Open Source Biotechnology for Global Health: two case studies

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Summary

Using a case study approach, we examine the potential for open source biotechnology for global health. Two open source biotechnology initiatives are analyzed: projects by the non-profit Cambia institute, and India's Open Source Drug Discovery project (OSDD). Cambia is addressing neglected diseases by making relevant patent information available through its Patent Lens project and Initiative for Open Innovation. OSDD complements this initiative through a collaborative platform and open-source practices to accelerate drug development for neglected diseases.

While practices and licensing models differ between the software and biotech industries, Cambia and OSDD have each implemented principles of the open source movement, including licensing innovations, open access, and collaborative platforms. While different in approach, scope, and successes to date, they share the common goal of creating platforms and practices that promote technical advancement in the service of basic needs of the developing world. We conclude that the metaphor of open source as it has developed in the software industry imperfectly describes what is happening in biotechnology, but that biotechnology for global health can move ahead through its own version of open source principles and practices.

Contents

Introduction

This paper examines the potential of open source biotechnology in global health. We start by summarizing the controversial role of patents in innovation, and the open source approach as one response.

Two case studies are then described in depth: Cambia and India`s Open Source Drug Discovery project (OSDD). (The methodology used is an analysis of semi-structured interviews conducted by the authors with key actors in the two projects, along with analysis of related secondary data.)

The next section after the case studies looks ahead at other initiatives underway, and suggests open issues that merit further exploration. Finally, the conclusion summarizes the paper, and suggests what might be needed to build on the modest successes to date.

The controversial role of patents in innovation

It has been a long-standing view that patents are directly linked to innovation, as enablers of technological advancement that contribute to economic development (Gollin, 2008). Patents provide a limited monopoly, and are filed by research institutes, firms, and inventors to ensure compensation through product development and marketing by the inventor, or through licensing arrangements. Funds invested in creating new innovations are thereby expected to be recouped, which provides incentives for future innovation funding. Patents are published, making their contents available to those skilled in the art.

However, a number of issues surrounding intellectual property (IP) and innovation have been raised, with respect to the international development agenda in general (Netanel, 2009; U.K., 2002; UNCTAD, 2007) and global health solutions in particular (WHO, 2006). For patents, these issues include quality of issued patents, overriding patent protection for humanitarian reasons, the potential barriers to innovation of the complex patent landscape, research exemptions, and the unique needs of inventors, non-profit foundations, universities, and small firms working in global health.

Examples of enabling platforms that have been patented are genes of important organisms like humans, rice, and maize, and more recently technologies related to RNAi (Schmidt 2007). Many academics see discoveries related to the human genome as being vital to future biomedical innovation. However, it is estimated that 20% of the human genome is claimed by patents. Two-thirds of these patents are owned by private firms. Additionally, two-thirds of the patents are legally questionable because they overlap other patent claims. (Cukier, 2006) Such “patent thickets” have led to what some experts call the "tragedy of the anti-commons" – instead of resources being over-used, the proliferation of patents blocking fundamental tools in biotechnology research has led to the under-use of resources from lack of cooperation between patent holders (Shapiro, 2001; Maurer, 2006; Joly, 2007).

Patent pools are consortiums of cross-licensing entities which have recently been used to help stimulate research in neglected diseases, allowing access to select patents and technologies (Van Overwalle, 2009). However, enabling tools and collaborative practices

are required to make the patent landscape accessible – including follow-on applications, new uses, and new research for global health solutions.

The open source approach

In his now-famous essay "The Cathedral and the Bazaar" (Raymond, 2000), Eric Raymond described two methods for producing computer software. According to his analogy, the "cathedral" is any top-down, hierarchically driven "closed shop". In contrast, the "bazaar" is the relative anarchy of open source development, whereby software is available for modification and use by all, for free. Microsoft and IBM have historically both been cathedrals in this sense (although IBM has recently become a major advocate of open source). Such companies have historically guarded the source code of their software, kept it secret, and treated it as valuable intellectual property. Open source projects such as Linux and the Firefox web browser, on the other hand, make their source code available for anyone to examine and modify.

The open source movement has had an enormous impact on the global software industry (St Amant & Still, 2007; Feller et al, 2005). A majority of web servers on the internet run the open-source Apache web server, and the Linux operating system has grown from a part-time student project to a significant global presence. Both of these are open source packages, and their economic impact can be roughly calculated by estimating how much money would have to be spent to replace them on their respective machines with a closed-source equivalent. (The calculation should also include any net difference in technical support and consulting charges between the two options.) It is harder to estimate how many open-source servers would not exist at all if their operators had to pay for their existence.

