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What Synthetic Genomes Mean for Our Future: Technology, Ethics, and Law, Interests and Identities

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SYMPOSIUM: BIOETHICS, LAW, AND SYNTHETIC BIOLOGY

WHAT SYNTHETIC GENOMES MEAN FOR OUR FUTURE: TECHNOLOGY, ETHICS, AND LAW, INTERESTS AND IDENTITIES

Thomas H. Murray, Ph.D.*

Is synthetic biology best understood as a continuation of the more than three decades of scientific activity aimed at “hacking” biology, beginning with the first successful attempts to recombine DNA? Or is it a distinctive and novel endeavor with profound implications for public policy—for how we think about and manage risks? Is it so distinctive that it threatens to arouse conflicts over the identities through which we understand and shape our lives?

Part I of this article will show how synthetic biology is being defined, provide examples of proposed applications, and describe four major streams of scientific and technological developments, all of which fall under the umbrella of synthetic biology.¹ It will then take up two

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¹ See *infra* Part I (discussing the different conceptions of the definition of synthetic biology).

1316 VALPARAISO UNIVERSITY LAW REVIEW [Vol. 45]

interrelated questions.² First, is synthetic biology best understood as a series of incremental developments in the decades-long scientific effort to “hack” biology, or should it be seen as a sharp departure from the past? Second, how significant is the shift in emphasis from hypothesis-driven science aimed at explaining biology to an engineering mindset that regards explanation and understanding as far less important than control and predictability?

Part II will examine the challenges synthetic biology poses to policy. What risks have aroused the greatest concern?³ What policy responses have been proposed and how likely are they to achieve important goals such as protecting against the use of synthetic biology for biological warfare or bioterrorism as well as against inadvertent harms (sometimes called “bioerror”)?

Part III delineates and critically examines three broad principles or stances that frame both ethical analysis and policy.⁴ The first, the precautionary principle, is often invoked by those suspicious of or opposed to some technology.⁵ The second, the proactionary principle, opts to give the benefit of the doubt to such innovations.⁶ In practice, neither the precautionary nor the proactionary principle routinely dominates in national policies, and there are many variants of both. The Presidential Commission for the Study of Bioethical Issues (“PCSBi”), in its report on synthetic biology, proposed a third principle, a *via media*, which they have labeled “prudent vigilance,” a concept that warrants explication and critical analysis.⁷

The content of disputes involving technology, ethics, and policy include more than enthusiasm for technological innovation, and fears of

² See *infra* Part I.B (explaining major changes that have occurred in the development of synthetic biology such as the application of an engineering mindset and the differences in expectations, training, and culture that accompany it).

³ See *infra* Part II.A (proposing that the biosecurity risks posed by synthetic biology are of great concern to the public).

⁴ See *infra* Part III.B (discussing the differing ways the United States and Europe view the advance of synthetic biology).

⁵ The precautionary principle holds that “in the face of reasonable fear of severe harmful effects on people or the environment, governments may be justified in imposing measures to prevent this harm, even in the absence of conclusive scientific evidence.” Karsten Klint Jensen, *The Moral Foundation of the Precautionary Principle*, 15 J. AGRIC. & ENVTL. ETHICS 39, 39 (2002).

⁶ “[T]he Proactionary Principle urges all parties to actively take into account *all* the consequences of an activity—good as well as bad—while apportioning precautionary measures to the real threats we face, in the context of an appreciation of the crucial role played by technological innovation...” Max More, *The Proactionary Principle*, MAXMORE.COM (July 29, 2005), <http://www.maxmore.com/proactionary.htm>.

⁷ PRESIDENTIAL COMMISSION FOR THE STUDY OF BIOETHICAL ISSUES, *NEW DIRECTIONS: THE ETHICS OF SYNTHETIC BIOLOGY AND EMERGING TECHNOLOGIES* 4 (2010).

2011] *What Synthetic Genomes Mean for Our Future* 1317

innovation's unanticipated or unwelcomed consequences. Part IV describes how debates on two controversies—embryonic stem cell research and genetically modified foods—received very different treatments in the U.S. and the UK.⁸ Perhaps viewing public policy disputes as a conflict of competing interests will be helpful in discerning the major disputes in synthetic biology.⁹ Part IV also introduces the distinction between conflicts that revolve around disputes over interests and conflicts over identities.¹⁰ The article concludes with reflections on the usefulness of the interests/identities distinction for coming conflicts over synthetic biology.¹¹

I. WHAT IS THIS THING CALLED SYNTHETIC BIOLOGY?

The Royal Academy of Engineering offered this definition in 2009: “Synthetic biology aims to *design and engineer* biologically based parts, novel devices and systems as well as redesigning existing, natural biological systems.”¹² The European Commission described synthetic biology as

... *the engineering of biology*: the synthesis of complex, biologically based (or inspired) systems which display functions that do not exist in nature. This engineering perspective may be applied at all levels of the hierarchy of biological structures In essence, synthetic biology will enable the design of ‘biological systems’ in a rational and systematic way.¹³

The President's Commission stuck a similar tone in its December 2010 report: “synthetic biology [] aims to apply *standardized engineering techniques to biology* and thereby create organisms or biological systems with novel or specialized functions to address countless needs.”¹⁴ This

⁸ See *infra* Part IV.A (delving into the specific aspects of synthetic biology that are in controversy in the U.S. and UK).

⁹ See *infra* Part IV.B (using the Chrysler corporation's near failure to illustrate the competing interests that must be considered in public policy disputes).

¹⁰ See *infra* Part IV.C (proposing that issues of identity which arise in the abortion debate present an alternative dynamic to public policy disputes).

¹¹ See *infra* Part V (examining the effect that conflicting interests and identity disputes have on the burgeoning field of synthetic biology).

¹² ROYAL ACADEMY OF ENGINEERING, SYNTHETIC BIOLOGY: SCOPE, APPLICATIONS AND IMPLICATIONS 13 (2009) (emphasis added).

¹³ EUROPEAN COMMISSION, SYNTHETIC BIOLOGY: APPLYING ENGINEERING TO BIOLOGY 5 (2005).

¹⁴ PRESIDENTIAL COMMISSION FOR THE STUDY OF BIOETHICAL ISSUES, *supra* note 7, at 2 (2010) (emphasis added) (internal quotation marks omitted).

1318 VALPARAISO UNIVERSITY LAW REVIEW [Vol. 45]

sampling of definitions is reasonably consistent with a surprisingly wide range of definitions that have been offered for such a nascent enterprise.¹⁵

These and other typical efforts to define synthetic biology are as interesting for what they leave out as for what they include. First, they make no attempt to specify the disciplines or professions that may claim to be practicing synthetic biology. Biologists of many stripes, of course, may be practicing synthetic biology, but so may engineers, mathematicians, computer scientists, physicists and biochemists. Indeed, some of the ambitions of synthetic biologists stretch or burst the boundaries of biochemistry. The eminent scientist and business leader George Poste has suggested that synthetic biology is by definition not what we have traditionally regarded as biological: “The boundary between synthetic biology and systems biology should reside in a single criterion: has the engineered process, product or organism been fabricated from natural materials (systems biology) or from components not adopted in natural evolution (synthetic biology)?”¹⁶

Second, the various definitions of synthetic biology do not try to claim any particular set of tools and methods. Those employed can vary hugely and still be considered the practice of synthetic biology. This includes old and new tools in genetic engineering (sequencing, DNA synthesis, assorted methods for manipulating genomes and DNA sequences) and what Ron Weiss, an engineer at MIT, lists as the “engineering principles and methodologies that have worked well in other established fields (e.g., modularity, system fabrication using libraries of well-characterized and interchangeable parts, rapid prototyping, predictive models and robust designs).”¹⁷

Third, the definitions do not declare any fixed set of goals beyond developing the tools and knowledge to bend or alter natural systems to serve human intentions. Adam Arkin, a bioengineer at University of California-Berkeley, asserts “[s]ynthetic biology aims to make the engineering of new function in biology faster, cost effective, scalable, predictable, transparent and safe.”¹⁸

¹⁵ See generally *What's in a Name?*, 27 NATURE BIOTECHNOLOGY 1071 (2009) (providing the range of definitions of synthetic biology and the key disputes about its boundaries with genetic engineering, systems biology, and metabolic engineering). Twenty commentators including leading researchers in synthetic biology and scholars on its legal and ethical implications offer their often competing definitions of the field. *Id.*

¹⁶ *Id.* at 1073. Other leaders in the field disagree and propose more inclusive definitions of synthetic biology. *Id.*

¹⁷ *Id.*

¹⁸ *Id.* at 1071.

