Connecting Philosophy, Science and Sociology through Example: Weak Emergence and Computation
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The whole-versus-parts debate is a longstanding discussion in philosophy that has broad social relevance. This tension can be seen in how we conceptualize living organisms: are they a collection of cells programmed by DNA or is there something to be learnt from looking at the capacity for these cells to form organs, systems and organisms? Since the relationship between wholes and parts applies to the nature of explanation, the structure of scientific theories and so forth, it is a genre that has flourished within the philosophy of science and interested many outside the academy. I put forward the example of emergence as a case for how themes in one discipline can be used to reach out to other disciplines and hold appeal for the general public.

One aspect of the discussion of whole-versus-parts is the concept of emergent phenomena. Emergent phenomena are events that occur at high-levels within a system and are unpredictable from the lower-level components of the system. Note that ‘what constitutes a level’, the ‘number of levels’, what is a high relative to a lower-level, are all dependent on the system. The designation of what determines a system is also context dependent and can range from atom to organism. Emergence is also used to describe human behaviour.

The relationship between high-level emergent phenomena and lower-level parts is a matter of debate that has resulted in two main categories: strong and weak. The argument between strong and weak emergence regards whether or not higher-level phenomena can be reduced to lower-level phenomena. Strongly emergent phenomena are described as being irreducible whereas weakly emergent phenomena can be reduced to lower-level components. Reduction is the defining distinction between the two emergent categories and has led to conflict within the emergence literature and how we discuss living organisms.

The reason philosophers keep returning to emergence is because it offers potential to reconcile basic philosophical discrepancies between higher and lower-level parts. From an alternative perspective, contemporary theories of emergence actively critique classic reductionism but what ought to be even more compelling is how systems biologists can contribute to philosophy by providing us a means to forward our own understanding of the concept. This not only gives a novel view of the issue, but acts as a way for philosophy to connect with other disciplines including science and sociology.

My research supports philosopher Mark Bedau’s notion of computation\(^1\) for reduction while moving forward his claim that computation is a way to enlarge the category of weakly emergent phenomena by giving two examples. The use of computation is a reflection of the relationship between technology and knowledge which is directly related to what we value and prioritize as research worthy.

i) **Distinguishing between Strong Emergence and Weak Emergence**

An effective way to deliberate about the definition and potential of weak emergence is to consider the limitations of strong emergence. A classic example of strong emergence is consciousness. Consciousness does not seem predictable from lower-level atomic reactions and appears to be impossible to trace back to this lower-level. In the case of strong emergence, the relationship between higher-level and lower-level phenomena is not reductive and so does not have a complete mechanistic explanation.

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On the contrary, the defining characteristic of weak emergence is that it is reducible to lower-level elements. Classic examples of weakly emergent phenomena are the flock formations of birds and the swarming behavior of insects. These patterns are novel, but explicable. Though these high-level phenomena are reducible to the movement of their individual parts, they remain unpredictable from the starting conditions of the system. As a result of this reduction, it is possible to have a mechanistic explanation of the relationship between higher-level and lower-level phenomena. Depending on the degree of complexity of the higher-level phenomena, computational assistance in the form of mapping interactions or tracking elements may be required for the reduction.

Discussions of consciousness and flock formations along with other emergent phenomena have implications across disciplines. Emergence can serve as a concept to promote cross-disciplinary work and engagement with the public because of the familiar examples it describes. Thus, emergence lends itself to assessment through various philosophical, social, technological and scientific lenses.

ii) The Connection between Examples (philosophy) and Explanation (science)

What is valuable about a mechanistic explanation is that it is subject to empirical testing. Strong emergence cannot be reconciled with empirical investigation because the fundamental irreducible feature of strong emergence produces an explanatory gap that distorts causal relationships. The explanatory gap is the area between the higher-level emergent phenomenon and the lower-level parts of the system through which a reductive relationship cannot be constructed.

I look at examples in proteomics because biological organisms have complex top-down and bottom-up relationships many of which, like consciousness, are thought of as strongly emergent. Instead I argue that these phenomena are actually weakly emergent. This is important socially because of science’s role in the public perception of explanation and justification.

iii) The Relationship of Synthetic and Systems Biology to Emergence

Since several proteins are able to perform multiple tasks depending on the environmental conditions of the organism, tracking their interactions can be challenging. However, computation has allowed systems biology to map and track these proteins at this higher-level as well as verify these lower-level relationships by using synthetic biology to enhance or delete certain genes to test the integrity of the system. The higher-level systems’ interactions of the proteins are reducible to the lower-level synthetic markers in the organism making this method of verification weakly emergent. What is most interesting is that scholars like Bar-Yam (2004) and Boogerd et al. (2005) have mistakenly used similar proteomic examples as strongly emergent which suggests there might be several other examples thought to be genuinely strongly emergent that can be reduced through computation and considered weakly emergent.

I propose that weak emergence is able to reduce novel higher-level phenomena to lower-level phenomena with the assistance of computation which can significantly reduce the number of strongly emergent phenomena and show the category of weakly emergent phenomena to be much larger than initially believed. Specifically this can have a societal impact on how we view reductionism; but more broadly, emergence shows how philosophers can connect across disciplines and discuss matters relevant to the general public.

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Experimental Collaborations
Jane Calvert and Emma Frow, University of Edinburgh
(Owing much to discussions with Andrew Balmer, Susan Molyneux-Hodgson, Claire Marris, Morgan Meyer and Matt Kearnes.)

We are social scientists who work closely with synthetic biologists, and in this short paper we argue for the value of a certain type of interdisciplinary collaboration: one that is experimental and emergent and has the potential to create new knowledge. We think that this type of experimental collaboration should be more actively supported and resourced.

As researchers in Science and Technology Studies (STS), our desire for more experimental collaborations is partly a response to our observation that discussion of the ethical, legal and social implications of synthetic biology in policy reports has become calcified around a pre-defined list of ‘issues’ (such as biosafety, biosecurity, intellectual property, and public engagement). This continued re-articulation of a small number of ELSI concerns has set up a division of labour and responsibility that we think does not encourage genuine interdisciplinary collaboration, but positions ELSI in a service role to scientists and research funders. Our proposal for slightly more radical, less instrumental collaborations may help to establish partnerships that can ‘open up’ entrenched problem-solution framings, and suggest more creative ways forward.

So what would these experimental collaborations entail? We are contributing authors on a forthcoming paper that proposes the following: “Much like experiment in science, we must be adventurous and playful, willing to explore the unknown, tinker with our practices and be resilient in the face of failure” (Balmer et al. forthcoming). Experimental collaborations are necessarily risky and carry with them high levels of uncertainty about both processes and outcomes, but an activity that is risky also has the potential to be thrilling.

We think that examples of such experimental collaborations can be found in the Synthetic Aesthetics project,1 which brought together six synthetic biologists with six artists and designers in paired exchanges. The pairs were tasked with investigating design and synthetic biology, with the explicit freedom to take their work in any direction they chose. The artists and designers spent two weeks in the science laboratory, but, significantly, the exchanges were reciprocal, so the scientists and engineers spent an equal amount of time in the art/design studio.

The pairs had to identify questions that were of interest to them both. For example, one pair decided to look at synthetic biology from the perspective of geological time (the sweep of which extends from the beginning to the end of the Earth). This radical shift in our temporal perception of synthetic biology raises issues of humility and hubris in challenging and unconventional ways. Another pair made cheeses from the bacteria that grow on human skin. They used this playful project to argue that cheesemaking is a more appropriate metaphor for synthetic biology than computer engineering, since it draws attention to “complex living worlds performing incredible feats of metabolism” (Agapakis and Tolaas 2014, p.282).

These joint projects were between synthetic biologists and artists and designers, but we think that we can learn from them to inform collaborations between synthetic biologists and social scientists, although we may have to change some of our methodological habits.

We believe that to engage in experimental collaborations as social scientists it is necessary to think with scientists and engineers instead of making studies of them (see Ingold 2013). We will have to shift from seeing synthetic biologists as our ‘informants’, to thinking of them as our
‘epistemic partners’ (Holmes and Marcus 2008) – as people with whom we can create new objects, new practices, and new knowledge (Barry et al. 2008). This may require that we come to see ourselves as participants rather than spectators in synthetic biology, and face up to our complicity and the fact that we become part of the fields we study.

We do realise that there are considerable challenges to setting up novel forms of collaboration between social scientists and synthetic biologists. Rabinow and Bennett (2012) have shown how they had to confront issues of power, control over the research agenda, and divergent expectations from both scientists and research funders. Reflecting on their experiences, and our own, we think that for experimental collaborations to be successful they need to possess certain features.

First, time needs to be devoted to developing and articulating topics of shared interest. Being ‘tacked on’ to an already-defined synthetic biology research grant does not facilitate the kind of “inventive problem making” (Michael 2012, p.539) that we advocate here. Our experience in the UK suggests that developing shared concerns can happen through a process of spending extended periods of time with the same scientists and engineers. In our case, this was facilitated through our involvement in a multi-institutional UK research network called SynBioStandards (from 2008-2011), which was funded to build relationships rather than produce specific outputs.

Second, experimental collaborations should not be primarily motivated by instrumental aims; they should not be driven by a top-down political agenda or demand pre-defined deliverables. If a large flagship research programme depends on the success of a collaborative activity, where ‘success’ has already been defined according to measures like industrial investment, patents, new biosafety proposals, etc., then there is little scope for experimentation.

Importantly, these types of collaboration also require certain dispositions on the part of all those involved. Social scientists, natural scientists and engineers need to be willing to challenge their own assumptions, and respect unfamiliar epistemologies and methodologies. Research funders also have to be open to investing in activities where the outcomes are not necessarily obvious from the outset, but emerge from the process of collaboration itself. Experimental collaborations may also require the creation of new physical (or virtual) spaces to facilitate discussions across disciplines and professions (Reardon 2013). These may have to be neutral spaces, not clearly associated with scientific (or social scientific) work.

We realise that these are not the only types of collaboration that we and other social scientists will engage in, and that they are not always necessary or appropriate. But we think that experimental collaborations have the most potential to challenge the narrow ways in which ELSI research is often framed, and stimulate more unexpected and creative thinking.


1 Funded by the NSF and the EPSRC. See www.syntheticaesthetics.org
2 Funded by four UK research councils. See www.synbiostandards.co.uk
Towards Imperfection: Science Communication, Dialogue and Interdisciplinarity in Synthetic Biology

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This paper is concerned with the form that collective reflection on synthetic biology should take. It draws on our experiences working with natural scientists and project managers in synthetic biology to develop an interactive, dialogic – but also informative – installation in order to reflect on the challenges and opportunities that such interdisciplinary work presents.

We take as our starting point for this paper the understanding that synthetic biology is an exciting field of research, but that there are a diverse set of imaginaries of how this field can and should be used to make a better society (Balmer and Wood 2008; Yearley 2009). In order to develop the field in a robust way, we need to make sure that all of these imaginaries are heard and taken into consideration.

We therefore take for granted that synthetic biology, in its practice and policy, should be ‘opened up’ to broad societal debate (Stirling 2008). It should be interrogated from a wide range of perspectives, including those from lay publics, diverse stakeholders, the humanities and social sciences, and the natural sciences themselves (Balmer et al 2012).

Such an integrative agenda is, however, highly costly for all involved, with regard to finances, time, personal comfort, and intellectual autonomy. It places significant demands on individuals and research projects, may be read as intrusive by natural scientists and uninteresting by lay publics, and calls into question the very nature of interdisciplinary engagement (Fitzgerald et al 2014; Rabinow and Bennett 2012). Previous experience – with synthetic biology and other emerging technologies, as well as with European moves towards the use of frameworks for ‘Responsible Research and Innovation’ (Koops et al in press) – indicates that such integration will be difficult to establish top-down.

Our central argument is that we need to acknowledge the challenges that integration presents. It is important for ‘us’ (here: social researchers and policy makers) to take into account that we are working under conditions that preclude ideal-type deliberation, or collaboration. We need to embrace the imperfections of the systems we work within.

Our experience has been that integration agendas are most productively implemented on the small scale, through seemingly mundane things such as personal friendships, moments of patience and generosity, and the shared experience of institutional or organisational demands (such as communication activities or reporting; cf Fitzgerald et al 2014). Rather than seeking to impose reflection and dialogue through top-down frameworks or projects, the other option is thus to support it from the bottom-up, performing and collecting various smaller-scale experiments that contribute to this integrative agenda. None of these experiments will be ideal: they may involve misimaginations of publics, the dominance of traditionally powerful actors, or simple failure to meet their aims. But such imperfect engagements may still open up spaces for shared reflection and for change.
As an example we want to reflect on practices of science communication. STS scholarship has tended to focus on public and stakeholder engagement that seeks to inform, as directly as possible, scientific practice or policy (PitlikZilig and Tomkins 2011); science communication, on the other hand, is often informal, small-scale, and ad-hoc. Its practice – as part of a process of engaged and reflective research – raises a number of interesting questions as to how synthetic biology may be productively ‘opened up’ at the local level.

It demands, for instance, that we find forms of communication that make scientists and other scholars work together. The tendency to establish a division of labour such that scientists are in charge of the science, and scholars for social science and humanities are in charge of the ‘other stuff’ (ethics, societal implications, public views, communication…), is detrimental for integrated public discussion of how we want to develop synthetic biology. We therefore need to take seriously the needs and desires of our natural science partners as well as questions of how best to open up their science to integrative debate. We will also need to develop new methods of science communication which integrate what has traditionally been seen as divided: dissemination, diffusion and other one-way communication formats with dialogue, engagement, democratic discussion and openness.

We also need to think of science communication as something that is not just about communication, but which concerns the practice of science itself. Public communication shapes expectations of what types of research society should invest in: in this sense, science communication is part of the big business of science and should be acknowledged as such. Communication is performative, and will change how synthetic biology is imagined by ourselves and others. Similarly, science communication is an identity-shaping activity. Synthetic biology, because of its potentially controversial nature, has the potential to be exemplary of discussions of what type of activity science is – and of what type of actors scientists are. Again, communication of synthetic biology will perform diverse identities, including the nature of scientific citizenship, scientific organisations and scientific nations.

Finally, science communication teaches us that non-scientists have a diverse set of reasons for engaging with science, and use and re-shape scientific knowledge in a variety of ways. We will therefore need to think about public communication about synthetic biology in a way that acknowledges and meets these reasons, taking seriously, for instance, the thrill of spectacle, a hunger for usable knowledge, or the co-option of communication for individuals’ own identity-forming practices.

Science communication, in our experience, offers opportunities to build long-term collaborative relationships between scholars from different disciplines, as well as to enable space for diverse forms of public debate. Its practice requires some level of comfort with the imperfect – flawed public dialogue, dubious motives, or the ‘selling’ of science. But our point has been that it is better to thoughtfully work with the imperfect than attempt to impose an idealised model of integration that is ultimately unrealisable.

See english.breaking-entering.dk for an account of one experiment in communicating synthetic biology.
Grasping Synthetic Biology

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My vision for engaged social science scholarship in the field of synthetic biology employs the image of grasping as a double metaphor. First, to grasp is to know - not just to know about or know of, but to achieve a tangible, visceral understanding. Grasping thus connects to notions of tacit knowledge, embodied expertise, and professional habitus. Second, to grasp another’s hand – to engage – is not only to create the possibility that your power will move the other but also to risk that the other’s power will move you. Grasping thus opens possibilities for deep knowledge across communities, but at the price of vulnerability. With engagement, protective distance – intellectual, social, professional, even physical – evaporates and the opportunity for intimate critique emerges.

Those of us involved in the Genetic Engineering and Society (GES) program at North Carolina State University have struggled with this “grasping.” We employ a vision in which scientists are not “defecting” and social scientists are not “studying up.” Instead, a group of scholars is learning, searching, and communicating together to understand genetic engineering in global, social, and cultural contexts. The academic engagement—grasping hands—aims to model engagements for other social groups interested in genetic engineering, including proponents and detractors but also the merely curious or concerned.

Interdisciplinary collaboration is key to the GES program’s rigor and trustworthiness. We have often discussed the lack of trust among individuals and groups with divergent interests in genetically engineered organisms. Our historians, anthropologists, political scientists, and biologists recognize that it may be impossible to build an organization trusted by all parties in the dialogue. Despite this challenge, there are paths for putting together a generally trustworthy organization that provides global leadership on the topic. The GES program is starting down this path by emphasizing transparency and a diversity of voices. Some of our participants are strong advocates of genetic engineering, and others are skeptical or generally oppose it. We have been able to benefit from this contrast through honest and open dialogue with high standards of academic engagement. The challenge of speaking—and, more importantly, listening—across very distinct academic cultures is not trivial. Yet, the GES group has grasped one another with the intention of modeling such engagement for broader academic and public communities.

Where we may have fallen short, however, is in grasping and holding on through the full research process. We come together, but only partially, and rarely to pursue a common goal beyond the design and delivery of an interdisciplinary course or symposium. I suspect that we would need to overcome three barriers:

1. **Conflict avoidance.** Most researchers seem to avoid conflict, and to integrate multiple disciplinary ways of asking and answering questions will produce conflict. One potential solution would be to engage a third kind of professional in the research team – someone who is managing the group without a stake in the production of scholarship. Too often, in my experience, interdisciplinary groups look to the social scientists/humanists when conflict arises, as if their “softer” fields of expertise prepare them better to manage such
conflict. It is not clear to me that this assumption is accurate, and even if it were, it places an extraordinary and uneven burden on one part of the group.

a. What if conflict was expected in an interdisciplinary effort and planned for?
b. What would working through conflict expose within and between disciplines that surround synthetic biology?

2. **Power inequities.** The large and small scale projects that bring together natural/physical scientists and social scientists/humanists tend to reify, structurally and rhetorically, the power disparity between these disciplinary traditions. I see no need to name specific projects here. When a system of research embodies this disparity from the very beginning, the grasping is uneven, in both senses of the word. I have witnessed and heard about too many examples where social scientists/humanists come to occupy the role of critics from the margins, or more disturbingly, embedded apologists.

a. What if an interdisciplinary program in synthetic biology were structured to have an even balance of power between disciplinary traditions?
b. Could we imagine new roles for social scientists and humanists that disrupt the traditional narratives of marginal critics or embedded apologists?

3. **Resource constraints.** Within GES, the closer we have come to this model of grasping, the more we have witnessed the need for huge investments of resources. It takes tremendous time, energy, and mental space to grasp another discipline, another way of knowing, another researcher with different priorities and understandings than you. To be frank, a serious attempt at this project would require a strategy to free a group of interdisciplinary researchers from the normal constraints of academic life. While we might imagine recruiting only the most senior professors, who would presumably be less preoccupied with short-term production for tenure and promotion, this would sadly leave out the younger generation of scholars who may have been trained more explicitly in interdisciplinary collaboration.

a. What if participants had the time and space to focus on grasping without needing to produce according to the typical academic timeline?
b. How could such a project support rather than disrupt the career of young academics?

This paper is meant to serve as a call and a warning. The call is for the exploration of grasping synthetic biology in a deep way that destabilizes current traditions in interdisciplinarity that have resulted in conflict avoidance and power inequities. The warning is that doing so half-heartedly could be damaging and wasteful.
**Socio-Technical Integration.** Around the world, policy demands for socially responsible development of critical yet potentially controversial areas of emerging science and technology have intensified. At the same time, social researchers are developing and testing new engagement methods for bringing publics, stakeholders, and policy makers together in dialogue. Yet, as scholarly and public engagement around synthetic biology moves forward, it will be important to connect it with the actual practices of scientists and engineers. If this can be done, research pathways and technological trajectories will stand a greater chance of developing in ways that are responsive to public values and ethical concerns.

Socio-technical integration entails any process by which scientific experts account for the societal aspects of their work as an integral part of this work. At the heart of this idea is the proposition that scientific and engineering decisions play a crucial yet often overlooked role in the societal governance and shaping of emerging technologies. Routinely and explicitly reflecting on societal aspects during laboratory research can lead to opportunities to incorporate these considerations directly into technical decisions. This not only builds deliberative and anticipatory capacities into the heart of the scientific enterprise, in theory it can influence the direction of scientific and technological developments and thus help strengthen important links between science and society.

In practice, socio-technical integration faces numerous challenges and tensions: the connections between societal aspects and scientific practices are not always self-evident, meaningful collaboration between physical and social scientists can be difficult to achieve, and the idea of integration can trigger longstanding fears that it might harm scientific productivity and infringe on scientific autonomy.

**STIR Project and Results.** The Socio-Technical Integration Research (STIR) project coordinated 30 laboratory engagement studies in which social science and humanities scholars interacted regularly with scientific and engineering researchers working in nanotechnology, biotechnology and other basic and applied research areas. The project goal was to investigate the possibility and utility of socio-technical integration during routine laboratory practices. Following the “midstream modulation” framework, integration during laboratory research was conceived to take place midway between traditionally opposing categories such as research policy and technology regulation, promotion of innovation and its social control, social scientific observation and ethical advocacy.

