Synthetic biology, patenting, health and global justice

Contribution to the SYBHEL Workshop in Bilbao, November 4-5, 2010

Henk van den Belt
Applied Philosophy
Wageningen University
The Netherlands
Email:henk.vandenbelt@wur.nl

> "… the patent system is inherently political. This implies that its design and reform will never be based on legal nicety, scientific fact or disinterested economic calculation alone. Politics is almost inevitably a part of the equation, and nowhere more so than in the life sciences field ..." (Graham Dutfield 2009, p. 4)

> "I hate Myriad [Genetics] the way some people hate Goldman Sachs. [By patenting genes], they made enormous profits [but] they are also raising the cost of medicine." (James Watson, April 28, 2010)

> "The danger isn't that Craig Venter has become God, it is that he might become Bill Gates. We do not want a monopolist over the code of life." (James Boyle, May 28, 2010)

Introduction

Forecasting is a rather hazardous exercise, especially if the aim is to predict the future. Any sketch of the likely development of synthetic biology in the near and more remote future is speculative, as would be an outline of expected trends in patent law. So an exercise in which these two forecasts or explorations are to be combined, would be doubly speculative. The problem becomes even worse if we have to zoom in on the *medical applications* of synthetic biology and the legal and moral issues they are going to raise with regard to property and ownership – because it is not yet very clear what medical applications may stem from synthetic biology in the short and middle term. To raise the question, 'Should we patent synthetic biology products when they are related to human health?' – as the outline of the program for this workshop does – may be useful and admirable as an attempt to force the issue and bring matters to a head, but also seems to betray a certain political naiveté. One might also think that the picture for *medical* synthetic biology is still too hazy to make any discussion of the need for a new legal framework for patents in this special field opportune and fruitful at this early day.

Consulting the SYBHEL website does not help us much in finding any clues and leads to develop a more elaborate position with regard to the questions raised. One issue that is mentioned is the ethical implications of "creating life" – indeed an issue that is already widely

discussed but one that does not relate specifically to medical applications (I have indulged to engage in that debate myself, see Van den Belt 2009b). It is furthermore stated that synbio "may alter our conceptual understanding of the nature of health, well-being, disease and therapy". This may be a rather grand claim. My impression is that many of my colleagues in philosophy and ethics and in science and technology studies (STS) are fond of making such claims. It would be rather trivial and prosaic to simply say that new developments in medical science have an impact on our health and well-being and enlarge the therapeutic arsenal to combat the diseases from which we suffer, so it sounds much more exciting to say that our conceptual understanding itself is affected by such developments. But *when* exactly would it be justified to claim that our *concepts* of what it *means* to be ill or healthy have been altered? (Did the conquest of tuberculosis in the developed world alter our very concepts of disease and health? It certainly brought an end to the enchanted world of the Magic Mountain!) My point is that ELSI scholars should be wary of hyperbolic claims that may play too easily into the strategic schemes of raising great expectations for a new field of science and technology (cf. Alfred Nordmann's [2007] criticism of speculative 'if-and-then' ethics). Some skepticism would also be appropriate with regard to the claim that "Synbio could help design truly personalized drugs specific to individual needs", as this seems just a recycling of the old promise that genomics and nutrigenomics raised about ten years ago but were unable to fulfill in the past decade.[1]

What then would be the best approach, in the light of the difficulties and pitfalls sketched above, to tackle the legal and moral issues raised by synthetic biology and its medical applications with regard to property and patenting? My preferred strategy would be a two-pronged approach. On the one hand I would like to put contemporary developments in a historical perspective. This provides some immunity against the hypes and exaggerated expectations that inevitably surround a new field like synthetic biology. The rise of synbio can be seen as a continuation, and provisional culmination, of some longer-term trends that are characteristic of major strands in western science and technology, e.g. the "informatisation" of life since the beginnings of molecular biology or the attempted implementation of the Kant-Vico-Feynman principle "What I cannot create I do not understand", which has previously been followed in organic chemistry (Van den Belt 2009a). Synbio is also a continuation and radicalization of genetic engineering or biotechnology. Thus there is historical continuity as well as discontinuity. That also applies to the development of patent law (or more broadly

[1] The SYBHEL website also mentions the 'poster-child' of synthetic biology (or more exactly metabolic engineering): the synthetic production of a pre-cursor of artemisinin (an effective anti-malarial drug) by Jay Keasling's team at Berkeley, funded by the Bill and Melinda Gates Foundation. The website remarks: "Ironically, however, this scientific development could have a detrimental impact on the communities in developing countries who currently produce the rare precursor to amorphadiene as a synthetic substitute could cause a loss of value of the product supports their livelihood." This issue has been discussed more extensively in a brochure of the Ottawa-based ETC Group (see ETC Group 2007, pp. 52-55). One would like to know how specific and idiosyncratic this particular case is, and how compelling the evidence is on which it is based. Does it really cast an ethical shadow over the synthetic artemisinin initiative? To what extent could the lesson be extrapolated to similar initiatives involving synthetic biology? Such questions are still hanging in the balance.

intellectual property law). It is very important to realize that "the history of intellectual property rights is a history of contestation" (May and Sell 2006), so as to avoid the widely held misconception that IP issues have become controversial only recently. The other prong of my two-pronged approach would be to give free reign to the moral imagination by proliferating possible scenarios for the future of IP and synbio (as was done in a major study commissioned by the EPO) and by elaborating institutional re-designs explicitly aimed at the normative goal of global justice (as is done, for example, by Thomas Pogge and other advocates of the Health Impact Fund). In a sense, this is making a virtue out of necessity, as it is openly acknowledged that the future is radically uncertain. The two prongs of my approach are held together by an historically informed interpretation of the current international situation in IP law as representing a major political contest between two frames, namely the "IP frame" and the "A2K frame" (access-to-knowledge frame) (Kapczynski 2009). The first frame has dominated the past three decades, but the latter frame is in the ascendance.

Technology-neutrality of patents versus "co-construction"

The debate on synbio and patents is often framed by the prior assumption that the patent system is, or should be, "neutral" with regard to the kind of technologies for which legal protection is being sought. This neutrality is even enshrined in the TRIPS agreement. Article 27.1 states that "… patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application". Thus in a recent article on synbio and patents, EPO official Berthold Rutz remarked: "One of the reasons for the long-lasting success of the patent system is its *non-discriminatory character*. The same basic patentability criteria apply to all fields of technology: novelty, inventive step and industrial application" (Rutz 2009, S14).[2]

I think the technology-neutrality of the patent system is a myth. There has never been a patent system that is completely or even approximately "technology-neutral", nor can there be such a system. The myth presumes that the three basic requirements can be applied to any newly emerging field of technology in a straightforward and "mechanical" way, without needing much additional interpretation. It also passes over the problem of patentable subject matter.

