Population suppression with dominant female-lethal alleles is boosted by homing gene drive

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August 26th, 2024

Applicant for PAYS

Mosquitoes as pests

Anopheles gambiae
(transmitting malaria)

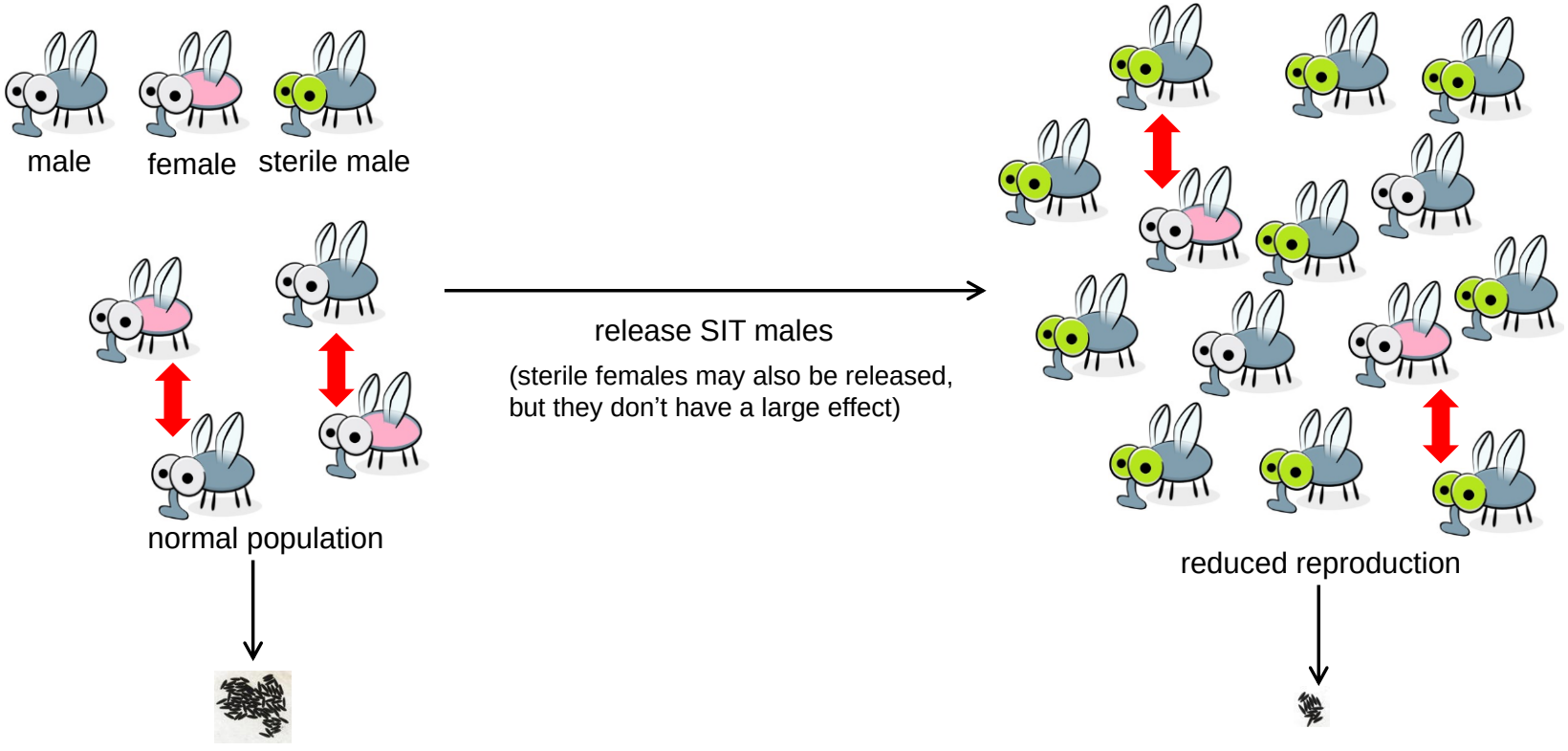
Aedes aegypti
(transmitting dengue, yellow fever, zika, etc.)

Vectors	Disease caused	Type of pathogen
Aedes	Chikungunya	Virus
	Dengue	Virus
	Lymphatic filariasis	Parasite
	Rift Valley fever	Virus
	Yellow Fever	Virus
	Zika	Virus
Anopheles	Lymphatic filariasis	Parasite
	Malaria	Parasite
Culex	Japanese encephalitis	Virus
	Lymphatic filariasis	Parasite
	West Nile fever	Virus

