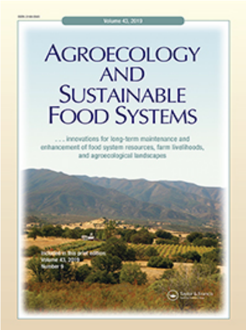


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# Gene driving the farm: who decides, who owns, and who benefits?

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# Gene driving the farm: who decides, who owns, and who benefits?

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**ABSTRACT**
Since the mid-1990s, the emphasis of genetic engineering in agriculture has been squarely on the crops and livestock that farmers long ago domesticated and now cultivate. With CRISPR-Cas9, the modification of seeds and breeds continues apace – but the technology has also cracked open something new. Gene drives, newly enabled by CRISPR, have brought an unprecedented possibility to propel mutations through populations in the wild. With gene drive has come the promise not just of modifying seeds but of reshaping weeds, insects, and many other organisms comprising the larger-farm ecosystem. This commentary essay explores the social and ecological implications of gene-driving agriculture. What does it mean for biologically diversified agriculture? For IP rights over wider spheres of knowledge and nature? What are the limits of knowledge to predict outcomes in complex agroecosystems, and who gets to decide what gene drives will do?

**KEYWORDS**
Gene drive; CRISPR-Cas9; agroecology; knowledge diversity; risk

Roughly 6 million metric tons of herbicides, insecticides, and fungicides are sprayed onto the global landscape each year (Bernhardt, Rosi, and Gessner 2017). Mounting recognition that chemical-based farming contributes substantially to this figure – polluting waterways, damaging farmworker health, and building up in the tissues of organisms from humans to tadpoles – is forcing a reckoning to try something different. Now, a technology known as gene drive holds the potential to eradicate crop pests without the use of chemicals (NAS 2016). It could be used to suppress troublesome fungi, nematode, and rodent populations, and to control pernicious weeds. Certain types of drives, scientists say, might even improve the sustainability and safety of pesticides and herbicides. With such prospects being floated, one expects that boosters of organic and diversified agriculture would listen up, and possibly, cheer.

But in mid-October 2018, more than 200 farmer, peasant, and civil society organizations around the world published a sign-on letter calling for a moratorium on gene drive technology (ETC 2018a). Endorsed by the

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International Federation of Organic Agriculture Movements (IFOAM), the International Union representing Food and Farmworkers, the African Food Sovereignty Alliance, and La Vía Campesina, among others, the letter called on governments to establish participatory technology assessment processes "and to respect and fulfill the full free, prior and informed consent of Indigenous Peoples and other affected populations for all emerging biotechnologies, including gene drives."

The letter was also supported by no less than three former and current UN Special Rapporteurs on the Right to Food, including Olivier De Schutter, who said in a news release accompanying the letter, "Applying gene drives to food systems threatens to harm farmers' rights and the rights of peasants as enshrined in international treaties" (ETC 2018b). Gene drives, De Schutter argued, "would undermine the realization of human rights including the right to healthy, ecologically-produced and culturally appropriate food and nutrition."

Likened by its creators to "sculpting evolution" and by its detractors to "reckless driving," gene drive technology is sparking considerable attention – and considerable debate.[1] Though no drives have yet been released into nature, let alone farming systems, evidence from patent filings and biotech investments suggest they soon will. Meanwhile, the funding of gene drive research is raising questions about whose priorities are behind the wheel.

Scientists, farmers, and social movements flank various sides of these contestations. While some researchers argue that drives could benefit agriculture by reversing pesticide and herbicide resistance in insects and weeds, others wonder if those moves don't mostly translate into more agro-chemical sales. In California, a hotbed of drive research, several large-scale fruit growers welcome drive technologies that could get rid of their insect pests (Regalado 2017). But internationally, many peasants have organized alongside sustainability scholars and food movement leaders to petition for a full moratorium on gene drives in agriculture.

If you've been following the GMO wars over the past couple decades, the fault lines of this gene drive debate may sound very familiar.

But there is also something new. For the first time since GMOs came into farm fields in the mid-1990s, the emphasis is not on engineering crop seeds or livestock directly. Rather, it's on engineering the ecosystem around the farm. With prospects of driving genes through wild populations, a new world of engineering agroecosystems has cracked open into view. That calls, at the very least, for honest brokers to help us reckon with gene drive technology. Is driving genes something for advocates of sustainable food systems to consider? Something to fear or contest? What *is* a gene drive in the first place, and who gets to decide how one is used?

But there is also something new. For the first time since GMOs came into farm fields in the mid-1990s, the emphasis is not on the crop seeds or livestock. Rather, it's on genetically engineering ecosystems around the farm. Agroecologists will recognize that ecosystems have long been shaped by agricultural biotechnologies. Bollworms have evolved resistance to Bt and pigweed to glyphosate; Indigenous landraces have been contaminated with corn transgenes. For the most part, however, first-generation GM organisms spread their genes mostly by accident. The business model of GMOs has been driven by maximizing production. Some superweeds and gene flow are seen as acceptable risks.

