

SYNTHETIC BIOLOGY AND ENGINEERING ETHICS WORKSHOP

National Academy of Engineering
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2nd Floor; Room 213

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RESEARCH QUESTIONS

■ FOR EXPERTS IN ENGINEERING ETHICS

- After reading the one-pager, can you come up with two questions focused on ethical issues that seem key to developing socially responsible synthetic biology?
- Can you also formulate one personal reflection about the shape that collaborations between engineering ethics and an emerging technology like synthetic biology should take?
- What activities and materials should have priority in ethics training in synthetic biology?

■ FOR EXPERTS IN SYNTHETIC BIOLOGY

- After reading the one-pager, can you come up with two ethics-related questions that seem key or unaddressed, or that you have encountered while practicing bio-engineering/synthetic biology?
- Can you also formulate one personal reflection about the shape that collaborations between experts in synthetic biology and experts in engineering ethics should take?
- What activities and materials should have priority in ethics training in synthetic biology?

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Deborah G. Johnson

Anne Shirley Carter Olsson Professor of Applied Ethics in the Department of Science, Technology, and Society in the School of Engineering and Applied Science of the University of Virginia

Two questions key to developing socially responsible synthetic biology:

Perhaps this is too obvious, but the central question has to do with understanding the uncertainties and risks of undertaking synthetic biology? Uncertainty is at the heart of anxieties about synthetic biology. Providing trustworthy accounts of the risk involved in this endeavor is important, but the daunting challenge is in managing the risks of use and misuse. In this sense, the big question is whether systems of accountability can be put in place that will protect humanity from the risks.

A second (more subtle) key question has to do with how synthetic biology is presented to the public. The meaning and significance of synthetic biology is, in some sense, still in the making. On the one hand, there is the worry that synthetic biology comes to be known as the equivalent of 'Franken Food'; on the other hand, it is important that scientists and engineers do not mislead the public. The public is becoming increasingly mistrustful of science (as they should). Thus, the synthetic biology community should consider how synthetic biology is public understood; are they "crossing lines that have never been crossed before"? are they creating Frankenstein beings? Or what? They also have to be careful about not overestimating the benefits or underestimating the risks.

A personal reflection about the shape that collaborations between engineering ethics and an emerging technology like synthetic biology should take:

Whatever shape the collaboration takes, there has to be recognition that both synthetic biology and ethics are moving targets. Both are fluid. As a technology or technologies, synthetic biology, like all developing technologies, isn't a fixed or already known set of techniques and know-how that studied in practice and regulated. Likewise, ethical concepts (in general and in engineering ethics) are also fluid. Although some fundamental ethical principles and concepts persist, their meaning often has variable interpretations and their application to new situations is often contested. This fluidity means that collaborating is a daunting challenge, though the collaboration offers the best opportunity for ethical perspectives to influence the development of the technology, i.e., while it is still in the early stages, while it is still 'in the making'.

Ideally the shape of the collaboration would involve synthetic biologists taking the lead and viewing the collaboration with ethicists as an opportunity, not a threat. For this reason use of the phrase “ethical boundaries” is problematic. It implies that the role of ethics is to constrain science rather than be part of it or even to lead science. Science is a social endeavor (funded and directed by government and private organizations, consisting of beliefs and practices that change over time) and as such consideration of the social implications of any particular scientific enterprise should be understood as an essential part of the undertaking.

Ideally the collaboration would lead to the development of a synthetic biology community that would institute practices that involve ongoing evaluation of the field’s social implications. I draw here on Wetmore’s piece on automobile air bag performance monitoring; he uses this as an exemplary case of engineers who don’t abandon what they develop once it is put into the marketplace. They continue to track and monitor performance, and make recommendations for future development [See: J. M. Wetmore, *Engineering with Uncertainty: Monitoring Air Bag Performance*. *Science and Engineering Ethics* 14 (2) 2008]. Ongoing monitoring and a system of accountability for the field of synthetic biology is what should be sought by the collaboration (and, of course, the monitoring should be done by those who do not have financial interests in the development of the field).

What activities and materials should have priority in ethics training in synthetic biology?

I don’t know the answer to this question. All I know is that the field of engineering ethics makes use of a set of concepts, a language, and lessons learned from past cases that allows one to think about and see technology and engineering in a particular way. The lens of ethics allows one to examine the implications of technological development with an eye to human values and to individual and social well-being. Engineering ethics is a discourse; a discourse involving engineering ethics and synthetic biology could facilitate an understanding of the implications of synthetic biology that could in turn influence how the technology develops.

Jim Kealey

Director of Molecular Biology at Amyris

Questions/reflections focused on ethical issues that seem key to developing socially responsible synthetic biology:

- What mechanisms are most conducive to establishing fruitful collaborations between social and natural scientists, to help transcend “catchy rhetoric” and add value for science and society?
- What ethical boundaries should govern enabling technologies in Synthetic Biology? Can we construct an “ethics meter” that measures societal concern for synthetic biology applications? Such a tool could help scientists and the general public gauge which activities rank low versus high in terms of societal concern. For example, the use of synthetic biology tools for manipulation of microorganisms might register lower on the ethics meter than manipulation of plants. The manipulation of plants might register lower than manipulation of mammals etc.

Personal reflection about the shape that collaboration between engineering ethics and an emerging technology like synthetic biology should take?

