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Mapping Global Status and Trends in Patent Activity for Biological and Genetic Material

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Abstract

The extension of intellectual property rights into the realm of biology has emerged as an increasing focus of controversy in relation to science,[2] biodiversity,[3] agriculture,[4] health,[5] development,[6] human rights[7] and trade.[8] This paper presents the results of a review of international trends in activity for patent protection between 1990-2000 and provisional data to 2004 and 2005 from over 70 national patent offices, four regional patent offices and the World Intellectual Property Organisation (WIPO) using the European Patent Office esp@cenet worldwide database.[9] The review employed patent publication counts as an indicator of activity for traditional medicines, pharmaceuticals, agriculture, and biotechnology. The research provides insights into the internationalisation of patent activity in multiple areas of biology. The review emphasises the need to combine the further development of quantitative methods with qualitative analysis of the implications of international patent activity in relation to biological and genetic material for science, society and policy.

Introduction

A patent is a legal certificate awarding temporary protection over a claimed invention for a period that is at least 20 years.[10] During this period, patent holders enjoy a range of monopoly rights over the claimed invention including the right to exclude others from “making, using, offering for sale, or selling” the invention and the associated right to exclude others from “importing” the invention into jurisdictions where the patent is in force.[11] During the period of protection the patent holder may be able to commercially exploit the claimed invention either by bringing a product to market or licensing the intellectual property to others.[12]

Patents have commonly been presented in terms of a bargain between society and inventors whereby society accepts the burden of a temporary monopoly to encourage innovation and in return inventors disclose new and useful inventions which become available to serve the wider public good once the period of protection expires. The 1990s witnessed the extension of this logic to biological and genetic material on the international level.

The internationalisation of patent protection in the realm of biology has been justified in terms of the promotion of science and innovation, Foreign Direct Investment (FDI), technology transfer and enhanced trade in goods and services.[13] In the context of the rise of the “knowledge economy” and what is now being called the “bioeconomy” the provision of intellectual property protection is increasingly seen as central to providing incentives for research and innovation across a spectrum of biotechnologies.[14] The pursuit of intellectual property in this arena is also being promoted among universities as part of a wider process of “turning science into business.”[15]

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However, the internationalisation of patent protection raises substantive issues surrounding the human rights, ethical, social, scientific, economic, environmental and legal implications of the extension of particular forms of property and property relations into the realm of biology. These concerns range from the human rights of indigenous peoples in relation to traditional knowledge and resources,[16] the ethics of patenting embryonic stem cells,[17] the interests of developing countries in relation to biodiversity, conservation and development,[18] the impacts of patent protection on access to affordable medicines,[19] innovation in biomedicine,[20] the implications of processes of "enclosure" for the openness of science[21], the future of the public domain,[22] and the principle of "common heritage."[23]

One problem confronting civil society organisations, members of the research community and policy makers in debates surrounding intellectual property is the lack of visibility of patent activity in relation to biological and genetic material. This paper seeks to contribute to addressing that problem and presents the basic results of a review of international patent activity across a spectrum of biological and genetic material.

Approaching the Patent System

According to statistics compiled by the World Intellectual Property Organisation (WIPO), between 1990 and 2000 an estimated 7.6 million patents were granted across all areas of invention.[24] Calculating the number of patent applications worldwide is fraught with difficulty and the available data are unreliable.[25] However, according to the major patent offices, in the region of 10 million applications are estimated to have been submitted by the year 2000.[26] The global nature of the patent system presents a complex array of methodological obstacles for researchers.

In practice, two main instruments are responsible for the international expansion of patent protection over the last decade in the realm of biology. The first of these, which has been the subject of extensive scholarly and policy debate, is the Agreement on Trade-Related Aspects of Intellectual Property (TRIPS) under the World Trade Organisation (WTO).[27] For our purposes it is sufficient to highlight that the TRIPS agreement extended patent protection to all areas of invention, including biology. Specifically, the TRIPS agreement introduced a requirement for member states of the WTO to provide patent protection for microorganisms and microbiological process and an additional requirement for either patent protection or *sui generis* (of its own kind/specially generated) protection for plants (or both).[28] The TRIPS agreement provides for the possibility of exclusions from patentability in order to "…protect *ordre public* or morality, including to protect human, animal and plant life or health or to avoid serious prejudice to the environment…" (Article 27.2). However, these exclusions are limited by the condition that "…such exclusion is not made merely because the exploitation is prohibited by their law." In addition, exclusions are possible for "diagnostic, therapeutic and surgical methods for the treatment of humans or animals" (Article 27.3 a).[29]

The second main instrument is the 1970 Patent Cooperation Treaty (PCT) (modified 2001).[30] The Patent Cooperation Treaty introduces a major multiplier effect into the international patent system by allowing a single application to be filed for potential

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protection in up to 133 countries.[31] In contrast to the TRIPS agreement, which refers to the subject matter of patent protection, the PCT is the main vehicle for the internationalisation of patent protection on an operational level.[32] The multiplier effects of the PCT are accentuated by regional patent instruments such as the European Patent Convention and similar arrangements in Africa, the Middle East, and Eurasia through which applicants can seek protection in multiple jurisdictions.[33]

Methodological Foundations

A variety of methods are now available for examining the relationship between patent activity and innovation. In particular, the OECD has pioneered the development of methods for international comparative analysis ranging through patent counts by filing (priority) date,[34] the creation of patent families for particular country groupings and areas of technology,[35] and a framework for the development of biotechnology statistics.[36] These methods are complemented by additional techniques such as the use of patent citation analysis.[37] In the arena of biological and genetic material, a growing body of work within the scientific journals employs combinations of patent counts with qualitative analysis (typically from the United States Patent and Trademark Office). However, the development of methods in this area is affected by issues of data availability, data comparability, data disclosure and the lack of an international contextual framework for analysis of patent activity.

Our research was directly informed by the wider methodological work of the OECD in developing an international framework for the analysis of patent activity. However, the research was not concerned with the use of patent counts as a measure of innovation but focused on the basic question of the identification of biological and genetic material within the international patent system in the context of debates under the Convention on Biological Diversity. In particular, in view of the scale of the international patent system the research was concerned with exploring the development of what might be called “open” methods for patent research using a data source that is readily accessible to researchers in both developed and developing countries.

For this reason the research focused on the identification of biological and genetic material (broadly conceived) within the patent system using the freely available European Patent Office esp@cenet “worldwide” database.[38] While a variety of commercial database services are available for patent research these will generally be beyond the budgets of most researchers. In contrast esp@cenet is the largest freely accessible database of its type and encompasses patent documents from over 70 countries, 4 regional patent offices and the World Intellectual Property Organisation (for the PCT). At the time that research was initiated in 2004 esp@cenet contained approximately 48 million patent and related documents. By May 2006 this had increased to a reported 54 million patent and related documents.[39] As of July 2006 esp@cenet contained approximately 44.5 million documents that are directly concerned with patents.[40] esp@cenet is increasingly a focus of efforts to make patents in the life sciences more widely available through initiatives such as the BIOS Patent Lens developed by CAMBIA in Australia.[41]

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In order to identify biological and genetic material within the patent system the research focused on the identification of International Patent Classification (IPC) codes for biological and genetic material and relevant technology sectors. The IPC is a hierarchical classification system of approximately 70,000 alphanumeric codes that are used by patent examiners in patent offices around the world to describe the contents of patent applications.[42] The IPC is the main tool that can be used to identify patents relating to biological and genetic material. Thus, patent activity relating to traditional medicines can be identified using the codes A61K35/78 or A61K36, while activity for genetic engineering for plants can be identified using the code C12N15/82. In short, an understanding of classification codes provides a short-cut to identifying areas of the patent system relating to biological and genetic material.[43] The IPC also overcomes the difficulties represented by the use of multiple languages within the patent system.

