A comparative study between scientific publications and patents: a case of a neglected disease, Leishmaniasis

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Résumé

L'objectif principal de cette recherche était de mettre en avant des méthodes qui pourraient aider et nourrir les gestionnaires de la santé de prendre des décisions sur les maladies négligées et les plus précises sur la leishmaniose. Le présent ouvrage est une étude comparative évaluer les facteurs présentés dans un environnement de recherche à travers l'analyse des publications scientifiques et dans le secteur de la santé à travers l'analyse des brevets et comment ces deux zones sont reliées entre elles, le cas échéant. Au cours de cette recherche, nous avons appliqué des méthodes de données et d'analyse des réseaux sociaux dans la recherche, le traitement et l'analyse de ces informations et des réseaux en évaluant les relations entre les entités, les chercheurs et les brevets au fil des années. Autre tentative de ce travail était de cartographier les intérêts sur la leishmaniose parmi les pays du monde et de sa dynamique sur les 13 dernières années.

Abstract

The main objective of this research was to bring forward methods that might help and nourish health managers take decisions about neglected diseases, and more specific on Leishmaniasis. The present work is a comparative study evaluating factors presented within a research environment through the analysis of scientific publications and within the health industry through the analysis of patents and how those two areas are interconnected, if so. During the course of this research we applied methods of Data and Social Network Analysis in the search, treatment and analysis of such information and networks by evaluating the relationships between the entities, researchers, and patents along the years. Another attempt of this work was to map the interests on Leishmaniasis among the countries in the world and its dynamics on the past 13 years.

1 Introduction

The research universe defined for this study is on Leishmaniasis disease contained in the so-called neglected tropical diseases (NTD). The term NTD, which has been used since the mid 1990s, has become a “brand-name” referring to a group of diseases that are especially endemic in low-income populations living in tropical and subtropical countries [1]. However, up to this date, there are no clear or agreed definitions for what constitute a neglected disease. According to the 2010 report from the World Health Organization (WHO) “Working to Overcome the Global Impact of Neglected Tropical Diseases” the NTDs affects more than 1 billion people around the world.

The known diseases are defined by the WHO as types I, II and III where Leishmaniasis is considered a type III disease. This definition is followed by a great number of health organizations and ministries around the world. The definition in itself brings different concepts together including the wealth of a country between rich and poor; the state of its development between developed and developing and most importantly a measure of the burden of diseases by the incidence of the disease within the population (CEWG 2012). The definitions themselves are combined such that:

- Type I diseases: are incident in both rich and poor countries, with large numbers of vulnerable populations in each.
- Type II diseases: are incident in both rich and poor countries, but with a substantial proportion of the cases in poor countries.
- Type III diseases: are those that are overwhelmingly or exclusively incident in developing countries.

With regard to investments in the area, those diseases do not receive adequate attention for its treatment and eradication, which perpetuates the condition of people who are exposed to them [2]. In order to treaty the problems involved with NTDs, or Leishmaniasis specifically, it is necessary to understand its complexity. One of the ways to help this situation through research is to provide methods to analyze the context using a number of different instruments and approaches. The study of scientific publications and patents is part of what is involved and this present work intends to show some of its benefits.

In regard to scientific publications, there are a number of databases that catalogue journals on specific areas. Those databases are a very rich environment to understand the research world with information such as countries involved on research, number of publications per year and collaboration among institutions, countries and researchers. However, due to the large number of publications, journals and databases it is necessary to define clear methods that can bring valuable information at the right time. The analysis of patents is also used to measure and understand the growth or declined interest of countries and organizations within the NTD context. Through its analysis a great number of information might surface, such as companies and research institutions involved, countries health and economical policies and others.

A number of publications on co-authorship and patents on NTDs specific diseases have been published in recent years. It's imperative that new tools and approaches being developed focus on facilitating public policy planning and foster the management of innovation in countries' public health systems [3]. On Leishmaniasis a recent bibliometric study [1] used one of the databases included in our work, helping making a comparison of the results. One of the results found was that the number of publications on the area has increased considerably on past years. A comparison with results from another research [4] has also been made in regards to the same database using a co-authorship analysis.

2 Data Analysis of a Neglected Disease

The research universe on Leishmaniasis for this paper has been made through the analysis of two different databases, PubMed and PASCAL, for scientific publications and one agency, The United States Patent and Trademark Office (USPTO) for patents and patent' applications. The reason behind the use of two different databases on scientific publications was to analyze if there were significant differences that might bias ones research. The access to the databases occurred during the month of May and June, 2013. We have decided to take into consideration only the publications and patents from 2000 to 2012 included.

2.1 Method for Data Treatment

For the data treatment and analyses we used the software Tetralogie. The software allows (several and remote users) to conduct strategic analysis from heterogeneous textual data through analysis of conventional and innovative methods. With statistical methods and exploratory data analysis methods, it shows strategic information such as actors identity, mobility, emergence and evolution of topics, concepts and terminology. Another feature of the software is that it allows graphical visualization for understanding human activities and their interactions as well as their evolution in a decision-making perspective. It combines static and dynamic visualization where the static aspect is based on a representation space, in which the precepts of graph theory are applied. The dynamic visualization applies features and capabilities to further understand evolution of the data and facts in respect to time. Tetralogie allowed us to identify the role of data within the structure, analyzing their neighborhood, filtering, k-core, transitivity, back to the source documents, to partition the graph or to focus on its structural features[5].