- Synthetic biology is sometimes described as an extension of genetic engineering technology. As a scientific discipline, genetic engineering has a long and safe track record and has been the subject of prior ethical scrutiny. To what extent should synthetic biology be covered under the genetic engineering ethical umbrella?

What activities and materials should have priority in ethics training in synthetic biology?

Materials and activities given priority: Case studies or examples of constructive collaboration between social and natural scientists would provide guidance for establishing a framework for future projects and outreach activities.

Michael C. Loui

Professor of Electrical and Computer Engineering at University of Illinois at Urbana-Champaign

Two questions about synthetic biology and engineering ethics that seem key to developing socially responsible synthetic biology:

- Engineering codes of ethics emphasize competence in undertaking assignments: engineers should practice only areas of technical competence, as qualified by education or experience. How can engineers participate in synthetic biology when they do not have the technical competence?
- Engineering is devoted to the economical production of safe and useful objects, to serve the public good. All engineering codes of ethics prioritize the safety of the public. Obviously engineers would strive to ensure the safety of any products of synthetic biology. When risks are poorly understood, and there are few standards for safety factors, engineers usually insist on safety features: for example, large containment vessels for nuclear reactors. Engineers also install monitoring devices, they collect data, and they introduce modifications to continually improve the safety of their products. How can engineers assist synthetic biologists when it is difficult to determine the risks, and when no safety standards exist?

Initial personal reflection on collaborations between engineering ethics and synthetic biology:

- Does engineering ethics have anything to say about synthetic biology? Does synthetic biology pose any new questions for engineering ethics?
- Synthetic biology is evidently not an engineering activity in the usual sense because
 1. The field seems to lack technical standards such as safety standards
 2. Practitioners do not hold professional licenses, which would certify that they have a minimum level of technical competence
 3. The experience base is insufficient to reliably estimate time and costs for large projects

The third point suggests an important distinction between science and engineering: the concern for economics and efficiency. This concern distinguishes synthesis in organic chemistry from process design in chemical engineering. Put another way, while engineering is characterized by the design and manufacture of new devices and processes, not all who create are engineers. I can build a tool shed in my back yard, but I am not a civil engineer. If you want to build a skyscraper, you need a team of engineers.

At this time, synthetic biology resembles synthetic organic chemistry rather than engineering design. Once synthetic biology reaches the point of large-scale production, with large expenditures for people and materials, it would become an engineering activity. To speculate on the ethics of engineering problems posed by production-level synthetic biology seems premature to me.

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Carl Mitcham

Professor of Liberal Arts and International Studies and Director of the Hennebach Program in the Humanities, Colorado School of Mines

Initial, provisional response:

– **After reading the one-pager, can you come up with two questions focused on ethical issues that seem key to developing socially responsible synthetic biology?**

Four qualifiers:

First, I do not yet know much about the synthetic biology field. I look forward to learning more.

Second, I am slightly uncomfortable with the term “expert” in engineering ethics (or anything else). Whenever I hear the word “expert” I remember my high school math teacher’s definition of an “expert” as a “former drip.” My preferred self description is as an interdisciplinarian. Indeed, I would argue that the core activity of ethics is interdisciplinarity.

Third, I am equally uneasy with the concept of “social responsibility.” As someone who was a draft resister in the 1960s, I can recall how the concept of responsibility was often used against me and others to try to quiet our protest of an unjust war. The practice of *irresponsibility* can be and often grows out of a commitment to truth or the good beyond the merely social.

Fourth, the term “synthetic biology” deserves questioning. During the 1970s there was some debate about the terms “synthetic” and “artificial” as applied to the results of scientific and technological research. One corporation published an advertorial in *Time* complaining about use of the term “artificial” (as in “artificial flowers” and “artificial intelligence”), with the connotation of “less than real.” Instead, the advertorial argued for a broad use of the term “synthetic” (as in “synthetic fibers,” “synthetic oil,” and “synthetic diamonds”) to replace “artificial” (especially in “artificial sweeteners” and “artificial chemicals”). We should, the argument went, use the more positive qualifier with weaker negative connotations. Humans were just being naturally creative when inventing new processes and products better than those found in nature. Synthetic materials (from steel to nylon) and pharmaceuticals (antibiotics, Tylenol, and more) were all argued to be both “natural” (because created by a naturally creative humans) and better than nature (because they helped humans live better). Recall the DuPont slogan: “Better things for better living through chemistry.” It is probably not accidental that a rhetoric of “synthetic biology” was chosen by the scientific community over “artificial biology” and that this successful branding has modulated public acceptance. (I note, however, that in at least one of workshop readings the artificial vs synthetic issue is alluded to.)

With this fourth qualifier in mind, one important question would thus focus on a critical analysis of the terminology: What is the basis for using the term “synthetic biology”? How did this develop? Are there more accurate alternatives? (This question is clearly related to one of the most fundamental questions in the philosophy of engineering: To what extent is engineering natural?)

As a second question, it would be appropriate to return to the issue of social responsibility: Do “synthetic biologists” have obligations to think beyond “social responsibility”? If so, how? What might this mean? (Again, this is simply a restatement in a new context of a fundamental question in engineering ethics concerning the character of responsibility in the engineering profession.)

– Can you also formulate one personal reflection about the shape that collaborations between engineering ethics and an emerging technology like synthetic biology should take?

