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Gene Drives as Interventions into Nature: the Coproduction of Ontology and Morality in the Gene Drive Debate

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Abstract Gene drives are potentially ontologically and morally disruptive technologies. The potential to shape evolutionary processes and to eradicate (e.g. malaria-transmitting or invasive) populations raises ontological questions about evolution, nature, and wilderness. The transformative promises and perils of gene drives also raise pressing ethical and political concerns. The aim of this article is to arrive at a better understanding of the gene drive debate by analysing how ontological and moral assumptions are coproduced in this debate. Combining philosophical analysis with a critical reading of the gene drive literature and an ethnographic study of two leading research groups, the article explores the hypothesis that the development of and debate about gene drives are characterized by a particular intervention-oriented mode of coproduction. Based on the results of this exploration, we highlight the need for a broadening of the perspective on gene drives in which empirical, moral, and ontological concerns are addressed explicitly in their interplay rather than in (disciplinary) isolation from each other.

Keywords Gene drives · Coproduction · Interventionism · Human-nature relations

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Introduction

Gene drives are inheritance-biasing biotechnologies, considered promissory for their potential to revolutionize approaches to disease eradication and prevention, protection of wild populations, species, ecosystems and biodiversity, and protection of agricultural crops [1]. Projected applications are based on the gene drive construct's ability to copy itself such that it allows spreading genetic alterations through wild populations [2]. As for many related biotechnological fields, the advent of CRISPR as a genome editing technique has led to recent claims of revolutionizing development of synthetic (human-made) gene drives[1]. After a first article outlining the technological specifics and potential fields of application of CRISPR-based gene drives in 2014 [3], proof-of-concept under laboratory conditions quickly followed

[1] Theoretical accounts of using gene drive mechanisms have been around for a while; with the advent of CRISPR as a revolution in human-directed genome editing, the possibility of developing gene drives mechanisms that actually work has reemerged with fervour since 2014.

for yeast [4], fruit flies [5], mosquitos [6–9], bacteria [10], and mice [11][2].

The revolutionary promises and core features of gene drive technologies give rise to both moral and ontological (or metaphysical[3]) issues. Starting with the former, a noteworthy feature of the gene drive debate is how explicitly morally charged it has been from the outset (since 2014). The commonly highlighted potential benefits in health, conservation and agriculture—contributing to the values of health through disease eradication, biodiversity through population and ecosystem management and food safety and security through pest control—are often presented as not only supporting the use of gene drives but as making their further development and testing close to morally obligatory [12–17]. At the same time, gene drives raise strong moral concerns. The technology's potential for triggering rapid, possibly irreversible spread of genetic modifications to target populations in the wild [1] led to concerns about security and unintended consequences that have become widely discussed in the literature [1, 15, 18–26]. Recognition of these concerns triggered policy, regulation, and governance proposals from an unusually wide range of contributors, who at times also collaborated in preparing these proposals: policy and regulation makers, (popular science) media, academics from the social sciences and humanities (particularly those interested in governance and policymaking and those interested in ethics), and—of particular noteworthiness—individual scientists working on the technology [1, 14, 15, 21–23, 25, 27–42]. The main risks initially focussed on were the accidental, premature or ill-intentioned escape or release of gene drive-modified organisms with negative and potentially irreversible ecological consequences [4, 27]. Subsequently, more attention has been devoted to the potential for negative impacts from gene drive releases conducted intentionally and with the best of intentions ([43–45] provide overviews of such considerations; publications about safely trailing gene drives can be considered part of this category as well, e.g. [22, 33, 46–50]).

On the ontological side, gene drives can be regarded as transforming our conceptions of nature and natural phenomena, as a select number of contributions to the gene drive debate have suggested [1, 19, 43–45]. While all biotechnologies intervene into nature in one way or another, gene drives have been positioned as a way of "sculpting evolution" [51, 52] due to their inheritance-biasing features. This has led to the suggestion that gene drives transform our understanding of the givenness of this fundamental mechanism of the living world [1, 2, 19, 24, 32, 44, 53]. The potential ontological ramifications of gene drive applications also involve understandings of nature as wilderness. While gene drives are often referenced as a way of targeting wild populations, these projected applications simultaneously seem to challenge the very idea of wildness or wilderness as characterized by its relative distance from human intervention [1, 3, 18, 19, 24, 43, 53, 54][4]. Gene drive technologies are thus potentially ontologically disruptive in the sense that they challenge the boundaries and sometimes even the coherence of core concepts for navigating the biological world from "evolution" to "nature" to "wild(er)ness".

The aim of this article is to arrive at a deeper understanding of gene drives by analysing these assumptions in tandem; that is, by analysing the specific ways in which ontological and moral assumptions—about gene drives, nature and human action—are *coproduced* [55] in the gene drive debate, and by critically

[2] Although the latter publication indicated more mixed results; the encountered technical difficulties were grounds for the authors to conclude that 'both the optimism and concerns are likely to be premature' [11, p. 108].

[3] Philosophically, the terms "ontology" and "metaphysics" can be differently defined and distinguished. We use the following distinction: whereas metaphysics involves accounts of the fundamental nature of being, reality or nature, ontology tends to be more specifically concerned with providing accounts and categorizations of the entities, processes, and relations of which (certain domains of) reality consist. In this article, for purposes of consistency, we have chosen to adopt the term ontology instead of metaphysics to refer to those assumptions that concern reality and/or nature and the different entities or other phenomena it consists of. We consider metaphysics to be the more appropriate term for referring to (culturally specific) systems of understanding and giving meaning to the world, nature, and the place of humans in it.

[4] Within the environmental philosophy literature the meaning of wilderness and wildness are contested. While some regard wildness as the characteristic of a natural entity that has never been touched by human hand [152, 153], others argue that this is premised on a false dichotomy between human and nature [154] and rather focus on autonomous processes. Vogel [155, p.112] for example interprets wildness as the 'operation of forces in an object or organism that operate unpredictably and beyond the grasp of any human actor'. Others [156, 157] distinguish different dimensions of wildness and present it as a more gradual concept.

questioning these framings of gene drives in terms of what they highlight and what they fail to accentuate. The notion of coproduction suggests that ontological and moral claims and assumptions are inseparably connected and mutually define each other in scientific and technological development and debate. As Scott and Marshall [56, p. 531] point out, any 'understanding of the world, or some part of it, must make assumptions (which may be implicit or explicit) about what kinds of things do or can exist in that domain, and what might be their conditions of existence, relations of dependency, and so on. Such an inventory of kinds of being and their relations is an ontology.' An ontological assumption is then an assumption about what kinds of things do or can exist, and what might be their conditions of existence, relations of dependency, and so on[5]. We explore the connection of ontology with morality in light of the recurrent framing of gene drives as potential future *interventions into* (parts or dimensions of) *nature*. Our point of departure is that the idea of an intervention, and of an intervention into nature more specifically, relies on connecting morality and ontology in particular ways. By devoting our attention to these particular ontology-morality connections, we provide a new perspective on what is at stake in considerations of the future use of gene drives. Looking through the lens of the coproduction framework reveals that gene drives are framed as demarcatable, local, specific, well-considered and therefore legitimate interventions. However, such a framing of a gene drive intervention into nature as an isolated event into a neatly demarcated piece of the world is inherently incomplete. Our framework further highlights how the gene drive debate's early emphasis on ethical issues is troubled by the fact that it is difficult to engage in such normative evaluation if normative disagreements arise partly from different ontological perspectives of how to situate gene drives in competing understandings of nature.

We elaborate this framework of coproduction and intervention in the "Coproduction of Morality and Ontology" section of the paper. The section "The Gene Drive Debate" first explains the literature study and ethnographic material and method that support the article's conceptual-philosophical narrative, and provides a brief account of the gene drive debate. In "Gene Drives as Interventions" we present the analysis of gene drives as interventions and the ontological and moral assumptions this involves. We subsequently discuss the implications of adopting a framework that takes coproduction seriously for our understanding of gene drives and intervention in "A Perspective that Acknowledges Coproduction—Discussion". We conclude the article in the "Conclusion" with a brief summary and reflection on the question of the relevance of our argument for the political and ethical dialogue on the use of gene drives.

The Gene Drive Debate

Literature Analysis and Ethnography

The following account approaches gene drives by integrating an analysis of the gene drive literature and an ethnographic study of two research groups with a philosophical analysis of coproduction of ontology and morality. We explore a (hypo)thesis about intervention-oriented coproduction through the observational detail of ethnography and framing analysis. The findings from our reading of the literature provide a more general framework for the conceptual analysis, with observations from the ethnography providing more detailed illustrations around particular themes. The literature analysis aims at understanding the gene drive debate *in terms of its discourse on the implications of gene drives and how to deal with these*. The analysis focused on publications in academic journals about gene drives since 2014—which is when the article by Esvelt et al. [3] was published which kickstarted the recent attention the technology has received; when referring to "the gene drive debate", we thus refer to publications from 2014 onwards—that addressed the wider (e.g. ethical, safety, responsibility) implications of gene drives. Also included was "grey" literature on gene drives from policy advisory organizations. "Hard science" publications that focus only on the technical side of developing gene drives were excluded[6]. The aim of the literature analysis was not a systematic, categorizing, descriptive overview, but to arrive

[5] We thank our colleague Julia Turska for suggesting this definition to us.

[6] Also excluded were publications that presented methods and results of modelling the effects of gene drive releases.

at a critical reading of the discourse on gene drives on the basis of noticeable ways of framing the moral and ontological implications of gene drives.

While we do not focus on the technical, state-of-the-art side of gene drive development (for recent overviews that do, see [57, 58][7]), we want to point out that recent reviews of the science behind gene drives [57, 58] convey two core points: first, that it has proven difficult to design gene drives that would actually be effective and safe in the wild, due particularly to the development of resistance to the drive and reduced fitness as a result of the drive, which hamper the evolutionary stability of the drive construct in the wild; and secondly, that there has been remarkable promise and success in addressing these issues.[8]

The ethnographic study focused on two case studies of research groups involved in gene drive development (the second group worked on a particular type of drive, a *split* drive, that is not formally a full gene drive; when we refer in this article to gene drive technology, we refer to a collection of variants that include full gene drives and split drives—more on the variants in The Current State of the Gene Drive Debate). The studies were conducted by the first author between the end of 2018 and the middle of 2020. The first case study involved a three-month engagement with MIT's Sculpting Evolution lab in Cambridge, Massachusetts. Data was gathered by attending group meetings, observing lab-work, holding one-on-one conversations with group members and a number of social scientists and humanities scholars who had recently worked with and/or researched the group, studying the group's website, and analysing the literature which has already been published about the group. The lab was selected for their prominence in the gene drive debate. The group's director, Kevin Esvelt, has been a highly visible figure in the gene drive debate, with many academic and popular (science) publications referencing him, profiling him, or being (partly) by his own hand; the PhD researcher from the other research group (introduced below) even suggested he had single-handedly set the course for both the gene drive debate and the technology's research agenda since 2015. Particularly striking has been his vocality concerning the non-scientific side of gene drives. This is unusual for a scientist/biotechnologist, at least to this degree, and as such should not be taken as typical for today's technoscience. The group's projects (at or just prior to the time of visiting) involving the development of or the consideration of using a gene drive to address a societal problem include[9]: studying the evolutionary stability of gene drives using nematodes (roundworms) as a model organism; inventorying and improving upon existing mathematical modelling of gene drive dynamics "in the wild"; (exploring the possibilities for) designing pain-free mice; designing mice for field-release to combat tick-borne diseases on islands in the vicinity of MIT; (exploring the possibilities of) combatting invasive species for conservation purposes, with Australia and New-Zealand as prime locations[10]. Other projects included developing non-gene-drive mammalian population control systems for conservation; developing viral defense models; conducting "directed evolution" using viruses to develop proteins and other microbiological "products"; and developing algorithms for biosecurity purposes.

The second case study involved the Laboratory of Microbiology at Wageningen University in the Netherlands and focused specifically on one PhD researcher working on the development of a

[7] The focus in these reviews is particularly on gene drives in insects, although other organisms are also addressed. [158] provides an additional overview of the state of gene drive development for insects specifically. [159] provides an example of one additional recent development in the field: the use of gene drives as tools for laboratory research.

[8] For mosquitoes, Bier [57, p. 19] remarks on the basis of his extensive review of the research in the field: 'Progress in the gene-drive field has been remarkable over the past 5 years. In this brief period of intensive productivity, nearly all substantive technical barriers have been overcome for drive systems either modifying or suppressing mosquito populations.' He adds that therefore, 'it is now possible to define relatively precise target–product profiles defining detailed characteristics of drive systems that would be suitable for advancing to the next phase of testing in physically or ecologically confined outdoor […] field tests' [57, p. 19]. Similarly, Gantz & Bier [58, p. 17] conclude that 'The promise of active genetics at its dawn in 2016 has been fulfilled in nearly all spheres initially envisioned including the development of efficient next-generation gene-drives, allelic-drives, drive neutralizing elements, and adaptation of these systems to other organisms including additional insect species, mammals, bacteria, and viruses'.

[9] Many of these projects have clear names that are much more enticing than the awkward descriptions provided here—for the sake of anonymity these are not mentioned.

