This is an Accepted Manuscript of a book chapter published by Routledge in *Wild Animal Ethics: The Moral and Political Problem of Wild Animal Suffering* on October 30, 2020, available online: https://www.routledge.com/Wild-Animal-Ethics-The-Moral-and-Political-Problem-of-Wild-Animal-Suffering/Johannsen/p/book/9780367275709

Chapter 5 – Editing Nature

Kyle Johannsen

Abstract:

In light of the extent of wild animal suffering (WAS), some philosophers, myself included, have adopted the view that we should cautiously assist wild animals on a large scale. However, there isn't yet a consensus on what types of intervention to research, or on what the specific goals of intervention should be. In this chapter, I argue that using gene drive to beneficially modify wild animal populations is a type of intervention especially worthy of research. Focusing on CRISPR in particular, I argue that the moral costs of the alternative - the perpetual interference with wild animals' liberties associated with conventional wildlife management - are far greater. Additionally, I compare a number of different goals that CRISPR could be used to try to achieve. Potential goals include making certain species, such as r-Strategists or predators, go extinct; removing the capacity to suffer from certain animals; or changing animals' dietary and reproductive behavior, e.g., turning carnivores into herbivores or r-Strategists into K-Strategists. Though I argue that behavior change is ideal, I allow that removing the capacity to suffer is a promising, second-best option should behavior change prove infeasible to safely implement.

1. Introduction

In previous chapters, I hope to have established that there's a strong case for large-scale, humanitarian intervention in nature. Predation, the r-Strategy, and other natural processes are responsible for a tremendous amount of suffering, and though the risks of intervention must certainly be considered, they don't suffice to undermine a cautious commitment to large-scale assistance.

In this chapter, I'll argue that genetically editing wild animal populations is a type of intervention especially worth of researching. Particular attention will be devoted to CRISPR,[i] a recent type of gene editing with the power to significantly change the natural world. In section 2, I describe how CRISPR works and explain why it's such a powerful form of intervention. Though CRISPR has various virtues, its greatest one, arguably, is that CRISPR-created traits can be designed so that they're inherited by nearly all of an edited organism's descendants. In other words, CRISPR can 'drive' traits through wild populations.[ii]

Section 3 compares conventional wildlife management to gene drives. In it, I argue that the moral costs of the former are far greater than those of the latter.[iii] I also respond to the objection that gene drives, even if better than conventional management, are impermissible because developing them requires experimenting on animals. I argue that such experiments are justified so long as we're also justified in believing that they'll lead to the implementation of successful, large scale interventions, and I recommend that initial experiments be conducted on animals who lack the capacity to suffer.

Section 4 compares a number of different goals that gene drives could potentially be used to try to achieve: (a) to make certain species go extinct;[iv] (b) to remove the capacity to suffer from certain animals;[v] or (c) to change animals' dietary and reproductive behavior.[vi] Though I argue that behavior change is ideal, I concede that it's sensible to eliminate at least some species of non-sentient parasite. Furthermore, I concede that in the event that it proves infeasible to safely change wild animals' dietary and reproductive behavior, removing certain animals' capacity to suffer is a second-best option worth exploring.

2. CRISPR

One especially promising type of intervention is gene editing. CRISPR, the latest form of gene editing, has received a considerable amount of attention from in the media over the last four years, and for good reasons. For one, it's both cheap and easy to use. Whereas earlier forms of gene editing required costly materials and a considerable amount of specialized expertise in protein engineering, CRISPR has comparably low material costs, and it edits the desired part of a genome via an easily modified RNA molecule.[vii] This comparative inexpensiveness and ease of use has democratized gene editing, making it possible for labs of modest means to use gene editing in their research. In fact, CRISPR is so accessible that amateurs called 'biohackers' are able to use it,[viii] a fact that was dramatically demonstrated when Josiah Zayner live-streamed himself self-administering a CRISPR-based muscle enhancer. Since Zayner's live-stream, a number of other live-streamed publicity stunts have been pulled by biohackers. Though Zayner himself has decided to abstain from further stunts, he still involves himself in a variety of CRISPR-related activities.[ix] Among other things, he owns a company called 'The Odin' that sells do-it-yourself CRISPR kits. The kits available for purchase include one for creating fluorescent yeast, and one that can be used to create 'bioart' via different colored bacteria.[x]

