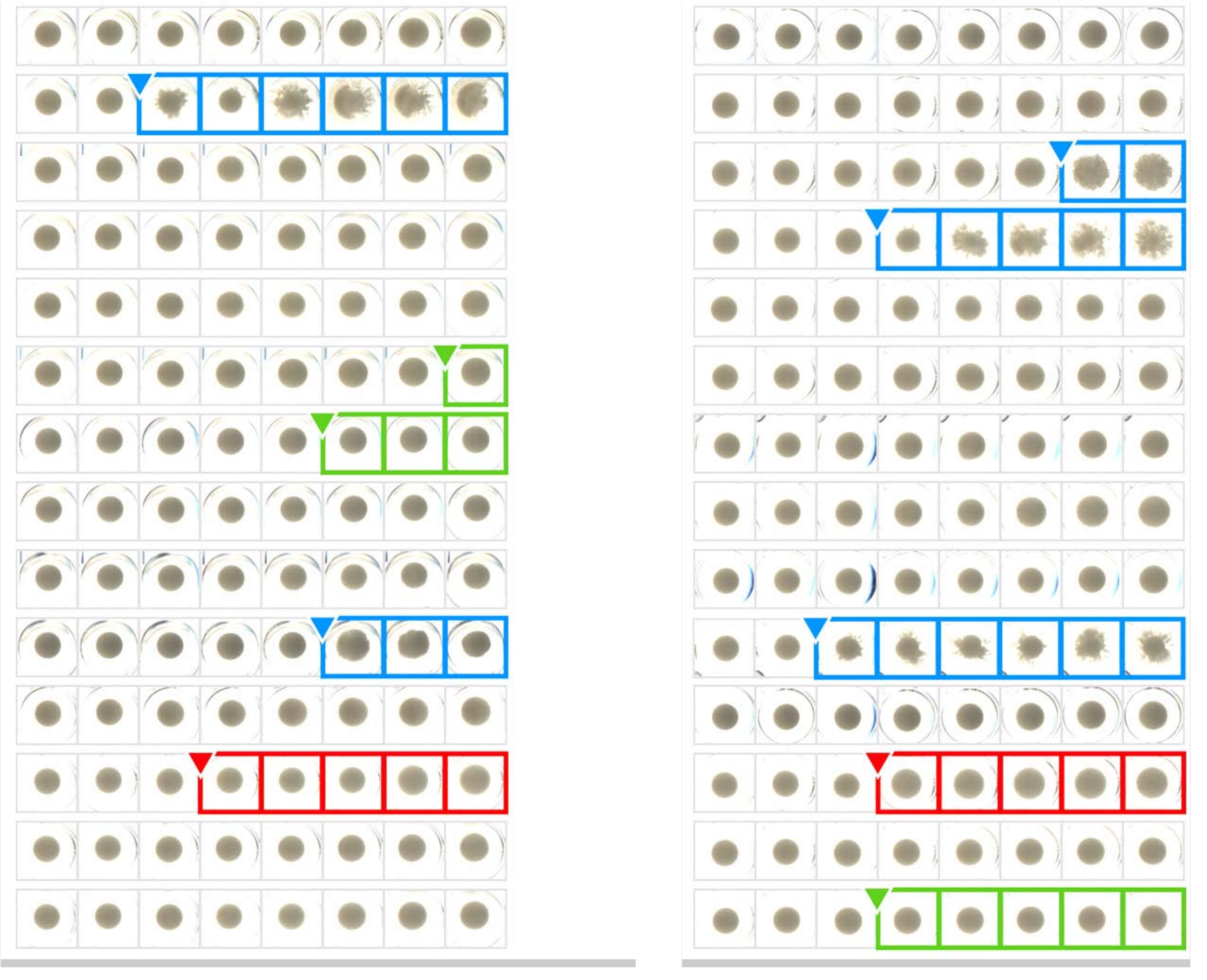
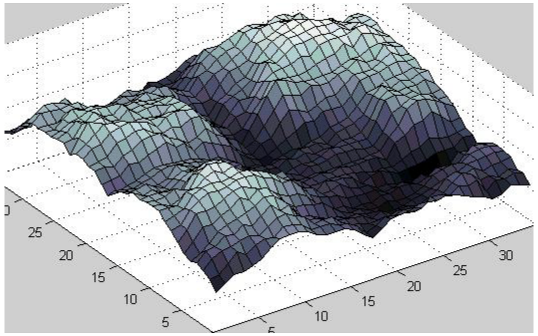
What I saw when I watched some evolution



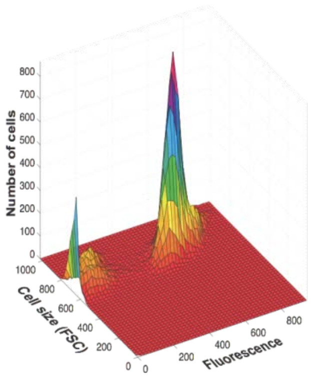
Michael Desai, Harvard University

Things I might say



1. What could evolution do?

   A set of possibilities

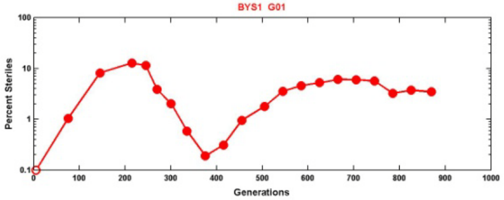


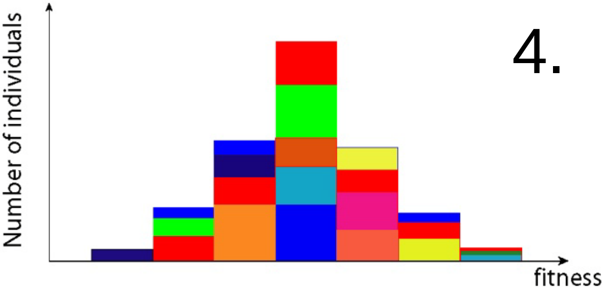
2. A System to Visualize Adaptation

   The rise and fall of sterile mutations

3. Adaptation in Experimental Yeast Populations

   An array of observed dynamics

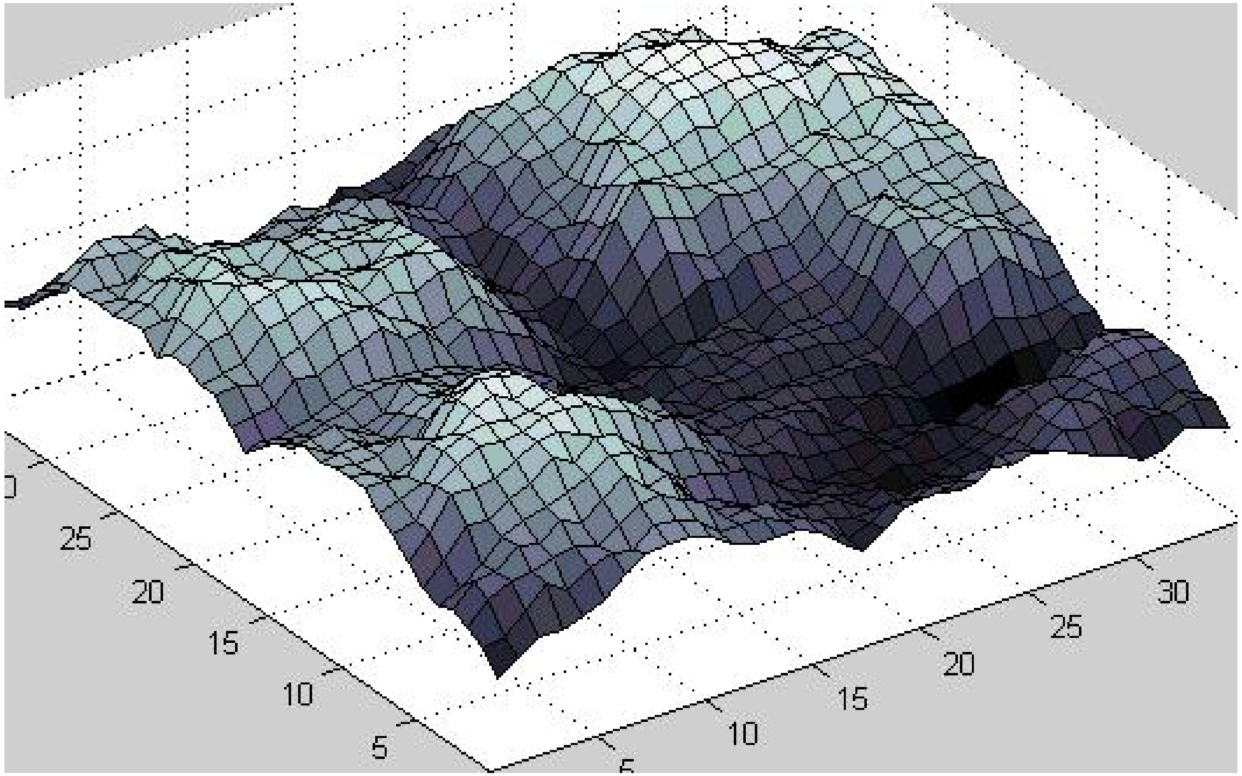




4. What Has Evolution Done?

   Genetic variation in selected asexual populations

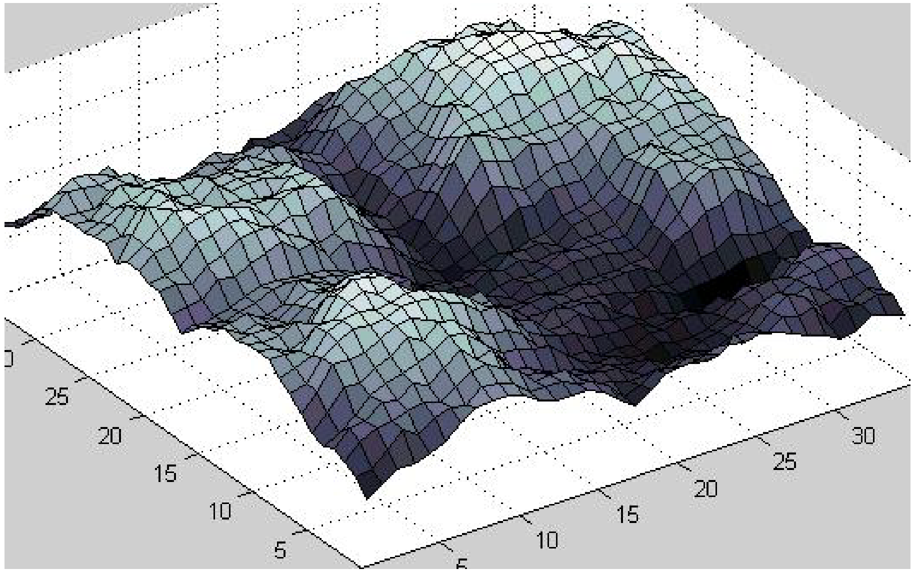
What *could* evolution do?
What *will* evolution do?



