What's in a name?

Defining an emerging field can be challenging. *Nature Biotechnology* asked 20 experts for their views on the term 'synthetic biology'.

Similar to other new and trendy fields, synthetic biology has been defined so loosely that it can seem like all things to all people. Traditional genetic or metabolic engineering has been rebranded as synthetic biology, often to take advantage of the hype cycle that fuels investor interest. Below, 20 experts give their own definitions. The diversity of responses indicates that consensus as to the meaning of synthetic biology still lies some way off.

Adam Arkin, professor, Department of Bioengineering, University of California, Berkeley, California.

Synthetic biology aims to make the engineering of new function in biology faster, cost effective, scalable, predictable, transparent and safe. It focuses on improvement of standard genetic engineering technology; development of standards for genetic assembly and rapid characterization; creation of families of genetic 'parts' that behave reliably in designated hosts and have no undesigned interactions; and generation of safe, robust host cells. That is, it aims to remove the burden of synthesis and endless rounds of optimization of functional performance and thereby facilitate the design of increasingly complex systems. Although chemical production is the most powerful current application, synthetic biology seeks to address a much broader class of problems, including programmable materials, therapeutic organisms and systems that support agricultural and environmental services. Many of these systems will be engineered for operation beyond the bioreactor, requiring sophisticated sensing, computing and actuating systems to perform effectively and safely in complex environments.

Frances Arnold, professor, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California.

Synthetic biologists construct new biological entities—molecules, pathways, regulatory networks, organisms and ecosystems—by programming them, or reprogramming them, at the level of the DNA code. The new name 'synthetic biology' reflects an explosion in our ability to genetically engineer increasingly complex systems and the desire of scientists and engineers from fields outside molecular biology and genetics to participate in the fun, contributing to the technology and its applications.

David Berry, partner, Flagship Ventures, Cambridge, Massachusetts.

The term synthetic biology should really be synthetic biotechnology. The reason for that is, effectively, it is using tools of modern biology, including DNA sequencing, DNA synthesis, cell analytics, etc., to design biological tools to accomplish tasks. The goal is to leverage exponential information-generation with the precision of biology to create these tools. The use of them can be broad, including sense-response proteins or cells, engineered biocatalysts, or cells that undergo conversions. On this last point, the difference between metabolic engineering and synthetic biotechnology is that only with the latter can you design cells that accomplish a task that is independent from what the cell normally does—that is, causing a heterotrophic organism to be autotrophic, not improving a yeast's ability to make ethanol.

Joachim Boldt, assistant professor, and **Oliver Müller**, junior research group leader, Department of Medical Ethics and the History of Medicine, Freiburg University, Germany.

Synthetic chemistry has shown the way: from systematic analysis of chemical processes to synthesis of novel products. Synthetic biology does the same, but in the realm of the living. It leads us from analyzing complex molecular processes inside the cell to generating novel cellular functions and novel single-cell organisms. As such, synthetic biology comprises our full-blown ability to technically manipulate genetic, metabolic and signaling processes inside and in between cells. It is turning us into creators of the most basic parts of living nature. Synthetic biology opens up the possibility to augment nature with neo-microbes by an effort of engineering, thus aiming at controlling the uncontrollable. Philosophically speaking, the project of synthetic biology crystallizes in one single question: can we or should we, undoubtedly being part of nature, understand ourselves as co-creators of the evolution?

George Church, professor, Department of Genetics, Harvard Medical School, Boston, Massachusetts.

Genetic engineering focuses on individual genes (typically cloning and overexpression). The logical extension of that to system-wide change is genome engineering. Intermediate between these is metabolic engineering, which involves optimizing several genes at once. Synthetic biology is 'meta' to all of these in establishing standards for modules, intentionally interoperable in their assembly and functioning. Hierarchical properties permit computer-aided design at different levels of abstraction, from the sub-molecular level to supra-ecosystem levels.

Andrew D. Ellington, professor, Institute for Cellular and Molecular Biology, University of Texas, Austin, Texas.

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.

© 2009 Nature America, Inc. All rights reserved.

© 2009 Nature America, Inc. All rights reserved.

Drew Endy, assistant professor, Department of Bioengineering, Stanford University, Stanford, California.

We human beings belong to the clan of the opposable thumbs; we are very good at discovering and making new things by building. Synthetic biology, by exploring how to remake or assemble the molecules of life, provides a complementary scientific approach for learning how life works. Synthetic biology also celebrates getting much better at constructing new living things by recognizing that a good biological engineer will not just deliver on any one biotechnology application but will also contribute to the development of tools, so that all who might follow will find a safer and easier path.

