Spread of introduced *Wolbachia* in natural insect populations: robust predictions relevant to dengue control

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Keywords: reaction-diffusion, bistability, wave speed, wave initiation, wave stopping

Wolbachia are maternally inherited endosymbiotic bacteria that generally live inside the cells of invertebrate hosts [1]. *Wolbachia* can spread through populations by manipulating host reproduction to favor infected females – and they also can protect their hosts from other microbes, including agents such as the dengue virus that cause human disease [2]. Since 1984, Hoffmann, Turelli and collaborators have documented three examples of rapid spatial spread of *Wolbachia* through natural populations of *Drosophila simulans*, starting with spread through California at about 100 km/year [3, 4]. This rapid spread helped motivate ongoing *Wolbachia*-based population manipulations aimed at dengue control in Australia, Vietnam, Indonesia, Brazil and Colombia. The original interpretation of *Wolbachia* spread invoked "bistable" frequency dynamics, in which reproductive manipulation by *Wolbachia* overcame both imperfect maternal transmission and fitness costs associated with the infection. But bistable dynamics are difficult to reconcile with very rapid spatial spread. We will discuss models and data relevant to understanding *Wolbachia* spread in nature. Although bistability now seems implausible for natural *Wolbachia* infections [4], it almost certainly describes artificially introduced *Wolbachia* infections, specifically the transinfection of *Aedes aegypti* with *w*Mel, a *Wolbachia* strain native to *D. melanogaster* that suppresses transmission of the dengue virus. The mathematics of bistability implies that contrary to the very rapid spread of native *Wolbachia* through *Drosophila* populations, introduced *Wolbachia* will spread much more slowly, on the order of 100-300 m/year (versus 100 km/year), through *Aedes aegypti* populations. This prediction is consistent with new data from Australia. We present results describing the robustness (and limitations) of reaction-diffusion-based predictions [5] concerning wave speed, wave width and wave initiation to long-tailed dispersal. In principle, even slow spatial spread can contribute to area-wide control of vector-borne diseases such as dengue. However, spread may be regularly halted by barriers to dispersal.

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