Connecticut Debate Association
February 2, 2019
Daniel Hand High School and New Canaan High School

Resolved: Genetic modification of species in the wild is on balance unethical.

Gene Drives

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For many years now, scientists have been able to alter genes inside microbial, plant, and animal cells to change organisms' traits, creating, for example, plants that produce their own protective insecticides and fish that grow to maturity almost twice as fast as normal. But while it has become practically routine for scientists to genetically alter individual organisms, a new set of advances promises something much more ambitious: the ability to propagate new genetic traits* into entire populations over just a few generations. Rapid, population-wide dissemination of new traits is challenging because in most sexually reproducing species, only half of an individual's offspring will inherit any given version of a gene.

An emerging technology called a "gene drive" could solve this problem by overriding standard molecular mechanisms of inheritance and ensuring that virtually all offspring inherit a newly engineered trait, instead of just half. The prospect of accelerating the pace at which traits spread through a population from generation to generation is enticing. Imagine a few mosquitos, engineered so they can't transmit malaria, passing that trait to every one of their many offspring until, over the course of just a few months, virtually no mosquitos in the area pose a risk of spreading malaria. But gene drives also present risks and ethical quandaries.…

What does gene-drive technology do?

Sexually reproducing individuals typically have two copies of every gene—one inherited from each parent—and only one of those versions is passed on to each offspring. That means if a parent's genome includes version A and version B of a given gene, each version has a 50 percent chance of getting passed along to a given offspring. Put differently, on average, half of one's progeny are likely to end up with version A, and half will inherit version B. Gene drive technology changes those odds, so that a selected gene version has a near-100 percent chance of being passed down to all offspring.

How does a gene drive work?

In effect, it changes one version of a gene—inherited from one parent—into a duplicate of the version inherited from the other parent. As a simple example, now there are two copies of version A and no version B, so the odds of passing A along to any individual offspring double to about 100 percent ("about" because biology is complex and many factors affect outcomes).

To start a gene drive, scientists introduce the desired gene into an organism or edit an existing gene to confer a new trait or to disable an unwanted trait. They also add a specialized set of molecular instructions—the recently developed gene-drive elements—which effectively duplicate that genetic change and ensure that not just half but virtually all offspring inherit it. (These gene-drive elements are themselves passed to offspring along with the altered gene, so the prevalence of that altered gene grows quickly with every generation.)

In a mosquito, for example, this change might block the insect's ability to transmit malaria to people. Within a few generations–which can mean less than six months, since mosquitoes reproduce about every two weeks—a large proportion of mosquitos in a given area might be expected to now carry this new trait.

Results will depend a lot on such things as whether there are geographic or other barriers to the altered insects spreading out or getting diluted. But as an approximation, release of one gene-drive-altered mosquito for every 100 in a wild population would result in nearly all members carrying the gene within 10 generations.

Without a gene drive, the new trait would in most cases remain rare or disappear over time (especially if it offered no particular advantage to the mosquito), diluted in every generation by the far more prevalent, normal, "wild-type" genes found in everyday mosquitos.

In which organisms have scientists experimented with gene drives?

Primarily mosquitoes, fruit flies, and sexually reproducing yeast, whose short generation times make them excellent test subjects for this technique, as well as some studies in mice—in all cases in enclosed, specially protected laboratories to prevent escape. Bacteria and viruses, which reproduce asexually, are not candidates because gene drives work only on sexually reproducing species.

Could gene drives work in people?

In theory, yes. But gene drives have their most notable impact on species with very large numbers of offspring and very short generation times—not decades, as with humans.

What are the potential benefits of gene drives?

By significantly accelerating the propagation of a new trait in a population, gene drives could:

- reduce or eliminate species' ability to spread human diseases, greatly reducing the toll of some longstanding human scourges;
- suppress plant pests that can otherwise decimate agricultural production; and
- help restore disturbed ecologies by weakening invasive species.

So powerful is a gene drive's "finger on the scale" of inheritance, it can even increase the prevalence of genetic traits that evolution would normally cull over time, such as reduced fertility. With gene-drive technology, organisms would persistently pass this trait to virtually all offspring, despite the toll it was taking on them.

Gene drives could help tackle major public health issues without expensive and difficult-to-implement strategies that rely on personal behavior changes and high degrees of compliance, such as taking medications every day, buying and using bednets correctly, or trying to eliminate the countless places where mosquitos breed.

What are the potential risks of gene drives?

Because of the complexity and interconnectedness of the Earth's web of life, seemingly desirable genetic changes in one species may turn out to have unanticipated, disruptive effects on others. Taken together with models suggesting that once a gene drive becomes established in a population it could be difficult or even impossible to stop, that means a gene drive could inadvertently cause long-lasting harm to the environment, the economy, or human health.

Case by case, such risks would need to be balanced against the risk of pursuing less effective strategies or of doing nothing.