2.2 Database

The research have been made taking into consideration authors of articles and patents, countries where those authors were from, journals used for the scientific publications besides companies, universities and research institutions involved on both articles and patents. For all the information analysed the years of publication for scientific publications and of deposit for the patents were added to the analysis in order to understand the dynamics of the area within the past 12 years. The PubMed platform, which holds the Medline Database, was used for the research as one of the databases. PubMed is a free database accessing references and abstracts on life sciences and biomedical topics. Data files were retrieved from PubMed with the Medical Subject Headings (MeSH) terms or descriptors "Leishmaniasis" and "Leishmania" for title and abstract, for the years 2000 to 2012. The second database used for the scientific publications was PASCAL. Pascal is a multidisciplinary and multilingual bibliographic database. It covers most of the worlds' literature in Science, Technology and Medicine since 1973. The same search terms, dates and review of the data applied to PubMed was applied to PASCAL. After reviewing the data we decided to discard all the articles which contained the word "clinical" explicitly on their titles or abstracts. We decided for this path on the bases that clinical trials is a post discovery phase which might bias the understanding of innovative contribution on the area and the consequent interest of scientific community and corporations. For the patents we have used the USPTO web site for the data retrieval. The search terms used had the same characteristics as for the scientific publications plus the medicines used to treat the illness as stated on the United States National Institute of Health (NIH) web site (http://www.ncbi.nlm.nih.gov/ access june 2013); sodium stibogluconate, meglumine antimoniate, macrolide, benzamidine, phosphorylcholine and neomycin.

2.2.1 PubMed and PASCAL scientific publications

The scientific databases are both well known and largely used by the academic community. Their differences however could help future researches taking into consideration aspects that might be important for more precise studies. The total number of publications between both databases diverge almost 3 folds for PubMed having a total of 9,210 articles for the period with the filtering mentioned before against 3,650 publications in PASCAL. The total number of Journals has also a great difference with PubMed covering 1,114 journals while PASCAL covers 362. This difference suggests that PuBMed has a much higher coverage in terms of absolute numbers. However, PASCAL has a more detailed qualification of the data concerning the countries where the authors are coming from. This is an important information if ones research aims to understand which countries are making the most contribution and the cooperation existent on research world. A difference in regards to country publications rank was noticed on the total number of articles per country, where USA, France,

Belgium, Tunisia and Turkey had one or two places higher ranked in PASCAL, while Italy is 5 times lowered ranked. We also analyse the average of information per article concerning MESH words and key words per article but it was not found any significant difference among the databases.

2.2.2 Patents

For the patents we used the USPTO database, retrieving data for patents that has already been published as well as patents applications. The total number of patents and applications found were respectively 810 and 680. The number of authors for those patents and applications were respectively 1,610 and 1,435. We will discuss further on how those authors interact with each other showing a clear difference from collaboration in comparison to academic researchers. In respect to the number of companies or organizations whom own the patent there are further analysis that must be done in regards to the applications, which shows in most cases not the owner but its legal representative. In total there were 332 different organizations for the patents and 217 for the applicants. Out of those organizations 15 of them have 5 or more patents and 9 of them has 5 or more applications with United States, Japan and Germany alone with more than 50% of all the patents and applications on the area.

3 Results

One of the results of our study was the absolute number of publications for each database per year as shown on figure 1. Figure 1 shows a steady increase for the scientific publications with a greater ratio for PubMed in comparison to PASCAL. For the year 2012 the PASCAL data shows a decrease in numbers of publications compared to 2011, however this might happen due to a delay on the processing of new publications. This difference for the year 2012 for PASCAL database deserves a further study. As for the patents and patents' applications the number of deposits have reached its peak between the years 2003 and 2005 with patents reaching 57 deposits for the year 2003 and applications 101 deposits for the year 2005. However, due to a processing delay for patents, which might take from 2 to 12 years in some cases, the actual numbers of approved patents might change significantly and the consequent results in regards to the interest in the area through the study of patents is not conclusive.

The comparison between the academic and commercial publications and deposits is an interest issue, especially due to its differences. The countries with most scientific publications are not necessarily the ones with the highest patents applications, with an exception of USA, which demonstrate a different form of approaching on both areas and a lack of penetration on patents from countries with highest incidence of the disease. A correlation in regards to the numbers of publications and deposits are not to be found, maybe in great reason for the different processing time. On the other hand, the problem for developing countries

and the number of people affected by those illnesses has forced emerging countries such as Brazil and India to invest on scientific research. Another very important player on the area are the Non Governmental Agencies (NGO), such as *Medecins Sans Frontiers* (MSF) and Drugs for Neglected Diseases initiative (DNDi), which has helped bring lowered prices medicines and treatments for the needs. The study of the NGOs are not part of our study, however we understand its great influence.