STIR studies generally followed the same basic methodology, although several experimented with alternative approaches. In general, social researchers learned the theory and observed the methods of their laboratory counterparts; but they also were asked to introduce a decision protocol that was designed to unpack social and ethical dimensions of the lab science itself in a real-time, hands-on, collaborative manner. Ideally, the social researchers, their methods and inquiries became embedded in the laboratory during each 12-week engagement study.
In addition to co-authored publications and the acquisition of interactional expertise, the STIR project correlated several types of outcomes to its interdisciplinary activities: Nearly all of the 30 studies documented *heightened reflexive awareness* among research participants of interrelations among research developments, societal contexts, and laboratory decision-making. Similarly, a large majority of the studies also documented *deliberative reflection* on the societal aspects thought to be at stake in research. By comparison, only about half of the studies actually documented *practical adjustments* to research procedures and to laboratory strategic thinking that were correlated with the interdisciplinary dialogues. Approximately one-third the studies routinely used the semi-structured decision protocol that was originally designed to guide the interdisciplinary interactions. Interestingly, all studies in this sub-set documented *heightened reflexive awareness, deliberative reflection and practical adjustments*.

STIR project results suggest that thinking and talking about the societal aspects of their research while scientists and engineers went about their normal work routines did not entail a sacrifice in scientific productivity. Rather, reports of enhanced creativity and productivity during lab research were not unusual. Thus, integrative efforts to enhance societal responsiveness and scientific creativity can be mutually reinforcing.

**Integration in Synthetic Biology.** Diverse social scientific engagements with synthetic biologists have meaningful opportunities to develop the theory, refine the methods, and deepen the practical impact of integrative efforts such as those conducted by STIR. Projects and activities can vary the sites, participants, frequency, intensity, questions, and relative structuring of embedded socio-technical collaborations and interactions. Combined with other engagement tools and forums, diverse aspirations for integration and rationales for engagement can be both deepened and put to empirical test. Ideally, future efforts will attend simultaneously to the conditions under which collaborative skills are acquired, material configurations are shaped and normative concerns are articulated and negotiated.

It is important to acknowledge the numerous challenges and relatively high stakes involved in expanding both scientific and social scientific capacities for productive collaboration. STIR shows the importance of sustained interaction over time for catalyzing changes in trust, understanding, materiality and human agency. Essential tensions—typically viewed as barriers—between observation and action, social learning and material durability, and involving the instrumental, normative and interpretive roles of social science can also be viewed as design criteria and hence productive resources. The same might even be said about inevitable power relations and their imbalances. Above all, integration can both explore, and possibly seek to inform, the relationship between two central modern institutions: the social organization of science and its broader context of democratic norms and values.

The contribution of social sciences in the governance of emerging sciences and technologies has been the focus of much attention over the last few years. The usual narrative suggests that the contribution of social sciences may be identified as an overlapping sequence of three waves: analysis of ethical legal and social implications (ELSI), contribution to democratization of choices through public engagement, and more recently integration of social scientists in research laboratories in order to perform real time assessment and foster reflexivity. Programs for ‘anticipatory governance’ performed at ASU, ‘human practices’ at SynbERC, ‘constructive Technology Assessment’ in the Netherlands, or collaborative projects in the UK are among the most prominent examples of this third wave. In this short note, I argue that this later form of contribution of social sciences has serious limitations. To put it in a nutshell, such an engagement in local forms of co-production overlooks key transformations in the regime of production of knowledge that go along with the emergence of SB. To support this argument, I start by referring to an analysis of the current emergence of SB (Raimbault et al. 2014) and then turn to more general analytical questions.

Although SB is still an emerging field, we used a delineation strategy to identify 3000 scientific papers published until end 2013. Most of the 10 000 authors that appear in the corpus only appear once. We identify a core set of about 300 researchers and a smaller set of less than a dozen Institutional Entrepreneurs that both play a key role in the construction of the cognitive dimensions (they have published in the top 100 highly cited papers of the corpus) and in the social dimensions (they are involved in institutional setting) of the field. The high rate of self-references (most of top papers cited by the corpus belong to the corpus) is a good indicator of the growing level of autonomy of the field. Members of the core group formulate a scientific promise that plays a key role for mobilizing resources and attracting researchers. They also play a key role in shaping a local order that involves inter alia communication channels, training, social norms of behavior, etc. The definition of standards of proof is crucial and this involves both cognitive and social dimensions. We call this dynamics –which is internal to the scientific field – the "credibility circle".

Our analysis also shows the central role of applications in the dynamic of the field, which leads us to characterize it as a techno-scientific field (TSF). Co-word mapping allows us to identify three clusters of research organized around applications: medical applications; biofuels; and tools for engineering biology. Thus, the dynamic of the field is not only related to credibility circles but also to external forms of valuation of the relevance of the research. The crucial point for a TSF lies in the translation of the scientific promise into promises of application. This is instrumental for building the legitimacy of the emerging field and gaining public support. This public support may translate into additional resources (through specific public programs for
research and/or innovation) and may reinforce expectations and hence attract researchers and companies into the field. We call this dynamic the "legitimacy circle".

Our claim is that the coupling of the credibility and the legitimacy circles plays a key role in the emergence of a TSF. Within the core group, Institutional Entrepreneurs are crucial for such coupling. They span boundaries not only across scientific disciplines but also across social worlds. Hence, they play a key role in translating the scientific promise into promises of application, in constructing the image of synthetic biology in the public sphere to gain public support, and so on. Therefore, they not only act within the scientific world but also construct the conditions of emergence of the new specialty through the making of its socio-political environment. Overall, synthetic biology exemplifies what we have called a regime of techno-scientific promises (Joly 2010).

Our empirical work and analysis of the emergence of SB as a techno-scientific field that contributes to a regime of techno-scientific promises, and of the important role of credibility and legitimacy circles, has important implications for research agendas for social sciences. Social scientists are well placed to ask important questions such as: what are the type of relations between science and society within such regimes? What are the processes of techno-scientific promise making? What is valued and how –and how does it affect research agendas? What does it mean to govern through promises?

Social scientists can also contribute to debates around the growing reference to responsibility. What are the implications on research objectives and laboratory practices? Is it mainly a way to ensure self-regulation of the field and prevent external forms of compulsory control? What does it mean to be responsible and reflexive in a regime of techno-scientific promises? What is the expected role of social sciences in this context? Is it just about fostering acceptability?

References


Controlling Life? Implications of the mathematisation of biology & other topics

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Background
Research at University of Sheffield on the social study of synthetic biology – using primarily STS\(^1\) approaches - began in 2007. Based in the sociology department, a programme of work was developed out of existing interests on the dynamics of techno-scientific communities, with a particular empirical focus on physical sciences and engineering fields. Most of our sociological research so far has focussed on understanding different aspects of scientific field development e.g. how new scientists are trained; how new scientific communities are formed from existing interests; how attempts to generate knowledge production in inter-disciplinary settings are organized etc. Yet we have barely scratched the surface of several key sociological research questions. The long term engagement with particular science and engineering research groups is central to our research programme and we have gained funding to work on several collaborative projects. It is from this context that the following ideas emerge.

Some research areas, challenges and questions
- Implications of the mathematisation of bioscience

While aspects of computing, systems engineering, control sciences and mathematics are central to the ideal-type processes and the goals of synthetic biology, these engineering and mathematical fields are not only playing a role in the development of synbio but currently impacting in many other areas of bioscientific work. As a result, it may not be wise to separate out (completely) synbio from other trends and developments in bioscience and a sociological research agenda should perhaps not confine itself to synthetic biology (as it is currently defined). We need to understand the ongoing drive to quantify / mathematise /automate the biological sciences and what falls out from that. The translation of the biorealm through, not only quantification, but a mathematical worldview, has practical and epistemological implications that are currently unexplored.

- The practical accomplishment of synbio as an interdisciplinary field

Synbio lays claim to multiple disciplines in pursuit of its goals. Yet it is well known that inter-disciplinary research can be challenging. Is synbio getting it right or not? If it is, what lessons may work for other areas of research and other emerging fields? Are we sure we know what success looks like in interdisciplinary research?

- Industry-academia relations in synbio

In the UK, as elsewhere, synbio appears to be playing a particular kind of economic role. The prospect of economic returns, jobs etc is regularly mobilised to justify continued public investment. This can only be brought about however by bridging an ‘innovation gap’ (or crossing the dramatic ‘valley of death’). Hence the role of industry is

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\(^1\) STS – Science and Technology Studies
perceived as key to the success of the synbio endeavour. Realising this vision of industry – academic relations is not necessarily straightforward and it is not yet clear what appropriate forms of relation might emerge between public and private sectors, nor (again) how ‘success’ might be recognised.

- Expanding current notions of social study of science

The practice of synbio as an everyday science remains elusive. Whether the field will ever stabilise remains an open question. This means that the terrain that STS would like to explore is ever-changing and the ethical landscape is evolving. Alongside, it also provides an opportunity for the co-development of research agendas across disparate research areas. We need to broaden our notions of what social and humanist study of synbio may involve and we need to develop our repertoire of resources (conceptual, theoretical and practical) to analyse and explain and to inform policy and practice.

- Training (who, what, when)

To what extent does training of the technically competent need to include development of competency in the social dimensions of the field (the politics, economics, sociological, ethical etc). If responsible research and innovation is important, then whose notions of ‘responsibility’ will count? We also have to consider the training of social scientists, to ensure the ongoing analysis of this technical domain (& subsequent emerging technologies yet to be envisaged). Can we experiment with joint training?

- The problem with the term ‘social acceptance’

What would be a better concept than ‘social acceptance’? Acceptance is a problematic notion for a number of reasons and there is sufficient STS knowledge available to counter the utility of the idea. What sociologically-acceptable ideas could replace it?

- Equity and access

What do emerging technologies in emerging economies look like? Who are the winners and losers as time goes on? Science is a global activity but do we have the capacity to comprehend implications on global scales? Do we have the sociological apparatus to handle uncomfortable questions around equity and economics?

- Open and closed innovation

What are the implications of parallel developments in synbio of open source and closed (IP protected) approaches to the field? Do we assume a mixed economy will ensue and what might the interplay be? How may open-source be policed? Should it be?

- Collaborative experimentation

Synbio has offered intriguing possibilities for collaboration across social and technical communities. We need to get beyond simplistic ideas of what makes interdisciplinary research hard e.g. language, and reach to deeper concerns of an epistemological nature in exploring new forms of knowledge generation. Could we mess with institutional boundaries in relation to synbio in ways not available in other domains? How can social science participate in these experiments? Will participation be possible without sacrificing key parts of disciplinary integrity, our promotion prospects & our need to fulfil institutional success metrics?
Experiments in Practices: A Few General Lessons  
Megan J. Palmer, PhD, Stanford University

- **Societal goals must be driving, not subservient to, technical goals.** If this is not recognized across the many levels of agenda setting then we are probably doomed.

- Sustaining a societal research agenda, and the multi-disciplinary teams to drive that agenda, requires **organizational and power structures that promote (not discourage) critique.** Otherwise, uncomfortable knowledge can lead to disempowerment, and even worse, rejection.

- For institutions to mature (i.e. learn, adapt), they must include **mechanisms for (1) identifying emerging issues, and (2) changing their practices in response to new knowledge.** Leadership must co-develop and revisit agendas and not restrict activities to pre-defined issues.

- We should **expect and embrace persistent and fundamental tensions** regarding the relevance of societal research agendas, as they are functions of changing values and politics. Tensions may well **exacerbate** as technologies and investments mature. Acknowledging and creating space to explore and (re)balance tensions may help protect against polarization and gridlock – and are functions foundational to democratic processes.

- **Societal research should be flexibly organized, both intellectually and operationally, to include both components integrated with technical work, and components independent of technical work, with transitions over time.** The model for organization will vary with the questions/goals pursued and the interests at play. Some problems require primarily social science or technical expertise; some require a mix of disciplinary expertise. Supporting a combination of activities both within and outside any given mission-driven research center, with support for active communications between them, is necessary to allow both learning and oversight. There is a need for more rigorous empirical work on how different organizational forms have fared so far– with a recognition that the results of such studies are will be sensitive, and their scholars vulnerable.

- Societal research agendas require **institutional support for unique but complementary types of activities**, including research, education, strategy and management, communications, and brokering. Too often ‘brokering’ functions are neglected and under-resourced, but they are essential to catalyzing and managing relationships between interdisciplinary groups and interests.

- Bolstering a now-weak infrastructure for societal aspects of research requires **long-term sustained attention, leadership and resources.** The often-longer return time on investment for these efforts means they are often neglected under resource constraints.
These lessons are not unique to synthetic biology. The organization and governance of science and technology has been, and continues to be, a subject of study in many fields (not simply those that are “emerging”) by scholars and practitioners across a variety of disciplines. Unfortunately, there is a dearth of scholarship and practice that recognizes connections between these fields. Advances in the study and manipulation of living systems allow us to test our conceptual and operational models for the governance of science and technology. In particular, along with other areas like cyber and advanced manufacturing, they challenge whether existing models can account for quickly proliferating and globalized technologies and practices that may not be shaped through traditional hierarchical institutions or market forces. Rather, we need to develop our conception of network governance and how institutions, infrastructure, and management that can balance centralized and decentralized control in global contexts.
Responsive Novelty: Taking Innovation Seriously in Research Agendas for Synthetic Biology

Sujatha Raman, Deputy Director, Leverhulme Making Science Public Research Programme & Institute for Science and Society (ISS), University of Nottingham and Visiting Scholar, Consortium for Science, Policy and Outcomes (CSPO), Arizona State University

The Research Problem

Approaches in synthetic biology have been put forward as novel options for addressing grand challenges such as climate change and antimicrobial resistance. In this context, societal research agendas must include the following questions:

What might constitute novelty in domains interpolated by synthetic biology; according to which criteria; and as determined by whom? Can different visions of novelty be creatively synthesised - if so, how, and to what effect?

At first, such questions seem contrary to the goals of developing a societal agenda around synthetic biology (SB) research. Societal research is normally expected to fill in the gaps in knowledge produced by scientists and engineers, exploring questions that are not formally part of the scientific/technical agenda for investigation. Such presumed knowledge gaps include questions of the following nature. What are the ethical implications of developing and using SB applications? How do different public and stakeholder groups perceive SB? What might be the unforeseen side-effects of SB? How should SB research and innovation be regulated? These are all important questions. But, as many social researchers have pointed out, the institutional arrangements and norms that structure how research in SB and other emerging technology areas is done and validated have inadvertently created their own blind-spots and knowledge gaps.

The gap in knowing how to make social dimensions really matter to research and innovation is particularly glaring for reasons outlined below.

- Social/ethical matters are treated as spatially, temporally and substantively separate from technical ones. That is to say, they are seen as lying outside the normal spaces of scientific research (e.g., laboratories, journals), to be determined by non-scientists (e.g., ethicists, social scientists, publics, stakeholders, policymakers) either before technical work begins or after technical challenges have been solved, and to be about opinions and values that cannot themselves be incorporated into research practice.

- These divisions mean we know a great deal about how to elicit different societal perspectives but less about how to integrate them into research so that ethical questions such as those framed in terms of ‘social’ or ‘economic’ sustainability (e.g., justice, equality, livelihood, human well-being) come to be investigated simultaneously and together with scientific/technical ones.

- This demarcation arises because scientists and engineers are expected to determine what is novel or innovative while social scientists and ethicists are expected to determine how innovation can be done responsibly. In neither case is the question of what constitutes or might constitute innovation considered worthy of systematic investigation in its own right. Rather, what is novel is taken to be a given at the start of new research rather than as a subject of this research.

- The need for more integration of the social and the scientific is important because interventions for innovation are frequently experienced as being not innovative enough,
even where the fulfilment of societal need is meant to be its purpose. Rather than treating this lack as a problem of societal resistance or lack of responsibility, it is at least equally valid to take it to be one of insufficient novelty if SB or other emerging technologies are seen as extensions of existing socio-economic-systems and their problems.

- There is insufficient attention paid to a.) ways in which a specific intervention might or might not be novel according to different actors and b.) the landscape of different visions for novel interventions. These aspirations are central to ideas of responsible innovation that emphasise the need to open up the innovation process to different visions of innovation, thereby asking not only ‘what if’ questions (e.g., what if a technology produces undesirable impacts) but also ‘what else’ ones (e.g., how can innovation be done differently). For example, bioenergy is likely to require significant changes in agri-economic and global trade systems in conjunction with technological novelty if it is to be really innovative. If synthetic biology is to be applied to bioenergy, this challenge will need to be considered.

**Societal Approaches to Researching Novelty**

Expanding and investigating the landscape of novelty in response to different visions of innovation (hence, *responsive novelty*) requires more support for integrative approaches. One approach is to begin with lab-based research projects or methods and look for ways of integrating societal matters into these domains. Examples include the socio-technical integration of research (STIR) framework, anticipatory life cycle assessment, and systems engineering. We also need approaches that begin from outside of the lab in policy, economic and socio-cultural systems and work their way back in – these might draw from problem structuring methods and whole system analysis in policy studies. The key with all of these is to draw out the novel insights that emerge from these different interfaces to clarify that the social is not merely an add-on, but is rather central to generating knowledge for innovation.

In conclusion, I will look briefly at how this might work around SB approaches to drug discovery in the face of antimicrobial resistance (AMR).

**Investigating Epistemic novelty** – It has been suggested that SB approaches to new antibiotics would pre-empt the development of resistance because of their novel biological mechanism of action. A key societal question for research would be to investigate this further by looking at how representatives of different scientific, clinical, epidemiological and healthcare fields envision novelty in the face of antimicrobial resistance. For example, how do advocates of evolutionary medicine or imagine novel solutions to AMR and how do the se compare with SB? Eliciting different perspectives could be followed by integrative exercises in problem structuring and synthesis, keeping in mind that not all differences can be reconciled and reporting needs to be transparent on what has been left out.

**Investigating Socio-economic novelty** – A recent policy paper on synthetic biology for AMR suggests that SB approaches are highly efficient, hence representing an economically attractive option for less-affluent parts of the world where infectious diseases are more of a threat. Here, one might look at which socio-economic and institutional models would allow SB to be innovative rather than assume that SB is intrinsically novel because of its efficiency. One could also draw on knowledge and experience of how poverty not only shapes the spread and impacts of disease but also the impact of technological interventions (medicines) on the body, investigate what might be done about this and then ask where SB fits in this broader picture.
In conclusion, to make societal research on emerging technologies matter, we need to respond to the possibility of innovating in social, industrial, economic, policy and cultural systems as much as and in conjunction with technological innovation. This might allow for synthetic biology to be novel in ways not envisaged within current market-based economic models (for example, by creating the space for new ways of building social value rather than just private value). It might also allow for ways of transforming the social world (for example, dealing with poverty and inequality) to be explored in conjunction with SB rather than taken to be separate from it. Through this there may be opportunities for synthetic biology to reconnect with older visions of ‘biological engineering’ which were seen as distinctive from and a corrective to the problems of industrial systems.

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5 This formulation of the problem of innovation is drawn from Safalaoh, Andy. 2014. The Elusiveness of pro-poor innovation benefits: lessons from the smallholder livestock sector in Malawi. PhD thesis, University of Nottingham.


7 See: [https://andybalmer.wordpress.com/2013/07/30/can-scientists-engage-critically-with-capitalism/](https://andybalmer.wordpress.com/2013/07/30/can-scientists-engage-critically-with-capitalism/); Also, Raman et al. op cit 3.


9 See Takano and Breitling 2012, op cit 1.

10 On the relationship between drugs, drug resistance and poverty, see the extensive work of Paul Farmer.


Societal Aspects of Synthetic Biology: Organisms and Applications Matter!
Amy K. Wolfe, Society-Technology Interactions Science Team Leader, Oak Ridge National Laboratory

This background paper\(^1\) constitutes an entreaty to scholars investigating societal aspects of synthetic biology: approach synthetic biology specifically, not generically.

*Synthetic biology is defined in numerous ways. It can be conducted through diverse processes on divergent types of organisms. It also can be ‘used’ or ‘applied’ in potentially unlimited venues to accomplish any of a number of objectives.* These sorts of statements should become more than familiar, nearly obligatory introductions to studies of societal aspects of synthetic biology that subsequently fail either to account for or to address the extraordinary variability encompassed by the phrase “synthetic biology.” Instead, synthetic biology-related specificity should be used to sharpen inquiries and add analytical depth. Doing so potentially can impart new levels of credibility or power to resulting findings and recommendations.

I am among a set of authors who made a similar point about nanoscale science\(^2\), arguing that “ELSI [ethical, legal, and social issues] scholars should add technical- and application-related forms of specificity to their work and their writings to enhance effectiveness and impact in communicating with one important target audience—members of the nanoscale science community” (p. 193). We asked our fellow ELSI scholars, “what is it, exactly, that we…want nano-scientists, -managers, or –funders to do as a result of our scholarship?” (p. 199). By extension, what goals do those of us participating in this workshop have for the outputs of any research agenda we may propose? Those goals may change over time, but they provide an explicit framework upon which to build a research agenda. That framework also provides a way of gauging the extent to which agenda items individually and collectively align with research goals.