There is also a risk of intentional misuse; a gene drive released by terrorists or a rogue state against, say, an agricultural target might cause significant damage and be difficult to counter.

Is there a way to limit, turn off, or reverse a gene drive?

Maybe. Scientists are studying whether:

molecular toolsets could be embedded within altered organisms to limit or even halt the spread of a gene drive to nearby populations outside the desired impact area; or

a new gene drive, using the original unaltered gene, could revert things to normal.

Experiments also suggest that gene-drive efficacy may sometimes naturally dissipate over time, whether scientists want it to or not, through the development of genetic "resistance" within the altered organisms that gradually suppresses the gene-drive elements.

What are some of the ethical questions to consider related to gene drives?

Is it acceptable to start a self-propagating change in the natural ecosystem without having a sure way to stop it or reverse it?

Who gets to decide whether to launch a gene drive given the possibility that impacts could cross political or geographic boundaries, and recognizing that each case may be different?

Should gene drives aim merely to reduce pest species' numbers or their damaging behavior, or in some cases might it be appropriate to engineer a species to extinction?

Has anyone ever released a gene drive into the environment?

No team has reported releasing a gene drive into the environment or is even known to have formally asked permission to do so. Some researchers have proposed approaches for how to conduct such an experiment responsibly and with full transparency, for discussion purposes.

Who has oversight over gene drives?

In the United States, environmental release of gene-altered organisms falls under the shared regulatory jurisdiction the Environmental Protection Agency, the U.S. Department of Agriculture, and the Food and Drug Administration.

Internationally, in December 2016, member nations of the United Nations Convention on Biological Diversity rejected calls by 170 environmental groups to declare a moratorium on the development and release of gene-drive technology and instead released a statement urging caution if gene-drive experiments were to be attempted in the field.

Nearly 200 nations—including all United Nations member states except for the United States—are parties to that Convention.

Gene-drive technology is expected to be on the agenda again when those nations meet in November 2018 in Egypt.

Is gene-drive science ready for testing in the open?

In June 2016, the U.S. National Academies of Sciences, Engineering, and Medicine released a report, “Gene Drives on the Horizon,” prepared by a committee of experts in the natural and social sciences, ethics, and the law. The report referred to the “breathtaking” pace of change in the gene-drive field in recent years as “both encouraging and concerning”, concluded that “There is insufficient evidence available at this time to support the release of gene-drive modified organisms into the environment. However, the potential benefits of gene drives for basic and applied research are significant and justify proceeding with laboratory research and highly controlled field trials.

called for improvements in the ability to model, or predict, the effects of a proposed gene drive, by better understanding such key factors as the affected species’ role in the environment; whether other species would fill a similar ecological niche if the affected species were to disappear; the likely impact on other species that have co-evolved with the affected species; and whether mechanisms of resistance would naturally emerge, which could slow or stop a gene drive, for better or worse.

called for a “precautionary, step-by-step” sequence of contained experiments to gain knowledge about potential benefits and risks, to provide time for public engagement, and to resolve issues of governance, but it does not preclude moving ahead with field tests under some conditions.

*The relationship between “genes” and “traits” is complicated. Some individual genes can result in a trait all by themselves. Other genes may only do so in conjunction with other genes, or with other limits. For simplicity, we limit our discussion here to simple traits that can be programmed with a single gene.

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DRIVING (GENES) WITHOUT (MORAL) BRAKES

Center for Humans and Nature Blog, By: Bruce Jennings

“Can the human mind master what the human mind has made?” —Paul Valéry

Human beings have always been creatures who create in various ways, but at last we stand poised on the threshold of new power to genetically enhance individual human beings and to intervene in the evolutionary shaping of nonhuman species. We can now understand and engineer the structure and function of genomic and cellular activity, and we can bring into existence organisms that have never before been produced by evolution and natural selection. Henceforth, anthropogenic life will share the earth with natural life. The era of human biopower has arrived and has placed unprecedented willful control of the conditions of life in human hands.

Human biopower permeates the material and the living world on a planetary scale and at the molecular level. The planetary effects of biopower—such as biodiversity loss and climate change—have been largely the byproducts of collective economic activity (agriculture, mining, manufacturing, petrochemicals) within which many kinds of technologies, including genetics, play an important role. But the planetary effects of synthetic biology and the new biotechnology are beginning to be felt throughout the economy and will increase over time in what is referred to as the global “bioeconomy.”[1]

Biopower proffers dreams-come-true for some, perhaps nightmares for others. Either way, it raises fundamental ethical, political, and economic questions that cannot be ignored. These questions tax the limits of our understanding of responsible innovation and governance. How they are answered will show whether we have the capacity to use biopower for just ends and to control its use effectively. The jury is still out, and the social cost-benefit balance sheet of past uses of genetic engineering—especially in agriculture—is in the red, in my judgment. Biotechnology is inherently shaped by political and economic forces. Unfortunately, it is not also inherently shaped by ethical constraints, or what we might call “moral brakes.” But it should be, and it can be if our governance is informed by prudence, humility, and an abiding interest in the common good of all life. So far the economics and politics of biotechnology have been markedly deficient in these virtues.

