" A MIXED METHOD GROUNDED THEORY(MM-GT) WITH INTELLIGENT GIS AND MACHINE LEARNING APPROACH TO UNIVERSITY BASED BIOTECH BUSINESS INCUBATORS(UBBI) CLUSTERS: A STRONG STRUCTURATION AND SPATIAL AGGLOMERATION VIEW "

Research Paper

Ademola Taiwo, SSBM, Geneva, Switzerland, ademola@ssbm.ch

Abstract

This study investigates and integrates University Based Biotech Business Incubators(UBBI) and tech transfer clusters based on several cases from different Regional Innovation System(RIS). The study further develops a conceptual framework based on the ensuing themes, patterns and categories with grounded theory for UBBI Clusters and tech transfer spinoffs, their embedded Regional Innovation System (RIS) and UBBI roles. The study also includes an assessment on how UBBIs clusters are formed, Universities roles and perspectives, knowledge flow and innovation ecosystem development, UBBI regional transformation or changes and their substantive and Dynamic Capabilities. This study also explores how these UBBIs absorb the attributes and elements within their ecosystem to facilitate research and product development and the specific capabilities these UBBIs have developed overtime in their value chain based on the Biotech Cluster's life cycle.

Based on a Mixed Method Grounded Theory Approach(MM-GT) with Intelligent GIS and an application of Strong structuration theory(SST), this study examines the impact of external conditions on UBBI clusters' structures and how the actors respond and build resilience to disruptions and bottlenecks such as influence of regulation, policies development on the UBBI's Cluster and impact of the social structure and active agents or actors on the ecosystem. Using the cases from different RIS, this study further uses ensuing grounded theory to develop a model based for Intelligent Geography Information System(GIS) with Machine and Deep Learning (ML, DL with Generative AI) that could be used for the simulation of UBBI's spatial agglomeration and clusters formation with their dynamic capabilities.

Keywords: University Based Biotech Business Incubators, Universities Biotech based Spinoffs, Biotech Clusters, Regional Biotech Innovation System.

1 Introduction

Universities role in their regional innovation ecosystem involve not only research and academic influence or impact, but also the facilitation of knowledge and information development, generation, spillover, ecosystem transformation, spinoffs, stimulating entrepreneurial activities and value creation(Allen and McCluskey, 1991; Etzkowitz, 2002; Lee and Osteryoung, 2004; Mubarak AL-Mubaraki and Busler, 2014). Universities and their Business Incubators absorb elements, dimensions and attributes from their regional ecosystem(Brown and Mason, 2017; Malecki, 2018) through a

transformative process based on their capabilities re-combination and re-integration(Heaton, Siegel and Teece, 2019; Heaton, Lewin and Teece, 2020).

In addition to these, UBIs combine their initial substantive capabilities such as research labs, academic absorptive capabilities with their external networks in creating spinoffs and tech transfers in specific industry sector(Rasmussen and Borch, 2010; McAdam, Miller and McAdam, 2016; Rasmussen, Benneworth and Gulbrandsen, 2020) via the establishment of incubators, science parks and technopoles. Using combination of the RIS based infrastructures and their capabilities several industrial specialized or focused business incubators and cluster agglomerations have been established. An example is the Biotech Based University Business Incubators(UBBI) with focus on product development in biomedicine, biopharma and protein recombination and DNA(Cooke, 2001c, 2008).

UBBIs are developed with the cluster actors (firms, specialized biotech firms and Multinational Biotech Corporations) with specialties in investing in Universities spinoffs or license purchase from Universities. Agglomeration of these Biotech based clusters and the UBBIs occur in different RIS modes and types, so also is the influence of these UBBIs and the roles they play within these RISs due to the evolving Innovation development ecosystem(Asheim and Coenen, 2005; Spigel, 2017). In line with this, this study investigates the UBBI clusters in different RIS modes, their spinoffs and technology transfers based on a mixed method grounded theory approach(MM-GT).

The MM-GT study design is divided into four stages(a multi-strand mixed method design). In the first phase, the qualitative thematic analysis and aggregation of distinct ten cases of UBBI clusters are used to develop the conceptual framework. The extracted codes and code maps are then transformed for further initial quantitative analysis. Codes co-occurrence, Sankey Diagrams, code network maps are generated for visualization.

With the conceptual framework,synthesis and categorization of the patterns and themes in the study grounded in the qualitative cases were formed. Based on these patterns,themes and categories that ensued,some UBBI clusters' themes are categorized and classified such as: the UBBI cluster formation, approach, characteristics, value chain and strategies, impact of external conditions and tensions on their socio-human structure.