Biology → Space of Possibilities → Distribution of Outcomes

How do we characterize what could happen?
Given what could happen, what will?
Given what did happen, what could?

Characterizing the Spectrum of Possibilities



Biology ⟶ Space of Possibilities ⟶ Distribution of Outcomes

What does a typical space of possibilities look like?

Global structure? Hopeless

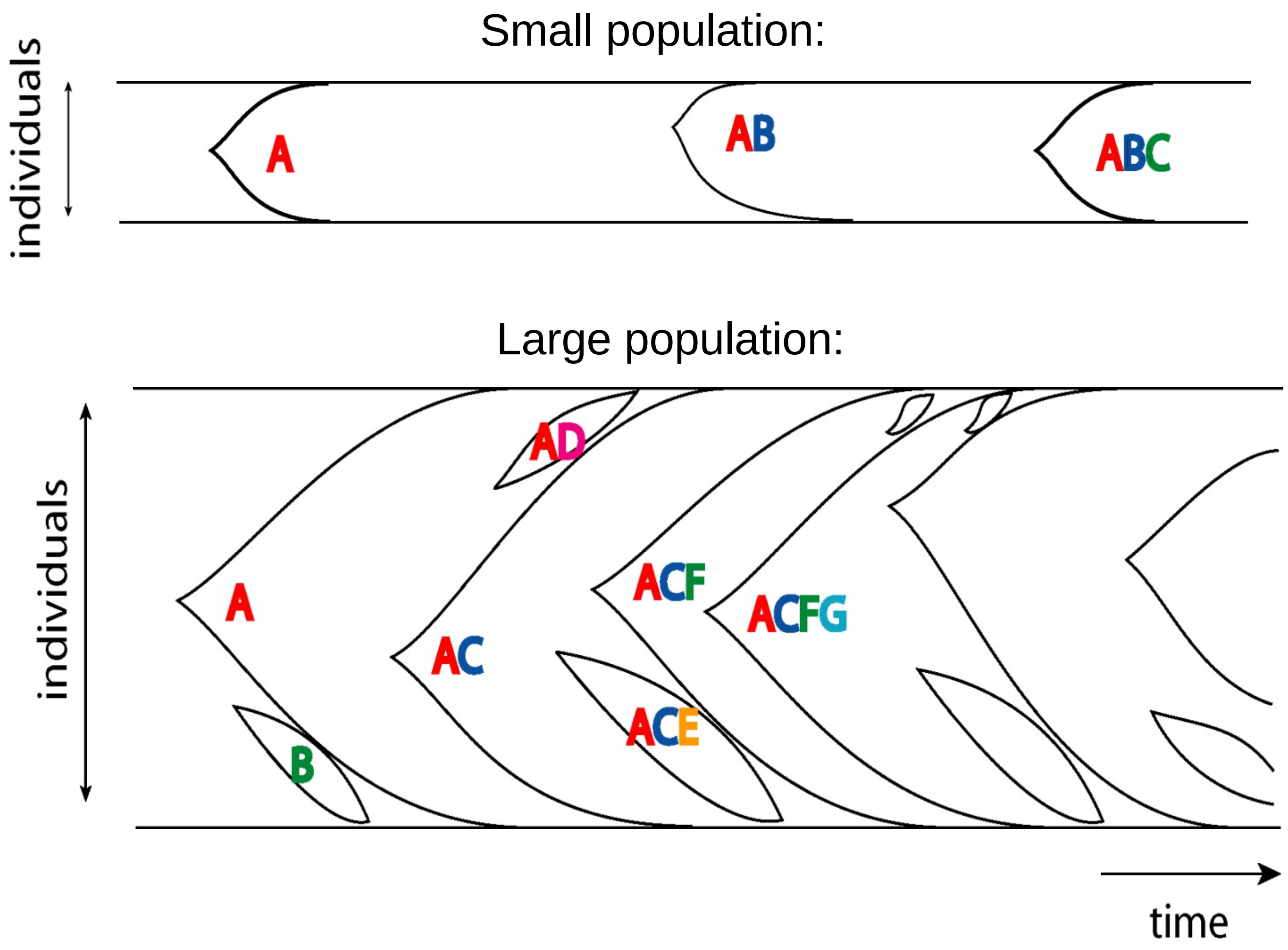
Local structure? DFE, epistasis

Statistical structure?

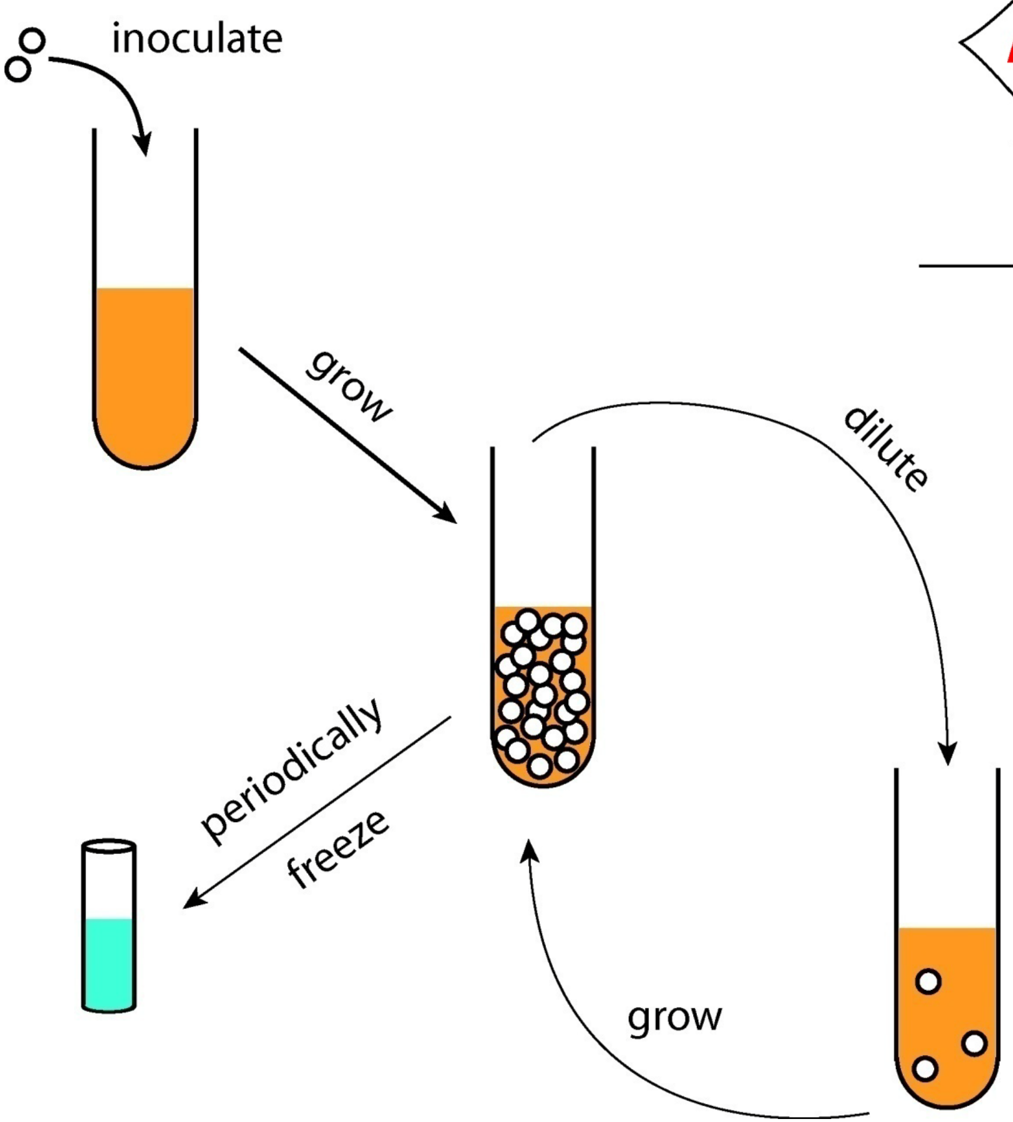
How does biology constrain the possibilities?

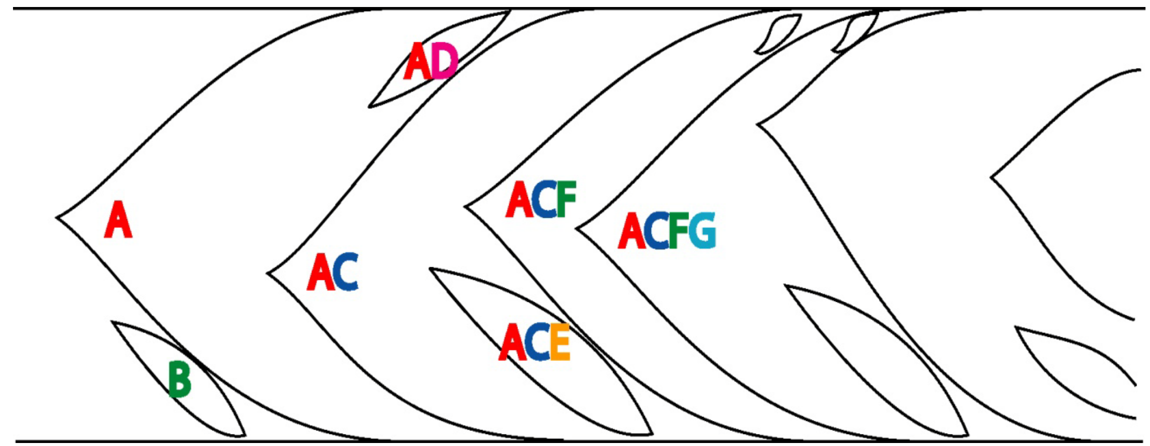
How does evolution constrain the possibilities?

