from issues of spatial resolution. Intriguingly, Morley and co-workers' observations suggest a possible workaround for tissue engineering: they find that filaments contract within a certain parameter regime. In this regime, tissues would behave like Shrinky Dinks — toys that shrink when heated, but retain their initial shape[10]. The effective spatial resolution of printed tissue constructs might therefore be much better than the diameter of the printer's nozzle would typically allow, because of the compacting effect of cell tractions throughout the printed object. The challenges of 4D bioprinting thus provide exciting opportunities for engineers to grapple with tissue-developmental processes, and to treat them as controllable design motifs. ■

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INFECTIOUS DISEASES

A trial to tackle tiger mosquitoes

A fresh approach to suppressing the Asian tiger mosquito, a highly invasive species that transmits disease-causing viruses, has been used to nearly eradicate these insects from two test sites in China. SEE ARTICLE P.56

PETER A. ARMBRUSTER

Mosquito-borne viruses, including dengue, chikungunya and Zika, are major public-health threats[1]. Because neither vaccines nor effective drug treatments are available for most mosquito-borne viruses, vector control — that is, suppression of the mosquito populations that transmit viruses — remains the primary means of reducing disease incidence. The Asian tiger mosquito (*Aedes albopictus*) has spread rapidly in recent years, is increasingly prevalent in densely populated urban environments and is resistant to conventional vector-control practices[2]. On page 56, Zheng *et al.*[3] describe a new control strategy that almost completely eliminated *Ae. albopictus* from two experimental field sites, providing encouragement for future approaches to control *Ae. albopictus* and other vector mosquitoes.

Over the past two decades, various innovative strategies to reduce the transmission of disease-causing viruses and microbes by mosquitoes have been developed[4]. These strategies aim either to reduce mosquito populations (known as population suppression) or to make wild mosquitoes unable to transmit infectious diseases by spreading genetic modifications or bacterial infections through natural populations (known as population replacement).

Bacteria from the genus *Wolbachia* live in the cells of insect hosts, are maternally inherited and affect the reproduction of their host in such a way that they can be leveraged for both population suppression and population replacement. For example, when male mosquitoes infected with certain *Wolbachia* strains are released and mate with wild females that are not infected with the same *Wolbachia* strain, the females are unable to produce viable eggs (Fig. 1a). Alternatively, releasing males and females that are all infected with a strain of *Wolbachia* that makes mosquitoes less able to transmit viruses can lead to the spread of this strain through the wild population (Fig. 1b). Indeed, field trials of *Wolbachia*-based population replacement of the closely related *Aedes aegypti* are currently being conducted in five countries[4]. In addition, previous attempts at *Wolbachia*-based suppression of populations of several different mosquito species have shown some success[4].

Ae. albopictus is highly invasive and has spread rapidly from its native Asia to all continents except Antarctica over the past 40 years[5]. This mosquito is difficult to control, in part because larvae develop in a wide variety of artificial containers that are challenging to treat thoroughly with insecticides, and its desiccation-resistant eggs can survive in a dormant state for long periods.

Zheng and colleagues aimed to release male *Ae. albopictus* infected with a selected *Wolbachia* strain to suppress established populations in residential areas of two islands in a river in Guangzhou, China. Wild populations of tiger mosquitoes are infected with two strains of *Wolbachia* that do not block virus transmission[6]. The authors therefore infected *Ae. albopictus* with a third strain of *Wolbachia*, called *w*Pip, from the mosquito *Culex pipiens*, to produce a laboratory colony of mosquitoes that they called the HC population.

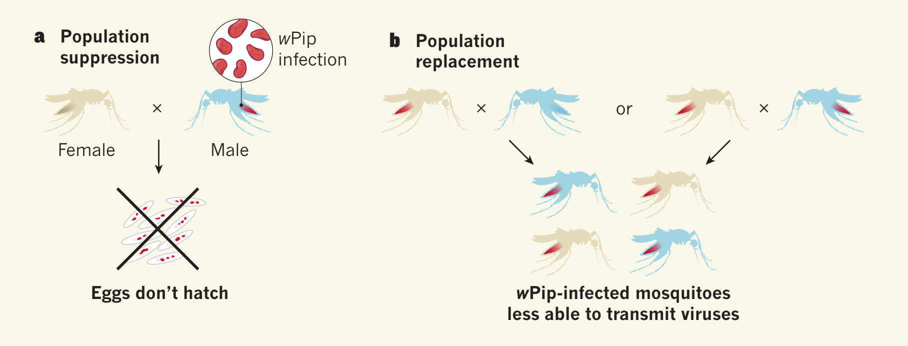

Figure 1 | Controlling populations of disease-transmitting mosquitoes using *Wolbachia* bacteria. **a**, One method of suppressing a mosquito population, termed population suppression, is to release male mosquitoes that are infected with a strain of *Wolbachia* bacteria that makes them unable to produce viable offspring with females that are not infected with the same *Wolbachia* strain. Zheng *et al.*[3] aimed to suppress tiger mosquito (*Aedes albopictus*) populations in this way by releasing male tiger mosquitoes carrying a *Wolbachia* strain called *w*Pip from another species of mosquito (*Culex pipiens*). **b**, Females infected with a given strain of *Wolbachia* can produce viable offspring with males regardless of whether the males are infected with the same strain. Thus, if *w*Pip-infected females were accidentally released, wild females would produce fewer offspring than the *w*Pip-infected females, and the *w*Pip infection would spread rapidly, leading to population replacement. However, Zheng *et al.* showed that *w*Pip-infected mosquitoes were less susceptible to infection by disease-causing viruses than were wild mosquitoes. Therefore, population replacement would still have resulted in reduced virus transmission.

