Modelling resistance to genetic control of insects

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RIDL® (Release of Insects Carrying a Dominant Lethal)

is a genetic variant of the Sterile Insect Technique (SIT).

It is under trial in mosquitoes & crop pests.

The insects are "genetically sterile", rather than sterilised using irradiation.

Thomas et al. (2000) Science 287:2474

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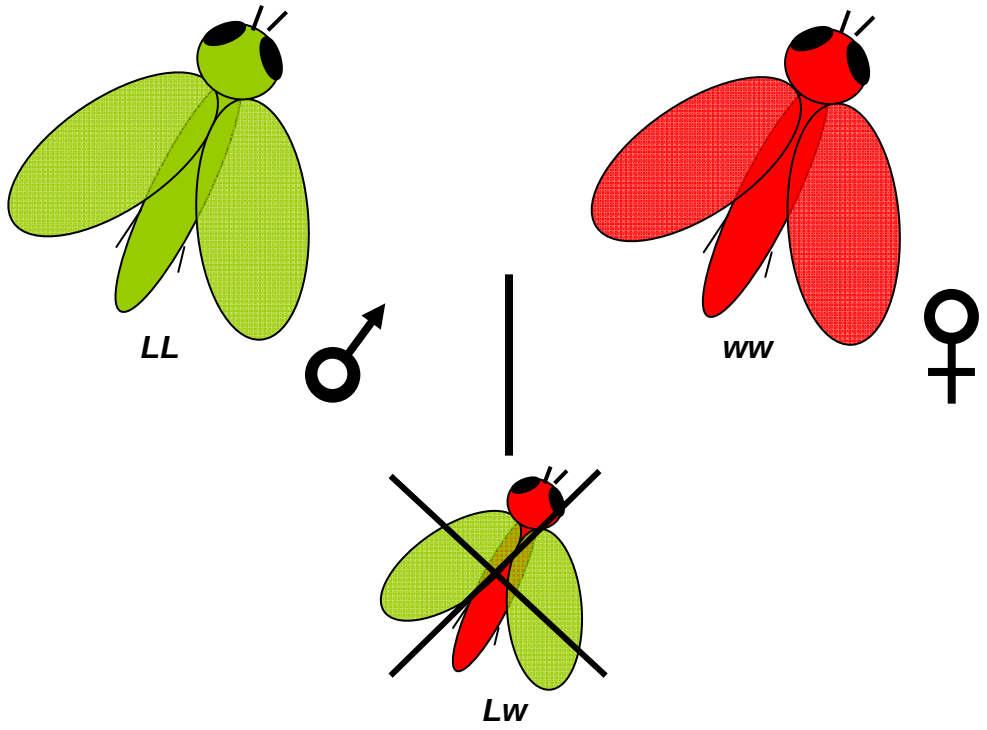
Released males carry two copies of a dominant lethal genetic construct ("LL").

Wild type ("ww") females that mate with those males have no progeny.



Thomas et al. (2000) Science 287:2474

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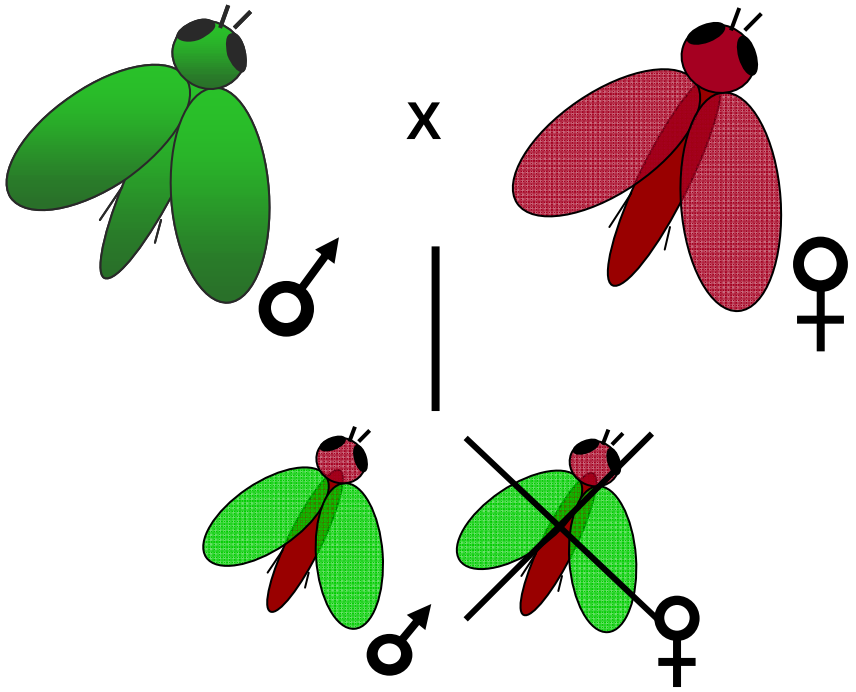
The genetics can be made sex-specific; in a female-lethal version, daughters die, but sons are unaffected (and half their daughters die, half their sons inherit…)



