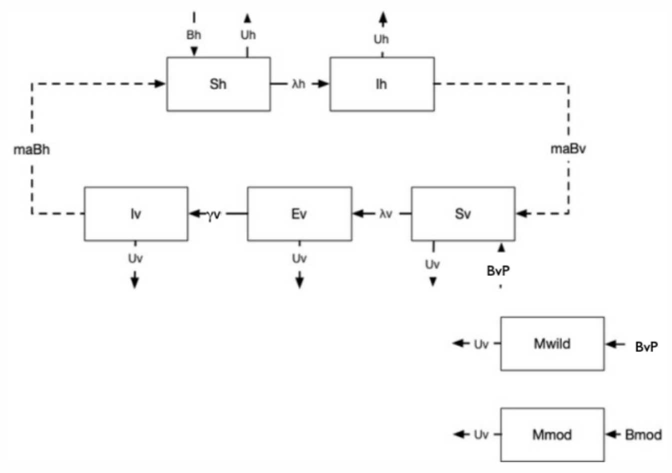
How many genetically modified Anopheles gambiae mosquitoes need to be released into endemic regions in Africa to eliminate Plasmodium falciparum malaria?

Background

In 2015, approximately 3 billion people were at risk of contracting malaria, while 429,000 deaths were estimated to occur as a result of the disease[1]. The disease burden is reflected through morbidity and mortality, but also an economic impact estimated to cost Africa $12 billion annually[2]. A reduction in this burden can be achieved by investing in technology-based interventions. The CRISPR-Cas9 is a gene drive system which influences female mosquito species such as Anopheles gambiae, the primary vector for malaria, to inherit male characteristics, thus supressing malaria transmission[3]. We are investigating the number of genetically modified mosquitoes needed eliminate malaria.

Methods

In order to project the outcome of a CRISPR-Cas9 intervention, the Odin programming language was used to run a model. We are assuming a 100% efficiency in the gene drive. The model considers the birth rate for both humans and modified mosquitos, as well as the death rate. We are especially interested in the death rate of the infected humans. The intermediate step between a susceptible and infected human is detailed as the force of infection, while for the mosquito this is the step between being susceptible and exposed. A significant component of the model is the parameter for the modified mosquito birth rate. This takes into account a 45% reduction in fecundity due to the gene drive. Due to the assumption that this system is 100% efficient, all mosquito offspring are modelled as being modified males.



Parameters:

- Bh/Bv: Birth rate human/vector
- Uh/Uv: Death rate human/vector
- λh: FOI human
- λv: FOI vector
- γv: Extrinsic incubation period
- P = Proportion of males that are wild type
- Bmod = Birth rate of modified mosquitoes taking 45% reduced fecundity into account

Figure 1: Gene Drive System Model Flowchart

Results

Computing the model in Odin found that a 100% efficient gene drive system would eliminate an Anopheles gambiae population irrespective of the number of genetically modified mosquitos released into the wild population. Figure 2a displays the number of infected humans decreasing over time as 100 modified mosquitos are released into the population. Eventually there are no infected humans after 800 days.

Figure 2b shows how sensitive the time frame for eradication of a population is to the number of mosquitos released.

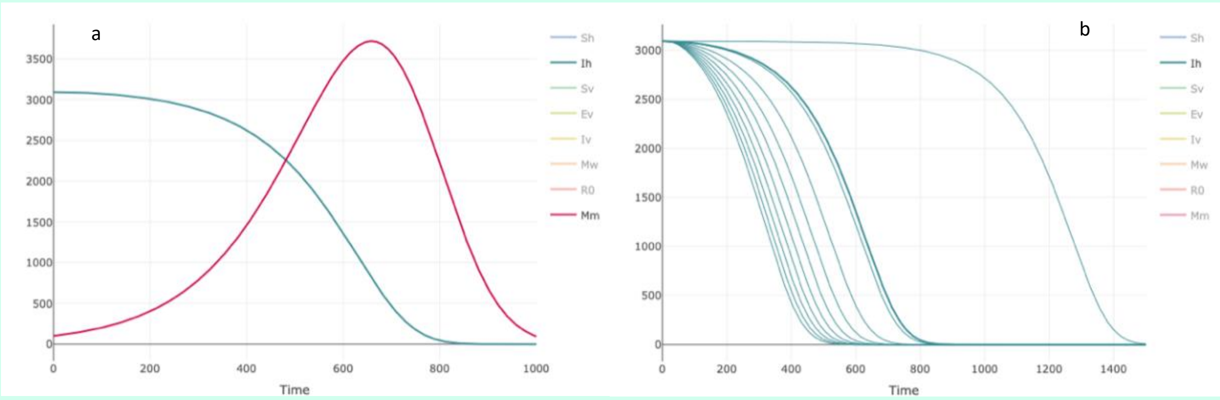


Figure 2: Model Graphical Outputs

Interpretation

Finding an effective vaccine against malaria appears to be a challenging public health objective[4]. Genetic modification carries the potential as an alternative intervention in reducing incidence through elimination of the vector. The model has shown that any number of modified mosquitos are able to cause wild populations to collapse within a respective time frame. A potential limitation, however, would be the assumption that the gene drive is 100% efficient – this is unlikely to be the case when carrying out the gene drive.

References:

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