World Patent Information 52 (2018) 42–49

Contents lists available at ScienceDirect

World Patent Information

journal homepage: www.elsevier.com/locate/worpatin

Analysis of technological production in biotechnology in northeast Brazil

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ARTICLE INFO

Article history:
Received 8 November 2016
Received in revised form
12 December 2017
Accepted 21 January 2018

Keywords:
Bibliometrics
Innovation indicator
Cooperation network

ABSTRACT

The aim of the article was to analyze the technological production in Biotechnology in the northeast of Brazil between 1983 and 2012. Data were collected from the analysis of patent applications submitted by professors affiliated to graduate programs in Biotechnology in the region. The research sources were as follows: institutional websites of the northeastern graduate programs, patent bank of the National Institute of Industrial Property (INPI) and the Lattes platform maintained by the National Research Council (CNPq). A total of 191 patent applications submitted by researchers residing in the region were identified. Data were analyzed using bibliometrics. The results point to a growing trend in the technological production of biotechnology in the region, with universities and research institutes accounting for the largest number of applications. There was also intense cooperation with public universities in the southern and southeast regions.

1. Introduction

The actions of Science, Technology and Innovation (ST&I) implemented by the Brazilian government over the last decade has promoted investments in the area of biotechnology. In agreement with the Science, Technology and Innovation Plan (PADCTI) [1], which considers Biotechnology as a strategic area, the ST&I actions have enabled the training of human resources, construction and approval of a legal framework aimed at establishing cooperation between universities and companies. In addition, the implementation of the Sectorial Biotechnology Fund and an endeavor to decentralize the infrastructure of biotechnology support must be pointed out, as investments had been only focused on developing the Brazilian southeast and southern regions.

As a result of these actions, the overall growth rate of Brazilian scientific production in 2011 surpassed the international average, ranking 13th position [2] in 2011, while in 2002 it ranked 17th in scientific production. The highest rates of articles are in the fields related to biotechnology, particularly applied chemistry and chemical engineering [3].

In terms of technological production, the Brazilian growth pattern was significant, albeit on a smaller scale. The number of filings of patent applications in the United States Patent and Trademark Office (USPTO) from 1990-2000 increased 150% in Brazil [4]. Although the Brazilian participation in the International Patent System is limited, it has been growing rapidly. Among the BRICS[1] countries, Brazil currently ranks 4th in terms of patent applications in at least one or two countries, and it ranks 56th in the international scenario [5].

As for the Brazilian scenario for patent applications in biotechnology, studies [6] report a linear growth over the last decade, particularly for the biennium 2007-2008, as there was an increase of 30% compared to previous years. When analyzing patent

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[1] In economy, BRICS is an acronym that refers to the founding member countries (the BRICS group: Brazil, Russia, India, China, South Africa), which together form a political cooperation group.

https://doi.org/10.1016/j.wpi.2018.01.006
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applications in the subclass C12n retrieved from INPI (National Institute of Industrial Property) between 2001 and 2008, Brazil ranked fifth among the ten countries with patent applications [7].

In an analysis of patent applications, INPI states that 194 patents were filed in Brazil from 2001 to 2005, which corresponds to 8.3% of all patent applications [8]. Of the patent applications in Brazil, 73.5% of them were from institutions located in the southeast and southern regions. It should be emphasized that in order to mitigate the differences in indicators in the ST&I field, the Brazilian government has been promoting decentralization actions of the ST&I infrastructure. Thus, considerable efforts have been made to strengthen the Brazilian regions, particularly the mid-western, northern and northeast regions, to increase cooperation with the federal system by strengthening and decentralizing the national system of research and development. Within this perspective, specific actions have been carried out in the mid-western, northern and northeast regions, among them the allocation of 30% of the resources of the science and technology sector funds and the increase of graduate programs in biotechnology aiming to train human resources.

Among these regions, the Northeast Regional Development Plan (PRDNE) in the northeast is one of the pillars to improve ST&I indicators and "promote competitiveness of the productive sector" [9], which has been led to an increase in scientific and technological productions in the field of biotechnology [10].

In view of the regional context, as biotechnology is a strategic area to improve ST&I indicators and has changed the Northeast region, the present research proposes to map the technological production in biotechnology in the Brazilian Northeast to indicate elements for a governmental decision making that favors the dissemination of biotechnology in technological areas.

From these general objectives, the specific objectives of the study were: (a) to present an overview of the activity of patenting in biotechnology in the Brazilian Northeast; and (b) to analyze the technological cooperation among institutions regarding this activity, with emphasis on the scientific characteristics of the inventors.