Splicing Life and Driving Evolution

In 2010 a powerful and precise new technique of altering the DNA sequence using a protein called CRISPR-Cas9 was developed making altering genes much easier and less expensive to accomplish than ever before. We have gone from “recombinant-DNA engineering” to “genomic editing.” CRISPR-Cas9 is going viral, one might say, in research laboratories around the world. It will open new doors to many practical applications on plants and nonhuman animals, and in human medicine as well. Editing somatic cells in this way will alter the genetic functioning of an individual organism; editing a germ line cell (an egg or sperm cell) will alter successive generations of offspring who inherit the anthropogenic trait. Somatic gene editing in human beings cannot yet be done safely and ethically, but, in combination with medically assisted reproduction, it offers promise for preventing some terrible diseases and genetically enhancing individuals.[2]

Moreover, a second new development known as “gene drives” is on the horizon. By encoding the CRISPR mechanism and a particular DNA sequence in the reproductive cells of an organism, we could greatly increase the probability that certain traits will in fact be replicated by offspring and continue to be propagated in subsequent generations. Passing a given trait along is normally an even bet. Gene drives greatly increase the natural odds and rig the Roulette wheel of evolution. This technology may be able to drive particular genetic characteristics through the genotypes and phenotypes of an entire species within a few generations, which is a very short time for some species, such as insects. It can also be a platform for deliberate extirpation of an entire species by altering its sexual balance (e.g. by ensuring that male offspring are sterile), resulting eventually in severe population decline. Gene editing, although not yet involving gene drives, is being used today to similar effect with Ades aegypti mosquitoes that carry Zika and other pathogenic viruses.

Gene editing to avoid a defect in a given individual may be acceptable if doing so is safe and effective, but editing to change the genetic make-up of a person’s progeny (germ line engineering) in human beings has been strictly off limits. Indeed, it is one of the clearest examples of a principled ethical brake pedal in the domain of biotechnology. The use of gene drives to reshape the traits and evolution of human populations is not in the cards. On the other hand, gene editing in nonhuman beings is well underway today, and potentially, gene drives will also be used to alter the evolutionary traits of plants and animals in the future. Indeed, the nonhuman environmental uses are being promoted and welcomed around the world with open arms. One scientist was quoted by the New York Times as saying, “We are going to see a stream of edited animals coming through because it’s so easy.”[3]

Because it is so easy? Being driven by what’s easy is driving without moral brakes.

Gene editing and gene drives clearly raise important questions about moral imagination and responsibility—about precautionary government regulation of scientific research and about commercial technological applications that present great uncertainty and pose potentially severe, irreversible risks to health and to the environment. These are not unimportant questions. However, I suggest that underlying precautionary governance and responsible innovation is a yet more fundamental question: With nonhuman beings, can we ever resist the so-called “technological imperative” by saying no to a technique for engineering life that actually works? And can we ever resist the anthropocentric imperative by saying no to engineering life that actually serves human interests or desires but carries with it deleterious effects for nonhuman species and for ecosystems? In other words, do we still have ecological moral brakes, and are we still capable of stepping on them in the age of biopower?

An Ecological Conscience

How do we know when to step on the moral brakes? Here is one rule of thumb: Do so whenever we are tempted by the technological imperative and the anthropocentric imperative to deny moral considerability to nonhuman beings and to see our species as apart from and above the “rest” of nature. We should speed up or slow down depending on the effect that technological innovations have on the health and integrity of webs of life and on the species-being of individual forms of life within that web. Integrity here has to do with the sustainability, resilience, and capacity for self-renewal of systems that have been shaped by a long process of evolutionary adaptation. This rule of thumb illustrates what can be called an ecological conscience. This conscience, these moral brakes, is not starry-eyed at all, but can be put into practice. I regard it as in keeping with a broad-based consensus in the conservation community today, which is reflected, albeit not perfectly, in the “Aichi Biodiversity Targets” adopted in 2010 by the Convention on Biodiversity.[4]

In order to think with an ecological conscience and to drive genes with moral brakes, we need to think seriously about the ethical significance the natural evolutionary process may have in and of itself. We also must consider the value that emerging from it confers on all species, particularly those pestiferous ones that only moral brakes and conscience will make humans tolerate and accommodate.

