The Ethics of Protocells

Moral and Social Implications of Creating Life in the Laboratory

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Introduction to the Ethics of Protocells

Mark A. Bedau and Emily C. Parke

Protocells are microscopic, self-organizing, evolving entities that spontaneously assemble from simple organic and inorganic materials. They are also known as artificial cells; however, that phrase is sometimes used to refer to things like artificial red blood cells, which are more inert than alive. By contrast, protocells are alive; they are similar to single-celled organisms like bacteria, in that they grow by harvesting raw materials and energy from their environment and converting it into forms they can use, they sense and respond to their environment and take steps to keep themselves intact and pursue their needs, and they reproduce and ultimately evolve. They are a new kind of technology that can, for all intents and purposes, be considered literally alive. Indeed, they are sometimes called "protocells" to emphasize their similarity to simple single-celled life forms. But protocells are simpler than any existing bacterium. And unlike bacteria, they are not natural but artificial, and exist only through human creation. Or at least this is what protocells will be like when they exist, for they do not exist now. However, that will change sooner than many people realize. Teams of scientists around the world are racing to create protocells, and incremental success is continually yielding more and more lifelike systems. The creation of fully autonomous protocells is only a matter of time.

Protocells are capturing growing public attention. New companies for creating artificial life forms are now being created in Europe and America,[1] and the commercial and scientific advances are attracting increasing media attention.[2] The increasing pace of breakthroughs in protocell science will increasingly heighten public interest in their broader implications.

The prospect of creating protocells raises some pressing social and ethical issues. Protocells will offer new benefits to individuals and to society and vast new economic opportunities, but they also have the potential to pose risks to human health and the environment, as well as to transgress cultural and moral norms. Because

protocells are living matter created from nonliving matter, they will be unlike any previous technology humans have created, and their development will take society into uncharted waters. This book aims to inform interested parties about these new developments and to promote an open and responsible process of evaluating the prospect of protocells.

The essays in this volume were written by a variety of experts who explore different aspects of the social and ethical implications of protocells. The authors reflect many different professions and intellectual traditions, so the chapters provide a diversity of perspectives on the relevant issues. The aim is not primarily to settle all questions, for that aspiration is unrealistic today. The questions are too complex and unexplored, and the discussion too preliminary to produce unequivocal answers. By providing relevant detailed information that reflects the complexity of the issues, this book can foster constructive reflection and discussion that will help stakeholders become informed and involved. Since the creation of living technology will, in time, profoundly change the world we live in, we think the stakeholders include all concerned individuals.

The State of the Art in Protocell Research

Nobody has yet created a protocell, but research aimed at this goal is actively under way. A comprehensive survey about the state of the art in protocell science is well beyond the scope of this introduction; such a survey can be found in the book *Protocells: Bridging nonliving and living matter* (Rasmussen et al., 2008). Protocell research strategies can fall into one of two categories: the "top-down" and "bottom-up" approaches. The top-down approach involves creating new kinds of life forms by modifying existing ones. The bottom-up approach involves creating living systems from nonliving materials, or "from scratch."

In 2002, J. Craig Venter and Hamilton Smith publicized their intention to create a partly manmade artificial cell, with $3 million in support from the U.S. Department of Energy (Gillis, 2002; Zimmer, 2003); the Department of Energy subsequently increased its support by an order of magnitude (Smith, personal communication). Venter and Smith are using the top-down approach to simplify the genome of the simplest existing cell with the smallest genome: *Mycoplasma genitalium*. Sequencing showed that the 580 kb genome of *M. genitalium* contained only 480 protein-encoding genes and 37 genes for RNA species, for a total of 517 genes (Fraser et al., 1995). Random shotgun gene knockout experiments subsequently determined that approximately 300 of those genes were essential for *M. genitalium* to survive and reproduce in laboratory conditions (Hutchison et al., 1999).