2011] *What Synthetic Genomes Mean for Our Future* 1319

Some practitioners of synthetic biology attach little importance to definitional exercises. Andrew D. Ellington at University of Texas-Austin writes:

These words [synthetic biology] don't have much meaning. The definition of a new field is either based on a discovery or redefinition, and – because I can't point to a single great discovery in this field – synthetic biology is really more about a redefinition of biotechnology. It encompasses the rather old notion that you can engineer living systems, but updates that notion with the universal realization that the ability to synthesize lots of DNA and do mathematical modeling is a very powerful combination. But I'd say synthetic biology's key utility is to excite engineers, undergraduates and funding agencies. Its key disadvantage is to create hysteria in the defense community.¹⁹

The theme that runs through the disparate efforts to define synthetic biology is the application of an engineering mindset to biological or quasi-biological systems. Proposed applications cover a great range. Bacteria and yeast have had their metabolism altered so that they produce artemisinic acid, a precursor of the potent anti-malarial drug artemisinin. The microbe *pseudomonas* can now degrade certain pesticides, thanks to intentional changes wrought by human hands. High-value industrial chemicals can be produced by yeast.²⁰

A. Major Streams of Scientific and Technological Developments

Not surprisingly, in such a dynamic and youthful enterprise, commentators are not unanimous in how they carve up the field. The four major streams described here are not meant as magisterial pronouncements, only as helpful descriptions that will surely become outdated as the field expands.

The first stream is advanced genetic engineering. It employs the relatively familiar but increasingly powerful tools that scientists have been perfecting since the recombinant DNA era began in the mid-1970s, and it is supplemented by the knowledge and tools developed through

¹⁹ *Id.* (alteration in original).

²⁰ See Press Release, Amyris, Amyris's First Commercial Production Facility Complete and Operational (Apr. 29, 2011), available at <http://www.amyrisbiotech.com/en/newsroom/202-amyriss-first-commercial-production-facility-complete-and-operational>. Amyris is producing farnesene in Brazil at an industrial scale. *Id.*

1320 VALPARAISO UNIVERSITY LAW REVIEW [Vol. 45]

genome sequencing. According to leading researchers such as Jay Kiesling, whose teams are responsible for both the artemisinin acid and farnesene producing organisms, success depends upon serendipity as much as engineering-like design.²¹ Products from this stream are on a faster track towards commercial production than the other streams.

The second stream is DNA-based device construction. Taking its inspiration directly from engineering fields such as electronics, this movement envisions building catalogues of well-characterized standard parts that can be assembled into systems or “circuits” that would reliably accomplish whatever task the designing engineer wished. Like their counterparts in electronic engineering, designers could pluck whatever transmitters, actuators, sensors, or other components they needed from the available parts list. The movement has created its own institutions such as the BioBricks Foundation and the MIT Registry of Standard Biological Parts.²² Simplification and standardization are key aims; the BioBricks movement has also embraced the open source concept, encouraging innovators to deposit their bioparts into a common registry that is available to all. Drew Endy, one of BioBricks’ most visible and charismatic advocates, sums up the movement’s guiding spirit: “if you consider nature to be a machine, you can see that it is not perfect and that it can be revised and improved.”²³

Creating a Lego-like biology has many appealing features. Imagine a world of synthetic biology where anyone with a good idea can take freely from a public registry whatever components are needed to assemble a device that could solve an important problem, entertain, decorate, or do any of a host of things humans desire. However, the BioBricks movement faces serious challenges. It has proven fairly easy to create bioparts, but standardizing them and getting them to work in predictable ways has been more difficult. Feedback loops are familiar problems in electronic systems and software development, but the complex interactions within even relatively simple biological systems may be more challenging to cope with. Also, the democratization of biological innovation spurred by open access to bioparts must confront the likelihood that not all cherished ideas will be good ideas. Some will lead to inadvertent dangers; in other cases, the designer may have

²¹ ROBERT CARLSON, *BIOLOGY IS TECHNOLOGY: THE PROMISE, PERIL, AND NEW BUSINESS OF ENGINEERING LIFE* 101 (2011).

²² BIOBRICKS FOUNDATION, <http://biobricks.org/> (last visited June 28, 2011); REGISTRY OF STANDARD BIOLOGICAL PARTS, MIT, http://partsregistry.org/Main_Page (last visited June 28, 2011).

²³ RINIE VAN EST, HUIB DE VRIEND & BART WALHOUT, *CONSTRUCTING LIFE: THE WORLD OF SYNTHETIC BIOLOGY* 2 (2007).

2011] *What Synthetic Genomes Mean for Our Future* 1321

malign intentions. How to discourage or head off such dangers is a challenge to be taken very seriously.

The third stream entails the creation of a minimal cell that could be used, for example, as a “chassis” onto which different parts assemblies could be mounted. The analogy here is with automobile manufacturers who can use a basic structure to build many types of vehicles, from family sedans to SUVs. Scientists at the J. Craig Venter Institute (“JCVI”) announced the creation of a “synthetic bacterial cell” in May 2010.²⁴ The scientists obtained the sequence of *Mycoplasma mycoides*, a bacterium with a relatively small genome (1.08 million DNA base pairs).²⁵ They then designed 1,078 “cassettes” each 1,080 base pairs in length and had them manufactured by a commercial DNA synthesis company, Blue Heron Biotechnology.²⁶ Yeast cells were used to stitch the cassettes together into ever-longer sequences in three stages until the full-length genome, with such added texts as quotes, authors’ names, and an email address, was assembled. The artificial chromosome was then inserted into the cell of a closely related bacterium, *Mycoplasma capricolum*, whose enzyme that protects the cell against the invasion of foreign DNA had been disabled. The synthetically designed genome took over the intracellular mechanisms of *Mycoplasma capricolum* yielding cells containing only the inserted DNA within two days.

The larger significance of this research is in dispute. The JCVI describes it as a “proof of principle that genomes can be designed in the computer, chemically made in the laboratory and transplanted into a recipient cell to produce a new self-replicating cell controlled only by the synthetic genome.”²⁷ They predict ever-wider uses of their technology that “will undoubtedly lead to the development of many important applications and products including biofuels, vaccines, pharmaceuticals, clean water and food products,”²⁸ while others are more skeptical.

The fourth stream does not attempt to redirect existing biological entities but rather to create entirely new ones. For example, the effort to construct protocells proposes to redesign, synthesize and assemble basic cellular components using combinations not found in nature. The ProtoLife project surrounds RNA ribozymes with a fatty acid membrane.

²⁴ Press Release, J. Craig Venter Institute, First Self-Replicating Synthetic Bacterial Cell (May 20, 2010), available at <http://www.jcvi.org/cms/press/press-releases/full-text/article/first-self-replicating-synthetic-bacterial-cell-constructed-by-j-craig-venter-institute-researcher/>. [hereinafter J. Craig Venter Institute].

²⁵ *Id.*

²⁶ *Id.*

²⁷ *Id.*

²⁸ *Id.*

1322 VALPARAISO UNIVERSITY LAW REVIEW [Vol. 45]

This stream's vision of a new biology is ambitious. One of its leaders described its goal as the creation of

a new form of life . . . a genuinely new living entity, albeit one not based on biology and not made out of the customary biological ingredients: no DNA, no conventional biomolecules, no cell membrane of the ordinary type, no nucleus, no mitochondria, no endoplasmic reticulum or any of the other innumerable vital trappings of normal, orthodox biological cells.²⁹

Whether this movement will achieve its goal is uncertain.

B. Understanding the Evolution of Synthetic Biology

How is synthetic biology's relationship with more than three decades of efforts to "hack" biology best understood? Are the various streams of synthetic biology merely the latest in a long series of incremental developments? Or do the collection of activities under the rubric of synthetic biology depart in fundamental ways from the past? What clues may be found in the shift in emphasis from hypothesis-driven science aimed at explaining biology to an engineering mindset that regards explanation and understanding as far less important than control and predictability?

