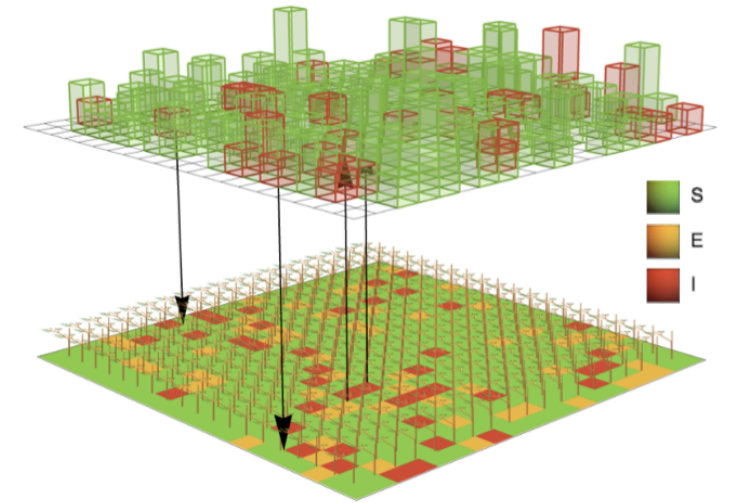
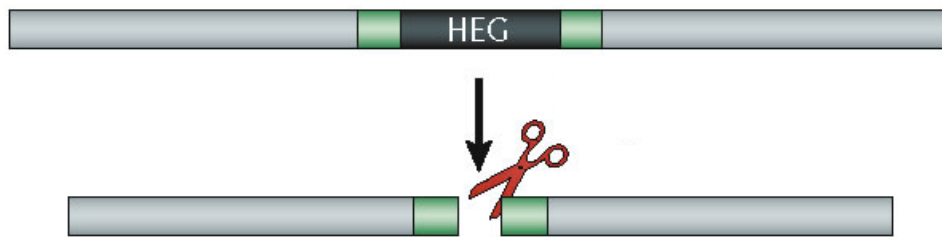


# CRISPR-Cas9-based gene drive architecture for control of agricultural pests

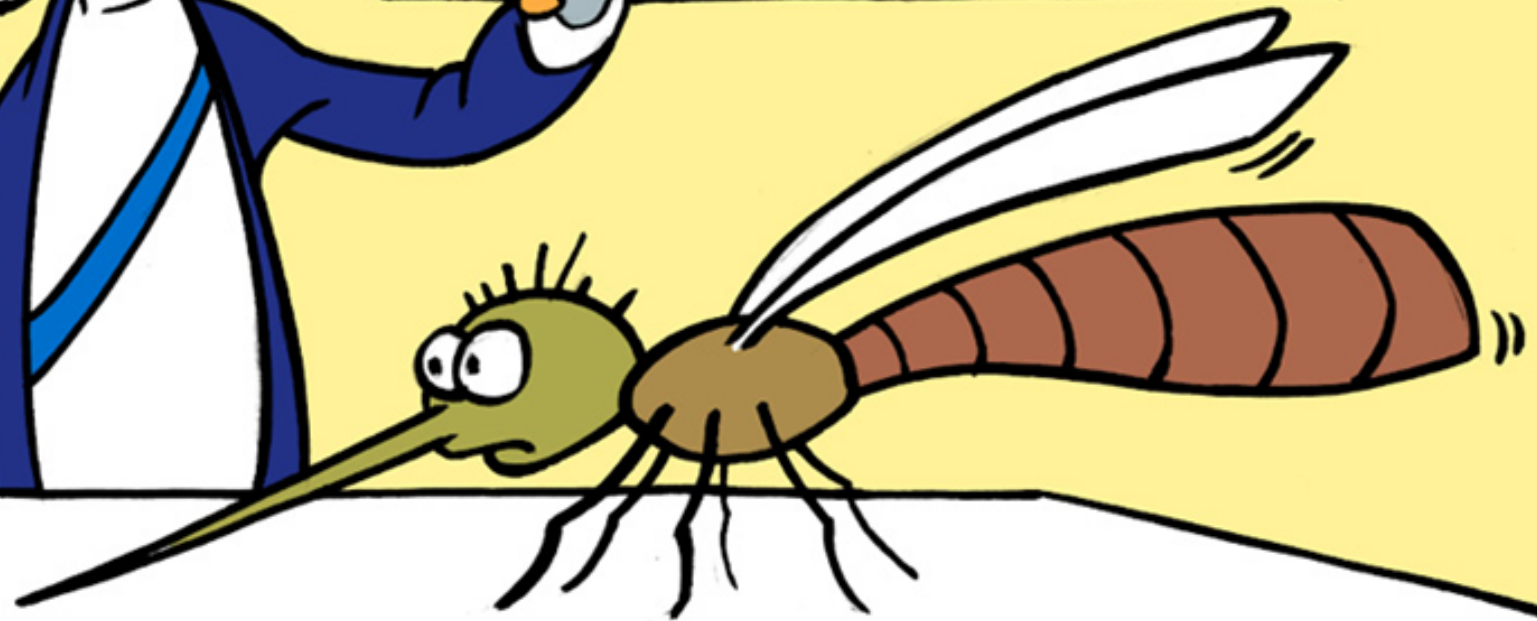


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Division of Biostatistics and Epidemiology  
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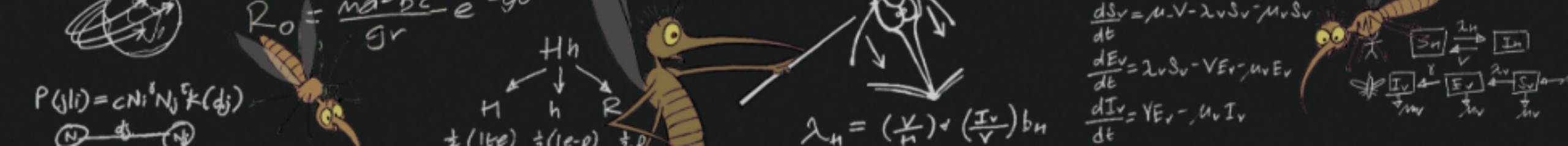
 School of  
Public Health

**M**  
LABS INC









**John Marshall**

**Samson Kiware**



**Hector Sanchez**



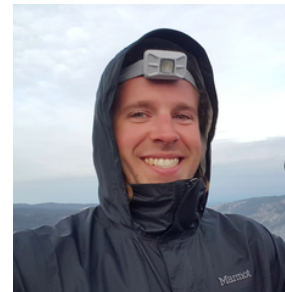
**Gordana Rašić**



**Yogita Sharma**



**Sean Wu**



**Jared Bennett**



**Partow Imani**



**Tomas Leon**



**Sarafina Smith**



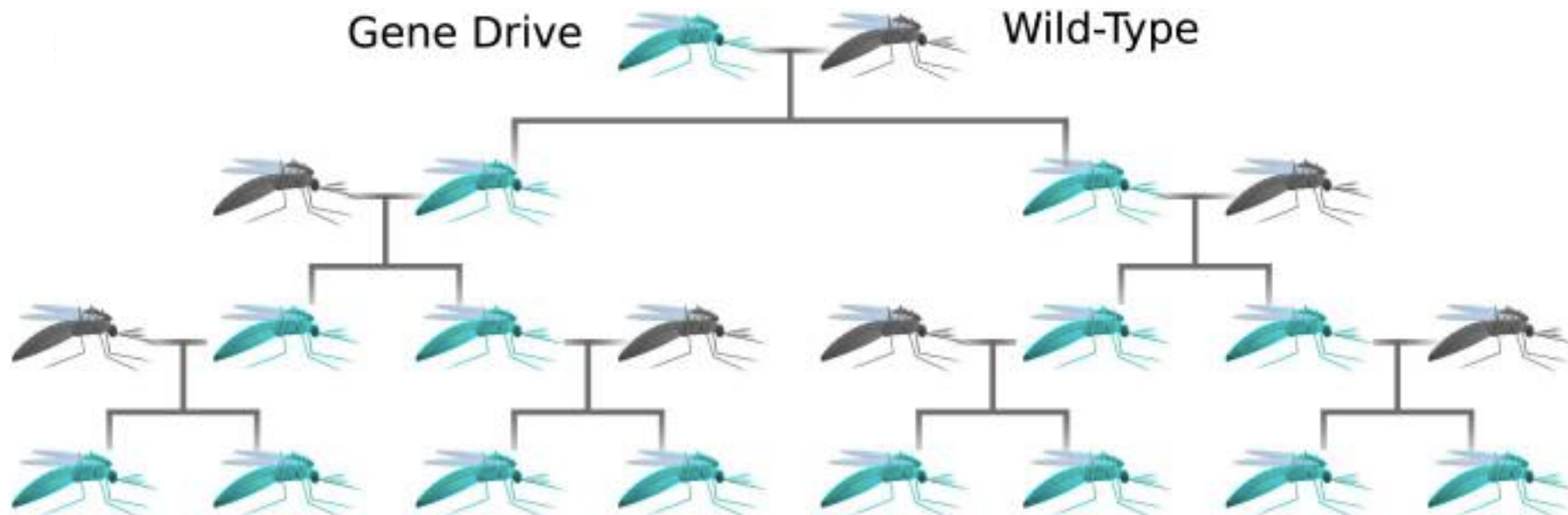
**Biyonka Liang**



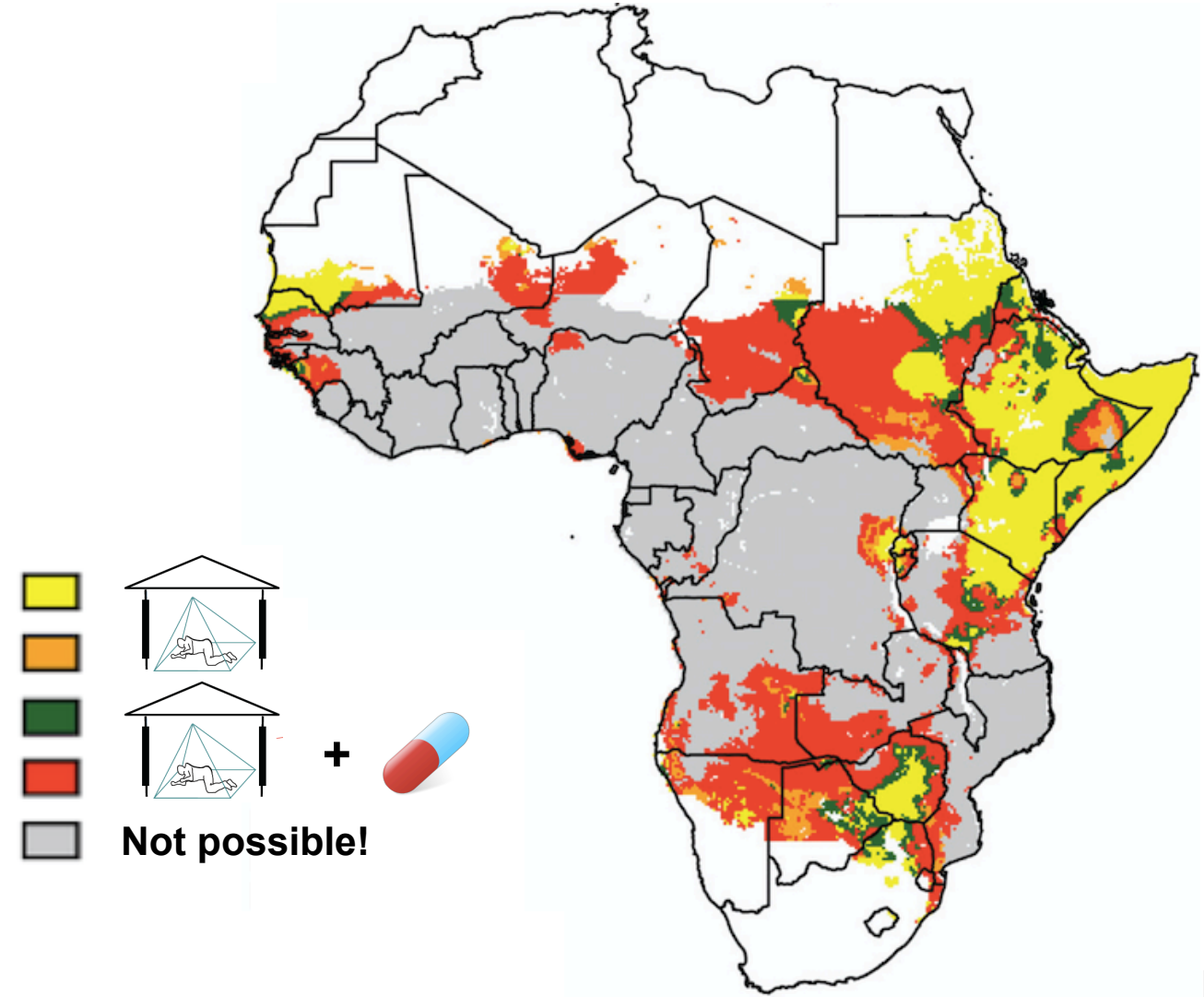
# Homing-based CRISPR-mediated gene drive