Fu et al. (2007) Nature Biotechnology 25:353

Fu et al. (2010) PNAS 107: 4550

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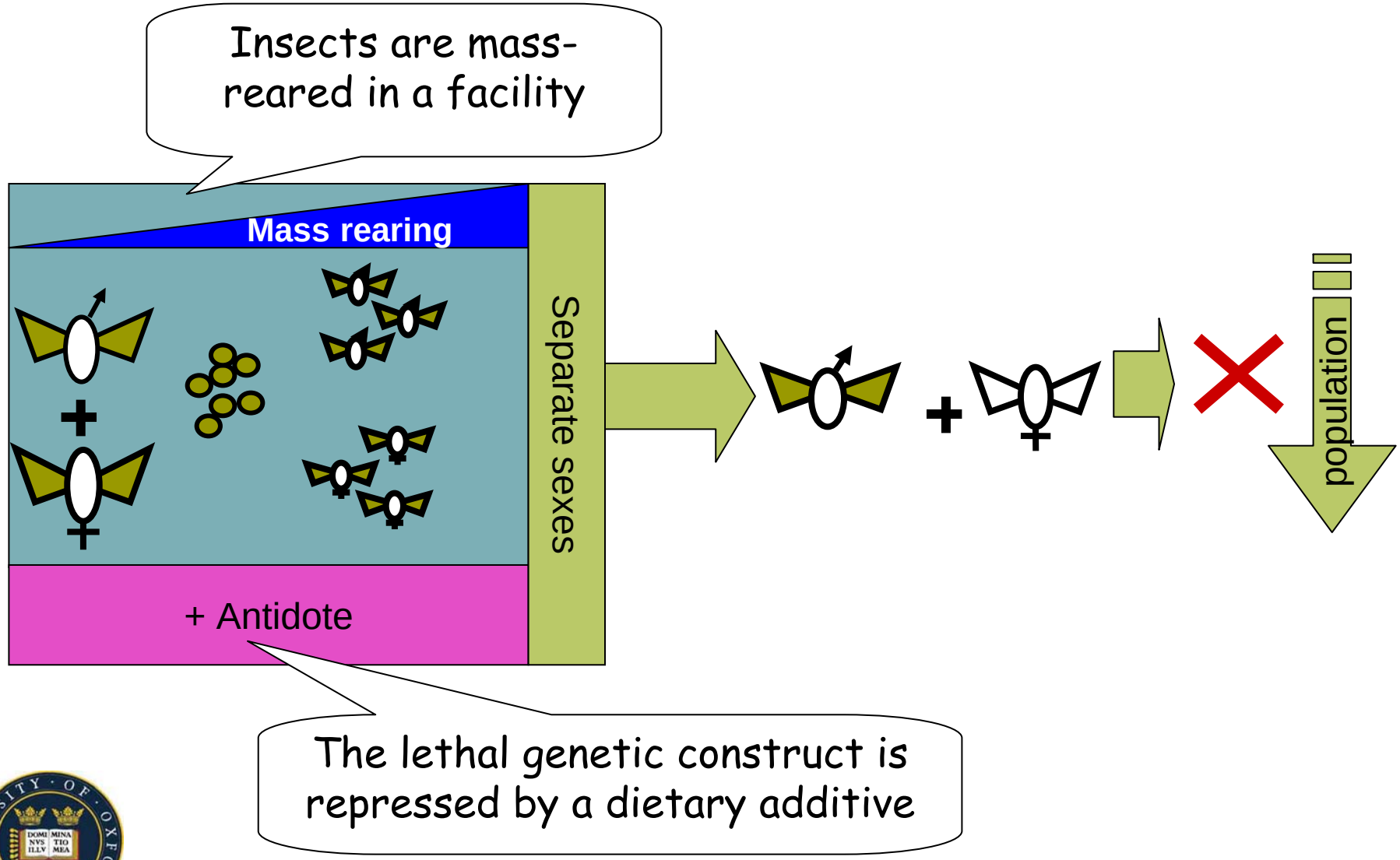

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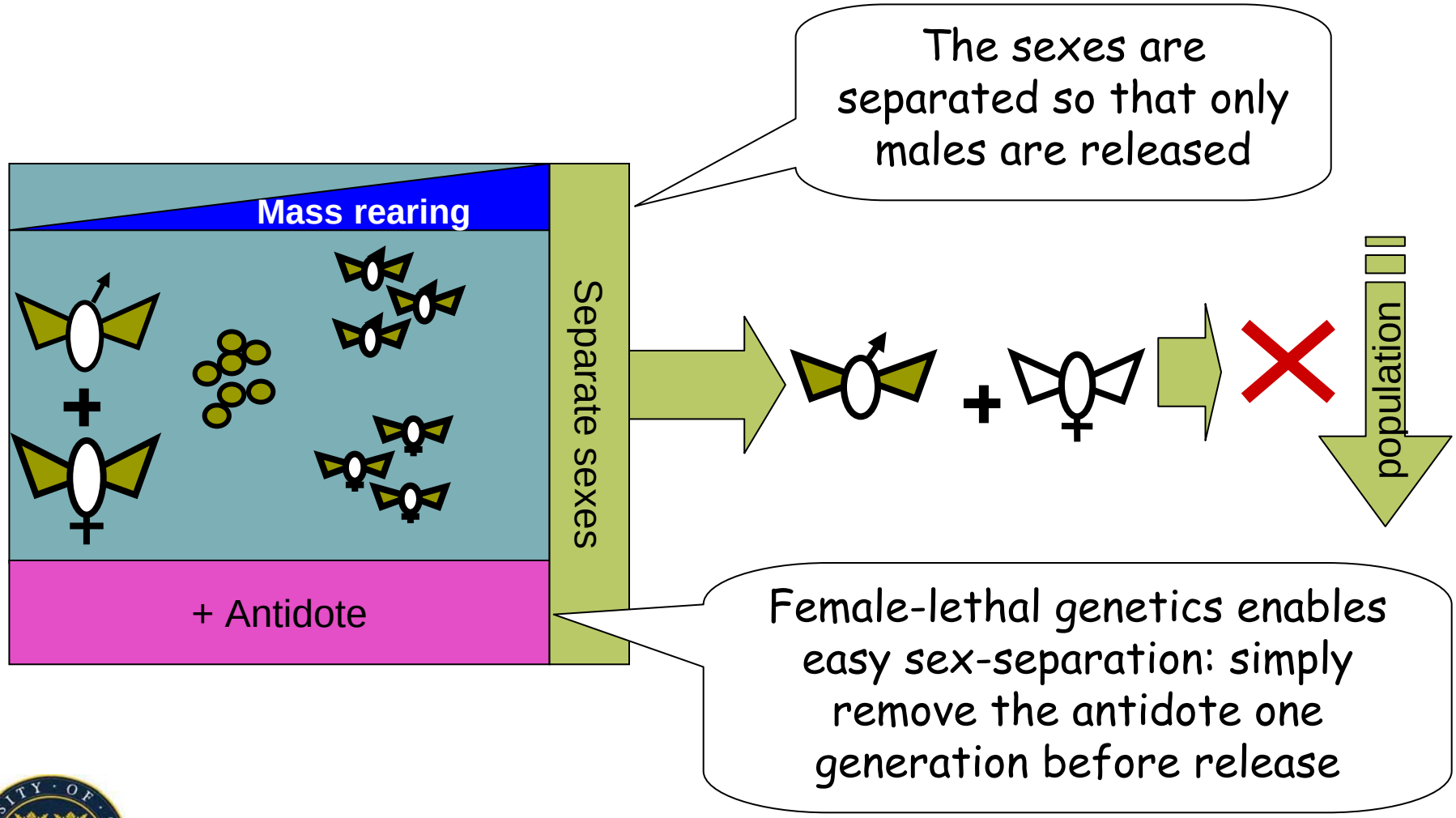