For the purposes of the research, a review of the IPC (IPC7 and IPC8) was conducted with the aim of identifying the main classifiers and combinations of classifiers relevant to biological and genetic material and areas of science and technology.[44] Over 700 classifiers were identified as part of this process.[45] In particular, the research was concerned with isolating the main areas of the patent system that involve direct claims over biological and genetic material. The main classifiers for biological and genetic material and sectors of patent activity are provided in Table 1.[46]

Table 1. Main IPC Classifiers for Biological and Genetic Material

IPC Code	Classifiers (*Class* and Sub-Class Level)
Section A	**Human Necessities**
A01	*Agriculture*
A01H	New plants or processes for obtaining them
A01K	Animal Husbandry…New breeds of animals
A01N	Preservation of Bodies of Animals or Plants or Parts thereof; biocides
A23	*Food or Foodstuffs*
A23L	Foods, Foodstuffs, or Non-Alcoholic Beverages
A61	*Medical or Veterinary Science; Hygiene*
A61K	Preparations for Medical, Dental or Toilet Purposes
Section B	**Transportation**
B82	*Nanotechnology*
B82B	Nanostructures, Manufacture or treatment thereof
Section C	**Chemistry; Metallurgy**
C07	*Organic Chemistry*
C07C	Acyclic or Carbocyclic compounds
C07D	Heterocyclic compounds
C07H	Sugars; derivatives thereof; nucleosides, nucleotides; nucleic acids
C07K	Peptides
C08	*Organic macromolecular compounds*
C08H	Derivatives of natural macromolecular compounds
C08L	Compositions of macromolecular compounds
C09	Dyes (C09B); Paints (C09D); Natural Resins (C09F); Polishes (C09G); Adhesives (C09J); Other Applications (C09K)
C11	*Animal or vegetable oils, fats, fatty substances or waxes*

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C11B	Producing, refining preserving fats, fatty substances, waxes
C11C	Fatty acids from fats, oils, waxes
C11D	Detergent compositions
C12	*Biochemistry, Beer, Spirits, Wine, Vinegar, Microbiology, Enzymology, etc.*
C12N	Microorganisms or Enzymes; Compositions thereof…; Mutation or genetic engineering…
C12P	Fermentation or Enzyme using processes to synthesise chemical compounds
C12Q	Measuring or testing processes involving enzymes or microorganisms
C12R	Indexing classifier for microorganisms & biochemistry.
C12S	Processes using enzymes or microorganisms to liberate, separate or purify a compound, to treat textiles or clean solid surfaces
C40	*Combinatorial Technology*
C40B	Combinatorial Chemistry; Libraries
G01	*Measuring; Testing*
G01N	Investigating or analysing materials by determining their chemical or physical properties i.e. for biochemical electrodes
G06	*Computing*
G06F	Electrical Digital Data Processing

The classifiers and combinations of classifiers were entered into the esp@cenet "worldwide" database using the advanced search page to elucidate data on trends in activity by patent publication year.[47] For areas of patent activity that do not possess clear classification codes (i.e. stem cells, genomics, proteomics, bioinformatics) additional research was conducted using the commercial whole text Micropatent Aureka Gold patent database to identify the main areas of the patent system for these emerging areas of activity.

Searches of esp@cenet using IPC indicators and combinations of indicators were conducted in 2004 (x 3), 2005 (x 1) and 2006 (x 2). This extensive dataset is made available in stand-alone form through this open access journal in order to encourage open research methods for patent activity.[48] This paper reports on patent activity and indicators for ethnobotanicals and traditional medicines, pharmaceuticals, agriculture and biotechnologies. Researchers interested in other areas of activity, such as biocides, industrial chemistry, microorganisms or other areas will find further information in the dataset. In approaching the results presented in this paper it is important to emphasise three points.

The use of patent publication counts with esp@cenet has a number of implications and limitations when compared with alternative methods. Thus, in contrast with the use of patent counts by filing date (priority date) for the purposes of economic analysis, patent counts by publication date refer to applications that were filed at least 18 months prior to publication. This introduces a significant lag time from the perspective of economic analysis. Furthermore, publication data from esp@cenet include the original publication of applications and the re-publication of applications over time as they move through the patent procedure in multiple jurisdictions on the route to becoming patent grants.[49] This is a common issue confronting patent

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research and it is not readily possible to isolate the different types of patent publication within the esp@cenet public interface.[50]

As such, the data do not discriminate between patent applications and grants and include data on the movement of applications through the procedure. Here we would note that patent applications and patent grants differ in their importance and implications.[51] The data presented in this paper refer to the overall behaviour of the international patent system and encompasses the behaviour of applicants, the multiplier effects of international and regional instruments, and the activity of patent offices. This has the significant strength of providing an overview of the workings of the international patent system on the systemic level in relation to biological and genetic material. The increasing use of esp@cenet by national patent offices may provide important opportunities for similar analysis of national level trends and initiatives such as the BIOS Patent Lens provide increased access to patent documents for qualitative analysis. The forthcoming release of the European Patent Office Worldwide Patent Statistics Database (PATSTAT) that has been developed as part of the Patent Statistics Taskforce led by the OECD should considerably strengthen capacity for detailed econometric analysis of patent activity.[52]

The second point relates to the use of patent databases. The expansion and internationalisation of the patent system has led to increasing dependence on the use of databases. However, research using patent databases is critically dependent on four factors: a) the contents of the database and country coverage; b) the stability of the underlying database architecture over time; c) the accuracy of the search algorithm, and; d) the behaviour of searchers.

In order to test these issues, the methodology focused on the use of repeat searches of esp@cenet in order to generate comparative data over time. This revealed that the coverage of the database is expanding over time but that issues surrounding changes to the underlying structure of the database, the reclassification of documents and user behaviour also need to be borne in mind.[53] In general, as we might expect, the repeat searches revealed that the data demonstrate significant change in the period closest to the present (i.e. 2000-2005) that reflect the addition of documents by patent offices. Data for recent years (i.e. 2004 and 2005) will frequently display an apparent steep decline in activity. This generally corresponds with a lack of available data.[54] The numbers provided in this paper thus reflect the status of documentation within esp@cenet at the time of the searches. The numbers are approximate in nature and intended to serve as indicators of system level trends for particular areas of activity.[55] Data comparability graphs and tables for the main indicators are provided with the accompanying dataset. The present article reports on the June 2006 dataset except where otherwise stated.

Finally, it is important to note that patent documents are frequently awarded more than one classification code in order to adequately describe the claimed invention and the contents of applications. This trend will increase under the latest version of the IPC (IPC8) which entered into force in January 2006.[56] As a consequence, patent publications featuring in one area of the data may also appear in other areas of the data. However, as we will see, the use of combinations of classifiers provides

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important opportunities to define sectors of activity and areas of technology in relation to biological and genetic material.

Patent Trends for Ethnobotanicals and Traditional Medicines

During the 1990s traditional knowledge of plants and other organisms became an important focus of attention in the form of biological prospecting, or "bioprospecting," for new and useful compounds and biological materials in a variety of industry sectors, notably pharmaceuticals. [57] Proponents of bioprospecting argued that developing countries who are rich in biodiversity would obtain benefits through bioprospecting contracts in the form of revenue from milestone payments, funding for scientific capacity-building and, potentially, significant royalty streams arising from product development.[58]

However, the rise of bioprospecting rapidly became a focus of controversy. In particular, research and patenting involving knowledge and material collected among indigenous peoples, local communities and farmers in developing countries led to allegations of "biopiracy."[59] This has served to highlight issues surrounding the human rights and ethical dimensions of patent activity in relation to the rights of indigenous peoples, the extraction and patenting of biological diversity from developing countries by individuals, universities and companies in developed countries, and the wider implications of intellectual property in relation to biological and genetic material. Attempts to address these issues are an important focus of the work of the Convention on Biological Diversity and include the potential development of one or more new instruments as part of an international regime on access to genetic resources and benefit-sharing.[60] Developing countries are also promoting new instruments under the Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore (IGC)[61] under WIPO and amendments to the TRIPS agreement in relation to traditional knowledge.[62]

Growing international debate surrounding traditional knowledge, the human rights of indigenous peoples and local communities and the interests of developing countries has been accompanied by reports of limited, and declining, interest in natural products as a route to drug discovery among pharmaceutical companies.[63] Indeed, for much of the 1990s it appears that the major pharmaceutical companies focused on the apparent promise of synthetic combinatorial chemistry (see below).[64] However, in practice, what may be called ethnobotanicals and traditional medicines emerged as one of the strongest areas of international activity in the review and significantly outstrip trends in areas such as agriculture.[65]

Ethnobotanicals and traditional medicines are mainly situated within "medicinal preparations with undetermined constitution" (A61K35).[66] In the period 1990-2000 there were approximately 52,248 publications under "medicinal preparations with undetermined constitution" (A61K35), with a provisional 99,339 publications by 2004 and 114,272 by 2005 (Figure 1).[67] This category includes a wide range of materials (i.e. from embryos, ovaries, snakes, leeches, algae etc.) but is dominated by material from plants (A61K35/78) with 25,803 patent publications recorded between 1990-2000, 51,060 by 2004 and 60,538 by 2005.