The continuity/discontinuity distinction is not central to understanding what is new and important in synthetic biology. The most significant change is not the increasingly sophisticated tools but instead, the application of an engineering mindset to biological systems, and the differences in professional expectations, training, and culture that accompany it. The differences are not all-or-none in nature, and the generalizations to come are admittedly crude efforts to mark a complex and uneven terrain. But even subtle differences can have important consequences. Biologists, as scientists, aim to understand the complexity of biological entities and processes. Engineers can have a different attitude towards complexity. Tom Knight, one of the founders of the BioBricks movement put it this way: "[a]n alternative to understanding complexity is to get rid of it."³⁰

Along with the differences in expectations, such as understanding versus control, come differences in training and culture. Physics may have been the first of the natural sciences to confront the life-altering,

²⁹ ED REGIS, WHAT IS LIFE?: INVESTIGATING THE NATURE OF LIFE IN THE AGE OF SYNTHETIC BIOLOGY 3 (2009).

³⁰ Philip Ball, *Starting from Scratch*, 431 NATURE 624, 625 (2004).

2011] *What Synthetic Genomes Mean for Our Future* 1323

even planet-altering, power of their science with the creation of nuclear weapons, but biology was compelled to confront its moral responsibilities in the 1970s when it devised the tools that allowed biologists to move bits of DNA between organisms. The famous Asilomar Conference in 1975 was in effect a formal acknowledgement that biology now possessed powers to do great good—or great harm.³¹ Biological scientists since Asilomar have been exposed to ethical debates over the aims and consequences of their research. Engineers may also receive formal training in professional ethics, but their deep involvement in the complexities of biology is of more recent vintage.

To summarize, where molecular biology emphasizes discovery and explanation, molecular engineering prizes the capacity to design. Molecular biology attends to emergent properties, while molecular engineering focuses on control and prediction. Finally, where molecular biology struggles to understand complexity, molecular engineering desires to simplify and streamline.

At present, it is unknown how readily biological complexity will yield to engineers' aspirations for simplification, predictability and control. If the complexity of biological systems turns out to be an enduring impediment for some of the principal streams in synthetic biology, at least two important implications emerge. First, investments—from government and foundation grants to angel and venture capital firms—may become more difficult to obtain for those streams. Second, both technical analyses and public perceptions of the risks from synthetic biology will be more cautious as predictability and control is less certain.

II. SYNTHETIC BIOLOGY AND PUBLIC POLICY

The ability to reconstruct virulent organisms eventually gets the attention of policy makers and the public.³² The power to tinker with such organisms to enhance their virulence or to add pathological

³¹ See generally Paul Berg et al., *Summary Statement of the Asilomar Conference on Recombinant DNA Molecules*, 72 PROC. NAT'L ACAD. SCI. 1981 (1975) (summarizing the Asilomar Conference).

³² See e.g., Ray Kurzweil & Bill Joy, *Recipe for Destruction*, N.Y. TIMES, October 17, 2005, at A19 (urging discretion in publishing genetic information to prevent dangerous viruses from reaching the public). The reconstruction of the 1918 influenza virus in a lab in 2005 set off a host of security and public health concerns. *Id.* If one were able to create new pathogens, such as the H1N1 virus, and these pathogens accidentally escaped, they could pose a severe threat to public health. *Id.* See also *General Information*, FLU.GOV, <http://www.pandemicflu.gov/general/> (last visited June 28, 2011). The discovery of the H1N1 virus led to the announcement of a nationwide public health emergency in late March and early April 2009. *Id.*

1324 VALPARAISO UNIVERSITY LAW REVIEW [Vol. 45]

properties to currently benign ones increases our interest further. Part II.A will discuss the distinguishable concerns of biosecurity and biosafety in synthetic biology. Then, Part II.B will propose three plausible avenues that could advance biosecurity and minimize harm.

A. *Concerns of Biosecurity and Biosafety*

One useful distinction is between concerns over biosecurity and biosafety. Biosecurity includes both state-based biowarfare and non-state sponsored bioterrorism. Biosafety concerns, which some call “bioerror,” include laboratory accidents, inadvertent releases of modified organisms into the environment, horizontal gene transfer between modified and unmodified organisms, and the capacity of living organisms to evolve and adapt in ways we cannot anticipate.

Biosecurity concerns in synthetic biology have drawn the attention of policy makers and scientists for many years.³³ Political defenses, from treaties and international covenants to foreign aid and other forms of influence, are available when dealing with state actors. Non-state actors, such as would-be bioterrorists, are more elusive targets. Scientists familiar with synthetic biology have both good and bad news to offer. The bad news first: the “de-skilling” of synthetic biology makes it easier for malevolent actors to manufacture pathological organisms. DNA synthesis firms have been screening for suspect sequences, but the effectiveness of such procedures is disputed,³⁴ and the spread of DNA synthesis technology around the world constrains any single nation’s ability to limit access to synthetic DNA sequences that might be used to assemble a harmful microbe. Now, the good news: weaponizing

³³ See generally Screening Framework Guidance for Synthetic Double-Stranded DNA Providers, 74 Fed. Reg. 62319 (Nov. 27, 2009) (providing voluntary guidance to “the gene and genome synthesis industry”); MICHELE S. GARFINKEL, SYNTHETIC GENOMICS: OPTIONS FOR GOVERNANCE (2007); NATIONAL SCIENCE ADVISORY BOARD FOR BIOSECURITY, ADDRESSING BIOSECURITY CONCERNS RELATED TO THE SYNTHESIS OF SELECT AGENTS (2006) [hereinafter NSABB, ADDRESSING BIOSECURITY CONCERNS]; NATIONAL SCIENCE ADVISORY BOARD FOR BIOSECURITY, PROPOSED FRAMEWORK FOR THE OVERSIGHT OF DUAL USE LIFE SCIENCES RESEARCH: STRATEGIES FOR MINIMIZING THE POTENTIAL MISUSE OF RESEARCH INFORMATION (2007) [hereinafter NSABB, PROPOSED FRAMEWORK]; MICHAEL RODEMEYER, NEW LIFE, OLD BOTTLES: REGULATING FIRST-GENERATION PRODUCTS OF SYNTHETIC BIOLOGY (2009); PRESIDENTIAL COMMISSION FOR THE STUDY OF BIOETHICAL ISSUES, *supra* note 7; MILDRED K. CHO & DAVID A. RELMAN, *Synthetic “Life,” Ethics, National Security, and Public Discourse*, 329 SCI. 38 (2010).

³⁴ Markus Fischer & Stephen M. Maurer, *Harmonizing Biosecurity Oversight for Gene Synthesis*, 28 NATURE BIOTECHNOLOGY 20, 20 (2010) (explaining that these are not as effective because “each DNA synthesis company implements [the procedures] differently”); David A. LaVan & Louis M. Marmon, *Safe and Effective Synthetic Biology*, 28 NATURE BIOTECHNOLOGY 1010, 1010–12 (2010) (noting that current procedures “could be improved” because they “rely on voluntary participation”).

2011] *What Synthetic Genomes Mean for Our Future* 1325

biological pathogens is a significant challenge, one unlikely to be met by non-state actors. The possibility remains of less sophisticated strategies, for example, the bioterror equivalent of a suicide bomber who is infected with some pathogen and then attempts to spread it to individuals in the target locality.

One additional possible bit of good news: complexity and emergent properties may be our friends. Both the manufacture and the spread of effective synthetic biological weapons are beset with uncertainty. The National Science Advisory Board for Biosecurity noted in 2006:

Current scientific understanding reveals that it is often the combination or interaction of genetic elements that underlie these properties rather than one specific gene sequence. Furthermore, the harmful consequences of biological agents are dependent upon the coordination [of] multiple factors, including host susceptibility, the agent's infectivity, transmissibility and virulence, and the availability of prophylactic or therapeutic interventions.³⁵

It may prove difficult to prevent bioterrorists from trying to create a biological weapon. But the potency of any such weapons will be difficult to predict, and their "success" will be a function of multiple factors including many—such as the range of public health responses to other infectious agents, vaccines, and therapies—over which we have control and can deploy to minimize the harm done.