In the second stage, a sequential explanatory mixed method will be used based on the resulting UBBI cluster categories and classifications, a survey is generated from the categorization and classifications followed by a quantitative predictive modeling from the resulting survey results. Further more, specific cases are selected for the survey and indepth interview is also applied in this stage based on the findings and an inference is made to understand the results of stage one(conceptual) and stage two(sequential explanatory-survey and interviews). The ensuing meta-inference is combined and forms the first theoretical base.

In the third stage,based on the initial research questions defined, a sequential exploratory mixed method is then applied on the cases in stage two based on differing regional contexts for further theoretical sampling. For this research due to the stages and phases involved,purposive,identical and nested sampling designs and schemes will be used.

This stage seeks to examine:(a) what University Based Biotech Incubators and clusters patterns, themes and classifications exist? (b) How have these clusters formed and developed their network of linkages and institutional and legitimate structures overtime? (c) How has their network of actors changed overtime due to varying dynamism and factors internally and externally? (d) What existing structures, patterns and classifications exist that facilitate huge regional success overtime and how do they adapt to disruptions and bottelnecks within the clusters? (e) What lessons can other regional clusters (within their RIS, NIS or SIS) learn and how can they adapt their existing structures for better progress?

In the fourth and final stage, a comparism is made between findings in phase 2 and phase 3 for further meta-inferencing and theoretical grounding.

2 UBBI and Spinoffs' Clusters

Several UBBI based clusters exist around the globe with different agglomeration formation approaches due to the different RIS types and entrepreneurial ecosystem transformation overtime. These UBBI roles within these clusters include: incubating biotech based startups, facilitating cross academic and industry research development projects and licensing of intellectual properties(IPs) and spinoffs to SBFs (specialized Biotech Firms). While clusters consist of interrelated actors and elements within a region combining resources and capabilities to create economic and growth development, UBBIs including Biotech Tech transfer offices embedded within these regions via their alliances and partnerships engage in cluster formation and activities based on their close proximity to firms and SBFs. These alliances and cluster formation could be triggered or initiated via government and private and public partnerships, University initiated cluster formation or firm initiated networks due to personal and former companies or place of employment networks(Asheim and Coenen, 2005; Cooke, 2008).

The UBBI clusters examined in this study includes the MIT Boston 128 cluster(US) in the Massachusetts Region, (with Stanford, Boston and Harvard Universities), Swedish Karolina Institute and Med Valley Cluster with the neighboring Scandinavian Universities (Waxell and Malmberg, 2007; Baraldi, Ingemansson and Launberg, 2014) and Firm Alliances, Bio Region (Germany), Bio Alps and Bio Valley (Switzerland) (Carrin, Mack and Zarin-Nejadan, 2004), Austria (Tyrol, Styria and Wien), Israel (Jerusalem), South Africa (Gauteng Cluster), France (Mytelka, 2004), Italy (Conicella,

2011), Japan (Edgington, 2010; Wakabayashi and Takai, 2016) and India (Natesh and Bhan, 2009).

Based on the thematic analysis, the following major categories and themes are formed: (a) Category A: UBBI Biotech Clusters with Sub-categories (cluster formation, approach, characteristics, Innovative clusters and alliances, clustering models).

(b) Category B: UBBI Clusters' Actors, Linkages and Partnerships

(c) Category C: Impact of External Conditions on UBBI Clusters, with sub-categories: bottlenecks and challenges in UBBI clusters,

(d) Category D: UBBI and their Regional Innovation System with sub-categories such as: Regional Biotech Transformation and Changes, UBBI RIS Components and Characteristics. The next sections discuss these categories and the grounded theory mixed method approach (add the unit of analysis approach-trans regional, regional, cluster), national, regional and local levels).

3 Category A: UBBI Clusters

3.1 UBBI Clusters Overview:formation, approach and characteristics

A major prevalent theme is UBBI cluster formation,approach and characteristics and it is pertinent to understand the several cases of UBBI' cluster formation triggers and drivers,approaches and characteristics of the UBBI clusters. From the cases investigated, an important trigger in the cluster formation is the initial regional infrastructure and established networks. A related case is the Boston 128 cluster which has universities such as Harvard, MIT, Boston and Stanford and the bustling entrepreneurial landscape. The establishment of such a biotech based cluster was built on the already dynamic MIT entrepreneurial pedigree known for spinning out unicorn startups. MIT also operate a virtual biotech incubator and handles responsibilities of liaising for the licensing of patents and investors for spinoffs. Another important factor is the level of tolerance of failure of entrepreneurs which has been a major motivating factor for student entrepreneurship within MIT and the Boston Massachusetts region(Nelsen, 2005). A critical look at the North American UBBI clustering model shows a hybrid of both large firms investments and Universities spinoff modes. Large firms collectively involve with the Universities to collaborate in Research and Development projects thereby developing both analytic and synthetic forms of knowledge bases(Asheim and Coenen, 2005). This

form of clustering is due to the readily available biotech research labs and venture financing firms in major biotech clusters like Boston, San Diego and North Carolina.

