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Research Tool Patents and Free-Libre Biotechnology: A Suggested Unified Framework

This is Working Paper
No 36 (April 2008)

Research Tool Patents and Free-Libre Biotechnology: A Suggested Unified Framework

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This draft: March, 12th, 2008

Abstract

This paper proposes a unified conceptual framework to analyse the multiple role and consequences of patents in the case of biotechnology research tools. We argue that the knowledge/information and independent/complementary nature of research tools define heterogeneous frameworks in which the patent system plays different roles. In particular, using the analogy with the free-libre open source movement in software, we show that patents can promote open innovation by ensuring the freedom of some pieces of knowledge. A strong conclusion of the paper is therefore that, against common belief, an adequate use of the patent system may contribute to preserving freedom of access to upstream research tools within a framework that we call free-libre biotechnology.

Keywords: Intellectual property rights, sequential innovation, open source, knowledge, collective invention
JEL classification: D2, O3

1. Introduction

This paper proposes a unified conceptual framework to analyse the multiple role and consequences of patents when innovation is sequential, i.e. when second stage innovations build on first stage innovations. Specifically, we consider the case of biotechnology research tools, which are inputs into the process of developing new biotechnology drugs, plants, etc. Using the analogy with the free-libre open source software movement, we propose an enlarged view of the patent system by arguing that patents can provide different outcomes when confronted with varied situations (Cohen *et al.*, 2000; Arora *et al.*, 2003; Bureth *et al.*, 2005; Cohendet *et al.*, 2006).

In particular, we assume that the knowledge/information and independent/complementary nature of research tools define heterogeneous frameworks, in each of which the role of the patent system is different. A strong conclusion of the paper is that, against common belief, an adequate use of the patent system may contribute to preserving free access to research tools within a framework that we call free-libre biotechnology (Burk, 2002; Maurer, 2003; Burk and Boettiger, 2004; Hope, 2004; Rai, 2005; David, 2006).

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We are particularly grateful to Patrick Cohendet, Monique Flasaquier and two anonymous referees for helpful comments. The usual disclaimers apply.

There has been a recent focus of attention on research tools within academic and policy-related literature, as indicated by the abundant literature on this topic (NRC, 1997; Heller and Eisenberg, 1998; Walsh, Arora and Cohen, 2003; Nelson, 2004). Research tools' foundational position within the innovation process in modern biotechnology makes their mode of appropriation a core issue. Since they are inputs in the development of further applications it is highly important that they remain easily available. Strategies of exclusion based on strong patents may impede second stage innovations that need to use research tools. Conversely, lack of an adequate appropriation environment may decrease the incentives to construct research tools. A fine balance must therefore be respected when dealing with the issue of research tool patents[1].

Now, although the central role of patents in the birth and development of the biotechnology industry three decades ago is not questioned, there are many concerns nowadays that research tools are over protected and that too strong patents lead to restricting access to materials and techniques that are critical for future research in life sciences (Heller and Eisenberg, 1998; Nelson, 2004).

Regarding the double objective to allow for a wide use of research tools and to provide firms with incentives to innovate and build new research tools, we explore in this paper the solution provided by the pioneering example of free-libre open source software (FLOSS)[2]. It is indeed appealing to transpose the FLOSS model to biotech research tools, since detailed analysis of the software industry suggests that FLOSS can provide a solution to reconcile incentives to innovate with wide dissemination of software outputs (Lerner and Tirole, 2001; Nuvolari, 2001; Bonaccorsi and Rossi, 2002; Dalle and Jullien, 2003; Lakhani and von Hippel, 2003; Jullien and Zimermann, 2006).

We propose therefore a framework based on the example of FLOSS that would favour collaboration, collective innovation and ensure the freedom of research tools (Hope, 2008). This framework we call free-libre biotechnology. Much as copyright in software has been turned to copyleft, we show that patents can be used in such a way as to ensure free utilisation of research tools and therefore can help to promote free-libre biotechnology. Patents are flexible instruments that can be used in multiple manners. As David (2006) proposes, one can

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[1] The question of the effect of patents on incentives to produce and circulate research tools is far from straightforward. As emphasised by many examples, a wide circulation of the research tools based on low licensing fees does not mean to renounce making important profits out of the research tool (see for instance the Cohen-Boyer patent on recombinant DNA). Similarly, high licensing fees may not always prevent the diffusion of the research tool (as suggested by the example of the Polymerase Chain Reaction (PCR) technology) (NRC, 1997).

[2] The FLOSS movement was developed in the 1980s and was linked to the emergence of strategies of appropriation and exclusion within the software industry (Lessig, 2001). Worried about the consequences of the surge in appropriation, which may deter collaborations and open access to software, Richard Stallman founded the Free Software Foundation (FSF) in 1984. The latter aimed at promoting collective and decentralised development of free software, an important feature of which was disclosure of the source code. In order to ensure the freedom (in the sense of the French meaning of the word, i.e. *libre* and not *gratuit*) of software the FSF developed an original exploitation licence: The GNU General Public Licence (GPL) also known as copyleft. The GPL ensures that everybody can use, modify, copy and even distribute any software “protected” by the licence under the unique condition that these changes continue to be copylefted, meaning that improvements must remain accessible and open to modifications by everybody. GPL is therefore a viral license since it reproduces itself with each modified or extended version of software that used copylefted software. In the last decade FLOSS has proved to be a major success with some libre-software, such as Linux, Apache, Sendmail, MySQL and Perl (LAMP), widely adopted all around the planet.

envisage hijacking the traditional role of patents by “using intellectual property rights to expand the commons for science”:

> *“Less notice has been taken, however, of what may be called “the third face of IPR.” This is the legal protection of private rights to arrange contracts for common-use, thereby creating “club goods” that permit the participants to share access to the information and its utilization under conditions that emulate those of the public domain, but which may be enforced by invoking the rights of the original intellectual property owners. The contractually constructed, IPR-based “information commons”, thus, is a natural device for the socially efficient pooling of research results, particularly those that take the form of tools for exploratory science. It is, like the application of certain forms of copyright licensing such as the GNU GPL in the case of open source software, a form of ‘legal jujitsu’, Yochai Benkler’s (2006) marvellously acute characterization of the strategy of deploying the laws on intellectual property rights to achieve a purpose quite opposite to the one for which is usually is intended.”*
>
> David (2006)

This possibly new role for the patent system leads us to propose a unified framework to analyse the many different uses of patent with respect to research tools. We consider two dimensions of research tools: as complementary vs. independent in use and knowledge based vs. information based, which defines four very different contexts for conceptualising research tools. For each one of these contexts, we analyse the role of the patent system and discuss the strengths and weaknesses of this instrument. The basic idea being that the more we converge towards a complementary and knowledge based view of research tools, the more important it is to guarantee the freedom of research tools and therein lies the important role of the third face of intellectual property rights as mentioned above by David.