B. Proposed Policy Responses to Curtail Biosecurity Concerns

Of the regulatory frameworks proposed for synthetic biology, three will be considered here: self-governance; government regulation; and international agreements.

The American Society for Microbiology ("ASM") provided a cogent example of self-regulation by the scientific community with its 2003 initiative to screen manuscripts to protect against publishing information that would threaten biosecurity, including the possibility of dual-use. Over 16,000 manuscripts were reviewed.³⁶ Three received special scrutiny, one was modified, and not a single manuscript of the more

³⁵ NSABB, ADDRESSING BIOSECURITY CONCERNS, *supra* note 33, at 14.

³⁶ Brian Rappert, *The Benefits, Risks, and Threats of Biotechnology*, 35 SCI. & PUB. POL'Y 1, 2 (2008).

1326 VALPARAISO UNIVERSITY LAW REVIEW [Vol. 45]

than 16,000 reviewed was withheld from publication because of biosecurity concerns.³⁷

What lesson are we to draw from this experiment in self-governance? The tiny number selected for scrutiny is notable. It may be that scientists know better than to try to publish papers that could threaten biosecurity, or perhaps they sent such papers to other journals during that interval. It is possible that the reviewers were reluctant to deny publication for their fellow scientists and used a very high threshold before deeming a paper worthy of special attention. The ASM initiative constitutes a proof of principle: that scientific societies are capable of organizing a process designed to forestall the publication of threatening material. Absent additional information shedding light on the process, however, it is difficult to judge whether the initiative was successful in its ambition to advance biosecurity.

Government regulation is another plausible avenue. The case of DNA synthesizers provides an illuminating illustration of the difficulties any single nation will face in attempting to keep crucial equipment out of the hands of those intending harm. A recent search on eBay turned up a used DNA synthesizer for US\$2,500.³⁸ Such machines vary from the size of a microwave to a refrigerator. Top-of-the-line new devices can cost in excess of \$100,000, but as the eBay example shows, used ones can be found for far less. There are more than 20 manufacturers worldwide and alternative technologies, such as DNA synthesis chips, are in development.

Analysts have examined a range of strategies governments might pursue to control the availability of DNA synthesizers including registration, licensing and service. For example, governments could attempt to limit the availability of raw materials such as essential reagents or crucial spare parts such as capillary tube assemblies by allowing manufacturers of such items to ship only to licensed owners of DNA synthesizers. A machine with worn out capillary tubes or lacking fresh reagents, on this reasoning, is useless. Without international harmonization, however, the efforts of any one nation are unlikely to result in much more than added inconvenience to those with malign intentions.

³⁷ *Id.*

³⁸ *Beckman DNA Synthesizer Oligo 1000M & Manual*, EBAY, http://cgi.ebay.com/Beckman-DNA-Synthesizer-Oligo-1000M-Manual/180678971753?pt=LH_DefaultDomain_0&hash=item 2a114e5169 (last visited June 21, 2011).

III. PRINCIPLES FOR ETHICS AND POLICY TOWARDS SYNTHETIC BIOLOGY

There is an ongoing debate about methods for evaluating risks and weighing costs and benefits. In much of the existing literature, the debate is framed as a choice between two poles—a “precautionary” pole, which is skeptical about the outcomes of new technologies, and a “proactionary” pole, which is optimistic. In fact, a range of positions are possible, and there is growing belief that the ideal position would be somewhere between these two poles. Thus, the debate should be understood not as a choice between two extreme alternatives, but as a more nuanced decision about the appropriate degree of precaution to take with respect to an emerging technology and the appropriate level and kind of support to offer it.

A. *Evaluating Potential Outcomes Using Risk Assessment and Cost-Benefit Analysis*

The standard methods of evaluating outcomes in the United States employ risk assessment procedures and economic tools, such as cost benefit analysis. Often, the ostensible goal with these methods is to treat the process of evaluating potential outcomes as an endeavor grounded in technical expertise and the employment of quantitative models, making it objective and analytic to the greatest extent possible. Risk assessment provides tools for addressing three inquiries as objectively as possible: whether a causal relationship exists between an entity or a project and the particular effects on human health and the environment; what the strength of the relationship is between that entity or project and the effects; and what the extent of exposure is to the hazard.³⁹ Cost-benefit analysis is a way of deciding whether to proceed with a project by estimating in monetary terms the public’s views of the project.⁴⁰ By looking to preference, understood as a matter of market choice and averaged across a community, cost-benefit analysis also seeks to model decision-making in a way that is value-neutral and objective.

Criticisms of these tools include concerns about the plausibility of an objective, analytic method for identifying risks, gauging their severity, and comparing costs against benefits. A number of commentators hold that risk assessment fails to account adequately for the fact that the identification of risk is unavoidably normative, depends partly on

³⁹ NATIONAL RESEARCH COUNCIL, *RISK ASSESSMENT IN THE FEDERAL GOVERNMENT* 3 (1983).

⁴⁰ CASS R. SUNSTEIN, *RISK AND REASON: SAFETY, LAW, AND THE ENVIRONMENT* 291 (2002) [hereinafter *SUNSTEIN, RISK AND REASON*]; CASS R. SUNSTEIN, *LAWS OF FEAR: BEYOND THE PRECAUTIONARY PRINCIPLE* 129 (2005) [hereinafter *SUNSTEIN, LAWS OF FEAR*].

1328 VALPARAISO UNIVERSITY LAW REVIEW [Vol. 45]

nonanalytic and emotional aspects of human nature, and is significantly shaped by culture.⁴¹ Cost-benefit analysis has been criticized on grounds that it distorts individuals' values by representing them as a single unit of measure⁴² and wrongly assumes that individuals' preferences, as reflected in market choices, accurately reflect their values.⁴³ Cost-benefit analysis has also been charged with failing to account adequately for costs that will not surface for many years or that may affect only distant people or nonhuman forms of life. These problems suggest that cost-benefit analysis distorts or omits considerations important for public policy. Critics also maintain that cost-benefit analysis functions poorly when data about outcomes is scarce or unreliable.

Various commentators have discussed the concerns raised by synthetic biology's potential risks, costs, and benefits. Recommendations for addressing these concerns range from improved self-governance by scientists to restrictions on the publication of research that might pose security threats, mechanisms for regulating the trade of DNA sequences,⁴⁴ centralized regulation, and outright prohibition of the technology.⁴⁵ If risk were addressed largely as a matter of self-governance, then questions arise about how self-governance should be monitored or enforced. If risk were addressed through more centralized oversight and control mechanisms, questions would arise about whether those mechanisms were unacceptably holding back the science. However risk is addressed, those mechanisms should extend to activities in the private sector, and they should be flexible enough to deal with an evolving technology, as the International Risk Governance Council has stressed.

⁴¹ Paul Slovic et al., *Risk as Analysis and Risk as Feelings: Some Thoughts About Affect, Reason, Risk, and Rationality*, 24 RISK ANALYSIS, 2008, at 1; Dan M. Kahan et al., *Cultural Cognition of the Risks and Benefits of Nanotechnology*, 4 NATURE NANOTECHNOLOGY 87, 87–90 (2009) (explaining that “public attitudes are likely to be shaped by psychological dynamics associated with cultural cognition”).

⁴² Douglas MacLean, *The Ethics of Cost-Benefit Analysis: Incommensurable, Incompatible, and Incomparable Values*, in DEMOCRACY, SOCIAL VALUES, AND PUBLIC POLICY 107 (Milton M. Carrow, Robert P. Churchill & Joseph J. Cores eds., 1998).

⁴³ Douglas A. Kysar, *It Might Have Been: Risk, Precaution, and Opportunity Costs*, 22 J. LAND & USE 1, 17–18 (2006); Douglas MacLean, *Ethics, Reasons, and Risk Analysis*, in THE ETHICS OF TECHNOLOGICAL RISK (Lotte Asveld & Savine Roeser eds., 2009).

⁴⁴ GARFINKEL, *supra* note 33; Hans Bügl, et al., *DNA Synthesis and Biological Security*, 25 NATURE BIOTECHNOLOGY 627, 627–29 (2007).

⁴⁵ JIM THOMAS, *EXTREME GENETIC ENGINEERING: AN INTRODUCTION TO SYNTHETIC BIOLOGY* (2007).

