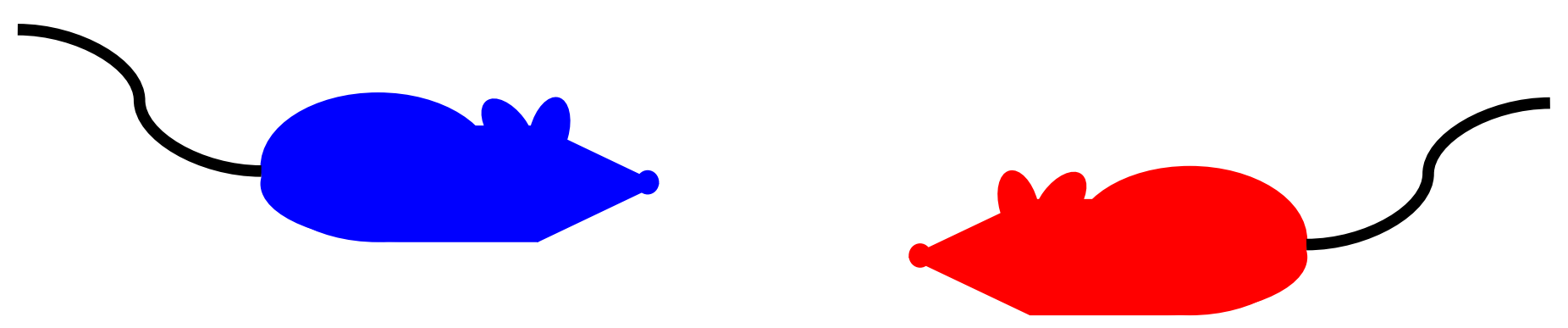
Genetically engineered mice for eradicating invasive mouse populations



Modeling the efficiency and ecological impacts

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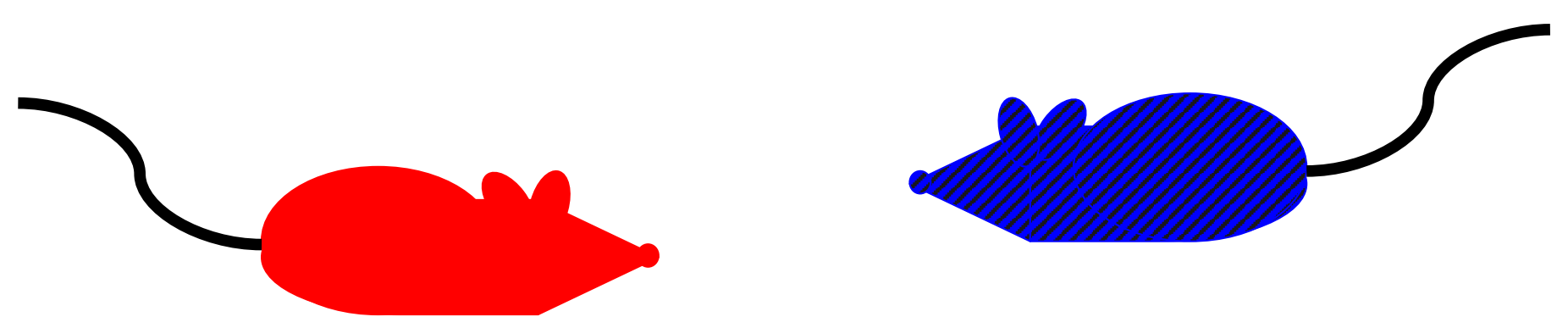

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Current invasive rodent eradication methods are often impractical