With gene drive, the inherent design and intention is to spread through ecosystems, with little respect for property lines or international borders. Drives hold particular importance because they are designed to overcome the checks of natural selection that ordinarily prevent detrimental traits – like infertility – from becoming fixed in a population. With gene drive, such mutations can potentially reach every member of a species.

This new capability calls, at the very least, for honest brokers to help us reckon with gene drive technology. Is driving genes something for agroecologists to consider? Something to fear or contest? What *is* a gene drive in the first place, and who gets to decide how one is used?

## Learning from selfish genes

Usually, a genetic change in one organism takes a long time to spread through a population. For more than a century, geneticists have known that in organisms that pair up to reproduce, most genes have a 50–50 chance of being inherited, as Moravian scientist Gregor Mendel famously demonstrated using pea plants. Similarly, evolutionary biologists have known since Charles Darwin's time that natural selection eliminates inherited traits that reduce an organism's fitness, such as a mosquito's susceptibility to insecticide.

In the early 2000s, Austin Burt, a professor of evolutionary genetics at the Imperial College in London, outlined an ingenious way to flout the laws of both inheritance and evolution. Gene drives, Burt understood, were not new. Observed by scientists since the 1960s, such "selfish" genetic elements exist in nature and have long fascinated scientists who wondered why inheritance patterns were defying both Darwinian theory (survival of the fittest) and Mendel's Laws (of inheritance) (Craig, Hickey, and VandeHey 1960).

Dr. Burt showed that certain tricks of molecular biology could achieve the same results as natural drives – causing a gene to be inherited by many more organisms through many more generations than standard genetics allow. His

2003 paper laid out an eloquent theory of gene drives and their possible applications (Burt 2003).

What Burt described in this landmark paper was a way to harness natural gene drives based on endonucleases, or types of enzymes that can cut double-stranded DNA. Natural "homing" endonuclease genes exhibit drive behavior by cutting the site on the corresponding chromosome that lacks the drive element. This induces the cell to repair the break by copying the endonuclease gene onto the normal (or wild-type) chromosome. (Scientists term the copying process "homing," while the endonuclease-containing chunk that is copied is referred to as a "gene drive" or simply a "drive.")

Because copying causes the fraction of offspring that inherit the drive to be greater than 50%, the genes can drive through a population even if they reduce the reproductive fitness of the individual organisms that carry them. Over several generations, as Figure 1 shows, such selfish inheritance should theoretically propel a gene from a small number of individuals until it is present in all members of a population.

Since that time, many labs have tried to follow Burt's proposal, using a variety of homing endonucleases. But since all such drives cut the *natural* recognition site of the relevant enzyme, designing drives to cleave *new* target sequences of interest has been a major challenge. The few attempts to do so struggled to cut sequences at high efficiency. Ten years after Dr. Burt's landmark paper, no drive capable of spreading efficiently through a wild population had yet been developed.

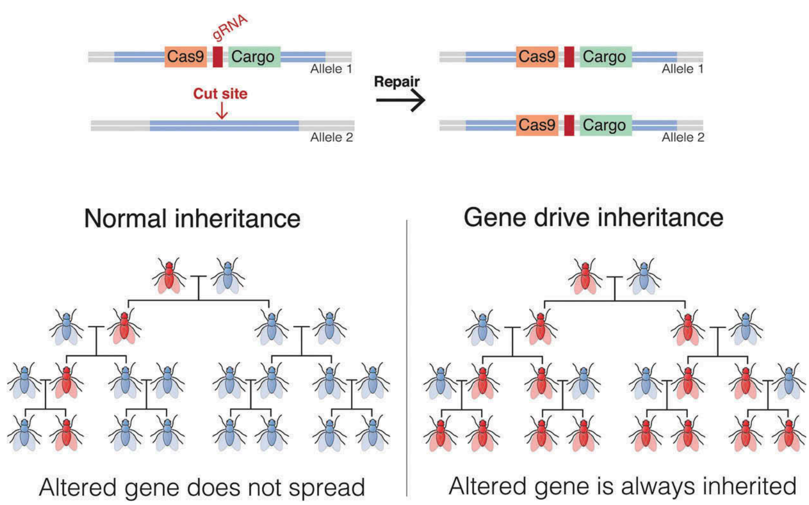


**Figure 1.** Inheritance pattern of gene drive in flies. Credit: Mariuswalter [CC BY-SA 4.0 (https://creativecommons.org/licenses/by-sa/4.0)].

## From idea to working system

The advent of CRISPR-Cas9 in the past five years has blown past these previous limitations (Montenegro 2016). CRISPRs are segments of bacterial DNA that, when paired with a specific guide protein, such as Cas9 (CRISPR-associated protein 9), can be used to make targeted cuts in an organism's genome. With the discovery of the guided Cas9 enzyme, researchers have found a gene editing tool that works across numerous kingdoms, from plants and fungi to insects and animals. They have also been given a straightforward method – relying on the same basic homing mechanism employed in nature – for targeting drives to wherever they wish.