However in Canada, the major clusters are found in Toronto and Montreal where multi-national corporation both invest in projects with Universities but also acquire smaller firms and patents or licenses. This clustering model is different in comparism to some parts of Europe where major initial cluster concentration had been on University spinoffs and tech transfer offices and also joint regional project initiation and collaboration(Niosi and Bas, 2003). While this approach is safe and reduces the risk of failed projects, the radical and highly risky innovative approach of the North American counterpart probably makes it the largest and highly funded global UBBI cluster. Scholars and cluster actors have also liased for more investment keen approach and increase in the level of tolerance to failure of projects in Europe(Cooke, 2001a; Cooke and Huggins, 2004).

3.2 UBBI Clusters Modes of Formation:

Several modes of UBBIs cluster formation could be seen. One of such is the German BioRegional competition and regional government involvement in creating biotech based clusters with the Universities playing a major role. One of such formation is the Bio Region contest or competition established for all 16 regions for innovative biotech based development and access to government funding. Three major regions were selected for the initial biotech based development which are Munich (Bavaria Region), NRW and Rhein Neckar (Heidelberg, Ludwigshafen)(Dohse, 2000). An important factor with these regions is the presence of reputable biotech based university research and infrastructure. One of such is in Heidelberg' Max Planck institute known for its long term pedigree in biomedicine spinoffs companies. Same could also be said of the other two regions with profound tech based universities e.g TU Munich, RWTH Aachen in NRW. These Universities and their tech transfer offices have over the years spinoff several successful high tech based startups which facilitated the establishment of the Biotech clusters in the region. However, scholars have suggested for further investment for the other less favored biotech regions

Another form of UBBI cluster formation is due to the role of Universities and their proximity to firms and also the presence of critical mass of large biotech firms within a region. Such example could be found in Sweden and Switzerland. The Karolina Institute in Uppsala, Sweden is a typical example with a robust funding and support programs and organizations such as the KIDB (Karolina Institute Development Board) and the KIAB which aid the institute in establishing a strong venture based and tech transfer offices. The institute also has a large concentration of Pharma and Biotech firms with a trans-regional network with links to Aarhus University in Denmark and Finish Universities(Baraldi and Waluszewski, 2011; Baraldi and Havenvid, 2016).

The Swiss Biotech clusters are initiated and built on strong strategic alliances and partnerships which has resulted in the formation of Biotech clusters like the BioAlps, Bio Valley and BioPole and a strong broker partnership initiated by the BioPartner which links several firms, developers, suppliers and researchers within all the regions and trans-national to the Biotech clusters. These clusters are strengthened via regional and cross regional co-development and co-evolution processes involving regions like Basel, Zurich and Bern which formed the tech transfer offices of Unitectra and the BioPole cluster involving the Geneva, Lausanne, Neuchatel, Freiburg and Vaud Region(Carrin, Mack and Zarin-Nejadan, 2004). A critical factor to the success of the Swiss clusters has been its pedigree for quality and competitive startup ecosystem with readily available support and funding, and the presence of EPFL, Lausanne, ETH, Zurich and University of Zurich and also UNIGE (University of Geneva) renowned for global research and academic pedigree(Cooke, 2001a; Cooke *et al.*, 2011).

A similar profound success of biotech cluster is also in the UK in the region Cambridge and Oxford which is also buoyed by the presence of the two major renowned Universities (Oxford and Cambridge Universities) known for its research infrastructure and presence of academic professors with focus on tech transfer. However the major contributing factor to the development of this cluster is the high level of labour mobility to the regions which has created attractiveness, expertise and knowledge generation

and supply needed for the creation of such cluster. This also corroborates the Potter Diamond model for cluster formation(Cooke and Huggins, 2004).

While there have been notable successes in these regions, other clusters within the same country have not been able to develop their UBBI clusters as compared to the successful ones in the same country. A critical factor that determines yet undermines the development of most high-tech based regional cluster and ecosystem is the presence of already established high tech capabilities(substantive) that these newly established clusters can leverage on. The presence of venture champions and actors with large personal networks that could facilitate the creation of those clusters is also essential(Rasmussen and Borch, 2010). It is also worth noting that the Regional mode or type is critical in the formation of UBBI clusters. Weak or less favoured entrepreneurial regions, require highly innovative capabilities and partnerships to succeed while also potential and cross border regions engage in cross regional partnerships and alliances for cluster formation. One of such cluster partnership could also be seen in the BioAlps (Freiburg, Strasburg and Basel).