The economic impact of the open source movement is undeniable – for example, one study found the notional value of Europe's investment in open source software to be 22 billion Euros in 2006 (Ghosh, 2006). This economic impact is also, to a degree, a metric for open source's true importance, which according to the movement's founders is more than financial. Richard Stallman, who is widely considered the founding father of the movement, emphasizes that software should be both open and *free* – in his phrase, free as in "free speech", not free as in "free beer" (Williams, 2002). This is an important distinction and pertains to rights rather than price. Free and open software, as Stallman defines it, is software that not only is not proprietary, but cannot be made proprietary by any commercial or governmental entity. Access to it is an inalienable right regardless of location or income, and other software can build on it to create new solutions. A range of incentives push people and organizations to write such software, including building reputation, providing a public good, tapping into volunteer contributions, and undercutting for-profit rivals (Weber, 2004).

The licensing aspect of the open source movement is often taken for granted today, but there was nothing inevitable about its development. Richard Stallman was the first software developer to codify into law a license for open source development. His GNU Public License (GPL) became the template for modern open licensing schemes, and arguably the inspiration for new instruments such as the Creative Commons licenses, which are used in areas such as publishing and the arts. Creative Commons licenses, like other licenses that have evolved after the GPL, have "some rights reserved"; users of such

licenses can choose which specific obligations to impose, such as a book author who chooses to give readers the ability to download or pass on the book for free, as long as no money is charged and the book's author is appropriately attributed (Boyle, 2008).

Hence, the open source movement in software has spawned a licensing renaissance of sorts. The analogy of open source is now being applied in different sectors of society. Biotechnology is one of these.

It is perhaps natural that the first people to attempt an implementation of open source in a new area will try to make a one to one comparison between software development and the new domain. This appears to have happened with open source biotechnology, because current projects tend to emphasize sharing of data through open licensing schemes. However, when the metaphor of open source is transferred to biotechnology for global health, it naturally needs adaptation, because biotechnology industries and research efforts are not structured like the software industry. New biotechnologies are generally patented, whereas software source code is covered by copyright law. New biotechnology may require long and expensive laboratory development followed by even more expensive clinical trials, whereas new software can be developed in a more incremental and typically less expensive fashion.

What is important about open source (and arguably, what motivates people to try it in new areas in the first place) is the multiple freedoms it brings. Richard Jefferson, founder and CEO of the world's first biotech licensing organization, Cambia, puts it this way: "Open source [is not only] about the freedom to look at things. It's not about sharing. It's about preserving the right to actually act, using it."

In the remainder of this paper, we will explore the Cambia and OSDD initiatives to understand how principles and practices from open source are being applied in biotechnology for global health. We then return to the question of whether an open source model for health care research and development might be of benefit to organizations and individuals working in and for the developing world, and suggest some principles and open questions for future work.

Cambia

Richard Jefferson founded Cambia in 1991, as a private, non-profit institute based in Canberra, Australia. Initially, Cambia used its first grants from the Rockefeller Foundation to develop training and technology to support rice scientists in Asia, Africa, and Latin America. During the 1990's, Jefferson traveled to almost every lab that was doing biotechnology in the developing world. His experience with these communities colored his philosophy on access to tools.

Cambia's mission as stated on its web page is "to democratize innovation: to create a more equitable and inclusive capability to solve problems using science and technology".

BIOS: an open source licensing solution for biotech

In 2006 Cambia launched the BIOS Initiative (Biological Innovation for Open Society) with funding from the Rockefeller Foundation. Its aim was to create a "protected

commons" with legal structures to allow users to access, improve, and modify enabling technologies based on their local situations, without infringing proprietary rights. A protected commons is a secure platform where dialogue concerning inventions or improvements can take place without the invalidation of future patent applications or the misappropriation of information by third parties. The BIOS Initiative is not about creating free products; it is about creating the freedom to innovate using past knowledge and technologies, and about reducing the barriers surrounding deliverability.

> Agriculture R&D for the developing world could be lost without a concept like BIOS and open source.
>
> – Gary Toenniessen, Director of Food Security Rockefeller Foundation

The heart of the BIOS Initiative is the development of certified open-source BIOS licenses and BIOS-compliant agreements. They are designed to cultivate collaboration and deter secrecy, monopolistic strategies, and exclusiveness.

The BIOS licensing structure goes back to Jefferson's fundamental belief in the enabling power of legal tools, and aims to allow access to enabling technologies and improvement of these tools. This in turn is hoped to lower barriers to product development, and to further modification to allow products to suit local needs.

The specifications of the BIOS licensing structure attempt to ensure enabling technologies are not appropriated by individual private parties. Rather than accepting strict conditions on the use and dissemination of technical knowledge as traditional patents impose, BIOS licensees must agree to binding legal requirements to preserve the right of others to use the technology; in exchange, they gain access to the technology (BIOS, 2009).