Figure 1: Medicinal Preparations with undetermined constitution

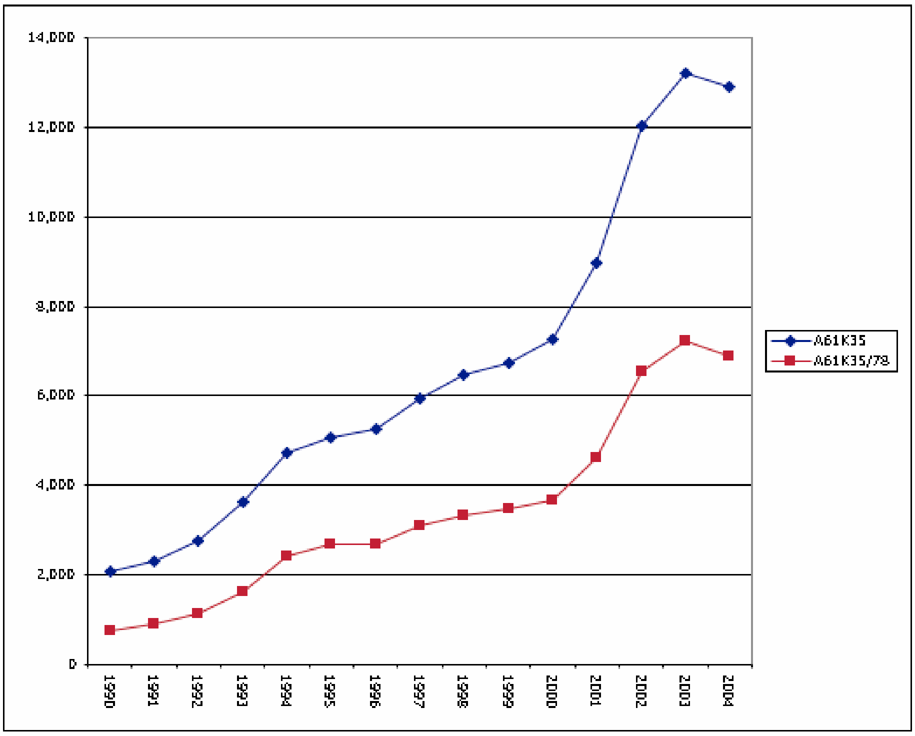
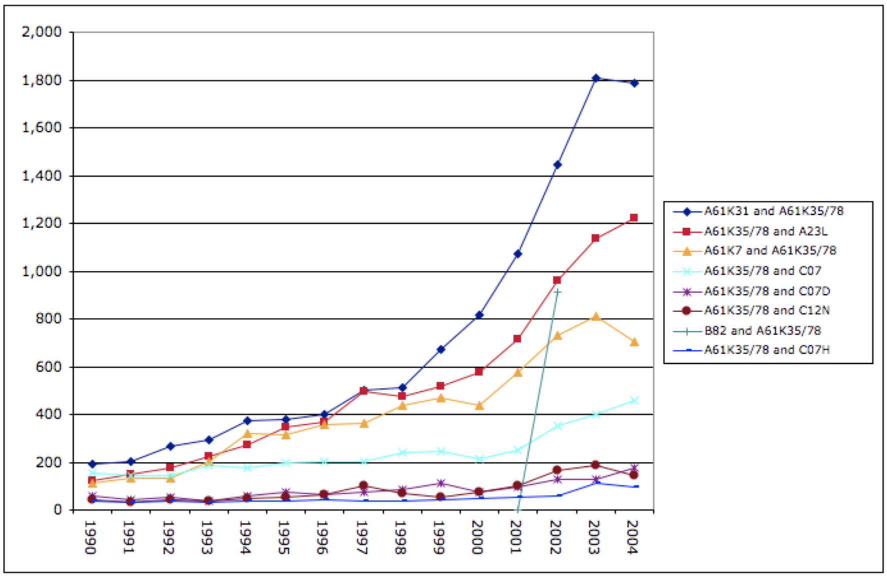


Figure 2: Emerging Activity for Ethnobotanicals and Traditional Medicines



Patent publications in relation to plant material are predominantly awarded a single classification code by patent examiners. This in part reflects the way in which examiners use patent classification codes but also suggests that activity in this area is mainly concerned with raw extracts from plants for use as ingredients or partially characterised compounds. However, an insight into the emergence of a range of sectors and technologies relating to plants and their components can be gained by combining IPC indicators. This is achieved by conducting searches for more than one classifier (i.e. A61K35/78 and A61K31) to identify documents that refer to both ethnobotanicals and traditional medicines and other areas of activity (i.e. pharmaceuticals under A61K31) (Figure 2). An extensive list of such combinations for multiple areas of activity is provided in the accompanying dataset as an aid to further research.[68]

The most notable areas of activity in relation to plant material include pharmaceutical compounds (A61K31) with 4,609 publications between 1990-2000, 10,723 by 2004 and 12,347 by 2005. This is followed by foodstuffs (i.e. dietary supplements and nutraceuticals under A23L) with 3,728 publications between 1990-2000, 7,758 to 2004, and 9,147 to 2005. The emerging importance of ethnobotanicals in relation to patent activity for cosmetics (A61K7) is reflected in 3,274 publications between 1990-2000, 6,094 to 2004 and 6,784 to 2005.

However, Figure 2 also reveals the emergence of patent activity in the realm of biotechnology. Thus, 619 patent publications linked to the main indicator for biotechnology (C12N) are recorded between 1990–2000, 1,212 by 2004 and 1,338 to 2005. Indicators are also beginning to emerge for DNA (C07H) with 422 publications recorded to 2000, 740 publications to 2004 and 848 in the period to 2005. While the numbers are small relative to wider trends they are suggestive of the increasing application of biotechnology related knowledge and techniques to ethnobotanicals and traditional medicines.

A striking spike in activity emerges in 2002 in relation to traditional medicines and nanotechnology (B82) with a total of 914 patent publications in this area. However, it is intriguing to note that one individual, a Yang Mengjun from China, accounts for 905 of these publications.[69] A review of the abstracts for these applications reveals that the applicant is listing large numbers of Chinese medicines on the nano scale and claiming efficacy in the treatment of disease. Taking into account that these applications all appear to have been published on the 11 September 2002 it is tempting to conclude that we are confronted with a hyper-inventor. In practice, a more likely explanation is that this individual was engaged in speculative patenting of traditional medicines on the nano scale with a view to maximising the potential to secure licensing revenue (rents) from other actors who may be interested in this area of activity. This phenomenon can be described as “biosquatting” and can be characterised as exploitation of the availability of monopoly for the purposes of rent extraction.[70] Biosquatting is similar to the phenomenon of domain name squatting that beset the internet in the 1990s.[71]

The challenging nature of patent activity for ethnobotanicals and traditional medicines is also suggested by a detailed review of activity in relation to *Lepidium meyenii* (Peruvian ginseng) which has been a focus of debate surrounding biopiracy.[72] A review of activity for *Lepidium meyenii* suggests a tendency for applicants, or their lawyers, to seek protection for the components of plants at the genus or family level (i.e. *Lepidium* or *Brassicaceae*) rather than at the level of an individual species.[73] This suggests that applicants are seeking to maximise the scope

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of protection for the claimed invention with a view to maximising opportunities to secure rents. However, the nature of patent claims in relation to ethnobotanicals and traditional medicines merits much more detailed research. For the present purposes this example provides an insight into the growing challenges involved in assessing patent activity in the realm of biology. Put simply, the biological components of one organism may be shared across species, genera and families of organism (see below).

In the context of international debates under the Convention on Biological Diversity and related policy arenas, much attention has focused on the presumed interest of major pharmaceutical companies in relation to traditional knowledge. In practice, more detailed quantitative research is needed on the structure of international activity in relation to ethnobotanicals and traditional medicines. However, preliminary research for activity in the main jurisdictions using Micropatent Aureka Gold suggests that activity in this area is characterised by a wide range of individuals, small companies and public research organisations (PROs) such as universities.

Existing debates about the problem of biopiracy have primarily focused on the patenting of traditional knowledge and materials originating from indigenous peoples and local communities in developing countries by individuals, universities and companies based in developed countries. However, it is interesting to observe that individuals, universities and companies from developing countries are becoming increasingly active in this area.[74] For example, the Council for Scientific and Industrial Research (CSIR) in India has been particularly active in patenting.[75] The most striking example of this is China which accounts for approximately 40% of 66,434 publications across the database as a whole.[76] These patent applications are mainly being submitted on the national level but the Chinese authorities are now reported to be promoting applications on the international level through the use of the Patent Cooperation Treaty.[77]

Emerging trends in activity for ethnobotanicals and traditional medicines in both developed and developing countries raise a variety of issues requiring further research. Thus, a clearer assessment is required of patent activity in both developing and developed countries in relation to the terms and conditions under which material and knowledge is submitted for protection, in relation to the human rights of indigenous peoples and local communities, the nature of patent claims, the actors involved and the nature of markets. The potential or actual impacts of patent activity in the main markets in relation to knowledge and material originating in developing countries (i.e. in relation to trade barriers for local producers, also merits further research). Finally, the rise of patent activity involving raw extracts raises potential issues surrounding the conservation status of the plant and other species involved and may merit further research in relation to issues under the Convention on Biological Diversity and the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES).[78]