Among the indicators to measure innovation and/or understand the production of knowledge, experts of innovation have been adopted the study of patents as one of these indicators [11,12]. One of the methods that can help to classify, map, and systematize scientific and technological production is bibliometrics [13]. According to the authors, this method has become an increasingly significant indicator of scientific and technological production in certain fields and it is a valuable strategy for the generation, systematization, and dissemination of knowledge.

It is also worth noting that bibliometric techniques are extended to the study of knowledge in technological production, since articles and patents, from a documentary point of view [14], have similar characteristics (author/inventor, institution/applicant, bibliometric/official classifications, etc).

2. Theoretical background

2.1. Patents as an innovation indicator

Among the innovation indicators, patents can be used to identify and evaluate innovations at different levels [11,15–22]. Thus, analyzing patents to measure the process of transformation and application of knowledge and map the evolution of new fields of science and technology according to the number of patents indicates the level of technological activity and the outcome of the inventive process [23].

In contrast to the above and at the same time complementing the discussions, it has been argued that patents can be used to identify and evaluate national, sectorial and regional innovations; however, patents are only a partial indicator of innovation [24]. Among the innovation indicators based on patents, the authors cite the number of patents as a way to verify the willingness of a company, sector or country to apply for patents. Nevertheless, as patenting occurs during the process of research development as a means of protecting knowledge, this may not provide the adequate measurement of the economic or commercial potential of innovation. In this aspect, it is important to note that not every patent granted becomes a commercial product.

Another point to consider, when using the patent indicator, is the structure of the national innovation system. The number of patents is unattractive in countries with a poor national innovation system. While searching for an alternative to measure the degree of innovation, these countries have adopted the number of patent applications as an alternative to check which institutions, sectors, and regions are developing innovation. In this perspective, the number of patent applications enables the analysis of safety activities for the production of knowledge, with the main objective to guide ST&I policies of a country, sector or region.

Thus, this paper aims to contribute to the understanding of safety activities for the production of knowledge generated by researchers, laboratories, and companies, particularly in the field of biotechnology, in a country with a poor national innovation system [25].

2.2. Patents in biotechnology

Due to the interdisciplinary nature of biotechnology and its commercial potential [26,27], the term *biotechnology* has different definitions, which depend on each author or situation, as well as the time and place analyzed. Because of this dynamics, it is appropriate to discuss the concept of biotechnology adopted by the Brazilian government and the definition of patents in biotechnology, considering the statistical summary of patents.

According to the Convention on Biological Diversity – CBD – the Brazilian government understands the concept of biotechnology as "any technological application that uses biological systems, living organisms, or derivatives to make or modify products or processes for specific use" [28]. This concept has also been adopted by the Biotechnology Development Policy - BDP [29].

On the other hand, the OECD (Organization for Economic Cooperation and Development) understands the term biotechnology as being the "application of science and technology to living organisms as well as parts, products and models to alter living organisms or not, with the purpose of producing knowledge, goods or services" [30]. The techniques of modern biotechnology include the following: DNA (deoxyribonucleic acid); RNA (ribonucleic acid); proteins and other molecules; cell cultivation and tissue engineering; biotechnology processes; subcellular organisms; bioinformatics and nanobiotechnology.

In general, it is understood that the BDP definition includes the techniques of traditional, intermediate and modern biotechnology, of which Brazil makes no distinction; the OECD, on the other hand, only includes modern biotechnological techniques, as noted in the above definition. Thus, the Brazilian definition of biotechnology does not follow the strict framework codes of the International Patent Classification (IPC).

These discussions directly impact the analysis of patents in biotechnology because the concept defined by the OECD only lists 30 IPC codes corresponding to biotechnology patents to generate biotechnological statistics.

Among the studies that deal with the analysis of biotechnology patent applications in the Brazilian scenario, it has been observed that the concept of biotechnology sometimes follows the BDP guidelines [31–34] and other times the OECD definition [6,8,35,36].

Overall, these studies seek to obtain feedback on the technological production in biotechnology in the Brazilian scenario to understand the development of biotechnology in the technological field.

On the other hand, studies on regional technological production are scarce in Brazilian literature. It is this aspect that this study seeks to provide input to further discuss the ST&I policies in the area of technological production in biotechnology from a regional point of view.

3. Materials and methods

This is a quantitative approach, of an exploratory and descriptive study [37,38] with the application of statistical methods combined with Bibliometrics and Social Network Analysis - SNA. To achieve the objectives of the study, we considered biotechnology research to be directly related to public institutions and the main drivers for the development of scientific and technological production are graduate programs.

First, we researched the location of professors affiliated to graduate courses in biotechnology in the northeast of Brazil. Currently, the northeast region has eight master's degrees and four doctoral programs in biotechnology, involving a total of 415 professors affiliated to institutions in the northeast.

