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"HOW COGNITIVE PROXIMITY ENABLES AN ENTREPRENEURIAL ECOSYSTEM WITH LIMITED RESOURCES TO SUPPORT BIOPHARMA SMEs."

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Abstract

This thesis employs cognitive proximity as a theoretical lens to understand how an entrepreneurial ecosystem in a second-tier region supports biopharma SMEs whilst being constrained by limited access to funding and a lack of sustained sector-specific support from the government. Cognitive proximity is chosen to address the research question "how does a second-tier region support SME activity in the biopharma industry?" as it considers the importance of common languages, similar knowledge bases, and shared goals to facilitate interactions between organisations in an entrepreneurial ecosystem.

The first objective of this thesis was to explore the interactions between inputs and mediators in an entrepreneurial ecosystem for biopharma SMEs in a second-tier region. Taking an embedded case study approach and drawing upon interview data with a diverse group of key actors in such an ecosystem, the study develops a framework to identify and understand the contextual factors and their interactions to the genesis and development of the entrepreneurial ecosystem. Here a new type of actor, defined as an "anchor mediator" was found to play a pivotal role in addressing resource deficiencies in the region.

The second research objective was to understand the lifecycle of partnerships in the biopharma industry from the perspective of the SMEs in this second-tier region. Through in-depth interviews with SME managers and their key stakeholders, the study was able to understand and represent the lifecycle of partnerships in the biopharma industry. Therefore, the second contribution of this research is an articulation of the enabling role of cognitive proximity to the formation and management of partnerships in the biopharma industry for SMEs lacking key financial and policy support.

This thesis concludes that cognitive proximity can be used as a theoretical lens to help researchers better understand the role that interactions play in supporting biopharma SMEs within entrepreneurial ecosystems in second-tier regions whilst enabling the development of new knowledge in the literature regarding regional development and partnerships in the biopharma industry. For policymakers, this research highlights the importance of a public sector supported anchor mediator taking a long-term role in addressing cognitive proximity between organisations.

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"Work hard, study well, and play. Eat and sleep plenty… That's the way to learn."

-Akira Toriyama.

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Chapter One – Introduction

This thesis employs cognitive proximity as the theoretical lens to understand how biopharma SMEs are supported by an entrepreneurial ecosystem in a second-tier region presenting positive outcomes despite only having access to a limited amount of resources in terms of funding and sector-specific support from the government.

Cognitive proximity is the chosen theoretical lens to address the research question “how does a second-tier region support SME activity in the biopharma industry?” as it considers the importance of common languages, similar knowledge bases, and shared goals to facilitate effective collaboration between organisations. Though it has been traditionally used as a theoretical construct in multidimensional research regarding regional development and open innovation, this research argues that employing cognitive proximity can help to build new theory by allowing a better understanding of the interactions necessary to support SMEs in the biopharma industry based in second-tier regions.

The first objective of this thesis is to explore the interactions between inputs and mediators in an entrepreneurial ecosystem for biopharma SMEs in a second-tier region. To do so, this research investigates the available contextual factors in the chosen entrepreneurial ecosystem while deploying cognitive proximity to explore the importance of shared goals between the most relevant actors within an entrepreneurial ecosystem.

The second research objective is to understand the lifecycle of partnerships in the biopharma industry from the perspective of SMEs in a second-tier region. This research

objective acknowledges the importance of cognitive proximity for establishing and managing partnerships in the biopharma industry by investigating how common languages, similar knowledge bases, and shared business goals facilitate establishing and managing such partnerships.

Thus, the work of this thesis is positioned within two academic conversations. First, it contributes to the rising theme of entrepreneurial ecosystems and the recent calls for the study of this “umbrella concept” (Theodoraki and Messeghem, 2017) through exploratory research to allow the conceptualisation of theoretical constructs. Finally, this research also aims to contribute to the literature regarding the complex interactions required to consummate partnerships in the biopharma industry from the perspective of SMEs in a second-tier region as this is a rich setting for building theory.

1.1 Background to the Study

The following section introduces the importance of considering cognitive proximity as the theoretical lens for this research and how this research advances the current knowledge of two academic conversations: entrepreneurial ecosystems and partnerships in the biopharma industry.

1.1.1 Cognitive Proximity as a Theoretical Lens

Cognitive proximity, also referred to as Cognitive Distance, Cognitive Dimension, or Common Ground through the literature in regional development and open innovation (Boschma, 2005; Theodoraki, Messeghem and Rice, 2018; Mao *et al.*, 2019), is usually

considered one of the factors involved in the effectiveness of collaborations between organisations.

This theoretical construct is considered as the manifestation of the homogeneity between organisations by including commonalities in knowledge bases, languages, goals, and norms (Boschma, 2005; Capello and Caragliu, 2018; Hauge, Pinheiro and Zyzak, 2018; Werker, Korzinov and Cunningham, 2019). This research chooses cognitive proximity as the theoretical lens to contribute to the knowledge of entrepreneurial ecosystems and partnerships in the biopharma industry for the following reasons.

First, in terms of entrepreneurial ecosystems, it has been argued that shared goals for regional development grounded in common culture, language, and norms facilitate the communication between the relevant members of an entrepreneurial ecosystem, therefore making a positive impact on the ecosystem's performance (Theodoraki, Messeghem and Rice, 2018). This approach to understanding entrepreneurial ecosystems highlights the importance of not only exploring who the most relevant members are but also investigating the interactions between them through cognitive proximity.

Secondly, regarding the conversation around partnerships and collaborations in knowledge-intensive industries, it is suggested that cognitive proximity affects the establishment and management of partnerships as collaborating organisations are required to find a "common ground" (Mao *et al.*, 2019). This "common ground" can be established through the sharing of similar knowledge bases, scientific language, and

business goals (Cunningham and Werker, 2012; le Duc and Lindeque, 2018; Ooms, Werker and Caniëls, 2018; Werker, Korzinov and Cunningham, 2019; McGreevy *et al.*, 2020; O' Connor, Doran and McCarthy, 2020).

By considering cognitive proximity as a theoretical lens rather than a quantifiable construct, it is possible to better understand how an entrepreneurial ecosystem in a second-tier region "punches above its weight class" by supporting entrepreneurial activity and innovation for biopharma SMEs.

1.1.2 Advancing Knowledge in Entrepreneurial Ecosystems

Entrepreneurial ecosystems are a rising subject area in academia as governments have adopted them as a policy initiative to try to improve regional entrepreneurship and innovation (Acs *et al.*, 2017; Theodoraki and Messeghem, 2017; Robertson, Pitt and Ferreira, 2020). Entrepreneurial ecosystems are rooted in systems theory as an ecological metaphor (Velt, Torkkeli and Laine, 2020) as they are settings in which a heterogeneous group of interconnected actors formally and informally cooperate to promote and facilitate entrepreneurial activity and innovation within a specific region.

If explored through a systems-based approach, entrepreneurial ecosystems require inputs that can be transformed into outputs through interactions (Acs et al., 2017) of the members of the ecosystem. Most contemporary research usually focuses on assessing the outputs of entrepreneurial ecosystems to understand the socio-economic differences between different regions by assessing their economic performance, start-up activity, or the number of "blockbuster companies" (Theodoraki and Messeghem, 2017). By focusing

on these outputs, policymakers aim to create entrepreneurial ecosystems whose performance is based on first-tier regions such as Silicon Valley in the US or the Golden Triangle in the United Kingdom. However, an outputs-focused approach can be problematic as it tends to simplify the interactions within entrepreneurial systems, therefore leading to theoretical and practical limitations around this concept (Brown and Mason, 2017; Dedehayir, Mäkinen and Roland Ortt, 2018; Muñoz *et al.*, 2020; Velt, Torkkeli and Laine, 2020).

The first limitations in understanding entrepreneurial ecosystems are conceptual as literature has tended to overlook the heterogeneous nature of these systems (Brown and Mason, 2017; Muñoz *et al.*, 2020). It is argued that this lack of conceptualisation for the study of entrepreneurial ecosystems is a result of their rapid adoption as a policy initiative (Brown and Mason, 2017). Therefore, as attractive as the concept can be for policymakers, an incomplete understanding of the phenomena can lead to misapplications. Without a full understanding of the interactions between SMEs, inputs, and mediators that lead to outputs, it is difficult to promote and facilitate the genesis and development of entrepreneurial ecosystems, especially in regions lacking significant amounts of private funding and ad-hoc policy initiatives, which are known as second-tier regions. The way entrepreneurial ecosystems are established and developed is likely to vary depending on the context of the region that the ecosystems inhabit and the interactions between its more relevant members.

Another limitation in the study of entrepreneurial ecosystems is that, as in nature, every entrepreneurial ecosystem is unique, different, and presents idiosyncratic relationships among its members that are likely to depend on the specific context they are located in (Autio *et al.*, 2014; Theodoraki and Messeghem, 2017; Robertson, Pitt and Ferreira, 2020). In nature, ecosystems evolve as a response to the environment (context) available to the organisms within it, and the same can be argued for entrepreneurial ecosystems (Autio *et al.*, 2014; Muñoz *et al.*, 2020; Robertson, Pitt and Ferreira, 2020). The genesis and development of an entrepreneurial ecosystem will depend on the context and the relationships within it; consequently, entrepreneurial ecosystems in first-tier regions are likely to be established and developed differently from those in second-tier regions. As a consequence, it has been suggested that entrepreneurial ecosystems can be explored on a case-by-case basis that allows for more targeted policy interventions to enhance the entrepreneurial activities and innovation efforts already occurring in these regions (Autio *et al.*, 2014; Muñoz *et al.*, 2020; Velt, Torkkeli and Laine, 2020).

There is a lack of theoretical frameworks that take the aforementioned issues into account to allow academics to investigate, conceptualise, and empirically explore entrepreneurial ecosystems closely. This issue can be a result of the lack of theoretical conceptualisation; nonetheless, there have been efforts to explore the components of entrepreneurial ecosystems. The better-known efforts are the triple, quadruple, and quintuple helixes models addressing knowledge-based entrepreneurship (Rosenlund, Rosell and Hogland, 2017; Todeva and Ketikidis, 2017; Carayannis *et al.*, 2018). Each helix model is an improvement upon the previous one; nevertheless, this research aims to build upon them

by using cognitive proximity to better understand the interactions between the organisations within an entrepreneurial ecosystem.

Therefore, there is an opportunity for this thesis to empirically examine contemporary frameworks such as the inputs, mediators, and outputs framework – the IMO framework – (Lecluyse, Knockaert and Spithoven, 2019). In the IMO framework, the inputs within a system interact with relevant mediators to facilitate the outputs of such a system. According to recent research (Dedehayir, Mäkinen and Roland Ortt, 2018), by employing explorational frameworks for the study of entrepreneurial ecosystems, it is possible to identify the roles that relevant organisations assume within the ecosystem. This is important as recent research suggests that the interactions between relevant organisations can be an effective substitute for private funding or beneficial government policy (Muñoz *et al.*, 2020).

We propose that an ideal setting to explore the utility of the interaction-based IMO framework is within a second-tier region as they tend to lack resources such as private funding and supportive government policies that are available within ecosystems studied using predominantly output-focused perspectives. Looking outside first-tier regions also provides the opportunity to explore SMEs, which provide the majority of economic activity, yet questions remain regarding how to best facilitate the development of such SMEs, especially in knowledge-based industries such as the biopharma industry that offer significant growth potential (Cardoso and Meijers, 2016; Rossiter and Smith, 2017a; Wang et al., 2015).

We focus upon the City of Nottingham as a second-tier region in the United Kingdom as it is a typical example of an overperforming second-tier region. It ranks tenth in terms of private funding for the biopharma sector within the twelve regions in the UK with entrepreneurial activity in this industry (Crocker, 2019). Nonetheless, it produces remarkable outputs as it ranks sixth in terms of start-up and SME activity in the UK's biopharma industry, and the science parks for life sciences in this entrepreneurial ecosystem presented a survival rate of 91% on average from 2007 to 2019 (Crocker, 2019).

To shed light on how the current contextual factors (McAdam et al., 2014) interact to produce positive outcomes for the Nottingham Biopharma Ecosystem, this research aims to build upon the inputs, mediators and outputs framework (IMO framework) for the contribution of science parks depicted by Lecluyse (2019). This is achieved through using cognitive proximity to understand how the interactions between inputs and mediators facilitate the positive outputs for the Nottingham Biopharma Ecosystem. This contributes to the literature in entrepreneurial ecosystems by exploring the genesis, development, and current state of the contextual factors within one entrepreneurial ecosystem, while building upon a theoretical framework for the exploration of such factors by using cognitive proximity to better understand the interactions between inputs and mediators within the ecosystem.

Therefore, this research identifies an opportunity to undertake exploratory research to investigate the genesis and development of entrepreneurial ecosystems for biopharma

SMEs as this second-tier region is a specific context that allows for the conceptualisation of theoretical constructs (Dedehayir et al., 2018). As a result, this research seeks to explore the specific context that allowed the genesis, development, and current state of an entrepreneurial ecosystem for SMEs in the biopharma industry within a second-tier region.

As entrepreneurial ecosystems are defined by the context they are based on and the interactions within them, this research builds upon the contextual factors explored by McAdam (2014). McAdam (2014) investigates these factors for collaborative social networks; however, they are suitable for entrepreneurial ecosystems as both constructs depend on the context and interactions available to them. The contextual factors are related to the support mechanisms (government policy, funding opportunities, support organisations, and science parks) available in the genesis and the development of an entrepreneurial ecosystem, and they could be suitable depending on the industry sector and target market (McAdam *et al.*, 2014; Lecluyse, Knockaert and Spithoven, 2019). Through employing cognitive proximity, it is possible to unveil the importance of shared regional goals between the relevant members of the ecosystem so they can take advantage of such contextual factors.

Recent research has tried to understand different dimensions of context for entrepreneurial ecosystems such as the temporal context, the industrial context, or the social context (Autio *et al.*, 2014; Robertson, Pitt and Ferreira, 2020); nevertheless, the combination of all these dimensions comprises the contextual factors investigated by

McAdam (2014). Hence, the first research objective of the thesis is to explore the interactions between inputs and mediators in an entrepreneurial ecosystem for biopharma SMEs in a second-tier region.

1.1.3 Advancing Knowledge Regarding Partnerships in the Biopharma Industry

This research also contributes to the literature regarding collaborations and partnerships within the biopharma industry. Collaborations and partnerships in the biopharma industry are usually explored through the interactions of large biopharma companies (Schweizer and He, 2018) with external organisations, especially SMEs located in first-tier regions (Chakraborty *et al.*, 2020; DeCorte, 2020). Nevertheless, it is important to explore these collaborations and partnerships between SMEs in the context of a second-tier region as they are thought to be an effective strategy for leveraging knowledge and expertise (Wang, Lestari and Yang, 2015).

In an entrepreneurial ecosystem within a second-tier region, partnerships are important for biopharma SMEs as these interactions are useful to leverage resources that are difficult to otherwise access in these regions such as funding for research and development (R&D), broader expertise within a different area of the biopharma industry, or access to relevant technology and knowledge (Wang, Lestari and Yang, 2015; Huang and Wang, 2018). Collaborations and partnerships between organisations can be explored by considering the role of cognitive proximity for the establishment and management of these partnerships through proposed phases of engagement explored by Schweizer and He (2018).

Therefore, another research objective for this thesis is to understand the lifecycle of partnerships in the biopharma industry between SMEs in a second-tier region. This approach to exploring collaborations and partnerships is relevant because it expands the concept of cognitive proximity as the perceptions that SMEs have on external organisations are likely to be mediated by these theoretical constructs.

It is argued that in terms of cognitive proximity, the closer different organisations are, the better relationship they will have (Capello and Caragliu, 2018; Garcia *et al.*, 2018; le Duc and Lindeque, 2018). Therefore, this research also aims to explore how SMEs interact with external organisations. By doing so, this research can expand our knowledge on the lifecycle of the partnerships between SMEs in the biopharma industry and external organisations. This second research objective contributes to the literature addressing the complex nature of partnerships in the biopharma industry by expanding the importance of the theoretical construct of cognitive proximity as an enabler of partnerships affecting SMEs within an entrepreneurial ecosystem in a second-tier region.

This research reaches two main conclusions. First, it concludes that the organic development of an entrepreneurial ecosystem in a second-tier region depends on its context through the available inputs and mediators, their interactions, and their cognitive proximity. Finally, when considering the key interactions over time, it concludes that the lifecycle of partnerships and collaborations in the biopharma industry depends on complex interactions that can be better understood by expanding on the concept of cognitive proximity as an enabling element.

1.2 Thesis Structure

The thesis is comprised of seven remaining chapters summarised as follows.

Chapter Two is divided into three parts. Part one discusses cognitive proximity, its interchangeable use throughout the literature, and the most relevant constructs to consider when employed as a theoretical lens. Part one of Chapter Two also addresses the relevance of cognitive proximity for the exploration of entrepreneurial ecosystems and its role in understanding the lifecycle of collaborations and partnerships in the biopharma industry.

Part two discusses entrepreneurial ecosystems as an umbrella construct, the importance of context to differentiate between entrepreneurial ecosystems, the differences between first-tier and second-tier regions, the importance of science parks within entrepreneurial ecosystems, the contextual factors within entrepreneurial ecosystems, and current frameworks for the contextual exploration of entrepreneurial ecosystems.

Part three reviews the literature concerning SME collaborations and partnerships in the biopharma industry'. It explores the central arguments that relate to the importance of cognitive proximity when exploring collaborations and partnerships in the biopharma industry, the types of knowledge shared through these partnerships, the barriers hindering such partnerships, and the current frameworks to explore partnerships between different organisations in the biopharma industry.

Chapter Three presents the interpretivist approach undertaken by this research while providing the philosophical assumptions made by the researcher. This chapter also

justifies the use of the case study methodology as the most suitable methodological framework to answer the research question and achieve the research objectives.

Chapter Four presents the units of analysis within the embedded case study to contextualise their role within the entrepreneurial ecosystem and their experiences regarding partnerships with external organisations.

Chapters Five and Six comprise the empirical findings relevant to each of the research objectives laid down by this study.

Chapter Seven consolidates the findings from Chapter Five and Chapter Six. It represents the theoretical discussion chapter by highlighting the theoretical significance and contributions of the empirical findings to the relevant literature.

Chapter Eight presents the conclusions from this research project and consolidates the theoretical and empirical contributions. This research also presents the limitations of the study while providing ideas for future research that can expand the contributions made by this study.

Chapter Two – Literature Review

In this chapter, the literature underpinning this research is reviewed in three parts. Part one of this chapter addresses the concept of cognitive proximity, its interchangeable use in different academic fields, and the more relevant constructs to consider when employing cognitive proximity as a theoretical lens. This part also summarises the role of cognitive proximity when exploring entrepreneurial ecosystems and its role in the formation and management of partnerships in knowledge-intensive environments.

Part two explores the literature concerning entrepreneurial ecosystems as an umbrella concept, the relevance of context when investigating entrepreneurial ecosystems, the differences between the context in first-tier and second-tier regions, and the importance of science parks as part of entrepreneurial ecosystems and their shortcomings. Part two also delves into the relevance of considering context when exploring entrepreneurial ecosystems, different dimensions that form the contextual factors within entrepreneurial ecosystems, and current frameworks for the contextual exploration of entrepreneurial ecosystems.

Part three reviews the literature concerning collaborations and partnerships in the biopharma industry from the perspective of SMEs. It explores the central arguments that relate to the importance of cognitive proximity when exploring collaborations and partnerships in the biopharma industry, the types of knowledge shared through these partnerships, the barriers hindering such partnerships, and the current frameworks to explore partnerships between different organisations in the biopharma industry.

2.1 Part One: Cognitive Proximity as a Theoretical Lens

During the last two decades, there has been a growing interest in studying collaborations between organisations (Yun and Mohan, 2012; West and Bogers, 2014; Bogers, Chesbrough and Moedas, 2018). Therefore, academics have been exploring the establishment and management of collaborations between organisations by redefining the concept of distance (Boschma, 2005; Mao *et al.*, 2019). Rather than simplifying distance as a one-dimensional unit measured through the actual geographic distance between organisations, Boschma (2005) redefined distance between organisations as a multidimensional concept to allow for a more robust understanding of the interactions between collaborating organisations.

Boschma (2005) argues that the overall distance between organisations is composed of their geographical proximity, cognitive proximity, social proximity, and institutional proximity. Boschma (2005) also suggests that deconstructing distance into these different dimensions facilitates the analytical and empirical isolation needed to explore the role of each dimension in collaborations. From these dimensions of distance, this research considers that cognitive proximity could reveal new insights on the underpinning interactions within entrepreneurial ecosystems and the formation and management of partnerships in the biopharma industry.

A phenomenon around the construct of cognitive proximity is that it is not uniformly used through literature. In the literature investigating entrepreneurial ecosystems, it is referred to as the “cognitive dimension” of the system (Theodoraki, Messeghem and Rice, 2018),

whereas as in the literature regarding the lifecycle of partnerships and collaborations, it can be found as “common ground” (Mao *et al.*, 2019) or the “interactional factors” (McAdam *et al.*, 2014). This research keeps the concept of cognitive proximity as it is since cognitive proximity considers the manifestation of homogeneity between organisations that includes language, knowledge base, goals norms, rules, and values (Molina-Morales, García-Villaverde and Parra-Requena, 2014; Capello and Caragliu, 2018; Hauge, Pinheiro and Zyzak, 2018; Theodoraki, Messeghem and Rice, 2018; Werker, Korzinov and Cunningham, 2019; McGreevy *et al.*, 2020).

Cognitive proximity is thought to be relevant for collaborating organisations as having similar ideas on how to act when interacting helps organisations to establish norms, rules, and goals as well as reducing the risk of misunderstandings and opportunistic behaviour, through effective communication (Torre and Rallet, 2005; Molina-Morales, García-Villaverde and Parra-Requena, 2014; Garcia *et al.*, 2018; Mao *et al.*, 2019; O’ Connor, Doran and McCarthy, 2020). Cognitive proximity between organisations can be considered ideal when they possess a similar knowledge base at a technical, organisational, or market level as this promotes effective understanding across firms (Garcia *et al.*, 2018).

The following section in part one of this chapter introduces the relevant constructs when using cognitive proximity as a theoretical lens (language, knowledge base, and goals), followed by the relevance of cognitive proximity when exploring entrepreneurial

ecosystems, and the role of cognitive proximity for the establishment and management of partnerships in knowledge-intensive environments.

2.1.1 Common Language, Knowledge Base, and Goals

Research considering cognitive proximity assumes that organisations are able to effectively communicate through sharing similar languages, knowledge bases, business goals, values, and norms (Molina-Morales, García-Villaverde and Parra-Requena, 2014; Presutti *et al.*, 2017; le Duc and Lindeque, 2018; O' Connor, Doran and McCarthy, 2020). This section explores the relevance of similar languages, knowledge bases, and business goals for cognitive proximity as these are considered the key constructs involved with "kicking off" new relationships between organisations (Molina-Morales, García-Villaverde and Parra-Requena, 2014; Mao *et al.*, 2019; McGreevy *et al.*, 2020; O' Connor, Doran and McCarthy, 2020), whereas similar values and norms can be a result of successful interactions (Bertin, 2019; Mao *et al.*, 2019; Gao *et al.*, 2021).

Language not only considers the linguistic aspects but also includes the technical and scientific jargon used in conversations (Hauge, Pinheiro and Zyzak, 2018; Ooms, Werker and Caniëls, 2018; Mao *et al.*, 2019; Werker, Korzinov and Cunningham, 2019). Similar language in the context of the interactions between organisations encompasses the concepts of "know-what" and "know-why" (Cunningham and Werker, 2012; Ooms, Werker and Caniëls, 2018), which are important for effective communication between organisations and individuals. Through a common language, it is possible to avoid losing any information as agreements and knowledge can be made explicit and then shared

(Hauge, Pinheiro and Zyzak, 2018). Therefore, the first barrier that collaborating organisations overcome is a gap in their language (Hauge, Pinheiro and Zyzak, 2018; Errecaborde *et al.*, 2019; McGreevy *et al.*, 2020).

The construct of knowledge base refers to the tacit and explicit knowledge that an organisation possesses and encompasses the concept of “know-how” (Hauge, Pinheiro and Zyzak, 2018). Knowledge bases are important for interactions between organisations as they determine the type of knowledge that can be shared (Salavou, Baltas and Lioukas, 2004; Kruse, 2012; Bigliardi and Galati, 2018; Santoro *et al.*, 2018). For knowledge-intensive contexts such as the biopharma industry, the knowledge base is actioned through standardised terminology that feeds the common language between organisations (Hauge, Pinheiro and Zyzak, 2018). The more similar the knowledge base between organisations, the easier it is to establish effective communication through common language so these organisations can either find or set common goals.

Common goals, also referred to as common objectives (Rybnicek and Königsgruber, 2019), are helpful to focus the efforts of collaborating organisations as they facilitate the desired outcomes of collaborations (Theodoraki, Messeghem and Rice, 2018; Rybnicek and Königsgruber, 2019). Through understanding their shared goals, collaborators can work on developing the strategies, work plans, and communication channels while managing the expectations of the involved parties for effective collaborations (Hong, Heikkinen and Blomqvist, 2010; Attia, 2015). Unclear goals are likely to result in collaborations with unrealistic expectations affecting the trust between the involved

organisations. Ultimately, an “ideal cognitive proximity” can facilitate trust-building interactions between organisations through their shared language, knowledge bases, and goals (Diez-Vial and Fernández-Olmos, 2017; Díez-Vial and Montoro-Sánchez, 2017; le Duc and Lindeque, 2018; Theodoraki, Messeghem and Rice, 2018; Giuliani, Balland and Matta, 2019; Leon *et al.*, 2019; Ng *et al.*, 2019; Rybnicek and Königsgruber, 2019).

The following sections of Chapter Two, part one will explore the relevance of cognitive proximity at two different levels: the regional level, which is relevant to the first research objective of this thesis (to explore the interactions between inputs and mediators in an entrepreneurial ecosystem for biopharma SMEs in a second-tier region), and the SME level, which is relevant to the second research objective of this research (to understand the lifecycle of partnerships in the biopharma industry from between SMEs in a second-tier region).

2.1.2 Cognitive Proximity in Entrepreneurial Ecosystems

Cognitive proximity is an integral component of entrepreneurial ecosystems that can help us better understand how to better support SMEs in them. Taking cognitive proximity into account when developing frameworks for the exploration of entrepreneurial ecosystems is relevant as it can help to better understand the relationships between SMEs, inputs, and outputs of a system, especially when building upon the IMO framework (Lecluyse, Knockaert and Spithoven, 2019) as this research does. Therefore, cognitive proximity is an appropriate theoretical lens to explore the interactions between inputs and mediators in an entrepreneurial ecosystem for biopharma SMEs in a second-tier region.

Theodoraki (2018) refers to cognitive proximity as the “cognitive dimension” of entrepreneurial ecosystems and suggests that it can contribute to the sustainability of such ecosystems. Establishing a common language by consolidating similar knowledge bases facilitates the necessary discussions for setting shared regional goals (Inkpen and Tsang, 2005). Then a positive loop can start within the entrepreneurial ecosystem, where cognitive proximity helps to define common goals that lead to greater cognitive proximity if these goals are met. Figure 1 represents the relationship between cognitive proximity and shared regional goals in entrepreneurial ecosystems.

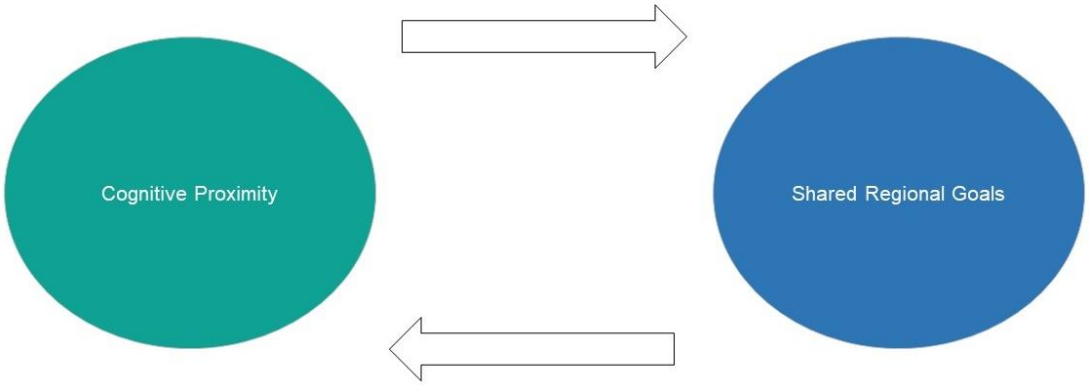


Figure 1. Cognitive Proximity and Shared Regional Goals (Inkpen and Tsang, 2005; Theodoraki, Messeghem and Rice, 2018).

Having ideal cognitive proximity between relevant members of entrepreneurial ecosystems helps to construct collective narratives by highlighting success stories and positive experiences within the ecosystem (Theodoraki, Messeghem and Rice, 2018). At a firm level, cognitive proximity helps companies within an ecosystem to legitimise their

organisation by having access to the contextual factors within it (Rybnicek and Königsgruber, 2019).

Contemporary research has begun to question the role of similar knowledge bases within systems, and an interesting example is an exploration of the interactions within life science parks in the Netherlands (le Duc and Lindeque, 2018). The more similar the knowledge base, the easier it is to find and keep partners for collaboration, and a good example can be found when looking at an integral part of entrepreneurial ecosystems, science parks. The Leiden Bio Science Park in the Netherlands only accepts companies developing products or services based on DNA technologies (le Duc and Lindeque, 2018). Site management carefully assesses applications to join the site by evaluating applicants' business profile, knowledge base, and existing relationships with actors within the cluster. This is a control mechanism as by only accepting applications from firms fitting Leiden Bio Science Park's profile, site management enhances cognitive proximity between companies based there (le Duc and Lindeque, 2018).

Controlling the knowledge base within a science park is likely to promote the growth of intra-park social networks for collaborations as this focuses on knowledge-sourcing activities (le Duc and Lindeque, 2018). Nevertheless, this will eventually place sites such as Leiden in an inertia or lock-in situation thus preventing new knowledge from entering the system (Molina-Morales, García-Villaverde and Parra-Requena, 2014; Presutti *et al.*, 2017). Therefore, a careful balance and management of different knowledge bases could be maintained by science park managers. Science parks can be important elements

helping controlling knowledge bases (le Duc and Lindeque, 2018; Thompson, Purdy and Ventresca, 2018; Lecluyse, Knockaert and Spithoven, 2019); therefore, these findings are relevant when exploring entrepreneurial ecosystems.

Molina-Morales' (2014) findings can help us to further understand the importance of considering cognitive proximity when exploring entrepreneurial ecosystems. Their research included the relationship between the geographical and the cognitive dimensions of proximity to knowledge flow and overall innovative performance as it was thought that both dimensions would have a complementary effect on the innovative performance of a company. However, the findings concluded that cognitive proximity is more relevant for a successful collaboration and that differences between cognitive proximity can suggest why not all the companies within an entrepreneurial ecosystem perform similarly (Molina-Morales, García-Villaverde and Parra-Requena, 2014; Bigliardi and Galati, 2016, 2018).

Cognitive proximity can also help us to understand the interactions between the members of entrepreneurial ecosystems by considering the "small world" characteristics connecting relevant actors within a specific industry. Cognitive proximity between individuals (le Duc and Lindeque, 2018) appears to be key to engage in informal interactions while cognitive proximity between companies seems vital to reach formal partnerships (Boschma, 2005; Molina-Morales, García-Villaverde and Parra-Requena, 2014; Garcia *et al.*, 2018). A "small-world" social network refers to a network that is formed by several dense clusters (groups of collaborating actors) linked together by their interactions.

“Small-world” networks are likely to be important for establishing interactions within entrepreneurial ecosystems as this network configuration allows two or more members of a network to be closer than it may appear as they would be connected by a small number of steps (van Egeraat and Curran, 2014). The dense clusters in a “small-world” network do not disappear easily due to their similar knowledge base, which makes the structure of the overall network stable through time.

The stability of a “small world” network facilitates bringing in new members that can embed themselves into an already established entrepreneurial ecosystem while allowing them to quickly scout for organisations for potential collaborations and partnerships. In a “small world”, reachability is expected to be tight and to strengthen as time passes if common values and business goals are introduced; this helps the actors to connect easily regardless of a considerate geographic distance (Shaw, 2006). The properties of a “small world” have been helpful to compare the Cambridge bio-cluster in the United Kingdom (part of the “Golden Triangle”) and the Munich (a German first-tier region) bio-cluster in Germany (Casper and Murray, 2005), to explore the structure of the Irish biotechnology sector network (van Egeraat and Curran, 2014), and to illustrate the networks for R&D strategic alliances in the US biopharma sector (Jacob and Duysters, 2017).

When members of a “small world” network have ideal cognitive proximity, it is possible that relationships can evolve from informal to formal and the intensity of their ties vary from weak to strong. On the one hand, informal collaborations are mainly formed by inter-personal linkages between specific individuals across different organisations and often

lack commercial goals. Informal partnerships provide troubleshooting knowledge that does not compromise any kind of intellectual property or confidential information. On the other hand, formal collaborations are oriented towards business goals and include joint ventures, joint-products/services, commercial agreements, and innovation partnerships (van Egeraat and Curran, 2014).

Overall, cognitive proximity can be considered as the glue that holds together interactions within entrepreneurial ecosystems by helping its members to focus their efforts towards shared regional goals through maintaining the “small world” configuration (Inkpen and Tsang, 2005; le Duc and Lindeque, 2018; Theodoraki, Messeghem and Rice, 2018; Rybnicek and Königsgruber, 2019). Therefore, using cognitive proximity as a theoretical lens to explore the complex interactions within entrepreneurial ecosystems can help build knowledge while providing an understanding of how to better support SMEs within entrepreneurial ecosystems in second-tier regions (Theodoraki, Messeghem and Rice, 2018).

The next section addresses the importance of cognitive proximity and its relevant constructs to understand the lifecycle of partnerships in the biopharma industry from between SMEs in a second-tier region.

2.1.3 Cognitive Proximity in Company–Company Partnerships

The previous section of this thesis explores how cognitive proximity helps to determine shared regional goals within an entrepreneurial ecosystem. However, when exploring partnerships between companies, cognitive proximity can facilitate the complex

interactions required to manage those partnerships (McAdam *et al.*, 2014; Beck *et al.*, 2017; Vangen, 2017; Errecaborde *et al.*, 2019; Ingstrup, Aarikka-Stenroos and Adlin, 2020). Therefore, this research presents cognitive proximity as an appropriate theoretical lens to understand the lifecycle of partnerships in the biopharma industry between SMEs in a second-tier region.

Partnerships are inherently difficult to manage as they require the combination of different resources, skills, and expertise (Vangen, 2017). Contemporary research suggests that cognitive proximity is an important element for creating environments for effective partnerships as it helps to set the ideal starting conditions, organisational structures, and evaluation methods for these collaborations to reach the established shared goals (Errecaborde *et al.*, 2019). This is also referred to as “common ground” in contemporary research (Mao *et al.*, 2019).

According to Errecaborde’s findings (2019), effective communication is a significant element for building trust when establishing and managing partnerships. These findings highlight the importance of the constructs of common languages and overlapping knowledge bases at an organisational level (Beck *et al.*, 2017; Errecaborde *et al.*, 2019; Rybnicek and Königsgruber, 2019). Recent research (Garcia *et al.*, 2018) concludes that collaborations between organisations are fostered through effective communication rather than constant communication, which suggests that cognitive proximity plays a key role when building partnerships in knowledge-intensive environments such as the biopharma industry. Effective communication can be important for partnerships by

promoting regular and effective interactions which are beneficial to coordinate efforts (Beck *et al.*, 2017), monitor the progress of the projects (Errecaborde *et al.*, 2019), and define the review mechanisms at the end of a project.

At the organisational level, knowledge bases are important because they promote a mutual understanding between the individuals representing the involved parties (Beck *et al.*, 2017). According to Rybnicek (2019), mutual understanding through a common language and similar knowledge bases can help to close the gap if collaborators come from different backgrounds and hence encounter cultural differences (Vangen, 2017). However, there is also an individual level when considering partnerships as they are usually partnerships started and managed by key individuals called champions (Hamadi, 2018). It is suggested that these champions could aim to have ideal cognitive proximity at a personal level (le Duc and Lindeque, 2018). Even when organisations are cognitively close, relationships will be difficult if their champions are not.

Finally, it is argued that the ability to find or setting shared goals is an important determinant of success for partnerships (Vangen, 2017; Ingstrup, Aarikka-Stenroos and Adlin, 2020) as these partnerships are “a mean to obtaining outcomes too ambitious for any single organisation to deliver on its own” (Vangen, 2017). Research usually focuses on finding new ways to measure cognitive proximity, assessing its impact on companies engaging in partnerships (Capello and Caragliu, 2018; Garcia *et al.*, 2018), or exploring the type of distance that is more relevant for high-tech SMEs (Boschma, 2005; le Duc and Lindeque, 2018). Nevertheless, cognitive proximity can also be a relevant theoretical

lens to better understand partnerships in a complex, highly regulated, and result-oriented environment such as the biopharma industry (Theodoraki, Messeghem and Rice, 2018).

The next section of this chapter introduces the literature on entrepreneurial ecosystems, the relevance of setting the research in a second-tier region by contrasting it to first-tier regions, the relevance of science parks within entrepreneurial ecosystems, the importance of contextual explorations for entrepreneurial ecosystems, and the current frameworks used for investigating entrepreneurial ecosystems.

2.2 Part Two: Entrepreneurial Ecosystems

Recent research suggests that by focusing on cognitive proximity it is possible to gain a better understanding of entrepreneurial ecosystems so novel contributions to already established theoretical constructs can be developed (Theodoraki, Messeghem and Rice, 2018). Chapter Two, section two of this thesis addresses the literature on entrepreneurial ecosystems by focusing on the opportunities for academic researchers and practitioners. This section explores what entrepreneurial ecosystems are, the differences between ecosystems in first-tier and second-tier regions, science parks as a component of entrepreneurial ecosystems and their shortcomings, the importance of considering context when exploring entrepreneurial ecosystems, and the current frameworks for the understanding of entrepreneurial ecosystems.

Entrepreneurial ecosystems are a rising theme in academia because they are a recent initiative of policymakers to promote innovation and entrepreneurship at a regional level as this concept has its roots in the literature of regional development and strategy (Acs *et al.*, 2017). While other related concepts such as industry clusters or science parks try to understand regional development purely through the effect of the agglomeration of organisations (Molina-Morales, García-Villaverde and Parra-Requena, 2014; Minguillo, Tijssen and Thelwall, 2015; Lecluyse, Knockaert and Spithoven, 2019), the concept of entrepreneurial ecosystems highlights the importance of different organisations connecting to form social networks to reach common regional goals while facilitating collaborations and entrepreneurial activities (Acs *et al.*, 2017; Theodoraki, Messeghem and Rice, 2018). Henceforth, cognitive proximity can be an important theoretical lens for

investigating the interactions between relevant members of entrepreneurial ecosystems (Molina-Morales, García-Villaverde and Parra-Requena, 2014; Capello and Caragliu, 2018; Theodoraki, Messeghem and Rice, 2018).

The literature exploring entrepreneurial ecosystems is in constant review and development so there is not a uniform definition for the concept yet (Brown and Mason, 2017; Robertson, Pitt and Ferreira, 2020). Nevertheless, this research chooses to adopt the working definition of entrepreneurial ecosystems as "localised settings in which a heterogeneous group of interconnected actors formally and informally interact to facilitate the entrepreneurial activity that adds value to a specific industry sector" (Brown and Mason, 2014, 2017; Theodoraki and Messeghem, 2017). The lack of a general definition for this theoretical concept is a result of the different approaches used to explore entrepreneurial ecosystems through their organisational, cultural, behavioural, and even biological characteristics. Therefore, it is argued that the construct of an entrepreneurial ecosystem serves as a "conceptual umbrella" (Brown and Mason, 2017; Theodoraki and Messeghem, 2017) that encompasses different perspectives that allow the potential development of new contributions for analysing the underlying context in which they exist.

In practice, just as in nature, entrepreneurial ecosystems are heterogeneous systems as they include not only firms in a certain industry but also other actors such as public and private stakeholders, investors, universities, and service providers for all of these organisations (Theodoraki and Messeghem, 2017). Consequently, entrepreneurial ecosystems are a result of these actors, their interactions, the physical infrastructure in a

given region, and the culture of the individuals and organisations within an entrepreneurial ecosystem (Acs *et al.*, 2017; Theodoraki and Messeghem, 2017; le Duc and Lindeque, 2018). However, the literature exploring entrepreneurial ecosystems has traditionally overlooked the heterogeneity by mostly focusing on one of the determinants at the time by trying to explore either the firms, the infrastructure, isolated components of culture, or the effect of one of these attributes on the economic or innovative performance of the firms within it (Acs *et al.*, 2017; Brown and Mason, 2017; Theodoraki, Messeghem and Rice, 2018).

It is argued that the heterogeneity of organisations makes it difficult to establish common goals for the region (Theodoraki and Messeghem, 2017) as these actors usually have conflicting business goals. Nevertheless, this is a result of the traditional literature mostly focusing on individual firms or individuals within them. Therefore, it is relevant to develop theoretical frameworks that take these issues into account so they can help to better conceptualise entrepreneurial ecosystems for empirical explorations.

2.2.1 Entrepreneurial Ecosystems

Though the concept of entrepreneurial ecosystems is traditionally explored in the literature concerning regional development and strategy, the concept finds its rooting in the systems theory which is based on the concept of ecosystems explored in ecology (Acs *et al.*, 2017; Velt, Torkkeli and Laine, 2020). As a concept rooted in systems, entrepreneurial ecosystems require inputs that can be transformed into outputs through the interactions between the members of the ecosystem.

Nonetheless, research in this area usually focuses on measuring certain outputs of entrepreneurial ecosystems such as the economic performance of individual firms, start-up activity in the region, or the number of “blockbuster companies” coming from an entrepreneurial ecosystem (Theodoraki and Messeghem, 2017). Focusing on the outputs of the system contributes to disregarding the heterogeneity of entrepreneurial ecosystems while preventing the conceptualisation of the interactions that transform the inputs into outputs.

Research assessing the outputs of these systems aims to understand the socioeconomic differences between entrepreneurial ecosystems and has been used by policymakers to try to “create” entrepreneurial ecosystems (Brown and Mason, 2017; Theodoraki and Messeghem, 2017; Lecluyse, Knockaert and Spithoven, 2019). These “artificial” efforts usually try to emulate the established outputs presented by entrepreneurial ecosystems based in first-tier regions such as Silicon Valley in the US or “the Golden Triangle” in the United Kingdom. Nevertheless, “artificial entrepreneurial ecosystems” do not usually perform as effectively as the template regions as the interactions between the members of the ecosystem, the context in which these interactions occur, and the legacy that a specific region carries are overlooked (Autio *et al.*, 2014; Brown and Mason, 2017; Robertson, Pitt and Ferreira, 2020). Disregarding the uniqueness and heterogeneity of entrepreneurial ecosystems can lead to misapplications of this concept by policymakers and a lack of theoretical grounding of the construct by academics (Muñoz *et al.*, 2020; Velt, Torkkeli and Laine, 2020).

In nature, every ecosystem is unique as they depend on their environment, which is an analogue to what research considers as context. It is the specific context of biological ecosystems which in turn determines the relationships between the organisms inhabiting it. Therefore, it is relevant for this literature review to acknowledge the importance of context when trying to explore an entrepreneurial ecosystem and how the different dimensions of context can help to develop theoretical frameworks for the exploration of the contextual factors (McAdam *et al.*, 2014) in an entrepreneurial ecosystem.

The following section of this chapter explores the literature concerning two contrasting contexts for entrepreneurial ecosystems, which are first-tier and second-tier regions, while providing examples for each of these in the United Kingdom.

2.2.2 First-tier Regions and the Golden Triangle

First-tier regions are defined as the regions in a country that present the foremost importance in terms of political influence, economic performance, and “attractive pull” (Cardoso and Meijers, 2016). First-tier regions tend to be the centre of attention of academics, practitioners, and policymakers as they are the “gold standard” of what other regions in a country could aspire to be.

From revealing the shape of the DNA molecule in 1953 to the first efforts in manipulating the protein structure of an antibody in 1998, the United Kingdom has been a major player in providing ground-breaking innovations to the life science sector in general (Cooke, 2001). In the United Kingdom, many of the paradigm-breaking innovations that helped to shape the state of the life science sector through the 20th century were mostly

accomplished in either London, Cambridge, or Oxford. The pivotal role of these regions earned them the title of the “Golden Triangle.” The regions forming the “Golden Triangle” are an exceptional example of first-tier regions, and such recognition is not only a result of their historical contributions but also because they have consistently stimulated the life science industry sector for the United Kingdom. The three regions comprising London, the South East, and the East of England accounted for more than 80% of the total private investment in life science-oriented companies for the period comprising 2012-2017 (Crocker, 2019) in the United Kingdom.

A more detailed analysis of these regions provides interesting information on the number of new spin-off companies created in such a period. The University of Oxford accounts for 27 life-science spin-offs and the University of Cambridge accounts for sixteen, which is respectively two and four times more than the reported figures for the year 2011. This trend is also found in University College London. Therefore, it is suggested that the overall state of the life science industry in the United Kingdom depends closely on the performance of companies spinning off from the regions forming the “Golden Triangle” (Bio City Group, 2017; Crocker, 2019).