Construct cuts recognition site and serves as template for repair



# Optimal interventions to eliminate malaria



• Walker PGT, Griffin JT, Ferguson NM, Ghani AC (2016) Lancet Global Health

# Public attitudes to gene editing for malaria control in Mali



***“You have to start somewhere. From this, people will know whether it’s good or bad... I would like you to conduct a trial in my village because I would like to be an example for another community.”***

Elder, Koporo-na, Mali

***“I would have to see an example of modified mosquitoes reducing malaria in another village before I believe this claim”***

Elder, Tienfala, Mali

- Marshal JM, Toure MB, Traore MM, Famenini S, Taylor CE (2010) Malaria Journal 9: 128



# Can we conduct a confined field trial of gene-edited mosquitoes?

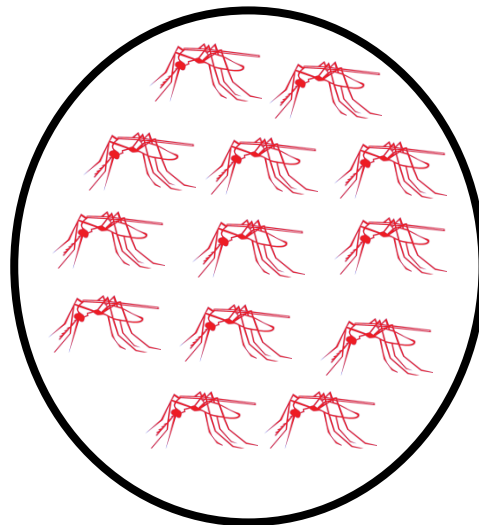


**Banambani, Mali**

7 km  
←→

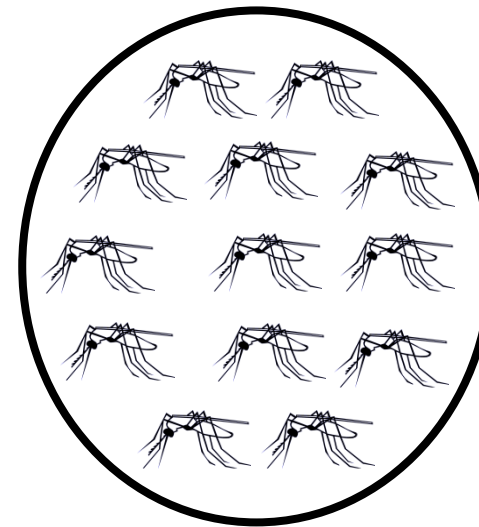


**Doneguebougou, Mali**



**Gene-edited mosquitoes**

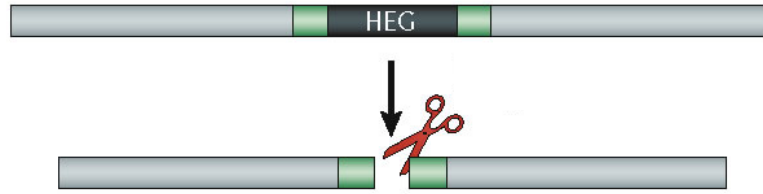
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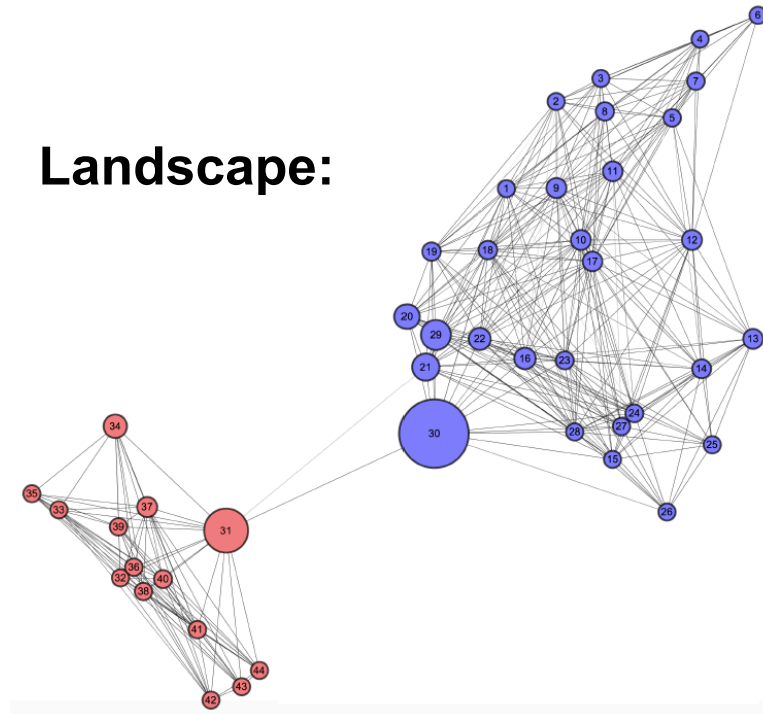
**Wild-type mosquitoes**

# Modeling as data integration to address specific questions

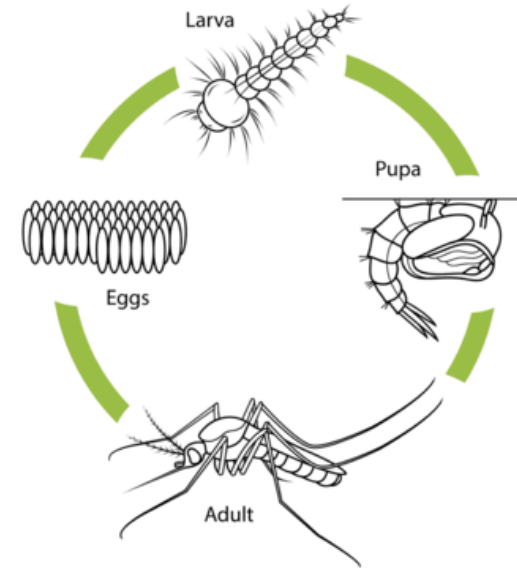
## Inheritance pattern:



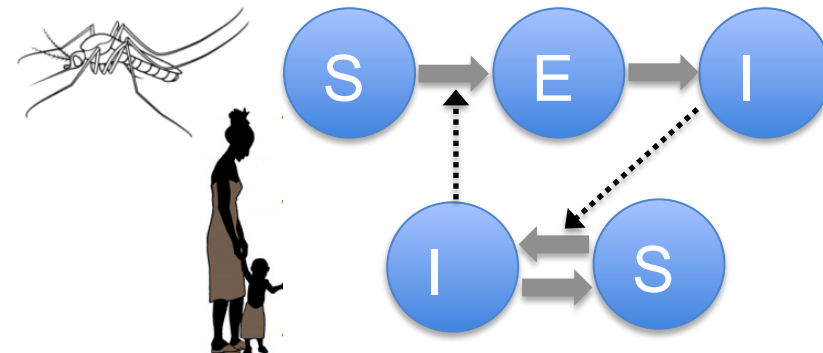
## Landscape:



## Mosquito life cycle:



## Disease epidemiology:



# Mosquito Gene Drive Explorer (MGDrivE)

## MGDrivE

Mosquitos + Tensors +  
Genetics + CS + Networks +  
Math + Coffee

View  
Releases List

Browse  
Documentation

View on  
Youtube

Fork on  
GitHub

Download  
ZIP File

Download  
TAR Ball

Developed in [John Marshall's Lab](#) by:

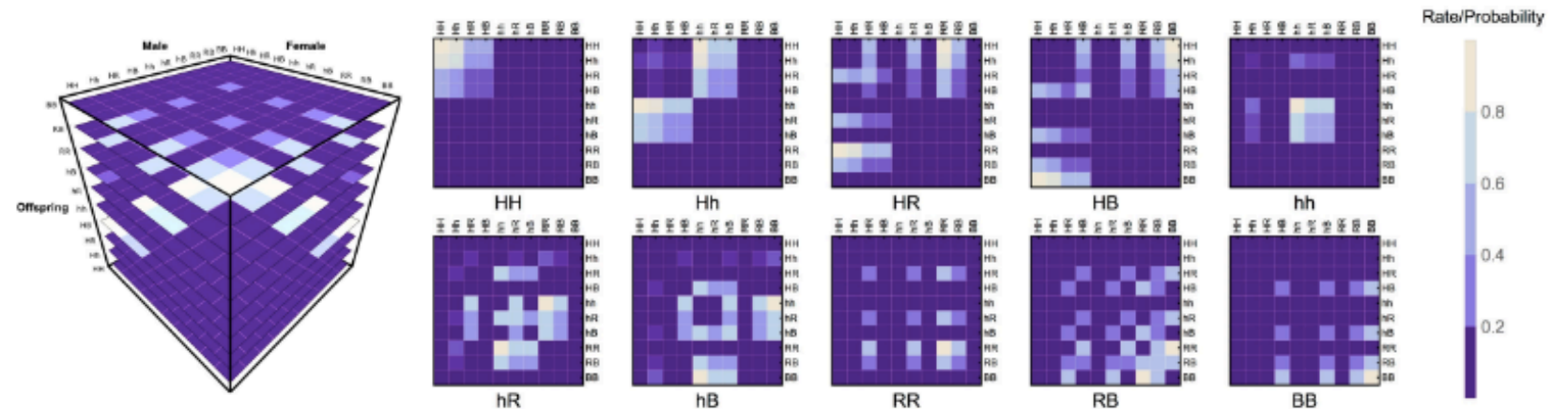
-Lead: [Héctor M. Sánchez C.](#)  
-Core Dev: [Sean L. Wu](#), [Jared Bennett](#)  
-Spatial Analysis: [Biyonka Liang](#), [Sarafina Smith](#),  
[Sabrina Wong](#)  
-Movement Kernels: [Partow Imani](#)

...and, of course, our PI: [John M. Marshall!](#)