Beyond natural consequences, there are also cultural consequences to consider. An ecological conscience will ask whether a given technology enables or impedes our ability to see ourselves as engaged in interdependent, ecosystemic transactions with the biophysical world, where we are responsible citizens or members, not lords and masters. It is a mistake to leave the possible impact of a given technology on cultural meaning and moral learning out of the conversation. If science defines what authentic knowledge is, technology defines what legitimate human agency entails. Together they claim to provide humankind with value-neutral means, but in fact they valorize particular ends of knowing and acting, while marginalizing others.[5]

Driving in Low Gear

Although quite prepared to apply the moral brakes to the new biotechnology of gene drives and to the biopower genomic editing confers, an ecological conscience, as I understand it, will not necessarily tell us to come to a complete stop in all contexts. Sometimes it is ethically enough to slow down and look both ways. Neither the technological imperative nor the anthropocentric imperative adequately justifies these technologies. However, appeal to the health and integrity of the web of life, now threatened on the planetary scale, may provide strong ethical arguments in favor of putting molecular genome technologies to work in the service of conservation. If governed and deployed with prudence and humility—large ifs—gene drives can and should be used to achieve ecosystemic and conservation outcomes that support biodiversity, integrity, and resilient functioning. Our species is running out of time to redeem itself for the destruction it has wrought on the Earth in the last century. Biopower—rightly understood and used—can be a part of that redemption. But two things are for sure: we will be sorely tempted to go too far, too fast; and driving genes safely and justly won't be so easy.

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DRIVING GENES ON A SLIPPERY SLOPE

Center for Humans and Nature, By: Curt Meine·

In some ways, it has been a classic October in southwestern Wisconsin. Wooded hillsides have turned red and yellow and orange. Pumpkins have migrated from fields to front porches and storefronts. Slow-moving combines and tractors block impatient cars as the corn harvest proceeds.

In other ways, it's an unusual fall. The average temperature for the state of Wisconsin as a whole this year is running almost five degrees above normal. It's November 2 and so far there have been only a couple light frosts—so light that my garden beans and even some tomatoes are still producing. We are some three weeks past the average first frost date. The long-range forecast, stretching into mid-November, shows nothing close to freezing. In our locale, we also had an unusually rainy and humid summer, with several extreme episodes of rain.

Climate scientists are accustomed to cautioning that any given stretch of atypical weather does not a climate change signal make. However, we are all increasingly sensitive to possible signals where we might have heard only noise before.

In this year of heat, rain, and humidity, the sound of abnormality has been quite literal: the buzzing of mosquitoes. At my place—a rural setting along the Wisconsin River—we have had bad mosquito seasons before, but I do not recall one so long-lasting. Even as I type these words, a mosquito flits along the screen in the window next to my desk. On November 2. In Wisconsin. This is weird—and consistent with global weirding.[1]

Several weeks ago I was walking one late afternoon with friends in a nearby field. The long rays of sunlight illuminated squadrons of dragonflies cruising over the tall grasses, busily providing free ecosystem services. The dragonflies, hundreds of them in all directions, were gorging themselves on the abundant mosquitoes. In some parts of the South, dragonflies are called "mosquito hawks." Amid the frenzy, one could almost see the graph of their matched population growth curves: the outbreak of mosquitoes closely synchronized with the dragonfly hatch. Such dragonfly-on-mosquito predation occurs not only among the adults, but among their respective larvae as well.

Mosquitoes have also been abundant in the news recently, headlined as carriers of the Zika virus. Debates are being waged over the potential uses, risks and benefits, and ethical implications of emerging technologies in synthetic biology to control and even eliminate mosquito populations. In particular, the development of the gene-editing tool CRISPR-Cas9, has opened up new possibilities for rapidly driving genetic modifications through populations of plants and animals, enabling us to alter the genomes—and hence to intentionally redirect the evolutionary pathways—of entire species.

Proposals are now being developed to deploy CRISPR technologies in response to the spread of Zika. Those headlines are provocative: "We Have the Technology to Destroy All Zika Mosquitoes"[2]; "Mosquitoes Are Deadly, So Why Not Kill Them All?".[3] Work on CRISPR techniques is advancing quickly, and debate over its applications is ramping up. In June, the National Academy of Sciences released its report Gene Drives on the Horizon.[4] The report states that "the potential of gene drives for basic and applied research are significant and justify proceeding with laboratory research and highly-controlled field trials." Committee co-chair James Collins noted that "a lot more research is needed to understand the scientific, ethical, regulatory, and social consequences of releasing such organisms," while the committee's report advocated strongly for full public engagement in making any proposals to deploy the new technologies. In September the World Conservation Union (IUCN) adopted a motion at its quadrennial congress recommending that the IUCN fully assess the impact of the new technology and "[refrain] from supporting or endorsing research, including field trials, into the use of gene drives for conservation or other purposes until this assessment has been undertaken."[5]

As the debate swirls, I see the field teeming with dragonflies—a reminder of the ongoing ecological and evolutionary processes that provide population checks-and-balances in the invertebrate world. Dragonfly predation can play a role in providing biocontrol of mosquitoes.[6, 7] That said, in a biosphere where humans are driving extensive, rapid, and accelerating changes, dragonflies are unlikely to come to the rescue. We ought not to expect that they can kick in ecologically, like the seagulls miraculously saving the Mormons' crops from the insect hordes, or the indigenous Earthly microbes that ultimately brought down H. G. Wells' invading Martians. But the dragonflies do remind us that, in all our actual and imagined interventions, we are always dealing not simply with species, but complex systems.