Venter and Smith have used off-the-shelf DNA synthesis technology to construct an entirely artificial genome for *M. genitalium* (Gibson et al., 2008), having first proved the methodology on the significantly smaller genome of a virus (Smith et al., 2003). They have also transplanted the genetic material from one bacterium into another, and expressed the transplanted genes (Lartigue et al., 2007). The final step is to put those two pieces together, and transplant a fully synthetic whole genome into a bacterium, express the genome, pass on the synthetic genome to daughter cells, and initiate a lineage of artificial cells. When the bacterium cytoplasm expresses that synthetic DNA, it will grow and reproduce and thus start a lineage of bacteria that has never existed anywhere before (Gillis, 2002). Once perfected, the process can be repeated to add new genes that perform various useful functions, such as generating hydrogen for fuel or capturing excess carbon dioxide in the atmosphere. By the time this book appears in stores, we expect that Venter and his associates will have succeeded in expressing a wholly synthetic *Mycoplasma* genome inside a donor *Mycoplasma* cell.

Venter recently (in 2005) created a company, called Synthetic Genomics Inc., to commercialize artificial cells. The company aims at producing, among other things, bio-factories for environmentally friendly forms of energy. Synthetic Genomics has applied for a patent for life forms created with the minimal *Mycoplasma* genome that they have discovered (USPTO, 2007). At the same time, a group of new similar companies (e.g., Amyris Biotechnologies, Codon Devices, LS9 Inc.) are reengineering existing life forms for various purposes, such as bio-factories for pharmaceuticals and other useful but rare chemicals, calling their work "synthetic biology."

The synthetic biology approach to making protocells is a logical extension of our experience with genetic engineering over the past thirty years. It has the virtue of allowing one to take advantage of all the complexity and biological wisdom produced by millions of years of evolution and currently embodied in the biochemistry of living organisms, without needing to fully understand the underlying mechanisms that produced them. It has the corresponding disadvantage that its insights will be constrained by the same evolutionary contingencies. If the fundamental problems simple cells must face have essentially different solutions, these will not be discovered by building on the minimal genetic requirements of *Mycoplasma*.

The alternative, bottom-up approach to creating protocells sacrifices the head start existing life forms provide, and instead attempts to create protocells de novo, entirely from nonliving materials. The goal is to create an aggregation of molecules that is simple enough to form by self-assembly, but complex enough to grow, reproduce itself, and evolve without using any products of preexisting life forms such as ribosomes and enzymes. The advantage of this approach is that, freed from the contingent constraints within existing life forms, it can explore a broader canvas of

biochemistries and thus eventually reach a more fundamental understanding of the molecular mechanisms required for life.

Several research groups are currently working toward building protocells from the bottom up (Rasmussen et al., 2008). Many groups are expressing more and more complicated genetic networks inside vesicles, typically using an enzyme found in living cells, and often using all of the cellular material found in cell-free extract, including ribosomes and hundreds of additional enzymes. More strict bottom-up groups avoid using materials derived only from living cells, although they do use DNA, RNA, and some other molecules distinctive of life on Earth.

Most bottom-up protocell research draws inspiration from existing cellular biology. The three primary elements of most protocells are the formation of enclosed membranes from amphiphilic lipids, the replication of information-carrying molecules such as DNA or RNA through a templating process, and the harvesting of chemical energy to construct cellular structures from small molecules that are transported across the membrane from the environment into the cell (Szostak, Bartel, & Luisi, 2001; Pohorille & Deamer, 2002). Nucleic acids like DNA and RNA will replicate under appropriate laboratory conditions, but a container is needed to maintain reactants at sufficient concentrations and keep molecular parasites out. A population of such containers encapsulating differently functioning molecular species would allow competing reaction systems to evolve by natural selection. So, the general consensus in the protocell community is that a protocell must have three functionally integrated chemical systems: an informational chemistry with some combinatorial molecule like DNA that programs vital cell functions, an energy-harvesting chemistry (metabolism) that drives all the chemical processes in the cell, and a self-assembling container (cell wall) that keeps the whole cell intact.