Interdisciplinary collaboration is both increasingly important and complex (see Robert Frodeman, Julie Thompson Klein, and Carl Mitcham, eds., *Oxford Handbook of Interdisciplinarity* [2010]). Two persistent dangers:

- (a) Failure sufficiently to distinguish such different phenomena as multi-, cross-, inter-, and trans-disciplinarity (for all of which “interdisciplinarity” often functions as an umbrella term) and simply to invoke all interdisciplinarity as a good thing.
- (b) The coopting of one “discipline” by another. The latter may be a special problem in interdisciplinary collaborations between technoscience and ethics. The coopting works both ways. Sometimes a technoscience will try to use ethics to give it a clean bill of health for the public. Other times ethics will just try to flex its muscles with insufficiently informed criticisms of the technoscience. Both extremes need to be avoided. But how?

These two issues (and more) about interdisciplinary collaborations and how they work deserve extended exploration (with case studies) in relation to synthetic biology and ethics.

– What activities and materials should have priority in ethics training in synthetic biology?

Not sure. But again we ought to include critical reflection on the rhetoric used here: Ethics “training”?

There exists a serious tendency to dumb down ethics if not emasculate it. Training is very close to indoctrination. Some training may be appropriate, but it should be limited, and more important is the cultivation of critical reflection on any training that takes place – transforming training into education. Ethics should not be limited to the delivery of trade school or vocational propaganda.

The overview of “Ethical Issues in Synthetic Biology” by Erik Parens, Josephine Johnston, and Jacob Moses is especially good in this regard. The implicit argument for not limiting education to physical harms but including as well critical reflection on non-physical harms, deserves support. Indeed, the argument in this report for making explicit the linkages among synthetic biology, genetic engineering, nanotechnology, information technology, and other emergent sciences and technologies, would be good to make part of any synthetic bioethics education practice.

Furthermore, I’d suggest it might be worthwhile that in thinking about this question we at least revisit the argument from a report on *The Teaching of Ethics in Higher Education* (1980) that emerged from a study by the Hastings Center. The report – to which more than fifty scholars contributed – set forth five goals for university level ethics education:

- (1) stimulating the moral imagination,
- (2) recognizing ethical issues,
- (3) developing analytic skills,
- (4) eliciting a sense of moral obligation and personal responsibility, and
- (5) tolerating and resisting disagreement and ambiguity.

To what extent should these be the goals as well of any ethics and synthetic biology collaboration?

Two qualifiers from *Teaching of Ethics in Higher Education* that deserve emphasis: The report also argued that ethics courses “ought not explicitly to seek behavioral change in students.” Instead, ethics ought simply “to assist students in the formation of their personal values and moral ideals, to introduce them to the broad range of moral problems facing their society and the world, to provide them contact with important ethical theories and moral traditions, and to give them the opportunity to wrestle with problems of applied ethics, whether personal or professional” (p. 81).

Second,

Courses in ethics should respect the pluralistic principles of our society, acknowledging the variety of moral perspectives that mark different religious and other groups. Indoctrination, whether political, theological, ideological, or philosophical, is wholly out of place.... Although

students should be assisted in developing moral ideals and fashioning a coherent way of approaching ethical theory and moral dilemmas, the task of the teacher is not to promote a special set of values, but only to promote those sensitivities and analytical skills necessary to help students reach their own moral judgments" (p. 81).

This latter point appears modestly contradictory. In the name of rejecting indoctrination, is not a commitment being advanced to indoctrinate ethical pluralism? Would it not be better simply to affirm and argue for ethical pluralism as a basic good?

In the ethics of science and engineering it is useful to draw a distinction between critical reflection on "doing things right" (means) versus "doing the right things" (ends). The former tends to be the primary focus in ethics education (understood as training) in the technosciences. One may grant its importance. But it should not be pursued at the exclusion of the latter.

What kind of critical reflection on ends is possible in a pluralist, globalizing world context? A quotation from Gianni Vattimo is worth considering:

What I have said so far does not imply that philosophy [or ethics] ought to be cut off completely from science. Rather, it interests me greatly to learn what the impact is of certain scientific achievements, what has changed in the history of our existence, our culture, our human community in consequence. For me, the philosophy [and ethics] of science is basically, whether it likes it or not, a species of sociology or philosophy of culture.... Philosophical reflection on science should be historical reflection on the aftermath of the transformation of our existence by this strain of cultural activity. (*The Responsibility of Philosophy* [2010], pp. 51-52.)

Such reflection deserves to be included in both ELSI (Ethical, Legal, and Social Issues) in relation to human genome research and SEI (Societal and Ethical Issues) in relation to nanoscience and technology. In conjunction with genomic and nanotechnoscience, humans are in the process of remaking the world, turning it into an artifact. Surely it is crucial to reflect on the ways in which this is transforming not just the human condition but what it means to be human.

Brian Pfleger

Assistant Professor of Chemical and Biological Engineering at the University of Wisconsin-Madison

- After reading the one-pager, can you come up with two ethics-related questions that seem key or unaddressed, or that you have encountered while practicing bio-engineering/synthetic biology?

I think the major ethical question that we face as practitioners of synthetic biology is “what is life”? This question is a driver for the synthetic genomics studies mentioned in the one page write up and a fundamental question that motivates many researchers in various fields. The delicate nature of this question in relation to one’s spiritual or religious beliefs could lead to internal conflict, dramatic changes in regulation, public opinion, and/or the ability to conduct synthetic biology experiments. While synthetic biology is in its infancy, we must train new scientists to be conscious of the sensitive nature of addressing this question and how it can impact non-scientists and scientists alike. I have heard from colleagues who have described their work in synthetic biology to elected officials only to be chastised for “messing with God’s plan”. In my opinion, developing a consistent educational message that addresses the ethical concerns related with this issue is vital to the continued growth of synthetic biology as a discipline.