By November 2015, just four years after the first published reports on CRISPR-Cas9, the first effective gene drive was reported in *PNAS* by scientists at UC Irvine and UC San Diego who introduced a cargo of malaria-resistance genes into lab mosquitoes (Gantz et al. 2015). Less than a month later, researchers Andrea Crisanti and Tony Nolan at Imperial College, London reported on a population control approach for tackling malaria (Hammond et al. 2016). Disrupting three mosquito genes for female fertility, their system was a type of "genetic load drive" that spreads sterility slowly throughout insect populations, eventually dwindling their numbers to zero. Another eradication method relies on biasing the sex of the target organisms. One nicknamed "crash drive" works when a gene engineered into the Y chromosome literally shreds the X chromosome in the cells that make the mosquito's sperm, thus ensuring that all offspring are male. In principle, the number of females should erode generation by generation until the population collapses.

In September 2018, Crisanti's team reported in *Nature Biotechnology* the first successful elimination of laboratory mosquitoes in less than 11 generations (Kyrou et al. 2018). While the researchers anticipated it would be 5–10 years before gene drives were ready for environmental release, by February 2019, another milestone was reached: scientists in Italy began the world's first large-scale release of drive mosquitoes – created with help from the Imperial College team – into a high-security laboratory. Ruth Mueller, an entomologist who runs the lab, told reporters, "This helps us understand better how a gene-drive release would work in the real world" (Stein 2019).

Encouraged by successes in lab mosquitoes, geneticists now suggest that drive potential is much bigger. While most research to date has focused on disease control – using drives to combat mosquitoes carrying malaria, West Nile, Lyme, and dengue – geneticists who work in this arena are calling drive "an entirely new approach to ecological engineering with many potential applications relevant to human health, agriculture, biodiversity, and ecological science" (Esvelt et al. 2014)

## Gene driving the farm?

In agriculture, the immediate utility of drive was not immediately apparent. After all, most industrialized-nation farmers get their livestock from breeders and their seeds from companies. Those seeds and breeds are not reproducing on the farm, so there is little chance of the drive being able to spread. Of course, the "GMO" does not need to be the corn or the pig, researchers have realized. It is also possible to engineer the environment *around* the crops and livestock. The plants that act as weeds. The insects or rodents that behave as plant and post-harvest pests. If biotech in agriculture was once the domain of what farmers grow – RoundUp Ready Corn, Bt Cotton, SmartStax corn, and so on – scientists and industry are now looking at intentional genetic engineering of the larger ecosystem surrounding the farm.

One key way drives can be used in agriculture is much along the lines of mosquitoes: using genetic load drives or sex biasing drives to bring agriculture pest population numbers down, potentially to zero. At the University of California, San Diego, research led by data analyst Anna Buchman and Omar Akbari, professor of entomology, is focusing on how to engineer drives into the spotted wing fruit fly (*Drosophila suzukii*). These fruit flies are considered invasive pests that have long affected the productivity of peach, cherry, and plum plantations in industrialized agriculture regions of East Asia. More recently, the flies have become a major nuisance in orchards in North America and Europe. For the UC San Diego researchers, drive offers the possibility, Buchman told the campus news, of dealing with insects that "don't belong here in the first place" (Aguilera 2018).

The insects have a different perspective, of course, which is also important for research. Gene drive enables the rapid spread of engineered transgenes. But as any good biologist knows, natural selection remains at work. Lab and modeling experiments have shown that drive resistance can result in many ways: from inefficient drive constructs, from mutations that arise during repair of cut DNA, and from natural sequence variations that prevent cutting by CRISPR-Cas9 (Noble et al., 2017). Any alleles that confer resistance, moreover, will typically increase in abundance because most drives – like most transgenes – are likely to reduce the fitness of the organism (Esvelt et al. 2014). Scientists will therefore need to prevent such resistance from arising, whether in a mosquito or a farmers' fruit fly. One tactic is to target two or three sites for fertility genes in crop pests, giving natural selection a much higher barrier to overcome.

A different application in the gene drive toolkit is to call in the chemicals, reversing pesticide resistance in insects and weeds. Already four years ago, Wyss Institute researchers led by genomics guru George Church described ways that they felt gene drives could support agriculture. A class of so-called "sensitizing drives," they explained, could potentially reverse mutations allowing the western corn rootworm to resist Bt toxins (research by Gassmann et al. 2014). Similarly, horseweed and pigweed could be induced to resist the herbicide glyphosate (Gaines et al. 2010; Ge et al. 2010), which is often used in no-till agriculture. With careful timing and localizing of drive releases, they suggested, "periodically releasing new drives could potentially allow any given pesticide or herbicide to be utilized indefinitely" (Esvelt et al. 2014).

While some sensitizing drives reintroduce organisms' vulnerability to pesticides, a different form of sensitizing drive could possibly render pest populations vulnerable to molecules that never previously affected them. For example, Wyss researchers say, it might be possible to replace a gene that is important to an organism's fitness (a prerequisite in order for drive to spread and become fixed in a population) with a version from another species whose function is sensitive to a particular compound. This approach, they suggest, could lead to safer and more species-specific pesticides and herbicides.