Article 27.1 of the TRIPS agreement unjustifiably grants the moral high ground to pharmaceutical companies opposing provisions in national patent laws that exclude product patents for drugs, as if "Thou shalt not discriminate!" were the first of the Ten Commandments in patent legislation. In the past, however, many countries (e.g. Germany, Italy, India) have excluded medicines from patenting on the legitimate and respectful grounds that this would serve public health best. What deserves ethical censure is rather that such provisions have been outlawed by the TRIPS agreement. At any rate, patents in the area of health have always been a sensitive issue.[3] Thus Howard Florey and his team at Oxford

[2] Despite these opening remarks, Rutz acknowledges that the emergence of new technologies regularly raises questions about the working of the patent system. He also deals with the question whether the latter is still suitable with regard to inventions in synbio. Why, then, does he pay lip-service to the principle of technology-neutrality of the patent system?

[3] Significantly, in former times, so-called "patent medicines" (although seldom actually

University did not file patents on penicillin in 1940-41 "because patenting was then against ethical medical principles" (Macfarlane 1980, 369). The earlier example of insulin (1920-21) is only an apparent exception: "… medical men, such as Macleod and Banting, were bound by their profession's code to make all advances in health care freely available to humanity… [I]t would violate a physician's Hippocratic oath to engage in the profiting from a discovery that patenting normally implied" (Bliss 1988, 133). When the University of Toronto nonetheless decided to patent the insulin extract it was only as a purely defensive measure that would stop nobody from making the extract: "In fact the point was to stop anyone from ever being in a position to stop anyone else" (*ibid.*). In others words, the university made an attempt at "copylefting" the patent system. Finally, when Jonas Salk was asked in the 1950s why he hadn't patented his polio vaccine, he is famously reported to have answered: "Can you patent the sun?". (However, his legacy does not prevent the Jonas Salk Foundation today from aggressively patenting as much of their research outcomes as they can, including new vaccines.)

If technology-neutrality were really a sacrosanct principle of patent law, it would hardly be defensible and in fact downright inconsistent for the TRIPS agreement to allow Members to exclude diagnostic, therapeutic and surgical methods (Art. 27.3.a) or plants and animals from patentability (Art. 27.3.b). (For plants, Members must provide either protection by patents or an effective *sui generis* system of plant variety protection or any combination thereof.) However, the proponents of plant and animal biotechnology have no reason to complain about "discrimination", as the North American and European patent authorities have granted very special concessions to the holders of patents in this area by allowing them to also claim the transgenic offspring of genetically modified organisms and to extend the protection of patented genes to every organism in which such genes may be found, thus turning "natural" processes of reproduction and multiplication potentially into acts of infringement (as is illustrated by the notorious case of Monsanto versus Percy Schmeiser). Around 1900 the influential German jurist Josef Kohler argued that patents on living, self-reproducing organisms would be absurd because "patent law can govern only human action, it cannot constrain nature in those cases in which nature causes everything or at least the main part" (see the discussion of his views in Van den Belt 2009a, 1322-1326). Patent law in western countries has moved a long way from Kohler's common sense.

Against the myth of technology-neutrality we can put the idea of the "co-production" or "co-evolution" of technology and patent law. In science and technology studies (STS) it is indeed not unusual to conceive of the relationship between science/technology and society (or the social, legal and political order) as one of mutual shaping, thus avoiding the extremes of scientific/technological determinism and social determinism. When a new field of technology emerges, patent law does not provide a list of ready-made criteria by which the technical

---

patented) had acquired a rather notorious reputation (cf. "snake oil"). An editorial comment in the *American Journal of Public Health* stated in 1926: "One of the glories of the medical profession has been that discoveries for the betterment of mankind and the relief of suffering have always been given freely to the public.[…] Patent and proprietary medicines have been and are a stench in the nostrils of the profession" (Editorial 1926).

accomplishments in the new field can be judged as patentable inventions. Instead, the conditions of patentability have first to be worked out and elaborated vis-à-vis the new technology, if only because the notion of "invention" is not strictly and universally defined but open to historically variable interpretation.[4] Thus with the rise of synthetic dye chemistry in the second half of the 19th century decisions had to be made about the precise meaning and scope of "a *particular* process" to which the German Patent Act of 1877 had limited the patentability of chemical inventions; or on how high (or rather low) the bar for inventiveness had to be put to allow the patenting of "inventions" routinely produced on a large scale by the new R&D laboratories of the chemical industry (Van den Belt and Rip 1987). As a major stakeholder, the German chemical industry often lobbied vigorously to influence the shaping of patent law (see also Dutfield 2009).

The development of patent law and biotechnology provides another clear example of "co-construction" or "co-evolution". The first question to be answered was if this part of law applied at all to this new area of technology. In the landmark case of *Diamond v. Chakrabarty* a 5-to-4 majority of the US Supreme Court held in 1980 that anything new under the sun that is made by man, whether living or non-living, can in principle be patented. Chief Justice Burger argued on behalf of the majority: "[T]he patentee has produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility. His discovery is not nature's handiwork, but his own; according it is patentable subject matter under § 101." This verdict occasioned a huge capital influx into the emerging biotech industry in the following years.[5] During the 1980s the patentability of living organisms was further extended from bacteria to multi-cellular organisms and to higher plants and animals (cf. the "oncomouse" patent of 1988). Equally important for the biotech industry was that patents on isolated and purified genes and DNA sequences have also been recognized as legally valid. The reasoning behind this view was that a gene is just a chemical compound and that the isolation and purification of a particular DNA sequence from the body turns it in something radically different from its natural state and thus into an invention eligible for patenting.[6] This doctrine would seem to be a rather thin justification – the Australian jurist Luigi Palombi disparagingly calls it the "isolation contrivance" (Palombi 2009, 205-225) – but nonetheless it has provided the legal underpinning for the practice of

[4] In 1886 an official Commission of Inquiry on the German Patent Law appropriately spoke about "der im Culturleben flüssige und wandelbare Begriff der Erfindung" (the culturally fluid and variable concept of invention). The Commission was against an explicit definition, as this would frustrate the needed "vernünftige Ermessen" (reasonable judgment). See *Die Chemische Industrie* 10 (1887): 379.

[5] Together with the Bayh-Dole Act of 1980, which allowed universities to take out patents on the results of federally funded research, it also led to a rapid commercialization of molecular biology. In the introduction to his novel *Jurassic Park*, the late Michael Crichton wrote in 1991: "The commercialization of molecular biology is the most stunning ethical event in the history of science, and it has happened with astonishing speed".