The spontaneous growth and replication of lipid bilayer vesicles has already been demonstrated in the laboratory (Walde et al., 1994), as has the synthesis of information-carrying molecules inside lipid vesicles (Oberholzer, Albrizio, & Luisi, 1995; Pohorille & Deamer, 2002). Furthermore, self-replicating RNA molecules can be encapsulated in self-replicating lipid vesicles. Monnard and Deamer (2002) encapsulated T7 polymerase and a 4,000-base-pair plasmid inside lipid vesicles, and added the ribonucleotides ATP, GTP, CTP, and UTP to the surrounding broth. By carefully cycling the temperature in a polymerase chain reaction (PCR) machine, they were able to achieve RNA synthesis inside the vesicles. This worked because the lower temperature permitted the RNA substrates to cross the vesicle membrane and the higher temperature activated the polymerase, catalyzing the production of more RNA.

Those using the bottom-up approach to protocells have no qualms about using external, manual methods to accomplish cellular functions that natural life forms

carry out internally and autonomously, for such artifices can achieve important intermediate milestones and then can be removed at a later stage. Hanczyc, Fujikawa, and Szostak (2003) have used external, manual extrusion and serial transport methods to achieve a complex vesicle system that repeatedly grows and divides. This system uses the clay montmorillonite, which is known to catalyze the polymerization of RNA from activated ribonucleotides. In Hanczyc's system, the clay serves two functions: It catalyzes vesicle growth by converting fatty acid micelles into vesicles, and it promotes RNA encapsulation into the vesicles. The enlarged vesicles can then be manually extruded through tiny pores, which causes them to divide into smaller vesicles that retain their original content. Putting this all together produces a complex vesicle-based system consisting of lipids, genetic material, and mineral catalysts that can be made to undergo continual cycles of growth and division.

Much effort in bottom-up protocell research is directed at finding an appropriate RNA replicase, that is, an RNA molecule that functions both as a repository for genetic information and as an enzyme directing replication of RNA itself. A single molecule that performs both critical functions could vastly simplify the protocell's biochemistry, because an RNA gene for the replicase could be copied using that very same RNA molecule as a catalyst. A promising initial step toward this goal includes using in vitro selection to find ribozymes (RNA enzymes for breaking down RNA) that act as primitive polymerases (enzymes for building up RNA) (Ekland & Bartel, 1996; Bartel & Unrau, 1999). Key remaining challenges are to find an RNA replicase efficient enough to accurately replicate all of itself, and to get this function to work quickly inside a self-replicating vesicle.

A third challenge in the bottom-up approach to protocells is to combine the functioning of the genetic, metabolic, and container chemistries so that the entire system evolves as a unit. Rasmussen, Chen, Nilsson, and Abe (2003) proposed a protocell in which these three chemical systems are explicitly combined in a very simple fashion. The unnaturalness of this design is especially striking in several ways. First, because of various advantages it affords, the synthetic and completely artificial nucleotide PNA (Nielsen, Egholm, Berg, & Buchardt, 1991) replaces RNA and DNA. Second, the protocell has no proteins. The PNA programs cellular functionality, but not by producing structural proteins or catalysts. Instead, the sequence of nucleotides directly modulates the amphiphile synthesis that drives the growth and reproduction of the protocellular containers. Third, these containers might not be vesicles formed by bilayer membranes but micelles, which are many orders of magnitude smaller than vesicles. In contrast to the aqueous interior of vesicles that usually house protocellular components, Rasmussen's design encapsulates the protocell's metabolic and genetic chemistry in the oily micellular interior and in the

micelle-water interface. Rasmussen's design illustrates how far bottom-up protocell designs have deviated from any form of life known today.[3]

The top-down and bottom-up approaches represent alternative tendencies in protocell research, but they are not necessarily diametrically opposed. Many lines of research combine elements of both; a good example is research using cell-free extracts. Cell-free extracts are complex mixtures containing the cytoplasmic and nuclear material of living cells. Different cell-free extracts can be made, containing different cytoplasmic or nuclear components. For example, a cell-free translation extract contains all the cellular components needed to synthesize proteins from messenger RNA (mRNA). Recent work with cell-free extracts has yielded some impressive results. Noireaux and Libchaber (2004) created a vesicle system in which two genes are transcribed and translated into proteins that function in tandem. They encapsulated a plasmid with two genes inside vesicles containing cell-free extract. One gene produced green fluorescent protein (GFP), and the other produced alpha hemolysin, a protein that forms pores in bilayer membranes. This pore-forming protein spontaneously embedded itself inside the vesicle membranes. The resulting pores permitted amino acids to continually resupply the GFP synthesis process controlled by the second gene. This sustained GFP production for an order of magnitude longer than occurred without the pores.