Gene drives do offer the promise of finer-grained and precisely targeted interventions—a more direct silver bullet, as it were. But we soon find ourselves on a classic slippery slope. Once a species is targeted or a situation identified for gene-drive-enhanced intervention, when do (or can) we stop? In the case of Zika and mosquitoes, the case and the reasoning is relatively straightforward: apply the new gene drive technology to address an imminent threat to human health. Yet, even if the technique works as prescribed and intended, questions arise. How quickly will new populations of Zika-carrying mosquitoes arrive to fill the void created by the eradicated population? How many times will the application of the technology be required? How will climate change affect the future incidence and spread of Zika (and other emerging mosquito-borne diseases) in the locale? In the region? Globally?

Take another case: the proposed release of gene-drive-altered mice to control the spread of Lyme disease on Nantucket Island. "Nantucket boasts some of the highest Lyme infection rates in the country, and the idea… would involve modifying the genes of tens of thousands of mice to keep them from spreading the Lyme bacterium to ticks, which in turn infect people."[8] If approved, this would constitute the first release of animals modified with CRISPR technology with the intent of altering the genome of the target species. At this inflection point on the slippery slope, the caution signs are more evident, and more questions again arise. Will treating one particular vector break the ecological chain that results in the high incidence of Lyme disease? Will we need to modify the genomes of other mammals that contribute to the prevalence of Lyme? What of the other landscape factors—high white-tailed deer populations, changing forest cover and composition, disrupted fire regimes, the presence of tick predators—that affect Lyme? If the mouse species becomes a vector for another communicable disease, will we alter its genetic makeup again?

Or take another case, involving the application of gene drives to biodiversity conservation efforts. Among the most prominent interventions being proposed is the use of gene drives in Hawaii to eradicate the mosquitoes that carry avian malaria, a main factor in the demise of Hawaii's native honeycreepers and other threatened songbirds.[9] Mosquitoes are a recent arrival to the Hawaiian chain, and the intervention would in fact be a response to an already highly altered ecological condition, with the aim of enhancing elements of native biodiversity. Even the most risk-averse conservation biologists are likely to give some deeper consideration to this application of the technology.

Anne and Paul Ehrlich famously compared the loss of species to the careless popping of rivets on an airplane.[10] Now, in cases such as mosquitos and the Zika virus, we face the possibility of deliberate rivet removal, weighing a human health risk against a conservation risk. With the Nantucket mice, we are proposing to enhance public health by replacing one rivet with a new-and-improved one. In Hawaii—to stretch the metaphor a bit more—we are considering the possible conserving of some rivets through the removal of other rivets that have been inadvertently drilled into the fuselage.

Such human health and conservation applications of gene drives only invite yet more questions about the profile and contours of the slippery slope we face. Where do we draw the line between an imminent health risk or clear conservation threat, and a mere annoyance? Why not eradicate all human-biting mosquitoes on the basis that… they bite humans? What is the line between a real threat and discomfort? Why not eradicate any species that inconveniences us in any way? Why not eliminate all bees that sting, all flies that buzz, all the serpents from our gardens? If and when such technologies become inexpensive and readily available, will a profit-driven marketplace seek to relieve any and all of our irritations, maximizing our individual self-interests, dismissing ecological concerns, and externalizing costs all along the way? When, in some future hot and wet summer, the mosquitoes are gene-driven from my back yard, will I be grateful for the effective (if limited) climate-change fix? Or will I miss the darting dragonflies, flashing in the sun?

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CHALLENGING EVOLUTION?

Center for Humans and Nature, By: Gregory E. Kaebnick·

We have long had the ability, we humans, to work outside the bounds of evolution. Dairy cattle, maize, and all sorts of dog breeds attest to that. It is unlikely that natural evolution alone would have produced these things. They depended on human intervention. However, in the past, the scope of human intervention was rather limited. The newly emerging tools for genome editing are widely thought to mark a significant advance in our ability to get what we want out of nature. We seem to be challenging evolution head on, maybe trying to render it obsolete. For those environmentalists or conservationists who want to limit the human alteration of nature, the challenge to evolution posed by genome editing looks like an awful new threat and raises telling questions. What should be the proper relationship between humans and the biological evolution of life on Earth? From the standpoint of care and concern for the natural world, a desire to protect nature from human encroachment, how should we think about gene editing technologies?