My proclivity is to establish goals that involve the *use*, and not just the production, of research findings. This use- and goal-oriented proclivity undoubtedly influences the emphasis I place on

\(^{1}\) This material is based upon work supported by the U.S. Department of Energy, Office of Science, Office of Biological and Environmental Research. However, the opinions expressed are my own.

specificity, as does our relatively recent focus on “members of the [salient] scientific community”\textsuperscript{3} as one target “user” population. Regardless, I believe that specificity can:

- enhance research on an array of societal aspects of synthetic biology, including upstream or public engagement, responsible innovation, public attitudes and opinions, communications, bioethics, governance, costs vs. benefits, and risk;
- improve our collective ability to achieve multiple research goals; and
- increase the “usability” of our research results among multiple target user populations.

To illustrate these points and spur workshop discussion, I briefly mention just two interrelated forms of specificity—type of organism and potential application. Consider, as examples, a few possible types and applications of new or altered DNA: in bacteria intended for therapeutic medical treatment; in bacteria intended for environmental remediation; in algae intended for biofuel production; and in plants intended for food. It seems obvious that societal aspects of synthetic biology vary when used directly in the human body versus in soil, water, or plants. Certainly governance issues vary. Different regulations apply to microbes, plants, and algae within and across agencies. For instance, under the US Environmental Protection Agency's purview, the Toxic Substances Control Act applies to microbes and some algae, but not plants; the Federal Insecticide, Fungicide, and Rodenticide Act applies to plants, not microbes or algae; and the Clean Water Act may apply to algae. Moreover, attitudinal and acceptability issues may vary. We do not currently know what internal calculus respondents use in answering questions about synthetic biology when they are presented with an assortment of potential uses, benefits, or risks. For instance, we do not know whether respondents anchor their responses to what they see as the most positive versus most negative aspects of synthetic biology, or the extent to which answers represent some 'average'. Likewise, we neither know what bias we inadvertently may impose on research in our selection of examples or illustrations nor the extent to which answers based on one set of examples apply to other possibilities.

Even just two specific synthetic biology attributes—organism and application—have substantive, potentially significant, implications for social science research. These attributes influence the settings, processes, and practices associated with R&D, production, and deployment; invoke different sets of regulations; generate different economic or other cost-benefit parameters and ratios; produce different human health and environmental risks, with varying magnitudes and duration; and may lend themselves to markedly different potential misuses (dual use). We should craft a research agenda on societal aspects of synthetic biology that is attentive to specificity.

\textsuperscript{3} In particular, our team has focused on scientists, science managers, and science funders who shape choices about what research to conduct and what to do with the results of that research.
Moral Status, Illicit Bio-Economies, and Equity/Parity
David M Berube, GES Fellow, NCSU

There are three issues about which I have some interest as both a rhetorician and a social scientist. First, there is the issue of defining “life” and moral status. I would argue that both removing the attribute “living” from any organism will change its moral status and adding the attribute “living” to a machine will change its moral status as well. The implications associated with moral status are important.

During wartime we observe the dehumanization of the enemy. Without defending the activities of ISIL/ISIS per se, we are already hearing them referred to as monsters. David Cameron on September 13 of this year pledged to work with Britain’s allies to destroy the Islamic State, saying of the group’s members, ”They are not Muslims, they are monsters.” A less articulate Ted Nugent on the 17th commented: “We should rain hell down on these Muslim monsters and all who provide them safe haven until there is nothing left of their hate and evil ways. A scorched-earth policy is a good policy as it pertains to exterminating these devils. Killing them all would send a message to every other voodoo nut job that America once again is all business.” Demonizing has long been a dehumanizing strategy in times of war. Said explained defense of his major work Orientalism that very little of detail reached American audiences and policy makers understanding that over simplified complex international issues by over generalizing the other, the enemy especially.

With “otherizing”, demonization, and dehumanization we are changing the moral status of people, moving them into a category of thing. Much like reservations over cloning, we know that early attempts to produce viable “living” machines will be fraught with failure. Some of our creations will not live and indeed may die at our own hands because they are not optimally viable. Witness the “Dolly” rejects.

While we kill bacteria when we wash our hands and brush our teeth, we are talking about creating life and extinguishing life. As we move up the developmental ladder from bacteria and viruses to more complex life forms, we need to ask ourselves what moral status we are willing to award our creations as well as how we decide to remove its/their moral status.

Second, we need to consider the role synthetic biology might serve in the illicit bio-economy. This issue has mostly been raised by Markus Schmidt from the Organisation for International Dialogue and Conflict (Vienna) in two of his pieces. Schmidt in writing about the DIYBio movement and its members wanted to make certain that while he found them mostly harmless, there were other free agents with highly suspicious motivations.

In contrast to the amateur biologists who try to do things with a low budget, the illicit bio-economy and its players are known to have a very high budget. It is easily imaginable that drug cartels set up (semi-) professional laboratories using an easily available biological toolbox to design microorganisms to produce not the plant
product artemisinin acid but a plant derived semi-synthetic cocaine or heroin (2009: 96)

Schmit postures “there is no reason to believe that full biosynthetic of currently semi-synthetic drugs or fully synthetic amphetamine-type stimulants will not be possible and economically attractive using the toolkit of synthetic biology in the near future.... [T]he future illicit bio-economy could see some dramatic changes one the technology to manufacture metabolisms a la carte is out there” (2008: 3).

Third, there is the equity/parity issue associated with the costs and benefits shared by the same population. For me, this is a rhetorical issue. I have grown weary with the usefulness of the poor and marginalized as the backing for claims about the importance of scientific and technological developments especially when the benefits associated with advanced science and technology at best trickle down to the poor.

When we ask about drawbacks, we hear about applications as a counterbalance. The applications involve extrapolating discoveries and positing arguments about humanitarianism. When we complain about some futuristic down side to a new technology, we hear that we are not even close to developing the technology to the point where it might trigger the down side. Applications are a justified use of speculation but drawbacks and disaster scenarios are not. One begins to question this logic of scientific and technical rebuttals when populations of arguments as well as populations of fauna, including humans, are treated very differently.

Speculating about future contexts cannot justifiy accelerated development while at the same time discrediting reservations and precautionary trending.

Just three issues I think we need to address.

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Context is Everything: Time Frames, Impacts & Risk Communication in Synthetic Biology Decision Making Processes
Margaret S. Race, SETI Institute

The synthetic biology community is engaged in a multi-decadal process focused on scientific expansion, development of new applications and eventual large-scale implementation of promising methods applicable for diverse uses across wide geographic areas—domestically and internationally. In the public discussions about synthetic biology, proponents have generally focused on how advances in basic science will lead to promising applications and uses for societal benefit, while opponents raise questions about the potential risks, the many uncertainties and unknowns, and concerns about societal impacts and implications in both the short- and long-terms.

Before attempting to identify important research areas associated with the societal aspects of synthetic biology, it will be important to have a realistic overview of the scenarios that may arise at different time frames and under different contexts in the public decision making processes ahead. This involves identifying what institutions and experts are involved at different stages of decision making, what types of applications and uses are anticipated as the field expands, and how risks and impacts are understood, managed and mitigated (from the lab bench, through R&D efforts, to the end-of product life-cycle). It is likewise important to distinguish the perspectives and assumptions of the different people involved in deliberations at particular times—from science and technology experts, to government policy makers, commercial and industry representatives, individuals, and public audiences in all their diversity. Finally, because synthetic biology involves the very nature of life and its deliberate manipulations for human purposes, discussions of research agendas must also include the foundational perspectives of philosophers, ethicists and other humanities disciplines.

All the information outlined above will be needed to design effective communication plans that clearly and accurately explain the risks, impacts, uncertainties and mitigation options, as well as address societal non-scientific concerns. Thus, when planning a long term research agenda for addressing societal concerns and engaging/informing the public, it will be important to acknowledge and clearly articulate:

1) **What specific time frame and context is being addressed**—and what stakeholders, institutions and issues arise at different stages of the overall public decision making process. The road ahead should not be viewed as a single decision making process—rather it involves multiple decisions and processes—with each ‘solution’ potentially resulting in new or different problems, with different societal concerns at each step. For the purposes of designing a research agenda, it may be useful to examine (compare and contrast) four representative times in the process. (It is arguable that in first two phases, input from the scientific/technical and legal/policy communities predominate —while societal awareness and opportunities for involvement increase gradually over time —as the applications (or problems) become more individually relevant).

   a. Early stages. From the Asilomar era of early research in genetic engineering in high containment labs; to the Ice Minus era and controversies associated with deliberate outdoor release and pilot projects; through the early sybbio era of R& D (to ~ 2000?). This era involved questions of government funding, applicability of existing laws/institutions;
environmental impact statement; and populations addressing mainly local/regional controversies, at least initially.

b. The current situation: the era of deliberative democracy – which includes discussions of bioethics, adequacy of laws, regulations and institutional oversight; concerns about responsible research (biosafety and health), especially at academic institutions; deliberations about potential dual use problems; and growth of DIY-ers, IGEM competitions, commercial ideas and venture funding.

c. NEXT: coming era of commercial scale ups & Industrialization (many new and different issues, laws, institutions, and practitioners—a sequential decision making process). The period of expansion beyond pilot scale R&D to large-scale industrial operations with product-lifecycles, international markets, wide distribution, and concerns about end-of-life disposal etc. (comparable to chemical industry; big-pharma; food-agricultural sectors)

d. ALSO-- Need to focus on representative, potential accident scenarios and time frames—involving many different syn-bio products/uses, institutions, publics and issues involved. No one-size-fits-all approach.

2) look at specific **Risks, impacts, and uncertainties associated with the different time frames and situations**—where do info gaps & uncertainties exist or will likely remain—especially for industrial and outdoor applications

Compare and contrast the issues for synbio applications/uses under **controlled situations in labs or large commercial facilities** vs.

Consider how qualitative questions about long term impacts from **deliberate outdoor releases and uses—and associated product life cycle and disposal issue**—will impact the public (similar to questions about GMOs and environmental long term changes?)

3) **Risk Communication needs** – For each time frame or context, determine the different societal information needs; & consider analogue or historical information on how to address them. There is an extensive literature on risk analysis and public decision-making, with relevant research on risk communication, risk-perceptions, foundational values, and public involvement. It may be useful to examine existing research findings on effective and ineffective communications as seen in diverse sci-tech analogues [e.g., chemical industry, oil & gas—fracking; GMOs—over time & in different locations -- US vs European); nuclear industry and applications; and even climate change-- for aspects of gradual emergence of problems and public views about accepting/rejecting expert advice and opinions]

   a. Consider adoption of best practices for effective communication and outreach efforts (ex. avoid disseminating info in monologues or enthusiastic 'infomercials" and avoid the Deficit Model of risk communication.)

   b. Prepare to discuss risks, mitigation, and remediation options in advance? Who are the 'experts' who can engage in true dialogue at different times? (especially if and when accidents occur (the latter is important because there are few or no equivalents of
environmental impact assessments for advance public discussions and hearings)

c. Gather systematic information on public understanding & views of synbio. Surveys indicate that the public is generally uniformed about synthetic biology. Are there opportunities for research on public understanding, risk perceptions, & values of concern?
The monster and the polar bears: Constructing the future knowledge landscape of synthetic biology to inform responsible innovation

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Nearly two centuries ago Mary Shelley’s Frankenstein envisioned with prescience the future of health innovation and technology. Shelley’s tale of the ambitious doctor, Victor Frankenstein, who generated near-human life, “the Monster”, with unintended consequences helped inspire the field of bioethics to attend to issues such as the philosophical and moral standing of humans, machines, and their novel interactions. But since Frankenstein’s Monster was left to perish at the North Pole, few, if any, have stopped to consider what impact this might have had on the arctic ecosystem, the iconic polar bears (ever the image of man’s recklessness), or the local Inuit communities. Innovations in health technology and health systems have considerable implications for the sustainability of broader socio-ecological-technical systems, which extend beyond debates on the morality and ethics of individual patients and doctors. As the bicentennial of Frankenstein approaches, advances in synthetic biology are drawing attention back to health innovation and challenging previously accepted moral and ethical boundaries. Attention should also be paid to how synthetic biology may redefine social-ecological interactions and shape visions, expectations, and fears about the future. The promise of synthetic biology for health is based on Western notions of ideal physical health for the individual, but that ideal does not necessarily scale up to communities or society, nor does it translate to social-ecological system wellbeing. It is critical to understand whether the practice of synthetic biology research and its implications for discrete groups (doctors, patients, insurers) meet established standards — the questions inspired by Frankenstein centuries ago. But now is also the time to start investigating whether synthetic biology can contribute to or hinder progress toward sustainability goals from a broader social-ecological-technical systems perspective.

Considering the future contributions of synthetic biology requires first anticipating what may come from innovations in the field. To anticipate is not to predict, but rather to seek out pieces of the future that inform how one acts today (Guston 2013). Knowledge about the future is constantly being socially constructed by a wide diversity of special interests; for emerging technologies, these interests are often scientists, product marketers, and issue advocates. This breadth of knowledge, having distinctly different ontological and epistemological characteristics constitute a multi-dimensional and pluralistic future knowledge landscape, which is continuously reformulated and can be enacted to inform present-day actions and planning efforts (Withycombe 2010). So while it is not possible to know exactly what the future holds, one might look at a diverse and broad future knowledge landscape, reflect, and prepare for different futures. Scenario construction and visioning are two anticipatory methods commonly used to construct future knowledge. Such construction is usually done in relative isolation with minimal engagement with other ongoing or past future knowledge construction processes. In these cases, only a small portion of the future knowledge landscape informs decisions—a move from tunnel vision to funnel vision. A full picture of the future knowledge landscape is needed for responsible innovation in synthetic biology, where the very building blocks of life are altered or reassembled. A number of anticipatory activities have been undertaken to examine the future of human health, health systems, health technology and even synthetic biology, specifically. By investigating anticipation around these themes, a rudimentary future knowledge landscape of
Mapping the future knowledge landscape for synthetic biology can serve as the basis for answering several important questions, including: who is shaping which pieces of synthetic biology’s future; what are the values imbued in those futures; and what large-scale socio-ecological-technical transformations may arise from those futures? Sustainability provides a framework to analyze what is emphasized in the future knowledge landscape and what is marginalized or absent (like the polar bears). The future knowledge landscape can also be assessed against normative sustainability criteria including livelihood opportunity, human flourishing, and socio-ecological integrity across intra- and inter-generational scales. Such analysis and assessment are critical for developing anticipatory capacities among scientists, policy makers and the broader public whose tax dollars help fund research and who (or perhaps their descendants) will ultimately live with the consequences of innovations in synthetic biology.

At first glance, public as well as scientific discourses on the future of synthetic biology appear to coalesce around extreme promises and perils for humans. This is not uncommon for emerging technologies. Recent bibliometric analysis by Youtie and Shapira (2014) on the future of synthetic biology concludes that the discourse predominately reflects historical approaches to bioethics. Techno-ethical scenarios are also an important part of the scientific dialogue on the future implications of health innovation, while socio-technical systems including physical infrastructures, demographics, as well as the politics and power therein are infrequently referenced. So while bioethical work continues to attend to the individual (e.g. patient rights) and professional societies (e.g. doctors), there is limited understanding of the future implications of synthetic biology for the complex socio-technical systems that encompass health innovation, let alone for social-ecological systems, where there may be potentially significant implications for sustainability. A full literature review is needed which includes a document analysis, with grey literature, focusing on the future of synthetic biology and health innovation more broadly.

At present it appears that the future knowledge landscape of synthetic biology specifically, but also health innovation more broadly, is not fully developed enough to inform responsible innovation. Additional future knowledge is needed to fill critical gaps in the future knowledge landscape, but this knowledge must be co-constructed with new and different perspectives.

The construction of future knowledge is often the purview of the powerful—there are future makers and future takers—giving a distinct perspective to the future that possibly diminishes or ignores other important perspectives. Future scenarios of synthetic biology should be constructed, paying particular attention to unexplored areas of the future knowledge landscape, including the impact of synthetic biology on the broader public, marginalized groups, future generations and social-ecological systems. This requires transdisciplinarity (generating knowledge with communities of practitioners and laypersons) to draw upon multiple perspectives with the goal of broadening the future knowledge landscape into new territory. This also requires tools that encourage divergent thinking and inspire creativity in thinking about the future. To return to Frankenstein, a research agenda on the societal aspects of synthetic biology should consider the moral and ethical implications of the Monster as well as the human and non-human life he encountered, which might be forever altered. The aim of such a research agenda would be to bring anticipation closer to decision-makers shaping synthetic biology, construct a broader future knowledge landscape for the field, and contribute to the theory and practice of responsible innovation and sustainability.
References:


Multi-Site Public Engagement with Science – Synthetic Biology
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David Sittenfeld, Forum Program Manager, Museum of Science

The Museum of Science has just received an award from the Advancing Informal Science Learning (AISL) program at NSF, with co-funding from ENG and BIO, for a project to conduct public engagement activities at multiple science museums. AAAS, Science Museum of Minnesota, and Ithaca’s Sciencenter are subawardees, and SynBerc is a project partner. This project is just starting up, so I am reporting on it here even though the funding is already in hand.

The MSPES-SynBio project is aimed at building capacity among institutions of informal science education (ISE) to develop and implement multi-site public engagement with science (MSPES) activities in partnership with scientists working in the field of synthetic biology (synbio). In the first year of the project, materials will be developed collaboratively by participants from eight ISE sites, in partnership with local synbio scientists, with support from a central team of ISE professionals, synbio researchers experienced in public outreach, and experts on public engagement, science and society, and science communication. Materials tested at the eight pilot sites in year 1, will be revised and packaged into a kit like those developed by the Nanoscale Informal Science Education Network (NISE Net) for annual NanoDays events. The MSPES project will leverage work done by the NISE Net to disseminate 200 SynBio Kits to sites across the U.S. and help recipients to incorporate public engagement with science (PES) activities about synbio into their educational programs.

In addition to summative evaluation to identify project outcomes, an internal team of evaluators will develop approaches to evaluating PES activities that have intended outcomes for both public and scientist participants and are different from those of most ISE work that is firmly based on “public understanding of science” goals. All the material developed will be revised and posted online for open access to all who want to use them. In addition, a guide to developing single-site and multi-site PES activities more generally will be developed, shared online, and presented in publications and at professional meetings of informal educators and scientists.

The MSPES project builds upon the work of several prior NSF-funded projects including one that explored the extent to which ISE organizations are implementing PES as differentiated from “public understanding of science” in the Center for the Advancement of Informal Science Education 2009 report Many Experts, Many Audiences: Public Engagement with Science. Despite calls from social scientists and science policy experts for a decade, this prior work found that PES strategies are far from fully implemented in the work of ISE organizations. At a workshop held as part of the pathways project, 55 ISE professionals interested in PES outlined nine priority areas for further development of PES in ISE. The proposed MSPES project will address several of those priorities.

The team for this project includes the Museum of Science, public engagement leaders at the American Association for the Advancement of Science, scientists with particular interest in public engagement from the NSF-funded Synthetic Biology Engineering Research Center, ISE educators from the Science Museum of Minnesota, and Ithaca’s the Sciencenter, social and political scientists associated with ASU’s Center for Nanotechnology in Society (CNS) and Consortium for Science, Policy, and Outcomes (CSPO); and the Expert & Citizen Assessment of Science & Technology (ECAST) Network. Additional support from experts in engaging diverse
audiences, as well as from pilot site participants and NISE Net regional hub leaders, will ensure not only the development of new knowledge in this project but also its wide dissemination.

The ISE, SynBio, AAAS and science policy communities are all at a crossroads in terms of recognizing the importance of convening multidirectional conversations between scientists and the public around these kinds of issues, and synthetic biology provides a clear and rich path forward in terms of doing this that will allow us to build upon the work that CNS-ASU did with ISE people from the NISE net but brings in a different group of scientists. The hope is that this will provide a basis for approaching other groups of scientists with the tools that we will develop in partnership with AAAS and our colleagues.

The public will benefit from the MSPES project in several ways. The project will create materials, activities, and increased capacities among ISE organizations and scientists to engage the public in learning about synthetic biology—a topic about which a Presidential Commission has said that public deliberation is particularly valuable. It will also further develop PES in both ISE and science communities. Broader implementation of PES will help members of the public discover ways to engage with scientists to consider impacts and policies related to emerging technologies, feel a connection to the enterprises of scientific research and technological development, and even contribute to efforts to maximize their benefits to society.

Project deliverables are designed to have strategic impact on the field by building the capacity of ISE professionals to be developers, facilitators, and evaluators of PES activities, with scientists as potential partners or “clients” for whom the ISE professionals organize the engagements.

As the content of the MSPES project is developed, special emphasis will be placed both on questions that scientists would like to explore in discussion with the public, and that the public can contribute to in significant ways. A starting point for developing content will be consideration by the project team of topics like:

**Risk Management**: What processes should be put into place to ensure that health or environmental risks from synthetic biology are appropriately assessed and risks minimized?

**Openness and Transparency**: How transparent should the outcomes of synbio research be, including genetic information about novel organisms, given concerns about the potential for bioterrorism?

**Community Coordination**: How should the academic scientific community, the industry, and the DIY bio community work together?

**Oversight and Regulation**: How should we build a regulatory environment that reduces hurdles to innovation while protecting the public from unanticipated consequences?

