EDITORIAL—SYNTHETIC BIOLOGY

Synthetic biology builds upon over 35 years of genetic engineering. For example, in the 1970s methods were invented for using enzymes to rework DNA. Applying these tools, bacteria were engineered to yield relevant products such as growth hormones and insulin. Although many pioneering engineers were involved in such work, still more missed this biotechnology revolution or did not consider genetic engineering ‘real engineering’. This framing began to change in the late 1990s as the early genome projects neared completion. With several organisms sequenced and so-called ‘parts lists’ of natural genetic components growing exponentially, the biological sciences community became pressed to develop better methods for understanding how genes and proteins comprise healthy cellular systems, and how diseases arise in response to underlying molecular changes. Many engineers, often trained to deal with complex systems, saw a new opportunity to join in biological research at the cellular and molecular levels.

But some who entered were taken aback at the complexity of natural biomolecular systems. Luckily, a few researchers learned enough molecular biology to realize that instead of directly grappling with nature’s inherent complexity, simpler synthetic gene ‘circuits’ could be manually crafted using the tools of genetic engineering. For example, genetic analogs of basic electronic circuits were engineered and natural organisms slightly rewired, with an optimism and excitement similar to tinkering with a radio and with a resultant building of confidence and framing of new scientific questions.

However, a new set of frustrations emerged as the pace, cost, and uncertainty of working with biology became apparent to engineers more familiar with advanced systems engineering approaches based on electronic design automation and rapid prototyping. Thus, some researchers began to explore if and how to make the entire process of engineering biology easier. Under the label ‘synthetic biology’, we can now recognize a vibrant and sustaining research community working to improve the process of engineering biology, in addition to producing specific biotechnology products. Importantly, rather than separating science from engineering, the needs of the tool builders and the new questions posed by the early ‘tinkers’ have created and amplified opportunities at the intersections of chemistry, physics, biology and engineering.

As one prominent example, direct chemical synthesis has become a practical alternative to cut-and-paste methods for constructing large DNA molecules that encode entire biochemical pathways, or other functional genetic modules. This approach has the benefit of allowing complete flexibility of design, with no requirements for placement of restriction sites or other features that are not critical to the ultimate biological function of the designed sequence. Methods for seamless assembly of synthetic DNA have enabled the complete synthesis of viral genomes and even a small bacterial genome. Recently much progress has been made in our ability to manipulate and clone large pieces of DNA, both natural and synthetic. For example, small bacterial genomes can be cloned in yeast, and then transferred back into a bacterial cell where they ‘boot-up’ to direct the activities of the cell. These methods for synthesis and engineering, at the gene and genome scale, have the potential to provide new insights into fundamental biological problems, such as defining the minimal genetic requirements for cellular life, while also allowing a subset of engineers to specialize in the design of genetic systems.

For historical context, in the 19th century, chemists moved from describing the composition and structures of the molecules with which they worked to synthesizing known compounds and inventing new ones. The resulting work led to new scientific discoveries and many new chemicals, materials, and industries. We believe that the sciences of genetics and molecular cell biology have now firmly entered their synthetic era. In addition to describing the physiology and behavior of organisms, to determining the genetic sequences and identifying the molecules that make life work, biologists are now able to learn by building, to discover by construction what is needed for life to work, and to explore what might evolve next or be made anew. This is obviously an exciting time to be a biologist or biological engineer, as new discoveries pour in and the next steps are taken to engineer organisms that contribute to human flourishing and diverse, sustaining environments.

As a journal, Nucleic Acids Research has constantly been at the forefront of innovative publishing practices relevant to the genetic material and information. We were the first to encourage computational biology papers, to require the deposition of sequences in the GenBank/EMBL/DDBJ database, to devote special issues to Databases and Web Servers and among the first to move from a traditional subscription-based journal to a truly open access one. Recognizing the importance of synthetic nucleic acid sequences and the further ramifications of those sequences, the Journal is moving beyond mere description. We intend to provide a useful and innovative forum for publishing advances in the dynamic area of synthetic biology. On an ongoing basis, we welcome your suggestions for what the field needs from a research journal, as well your manuscripts contributing to this exciting frontier at the confluence of biology and technology.

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