Section 2 defines research tools and discusses the merits of patents with respect to the production and distribution of research tools. Section 3 introduces and discusses, through various examples, the notion of free-libre biotechnology. Specifically it explores the role of patents to promote the construction and preservation of a research tool commons. Finally, in section 4 we propose a framework to analyse the role of patents according to two dimensions of research tools - complementary vs. independent in use and knowledge vs. information based.

2. Research tools and the patent issue

A research tool is used for research purposes and is not considered, in its own right, as an application. In particular, research tools are knowledge that may either be: embodied, such as in scientific instruments and research materials; or disembodied, such as a technique employed during research (Scotchmer, 2004). Specifically, in biomedical science a research tool is “any tangible or informational input into the process of discovering a drug or any other medical therapy or method of diagnosing a disease” (Walsh, Arora and Cohen, 2003, p. 287).

Research tools are part of a sequential process of innovation, being situated upstream from the development of applications such as new drugs for instance. These follow-on innovations are thus drawn from the previous invention, diffusion and usage of research tools, which serve as a springboard for downstream innovations. Researchers are in a sense consumers of research tools. This attribute of research tools as feeding further research has led the academic literature to refer to research tools as: “enabling technologies” (Burk and Boettiger, 2004) or “platform-technologies” (Pray and Naseem, 2005).

Examples of research tools are many. For instance, the technique of recombinant DNA invented by Stanley Cohen and Robert Boyer is a research tool that has proved to be essential in the spawning of advances in molecular biology (National Research Council, 1997; Oliver and Liebeskind, 2003). This technique is essential in the manipulation of DNA segments but, in itself, it is not an application. It is of great usefulness only in upstream research tasks. Likewise, instruments in spectroscopy concerning the study of matter generate usefulness predominantly in research activities. The continued innovation in spectroscopy and the embodiment of this knowledge into scientific instruments has led to many advances (Riggs and von Hippel, 1994). Other examples of biotechnology research tools are polymerase chain reaction (PCR), high-throughput screening technologies, genomic databases, transgenic mice, modelling programs or knowledge of a target that is involved in a disease and as such represents a potential drug intervention.

In the context of sequential innovation, where the value of an invention may be in boosting further innovation, the question of the adequate patent dimension is as vital as it is delicate (Scotchmer, 1991; Green and Scotchmer, 1995; Scotchmer, 1996; Bessen and Maskin, 2000; Scotchmer, 2004). A first generation research tool is an essential element to develop a second generation application. In this situation, the development of the application is not possible without the prior invention of the research tool. However, since commercial value usually resides in products that are developed later and not in the research tool itself, the invention of the research tool will only be rewarded if it can get a part of the returns from the sale of the application. A central point is hence to make sure that earlier innovators are compensated for their contribution, while ensuring that later innovators also have an incentive to innovate.

Intellectual property rights can structure and organise the division of profits among sequential innovators. The patenting of the research tool allows for the negotiation of “reach-through” licensing terms between the two entities. Scotchmer (1991) insists on the importance of the scope of the research tool patent in determining the redistribution of the value from the sale of the second generation application. Too broad a patent will lead to excessive appropriation by the research tool inventor and insufficient returns for the second generation inventor. Whereas if it is too narrow, then the application may be able to work around altogether the research tool patent thus not rewarding the first generation inventor at all. In short, the design of patents is essential in ensuring sufficient incentives to invent for both the first and second generation inventors.

Furthermore, the search process of research paths involves, by nature, uncertainty, since at the onset it is impossible for any one participant to foresee the most performing trajectory. As a matter of fact, a variety of participants will interpret differently what they believe to be the best path to pursue (Simon, 1982; Nelson and Winter, 1982). It is thus socially desirable in this context of uncertainty that numerous entities partake in the search of a particular research area in order to find the most performing route (Merges and Nelson, 1994). For this to be so, the research tools essential to the domain must not remain exclusive to a few so that there can still be numerous forages into the research path (Nelson, 2004).

Yet, patents on research tools give rise to an element of *control* to the patent owner who has the choice to exert rights to exclude others from the concerned research paths. Therefore, research tool patents may influence the development of research tools and applications along technological trajectories (Dosi, 1988; David, 2004). Too wide patents may decrease incentives for follow-on innovators because the latter may be held hostage by the first generation patent holder. Furthermore, patents on research tools, and the consequent necessity of extensive licensing, invariably raise the cost for other participants to participate in the construction of a trajectory. Such “toll booths” (David, 2004, p. 17) are likely to further put off participation in research paths that involve the licensing of many patents. Concerning the domain of biomedical science, this issue has been expressed as a potential “tragedy of the anticommons” (Heller and Eisenberg, 1998).

In short, with regard to biotechnology research tools, patents offer contrasted results. On the one hand, there is no doubt that they increase incentives to produce first generation innovation. It is widely acknowledged that patents are essential elements to spur biomedical innovation (Levin *et al.*, 1987; Cohen *et al.*, 2000). But on the other hand, there are concerns that in life science we may have gone too far into offering patent protection and that patents may increase the cost of access to research tools, which may preclude further second generation innovations (NRC, 1997; Heller and Eisenberg, 1998; Nelson, 2004; David, 2006). In recent studies, Walsh, Arora and Cohen (2003) and Pray and Naseem (2005) do not find evidence of such holding-up due to research tool patents, mainly because actors of the innovation process are able to develop “working solutions”[3]. But the authors conclude that despite their reassuring finding, “aggressive patent behaviours can always threaten basic scientific research”, which calls for “a continuous need for active defense of open science” (p. 335). Free-libre biotechnology pursues this objective. Specifically, it aims at reconciling two apparently contradictory goals: (1) To provide incentives to economic actors to engage into the production of further research tools and (2) to ensure the freedom of the produced research tools.