**Public Involvement**: How should synthetic biology research be shared and communicated with the public, and what should the public role be in decision-making about synthetic biology policy?

**Ethics and Equity**: What process should be implemented for considering and responding to ethical concerns or objections to synbio research as they arise?

Workshops to develop public engagement materials and prepare participants to use them will take place on Oct 2014, Feb 2015, Jun 2015, and Oct 2015. Pilot engagement activities at eight host sites will take place in the summer of 2015, with engagement activities at 200 sites in the summer of 2016.
Design Fiction as Public Engagement with Synthetic Biology
Megan K. Halpern, Postdoctoral Researcher, ASU

The abstract concept of the future often conjures images of post-apocalyptic landscapes or naive utopias. In these scenarios, new and emerging technologies like those developed for synthetic biology are painted as the instruments of our destruction or our salvation, making nuanced discussion about these technologies a challenge for those working to engage publics in shaping technology policy. Participatory exercises and deliberations surrounding anticipatory governance and forecasting are often used to begin these more nuanced conversations. These methods of engaging publics have been successful; however, like consensus conferences and other forms of public deliberation, they may attract a specific, highly motivated, already engaged group of citizens, whereas participation in activities like those developed in informal science learning settings, like science museums, may engage a broader range of people in activities. This paper will briefly sketch an idea for a set of activities that may spark discussion around the ethical and social implications of emerging technologies like synthetic biology.

A number of science fiction authors and designers have begun to develop the concept of design fiction as a way to mitigate these wild musings about the future by focusing on something tangible: a designed object, albeit a fictional one. Bruce Sterling is often credited with coining the term design fiction, however, Julian Bleecker is perhaps the best-known designer working with, and writing about, the genre. His group, the Near Future Laboratory, recently published the TBD Catalog, a book of objects and services from the near future. The Near Future Laboratory describes design fiction as “the platform best suited for taking a sideways glancing blow at a set of open issues, exploring unknown unknowns, working through turbulent alternatives, contesting the status quo and walking down strategic alternatives.” Thus far, design fiction has rested in the hands of science fiction writers and designers, but I believe the design process can be opened up to publics to provide a playful way of beginning conversations about the future. Previous projects provide an indication that 1) Activities that ask participants to engage in an activity rather than a dialogue tend to create more focused outcomes, and 2) that speculative prototyping, or design fiction, provides an excellent strategy for such an activity.

Example: Future of Work Prototyping Activity
To provide a more clear picture of the kinds of activities I envision, I will describe an activity used in a recent workshop Professor Laura Forlano (Chicago Institute for Design) and I created for labor advocates and activists, digital activists, and others interested in technology and the future of labor. During the second part of the workshop, teams were asked to consider the most surprising or unexpected aspect of their experience at the workshop thus far, and to develop it into a prototype. Our initial observations indicated that the groups often began to build their prototype before they knew what they were building. In my own group, we began to discuss ways of rethinking the relationship between employees and healthcare workers. However, we had trouble arriving at a plan of action until we stopped deliberating and began to build. One group member assembled a cardboard box. Another added a head of yarn, and then two more members attached arms and legs. Soon we had created a healthcare robot that we imagined would be owned and maintained by primary care providers, like nurses (see Fig 1). These robot companions would complete the more mechanical tasks, like recording vital signs and taking

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blood samples, while the healthcare worker was able to speak with the patient about their history and symptoms. As we built, we began to think and talk about the implications of such a robot for the healthcare worker and the patient. We also talked about an economic structure where the nurses owned the robots, thus, retaining their job security. Being given cardboard boxes, blue tape, markers, and other supplies, as well as a time limit, suggested the prototypes should be unpolished mock-ups. This created freedom for groups to play with the materials rather than pressure to build something beautiful.

**Pop-up Public Biodesign Fiction Labs**

There are many ways to adapt the concept of design fiction as a way to engage publics, here, I sketch out one possible way. The pop-up biodesign fiction lab can be deployed in museums, schools, or other public spaces. This activity could easily be tailored to specific age groups. The labs should provide inspiration and opportunities to explore the kinds of work being done in synthetic biology, and encourage low-fi prototyping similar to the exercise described in the future of work example above.

**Performative Aspects of the Lab**

The lab space should provide a performative, ritual space. When visitors step into the lab, they become bio designers. Perhaps they are given lab coats to wear, or initiated in some way. Similarly, any inspirational or learning materials should be designed as a part of their process. What might be information cards become design briefs. The look and feel of the materials should strike a balance between highly designed space that evokes the character of a lab and an unpolished, almost home-made feel. The idea is to invite visitors to play and create whether or not they are skilled. The materials with which they will create their prototypes might be recycled paper and plastic, or other incongruous artifacts. Design protocols, inspirational prompts, or other activities may guide users toward a particular project.

**Discourse Surrounding Creations**

The creation of the prototypes itself provides the initial opportunity for discussions about the ethical and social implications of the work, and groups working together or simultaneously will likely begin these conversations. However, in order to gain a sense that their designs are part of a larger conversation, and to begin that conversation, their prototypes should be shared or displayed, or even used in scenarios. One option may be to host improvisational performances surrounding objects created in the lab. Catalogs similar to the TBD Catalog created at Near Future Laboratory may be created as well, and these catalogs may be used as a starting point for further discussions.

**Opportunities for Research**

Research questions about the way we think and talk about the future might accompany questions about the efficacy of design fiction as a method of public engagement in science and technology. In the future of work prototyping activity, participants thought in nuanced ways about the use of their prototypes. They were able to pose questions and engage in discussions through the design of the prototype. Ethnographic observations of the design process will provide interesting material for analysis, as will the artifacts themselves. Additionally, individual and group interviews with participants about their creations may be framed as a part of the performative experience. For example, interviewers may play the role of reporters, asking designers about their work.
In 2012 CNS-ASU faculty Jameson Wetmore and Ira Bennett were invited to develop a “Societal and Ethical Implications” component of a Next Generation National Nanotechnology Infrastructure Network (NG-NNIN) proposal with an annual budget of $525,000. NSF decided to cancel that funding stream at the last moment, but the network within a network that was designed might be a useful tool for thinking about social science research and engagement in synthetic biology. The basic framework was as follows:

NG-NNIN Societal & Ethical Implications Program Proposal
Jameson Wetmore & Ira Bennett, Arizona State University

Recent scholarship has demonstrated that one of the most effective ways to both research the societal and ethical aspects of nanotechnology and feed the insights gained in this process into decision making at many levels is to bring together social scientists, natural scientists, engineers, and the public to work collaboratively. The NG-NNIN, with its broad national coverage and thousands of users, is in a unique position to facilitate this type of work by serving as a nation-wide convener of these activities at its 17 universities. The NG-NNIN Societal & Ethical Implications (SEI) Program will create an infrastructure for developing new programs, facilitating collaborations, promoting research, and disseminating content and best practices that address the relationship between nanotechnology and society. The NG-NNIN SEI program will be administered at Arizona State University (ASU) and will focus on three major areas:

1. **Professional Development.** The NG-NNIN will aim to increase science and engineering undergraduate, graduate student, and postdoc’s understanding of the social, political, and ethical implications of their work:
   a) *New methods for professional development.* The NG-NNIN will develop new programming and pilot such programs at ASU, which will then be distributed more broadly through the mechanisms that follow.
   b) *Science Outside the Lab.* Each year four graduate students affiliated with the NG-NNIN will be selected to attend CSPO’s flagship educational program: “Science Outside the Lab” a two week program in Washington, DC that introduces students to how government agencies, corporations, and NGOs make decisions about science and engineering.
   c) *Mini Grants for Engagement Development.* The SEI program at ASU will coordinate the distribution of $3,000-$10,000 grants to facilitate activities at NG-NNIN universities for things like paying for an assistant to develop course material, travel for program participants, or providing extra salary for a professor with an existing full teaching load to co-teach a course with a scientist.

2. **Interdisciplinary Research and Programs.** While it is important to offer graduate students professional training to develop individuals with interdisciplinary skills, much of the future of science and technology will be developed by groups of people, often in laboratories. Thus a major component of the SEI Program will focus on fostering interdisciplinary collaborations.
   a) *Anticipatory Workshops.* These two day workshops will bring together the wide expertise of social scientists, natural scientists, museum professionals, and others from within and outside the NG-NNIN nodes to brainstorm future technological possibilities and implications of specific nano-enabled fields.
b) **Mini Grants.** Grants between $3,000 and $15,000 will be made available to groups wishing to do interdisciplinary work on the societal and ethical implications of research.

3. **Museum Collaborations.** In order for social scientists, natural scientists and engineers to truly understand the links between nanotechnology and society we must work with and learn from the public.

   a) **Partnerships between nodes and local science centers.** The NG-NNIN SEI Program will identify and facilitate partnerships between scientists, engineers, and museum professionals with complimentary expertise and common goals. These partnerships will help the public understand our work and, more importantly, help our researchers understand the public.

   b) **Annual network wide museum collaborations.** The SEI Program will pilot a different interdisciplinary program each year, drawing from multiple museums and NG-NNIN nodes. These could include a workshop for graduate students and PIs on how to present research to a broad audience or a competition for graduate students and lab groups to develop tabletop demonstrations that help the public to understand the technical and social aspects of their work.

   c) **Mini Grants for Science Museum Development and Collaboration.** The SEI program will offer partner science centers grants of $3000 to facilitate their collaboration with NG-NNIN researchers.

**Building an SEI Network**

While much of the NG-NNIN’s SEI work will be facilitated through the ASU node, a number of strategies will be employed to capitalize on the strength of the entire network.

1) **Congress on Collaboration in the Social and Ethical Implications of Research.** In years two and four the SEI Program will host a Congress that brings together representatives from every node to work with and learn from professionals from across the country and other large networks and centers.

2) **Development Charettes.** In conjunction with the Congresses, the SEI Program will sponsor one day workshops that give scholars from NG-NNIN nodes a collaborative space for developing new professional development programming.

3) **SEI Fellows.** In the first generation NG-NNIN it was difficult to find reliable SEI coordinators at every site, but a handful of scholars stood out, doing very good work. These fellowships will recognize SEI leaders at NG-NNIN nodes, give them funds to continue the SEI work they do and strengthen their relationship to the NG-NNIN, and provide incentive for NG-NNIN nodes to recruit faculty at their universities to do SEI work.

4) **Travel funding for Collaborative work.** The SEI Program will sponsor trips for scholars looking to pick up new skills and approaches by spending time embedded at an aspirational peer site for up to a week. Money will also be set aside to make sure that the director and associate director are able to engage in site visits at various nodes.

5) **Clearinghouse Website.** To further disseminate established programs and prevent continued reinvention of engagement programs, the SEI Program will collaborate with Purdue University’s NanoHub to develop a website dedicated to providing syllabi, tips, and pitfalls to avoid.

6) **Evaluation.** In an effort to continually improve these programs and develop data for publishing and promoting them, we will hire an outside consultant for evaluation. They will provide an overall analysis of activities and an analysis of at least one targeted program each year.
China’s role as the world’s factory – a role it has played for the last three decades – is undergoing a major transition: from ‘made in China’ to ‘designed and created in China,’ from imitator to innovator. Like the “newly industrializing economies” of East Asia a generation ago, China’s meteoric economic growth has been fueled by export-oriented industrialization. The extraordinary amount of Foreign Direct Investment China receives was originally driven by its plentiful supply of cheap labor. In recent years, however, as its economy has grown at historically unprecedented rates, its investments in science and technology have started to pay off. As labor costs have risen, foreign firms are increasingly drawn to China for two other reasons: the ability to partner with China’s growing (and relatively inexpensive) science and engineering talent pool, and access to what is becoming the world’s largest consumer market. China has grown to become the world’s second-largest economy, its GDP surpassing Japan’s in 2010. Corrected for purchasing power parity, PPP, the IMF estimates that China’s economy will surpass that of the U.S. in 2016 – assuming, of course, that current trends continue.

Despite its frequent assertions to the contrary, China clearly sees itself as an emerging world power, bent on becoming globally competitive both economically and technologically, and thereby resuming what the Chinese increasingly feel is their rightful place in history. Shortly after his appointment as the general secretary of the Chinese Communist Party, during a visit to the National Museum off Tiananmen Square, President Xi Jinping stood in front of an exhibit called ‘The Road to Rejuvenation,’ and reminded the assembled dignitaries and reporters that

After the 170 or more years of constant struggle since the Opium Wars, the great revival of the Chinese nation enjoys glorious prospects… Now everyone is discussing the Chinese dream, and I believe that realizing the great revival of the Chinese nation is the greatest dream of the Chinese nation in modern times.  

Since its adoption of the 15 year Medium and Long Term Plan for Science and Technology (hereafter MLP) in 2005, China’s leaders have been investing increasingly in ‘indigenous innovation’ in advanced technologies, as a means to realizing the “Chinese dream.” The MLP calls on China to invest heavily in advanced technologies, with nanotechnology identified as one of four ‘science megaprojects’ for special attention. The MLP, reinforced by China’s 11th and 12th Five Year Plans, and buttressed by similar plans and spending at the provincial and local levels, can be seen as state-led industrial policy. This investment in science and technology has

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3 The others are reproductive biology, protein science, and quantum research. The MLP also identifies thirteen ‘engineering megaprojects,’ eight ‘frontier technologies,’ and eleven ‘key areas’ for targeted investment.
yet to pay big dividends, but the trend lines are promising. China’s universities and science parks are impressive to look at, with labs and facilities that rival those of the U.S. and Europe. Sparkling facilities, however, do not automatically translate into innovative breakthroughs.

In our past research at CNS-UCSB, my group has utilized a mixed-method approach to studying China’s success in promoting nanotechnology. We have conducted numerous field trips to universities in Beijing, Tianjin, and the Shanghai area and interviewed leading scientists, engineers, and architects of China’s nanotechnology programs. Our initial research focused primarily on basic research; more recently, we have looked at the commercial results of this research, including a case study of Suzhou Industrial Park. We have also analyzed publications and patents, using bibliometric data-mining techniques. In both cases our central questions have been twofold: (1) How effective is Chinese state policy in fostering innovations in nanotechnology – particularly innovations that result in products that could result in sustainable economic growth? (2) What is the role of international collaboration in fostering S&T development in China?

These questions, and methods, could be readily adapted to the study of synthetic biology in China. Despite the absence of an agreed-upon definition of synthetic biology, it is high among China’s future investment priorities, seen as having the potential to create breakthroughs in both basic science and practical applications. Research in areas related to synthetic biology began as early as the 1960s, when Chinese scientists made synthetic insulin; China is active in the Human Genome Project, contributing to its database; and China has been investing in emerging technologies such as genomics, bioinformatics, stem cell research, and, of course, nanotechnology. All of these are fields related to synthetic biology, providing a strong foundation on which to build (Pei, Schmidt, and Wei, 2011). Five British universities have recently received grants from Britain’s Synthetic Biology China Partnering Award program; in the words Douglas Kell, head of Britain’s Biotechnology and Biological Sciences Research Council (BBSRC), “co-funded initiatives such as this scheme will see British and Chinese scientists learning from each other’s expertise and benefiting from the globalization of excellent science.” And the third annual Cold Spring Harbor Asia conference on synthetic biology will be held in Suzhou, is scheduled for December 1-4, 2014.

A future societal initiative on synthetic biology would be remiss in overlooking the global role that China will play in basic research, development, and commercialization, the result of both aggressive state policies and international collaborations.

4 It is included in the Chinese Academy of Science Roadmap for Innovation 2050; CAS roadmap Innovation 2050 (http://www.edu.cn/html/rd/z/cxlx.shtml)
6 The 3rd Cold Spring Harbor-Asia meeting on Synthetic Biology will cover recent exciting developments in synthetic biology research around the world covering novel genome engineering tools and strategies for both prokaryotes and eukaryotes. One of the core synthetic biology themes, designing cellular circuits, will also be covered. This meeting will also cover recent advances in metabolic engineering, which upon integration with synthetic biology, is playing increasingly important roles in moving towards bio-based economy through the establishment of bioprocesses for the sustainable production of chemicals, fuels and materials from renewable non-food biomass. More exciting emerging tools and techniques of synthetic biology will also be covered (http://www.csh-asia.org/2014meetings/synthesis.html)
In this paper we focus on the collaboration that has been established in the field of synthetic biology between the European project SYNENERGENE (www.synenergene.eu) and student teams participating in the annual undergraduate international Genetically Engineered Machines Competition iGEM (www.igem.org).

SYNENERGENE is a Mobilisation and Mutual Learning Action Plan on challenges in Responsible Research and Innovation (RRI) in synthetic biology within the European Commission’s FP7 Science in Society Work Program. As a new emerging field synthetic biology offers huge potential for novel drugs and vaccines, as well as for ‘greener’ chemicals and biofuels. Nonetheless, this field, about which there is as yet fairly scant public knowledge, also brings with it various challenges, ranging from regulatory issues of biosafety, biosecurity and intellectual property rights to potential environmental and socio-economic risks in developing countries. Thus, in the context of RRI, synthetic biology raises questions relevant to many different stakeholders, policy makers and the general public. SYNENERGENE aims at mobilizing a wide variety of stakeholders and members of the public, bringing them together and facilitating a sustainable and fruitful dialogue in order to promote responsible research and innovation in synthetic biology.

iGEM represents a growing community of dedicated young science students who already work in the spirit of RRI, contributing to the development of synthetic biology as a new field of engineering. At the beginning of the summer, student teams are given a kit of biological parts from the Registry of Standard Biological Parts. Working at their own schools over the summer, they use these parts and new parts of their own design to build biological systems and operate them in living cells. This project design and competition format is an exceptionally motivating and effective teaching method which also strongly fosters the spirit of RRI. So-called ‘policy and practices’ work is an inherent part of each iGEM project. One of the aims of the established collaboration is to extend these practices of RRI by stimulating interaction between the iGEM community and partners in the SYNENERGENE network and to get inspired by the work and creative ideas of the iGEM teams in its own activities.

The collaboration provides for an iGEM Fund offering small grants to iGEM teams for contributions to the program of activities undertaken by SYNENERGENE partners. One example is a series of ‘real-time technology assessments’ to explore possible futures for synthetic biology, which will be carried out by SYNENERGENE partners in collaboration with iGEM teams working on particular creative and significant ideas for innovation. Other examples include contributions from iGEM teams to: anticipatory and adaptive forms of biosafety assessment in the field of synthetic biology, the development of a web-based educational platform introducing synthetic biology and its potential applications and implications in a playful way, and the development of design ideas for exhibitions aiming to expose the public in imaginative and artistic ways to different dimensions of synthetic biology.
In this paper we discuss our experiences with a recent call for proposals from iGEM teams with an interest to collaborate in a process of real-time technology assessment supported by partners from SYNENERGENE. iGEM teams will have to contribute in their policy and practices work to a process of real-time technology assessment by elaborating two different kinds of future scenarios relating to SynBio applications envisaged by the teams:

*Application scenarios*
Application scenarios offer detailed and realistic descriptions of how SynBio ideas can lead to actual applications in society, including: design criteria for the products proposed, target producers and users of the products, the needs and costs involved, legal issues of patenting, regulatory requirements, potential safety, social and ethical implications, and available or conceivable alternatives.

*Techno-moral scenarios*
A techno-moral scenario is a tool to stimulate imagination, reflection and debate about ways in which SynBio applications may transform our society through wider impacts, including ethical, legal and social issues.

SYNENERGENE partners will take up the scenarios as a starting point for an interactive process of technology assessment, involving a variety of stakeholders and iGEM team members in workshop settings with the aim to develop socially robust agendas for SynBio innovation. Scenarios will also be used by SYNENERGENE partners as a tool in organizing public debates on SynBio futures.

An important step in the development of application scenarios is to identify and specify the practices and conditions in which particular SynBio applications envisaged by iGEM teams might be produced and used. How does these practices look like, who is involved in what role, and how will these practices be changed and affected by the new applications? Knowledge about the experiences and visions of actors involved in these practices is vital for the elaboration of future application scenarios.

While application scenarios focus on the prospects and challenges for innovation and related regulatory concerns in regard to risks and ownership, ‘techno-moral scenarios’ highlight the wider transformative potential of future applications of synthetic biology in society. Techno-moral scenarios explore the ways in which new technologies may challenge and shape what we want, how we relate to each other, and how we relate to the world. Thus they invite audiences to imagine and appraise ways in which particular SynBio applications might change our world, our ideas, values and ideals.
The biosecurity, biosafety, bioweapon, and biodefense risks of synthetic biology are enormous and have been discussed in some detail (e.g. Petro et al., 2003, Lemon and Relman et al., 2006). Such risks may include everything up to the destruction of most of life on Earth. These worst-case scenarios should not be discounted, because there are not only individual cults and terrorist groups that would be happy to perform such heinous acts, but also possibly entire states, such as North Korea. Historically, many states have been involved in bioweapon research and production, and as the power of biotechnology is democratized we should also expect non-state actors to become involved, as indeed some already have (e.g. the Rajneeshees in 1984, the 2001 Anthrax attacker, etc.).

