Synthetic Biology

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Agomoni Ganguli-Mitra · Huib de Vriend
Editors

Synthetic Biology

The Technoscience and Its Societal Consequences

Springer

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Chapter 1
Introduction

Markus Schmidt

Synthetic Biology, the design and construction of new biological systems not found in nature, is developing rapidly as a new branch of biotechnology, with many anticipated benefits and a high impact on society. As a result, the societal aspects of this discipline, as well as its possible risks, are becoming increasingly prominent. It is therefore crucial that the societal dimensions develop side by side with the field, engaging all stakeholders, including scientists, other experts and society at large.

This book represents the first edited volume of original research on a variety of societal issues related to synthetic biology. Part of it is also the outcome of the project SYNBIOSAFE, the first European project focused particularly on the safety, security and ethical aspects of synthetic biology. SYNBIOSAFE also aimed at stimulating an international debate on the societal consequences of synthetic biology in a proactive way, and we hope this book will serve as a crystallization point of such a debate for the years to come.

In addition to the project participants' chapters on ethics (Chapter 5), biosafety (Chapter 6), biosecurity (Chapter 7), and conclusions (Chapter 11), we also invited distinguished scholars to complement our work with chapters on the history of synthetic biology (Chapter 2), an introduction to the science and technology behind synthetic biology (Chapters 3 and 4), a chapter on the questions on intellectual property rights (Chapter 8), governance of new and emerging technologies (Chapter 9), and the role of civil society organizations (Chapter 10).

In **Chapter 2 "That Was the Synthetic Biology That Was"** Luis Campos shows that the term and the concept of synthetic biology has a history that dates back at least to the nineteenth century. Campos demonstrates in an intriguing way that the will to create "a technology of the living substance" has fascinated scientists for decades and centuries and has led to several moments in history when scientists claimed they were about to "create life in the test tube", produce "synthetic new species" at will, or otherwise engage in the engineering of genes and chromosomes.

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This constructive notion is also the Leitmotiv of contemporary synthetic biologists such as Carolyn Lam, Miguel Godinho, and Vítor Martins dos Santos, who present **“An Introduction to Synthetic Biology” in Chapter 3**. They emphasize that, although the wish to engineer life is decades old, only recent scientific developments allow for the application of true engineering principles to living organisms as outlined in this chapter. The authors show that synthetic biology is less of a homogenous undertaking but includes several major categories of research and engineering, each with a distinct area of focus, such as DNA circuits, synthetic metabolic pathways, protocells, genome minimization, use of unnatural biochemical components, and synthetic microbial consortia.

The cross-disciplinary feature of synthetic biology is unprecedented and involves fields such as chemistry, molecular biology, process engineering, nanotechnology and information technology. The use, for example, of automated design and IT resources for the design of living organisms is described in **Chapter 4 “Computational Design in Synthetic Biology”** by Maria Suarez, Guillermo Rodrigo, Javier Carrera, and Alfonso Jaramillo.

Following two chapters describing the scientific and technical aspect of synthetic biology, Anna Deplazes, Agomoni Ganguli-Mitra, and Nikola Biller-Andorno discuss its ethical implications in **Chapter 5 “The Ethics of Synthetic Biology: Outlining the Agenda”**. This chapter addresses ethical issues by assigning them to three main categories: method-related, application-related, and distribution-related issues. The authors also address a statement that is often raised in the discussion about ethics of synthetic biology, namely that the ethical issues of synthetic biology have been discussed in previous debates and therefore do not need to be addressed again. Contrary to the beliefs of many scientists they argue that preceding debates do not render the discussion of ethical issues superfluous because synthetic biology sets these issues in a new context and because the discussion of such issues fulfills in itself an important function by stimulating thought about our relationship to technology and nature. Furthermore, given that synthetic biology’s aims go beyond those of previous technologies, it does in fact raise novel ethical issues. By presenting an overview of the various ethical issues in synthetic biology and their actual and perceived importance, this chapter aims at providing a first outline for the agenda for an ethics of synthetic biology.