Combining population control with the introduction, deletion, or mutation of specific genes or sequences, gene drive in agriculture has now expanded into a whole R&D pipeline of possible applications. Altering the makeup of grasshoppers to prevent swarming. Eradicating aphids that spread greening disease in citrus (NIFA 2016). Eliminating populations of rats, mice, and flour beetles that infest grain silos. Crashing populations of screw worm flies that prey on cattle. Increasing the "genetic gain" in such cattle – and other livestock (Gonen et al. 2017). Even using drive to introduce an "optogenetic" (light controlled) gene into honeybees of intercepting olfactory and neural pathways that control feeding, mating, flying, and orientation (USPO 2015).

Not all of these are close to being released into ecosystems, to be clear. Many are unlikely to make it past blueprint stages. But in the gap between hypothetical scenarios and reality, many concerned farmers, civil society organizations, and food security experts have begun to raise concerns about the wisdom – and utility – of gene driving the farm.

## High tech magic bullets and monopolies

As delegates around the world convened in Rome in mid-October 2018, for the annual meeting of the FAO Commission on Food Security, the Canada-based organization ETC Group teamed up with the German-based Heinrich Böll Foundation to unveil a new report, warning of the perils of gene drive. Building on a previous report from 2016, *Forcing the Farm* goes into further depth on agriculture and food-specific applications of drive interventions (ETC 2018a). It also highlights prominent investors in gene drive technology, including the US Defense Advanced Research Projects Agency (DARPA), the

Gates Foundation, Tata Trusts, and the Facebook-backed Open Philanthropy Project.

In this report, the optimistic tones of Wyss Institute researchers – envisaging how drive will help farmers who struggle with weeds and pests – are turned squarely on end. “Gene drive organisms,” the authors suggest, “are merely the latest in a volley of high-tech “magic bullets” that have been imposed on agricultural systems by industrial agriculture players as supposed solutions to ongoing food and agriculture crises” (ETC 2018a, 6).

While the first generation of GMOs ran into problems when benefits to farmers failed to materialize and consumers shirked from GM foods, the report suggests, the new drive technologies offer another strategy: “Now biotechnologists are contemplating a new strategy – to engineer newly developed invasive forms of genetic modifications to control insects, weeds and create new monopolies” (ETC 2018a, 2).

For ETC Group and its allies, the creation of invasive “GDOs” (gene drive organisms) takes “one of the worst scenarios envisaged for genetically modified organisms” – that is, release into the wild – and turns it “into a deliberate industrial strategy” (ETC 2018a, 2).

## In need of honest brokers

ETC’s lexicon of GDOs, “genetic pollution,” and biotechnologists strategizing to create new monopolies – well, it tends to rub scientists the wrong way. So, it is worth pausing for a moment to focus on the role of scientists in today’s food system predicament. I refer here to what environmental anthropologist Glenn Davis Stone calls “the honest brokers” (Stone 2017). New biotechnologies force us all – scientists, policymakers, and the broader public – to confront problems of extraordinary complexity. They challenge our worldviews, our ideological commitments, our visions of the past and the future.

An honest broker, in Stone’s assessment, is someone who is skilled at “providing information to expand and clarify a scope of choice, but allowing others to make decisions according to their own values” (Stone 2017, 3). This notion is not Stone’s invention; he draws upon climate scientist Roger Pielke, who in turn was inspired by the philosopher of science Robert Merton. At times when the dizzying speeds of changing technologies beckon for deep understandings of nature, basic scientists are not the only source of knowledge, but they can be particularly valuable for three reasons.

First is knowledge. Basic scientists have understandings of biology and ecology and matter and energy. Their explanations are badly needed, especially at times when the media lacks fact-checking or accountability. Second, Merton suggested, is knowledge of uncertainty. Technologies like gene editing are riddled with the unknown. Good science takes as its starting point uncertainty; there are methods of accounting for the strength of what is known. Neither pro-GMO executives nor anti-GMO activists are bound by these knowledge constraints, nor do they claim to be. Third are career and reward structures. While we might argue how much these actually hold muster in neoliberal educational institutions of today, in Merton's eyes anyway, scientists are buoyed by institutional policies and self-policing that enforce basic norms of universalism, communitarianism, disinterested behavior, and organized skepticism.

Stone argues – and I agree – that instead of honest brokers right now, the field of biotech science is littered by much of the opposite: many who are active as public intellectuals on GMO issues "fit the definition of stealth-issue advocates, claiming scientific knowledge as a sole motivation, while acting as belligerents in a polarized war of rhetoric" (Stone 2017, 4).

Some honest brokerage is badly needed in the many ecological, economic, and democratic questions that swirl around gene drive. Bridging the gap between biotechnicians and activists, then, might begin with a few frank conversations about gene drive's role in contributing to a sustainable food system.