The Problem with Adaptation in Large Populations



An Experimental Approach



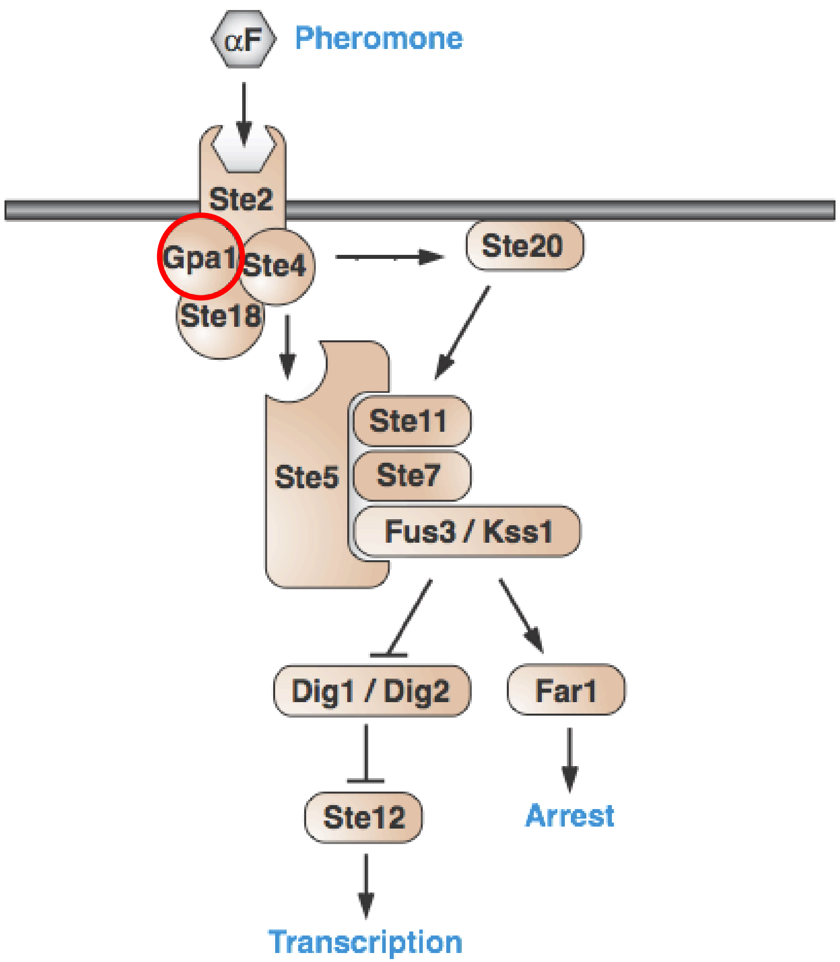


Fitness = How many offspring get through the dilution

But what do we see?

Interesting things are rare and rare

Sterile Strains Have a Selective Advantage



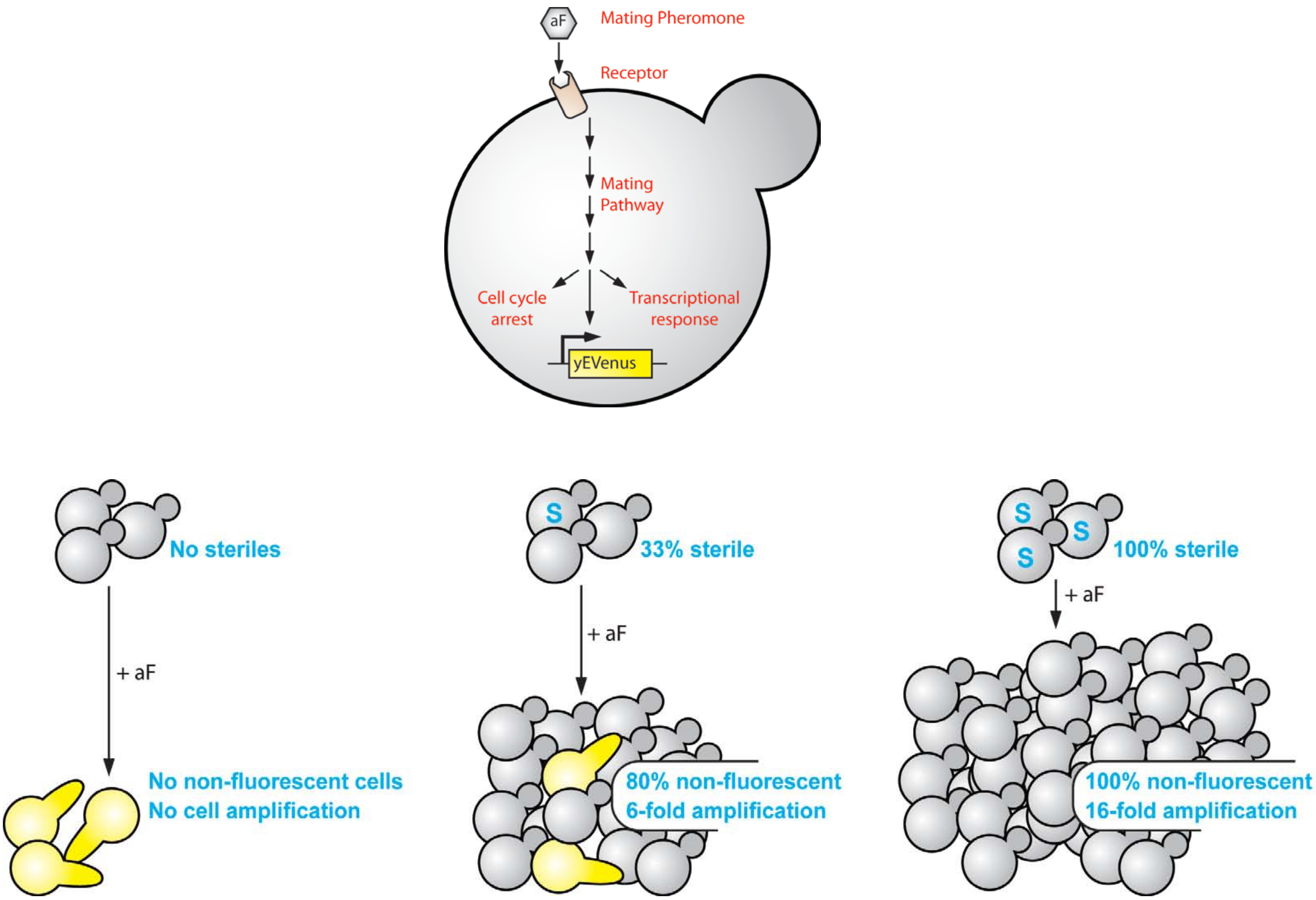
Selective advantage of sterility

BY allele of *GPA1*: *s* = 1.5%

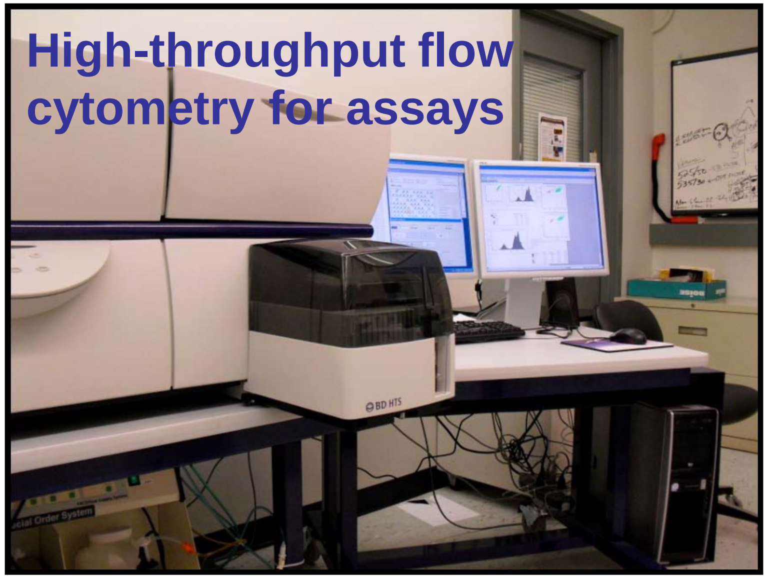
RM allele of *GPA1*: *s* = 0.6%

Lang, Murray, Botstein. 2009. *PNAS*.

A System for Visualizing Sterile Mutations



We Can Watch Hundreds of Replicates



Experimental Parameters

Mutation rate:

$U_{sterile} = 6 \times 10^{-6}$

Selective advantage:

RM: $s = 0.6\%$

BY: $s = 1.5\%$

Population size

Big: Ne ~ 2,000,000

Small: Ne ~ 100,000

148 replicates each (~600 cultures)

Eight plates

RMS1

RMS2

BYS1

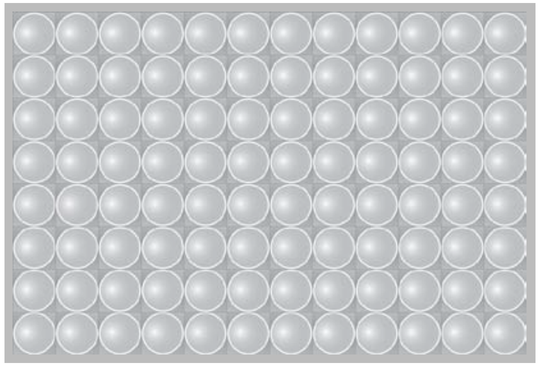
BYS2

RMB1

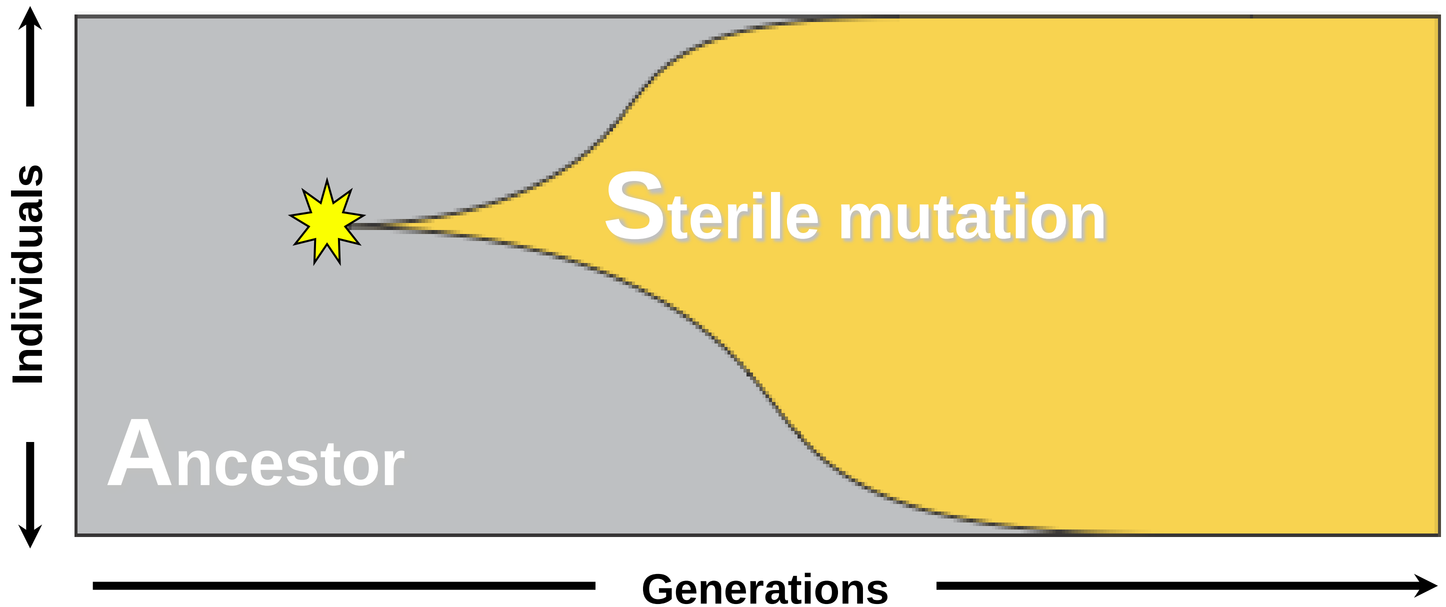
RMB2

BYB1

BYB2



If There Were Nothing Else



Mutation rate:

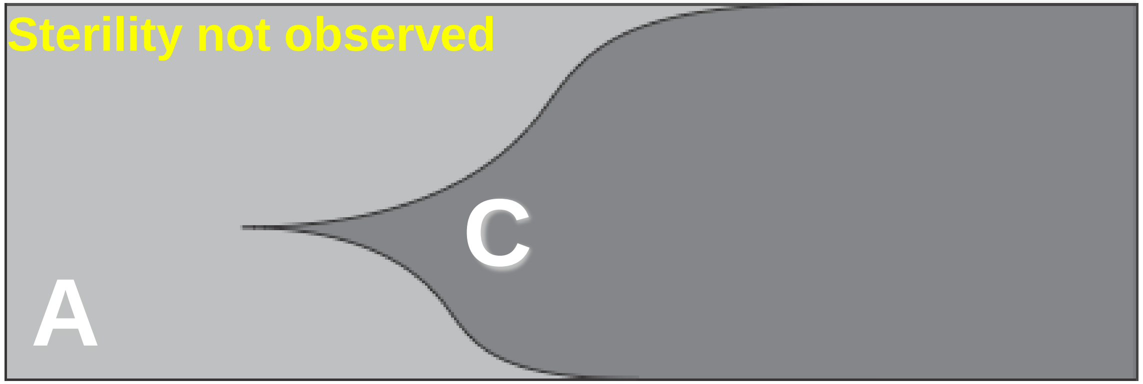
$U_{sterile} = 6 \times 10^{-6}$

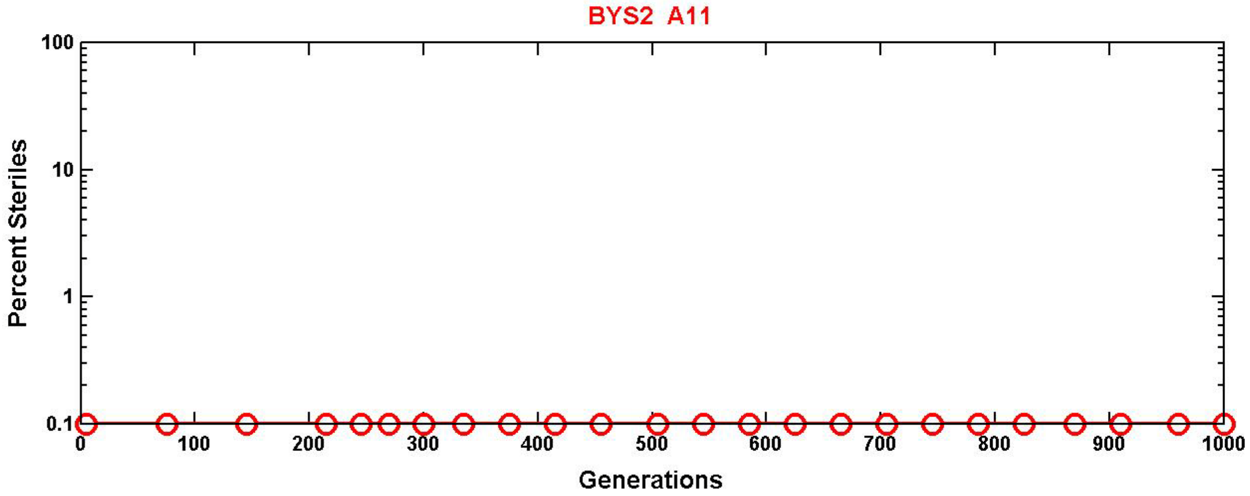
Selective advantage:

RM: $s = 0.6\%$

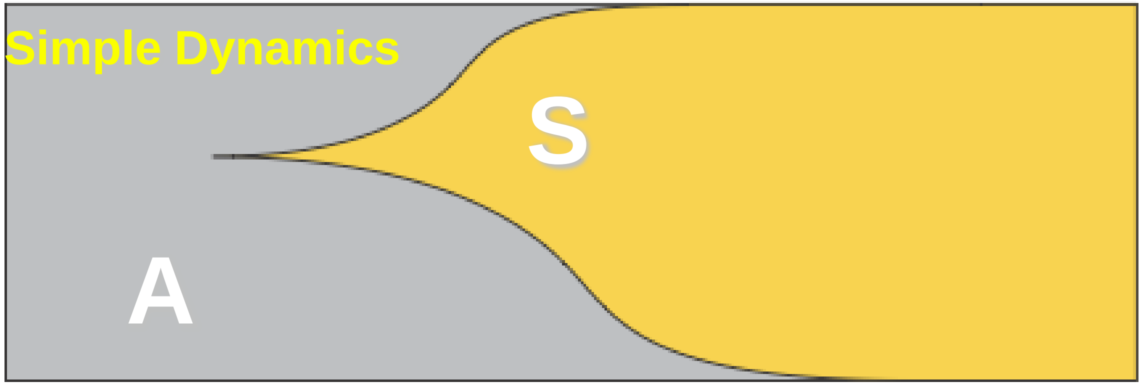
BY: $s = 1.5\%$

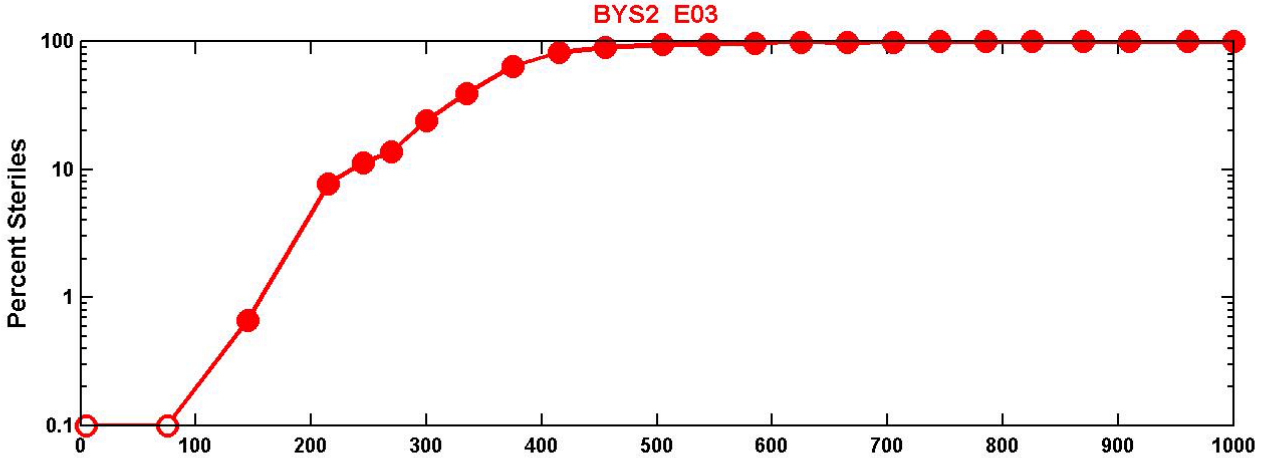
The Most Common Result

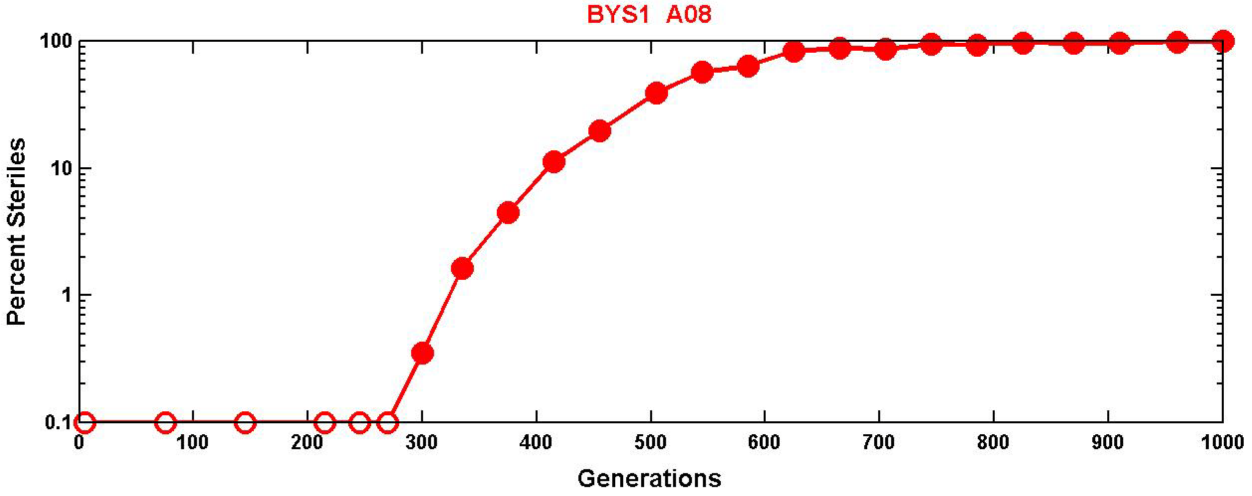




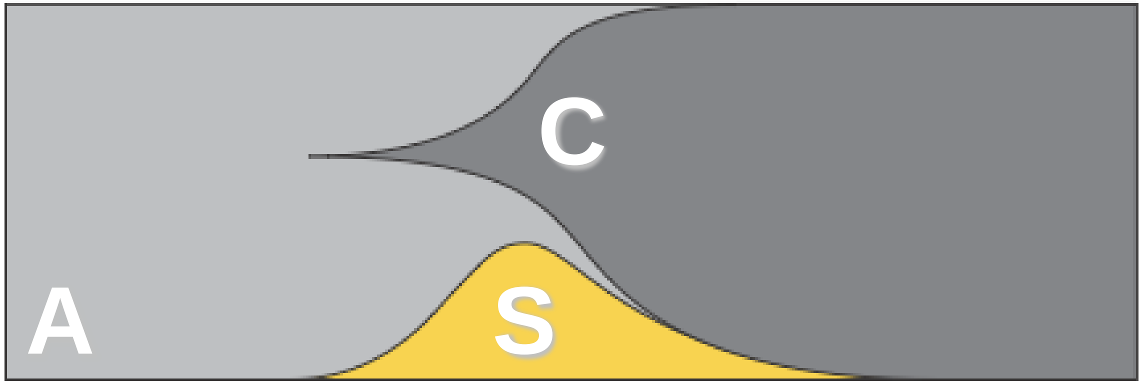
Simple Selective Sweeps

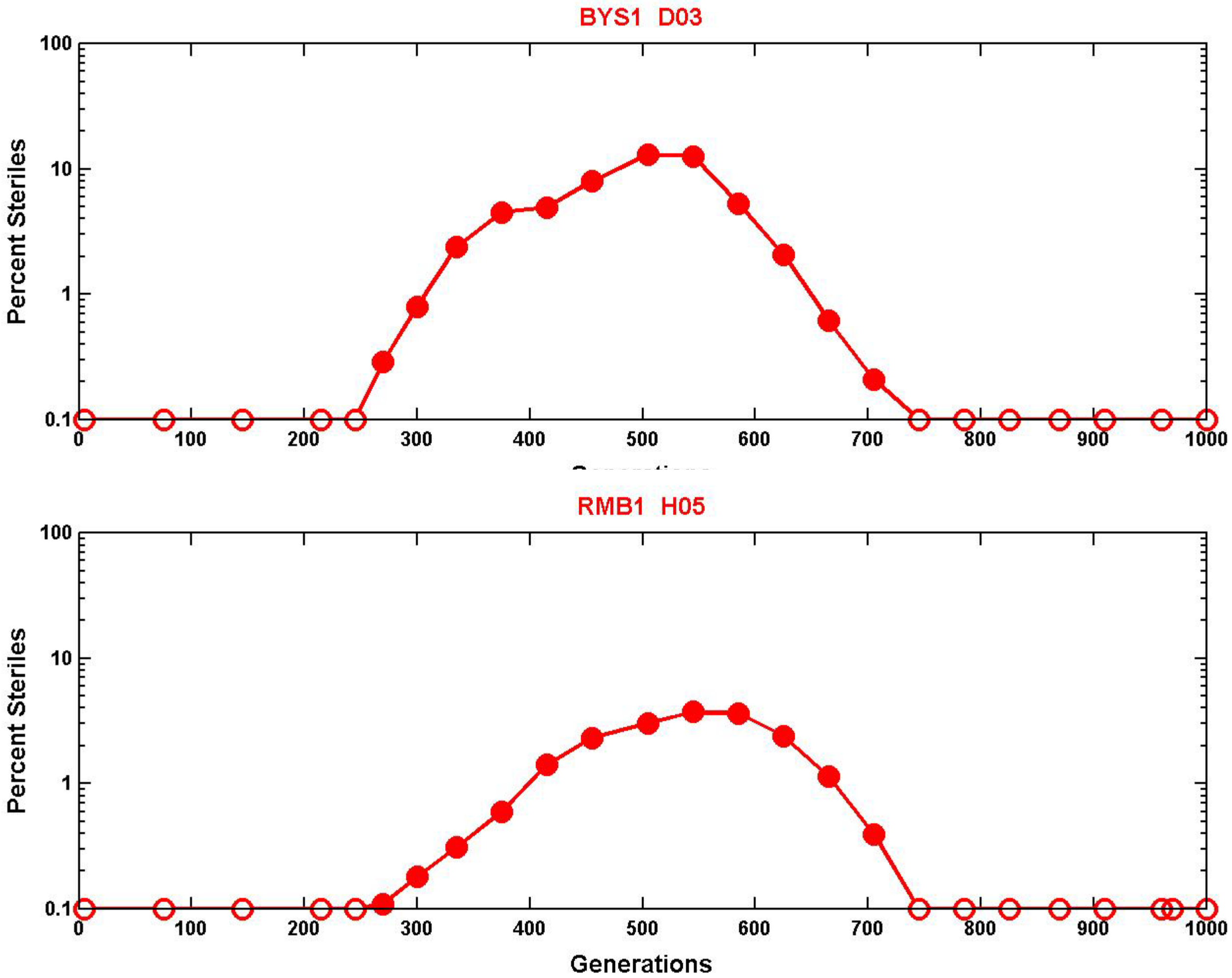




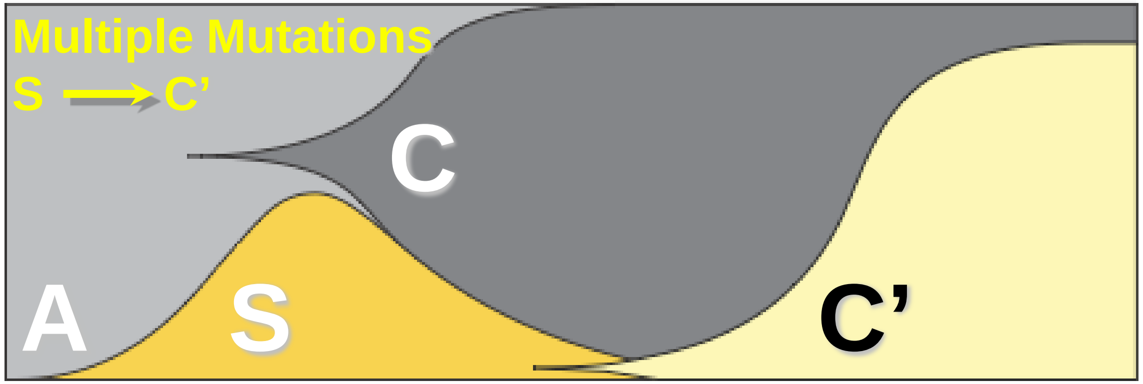