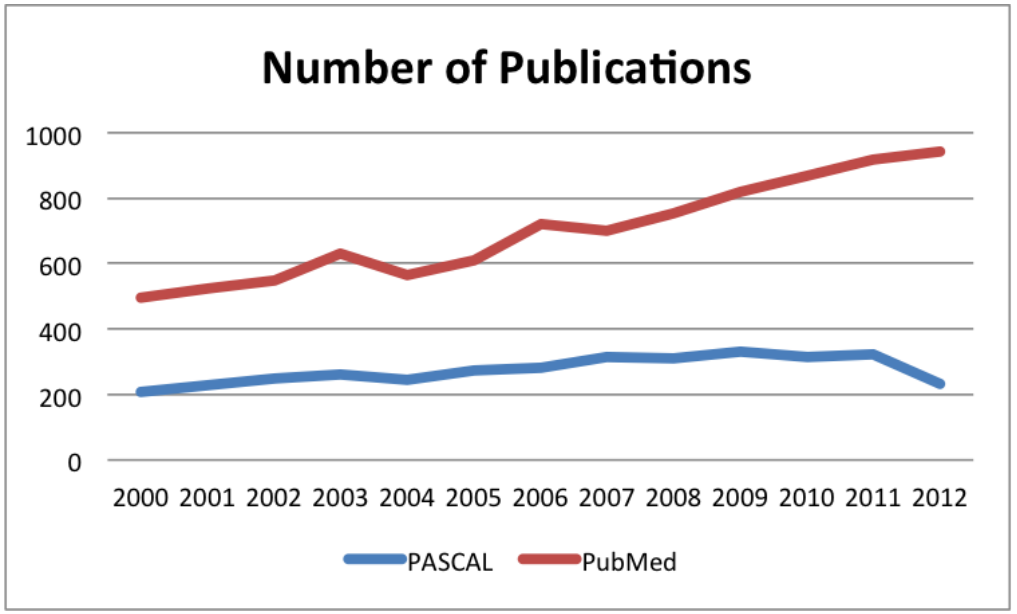

Figure 1 – Total Number of Scientific Publications

Concerning the journals used by the researchers for publications the 20 most frequent journals in PASCAL where found amongst the first 30 journals in PuBMed. On the other hand, out of the 20 journals most used by researchers on PubMed only 9 were found amongst PASCAL database. A list of the first 20 journals for each database is shown on table 1 with the numbers of publications for the period analyzed on the left column. Noticed that the first journals on PASCAL database, marked with the arrowed lines, are all present on PubMed but it doesn't hold true for the other way around.

The study of the journals and its publications might help understand the interest that the journals might have. For the purpose of this study we concerned ourselves with the absolute number of publications in order to understand the increase or decrease of interest over the years. We have not used the impact

factor for each journal in this study because we understand that there is a further analysis that might be necessary. This analysis is concerned with the characteristic of each journal. Some journals want to be on the leading edge of scientific publications, other journals might start publications in a certain area only after a few years that a topic became settled among the scientific community. This type of study would help understand and better qualify journals and its time of entrance on the field.

Table 1 - Journals with most Publications from 2000 to 2012

# Pub	PASCAL Database	# Pub	PubMed Database
200	The American Journal Of Trop Medicine And Hygiene	253	Molecular And Biochemical Parasitology
197	Experimental Parasitology	237	Experimental Parasitology
192	Infection And Immunity	213	Memorias Do Instituto Oswaldo Cruz
178	Parasitology Research	210	The American Journal Of Tropical Medicine And Hygiene
143	Acta Tropica	197	The Journal Of Biological Chemistry
127	Transactions Of The Royal Society Of Trop Med & Hygiene	197	Infection And Immunity
117	International Journal For Parasitology	183	Parasitology Research
113	Antimicrobial Agents And Chemotherapy	173	Journal Of Immunology (Baltimore Md. : 1950)
102	Vaccine	158	Transactions Of The Royal Society Of Tropical Medicine And Hygiene
100	Annals Of Tropical Medicine And Parasitology	156	Revista Da Sociedade Brasileira De Medicina Tropical
99	Parasitology	154	Acta Tropica
69	Journal Of Medical Entomology	138	Plos Neglected Tropical Diseases
68	Microbes And Infection	127	International Journal For Parasitology
67	Bioorganic & Medicinal Chemistry	122	Veterinary Parasitology
66	European Journal Of Medicinal Chemistry	120	Antimicrobial Agents And Chemotherapy
61	Trends In Parasitology	109	Vaccine
58	Bioorganic & Medicinal Chemistry Letters	107	Plos One
57	The Journal Of Infectious Diseases	106	Annals Of Tropical Medicine And Parasitology
56	Tm & Ih. Tropical Medicine & International Health	105	Parasitology
54	Molecular Microbiology	82	European Journal Of Immunology

On tables 2 to 5 we show the number of publications for each database by year and per country. The first two tables, 2 and 3, shows the publications for PASCAL and PubMed. It can be seen that there is very few differences among the leading countries concerning the total number of publications with Brazil, USA, India, UK and France as the top 5 countries. In regard to the years we can see a steady increase in publications over the years, as shown also in figure 1, with a decrease for the year 2012 for PASCAL database. On all the tables we show on the second line the sum for that specific year concerning all the publications and not only the countries shown on the table.

