

Article

Global–Local Knowledge Spillover Strategic Coupling Network: Biopharmaceutical Industry Study of GBA, China

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Abstract: Strategic coupling is a hot field in the research of global production networks. The existing literature mostly consists of studies from the perspective of countries, regions, and enterprises, and relatively lacks the content for describing global–local strategic coupling networks and their evolution path with industries as carriers. The GBA is a bridgehead for China to participate in the global production network. Based on the systematic construction of the strategic coupling network analysis framework of global–local knowledge spillovers, this paper, taking the biopharmaceutical industry of GBA as an example, depicts the evolution process of its coupling network nodes, structures, and networks from 1990 to 2019 by using system analysis, social network analysis, and other methods, and analyzes node centrality, network structure, coupling paths, and their influencing factors. We found that the strategic coupling of global–local knowledge spillover is typically a networked structure, with the network organization presenting a multi-element sub-system hierarchical state. The overall network structure, with knowledge spillover as the carrier, shows obvious phased differences, having gone through three path stages from exploratory to expanding to stable. The path selection shows a spatial progression and a temporal sequence. The main factors affecting the path selection of the coupling network are the bargaining power of regional knowledge, behavioral subjects' will, and multi-dimensional proximity.

Keywords: strategic coupling; knowledge spillover; global production networks; biopharmaceutical industry; Guangdong-Hong Kong-Macao Greater Bay Area (GBA)



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1. Introduction

Since the beginning of the 21st century, the global production network (GPN) has become an important driving force of economic globalization, as well as the primary organizational carrier of global innovation [1,2]. As the central concept of global production network theory, strategic coupling establishes an important variable characterizing the relationship between regional and global production networks [3]. Coe attributed strategic coupling to the complementary effect between global and local production networks; local advantages are complementary to the strategic needs of leading enterprises in the global production network, and strategic coupling occurs as a result of value creation, enhancement, capture, and other factors [4]. When relevant scholars discuss its connotation and theoretical model further, they define it as the process of coordination, cooperation, and exchange between regional producers and flagship enterprises of the global production network, forming stable cooperative relations between them, and summarize three basic types of strategic collaboration, namely strategic cooperation, endogenous innovation, and production hubs [5,6]. With the rise of the research paradigm of economic geography evolution, MacKinnon further stated that the process and mode of strategic coupling over time show significant differences between different places and industries, and the original three types of strategic coupling cannot comprehensively and profoundly reflect the process of strategic coupling development [7]. As a result, Yeung narrowed his focus

to the dynamic evolution process and nature of strategic coupling, classifying it into three stages: functional coupling, native coupling, and structural coupling [8]. Countries, regions, and multinational enterprises are commonly regarded as strategic initiators of strategic coupling, resulting in a relative lack of research on describing the process and characteristics of strategic coupling networks with different industries as carriers [4,7,9–11]. During the institutional transformation of economic geography research, scholars suggested that the research focus be shifted from the early description of production organization to the description of production organization [12,13]. Industries are the carriers of the organizational relationship between enterprises, economic and social integration. As a result, different types of industries must be used as research objects to depict the mode, path, formation, and evolution mechanism of strategic coupling and the differences in strategic coupling among different industries.

In China, cities are transitioning from factor-driven models to models driven by innovation. Knowledge spillover is a crucial illustration of the spatial stickiness of a region, which is also viewed as a resource that promotes regional development through innovation following investments [14–16]. The geographic pattern of knowledge, influencing factors, and the spatial mechanism of knowledge diffusion are the main research topics of the current knowledge spillover studies; data methods such as patent cooperation and document tracking are primarily used to characterize the creative knowledge spillover network [7,17–21]. Specifically, cities, businesses, universities, and other knowledge spillover network nodes have spatial heterogeneity in different properties and regions based on various data sources, and regional organization mode, spatial absorption capacity, and network fundamental knowledge will all have a significant impact on the structure of knowledge spillover networks [22,23]. Knowledge spillover follows the laws of multi-dimensional proximity (geography, cognition, organization), hierarchical diffusion, distance attenuation, and other aspects due to the influence of regional innovation, agglomeration effect, proximity effect, and other causes [24,25]. It is clear that knowledge spillover has grown to be one of the crucial elements influencing the strategic coupling between the global and local levels; the paths and modes of various types of industries based on knowledge spillover in the process of integrating into the global innovation network will also show great differences because of the spatial and temporal heterogeneity of regional spatial stickiness and bargaining power, as well as the significant differences in knowledge production and innovation development modes of various types of industries [26,27]. The biopharmaceutical industry, which depends heavily on innovation and has a high level of scientific and technological content, will show knowledge spillover in space in the three links of the industrial chain: fundamental research, applied research, and product production [28]. Therefore, focusing on the establishment and evolution of the strategic coupling network of global–local knowledge spillover, starting from the city with a solid biopharmaceutical foundation, is one of the significant attempts to quantitatively characterize the strategic coupling network.

In the era of globalization, economic activity has a multi-scale of “local-national-regional-global” dimension. Two schools of thought have emerged in the study of innovation geography, with the global production innovation network focusing on multinational corporations and the regional production innovation network emphasizing local enterprises (industrial clusters) [11,29–31]. Swyngedouw believes that since economic globalization is actually “global-localization”, which can reflect the coordinated development of global and local levels, it is difficult to describe the global characteristics solely by describing the network of a single scale [32]. Si defined the concept of “global-local innovation network” in the study of “global-local innovation and knowledge network,” emphasizing that “global innovation systems” such as “knowledge spillover” and “technology diffusion” are not just a simple local innovation network superposition, but rather a new global innovation network created by coupling various local and global subjects [33]. The research topic of this paper, “global–local knowledge spillover strategic coupling network,” has the following connotations in light of the aforementioned factors. First of all, this network is a crucial component of the world innovation network. Secondly, it is created through the strategic linking of the local and global knowledge spillover networks. Thirdly, the network uses knowledge spillover as the

medium and depicts the networked outcomes of inter-subject linkages and strategic coupling of subjects at the local and global levels.