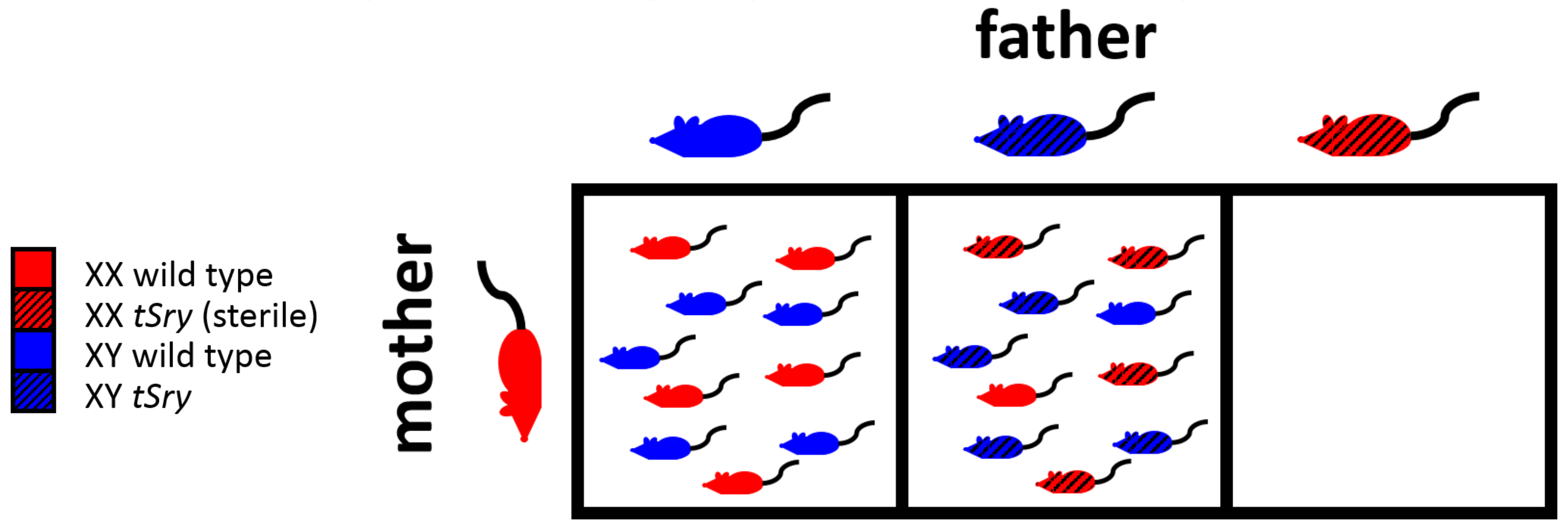
- Invasive rodents are found on 80% of islands and have contributed to the extinction of at least 50 vertebrates (Towns et al. 2006).
- Rodents are eradicated with high concentrations of rodenticide, causing slow internal bleeding and non-target lethality.

House mouse (*Mus musculus*)
Image from Wikimedia commons user 4028mdk09

- Recent advances in genetic engineering could allow for a species-specific non-target alternative (Campbell et al. 2015).
- This approach is more common for insect pests (Burt 2003, Esvelt et al. 2014), but there are new ecological questions and concerns with mammals.

An engineered gene drive would alter sex ratios, reducing mouse populations

- The proposed *t-Sry* construct would be engineered in house mice (*Mus musculus*) with the following genes.
  - ***Sry* gene**: Induces testis development (usually found on the Y chromosome). On an autosome, it causes sterility in XX offspring.
  - ***t*-haplotype**: Meiotic drive found naturally in house mice. If father carries one copy of the *t*-haplotype, over 50% of offspring inherit it.



Modeling density dependent population dynamics of gene drive eradication

- Logistic growth in absence of *t-Sry* construct
- *t-Sry* mice added at release rate of μ per month
- Simplifications: polygamous random mating, no migration, no mutation
- $0.5 < \tau \leq 1$ proportion of offspring from *t-Sry* father will also inherit the *t-Sry* construct
- The *t-Sry* construct alters the natural death rate with c
- Each genetic combination changes at the following rates.

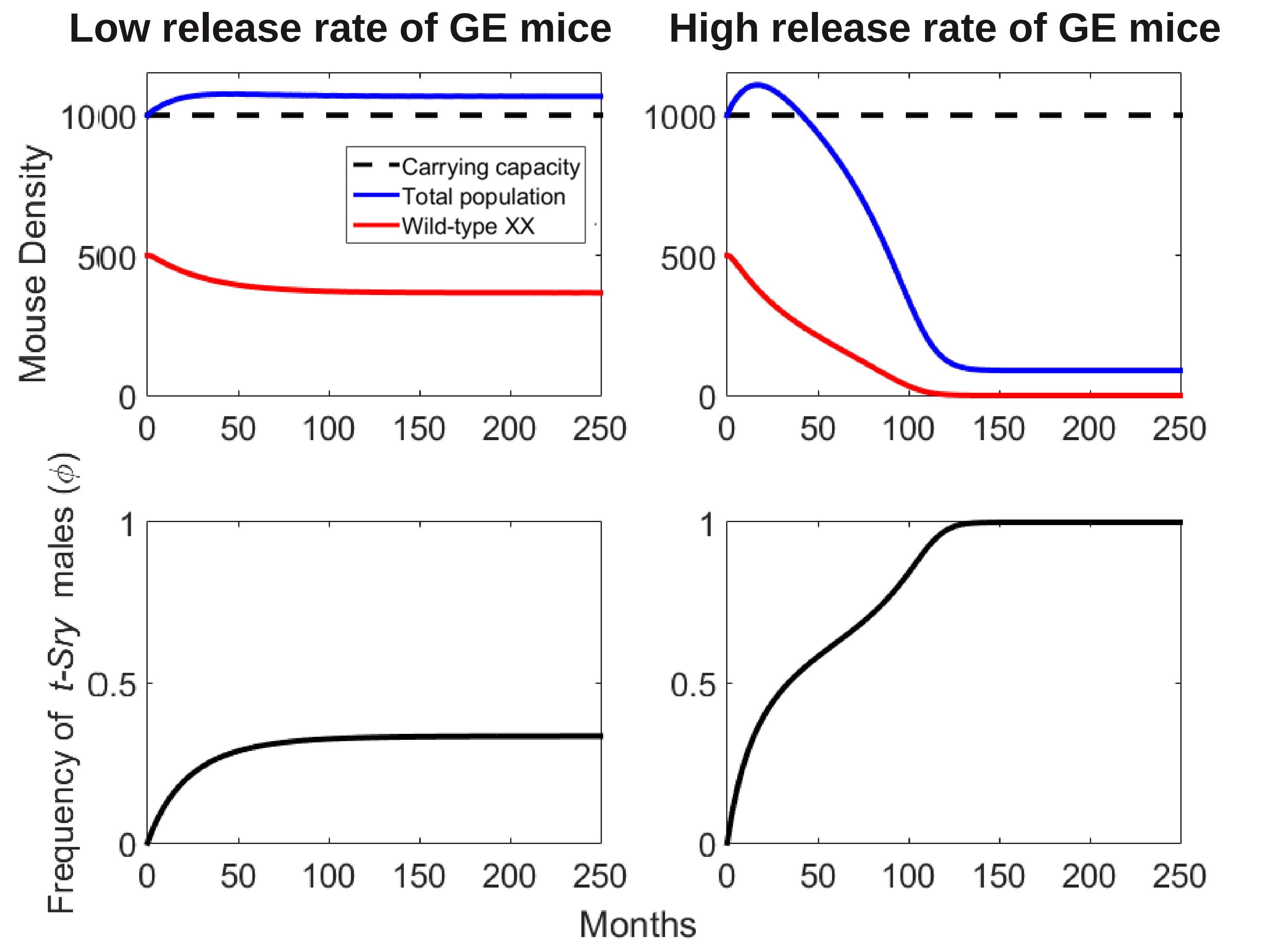
XX WT $$\frac{dW_X}{dt} = (a_1 - a_2 W_X)\left(\frac{W_Y}{W_Y+G_Y}\right)W_X + (1-\tau)(a_1 - a_2 W_X)\left(\frac{G_Y}{W_Y+G_Y}\right)W_X - (b_1 + b_2 N)W_X$$