In response to growing demand for patent protection for medicinal plant material, a new series of classifiers for species and genera have been introduced under indicator A61K36 (which replaces A61K35/78 from January 2006). The introduction of these classifiers is likely to assist in clarifying the nature of activity in relation to ethnobotanicals and traditional medicines. As we will now see, this extends to the

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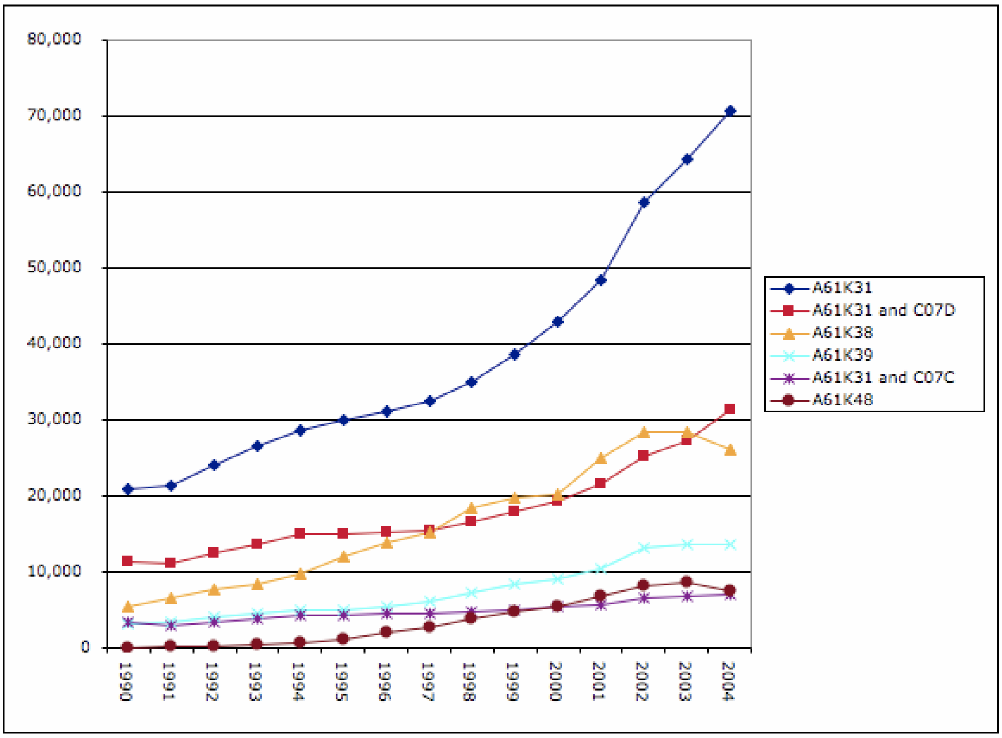
need for a better understanding of the transition between traditional medicines and pharmaceutical compounds and the wider role of compounds originating in nature in the pharmaceutical sector.

Patent Trends for Pharmaceuticals

Patent protection in relation to pharmaceutical compounds is a focus of international policy debate in relation to bioprospecting, access to affordable medicines in developing countries, and the costs, orientation and performance of the pharmaceutical sector in developed countries.[79]

Pharmaceuticals are located under a variety of classifiers within the patent system (Figure 3). The main indicator for pharmaceutical compounds that have been wholly or partially characterised is "Medicinal preparations containing organic active ingredients" (A61K31). Approximately 332,270 publications are recorded in this category between 1990-2000 rising to a provisional 574,386 by 2004 and 637,960 publications by 2005. With the exception of the activity under organic chemistry, this was the main area of international patent activity across the dataset.[80]

Figure 3: Patent Publication Trends for Pharmaceuticals



Patent activity in relation to pharmaceutical compounds can be divided into two broad categories. In cases where a new use is claimed for a previously characterised compound the application is classified under A61K31 and protection is limited to the specific use of the compound. Figure 3 suggests that this remains an important area of activity within the patent system. However, where a compound is new, a classifier will also be awarded in the relevant area of chemistry and "per se" (as such) protection is provided for the compound during the period of the patent. The data reveal that trends in this area are dominated by heterocyclic compounds (C07D) with 163,092 publications between 1990-2000 rising to 268,570 by 2004 and 295,188 by 2005. In contrast trends in relation to pharmaceuticals and acyclic or carbocyclic compounds (C07C) are less significant with 46,805 publications between 1990-2000, 72,856 to 2004 and 78,546 to 2005.

Activity in relation to pharmaceuticals begins to enter what appears to be a cross-over zone between pure chemistry and biotechnology in relation to medicinal preparations containing peptides (i.e. short strings of amino acids that form part of a protein under A61K38) and preparations containing antigens or antibodies (A61K39). This is a cross-over zone in the sense that activity in this area may involve pure chemistry and biochemistry and the increasing shift within the pharmaceutical sector towards alliances between the major pharmaceutical companies and biotechnology companies.[81]

Figure 3 suggests that trends in activity in relation to peptides and pharmaceutical preparations are beginning to catch up with new heterocyclic compounds with 137,542 publications to 2000, 245,805 publications to 2004 and 266,827 publications for peptides to 2005. Patent activity in relation to peptides has led to debate over whether biotechnology patents over peptides may stifle research in pure chemistry.[82]

In the second cross-over category, "medicinal preparations involving antigens or antibodies" (A61K39), approximately 61,511 publications are recorded between 1990-2000, 112,123 by 2004 and 124,267 by 2005. Antibodies (i.e. monoclonal antibodies) have emerged as a major focus of activity in relation to biotechnology.[83] There is a strong association between patent activity for peptides and antigens and antibodies under peptides (C07K) within organic chemistry.[84] As we will see below, there is also a strong association between patent activity in relation to peptides, antigens and antibodies and areas such as stem cells, genomics, proteomics, and bioinformatics.

Patent activity for gene therapy (A61K48) is a discreet area of activity with 22,003 publications between 1990-2000, 53,379 by 2004 and 59,692 by 2005. This is therefore the logical starting point for further research on gene therapy. Patent activity for pharmaceuticals and DNA begins to come into focus by combining indicator A61K31 with C07H (sugars, nucleotides, nucleosides, nucleic acids) with 22,012 publications recorded between 1990-2000, 33,409 in the period to 2004 and 35,984 to 2005. This is followed by the main indicator for biotechnology, "microorganisms or enzymes" (C12N), with 13,085 publications between 1990-2000, 26,201 publications by 2004 and 28,735 in the data to 2005. Activity in this area, as we might expect, is dominated by genetic engineering (C12N15) with 20,214 publications recorded in the data to 2005.

As these multiple indicators suggest, additional research is desirable in order to define and disaggregate sectors of activity in relation to pharmaceuticals across the spectrum from pure chemistry to biotechnology. However, the basic principle that is established here is that it is possible to begin separating out the main areas of

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international activity through an understanding of patent classifiers and combinations of classifiers. Additional information in the dataset may assist in further clarification of trends within the pharmaceutical sector.

A further challenge to assessing patent activity in the pharmaceutical sector is understanding trends in relation to disease. This is particularly relevant in the case of debates surrounding neglected diseases.[85] In recognition of the desirability of improving indicators in this area, in 2000 a new set of indicators (A61P) were introduced for disease categories. A review of the contents of esp@cenet for all years across the database within the 2005 dataset revealed the dominance of activity in relation to anti-cancer drugs (40,859), treatments for nervous system disorders (37,643), anti-infectives (31,939), heart disease (30,145) and disorders of the metabolism (23,249). Activity for disease categories of relevance to developing countries, i.e. HIV (5,269), antiparasitics (3,905), antiprotozoals for diseases such as leishmaniasis, trichomoniasis (963), antimalarials (815) and TB (705) ranked much lower. However, it should be noted that these indicators are relatively new and their use by patent offices world-wide may be limited. Furthermore, a variety of other factors may also affect patent activity in this area.[86] In the context of ongoing debates relating to intellectual property and pharmaceuticals under the World Health Organisation further research is highly desirable in this area.[87] Future research would ideally combine the use of indicators with the use of whole text databases to test and enhance data capture for patent activity and neglected diseases.

Other important areas for clarification relate to the role of compounds from natural products in patent activity. Thus, trends in demand for ethnobotanicals and traditional medicines would suggest that activity in this area should filter through to the main areas of activity for pharmaceutical compounds. However, as Figure 2 demonstrates, while the trends are significant overall numbers are low. This appears to reflect the problem that a linkage between the origin of a compound with a plant or other organism within the patent system is not maintained at the level of the classification of applications once the compound is characterised or synthesised.