[6] This view is often presented as if it were a logical consequence of the Chakrabarty decision, but Palombi argues that the case for patents on isolated and purified genes would not pass the US Supreme Court's criteria, as such genes do *not* have "markedly different" characteristics from their natural counterparts (Palombi 2009).

granting gene patents by the US, European and Japanese patent office for more than two decades.[7] By 2005, it was found that some 20 percent or one-fifth of human genes had already been captured by US patents (Jensen and Murray 2005). One can therefore imagine that the recent decision by Judge Robert Sweet on May 29, 2010, in the high-profile case against the patents of Myriad Genetics on the BRCA1 and BRCA2 genes related to breast and ovarian cancer, must have sent shock waves through the entire biotech industry. Judge Sweet dismissed the isolation doctrine as a "lawyer's trick" and declared that human genes constitute unpatentable subject matter (Schwartz and Pollack 2010). The biotech industry hopes that his decision will be reversed by the higher courts.

From about 1980, modern biotechnology has "co-evolved" not just with patent law, but also with other parts of the social and political order. Indeed, the extension of patentable subject matter to include genes and DNA sequences, cultivated cells and tissues and transgenic organisms was itself part of a wider movement of strengthening and extending intellectual property rights (not just patents, but also copyrights and breeders' rights) on national, regional and worldwide scales that fitted well with a neoliberal agenda of privatization, globalization and the reduction of the public sector.[8] In recent years, however, this dominant "IP frame" is increasingly challenged by the "A2K frame" or "access-to-knowledge frame" (Kapczynski 2009).

One possible effect of "co-construction" or "co-evolution" between technology and patent law is that it may lead to *path effects* that may in turn give rise to *mismatches* between subsequent technologies and intellectual property regulation. Thus the proliferation of patents covering hundreds of thousands of genes or DNA sequences on the human genome and the genomes of other organisms, a direct outcome of the prior "co-evolution" of classical biotechnology and patent law, may constitute a formidable obstacle for the development and application of new technologies like DNA-microarrays ("gene chips") and whole-genome sequencing. Synbio will also have to confront the legal legacy of the biotech gold rush.

---

[7] In 1988 the European Patent Office, the US Patent and Trademark Office and the Japanese Patent Office issued the following joint statement: "Purified natural products are not regarded under any of the three laws [US; EU; Japan] as products of nature or discoveries because they do not in fact exist in nature in an isolated form. Rather, they are regarded for patent purposes as biologically active substances or chemical compounds and eligible for patenting on the same basis as other chemical compounds." It may be noted that in Europe the patentability of genes and DNA sequences was only officially established with the passing of the European Directive for the Protection of Biotechnological Inventions in 1998 (European Directive 98/44/EC), so the EPO already ran ahead of the political decision.

[8] Amy Kapczynski cites William Landes and Richard Posner, who point to the "free-market ideology" that came to prominence in the late 1970s and argue that "it was natural for free-market ideologists to favor an expansion of intellectual property rights" (Landes and Posner, quoted in Kapczynski 2008, 842). However, a longer historical perspective should warn us against the "naturalness" of a close relation between economic liberalism and a pro-IP stance. In the mid-19th century the adherents of Free Trade in Europe were generally *against* patents, which they saw as obsolete "privileges" of the *Ancien Régime* and as impediments of free competition.

Synbio at the crossroads

It is not difficult to understand why patents could be a major threat to the realization of that particular strand of synbio that aims at the construction of complex biological systems on the basis of well-defined standard parts, i.e. genetic sequences with known functions that can be used as building blocks in biological syntheses. Construction of one biological system may easily require hundreds or even more than 1000 different components. If only a small percentage of the needed parts were encumbered with patents (or other IP constraints), it could become prohibitively costly to obtain "freedom to operate" to assemble the entire system. A patent thicket would doom the prospects of this strand of synbio: "One roadblock to synbio's future is the messed-up patent environment in biotech, where every tiny protein pathway and gene sequence has an owner wanting to get paid … [U]nless basic components are made freely available it will be too expensive to make anything useful or complex" (Herper 2006).

Deeply concerned that their fledgling field could be smothered already in its cradle, several synbio enthusiasts from MIT, Harvard and the University of California have set up the *BioBricks Foundation*, which administers the Registry of Standard Biological Parts, a steadily growing online collection of parts on which synbio practitioners can draw at will to engineer new life forms and to which they can contribute their own components. From the outset leaders of the field like Drew Endy and Tom Knight have also been groping for suitable legal instruments to ensure that BioBrick™ standard biological parts remain freely available to the synbio community. They have been inspired by the open source movement in software development, which uses copyright law in a creative way by devising licenses like the GPL or General Public License ("copyleft") to ensure that newly written software code is not privately appropriated but remains free to use for all. The problem for synbio is that legal devices like the GPL that are based on copyright law cannot easily be transferred to the biological field. Due to its "viral" effect a GPL-like license might also be considered too strong in that it would prevent the patenting of any final products such as pharmaceuticals that could be made by synbio methods. It is all very well to keep the basic tools and building blocks freely available to the research community, but some synthetic biologists argue that such a viral effect would be undesirable as patents are still a cornerstone in our current system of pharmaceutical innovation. The legal experts Arti Rai and James Boyle advise the synbio community to follow the example of the (public leg of the) Human Genome Project and make new building blocks publicly available as soon as possible: "Placing parts into the public domain not only makes parts unpatentable, but it undermines the possibility of patents on trivial improvements" (Rai and Boyle 2007, 392). This strategy does not provide a watertight guarantee, however, that such parts will be preserved for the public domain or the commons. It is not certain either whether the parts that are already in the Registry are unencumbered by any patent rights. On a workshop held in Berkeley on March 31, 2006, Drew Endy estimated or rather speculated that perhaps one-fifth of Biobricks parts were patented. So it is not unthinkable that in future when synbio yields commercially interesting applications in the fields of health, energy or bioremediation, "patent trolls" claiming intellectual ownership of

some of the used parts may suddenly turn up to assert their rights. In October 2009 the so-called *BioBrick™ Public Agreement* (BPA) was proposed as a new legal framework for regulating the rights and duties of the contributors and users of the parts collection. Basically, the Agreement amounts to "an irrevocable promise not to assert any property rights held by the Contributor over Users of the contributed Materials" (http://bbf.openwetware.org/BPA). It has no viral effect, so it does not prevent users employing parts from the collection to patent any final products they may develop from these starting materials. One might question whether this proposed arrangement provides sufficient incentives for potential contributors to donate their materials to the Registry (Henkel and Maurer 2009, 1097). The BPA is currently still being discussed in the synbio community.

There is no doubt that the synthetic biologists who established the BioBricks Foundation are strongly committed to open-source principles and an ethos of sharing, but they too are forced to accommodate to the realities of an IP-dominated world. Their attempt to carve out a little niche of a commons comprising the building blocks and basic tools of their trade thus continues to rest on a fragile legal base.