2011] *What Synthetic Genomes Mean for Our Future* 1329B. *Precautionary versus Proactionary Views of Risk Assessment*

The use of risk assessment methods and economic analyses is sometimes thought to constitute a generally proactive policy stance toward a technology and is contrasted to the precautionary stance, thought to be characteristic of European policy. As noted, the precautionary principle comes in a variety of flavors, with different implications for policy. Also, while Europe has favored a precautionary stance on some issues concerning biotechnologies, such as genetically modified crops, it has been markedly proactionary on other topics, such as construction of nuclear power plants, where the United States has been more cautious.⁴⁶

The precautionary principle is intended to address scenarios involving uncertainty. Most commentators agree that the central idea behind it is that plausible reasons to believe that a project may have harmful effects provide justification for imposing measures to prevent those effects, even in the absence of conclusive scientific evidence that the effects will be realized.⁴⁷ The precautionary principle shifts the burden of proof from showing that harms will occur to showing that harms will not occur.

Many acknowledge that the precautionary principle has considerable intuitive appeal, as its central point is captured by such maxims as "Look before you leap" or "Better safe than sorry." Nonetheless, it has come under fierce criticism. Where risk assessment and cost-benefit analysis are seen as implausibly value-neutral and analytic, the precautionary principle is seen as hopelessly vague and as grounded only on emotions and, in particular, on crude fear.⁴⁸ Where cost-benefit analysis is seen as undercounting costs, the precautionary principle is seen as dramatically overweighting them (indeed, critics see it as blatantly anti-science).⁴⁹ Cost-benefit analysis is thought to deal

⁴⁶ Jonathan B. Wiener & Michael D. Rogers, *Comparing Precaution in the United States and Europe*, 5 J. RISK RES. 317, 318-19 (2002) (comparing European and United States approaches); see also generally, David Vogel, *The Politics of Risk Regulation in Europe and the U.S.*, 3 EUROPEAN ENVTL. L. 1, 1 (2003) (explaining that the United States has historically been more cautious though the trend is changing).

⁴⁷ Jensen, *supra* note 5, at 39 (defining the precautionary principle); David B. Resnik, *The Precautionary Principle and Medical Decision Making*, 29 J. MED. & PHIL. 281, 285-90 (2004).

⁴⁸ See generally Jonathan B. Wiener, *Precaution in a Multirisk World*, in HUMAN AND ECOLOGICAL RISK ASSESSMENT: THEORY AND PRACTICE 1509 (Dennis J. Paustenbach ed., 2007) (explaining three versions of the precautionary principle); MAXMORE.COM, *supra* note 6 (explaining the shortcomings of the precautionary principle).

⁴⁹ See Letter to Dr. Amy Gutmann, Chair, Presidential Commission for the Study of Bioethical Issues 2 (Dec. 16, 2010), available at http://www.foe.org/sites/default/files/Letter_to_Commission_Synthetic_Biology.pdf ("The precautionary principle often is mischaracterized as anti-science, anti-technology, or anti-progress.").

1330 VALPARAISO UNIVERSITY LAW REVIEW [Vol. 45]

poorly with uncertainty, while the precautionary principle is thought to give so much weight to uncertainty that—because uncertainty abounds in all possible courses of action—it will lead to paralyzed inaction.⁵⁰

Some of these criticisms oversimplify the precautionary principle. Different versions of the principle endorse varying degrees of precaution, and some versions spread the burden of proof. For example, the precautionary principle could require that not just *any* state of uncertainty is sufficient to support imposition of constraints; rather there must be a plausible causal story about possible harms.⁵¹ Meanwhile, among proponents of a more proactionary stance, Cass Sunstein has recently argued for a more moderate form of the cost-benefit paradigm. He proposes, in place of the precautionary principle, a more limited and focused “anti-catastrophe principle” for projects that may bring about particularly dire risks or costs, but in which the probability of those risks or costs occurring is highly uncertain.⁵²

In a report on synthetic biology issued at the end of 2010, the PCSBI recommended that policy toward emerging biotechnologies, including synthetic biology, should be based on a “principle of *responsible stewardship*” toward collective human well-being and the environment, which in turn “calls for *prudent vigilance*.”⁵³ The content of this recommendation remains ambiguous, however. Although the notions of “responsibility” and “prudent vigilance” suggest some degree of precaution, the PCSBI did not attempt to fit its recommendations into the existing literature on the precautionary principle. It also failed to explain which evaluation processes are appropriate, even though it said that evaluation of the technology should be “ongoing.” Furthermore, it did not call for any particular constraints on synthetic biology; thus, critics were left with the impression that the PCSBI had not called for any substantive policy changes.⁵⁴

Several considerations discussed in this section reveal that confusion reigns over how to evaluate outcomes. Such considerations include: the range and variety of positions about precaution; the growing sense of compromise between seemingly opposed positions; the recognition that countries once thought to favor one or the other stance turn out (on a

⁵⁰ Cass R. Sunstein, *The Precautionary Principle as a Basis for Decision Making*, 2 THE ECONOMISTS’ VOICE 1 (2005) (explaining that this would “eliminate *all* policies from consideration—including the status quo—because almost all policies impose risks”).

⁵¹ Resnik, *supra* note 47, at 286.

⁵² SUNSTEIN, LAWS OF FEAR, *supra* note 40, at 109.

⁵³ Presidential Commission for the Study of Bioethical Issues, *supra* note 7, at 4.

⁵⁴ Kelly Trout, et al., *NGOs Blast US Presidential Commission on Bioethics*, THE ETC GROUP (Dec. 16, 2010) <http://www.etcgroup.org/en/node/5244> (outlining critiques of the PCSBI recommendations).

2011] *What Synthetic Genomes Mean for Our Future* 1331

broader analysis) not to have a general principled preference for either; and the questions about the value assumptions in risk assessment, cost-benefit analysis, and the precautionary principle collectively point to the need for a deeper understanding of these issues.

IV. INTERESTS AND IDENTITIES

Some public policy disputes, even those with a great deal at stake, can be brought to apparent closure. Other disputes continue to fester despite repeated efforts to reach a compromise. Consider two disputes about biotechnology that took divergent paths in the U.S. and the UK: human embryonic stem cell ("HESC") research; and genetically modified organisms ("GMOs").

A. *Comparing Biotechnology Disputes in the US and UK*

On August 9, 2001, President George W. Bush ordered that federal funding for HESC research would be allowed, but only on cell lines created prior to the moment his policy was announced.⁵⁵ A fierce battle over public policy and public opinion followed swiftly. It was little noted at the time that some sanctity-of-life advocates condemned the President's policy⁵⁶ even as conservative defenders praised him as Solomonic.⁵⁷ The President was hemmed in by enthusiasm among scientists and many Americans for what were depicted as the abundant possibilities that HESC research could lead to treatments for dire diseases on the one hand, and the adamant resistance on the other by opponents of embryo research and abortion, who were among the President's and his party's most committed supporters.

It took the election in 2008 of President Barack Obama for any change in policy on HESC research. Within weeks of his inauguration, President Obama rescinded the Bush policy and permitted, with limits, federal funding for HESC lines created after August 9, 2001.⁵⁸ On

⁵⁵ *President George W. Bush's Address on Stem Cell Research*, CNN.COM (Aug. 9, 2001), <http://edition.cnn.com/2001/ALLPOLITICS/08/09/bush.transcript/index.html>.

⁵⁶ Cal Thomas, *President Bush's Compromise*, TOWN HALL.COM (Aug. 14, 2001), http://townhall.com/columnists/calthomas/2001/08/13/president_bushs_compromise.

⁵⁷ George Will, *Bush's Stem Cell Decision was Brilliant*, TOWN HALL.COM (Aug. 14, 2001), http://townhall.com/columnists/georgewill/2001/08/14/bushs_stem_cell_decision_was_brilliant.

⁵⁸ See generally President Barack Obama, *Signing of Stem Cell Executive Order and Scientific Integrity Presidential Memorandum* (March 9, 2009), available at http://www.whitehouse.gov/the_press_office/Remarks-of-the-President-As-Prepared-for-Delivery-Signing-of-Stem-Cell-Executive-Order-and-Scientific-Integrity-Presidential-Memorandum/ (announcing the change in US policy toward HESC).