Others have described the impact of engineered microorganisms on the environment, so I will raise a security concern. The ethics of working with dangerous or even lethal organisms are well covered in biological disciplines, but not in engineering. Students must be exposed to what could happen if synthetic biology was applied to engineering select agents.

- Can you also formulate one personal reflection about the shape that collaborations between experts in synthetic biology and experts in engineering ethics should take?

I have not had a great deal of experience working with bioethicists or engineering ethics researchers. So, I cannot comment at this point on how best to collaborate with experts in these fields. Naively, I would like to say that students should possess an internal moral compass that steers them in the proper direction, but I recognize that this is not always true.

- What activities and materials should have priority in ethics training in synthetic biology?

Sensitivity to religious and spiritual beliefs, biosecurity, environmental impact.

Bruce Rittmann

Director of the Center for Environmental Biotechnology in the Biodesign Institute at Arizona State University

A few ideas about challenges and issues with regard to engineering ethics and synthetic biology:

- Traditionally, when engineers are taught about "engineering ethics," the focus is on their responsibility to serve the client with competence and honesty. Engineering codes of ethics are strongly slanted to this interpretation of ethics. A problem is that "client" can be and often is defined rather narrowly: the entity that pays for the service. Particularly for those of us who deal with technical aspects of environmental quality and public welfare, we have come to realize that the "client" often has to be viewed more broadly: e.g., the community, the nation, a functioning ecosystem. Should synthetic biology take off as a technology, those who practice it will be prudent to ask "whom do I serve?" The menu of alternatives will look like the list I just made. Conflict may arise among the different clients.
- Many of the potential applications of synthetic biology are BIG in scale. I am thinking specifically of producing feedstock for renewable energy or the chemical industry. In this case, BIGNESS itself is an issue of ethical concern. Even if the technology or its product is benign (even thoroughly beneficial), the fact that it is produced on a very large scale will mean that the technology has environmental and social impacts. This issue is not unique to synthetic biology, but it is not often deliberated as technologies move from emergent to worldwide. Did we contemplate at the beginning of the 20th century what would be the environmental and social impacts of widespread use of fossil fuels? Not really. (The impacts run the gamut of positive to negative, but are huge and are defining they way in which synthetic biology may be used.) What about the impacts of using synthetic biology (or anything else) to replace fossil fuels over the next 50 years?
- The last item on my mind is that whatever we do in synthetic biology in the realms of interest to me (e.g., renewable energy) CANNOT BE CONTAINED. The organisms we create with get out and about. They will interact with the rest of Nature. What should we do to predict the consequences? How can we deal with the inevitable uncertainty? How much effort ought we make to prevent the inevitable in order to assuage concerns?

Mariachiara Tallacchini

Professor of Philosophy of Law at the Law Faculty of the Catholic University of Piacenza (Italy)

“Meta-framing” and “re-connecting”: what is new in Synthetic Biology and what can be reflected on from the past?

As has already happened widely with biotechnology, the double rhetoric of the “everything is new” and “everything is the same” is also likely to be displayed with Synthetic Biology (SB). From time to time supporters and opponents of new technologies have argued for maintaining the continuum or for breaking with the past as reasons to support their positions.

There is important knowledge about past ways of framing the issues and of intervening that should be critically compared and taken into account in order not to be caught in the new v. old rhetoric; it is possible to try to really be more imaginative and open toward the challenges and opportunities of SB. It has been pointed out that “(e)very descriptive language, including those that are used to describe technical or scientific systems, is ultimately metaphorical; it carries a meaning and has an agenda” (De Lorenzo, Danchin 2008). These metaphorical

assumptions should be taken into account as words and concepts travel from descriptive to prescriptive contexts and languages (Stengers 1987).

This “new v. old rhetoric” is widely used for several purposes, from science and technology to ethics, law, and politics. It is also partially engendered by the different existing normative structures. For instance, in the European Union (EU), taking into account all the existing legal sources regulating scientific fields analogous to or potentially connected to SB, and thus to adopt the point of view of continuity, is a consequence of the “civil law” system requiring in advance the harmonization amongst Member States’ laws. The European Group on Ethics (EGE) document on SB, in fact, starts with a long list of relevant laws already potentially (although only partially) regulating the field (EGE 2009).

The same is not true of the US system, where the “common law” court-based approach (though partially modified by laws, technical guidelines, commissions’ opinions, etc..) has to some extent more freedom to experiment with new fields and is less bound to general harmonization.

However, even in light of the EU assumptions about the numerous laws covering different aspects of SB, such as advanced therapies in the medical fields, safety aspects of several products, contained use or deliberate

Questions:

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release of GM micro-organisms and organisms (just to mention a few), no provisions deal with the relationships or the gaps amongst the topics, and existing institutions (and the very structure of the EU Commission separated in Directorate Generals - DGs) are often unrelated and do not interact in a coordinated way.

In dealing with how to frame the novel features of SB and how to contextualize it within the existing techno-scientific and regulatory environment, my comments strongly relate to the interactions between the scientific and the normative levels, and to how they influence (or co-produce) each other.

Past techno-scientific and regulatory experiences should not be seen as forms of normalization or legitimation of SB but as opportunities to understand failures, missed lessons, etc..