Nevertheless, the success of these regions in supporting life science SMEs is not only achieved through the aid of government initiatives to push the sector forward. Several private investors exclusively fund companies located in the “Golden Triangle” through different capitals, such as the Oxford Sciences Innovation Fund or Cambridge Innovation Capital (Bio City Group, 2017; Crocker, 2019). These regions with the utmost national

importance in terms of entrepreneurial activity and innovation are labelled as first-tier regions (Cardoso and Meijers, 2016; Mayer, 2013; Wang et al., 2015).

Despite the intensive funding and policy support for the “Golden Triangle”, other regions in the United Kingdom have developed entrepreneurial ecosystems for biopharma SMEs, such as the East Midlands. Regions outside the main hubs for the economy and innovation are referred to as second-tier regions. An analysis by Cardoso and Meijers (2016) classifies Nottingham as one of the most promising second-tier regions in the United Kingdom.

2.2.3 Second-tier Regions and the Nottingham Biopharma Ecosystem

In recent years, research has begun to pay attention to entrepreneurial activity and innovation outside first-tier regions (Mayer, 2013; Wang, Lestari and Yang, 2015; Cardoso and Meijers, 2016). Second-tier regions do not offer the same attractiveness (access to several sources of specific investment, human and social capital) as their first-tier counterparts; however, they can play a relevant role on a national or international scale (Cardoso and Meijers, 2016).

Some second-tier regions present a surprising performance despite their deficits, and are, therefore, appropriate sites to build new theory around entrepreneurial ecosystems. Some examples of entrepreneurial ecosystems in second-tier regions that present inviting environments for SMEs in knowledge-based industries are the cluster for regenerative medicine in Edinburgh, Scotland, and the Nottingham Biopharma Ecosystem in England. An exploration of the cluster of regenerative medicine in Edinburgh highlights the

importance of an established regional legacy to support the advent of SMEs in a specific industry sector (Johnson and Bock, 2017). These regions are important as they are not only limited by their size but they might also be constrained by the limited contextual factors within entrepreneurial ecosystems in second-tier regions.

SMEs based in second-tier regions usually manage to grow by leveraging assets from other organisations in the region causing the whole location to thrive and grow (Mayer, 2013). This effect relates to the economic agglomeration due to clustering investigated by Delgado (2014); nevertheless, second-tier regions heavily depend on the interactions between the key members of the entrepreneurial ecosystems in these regions. Research in Chinese second-tier regions hosting biopharma companies supports these ideas. It was found that such regions grew their GDP at a higher rate than most Chinese first-tier regions (Wang, Lestari and Yang, 2015). Furthermore, Wang (2015) points out that biopharma companies in first-tier regions usually allocate more resources on efforts to handle existing competitors and operational activities rather than in actions that allow new products or services to enter the market.

Biopharma SMEs based in second-tier regions can overcome competition and entry barriers found in first-tier cities while broadening the existing market and achieving a better understanding of macroeconomic and socio-political factors that might affect the company's future performance (Wang, Lestari and Yang, 2015). Wang (2015) supports the idea that an optimal ecosystem for entrepreneurship facilitates entrepreneurial activity by providing appropriate local support mechanisms and interactions that add value to

biopharma SMEs in second-tier regions. The benefits of a second-tier region are likely to help SMEs in this industry sector to diminish operative and administrative risks while potentially having access to specialised knowledge and information, and potentially to collaboration networks.

Nottingham City, part of a second-tier region in the United Kingdom, has benefited from some of the characteristics previously explored in this section as not only have biopharma SMEs been established but also organisations and firms that offer specialised support services such as marketing strategy, communications, and legal advice have grown since the founding of the first science park in this entrepreneurial ecosystem in 2003. Support services are an important factor within science parks and entrepreneurial ecosystems as SMEs in this industry rely on them to meet needs regarding business services and innovation, and networking activities that would not be affordable otherwise (Minguillo, Tijssen and Thelwall, 2015; Lecluyse, Knockaert and Spithoven, 2019; Ng *et al.*, 2019).

According to a Bio City Group Report (2019), the life science sector in Nottingham has grown at a faster and more favourable rate in the last twenty years when compared to other second-tier regions in the UK such as Newcastle (Bio City Group, 2017; Crocker, 2019). Despite ranking tenth out of the twelve regions in the UK with activity in the life science sector, Nottingham consistently ranks in the top six regions regarding start-up and SME activity for this industry sector (Bio City Group, 2017; Crocker, 2019). To accomplish such regional performance has been a significant challenge for Nottingham

as it had historically been a manufacturing hub with little influence in developing innovative services or products for the life science sector.

A notable exception is the discovery, development, and commercialisation of ibuprofen in the 1960s thanks to R&D efforts by Boots. After this blockbuster drug, Boots faced several unsuccessful attempts to develop novel pharmaceuticals that led the company to give up its historical R&D facilities. It was in that building that Bio City Nottingham was established thanks to private and public support.

Bio City provides a physical space not only for new companies but also for companies that were already established in and around the East Midlands (Ehret, McDonald-Junor and Smith, 2012). Bio City Nottingham and the local council provide local support mechanisms that encourage biopharmaceutical start-ups to start operations in the region (Bio City Group, 2017). The presence of these support mechanisms has been suggested as an important aspect that promotes high-tech entrepreneurship and can also be a determining factor for start-ups when choosing the ideal location to start operations (Fini *et al.*, 2011; Ehret, McDonald-Junor and Smith, 2012; Lecluyse, Knockaert and Spithoven, 2019).

For the 2012-2016 period, companies based in the East Midlands managed to secure only 0.9% of the available funds for investment in the life science sector nationwide (Bio City Group, 2017). A reason for such a small figure is that only a handful of companies are spinning off from the local universities. The University of Nottingham is one of the top fifteen universities in the United Kingdom (Bio City Group, 2017); however, the number

of companies spinning-off from it is not close to those of the universities in the Golden Triangle, and Nottingham Trent University stays even further behind in this aspect. From the nearly 70 companies that have been tenants of Bio City Nottingham, only around 10% are a result of research projects from local universities, while for the “Golden Triangle” this figure is close to 50% (Bio City Group, 2017). This impact of the local universities on the footprint of life science entrepreneurship in the region could be the result of a misalignment of goals between them and the local industry. It is argued that cognitive proximity between universities and the local industry is important to promote and sustain academic entrepreneurship in entrepreneurial ecosystems (Ingstrup, Aarikka-Stenroos and Adlin, 2020).

Another reason for the difference in private investment between the “Golden Triangle” and the East Midlands might be the business models followed by the companies in each region. In Bio City Nottingham, only one-third of the companies rely on a product-based business model while two-thirds of the companies are service-oriented whereas most of the companies from the “Golden Triangle” depend on the development of products with a strong intellectual property – IP (Bio City Group, 2017; Crocker, 2019). By taking these factors into account, it is evident that in the biopharma industry, drug discovery companies require more substantial funding for introducing novel products to the market (DiMasi, Grabowski and Hansen, 2016).

As a region, the “Nottingham Biopharma Ecosystem”, and organisations within the ecosystem such as the science parks managed by BioCity Group, present outputs that

are above the expectations of an average second-tier region (Crocker, 2019). From these outputs, it can be argued that science parks are an important component of the makeup of entrepreneurial ecosystems for SMEs in the biopharma industry in a second-tier region.

The next section of this literature review addresses the relevance of science parks, their shortcomings, and the importance of considering them an integral component of the contextual factors of entrepreneurial ecosystems.

2.2.4 Science Parks within Entrepreneurial Ecosystems

Since companies tend to agglomerate within science parks, and science parks embed themselves within entrepreneurial ecosystems, it becomes important for research in entrepreneurship and innovation to explore the contextual factors of entrepreneurial ecosystems while considering the role of science parks for SMEs in the biopharma industry (Autio *et al.*, 2014; Diez-Vial and Fernández-Olmos, 2017; Díez-Vial and Montoro-Sánchez, 2017; Lecluyse, Knockaert and Spithoven, 2019).

Before the trend of entrepreneurial ecosystems, science parks were the prevailing policy tool to encourage knowledge-based innovation and entrepreneurship (Lecluyse, Knockaert and Spithoven, 2019; Robertson, Pitt and Ferreira, 2020). Among the benefits of science parks, access to new information is one of the most important as information is central to knowledge-based entrepreneurship (Porter, 2000).

Science parks are often located in regions where there is an existing pool of emerging and highly specialised talent (Casper and Murray, 2005) and government local support systems (Fini *et al.*, 2011). Regions hosting science parks usually provide a welcoming

culture for innovation and entrepreneurship, experienced mentors to help SMEs to sustain growth, brokers and deal-makers, industry gatekeepers, and access to networks for collaboration and support (Spigel, 2017).

The relationships between the contextual factors are important for the genesis and development of regional entrepreneurial ecosystems as they depend on the interactions of entrepreneurs in a certain sector with the local economy, support systems, and economic and social environments (Acs *et al.*, 2017; Theodoraki and Messeghem, 2017; Qian, 2018). Positive interactions between these factors facilitate local entrepreneurship (Qian, 2018), especially for knowledge-based organisations (Stam, 2015).

Specialised high-tech science parks are usually at the centre of what has been defined as the “triple helix” perspective for regional innovation systems (Leydesdorff and Zawdie, 2010). The triple-helix perspective suggests that a region can empower innovation through knowledge exchange between academia and industry with the support of a set of government initiatives. In a triple-helix configuration, industry stakeholders and regional governments offer different local support mechanisms to academia spin-offs that are important for a starting high-tech company (Fini *et al.*, 2011).

In the United Kingdom, government initiatives aiming to promote science parks for the life science sector can be traced back to the late 1990s and early 2000s (Ehret, McDonald-Junor and Smith, 2012). These efforts positioned the sector (more specifically biotechnology and biopharma) as part of what was defined as a knowledge-based economy is the purpose of which is to promote the economic development of different

regions across the country (Smith and Ehret, 2013). The efforts did not stop by giving the life science sector an important role in the future economic development of the nation; tax incentives for start-ups and programmes to facilitate technology and knowledge transfer between industry and academia were also set in place. However, these programmes focused on incubating companies rather than sustaining the growth of SMEs. These government initiatives favoured the creation of science parks for the life sciences across the whole nation instead of exclusively settling down in any of the regions of the "Golden Triangle" formed by London, Cambridge, and Oxford (Smith and Ehret, 2013).

Science parks are a place not only for high-tech based SMEs but also for universities' research facilities, business incubators, private investors, government agencies, and companies from the support services sector (Theodoraki, Messeghem and Rice, 2018). The interactions between organisations with different origins create a heterogeneous environment for collaboration (Geenhuizen and Soetanto, 2008). Heterogeneity is thought to be beneficial not only for the companies embedded in a science park but also for the regions hosting them as regional economic growth is expected (Porter, 2000). New companies might arise from the needs that SMEs within the cluster have, which enhances the region's economy through the effects of economic agglomeration (Delgado, Porter and Stern, 2014).

Science parks also facilitate knowledge sharing through what has been defined as the "spillover effect" (Argote and Ingram, 2000; Delgado, Porter and Stern, 2014; Diez-Vial and Fernández-Olmos, 2017; Qian, 2018; Triguero and Fernández, 2018). This effect

refers to knowledge that is not formally acquired by companies from collaborating with external partners (Argote and Ingram, 2000). The “spillover effect” is valuable for SMEs as they benefit from not only the activities towards innovation but also their enhanced managerial experience when handling specialised projects. Spillovers in a localised geographic area can either be regional or local (Triguero and Fernández, 2018). Regional spillovers involve companies in the same region but operating in different industries, while local spillovers occur in the same region and the same industry (Ma, 2009).

Nevertheless, science parks have their shortcomings. Recent research has argued that only focusing on science parks might hinder innovation and entrepreneurship as these locations are not isolated islands, but are part of a larger regional context (Molina-Morales, García-Villaverde and Parra-Requena, 2014; Lecluyse, Knockaert and Spithoven, 2019). The following section will address the theoretical and practical limitations of science parks and why it is important to acknowledge them as an integral part of entrepreneurial ecosystems in second-tier regions for biopharma SMEs.

2.2.5 The Shortcomings of Science Parks

Science parks were established as policy tools to promote innovation and entrepreneurship in knowledge-based economies (Porter, 2000) as it was expected that the firms occupying these spaces would closely collaborate as a result of geographical proximity (Bell, 2005; Bigliardi and Galati, 2016). Policymakers and researchers such as Porter (2000) regarded science parks and industry clusters as having a pivotal role in innovation and entrepreneurship; nevertheless, recent findings question the importance

of geographical proximity as the main driver for innovation and entrepreneurship for clustered companies (Presutti *et al.*, 2017).

It has been suggested that geographical proximity puts innovation and entrepreneurship activity on a plateau that is difficult to overcome without introducing external (off-science park) knowledge (Molina-Morales, García-Villaverde and Parra-Requena, 2014). Though agglomeration of organisations facilitates access to information, this information is the same for all the neighbouring companies. This stiff geographical arrangement isolates the region and avoids new knowledge from reaching companies within the entrepreneurial ecosystem resulting in what is known as the "network inertia problem" (Presutti *et al.*, 2017) or "spatial lock-in" (Molina-Morales, García-Villaverde and Parra-Requena, 2014). Presutti (2017) claims that this phenomenon affects organisations not only at an R&D level but also at operational and marketing levels having a potentially negative effect on innovative efforts and entrepreneurial activity.

To overcome these negative effects of science parks on innovation and entrepreneurial activity, companies are likely to take part in collaborations beyond their geographical proximity (Minguillo, Tijssen and Thelwall, 2015). Minguillo (2015) reached this conclusion after a critical analysis based on the relationship between the number of research papers written through collaborations inside science parks and the number of research papers written through collaborations outside such parks. Minguillo (2015) research only explores the result of these two options for collaboration; therefore, it becomes relevant to explore

the attitudes and managerial processes that are involved in the decision-making process of allocating resources and efforts for collaboration.

Giulani (2018) analysed underperforming science parks and found that in the relationships that site managers promoted, they were struggling to promote cognitive proximity between their tenants through common interests between their tenants. Some companies would then adopt “anti-social” behaviours and begin to scout for collaborators outside their cluster, favouring former colleagues and friends (Giuliani, Balland and Matta, 2018). Eventually, the most successful companies in underperforming science parks would be the ones making effective use of partnerships and collaborators outside the science park.

Giuliani’s research supports Molina-Morales’ (2014) arguments illustrating that companies in the same science park do not perform equally in terms of business or innovative performance. Furthermore, this irregular distribution of knowledge is not exclusive to underperforming science parks as even in the ones that are thriving, organisations that do not engage in collaborations and partnerships tend to underperform compared to those with the resources and managerial skills to foster external relationships (Presutti *et al.*, 2017).

Management in companies that are underperforming in financial and economic terms compared to other tenants in the same science park might experience dissatisfaction and will try to improve their situation without planning effective strategies (Giuliani, Balland and Matta, 2018). These companies usually ascribe such underperformance to the

science park management's inefficiency to care for all members the same way (the lack of meaningful opportunities to foster social connections, ineffective communication within members, and lack of internal advertisement), to environmental factors (political or economic instability), and to the lack of local support for all the members of the science park (Giuliani, Balland and Matta, 2018).

The factors that hinder relationships between SMEs in the context of a science park are likely to be more noticeable within second-tier regions as a result of the limited contextual and interactions in these regions. Academic research could explore how SMEs in the biopharma industry interact within science parks and the role that science parks might play in those interactions within the context of entrepreneurial ecosystems. Hence, it is relevant to understand the contextual and interactional factors around successful science parks and entrepreneurial ecosystems for SMEs in the biopharma sector in the United Kingdom. Taking into consideration these factors is likely to provide a better understanding of the heterogeneity of entrepreneurial ecosystems that facilitates a more accurate conceptualisation of entrepreneurial ecosystems.

The following section addresses the relevance of considering the different dimensions contributing to the contextual factors (McAdam *et al.*, 2014) in entrepreneurial ecosystems so they can be taken into account when investigating the genesis and development of entrepreneurial ecosystems within a specific context while allowing for the conceptualisation of theoretical constructs (Dedehayir, Mäkinen and Roland Ortt, 2018).

2.2.6 Exploring the Context of Entrepreneurial Ecosystems

The differences in access to financial resources and contextual support mechanisms such as science parks between entrepreneurial ecosystems in first-tier regions and second-tier regions suggest the acknowledgement of these differences when exploring the development of entrepreneurial ecosystems in second-tier regions for biopharma SMEs. The traditional approach to exploring the influence of context usually focuses on the formal structures and institutions within national systems that promote innovation (Zahra and Wright, 2011).

Academic research has only recently begun to recognise that the role of contextual mechanisms also expands to entrepreneurial activity as this activity is likely to vary across different regions within the same country and different industries (Autio *et al.*, 2014; Diez-Vial and Fernández-Olmos, 2017). Most of the academic efforts to understand the importance of context emphasise the performance (outputs) of innovation and entrepreneurial processes by measuring and assessing generated forms of intellectual property (Autio *et al.*, 2014). However, it is argued that the context within an entrepreneurial ecosystem is likely to influence innovation and entrepreneurship in these regions (McAdam *et al.*, 2014; Giuliani, Balland and Matta, 2018). The following sections will review the different dimensions of context and proposed frameworks for its exploration.

2.2.7 Dimensions of Context within Entrepreneurial Ecosystems

Contemporary research exploring the importance of context for entrepreneurial ecosystems recognises that the contextual factors within a specific region are influenced by the different agents that coexist in such environments (Autio *et al.*, 2014; Bonacina Roldan, Hansen and Garcia-Perez-de-Lema, 2018; Giuliani, Balland and Matta, 2018; Robertson, Pitt and Ferreira, 2020).

McAdam (2014) suggested that the contextual factors influencing entrepreneurial activities depend on the support mechanisms available to SMEs, such as government policies, funding opportunities, or physical infrastructure. Therefore, it can be argued that the support mechanisms available within a specific region are likely to influence the strategic decisions that individuals within biopharma SMEs make, the business models the companies adopt, and the type of support needed from external organisations (Autio *et al.*, 2014; Diez-Vial and Fernández-Olmos, 2017; Giuliani, Balland and Matta, 2018).

Autio (2014) highlighted the importance of exploring context while recognising its multidimensional components by presenting different components for context that are likely to influence the contextual and interactional factors within entrepreneurial ecosystems. Table 1 summarises the different types of context considering their traditional exploration in literature around innovation processes and social networks, and the reach this research assigns them for the exploration of entrepreneurial ecosystems.

Contextual Dimension	Traditional Levels of Exploration	Influenced Activity	References
Industrial and Contextual	National and Regional	Innovative Activity	(Autio *et al.*, 2014; Wang, Lestari and Yang, 2015; Robertson, Pitt and Ferreira, 2020)
Organisational	Firm and Network	Innovative Activity	(Nanda and Sørensen, 2010; Autio *et al.*, 2014; McAdam *et al.*, 2014; Giuliani, Balland and Matta, 2018)
Institutional and Policy	National and Regional	Innovative and Entrepreneurial Activity	(Autio *et al.*, 2014; Lee, 2017; Bogers, Chesbrough and Moedas, 2018; Flanagan and Wilsdon, 2018)
Social	Network	Innovative Activity	(Bozeman and Corley, 2004; Autio *et al.*, 2014; McAdam *et al.*, 2014; Robertson, Pitt and Ferreira, 2020)
Temporal	National and Regional	Innovative and Entrepreneurial Activity	(Autio *et al.*, 2014; Carvalho and Van Winden, 2017)

Spatial	Global, National, Regional, and Local	Innovative Activity	(Autio *et al.*, 2014; Rosenlund, Rosell and Hogland, 2017; Carayannis *et al.*, 2018)

Table 1. Dimensions of Context (Autio *et al.*, 2014).

The organisational context involves the business practices, expertise, and organisational culture within the organisations in an entrepreneurial ecosystem (Autio *et al.*, 2014), and it is likely to be impacted by the previous experiences of key individuals within such organisations (Nanda and Sørensen, 2010). This dimension of context is closely related to the concept of cognitive proximity underpinning this research; henceforth, it is likely that the contextual factors and cognitive proximity promote and facilitate the relationship between biopharma SMEs and other members of the entrepreneurial ecosystem they are embedded in.

Traditionally, the industry and technological contexts are related to the underpinning technology on which companies within a specific sector network rely in their development within an entrepreneurial ecosystem (Autio *et al.*, 2018). When considering this type of context within the environment of an entrepreneurial ecosystem, it might allow the phenomena of agglomeration that leads to the formation of industry-specific clusters (Lecluyse, Knockaert and Spithoven, 2019), therefore shifting from a type of context influencing companies to one influencing the trend for business models within an entrepreneurial ecosystem.

Other dimensions of contexts that might affect entrepreneurial activity within entrepreneurial ecosystems are the institutional and policy context, the social context, the temporal context, and the spatial context (Autio *et al.*, 2018). The institutional and policy context concerns formalised organisations such as venture capitalists and science parks that facilitate innovative activities within companies. The social context involves the heterogeneity of actors within an entrepreneurial ecosystem and their ability to collaborate to complement their specific expertise to promote innovation and entrepreneurship. Considering the social context for entrepreneurial activities within an entrepreneurial ecosystem is likely to provide a context-specific understanding of the organisations that facilitate activities for innovation and entrepreneurship (Autio *et al.*, 2014; Robertson, Pitt and Ferreira, 2020).

The temporal context for innovative activity is concerned with the changes through time in policy incentives that might influence the lifecycle of an industry sector (Hoskisson *et al.*, 2013; Autio *et al.*, 2014). Moreover, the temporal context is also thought to play a role within the development of entrepreneurial ecosystems (Feldman, Francis and Bercovitz, 2005; Feldman, Siegel and Wright, 2019). Finally, the spatial context is related to the influence of a firm's location on its innovative activity while considering its physical presence from a local to an international distribution (Welter, 2011; Autio *et al.*, 2014).

Contemporary researchers have highlighted the importance of contextual factors for innovation and entrepreneurial activity due to the differences across different regions promoting the same industry sector within a country; nevertheless, there is an ongoing

academic discussion that aims to develop robust tools for contextual exploration (Carvalho and Van Winden, 2017; Diez-Vial and Fernández-Olmos, 2017; Autio *et al.*, 2018; Lecluyse, Knockaert and Spithoven, 2019).

In entrepreneurial ecosystems, the contextual factors (McAdam *et al.*, 2014) are formed by the different dimensions of context interacting within them. Therefore, adopting robust frameworks to explore the contextual factors influencing the genesis and development of entrepreneurial ecosystems through their interactions can help to build new knowledge by considering the heterogeneity, their dependence on context, and the interactions within them.

2.2.8 Frameworks for the Exploration of Contextual Factors within Entrepreneurial Ecosystems

Different theoretical models and frameworks for the exploration of contextual factors have been developed since contemporary research started to acknowledge the importance of context when exploring ecosystems for innovation and entrepreneurship (Muñoz *et al.*, 2020). This section reviews these theoretical models and frameworks while pointing out gaps in knowledge where this research can contribute.

With the advent of knowledge-based economies, technology transfer initiatives within universities, and the proliferation of science parks, a system where these organisations collaborate with governments to promote innovation and entrepreneurship was suggested. In the triple-helix framework, government, universities, and private industrial sectors collaborate to facilitate market introduction of knowledge-based products or services first developed within academic research groups (Kimatu, 2016; Rosenlund, Rosell and Hogland, 2017). The interactions proposed by the triple-helix framework are

suggested to promote a sustainable strategy for technological innovation while facilitating the empowerment of regional economies (Kimatu, 2016).

Since the triple-helix framework only considers some of the contextual dimensions explored by other authors (Autio *et al.*, 2014), it has been improved by integrating more helixes. In a four-helix model (Kimatu, 2016), civil society is integrated into the framework as a group of stakeholders to take into consideration rather than an active part of the ecosystem. A recent effort to advance the helix frameworks introduced the concept of "environment" as a dimension that "takes into account the national and regional economic interests and contributes to the activation and enhancement of innovations, technologies and human capital" (Carayannis *et al.*, 2018).

Overall, the different iterations of the helix framework have attempted to operationalise an ideal reality on which knowledge-based entrepreneurship is a result of intensive knowledge-based innovations (Kimatu, 2016; Rosenlund, Rosell and Hogland, 2017). The different iterations of these frameworks could be a result of not taking into consideration a wider definition of the contextual factors within an entrepreneurial ecosystem; therefore, other theoretical models for exploring contextual factors have been also proposed.

Autio (2014) discussed the different contextual interactions within an entrepreneurial ecosystem while suggesting a theoretical framework considering the interactions and relationships between contexts, entrepreneurs, entrepreneurial behaviour, types of entrepreneurial innovation, and performance.

Autio's framework depicts the different contextual dimensions as interrelated dimensions that influence the innovative performance of an entrepreneurial ecosystem (Autio *et al.*, 2014). However, it does not explore in detail how the interactions between these contextual dimensions are facilitated as it only proposes that the contextual dimensions influence entrepreneurial behaviour through time. Autio's framework (2014) can be considered as an advancement of the helixes that takes temporal context into account. Different contemporary researchers have argued for the importance of exploring specific contextual factors and interactions (Giuliani, 2013; Bonacina Roldan, Hansen and Garcia-Perez-de-Lema, 2018; Theodoraki, Messeghem and Rice, 2018) while considering their changes and developments through time (Carvalho and Van Winden, 2017). Figure 2 depicts the relationship between the quintuple helix framework and Autio's multidimensional framework for context.

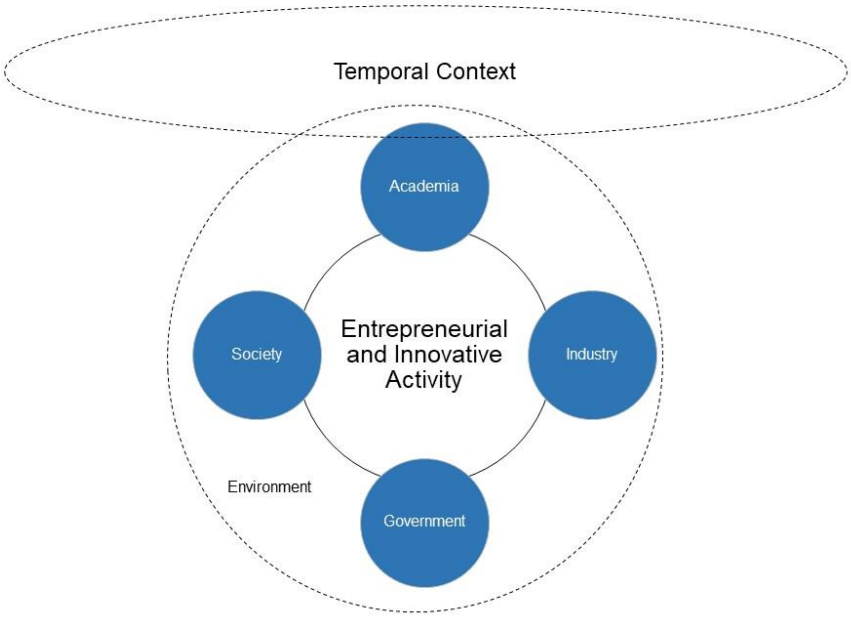


Figure 2. Helixes Models and Temporal Context. Representation of the Helixes model (Leydesdorff and Zawdie, 2010; Rosenlund, Rosell and Hogland, 2017; Carayannis *et al.*, 2018) taking into account the temporal context explored by Autio et. al (2014).

The different efforts to represent the influence of contextual factors on either innovative or entrepreneurial ecosystems are difficult to utilise as they do not take into consideration how the interactions between different organisations help to develop entrepreneurial ecosystems. However, a framework that has been recently employed to organise literature reviews on the contribution of science parks might be useful for empirical contextual explorations as well.

The Inputs-Mediators-Outputs Framework (IMO) was recently utilised by Lecluyse (2019) to organise literature regarding the contribution of science parks. By approaching the contribution of science parks as part of a system, this framework can be built upon to

acknowledge entrepreneurial ecosystems as a concept derived from a systematic view where inputs are transformed into outputs (Acs *et al.*, 2017; Brown and Mason, 2017; Theodoraki and Messeghem, 2017).

Within the IMO framework, the inputs allow for the understanding of the different features and attributes that impact the contribution of a science park in a firm's performance; the mediators are the mechanisms that facilitate the transformation of such inputs into desirable outcomes which are indicators of success (Lecluyse, Knockaert and Spithoven, 2019). This framework suggests that there is an interaction between a science park, the firms within the science park, and their goals in a knowledge-based economy. However, it does not take into consideration how the interactions between inputs and mediators promote the development of an entrepreneurial ecosystem to deliver regional specific outcomes. Figure 3 presents the IMO framework as depicted by Lecluyse (2019).

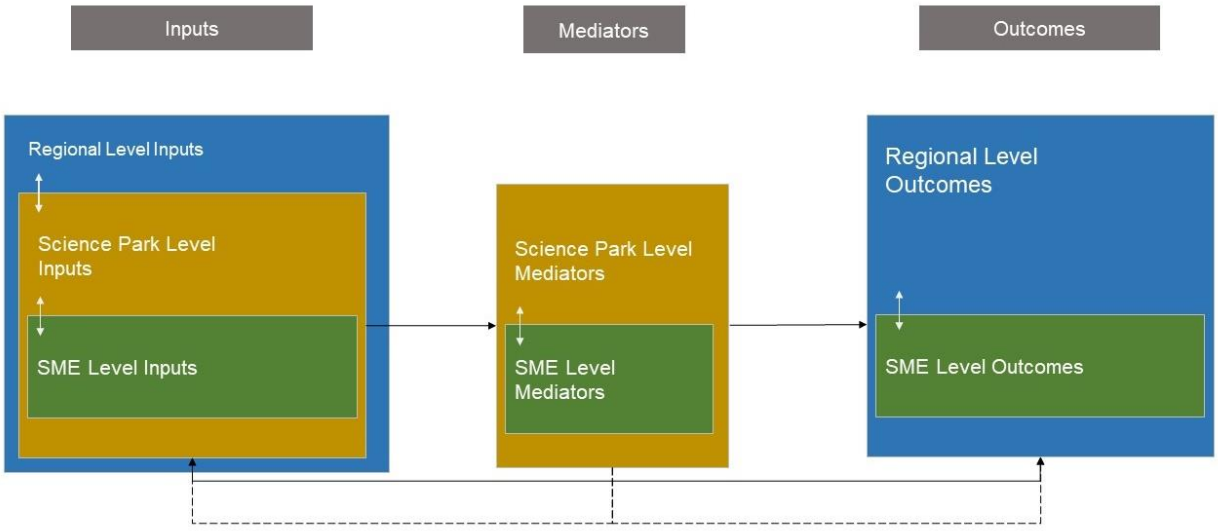


Figure 3. IMO Framework for Science Park Contributions (Lecluyse, Knockaert and Spithoven, 2019).

This research aims to build on the presented framework for the analysis of contextual factors so a more fined-tuned framework that considers how the relationships between the different contextual factors facilitated the development of an entrepreneurial ecosystem for biopharma SMEs in a second-tier region can be presented.

This research considers that cognitive proximity is an adequate theoretical lens to build upon the IMO framework to obtain a representation of the interactions between inputs and mediators within an entrepreneurial ecosystem for biopharma SMEs in a second-tier region. By using cognitive proximity to explore this entrepreneurial ecosystem, it is possible to gain a better understanding of the composition and inner functioning of the ecosystem (Theodoraki, Messeghem and Rice, 2018).

The next section of this chapter introduces the literature regarding partnerships and collaborations between SMEs, especially in the biopharma industry. It presents their

relevance, the type of knowledge exchanged through partnerships, the relevance of exploratory research to investigate partnerships, the factors involved in starting and managing partnerships, and the importance of considering the lifecycle of partnerships.

2.3 Part Three: Partnerships in the Biopharma Industry

Cognitive proximity is considered to be an important factor influencing the formation and management of partnerships in knowledge-based industries as reviewed in part one of this literature review. Chapter Two, part three of this thesis addresses the literature regarding the importance of considering partnerships between SMEs in the biopharma industry, the relevance of engaging in exploratory research to better understand partnerships, the barriers that partnerships might encounter, and the importance of investigating the lifecycle of partnerships in the biopharma industry.

2.3.1 Partnerships in the Biopharma Industry from an SME Perspective

The unprecedented events derived from the Covid-19 pandemic highlight the importance of partnerships between organisations within the biopharma industry (Chakraborty *et al.*, 2020). In this industry, the model for research and development (R&D) of new drugs and vaccines has shifted from solely relying on a company's internal R&D efforts towards an open and collaborative approach (Boni, 2018; Russo-Spena and Di Paola, 2018) where different parties are involved throughout pre-clinical development, clinical trials, and commercialisation activities (DiMasi, Grabowski and Hansen, 2016).

While the 20th century was dominated by the progress made by in-house R&D teams at large biopharma companies, the last two decades have seen academic research groups and highly specialised SMEs taking an increasingly major role in activities such as lead identification and validation respectively (DeCorte, 2020). With the growing implementation of this approach for the development of drugs and vaccines, it is argued

that the most cost-effective companies in the biopharma industry will be at the focal point of collaboration networks for the development of new products and services (Hunter, 2014). According to Chakraborty and collaborators (2020), SMEs are already key players in the partnerships needed to drive innovation while diminishing risk in the biopharma industry. Moreover, SMEs in this industry are important contributors to the economy as approximately 70% of the companies in the UK's biopharma sector fall within this category (Office For Life Sciences, 2020), yet questions remain regarding how to best facilitate the development of partnerships between and with such SMEs.

SMEs in the biopharma industry are usually launched around the specific expertise of the founding team while having the opportunity to adapt to changes in the market with more ease than large organisations (Huang, Soutar and Brown, 2002). Therefore, large biopharma organisations are becoming more interested in collaborating with SMEs as these partnerships are likely to add value while reducing the costs and risks associated with the development of new products and services in this industry (Michelino *et al.*, 2015; Chakraborty *et al.*, 2020; DeCorte, 2020).

On the other hand, SMEs in the biopharma industry tend to collaborate with external organisations to leverage resources that are difficult to access due to their inherent limitations as SMEs (Elfring and Hulsink, 2007; Pullen *et al.*, 2012; Sullivan and Ford, 2014). These resources are usually related to scientific knowledge, market knowledge, media knowledge, and organisational knowledge (Avermaete *et al.*, 2003; Salavou, Baltas and Lioukas, 2004; Brunswicker and Vanhaverbeke, 2015; Bigliardi and Galati,

2018; Santoro *et al.*, 2018). Table 2 presents the different types of knowledge that SMEs can leverage through partnerships.

Type of Knowledge	External Source of Knowledge	References
Scientific Knowledge	• **R&D partners.** • Research Centres. • Specialised Suppliers.	(Avermaete *et al.*, 2003; Salavou, Baltas and Lioukas, 2004; Kruse, 2012; Bigliardi and Galati, 2018; Santoro *et al.*, 2018)
Market Knowledge	• Customers. • Suppliers. • Competitors.	
Media Knowledge	• Scientific Conferences.	
Organisational Knowledge	• R&D Partners.	

Table 2. Sources of External Knowledge.

Bigliardi and Galati (2018) identified three major types of knowledge to be shared through collaborations and partnerships: market knowledge (obtained from customers, suppliers, and competitors), scientific knowledge (obtained from universities, specialised suppliers, and research centres), and media knowledge (obtained from licensing patents, information from specialised websites, and industry/scientific conferences). With this

classification, Bigliardi grouped the findings of Brunswicker (2015), Kruse (2012), and Santoro (2018); however, organisational practices that can add value and improve an organisation's performance are left out of the classification.

This research focuses on the scientific knowledge leveraged from R&D partners as exchanging this type of knowledge depends on complex interactions that can be better understood through cognitive proximity as "a mean to obtaining outcomes too ambitious for any single organisation to deliver on its own" (Vangen, 2017). Furthermore, exchanging scientific knowledge in the context of the biopharma industry is a lengthy process in which projects can be affected if there are changes in the cognitive proximity between the partners. A single drug development project can last up to 81 months from the beginning of clinical studies until the submission of the relevant paperwork to the regulatory agencies with an average cost of approximately 1,460 million USD (DiMasi, Grabowski and Hansen, 2016). Therefore, it is important to acknowledge that these partnerships go through different stages that can be better understood if identified as a lifecycle.

Leveraging resources is important for SMEs as it allows them to diminish risk without incurring high operational costs; nevertheless, the amount of funding needed to engage and manage these partnerships is even more limited within second-tier regions (Wang, Lestari and Yang, 2015; Cardoso and Meijers, 2016). This is relevant for SMEs based in second-tier regions where funding opportunities and supportive industry-specific policy initiatives tend to be limited (Wang, Lestari and Yang, 2015). Wang (2015) supports the

idea that second-tier regions facilitate strategic activities such as partnership management for SMEs as companies in these regions do not face the struggle of high operational costs related to facilities and market entry that are common in first-tier regions.

The SMEs in the City of Nottingham have benefited from some of the characteristics previously explored and, as a result, the life science sector in this region has grown at a faster and more favourable rate in the last twenty years when compared to other second-tier regions in the UK such as Newcastle (Crocker, 2019). From these outcomes, it can be argued that funding and high levels of human and social capital may not be the primary determinant elements supporting SMEs in a second-tier region (Wang, Lestari and Yang, 2015; Muñoz *et al.*, 2020) and that partnerships and collaborations can be an effective substitute for the lack of private capital for SMEs to access scientific knowledge through R&D partners (Wang, Lestari and Yang, 2015; Schweizer and He, 2018; Chakraborty *et al.*, 2020; DeCorte, 2020).

Despite the importance of SMEs in the economy and regional development of second-tier regions, partnerships in the biopharma industry are usually investigated from the perspective of large biopharma and biotech companies, and researchers have not yet determined the best way to explore these collaborations between SMEs (Schuhmacher *et al.*, 2013; Michelino *et al.*, 2015; Schuhmacher, Gassmann and Hinder, 2016). Moreover, research investigating partnerships in the biopharma industry usually tries to

assess the impact of these practices from the perspective of large companies (Michelino *et al.*, 2014, 2015; DiMasi, Grabowski and Hansen, 2016).

In recent years, scholars had begun to argue for the importance of investigating partnerships in the biopharma industry from the perceptions of SMEs (Bigliardi and Galati, 2018). This takes special importance as innovation and entrepreneurial activity in the biopharma sector would be more difficult without the role of SMEs (Chakraborty *et al.*, 2020; DeCorte, 2020). SMEs are usually formed around an innovative product or service; however, they can adapt to changes in the market with more ease than large firms (Huang, Soutar and Brown, 2002). The following section reviews the importance of engaging with exploratory research when investigating the role of partnerships. This is relevant as it allows this research to explore the lifecycle of partnerships in the biopharma industry between SMEs while taking into account the complex interactions in this sector.

2.3.2 Exploratory Research for Investigating Partnerships

Partnerships in the biopharma industry are traditionally explored in the setting of large companies by assessing the effect of these activities through defined outcomes (Michelino *et al.*, 2014, 2015; DiMasi, Grabowski and Hansen, 2016). These outcomes are usually related to the time needed to implement a joint project, the intellectual property generated through partnerships or the economic and financial impact of these partnerships for the involved parties (Michelino *et al.*, 2015). Though these metrics might be relevant in the context of large biopharma companies, they present SMEs with benchmarks that are difficult to accomplish due to their inherent limitations such as a lack

of human capital and funding to actively engage with partnerships. Hence, there is an opportunity to empirically explore how SMEs in a region constrained by lack of funding and human capital manage partnerships to leverage scientific knowledge.

While the traditional approaches for understanding the impact of collaborations in the biopharma industry focus on the measurement and assessment of arbitrary qualitative data (Michelino *et al.*, 2015), a recent call for longitudinal explorations has been made by contemporary research (Bigliardi and Galati, 2018). Longitudinal explorations are important as they have the potential of exploring how the outcomes assessed by the traditional approaches are met through deploying relevant theoretical constructs such as cognitive proximity.

To engage with longitudinal explorations of the development of partnerships in knowledge-based industries, a model with four dimensions is proposed by Bigliardi (2018). These dimensions investigate i) the reasons to engage (or not to) with collaborations (why); ii) the type of information, knowledge, or resources that are exchanged (what); iii) the managerial process to facilitate these collaborations (how); and iv) the actors that participate in these collaborations (with whom).

The reasons behind engaging with a collaboration (why/why not dimension) can be grouped into two main themes: financial and entrepreneurial reasons, and innovative reasons (Bigliardi and Galati, 2018). Companies seeking to collaborate for financial and entrepreneurial reasons are interested in maintaining growth while increasing profits (Yun and Mohan, 2012), alleviating the risk and cost involved with the development of lengthy

projects, and increasing organisational and operational flexibilities (Bigliardi and Galati, 2018). As for companies engaging with collaborations for innovative reasons, they seek to develop and commercialise new products or services (Pullen *et al.*, 2012; Vangen, 2017) or to access specialised R&D services (Hossain, 2015). The reasons to engage in partnerships also include getting access to missing knowledge, leveraging complementary resources, and expanding their presence in social networks for potential collaborations (Pullen *et al.*, 2012).

The assets that are shared and exchanged through partnerships (what dimension) are different from company to company as they depend on specific needs (Bigliardi and Galati, 2018). Companies can collect information and data from customers to investigate their experiences and preferences (Brunswicker and Vanhaverbeke, 2015). Feedback from customers is also helpful to recognise opportunities for new products, services, and/or business models (Santoro *et al.*, 2018). When partnerships are formed with suppliers, the collaborations usually aim to explore and exploit specialised technical knowledge to add value to products, services, and manufacturing processes (Brunswicker and Vanhaverbeke, 2015). Additionally, companies share and exchange information on legal and industry requirements (Kruse, 2012).

When exploring partners for collaborations (the whom domain), Bigliardi (2018) grouped them in two main areas: market-related (these associates can provide market and media knowledge) and technology-related partners (these associates can provide scientific knowledge). Organisational knowledge is usually identified and adopted through

spillovers while exchanging market or scientific knowledge (Argote, 2000). A dimension that was not considered by Bigliardi is the timing for collaboration. The length and the different aims of each stage in the drug development process make it difficult for an external partner to add value through lengthy projects. Due to the duration and specificity of the discovery, development, and commercialisation processes for a new drug, the domain “when” also becomes important when investigating collaborations and partnerships, especially in the biopharma industry (Huizingh, 2011).

Partnerships are not without issues as the different directionality for knowledge sharing might affect the willingness to collaborate with an external company (Lichtenthaler, Hoegl and Muethel, 2011). Hence a company could be ready to engage with external collaborators (Lichtenthaler, Hoegl and Muethel, 2011; Bigliardi and Galati, 2016; Calof, Meissner and Razheva, 2018). Hoegl (2011) suggested that the top executives in the company require a willingness to provide support to the process. Secondly, an open attitude towards accepting new ideas from an external organisation is desirable for the employees (Lichtenthaler, Hoegl and Muethel, 2011). Finally, individuals designated to overlook these organisational changes must be able to communicate the internal strategy for the collaboration through the company and to any shareholder in a timely manner. This key figures with the responsibility of managing and promoting collaborative activities are known as champions (Fichter, 2009; Hamadi, 2018).

Champions have been studied by research in entrepreneurship and innovation, and four different types have been investigated (Hamadi, 2018). Power champions are individuals

that support collaborations from a top management position and use their organisational hierarchy to promote innovative projects (Witte, 1973). Expert champions possess the specialised technical know-how to develop a novel product/service (Gemünden, Salomo and Hölzle, 2007) and are heavily involved in inter-organisational interactions required for open collaborations and partnerships (Rese, Gemünden and Baier, 2013). Organisational champions provide the organisational expertise needed to effectively manage communications between the involved shareholders and key individuals and to overcome any administrative barriers. Organisational champions also connect the relevant people to facilitate collaborative projects while coordinating key activities (Goduscheit, 2014). Finally, relationship champions are individuals who are connected with external actors that can support the project with the market, scientific, media, and organisational knowledge. Relationship champions have high network-making and network management skills (Goduscheit, 2014). These champions play an important role when scouting and engaging partners for collaborations and partnerships (Gemünden, Salomo and Hölzle, 2007). Overall, these champions are tasked with the goal of not only promoting collaborations and partnerships within an organisation but also liaising with potential partners while overcoming different barriers for open innovation activities.

There are different barriers to collaborating with external organisations. The next section of this thesis addresses the literature concerning these barriers so the relevance of the cognitive proximity for establishing and managing partnerships is palpable.

2.3.3 Barriers for Establishing and Managing Partnerships

A lack of knowledge and information about the implementation and benefits of collaborations and partnerships, a lack of awareness of the potential partners, and a lack of trust in external organisations play a key role in companies that engage in unsuccessful partnerships (Hewitt-Dundas and Roper, 2018). This lack of knowledge and trust can be the result of non-ideal cognitive proximity and makes external partnerships hard to formalise as a result of four main barriers for collaborations and partnerships (Bigliardi and Galati, 2016).

Organisational barriers are related to the lack of an official structure for the management of collaborations with external organisations. Without this structure, a company will probably lack the skills to establish an effective relationship with an external party while driving the internal change of attitude needed within the company's staff (Lichtenthaler, Hoegl and Muethel, 2011). The lack of power and administrative champions to support collaborations and partnerships affects the internal structure of a company when trying to use them as a regular practice.

Financial and strategic barriers are likely to arise from the cost related to new collaborations and the disagreement of the related parties on the strategic goal of the partnership (Christensen, Olesen and Kjær, 2005). This usually is a result of a lack of vision from management as a budget to manage external collaborations might not be promptly and adequately allocated (van de Vrande *et al.*, 2009).