Based on the connotations of “global-local knowledge spillover strategic coupling network”, we sorted out the latest authoritative literature on knowledge spillover and global-local strategic coupling, and summarized the recent main progress into three aspects. First, multi-scale coupling research on knowledge spillover is conducted from a single or multiple scales, such as global, global-local, interregional, internal EU, US-global, and other scales. The knowledge spillover network and coupling network in multi-scale spaces, such as global and interregional, are analyzed, and the concept, structure, formation, and evolution path are summarized [34–37]. Second, special research perspectives, such as technology hierarchy, diversity, multinational companies, R&D laboratories, renewable energy, enterprises, etc., can be generalized and seen in the papers; they analyze the knowledge spillovers contained in them, and explain how they build and participate in multi-scale coupling networks through knowledge spillovers [38–44]. The third aspect is to study the regional characteristics of knowledge spillovers and strategic coupling for typical geographical regions. The main studies mainly focus on China, ASEAN, EU, and other regions, revealing the typical characteristics within these regions [45–51]. In addition, relevant studies also studied the knowledge spillover and strategic coupling after the global pandemic COVID-19, believing that the COVID-19 epidemic has significantly affected the position of economies in the global knowledge system, and significantly affect their ability to produce, mediate, and acquire global knowledge [52,53].

Thus, we identified two gaps for further study through the literature review. First, knowledge spillover is thought to have a significant impact on global-local strategic coupling, but the theoretical mechanism and direction of impact are still unclear. Second, from the perspective of the multi-scale effect of geography, there are clear individual differences between various regions, historical eras, and industrial clusters in the global-local multi-scale. Therefore, this paper aims to conduct an empirical study on the global-local strategic coupling network of the GBA biopharmaceutical industry from the perspective of dynamic evolution, with knowledge spillover as the coupling carrier, focusing on answering the following questions: Using knowledge spillover as the carrier, how should the global-local strategic coupling system’s framework be built? How is global-local strategic coupling impacted by knowledge spillovers? From an evolutionary perspective, what are the spatiotemporal evolution trends, traits, network structure, and coupling path of the global-local knowledge spillover strategy of the biopharmaceutical industry in GBA? What are the staged differences in the dynamic evolution of the above coupling networks and paths?

The structure of this article is as follows. First, this paper presents the study topics and clarifies the theoretical and practical contributions of this work based on a review of the literature on knowledge spillovers and global-local strategic coupling. Second, the research area (GBA), as well as the research data, particularly the data processing procedure of patent collaboration, are then thoroughly discussed. Then, this study builds a framework for global-local strategic coupling analysis system based on knowledge spillover, and analyzes its characteristics and multi-level structure. In the fourth section, this article defines the network characteristics and phase characteristics of global-local strategic coupling based on knowledge spillover of the biopharmaceutical industry in GBA. In light of these considerations, the fifth section of this work summarizes the general laws, theoretically explores the evolution laws of the global-local strategic coupling based on knowledge spillover in time and space, and summarizes the factors of coupling path selection. The main direction of furthering this work is also presented in the Discussion section of this paper.

2. Materials and Methods

2.1. Research Area and Object

The Guangdong-Hong Kong-Macao Greater Bay Area (the GBA) is made up of nine cities in Guangdong Province, including Guangzhou, Shenzhen, Zhuhai, Foshan, Huizhou, Dongguan, Zhongshan, Jiangmen, and Zhaoqing. It also includes Hong Kong and Macao, two special administrative regions. The GBA has a total size of 56,000 km² and a population of 72.7 million, making it one of the regions in China with the greatest levels of economic development and innovative capacity. The Pearl River Delta has been at the forefront of opening up and cooperation since China implemented the reform and opening-up policy in 1978. This is largely part due to its unique geostrategic location beside Hong Kong and Macao, as well as its superior background conditions, including high-quality and affordable labor, a pleasant climate, and a well-known hometown for Chinese who have emigrated outside of China. With the continuous promotion of “The Belt and Road Initiative (BRI)” and RCEP (Regional Comprehensive Economic Partnership), the GBA has developed into a crucial component of the new era’s national “dual circulation” strategy and a decisive spatial conduit for China’s efforts to create a world-class urban agglomeration and more effectively compete on the global stage. Regarding the GBA, attaining innovation-driven development is a crucial step toward high-quality transformative development in the area.

Additionally, one of the GBA’s representative industries is the biopharmaceutical sector. It dates back to the 1970s and has a broad scope of topics covered. In a narrow sense, the term “biopharmaceutical industry” refers to sectors of the economy where human-related biotechnology serves as the foundation, including genetic engineering, medication production, the production of medical devices, etc. It encompasses several industrial sets in the fields of production and uses, taken in its broadest sense [54]. The biopharmaceutical industry has the following characteristics when compared to other industrial sectors: For starters, it contains a lot of technology and a lot of knowledge. Second, technological innovation has grown in importance in the biopharmaceutical industry. Third, innovation is highly dependent on capital, manpower, and material resources, as well as having high benefits and risks. Fourth, the biopharmaceutical industry’s development guidance in different countries and regions has both commonality (theoretical review, etc.) and a distinct control mechanism [55]. To reduce investment risks, biopharmaceutical enterprises choose multi-agent cooperation and joint development mode of enterprises, scientific research organizations, colleges, and universities during the R&D process. In the biopharmaceutical industry, collaborative innovation and innovation networks are prominent. Because of this, it is a representative industry for studying the global–local knowledge spillover strategic coupling network. Although the biopharmaceutical industry in the GBA began later than in Shanghai, Suzhou, and Beijing, it remains one of the key areas where China’s biopharmaceutical industry congregates. The GBA’s biopharmaceutical industry development has a solid economic foundation and industrial environment. Because the GBA is the bridgehead of China’s opening-up and international innovation cooperation and is an appropriate area for studying global–local coupling, the biopharmaceutical industry in the GBA was selected as the case industry that makes this study typical.