3. Free-libre biotechnology

3.1 Definition, objectives and functioning

We do not find yet a clear definition of free-libre or open-source biotechnology in the literature[4]. Maurer *et al.* (2004, p. 183) envisage open source biotech as a: “decentralised web-based, community-wide effort, where scientists from laboratories, universities, institutes,

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[3] “We find that there has in fact been an increase in patents on the inputs to drug discovery (“research tools”). However, we find that drug discovery has not been substantially impeded by these changes. We do not observe as much breakdown or even restricted access to research tools as one might expect because firms and universities have been able to develop “working solutions” that allow their research to proceed. These working solutions combine taking licenses, inventing around patents, infringement (often informally invoking a research exemption), developing and using public tools, and challenging patents in court […] Many of our responding firms suggested that if a research tool was critical, they would buy access to it. We also observe that most of what might be called “general purpose” tools—tools that cut across numerous therapeutic and research applications that tend to be non-rival-in-use—tend to be licensed broadly” (Walsh, Arora and Cohen, 2003, p. 286).

[4] In a recent paper Maurer (2003, p. 3) explains that: “Several authors have recently suggested that a new method of doing science, variously called *open source genomics*, *open source biology*, or *open source biotech* is about to emerge. The idea is intriguing. Although currently confined to computer software, open source methods present an interesting alternative to traditional R&D institutions like intellectual property. So far, however, it is not clear what *open source biology* would actually look like. Articles describing open source biology typically point to (a) computer software written by and for biologists, or (b) projects where biologists publish data but waive intellectual property protection […] Somehow, one expects more”.

and corporations could work together for a common cause". Hence, such an institution should be based on voluntary collaborations, it should be non-hierarchical and decentralized. While we fully agree on this description of free-libre biotech as involving collaboration among heterogeneous actors, we insist here on the fact that one of the central features of free-libre biotechnology must be the freedom of access to past research. It is only this freedom that can sustain continuous exchanges and interactions among participants, as illustrated by the free-software example.

But what does "free" mean exactly? Following Lessig (2001), "a resource is "free" if (1) one can use it without the permission of anyone else; or (2) the permission one needs is granted neutrally" (Lessig, 2001; p. 12). This definition implies, among others, that the permission to access the resource is not granted at the discretion of an "owner", who could therefore choose arbitrarily to refuse or grant access to others. With respect to upstream research tools this definition of freedom has one important consequence: The access to the "free" research tool needs not automatically to be free of charge. The central characteristics of a free research tool is that it must remain accessible for everybody under conditions that are not too difficult to meet ("reasonable") and not discriminatory.

This definition of a free research tool, which insists on the necessity to make the tool easily available to everybody and not on the price, converges with the point of view of Nelson, who confesses that: "With respect to patented research tools created by industry research, my concern is less with open use at a fee, but with decisions not to make the tools widely available" (Nelson, 2005, p. 137).

A patented research tool is not free according to our definition, because the owner can choose whether or not to grant a licence. Yet, it is open source in a weak sense, since the application to a patent entails an obligation to disclose the innovation publicly. Similar to FLOSS, where projects disclose their underlying source code, thus allowing other programmers to learn from them, patents contain a description of the innovation they intend to protect, therefore participating in the dissemination of the protected knowledge within the economy (Burk and Boettiger, 2004). This disclosure is specifically important in the case of sequential innovations, for which secrecy would highly hinder technological progress.

Yet, when innovations are sequential, the disclosure of the knowledge underlying an innovation may not be sufficient. What is often needed is also that the upstream innovation itself is free so that the next stage innovation can be built upon it. In this pursuit of ensuring freedom to biotechnology research tools, organizational designs and numerous licenses analogous to those used in FLOSS can be ported from the software sector to the biotechnology one. For instance, in the case of research collaboration this may simply concern the signing of a waiver agreement in which participants into the collaboration engage themselves not to patent their output, so that the latter remains free to re-use. This kind of agreement was used in the Alliance for Cell Signalling (Maurer *et al.*, 2004)[5]. A further license could be an "open access" type license (Guadamuz, 2006) in which licenses allow for the research tools to be openly accessible to all who wish to use them, without any constraint attached to the license.

Those licenses may ensure the freedom of a research tool but not of all the follow-on research tools. Yet, we believe that the purpose of free-libre biotechnology must be to ensure the

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[5] www.AFCS.org

freedom of all research tools, to keep the whole platform open and not only some parts of it. It is not enough to make sure that one research tool cannot be appropriated. All the research tools related to a given technology must be kept free.

In order to achieve this continued freedom of all research tools related to a given technology, patents can be used in a performance of legal jujitsu (Benkler, 2006). Patents can mimic copyleft type licenses by adopting a “grant back mechanism”, which would imply that users of patented research tools may be granted a license only if they agree to put further improvements under the free regime (Burk and Boettiger, 2004). Such a research tool license would therefore stipulate that users of research tools are required to grant back the rights on follow-on inventions to original inventors. Given that the original inventor chooses to license freely the research tools, this viral clause effectively guarantees that the sequence of innovations arising from a research tool will be enduringly free to re-use to all those who abide by the licensing terms[6].

The rationale in using patents to free research tools can be understood through the analogy with jujitsu (Benkler, 2006; David, 2006), which is a martial art oriented towards active self defence. Jujitsu practitioners are never offenders but once they are attacked they practice a pro-active and offensive defence. Having developed several skilful techniques, they are experts in using the strength of their adversaries to their advantage. Similarly for free-libre biotechnology, patent owners use the strength of the patent system against its primary purpose. In line with the state of mind of martial art practitioners, free-libre biotechnology therefore suggests to use the patent system to prevent that entire streams of research are closed down by patent thickets.

The following two examples of the BIOS initiative and the International HapMap project illustrate the application of these viral licenses.