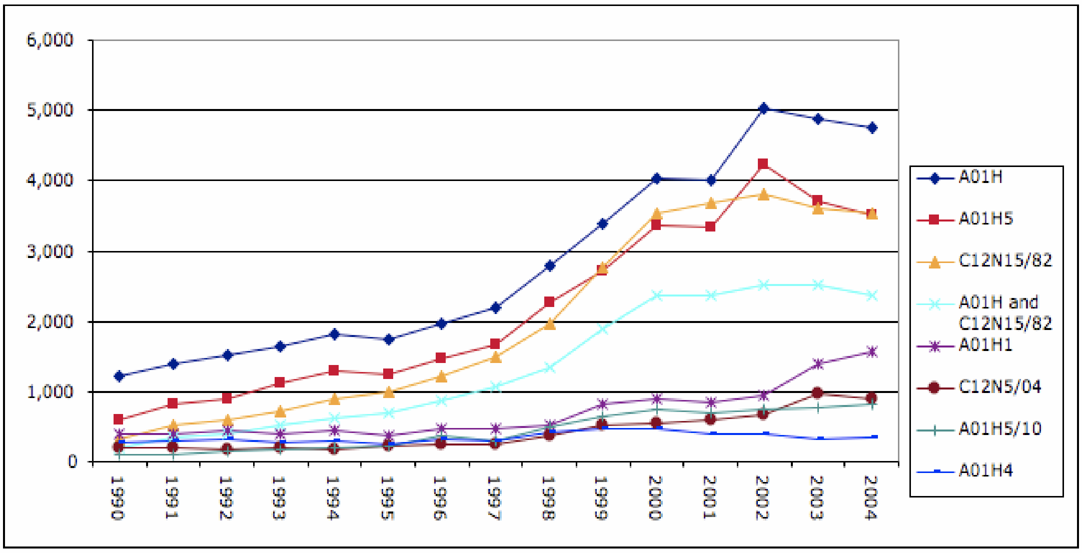
In practice, as Newman, Cragg and Snader (2003) have demonstrated "yet again," compounds originating from, modelled on, or mimicking, natural products are of central importance within the pharmaceutical sector at the level of actual approvals of new drugs by the United States Food and Drug Administration.[88] As Newman, Cragg and Snader also highlight, in reviewing approvals between 1981 and 2002, they were not able to identify a single *de novo* combinatorial compound that was approved as a new drug during this period.[89] In short, debates focusing on the promise of *de novo* combinatorials appear to overestimate their potential and underestimate the ongoing importance of natural products at the level of actual outputs. This suggests a need for further research on the relationship between compounds from nature and pharmaceuticals and international patent activity in the context of debates surrounding bioprospecting and access to genetic resources and benefit-sharing under the Convention on Biological Diversity. One potentially fruitful avenue of enquiry for such research might focus on the nomenclature of natural compounds developed by the International Union of Pure and Applied Chemistry.[90]

This in turn suggests a need for a wider assessment of the relationship between patent protection and outputs in the form of approvals in the pharmaceutical sector. It should be emphasised that the data on international trends presented in this paper refers to overall publication activity rather than priority applications (first filings) and patent grants.[91] However, when international trends are viewed in the context of declining approvals in countries such as the United States we can perhaps begin to legitimately ask the question: where are all the new drugs?[92] That is, bearing in mind the complexities of drug development, is the patent system performing its avowed function or generating other effects?[93] In the context of ongoing international debates surrounding the role of patent protection in the pharmaceutical sector, this draws attention to the need for closer attention to quantitative analysis of patent activity relative to actual outputs in the form of approvals of new drugs.[94] Taking into account the long lead-in time for the development of new pharmaceuticals, this might usefully take the form of country-level studies of patent activity relative to actual approvals over a 20-30 year period.[95]

Patent Trends for Agriculture:

Intellectual property protection for plants takes three main forms: plant variety protection, plant patents and industrial patents.[96] The present review focuses on industrial patent activity (Figure 4).

Figure 4: Main Trends for Agriculture



The main indicator for agriculture is "new plants of processes for producing them" (A01H). Approximately 23,689 patent publications registered with esp@cenet between 1990-2000, 42,371 by 2004 and 46,509 by 2005. Demand in relation to agriculture is dominated by the general category of flowering plants (A01H5) with approximately 17,455 publications recorded between 1990-2000, 32,210 by 2004 and 35,100 by 2005. This category includes United States plant patents.[97]

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The most striking feature of patent activity in relation to agriculture is growing trends towards recombinant genetic engineering for plants (C12N15/82). Between 1990 and 2000, approximately 15,064 publications emerge in the data, 29,684 by 2004 and 32,667 by 2005. While Figure 4 suggests that activity is now levelling out, it is also interesting to note that patent examiners predominantly award patent applications under C12N15/82 rather than both A01H and C12N15/82 (see Figure 4). This suggests that further research should concentrate on C12N15/82. Additional biotechnology-related indicators include "modification of plant genotypes" (A01H1), "plant reproduction by tissue culture techniques" (A01H4) and "undifferentiated plant cells and tissues" (C12N5/04). In contrast with biotechnology-related activity trends in relation to the modification of plant phenotypes (A01H3) are much lower with 416 publications recorded between 1990-2000, 789 to 2004 and 861 to 2005.

The implications of intellectual property protection in the realm of agriculture, notably in connection with plant variety protection under the Union for the Protection of New Varieties of Plants (UPOV) and debates surrounding patents, biotechnology and agriculture in developing countries are a significant focus of ongoing public, scientific and policy debate.[98] The importance of balancing quantitative analysis of patent activity in this area with qualitative analysis of the implications of emerging areas of activity such as genomics can be briefly illustrated through reference to the rice genome *(Oryza sativa)*.[99]

In 2001 Syngenta Biotechnology Inc. and Myriad Genetics announced the completion of the draft of the rice genome.[100] This sparked concern that the genome of the world's major cereal would be patented.[101] In response, Syngenta announced in 2002 that the genome data would be made available to the publicly funded International Rice Genome Sequencing Project.[102] However, in 2002 Syngenta also submitted a Patent Cooperation Treaty application naming 115 countries entitled "Identification and Characterization of Plant Genes" which claimed to have identified the genes regulating flowering, head formation and plant morphology in rice, wheat, maize and banana (WO03000904). The application described over forty species and genera, of which at least 23 are protected under the International Treaty on Plant Genetic Resources for Food and Agriculture, as falling within the scope of the claimed invention.[103] This extended to plants yet to be described by taxonomists: "Any other genera or species of Lemmaceae, if they exist, are also aspects of the present invention."[104] The specific claims were constructed in terms of the percentages of activity of whole or partial DNA and protein molecules, i.e. in determining flower meristem identity, such that the discovery and use of "substantially similar" or "homologous" DNA and protein molecules from other plants for research or product development would infringe the patent. In short, the application sought to stake a claim to the fundamental genetic components of flowering plants.[105]

This application was the subject of an unfavourable search report from the European Patent Office in relation to prior art in late 2004. In particular, the search report identified existing prior art from the University of Washington (US5861542) and Max Plank Gesellschaft (WO0037488) in relation to MADS-box proteins for rice, grasses and other plants.[106] The application also became a focus of an international campaign led by the international civil society organisation ETC Group in January

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2005.[107] In February 2005 the company informed ETC that it would allow the application to lapse world-wide and the application is now dead.[108] However, the application formed part of a wider family of applications relating to the rice genome that are linked to an underlying patent filing that is 12,529 pages long.[109] The patent family for the application consists of 23 basic members (as of July 2006) and the company is continuing to pursue a small number of applications on specific components of the rice genome within this wider patent family.[110] Greenpeace, The Berne Declaration, No Patents on Life and Swiss Aid are hoping to persuade the company to withdraw the remaining applications.[111]

As this suggests, in considering trends in agricultural biotechnology, the scope of patent claims made possible by the mapping of the genomes of organisms may be as important as the overall number of patent applications and grants.[112] Specifically, genomics is dependent upon the identification of genetic similarities (homologies) between organisms across species, genera, and classes of organism. Thus, the identification of the genetic components of the model plant *Arabidopsis thaliana* which falls into the dicot (dicotyledon) class provided the keys to unlock the genome of rice which is a monocot (monocotyledon). This in turn provides the keys to unlock the genomes of other major food crops (i.e. wheat, maize etc).[113] The reason for this is that organisms such as plants are ultimately linked through evolution to common ancestors and conserve key elements of their genome over evolutionary time.[114] In the realm of intellectual property, genomics thus makes possible claims at the level of the fundamental common elements of genomes across classes of organism.[115]

The analysis of the positive and negative implications of patent and related forms of intellectual property in the realm of agriculture deserves much greater attention than can be provided here. This is particularly true in relation to plant genomics but also extends to detailed consideration of biotechnology in relation to animals and agriculture. In moving forward with understanding the implications of trends in agriculture for plants and animals in both developed and developing countries, this suggests the need for closer attention to the development of international indicators and combining quantitative analysis with qualitative sampling techniques to generate representative data on particular sectors of activity, i.e. plant genomics, biotechnology and animals.