After collecting the names of the professors, we began the search for patents in the INPI database, available at http://www.inpi.gov.br/portal/, using the search box *Inventor's name*. Information was collected according to the following definitions:

Inventor/co-inventor - the intellectual party responsible for the patent, who may or may not be the applicant.

Institution - affiliation of the inventor.

Applicant or assignee - the one who has the right to apply for the patent and to whom the patent is granted. It should be noted that the applicant can be an institution or an individual.

Classification - patent classification codes (PCC) with which the patent was indexed.

3.1. Filing date - date of patent filing

The research parameter adopted was the patent applications and not those granted in the region, since the patent application indicates the will of the inventor to proceed with the request. This action can be understood as an internal policy of existing intellectual property in the institution.

To complement the information, the database of Lattes Platform was used (available at http://lattes.cnpq.br/) to identify the employment status and institutions of applicants when the patent application was filed. Moreover, we found that professors had more than one employment status. In this case, we decided to collect the data from the institution in which they had longer professional experience.

The data of patent applications were researched from 1983 to 2011. The choice of the initial survey period took into account that this was the first research involving technological production in the Northeast and also that the first patent filed by professors was also during this period. As for the final period, we took into account that patent applications are confidential for 18 (eighteen) months from the date of filing. It is important to note that information was collected from September to December 2013.

The information was organized in Excel software spreadsheet. The data analysis focused on procedures based on bibliometrics and Social Network Analysis (SNA), which verified information sharing that shapes and drives technological cooperation network in Biotechnology.

To achieve this purpose, two metrics from SNA were adopted: *centrality of degree and density*.

According to Everett [39], *centrality* is the most frequent concept used to identify the most important players in the network. Among the measures, the *centrality of degree* is the number of ties that a player has established with other different players throughout production activity. The player who has a higher degree of centrality is seen in the network as a facilitator of information [40].

Regarding *density*, this considers the relationship between existing links among the players of a network and the total number of possible connections. With values between 0 and 1 indicate the high or low network connectivity. The closer to 0, the lower the connectivity, and the closer to 1, the greater the connectivity.

The data were analyzed using the following software:

- Ucinet, version 6 [41] - calculation of centrality and density measurements;
- Netdraw, version 2.09 [42] construction of co-authorship networks of the most cooperative institutions.

4. Results and discussion

From the data collected from the INPI website and Lattes platform, tables, graphs and co-authored maps were developed to help understand the technological production in biotechnology in the northeast. This analysis is organized according to the four selected items, namely: i) development of technological production within the period established; II) key institutions in the northeast with patent applications in biotechnology; III) major subject areas of patents - IPC; IV) social network analysis among northeast institutions and partners for the development of biotechnology in the region.

In total, 178 patent applications were identified. The predominant type of patents for the analysis was Patents of Invention (PI), totaling 170 cases (95.5%). There were only eight (4.5%) for patent types “Model of Utility” (MU). Therefore, only invention patents were selected for this study.

By analyzing the academic degrees of the inventors responsible for the patent applications, we found that 87.8% had graduate training. From the total, 66.9% have post-doctoral fellowships, 13.1% doctoral degrees, 7.8% Master's degrees, 6.3% specialization degrees and 5.9% undergraduate degrees.

The average number of patent applications per researcher-professor is 2.3, considering that 53.55% of the researchers had only one patent application within the period analyzed. The professor with the highest number of patent applications is a researcher from the Tiradentes University - UNIT, who has 12 patent applications and conducts research in the areas of natural products and biodiesel.

Fig. 1 shows that the number of patent applications in biotechnology of professors affiliated to graduate programs in the northeast region has increased over the years with a significant increase as of 2009, showing a growing trend of technological production in the region.

The first patent application in Biotechnology in the northeast was in 1983 (PI process number 8306340-4) entitled “Process for obtaining biopolymers by gelatinous fungus”. The application was filed at the Federal University of Paraíba (UFPB) and the patent was granted in 1992.