These questions are sharpened a bit more by the recent discovery of "gene drive" systems—genetic phenomena that are transmitted from an organism to its progeny at rates greater than would be predicted by normal inheritance patterns. Normally, a gene is inherited by 50 percent of an organism's offspring. A gene that is part of a gene drive system will be passed along at higher rates, perhaps much higher rates, and so "driven" through the organism's descendants.[1] Gene drive systems occur naturally but can also be created in the laboratory. As described by a report released in June by the National Academy of Sciences, artificial gene drive systems could be used to edit not just individual organisms, but whole populations, even entire species.[2]

The bottom line in the NAS report is that no artificial gene drives are ready for environmental release and that much work would be necessary before any were, but that they might prove to be very useful tools, and therefore that the work—which includes basic science, risk assessment, public discussion, and governance—is worth doing. We (meaning scientists, funders, oversight agencies, and the public) should go case by case; some proposed uses (maybe many or most) will turn out to be unacceptable, but some might make sense.

That claim, that gene drives might turn out to be bad or good, also depends on how we think about the proper relationship between humans and the biological evolution of life.

The sense in which gene editing and gene drives seems to change the relationship between humans and evolution is easy to see intuitively. When we breed exotic rose cultivars, for example, there's a sense in which we are working with evolutionary processes at the same time that we may be trying to overcome evolutionary constraints. We can think of ourselves as engaged in what Michael Pollan calls a "conversation" with nature—an ongoing exchange in which nature, through the sexual recombination and random mutation of genes, suggests new genetic possibilities and humans respond to nature by selecting the possibilities they like. And it's not always obvious who's in charge: sometimes, whether humans are creating the creature or the creature is evolving to exploit a niche is not even clear. The emergence of dogs from wolves attests to this complexity; possibly humans deliberately bred dogs from wolves, or possibly some wolves gradually developed traits that allowed them to live alongside—and essentially live off—humans.

Technologies for genetically modifying organisms arguably look more like command-and-control than conversation. They don't depend on evolutionary processes to generate new genetic possibilities. They let scientists create and arrange genes themselves, and they allow for a wider range of genetic possibilities as well—mustard plants that glow faintly in the dark, for example.

Artificial gene drive systems take the command-and-control metaphor even further. They could overcome the familiar Mendelian patterns of inheritance, they could let us modify populations. They might allow us to alter populations in ways that are harmful to the organism, appearing thereby to overcome the evolutionary principle of the survival of the fittest. In fact, it is possible that gene drive systems could be designed to eliminate a species altogether. A drive that caused all offspring to be males might lead to a population collapse and eventual extinction, for example. And because gene drive systems spread themselves, they would let us try this power in the wild. A genetic change that is not driven would survive and spread in the wild only if it conferred a benefit, as in the case of American Chestnut Trees that are altered to withstand chestnut blight.

To be sure, the power has limits. Gene drive systems will not work in most organisms (all micro-organisms and any plants that are self-pollinating) and would be ineffectual in many others (including anything with a slow reproductive cycle and anything that has reproductively isolated subpopulations). Gene drive systems would sometimes fail. This could happen if, for example, the drive harms the organism but does not work in a part of the organism's population; that subpopulation would likely outcompete the portion that has been altered with the drive. Still, the basic point is rather shocking from an environmentalist's perspective: gene drives hold out the prospect of altering species in a way we have not been able to do before.

So is this good or bad? How should someone who cherishes nature think about gene drives?

To begin with, we should recognize that the challenge is not as great as it may seem. Evolutionary processes would hardly be nullified by gene drives. A gene drive that failed to penetrate a population and got squeezed out of existence would be an example of the organism evolving resistance to the drive. A drive that succeeds, on the other hand, must also still be subject to evolutionary pressures. The fact that gene drives occur in nature makes it plain that gene drives are simply part of the overall biological buzz and whir that evolution acts upon.

What we decide about gene drives will depend partly on how environmental goals are balanced against other goals, especially public health goals. There's a possibility that gene drives could be used to prevent mosquitoes from transmitting the parasite that causes malaria, which kills around half a million people each year—mostly children, mostly in low- and middle-income countries. Other contemplated uses might take aim at dengue fever, chikungunya, and Zika.

The answer also depends on what it is in the human relationship to nature that we want, as environmentalists, to protect. If challenging evolution looks like an unacceptable human incursion into nature, maybe that's because we think natural genomes deserve special protection. Science has to some extent taught us to think of genomes as morally special. We sometimes hear, for example, that genes are "the book of life"—the record of a master plan of sorts that makes organisms what they are. If we value the living world around us, then such "book of life" language may lead us to think of genomes as the ultimate location of the value of the living world. Genomes may then become sacred.