Unlike some other open-source licenses, BIOS licenses do not prohibit licensed technology from being used to develop downstream proprietary products. In this way, Cambia distinguishes between tools and applications.

BIOS licenses ensure that the base technology remains the property of the first developer, but that all licensees have a world-wide, non-exclusive, royalty-free right to use the technology and improvements. Improvements remain the IP of the developer. Owners of technology or an improvement made available under a BIOS license may not assert IP rights over that technology or improvement against other BIOS licensees, and must share biosafety data; they benefit from access to the technology of other BIOS licensees. Users must agree to support the development of a protected commons around the technology. BIOS licenses and BIOS-compliant agreements cannot be restricted for a particular use, and there is no differentiation between a research license and a commercial license, as BIOS allows for the development of products for profit or for public good.

Permission to use Cambia's technologies is available at no cost. However, there is a technology support agreement with each BIOS license in which for-profit companies based in OECD countries must pay a fee based on the size of their operations, and there is an optional support agreement for other companies.

Cambia's first license was developed for plant molecular enabling technologies, and was aimed at companies and non-profits of all sizes from both developing and developed countries. A license for genetic resource indexing technologies is also available, and one

for health-related technologies is currently being drafted. The goal is that, as more technology is made available, additional agreements can be developed.

Cambia's website sums up the benefits of the BIOS licenses as follows:

- Ability to access the intelligence, creativity, goodwill, and testing facilities of a larger and wider community of researchers and innovators;
- Decreased transaction costs relative to out-licensing or obtaining technology via bilateral license agreements;
- Portfolio growth through synergies obtained by combining pieces of technology that may, by themselves, be too small to make a profit, or lack sufficient freedom to operate or enablement;
- High leverage of costly investments in obtaining proofs of concept, developing improvements, and obtaining regulatory and utility data;
- Ability to commercialize products without an additional royalty burden.

Cambia suggests that BIOS licenses may be of interest to several kinds of scientists, organizations and firms. First, anyone interested in materials and technology from Cambia such as GUSPlus or TransBacter which are available only under BIOS-compatible agreements. Second, research organizations that want access to information that might help complete a project they are working on, and bring it to successful real-world implementation. Third, small and medium enterprises that want some protection from the "patent thickets" described earlier that impede their progress. Fourth, large companies that can see how sharing information in particular domains would not be detrimental to their profit margins, but may actually help them leverage investment by obtaining the improvements of others (as has happened with some large companies in the software industry like IBM).

Some conclusions can be drawn from Cambia's experience with BIOS. Various firms did express enthusiasm towards the BIOS licensing structure during the first years of the initiative; however, the licenses still need to be worked upon to have the effect Cambia desires. Certainly BIOS has not resulted in a flowering of free and open projects in the way that the GNU Public License and its offspring produced in software. There are several reasons for this.

The primary one may be that software is intrinsically cheap to produce. One programmer working in his basement may create an entirely new product; Linus Torvalds created the kernel of the Linux operating system by himself, with no financial aid and without requiring the use of sophisticated laboratory equipment. Once created, software is easy to reproduce—it is, in fact, very difficult to *stop* it from reproducing.

As intellectual property, software's source code can be adequately protected by copyright law or by relatively simple licensing schemes such as the GPL. In contrast, biological innovations currently require patent law for their protection. Working with patents is not easy. To establish a new patent one must do a search to make sure that a patent does not already exist for the innovation; costly lawyers may need to be consulted to determine the patent's likely viability against court challenges by rivals; patents must be registered in all countries of interest, and fees paid both up-front and on an ongoing basis. While large

or mid-sized organizations will have the resources to pursue Cambia's licensing scheme, it is not clear that small ones will, such as when licenses require searches, authentication, and monitoring against violation. (That said, small firms face even greater difficulties if they attempt to accommodate the existing patent system.)

Another problem with the patent approach is that, in order to create a pool of components large enough that users can research areas of interest freely, many hundreds or thousands of methods may need to be licensed. There is thus a critical mass barrier to be overcome. Observers of the intellectual property scene have suggested an overarching need for "cultural environmentalism" to protect and expand the public domain of ideas on which innovation rests (Boyle, 2008).

More subtly, cultural and inertia barriers also exist for adopting new IP innovations, especially where institutional and support mechanisms are geared toward rewarding traditional patents as a measure of productive output. A lesson for future initiatives may be the importance of considering cultural and workflow barriers to adopting new IP innovations, and thinking through the motivations and incentives necessary to attract sufficient early adopters for the IP innovation to become self-sustaining.