2.2. Data and Preprocessing

Paper cooperation data are commonly used to characterize theoretical innovation in the method of describing knowledge spillover, and patent cooperation is a common indicator to measure technological innovation. This paper investigates the strategic coupling network structure of the GBA biopharmaceutical industry’s global–local knowledge spillover as well as the spatiotemporal evolution of the coupling path. Because the biopharmaceutical industry has the characteristics of a high-tech added value industry, its products will eventually enter the market as high-tech medical products, so relevant researchers frequently obtain intellectual property law protection through patent applications. As a result, using patent cooperation data can better depict the current state of transnational cooperation in the biopharmaceutical industry in the GBA. The data for this study were gathered

from the “PatSnap Patent Database” (PPD, <https://analytics.zhihuiya.com/>, accessed on 26 January 2021), primarily using World Intellectual Property Organization patent data (WIPO). PPD is a global patent search database that integrates patent databases such as the World Intellectual Property Organization and the European Patent Office (EPO), covering patent data from 116 countries and regions and accumulating over 135 million pieces of data. WIPO is a United Nations global knowledge forum organization involved with policy, information, and cooperation. It collects a wide range of knowledge cooperation data on patents, trademarks, industrial design, and so on. The patent data collected by WIPO has the characteristics of rich regions, broad industry coverage, and remarkable innovation cooperation, which can closely match the research needs of this study.

This study’s data were drawn from WIPO patent data on invention applications filed between 1990 and 2019. Because patent applications are filed through the Global Patent Cooperation Treaty (PCT) at WIPO, the patent data contained in the organization typically does not represent the time of patent authorization, but rather the time of patent application. Data preprocessing is divided into three steps. The first step is data retrieval. The patent retrieval method involves searching the biopharmaceutical industry’s patent data using the IPC industry classification number and screening the patent data with only one original patent applicant’s address located in the GBA. Following the search, 10,030 patent data entries from the GBA biopharmaceutical industry were obtained. The data were then filtered in the second step, with the filtering standard being that if the original patent includes the applicant’s address in and out of the GBA at the same time, the data were considered effective patent data with international cooperation; 487 pieces of data were retained. To ensure the consistency of the total amount of patent cooperation data, the third step is to identify the type of patent data. There are different identification methods for two different situations—if multiple personnel or units participate in one single patent cooperation datum, this research identifies this patent cooperation data as just one piece of datum; if one patent datum has multiple authors or units, the number of paths in the matrix depends on the number of authors or units. Furthermore, to reduce the abrupt change in patent application data between years, the patent data from 1990 to 2019 were divided every five years as a period, and six periods (1990–1994, 1995–1999, 2000–2004, 2005–2009, 2010–2014, and 2015–2019) were identified covering 4, 17, 99, 135, 121, and 111 pieces of patent data respectively with international cooperation.

2.3. Methods

2.3.1. Systematic Analysis

In terms of theoretical discussion, this study takes knowledge spillover as the research object, attempts to build a theoretical analysis framework of global–local knowledge spillover strategic coupling, analyzes the system characteristics of the global–local knowledge spillover strategic coupling network and its path under the assumption that the network is an open and complex system [56], and reveals the overall system internal logic and interaction between subsystems and system elements.

2.3.2. Social Network Analysis

A common method for studying the characteristics of individuals and networks in network structure, as well as their network relationships and network structures, is social network analysis [57]. This study describes the centrality and network connection strength of the GBA biopharmaceutical industry’s strategic coupling network using the social network analysis method and patent cooperation data representing knowledge spillover between global and local cities. The following are the specific methods:

Node centrality. Node centrality includes node centrality, proximity centrality, and intermediate centrality. Since the data used in this study are patent cooperation data, and the network formed by its combination is an undirected asymmetric network, this

study only considers the selection of node centrality index to examine the centrality of network nodes.

$$C_{D(i)} = \sum_{j \in N} X_{ij} \quad (1)$$

In Equation (1), $C_{D(i)}$ is the knowledge spillover centrality of node cities in the network, and X_{ij} is the number of knowledge spillover contacts of node cities after bisection. In the specific calculation process, the number of knowledge spillover connections of a node city is the number of times that the city appears in the knowledge spillover matrix.

Network connection strength. In this study, the general model of spatial connection strength—the gravity model—is used to measure the knowledge spillover connection strength between different node cities in the network.

$$C_{L(i)} = V_i \times V_j / D_{ij} \quad (2)$$

In Equation (2), $C_{L(i)}$ is the knowledge spillover connection strength between node cities in the network, V_i and V_j are the node centrality of node cities i and j , and D_{ij} is the spatial distance between node cities i and j . In the specific calculation process, it is the topological adjacency of network connections between node cities i and j , that is, the number of connection axes between different node cities in the network.

3. Strategic Coupling System Analysis Framework of Global–Local Knowledge Spillover

3.1. Global–Local Knowledge Spillover Strategic Coupling System Network

The coupling process of global–local knowledge spillover strategy in the regional space evolves from an axis structure to a network structure. Strategic coupling of global–local knowledge has specific spatial and regional characteristics [17,58–61]. Most regions initially coupled with countries and regions that had close kinship, strong knowledge production capacity, convenient spatial and regional communication channels, or a high demand for knowledge spillover markets. The initial coupling has a small number of subjects, a concentrated spatial and regional distribution, and obvious commonality. The initial coupling has a small number of subjects, a concentrated spatial and regional distribution, and obvious commonality. As a result, at this stage, the spatial structure of the global–local knowledge spillover strategy coupling mostly presents a simple axis structure, that is, the coupling mode is also relatively single due to the small number of coupling subjects, the concentration of kinship attributes, and the high concentration of regions [62,63]. The spatial structure of the strategic coupling of global–local knowledge spillover has gradually evolved from the axis structure to the network structure as the coupling process has deepened and upgraded, exhibiting the three characteristics listed below: First, the number of subjects participating in the coupling process is increasing, which is not only due to an increase in regional subjects of the coupling space, such as China and India's participation. It is also the pluralistic proclivity of the coupling type subjects. This coupling process is being participated in by an increasing number of multinational corporations, international organizations, scientific research institutions, and other multi-subjects [20,64]. Second, the coupling mode has been constantly innovated, from the early days of joint development of single advanced manufacturing equipment to the coupling mode of patent research and development, paper cooperation, and other theoretical and technological innovation. The new mode has also significantly boosted the coupling space structure's networking [15,65,66]. Third, the coupling effect is more widespread. The strategic coordination of global–local knowledge spillover is primarily an economic behavior. Initially, the coupling primarily encourages the spatial transformation of innovative economic benefits to achieving greater innovative economic benefits in a larger space on a global scale. Later on, the coupling focuses not only on economic benefits, but also on the comprehensive realization of social and ecological benefits. For example, the strategic coupling of global–local knowledge spillover in the process of COVID-19 vaccine research and development is also committed to achieving social and political benefits to some extent [67–69].