Table 2 - PASCAL Number of publications by country and year

PASCAL		2012	2011	2010	2009	2008	2007	2006	2005	2004	2003	2002	2001	2000
	SUM	363	508	499	493	436	467	419	429	371	399	388	330	286
usa	720	41	64	49	60	60	59	67	55	58	58	48	49	52
brazil	704	44	77	72	65	65	66	55	57	36	51	45	40	31
france	453	24	27	28	42	23	42	38	46	32	41	39	39	32
uk	393	15	25	39	36	23	23	24	43	35	35	42	23	30
india	381	42	45	43	43	43	38	21	29	19	10	17	15	16
spain	290	21	29	15	20	30	33	17	16	24	23	36	11	15
germany	205	10	26	20	13	15	12	9	12	18	15	21	21	13
switzer	181	12	25	20	20	10	22	9	14	13	17	7	8	4
iran	155	15	22	18	22	20	13	10	9	6	6	9	4	1
canada	120	7	9	16	9	11	12	11	8	7	11	10	9	0
venezue	111	4	7	6	15	4	10	11	11	5	10	10	10	8

Table 3 - PubMed Number of publications by country and year

PubMed		2012	2011	2010	2009	2008	2007	2006	2005	2004	2003	2002	2001	2000
	SUM	938	892	831	799	727	679	702	596	552	613	528	505	474
brazil	1698	226	180	173	174	152	147	130	108	102	94	78	82	52
usa	1280	102	105	96	82	108	91	112	99	99	116	89	81	100
india	860	120	123	93	80	79	68	55	60	48	39	32	33	30
uk	568	38	43	55	49	37	28	45	48	43	49	49	34	50
france	490	40	41	33	36	33	38	45	36	27	41	45	36	39
spain	411	43	32	26	34	43	39	21	27	30	34	31	29	22
germany	354	28	34	31	29	31	27	22	22	19	32	23	25	31
iran	318	65	63	41	40	29	22	13	12	8	7	6	7	5
canada	247	29	14	25	19	24	18	17	18	10	16	21	20	16
italy	197	13	13	23	24	20	14	19	15	20	11	7	10	8
venezue	143	6	4	11	15	9	12	14	9	9	13	14	13	14

Figures 2 and 3 show the data on tables 2 and 3 in a graph format without the total sum.

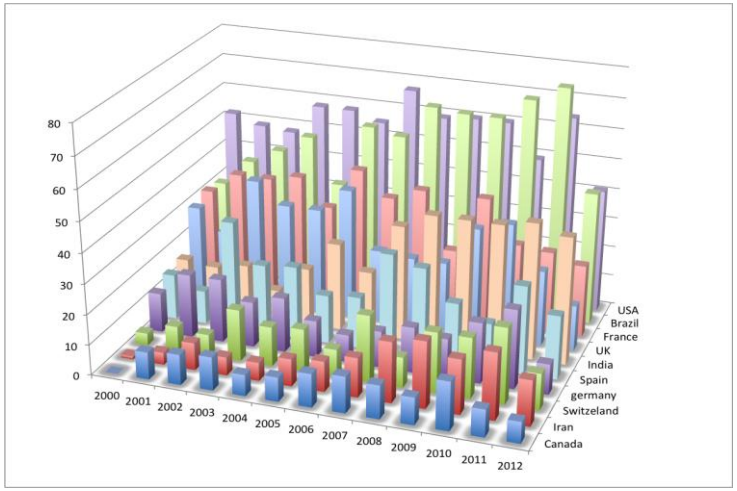

Figure 2 – PASCAL top countries Publications

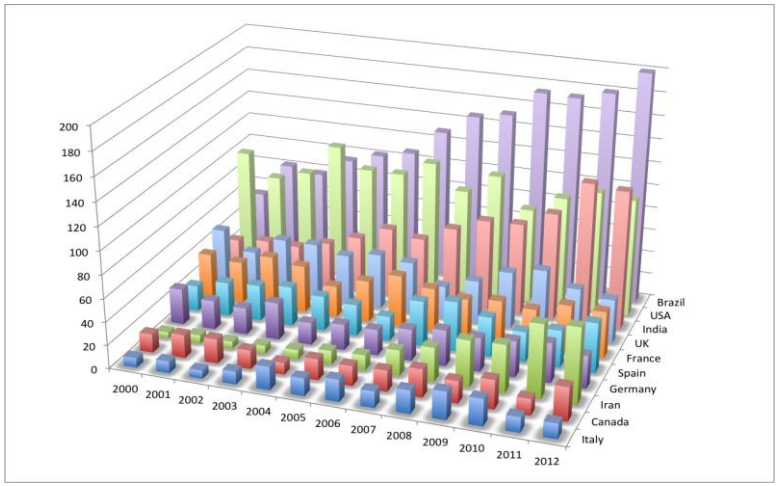

Figure 3 – PubMed Top countries Publications

The same data used on table 2 and 3 is showing on figures 4 to 5 in terms of publications and patents per country. The figures only show the sum over the 12 year period. The lighter the green the greater the number of publications and patents. The countries in red or orange have no recorded publication or patent on the databases used. This map can give an idea of how spread is the scientific publications and patents around the world.