Patent Trends for Biotechnology

The discussion in preceding sections illustrates the increasing penetration of biotechnologies across a spectrum of sectors of activity and corresponds with increasing trends to convergence of science and technology around the “bio”.[116] However, identifying trends in relation to biotechnology as a spectrum of diverse sub-sectors of activity encompassing areas such as stem cells, genomics, proteomics, bioinformatics, systems biology, bionanotechnology and emerging areas such as synthetic biology presents significant challenges.[117]

A variety of approaches to analysis of patent activity are emerging in this area. These include key word searches of the main patent offices and combinations of classifiers, i.e. DNA patents,[118] diagnostic testing,[119] and sophisticated searches of sequence databases for patented sequences as a basis for detailed analysis, i.e. the landscape of

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intellectual property for the human genome.[120] Taking into account that applications from residents of developed countries are the main drivers of patent activity in this area, these approaches also provide important insights into wider trends in activity. However, in approaching the patent system as a global system, researchers are confronted by the use of an increasing number of languages and the lack of availability of the whole text of patent documents.[121] The identification of key indicators for activity is therefore desirable to provide the quantitative context and to identify areas for more detailed research.

As a contribution to methodological development, the present research employs a provisional IPC based working definition of biotechnology developed by the OECD.[122] The working definition employs 30 IPC classifiers and indicator C07H for DNA was added to improve the data coverage. The results of the searches were then ranked to identify the main indicators (Figure 5).

Figure 5: Main Trends for Biotechnology

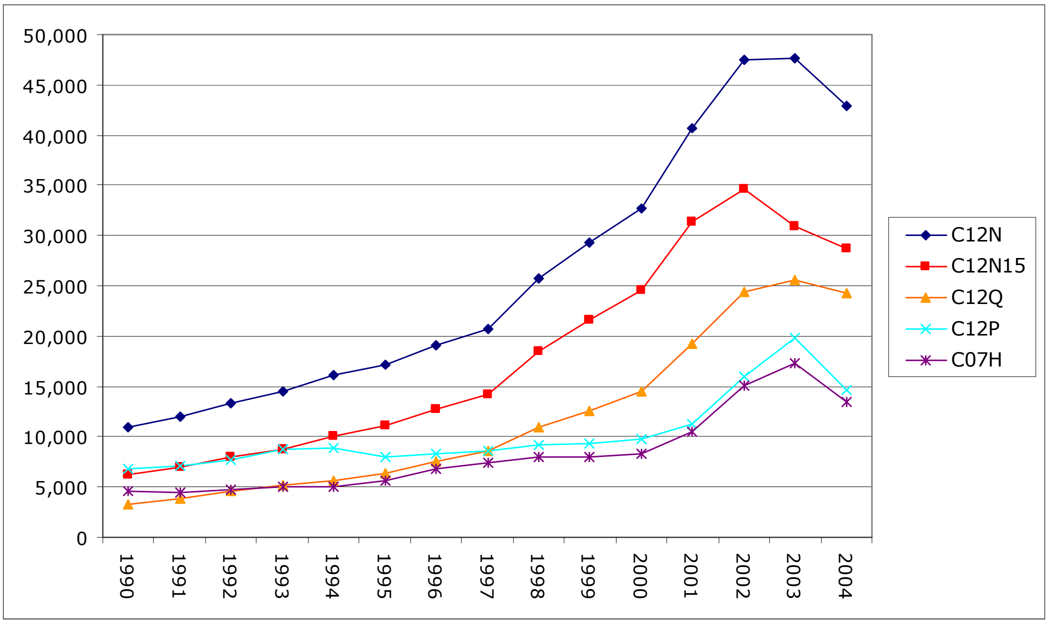


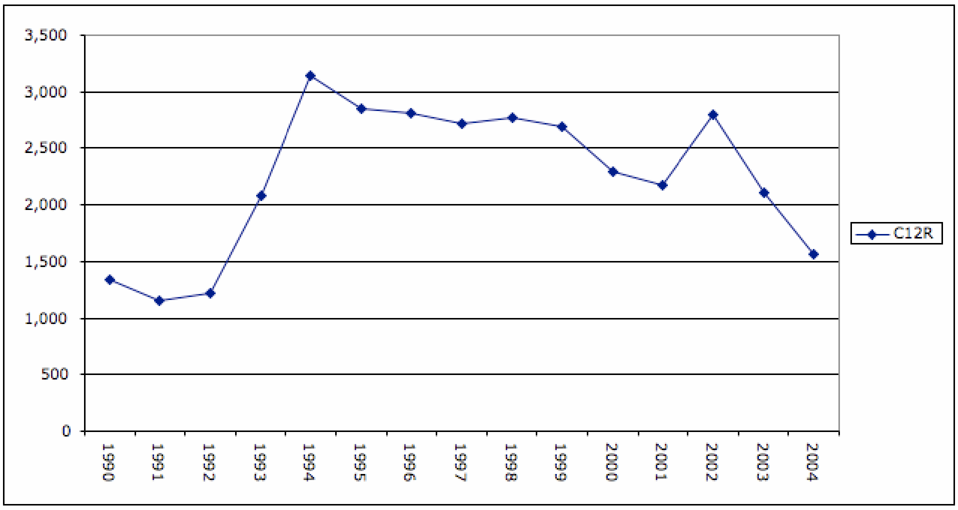
Figure 5 reveals that "microorganisms or enzymes" (C12N) is the main indicator for patent activity relating to biotechnology with approximately 211,663 publications recorded between 1990 and 2000, 390,252 by 2004 and 426,845 by 2005. Trends under this indicator are dominated by "mutation or genetic engineering" (C12N15) with 142,556 publications to 2000, 268,092 by 2004 and 292,437 by 2005. Other strong areas of activity include "measuring or testing processes involving enzymes or microorganisms"(C12Q) with 83,077 publications between 1990-2000, 176,530 by 2004 and 197,612 by 2005. This is followed by "fermentation or enzyme using processes to synthesise compounds" (C12P) with 92,322 publications between 1990-2000, 153,881 by 2004 and 167,008 by 2005.

As noted above, the main classifier for DNA is C07H (sugars, derivatives thereof; nucleosides, nucleotides and nucleic acids) with approximately 67,942 publications recorded between 1990-2000, 124,518 by 2004 and 135,625 by 2005.[123] However, it appears that this indicator under organic chemistry is now being superseded by the use of indicators such as C12N under biochemistry. For this reason, while it remains important, an exclusive focus on C07H will underestimate patent activity in relation to DNA and biotechnology. Other important areas of activity in relation to biotechnology include immunoassays (G01N33/53) in the area of physics with 25,474 publications between 1990-2000, 55,740 by 2004 and 62,129 by 2005. As discussed above, peptides (A61K38 and C07K), antigens and antibodies (A61K39), and gene therapy (A61K48) are also very significant areas of activity.

One of the most striking features of patent activity in relation to biotechnology is the predominance of patent indicators that refer to microorganisms or enzymes.[124] In practice, microorganisms are an important focus of interest across a range of research and industry sectors and are an increasing focus of bioprospecting activities in areas such as Antarctica[125] and the deep sea bed.[126] The sequencing of the genomes of microorganisms (i.e. Archaea and Bacteria) are also a key focus of research activity.[127] Patent activity in this area now extends to claims to the whole genomes of organisms.[128]

Figure 6 sets out trends in activity relating to microorganisms that have been taxonomically described using *Bergey's Manual of Determinative Bacteriology* (Eighth edition, 1975) under indicator C12R. This reveals approximately 25,062 publications between 1990-2000, 33,707 publications to 2004 and 34,898 by 2005. In practice, the extent to which patent offices consistently use the descriptive indexing classier C12R is open to question and the classification system may not be keeping pace with patent activity in this important area.[129] Further research is desirable on this issue. However, it appears reasonable to assume that microorganisms as they are ordinarily understood (i.e. Archaea and Bacteria) cannot account for levels of patent activity within these areas of the patent system.