Natural living cells do not only contain many genes producing proteins with interlocking cellular functions; these genes often regulate one another, in complex genetic networks. Yomo and colleagues (Ishikawa et al., 2004) have demonstrated the first vesicle system with a two-stage functioning genetic network. They also encapsulated a plasmid with two genes in a vesicle containing cell-free extract. One gene produces T7 RNA polymerase, and this enzyme produces mRNA for GFP from the second gene. They demonstrated that these two genes acted in concert, with the polymerase significantly promoting the production of the GFP. A natural generalization of their achievement is to encapsulate genetic networks with three or more stages.

Risks and Benefits of Protocells

There are two main motivations behind protocell research. One is pure science. The ability to synthesize life in the laboratory will be a scientific milestone of immense proportions. Achieving it will mark a profound understanding of the biochemical systems that embody life, and it will also open a fast track to a series of further fundamental insights. Every step along the way toward building a protocell allows researchers to learn more and more about life and living systems. The ability to

create such systems in the laboratory is an acid test of the extent to which one really understands how such systems work.

But there is also a practical motivation behind creating protocells. Natural cells are much more complicated than anything yet produced by man, and many people believe that the next watershed in intelligent machines depends on bridging the gap between nonliving and living matter (e.g., Brooks, 2001). So, making protocells that organize and sustain themselves and evolve in response to their environment will lead to the creation of technologies with the impressive capacities of living systems. The promise of harnessing those capacities for social and economic gain is quite attractive.

Many technological, economic, and social benefits can be expected to follow the creation of protocells, because protocells are a threshold technology that will open the door to qualitatively new kinds of applications. Pohorille and Deamer (2002) note numerous pharmacological and medical diagnostic functions that protocells could perform. One application is drug-delivery vehicles that activate a drug in response to an external signal produced by target tissues. Another function is microencapsulation of proteins, such as artificial red blood cells that contain enhanced hemoglobin or special enzymes. A third application is multifunction biosensors with activity that can be sustained over a long period of time. After reviewing these examples, Pohorille and Deamer (2002, p. 128) conclude that "Protocells designed for specific applications offer unprecedented opportunities for biotechnology because they allow us to combine the properties of biological systems such as nanoscale efficiency, self-organization and adaptability for therapeutic and diagnostic applications. . . . [I]t will become possible to construct communities of protocells that can self-organize to perform different tasks and even evolve in response to changes in the environment." It is easy to expand the list of hypothetical protocell applications with possibilities ranging from molecular chemical factories and the metabolism of environmental toxins to smart defenses against bioterrorism and a cure for heart disease (e.g., protocells that live in our bloodstream and keep it clean and healthy by ingesting atherosclerotic plaque).

Protocells are the tip of an iceberg of opportunities provided by living technology. Living systems have a remarkable range of distinctive useful properties, including autonomous activity, sensitivity to their environment and robustness in the face of environmental change, automatic adaptation and ongoing creativity. There is increasing need for technology that has these features; such technology could be said to be literally "alive." Conventional engineering is hitting a complexity barrier because it produces devices that are nonadaptive, brittle, and costly to redesign. The only physical entities that now exhibit self-repair, open-ended learning, and

spontaneous adaptability to unpredictably changing environments are forms of life. So, the future of intelligent, autonomous, automatically adaptive systems will be living technology. And protocells will be the first concrete step down this path.

