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Assessing the Knowledge-Building Dynamics of Countries in the Formation of Emerging Fields: A Bibliometric Approach on iPS Cells

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Abstract--**This paper seeks to demonstrate a method for assessing the dynamics of the knowledge-building of countries active in the formation of technological fields at early stages of development. The empirical case of induced pluripotent stem (iPS) cells, a newly discovered stem cell species, is chosen. Conceptually, we visualize knowledge-building efforts surrounding an emerging field as involving the formation of knowledge networks. According to the way countries participate in these knowledge networks, insights into their knowledge-building dynamics can be gained. Three types of dynamics are evaluated in this study: 'knowledge exploration', 'knowledge nurturing', and 'knowledge exploitation'. For that purpose, an integrated and multi-dimensional bibliometric mapping approach encompassing both the intellectual bases and research fronts, and a conflated techno-scientific layer is used. Three types of networks were built: bibliographic coupling, co-citation clustering, and citing-cited networks; each network for each of the dynamics analyzed in this paper. By looking beyond the simplistic façade of general bibliometric indicators, the results of this paper are believed to provide a more complex picture of the dynamics involved in potentially rewarding emerging fields.**

I. INTRODUCTION

Technological change has become more frequent and more severe over the years. A natural outcome of this relentless change has been the continuous formation of new technologies propagating across countries, industrial sectors, and markets [1]. These new technologies, typically referred as emerging technologies, have been regarded as essential to successful growth, employment, competition and sustainability, and in the formation of new and transformed industries [2]. With such potential benefits, it is not surprising that actors, be it countries, organizations, or individuals, are willing to take the risk of being involved in the formation of newly emerging fields. The latter, despite the well-known market and technical uncertainties surrounding technologies at early stages of development [3], as well as their speculative features in which expectations, controversies, and even hype play crucial roles [4]. As may be inferred, not every actor can successfully accrue value from the potential opportunities of emerging fields; here, reasons behind these discrepancies are: differences in the competence-building efforts [5], the path-dependent nature of research efforts [6], external aspects such as laws and regulations, etc. In this paper, the role of knowledge-building as a crucial aspect in exploiting the opportunities of newly emerging fields is stressed. Conceptually, we visualize the knowledge-building efforts around emerging fields as involving the formation of a knowledge network tightly knitted to the technological innovation system that usually accompanies the emergence of new technologies [7]. The way countries take part in these knowledge networks is regarded as crucial aspect for defining the influence of countries on maneuvering the developments of a particular field. Within this mind, the aim of this paper is to assess, in quantitative terms, the dynamics of the knowledge-building efforts of countries active in newly emerging fields as inferred from the knowledge networks. Here, the empirical case of induced pluripotent stem cells (iPS cells), which are a newly discovered stem cell species that can be generated by the reprogramming of somatic cells, is used. For the particular case of Japan, iPS cells have become one of the pillars of the current government's economic growth strategy. As part of the innovation strategy 'substitution and supplement of body and organ functions', earlier approvals of regenerative medicine products for the promotion of the practical use of iPS cells and a 110 billion yen-fund in support of stem cell research over the next 10 years have been recently introduced in Japan [8-10].

Typically, simple bibliometric indicators such as publication outputs, growths or citation impacts have been used in practice to measure the knowledge-building efforts of countries. Despite its simplicity, such approaches suffer from several major drawbacks; particularly, their 'conceptual narrowness' prevents them from taking into account the interdependencies between publications and patents, and thus fail to provide deeper insights into the knowledge-building dynamics. Recently, Rafols et al [11] have advocated for the 'opening-up' of science and technology indicators. For them, "both broader and more plural forms of S&T indicators and visualization tools are needed" [11]. This paper closely resonates with Rafols et al [11]'s demands by making use of a bibliometric approach integrating an array of quantitative indicators and knowledge mapping approaches across an array of analytical layers. Two main layers of analysis are used. First, emerging disciplines are visualized in terms of both the intellectual base on which emerging fields are built upon and the research fronts along which they are heading to [12]. Second, scientific and technological aspects are conflated into a techno-scientific layer by integrating the totality of publications and patents of an emerging field into a single framework. Under the assumption that bibliometric-based networks can be used as proxies of the knowledge networks building around emerging fields, co-citation clustering, citing-cited and bibliographic coupling networks integrating both the full of scientific papers and patents of the emerging field of iPS cells were constructed. By observing the way relevant countries – United States, Japan, United Kingdom, Germany, and China – take part in these networks, their dynamics of knowledge-building were evaluated. In this paper, three main roles are assessed: 'knowledge exploration', 'knowledge exploitation, and 'knowledge nurturing'. The results of this paper are expected to provide a visual and quantitative method for assessing the paths to be taken by countries in order to increase their relevance in potentially rewarding emerging fields.

This paper is structured as follows. Section 2 begins with a brief description of the field of iPS cells. Section 3 continues with the description of the framework of analysis underpinning this paper. Next, Section 4 provides a description of the data and methods of analysis. Following, Section 5 describes the results of this analysis. Finally, Section 6 closes by providing the conclusions and implications drawn from this paper.