1332 VALPARAISO UNIVERSITY LAW REVIEW [Vol. 45]

August 23, 2010 the District Court for the District of Columbia issued a temporary injunction blocking President Obama's executive order.⁵⁹ Roughly one month later on September 28, an appeals court ruled that funding could proceed while arguments were being heard.⁶⁰ Then, on April 29, 2011, a three-judge panel of the U.S. Court of Appeals for the District of Columbia Circuit by a 2-1 vote vacated the district court's injunction.⁶¹ The judges, all Republican appointees, ruled that the challengers were unlikely to prevail on the merits of the lawsuit. No one who understands the determination of sanctity-of-life advocates in the U.S. could think that this court ruling, or any future one, could end the conflict over HESC research. Something beyond merely the interests of the parties seems to be at stake in the dispute over HESCs.

In sharp contrast, the UK has allowed research on embryos remaining after assisted reproductive procedures since 1990. UK law also allows for the creation of embryos to be used in research. Most such research falls under the authority of the Human Fertilisation and Embryology Authority ("HFEA").⁶² The 1990 law was initially interpreted as allowing research on embryos only in the field of reproductive biology; a new interpretation in 2001 gave permission for many kinds of basic research in addition to reproduction.⁶³ The HFEA was also willing to allow human embryos to be used in certain lines of research involving cloning, but this authorization has been challenged. Conflicts over embryo research have occurred, but they have failed to engender the fierce and implacable character of such debates in the US. Could this be merely a reflection of national character, perhaps an aversion to political conflict? The evidence suggests otherwise.

Consider the response of the UK and its fellow nations in the European Union to GMOs, particularly as they affect the foods available to people. In the UK and other European Union member nations, GMO food products inspired energetic public resistance; the regulatory scheme devised is meant to ensure that GMO foods must endure a rigorous approval process. Producers are required to demonstrate that the genetically modified trait is as safe as comparable conventional products, rather than the burden of proof resting on those concerned over the

⁵⁹ *Sherley v. Sebelius*, 704 F. Supp. 2d 63, 73 (D.D.C. 2010).

⁶⁰ Order Granting Motion for Stay Pending Appeal, Case No. 10-5287 (Sept. 28, 2010).

⁶¹ *Sherley v. Sebelius*, 2011 WL 1599685 (D.C. Cir. 2011); George J. Annas, *Sudden Death for a Challenge to Federal Funding of Stem-Cell Research*, 364 NEW ENG. J. MED. e47 (2011); I. Glenn Cohen & Eli Y. Adashi, *Human Embryonic Stem-Cell Research Under Siege: Battle Won but Not the War*, 364 NEW ENG. J. MED. e47(1) (2011) (describing the District of Columbia Circuit opinion interpreting the Dickey-Wicker Amendment).

⁶² Human Fertilisation and Embryology Act, 1990, 37 HMSO (Eng.).

⁶³ *Id.*

2011] *What Synthetic Genomes Mean for Our Future* 1333

suspected dangers of the new GMO product. Producers also have to test for changes in plant metabolism that may have been caused by the genetic manipulation.

In sharp contrast, the US regulatory scheme for GMO foods gives authority to the Food and Drug Administration under the Federal Food, Drug & Cosmetic Act,⁶⁴ just as it does for other food products. No unique consideration is mandated for genetically modified foods. Complaints by the public have been isolated and sporadic.

B. The Effect Conflicting Interests Have on Public Policy

There may be an alternative way of looking at policy disputes. Some flare fiercely for a time then subside as the policy is more or less begrudgingly accepted by both sides. Others, like HESC research in the US and GMOs in the UK, prove to be far more enduringly contentious, with the losers merely biding their time until circumstances allow the battle to be renewed.

The contrast between the two types of disputes is portrayed nicely by the differences between two recent major policy fights. As the U.S. plunged into deep recession in 2008, the very existence of its big three automobile manufacturers was in doubt. If they collapsed, so would many smaller companies that provided parts to them. Many manufacturing jobs were at risk. The Chrysler Corporation came closest to folding. Its survival depended upon restructuring: the only certainty was that there would be plenty of losers. Retired workers faced reduced pensions and health benefits; current workers feared closed factories, eliminated jobs, and reduced salaries and benefits; and new employees confronted sharply lower wages and benefits. Creditors risked their invoices going unpaid. Investors who bought Chrysler's bonds and stocks over the years faced the prospects of their holdings plummeting in value or even becoming worthless.

The battles over whose interests would be protected and to what extent were fierce and prolonged. In the end, though, the restructuring was accomplished. Each party extracted what they could, and life went on for everyone concerned, not least the Chrysler Corporation (and its new partner and possible eventual majority owner, Fiat).

The restructuring of Chrysler was an example of a public policy conflict over interests. Disputes over interests have noteworthy characteristics. First, tradeoffs are permitted and regarded as legitimate; they are essential components of bargaining and negotiation. Second, genuine compromises are both possible and anticipated. A key element

⁶⁴ Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301–399d (2010).

1334 VALPARAISO UNIVERSITY LAW REVIEW [Vol. 45]

in compromises in disputes over interests is that in practice as well as in principle all parties can accept such compromises with no one feeling violated. If one party felt it was treated badly, either it failed to understand the nature of such disputes or the resolution failed to balance the parties' interests equitably. It is not uncommon for parties to step away from hard-fought battles over interests with grudging respect for their counterparts who were, after all, playing with great skill by the same rules and for comparable stakes. Third, public interests can also be represented in policy disputes over private and commercial interests. The federal government's sense of urgency in the Chrysler restructuring had many contributing causes, but among them was surely the concern over the waves of industry destruction and the hemorrhaging of job losses that would come in the wake of Chrysler's impending demise. Such losses would further endanger the prospects for economic recovery as well as increase government expenditures for unemployment compensation and other social safety net programs.

C. *Public Policy Issues in the Context of Identity*

The dynamics of certain other public policy disputes, however, look quite different. Kristin Luker, in her landmark 1984 book, *Abortion and the Politics of Motherhood*, shows the nature of this difference.⁶⁵ Luker describes the explosive growth of the pro-life movement after the Supreme Court's 1973 decision in *Roe v. Wade*.⁶⁶ This movement, which had been largely populated by men, suddenly found a wave of women rushing forward, many of whom had never before been politically active. Luker writes: "this round of the abortion debate is so passionate and hard-fought because it is a referendum on the place and meaning of motherhood."⁶⁷

After *Roe v. Wade*, the battle over abortion in the U.S. was no longer being fought over fine points of theology or moral philosophy (though it was never entirely that simple). Now, it was clearly also a dispute over identities, over what gave the lives of many Americans meaning and significance. Disputes over identities are arguments over core beliefs about one's place in the world and the possibilities for flourishing. Such beliefs are not subject to tradeoff; compromise, if it is possible at all, is never more than tactical and temporary. For any stable, lasting policy to emerge identities must either prevail or evolve.

⁶⁵ KRISTIN LUKER, *ABORTION AND THE POLITICS OF MOTHERHOOD* (1985).

⁶⁶ *Id.* at 193 (describing the effect of *Roe v. Wade*, 410 U.S. 113 (1973) on the pro-life movement).

⁶⁷ *Id.*

2011] *What Synthetic Genomes Mean for Our Future* 1335

Evolution of identities seemed a possibility in the abortion debate with the rise in two-worker families and increasing concern for wage equality between men and women. On the pro-choice side of the debate, women should have the option of a life as both a mother and a worker; uncontrolled fertility was the principle threat to success in the workplace, therefore options for preventing the birth of unplanned children, from birth control to abortion, were seen as instrumental to the possibility of women's flourishing. In recent decades, spurred by economic aspirations and often by necessity, many women—who were primarily identified as mothers—entered the workforce. The possibility existed that women in these circumstances might come to share the concerns of pro-choice advocates about uncontrolled fertility as a barrier to financial success. To the extent such women came to value their identities as workers as well as mothers, their attitudes towards abortion may evolve as well. I offered this speculation in *The Worth of a Child* in 1996⁶⁸ but I am not aware of any evidence such changes have taken place.