Many applications (90.59%) were filed after 2001. With respect to the low numbers during the previous decade, it should be noted that Industrial Property Law - IPL No. 9279/96 from May 15, 1997 is the current legal framework that establishes the main guidelines for the use of industrial property system and it provides incentives for innovation and scientific and technological research [43]. It provided a new stage for evaluating innovation, which led to the

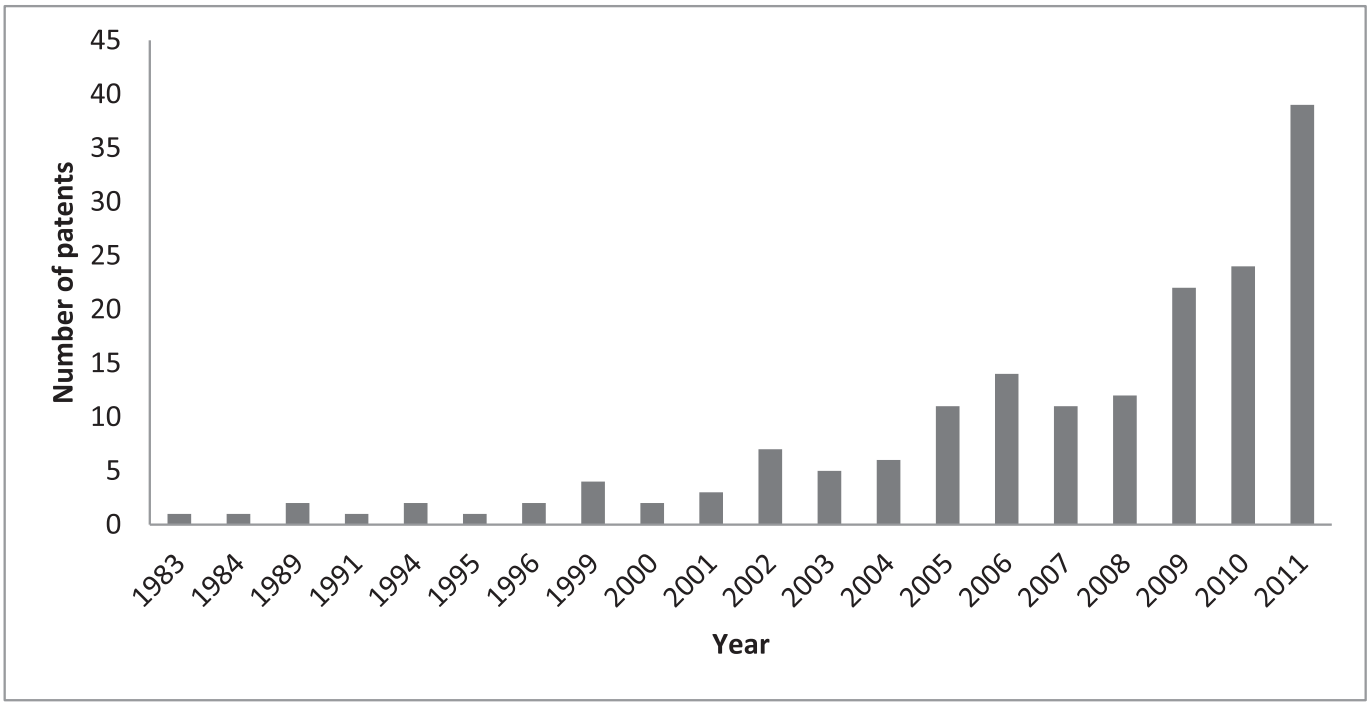

Fig. 1. Evolution of patent applications in Biotechnology in the northeast of Brazil (1983-2011).

continuous learning of a country that had devoted little attention to protection.

Given this situation, it is relevant to highlight the Innovation Law (Law No. 10.973 of 02/12/2004), more specifically the part that proposes the creation of the Technological Innovation Centers (TIC), as this law promoted the participation of universities and research institutions in the innovation process through the TIC, which stimulated research [44].

In this context, it should be emphasized that graduate courses in biotechnology and related fields in the northeast region have required the submission of patent applications as part of the dissertation and thesis defense since 2006, which has been a stimulus to increase technological production.

Regarding the judicial nature of applicants, universities submitted 60% of applications, followed by individuals (18.38%), public research centers (14.05%), private companies (5.41%), and mixed companies (2.16%). Of these, only Petróleo Brasileiro S.A. (Petrobras) has four patent applications. It is important to note that 44.44% of private companies are located in the state of Ceará.

By analyzing the number of applicants for patent applications, it was found that 80.59% of applications had a single applicant. The remaining applications had an average of three applicants. The patent applications with more researchers (eight) are from institutions in the states of Pernambuco and São Paulo.

The maximum number of co-invention of a patent was 84 researchers from different Brazilian institutions. Regarding this patent, it is related to the participation of researchers from the northeast region in the Brazilian Genome Project, referring to the study of the *Chromobacterium violaceum* organism. In a depth analysis, it was found that researchers from three institutions in the region (Federal University of Rio Grande do Norte - UFRN, State University of Santa Cruz-UESC and the Federal University of Ceará - UFC) participated in the research, resulting in the patent application No. PI 0207239-4 at the INPI, under the title "Polynucleotides encoding genes of chromosome of bacterium *Chromobacterium violaceum*, and expression and activities of these polynucleotides and their application", filed by the National Laboratory for Scientific Computing in 2002.