[10] For this latter project in particular, the situation is that a gene drive was discussed as an option early on, but had been discarded by the time of the first author's research visit.

functional split drive in yeast. A split drive is a particular design that separates two necessary components of a full gene drive in order to prevent autonomous spreading. The group was selected for being the only group in the Netherlands working on drive development (at least at the time, to our knowledge) and for its prominence in the development of CRISPR-technologies and the CRISPR-debate. This study was much longer in duration, involving the presence of the first author during weekly meetings for a period of 1.5 years, and focused mainly on the development of the PhD researcher's project and the interactions between the PhD researcher and this researcher's supervisor. Important additional data sources were the PhD researcher's educational duties during this period, during which the first author was also present, and a number of conversations the researcher had with people expressing interest in gene drives and the project.

For both case studies, observations, conversations and interviews were written down (permission for audio-recording was not granted) and these transcripts were subsequently analysed for how they involved ontological and morality-related matters. As with the literature analysis, the analysis of the ethnographic material was not aimed at being encompassing or systematic, but at coming to what in our view were the most interesting and remarkable features of the bioengineer's practices and views.

The Current State of the Gene Drive Debate

What image of the discourse on the implications of gene drives and how to deal with them emerges from our reading of the literature? As can be expected for an emerging technology, accounts of gene drives lie somewhere on the spectrum between emphasizing unprecedentedness, radicalness and uniqueness, and claiming continuity and drawing parallels with other developments and technologies, with many accounts acknowledging both sides. The influential NASEM-report from 2016 [1], which has since become a benchmark for subsequent publications, defined gene drives according to two features: the intentional rapid spread in the wild of the genetic trait, and the potential irreversibility of environmental consequences that result from their release. Simon et al. [59] characterize gene drive organisms as between continuity and novelty and stress how, on the side of novelty, the inheritance and spread of a transgene in wild populations becomes the explicit aim with gene drives, as opposed to the danger or risk such spreading represents in considerations of traditional genetically modified organisms. Moreover, the aim to change wild species comes with unpredictability in terms of effects in the target population, their environment, and ecosystems beyond the area of release, since modifications are unlikely to be limitable to the area of release.

The initial spur of excitement about gene drives can be explained by their potential to target difficult-to-control wild species: they are held to provide a solution to a specific set of problems in health, conservation and agriculture for which current solutions are considered lacking or unsatisfactory [1, 17, 19, 60]. However, the debate has arguably been characterized more strongly by claims of the technology's potential risks and negative consequences (e.g. [1, 15, 18–24, 26]). Theoretically, the release of even a few organisms could lead to the introduction of beneficial or harmful genes in entire wild-type populations, leading commentators to consider gene drives 'highly contentious' [61, p. S203]. CRISPR-developer and Nobel Prize winner Jennifer Doudna refers to gene drives as a way 'in which the power to edit the genes of other species could prove to be more dangerous than any changes humans have made to the planet so far' by causing 'unstoppable, cascading chain reaction[s]' [62, p. 147] and a *The New Yorker* profile of Kevin Esvelt's gene drive efforts states that 'there has never been a more powerful biological tool, or one with more potential to both improve the world and endanger it' [63, n.p.]. Claims of gene drives' power potential relate not merely to their possible effects, but also to the easy access to that power[11] [15, 27, 32]. The highly critical Sustainability Council of New Zealand regards gene drives as a technology that 'radically exceeds the existing boundaries of human power over nature' due to it conferring 'the ability to rapidly eliminate or reengineer entire species that have evolved over millions of years' [43, p. 16] and to deliver 'extinction to order or […] permanent reengineering of wild species' [43, p. 62].

[11] Especially since CRISPR made genome editing far more accurate and far less expensive and labour-intensive.

Part of what makes gene drives such an interesting case is that they were kind of "stumbled upon" in laboratory settings [3, 5], after which their potential real world effects—both intended and unintended, both beneficial and undesirable—were quickly realized and became guiding for both the development of the technology and the debate surrounding it. In this context, much of what has triggered attention and subsequently been said about gene drives has been a reaction to the hypothesized variant that "started it all": what has, with some hindsight, been labelled the universal or standard drive, which does not limit itself to local members of the species and has potentially wide population and ecosystem effects [15, 21]. Combined with the option of using a gene drive to eradicate, not modify, a population, this has led to the (un) popular image of this technology driving entire species extinct [43, 64, 65]. Given the obvious gravity of this ultimate possibility, a lot of attention has since gone out to softening the sharp edges of the (image of the) universal extinction drive. This has been done in a number of ways.

First of all, there were the initial calls for laboratory safety and science self-regulation that emerged together with the first publications on the newly discovered potential of synthetic gene drives [4, 15, 27, 59, 66–68] ([69] provide a more recent reiteration). The aim of these calls was to prevent potentially highly effective gene drives from either escaping the lab or leaving it without due consideration, in the absence of a regulatory system catered specifically to gene drives. The underlying concern for some of these authors was to prevent harm to public trust in gene drive development and science more broadly [15, 66, 68]. Secondly, and in further regard to this regulatory void [70], calls have been made to adjust existing risk assessment and regulatory frameworks to accommodate the novel features presented by gene drives[12] [1, 15, 33, 39, 40, 42, 53, 59, 61, 71–81]. The point here is that existing frameworks are too restrictive to allow for the proper assessment and testing of gene drives, being based on prior biotechnological developments that lacked gene drives' spreading properties. These proposed adjustments to existing frameworks thus support the third category of responses, those that emphasize the need for further experimentation and testing, from laboratory to highly controlled field trail to first field release [1, 13, 15, 16, 39, 71, 77, 82]. The great potential of gene drives for both benefits and harms is here suggested to vindicate conducting further research under careful conditions in order to understand effects in natural systems and to assess the risks involved. Publications detailing the conditions for safe field trials belong to this category [22, 33, 46–50]. Fourthly, and responding to the diagnosis of a regulatory void in a different way, various publications have stressed the need for international governance agreements to fit gene drives' disregard for human legislative boundaries [1, 14, 15, 21, 24, 29, 31, 36, 42, 43, 46, 48, 75, 83–86]. Gene drives' spreading properties are here taken to mean that a decision on a gene drive release ought to include governments of all territories where the gene drive modification might spread towards.

Fifthly, a substantial proportion of the more recent gene drive debate has revolved around the advocacy of public inclusion in general and of local community engagement and decision-making regarding gene drive releases in particular [14, 25, 38, 41, 42, 46, 48, 50, 69, 71, 84, 87–98]. While endorsement of community engagement as a principle of decision-making is not specific to gene drives or to technology development, the emphasis it receives in the gene drives debate does appear linked to the technology's idiosyncrasies. The combined features of deliberately causing modification or decimation of a local population and the use of a novel mechanism of deliberate rapid genetic spread appear to strengthen these calls, as does the fact (in principle not gene drive specific) of the colonial history of the parts of the world where currently considered gene drive applications are located (such as New Zealand and Burkina Faso). Finally, and in close relation to the advocacy of community decision-making, more technical responses to gene drives' controversiality have proposed the development of altered or augmented drive systems that are *local* [15, 99]. The idea here is to limit the universality or irreversibility of the gene drive spread, or both, with proposals suggesting the development of drives that are self-exhausting [4, 100, 101], only spread if released above a certain threshold

[12] This is what Evans and Palmer [160] call anomaly handling through system modification: changing the regulatory framework (the system) in order to accommodate gene drives (the anomaly).

[102–104], reverse the change made by a previous gene drive release [3, 105, 106][13], or are designed to target specific parts of genes (alleles) that occur exclusively in particular local populations [47, 48, 99, 107]. There have also been proposals for "split-drives", which separate the core components required for a fully functional gene drive [105, 108–114][14]. The connection to the community engagement proposals is that these augmented drives would make local decisions on a gene drive release legitimate decisions: a local decision about a local technology [32, 100].

The relevance for our purposes of these six categories of proposals for responsible gene drive development is that despite their obvious specificities, each aims at defusing concerns over gene drives, at reducing the technology's controversiality, at making their future use morally legitimate. Gene drives were stumbled upon, after which their promises and perils were soon realised and strategies to neutralise concerns and legitimize their application were adopted: calls for (self)regulation that would not block further research and testing, calls for community engagement, and the development of technical solutions to control potential negative effects. We return to this legitimizing tendency in the gene drive debate in our analysis of Gene Drives as Interventions. What is important to note is that in its legitimizing and defusing focus, the gene drive debate tends to misrepresent scientific and technological development. The quick and prominent emphasis on addressing the normative, ethical or moral implications of gene drives disregards how these implications are deeply interrelated with fundamental questions about what gene drives are; that coproduction is taking place. As we will explain in the next section, how gene drives are ontologically framed cannot be regarded separately from moral views about gene drives.

[13] Combinations of these types are also suggested [15].

[14] These drives are more focussed on safety and controllability than localness per se. In what follows we devote more attention to the idea of "local" drives.

Coproduction of Morality and Ontology

The Coproduction Thesis

Inspired by contemporary scholarship in Science and Technology Studies and philosophy of technology, we have analysed the empirical (ethnographic and literature) material through a theoretical framework of *coproduction* that focuses on the interplay between ontological and moral assumptions in the gene drive debate. Frameworks of coproduction have become widely used to explore dynamic processes and feedback loops at the interface of science and society [115–117]. The basic underlying idea is simple: 'the ways in which we know and represent the world (both nature and society) are inseparable from the ways in which we choose to live in it' [55, p. 2]. While in Jasanoff's [55] influential framework the emphasis tends to be on the coproduction of "knowledge and norms"—or epistemological and moral assumptions—our particular focus on *ontology* and morality can be regarded as included in her notion of 'how we know and represent the world'. Coproduction for Jasanoff is not primarily about normativity in relation to how we gain knowledge, but in relation to that which knowledge is about: reality, the world, nature—the domain of ontology. Highlighting specifically the ontological dimension of coproduction allows us to focus on a particular dynamic of the gene drive debate that is crucial for understanding its moral and societal dimensions: its deep entanglement with assumptions about the status, demarcation and properties of nature and human action.

Our reading of the gene drive debate suggests three limitations of the debate in terms of ontology-morality coproduction. First, whereas the debate has been strongly and explicitly concerned with gene drives' moral implications, their ontological implications have received far less explicit attention. As will be illustrated, gene drive development is suffused with often implicit ontological assumptions about nature and human action. Secondly, if explicitly discussed, the ontological implications of and assumptions underlying gene drive development tend to be presented in a rather abstracted fashion—gene drives would change how we understand and give meaning to evolution, nature, or wilderness. This leads to stalemates in the debate between those concerned with specific, problem-solving applications and those concerned with moral and/or ontological questions. Finally, there is the divorce of the moral debate on gene drives from explicit recognition of ontological matters; the issue of misrecognition of their coproduced nature.

A key point of the coproduction framework is that coproduction is a pervasive and unavoidable social phenomenon. The coproduction thesis itself can therefore be regarded as an ontological claim about social reality. As a result, the concept of coproduction gives rise to a number of profound metaphysical questions[15]. We acknowledge these questions and their relevance, but consider addressing them beyond the scope and purpose of this article. Instead, we adopt the relatively uncontroversial version of the thesis that states that ontological and moral claims and assumptions are interconnected in scientific and technological development and debate. Against the backdrop of the wider coproduction thesis, we consider the main question to be not whether gene drives give rise to coproduction but rather *what kind* of coproduction. The answer to this question comes in two parts. First, gene drive coproduction relates explicitly to the ontology and morality of (parts of) *nature*; secondly, it relates to the idea of *interventions into* nature.

Gene Drives and the Coproduction of Nature

While any emerging technoscientific development can be analysed on the basis of ontological implications—what does it mean for our conceptions of ourselves, of reality, of the world, of categories used to distinguish between them?—due to their core features gene drives specifically draw the ontology *of nature*, and related questions of morality, right into the middle of technoscientific development. In a general sense, gene drives can be said to give rise to a coproduction of ontology and morality regarding nature in at least the following respects. First, gene drives make salient the question of the ontological and moral status of *evolution* (as part of the natural world more broadly), as they have been referred to as an intervention into evolution, as surpassing the rules of evolution, cheating evolution, and sculpting evolution [2, 24, 43, 51, 118]. Second, gene drives' potential lays primarily with their use to target *wild* populations, bringing the ontological and moral distinction between the human-controlled and non-human world to the fore [1, 3, 18, 19, 24, 43, 53, 54]. Third, and closely related, because gene drives are a naturally occurring phenomenon that has been discovered and subsequently noticed for its potential to be "harnessed" to devise human-designed variants [15, 119], gene drives foreground questions of the ontological and moral status of artefacts and hybrids ([17, 67, 92] illustrate gene drives giving rise to questions of naturalness; explicit ontological questions are raised by [1, 19, 44]). Fourth, certain potential gene drive applications give rise to the possibility of *species* eradication or modification, triggering discussion on what defines species and what their moral status is [42–44, 120, 121]. Finally, the debate about gene drives has been strongly steered by the suggestion of their highly efficient and irreversible spread and various attempts to downplay that high potential on the basis of the "reality" of natural processes. Because of this, gene drives have given rise to questions of the ontology of nature in terms of the intricacies of its actual functioning—its processes, its mechanisms, its relations, its connectivities, its components, its predictability vs. its unexpectedness—and our morally charged reverence thereof [43, 44, 122, 123].

