2023_85_SPH_Hancock: Modelling strategies for the release of genetically-modified mosquitoes for arboviral control across different environmental settings

Supervisors: Dr Penny Hancock (mailto:p.hancock@imperial.ac.uk); Dr Ilaria Dorigatti (School of Public Health), Dr Andrew Hammond (Biocentis)

Department: School of Public Health

We will develop mathematical models to investigate the potential of novel strategies for controlling populations of insect pests and disease vectors that utilise cutting edge approaches in genome engineering. These strategies involve releasing insects carrying genes that spread through wild populations despite incurring fitness costs. These genes spread because they use CRISPR-based molecular mechanisms to bias their own inheritance above the normal Mendelian rate of 50%, a process known as “gene drive”. As the genes increase in frequency, the population undergoes phenotypic transformation that can manifest as population suppression or reduced rates of insect-to-human disease transmission. For instance, a gene-drive that confers female sterility has been shown to induce complete suppression of caged populations of *Anopheles gambiae* mosquitoes, a major vector of malaria. Traditional vector control methods based on the mechanical removal of breeding sites and insecticide spraying are known to have a negative impact on the environment. Gene drive technologies offer an environmentally beneficial alternative, because their impacts are restricted to the target organism.

Arboviruses transmitted by *Aedes aegypti* mosquitoes, such as dengue and Zika, represent a huge public health burden in the tropics and sub-tropics. Arbovirus transmission is highly sensitive to climatic conditions, and it is critical to understand how climate change will influence their distribution and spread. Our modelling approach will represent key aspects of the ecology of *Ae. aegypti* mosquitoes, and how these respond to endogenous and exogenous environmental variation. We will use empirical data to capture ecologically realistic patterns of mosquito life history, including density-dependent population regulation, temperature dependancy, and spatial landscape connectivity. Model sensitivity analyses will identify key ecological processes that influence the fate of introduced gene drive constructs, considering different environmental settings and projected climate change scenarios. We will link these ecological models to epidemiological analyses to investigate the potential of gene drives to reduce the burden of arboviruses across the global environmental range of *Ae. aegypti* under climate change. Our candidate will be part of an industrial collaboration with Biocentis (https://biocentis.com/), a biotechnology company building sustainable solutions for genetic control of insect pest and vector species. Biocentis uses genome engineering to develop novel insect strains that can be released to reduce populations of harmful insect species that threaten agriculture, human health, and the environment. The candidate will benefit from a placement abroad with Biocentis (Terni, Italy) providing interdisciplinary training across academic and industrial settings. This exposure will provide unique insight into the translation from genome engineering and product development through to field trials.

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