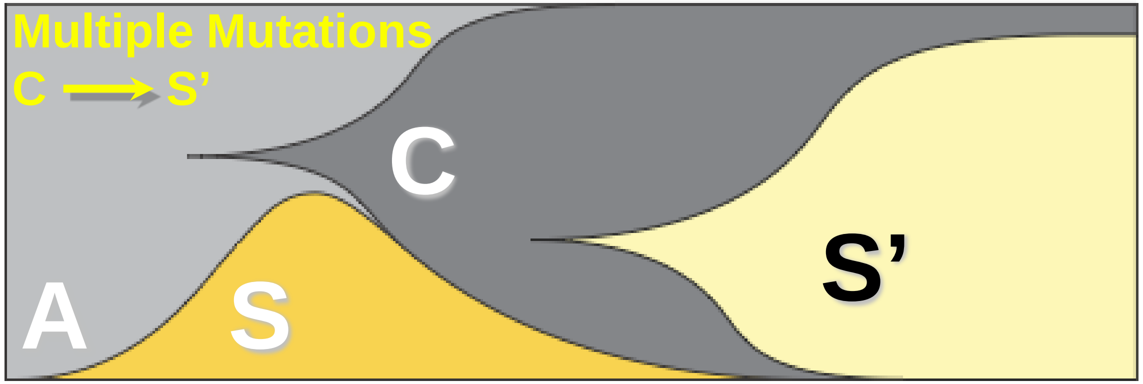
Clonal Interference

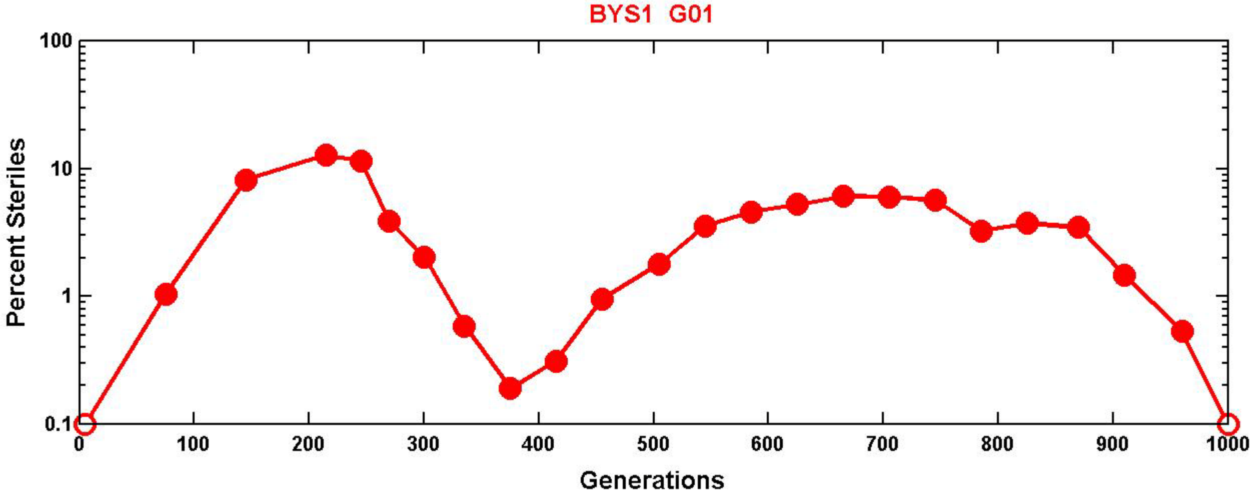




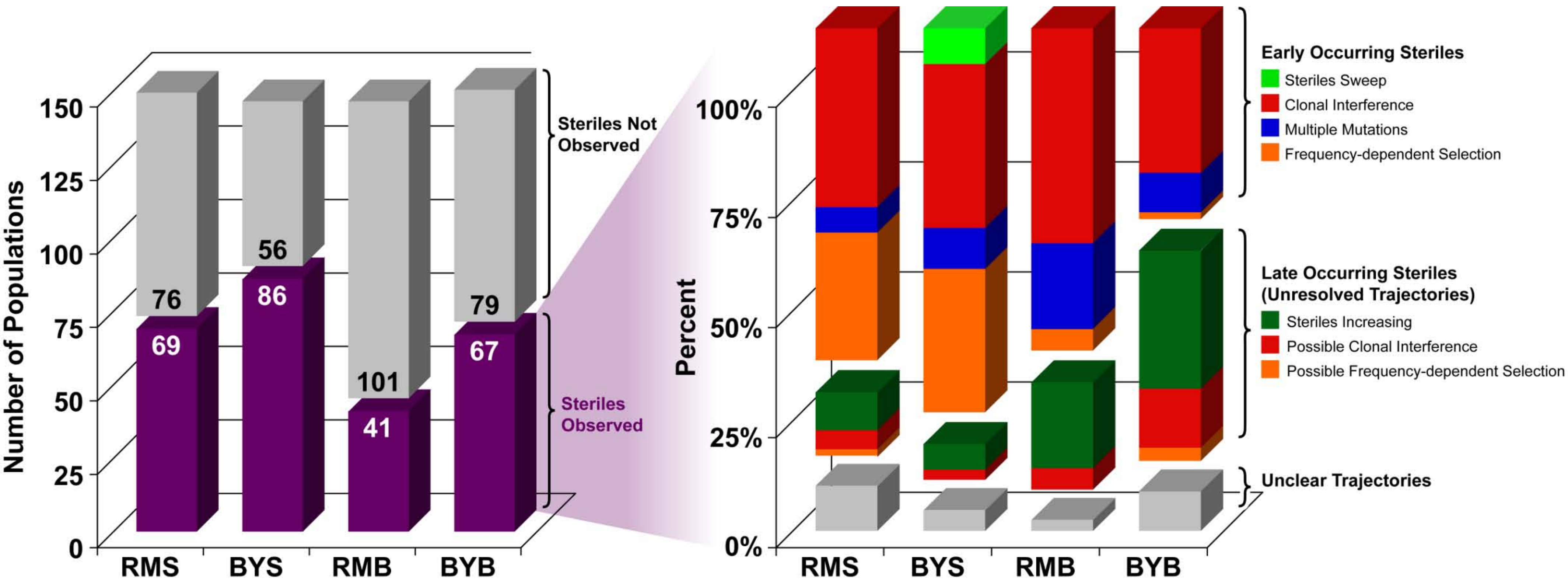
More Complex Dynamics



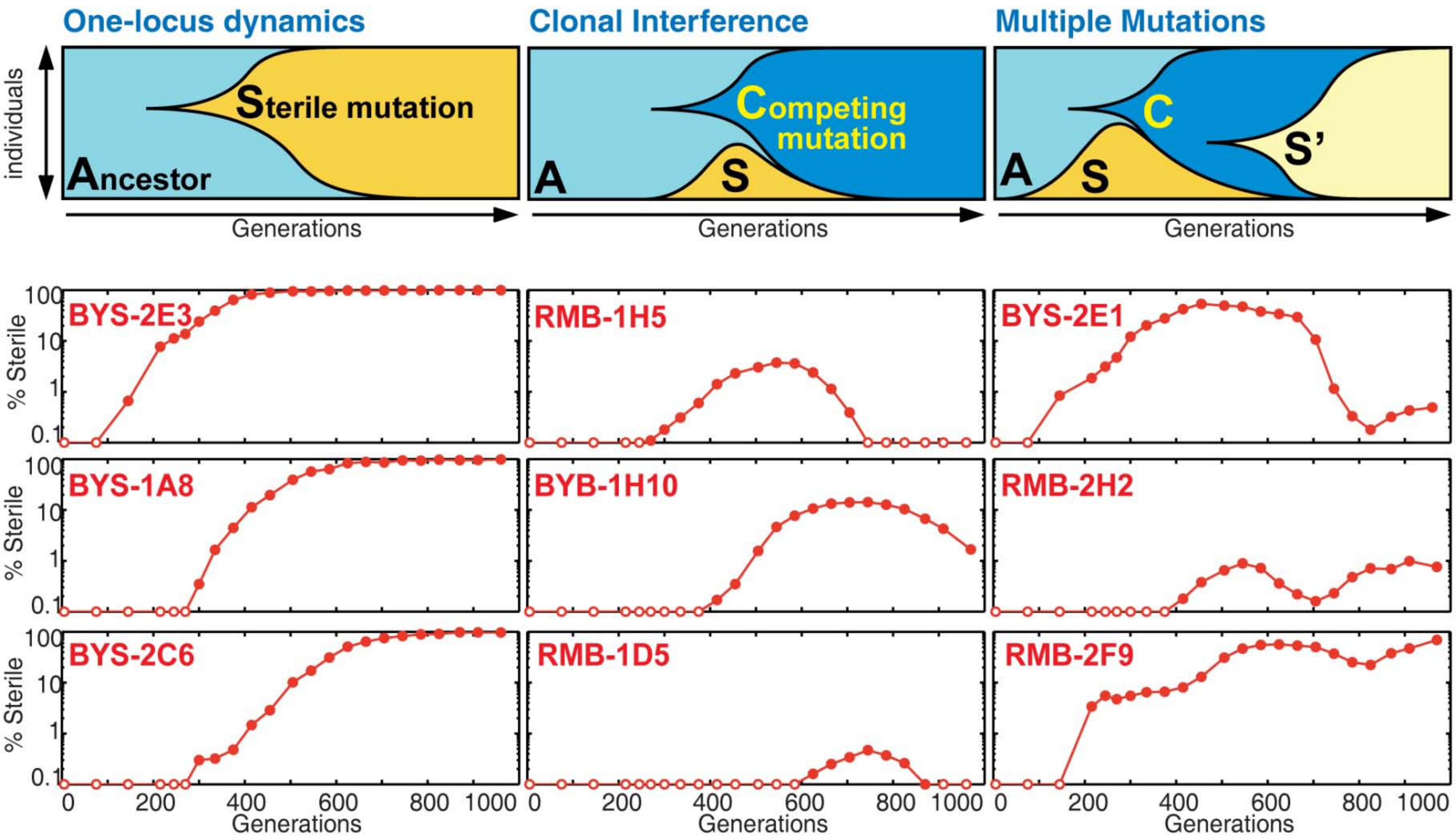




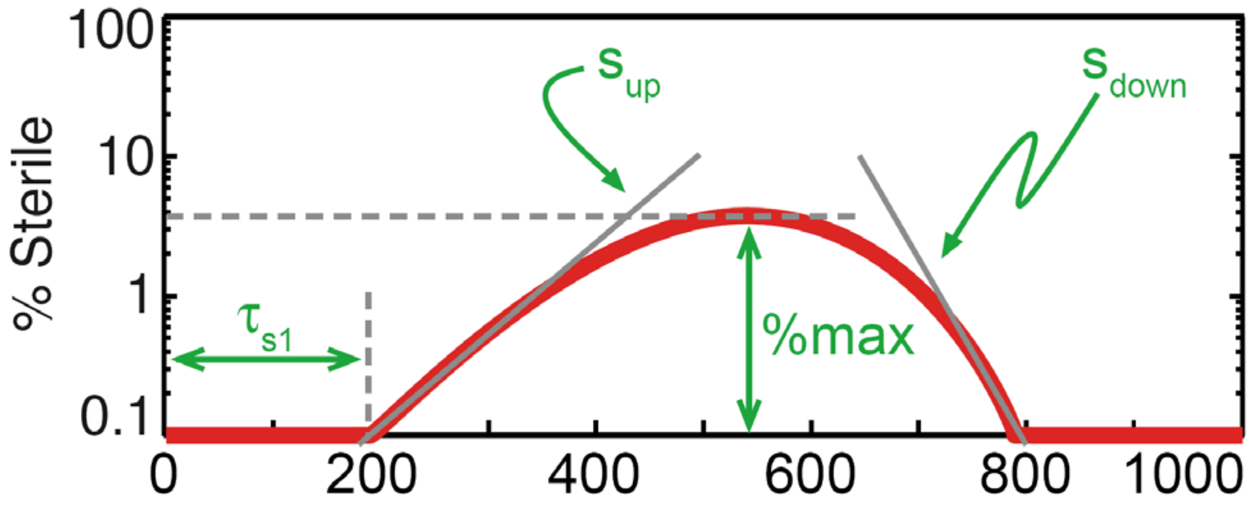
Summary of Dynamics

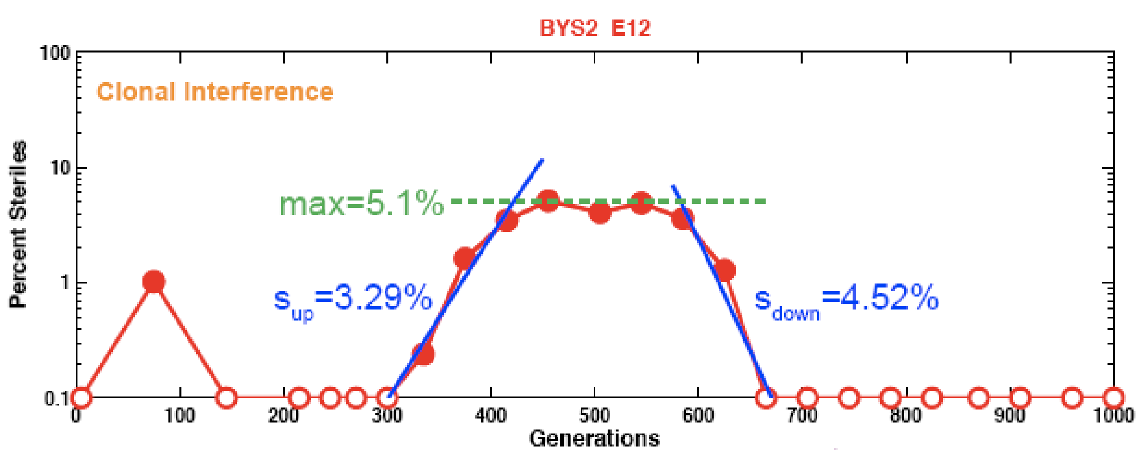


Timings of Observed Dynamics