The prospect of protocells also raises significant social and ethical worries. Ethical issues concerning the creation of artificial forms of life have a long history, dating back at least to the artificial production of urea in 1828, the first manmade organic compound synthesized from inorganic materials. Concerns about nanostructures proliferating in natural environments were expressed in the nanotechnology community almost a generation ago (Merkle, 1992), and in the past decade Bill Joy's cautionary piece about the combination of nanotechnology with genetic engineering in *Wired* (Joy, 2000) sparked extensive commentary on the Web. Similar public concerns have surfaced over the minimal cells of Venter and Smith's research, which are sometimes dubbed "Frankencells." Mindful of this public outcry, Venter halted research and commissioned an independent panel of ethicists and religious leaders to review the ethics of synthesizing protocells (Cho et al., 1999). When this panel subsequently gave a qualified green light to this line of research, Venter and Smith resumed their project (Gillis, 2002). This move attracted some commentary on editorial pages (e.g., Mooney, 2002). Events like these are increasingly bringing the social and ethical implications of protocells to the attention of a wider and wider audience.

One of the most widespread worries about protocells is their potential threat to human health and the environment. Bill Joy's *Wired* article did not mention protocells specifically, but he worried about essentially the same thing: molecular machines with the ability to reproduce themselves and evolve uncontrollably. Referring to the dangers of genetic engineering and Eric Drexler's (1986) warnings about the dangers of self-reproducing nanotechnology, Joy concludes that "[t]his is the first moment in the history of our planet when any species, by its own voluntary actions, has become a danger to itself—as well as to vast numbers of others." He describes one key problem thus:

> "Plants" with "leaves" no more efficient than today's solar cells could out-compete real plants, crowding the biosphere with an inedible foliage. Tough omnivorous "bacteria" could out-compete real bacteria: They could spread like blowing pollen, replicate swiftly, and reduce the biosphere to dust in a matter of days. Dangerous replicators could easily be too tough, small, and rapidly spreading to stop—at least if we make no preparation. We have trouble enough controlling viruses and fruit flies.

Joy later adds the threat of new and vastly more lethal forms of bioterrorism to the list of health and environmental risks of protocells.

These possible dangers stem from two key protocell properties. First, since they self-replicate, any danger that they pose has the potential to be magnified on a vast

scale as they proliferate and spread in the environment. Second, because they evolve, their properties could change in ways that we never anticipated. For example, they could evolve new ways of competing with existing life forms and evading our control methods. This potential for open-ended evolution makes the long-term consequences of creating them extremely unpredictable. Much of the positive potential of protocells stems from their ability to self-replicate and evolve, and the very same power raises the specter of life run amok.

There are obvious possible strategies for coping with these risks. One is simply to contain protocells strictly in confined areas and not let them escape into the environment. This is a familiar way of addressing dangerous natural pathogens (for example, the Ebola virus). Another method is to take advantage of the fact that protocells are artificially created and build in mechanisms that cripple or control them. A third method is to make them dependent on a form of energy or raw material that can be blocked or that is normally unavailable in the environment, so that they would survive in the wild only if and when we allow them to. A fourth method is to engineer protocells to have a strictly limited life span, so that they die before they could do any harm. Or one could engineer them to remain alive only on receiving regular external signals, or to die when an externally triggered on/off switch is tripped. For example, there is evidence that magnetic fields can be used to turn genes on and off (Stikeman, 2002). A further form of crippling would be to block their ability to evolve. For example, one could hamper protocell evolution by preventing recombination of genetic material during reproduction. Merkle (1992) has also proposed encrypting artificial genomes in such a way that any mutation would render all the genetic information irretrievable. A further suggestion is to put a unique identifier (a genetic "bar code") inside each protocell, so that we can identify the source of any protocell that does damage and seek redress from the responsible parties.

Such measures would not placate concerns about protocells, though. All such safeguards are fallible and costly. No containment method is perfect, and more effective containment is more expensive.

