Gene drives accelerate evolution – but we need brakes

July 6 2018, by Yu-Hsuan Tsai And Tony Perry

Credit: AI-generated image (disclaimer)

Worried about mice in the kitchen? Fed up with pigeons on your way to work? Teed off by weeds on your lawn? Recent work points to a way that might just reduce – or even eliminate – unwanted species in a short period. The method is based on something called a gene drive – a method of making changes to an entire population of a specific species by altering its genetic material (its genome).

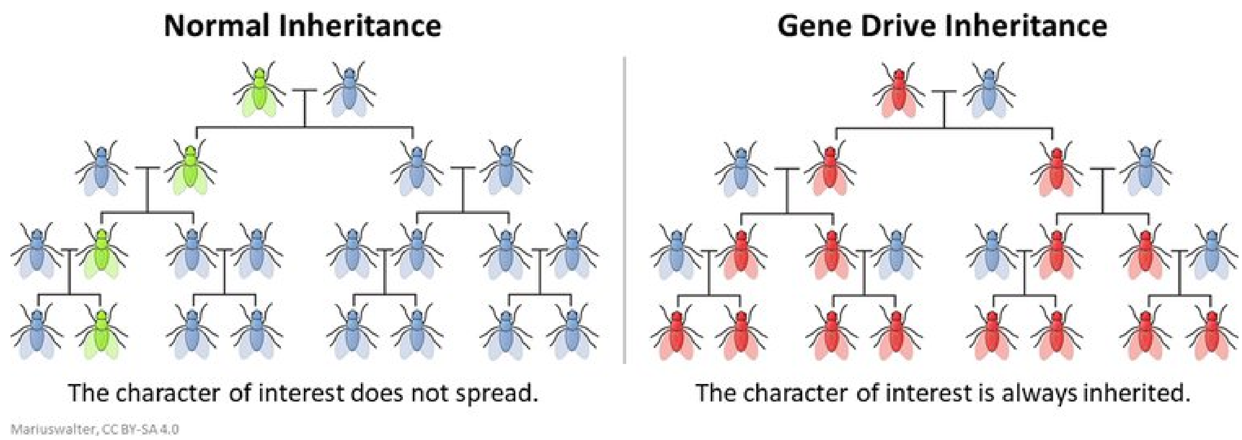
Although gene drives are today restricted to the confines of a few laboratories, they have immense promise. In addition to potential pest removal they might, for example, allow us to make livestock more resilient to disease, enhance the nutritional value of crops, or eliminate the mosquitoes that transmit infectious diseases such as zika and malaria.

Using gene drives also carries risks. Removing a species from its environment could have unforeseen environmental consequences, or organisms could become resistant to the gene drive – instantly removing all of its advantages. Gene drives authorised in one country could also spread to countries that didn't want it.

The problem is that there is currently no way to control a gene drive once it has left the lab. But new research elaborates on how we could control gene drives to throw on the brakes and even reverse their effects.

A gene drive spreads one or more inherited characteristics in sexually reproducing species faster than could happen naturally. The characteristic might be skin colour, gender or immunity to certain diseases. Or it might eventually kill or make sterile an entire population, for example via a gene drive that led solely to male offspring.

So how does the gene drive work and how can it be made switchable? In most cases offspring naturally have a 50% chance of inheriting a particular gene variant (allele), from each parent. If the variant has a positive effect, offspring that inherited it are more likely to thrive, so that over time there are more of them and the variant effectively spreads through the population. If the gene variant is a dud, the opposite occurs. This is the principle of natural selection.



Left: a normal inheritance pattern via sexual reproduction. Right: inheritance via a gene drive. Credit: Mariuswalter

But a gene drive element is inherited by all offspring, regardless of whether or not it contributes to the ability to thrive, so natural selection is subverted and the entire population quickly carries the element.

