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BOOK REVIEW

Just because we can…: a review of Beth Shapiro, Life as we made it: how 50,000 years of human innovation refined- and redefined-nature

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Daniel T. Blumstein[1]

In this wonderfully written book Beth Shapiro makes a strong case for the moral imperative of synthetic biology. Not only will CRISPR-based gene editing tools and other technologies permit us to address climate, food, and biodiversity crises, she argues, but these technologies have the opportunity to save us from pandemic disease. She supports her position with her deep evolutionary view of life – she studies ancient DNA – and is as comfortable mucking (literally!) around the field searching for fossils and subfossils as she is in the laboratory pushing her field forward with new techniques and analyses.

Her argument in a nutshell is that humans have been domesticating animals and plants for at least 50,000 years. Some of this domestication relied on animals becoming tolerant of us and ultimately creating mutualistic relationships, as seen in wolf-to-dog domestication. Others involved us selecting for certain traits that we found useful, as seen with many food plants and in the animals we eat. Yet, such artificial selection, she argues, because it works with existing variation, and hence is in some sense 'natural', is a dull tool. Synthetic biology, however, is a kit filled with sharp tools. We can speed up selection of existing variation within a species using cisgenic manipulations, or we can create genuinely novel transgenic organisms where traits from different lineages are combined. Why are transgenic manipulations required?

She begins outlining a problem I resonate to – anthropogenically driven extinction. The single best seminar I took in graduate school focused on Martin and Klein's (1984) large edited book about extinction where we discussed the cause of rapid extinctions that were seemingly associated with human expansion. Everyone had the same data but people's interpretations about Martin's Pleistocene overkill hypothesis led to stimulating debates. Shapiro updates this nearly 40-year old argument with many

✉ Daniel T. Blumstein
marmots@ucla.edu

[1] Department of Ecology and Evolutionary Biology, University of California Los Angeles, Los Angeles, CA, USA

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new results; some of which were made possible by her (and others') pioneering work using DNA collected from fossils (ancient DNA) to create better timelines of human expansion and species extinctions. Spoiler alert: humans arriving on islands have a terrible record of quickly driving many species extinct, but their effect of moving around continents is a bit less clear cut (ecology is complex!).

From this Shapiro argues that humans have the unique ability now, more than ever in the past, to reverse extinctions. She uses the Public Trust Doctrine (nicely described in Sagarin & Turnipseed 2012) to argue that we are obligated to protect nature for everyone. And, because we're driving so many of the extinctions in our current biodiversity crisis, we are morally responsible through whatever means to do so.

The saga to get where we are today with synthetic biology takes us through incidental domestication to tinkering via selective breeding, hybridization, artificial insemination, embryo transfer, gene guns that insert genes into plants, and now to technologies like CRISPR which can edit single genes in a variety of organisms. Of course there are consequences of such manipulations; we reduce genetic variation in our food and livestock making them susceptible to disease, and maladaptive traits may become common in the population. But, she argues, we can fix these too once we're aware of them.

Yet the application of modern genetic tools is not without controversy and she clearly explains the controversy. She describes the history of the FLAVR SAVR tomato, which was the first successful genetically modified novel food, but failed commercially for other reasons. And she talks about Golden Rice and its ability to increase nutrition to many people who rely on rice as their staple starch. She talks about the ethical quandary of editing human DNA. She asks all the right questions about our ability to bring back mammoths as well as outlining the challenges of doing so (amongst them – the inability with current technology to change about 1 million different genes that separate mammoths from Asian elephants). And she writes clearly about the promise and the peril of gene drives – a promising or terrifying tool (depending on your perspective) that capitalizes on what she calls 'evolutionary villains' to rapidly spread traits that produce sterile individuals which can drive a population to extinction. Synthetic gene drives have the potential to eliminate malaria, zika, and dengue-causing mosquitoes, as well as remove invasive species, such as brush-tailed possums from New Zealand. Their risk is that the genes escape their target area and for species like brush-tailed possums, which are native to Australia, drive an endemic species extinct.

While reading all of this I kept thinking, just because we can doesn't mean we should. I also thought of the remarkable hubris we have to believe that we can control nature. At a party years ago I was talking to a physicist about how people in my field (ecology and evolutionary biology) have physics envy because they can predict things with incredible precision while we're happy if we can explain 20% of the variation in something we study. His response was that physics is easy and the natural world is complex. He was impressed that we even tried to understand such complex systems! A lesson we shouldn't forget. Particularly given the long history of human biocontrol interventions to save wildlife that have failed (cane toads in Australia, stoats and pretty much everything else in New Zealand, mongooses in Hawaii, and many, many more things). This is not to say that all wildlife conservation has been a failure,

but rather that we simply don't know as much as we should about these complex systems, characterized by non-linear responses, and tipping-point dynamics, than we must to properly design interventions. Wisely, Shapiro notes that if we're going to introduce synthetic gene drives, we should simultaneously make kill switches prior to introduction.

I teach an ecological ethics course that debates some of the topics that Shapiro so beautifully discusses. Despondent over the controversies (killing one endangered species to save another, immunocontraception to control exotic and native animals, the ethics of gene drives and other transgenic manipulations, and many other topics) my students come to realize that these are often lose-lose problems that humans created. Many of these problems are driven by habitat loss and over-consumption, which are often related to over-population. Many of these complex problems are driving humanity towards a ghastly future (Bradshaw et al., 2021). It is these bigger problems that have created these lose-lose situations. It is these bigger problems that ultimately must be addressed. Why are we at the point where we're even discussing killing Steller or California sea lions that are eating 13 endangered species of salmonids? What drove the salmonids to this state in the first place? Well, we destroyed their headwaters and breeding grounds. We over-fished them. We polluted their habitat. Addressing these bigger problems is essential to remove the proximate problem which creates the fraught situations we find ourselves in.

To address our biodiversity crisis, I think we need to move beyond sharp tools (however useful they may be in certain proximate situations) and address the hard problems that drove us to open up our toolbox in the first place. I say this as someone who develops dull tools – behavioral interventions to manage human-wildlife conflicts and increase the size of vulnerable populations. I say this as someone who is working to share any tools and approaches with the broadest possible audience, including the genomic tools that Shapiro so ably describes. But I also question the utility of doing so without addressing the root causes of our proximate biodiversity crisis. I struggle with novel creations to save natural species. I struggle with the meaning of natural.

That said, I fully agree with Shapiro when she discusses the achievements and promise of a set of sharp tools to modify plants and animals for our use, and ultimately, to address human disease. I've used the same arguments she uses to defend GMO foods (her explanations are better!) and see that with more efficient production and less food waste we can feed humans and conserve biodiversity. Of course, caution is required before we release novel organisms into the environment. But we have already driven the environmental changes that will require us to change our agricultural practices to grow plants (and animals) that require less water, those that are more heat tolerant, and those that can survive the increasingly variable weather that is the new normal. If we want to feed humanity, we need modern synthetic biology. And, the promise of synthetic biology to help improve health by targeted gene editing seems, to me, to be both morally defensible and, in many situations, very desirable.

Your perspective on these arguments and controversies might be developed or even shifted by reading this excellent book that captures both the excitement of being in the field as well as the laboratory to understand and address not just our biodiversity crisis but our challenges to feed humans in a rapidly changing world. These are important issues for our times and the ethics and policy associated with applying this technology

is actively debated (e.g., Gutmann, 2011). Since these ethical issues are likely to impact many, thus both scientists and non-scientists will benefit from reading and discussing this exciting book.

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