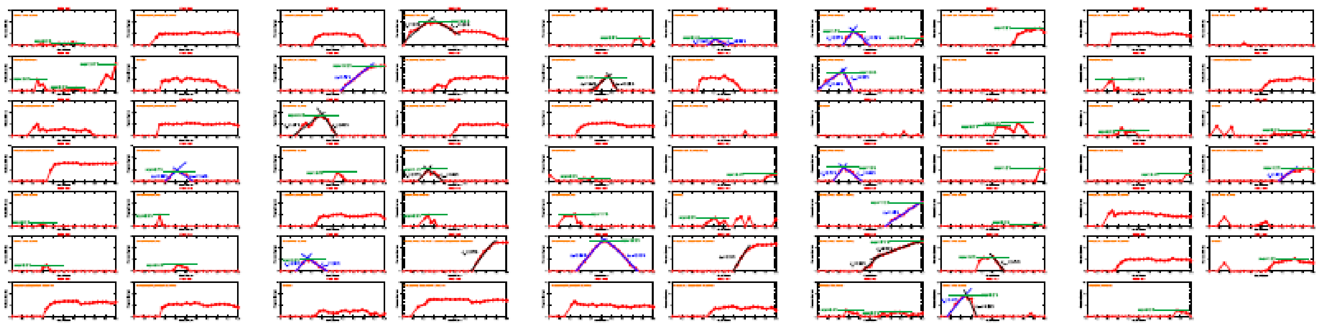


Details of Observed Trajectories

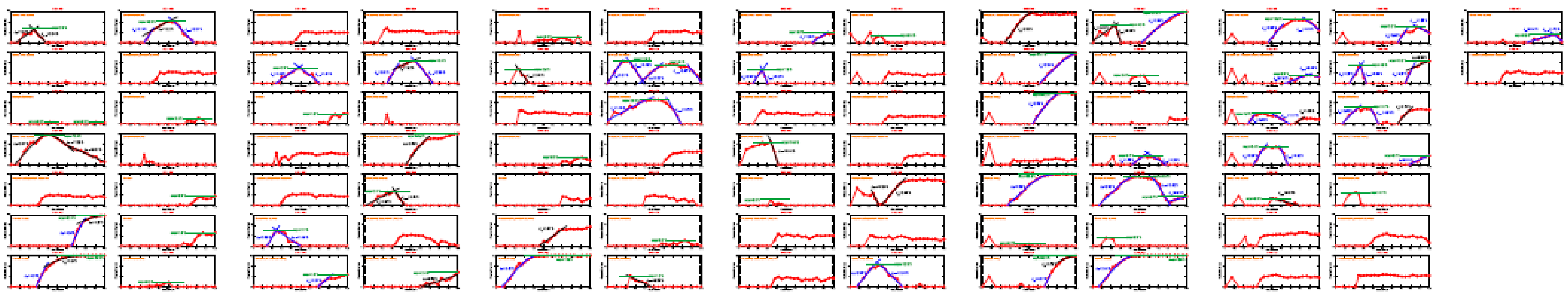




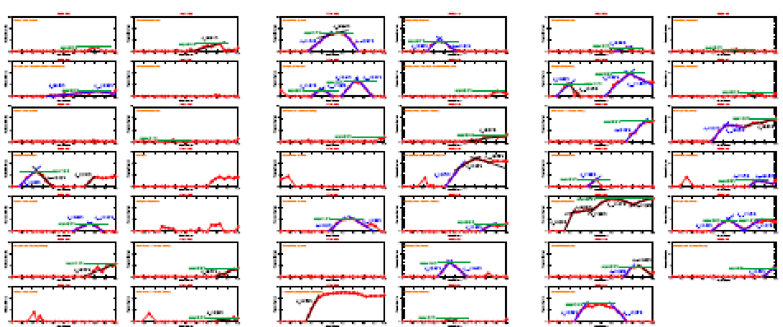
Distributions of Dynamics



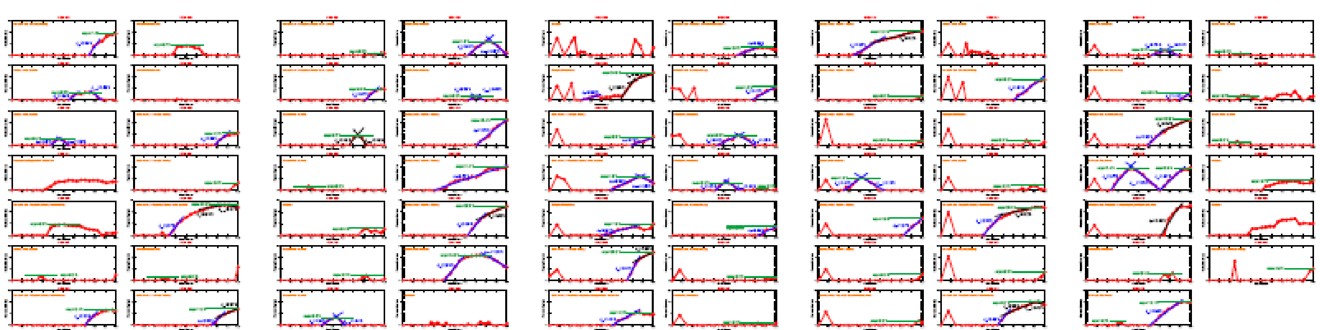
RMS



BYS

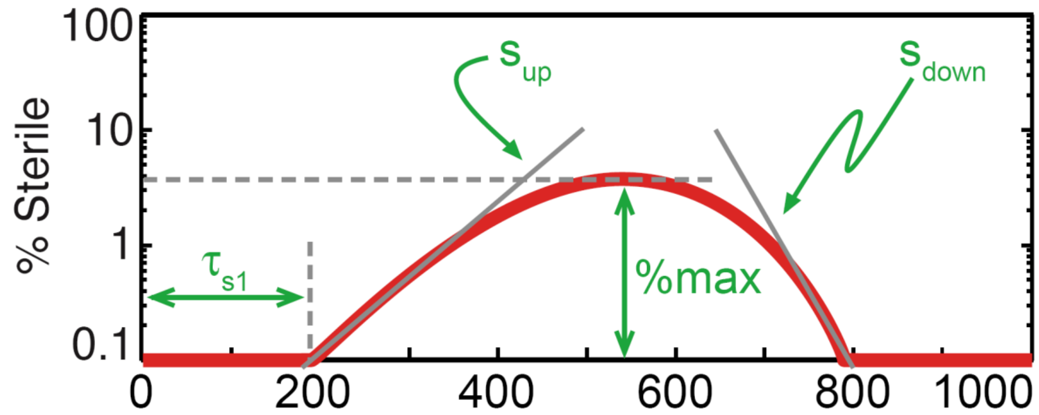


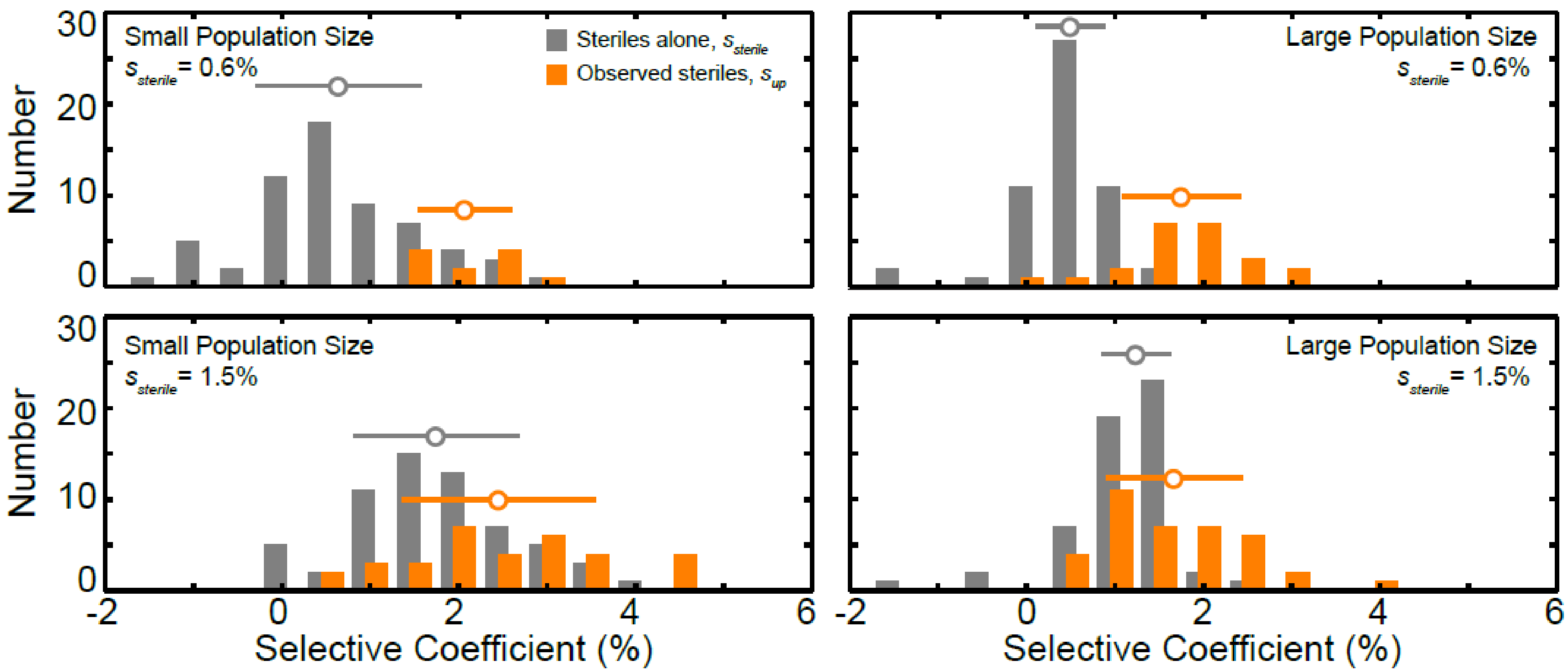
RMB



