CRIBSHEET #16

SYNTHETIC BIOLOGY

THE KEY QUESTION OF SYNTHETIC BIOLOGY:

Can we learn to program DNA and living organisms as well as or better than we currently program computers?

Life, even at its most minuscule, can elicit incredible change on a planetary scale. Consider the oxygen you're breathing. Its presence in Earth's atmosphere is a biochemical accident, a waste product of photosynthesizing organisms. Together, organisms cycle essential nutrients like carbon and nitrogen around the planet; even on its own, an organism can fabricate useful materials, and each—thanks to its cellular machinery—is capable of processing the information found in its genetic code.

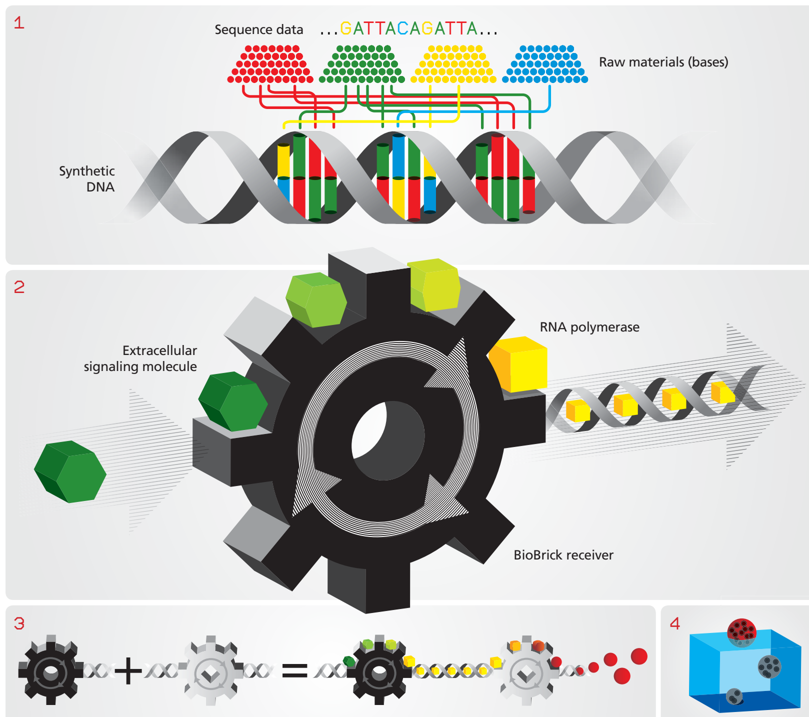
After biologists learned to decode genes, they soon learned to redirect the power of life by **manipulating DNA**. Scientists have developed numerous techniques to **read** and **modify** DNA; those techniques form the basis of genetic engineering, but many are inefficient. **Synthetic biology** is an effort to develop better tools and technologies for engineering biological systems, with the overarching goal of creating **new biological functions** and enhancing those that already exist.

CONSTRUCTING DNA

DNA sequencing allows researchers to read genetic material, converting information encoded within DNA molecules into sequence data. **DNA synthesis** allows biologists to write genetic material from scratch, using sequence data to assemble DNA molecules 1. Researchers are working to improve the power of DNA synthesis technology, but the bigger challenge is to invent new languages and grammars that enable the writing of many new **genetic "programs,"** each coding for useful behaviors, such as the production of fuels, foods, or medicines.

GENETIC PROGRAMS

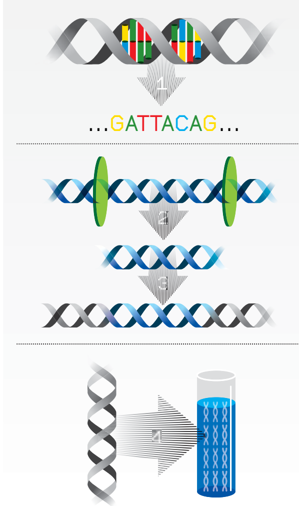
To make programming DNA easier, synthetic biologists are creating banks of standardized DNA sequences, or parts, that each perform a specific function. For example, the BioBricks Foundation, an open-source initiative from MIT, Harvard, and the University of California, San Francisco, is doing this by developing **BioBrick** parts, functional sequences of DNA with uniform prefix and suffix sequences. This **structural standard** allows BioBrick sequences to link together and act as **interchangeable parts**.