# Mosquito Gene Drive Explorer

## Brief Description

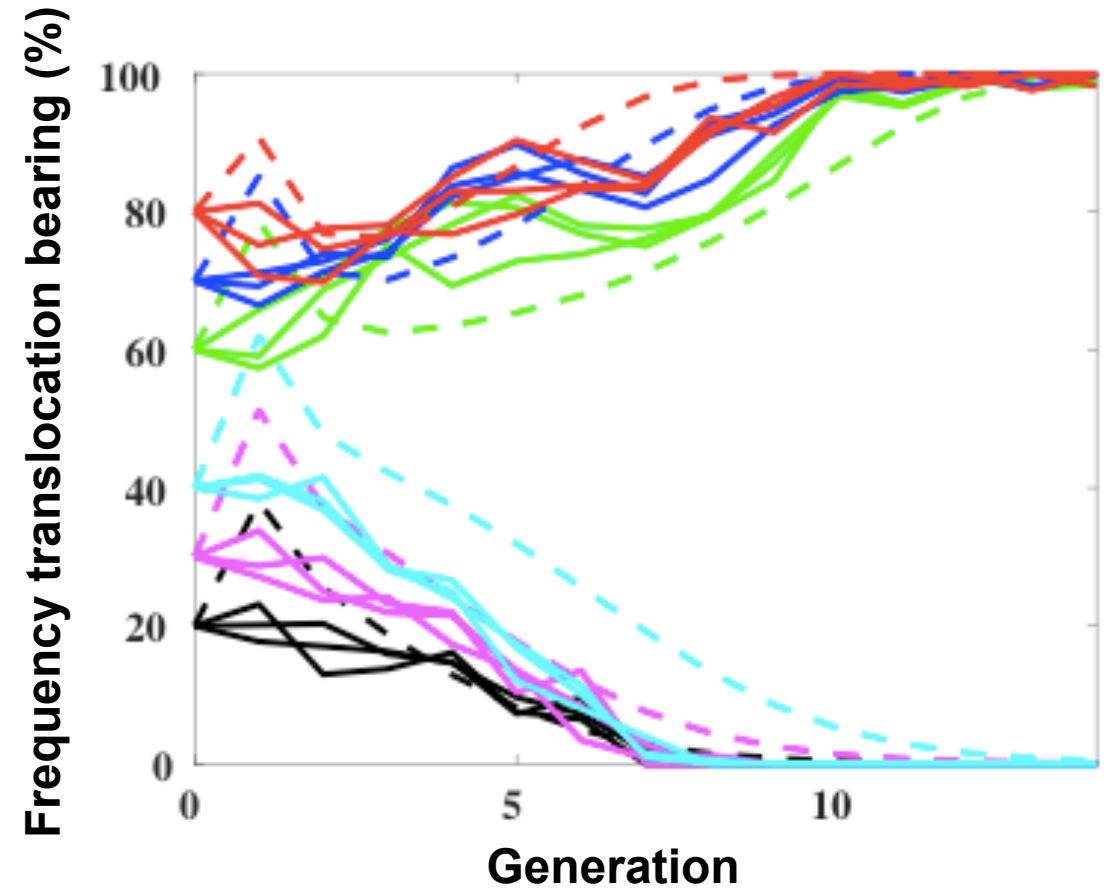
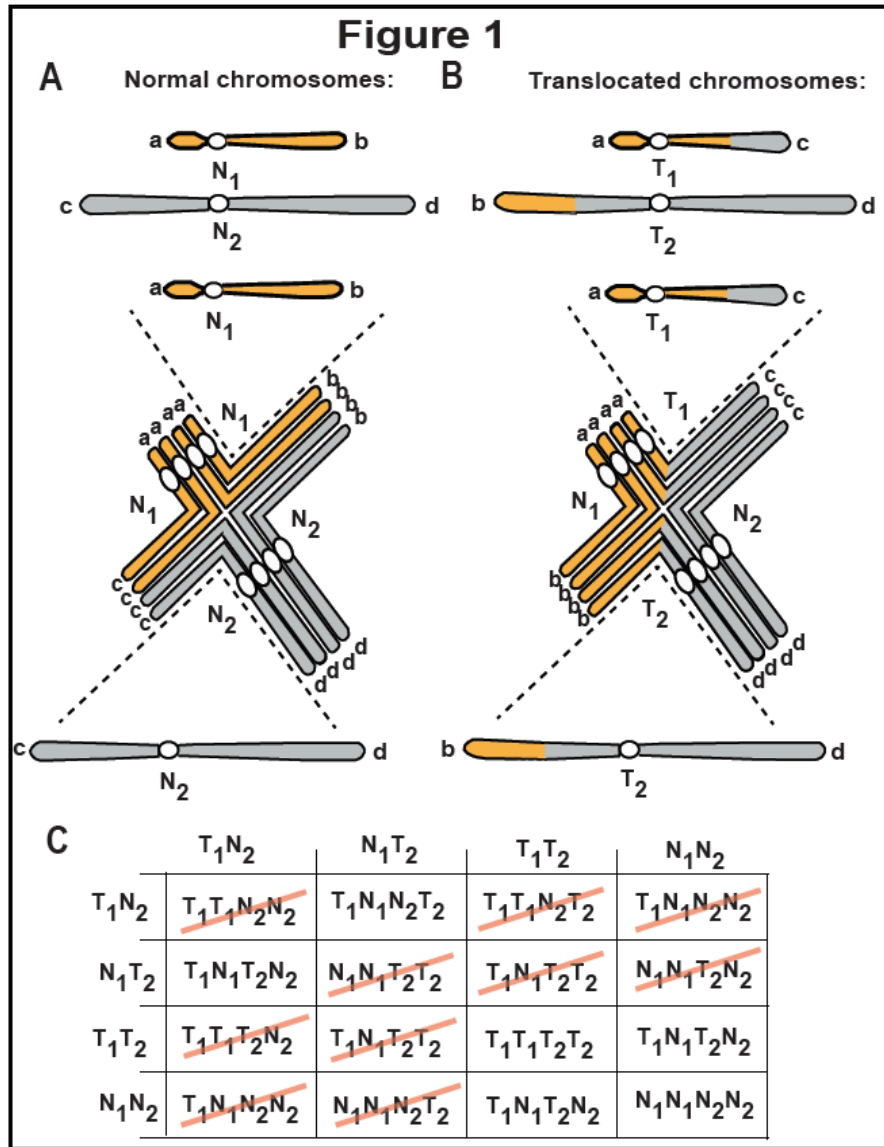
**MGDrivE** is a framework designed to serve as a testbed in which gene-drive releases for mosquito-borne diseases control can be tested. It is being developed to accommodate various mosquito-specific gene drive systems within a population dynamics model that allows migration of individuals between nodes in a spatial landscape.



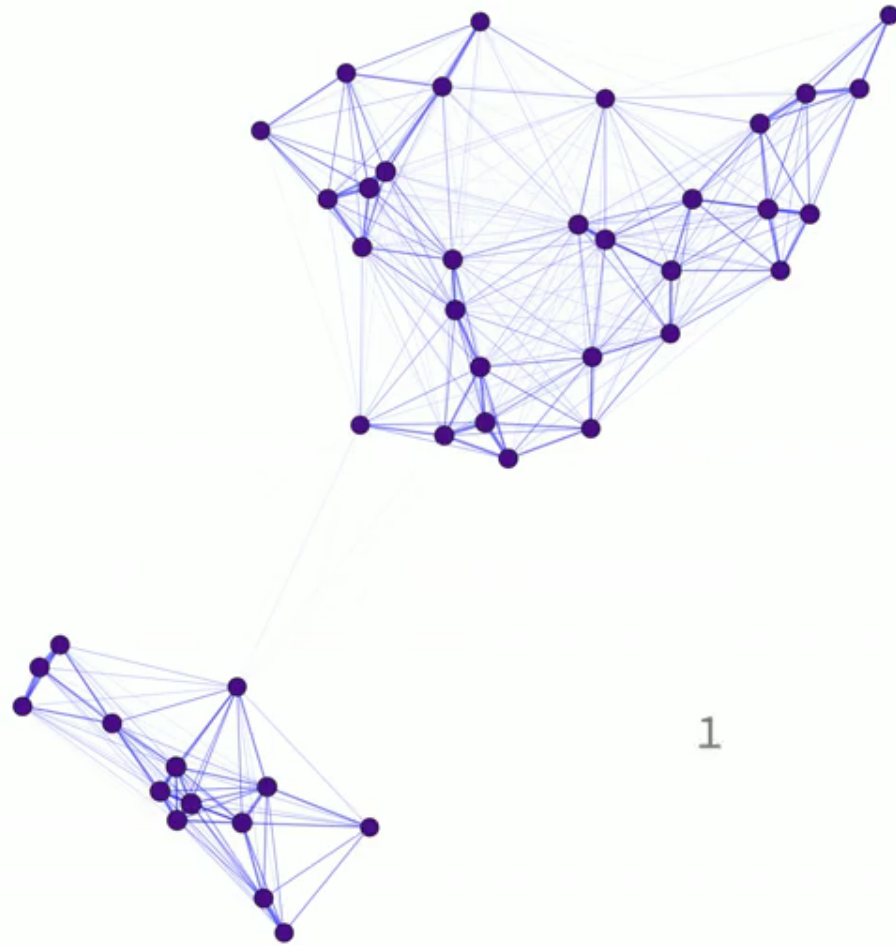
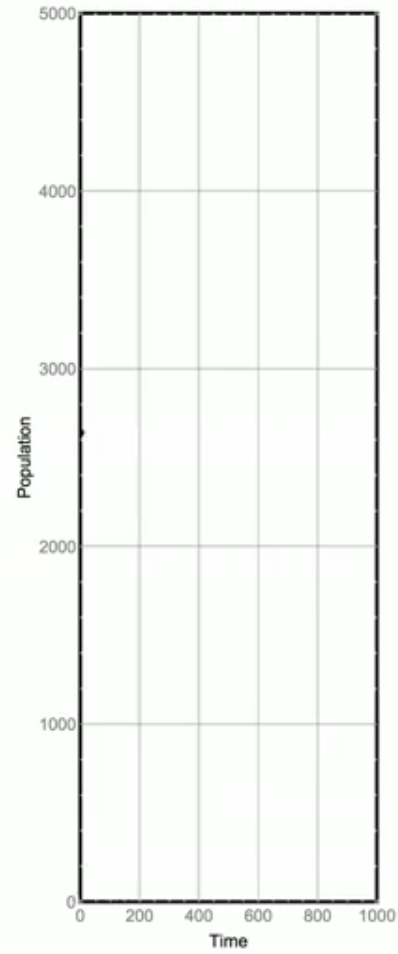
## Demonstration



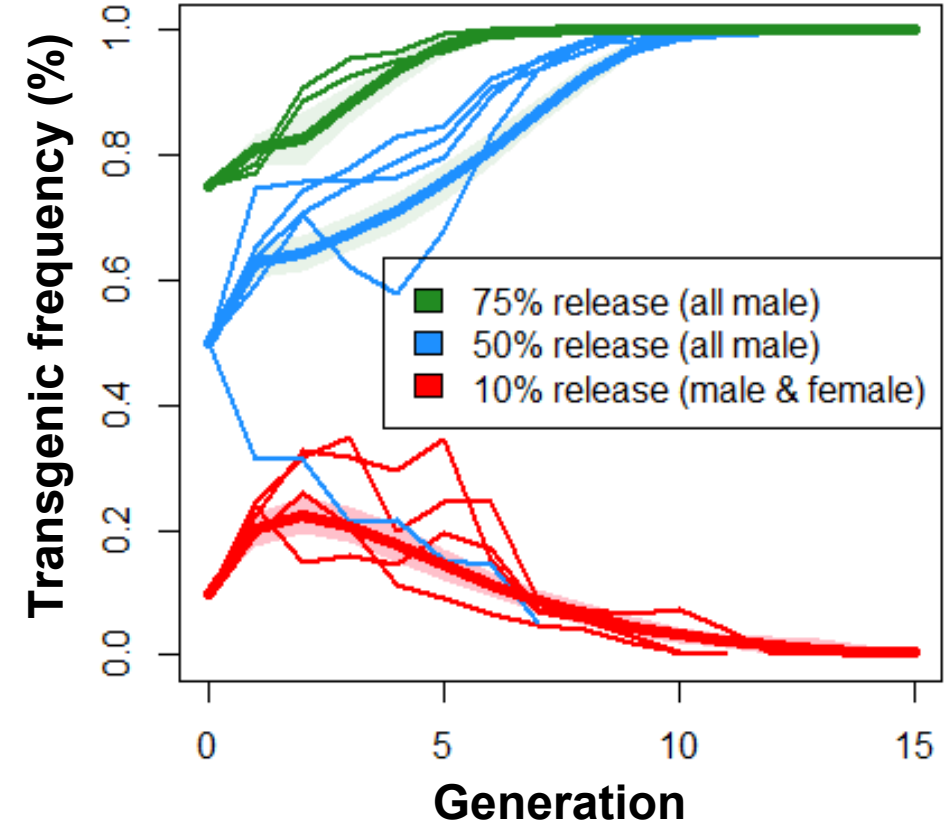
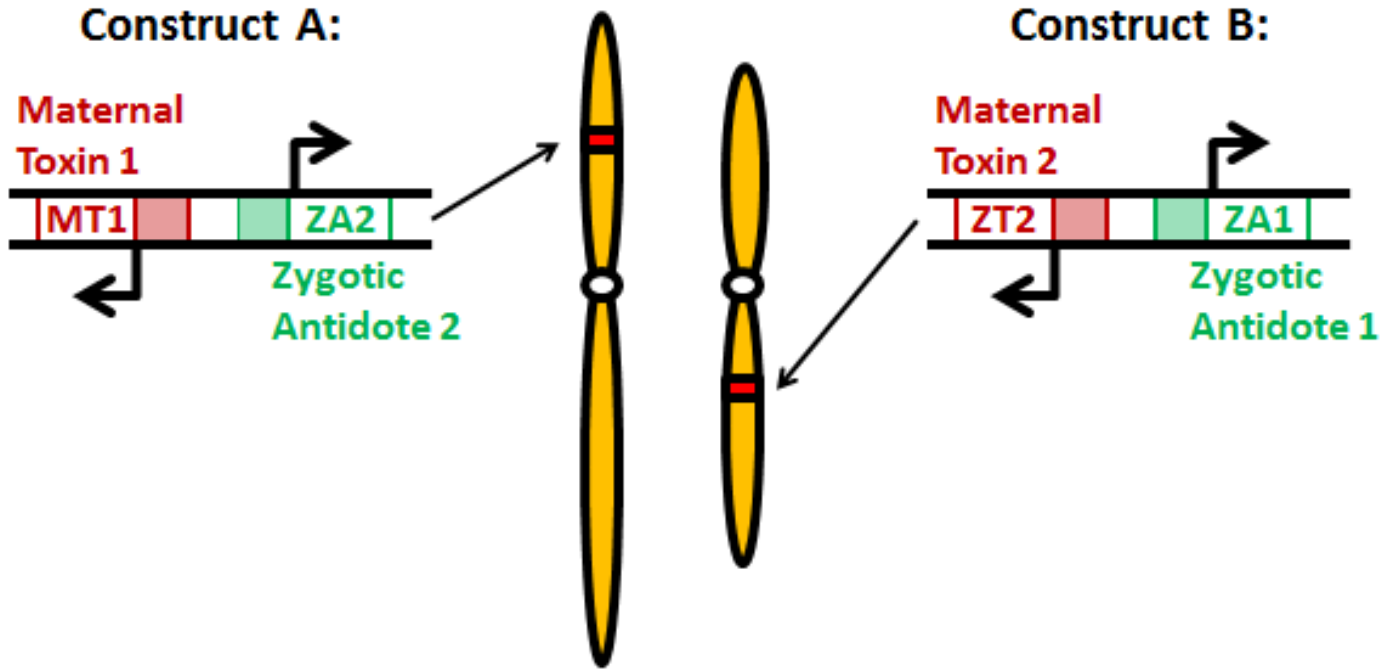
# Application to chromosomal translocations