The BioBricks approach is not the only strand in synbio. There is also the "chassis school" represented by Craig Venter and his team. Their favored procedure is to assemble a "minimal genome" (i.e. a microbial genome stripped of all dispensable genes) from synthesized DNA, transplant it into a recipient cell whose own genome has been removed, and use the artificial creature thus obtained as a "chassis" upon which all kinds of economically useful genes can be mounted. On 31 May 2007 the US Patent and Trademark Office caused a stir when it published the patent application that the J. Craig Venter Institute had filed in October 2006 on a new artificial life form called *Mycoplasma laboratorium* (US Patent Application 20070122826, filed 12 October 2006). The announcement was somewhat premature, because the first artificial creature was only to see the light of day almost three years later, on 29 March 2010. However, the claims of the first patent application, to which other applications would follow, were already quite sweeping. They are formulated successively as of increasingly wider scope. Thus the set of 381 essential genes making up a "minimal bacterial genome" is being claimed (claim 1); the synthetic organism that can be made from these genes; any variant of the organism that can produce ethanol or hydrogen (claim 20); any scientific method for assessing the functions of genes by inserting those genes into the synthetic organism (claim 22); and any digital version of the synthetic organism's genome (claim 19). Among the intended applications the creation of synthetic organisms for the production of biofuels like ethanol and hydrogen is particularly emphasized. At present, such applications may sound futuristic, but it seems that Venter wants to signal to the general public that his enterprises (consisting not only of the nonprofit *J. Craig Venter Institute* but also of the private company *Synthetic Genomics, Inc*.; patent rights will all be assigned to the latter) intend to play a key role in solving the urgent problems of energy supply and climate change. In his Richard Dimbleby Lecture delivered on 4 December 2007 on BBC One, he went so far as to suggest that synbio may save the world and effectively constitute humanity's last chance for survival (Venter 2007).

Contrary to the BioBricks school, which attempts to establish a practice of sharing inspired by open-source models in software development, Venter continues the strategy of aggressive patenting of classical biotechnology with a vengeance. The two strands of synbio thus illustrate the tension between the old "IP frame" and the new "A2K frame" (Kapczynski 2009).

The suite of patents that the J. Craig Venter Institute subsequently filed also have very broad claims. John Sulston, Venter's old rival in the race to sequence the human genome, recently sounded the alarm on the extremely wide scope of the claims in the patent applications, suggesting that they might, if granted, give Venter's enterprise a monopoly on a wide range of techniques (Chan and Sulston 2010). James Boyle also warns that Venter might become "a monopolist over the code of life" and that the efforts of the BioBricks community to create an open source collection of standard biological parts might be endangered by "the threat of overbroad patents on foundational technologies" (Boyle 2010).

Let us assume, for the sake of the argument, that the plans of Venter's company Synthetic Genomics Inc. to develop highly advanced "fourth-generation" biofuels using carbon dioxide as feedstock will indeed come true and that the new techniques as a matter of course will be heavily protected by patents. This would conjure up the morally problematic scenario in which technological solutions that might be humanity's last hope for survival (as Venter himself suggested in his lecture before the BBC) are locked up in patents that serve to make them inaccessible to any but the most wealthy users. The company will have to tell its impecunious non-clients: "Sorry, you won't be saved, if you are not willing to pay the price of your survival!". But in this case, unlike the users of high-priced patented medicines that are effectively denied to poor patients, the wealthy users of expensive high-tech biofuels won't be saved either. Climate change will not be sufficiently mitigated if only the wealthy inhabitants of the earth use "climate-neutral" energy.

Important medical applications of Venter's synbio approach are expected in the area of vaccine development. In October 2010 his institute and his company set up a new venture, *Synthethic Genomics Vaccines Inc.* (SGVI), in collaboration with the Swiss pharmaceutical company Novartis, to develop next-generation vaccines. The J. Craig Venter Institute will bring its synthetic genomic research expertise to this venture, "coupled with the intellectual property and business acumen of SGI [Synthetic Genomics Inc.]" (press release October 7, 2010). The direct aim of the venture is to accelerate the production of the influenza seed strains required for vaccine manufacturing, so that the time needed to start vaccine production can be cut short by two months (with the so-called swine flu "pandemic" of 2009 serious vaccine production only got started after the peak of the "pandemic" was over). This is a respectable aim, of course (though one might question whether the world might be "prepared" in time if a pandemic outbreak of the rapidity and seriousness of the Spanish flu of 1918 would strike again, even with a time saving of two months). There is no doubt, however, that the new venture will pursue a strategy of aggressive patenting. Yet the area of vaccine development for influenza epidemics is precisely an area where intellectual property rights clash with global public health needs (Andrews and Shackelton 2008). Under the rules of the WHO countries affected by flu outbreaks are expected to send samples of viruses to the

WHO's collaborating research centers and laboratories, which are all located in the USA, Europe or Japan. These laboratories cooperate with western pharmaceutical companies that take out patents on genetic sequences and vaccines derived from these virus samples (for an expert report on patentability issues related to viruses, see WIPO 2007). Developing countries contributing samples to the WHO are often unpleasantly surprised when they subsequently find out that they cannot afford the patented vaccines that are developed from these materials. No wonder then that in 2007, during the avian flu epidemic, Indonesia refused to further share its H5N1 virus samples if it would not get access to affordable vaccines (Hammond 2009). This is a very serious threat as worldwide sharing of virus samples is a vital requirement for the effective working of WHO's Global Influenza Surveillance Network. Within the WHO parties are still negotiating about access and benefit-sharing arrangements for virus samples and vaccines.

As the above examples of biofuels and vaccines illustrate, we have to consider patent issues in the broader context of sustainable development and global health and global justice. Moreover, the traditional justification of intellectual property rights as indispensible incentives for innovation is increasingly challenged as alternative models have emerged in the wake of the open-source movement. Chan and Sulston put the controversy over Venter's patents in the perspective of an epochal confrontation between the IP frame and the A2K frame: "The conflict between private interests in science, protected by patents and cloaked in secrecy, and open access research remains one of the most contentious issues in modern science *and affects us all*" (Chan and Sulston 2010, 1316; italics mine).

Commodification, property and intellectual property

The rise of synbio may have a disenchanting effect on our general view of life. It is said to undermine the categorial distinction between the "made" and the "grown", which is supposedly constitutive for the way we see ourselves and the rest of living nature (Pottage 2007, 323, citing Habermas). The ethical panel that was installed by Venter himself hinted in 1999 that the general public might wrongly interpret the new developments in science as if life were reducible to or nothing more than DNA, thus threatening the view that "life is special" (for a discussion, see Van den Belt 2009b).