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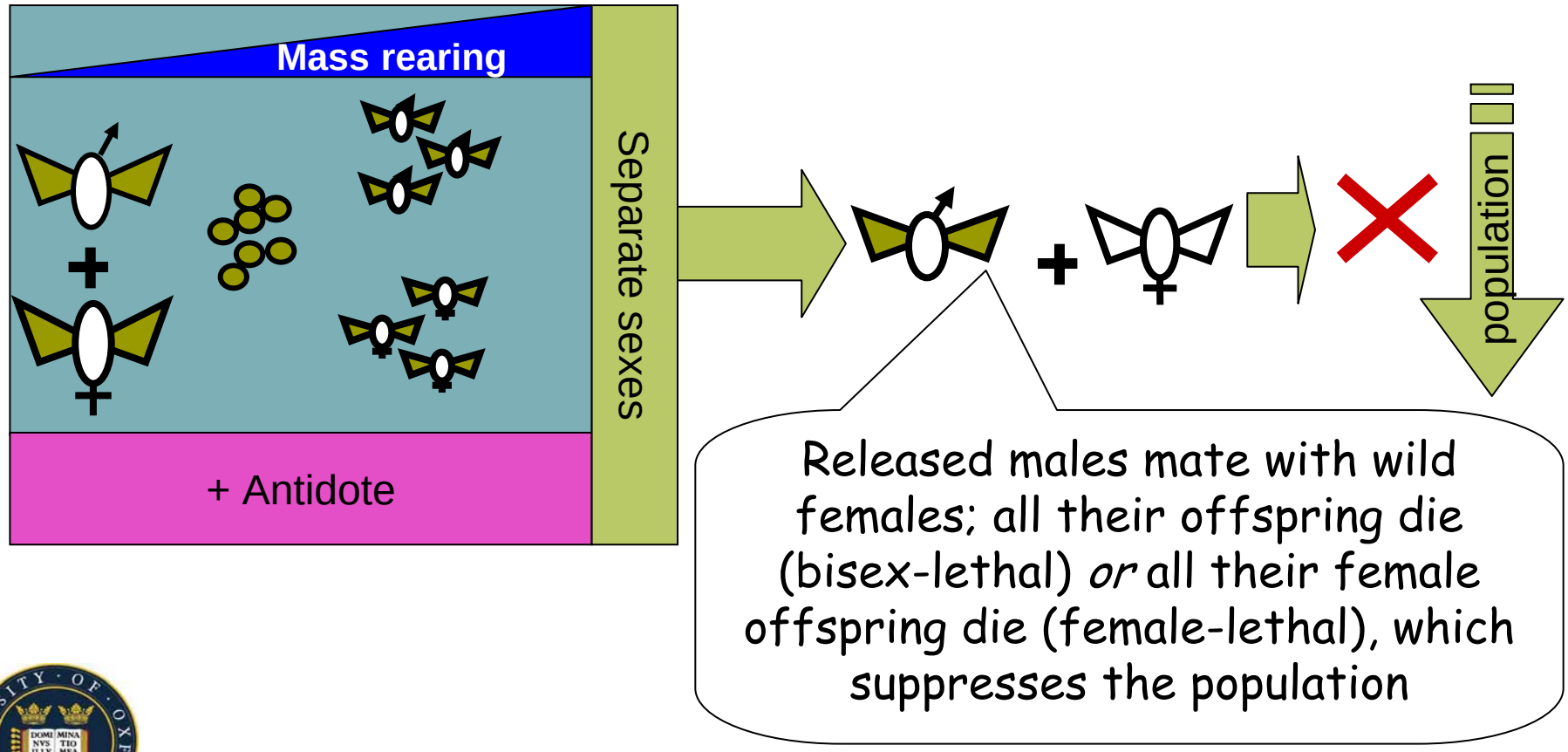

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What are the consequences if heritable resistance arises to the RIDL genetic construct?

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We developed mathematical (population genetic and population dynamic) models to find answers.

N. Alphey et al. (2011) J Theor Biol 270:42

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Resistance has not (yet) been detected in any RIDL strains.

Imagine a hypothetical resistant gene *R*, which reduces the lethality of the RIDL construct - some, perhaps all, affected individuals survive.

(unspecified biochemical mechanism)

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The resistant gene *R*, might have some fitness cost, relative to the susceptible allele *S*.

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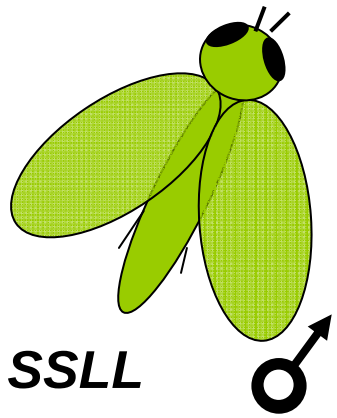
Assume that all released RIDL males have no resistant alleles.



So their progeny will inherit:

- a susceptible *S* allele, providing an element of resistance dilution

  and

- a lethal *L* allele, which would favour resistance

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How will these competing forces play out?

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It depends on properties of the *R* allele (degree of susceptibility & fitness cost) and the ratio of released *SSLL* males to males emerging in the wild.

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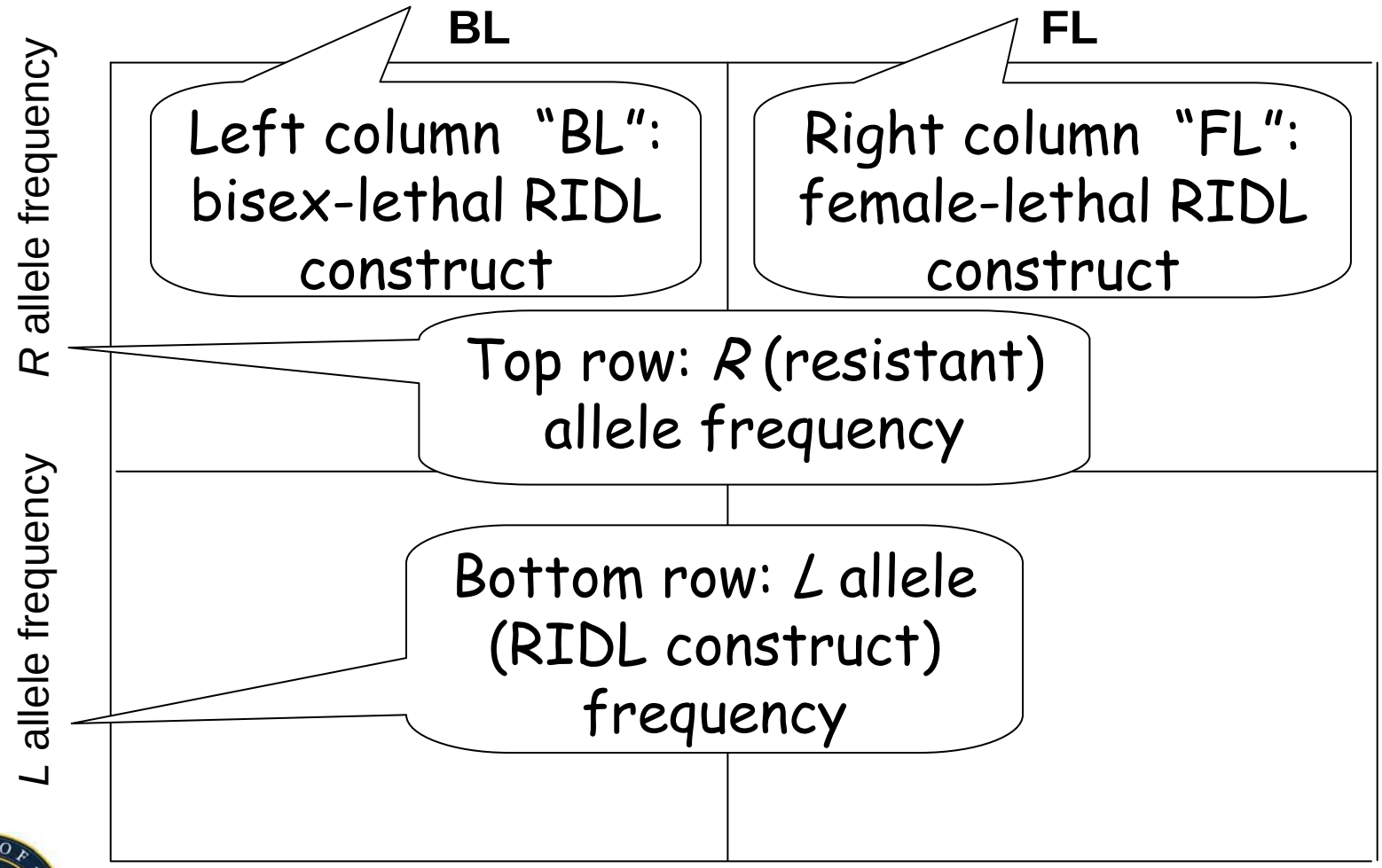
Layout of diagrams that follow