A second reason for all of the media attention is that CRISPR-created traits can be quickly dispersed through a target population via 'gene drive'. In general, the term 'gene drive' refers to the process that occurs when a gene increases its odds of being passed on. There are a number of methods via which genes may do this,[xi] but the method associated with CRISPR is called an 'endonuclease drive'. Endonuclease drives occur when a gene possessed by one of a pair of chromosomes cuts the associated area of the partner chromosome. The cell, in turn, repairs the damage to the partner chromosome by copying the 'attacking' gene onto it. The gene's subsequent presence in both chromosomes ensures that it will be inherited by nearly all of its organism's offspring.[xii] The reason CRISPR is well-suited for implementing endonuclease drives is because it works in a similar manner: it cuts the targeted part of the genome, and this cut is in turn repaired using an edited gene. Via an endonuclease gene drive, then, CRISPR can spread a genetically engineered trait through a target population, and a number of studies have already done so with insects, albeit in a laboratory setting.[xiii]

In combination, CRISPR's inexpensiveness and ability to start gene drives make it a potentially powerful tool for assisting wild animals. Traits that would benefit wild animals could be developed in the laboratory and then spread through wild animal populations. Though it's hard to predict exactly which traits we'll be able to develop, CRISPR's record of success in modifying insects and animals gives us reason to be optimistic. Consider the research being done on mosquitos. It has already been demonstrated, in the laboratory setting, that modifications which spread sterility through female mosquitos (thereby reducing population size) or which make mosquitos resistant to malaria parasites, can be driven through mosquito populations.[xiv] And the animal farming industry has had some success at modifying cows in ways intended to make both raising and killing them more 'humane.' Examples include the development of cows who are resistant to bovine tuberculosis,[xv] and the development of bulls that don't grow horns and thus who won't eventually be made to undergo a painful dehorning.[xvi] Whether welfarist modifications are morally good, all things considered, is an open question, but they certainly demonstrate CRISPR's huge potential for producing new phenotypes.[xvii]

3. Justifying the Moral Costs of Gene Drive

Gene drives are appealing not only in light of their potential for benefitting wild animals, but also because the moral costs of using them are small relative to conventional wildlife management. When writers imagine what it would mean to assist wild animals on a large scale, they often imagine a zoo-like scenario that involves significant restrictions on wild animals' liberties.[xviii] Examples of such restrictions include using fences to separate predators from their prey, and feeding predators a plant-based source of protein; as well as using sterilization or contraceptives to restrict the reproduction of all but a small number of r-Strategist individuals and subsequently caring for those infants who are born.

The main reason gene drives are preferable to conventional wildlife management is because the harms of gene drive are initial, rather than perpetual, and because those harms are inflicted on only a small subset of each target population, rather than the entire population. As we noted earlier, gene drives are conducted by modifying a small number of edited organisms who, upon release into the wild, spread the relevant trait or traits throughout wild populations. Though being experimented upon and held captive in a lab are certainly significant harms for the animals who must undergo it, only a small proportion of the current population are required to endure these harms, and future members of the population needn't endure any harms at all. In comparison with a zoo-like scenario, then, the moral costs associated with gene drives are quite small. Using gene drives to assist wild animals is compatible with leaving most wild animals free to live their lives.

It might be objected that gene drives, though less morally costly than conventional wildlife management, are still too costly to be permissible. One obvious worry is the possibility of unintentionally causing significant ecological damage. I discussed fallibility at length in Chapter 4, so I won't discuss it much here. However, I will say that significant research and testing would have to be conducted before beneficent gene drives could be conducted responsibly. I'll also note that research has already been conducted on 'daisy-chain' gene drives – a technique that promises to allow for localized drives that don't spread beyond a certain geographical area.[xix] Unlike a standard gene drive, a daisy-chain drive operates via a series of linked elements. Each element in the chain drives the next, and as a consequence, links in the chain disappear from the target population over time. When the chain eventually runs out, so does the drive.[xx] The built-in expiry date that daisy-chaining creates is useful for purposes of conducting safe field tests, as well as for ensuring that the wishes of particular nations are respected.[xxi] As we noted in Chapter 3, eco-systems span state border, and thus large-scale interventions will often affect multiple nations' environment. In the event that some nations aren't interested in having their environment affected by a particular gene drive, daisy-chaining could be used to let them opt out.[xxii]