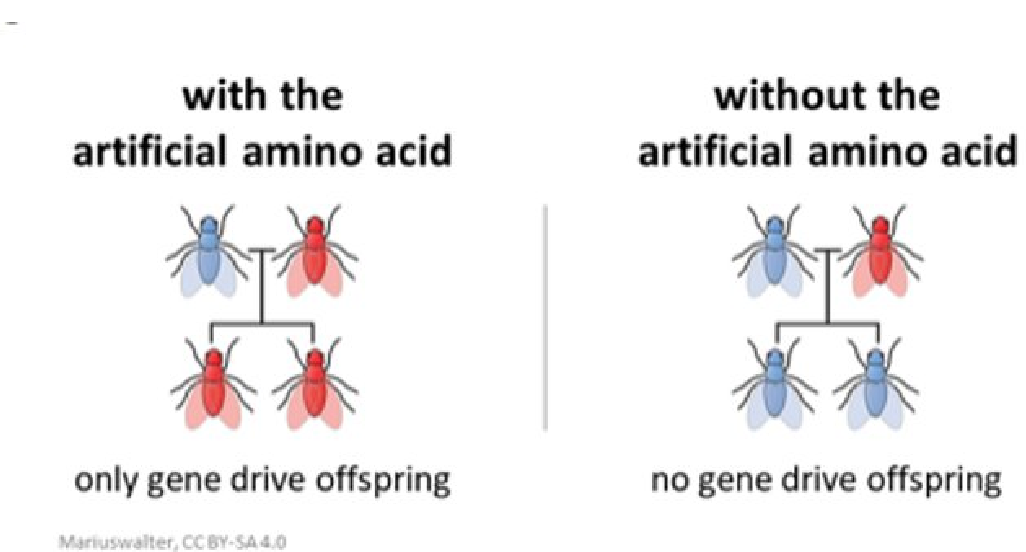
A study found that within three generations, an introduced gene drive could be present in an entire population of flying insects (image on right). This has sparked interest in the use of gene drives to control disease vectors such as mosquitoes, which carry zika and malaria. Although the technology is arguably ready, especially in the case of eliminating diseases from mosquitoes, gene drives have not yet been field tested due to safety concerns.

With great power, comes great responsibility. Even after thorough research, it is at best difficult to predict the environmental impact of releasing a gene drive organism into the wild.

Popular culture reflects a nervousness around genetic modification in movies such as Piranha and Deep Blue Sea. These scenarios remind us of how little we still know about the long-term consequences of gene modification and the importance of safeguarding and regulating its use so that we may even reverse the process if needed.

To limit their spread, the essential first step is to stop generating more gene drive organisms. This can be achieved by either killing all existing individuals or undoing their genetic change. Unfortunately, the first approach is likely to be impractical and we still have no clear way of achieving the latter.

Instead, we suggest making the gene drive switchable. The idea is to change the gene drive process so that the altered genes are only guaranteed to be passed on if the organism ingests a certain type of amino acid (all proteins are made out of 20 naturally occurring amino acids).



Amino acids could become the key to controlling gene drives outside of the lab. Credit: Mariuswalter, CC BY-SA

Like a key in an ignition, the gene drive only works with the amino acid present. Without the amino acid the gene drive is switched off – and even offspring that contain the gene drive become subject to natural laws of inheritance. By using an amino acid that does not naturally exist in nature, we can use it to precisely control gene drive activity in the wild.

This could be an affordable way of ensuring we stay in the gene driver's seat. The amino acid that controls it can be bought for as little as £0.40 per gram and would probably be required in concentrations of less than 0.1 gram per litre for most applications.

Because the gene drive is controlled by an amino acid, it's readily broken down and should be environmentally friendly – but we don't know how stable it is outside of the laboratory or how much exactly would be needed for each application.

But it's safe to assume that using gene drives to propagate disease resistance in a population of livestock would require fewer resources than spraying an area the size of Utah to control mosquitoes. If we can ensure the animals are only exposed to the amino acid while in the controlled area then we can contain gene drive activity, even if animals drift across borders.

This is tomorrow's biology, if we want it – today it is hypothetical. Tentative steps towards this future will involve demonstration in model animals that, if successful, might lead to applications to improve livestock. Gene drives in this sector would be relatively easy to monitor and could also be economically attractive.

In medicine, controllable gene drives in cell therapy may help to ensure that all of the targeted genome contains the desired change. More generally, the faculty of switching gene drives off will reduce the risk of immunity to them emerging – if gene drive components are absent, there's nothing for an immune system to respond to.

It might even be possible for any kind of amino acid to work as our fail safe once the technology has improved. Before we embark on the road to gene driving nature, it helps to know we can always kill the engine if we don't like the destination.

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