3.2. Multi-Layered Structure of the Global–Local Knowledge Spillover Strategic Coupling Network

The strategic coupling network of global–local knowledge spillover exhibits hierarchy and diversification in terms of network element structure. According to the spatial unit subsystem of the coupling network, the coupling process of the networked structure typically includes three or more spatial units, which are primarily made up of global and local units (Figure 1). The global unit is generally made up of companies, organizations, and scientific research institutions that operate and exchange on a global scale. The local unit is made up of the government and local businesses. In the process of forming the global–local coupling network, the global unit has significantly greater control over the network than the local unit, but the willingness and ability of the local unit to cooperate (resource endowment, economic conditions) are equally important to the network. The connection and interaction within and among the node units of the coupling network are also hierarchical and complex as a result of the interaction of each coupling network sub-system. The strength, breadth, and depth of the interaction and game between the actors (enterprises, governments, scientific research institutions) within the local unit, between different local units, between local and global units (multinational companies, organizations, scientific research institutions, etc.), and other subsystems can influence the coupling network structure and network density to varying degrees [7,15,70–72]. As shown in Figure 1, if local unit B's ability to integrate innovation resources is greater than that of local unit A, the strength, stage, and mode of the two in the coupling process in a pair of opposite directions will demonstrate the “law two of hot knowledge”, that is, the stronger of the pair can determine the coupling mode and strength, and knowledge will overflow from the dominant to the weaker.

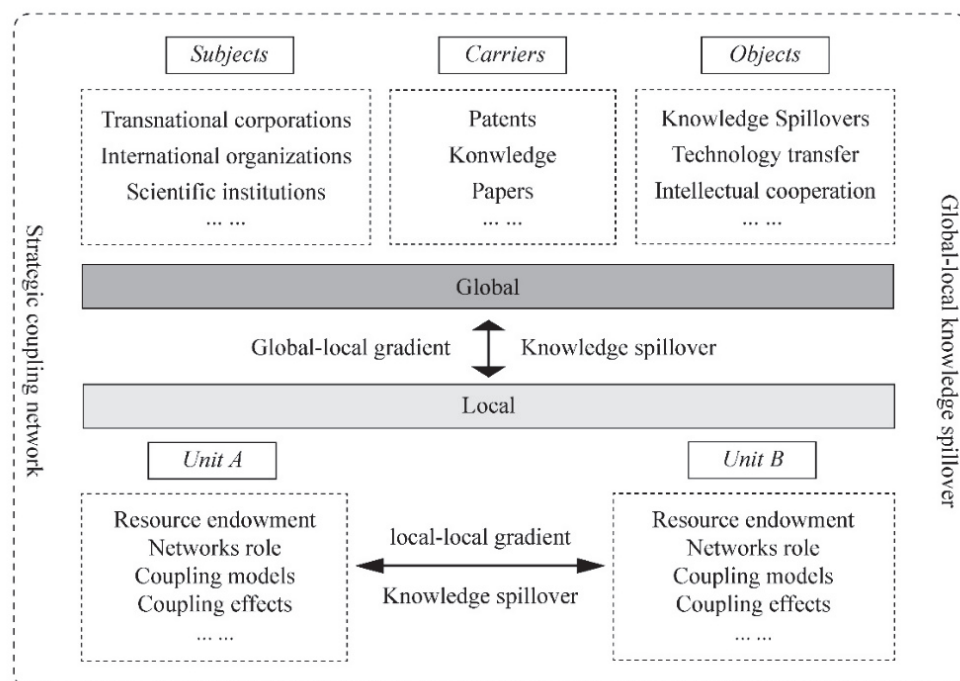


Figure 1. Analysis framework of global–local knowledge spillover strategic coupling system.

4. Biopharmaceutical Industry Global–Local Strategic Coupling Network in the GBA

4.1. Global–Local Strategic Coupling Network Structure of the Biopharmaceutical Industry in the GBA

4.1.1. Evolution of Overall Coupling Network Structure

Using the social network analysis method and the Gephi software, we visualized the centrality strength and grade of each node city in the coupling network (Figure 2). The findings indicate that: (1) From 1990 to 2019, the strategic coupling network structure of global–local knowledge spillover of the biopharmaceutical industry in the GBA was

complicated, the network density of 6 periods increased from 0.026 to 0.089, and the network connection strength was also promoted from 0.020 to 0.043. (2) The core node of the global–local strategic coupling network evolved in three stages: “single core; three weak cores; three strong cores”. During the first stage (1990–1999), Hong Kong was the dominant core node city in the GBA for global–local coupling with a node centrality of 26. In the second stage (2000–2014), Hong Kong’s dominance weakened due to its node centrality declining from 160 to 106; the entire GBA network evolved into a structure of “one center and two sub-centers” with Hong Kong as the primary core node and Guangzhou and Shenzhen as the two secondary core nodes, and the node centrality of Hong Kong, Guangzhou, and Shenzhen are 106, 88, and 30, far ahead of other cities. During the third stage (2015–2019), the three core node cities of Hong Kong, Shenzhen, and Guangzhou maintained network equilibrium with node centrality of 86, 104, and 80, forming a global–local coupling pattern of tripartite collaboration in the GBA, and the overall network completed the transformation process from a simple axis type of single core to a complex and diverse type of multi-core. (3) In the evolution of the global–local coupling network of the biopharmaceutical industry in the GBA, Beijing, Shanghai, Nanjing, Suzhou, Wuhan, Xi’an, and other Chinese cities, as well as London, Tokyo, Paris, Los Angeles, Washington, New York, Boston, Houston, and other cities around the world, serve as intermediary node cities in the coupling network, which means that the cities mentioned above have knowledge spillover with the GBA cities in the global–local biopharmaceutical industry patent cooperation applications at the same time, and they are important node cities on which the global–local coupling network is dependent.