A second worry is that genetic experiments must first be conducted in order to develop a genetic intervention, and that such experiments risk harming their subjects. As I mentioned earlier, the harms risked by genetic experimentation are initial, rather than perpetual, and only a small sub-set of the target population are put at risk. Still, it's worth asking whether imposing those risks is justified. The main harms risked by genetic experiments are those associated with the unintended consequences an edit may have for a research subject. Consider a horror story from the 80's. In 1985, the United States Department of Agriculture attempted to engineer pigs who would grow faster and thus consume less grain before becoming fit for slaughter. The researchers' approach involved inserting a human growth hormone gene into a series of pig fetuses, 19 of which ended up surviving birth and reaching maturity. In all 19 cases, however, the genetic modification had unintended consequences. In particular, all of the pigs were sterile, and a number of them experienced medical issues such as physical deformity, ulcers, arthritis, and a compromised immune system.[xxiii] Genetic engineering today is much more advanced than it was in the 80's, but risks are still present. Unintended consequences can occur when an edit is 'off-target', i.e., when experimenters accidentally cut the wrong part of the gene, but even 'on-target' edits can produce unexpected physical consequences.[xxiv]

In previous work, I've argued that the risks of genetic experiments are justified by the sheer scale of wild animal suffering. Though exposing animals to risk (not to mention the discomfort of being held captive in a laboratory) is regrettable, only a very strict deontologist should think that those risks aren't outweighed by the interests of the great many future animals – trillions, perhaps – who we could potentially save from a dismal fate.[xxv] There is one complication, however. In order for the potential benefits of gene drives to trump the risks of experimentation, we must have good reason to believe that those potential benefits will be actualized. If safe gene drives that effectively assist wild animals are, despite researchers' best efforts, unlikely to ever be developed, then the risks of experimentation are unjustified.[xxvi] In light of this, I think it's important for researchers to do a certain amount of knowledge and capacity building before they move on to experiments that involve sentient animals. For example, researchers interested in developing gene drives that reduce r-Strategist birth rates might begin by experimenting on r-Strategists who probably aren't sentient, such as insects (it's worth noting that, as I mentioned above, successful gene drives have already been performed on laboratory mosquito populations).[xxvii] Researchers might also wait until the political support necessary to implement gene drives hopefully develops, as well as contribute to the public dialogues necessary to create that support.

A noteworthy point about CRISPR is that it may have the power to ameliorate some of the ethical concerns it raises. As we noted above, CRISPR has already been used, with some degree of success, to perform gene edits that promise to improve the welfare of farmed animals, e.g., by creating resistance to tuberculosis and by preventing horn growth. Adam Shriver argues that we should take this sort of research a step further and attempt to engineer farm animals whose capacity to experience pain is reduced – a possibility that might well be pursued with respect to lab animals, as well.[xxviii] In fact, a couple of past studies have already succeeded in creating genetically engineered mice who possess a lesser capacity for pain. In both cases, genetic modification succeeded (either wholly or partially) at inhibiting the affective dimension of pain, i.e., the extent to which one is disturbed by or minds their pain, rather than one's sensory experience of it. Put another way, the mice were engineered to be incapable of *suffering*, but they were still able to experience *mere pain*.[xxix] Though the researchers performing these studies weren't specifically interested in benefitting animals, the Sculpting Evolution group at the MIT Media Lab is currently working on a project that aims to improve animal welfare. More specifically, they aim to develop CRISPR-modified lab mice who are suitable for use in experiments, but who won't experience suffering in the process. Their hope is to engineer a sort of trigger that, when activated, would completely block any suffering (without the use of pain killing drugs).[xxx]

Again, it's an open question whether using CRISPR to pursue welfarist goals is morally justified. The obvious worry is that such projects will contribute to the perception that animal exploitation is justified and thus impede the reformist efforts of animal rights advocates. In the event that CRISPR-modified lab animals do become available, though, using them would at least be less morally costly than using animals who would experience significant suffering. Researchers might, for example, develop birth-rate-reducing gene drives in suffering-inhibited lab mice before attempting to develop those drives in wild rodents. In this way, suffering-inhibited lab animals could be incorporated into the capacity building phase. Furthermore, in the event that replicating suffering inhibition in other species is something that could be done easily and at little risk to research subjects, researchers might first produce a suffering-inhibited population of the relevant species before doing gene drive research on it, e.g., produce a suffering-inhibited population of meadow voles who could then be used in experiments that aim to reduce meadow vole birth rates. In this way, suffering-inhibited lab animals might also be used in the final stages of research.