As we will show in the following section, gene drives give rise to a coproduction of ontology and morality regarding nature in a particular way: they entail *interventions* into natural systems. The Sculpting Evolution lab defines its mission in part as seeking 'to develop tools capable of *precisely intervening* in the evolution of ecosystems' [52, n.p., emphasis added]. Preston and Wickson [44] argue that gene drives have ethical implications on three levels: their impacts on human and planetary wellbeing, the intentions driving the technology forward, and *the character of the interventions* they entail. More generally, various policy, regulatory and ethical publications represent the end point of current gene drive development in terms of future gene drive interventions [1, 13, 15, 16, 18, 30, 32, 45, 53, 77, 84, 91–94, 97, 118, 120, 124–131].

We hypothesize that the idea of an intervention, and of an intervention into nature more specifically, comes with particular ways of making the connection between morality and ontology salient and that the understanding of gene drives as interventions into nature matters for the coproduction dynamic of gene

[15] E.g.: whether ontology and morality are *always and necessarily* connected; whether it is a thesis about social reality only or about reality as such; whether the interconnection of ontology and morality pertains to human representations of reality only, or has some sort of "external", "worldly" existence beyond such representations.

drives. An intervention relation carries assumptions about what is intervened into or upon, but also about the intervener and the means and relation of intervention itself. Thus, an ontological assumption about what gene drives would intervene into is always also, at least implicitly, an assumption about the intervener and the nature of the action relation between the two. Moreover, importantly, the understanding of a gene drive as a specific intervention into a specific natural system or population is itself a powerful ontological representation, as it suggests the very possibility of cutting up reality into an intervention situation on the one hand and "the rest of the world" on the other.

Understanding gene drives in terms of an intervention-oriented coproduction dynamic has implications for our ability for and approach to critical engagement with the technology. It highlights how critical engagement with gene drives needs to address empirical, moral and ontological concerns together, and that this in turn requires a perspective that zooms out from a narrow focus on specific intervention context and relation. Such a perspective reveals how a view of gene drives as specific interventions into nature obfuscates the interventionism already present in the bioengineer's lab prior to any field release. A Perspective that Acknowledges Coproduction—Discussion returns to these implications. In the following section Gene Drives as Interventions, we first elaborate the specific ways in which gene drives have been framed in terms of the different dimensions that constitute an intervention.

Gene Drives as Interventions

Adapting the notion of "intervention" from political science [132], we argue that potential gene drive applications have been represented, and can be analysed, in terms of the ontology and morality of intervention along four dimensions [133]. First, because interventions occur between two parties or entities, the intervener and the intervened-upon, they come with distinctions between and definitions of who is causing change (the intervener) and who or what is being changed (the intervened-upon). Second, because interventions are cases of deliberate action, the boundary between intentional action and accidents and unintended consequences becomes ontologically and morally important. Thirdly, an intervention aims at realizing a desired change, and this aim is in turn based on regarding the intervened-upon as steerable, guidable, manageable and correctable and as in need of the projected change—all involving ontological and moral assumptions. Finally, interventions are deliberate actions for which the intervening party claims to have legitimating reasons[16], which creates a space for asking for moral justification. The moral justification relies on the definitions of who intervenes, who is intervened into, intentionality, problem, goal, and control of the other dimensions—on the definitions of the ontology of the gene drive intervention.

We maintain the fourfold typology as much as possible in what follows; however, because the dimensions clearly overlap, the discussion at times takes up two or more dimensions together.

Gene Drives as Externally Initiated Interventions: The Intervened-Upon

One of the key ontological questions to ask about gene drives is: what is the "intervened upon", exactly? The different ways gene drives give rise to coproduction of *nature* return here, now seen through the intervention lens. Is the intervened-upon the population that is being targeted by the gene drive? Is it the genetic composition of the population/species first and foremost? Or is it the local ecosystem, in which said population has created the problem of invasion or disease it is now being targeted for? Given gene drives' self-propagating feature, can we understand the intervened-upon as something circumscribed in time and space in the way the designation ecosystem suggests? And does "ecosystem" do enough justice to the human presence in those local systems where gene drives are to be deployed[17]? These definitional

[16] We emphasize that while a legitimation is always provided by the intervener, this is not the same as the suggestion that the intervention *is* legitimate. That an intervention occurs is also not necessarily a sign of its legitimacy, only of a particular legitimation context which grants that intervention its power. Legitimation and legitimacy mean different things—the former suggests that legitimation is provided, the latter something more, that it enjoys a widespread support (political definition) or adheres to certain principles of morality (philosophical definition).

[17] As all suggested "real world" applications of gene drives are clearly proposed to address problems-for-humans, it can be argued that it is into a human-nature problem field that the gene drive intervenes.

questions suggest a tension between acknowledging connectivity in nature and the ability to demarcate a gene drive intervention to convey legitimacy. We return to this tension in the sections below.

As indicated earlier, some commentators take a step further and argue that gene drives intervene into *evolution*, the evolutionary process, or evolutionary principles [1, 24, 32, 43, 44, 51, 53, 118]. Such suggestions raise the question what evolution is, and whether it is best understood as one big process or as many different smaller ones. It also raises questions about its relation to the concept of nature—for example, is evolution the process that gives rise to nature, or does nature encompass evolution? Our case study of Sculpting Evolution provides illuminating reflections on this point. The ethnography revealed at least six understandings or uses of evolution employed by the lab members: (1) natural evolution, the evolution of evolution theory, involving selection pressure, reproduction and fitness; (2) evolution as directed evolution, analogous to dog or flower breeding: changing the genetic composition of a population in response to a chosen and imposed selection pressure; (3) evolutionary stability, or the maintenance or restoration of a population's genetic composition after disturbance; (4) evolution of information, or the view that development of informational patterns and complexity is the most fundamental ontological and moral feature of the universe; (5) evolution as our most important source of inspiration or teacher; (6) evolution as a metaphor for required changes to the scientific enterprise.

But regardless of whether the application of the group's technologies lies in using bacteria to optimize the functions of proteins or in eradicating invasive species with ecological purposes in mind, the actual mechanism of evolution the group works with is evolution on the *molecular* scale, not the ecological scale—with the latter being the realm of evolution of organisms, populations or species. Therefore, in the group's consideration of using a gene drive mechanism for ecologically informed purposes, two understandings or meanings of evolution are involved: evolution as any change in the genetic composition of a (natural or laboratory) population in response to a (natural or deliberately introduced) selection pressure, and evolution as the grand natural process of biology—Nothing in Biology Makes Sense Except in the Light of Evolution[18]—which explains life on earth as we know it today and which helps us understand how and why ecological problems arise in the first place (populations coevolve with their environments). In the case of directed evolution, the group changes the selection pressure in order to stimulate a certain molecular composition to optimization—this is protein breeding[19], as it were. In the case of using a gene drive in natural contexts, the group would change not the selection pressure—that would be classic conservationism—but the genetic composition of *organisms* (see also [45] on gene drives in conservation). An answer to the question of what a gene drive intervenes into depends on the understanding of evolution. The bioengineers entertain different uses of the concept, and work in their daily practices with a conception of evolution that only formalistically shares its meaning with what is commonly invoked with the concept of evolution as the grand process of life on earth.

Furthermore, the bioengineers of both groups connect a sense of awe in the face of evolution[20] to taking design inspiration from evolution for new biotechnologies[21]. To them, evolution is not something you intervene into, but something you can use. Evolution thus shifts from being defined as the

[18] The title of a 1973 essay by evolutionary biologist Theodosius Dobzhansky.

[19] This metaphor was used by one of the group members during a conversation with the first author.

[20] While Preston's [44, 51, 161] suggestion that gene drives intervene into evolution is connected to a moral position of non-interference into nature, it shares with the Wageningen and MIT groups' bioengineers a sense of awe in the face of the process of evolution.

[21] One of the most interesting tensions encountered in Sculpting Evolution's written representations of their objectives and in observed meetings and conversations is that between, on the one hand, the desire and professed need to understand evolutionary mechanisms (as the group's website reads: 'Our laboratory seeks to understand why systems evolve in the ways that they do') and, on the other hand, the resignation to not understanding how it works, as long as it works. The group's director often alluded to this (not without a sense of humour): 'I've given up on trying to understand'; 'you keep saying you want to understand it, whereas I'm like: I don't give a damn how it works, just that it works'. Particularly concerning their "directed evolution" projects, various other group members remark on not knowing exactly why what happens, happens—the aim is to get reliable, repeatable results. This is a tension also present in the discussions of the Wageningen Microbiology group.

"intervened-upon" to being part of the intervention tool, and this shift in the ontological understanding of evolution in the intervention relation has implications for the moral evaluation of intervention and a gene drive intervention specifically. When evolution is not that which you intervene into using a gene drive, but that which you use to intervene, evolution has already been usurped into dominant practice, into the box of tools at our disposal. In this understanding of gene drives and evolution, gene drives would both work with and against evolution at the same time, and therefore cannot so easily be understood as the intervened-upon.

Gene Drives as Externally Initiated Interventions: The Intervener

Moving from the intervened-upon to the identity of the intervener, the gene drive debate shows a further interesting dynamic. In the case of Sculpting Evolution's early gene drive and similar initiatives, the developer of the intervention technology was to an important degree also the intervening party. Esvelt explicitly approached local communities in an attempt to connect the technology to a local problem. This double identity, manifested in an individual person, of lab scientist and technology 'marketer' is unusual in science. However, it reveals that the link between biotechnology developer and real world application is always there to a degree, if only for the reason that the biotechnology developer often needs the prospect of application in order for the technology to become successfully developed. It is precisely this link that becomes blurred in the emphasis on local community engagement and decision-making, central to the responses of the gene drive debate [14, 25, 38, 41, 42, 46, 48, 50, 69, 71, 84, 87–98]. The community engagement framing—that local communities are the most legitimate party to decide about gene drive interventions, coupled to proposals to develop "local" drives that allow incorporating local views into their design—leads to a transposal of the identity of the "intervener" from the bioengineer to the local community, and with this of the locus of the legitimacy requirement of the intervention. It is local communities that are seen as the legitimate party to intervene using a gene drive, and with this, their justifications become the focus of moral concern.

Moving towards a next dimension of intervention—the specific goal of bringing about a change to address a problem—there is an important further implication of this shift. The bioengineering potential of gene drives was first discovered or realized, and potential domains of application and actual contexts of use were only then envisioned and pursued. For a local community, however, dealing with a dire problem such as local biodiversity threats or malaria, the goal clearly precedes the means of intervention: the gene drive is the tool, one potential option among others. Various Sculpting Evolution members explicitly acknowledged the existence of these other options in conversation; however, their focus is necessarily circumscribed by the kind of contribution they can deliver, given their skills and expertise—if they want to contribute something to these problems, it will be a bioengineering solution. Yet, were the solution to follow the problem, rather than the other way around, gene drives may be more morally legitimate in the eyes of many.

Gene Drives as Forms of Deliberate Action

A lot of the initial energy in the gene drive debate went into drawing boundaries between accidental, unreflective, and malicious releases on the one hand, and deliberate, reflective, and benevolent releases on the other [1, 3, 27, 28][22]. This initial dynamic is understandable, given the stumbled-upon nature of the contemporary gene drive discoveries [3, 5] and the spreading properties of gene drives: the atmosphere upon publication of the first proofs-of-principle in 2014 and 2015 tended towards crisis management, of making sure no disasters would occur, and the involved scientific community accordingly emphasized assuming responsibility and applying self-regulation.

The gene drive community attempted to distinguish *interventions* (deliberate, well-conceived, legitimated) from accidents and ill-conceived releases, and to distinguish "actual" interventions

[22] Aside from the energy that naturally went into distinguishing these different options from each other, such as accident from malintent; the point here is that the debate centered on distinguishing wrongful gene drive development and release from good or right gene drive development and release, or—in other words—distinguishing legitimated interventions from wrongdoing.

from the experimentation and testing that leads up to them, which are not considered interventions yet. An important effect of this initial dynamic has been that the category of deliberate, reflective and benevolent gene drive uses received less attention as a potentially morally problematic domain. The separation between intentional/deliberate/benevolent and unintentional/accidental/malicious serves to distinguish proper source of moral concern from its neutral opposite, but this neutral opposite is then also represented as the solution to the morally problematic versions: embracing gene drives intentionally, deliberately, and benevolently is the antidote to unintentional, accidental or malicious gene drive releases [3, 15, 27, 28]. Particularly the initial narrative put forward by Sculpting Evolution's director Esvelt, subsequently resounded in many publications and media outlets, centres on the figure of the careless or inconsiderate (does not know any better) scientist or local community, who either develops or deploys a gene drive without the proper precautions and procedures in place ([32, 66, 68]; examples of popular media outlets profiling this message are [60, 134]). But with gene drives, there are reasons to question the outcome of this boundary work. With gene drives, there is a sense in which there is no neat separation between the intentional and unintentional, between the deliberate and the accidental. The very mechanism that explains gene drives' desirability when applied intentionally—rapidly spreading a genetic trait in the wild with certain permanent environmental effects—is also the mechanism that makes them undesirable. Precisely because the gene drive is designed to create a cascading population effect through rapid sexual reproduction, and to do so in a "wild" context, a natural context of interactivity—which is in terms of application its raison d'être—it can lead to all sorts of unintended consequences.