Such cultural responses have much to do with the relentless "informatization" of the biological world that is going on for some decades now and of which synbio is only the most recent expression. In the early 1980s Jeremy Rifkin, the well-known critic of biotechnology, was already exceptionally farsighted when he speculated that future generations would inhabit a world in which nature was "no longer something they are born into but rather something they program" (Rifkin 1984, 23). He expected the computer and information sciences to become "the means of communication humankind will use to reorder living material in the biotechnical age" (ibid., 21). His prophecy seems realized at last in the current age of synbio. Life itself is increasingly understood in terms of "information processing" or "computation" and cells and organisms are seen as computers that can be easily (re)programmed according to our wishes. Rather than evolving naturally (the "grown"), living beings become the product of deliberate design (the "made").

Such views also tend to inform intellectual property legislation. A case in point is the way living organisms are considered in patent law. The *European Directive on the Legal Protection of Biotechnological Inventions* (Directive 98/44/EC) gives the following definition of the key object of protection: "… 'biological material' means any material containing genetic information and capable of reproducing itself or being reproduced in a biological system" (art. 2.1 sub a). Notice that not just genes and cells but complete organisms can be brought under this definition. During political debates on the implementation of the Directive in the Netherlands in 2003-2004, several members of parliament expressed concern that the new legislation would reduce living beings to the status of biological material. In response to this concern, cabinet ministers pointed out that "all living beings *consist of* biological material, but of course *are* more than just biological material" (Dutch Parliament 2004, 23ff). This facile defense is rather disingenuous, however, as organisms clearly *meet* the definition of "biological material" given in the Directive and on that count must be held to *be* such material (besides, the Directive declares entire organisms to be patentable). There is no escape from the conclusion that in modern patent law plants and animals are being reduced to the status of raw material or carrier of genetic information. To some extent this even holds for human beings, although the human body and its parts have been expressly declared unpatentable – at least in their "natural state", because isolated human genes are patentable just like other isolated genes.[9]

Jane Calvert has moved the "co-construction" thesis one big step further by arguing, somewhat speculatively, that the requirements of intellectual property law may in their turn also influence the very *content* of science (Calvert 2008; Calvert 2010). She propounds the tentative argument that synbio is following a reductionist engineering approach to biology precisely, or at least partly, with the preconceived aim of making biological systems or parts of biological systems better conform to the characteristics of fungible "*commodities*", that is, "things" or objects of property that can be exchanged on the market. This aim is promoted by making biological parts discrete and interchangeable, by ensuring modularity, and by realizing reliable and predictable performance of the assembled systems: "In forcing biology into the mould of engineering, by developing discrete and substitutable parts, synthetic biology is simultaneously making biology better fit intellectual property regimes. This is no coincidence, because patent law developed in the context of industrial manufacturing … It is also consistent with the direction of biotechnology more generally, which can be seen as 'relentlessly pursuing the program of making every element of the world programmable or susceptible to engineering' (Pottage, 2007: 340)" (Calvert 2008, 392-93).

Calvert addresses an obvious objection against her sweeping thesis. How about the synthetic biologists of the BioBricks school who are enthusiastically creating a commons of standard

[9] Article 4 of the Universal Declaration on the Human Genome and Human Rights, adopted by the UNESCO in 1997, states: "The human genome *in its natural state* shall not give rise to financial gains" (my italics). Due to the added qualification "in its natural state", this article is completely toothless and meaningless. It is an empty gesture to defend human dignity that does not prevent the patenting of parts of the human genome by invoking the "isolation contrivance" (Palombi). By the way, how *could* you obtain financial gain from the human genome "in its natural state"?

biological parts? Aren't they precisely motivated to keep patents at bay as much as they can, rather than trying to lock up their materials and tools in exclusive property rights? Calvert recognizes that the BioBricks program with its stress on modularity and the use of interchangeable parts makes the biological components more similar to software code: "One advantage of modularity is that several different researchers can work on different parts simultaneously, meaning that the field can develop faster. In this way, *modularity is well-suited to open source principles*, and many synthetic biologists are ideologically committed to open source, to such an extent that the aspiration to make their work open source is a guiding principle of the field" (Calvert 2010; italics mine). Calvert points out, however, that open source itself depends on the existence of prior property rights, as in the case of free software where the GPL license is based on copyright: "Rather than being a substitute for intellectual property, open source is perhaps more correctly conceived of as a mosaic of private property [ref. omitted]. For this reason appropriation is just as important in open source as it is in more conventional property rights [ref. omitted]" (Calvert 2008, 392).

Calvert's point is formally correct, but also tends to inflate the influence of (intellectual) property norms on the content of biological science beyond measure.[10] Another critical point is her assumption that so-called "intellectual property rights" (here used as an umbrella term for patents, copyrights, trademarks, breeders' rights and the like) can indeed be considered a proper subset of property rights. The meaning of the term "commodities" in both contexts is quite different. In the economic world of Adam Smith and Karl Marx, "commodities" were first and foremost material goods possessing both use-value and exchange-value that could literally change hands on the market, or in other words, objects of real, tangible property (for Marx, "labour-power" was already a very special and exceptional "commodity"; it took a real *tour de force* to fit that notion into the framework of political economy). It has always been extremely difficult to see what the exact "object" is that is protected by an intellectual property right – such as a literary "work" in copyright law, or an "invention" in patent law. So much is clear that a "work" may not be identified with a particular copy of a book and an "invention" may not be identified with the concrete technical "embodiment" of the inventive idea. The "objects" of IP rights are rather to be seen as "abstract goods" (Drahos 1996). This would make them very spooky "commodities" indeed. In fact, they only become tradable "commodities" of sorts thanks to the granting of exclusive rights, that is, rights of exclusion – and not the other way around, i.e., they do not have to be "commodities" (in whatever sense) to fulfill the requirements of copyright or patent law.

The term "intellectual property" has only come into general use after 1970. The fact that a variety of disparate rights have been successfully lumped together under this general heading

[10] Amy Kapczynski makes a similar point: "The GPL, of course, also necessarily relies on copyright law for its effects, and it is now frequently pointed out that in this sense, its licensing scheme depends upon copyright law" (Kapczynski 2008, 877). For her, however, this is an illustration of what she calls "law's gravitational pull" and of the framing effect of the dominant IP frame on the adherents of the A2K frame. One is also reminded of the rather hilarious fact that the founder of the free software movement, Richard Stallman, was alarmed by the proposal of the Swedish Pirate Party to limit the copyright term to five years only, as this would also undermine free software (Stallman 2009).

is itself a sign of the "propertization" of IP rights (Lemley 2005). The uncritical, taken-for-granted use of the expression "intellectual property" has also contributed to the rise of the "IP frame" since about 1980 due to its powerful framing effects (Kapcynski 2008, 842 ff). In earlier times, the expression was used much more sporadically and not always with the same meanings that are nowadays attached to it. In Robert Merton's sociology of science, for instance, intellectual property rights primarily refer to the recognition and esteem, or academic "credit", which are due to scientific researchers who have made important discoveries, and surely not to any economic exploitation rights with regard to these discoveries (for a more extensive discussion, see Van den Belt 2010).