The construction of biological systems through the application of engineering principles is the declared goal of synthetic biologists who frequently cite genius physicist Richard Feynman “What I cannot create I do not understand”. This leitmotiv is the starting point for the question Markus Schmidt asks in **Chapter 6 “Do I Understand What I Can Create?”** reflecting on biosafety issues in synthetic biology. He argues that the design of larger DNA-based bio-circuits requires risk assessment tools that go beyond those used in traditional genetic engineering, and that have not been developed yet. Avoiding risk is one part, the other one should be to make biotechnology even safer. This aim could be achieved by introducing concepts of systems engineering, especially from safety engineering, to syntheic biology. Some of these concepts are presented and discussed by the author, such as Event Tree and Fault Tree Analysis. Finally the author discusses the impact of the de-skilling agenda in synthetic biology, allowing more and more people to engineer biology. This development needs to be monitored, to avoid amateur biologists causing harm to themselves, others and to the environment.

While the biosafety chapter deals with unintentional consequences, the biosecurity **Chapter 7 "Security Issues Related to Synthetic Biology: Between Threat Perceptions and Governance Options"** by Alexander Kelle, targets the intentional misuse such as terrorism and warfare. Based on the realisation that past breakthroughs in the life sciences have regularly been misused for weapons purposes, this chapter argues that the security implications of synthetic biology need to be taken seriously. Kelle argues for a continued exposure of synthetic biologists to the notion that biosecurity considerations form part of their responsibilities as practicing life scientists. Also current efforts to address biosecurity risks related to synthetic biology need to be further broadened. To facilitate this, a comprehensive biosecurity governance system – the 5P-strategy – is proposed that focuses on the provider and purchaser of synthesised DNA, but also on the principal investigator, the project, and the premises at which research is being conducted. Once the ideal policy intervention points and the measures with which to address them are determined, a discussion involving the relevant stakeholders about the content of the measures to be adopted can be started.

The impact of sharing and ownership issues on the development of synthetic biology is presented in **Chapter 8 "The Intellectual Commons and Property in Synthetic Biology"** by Kenneth A. Oye and Rachel Wellhausen. The authors introduce a conceptual framework for the analysis of ownership and sharing in emerging technologies, organized around two dimensions: a private ownership vs commons axis and a clarity vs ambiguity axis. Using the general framework they assess the fit between de jure and de facto conventions governing intellectual commons and property and the elements of synthetic biology that are objects of ownership and sharing. They also describe positions on ownership and sharing within the community of synthetic biologists, highlighting areas of agreement on common ownership of infrastructure, including registries of standardized biological parts; and agreement on private ownership of designs of devices ripe for commercialization. Finally they discuss the varied views of synthetic biologists on precisely where to draw the line on public vs private ownership.

Chapter 9 "Governing Synthetic Biology: Processes and Outcomes" by Joyce Tait, describes how the governance of new areas of development in life sciences has in the past led to an increasingly onerous and lengthy regulatory process which ensures that "only major multinationals can play", eventually stultifying the entire innovation system. She analyses that public and stakeholder pressures tend to reinforce demands for more regulation and stricter governance, in the case of synthetic biology related to biosafety, biosecurity, trade and global justice, and the morality of creating novel life forms. However, the policy makers' responses to these pressures can have counter-intuitive implications for innovation. Comparing synthetic biology with nanotechnology and GM crops, she provides insights into the nature and impacts of future pressures on synthetic biology governance and how they could contribute to better decision making in future. The author concludes that concerted international dialogue will be needed that takes account of the interplay between scientists, medical professionals and engineers; policy makers and regulators; and citizens and advocacy groups of all shades of opinion.

The need for international dialogue is also the basis of **Chapter 10 "Synthetic Biology and the Role of Civil Society Organisations"** by Dirk Stemerding, Huib de Vriend, Bart Walhout, and Rinie van Est. According to the authors, civil society organizations (CSO) often take the lead in these debates and as such play an important mediating role between scientific and governmental institutions and wider publics. The mediating role of CSOs is especially important in a globalizing world in which scientific and technological innovation is increasingly taking place in an international context and is strongly driven by the commercial interests of large multinational corporations. In this chapter the authors discuss the potential role of CSOs in future societal debates from three different perspectives. First, they describe the recent and early involvement of CSOs in debates about synthetic biology. They then go on to discuss some of the main social and ethical issues that have been raised in these debates. Finally in addition to their more general observations, the main findings from a survey in which the authors have enquired a number of CSOs about their (intended) involvement with synthetic biology are presented.