# MGDrivE: Translocations with remediation

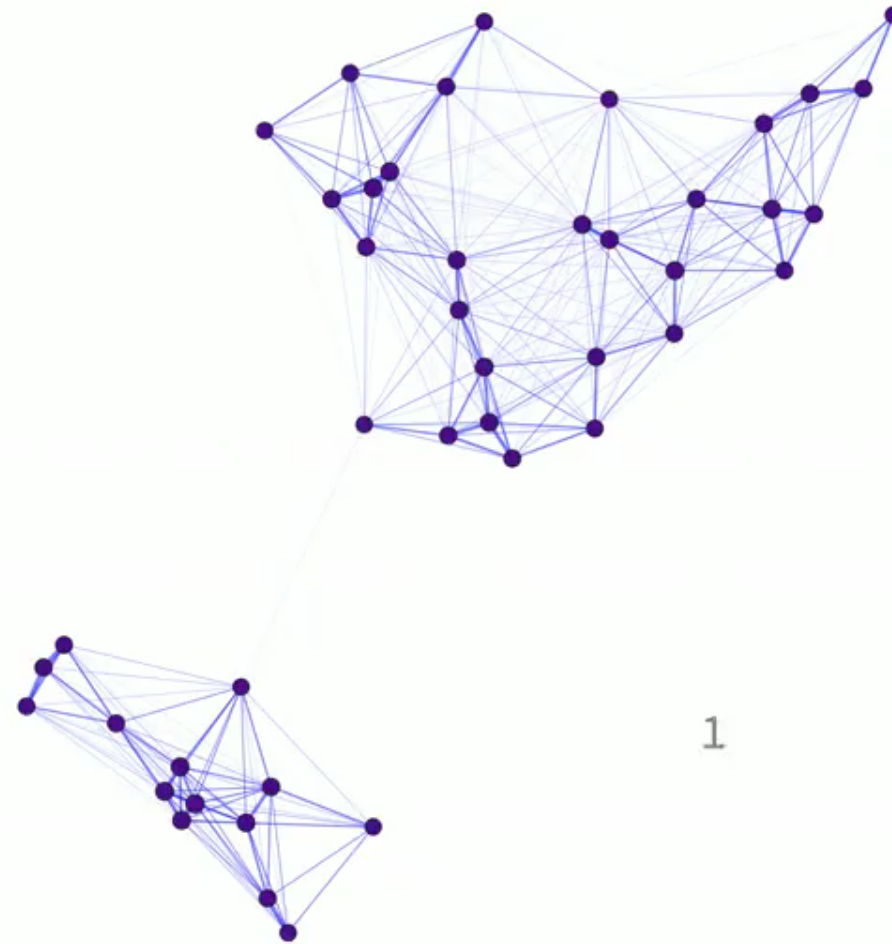
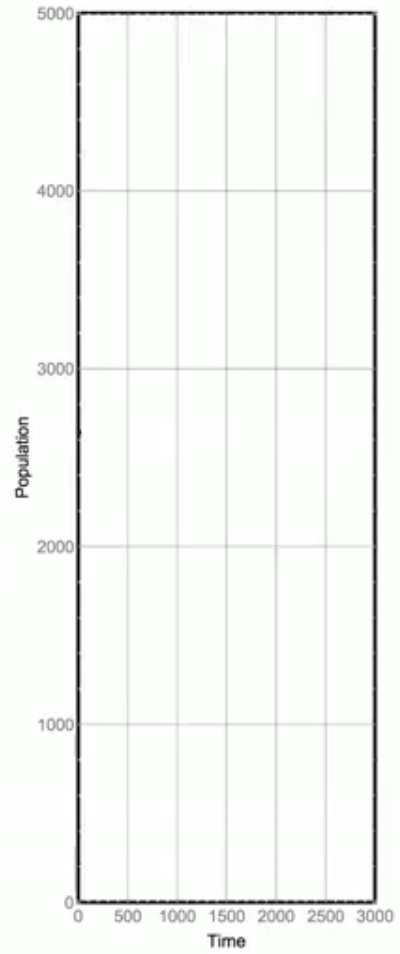


# Application to toxin-antidote-based underdominance

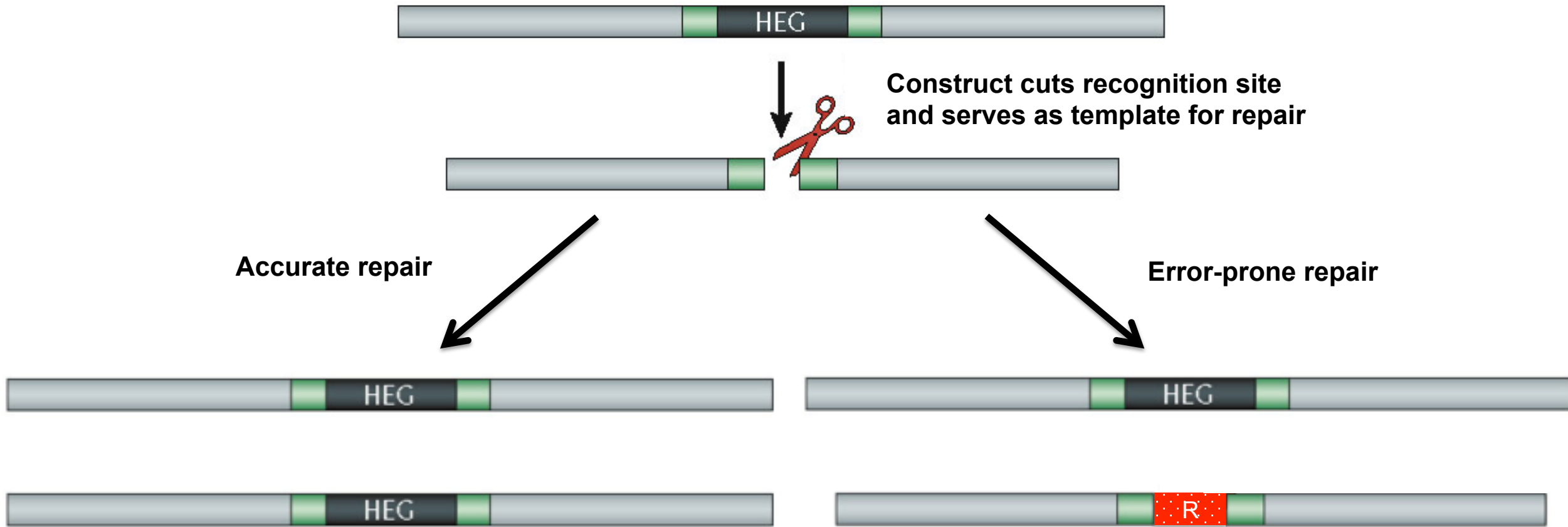




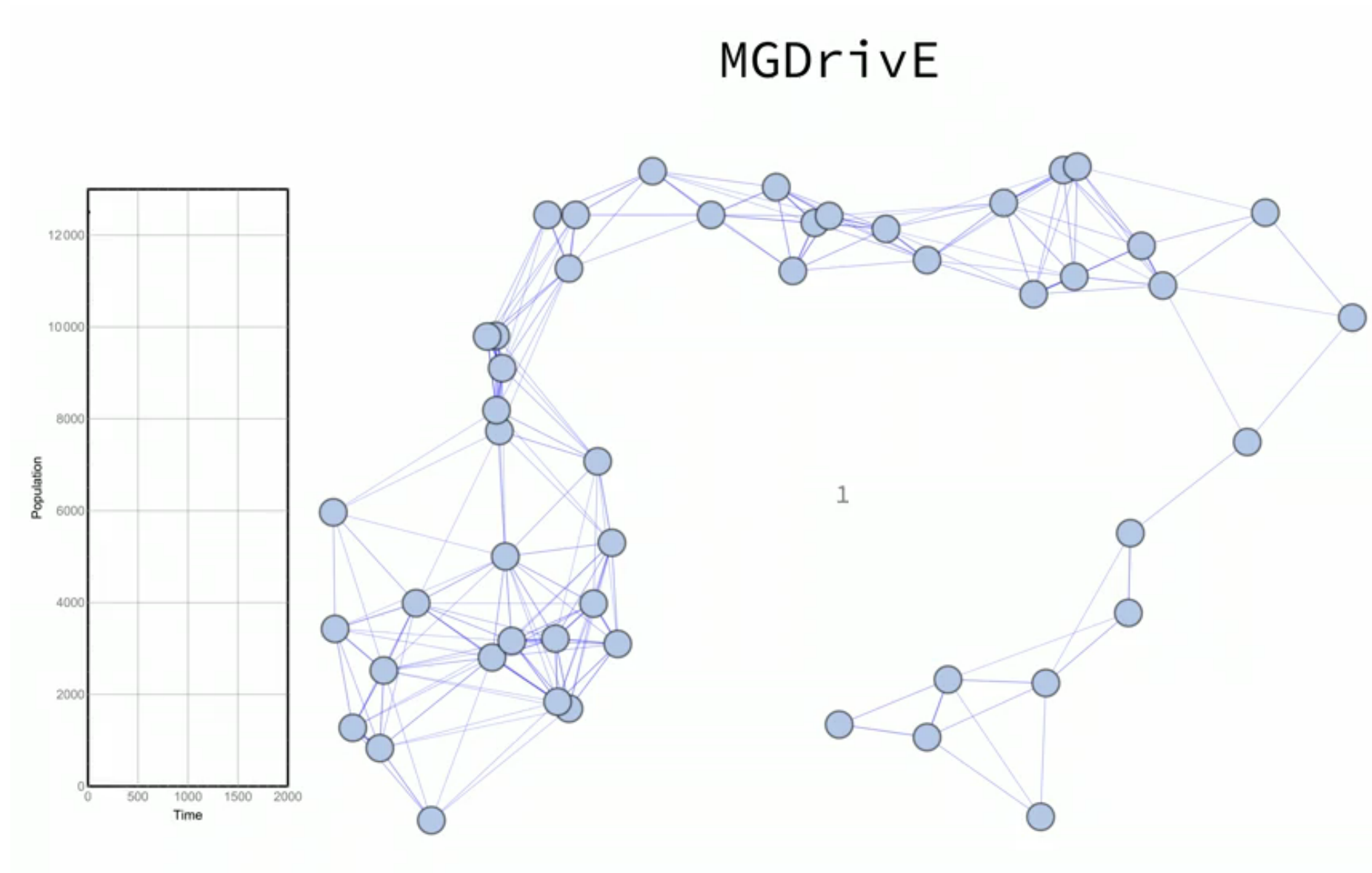
# MGDrivE: Toxin-antidote-based underdominance



