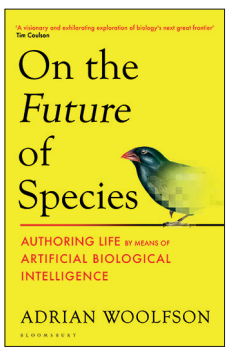
Book

Dreams of a synthetic genome



On the Future of Species: Authoring Life by Means of Artificial Biological Intelligence
Adrian Woolfson
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In June, 2025, the Wellcome Trust announced an ambitious £10 million UK project called the Synthetic Human Genome Project (SynHG) and claimed it "will unlock a deeper understanding of life, leading to profound impacts on biotechnology, potentially accelerating the development of safe, targeted, cell-based therapies, and opening entire new fields of research in human health". Some saw it differently, warning melodramatically about the horrors of laboratory-grown body parts. In *On the Future of Species: Authoring Life by Means of Artificial Biological Intelligence*, biologist Adrian Woolfson, whose company Genyro is aiming to develop some of the technical methods needed, sets out his vision of the potential of total synthesis of genomes. He offers a manifesto that would, he argues, allow the technology to develop in a way that respects human autonomy, dignity, and safety.

With a capability to programme and make genomes to order, Woolfson says, "it should be possible to meet most of humanity's needs through biologically inspired designs"—to solve many global problems, revolutionise health care, extend human lifespan, and create other organisms to order. Yet these grand claims are not merely unsubstantiated in the book, they are actually undermined by it. *On the Future of Species* emerges as an internal Socratic dialogue between an author presenting fantastical visions of what synthetic genomes might enable and at the same time clearly and honestly explaining why the complexities of the genome and the organism probably preclude many of them. Woolfson apparently shares much of my scepticism, when he remembers to.

We have been here before. In 2016, a US-based consortium of researchers announced a venture they called the Human Genome Project-Write. That initiative petered out, partly because the technology was not even close to such capabilities. Woolfson argues that we have come a long way since. But some fundamental problems remain to hinder this dream of engineering biology by design from the bottom up.

Woolfson acknowledges that the complexity of the human genome might impose severe constraints on the degree to which it can be engineered at all. "In their current form", he writes, "biological machines [the metaphor is itself questionable] are barely engineerable, yet alone programmable." His answer is that we can simplify genomes to eliminate these quirks. This argument is not without some support. In 2016, researchers at the J Craig Venter Institute in La Jolla, CA, USA, made a "simplified" version of the genome of the bacterium *Mycoplasma mycoides* stripped down to just 473 genes. 2 years later, researchers in New York, NY, USA, fused the 16 chromosomes of yeast into two giant ones without loss of viability. And most impressively, in 2023 an international consortium called the Synthetic Yeast Genome Project announced the total synthesis of all 16 chromosomes of yeast and showed that yeast strains with more than half of the genome made synthetically were still viable. But—this is a caveat that should be kept in mind throughout the book—we now know that French biologist Jacques Monod's famous claim that "what is true for *E coli* is true for the elephant" is not correct in key respects. The molecular rules of the biochemistry of protozoa and even of single-celled eukaryotes are qualitatively different in some important ways from those of metazoa. For example, humans have more protein disorder, more multidomain proteins, more non-coding DNA, different kinds of gene regulation, and multiple cell types. Woolfson is keen to attribute the apparent perversity of human genomic complexity to evolution's indifference to optimisation and willingness to accept jerry-rigged, short-term solutions. There is surely some of that. But to suppose that the human genome can be reorganised and streamlined into a form that we can then rationally engineer is an act of faith. It seems very possible that what looks to us like messiness is in fact a vital aspect of how our genomes work. Woolfson's claim that "If you can program a bacterium, you can program a human" might be too simplistic. A 2026 review of the state of play in "mammalian genome writing" made the magnitude of that task bracingly plain.