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Consider the "worst-case" scenario: the *R* allele is dominant, has no fitness cost, and confers complete resistance (i.e. any *RR* or *SR* individual ignores the *L* allele)!

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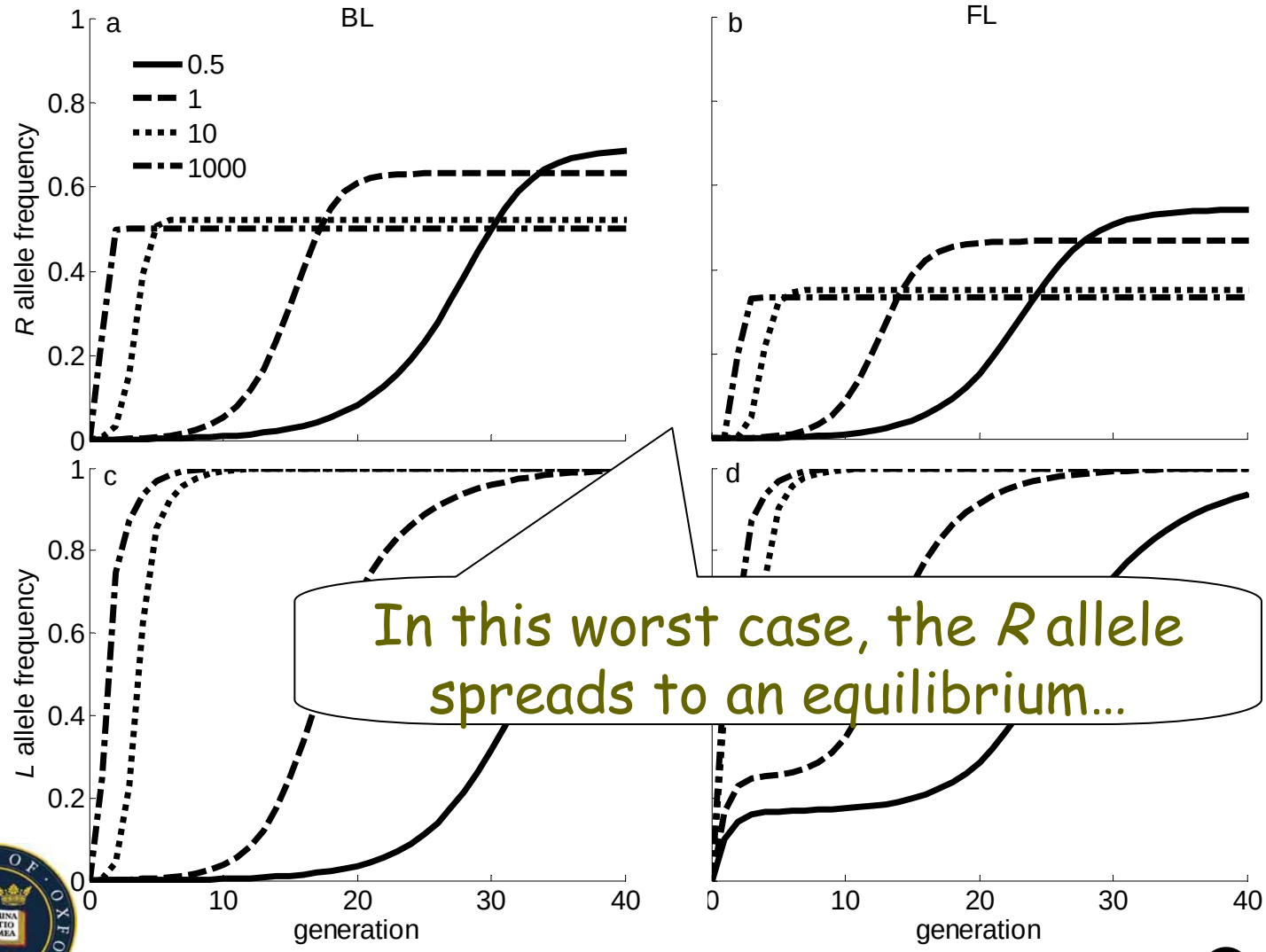
Allele frequency evolution: WORST-CASE SCENARIO