XY WT $$\frac{dW_Y}{dt} = (a_1 - a_2 W_X)\left(\frac{W_Y}{W_Y+G_Y}\right)W_X + (1-\tau)(a_1 - a_2 W_X)\left(\frac{G_Y}{W_Y+G_Y}\right)W_X - (b_1 + b_2 N)W_Y$$

XX *t-Sry* $$\frac{dG_X}{dt} = \tau(a_1 - a_2 W_X)\left(\frac{G_Y}{W_Y+G_Y}\right)W_X - (1+c)(b_1 + b_2 N)$$

XY *t-Sry* $$\frac{dG_Y}{dt} = \underbrace{\phantom{(a_1 - a_2 W_X)\left(\frac{W_Y}{W_Y+G_Y}\right)W_X}}_{\text{birth rate from wild-type fathers}} \underbrace{\tau(a_1 - a_2 W_X)\left(\frac{G_Y}{W_Y+G_Y}\right)W_X}_{\text{birth rate from } t\text{-}Sry \text{ fathers}} - \underbrace{(1+c)(b_1 + b_2 N)G_Y}_{\text{death rate}} + \underbrace{\mu}_{\text{release rate}}$$

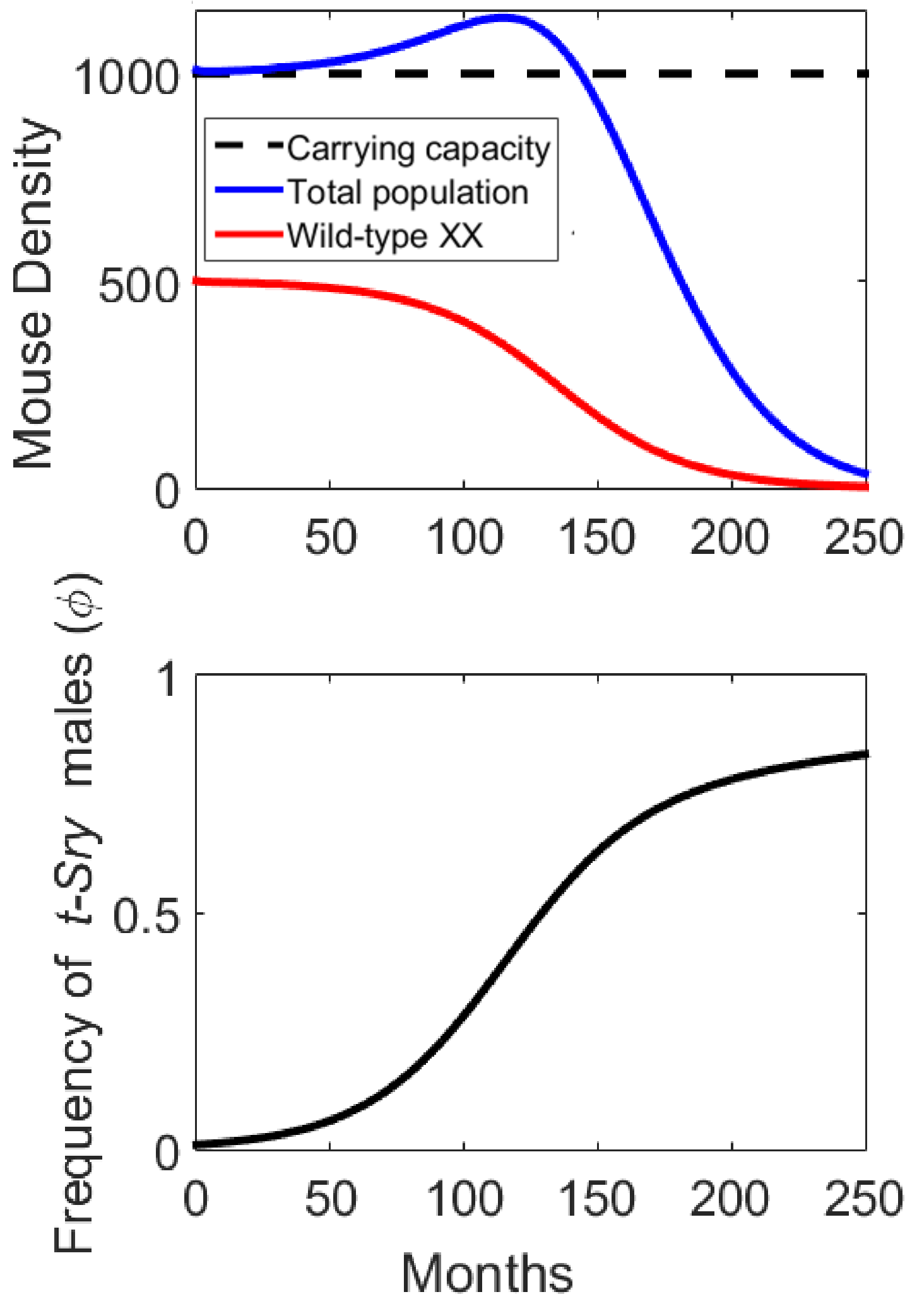
Long-run population dynamics depend on the fitness of GE mice



Low release rate of GE mice | **High release rate of GE mice**

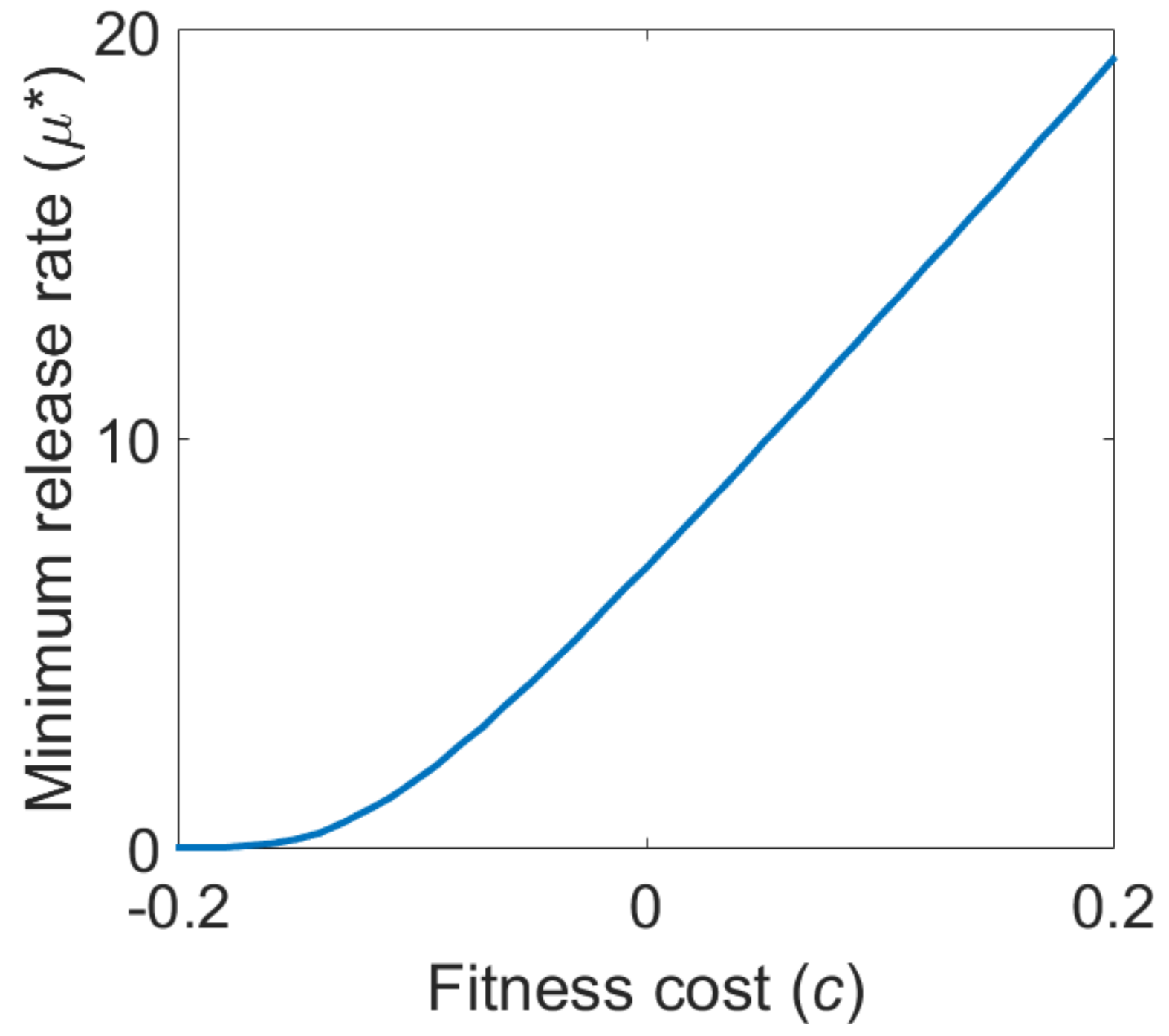
- The *t-Sry* construct will likely impose a fitness cost, so it is not expected to spread through a population on its own.
- Only high release rates can eradicate the population in this case.