BioForge: the first open biotech web portal

Launched by Cambia in 2005, BioForge was a project designed to provide a protected commons where users could announce details of new projects, collaborate on new technologies and improvements, and share experiences and findings with other users. It was a web portal where different problem solvers could come together and develop and share protocols, comment on patents and potential restrictions, and access tools in a public but secure environment.

BioForge was explicitly patterned on successful software development portals such as SourceForge. Its purpose was to create an active development community similar to the open source software community. BioForge is an example of attempting to transplant an aspect of open source in one domain (software development) to another (biotech).

To kick-start BioForge in 2005, Jefferson seeded it with a number of Cambia's patented technologies, including GUSPlus (an enhanced version of GUS) along with a number of technologies still in early-stage development such as TransBacter.

Within two months of its launch, BioForge had 2000 registered users. What was expected from BioForge was a place for positive debate, cooperative development of concepts, novel project management, and solving problems that were being unmet by current innovation practices.

However, within the first year of BioForge's launch, it became clear that collaborating online was not within the culture of the target life sciences community. BioForge did not continue to grow.

Several factors may have contributed to this. It may be that the majority of scientists do not have the time to regularly be active on an online platform. Similarly, Janet Hope has suggested that the costs of communication and collaboration between workers in biotech may be higher than in software, because of the lack of codification and standardization within many of its methodologies (Hope, 2008). She gives the example of experimental

protocols, which may differ from lab to lab. It is not clear that a portal like BioForge could facilitate the sharing of corporate or lab culture, much less the many unwritten assumptions that specialists in diverse fields have developed. For instance, in software development both the platform and the programming languages are formalized and standard; this is not the case in biotechnology.

Whatever the details, the main lesson is that both the culture and the physical practices of biotechnology are not a perfect fit to those of software development. The direct analogy of SourceForge to BioForge was incorrect.

The BioForge project did not thrive, and, since it also turned out to be high maintenance for Cambia, it was discontinued. A follow-up platform that learns from BioForge's difficulties may yet prove valuable:

> Now can we do [BioForge] differently? Absolutely. If we set up public metrics…community credits for whether you are a contributor in a substantive way that can go toward professional prestige and advancement…Now when we get that properly integrated in so that there actually is, not a popularity contest, but a sensible accreditation and value is ascribed to a contribution, then it'll have merit. It really will.
>
> – Richard Jefferson, Founder & CEO Cambia

Patent Lens: an open patent research system

Obtaining dozens of licenses from dozens of patent owners may be necessary for a researcher to use, improve upon, or conduct research using a technology. Large transaction costs risk hampering follow-on innovation, and some argue that patents have been granted for innovations that are not truly novel (Heller, 2008). The increasing complexity of the patent landscape has led to what has been called a "patent thicket" – a maze of overlapping IP rights (Shapiro, 2001). Each patent holder can prevent others from using the invention and, thus, hinder its commercialization or follow-on development.

Patent Lens is Cambia's response to the complexity of the patent world. It is a free full-text patent informatics resource. As of 2009, the database contains more than 9 million patent documents from the U.S., Europe, Australia, and WIPO and over 68 million DNA and protein sequences disclosed in patents. It includes lapsed, abandoned, and expired U.S. patents.

Patent Lens also allows scientists, business people, and the public to contribute comments on a patent. Although there are commercial information providers who have patent searching services, many of these corporations charge heavy fees for their services.

> Patents are not about science, they're about the conversion of science into perceived economic value, and that specialized language and capability has emerged as the ecclesiastical elite. What we wish to do is democratize that process.
>
> – Richard Jefferson, Founder & CEO Cambia

Patent Lens is more than a powerful search engine. It is a public platform to allow diverse players to investigate and analyze key IP issues, and to facilitate community involvement in overseeing and guiding the patent system. Patent Lens has tried to provide its users

with guidance over the nature of rights being appropriated and continues to improve its services.

Cambia plans to integrate business information into the database to allow people to see the power chains developing as a result of acquisition of IP, e.g. who owns what, and dependencies between different technologies. Patent Lens also has free tutorials and documents to acquaint users with concepts, and offers practical advice on IP issues – helping ensure the basics of IP are more accessible to scientists and others.

Patent Lens was first developed when the Rockefeller Foundation, which was working with developing world scientists on rice biotechnology, saw that industrialized countries were seeking patents on fundamental processes and components of the rice genome. These patents could inhibit the development of a sustainable sector that would improve rice in the developing world. To address this problem, Rockefeller funded Cambia to begin what was then the first public sector, full-text patent database. This database was integrated between jurisdictions and allowed its users to see what patents existed, what each was blocking, and whether there were ways of navigating around them.