In the next section, I consider a variety of ways that gene drives might be used to reduce wild animal suffering. One of the possibilities I'll consider is whether modifications that inhibit suffering should be used not only to reduce the harms of experimentation, but to help wild r-Strategists, too.

4. What to Do with Gene Drives?

Thus far I hope to have shown that gene drive research has the potential to develop morally acceptable, effective means of assisting wild animals on a large scale. I have not, however, said much about what sorts of gene drives may be worth researching. In previous work, I've argued that we should try to develop gene drives that would change r-Strategists into K-Strategists, i.e., gene drives that would reduce r-Strategist litter and clutch sizes, and increase the amount of energy r-Strategist parents devote to each of their offspring.[xxxi] In a similar vein, other authors have suggested that we attempt to change carnivores into herbivores.[xxxii] Such proposals are obviously very ambitious and may turn out to be impossible. They would also cause various ecological side effects that would have to be offset by supplementary drives, e.g., if we change carnivores into herbivores, then we should also be mindful of controlling the size of the populations our former carnivores preyed on. Considering the sheer scale of wild animal suffering, though, it's worth doing the research necessary to determine whether radical forms of behavior change are feasible and could be safely implemented. Furthermore, even if it turns out that behavior change is often too ecologically dangerous, there may still be some eco-systems in which implementing it would be safe, e.g., eco-systems where predators play a smaller role and could be modified without causing too much disruption.[xxxiii]

In what remains of this chapter, I'm going to consider some alternatives to large scale behavior change. In particular, I'll consider whether we should try to make certain species go extinct,[xxxiv] and whether we should try to remove animals' capacity for suffering.[xxxv] Though I'll argue that behavior change is ideal, I'll also argue that the above-mentioned alternatives are appropriate in some contexts.

Let's consider extinction first. Is there any merit in the proposal that we should make predators or r-Strategists go extinct? On the one hand, doing so would certainly prevent a great deal of harm from occurring. Extinction would prevent further acts of predation, and it would prevent doomed r-Strategist infants from being brought into existence. What's more, so long as extinction is achieved by spreading sterility (a feat which, it turns out, gene drives can accomplish),[xxxvi] existing predators and r-Strategists won't lose their lives (unlike when habitat is destroyed).[xxxvii] On the other hand, there are a number of costs associated with causing extinction. First, sterilizing predators and r-Strategists would deprive some existing animals – specifically K-Strategist predators – of the opportunity to raise children. For animals who have an interest in forming a family and raising their young, becoming sterile is a significant loss. Second, widespread extinction would be ecologically risky - maybe even more so than widespread behavior change. Third, even if we could, perhaps with the use of supplementary drives, safely cause predators and r-Strategists to go extinct, it seems clear to me that behavior change is preferable to extinction. My thought is a simple one – a world that contains many animals is better than a world that contains very few animals, so long as most of the animals live good lives. The main reason for this is because a world with many animals (all or most of whom flourish) contains greater total utility than a world containing fewer animals. Though promoting total utility to the exclusions of all else has counter-intuitive consequences – among other things, it leads us to the conclusion that we should produce large, unhappy populations instead of smaller, happy populations – it remains true that considerations of total utility carry some moral significance. As we noted in Chapter 4, total utility matters a great when utility levels are negative, i.e., since a large population of beings who lives aren't worth living is far worse than a small population of beings whose lives aren't worth living. But even when utility levels are positive, total utility matters – just not as much as average utility does.

In addition to possessing greater total utility, a world with more animal individuals and animal species is a more biodiverse one. The appeal of biodiversity is partially aesthetic, at least for those of us who enjoy the experience of observing different animals, or who even just like the thought that many different animals share the word with us. More substantially, though, biodiversity is important for stability, as eco-systems that contain higher levels of biodiversity are better able to withstand disruptions. After all, implementation is about more than just bringing something about. In addition to doing what's needed to create better states of affairs, we should also do what's needed to ensure that they remain in place.[xxxviii] In the event that we do manage to create eco-systems where most wild animals live flourishing lives, biodiversity would presumably have a role to play in ensuring that those eco-systems don't collapse.

Though behavior change is preferable to making sentient r-Strategists and sentient predators go extinct, we may wish to make certain other organisms go extinct, namely organisms that cause harm to wild animals and which do not themselves possess morally significant interests, e.g., harmful bacteria and parasites. A proposal along these lines was recently suggested by Kevin Esvelt, who argues that CRISPR can and should be used to wipe out the screw fly.[xxxix] The screw fly – a nasty parasite that lays eggs in open wounds so that its larvae may eat the flesh of living mammalian hosts – was wiped out in North America a couple of decades ago. Though they were wiped out primarily in order to protect livestock, wild mammals benefitted immensely, too. Unfortunately, the method used to exterminate them (the Sterile Insect Technique) is not effective in all areas of the world, and thus the screw fly still exists in South America and other places. CRISPR could be used to wipe these parasites out for good, and there doesn't seem to be any good reason not to do so.