## Does driving genes through wild populations resonate with biologically diversified farming?

Does it seek to control and simplify agroecosystems rather than cope with organisms (like pests) that may not always behave as we want but that serve important roles in complex ecological webs? While most current drive experiments are confined to laboratory settings, with sophisticated biosecurity protocols in place, the entire point of drive is to eventually introduce genes into wild populations to propagate virally. We need ecologists and agroecologists to help us better understand what the effects of such releases might be. If, for example, we successfully wipe out a problematic pest, what happens to the beneficial insects or birds that used to rely on them for food? Or what happens if collapsing one population opens up food resources or habitats for new types of pests to move in? In what ways – if we can even count them – will gene drive ripple across the food web in ecosystems in and around the farm?

## What are the risks – ecological and social – of ecosystem engineering and are they being seriously appraised?

The idea implicit in gene drive is that scientists can know the risks and can steer the trajectory of drives, stopping them from spreading or running amok. But gene drive researchers themselves acknowledge great uncertainties in the scope, durability, and control of drives. For example, Kevin Esvelt, a prominent drive expert at MIT, has become something of a maverick in his field for publicly criticizing the hubris of many biotechnologists. When the first UC Irvine demonstration of drive was published in 2015, Esvelt told MIT Technology Review that, in his opinion, the California researchers had not used strict enough safety measures. Locked doors and closed cages are not enough, he said. Instead, they could be installing a genetic "reversal drive" so the change can be undone, if necessary (Regalado 2015). Similarly, Hank Greely, a bioethics law specialist at Stanford, says environmental uses are more worrisome than a few modified people. "The possibility of remaking the biosphere is enormously significant, and a lot closer to realization," he told the Technology Review (Regalado 2015).

More recently, scientists have gone even further to say that gene drives are too risky for field trials (Zimmer 2017). In 2017, a team of Harvard and MIT researchers created a detailed mathematical model to describe what happens following the release of gene drive organisms. In a paper published on the preprint bioRxiv server, they discovered unacceptable risk: "Current CRISPR gene drive systems," they said, "are likely to be highly invasive in wild populations" (Noble et al. 2017). In other words, in the name of conservation a drive might spread to places where the species isn't invasive at all, but is part of a well-established ecosystem.

What does this mean for agriculture? Can we expect that releasing gene drives to eliminate invasive insects or plants in one territory will not spread into agroecosystems that depend on a variety of "unplanned" pollinators, predators, habitats, and food-providers? Can we be confident that drives will preserve the integrity of agrobiodiversity, especially in Indigenous and traditional cropping systems where boundaries between "wild" and "domesticated" are porous and intentionally traversed?

Championing the notion of releasing drives into nature, Esvelt admitted in 2017 was "an embarrassing mistake" (Zimmer 2017). While other scientists express similar precautions about gene driving wild ecosystems, agriculture, as a "human-dominated" system, is a likely space for more aggressive interventions to seem acceptable. Thus, it is here especially that we need agroecologists to help us understand the complex dynamics of patchy landscapes, where conservation and agriculture, cultivated and noncultivated converge (Perfecto and Vandermeer 2010). And we need geneticists like Esvelt to own up to the limits of certainty – and the known and unknown risks of what gene drive can do.

## Can we actually reverse drives? is there going back?

Reversal drives are being proposed as a safety mechanism to contain gene drive. A reversal drive would cut out an errant drive and restore the target organism almost to its previous state. Of interest to many GMO critics, researchers even propose that reversal drives could remove conventionally inserted transgenes that entered into indigenous crop and wild relative populations through cross-pollinating with GMOs. This means, in theory, that drive could be harnessed to remove relics of transgenic corn from native Mexican maize, or the contamination of organic farmers' crops with GMO varieties.

But even drive experts acknowledge that reversal is never fully restorative. It is important to note, they say, that "even if a reversal drive were to reach all members of the population, any ecological changes caused in the interim would not necessarily be reversed" (Esvelt et al. 2014). For farmers caught in the crosshairs of such experiments, this may be putting it mildly. What happens "in the interim" might be the loss of crops, the piling up of debt, the stress and psychological trauma of struggling to hang onto the farm. None of that could necessarily be reversed.

## How might drives for conservation, human disease, or war affect food and farming?

Currently drives are being hypothesized and developed to tackle issues in conservation (e.g., controlling invasive species), public health (eliminating disease vectors), military (developing biological weapons), and agriculture (CSWG 2016; NAS (National Academies of Sciences, Engineering, and Medicine) 2016; Specter 2017). But these are also non-exclusive applications. Around the world, people who suffer from malaria, dengue, and other water-borne illnesses are mostly living in agrarian communities dependent on agriculture for their livelihoods. How their health is affected or not by gene drive will have direct ramifications for food security and nutrition. Similarly, controlling invasive species for conservation in tropical forests could quickly ripple out into the trophic webs supporting farms. Farming and conservation in fragmented habitats are not so easily teased apart. Finally, military applications of gene drive being developed by the US Department of Defense could be targeted against crops of countries considered to be adversaries (Neslen 2017, DARPA n.d.). The weaponization of food is nothing new, but gene drive takes it to another level, potentially threatening a whole country's food supply through the spread of noxious mutations.

