

# Open Access, Intellectual Property, and How Biotechnology Becomes a New Software Science

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## Abstract

Innovation is slowing greatly in the pharmaceutical sector. It is considered here how part of the problem is due to overly limiting intellectual property relations in the sector. On the other hand, computing and software in particular are characterized by great richness of intellectual property frameworks. Could the intellectual property ecosystem of computing come to the aid of the biosciences and life sciences? We look at how the answer might well be yes, by looking at (i) the extent to which a drug mirrors a software program, and (ii) what is to be gleaned from trends in research publishing in the life and biosciences.

## 1 Introduction: Convergence of Computing and the Life Sciences

The term ICT, information and communications technologies, will be used here to denote computing-in-the-large, including telecoms, networking, hardware including photonics, design, applications, and so on. We will use the term computing to be somewhat more restrictive, involving software, software engineering, applications – all areas built on computational thinking [22].

ICT has a crucial role to play in drug creation; in early warning and rapid response systems when faced with pandemics; in developing new, responsive technologies to face the threats of epidemics and pandemics. But ICT goes way further than just an infrastructure for the life sciences or for any other area. In fact [12], “Software and networks can express ideas in the conventional written sense as well as create (express) infrastructures that allow ideas to circulate in novel and unexpected ways.”

## 2 Intellectual Property in the Life Sciences: Current Focus on Patents

### 2.1 Crisis of Innovation in the Life Sciences

Life sciences dominate the patent system. “Life sciences contribute the lion’s share of patent revenues at leading US universities, outpacing contributions from physical science, information technology, and other fields. Life scientists also supply most of the inventions patented by the 10 technologically strongest US institutions” according to [1]. “In 2001, the top 10 US universities generated 689 life science patents, compared with 263 in information technology and 245 in all other technology categories.

These life science discoveries contribute 42% to the overall tech strength portfolio at these universities, compared with a 35% contribution by information technology and a 23% contribution from all other technology categories. The technical strength of a university indicates the extent to which its inventions influence others in their fields, as determined by how often its patents are cited by other patents.

Life sciences contribute more than do other fields to institutions' technological and research strengths because "companies in the life sciences have a lot of experience in commercializing ideas from universities," [1], who continues: "[Companies in] engineering and other fields do not have this same experience because they tend to develop ideas themselves. The engineering fields also are more process oriented, while the life sciences are more product oriented. That makes a difference."

Linking the patent system with innovation in universities, a journalist view [18] is: "it was the life sciences – in particular, biotechnology – that started universities down the slippery commercial slope in the first place. Even before the Bayh-Dole Act, pharmaceutical companies were eagerly trolling campuses, looking for projects to finance. After the law was passed, they stepped up their efforts, but now with renewed zeal for keeping potential trade secrets from competitors."

There is however a growing problem with the innovation process in pharmaceuticals. A leading researcher in the field has sketched out this situation as follows [8]: "The number of new drugs approved by the FDA has fallen linearly from 53 in 1996 to 17 in 2007, the same number as in 1983. A slight bump upwards to 21 approvals in 2008 includes 3 drugs eventually approved on reconsideration and 3 radiocontrast agents. In other words, it doesn't buck the trend. This coincides with downward pressure on drug pricing. The growth in prescription drug sales – 10% of the \$286.5 billion US healthcare budget in 2007 – had plummeted even before the present crisis: generics now account for roughly 60% of the market and are rapidly growing in market share.

Pharma has reacted by shedding jobs in the US – more than 100,000 over the past 5 years – and moving research to join drug production in lower cost economies overseas. Anticipated future revenue for the industry has shifted dramatically towards Asia. The current crisis is likely to accelerate these trends."

Walton and Frank [21] give indicative figures of 80% of all scientists who ever lived being alive today; only 10–20 new drugs approved each year; to get a drug to market it costs now \$1 billion and takes 15 years. Now, they state, an estimated \$13.1 billion of drugs are going generic in 2008 and \$6.7 billion in 2009.

## 2.2 Exclusivity of Exploitation by Pharmaceutical Companies and Its Loss

Companies in the "highly regulated and R&D driven" pharmaceutical sector are considered as (i) originating, driving research and the regulatory process including clinical trials, and protecting products through time-limited patent protection; and (ii) generic companies, entering markets post-patent protection with equivalent products. Interestingly, 35% of the compounds taken on board by originator companies are acquired or licensed from third party, often small or medium sized biotech, companies.