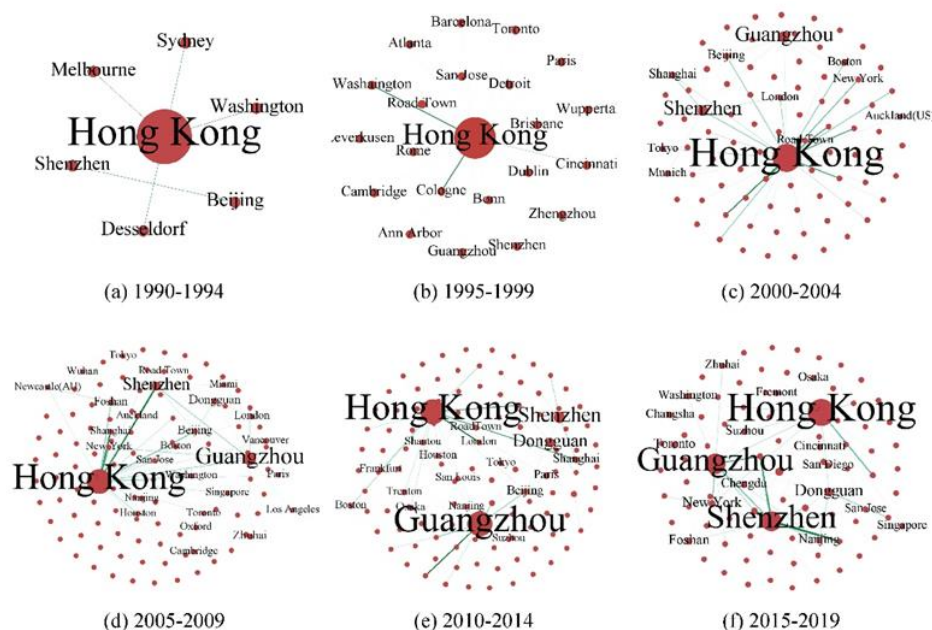


Figure 2. Global–local strategic coupling networks of the biopharmaceutical industry in the GBA.

4.1.2. Evolution of Individual Coupling Network Structure

The cities in the GBA are divided into four levels to reveal the individual networks of different node cities in the network, namely, Hong Kong, Guangzhou, Shenzhen, and other urban clusters, and the dynamic evolution characteristics and processes of their global–local coupling networks are revealed respectively (Figure 2). The research finds that: (1) Hong Kong is the “antenna” of the GBA’s global–local knowledge spillover strategy coupling network, according to the research. From 1990 to 1999, Hong Kong was the only city in the GBA to generate strategic global–local knowledge spillover coupling; since Hong Kong’s return to China in 1997, knowledge spillover between Hong Kong and surrounding cities such as Shenzhen and Guangzhou has been continuously strengthened.

Hong Kong has gone through a “rising–growing–maturing” process in the GBA knowledge spillover’s global–local coupling network, and the network function of Hong Kong has also changed from “antenna” to “window”. (2) Guangzhou’s integration into the GBA knowledge spillover’s global–local coupling network began later than Hong Kong’s, and its medium-term growth momentum is strong, but its stamina is slightly insufficient. From 1995 to 1999, Guangzhou officially joined the coupling network, and only one global city (Cincinnati, OH, USA) was strategically coupled during this time; from 2000 to 2014 (2000–2004, 2005–2009, and 2010–2014), the number of global cities strategically coupled with Guangzhou increased to 8, 15, and 32, respectively. The number of global cities coupled with Guangzhou dropped to 14 from 2015 to 2019, because after Guangzhou experienced the rapid growth stage of the coupling network (2000–2014), the strategic coupling network of global–local knowledge spillover reached a relatively stable state. There are risks and uncertainties in coupling with new network nodes at this stage, and the current coupling pattern is difficult to break; additionally, the cost of maintaining good coupling with all nodes in the network is quite high, so coupling nodes with higher costs will be gradually abandoned. (3) Shenzhen only gradually entered the GBA global–local strategic coupling network in 2000, and it is the city with the most recent but strongest development momentum of the three core cities. From 2000 to 2009, Shenzhen’s strategic integration with global cities was primarily dependent on Hong Kong. Following the “Hong Kong–Shenzhen” cooperation, Shenzhen’s participation in the global–local coupling network became the main feature of this period; from 2010 to 2019, Shenzhen gradually lost its reliance on Hong Kong and became a network core city with a certain independent coupling capacity, so the number of strategic couplings with global cities continued to rise, rapidly increasing from 14 in the initial coupling period to 31 in 2019. (4) In terms of other cities in the GBA, their participation in the global–local strategic coupling of knowledge spillover in the biopharmaceutical industry has increased from 1990 to 2019, particularly in important node cities such as Foshan, Zhuhai, and Dongguan. According to coupling approaches, the proportion of direct coupling between these cities and global cities is negligible, with the majority of them being indirectly coupled through three core cities: Hong Kong, Shenzhen, and Guangzhou. For example, from 2000 to 2004, Foshan used Guangzhou as a springboard to conduct knowledge spillover cooperation with Chennai, India; Zhuhai and Dongguan collaborated with Durham, Raleigh, Chapel Hill, and other regions of the United States via Hong Kong.