As for the patent approval in general, only 3.5% of the patent applications in Biotechnology in the region during the period under analysis were granted. Regarding the other patent applications, it was found that:

- 41.8% were denied because they did not comply with the requirements of articles 33 or 86 of the LPI, which consist of the issuance of an opinion on the non-patentability, non-compliance of the application in the correct patent area (Art. 33), or non-payment of the annual fee (Art. 86);
- 3.5% were suspended for not meeting the requirements of Art. 34 of the IPL. These applications are those that did not submit the documentation required for the evaluation within the 60-day period, in accordance with article 34.
- 6.5% had their applications denied for not meeting the requirements of articles 8, 10, 11, 13, 18, 22, 24 and/or 25 of the IPL. These applications fall within the scope of the concept of non-patentable inventions (Articles 9, 10, 11, 13, 18 and 22) or the patent application was not developed in a way that it showed to be a single inventive concept (Art. 22). It should also be pointed out that applications that were not present clear or precise in the descriptive report (Articles 24 and 25) were also denied, based on the conditions of the application.
- 44.7% of applications are waiting for a reply.

By tracking the processes related to the institution and researcher with the largest number of patent applications, it was possible to observe that the above-mentioned dynamics need to be discussed with the TICs and developers of the ST&I policies. After all, approximately 60% of patent applications — individually submitted - have been shelved or denied because they fail to meet the criteria in the articles cited above, particularly Arts. 33, 34 and 86 of the IPL.

Thus, it is clear that monitoring the application may be decisive

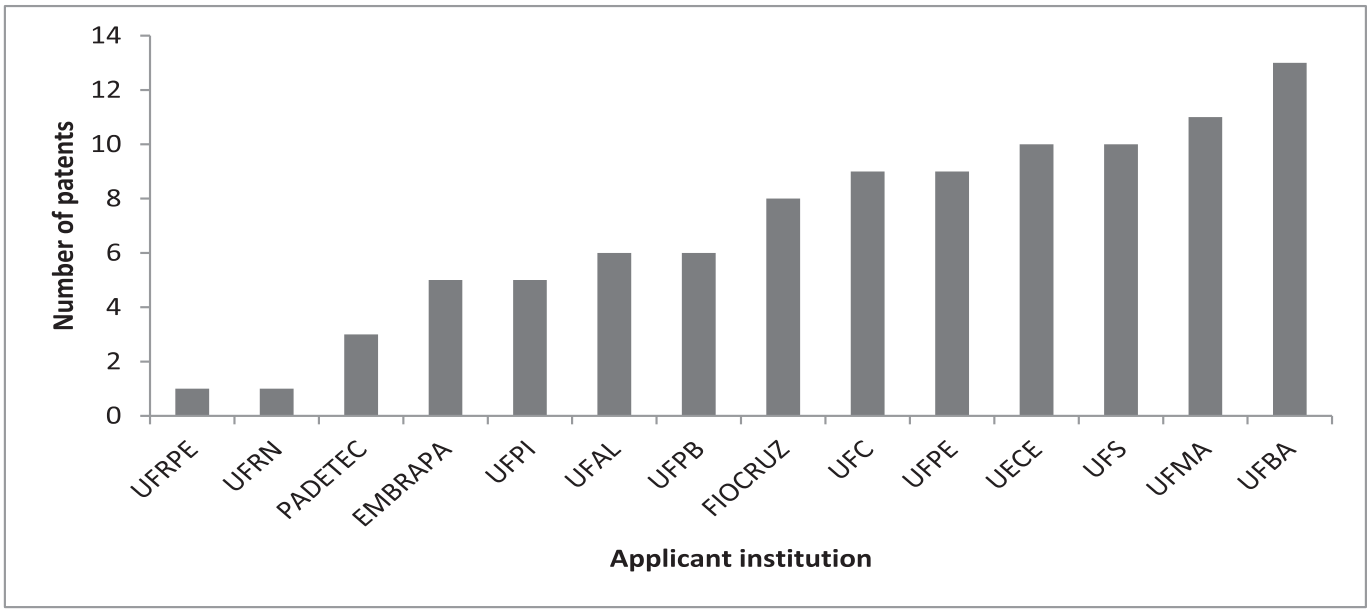

Fig. 2. Main institutions in the northeast of Brazil of patent applications in Biotechnology (1983-2011).

for the development of technological production in the region. Therefore, the action of TIC is essential as, among their duties, according to item VI of the first paragraph of Art. 16 from Law 10,973 of 2004, it must "keep up with the application process and the maintenance of property intellectual of the institution" [44].