4 Category B: UBBI Clusters Actors, Partnerships and Alliances

This category highlights the actors within a typical UBBI cluster, their roles, the type of networks formed and the relationships and partnerships that evolve. It is important to understand the set of actors that facilitate the agglomeration of UBBI Clusters. Generally, UBBI clusters can be initiated by higher institution of learning in connection with other research organizations or clinical research institutes. Other initiators of UBBI clusters and agglomeration could be large firms and SBF(specialized biotech firms) with close proximity to Universities to facilitate research and development collaborations and licensing of intellectual properites(IPs). In general actors in the UBBI clusters include Governement with the responsibilities of specifying regulations and policies that guides the biotech value chain product development, protection of customers and end users, creating standards and ensuring compliance in the production process, facilitating and corroborating in regional IP development processes, providing funds or acting as public venture capitalists for major projects and creating entrepreneurship based support programs for universities and regional based biotech startups.

Major actors within these clusters include: Large firms, MNC(multi-national corporations and specialized biotech firms(SBFs), suppliers which include biomed devices, regional development agencies and partnering facilitators. These organizations develop formal and informal networks based on their existing relationships with past employers and long standing industry experience to initiate cluster networks and collaborations with Universities for knowledge spillover and innovation(Audretsch and Keilbach, 2007; Cooke, 2013).

Universities and their UBBI's play important roles in the cluster as they aid the commercialization of research via the establishment of the transfer offices and also the spinoff or startups creation. Universities and UBBIs earn revenues via the royalty sales and the patenting returns. Large firms also invest in some of the spinoffs or partake in projects and research funding with the Universities(Niosi and Bas, 2003; Rothaermel and Thursby, 2005).

Other actors within the value chain also include Research institutions, government development agencies, Pharma Based firms and Clinical Research Organizations which form alliances with Universities for Research and Development.

4.1 UBBI Linkages and Relationships

Linkages in UBBIs are formed based on mutual interests and existing behavioural patterns which had culminated in formal or informal networks. These linkages exist among firms which could be initiated by individuals from a former company or Universities alumnis. Linkages also exist between Universities and industries based on closeness or proximity. These linkages form the bases for strategic alliances and partnerships. Universities play essential role in developing and facilitating the social capital required for the cluster formation and success based on structural and relational levels(Uctu and Jafta, 2014). Mutual interests in biotech based projects also aid social capital creation on a cognitive level.

5 Category C: External Impact on UBBI Clusters

An emerging category among UBBI clusters was the effect of external impact, bottlenecks and crisis on the cluster. UBBI clusters are subjected to the impact of external constaints and disruptions. These bottlenecks, constraints or disruptions could arise from government policies as Biotech is a highly regulated institutions and the UBBIs are also different from the traditional UBIs due to the time involved in product development (10 years). Government policies and regulations on biotech firms aims at preventing end-users and ensuring product and device compliances. However this also generate responses from the actors within the clusters. The different IP strategy differentiation and pathways is also a major constraints among the clusters.

5.1 UBBI Bottlenecks and Challenges

There are also other bottelenecks such as reliance on heavy infrastructures and research labs for product development,tolerance to failure and factoring in losses incurred during product development process or risk aversness. Lack of entrepreneurship support and facilitation in some regions or Universities is also a bane to the success of some UBBI clusters. Different pathways and strategies for Intellectual property procedures among Universities and Firms also generate constraints and bottlenecks. Inavailable or insufficient funding and lack of venture capitalists in some weak potential regions cause failure or abandonment of research project(Breznitz, O'Shea and Allen, 2008).

In combating these challenges and constraints, it is relevant to develop a theoretical perspective to understand the nature of the external conditions and impact and also how the actors within these UBBI clusters respond to the constraints based on perceived behavioural patterns and innate views or perspectives of the ecosystem. The Strong Structuration Theory(SST) will serve as a guide based on the quadripartite framework in classifying the UBBIs various external conditions and structures, the internal structures(conjectures and habitus which are based on sets of legitimation, significance and domination which include rules, norms and policies and also the culture and perpectives of individuals), the active agents and actors and typical expected results or outcomes of the external conditions.

SST with other theories such as actor network theory and Personal Construct Theory(PCT) will aid the understanding of how the UBBI Clusters' actors respond based on their behavioral construct initiated by environmental,firm culture or conditions,normative expressions and legitimation(Jack and Kholeif, 2007; Makrygiannakis and Jack, 2018). In achieving this, the ensuing codings from categories C(external impact on UBBI) were classified into the external structures which include: tolerance to failure, failed product development, selection decision critieria, consumer sentiments, government policies and regulations effect,different Universities IP licensing pathways strategies, lack of entrepreneurship facilitation in weak potential regions and lack of funding).

The internal structure classification include:Mutual interests,competencies,knowledge experience,level of power response and interest protection against circumstances(e.g recession),Government regulations,policies and norms(or rules),industry standards and compliances,RIS entreprenurial climate and culture,patenting perspectives,cluster missions and objectives.