https://www.who.int/

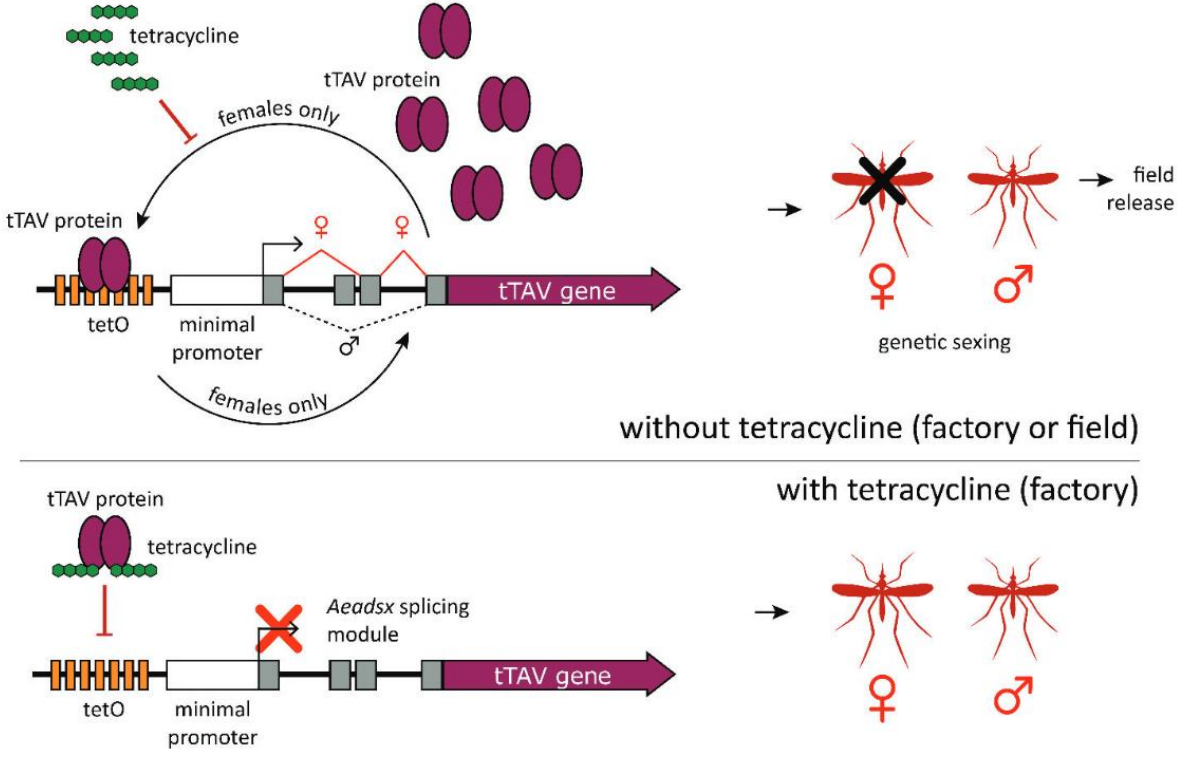
Population genetic control

Sterile Insect Technique (SIT)