In this worst case, the *R* allele spreads to an equilibrium…

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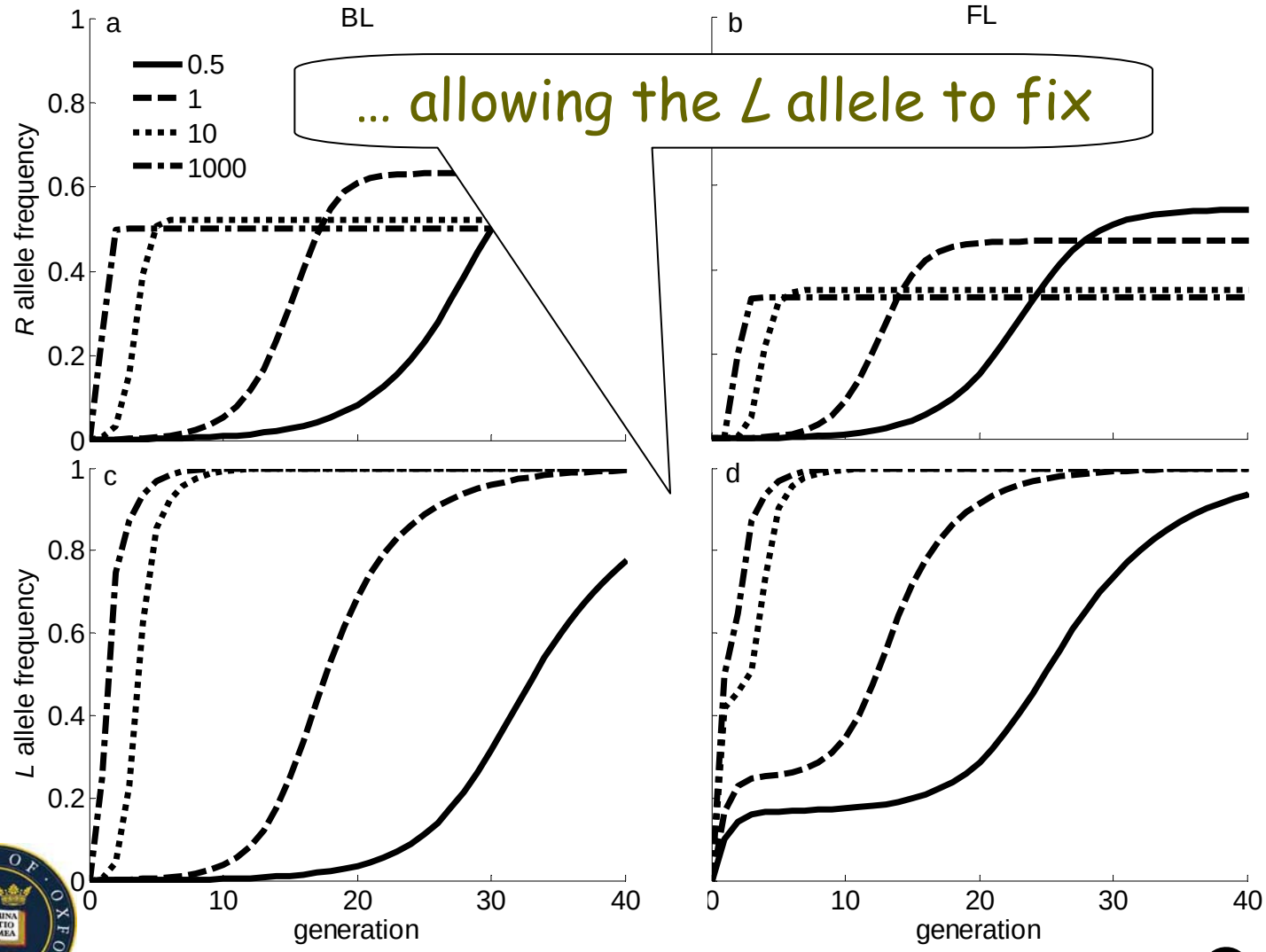

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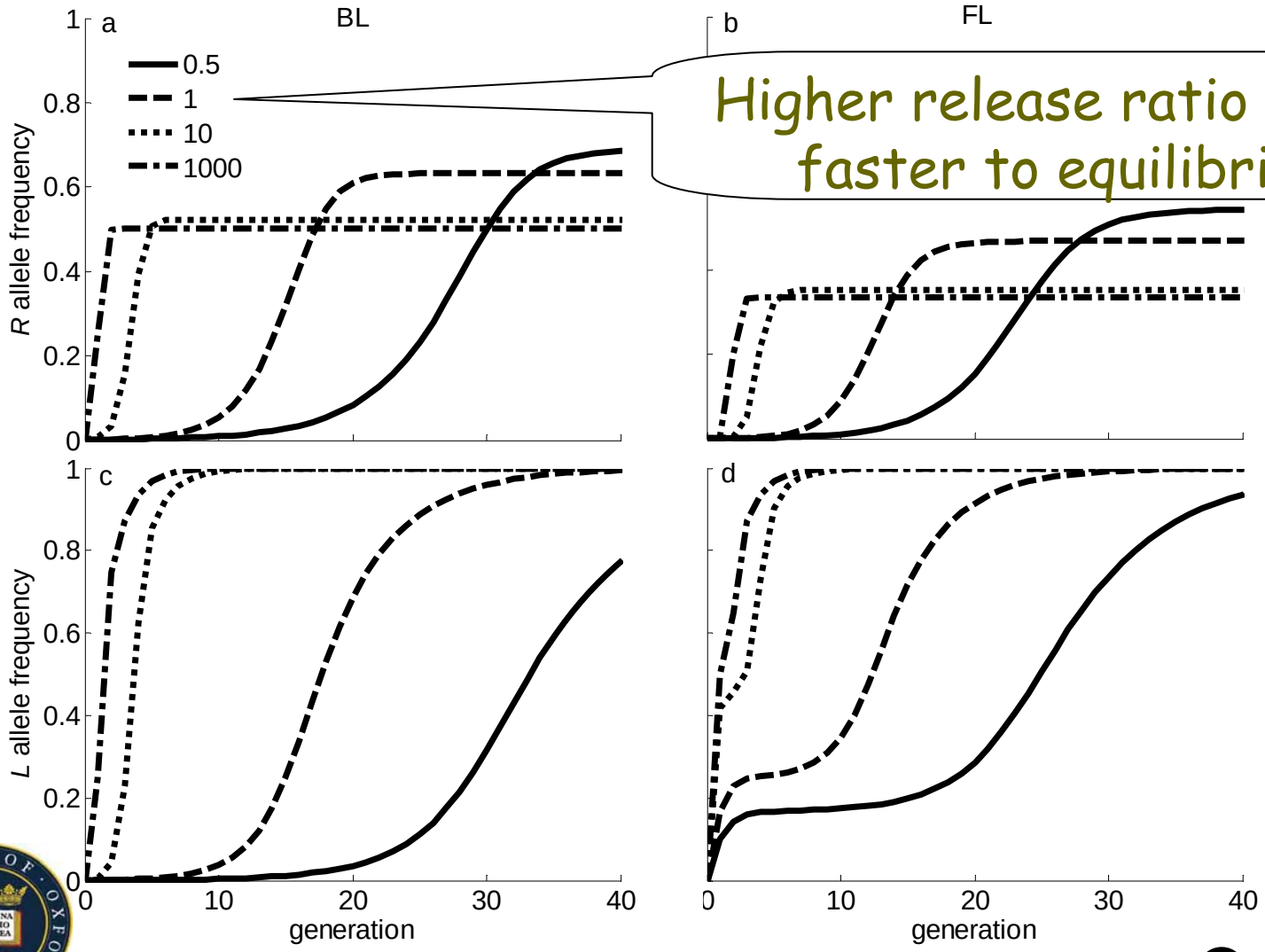

Higher release ratio means faster to equilibrium

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The next graphs again show dominant resistance, with no fitness cost. The solid line is complete resistance, the other lines are increasing *susceptibility* to the genetic lethality (i.e. less effective resistance).