In the final **Chapter 11 "Summary and Conclusions"** we draw conclusions from our 2-year project SYNBIOSAFE studying the ethical, safety and security aspects of synthetic biology. This chapter presents a compilation of what we consider priority topics regarding societal issues of synthetic biology for the years ahead. The points collected are intended to encourage all stakeholders to react to the various issues presented, to engage in the prioritisation of these issues and to participate in a continuous dialogue, with the ultimate goal of providing a basis for a multi-stakeholder governance of this field. The points made in this chapter address the societal dimensions in two ways. First, they deal with novel issues that accompany synthetic biology, which are different from those associated with other life science activities. And second, they also address the fact that "old" issues will resurface in the discussion of societal aspects of synthetic biology. Although some of the topics have been debated for over 30 years now (e.g. since Asilomar), the contemporary political and societal contexts are quite different compared to the mid-1970s. Thus old issues may be revisited and revised in the light of this contemporary context.

We hope that this book stimulates further constructive research and discussions on the societal consequences of the technoscience of synthetic biology.

Chapter 2
That Was the Synthetic Biology That Was

Luis Campos

Contents

Abstract Visions of a synthetic engineering-based approach to biology have been a prominent and recurring theme in the history of biology in the twentieth century. Several major moments in this earlier history of attempts to redesign life are discussed: the turn-of-the-century prominence of experimental evolution and the coining of "synthetic biology" in 1912; early synthetic approaches to experimentally investigating the historical origin of life on the early earth; the goal of developing a "technology of the living substance" and the creation of life in the test tube as the ultimate epistemic goal for an engineered biology; the creation of synthetic new species in the first explicitly labeled efforts at "genetic engineering" in the 1930s; and the re-emergence of "synthetic biology" during the rise to prominence of novel recombinant DNA technology in the 1970s. The use of synthesis as a both mode of inquiry and of construction is highlighted. Aspects of the more recent history (the last decade) of contemporary synthetic biology are also explored.

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2.1 Introduction

"The first attempts to write the history of a scientific discipline often presage its imminent senescence" – or, in the case of synthetic biology, its imminent adolescence.[1] Most accounts of synthetic biology place its origin in the relatively recent past – if not just a few years ago, then perhaps in the 1990s or at a far reach in the 1970s. One frequently heard claim for the origin of the field dates to an editorial in *Gene* in 1978 describing the implications of the discovery of restriction enzymes, and making reference to "the new era of synthetic biology" (Szybalski 1978). Others trace the term back to less prominent pieces written a few years earlier, but all of which had been effectively forgotten and unknown to today's "founders" of the field.[2] Tracing a disciplinary label can certainly be a useful tool for uncovering the past of a field, but too exclusive a focus on the history of the label itself, rather than the field it represents, may exclude many more interesting and important developments.[3] Disciplinary godfathers have their purposes, but coinages alone do not a new field make.

The idea that a synthetic, engineering-based approach to life could serve both as an ultimate font of biological knowledge and that such knowledge could be directly and immediately applied to human purposes and for human benefit, is a prominent and recurring theme in the history of biology of the twentieth century. If "synthetic biology" is understood more broadly in this sense, then the twentieth century is replete with instances where this vision of biology led to important developments and transformations. Although the label was first coined shortly after the turn of the twentieth century, more significantly it was also at this time that a distinctively synthetic engineering-oriented standpoint to life gained dominance. The founding of the Carnegie Institution's Station for Experimental Evolution at Cold Spring Harbor serves as one useful entry point into this twentieth-century story of life by design.

Inaugurated on June 11, 1904, by the renowned Dutch botanist and author of *Die Mutationstheorie* Hugo de Vries, the Station was on the cutting-edge of biological research intended to turn the study of living things to the greater service of humanity. In his 45-min dedicatory address, de Vries was reported as saying that "evolution has to become an experimental science, which must first be controlled and studied, then conducted and finally shaped to the use of man."[4] At a time when Darwinism was relatively out of fashion as outmoded, slow, and incomplete as a

[1]The title of this piece and the first sentence are taken from Gunther Stent's landmark review (Stent 1968).

