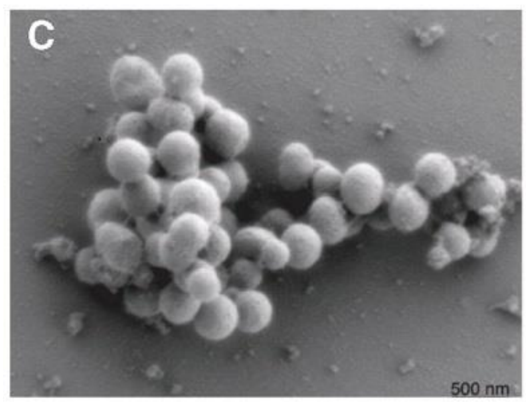
The Biorevolution is Enabling New Opportunities

Rapid advances in the scientific understanding of living organisms are producing new technological capabilities

We are living through a period of what may justly be called a revolution in our understanding of living organisms and how they operate. One eminent biologist has called the present period "the Golden Age of Biological Science". As is often the case when scientific understanding of natural phenomena advances, new technologies – tools intended to "harness that understanding to human purpose"[1] – quickly follow. The biorevolution has generated and benefited from an array of new technologies that endow us with new powers to manipulate microbes, plants, animals, and even whole biosystems. These capabilities will be hugely beneficial to humankind, and will be useful across a wide range of applications, from medicine to agriculture to food production and materials science. But as with all powerful technologies, biotechnologies are "dual-use", and can be used for malignant purposes.

Decoding and recoding the "code of life"



SEM of M. mycoides JCVI-syn1.0, first self-replicating cell with synthetic genome.
Source: Gibson et al, Science (2010) 329: 52-56 (Fig 5C)

The breadth and rapidity of our increasing comprehension of the biological world is made possible by the technological fruits of the 20th century digital revolution. There is no obvious start to the biorevolution, but the current capacity to read, write and edit genomes can be said to have begun with Watson and Crick's 1953 discovery that the nucleotide sequences in DNA constituted the "code of life". The Human Genome Project (1988-2000)[2], biology's first "big science" project, established the viability of decoding and digitizing the three billion base pairs in the human genome. J. Craig Venter and others have since demonstrated the feasibility of editing an organism's digital code, chemically synthesizing the specified DNA and then precisely assembling the encoded sequence of nucleic acids to yield a functioning microbe[3]. Meanwhile, the speed, accuracy and decreasing cost of the tools and machines that read the code of life are progressing faster than Moore's Law.

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1 Arthur, W. B. (2009). The nature of technology: What it is and how it evolves. New York: Free Press.

2 https://www.genome.gov/10001772/all-about-the--human-genome-project-hgp/

3 Gibson DG, et al. (2010). Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome. *Science* 329 (5987): 52-56. DOI: 10.1126/science.1190719

The 20th century digital revolution made the biological revolution possible

The genomic revolution was made possible by broad access to advanced computing and the capacity to store and analyze vast quantities of data. Other products of the digital age were also critical to the biorevolution. The "resolution revolution" has produced powerful machines such as cryo-electron microscopes that enable precise visualization at the level of biomolecules. Robotics make it possible to execute thousands of experiments very rapidly, yielding huge amounts of data. This information is then transmitted at the speed of light to scientists all over the world, where it is incorporated into new experiments, yielding new knowledge, and translated into new applications. Bioscience is a global enterprise: the majority of publications in top peer-reviewed journals are authored by international research teams.

Robotic lab accessible through the cloud.
Source: Emerald Therapeutics

Synthetic Biology: Engineering Life

Synthetic biology (synbio) is focused on learning how to "engineer biology". The aim is to make the assembly and recombination of biological "parts" standardized, predictable and routine. Synbio holds promise for allowing humans to make use of the enormous creative capacity of the living world and to repair defective or diseased organisms. In 2015, a Stanford research scientist successfully combined 23 genes from six different species to create a yeast cell that synthesizes opioids[4]. The researchers hope to create drugs that will block pain without dangerous side effects.

> "Research in genome editing conducted by countries with different regulatory or ethical standards than those of Western countries probably increases the risk of the creation of potentially harmful biological agents or products. Given the broad distribution, low cost, and accelerated pace of development of this dual-use technology, its deliberate or unintentional misuse might lead to far-reaching economic and national security implications."
>
> James R. Clapper, DNI
> 9 Feb 2016 Statement for the Senate Armed Services Committee
> on *Worldwide Threat Assessment of the US Intelligence*

This exceedingly challenging, scientific feat was the result of a decade long effort, and was accomplished *without* CRISPR, a microbial defense against viruses, which has been adapted to create precise gene editing tools that enable researchers to make changes in the DNA of any organism. Gene editing has been practiced since the 1970s, but CRISPR-based techniques are cheaper and faster and much easier to use than previous approaches. Different types of CRISPR systems have been identified and scientists are learning to modify these systems for a range of

4 Galanie S, et al. (2015). Complete Biosynthesis of Opioids in Yeast. *Science* 349(6252): 1095–1100.

research purposes. The accessibility and ubiquity of CRISPR gene editing has raised concerns that the tool could be used to engineer bioweapons that might be designed to resist existing countermeasures.

While still largely a research technique, engineering of biology is penetrating the commercial markets. In 2016, US-based start-up companies using synbio techniques raised hundreds of millions of dollars from venture capital and public offerings[5]. These companies are pursuing products that range from engineered silk fabrics and leather replacement products to fragrances and flavors synthesized by engineered yeasts and bacteria, to seed coatings and new approaches to drug delivery.

The Biorevolution is Global

Although the biorevolution was catalyzed by decades of US investments in basic research, it is a global phenomenon. In contrast to some other industries, barriers to entry into the biotech industry are relatively low. Numerous countries, developed and developing, recognize that biotechnology will be a key driver of the global economy and have incorporated biotech development into their national strategic economic plans[6].

China, in particular, is determined to lead the biorevolution. China could soon become the world's second largest drug market. State-owned CNBG (China National Biotec Group) is already the world's largest vaccine manufacturer. The biotech industry is a central pillar of China's 13th Five Year Plan. and there is increasing early-stage financing activity in, around, and from China[7].

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5 Cumbers, J. These 33 Synthetic Biology Companies Raised More Than $900 Million in 2016. Synbiobeta. 28 Sept 2016. Accessed 10 April 2017. https://synbiobeta.com/33-synthetic-biology-companies-raised-900m-2016/

6 Nath, Indira. (2008). Developing countries have joined the front lines of the biotechnology revolution in health and agriculture. *Nature* 456:40. doi:10.1038/twas08.40a

7 Roy K. McCall. Investing in China's Biotech Industry. 16 Mar 2016. Accessed 19 Dec 2016. http://www.china-briefing.com/news/2016/03/16/investing-in-chinas-biotech-industry.html