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Gene Drives, Nature, Governance: An Ethnographic Perspective

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Chapter 3

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We are, at long last, learning to speak the language of nature. With sufficient cooperation and humility, we might even use it wisely.

---Smidler, Min, and Esvelt 2016, n.p.

Although evolution has enabled some naturally occurring genes to propagate above their expected frequencies, the recent discovery of CRISPR-Cas9 has enabled geneticists to cause this to happen at exceptionally high rates for chosen genes in the form of "gene drives." By encoding the CRISPR editing system into the DNA of certain organisms, geneticists can make a desired edit reoccur in each generation, driving the trait through the entire population by modifying only a few individuals (Esvelt et al. 2014; Harmon 2016).

Synthetic gene drives hold incredible promise, according to certain scientists at least. It is said that this technology has the potential to wipe out infectious disease vectors such as malaria-bearing mosquitoes, who kill hundreds of thousands of African children and adults each year, and thus to massively impact human health, especially in developing countries. Some have also suggested that gene drives could assist in the conservation of endangered species by eliminating the parasites and invasive predators who threaten their existence, such as in the cases of sylvatic plague for black footed ferrets (Novak, interview) and of invasive rodents on islands (National Academies of Science 2016). Gene drives could, to take another example, suppress the avian malaria-bearing mosquitoes who transfer disease to endangered honeycreepers in the Hawaiian Islands (ibid.). By using targeted modifications within an organism's DNA in order to impact certain populations or even entire species, gene drives could minimize the ecological effects of insecticide and rodenticide use—thus providing what some say are clear advantages for the natural environment.

Alongside what is presented by scientists and the media as incredible promise, the introduction into the wild of individuals containing gene drives involves major risks. “DDT only goes where you spray it, [but] a gene drive will keep going beyond; unless you design it otherwise,” geneticist Andie Smidler told me in an interview we held at the Harvard School of Public Health. Along these lines, a report issued by the expert committee convened by the National Academies of Science, Engineering, and Medicine in June 2016 warns about the “cascade of population dynamics and evolutionary processes” that might be initiated by the introduction of an artificial gene drive into the wild (National Academies of Science 2016). Even with sophisticated computer models and ecological risk assessments, such a cascade of effects would be difficult to predict, according to the report.

Given the intentional design of gene drives to spread like fire and that of impacted organisms to cross jurisdictional borders, the National Academies of Science report cautions that there is currently no effective regulatory mechanism to oversee gene drive research and field trials (ibid.; see also Akbari et al. 2016; Charo and Greely 2015; Oye 2015). As a result, some have pointed out that in the context of genetic engineering, “the implementation of social responsibility in the United States has been left virtually solely to scientists” (Sankar and Cho 2015, 23). It is in this regulatory void that the operating scientist becomes a self-regulator, her values and visions that much more important as they at least partly determine the scope of the research that she will undertake and its normative dimensions. A new scientist-regulator hybrid thus emerges at the center of gene technology governance.

My chapter moves away from the usual discussion of gene drives to consider the emotional and relational landscape of gene drive scientists. Specifically, I draw on in-depth discussions with several gene drive scientists and related experts to explore their personal perceptions of nature and their relationship toward the animals they edit and engineer. Arguably, the underlying relationship of the scientists I have interviewed toward nonhumans and the environment informs, even paves, their research path. Their perceptions about nature in particular provide these scientists with the normative justification to pursue research that would alter not only individual DNA but also entire populations and the ecosystem. This chapter seeks to discover how gene drive scientists think and feel about the impact of their research.

I will begin this ethnographic contemplation with a hands-on description of how gene drives work and a brief account of the ecological implications of this technology. Next, I will discuss the attitude expressed by prominent gene drive engineer Kevin Esvelt toward nature and about the relationship between humans and nonhumans. Finally, I will present my conversations with three biologists who are working on gene drives in mosquitoes about the role of nature and the value of life. I should note at the outset that this is by no means an exhaustive study of gene drive scientists, nor is it necessarily representative of the larger gene editing community. Nonetheless, the discussions below expose some of the major emotional and relational questions and concerns facing contemporary scientists in the nascent field of gene editing and how they conceive of and implement the self-regulation of their research.