Part of the new is also “dealing with the past”, namely the fact that SB is going to interact with existing technologies (and their normative counterparts), with already existing gaps amongst them, and with the complex larger techno-scientific, cultural, social and regulatory environments.

In these dynamic relationships between new and old, future and past, , I would like to propose the key-terms META-FRAMING and RE-CONNECTING to summarize my perspective on SB as my two main points/issues are concerned. In fact, both my general points refer to the importance, in the dialogue between “engineering ethicists” and “synthetic biologists”, to look at the implied and implicit assumptions lying behind their descriptive and normative frameworks. Though I can offer here only a few hints of a far more complicated discourse, I would like to suggest the following items:

1) the need to be aware of the metaphors and images used to represent the new innovative processes and products by looking at representations and images lying behind previous techno-scientific exercises to make sense of the “new” (primarily biotechnology both in the agro-food and medical sectors),- and to be aware of how these images have affected the normative imagination (ethical and legal) as to the setting of regulatory boundaries, and in thinking about safety/security, and intellectual property;

2) the need to reflect broadly on the normative and regulatory dimensions and on the existing normative tools. In general, I think that what needs to be stressed about the role of a normative framework is more about its “descriptive” potential to organize and facilitate knowledge, knowledge exchange, setting of standards, etc...more than about its “prescriptions/prohibitions,” an old but highly misleading conception of the law in this context. As far as ethics is concerned, we should reflect on what “ethics” is today, what kind of “tool” it has become in framing, establishing, and implementing values in different legal systems and with a comparative approach.

Though seemingly not focusing on ethical issues in SB and on collaboration between engineering ethicists and SB scientists, an awareness about the background and context for SB may be directly relevant to how ethical questions are shaped and how forms of interaction are established. In other terms, becoming aware of the assumptions in imagining both the techno-scientific and the regulatory domains is strategic to broadening our vision of SB.

1. Reflecting on how SB is represented and imagined: how mechanistic metaphors and images are going to structure the field and how are they also going to inform normative (ethical and legal) imagination?

SB seems to incline toward strongly endorsing mechanistic models about biological processes and products. These mechanistic representations are anything but new in biotechnology and genetic engineering, where metaphors or images or drawings constructed to represent new processes, products, and their potential effects have widely adopted mechanistic models.

Beyond the need to show the functioning of biological systems in a simplified way, these models also convey the implicit reassurance that these systems are reliable and under control, and that their behavior is predictable.

This reassuring effect has also entered regulations where it has been used as evidence for regulation to be in control of safety aspects.

As these images are becoming the maps of a new territory (SB), their rhetorical effect is even stronger, because, as SB territories do not exist yet, their mapmakers (cartographers) are in charge of mapping something that they are at the same time inventing.

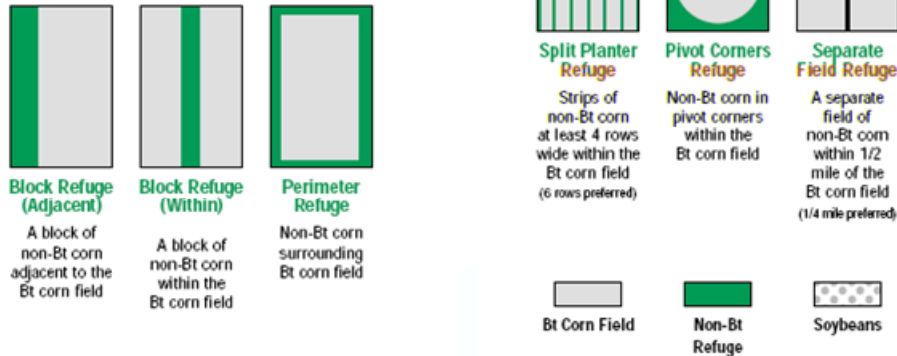
Some examples taken from biotechnology may illustrate how the visual dimension has been used to convey much more than specific functions (here, providing suggestions for GMO cultivation and a drawing for a patent application).

a) The case for containment

The representation of the contained use of GMOs by some groups of American Farmers is a nice example of the descriptive/prescriptive character of this strategy. In fact, while showing a variety of ways to isolate the fields planted with GM seeds with layers of trees, the image also gives a sense of an efficient, safe, and also beautiful use of a contested technology.



As illustrated below, the appropriate size non-Bt corn refuge may be planted a number of ways:



Over time several investigations have challenged the safety of these “beautiful geometries”. The most recent findings in North Dakota about the contamination of lands by GM canola (Nature news, August 6, 2010), may provide, along with other evidence, strong arguments against these misleading overlaps between maps and territories, models and reality.

b) The case for patenting organisms

Legal imagination has traditionally been strongly affected by mechanistic representations of reality, not only in regulating science and technology, but also in creating an objective and value-free image of its features and procedures.

Interesting examples are found in the patent domain, and especially in the attempt to extend patentability from mechanical inventions to “biological artifacts”. Drawings of the inventions for which a patent is claimed are enclosed among the filed documents. These drawings have to show the object of the invention. However, while mechanistic artifacts represent the object, in the case of engineered organisms, what is shown is only the representation of the engineering process, and not the organism as such. Of course, the implicit assumption here is that the organism can be reduced to the genetic modification because nothing else is going to change except for the directly-engineered sequence. However, that this is the case was more a matter of hope and persuasion than a mere self-evident statement, and the mechanistic representation of the Oncomouse was strategic in this respect.