3.2 Two examples: BIOS and HapMap

In the domain of agricultural biotechnology, the BIOS initiative – BIOS as Biological Innovation for Open Society - aims at developing free plant transformation research tools in view of their re-use to create applications such as improved strains of crops. Specifically, the BIOS initiative is seeking to develop a set of research tools that would operate freely of current patents on plant transformation methods. The BIOS initiative currently covers 12 research tools including the techniques of Transbacter and the popular GUS gene reporter. Those research tools are all patented and can be used only under specific conditions. In order to use them, a third party has to agree to the BIOS license that adopts a copyleft style “grant back mechanism” forcing the licensors into agreeing to share back to the BIOS initiative the rights to re-use the improvements that are made to BIOS research tools as well as all the information concerning that improvement. In a dynamic perspective, this creates an environment: “in which a material or invention can be improved by the ideas of many, but access is maintained for all who agree to the terms, without exclusive capture by anyone” (BIOS homepage[7]). Furthermore, although the use of a BIOS patent is *libre* it may not

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[6] Compared to such viral licensing agreements, releasing merely the research tool into the public domain or granting an open access license cannot ensure the freedom of the entire field. Indeed, those strategies entails the risk that follow-on innovators appropriate some part of the set of research tools and therein control their use.

[7] http://www.bios.net (accessed [09/17/06]). It is further mentioned on the website that: “Instead of royalties, BIOS licensees must agree to legally binding conditions in order to obtain a license and access to the protected

necessarily be free of charge. Private members of OECD countries are required, in addition to agreeing with the licensing terms, to pay a participation fee.

This viral clause of licensing implies that research tools that build on a technology patented by BIOS cannot be appropriated. Yet, this regards only upstream research tools. The treatment of applications derived from those research tools is completely different. Developers of potential applications of the BIOS research tools have the liberty to individually control new strains of plants, through patents if so wished. This frontier put to the free environment is linked to the specific features of innovation in biotechnology. As emphasized by Maurer *et al.* (2004), there has to be some appropriation in the innovation process so that, at the end, firms are encouraged to put end products on the market. Indeed, although prices for equipment in biotechnology may be declining (Carlson, 2003), there remains large costs in the development of biotech applications, such as the testing of drugs (Lerner and Tirole, 2001). Those costs mean that an organization that is based solely on the decentralized contributions by a community of private, garage-based scientists with intrinsic and, limited, extrinsic motivations, is unlikely to reach the commercial success of FLOSS projects. The BIOS initiative aims therefore at preserving the freedom only of upstream research tools, without impeding the commercial exploitation of their direct applications.

A downside of this BIOS viral licence is that it proves very black or white. As explained by the Public Intellectual Property Resource for Agriculture (PIPRA), the BIOS licence has two major drawbacks when BIOS licensed research tools are used with another set of non BIOS licensed research tools. Firstly, all improvements made to the research tools irrespective of their origin would fall under the BIOS licensing terms. Therein, even though the BIOS research tool played only a small role in the set of research tools as compared with other non-BIOS components, the grantback mechanism would concern the rights of use of all the improvements. Secondly, the BIOS license mentions that it “will in no way be waived, modified, negated, or otherwise diminished due to [the licensee's] contractual obligations to third parties”. In the context of publicly funded research this was deemed to contravene with current practices. These two issues led the organisation to not adopt the BIOS licensing terms on its projects (PIPRA, 2006). Paradoxically, it is therefore possible that the BIOS licence, far from encouraging collaboration, deters it.

A similar kind of license that tries to dynamically protect the freedom of the sequence of developments of a research tool was used in the domain of human genetics by the International HapMap project. This project aimed at developing a database of haplotypes, which are variations in the human genome that can help researchers to inquire into hereditary, genetic diseases. The value of this data is in comparing multiple genomes from around the world. Therefore it requires collaboration between numerous laboratories and it is essential that all haplotype information remains in one single database. Yet, during the construction of the database there is a risk that individual parties appropriate parts of the database either through patents or through database laws.

A specific licensing agreement was designed with the aim of preserving the free use of the entire database. The HapMap license requires, instead of royalties, that the user of the database agrees not to appropriate the database, nor to exclude other parties from using the data. In addition, if the user passes on the data to a third party, the same license would apply, as well. In other words, the HapMap license tries to defend the free re-use of the database by

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commons. These conditions are that improvements are shared and that licensees cannot appropriate the fundamental kernel of the technology and improvements exclusively for themselves”.

blocking property rights that might affect its free re-use and is enduring in the sense that it reproduces itself with all uses of the data.

The HapMap project has advanced to produce significant research results and it is now possible to benefit from hindsight in analysing the practicality and usefulness of this licensing agreement (Eisenberg, 2006; Gitter, 2007; Hope 2008). Although there are advantages of the licensing requirements demanding that all third party users of the data agree to the same obligations, this posed a major disadvantage with regards to the publishing of data in peer-reviewed publications. Given that the data in publications could not be subject to the same licensing terms, as long as the licensing terms had to be upheld, the research data remained unpublishable in journals. However, the matter was resolved in 2005 as the HapMap licensing terms were retracted. The database having effectively entered the public domain, this rendered the terms of the licensing agreement obsolete and the data results publishable.

3.3 Where do we go from here?

Free-libre biotechnology has been compared to jujitsu. Yet, in martial arts, like all practices, there is a necessary preparation time or “training” before the correct performance can be attained. For instance, the success of the FLOSS movement rests much on the work of the FLOSS community over the last twenty years. The ex-ante job of developing the licensing mechanisms, of convincing the actors, of reconciling the incentives of the community with the pursuit of a particular project, etc., entails sunk costs and implies that such communities can only become operational after a long preparation time. During this lengthy search process, the pioneering adopters, such as BIOS and the HapMap, are likely to bear the brunt costs for exploring and testing these licenses.

One of the first and major tasks to implement free-libre biotech will be to imagine and design licences that are likely to be accepted by most players in the field and to fit with the specificity of each technology. For instance, the case of BIOS license is very much tailored to the fact that the mother-owner CAMBIA (for Centre for the Application of Molecular Biology to International Agriculture) owned valuable intellectual property to build on, and that the domain allows separating the application from the research tool (basically, new plants are applications and everything to make possible a new plant is research tool). In this way, BIOS, through a well designed license, is able to guarantee that the research tools and continued development is enduringly free. But other contexts will be different and will require subtle modifications to the license. It may not be so easy to separate a free layer from the controlled layer as other situations may require more upstream appropriation due, for instance, to the necessary investments to develop research tools.