Cambia's team used the Patent Lens technology to map out the patent landscape of Agrobacterium, one of the most widely used tools for making transgenic plants. When developing new plant varieties, GUS can be used to monitor what implanted genes are expressed; to actually get the genes into the plant requires Agrobacterium. However, Agrobacterium is tied up in dozens of patents, now mainly owned by a few large life sciences companies. By mapping out all the patents on Agrobacterium, Cambia was able to develop TransBacter, a way to implant genes into a plant using a different family of bacteria than that used by Agrobacterium. However, Jefferson does not simply see TransBacter as working around Agrobacterium.

> …we don't want to simply work around a cumbersome set of restrictions: we want to treat those restrictions as both a challenge and as an inspiration, and go way beyond them. We want to ensure that the next technology to emerge not only has the freedom to operate that our license provides, but is actually better than the one it is replacing. So we want it to be a very positive move.
>
> – Richard Jefferson, Founder & CEO Cambia

Patent Lens has been used by individuals and groups from around the world, and its work praised by the WIPO (World Intellectual Property Organization) and many commentators. It has shown the value of building tools that summarize and map out complex policy areas, making information "practically accessible".

While Patent Lens is helping to create a more transparent patent landscape, the next step Jefferson sees is to develop informatics for analyzing patents, as discussed later. This will present patents in such a way that non-specialists can understand how they fit into larger patterns of activity in biotechnology, and identify areas of potential opportunity.

With an understanding of Cambia's history and projects, we turn now to a description of the second of this paper's case studies in open source biotechnology.

OSDD: Open Source Drug Discovery

India's Open Source Drug Discovery consortium (OSDD) was launched in 2007 by the country's Council of Scientific and Industrial Research (CSIR). CSIR's stated mission is "to provide scientific and industrial R&D that maximizes the economic, environmental and societal benefits for the people of India." OSDD has been strongly supported by CSIR's director, Professor Samir Brahmachari.

CSIR's mandate is to partner with industry and technological leaders to improve the quality of life of the Indian population. The organization aims to assist Indian companies in becoming world leaders in their respective areas, while contributing to the common good. OSDD goes beyond this, however, because its open-source philosophy does not recognize borders.

The OSDD initiative attempts to encompass all the activities in the drug discovery process: identification of nontoxic drug targets; in vitro and in vivo validation; in-silico screening of small molecules; lead optimization; pre-clinical toxicity; and clinical trials. OSDD's vision is to achieve affordable healthcare in the world through a global platform where expertise and talent can be pooled together to discover novel therapies. Its mission is to apply openness and collaboration to the entire drug discovery process through an open-source approach, and keep drug costs low.

Brahmachari talks about the necessity of retaining patent protection alongside open source development, rather than in opposition to it (Kochupillai, 2008):

> We will not put a wall around drugs that are required by the masses and which we want to sell cheaply (such as Hepatitis or TB drugs), but will put a wall around drugs that have high market affordability, where the diseases that these drugs treat are not yet prevalent among lower income groups. In addition, by patenting, we can also challenge monopolies.
>
> – Samir Brahmachari, Director General CSIR India

For Brahmachari and OSDD, therefore, open source represents an instrument – one that, like patent law itself, is to be used to achieve certain specific goals. Openness is not an ideal to be pursued for its own sake; OSDD's focus is on the ultimate social result. Similar paths have been explored by other life sciences research groups, such as SARS-related patents applied for by research labs which worked out the basic science of SARS – a key motivation for patenting was to stop others monopolizing SARS diagnostics and treatments (Simon et al, 2005), and proposals have been made for policies that would make this sort of public-interest patenting a normal practice for publicly-funded genomics research (Gitter, 2008).

How OSDD works

Until recently, drug discovery was a "wet" science; if scientists wanted to identify potentially therapeutic chemicals, they had to do experiments in test tubes and use live cultures or animals. Developments in bioinformatics have enabled researchers to do drug discovery in silico, by sitting in front of their computers. This process of drug discovery is what OSDD is based upon. The linkages allowed by internet technology mean that researchers can now be united to tackle drug discovery.

CSIR has set up a collaborative online platform, SysBorgTb, for the exchange of ideas, data, projects, and resources for drug discovery focused on tuberculosis. The web portal provides bioinformatics tools, biological information, data on the pathogens, tools for data analysis, projects for students to participate in drug discovery, and discussion forums for members to share ideas. A core committee of expert scientists monitors the entire process. As of October 2009, there were more than 1700 registered participants for OSDD (SysBorgTb, 2009).