II. THE TECHNOLOGY UNDER STUDY: INDUCED PLURIPOTENT STEM CELLS (IPS CELLS)

Stem cells are the foundation cells of living multicellular organisms. They are characterized by two main properties: self-renewal and differentiation into a wide range of specialized cell types. Over the years, a wide range of stem cells have been reported: embryonic, mesenchymal, hematopoietic, endothelial, and induced pluripotent stem cells, among many others. Typically, stem cells have been divided according to their ability to differentiate, i.e. change, into other cell types, also referred as cell potency. From their greatest to their lowest cell potency, stem cells are classified into totipotent, pluripotent, multipotent, oligopotent and unipotent stem cells. In particular, pluripotent stem cells refer to those cells capable of becoming all cell types, except for embryonic components. Recently, stem cell research has experienced a renewed interest within the scientific community, particularly driven by the emerging field of induced pluripotent stem cells (iPS cells) [13]. iPS cells are non-pluripotent mature cells that have been reversed to become pluripotent by introducing, through an array of different methods, a series of pluripotency-related genes. iPS cells were first reported in 2006 in mice and in 2007 in humans by Shinya Yamanaka and his group at the Kyoto University in Japan. The groundbreaking nature of their discovery has been internationally acknowledged through the conferral of the Nobel Prize in Physiology or Medicine to Shinya Yamanaka in 2012 jointly with John B. Gurdon. Research on iPS cells has dramatically accelerated worldwide because of their therapeutic potentials allowing treatments without the ethical and political debates surrounding embryonic stem cells. In particular, four potential avenues of application of iPS cells are typically highlighted [14]: (a) basic or academic research tool and drug discovery tools particularly toxicity testing, (b) disease modelling or the ability to generate pluripotent cells from patients afflicted with diseases, (c) personalized medicine whereby therapeutic regimes are optimized to minimize side-effects and maximize efficacy at an individual patient basis, and (d) cell implantation therapies or regenerative medicine through regeneration or repair of organs and tissues damaged by diseases. For the particular case of Japan, iPS cells have become one of the pillars of the current government's economic growth strategy. As part of the innovation strategy 'substitution and supplement of body and organ functions', earlier approvals of regenerative medicine products for the promotion of the practical use of iPS cells and a 110 billion yen-fund in support of stem cell research over the next 10 years have been recently introduced in Japan [8-10].

III. FRAMEWORK OF ANALYSIS

Knowledge has been regarded as what makes technologies possible [15]; as such, it is not only an outcome, but also a condition for the generation of innovations [16]. In terms of its dynamics, knowledge has been regarded as an uncertain, open-ended, and dynamically uneven process brought about by learning and cumulative interactions [17, 18]. Two properties of knowledge important for this paper are its co-relational structure, i.e. knowledge establishes connections between concepts, and its retrieval and interpretative structure, i.e. knowledge can be recovered [19]. Following Krafft et al [16], it can be inferred that knowledge can be represented in terms of networks. Different names have been used to refer to these knowledge networks, such as knowledge bases, knowledge structures, etc. Conceptually, these knowledge networks are believed to reflect the knowledge-building efforts surrounding an emerging field. What is more, given the above-mentioned duality between knowledge and technology, we may expect these knowledge networks to be closely intertwined to the embryonic technological innovation systems that have been typically assumed to be building around newly emerging technologies [7]. The structure and nature of this knowledge network is expected to be an emerging property of the innovating agents or actors [16]. These actors are the individuals or organizations – be it public research organizations, universities, firms, government agencies, individuals, etc. performing innovation activities and pursuing deliberate strategies [20]. Moreover, they are characterized by particular learning processes, competencies, beliefs, objectives, organizational structures and behavior-interacting through processes of communication, exchange, cooperation, coopetition, and command [20]. From what has been said, it can be inferred that the way actors take part in the knowledge networks building around emerging technologies may provide insights into their influence on maneuvering the developments of a particular field. Given the complexities involved in these processes, the understanding of the role of countries in the knowledge networks demands a multi-dimensional and integrated approach. In this paper, as shown in Fig. 1 we attempt to do so by visualizing the knowledge networks building around emerging technologies in terms of the intellectual bases on technologies are built upon (backward looking) and the research fronts along which they are heading to (forward looking) [12], as well as the confluence of both scientific and technological issues into a single techno-scientific layer.

A method has been advanced for integrating both scientific and technological layers into a single knowledge network, what we refer as techno-scientific networks. In contrast to scientific linkage approaches in which only the non-patent references of patents are used, our approach encompasses the totality of patents and publications, and their cited patents and publications, encompassing an emerging field. Building upon the framework shown in Figure 1, in this paper we would like to explore the way relevant countries participate in the knowledge-building efforts within the emerging field of iPS cells as reflected on their techno-scientific, backward/forward-looking networks.

Empirically, these knowledge networks are visualized through bibliometric mapping approaches. As shown in the bottom of Fig. 1, three different networks are used – co-citation clustering, bibliographic coupling, and citing-cited networks – from which three roles related to knowledge-building efforts are discerned: knowledge exploration, knowledge nurturing, and knowledge exploitation. As later sections will show, each of these roles was visualized in terms of quantitative indicators drawn from bibliometric mapping approaches. Following, each of these roles will be described:

- **Knowledge exploration** – It relates to the ability of countries to actively contribute to the research fronts of an emerging field. As such, an influential role in knowledge exploration endows countries with an ability to advance a field. This is the forward-looking perspective. Assuming the use of bibliographic coupling networks as proxies for assessing the research fronts of a particular field [21-23], knowledge exploration was analyzed through the role played by relevant countries in the techno-scientific bibliographic coupling networks. This role is related to the way a country opens up research avenues in an emerging field.
- **Knowledge nurturing** – It points to the ability of countries to add up to the intellectual base underpinning a field. A strong role on knowledge nurturing points to countries with a high cognitive influence on the other countries. As such, this refers to the 'backward-looking' perspective. Relying on the use of co-citation clustering as a proxy for the intellectual bases of fields [12, 22, 23], knowledge nurturing was evaluated by assessing the role played by relevant countries in the techno-scientific co-citation clustering network. This role is related to the way a country influences the cognitive structure underpinning an emerging field.
- **Knowledge exploitation** – It refers to the ability of countries to make use of or exploit knowledge previously generated by other countries. In bibliometric terms, knowledge exploitation can be inferred by evaluating the citing-cited relationships among countries.

Each of the networks built for describing each of the three roles was evaluated through a series of bibliometric indicators, which will be described in detail in the following section.