Martin Fussenegger, professor, Swiss Federal Institute of Technology, Zurich, Switzerland.

Since its inception some 40 years ago, molecular biology has largely remained a descriptive discipline using a rather childish strategy to unravel the inventory of biological parts that are essential for life on this planet: disassemble to understand. Life becomes a lot more thrilling when we are assembling parts to make functional systems. With the post-genomic era having provided encyclopedic information on gene-function correlations, and systems biology now delivering comprehensive details on the dynamics of biochemical reaction networks, molecular biology has come of age and life scientists are now adult: ready to reassemble these cataloged items in a systematic and rational manner to create and engineer functional biological designer devices and systems with novel and useful functions. A new type of constructive systems biology—synthetic biology—is born.

E. Richard Gold, professor, Faculty of Law, McGill University, Montreal, Quebec, Canada.

Synthetic biology comprises the research necessary to develop a living organism that can be described without reference to an existing organism. Drawing on my patent law background, what seems critical to me is that any resulting organism can be described in words without having to refer, directly or indirectly, to any living organism. The end result will therefore be something completely new rather than a modification or change to an existing organism. By defining the field in terms of a result, it leaves the specific disciplines that are included open. For example, I would imagine that the fields include not only biology, but computer science and even social sciences to the extent that these help overcome important roadblocks to researchers' ability to do their work.

Jim Greenwood, president and CEO, Biotechnology Industry Organization, Washington, DC.

Synthetic biology is an interdisciplinary approach that applies engineering principles to biology. It builds on both improvements in the speed and cost of chemical synthesis of naturally occurring DNA and growing knowledge of genomics to enable researchers to design and synthesize modified microorganisms, such as bacteria, that can produce useful products in the pharmaceutical industry, personal care, specialty chemicals and biofuels. Whereas systems biology studies complex natural biological systems using modeling and simulation comparison to experiment, synthetic biology studies how to build artificial biological systems and synthesize industrial products. The focus is often on taking parts of natural biological systems, characterizing and simplifying them, and using them as components of an engineered biological system.

Sang Yup Lee, distinguished professor and LG Chem Chair professor, Korea Advanced Institute of Science and Technology, Daejeon, Korea.

Originally, synthetic biology sought to redesign and rebuild biological parts and systems without specific biotechnological objectives, whereas metabolic engineering aimed at purposeful modification of metabolic and other cellular networks to achieve desired goals, such as overproduction of bioproducts. Recently, it has become more difficult to distinguish the two disciplines as each is employing the other's approaches. Metabolic engineering is adopting synthetic biology's strategies of gene synthesis, very fine control of gene expression, etc., while synthetic biology is taking metabolic engineering's objective-driven strategies of engineering circuits and consideration of whole-cell metabolism. And both are moving towards integration with systems biology. We do not need to argue about what synthetic biology is and what is different about it as we want to honor people's diverse thinking.

Wendell Lim, professor, Department of Cellular & Molecular Pharmacology, University of California, San Francisco, California.

Synthetic biology is the application of engineering principles towards the construction of novel biological systems. At its heart, all synthetic biology shares a constructivist philosophy of trying to figure out how simpler parts can be combined to build systems with much more sophisticated behaviors, whether the goal is to build something useful or to increase our basic knowledge. Although most synthetic biology uses modules of biological origin as its toolkit, I am agnostic about whether this must be part of the definition of synthetic biology. For example, if someone figured out how to use abiotic components to build a material with the very 'biological' behavior of self-repair, I would consider that synthetic biology. In many cases we learn more about the 'rules of living systems' if we mimic them with a range of completely different parts.

Jeremy Minshull, CEO, DNA2.0, Menlo Park, California.

Synthetic biology began in earnest when phosphoramidite chemistry first allowed us to design and synthesize DNA sequences *de novo*. Now, we can make genes easily and are on the brink of synthesizing functional genomes, but we are only starting to learn how to design the sequences we really want. Scientific progress is incremental, but people holding purse strings, public or private, are most excited by paradigm shifts and the prospect of quick payoffs. Synthetic biology, then, is a useful term to attract funding for the ongoing (~30-year-old) biological revolution, powered by advances in molecular biology techniques coupled with increases in computing power. It means whatever the listener wishes to hear.

Thomas H. Murray, president, The Hastings Center, Garrison, New York.