At this point, two recent actions to guide Brazilian Institutions regarding the scientific and technological development of the country must be pointed out. The first one is the publication of Resolution No. 144/2015 that establishes the *Patent Applications Exam Guidelines in the field of Biotechnology* which aims to improve the processing procedures of patent applications in biotechnology [45]. The second one was the publication of Law 13,243 of January 11, 2016 [46], which establishes incentives for the development of scientific research, scientific and technological capacity and innovation in production environment, as well as Law 10.973/2004 [34], among others.

According to Fig. 2, public institutions are responsible for the technological knowledge in Biotechnology in the northeast: universities and government research centers, particularly: UFBA, UFMA and UFS. Thus, the northeast region is consistent with the national scenario, which points to the public sector as the main responsible for the development of Biotechnology in Brazil [6–8] with 80% of investments and research activities [47].

The privileged position of UFBA is explained, among other factors, by the partnership with Petrobras and because it relies on the coordination of TIC-NE Network that acts as a mechanism of TIC integration in the northeast [48]. It should be noted that the analysis of the processes indicated that nine UFBA applications were filed, since they did not meet the Art. 33, 34 and 86 of the IPL.

Regarding UFS, it is worth noting that the experiences in the field of technological production boosted the approval of the first master's degree in the field of Intellectual Property Science in 2012.

The 170 patent applications registered in the period were distributed according to the IPC subclasses (8 t h ed.), which features the following sections/areas [49]: A - Human Necessities; B - Processing Operations; Transport; C - Chemistry and Metallurgy; D - Textiles and paper; E — Fixed Buildings; F - Mechanical Engineering; Lighting; Heating; Weapons; Explosion; G - Physics; H - Electricity.

Each of these large sections has subdivisions, which allows the types of technologies developed and thematic trends in research on biotechnology in the region to be analyzed. Fig. 3 shows the distribution of patents in the study according to IPC.

As shown in Fig. 3, most of the patents are related to Section A (Human Necessities). It is noteworthy that the classification under code A61K (preparations for medical, dental or hygienic purposes) in this study represent 64 (37.6%) of the patent applications identified. Following, the A61P classification (specific therapeutic activity of chemical compounds or medicinal preparations) has 56 patents (32.9%), and C07D (Heterocyclic compounds) has 16 patents (9.4%); each application can contain one or more classifications.

Thus, the field of Human Necessities has 141 (82.9%) patent applications, Chemical and Metallurgical has 100 (58.8%), Physics has 16 (9.4%) and Processing and Transport Operations has 6 (3.5%). It is worth noting that 24.1% of the patents found fall within the concept of biotechnology adopted by the OECD.

In Fig. 4, the intra-institutional and inter-institutional cooperation network shows the 16 most collaborative institutions.

Having as reference the institutions in which researchers in biotechnology are inserted, Fig. 4 shows that among the 16 institutions, UFS is the one with the largest number of collaborators, followed by UFPE and UFMA. UFS has 81 collaborators, and of these, 12 are with the UFPE, 10 with UFRGS, among other cases with minor occurrences, generating a percentage of 44.44% of cooperation among universities. In sequence, the UFPE has 73 collaborative occurrences and of these, 67.12% is internal collaboration. The main partners of this institution are: UFS, UFC and USP. UFMA has 59 collaborators and of these, 18.64% of partnerships are co-owners with higher education institutions. The main partner institutions of UFMA, in descending order, are: RENORBIO, Unicamp, UFS and UECE.

With regard to interregional cooperation, it should be noted that all institutions except UFRS, are located in the southeast region (Fig. 4). It should be noted that research in biotechnology in the southeast region is more dynamic as pioneering studies in the area are conducted there because their specialized laboratory structure is greater. The universities Unicamp, USP and UFRS are the ones [7]