But we might also take a more systemic view. We might hold, that is, that genomes are particularly important parts of organismal systems, and that organisms are important parts of ecosystems, and that it is the larger systems and patterns that we want to protect. If we take that view, then we should be careful with any proposed alterations to genomes but should not foreclose such alterations right from the start—not, at least, if the alterations can achieve larger environmental aims.

And, perhaps surprisingly, environmental protection and restoration is one of the goals that gene drives could serve. One use described in the NAS report is to prevent avian malaria in Hawaii. Neither avian malaria nor the species of mosquito that transmits it is native to Hawaii, and native birds, with little to no immunity to malaria, have been in severe decline. Island-wide spraying of insecticides is out of the question. Vaccinating the birds is not possible. A gene drive technique--either preventing the mosquito from transmitting malaria or simply eliminating the mosquito—might be the only feasible solution.

Another example is a gene drive system to eliminate mice or rats that have become invasive on other Pacific islands. Here, too, native birds are severely threatened. The usual way to control the rodents requires the placement of traps or poisons around the island, but that's often invasive, expensive, and painful to the rodents, and it may kill other animals who should be saved while failing to control the rodents anyway. Again, a gene drive might be the only feasible solution.

Careful study of the drive, the target animal, and the affected ecosystem would be needed to know for sure. There are many questions to be answered: Has the animal, even though invasive, become environmentally important? Would the effect be limited to the local population, or would it jump to places where the animal is native? Could the drive have unwanted effects in the organism? Could it jump to other organisms, and with what effects?

Releasing a gene drive into the environment without studying these questions could have awful results even if the goals were admirable. For that matter, a release could be awful precisely because the goals were awful. Big public health and environmental goals could give way to more trivial interests. In principle, people might use gene drives to modify or eliminate organisms merely to remove nuisances. But to turn our attention to the goals and results is to recognize that the issue is not the genetic intervention itself, but what we do with it. Given the possible uses, we should regard gene drives both with alert concern and cautious hope.

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FUTURE GENERATIONS AND GENE DRIVES: THE IMPORTANCE OF INTERGENERATIONAL EQUITY

Center for Humans and Nature, By: Jennifer Kuzma·

The Problem

A few years ago, I was preparing a slide presentation at home with my oldest daughter sitting next to me. As an artist, writer, and musician, she has little interest in what I do for a living. Yet that day she looked over my shoulder, saw my title slide, and asked, "What is synthetic biology?" After my initial shock that it should interest her at all, I tried to explain synthetic biology to her in the most neutral and balanced way possible. I said something about how synthetic biology involved the design and construction of new biological parts and systems, (sometimes living systems), or the redesign of existing living or non-living biological systems for useful purposes, such as energy, clean water, food, or chemical production. She replied "Yuck, why would anyone want to do that?"

Her immediate and strong reaction surprised me. After all, her generation lives on hi-tech and social media, and she inhabits a highly managed suburban ecosystem. The artificial world is "natural" to her. Exposure to "untouched" nature has been limited to occasional excursions to National Parks and even rarer camping trips. Our family is not outdoorsy or all-organic, and many a genetically-engineered food can be found in our household at any given time. Why then did she intuitively reject synthetic biology and the human desire to alter living organisms? Do most kids feel this way? Do children have an innate sense that the "natural" world, untouched by human interference, has the greatest value? I searched for national polls or discussions with youth about emerging applications of genetic engineering and could find none. Although my daughter's generation will inherit the consequences of today's deployment of new genetic engineering technologies, no one seems to be asking them what they desire of their future world.

The Technology

Today's genetic engineering methods are allowing scientists to insert genes into organisms that have the potential to spread themselves throughout natural populations. These are called gene drive systems. Gene drive systems are based on gene editing proteins and cellular repair machinery. They can be designed to cut an essential target gene in the organism and deactivate it, so that the population dies off, or they can be used to carry extra "cargo" genes into populations to confer desirable traits.

To date, most genetically engineered organisms (GEOs) released into natural or agricultural environments are not expected to spread over time because they are usually less fit than native populations. Also, regulatory systems have stressed the need for plans to contain GEOs to certain areas like field trials, food production systems, or geographic regions that have given approval for their release. Yet GEOs with gene drive systems are designed to do the opposite, to spread and mate with wild relatives in order to drive their genes into the native population.

Specific purposes of gene drives are limited only by the traits that can be inactivated, replaced, or introduced. Proposed applications for deploying gene drives into the environment include: eradicating insect populations that carry human disease; enhancing agricultural safety and sustainability; protecting threatened species, and controlling invasive species.