The Labor of Gene Drives

The actual work of gene drive scientists didn't hit home until I sat with Andie Smidler. Smidler is a Harvard School of Medicine graduate student working with two prominent scientists, Kevin Esvelt and Flaminia Catteruccia, and an unusually energetic woman. She doesn't have an office, which is why we convened in the kitchen behind Catteruccia's lab at the Harvard School of Public Health. When I complain to Smidler about my inability to wrap my head around gene drives, she readily takes on the challenge. "Everybody has two copies of every gene, one from mom and one from dad," she tells me matter of factly. "These genes are usually very similar, but where they differ is where you get all different types of humans. Dad has a gene for tallness and mom has a gene for shortness, for example." I am able to follow her to this point, but then things get more complicated:

> A cell normally repairs its DNA by searching for the other copy to say, "Hey, I'm broken, I need to fix myself, but that one is still intact, I bet that's the right gene." So [if mom's gene is broken,] dad's gene drive cuts mom's empty DNA and then mom's broken DNA is like, "I need to fix myself." So the cell has a natural DNA repair mechanism. And it uses DNA from the [synthetic] gene drive as the template for repair. And it says, "I'm replicating to fix myself, but oh hey look, this gene drive looks similar enough, I'll copy it over," and it copies it over. So you're born with one copy, and now you have two copies. If this happens in the germline . . . , what you get is biased inheritance. Now that both mom and dad's copies are gene drives, all of their kids are going to get one copy of the gene drive, and then it does the same thing in the kid as it did in the parents. It cuts the other version, copies itself over and it keeps spreading that way. So it artificially gets inherited at a higher frequency than normal. And that's the basic concept behind most of these modern gene drives (ibid.).

The process of designing a stable drive is apparently a more complicated matter altogether. Smidler explains:

> To make an evolutionarily stable drive, you have to put the drive into these really critically sensitive genes in a very specific way. And you have to engineer them so precisely because you have to insert this massive genetic cargo in the middle of this gene that normally can't be disrupted. You design it so that it can survive, but it's very tedious and difficult to do. These are genes that you can't cut in the first place and have the cell survive, but to build our gene drive, not only do we have to cut it, but then we have to do all this crazy genetic engineering stuff, get the cell to live, and then get the product that we want. So it took us the last two and a half years to be able to make the genetic engineering change in that essential gene and get that cell to live. We have it now. We don't have the drive. To build the drive, we have something called a docking line, and basically it's a sequence that you can put on your transgenes (ibid.).

This account affords a glimpse into the on-the-ground trials of gene drive scientists. It is surely the closest I've gotten to comprehending the scientific labor involved in gene drives on the micro scale of the DNA and the immense battles over harnessing life into a digitized and predictable form (see Chapter 9, this volume).

The Ecologies of Gene Drives

Beyond the individual, gene drives could also impact life at the level of populations, species, and ecosystems. Science and technology studies (STS) scholars Javier Lezaun and Natalie Porter refer to gene drives as a "transgenic technology." They explain that "transgenic technologies hope to find in the genome of the pertinent animal species a molecular 'switch' that would short-circuit transmission to humans" (2015, 4). Contrasting this with the One World, One Health (OWOH) approach that attempts to contain the circulation of pathogens among species, Lezaun and Porter caution that genetic modification "promises a kind of directed animal evolution, which would absolve humans from the need to alter their behavior in the service of disease prevention” (ibid., 97). Instead of alertness to the animal-human interrelations prescribed by the OWOH model, transgenic technologies present “entirely new dynamics of intra-species competition,” giving rise to “qualitatively different human-animal ecologies” (ibid., 99; see also Chapter 2, this volume). Along these lines, in his in-depth documentation of the path of dengue fever, mosquitoes, health providers, and poor communities in Nicaragua, STS scholar Alex Nading develops the term “the politics of entanglement.” This term serves Nading to highlight the strife of local communities “to remain alive to the world around them despite global health strategies that seek to insulate them from their environments” (2014, back cover).

The National Academies of Science, Engineering, and Medicine expert committee on gene drives seemed less apprehensive of transgenic technologies generally and of the disentanglements that may occur as a result of their anthropocentric focus in particular. After a yearlong study of six potential sites for gene drive use, the long awaited report, released in June 2016, called for “carefully controlled field trials,” effectively giving experiments outside the lab a green light to proceed. The report nonetheless cautions that “before field testing or environmental release of gene-drive organisms, it is crucial to establish a detailed understanding of the target organism, its relationship with its environment, and potential unintended consequences. It is also essential to consider confinement and containment strategies to reduce the potential for unintended releases” (National Academies of Science 2016, 2). Harvard biologist Flaminia Catteruccia, who is part of the small team developing gene drives for nonhuman species, responded to the report: “If you use a gene that kills the plasmodium parasite in mosquitoes, how will it behave with other pathogens? Will it affect, for instance, insecticide resistance? If you affect dengue, how will that behave with yellow fever or, now, with Zika virus? . . . There are lots of questions to be addressed before we can safely release them" (quoted in Powell 2016). One concern is that the drive could "jump" to other organisms besides the targeted ones (Ledford and Callaway 2015).