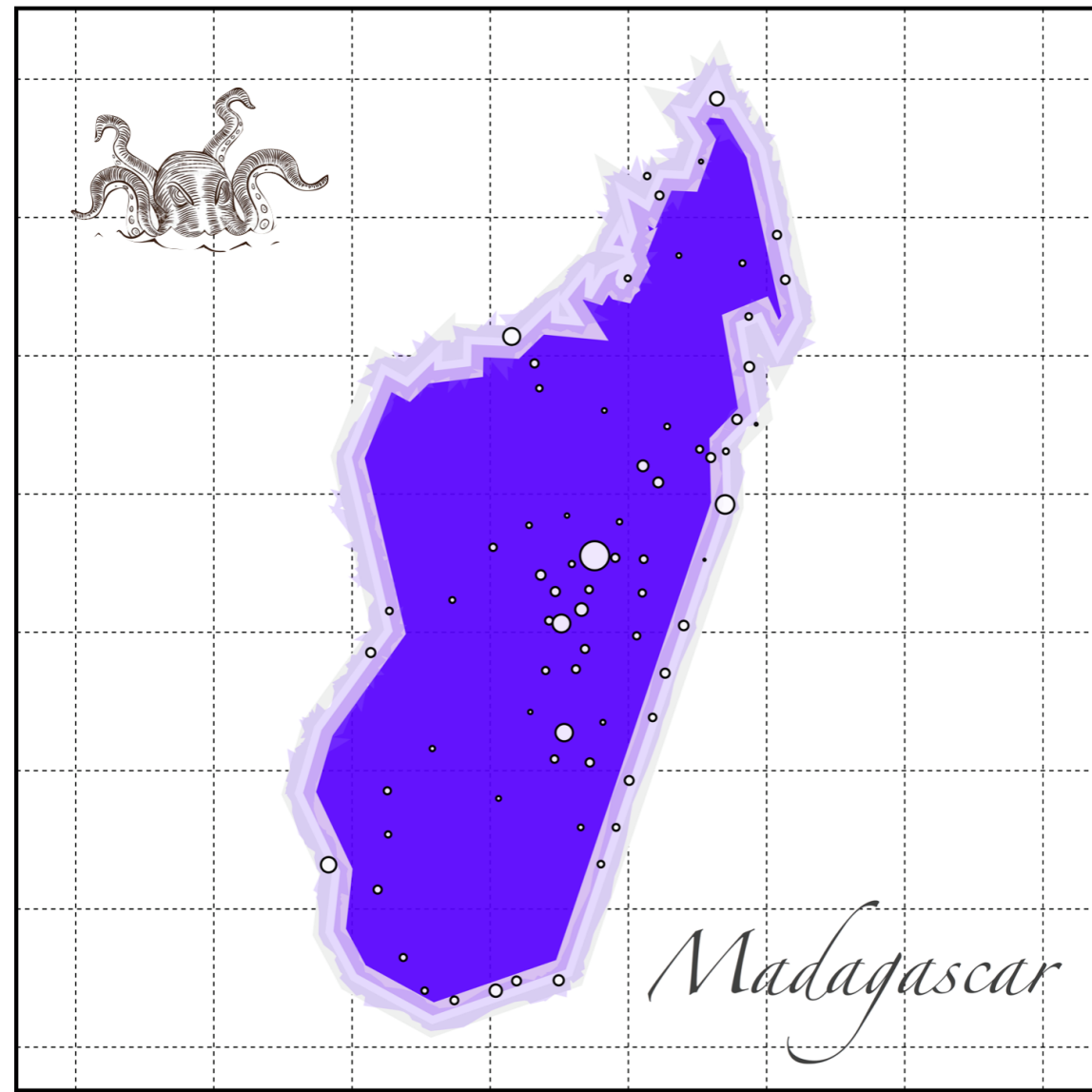
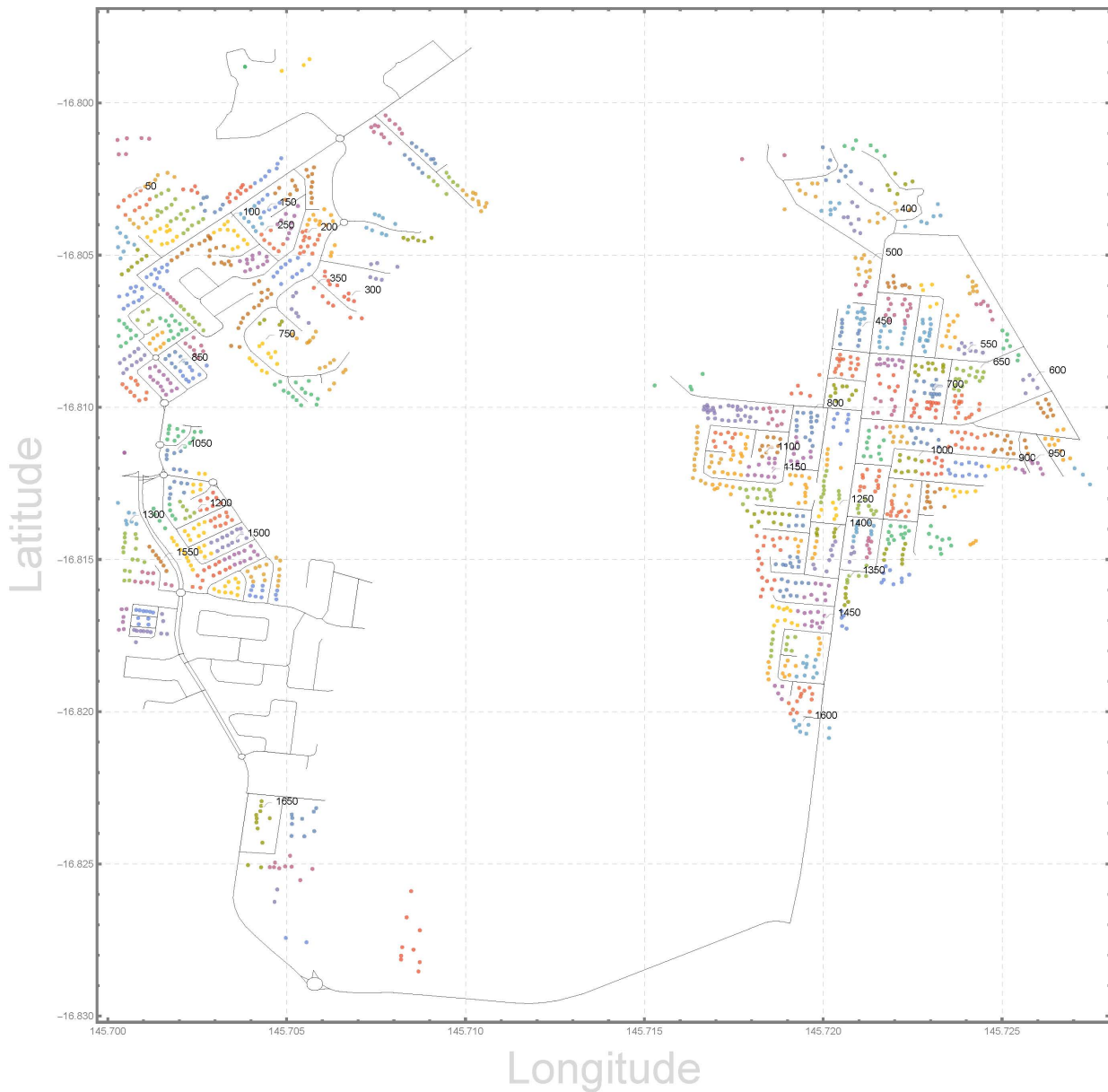
# Homing-based gene drive with resistant alleles



# MGDrive: Homing-based gene drive with resistance

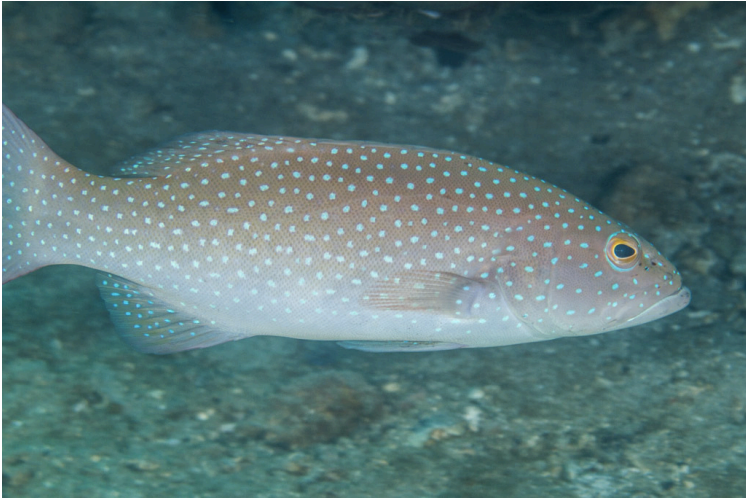
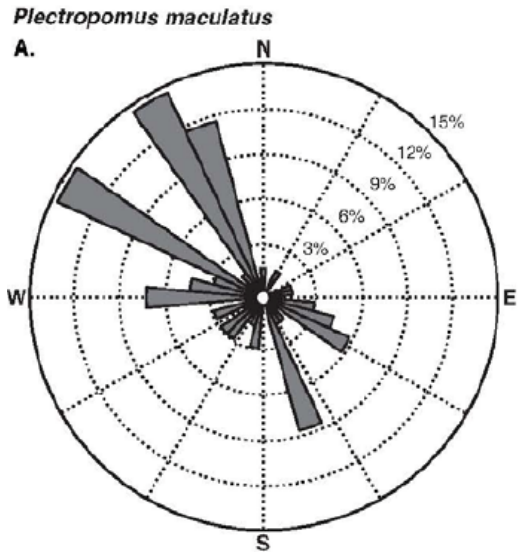
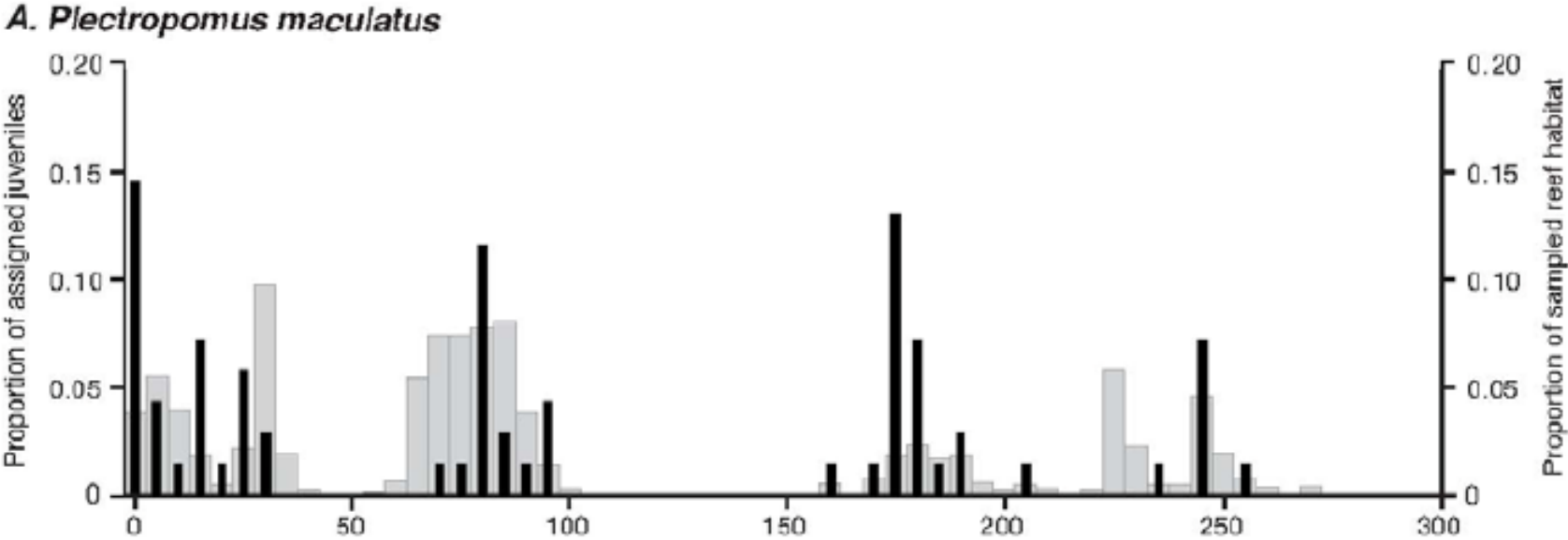