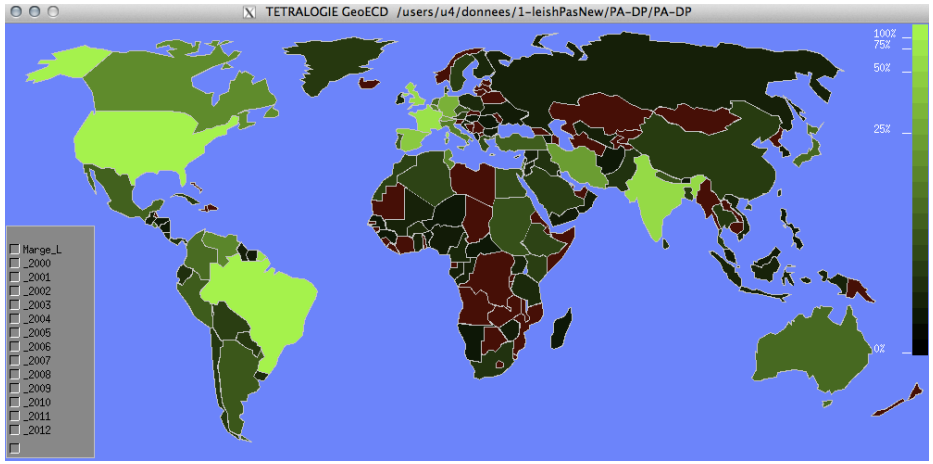

Figure 4 – PASCAL – Global view of Scientific Publications

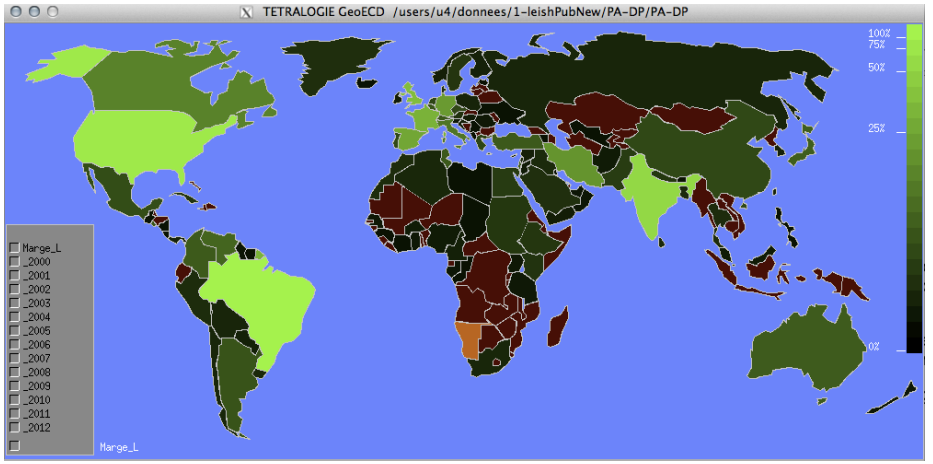

Figure 5 – PubMed - Global view of Scientific Publications

As for the patents and applications, the tables 4 and 5, we have both USA and Japan as the main countries with patents over the disease with countries in west Europe following the lead. As we have mentioned, the countries most affected by the diseases have small influence on the production, with India being the only one among the first 10 countries for applications. Concerning the number of patents over the years we can't see an increase in interest over the area which diverges from the scientific community publications.

Table 4 - Number of Patent publications by country and year

Patent		2012	2011	2010	2009	2008	2007	2006	2005	2004	2003	2002	2001	2000
	SUM	3	16	14	24	25	27	23	39	35	57	54	59	63
usa	153	0	8	3	9	11	8	7	12	13	18	22	20	22
japan	63	0	2	2	2	3	4	3	11	4	6	11	5	10
germany	31	1	1	2	1	3	4	1	3	1	3	2	3	6
france	23	0	1	0	1	0	2	2	0	2	4	4	3	4
switzer	22	1	0	0	1	0	3	2	0	3	3	3	4	2
canada	16	0	0	0	0	0	0	1	0	0	2	0	5	8
croatia	14	0	0	1	0	1	0	1	0	2	6	1	1	1
uk	13	0	0	1	0	0	1	0	1	2	3	1	2	2
south-k	12	0	0	2	2	1	1	0	3	0	0	1	2	0
italy	11	0	0	0	0	3	0	2	1	1	2	1	1	0
india	11	0	0	0	1	0	0	1	1	0	2	5	0	1

Table 5 - Number of Patent applications by country and year

Application		2012	2011	2010	2009	2008	2007	2006	2005	2004	2003	2002	2001	2000
	SUM	20	48	59	65	59	78	78	101	90	90	75	71	13
usa	296	9	22	14	26	22	27	23	27	30	31	30	29	6
japan	97	0	3	5	7	9	6	12	16	11	9	11	7	1
germany	70	4	4	9	3	4	8	3	12	8	7	4	3	1
switzer	60	3	4	5	2	1	7	4	7	10	6	4	6	1
france	49	0	2	6	3	2	4	3	5	7	8	4	4	1
india	27	0	1	2	1	1	1	4	5	1	4	5	1	1
croatia	22	0	0	1	0	1	0	4	3	3	7	2	1	0
canada	22	1	1	1	2	2	2	2	0	0	3	3	5	0
uk	21	1	0	2	0	0	5	2	2	3	1	2	3	0
italy	20	0	1	0	0	4	1	6	2	1	2	1	2	0
south-k	18	0	0	2	2	3	1	0	6	0	1	2	1	0

3.1 Author Turnover

Another approach on our study have been done on author turnover for scientific publications attempting to understand how often there are new people coming in to the field and if experienced researchers are leaving to other areas of study. This analysis might show how settled an area of research is and how it brings interest for new scientists. This analysis must take into consideration the mean time for a researcher to reach 5 publications on the area. Due to this delay in time for the publications we have analysed publications from 1949 to 2012, however the last 6 years, from 2006, and mark in grey, should not be taken into consideration. If an author publishes an article after 4 years of not publishing on the area he is considered, on our measures, a new entrant or start. If an author, after publishing on the field stop publishing for at least 4 years, on the fifth year he is marked as leaving the field or stop. The graph on figure 6 shows that there was a great instability of people leaving and entering the field but by the year 1988 it became stable with an absolute steady increase of researchers on the area since there has been always more people entering than leaving. The absolute number of new entrants has grown each year.