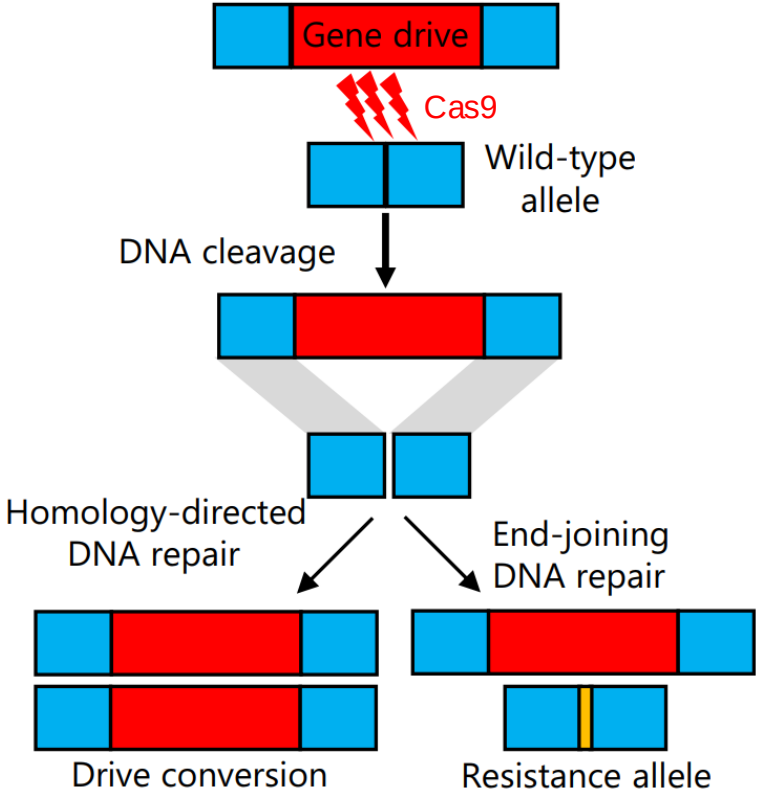


Population genetic control

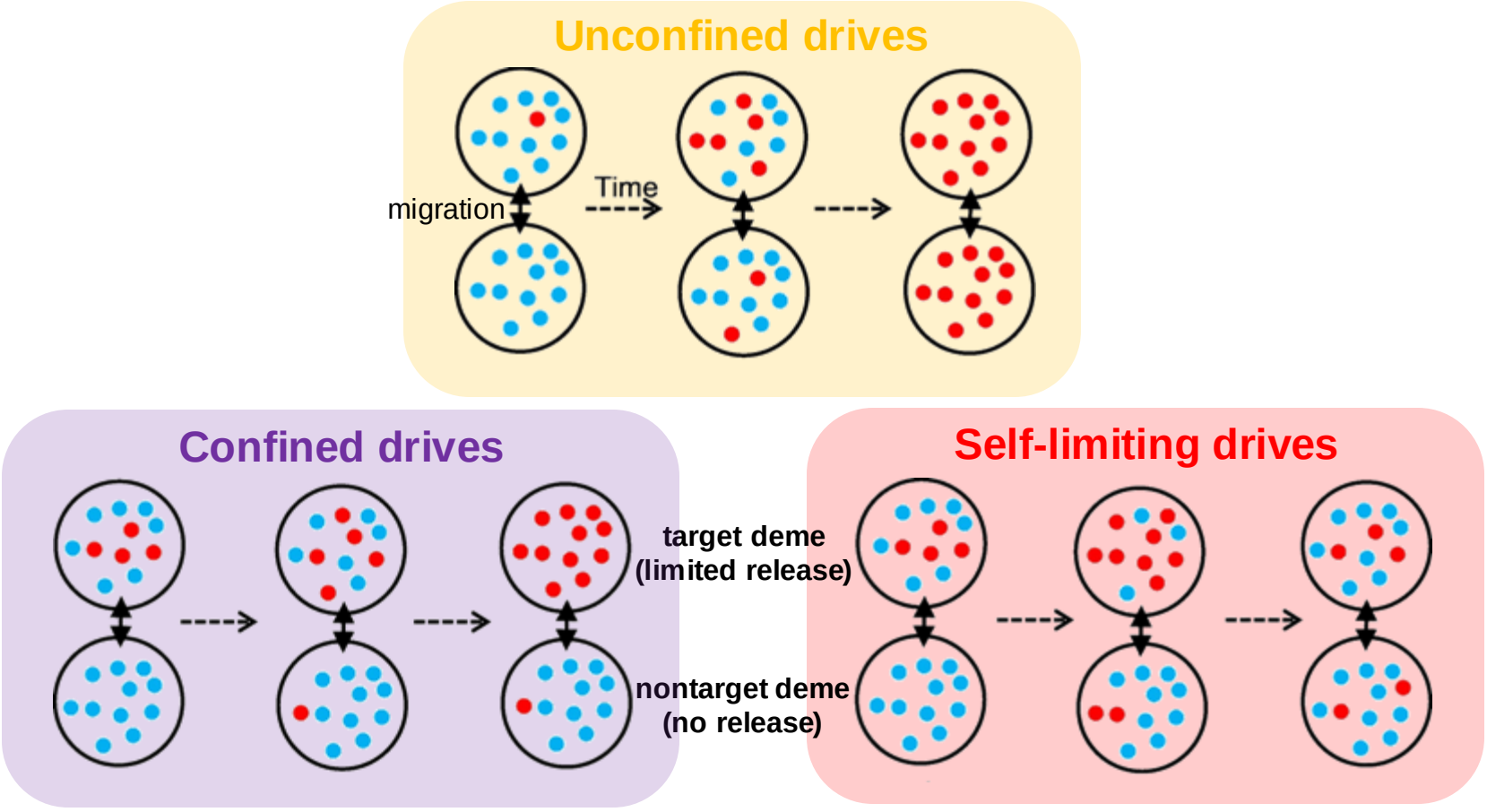
Female-specific Release of Insects carrying Dominant Lethals (fsRIDL)



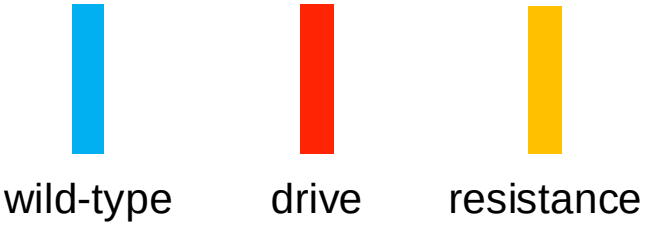
Homing gene drive



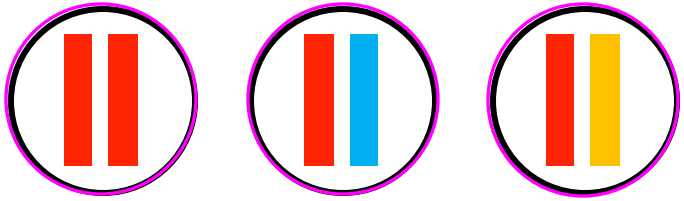
Biosafety concern: confinement of gene drives