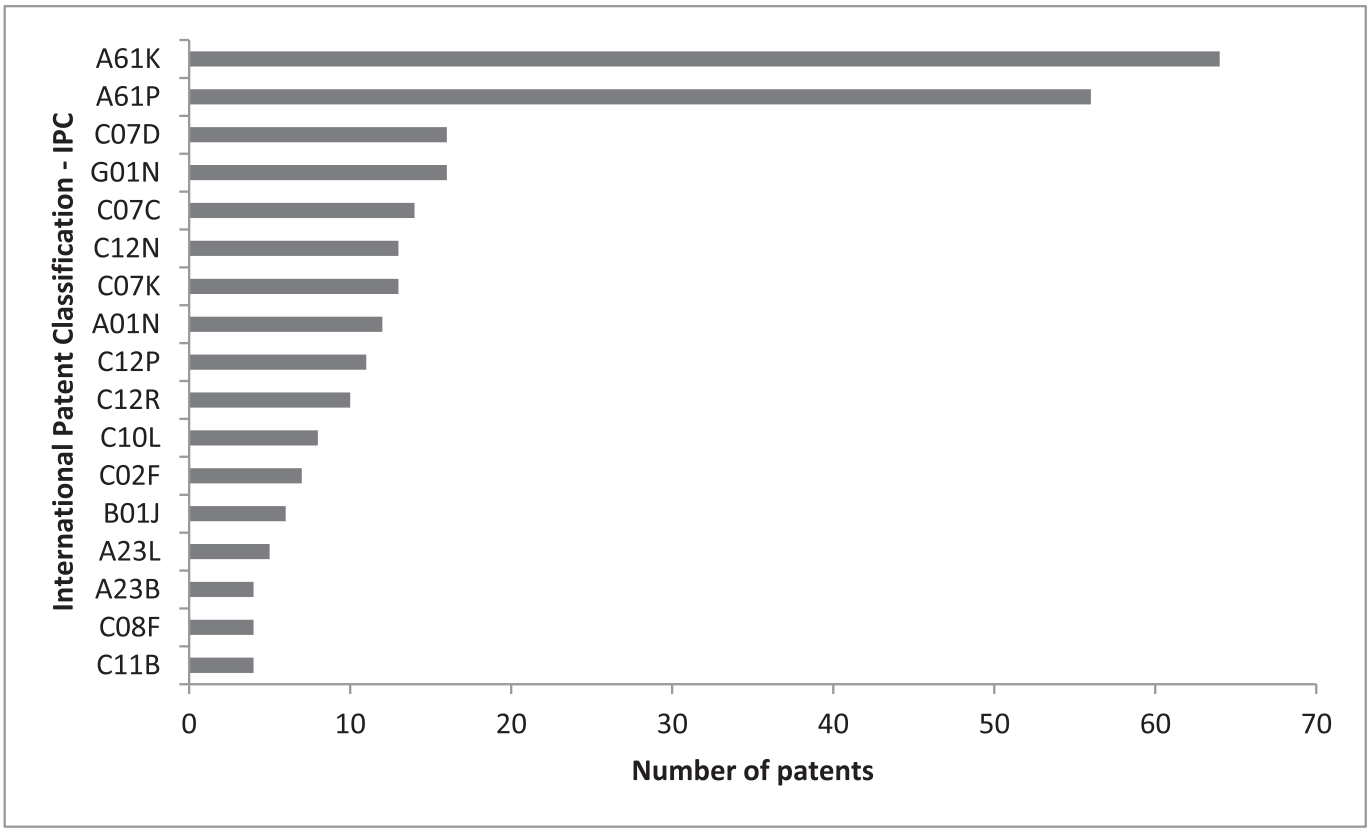

Fig. 3. Distribution of patent applications filed in Biotechnology in the northeast by IPC (1983-2011).