Active agents include:SBFs(specialized biotech firms),UBBIs,CROs,Research Institutes,Regional Development Agencies,Government(Regional,National and Trans-National-EU).

Expected outomes are: Successful Research and Development projects, collaboration on research projects and successful licensing and spinoffs. Table I shows the SST Quadripartite Framework.

SST will be further applied on other UBBI Clusters' cases to ascertain the validity of this initial framework from the study.

6 Category D: UBBI Regional Innovation System

Another ensuing category in the conceptual framework development is the UBBI Regional Innovation System. Formation of UBBI clusters and agglomeration is dependent on the regional type or mode and the characterisitics of the regional innovation system. There are variation in the need, attractiveness and absorptive capacities of regions based on the support and infrastructure available. This gives rise to the different modes of regional innovation system which could be thick or thin;peripheral, municipal or old industry regions (Cooke, 2001b). Weak potential and cross border regions also exist which are less entrepreneurially favoured. These regions require different levels of entrepreneurial engagement and alliances compared to the thick RIS mode with available entrepreneurial and robust cluster. While clusters like the Boston 128 could boast of highly robust thick RIS modes facilitated by the presence of Ivy league Universities, other UBBI clusters with thin RIS have also designed measures to facilitate biotech cluster formation due to their available regional capabilities. An example is in Austria with three major biotech regions :Wien(Vienna). Tyrol and Styria. While Wien initially has a well funded and infrastructure available that faciliatated the establishment of a biotech cluster, the other regions depended on their already established high tech ecosystem to initiate the biotech cluster. The initial focus or concentration in Tyrol was on biotech devices manufacturing(Trippl and Tödtling, 2007).

In South Africa, the Guateng Region with Universities like Stellenbosch and Capetown concentrate more on biomed based technologies startups as research based project is inhibited by lack of sufficient funding and few expertise in the region(Pillay and Uctu, 2013). Jerusalem and Tel Aviv Universities in Israel with the clusters also deployed measures to concentrate on a segment of the value chain (R&D) due to availability of funds. However the Israeli cluster has been able to leverage on its regionally successful high-tech startups ecosystem for its UBBI cluster agglomeration(Breznitz, O'Shea and Allen, 2008; Breznitz, 2013).

7 Methodology: Mixed Method Grounded Theory Approach (MM-GT)

The study is designed by combining the beauty and benefits of a mixed method research with the thorough data explication of the grounded theory in developing a theory for UBBI clusters and ecosystem structures and impact of external conditions. Due to the complexity of the study and several theories and concepts surrounding it(such as knowledge spillover,entrepreneurial activities,dynamic capabilities,social networks,structuration theory,regional innovation system and urban and regional development theories),the research design is divided into different stages so as to inculcate these concepts. To diffuse the dichotomies behind the research questions,it is deemed fit to select an aggregration of a research design that is transparent,robust and encourages continuous inferencing until data saturation ensues.

In this regard, a methodology such as MM-GT is suitable which combines both theoretical objectivism and constructivism(Creamer, 2018). The research is based on mixed method multi-strands design(Creswell *et al.*, 2003; Johnson and Onwuegbuzie, 2004; Tashakkori and Creswell, 2007; Tashakkori and Teddlie, 2021) with constant data comparism at each phase in the design. The MM-GT procedural approach is shown in Figure 3. The design is divided into four stages. In stage one, qualitative thematic analysis is applied with the resulting codes categorized into patterns and themes for conceptual development as explained above. The codes and code maps are then quantitatively analyzed.

In the second stage, sequential explanatory mixed method will be applied by first developing survey from the ensuing conceptual framework followed by an indepth interview to both clarify the results from the survey and conceptual framework using selected cases based on purposive, nested and identical sampling scheme and design. At this stage a combined result ensues based on the theoretical sampling and constant comparism.

In the third stage, using the research questions highlighted in section one above, a sequential exploratory mixed method is used and selected cases from an in-depth interview will be transcribed and coded with emerging categories classified and compared with the initial findings of stage one and two. A resulting survey then ensues and will be distributed to selected UBBI BioRegions as in stage two. Data integration and theoretical sampling occurs at this stage based on purposive, nested and identical sampling scheme. The emerging findings from the qualitative and quantitative mixed methods will be combined as another theoretical base.

In the fourth and final stage, the results from stages two and three are compared for divergence or convergence and will be merged for further constant data comparism and theory development grounded in the data collected.

8 Spatial Agglomeration and Intelligent GIS with ML and DL

Based on the final theory and ensuing model developed from the mixed method grounded theory approach, the model will be fitted with the use of Geographical spatial analysis for spatial agglomeration modelling and simulation with spatial analysis GIS software.