This raises the question of global catastrophic and existential risks. The philosopher Nick Bostrom has described global catastrophic risks as risks which threaten massive global disaster and existential risks as risks which threaten human extinction (Bostrom, 2002). Synthetic biology presents such risks, especially if permitted as a DIY hobby that anyone, including terrorists, could pick up. Because synbio permits such significant changes to living organisms, we should not expect to be able to prepare for all the various diverse and unpredictable bioweapons that could be produced by a fully democratized DIY synbio milieu. Indeed, we cannot even effectively deal with the natural biological problems that nature throws at us now.

The philosopher Hans Jonas has argued that the first and most important rule of ethics, his “imperative of responsibility,” is that humankind must exist in the future (Jonas, 1984). One is not allowed to play a “va banque” game with humanity. Therefore anything that puts humanity at risk ought to be carefully controlled or eliminated, if possible. There are many risky things that we cannot control, but synthetic biology need not be one of them.

Recalling the “risk equation” (risk = harm x probability), Michael Davis has argued that for any unacceptable harm with a non-zero probability the risk is too high (Davis, 2012). Human extinction should qualify as an unacceptable harm; therefore, since DIY synbio permits a certain non-zero probability of that harm, it presents an unacceptable risk that ought not be permitted. As we enter the risk terrain of DIY synbio, we – or at least some of us – are deciding that we are willing to risk everything on the possible finite goods synbio might give to us. Reasonable gamblers should not risk everything, including their own lives, on a finite win.

Given the dangers presented by synbio and the ethical rule that humans ought to exist in the future (which we ought hardly to need, as self-interest would hopefully suffice), we need a strong governance and policy response to this threat. The current Presidential Commission for the Study of Bioethics Issues response of “prudent vigilance” is insufficient. “Prudent vigilance”
would have been an odd solution to the dangers of nuclear power, for example. Synthetic biology permits the creation of destructive capacities worse than nuclear weapons and at much less difficulty. Adaptation to and mitigation of these risks will likely need to be, therefore, even more significant than the changes to the world that occurred due to the advent of nuclear weapons. Perhaps it is only because the power of nuclear weapons was made clear on Hiroshima and Nagasaki that nuclear technology has been controlled as well as it has. In lacking examples of the destructive power of synbio, our collective imaginations seem to fail. How can we respond to this failure of the imagination? We need to present these ideas to the public as best we can.

Mitigation of and adaptation to the risks of synbio should be a top priority. This will require policy responses which include governance over scientific research and technological development. When people try to make nuclear reactors at home (as has happened more than once), the public and the government should be concerned. Reactors are peaceful uses for nuclear power, but they still do not belong in people’s homes. Likewise, when someone tries to do synthetic biology “at home,” the public and the government should be concerned. Glowing plants are not weapons, but the same methods which produce them could produce much worse things. No finite benefit can justify the risk of human extinction, but what of the risks of smaller accidents or attacks that might kill “only” millions of people? Can any benefit justify that level of risk? I would think not, but this is a question for the public to decide, not for academics, scientists, engineers, DIY inventors, or any one group. This is a question of the common good, and so the decision makers should be everyone. Synthetic biology needs intense scrutiny, public discussion, democratic process, and limitations and enforcement to prevent unacceptable scenarios, so that we produce the best possible future with these technologies and not the worst.

References


Sparse Information Mitigation Strategies for Managing Emergent Risk in Synthetic Biology

George Khushf, University of South Carolina
in collaboration with Chris Anderson, UC Berkeley

Our research considers the following questions related to emergent risk, biosafety, and security:

(1) How are questions of risk, safety and security best addressed in an emerging area where there is sparse information for working up risk questions, and where simple allocation of burden of proof along traditional fault lines of precautionary vs risk-based management strategies only leads to polarization and counter-productive posturing? Which aspects of risk, safety, and security can be addressed as technical problems (e.g., design of safe organisms or algorithms for screening orders to sequencing companies) and which aspects are better addressed in terms of institutions and policies and in terms of new forms of governance and/or norms and cultures of responsible innovation? Where are collaborations needed between social impacts/ELSI researchers, scientists and engineers to develop strategies for managing risk, safety, and security associated with synthetic biology? Alternatively, where is research and development best handled in terms of more specialized, disciplinary projects?

(2) How can synthetic biology inform and extend our capacity to monitor and manage risk, assure safety and promote security? Social impacts research is usually oriented toward the ways synthetic biology generates problems of risk, safety, and security. However, the field also provides a host of new tools for conceptualizing and addressing such problems. In what ways might synthetic biology help us better understand and manage risks? Bioinformatics initiatives used to identify commercially viable targets of microbial chemical factories might also enable us to better understand the nature of the risks associated with specific research areas. There are also various technical strategies that can be used to design organisms so they are safe, e.g., to assure containment, establish dependence of organisms on artificial environments, bar code or preserve memory of development that can be used for tracing, or protect with safety mechanisms like kill switches and control circuits. Beyond these technical solutions, synthetic biology offers more general ways of understanding and interfacing with living systems that might inform governance; e.g., evolutionary and combinatorial design strategies commonly used in synthetic biology provide ways of managing systems that remain opaque to users; and new regulatory and control strategies might be generalized to monitor and manage error and failure. Traditional discourse on risk and governance often assumes a capacity to gate, monitor and control technological developments that is unrealistic, and it often requires extensive data that is not available at early stages of research and development. This, in turn, leads to huge discrepancies between the rates of technological development and those of social oversight mechanisms. In what ways do our approaches to risk and governance work with assumptions about how we understand and manage technology that are no longer fit for the practices and products associated with synthetic biology? Are there ways a philosophy of the emerging science and technology can inform approaches to governance that are more agile and better track the current realities of the science?

(3) How do we identify and understand emergent risk? Synthetic biology involves an extension of tools associated with recombinant DNA research and, more generally, molecular biology and biotechnology. The risk space for these antecedent fields has been partially mapped, and there are an extensive range of policies for
managing these risks. When asking about the risks associated with synthetic biology, we are thus not asking about the risks of a technological capacity that is viewed independent of policy. Instead, we are concerned with the differential elevation in risk associated with managing the emerging research as if it were of a conventional sort. The risk associated with an emerging STEM field is the elevated, unmanaged risk that potentially calls for some extension of policy. Mapping this emergent risk is especially difficult because it requires specification of a relevant extension of the emergent field over the conventional field of research together with an appreciation of how this specific difference leads to an elevated residual risk. When does the relevant specific difference involve an unmitigated risk that is above a threshold that calls for an extension of policy to manage that risk?

How do we best identify and manage these emergent risks in synthetic biology? Are there strategies that can be used to rapidly work up questions of realistic emergent risks, so we can initiate research that enables us stabilize and extend the policy infrastructure at a rate that roughly tracks the rate of technological development?

(4) What policies and initiatives are relevant when considering emergent risk, and what assumptions about the development, use, and associated practices of technology are implicit in such policies? As noted in (3), emergent risk is a complex function of the difference between emergent and conventional technology and the background policies for managing the conventional risk. To clarify the policy challenge associated with an emergent domain, we thus need to understand the relevant background policy and recognize mismatches between assumptions about technology integral to the policy and the current realities of the technology to be managed by the policy. Similarly, new initiatives to manage risk involve assumptions about technology that may or may not be appropriate; for example, DARPA initiatives assume virulence of a pathogen can be specified at the level of a gene, and thus handled as a modular component that is transported from one organism to another. This assumption also informs strategies for determining biosafety levels of research based on the risk group of the wild type of an organism or that of a gene derived from a pathogen. Related assumptions maintain a focus on select agents when considering bioweapons. Are these assumptions appropriate? Any gap analysis of the policy infrastructure depends on recognizing the messy patchwork of relevant policies and the assumptions about technological types and uses implicit in those policies. How do we clarify the relevant patchwork, identify the problematic assumptions, and advance an understanding of gaps in ways that can constructively inform new, more fitting approaches to governance?

(5) How can we develop forms of risk analysis and management that work with sparse information? In emerging research areas there is often insufficient data for conventional risk analysis. Even in areas where a risk scenario can be specified, many or even all of the steps in the risk pathway may be poorly understood. It may be very costly to obtain data on the probabilities of steps in the risk pathway and obtain reasonable estimates of the harm should the risk scenario occur. Generally, risk analysis is data hungry and expensive, and it can divert resources away from promising lines of research that can have a significant, positive social impact. Strategic decisions must thus be made about where to allocate scarce funds for obtaining risk data and for balancing research on risks against research directed toward promising new applications. Are there ways of understanding and managing risks that are less data hungry, and that can work with the sparse information associated with emerging research in synthetic biology?

We are working on sparse information mitigation strategies that can address these challenges.
Risk Assessment of Genetically Engineered and Synthetic Biology Microorganisms by EPA under the Toxic Substances Control Act

Gwendolyn McClung, US Environmental Protection Agency

Risk evaluation is an important societal aspect of synthetic biology, as the public expects that new technologies, and the products of those technologies, will be safety introduced into society. Under the Toxic Substances Control Act (TSCA) implementation of the Coordinated Framework for Regulation of Biotechnology, the U.S. Environmental Protection Agency (EPA) is responsible for assessing the risk of certain genetically engineered microorganisms (GEMs) that are “intergeneric,” meaning that they are formed by the deliberate introduction of genetic material from a genus different from that of the recipient microorganism. The term intergeneric can include those GEMs created through the use of synthetic biology techniques if the introduced genetic material is not identical to that which could be found in the genus of the recipient. GEMs falling under TSCA’s jurisdiction may be used for a variety of purposes including, but not limited to: fuel production, biomass conversion, waste treatment, biofertilizers, biomining, bioremediation, biosensors, microbially enhanced oil recovery, desulfurization of fossil fuels, and closed system fermentation for the production of enzymes and commodity or specialty chemicals.

EPA evaluates the risk posed by a use of a GEM under the paradigm of Risk = Hazard x Exposure. Because EPA under TSCA is responsible for premanufacturing review of GEMs, its analyses are necessarily predictive and need data and tools to perform those predictions. Because premanufacture notifications typically do not come with sufficient data to assess the substance, EPA must necessarily use indirect data, such as literature on the recipient and/or analog microorganisms, to predict how the prospective product organisms might behave under a wide range of circumstances.

In conducting its GEM risk assessments, EPA details the genetic modifications to the recipient organism and identifies the original donor organisms. The hazard assessment evaluates potential hazards posed by the introduced genetic material and includes an evaluation of the potential for horizontal gene transfer of this genetic material to other microorganisms in the environment. For human health, the assessment evaluates the potential pathogenicity/toxicity and allergenicity of the GEM. For ecosystems, it examines the potential for pathogenicity/toxicity to terrestrial and aquatic animals and plants. Potential hazards also include interactions of the GEM with other microorganisms in the environment and its effects on environmental processes such as biogeochemical cycling.

EPA’s estimate of exposure considers production volumes and evaluates exposure of the GEM to workers, and releases of the GEM from production facilities or during field testing if the use anticipates an intentional environmental release. In addition, release estimates are used to estimate inhalation and drinking water exposures of the GEM to the general human population and exposures to the environment.

Synthetic biology may lead to novel microorganisms that make risk assessment challenging. Synthetic biology is usually thought of as a continuum from the use of just one or several chemically synthetized genes to extreme metabolic engineering to extreme novelty, such as the creation of organisms with alternate codon usage, or organisms with xenonucleic acids. If the
traits of a microorganism are radically changed from those of the recipient strain, comparison to the parental strain may no longer be appropriate.

In the absence of comparator microorganisms such as the wild-type, it may not be possible to predict the behavior of newly developed synthetic biology microorganisms in the environment and their interactions with other microorganisms. Likewise, there may be unknown effects on terrestrial and aquatic flora and fauna that cannot be predicted.

Completely synthesized genomes are another example of when there is no comparison to a wild-type organism. Even alterations in the cell wall or cell membrane of a microorganism for some useful purpose through synthetic biology techniques may make risk assessment difficult.

These issues create the need for additional research to support GEM risk assessment. They include the following:

- There is a need for extensive testing of some types of synthetic biology microorganisms before they are released into the environment. Research is needed to develop testing approaches that are inexpensive, reliable/reproducible, and generalizable over broad categories of GEMs.

- Microorganisms are typically considered to be sensitizing agents. Unfamiliar cell wall or membrane proteins may change their allergenic potential, and research is needed to develop methods for evaluating the allergenicity potential of GEMs.

- Comparison of orthogonal life to wild-type organisms cannot be made. Although the design of an organism by replacement of all copies of a particular codon with a different codon not found in naturally occurring microorganisms may be an intentional biocontainment strategy, research is needed to determine the stability of this strategy and whether reversion to naturally occurring codons can occur, particularly with DNA repair mechanisms inherent within the cell, or even uptake of naked DNA from the environment.

- The possibility for transfer and incorporation of xenonucleic acids into naturally occurring microorganisms and what effects may result in these microbial cells also needs investigation.

- Likewise, research is needed on the stability of use of xenonucleic acids as a biocontainment measure.
Modeling Risk in Complex Bioeconomies
Clark A. Miller, Associate Director, Consortium for Science, Policy & Outcomes, ASU

Economic theories—and their applied variants in business practice—are almost entirely grounded in abstract concepts (e.g., supply, demand, labor, capital) that divorce market phenomena from the specific social, political, and technological contexts within which they occur. Social scientists have studied the processes and practices by which actors make market abstractions, noting that they do so simultaneously, across epistemic, performativity, and materiality dimensions (e.g., Cronon 1991; Steinberg 1994; Sunder Rajan 2006; Mackenzie 2008; Busch 2013). Yet, as recent concerns about sustainability highlight, even the simplest of markets, such as commodity markets, can never fully be isolated from the complex webs that link key aspects of these markets to diverse social, ecological, technological, and geophysical systems. How much worse, then, complex market phenomena—that cut across biology, society, economy, engineering, and ecology—such as those envisioned in novel synthetic bioeconomies?

Bioeconomies have a lengthy historical record that testifies to the problem of market abstraction. Agriculture has fed large populations for thousands of years; yet, great famine has also persisted as a systemic feature of the political economy of agricultural markets (Sen 1981). For the vast majority of agricultural history, slavery and indentured servitude were common. Today’s agricultural system has perhaps escaped famine and slavery (although hunger and malnutrition persist at high levels, globally, as do mistreated farm workers), at the expense of massive resource inputs that have contributed to land degradation, disruptions of carbon and nitrogen cycles (and associated impacts, such as climate change, deforestation, ocean acidification, and ocean dead zones), widespread pollution from agrochemicals, the construction of massive water systems (with their own disruptive effects), and the rise of monocultures that are highly vulnerable to increasingly pesticide-resistant diseases and demand constant innovation in order to fend off rapid declines in yield and productivity. Likewise, today, agro-food systems have hugely distorted human nutritional patterns, especially around the overconsumption of sugars, contributing to rapid increases in the United States in childhood obesity, diabetes, and other diseases.

Other modern bioeconomies have also had their share of problems. Blood manufacturing systems, crucial to the practice of surgery and emergency medicine, as well as treatments for hemophilia and other diseases of the blood, have experienced numerous episodes of disease transmission, including hepatitis C and AIDS (Dubin and Francis 2013). Hospitals and feedlots have combined to produce super-resistant microbes that cannot be treated by any known antibacterial medicines. Interwoven food and transportation markets combine with migratory bird ecologies to annually generate and spread deadly infectious diseases among people, pigs, and avians. Other market interactions generate sporadic but seemingly inevitable outbreaks of foodborne pathogens—e.g., periodic outbreaks of Ebola from bushmeat markets and e. coli infections in hamburger. Recently, complex interactions between food and fuel markets contributed to price spikes for staple foods in poor communities around the globe. These risks are compounded when we go beyond considerations of health and biophysical harm to include consideration of social and economic risk, power, identity, justice, and ethics.

The risks associated with complex bioeconomies arise both because: (1) markets transform complex relationships among social, technological, biological, organizational, economic, and ecological systems, and (2) existing forms of knowledge have a great deal of difficulty in
capturing the complexities of cross-system dynamics. While synthetic bioeconomies are hardly unique, they complicate concerns about risks for several reasons. First, they create novel forms of life whose biological properties are not fully known or predictable when integrated into complex biological and ecological systems. Second, they unsettle taken-for-granted social, political, and cultural assumptions around which (sometimes only modestly) stable social orders have been established. Third, they create new demands for biological production (e.g., biofuels) that may stress already overwrought relationships among social, technological, and biological systems. Fourth, they potentially disrupt (sometimes only modestly) stable markets that provide critical services (e.g., food and health) to large populations. Peoples’ lives, livelihoods, identities, relationships, institutions, and communities are bound up with biomarkets—to transform such markets is inevitably to transform society.

To develop a capacity to address these concerns in an anticipatory fashion—as opposed to simply reacting to surprises that occur—requires a capacity to model complex bioeconomic transformations that straddles biological (including medical and ecological), economic, engineering, and sociological disciplines. By model, I mean significantly more than computational modeling. While some risks may occur as a result of dynamics that are fully quantifiable, others may not. Social practices, meaning and identity formation, ethical norms, and organizational and institutional dynamics are frequently critical elements in the rise and propagation of risks. Often risks arise as a result of social practices, or of social responses to new possibilities or events, as the recent outbreak of Ebola virus in W. Africa is revealing. Just as significantly, these challenges demand analyses that extend across supply chains and over the full lifecycle of synthetic bio-products, and they demand a capacity to model both functioning systems/markets and the ways in which systems/market transformations come into being and take shape, sociologically.

Accomplishing these goals will require unprecedented interdisciplinary collaboration. It will require new forms of synthesis in systems modeling that provide meaningful insights across social, organizational, technological, biological, ecological, and economic models built on radically different epistemologies. It will also require greater transparency in the early phases of synthetic bio-product and bioeconomy formation than is common in current intellectual property regimes or innovation policies. It will require a robust capacity to anticipate the social dynamics of new bio-capabilities and to monitor evolving social dynamics to compare real-world developments to modeled and anticipated expectations. Finally, it will require new forms of inquiry and organization to feed the insights of these types of knowledge into practices of responsible innovation within the synthetic biology industry.

Due to the relatively early stage of synthetic biology research and development, NSF has the opportunity to invest in the research necessary to develop tools and methods for critically and comprehensively assessing risk in emerging synthetic bioeconomies, but only if they begin now. Work under programs such as the now ended Biocomplexity program, the just beginning Resilient Interdependent Infrastructures Processes and Systems program, and the long-running Coupled Natural-Human Systems program could potentially serve as a model for such an initiative, but each is structured in ways that limit inquiry so as to prevent the development of the kinds of tools and expertise necessary. In particular, new initiatives should find strategies for studying complex multi-system dynamics that blend what can be measured quantitatively and modeled computationally with research strategies that examine social, institutional, and other dynamics that cannot. Absent such an effort, synthetic biology will, without warning, as history suggests of all previous bioeconomies, generate new risks that surprise us and create destruction and havoc.
Synthetic Biology to Create Cyanobacterial Biocatalysts for Green Chemistry
Wim Vermaas, Foundation Professor, Arizona State University

**Synthetic biology.** Synthetic biology is a broad term with at least two fundamentally different meanings or connotations (Stephanopoulos, 2012). One is metabolic engineering on steroids, where multiple genes are deleted, introduced, or modified in an existing organism, usually with the goal of having the organism produce desired compounds or carry out desired functions. The other is –ideally- a synthetic cell or de novo design of an organism to carry out novel functions. Whereas there are many examples of the former type of synthetic biology, a de novo design of an organism has not yet been accomplished and most likely is well into the future. The reason for difficulties in de novo design is not that it is too challenging to chemically synthesize and assemble a large genome of 1 Mbp (1 million nucleotide pairs) or more; indeed, this has been proven to be feasible (Gibson et al., 2010). Instead, making a “new” organism de novo has not yet been feasible because we do not understand the intricate regulation of the cell that allows proteins to be expressed in the right amount and at the right time. Thus far, organisms with synthesized genomes have been built solely on the blueprint of existing organisms, with rather minor modifications (Gibson et al., 2010; Annaluru et al., 2014). As de novo design of viable organisms with desired functions is still outside the realm of present reality, societal discussions on this may be deferred until there is more clarity on what new life forms may be possible. Therefore, I will focus here on synthetic biology as “metabolic engineering on steroids”.

**Metabolic engineering.** Molecular biology advances in the past decades have enabled the development of organisms with new functions, often to produce desired compounds. This has led to the facilitation of “green chemistry”, where compounds that are typically made from petroleum can now be made biologically, thus providing a sustainable way to produce compounds that currently originate from non-renewable resources such as oil. Therefore, metabolic engineering has significant potential in making our lifestyle more sustainable.

Metabolic engineering often makes use of yeast or *Escherichia coli*, microbes that have been genetically engineered to be able to produce the appropriate products and that are grown to high cell density in large fermenters. However, in typical applications biological production with these organisms requires that one feeds the metabolically engineered organism with a fixed-carbon source such as sugar, which is converted to a desired compound, such as a building block for polymers. These sugars, directly or indirectly, come from plants that made them through photosynthesis. At large scale this is one more way that the human population uses plant material, providing competition with crops grown for food, feed or biofuel. As agricultural production will need to grow significantly in the coming decades just to keep up with increased demand for food, feed and fuel, alternate ways for sustainable production of petroleum substitutes are desired. A more direct way to provide fixed carbon for production of desired products is to have the organism perform photosynthesis itself, so that it can make the fixed carbon that it can convert into desired products (reviewed in Oliver and Atsumi, 2014). This “one-stop-shop” approach has many advantages, including that it does not divert crop production towards yet one more important use, but requires that the genetically modified organisms used for production of desired chemicals are grown outside, exposed to sunlight.