Collaboration barriers include the fear of encountering an opportunist while trying to collaborate with companies that are not closely related in terms of cognitive proximity (Bigliardi and Galati, 2016). An effective strategy with key phases to scout potential partners can help to diminish risks related to collaboration barriers (Schweizer and He, 2018).

Finally, knowledge barriers are related to the loss of important knowledge without the proper compensation as well as not wanting competitors to imitate a technology or to copy a flagship product (Bigliardi and Galati, 2016). Not having access to up-to-date knowledge also affects the willingness to collaborate with external partners (Breschi, 2005). An environment with poor sources of knowledge and information is likely to affect collaborations and partnerships with external organisations greatly (Verbano, Crema and Venturini, 2015).

To overcome these barriers, a slow and strategic change of perception needs to be made within the people liaising these relationships between SMEs in this industry. Biopharma companies need to become aware not of the benefits of collaborations, but of the opportunities and challenges for the industry sector as a whole (Zynga *et al.*, 2018). Awareness of the assets and strategies required to help maintain a relevant portfolio of products and services is likely to encourage a company's management team to enlarge (or even begin to nurture) network connections to scout for potential collaborators.

Eventually, experienced mentors and champions within the company could help to establish managerial processes to liaise with external organisations. Trying to collaborate

with external partners without an in-depth understanding of good practices and process architectures usually leads to failed projects (Zynga *et al.*, 2018), and differences between the performance of SMEs within the same entrepreneurial ecosystem (Giuliani, Balland and Matta, 2018).

This research explores whether cognitive proximity can act as an enabler to overcome any of these collaboration barriers as they manifest through the lifecycle of partnerships.

2.3.4 Exploring the Lifecycle of Partnerships in the Biopharma Industry

This research suggests that cognitive proximity is likely to mediate the formation and management of partnership between SMEs in the biopharma industry, so it becomes important to explore how companies engage, manage, and take advantage of collaborations through this theoretical lens. Cognitive proximity has been found to play an important role when leveraging resources and sharing social capital between the organisations involved in partnerships (Partanen, Chetty and Rajala, 2014; Presutti *et al.*, 2017; Vangen, 2017; Rybnicek and Königsgruber, 2019; Ingstrup, Aarikka-Stenroos and Adlin, 2020; McGreevy *et al.*, 2020).

There is a rising interest in exploring the development of partnerships and collaborations in the biopharma industry between SMEs (Schweizer and He, 2018; Chakraborty *et al.*, 2020; DeCorte, 2020), especially in second-tier regions (Wang, Lestari and Yang, 2015). Schweizer and He (2018) identify stages and phases that companies go through when setting up partnerships. These phases are defined as inception, ignition, and implementation (Schweizer and He, 2018).

The inception stage begins with companies scouting for experts (either in industry or academia) that might become collaboration partners (Ashkenazy, 2018). Such opportunities might be created by assessing companies through business development techniques such as the BANT methodology (Kimla, 2013), which assesses a company´s budget, authority figures, need, and timing for the engagement, or by mere chance (Schweizer and He, 2018). It is suggested that managers also consider the knowledge and technical complementarity when assessing potential partners as these factors can facilitate resource allocation (Rojas, Solis and Zhu, 2018). Then, firms evaluate the potential benefits from the collaboration; this assessment of benefits is the start of the ignition stage. The goal of the ignition stage is an in-depth assessment of the technologies to observe if they can work together at a technical or market level and if the collaboration is in line with the business goals. When negotiations are successful, the firms will then draw a plan for collaboration.

Finally, the implementation stage involves the activities needed to execute the plan. However, during this stage, the agreements and plans developed during the ignition stage are usually reassessed if eventualities are presented (Marshall, 2004). The value and benefits of the collaboration are evident at this stage (Schweizer and He, 2018). Schweizer and He represented these phases within a model that resembles an S-curve as presented by McAdam's research (2014) on the development of collaborations in the UK's agri-food industry.

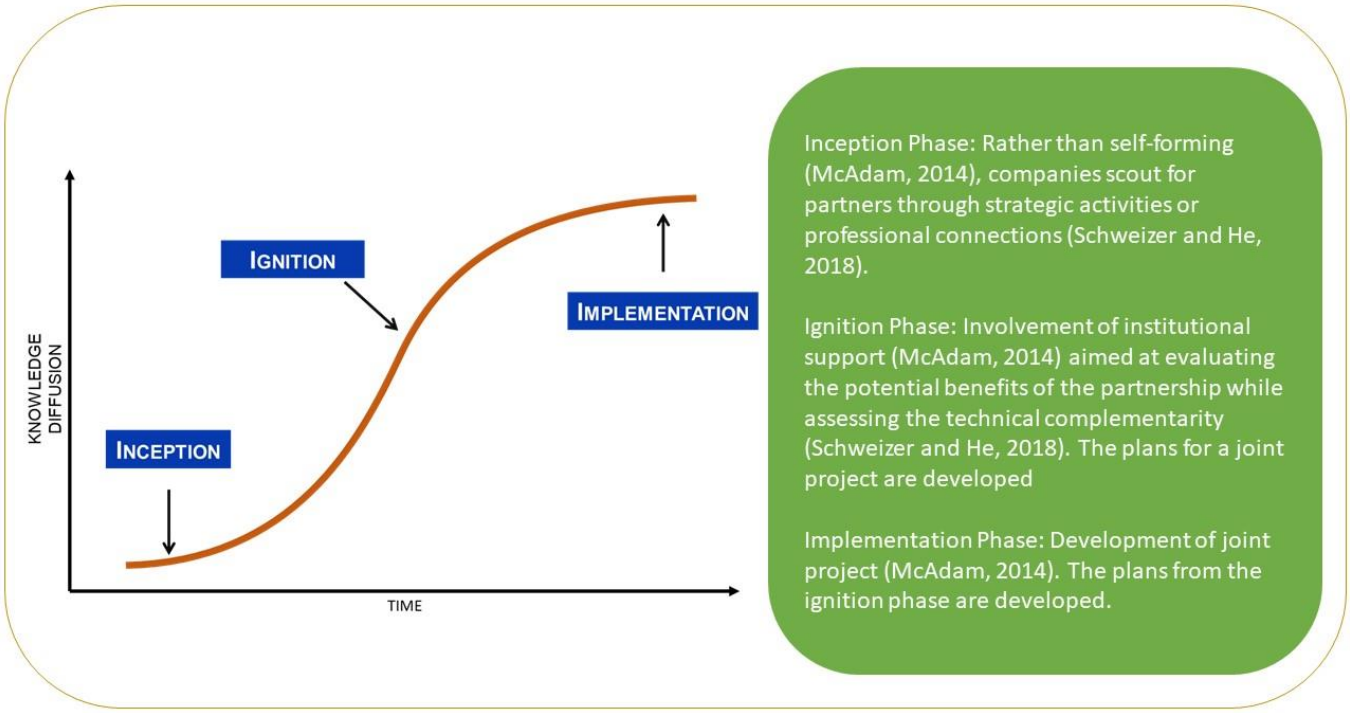


Figure 4. S-Curve Model with Phases. Consolidation of the contributions by McAdam (2014) and Schweizer & He (2018) within the S-Curve lifecycle model.

Schweizer and He's research (2018) focused on assigning values to evaluate the potential benefits of a potential collaboration through these stages; nevertheless, they did not explore the managerial strategies and practices that companies engage with to achieve a successful partnership. Therefore, this research aims to provide a more fine-grained model for the lifecycle of partnerships, especially between SMEs, in the biopharma industry through the exploration of qualitative data while using cognitive proximity as a theoretical underpinning for this model. Figure 4 consolidates the contemporary research this project aims to contribute forwards through addressing the

second research objective of understanding the lifecycle of partnerships in the biopharma industry from the perspective of SMEs in a second-tier region.

2.4 Chapter Summary

Cognitive proximity was originally proposed as a component of distance to quantitatively assess the outcomes of collaborations between organisations (Boschma, 2005; Molina-Morales, García-Villaverde and Parra-Requena, 2014). This construct to explore distance has been included in academic conversations regarding regional development and open innovation (Theodoraki, Messeghem and Rice, 2018; Mao *et al.*, 2019) as it ponders the manifestation of homogeneity between organisations that includes common languages, similar knowledge bases and shared goals (Molina-Morales, García-Villaverde and Parra-Requena, 2014; Capello and Caragliu, 2018; Hauge, Pinheiro and Zyzak, 2018; Theodoraki, Messeghem and Rice, 2018; Werker, Korzinov and Cunningham, 2019; McGreevy *et al.*, 2020).

This research proposes that deploying cognitive proximity as a theoretical lens can help to build new theory by addressing the research question “how does a second-tier region support SME activity in the biopharma industry?” To approach this research question through cognitive proximity, this research considers two levels on which this theoretical lens can be useful to gain new knowledge: the entrepreneurial ecosystem level and the firm level.

At the entrepreneurial ecosystem level, cognitive proximity is also known as the “cognitive dimension” (Theodoraki, Messeghem and Rice, 2018), and it argues that through a

common language and similar knowledge bases it is possible to set regional goals. Meeting these shared regional goals assists in increasing the cognitive proximity between the relevant members of the ecosystem through a positive loop that helps to sustain the ecosystem through collective narratives of success. Ideal cognitive proximity also helps to maintain closeness in the interactions between relevant members of an entrepreneurial system by supporting the “small-world” dynamic characteristic of organisations embedded in networks in the biopharma industry. This research considers cognitive proximity as a “glue” that holds together interactions within entrepreneurial ecosystems by helping its members to focus their efforts towards shared regional goals by maintaining the “small world” configuration (Inkpen and Tsang, 2005; le Duc and Lindeque, 2018; Theodoraki, Messeghem and Rice, 2018; Rybnicek and Königsgruber, 2019).

Entrepreneurial ecosystems are a rising subject area in academia as governments have adopted them as a policy tool to try to improve regional entrepreneurship and innovation. This concept finds its academic rooting in the literature in regional development and strategy, but it is deeply connected to a lineage of research based on understanding systems. Research on business systems is inspired by the concept of ecosystems studied in ecology and has as one of its main premises that a system requires inputs that can be transformed into outputs through the interactions of the members of the system.

As a result of this premise, research investigating entrepreneurial ecosystems traditionally focuses on measuring their outputs through arbitrary measures of performance with a quantitative value such as economic performance, start-up activity, or the number of

“blockbuster companies” (Theodoraki and Messeghem, 2017). By focusing on desirable outputs, policymakers usually try to create entrepreneurial ecosystems based on the outputs of those based in first-tier regions as a benchmark; however, this approach is likely to result in misapplications of the concept of entrepreneurial ecosystems as there are still theoretical and practical limitations of the concept that require a better understanding.

Understanding the different contexts for the genesis and development of entrepreneurial ecosystems is of relevance. This research identifies first-tier and second-tier regions as two major contexts for the genesis and development of entrepreneurial ecosystems. First-tier regions are those with major national importance in terms of economic performance and pulling resources from the rest of the country. These regions usually benefit the most from government policy promoting regional entrepreneurship and innovation. Second-tier regions are usually defined for what that they are not, so this research labels them as “regions outside the main hubs for innovation and entrepreneurship that successfully promote regional innovation and entrepreneurship despite their limited resources.” In the United Kingdom, the first-tier regions for the biopharma sector are London, Oxford, and Cambridge, which are collectively known as the “Golden Triangle”.

This research focuses on a second-tier region because these regions provide an interesting context for research as entrepreneurial ecosystems in these regions usually lack key resources such as private funding and tailored-made government policies to facilitate the development of SMEs in knowledge-based industries. Therefore, biopharma

SMEs in these regions are likely to be constrained by the limited contextual and interactional factors available to them. The City of Nottingham is a second-tier region in the United Kingdom, and it is a typical example of one as it ranks tenth in terms of private funding for the biopharma sector within the twelve regions in the UK with entrepreneurial activity in this industry (Crocker, 2019). Nonetheless, it produces remarkable outputs as it ranks sixth in terms of start-up and SME activity in the UK, and the science parks in this entrepreneurial ecosystem presented a survival rate of 91% on average from 2007 to 2019 (Crocker, 2019).

Another integral part of the contextual factors involved in an entrepreneurial ecosystem is the presence of science parks. Science parks are the policy tool preceding entrepreneurial ecosystems on which policymakers relied. Research on science parks suggested that they would foster entrepreneurship and innovation in the biopharma sector by agglomerating SMEs and other organisations providing support services. Nevertheless, science parks have their shortcomings, and recent research advocates for considering science parks as part of their entrepreneurial ecosystem and its interactions

To have a better understanding of the contextual factors surrounding an entrepreneurial ecosystem, Autio (2014) explores the different dimensions that form context. Different theoretical frameworks have tried to represent the context affecting knowledge-base entrepreneurship and innovation, but they usually overlook the heterogeneity and the interaction between the relevant actors in an entrepreneurial ecosystem. However, this research identifies the IMO framework as a suitable theoretical one that can be improved

on through this research for the exploration of the contextual factors in an entrepreneurial ecosystem as it takes into account the interactions between inputs and mediators to produce outputs.

Understanding how the contextual factors of an entrepreneurial ecosystem interact through cognitive proximity is important to better understand its genesis and development.

At a firm level, cognitive proximity can help us to comprehend more fully the lifecycle of partnerships between SMEs in the biopharma industry. Partnerships in this industry are inherently complex to establish and manage and might span lengthy periods; henceforth, cognitive proximity is an important element for creating environments for effective partnerships as it helps to set the ideal starting conditions, organisational structures, and evaluation methods for these collaborations to reach the established shared goals (Errecaborde *et al.*, 2019). This is also referred to as “common ground” in contemporary research (Mao *et al.*, 2019).

Understanding how collaborations are established and managed between SMEs in the biopharma industry is important as this sector has shifted its R&D model from a closed one to one depending on collaborations and partnerships between external organisations. Research exploring collaborations and partnerships in the biopharma industry usually observes these phenomena from the perspective of large biopharma companies located in or near first-tier regions. Thus, it is relevant to understand the lifecycle of and partnerships between SMEs based in second-tier regions.

The different barriers to collaborations and partnerships in this industry are, to some degree, a result of a lack of trust and fear of opportunistic behaviours from potential partners derived from a lack of cognitive proximity. Therefore, there is an opportunity to advance the current models exploring the lifecycle of these interactions by considering cognitive proximity as an enabler.

Chapter Three – Methodology and Research Design

Chapter Two reviewed the literature addressing the importance of cognitive proximity as a theoretical lens to understand how to support biopharma SMEs in second-tier regions at two different levels: the entrepreneurial ecosystem level and the firm level. Chapter Two also explored how finding a common language and sharing similar knowledge bases between organisations helps them in establishing shared goals to support the ecosystem and their partnerships, respectively. Finally, Chapter Two elucidated the literature and theoretical gaps regarding the literature on entrepreneurial ecosystems and partnerships in the biopharma industry.

This chapter now explores the methodological approach that will be adopted to address the research objectives and theoretical gaps presented across Chapters One and Two. It begins with a review of the philosophical underpinnings of social science research while discussing the ontology and epistemology better suited to accomplish the research objectives.

The chosen methodology, research design, and research methods that this research employs are then discussed while justifying the method of analysis. Finally, given the nature of the research, the concept of reflexivity is included to acknowledge the impact of the researcher on the research process and resultant findings.

3.1 Philosophy and Research Paradigms

When studying social science, it is important to determine the philosophical assumptions that will allow the researcher to understand the phenomena that is being studied (Tsang,

1999). The philosophical paradigms of research help to reflect on the contribution to knowledge, the importance of the project, and can be used as a research guide. These paradigms can also influence the ontological and epistemological position of the research, data collection methods, and even the interpretation of the findings (Guba and Lincoln, 1994). An ontological position provides a statement of what is the nature of the reality for the research topic according to the researcher (Creswell *et al.*, 2007), while an epistemological position involves how the researcher collects information (Morgan, 1980).

There are a wide range of philosophical viewpoints that differ in their consideration of reality. Empiricism, positivism, and post-positivism are connected to natural and exact sciences, while social sciences tend to approach reality through approaches such as post-modernism, constructivism, and constructionism (Morgan and Smircich, 1980; Guba and Lincoln, 1994).

Positivist and post-positivist views consider reality as something objective that cannot be affected or changed by individuals as it external to them, therefore, only answers that can be translated as conclusive knowledge are accepted, whereas approaching reality through a post-modernist, constructivist, or constructionist position implies that there can be multiple realities that depend on the individuals within them (Cunliffe, 2011), so there are possible answers which are not definitive and vary depending on different environments.

Hence, a positivist and post-post-positivist approach is connected to the philosophical paradigm of realism, while the approaches that accept multiple realities are related to

relativism (Guba and Lincoln, 1994). Other philosophical paradigms that seek to reconcile both views of reality are critical realism and pragmatism. On the one hand, critical realism argues that reality is made up of the interactions between specific mechanisms and events through different domains: the real domain, the actual domain, and the empirical domain (Tsang, 1999). On the other hand, pragmatism presents an objective reality that still allows external influences that shape such reality (Tsang, 2016). Though there is a differentiation between these philosophical paradigms, the approach in which a concept is studied varies significantly in social sciences (Alavi, Maryam, 2001).

The following sections will review the ontology and epistemology that better helps to answer the research question: how does cognitive proximity enable a second-tier region to support biopharma SMEs?

3.1.1 Ontology

Ontology is concerned with how social objects can be viewed by researchers (Alavi, Maryam, 2001), and qualitative research usually takes the position in which multiple subjective realities exist. Therefore, social objects can be considered as objective entities, social constructions, an existing part of social actors, an abstract object shaped by cognitive processes, or as the actions taken by individuals as they act in the world (Morgan and Smircich, 1980; Carlsson *et al.*, 1996; Creswell *et al.*, 2007).

This thesis adopts the interpretive paradigm while taking the ontological position that reality is socially constructed through the subjective experience of the individuals involved (Morgan and Smircich, 1980). By doing this, the narrative and the meaning of it are

produced by individuals through their interactions and specific actions (Creswell *et al.*, 2007). This means that social phenomena are in constant change and development.

This research seeks to understand the subjective meanings that emerge as individuals act in their environment by taking an inductive stance to clarify the foundational reasoning for this work. Through an inductive approach, the research can focus on the experiences of individuals and on how they interpret reality through their individual and shared experiences (Bell and Bryman, 2007). This approach is quite flexible as does not require a pre-determined theory to begin and relies upon the data analysis to reach meaningful conclusions (Eisenhardt and Graebner, 2007). By going in hand with the interpretivist paradigm, this approach allows this research to understand contextual factors that facilitated the genesis and development of an entrepreneurial ecosystem in a second-tier region and to explore the lifecycle of partnerships in the biopharma industry between SMEs.

Henceforth, this research proposes an exploratory interpretivist approach for the investigation of the contextual factors that facilitate the development of an entrepreneurial ecosystem, and for the understanding of the complex interactions involved in the lifecycle of partnerships between SMEs in the biopharma industry.

3.1.2 Epistemology

This research explores how reality looks like so a second-tier region can support an entrepreneurial ecosystem for biopharma SMEs. Through an interpretivist ontological approach, this research can collect data on one of the multiple realities that facilitated the

development of an entrepreneurial ecosystem within a second-tier region, and the formation of collaborations and partnerships from the perspective of SMEs.

The chosen philosophical framework considers that there is a component of rationalism and voluntarism and favours ideographic methods for data collection (Packard, 2017). Interpretivism drifts away from realism as it views social interactions as a voluntary act in nature, so they could be explored at the individual levels as individuals confer different meanings to these interactions. Moreover, through interpretivism, engaging with external organisations is a choice that certain individuals make towards a personal and organisational benefit. Thus, this research seeks to understand such choices and the consequences they instigate.

Interpretivism helps in considering reality as a continuous process that is modified and further unfolded by decision, rather than a fixed set of activities (Packard, 2017). Once the data is collected, the interpretation of such a data set allows the researcher to perform a reverse-engineering process known as retrospection. Through retrospection, this research uses the collected data and information to explore why and how the interactions between different actors produced specific events (Tsang, 2016). Moreover, by obtaining knowledge through the interpretation of qualitative data through idiographic methods, the researcher can analyse the data as a result of a specific context.

Since the objective of this thesis is to understand and explore the subjective experiences of the actors within an entrepreneurial ecosystem and of the people involved in liaising with external organisations for partnerships, this research uses the case study

methodology (Eisenhardt and Graebner, 2007; P. Swanborn, 2010; Eisenhardt *et al.*, 2018).

3.2 Methodology

This section approaches the methods for data collection and the data analysis used to generate knowledge (Cunliffe, 2011). Defining the philosophical underpinning of the research dictates to some extent the chosen methodology.

On the one hand, positivist approaches favour methods that analyse quantitative data and aim to measure and determine the effect of different constructs of a theory on a phenomenon (Tuli, 2011). On the other hand, interpretivist explorations allow for the inductive nature of the methods for the collection and analysis of qualitative data, which enables a researcher to explore insights and experiences in a specific context. Analysis of qualitative data facilitates an in-depth investigation of “how” and “why” a social phenomenon is manifested (Mohajan Kumar Haradhan, 2018).

Methodologies that collect qualitative data are useful to understand the relationships between actors from their experiences while engaging in social interactions and to construct an interpretation of the social reality from the life experiences of people fitting a certain criterion (Atkinson, Coffey and Delamont, 2001). Analysing qualitative data is useful in areas such as management and information systems as it helps to obtain a profound understanding of particular issues (Mohajan Kumar Haradhan, 2018). Collecting qualitative data usually involves forming connections with research participants; these

personal connections usually add richness and depth to conclusions drawn from qualitative data analysis (Tuli, 2011).

Collecting qualitative data does not rely on a single method; therefore, the nature of the research question defines the data collection method (Tuli, 2011). From the different methodologies to collect qualitative data, a case study allows the researcher to explore the questions proposed in this thesis.

3.2.1 The Case Study Methodology

A case study is usually defined as an intensive investigation of a research unit (a person, a group of people, or a specific location) aimed at extrapolating conclusions for a larger set of similar units (Gerring, 2004). By using a case study methodology, a researcher can narrow down a complex and broad theme into manageable research questions (Peter Swanborn, 2010). In a case study, a population is formed by a sample of studied and unstudied cases. Each sample is comprised of several units, and each unit is observed at a certain point in time comprising a case. Due to its nature, a case study is a tool that can either illustrate established concepts or help to create new theories (Gustafsson, 2017) while providing a framework to explore and analyse complex themes (Haele and Twycross, 2018).

Each case is formed by several dimensions that are built upon observation (Gerring, 2004). A case study allows the researcher to know what is specific to a unit, and what from that unit can be generalised to other units; henceforth, allowing a case study to provide original research of some sort (Gerring, 2004). Therefore, it is important to

differentiate between formal and informal units within a case study. On the one hand, formal units are chosen to be extensively investigated while, on the other hand, informal units are brought into the analysis as accessories to help set up the introduction to the research or to illustrate some of the conclusions. Informal units are surveyed in less detail as conclusions about these units are usually collected from secondary data and their state as informal units is often left implicit (Gerring, 2004). To avoid confusion in the experimental design, the units need to be defined clearly so the conclusions can be generalised only for other units meeting such characteristics.

The case study methodology also permits the examination of correlative relationships in a simple but still highly informative manner (Gerring, 2004), thus providing a groundwork to explore the research question in this thesis: “how does cognitive proximity enable a second-tier region to support biopharma SMEs?”

A how question can be answered without the need for a cross-unit analysis as these explorations can go as far as illustrating how a research unit is different or similar to other research units. However, by doing so, there is no way to make any assertions about causal relationships occurring within and between the different units. Therefore, the researcher needs to choose between analysing a single unit (single-case study) or several units (multiple case study) as different contexts allow for different possible conclusions (Gustafsson, 2017). In either case, it is recommended to explore cases that can be considered crucial or highly representative of the explored phenomenon (Gerring, 2004) in a well-defined context. Therefore, this research is set in Nottingham City as it is

a second-tier region that supports an entrepreneurial ecosystem for biopharma SMEs that performs better than other second-tier regions in the UK (Crocker, 2019).

In a single case study, a researcher can explore and contrast old theories against new coming paradigms because a more careful and in-depth analysis of the unit is made (Dyer and Wilkins, 1991; Gustafsson, 2017).

3.2.2 Building Knowledge from the Case Study Methodology

When collecting data through the case study methodology, it has been deemed important for the study to start with a research question that provides the researcher with a well-defined focus (Eisenhardt and Graebner, 2007; Eisenhardt *et al.*, 2018). Doing this diminishes the possibility of being overwhelmed by the volume of data while forcing the research to specify the objectives of the exploration and the type of data to be collected. An approach for accomplishing the desired focus is by defining a priori constructs in the initial phases of the theory-building research. In her research addressing the case study methodology, Eisenhardt (1989, 2007, 2018) argued that a priori constructs are important as themes start to emerge from the collected data. Nevertheless, she also advised against rigidity and certainty when defining research questions and specifying constructs as in this methodology the most important part is a resultant theory closely linked with the collected data.

The selection of cases is another important consideration for the theory-building process from a case study. The population of the case is a key issue as it defines the research units from which the research sample will be drawn. Furthermore, selecting the population

for the case study allows for the control of any extraneous variation. Participant selection is based on a replication logic (Eisenhardt and Graebner, 2007; P. Swanborn, 2010) where each research unit either predicts the same results or predicts contrasting results that can be used to refine the theory-building process while extending its applicability.

A case study traditionally employs the combination of multiple data collection methods, with interviews, direct observations, and archival sources of documentation being particularly common (Eisenhardt and Graebner, 2007; P. Swanborn, 2010; Eisenhardt *et al.*, 2018). The collection of data from multiple sources is important as it allows for data triangulation, which refers to the use of multiple sources of data obtained at different places and different moments for comparison and cross-referencing (Merriam, Sharan B., 2015).

Another key element of the case study methodology is that it encourages the overlap of data collection and data analysis. This overlapping is considered beneficial for the researcher because it allows for adjustment to the data collection methods as data analysis may unveil unexplored themes that the researcher might further explore. This characteristic of the case study methodology provides the researcher with the flexibility needed to either ground theory or to provide new theoretical insights (Eisenhardt and Graebner, 2007).

Analysing the data collected for a case study will produce themes, concepts, and relationships among the data that must be compared to the relevant literature (Eisenhardt and Graebner, 2007; P. Swanborn, 2010). A key element to this process is to consider a

broad range of literature as literature discussing similar findings will help to tie underlying similarities together while resulting in a stronger internal validity and a greater potential for generalisation whereas examining contrasting literature provides an opportunity to make a novel contribution. The revision of the extant literature is important for the theory-building process as the case study methodology is a bottom-up approach where the specifics of the collected data try to provide generalisations of theories; therefore, there is the risk of developing an idiosyncratic theory with limited applicability (Eisenhardt *et al.*, 2018). Table 3 provides an overview of the theory-building process from a case study.

Stage	Task	Justification
Preparation	• Defining the research question. • Elucidating a priori constructs.	• Directs efforts. • Provides better grounding for the construct measurements.
Case Selection	• Defining the research participants through theoretical sampling.	• Prevents extraneous variation and sharpens validity. • Directs the data collection efforts towards theoretically useful cases.
Definition of Data Collection Methods	• Defining the multiple data collection methods.	• Strengthens the theory-building process by triangulation of evidence.
Fieldwork	• Overlapping data collection and data analysis. • Integrating field notes into the analysis.	• Speeds the analysis up and might unveil unexplored themes. • Allows for adjustments to the data collection methods. • Allows for the discovery of theoretical saturation.
Data Analysis and Development of Theoretical Constructs	• Applying reduction techniques that produce themes.	• Allows for the grouping of data for further comparison to relevant literature.
Literature Comparison and Closure	• Comparing the analysed data to relevant literature (either similar or conflicting). • Providing conclusions and contribution.	• Improves generalisability, construct definition, and internal validity.

Table 3. Theory-building Process (Eisenhardt and Graebner, 2007; P. Swanborn, 2010; Eisenhardt *et al.*, 2018).

3.3 Research Design

This study employed an inductive case study research design to explore “how does cognitive proximity enable a second-tier region to support biopharma SMEs?” This

research collected data from seven SMEs, some of their collaboration partners, and relevant stakeholders in the “Nottingham Biopharma Entrepreneurial Ecosystem” from November 2018 to November 2019. The research participants were theoretically selecting following the recommendations of Swanborn (2010) and Eisenhardt (2007, 2018). A combination of the retrospective and snapshot approaches to the case study methodology was chosen for this study (Mohajan Kumar Haradhan, 2018).

3.3.1 Population

The research participants were drawn from a single entrepreneurial ecosystem, defined by the researcher as the Nottingham Biopharma Entrepreneurial Ecosystem. This entrepreneurial ecosystem for SMEs in the life sciences is located in a second-tier region within the East Midlands region in the United Kingdom.

The Nottingham Biopharma Entrepreneurial Ecosystem is an interesting second-tier region, as despite lacking the private funding designated to the “Golden Triangle” or “The Northern Powerhouse” (Bio City Group, 2017; Crocker, 2019), it presents one of the highest start-up and SMEs activities in the life sciences among other second-tier regions in the UK, such as Newcastle, Leeds, or Sheffield (Crocker, 2019). Therefore, this entrepreneurial ecosystem provides an ideal setting to explore how specific contextual factors facilitate the development of an entrepreneurial ecosystem (Autio *et al.*, 2014; Lecluyse, Knockaert and Spithoven, 2019; Robertson, Pitt and Ferreira, 2020). It is also an interesting setting to investigate the lifecycle of collaborations and partnerships in the biopharma industry from the perspective of SMEs in a second-tier region.

3.3.2 Research Participants

Within the specified population, the research participants were chosen theoretically as suggested by Eisenhardt (1989, 2007). The participant companies were SMEs in the biopharma industry offering products or services for any of the development stages (pre-clinical, clinical, or review process) of the drug development process (DiMasi, Grabowski and Hansen, 2016).

Defining this was important as it allowed the research to include not only drug development companies but also contract research organisations (CROs), and contract research and manufacturing organisations (CRMOs). CROs and CRMOs are important as they provide highly specialised peripheral services that even large biopharma companies need through a drug development project (DeCorte, 2020). These services usually involve lead identification and assessment, formulation and manufacturing of the molecule and its delivery method, and the evaluation of effects of such molecules in vitro and in vivo. Being able to identify companies that participate in different stages of a drug development project is concurrent with the open innovation paradigm in the biopharma industry (Boni, 2018; Chakraborty *et al.*, 2020). Table 4 provides a profile of the participant organisations in this study.

This research undertook a primary identification of the local organisations that facilitate entrepreneurial activities for biopharma SMEs within the entrepreneurial ecosystem (Carayannis *et al.*, 2018; Lecluyse, Knockaert and Spithoven, 2019). The list of relevant

stakeholders was updated after identifying unveiled themes during the overlapping process of data collection and data analysis (Eisenhardt and Graebner, 2007).

Participant Organisation	Internal Respondents	External Respondents	Time Spent with Unit of Analysis	Archival Data
Participant SMEs				
Company Alpha	Head of Partnerships & Licensing (Alpha 1)	Not Available	165 minutes	Company website and press releases.
Company Bravo	Founder (Bravo 1)	Not Available	165 minutes	Company website and press releases.
Company Charlie	Head for Global Business Development (Charlie 1)	External Marketing Director (Charlie 2) Marketing Intern (Charlie 3)	220 minutes	Company website and press releases.
Company Delta	Founder & CEO (Delta 1) Operations Manager (Delta 2)	Not Available	212 minutes	Company website and press releases.
Company Echo	Pain Development Director & Site Director (Echo 1)	Not Available	188 minutes	Company website and press releases.
Company Foxtrot	Director of Marketing (Foxtrot 1)	CEO of an acquired company (Foxtrot 2) and BioCity's Corporate Development Director (BIO1)	200 minutes	Company website and press releases.
Company Golf	Chief Scientific Officer (Golf 1) and Marketing Manager (Golf 2)	CEO from technology development partner (Golf 3)	266 minutes	Company website and press releases.
Participant Ecosystem Stakeholders				
BioCity Group	Corporate Development Director (BIO1)	Not Applicable	300 minutes	Company website, press releases, bi-annual reports.
Medilink East Midlands (MEM)	Project Manager/ Business Development (MEM1)	Not Applicable	360 minutes	Organisation website and press releases.
Academic Health Science Networks (AHSN)	Commercial Manager (AHSN1)	Not Applicable	180 minutes	Organisation website, press releases and annual reports.
Mentor, Ohio Department for Economic Development and Internationalisation	Director (DED1)	Not Applicable	225 minutes	Organisation webpage and press releases.
Company Vent	Director & Chairperson (VENT1)	Not Applicable	200 minutes	Company website and press releases.

Table 4. Research Participants.

3.3.3 Unit of Analysis

Given that for small and medium organisations the responsibility of connecting with external organisations is claimed by a key individual (Fichter, 2009; Hamadi, 2018), this study identified the more influential external liaisons for each company, usually holding positions as CEOs, CSOs, or Business Development Directors/Managers.

Since the concept of cognitive proximity can manifest between organisations and individuals (Molina-Morales, García-Villaverde and Parra-Requena, 2014; le Duc and Lindeque, 2018), this research focused on the strategic decisions that individuals representing different organisations embedded within this specific entrepreneurial context made as a result of the contextual and interactional factors (Autio *et al.*, 2014; McAdam *et al.*, 2014; Lecluyse, Knockaert and Spithoven, 2019) available. This is therefore an embedded single-case study, in which the relevant case (the Nottingham Biopharma Ecosystem) is explored through the investigation of different units of analysis embedded within it. Figure 5 presents the different typologies of single case studies.

Therefore, this research is an embedded single-case study, in which the units of analysis are the individuals within the SMEs embedded in the entrepreneurial ecosystem and the stakeholder organisations tasked with facilitating the interactions between the actors within the entrepreneurial ecosystem.

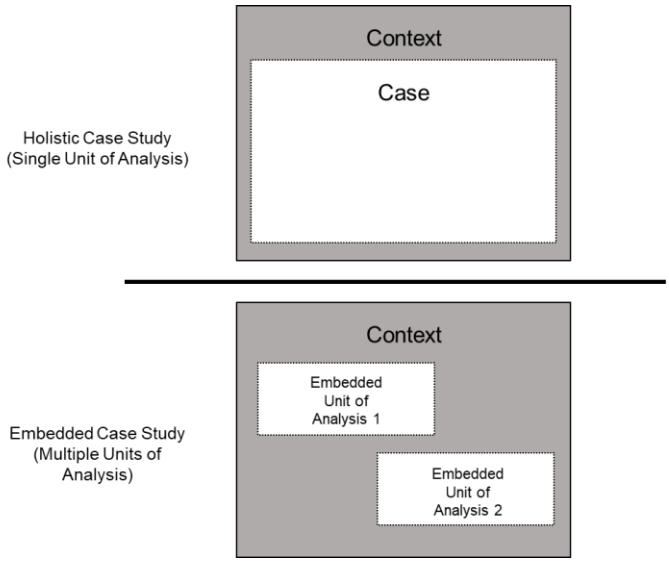


Figure 5. Typologies of Single Case Studies.

3.3.4 Synergy of Retrospective Analysis and Snapshot Analysis

There were twelve participant organisations for the study, which comprised both a retrospective account of the individuals' experiences and an in-depth snapshot analysis of specific events identified within the retrospection. On the one hand, a retrospective exploration allows the study of past events with historical relevance to the companies (Mohajan Kumar Haradhan, 2018), while the snapshot approach is useful to investigate the impact of a specific event that can stretch through a period of days to even months by connecting the significance of the event to the companies' internal environment.

The approach employed in this study also offers an opportunity to identify the dynamic processes involved in the development of an entrepreneurial ecosystem within a second-tier region. This retrospective/snapshot analysis is likely to allow the researcher to keep

focus by highlighting patterns and common themes that can be useful as starting points for other types of studies (longitudinal study, ethnography, etc).

However, there is a danger of accepting unconscious biases from the research participants, forcing the researcher to carefully analyse the data while reflecting on the a priori constructs, the extant literature, and their reflexivity. The concept of reflexivity and its importance to this research is explored in section 3.3.6 of this chapter.

3.3.5 Data Collection Methods

As mentioned in section 3.2.2 of this chapter, data for a case study analysis can be collected from varied sources (P. Swanborn, 2010). For this study, the following sources have been selected: direct interview with participants, confirmatory interviews with collaboration partners of the participant SMEs, and documentation from publicly available data. Participants were provided with an information sheet (see Appendix 1) regarding the ethical considerations applicable before the fieldwork process.

The Interview Method

For this research, data collected from the interviews was the most important source of information for the case study. Within interview types, there are in-depth interviews and focused interviews (Dyer and Wilkins, 1991; P. Swanborn, 2010), with the first type taking the form of guided conversations while the latter relies on structured questions.

In-depth interviews are guided conversations in which the research participants answer facts as well as providing their opinions about specific events and circumstances. The researcher is interested in both the facts and the participants' insights and personal

perceptions about the research question. In-depth semi-structured interviews were a key part of the case study as they allowed for the discovery of themes relating to the development of an entrepreneurial ecosystem within a second-tier region, and the lifecycle of the partnerships in the biopharma industry between SMEs.

Yin (2009) differentiates two levels for interview questions during a data collection interview. Level 1 questions form the initial line of enquiry and allow the creation of rapport between the researcher and the participants, while level 2 questions are the actual conversational questions posed in a non-threatening manner. The interview guides for research participants can be found in the Appendices section of this thesis (Appendix 1 and Appendix 2).

Data from semi-structured interviews with research participants and archival documentation was collected from November 2018 to September 2019, and then again in January 2020. Direct observation of meetings between SMEs and relevant stakeholders within the entrepreneurial context was undertaken in November 2019 and December 2019.

The semi-structured interviews were conducted at the convenience of the participants at either their workplace or through telephone calls and varied in length between 60 and 90 minutes. Semi-structured interviews are guided conversations rather than strict questionnaires that help to suggest explanations as to the how and why of key events for a company by following a planned line of inquiry while allowing the interviewee to verbalise their experiences and thoughts on certain themes (Haele and Twycross, 2018).

Given that the research focuses on the development of the entrepreneurial ecosystem and the lifecycle of partnerships in the biopharma industry between SMEs, the use of semi-structured in-depth interviews is a fitting approach as interviews focus on personal decisions while providing verbal reports of specific actions after an internal process of self-reflection (Dyer and Wilkins, 1991; Eisenhardt, 1991; Van Hilten, 2018). Nevertheless, there are limitations to this method such as interviews bias, insufficient information, poor information recall by the participants, or an inaccurate recollection of events. To have a more precise version of the events during the interview process, all interviews were digitally recorded with the participants' consent. Recordings allowed special attention to be given to visual cues and body language.

The Direct Observation Method

A benefit of doing a case study is that the researcher can draw information from the phenomena being studied in its natural environment as the relevant contextual and interactional factors associated with the research question will be available for observation (P. Swanborn, 2010). Therefore, direct observations were an important part of this study.

For this research, the researcher engaged with casual data-gathering activities to enhance the data collected from the in-depth interviews. The observational evidence was useful to provide additional information about the entrepreneurial ecosystem itself and the relationships between SMEs and relevant stakeholders.

The interactions between SMEs in the entrepreneurial ecosystem and the relevant stakeholders were observed on two occasions. They were first observed at the Annual General Meeting organised by Medilink East Midlands, where they reviewed the progress of the membership organisation for the 2018-2019 period. The second observation occurred at the presentation of the 2019 Life Science Industry Report by the BioCity Group, where the organisation managing the life science parks in the entrepreneurial ecosystem presented a summary of the start-up and entrepreneurial activity in the UK. In both meetings, I observed participants and questioned some of them on the opportunities for the further development of the Nottingham Biopharma Entrepreneurial Ecosystem and their concerns when collaborating with external organisations for open innovation and network formation activities (Bigliardi and Galati, 2016; Calof, Meissner and Razheva, 2018).

Documentation Method

Documentation is relevant for a case study, and it can take the form of emails, diaries, minutes, proposals, news clips, press releases, and media articles. Relevant documentation serves to augment and corroborate evidence from other data sources (P. Swanborn, 2010; Vannoni, 2015). Documentary evidence allowed the researcher to make inferences about specific events as it reflects the message that the participant organisations conveyed for external organisations with a specific objective at a particular time within a particular context (P. Swanborn, 2010).

Archival information included documentation made publicly available by the participant organisations. It included news on specialised websites, media interviews, and company profiles obtained from the press section of their webpage. The different sources of data for the case study are highly complementary and allow for the creation of a case study database that helps the researcher to maintain a chain of evidence (P. Swanborn, 2010).

The sources of archival data cannot be listed for those research participants (participant SMEs) that agreed on participating in this research anonymously.

3.3.6 Reflexivity

A theme to address regarding this study is the influence of the researcher when collecting, coding, and interpreting the data. This is known as reflexivity or the researcher's position.

Reflexivity is often defined as the underlying beliefs, values, and experiences held by the researcher when selecting study cases and providing justification for the methodological design (Reid *et al.*, 2018). Recognising the researcher´s position is important in qualitative research as it allows potential assumptions and biases to be judged to assess the authenticity of the findings; hence, it has become an important issue to address in qualitative research (Doyle, 2013). To state the researcher's position and previous experience is important as they might influence what the researcher understands from the data collection and interpretation (Doyle, 2013). This concept recognises the importance of context and the co-creation of knowledge during the interviewing process (Van Hilten, 2018).

Reflexivity as a concept also involves a certain level of consciousness; hence, it requires self-awareness (Palaganas *et al.*, 2017) through active involvement in the research process (Lambert, Jomeen and McSherry, 2010). As a researcher, I am able to recognise that I am part of the social world that I am exploring through this research. However, reflexivity is also an ongoing process through the research project. Reflexivity becomes a continuous process of introspection and reflection by the researcher, and it aims to assess and understand how one's social and professional background might affect the research (Palaganas *et al.*, 2017). The main goal of reflexivity is to make explicit the relationship between the researcher's background and the effect this might have on the participants. The practice of a reflexivity process is an important component of qualitative research as this process ensures an appropriate engagement with the principles of qualitative research (Palaganas *et al.*, 2017).

In terms of the project's scope, the researcher benefits from industry experience as Marketing & Business Development Intern, Online Researcher, and Business Development Manager for life science companies in both the United Kingdom and Mexico. This international experience provides the research with an industry insight that helped the researcher to recognise areas of opportunity for academic research, policymakers, science park managers, and life science entrepreneurs.

Concerning the interview process with the participants, I can understand the main technical details of the products and services offered due to my academic background. I graduated with a bachelor in Genome Biotechnology and a postgraduate degree in

Applied Biopharmaceutical Biotechnology and Entrepreneurship. This life science background facilitated the conversation between the researcher and the interviewees as they did not need to explore in detail the technicalities about their offering; thus, they could focus on providing the strategic information that the researcher was interested in. Moreover, bonding through science helped to build rapport and allowed the interviewees to open up and easily talk about the themes explored in this research.

The fieldwork presented unplanned challenges. Initially, the aim of this research was to collect data from at least one external collaboration partner for each participant company, the regional office for the UK's Department for International Trade (DIT), and staff involved in the Midlands Engine. However, contacting these organisations was challenging as they could not accommodate time for this research for several reasons, including organisational changes or lack of time. Given the research timescale, and the reach of theoretical data saturation (Gioia, Corley and Hamilton, 2013), I modified the data collection methods to the ones presented across section 3.3 in this chapter.

In an attempt to remain close to the data while allowing for the overlapping of data collection and data analysis, I transcribed all interviews in an iterative process. As a non-native English speaker, I had to listen to some of the recordings more than three times to make sure I represented the recordings accurately during the transcription process. When in doubt of certain terms, I would corroborate with documentary evidence.

The data analysis was a valuable time in which different methods were used in a trial-and-error process. This process spanned six months, but by following the case study

theory-building process (Eisenhardt and Graebner, 2007; Eisenhardt, 2018), I was able to navigate through the data to develop the theoretical frameworks required to reach the research objectives presented in Chapter One.

3.4 Method for Data Analysis

As explored in section 3.3 of this chapter, this study follows the case study methodology through the different stages suggested by the relevant literature (Eisenhardt and Graebner, 2007). Data collection began in November 2018 and was carried out until mid-January 2020 after follow-up interviews with relevant stakeholders for the entrepreneurial ecosystem.

The study began with a pilot interview in November 2018 that served as a testing ground for the interview protocol. Since this pilot interview resulted in the discovery of themes in line with the a priori constructs, it was included in the final interview set and used as the template for the rest of the interviews. Data from interviews and documentary evidence was collected from November 2018 to January 2020. Observational data was collected from November 2019 to December 2019.

3.4.1 Interview Transcription and Coding

All the interviews were recorded and then fully transcribed by the researcher. This aided closeness to the data that would have been difficult to replicate had the services of a professional transcriber been hired. Twenty out of the total twenty-two interviews were manually transcribed for their coding.

The first round of coding employed descriptive coding to provide an inventory of specific topics to create themes and categories across the different sources of information. This approach had the goal of maximising the data analysis through a system for data reduction (Gioia, Corley and Hamilton, 2013).

Coding Each Interview

The researcher assigned each interview transcript its unique code derived from the company code. For example, Company Alpha was coded as ALPHA. Then each interview transcript within the unit of analysis was given a number relating to the research participant. For example, the Head of Partnerships & Licensing in Company Alpha was labelled Alpha 1. Each interview transcript was kept as a separate Word document; however, master copies of the transcripts were left untouched. The list of the codes for the research participants is in Table 4 in section 3.3.2 of this thesis.