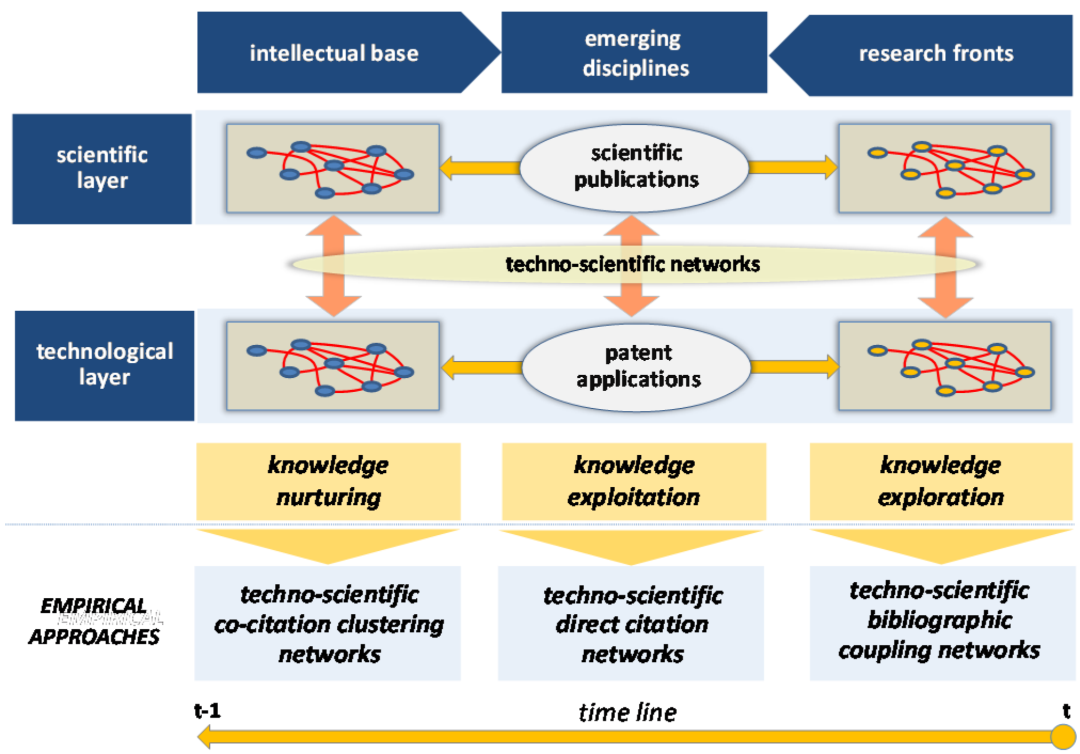

Fig. 1 Conceptual and empirical approaches analyzed in this paper

IV. DATA AND METHODS OF ANALYSIS

This section briefly describes the data and methods of analysis used in this study. Both, publication and patent data relevant to the iPS field were used. As previously described, in contrast to extant research efforts both bibliometric sources were used in an integrated framework. Publication data were extracted from the Thomson Reuters' Web of Knowledge (WoK). For that purpose, the following search query was used: TS=((induc* NEAR/25 pluripoten* NEAR/25 stem) OR ((IPS OR IPSC) AND (stem NEAR/5 cell*))). This search was restricted to the titles, abstracts and keywords of articles and proceeding papers written in English and published within the time period 2006-2012. The year 2006 was used as it was the year when the pioneering paper by Takahashi and Yamanaka on the discovery of iPS cells derived from mice was published. A total of 2,283 publications were originally collected, which were manually read in order to identify those documents relevant for the field of iPSC technologies. At the end, 1,536 publications were selected for this study. From these, 27,773 cleaned cited references were extracted. Patent data were extracted from the Thomson Reuters' Derwent Innovations Index (DII). In contrast to publication data, a much broader keyword-based search query was used: TS=(pluripoten* AND "stem cell*"). This search embraced the titles and reviewed abstracts of patent documents. In order to take into account the 18-month time lag until patents applications are published, patents with publications years until 2013 were considered. A total of 1,916 patent families were collected. After manually reviewing the full text of each of these documents with Google Patents and other publicly available patent databases, 1,143 patent documents were considered. In this case, the criteria for the selection of relevant patents was based on the use of iPS cells at its broadest sense; that is, patents directly stating a direct or intended use of iPS cells on the claims or as an embodiment of a patent were considered for this study. In total, 7,324 cited patents and 21,441 non-patent references (NPR) were extracted from the full text of these patents through the use of the software application Grobid developed by Patrice Lopez from the INRIA research institute in France [24].

In a subsequent step, the collected data underwent a series of cleaning and sorting procedures consisting mainly of manually grouping together similar references, correcting input errors in their bibliographic information, etc. Of particular importance for this study, the labels of patents and publications, sources and cited references, underwent an exhaustive standardization in order to integrate patent and publication data into single networks. Following, the software VantagePoint was used to merge the datasets required for the construction of the different techno-scientific networks: co-citation clustering networks, citing-cited networks, and bibliographic coupling networks. These networks were visualized and analyzed with the software UCINET/NetDraw. In total, two sets of networks were constructed, one for each of the time periods under study, namely 'up to 2009' and '2010-2012'. A crucial step for this research consisted in the extraction of countries from these networks. This was done by allocating the countries where the authors of publications and the assignees of patents come from. For the cases of nodes with multiple countries, the contribution of each country was counted as a unit. Moreover, given their predominant position on the field of iPS cells, the USA, the UK, Japan, Germany, and China were selected for this study. For the construction of each of these networks a series of thresholds were used to restrict our analysis to relevant network nodes. As previously described, these networks were used to assess the roles of countries in knowledge-building efforts surrounding the emerging field of iPS cells. For this purpose, a series of bibliometric indicators were estimated for each of the constructed networks (co-citation clustering, bibliographic coupling, and citing-cited networks). For the case of the co-citation clustering and bibliographic coupling networks, the following indicators were used:

- **Significance of countries in the intellectual bases and in the research fronts** – The significance of the participation of countries in the knowledge networks building around the emerging field of iPS cell, in terms of the intellectual base and research fronts, was measured through the shares of nodes in which countries are present in the co-citation clustering and bibliographic coupling networks, respectively. Additionally, the shares of records were evaluated for the nodes of each country. Both measures of significance were recorded in percentage units.
- **Predominance of countries in the intellectual bases and in the research fronts** – For these indicators, average degree and betweenness centrality values of the nodes in which countries are present in the co-citation clustering and bibliographic coupling networks were evaluated. In contrast to the previous indicator, predominance takes into account the interrelationships among network nodes, and therefore the locational quality and influence of the nodes within the network. Degree centrality defines the number of edges incident on a node in a network. As such, it indicates the degree to which a particular country exists in the network. Betweenness centrality refers the extent to which a node lies on the shortest path between pairs of nodes in the network. This centrality value determines the locational quality of the problem areas; usually, those with high betweenness centrality tend to be located closer to the center of the network.