Luker's interviews with advocates in the pro-life and pro-choice communities revealed intriguing differences far more extensive than their attitudes towards abortion. Advocates differed on a number of values, on their beliefs about the essential natures of women and men, and on what constitutes flourishing for women and men. An image that may be useful is that of the paths women and men must travel if they are to flourish. The details of the journey are not central here: what matters is whether the paths are seen as essentially separate or as overlapping.

In this metaphor, pro-life advocates tended to view women and men as walking separate paths—complementary and parallel perhaps, but mostly distinct. If women are by their nature nurturing, parental, and ill-equipped for the cold competitive world of employment, men were less well suited to be parents but eager for the gladiatorial battles of factory, sales floor and office. For pro-life advocates, women's and men's natures directed them down different paths toward flourishing.

Pro-choice advocates on the other hand were inclined to draw far less sharp boundaries, if they acknowledged such differences at all. Women could find great satisfaction in being nurturing parents, but so could men. Men might or might not relish competition at work, but women could also enjoy the challenges of a career and the satisfaction of bringing home a paycheck. In the worldview of pro-choice advocates, the paths to flourishing for women and for men may be indistinguishable or, at the least, considerably overlapped.

⁶⁸ See generally THOMAS H. MURRAY, *THE WORTH OF A CHILD* (1996).

1336 VALPARAISO UNIVERSITY LAW REVIEW [Vol. 45]

Given the far-reaching differences in identities between pro-life and pro-choice advocates, it should be no surprise that arguments between the two camps often break down into mutual unintelligibility with each side wondering of the other: How could anyone think such a thing?

Of course, to claim a simple dichotomy between interest-based and identity-based disputes underestimates the complexities of both the concepts and of the disputes to which they may be applied. Luker found that pro-life and pro-choice advocates differed significantly in their education, work experience and job qualifications.⁶⁹ Interests, that is, seemed to track identities. It is likely that people fashion their identities, at least in part, according to their interests; it is also likely that their interests take a shape that is consistent with their identities. Identities and interests, that is, develop together and affect one another.

How can we know when we confront a dispute over identities rather than mere interests? One clue is the question at issue. Identity disputes tend to be over questions like: Who am I? Does this threaten how I understand the meaning or significance of my life, my place in the world? Would the likely changes or losses to follow rock the foundation of my being? People can experience events that are simultaneous blows to identities and interests. Millions of Americans who lost their jobs in the Great Recession and have not found new ones are suffering a double loss: to their economic interests, income and life opportunities, and also to their identity as a reliable provider for their family.

Understanding the heightened stakes when identities are threatened may illuminate why disputes over estates and inheritances are often so volatile and painful. Because they are often not only over interests such as property and money, they can also be fresh fields for battle over one's identity and status within the family, over the relationships—good and awful—that formed one's personality and identity. Tommy Smothers regularly complained to his brother Dick: "Momma always liked you best!" For them it was comedy; for many parties to inheritance disputes, sentiments like these are excruciatingly deep and painful. So it is with disputes that engage identities.

V. INTERESTS, IDENTITIES, AND SYNTHETIC BIOLOGY

Because synthetic biology is not one thing but rather multiple streams, each proceeding at its own pace and towards its own goals, we should not expect any singular answer to the question whether conflicts over synthetic biology will encompass identities as well as interests. It will depend on the actors, the goals, and the stakes. In many cases, the

⁶⁹ LUKER, *supra* note 65, at 194–97.

2011] *What Synthetic Genomes Mean for Our Future* 1337

ethical concerns raised by synthetic biology are likely to be intelligible in terms of consequences and interests. Policy makers, the public, and health professionals worried over the possibilities of bioterror, biowarfare and bioerror will press their case against other actors who believe the fears are exaggerated and worry that scientific progress—and ultimately product development and profits—will be slowed.

Similarly, concerns over social and economic dislocations caused by developments in synthetic biology appear to be mostly over interests, though often not the interests of the parties carrying forward the argument. For example, advocacy groups such as ETC claim that using synthetic biology to help produce the anti-malaria drug artemisinin would deprive harvesters of sweet wormwood bark—the current source of artemisinin—of their livelihood.⁷⁰ In a comparable vein, advocates for the poor and people in the developing world sound warnings over the possibility that large scale biosynthesis for biofuels or industrial chemicals could lead to the displacement of food crops in favor of producing raw agricultural materials for synthetic biology manufacturing, thereby making food more expensive and scarce.

In principle, conflicts such as these could be negotiated, compromises reached that would give all parties at least a portion of what they want, and though not everyone may be happy, no one need feel violated. Are there concerns about synthetic biology that could result in conflicts over identities? This section will focus here on one such concern: humankind's relationship with the natural world.

Boldt and Müller sketch one approach.⁷¹ They argue that synthetic biology marks a fundamental shift in our relationship with nature that translates readily into consequences: people will become overconfident in their abilities to control life and overreach with potentially dire consequences; the more we come to regard life as mere artifact, the greater the risk that we will regard—and treat—higher organisms with diminished respect and protection.⁷² Though their basic stance appeals to identity—humankind's place in the cosmos—their worries concentrate on the bad things that will happen as we humans, in bliss and ignorance, shed the modest cloak of manipulators of what exists in favor of the power suit worn proudly by those who want to recast life according to their whims.⁷³ While such a gradual transformation of human identities

⁷⁰ ETC GROUP, THE NEW BIOMASTERS: SYNTHETIC BIOLOGY AND THE NEXT ASSAULT ON BIODIVERSITY AND LIVELIHOODS 40 (2010).

⁷¹ Joachim Boldt & Oliver Müller, *Newtons of the Leaves of Grass*, 26 NATURE BIOTECHNOLOGY 387 (2008).

⁷² *Id.* at 388.

⁷³ *Id.*

1338 VALPARAISO UNIVERSITY LAW REVIEW [Vol. 45]

may have consequences, it does not seem all that different from other ways humankind has devised to assert control over nature from agriculture and plant breeding to the refining and shaping of metals. These may have altered human identities for better or worse, but they did not commonly erupt into conflicts over clashing identities among different groups of people. The consequences of such evolutionary changes in identity are well worth attending to; but they do not amount to conflicts over identities on the order of embryo politics in the U.S.

The clearest encroachment on “creation” would be to create life out of inanimate matter, at the hand of and according to the precise design of humans—a goal that was approximated in the recent claim to have created a synthetic cell.⁷⁴ The initial claims were colorful and bold. Craig Venter at a press conference described the cell line as “the first self-replicating species we’ve had on the planet whose parent is a computer.”⁷⁵ Another leader of the team of scientists who accomplished this feat, Clyde Hutchison, acknowledged that “‘synthetic’” means a “‘chemically synthesized’” genome, not an entirely novel life form.⁷⁶ “‘You’d like to design a genome from scratch,’ he says. ‘You’d like to put it into a cytoplasm that you built up from scratch. But we’re trying to do something we can do.’”⁷⁷ David Baltimore, a distinguished scientist, described the accomplishment as “a technical tour de force” rather than breakthrough science.⁷⁸ Referring to Venter, he remarked “He has not created life, only mimicked it.”⁷⁹

Is this technological accomplishment an example of what Boldt and Müller call “*manipulatio*,” “*creatio ex existendo*,” or is it the further leap into “*creatio ex nihilo*”—creation out of nothing?⁸⁰ A cautious appraisal seems in order. In producing the cell line it dubbed *Mycoplasma mycoides* JCVI-syn1.0, the JCVI team used the sequence of a naturally occurring microbe. Into that functional genome they inserted a number of non-coding, non-functional sequences—call them genetic tattoos—including three brief quotations, the names of the article’s authors, and an email address.⁸¹ In an interview, Venter noted that fourteen genes

⁷⁴ Daniel G. Gibson et al., *Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome*, 329 SCI. 52, 52-56 (2010).

⁷⁵ Nicholas Wade, *Researchers Say They Created a ‘Synthetic Cell’*, N.Y. TIMES, May 20, 2010, available at <http://www.nytimes.com/2010/05/21/science/21cell.html>.

⁷⁶ Roberta Kwok, *DNA’s Master Craftsmen*, 468 NATURE 22, 25 (2010) (internal quotations omitted).

⁷⁷ *Id.*

⁷⁸ Wade, *supra* note 75.