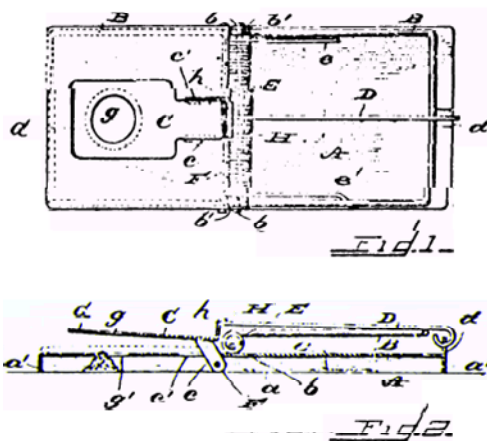
In 1989, almost coincidentally with the release of the first US patent on a complex organism, the Oncomouse, the Office of Technology Assessment published the report “Patenting Life” (OTA 1989). In order to stress the analogy between mechanical and biological inventions, and

thus the inevitable patentability of organisms, the OTA showed, side by side, the two drawings accompanying, respectively, the Mousetrap (patented in 1900) and the Oncomouse. And certainly the effect that the two different representations convey is that they are strongly similar and, therefore, that the real inventions presumably also share the same “nature”.

This legal representation of the Oncomouse as a “bioartifact” is a “normative description” for two different reasons. It not only simply assumed and did not discuss whether its premises were acceptable: its correspondence to what was actually done (no precise gene insertion but random microinjection in the embryos); the absence of interactions among genes and at the more general physiological level; etc...

It also suggested that, given the Oncomouse’s essential reducibility to a mechanical representation, it could by analogy be patented as the mousetrap was.

Figure 1-2-Figures, Mousetrap and Mouse Patents



Above--Two figures were submitted for U.S. Patent No. 661,068, the mousetrap, which was issued in 1900. The invention is “a trap of simple construction which can be manufactured inexpensively” in which “the bait cannot be removed without releasing the engaging jaw.”

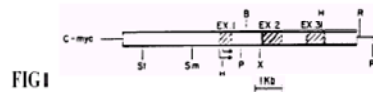


FIG 1

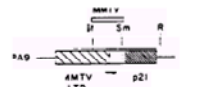


FIG 2

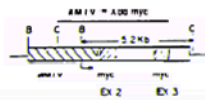


FIG 3

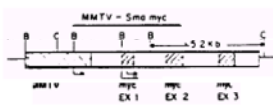


FIG 4



FIG 5

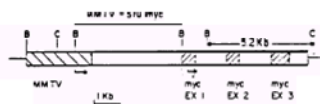


FIG 6



As is well-known, the patentability of complex organisms was not accepted by the Canadian Supreme Court which directly contested the mechanistic representation of reality lying behind such representations (). The Canadian justices proposed instead an organicistic vision implying that the inventor lacked complete control and the ability to reproduce the Oncomouse, as in organisms A+B+C lead to a variety of potential combinations which cannot be known in advance. The main differences in terms of protection are the patentability of the

process and not of the product, the impossibility of applying the concept of “composition of matter” (contained both in the US and in the Canadian patent law) to an organism, and therefore the necessity for public participation and dedicated new legislation in order to modify the existing provisions.

The mechanistic representations of “biological inventions” in the patent domain and generally in Intellectual Property Rights (IPRs) domains have broader consequences beyond those limited to the protection of innovation. In fact, patentability and safety aspects have been, at least in the US and the EU legal systems, strongly associated and reinforcing each others. Patenting, as it implies control of the patented invention, helped promote thinking that bioartifacts were safe.

But also, the rejection by the Canadian SC of the mechanistic epistemology has led to two different epistemological-legal models that are now competing at the transnational legislative and courts levels.

I will say something more about the role of normativity (and legal normativity) in co-producing the way we imagine and construct realities. My point here concerns the powerful implications of mechanistic representations and how they can also be endorsed by laws and can limit legal imagination.

c) The principle of substantial equivalence

Also, some normative elements should be rethought as depending on these kinds of mechanistic assumptions.

Though not directly expressed and exposed through images, the principle of substantial equivalence is another example of a “heuristic” established under mechanistic assumptions. Substantial equivalence refers to reducing a novel engineered food to an existing conventional one, by comparing some of their common features.

Does SB also involve rethinking the “principle of substantial equivalence” adopted in the GM field (endorsed primarily in the US)?

What failed about the mechanistic model of control? What might be rethought and revisited?

Does SB involve rethinking about precaution ?

There is the need for broader and multiple forms of imagination and representation, other than the mechanistic one. Not being caught in just one imaginary (Wynne et al. 2007; Jasanoff, in press) is strategic to feed alertness about the limits of our imagination.

2. Rethinking normativity, between description and prescription

In some SB literature the assumption is often made that the legal dimension is concerned with limitations and prohibitions (as to scientific freedom of research, experimentation in new fields, etc...).

However, today the roles of the law and of a regulatory framework are wider and call for innovation. First of all, a normative framework has to deal with prescriptive provisions as well as with the definition of the field and with the organization of all relevant knowledge: what counts as knowledge and who is going to define it, how to collect it, how to transfer it, what has to be made public, etc...

These functions about the “legitimate knowledge” that has to be taken into account have been explored and also criticized in the construction of risk- and precaution-related regulations, where, for instance, the concept and the model of an “extended peer-reviewed” knowledge has already been proposed (Funtowicz 2010).