From the perspective of the coproduction framework, these dynamics of the gene drive debate involve connecting a certain ontological definition of gene drives to their moral evaluation. Attempts are made to associate conceptions of gene drives with the image of carefully considered interventions—although this occurs implicitly to an important degree. Recklessness and malintent are obviously morally wrong, but are not considered inherent to what gene drives are—the wider condition or context of their application determines their moral character. These (implicit) attempts at aligning the ontology of gene drives with that of the carefully considered (and thus morally legitimate) intervention trade on ambivalence in the ontology of gene drives. What is, and what is not, "part of" the gene drive? Should the effects of a gene drive release, both foreseen and unforeseen, both desired and undesired, both to the target population and to the wider ecosystem, be understood as part of what a gene drive is? Or are they outside of the definition of a gene drive, are they just "effects of"? Clearly, the more one includes such potential for harm, risk, uncertainty, and irreversibility into the understanding of what the gene drive is, the more difficult it becomes to argue that the legitimacy of a gene drive application is dependent on the specific application context. We return to these ambivalences in the next sections.

Gene Drives as a Specific Intervention—Steerable, Guidable, Manageable and Correctable

Part of the debate about gene drives has turned on whether that which the gene drive intervenes into can actually be considered steerable, guidable, manageable and correctable[23]. May we assume this for both the gene drive mechanism over successive generations of sexually reproducing organisms and for the local ecosystem in which it is deployed? To what extent? While the power of gene drives to affect natural populations is what triggered the specific trajectory the debate took, the extent to which gene drives would be precise and efficacious is very much dominating the scientific development of the technology at the moment [57, 58]. In both the Wageningen and MIT group, experimentally attaining a functional (gene) drive proves to be more difficult than expected[24]. Various scientific publications similarly indicate partial success stories [1, 11, 135–141], with stability of the gene drive mechanism over subsequent generations being the main issue.

[23] Four concepts derived from our definition of intervention [133].

[24] Moreover, both groups are engaged with modelling exercises on gene/split drives, attempts not at decisively proving that drive systems would work as projected, but at showing what factors would determine this success. This further suggests the state of uncertainty gene drive development finds itself in.

While many characterizations of gene drives refer to the effects on the target species, a common concern is the irreversibility of wider ecological consequences following gene drive release: 'no matter how we alter an ecosystem […] we can't guarantee that it will return to its original state, even if we remove the source of the change' [32, pp. 23–24]. Similarly, Esvelt & Gemmell [21, p. 2] state that 'the bottom line is that making a standard, self-propagating CRISPR-based gene drive system is likely equivalent to creating a new, highly invasive species: both will likely spread to any ecosystem in which they are viable, possibly causing ecological change'. Even regarding the proposals for drive systems that would not have these universal (standard, self-propagating) tendencies, Oye et al. [28, p. 1] remark that 'ecological effects would not necessarily be re-versed'. A recurring related topic in the gene drive literature is the complexity of the systems in which gene drives are to be deployed and the lack of knowledge and uncertainty this entails. Here, we recognize the final dimension of the coproduction of nature (see Gene Drives and the Coproduction of Nature) that revolved around the "reality of nature" being one of recalcitrance and unpredictability. When molecular biologists and chemists take their synthetic creation out of the laboratory and into the wild, they enter the realm of ecology, where the regularities of experimental conditions are nowhere to be found: 'our knowledge of ecosystem-level species interactions is limited' [15, p. S51][25].

In these contributions to the debate, specification of the uncertainty of engineering complex systems thus amounts to providing an overview of the potential wider risks of gene drives. In this regard, many of the factors commonly referred to under the rubric of "risks" in gene drive publications may be more appropriately understood as uncertainties, given that little or no reasonable estimate of the likelihood of occurrence nor a specific description of the effects can be provided. These characterizations of gene drives challenge the assumption that the involved intervention is based on knowing that the projected effect will actually be realized. The ethnographies revealed an interesting parallel between conversations of the two groups in this regard. In both cases, the bioengineers showed themselves concerned mainly with getting something to work, not with understanding why or how it works the way it does. Moreover, both groups displayed an ambivalent attitude to acknowledging uncertainty and unexpectedness. The role of uncertainty is acknowledged, but to a degree. Reference is often made to biology or nature "always finding a way" and being "unpredictable", while working on "reliable" and "safe" interventions into biology or nature; a vision of the recalcitrance of nature and life is combined with the effort to design reliable tools from and for natural and living systems, as if the two visions were not mutually exclusive.

In navigating this space between gene drive, wider ecosystem, control and uncertainty, there is discursive boundary drawing at play regarding the steerability, guidability, manageability and correctability of the intervened-upon. The development and discursive legitimation of nonuniversal and reversible drives [15, 100] accepts the possibility of the universal drive or the priorly released drive not doing what you want it to do—either explicitly or implicitly—and responds by providing an antidote, as it were. But what provides the certainty for the antidote working as planned, when it is designed to counter the lack of certainty of the original gene drive construct? Furthermore, these proposals for augmented drives rely on the narrow circumscription of the intervention situation. They appear intended to bring the geographic and temporal scales implied by the universal gene drive [142] down to a level where steerability, guidability, manageability and correctability seem more plausible.

It is relevant to return here to the early dynamics of the gene drive debate. The recognition of the power of gene drive technology (see The Current State of the Gene Drive Debate) led to calls for limiting the technology's power by designing modified drives [21, 27, 58, 99, 100]. A relevant question here is the extent to which the "power" of the gene drive mechanism should be assessed depending on *how far its effects reach*. Would a highly localized, but highly effective gene drive not be a very powerful technology? Would it not, in a way, be *more* powerful than

[25] Some authors have specified such general references to uncertainty and lack of knowledge into overviews of knowledge and research gaps [1, 17, 18, 22, 92, 128], which converge on mentioning factors such as mutations of the gene drive genetic element, gene transfer outside of the target species, reproduction and mate selection patterns, effects of species decline or eradication on ecosystem functioning, and likelihood of ecological niche of eradicated species becoming filled by other species.

one that is less "controlled"? Here, we see an important point of division between those that would challenge gene drives' moral justifiability on the basis of its unforeseen effects and those that would do so on the basis of its intended effects. For the former, improved controllability means reduced power; for the latter, it can also mean increased power of the technology.

Gene Drive Intervention as Coproduction

The previous sections showed how diverging understandings and representations of intervener, intervened-upon, intervention tool, intentionality, problem-solving and manageability shape moral reasoning about the legitimacy of a gene drive intervention. The morality of a gene drive intervention runs through each of these attempts at settling the ontology of the intervention and the domains—human and nature—it connects. In one sentence: the ontological dimensions of the intervention relation are inseparable from its moral dimensions.

The following self-description by MIT's Sculpting Evolution provides as good a summary illustration as any of how ontology and morality come together in the development of gene drives:

> Evolution gave rise to every living thing and all of human culture, but evolved systems are very different from those designed by humans. They're harder to predict and to design, and exhibit a frustrating tendency to evolve away from engineered behaviors. At the same time, harnessing and directing evolution can generate useful organisms and biomolecular tools that we could never have rationally designed. Our laboratory seeks to understand why systems evolve in the ways that they do, to develop tools capable of precisely intervening in the evolution of ecosystems with the guidance of interested local communities, and to cultivate wisdom sufficient to know whether, when, and how to proceed. [52, n.p.]

The passage reveals the ambivalent attitude towards evolution: the source of all of life, including human life; the superior process for designing organisms and molecules; the frustrating, ungraspable phenomenon which we need to understand better; the mechanism we can put to use, even without fully understanding it. It includes explicit reference to *intervening* in *the evolution of ecosystems*. It introduces the notion of community guidance in relation to ecosystem intervention. It implicitly refers to the demarcation between lab and outside world in the idea of *precise* intervention in the field through the tools developed by the group in the lab. And it alludes to wisdom and its cultivation, introducing a (perhaps *the*) fundamental philosophical and moral concept into the group's main objectives.

The above analysis supports the hypothesis that the idea of an intervention, and of an intervention into nature more specifically, comes with a particular mode of making the connection between ontology and morality salient. Who the intervener is, how we define the intervened upon, how we circumscribe and distinguish the two; when a course of action is deemed an intervention, a form of deliberate action, and when it is something else; who is considered to legitimately speak on behalf of the intervened-upon and its needs—these are all matters bringing ontological and moral concerns together, foregrounded by the idea of intervention. Furthermore, questions about what nature is, how its relations, processes or components should be understood regarding the idea of nature, how fundamental and unchangeable or dynamic and malleable it is, what evolution is and means, and how human beings should act towards, within, or as part of nature are additionally triggered by the idea of a gene drive as an intervention *into nature*.

However, what also emerges from the analysis is that if a gene drive is an intervention into nature, it is a quite particular one. The explicit aim of causing deliberate, rapid spread of genetic modification through a population (something to be avoided at all cost with regular GMOs [59]); the type of thinking about scales and demarcation such spreading triggers; evolution as that which the gene drive intervenes into, but also that which the technology uses or is based on—these and other dimensions of gene drives give a particular ring to its coproduction of ontology and morality along the intervention axis. Moreover, the analysis shows that a lot of discursive work goes into bringing morality and ontology into alignment in such a way that the image of a legitimate gene drive intervention results—an endeavour that proves difficult, given gene drives' particularities. Gene drive development is imbued with particular, partly contradictory, conceptions of nature, ranging from biochemistry-based denials of boundaries between artificial and natural, to defenses of gene drives on the basis of their "naturalness" and pleas against the technology for interfering with natural processes.

To what degree gene drive interventions should actually be embraced remains deeply contested (e.g. [43, 44]; see also various responses to gene drives by NGOs and activist groups such as the ETC Group [143] and Friends of the Earth [144]). The aforementioned particularities explain why gene drives are a controversial emerging technology, and why so much work has gone and is going into turning the initial image of a universal, irreversible, globally spreading, species-eradicating gene drive into something less controversial, something more politically and socially legitimate(d), something more morally acceptable. In the next section, we reflect on these efforts of gene drive development and debate by proposing what our framework of intervention-oriented coproduction could bring to the way we understand and give meaning to gene drives and by extension to technoscientific development more broadly.

A Perspective that Acknowledges Coproduction—Discussion

We have seen how gene drives can be analysed in terms of their character as interventions, and how this reveals particularities of their coproduction dynamic. One issue that has remained implicit in this discussion, however, is that the representation of gene drives as involving particular, discrete interventions is allowing only certain ethical or moral issues to come into view; that is, only those issues that relate to the particular intervention context and relation. This implicit representation relies on coproduction for its framing: it connects ontology and morality in a certain way and represents them as local phenomena. In what follows, we suggest that adopting a wider analytical perspective that takes the coproduction thesis seriously challenges the ontological and moral assumptions of gene drives as specific, future interventions into nature.

A perspective that acknowledges coproduction provides a crucial challenge for the moral evaluation of gene drives. After the high-profiled 2014 and 2015 publications, the debate turned to case-specific descriptive and normative ethics [18, 26, 69, 91, 94, 125, 127, 145–148] and proposals for responsible further development [1, 14, 15, 21–23, 27–35, 37] quickly—perhaps too quickly. However, it is difficult to engage in a first-order normative evaluation if normative disagreements partly arise from different ontological perspectives of how to situate gene drives in competing understandings of nature. Furthermore, proposals for responsible further gene drive development tend to cherry-pick, locating ontology and morality in some places but not others, and denying their entanglement. These quick turns to normative ethics and responsible science proposals leave a number of key fundamental questions of coproduction unturned. One of these asks whether human beings are capable of including the nonhuman world into their ethical analyses nonanthropocentrically, and if so, how this can be done. A second asks to what extent and in what way we can ask and attempt to answer ethical questions without talking about ontology at the same time (or at least without accepting that one is grossly oversimplifying the answer). A third, in close relation to the former, asks to what extent the clearly demarcated case of the ethical analysis has truth-value concerning the actual, much more fluid, moral universe.

Asking such questions of coproduction leads to a number of insights about ontological and moral considerations relevant to gene drives that escape the particular intervention context. First of all, if our moral concerns only focus on specific gene drive interventions this would leave concerns about a wider context of interventionism outside of the consideration. Secondly, interventionism is revealed to already start in the lab, prior to any potential "real-world" intervention. These two insights are addressed in what follows.

A Wider Context of Interventionism as the Key Moral Issue

The focus on gene drives as particular interventions has as part of its coproduction dynamic the effect of leaving a broader cultural context of interventions outside of the normative consideration. However, this wider cultural context of human interventions into nature—of intervention*ism*—forms for many the very moral background condition to the question of why gene drives are morally relevant or controversial in the first place. One direction for the future of gene drives would be to embrace their transformative potential as part of a wider interventionist perspective on technology as tools for fundamentally reshaping nature and its underlying mechanisms (as discussed by Sandler [45]). However, interventionism is deeply contested and is not the only choice for the future of human-nature relations, nor more specifically for the coproduction of ontology and morality regarding nature [149]. Traditional conservationism, for example, resists the promises of reshaping nature through the power of technologies, diverging from interventionism in its normative assessment and in defending a stricter ontological-moral division of nature and culture. Alternatively, for approaches inspired by (among others) ecofeminism, political ecology, and Indigenous ethics that emphasize reciprocal relationality with and agency of nonhumans [150, 151], the ontological-cum-moral objection to interventionism is directed at the hierarchical structure of its human-nature relations, in which humans intervene and nonhumans are intervened-upon.