For the case of the citing-cited network, the following indicators were used:

- **Degree of external cognitive influence** – The degree of external cognitive influence of relevant countries was measured through the percentage of self-citation observed in the citing-cited relationships across countries.

- **Breadth of country influence** – This indicator measures the breadth of countries influencing the technoscientific activities of a particular country. For that purpose, the Shannon's entropy of the proportions of countries being cited by the nodes of a particular country was estimated.

V. RESEARCH RESULTS

This section describes the results of this paper. Before describing the assessment of the dynamics of the knowledge networks, next section presents a general bibliometric analysis of the total of scientific papers and patents collected for the emerging field of iPS cells.

A. General bibliometric analysis

This section provides preliminary insights into the roles played by relevant countries in the knowledge building efforts surrounding the emerging field of iPS cells through the use of simple bibliometric indicators (Fig. 2).

In line with Boyack et al [25], Fig. 2 relates the total of publications and patents on iPS cells for relevant countries over the periods of time 'up to 2009' and '2010-2012'. As can be seen in this figure, the USA and Japan are leading the field of iPS cells; particularly, the outstanding performance of the USA during the period 2010-2012 should be highlighted. Despite its pioneering efforts in this field, Japan appears to be lagging behind. Moreover, based on the slope of their line graphs, the USA and Japan appear to be experiencing balanced growth rates in publications and patents. The performance of the rest of the countries is shown in the inset of Fig. 2. As shown in this figure, the performances of Germany, the UK, and China outstand relative to other countries (Singapore, South Korea, and France). Nevertheless, as suggested by the slope of their line graphs, their performance appears to be mainly focused on scientific publications. In this regard, the case of China should not be overlooked, particularly during the second time period. During this time period, at least for the case of publications, China has achieved performance levels closer to Japan.

Although some interesting aspects can be drawn from the analysis presented in this section, next section will show that greater insights can be gained from evaluating the performance of countries from a network perspective.

B. Evaluation of the dynamics of knowledge-building for relevant countries

This section presents the results from the evaluation of the different techno-scientific networks constructed in this paper: co-citation clustering, bibliographic clustering and citing-cited networks (Fig. 4); one type of network for each of the three types of knowledge-building roles analyzed in this paper. Moreover, two periods of time are shown in Fig. 3, namely 'up to 2009' and '2010-2012'. As previously described, these networks include the totality of publications and patents for the field of iPS cells. For the purposes of this section, the countries participating in each of the nodes of the networks were collected. Following, the bibliometric indicators estimated from this network-based country data will be described.

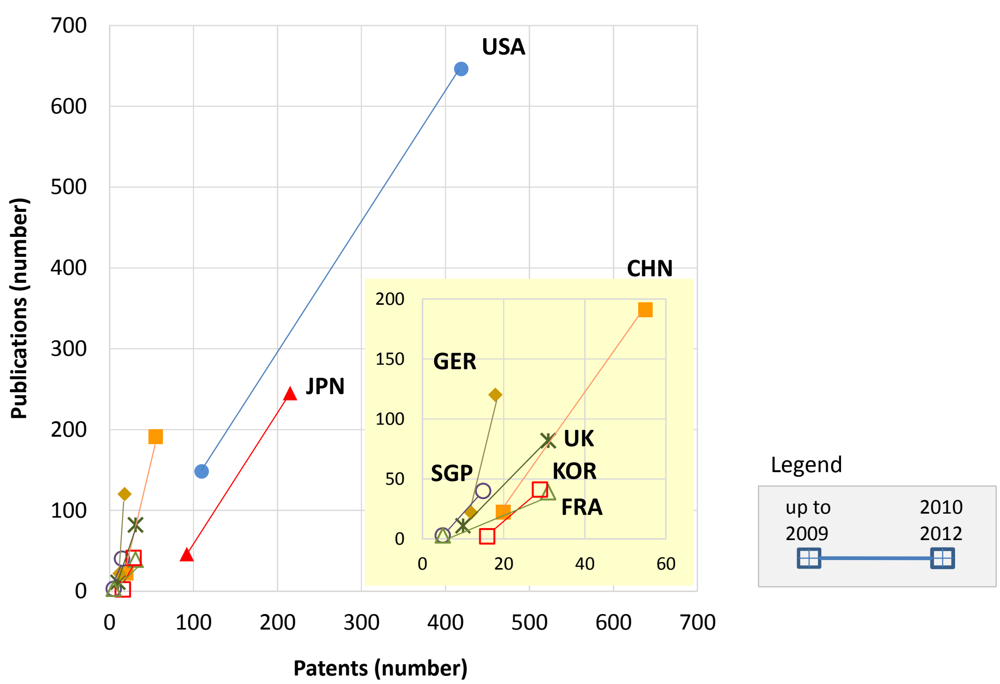

Fig. 2 Patents and publications for the field of iPS cells for the time periods: up to 2009 and 2010-2012.