[2]"I didn't realize I was associated directly with invention," Szybalski said in an address delivered at the Synthetic Biology 4.0 conference in Hong Kong in October 2008. "I found out there was article in Wikipedia crediting me... I had to find it because I forgot about it."

[3]It will also include what may seem to be false positives, like (Huxley 1942) and (Reinheimer 1931) which – without much more interpretive work being done – seem at first glance to have relatively little to do with most contemporary understandings of "synthetic biology."

[4]"Scientists Assembled at Cold Spring Harbor: Formal Opening of the Carnegie Station for Experimental Biology," *Brooklyn Daily Eagle*, June 12, 1904.

description of evolutionary change – and when de Vries' own recently published mutation theory was in the ascendant – such vigorous proclamations that evolution could now come under experimental investigation and ultimately under human control matched the hopes of the new century. Here "[i]n this ten-acre plot" one newspaper reported, "man – long content with his part as caretaker and subjugator of living species – is now learning the new role of creator." Side by side with the human-focused interests of the other wing of the Laboratory, the Eugenics Record Office, the Laboratory's first director Charles Davenport declared that "the principles of evolution will show the way to an improvement of the human race" just as it would show "how organisms may be best modified to meet our requirements of beauty, food, materials and power."[5]

From the earliest years of the century, de Vries and other scientific breeders referred to their experimental breeding work as "synthetic" with the ultimate goal of creating novel, useful forms of life. "[Luther] Burbank crosses species," de Vries once said, referring to the traditional California breeder known for his almost magical ability to produce strikingly new and valuable varieties of flowers and fruits. "I seek to create new ones". Many of de Vries' contemporaries agreed, and declared of his work: "This is 'creating' life" (Huneker 1920). More than a sensational claim, it was precisely this "dissolution of the distinction between artificial and natural creations" that was de Vries' signature achievement, that guided much work at the Station, and that helped pave the way for the engineering of biology as a central goal of the twentieth century (Kingsland 1991).

2.2 Coining "Synthetic Biology"

While the synthetic approach to life was already underway at Cold Spring Harbor, the earliest explicit reference to "la biologie synthétique" appears to come from the French professor of medicine Stéphane Leduc (1853–1939), who published his *La Biologie Synthétique* in 1912 after years of experimentation. Leduc's work is significant for more than the happenstance fact that he called his efforts by the same label we use today. As he grew a variety of osmotic and crystalline growths in solution in his various "jardins chimiques," Leduc hoped to show how basic physicochemical processes like osmosis and diffusion could produce new and complex, even recognizably "organic" forms. A distinctively "synthetic" approach to the problem of biological morphology, Leduc's approach and findings were contested by numerous contemporaries who saw in his osmotic growths merely pale imitations of life, irrelevant for a true and better understanding of living things.

In his role as one of the first to experimentally attempt to use *synthesis* as a means to understand the basic biology of organic growth and morphology, however,

[5]"Man as Creator, Wonders of New Station for Experimental Evolution," *Los Angeles Times*, "Illustrated Weekly Magazine," February 24, 1907, p. 11.

Leduc's early work provides a recognizable affinity with a primary goal of today's synthetic biology. Leduc was a firm believer in the epistemic virtues of synthesis, and not just analysis, in the progress of biology:

> Jusqu'à present la biologie n'a eu recours qu'à l'observation et à l'analyse. L'unique utilisation de l'observation et de l'analyse, l'exclusion de la méthode synthétique, est une des causes qui retardent le progrès de la biologie... [La méthode synthétique] devoir être la plus féconde, la plus apte à nous révéler les mécanismes physiques des phénomènes de la vie dont l'étude n'est même pas ébauchée. Lorsqu'un phénomène, chez un être vivant, a été observé, et que l'on croit en connaître le mécanisme physique, on doit pouvoir reproduire ce phénomène isolément, en dehors de l'organisme vivant.