4.2. Global–Local Strategic Coupling Network Path of the Biopharmaceutical Industry in the GBA

4.2.1. Evolution of Transnational Coupling Paths

In general, the global–local coupling network nodes of the biopharmaceutical industry in the GBA are primarily made up of developed countries in the northern hemisphere, with noticeable annual changes between countries (Table 1). It can be broken down into three stages: (1) From 1990 to 1999, there was little external knowledge spillover from the biopharmaceutical industry in the GBA. It first made contact with Germany, Australia, the United States, and other countries before spreading to the United Kingdom, Ireland, France, Italy, Spain, and other Western European countries. (2) From 2000 to 2009, the knowledge spillover of the biopharmaceutical industry in the GBA increased significantly, gradually spreading from Britain, France, Germany, and Italy to Belgium, the Netherlands, Switzerland, Sweden, Portugal, Sweden, Russia, and other European countries; in North America, the connection with the US and Canada gradually occupied the dominant position of the coupling networks; and in Asia, it has gradually spread from Singapore. (3) From 2010 to 2019, the global–local coupling paths of the biopharmaceutical industry in the GBA followed the pattern of “local penetration and overall stability”. Cities and global countries and regions are concentrated in Europe (Britain, France, and Germany), North America (the United States and Canada), Australia, Japan, and other newly developing countries such as India, Sri Lanka, and Argentina.

Table 1. Global–local strategic coupling paths of the biopharmaceutical industry in the GBA ¹.

Periods	Core Cities	Coupling Countries	Coupling Cities
1990–1994	Hong Kong	Australia (2), USA (1), Germany (1)	Sydney, Melbourne, Washington, D.C., Dusseldorf
1995–1999	Hong Kong	USA (10), Germany (7), Australia (2), Britain (1), France (1)	Washington, Cincinnati, Cologne
2000–2004	Hong Kong, Guangzhou	USA (80), Britain (15), Japan (12), Germany (9), Canada (8), Australia (8)	Boston, Los Angeles, London, San Diego, Raleigh, Carrey, Tokyo, Hillsborough, Munich, Melbourne, New York
2005–2009	Hong Kong, Guangzhou, Shenzhen	USA (86), Britain (17), Japan (8), Germany (8), Canada (15)	New York, Boston, Washington, San Jose, London, Houston, Vancouver, Singapore, Paris
2010–2014	Hong Kong, Guangzhou, Shenzhen	USA (68), Britain (16), Japan (8), Canada (7), France (3),	London, New York, Los Angeles, Paris, Osaka, Rhode City, Cincinnati, Singapore, Vientiane, Minneapolis
2015–2019	Hong Kong, Guangzhou, Shenzhen	USA (77), Japan (8), Britain (5), Singapore (3), Canada (3)	New York, Oxnard, Kyoto, Los Angeles, Atlanta, Houston, Trenton, Fremont, Singapore

¹ Due to the limitation of space, the country only represents the countries with the top 5 coupling times, and the city only represents the cities with the top 10 coupling times. When making statistics, list all the parallel countries (cities) in the parallel situation.

4.2.2. Evolution of Geographical Coupling Paths

This study discovered, based on the geographical characteristics of the node cities of the coupling networks (Table 2), that: (1) When strategic coupling occurs with new countries (regions), cities with national capitals, developed economies, and rich innovation resources are frequently the first choice. When the GBA biopharmaceutical industry collaboration network expanded to Europe, Dusseldorf, Germany, was chosen as the capital city of North Rhine Westphalia, Europe's most densely populated and economically developed region. Then, in the process of diffusion in European countries, economically developed and densely populated cities such as London, England, Paris, Ireland, Dublin, Rome, Italy, and others were chosen first. (2) In the diffusion process of the coupling network, the coupling nodes show an obvious evolution process from coastal ports or border cities to inland cities based on the evolution of the geographical location path of the coupling network nodes. For example, in the connection with North America, the network first chose to couple with the urban agglomeration on the east coast of the United States (Washington, New York, and Boston), and then expanded to the San Francisco Bay (San Diego, San Francisco, San Jose, and Mountain View City), the areas near the Great Lakes (Chicago, Detroit in the United States, Toronto, Ottawa, and other cities in Canada), and finally spread to Cincinnati North Carolina Research Triangle Park (Raleigh, Chapel Hill, Durham) and other cities. (3) The regional industrial base, culture, and institution all have a significant impact on coupling path selection. For example, in the European coupling network, Lausanne, Basel, and Zurich in Switzerland, and Brussels in Belgium have become important nodes in the coupling network since 2005, with the continuous deepening of cooperation with Germany, Britain, France, and other regions. Among them, the biopharmaceutical industry in Switzerland is one of the most developed and innovative industries in Switzerland. The four most well-known biotechnology industry clusters in Switzerland are Geneva Lausanne, Basel, Zurich, and Ticino. It has been discovered that

the knowledge level of network destinations is also an important determinant of whether the subjects can be coupled.

Table 2. Distribution of invention patent applications of biopharmaceutical countries ¹.

Ranking	Country	Scale	Ranking	Country	Scale
1	USA	48	8	Korea	3
2	Japan	12	9	Denmark	2
3	China	8	10	Belgium	2
4	Germany	7	11	Italy	1
5	France	5	12	Netherland	1
6	Britain	5	13	Sweden	1
7	Switzerland	4	14	Ireland	1

¹ Data source: IncoPat domestic and foreign patent search platform (<http://www.incopat.com>, accessed on 26 January 2021).