A further need of free-libre biotechnology licenses shall deal with the specificities of biotech as compared to software. First, as already mentioned above, licenses will have to consider the fact that research in biotech is often more costly than in software, where the sole cost for programmers is often the time they spent in front of their machines. Also, due to the high capital intensity in biotech, licenses shall be clearly designed to allow business opportunities. Free-libre biotechnology can only work if there is alternative opportunity of profits (Hope, 2004). This point makes the former question on the possibility to distinguish between research tools that must remain free and application that can be appropriable, all the more relevant.

Second, knowledge is highly codified and modular in software. Modularity helps the FLOSS community to coordinate and operate in a decentralized way. An important issue deals therefore with the question of modularity in life sciences. Although we do not have results for the entire biotech field, we can provide insights drawn from the specific case of DNA vaccines, for which modularity has been put forward (Bureth and Pénin, 2008). Therefore, at least in some biotech fields, the absence of modularity cannot be put forward to explain the failure of a free-libre model.

Another important part of the preparation stage will involve the diffusion of the licenses within the domain. Although single efforts are to be acknowledged for their individual worth, a collective innovation process means that there would have to be a commonality in the use of free licenses. Much as norms and rules are situated within communities, the adoption of free licenses is likely to be localized in communities. How this may spread through from community to community of different typologies is an interesting question to be pursued.

To summarise, we discussed here an original way to use the patent system. Contrary to its primary purpose, which is to exclude potential imitators and thus to enable innovators to appropriate their innovation, patents may also preclude appropriation and ensure the freedom of innovations. How can we reconcile this original use of patents with more traditional ones? Economic theory has indeed identified many different rationales for the patent system. It has been shown that patents may prevent imitation, contribute to disseminating knowledge within an economy, help create a market for technologies (Arora and Fosfuri, 2000; Arora, Fosfuri and Gambardella, 2000), ease inter firms negotiations and collaborations (Bureth *et al.*, 2005) or signal competences (Pénin, 2005). Our goal in the next section is to construct a unified framework to analyse the role of patents with respect to biotech research tools. We propose that each particular use of patents may correspond to a specific situation that depends on the properties of research tools.

4. A unified framework to analyse research tool patents

4.1 Conceptualizing research tools

The variety of economic properties that one can attribute to research tools leads to subtleties in their analysis. In order to highlight the nuances, we shall examine research tools along two principal dimensions: First, research tools can be depicted as either independent or complementary inputs in the development of downstream applications. Second, we can consider research tools as being information, such as in the seminal work of Arrow (1962), or as being knowledge, following Nelson and Winter (1982).

Independent vs. complementary research tools

A first dimension that is central to understand the variety of research tools deals with their independent vs. complementary nature. An independent research tool can be used alone into the development of an application. It does not need to be combined with other research tools. Conversely, complementary research tools cannot be used by themselves. They are useful to develop applications only when they are combined with other research tools. As such, independent research tools have a direct value to their users while a research tool that is complementary: “has no value to the user at all unless the user has access to its complements” (Scotchmer, 2004, p. 144).

This design element of research tools as either an individual input or as complementary inputs affects the interdependency between producers of research tools and developers of applications. An individual input leads to a simple one-to-one interaction between a research tool producer and potential developers, whereas the design element of complementary research tools means that multiple inputs are required to develop a particular application. In the latter situation developers will therefore have to interact with many different research tools producers, which may increase the overall price to develop applications.

Information vs. knowledge based research tools

A second essential dimension of research tools deals with their contents, which can be assimilated either to information or to knowledge. In the former case, production and diffusion of research tools can be modelled by using the seminal framework defined by Arrow (1962). When considered as information, research tools share to some extent the properties of a public good, i.e. it is very difficult or even impossible to exclude individuals from re-using freely a research tool.

To consider research tools as information leads to a classical problem of incentives. Since new knowledge can hardly be appropriable by the innovator, incentives to invest in R&D are low and, without State intervention, there will be an under-investment of resources into the invention of new research tools as compared to society's preferred level.

As long as research tools are considered as information one can distinguish between the creation of the research tool, its commercialisation and its use. Yet, as soon as research tools are assimilated to knowledge, the frontier between their creation and their transfer is blurred. Transferring the research tool involves an activity of creation, not of mere reproduction of an already existing artefact (Amesse and Cohendet, 2001). Here, the public good problem is not relevant any more, since knowledge is usually sticky, i.e. it is embodied within its holder and benefits other individuals only after a long and costly work of transmission and assimilation. To absorb some knowledge that is transmitted by a given source requires a cognitive re-appropriation by the receptor, which means that knowledge is, in a sense, “personal” (Polanyi, 1958). It cannot be fully replicated and transferred from one individual to another.

When considering research tools as knowledge, the inventor and society no longer face the prospect of the provision of a new public good. Knowledge is marked by strong rivalry (it is hard to reproduce it outside the local context where the discovery has been made) and strong exclusivity (the invention is linked to the mental map of the inventor). In this case, the challenge rather concerns the intricate task of the transmission of the research tool, which may require a costly process of codification (Cowan *et al.*, 2000). Furthermore, in order to be able to use the research tool, the user is also required to be endowed with the necessary knowledge to understand the message and to absorb the knowledge embodied into the research tool (Cohen and Levinthal, 1989). Undertaking the transmission process of the research tool is therefore an essential but resource-consuming step for both the inventor and the user(s).

For the research tool inventor, the priority is now to manage the transfer of his knowledge for its re-use in the development of an application. In this task, the fundamental problem for innovators is less a capacity to claim ownership over knowledge but more the ability to explain and diffuse it to others, i.e. how to make oneself understood. Much as the musician who is new on the scene is required to play his music otherwise no one will listen and possibly enjoy it, inventors must undertake repeated investment in making themselves known and understood through “seeking interest” in their knowledge (Callon, 1993 and 1999; Amin and Cohendet, 2004). Conversely, by considering research tools as information, this vital collaborative process of the inventor garnering interest is abstracted from the diffusion of research tools.