Reading Each Interview

Reading the interview was important to familiarise oneself with the collected data. Transcribing the interview was beneficial as it allowed the researcher to go over notes recorded during the interview process that the recorder could not capture. These notes could be referred to using archival data to verify dates or considering the actions and facial movements of an interviewee that helped to make emphasis on key points.

Identifying Themes and Categories – First Round of Coding

Closeness with data allowed the researcher to develop themes and categories. When reading the interviews, notes were made on the different themes and categories concerning the research question and objectives. This helped to identify the reoccurring themes and categories that were evident from the interview transcript.

The themes and categories required a colour code to aid easy identification. For example, the theme Nottingham's Regional Legacy was assigned green, so the sections of the transcript referring to this were highlighted on the Word documents with the transcripts. Figure 6 presents an example of this on interview ECHO1.

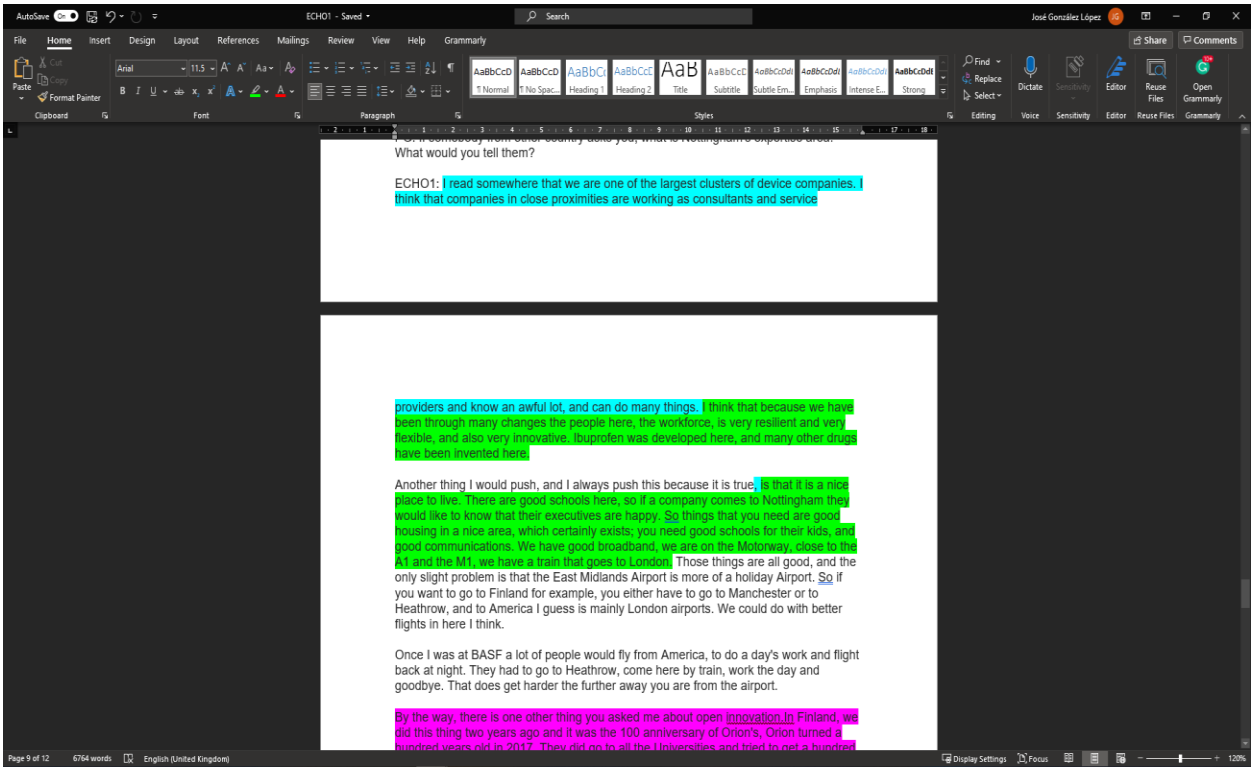


Figure 6. Sample of Coded Interview.

Post Coding and Data Analysis

A descriptive narrative was written for each of the units of analysis. This narrative included relevant information from the different sources of documentation, and a thematic analysis was undertaken moving between the raw data collected from the semi-structured interviews, the archival data, and the extant literature to create themes, causal explanations, and relationships between the actors and relevant theoretical constructs.

The data analysis started with a priori codes related to the research question and existing literature (Hoyte *et al.*, 2019) for the different levels of exploration within this research. To explore the role of cognitive proximity at the entrepreneurial ecosystem level, a priori codes draw from the literature on industry clusters, entrepreneurial ecosystems, and second-tier regions, whereas the exploration of partnerships between SMEs in the biopharma industry relies on the literature on open innovation, social network theory, and cognitive proximity. Categories were created to maintain and organise large batches of data. Table 5 presents a summary of the a priori codes and the literature involved.

A priori codes	Relevant literature
Entrepreneurial Ecosystems (Local Support Mechanisms and their interactions through cognitive proximity).	(Cooke, 2001; Fini *et al.*, 2011; Mayer, 2013; Wang, Lestari and Yang, 2015; Cardoso and Meijers, 2016; DiMasi, Grabowski and Hansen, 2016; Carayannis *et al.*, 2018; Meijers, Hoogerbrugge and Cardoso, 2018; Lecluyse, Knockaert and Spithoven, 2019)
Partnerships between SMEs in the biopharma industry (Cognitive proximity as an enabler to establish and manage partnerships).	(Marshall, 2004; Johnson and Bock, 2017; Presutti *et al.*, 2017; Ashkenazy, 2018; Bigliardi and Galati, 2018; Capello and Caragliu, 2018; Hamadi, 2018; le Duc and Lindeque, 2018; Rojas, Solis and Zhu, 2018; Schweizer and He, 2018)

Table 5. A Priori Codes for Coding.

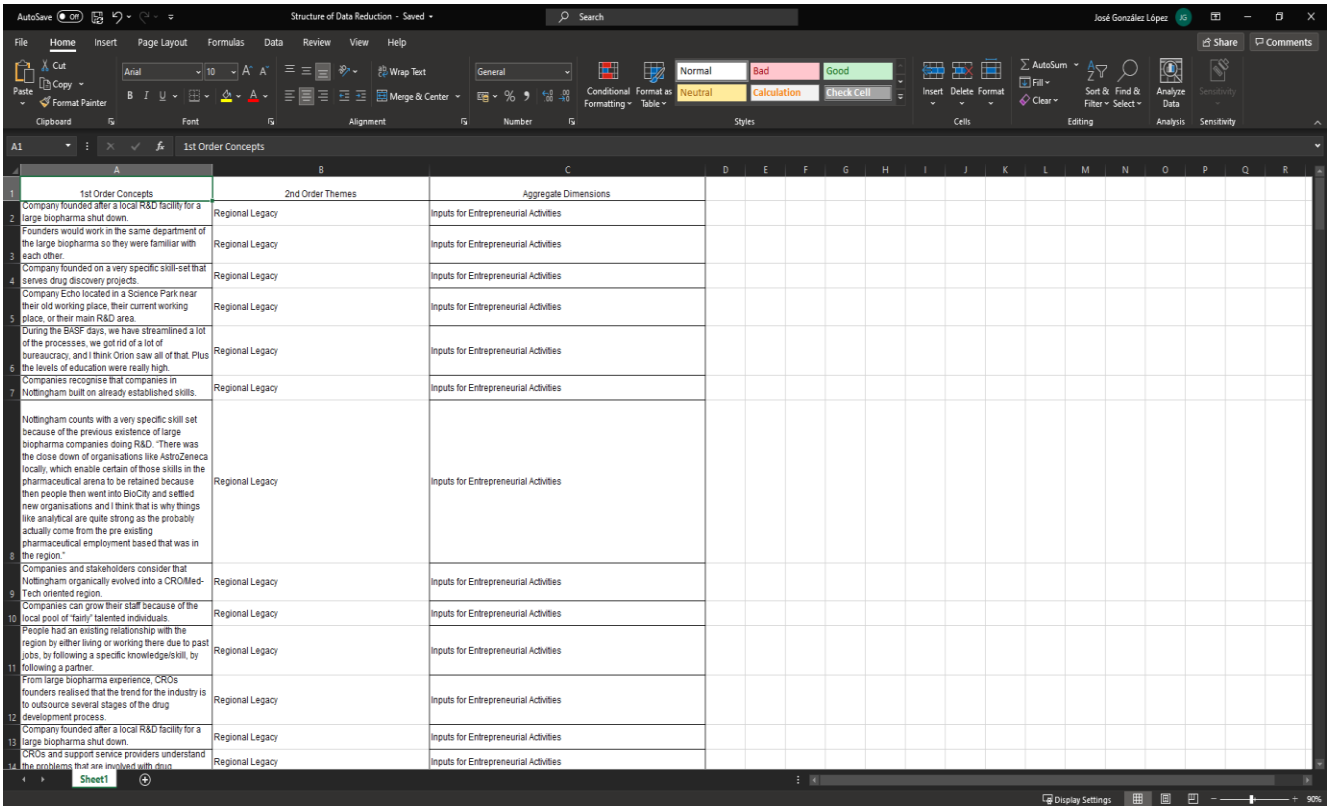
The codes were sorted into sections related to the research themes and objectives. A narrative, interpretivist approach was adopted to enable an accurate description of the data. To interpret which choices and experiences were linked to operating an SME biopharma company in Nottingham and the social interactions that facilitate interactions for and between organisations in the ecosystem was an iterative process involving follow-up interviews with some of the participants and stakeholders, and a constant update of the archival data. Although time-consuming, this method was the most appropriate to elucidate data from the interview transcripts and documentary data.

The system for data reduction presented by Gioia (2013) assumes that the organisational world is a social construction where the people and organisations involved in the phenomena are aware of what they are trying to accomplish and therefore can help understand the intentions behind their actions. This reductionist system requires the themes to be identified in the first round of descriptive coding so they can be consolidated into second-order themes. Once there is a full set of first-order and second-order themes, the second-order themes are grouped in aggregate dimensions that allow for the development of a data structure (Gioia, Corley and Hamilton, 2013).

Structured data allows the researcher to approach the data theoretically rather than just methodologically, as the higher abstraction level lays the foundation needed for comparing the collected data to the extant literature (Gioia, Corley and Hamilton, 2013). Overall, the reduction and abstraction of collected information through a reduction system

allows a researcher to see if there are precedents to the findings or if new concepts missing from the extant literature have emerged.

The structure for data reduction was manually curated from the narrative of each unit of analysis into a Microsoft Excel spreadsheet. Figure 7 presents an overview of the abstraction level achieved during the data analysis.



1st Order Concepts	2nd Order Themes	Aggregate Dimensions
Company founded after a local R&D facility for a large biopharma shut down.	Regional Legacy	Inputs for Entrepreneurial Activities
Founders would work in the same department of the large biopharma so they were familiar with each other.	Regional Legacy	Inputs for Entrepreneurial Activities
Company founded on a very specific skill-set that serves drug discovery projects.	Regional Legacy	Inputs for Entrepreneurial Activities
Company Echo located in a Science Park near their old working place, their current working place, or their main R&D area.	Regional Legacy	Inputs for Entrepreneurial Activities
During the BASF days, we have streamlined a lot of the processes, we got rid of a lot of bureaucracy, and I think Orion saw all of that. Plus the levels of education were really high.	Regional Legacy	Inputs for Entrepreneurial Activities
Companies recognise that companies in Nottingham built on already established skills.	Regional Legacy	Inputs for Entrepreneurial Activities
Nottingham counts with a very specific skill set because of the previous existence of large biopharma companies doing R&D. "There was the close down of organisations like AstroZeneca locally, which enable certain of those skills in the pharmaceutical arena to be retained because then people then went into BioCity and settled new organisations and I think that is why things like analytical are quite strong as the probably actually come from the pre existing pharmaceutical employment based that was in the region."	Regional Legacy	Inputs for Entrepreneurial Activities
Companies and stakeholders consider that Nottingham organically evolved into a CRO/Med-Tech oriented region.	Regional Legacy	Inputs for Entrepreneurial Activities
Companies can grow their staff because of the local pool of "fairly" talented individuals.	Regional Legacy	Inputs for Entrepreneurial Activities
People had an existing relationship with the region by either living or working there due to past jobs, by following a specific knowledge/skill, by following a partner.	Regional Legacy	Inputs for Entrepreneurial Activities
From large biopharma experience, CROs founders realised that the trend for the industry is to outsource several stages of the drug development process.	Regional Legacy	Inputs for Entrepreneurial Activities
Company founded after a local R&D facility for a large biopharma shut down.	Regional Legacy	Inputs for Entrepreneurial Activities
CROs and support service providers understand the problems that are involved with drug	Regional Legacy	Inputs for Entrepreneurial Activities

Figure 7. Manually Created Structure for Data Reduction.

3.4.2 Structure for Data Reduction

The inputs were identified in instances where references were made to the contextual factors (Autio *et al.*, 2014; McAdam *et al.*, 2014; Brown and Mason, 2017) that promote entrepreneurial activity and innovation in the entrepreneurial ecosystem from the

perception of the resident biopharma SMEs in it. Table 6 presents the data reduction structure for the aggregate dimension regarding the ecosystem inputs for entrepreneurial activity in this second-tier region.

The mediators were identified in instances where research participants detailed how certain organisations facilitate specialised networking activities to scout for collaboration partners and business support services. The data reduction structure for the aggregate dimension regarding the ecosystem mediators for entrepreneurial activity and innovation can be found in Appendix 4.

The interactions within the entrepreneurial ecosystem were identified from instances where research participants commented on the relationships between SMEs and the different inputs and mediators within the entrepreneurial ecosystem in this second-tier region. The data reduction structure for the aggregate dimension regarding the interactions within the entrepreneurial ecosystem can be found in Appendix 5.

Finally, to identify the phases (Schweizer and He, 2018) for the lifecycle of partnerships in the biopharma industry, the data reduction identified instances where participant SMEs detailed their interactions when engaging in business partnerships to leverage scientific knowledge from R&D partners. The data reduction structure for the lifecycle of partnerships in the biopharma industry from the perspective of biopharma SMEs in a second-tier region can be found in Appendix 6.

1st Order Concepts	2nd Order Themes	Aggregate Dimensions
• Companies were founded on already established skills. • The ecosystem counted with a very specific skill set because of the previous existence of large biopharma companies doing R&D.	Regional Legacy	Inputs for Entrepreneurial Activity in the Entrepreneurial Ecosystem
• In terms of networks, support, and the local ecosystem for start-up companies, there is a lot better infrastructure now than twenty years ago. • The BioCity Science Parks offer the best space, at the best price in the region.	Incubation	
• Training on pitching high-tech business ideas has been important for competing and securing funding. • Companies attended BioCity Accelerator Programme to understand how to set up and run an early-stage company.	Developmental Programmes	
• Companies tap into national grants to engage with R&D activities. • Companies tap into local grants to sort out business activities.	Funding	
• Universities “have their research” that not always matches the industry needs. • Companies sometimes find it difficult to collaborate with universities due to differences in working pace, goals, and a lack of parity.	Higher Education Institutions (HEIs)	

Table 6. Structure for Data Reduction for the Ecosystem Inputs.

3.5 Chapter Summary

This chapter explored the philosophical underpinnings of research in social science and the epistemology and ontology dictated by the research question, the research objectives, and research paradigms. This research considers entrepreneurial ecosystems and partnerships between organisations as social constructions; therefore, it adopts an interpretative paradigm for the ontological and epistemological positions.

An embedded single case study methodology was chosen for the theory-building process (Eisenhardt and Graebner, 2007) that would allow the research question to be answered by exploring the proposed research objectives. The different sources of qualitative data for the case study were then explored, discussed, and justified while highlighting their complementarity. A section addressing reflexivity was included to address awareness about the role of the researcher as part of the knowledge-building process in the context of a case study. Finally, this section presented the method for data analysis based on the first round of descriptive coding, followed by the data analysis based on a system of data reduction (Gioia, Corley and Hamilton, 2013) that allowed for comparison of findings to the extant literature.

Chapter Four – Exploring the Units of Analysis

This chapter contextualises each of the units of analysis in this embedded case study after consolidating the data collected from the semi-structured interviews and the archival data.

For the participant SMEs, the narratives are organised as follows. First, a profile of the research participants and their role in the SME is presented. The profile of the research participant is important as it allows the researcher to understand the language and knowledge bases they are more familiar with. Their individual profile is followed by the company's profile, which includes the story behind their founding, their business model, and technical expertise. Then their rationale for choosing the Nottingham Biopharma Ecosystem, their interactions with relevant stakeholders (inputs and mediators), and their overall perceptions of the contextual factors in the Nottingham Biopharma Ecosystem are presented. These factors will help with the exploration of the entrepreneurial ecosystem through investigating inputs, mediators, and their interactions through cognitive proximity presented later on through Chapter Five.

Then, the interpretivist narrative regarding the partnership management of the SME is presented. The research provides the participant's recollection of their successful and unsuccessful experiences when trying to establish and manage partnerships with external organisations using cognitive proximity as a theoretical lens. These findings are then reflected upon later on through Chapter Six.

For the participant SMEs, the interpretivist narrative is presented through the following sequence. First, a profile of the participant and their role in the organisation is provided. The profile of the research participant is considered as it allows the researcher to understand the

language and knowledge base they are the most familiar with. Then the research presents the overall goal of the organisation. These findings related to the exploration of the entrepreneurial ecosystem are consolidated later on through Chapter Six.

Afterwards, the interpretivist narrative of how the stakeholders support SMEs to establish and manage partnerships is presented. The research introduces the way these stakeholders support SMEs to connect with organisations they can use to leverage knowledge. These findings related to the lifecycle of partnerships between SMEs in the biopharma industry are established in Chapter Seven.

Figure 8 presents a timeline of the relevant milestones for the Nottingham Biopharma Ecosystem while contextualising the units of analysis within it.

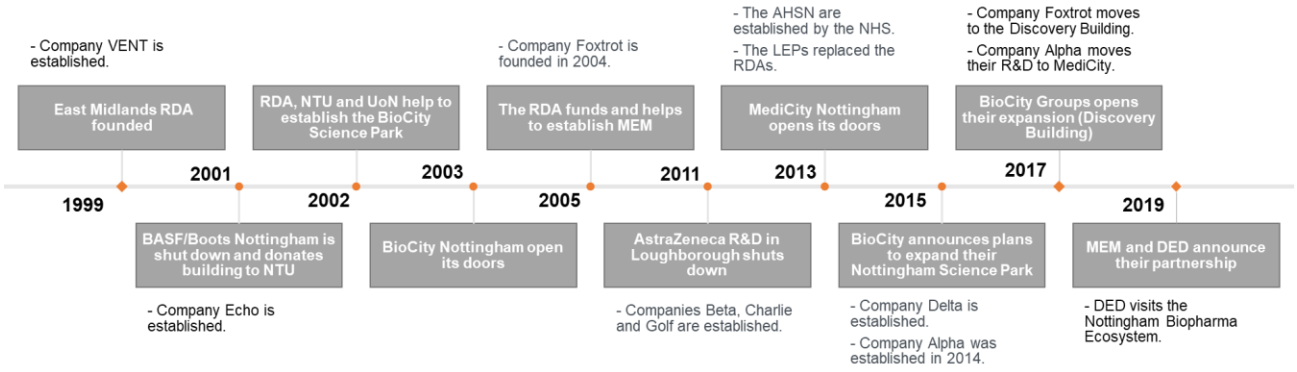


Figure 8. Timeline of the Nottingham Biopharma Ecosystem.

Figure 9 presents the network formed by research participants to illustrate the better-connected organisations in the Nottingham Entrepreneurial Ecosystem and the potential reach of the network.

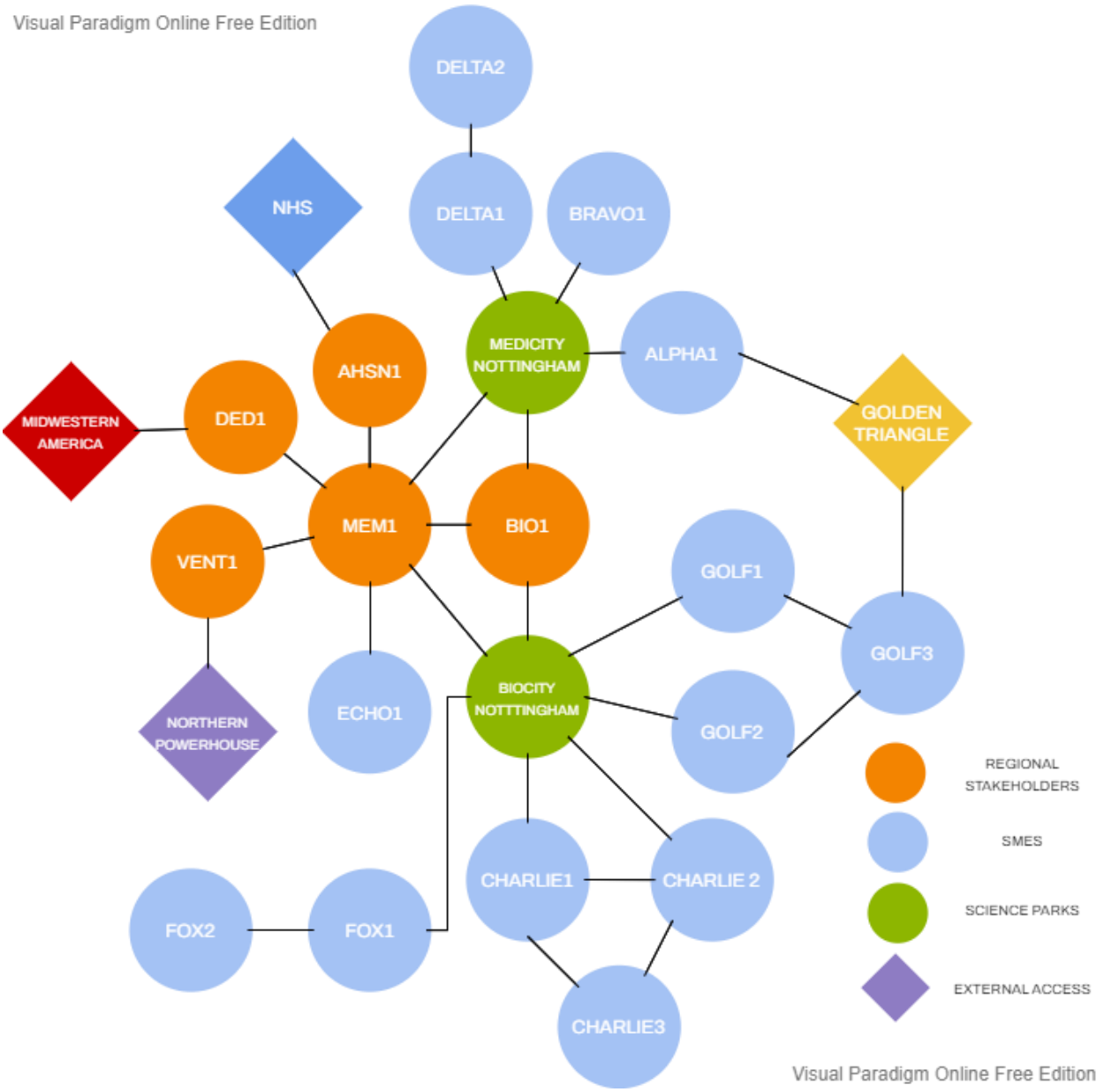


Figure 9. Research Participants Network Map.

4.1 Company Alpha

The interview transcript for this unit of analysis was coded as Alpha1. Information from the company's website and press releases by third parties were used as archival data.

4.1.1 Research Participant's Profile

The research participant for Company Alpha is the Head of Partnerships & Licensing. They have an undergraduate degree in Molecular Genetics and Biotechnology from Sussex University in the UK. The undergrad programme included a year in the industry where the participant gained experienced in Bioinformatics while working in a large biopharma company based in the "Golden Triangle". After graduating from undergrad, the participant worked in positions that were not related to the biopharma or biotechnology industry. They worked as a recruiter for an investment bank and as a sports coach and personal trainer for some years. After these experiences outside the biopharma industry, they enrolled in a master's programme in Applied Biosciences and Biotechnology at Imperial College London. Here they met Company's Alpha founding team and became their first employee once they finished their master programme. They argue that their role is generally known as business development as they "organise partnerships with both academic groups and companies."

4.1.2 Company's Profile

Company Alpha was founded in 2014 by an academic researcher from Imperial College London working with bacteria to produce and deliver therapeutic payloads to the gastrointestinal tract. Through this platform, therapeutic molecules can be produced at a large scale and then

delivered orally without the risk of being affected by the acidity of the gastrointestinal tract. Their business model is to license therapeutics to larger biopharma companies.

Company Alpha is an evolution from a company its founder first started in 1999. The company preceding Company Alpha relied on traditional fermentation that used bacteria to produce commodity chemicals for different applications in the industrial biotechnology space. These commodity chemicals were naturally occurring in the bacteria, and their production was expensive when compared to traditional chemical synthesis; therefore, this academic researcher decided to abandon traditional fermentation and explore the options provided by genetic engineering.

Company's Alpha founder leveraged the scientific knowledge necessary for the genetic manipulation of bacteria from an academic research group based in the University of Nottingham. When Company Alpha started operations in 2014, it was located in the business incubator at Imperial College (where the founder still is an academic).

4.1.3 Rationale for Choosing the Nottingham Biopharma Ecosystem

As the collaboration between Company Alpha and a group of Nottingham University academics delivered the expected results, the business incubator at Imperial College London closed. Without a physical space for the scientific operations of the company, the scientific team decided to keep on working, then inside a lab facilitated by the Nottingham academics.

As the company required more space, they decided to move into one of the specialised science parks in the Nottingham Biopharma Ecosystem, MediCity Nottingham. According to the participant, the founder and CEO chose MediCity over BioCity because it was geographically

closer to their academic collaborators and also because BioCity did not have enough available space to accommodate Company's Alpha laboratory needs. Both MediCity and BioCity science parks are managed by the BioCity Group.

Though the scientific branch of the company is based at MediCity Nottingham, the management team's office space is located within the "Golden Triangle". According to our research participant, this allows the company to keep the costs related to scientific and production activities low while allowing team management to be geographically near to the main hubs for innovation and entrepreneurship in the United Kingdom. They acknowledge that companies completely based outside the "Golden Triangle" struggle to get the visibility needed for prospecting customers or scouting for collaborators.

4.1.4 Relationships with Inputs and Mediators in the Ecosystem

Though their scientific branch is located in MediCity Nottingham, Company Alpha does not have a relationship with BioCity Group Management. Our research participant comments that they receive BioCity's communications; however, they do not interact with science park management as their management branch is located in the "Golden Triangle". So, they do not interact with science park management or other SMEs within the science park for entrepreneurial activities. Company Alpha is not a member of the regional membership organisation supporting SMEs and does not try to access regional funding'.

The only interaction Company Alpha has within the Nottingham Biopharma Ecosystem is with the academics they worked with to develop a bacterial platform to produce and deliver therapeutic molecules. However, they argued that liaising with universities rather than this

specific group at the University of Nottingham is difficult. They said that projects with academics "can be a bit frustrating" as academics "don't really communicate very well" and struggle to share relevant pieces of work. Another issue that they commented on is that the goals between academics and SMEs tend to be different. While Company Alpha is constantly trying to generate "the right information that is going to be important commercially", the academics are "typically more motivated by fundamental research as publications."

4.1.5 Partnerships Management

The participant's role within Company Alpha is to organise partnerships with other companies and academic groups. Company's Alpha Head of Partnerships commented that they have an internal list of organisations they try to contact to collaborate with; however, they do not have a standardised strategy for approaching these potential partners. They commented that their approach is to try to attend networking events held in the context of scientific and industry conferences so they can reach out to the relevant people they think they can partner up with. Nevertheless, contacting large biopharma companies requires more effort, as those organisations already have a list of contacts, which represents an entry barrier for companies such as Alpha.

Company Alpha's participant commented that they also have employed business consultants and that their latest partnership came through a referral from a business consultant. The business consultant had worked with a "Golden Triangle"-based company in the arena of vaccine development and thought that Company's Alpha expertise could benefit such a company. After the introductions were made through this business consultant, the companies

realised that their technologies were complementary as “they (the Golden Triangle Company) are creating specific peptides and we have a system that could produce and deliver peptides.”

Company’s Alpha participant commented that even if the scientific technologies are complementary and could benefit both parties, “it all comes down to personalities.” Company Alpha considers that “a fit” between individuals or a group of people, their openness to share information, and their ability to effectively communicate are the most important attributes of a successful partnership. Company Alpha argues that for a transparent partnership it is necessary to set up a detailed work plan with milestones and work packages. Finally, Company Alpha thinks that partnerships could be reviewed throughout the project to make sure that the milestones are being met in time. According to this research participant, evaluating the results of a partnership is important as it helps them to plan the potential next steps of a partnership.

4.2 Company Bravo

The interview transcript for this unit of analysis was coded as BRAVO1. Information from the company’s website and press releases by third parties were used as archival data.

4.2.1 Research Participant’s Profile

The research participant for Company Bravo is the Chief Operating Officer and co-founder. They have an undergrad degree in Pharmacy from the University of Nottingham, and after finishing the programme they did an industrial pre-registration placement. However, after finishing the pre-registration placement, they went back to the University of Nottingham to study a PhD in Pharmaceutical Sciences with an interest in the area of tissue engineering which falls under the umbrella of regenerative medicine. After finishing the PhD, they helped the academic

group they were a part of to settle a spinout in 2000. The research participant has been involved with two university spinouts since then and studied for an Executive MBA at the University of Nottingham Business School.

4.2.2 Company's Profile

Company Bravo was founded in 2011, and its business model is to develop platforms for the field of tissue-specific regenerative medicine. These platforms aim to facilitate the recovery of tissues post-surgery and will eventually be able to deliver therapeutic molecules to tissues that are difficult to access with current technologies, such as those forming bone and the nervous system.

Company Bravo builds upon a previous company founded by the same group of academics in the year 2000. The model of this company was doing contracted research for clients in the biopharma sector. Company Proto-Bravo started operations within the School of Pharmacy at the University of Nottingham, but it was difficult for the company as they felt that they were fighting for resources such as equipment and space. This helped the company to start operations cost-effectively before outgrowing the lab space provided by the university. Proto-Bravo then moved to business units owned by the University of Nottingham; according to the research participant, they were "given a shell of a facility that then you had to refurbish to meet your requirements. If you were successful, you could quickly outgrow the facility, so it was cost-prohibitive."

The precursor to Company Bravo then moved to BioCity Nottingham when the science park started operations in 2004. They were among the first tenants ever in the science park and

were offered a flexible tenancy model where they could expand or reduce their footprint in the building if needed. The science park provided equipment and spaces that were ready to use. However, after years of struggling with the amount of capital needed to capitalise from their business model, they decided to change the business model and cease operations for administrative reasons, and they became Company Bravo in 2011. Company Bravo is based at MediCity Nottingham as it is geographically closer to the School of Pharmacy than BioCity.

4.2.3 Rationale for Choosing the Nottingham Biopharma Ecosystem

The main reason for Company Bravo choosing Nottingham, even after their first unsuccessful experience incubating and trying to grow a company, is their relationship with the School of Pharmacy at the University of Nottingham. The founding team are still academics at the University of Nottingham and live in the region.

The second reason is that they witnessed the development of a strong entrepreneurial ecosystem that now provides more support to SMEs than it did in the year 2000. According to the research participant, the few relevant stakeholders were “a lot less connected back then. In terms of networks, support and the local ecosystem for companies, there is a lot better infrastructure now than what there was twenty years ago.”

The research participant from Company Bravo commented that now they can get better support from the group managing the science parks specialised in life sciences by allowing support organisations to enter the ecosystem. From only offering a physical space, now they provide tutoring, business support services, and continued education.

4.2.4 Relationships with Inputs and Mediators in the Ecosystem

Company Bravo acknowledges that “BioCity and Medilink are the key players in terms of providing infrastructure and cross-talk, respectively.” BioCity is the group that manages the science parks specialised in life sciences in the Nottingham Biopharma Ecosystem.

Company Bravo “does not tend to tap into much of what is available” from the science park’s management. They think that science park management’s support is mostly tailored towards the early-stage support of start-up companies, which they think they do not need from their previous entrepreneurial experience. However, Company Bravo taps into the science park reach and network whenever they require support with signposting or scouting as they will help Company Bravo to “identify groups in local universities or companies” they can connect with “to access particular expertise.”

On the other hand, Company Bravo has a more active relationship with Medilink East Midlands (MEM). MEM is a regional membership organisation that aims to support life science SMEs through offering spaces for specialised networking and managing local grants for business activities. According to Company Bravo, MEM’s support starts by trying to understand what type of support the local SMEs need through periodical one-on-one meetings between a MEM representative and Company Bravo. Company Bravo has applied for local funding through MEM for business growth activities such as expanding lab space.

Company Bravo has also benefited from MEM’s efforts of promoting interactions within the entrepreneurial ecosystem through special interest groups. The research participant from Company Bravo argues that these groups “work very well because they obviously tend to be

more focused", which is very useful for companies that cannot allocate an important number of resources for scouting potential partners or collaborators.

4.2.5 Partnerships Management

Company Bravo states that their main collaborators to leverage scientific knowledge are based in the Far East and the United States. To identify potential partners, Company's Bravo participant highlights the importance of "meeting people, understanding what their capabilities are, and then keeping them in mind as to when they might be needed." To meet people, they attend scientific or industry-specific conferences where the attendees share a common language (science) and a similar knowledge base (regenerative medicine and therapeutic molecules). When scouting for collaborators, Company Bravo also taps into their relationship with academics through their links with the School of Pharmacy at the University of Nottingham.

Nevertheless, the common language and the similar knowledge base are only a part of what Company Bravo looks for in a partner. Company's Bravo participant suggests that the way that the partner works is as important as their knowledge and expertise. Company Bravo deems effective communication and the "codification of information" as important as scientific expertise. For Company Bravo, "codification of information" means "how the information is written down and communicated, what is included, what is left out, and whether they are prone to any errors or if there are any misunderstandings."

Before committing to a partnership for a lengthy project, Company Bravo tries to develop a "short-term feasibility piece of work" where they can assess the work culture and communication skills of their partner. From this assessment, they can either "continue or

discontinue to work with a particular company." Moreover, Company Bravo usually sets frameworks for partnerships that depend on constant communication, weekly progress meetings, and on-site visits when a project's milestone is met.

4.3 Company Charlie

The interview transcripts for this unit of analysis were coded as CHAR1, CHAR2, and CHAR3. Information from the company's web site and press releases by third parties were used as archival data.

4.3.1 Research Participant's Profile

Research participant CHAR1 is an employee of Company Charlie working as the Head for Global Business Development (HBD). Participant CHAR1 is a trained scientist with a degree in Biology and a PhD looking at signalling in transduction cascades, followed by a post-doctoral position at the John Innes Centre. After this extensive training as a scientist, participant CHAR1 became interested in the applicability of academic research as commercial products and services, which led to a "jump" into tech transfer. They completed a PGD in Marketing supported by government incentive.

After the training in marketing, they got a position at UCL, where they were in charge of tech transfer for biopharma research. While at UCL, they were involved with evaluating the feasibility of tech transfer projects, raising funds for tech transfer projects, and negotiating exits for the projects in the form of licensing agreement or spinout companies.

In their current position at Company Charlie, they are in charge of prospecting customers and liaising with collaboration partners on demand.

Participant CHAR2 is an external partner to Company Charlie. Participant CHAR2 is one of two Managing Directors for a support service company that provided Company Charlie with support in marketing and business development. As Company Charlie grew and became more successful, they agreed to a partnership with Participant CHAR2 where Participant CHAR2 became the Marketing Director for Company Charlie. Research participant CHAR2 has a degree in European Studies with German from the University of Nottingham and acquired experience in the biopharma industry after working in Germany for a large biopharma company in the areas of Public Relations and Product Management. Participant CHAR2 and Company Charlie's founder and CEO connected through a common personal relationship with a Non-Executive Director in Company Charlie.

Participant CHAR3 is an intern at Participant CHAR2's company working on a placement project under Participant CHAR1 at Company Charlie. They have a degree in Microbiology from the University of Nottingham and a master's in applied Biopharmaceutical Biotechnology and Entrepreneurship from the same university. As a part of their master's programme, they undertook a placement in CHAR2's company. Through this placement, participant CHAR3 worked for Company Charlie under CHAR1 doing market research to reconnect with past customers and connect with new prospects in the United States. According to CHAR3, their background in life sciences was important to adapt to the environment within Company Charlie.

4.3.2 Company's Profile

Company Charlie is a laboratory-based Contract Research Organisation (CRO) founded in 2011 by a team of three scientists after AstraZeneca closed their Charnwood site. From a team

of three scientists, Company Charlie has “grown organically” (CHAR1) and was employing 28 people across lab-based and administrative roles at the time of the interview in winter 2019. Company Charlie has favoured a “flat management structure” (CHAR1) that facilitates communication across the company and allows employees to “bring up” (CHAR1) suggestions when working on complex projects.

Company Charlie is a company that specialises in Drug Metabolism and Pharmacokinetics (DMPK) and offers in vitro assays to understand the properties of therapeutic molecules during their development. Company Charlie helps their customers choose the therapeutic molecules with better chances of becoming a “winner molecule” (CHAR1) through a “consultative approach” (CHAR2).

4.3.3 Rationale for Choosing the Nottingham Biopharma Ecosystem

When the AstraZeneca site on Charnwood (located in the Midlands region in the United Kingdom) closed, BioCity’s CEO visited the site and told people that if they wanted to start up a company in BioCity Nottingham, they would get one year of subsidised rent. The rent incentives, the lab facilities available at BioCity Nottingham, the money the founding team got from their termination, and the geographical proximity between Charnwood and Nottingham were the most important reasons for choosing Nottingham and BioCity as a place to start the company.

4.3.4 Relationships with Inputs and Mediators in the Ecosystem

Company Charlie has been actively involved with some of the major stakeholders within the Nottingham Biopharma Ecosystem. First, they took part in the developmental programmes

offered by BioCity's management. These programmes helped the founding team to acquire helpful skills for setting up and running an early-stage company. However, after Company's Charlie time in these programmes ended, BioCity's Chairman took an interest in the company's growth potential and became a Non-Executive Director in Company Charlie. This helped Company Charlie as they could start to leverage knowledge and resources through deploying BioCity's infrastructure and already established network.

Company Charlie is also a member of MEM. They acquired the MEM membership to raise the company's profile, to legitimise their position within the entrepreneurial ecosystem, and to have access to the better-connected stakeholders in the ecosystem for business development.

Company Charlie also tried to tap into government offices for support. CHAR1 argued that the CEO had spoken to a range of different people across different government offices but only managed to establish a connection with the people running the Midlands Office of the Department for International Trade (DIT). The DIT is a government office that supports companies trying to expand their offering beyond the UK. The DIT offers UK SMEs (regarding the industry sector) a platform to display their expertise at industry-specific congresses through offering funds to attend specialised events abroad. Company's Charlie success has helped them to successfully secure DIT funding when necessary, which has been important in increasing their exports by 78% in 2019 from 2018. Currently, exports represent 50% of the company's revenue.

4.3.5 Partnerships Management

Upon establishing Company Charlie at BioCity in 2011, the company's CEO would go door to door in the science park asking the neighbouring companies about their expertise and their previous life before starting a company in the science park. From these early efforts, Company Charlie established on-demand partnerships with two companies that specialised in chemical-based analysis and molecule purification. Another partner for Company Charlie was based outside the science park and was a CRO offering expertise in the analytical chemistry of small molecules. According to participant CHAR1, these efforts became the blueprint for partnerships and collaborations as they only consider partnerships with companies that are "complementary but not competing."

According to participant CHAR2, Company Charlie assesses potential partners through two major themes. First, they assess their "hard skills", which are related to the scientific knowledge and industry expertise the potential partner has to offer – "we have to know they are experts in their area, that they have high-quality research or high-quality services" (CHAR1). Company Charlie also focuses on the "soft skills", which are related to the theoretical lens of cognitive proximity utilised in this research.

Research participant CHAR1 highlights the importance of establishing channels for effective communication, setting regular meetings, and running and attending events together as partners. Therefore, Company Charlie's approach to partnerships is to connect the key individuals across organisations to help the partnership grow while increasing the trust – "what you want to do is you want to get your pharmacologist speaking with pharmacologists, your

bioanalysis speaking to bioanalysis and your BD guy speaking with the BD, and your lawyer speaking with their lawyer. So you need to have certain parity of messages and people who can cross communicate" (CHAR1).

Finally, for Company Charlie, the common goal between them and any partner is to provide the best support possible to a customer. Company Charlie "takes pride" (CHAR1) in its good customer relationship management and avoids partnering with companies that are not "willing to go the extra mile for clients rather than just a cash-out" (CHAR1). Company Charlie is now in a position in which potential partners reach out to them and not the other way. Therefore, the companies pitching potential partnerships to Company Charlie are asked to demonstrate how they are complementary but not competing while providing excellent customer support.

4.4 Company Delta

The interview transcripts for this unit of analysis were coded as DELTA1 and DELTA2. Information from the company's website and press releases by third parties were used as archival data.

4.4.1 Research Participant's Profile

Research participant DELTA1 is the Chief Executive Officer and founder of the company. They have a degree in Biomedical Sciences from Nottingham Trent University and a PhD from the University of Nottingham specialising in amniotic membranes and tissue regeneration. They were awarded their PhD in 2005, and the research undertaken during their studies generated a patent filed by the University of Nottingham. Participant DELTA1 continued to work in academia by expanding their academic focus to stem cell research and produced more

intellectual property for the university that was filed in 2013. However, the university administration was having difficulties when trying to license the patents, so research participant DELTA1 decided to create a spinout company after fourteen years as an academic.

Research participant DELTA2 is the Operations Manager at Company Delta. They have a degree in Biotechnology Engineering from ITESM in Mexico and a master's in applied Biopharmaceutical Biotechnology and Entrepreneurship from the University of Nottingham. Upon completion of their master's, they returned to Mexico to work as a university lecturer and lead-scientist at a company manufacturing recombinant proteins. Then they returned to the UK as a lab technician for Company Delta, where they later became Operations Manager. At the time of the data collection interview, they were enrolled in an MBA at Nottingham Trent University.

4.4.2 Company's Profile

Company Delta was founded in 2015 after the founder decided to start a spinout company to take advantage of the patents generated during their years in academia. The company is based in MediCity Nottingham and develops biotherapies for their use in ophthalmology. Company Delta's founder stated that as an SME the company has been able to quickly adapt and pursue business opportunities as they appeared; however, they would struggle to consolidate any efforts due to a lack of resources. The founder secured the funding needed to start the company after attending the BioCity Developmental Programmes.

4.4.3 Rationale for Choosing the Nottingham Biopharma Ecosystem

Participant DELTA1 is still working as an academic for the University of Nottingham, and the company's R&D is linked to their academic research, so this is one of the main reasons for choosing the Nottingham Biopharma Ecosystem. In terms of choosing a location within the ecosystem, the company's founder commented that MediCity was better equipped in terms of laboratory facilities than BioCity. Moreover, MediCity is geographically closer to their workplace as an academic.

4.4.4 Relationships with Inputs and Mediators in the Ecosystem

Participant DELTA1 took part in the developmental programmes offered by BioCity Group. Participant DELTA1 argues that these programmes gave Company Delta's founder knowledge and skills on how to get funding by presenting a scientific idea to potential business investors. After this training, BioCity Group was keen on helping Company Delta out and introduced them to a private investment fund, which then provided seed funding. Having secured seed funding, BioCity offered Company Delta a year of subsidised rent at either of the group's science parks in Nottingham. BioCity Group has taken such an interest in Company Delta that they have also invested in the company through their own investment fund.

However, research participant DELTA1 does not get involved with other services provided by BioCity. Research participant DELTA1 commented that they do not attend general networking events or social gatherings organised by science park management. They commented that for these events, they tend to send middle management employees such as DELTA2. Research participant DELTA2 commented that attending general networking events and social gatherings

is not helpful for entrepreneurial activities. Participant DELTA2 commented that general networking events hosted by BioCity Group have a limited diversity of attendants as people usually go to enjoy free food and do not interact with other attendants. Furthermore, research participant DELTA2 argued that the company prefers to attend the specialised events organised by Medilink East Midlands such as the “special interest groups”. They also find that the communications and information circulated by MEM is more useful than those shared through BioCity Group.

Despite being a spinout from the University of Nottingham, Company Delta does not have a working relationship with them other than the research group where the founder is an academic. Research participant DELTA1 commented that it is difficult to balance their work as an academic and an entrepreneur as the university measures their performance as an academic with certain benchmarks as “there are no other allowances or recognition if you are not actually generating ten papers a year, but you got a company taking a product forward that is actually saving sight which was developed in Nottingham” (DELTA1). Company Delta’s founder highlights that it has been difficult to collaborate with the University of Nottingham as an entrepreneur because the university’s goals are not aligned with the industry.

They commented that not being able to validate their technology in the hospitals associated with the university has led Company Delta to partner up and collaborate with other universities and hospitals across the United Kingdom to obtain data. They commented that is difficult to collaborate with a university hospital that expects a local spinout company to pay large amounts of money for a partnership that validates the research produced within the same university.

4.4.5 Partnerships Management

Company Delta's founder reveals that working with clinicians is a challenge as they are difficult to reach; however, scientific conferences and industry-specific meetings provide a "more relaxed" environment to scout and approach potential partners. They argue that once the first contact is made, it is not difficult to follow up on a potential partnership as clinicians and Company Delta have the common goal of providing patients with the best care possible.