A shift in perspective from intervention to interventionism has implications for claims to legitimacy of particular gene drive interventions, that rely—as we have seen—on an assumption of demarcatability. It raises doubts about whether considerations of specific gene drive interventions can actually exclude a wider cultural context of interventionism. Gene drives can be regarded as reflecting a history of human interventions into nature and a wide range of contemporary technologies and interventions. Moreover, the use of a gene drive to address conservation, disease eradication, and agricultural problems can be seen to reflect the grand contextual issue of human dominance on a planet of anthropogenic climate change and ecological crises. In conservation, for example, gene drives are considered and defended according to an "end justifies the means" argument [45], where the end entails maintaining the state of the system as it has recently existed. However, today's ecological disruption is not locally determined—its root is understandable only as a to an important degree supralocal—global, earth system—phenomenon. To fight the ecosystem disruption using a gene drive under a last resort legitimation is to leave the root problem—a state of heightened disruption due to anthropogenic (climate) change—outside of the definition of the intervention context and outside of the legitimation.

The gene drive debate has tended to steer our imagination of the relevance of gene drives towards the extremes of reckless accidental and deliberate release, and at times malicious release [1, 3, 27, 28]. But recklessness and maliciousness are morally unambiguous—we know that they are wrong, and thus we concern ourselves with ways of preventing them[26]. From the perspective of a critical outlook on interventionism, however, the most important realm of morality for gene drives lies in the in-between of these two unambiguous extremes: the realm of deliberate, well-intended release or intervention. Particularly the emphasis on unforeseen consequences, risk and uncertainty [1, 15, 19–21, 23, 27] illustrates how interventionism itself is not what is normatively on the table: we are not challenging the use of interventions to address human-nature problems, we are challenging "reckless" intervention or non-intervention (accidents). If there is reasonable certainty that the desired change to the intervened-upon is to occur as projected, we allow for it.

The Interventionism in the Bioengineer's Lab

In this regard, interventionism arguably becomes a stronger presence with every attempt to technically modify gene drives such that they become more localizable and controllable. By moving from the possibility of accidental releases and safety measures to guard against those to deliberate releases, for the purpose of great benefits, and the specific conditions under which those may occur, the gene drive discourse moves further and further towards interventionism. Limiting the gravity of the intervention "in the wild" can only be accomplished by increasing the interventionism "in the lab". A wider coproduction perspective challenges the commonsensicality of the view that gene drives would involve interventions only once they are field-released. Important boundary work occurs here: the moral questions arise only once the gene drive gets into contact with the "outside world". What precedes the real world gene drive application, however, is the bioengineer's development of the technology. The split between outside and inside the laboratory—a powerful ontological

[26] Which is not to say that determining the extent to which a technology allows for/plays into recklessness or maliciousness is similarly straightforward, nor that attributing them to specific instances of behaviour is.

representation—masks how interventionism starts in the lab.

To illustrate the looming presence of interventionism in the lab, consider the Wageningen group's PhD researcher. The project revolved around the creation of a split drive in yeast with *further research* as its main application. Thus, the precise design is not to be applied to one of the main "real world" problems of human health and environmental and biodiversity challenges. This particular feature of the involved design suggests a distance from the interventionist potential of gene drive technology mentioned earlier. However, what became clear during the ethnography was that this potential was always present in the background of the daily work of the PhD researcher's project. While getting a functional split drive in the lab was the (at times frustratingly difficult to achieve) objective, the envisaged subsequent step was to work on a drive system to support the work of using them "in the wild" in a hoped-for acceptable manner. Furthermore, in explaining the research to students and interested parties, the morally controversial nature of gene drives and their future use as interventions was a central part of the PhD researcher's narrative. The key take-away here is that in both the experimental work and in the context the PhD researcher tried to navigate, the intervention(ist) potential of gene drives was always present in the background.

More importantly perhaps, questioning the view of nature as that which exists "out there" recognizes that the core of the bioengineer's work *is* intervention into nature. The idealized image of the scientist is that of someone who attempts to *understand* nature. Our experience in observing conversations between bioengineers conversely emphasizes the extent to which these scientists do not necessarily know *how* things work, but *that* they work and *to what effect*. Their objective is to realize an effect, to execute a desired change. Sculpting Evolution's aforementioned views on "directed evolution" are a case in point here. What further emerges from both ethnographies is that bioengineering is discursively represented as a domain of ultimate opportunity. *The sky is the limit, the only limitation is your imagination* is what the Wageningen group's PhD supervisor tells bioengineering graduate students during a lecture on the future of CRISPR; *you can engineer (almost) anything* is the name of a bioengineering course provided at MIT in which Kevin Esvelt participates. The limitation to what is possible is considered in principle not to exist *scientifically*, and limitation can therefore only stem from two sources: your own limitedness of imagination and ability, or the outside world that imposes it.

In the latter regard, it is worth mentioning that the Wageningen group's PhD supervisor, during the aforementioned lecture, referred to "ethics" as one of three challenges to further CRISPR development. When asked about this representation, the PhD supervisor explained that we should stop doubting the technical side of CRISPR and that we should move on to addressing the involved questions of ethics—questions "we as scientists cannot provide" and need to be provided by society (personal communication). This underlines how the demarcation of lab from outside world is often also understood as a moral demarcation. For the PhD supervisor, ethics is perceived as something belonging to the domain outside of the lab, to society. More generally, the gene drive debate has tended to embrace similar representations from the outset: once something *escapes* from the lab, we enter the domain of ethics—the moral world is the outside world, and it invades the lab only by grace of a projected potential mishap, the origin of which can be traced back to the lab.

Conclusion

The debate about gene drives has been explicitly moral from the outset. The concerns about undesirable releases of gene drives that emerged together with their initial promises and the technology's poster child applications in health and conservation pulled the gene drive debate—including, notably, individual scientists and research groups—deeply into discussions about the ethics and politics of science and technology. However, the connection between this normativity on the one hand and underlying ontological assumptions about gene drives, nature, and human-nature relations on the other—so important to understanding the precise nature of the moral claims being made—has tended to remain implicit.

Our focus on intervention has aimed to make these connections more explicit. The intervention concept focuses our attention on the intervener, on what is to be implemented, and on the relation between the two. It emphasizes the importance of projection into the future, a feature central to technoscience in its concern with providing "real world solutions". With gene drives, this temporal dimension is crucial. After gene drives were stumbled upon in laboratory settings, their potential future effects were quickly realized and became guiding for both the development of the technology and the surrounding debate. Thus, in a leap of imagination, as it were, the potential future effects of gene drives were projected and made into a constitutive part of the technology in one move. Nowhere in this process—that occurred rapidly and outside of formal regulative and policy-making institutions—was there a real world application or experiment present yet.

Developing a critical, considered account of gene drives requires recognizing the coproduction of ontological and moral assumptions and recognizing that it is channelled by a framing of gene drives as potential future interventions into nature. Our ethnographic and literature analyses have shown that gene drive development is not a value-free repository of facts from which others develop ontological and moral assessments. Contemporary gene drive development is guided by a specific, intervention-oriented, form of coproduction. These considerations highlight the need for a broadening of the perspective on gene drives in which empirical, moral, and ontological concerns are addressed explicitly and in their interplay rather than in (disciplinary) isolation from each other.

What could such an integrated perspective bring? We conclude with an illustration. A critical reading of an article in *Science* [39] by a group of key contributors to gene drive development and debate[27] suggests how the advocacy of local community engagement provides only partial recognition of—or "cherry picks"—morality and ontology and their interplay. The authors introduce the relevance of gene drives by suggesting that their transformative potential does not in the first place reside in the actual transformations to the natural environment they would effect, but rather in their potential influence on 'the way societies address a wide range of daunting public health and environmental challenges' [39, p. 1417]. In the vocabulary of this article: gene drives' transformative potential lies in embracing a particular variant of intervention(ism) to address certain human-nature problems. This is an astute observation very much in line with a more considered view on technology, intervention, and the coproduction of ontology and morality. However, while the authors frame the stakes of gene drive development in terms of this *substantive* point, the actual normative content of the article does not reflect this insight[28]. The article is about due (fair, just) process of gene drive field testing.

It is to an important degree appreciable that the authors leave the "substance" to others, to the public, to the local communities where gene drive interventions may be deployed; all they want is a good process that makes sure the public can bring *their* substantiveness to the table. But there are issues with this position. Given the repeated emphasis on the centrality of local community involvement, it suggests that the substance of gene drives—their moral and ontological implications—is a local affair. Interestingly, this representation of gene drives implicitly presents a meta-position on coproduction; namely, one which does not so much suggest that certain moral and ontological assumptions come together, but that ontology and morality—as social phenomena—themselves exist and interact locally. In other words, this group of initiates, representative of the gene drive debate, is engaging in coproduction as a framing strategy (though they may not be aware of this). However, while recognition of cultural diversity, democratic decision-making and colonial past rightly supports the attitude of giving local communities the determining voice in these matters, we can question the extent to which ontology and morality and their coproduction can be understood as local. In an important sense, ontological and moral commitments and assumptions are considered to be true *non*-locally by those espousing them. Acknowledging ontology-morality coproduction in relation to interventionism (as we introduced in A Perspective

[27] Both scientific and beyond, and including Esvelt among various authors who figure prominently in the references of our analysis of the gene drive debate. See [39] in reference list for full overview of involved authors.

[28] As the following quote summarizing the authors' intentions indicates: 'By presenting our commitments for field trials of [gene drive organisms], we aim to prepare for potential field trials that are scientifically, politically, and socially robust, publicly accountable, and widely transparent. Our intent is to contribute to public policy decisions on whether and how to proceed with GDOs, based on evaluations conducted in fair and effective partnerships with relevant authorities and other stakeholders.' [39, p. 1419]

that Acknowledges Coproduction—Discussion) further supports viewing gene drives as a non-local technology.

Adopting a more integrated coproduction perspective can thus help bring to light particular tensions in proposals for morally and politically sound gene drive development. It suggests that the global vs. local gene drive juxtaposition of the gene drive debate has fed into a very spatial, scalar conception of technological intervention and its influence: *in order to* make the decision-making context a manageable, local one, the gene drive ought to be made such that its effects are local as well. But does technological influence work that way? Can we simply trace the lines of the genetic inheritance pyramid to see where a gene drive's effects lead or end? The implicit suggestion in the proposals for local community engagement in combination with local drives is that if the gene drive is not universal/self-propagating, is limited spatially, temporally, or both, it loses much of its controversiality. As long as the decision-making process is ethically sound, the resulting gene drive interventions will be so as well. Philosophically speaking, this is debatable, for it makes morality a matter of decision-making processes—it confuses politics with morality.

The point in raising these considerations is not to challenge the obvious necessity or unavoidability of localizing decision-making—of narrowing-down—in order to make matters concrete and practicable. The point is to reveal the underlying implicit ontological-moral assumption that such a narrowing-down is more than an unfortunately necessary reduction of ontological and moral complexity; that by such narrowing-down and cutting up the world into specific intervention contexts, all factors and considerations considered non- or supralocal are excluded not because they are too difficult to incorporate, but because they actually do not form part of the ontological and moral reality of the local situation. Neither the development nor ethical assessment of gene drives can circumvent the wider challenge of competing modes of coproducing ontology and morality of gene drives and the issues with demarcatability these suggest.

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Declarations

Ethical Approval Keje Boersma's PhD research project has been approved by the Social Sciences Ethics Committee of Wageningen University.

Informed Consent Informed consent was provided by the members of the two research groups who participated in the study. The directors of both participating research groups approved of the final manuscript in terms of references to their group and its members.

References

1. National Academies of Sciences, Engineering, and Medicine (2016) Gene drives on the horizon: Advancing science, navigating uncertainty, and aligning research with