Multiple streams of scientific inquiry and engineering practice, some decades old, converge under the marketing banner 'synthetic biology'. The ways we think and feel about biology are evolving along with the technologies used to manipulate it. Synthetic biology embodies: a faith that biological systems can be brought to heel, and made predictable and controllable; a stance toward the intricacy of biological organisms aptly described by Tom Knight [MIT] as an "alternative to understanding complexity is to get rid of it"; a confidence that biological entities can be hacked apart and reassembled to satisfy human curiosity and to serve important, legitimate human purposes; a *hope* that error and malevolence can be deterred, contained or outmaneuvered through the vigilance of governments and, especially, the collective efforts of well-intentioned scientists, engineers and garage biologists. Will what we might dub the 'Legoization' of biology fully justify the faith, stance, confidence and hope invested in it? The answer to this question will help to shape the future of humankind and the world we inhabit.

George Poste, chief scientist, Complex Adaptive Systems Initiative, Arizona State University, Phoenix, Arizona.

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)? Non-natural substrates include novel nucleotides and amino acids, proteins with unique tertiary structures, hybrid organic–inorganic molecular assemblies, biomimetic nano- and meso-scale materials and devices, and genetic sequences that did not arise through natural evolution. The construction of complex multigenic assemblies from known genetic sequences to synthesize biofuels or natural biomolecules that cannot be readily produced by chemical synthesis represents advanced genetic engineering and not synthetic biology. If such manipulations were classified as synthetic biology, the entire history of biotechnology and heterologous gene transfer would warrant redefinition as synthetic biology. The prospect of novel organisms created by synthetic biology has provoked scrutiny about potential health and environmental risks and dual-use abuse. Inaccurate definitions of the field, driven by efforts to attract publicity or funding, run the risk of attracting regulatory oversight to advanced biotechnology activities that do not pose the complex public policy issues raised by synthetic biology.

Kristala L.J. Prather, assistant professor, Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts.

If you ask five people to define synthetic biology, you will get six answers. I'd say it is the (re-)design, construction and analysis of biological systems or sub-systems. It is an effort to apply engineering principles in the context of biology and includes a focus on the development of well-characterized parts from which higher-order devices and systems can be reliably and robustly assembled.

Hana El-Samad, assistant professor, Department of Biochemistry and Biophysics, California Institute for Quantitative Biosciences (QB3), University of California, San Francisco, California.

Synthetic and systems biology are the ultimate synergetic partners for ushering in an era of rapid and provably systematic biological discovery. There are two ingredients necessary to unravel a biological system: the ability to generate perturbations that are maximally informative, and the ability to accurately measure the impact of such perturbations and organize the information they yield into a framework that can be easily queried and methodically analyzed. Synthetic biology could provide the first ingredient by generating genetically encoded 'perturbation' generators that are well-designed and characterized, while being tunable and portable. Conversely, systems biology should provide the technological innovations necessary to measure quantitatively the dynamical outcomes of these perturbations in any system of interest. It should also provide the computational innovations that are appropriate for a brand of system identification tailored to biological questions, in addition to analysis tools that can transition between different biological scales. This last feature is absolutely necessary—whereas the immediate goal might be investigation of a given biological mechanism, the ultimate goal should be the identification of the overarching organizational principles of cells and organisms. Systems and synthetic biology share this common vested interest, and a close-knit collaboration will reap many benefits for both fields.

Christina Smolke, assistant professor, Department of Bioengineering, Stanford University, Stanford, California.

Synthetic biology involves the development and application of engineering principles to make the design and construction of complex synthetic biological systems easier and more reliable. It is the focus on the development of new engineering principles and formalism for the substrate of biology that sets it apart from the more mature fields upon which it builds, such as genetic engineering. Synthetic biology represents an approach to biological design and genetic programming that can be used in a variety of different application areas in biological engineering, such as metabolic engineering or genetic/cellular therapies. However, one can conduct projects in these application areas (that is, metabolic engineering) without them falling into the category of synthetic biology, depending on the approach and tools implemented in the design, construction and characterization processes.

Ron Weiss, associate professor, Department of Biological Engineering and Department of Electrical Engineering and Computer Science, Massachusetts Institute of Technology, Cambridge, Massachusetts.

Synthetic biology is the engineering discipline for building novel and sophisticated living systems. In this discipline, we view cells as 'programmable matter', and strive to design and control complex intracellular and extracellular activities that allow us to achieve precisely defined engineering or scientific goals. To be successful, we will need to incorporate 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). But at the same time, we must also be cognizant of the interesting and challenging features of the biological substrate that make it different from all other existing engineering disciplines (e.g., self-replication, self-repair, mutation and evolution, high degree of noise, incomplete information and the importance of cellular context).

© 2009 Nature America, Inc. All rights reserved.