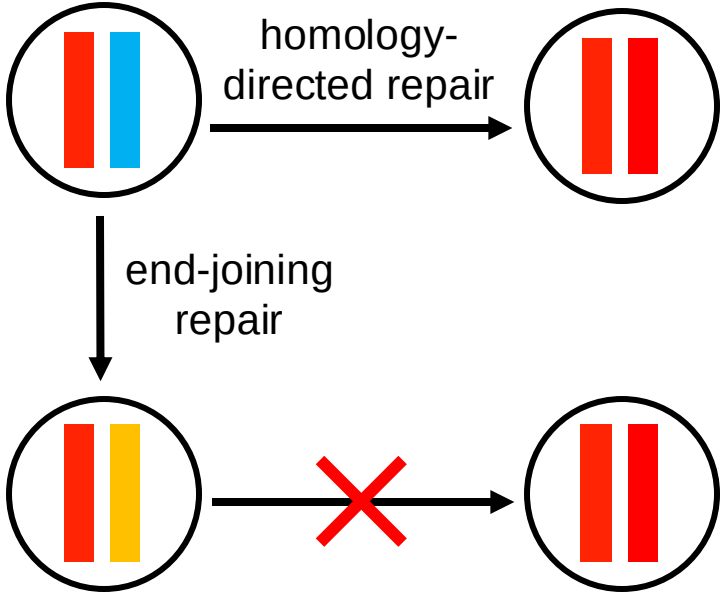
Design: Drive-RIDL



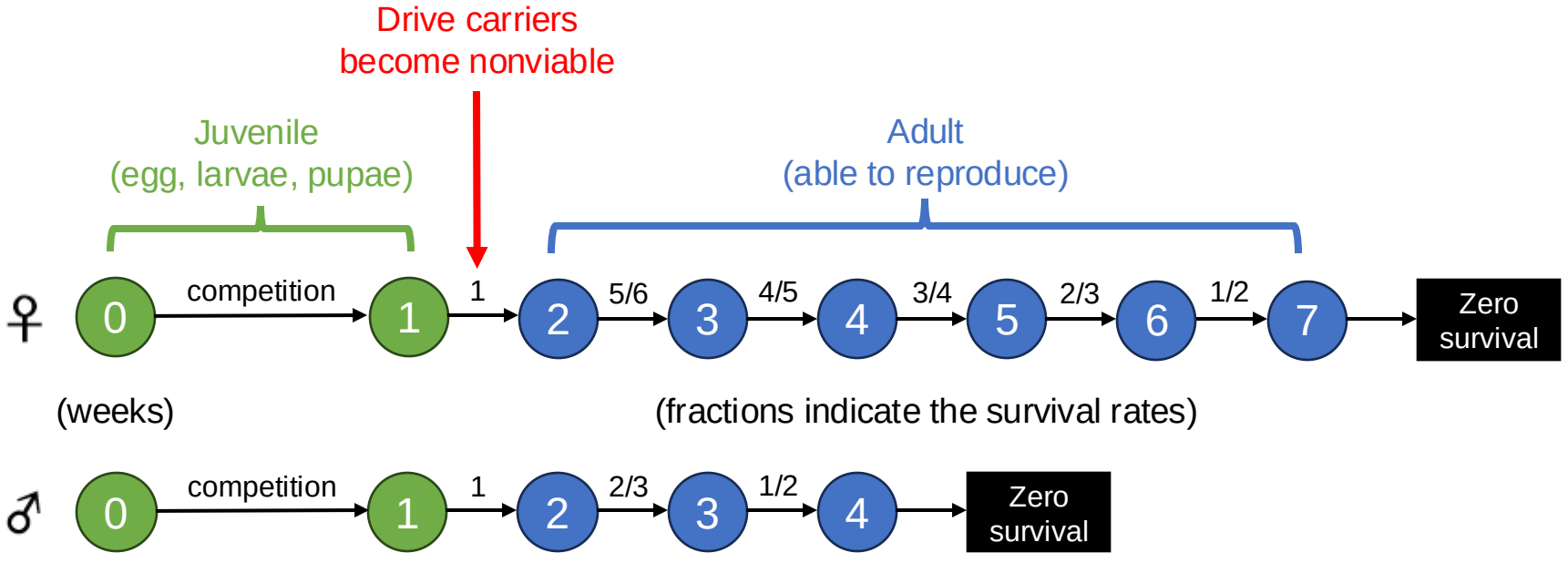
Females with the following genotypes are not viable without antibiotic:



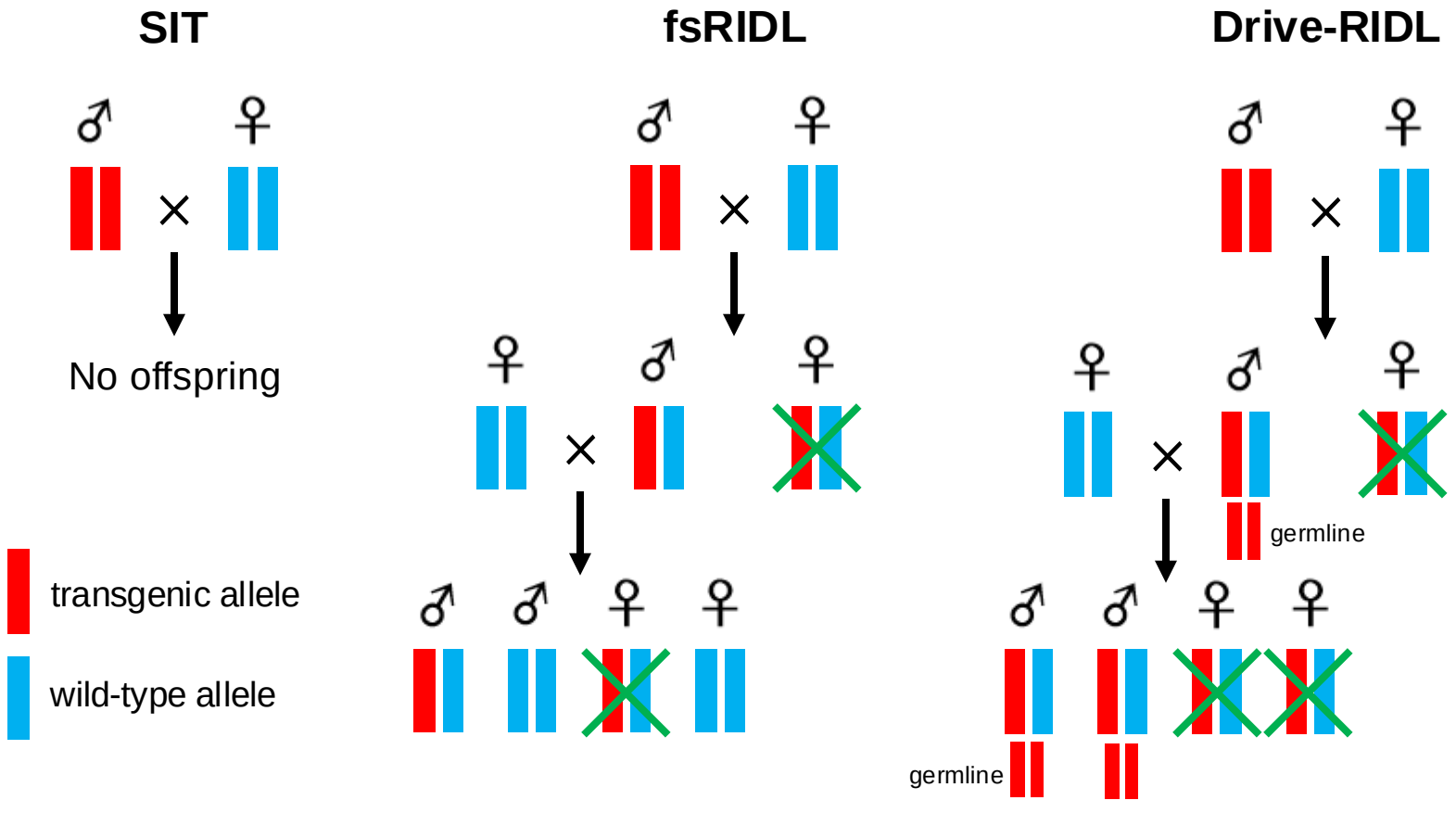
Drive conversion in male germline:



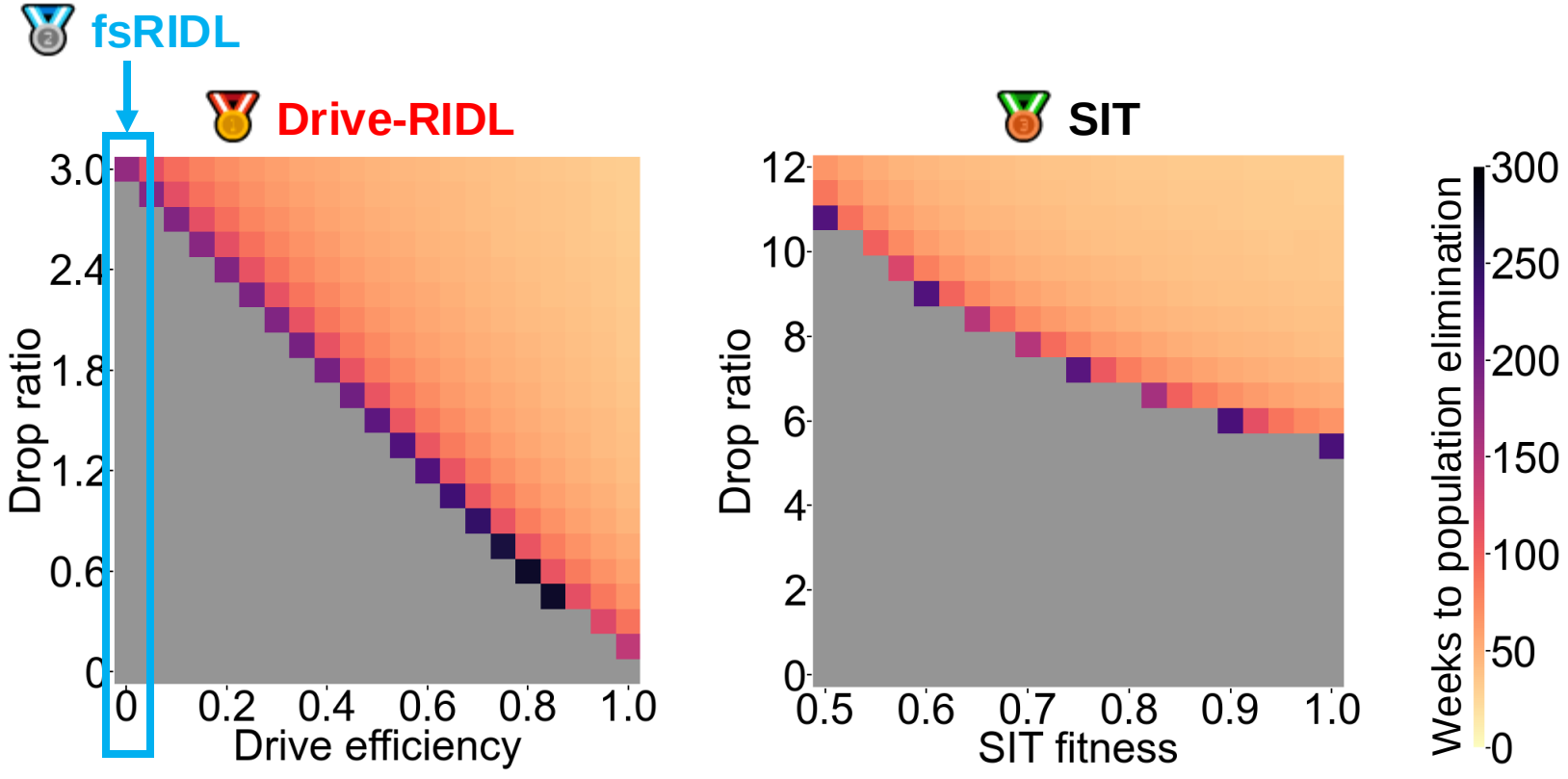
Simulating Drive-RIDL using a mosquito model