To show the historical contrast with an earlier century, I will quote extensively from a parliamentary speech of the Dutch Minister of Justice, Anthony Modderman, who in 1881 defended a new bill for the regulation of copyright (or authors' right) *by explicitly rejecting the very notion of "intellectual property rights"*:

> "All property rests on the possibility of a perfect physical possession; furthermore, it is also characteristic for property that its enjoyment by one person excludes or limits its enjoyment by another. […]
>
> Why do we say that the sea – properly understood, the *open sea*, not the coastal waters – is not susceptible to property?
>
> Hugo Grotius already taught us why. It is because the open sea does not lend itself to exclusive physical possession; also, because its enjoyment by one person does not exclude the enjoyment of it by another.
>
> The same holds, despite all other differences, for our divulged thoughts – in whatever form they may have been revealed.
>
> One may keep one's thoughts to oneself or one may express them; but once one has expressed one's thoughts, they become the common property [*gemeen goed*, literally "common good"] of all who have been willing to listen to us or to read us and who have absorbed these thoughts. Furthermore, the enjoyment or the benefit that one person derives from them in no way diminishes the enjoyment or the benefit that they may yield to someone else.
>
> You will understand the tenor of these remarks. They do not aim to dispute the awarding of a (temporary) exclusive right to reproduce the products of our minds. They rather intend to remove from the debate the false name of 'intellectual property right'; a name destined to lighten the burden of the opponents [of copyright protection]. What the Government defends is a right on its own; a right *sui generis*, to be assigned as such and to be regulated by law." (Auteurswet 2006, 59; my translation).

Minister Modderman thus argued that what is sometimes called "intellectual property" is not property at all. We can find echoes here of Thomas Jefferson's famous comments on the non-rivalry and non-excludability of ideas, which make them singularly unfit for property (Jefferson 1813). The government may grant temporary exclusive rights to protect literary works (copyright) or inventions (patent law), but such legal protection is *not* based on the (false) notion of "intellectual property rights". This was the view behind the so-called "IP

clause" (a retrospective name!) in the US Constitution of 1787 as well as the Dutch copyright bill of 1881.

Patents, health, and global justice

It is still too early to discuss the potential medical applications of synbio and the ethical and legal questions they would raise with regard to patenting in concrete detail. However, an intense international debate is already going on about the ethical implications of patents in the medical area in terms of the human right to health, access to essential medicines and global justice. As the discussion on the ethical aspects of medical synbio applications is likely to be placed into this wider debate, it may be useful to sketch the main outlines of this debate in the final part of this paper.

It was the worldwide HIV/AIDS crisis that raised widespread awareness about the morally problematic character of drug patents, especially when western pharmaceutical companies were at first emboldened by the TRIPS Agreement of 1995 to assert their enhanced IP rights with much more vigor than before. A temporary (20-year-long) monopoly on a new drug that a patent affords may help a pharmaceutical company to recoup its investments in research and development. The other side of the coin is that millions and millions of poor patients, especially in sub-Saharan Africa, are doomed to die prematurely while the patented medicines that could save their lives or at least alleviate their suffering are beyond their reach due to high monopoly prices (Forman 2007). Economist Joseph Stiglitz even compared the pharmaceutical companies with Scrooge, the repulsive character in Charles Dickens's *Christmas Carol*, because they seemed to care so much more for their sacrosanct IP rights than for the horrible fate of poor Africans (Stiglitz 2006).

As any economics textbook explains, a monopoly will lead to a static inefficiency or welfare loss that is known as a "deadweight loss". Because the monopoly price is so much higher than the marginal cost price, a patent monopoly on a drug will prevent transactions with all those potential users who are able and willing to pay more than the marginal cost but not the full monopoly price of the patented drug.[11] In the case of patents for essential, live-saving medicines, this "market failure" leads to morally unacceptable situations.

Since the turn of the century the situation with regard to HIV/AIDS has considerably improved, as a consequence of the heavy moral pressure exerted by NGOs like Oxfam and Médecins Sans Frontières on pharmaceutical companies to lower drug prices, the increased credibility of the threat of compulsory licensing in the wake of the Doha Declaration of 2001, and increased competition from generic manufacturers. In general, prices for HIV/AIDS medicines in developing countries have dropped quite drastically in the last decade.

[11] Grootendorst (2009) cites quantitative calculations that indicate that the dead-weight loss in the US pharma market may be no less than 60 percent of sales revenues, while other investigations show that the relative size of the dead-weight loss in developing countries might even be much higher. It is clear that, simply in economic terms, enormous amounts are involved.

Although NGOs hold that what has been achieved until now is not nearly enough, others might have doubts about whether continuing to put pressure on companies to lower their prices still further until they come close to the level of marginal costs is the right way to proceed in the search for solutions to global health problems. Pharmaceutical companies wonder why they are singled out for special treatment to contribute to the solution of a problem that they did not create. They also point out that it is incorrect to look at the prices of patented medicines only from a static point of view. After all, patents are temporary monopolies that are precisely intended as incentives to stimulate the search for new medicines. No patents, no innovation. Higher prices in the present (until the competition of generics after the expiration of the patent brings them down) are simply the "price" we all have to pay to enjoy the fruits of progress. A substantial erosion of price margins might well endanger pharmaceutical innovation. Finally, a strategy of *differential pricing* (i.e. charging low prices in poor countries and high prices in wealthy countries) is also not sustainable, as the low-priced medicines will easily find their way to high-income countries through smuggling.

The philosopher Thomas Pogge, who has thought long and hard about the working of the international patent system from the perspective of global justice, agrees that one should not consider the problem exclusively from the point of view of static efficiency but also take into account the dynamic role of the patent system to foster innovation (Pogge 2005). However, one cannot simply trade off dynamic efficiency (innovation) against static inefficiency (lack of access to existing medicines). Pogge insists that access to essential medicines is a human right that is to be secured by a just international system. This human right cannot be sacrificed on the altar of pharmaceutical innovation. Even more, when looked at from a dynamic perspective, the international patent system does not meet the requirements of global justice either: it generates innovations, indeed, but it does not generate the right kind of innovations. As financial incentives, patents operate by orienting research towards the needs of the wealthy and the affluent, that is, those who exercise effective demand backed up by purchasing power, and not towards the needs of the poor and needy who are unable to do so. The well-known "10/90 gap" illustrates this defect: "Only 10 percent of global health research is devoted to conditions that account for 90 percent of the global disease burden" (Drugs for Neglected Diseases Working Group 2001, 10). There are therefore many "neglected" diseases, especially in the Tropics, which fail to receive adequate attention from the international research community.