Importantly for this chapter's purpose, the National Academies of Science report also briefly considered the broader role of nature and the meaning of human-nonhuman relationships when it adopted the following statement on human values:

> Perspectives on the place of human beings in ecosystems and their larger relationship to nature—and their impact on and manipulation of ecosystems—have an important role in the emerging debate about gene drives. The increased power for human beings to alter wild species and perhaps to eliminate them, thereby altering the shared environment—will be intrinsically objectionable to some people. Proposals to use gene drives in ways that might lead to the extinction of species or significantly alter the environment will require especially careful review (ibid., 18).

Only a couple of months after the report was released, thirty environmental leaders who convened at the 2016 World Conservation Congress issued the following statement: "Given the obvious dangers of irretrievably releasing genocidal genes into the natural world, and the moral implications of taking such action, we call for a halt to all proposals for the use of gene drive technologies, but especially in conservation" (Friends of the Earth 2016). Founding signatories of this statement include Jane Goodall, David Suzuki, and Vandana Shiva.

I would propose that the differences in approach toward the desirability of gene drives and their regulation are caused by divergent foundational approaches toward the meaning and value of nature. Whereas environmental leaders seem to see an inherent and intrinsic value in the "natural world" and its conservation and thus highlight the dangers in gene drive technologies (see Chapter 5), geneticists either do not see the value in conserving existing nature as is, or they do not see this world as natural to begin with. These bifurcated views about nature tend toward either cautionary or interventionist approaches, in turn engendering divergent modalities of governance.

Gene Drives vs. Nature

Kevin Esvelt is a prominent scientist in the gene drive community and much respected within this community for his consistent call for responsible, responsive, open, and transparent science (see, e.g., Chapter 1, this volume). He is strongly influenced by utilitarian thinker Peter Singer and is quite outspoken about his views toward nature. Specifically, Esvelt is quick to assert the immorality of nature, which he sees as "red in tooth and claw," an expression he is particularly fond of. "Existence in the wild is basically unmitigated pain and suffering," Esvelt told me as we were sitting in one of Boston's gardens, observing squirrels and rabbits. "No ethics committee would ever approve the [creation of] organisms [who] live their lives in the wild, [are] eaten alive by parasites, [are] taken out by nasty diseases, and [are] constantly having to evade predators—with horrific suffering when the predator eventually catches you" (interview). Wilderness is immoral and evolution is immoral—or amoral—Esvelt seems to use these two terms interchangeably. He explains: "Darwin probably lost his faith. He didn't quite say it, because it was politically impolite at the time, but he said he could not conceive of how a good creator could have created the [spider wasp], which are the wasps that paralyze their prey, and inject them with eggs that then grow into larvae and eat them from the inside—using no painkiller, of course. Why would you do that? That's not evolutionarily advantageous. So evolution . . . [is] outrageously cruel" (ibid.).

As part of his stance toward nature and evolution, Esvelt is most interested in directing his talents toward "urgently solving the problem of animal suffering and human suffering." "Once we get the ball rolling," he tells me, "then I'll be able to think about changing the cultural perceptions on suffering, and cultural perceptions of nature, and what is defined as pure and good." The romanticization of nature has always bothered him, Esvelt says in our interview. "People who have lived in cities long enough start to romanticize what is out there, because living in a city is bad, of course. Until very recently it was bad—it was disease-ridden, crime-ridden, life expectancy was shorter than in the countryside. [But] now it's flipped." Still, the grass stayed greener on the other side, according to Esvelt. And "that's where this notion of nature being the font of purity and goodness came from. Before that, . . . the notion that you would go camping was insane. Why would you do that? Why would you give up everything that we've worked to achieve?"

Esvelt finally compares the suffering that occurs in nature to lemons, and human progress to lemonade. "I'm very much of the opinion that life is made of lemons and we're slowly making lemonade. I mean, more lemonade than we ever have before. . . . We're better off now than we have been. I think that's pretty much indisputable." He then proceeds to ask rhetorically: "Would I rather exist in a world in which we tweaked things in order to reduce the nasty parasites that lay their eggs in you and those larvae eat you alive from the inside, or one in which we didn't?" The notion that technology makes lemonade out of nature's lemons calls to mind John Locke's views on nature and progress that underlie modern theories of property. The idea that humans improve on nature also feeds into a regulatory approach that valorizes technological progress, with the only relevant concern being the proper allocation of the lemonade, and not the very existence of lemonade and the ever-growing need for more of it.