## Who gets to decide what drive can do?

By 2016, the National Academies of Sciences, Engineering, and Medicine had assembled a full 220-page study on gene drives (NAS (National Academies of Sciences, Engineering, and Medicine) 2016). Acknowledging the risks inherent in the new technology, the NAS wrote: "The potential for gene drives to cause irreversible effects on organisms and ecosystems calls for a robust method to assess risks."

Many experts feel that robust risk assessment is only a start. Esvelt, for one, had major issues with the NAS guidelines, which did not explicitly require scientists to publicly disclose their experiments before conducting them. As he told the Genetic Experts News Services (GENeS) at the time: "Everything in the Academy report points to this same conclusion about public disclosure. They just don't explicitly acknowledge it. And that's a pity, because gene drive systems are intrinsically about altering the shared environment. We should at the very least have the courtesy to inform people what is being planned – and let them voice their opinions – before we begin" (Loria 2016).

Scientists must reach out to policymakers, NGOs, and communities at-large to build better processes for assessing risk and involving the public.

## Who will benefit from drives?

Esvelt is an example of the complicated trajectories of modern biotech science. A proponent of open science, he publishes details of RNA sequences and gene drive constructs on his laboratory webpage, "sculptingevolution.org." He invites public access to these pages and has called CRISPR (as opposed to other proprietary platforms[2]) a means of democratizing gene editing.

Yet, in agriculture, public–private partnerships and licensing agreements complicate the picture of who benefits. The foundational Esvelt/Harvard patent application on RNA-guided gene drives lists 167 common herbicides to which plants could be made susceptible via drive. Additional analyses by ETC Group of this patent application, together with a second patent, show that each patent references around 500–600 agricultural uses – 186 herbicides, 46 pesticides, 310 agricultural pest insects, nematodes, mites, moths, and other pests. These numbers suggest much R&D in the drive pipeline is tied to sales of agrochemicals. Beyond chemical sales per se, the patents on drive make way for a new business model for agroecological engineering. In this scenario, owners of the IP could sell proprietary compounds, their new classes of drive-associated molecules, and even older, more toxic chemicals (with plants made newly susceptible) into the marketplace. Researchers must be willing to learn about and talk through the implications of IP rights in CRISPR and whose priorities are put first (Parthasarathy 2018).

## Who is the public? is gene drive democratic

As the new wave in genetic engineering opens many possibilities to change agriculture for better or worse, several scientists are striving to be the honest brokers. They are holding townhalls in Nantucket to discuss how gene drives for mice might combat Lyme disease. They are writing precautionary op-eds and calling for "community-guided eco-engineering research" (Esvelt and Gemmell 2017). Most recently a team of journalists and academics suggested in *Science* that gene drive should have "locally based, globally informed governance." To inform decision-making, they proposed, a neutral coordinating body aided by expert facilitators could convene communities, technology developers, and governmental and nongovernmental organizations "in ways that ensure inclusive deliberation" (Kofler et al. 2018).

This is a start. Certainly, efforts to involve local communities in participatory decision-making should be lauded. But it is also possible to see something else afoot here. Kofler and colleagues argue that current international frameworks are not equipped to face the new challenges brought by gene drives. Neither the Convention on Biological Diversity (CBD) nor the IUCN, they suggest, offer the kind of "broad and open deliberative process we advocate."

Yet civil society actors with whom I spoke view this critique of international governance another way. As movement groups prepared to travel to Sharm El-Sheik for the annual CBD meeting last November, many expressed concern about scientists' attempt to bypass the Cartagena Protocol, which has existing mechanisms for engaging civil society groups.

The CBD has in fact enlisted a Technical Expert Group on Synthetic Biology to update the Protocol's rules on living modified organisms to accommodate gene drive-bearing organisms. In December 2017 this ad hoc group flagged "FPIC" – Free, Prior, and Informed Consent of local communities – as an essential concern for gene drive projects. Enshrined by the UN Declaration on the Rights of Indigenous Peoples, FPIC guidelines suggest that any parties wishing to introduce gene drive organisms would not only need to obtain prior and informed consent from national governments for potential transboundary movements, but also from Indigenous peoples whose lands and territories might be affected.

The IUCN, meanwhile, has since 2016 adopted a de facto moratorium on support for or endorsement of research into gene drives for conservation or other purposes. This halt came about when 71 governments and 355 NGOs (out of a total 554 votes cast) – asked the conservation body to refrain from supporting research into gene drives until it completes an ongoing assessment of the technology (*The Ecologist* 2016, IUCN 2018).