Pogge concludes that any proposal for a re-design of the international patent system in the field of medicines has to solve *two* problems simultaneously:

(a) The access problem (cf. deadweight loss)

(b) The availability problem (cf. the 10/90 gap)

Pogge has proposed his own institutional solution for dealing with these two problems, the so-called *Health Impact Fund*, which has been further elaborated with the help of others (see Hollis and Pogge 2008; Singer and Schroeder 2010). Whatever one thinks of the merits of

Pogge's reform proposal, he certainly deserves credit for bringing home so clearly that these twin problems define a major part of the task-set for any attempt at institutional re-design.

In Pogge's view, an international public fund based on obligatory contributions (mostly) from developed countries, the *Health Impact Fund*, should be established to create the possibility of rewarding pharmaceutical companies for developing essential medicines, the size of their reward being proportional to the impact of their invention on the global disease burden. In essence, the scheme means that companies are offered a choice. Once they have taken out a patent for a new drug, they can either attempt to earn money on it in the usual way by exploiting the monopoly and setting prices that affluent markets can bear, or they can choose the option of registering with the Fund and being rewarded according to a formula that is geared to the health impact of the new drug (measured in terms of QALYs). In the latter case the drug is made available to generic manufacturers who will offer it at a price slightly above production cost. The second option would entail a different *metric of success* for the drug company. Success will not be measured then in terms of net sales to those who can afford to pay the high prices of a monopolized invention, but in terms of the reduction of the global disease burden, irrespective of the purchasing power of those who suffer from it. In this way it is hoped that the Health Impact Fund will redress the existing imbalance of availability (epitomized by the "10/90 gap") by providing incentives that are not geared to purchasing power but to medical need. Competition from generic manufacturers will ensure that the problem of access is also addressed. (For a detailed exposition of the whole scheme, see Hollis and Pogge 2008).

Several commentators have questioned the political and practical feasibility of the Health Impact Fund. One critical issue is funding. The whole initiative needs initially some 6 billion dollars from governments or other contributors to take off. Will such funds really be forthcoming and can pharmaceutical companies base their long-term R&D decisions with any confidence on government pledges to provide funds over a longer period of time? "Providing public funds to drug companies is unlikely to be politically popular: competing demands will always seem more urgent and desirable" (Buchanan, Cole and Keohane 2009, 21). It has also been pointed out that the measurement procedure for assessing the impact of a new medicine on the global disease burden is rather complex, which would make the assessment vulnerable to corruption (Sonderholm 2010).

Here I would like to draw attention to another critical feature of Pogge's reform proposal, namely the notable fact that the whole scheme still relies very strongly on the "incentivizing" effect of patents.[12] The main problem with the present patent system, in Pogge's view, is that

[12] As Singer and Schroeder explain: "The Health Impact Fund leaves intact strong incentives for the pharmaceutical industry around the globe, thereby preserving the TRIPS advantages, whilst mitigating its main challenge, namely to block access to life-saving medicines to the poor. By registering a patented medicine with the Fund, a firm would agree to sell it globally at cost. In exchange, the firm would receive, for a fixed time, payments based on the product's assessed global health impact. The arrangement would be optional and it would not diminish patent rights, it therefore aligns the interests of pharmaceutical companies with the interests of poor patients. Such a win-win situation has to be welcomed!" (Singer and

the incentives are geared to (potential) market demand in wealthy countries that is backed up by purchasing power. The "trick" of Pogge's scheme is to leverage the unmet medical needs of the South by backing them up with additional funds, so that they too carry some weight in the market pull directing pharmaceutical innovation. It is all a matter of setting the incentives "straight" – but by the same token the scheme still counts on the role of patents as incentives.

The pharmaceutical industry is usually seen as a sector where patents are indispensible for innovation, due to high investment costs of R&D and the relative ease to reverse engineer any resulting product. Lately, however, the presumed "incentivizing" effect of patents even for the pharma sector is increasingly called into question. For one thing, the track record of the industry over the recent period is not particularly impressive (even apart from the global imbalance epitomized in the 10/90 gap). Official figures show that in the last three decades "the productivity of the pharma R&D enterprise – the number of new molecules brought to market per dollar spent on R&D – has declined markedly" (Grootendorst 2009, 2). This productivity slowdown occurred in a period when new technologies like genomics, combinatorial chemistry and knock-out mice were supposed to make the drug discovery process more rapid and more efficient. The conditioned reflex of the pharma industry to a drying pipeline of new inventions is to clamor for more patent protection, but the fact of the matter is that their wishes on this score have been answered rather well during the past decades. Ironically, some hard-boiled economic analyses locate the root of the problem in the patent system itself and the very high profit margins that it generates. Grootendorst sums up the social costs that are caused by the current system of pharmaceutical innovation centered on patents: (1) the costs to the healthcare system of medication non-compliance due to higher drug prices; (2) the resources consumed in the battle over the innovator's profits; (3) the resources spent by the innovator to expand unit sales and extend patents; (4) the increased costs of pharma R&D when this R&D builds on patented upstream discoveries; (5) the distortions in research direction caused by non-patentability of certain compounds; and (6) the administrative costs of the patent system (Grootendorst 2009, 32).[13] To this list can be added the unknown but most likely very considerable extent of bias and distortions in the medical literature due to widespread practices like "ghost management" and "publication planning" that result from the dominance of marketing imperatives over the research process (Sismondo and Doucet 2010).

Thus there is every reason to question Pogge's assumption that patents are indispensible as incentives for innovation. For the members of the "A2K" coalition there is, of course, nothing extraordinary in this conclusion. As Amy Kapczynski remarks: "The production process of free and open-source software is central to the imaginary of the A2K mobilization because it

---

Schroeder 2010, 17).

[13] In Grootendorst's paper, each of these rubrics of social costs is further specified and discussed in detail. A very interesting category is the second rubric. When a patent allows very high profit margins on a certain drug, this will attract others seeking their share of the spoils. A lot of effort is simply wasted on keeping these rent-seekers at bay: "The innovator will need to spend resources fending off counterfeiters, resellers, competing drug companies (both generic and branded me-toos), and negotiating with and lobbying price regulators and drug insurers …" (Grootendorst 2009, 32).

offers a model of collaborative, distributed innovation that does not rely on the incentivizing effect of IP rights" (Kapczynski 2008, 869-870). Another plank of the "A2K" platform is that "under no circumstances can human rights be subordinated to intellectual property protection" (Kapczynski 2008, 866). It seems that Pogge got stuck half-way between the IP frame and the A2K frame.

References

Andrews, L., and L.A. Shackelton (2008). Influenza genetic sequence patents: where intellectual property clashes with public health needs. *Future Virology* 3(3): 235-41.

Auteurswet (2006). *Auteurswet 1881: Parlementaire geschiedenis wet 1881 – ontwerp 1884*, with an introduction by M. Reinsma. Zutphen: Walburg Pers.