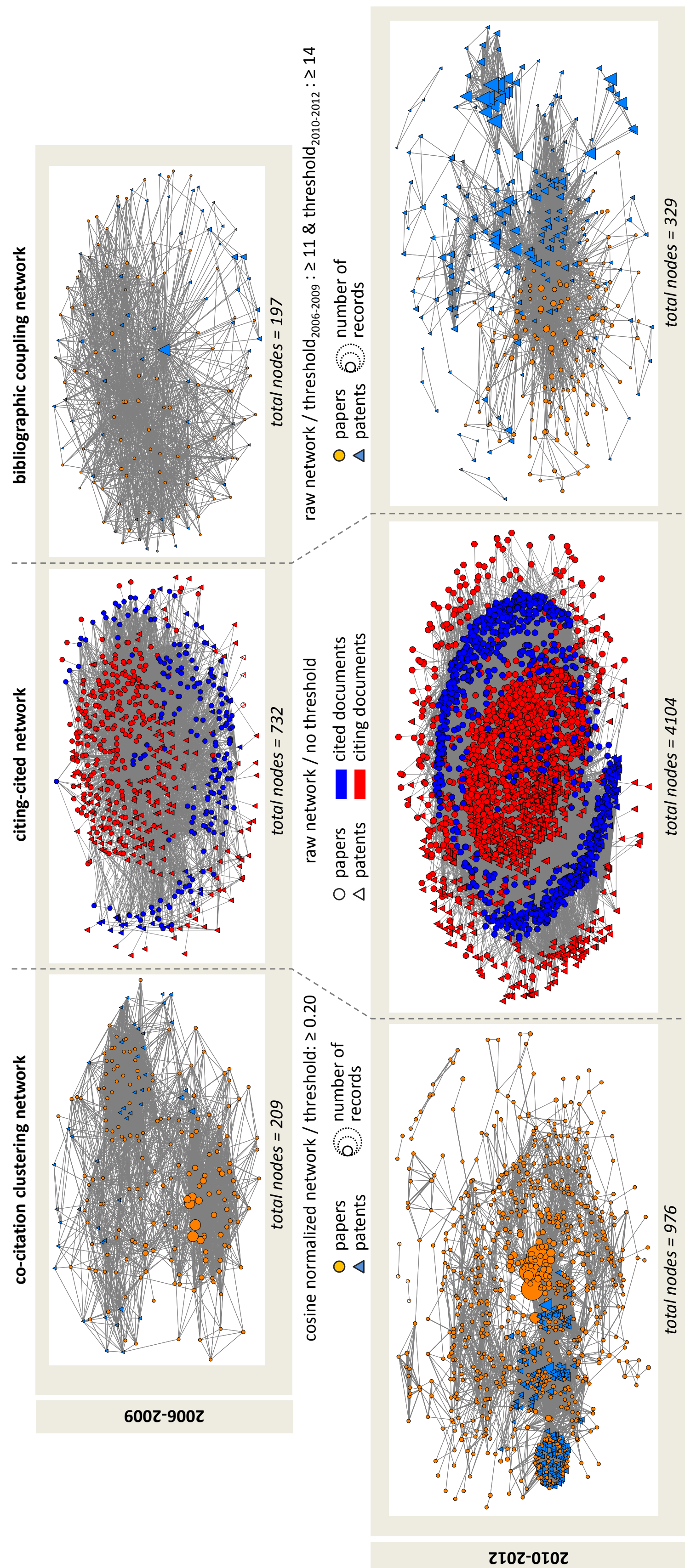

Fig. 3 Co-citation clustering networks, citing-cited networks, and bibliographic coupling networks

TABLE 1 SIGNIFICANCE AND PREDOMINANCE OF COUNTRIES IN THE INTELLECTUAL BASE (ALL, ONLY PATENTS, AND ONLY PUBLICATIONS)

co-citation clustering

2006-2009

(ALL)					(ONLY PATENTS)					(ONLY PUBLICATIONS)				
country	% nodes	% rec	av. degree	av. betw	country	% nodes	% rec	av. degree	av. betw	country	% nodes	% rec	av. degree	av. betw
China	1.4%	0.6%	28.8	20	China	-	-	-	-	China	1.7%	0.6%	28.8	20.0
Germany	7.2%	5.8%	43.3	56.9	Germany	-	-	-	-	Germany	8.8%	6.2%	43.3	56.9
Japan	13.1%	23.3%	47.5	137.8	Japan	10.0%	21.0%	29.2	43.0	Japan	13.8%	23.5%	50.3	152.2
UK	8.3%	4.8%	35.2	73.9	UK	4.0%	2.5%	45.0	72.0	UK	9.2%	5.0%	34.3	74.1
USA	53.4%	55%	40.1	90.2	USA	64.0%	61.7%	26.3	59.5	USA	51.3%	54.5%	43.6	98.2

2010-2012

(ALL)					(ONLY PATENTS)					(ONLY PUBLICATIONS)				
country	% nodes	% rec	av. degree	av. betw	country	% nodes	% rec	av. degree	av. betw	country	% nodes	% rec	av. degree	av. betw
China	3.7%	2.4%	23.1	884.4	China	-	-	-	-	China	4.0%	3.0%	24.3	901.9
Germany	5.3%	5.1%	34.2	937.2	Germany	1.2%	1.1%	36.0	131.4	Germany	5.7%	6.0%	34.1	951.3
Japan	10.5%	16.0%	29.9	1769.9	Japan	10.6%	15.2%	69.8	333.4	Japan	10.5%	16.2%	26.5	1893.1
UK	7.7%	6.1%	42.6	775.3	UK	8.2%	7.1%	147.4	23.6	UK	7.7%	5.9%	33.1	843.7
USA	50.1%	54.3%	46.9	1074.4	USA	71.8%	69.7%	106.5	308.5	USA	48.3%	50.8%	39.3	1170.9