However, as ethics is concerned, in ethical discourses, as ethics committees are usually limited to the analysis of “ethical implications” of science and technology, scientific knowledge is often assumed as a given and is rarely challenged.

The cognitive domain should therefore be broadened for both scientific and democratic reasons. Collecting all relevant knowledge from all relevant social sources for decision-making purposes, as Funtowicz has suggested, represents a requirement from both a democratic and a scientific perspective.

Also, an important part of a “constitutional” approach consists of organizing the different sources of normativity, comparing the different existing normative frameworks, opening up to new ways of harmonizing new activities and actors with new forms of protections. Ethics, for the reasons summarized below, also needs to be relocated and reshaped in this more complex normative landscape.

2.1 Reconnecting separated normative domains

Synthetic Biology (SB) provides a unique opportunity to rethink the domains of human (primarily medical), animal, and environmental ethics in connection with each other. Even though this interrelated perspective had been envisaged (maybe naïvely) in early bioethics reflection (Potter 1975), the disciplinary boundaries and the spheres of influence built to separate medical ethics from animal and environmental ethics on the other side, have de facto disconnected the potentially related domains. The ultimate goal of this understanding of bioethics was “not only to enrich individual lives but to prolong the survival of the human species in an acceptable form of society” (Potter 1975, 67).

The individualistic character that, for well known and understandable reasons, framed most bioethical approaches has become through time a major obstacle to connecting and making sense of biomedical technologies where individual rights have to be harmonized with collective rights and public health needs. In this respect, the attempts to elaborate models to allocate rights and risks in xenotransplants may provide insights and lessons for the current understanding of potential challenges involved by SB (Tallacchini, in press).

The early development of biotechnology offered another chance for taking into account the relationships and inseparability between what was happening in the laboratory and the potential effects on the larger environment. But the willingness to show that technology is under control has led to formulations (including legal formulations) where the separation between “contained use” and “deliberate release” (e.g., as in the European Union’s directives) is taken for granted.

2.2 Meta-framing safety: reconnecting individual rights and public health protection

The global spread of several infectious diseases in the last fifty years, the majority of which has been caused by cross-species pathogens (Jones, Patel, Levy 2008), and the more recent lasting fears about influenza, especially about avian flu, is giving rise to a sort of “paradigm change” in bioethics. In fact, a number of bioethicists have started talking about the need to invent an ethics for pandemics, a so-called “pandethics” (Selgelid 2009), that is not simply reduced to the draconian necessities of “legal preparedness”. These authors have outlined how bioethics (for well known historical reasons) was framed according to individualistic approaches which now appear inadequate when confronted with public health needs. Pandethics is about confronting and harmonizing individual rights and collective safety. However, it may imply the ethical justification for application of compulsory and restrictive measures to individuals as they become a risk for the community.

Interestingly, contributions to the new field discuss pandemics and pandethics without making any distinction between “naturally occurring” and “technology-related” emerging infections, suggesting that the same control strategies and measures should apply whenever these situations appear. However, even if this may be the case once an emergency is already in place, it is hard to think of it as a general condition for ethical approval and legitimization of new technologies.

These reflections may apply to SB as the potential for spreading new pathogens is a main concern in synthetic biology as well whether the spread is accidental, intentional or any possible combination between chance and willingness, as the actual separation between safety and security is far from clear here.

In this context, the case of xenotransplantation (the use of cells, tissues and organs from nonhumans in humans) (XT) is directly relevant here as an existing resource to reflect on. Xenotransplantation is today in the unique position of having encouraged the exploration of schemes for public health protection which do not suppress individual rights.

One main concern about performing clinical xenotransplants is the risk of transmitting pathogens (and creating new pathogens) from the animal source to the human recipient and to the general population. XT represents the most prominent case of a technology whose implementation required compromising and theorizing acceptable trade-offs in order to maintain individual rights while keeping safety conditions for the public. Because it can involve the transmission of infections, XT breaks the common rules of individual informed consent, by asking patients, in conditions of uncertainty about potential risks, to accept giving up some of their rights. The threats to collective safety that known or unknown infectious agents (so-called xenogeneic infections) may spread to the population at large not only require new ways of thinking about individual and collective rights, but also represent a challenge for bioethics in individually-oriented liberal democratic societies.

In this respect XT has involved almost unique regulatory exercises aimed at harmonizing and combining in general frameworks the individual medical dimension, the public health level, and concerns for animals and the environment. Also, XT represented the first domain where the application of the precautionary principle was evoked outside environmental issues (Nuffield Council 1996).

At the beginning of the 21st century, as conditions for the delicate passage from preclinical to clinical trials seemed near, different regulatory frameworks were developed to normalize XT, primarily by mitigating the potential risks of infections while protecting involved subjects. Different legal and policy approaches to XT were framed in that period. These include the US (2001), the European (Council of Europe and European Union) (2003), the Canadian (2002) and the Australian regulations (2004) (the last two as variants of the same model). Each used a different strategy to build XT as a socially acceptable and legitimate technology, by reciprocally adjusting science and norms. Each model speaks politics as well as science. Without entering into a detailed description of the models, a few hints about them are useful to show how they can be lessons from which to learn.