So far, governance of gene drive systems has focused on questions of ecological risk and benefit. For example, for gene drives designed to eliminate pest populations, how would the disappearance of a species affect ecosystem functioning or services? Could other more harmful species fill the ecological niches of the eradicated organisms, perhaps ones spreading even more detrimental human, agricultural, or ecological disease? What is the potential for horizontal gene transfer of the gene drive system into other species like predators, and would the impacts be harmful to these populations? Although ecological risk assessment should be a key part of decisions whether to release a gene drive (and indeed most regulatory policies are based on risk-benefit estimations), there has been a push for a broader framing of issues that should be considered in decision making about gene drives. The eradication of wild pigs in Hawaii using population suppression (by conventional techniques, not gene drives) illustrates the importance of broader assessments. Feral pig eradication is desirable to reduce ecological damage to indigenous species, but Native Hawaiian communities and others who rely on the pigs for cultural events and food are opposed to it. Values of ecosystem protection and cultural preservation appear in conflict. In some cases, hunters have formed alliances with Native Hawaiian cultural groups against such efforts, and the controversy over pig eradication continues today.

Intergenerational Equity

Although discussion of some of the societal issues for gene drives has begun in the scientific literature, the media, and among key scientific and policy organizations, consideration of the potential consequences of gene drives for future generations has been virtually absent.[1] Work on intergenerational justice and obligations is not well developed in the field of ethics. Some proposed principles of intergenerational equity (IE) would require that the well-being and desires of future generations be taken into account when making decisions. This is based on the premise that all generations are partners in ensuring human survivability and well-being. Because the goals and objectives of society extend beyond the current generation and cannot often be achieved in the present, each generation is morally obligated to support human continuity by protecting resources essential for life to ensure the dignity and well-being of Earth's current and future inhabitants. Present generations are indebted to past ones for the resources that ensure their well-being and hold these resources in trust for the next generation.

Although intergenerational equity has been a prominent concern in international policy making in areas of climate change and sustainability, it is seldom discussed in the context of genetic engineering of species destined for environmental deployment.[2] Questions associated with IE include: (1) How would the deployment of gene drives likely affect the ability of future generations to use the natural world to ensure global health and well-being? (2) How would the deployment affect the ability of future generations to apply their own values to enjoy or appreciate the natural world? (3) How reversible is the deployment so that future generations could apply their own values to restore their options for use or nonuse decisions?

Three generations of hands stacked on one another

Ecosystems are complex and sensitive. Unintended effects could accompany the engineering of species with gene drives in the wild. For example, a more dangerous pest might fill a niche left vacant by a population suppression gene drive, or beneficial predators might be harmed from eating prey with killer-gene drives. Although researchers are working on systems to recall gene drives, certain effects could be irreversible, and others unpredictable. Thus, humanity's ability to alter populations within ecosystems through genetic engineering raises issues associated with biodiversity and conservation that, in turn, may affect the abilities of current and future generations to use and enjoy the benefits of the natural world. Furthermore, there are important IE issues to consider from a non-use standpoint. Visions of the natural world may change over generations, and the attitudes of future generations toward having permanently engineered populations in their natural world need to be considered. Will future inhabitants of the planet view these species as wild ones? Will they cease to enjoy their surroundings if they know that the species are genetically altered or manipulated by humans?

Principles of IE should be incorporated into contemporary decision-making about whether, when, and how to deploy gene drives. The range of ethical issues will vary according to what the gene drive is designed to achieve in the organism, such as whether it will: (1) immunize a population against a health hazard or the ability to carry it; (2) decrease the organism's fitness to suppress the population; (3) enhance or protect the population itself against threats; or (4) make the population newly susceptible to chemical or biological agent. IE issues will also differ according to broad purpose categories of improving agricultural production, protecting human health, controlling invasive species, or preserving endangered species.[3]

For example, applications of gene drives to human disease eradication and agricultural production primarily benefit the current generation with secondary benefits and potential risks to future generations. In these cases, the irreversibility and uncertainty surrounding the deployment may not be acceptable from the standpoints of conserving options, access, and quality associated with the environment. Perhaps in these cases, we should proceed cautiously and deploy gene drives only if uncertainties can be reduced and only with public dialogue to envision the concerns of subsequent generations. In contrast, there seems to be more latitude—and perhaps even an ethical imperative—to develop gene drive technologies for protecting threatened species, perhaps through a disease immunization approach. In this category, irreversibility and greater uncertainty might be tolerated in order to conserve the natural and cultural world for future generations, especially if alternatives to protect the species are not viable.

Next Steps

With increasing proposals for the use of genetic engineering in the wild, there is a strong argument to be made for consulting with the generations that are to inherit the world altered through this technology. A simple, first step to considering intergenerational equity issues in decision making could be a national effort to consult the next generation and report their concerns and hopes for gene drives back to policy makers.[4] The idea of "nature" and human relationships with it are shifting, and today's youth are most likely to experience the changes we make today. Yet they are left out, and their voices are not heard by policy makers. As adults working in this area, we can at least provide opportunities for youth to discuss their hopes, concerns, and attitudes about next generation genetic engineering including gene drives, while we encourage policy makers to adopt a long-term perspective for other future generations.

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