Alongside his views toward nature, another important aspect of Esvelt's philosophy that arguably impacts his work as a genetic engineer regards the relationship between human and nonhuman animals. Esvelt readily admits to being a speciesist in this context. In his words: "there are lots of different forms that [life] can evolve into, and some particular forms cause more negative net utility to other species than is counterbalanced by the positive utility of them existing." Esvelt has been influenced by Brian Tomasik's philosophy, which contends that even if insects suffer twelve orders of magnitude less than humans, their suffering outweighs ours and every other mammalian life on earth (2015, 139). Nonetheless, because Tomasik believes that the insects' life lacks happiness and is outweighed by the pain of death, he eventually encourages the extinction of such insect populations.

While Esvelt does not agree with Tomasik's mode of counting insects versus humans (in his words: "I don't go that far, and that's partly because I grade things with cognitive complexity to a much greater extent"), he is clearly on board with the utilitarian mode of thinking that determines and distinguishes life's value based on degrees of suffering. When I am slow to follow his calculus of positive, negative, and neutral utility, Esvelt points to a baby bunny that happened to cross the path behind our bench, stating: "That baby bunny probably has it better off than most insects, depending on its current parasite load, and how it dies. It's probably better to be larger and comparatively cognitively sophisticated, in most cases, because you're likely to be longer lived and have a longer youth and positive utility" (Esvelt, interview). Using a similar calculus, Esvelt argues that because humans are the most sophisticated cognitive creatures on earth, our suffering and pleasures balance out in relation to those of insects, despite their incredible quantities. And although he admits that humans have been causing mass extinction to numerous life forms on this planet, he reasons that "if we terraform Mars and seed it with life, that will more than outweigh any of our past sins." While this may sound like a scene from a science fiction movie, the project of populating Mars with life is already in progress at George Church's lab (Davis, interview), where Esvelt conducted his postdoctoral research.

Esvelt's utilitarian philosophy is not limited to living forms, however. "I try not to be too much of a materialist, or a life-ist," he tells me. "What's so special about life, anyway?" he asks, explaining that "in many ways, biological evolution is inferior to the cultural kind, and [to the] technological kind." There are other considerations to life and biodiversity, he continues. "A virus is an interesting information string, but is it more valuable than an idea? An idea is a different form of evolutionary replicator; it's a different form of information. But why is the virus more or less valuable just because it happens to be encoded in DNA, rather than in neurons, or magnetic strips, or ink on paper? There are so many different potential forms of information, and what I'm interested in, literally, is informational patterns and complexity" (for an in-depth analysis of this approach see Chapter 9, this volume). And if life isn't all that special, death is definitely overrated, according to Esvelt. "I am one of those people who sees no particular purpose in death and I would abolish it if I could," he tells me in our interview. "Not because it's so tragic when you're dead, it's just unfortunate for everyone else and you can no longer gather positive experiences." Not only the quality of life, but also the very essence of life and its relationship to its other, death, are newly called into question.

But Esvelt was not always a utilitarian. "I was a radical environmentalist in high school," he admits. "I viewed humanity as extinguishing patterns that nature had created [and] that had their own intrinsic beauty." Generally, the intrinsic value approach to nature is juxtaposed with the instrumental value approach that sees nature as valuable only so far as it is useful for humans (Callicott 1995; see also Chapter 5, this volume). Yet Esvelt tells me that his views had radically changed when he realized, in his early college years, that "if what I really care about is the diverse patterns created by life, then humanity is the one species that's going to get life off this planet and create new forms of life. . . . [T]hat is more important than anything else; it's more important than conservation [on earth]." Esvelt emphasizes: "I've never seen anything particularly spectacular and holy about the fact that most of the universe is barren [and] lifeless rocks, and more hydrogen." "Life is far more interesting. Life evolves," he tells me. "Our overall purpose, insofar as we have one, is to spread interesting patterns throughout the universe." "We have a duty to expand our garden," he continues. "[But] we need to make sure that it is a garden, and not the gladiatorial arena [that wilderness is]" (interview). The scientist thus emerges as the knight whose responsibility it is to govern nature and improve on it. Furthermore, conservation is configured as a marginal concern in comparison to the much broader concern with life as a mode of information and its expansion beyond planet earth.

The Nature of Transparency

Reading and re-reading the long transcripts of our conversations, I find it hard to reconcile Esvelt's all-encompassing utilitarianism and almost-contemptuous attitude toward nature with his call for full transparency in gene drive research and his insistence on democratic decision-making in this regard. In his June 2016 contribution to *Nature*, Esvelt explains that "gene editing can drive science to openness." "Because the consequences of mistakes involving gene-drive organisms could affect communities outside the laboratory," he writes, "scientists have an obligation to openly share their plans, invite suggestions and concerns, disclose experimental results as soon as possible, and redesign the technology as needed. Applied to gene drives, such an approach will also have a greater chance of earning popular support for applications that could save millions of human lives and rescue numerous species from extinction" (ibid.). In Chapter 1 of this volume, Esvelt repeated his concern that if scientists do not govern themselves properly by involving the relevant publics, such publics will lose their trust of these scientists and react by taking away their social and normative license to save the world (page ___, this volume).