public values. Committee on Gene Drive Research in Non-Human Organisms: Recommendations for Responsible Conduct. Available online: https://nap.nationalacademies.org/catalog/23405/gene-drives-on-the-horizon-advancing-science-navigating-uncertainty-and
2. Champer J, Buchman A, Akbari OS (2016) Cheating evolution: Engineering gene drives to manipulate the fate of wild populations. Nat Rev Genet 17:146–159. https://doi.org/10.1038/nrg.2015.34
3. Esvelt KM, Smidler AL, Catteruccia AL, Church GM (2014) Emerging Technology: Concerning RNA-guided gene drives for the alteration of wild populations. eLife 3:e03401. https://doi.org/10.7554/eLife.03401
4. DiCarlo JE, Chavez A, Dietz SL, Esvelt KM, Church GM (2015) Safeguarding CRISPR-Cas9 gene drives in yeast. Nat Biotechnol 33:1250–1255. https://doi.org/10.1038/nbt.3412
5. Gantz VM, Bier E (2015) The mutagenic chain reaction: A method for converting heterozygous to homozygous mutations. Science 348(6233):442–444. https://doi.org/10.1126/science.aaa5945
6. Gantz VM, Jasinskiene N, Tatarenkova O, Fazekas A, Macias VM, Bier E, James AA (2015) Highly efficient Cas9-mediated gene drive for population modification of the malaria vector mosquito Anopheles stephensi. PNAS 112(49):E6736–E6743. https://doi.org/10.1073/pnas.1521077112
7. Hammond A, Galizi R, Kyrou K, Simoni A, Siniscalchi C, Katsanos D, Gribble M, Baker D, Marois E, Russell S, Burt A, Windbichler N, Crisanti A, Nolan T (2016) A CRISPR-Cas9 gene drive system targeting female reproduction in the malaria mosquito vector Anopheles gambiae. Nat Biotechnol 34:78–83. https://doi.org/10.1038/nbt.3439
8. Kyrou K, Hammond AM, Galizi R, Kranjc N, Burt A, Beaghton AK, Nolan T, Crisanti A (2018) A CRISPR-Cas9 gene drive targeting doublesex causes complete population suppression in caged Anopheles gambiae mosquitoes. Nat Biotechnol 36:1062–1066. https://doi.org/10.1038/nbt.4245
9. Li M, Yang T, Kandul NP, Bui M, Gamez S, Raban R, Bennett J, Sánchez CHM, Lanzaro GC, Schmidt H, Lee Y, Marshall JM, Akbari OS (2020) Development of a confinable gene drive system in the human disease vector Aedes aegypti. eLife 9:e51701. https://doi.org/10.7554/eLife.51701
10. Valderrama JA, Kulkarni SS, Nizet V, Bier E (2019) A bacterial gene-drive system efficiently edits and inactivates a high copy number antibiotic resistance locus. Nat Commun 10:572. https://doi.org/10.1038/s41467-019-13649-6
11. Grunwald HA, Gantz VM, Poplawski G, Xu X-RS, Bier E, Cooper KL (2019) Super-Mendelian inheritance mediated by CRISPR–Cas9 in the female mouse germline. Nature 566:105–109. https://doi.org/10.1038/s41586-019-0875-2
12. Kahn J (2016) Gene editing can now change an entire species – forever. TEDTalk Febuary 2016. https://www.ted.com/talks/jennifer_kahn_gene_editing_can_now_change_an_entire_species_forever?language=so. Accessed 28 Mar 2022
13. James S, Tountas KH (2018) Using Gene Drive Technologies to Control Vector-Borne Infectious Diseases. Sustainability 10(12):4789. https://doi.org/10.3390/su10124789
14. Kofler N, Collins JP, Kuzma J, Marris E, Esvelt K, Nelson MP, Newhouse A, Rothschild LJ, Vigliotti VS, Semenow M, Jacobsen R, Dahlman JE, Prince S, Caccone A, Brown T, Schmitz OJ (2018) Editing nature: Local roots and global governance. Environmental gene editing demands collective oversight. Science 362(6414):527–529. https://doi.org/10.1126/science.aat4612
15. Min J, Smidler AL, Najjar D, Esvelt KM (2018) Harnessing gene drive. Journal of Responsible Innovation 5(S1):S40–S65. https://doi.org/10.1080/23299460.2017.1415586
16. The Royal Society (2018) Gene drive research: Why it matters. The Royal Society. https://royalsociety.org/-/media/policy/Publications/2018/08-11-18-gene-drive-statement.pdf. Accessed 28 Mar 2022
17. Alphey LS, Crisanti A, Randazzo F, Akbari OS (2020) Standardizing the definition of gene drives. PNAS 117(49):30864–30867. https://doi.org/10.1073/pnas.2020417117
18. Kuzma J, Rawls L (2016) Engineering the Wild: Gene Drives and Intergenerational Equity. Jurimetrics 56:279–296
19. Nuffield Council on Bioethics (2016) Genome editing: An ethical review. The Nuffield Council, London. http://nuffieldbioethics.org/project/genome-editing/ethical-review-published-september-2016. Accessed 28 Mar 2022
20. RIVM (2016) Gene drives. Policy report. Letter report 2016–0023. Dutch National Institute for Public Health and the Environment. https://www.rivm.nl/bibliotheek/rapporten/2016-0023.pdf. Accessed 28 Mar 2022
21. Esvelt KM, Gemmell NJ (2017) Conservation demands safe gene drive. PLoS Biology 15(11):e2003850. https://doi.org/10.1371/journal.pbio.2003850
22. Moro D, Byrne M, Kennedy M, Campbell S, Tizard M (2018) Identifying knowledge gaps for gene drive research to control animal species: The next CRISPR step. Global Ecology and Conservation 13:e00363. https://doi.org/10.1016/j.gecco.2017.e00363
23. Noble C, Adlam B, Church GM, Esvelt KM, Nowak MA (2018) Current CRISPR gene drive systems are likely to be highly invasive in wild populations. eLife 7:e33423. https://doi.org/10.7554/eLife.33423
24. Norwegian Biotechnology Advisory Board (2017) Statement on gene drives. Biotecknologiradet, Oslo. http://www.bioteknologiradet.no/filarkiv/2017/02/Statement-on-gene-drives.pdf. Accessed 28 Mar 2022
25. Rudenko L, Palmer MJ, Oye K (2018) Considerations for the governance of gene drive organisms. Pathogens and Global Health 112(4):162–181. https://doi.org/10.1080/20477724.2018.1478776
26. Thompson PB (2018) The roles of ethics in gene drive research and governance. Journal of Responsible Innovation 5(S1):159–179. https://doi.org/10.1080/23299460.2017.1415587
27. Akbari OS, Bellen HJ, Bier E, Bullock SL, Burt A, Church GM, Cook KR, Duchek P, Edwards OR, Esvelt KM, Gantz VM, Golic KG, Gratz SJ, Harrison MM, Hayes KR, James AA, Kaufman TC, Knoblich J, Malik HS, Matthews KA, O'Connor-Giles KM, Parks AL,

Perrimon N, Port F, Russell S, Ueda R, Wildonger J (2015) Safeguarding gene drive experiments in the laboratory. Science 349(6251):927–929. https://doi.org/10.1016/j.socscimed.2021.113850
28. Oye KA, Esvelt K, Appleton E, Catteruccia F, Church G, Kuiken T, Lightfoot SB-Y, McNamara J, Smidler A, Collins JP (2014) Regulating gene drives. Science 345(6197):626–628. https://doi.org/10.1126/science.1254287
29. Webber BL, Raghu S, Edwards OR (2015) Is CRISPR-based gene drive a biocontrol silver bullet or global conservation threat? PNAS 112(34):10565–10567. https://doi.org/10.1073/pnas.1514258112
30. Burt A, Coulibaly M, Crisanti A, Diabete A, Kavondo JK (2018) Gene drive to reduce malaria transmission in sub-Saharan Africa. Journal of Responsible Innovation 5(S1):S66–S80. https://doi.org/10.1080/23299460.2017.1419410
31. Convention on Biological Diversity (2018) Decision on synthetic biology. Fourteenth meeting of the Conference of the Parties to the Convention on Biological Diversity, Sharm El-Sheikh, Egypt, 17–19 November 2018; CBD/COP/14/L.31, 28 November 2018 Page 2. https://www.cbd.int/doc/c/2c62/5569/004e9c7a6b2a00641c3af0eb/cop-14-l-31-en.pdf. Accessed 28 Mar 2022
32. Esvelt KM (2018) Rules for sculpting ecosystems. Gene drives and responsive science. In: Braverman I (ed) Gene editing, law, and the environment: Life beyond the human. Routledge, New York, pp 21–37
33. Hayes KR, Hosack GR, Dana GV, Foster SD, Ford JH, Thresher R, Ickowicz A, Peel D, Tizard M, De Barro P, Strive T, Dambacher JM (2018) Identifying and detecting potentially adverse ecological outcomes associated with the release of gene-drive modified organisms. Journal of Responsible Innovation 5(S1):S139–S158. https://doi.org/10.1080/23299460.2017.1415585
34. Leitschuh CM, Kanavy D, Backus GA, Valdez RX, Serr M, Pitts EA, Threadgill D, Godwin J (2018) Developing gene drive technologies to eradicate invasive rodents from islands. Journal of Responsible Innovation 5(S1):S121–S138. https://doi.org/10.1080/23299460.2017.1365232
35. Medina RF (2018) Gene drives and the management of agricultural pests. Journal of Responsible Innovation 5(S1):S255–S262. https://doi.org/10.1080/23299460.2017.1407913
36. Novak BJ, Maloney T, Phelan R (2018) Advancing a New Toolkit for Conservation: From Science to Policy. The CRISPR Journal 1(1):11–15. https://doi.org/10.1089/crispr.2017.0019
37. Scott MJ, Gould F, Lorenzen M, Grubbs N, Edwards O, O'Brochta D (2018) Agricultural production: Assessment of the potential use of Cas9-mediated gene drive systems for agricultural pest control. Journal of Responsible Innovation 5(S1):S98–S120. https://doi.org/10.1080/23299460.2017.1410343
38. Buchthal J, Evans SW, Lunshof J, Telford SR III, Esvelt KM (2019) Mice against ticks: An experimental community-guided effort to prevent tick-borne disease by altering the shared environment. Phil Trans R Soc B 374:20180105. https://doi.org/10.1098/rstb.2018.0105
39. Long KC, Alphey L, Annas GJ, Bloss CS, Campbell KJ, Champer J, Chen C-H, Choudhary A, Church GM, Collins JP, Cooper KL, Delborne JA, Edwards OR, Emerson CI, Esvelt K, Evans SW, Friedman RM, Gantz VM, Gould F, Hartley S, Heitman E, Hemingway J, Kanuka H, Kuzma J, Lavery JV, Lee Y, Lorenzen M, Lunshof JE, Marshall JM, Messer PW, Montell C, Oye KA, Palmer MJ, Papathanos PA, Paradkar PN, Piaggio AJ, Rasgon JL, Rasic G, Rudenko L, Saah JR, Scott MJ, Sutton JT, Vorsino AE, Akbari OS (2020) Core commitments for field trials of gene drive organisms. Science 370(6523):1417–1419. https://doi.org/10.1126/science.abd1908
40. Devos Y, Mumford JD, Bonsall MB, Glandorf DCM, Quemada HD (2022) Risk management recommendations for environmental releases of gene drive modified insects. Biotechnology Advances 54:107807. https://doi.org/10.1016/j.biotechadv.2021.107807
41. Kormos A, Lanzaro GC, Bier E, Santos V, Nazaré L, Pinto J, Aguiar dos Santos A, James AA (2022) Ethical considerations for gene drive: Challenges of balancing inclusion, power and perspectives. Frontiers in Bioengineering and Biotechnology 10:826727. https://doi.org/10.3389/fbioe.2022.826727
42. Wise IJ, Borry P (2022) An ethical overview of the CRISPR-based elimination of Anopheles gambiae to combat malaria. Bioethical Inquiry 19(3):371–380. https://doi.org/10.1007/s11673-022-10172-0
43. Sustainability Council of New Zealand (2018) A constitutional moment. Gene drive and international governance. Sustainability Council of New Zealand. http://www.sustainabilitynz.org/wp-content/uploads/2018/10/AConstitutionalMoment_September2018.pdf. Accessed 28 Mar 2022
44. Preston CJ, Wickson F (2019) Ethics and governance. In: Gene drives. A report on their science, applications, social aspects, ethics and regulations. Joint report by Critical Scientists Switzerland, European Network of Scientists for Social and Environmental Responsibility, and Vereinigung Deutscher Wissenschaftler, pp 215–253. https://genedrives.ch/report/
45. Sandler R (2020) The ethics of genetic engineering and gene drives in conservation. Conserv Biol 34(2):378–385. https://doi.org/10.1111/cobi.13407
46. Barnhill-Dilling SK, Serr M, Blondel DV, Godwin J (2019) Sustainability as a framework for considering gene drive mice for invasive rodent eradication. Sustainability 11(5):1334. https://doi.org/10.3390/su11051334
47. Campbell KJ, Saah JR, Brown PR, Godwin J, Gould F, Howald GR, Piaggio A, Thomas P, Tompkins D.M, Threadgill D, Delborne J, Kanavy DM, Kuiken T, Packard H, Serr M, Shiels A (2019) A potential new tool for the toolbox: Assessing gene drives for eradicating invasive rodent populations. USDA Wildlife Services - Staff Publications 2235. https://digitalcommons.unl.edu/icwdm_usdanwrc/2235
48. Godwin J, Serr M, Barnhill-Dilling SK, Blondel DV, Brown PR, Campbell K, Delborne J, Lloyd AL, Oh KP, Prowse TAA, Saah R, Thomas P (2019) Rodent gene drives for conservation: Opportunities and data needs. Proc R Soc B 286(1914):20191606. https://doi.org/10.1098/rspb.2019.1606