# Extrapolating to more realistic landscapes



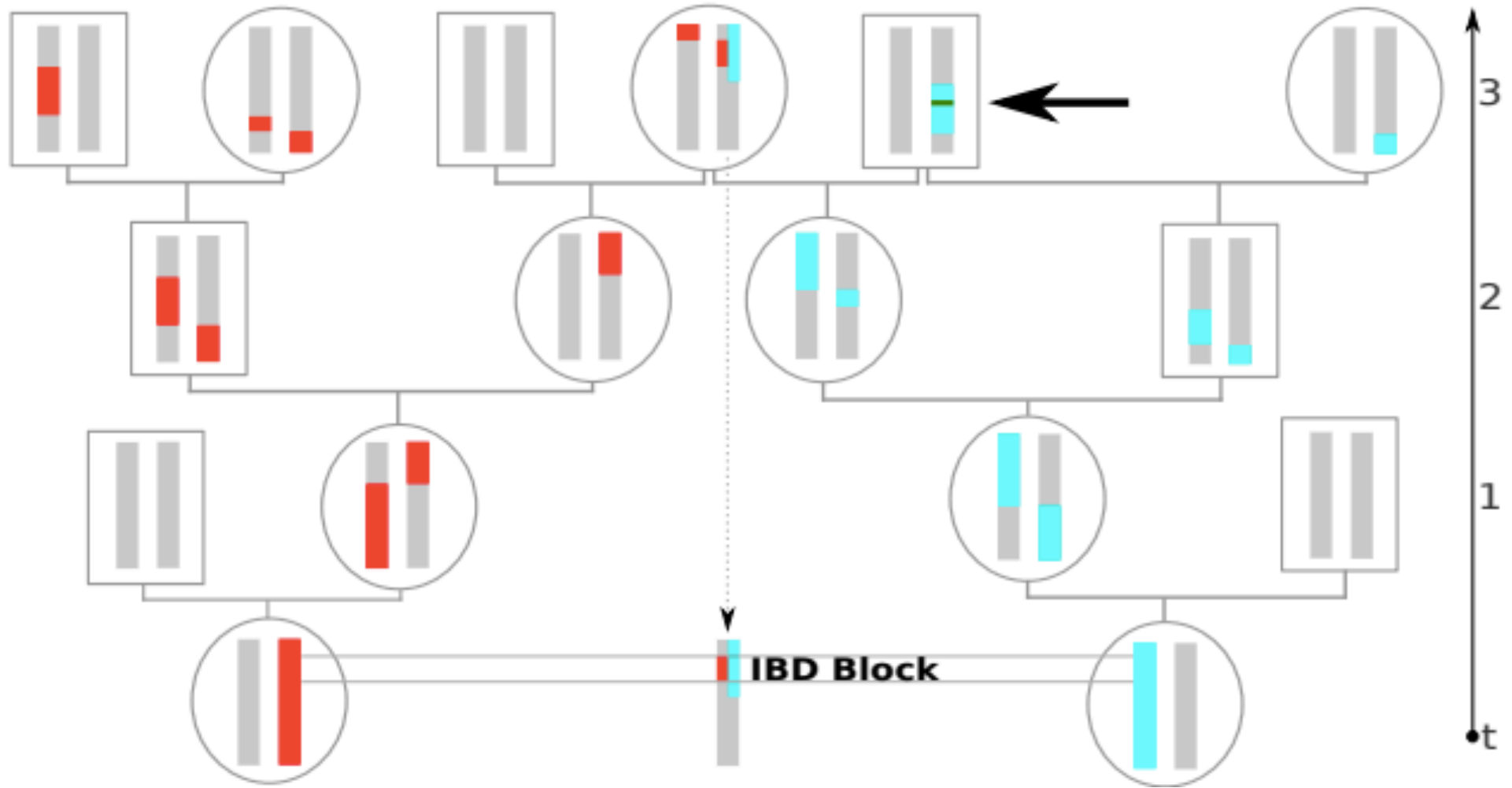


# Fine-scale movement patterns from parentage analysis



- Williamson DH, Harrison HB, Almany GR, Berumen ML *et al.* (2016) *Mol. Ecol.* 25L 6039-6054

# Intermediate movement from identity by descent (IBD)



- Ringbauer H, Coop G, Barton NH (2017) Genetics doi: 10.1534/genetics.116.196220.

# Insect agricultural pests of interest



***Drosophila suzukii***



***Ceratitis capitata***



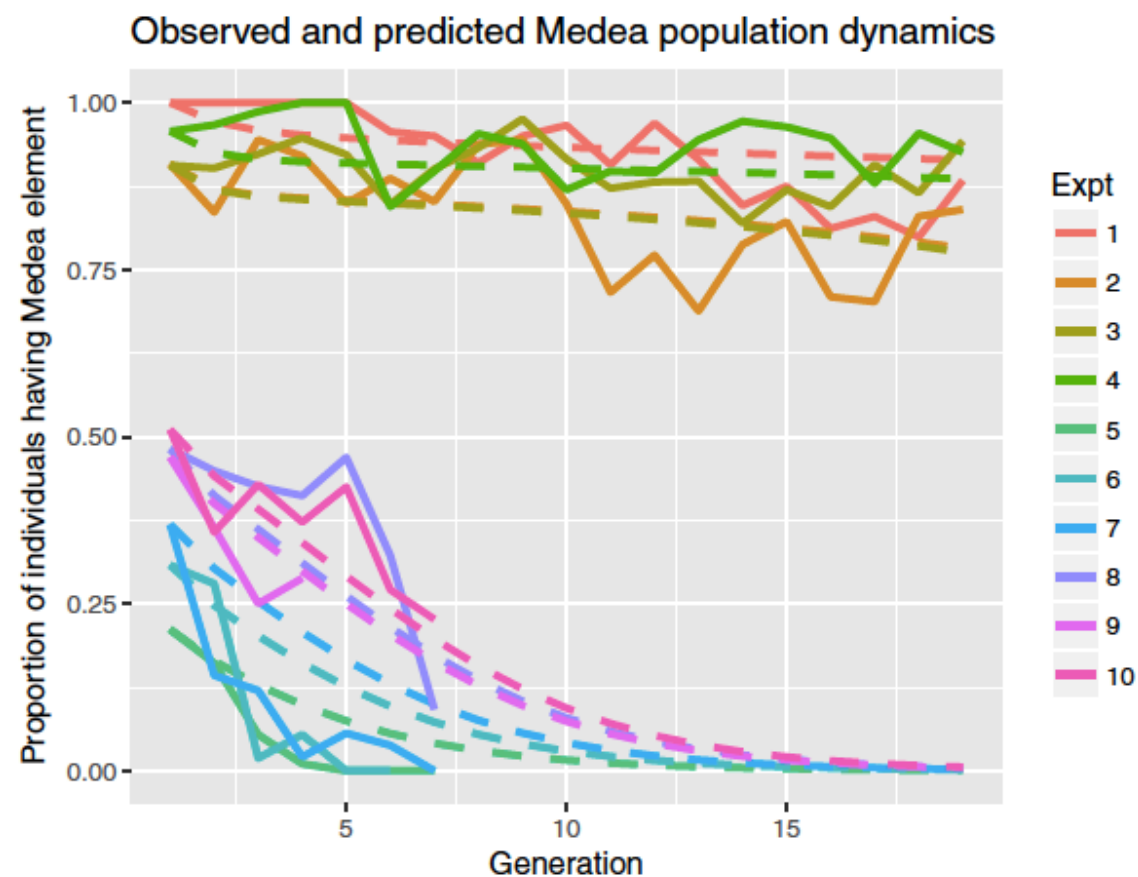
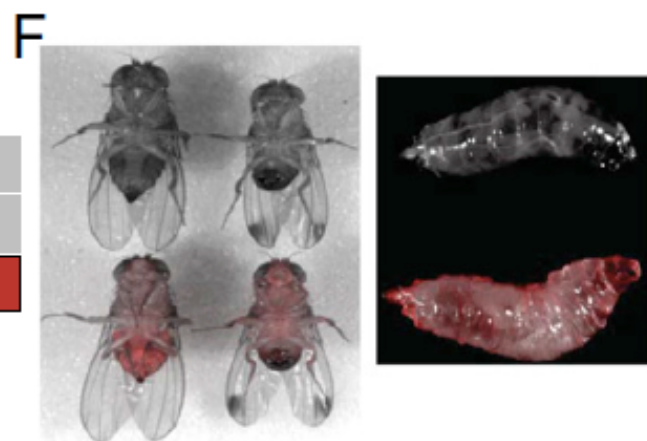
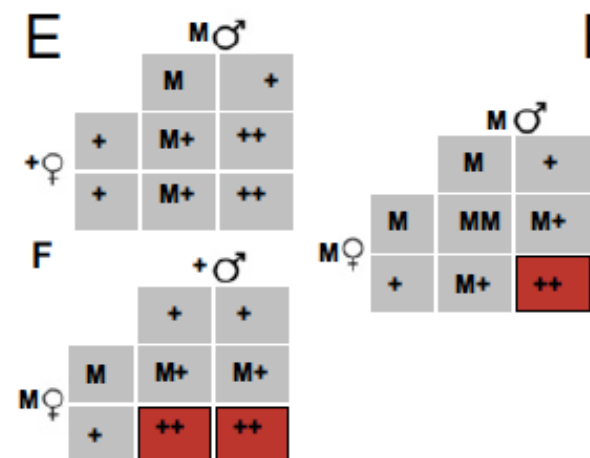
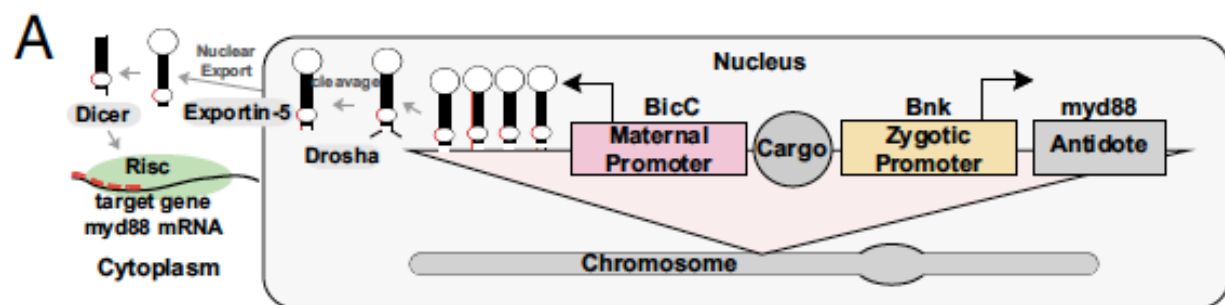
**Asian citrus psyllid**



**Pink bollworm**

# Synthetically engineered *Medea* gene drive system in the worldwide crop pest *Drosophila suzukii*

Anna Buchman<sup>a,b,c</sup>, John M. Marshall<sup>d</sup>, Dennis Ostrovski<sup>a,b</sup>, Ting Yang<sup>a,b,c</sup>, and Omar S. Akbari<sup>a,b,c,e,1</sup>