⁷⁹ *Id.*

⁸⁰ Boldt & Müller, *supra* note 71, at 388.

⁸¹ J. Craig Venter Institute, *supra* note 24.

2011] *What Synthetic Genomes Mean for Our Future* 1339

suspected of being pathogenic (the naturally occurring bacteria that infects goats) were cut out.⁸² The original genome was thus somewhat modified in both nonfunctional and possibly functional ways, but the overall architecture of the genome was a more or less faithful replica of a naturally occurring organism. Furthermore, stitching the DNA sequences together took place in yeast cells, and the cytoplasm and cell membrane—everything but the genome—began as a healthy, normal *Mycoplasma capricolum* into which the chemically synthesized and yeast-assembled genome was placed. An impressive accomplishment, no doubt; but far short of “*creatio ex nihilo*,” and possibly even short of “*creatio ex existendo*”—a “mere” “*manipulatio*,” perhaps.⁸³

There is another way to think about synthetic biology’s impact on our relationship with nature. Paul Lauritzen’s chapter in Greg Kaebnick’s new book, *The Ideal of Nature*, draws inspiration from the work of two notable authors, Cormac McCarthy and Wendell Berry. Lauritzen writes of McCarthy’s novel *The Crossing*⁸⁴:

This is the central worry of *The Crossing*: human overreaching has the potential irrevocably to change the world in ways that humans cannot, or at least do not, begin to comprehend. And some things, when they are changed, cannot be made right again. In exercising our power, whether in relation to the environment or in relation to agriculture or biomedical technology, the appropriate attitudes are awe and respect for the mystery of the world around us. The appropriate virtue is humility. Instead we act like “a god insatiable whom no ceding could appease.”⁸⁵

Bonnie Steinbock’s chapter in the same book warns against any simple acceptance of nature or human nature as a clear guide for moral action. But she also cautions against hubris: “Humility in the face of unknown risks and limited human knowledge is clearly warranted, especially in light of human destruction of fragile ecosystems. Moreover, another aspect of humility is to be awed by the power and beauty of nature. To

⁸² Wade, *supra* note 75.

⁸³ Boldt & Müller, *supra* note 71, at 388.

⁸⁴ Paul Lauritzen, *Thinking Like a Mountain: Nature, Wilderness, and the Virtue of Humility*, in *THE IDEAL OF NATURE: DEBATES ABOUT BIOTECHNOLOGY AND THE ENVIRONMENT* 114–29 (2011).

⁸⁵ *Id.* at 120–21.

1340 VALPARAISO UNIVERSITY LAW REVIEW [Vol. 45]

reduce nature to its commercial value is crass.”⁸⁶ The notable British philosopher Kate Soper’s contribution provides a similar caution:

There are, after all, aspects of human existence and response we may do better to acknowledge rather than seek to rationalize. Even if we cannot point to any essential or universal aspects of ourselves that underlie our forms of resistance to specific forms of biotechnology, such intuitions are always to be attended to as signaling, not so much the limits of what we *can* do to ourselves and other creatures and the rest of nature, but what we can do and *still expect to live well*, to be happy, and to experience the rewards of membership of an ethical community.⁸⁷

These authors are not indifferent to consequences or interests, but their principle focus is on cultivating moral virtues such as humility, morally fraught attitudes such as awe, and on preserving the possibilities for human flourishing in moral communities—that is, on matters not readily reducible to consequences or interests. Do these concerns about our relationship with nature and human nature amount to differences in identities?

Consider the worldview of the noted author Wendell Berry as described by Lauritzen: “The traditional respect, reverence, and awe with which humans approached nature have been lost. In their place, we find a consumerist mindset that sees nature merely as raw material to be used without limit or constraint.”⁸⁸ It would be difficult to reconcile this view with the consistent thread that runs through all the major variants of synthetic biology: an engineering mindset that aims to replace complexity with control and predictability. Engineering metaphors of mechanisms, devices and circuits run squarely up against Berry’s warning: “By means of the machine metaphor, we have eliminated any fear or awe or reverence or humility or delight or joy that might have restrained us in our use of the world.”⁸⁹

Of course, it is possible that Berry’s worldview is idiosyncratic, not a widely shared mark of identity. But there are hints of a wider uneasiness

⁸⁶ Bonnie Steinbock, *The Appeal to Nature*, in *THE IDEAL OF NATURE: DEBATES ABOUT BIOTECHNOLOGY AND THE ENVIRONMENT* 98, 110 (2011).

⁸⁷ Kate Soper, *Disposing Nature or Disposing of It: Reflections on the Instruction of Nature*, in *THE IDEAL OF NATURE: DEBATES ABOUT BIOTECHNOLOGY AND THE ENVIRONMENT* 1, 14 (2011) (citations omitted).

⁸⁸ Lauritzen, *supra* note 84, at 122.

⁸⁹ WENDELL BERRY, *THE UNSETTLING OF AMERICA: CULTURE & AGRICULTURE* 56 (1977).

2011] *What Synthetic Genomes Mean for Our Future* 1341

with the ambitions of synthetic biology. A 2010 survey asked respondents to choose their top concern about synthetic biology from among five options.⁹⁰ A quarter of the respondents chose as their primary concern that it is morally wrong to create artificial life, and more than a quarter were most worried that synthetic biology could be used to create harmful things such as biological weapons.⁹¹ Twenty-three percent chose “negative health effects for humans” as their primary fear, thirteen percent picked damage to the environment.⁹² Only eight percent claimed none of these were a worry.⁹³ All surveys have their limitations and no simple translation is possible between this survey’s results and Berry’s call for fear, awe, reverence and humility—to say nothing of delight or joy. But neither should we dismiss the concerns expressed here as merely confused or ignorant.

Recall the markers of conflicts over identities: tradeoffs are not readily available; integrity-preserving compromises are elusive; and mutual unintelligibility prevails. It is concerning that this last feature, mutual unintelligibility, may have already appeared. Synthetic biology enthusiasts often take it as a matter of faith that if the public understood their aims and methods, their enthusiasm would be universally embraced. But this may be prematurely optimistic. The same survey found a majority of Americans supporting the further cautious development of synthetic biology, but also a majority wanting federal regulation rather than leaving it up to voluntary guidelines.

One finding, though, is particularly striking. When respondents were asked their initial impressions of synthetic biology, nineteen percent said that the “benefits [would] outweigh the risks;” only sixteen percent worried “that the risks will outweigh the benefits.”⁹⁴ A third of those polled judged risks and benefits to be about equal with the remainder saying they were not sure.⁹⁵ Respondents were then given what was designed as a neutral description of synthetic biology. After that brief explanation, the percentage of those worried that risks will outweigh benefits more than doubled to thirty-three.⁹⁶ Those who were initially not sure broke roughly two-and-a-half to one in favor of risks outweighing benefits.⁹⁷ Proponents of synthetic biology who are

⁹⁰ See generally HART RESEARCH ASSOCIATES, AWARENESS & IMPRESSIONS OF SYNTHETIC BIOLOGY (2010) (reporting the results of these findings).

⁹¹ *Id.* at 14.

⁹² *Id.*

⁹³ *Id.* at 15.

⁹⁴ *Id.* at 5.

⁹⁵ *Id.*

⁹⁶ *Id.* at 7.

⁹⁷ *Id.* at 6–8.

1342 VALPARAISO UNIVERSITY LAW REVIEW [Vol. 45]

confidant that the more the public knows, the more favorable their attitudes will become should attend to the implications of this study. The simplistic assumption that the problem is the public's ignorance is unhelpful here.

VI. CONCLUSION

It cannot be said whether synthetic biology will provoke deep, persistent disputes like those over embryo research in the U.S. or GMOs in Europe. It's wise, though, to be patient with serious efforts to articulate concerns that cannot be readily cashed out in terms of consequences. Identities locate people in their cultures and moral worlds; they provide narratives of meaning, and map pathways to flourishing. We should acknowledge that not all efforts to reengineer biology are hubristic overreaches, but also recognize that humility and awe are important moral attitudes in shaping our identities, particularly our relationship to nature and to powerful means for altering that relationship, such as those given by synthetic biology. The paths to flourishing available to us, and the prospects for fruitful voyages along those paths, may call for uncommon vision and wisdom that see beyond stale and comforting metaphors.