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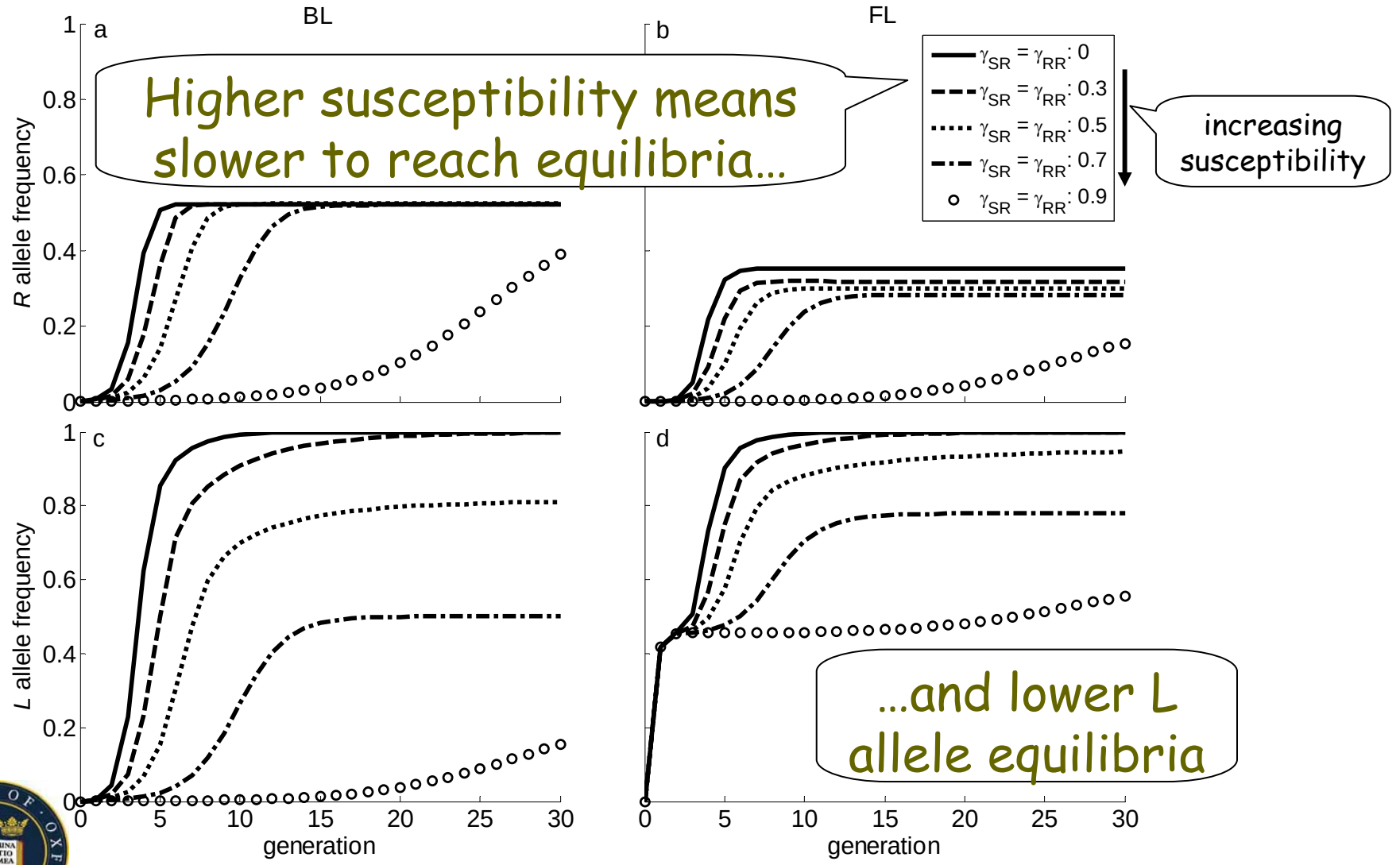
Allele frequency evolution: NEARLY-WORST CASE



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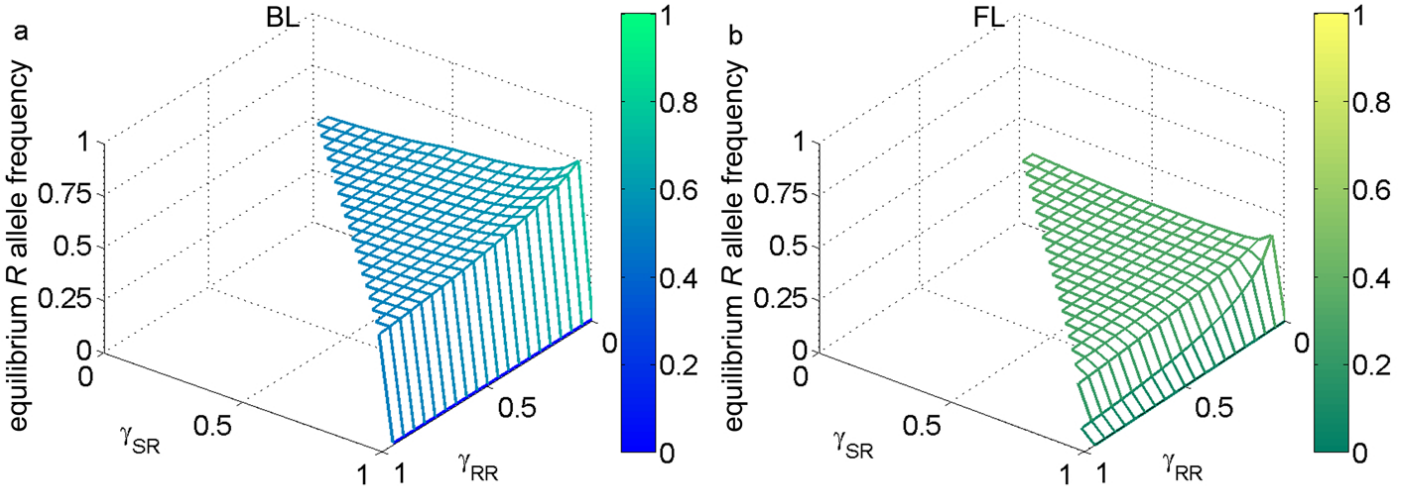
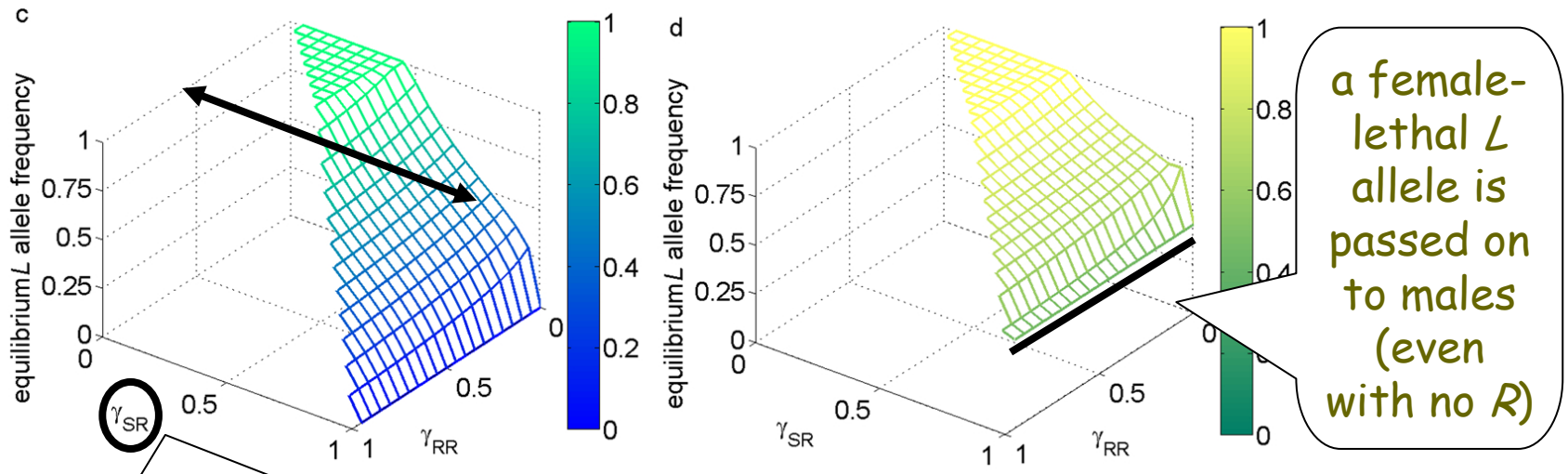
Allele frequency equilibria depend on *SR* and *RR* susceptibility (γ) to the lethality