Single release of GE mice with a strong fitness advantage

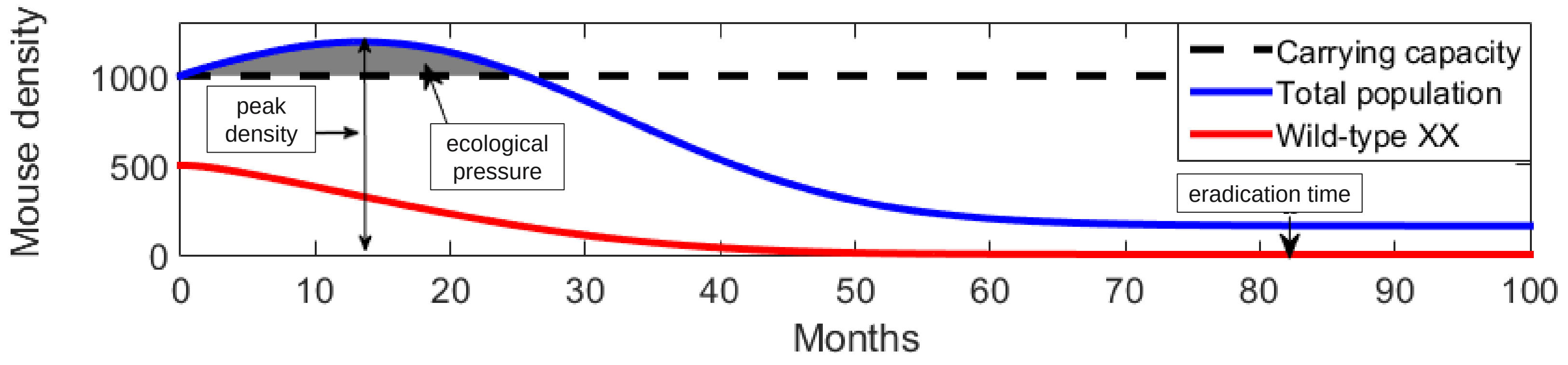


- In theory, backcrossing with mice from a highly competitive population could give the *t-Sry* mouse a substantial fitness advantage.
- In this case, the *t-Sry* construct could spread and eradicate the population with a single release.
- This is problematic if *t-Sry* mice escape to a non-target population.