Based on the extracted categories and ensuing grounded theory, survey and interviews would be conducted with other regional based UBBI clusters to apply the theory based on the UBBI RIS modes, characteristics, Universities roles, sets of constraints and challenges faced by the UBBI clusters. Based on these categories, the inputs will be trained into an intelligent GIS to understand the varying characteristics that occurs among UBBI clusters and how they transform overtime. The ML and DL based spatial analysis could be used to predict future UBBI RIS characteristics and how they can adjust to different constraints, the sets of capabilities within their RIS they can leverage on to enhance more value creation. Simulations and visualization based on different bottlenecks or challenges that can occur and how the UBBI cluster structures could respond would be determined.

The application of the intelligent spatial agglomeration will enable regional governments and cities to understand the various cluster classifications and their characteristics and how they can leverage on existing capabilities or infrastructure within their regions to attain or enhance further UBBI cluster developmental successes. The regional transformation and innovation development changes they undergo could also be simulated based on the ensuing cluster characteristics. This will aid the quest for Regional Innovation System or ecosystem renewal and technological adaptation.

Spatial Analyst based software integrated with intelligent geographical information system(GIS) used for urban and regional planning would be integrated with this study to simulate typical RIS based on the ensuing theoretical grounded theory framework. The UBBI cluster characteristics and RIS components will be designed in the spatial analyst software. An Intelligent GIS combines the power of Artificial Intelligence,Machine Learning and Deep learning to predict regional and urban characteristics formation and development.

8.1 Figure



Figure 1. Conceptual model and study framework research model.



Figure 2. Actors in UBBI Clusters' Value Chain





Figure 3. UBBI Clusters' Study design

8.2 Table

Strong StructurationTheory (QUADRIPARTITE FRAMEWORK)								
1. EXTERNAL STRUCTURE								
Tolerance to failure,								
Selection decision critieria,								
Consumer sentiments,								
Government policies and regulations effect,								
Different Universities IP licensing pathways strategies								
2. INTERNAL STRUCTURE(CONJECTURES)	INTERNAL STRUCTURE(HABITUS)							
Level of power response and interest protection against	RIS entrerpenurial climate and culture,							
circumstances(e.g recession),	Mutual interests,							
Government regulations, policies and norms(or rules),	Competencies, knowledge and experience							
Industry standards and compliances,								
3. ACTIVE AGENTS or ACTORS								
SBFs,UBBIs,Univeristies,Large Firms,University Alumni,Virtual Incubator Representatives,Tech								
Transfer Offices, Government Agencies, Regional Development Agencies,								
4. OUTCOMES								
Biotech Universities Based Spinoffs								
Partnerships and Strategic Alliances for Collaboration								

Table 1.UBBI Clusters' SST Quadripartite Framework.

Description	Year	Author	Country	Comment
Clustering, Long Distance Partnerships and the SME: A Study of the French Biotechnology Sector	2011	Lynn K. Mytelka	France	
A Tale of two clusters; high tech industries in UK	2004	Phillip Cooke and Robert Huggins	UK	
Developing Biotech Clusters in Non-High Tech Regions:The Case of Austria	2007	Michael Trippl & Franz Todtling	Austria	
The role of research institutions in the formation of the biotech cluster in Massachusetts: The MIT experience	2005	Lita L. Nelsen	US	
Biotech Megacenters:Montreal and Toronto Regional System of Innovation	2003	George Niosi and Tomas Bas	Canada	
The Biosciences Knowledge Value Chain and Comparative	2006	Phillip Cooke, Dan Kaufmann Chen	US,UK,Germany	Knowledge,Value Chain,BioIncubators

Incubation Models		Levin, Rob Wilson		comparism
Biotehnology Strength in India:Strength,limitation and outlook	2009	Natesh and S.K Bahn	India	
Japanese Approaches to Biotech Clusters:Impication for British Columbia	2008	David Edgington	Japan & Canada	
Institutional Policy and Network Evolution in Industry University Collaborations:Longitudinal Analysis in Japanese Biotechnology Cluster during 2000s	2016	Naoki Wayakabashi,Keigo Takai	Japan	
What is glocal and what is local in knowledge generating interaction? The case of biotech cluster,Upsala,Sweden	2007	Anders Waxell and Ander Malmberg	Sweden	
(2016) 'Identifying new dimensions of business incubation: A multi-level analysis of Karolinska Institute's incubation system	2016	Baraldi, E. and Havenvid, M.I.	Sweden,	Unique description of a UBI focused in Biomed
Biotechnology clusters as regional, sectoral innovation systems	2002	Phillip Cooke	RIS,US,Germany,UK	RIS of Biotech Clusters
Science-technology-industry network "the competitiveness of swiss biotechnology": a case study of innovation	2004	J.Bart Carrin, Yuko Harayama, J. Alexander K. Mack,and Milad Zarin-Nejadan	Switzerland	
Cluster sustainability: the Israeli life sciences industry		Shiri M,Breznitz	Israel	
A snapshot of the successful bioclusters around the world: Lessons for South African biotechnology	2012	Nirvana S. Pillay,Razman Uctu	South Africa	
Technology policy and the regions the case of the BioRegio contest	2009	Dirk Dohse	Germany	
Innovative Ecosystems in Biotechnology: the bioPmed case	2011	Fabrizio Conicella	Italy	
Regional differences in the development of Biotechnology in SouthAmerica:the case of Brazil and Mexico	2014	Miroslaw Wojtowicz and Slawomir Dorocki	Brazil,Mexico	