In this context of research tools as knowledge, the risk is therefore that research tool inventors and users fail to construct a common knowledge base that makes the development of applications possible. The rationale for State intervention rests here on solving issues of collaboration between the actors with at the root, the problem involving the transfer of the research tool from inventor to user(s).

To summarise, one can represent research tools along two dimensions: information vs. knowledge based and independent vs. complementary. Crossing those two dimensions leads to four different conceptualizations of research tools.

Table 1: A quadrant to conceptualize research tools

Research tools as	**Independent**	**Complementary**
Information	**I** *Incentives*	**II** *Coordination*
Knowledge	**III** *Collaboration*	**IV** *Collective invention*

I. This configuration, where research tools are used individually and can be assimilated to information, corresponds to the traditional arrovian framework. Research tools are easily reproducible by a technician without any need of assistance, which implies that the main concern deals with incentives to produce such research tools since, as emphasised above, their appropriation is not straightforward.

II. This second configuration depicts research tools as being information and complementary[8]. Here the major concern deals not only with incentives but also with coordination problems, since for the user it is necessary to assemble many research tools. A deficit of coordination among the different producers and users may prevent the development of some applications.

III. Considering research tools as being independent and knowledge based emphasises the importance of collaboration among users and producers. Conversely to former cases, here there is little free-riding possible. The understanding of the research tool’s intricacies remains the sole possession of the inventor, who therefore controls its reproduction. It is only after an effort of learning that the user will be able to operate the research tool. The major concern here has shifted from incentives problems to problems of transferring the research tool. It is necessary to

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[8] An example of such research tools is Polymerase Chain Reaction (NRC, 1997; Fore *et al.*, 2006). In the domain of molecular biology the use of PCR has applications in domains such as diagnosis of hereditary diseases or forensics. PCR is a complementary research tool in the sense that it can not be performed without the use of other research tools- the technique, material and instrument. Yet, these research tools can be easily transferred and re-used by technicians, which makes them comparable to information.

set up a tight cooperation among producers and users in order to transfer the knowledge based research tool.

IV. Finally, research tools can be viewed as knowledge and complementary. In this case, the situation requires the development and preservation of a common base of knowledge to use the research tool. Applications can only be derived from a tight collaboration among all the research tools producers and application developers. This configuration may therefore correspond to what several authors refer to collective invention (Allen, 1983; Schrader, 1991; Nuvolari, 2001).

In the next section, we shall analyse the varied uses of patents through this depiction of different conceptualizations of research tools. Depending on the information or knowledge and the independent or complementary view, the patenting of research tools follows either a classical logic of appropriation or a logic of collaboration and even of liberation of the patented knowledge.

4.2 Different roles for research tool patents

Independent and information based research tools: Incentives

The upper-left part of the quadrant depicts the traditional arrovian framework. Research tools are information, which implies that their commercialisation will be confronted to the paradox of Arrow (1962), which can be summarised as follows: The decision to purchase and use a research tool depends on the user's ability to measure up its value and, thus, on possessing the information. But, if the information is already possessed by the user then there is no longer the need to purchase it anymore. The characteristic of information as an economic good undermines the possibility to trade research tools on a market[9]. Hence, in this basic configuration, without property rights, producers can hardly trade research tools to users. Since only the latter can derive profit out of the research tool, incentives to invest into the creation of first generation research tools remain very low.

Patents can provide an alternative outcome to this paradox. The combination of the elements of exclusivity and revealing inherent to a patent are essential with respect to the implementation of a market for information. The coupling of these two properties of disclosure and protection allows in some sense to solve the paradox of Arrow (1962). Patents both disclose and protect information, thus preventing free riding from occurring. They enable innovators to sell their innovation with the peace of mind that no entity will "hijack" it. Therefore, property rights may often favour information transfer. In a sense, the patent system allows the creation of a market for technologies and highly codified knowledge (Arora and Fosfuri, 2000; Arora, Fosfuri and Gambardella, 2000).

In a sense, patents enable the separation between users and producers therefore allowing gains in specialisation by the respective entities. In this context, the inexistence of patents would mean that the same entity would have to be both the producer and the user of the research tool. Patents provide incentives for some firms to specialise in the production of research tools, to patent their research tools and then, to commercialise them to users through licensing

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[9] A famous illustration of this problem is given by Tirole (2003, p. 23) who tells us the story of Robert Kearns, the inventor of the windshield wiper. Having no possibilities to commercialise alone his invention Robert Kearns proposed collaboration to Ford, to whom he disclosed the idea and some of the technical aspects. Ford refused the collaboration and some time later introduced on the market a similar product with only slight technological differences.

contracts that specify the price and the terms of the transaction[10]. As emphasised by Scotchmer (2004), within this simple configuration patents enable the sharing of the benefits along the invention chain, allowing the remuneration of upstream inventors, who would not be induced to invent otherwise.

Yet, economic theory has also extensively demonstrated that the element of exclusivity granted to the patent owner generates a dead-weight monopoly loss for society. Monopoly pricing will lead to under-use of the research tool as compared with an ideal, i.e. some applications may not be implemented although socially desirable. This dead-weight loss is usually considered as the price to pay in the short run to ensure ongoing technological progress and therefore increased welfare in the long run.

Complementary and information based research tools: coordination

The upper-right part of the quadrant views research tools as being information based but complementary. In this case, beyond the problem of incentives described above, there is also a problem of coordination among the research tool users and the different producers.

This need of coordination can be solved (at least partly) by the patent system. Indeed, patents, by creating a market for research tools, may be a powerful device to coordinate innovative activities and to ensure that users can access all research tools. It is a central axiom of standard economics that the market acts as a coordination device. The commodifying of inventions allows the market to be the coordination device for bringing together a large number of upstream sellers of research tools and buyers looking for developing applications. This allows a powerful decentralised guidance through price signals on research tool licenses.

However, here the implementation of applications may be confronted to a problem of “anticommons” (Heller and Eisenberg, 1998). The expression “tragedy of the anticommons” relies on the notion of “tragedy of the commons” stressed by Hardin (1968). As stated by this biologist, the lack of property rights on a common good can lead, if the good is used above its regenerative capacities, to its entire destruction. The idea of the anti-common tragedy deals with the exact reverse problem. In the case of fragmented property rights over a resource there is a risk of suboptimal use of this resource due to the addition of monopoly situations that increases the overall price to exploit the resource. A tragedy of the anti-commons therefore means that an application derived from research tools may not be implemented due to too high a price induced by the addition of monopoly positions on intermediate research tools.