% nodes: share of network nodes by country
% records: shares of records allocated to network nodes by country

av. degree: average degree centrality
av. betw: average betweenness centrality

1) Significance and predominance of relevant countries in the intellectual base

Table 1 presents the results of the bibliometric indicators obtained from the techno-scientific co-citation clustering networks over time. Three types of tables are included: one table including both publication- and patent-related network nodes, another table including only patent-related network nodes, and other table including only publication-related network nodes. The values across different countries do not add up to 100% as only the values for relevant countries are included in this table. As can be observed in Table 1, the intellectual base underpinning the field of iPS cells is dominated by the USA. Here, more than half of the shares of nodes and records of the intellectual base belong to American actors. In particular, USA's significance appears to be particularly evident for the patent-related network nodes which reach levels around 65-70%. Additionally, this is accompanied by a large predominance in the network in terms of their average degree and betweenness centrality values. This result may be related to the traditionally strong competences of the USA on the field of embryonic stem cells, one of the greatest cognitive influences for the field of iPS cells, as well as by the high competence of the USA in relevant general technologies for iPS cells, such as gene or virus delivery, gene editing, etc. Despite the pioneering efforts of Japan in this field, Japanese network nodes account merely 11-13% in the intellectual base. As shown in Table 1, the shares of countries tend to decrease over time as more countries join the field. However, Japan has experienced the largest decrements in significance over time, particularly for the case of publications. This may suggest a decreasing interest, although still strong, for the Japanese contributions in the intellectual base. Despite this, Japan still holds the largest predominance in the intellectual as shown in their highest centrality measures; that is, Japanese contributions are believed to occupy key positions within the intellectual base. This may be directly related to Japan's pioneering contributions in the area, particularly Prof. Yamanaka and colleagues' papers and patents. Germany and the UK are characterized by significance levels reaching 7-8% of the shares of nodes in the intellectual base, but slightly less values for the percentage of records. Two differences can be observed between both countries. First, whereas Germany displays the greatest levels of significance in publication-related nodes, the UK shows more balanced levels for both types of nodes. Second, despite the lower shares of nodes for Germany vis-à-vis the UK, it appears to enjoy higher levels of predominance, particularly for its patent-related nodes. The case of China shows an interesting pattern. China is the only country with increasing levels of significance values in the intellectual base; its values for publication-related nodes reach 4.0% for the second time period, getting closer to those of Germany and the UK. However, no patent-related network nodes can be observed for China.

2) Significance and predominance of relevant countries in the research fronts

Following a similar arrangement to Table 1, Table 2 describes the significance and predominance of relevant countries in the research fronts along which the field of iPS cells is directed. As can be observed in this table, similar to the intellectual base, the USA shows the largest significance. Whereas the significance of the USA along the technological layer has increased to reach levels around 60%, their influence on the scientific layer has decreased to levels of significance reaching 37%. The predominance of the USA, although still high, has been contested by other countries – Germany and the UK – particularly for scientific-related research fronts. Over time, the highly significant and predominant position of Japan in the research fronts in the first time period has eroded over time. For the case of the scientific-related research fronts, Japan appears to be outdone in significance and predominance by China. It would be interesting to further investigate the reasons behind such backwardness. Nevertheless, Japan still displays a significant and predominant influence in the technological-related research fronts. Over the years, Germany's significance has been mainly focused in scientific-related nodes reaching 7-8% for both nodes and records. Despite their relative low shares, German publication-related nodes display the largest predominance in the research fronts. In contrast to the rather influential role of the UK in the intellectual base, this country shows the lowest levels of significance in the research fronts. Despite their low significance, UK nodes appear to be well-positioned in the network, even reaching the highest values for patent-related nodes. Similar to their performance in the intellectual base, the relatively low and significant predominance of China in technology-related nodes is contrasted with strong scientific-related nodes reaching significance levels around 12-13% and similarly strong centrality values. In terms of the scientific-related nodes, China appears to have even overpassed Japan in significance and predominance.

3) Degree of influence of external countries

This section now discusses the influence of external countries on each relevant country's research efforts, as well as the breadth of their influences over time (Table 3). As the results obtained for the three tables – including both publications and patents, including only patents, and including only publications – were rather similar, Table 3 only shows the results for the citing-cited relationships including both publications and patents.

The relative low self-citation rates shown in Table 3 may point to the broad array of countries that are taken into account by each country's research efforts, even for strongly positioned countries such as the USA and Japan. Nevertheless, the percentages of self-citation do show some differences across countries, as described below. The decreasing self-citation rates and increasing entropy values discerned across countries may be attributable the increasing

TABLE 2 SIGNIFICANCE AND PREDOMINANCE OF COUNTRIES IN THE RESEARCH FRONTS (ALL, ONLY PATENTS, AND ONLY PUBLICATIONS)

bibliographic coupling

2006-2009

(ALL)					(ONLY PATENTS)					(ONLY PUBLICATIONS)				
country	% nodes	% rec	av. degree	av. betw	country	% nodes	% rec	av. degree	av. betw	country	% nodes	% rec	av. degree	av. betw
China	6.9%	6.7%	26.2	27.0	China	2.9%	2.9%	19.0	29.2	China	8.8%	9.0%	27.3	26.6
Germany	6.3%	6.9%	43.7	73.2	Germany	4.9%	4.4%	30.6	10.6	Germany	6.9%	8.3%	48.1	94.1
Japan	18.1%	18.8%	30.8	100.4	Japan	28.2%	29.1%	24.2	69.7	Japan	13.4%	12.6%	37.4	131.1
UK	3.1%	3.1%	29.9	52.8	UK	1.9%	1.9%	41.5	69.1	UK	3.7%	3.7%	27.0	48.7
USA	51.9%	52.0%	32.6	87.9	USA	52.4%	52.5%	19.5	62.4	USA	51.6%	51.8%	38.9	100.4