**Phototrophic production of desired compounds.** The phototrophic organisms that are used for production of “green chemicals” typically are cyanobacteria, which are photosynthetic bacteria that perform the same type of photosynthesis as plants. In fact, they are the evolutionary
progenitor to chloroplasts, the photosynthetic organelles in plants. Some strains of cyanobacteria are readily transformed, and a number of strains have been developed that form desired products (Oliver and Atsumi, 2014). However, large-scale application of these organisms requires these organisms to be grown in extensive photobioreactor systems. These systems may cover large areas, and leakage etc. cannot be totally excluded. Therefore, any organisms grown there must be safe, must not persist in the environment, and must be approved for potential release. Fortunately, organisms that produce compounds for human use typically do not grow as quickly as the wild-type strain as they need to invest energy and resources into producing compounds for us. Therefore, strains that have been genetically modified in this way typically do not have the potential to become invasive species. Nonetheless, it is important to perform thorough studies regarding the safety and ecological effects to avoid potential issues.

The issue of release of genetically modified photosynthetic microbes is not fundamentally different than that of release of GMO plants. The majority of corn, soybean and cotton grown in the US is genetically modified, and there is no indication of inherent negative effects of the GMO plants during the past dozen or so years that they have been routinely planted. Any genetically modified photosynthetic microbes that are considered for large-scale production outdoors should have been demonstrated to be harmless and not particularly invasive, and any genes that have been added should not have the potential for toxicity. Genetically modified photosynthetic microbes are going through testing for EPA review of outdoor cultivation (http://www.epa.gov/biotech_rule/pubs/submiss.htm) and several strains can now be grown outdoors. The biggest differences in terms of the risks of the plant and microbial systems are (1) microbes are more prone to horizontal gene transfer, leading to potentially increased rates of gene flow from one organism to the other in microbes vs. plants, and (2) in aqueous media there is increased potential for movement and thus genetic exchange vs. in terrestrial plants, although in plants pollen has great potential for spreading as well.

Overall, society will need to weigh the advantages of metabolically engineered photosynthetic microbes in their contribution to a more sustainable society, vs. the potential risks (currently viewed to be rather minimal) that may come with inadvertent gene transfer or with issues that we currently have not considered. The potential risks related to the latter category obviously are unknown, but in view of the maturity of the field it seems unlikely that major surprises are still in store. One additional societal question to be considered in the risk/benefit analysis is what alternatives might be available and preferable to provide polymers (plastics, nylon, etc.) without the use of oil. After considering all major factors, it is my view that sustainable production of “green” chemicals in photosynthetic microbes that have been modified to produce large amounts of such compounds carries an acceptable risk and has many benefits, including reducing our oil dependence.

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An International Look at Regulatory Oversight of Synthetic Biology: 
Focus on Engineered Organisms with Intended Environmental Use
Sarah R. Carter, Policy Analyst, J. Craig Venter Institute
Robert M. Friedman, VP for Policy and University Relations, J. Craig Venter Institute

Synthetic biology is part of a new generation of biotechnology that will enable new types of products not easily achieved with today's genetic engineering. In the next 5 to 10 years, this expansion is likely to include new technologies with intended uses in the environment. Examples include organisms developed for biofuel purposes include algae that produce fuel from sunlight and plants genetically engineered for use as biofuel feedstocks. While some of these technologies are likely to be developed in the United States, product developers in other countries will employ synthetic biology and other newer generation biotechnologies as well. Moreover, product developers will be looking for production opportunities and markets for their products throughout the world. An understanding of the complex and varied regulatory oversight that currently exists for organisms engineered using synthetic biology is a necessary and vital component for understanding the societal implications of this new technology.

For example, we recently completed a report, funded by the Department of Energy and the Alfred P. Sloan Foundation, on the challenges that will arise for the U.S. biotechnology regulatory system with the increasing use of synthetic biology and other new genetic engineering techniques, with a focus on organisms with intended uses in the environment (Carter, et al., 2014: http://www.jcvi.org/cms/research/projects/synthetic-biology-and-the-us-biotechnology-regulatory-system/overview/). We found that the U.S. regulatory system is well equipped to address most, but not all, health, safety, and environmental risks that these organisms are likely to pose. Our report detailed two key challenges and three additional issues that are likely to arise for the regulatory system and offered options that policy makers could consider in addressing those challenges.

The first challenge arises because synthetic biology and other new genetic engineering techniques may increase the likelihood that engineered plants will fall outside of the U.S. Department of Agriculture’s (USDA’s) authority to review. USDA currently regulates most genetically engineered plants because they have been transformed using a plant pest (usually Agrobacteria) or incorporate DNA from a plant pest. These newer techniques may no longer require plant pests for transformation.

The second challenge for the U.S. regulatory system will arise primarily for the Environmental Protection Agency (EPA), which regulates genetically engineered microbes under the Toxic Substances Control Act. As synthetic biology increases the number and the diversity of engineered microbes for commercial use, EPA’s resources and expertise will become increasingly stretched. If it is not addressed, this situation could lead to delays, inadequate reviews, and potential legal challenges.
Clearly, such conclusions are specific to the United States. A comparative international analysis would help us better understand the oversight of organisms with intended environmental use are likely to face worldwide. Such organisms are subject to a wide range of risk assessment and regulatory oversight during their development and deployment that varies from country to country. However, while regulation of genetically engineered food crops has been well established in many countries, how such regulation will apply to plants engineered using newer genetic engineering techniques or for other purposes (e.g. biofuel feedstocks) is not well understood. Furthermore, while there has been some analysis of the European Union and the challenges that it faces in the regulation of newer generations of biotechnology, there has been virtually no discussion of these issues for Brazil, Argentina, and other countries that will be most likely to take advantage of the new economic opportunities that these organisms will present.

This type of analysis should focus on those countries that are most likely to embrace genetically engineered organisms with intended environmental use and/or have significant amounts of synthetic biology research underway. An initial list might include: Brazil, Argentina, UK, Germany, Spain, Israel, South Africa, Australia, and China. Some of these countries have policies and publics that are very restrictive of environmental use of genetically engineered organisms (e.g. UK, Germany), but have significant investments in synthetic biology and have also made commitments to biofuels and renewable energy. Others have less investment in synthetic biology (e.g. Argentina, South Africa), but have adopted previous generations of biotechnology for large-scale commercial production.

All of these countries and their regulatory systems exist within the complex frameworks of international treaties and agreements, import-export controls, and economic and environmental incentives. While these factors are not explicitly part of the regulatory oversight of genetically engineered organisms, they are very important in understanding the context in which these organisms will be assessed and managed. For example, how an algae-derived biofuel falls within a renewable fuel standard framework may impact its assessment in a risk-benefit analysis.

There has been limited comparative analysis of biotechnology regulatory systems (outside of the U.S. and the European Union) and virtually none in the context of newer generations of biotechnology. Such a study or studies would help to understand the regulatory pathways that these organisms are likely to face, sources of regulatory uncertainty, key economic and trade issues, and any country-specific factors that may facilitate or block development or use of these organisms as they move from the laboratory to commercial use. We hope to pursue this topic to follow up on our previous work on the U.S. regulatory system.
Frankenstein is everywhere. He is ubiquitous, as omnipresent as Waldo but a lot easier to spot. *Frankenstein* is an Ur-narrative of synthetic biology, and haunts public discourse about it.

Victor Frankenstein and the creature he made from dead body parts is a recurrent theme in policy arguments about new life forms and the role of human intervention in nature. When the President’s Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research was addressing oversight of recombinant DNA in *Splicing Life*, it devoted an entire section to the “Deeper Anxieties” that featured the Frankenstein tale. Frankenstein appears in countless reports on human cloning. *Amicus curiae* briefs to the Supreme Court in *Diamond v Chakrabarty* invoked Frankenstein as a cautionary tale, arguing against deciding that life forms could be patented. In his majority opinion, Chief Justice Burger explicitly dismissed the “parade of horribles” in which Frankenstein’s creature was marching prominently. Frankenstein lurks in subsequent lower court decisions about patenting transgenic mice.

The Frankenstein tale resonates through popular culture and is brought to bear in policy debates in many ways, at many times, in many contexts. It is a cautionary tale, but invoking Frankenstein is also a rhetorical device to dismiss cautionary tales.

We will use the November conference in Tempe to launch a crowdsourcing project to collect documents, images, and instances of using Frankenstein when public policy decisions are being made. We will invite contributions in an open process. We will then create a taxonomy of uses of the Frankenstein tale and Frankenstein images at different times in different cultures for different policy decisions.

We will link our effort to the ASU Frankenstein Bicentennial project, and will also use it as an input to the proposed June 2016 workshop at the Fondation Brocher near Geneva.
Two years ago, a group of us developed a document called: “Principles for the Oversight of Synthetic Biology”. The eight principles recognized that much of technology assessment/risk assessment misses having an integrated approach that looks at public health, worker safety, environmental protection, communities’ right to know, democratic participation, corporate responsibility, manufacturer liability, and economic justice at the same time as approval of a new application of a technology.

PRECAUTIONARY PRINCIPLE

The Principles start with the Precautionary Principle. US Politicians like to deride the European Union for its use of the Precautionary Principle, but I would note that we are seeing extreme examples of the Precautionary Principle play out in US politics with Governors who have previously proclaimed that they are not scientists when it comes to Climate Change, suddenly becoming epidemiologists when it comes to Ebola. Our application of the Precautionary Principle is more nuanced.

We suggested that when applying the Precautionary Principle to Synthetic Biology we should first have a moratorium on the release and commercial use of synthetic organisms, cells or genomes until government bodies with full public participation have:

* Developed a research agenda that address the full breadth of the public’s interest
* Assessed Synthetic Biology approaches against alternative approaches
* Conducted full and inclusive assessments of the technology including human health, environmental and socio-economic impacts of synthetic biology.
* Developed national and international oversight and security mechanisms that can keep pace with the risks of synthetic biology technologies.

REQUIRE MANDATORY SYNTHETIC BIOLOGY SPECIFIC REGULATIONS

We were criticized as calling for a moratorium as a way to kill synthetic biology. (In fact, two major environmental organizations would not sign on because we were not calling for a ban.) One of the things that could kill synthetic biology would be a continued failure to revamp the regulations for genetic engineering in the US and other countries to account for synthetic biology. The US government relies on the so-called “coordinated framework” developed in 1986 as a way to quickly shoe horn genetic engineering into existing regulations. It does not work well for genetic engineering and except perhaps in the area of synthetic biology derived drugs fails entirely for most synthetic biology products moving to market.

FDA

The US FDA has been using a process called “Generally Regarded As Safe” to approve genetically engineered plant based foods. This process should not be used for Synthetic Biology. Companies cannot be expected to do their own reviews and keep them secret from the...
public. The FDA reviews genetically engineered versions of insects that care human disease as “New Animal Drugs”. FDA is currently reviewing Oxitec’s GE mosquitos. Synthetic Biology products that might be used for dietary supplements will generally escape any review by the FDA. Synthetic biology derived food flavorings will also sidestep most review. Vanillins derived from synthetic biology like that being developed by Evola might get the most review, but not because they are synthetic biology, but because vanilla has more comprehensive definitions in food law. The FDA needs to revamp its regulations related to GRAS, food additives, flavorings, genetically engineered animals, animal feed additives, cosmetics and dietary supplements to adequate review synthetic biology products.

EPA

The US EPA reviews genetically engineered microbes through the Toxic Substances Control Act. It does not approve the microbes, just looks at them before they enter commerce via a Microbial Activity Review Notice. Most of the US companies that submit these tell the EPA that everything in them is confidential business information. (I will show two of the recent MCANs from Solazyme, a synthetic biology company that are completely redacted.) If a company changes through the process of synthetic biology one of a dozen microbes commonly used in synthetic biology, they don’t have to submit anything at all. If an organism is to be deliberately released from containment into the environment, EPA regulations require that submission of a TSCA Environmental Release Application and EPA approval before the organism is released into the environment. The number of applications for TERA and MCANs are increasing rapidly. The funding of EPA reviews of these TERA and MCAN documents is not going up. The staff in the division are nearing retirement age. The rewrite of TSCA now being considered by the US Congress needs to include updates to EPA’s authority to regulate biotechnologies. The pesticide law likewise needs revisions for microbes engineered to function as biocidal agents.

USDA

The US Department of Agriculture has regulated genetically engineered organisms used in agriculture through its authority to regulate plant pathogens. This authority is already allowing genetic engineering that does not use pathogens like agrobacterium to perform the gene transfer. The USDA has no authority to regulate products of synthetic biology. The Inspector General of the USDA directed the APHIS branch to develop regulations for the oversight of genetically engineered animals and insects, but APHIS still has not developed those regulations. Field trials for one genetically engineered insect, a pink boll worm, were approved for Arizona, but suspended due to outcry from organic cotton growers worried that their crops would become contaminated by the insects and they would not be able to sell their crops as “organic”. APHIS is considering allowing the release of genetically engineered diamondback moths in upstate New York despite still not developing regulations for their oversight.

THE COURTS

If the US fails to develop adequate regulations for the oversight of synthetic biology derived plants, animals and microorganisms. It is likely that de-facto regulations will come primarily through tort law and national environmental policy act law suits. Already, US rice growers have lost Asian markets when experimental “pharma” rice contaminated shipments to Asia. US wheat growers lost sales to Asia and Europe last year when Monsanto’s experimental GE wheat was found in Oregon and Montana. If microorganisms that have been engineered by synthetic biology contaminate the beer of a local brewery in Berkeley, Boston, or Rockville, all center of synthetic biology experiments, expect lawsuits. Big firms will be able to survive these lawsuits, the little ones won’t. For the sake of the little guys, the US had better get the regulation right.
Reimagining Responsibility in Synthetic Biology
J. Benjamin Hurlbut, School of Life Sciences, Arizona State University

Synthetic biology is as yet a scientifically nascent field whose identity has taken shape primarily as a vision—a vision of a field that pivots from understanding living systems, to rendering life a repertoire of parts for use-inspired design. In practice, synthetic biology has thus far been defined less by actual uses, and more by an imagination of the eventual usefulness of synthetic biology’s (future) achievements: it will engineer life to achieve forms of human benefit that would otherwise be unattainable. Thus the project of synthetic biology is, in a fundamental sense, predicated on its promise to address, and to take responsibility for, certain societal problems: the field has constructed itself as able to respond, and thus as the right response, to basic problems of human welfare and security. This move of linking (imagined) technological futures to responsibilities of governance is potentially highly consequential on three levels: first, for the way synthetic biology itself develops as a field; second for relations between synthetic biology and society, including especially in the forms of autonomy the former enjoys, the kinds of assessment and oversight it is subject to, and the expectations that underwrite public trust in and support for research; third, for the ways institutions of governance imagine and execute their own responsibilities.

In this short statement, I am primarily concerned with the last of the three. Many fields in the biosciences have taken to justifying research by reference to the putative benefits that will flow to society. This turn towards (promising) usefulness has become a powerful mode of self-justification. As the case of synthetic biology shows, it goes beyond the mere instrumentalization of knowledge production to positioning technoscience as an institution of governance; that is, not merely as a source of potentially useful technologies, but as supplying a conceptual frame—and the institutionalized authority—whereby responsibilities of governance are articulated. For instance, a recent NAS report on the future of the biosciences asserts that the “new biology” (for which synthetic biology is the exemplar) “would enunciate and address broad and challenging societal problems” (National Research Council 2009) This is not merely a vision of technoscience, but of governance: with the capacity to “address” societal problems, the New Biology likewise claims the authority to “enunciate” them, to designate what challenges warrant worry, and what sociotechnical futures are possible, desirable and good.

This represents not only a moment of transmutation in the biosciences, but a transfiguration of imaginations of responsibility: of science to society, but likewise of society to science, lest society stand in the way of the forms of technical advance that it ostensibly needs. These re-imagined responsibilities have potentially far-reaching effects. They may come to be (and to some degree already have been) codified in notions of how law, democracy and market should be configured in deference to the futures that the biosciences promise (e.g. (Presidential Commission on Bioethical Issues in Biomedical Research 2010; U.S. White House 2012). In this sense, the New Biology represents a significant intervention in orderings of democratic governance, irrespective of whether its technological promises (or risks) are actually realized. It is an intervention that touches upon how the public good is imagined, and upon what forms of deliberation and collective moral sense-making are called upon—or are silenced—in the work of governing science and technology.
Of course, the New Biology’s ability to play this role depends on the willingness of democratic institutions to defer to such scientifically authorized accounts. In important respects, therefore, felt social insecurities over the project of synthetic biology are at once over the forms of collective sense-making and institutionalized modalities of public reasoning whereby research agendas are subject to democratic accountability.

On the whole, the forms of capacity for attending to “social and ethical issues” in scientific research that have been institutionalized since the 1970s are insufficient to address these problems, to a large degree because they have contributed to them in subtle and underappreciated ways. They have tended to treat society as always only able to react to the forms of novelty that science produces: science acts, and society reacts. Science makes revolutions, and society is revolutionized by them. Hence, ELSI research has generally focused on “impacts” and “consequences,” chasing after the implications of technological futures that science has first declared to be plausible, and thus deferring to the scientific community to decree what forms of novelty warrant societal attention. This is de facto a programmatic vision of the right allocations of responsibility between institutions of governance, but one whose political and normative dimensions are occluded.

This has a number of implications for how “societal dimensions” of synthetic biology should be approached.

1. **Forms and fora of Deliberation.** Systematic attention should be given to understanding: a) what opportunities for deliberation exist, b) what institutional arrangements—both scientific and democratic—engender opportunities for, or deficiencies in deliberation, and c) what underlying norms of reasoning and participation configure deliberation and/or render existing regimes immune to democratic correction. I wish to emphasize in particular the quotidian spaces in which deliberation about the appropriateness of research takes place, from the micropractices of institutional biosafety committees, to the macro-scale roles of scientific experts, public bioethics bodies, etc. in addressing publicly controversial issues and in disciplining public discourse. These are sites in which the terms of controversy and the frameworks of adjudication take shape. Before we can ask whether they function well—whether they are democratic, reasonable and good—we must interrogate the notions of reasonableness, the visions of the good, and the imaginations of democracy that are incipient in them. Attention to deliberation requires not merely asking whether there could be more of it, but asking what institutionalized imaginations of how we should reason together about morally and technically complex matters discipline practices of democratic oversight, and with what consequent silencing of voices and occlusions of concerns.

2. **ELSI Research.** Since the 1970s, social and ethical issues have generally been approached in a reactive mode. They attach to particular technological domains as questions about impacts and implications. This is partly because particular emerging technologies have been treated as the warrant for raising ethical concerns, and scientific declarations about the (im)plausibility of particular technological futures has tended to initiate or close down normative deliberation. However, technological controversies have come and gone, but modes of reacting to them have come to be patterned and institutionalized. ELSI research has directed remarkably little attention to its own institutionalization, and the forms of power and authority it has thereby acquired. This
is a serious deficiency, both because it neglects a critical dimension of the landscape of the contemporary biosciences, and because it occludes a range of fundamental normative questions about how societies reason together about, evaluate, and govern their scientific and technological undertakings. Ethical and social issues must be attended to as political and institutional features of the biosciences, not as consequentialist epiphenomena of scientific creativity. The latter approach systematically occludes questions about the forms of authority that systemically configure science-society relations, and that have become powerful resources for the political and normative identities of bioscience domains. This applies particularly for a field like synthetic biology that claims the authority to enunciate and address societal problems.

3. STS Research. In the last several decades, the field of Science and Technology Studies (STS) has developed the most salient insights and powerful critical tools for addressing the kinds of issues outlined above. Yet STS remains relatively marginal in forms of ELSI capacity that public agencies have supported and nurtured. This should change. STS brings a critical repertoire for understanding the social, historical, institutional, political and moral underpinnings of contemporary technological societies. Given that the relevant object of analysis in synthetic biology is not a particular technique or technology, but the project and vision of the field itself, STS represents the most robust, existing intellectual capacity for attending to the social and ethical significance of this emerging field. Yet an additional strength of STS is that it is not issue-bound. That is, it attends not only to issues that are marked as “ethical,” but the processes whereby they come to be marked as such, the prior work that goes into differentiating domains of expertise and authority, for instance into issues of science and politics, or facts and values, and it examines these processes as features of institutions, rather than as epiphenomena circumscribed to particular scientific fields or technological developments.

The greatest, but most fragile achievement, of democracy is a social order in which the visions of progress and the good that underwrite imperatives of the present are products of collective imagination. Understanding the place of science in democratic societies requires attending to the ways democracies draw on science to know, reason together, and articulate what is right, in both the epistemic and normative sense of the word. A commitment to responsible research and innovation requires that such capacities of understanding are supported and nurtured.