Figure 6: Patent activity for taxonomically described microorganisms



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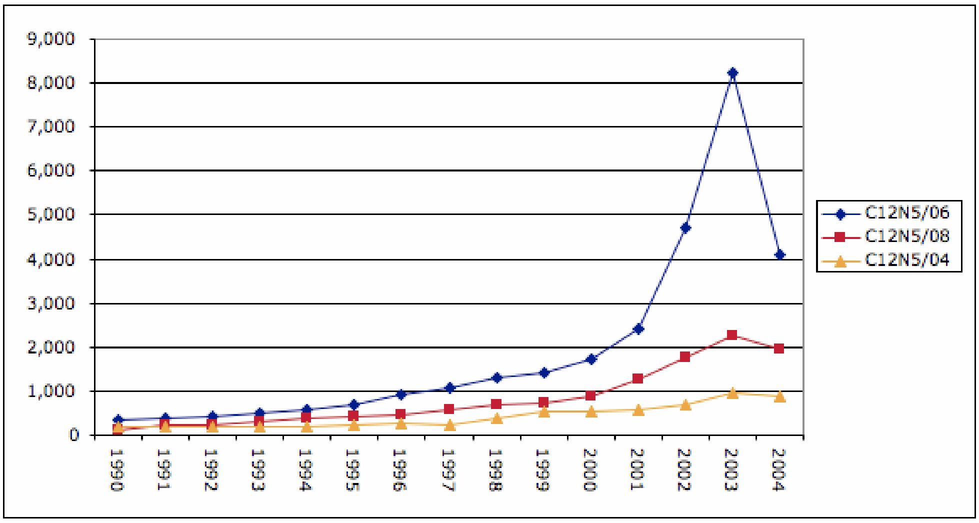
In considering this apparent conundrum it is important to recall that patent activity in the realm of biotechnology has its origins in the 1980 United States Supreme Court decision *Diamond v. Chakrabarty* which found that a microorganism that had been genetically engineered could be considered to be a product of "human ingenuity" and consequently patentable.[130] It appears that in the context of the subsequent expansion of patent activity in the realm of biotechnology, the categories of the patent system that relate to microorganisms and enzymes have been converted into catch-all categories for a wide range of biological and genetic material. This also serves to highlight the wider significance of the requirement within the TRIPS agreement that patent protection must be provided for microorganisms and microbiological processes.[131]

Thus, the guidance notes for the Biochemistry class (C12), within which C12N and the other major indicators are located, explains that: "In this class, viruses, undifferentiated human, animal or plant cells, protozoa, tissues and unicellular algae are considered as micro-organisms".[132] In the case of "undifferentiated human, animal or plant cells" this extends to stem cells and plant meristems, tissues, cell lines and culture media (Figure 7).[133]

Figure 7: Undifferentiated Human, Animal or Plant Cells or Tissues



The main indicator for undifferentiated human, animal and plant cells or tissues is C12N5. A total of 53,885 publications were recorded between 1990-2000, 109,234 by 2004 and 119,525 by 2005 (not shown). In practice, on the international level patent offices classify at different levels of detail and the use of C12N5 appears to predominate. However, Figure 7 reveals significant activity in relation to undifferentiated animal cells or tissues (C12N5/06) with 9,139 publications recorded between 1990-2000, 28,771 by 2004 and 31,965 by 2005. In the case of undifferentiated human cells or tissues (C12N/08) 4,984 publications were recorded between 1990-2000, 12,226 by 2004 and 14,195 by 2005. Activity in relation to plants (C12N5/04) registered 3,109 publications between 1990-2000, 6,244 by 2004 and 7,002 by 2005.

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Patent activity in relation to undifferentiated animals cells or tissues (C12N/06) encompasses embryonic stem cells such as the University of Wisconsin Alumni Research Foundation (WARF) patent applications and grants on primate embryonic stem cells arising from research with marmosets and rhesus monkeys (i.e. WO9622362).[134] These patent applications were constructed in such a way that claims relating to embryonic stem cells in rhesus monkeys and marmosets extended to primates and thus to humans. As in the case of genomics, this exposes the issue that patent claims may be constructed to encompass homologous material in other organisms.[135] These patent grants are a significant focus of debate within the literature.[136] Looking beyond the substantive ethical debates that revolve around embryonic stem cell research and patenting, this exposes the difficulties presented for scientific research by expansive claims across organisms.[137]

Patent activity in relation to stem cell related indicators also provides an insight into areas such as cloning.[138] Thus, Patent Cooperation Treaty applications submitted by former Seoul National University Professor Hwang Woo Suk and colleagues in relation to an embryonic stem cell line (WO2005063972), a transgenic cloned cow (WO2004016773), a cloned pig (WO03089632), a method for producing a cloned tiger through inter-species nuclear transfer (WO0100794) and the same methods for producing a cloned human embryo (WO0100793) are classified under C12N5 but may also cross-link to “mutation or genetic engineering” (C12N15) and new breeds of animals under agriculture (A01K).

Hwang Woo Suk and his colleagues published two articles relating to cloning and stem cell research in the journal *Science.* These papers, *Evidence of a Pluripotent Human Embryonic Stem Cell Line Derived from a Cloned Blastocyst*[139] and *Patient-Specific Embryonic Stem Cells Derived from Human SCNT Blastocysts*[140] have been the subject of much media discussion, and have been retracted by the journal’s editors[141]. The investigating committee of Seoul National University (SNU) concluded that the data and claims presented in relation to stem cells lines were fabricated.[142] In addition to the legal and ethical issues raised by this level of alleged scientific misconduct, this raises questions about the technical validity of the inventions claimed within the patent applications. The wider implications of scientific misconduct for the international intellectual property regime in areas of ‘breakthrough’ science merit fuller consideration than can be provided here. However, ongoing controversies about patent applications arising from this research suggest a need to question the role of intellectual property in ‘turning science into business’ in such sensitive areas.[143]

For our present purposes the important point here is that we now have a clearer idea where to begin looking for patent activity in relation to stem cells and cloning. However, stem cell-related patent activity also introduces the wider methodological challenge that new areas of science and technology do not necessarily fall into single areas of the patent system. As a contribution to further methodological development, research was conducted using the Micropatent Aureka Gold patent service in order to begin defining the main areas of patent activity for stem cells, genomics, proteomics, and bioinformatics. The searches were confined to United States applications and grants, European Patent Convention applications and grants, PCT applications,

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applications and grants for Germany, and applications for the UK, Japan and France. The searches covered the period from 1 January 1990 to 31 December 2005.

A search of the main jurisdictions using the Micropatent Aureka Gold whole text service for the simple terms “stem cell or pluripotent or totipotent” revealed a raw sample of 32,490 documents.[144] Of these 25,458 (78%) were published between 1 January 2001 and 31 December 2005. Refinement of the search terms may be desirable to enhance data capture. However, this example serves to suggest a dramatic increase in patent activity in the main jurisdictions and is mirrored in areas such as genomics (see below).

A total of 20,458 (63%) of these publications were classified under C12N for microorganisms or enzymes. On a more detailed level of the 32,490 documents a total of 12,676 (39%) were classified under C12N5 (for undifferentiated material) while 11,283 (35%) were classified under C12N15 (for genetic engineering). Taken together these two indicators accounted for 19,040 (59%) of the overall sample and 93% of documents under C12N and confirms that this is the logical starting point for research.[145] However, the research also revealed that documents are classified under 10 main IPC classifiers ranging from agriculture, to pharmaceuticals, and physics. In total the 10 classifiers encompassed 31,423 documents (97%) of patent activity for the sample. However, 64 classifiers are required to reach 99.68% and some documents go unclassified.

In the case of genomics, a total of 128,400 publications containing the term “genome” were published in the main jurisdictions between 1990-2005.[146] Of these, 39,542 documents were published between 1990 and the end of 2000 while 88,858 documents (69%) were published between 2001 and the end of 2005. As this makes clear, patent activity in relation to genomics has undergone dramatic expansion in recent years and corresponds with the completion of the maps of the human genome and the first genomes of plants (i.e. *Arabidopsis thaliana* and *Oryza sativa*), animals, insects and microorganisms.[147]

A sample of 50,454 documents published between 2001 and 2003 containing the term genome was analysed in order to identify the main classifiers relating to genomics. This revealed that 32,476 (64%) of the sample falls within C12N. Other significant areas include C12Q (36%) C12P (26%) and C07H (29%). Combined, these four indicators capture 41,755 (83%) of genome related publications. As noted in the discussion of pharmaceuticals, indicators for peptides (A61K38 and C07K), antigens and antibodies (A61K39) and gene therapy (A61K48) are also significant in this area. Coverage improves to 47,810 (95%) through the inclusion of medicinal preparations (A61K) and peptides (C07K). However, patent activity in relation to genomics also reveals the importance of activity falling in the area of physics within the international patent classification. Thus, a total of 14,591 documents in the sample are awarded classifiers in relation to “investigating or analysing materials by determining their chemical or physical properties” (G01N) and “electrical digital data processing” (G06F). When these indicators are included data capture increases to 48,364 (96%) of the sample. Data capture can be increased to 99.93% by using 65 classifiers but becomes increasingly fragmentary.

The increasing importance of activity classified under physics is also revealed in relation to proteomics and bioinformatics. Here we should emphasise that further research is required on the extent to which activity under physics involves *per se* claims over biological and genetic material.