"The pharmaceutical sector is one of the main users of the patent system." This is quite an interesting assertion, because it is so clearcut, from the Executive Summary of the Final Report on the EC (European Commission) Competition Inquiry [6]. And: "Contrary to what might be assumed, blockbuster medicines' patent portfolios show a steady rise in patent applications throughout the life cycle of a product. Occasionally they show an even steeper increase at the end of the protection period conferred by the first patent" [5].

The EC initiated the inquiry into competitiveness in the pharmaceutical sector in January 2008, leading to the Final Report in July 2009 [6]. Motivations were "delays in the entry of generic medicines to the market and the apparent decline in innovation as measured by the number of new medicines coming to the market". Prescription medicines for human use only were at issue.

The decline in novel medicines reaching the market was such that there were on average 40 new medicines per annum between 1995 and 1999, and in the 2000s this has averaged 27 [7]. The effective patent protection period from product launch to the first generic launch is over 14 years in 2009, up from 10 years in 2000 [7]. After about two years, generic companies have the effect of taking the erstwhile price for the drug down by 40%. Generic market share varies a lot between countries: in Poland it is highest at 56%, whereas it is lowest in Ireland (13%), France (15%) and Finland (16%) [5].

The industry distinguishes between primary and secondary patenting. The latter include “different dosage forms, the production process or ... particular pharmaceutical formulations” [6]. Further, in order to prolong the exploitation of (time limited) protected pharmaceutical products use is made of numerous defensive patents, referred to as “patent clusters” or “patent thickets”. The Final Report notes that “individual medicines are protected by up to nearly 100 product-specific patent families, which can lead to up to 1,300 patents and/or pending patent applications...”. The Final Report notes some “awareness by patent holders that some of their patents might not be strong”, and also that defensive patenting has the clear benefit of slowing down the ability of generic products to come forward and take over the role of the originating company’s product.

Outcomes of the Final Report are recommendations for a faster and more efficient intellectual property system, including a (European) Community patent and a unified litigation system. Promised for 2010 is a new consideration “on the use of personalized medicines and ‘-omics’ technologies in pharmaceutical research and development and on the possible need for new ... instruments to support them”.

At issue here are “new technologies like pharmacogenomics and patient-specific modelling and disease simulators” for personalized medicine. The prospects for personalization of health and medical care based on the association of human illness with genetic make-up is not always viewed with optimism though [20]. This is due to the complexity of common diseases like cancer and diabetes, linked to multiple genetic variations.

### **3 Intellectual Property: Between Patents and Other Forms of Property Rights that Include Research Publishing**

#### **3.1 Implications of Pandemics for Patent Protection**

Apart from legal exclusivity running out, there is a further possible stress point on exclusivity.

To tackle the expected influenza A/H1N1 pandemic, in May 2009 the World Health Organization (WHO) allowed the leading Indian pharmaceutical corporate Cipla to produce the generic version of the anti-viral medication, Tamiflu. Hoffmann-La Roche’s oseltamivir, branded as Tamiflu, and GlaxoSmithKline’s (GSK) Relenza are the only two recognised drugs to treat the pandemic swine flu, H1N1 [14]. Cipla brought a generic drug, zanamivir, substituting for oseltamivir to market in August 2009. The inhalatory drug zanamivir was branded as Virenza in India. By August 2009, in view of the less critical threat posed by the A/H1N1 virus, a withdrawal of zanamivir was planned by regulatory authorities in India. The Hoffman-La Roche drug, Tamiflu, only was to be used. Meanwhile GSK’s Relenza is a pre-1995 drug and lacks patent protection in India.

What is of note here is the readiness of generic companies to step into the production and distribution breach, and how such a situation unfolds in a possibly socially threatening context.

#### **3.2 The Changing Culture of Publishing and Open Access**

The first scientific journals, as we recognize them, go back to the 17th century. Major aspects of the research process have remained close enough to how things were done those few hundred years ago, including the research reporting process through publication.

Increasingly now, open access is gaining ground. What this implies is that journal or conference proceedings articles ought to be put in institutional or discipline repositories six months (or immediately) following publication.

It is interesting to probe further and see who or what is leading the charge towards open access. This movement is led clearly enough by the medical and health sectors. Firstly it is in these areas that there is potentially a resonance with the marketplace for commercialization, and with an expressed need for application and deployment. (See section 4.1 below.) Secondly, medical and healthcare research is one opening – one vantage point – in regard to the large life sciences sector. Thirdly and most of all, it is organizations like the National Institutes of Health that have gone furthest, most quickly too, in introducing

open access policies. Between April and May 2008, for example, NIH policy of mandated depositing of peer-reviewed publications in PubMed Central became finalized [16].