At stake in the US regulatory model was the maintenance of a coherent, contractual, liberal vision of society, namely how to make the unknown effect of XT compatible with a legal framework based on individual rights and responsibilities. In the European Union (EU) and Council of Europe (COE) model, the paternalistic and vertical structure and construction of Europe, still based on national sovereignties, combined with the need to boost European competitiveness was the prevailing reason for invoking and applying the precautionary principle not toward the potential risks of technology, but against the patients' dangerous behaviors by legitimizing the concept of patient's "lawful detention" and consent to "waiving some fundamental rights" (COE 2003; European Commission 2001). In the cases of Canada and Australia, a partial attempt to cope with potential infections by involving citizens as responsible lay experts was made as an effort to integrate the realities of state and society in a renewed idea of democracy. However, eventually both governments stepped back from thoroughly endorsing this reform.

In these mixed scientific and political contexts and reasons, the relationships between facts and norms were anything but linear. In the US case, in order not to disrupt the individualistic, liberal political model, the legal imagination about potential infectious diseases was framed around HIV, namely a pathogen whose spread is highly controllable based on responsible individual conduct. Of course, the same could not be said if the imagined pathogens were airborne diseases such as SARS and Ebola. These kinds of epidemic threats directly call for constraints and public health safety measures. But assuming that safe conditions for implementing a new technology imply the suspension of fundamental rights would obviously have been socially unacceptable. Therefore, a quite disputable scientific assumption, namely HIV as the default pathogen informing the guideline on safety, was adopted to normalize and legitimize the practice of XT.

Certainly AIDS was a relevant scientific model, especially at that time, as knowledge acquired about how to alert, organize and control the more exposed communities constituted an important learning experience about infectious diseases. However, using HIV as a general model for disease transmission reinforced the assumptions that epidemics can be managed and controlled through educating individuals, and is completely compatible with a frame of rights and responsibilities.

The case of XT also shows how complexities concern not only the uncertainties about new technologies, but also the complexities of the environments where they are going to be implemented. Not only SB, but most so-called 'advanced therapies' already represent and can be defined as "garage biology, as they may happen in non-sophisticated technological contexts. Just to provide an example, almost at the same time as when the first cases of H1N1

started manifesting in Mexico, a clinical trial with swine pancreatic islets was proposed to the Mexican government. It is well known that countries which already have poor public health and general safety conditions (which are also likely to be connected to inadequate rights protection) become the sites for inexpensive experimentation with new technologies ().

**Meta-framing safety:
re-connecting individual rights and public health**

	Science policy model	Imagined infection	Measures adopted	Main actors	Role for public	Political vision
US	Science-based policy	HIV	Individual Right/ Responsibility	Sponsor/ Patient	Transparency	Liberal
EU	Policy-related science	Airborne infections	Precaution against patient	Government	Public health	Sovereignty
CA/AU	Extended peer-review	Airborne infections	Precaution toward technology	Citizen scientist	Scientific citizenship	Participatory democracy

2.3 Reframing ethics: what is “ethics” and what normative source has it become?

The vision of the ethics undertaking as “the determination, so far as that is possible, of what is right and wrong, good and bad, about the scientific developments and technological deployments of biomedicine” (Callahan 1999, 276) has accompanied and justified the rise and role of ethics as a means to improve the rationality and the rationale of public decisions in the domain of life sciences and technology.

The institutionalization of ethics through ethics commissions and committees, namely appointed bodies with consultative and administrative functions, has been seen as the beginning of the blurring of boundaries between a supposedly rational programme and a practice to implement political will (Galloux et al. 2002). In fact, the creation of ethics committees and commissions as a method for decision-making produced a radical transformation of the fundamental needs for a public ethical discourse in modern democracies, namely a more intense and open dialogue between science and society.

What really counts as relevant socially acceptable behaviors, what people care about and may be responsible for, has often been discussed and decided in quite restricted circles, far from any forms of participation. The recent fate of the concept of privacy may provide a good example. After having dominated ethical discourse for decades (with no concern for the degree of actual public interest in it) the idea of privacy has become much less ethically fashionable --at least in some fields and primarily in the European context) as the needs to make biobanks freer in using biological and genetic data and to safely dispose of human tissues have transformed availability (described as solidarity) and traceability of biological materials and information into higher priorities. The very same supporters of privacy as the main expression of the autonomy of the subject are now arguing that autonomy implies solidarity, namely giving up privacy for the sake of medical progress.

If the criticism of bureaucratized ethics as a governmental instrument—more of government than of governance—is now widely recognized, still under-examined are the questions about what kind of “normative tool” “ethics” has become, namely what is its statute within the formal sources of normativity in the State under the rule of law. In Europe, as “ethics” is formally dependent on the principle of subsidiarity, namely on Member States’ sovereign power, European citizens are de facto subjected to “State-sponsored” or “government-sponsored” ethics. This is no different from what happened in the US in the case of public funding of stem cell research.

In this respect I strongly agree with Rabinow’s criticism of the word *ethics* itself (Rabinow 2010), as a key-term that is now limiting more than enhancing our imagination about how “human choices and practices” are evolving, where they are going, and how they will be negotiated/deliberated about within similar and throughout different world regions.

The abstract starting points and the concrete outcomes of the ethical discourse have become contradictory. Theoretically informed with the (unrealistic) assumptions about its universality (even when limited to professional domains) and rationality; and supposedly performing the functions of representing public choices and of being politically-neutral expert judgment, ethics has actually evolved into a power to create and implement “values” (Tallacchini 2009). In order to be helpful as a soft law tool and not to lose its credibility, “ethics” needs to be rethought and reframed.

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