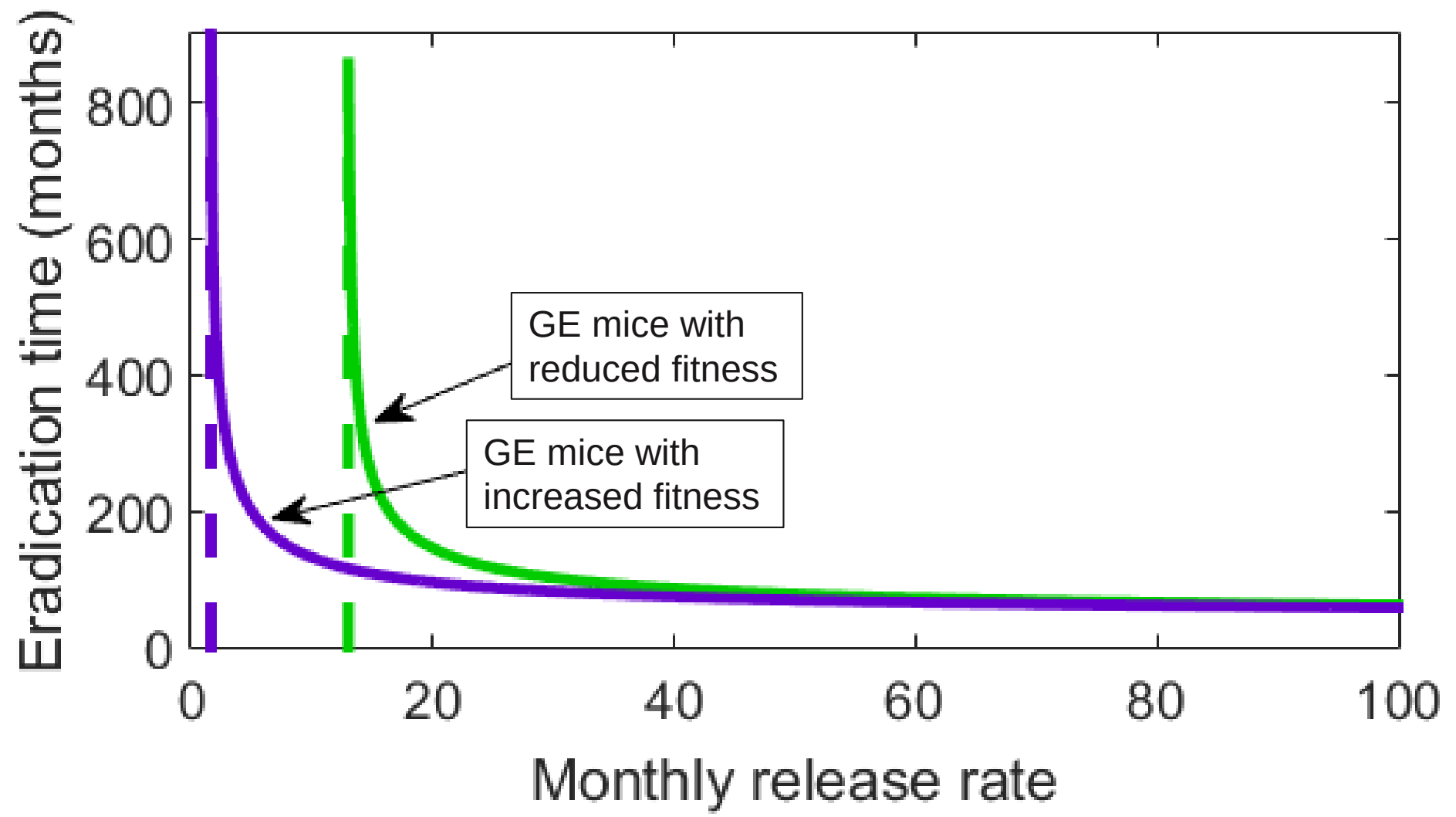
- Overall, *t-Sry* mice need to be released above a minimum rate.
- This minimum rate increases as the fitness cost increases.