A second alternative to behavior change is removing r-Strategists', and perhaps K-Strategist prey species', capacity to suffer. This proposal is premised on the above-mentioned distinction that some philosophers and cognitive scientists draw between the affective dimension of pain - the extent to which one is disturbed by or minds their pain – and one's sensory experience of it. Experiencing mere pain (pain without or with little of its affective dimension) would still function to help an organism avoid harmful stimuli, but it's also far less unpleasant than suffering. Removing r-Strategists' capacity to suffer without removing their capacity to feel mere pain is similar to giving them a permanent pain killer. It promises to significantly reduce the unpleasantness of their lives without making them less well-adapted to their environment.

This proposal has one major virtue relative to extinction and behavior change – it has the potential to significantly improve r-Strategists lives without significantly impacting the eco-systems they live in. More specifically, it would allow us assist r-Strategists without affecting their birth rates, reducing their evolutionary fitness, or interfering with the relevant predator-prey relationships.

Though the above proposal is admittedly quite promising, I do have a number of reservations about removing r-Strategists' capacity to suffer. First, the capacity to suffer certainly makes some contribution to how well-adapted a species is. Though it's true that physical discomfort can motivate animals to avoid harmful stimuli, real suffering is far more memorable than physical discomfort. An animal that's capable of suffering is likely better at learning from its negative experiences, and at avoiding that which it identifies as the cause of negative experiences, than an animal that's incapable of suffering. I'm not just speculating – Shriver, in his discussion of suffering-inhibited lab mice, admits that pain's affective dimension is associated with some behavioral responses (which is how the researchers were able to tell that their experiments worked), and that the loss of those behavioral responses might make an animal less capable of learning to avoid dangerous parts of its environment.[xl] Second, removing the capacity wouldn't suffice to make r-Strategists' lives good - it's would only make them less terrible. Third, it would be very surprising if removing the capacity to suffer didn't also reduce a being's capacity to have positive experiences. After all, deadening sensitivity, whether it be emotional or physical, does more than just reduce a being's capacity for negative experiences. People who use anti-anxiety medication, for example, often report that it deadens not only their ability to feel anxiety, but also their ability to feel emotions like humor or excitement.[xli] But even if the capacity to suffer could be removed without deadening one's general sensitivity, I still think that being unable to suffer would negatively affect one's positive experiences. The reason is because our ability to appreciate positive experiences is likely, at least to some extent, contingent upon our having had negative experiences to compare them to, e.g., excitement is pleasant in part because we know what boredom feels like, and joy is pleasant in part because we know what sadness feels like. As a result, being incapable of suffering would almost certainly reduce one's ability to experience pleasure.

It's worth noting that it may be possible to design gene drives that circumvent at least some of the above problems. For example, we might design gene drives that remove r-Strategists' capacity to suffer, but only during the period of time when they're most likely to die a painful, premature death, e.g., for the first few weeks of their lives. Such gene drives would significantly benefit those who die a terrible death shortly after birth, but it wouldn't impede the evolutionary fitness of those lucky enough to live longer, nor would it impede their capacity to appreciate positive experiences. It is tempting to go even further and attempt to deprive young r-Strategists of sentience altogether. That way, they wouldn't even experience mere pain. I suspect, however, that even the temporary removal of sentience would significantly impact r-Strategists' adaptability. Merely removing the capacity to suffer is a much safer bet, even though it would mean that most r-Strategists continue to die painfully and prematurely.

In light of the above, it seems clear to me that removing r-Strategists' capacity to suffer is not an entirely adequate substitute for behavior change. That said, if it turns out that, even after considerable research, changing the behavior of r-Strategists is infeasible, then removing their capacity to suffer is a second-best option that may be worth pursuing. Similarly, if behavior change does turn out to be feasible but too dangerous in some ecological contexts, removing r-Strategists' capacity to suffer may be a desirable alternative in those contexts. In fact, if it turns out that we can limit the removal of suffering to r-Strategists' early life, we may wish to conduct such gene drives alongside any behavior-change drives we implement. That way any r-Strategists who, despite our best efforts, do die a painful and premature death, at least won't suffer in the process.