2010-2012

(ALL)					(ONLY PATENTS)					(ONLY PUBLICATIONS)				
country	% nodes	% rec	av. degree	av. betw	country	% nodes	% rec	av. degree	av. betw	country	% nodes	% rec	av. degree	av. betw
China	9.7%	8.4%	53.0	701.0	China	1.9%	1.6%	100.0	415.7	China	12.5%	13.1%	50.5	716.5
Germany	5.2%	4.6%	50.1	1124.4	Germany	1.6%	1.1%	34.7	463.2	Germany	6.5%	7.0%	51.5	1183.7
Japan	14.1%	13.6%	67.8	593.7	Japan	20.6%	18.0%	115.3	757.2	Japan	11.7%	10.6%	37.4	488.7
UK	3.6%	3.2%	38.8	1046.3	UK	2.7%	1.7%	40.4	1198.1	UK	4.0%	4.3%	38.5	1009.2
USA	42.5%	48.0%	43.0	888.2	USA	57.8%	63.1%	43.3	1009.9	USA	37.0%	37.5%	42.8	818.9

% nodes: share of network nodes by country
% records: shares of records allocated to network nodes by country

av. degree: average degree centrality
av. betw: average betweenness centrality

TABLE 3 SELF-CITATION AND ENTROPY OF THE CITING-CITED RELATIONSHIPS ACROSS RELEVANT COUNTRIES

	2006-2009		2010-2012	
country	% Self-citation	Entropy	% Self-citation	Entropy
China	6.3%	2.26	8.9%	2.77
Germany	13.9%	2.13	10.7%	2.89
Japan	22.7%	2.28	18.3%	2.62
UK	11.1%	2.21	8.9%	2.83
USA	22.2%	2.36	17.3%	2.77

number of countries joining this 'hot' field of research. The data on Table 3 helps us infer that the USA and Japan display the largest percentages of self-citation in the two time periods. Despite their large self-citation rates, both countries display a diverse range of countries influencing their research efforts as shown in their entropy values. In terms of their self-citation rates, the UK and Germany find themselves in a second-tier position with values around 10-11%. In particular, both countries are characterized by the largest entropy values. China shows the lowest rates of self-citation, which may point to their still peripheral influence in the field of iPS cells. However, for the time period 2010-2012, China has reached similar levels of self-citation as the UK as well as relatively high entropy values, which may suggest the catching-up efforts of China in the field of iPS cells.

VI. CONCLUSIONS AND DISCUSSIONS

In this paper, we have attempted to look behind the simplistic façade of general bibliometric indicators through the use of an analytical approach involving multiple sources of data and an array of different analytical perspectives: scientific/technological, forward-backward looking, bibliometric indicators and bibliometric mapping approaches, etc. Through this, a more complex picture of the dynamics of the contributions of countries to the knowledge-building efforts surrounding emerging fields, in our case the field of iPS cells, could be discerned. After constructing three different networks – co-citation clustering, citing-cited and bibliographic coupling networks – over two periods of time, a series of bibliometric indicators were extracted from these country-based networks to assess the three different knowledge-building roles evaluated in this paper: 'knowledge exploration', 'knowledge exploitation', and 'knowledge nurturing'. Compared to the general bibliometric analysis, we believe that our approach has come up with fuller insights into the dynamics taking place in this emerging field. By taking a network-based approach, the patterns of interdependency within and among the patents and publications encompassing an entire emerging field were taken into account.

In terms of 'knowledge nurturing', it was found that the USA has the most significant and predominant influence. Despite its pioneering efforts in the field of iPS cells, the significance of Japan was not as strong as we had expected. Japan's influence appears to be highly significant in the technological layer. Moreover, Japan still enjoys the highest predominant position in the intellectual base. The role of Germany, China, and the UK is mostly restricted to knowledge nurturing on the scientific layer of the intellectual base. In particular, the significance and predominance of China have reached levels closer to those of Germany and the UK. For the case of 'knowledge exploration', it was shown that the USA displays the strongest significance and predominance; however, its significance and predominance has been contested over time. Despite its decreasing significance and predominance in the scientific knowledge exploration, Japan still exerts a high influence on technological knowledge exploration. Chinese presence in 'knowledge exploration' efforts appears to have increased rapidly, particularly stressing the scientific domain; here, China appears to have overpassed Japan in both significance and predominance. Germany and the UK's roles have been meager in terms of the technological research fronts. Interestingly, despite their relatively low levels of significance, the UK displays the highest predominance in the technological research fronts and Germany the highest predominance in the scientific research fronts. For the case of 'knowledge exploitation', it was shown that despite the dominance of few countries in the field, it was observed that all countries were using a more or less similarly diverse country sources. Nevertheless, differences were observed for the rates of self-citation across countries. Here, significant and predominant countries such as the USA and Japan displayed a larger tendency to rely on knowledge sources from their own countries. This is not surprising giving their higher influence on this field. In contrast, China may be regarded as undergoing the largest knowledge exploitation, although its levels for the second period of time got closer to those of Germany and the UK.

A series of implications can be drawn from the results of this paper. First, feedback loops between intellectual bases and research fronts, i.e. 'knowledge nurturing' and 'knowledge exploration', appear to be playing a crucial role in the dynamics of emerging fields. For the case of the iPS cells, the intellectual base is not necessarily related to iPS cells per-se but rather to the wide range of related and peripheral technologies surrounding this field, such as embryonic stem cells, delivery methods, gene editing techniques, and so on. These peripheral competences may have allowed other countries to 'relatively easy' grasp this new technology and successfully jump into the 'iPS cell bandwagon'. Second, we could observe that the entrance to emerging fields was usually carried out through the scientific domain. In this case, the significant and predominant technological strength of dominant countries, USA and Japan, gives them an edge relative to other countries. Third, progress in this field cannot be considered to be related solely to scientific and technological aspects. As defined by Morlacchi and Nelson [26] and Nelson [27], it appears to follow three closely interrelated pathways: (a) advances in biomedical scientific understanding, (b) improvement of ability to develop and use medical technologies, and (c) learning in practice. The case of Japan is useful for this purpose, despite their lower influence vis-à-vis the USA, Japan has been the first country to announce a pilot study involving iPS cells, particularly for patients suffering from wet-type age-related macular degeneration.