Another indirect cost of stringent containment procedures is that they would significantly hamper protocell research. This, in turn, would impede the growth of our knowledge of how protocells work and what beneficial uses they might have. Many envisioned benefits require protocells to inhabit our environment or even our bodies. Such applications would be impossible if all protocells were isolated inside strict containment devices. Furthermore, methods for crippling or controlling protocells could well be ineffective. When humans have introduced species into foreign environments, it has often proved difficult to control their subsequent spread. More to the point, viruses and other pathogens are notorious for evolving ways to

circumvent our methods of controlling or eradicating them. This implies that protocells could experience significant selection pressure to evade our efforts to cripple or control them. Another kind of social cost of crippling protocells is that this would sacrifice a key benefit of living technology—taking advantage of life's robustness and its flexible capacity to adapt to environmental contingencies.

Themes in the Chapters

The chapters in this book weave together various themes, in three broad sections. The first section treats risk, uncertainty, and precaution with protocells. The second section draws lessons from recent history and related technologies. The third section explores how society should approach ethical questions in a future with protocells. Many chapters discuss issues that fall into two or all three of these categories, so chapters are placed within individual sections somewhat loosely.

Protocell technology is too novel to have yet generated a substantial literature. One way to start thinking through their social and ethical implications is to identify basic methodological lessons about good and bad arguments for and against protocells, as Boniolo argues in chapter 17. Another strategy is to empirically compare related technologies that have received significant public attention. A number of new biotechnologies are already pressuring our values and preconceptions about life. Stem cell research, cloning, and genetic engineering, for example, are increasingly changing the nature of the life forms that exist in our world. This is causing more and more people to think about the importance and sanctity of life, and the very notion of what it is to be alive. A number of chapters draw lessons from our track record with related biotechnologies, including genomics and the chemical industry (chapter 4), modern agriculture (chapter 2), biomedical science (chapter 16), synthetic biology (chapters 9, 11, and 14), and nanotechnology (chapter 8). These related areas are mirrors in which we can glimpse our future with protocells.

Another way to triangulate our future with protocells is to examine their implications for intellectual property rights. Pottage, in chapter 10, identifies some distinctive aspects of patents for protocell innovations, and explores how protocell patents disturb the political and institutional foundations of our current intellectual property practices. Hoping to foster the generation and diffusion of protocell innovations, some take inspiration from the open-source movement in software, typified by the Linux operating system, created through the collaboration of a wide network of interested individuals and then distributed for free. Hessel argues in chapter 11 that open-source biology would allow science and commerce alike to benefit from

innovations in living technology while minimizing the potential for harmful applications.

Each new technology has heightened public awareness and sensitivity about potential technological risks. Most would agree that decision makers should take account of the public's concerns about protocell technology. However, doing so is not easy. A number of chapters concentrate on the complexity of the relationship between public perception and the progress of new technologies. Citing examples from recent history, in chapter 7 Durodié discusses the simultaneous importance and difficulty of making sure that the public's actual voice is heard, rather than just the voices of interest groups that purport to represent the public but are actually driven by their own private agendas.

Several chapters examine the relationship between the public and those actively engaged in protocell research. The latter group involves not only scientists but also entrepreneurs. Some scientists and businesspeople proactively engage other stakeholders and the general public, elicit their views and concerns, and respond to them. Others try to lay low, out of the public eye, for as long as possible. Johnson, in chapter 2, argues for the wisdom of proactive engagement with stakeholders, drawing on examples from recent history. The public's role in decision making about new technologies is a contentious issue, for reasons examined by Hantsche in chapter 12. Hantsche emphasizes the difficulty of giving due weight to societal values when making decisions about our future with protocells, since there is no clear precedent on which to base these decisions.

One natural response to the complexity of the social and ethical questions about protocells is to engage the assistance of professional ethicists. Precedents for this include the earmarking of a small fraction of the human genome project budget for studies of the ethical, legal, and social implications of sequencing the human genome, and the existence of a number of professionally staffed institutes and centers for examining social and ethical implications of nano- and biotechnologies. But the advice of such studies and institutes is no quick fix that resolves ethical dilemmas and absolves scientists from making difficult ethically laden decisions. In chapter 15, Gjerris emphasizes that enlisting the help of professional ethicists will not eliminate the ethical problems raised by protocells but might, in fact, magnify them.