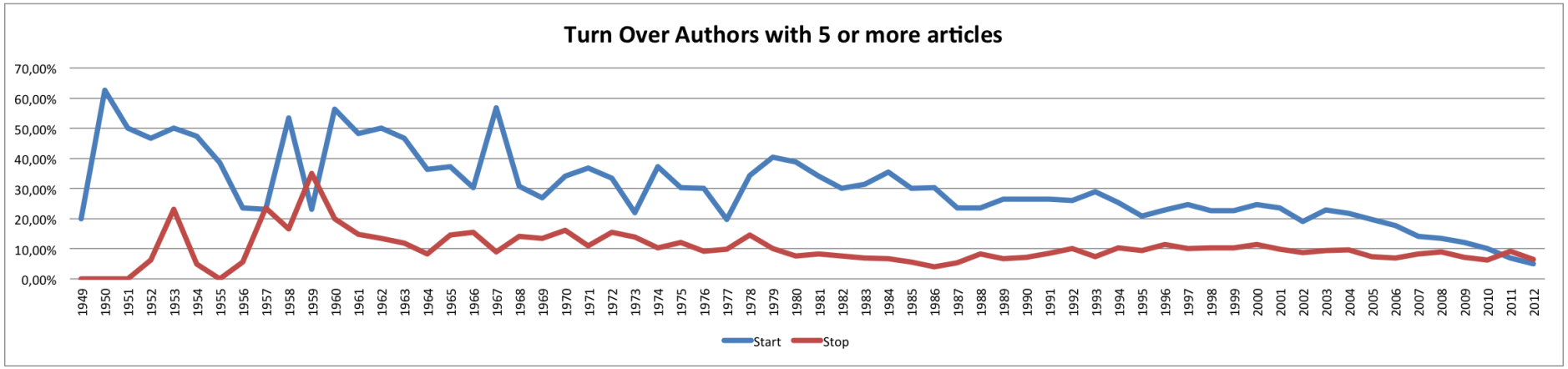

Figure 6 – Author Turn Over

Figure 7 brings the same information for author turnover using factorial Correspondence Analysis [6]. A Correspondence Analysis method takes as input a cross value over time and publications per author, for example, and outputs its distribution of values and variables over a multi dimension table. The years, as

shown in the top left part of the figure and pointed out in red on the bigger picture, show the years spread across the quadrants in a two dimension view. The circles in yellow show the concentrations of authors which have published around those periods.