OSDD breaks downs the large complex process of drug discovery into smaller sets of activities that have clear and defined scope and deliverables for participants to tackle. These small sets are called work packages, which are posted on the OSDD web portal. The goal is for participants to contribute ideas, software, articles, IP, molecules, or anything that can help in solving these work packages.

Users of the portal must comply with OSDD's Terms and Conditions, policies, and the relevant applicable laws of the user's jurisdiction. The Terms and Conditions have been developed to reflect the mission and vision of OSDD. The agreement covers topics including use of services, appropriate content, proprietary rights, and users' rights. The agreement aims to preemptively prevent the potential problem of third parties acquiring proprietary rights based on information available on the portal – either pre-existing or generated by the OSDD community, during the drug discovery process or otherwise – without contributing improvements made back to OSDD. The Terms and Conditions authorize CSIR (India) to act on behalf of OSDD to sue for violation of these terms.

Like the BIOS license, OSDD allows users to commercially or non-commercially use any improvements, additions, or modifications of the information available in the portal that the user has made. Users must grant back an unencumbered worldwide non-exclusive right to OSDD for use of any IP rights acquired by making improvements or modification of any part of the portal information. OSDD can use these rights for further research in accordance to its vision and mission.

A key way in which SysBorgTb differs from BioForge is that it provides clear incentives for participants. This is an element that Jefferson identified as missing from BioForge. All contributions are planned to be peer-reviewed, with appropriate credits assigned for each contribution. Based on the credits accrued by contributors, they will be awarded different levels of membership, with each level entailing certain rights, privileges, and responsibilities in the entire process.

Now in its first phase, the OSDD project has begun to investigate the genetics of Mycobacterium tuberculosis, with a view to finding new drugs or treatments. These may include treatments against both drug-resistant and latent tuberculosis. In October 2009, OSDD announced a collaborative project to be completed in 2010, to re-annotate the entire Mycobacterium tuberculosis genome in order to systematically make all information available on each gene easily accessible and searchable. The project followed the earlier successful completion by OSDD of "TBrowse", a tool for integrative analysis of the tuberculosis genome (Bhardwaj et al, 2009).

Treatment of Mycobacterium tuberculosis has evaded drug discovery despite enormous scientific progress in other areas, though there has recently been increased activity in both research for new treatments and access to inexpensive existing treatments (WHO, 2009).

OSDD believes that what is required is a holistic approach to understanding the biology of infection, so as to design better treatments. The complexity of this task and past attempts to tackle this complex disease highlight the need for the best minds to collaborate, and share expertise in an open environment.

Scarecrow or wall: using the right form of protection

Samir Brahmachari's approach to open-source is to add it to the toolkit next to patent protection. CSIR does not see the OSDD initiative as being superior to patents, but as being different. Brahmachari likens the difference between the two approaches to the difference in how you protect a factory (by erecting an expensive wall) as opposed to how you protect a rice paddy (by erecting a cheap scarecrow):

> Thus, in growing a paddy, we will use an open source model. While building a factory, we will patent. If my discovery benefits millions, and I want to give it to them cheaply, I do not want to raise the costs by spending a lot of money in protecting. But if the R&D is highly expensive, then we will patent.
>
> – Samir Brahmachari, Director General CSIR India

In addition, he sees open source as a methodology for side-stepping certain issues rather than meeting them head-on. For instance, by developing free diagnostics based on pharmacogenomic principles, an open-source initiative can revive older, inexpensive drugs, thus sidestepping the arduous process of developing new drugs. A small change, in this case, could make a large difference.

Looking Ahead

The Initiative for Open Innovation

Cambia's BIOS initiative was undertaken from 2006 to 2008, and had some successes and some failures. The Patent Lens project was a significant success, and is now one of the world's most popular open web resources for patent search and analysis. The BIOS licensing infrastructure was met with enthusiasm by some companies, but had intrinsic problems that needed to be solved for it to become truly effective in its goals. BioForge did not complement the culture of scientists, and this first attempt at a collaborative portal for biotech was not successful.

With these lessons learned, Cambia is moving ahead with the new Initiative for Open Innovation (IOI), an evolving joint venture based at Cambia and Australia's Queensland University of Technology. IOI's goal is to increase the effectiveness, efficiency, and equity of science and technology enabled innovation for public good, while retaining Cambia's focus on patent system transparency and navigation.

IOI will explore, test, and validate new collaboration and licensing tools with the aim of fostering an effective "commons of capability". This commons is hoped to lower monetary and complexity costs to creating new biotechnology solutions, by providing open decision support tools.