Along the same lines, Esvelt is also concerned about the existing regulatory system and, in particular, about the way that patents and publications are managed, which disadvantages open science and punishes those who practice it. In his words: "sadly, open and responsive science flies in the face of current incentives. Scientists who disclose their ideas are often 'rewarded' by being scooped by another lab, rather than by being recognized for their creativity. It is a prisoner's dilemma. The benefits come from cooperation by everyone. But by participating, you risk being exploited by people who steal your idea, get it working before you do, and claim the credit" (Esvelt 2016, 153; see also page __, this volume).

James (Jim) A. Collins is professor of biology at Arizona State University and the co-director of the expert committee that released the National Academies of Sciences, Sciences, Engineering, and Medicine report on gene drives. Collins tells me in our interview that upon the report's release, Esvelt called him to complain that the transparency of research and the importance of biological containment were not emphasized enough and that the public should always have a say about the introduction of gene drive organisms. Collins comments in response: "When he says that residents need to have a say, Kevin's thinking [of] Lyme disease in Martha's Vineyard. But why stop at this island? Who is the relevant public? And what does 'have a say' mean, anyway? Is it a vote? What kind of a vote? How will it all work?" (interview). When assigning a decision to a group of people, one must adhere to their decision, even if it is objectionable, Collins tells me, implying that he is not sure that Esvelt truly endorses this particular aspect of democratic decision-making process. Esvelt responds with his own critique: "I personally believe the current system of do-everything-in-secret-until-submitting-the-product-to-regulators is a pretty terrible system for inspiring public confidence in the governance of technology" (e-mail communication). While everyone seems to agree that the public must be involved, the question is, more precisely, who the public is—and who gets to decide on this question.

Another question that has until now remained at the margins of the discussion is whether the relevant "public" should include nonhumans. "At the Committee, no one really spoke for Nature," Collins admits. "But what would that mean, anyway? I can't imagine how this would work. From the local frogs to the local birds to the mosquitoes themselves—they all have a stake. This is why it's an out-of-bounds question. Anyway, it didn't come up in our statement of task, and with the limited time we had, we needed to stay on task" (Collins, interview). Over two decades ago, French STS scholar Bruno Latour called to initiate a "parliament of things" to take nonhumans into account in democratic decision making (Latour 1993). How to work around human agency and move toward nonhuman actancy has been a topic of much discussion among posthumanists (see, e.g., Kohn 2013) and one that could use a more serious discussion in this context, too.

Another curious aspect of Esvelt's philosophy of governance is his view on patenting gene drives. "I opened this dangerous box, therefore I better make sure it doesn't fall into the wrong hands," Esvelt says in response to my question about why he had applied for a patent on CRISPR gene drives. Yet despite his repeated calls for collaboration rather than competition and for openness in place of secrecy, durin g a gene drive conference I observed in February 2016, Esvelt was reluctant to share the news about his application for a gene drive patent with the gene drive community. When I asked him about this, Esvelt blamed the patent system. In his words: “The primary link between [intellectual property] and openness is that even though the patent system was explicitly set up to encourage disclosure, the current system makes it very hard to openly share your ideas without losing your ability to patent them, and therefore to give them away. We are forced to file provisionally and prophetically, then race to demonstrate that it works within a year when we have to file the real thing” (e-mail communication). As I have mentioned in the introduction, Esvelt has sought to use patents to protect the public from what he conceives as dangerous private interests. Andie Smidler explains: “Kevin [and I] decided to patent the CRISPR gene drive concept because . . . we wanted to . . . make sure that no one could try and turn it into a Monsanto situation, where everyone hates it, it’s loathsome, it’s terrible, it’s mismanaged, [and certain] people are just itching for a profit” (interview). Here, not only does the hybrid role of the scientist-regulator emerge, but the responsible scientist also ends up representing the public interest in place of the incompetent state.