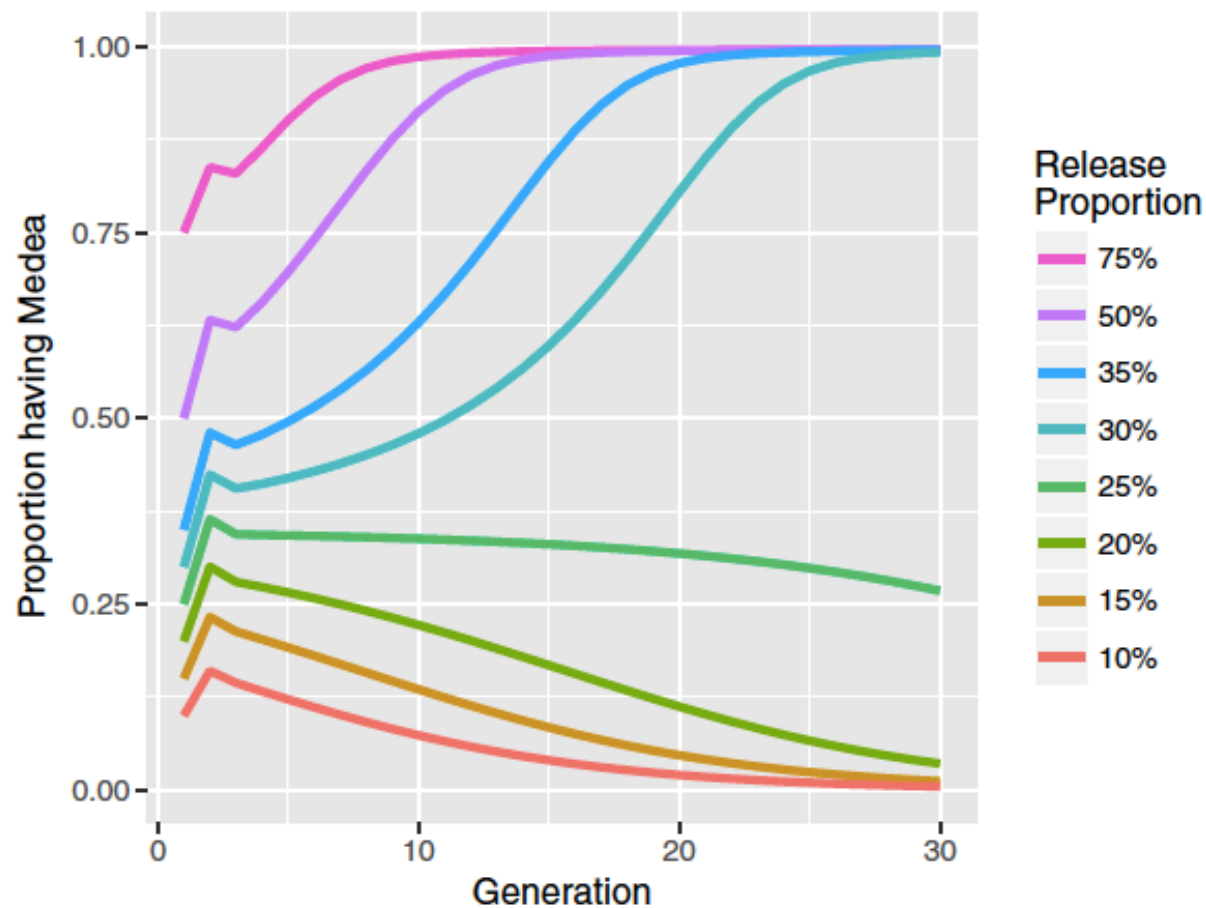




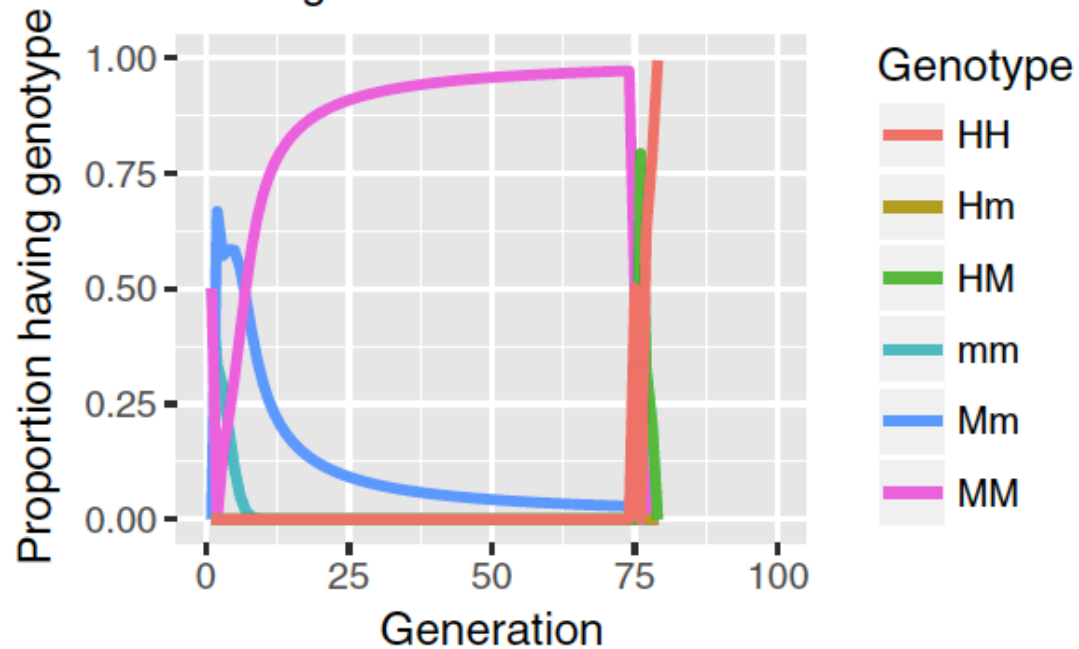
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Fitness costs halved, 93% toxin efficiency

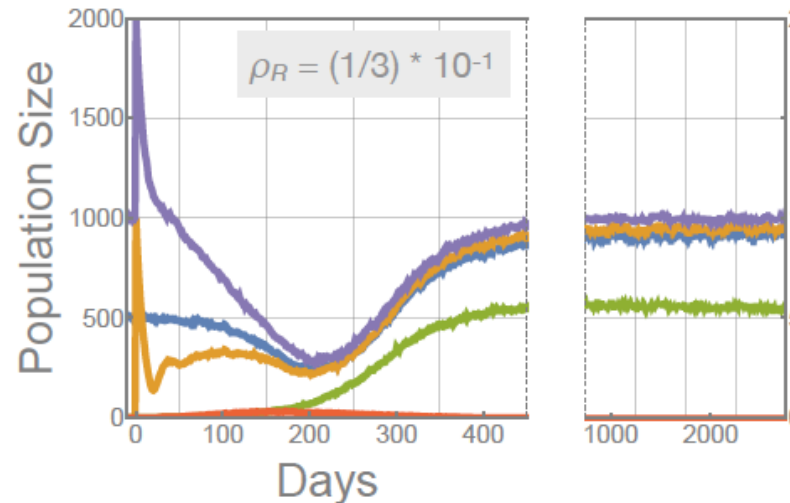
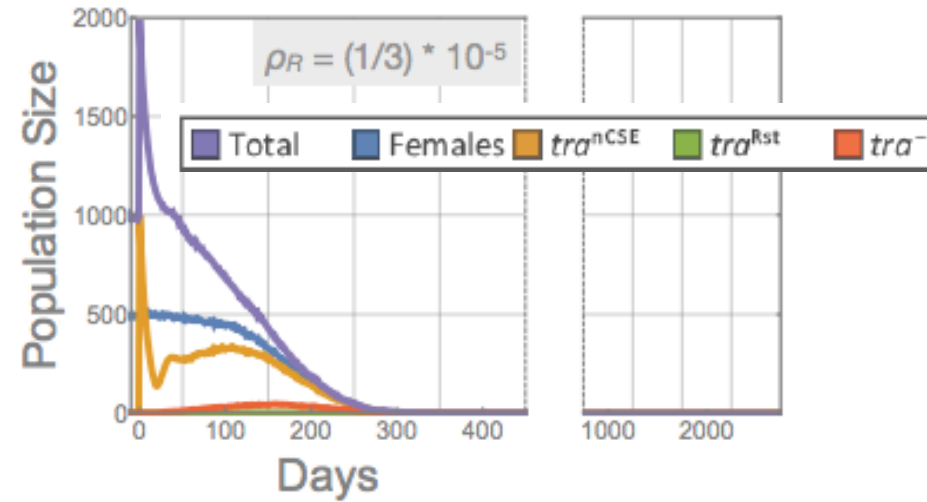
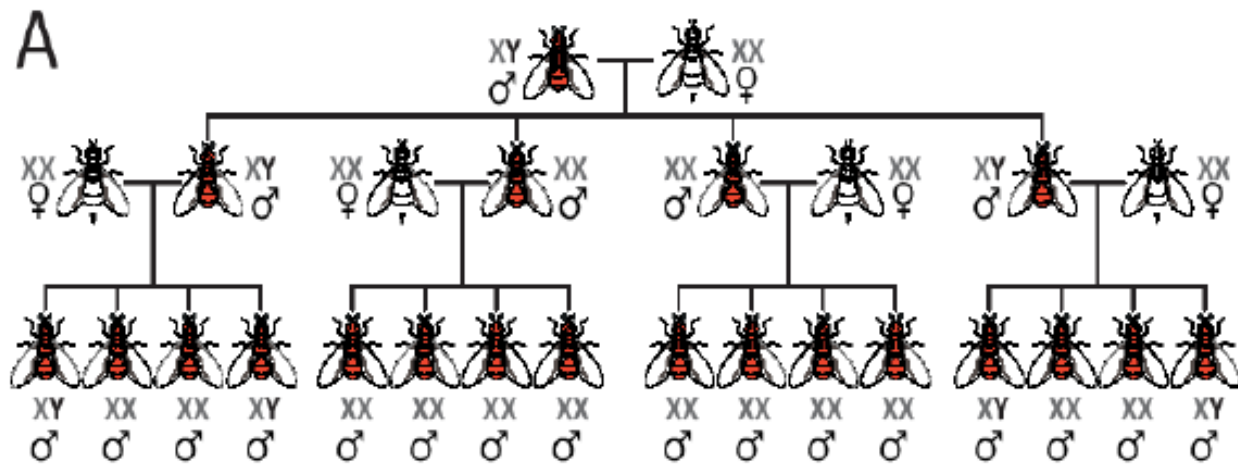
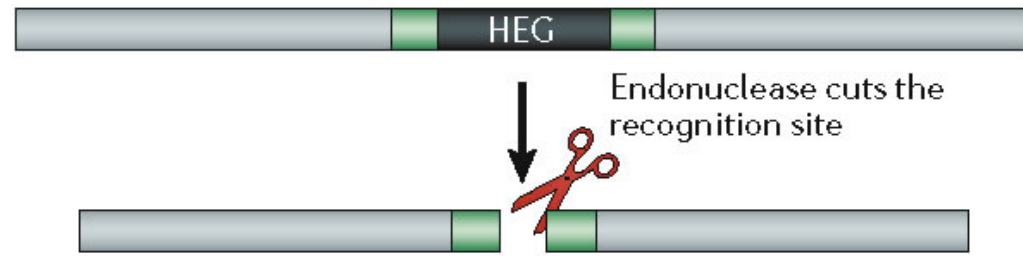


D. Ideal Medea, homing construct with antidote



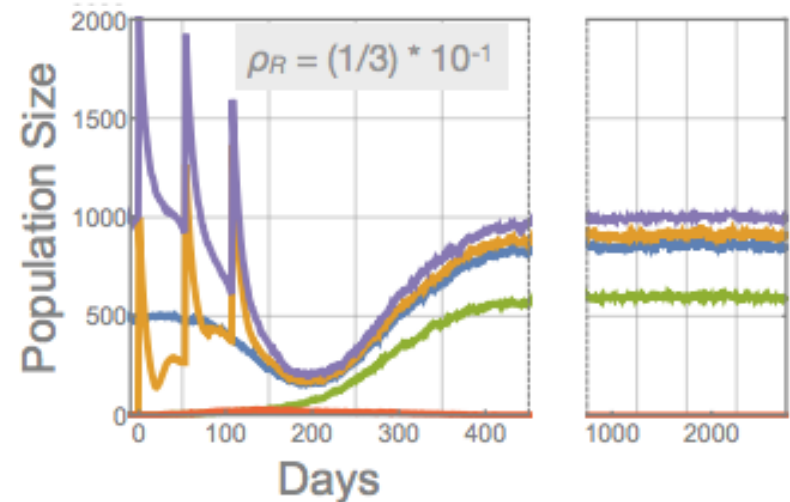
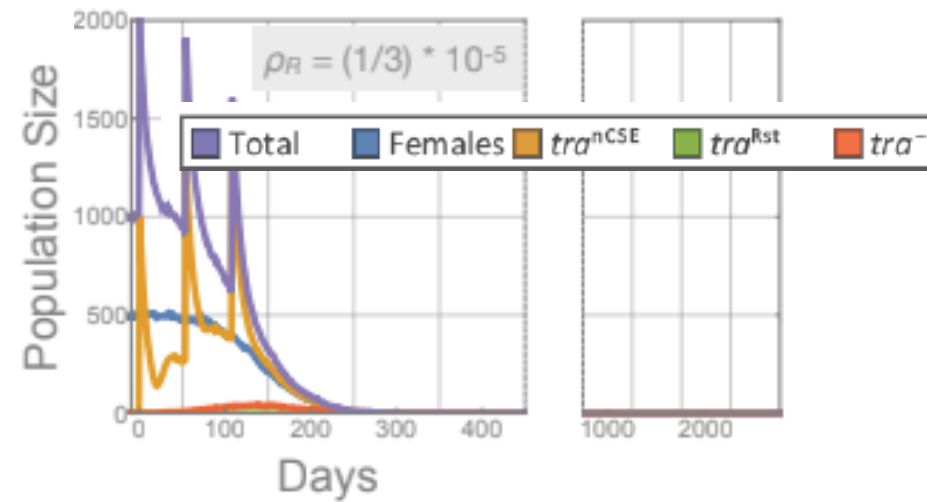
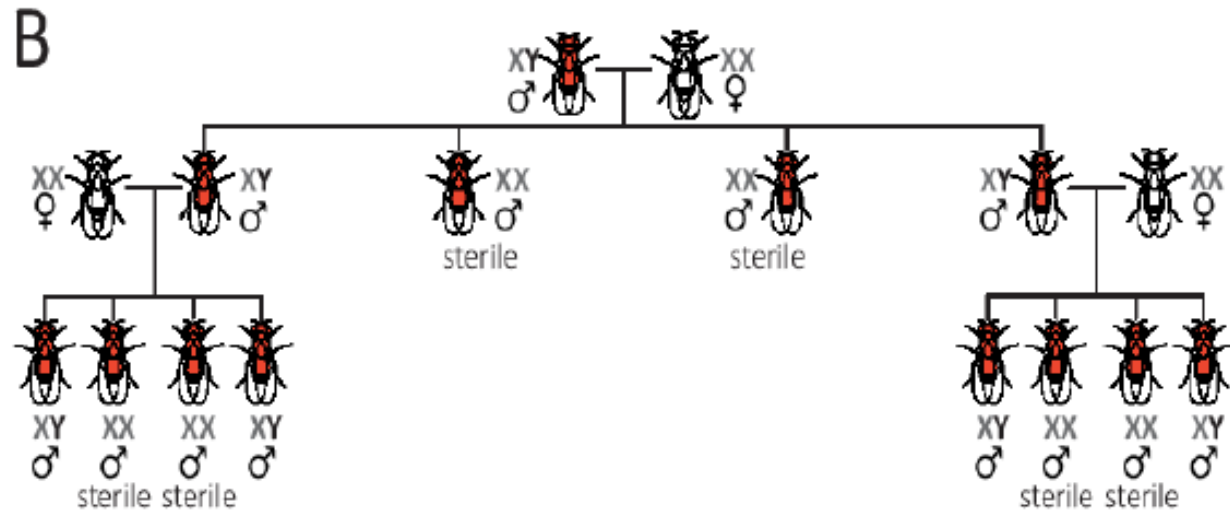
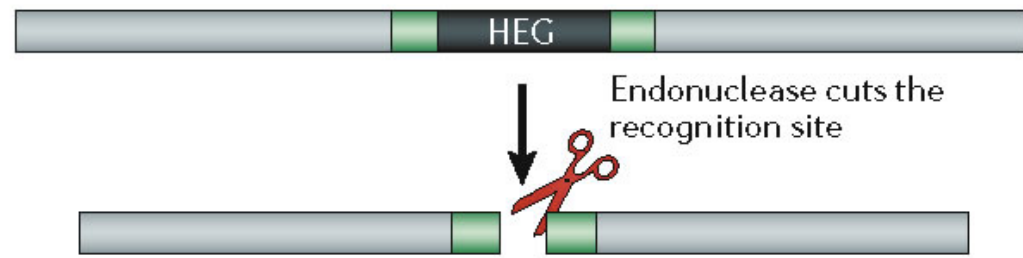
# Consequences of instant induction of resistance evolution on a sex conversion-based suppression gene drive for insect pest management