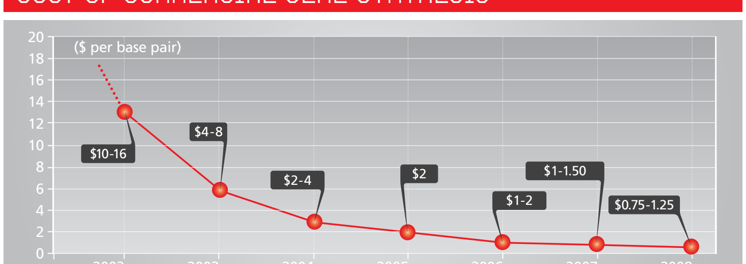
An efficient genetic machine also requires a **communications standard**. For example, one type of BioBrick part acts as a **receiver** for extracellular signals (conveyed via a modified sugar molecule, $3OC_6HSL$ ●) and produces an intracellular signal that other BioBrick parts can respond to. BioBrick parts communicate using **RNA polymerase** ■; the more sugar fed to a receiver, the more polymerase it will emit each second 2. There is a direct analogy to electricity: Just as an ampere is the unit that describes how many electrons flow past any given point on a wire each second, **polymerase per second**, or **PoPS**, describes the rate at which polymerase molecules flow down a DNA strand. The strength of the PoPS current controls how strongly a "plugged in" BioBrick part will respond. A BioBrick sequence recently developed by college students produces bubbles of protein, called vesicles ●, inside a cell. Plugging the bubble BioBrick part ✲ into the PoPS current from a BioBrick receiver ✲ creates a new genetic program 3 that can alter the number of vesicles created within a cell; more sugar means more PoPS, which in turn produces more vesicles and a more buoyant cell 4. This is but one example of a genetic program made possible by standardized synthetic biological parts.

BIOTECHNOLOGY BASICS

Genetic information is encoded by four nucleotides, or **bases**, that are part of DNA's molecular structure. To obtain this information, scientists read these bases in a process called **DNA sequencing** 1. Once a sequence is known, it can be **isolated** by restriction enzymes, proteins that sever DNA strands at specific sequences 2. A genetic engineer can insert such snippets of DNA into other DNA strands 3. Snippets of DNA can also be **amplified** (copied many times) by the polymerase chain reaction (PCR), making them easier to work with 4. Polymerases are molecules that travel along a strand of DNA to perform various tasks. Researchers also use PCR to selectively mutate small portions of genes. These methods enable researchers to **manually edit** DNA, which can then be incorporated into living organisms via several techniques collectively called **DNA transformation**.

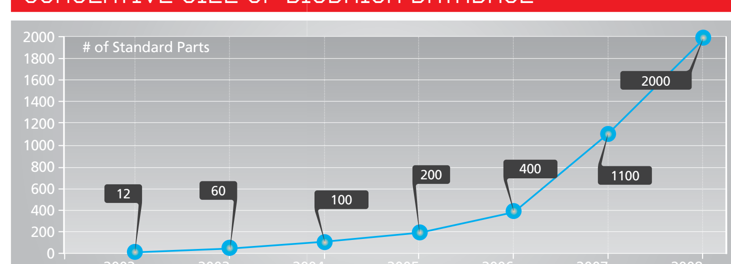


COST OF COMMERCIAL GENE SYNTHESIS



As costs plummet, the largest barrier against more individuals taking advantage of DNA synthesis is the inherent complexity of biological systems. Just as software developers used to painstakingly program in binary machine language but now rely on software compilers and sophisticated programming languages, synthetic biologists today await powerful computer-aided abstraction tools that simplify biology's complexity into easier formats. Many need to be developed.

CUMULATIVE SIZE OF BIOBRICK DATABASE



Since BioBrick parts are open source and in the public domain, anyone can use or modify existing BioBrick sequences free of charge and also submit new ones to online databases. This openness has driven significant growth in the number of BioBrick parts, as well as the creation of academic contests like the annual international Genetically Engineered Machine (iGEM) competition. As more BioBrick sequences accumulate, the collective power of synthetic biology increases.

THE ISSUE: THE DEMOCRATIZATION OF BIOTECHNOLOGY

If synthetic biologists continue crafting tools that simplify genetic engineering, it will become much easier for anyone, regardless of training, to construct novel biological systems. Synthetic biology techniques are "dual use": The same methods that could lead to a cancer-fighting bacterium might also make deadly biological weapons; the same methods that promote ecologically unsound crop monocultures could also cause beneficial flowerings of engineered biological diversity. Ultimately, governments, large corporations, and international regulatory bodies by themselves may not be able to control whether synthetic biology is wisely used—that choice will also be up to each of us.

SOUNDBITE

Powerful new tools and technologies will ultimately give individuals the ability to design and modify custom genomes and construct artificial living organisms from scratch.

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