Gene Drives in Mosquitoes

To date, CRISPR gene drives have been used in four different species: yeast, fruit flies, and two different mosquito species (National Academies of Sciences, Engineering, and Medicine 2016, 1). Mosquitoes are by far the most urgently and comprehensively studied species for gene drive applications. Their genetic editing is also probably the most advanced experiment in gene drives. The goal of scientists has been to alleviate human diseases transmitted through mosquitoes, such as malaria, dengue, and Zika. The work of controlling certain mosquito species through genetic editing is not new: the for-profit company Oxitec has already paved the path for genetic work on mosquitoes through its introduction of sterile male mosquito populations. Oxitec has not been using gene drives, which means that they must perform periodical releases, which makes for a better business model than global gene drives (Alphey, personal communication).

Oxitec's "environmentally friendly OX513A male mosquitoes" were introduced in five separate efficacy trials—in Brazil, the Cayman Islands, Panama, and Malaysia—leading to a greater than 90 percent reduction in the local *Aedes aegypti* (disease-borne) populations (Oxitec 2016, 3). Once the "friendly male" mates with the relevant females, the offspring inherit a self-limiting gene and die before becoming functional adults, thereby reducing the size of the wild population. By 2016, over 150 million Oxitec mosquitoes were released in field suppression programs. A built-in fluorescent marker was designed into the engineered mosquitoes in order to track them in the field and the lab (see, e.g., Figure 3.2).

Although the local community in South Florida refused Oxitec's engineered mosquitoes in the recent past, a new debate is currently unfolding about the release of a new type of Oxitec mosquito to Key Haven in order to control the spread of Zika. In August 2016, the FDA found "that the proposed field trial will not have significant impacts on the environment" (FDA 2016). Being the hot potato that it is, the mosquito control board nonetheless decided to defer the final decision to "the people." A referendum held in fall 2016 produced split results: while the voters of Monroe County voted 58 to 42 percent in favor of releasing the genetically modified mosquitoes, the community of Key Haven, where the mosquitoes would be released, opposed the resolution by a 65-35 margin (Mother Jones 2016).

Flaminia Catteruccia is a molecular entomologist who studies mosquito reproduction and conducts research on gene drives at the Harvard School of Public Health. She has been part of the Harvard collaboration on gene drives in mosquitoes that also includes Esvelt, Smidler, and Church. We spoke at her office, and then she showed me her lab, abuzz with thousands of mosquitoes. As with Oxitec's approach, rather than kill the baby mosquitoes, Catteruccia's model is to null the reproductive act, namely: to have sterile males mate with females. Since the females mate only once in their lifetime, such females will not have offspring. Catteruccia's program does not kill any mosquitoes, only limits their reproduction. Catteruccia is proud of her non-lethal method, as she admits to having a special relationship with the mosquitoes she works with. "We originally captured those mosquitoes and then we colonized them and brought them back to the lab," she tells me about the origin of her lab's mosquitoes. "So these are [lab] colony mosquitoes," she continues. "But from time to time, you might want to refresh your colony with a few mosquitoes [from the wild] to make it as field-like as possible" (interview).

"Mosquitoes are the least-liked animals in the world," Catteruccia laments. "People are disgusted by rats, but I think everyone hates mosquitoes." As for her own feelings toward mosquitoes, while she admits that the first time she saw a mosquito under a microscope was scary ("It had big eyes, and was furry, it was a bit like, 'What am I looking at?'"), Catteruccia has since then fallen in love with this organism. "There are 5,000 different mosquito species, but only a handful of them transmit malaria," she says in their defense. "We study them because they are a fascinating organism that transmits a disease that kills. They don't kill, themselves, they just carry these pathogens," she continues. "The whole world would be a very sad place without mosquitoes," she adds. And while "there are not many organisms that feed on a specific and exclusive mosquito diet," eliminating mosquitoes would definitely change the environment, according to Catteruccia. Birds both feed on mosquitoes and determine their migration patterns partly in order to avoid their bites. An elimination of mosquitoes would affect the food chain in the other direction, too, as mosquitoes feed on bacteria, fungi, and algae. But there isn't much concern that mosquitoes will become extinct, Catteruccia assures me. In her words: "we're never going to get rid of mosquitoes. They're going to outlive us. They were on this planet 200 million years ago" (see also Webber et al. 2016).

Catteruccia studies the interactions between male and female mosquitoes, among the females, and between the mosquitoes and the disease-bearing parasite. "So it's a really a complex series of interactions that you study *in vivo*, in the whole organism. And that's what I love about this," she reflects. In her lab, Catteruccia houses thousands of mosquitoes at one time, from which she takes 50 to 100 females and infects them with the malaria parasite to conduct genetic experiments. She explains the multiple layers of physical containment for the infected mosquitoes: "There's a room within a different room, [and] within this room there is a glovebox. And then the [infected mosquitoes] are in cages within the glovebox. So there are four levels of separation from the rest of the population." When she or her staff work on the mosquitoes, they always use gloves, and they always handle the mosquitoes within the cages. "The only way they come out of the cage is when they are dead," Catteruccia assures me. The geographical design of the lab embodies normative codes of confinement and separation (for more about physical and biological containment, see Chapter 4, this volume).