Bliss, M. (1988). *The Discovery of Insulin*. London: Faber and Faber.

Boyle, J. (2010). Monopolist of the Genetic Code?, May 28, 2010 (http://www.thepublicdomain.org/2010/05/28/monopolist-of-the-genetic-code/)

Buchanan, A., T. Cole and R.O. Keohane (2009). Justice in the Diffusion of Innovation. *Journal of Political Philosophy*, no. doi: 10.1111/j.1467-9760.2009.00348.x

Calvert, J. (2008). The Commodification of Emergence: Systems Biology, Synthetic Biology and Intellectual Property. *BioSocieties* 3: 383-398.

Calvert, J. (2010). Synthetic biology: constructing nature? In *Nature After the Genome*, edited by S. Parry and J, Dupré, pp. 95-112. Oxford: Blackwell.

Chan, S., and J. Sulston (2010). Patents in synthetic biology may hinder future research and restrict access to innovation. *BMJ* 340 (19 June 2010): 1315-16.

Drahos, P. (1996). *A Philosophy of Intellectual Property*. Dartmouth: Aldershot.

Drugs for Neglected Diseases Working Group (2001). *Fatal Imbalance: The Crisis in Research and Development for Drugs for Neglected Diseases*. Geneva: Médecins Sans Frontières.

Dutch Parliament (2004). *Kamerstukken I 2003/04, 26 568 (R1638), B* (Parliamentary proceedings).

Dutfield, G. (2009). *Intellectual Property Rights and the Life Science Industries: Past, Present and Future*, second edition. New Jersey etc.: World Scientific/

Editorial (1926). Ethics and Patents. *American Journal of Public Health* 16(9): 919-920.

ETC Group (2007). Extreme Genetic Engineering: An Introduction to Synthetic Biology (www.etcgroup.org).

Forman, L. (2007). Trade Rules, Intellectual Property, and the Right to Health. *Ethics & International Affairs* 21(3): 337-357.

Grootendorst, P. (2009). *Patents, Public-Private Partnerships or Prizes: How should we support pharmaceutical innovation?* University of Toronto, 22 September 2009.

Hammond, E. (2009). Indonesia fights to change WHO rules on flu vaccines. *Seedling*, April 2009.

Henkel, J., and S.M. Maurer (2009). Parts, property and sharing. *Nature Biotechnology* 27 (12): 1095-90.

Herper, M. (2006). Architect of Life: Drew Endy aims to reinvent the biotechnology industry. *Forbes*, 10 February 2006.

Hollis, A., and Th. Pogge (2008). *The Health Impact Fund: Making New Medicines Accessible to All*. Incentives for Global Health (IGH).

Jefferson, Th. (1813). Letter to Isaac McPherson, Monticello, August 13, 1813 (http://odur.let.rug.nl/~usa/P/tj3/writings/brf/jefl220.htm).

Jensen, K., and F. Murray (2005). Intellectual Property Landscape of the Human Genome. *Science* 310: 239-40.

Kapczynski, A. (2008). The Access to Knowledge Mobilization and the New Politics of Intellectual Property. *The Yale Law Journal* 117: 804-885.

Lemley, M. (2005). Property, Intellectual Property, and Free Riding. *Texas Law Review* 83: 1031-65.

Macfarlane, G. (1980). *Howard Florey: The Making of a Great Scientist*. Oxford: Oxford University Press.

May, C., and S. Sell (2006). *Forgetting History is Not an Option! Intellectual Property, Public Policy and Economic Development in Context*. Paper Birkbeck College, London, September 15, 2006.

Nordmann, A. (2007). If and Then: A Critique of Speculative NanoEthics. *Nanoethics* 1(1): 31-46.

Palombi, L. (2009). *Gene Cartels. Biotech Patents in the Age of Free Trade*. Cheltenham: Edward Elgar.

Pogge, Th. (2005). Human Rights and Global Health: A Research Program. *Metaphilosophy* 36 (1/2): 182-209.

Pottage, A. (2007). The Socio-Legal Implications of the New Biotechnologies. *Annual Review of Law and Social Science* 3: 321-44.

Rai, A., and J. Boyle (2007). Synthetic Biology: Caught between Property Rights, the Public Domain, and the Commons. *PLoS Biology* 5(3): 389-393.

Rifkin, J. (1984). *Algeny: A New Word – A New World*. Harmondsworth: Penguin Books.

Rutz, B. (2009). Synthetic biology and patents. A European perspective. *EMBO reports* 10: S14-S16.

Schwarz, J., and A. Pollack (2010). Judge Invalidates Human Gene Patent. *New York Times*, March 29, 2010.

Singer, P., and D. Schroeder (2010). *Ethical Reasons for Intellectual Property Rights Reform: A Report (D1.3) for Innova P2*. IGH Discussion Paper No. 7, February 16, 2010.

Sismondo, S., and M. Doucet (2010). Publication Ethics and the Ghost Management of Medical Publication. *Bioethics* 24 (6): 273-283.

Sonderholm, J. (2010). *Intellectual Property Rights and the TRIPS Agreement. An Overview of Ethical Problems and Some Proposed Solutions*. World Bank: Policy Research Working Paper 5228.

Stallman, R. (2009). How the Swedish Pirate Party Platform Backfires on Free Software (http://www.gnu.org/philosophy/pirate-party.html)

Stiglitz, J. (2006). Editorial: Scrooge and intellectual property rights. *BMJ* 333: 1279-1280.

Van den Belt, H. (2009a). Philosophy of Biotechnology. In *Philosophy of Technology and Engineering Sciences*, edited by Anthonie Meijers, pp. 1301-1340. Amsterdam: Elsevier.

Van den Belt, H. (2009b). Playing God in Frankenstein's Footsteps: Synthetic Biology and the Meaning of Life. *Nanoethics* 3: 257-268.

Van den Belt, H. (2010). Robert Merton, Intellectual Property, and Open Science. A Sociological History for Our Times. In *The Commodification of Academic Research. Science and the Modern University*, edited by Hans Radder, pp. 187-230. Pittsburgh: University of Pittsburgh Press.

Van den Belt, H., and A. Rip (1987). The Nelson-Winter-Dosi Model and Synthetic Dye Chemistry. In *The Social Construction of Technological Systems. New Directions in the Sociology and History of Technology*, edited by W.E. Bijker, Th. P. Hughes and T. Pinch, pp. 135-158. Cambridge MA: MIT Press.

Venter, J.C (2007). A DNA-driven world. The 32nd Richard Dimbleby Lecture. BBC One. December 4, 2007 (www.bbc.co.uk/pressoffice/pressreleases/stories/2007/12_december/05/dimbleby.shtml).

WIPO (2007). Patent issues related to influenza viruses and their genes. Working Paper.