> **"More generally, there is something profoundly dispiriting about seeing speculative high-tech solutions proposed in health care when we already know how to solve a huge amount of disease in the world if only there was the political will to address societal deprivation, health inequities, and inadequate access to medicines and health care."**

As for how we will plan phenotypes from genotypes: here I was reminded of the well known cartoon in which a physicist explains his theory to a colleague on the blackboard, which includes a step labelled "Then a miracle occurs". Today that miraculous step is allegedly going to be provided by artificial intelligence (AI). Woolfson accepts that we might never develop an intuitive understanding of our own molecular biology or a theoretical framework that will allow for the prediction of phenotypes. But no matter, because AI will do it for us, as a part of what Woolfson calls artificial biological intelligence (ABI)—the

attainment of which "must become the central objective of the biological sciences". By way of example, he cites "biological foundation models" such as Evo 2, developed by an academic and commercial consortium, which predict the phenotypic consequences of some genetic mutations even in humans. (We can now add Google DeepMind's AlphaGenome to that list.) With such a capability, he suggests, we will become fluent in "the language of life", decode the "generative laws of biology", and be able to dial into a genome and any chosen phenotype. That, Woolfson claims, could be a microbe that synthesises rocket fuel or waterproof fabrics, or a "synthetic emotion that evokes qualitatively new mental states", or a human mind that lacks free will.

Yet Woolfson also acknowledges that, not only do we know very little about "the grammatical rules and design principles governing life's complexity", but also that phenotypes are not after all even wholly encoded in genotypes. He explains that morphologies and traits of organisms arise from what he calls "informiomes": informational inputs of many kinds, including the environment. "Much of the cellular information required for life is not coded at all", he points out. In particular, morphologies are shaped by rules of self-organisation of cells and tissues and governed by collective interactions, materials properties, and other factors. Genes, he rightly says, do not specify these processes but rather, fine-tune them towards specific ends.

This does not in itself preclude genomic design of phenotypes, because if we can understand the rules of those genomic tweaks, we can redirect the outcomes accordingly. But there are many problems with that idea, some of which Woolfson also identifies. For one thing, there is pleiotropy—each gene typically influences many traits—and polygenicity—most traits are influenced by many genes. So traits cannot be specified independently of one another. If we want to engineer one complex phenotype, such as cognition or resistance to neurodegenerative disease, we are sure to be affecting another. We could not be sure what we are making unless we make it.

For this reason, Woolfson wisely says that it is hard to see how making a human with a redesigned wholly synthetic genome "could ever be considered safe, ethical or justifiable". Just so—and there, at a stroke, go many of the science-fictional visions he paints elsewhere of humans engineered for space travel or settlement, or to experience synthetic emotions, or to be immortal.

One goal that seems more achievable and less ethically fraught would be the creation of "designer cells" with specified tasks such as supercharging the immune system. These cells might carry out functions not known in natural systems. Indeed, one of the goals suggested for SynHG is to make therapeutic cells with "hardwired" cell fates, obviating the risk (inherent in some stem-cell therapies) of cells switching to tumourigenic forms. This is an exciting idea. Whole-genome synthesis could also be a useful tool for basic science—for example, allowing researchers to access regions of sequence space not easily reachable with conventional gene-editing technology and helping to investigate the roles of complex non-coding regulatory regions.

When he stays on such solid ground, Woolfson tells an intriguing tale. But he is often tempted towards the more spectacular. He dangles the prospect of "the end of illness"—a rather meaningless notion floated by AI leaders, such as Demis Hassabis of Google DeepMind, as something that might be achievable with AI within a decade—only to admit that genomic complexity will probably preclude it. Of course, a great deal of disease is not fundamentally genetic. More generally, there is something profoundly dispiriting about seeing speculative high-tech solutions proposed in health care when we already know how to solve a huge amount of disease in the world if only there was the political will to address societal deprivation, health inequities, and inadequate access to medicines and health care. Past experience suggests that the more high-tech a solution, the smaller the portion of the health-care burden that can be addressed with it—not only because of cost, but also because there are easier solutions to many common problems that are simply neglected. Woolfson's claim that "If the ultimate goal of clinical medicine is to liberate humankind from disease, then large-scale genomic reprogramming may ultimately be the only way to achieve this" is therefore not only scientifically and societally questionable, but also fundamentally ambiguous—it is not clear what a "disease-free genome" could even mean.

In discussing species de-extinction Woolfson points out that this is not a matter of phenotype but also of ecological context. Species, he rightly says, are not only genetically defined but are "inseparably connected to a series of higher-dimensional informational spaces". Nonetheless, he claims elsewhere that command of the "language of DNA" via ABI will offer us any organism we care to imagine.

On the Future of Species, then, should come with a health warning: danger of whiplash, as the reader is carried from thoughtful analysis of the real complexities of genomics to far-fetched claims about what genome synthesis will make possible. It contains much that is fascinating, enticing, and usefully provocative, but the ultimate vision is an article of faith. I for one do not see it ever being realised, mostly because life just does not work this way.

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Philip Ball's latest book is *How Life Works: A User's Guide to the New Biology* (Picador, 2024).

Further reading

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