SR susceptibility has more effect than *RR*

a female-lethal *L* allele is passed on to males (even with no *R*)

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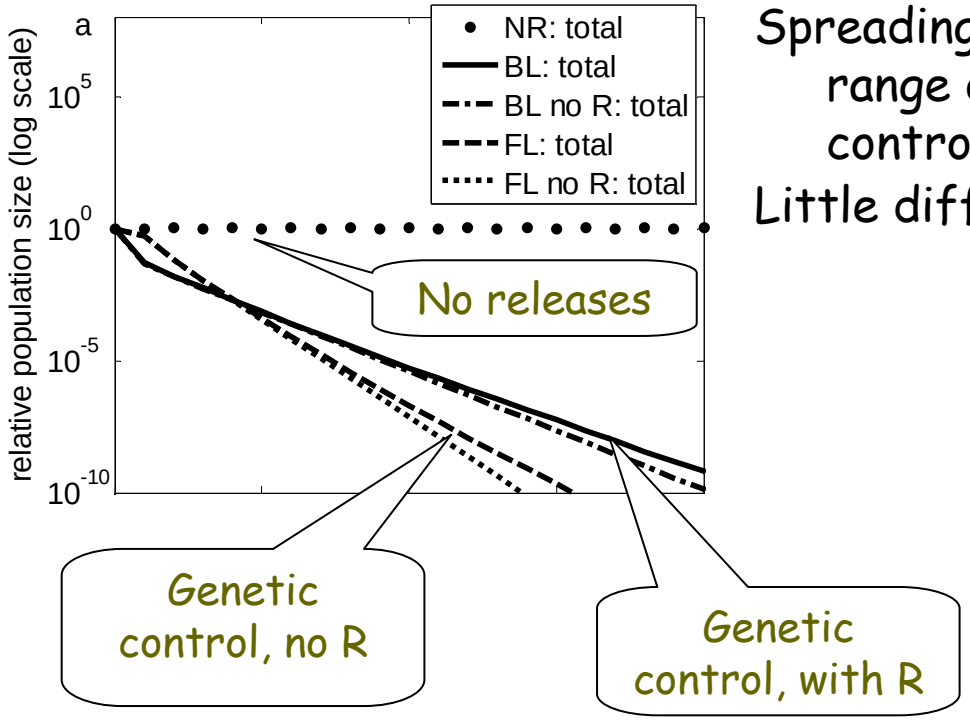
Effect of spreading *R* and *L* on population control



Spreading *R* and *L* alleles can have a range of impacts on population control:

Little difference (a)

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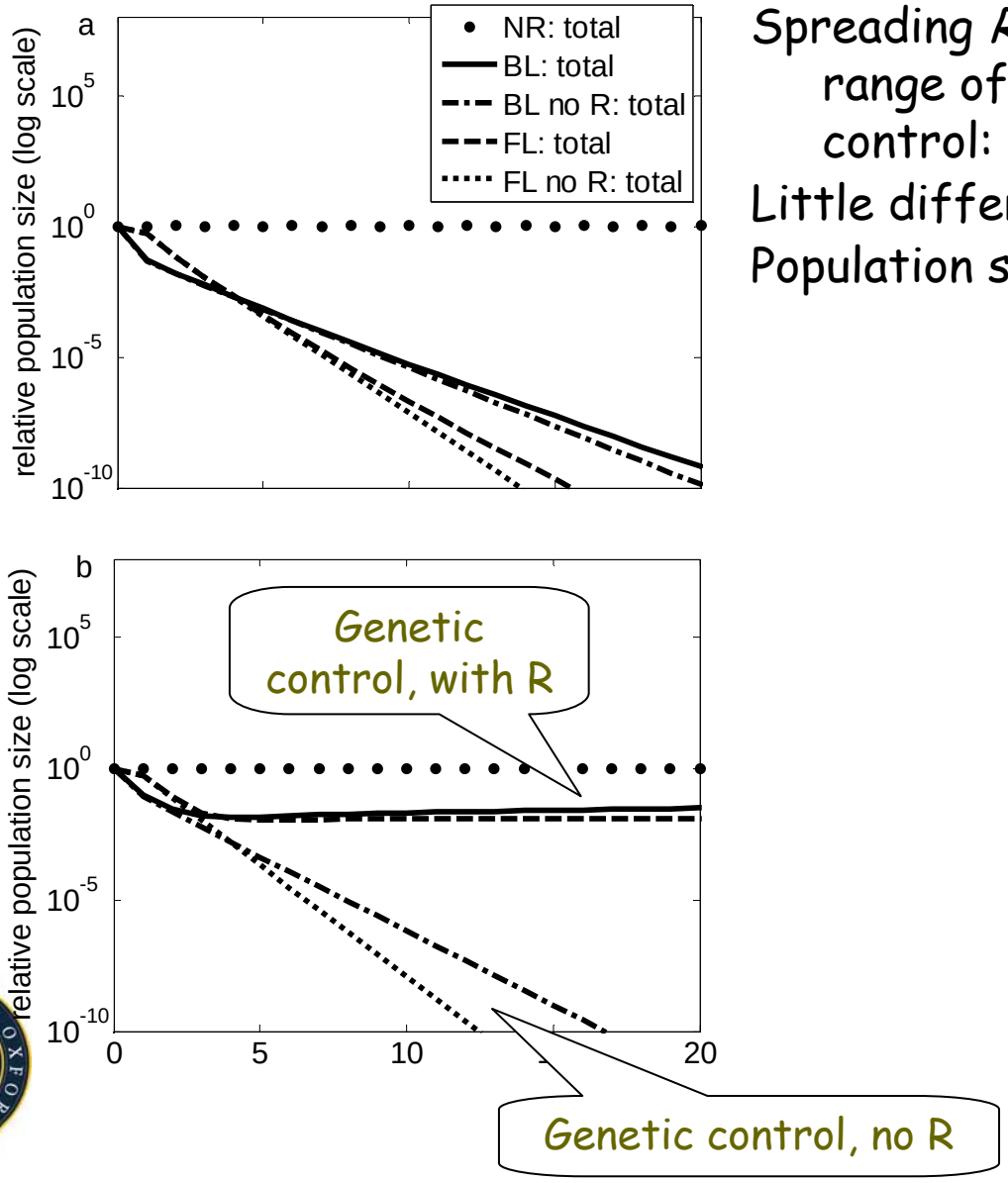
Effect of spreading *R* and *L* on population control