5. Conclusion

In conclusion, I've argued that gene editing technology provides a particularly promising means of assisting wild animals. Though gene drives do carry certain moral costs, those costs are considerably less than the costs of conventional wild life management. The reason is that unlike conventional management, a gene drive's harms are merely initial, and they only affect a small subset of the target population.

In addition to arguing the merits of gene editing, I argued that it should ideally be used to change animals' dietary and reproductive behavior, i.e., to turn predators into herbivores and r-Strategists in K-Strategists. However, I admitted that gene drives should sometimes be used to eliminate species, particularly non-sentient parasites, and that gene drives should perhaps be used to remove r-Strategists' capacity to suffer in the event that behavior change proves infeasible.

References

Alphey, L. 2014. “Genetic Control of Mosquitoes.” *Annual Review of Entomology* 59: 205-24.

“Biotech Kits & Classes.” Available at: https://www.the-odin.com/ (accessed Feb 29th, 2020).

Burt, A. 2003. “Site Specific Selfish-Genes as Tools for the Control and Genetic Engineering of Natural Populations.” *Proceedings of the Royal Society of London* 270: 921-8.

Cochrane, A. 2018. *Sentientist Politics: A Theory of Global Inter-Species Justice* (Oxford: Oxford University Press).

Cohen, G.A. 2009. Why Not Socialism? (Princeton: Princeton University Press).

Comstock, G. 1992. "Should We Genetically Engineer Hogs?" *Between the Species* 8: 196-202.

Cooper, Jr., W.E., R.A. Pyron, and T. Garland Jr. 2014. “Island Tameness: Living on Islands Reduces Flight Initiation Distance.” *Proceedings of the Royal Society B: Biological Sciences* 281: 20133019

Donaldson, S., and W. Kymlicka. 2011. *Zoopolis: A Political Theory of Animal Rights* (New York: Oxford University Press).

Donaldson, S., and W. Kymlicka. 2013. “A Defense of Animal Citizens and Sovereigns.” *Law, Ethics, and Philosophy* 1:143-60.

Doudna, J.A., and E. Charpentier. 2014. “The New Frontier of Genome Editing with CRISPR-Cas9.” *Science* 346: 1258096.

Esvelt, K.M., A.L. Smidler, F. Catteruccia, and G.M. Church. 2014. “Concerning RNA-Guided Gene Drives for the Alteration of Wild Populations.” *eLife* 3: e03401.

Esvelt, K.M., and N.J. Gemmell. 2017. “Conservation Demands Safe Gene Drive.” *PLOS Biology* 15: e2003850.

Esvelt, K.M. 2018. “When Are We Obligated to Edit Wild Creatures?” Available at: https://leapsmag.com/when-are-we-obligated-to-edit-wild-creatures/ (accessed July 7th, 2020).

Gantz, V.M., N. Jasinskiene, O. Tatarenkova, A. Fazekas, V.M. Macias, E. Bier, and A.A. James. 2015. “Highly Efficient Cas9-Mediated Gene Drive for Population Modification of the Malaria Vector Mosquito *Anopheles Stephensi*.” *PNAS* 112: E6736–43.

Gantz, V.M., and E. Bier. 2015. “The Mutagenic Chain Reaction: A Method for Converting Heterozygous to Homozygous Mutations.” *Science* 348: 442-4.

Gao, Y., W. Haibo, W. Yongsheng, L. Xin, C. Linlin, L. Qian, C. Chenchen, L. Xu, J. Zhang, and Y. Zhang. 2017. "Single Cas9 Nickase Induced Generation of *NRAMP1* Knockin Cattle with Reduced Off-Target Effects." *Genome Biology* 18: 13.

Gersbach, C.A. 2014. "Genome Engineering: The Next Genomic Revolution." *Nature Methods* 11: 1009-11.

Hammond, A., R. Galizi, K. Kyrou, A. Simoni, C. Siniscalchi, D. Katsanos, M. Gribble, D. Baker, and E. Marois. 2016. "A CRISPR-Cas9 Gene Drive System Targeting Female Reproduction in the Malaria Mosquito Vector *Anopheles Gambiae.*" *Nature Biotechnology* 34: 78–83.

Johannsen, K. 2017. "Animal Rights and the Problem of r-Strategists." *Ethical Theory and Moral Practice* 20: 333-45.