To validate their technology, Company Delta has collaborated with hospitals and research centres in India. The connection with the India-based organisations is a result of the network of academic collaborators research participant DELTA1 built before starting the company. Research participant DELTA1 reveals that the cultural differences between companies from different countries are an important theme to consider; therefore, they have built a multicultural team, so they are ready to collaborate with organisations from different backgrounds without a problem.

4.5 Company Echo

The interview transcript for this unit of analysis was coded as ECHO1. Information from the company's website and press releases by third parties were used as archival data.

4.5.1 Research Participant's Profile

Research participant ECHO1 is the Site Director and Pain Development Director for Company Echo. They have two undergraduate degrees in Medicine and Biochemistry from Queen's University. After finishing both degrees, they registered in the General Medical Council (GMC)

and worked as a physician for a few years until applying for a job as a Biochemist within the Clinical Pharmacology Division at Boots in Nottingham City.

They worked for Boots for ten years until the R&D Division was acquired by BASF. They stayed on-site working now for BASF until the company closed and withdrew the Nottingham site. Then they helped to set up Company Echo in the Nottingham City Centre as an R&D branch of a larger European biopharmaceutical company based in Finland.

4.5.2 Company's Profile

Company Echo is a Research & Development branch of a larger European biopharma based in Finland. Company Echo was established in Nottingham City Centre in 2001 just after the R&D division of BASF was shut down. They operate as an SME within the entrepreneurial ecosystem but are able to tap into the resources of their parent company when necessary.

Company Echo's founding team originally wanted to pitch the vacant BASF site (now the BioCity Science Park) and the skills of the scientists working there to large companies so they could be absorbed. However, the growing paradigm of open innovation and outsourcing for the biopharma industry and the UK's policy of promoting the creation of science parks prevented any large company from acquiring the BASF site.

Research participant ECHO1 pitched the site and their staff of experts to ten large biopharma companies and was then contacted by the representative of a Finnish company. After recognising the skill set and expertise of the scientists formerly working for BASF, the Finnish company offered them the opportunity to start an R&D branch in the UK where they could work

on their drug development in their areas of expertise while being able to tap into the resources of the larger parent company when necessary.

With a staff of twenty people, Company Echo is the only foreign R&D subsidiary of the Finnish company and works in drug development projects for the areas of oncology, respiratory diseases, neurodegenerative diseases, and pain control.

4.5.3 Rationale for Choosing the Nottingham Biopharma Ecosystem

Company Echo decided to stay in Nottingham as the “previous life” of all the employees and the founding team was based in and around Nottingham. Research participant ECHO1 also highlighted that Nottingham was a cheaper option than trying to move to the “Golden Triangle”, which is the region in the United Kingdom where most of the drug development SMEs are based.

Participant ECHO1 commented that after the regional AstraZeneca R&D facilities were shut down a few years after BASF, a large pool of experts clustered within the Nottingham Entrepreneurial Ecosystem and have become an asset to leverage scientific knowledge when needed. Participant ECHO1 revealed that the large companies “have fragmented and there are lot of companies that were founded on the expertise they had from working in the large companies.” Participant ECHO1 also argued in favour of Nottingham and stated that the area is a “nice place to live.”

4.5.4 Relationships with Inputs and Mediators in the Ecosystem

After finalising the deal with the large Finnish biopharma company, Company Echo needed to find a place to start operations. BioCity Group allowed them to occupy the old BASF facilities

where they had worked for twenty years and offered Company Echo a place within the science park when it opened in 2003. However, research participant ECHO1 decided to set up in a new space, as they and their team wanted a “new beginning”, and moved to a building in Nottingham City Centre, not far from the BioCity Science Park. Their relationship with BioCity Group has been that of “good neighbours” since then as Company Echo is usually invited to participate in general networking events held at the science park.

The strongest relationship Company Echo has within the ecosystem is with Medilink East Midlands (MEM). According to research participant ECHO1, MEM is “the glue that holds us all together” in the entrepreneurial ecosystem as they excel at connecting the right people. Participant ECHO1 highlights the contact list they can access through MEM and the importance of the special interest groups they organise. Connecting with and through MEM helps Company Echo to behave as an ambassador for their parent company while scouting partners for drug development projects.

Research participant ECHO1 has tried to build a relationship with the local universities but has struggled to do so. Company Echo argues that collaborating with prestigious universities such as the University of Nottingham could benefit their projects; however, upon a meeting with the Deputy Director of Research, they could not find overlapping interests or common goals. However, research participant ECHO1 reveals that whenever they have contacted an academic research group, it has been through MEM rather than the university. They argue that MEM has a better knowledge of the needs that SMEs in the ecosystem have and are able to connect them with the relevant academic groups.

4.5.5 Partnerships Management

Company Echo usually scouts for partners through MEM's network. If they need to leverage scientific knowledge from a company or an academic group, research participant ECHO1 usually reaches out to MEM. According to research participant ECHO1, this is helpful as MEM will direct them to people who can help them. MEM act as a broker by connecting people from relevant organisations who already share a common language and have overlapping knowledge bases.

Research participant ECHO1 revealed that after the connections are made, it might take months or even years before a partnership can be established due to the lengthy organisational process required by their parent company in Finland. After establishing a connection with the relevant people in Company Echo, a potential partner needs to contact the relevant people from the partner company. If the second stage of talks is successful, a potential partner would be required to contact the parent company's Alliance Management Division so they can learn what will be expected from them in terms of communication, accountability, values, and culture. According to research participant ECHO1, finding commonalities in these themes is important as it is a step towards defining common goals for a partnership. If there is a mismatch in any of the before-mentioned areas, the parent company will not allow Company Echo to go through with the partnership.

4.6 Company Foxtrot

The interview transcripts for this were coded as FOX1 and FOX2 while the research participants BIO1 and CHARLIE2 also contributed to the understanding of Company Foxtrot. Information from the company's website and press releases by third parties were used as archival data.

4.6.1 Research Participant's Profile

Research participant FOX1 is the Director of Marketing at Company Foxtrot. They have an undergrad degree in Marketing followed by an MBA. Before joining Company Foxtrot, they worked for a large company in the energy sector for eight and a half years doing marketing, business strategy, and sales. Though Company Foxtrot was founded in 2004, research participant FOX1 is the first person to formally be in charge of marketing upon joining the company in 2019. Research participant FOX1 revealed that learning the language of the biopharma sector has been a challenge, but their colleagues and science park management have helped them to ease into the role.

Research participant FOX2 was the Chief Executive Officer of an external partner based within the Nottingham Biopharma Ecosystem whose company was later acquired by Company Foxtrot. Participant FOX2 was awarded a PhD by St George's Hospital Medical School and then went on to work for Boots in Nottingham in 1988. As research participant ECHO1, they worked for Boots and then for BASF until the Nottingham R&D branch was closed in 2001. Their company was founded in 2001 and acquired by Company Foxtrot in 2019.

The profile of research participant BIO1 will be provided when exploring the unit of analysis BioCity Group.

4.6.2 Company's profile

Company Foxtrot is a Contract Research Organisation (CRO) established in 2004 after a large biopharmaceutical company shut its R&D branch in Nottingham. The company started as a "small clinical group" providing support to drug development projects. After AstraZeneca closed in 2011, Company Foxtrot was able to attract talent to broaden their offering and added scientists to work on biotechnology, DMPK, computational chemistry, and in vivo assessment of drug interactions. The company was founded by a team of four people in 2004 and grew to a staff of over 200 people by late 2019.

According to research participant BIO1, the company started occupying a small lab space in BioCity Nottingham's first building. They then expanded to occupy a whole floor, and in 2017, Company Foxtrot moved into BioCity's new building, where they occupy two floors.

4.6.3 Rationale for Choosing the Nottingham Biopharma Ecosystem

As with previous founding teams, Company Foxtrot's founding team was working for a larger biopharma company that shut down. They were offered rent incentives to start the company within the BioCity Science Park and thought that being part of a science park would present them with more networking opportunities.

According to research participants FOX1 and FOX2, the companies at the early stages of the entrepreneurial ecosystem would work with the remaining large biopharma companies. After the last of these large companies based in the East Midlands shut down, Company Foxtrot benefited from the pool of available talent and attracted new staff to expand their offering. This

growth and ability to attract talent can be seen as a benefit from operating in a second-tier region.

4.6.4 Relationships with Inputs and Mediators in the Ecosystem

According to research participants FOX1 and BIO1, Company Foxtrot has been in a closed relationship with BioCity Group management. Research participant FOX1reveals that science park management is not only a “landlord” to Company Alpha but also a collaborator as they organised joint networking events. Moreover, BioCity’s marketing team has helped research participant FOX1 to ease into the biopharma industry language.

Company Foxtrot is a member of Medilink East Midlands (MEM) and attends some of their events; however, research participant FOX1 highlighted that the company has outgrown the support that BioCity and MEM can provide them. The company now scouts for opportunities for partnerships and collaborations through their internal processes.

4.6.5 Partnerships Management

Research participant FOX1 detailed that Company Fox’s initial approach to partnerships was to find companies with complementary skills. Participant FOX2 reflected on this and revealed that the companies “were highly complementary businesses.” However, research participant FOX1 commented that Company’s Foxtrot strategy is to consolidate complementary skills under an umbrella of companies. The acquired companies were recurrent partners of Company Fox who would help them to deliver drug discovery and development projects to their customers. Participant FOX1 highlighted the importance of their Director of Research to identify the opportunities for complementary partnerships.

Research participant FOX1 detailed that the company is aware of the cultural differences across the globe, so they have a multicultural team. Team diversity has been important as they have been able to connect with companies in places such as Japan, Korea, and the United States. According to research participant FOX1, understanding how other companies approach establishing partnerships and making business has been important for Company's Foxtrot growth.

4.7 Company Golf

The interview transcripts for this unit of analysis were coded as GOLF1, GOLF2 and GOLF3. Information from the company's web site and press releases by third parties were used as archival data.

4.7.1 Research Participant's Profile

Participant GOLF1 is the Chief Scientific Officer and founder of Company Golf. They have a degree in Applied Biology specialised in Human Biology and Pharmacology from the North East London Polytechnic. After a year of working as a graduate, they enrolled in a PhD studying chemicals affecting female fertility at the Institute for Reproductive Biology in Edinburgh. After a post-doctoral experience in the US and a few years in a Golden Triangle-based large biopharma company, they moved to AstraZeneca, where they worked for eleven years until the site was shut down. They decided not to continue at AstraZeneca and started Company Golf.

Research participant GOLF2 is the Marketing Manager for Company Golf. They have a degree in Applied Biopharmaceutical Biotechnology and Entrepreneurship from the University of

Nottingham. After finishing their master's, they obtained a certificate in Innovation Management while working for another SME specialised in platelets research before joining Company Golf.

Research participant GOL3 is an external collaborator of Company Golf. They have a PhD in Biological Sciences from the University of Cambridge. Before joining Company's Golf collaborator as CEO, they worked in large biotechnology companies for over twenty years in areas related to business development.

4.7.2 Company's Profile

Company Golf is a preclinical Contract Research Organisation (CRO) based in BioCity Nottingham. It was founded in 2011 by a team of three scientists who were working at the AstraZeneca R&D facility in Loughborough. After AstraZeneca in Loughborough shut down, they decided not to continue working for the company and started a new company.

Company Golf supports the early stages of drug development projects by helping organisations to identify and validate therapeutic targets. This is important for drug development projects as it is an effort to identify the therapeutic molecules that have the best chances to make it through the development pipeline.

4.7.3 Rationale for Choosing the Nottingham Biopharma Ecosystem

The members of the founding team were living and working near Nottingham City, and while looking for a place to establish their start-up, they discovered BioCity Nottingham. The science park offered facilities that were ready to move in and lab equipment on demand at reasonable prices, so they decided to set up the company in the BioCity Nottingham science park.

4.7.4 Relationships with Inputs and Mediators in the Ecosystem

Research participant GOLF1 reveals that the first eighteen months of their time at BioCity Nottingham “were brilliant.” Through funding allocated by the European Union, science park management provided Company Golf with twelve months of an entrepreneur in residence. This entrepreneur in residence helped Company Golf with setting a business strategy to achieve the company’s goals. However, after the incubation time, research participant GOLF1 has not been happy with the support provided by science park management.

Research participant GOLF1 revealed that science park management makes it difficult for the tenants to meet up through scientific conversations. Participants GOLF1 and GOLF2 argued that science park management has traditionally focused on offering social events which have little value for the companies on-site. Though Company Golf has tried to organise scientific talks, they have been met with resistance from the team managing the science park. The unsuccessful efforts at promoting scientific conversations on-site have created a “silo mentality” (GOLF1), where Company Golf considers the science park as a landlord and not as a support organisation.

Company Golf has tried to tap into the scientific knowledge of research groups at the local universities, but these efforts have not been successful. Research participant GOLF1 revealed that working with universities is a slow process in which it is difficult to establish common goals as Company Golf tries to secure funding to produce results that can validate their expertise through generating “specialised marketing material” (GOLF1), while universities are focused on

securing funding to fund postgraduate researchers and post-doctoral employees to generate academic papers.

Company Golf are members of Medilink East Midlands (MEM) to increase their exposure while validating their position as members of the entrepreneurial ecosystem; however, they do not have an active relationship with the membership organisation. This could be a result of MEM's struggles to set up a special interest group for CROs (MEM1).

4.7.5 Partnerships Management

For Company Golf, the first step towards establishing a partnership is to be able to communicate with a potential partner. Research participants GOLF1 and GOLF2 claim that science is the common language that enables the communication between Company Golf and potential partners. Company Golf attempts to communicate with companies on the setting of scientific conferences, which is how they connected with participant GOLF3. According to participants GOLF1 and GOLF3, scientific conferences provided an inviting environment where the individuals attending are likely to share a common language.

After the initial contact, Company Golf assesses the expertise of their potential partner and the scientific knowledge they can leverage for them. Research participant GOLF3 reveals that this assessment involved on-site meetings where their scientific experts discussed how they could complement their skills. After establishing the common goal of developing a platform for cell cultures, they applied for R&D funding through a government office that supports research and development by SMEs at a national level.

From their partnership, Company Golf and research participant GOLF3's company produced a patent; however, they have struggled to "take it forward" (GOLF1) after they ran out of government funding for the project. The lack of funding has affected their relationship as they can no longer allocate resources for the joint commercialisation of the patent.

Research participants GOLF1 and GOLF2 argue that a critical milestone in the process of establishing a partnership is to determine the common goals for the partnership at different stages. According to participant GOLF1, failing to establish how the involved parties will benefit from a partnership leads to a "mission creep", where companies will not collaborate (or stop collaborating if they had partnered up for a specific project).

Finally, Company Golf asks for a commitment from their partners. According to research participant GOLF1, commitment means attending events and conferences as partners so they can effectively communicate to the industry about their joint projects and the value they can add to preclinical drug development projects. If partners do not meet Company Golf's expectations and requirements, the collaboration is likely to stop after evaluating the benefits it provided both parties.

4.8 BioCity Group

The interview transcript for this unit of analysis was coded as BIO1. Information from the organisations' website and press releases by third parties were used as archival data.

4.8.1 Research Participant Profile

Research participant BIO is the Corporate Development Director in BioCity Group. They have a degree in Business and Finance, and after their degree, they worked for several years in the

British Consulate in Lyon, France. Their last project for the British Consulate was to organise a trade mission between British and French companies; one of the British organisations in the mission was BioCity.

After moving to Nottingham for personal reasons, they approached BioCity Nottingham and were hired in a business development role. Their role involved growing the tenant base of the science park while building relationships with other organisations within the entrepreneurial ecosystem, such as Medilink East Midlands (MEM) and the local universities. Their success at growing the tenant base in BioCity Nottingham and helping create Medilink Nottingham opened an opportunity for a job in a Golden Triangle-based science park. After a successful run in the Golden Triangle, they went back to BioCity Nottingham to overlook a corporate role.

4.8.2 Organisation's Profile and Role in the Ecosystem

The BioCity Nottingham science park was established in 2003 as an effort by the University of Nottingham, Nottingham Trent University, and the East Midlands Development Agency using the building and equipment that BASF donated to Nottingham Trent University upon shutting down their R&D site in 2002. After successfully growing their tenant base, they expanded their science park offering by establishing a second science park called MediCity Nottingham. Both science parks are oriented at supporting life science-oriented companies but also house support service organisations that offer services oriented to business administration and management such as consultancies.

BioCity Group is the organisation that manages these science parks while providing complementary services for incubation. First, they offer business incubation programmes

known as the “pre-accelerator” and “accelerator” programmes. According to research participant BIO1, these developmental programmes have the goal of closing the gap between science and business by providing scientists with the skills to turn research into a viable business idea. Secondly, BioCity Group manages a private investment fund they use to support viable business ideas presented through the developmental programmes or established companies within their science parks that showcase market growth potential. According to research participant BIO1, the combination of science parks, incubators, and an investment fund is unique and unprecedented in the United Kingdom.

BioCity Group is currently working on establishing a process in which all its tenants can benefit from the group’s network of experts. Research participant BIO1 claims that BioCity Group has formed an extensive network of mostly retired life science entrepreneurs who support the developmental programmes. However, it has been difficult for BioCity Group to find a process for these experts to support already-established SMEs looking to grow.

BioCity can be classified as an input within the IMO framework by providing two science parks, developmental programmes, and an investment fund. They aim to provide an inviting environment for start-up formation and SME entrepreneurial activity.

4.8.3 Supporting SMEs for Partnerships Management

Research participant BIO1 recognises that BioCity Group has excelled at growing its tenant base while establishing more science parks across the Midlands and Scotland; however, they recognise an opportunity to better support SMEs trying to leverage scientific knowledge through on-site interactions. The current efforts involve promoting interactions between tenants through

social activities such as pizza nights, ice cream afternoons, and joint activities with the city's alternative quarter. Through these activities, BioCity Group attempts to support SMEs' partnerships management by facilitating the interactions necessary for the inception stage of the partnership's lifecycle.

From other research participants, there is a perception that BioCity is more active at supporting tenants with a larger footprint in the science park and those with higher growth potential. This can lead to a "silo" mentality as detailed by research participant GOLF1.

BioCity's relationships with other stakeholders are explored in the next chapter when this research examines the entrepreneurial ecosystem through cognitive proximity.

4.9 Medilink East Midlands

The interview transcript for this unit of analysis was coded as MEM1. Information from the organisation's website and press releases by third parties were used as archival data.

4.9.1 Research Participant Profile

Research participant MEM1 is a Project Manager and Business Development Specialist for Medilink East Midlands. They have a business-related degree from the University of Pretoria in South Africa, and before joining MEM they worked as a Consultant in South Africa and as an employee of the UK's Department for International Trade (DIT). They joined MEM in 2009, where they are responsible for business development activities and organising events for members. They are also responsible for engaging with external organisations.

4.9.2 Organisation's Profile and Role in the Ecosystem

MEM is a membership organisation with the goal of helping life science-oriented companies establish, develop, and grow. The organisation was founded in 2005 as an initiative of the East Midlands Regional Development Agency (RDA) so local companies in the life science sector could meet "the various stakeholders to talk to each other in a non-threatening environment to facilitate relationships within the ecosystem" (MEM1).

The RDA was a government office that operated from 1999 to 2012 to support the economy in the East Midlands, which included Nottinghamshire, Leicestershire, Derbyshire, and Loughborough. They were especially keen on supporting knowledge-based economies as Nottingham was named one of the six science cities in the United Kingdom in the mid-2000s. The RDA was dissolved in 2012 with a change in government and replaced with Local Enterprise Partnerships (LEPs). MEM remains as a legacy of the efforts by the RDA on supporting knowledge-based industries and has been funded through membership and event fees.

MEM network of contacts expands through the East Midlands and accounts for over 4,000 individuals from over 700 different organisations available to the 150 members. According to research participant MEM1, around 50% of the members are located in the Nottingham Biopharma Ecosystem, around 15% in Leicestershire, about 12% in Derbyshire and the rest are distributed throughout the East Midlands. However, nearly 10% of their members are based outside the East Midlands and joined MEM to have access to the ecosystem. From the

membership base, around 15% operate within the biopharma and biotechnology sector and are clustered in the Nottingham Biopharma Ecosystem.

A summary of the membership services offered by MEM is as follows. First, MEM organises events that connect organisations and individuals with close cognitive proximity, which are known as “special interest groups”. Second, they facilitate discounts so their members can attend exhibitions and industry-specific trade shows. Third, they provide their members with discounts to access support services such as legal consultations or risk assessment. Fourth, they organise a lobby group to understand the needs of regional SMEs so they can liaise with government offices for better support.

Furthermore, MEM also provides some support to non-members. Research participant MEM1 labels this support as “special projects” in which MEM manages small grants on behalf of the government. SMEs (regarding their membership status) can apply for these grants through MEM. The “special project grants” have the goal of supporting SMEs with entrepreneurial activities such as paying for business strategy or marketing consultancy.

Medilink East Midlands can be considered as a mediator within the Nottingham Biopharma Ecosystem as it facilitates the interactions between SMEs, inputs, and mediators.

4.9.3 Supporting SMEs for Partnerships Management

There are two main mechanisms in which MEM supports SMEs with partnership management and are directed to the inception stage of the partnership life cycle. The first mechanism involves the “special interest groups” while the second depends on direct referrals.

The special interest groups are meetings directed to a specific sector of the life science industry. These events are not directly organised by MEM, but by members of their network. They identify a relevant champion for a specific interest area who then finds speakers who can provide relevant talks. The only supervision by MEM is that the content of the meetings is required to start with a scientific or technological trend to be followed by a discussion on the implications for the industry. There are special interest groups for medical technologies and the treatment of infectious diseases; nevertheless, MEM has struggled to establish a special interest group for CROs (which represent the main business model of biopharma companies in Nottingham).

MEM also supports the inception stage of the partnership's lifecycle through referrals and direct connections on demand. As mentioned by some of the research participants from the local SMEs, they reach out to MEM if they need to find specific knowledge. According to research participant MEM1, these introductions are important as the involved parties are aware that MEM only connects individuals and organisations that are cognitively close and therefore could become a good match as partners. Research participant MEM1 commented that "If we make an introduction, is not just an introduction for the sake of an introduction, that's because there is a meaningful connection that can be made in terms of somebody providing something… Frequently, the connections we make are very fruitful" (From interview MEM1).

4.10 East Midlands Academic Health Science Networks

The interview transcript for this unit of analysis was coded as AHSN1. Information from the organisation's website and press releases by third parties were used as archival data.

4.10.1 Research Participant Profile

Participant AHSN1 is the Commercial Manager for the East Midlands Academic Health Science Networks (AHSN). They trained as Dental Technician and worked in a hospital in London for five years; then they got a job for a company selling medical kits. After a career of 25 years in commercialising medical technologies, they joined AHSN in 2015 to have a job that required less travelling.

4.10.2 Organisation's Profile and Role in the Ecosystem

The East Midlands Academic Health Science Networks (AHSN) is an organisation set up by the National Health Service (NHS) in 2013 which operates as the innovation arm of the NHS. The East Midlands AHSN is one of fifteen regional AHSN offices across the United Kingdom.

According to research participant AHSN1, they are tasked with helping new innovations to enter the health system. AHSN usually work with SMEs and individual innovators to help them understand the NHS system and its requirements. Their support also includes organising workshops aimed at providing SMEs or individual innovators with information on where to get funding, where to get support to incubate their ideas, and how to engage with the NHS system.

AHSN is considered a mediator in the IMO framework as this organisation facilitates interactions that enables SMEs entrepreneurial activities. The interactions between AHSN and other inputs and mediators are explored in Chapter Five.

4.10.3 Supporting SMEs for Partnerships Management

AHSN supports the inception stage of the partnership lifecycle through their workshops. These workshops are usually a joint effort between AHSN and either MEM or BioCity, so they are a

good place for local SMEs to realise they are cognitively close. Research participant AHSN1 reveals that the organisation cannot support SMEs even further due to budget restrictions as they received their funding from the government through the NHS.

4.11 Mentor, Ohio Department for Economic Development and International Trade

The interview transcript for this unit of analysis was coded as DED1. Information from the organisation's website and press releases by third parties were used as archival data.

4.11.1 Research Participant Profile

Research participant DED1 is the Director of the Department for Economic Development and International Trade in the Midwestern city of Mentor, Ohio, in the United States. Before taking on this role, they had a career in different areas such as government service, business, and higher education.

4.11.2 Organisation's Profile and Role in the Ecosystem

The Department for Economic Development and International Trade (DED) is an office created by the government of the city of Mentor to attract, retain, and maintain businesses in this city. This city was interested in connecting with Nottingham due to their similarities in size, industries they support, and limitations.

Mentor, Ohio, is a second-tier region in the Midwest of the United States with a strong presence of life science-oriented companies. The city is home to the headquarters of a large Medtech manufacturer and that has attracted other Midwestern companies into their ecosystem. One strategy that the DED is using to strengthen their ecosystem is to help their local companies to connect (and eventually partner up) with foreign companies.

Their trade programme started by connecting with UK companies through MEM. This organisational partnership was announced in 2019 and led to establishing trade missions including companies from both ecosystems. DED aims to support UK SMEs by facilitating their access to the American market by connecting with potential business and innovation partners.

The DED is considered a mediator in the IMO framework as its main goal within the ecosystem is to support SMEs in the Nottingham Biopharma Ecosystem with entrepreneurial activities related to entering the American Midwest market. The interactions between the DED and other inputs and mediators are explored in Chapter Five.

4.11.3 Supporting SMEs for Partnerships Management

The DED supports the inception stage of the partnership lifecycle through their trade missions. For their trade missions, the DED and MEM select the organisations that they consider to be cognitively close enough to potentially create a partnership.

4.12 Company VENT

The interview transcript for this unit of analysis was coded as VENT1. Information from the organisation's website and press releases by third parties were used as archival data.

4.12.1 Research Participant Profile

Research participant VENT1 is the Chair of the Investment Committees in Company VENT1. They have a degree in Pharmacy, and after a few years of working experience, they joined Nottingham-based Boots, where they worked for ten years. During their time in Boots, they studied a company-sponsored MBA. After leaving Boots, they established company VENT1 in 1999, where they were Managing Director from 1999 to 2013.

Their education as pharmacists and prior work experience at Boots have helped them to successfully invest in early-stage life science companies.

4.12.2 Organisation's Profile and Role in the Ecosystem

Company VENT1 is an independent fund manager established in 1999. Their experience spans a range of sectors such as luxury consumer brands and software; however, they have found a niche in the healthcare and biopharma sector. Company VENT1 were among the first residents of the BioCity Nottingham science park; however, due to strategic reasons, they decided to move their Midlands offices to Leicester. Their role in the ecosystem is to invest in early-stage companies through the investment funds they manage.

Research participant VENT1 reveals that science parks facilitate their selection process when assessing which companies to support. Company VENT considers that companies based in science parks have support mechanisms in place that will diminish the risk of the companies not meeting their strategic goals. Therefore, Company VENT has established its Northern offices within the BioCity Group managed science park, Alderley Park.

Though their Midlands offices are not based within the Nottingham Biopharma Ecosystem, Company VENT can be considered as an input of the IMO framework within the Nottingham Biopharma Ecosystem as they invest in companies located in this entrepreneurial ecosystem.

4.12.3 Supporting SMEs for Partnerships Management

Company VENT supports the inception stage of the partnership lifecycle. According to research participant VENT1, while investing in a company they will introduce the investee to potential partners and direct them to the relevant mediators that can support with further introductions.

Research participant VENT1 revealed that they expect the investees to take their advice regarding potential partners into consideration.

4.13 Chapter Summary

This chapter helps to contextualise the units of analysis explored for the embedded case study methodology employed in this research. Through this contextualisation, the research is able to determine the different components of the IMO framework so their role and interactions can be explored in detail in Chapter Five.

Through this chapter, this research starts to identify the key components to explore this entrepreneurial ecosystem through cognitive proximity. In terms of inputs for the IMO framework, this chapter identifies the regional legacy in the biopharma industry, the developmental programmes for aspiring life science entrepreneurs, and funding opportunities as the most relevant ones. Higher education institutions (HEIs) are also an important part of this entrepreneurial ecosystem as they provide human capital for the local organisations. In terms of mediators, this research identifies a number of organisations that can be divided into mediators for networking and social interactions, government-led mediators, and external mediators. These components of the IMO framework and their interactions through cognitive proximity are explored in Chapter Five.

This chapter also presents the importance of cognitive proximity to better understand the lifecycle of partnerships in the biopharma industry from the perspective of SMEs. According to research participants, sharing a common language (science) and complementary knowledge bases is important for companies when exploring a partnership opportunity. The implications of cognitive proximity through the lifecycle of partnerships are explored in depth through Chapter Six.

Chapter Five – Empirical Findings I

This chapter explores the inputs, mediators (Lecluyse, Knockaert and Spithoven, 2019), and their interactions forming the contextual factors of an entrepreneurial ecosystem for biopharma SMEs in a second-tier region. Second-tier regions typically lack key resources such as funding or targeted government policy for entrepreneurial activities and innovation (Mayer, 2013; Wang, Lestari and Yang, 2015; Cardoso and Meijers, 2016).

The contextual factors help in understanding the key components and organisations, and their interactions in the region while taking into account how they promote and facilitate entrepreneurial activities and innovation through incubation, providing access to funding and local talent. These factors also illustrate how the local legacy of drug discovery fuels the region's current industry mainly focused on contract research organisations (CROs). It also seeks to understand their perceptions of the interactions between ecosystem stakeholders such as the local science parks management, government offices, and research groups in universities.

This chapter presents findings for the contextual factors for the Nottingham Biopharma Ecosystem while exploring the interactional factors between them.

5.1 Exploring an Entrepreneurial Ecosystem in a Second-Tier Region

This chapter provides an in-depth exploration of the inputs and mediators forming the contextual factors that facilitated the genesis and development of an entrepreneurial ecosystem for biopharma SMEs in Nottingham City, United Kingdom.

The participant companies have different specialised skills through early-stage activities in the drug development pipeline, and six out of the seven have a link to Nottingham or the East

Midlands regions before founding. Table 7 summarises the analysis of the participant SMEs explored in detail in Chapter Four.

Unit of Analysis	Company Profile	The Rationale for Choosing the Nottingham Biopharma Ecosystem	Relationships with Inputs and Mediators
Company Alpha	• Founded in 2014 at a university in the Golden Triangle. • Licenses therapeutic molecules to larger biopharma companies. • Moved their R&D area to Nottingham in 2017. • Based at MediCity Nottingham.	• They partnered with a research group at the University of Nottingham to leverage scientific knowledge, so they opted to be near them. • The leasing in Nottingham was more affordable than anything in the Golden Triangle.	• They are invited to social events organised by science park management; however, they do not attend such events. • They do not belong to the local membership organisation for SMEs in the life science sector.
Company Bravo	• Founded in 2011 as a spin-off company of a local university. • Founded after the restructuration of a precursor company. • Develops and commercialises platforms for tissue-specific regenerative medicine. • Based at MediCity Nottingham.	• The company is a spin-off from a local university, so the managing team are still academics there. • The life science parks offered on-demand space and equipment that fit the company's needs.	• They are invited to social events organised by science park management. However, they do not see value in social events. • They are members of the local membership organisation and attend their science-oriented events. • They have a link with a local university as their company is based on academic research.
Company Charlie	• Founded in 2011 after the regional R&D labs of a large biopharma were shut down. • The company is a contract research organisation (CRO) specialised in *in vitro* DMPK assays. • Based at BioCity Nottingham.	• The founding team were offered incentives as subsidised rent and on-demand lab facilities by science park management. • The founding team wanted to start their company while remaining geographically close to their previous place of work.	• The company actively attends the social events organised by science park management. • The company is a member of the local membership organisation for life science SMEs.
Company Delta	• Founded in 2015 as a spin-off company from a local university. • The company develops biotherapies for their use in ophthalmology. • Based at MediCity Nottingham.	• The company is a spin-off from a local university, so the founder & CEO still works as an academic there. • The company was offered rent incentives to move to one of the science parks for life science companies.	• The science park management helped them to obtain seed funding. • They attended the developmental programmes offered by the science park. • The company managing team are invited to social events organised by science park management but do not usually attend. • They are members of the local membership organisation and attend their science-oriented events.
Company Echo	• Founded in 2001 after a Nottingham-based R&D biopharma was shut down. • The company is the R&D branch of a large biopharma company based in Europe. • The company operates within the ecosystem as an SME. • Based in Nottingham City Centre.	• The managing team were made redundant and wanted to stay in Nottingham. • Setting the company in Nottingham was more affordable than anything in the Golden Triangle to their new employers.	• They are members of the local membership organisation and attend their science-oriented events. • The company uses the local membership organisation to connect with relevant individuals. • They struggle to connect with the local universities.
Company Foxtrot	• Founded in 2004 after a Nottingham-based R&D biopharma was shut down. • The company is a CRO for drug discovery projects. • Based at BioCity Nottingham.	• The managing team were made redundant and wanted to stay in Nottingham. • The founders were offered rent incentives to move to the science park.	• They are members of the local membership organisation and attend their science-oriented events. • They are in constant communication with the science park where they are considered the star tenant. • They struggle to connect with the local universities.
Company Golf	• Founded in 2011 after the regional R&D labs of a large biopharma were shut down. • The company is a contract research organisation (CRO) specialised in preclinical assays. • Based at BioCity Nottingham.	• The managing team were made redundant and wanted to stay in the region they lived and worked in for twenty years. • The science park offered the founding team rent incentives and support to incubate a company.	• They attended the developmental programmes offered by the science park. • The company managing team are invited to social events organised by science park management but do not usually attend. • Members of the membership organisation but do not engage with the events.

Table 7. Profile of Participant SMEs.

Nottingham, a second-tier region in the East Midlands area of the United Kingdom, has developed a series of inputs that interact with local mediators to facilitate the creation and growth of SMEs in the biopharma industry as introduced previously in Chapter Four. Table 8 presents a summary of the participant inputs and mediators.

Unit of Analysis	Organisation Profile	Role in the Ecosystem	Role in the *IMO framework*
BioCity Group	• Established in 2003 after the R&D labs of a large biopharma were donated to a local university.	• To manage the two local science parks specialised in the life science sector. • To provide incubation infrastructure, developmental programmes for aspiring entrepreneurs, and capital funding for life science companies.	• Inputs in the form of incubation infrastructure, developmental programmes, and funding.
Medilink East Midlands (MEM)	• Established in 2005 by the Regional Development Agency that was active from 1999 to 2012.	• Membership organisation that specifically supports life science SMEs. • To organise scientific-oriented meetings for SMEs to connect between them and with academia. • To manage government funding for business support activities. Non-members can apply for this.	• Anchor mediator.
Academic Health Science Networks (AHSN)	• Established in 2013 to help SMEs and sole innovators to access the National Health Service (NHS).	• To organise workshops with information on where to get funding, incubation support, and how to engage with the NSH.	• Government-led mediator.
Mentor, Ohio Department for Economic Development and International Trade	• Connected with MEM in 2018. • They aim to attract, retain, and maintain businesses in the Midwestern city of Mentor, Ohio in the US.	• To connect the Nottingham Biopharma Ecosystem with organisations in Mentor, Ohio. • Support MEM in connecting SMEs with a potential to collaborate across countries.	• External mediator.
Company Vent	• Founded in 1999 after the Director left the biopharma industry.	• To scout and fund companies within the entrepreneurial ecosystem. • To direct their investees to the relevant support organisations.	• Input for funding.

Table 8. Participant Inputs and Mediators.

These contextual factors and their interactions are explored after an inductive exploration of the contextual factors for the Nottingham Biopharma Ecosystem; they include the local support

mechanisms present in the city, and their interactions are explored through the construct of cognitive proximity.

5.2 Inputs for Entrepreneurial Activities

The contextual factors consider the key components and organisations in an entrepreneurial ecosystem that promote and facilitate entrepreneurial activity and innovation (Autio *et al.*, 2014; McAdam *et al.*, 2014; Velt, Torkkeli and Laine, 2020). This research classifies these contextual factors into inputs and mediators and explores their interactions through the construct of cognitive proximity. According to our findings, the interactions between the biopharma SMEs, the inputs, and the mediators promote and facilitate entrepreneurial activity and innovation within the entrepreneurial ecosystem in this second-tier region.

In terms of inputs, this study identifies regional legacy, incubation infrastructure, developmental programmes, access to funding, and higher education institutions (HEIs). The mediators mostly liaise interaction between SMEs and third-party organisations; therefore, this research explores mediators for network formation and social interactions, government-led mediators, and external mediators.

5.2.1 Regional Legacy

Nottingham's legacy in drug discovery and commercialisation began with the launch of ibuprofen by the local company Boots in the 1970s (Ehret, McDonald-Junor and Smith, 2012). This major milestone promoted the growth of drug discovery and development efforts in Nottingham City as Boots invested in creating an R&D Campus in the City Centre (Ehret, McDonald-Junor and Smith, 2012; Smith, Rossiter and McDonald-Junor, 2017).

This campus was later acquired by a large biopharma company with international reach in the 1990s (BASF); however, the shift towards collaborative practices became stronger at the turn of the new millennium (Bianchi *et al.*, 2011; West *et al.*, 2014; Schuhmacher, Gassmann and Hinder, 2016; Bigliardi and Galati, 2018; Bogers, Chesbrough and Moedas, 2018; Russo-Spena and Di Paola, 2018) and left an unoccupied R&D campus with state-of-the-art equipment, and a pool of expert scientists on drug discovery, development, and validation looking for employment. During the first decade of the 2000s, this effect was replicated in nearby regions such as Loughborough and Alderley (Ehret, McDonald-Junor and Smith, 2012).

Participants from Medilink East Midlands (MEM) and companies Echo, Charlie, Echo Foxtrot, and Golf agreed on the importance of having an empty R&D campus and access to a significant amount of highly skilled people made redundant for the genesis of an entrepreneurial ecosystem for Biopharma-oriented SMEs in Nottingham. Companies Charlie, Echo, Foxtrot and Golf originated after these events throughout the first decade and a half of the 2000s (between the years 2004 and 2015) as start-ups spinning off from these large biopharmaceutical companies as a consequence of a large-scale shutting-down of research and development sites across the region. The internal participant from Company Echo mentioned that each funding team for the before-mentioned companies had differentiated skills through the development pipeline, which provided BioCity with a portfolio of companies with complementary services, to begin with.

Research participant from Company Bravo reflected on the available talent at the time the ecosystem started: “There was the closedown of organisations like AstraZeneca locally, which

enable certain of those skills in the biopharmaceutical arena to be retained. Because then people went into BioCity and settled new organisations and I think that is why things like analytical are quite strong as they probably actually come from the pre-existing biopharmaceutical employment base that was in the region" (From interview BRAVO1).

The internal participant from Company Bravo commented that BioCity Group management pitched the site to the funding teams while the large biopharmaceutical companies were shutting down and offered risk-diminishing incentives such as a year's rent-free, dedicated staff for cleaning, reception, and security, and most importantly, the rental of on-demand equipment that would be expensive for a start-up to acquire. Participants from Companies Bravo and Delta, spinouts from a local university, commented that their companies also considered their links to Nottingham-based academics as BioCity Nottingham and MediCity Nottingham offer very close proximity to the local universities' main campuses.

A more recent example from December 2018 is Company Alpha. This company spun out from a Golden-Triangle university but saw Nottingham as a good place to set up their R&D site. The internal participant from Company Alpha commented that their R&D activities led them to connect with a Nottingham-based research group, and as they started to do more work with the University of Nottingham, they moved those activities to a University of Nottingham lab for a couple of years before moving to MediCity Nottingham. MediCity provides them with the necessary equipment to develop their projects at a more affordable price than those available in the "Golden Triangle" area.

5.2.2 Incubation Infrastructure

The specialised organisation for incubating life science SMEs in the Nottingham Biopharma Ecosystem is the BioCity Group through the science parks BioCity and MediCity Nottingham. The Corporate Development Director for BioCity Group commented that when they started filling the sites, the group provided a wide range of incentives to life science entrepreneurs to start their companies there if they came from any of the local large biopharma companies that were shutting down in the mid-2000s.

When BioCity Nottingham Science Park started operations, they focused mainly on offering affordable leases and high-end equipment left behind by the large company that occupied those facilities. Moreover, research participants from Companies Bravo, Charlie, Foxtrot, and Golf confirmed that BioCity provided their start-ups with mentoring through European Union funding. This funding did allow science park management to allocate an “entrepreneur in residence” to help these companies refine their business plans and strategies to ensure their efforts proceeded in the right direction. This support was provided for a period of twelve to eighteen months, and as detailed by an internal participant from Company Golf, it consisted of a business strategy coach that would consult the companies “few days a month” on key aspects such as business strategy and business development.

The internal participant from Company Bravo stated that they had previously been involved as the founder of a company that was among the first tenants in the science park and clarified that the management group offered a dynamic business model of leasing space for their tenants after a free-trial experience. The contracts were flexible, and companies were able to take more

space office and laboratories (if available) as needed, or if companies increased their outsourcing and reduced the footprint in the building, they could give up space quickly. This meant that companies could re-arrange their footprint within the science park on demand if necessary.

In addition to the “entrepreneur in residence”, the flexible occupation contracts, and specialised equipment, the science park also provided these companies with secondary support services that could be operationally prohibitive for the companies, such as a general reception, security, and centralised services for heating, electricity, and water. The access to these resources enabled the companies to meet everyday needs at a low cost according to research participants from Companies Bravo, Foxtrot, and Golf.

As the first science park site filled up, BioCity Group expanded their local presence and opened another science park for incubation inside Boots’ campus called MediCity Nottingham. MediCity Nottingham provides the same support as the BioCity site but aims to help incubate companies with a focus on the health sector and the nutrition industry.

5.2.3 Developmental Programmes

Science park management detailed that as the sites grew their tenant base, they identified the need for providing more support to potential tenants as they realised most of them came from purely scientific and academic backgrounds and were therefore lacking prior entrepreneurial experience.

To tackle the lack of prior entrepreneurial experience among their potential tenants, the science park management started developmental programmes known as pre-accelerator and

accelerator programmes. Science park management uses these programmes to provide scientists and academics without prior entrepreneurial experience with knowledge on how to present their innovative ideas through a business plan that can appeal to potential investors. Science park management also uses these programmes to find good ideas with a market potential so they can secure a tenant for the short and mid-term.

The content of these developmental programmes is aimed at closing a knowledge gap between problem identification and venture creation for people without prior entrepreneurial experience as confirmed by an internal participant from Company Delta: “As a result of that training, we secured the full money that we needed from one investor” (From interview DELTA1).

According to the science park’s management, refining these programmes is an active and evolving activity in which they constantly revise the contents of the programmes according to the feedback from the attendees. In the beginning, these programmes were short and intense as they took place in a week’s space; however, that did not work well for academics as they were not as focused since they were “juggling” the programmes with other commitments. Now the programmes have been extended to a couple of weeks for the pre-accelerator and a couple of months for the accelerator to avoid the scheduling conflicts from happening.

5.2.4 Access to Funding and Specialised Networks

In addition to two science parks for business incubation, BioCity’s Group support for companies also includes venture funding, whereby they try to allocate technologies with market potential identified after the developmental programmes

According to BioCity's Corporate Development Director, this combination of support mechanisms makes BioCity a unique place for companies: "That is what set us apart because you either have a science park or an accelerator, and on top, we have an investment fund to support companies we think have potential. Nobody has those three components" (From interview BIO1).

BioCity Group could not always invest in ideas they found interesting, but they could facilitate meaningful interactions for companies to secure key funding. The founder of Company Delta detailed how BioCity Group showed interest in their technology and market potential so introduced them to an investment company that supported them with seed funding.

In addition to funding opportunities, BioCity Group also provides access to a network of support services providers so their tenants can find support for activities related to marketing, business development, legal advice, and accounting. Research participants from Companies Charlie, Foxtrot, and Golf commented that BioCity Group also serves as a gatekeeper for the companies inside the science parks.

BioCity's support, combined with support from other mediators, allows the science park to have a "success rate" that, according to BioCity's Corporate Development Director, is "rare for the sector" as they detailed: "If you look at the success rate of companies in here, it is 93%, and that is massive, that is so high and that's quite rare for our sector" (From interview BIO1). This information is also available on archival data from the BioCity Report published in the years 2017 and 2019 (Bio City Group, 2017; Crocker, 2019).

5.2.5 Higher Education Institutions

In Nottingham City, there are two research-intensive higher education institutions (HEIs), The University of Nottingham and Nottingham Trent University. The findings suggest that their footprint is mostly related to providing human capital for local SMEs rather than collaborating with local biopharma SMEs. According to research participants from Companies Alpha, Delta, Echo, and Golf, the local HEIs excel at providing human capital; however, they struggle to fully exploit this input as the administrative processes of working universities are difficult to navigate for SMEs.

In the different frameworks for exploring entrepreneurial ecosystems based on the “triple helix” (Rosenlund, Rosell and Hogland, 2017; Carayannis *et al.*, 2018), universities are signalled as important partners for companies as they provide a pool of highly qualified human talent and specialised expertise. Therefore, this section explores the perceptions that local SMEs in the biopharma industry have on their collaborations with research groups from universities and the challenges they have encountered through such collaborations.

Perceptions and Benefits of Relationships with HEIs

Companies Alpha, Bravo, Delta, and external collaborators from Company Golf detailed that they have engaged with universities to develop research and development projects through government funding.