5. Evolution Mechanism of Global–Local Strategic Coupling Network in the GBA

5.1. Spatial Progression of Global–Local Coupling Network Evolution

The GBA's strategic coupling process of global–local knowledge spillover in the biopharmaceutical industry is marked by gradual spatial progression. Hagerstrand proposed three types of spatial knowledge diffusion: contagion diffusion, hierarchical diffusion, and relocation diffusion. Contagion diffusion is the gradual outward diffusion of knowledge spillover from the source; hierarchical diffusion is the initial flow of new knowledge among a small number of subjects with close kinship and similar scale, but new knowledge can flow among more subjects with similar grades as time goes on; and relocation diffusion is the knowledge spillover caused by the transfer of knowledge subjects [13,55,73]. According to the empirical study of the GBA biopharmaceutical industry, there are many types of spatial diffusion in the GBA biopharmaceutical industry's global–local coupling network: (1) From its diffusion path in North America (first select cities on the east coast, areas near the Great Lakes, the San Francisco Bay, and other regions, and then gradually spread to the United States and central Canada), it can be seen that the paths of the coupling network will first be selected in economically developed regions with close social contacts with their own countries (regions), and then gradually spread to other cities, which conforms to the characteristics of knowledge level diffusion. (2) The evolution of its coupling network paths in Europe (first in Germany's surrounding countries, then spreading to the rest of Europe) demonstrates that infectious diffusion is also the main form of the global–local coupling network's local diffusion.

5.2. Stage Evolution of Global–Local Coupling Network Evolution

The formation and evolution of the biopharmaceutical industry's global–local strategic coupling network path in the GBA have occurred in two stages: (1) The first stage (1990–1999) of strategic coupling network diffusion is the tentative path stage. It is emphasized that the global–local strategic coupling of the GBA cities was caused by Hong Kong's spillover as the coupling “window”. Hong Kong's “window” function of a regional strategic coupling is determined by historical reasons (colonial) and social system reasons (social system, economic system, etc.), and the special historical period endowed Hong Kong with an important historical position as the GBA's only core of the knowledge spillover network. (2) The second stage (2000–2010) is characterized by rapid growth in strategic coupling network diffusion. Guangzhou had also become the focal point of the GBA's strategic coupling at this point. The coupling network continuously established new coupling routes with North America (the United States and Canada), Europe (the United Kingdom, France, Germany, Italy, Switzerland, and so on), and Australia based on the original route (Dusseldorf, Germany, Melbourne, Sydney, Australia) (Australia, New Zealand, etc.). (3) The third stage of strategic coupling network diffusion (2010–2019) is the stable path stage. The main body and content of strategic coupling were solidified at this stage. In other words, after the knowledge spillover subject selects a tentative and rapidly growing coupling path, it

gradually maintains a relatively stable coupling network path in the large pattern, with only small local areas experiencing new path exploration. The most significant feature of this stage is the spatial differentiation of knowledge spillover between different cities within the GBA and the expansion state of the global–local strategic coupling network. Following self-improvement in path evolution, some cities' regional knowledge innovation ability and knowledge bargaining ability significantly improved. They continued to fortify the original coupling path while also exploring new coupling paths (such as Shenzhen). The strength and breadth of regional coupling continued to evolve, and the stage of decoupling and re-coupling was reached. However, due to insufficient innovation capacity in technical content and structure, some other cities have limited their competitiveness in the strategic coupling network of global–local knowledge spillover. They lack the stamina to explore new coupling paths, forming a path lock (such as Guangzhou), and gradually entering the stage of horizontal strategic coupling, that is, the strategic coupling between the region and the world has reached a relatively stable state, and the annual change of the coupling network is not visible.

5.3. Driving Mechanism of Global–Local Coupling Network Evolution and Path Selection

Because of different types of subjects, intentions, influencing factors, and so on, the route selection mechanism of the strategic coupling network of global–local knowledge spillover has different stages and thus produces different knowledge coupling effects.

(1) Motivating factors. The driving force behind the formation of the strategic coupling network of global–local knowledge spillover varies depending on the nature of the actors [25,60,69,74,75]. The internal driving force of the government, scientific research organizations, and other subjects is primarily to improve regional knowledge production and bargaining power, promote international cooperation, and enhance international innovation status while driving all subjects to the coupling through relevant policies (such as intellectual property protection law, taxation, talent incentives, etc.). From the standpoint of enterprises, it is primarily to achieve the goals of technology exchange, product innovation, and market expansion, as well as to achieve the goal of innovation gain through collaboration between enterprise R&D departments and other subjects.

(2) Influencing factors. The bargaining power of regional knowledge, the willingness of actors, and the role of multidimensional proximity are the main influencing factors in the formation and evolution of the coupling network of global–local knowledge spillover. The first is knowledge of the region and bargaining power. The ability of different regions to absorb, invest, innovate, and spread knowledge and new technologies are heavily influenced by regional economic and technological foundations. Under the influence of economic power, knowledge flow and coding will become more explicit and easier to spread across the globe. According to the research, the cities that occupy the core position in the process of the formation and evolution of the global–local strategic coupling network path of the GBA biopharmaceutical industry are frequently the regional economic, political, or cultural centers. As a result, one of the important deciding factors for global–local strategic coupling is the bargaining power of regional knowledge [7,13,14,61,76]. The will of the actor is also important. From the standpoint of knowledge spillover, scientific research institutions and transnational biopharmaceutical enterprises are the primary actors in the formation of global–local coupling networks. Strategic coupling is the active and conscious interaction of two actors. For example, the knowledge coupling between the Guangdong Hong Kong Macao Bay area and cities (towns) such as Chapel Hill, Durham, and Raleigh in the North Carolina Research Triangle of the United States demonstrates that research institutions, multinational enterprises, and the subjective will of regional government forces guided by common goals are important driving forces for the formation of strategic coupling. In addition to the two factors mentioned above, geographical proximity, social proximity, and organizational proximity are important considerations. One of the key theories used to explain the spread of technological innovation is multidimensional proximity. Multi-dimensional proximity, such as geographical proximity, social proximity, and organizational proximity, all play important roles in the formation and

evolution of the global–local knowledge coupling network path of the biopharmaceutical industry in the GBA [18,57,77–79]. For the global biopharmaceutical industry, geographical proximity (path selection in Europe) and social proximity (coupling with the United States east coast urban agglomeration, the Great Lakes urban agglomeration, the San Francisco Bay urban agglomeration, and other regions) between the coupling subjects in the global–local system are important factors in forming the coupling network, particularly those in Europe (Table 3). Furthermore, geographical location, social and cultural background, and institutional environment will all play a role in the formation of the knowledge spillover coupling network.

