A farmer carries freshly harvested genetically modified cauliflower in Panchkhal, Nepal, in 2020.

PHOTO: JONAS GRATZER/LIGHTROCKET/GETTY IMAGES

SYNTHETIC BIOLOGY

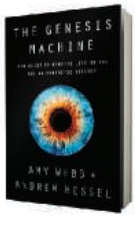
Life-changing biology

Genetically engineered genomes will disrupt the bioeconomy and rewrite human nature—are we ready?

By **Adrian Woolfson**

When interviewed in 1958 by *The Paris Review*, Ernest Hemingway confessed to having rewritten the ending of *A Farewell to Arms* a total of 39 times. The writer Raymond Chandler, on the other hand, adopted a different approach. He encouraged authors to "throw up" into their typewriters every morning and "clean up" at noon.

The strategy adopted by evolution by natural selection in authoring the genomes of living things has, by necessity, been more aligned with the latter approach than the former. While allowing individual letters in the genetic text to be edited, and facilitating the deletion, insertion, recombination, and duplication of more substantial genomic regions, evolution precludes throwing the entire folio away and starting again from scratch. Synthetic biology practitioners, however, are not necessarily bound by such constraints.



The Genesis Machine
Amy Webb and Andrew Hessel
PublicAffairs, 2022. 368 pp.

In their engaging and energetic new book, *The Genesis Machine*, Amy Webb and Andrew Hessel outline an optimistic manifesto for synthetic biology whereby "new biological circuits" and "programmable cells" will, if they are right, eventually upend traditional methods for building genomes. They assert that we are rapidly approaching a time when it will be possible to design and artificially synthesize the genomes of living things, including those of humans, from first principles.

The release of genomes from the constraints of evolution and the ability to prespecify genetic configurations are, the authors argue, likely to transform human nature and that of all living things. At a minimum, they may eliminate the "bad genes" underlying straightforward genetic diseases and remove some of the anguish and uncertainty of human reproduction. They will also establish the foundations of a biologically inspired industrial revolution and initiate a disruptive new bioeconomy.

DNA sequences might one day replace existing information storage technologies, the authors speculate. Meanwhile, the synthetic production of protein drugs by cells in the body, while having a beneficial effect on clinical medicine, may adversely affect the current biopharmaceutical industry. And genomically rewritten crops, while helping to achieve global food security, may restructure the agricultural industry.

Although existing biofoundries and related methods of DNA assembly have enabled the construction and recoding of simple genomes such as that of the bacterium *Escherichia coli* (*1*), the realization of the type of "genesis machine" envisaged by the authors—an entity capable of synthesizing the genomes of complex organisms from scratch—has remained elusive. A "DNA typewriter" will be required to achieve this goal. However, given that genome reading technologies have advanced to the point that human genomes can now be sequenced inexpensively within hours, it is not unreasonable to assume that genome writing technologies will follow suit.

Even more challenging and time-consuming than DNA writing is the debugging that synthetic genomes will likely require. Efficient genome writing will need to be tightly coupled to quality control.

It is one thing to have the ability to write genomes and another to know what to say. In this regard, databases of DNA sequences derived from natural organisms will help elucidate the principles necessary for effective genome authorship. The success with which machine learning enabled the artificial intelligence program AlphaFold to predict the unknown structures of proteins (*2*) vindicates this type of approach.

Biowarfare and the unpredictability of the ecological impact of bioengineering aside, and regardless of whether we will eventually be forced to choose between extinction or reengineering in order to survive, the issue of who will determine genome authorship, and how it will be deployed and regulated, is nontrivial. The power to control the essential substance of human nature may be a willing handmaiden of totalitarian agendas.

Ethical constructs, furthermore, are more fluid than we might like. The authors reference China's national DNA drive to "collect, sequence, and store its citizens' genetic data" and its prioritization of synthetic biology in a quest for "global science and tech hegemony."

It appears, however, that governmental agencies have largely ignored the strategic implications of synthetic biology. Without greater attention to this topic, we risk being blindsided by the "great transformation of life" that is already underway. ■

REFERENCES AND NOTES

1. J. Fredens *et al.*, *Nature* **569**, 514 (2019).
2. J. Jumper *et al.*, *Nature* **596**, 583 (2021).

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