Chapter 14, by Rabinow and Bennett, examines the two main existing modes in which professional ethicists interface with the scientific, regulatory, and policy-making communities, and advocates adopting a new, third mode of interaction that is especially appropriate for synthetic biology. Khushf makes a complementary point in chapter 13, arguing that ethical reflection must be an integral part of the

development of protocell science and technology. Scientists have often viewed their work as ethically neutral, appealing to a division of labor in which their job is to learn how nature works, and leaving it to policy makers to decide how this knowledge should be deployed. Khushf argues that this traditional separation of the scientific and ethical realms is no longer sensible, and that scientists need to get their hands dirty with the ethical complexities of their scientific investigations.

Protocells present an unusual challenge for society not only because their consequences are uncertain, but also because they force us to confront our views about life and its creation. In chapter 3, Bedau and Triant examine some related concerns, including the worries that protocells are inherently bad because they are unnatural, that they violate the sanctity of life, or that their creators are "playing God." Addressing the risks associated with the creation of life is an extremely value-laden undertaking. Hauskeller develops this point with details about comparable experience with biomedical science (chapter 16).

Addressing public concerns about protocells and making appropriately balanced decisions requires understanding the risks and benefits involved. With the potential for great benefit comes the potential for great harm and abuse. Because fully functional protocells have not yet been created, their actual risks are merely hypothetical today. Cranor, in chapter 4, discusses how society perceives risk, using examples from the chemical and genomics industries to draw conclusions about the perceived acceptability of protocell technology and the proper way to manage the accompanying risks.

The analysis and evaluation of the risks and benefits of protocells is so complex that deciding what to do is challenging. The stakes are high and any decision will have both good and bad consequences. The traditional tools policy makers use to weigh risks and benefits are decision theory and risk analysis, but Bedau and Triant point out that these methods offer scant help when we are in the dark about the ultimate consequences of our decisions.

A growing number of people have been arguing that society's traditional policy- and decision-making tools should be augmented with the precautionary principle, which states that precaution should be the overriding concern when considering new technologies. Several chapters deal with precaution as a decision-making tool, discussing the precautionary principle as a framework for evaluating critical policy issues involving new technologies. Parke and Bedau review various arguments for and against the precautionary principle in chapter 5, and in chapter 6 Sandin develops and defends a new virtue-based understanding of the precautionary principle. Durodié, in chapter 7, counters the contemporary popularity of precautionary thinking, arguing from recent history that too much precaution has led to bad decision making. And chapter 3 argues that following the precautionary principle is

itself too risky, because society cannot afford to forgo all the potential benefits of new technologies like protocells.

* * *

The creation of protocells promises to alter our world forever. Protocells could bring many impressive benefits for human health, the environment, and defense, and dramatically accelerate basic science. But they could also create new risks to human health and the environment, and enable new forms of bioterrorism. So, their potential upside and downside are both quite large.

In addition, creating life from scratch will fundamentally shake public perceptions about life and its mechanistic foundations, undermining certain entrenched cultural institutions and belief systems. Society should weigh all of these significant consequences when deciding what to do about protocells.

This book should help. The chapters offer a diversity of perspectives on the relevant issues and discuss the key questions. This volume does not indicate final solutions, but rather initiates an open, informed, and responsible discussion of the prospect of protocells. Rather than being the last step in understanding the moral and social implications of creating protocells, this book is the first.

Notes

1. For example, Synthetic Genomics Inc., ProtoLife Srl., and Codon Devices.

2. In addition to the publication of Michael Crichton's popular novel, *Prey*, about artificial cells, numerous news accounts have appeared in the past few years in, for example, *Science, Nature, The New York Times, The Wall Street Journal, The Chicago Tribune, NOVA, The Scientist*, and *New Scientist*.

3. Rasmussen's fully integrated design has not yet been experimentally realized; only pieces of the picture have been achieved in the laboratory, at the time of this writing.

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