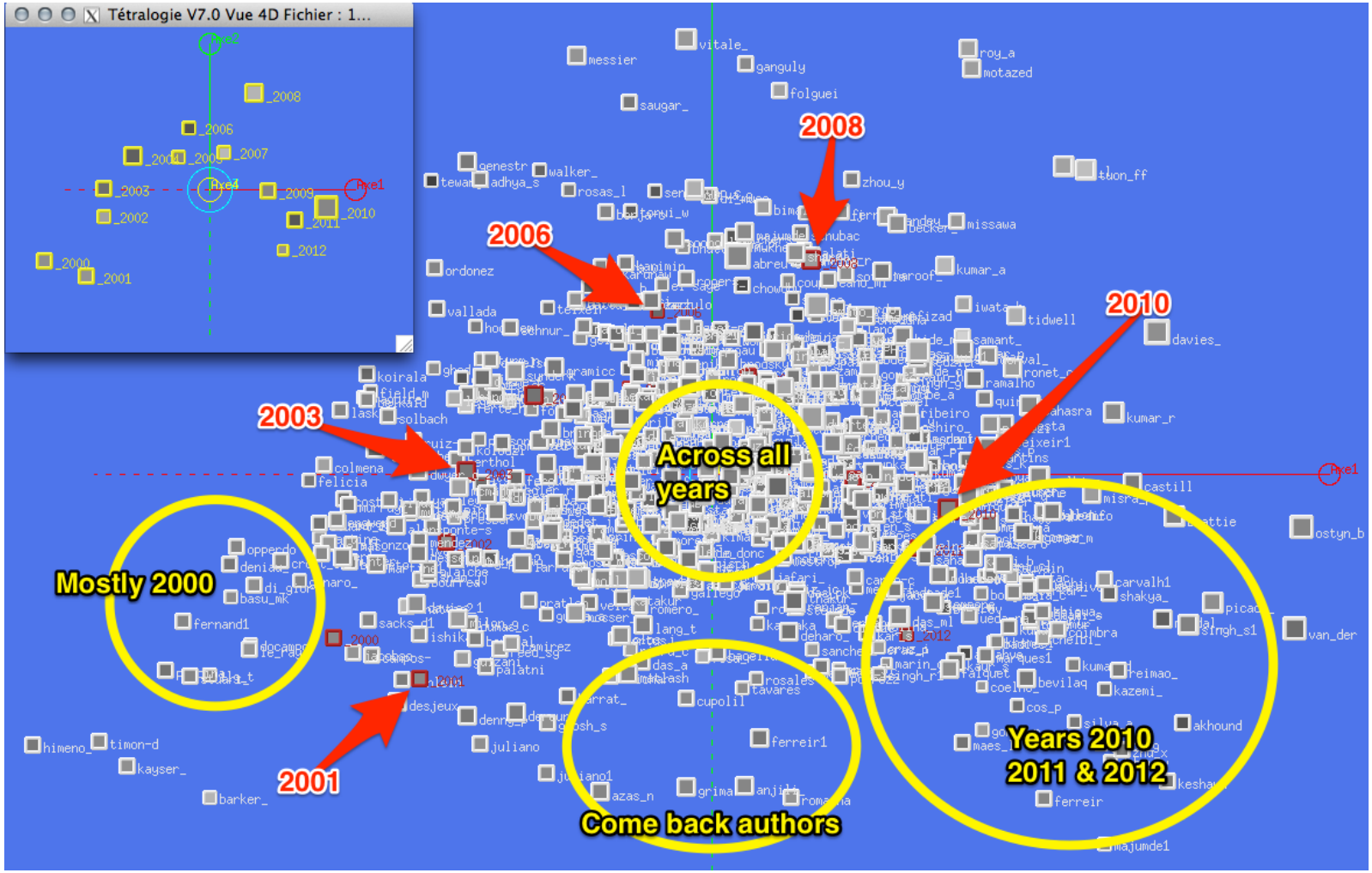

Figure 7 – PubMed – Author Turnover with 10 or more publications

A great majority of authors are in the field through out the entire period (centre of the graph) while others have written mostly around the year 2000, or around years 2010 to 2012 on leftmost and rightmost circles on the figure. The bottom circle show authors which have written in the begin of the period and have come back again on the last years. We can also see that the top right quadrant is the densest demonstrating a greater concentration of authors.