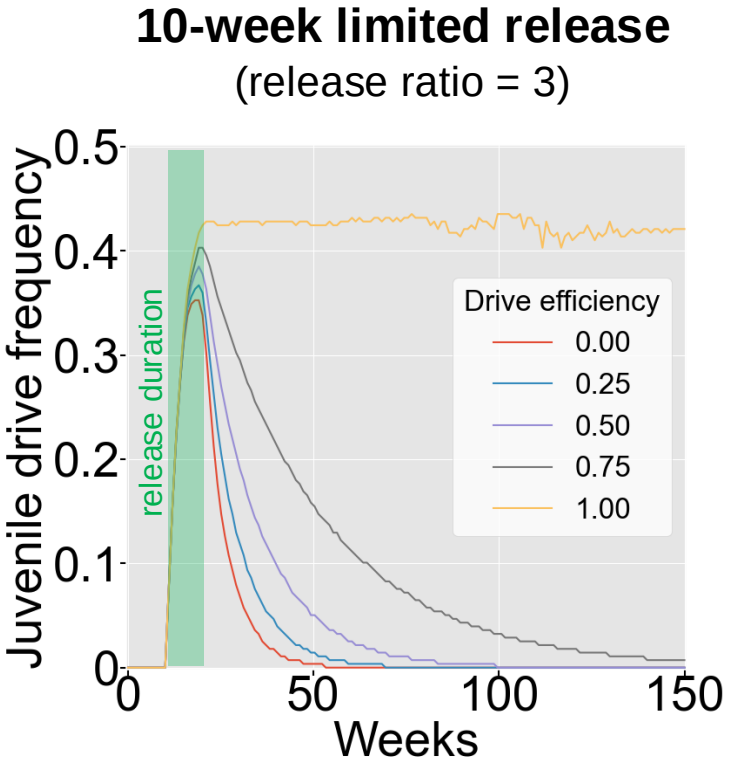
Modeling the three systems

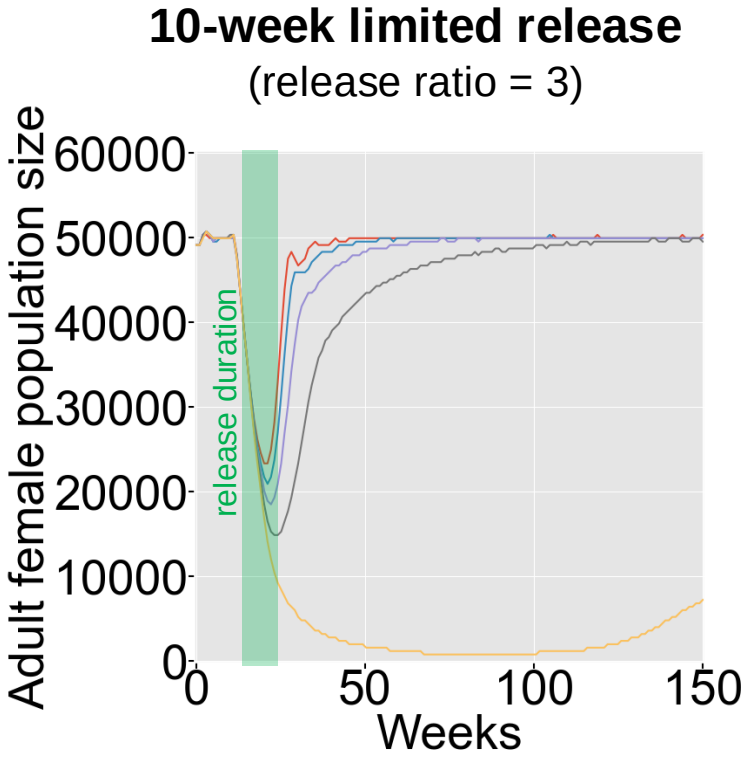


Population suppression is boosted by Drive-RIDL



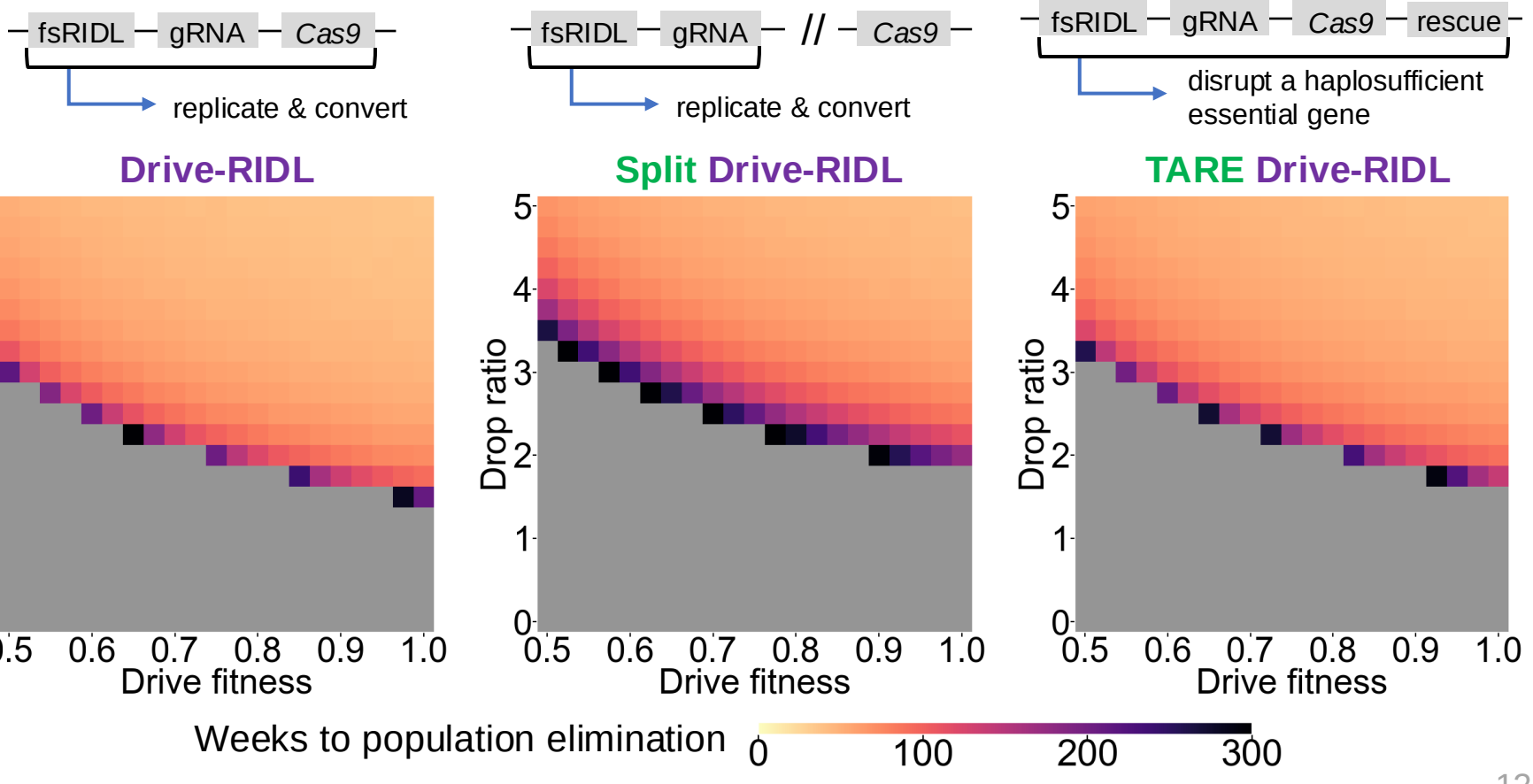
Drive-RIDL is self-limiting





Split and TARE drives exhibit similar performance

extra confinement, slightly lower power

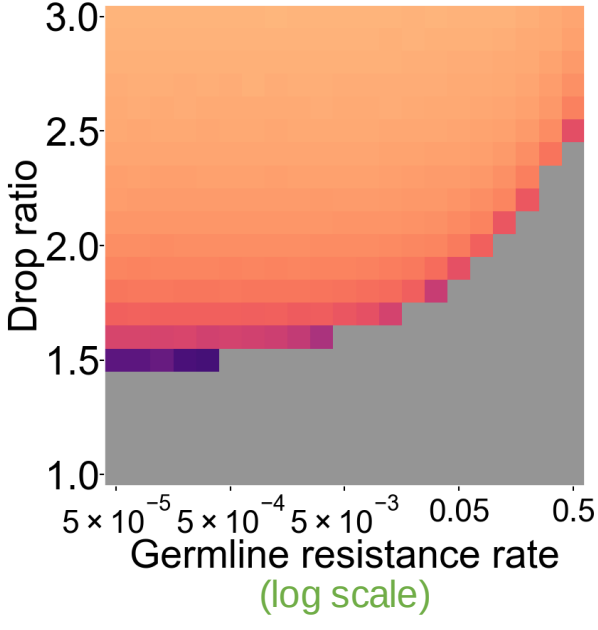


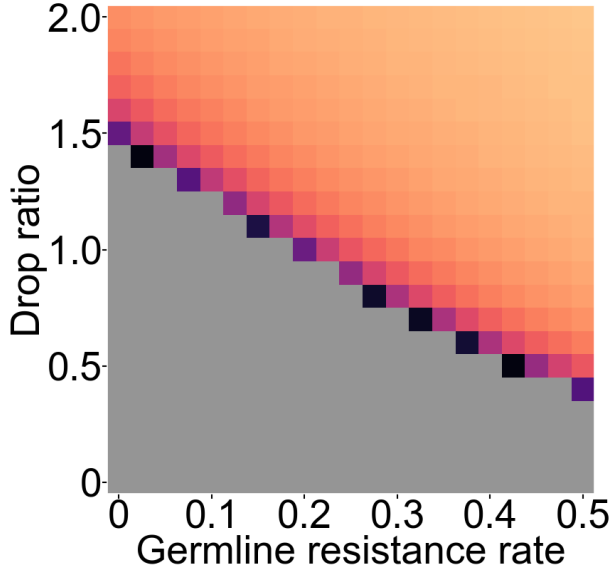
Rescue drives weed out resistance

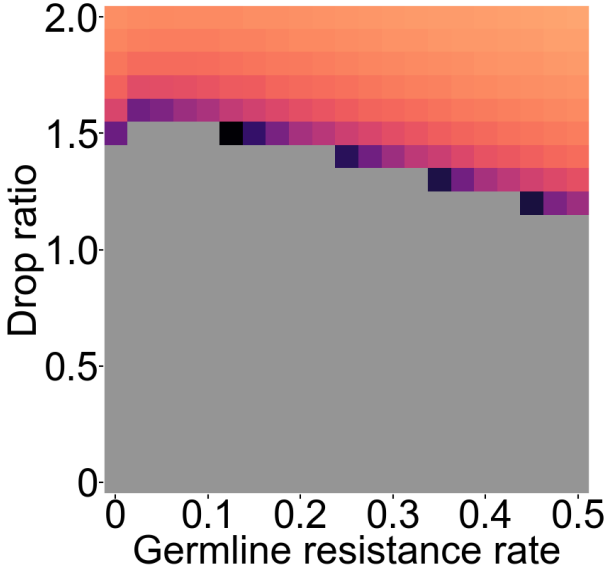