Spreading *R* and *L* alleles can have a range of impacts on population control:

Little difference (a)

Population still somewhat reduced (b)

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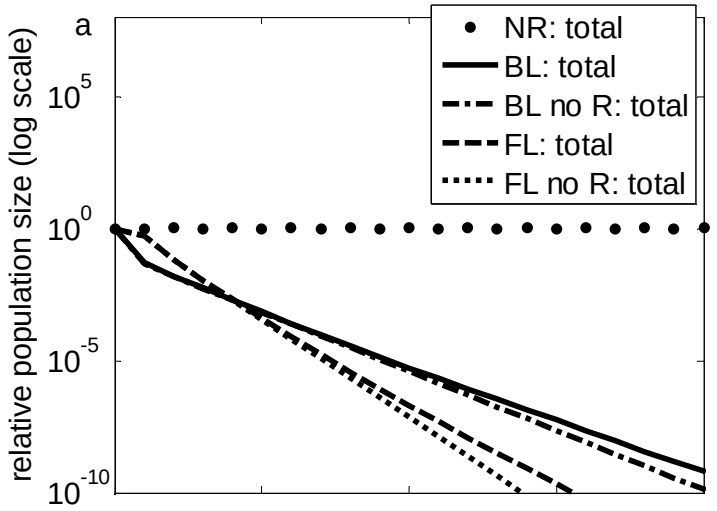
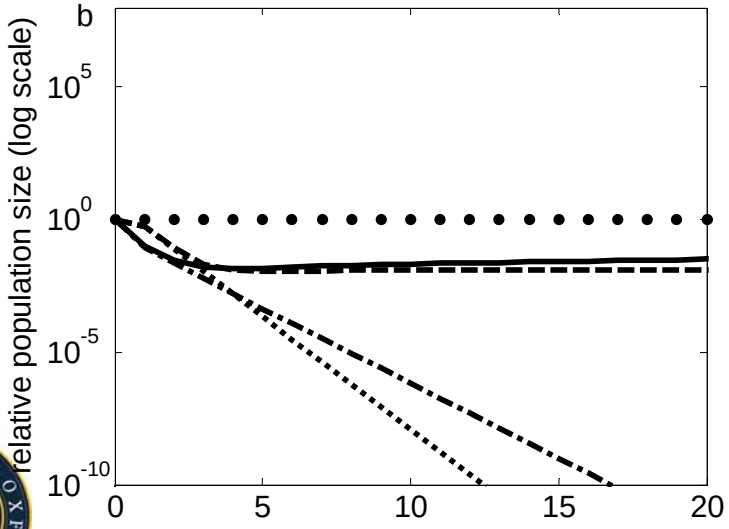
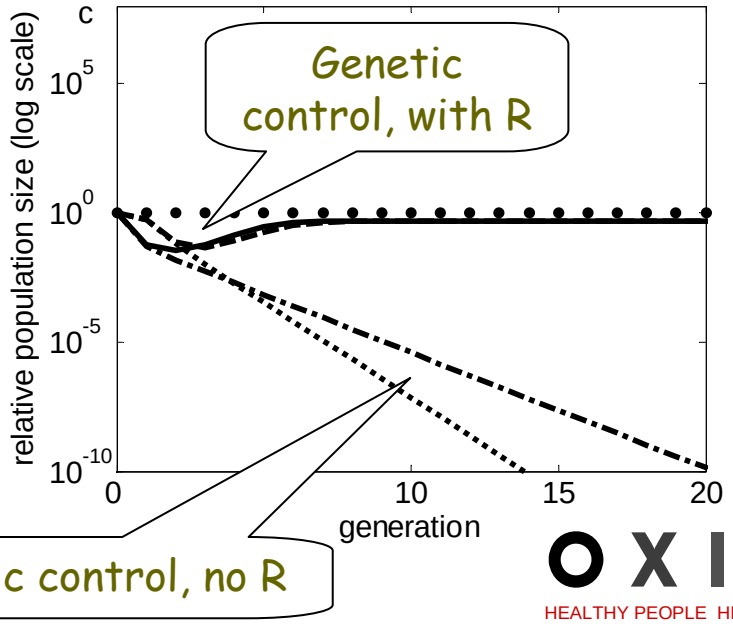
Effect of spreading *R* and *L* on population control







Spreading *R* and *L* alleles can have a range of impacts on population control:

Little difference (a)

Population still somewhat reduced (b)

Population rapidly rebounds, to slightly lower equilibrium (c)

Note the obvious "kinks" in b & c, as resistance starts to take effect

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Conclusions

- For given release ratio, the spread of *R* (and consequently *L)* depends on how effective *R* is and its fitness costs:
  - higher susceptibility *R* spreads less far, or goes extinct
  - higher cost *R* spreads less far, or goes extinct
- If *R* and *L* spread, the impact on a control programme could be negligible to significant
- The most threatening *R* (highly effective, little cost) would show up quickly in trials/results, allowing action (e.g. deploy alternative strains)

N. Alphey et al. (2011) J Theor Biol 270:42

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For more details

- See Journal of Theoretical Biology 270 (2011) 42-55 – available online now

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