For proteomics (the protein complement of a cell or organism) a search of the main jurisdictions for the term proteome revealed 3,671 publications between 1990 and the end of 2005. Of these 3,544 (96%) were published from 2001 onwards. The main indicator for proteomics is "investigating or analysing materials by determining their chemical or physical properties" (G01N) which accounts for 2,159 (59%) of documents in the sample i.e. mass spectrometry. This is followed by "measuring or testing processes involving enzymes or microorganisms" (C12Q) with 1,499 (41%) of the sample. When combined these indicators account for 2,758 (75%) of the sample. Other important areas of activity include peptides (C07K and A61K38) and C12N which push data capture to 3,351 (91%). Data capture can be enhanced to 3,587 (98%) through the addition of DNA (C07H), and pharmaceuticals (under A61K notably, antigens and antibodies, gene therapy), "digital data processing" (G06F), "apparatus and separation" (B01D) and "electric discharge tubes/lamps" (H01J). 100% of proteome related activity can be captured using 36 classifiers.

In the case of bioinformatics, a total of 9,567 documents were published in the main jurisdictions between 1990-2005 containing the term "bioinformatics" of which 8,855 (93%) were published since 2001. Activity in this area is dispersed across C12N (52%), peptides (under C07K) with 48%, C12Q (42%) and G01N (35%) and G06F for digital data processing (16%). Taken together these five indicators encompass 9,094 (95%) of activity. Data capture to 99.6% was achieved using 35 classifiers but became increasingly fragmentary.

These examples serve to demonstrate that it is possible to capture the main indicators for particular areas of activity as a basis for further research. However, problems of fragmentation also begin to emerge in demarcating areas of activity beyond approximately 95%. This reflects the dispersal of activity across a range of sectors. This problem has proved to be particularly marked in the case of nanotechnology which has undergone dramatic expansion in recent years.[148] In response, indicators for nanotechnology were introduced into the IPC (i.e. B82 and A61K9/51). However the pace of the 'nano rush' proved such that the USPTO introduced classifier 977 and the European Patent Office introduced a "tag" Y01N into esp@cenet documents under the European Patent Classification (ECLA). This can now be used to identify bionanotechnology patents i.e. Y01N and C12N produced 1,245 results in esp@cenet at the time of writing. Similar challenges may also emerge in relation to systems biology[149] and synthetic biology.[150]

Conclusions

This article has set out the basic results of a review of international patent activity in relation to biological and genetic material and provided suggestions for further research. In making the accompanying dataset available through an open access journal our aim has been to encourage the development of open research methods that will provide researchers, civil society organisations and policy makers in both developed and developing countries with a "clearer view" of patent activity in relation to biological and genetic material.[151]

As we have seen there are considerable challenges involved in addressing the international scale of patent activity for biological and genetic material and assessing the implications for science, society and policy. Addressing these challenges merits much greater attention from the research community. In particular, this research has demonstrated that biological and genetic material now occupies an increasingly prominent position within the international patent system. Patent activity in relation to biological and genetic material ranges from crude extracts from plants for use as ingredients in foodstuffs, medicines and cosmetics to pharmaceutical and industrial compounds, DNA and proteins, microorganisms, the genomes of organisms and their components and stem cells. Increasingly, activity is also moving into areas such as proteomics, bioinformatics, bionanotechnology, systems biology and synthetic biology.

The recent work of the OECD and the Patent Statistics Task Force in developing an international framework for statistical analysis and the new European Patent Office World Patent Statistics Database will greatly facilitate statistical analysis. However, it is also important to recognise that the characteristics and implications of activity in one area of the patent system (i.e. traditional medicines) will not be the same as those in other areas of the patent system (i.e. genomics or synthetic biology).[152] As we have argued in this paper, there is a need for a better understanding of the characteristics of sectors of activity and the actors and the markets involved as a basis for assessing their implications for science, society and policy.

When viewed from an international perspective this raises the challenge of how a structured approach might be developed that simultaneously recognises the scale and diversity of patent activity and the need for quantitative and qualitative analysis. In particular, how might international collaboration and data comparability be promoted in this area?

One answer to this question is to structure research around the International Patent Classification system. As the accompanying dataset reveals, in practice, the IPC operates at a considerable level of detail in relation to the type of material. This provides researchers with opportunities to target specific areas of activity and to situate their research within a wider context that can be linked with quantitative analysis.[153] Here it may be noted that areas such as genomics, systems biology and synthetic biology present complex methodological issues at the level of indicators. However, as existing research and the present paper highlights, it is possible to begin demarcating these areas as a basis for detailed research. In short, a structured approach to research that is linked to the IPC will provide a basis for the international comparability of research efforts on a variety of levels. Tools such as esp@cenet and the BIOS Patent Lens also provide researchers from both developed and developing countries with important free resources through which to interrogate the patent system in a structured way. This may then be linked with the use of sophisticated quantitative research tools.

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Finally, as noted in the introduction to this paper, the internationalisation of patent protection in the realm of biological and genetic material raises substantive issues across a spectrum from human rights and ethics to the future of science, innovation and world trade. In practice, the identification of the main indicators for biological and genetic material within the international patent system provides opportunities for targeted international policy responses. These opportunities include the potential introduction of new and more "open" models that recognise international concerns and promote the sharing of knowledge and resources to serve the wider public good. The exploration of those opportunities will be the focus of our future research.

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[40] Esp@cenet includes extensive information on utility models, designs, plant patents, certificates and other forms of intellectual property protection as well as non-patent literature ("XP" documents) that would presumably bring the total to the stated 54 million. Data coverage tables and calculations by document "kind codes" are provided with the dataset. The cited figure for patent documents excludes utility models, registrations, designs etc. but includes plant patents which feature in data contained in this paper under agriculture (A01H5). Detailed country coverage tables are provided in the annual European Patent Office publication entitled 'Global Patent Data Coverage: A comprehensive overview of the coverage of the worldwide patent database' http://patentinfo.european-patent-office.org/_resources/data/pdf/global_patent_data_coverage.pdf.
[41] http://www.cambia.org/patentlens/simple.cgi
[42] The IPC was established under the 1971 Strasbourg Agreement Concerning the International Patent Classification and at the time of writing there were 57 Contracting States to the IPC Union which governs the development of the IPC http://www.wipo.int/treaties/en/classification/strasbourg/.
[43] The latest version of the IPC (IPC8) consists of a core and an advanced level. IPC8 will be subjected to regular development on the advanced level, i.e. by major patent offices. It is anticipated that smaller patent offices will rely on the core level. For the purposes of international level analysis of patent activity, the core level (i.e. sub-class level) will generally enhance data capture and serve as a basis for more detailed analysis. See H. Wongel. The reform of the IPC - consequences for the users. World Patent Information 2005; 27: 227-231.
[44] The review mainly focused on IPC7 which forms the core of IPC8. The core of IPC8, which is available in published and electronic form, was also reviewed. However, the advanced level of IPC8 is only available in electronic form and will be subject to further development. Additional research is merited on both the core of IPC8 and the advanced level.
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[48] See the accompanying dataset.
[49] To a much more limited degree the data also include data on other forms of intellectual property protection notably utility models, plant patents and designs. This can be tested using kind codes (i.e. U) and IPC codes for the main indicators. Data coverage tables for esp@cenet are provided with the dataset.
[50] In part this reflects the complexity of the use of document "kind codes" (i.e. A, B, C) to describe different kinds of patent publication within the international system where different countries use different codes. A basic introduction to kind codes is available through esp@cenet and WIPO has developed "Standard ST.16" in relation to document codes http://www.wipo.int/scit/en/standards/pdf/03-16-01.pdf.
[51] Patent applications may involve speculative attempts to maximise ownership in emerging areas of science and technology for biological and genetic material. In contrast, the job of patent examiners is to award grants based on the criteria for patentability. This may involve rejecting claims or requiring modification of claims in the examination procedure. The analysis of patent applications thus provides insights into the behaviour of applicants while the analysis of patent grants speaks to the integrity of the patent system and the ability of patent holders to exercise particular rights. For discussion of patent applications in biotechnology see P. Oldham.. Global Status and Trends in Intellectual Property Claims: Genomics, Proteomics and Biotechnology. Global Status and Trends in Intellectual Property Claims 2004; Issue 1 http://cesagen.lancs.ac.uk/resources/docs/genomics-final.doc.
[52] For further details see OECD Work on Patents http://www.oecd.org/document/10/0,2340,en_2649_34451_1901066_1_1_1_1,00.html.
[53] For example, esp@cenet underwent a rebuild in 2005 and database performance was also reportedly degraded by users attempting to employ software robots to extract patent documents.

[54] It is for this reason, and in order to avoid confusion, that the graphs in the present paper cover the period 1990-2004.
[55] The repeat search methodology also revealed variability in the practical use of classification codes by patent offices (i.e. A61K39 rather than A61K39/00) that led to the adjustment of the searches to enhance data capture.
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