Leduc also held that his book offered a new and powerful mode of approaching life by analogy:

> La biologie synthétique représente une méthode nouvelle, légitime, scientifique; la synthèse appliquée à la biologie et une méthode féconde, inspiratrice de recherches; le programme consistant à chercher à reproduire, en dehors des êtres vivants, chacun des phénomènes de la vie suggère immédiatement un nombre infini d'expériences, c'est une direction pour l'activité. Les résultats, les faits exposés dans cet ouvrage: la reproduction des cellules artificielles, des structures, des tissus, des formes générales, des fonctions, de la circulation centripète et centrifuge, des mouvements et des figures de la karyokinèse, de la segmentation, des tropismes, tous ces résultats d'expérience et les expériences elles-mêmes seraient sans signification, sans intérêt, dépourvus de sens, si ces recherches n'étaient pas inspirées par l'imitation de la vie. C'est à l'analogie avec ce que l'on observe chez les êtres vivants que ces phénomènes doivent tout leur intérêt. (Leduc 1912)[6]

Although Leduc's work was not entirely mainstream, it was far from bunk science. The celebrated William Bateson – the man who coined the very word "genetics" – even made use of Leduc's work as an illustration of his own theory of life (Bateson 1913, Coleman 1970).

Synthetic in method and analogical in conceptual approach, Leduc's method could aim at a better understanding of "natural" living things even while producing artificial life-like forms: "C'est la méthode synthétique, la reproduction par les forces physiques des phénomènes biologiques, qui doit contribuer le plus à nous donner la compréhension de la vie." It remained for other pioneers in the prehistory of synthetic biology to move beyond such an analogical synthetic approach to the development of an approach more directly related to the potentialities of life.

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[6]Leduc's name seems to have been unknown to all participants at the 1.0 and 2.0 conferences: "We didn't even *know* our field had a history," the organizers told me when I applied to present on the history of the field at 1.0. At the 3.0 conference I presented a poster highlighting Leduc's role; he was also mentioned by another speaker, and Leduc has been routinely cited as a founding figure of the field since about that time. For further details on Leduc's work and its reception, and references to contemporaries also attempting to mimic living forms in this period, see Keller's "Synthetic Biology and the Origin of Living Form" in (Keller 2002).

2.3 Creating Life in the Test Tube

> On June 20th [1905] the scientific world was startled by the sensational announcement that a momentous discovery concerning the origin of life had been made by an English scientist. Working experimentally at the famous Cavendish laboratory in Cambridge, Mr. John Butler Burke, a young man in the prime of life... succeeded in producing cultures bearing all the semblance of vitality....

John Butler Burke, a young Irish physicist working at the Cavendish Laboratory in Cambridge, also turned to synthesis as a means to better understand the nature of life. While Leduc's efforts were focused primarily on proximate questions of form and shape, Burke's work had the higher aim of understanding something deeper and more fundamental about life itself: could life be produced from nonlife? In line with contemporary debates over the possibility of spontaneous generation, reports of his experiments proved to have immense popular appeal.[7]

As reported to *Nature*, Burke's sensational experiments involved plunking a bit of radium into a petri dish of bouillon, with the resulting production of cellular forms that were, if not quite living, at least *life-like*. Appearing to grow and subdivide over a span of days and demonstrating other life-like phenomena at the cytological level, they nevertheless decayed in sunlight and dissolved in water, proving that they were not simply bacterial contaminants. Existing at the limits of vision, Burke's growths were also extraordinarily difficult to see.

Burke was well aware of and readily acknowledged many others' contemporary attempts to create artificial cells, cells that incorporated foreign material, and cells that appeared to grow. He held that his own growths were something else altogether, however, in that the sheer number of life-related phenomena they exhibited far surpassed earlier attempts to merely mimic life. Burke didn't want to just mimic life – he wanted to get at its underlying features. Of Leduc's earlier forms, Burke argued that "*they have not the inherent and characteristic directive power of the living organism.*" A firm believer in the life-giving power of radium – a commonly held belief among both scientists and the public at this time[8] – Burke was convinced that he had produced something that was worthwhile even if not quite living, and contemporaries labeled his synthetic results "artificial life." Far enough from truly living things and yet just as far from being mere inorganic growths, he took his radium-induced growths to be new transitional forms of life with their own peculiar physical metabolism, and held that his growths were "suggestive" of both the nature and origin of life. It was far from mere wordplay to say that the element with a half-life (radium) had given rise to forms half-living.