49. Harvey-Samuel T, Campbell KJ, Edgington M, Alphey L (2019) Trialling gene drives to control invasive species: What, where and how? In: Veitch CR, Clout MN, Martin AR, Russell JC, West CJ (eds) Island invasives: Scaling up to meet the challenge. Occasional Paper SSC 62. IUCN, Gland. pp 618–627
50. Serr ME, Valdez RX, Barnhill-Dilling KS, Godwin J, Kuiken T, Booker M (2020) Scenario analysis on the use of rodenticides and sex-biasing gene drives for the removal of invasive house mice on islands. Biol Invasions 22:1235–1248. https://doi.org/10.1007/s10530-019-02192-6
51. Preston CJ (2018) The synthetic age. Outdesigning evolution, resurrecting species, and reengineering our world. MIT Press, Cambridge, MA
52. Sculpting Evolution (no year) Overview. https://www.media.mit.edu/groups/sculpting-evolution/overview/. Accessed 28 Mar 2022
53. Delborne J, Kuzma J, Gould F, Frow E, Leitschuh C, Sudweeks J (2018) Mapping research and governance needs for gene drives. Journal of Responsible Innovation 5(S1):S1–S9. https://doi.org/10.1080/23299460.2017.1419413
54. Courtier-Orgogozo V, Morizot B, Boëte C (2017) Agricultural pest control with CRISPR-based gene drive: Time for public debate. EMBO Reports 18(6):878–880. https://doi.org/10.15252/embr.201744205
55. Jasanoff S (2004) States of knowledge: The coproduction of science and social order. Routledge, New York
56. Scott J, Marshall G (2009) A dictionary of sociology, 3rd edn. Oxford University Press, Oxford
57. Bier E (2022) Gene drives gaining speed. Nat Rev Genet 23:5–22. https://doi.org/10.1038/s41576-021-00386-0
58. Gantz VM, Bier E (2022) Active genetics comes alive: Exploring the broad applications of CRISPR-based selfish genetic elements (or gene-drives). BioEssays 44(8):e2100279. https://doi.org/10.1002/bies.202100279
59. Simon S, Otto M, Engelhard M (2018) Synthetic gene drive: Between continuity and novelty. EMBO Reports 19:e45760. https://doi.org/10.15252/embr.201845760
60. Matthews D (2018) A genetically modified organism could end malaria and save millions of lives — If we decide to use it. Vox. https://www.vox.com/science-andhealth/2018/5/31/17344406/crisprmosquito-malaria-gene-drive-editing-targetafrica-regulation-gmo. Accessed 28 Mar 2022
61. Meghani Z, Kuzma J (2018) Regulating animals with gene drive systems: Lessons from the regulatory assessment of a genetically engineered mosquito. Journal of Responsible Innovation 5(S1):S203–S222. https://doi.org/10.1080/23299460.2017.1407912
62. Doudna JA, Sternberg SH (2017) A crack in creation: Gene editing and the unthinkable power to control evolution. Houghton Mifflin Harcourt Publishers, Boston
63. Specter M (2017) Rewriting the code of life. The New Yorker. https://www.newyorker.com/magazine/2017/01/02/rewriting-the-code-of-life. Accessed 28 Mar 2022
64. The Economist (2016) Extinctions to order. Gene-ocide. The promise and peril of “gene drives”. The Economist 17 September 2016. https://www.economist.com/leaders/2016/09/17/gene-ocide. Accessed 28 Mar 2022
65. Regalado A (2016) Bill Gates doubles his bet on wiping out mosquitoes with gene editing. MIT Technology Review 6 September 2016. https://www.technologyreview.com/2016/09/06/244913/bill-gates-doubles-his-bet-on-wiping-out-mosquitoes-with-gene-editing. Accessed 28 Mar 2022
66. Esvelt KM (2016) Gene editing can drive science to openness. Nature 534:153. https://doi.org/10.1038/534153a
67. Emerson C, James S, Littler K, Randazzo F (2017) Principles for gene drive research. Science 358(6367):1135–1136. https://doi.org/10.1126/science.aap9026
68. Esvelt KM (2017) Precaution: Open gene drive research. Science 355(6325):589–590. https://doi.org/10.1126/science.aal5325
69. Annas GJ, Beisel CL, Clement K, Crisanti A, Francis S, Galardini M, Galizi R, Grünewald J, Immobile G, Khalil AS, Müller R, Pattanayak V, Petri K, Paul L, Pinello L, Simoni A, Taxiarchi C, Joung JK (2021) A code of ethics for gene drive research. The CRISPR Journal 4(1):19–24. https://doi.org/10.1089/crispr.2020.0096
70. Braverman I (2018) Gene drives, nature, and governance: An ethnographic perspective. In: Braverman I (ed) Gene editing, law, and the environment: Life beyond the human. Routledge, New York, pp 55–73
71. Adelman Z, Akbari O, Bauer J, Bier E, Bloss C, Carter SR, Callender C, Costero-Saint Denis A, Cowhey P, Dass B, Delborne J, Deveraux M, Ellsworth P, Friedman RM, Gantz V, Gibson C, Hay BA, Hoddle M, James AA, James S, Jorgenson L, Kalichman M, Marshall J, McGinnis W, Newman J, Pearson A, Quemada H, Rudenko L, Shelton A, Vinetz JM, Weisman J, Wong B, Wozniak C (2017) Rules of the road for insect gene drive research and testing. Nature Biotechnology 35(8):716–718. https://doi.org/10.1038/nbt.3926
72. Krishnan P, Gillum D (2017) Gene Drive 101: A basic guidance resource for biosafety professionals. Applied Biosafety 22(4):181–184. https://doi.org/10.1177/1535676017731318
73. Benedict MQ, Burt A, Capurro ML, De Barro P, Handler AM, Hayes KR, Marshall JM, Tabachnick WJ, Adelman ZN (2018) Recommendations for laboratory containment and management of gene drive systems in arthropods. Vector-Borne and Zoonotic Diseases 18(1):2–13. https://doi.org/10.1089/vbz.2017.2121
74. Van der Vlugt CJB, Brown DD, Lehmann K, Leunda A, Willemarck N (2018) A framework for the risk assessment and management of gene drive technology in contained use. Applied Biosafety 23(1):25–31. https://doi.org/10.1177/1535676018755117
75. Rabitz F (2019) Gene drives and the international biodiversity regime. Review of European, Comparative & International Environmental Law 28(3):339–348. https://doi.org/10.1111/reel.12289
76. Dolezel M, Lüthi C, Gaugitsch H (2020) Beyond limits – the pitfalls of global gene drives for environmental risk assessment in the European Union. BioRisk 15:1–29. https://doi.org/10.3897/biorisk.15.49297
77. James SL, Marshall JM, Christophides GK, Okumu FO, Nolan T (2020) Toward the definition of efficacy and safety criteria for advancing gene drive-modified

mosquitoes to field testing. Vector-Borne and Zoonotic Diseases 20(4):237–251. https://doi.org/10.1089/vbz.2019.2606
78. Naegeli H, Bresson JL, Dalmay T, Dewhurst IC, Epstein MM, Guerche P, Hejatko J, Moreno FJ, Mullins E, Nogué F, Rostoks N, Sánchez Serrano JJ, Savoini G, Veromann E, Veronesi F, Bonsall MB, Mumford J, Wimmer EA, Devos Y, Paraskevopoulos K, Firbank LG (2020) Adequacy and sufficiency evaluation of existing EFSA guidelines for the molecular characterisation, environmental risk assessment and post-market environmental monitoring of genetically modified insects containing engineered gene drives. EFSA Journal 18(11):e06297. https://doi.org/10.2903/j.efsa.2020.6297
79. Then C, Kawall K, Valenzuela N (2020) Spatiotemporal controllability and environmental risk assessment of genetically engineered gene drive organisms from the perspective of European Union genetically modified organism regulation. Integr Environ Assess Manag 16(5):555–568. https://doi.org/10.1002/ieam.4278
80. Devos Y, Bonsall MB, Firbank LG, Mumford J, Noqué F, Wimmer EA (2021) Gene drive-modified organisms: Developing practical risk assessment guidance. Trends Biotechnol 39(9):853–856. https://doi.org/10.1016/j.tibtech.2020.11.015
81. Kuzma J (2021) Procedurally robust risk assessment framework for novel genetically engineered organisms and gene drives. Regulation & Governance 15(4):1144–1165. https://doi.org/10.1111/rego.12245
82. Mitchell PD, Brown Z, McRoberts N (2018) Economic issues to consider for gene drives. Journal of Responsible Innovation 5(S1):S180–S202. https://doi.org/10.1080/23299460.2017.1407914
83. Rabitz F (2022) The international governance of gene drive organisms. Environmental Politics 31(6):949–968. https://doi.org/10.1080/09644016.2021.1959756
84. Teem JL, Ambali A, Glover B, Ouedraogo J, Makinde D, Roberts A (2019) Problem formulation for gene drive mosquitoes designed to reduce malaria transmission in Africa: Results from four regional consultations 2016–2018. Malar J 18:347. https://doi.org/10.1186/s12936-019-2978-5
85. Reynolds JL (2020) Governing new biotechnologies for biodiversity conservation: Gene drives, international law and emerging politics. Global Environmental Politics 20(3):28–48. https://doi.org/10.1162/glep_a_00567
86. Reynolds JL (2021) Engineering biological diversity: The international governance of synthetic biology, gene drives, and de-extinction for conservation. Current Opinion in Environmental Sustainability 49:1–6. https://doi.org/10.1016/j.cosust.2020.10.001
87. Roberts A, Andrade PP, Okumu F, Quemada H, Savadogo M, Singh JA, James S (2017) Results from the workshop "Problem Formulation for the Use of Gene Drive in Mosquitoes." Am J Trop Med Hyg 96(3):530–533. https://doi.org/10.4269/ajtmh.16-0726
88. Brossard D, Belluck P, Gould F, Wirz CD (2019) Promises and perils of gene drives: Navigating the communication of complex, post-normal science. PNAS 116(16):7692–7697. https://doi.org/10.1073/pnas.1805874115
89. Hartley S, Thizy D, Ledingham K, Coulibaly M, Diabaté A, Dicko B, Diop S, Kayondo J, Namukwaya A, Nourou B, Paré Toé L (2019) Knowledge engagement in gene drive research for malaria control. PLoS Neglected Tropical Diseases 13(4):e0007233. https://doi.org/10.1371/journal.pntd.0007233
90. Resnik DB (2019) Two unresolved issues in community engagement for field trials of genetically modified mosquitoes. Pathogens and Global Health 113(5):238–245. https://doi.org/10.1080/20477724.2019.1670490
91. Singh JA (2019) Informed consent and community engagement in open field research: Lessons for gene drive science. BMC Med Ethics 20:54. https://doi.org/10.1186/s12910-019-0389-3
92. Wedell N, Price TAR, Lindholm AK (2019) Gene drive: Progress and prospects. Proceedings of the Royal Society B: Biological Sciences 286:20192709. https://doi.org/10.1098/rspb.2019.2709
93. Thizy D, Coche I, De Vries J (2020) Providing a policy framework for responsible gene drive research: An analysis of the existing governance landscape and priority areas for further. Wellcome Open Research 5:173. https://doi.org/10.12688/wellcomeopenres.16023.1
94. De Graeff N, Jongsma KR, Bredenoord AL (2021) Experts moral views on gene drive technologies. BMC Med Ethics 22:25. https://doi.org/10.1186/s12910-021-00588-5
95. Kormos A, Lanzaro GC, Bier E, Dimopoulos G, Marshall JM, Pinto J, Aguiar Dos Santos A, Bacar A, Rompão SPS, H, James AA, (2021) Application of the relationship-based model to engagement for field trials of genetically engineered malaria vectors. Am J Trop Med Hyg 104(3):805–811. https://doi.org/10.4269/ajtmh.20-0868
96. Resnik DB (2021) Precautionary reasoning in environmental and public health policy. Springer, Cham
97. Thizy D, Pare Toe L, Mbogo C, Matoke-Muhia D, Alibu VP, Barnhill-Dilling SK, Chantler T, Chongwe G, Delborne J, Kapiriri L, Nassonko Kavuma E, Koloi-Keaikitse S, Kormos A, Littler K, Lwetoijera D, Vargas de Moraes R, Mumba N, Mutengu L, Mwichuli S, Nabukenya SE, Nakigudde J, Ndebele P, Ngara C, Ochomo E, Odiwuor Ondiek S, Rivera S, Roberts AJ, Robinson B, Sambakunsi R, Saxena A, Sykes N, Tarimo BB, Tiffin N, Tountas KH (2021) Proceedings of an expert workshop on community agreement for gene drive research in Africa - Co-organised by KEMRI, PAMCA and Target Malaria. Gates Open Research 5:19. https://doi.org/10.12688/gatesopenres.13221.2
98. Hartley S, Taitingfong R, Fidelman P (2022) The principles driving gene drives for conservation. Environ Sci Policy 135:36–45. https://doi.org/10.1016/j.envsci.2022.04.021
99. Sudweeks J, Hollingsworth B, Blondel DV, Campbell KJ, Dhole S, Eisemann JD, Edwards O, Godwin J, Howald GR, Oh KP, Piaggio AJ, Prowse TAA, Ross JV, Saah JR, Shiels AB, Thomas PQ, Threadgill DW, Vella MR, Gould F, Lloyd AL (2019) Locally Fixed Alleles: A method to localize gene drive to island