There is a tradeoff between speed and intensity of GE-assisted eradication

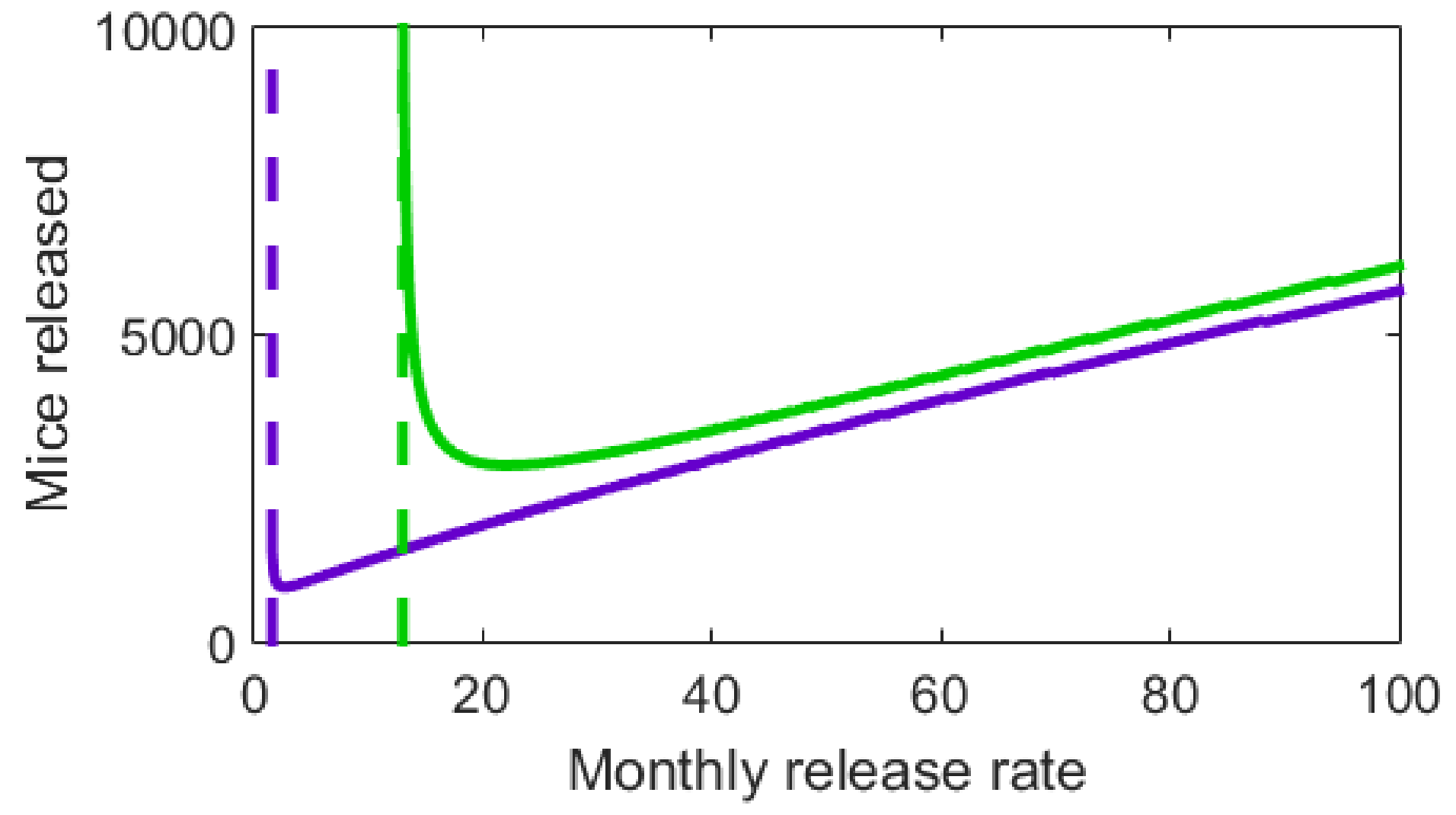


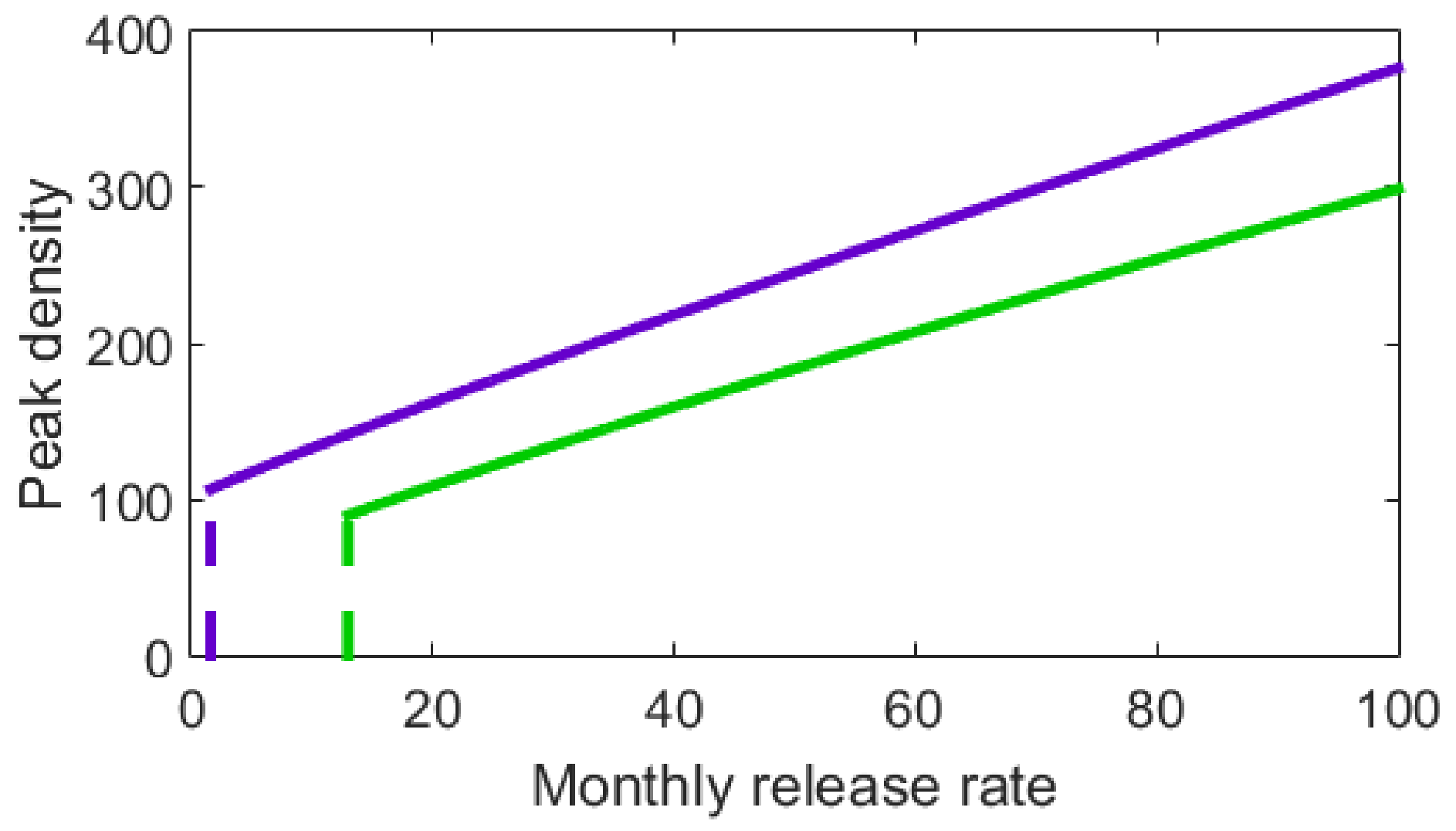
- Indirect transient costs and impacts could result from GE-assisted eradication.