Half-radium and half-microbe, these "radiobes" proved both immensely popular and controversial. The *New York Times* animatedly declared that these new forms existed "on the frontiers of life, where they tremble between the inertia of inanimate existence and the strange throb of incipient vitality." Burke himself said that

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[7] For more about Burke and further citations, please see (Campos 2006b), Chapter 2.

[8] For more on the connections between radium and life in this period, see (Campos 2006a) or (Campos 2006b) Chapter 1.

the interest his experiments unleashed "has been such that the brief note communicated to *Nature*, May 25th, 1905, and the few words uttered to a representative of the *Daily Chronicle*... have resounded from the remotest corners of the earth to an extent quite beyond the expectation even of my most apprehensive friends." Burke's experiments were hotly debated and contested on both sides of the Atlantic for months. By November 1906, Burke's findings were touted as "a discovery that has provoked more discussion, perhaps, than any event in the history of science since the publication of the 'Origin of Species,' for it has a direct bearing on all speculative theories of life."

Burke not only thought he had managed to produce at least "half-living" forms, somewhere on the border of life and not-life, but he used the controversy and fame that his work brought him to successfully reframe the terms of a contentious science-and-society debate about spontaneous generation with lasting effects. Although his experimental results were later discounted and explained away, and although he died unknown and almost completely ignored by the scientific community, he succeeded in laying the groundwork for the study of a new field: the experimental investigation into the historical origin of life. Synthesis was no longer about merely mimicking life; now it had been marshaled to help explore the more fundamental properties of life including its history and origin.

2.4 A Technology of the Living Substance

Not all pioneers in the prehistory of synthetic biology were interested in asking questions about the nature or history of life, however. Some – such as the German-American physiologist Jacques Loeb (1859–1924) – were much more interested in *doing* something with life, and in having full physiological and developmental control over it, developing new forms at will and as needed. As Philip Pauly has noted in his masterful biography, Loeb "considered the main problem of biology to be the production of the new, not the analysis of the existent" (Pauly 1987).

Loeb is most famed for, among other things, his mechanistic study of instincts and tropisms and his widely touted 1899 invention of "artificial parthenogenesis." This remarkable discovery, which cytologist and embryologist E. G. Conklin called "one of the greatest discoveries in biology," made Loeb a contender for the 1901 Nobel Prize. Loeb reported on his work in his *Mechanistic Conception of Life* (1912), the title punning on the new reality of artificial parthenogenesis and his own mechanistic view of life. The *Chicago Sunday Tribune* took similar license, trumpeting Loeb's work: "Science Nears the Secret of Life: Professor Jacques Loeb Develops Young Sea Urchins by Chemical Treatment – Discovery that Reproduction by This Means is Possible a Long Step Towards Realizing the Dream of Biologists, to Create Life in a Test Tube."[9] This was indeed not far from Loeb's own intentions. The discovery of artificial parthenogenesis – this "most vital discovery

[9] *Chicago Sunday Tribune*, November 19, 1899.

in the history of physiology," almost "the manufacture of life in the laboratory," as Loeb was reported to have said, meant that "we have drawn a great step nearer to the chemical theory of life and may already see ahead of us the day when a scientist, experimenting with chemicals in a test tube, may see them unite and form a substance which shall live and move and reproduce itself."[10] While Burke's forms may have had *some* but not *all* the properties of life, which was sufficient – indeed, exactly what was needed – for Burke's interests and purposes, Loeb's goal was otherwise. He dismissed Burke's attempts: understanding a phenomenon for Loeb meant being able to control that phenomenon. The test of ultimate control over life – Loeb's dream of "a technology of the living substance" – was not only to be able to do with life as one willed, but to eventually be able to create it oneself from scratch in the test tube.