Mohammad KaramiNejadRanjbar<sup>1</sup>, Kolja Eckermann<sup>1</sup>, Hassan Ahmed<sup>1</sup>, Hector Sanchez C.<sup>2</sup>, Stefan Dippel<sup>1</sup>, John Marshall<sup>3</sup>, Ernst A. Wimmer<sup>1</sup>

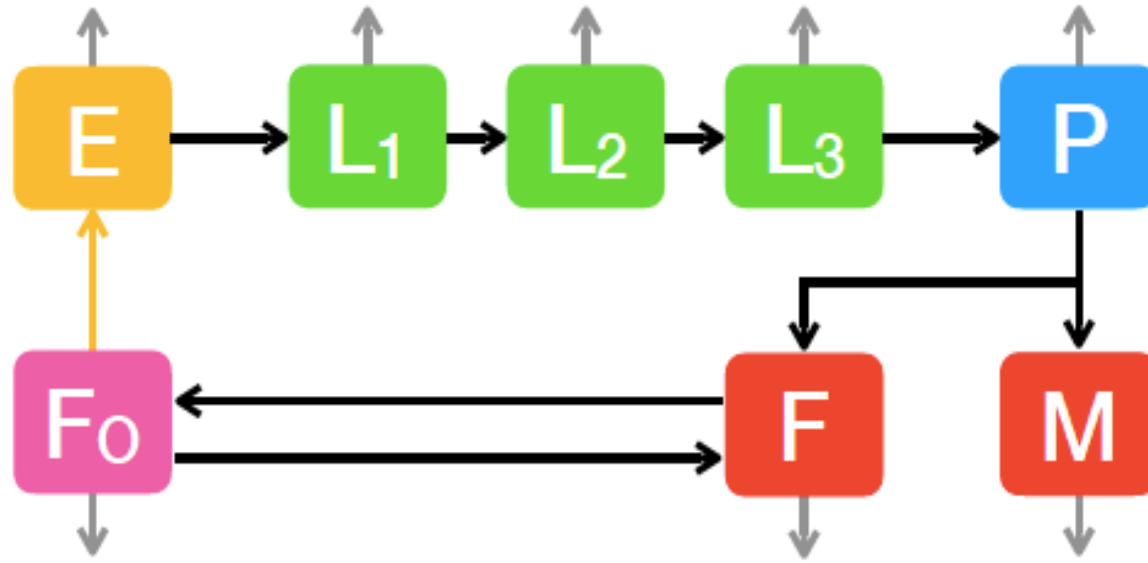


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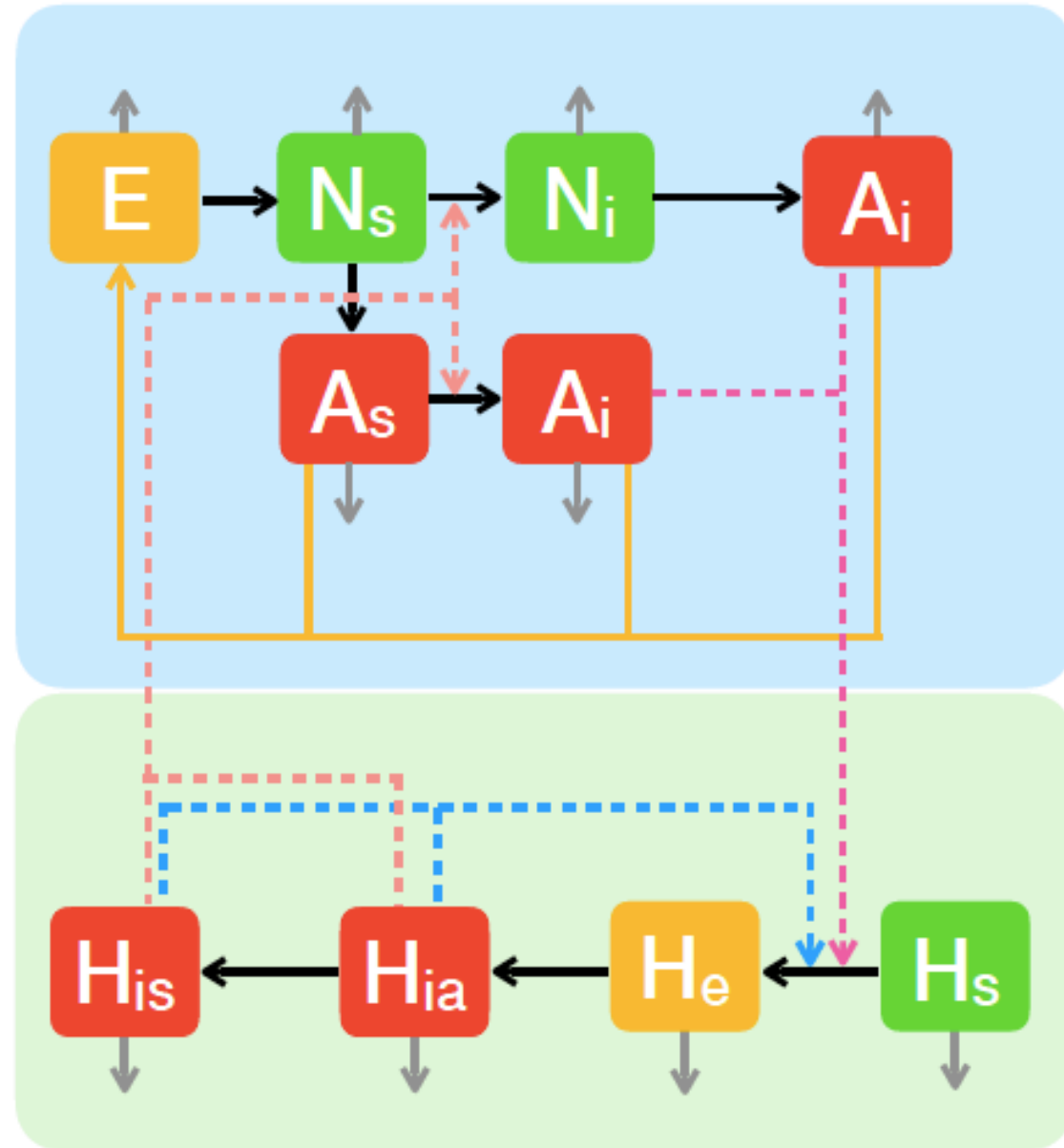


# Ecological models for agricultural pests

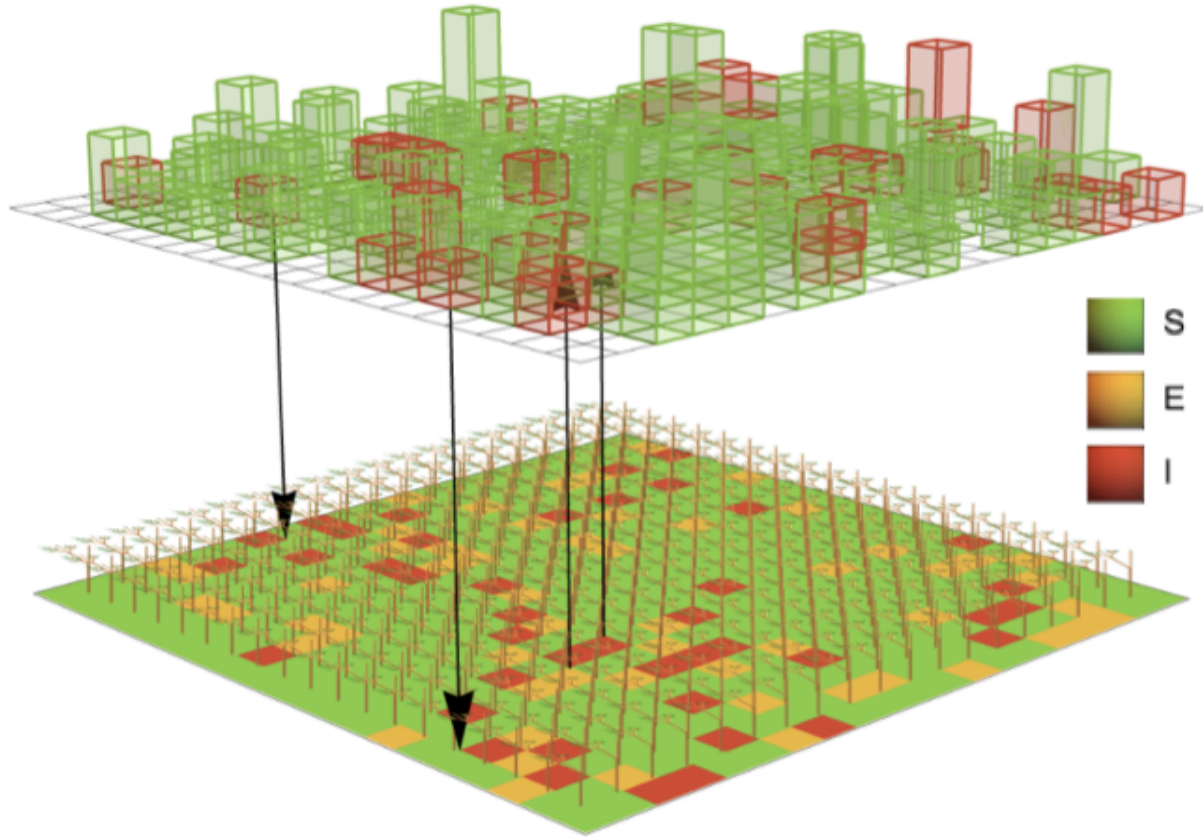




# Ecological models for agricultural pests



# Spatial habitat models for agricultural pests



# Questions for the group

1. Which agricultural pest species would be of most interest for gene drive applications?
2. Which crop species and geographies would be of most interest? At what scale?
3. What would the target product profile of the gene drive system be?
4. How could this strategy complement other agricultural pest control techniques?

# Acknowledgements

## COLLABORATORS:

### MARSHALL LAB @ UC BERKELEY



Hector M. Sanchez C., Sean L. Wu, Gordana Rasic, Jared Bennett, Yogita Sharma, Samson S. Kiware, Partow Imani, Biyonka Liang, Tomas Leon *et al.*

## OTHERS:

- Akbari Lab @ UC Riverside
- James Lab @ UC Irvine
- Bier Lab @ UCSD
- Hay Lab @ Caltech
- Lanzaro Lab @ UC Davis
- Malaria Elimination Initiative @ UCSF
- Prof David Smith @ IHME, UW
- School of Public Health @ UC Berkeley

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GATES foundation

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