IOI is being funded by the Bill and Melinda Gates Foundation and the Lemelson Foundation (a U.S.-based foundation with investments worldwide, that in its own words "sparks, sustains and celebrates innovation and the inventive spirit"). The initial funding of AUD 5.0M will be focusing on creating dynamic "patent landscapes" for malaria, tuberculosis, dengue, and other critical infectious diseases of the developing world – focusing on reducing barriers to developing new interventions in these diseases. The initial work will also expand the Patent Lens to Asia and other non-English speaking jurisdictions.

Having learned from the successes and failures of the BIOS licenses, Cambia is also developing legal agreements called *concordances*. With these concordances, Cambia aims to focus on community capability, not individual capability. The idea is for organizations to create a "free innovation zone" by not asserting their patented rights to technologies in the research, development, production, support, or distribution of a particular intervention (for instance, malaria).

> …University of Washington and Harvard, and Toronto, they all start signing these concordances with patents and you start building in a safe way what you might consider…a free innovation zone. And in that state, you can become increasingly attractive to small-medium enterprise and even other large players to come into that space, [to] start putting the pieces of this jigsaw together – knowing that each of the intellectual property holders reserves the right completely to assert their IP in other fields of activity.
>
> – Richard Jefferson, Founder & CEO Cambia

Concordances are intended to provide incentives for many players to enter an area that was otherwise fenced off. For this to be possible, patent transparency is a must, and Cambia plans on dynamically improving Patent Lens with this goal in mind.

Built on the platform of Patent Lens, IOI will create new Web 2.0 decision support tools aiming to allow diverse new entrants to access the innovation system in a fair and efficient manner. IOI also aims to create an evidence base on which to base policy and practice changes for public benefit, including internationally relevant patent law, policy, and practice guidance. IOI will liaise with key partners worldwide, including public sector agencies, patent offices, and the private sector.

Jefferson describes how these tools will help reduce barriers to innovation by reducing the need for expensive IP professionals or "clergy" to understand basic facts about patent landscapes:

> What we're trying to do with this, in terms of the low hanging fruit, is to bring in the world's patent information in a form that lends itself to much higher order mark-up and navigation tools. We're not interested in being a patent search facility…if you search and you find anything…How does it affect your life as a sociologist? How does it affect your life as a drug developer? Or as a citizen? There's no way to know that right now except through clergy interventions and our job is to break that down. So our low hanging fruit is to eliminate the inefficiencies in the system we have now, so people can rebuild their own incentive systems.
>
> – Richard Jefferson, Founder & CEO Cambia

One target of IOI will be creating patent landscapes relevant to tuberculosis. An official IOI liaison will be partnering with the Indian government to incorporate Indian patents into Patent Lens, and to work with OSDD. OSDD is adapting Cambia's philosophy on system-level barriers and its tools to navigate patents, to help its use of open-source as a way to develop new drugs.

Other relevant open-source biotechnology initiatives include an in-depth analysis of the "patent thicket" and patent pools (Van Overwalle, 2009), and an exploration of open source for neglected diseases (Maurer et al, 2004) and the subsequent development of the Tropical Disease Initiative's "computational kernel" for open source drug discovery (Orti et al, 2009). (The Tropical Disease Initiative is a community applying open source methods for neglected disease research.)

Three open issues

While the case studies covered in this paper indicate the potential and modest achievements to date of approaches to biotechnology that draw from the open source movement, many issues remain to be explored. Three of them are the use of collaborative platforms, integration with the broader IP reform debate, and understanding viable incentives and business models for innovation in an open-source context.

Collaborative platforms: Cambia and OSDD both deployed collaborative tools modeled on successful open-source software projects. OSDD's portal was SysBorgTb, which was intended to facilitate the exchange of ideas, data, projects, and resources for drug discovery. Cambia's tools were the Patent Lens and the now-discontinued BioForge, both of which were designed to complement the BIOS licensing scheme.

These tools illustrate how ideas taken from the software realm can, and sometimes can't, be translated to biotechnology. BioForge in particular presents a cautionary tale in how directly copying a successful tool from another discipline may not work. As Jefferson noted, providing metrics to signal users' contributions might help a follow-on platform work better; learning from the OSDD experience may also be helpful.

While Bioforge was not a success, Patent Lens and its subsequent development under the Initiative for Open Innovation suggest the potential of open platforms. There is room for detailed analysis of these platforms to understand what does and doesn't work, and to suggest specific feature sets that would be of most use to various constituencies developing health solutions.

The demonstrated value of collaborative platforms in both Cambia and OSDD also illustrates a point about the "open source" nomenclature. In the software world, open source literally refers to the ability to see the source code of programs. However, "open source" also embodies a set of cultural practices, licenses, and innovative collaboration methods. In biotechnology, therefore, at least three linked senses of open source should be considered for their value, both individually and in combination: open access to underlying information, open licensing practices, and open collaborative methods and platforms.