### 3.3 The Slow Move Towards Open Innovation Models in the Life and Biosciences

The rights management involved in open access can be seen as one element of a more general open innovation approach to intellectual property use and dissemination.

Open innovation is one among various collective activities that have been pursued in the ICT arena in particular. Examples noted by Broglia [3] include: Linus Torvalds and the development of the Linux operating system; Richard Stallman who established the GNU, “GNU’s not Unix”, repository of all levels of software from the early 1980s onwards; in conjunction with GNU, there has been the GPL, Gnu Public License or copyleft, which allows open redistribution and modification of software code so long as others can maintain these rights; the SourceForge repository of open source projects which according to [3] in July 2008 had 180,000 registered projects and 1.8 million users. Broglia proceeds to IBM’s use of Linux; the Red Hat distributor of Linux, set up by Bob Young; and Wikipedia. Extrapolating from these efforts, the point is made as to how collective, freely contributed effort and work – the “online volunteer” – is a new, remarkable and by now fully established model. The results are seen too in Second Life group practices, Amazon’s recommender system, and content on FaceBook, YouTube, eBay, and so on. Both free and commercial models exist side by side and are at times even intertwined.

Vingron [19] sees data as being a side of the life sciences that should be accommodated by open access. An element of change is seen in data: data sets are huge and so must be published (as ancillary to the paper) online. Meanwhile, “There is a strong push for all data to be public (genome sequence, protein structure)”.

Richard Jefferson’s BiOS, Biological Innovation for Open Society, [www.bios.net](http://www.bios.net), goes all the way, seeking a fully open innovation environment for data in the biosciences.

Open innovation can go hand in hand with more distributed and less centralized forms of development, and indeed this can even lead to more democratic organizational forms with fewer barriers to entry. While there is much to say in favor of open innovation, it is nonetheless clear that centralized and proprietary control can also lead to more reliable, more resilient, more robust and more recovery-enabled, forms of development. In the healthcare sector, software systems have been on occasion developed centrally, based on large state contracts, and have failed disastrously. For some, the blame lies in thoroughly inadequate requirements gathering. Others have seen the culprit as the refusal to access an open innovation model, incorporating open source. Johnson [10] presents a wide-ranging overview of these divergent views, based on case studies and experience with the US Veterans Health Administration (VHA). In passing we note that Johnson [10] includes examples of where centralized healthcare ICT systems have been developed and implemented with recognized success.

## 4 Pharmaceuticals as the New Software

### 4.1 Pharmaceutical, Software and Other Goods

Convergence between the computing sciences and the life sciences is ongoing but with a great deal of, as yet, unrealized targets [13]. We will now sketch out a scenario with clear implications for how the underpinning information-based sciences and engineering could relate to the life sciences in a very new way.

Consider for one moment the greatest product of all time in terms of return on investment and development. It is the drug Lipitor (atorvastatin calcium), used for cholesterol treatment, that cost Pfizer half a million dollars to develop, and had a return of over 13 billion dollars in 2007 [4]. The patent on Lipitor runs out in June 2011. This is only one drug among many where intellectual property rights are likely to change greatly in the next few years. Generics will step into their place, and will be priced far less.

Now consider software and pharmaceuticals. Both act on the environment. As such they have determinate inputs and they process these inputs in determinate ways. Assume that user interaction is part and parcel of

the software. So keyboard, visual, haptic, voice, sound, printer, display, etc. are input and output interfaces to the software's ambient environment. A drug has interaction too, in terms of influencing or discouraging cell growth, modifying in a positive or negative way the ecosystem of the human or animal, tempering inflammation or other secondary effects, and so on. The former is often macro level, and physical. The latter is often micro or nano level, biological and chemical. The essential analogies remain: both systems are carrying out interactions of a determinate and predictable kind on their environment.

Now consider how both are characterized by, or contrasted by, the following.

- Potentially huge costs to produce, refine: A drug takes, say, 15 years to produce. Consider the software in the Airbus 380 or Boeing 777 as a counterpoint to this.
- Validating shares engineering and art, statistical science and social sciences. But in neither domain (software, pharma) are the physical or natural sciences really to the fore. (Energy may yet change the picture here, and bring to the fore – for example – the thermodynamics of information: see [11].)
- Once developed and validated, the cost of reproducing software or a drug is effectively zero.