Translational Governance Research for Synthetic Biology

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Synthetic biology (SB) involves multiple techniques and tools to design and engineer complex or artificial biological parts, devices, and systems to achieve useful or novel properties. It resembles other “big science” fields like nanotechnology and genome sequencing in that it garners significant investment from the federal government and is drawing attention to not only its promise for addressing societal problems, but also to concerns about its potential impacts and its focus on “re-engineering life”. Categories of synthetic biology include, but are not limited to, synthesized or artificial genes, systems of engineered biological parts, and synthetic organisms. Although there are not clearly recognizable products of synthetic biology in the market yet, microorganisms with highly-engineered metabolic pathways to produce industrial or pharmaceutical compounds are now in use. More radical applications of SB, such as de-extinction of species or the creation of artificial cells, are emerging in the literature as successful in proof-of-concept stages. The ability to transform life is upon us, yet making societal decisions about what applications of SB are desirable to whom and under what conditions remains almost entirely in the hands of funders, the “free” market, and companies. Many citizens and scholars have argued that decision-making processes need to be open to a wider range of experts, stakeholders, and interested parties, especially in democracies. It is in this context that ethical, legal, and societal issues (ELSI) research becomes crucial to our future with synthetic biology.

ELSI research is primed to play an important role in societal decision-making process for SB. Through disciplinary, multi- and inter-disciplinary work, it can inform processes and methods for the design and implementation of governance systems and the choices made within them. However, historically, this potential has not been realized. Other ELSI programs such as those associated with the National Nanotechnology Initiative or Human Genome Initiative, have had marginal, ad-hoc influences on debates and courses of action, but have neither been integrated into decision-making processes nor had long-lasting, transformative impacts on those scientific fields. Although ELSI research efforts have yielded a mass of data, information, and better understandings of socio-technological relationships, they have not been given equal standing to natural science or engineering research and have not focused on practical and complex problems requiring decisions at the researcher, company, local, national or international levels. Simply put, the vast majority of ELSI research was neither translational nor integrated into society. ELSI researchers have been operating as the biological sciences did 30+ years ago, by doing research in “labs” without putting their ideas into the “marketplace” for useful purposes. For example, even public engagement efforts have been primarily used for research and not designed to have input into important and current societal decisions. With a few exceptions, there remains disconnect between ELSI findings and information and what to do about the future of technology, specifically synthetic biology.

This is not entirely or even largely the fault of the ELSI research community. Practically-inspired work does not traditionally get funded or rewarded. In the social sciences and humanities, “industries” do not exist to carry the ball for use-inspired research and develop products or processes. Yet, if we want to better inform and potentially improve our future with emerging technologies, it is important that we conduct ELSI research that is translatable and integrated into decisions about funding, governance, communication, R&D, and technological deployment.1

Whether this translation occurs is a two-way street. Societal decision-makers at all levels and in multiple institutions should be receptive to learning from ELSI research. In turn, ELSI researchers should

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1 I do not believe that all of ELSI research should be use-inspired or translational. Some basic ELSI research on theory and hypothesis testing needs to remain. It will be a balance. Perhaps start with a 50:50 split?
listen to the needs of practitioners and go out on the limb of engaged scholarship. Along these lines, I propose the following work to set the stage for ELSI research to better inform society, and in turn for ELSI research to be better informed by society: 1) host a series of pre-funding conversations among multiple relevant interested and affected parties (citizens reps, subject-matter-experts, stakeholders, groups) about what kind of ELSI knowledge and information matters to them and could be used for decision-making at multiple levels (this workshop may be a start), 2) identify the broad kinds of research that can best gather that knowledge and information, innovating with methods and cross-disciplinary approaches as needed, and 3) develop routinized and long-lasting governance systems to integrate ELSI research into societal decision-making in *timely, meaningful, and concrete ways*. In additional to laying the groundwork for translational ELSI work, these three areas also inspire research such as exploring mechanisms for conducting dialogues, developing mixed methods, and testing innovative governance systems.

In addition to the foundational work, I propose the following research areas for translational research. This list represents policy sciences work on governance systems, which currently has little place in the federal funding portfolio, yet it might be most important for making appropriate choices about SB:

- **Historical Analyses of Governance Systems**—
  o Explore the use of multiple natural & social science and ethical criteria and how to integrate them to analyze historical cases of governance and uncover patterns or features that are indicators of systems that lead to desirable outcomes for multiple stakeholders.

- **Experiments with Governance Systems**—
  o Test ways to anticipate and prepare for future technologies in governance systems with side-by-side comparisons of different features for these systems.
  o Explore alternatives for engaging “interested and affected parties” within these systems.

- **Methods to Deal with Uncertainty and Ambiguity in Governance.**
  o Improve upstream methods within governance systems to explore a broad range of harms and benefits and characterize uncertainty.
  o Test decision-science and future-studies approaches (scenario planning, Bayesian approaches, systems mapping, etc.) in governance systems.

- **Improve Ways to Explore Claims and Counterclaim in Contested Areas**
  o Develop balanced and more inclusive approaches for determining “weight of evidence” and for ways to minimize bias in interpretations of evidence.
  o Understand and acknowledge values behind multiple perspectives and interpretations of evidence.
  o Explore assumptions, contradictions, and correlation arguments on multiple sides of controversies.

Policy sciences and governance systems research is a tough sell, especially in the context of declining federal funding and animosity for political science research, which could be associated with ELSI governance work. However, SB is an area of technological development that not only has the ability to greatly impact society, but also the ability to fundamentally alter living things at their very core. There will be no stronger imperative for better integration of ELSI inquiry and research into societal decision making.

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2 Note this does not mean ELSI researchers should “vote” on societal decisions as in direct democratic fashion, but rather should have input into decisions—in other words, be seen and respectfully heard by those with power before decisions are made.

3 These exercises do not need to be “legally binding”; at least initially in the experimental stage, but should mimic conditions for direct input into decision-making authorities.
Synthetic Biology – An Opportunity for Soft Law Governance 2.0

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Synthetic biology is the latest emerging technology on a collision course with our traditional government regulatory paradigm. Such technologies have distinct characteristics that confound conventional regulation – including a rapid pace of development and change, unusually large uncertainties about future applications, benefits and risks, a diverse range of industries and users who will apply the technology in very different ways, and a broad set of potential risks and concerns that include but go beyond traditional regulatory triggers of environmental and health risks to also include bioethical, socio-economic, privacy and equity issues. While traditional government regulatory will play an important role in the oversight of synthetic biology, government regulation will likely be inadequate and too slow to provide satisfactory governance of synthetic biology.

“Soft law” governance approaches can supplement traditional government regulation. “Soft law” consists of private standards, guidelines, codes of conduct, principles, certification programs, voluntary programs, and partnership programs that establish substantive requirements that are not directly enforceable by government. Governmental agencies may play an important role in some soft law programs, but private companies, trade associations, non-governmental organizations, think tanks, standard-setting organizations and certification bodies may also play important roles. Soft law programs have several potential inherent advantages – they can be established and revised more quickly than government regulation, they often involve cooperative rather than adversarial relationships, and they extend across traditional legal jurisdictions and so can apply internationally. But soft law programs also have their problems, including limitations on public participation and transparency, incomplete participation and coverage, and inadequate enforcement and compliance.

Nanotechnology was the predicate test case for the soft law governance of synthetic biology. While soft law approaches have been applied to a wide variety of technologies and regulatory problems, nanotechnology represented the first major technology where soft law approaches played a dominant role. While regulatory agencies in the United States, European Union and elsewhere struggled to slowly define, characterize, evaluate and regulate nanomaterials, a wide variety of nanotechnology soft law programs were developed to try to fill the regulatory void. These soft law programs included nanotechnology risk management standards by international standard-setting organizations (e.g., ISO), government voluntary programs (e.g., EPA’s Nanoscale Materials Stewardship Program), industry-NGO risk management programs (e.g., EDF-DuPont NanoRisk Framework), codes of conduct (e.g., E.U. Code of Conduct for Responsible Nanosciences and Nanotechnologies Research), inter-governmental coordination networks (e.g., OECD Working Party on Manufactured Nanomaterials), industry consortiums for joint testing and research (e.g., NanoSafety Consortium for Carbon), and certification programs (e.g., CENARIOS). The effectiveness of these nanotechnology soft law programs was mixed, with some providing modest benefits while others were less successful.

Nonetheless, the experience with nanotechnology soft law programs can provide important lessons for synthetic biology. These lessons include the need for objective measures of accountability and enforcement, the importance of regulatory “backstops” to induce participation and compliance, and...
the potential leverage provided by insurance providers and liability avoidance to encourage participation in soft law programs.4

Soft law governance mechanisms are likely to play an even greater role in synthetic biology oversight given the inadequacies of existing regulatory programs to govern this diverse technology. There have already been a series of significant soft law applications in the synthetic biology space, including:

National Institute of Health Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines) are being adapted and revised for synthetic biology.

• The Synthetic Biology Project created by the Woodrow Wilson Center has launched a web-based Synthetic Biology Scorecard intended to follow and summarize both federal and non-federal efforts to enhance synthetic biology research and development governance, to minimize risk and maximize potential social and economic benefits.

• The Department of Health and Human Services released a Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA to minimize the risk of malicious misuse of synthetic nucleic acid technology.

• The National Science Advisory Board for Biosecurity (NSABB) has produced guidance documents and frameworks for the safe handling of dual use research.

• The International Association for Synthetic Biology, an association of genetic synthesis companies, has produced a Code of Conduct for Best Practices in Gene Synthesis.

• The Do-It-Yourself (DIY) segment of synthetic biology operates outside most formal research and environmental regulations, and has accordingly been the subject of innovative soft law programs such as voluntary guidelines, outreach and network building efforts, and educational programs.

Through these initiatives, soft law may have already played a more significant role for synthetic biology than any previous technology, but this is just the start, and proposals for new soft law initiatives abound.5 Much work and creativity is needed to make these soft law initiatives succeed – the outcome will play a major role in determining the future and viability of both synthetic biology and soft law approaches.

2 Diana M. Bowman & Graeme A. Hodge, Counting on Codes: An Examination of Transnational Codes as a Regulatory Governance Mechanism for Nanotechnologies, 3 REGULATION & GOVERNANCE 145 (2009).
Synthetic Biology and EHS Governance: The Coordinated Framework Case
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Liberal democracies confer to government the role of ensuring the safe introduction into society of technologies and the products of technology. In the United States, regulatory agencies that administer environmental, health, and safety (EHS) laws have been the principal actors playing this role. These agencies were set up to address 19th- and 20th-century problems, and have had notable successes in protecting people and safeguarding the natural environment. However, in the 21st century US agencies with EHS responsibilities are finding it increasingly difficult to ensure the safe and responsible introduction of new technologies into society.

The Coordinated Framework for the Regulation of Biotechnology exemplifies the stress that a new set of technologies, in this case biotechnology under the rubric of synthetic biology, has placed on EHS governance in the United States. The vulnerabilities that synthetic biology reveals in the Coordinated Framework also point to social science research needs around the governance of technology.

The Coordinated Framework was developed in 1986 as a set of policy statements organized by the White House Office of Science and Technology Policy and issued by five government units with responsibilities for biotechnology: the Food and Drug Administration, Environmental Protection Agency, Department of Agriculture, Occupational Safety and Health Administration, and National Institutes of Health. At the time, the creators of the Coordinated Framework believed that existing laws were sufficient to permit oversight of biotechnology. The framework therefore gave each agency with oversight responsibility wide latitude in how it implemented its regulations related to biotechnology. However, recognizing that lines of authority were not always clear, the Coordinated Framework established coordination among agencies with overlapping responsibilities.

The evolution of synthetic biology out of biotechnology raises concerns about the ability of agencies, within the Coordinated Framework, to exert effective governance over synthetic biology. For instance, under the old paradigm it was assumed that one organism would generate one product for one use, over which a single agency would have jurisdiction. Now, synthetic biology is creating conditions where a single organism may support the derivation of several products, each with multiple uses, leading to jurisdictional conflicts—or even gaps—between agencies. For example, chemical products of bacteria, yeasts or algae could have uses as food, feed, industrial chemicals, fuels, cosmetic ingredients, etc., depending on the customer and post-production processing. This is already creating problems for agencies. For instance, EPA has statutory time frames for new-substance review that could often require EPA to act well in advance of when FDA would have completed its necessary actions for a given case. This is particularly problematic because FDA nominally has the lead-agency role in many of these cases (e.g., food drug, and cosmetics cases).

Synthetic biology also raises issues related to the distinction between commercial and non-commercial research. Take the case of oversight of non-contained microorganism research that has no apparent commercial intent. Such basic research may not undergo the same type of risk-related federal review by a funding agency as would occur with a regulatory agency. Except for
compliance with National Environmental Policy Act (NEPA) requirements as exercised by the funder, generally, the focus of proposal reviews is on the likelihood of success of a given project. Funders may be reluctant to issue announcements for uncontained synthetic biology research if they believe they are responsible for risk evaluation.

The *Coordinated Framework* did not consider many issues that synthetic biology raises, such as energy policy and national security. As a consequence, agencies such as the departments of Energy and Defense, or NASA and NIST, are not part of governance under the framework.

The vulnerabilities to governance under the *Coordinated Framework* raise a number of research questions:

- Does the Coordinated Framework need to be updated to accommodate synthetic biology as a new part of biotechnology and if so, how? Would it change the overall product versus process philosophy of biotechnology governance?
- How do conflicting statutory imperatives affect implementation of the Coordinated Framework? Is the lead concept of the Coordinated Framework relevant now?
- What does “regulatory authority” over synthetic biology mean? If the United States does not have an adequate governance framework, what is in, and what is out, of agencies’ regulatory jurisdictions?
- What role can nongovernmental actors play in establishing and implementing EHS governance for synthetic biology?
- What are the implications for EHS protections that could arise from decentering the *Coordinated Framework* as a primary federal governance mechanism?
Inclusion of Environmental Justice Communities in Discussion on Governance of Synthetic Biology
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The field of synthetic biology (synbio) is a diverse field that covers many technological applications. Under the umbrella of synbio, there are many technologies that have environmental implications. These technologies include emerging developments such as engineered microbes for soil remediation (Wu et. al, 2006), nitrogen fixation in cereal crops using engineered microbes (Charpentier & Oldroyd, 2010), genetically modified corn for insect resistance (Hurley et. al, 2004), and biomining using engineered microbes (Moskvitch, 2012). Despite the diversity of synbio technological developments, one commonality shared by many of these is the need to think about potential environmental impacts that may occur, and how and when to use governance tools to address the potential risks and benefits of a given technology.

Currently there are many synbio applications in use and in the marketplace, as well as governance strategies in place to address potential risks that may come from these technologies. However, scholars have scrutinized the existing governance structure and questioned if the current systems are appropriate and able to fully address the challenges of synbio (Wiek et. al, 2012), (Marchant, 2013). Stakeholder feedback is needed from all potential affected parties, including environmental justice (EJ) members that may face implications from synbio technologies that have environmental applications. At this relatively early stage in both the development of synbio applications and relevant governance, scholars and policy makers have an opportunity to proactively seek input from EJ communities.

EJ communities have historically been marginalized and not had equal opportunity for meaningful input in governance strategies (Mohai et. al, 2009). At the same time, EJ communities have received a disproportionately high share of environmental burden from pollution and other environmental stressors. Known EJ burdens include hazardous waste facility sitting (Mohai et.al, 2009), cumulative pollutant exposure from multiple sources (Prochaska et. al, 2012), and mining waste disposal (Martinez-Alier, 2001); all of which have potential ties to emerging synbio applications.

There have been research efforts focused on public participation in synbio discussion, with some efforts seeking to gauge public opinion, while others have explored governance strategies (Pauwels, 2013) (Woodrow Wilson International Center for Scholars, 2014 ). These efforts have primarily focused on elicitation of governance strategy from the general public and/or field experts, and not specifically sought the opinions of EJ communities.

As an academic body, there does not appear to be much, if any, work being done to incorporate opinions of EJ communities on governance needs for synbio. A literature search for synthetic biology and environmental justice yields no results beyond broad discussions of ‘social justice’ (Reiss, 2014), (Hunter, 2014). Given the potential environmental impacts from some synbio technologies, and the potential disparities in access to the technologies, scholars are presented with an opportunity to encourage and promote early engagement of EJ communities in governance discussions for synbio.
The Genetic Engineering and Society Center at North Carolina State University is hosting a full day workshop designed to accomplish early inclusion of EJ communities in North Carolina in synbio governance discussions. This workshop is thought to be the first, or one of the first, of its kind. A goal of this workshop is to highlight governance needs and opinions that are specific to EJ communities, and to hopefully serve as a model that will be repeated in future studies. Given the priority of equal access to the decision making process as an EJ principle, it is important that these communities be able to take part in early discussions on governance needs for synthetic biology so that they can have input on these emerging technology.

REFERENCES


Synthetic Biology and the US Biotechnology Regulatory System
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Excerpted from: SYNTHETIC BIOLOGY AND THE U.S. BIOTECHNOLOGY REGULATORY SYSTEM: Challenges and Options
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This study addresses how well the current U.S. regulatory system for genetically engineered products is equipped to handle the near-term introduction of organisms engineered using synthetic biology. While the current regulatory system has generated debate from its inception, here we focus on whether the advent of synthetic biology will raise new issues for the regulation of these products. In particular, we focused on those engineered organisms (for example, bioenergy crops and biofuel-producing algae) intended to be used or grown directly in the environment, outside a contained facility.

Our research concludes that the U.S. regulatory agencies have adequate legal authority to address most, but not all, potential environmental, health and safety concerns posed by anticipated near-term microbes, plants, and animals engineered using synthetic biology. Such near-term products are likely to represent incremental changes rather than a marked departure from previous genetically engineered organisms. However, we have identified two key challenges to the current U.S. regulatory system posed by the introduction of organisms engineered using synthetic biology into the environment. For these challenges, we do not make specific policy recommendations, but rather set out options, including an analysis of the advantages and disadvantages of each option from a variety of perspectives for policy makers to consider. Policy responses will depend on the trade-offs chosen among competing considerations.

The key challenges and options to address them are:
Genetically engineered organisms are increasingly being developed in ways that leave them outside of the U.S. Department of Agriculture’s Animal and Plant Health Inspection Service’s (APHIS) authority to review, and synthetic biology will accelerate this trend. Currently, APHIS’ oversight depends on whether plant pests or some component of a plant pest is used to engineer the plant. These regulations covered almost all plants made using older genetic engineering techniques, but will not apply to plants engineered using several of the newer techniques. This shift will leave many engineered plants without any regulatory review prior to their cultivation in the environment for field trials or commercial production.

- Option 1: Maintain existing regulatory system and rely on a voluntary approach for those genetically engineered plants not subject to review. APHIS could maintain a voluntary system similar to their current regulatory procedures or product developers could use industry-developed standards to ensure that environmental risks are assessed and addressed.
- Option 2: Identify the most likely risks from newer generations of plant biotechnology and apply existing laws best able to mitigate them. One approach may be to use APHIS’ authorities over noxious weeds to regulate biotechnology products. In 2008, APHIS
issued a proposed rule for genetically engineered plants that incorporated both noxious weed and plant pest authorities, but even after extensive public comment and stakeholder input, the rule has not advanced.

- **Option 3:** Give APHIS additional authority to review and regulate genetically engineered plants. This option would require Congressional action, which might be difficult to achieve.

- **Option 4:** Promulgate rules under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) or the Toxic Substances Control Act (TSCA) for the Environmental Protection Agency (EPA) to regulate engineered plants. Both of these laws are broad enough to apply to genetically engineered plants, but such rules would be a major departure from the current regulatory system.

Synthetic biology will lead to an influx of genetically engineered microbes intended for commercial use, which may overwhelm EPA’s Biotechnology Program. While EPA regulators have successfully reviewed such engineered microbes to date, this influx will include a larger number and more diverse set of microbes than the program has seen previously, including many with intended or possible environmental exposure. Moreover, as engineered microbes become increasingly complex, risk assessments will pose a greater challenge. EPA will require additional funding to meet the increased workload and expertise requirements. In addition, the agency may be constrained by the authority given to it under TSCA, which has been criticized as inadequate, both in the context of engineered microbes and more broadly. These issues could lead to regulatory delays for microbial products, inadequate review, and/or legal challenges.

- **Option 1:** If and when needed, provide additional funding for EPA’s Biotechnology Program under TSCA and pursue efficiency measures to expedite reviews. Efficiency measures could include broadening exemptions for low-risk microbes and developing procedures to review environmental testing of engineered microbes on a programmatic basis (i.e. for multiple, similar microbes in a single submission).

- **Option 2:** Amend TSCA to strengthen EPA’s ability to regulate engineered microbes. This option would require Congressional action and could either address engineered microbes specifically or could strengthen TSCA for all chemicals subject to the law.

In addition to these major challenges, we have identified three additional issues in the regulation of new engineered microbes that should be periodically revisited as the technology advances, but in our view, do not require action today. These issues include the regulatory treatment of two classes of microbes that are exempted or excluded from review by EPA and EPA’s somewhat limited definition of “intergeneric microorganism.”