Company Alpha collaborates with academics in London, Cardiff, Oxford, and Nottingham for the improvement of their current technologies, while it is also engaging with Reading University through a Knowledge Transfer Partnership (KTP) sponsored by the UK government. They

clarified that a KTP is a scheme where Company Alpha partly funds a post-doctoral student to develop technology at a university that will later be transferred to the company's laboratories in Nottingham. Moreover, the company is hoping to offer such a post-doctoral student a job at the company to keep the expertise and knowledge they will have had invested in. An external collaborator for Company Golf is also involved with a university through a KTP and works with universities in Sheffield, Manchester, and Maastricht to build on collaboration projects for research and development. This research participant added that these relationships came from the personal relationships of current employees that had worked in research groups at these universities.

Company Bravo's founder commented that as a university spinout they still have very strong links with the University of Nottingham as they still work with "a number of research groups in the university" (From interview BRAVO1). Company Delta's founder revealed that the company has a research collaboration with a specific research group at the University of Nottingham, where the founder is still an academic researcher. Furthermore, Company Delta's Operations Manager is doing an MBA at Nottingham Trent University, where they have been able to signpost for laboratory intern roles that usually lead to permanent positions. Company Charlie's external collaborator agreed as their company also relies on local universities for attracting interns and permanent positions.

Challenges for Universities within an Entrepreneurial Ecosystem in a Second-Tier Region

Despite actively collaborating with a university group, Company Delta's founder detailed that the relationship with the university has had some difficulties as he considers that "the hardest context is mixing academics and industry" (From interview DELTA1). When trying to reconcile company work with university processes, they realised that the way of working is "really different as the industry is so fast, university is really slow, very caught up in red tape and bureaucracy" (From interview DELTA1). They also suggest that for academics who spinout companies, the balance and criteria for assessment in universities is difficult: "As an academic and a scientist you are measured against certain benchmarks, but there are no other allowances or recognition if you are not actually generating ten papers a year, but you got a company taking a product forward that is actually saving sight which was developed in Nottingham" (From interview DELTA1).

Company Golf's founder and CSO agreed that it is difficult to find a middle ground between universities and the industry and considers connections with research groups in universities "a waste of time" because in terms of timelines "they are incredibly slow and in terms of cost, they are incredibly expensive" (From interview GOLF1). They revealed that universities are not always aware of the awarding bodies that could fund a research project and commented that research groups try to get funding to employ post-doctoral researchers, which is not possible with the grants that Company Golf is eligible to apply for.

Research participant from Company Echo explored how local universities try engaging with universities by holding Open Days: "The University of Nottingham runs what is called a

showcase day, and they have presentations on things they are working on from the R&D side" (From interview ECHO1). They also detailed that Directors of Research from the local universities also contact people from companies or support organisations such as MEM if they believe they have something with the potential for technology transfer. They reflected that relationships with universities are difficult because universities usually have "so many interests all over the place" and when a company comes along and try to work with a university, they realise they have "a very small overlap with those interests which requires either party to make an effort to find those overlapping interests" (From interview ECHO1).

Research participants from Companies Bravo and Echo suggested that the lack of "overlapping interests" between universities and local SMEs could be addressed by having universities communicate more about what is done within their laboratories, as according to Company Echo's research participant, "there is a lot of going on here (local universities) that is probably not well known." Company Bravo's research participant agreed on this and detailed that as a University of Nottingham spinout, they are "somehow aware, there is a lot of stuff going on there". However, as a company, they are less familiar with what is going on at Nottingham Trent University.

Company Bravo's founders suggested that universities could provide more education and support to academic groups so they can improve their awareness around the commercial requirements about translational research and about how some key experiments could be structured "slightly different". That could help in terms of early-stage validation while adding

value creation and worthiness to any potential IP that could go then into the spinout companies so academics can get involved with entrepreneurial activities.

When collaborations with universities go through, there is yet another challenge that participant companies have encountered, and it is related to communication. Research participant from Company Alpha clarified that projects with academics within universities “can be a bit frustrating”, some might be more collaborative than others, but the overall experience Company Alpha has had is “that the academic does not really communicate well, usually keeps the work to themselves until last minute, and do not really reply to emails” (From interview ALPHA1).

According to participants from Companies Alpha, Delta, Echo, and Golf, the lack of effective communication and the intrinsic goals of academics (defined by the internal informant from Company Alpha as fundamental research and publications) make it “tricky” trying to tap into the knowledge and expertise within universities as an SME while trying to focus on obtaining data and information that companies can translate commercially as well.

In summary, in terms of inputs that support biopharma SMEs in this second-tier region, there are two specialised science parks in life science that provide developmental programmes for aspiring entrepreneurs while facilitating access to funding opportunities. Also, there are two HEIs that contribute to local SMEs by providing a pool of highly specialised human capital.

5.3 Mediators for Entrepreneurial Activities

This research defines mediators within the IMO network as the organisations within the entrepreneurial ecosystem that facilitate the liaison of local SMEs with other companies and organisations to facilitate entrepreneurial activity and innovation.

Mediators are likely to be important institutions for the success of an entrepreneurial ecosystem as they can foster collective growth by connecting and mobilising different stakeholders. This research classifies mediators as mediators for network formation and social interactions, government-led mediators, and external mediators.

5.3.1 Mediators for Network Formation and Social Interactions

Within the Nottingham Biopharma Ecosystem, there is one organisation that aims to promote social interactions between life sciences SMEs in the entrepreneurial ecosystem. Medilink East Midlands (MEM) is a membership organisation that was founded in 2005 by the then Regional Development Agency (RDA) with the idea of getting the various stakeholders in the life science sector to talk to each other in a non-threatening environment while facilitating relationships within the ecosystem (From interview MEM1).

According to MEM's Project and Business Development Manager, their goals are to facilitate networking and to provide business support to their members. According to the research participant from MEM, the organisation had approximately 150 members across the East Midlands in autumn 2019 with "probably around 50% in Nottinghamshire" being the Nottingham City area the major regional cluster for the sector. They added that nearly "15% of the membership are from the pharma and the biopharma sector, mostly clustered in Nottingham (From interview MEM1)."

They added that MEM provides a portfolio of services aimed at getting their members to connect, and to potentially collaborate with other companies and relevant stakeholders in the region as well. These services include regular meetings of special interest groups around

specific scientific topics and the industry opportunities around them, generic networking events to promote social interactions, and workshops and training courses for their members. Among the events MEM organises, the special interest groups are important according to research participants from Companies Bravo, Delta, and Echo, as these groups are sector-based.

When organising these special interests groups, MEM looks for a “champion” to help them organise the event. As explored by MEM’s participant, “For example, for the infectious diseases special interest group, we have a doctor from a regional university who runs that particular group. The doctor will identify the themes, the speakers, and run the events in conjunction with us” (From interview MEM1). MEM then ensures that what the champion organises is relevant to the industry and supports the event by providing industry speakers. These special interest groups have the goal of discussing relevant scientific advancements while trying to find opportunities to commercialise those technologies. The research participant from Company Bravo commented that these groups are very important for the company as they are focused on relevant technologies and problems for specific industries within the life sciences, specifically the biopharma and diagnostics sector.

Through what MEM’s research participant defined as “generic networking events”, the organisation provides a platform for SMEs and stakeholders to engage with social interactions and meet with relevant players in the local biopharma industry. As mentioned by Company Delta’s founder, these events might not lead to sales, but help to get key contacts for the company’s development. They added that being a member of MEM has benefited the company

as the membership organisation has pointed Company Delta in the right direction whenever they have a business need, such as recruitment.

These benefits were confirmed by the research participant from Company Echo as they commented that this relationship has facilitated “lots of important conversations” with other companies, stakeholders, and universities: “A nice thing about Medilink is that sometimes you almost collide with something you haven’t expected and that gives you ideas.” (From interview ECHO1).

The internal participant from Company Echo revealed that another benefit from being a MEM member is access to a contact list of experts in a broad range of areas that support SMEs in the biopharma sector. The Site Director for Company Echo detailed that when the company needed to find stem cell experts for a project, MEM connected them with companies commercialising products to manipulate stem cells and with an expert academic in the area.

MEM also provides support to non-members by organising events and managing funding on behalf of the national government and other local organisations that aim to support local SMEs, such as the Academic Health Science Networks (AHSN).

MEM’s Project Manager elucidated that they provide this type of support delivered through what they defined as “projects” which are mainly aimed at getting a good diagnostic of areas where SMEs need support and then to support them by facilitating access to funding and business consultants (From Interview MEM1). The projects are run independently from the services offered to MEM members; therefore, MEM’s events lead activities have to present something outside the scope of the projects as explored by MEM’s internal participant: “We try not to make

the grants so science-focused, we try to make them more commercially focused so they can understand what they are talking about and the commercial application of the science." (From interview MEM1).

5.3.2 Government-led Mediators

These mediators are government offices and initiatives to support entrepreneurial activities and innovation for different industry sectors regardless of the size of the company. These support SMEs in the process of supplying the National Health Service (NHS) and allow engagement with internationalisation activities.

Company Delta's founder revealed that accessing the National Health Service (NHS) as a technology supplier is a difficult process that requires meeting a very strict criterion in terms of providing scientific evidence supporting the technology and connecting with the right people in the system (From interview DELTA1). To facilitate this process, the national government have created the Academic Health Science Networks (AHSN) with specific branches for each region of the country, such as the East Midlands Office based in the Jubilee Campus of the University of Nottingham.

AHSN's Commercial Manager detailed that this organisation is tasked with helping innovations getting into the NHS. The organisation primarily works with companies and innovators to help them understand the NHS ecosystem and to direct them in the right direction for funding opportunities (From interview AHSN1).

The AHSN Commercial Manager revealed that they work closely with local inputs and mediators such as BioCity Group and Medilink East Midlands (MEM) as they are the two major

stakeholders in the Nottingham Biopharma Ecosystem. The relationship between the AHSN and MEM involves referring SMEs that need the specific support this organisation provides and organising workshops and training sessions that match the needs and interests that healthcare-oriented SMEs in the region have. The participant from the ASHN revealed that their organisation has delivered some of these workshops on behalf of MEM several times: “We just ran (in October 2019) (the) getting business cases NHS ready (workshop); we have run that about fifteen times as an organisation” (From interview AHSN1). This is confirmed by archival data on MEM’s webpage as this workshop ran again in February 2020.

The ASHN also gets involved with science park management by providing funding for their developmental programmes for life science entrepreneurs. The research participant for the AHSN explored this relationship: “We also work with the BioCity Group quite closely. So, they involved us with the accelerator and pre-accelerator programme which we fund” (From interview AHSN1). They added that the AHSN has limited funding and human capital to provide support to every company that comes to them; therefore, they rely on their relationships with other inputs and mediators to provide the best support to SMEs within the entrepreneurial ecosystem.

MEM’s research participant recognises the efforts of other government-led mediators such as the Office for Life Sciences and the Department for International Trade; however, these organisations do not fully understand the challenges for SMEs in niche industries according to research participants from Companies Golf, Charlie, and MEM. MEM’s Project Manager added

that Medilink is “probably the only organisation whose only agenda is to support businesses” and made clear that government offices such as the DIT have their internal objectives.

An external research participant from Company Charlie and the internal research participants from Company Golf agreed as they argued that the different agendas for each government office make it difficult to find the right person to talk to or to even follow up on previous government-funded projects through Innovate UK. The Marketing Manager for Company Golf commented on an experience trying to enrol on a government-organised training course: “I contacted everybody, and they would keep on sending me to different departments and I could not reach the final person. Because those government departments don’t really talk to each other.” Internal research participants from Company Golf highlighted the importance of finding the right people in the right government office to be able to benefit from their activities.

Research participants from BioCity Group, MEM, and the regional investment company have pointed out the importance of government support as they consider it promotes the development of high-tech industry clusters. BioCity’s research participant suggested that clusters in development need good regulatory environments so there is a clear landscape for the companies to operate within.

The need for further support from the government is mentioned by the research participant from the Investment Company: “Well, the government they talk a lot about supporting networks but in our experience that doesn’t really happen. Government just funds things, and if they choose the right manager then they will have the networks to add value” (From interview VENT1). This participant also suggested that the UK government “tends to be a very passive investor” that

relies on fund managers and other support organisations to facilitate the creation of networks for collaboration. They also added that the government could promote more activities related to creating “the entrepreneurial environment” for people to take the risk, and then let the business people find opportunities to get on with.

The research participants from Company Echo and the investment company share the perception that the support from the government has diminished in the last ten years as a result of a government restructuring. They acknowledged that with a former government, there was the East Midlands Development Agency, a government-led organisation whose role would be to get local companies and stakeholders in meetings to discuss and plan on projects to move the region forwards (From interview VENT1). The research participant from the investment company detailed that the Regional Development Agencies were transformed into Local Enterprise Partnerships, which had an impact on the meetings and plans involving the regional stakeholders: “I had more direct exposure to the RDAs than the LEPs, I was in the RDAs’ offices at least five times a year and I haven't been in the LEPs’ offices. I don't really know who the people are” (From interview VENTURE1).

Research participants from MEM and BioCity Group agreed that another important stakeholder is the UK’s Department for International Trade as it has the potential of supporting Nottingham-based companies to enter international markets. Research participants from companies Charlie and Delta commented that their companies have received support from the United Kingdom’s Department for International Trade (DIT); this support is well documented on several press releases on these companies’ websites.

This government office has the goal of facilitating the export of products and services by UK companies and supports them by providing funding to attend events abroad as confirmed by the founder of Company Delta: “Internationally you got the DIT who do support this. When we go to MEDICA (a large conference for healthcare companies) it would cost you about £10,000, but it cost us a couple of thousand to go so they have been very supportive” (From interview DELTA1).

During overseas events, the DIT sets up a stand that provides a focal point for the UK organisations attending the events as highlighted by a press release from Company Charlie’s website. This stand serves as a meeting point where companies interact not only with organisations from around the world but also with other UK-based companies that they might not be aware of as confirmed by the internal participant from Company Bravo: “Quite often, you go to these international trips, and actually the most value is from local, or UK-based companies that developed when going overseas” (From interview BRAVO1).

A Company Charlie research participant recognised the role of DIT events in enabling this to happen: “The founder and I were in Madrid last week, it was a DIT led event, and they would help facilitate some interactions, they set up events that we attended” (From interview CHARLIE1). From archival data on Company Charlie’s website, it is stated that export activities increased by 78% and represent 50% of the total revenue from the companies in 2019 as a result of the internationalisation facilitation. Company Charlie’s CEO confirmed their growth in a 2020 press release by commenting “We have seen significant growth in the USA market and

also in Europe as a whole and hope to build on our client base and continue working with businesses across these markets."

Moreover, participants from the relevant inputs for incubation and mediators for network formation highlight the importance of mediators external to the entrepreneurial ecosystem such as the Department for Economic Development of Mentor, Ohio, in the US.

5.3.3 External Mediators

This research defines an external mediator as an organisation that actively aims to liaise between organisations from different entrepreneurial ecosystems. For the Nottingham Biopharma Ecosystem, the findings identify the Department for Economic Development of Mentor (DED), Ohio, in the United States as an external mediator. The DED connected with MEM with the goals of facilitating and promoting business partnerships between SMEs in Mentor, Ohio, in the US, and the East Midlands, especially Nottingham, in the UK.

Mentor, Ohio, is a second-tier location in the US that shares some similarities with Nottingham in terms of size, local stakeholders (membership organisations, incubators, universities, and hospitals), and lack of private and government funding when compared to biopharma innovation hubs such as Boston (From interview DED1).

These similarities are not only perceived by the stakeholders in Nottingham as suggested by the Director of Economic Development from Mentor, Ohio: "the East Midlands is very good because we are very similar regions. Similar types of companies and similar demographic profiles so it kind of fits what we are doing here" (from interview DED1).

Through a collaboration agreement signed in 2019 with MEM, Mentor's Department for Economic Development (From interviews DED1 and MEM1) is now an international stakeholder for the biopharma, biotech, and med-tech industry in the East Midlands, especially in the Nottingham Biopharma Ecosystem. As detailed by MEM's Project Manager and Mentor's DED, the relationship with this overseas organisation aims to create a two-way business and knowledge flow between companies and support organisations in the East Midlands and their Mentor, Ohio, counterparts (From interview DED1).

The research participant from Mentor's DED detailed during the data collection interview that the relationship with MEM started with initial enquiries from a consultant formerly working for them on a project of internationalisation for local companies. These enquiries led to initial contact with MEM at a Med Tech conference that took place in Coventry in 2018 (From interview MEM1).

Research participants from Mentor's DED, MEM, and BioCity Group agreed that the knowledge flow between support organisations from the two regions is a key area for this partnership. BioCity's Corporate Development Director pointed out that, at an early stage, this international relationship is important in terms of sharing know-how with Mentor's incubator and introducing key gatekeepers in each location to companies from the other (From interview BIO1).

MEM suggested that they aim to use this relationship to provide further support to their members by helping them to establish international connections to promote their businesses in the US market. Furthermore, MEM is looking for Mentor's DED to "give them" American

companies that Nottingham-based companies can trade or collaborate with (From interview MEM1).

Mentor's DED has been looking to establish these relationships with other cities across the UK and Europe; however, the East Midlands interaction is the only one with a formal agreement due to MEM's role in the region (From interview DED1).

They further illustrated the role of MEM in the region by commenting that the way the organisation is run and the wide portfolio of members enables Mentor's DED to achieve their goals for internationalisation of Mentor's DED and added their perceptions on the city: "I think Nottingham, given its history and location, and demographics, is a very fertile ground for companies' development in these areas, there is no question about that." (From interview DED1).

Mentor's Director of Economic Development revealed that Mentor's long-term goal is to explore these relationships as far as possible so they can lead to a potential economic twinning between both regions. To accomplish this goal, they reciprocate MEM's efforts by providing Nottingham-based companies with the right connections to enter and explore the US market: "I couldn't tell you how thrilled we are to have the relationship with them because they are such an amazing facilitator of what we are trying to do. We want to make sure that we are reciprocating as much as we possibly can for their companies" (From interview DED1).

BioCity's Group Corporate Development Director suggested at first, this relationship will also provide an important platform for learning "best practices" for Mentor and Nottingham; however, they believe that the economic twinning (Mentor's DED long-term goal) is still a long way from

happening due to the limitations second-tier cities present: “I think that it will take time, but I think we need to get on that, and Medilink has been running missions, but I do think that they are not Boston, we are not Cambridge, so how in those second-tier regions can one make successful ecosystems (with a lack of significant private funding)?” (From interview BIO1).

Mentor’s DED is actively working to grow their relationship with MEM and BioCity and to potentially expand upon it. In November 2019, a delegation from Mentor’s DED visited Nottingham and other locations across the East Midlands to communicate their goals and the benefits that working with them can bring to UK-based companies. The connection with local companies and local stakeholders was facilitated by MEM. These missions are joint efforts and are expected to continue in the coming years as revealed by Mentor’s Director of Economic Development: “We just continued to grow that relationship (with MEM) and fostered that relationship since this point in time last year (2018)” (From interview DED1).

The Director of Mentor’s DED attended MEM’s Annual General Meeting in November 2019 and announced that the event for Nottingham-based companies visiting Mentor, Ohio, will be repeated in October 2020. Companies planning to attend will be able to apply for support from Mentor’s government through the DED, and the UK government through MEM and other offices that promote internationalisation for UK SMEs.

Overall, mediators in the Nottingham Biopharma Ecosystem aim to support business growth by facilitating interactions between SMEs within the entrepreneurial ecosystem, government-led agencies, and even foreign organisations. However, to have a better understanding of the

entrepreneurial ecosystem, it is important to address not only the heterogeneity of its members but also their interactions.

5.4 Cognitive Proximity in the Entrepreneurial Ecosystem

To have a better understanding of how a second-tier region can facilitate the genesis and development of an entrepreneurial ecosystem for biopharma SMEs, it is important to also acknowledge the interactions between the available inputs and mediators while assigning roles to those with the foremost relevance. Figure 10 presents an advancement on the IMO framework that showcases the interactions between SMEs, inputs, and mediators in the Nottingham Biopharma Ecosystem through operationalising the construct of cognitive proximity to explore the different state of the identified relationships.

This research identifies that the incubation infrastructure, the development programmes, and access to funding and specialised networks are tightly connected through the common goal of growing the tenant base of the life science-oriented science parks in the entrepreneurial ecosystem by increasing the cognitive proximity of these inputs. According to science park management, through consolidating a physical infrastructure, business acceleration programmes, and funding opportunities for their tenants, this entrepreneurial ecosystem offers an inviting environment to facilitate new venture formation in the life science sector.

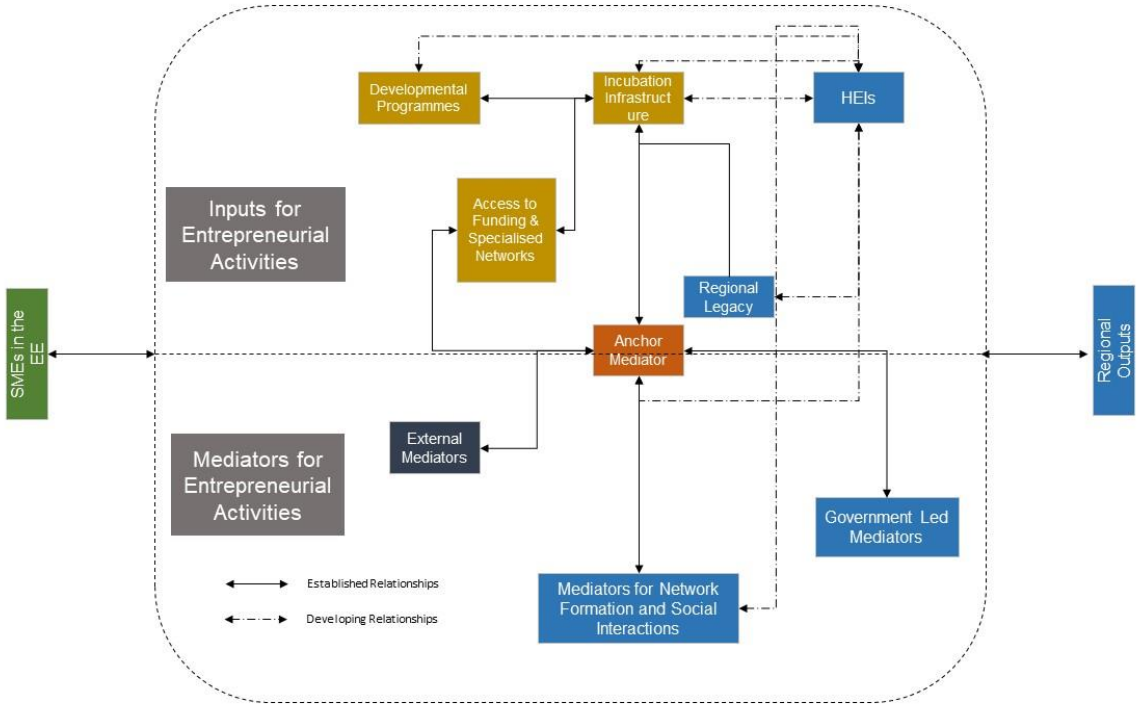


Figure 10. Interactions-based IMO Framework.

The findings suggest that MEM, a mediator for network formation and social interactions, not only is the better-connected member in this entrepreneurial ecosystem but also facilitates meaningful interactions that add value to the members of the ecosystem by supporting activities useful for the business growth of SMEs and innovation. This mediator consolidates the regional goals of supporting SMEs in the life science sector, especially in the biopharma industry by acting as the anchor mediator for the entrepreneurial ecosystem. From our findings, this research defines an anchor mediator as a networking support organisation tailored to the specific entrepreneurial activities and innovation capabilities of the region.

The following sections of this chapter will therefore explore the more relevant interactions within this entrepreneurial ecosystem in a second-tier region. First, this thesis will explore the

interactions between the anchor mediator and the incubation infrastructure managed by BioCity Nottingham.

Then, this study will present the findings regarding the interactions within the specialised science parks in this entrepreneurial ecosystem through cognitive proximity as it is argued that interactions in science parks are likely to facilitate entrepreneurial activities and innovation (Bonacina Roldan, Hansen and Garcia-Perez-de-Lema, 2018; le Duc and Lindeque, 2018; Lecluyse, Knockaert and Spithoven, 2019).

5.4.1 Cognitive Proximity Between the Anchor Mediator and the Incubation Infrastructure

MEM is the anchor mediator of this entrepreneurial ecosystem, and it is located within one of the specialised science parks in this entrepreneurial ecosystem and is in constant communication with the science park's management to avoid redundancy of support. MEM's Project Manager explained that they thought this was a logical place to locate as MEM considers BioCity Nottingham the centre of the ecosystem; nonetheless, this has resulted in members of the cluster having problems differentiating between the two organisations (From interviews BIO1 and MEM1). This reveals that the anchor mediator and the organisation managing the incubation structure share a common goal which helps to improve their cognitive proximity as shown in Figure 1 in Chapter Two.

According to BioCity's Corporate Development Director, through the lifecycle of the entrepreneurial ecosystem, both brands have had different levels of recognition and have even been thought to be the same organisation at times. This was confirmed by the internal participant from Company Bravo as they were not sure of which organisation delivers the

special interest groups the company has attended (From interview BRAVO1). For MEM's Project Manager, this confusion illustrates how closely both organisations work; however, he added that both organisations still need to work hard on creating and enforcing their own identities so they can highlight the benefits each organisation provides (From interview MEM1).

This close relationship helps MEM and BioCity Group to achieve their individual goals in the region of providing business support to their members and tenants respectively as MEM is a support organisation whereas BioCity Group is primarily a landlord for these SMEs.

MEM and BioCity Group have offices and science parks, respectively, across different regions in the United Kingdom (Alderly and Glasgow); nevertheless, the strongest collaborative relationship between a Medilink's office and a BioCity Group science park is found in Nottingham (From interviews BIO1 and MEM1). As confirmed by BioCity's Corporate Development Director: "I think that East Midlands is definitely one of the strongest… The East and West Midlands I would say that are probably the strongest. It helps that they are in here, based in our building, and I supposed that depends again on the make-up of your tenant base." (From interview BIO1).

BioCity's Corporate Development Director detailed that for MEM to achieve their goals, they have developed relationships with other regional stakeholders, such as BioCity Group, the AHSN, venture fund managers, and overseas organisations in other second-tier regions (specifically the Department for Economic Development in Mentor, Ohio).

Summarising the information from our participants, MEM has different roles in the cluster. Their primary role is to act as a membership organisation that facilitates social interactions between

their members through special interest groups, social events, and one-on-one feedback from their members. Their second role is to manage government (either national, regional, or local) funding to provide business support for healthcare SMEs in the region, including those that are not members, while another role is to help regional SMEs to enter foreign markets such as the American market. According to research participant MEM1, these roles have evolved according to the needs of the SMEs in the entrepreneurial ecosystem through constant feedback and communication. To achieve its goals, they have established relationships with the different inputs and mediators presented throughout this chapter.

5.4.2 Cognitive Proximity within the Specialised Science Parks

Enabling meaningful relationships between organisations based on the same science park can facilitate entrepreneurial activities and promote collaborations and partnerships within the science park (Porter, 2000; Delgado, Porter and Stern, 2014). These relationships are thought to facilitate access to wider networks and to new knowledge from other off-science park and off-ecosystem collaborators a company might have. To achieve this it has been mentioned a good relationship between companies based in the same science park and the science park management itself is needed (Giuliani, Balland and Matta, 2018).

Intra-science park relationships are important to consider when exploring an entrepreneurial ecosystem in a second-tier region, as these interactions have the potential of contributing to the outputs of the entrepreneurial ecosystem by promoting entrepreneurial activities and partnerships and collaborations within the science park.

For companies in the biopharma industry based in the specialised science parks, social interactions have the potential of promoting entrepreneurial activities while facilitating partnerships or collaborations. However, according to research participants from Companies Alpha, Bravo, Charlie, Delta, Foxtrot, and Golf, meaningful interactions are difficult to promote within the science parks in this second-tier region.

As mentioned, when exploring the contextual factors of the entrepreneurial ecosystem, BioCity Group manages both sites, and according to their Corporate Development Director, the group is making an effort to improve the company-to-company interactions, first, within the same science park, then across both sites, and eventually across all the BioCity Group locations in the United Kingdom.

Though companies within the Nottingham City science park have a common language in the form of the life science jargon, they do not have opportunities to scout for overlapping knowledge bases within the science parks. Participant companies based at the specialised science parks revealed that the management group promotes networking and interactions through social activities such as pizza meet-ups, ice cream afternoons, and joint activities with the “creative quarter” of the city. The Corporate Development Director detailed that these activities are planned to “create a good environment, but not so much about getting companies to formally interact” (From interview BIO1).

These events have a different reception depending on the background and the position of the research participants in their companies. On the one hand, the research participant from Company Foxtrot (with a background in marketing) commented that these social events are

good for people joining a company already established on the sites or for companies that are just starting up; while on the other hand, Company's Delta's founder (with a background in biotechnology) commented that people attending these events do not socialise with anyone else but the people they already know, usually from the same company they work in.

They detailed that they tried joining the monthly networking event, but they realised that "People mostly go just for the free food. And if you see the attendance, it is really, really poor. And it is always the same people that always attend the events" (From interview DELTA2). They also added that most of these events take place in BioCity Nottingham, so for people in Company Delta (and other MediCity Nottingham-based companies), it is difficult to attend these events just for "pizza and beers". Company's Golf founder agreed on this as they think that these events are great for everyone's morale but "…people go to the event, line up for whatever they are being handed out, but that doesn't create what you would call a company-to-company interaction" (From interview GOLF1).

Company Golf research participants suggested that the pizza nights and ice cream events could be complemented with short presentations where companies can be given a platform to present to other companies their expertise as they are "really not aware" of the different companies at BioCity Nottingham.

Company Delta's Operations Manager revealed that they do not know what people from the other companies on the same floor do, as the relationship goes as far as being "good neighbours" in that they greet each other in common areas or ask for some spare generic lab consumables. Company Delta's founder pointed out that companies could make a bigger effort

to attend the networking events, but running an SME just takes most of the time so they prefer to send over middle management: “The inter-company relationships aren’t probably as good as what they should be. MediCity makes an effort trying to facilitate and foster intercompany interactions, but in small companies, you always have to run” (From interview DELTA1). They also detailed that it is difficult for companies to attend social events as they cannot really “know” if the company will get something from them and added that if the company had to choose from a BioCity Networking event or Medilink Networking event, they would prefer to attend the Medilink one as it is “more likely” for them to find or even “run into” an interesting opportunity.

BioCity’s Corporate Development Director is aware of these concerns from some of the tenants and acknowledged that there are challenges with planning and booking these social events “…it is also about finding the times when I can or can’t run events. Here (BioCity Nottingham) I can do evening events, but at the Medicity site at five o’clock there is no one in the building” (From interview BIO1). They agreed and acknowledged that BioCity Group has an opportunity to improve the interactions within their science parks, and they revealed that this is one of the reasons BioCity Group ask them to return to the organisations after an experience as a Business Developer for a Science Park and Incubator in the “Golden Triangle” area.

With them as BioCity’s Corporate Development Director, BioCity has started a new event called “Come and meet your neighbour”; however, they think that BioCity Group still needs to “find out what they (the tenants) expect to see from other companies.” The research participant from Company Foxtrot suggested that BioCity Group could probably try a mix of events: “I think a

mix, probably. I think there is time for different purposes, so it varies" (From interview FOXTROT1).

The specialised science parks in the Nottingham Biopharma Ecosystem facilitate social interactions for SMEs sharing a common language; however, there is a lack of opportunities for connecting epistemic communities with an overlapping knowledge base. The knowledge bases within the science park are broad as they go from cosmetic or Medtech to CROs and drug discovery organisations.

5.4.3 Cognitive Proximity between Science Park Management and Tenants

In terms of having a relationship with science park management, there were contrasting findings between the participant SMEs. Science park management has selectively chosen companies to actively support, which has led other science park tenants to become cognitively distant from other organisations on-site. These differences in cognitive proximity between tenants and science park can promote a "silo mentality" as revealed by research participant GOLF1.

Research participants from companies Charlie, Delta, and Foxtrot commented that they have a good relationship with BioCity Group Management as they are in constant communication with people within the organisation. According to archival data from BioCity's web page, the founders and CEOs for Companies Charlie and Foxtrot have been involved with events organised by BioCity aimed at external audiences. Moreover, the Director of Marketing for Company Foxtrot explored the relationship the company has with the Science Park Management Group – "They very much pay attention to us, they are supportive of us, they are both or landlord and being supportive in many other ways." They added that BioCity Group also

organises events that are aimed at the commercialisation stage of the drug discovery pipeline that has been useful for them as Director of Marketing as they confirmed that “they (BioCity Group) do realise that they have a lot of people that are non-scientists, and who are working in-depth in science-oriented companies” (From interview FOXTROT1).

Company Delta’s founder revealed that the company has a close working relationship with BioCity Group. Company Delta attended the BioCity developmental programmes and raised BioCity’s interest as they wanted to invest in Company Delta but could not do it at the time: “So our investor was introduced to us by BioCity because BioCity, when I attended the course, wanted to invest but they weren’t able to so they introduced me to our investor, which then led to getting the funds” (From interview DELTA1). They detailed that having BioCity involved from the beginning helped to open the door of a lot of contacts that helped company Delta “get up and running.” They also added that BioCity’s Group interest in the company has been such that BioCity’s investment group has invested in the second seed funding round.

The relationship between Company Golf and science park management has not been constant through the years, according to research participants from the company. The CSO and founder of Company Golf commented that the relationship with science park management at the beginning “…was brilliant as they provided business strategy and development support for around eighteen months”; this support was provided through funding coming from a European Union Project. However, after this support ended, they have not been in constant communication with science park management as they consider that they have become “just landlords” since the group “started having aspirations of becoming a brand” to fill up the science

parks with companies. They also added that science park management has “kind of forgotten about their role as a support organisation” as they depend on the success of the companies within it.

Company Golf management revealed that they have tried to connect with other companies in the specialised science park; however, those efforts have been met with resistance from science park management. Company Golf’s founder detailed that they have tried to organise “pizza presentations” with a science focus for companies to showcase their “specialised marketing material” so everyone can be aware of what everyone else is doing. They believe that science park management prevents from organising events to avoid the companies from having a more recognisable brand than their own, which leads to “a silo mentality” among the tenants. An external collaborator for Company Charlie based in BioCity agreed and made clear that they tend to go to MEM instead of BioCity Group if they need any support.

5.5 Chapter Summary

This chapter reports on the contextual factors that this second-tier region provides to biopharma SMEs in the entrepreneurial ecosystem and their interactions through cognitive proximity. Through the IMO framework, this research identifies the relevant inputs and mediators in this entrepreneurial ecosystem for biopharma SMEs in a second-tier region and operationalises cognitive proximity to discover the interactions between them that promote and facilitate entrepreneurial activities and innovation efforts.

This study considers inputs as the contextual factors that promote start-up formation, innovation, and entrepreneurial activities for biopharma SMEs in an entrepreneurial ecosystem. Through the findings, this research identifies regional legacy, incubation infrastructure, developmental programmes, access to funding and networking opportunities, and higher education institutions as the relevant inputs in this entrepreneurial ecosystem. On the other hand, mediators are organisations that liaise between SMEs and other organisations to promote entrepreneurial activities and innovation. This research classifies mediators as mediators for social network formation and social interactions, government-led mediators, and external mediators. Furthermore, this research proposes the theoretical construct of the anchor mediator, which this research defines as a networking support organisation tailored to the specific entrepreneurial activities and innovation capabilities of the region.

This study utilises an interactions-based IMO framework to better represent the interactions within the entrepreneurial ecosystem through operationalising the construct of cognitive proximity. This framework allows for a better representation of the relevant inputs and

mediators, and their interactions within the entrepreneurial ecosystem. Finally, this chapter explores the interactions within the specialised incubation infrastructure by considering the relationship of SMEs within the science parks and the rapport between tenant companies and science park management.

A consolidation of the findings in this chapter suggests that this second-tier region overcomes a lack of funding and targeted government policy through the interactions between SMEs, inputs, and mediators. Most importantly, the shared goals of regional development and business support for life science SMEs allow for effective relationships that add value to SMEs in the ecosystem to be in constant development.

The next empirical chapter explores the interactions which are involved in collaborations and partnerships in the biopharma industry from the perspective of SMEs. The chapter will take into account the SMEs' perceptions of the interactions involved according to recently proposed research on the lifecycle of partnerships in the biopharma industry (Schweizer and He, 2018) by exploring the importance of cognitive proximity at each proposed phase.

Chapter Six – Empirical Findings II

The second objective of this research is to understand the lifecycle of partnerships in the biopharma industry from the perspective of SMEs in a second-tier region. Partnerships are relevant for SMEs in second-tier regions as they allow companies to leverage resources such as scientific knowledge even when constrained by the lack of resources characteristic of second-tier regions (Wang, Lestari and Yang, 2015; Bigliardi and Galati, 2018; Gillespie, Privitera and Gaspero, 2019). This chapter explores the lifecycle of partnerships in the biopharma industry from the perspective of SMEs within an entrepreneurial ecosystem in a second-tier region by deploying cognitive proximity as a theoretical lens.

To understand the lifecycle of collaborations and partnerships in the biopharma industry, this research builds upon McAdams's (2014) and Schweizer and He's (2018) findings by proposing cognitive proximity as an enabler to help for a better understanding of these interactions. According to McAdam (2014), the perception the different parties have on their relationship is important. Therefore, exploring the perceptions that companies have on their collaborations through cognitive proximity helps this research to understand the lifecycle of collaborations and partnerships in the biopharma industry from the perspective of SMEs as research usually focuses on collaborations involving large biopharma companies (Michelino *et al.*, 2015; Schweizer and He, 2018).

This chapter explores the perceptions these companies have during the phases of ignition, inception, and implementation investigated by Schweizer and He (2018) while exploring how

they affect organisation-to-organisation interactions. Table 9 presents a summary of how the participant SMEs engage with the different phases of the partnership's lifecycle.

This study considers cognitive proximity as a manifestation of the cultural homogeneity between organisations (Molina-Morales, García-Villaverde and Parra-Requena, 2014) rather than a measure of distance between them (Boschma, 2005). Therefore, this research proposes cognitive proximity as an enabler through the different phases (Schweizer and He, 2018) of partnerships and collaborations in the biopharma industry from the perspective of SMEs within an entrepreneurial ecosystem in a second-tier region.

Unit of Analysis	Company Profile	Ignition Phase	Inception Phase	Implementation Phase	Evaluation Phase
Company Alpha	• Founded in 2014 at a university in the Golden Triangle. • Licenses therapeutic molecules to larger biopharma companies. • Moved their R&D area to Nottingham in 2017.	• Establish a priority list to contact. • Attend networking sessions in specialised conferences. • Use intermediaries such as business consultants.	• Assess the skill set of a potential partner. • Assess personality traits in potential partners. • Consider that the fit between individuals is important. • Establish workloads and review processes. • Determine goals.	• Establish meetings to review project milestones. • Rely on constant communication.	• An active process through the partnership. • A detailed assessment is done at the end of a project.
Company Bravo	• Founded in 2011 as a spin-off company of a local university. • Founded after the restructuration of a precursor company. • Develops and commercialises platforms for tissue-specific regenerative medicine.	• Attend scientific conferences and "try to meet people." • Use intermediaries from their life in academia.	• Establish mechanisms for data sharing and communication. • Propose a short-term project before committing to a longer and more expensive partnership. • Determine goals.	• Establish a framework based on weekly meetings and on-site visits.	• An active process through their partnership.
Company Charlie	• Founded in 2011 after the regional R&D labs of a large biopharma were shut down. • The company is a contract research organisation (CRO) specialised *in vitro* DMPK assays.	• Upon foundation, the CEO would go door-to-door to meet other tenants in their building. • Use intermediaries from their previous employment. • Try to understand differences in culture.	• Assess their knowledge base and potential complementarity. • Investigate their personalities and "ethos". • Get the relevant teams in touch to plan workloads. • Determine goals.	• Communication is done between the relevant teams. • Rely on data sharing platforms.	• An active process through their partnerships. • Partnerships are reconsidered if there were problems during implementation.
Company Delta	• Founded in 2015 as a spin-off company from a local university. • The company develops biotherapies for their use in ophthalmology.	• Attend networking events within scientific conferences. • Use intermediaries from their life in academia. • Try to understand differences in culture.	• Use contracts to establish the activities for the implementation phase. • Use a multicultural team to engage with partners from different countries. • Determine goals.	• Communication and workloads are held as stated in their contracts.	• Partnerships are reviewed in terms of the established contract and might be reconsidered if certain goals are not fully met.
Company Echo	• Founded in 2001 after a Nottingham-based R&D biopharma was shut down. • The company is the R&D branch of a large biopharma company based in Europe. • The company operates within the ecosystem as an SME.	• Scout for partners through the intermediaries in the region. • Use intermediaries to make the scouting process more efficient while securing a good fit in terms of the knowledge base.	• Parent company accesses the cognitive proximity of a potential partner. • Parent company requires partners to attend a course about organisational culture. • Determine goals.	• Implement or adapt current IT resources to establish platforms for data sharing.	• Their parent company reviews if the goals of the partnership are met.
Company Foxtrot	• Founded in 2004 after a Nottingham-based R&D biopharma was shut down. • The company is a CRO for drug discovery projects.	• Use intermediaries to scout for potential partners. • Only contact companies that have complementary skills. • Try to understand differences in culture.	• Get people with similar knowledge base and culture together to interact. • Determine goals.	• Implement a platform for sharing data. • Have on-site visits to discuss milestones.	• An active process through their partnerships. • If the partnership is successful, they will begin to evaluate acquiring their partner.
Company Golf	• Founded in 2011 after the regional R&D labs of a large biopharma were shut down. • The company is a contract research organisation (CRO) specialised in preclinical assays.	• Attend networking sessions in specialised conferences. • Scout for companies that can add value to their offering. • Use partnerships to apply for R&D grants.	• Assess a partner's skills, personality, and work ethic. • Determine goals.	• Establish platforms for data sharing. • Constantly communicate through email and phone calls.	• An active process through their partnerships. • The partnership is reconsidered if the goals are not met.

Table 9. SMEs and the Phases of a Partnership.

6.1 Lifecycle for Partnerships from the Perspective of Biopharma SMEs

Schweizer and He (2018) identified three phases for large biopharma companies going through the process of collaborating with external organisations. These phases are part of a framework for a quantitative assessment of potential collaborators; however, this research also considers the importance of the perceptions that SMEs have on their potential collaborators (McAdam *et al.*, 2014) across the proposed phases of inception, ignition, and implementation.

Research regarding collaborations in the biopharma industry usually investigates secondary data publicly available from large companies to determine models for collaboration (Michelino *et al.*, 2015; DiMasi, Grabowski and Hansen, 2016; Schuhmacher, Gassmann and Hinder, 2016; Boni, 2018). Therefore, to have a better understanding of the processes required to engage in these collaborations, this study explores the lifecycle of these partnerships by using cognitive proximity as an enabler for the interactions between collaborating organisations. Figure 11 consolidates this research's findings regarding cognitive proximity as an enabler for the lifecycle of these collaborations while building upon the findings of McAdam (2014) and Schweizer (2018) on contextual factors and partnerships evolution, respectively.

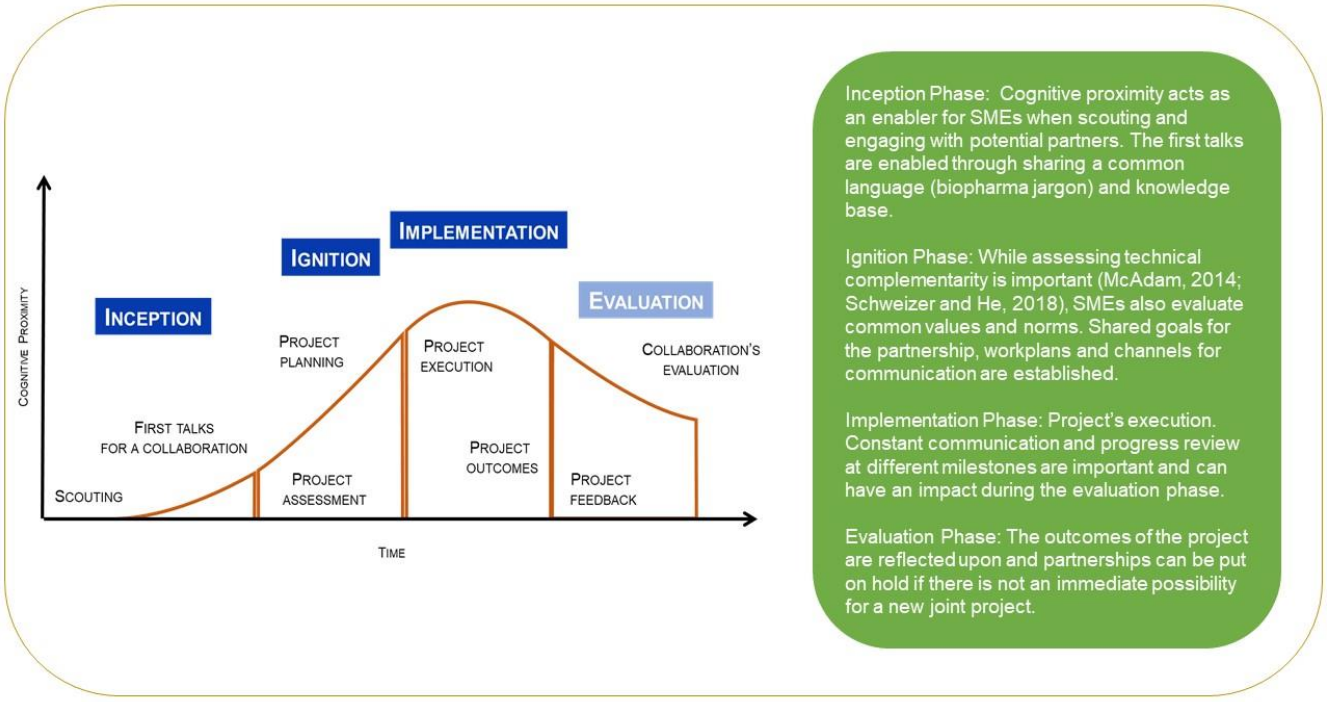


Figure 11. The Partnership Lifecycle Curve. This curve builds upon the phases for collaborations in the biopharma industry (Schweizer and He, 2018) by introducing a curve-like model for partnerships as suggested by McAdam (2014).