A drug can change its use and delivery, so the molecule or protein “platform” can change function or role. Cf. secondary patenting discussed in section 2.2. So it is for software. Computer software was always non-trivial to demarcate as a product. With reference to the US Copyright Act of 1976, and the US Code section 17 of 1980, Kelty [12] notes that: “During the 1980s, a series of court cases helped specify what counted as software, including source code, object code (binaries), screen display and output, look and feel, and microcode and firmware.”

Adaptability and modifiability are crucial. For software, “It is a peculiar feature of copyright law that it needs to be updated regularly each time the *media* change ...” We can consider “gramophones, jukeboxes, cable TV, photocopiers, peer-to-peer file-sharing programs”. Further, “new questions arise: how much change constitutes a new work, and thus demands a new copyright license? If a licensee receives one copy of a work, to which versions will he or she retain rights after changes? ... is the XML document equivalent to the viewable document ...? Where does the ‘content’ begin and the ‘software’ end?”. Kelty speaks of “denaturalization” of the software product.

So it is analogously with a drug. Faced with declining innovation in the pharma sector, and following the model of software that reuse is not simply a technical issue, then the thought arises as to how to harness collaboration. Some communities (e.g. humanities) would be aghast at liberal creation of derivative works. Other communities (e.g. computing and engineering) revel in reuse. Kelty ([12], p. 291) includes biology in the reveling category. Maybe the life sciences will follow suit, involving for example that the “compulsory licensing of pharmaceuticals [could be] open to analysis” according to the terms offered in [12] (p. 304).

In regard to software, Boyle [2] notes how a creative open “commons” in property rights contributed so much to spurring on the software industry. He notes, with worry, how synthetic biology “which shares aspects of both software (programming in genetic code) and genetic engineering” is threatened by the lack of open models of intellectual property.

In his concluding remarks on the evolution of biotech, with a particular focus on IPR (intellectual property rights), Pisano [17] stresses the need for organizational and institutional innovation in biotechnology, in order for it to overcome the slowness of productivity (i.e., rarity of new drug discovery and successfully bringing to market). In order to prevent under-exploited “islands of expertise” in biotech greater openness and disclosure are needed. Recall that both research publishing, and patenting and licensing, are forms taken by such expertise and knowledge. Pisano focuses on the latter areas of intellectual property – patenting and licensing. Among other recommendations, he proposes greater disclosure of clinical trial data much earlier in the development process, and not just after approval. While such disclosure does happen through journal publishing (cf. section 3.2), when this happens is at the discretion of the sponsoring drug company, and will not necessarily include negative as well as positive findings. Pisano's objective is to overcome the logjam of innovation in the biotechnology sector, and to facilitate investment decisions.

## 4.2 Conclusions

As patents run out, and as competitive pressure prizes open current intellectual property holdings, all of the pharma and bio sectors will be affected. The metaphor of a supernova would be apt. This is not just pointing to a massive economic and technological change. Rather, in analogy with, say, a black hole resulting from a supernova, it is a new source of tremendous dynamism – a melting together of pharma and software.

The implications of this would be profound. It would lead to a very different health system, including all of insurance, medical and public health domains. To have some feel for the direction of events, one need only look carefully at computer science and the ICT sector. Computer science and engineering are characterized by a wealth of “models” both in research and development and in the very rich ecosystem of intellectual property. The dream is one where “Everything that can be delivered digitally will be, at a cost approaching zero, through a bandwidth nearing infinity” [9], and IPR is adapted to fit this world view.

Creating of new drugs would result from ultra high dimensional search and discovery in truly massive, semantically rich data stores. Drug development would need a new pharma-oriented information search and fusion infrastructure at its core. Our health system would be even more integrally based on the information infrastructure. Fortuitously or presciently, the most advanced driver of open access in research outputs is the biomedical and health sector. The ground is already being prepared slowly, through data provision, for the search engines that will power the new pharma informatics and health informatics.

To envisage barriers between disciplines coming down is not a bad prospect. Computer science and engineering may be very different in one or two decades from now. An implication of such change is in research publishing. This is because one thing about the way we carry out our research and scholarly work is that we, across all science disciplines, have become very influenced by the biosciences. Take for example how journal citation rates are based on just two previous years. Extreme recency has come to count greatly in citation practices, and a very small number of highly profiled journals tower over all others. We know how different the scene is in computer science and engineering (cf. [15]). Perhaps the future of scholarly publishing across many disciplines is closer than we think to today’s variety of publishing practices in computing, both science and engineering, both theory and application, and embracing both open source and commercial rights and privileges.

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