Loeb's goal was not to shock the public or to distance or entice his colleagues – though it may have had these effects – but came simply a concomitant of what he viewed as a thoroughgoing engineering approach to life. According to Pauly, for Loeb, "the very fact that creation of life was a nonnatural act made it possible to specify the steps necessary for production. Scientists should create life just because nature could not do so; and on the way to such an achievement they would find the power to reconstruct the living world according to the principles of scientific reasoning." It is thus not without reason that Loeb described his theory of a chemical basis for evolution as the development of a "synthetic physiology" and that he was intensely interested in "the artificial production of matter which is able to assimilate," and in "producing living matter artificially." A sampling of passages from Loeb's writings clearly reveal these elements of his research agenda:

> The idea is now hovering before me that man himself can act as a creator, even in living nature, forming it eventually according to his will. Man can at least succeed in a technology of living substance [*einer Technik der lebenden Wesen*].
>
> It is possible to get the life-phenomena under our control... such a control and nothing else is the aim of biology.
>
> And ten years ago, when I went to Naples, I dreamed that I must soon succeed in producing new forms at will!
>
> Perhaps the most fundamental task of Physiology... to determine whether or not we shall be able to produce living matter artificially.
>
> It is in the end still possible that I find my dream realized, to see a constructive or engineering biology in place of a biology that is merely analytical.
>
> There is, therefore, no reason to predict that abiogenesis is impossible, and I believe that it can only help science if the younger investigators realize that experimental abiogenesis is the goal of biology. (Pauly 1987)

While other biologists saw the production of abnormalities and monsters – precisely the kinds of organisms Loeb regularly succeeded in producing – as irrelevant to the study of biology, Loeb held much like de Vries that it was only in breaking down such distinctions between the natural and the artificial that a program for an engineering biology could be fully explored. As Pauly noted, by 1900 Loeb

[10] "Creation of Life," *Boston Herald*, 26 November, 1899.

> had come to symbolize both the appeal and the temptation of open-ended experimentation among biologists in America, and he became the center of scientific and popular controversies over the place of manipulation in the life sciences.
>
> . . .The core of the Loebian standpoint was the belief that biology could be formulated, not as a natural science, but as an engineering science. More broadly, it means that nature was fading away. As biologists' power over organisms increased, their experience with them as 'natural' objects declined. And as the extent of possible manipulation and construction expanded, the original organization and normal processes of organisms no longer seemed scientifically privileged; nature was merely one state among an indefinite number of possibilities, and a state that could be scientifically boring. (Pauly 1987)

2.5 The Engineering of Experimental Evolution

This sort of celebration of the artificial did not sit well with many traditional biologists. "Thus one sitting in his study may blithely construct 'synthetic protoplasm' by 'a juggling of words,' or by a combination of ideas drawn from physics and chemistry," naturalist David Starr Jordan wrote scathingly in 1928 of newfangled attempts to engineer life.[11] The onetime president of Indiana and Stanford University, and an ichthyologist by training, Jordan was responding as most naturalists did to sensational claims like those of Loeb and others. Real biology was real biology: what Leduc, Burke, Loeb, and others were doing might be something interesting, but for Jordan it certainly wasn't biology. Many Progressive-era agriculturalists, breeders, and geneticists were more interested in altering protoplasm already in hand toward greater ends than they were in constructing synthetic protoplasm. Such concerns dovetailed in the American context not only with the establishment of new land-grant universities dedicated to the public good but also with the founding of experimental research stations like the one at Cold Spring Harbor. Gaining experimental control over evolution was seen as instrumental in such goods as improving crop yields or in developing new mutative varieties. Experiments in mimics of life, primitive life, or artificial life seemed less central.

Representing a parallel tradition in the engineering approach to life distinct from the work of Leduc, Burke, and Loeb, these investigators of a more traditional stripe – even as they ignored or derided artificial approaches – contributed in their own way to the development of an explicitly engineering-based approach to life, in their focus on improving species and varieties. Inspired by the work of de Vries, whose novel mutation-theory was sweeping biological circles in the first years of the century, many of these investigators began to envision a control of evolution that extended beyond the realm of basic *physiology* – where most of Loeb's research had concentrated – and into the phenomena of *heredity* and *evolution*.

In "The Aims of Experimental Evolution," his address at the dedication of Cold Spring Harbor, de Vries had suggested that organisms might mutate under the

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[11]D. S. Jordan, "A Consensus of Present-Day Knowledge as set forth by Leading Authorities in Non-Technical Language that All May Understand," in Frances Mason, ed., *Creation by Evolution*, New York, The MacMillan Company, 1928, p. 3.