In light of her high appreciation of this animal, how does she feel about killing mosquitoes? I ask. Catteruccia responds:

> I actually had an undergrad student who was doing a practical on mosquitoes. He refused to kill them. And that was the first time that [this] happened to me. Personally, there are some things that I don't like doing to them. And I always apologize when I do it. So I say, "Sorry," and [then] I chop their heads off, for instance. It's true! It's ridiculous, and I never thought about it. But now that you ask me, there is an element that is not 100 percent neutral for me. There is always "I'm killing a living organism," there is a little bit

of that. But, they don't live very long, so there's that element—I killed them [just] a week before they would die anyway. And also, we keep them in captivity and these ones definitely wouldn't [exist without our breeding]. The way we kill them is very fast. Not so much to alleviate suffering, but to make sure they don't fly around. So something that kills them very fast is to decapitate them. With needles. We anesthetize them with carbon dioxide, and then they go to sleep. And then you can kill them. I don't think anyone enjoys it. . . . We do it because we have to. We never discussed this, maybe we should? (interview)

Catteruccia goes on to compare lab work on mosquitoes and mice. She never wanted to work with mice, she admits, mainly because she couldn't deal with killing them. Catteruccia reflects about the regulatory aspect of working with these two animals in the lab: "the research on mice is much more regulated than with mosquitoes. No one asks you to kill mosquitoes humanely. For mice, you have to have certain protocols. I really think it goes hand-in-hand with our knowledge of their nervous system. Mosquitoes are much less sophisticated, so their suffering is more limited." Since they suffer less, it is implied, their life is worth less—yet another aspect of the utilitarian approach so prominent in Esvelt's philosophy and apparently underlying many of his fellow biologists' way of thinking. Another prominent gene drive biologist tells me along these lines: "A lot of biologists have to kill their subject matters; it's something we're accustomed to" (James, interview). Underlying these statements by scientists whose daily research involved nonhuman animals is the assumption that humans are superior to these animals. A second assumption is that humans must kill (certain animals) in order to make (certain humans) live. Thirdly, animals are ranked on a scale that renders some animals more equal than others. The death of certain species is grievable, while others are merely killable

(Braverman 2016). This biopolitical construction of relative worthiness is supported by existing regulations and guidelines, the value ascribed to certain animals is translated into their mode of governance, and vice versa.

Esvelt fills me in on another aspect of the mundane genetic lab work with mosquitoes. He explains that because mosquitos breed in swarms, getting two particular mosquitos to mate is a problem. The way that mosquito scientists get around this is "[to] take the male, lop his head off, then mount him, and [finally] knock out the female and forcibly mate her to the male. So behead the males, use drugs to knock the females unconscious, and forcibly mate the unconscious female to the dead headless male" (interview). Esvelt highlights the necessity of this procedure:

> A couple of times, the mosquito that [we] wanted was a rare male. So out of all these injections, only one male had the right fluorescent signature. You pull its leg off to sequence it, and it's like, "Yes, he's the one, we just need him to mate." And so you do the mating and you hope that she would find him, and he's on his last legs and clearly dying, and [we're] like, "Welp. Okay, I'll pull off the head and find an unconscious female." And that works. So yes, necrophilic rape is a thing that we do to mosquitoes (ibid).

Esvelt emphasizes that "to someone whose moral foundations are primarily based around harm and care—for example, a consequentialist—there is absolutely nothing wrong with this [practice]. The female mosquito is unconscious, will never know what happened, and being equipped with only the nervous system and cognitive capacity of a mosquito, certainly isn't programmed to react negatively in any way even if shown a video of what occurred." "Indeed," he concludes, "the very notion that a mosquito could be traumatized in that way is to anthropomorphize to a rather remarkable—and wholly inaccurate—extent."

Catteruccia strongly disagrees with Esvelt's description of mosquito lab work and is particularly rejecting of the term "necrophilic rape." "I found the term inaccurate and sensationalist," she writes me in an e-mail. "Some mosquitoes don't mate in captivity and the only way to maintain a colony and study them is to induce mating artificially, which is done by removing the male's head and putting the female asleep. The male is still physiologically alive when mating, so the term is at least inaccurate. The female is not stressed by the procedure, and behaves the same, lives as long, and reproduces as well as freely mating females" (e-mail communication).