Table 2.UBBI Clusters' extant literature and Cases

References

- Allen, D.N. and McCluskey, R. (1991) 'Structure, policy, services, and performance in the business incubator industry', *Entrepreneurship theory and practice*, 15(2), pp. 61–77.
- Asheim, B.T. and Coenen, L. (2005) 'Knowledge bases and regional innovation systems: Comparing Nordic clusters', *Research policy*, 34(8), pp. 1173–1190.
- Audretsch, D.B. and Keilbach, M. (2007) 'The theory of knowledge spillover entrepreneurship', Journal of Management studies, 44(7), pp. 1242–1254.
- Baraldi, E. and Havenvid, M.I. (2016) 'Identifying new dimensions of business incubation: A multilevel analysis of Karolinska Institute's incubation system', *Technovation*, 50, pp. 53–68.
- Baraldi, E., Ingemansson, M. and Launberg, A. (2014) 'Controlling the commercialisation of science across inter-organisational borders: Four cases from two major Swedish universities', *Industrial Marketing Management*, 43(3), pp. 382–391.
- Baraldi, E. and Waluszewski, A. (2011) 'Betting on science or muddling through the network: Two universities and one innovation commission', *The IMP Journal*, 5(3), pp. 172–192.
- Breznitz, S.M. (2013) 'Cluster sustainability: the Israeli life sciences industry', *Economic Development Quarterly*, 27(1), pp. 29–39.
- Breznitz, S.M., O'Shea, R.P. and Allen, T.J. (2008) 'University commercialization strategies in the development of regional bioclusters', *Journal of product innovation management*, 25(2), pp. 129–142.
- Brown, R. and Mason, C. (2017) 'Looking inside the spiky bits: a critical review and conceptualisation of entrepreneurial ecosystems', *Small business economics*, 49, pp. 11–30.
- Carrin, J.B., Mack, J.A.K. and Zarin-Nejadan, M. (2004) *Science-technology-industry network: the competitiveness of Swiss biotechnology: a case study of innovation*. Université de Neuchâtel Faculté de droit et des sciences économiques
- Conicella, F. (2011) Innovative ecosystems in biotechnology: the bioPmed case. working paper Bioindustry Park, May.
- Cooke, P. (2001a) 'Biotechnology Clusters in the UK: Lessons from Localisation in the Commercialisation of Science', *Small business economics*, 17, pp. 43–59.
- Cooke, P. (2001b) 'Clusters as key determinants of economic growth', *Cluster policies-cluster development*, 2, pp. 23–38.
- Cooke, P. (2001c) 'New economy innovation systems: biotechnology in Europe and the USA', *Industry and Innovation*, 8(3), pp. 267–289.
- Cooke, P. (2008) 'Regional innovation systems: origin of the species', *International Journal of Technological Learning, Innovation and Development*, 1(3), pp. 393–409.
- Cooke, P. et al. (2011) Handbook of regional innovation and growth. Edward Elgar Publishing.
- Cooke, P. (2013) 'Life sciences clusters and regional science policy', in *Clusters in Urban and Regional Development*. Routledge, pp. 143–161.
- Cooke, P. and Huggins, R. (2004) 'A tale of two clusters: high technology industries in Cambridge', *International journal of networking and virtual organisations*, 2(2), pp. 112–132.
- Creamer, E.G. (2018) 'Enlarging the conceptualization of mixed method approaches to grounded theory with intervention research', *American Behavioral Scientist*, 62(7), pp. 919–934.
- Creswell, J.W. et al. (2003) 'Advanced mixed methods research designs', Handbook of mixed methods in social and behavioral research, 209(240), pp. 209–240.
- Dohse, D. (2000) 'Technology policy and the regions—the case of the BioRegio contest', *Research Policy*, 29(9), pp. 1111–1133.
- Edgington, D.W. (2010) Japanese Approaches to Technology Clusters: Implications for British Columbia. Asia Pacific Foundation of Canada.