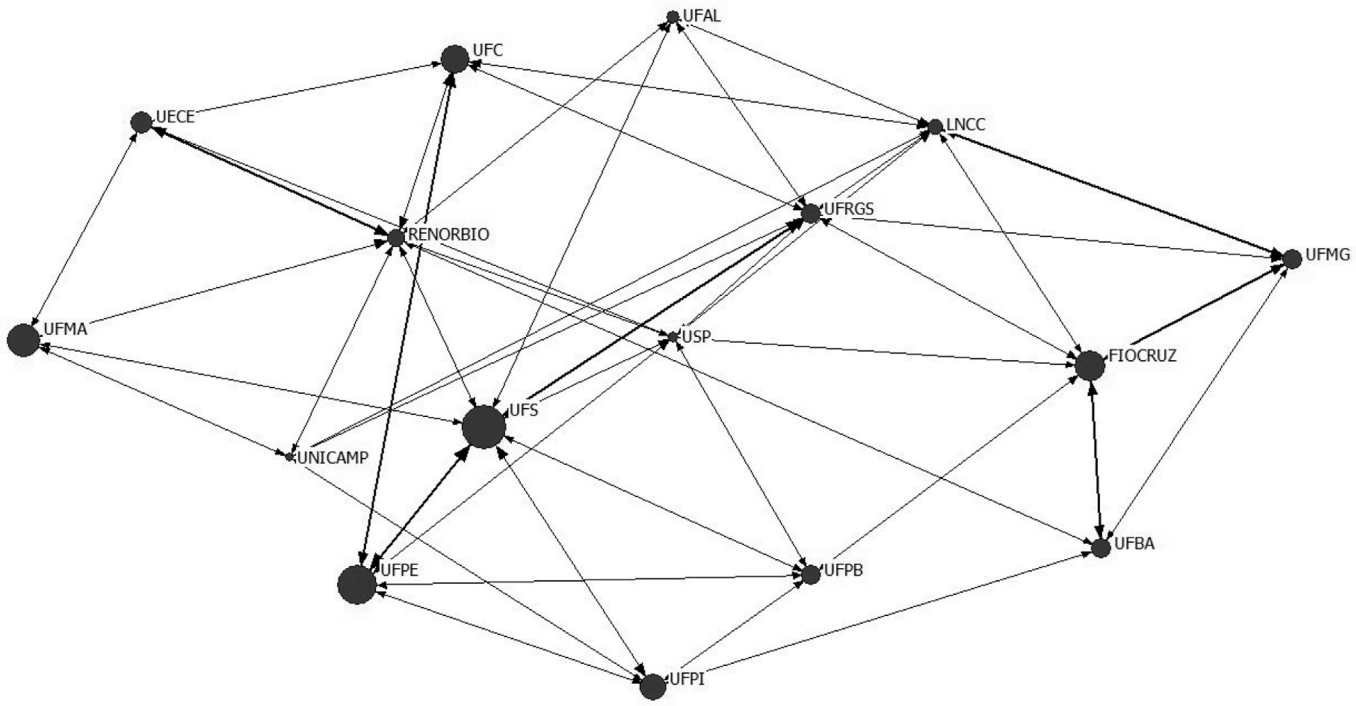

Fig. 4. Intra-regional and interregional technological cooperation network in the field of Biotechnology. Northeastern Brazil (1983-2011).

[8]; with the largest number of patent filings in the biotechnology field.

With respect to the structure of the cooperation network using the indicators of *centrality of degree* and *density* index, the following conclusions were obtained: the network centrality of degree is 11.83%, which confirms that the probability of all institutions obtaining information from the network is low. It should also be emphasized that the relative variability of institutions in the network obtaining information is 0.4661, indicating that, in the network under study, there are institutions with a higher degree of cooperation than others. On the other hand, there are institutions that have a low possibility of obtaining information as they have less interaction with other institutions.

Regarding the analysis of *centrality of degree* index per institution, the UFS shows the highest number of cooperation partnerships, followed by RENORBIO that plays a key role in the structure of Biotechnology cooperation network in the region because they are a link among institutions.

Reflecting on the strength of communication relationships mapped in cooperation network study, with dichotomized data, the *density* showed an index of 0.4417. When we use the interval of density values [50], we found that there is efficient communication in the network under study.

5. Conclusion

This study shows that there was increasing dynamics in technological research in Biotechnology in the northeast of Brazil as of 2009. Another aspect observed was that public institutions have been promoters of technological knowledge.

The area with the greatest number of applications were human needs and in the subclass A61K (preparations for medical, dental or hygienic needs). It is noteworthy that there are several healthcare graduate courses [10] in the region which provide human resources to develop the field in health biotechnology.

In this line, it should be noted that most inventors and co-inventors in the region with patent have graduate degrees, particularly postdoctoral fellowships. Therefore, the high level of academic maturity of the inventors in the region is outstanding.

Regarding the Social Network Analysis (SNA), it was found that there is a large cooperation network among players as well as the presence of institutions located in other regions of Brazil, for example UNICAMP and UFRGS, that maintain partnerships with northeast organizations. These partnerships are a positive factor in development of biotechnology in the region. It was also found that UFS is an information canal in technology cooperation network in biotechnology in the northeast and it has partnered up with most of the institutions that develop technological activities in the region.

Although the region has shown an increase in the number of patent applications, it was found that the procedures for obtaining patents in biotechnology is a bottleneck for the advancement of technological production. This statement is based on the fact that a significant percentage of applications have been denied for not meeting the requirements of IPL, such as the annual fee payment or inadequacy of application in the correct patent area. Thus, aiming to support these debates, it is suggested the qualitative research be conducted to analyze the possible factors that interfere in the follow-up actions of patent applications along with the INPI, and the motivations of researchers and institutions to submit these patent applications. Another aspect that needs to be analyzed is the perception of institutions and researchers who file for patents, regarding the technology transfer procedures generated from the patent granted.

The information reported in the present study has endeavored to understand the profile of technological development in Biotechnology in the northeast of Brazil and help the decision-making process of managers in the ST&I area concerning the technological development in the region.

Acknowledgements

This study was supported by grants from the Ceará State Foundation for the Support of Scientific and Technological Development - FUNCAP [Project Nº: BP2- 0107-00262.01.00/15 SPU Nº: 5708341/2015].

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