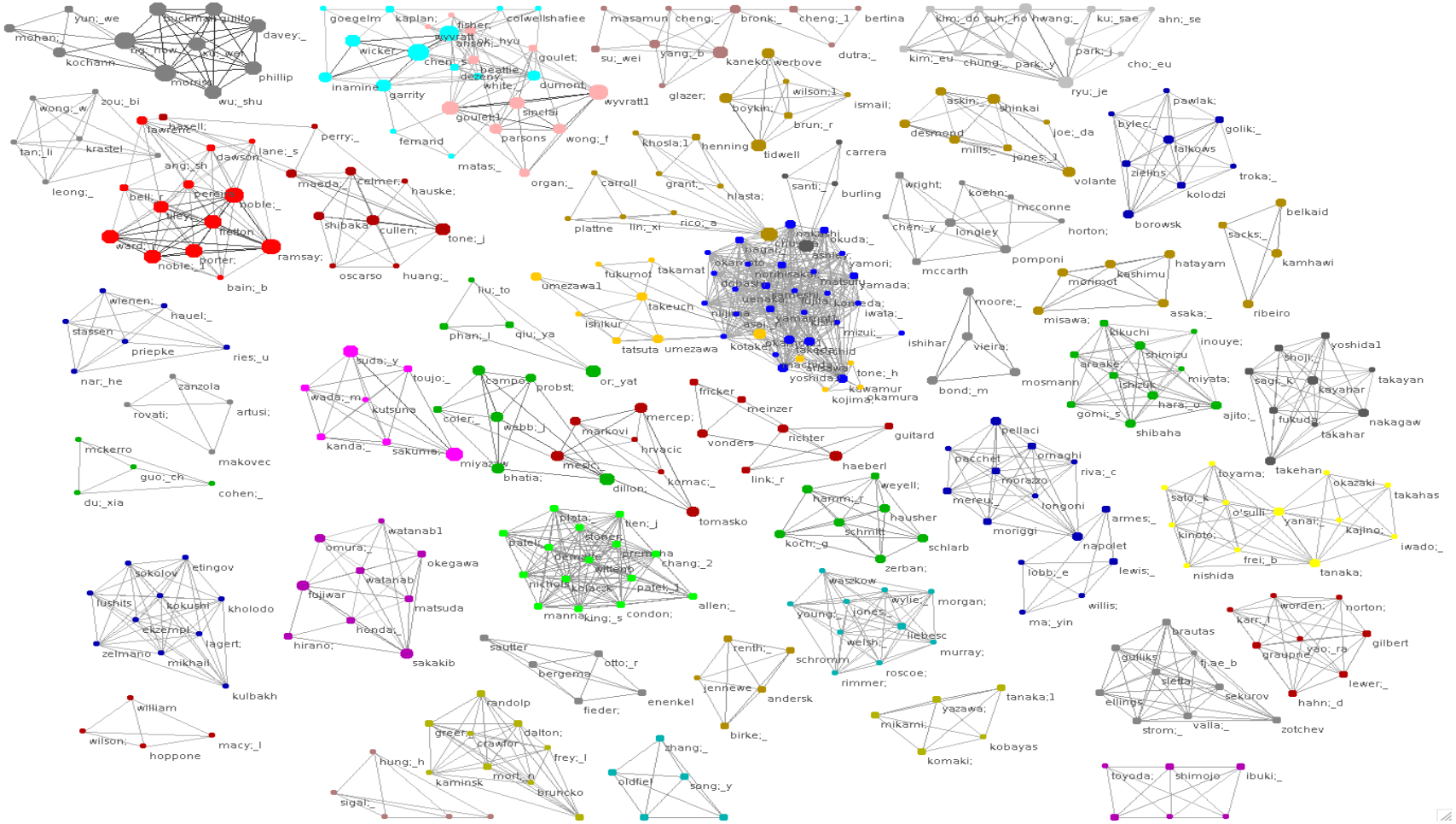

Figure 8 – Patent co-authorship

3.2 Social Network

Another line of study for the data collected for this work was the co-authorship on scientific publications and patents. People working together might demonstrate a type of relationship in which "most people who have written a paper together will know one another quite well" [7]. However this might not hold true for all the cases. In our study we have found 3 papers with more than 100 contributors for PubMed and 2 papers with more than 60 contributors for PASCAL. Those high numbers might suggest that on some cases the researchers do not necessarily know each other "quite well". Those articles with a high number of contributors are not the average, as the numbers of Authors per Article (6,24 and 5,47 for PubMed and PASCAL) have shown but must be taken into consideration, specially when reviewing the clustering coefficient [8]. The clustering coefficient measures network ''clustering'' or ''transitivity,'' which is the probability that two of a scientist's coauthors have themselves coauthored a paper. In science a high clustering coefficient would suggest that people are working together quite often, while a very detached network, as in patents, might suggest that people very rarely contribute with people outside its group. By removing some of the clinical trial papers from our database, some of the articles with an average of high contributors per paper have also been taken away.

For the scientific publications we used a similar approach from Newmans' coauthorship paper [4]. In his article he used three different databases to understand the relationship amongst authors in a field. One of the databases used were the Medline, also used on our research. The difference however was that Newman analysed all the fields on Medline together, while in our case we restricted ourselves to Leishmaniasis. This difference accounted for a divergence on the clustering coefficient in Medline data but in line with the other scientific databases studied. The table 6 show the numbers of articles, authors, authors per article, journals and clustering coefficient for PubMed and PASCAL.

Table 6 – Co-authorship table

	PASCAL	PubMed
Number of Articles	3650	9210
Number of Authors	11330	21957
Authors per Article	6,24	5,47
Number of Journals	362	1114
Clustering Coefficient	0,58	0,496

For the analyses of the co-authorship for patents we show on figure 8 the clusters which are formed amongst the authors. The figures gives a clear idea of how few contributions are made intra companies. Most of the authors shown on the figure works entirely for one corporation, with an exception of 3 clusters. The picture shows a great number of clusters very much disconnected. Besides very few authors do have relationships with other groups. This is a much different idea than with Academic collaborations, where the authors have a much higher tendency of sharing their discoveries and working with others in the field.

Another relationship we have analysed over the study was if there were companies or research institutions that publish scientific papers regularly and also has patents or applications in the field. We have found 35 organizations among universities and research institutions, both private and governmental, which worked on both areas. The name of the organizations are shown on table 7.

Table 7 – Organizations that has scientific publications and patents

Consejo Superior De Investigaciones Cientificas	Rosalind Franklin University Of Medicine And Science
Corixa Corporation	Swiss Tropical And Public Health Institute
Council Of Scientific & Industrial Research	The Ohio State University
Emory University	The Salk Institute For Biological Studies
Fundacao Oswaldo Cruz	The University Of Mississippi
Georgia State University	Tokai University
Hoshi University	Universidad De Granada
Indian Council Of Medical Research	Universite Laval
Infectious Disease Research Institute	Universite Pierre Et Marie Curie
Institut De Recherche Pour Le Developpement	University Of Alabama At Birmingham
Institut National De La Recherche Agronomique	University Of Bern
Institut Pasteur	University Of Mississippi
Institut Pasteur De Tunis	University Of Strathclyde
Intervet International B.V.	University Of Victoria
Johns Hopkins University	Virginia Polytechnic Institute And State University
Mcgill University	Washington University
National Institutes Of Health	Yale University
Rockefeller University	

4 Conclusion

This study was an attempt to bring forward some methods to analyze data focusing on a Leishmaniasis, a neglected disease. We have used data and network analysis tools on scientific databases and patents. This line of research have been made by different authors before and now we aimed at bringing together some of the techniques used.

As for the findings on the field we can say that there have been an increase interest by the scientific community over the years by the increase number of publications and a steady growth of new scientists on the area. In regard to the countries investing on the area, new players are coming forward, specially among the countries with high rate of neglected disease incidence, such as Brazil and India. For corporations we have not found an increase in interest over the area but was interest to see that the patents were mainly applied by a small group of countries such as USA, Japan and western Europe, specially France, UK and Germany. As for the collaboration we could see that on science there are higher levels of collaboration but in business or patents the collaboration is highly avoided. However recent studies have shown an interest over the field by median and small size pharmaceuticals due to public and private partnerships involving some of the NGOs in the area. This line of research deserve a further study in order to understand how those different groups interact with each other.

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