Integration into the broader IP reform debate: As mentioned previously, many issues and calls for reform have been raised regarding the intersection of IP and international development (U.K., 2002; UNCTAD, 2007; WHO, 2006; Gold et al, 2008). While global

health issues have featured prominently in some of these debates, such as deciding when compulsory licenses should be permissible to enable manufacture of medicines by lower-cost domestic entities, the use of open source for the development of new health solutions has thus far received relatively little attention.

Part of the reason for this may be the complexity of the issues involved. It is easy to understand a situation where a Brazilian, South African, or Indian company wishes to manufacture a low-cost version of an AIDS drug. It is much harder to grasp the opportunity costs of a complex patent regime, the unrealized potential of drugs that are *not* being developed when barriers to innovation are high, or the potential inhibiting effect on private sector innovation of relaxing IP protection.

To enable a more informed debate, looking at specific examples such as the case studies outlined in this paper may help to concretize issues. It could also be helpful to create metrics and simulation models that attempt to make clear the IP landscape – and the consequences of various policy options under consideration.

Incentives for innovation: A key issue raised by private sector entities in favor of stricter IP regimes is the maintenance of incentives for innovation. If innovators are not rewarded, who will invest in innovation?

There is a need to better understand viable business models that address this issue. For example, Janet Hope has proposed that a biotech company could remain profitable while open-sourcing its core technology (Hope, 2008). Her model makes the following three assumptions: increased access to a product or method will increase its adoption and thus the company's potential customer base; wide adoption may lead to improvements in the product or technology; the company positions itself to profit through analysis and contract research (positioning itself as the "expert" in the open-sourced technology).

This model is analogous to one that has proven successful for companies like Red Hat in the software world. Red Hat gives away its core Linux operating system for free, then charges for premium support services for it.

While intriguing, a much more thorough analysis is needed. Biotechnology innovations may be the result of a complex chain of discoveries, each of which entails risky investments that may fail. At which of these stages are open source approaches most viable? What partial rights regimes might for example release humanitarian rights promoting use in low-income countries, while keeping core rights that a company needs to maintain profitability (akin to the Creative Commons "some rights reserved" approach)? How can investments into enabling collaborative platforms be supported, as "pre-competitive tools" that may help all parties achieve more?

Both of the case studies in this paper were largely supported through government and foundation grants. However, patent pools are being explored by both public and private sector entities (Van Overwalle, 2009), and a variety of innovative funding mechanisms are being explored for global health that span the spectrum from for-profit to grant-based (Hecht et al, 2009; Hollis & Pogge, 2008). As has happened for the software industry, there is ample room for research into viable open source models that apply at each stage of the biotechnology value chain, differentiated by their requirement for public, foundation, and private funding.

Open source projects appearing in other areas of health care may provide insights. Most projects to date have aimed at creating free diagnostic or other medical software. However, the open source philosophy is spreading outside software. For example, there is now an open source prosthetics project (www.openprosthetics.org) that incorporates initiatives as diverse as shared CAD designs for prosthetic limbs and innovative financing and reimbursement systems for purchasing limbs. The open prosthetics group is explicitly targeting developing nations such as Cuba as collaborators.

Conclusion

The questions of what makes the open source approach works, and which aspects of it might be transferable to other domains, have been considered by several authors (Weber, 2004; Benkler, 2006). In this paper, we have explored two case studies of the application of the open source approach to biotechnology, and considered implications and open issues with respect to the creation of new solutions for global health.

The example of Cambia shows that the key open source principle of free access to technological tools appears to be transferable to other disciplines than software development. However, the licensing schemes that made open source so successful in the software world may not be easily duplicated in other areas. One lesson is that each area of endeavor that open source principles are applied to may require its own adaptation. First attempts at mapping the software analogy directly onto such areas (for instance, BioForge as an explicit copy of SourceForge) may fail; however they may fail in an educational way, indicating which alternative way forward may succeed.

The fact that organizations like India's OSDD are actively pursuing open source drug development is indicative of open source's potential in the developing world. While OSDD is at a very early stage, it has attracted thousands of contributors and received major funding from the Indian government. Such initiatives may provide a natural enabling environment for North-South collaborations to tackle neglected diseases.

As we have discussed, "open source" entails several linked yet distinct functions: open access to information, open licensing practices, and open collaborative platforms. The universal principle suggested by Richard Jefferson and others of *a right to access to enabling technologies* is more important than the details of a particular license, or arguments over copyright versus patents. The need now is for more well-informed pilot projects like those described in this paper, further research into which open source practices add the most value in global health and when, and subsequent policy development to harness open source approaches for solving global health challenges.

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