Ledford, H. 2015a. "Biohackers Gear Up for Genome Editing." *Nature* 524: 398-9.

Ledford, H. 2015b. "CRISPR, the Disruptor." *Nature* 522: 20–4.

McMahan, J. 2015. "The Moral Problem of Predation." In *Philosophy Comes to Dinner: Arguments about the Ethics of Eating*. Eds. A. Chignell, T. Cuneo, and M. Halteman (London: Routledge). Pp. 268-94.

Milburn, J. 2019. “Sentientist Politics Gone Wild.” In *Book Symposium: “Sentientist Politics: A Theory of Global Interspecies Justice.”* By A. Cochrane, J. Milburn, and S. O’Sullivan. Pp. 19-24 (*Politics and Animals*, Vol. 5).

Min, J., C. Noble, D. Najjar, and K.M. Esvelt. 2017. “Daisy Quorum Drives for the Genetic Restoration of Wild Populations.” *BioRxiv* 115618.

Noble, C., J. Min, J. Olejarz, J. Buchthal, A. Chavez, A.L. Smidler, E.A. DeBenedictis, G.M. Church, M.A. Nowak, and K.M. Esvelt. 2019. "Daisy-Chain Gene Drives for the Alteration of Local Populations." *Proceedings of the National Academy of Sciences* 116: 8275-82.

Nussbaum, M.C. 2007. *Frontiers of Justice* (Cambridge, MA: Belknap Press).

Pearce, D. 2015. “Reprogramming Predators.” Available at: https://www.hedweb.com/abolitionist-project/reprogramming-predators.html (accessed Jan 1, 2019).

“Reducing Suffering in Laboratory Animals.” Available at: https://www.media.mit.edu/projects/reducing-suffering-in-laboratory-animals/overview/ (accessed Feb 29, 2020).

Quinton, A. 2019. “Genome Edited Bull Passes on Hornless Trait to Calves: Study Sheds Light on Future of Genome Editing in Livestock.” Available at:

https://www.ucdavis.edu/news/genome-edited-bull-passes-hornless-trait-calves?fbclid=IwAR1mJAiqbd1C7pUOqvp5hvir8PQ3xJfPRzjpbd938I1oCmnHcSQ-QtwB2aM (accessed Oct 25, 2019).

Read, J., C. Cartwright, and K. Gibson. 2014. "Adverse Emotional and Interpersonal Effects Reported by 1829 New Zealanders While Taking Antidepressants." *Psychiatry Research* 216: 67-73.

Schultz-Bergin, M. 2018. "Is CRISPR an Ethical Game Changer?" *Journal of Agricultural and Environmental Ethics* 31: 219-38.

Shriver, A. 2009. "Knocking Out Pain in Livestock: Can Technology Succeed Where Morality Has Stalled?" *Neuroethics* 2: 115-24.

Shriver, A., and E. McConnachie. 2018. "Genetically Modifying Livestock for Improved Welfare: A Path Forward." *Journal of Agricultural and Environmental Ethics* 31: 161-80.

Soryl, A.A. 2019. *Establishing the Moral Significance of Wild Animal Welfare and Considering Practical Methods of Intervention* (Master's Thesis, University of Amsterdam).

Sun, Y., Y. Gao, Z. Zhao, B. Huang, J. Yin, G. Taylor, and Z. Chen. 2008. "Involvement of P311 in the Affective, but not in the Sensory Component of Pain." *Molecular Pain* 4: 23.

Wei, F., C. Qiu, S. Kim, L. Muglia, J. Maas Jr., V. Pineda, H. Xu, Z. Chen, D. Storm, L.J. Muglia, and M. Zhuo. 2002. "Genetic Elimination of Behavioral Sensitization in Mice Lacking Calmodulin-Stimulated Adenylyl Cyclases." *Neuron* 36: 713–26.

Young, A.E., T.A. Mansour, B.R. McNabb, J.R. Owen, J.F. Trott, C.T. Brown, and A.L. Van Eenennaam. 2020. "Genomic and Phenotypic Analyses of Six Offspring of a Genome-Edited Hornless Bull." *Nature Biotechnology* 38: 225-32.

Zhang, S. 2018. "A Biohacker Regrets Publicly Injecting Himself With CRISPR." *The Atlantic*. Available at https://www.theatlantic.com/science/archive/2018/02/biohacking-stunts-crispr/553511/ (accessed Feb 29, 2020).