In other words, while gene drive scientists and journalists lambast the CBD and IUCN as ineffective, it is less clear if their proposed alternatives will empower local communities as much as they say. One cannot help but be reminded of the "local turn" in recent development history. "Participatory development" became the buzzword in the mid-1990s across much of the global South, where structural adjustment was hitched to a newfangled localism, allowing scientific elites and transnational capital to continue cementing Eurocentric solutions to development problems (Mohan and Stokke 2000). Similarly in food systems, localism has often served to transfer power from government institutions to self-regulation by individuals, community institutions, public–private partnerships, and NGOs – not in order to back their sovereignty but to support market rule (Guthman 2007).

None of this is to say that international and national mechanisms are the only or best solutions to gene drive governance. Civil society groups continue to struggle – over safe containment, digital sequencing, intellectual property, and potential weaponization, amongst others – in these fora. As reported by the International Planning Committee for Food Sovereignty (IPC), which shared publicly its November 2018 CBD meeting notes on synthetic biology:

> Ongoing negotiations are long and difficult for this point on the agenda. The parties are not agreeing, trapped between the interests of the industry on the one hand, and those of the local communities, peasants and indigenous peoples on the other… We would like to see a solid text regarding free and informed consent with the full knowledge of indigenous peoples and local communities in paragraph 10. It seems that some parties are forgetting about their responsibilities with the three goals of the Convention, civil society and the citizens they represent.

Despite heavy pull by industry, however, and despite what the IPC called an "extremely worrying" position by the African Union, which continues to demand de-regulation of genome editing and to promote gene drive release for antimalarial efforts, Madagascar together with the Bolivian delegation argued for tighter regulations on synthetic biology (IPC 2018; Watts 2018). In the end, the 2018 CBD meeting fell short of the sovereignty movements' wishes: a full moratorium on gene drive research. Yet they also came away with wins from their perspective, including CBD requirements that countries must develop new safety guidance, assess environmental risks, and seek free, prior, and informed consent of local communities.

## A better way to govern drive?

If the proposals of Kofler et al. could be used to empower local communities in the CBD and similar spaces, rather than to provide voluntarist bypasses, their calls to include marginalized groups would be a welcome strategy. In addition, we could look for guidance to two further frameworks that have recently arisen.

The first, with the acronym ARRIGE, emerged in 2018 after a meeting in France gathered together patient associations, NGOs, governmental agencies, funding bodies, companies, and members of the general public. Lluis Montoliu, a researcher at Spain's National Biotechnology Center in Madrid and one of the ARRIGE founders, told *Nature News* (Smalley 2018, 485), that the assembly of diverse voices is key, and it must also include the global South – India, Southeast Asia, sub-Saharan Africa, and South America. "Do they know what we are planning to do?", he says. "Are they part of this discussion? Do they understand? Do they really accept? Do they know the challenges that [are] posed to the environment [by] the release of these genome edited mosquitoes?"

ARRIGE's design is to provide a permanent forum for international debate on risk-management that can inform ethical research, improve public engagement, and ultimately promote multisectoral governance of gene editing. Its noteworthy contribution, notes STS scholar Sheila Jasanoff, is the promise that "there will be more stakeholders at the table as the ethics of genome editing are worked out. This includes people who might be adversely affected by the technologies as well as those who might benefit from them" (Smalley 2018, 485).

Jasanoff herself has gotten into CRISPR governance. Along with colleague Benjamin Hurlbut, Jasanoff developed a framework they call a "global observatory for gene editing" (Jasanoff and Benjamin Hurlbut 2018). Somewhat different from ARRIGE in being comprised of mostly scholars and organizations from diverse cultural perspectives, the global observatory may be a bit underspecified, as Kofler et al. argue. But it is, to my mind, more subversive and epistemologically powerful. For example, attempts to include historically marginalized communities have often treated those groups as the "affected communities" or the "impacted communities" assuming that the introduction of biotechnology is a *fait accompli*.

Such was the case when a group of academics recently invited Dr. Esvelt to New Zealand to discuss the possible use of gene drives in conservation. As the *Wall Street Journal* reported in July 2018, New Zealand has plans to rid the country of non-native species such as possums and rats that threaten its indigenous flora and fauna (Marcus 2018). Gene drive, the government believes, could be a solution. On his visit, in addition to meeting with scientists, Esvelt met with members of the Te Tira Whakamataki (or the Maori Biosecurity Network), a group of elders, academics, tribal leaders and others who work to ensure Maorians participation in biodiversity decisions. Melanie Mark-Shadbolt, CEO of the network, told the *WSJ* that they liked Dr. Esvelt's idea of co-developing research and new technologies with community input. "We want to be active participants in research, not subjects," she said (Marcus 2018).

Soon after that visit, Dr. Esvelt and his New Zealand collaborator Neil Gemmell, published the previously mentioned perspective piece in the *Public Library of Science*, calling for community-guided research. But the Maori communities told the newspaper they felt blindsided. The scientists implied in their paper that actual use of gene drives in New Zealand was imminent rather than hypothetical. "When he met with us, he should have said, there is a paper coming out that talks about New Zealand and conversations I am having about gene drives, would you like to take a look?" she told the reporter.