This may arise when an application requires the combination of a high number of research tools, each of them being patented and therefore sold independently of the others. This multiplication of transactions leads first to an increase of transaction costs, the users of research tools being obliged to negotiate a license with each producer independently. But, most of all, this leads to a problem of multiple marginalisation, which was first raised by Cournot (1838) in his seminal contribution on the pricing of complementary intermediate goods[11]. Following Cournot, a surprising conclusion about licensing complementary goods is

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[10] The drug development industry is a prime example where division of labour induced by patents has changed completely the organisation of research. Typically in the 1980s and 1990s, the biotech paradigm generated a division of labour between biotechnology firms specialised in drug discovery techniques on the one hand and pharmaceutical companies specialised in bringing the end-applications to market on the other hand. Patents help to structure the transactions among those two worlds by easing the transfer of patented new molecules.

[11] Cournot (1838) showed that, in the case of complementary intermediate goods, sometimes one unique supplier (who has a monopoly position) is better for the overall social surplus than an addition of several

that the joint price is lower if they are sold as a unit by a single owner. Not only does collusion among research tool producers increases their profits, but it also decreases the overall price, thus benefiting users too (Cournot, 1838).

It is therefore in the interest of society that policy makers watch the risk of anticommons and, if necessary, try to improve interactions among research tools producers in order to decrease the overall price of developing applications. One widely debated solution to problems of anticommons lies in the implementation of patent pools (Shapiro, 2001). A patent pool is an agreement between two or more patent owners to licence one or more of their patents to third parties, set-up specifically to administer the patent pool. Hence, patent users, instead of having to bargain access with several independent owners will have to negotiate access only with one single entity that is in charge of all the relevant patents.

Patent pools may therefore decrease transaction costs as well as multiple marginalisation problems. Yet, two problems may affect the benefits of patent pools for society. First, costs for society may not be deleted but only displaced, since nothing is said on how research tool producers may bargain to set-up the patent pool. Second, public authorities must be very careful with anticompetitive behaviours. There is indeed a conflict between the formation of patent pools and antitrust policies. It is possible that patent pools are implemented not to solve anticommons but merely to decrease competition and to increase the margins of firms in the pool. Standard economic theory shows that patent pools are procompetitive and welfare increasing when gathering complementary patents but welfare decreasing when gathering substitute patents (Lerner and Tirole, 2004).

Independent and knowledge based research tools: Collaboration

So far, we have considered research tools as being information and as such we have supposed that they shared, at least to some extent, the properties of a public good. This may be the case for generic knowledge already disseminated within an economy. Yet, in the case of emerging and radically new techniques it is doubtful that the public good properties are satisfied. In this case, problems of free riders are less relevant for research tools' producers than problems of not being understood and therefore of not being able to implement the new techniques due to a lack of common cognitive grounds. Any attempt to disseminate and therefore to trade a research tool requires important and difficult preliminary work, as knowledge tends to adhere to its human support. This leads to reconsidering in depth the issue of research tools production and utilisation and the role of patents.

As argued by Cohendet *et al.* (2006), in a knowledge-based context, strategies of collaboration tend to overcome strategies of exclusion. It is only through in depth interaction among users and producers that research tools can be transferred. Mere licensing agreements are not sufficient to ensure the transfer of research tools because users usually do not have the ability to exploit them. They need assistance and face to face interactions to learn how to use the new technique. This does not mean that patents will be useless but it radically changes the role of patents and the way in which firms use their patent portfolios. In this context, patents are used as devices to collaborate and to diffuse knowledge. This role of patents to foster

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independent suppliers. The explanation relies on the existence of negative externalities. When a research tool producer increases his price, he decreases the demand for research tools, which affects other research tool producers. This negative externality implies that independent research tool producers will tend to ask too high prices for their research tools as compared with an ideal. Collusion among research tool producers may hence force them to internalise the externality and therefore to decrease the price of each research tool and the overall price to develop applications.

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inter-organisations collaborations has been raised by some recent studies (Arora and Merges, 2004; Bureth et al., 2006). It is only when techniques become more mature and languages are shared, that the importance of patents as an instrument of exclusion increases.

Patents may enable collaborations and therefore facilitate the exchange of tacit knowledge between research tool producers and users through various mechanisms. First, patents may signal the research tool to potential users, thus helping partners to identify each others. Indeed, all patent applications are published eighteen months after the first application, which means that by screening patent databases firms can identify potential partners. This signalling dimension of patents is all the more important as firms evolve in a context of incomplete information, usually not being able to infer what other firms are doing. For isolated research tool producers, patenting their technology may therefore be a way to advertise it and to ease the finding of users (Pénin, 2005).

Second, patents are a way to structure complex interactions among firms. They constitute legal devices that can help to structure collaborations and facilitate negotiations between research tool users and producers. For instance, patents reduce the risks linked to collaboration, therefore inducing firms to participate in the venture. Indeed, R&D cooperation is a risky process in the sense that participants must often share parts of their most important intellectual assets. Since patents protect the knowledge held by a firm from plundering by her partners, they decrease the risk of opportunistic behaviours and of hold up of competences. It follows that firms protected by patents may be more willing to be involved in R&D cooperation (Ordover, 1991). Furthermore, patents may also ease the transfer of the tacit component of technologies by including clauses of assistance and of exchange of employees in licensing contracts (Foray, 2004). Finally, all along the collaboration, patents can assist heterogeneous partners because they provide a common language that can be understood by many. A patent is therefore a key element in a shared culture, a prerequisite to bringing together actors around a common project.

Complementary and knowledge based research tools: Collective invention

Considering research tools as knowledge based and complementary reveals not only the issue of making oneself understood but also, in a context of uncertainty and multiple interactions, the importance of the construction of a common knowledge base. Not only is knowledge sticky, but the exploitation of a research tool requires the combination with many other research tools, i.e. users will have to collaborate with many producers. The key-point here is therefore the collective construction and preservation of a platform on which applications can be designed.