populations. Sci Rep 9:15821. https://doi.org/10.1038/s41598-019-51994-0
100. Noble C, Min J, Olejarz J, Buchthal J, Chavez A, Smidler AL, DeBenedictis EA, Church GM, Nowak MA, Esvelt KM (2019) Daisy-chain gene drives for the alteration of local populations. PNAS 116(17):8275–8282. https://doi.org/10.1073/pnas.1716358116
101. Min J, Smidler AL, Najjar D, Esvelt KM (2017) Daisyfield gene drive systems harness repeated genomic elements as a generational clock to limit spread. BioRxiv 104877. https://doi.org/10.1101/104877
102. Akbari OS, Chen C-H, Marshall JM, Huang H, Antoshechkin I, Hay BA (2014) Novel synthetic *Medea* selfish genetic elements drive population replacement in Drosophila; a theoretical exploration of *Medea*-dependent population suppression. ACS Synth Biol 3(12):915–928. https://doi.org/10.1021/sb300079h
103. Reeves RG, Bryk J, Altrock PM, Denton JA, Reed FA (2014) First steps towards underdominant genetic transformation of insect populations. PLoS ONE 9(5):e97557. https://doi.org/10.1371/journal.pone.0097557
104. Buchman AB, Ivy T, Marshall JM, Akbari OS, Hay BA (2018) Engineered reciprocal chromosome translocations drive high threshold, reversible population replacement in Drosophila. ACS Synth Biol 7(5):1359–1370. https://doi.org/10.1021/acssynbio.7b00451
105. Gantz VM, Bier E (2016) The dawn of active genetics. BioEssays 38(1):50–63. https://doi.org/10.1002/bies.201500102
106. Min J, Smidler AL, Najjar D, Esvelt KM (2017) Daisy quorum drives for the genetic restoration of wild populations. BioRxiv 115618. https://doi.org/10.1101/115618
107. Oh KP, Shiels AB, Shiels L, Blondel DV, Campbell KJ, Saah JR, Lloyd AL, Thomas PQ, Gould F, Abdo Z, Godwin JR, Piaggio AJ (2021) Population genomics of invasive rodents on islands: Genetic consequences of colonization and prospects for localized synthetic gene drive. Evol Appl 14(5):1421–1435. https://doi.org/10.1111/eva.13210
108. Xu XS, Gantz VM, Siomava N, Bier E (2017) CRISPR/Cas9 and active genetics-based trans-species replacement of the endogenous Drosophila kni- L2 CRM reveals unexpected complexity. Life 6:e30281. https://doi.org/10.7554/eLife.30281
109. Guichard A, Haque T, Bobik M, Xu X-RS, Klanseck C, Kushwah RBS, Berni M, Kaduskar B, Gantz VM, Bier E (2019) Efficient allelic-drive in Drosophila. Nat Commun 10:1640. https://doi.org/10.1038/s41467-019-09694-w
110. Champer J, Yang E, Lee E, Liu J, Clark AG, Messer PW (2020) A CRISPR homing gene drive targeting a haplolethal gene removes resistance alleles and successfully spreads through a cage population. Proc Natl Acad Sci USA 117(39):24377–24383. https://doi.org/10.1073/pnas.2004373117
111. Kandul NP, Liu J, Buchman A, Gantz VM, Bier E, Akbari OS (2020) Assessment of a split homing based gene drive for efficient knockout of multiple genes. G3 Genes|Genomes|Geneticsii 10(2):827–837. https://doi.org/10.1534/g3.119.400985
112. López Del Amo V, Bishop AL, Sánchez CHM, Bennett JB, Feng X, Marshall JM, Bier E, Gantz VM (2020) A transcomplementing gene drive provides a flexible platform for laboratory investigation and potential field deployment. Nat Commun 11:352. https://doi.org/10.1038/s41467-019-13977-7
113. Kandul NP, Liu J, Bennett JB, Marshall JM, Akbari OS (2021) A confinable home-and-rescue gene drive for population modification. eLife 10:e65939. https://doi.org/10.7554/eLife.65939
114. Terradas G, Buchman AB, Bennett JB, Shriner I, Marshall JM, Akbari OS, Bier E (2021) Inherently confinable split-drive systems in Drosophila. Nat Commun 12:1480. https://doi.org/10.1038/s41467-021-21771-7
115. Pickersgill M (2012) The co-production of science, ethics, and emotion. Sci Technol Human Values 37(6):579–603. https://doi.org/10.1177/0162243911433057
116. Filipe A, Renedo A, Marston C (2017) The co-production of what? Knowledge, values, and social relations in health care. PLoS Biology 15(5):e2001403. https://doi.org/10.1371/journal.pbio.2001403
117. Miller CA, Wyborn C (2020) Co-production in global sustainability: Histories and theories. Environ Sci Policy 113:88–95. https://doi.org/10.1016/j.envsci.2018.01.016
118. Montenegro de Wit M (2019) Gene driving the farm: Who decides, who owns, and who benefits? Agroecol Sustain Food Syst 43(9):1054–1074. https://doi.org/10.1080/21683565.2019.1591566
119. Burt A (2003) Site-specific selfish genes as tools for the control and genetic engineering of natural populations. Proceedings of the Royal Society B: Biological Sciences 270(1518):921–928. https://doi.org/10.1098/rspb.2002.2319
120. Rode N, Estoup A, Bourguet D, Courtier-Orgogozo V, Débarre F (2019) Population management using gene drive: Molecular design, models of spread dynamics and assessment of ecological risks. Conserv Genet 20(4):671–690. https://doi.org/10.1007/s10592-019-01165-5
121. Callies DE, Rohwer Y (2022) Justifying an intentional species extinction: The case of Anopheles gambiae. Environ Values 31(2):193–210. https://doi.org/10.3197/096327121X16081160834786
122. Čartolovni A (2017) Teilhard de Chardin's oeuvre within an ongoing discussion of a gene drive release for public health reasons. Life Sciences, Society and Policy 13:18. https://doi.org/10.1186/s40504-017-0064-8
123. Ledingham K, Hartley S (2021) Transformation and slippage in co-production ambitions for global technology development: The case of gene drive. Environ Sci Policy 116:78–85. https://doi.org/10.1016/j.envsci.2020.10.014
124. DeFrancesco L (2015) Gene drive overdrive. Nat Biotechnol 33:1019–1021. https://doi.org/10.1038/nbt.3361
125. Pugh J (2016) Driven to extinction? The ethics of eradicating mosquitoes with gene-drive technologies. J Med Ethics 42:578–581. https://doi.org/10.1136/medethics-2016-103462
126. Kolopack PA, Lavery JV (2017) Informed consent in field trials of gene-drive mosquitoes. Gates Open Research 1(14). https://doi.org/10.12688/gatesopenres.12771.1

127. Resnik DB (2018) Ethics of community engagement in field trials of genetically modified mosquitoes. Dev World Bioeth 18:135–143. https://doi.org/10.1111/dewb.12147
128. Critical Scientists Switzerland (2019) Gene Drives. A report on their science, applications, social aspects, ethics and regulations. Joint report by Critical Scientists Switzerland, European Network of Scientists for Social and Environmental Responsibility, Vereinigung Deutscher Wissenschaftler. Accessible online: https://genedrives.ch/report/
129. De Graeff N, Jongsma KR, Lunshof JE, Bredenoord AL (2021) Governing gene drive technologies: A qualitative interview study. AJOB Empirical Bioethics 13(2):107–124. https://doi.org/10.1080/23294515.2021.1941417
130. WYSS Institute (no year) Gene drives. https://wyss.harvard.edu/technology/gene-drives/. Accessed 28 Mar 2022
131. World Health Organization (no year) Summary of new interventions for vector control: Genetic manipulation. https://www.who.int/groups/vector-control-advisory-group/summary-of-new-interventions-for-vector-control/genetic-manipulation. Accessed 28 Mar 2022
132. Gelot L, Söderbaum F (2012) Rethinking intervention and interventionism. Development Dialogue 58:131–50. https://ssrn.com/abstract=2401025
133. Boersma K (2022) The Anthropocene as the end of nature? Why recognizing interventionism is key in coming to terms with the Anthropocene. Environmental Ethics 44(3):195–219. https://doi-org.ezproxy.library.wur.nl/10.5840/enviroethics202292643
134. Bouchard S (2017) Gene 'editing' on mice tested in war on ticks. The Working Waterfront Newspaper 17 November 17 2017. https://www.islandinstitute.org/working-waterfront/%E2%80%8Bgene-editing-on-mice-tested-in-war-on-ticks/. Accessed 28 Mar 2022
135. Callaway E (2017) Gene drives thwarted by emergence of resistant organisms. Nature 542:15. https://doi.org/10.1038/542015a
136. Champer J, Reeves R, Oh SY, Liu C, Liu J, Clark AG, Messer PW (2017) Novel CRISPR/Cas9 gene drive constructs reveal insights into mechanisms of resistance allele formation and drive efficiency in genetically diverse populations. PLOS Genetics 13:e1006796. https://doi.org/10.1371/journal.pgen.1006796
137. Unckless RL, Clark AG, Messer PW (2017) Evolution of resistance against CRISPR/Cas9 gene drive. Genetics 205(2):827–841. https://doi.org/10.1534/genetics.116.197285
138. Hammond AM, Kyrou K, Bruttini M, North A, Galizi R, Karlsson X, Kranjc N, Carpi FM, D'Aurizio R, Crisanti A, Nolan T (2017) The creation and selection of mutations resistant to a gene drive over multiple generations in the malaria mosquito. PLOS Genetics 13(10):e1007039. https://doi.org/10.1371/journal.pgen.1007039
139. Reed FA (2017) CRISPR/Cas9 Gene drive: Growing pains for a new technology. Genetics 205(3):1037–1039. https://doi.org/10.1534/genetics.116.198887
140. Champer J, Wen Z, Luthra A, Reeves R, Chung J, Liu C, Lee YL, Liu J, Yang E, Messer PW, Clark AG (2019) Multiple loci of small effect confer wide variability in efficiency and resistance rate of CRISPR gene drives. Genetics 212(1):333–341. https://doi.org/10.1534/genetics.119.302037
141. Dearden PK, Gemmell NJ, Mercier OR, Lester PJ, Scott MJ, Newcomb RD, Buckley TR, Jacobs JME, Goldson SG, Penman DR (2018) The potential for the use of gene drives for pest control in New Zealand: A perspective. J R Soc N Z 48(4):225–244. https://doi.org/10.1080/03036758.2017.1385030
142. Baltzegar J, Cavin Barnes J, Elsensohn JE, Gutzmann N, Jones MS, King S, Sudweeks J (2018) Anticipating complexity in the deployment of gene drive insects in agriculture. Journal of Responsible Innovation 5(S1):S81–S97. https://doi.org/10.1080/23299460.2017.1407910
143. ETC Group (2019) Gene Drive Organisms – An introduction to a dangerous new technology putting Africans at risk. Report co-published with Copagen, Terre à Vie, Alliance for Food Sovereignty in Africa and Health of Mother Earth Foundation. https://www.etcgroup.org/sites/www.etcgroup.org/files/files/etc_gene_drive_organisms-web_en.pdf. Accessed 28 Mar 2022
144. Friends of the Earth (2020) Open Letter: We need a global moratorium on the release of gene drive organisms. Letter addressed to European Commission 30 June 2020. https://friendsoftheearth.eu/publication/open-letter-we-need-a-global-moratorium-on-the-release-of-gene-drive-organisms/. Accessed 28 Mar 2022
145. Caplan AL, Parent B, Shen M, Plunkett C (2015) No time to waste – the ethical challenges created by CRISPR. EMBO Reports 16(11):1421–1426. https://doi.org/10.15252/embr.201541337
146. Callies DE (2019) The ethical landscape of gene drive research. Bioethics 33(9):1091–1097. https://doi.org/10.1111/bioe.12640
147. De Graeff N, Jongsma KR, Johnston J, Hartley S, Bredenoord AL (2019) The ethics of genome editing in non-human animals: A systematic review of reasons reported in the academic literature. Philosophical Transactions of the Royal Society B: Biological Sciences 374(1772):20180106. https://doi.org/10.1098/rstb.2018.0106
148. Nestor MW, Wilson RL (2020) Beyond Mendelian genetics: Anticipatory biomedical ethics and policy implications for the use of CRISPR together with gene drive in humans. Bioethical Inquiry 17(1):133–144. https://doi.org/10.1007/s11673-019-09957-7
149. Büscher B, Fletcher R (2020) The conservation revolution: Radical ideas for saving nature beyond the Anthropocene. Verso Books
150. Bormpoudakis D (2019) Three implications of political ontology for the political ecology of conservation. Journal of Political Ecology 26(1):545–566. https://doi.org/10.2458/v26i1.22014
151. Muller S, Hemming S, Rigney D (2019) Indigenous sovereignties: Relational ontologies and environmental management. Geogr Res 57(4):399–410. https://doi.org/10.1111/1745-5871.12362
152. Rolston H III (1991) The wilderness idea reaffirmed. The Environmental Professional 13:370–377
153. Katz E (1992) The Big Lie: The human restoration of nature. Research in Philosophy and Technology 12:93–107

154. Callicott JB (1991) The wilderness idea revisited. The sustainable development alternative. The Environmental Professional 13:235–247
155. Vogel S (2015) Thinking like a mall. MIT Press, Cambridge, Environmental Philosophy After the End of Nature
156. Palmer C (2016) Climate Change, Ethics, and the Wildness of Wild Animals. In: Bovenkerk B, Keulartz J (eds) Animal Ethics in the Age of Humans. Blurring boundaries in human-animal relationships. Springer, Dordrecht, p 131–150
157. Swart J, Keulartz J (2011) Wild animals in our backyard. A contextual approach to the intrinsic value of animals. Acta Biotheoretica 59(2):185–200. https://doi.org/10.1007/s10441-011-9126-0
158. Hay BA, Oberhofer G, Guo M (2021) Engineering the composition and fate of wild populations with gene drive. Annu Rev Entomol 66(1):407–434. https://doi.org/10.1146/annurev-ento-020117-043154
159. Bakerlee CW, Nguyen Ba AN, Shulgina Y, Rojas Echenique JI, Desai MM (2022) Idiosyncratic epistasis leads to global fitness–correlated trends. Science 376(6593):630–635. https://doi.org/10.1126/science.abm4774
160. Evans SW, Palmer MJ (2018) Anomaly handling and the politics of gene drives. Journal of Responsible Innovation 5(S1):S223–S242. https://doi.org/10.1080/23299460.2017.1407911
161. Preston CJ (2017) De-extinction and taking control of Earth's "metabolism." Hastings Cent Rep 47(4):S37–S42. https://doi.org/10.1002/hast.750

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