Finally, we should bear in mind that bibliometric data are limited in nature. Several studies have highlighted the English-biased nature of bibliometric studies, the influences of threshold setting on networks, the differences in the number of references across patent offices, etc. Furthermore, we have treated the network nodes in a lump manner without considering the specific type of knowledge embedded into them; doing so, may prove a more detailed description of the specific strengths of countries in the intellectual base and research fronts. This is a potential area for future development.

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REFERENCES

[1] Cozzens, S., Gatchair, S., Kang, J., Kim, K.-S., Lee, H.J., Ordonez, G., and Porter, A.; "Emerging technologies: quantitative identification and measurement", Technology Analysis & Strategic Management, 22, (3), pp. 361 - 376, 2010.

[2] Hung, S.-C., and Chu, Y.-Y.; "Stimulating new industries from emerging technologies: challenges for the public sector", Technovation, 26, (1), pp. 104-110, 2006.

[3] van Merkerk, R.O., and Robinson, D.K.R.; "Characterizing the emergence of a technological field: Expectations, agendas and networks in Lab-on-a-chip technologies", Technology Analysis & Strategic Management, 18, (3), pp. 411 - 428, 2006.

[4] Hilgartner, S., and Lewenstein, B.; "The speculative world of emerging technologies (unpublished work)", 2004

[5] Miyazaki, K.; "Building competences in the firm: Lessons from Japanese and European optoelectronics" St. Martin's Press, 1995.

[6] David, P.A.; "Why are institutions the ‘carriers of history’?: Path dependence and the evolution of conventions, organizations and institutions", Structural Change and Economic Dynamics, 5, (2), pp. 205-220, 1994.

[7] Bergek, A., Jacobsson, S., Carlsson, B., Lindmark, S., and Rickne, A.; "Analyzing the functional dynamics of technological innovation systems: A scheme of analysis", Research Policy, 37, (3), pp. 407-429, 2008.

[8] Economist; "Health care in Japan - Regenerative Medicine" The Economist, 2013.

[9] Yoneyama, K.; "Government to promote practical regenerative medicine" Yomiuri Shimbun/Daily Yomiuri, 2013.

[10] Kawano, S., and Matsuyama, K.; "Japan biotech firms jump as Abenomics cash spurs speculation" Washington Post, 2013.

[11] Rafols, I., Zwanenberg, P.V., and Stirling, A.; "Towards indicators for 'opening up' science and technology policy", Karlsruhe, Stuttgart: Fraunhofer Verlag, 2012.

[12] Chen, C.; "CiteSpace II: Detecting and visualizing emerging trends and transient patterns in scientific literature", Journal of the American Society for Information Science and Technology, 57, (3), pp. 359-377, 2006.

[13] Barfoot, J., Kemp, E., Doherty, K., Blackburn, C., Sengoku, S., van Servellen, A., Garavi, A., and Karlsson, A.; "Stem Cell Research: Trends and Perspectives on the Evolving International Landscape", 2013.

[14] Sengoku, S.; "Innovation and Commercialization of Induced Pluripotent Stem Cells", in Vertès, A.A., Qureshi, N., Caplan, A.I., and Babssis, L. (Eds.): *Stem Cell in Regenerative Medicine: Science, Regulation and Business Strategies*,Wiley, in press.

[15] Arthur, W.B.; "The Nature of Technology: What It Is and How It Evolves " Free Press, 2009.

[16] Krafft, J., Quatraro, F., and Saviotti, P.P.; "The knowledge-base evolution in biotechnology: a social network analysis", Economics of Innovation and New Technology, 20, (5), pp. 445-475, 2011.

[17] Consoli, D., and Ramlogan, R.; "Scope, Strategy and Structure: The Dynamics of Knowledge Networks in Medicine. ", Manchester Business School Working Paper No 569, 2009.

[18] Nelson, R.R.; "On the uneven evolution of human know-how", Research Policy, 32, (6), pp. 909-922, 2003.

[19] Saviotti, P.P.; "On the dynamics of generation and utilisation of knowledge: The local character of knowledge", Structural Change and Economic Dynamics, 18, (4), pp. 387-408, 2007.

[20] Malerba, F.; "Sectoral systems: How and why innovation differs across sectors", in Fagerberg, J., Mowery, D.C., and Nelson, R.R. (Eds.): *The Oxford Handbook of Innovation*,Oxford University Press, 2005.

[21] Jarneving, B.; "Bibliographic coupling and its application to research-front and other core documents", Journal of Informetrics, 1, (4), pp. 287-307, 2007.

[22] Shibata, N., Kajikawa, Y., Takeda, Y., and Matsushima, K.; "Comparative study on methods of detecting research fronts using different types of citation", Journal of the American Society for Information Science and Technology, 60, (3), pp. 571-580, 2009.

[23] Boyack, K.W., and Klavans, R.; "Co-citation analysis, bibliographic coupling, and direct citation: Which citation approach represents the research front most accurately?", Journal of the American Society for Information Science and Technology, 61, (12), pp. 2389-2404, 2010.

[24] Lopez, P.; "GROBID: Combining Automatic Bibliographic Data Recognition and Term Extraction for Scholarship Publications". Proc. Proceedings of the 13th European Conference on Digital Library (ECDL), Corfu, Greece2009.

[25] Boyack, K.W., Tsao, J.Y., Miksovic, A., and Huey, M.; "International trends in solid-state lighting: analyses of the article and patent literature (SAND 2008-4564). Sandia National Laboratories, Albuquerque, NM, USA.", 2008.

[26] Morlacchi, P., and Nelson, R.R.; "How medical practice evolves: Learning to treat failing hearts with an implantable device", Research Policy, 40, (4), pp. 511-525, 2011.

[27] Nelson, R.R., Buterbaugh, K., Perl, M., and Gelijns, A.; "How medical know-how progresses", Research Policy, 40, (10), pp. 1339-1344, 2011.