No rescue

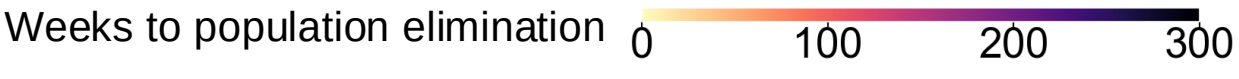
Haplolethal target

Haplosufficient target

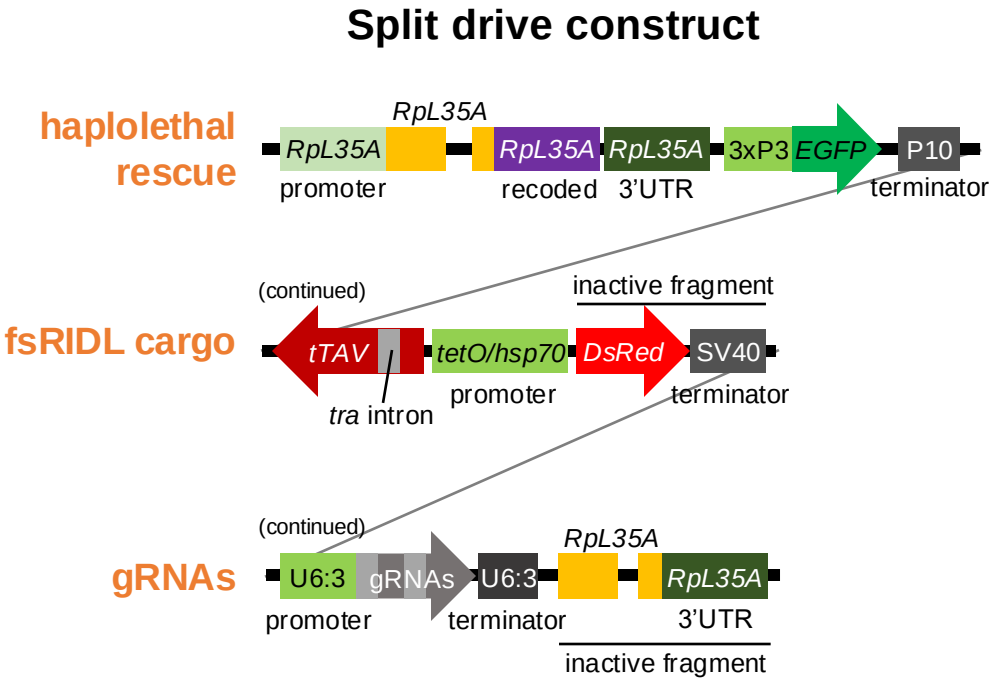


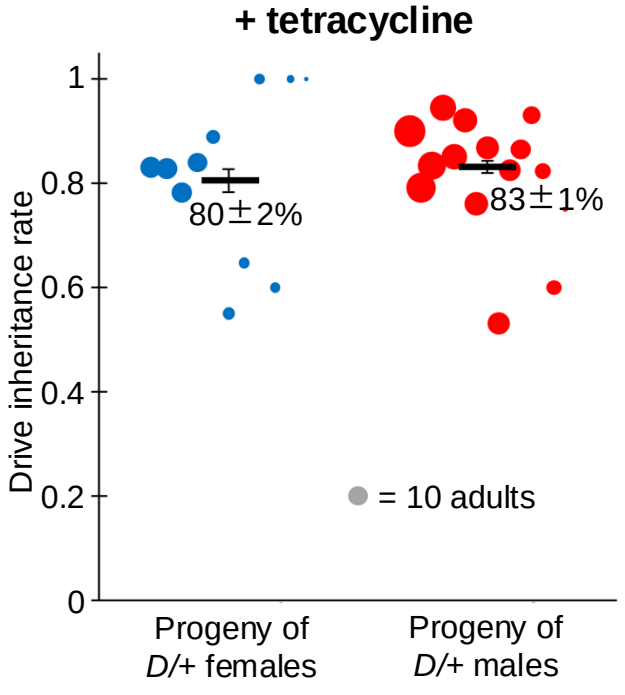






Experimental demonstration in *Drosophila melanogaster*

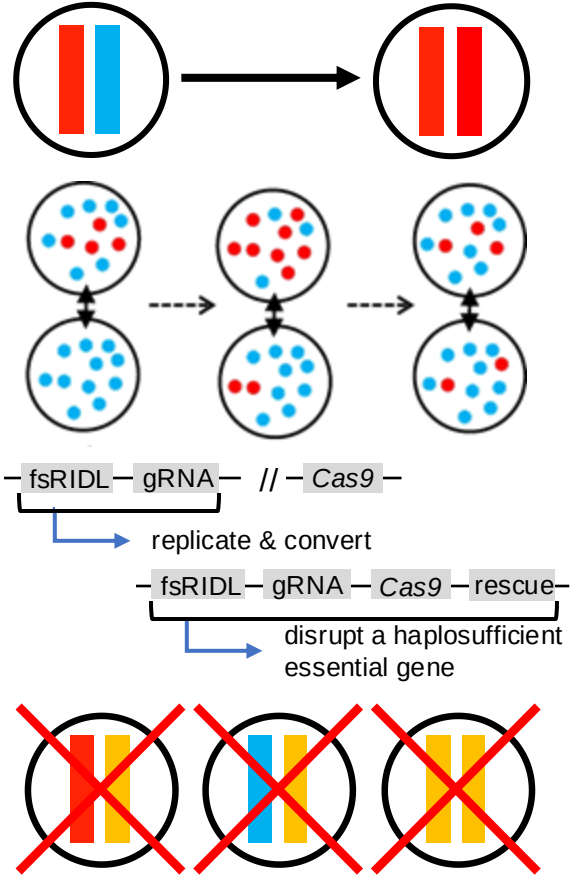




All *D*/*D* and most *D*/+ female offspring were nonviable without tetracycline

Conclusions

- Gene drives can substantially improve the population suppression power of female dominant lethal genes.
- Unlike typical homing drives, Drive-RIDL is self-limiting, making it potentially easier and safer to use.
- Split/TARE Drive-RIDLs provide extra confinement at a slight cost to the suppression power.
- A haplolethal/haplosufficient rescue improves the drive performance with a high germline resistance rate.



Thank you for listening!

Acknowledgement:

- Jackson Champer
- Yiran Liu
- Jingheng Chen
- Xuejiao Xu

Incomplete lethality of female heterozygotes