Table 3. Distribution of invention patent applications of biopharmaceutical enterprises ¹.

Ranking	Enterprise	Country	Scale
1	Roche	Switzerland	2122
2	Novartis	Switzerland	1336
3	Merck	USA	1222
4	Johnson & Johnson	USA	988
5	Bristol-Myers Squibb	USA	824
6	Bayer	Germany	694
7	Sanofi	France	670
8	Regeneron Pharmaceuticals	USA	662
9	GlaxoSmithKline	Britain	657
10	Boehringer-Ingelheim	Germany	588

¹ Data source: IncoPat domestic and foreign patent search platform (<http://www.incopat.com>, accessed on 26 January 2021).

(3) The effect of coupling. The strategic coupling network effect of global–local knowledge spillover has progressiveness and stage difference under the influence of different network path selection stages (tentative, expanding, and stable) and different coupling states. Inter-regional entities generate knowledge spillover associations in the first stage, driven by multidimensional proximity and innovation gain. The selection of coupling nodes at this stage varies due to the influence of the geographical distribution, history, institutional culture, organization, and so on of innovation elements. In the second stage, as the coupling state deepens, knowledge between regions exhibits the characteristics of orderly mobility, which is primarily manifested as follows: first, the regional spatial viscosity is enhanced, and the regional agglomeration of innovation exhibits the law of distance attenuation; second, knowledge spillover is primarily due to the non-local connection of R&D departments and scientific research organizations of enterprises and the e-commerce sector. The third stage is that the connection between nodes of the coupling network gradually forms a strategic coupling network of global–local knowledge spillover due to the interaction and influence of the orderly flow of knowledge in different regions.

6. Conclusions and Discussion

This paper takes the biopharmaceutical industry in the GBA as the research object, depicts the global–local strategic coupling network structure and path evolution process from 1990 to 2019, divides the evolution of its strategic coupling network path into stages, and summarizes its path selection mechanism based on constructing the analysis framework of the global–local knowledge spillover strategic coupling system. The following are the main conclusions:

- (1) The strategic coupling of global–local knowledge spillover is characterized by networking, as evidenced by an increase in the number of coupling network nodes and an increase in network density. The network subjects of global–local coupling are primarily composed of global units (multinational enterprises, international organizations, global scientific research institutions) and local units from the perspective of the coupling network’s subsystem (governments and local enterprises). The links and interactions between different subjects within the coupling network’s subsystem units

are hierarchical and complex, and knowledge spillover flows from knowledge-rich areas to relatively poor areas, demonstrating the regularity of knowledge as “the second law of heat”.

- (2) From 1990 to 2019, the strategic coupling network structure of the biopharmaceutical industry in the GBA, which uses knowledge spillover as a carrier, shows significant differences in stages. The GBA’s overall network structure evolution demonstrates a dynamic network evolution process of “single core; three weak cores; three strong cores”. Hong Kong, Guangzhou, and Shenzhen exhibit distinct development sequences of global–local strategic coupling networks in terms of the evolution of individual network structures. Hong Kong is the first city in the world to implement global strategic coupling. Guangzhou’s coupling network expanded significantly between 2000 and 2014, while Shenzhen gradually moved into the core position of the GBA’s global–local coupling network after 2014.
- (3) The path selection of the biopharmaceutical industry’s global–local coupling network in the GBA is spatially progressive and phased. The main factors influencing the coupling network’s path selection are the bargaining power of regional knowledge, the will of behavioral subjects, and multi-dimensional proximity. In terms of geographical characteristics, the main body will first choose the central city (center of politics, economy, and culture) or coastal port city related to the country (region) as the base point, and then gradually spread to the surrounding areas of these bases. The stages of the coupling path can be divided into three categories: the tentative path from 1990 to 1999, the expanding growth stage from 2000 to 2010, and the stable path from 2010 to 2019.

The GBA serves as a frontier window for China’s external opening and cooperation. As a critical strategic emerging industry in the new era, it is necessary to investigate the export-oriented knowledge coupling network of the GBA’s biopharmaceutical industry to demonstrate and guide its innovative cooperation on a global scale. The following research can be conducted based on this study: First, this study only uses GBA’s biopharmaceutical industry knowledge spillover as a carrier to depict the global–local coupling network and its path, without comparative research on different regions and different types of industries, and cannot explore the heterogeneity of coupling networks in different regions (such as the GBA, Beijing–Tianjin–Hebei Region, Yangtze River region) or industries (such as the high-tech industry, traditional manufacturing industry, and service industry). As a result, we can clarify the differences in future research by comparing the global–local coupling networks and their path evolution in different regions and industries. Second, this paper combines WIPO data on international patent cooperation. While it can better characterize patent cooperation links between GBA and global cities, it also weakens links between cities within the region (domestic, GBA) and cannot show the specific structure of the coupling networks at different geographical scales. We can continue to investigate the combination of regional and global patent cooperation in future research. Third, there are regional differences in the development of innovation networks across industries and regions. This paper focuses solely on the biopharmaceutical industry in the GBA. Although it quantitatively depicts the evolution path and state of strategic coupling of knowledge spillover in specific industries and regions, the theoretical refinement of the common development mode of innovation networks requires further investigation. In particular, the process of global–local coupling has been affected significantly due to the impact of COVID-19, mainly reflected in the network toughness damage caused by the blocked mobility in the global production network, which directly affects the scale, strength, and benefits of strategic coupling. Focusing on this, subsequent studies can explore the differences between real industries coupling (such as manufacturing) and knowledge-based coupling (innovation), the differences between formal knowledge spillover (patent cooperation) and informal knowledge exchange (social relationship), and the different impacts and responses to the impact of COVID-19.

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