6.1.1 Inception and Ignition Phases

The inception and ignition phases are related to the process of scouting or encountering potential partners, assessing the affinity between companies and individuals while setting a working plan to be executed (Schweizer and He, 2018).

The findings in this research suggest that cognitive proximity acts as an enabler during these phases, as according to our research participants, it is important to find a common language between organisations, to define the organisation's strategic plans for finding collaboration partners, and to be able to assess a potential collaborator's hard and soft skills. Furthermore,

research participants address the importance of acknowledging cultural differences and personal networks through cognitive similarities to facilitate engagement through these phases.

Establishing a Common Language

The founder and CSO of Company Golf revealed that before engaging in conversation with a potential collaborator, it is important to establish a common language so the involved parties can effectively communicate and signalled that for the biopharma industry the common language is science: “You need to be able to communicate science first of all… after that, we follow that with pounds signs, numbers, milestones, what they represent, etcetera. But predominantly the first thing should be science” (From interview GOLF1).

The importance of familiarity with the scientific language is confirmed by the research participants lacking formal education in life sciences. The Director of Marketing for Company Foxtrot suggested that even though it is not possible to become a scientist, it is possible to learn to speak the language. An external participant from Company Charlie agreed as they faced the “language barrier” when her company started collaborating with Company Charlie: “I never will understand a 100% of the science or will intend to, but what I need to understand: the features and benefits of what they do, who their audience is, and how to communicate to them, so you need to have some understanding” (From interview GOLF2).

Scouting for Partners through Common Language and Knowledge Base

When scouting for potential collaborators, research participants agreed on the importance of attending science-led events – either conferences, workshops, or trade shows – and pointed out the importance of the science component as attendees are more likely to share the common language.

Research participants commented on the importance of a strategic plan when attending events; as detailed by an internal informant from Company Delta, it is important to have an internal priority list of people and companies that could be suitable partners. Company Alpha also follows this strategy as the internal informant revealed that they have an internal priority list of people whom they think could be good partners and found that conferences have been a good way to connect with those people. An internal informant from Company Charlie commented in detail that, according to their experiences, collaborations in the biopharma are usually between companies that complement each other: “Well, we develop relationships with companies that don’t compete, but highly complement our offering” (From interview CHARLIE1). They also added that it is important for being proactive when approaching potential partners.

However, strategic planning is sometimes outweighed by coincidences and “unexpected interactions” as explored by one of the research participants from Company Delta. An external research participant from Company Golf mentioned that their involvement with Company Golf started after a scientific talk at a conference: “They (Company Golf’s CSO) saw me present at an event once, we started talking and over a couple of years we developed the idea” (From interview GOLF2). This is further supported by research participants from Companies Charlie,

Delta, and Golf. In fact, an internal research participant from Company Delta commented: “You might go to an event with something in mind, but then you might meet somebody who knows somebody and who then knows somebody, and that leads to something really interesting, so you never know” (From interview DELTA1). They revealed that most of the collaborators they have met came from engaging with people for one reason which then led to the company’s management becoming aware of another need they had. A research participant from Company Bravo commented that a key activity is “just meeting people, understanding what their capabilities are, and then keeping them in mind as to when they might be needed (From interview BRAVO1).”

Identifying Common Values and Norms

Another theme that research participants consider during the inception stage of the collaboration is the perception that the people involved have of the potential collaboration and more importantly, of the people representing a potential collaborating company.

As mentioned by a research participant from Company Golf, part of the strategic planning is assessing the technical and scientific skills of a potential collaborator; nevertheless, the personality and how easy they are to work with is a factor as important. The Head of Global Business Development in Company Charlie agreed on this by commenting: “So in order to work with a company, we have to know they are experts in their area, that they have high-quality research or high-quality services, and our personalities and ethos need to match as well. So, the soft skills are as important as hard skills” (From interview CHARLIE1).

The Director of Marketing for Company Foxtrot agreed on this by detailing that this is a reason why the company looks for credibility in the industry and credible people to collaborate with. The Research participant from Company Alpha revealed that before going into the ignition or implementation stage, “it all comes down to personality”. They also argued that “a good fit” between individuals or a group of individuals that can easily communicate and are open to sharing information makes collaboration projects smooth to run.

The Head of Global Business Development for Company Charlie argued that assessing the soft skills starts by analysing the core values of the potential collaborators. Since Company Charlie is known for their quality and good customer relationship management, they don’t want to collaborate with anyone who would detract from that ethos as it would eventually cause problems: “So you are looking for somebody similar. You are really lucky if you find somebody with focus, and that is willing to go the extra mile to help clients, rather than just cash out” (From interview CHARLIE1).

Company Charlie suggested the importance of both technical expertise and personal relationships and how easy it is to get along, as it would be difficult to have a potential collaborator they “might like as individuals but who cannot deliver the work”. The balance between technical expertise and “soft skills” was a theme that an external research participant from Company Golf agreed on as they consider that both companies (theirs and Company Golf) share “fairly similar” values as the CSO of Company Golf is very innovative, which they defined as “a good thing to have in a partner.”

An internal research participant from Company Charlie compared the process of scouting and getting to know a collaboration partner to “a courtship” where first the key individuals meet and try to get along, then you meet their team and afterwards you have your team meet their team. They also added that if you take on already established relationships, the worst thing to do is a “hard handover” as it is important to respect what the previous person accomplished so the collaborators are more open to accepting the new person in the role. This research participant went through this process of taking over an established partnership as the company’s CEO started to delegate some relationships: “So they have a history with the first person, and I need to respect that the first person has a background knowledge of them that I would never have so I need to get up onto speed” (From interview CHARLIE1).

The proposed phases of collaborations in the biopharma industry (Schweizer and He, 2018), as mentioned by a research participant from Company Charlie, are about “looking at the whole situation and finding a way to work together.” Nonetheless, they acknowledged that is difficult to assess every aspect of a potential collaboration before work starts, and “digging down” to look into a company’s quality and ethos becomes easier when work is undergoing as the “hard skills” are the ones that are noticeable first, “so it is easier to see what they do and then even easier to see if they do it well.”

Closing Cultural Differences through Cognitive Proximity

An important issue for participant companies while scouting and assessing the cognitive proximity between potential collaboration partners is to acknowledge the cultural differences between the people representing the companies.

Company's Foxtrot two main markets outside the UK are the United States and Japan. Their Director of Marketing revealed that, in Japan, the culture is more conservative in terms of risk, so the conversations and processes take longer as collaboration requires the people involved to build and earn each other's trust whereas, in the US, the talks tend to be more fast-paced. To navigate through cultural differences, the research participant from Company Foxtrot made it clear that the company uses people familiar with such cultures to liaise with these companies during the inception and the ignition stages: "Fortunately, in our company, we got two Japanese scientists, two very experienced scientists, who are working closely with our CSO, who is leading our efforts there with the Japanese market and customers." They added that for business development in the US, the company hired a person with already established connections and experience in the American market.

An internal research participant from Company Charlie agreed on the importance of considering these cultural differences at these stages of the collaboration by revealing that it is a key activity to identify if people would tend to be more transactional, like in the US or Germany, or if they would engage first in small talk such as "motorbikes or craft beer" as they do in countries like Spain.

Using Personal Relationships to Ensure Cognitive Proximity

To try to avoid collaborating with companies that cannot deliver on the technical skills or with organisations that might be cognitively distant, research participants commented that their size allows them to rely on referrals and recommendations from people within their network.

The Research participant from Company Alpha detailed that the company has engaged with a current collaborator using this strategy: “A collaboration with a Golden-Triangle university starting with a person who was coming to do some consulting for us on a technical side of biotechnology, and it was their idea to connect us with someone else they were working with” (From interview Alpha1). This collaboration started and was followed up by applying for an Innovate UK grant for a project that as of October 2019 was at early stages of development.

An external collaborator of Company Charlie commented that the relationship between their company and Company Charlie started after having them referred by a common personal relationship from a “previous life”. Research participants from Companies Charlie, Delta, Echo, Foxtrot, and Golf agreed on the importance of the support from networks from their previous roles in industry or academia for activities such as scouting and engaging with potential collaborators or recruiting new personnel for their companies.

A research participant from Company Delta confirmed that “previous life relationships” have helped the company to collaborate with research centres and companies in places such as India and Denmark as they have been involved in the field of their company services as an academic since 1999. Previous “network connections” can also be useful to improve add value for their current company as revealed by the Head of Global Business Development for

Company Charlie as they remarked that “Another reason I moved to Company Charlie is that I could see that my old network needed the services that Company Charlie offers” (From interview CHARLIE2).

Before entering the implementation phase, research participants commented that the parties need to establish processes to review the progress of the project and to quickly communicate if needed. The research participant for Company Alpha expounded that when companies are applying for Innovate UK funding, the application requires them to provide a work plan with milestones, work packages, and communication strategies they will use for the grant officer to monitor the progress of the project. Nevertheless, when collaborating outside the context of a grant, companies usually work hard to establish these processes as collaborations might fail at these phases if this is not accomplished. Moreover, identifying common values and cultural differences is not enough as mentioned by the participants since they consider that other components of cognitive proximity, such as common business goals, objectives, and balanced workloads, are important for mutually beneficial partnerships and collaborations.

6.1.2 Implementation Phase

During the implementation phase, the work plan created during the ignition phase is executed between the collaborating organisations (Schweizer and He, 2018).

Research participants from Companies Alpha, Charlie, Foxtrot, and Golf commented that for the implementation phase, communication, transparency, and effective exchange of information are important. A research participant from Company Golf defined “having transparency” as an effective way to show the data coming out of the project on demand to

every involved party, from the collaborator to the customer they are doing the project for. They added that relevant people across the different organisations need to be in the loop through an "effective IT platform" for data sharing during the project's duration.

The research participant from Company Foxtrot highlighted that only when the execution of the work plan starts can you see if collaborators can "pull their weight as well" as there are some companies that "just try to tag along" and do not add anything to the workload once the collaboration starts. For Company Golf's founder and CSO, a good collaboration depends on every involved organisation "putting in enough effort", which can be noticed if periodical meetings are set in place to monitor progress. Research participants from Companies Alpha, Bravo, Charlie, and Delta agreed about the importance of these type of meetings and added that inspection visits are usually needed for accountability.

An external collaborator for Company Charlie was in charge of overseeing the joint marketing and communication activities between Company Charlie and a former collaboration partner. According to Company Charlie's Head of Global Business Development, Company Charlie and their former collaborator complemented each other's expertise "quite well as one could do what the other could not." The external research participant's role was to put together a combined plan to communicate the joint services those companies were providing together at the time so it could be showcased at conferences and on their websites. Company Golf's founder and CSO agreed on the importance of communicating the success of collaborations as they become "specialised marketing material" which allows for the creation of new conversations with either

potential partners or customers at science-led events such as conferences, workshops, and webinars.

6.1.3 Evaluation Phase

Research participants from companies address the importance of evaluating collaboration partnerships after each project. According to research participants from companies Charlie and Foxtrot, meeting their partners at the end of each collaborative project (even unsuccessful ones) is important as this process allows them to reflect on any potential opportunities for further R&D projects or the production of “specialised marketing material”.

However, interactions to evaluate completed projects and the future avenues to explore for the partnerships are limited for SMEs in a second-tier region due to a lack of funding. A research participant related to the company Golf acknowledged that funding for collaborative projects is important to keep the relationships active. They detailed that once the Innovate UK grant funding the activities related to their collaboration ended, it has been difficult to “keep in touch” to build upon their innovation. The extra funding through the Innovate UK grant allowed both companies to engage in a project that adds to the core business of both companies while facilitating additional activities to monitor progress such as visiting each other and being able to contract another party to do some work they needed for the project. As a result of a lack of funding to support constant interactions, partnerships reaching the evaluation phase can become a loop of “hot and cold” interactions. Research participants from companies Golf and Charlie detailed that even successful relationships between collaborators tend to be “hot and cold” depending on the availability of a potential contract of funding.

Another relevant theme at the evaluation phase is that organisations can become cognitively distant as their future business goals from the partnerships can change. A research participant from the company Charlie commented that an increased cognitive distance between collaborators while evaluating projects can happen if one of their collaborators “didn't know what the aim was in the first place. Maybe because they didn't know where they were trying to go, and as a consequence of that, “what then happens is that you get what I would call mission creep.”

Finally, according to a research participant from company Charlie, a collaboration went “cold” and eventually ended because of changes in ownership in their collaborators so the new management had to assess the state of the partnership. According to archival data from company Charlie and their former collaborator, this relationship has ended as they are no longer listed as partners on each other’s web sites.

6.2 Chapter Summary

This chapter explores the lifecycle of partnerships and collaborations in the biopharma industry from the perspective of SMEs within an entrepreneurial ecosystem in a second-tier region. This exploration is accomplished by investigating the relevance of the construct of cognitive proximity through a series of phases investigated in recent research (Schweizer and He, 2018) illustrated through a curve-like model (McAdam *et al.*, 2014) defined by this research as the "partnership lifecycle curve".

The findings identify that cognitive proximity can be considered an enabler throughout the lifecycle of relationships that facilitate interactions between potential collaborators and their key individuals. During the ignition and inception phases, cognitive proximity is manifested as the need for establishing a common language between potential collaborators. Then it mediates the cultural differences while allowing the identification of relevant technical skills and personal values that are important to elaborate a work plan for the partnership.

During the implementation phase, cognitive proximity is important as it facilitates effective communication between partners and other stakeholders across the length of a partnership project. Effective means for communicating progress and organisational accountability are important to develop "specialised marketing material" that benefits the partners involved in a project. Finally, during the evaluation phase, cognitive proximity can act as an enabler that allows partners to critically assess the success of a project. During the evaluation phase partnerships can become a "hot and cold loop" as access to funding is a key factor to maintain

ongoing partnerships in the biopharma industry. Therefore, partnerships can be put on hold or end depending on the prospects of new projects.

Chapter Seven – Discussion

In this chapter, the findings presented in Chapter Five and Chapter Six are discussed in comparison with the relevant extant literature. The discussion begins with a reiteration of the main premise of the thesis while addressing the importance of context when exploring entrepreneurial ecosystems. The constructs of inputs and mediators and their interactions elicited in the proposed theoretical framework in Chapter Five are then discussed to explore what the empirical findings add to the literature in entrepreneurial ecosystems and science parks.

Then, this chapter discusses the significance of cognitive proximity as an enabler through the lifecycle of partnerships in the biopharma industry from the perspective of SMEs. The discussion regarding the lifecycle of partnerships explores the empirical findings presented in Chapter Six that contribute to the literature regarding partnerships and collaborations in the biopharma industry.

The implications for the current and future literature to the academic conversations around entrepreneurial ecosystems and partnerships in the biopharma industry are discussed in the chapter.

7.1 Cognitive Proximity as a Theoretical Lens

This study employs cognitive proximity as a theoretical lens to explore an entrepreneurial ecosystem for biopharma SMEs in a second-tier region. This is accomplished through addressing the following research question “How does a second-tier region support SME activity in the biopharma industry?” This research question was formulated to directly address gaps in the literature on entrepreneurial ecosystems and the academic conversations regarding collaborations and partnerships in the biopharma industry.

This research proposes that cognitive proximity can be used as a theoretical lens to better understand entrepreneurial ecosystems by exploring their members, their interactions, and how they facilitate partnerships for biopharma SMEs. The first research objective of this research was to explore the interactions between inputs and mediators in an entrepreneurial ecosystem for biopharma SMEs in a second-tier region. By using cognitive proximity, this research discovered that in the research setting, the inputs are cognitively close to the anchor mediator as they have the common goal of supporting biopharma SMEs to achieve their particular business goals.

The second research objective was to understand the lifecycle of partnerships in the biopharma industry between SMEs. The findings in this study reveal that cognitive proximity can act as an enabler for the interactions between biopharma SMEs seeking to establish a partnership. Therefore, this research has theoretical contributions to the academic conversations regarding entrepreneurial ecosystems and partnerships in the biopharma industry.

The first contribution of this research is to the literature around the rising theme of entrepreneurial ecosystems. According to Giuliani (2018), taking context into account when exploring entrepreneurial ecosystems can help to refine frameworks and theories while allowing a better understanding of how context shapes their genesis and development (Autio *et al.*, 2014; Robertson, Pitt and Ferreira, 2020). Exploring different contexts hosting entrepreneurial ecosystems can inform policymakers so government policy that better supports the specific members of such ecosystems can be created (Díez-Vial and Montoro-Sánchez, 2017; Lee, 2017; Flanagan and Wilsdon, 2018). Moreover, a call for exploratory research considering science parks as part of an entrepreneurial ecosystem has been made by recent research on innovation and entrepreneurship (Autio *et al.*, 2014; Díez-Vial and Montoro-Sánchez, 2017; Bonacina Roldan, Hansen and Garcia-Perez-de-Lema, 2018; Giuliani, Balland and Matta, 2018; Lecluyse, Knockaert and Spithoven, 2019).

To explore this specific context, this research aims to better understand the genesis, development and current state of the local support mechanisms that interact in the Nottingham Biopharma Ecosystem that facilitate entrepreneurial activities and innovation for SMEs in the biopharma industry. Therefore, this study has implications for researchers interested in entrepreneurial ecosystems in terms of providing empirical evidence that supports the importance of the context they are located in. Overall, the findings from this study regarding entrepreneurial ecosystems provide a theoretical framework for exploring and understanding the context of an entrepreneurial ecosystem where the actors within an ecosystem are classified according to their specific role.

This study supports the research suggesting that second-tier regions require specific research and policy categories that allow for the differentiation that the disparity between these locations and their first-tier counterparts creates (Cardoso and Meijers, 2016). The traditional approach of setting the same benchmarks for the different regions within a country can be problematic and unrealistic as entrepreneurial ecosystems are likely to differ in every region (Caiazza, 2014; Cardoso and Meijers, 2016; Ng *et al.*, 2019).

This research proposes the use of an interaction-based framework that allows for a contextual exploration of the inputs and mediators that promote and facilitate entrepreneurial activity and innovation for biopharma SMEs in a second-tier region. Furthermore, the findings from this study suggest that an effective collaboration between inputs, mediators and SMEs can substitute the lack of funding and targeted government policy which is common in second-tier regions. As the interactions between the members of an entrepreneurial ecosystem are important, this research explores such interactions for this entrepreneurial ecosystem through deploying the construct of cognitive proximity.

The second contribution of this research is to the literature regarding partnerships and the biopharma industry. While research has traditionally focused on investigating the different models for partnerships in the biopharma industry from the perspective of large companies (Michelino *et al.*, 2015; DiMasi, Grabowski and Hansen, 2016; Russo-Spena and Di Paola, 2018), this research explores the lifecycle of these partnerships from the perspective of SMEs within an entrepreneurial ecosystem in a second-tier region.

Exploring the development of these partnerships is important as biopharma SMEs in second-tier regions are more likely to utilise them to leverage resources and knowledge which would otherwise be difficult to access due to their size and underprivileged location.

This research confirms cognitive proximity as an enabler through the lifecycle of partnerships in the biopharma industry from the perspective of SMEs. Cognitive proximity allows a company to move from one phase to the next one while overcoming the different difficulties for establishing partnerships that have been explored in relevant literature (Michelino *et al.*, 2015; Calof, Meissner and Razheva, 2018; le Duc and Lindeque, 2018).

The findings in this research regarding partnerships in the biopharma industry highlight the importance of cognitive proximity as an enabler that can help to better understand the formation of partnerships rather than a quantitative measure of distance between organisations. Moreover, it provides empirical evidence for policymakers on how to facilitate relevant interactions between organisations in knowledge-based industries such as the biopharma sector.

7.2 Exploring Context Through the Inputs-Mediators-Outcomes Framework

The Inputs-Mediator-Outputs framework is usually employed to present literature reviews in several disciplines and has been recently used to identify relevant works on the contribution of science parks to their tenants (Lecluyse, Knockaert and Spithoven, 2019). When utilised as a framework for literature reviews, it allows for an understanding of the different features and attributes that impact the contribution of science parks (inputs) and the mechanisms (mediators) that transform inputs into arbitrary indicators of success (outputs).

This research builds upon such a framework by introducing an interaction-based IMO framework to explore and understand an entrepreneurial ecosystem for SMEs in the biopharma industry within a second-tier region through its inputs, mediators, and interactions between them. Figure 12 presents how this research contributes to the literature on entrepreneurial ecosystems by building upon the IMO framework for exploring the contribution of science parks propose by Lecluyse (2019).

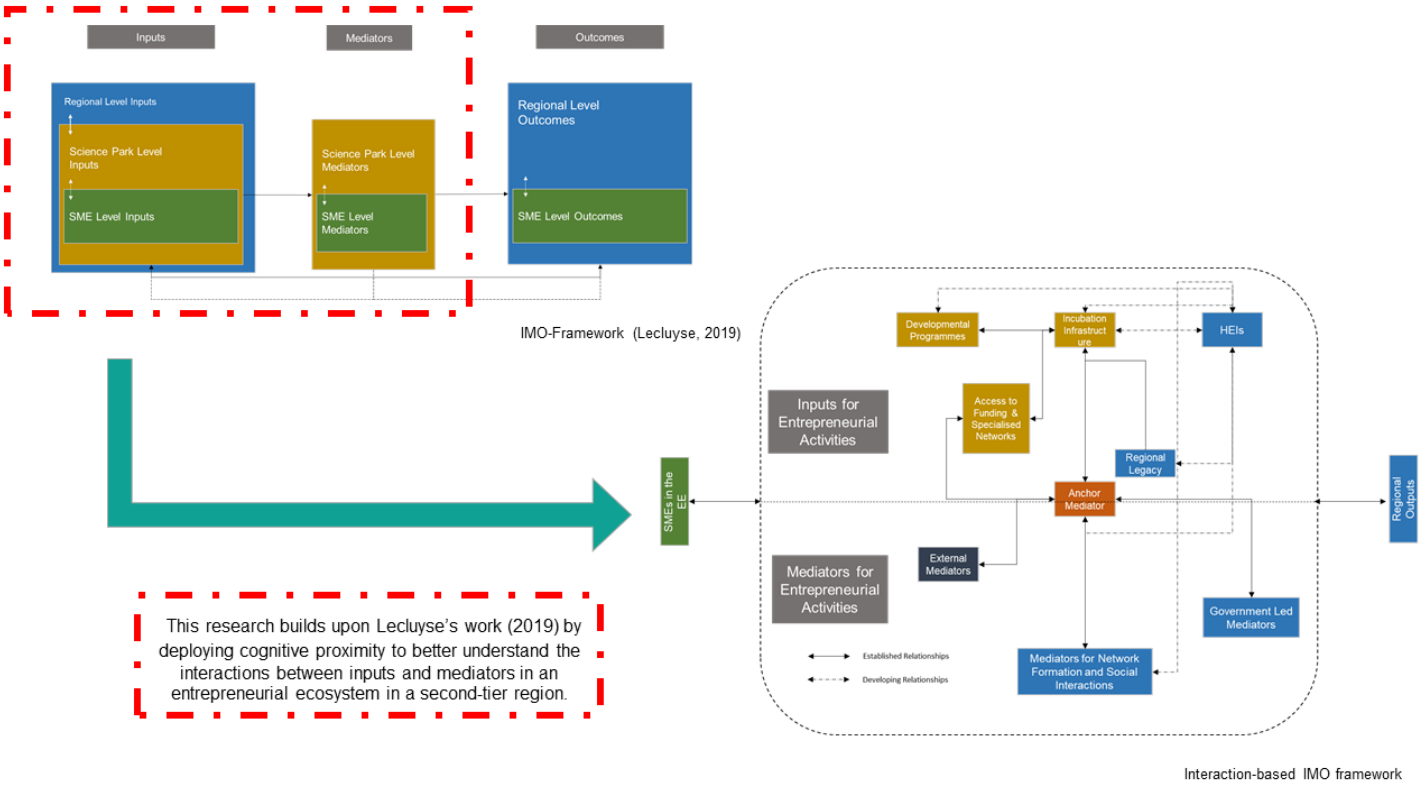


Figure 12. Contribution to Entrepreneurial Ecosystems

To understand the genesis and development of the Nottingham Biopharma Ecosystem, this research considers the contextual factors that facilitate start-up formation in the biopharma industry as inputs, while the organisations that liaise local SMEs with other companies and

organisations (either within or outside their entrepreneurial ecosystem) for networking formation or open innovation activities are considered as mediators.

The current research does not explore regional outputs as measurements for assessing the performance of biopharma SMEs as a result of their location are quite arbitrary, and are in constant development and refinement (Casper and Murray, 2005; Michelino *et al.*, 2014, 2015; Partanen, Chetty and Rajala, 2014; van Egeraat and Curran, 2014; Presutti *et al.*, 2017; Schweizer and He, 2018). Nonetheless, there are industry reports that provide regional-based outputs that illustrate the performance of Nottingham as an entrepreneurial ecosystem for biopharma SMEs (Bio City Group, 2017; Crocker, 2019).

To better understand the context for this entrepreneurial ecosystem, this research also explores the perceptions that SMEs have on the interactions between them and the regional inputs, mediators through cognitive proximity.

7.2.1 Inputs for Entrepreneurial Activities

There is a growing need for environments to support and foster new businesses and as shown by the Nottingham Biopharma Ecosystem Outputs, science parks can facilitate this goal (Anderson and AL-Mubaraki, 2012). Hence, it is important to understand how inputs, mediators, and their interactions form the contextual factors (McAdam *et al.*, 2014) that promote and facilitate entrepreneurial activity and innovation in an entrepreneurial ecosystem for biopharma SMEs in a second-tier region. Through this insight, there is an opportunity to better understand the differences between outputs across different second-tier regions in a given country (Diez-Vial and Fernández-Olmos, 2017).

This research adopts the Inputs-Mediators-Outputs (IMO) framework for literature reviews recently employed by Lecluyse (2019) and defines inputs as the contextual factors that promote start-up formation, innovation and entrepreneurial activities for the biopharma industry in an entrepreneurial ecosystem.

The following sections will discuss the implications of the findings involving the inputs in this entrepreneurial ecosystem. These implications address gaps or add to the literature on entrepreneurial ecosystems. The inputs to be discussed are the regional legacy, the incubation infrastructure, developmental programmes and higher education institutions.

Regional Legacy

The legacy of drug discovery and validation activities has had an impact on shaping the make-up of the current makeup of the Nottingham Biopharma Ecosystem as it is focused on Contract and Research Organisations (CROs) for drug development projects (Ehret, McDonald-Junor and Smith, 2012; Smith, Rossiter and McDonald-Junor, 2017; Alegre, Berbegal-Mirabent and Guerrero, 2019; Crocker, 2019). The presence of highly specialised CROs is likely to contribute to the positive outputs of this entrepreneurial ecosystem as they tend to be a major attraction for biopharma companies and academic research groups focused on drug discovery and development (Zhang, 2015).

The regional legacy within a niche process of the drug development process has allowed this entrepreneurial ecosystem to overcome the lack of private funding by promoting a large number of local SMEs to adopt service-based business models. In terms of private investment in life science start-ups and SMEs, the East Midlands ranks tenth out of the twelve regions with life

science entrepreneurial activity in the United Kingdom (Bio City Group, 2017; Crocker, 2019). However, this second-tier region ranks sixth from these twelve regions in terms of new life science start-ups for the period between 2014 and 2019 (Crocker, 2019).

The findings suggest that the positive outputs in terms of start-up formation and SME activity are also a result of the available incubation structure. Moreover, nearly 80% of the life science companies in the East Midlands are based in Nottingham (Crocker, 2019), and according to our research participants and archival data (BioCity, 2019), companies in the Nottingham-based science parks managed by BioCity Group have a survival rate of 93% on average when taking into account the period from 2007 to 2019.

Incubation Infrastructure and Developmental Programmes

As explored in a recent study (Rossiter and Smith, 2017b) and through data collected from research participants from companies Echo and Charlie, the creation of a life-science-oriented park was a collaborative effort that benefited from taking advantage of the region's context at the time it was founded in the early 2000s (Carvalho and Van Winden, 2017). The development of the science park that promoted the genesis of an entrepreneurial ecosystem for biopharma SMEs was facilitated by the availability of highly specialised talent (Casper and Murray, 2005) in drug development projects. These professionals provided a pool of talent and expertise that could populate the science park even before its formalisation (Alegre, Berbegal-Mirabent and Guerrero, 2019).

The idealisation and formalisation of this science park involved local leadership of the large biopharma company vacating the site, the local universities, and the RDA for the East Midlands

in a process that supports the literature exploring the development of science parks (Storey and Tether, 1998; Nahm, 2000; Shearmur and Doloreux, 2000; Lecluyse, Knockaert and Spithoven, 2019). The specific circumstances for the formation of the first life-science-oriented park illustrate that context is important when understanding entrepreneurial ecosystems (Autio *et al.*, 2014) as a pool of available resources, a desire for building an entrepreneurial ecosystem for the life sciences, and the UK's goal of empowering "science cities" (Flanagan and Wilsdon, 2018) contributed to the creation of the specialised science park in the city which promoted the genesis of the Nottingham Biopharma Ecosystem. Furthermore, science park management took the lead in managing and growing the science park as a private organisation. The growth of the science park that resulted in the creation of a second science park in the entrepreneurial ecosystem is an expected result from the private managerial and ownership structure of managing group (Sofouli and Vonortas, 2007; Hobbs, Link and Scott, 2017; Link and Scott, 2017; Lecluyse, Knockaert and Spithoven, 2019).

The implications of these findings for the literature on entrepreneurial ecosystems relate to the importance of understanding the inputs that promote and facilitate the genesis of an entrepreneurial ecosystem and how these inputs developed through time to meet the needs of its members. Furthermore, there are also implications for organisations looking to promote the genesis and development of entrepreneurial ecosystems and science parks.

These organisations could take into consideration the regional legacy and the available incubation infrastructure in the target region while managing to secure support from relevant stakeholders such as universities and government offices (Anderson and AL-Mubaraki, 2012).

Failing to do so might lead to an entrepreneurial ecosystem with science parks that require the constant support of local governments which has proven to be detrimental to science parks in the long term (Miao and Hall, 2014). Lecluyse (2019) identified that incubation infrastructure has been classified into three categories: property-related services, business and innovation support services and networking services to be discussed in the next section.

Property-related and Business & Innovation Services

Research participants' perceptions of the property-related services are consistent with the findings from relevant research on the area (Salvador, 2011; Rowe, 2013; Benneworth and Ratinho, 2014). Research participants based in the science parks find that such services helped them to lower operational expenses on community services such as reception, security staff and a renovated canteen. While research identifies (Salvador, 2011; Lecluyse, Knockaert and Spithoven, 2019) business and innovation services as customised advice in professional services areas such as marketing, business strategy, intellectual property, research activities, and access to public and private funding, BioCity Group provides developmental programmes for aspiring life science entrepreneurs.

However, some companies are left to find advice for sustained growth on their own once the developmental programmes for start-up incubation are finished; unless science park management has taken a special interest in them. Only a few of our research participants have been further supported by the science park's management through either their investment fund or by facilitating relevant network connections with private investors.

Once science park management starts connecting tenants with relevant stakeholders and gatekeepers, they become a mediator for certain companies. Some research participants perceive this as a “special treatment for star companies” that contribute the most to the SP management by leasing more space for offices and labs than “regular tenants”.

To address the gap in business and innovation services beyond the incubation stage, BioCity facilitates professional services organisations specialised in supporting life science companies with activities such as recruitment, marketing and business strategy, intellectual property and legal advice on-site. This is outside of the scope of the research by Salvador (2011) and Lecluyse (2019) on business and innovation services within science parks, as they do not consider support services complementation by independent on-site organisations. Therefore, science parks’ management promotes interactions between their tenants through offering networking services.

Networking Services

According to research on the services provided by science parks (Rowe, 2013; Koçak and Can, 2014; Lecluyse, Knockaert and Spithoven, 2019), networking services are meant to create opportunities for companies to engage with external organisations both within and outside the science park boundaries. When doing this, science park management becomes a partial mediator when facilitating these interactions for SMEs and support organisations within the sites. However, tenants perceive that on-site social interactions are not meaningful as they lack the specificity that companies with a science-oriented culture expect.

Science parks were intended as structures that would not only provide support services to start-ups and SMEs in early stages, but that would also foster and promote innovation and entrepreneurship through the social interactions between tenants, relevant stakeholders, and anchor organisations (Benneworth and Ratinho, 2014; Caiazza, 2014; Carvalho and Van Winden, 2017; le Duc and Lindeque, 2018; Lecluyse, Knockaert and Spithoven, 2019; Ng *et al.*, 2019).

To accomplish this goal of fostering innovation, science parks require tenants to engage in networking through social interactions; nevertheless, this research reveals that creating such engagement is difficult for high-tech science parks (Bonacina Roldan, Hansen and Garcia-Perez-de-Lema, 2018). This is especially complicated when tenants do not perceive straightforward benefits from what has been defined as “generic networking events” by research participants.

Networking services are difficult to plan and deliver for the BioCity’s Nottingham management as, although the local science parks are home to science-based companies, their expertise spans across the fields of Biopharma, Industrial Biotech, MedTech, and professional services (Ehret, McDonald-Junor and Smith, 2012; Bio City Group, 2017; Crocker, 2019). This heterogeneous mix has allowed for the science parks to grow their tenant base; nevertheless, it has prevented strong working relationships between the tenants except for on-demand intra-science park collaborations between some of the CRO companies on-site (BioCity, 2020).

Though all of the science-based companies in the Nottingham science parks operate within the life sciences, not all of them share the same knowledge base. Therefore, when people meet at

“generic networking events” they are less likely to be part of the same epistemic community which then has an impact on the cognitive proximity within the science park (le Duc and Lindeque, 2018).

Research usually considers universities as key members of entrepreneurial ecosystems (Kimatu, 2016; Rosenlund, Rosell and Hogland, 2017) that contribute to the outputs as there is a relationship between high-academic entrepreneurship and industry-academia partnerships in the “Golden Triangle” (Smith and Ehret, 2013; Bio City Group, 2017; Flanagan and Wilsdon, 2018; Crocker, 2019). Therefore, it is important to understand the perceptions that the members of the entrepreneurial ecosystem have on HEIs embedded in the entrepreneurial ecosystem.

Higher Educations Institutions (HEIs)

Though HEIs were an integral part of the genesis of the entrepreneurial ecosystem through collaborating for the establishment of a life-science-oriented park and providing human capital to biopharma SMEs, our findings suggest that the regional legacy oriented towards manufacturing and validation in the biopharma industry impacted the development and current makeup of this entrepreneurial ecosystem.

The University of Nottingham and Nottingham Trent University were part of the organisations that originally collaborated to create the BioCity science park (Ehret, McDonald-Junor and Smith, 2012; Smith, Rossiter and McDonald-Junor, 2017), and while research usually considers universities and government offices as important inputs and mediators within entrepreneurial ecosystems (Kimatu, 2016; Rosenlund, Rosell and Hogland, 2017; Flanagan and Wilsdon,

2018; Lecluyse, Knockaert and Spithoven, 2019; Ng *et al.*, 2019), this is not the perception that SMEs in this second-tier region have on them.

Through this research, it is noticeable that SMEs do not have enough resources to assess the high volume of local academic research that could add value to their organisations, and that universities could make more effort in terms of liaising between academic research groups and local SMEs in the biopharma industry. Therefore, local SMEs will tend to go the anchor mediator if there is the need to connect with a relevant academic group so they can have direct access to the academic expertise they are looking for.

Though universities were instrumental in the creation of this entrepreneurial ecosystem, the findings in this study suggest that SMEs are more likely to get involved with academic research groups when there are already established relationships from their "previous lives" in academia. This suggests that cognitive proximity through epistemic communities (le Duc and Lindeque, 2018) is as important for intra-entrepreneurial ecosystem relationships as it is for liaising with organisations outside the science parks. Personal relationships are important for collaborations within epistemic communities (Diez-Vial and Fernández-Olmos, 2017; Díez-Vial and Montoro-Sánchez, 2017; Giuliani, Balland and Matta, 2018) and as this research suggests, they can help to cope with the difficulties that working with universities present for SMEs in this entrepreneurial ecosystem.

This study reveals that SMEs in this second-tier region do not always collaborate with the local universities for some of the following reasons: i) there is not always an alignment between academic research and the problems local SMEs need solving; ii) decision-making processes

in universities move at a slower pace than within SMEs; iii) SMEs can't keep up with the high volume of academic research in the HEIs; iv) the goals of research groups do not usually match the business goals of an SME; and v) communication and data sharing between academics and SMEs are not always agile and timely.

Research in local support mechanisms and the helix models for technology transfer highlight the importance of relationships and the dynamics between universities and industry actors within an entrepreneurial ecosystem (Fini, Lacetera and Shane, 2010; Leydesdorff and Zawdie, 2010; Fini *et al.*, 2011, 2012; Rosenlund, Rosell and Hogland, 2017; Carayannis *et al.*, 2018); however, they usually do not consider the perceptions that the local industry has on their collaborations with academia or how to proactively promote the formation of these knowledge-based relationships (Benneworth and Ratinho, 2014). Therefore, this study suggests that research on entrepreneurial ecosystems and policy initiatives aimed at tech transfer through collaborations between academia and industry could consider what the perceptions, expectations and goals of the local industry are.

A mismatch on goals and scientific interest with the broader academic community is likely to motivate SMEs to pursue collaborations with academics they already know and that might be located outside of the entrepreneurial ecosystem (Benneworth and Ratinho, 2014; Naudé *et al.*, 2014; Minguillo, Tijssen and Thelwall, 2015; Diez-Vial and Fernández-Olmos, 2017; Presutti *et al.*, 2017; Ng *et al.*, 2019).

It is suggested that academic research is an integral part of the models for regional development through entrepreneurial activity and innovation based on a triple-helix

(Carayannis *et al.*, 2018) as they were designed through the outputs-focused perspective of first-tier regions where HEIs can contribute up to 50% of the new venture footprint in the biopharma industry (Bio City Group, 2017; Crocker, 2019). This is a clear contrast even in an overperforming second-tier region such as the Nottingham Biopharma Ecosystem where this figure reaches 10% (Bio City Group, 2017; Crocker, 2019). This suggests that there are opportunities to improve the cognitive proximity between biopharma SMEs and HEIs in this entrepreneurial ecosystem.

The next section of this chapter will address the discussion between the empirical findings regarding the mediators for entrepreneurial activities and the extant literature.

7.2.2 Mediators for entrepreneurial activities

Exploring an entrepreneurial ecosystem's mediators can help to gain a better understanding of the network relationships within a second-tier region while providing policymakers with empirical information that could help to improve region-oriented initiatives (Autio *et al.*, 2014; Giuliani, Balland and Matta, 2018; Robertson, Pitt and Ferreira, 2020).

In this second-tier region, the better-connected mediator is a membership organisation, Medilink East Midlands (MEM), located within the BioCity science park. In terms of helping SMEs connect among themselves, with academic research groups and government offices, it can be defined as the anchor mediator within this entrepreneurial ecosystem.

An anchor mediator helps to facilitate networking activities between local SMEs and other mediators with more specific roles such as facilitating access to private investment, helping companies to connect with the National Health Service (NHS), networking at international

knowledge-based events, and gaining access to entrepreneurial ecosystems abroad. This anchor mediator acts as a networking hub as it possesses a high number of relevant connections (Giuliani, Balland and Matta, 2018) at a local, regional, national and international level. However, access to the anchor mediator requires a membership which might mean that relevant networking opportunities and knowledge-sharing activities within the entrepreneurial ecosystem are distributed unevenly.

The anchor mediator also helps to facilitate networking activities between local SMEs and other mediators with more specific roles such as facilitating access to private investment, helping companies to connect with the National Health Service (NHS), networking at international knowledge-based events and gaining access to entrepreneurial ecosystems abroad. Furthermore, MEM can address the need of science-based SMEs as it provides tailored "science-based networking events" for every life science sector within the Nottingham entrepreneurial ecosystem that facilitate engagement to create "trust-based social relationships" between members of the same epistemic communities (le Duc and Lindeque, 2018). This anchor mediator acts as a networking hub as it possesses a high number of relevant connections (Giuliani, Balland and Matta, 2018) at a local, regional, national and international level.

7.2.3 Cognitive Proximity in the Entrepreneurial Ecosystem

There is a growing interest in exploring how SMEs and other members of entrepreneurial ecosystems perceive the incubation infrastructure provided by science parks management (Benneworth and Ratinho, 2014; Bonacina Roldan, Hansen and Garcia-Perez-de-Lema, 2018;

Lecluyse, Knockaert and Spithoven, 2019; Ng *et al.*, 2019) embedded in the ecosystem. A better understanding of the cognitive proximity between science parks and other members of an entrepreneurial ecosystem can provide empirical evidence to strengthen intra-science park relationships between tenants, anchor organisations and science park management (Giuliani, Balland and Matta, 2018; le Duc and Lindeque, 2018).

Cognitive Proximity Within Science Parks

According to the research participant from BioCity Group and relevant literature on science parks (Colombo and Delmastro, 2002; Durão *et al.*, 2005; Diez-Vial and Fernández-Olmos, 2017), it is suggested that incubation infrastructure that promotes and facilitates entrepreneurial activity and innovation differs greatly from one entrepreneurial ecosystem to the other. The findings in this research suggest that the relationship within the science parks in this entrepreneurial ecosystem are determined by the cognitive proximity created by the support services the science park management and the anchor mediator provide. Though the three categories of support services (Lecluyse, Knockaert and Spithoven, 2019) are available for the tenants of the science parks in the entrepreneurial ecosystem, not all of them are directly provided by the science park's management.

The findings suggest that the science parks in this second-tier region excel at providing property-related services while partially supporting business and innovation services. Moreover, research participants argued that there is a lack of "meaningful interactions" through the science park's networking-related services. Through employing cognitive proximity, the interactions within the science parks in this entrepreneurial ecosystem can be enhanced which

in turn would contribute to promote and expand innovation among the members of the ecosystem located in the science parks (le Duc and Lindeque, 2018; Giuliani, Balland and Matta, 2019).

Cognitive proximity refers to the knowledge base, cultural similarities and business goals between companies and their liaisons (Molina-Morales, García-Villaverde and Parra-Requena, 2014; Capello and Caragliu, 2018; Giuliani, Balland and Matta, 2018; le Duc and Lindeque, 2018). It has been suggested that networking interactions within science parks can be improved when reducing the cognitive proximity between their tenants (le Duc and Lindeque, 2018).

Contemporary research suggests that an effective manner to reduce cognitive proximity within a science park is to establish a tenant recruitment process that only allows companies from a certain discipline within the life sciences into the park (le Duc and Lindeque, 2018). Though this approach might create strong networks within the park as tenants would be working in similar (if not identical) fields, it may result in a knowledge lockdown (Boschma, 2005; Corrocher et al., 2019; Scott et al., 2019). Therefore, the findings in this research reveal that cognitive proximity can be improved without creating tenant homogeneity by facilitating “science-based networking events” led by tenants for tenants.

There is a desire from tenants to participate in scientific discussions, conferences and poster presentations as these activities allow for the creation of “trust-based social relationships” (le Duc and Lindeque, 2018), which then can be followed up for potential collaborations (Schweizer and He, 2018). This desire for organising “science-based networking events” is based on the collaboration projects that research participants have engaged with after attending these types

of events outside the science park. Ultimately, this is important as it has been suggested that relationships that start with specific knowledge sharing are most likely to be followed up by joint projects (Ng *et al.*, 2019).

A lack of overlapping knowledge bases within a science park is likely to be one of the reasons that tenants look for support or potential collaborations outside the science park. Though this is contrary to what has been traditionally expected in the literature from science parks and entrepreneurial ecosystems (Cooke, 2001; Minguillo, Tijssen and Thelwall, 2015; Kimatu, 2016; Lecluyse, Knockaert and Spithoven, 2019; Ng *et al.*, 2019), this research supports recent findings that suggest that the levels of social interactions within science park are low (Diez-Vial and Fernández-Olmos, 2017) and science park managers recognise these gaps in the network services they provide (Ng *et al.*, 2019). Ultimately, relationships between tenants in the Nottingham science parks have been explored by research participants as those of “good neighbours” that had the potential of creating personal friendships rather than business collaborations (Giuliani, Balland and Matta, 2018).

A perception of differentiated support among tenants and a lack of tailored networking services within a science park is likely to create a “silo mentality” that can have a negative impact on the performance of entrepreneurial ecosystems (Giuliani, Balland and Matta, 2018). To fulfil their needs for tailored events, BioCity and Nottingham tenants have made extensive use of the entrepreneurial ecosystem’s mediators. These mediators facilitate meaningful interactions among high-tech local SMEs, academics from universities, government offices and overseas entrepreneurial ecosystems.