To his credit, Esvelt (who is also a coauthor on the Kofler et al. paper) has apologized for this incident, issuing a public statement in the Medium. Reflecting on the experience, Dr. Esvelt told the *WSJ*, "I made the same mistake with respect to the local political environment that we're hoping to avoid with the natural environment: our lack of understanding leading to unwanted side effects" (Marcus 2018).

But it is precisely these unwanted side effects, environmental and political, that gives many agroecologists pause. Why must we contend with side effects from tools that are orthogonal to agroecological practices in their logic and design? Is there a drive that targets the structural roots of malaria? The chemical drivers of insect and weed resistance? The trade-driven routes through which invasive species spread?

"Why are we talking about governance at all?" said Devon Peña, a professor of American Ethnic Studies at the University of Washington in Seattle. Pena's work at UW and the non-profit Acequia Institute includes research on shifting mosaics of annual-perennial polycultures, plant-breeding, and participatory programs that conserve the integrity of local landrace varieties in the Upper Rio Grande. Crops like *maíz de concho* (white flint maize), he told me, have uncanny properties. They can randomly revert to rare intermediate forms, semidomesticated and semiwild. Yet these genetic regressions only occur in uncontaminated parent lines, meaning a gene drive could disrupt this curious rewilding behavior and along with it, what local communities view as evidence of its lineage of Mesoamerican origin and diversification.

For Peña, behaving as if the "genie is out of the bottle" with gene drive is a defeatist posture. Instead of asking the governance question, he said, "We should be asking the ecology question. Let's move to agroecology."

## Moving from neutral to dialogical

In 2015, an important milestone in gene editing governance was the International Summit on Human Gene Editing, held in Washington DC. At the event, Nobel laureate David Baltimore began the talks by invoking the 1975 Asilomar meeting on recombinant DNA research: "In 1975, as today, we believed it was prudent to consider the implications of a remarkable achievement in science. And then, as now, we recognized we had a responsibility to include a broad community in our discussions" (Baltimore 2016).

Asilomar is often recognized as a catalytic moment in biotechnology – a time when scientists affirmed their autonomy and committed to responsible research. Yet as Jasanoff and Hurlbut (2018, 436) point out, "the questions asked, the forms of expertise called upon, and the definition of stakes for science and human life were all shaped by those communities most aggressively advancing the research."

Just as we seldom trust parents to critically appraise their children – the creatures they created – gene drive should not be governed principally by the very experts whose livelihoods and legitimacy depends on advancing gene drive work. Gene drive cannot be a foregone conclusion before deliberations begin, as the Maori would tell us. And in creating space for such deliberations, we must also avoid well-intentioned, but slippery notions like "a neutral third party" (Kofler et al. 2018, 528), recognizing that no such thing as impartiality in science (as in life) exists. All actors have values and decision-making priorities.

Unfortunately, while academics in wealthy countries have the luxury of debating these particulars, farmers in the global South might have the most to lose. Burkina Faso is being prepared to receive the world's first field release of gene-drive mosquitoes developed in US and UK laboratories, with backing from the Gates Foundation (Swetlitz 2017, 2018). African biodiversity and food sovereignty groups are protesting these moves, calling it "colonial medicine" (ACB 2018). In January 2019, researchers in La Jolla, California reported the first successful drives in a mammalian system – a gene-driven mouse – that could have implications for agricultural animals on which smallholders depend (Conklin 2019; Grunwald et al. 2019). Seeds will also be a proving ground. In wealthy industrial economies with "formal" seed breeding systems, most farmers do not save their own seed, so it would be difficult for gene drive to spread. By contrast, say scientists, "developing countries that do not use centralized seed production and artificial insemination could be more vulnerable" (Oye et al. 2014).

Honest brokering begins, then, upstream from gene drive impacts and mid-stream among tributaries of value-laden, uneven, and partial knowledge. Here, as Jasanoff and Hurlbut (2018, 436) suggest, we can reflect more critically on key considerations: "What questions should be asked, whose views must be heard, what imbalances of power should be made visible, and what diversity of views exist globally."

Taking heed from agroecology's existing tenet, dialogue of knowledges (*diálogo de saberes*), agroecologists can intervene where they live and work, strengthening real processes of knowledge-making and biodiversity-renewing that gives farmers a practical alternative to industrial agriculture. They can back social movements in their negotiations with international governance frameworks and can write, speak, and remind the public and one another of Asilomar's promise. What are we doing? Why are we doing it? How do we solve the root problems – of poverty, inequality, and late-modern globalization – that propagate the crises gene drives are designed to address?

## Notes

1. “Sculpting Evolution” is the name of the laboratory and project site of Kevin Esvelt, a prominent gene drive researcher at MIT. “Reckless Driving” is the title of a report on gene drive produced in 2015 by the Civil Society Working Group on Gene Drives (CSWG 2016).
2. Calyxt is an example of a biotech firm that uses a non-CRISPR gene editing system known as TALENs. The first TALEN® was developed through a collaboration between the laboratories of Dan Voytas (CSO at Calyxt) and Adam Bogdanove at University of Minnesota and Iowa State University, respectively, in 2009.

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