It is important to note that although her recent career has been focused on conducting genetic research on mosquitoes, Catteruccia nonetheless acknowledges that the genetically tinkering with this organism to address human health issues is not the best solution from a societal point of view. Instead, she admits, it would have been much better to attend to conditions of poverty, inequality, and lack of education that have created such pockets of human vulnerability to mosquitoes in developing countries in the first place. But that seems to be a much harder challenge to address than fixing genes in mosquitoes, Catteruccia laments in our interview.

Place Figure 3.2 here: Adult female mosquitoes (*Anopheles stephensi*), vectors of urban malaria in India, transformed as part of a background experiment for gene drive. Courtesy of Anthony James.

Another molecular entomologist, Anthony James, has been working with gene drives and malaria for quite some time. He first became interested in this work when, as an undeclared undergraduate, he happened to get a job washing dishes at the local drosophila lab. Although he talks about collaborations within the small community of molecular entomologist working on mosquito-borne disease (less than a dozen around the globe, he points out), James is nonetheless convinced that his lab's approach of altering mosquito populations makes much more sense than

Catteruccia's approach of suppressing them. "With the suppression approach they will always come back, so this solution is not sustainable," he explains in our interview.

James also emphasizes that his use of the term sustainability does not carry any ecological meaning. "If I could, I would kill them all, but it is just impractical," he clarifies. Although he doesn't see mosquitoes as charismatic animals, James admits that they are exquisitely beautiful. Still, "would I want to mess with a beautiful tiger that's coming to attack me?" he asks, emphasizing that in his view, what we're dealing with here are dangerous animals. "When a female mosquito is fixated on you, it's either you or her," he tells me. As for how he feels about tinkering with nature, James admits that he grew up with the "back to nature stuff," so he is "quite respectful toward nature." At the same time, since he doesn't perceive the mosquitoes' environment as natural, but rather as human-created, he is not very concerned about tinkering with it. And as for his feelings about our rights, as humans, to engineer the molecular basis of life, James responds by referring me to the same day's headlines about the recent epidemic of lethal yellow fever. "We must respond," he tells me, implying that tinkering by scientists is not only a right but also a duty.

Conclusion

Synthetic gene drives raise ethical, ecological, and legal questions that are so broad and consequential that they can be difficult to grasp. What is clear, however, is that the power to directly alter not just a singular form of life but also the genetics of entire populations and species are currently both under-regulated and under-theorized. In place of state regulations, what seems to be emerging is a form of self-regulation by the gene drive scientists themselves. My chapter has drawn on in-depth interviews with several prominent gene drive scientists to explore their approach toward nature, animals, and the environment. My assumption has been that their approach impacts and regulates the way they work, and this assumption has been confirmed through the more personal stories that each of these scientists has generously shared with me. Although they have not contemplated these issues to the same degree, a few common assumptions about the role of nature and about animal-human relations did emerge from the interviews, most prominently the notion that killing insect populations, modifying their genes, and impacting the planet's ecological systems are justified in order to reduce human suffering and produce novel ecosystems. This is by no means a revelation; it is consistent with how humans have been treating insects, and nature more broadly, for centuries (see Chapter 2, this volume).

Nonetheless, the nuances are what have made this story interesting, and the differences between the scientists I have interviewed have revealed some of these nuances. What makes more sense: to sterilize mosquitoes or to alter their genes? How do scientists feel about, and go about, such killings, and how do they explain it to themselves? And finally: how do gene drive scientists view and regulate their power to genetically impact entire populations and ecosystems? I was struck by the differences I encountered between the biologists and the geneticists among my interviewees. Although my "n," or sample size, is clearly nothing close to statistical, my sense from the in-depth interviews was that as a biologist, Catteruccia holds a more intimate relationship with her animal "subjects," considers their suffering, and is sensitive to the possible conservation impacts of their modification. On the other hand, as a synthetic biologist and genetic engineer, Esvelt's thinking is more abstract and utilitarian. He is willing, happy even, to tinker further. Toward the end of our interview, Catteruccia encapsulated these differences: "These hardcore geneticists are so provocative in a way, and I think and my innate instinct is, 'Whoa, Whoa!' . . . I'm a more of a molecular entomologist. So I study insects, I'm definitely not hardcore like that. These guys are amazing with what they come up with and what they can do, with what they develop. With me, I'm just using those tools to study basic biology" (interview).

A final thought: while the gene drive scientists I've interviewed were all clearly intelligent, creative, and well-meaning, they were at the same time clearly under-educated in all matters ecology related. Their views about nature-human-animal relationships could benefit from some sophistication and historical contextualization. Maybe a workshop about nature with prominent cultural thinkers and ecologists would be a practical policy recommendation for this group of people, who in many respects hold the future of gene drive technology and its governance in their hands.

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