In developing this report, we consulted with a wide range of experts to ensure a broad representation of knowledge and viewpoints, including U.S. federal agency regulators, legal and science policy experts, representatives from the biotechnology industry, and non-governmental organizations. This cross-section of views informed this report, but this study does not represent a consensus: the findings and conclusions here are the authors’ alone, and not necessarily those of the institutions at which the authors work or the organizations that funded the study.
The UN Convention on Biological Diversity (CBD) is one of the few multilateral agreements to have specifically engaged with synthetic biology. Initially introduced through the CBD’s negotiations on biofuels, synthetic biology has been under consideration as a possible “New and Emerging Issue” since 2010. As a framework agreement, the CBD primarily produces “soft law.” Its political decision-making body, the Conference of Parties (COP), produces Decisions that are unlikely to establish new legal requirements but can be politically influential, mobilizing and guiding scientists, funding agencies, NGOs, businesses, and national governments. The CBD’s two protocols contain binding, ‘hard’ legal commitments on processes for the transboundary movement of living modified organisms and on access and benefit sharing of genetic resources. Neither protocol specifically addresses synthetic biology, but the CBD Secretariat’s analysis identifies that many current synthetic biology techniques likely fall within their scope.

This paper suggests research in two areas: 1) research to assist the CBD’s deliberations on synthetic biology; and 2) research on international decision-making processes around synthetic biology. These are based on participant observation of negotiating events, embedded work with the Secretariat, and interviews with involved actors as part of my dissertation research.

1) research for international deliberations on synthetic biology
CBD COP Decision IX/29 establishes seven criteria for identifying “New and Emerging Issues” to be added to the treaty’s agenda. Three criteria are highlighted here to indicate research that would respond to the CBD’s interests.

New evidence of unexpected and significant impacts on biodiversity: At meetings in June 2014, CBD Parties noted that both the “benefits” and “risks” of synthetic biology for biodiversity are “currently poorly understood” (SBSTTA 18 Recommendation XVIII/7). A responsive research agenda would consider current and anticipated applications of synthetic biology. Most current and near-term commercial applications are engineered micro-organisms for contained use. Research on the biosafety of such micro-organisms could examine industrial and research sites for the rate of survival and reproduction of escaped micro-organisms and the transfer of altered genetic material. Organisms intended for environmental release are broadly anticipated to result from synthetic biology research. As such organisms may present new biosafety concerns, a research agenda for monitoring their environmental impacts should be established while such organisms are still under development. Indirect impacts on biodiversity should be monitored too, such as land-use changes caused by expansion in the quantity or kinds of biomass for feedstock and population changes of wild animals or crops whose harvest has been displaced by products of synthetic biology. Ecologists and environmental scientists are particularly needed in developing this research agenda on impacts.

Evidence of the absence or limited availability of tools to limit or mitigate the negative impacts of the identified issue on the conservation and sustainable use of biodiversity: Based on the CBD Secretariat’s overview analysis of international law relevant to synthetic biology, CBD Parties have agreed that a “coherent and comprehensive international framework” to address synthetic biology is

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1 The CBD’s 12th Conference of the Parties has just convened (6-17 October 2014). At these negotiations, Parties may finally decide whether to add synthetic biology to the treaty’s agenda as a New and Emerging Issue.

2 In the context of the Cartagena Protocol on Biosafety (2005), “living modified organisms” (LMOs) are “any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology” (CPB Article 3(g)).

3 Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization (2010).
lacking, but they disagree on whether such a framework is desirable. In evaluating the international regulatory tools available to respond to synthetic biology, two areas of research may be helpful. First, an expansion of the Secretariat’s analysis could be carried out for each area of synthetic biology research. For example, analysis would determine how current international legal obligations would likely apply to the organisms that xenobiologists are aiming to produce. Understanding the potential legal landscape for their research results may influence the goals of synthetic biologists, while their feedback may help treaty bodies identify gaps or inconsistencies in their oversight. Second, risk assessment processes developed for genetically modified organisms should be re-examined as synthetic biology techniques make it possible to develop increasingly complex and novel organisms. The Cartagena Protocol on Biosafety’s risk assessment process takes into account the environment which will be exposed to the organism, the characteristics of the organism, and its intended uses. If many donor organisms and/or human-designed parts are used, such a comparative assessment system may not be adequate. Research is needed to identify the limits of current assessment methods and their applicability to near-term and anticipated products of synthetic biology. New methods of assessment may need to be developed in response to synthetic biology.

Magnitude of actual and potential impact of the identified issue on productive sectors and economic well-being as related to the conservation and sustainable use of biodiversity: Synthetic biology is relevant to the CBD not just for its impacts on biodiversity but also its impacts on associated socio-economic considerations. Research on the displacement effects of products of synthetic biology, such as semi-synthetic artemisinin, could help to establish the extent to which displacement is occurring, whose livelihoods are impacted, and the distribution of financial and other benefits from the new products. More broadly, research could track the differential global impacts of the expanding “bioeconomy,” in which synthetic biology is expected to play a key role.

These suggested areas of research indicate aspects of synthetic biology relevant to the objectives of the CBD (for additional aspects, please see UNEP/CBD/COP/12/20). I believe that the CBD’s considerations would also benefit from an analysis of the uncertainties of synthetic biology’s impacts on biodiversity. Some uncertainties may simply be gaps in knowledge, resolved by establishing monitoring and surveillance processes. Others may be a matter of waiting for the release of new applications and then tracking their anticipated impacts. More intractable uncertainties, however, are likely involved as well. Some direct impacts will be difficult to measure - the lag times will be too long, the limits of detection too high to register changes. As discovered with biofuels, tracking indirect impacts such as land-use change leads to wide-ranging results, due to fundamental differences in methodologies and the key assumptions of models. And there will be some impacts that cannot be anticipated, even with modified assessment processes. Thus far, CBD Parties have responded to synthetic biology by calling for gathering more information. More clarity on the nature of what is not known - probable timeframes for the resolution of information gaps and identification of the more intractable and indeterminate uncertainties - may help governing bodies identify where political responses to uncertainty are necessary and appropriate.

2) research on international deliberations on synthetic biology
The CBD’s deliberations on synthetic biology provide an opportunity to study the decision-making processes of an international environmental body as it grapples with an emerging biotechnology. How is synthetic biology defined by actors, and how is the CBD’s scope of engagement determined? How are uncertainties identified and framed? What sources and kinds of knowledge are drawn upon? Whose perspectives are reflected, and through what intermediaries? Such knowledge politics are key in the formation of international policy (Hulme 2012; Jasanoff 2004; Miller 2009; Scoones 2009). Research following the CBD and other governing bodies as they engage with synthetic biology could identify the epistemic foundations of resulting policy, analyzing how power is enacted and democracy performed through the contestations of claims of knowledge.
Ability Expectation and Ableism Studies (short Ability Studies): An innovative approach to catalyze a new community of practice to monitor, evaluate and address Synbio linked ability expectation challenges to how society functions: The Issue of Ability Expectation Governance
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First let me thank my students who do such an amazing job (more about them at http://www.crds.org/research/faculty/Gregor_Wolbring.shtml); their logo

Background
Ability Studies [1-3] investigates how ability expectation (want stage) and ableism (need stage) hierarchies and preferences come to pass and the impact of such hierarchies and preferences on multiple subject formations, social relationships and lived experiences based on diverse ability expectations and the actions linked to such expectations. Every individual, household, community, group, sector, region, and country cherishes and promotes numerous abilities and finds others non-essential. For example some individuals regard the ability to buy a given product as essential, while others do not; some perceive living in an equitable society as important, others do not; countries compare each other on whether one has certain abilities (e.g., provision of good education or high employment to its citizens) [1-2]. Furthermore negative treatments of others are often justified by a narrative where one powerful group decides that a certain ability is essential and that another group lacks the ‘essential’ ability[2]. The way humans interact with nature is also characterized by ability expectations with for example anthropocentrism and bio/eco-centrism exhibiting different ability expectations of what nature is to do for humans [3-4]. What abilities do we want to sustain? What new ability expectations are emerging? Who has the ability power to push their ability expectation agenda? How these questions are answered in the synthetic biology discourse will influence the cultural, social, economic and environmental impact of synthetic biology disrupting existing ability expectations. As such anticipatory governance of ability expectations [5-6] is a needed facet of anticipatory governance of technology in general and anticipatory governance of synthetic biology in particular. The Ability Studies framework allows for a new community of practice bringing together people and ideas in an innovative way, generating knowledge that will assist to advance a vision that enables maximum positive impact from the governance of synthetic biology. Ability expectations are linked to value, labeling, conflict, choice, identity, motivational, achievement, goal, self-determination, neo-institutional, body and social constructivism theories. Ability expectations are linked to the cultural reality of disablism experienced by entities labelled as lacking ‘essential’ abilities, as not fulfilling ability expectations of the ones setting the ability expectation agenda. As such ability expectation adds to the labeling theory discourse which focuses on the linguistic tendency of majorities to label negatively minorities or those seen as deviant from norms. Value theory records what people do value and attempts to understand why they value certain things. Ability expectation is about valuing certain abilities. Expectancy-value theory of achievement motivation (the ability desired) is used to analyze dynamics of various discourses. Ability desires are evident in the synthetic biology discourse. Conflict theory emphasizes possible conflict between social groups. Groups of people with different ability expectations are often in conflict with each other. Ability expectations influence and are shaped by the pillars and carriers of institutions and mechanisms and processes by which institutions persist or change identified by Scott[7]. Ability expectations are a factor in many of the
components of the discourse-institutionalist framework developed by Genus [8]. Finally one chooses between different abilities which can be classified as a ‘social choice’ problem [9]. The ability expectations we choose, whether as individuals or as another social entity impact and are impacted by the synthetic biology discourse. The abilities one favors within and outside of the synthetic biology discourse impact human-human, human-animal and human-nature relationships and how one defines ecological problems and identifies solutions to the problem. It also shapes which Ability privileges are accepted. Ability privilege is “the advantages enjoyed by those who exhibit certain abilities and the unwillingness of these individuals to relinquish the advantage linked to the abilities especially with the reason that these are earned or birth given (natural) abilities” (whereby down the road it will be interesting to see whether, and if yes how, synthetic biology will change the meaning of natural or the importance of natural as a qualifier) [4]. Ability privilege can play itself out between traditionally defined social groups (e.g. race, gender, class); for example if we look at the history of the Suffragette’s fight for women’s right to vote in USA the men constructed a narrative that valued rationality as an ability and men claimed that women were irrational and as such women were labelled as unfit to vote. This is an example of an ability privilege supporting male privilege. The claim that women are irrational beings is still used[10-14]. Irrationality is used as a tool to discredit one’s opponents in many discourses (see for example[15-16]). There continues to be constant formations of social groups that are defined by certain abilities and the privileges that come with it; for example people that are seen as productive versus non-productive or countries that are seen as competitive versus non-competitive. Technologies are one factor generating ability privileges; having the ability to access and to master certain technologies gives one access to better education and better paying jobs. Finally one new ability privilege on the horizon is linked to techno/genetic modifications of the body we perceive today as normal. These enhanced bodies will have abilities that will give them an edge such as in employment which, given today’s dynamics, will lead to the enhanced bodies having ability privileges (see the movie Fixed the science/fiction of human enhancement that covers certain ability expectation dynamics).

**Short analysis of 17 sources**

If one looks at the 17 reports for some keywords of importance if one looks at various aspects of Ability Expectation governance the following hits are obtained: ability 290; able 1152; challenge 406; choice; compet* 73; democra* 54; DIY 193; disab* 5; health 371; well-being/wellbeing 41; energy 237; ethic 671; expectation 18; govern 453; governance 128; igem 76; impact 163; independen* 51; issue 696; opportunity 240; option 135; patient 29; productive* 39; rational 37; regain 6; risk 892; stakeholder 106; gender 6; women 11; industry 273; NGO 60. To interpret some of the numbers, whose ability expectations are covered in the sources is mostly unclear as the sources often use the boiler plate term, “stakeholder” without identifying who they mean. In the cases that groups are mentioned there are visibility differences between groups (industry versus other groups such as women, disab*). Democratizing science and technology is discussed for a long time. When democratization of synbio is covered (source 1,9, 11 and 17) source 1 does link it to the DIY of synbio. Sources 9, 11 and 17 talk about Democratic deliberation and active participation of citizens but do not cover the abilities required by an individual or social group in order to participate in such deliberation. Indeed, there are assumptions as to the abilities that individuals and social groups have that are envisioned to participate in the discourse around democratizing technology (my Master student, Lucy Diep will be presenting on that topic at the CNS UCSB Democratizing Technologies Conference). When the sources talk about products linked to individuals the individual is mentioned within a
medical framework (patient, medical use of the term disabled, or health mostly with the meaning of medical health not social health) indicating the sales pitch for body linked interventions (including genomes) and the ability expectation discourse to come. As to abilities, to just mention sustainability (due to space restriction), sustainability is mentioned concretely around product sustainability (source 3), good health, reduction in Greenhouse gas as an example of a sustainability indicator (source 4) and natural resources/climate change (source 15) but for example social sustainability is not mentioned. As to applications energy is mention in all sources with the exception of source 6 and 8 but it is interesting to note that many ability expectations of synbio are not mentioned such as human enhancement which is only mentioned briefly in source 12 and 17 and the linkage between synbio and biological diversity (source 8) such as the proposal to generate biological diversity through synbio. Proposal: I suggest that an ability expectation taxonomy (e.g. which ability expectations are mentioned by whom, for whom, for which problems) including ability expectation synergy and conflict maps and ability expectation related decision trees and impact assessment are some concrete outputs the Ability Studies field can generate that would benefit the synbio discourse in general and the synbio governance discourse in particular. Ability Studies can be a catalyst for inter-, trans- and intra-disciplinarily innovation to practice and the emergence of a community of practice bringing together people and ideas in an innovative way filling the gaps evident so far in the synbio discourse.

The list of documents:
1) Next steps for European synthetic biology: a strategic vision from ERASynBio
2) Seven Myths & Realities about Do-It-Yourself Biology;
5) Perceptions of Synthetic Biology and Neural Engineering Key Findings from Qualitative Research April 18, 2014; http://www.synbioproject.org/publications/6684/
6) Synthetic Biology Report to Congress July 2013 Dept. of Energy
7) Synthetic Biology and the US Biotechnology regulation system: Challenges and Options Craig Venter Institute May 2014
8) The Nagoya Protocol and Synthetic Biology research: A Look at the Potential Impacts 2013
   http://scholarship.law.duke.edu/cgi/viewcontent.cgi?article=5916&context=faculty_scholarship

Wolbring, “Ability Expectation and Ableism Studies"

Reference List

Sociology seeks to understand why trademarks differentiate the value of products that are otherwise identical. The challenge to sociology is larger, however, when those trademarks apply to science and science funding. After all, science is supposed to be fact-based, rational, and different from non-science. Scientists should not be susceptible to branding. At least in theory.

Nanotechnology, systems biology, and synthetic biology are recently coined trademarks in science. All have elements of novelty, of course. “Systems biology”, for example, rests in the notion that the study of purified molecular components extracted from a living system (analysis) must lose some perspective on the “whole”. Systems biology was offered as a way to reconstruct the “whole” by enumerating its parts, putting numbers on their interaction parameters, and building a computer model to reproduce the performance of the whole. Likewise, nanotechnology began as an effort to gain for molecules the kind of predictability that is displayed by microcircuit design.

Beyond their core ideas, these trademarks have not been particularly useful, however. Systems biology turned out to be not greatly different from what had previously been called “physiology”, as Brent pointed out ("vague definition and unrealistic claims made for systems biology"). Efforts to get predictive medicine from computer simulations failed, primarily because the simulations were not robust with respect to uncertainties in the measured input parameters. Biology, complex chemistry, is more complicated than can be managed this way.

Likewise, nanotechnology has not produced much different from research that previously was called “materials science” or, more simply, “chemistry”. Molecules are, after all, nanoscaled. Further, the analogy between computer design and molecular design is flawed, in part because logic elements fixed at spots on a two dimensional surface do not diffuse to interact with other logic elements. Molecules in solution do just that. Indeed, for chemistry (biological and non-biological) to happen, molecules must do that.

Nevertheless, these trademarks attracted resources, often supporting quality science in the process. Thus, Leroy Hood founded the Institute for Systems Biology, which did excellent biological chemistry under his trademark. Harvard, whose own prestigious trademark allowed it to come late to the game, created two departments of systems biology. When the NIH awarded its first "pioneers" under its NIH Director Pioneer Award program in 2004, three of the first eight recipients carried the label “nanotechnology” in some form. It was the fad of those times.

Sociologists might look upon synthetic biology in the same way. Before they do, however, they must recognize distinct concepts associated with the trademark. For example, in 1912, Leduc published La Biologie Synthetique. Notwithstanding the need to translate the trademark from the French, his meaning was clear: Synthetic biology was the field seeking to create artificial life. Leduc was ahead of his time, but little imagination was needed even then to appreciate that if the analysis then underway to determine the structures of molecules of living systems was taken to its logical conclusion, it should be possible to create something unnatural that had properties that we value in life.
Indeed, chemists were already practicing the art of synthesis with this intent. In the 19th century, when chemists determined the arrangement of atoms in a natural product, they often attempted to re-synthesize the same arrangement from simpler starting materials. At first, their goal was simply to show that they had deduced correctly the molecular structure of the natural product. However, chemists eventually began to synthesize new forms of their subject matter. This synthesis allowed them to test theories that related molecular structure to chemical behavior. This synthetic capability drove structural theory in chemistry. Just imagine how much faster geology would progress if geologists could synthesize new planets.

This was the meaning of phrase “synthetic biology” when it was used again in the 1970’s by Waclaw Szybalski. Recombinant DNA technology was then becoming powerful enough to allow microbiologists to synthesize new forms of their subject matter. Szybalski recognized that this would open a new phase of research, where biologists would synthesize chemically altered microbes. By examining the resulting alteration in behavior, Szybalski expected to discover relations between biological parts and biological behaviors, just as chemist had done previously with their synthetic technology. Synthesis in biology would empower biological theory just as synthesis in chemistry had empowered chemical theory.

However, by the 1970s, chemists had discovered a still broader, and more powerful, role for synthesis. Famously articulated by R. B. Woodward in a 1968 lecture, synthesis can be part of a “grand challenge”, where chemists are forced to synthesize something difficult to synthesize. Pursuit of the synthetic grand challenge forces scientists to cross uncharted grounds where they must solve unscripted problems using available theory. When theory is inadequate, the synthesis fails, and fails in a way that cannot be ignored. Thus, synthesis can force discovery and paradigm change in ways that analysis and "hypothesis-based research" cannot.

Woodward had spoken an important truth: When scientists choose the hypotheses to test, they tend not to test hypotheses that challenge core theory. And if a scientist nevertheless seeks to test a hypothesis that actually challenges theory, the test will not likely be funded.

Even today, Woodward’s insight is not well appreciated by many biologists and the peer-review processes that they serve. Accordingly, “hypothesis-based research” remains the touchstone of “true science” across much of Federal science funding, outside of chemistry itself. Thus, relatively few resources support attempts to synthesize molecular assemblies that reproduce the behaviors of living systems, including their ability to reproduce, evolve, and adapt. Consequently, relatively little insight is emerging for biology in general, and natural biology in particular, of the type that could be provided by a Leduc-style “synthetic biology”.

Instead, most major Federal funding in "synthetic biology" has not moved conceptually beyond the 1980s. For example, DARPA is today investing tens of millions of dollars in its “Foundries 1000” program. This program seeks to rearrange natural enzymes in unnatural ways to create microorganisms that produce chemical products. The NIH has a parallel program entitled “Genomes to Natural Products”, albeit with a more modest budget.

Both programs fit squarely within the classical field known as “metabolic engineering”, a field that was already well developed in the 1980s. Examples from the 1980’s include the Cetus-Chevron process to co-synthesize fructose and propylene oxide, and the Genetics Institute-Chemie Linz process to manufacture phenylalanine. Both were gotten by rearranging enzymes from nature, the same process now funded by the DARPA and NIH programs.
The only distinction is one of scale. Today’s metabolic engineers rearrange perhaps 5-10 enzymes, not the 2-3 enzymes rearranged in the synthetic biology work done three decades ago. Rapid DNA synthesis, whole gene and genome assembly, xii,xiii,xiv and improved bioinformatics, *inter alia*, all make metabolic engineering faster and cheaper. But since the biological parts still can diffuse in solution to freely interact with each other (rather than being pinned down at specific spots on a circuit board), the rearrangement involves much “tinkering”. This was the word used a quarter century ago when engineers suggested that biological processing would be streamlined and vastly more productive once biological parts were altered via engineering strategies.xv

Intriguingly, synthetic biology appears to have created for itself a sociological problem by making claims of special powers for "engineering biology". Some members of the public have used the claims as grounds for alarm. For example, the Friends of the Earth recently objected to the use of the word "natural" to label products obtained by fermentation done with engineered microorganisms, evidently unaware that this has been the case 40 years.

It remains to be seen whether such claims will be realized, in particular, whether lay DIY individuals can engineer biology. Claire Maris in this symposium has a paper suggesting a very different reality. Among those who understand the supporting molecular sciences, is not clear that this claim can ever be realized. In any case, a new trademark does not create a new hazard.

References