[i] Technically speaking, CRISPR just refers to a structural feature present in the genomes of different bacteria. The actual gene editing is done by an associated enzyme called Cas9 in combination with a guide RNA molecule that targets the desired part of the genome to be modified. Nevertheless, the acronym 'CRISPR' is now typically used to refer to this new form of gene editing. See Doudna (2014) p. 1 and p. 3. For an informative and accessible article about CRISPR see Ledford (2015b).

[ii] The idea of dispersing a genetically engineered trait through gene drive has been around for a while. See Burt (2003).

[iii] Authors against intervention tend to assume that transforming nature into a zoo is the only available form of large-scale intervention. See Nussbaum (2007) p. 379; Donaldson and Kymlicka (2011) p. 164; and Donaldson and Kymlicka (2013) pp. 154-7.

[iv] For discussion of this possibility, see Milburn (2018) p. 24; and Soryl (2019) pp. 63-4.

[v] I originally encountered this idea when Andrew Fenton brought it up at a meeting of the Atlantic Regions Philosophers' Association. For discussion of a similar proposal, i.e., that we should remove farm animals' capacity to suffer, see Shriver (2009); and Shriver et al. (2018).

[vi] Pearce (2015); McMahon (2015); and Johannsen (2017).

[vii] Gersbach (2014) pp. 1009-10; Doudna (2014) p. 3; Ledford (2015b) p. 21.

[viii] Ledford (2015a).

[ix] Zhang (2018).

[x] See the company's website at https://www.the-odin.com/

[xi] For the types of gene drive that occur in nature, see Esvelt (2014) pp. 2-3.

[xii] Ledford (2015b) p. 22; Esvelt (2014) pp. 3-4.

[xiii] Esvelt (2014) pp. 4-9. For studies that have successfully used CRISPR to conduct gene drives, see Gantz and Bier (2015); Gantz et al. (2015); and Hammond et al. (2016).

[xiv] Gantz et al. (2015); Hammond et al. (2016). For a general discussion of genetic methods for controlling mosquito populations, see Alphey (2014).

[xv] Gao et al. (2017).

[xvi] For an accessible description of the relevant experiment, see Quinton (2019). For the academic article associated with the experiment, see Young et al. (2019).

[xvii] Section 2 of this chapter is a revised version of a discussion that was published in Johannsen (2017) at pp. 340-1.

[xviii] See footnote 3.

[xix] Esvelt at al. (2017); and Noble et al. (2019).

[xx] Min at al. (2017) p. 2; and Esvelt et al. (2017) p. 5.

[xxi] Esvelt et al. (2017).

[xxii] It's worth noting that some work has been done on combining daisy-chaining with 'genetic quorums' for purposes of making gene drives reversible. For a preliminary paper on daisy quorum drives, see Min et al. (2017).

[xxiii] Comstock (1992) p. 196.

[xxiv] Schultz-Bergin (2018) pp. 227-31.

[xxv] Johannsen (2017) p. 339 and p. 343.

[xxvi] Many thanks to Sue Donaldson for drawing my attention to this worry.

[xxvii] Gantz and Bier (2015); Gantz et al. (2015); and Hammond et al. (2016).

[xxviii] See Shriver (2009); and Shriver et al. (2018).

[xxix] For a helpful discussion of these studies, see Shriver (2009) p. 118. For the studies themselves, see Wei et al. (2002); and Sun et al. (2008). I also mentioned the distinction between suffering and mere pain in Chapter 2. Though I think the distinction is plausible, I suspect that the affective dimension is always present, at least to a small extent, in any experience we'd call 'pain'. See endnote vii in Chapter 2 for some thoughts about this.

[xxx] A description of the project is available at https://www.media.mit.edu/projects/reducing-suffering-in-laboratory-animals/overview/

[xxxi] Johannsen (2017).

[xxxii] Pearce (2015) and McMahan (2015).

[xxxiii] For example, it's common for predators to play a smaller role in island ecosystems. For a discussion of how this affects prey species behavior, see Cooper et al. (2014).

[xxxiv] See footnote 4.

[xxxv] See footnote 5.

[xxxvi] Hammond et al. (2016).

[xxxvii] For a discussion of habitat destruction, see Chapter 4.

[xxxviii] G.A. Cohen helpfully divides feasibility into two parts – accessibility and stability. See Cohen (2009) pp. 56-7.

[xxxix] Esvelt (2018).

[xl] Shriver (2009) p. 120.

[xli] See, for example, Read et al. (2014).