Since applications can only be based upon full access to this common platform of knowledge formed by all the research tools, the open dimension of the platform is central in order to allow its access at the lowest cost. In collective invention knowledge is re-used and partakes in a plurality of research potentially leading to numerous new research tools and downstream applications. Research tools as a free-libre resource is where researchers are able to unabashedly tinker and experiment without the necessary permission of “someone”. This whitespace is the vital open and unobstructed part of the researcher's workspace used for creative endeavours (Bollier, 2003). This research workspace can be seen as the layer preceding the development of follow-on inventions, i.e. the application layer. The vital importance of openness in such a complex and sequential innovation process was recently emphasised by Nelson (2004, p. 463), who reminds us that: “I do not know of a field of science where knowledge has increased cumulatively that has not been basically open.”

With respect to the construction and preservation of a common platform of knowledge it is often feared that patents may have a negative impact. They may split up and narrow the knowledge base and therefore decrease interactions among research tool users and producers. The complementary nature of research tools and the need to re-use them in the attempt to form an understanding and develop designs, interfaces and standards, may be impeded by the use of aggressive patent strategies.

However, we have seen in the previous section that patents can also help to preserve the features and vitality of a commons. The protection granted to the patent owner can serve to ensure the freedom of a research tool and can therefore foster collaborations and exchanges among research tool users and producers. We believe that it is in this context of complementary and knowledge based research tools, in which it is central to preserve the openness of all first stage research in order to foster the development of applications, that free-libre biotechnology is a helpful concept. In this case an increased number of patents on research tools can potentially serve to keep research areas open by reinforcing the freedom of common knowledge bases and thereby encouraging further the development of applications along multiple research paths.

5. Conclusion

This paper dealt with the availability of upstream research tools and the role of patents to ensure or to hinder their accessibility. This issue is central since, on the one hand there is a strong and steady trend towards patenting upstream research in life sciences, and on the other hand in upstream domains it is central to preserve a minimum level of freedom to foster the production of downstream applications. We must therefore implement levers to ensure both that individuals have strong incentives to produce research tools and that those research tools are easily available to users.

With this respect, we argued here that patents do not automatically prevent access to biotechnology research tools. Using the analogy with FLOSS, patents can also be used in order to help make first stage innovation free, thus facilitating the production of second stage innovations. One can operate the same hijacking of patents as has been done with the copyright to transform it into the so-called “copyleft”. FLOSS can serve as the inspirational basis for numerous free-libre biotechnology licenses that refer to how the rights to re-use an invention are attributed.

The question we addressed then was when shall we observe a use of patents as instrument of exclusion and when shall we observe a use of patents as instrument to ensure free access? Conceptualizing research tools in subtly different ways helped us to understand the underlying rationale for the various uses of research tool patents. Taking the perspective of research tools as being information leads to an understanding of the paradox of Arrow and of the problem of appropriability, which the patent may solve. In this framework there is no rationale for the freedom of research tools. Conversely, considering research tools as knowledge reveals the issue of the necessity to build a common knowledge base on which research tool users and producers will be able to interact. It is within this latter context that free-libre biotechnology is the most likely to be useful.

In conclusion, this paper showed that patents are very complex instruments that should not be reduced merely to tools of exclusion. Yet, some questions must still be addressed on the role of patents as instrument to preserve the freedom of technologies. Here are three important points that will have to be clarified in future research:

First, as noticed by one referee, even though this paper focused on biotech research tools, it is obvious that its conclusions may apply to all types of sequential innovations. Each time a second generation innovation builds on first stage research, patents may be interesting instruments to preserve both incentives and dissemination of first stage innovation. One needs therefore further theoretical analysis to explore the consequences of patents on the pace of innovation when technical progress is sequential. To this purpose, our work on the specific case of biotech research tools may provide a good departure point.

For instance, and it is our second point, theoretical modelling may be helpful to explore threshold effect in the formation of free patent pools. Due to the viral property of the licence, once a critical mass is attained the choice to agree or not to the licensing terms becomes obvious. As long as the number of patents is small and other firms can do without using the concerned patents, the set will grow slowly and will hardly impose itself. But as soon as the set is big enough, so that it cannot or it would be too costly to get around, firms must use patents in the platform and therefore have to agree on the terms of access to those patents. And the more firms use patents in the pool, the more patents are given back into the pool, thus contributing to increasing it and to reinforcing this size effect. To study this threshold effect, it may be interesting to apply models of increasing returns to adoption à la Arthur (1989). Related to this point it is also possible that the quality of the patent may replace the quantity. Even though the pool is small, if it encompasses one patent that is central in the field then it may also grow continuously. This was the case of the BIOS initiative, the success of which was partly due to the fact that the initiator already held one of the most important patents in the field and that many actors needed this patent.

The third central issue deals with drawing the borders between what is a research tool and what is an application. Put it otherwise, between what cannot be appropriated and must be put back into the pool and what can be patented and exploited individually by a firm. This question is central because it will determine the incentives of profit-driven organisations to invest in research tools and to participate in free-libre biotechnology. As illustrated by the BIOS case, a portion of the value chain will need to be appropriable in order to allow firms to make money. Yet, in most contexts it is likely to be very delicate to establish such a frontier.

Finally, we would like to end this paper with a discussion on the consequences our work may have on “open science”. It is indeed indisputable that patents have now entered the open science fortress and that most universities in the US and in Europe are widely patenting their research (Sampat and Ziedonis, 2001; Stephan, Sumell and Black, 2001; Cesaroni and Piccaluga, 2002; Mazzoleni and Sampat, 2002; Mowery, Nelson, Mowery and Ziedonis, 2002; Carayol and Matt, 2004). Many studies have documented the reasons and the consequences of this trend. Among others, concerns are dealing with the availability of academic research and with the long run dynamics of innovation. Most fears are coming from an aggressive and exclusive use of their patent portfolios by universities. Yet, our work may suggest another possible story. It is possible that patents reconcile incentives to do research and wide diffusion of these researches. The fact that patents can be compatible with a wide dissemination of technologies has been illustrated among others by the Cohen-Boyer patent (NRC, 1997).

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