- Eradication is faster when *t-Sry* mice are released at higher rates with reduced fitness costs.

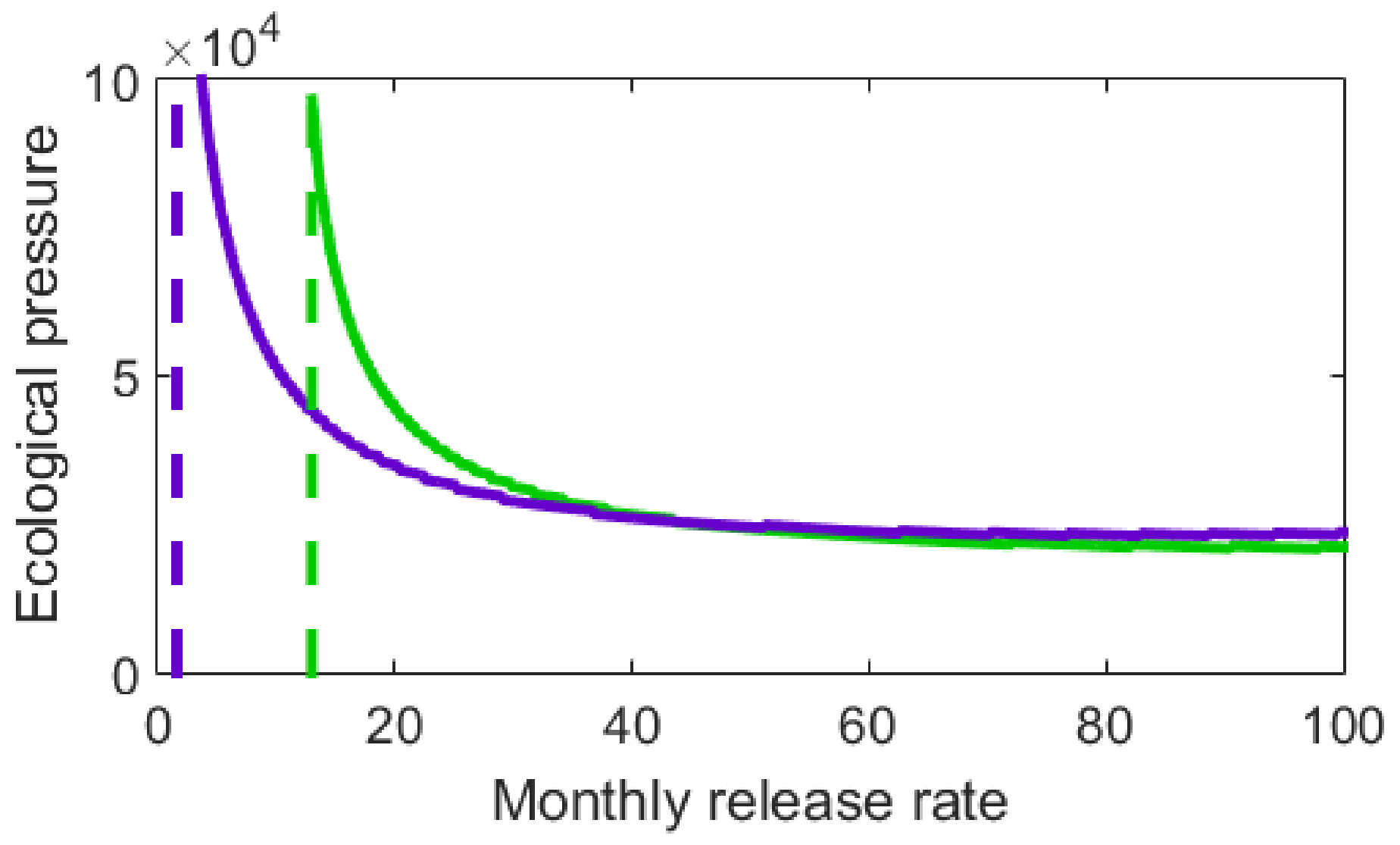
- The number of *t-Sry* mice needed for eradication is minimized at relatively small release rates.





- When far above their natural densities, invasive mice could intensify disruptive ecological interactions.
- Lower release rates reduce the peak population density.

- Both the duration and magnitude of increasing population size can be represented in a single metric.
- This is generally reduced with higher release rates of GE mice.



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References

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For more information about the ecological, ethical, historical, and societal complexities of this topic, see **https://research.ncsu.edu/islandmice/**