- Etzkowitz, H. (2002) 'Incubation of incubators: innovation as a triple helix of university-industrygovernment networks', *Science and Public Policy*, 29(2), pp. 115–128.
- Heaton, S., Lewin, D. and Teece, D.J. (2020) 'Managing campus entrepreneurship: Dynamic capabilities and university leadership', *Managerial and Decision Economics*, 41(6), pp. 1126–1140.
- Heaton, S., Siegel, D.S. and Teece, D.J. (2019) 'Universities and innovation ecosystems: a dynamic capabilities perspective', *Industrial and Corporate Change*, 28(4), pp. 921–939.
- Jack, L. and Kholeif, A. (2007) 'Introducing strong structuration theory for informing qualitative case studies in organization, management and accounting research', *Qualitative Research in Organizations and Management: An International Journal* [Preprint].
- Johnson, R.B. and Onwuegbuzie, A.J. (2004) 'Mixed methods research: A research paradigm whose time has come', *Educational researcher*, 33(7), pp. 14–26.
- Lee, S.S. and Osteryoung, J.S. (2004) 'A comparison of critical success factors for effective operations of university business incubators in the United States and Korea', *Journal of small business management*, 42(4), pp. 418–426.
- Makrygiannakis, G. and Jack, L. (2018) 'Designing a conceptual methodology for structuration research', *Meditari Accountancy Research* [Preprint].
- Malecki, E.J. (2018) 'Entrepreneurship and entrepreneurial ecosystems', *Geography compass*, 12(3), p. e12359.
- McAdam, M., Miller, K. and McAdam, R. (2016) 'Situated regional university incubation: A multilevel stakeholder perspective', *Technovation*, 50, pp. 69–78.
- Mubarak AL-Mubaraki, H. and Busler, M. (2014) 'Incubator successes: Lessons learned from successful incubators towards the twenty-first century', *World Journal of Science, Technology and Sustainable Development*, 11(1), pp. 44–52.
- Mytelka, L.K. (2004) 'Clustering, long distance partnerships and the SME: a study of the French biotechnology sector', *International Journal of Technology Management*, 27(8), pp. 791–808.
- Natesh, S. and Bhan, M.K. (2009) 'Biotechnology sector in India: strengths, limitations, remedies and outlook', *Current Science*, pp. 157–169.
- Nelsen, L.L. (2005) 'The role of research institutions in the formation of the biotech cluster in Massachusetts: The MIT experience', *Journal of Commercial Biotechnology*, 11, pp. 330–336.
- Niosi, J. and Bas, T.G. (2003) 'Biotechnology megacentres: Montreal and Toronto regional systems of innovation', *European Planning Studies*, 11(7), pp. 789–804.
- Pillay, N.S. and Uctu, R. (2013) 'A snapshot of the successful bioclusters around the world: Lessons for South African biotechnology.', *Journal of Commercial Biotechnology*, 19(1).
- Rasmussen, E., Benneworth, P. and Gulbrandsen, M. (2020) 'Motivating universities to support spinoff firms: Stakeholders and start-up incubation ecosystems', in *Research Handbook on Start-Up Incubation Ecosystems*. Edward Elgar Publishing.
- Rasmussen, E. and Borch, O.J. (2010) 'University capabilities in facilitating entrepreneurship: A longitudinal study of spin-off ventures at mid-range universities', *Research policy*, 39(5), pp. 602– 612.
- Rothaermel, F.T. and Thursby, M. (2005) 'University-incubator firm knowledge flows: assessing their impact on incubator firm performance', *Research policy*, 34(3), pp. 305–320.
- Spigel, B. (2017) 'The relational organization of entrepreneurial ecosystems', *Entrepreneurship theory and practice*, 41(1), pp. 49–72.
- Tashakkori, A. and Creswell, J.W. (2007) 'The new era of mixed methods', *Journal of mixed methods* research, 1(1), pp. 3–7.
- Tashakkori, A. and Teddlie, C. (2021) Sage handbook of mixed methods in social & behavioral research. SAGE publications.
- Trippl, M. and Tödtling, F. (2007) 'Developing Biotechnology Clusters in Non-high Technology Regions—The Case of Austria', *Industry and innovation*, 14(1), pp. 47–67.
- Uctu, R. and Jafta, R.C. (2014) 'Bio-entrepreneurship as a bridge between science and business in a regional cluster: South Africa's first attempts', *Science and Public Policy*, 41(2), pp. 219–233.

- Wakabayashi, N. and Takai, K. (2016) 'Institutional policy and network evolution in industry university collaborations: Longitudinal analysis of joint patent networks in a japanese biotechnology cluster during 2000's', in. 2016 Portland International Conference on Management of Engineering and Technology (PICMET), IEEE, pp. 1186–1194.
- Waxell, A. and Malmberg, A. (2007) 'What is global and what is local in knowledge-generating interaction? The case of the biotech cluster in Uppsala, Sweden', *Entrepreneurship and Regional Development*, 19(2), pp. 137–159.