When male *Ae. albopictus* from the HC population mated with females with the native double infection, all the resulting embryos died, as would be predicted because the females were not infected with the *w*Pip strain that infected the males (Fig. 1a). However, such embryo lethality did not occur when *w*Pip-infected males mated with females that were also infected with the *w*Pip strain (Fig. 1b). Thus, a risk in the authors' approach was that, if any *w*Pip-infected females were released along with males, they would spread the *w*Pip infection rapidly through the wild population, eliminating the population-suppressing effects of the *w*Pip-infected males. This risk was tempered by the finding that HC females were less susceptible than wild females to infection by dengue and Zika viruses. Therefore, although the goal was population suppression, if HC females were accidentally released, the worst-case scenario would have been population replacement (Fig. 1b) — still a net gain for public health.

Zheng and co-workers' major innovation was their method of preparing HC mosquitoes for release. In facilities that mass-rear mosquitoes, male pupae are usually mechanically separated from female pupae on the basis of size differences. Using this procedure to prepare groups of male mosquitoes led to a female contamination rate of approximately 0.2–0.5%, necessitating a secondary, manual screening to remove female pupae, recognized by their distinctive anatomy. However, this labour-intensive manual screen substantially limited the total number of mosquitoes that could be prepared. Zheng *et al.* eliminated the need for the manual screen by subjecting the HC pupae to low-dose radiation that sterilized females but that only slightly impaired male mating success. As a result of eliminating the manual screen, they were able to increase the number of male mosquitoes that could be released by more than tenfold.

Population-suppression strategies crucially depend on the ratio of released males to wild males. Thus, Zheng *et al.* used mathematical modelling and cage experiments to calculate the optimal sizes and timings of mosquito releases. During the peak breeding season, the rearing facility produced more than 5 million male mosquitoes per week, leading to the release of more than 160,000 mosquitoes per hectare per week at the test sites. Zheng *et al.* monitored the numbers and viability of eggs produced by wild mosquitoes, as well as the abundance of adult mosquitoes and the rates at which they bit humans at test sites and at nearby control sites (where no HC males had been released).

The releases produced striking results in two successive years. Relative to control sites, the average number of viable eggs produced by wild mosquitoes at test sites declined by 94% in both years, and the number of wild adult females collected in traps at the two test sites declined by 83% and 94% (only female mosquitoes take blood meals). Notably, the estimated human-biting rate decreased by as much as 96.6%. Surveyed support for the releases in the local communities, where residents were initially sceptical or indifferent to the trial, increased from 13% to 54%.

That Zheng and colleagues' trial almost eliminated a notoriously difficult-to-control vector mosquito from the test sites is remarkable. However, questions remain about the long-term sustainability of their approach. For example, immigrating mosquitoes would inevitably re-establish the natural population once the releases stop. Such recolonization might be prevented by the targeted release of a modest number of males or by conventional vector-control methods, but the required intensity and cost of these additional efforts are unknown. Also unknown is the extent to which this approach can be scaled up spatially. Efforts to develop automated release technologies and more efficient sex-separation methods (for example, see ref. 7), should substantially improve production and release capacity. However, whether such technological advances can overcome the financial and logistical challenges of implementing these approaches at a scale that reduces disease transmission across a major metropolitan area or nationwide remains to be seen.

No single vector-control strategy is expected to fully control populations of disease-carrying mosquitoes; combinations of approaches will probably be most effective[8]. Nevertheless, Zheng and colleagues' work represents a substantial advance, and demonstrates the potential of a potent new tool in the fight against mosquito-borne infectious disease. ■

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CONDENSED-MATTER PHYSICS

Spectroscopy with a magic twist

When two graphene sheets are stacked so that there is a specific angle between them, fascinating properties reminiscent of high-temperature superconductors emerge. Spectroscopy now provides insights into this behaviour. SEE LETTERS P.95 & P.101

MATHIAS S. SCHEURER

Rotating two overlapping mesh grids relative to each other produces interference patterns called moiré fringes. In the past few years, scientists have started to engineer moiré fringes at the atomic scale by twisting single-atom-thick layers of suitable materials, such as graphene (a 2D honeycomb lattice of carbon atoms). In 2018, it was shown that, as the twist angle between two graphene sheets is tuned to about 1°, the physical properties of the system change dramatically[1,2] to resemble those of high-temperature superconductors. To explore the microscopic physics of these surprising observations, four teams — Kerelsky *et al.*[3] (reporting on page 95), Xie *et al.*[4] (page 101), Jiang *et al.*[5] in a paper online in *Nature* and Choi *et al.*[6] in a paper on the arXiv preprint server — have carried out spectroscopic measurements on twisted bilayer graphene.

Many properties of single-layer graphene can be qualitatively understood in the free-electron picture, in which the repulsion between electrons is neglected. For instance, the relationship between the energy and the momentum of an electron in this material is, to a good approximation, independent of the density of surrounding electrons.

The situation is very different for twisted bilayer graphene at 'magic' twist angles[7], the largest of which is about 1°. In this case, electrons occupy flat bands — energy levels whose energies vary only weakly with electron momentum. Because of the small energy range of these flat bands, interactions between electrons cease to be weak perturbations, and the physical properties of the system depend crucially on the electron density. The interactions even induce phases that are not seen in single-layer graphene[1,2]: the system acts as an electrical insulator for certain electron densities for which the free-electron picture predicts a metallic phase; and, as in the case of high-temperature superconductors, increasing