7.3 Lifecycle of partnerships from the perspective of SMEs in the biopharma industry

Since collaborative projects for drug development projects have become the current paradigm for the biopharma industry (Bianchi *et al.*, 2011; Smith and Ehret, 2013; Schuhmacher, Gassmann and Hinder, 2016; Bigliardi and Galati, 2018; Crocker, 2019), there has been an interest in understanding the relationships that lead to these collaborations (Chakraborty *et al.*, 2020; DeCorte, 2020). However, research approaching the formation of these partnerships has mainly focused on the quantitative assessment of potential collaborations (Schweizer and He, 2018).

This research uses cognitive proximity to understand how cognitive proximity mediates the lifecycle of partnerships in the biopharma industry by proposing this construct as an enabler for the interactions leading to partnerships (Giuliani, Balland and Matta, 2019). Understanding the formation of these relationships and the context (Autio *et al.*, 2014; Robertson, Pitt and Ferreira, 2020) in which they occur can be helpful to explore the perceptions that SMEs in the Nottingham Biopharma Ecosystem have when liaising with external organisations such as collaboration partners. This research provides empirical evidence that can be used to tailor public policy and managerial practices that facilitate and promote interactions between SMEs in the biopharma industry.

The findings in this study highlight the importance of cognitive proximity as an enabler as it is important to determine a common knowledge base between organisations that are exploring potential collaborations for research-based activities (Partanen, Chetty and Rajala, 2014; Guo *et al.*, 2017; Presutti *et al.*, 2017; Hamadi, 2018; le Duc and Lindeque, 2018). This research

suggests that cognitive proximity is a key element that SMEs in the biopharma industry consider when engaging with and managing relationships with external collaborators rather than geographical proximity (le Duc and Lindeque, 2018). Furthermore, by promoting interactions based on cognitive proximity, it is possible to enable knowledge-sharing processes between key individuals from different organisations (Salvador, Mariotti and Conicella, 2013).

Distance between companies is considered as a multifactorial concept that involves the geographical distance, the base knowledge and business goals (Boschma, 2005; Torre and Rallet, 2005; Benneworth and Ratinho, 2014; Molina-Morales, García-Villaverde and Parra-Requena, 2014; Kim and Globerman, 2017; Presutti *et al.*, 2017; Garcia *et al.*, 2018; le Duc and Lindeque, 2018). The findings in this research suggest that cognitive proximity can be an enabler as it can be a substitute for other components of distance such as physical distance, a facilitator to reduce cultural distance and a key factor to help take advantage of temporary distance.

Contemporary research usually focuses on either assessing the impact that cognitive proximity has on the other dimensions of distance or the performance of collaborations between companies through analysing metrics such as the number of patents (Boschma, 2005; Kim and Globerman, 2017; Capello and Caragliu, 2018; Garcia *et al.*, 2018, no date; Giuliani, Balland and Matta, 2019). Nevertheless, this research presents a conceptualisation of the lifecycle of collaborations explored through cognitive proximity across the partnership (Schweizer and He, 2018).

McAdam's research (2014) on the formation and development of collaborations in low-tech industries proposes that these relationships can be illustrated using the S-Curve model to understand the role of knowledge diffusion during partnerships. McAdam's model is consistent with the literature in collaborations as it explores the diffusion of knowledge from its inception (McAdam *et al.*, 2014; West *et al.*, 2014; Bogers, Chesbrough and Moedas, 2018) and suggests that once relationships reach maturity through formal projects, the relationship is stable. However, when using cognitive proximity, the findings in this study indicate that for the biopharma industry these relationships are analogous to a Product Development Lifecycle curve.

Therefore, this research presents the Partnership Lifecycle Curve to understand collaborations and partnerships in the biopharma industry from the perception of SMEs by using the construct of cognitive proximity. This curve deploys the concept of cognitive proximity across the development of these relationships by using recently proposed phases for the assessment of potential collaborations in the biopharma industry (Schweizer and He, 2018). Figure 13 presents the contribution this research makes by building upon the research of McAdam (2014) and Schweizer (2018).

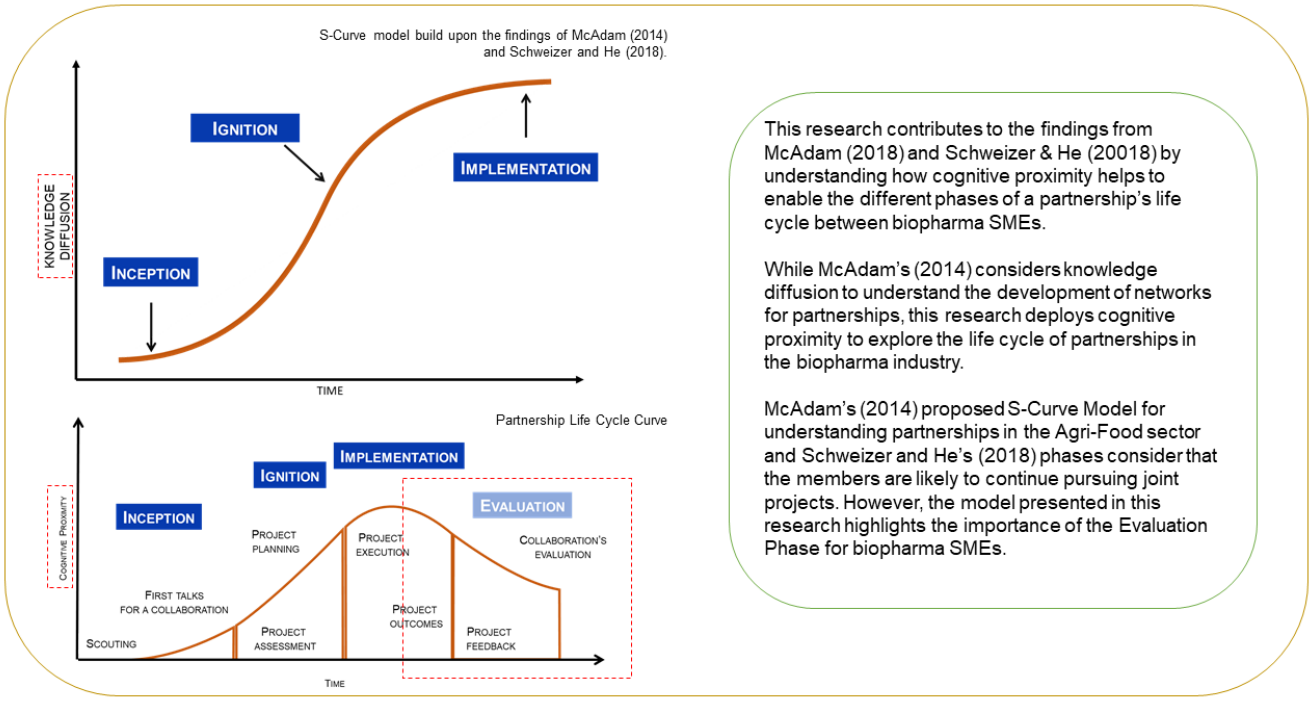


Figure 13. Contribution to partnerships between biopharma SMEs

As already mentioned, the findings in this research demonstrate the importance of "science-based networking events" to engage with activities for the ignition phase (Schweizer and He, 2018) as collaboration champions (Hamadi, 2018) are more likely to attend knowledge-specific events.

In specialised events, the epistemic communities with a common knowledge base can interact as science acts as a common language between people with different cultural backgrounds (le Duc and Lindeque, 2018). Overcoming the first barrier for communication through short cognitive proximity facilitates interactions between potential collaborators at an individual level so trust-building interactions can start (Diez-Vial and Fernández-Olmos, 2017; Díez-Vial and Montoro-Sánchez, 2017; le Duc and Lindeque, 2018; Giuliani, Balland and Matta, 2019; Leon

et al., 2019; Ng *et al.*, 2019) to facilitate the inception phase. These interactions are likely to help potential collaborators to conduct a preliminary assessment of the affinity between companies and the key champions for open innovation activities (Hamadi, 2018).

When there is ideal cognitive proximity but there are cultural differences (cultural distance), the presence of multicultural teams is important as these differences could have an impact on the development of the project (Leon *et al.*, 2019). This study suggests that when collaborating companies are based in different countries, multicultural teams can help to reduce the cultural distance. Furthermore, multicultural teams in SMEs have been found to adapt to changing environments while showing a good performance when engaging in collaborations and partnerships during the implementation phase (Korzilius, Bücker and Beerlage, 2017; Arslan *et al.*, 2020).

Literature addressing collaboration and partnerships identifies four main barriers that prevent organisations from collaborating: organisational barriers, financial and strategy barriers, collaboration barriers, and knowledge barriers (Christensen, Olesen and Kjær, 2005; van de Vrande *et al.*, 2009; Lichtenthaler, Hoegl and Muethel, 2011; Verbano, Crema and Venturini, 2015; Bigliardi and Galati, 2016; Schweizer and He, 2018). By conceptualising the lifecycle of these collaborations and operationalising the concept of cognitive proximity, this research can identify which barriers are determinant through the different phases of collaboration in the biopharma industry (Schweizer and He, 2018).

The findings drawn from this study indicate that during the inception phase the challenges for effective collaboration are usually the lack of funding (tackled by applying to government

funding through Innovate UK), a large social and cultural proximity (tackled through multicultural teams) and a difference of goals between organisations in the short term. These are barriers (Bigliardi and Galati, 2016) that are likely to prevent the involved companies from crossing the ignition phase of a potential collaboration (Schweizer and He, 2018).

Once companies are engaged in the ignition phase, they start to be in touch more often and other key individuals from the involved organisations enter the partnership lifecycle process. This is a potential barrier itself as even if there was a rapport between the first liaisons if the new people interacting are not able to manage the process, the collaboration could be negatively affected or even stopped (Leon *et al.*, 2019).

This research suggests the importance of establishing channels for effective communication between key individuals within and across the involved parties to overcome organisational barriers (Lichtenthaler, Hoegl and Muethel, 2011; Bigliardi and Galati, 2016). Furthermore, an effective system to store and share the project's data for on-demand access (Pitt *et al.*, 2006) creates a culture of transparency that according to the findings in this research is helpful to overcome the knowledge barriers related to a fear of losing relevant information without proper compensation (Bigliardi and Galati, 2016).

This study also shows that even when these barriers are overcome, partnerships in the biopharma industry will only last for as long as there is funding to engage with collaborative activities or while the strategic goals from the involved organisations are aligned. Government funding that allows for large research and development projects (Innovate UK) will only maintain these relationships for so long while the involved SMEs are developing new technology.

For biopharma SMEs with a service-based business model such as CROs, the funding depends on the availability of service contracts that require complementarity of services of two or more CROs. The findings in this research show that alliances and partnerships are in constant evaluation after each project finishes; therefore this study suggests the inclusion of an evaluation process in the phases for the lifecycle curve for partnerships (Schweizer and He, 2018).

Representing the lifecycle of collaborations in the biopharma industry from the perspective of SMEs through the Partnership Lifecycle Curve allows adding cognitive proximity as an integral part of the process. This model considers cognitive proximity as an enabler rather than a measure of distance while illustrating the potential barriers across the project's lifecycle while contributing to the literature on collaborations in the biopharma industry.

This conceptualisation is also important for champions (Hamadi, 2018) working for biopharma start-ups and SMEs, and mediators in entrepreneurial ecosystems as the findings suggest a set of activities and good practices based on cognitive proximity that facilitates collaborations and partnerships between different organisations in the biopharma industry.

7.4 Chapter Summary

This chapter discusses the empirical findings with the extant literature on entrepreneurial ecosystems and partnerships in the biopharma industry. The chapter also emphasises the use of cognitive proximity as a theoretical lens to meet the research objectives that answer the proposed research question in this thesis.

This chapter highlights the importance of context when aiming to the genesis and development of entrepreneurial ecosystems in second-tier regions as it recognises that these regions require specific research and policy initiatives. Tailored policies for these regions can allow them to provide an environment that facilitates growth and collaboration between SMEs and other regional stakeholders. To accomplish a contextual exploration of entrepreneurial ecosystems, this research proposes the adoption of the IMO framework and focuses on the relationships between SMEs, inputs, and mediators in the entrepreneurial ecosystem.

This study conceptualises the phases for collaborations in the biopharma industry, the barriers to such collaborations and the observed practices to facilitate the operationalisation of cognitive proximity through the Partnership Lifecycle Curve. This chapter also argues for the importance of providing life science entrepreneurs, stakeholders in entrepreneurial ecosystems and policymakers with empirical information on the activities that facilitate collaborative activities which will be explored in the next chapter.

In summary, this research responds to contemporary works that argue for the importance of understanding the context in which SMEs within entrepreneurial ecosystems operate in second-tier regions (Cardoso and Meijers, 2016; Autio *et al.*, 2018; Flanagan and Wilsdon, 2018;

Lecluyse, Knockaert and Spithoven, 2019; Robertson, Pitt and Ferreira, 2020) while using cognitive proximity to understand the lifecycle of collaborations and partnerships in the biopharma industry from the perspective of these SMEs (Boschma, 2005; Hidalgo and Albors, 2008; McAdam *et al.*, 2014; le Duc and Lindeque, 2018).

The following chapter will present a summary of the empirical findings of this research through a synthesis of the theoretical and empirical contributions made in this thesis while exploring its limitations and avenues for future research.

Chapter Eight – Conclusions, Limitations, and Future Research

In this chapter, a summary of the empirical findings is presented followed by a synthesis of the theoretical and empirical contributions made in this thesis. The limitations of this research are discussed, and a special emphasis is made to unveil future research directions that emerged from this study.

8.1 Introduction and Overview

This research employs cognitive proximity to understand how a second-tier region supports SME activity in the biopharma industry. This research uses cognitive proximity to understand the interactions involved in supporting biopharma SMEs at two levels, the entrepreneurial ecosystem level, and the SME level. Cognitive proximity can be used as a relevant theoretical lens as it considers the relevance of common languages, similar knowledge bases, and shared goals between organisations and SMEs. These constructs allow organisations to identify shared norms and values that promote transparency through effective communication (Boschma, 2005; Capello and Caragliu, 2018; le Duc and Lindeque, 2018).

Through addressing the research question “How does cognitive proximity enable a second-tier region to support biopharma SMEs?” this study uses cognitive proximity to better understand how an entrepreneurial ecosystem constrained by a lack of funding and government policies supports biopharma SMEs through promoting interactions between epistemic communities with similar knowledge bases.

This research laid out two objectives. The first one is to explore the interactions between inputs and mediators in an entrepreneurial ecosystem for biopharma SMEs in a second-tier region. The presence of inputs, mediators and their interactions explored through cognitive proximity are useful to understand the genesis and development of a successful entrepreneurial ecosystem within a second-tier region.

Through the literature review, gaps regarding entrepreneurial ecosystems were identified. First, there are conceptual limitations to understand entrepreneurial ecosystems as literature has tended to overlook the heterogeneous nature of these systems (Brown and Mason, 2017). Second, as in nature, every entrepreneurial ecosystem is unique, different and presents its idiosyncratic relationships among members that are likely to depend on the specific context they are located in (Autio *et al.*, 2014; Theodoraki and Messeghem, 2017; Robertson, Pitt and Ferreira, 2020). Third, there is a lack of theoretical frameworks that take all these issues into account that allow academics to investigate, conceptualise and empirically explore entrepreneurial ecosystems closely. Therefore, there are opportunities for exploratory research to investigate the genesis and development of entrepreneurial ecosystems within a specific context that allows for the conceptualisation of theoretical constructs (Dedehayir, Mäkinen and Roland Ortt, 2018). This research explores the specific context that promoted the genesis and facilitated the development of an entrepreneurial ecosystem for biopharma SMEs in a second-tier region.

The second research objective was to understand the lifecycle of partnerships in the biopharma industry between SMEs. Research exploring partnership formation and management in the

biopharma industry usually explores the outcomes of partnerships from the perspective of large biopharma companies usually located in first-tier regions.

Through the literature review regarding partnerships in the biopharma industry, this study identified the gaps in knowledge in this subject area. Collaborations and partnerships in the biopharma industry are usually explored through the interactions of large biopharma companies (Schweizer and He, 2018) with external organisations, especially SMEs located in first-tier regions (Chakraborty *et al.*, 2020; DeCorte, 2020). Nevertheless, it is important to explore these collaborations and partnerships from the perspective of SMEs in the context of a second-tier region. This approach to exploring collaborations and partnerships is relevant because it expands the concept of cognitive proximity as an enabler for biopharma SMEs in a second-tier region when engaging with external organisations for entrepreneurial activity and innovation.

The research consisted of an embedded case study research involving SMEs in the Nottingham BioCity Ecosystem and relevant stakeholders in this entrepreneurial ecosystem. The use of a qualitative research design employing interpretative means allowed an exploratory approach to be taken. This research sought to explore the phenomenon that has been occurring rather than test and validate since obtaining knowledge through interpretation of qualitative data through idiographic methods allowed the researcher to analyse the data as a result of the specific environmental situations (Tsang, 1999).

8.2 Contribution to Knowledge

The first objective of the thesis was to explore the interactions between inputs and mediators in an entrepreneurial ecosystem for biopharma SMEs in a second-tier region. Exploring this

research objective is relevant as second-tier regions lack key resources that are common in their first-tier counterparts such as private investment or tailored-made policies. To accomplish this, the research acknowledged the importance of the local context to determine the specific features and characteristics of an entrepreneurial ecosystem (Autio *et al.*, 2014; Robertson, Pitt and Ferreira, 2020).

To explore a specific context, this study builds upon the inputs, mediators and outputs (IMO) framework presented by contemporary research on the contribution of science parks (Lecluyse, Knockaert and Spithoven, 2019). This research advances the IMO framework by using cognitive proximity to better understand the interactions between relevant inputs and mediators in this entrepreneurial ecosystem. Therefore, the first contribution of this research is the implementation of an interaction-based IMO framework as a theoretical framework that allowed the researcher to identify and understand the actors and interactions within an entrepreneurial ecosystem while visualising the importance of these actors within it according to research participants.

The inputs were identified in instances where references were made to the contextual factors (McAdam *et al.*, 2014) that allow biopharma entrepreneurs to start their companies in the first place. With six out of seven participant companies being based in a BioCity Group science park, research participants highlighted the importance of an empty building with state-of-the-art equipment for a drug development project that would lease on-demand space at an affordable price when compared to other locations such as the “Golden Triangle”. In instances where research participants explored how certain organisations have the aim of facilitating specialised

networking activities to scout for collaboration partners and business support services, the mediators were identified. The outputs are the result of the interactions between SMEs and the inputs and mediators in a specific context; nevertheless, this research did not try to test and validate the aforementioned interactions.

The in-depth exploration of the inputs and mediators supported the understanding of the current context for this second-tier region. The findings in this research suggest that shared individual and regional goals between inputs, mediators, and SMEs are likely to have a positive impact on the outputs of an entrepreneurial ecosystem in a second-tier region; especially if a well-connected organisation is acting as the anchor mediator within the entrepreneurial ecosystem.

The contribution presented here is novel because it is one of the few studies that empirically captures the interactions between inputs and mediators in an entrepreneurial ecosystem for biopharma SMEs in a second-tier region through considering cognitive proximity. Furthermore, this research addresses recent calls to understand the context of entrepreneurial ecosystems (Autio *et al.*, 2014; Robertson, Pitt and Ferreira, 2020) through qualitative research that allows researchers to explore, and better understand a regional innovation system (Tsai and Chang, 2016; Bonacina Roldan, Hansen and Garcia-Perez-de-Lema, 2018) to be able to drive relevant context-specific policies (Brown and Mason, 2017; Theodoraki, Messeghem and Rice, 2018; Robertson, Pitt and Ferreira, 2020).

A second theoretical contribution to the literature in entrepreneurial ecosystems is the deployment of the construct of cognitive proximity as a theoretical lens. Employing this construct in the exploration of an entrepreneurial ecosystem allowed this study to understand

and contextualise the interactions between members of an entrepreneurial ecosystem for biopharma SMEs in a second-tier region. Contemporary research has suggested that the distance between organisations is a multidimensional construct that allows for a weighted measurement of its different components (Boschma, 2005; Torre and Rallet, 2005; Wuyts *et al.*, 2005; Kim and Globerman, 2017; Capello and Caragliu, 2018; Leon *et al.*, 2019). Nevertheless, this research deployed the concept of cognitive proximity to understand how this dimension manifests in the interactions between inputs, mediators and biopharma SMEs in the Nottingham Biopharma Ecosystem.

A second research objective of this study aims to understand the lifecycle of partnerships in the biopharma industry between SMEs. By investigating partnerships in the biopharma industry from the perspective of SMEs, this study was able to explore and represent the lifecycle of partnerships in biopharma while adding to the literature positioning cognitive proximity as an enabler for these interactions. Therefore, the second contribution of this research relates to understanding the formation and management of partnerships in the biopharma industry for SMEs lacking relevant resources to pursue such partnerships.

The partnership lifecycle model draws from the phases for assessing the potential of a collaboration (inception, ignition and implementation) in the biopharma industry (Schweizer and He, 2018). This research builds on Schweizer and He's (2018) work by adding an evaluation phase and identifying the barriers for collaboration (Christensen, Olesen and Kjær, 2005; van de Vrande *et al.*, 2009; Lichtenthaler, Hoegl and Muethel, 2011; Verbano, Crema and Venturini,

2015; Bigliardi and Galati, 2016; Schweizer and He, 2018) relevant for each phase and the importance of cognitive proximity to overcome them.

The contribution presented here is novel, as there is a limited amount of research exploring "how" partnerships in biopharma are built from the perspective of SMEs as research tends to explore the impact of collaborations and partnerships through the cause and effect studies using the economic and financial performance of large biopharma companies (Michelino *et al.*, 2014, 2015). Therefore, this study focuses on "how" the interactions between collaborating high-tech organisations can be initiated and managed by activities that promote interactions between organisations at an "ideal cognitive proximity"; therefore, providing a novel contribution to the literature regarding partnerships in the biopharma industry.

First, this research contributes to the literature in entrepreneurial ecosystems by exploring the context of an entrepreneurial ecosystem in a second-tier region through the interaction-based IMO framework. This provides an advancement in the literature advocating for a better understanding of entrepreneurial ecosystems (Autio *et al.*, 2014; Theodoraki and Messeghem, 2017; Robertson, Pitt and Ferreira, 2020).

This study also contributes to the literature regarding partnerships in the biopharma industry by exploring partnerships in the industry from the perspective of SMEs in a second-tier region while developing the partnership-lifecycle curve for this industry. This contribution is an advancement in the literature regarding partnerships in biopharma highlighted by recent research (Schweizer and He, 2018; Chakraborty *et al.*, 2020; DeCorte, 2020).

Moreover, the empirical findings and theoretical contributions of this research allow us to explore the current policy to produce suggestions to empower knowledge-based regional development and to provide actionable suggestions for biopharma entrepreneurs, science park management and policymakers.

8.3 Implications for Practitioners and Policymakers

The deep understanding of the context and the interactions within an industry cluster in an entrepreneurial ecosystem embedded in a second-tier region enables the creation of policy that leads to the formation of critical masses for high-tech entrepreneurship and innovation outside the “Golden-Triangle” (Flanagan and Wilsdon, 2018) and provides practitioners with empirical data on “how” to improve the relationships between SMEs, inputs and mediators within and across the different levels of an entrepreneurial ecosystem.

8.3.1 Implications for Science Park Managers

There are some implications for practitioners working in science parks. The first relates to providing empirical evidence on “how” to improve the networking services within science parks so they can facilitate meaningful interactions between the different organisations that operate within them (Giuliani, Balland and Matta, 2018; le Duc and Lindeque, 2018). This research reveals that despite the heterogeneous epistemic composition of the Nottingham City SPs, cognitive proximity between organisations could be reduced by facilitating “science-based networking events” led by tenants for tenants. This is relevant as tenant SMEs can identify companies with similar knowledge bases so they can engage with the inception phase of the partnership lifecycle.

There is a desire from the tenants to participate in scientific discussions, conferences and poster presentations as these activities allow for the creation of “trust-based social relationships” (le Duc and Lindeque, 2018), which can then be followed up for potential collaborations (Schweizer and He, 2018). This desire to organise “science-based networking events” is centred on the collaboration projects that research participants have engaged with after attending these types of events outside the science park. Ultimately, this is important as it has been suggested that relationships that start with the exchange of specific knowledge are most likely to be followed up by joint projects (Ng *et al.*, 2019).

8.3.2 Implications for Policymakers

This research is timely for policymakers as it provides empirical evidence that can facilitate a shift from the traditional approach, which considers the macroconditions of a country and results, towards research and policy that pays attention to second-tier regions trying to build or maintain entrepreneurial ecosystems (Miao and Hall, 2014).

Contemporary research identified a potential critical mass for life-science entrepreneurship including the Nottingham Biopharma Cluster which has been identified in the “M1 Corridor” (Mcdonald-junor and Ehret, 2015). This corridor considers the life science entrepreneurial activity occurring between Nottingham and Leeds and includes three second-tier regions with a high level of life science start-up activity: Nottingham, Sheffield, and Leeds. Table 10 shows the activity for life science entrepreneurship in these cities.

City	Region/Shire	Percentage of New Life Science Companies
Nottingham	East Midlands	96%
Sheffield	North Yorkshire	38%
Leeds	West Yorkshire	19%

Table 10. Critical Masses in the Midlands. 96% of the new life science companies in the East Midlands are located in Nottingham, 38% of the new life science companies in North Yorkshire are located in Sheffield, and 19% of the new life science companies in West Yorkshire are located in Leeds (Mcdonald-junor and Ehret, 2015).

Since life science, entrepreneurship is becoming urban-based (Zhang, 2015), and empowering the cities within the "M1 Corridor" might promote a geographical configuration that allows for specific policy and funding efforts for a critical mass (Lee, 2017; Flanagan and Wilsdon, 2018) while allowing every entrepreneurial ecosystem to develop around their unique strengths and challenges (Zhang, 2015). Furthermore, unifying the "M1 Corridor" might facilitate the creation of a brand that enhances the visibility of these three entrepreneurial ecosystems while reducing costs on promotion to raise brand recognition (Zhang, 2015; Flanagan and Wilsdon, 2018).

While Flanagan (2018) suggests that even with a lack of funding, a critical mass can be created by improving the connection between the neighbouring cities with the higher life science entrepreneurial activity, the findings in this research highlight the importance of appointing a figurehead to champion the region at relevant government lobby groups.

8.4 Limitations.

This research contributes to the literature on entrepreneurial ecosystems by exploring the context of a second-tier region through employing the interaction-based IMO framework while advancing the literature around collaborations in the biopharma industry. This is done by presenting the partnership lifecycle model to understand the evolution of collaborations from the perspective of SMEs. However, as with all research, this study was not without its limitations, and these are presented in the following sub-sections.

8.4.2 Analytical Limitations

As previously mentioned, this study focused on exploring the context of a specific entrepreneurial ecosystem in a second-tier region in the United Kingdom by operationalising the relevant stakeholders involved in supporting innovation and entrepreneurship.

During the analytic phase of this research, the emphasis was placed on exploring the contextual factors that would help to understand an entrepreneurial ecosystem, and less attention was given to the structural factor also explored by McAdam (2014), as the latter is related to specific organisational characteristics and practices outside the scope of this research.

Also, when exploring the evolution of collaborations and relationships from the perspective of SMEs in the biopharma industry through the partnership lifecycle curve, the importance was put on the constructs forming cognitive proximity without considering the behavioural factors that might affect those interactions, as it would require a deeper exploration of constructs from other disciplines such as organisational behaviour.

8.4.2 Theoretical Limitations.

The inputs, mediators and outputs were used in this study as a theoretical framework that allowed for the exploration and understanding of the contextual factors of an entrepreneurial ecosystem in a second-tier region. However, this research did not attempt to investigate their impact on the outputs as new measures that integrate more robust components of entrepreneurial ecosystems are yet to be fully developed (Lecluyse, Knockaert and Spithoven, 2019)

The partnership lifecycle curve is a model that represents the evolution of collaborations between SMEs operating in the biopharma industry and is a modification of the previous works exploring the evolution of collaborations and partnerships (McAdam *et al.*, 2014; Schweizer and He, 2018). And while it places special emphasis on the cognitive proximity between the organisations, it is less focused on other dimensions of distance such as culture, time, organisation or location (Boschma, 2005; Torre and Rallet, 2005; Wuyts *et al.*, 2005; Hobbs, Link and Scott, 2017; Kim and Globerman, 2017; Capello and Caragliu, 2018; Leon *et al.*, 2019).

8.4.3 Methodological Limitations.

The study was limited by its methodological framework in that the embedded case study was drawn from a second-tier city in a developed country with an already established legacy of drug development projects that resulted in available talent and facilitates that genesis of the entrepreneurial ecosystem.

The development of the partnership lifecycle curve, the exploration of the interactions between SMEs and inputs and mediators, and the analysis of the entrepreneurial ecosystem with the IMO framework depended on the anecdotal narrative that research participants provided on these themes.

Interviews with collaborators were not possible for every research participant. In some cases, the collaboration could not be explored as the identified organisation was changing management while in other cases it was due to the lack of response. Follow-up interviews were only done with two of the relevant stakeholders at the beginning of the year 2020 (Pre Covid-19 pandemic) to look for any changes in the contextual factors; however, no significant changes were identified that warranted a larger run of follow-up interviews.

Finally, the interviews did not cover the phenomenon of Brexit as it is considered a sensitive topic for some people in such a changing environment.

8.4.4 Empirical Limitations.

The findings in this study revealed a novel concept relating to the exploration and understanding of the context of the Nottingham Biopharma Ecosystem through the interaction-based IMO framework when suggesting the existence of an anchor mediator for this industry cluster in a second-tier region. Nevertheless, due to the current circumstances, follow-up interviews to discuss the relevance of the anchor mediator were not possible despite being within the context of the IMO framework.

When suggesting the partnership lifecycle curve, this research introduces the evaluation phase to the recent findings on the topic (Schweizer and He, 2018). While this study explores the

partnership lifecycle model through the concept of cognitive proximity, it does not evaluate the impact of cognitive proximity on each phase and its collaboration barriers.

8.4.5 Technical Limitations.

Finally, the study was not without some technical limitations. While there are many qualitative software packages such as NVivo, as well as either manual or automatic transcription services to speed up the transcribing process and the coding of the raw data, this study made use of neither. Interviews were performed in English and transcribed by one non-native-speaking researcher.

The coding adopted a system for data reduction (Gioia, Corley and Hamilton, 2013) and data analysis started with a priori codes related to the research question and existing literature (Hoyte *et al.*, 2019) for the different levels of exploration within this research. Then, categories were created to maintain and organise large batches of data. This was an iterative process involving follow-up interviews with some of the participants and stakeholders, and a constant update of the archival data. Data analysis took five months and the decision to not use specialised software to speed up the process resulted in closeness with the data that may have otherwise not occurred.

However, for future research projects, NVivo would be incorporated into the study as a data bank which would add transparency and portability. Also, transcription services may be employed for transcribing interview data generated if saturation allows for a second or third round of interviews.

8.5 Future Research.

The work on this thesis advanced our understanding of how a second-tier region can support an entrepreneurial ecosystem for biopharma SMEs by considering the context of the entrepreneurial ecosystem and the partnerships SMEs engage with.

As a result, this research presented the interactions-based IMO framework for exploring entrepreneurial ecosystems and the partnership lifecycle as a representation of the evolution of collaborations in the biopharma industry from ignition to maturity. However, the research presented its limitations that allow for future research avenues.

First, this research was contextualised within a second-tier city in a developed country. The theoretical framework to explore contexts presented in this study can therefore be used to examine and understand the entrepreneurial ecosystems of first-tier regions. In doing so, future research could determine if second-tier regions are more dependent on the interactions between SMEs, inputs and mediators. This would also require the testing and validation of the IMO framework by developing measures that consider the goals and contribution of inputs, mediators and SMEs to develop relevant outputs for a specific context as suggested by Lecluyse (2019).

A second avenue for future research involves the input of developmental programmes. These developmental programmes include mentorship in the aforementioned advice areas; nevertheless, they are directed to entrepreneurs in the process of creating new start-ups. While this research does not focus on the long-term benefits from these developmental programmes, the implications of these findings highlight the need for more detailed research exploring how

these initiatives can contribute to a deeper understanding of the differences of the context among the different entrepreneurial ecosystems across a country (Robertson, Pitt and Ferreira, 2020).

Another suggestion for future research relates to the development of the partnership lifecycle model which emerged from this study. This model was developed from operationalising the construct of cognitive proximity to advance previous works on this area (McAdam *et al.*, 2014; Schweizer and He, 2018); however, unlike McAdam's research (2014) this curve was created in retrospect considering positive experiences with collaborators. Therefore, future researchers could employ a longitudinal approach that allows for advancing the partnership lifecycle model while also considering other dimensions of distance such as time, culture, organisation and location.

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Appendices

Appendix 1. Information for Research Participants

Thank you for agreeing to participate in the research project. Your participation in this research is voluntary, and you may change your mind about being involved in the research at any time, and without giving a reason.

This information sheet is designed to give you full details of the research project, its goals, the research team, the research funder, and what you will be asked to do as part of the research. If you have any questions that are not answered by this information sheet, please ask.

This research has been reviewed and given favourable opinion by the Nottingham University Business School Research Ethics Committee.

What is the research project called?

HOW COGNITIVE PROXIMITY ENABLES AN ENTREPRENEURIAL ECOSYSTEM WITH LIMITED RESOURCES TO SUPPORT BIOPHARMA SMEs.

Who is carrying out the research?

Jose Francisco Gonzalez Lopez is carrying out this research as a part of his PhD research project in the University of Nottingham Business School

What is the research about?

My research is exploring how life science companies (biopharma sector) within a second-tier region, engage with external stakeholders to create networks for open innovation and collaboration. The information from this research will help to propose a set of good practices based on cognitive proximity that promote horizontal collaborations between SMEs within these regions to improve performance and increase the number of actors in the existing networks. Adding new actors to existing networks is important as they provide new sources of social capital that can prevent the innovative performance of a cluster to stagnate.

What groups of people have been asked to take part, and why?

CEOs, Innovation Managers, and Heads of Research in biopharma SMEs, as well as relevant stakeholders such as science park/cluster managers, VCs executives and managers, existing collaboration partners, membership organisations managers, and key members of the local and national government.	

What will research participants be asked to do?

You will be asked about your education and work experience. You will be also asked to recall on and explain the company's open innovation practices and your collaboration networks. You are likely to benefit from these reflective conversations and will be able to consult any piece of work resulted from this research on demand. Interviews will be recorded for analysis and a follow up meeting for confirmation of the findings might be necessary for methodological rigor. *You are free to withdraw from this research at any point up to publication.*

What will happen to the information I provide?

The audio from the interview will be recorded for codification and analysis. Companies and participant names will be given a data base nomenclature to preserve anonymity, although direct quotes might be included in the results interpretation if needed. Only the researcher and the project supervisors will have access to the information from the interviews.

Recorded files will be password protected and kept safe in the University of Nottingham servers for two years prior deletion.

What will be the outputs of the research?

This research will provide results for the researcher´s PhD thesis. It is also expected to potentially produce peer reviewed articles and case studies.

Findings, recommendations and other outputs of this research will be available to you on request.

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Complaint procedure

If you wish to complain about the way in which the research is being conducted or have any concerns about the research, then in the first instance please contact Dr. Simon Mosey and Dr. Hannah Noke.

Or contact the School's Research Ethics Officer:

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Appendix 2. Interview Guide for Participant SMEs.

- Year of foundation.

- Number of employees.
- Ownership and governance structure.
- Main reasons for choosing this cluster (Bigliardi and Galati, 2016, 2018; Giuliani, Balland and Matta, 2018).
- Support mechanisms from the cluster and the city council that you have found in this location (Fini *et al.*, 2011, 2012) .
- Products and services offered (Avermaete *et al.*, 2003).
- Main techniques and technologies employed (le Duc and Lindeque, 2018).
- Main suppliers, customers and support services partners (Avermaete *et al.*, 2003).
- Open innovation champions (Hamadi, 2018).
- Company links to universities in the Midlands (Geenhuizen and Soetanto, 2008; Fini *et al.*, 2011; Smith and Ehret, 2013; Bigliardi and Galati, 2018).
- Education (Degree and location) (le Duc and Lindeque, 2018).
- Prior work experience (le Duc and Lindeque, 2018)
- Role in the company (le Duc and Lindeque, 2018).
- Prior entrepreneurial experience (Guo *et al.*, 2017).
- Prior experience building collaboration networks (Elfring and Hulsink, 2007)

- Use of previous work or academic relationships in current position (Elfring and Hulsink, 2007).
- Process for opportunity identification (Guo *et al.*, 2017; Autio *et al.*, 2018).
- Main goals when collaborating with external partners (Kruse, 2012; Pullen *et al.*, 2012; Brunswicker and Vanhaverbeke, 2015; Hossain, 2015; Bigliardi and Galati, 2018; Santoro *et al.*, 2018)
- Open innovation model/strategy (Bianchi *et al.*, 2011; Lichtenthaler, Hoegl and Muethel, 2011; Schuhmacher *et al.*, 2013; Schuhmacher, Gassmann and Hinder, 2016)
- Key collaborators for social capital exchange (Coleman, 1988).
- Key partners for product and process development (Bianchi *et al.*, 2011; Russo-Spena and Di Paola, 2018).
- Network partners for product/service commercialisation (Cooke, 2001; Lawton Smith and Romeo, 2016; Lawton Smith, Bagchi-Sen and Edmunds, 2016; Schweizer and He, 2018).
- Formal joint-projects or forms of IP (Patent, trademarks, industrial design) resulting from collaborations with external partners (McAdam *et al.*, 2014).
- The fate of collaborative IP that does not fit the company's business model or goals (Williams, Young and Coffey, 2017).
- Initiators for the open innovation collaborations (McAdam *et al.*, 2014).

- Common business goal that promoted collaborations for open innovation (Boschma, 2005; Capello and Caragliu, 2018; Garcia *et al.*, 2018; le Duc and Lindeque, 2018).
- Personal relationships that promoted collaborations for open innovation (Boschma, 2005; Capello and Caragliu, 2018; Garcia *et al.*, 2018; le Duc and Lindeque, 2018).
- Organisational process to adopt collaborations for open innovation (West and Bogers, 2014; Bogers, Chesbrough and Moedas, 2018).
- Management of collaborators for product/service innovation and technological leverage (Spithoven, Vanhaverbeke and Roijakkers, 2013; Bigliardi and Galati, 2018)
- Management of support services partners for social capital (Coleman, 1988).
- Changes in the relationships with collaborators through first contact until now (Elfring and Hulsink, 2007; McAdam *et al.*, 2014; Partanen, Chetty and Rajala, 2014; Schweizer and He, 2018)
- Shared business practices and values that facilitated collaboration for open innovation with current and former partners (Boschma, 2005; Capello and Caragliu, 2018; Garcia *et al.*, 2018; le Duc and Lindeque, 2018).
- Factors determining the end of certain collaborations for open innovation (Huizingh, 2011; McAdam *et al.*, 2014; Bigliardi and Galati, 2016, 2018).
- Policy initiatives that facilitate collaborations for open innovation (Fini, Lacetera and Shane, 2010; Fini *et al.*, 2011; Laforet, 2013; Wang, Lestari and Yang, 2015).

- Cluster activities that promote social interactions (Lawton Smith and Romeo, 2016; Giuliani, Balland and Matta, 2018; le Duc and Lindeque, 2018).
- Cluster activities that promote the input of external information and knowledge (Molina-Morales, García-Villaverde and Parra-Requena, 2014; Presutti *et al.*, 2017).
- Opportunities for cluster managers to facilitate intra-cluster social interactions for open innovation (Garcia *et al.*, 2018; Giuliani, Balland and Matta, 2018; le Duc and Lindeque, 2018)
- Firms or individual outside the cluster that promoted and facilitated collaborations for open innovation (Elfring and Hulsink, 2007; Johnson and Bock, 2017; Ozmel *et al.*, 2017; Williams, Young and Coffey, 2017; Ashkenazy, 2018).
- Social and cultural bonds that facilitate collaborations for open innovation (Boschma, 2005; Molina-Morales, García-Villaverde and Parra-Requena, 2014; Capello and Caragliu, 2018; Garcia *et al.*, 2018; Giuliani, Balland and Matta, 2018; le Duc and Lindeque, 2018).
- Institutional characteristics that facilitate collaboration for open innovation (Capello and Caragliu, 2018; Garcia *et al.*, 2018; le Duc and Lindeque, 2018).
- Adaptability of the company for changing certain institutional characteristics to facilitate collaborations for open innovation (Knight, 2001; Avermaete *et al.*, 2003; Ferrary, 2011).

Appendix 3. Interview Guide for Stakeholders.

- Education (Degree and location)
- Prior work experience
- Role in the membership organisation
- Prior experience
- Use of previous work or academic relationships in current position.
- Year of foundation.
- Number of members from Nottingham.
- What are the business goals for the organisation?
- Support mechanisms from the city council and other government organisations to achieve the organisation's goals.
- Products and services offered to members.
- How do you identify upcoming challenges for your members?
- Is there a selection process for new members?
- Feedback process by members.
- Organisation's links to Nottingham Universities.
- Events to promote networking between members.

- Events to promote scientific knowledge sharing between members.
- Events to promote specialised industry requirements between members.
- How are these events related to the business goal of the site?
- What challenges do you face when trying to get members to participate on these events?
- How do you try to overcome these challenges?
- Which tenants are more involved with these events? Do you consider this reflects on their growth and performance?
- Are there examples of joint projects that started after members met at one of these events?
- What is the relationship with the members?
- Has the relationship with any of the members changed?
- What are some common factors between the organisation and the members you become more involved with?
- The traits of the ideal members.
- Are there differences between the members based in Nottingham and members based in other regions?
- Policy initiatives that facilitate collaborations for open innovation and network formation.

- Organisations that facilitate the engagement with open innovation and network formation activities within the UK
- What is your relationship with the local government to support life science SMEs?
- Are the business goals of the site in line with the regional and national goals for this industry?
- What is your relationship with other membership organisations in the region?
- Do you collaborate with industry clusters in the region to promote network formation and open innovation activities between tenants across those clusters?
- What are some social and cultural bonds that facilitate these relationships?
- What are some gaps that you consider policy makers should address to improve the environment for biopharma SMEs in the region?
- Organisations that facilitate the engagement with open innovation and network formation activities outside UK.
- Overall, what are your thoughts on Nottingham as a hub for biopharma SMEs? How does it differentiate to other similar regions? How does it thrive without the resources found in the Golden Triangle?

Appendix 4. Structure for Data Reduction for Ecosystem Mediators.

1st Order Concepts	2nd Order Themes	Aggregate Dimensions
• Companies join Medilink to raise their profile, to increase, their legitimacy, and to have access to regional and national stakeholders in the industry. • A lot is left to chance when you go to more broad, more general, and bigger events which is why I think the special interest groups work quite well.	Mediators for network formation and social interactions	Mediators for Entrepreneurial Activity in the Nottingham Biopharma Ecosystem
• SMEs in the area feel that they don't really have a voice. Government provides funding, but they don't really tap into SMEs to learn about their needs. • Government offices do not facilitate networking activities. • Losing the Local Government Agencies has been an issue.	Government Led Mediators	
• Medilink has signed an agreement for collaboration with the Development Agency in Mentor, Ohio. • Nottingham, and the Midlands in General, have a lot of similarities to the Mid-West in the US. • Medilink facilitates the due diligence for Mentor, and the companies they represent.	Eternal Mediators	

Appendix 5. Structure for Data Reduction for Interactions in the Entrepreneurial Ecosystem.

1st Order Concepts	2nd Order Themes	Aggregate Dimensions
• If we need access to a particular and unique skill set or piece of equipment MEM will help us to identify groups in local universities that we may not already be familiar with so we can access that expertise. • BioCity acts as a Landlord and Medilink as a support organization so there is no conflict and make sure they stick to their respective roles. • Medilink EM and BioCity Nottingham have a stronger relationship that any other Medilink-BioCity relationship.	Interactions between key inputs-mediators	Interactions within the Entrepreneurial Ecosystem
• Biocity organises talks that are quite broad as introduction to drug discovery or how to do marketing planning. • Companies complain that BioCity only takes them through their accelerator programmes, the 18-month coaching, and then just help a new batch of companies. Unless BioCity is involved with company (investor, or member of the board). • SMEs have a closer relationship with MEM than to the science park. MEM offered specialised interactions.	Interactions between SMEs and inputs and mediators	

Appendix 6. Structure for Data Reduction for the Lifecycle of Partnerships in the Biopharma Industry.

1st Order Concepts	2nd Order Themes	Aggregate Dimensions
• Informal social events on the setting of a scientific event are a good way to break the ice as the common language is there. • Science is the key element once conversations start. It serves as a common language. • Geographic boundaries are not important for collaboration efforts. Expertise and knowledge are more important than location.	Inception	Life Cycle of Partnerships for Open Innovation from the perspective of biopharma SMEs.
• Assessing hard skills (technical and scientific skills) requires due diligence and becomes easy until the joint projects start. • If a company excels at customer relationship management, they expect the same from collaborators. • Potential collaborations don't go through when one of the parties don't know what they want or think they will be getting something else in return.	Ignition	
• Collaborations require a commitment of resources, time, and accountability. • Relationships between organisations could fall to pieces if key individuals leave and are replaced with people having a different view if the relationships are not formalised. • Collaborations are not just an exchange of data. However, Communication, accountability, access to data, and progress meetings are important when working on joint projects.	Implementation	
• Collaborations tend to be "hot and cold" depending on the presence of funding. • Relationships can also get cold if there are management/ownership changes in a collaborator. • It is a loop of a relationship, from hot to cold to hot again.	Evaluation	