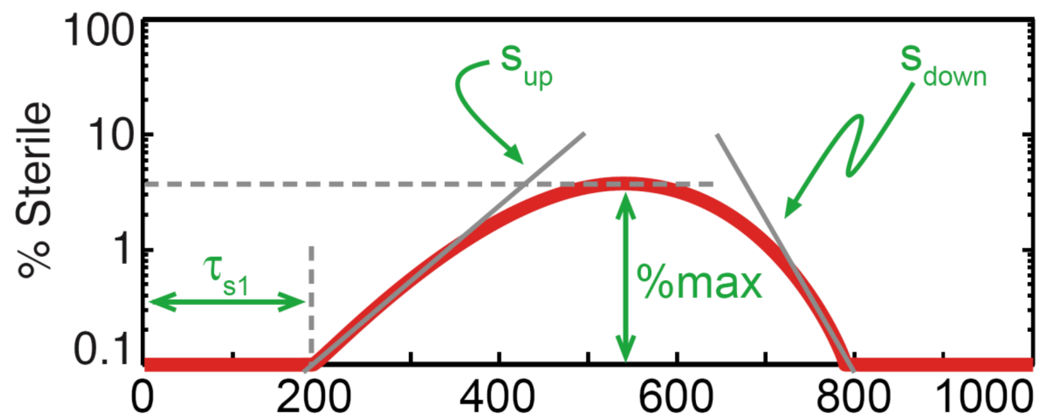
BYB

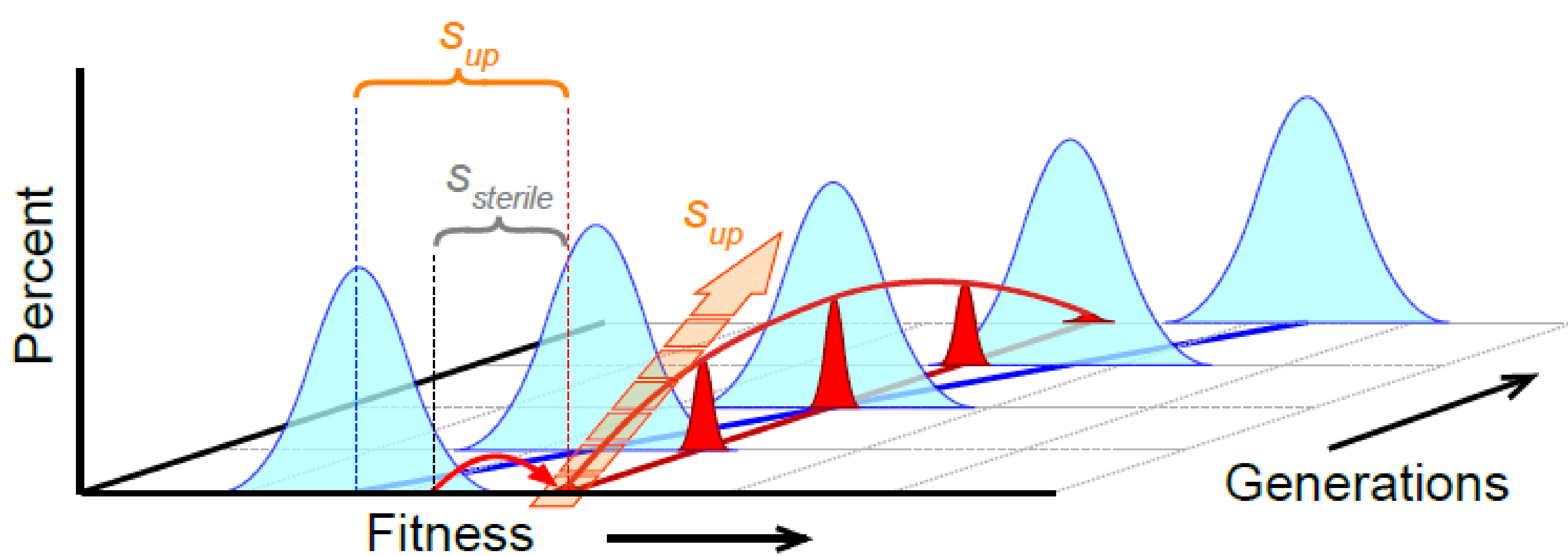
Distributions of Dynamics



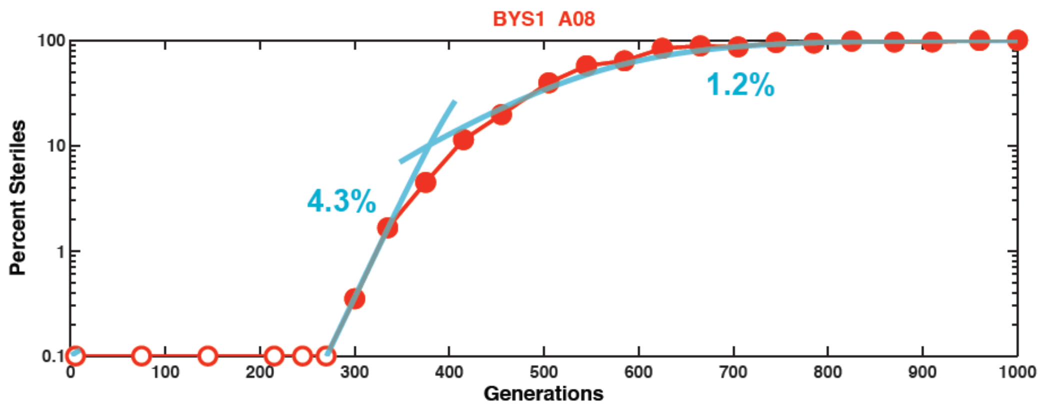


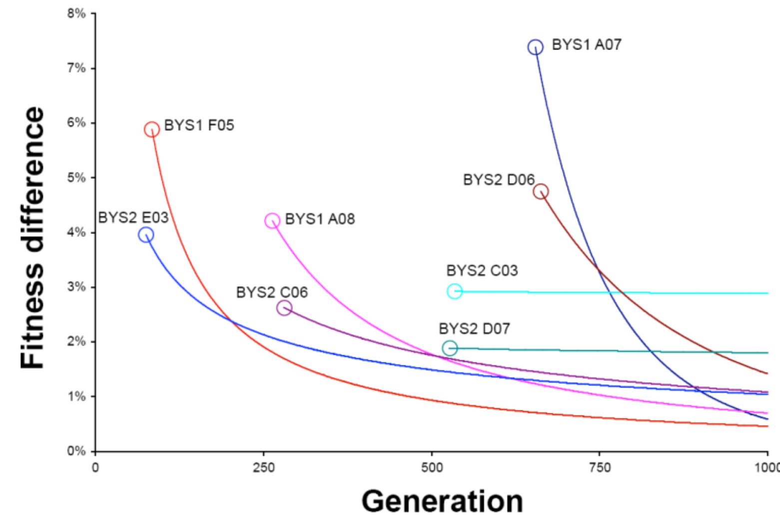
The Importance of Underlying Variation

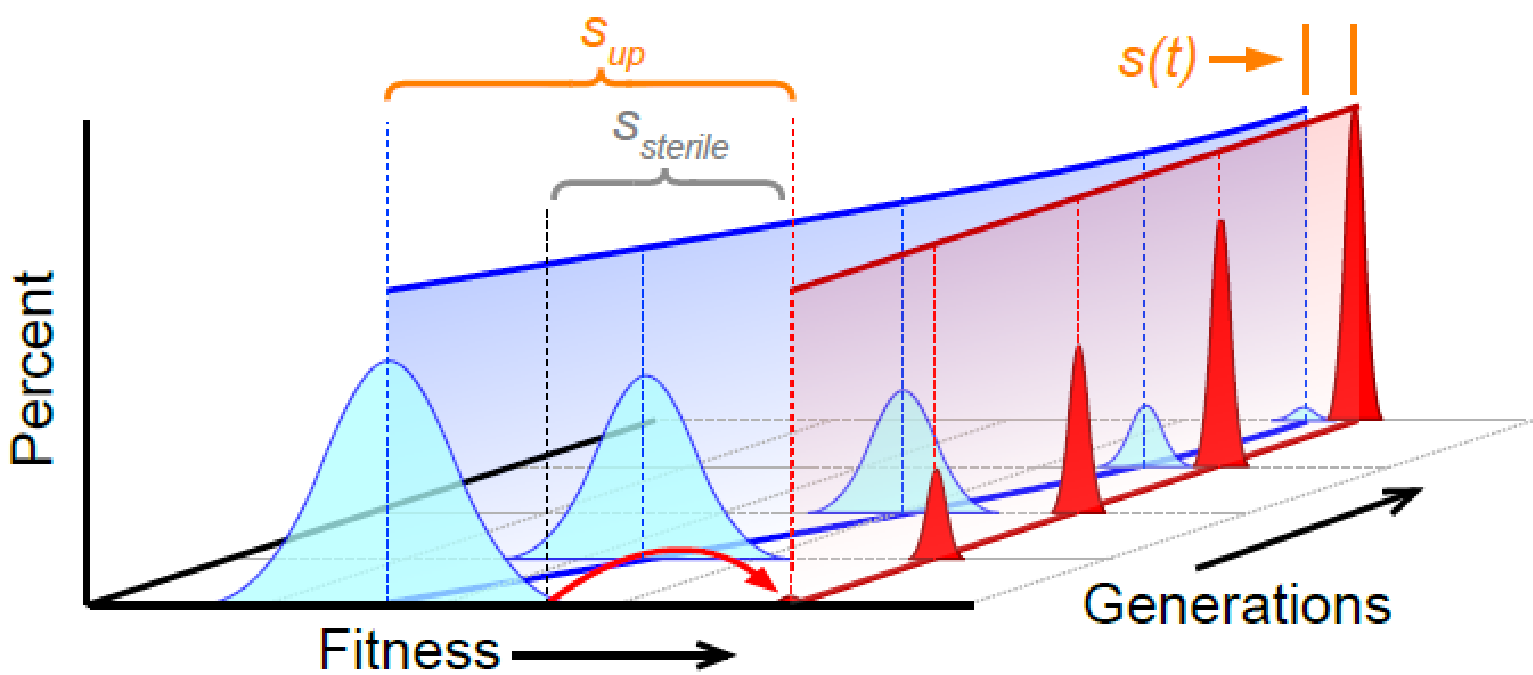




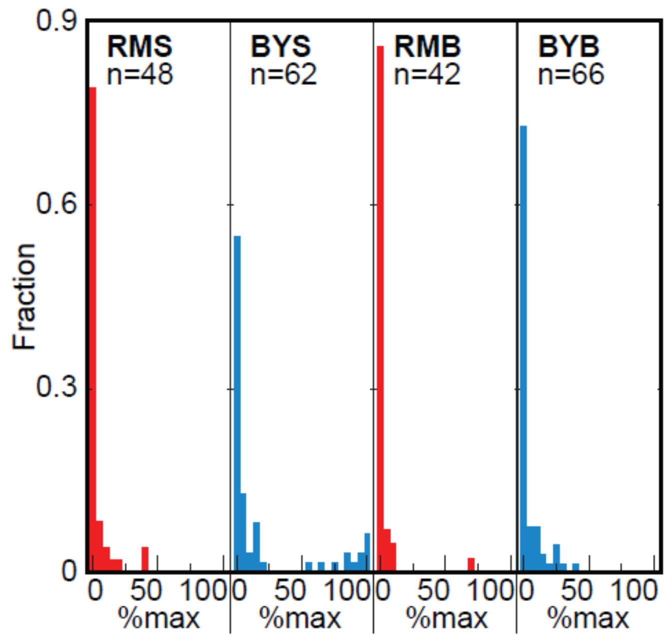
The Importance of Underlying Variation

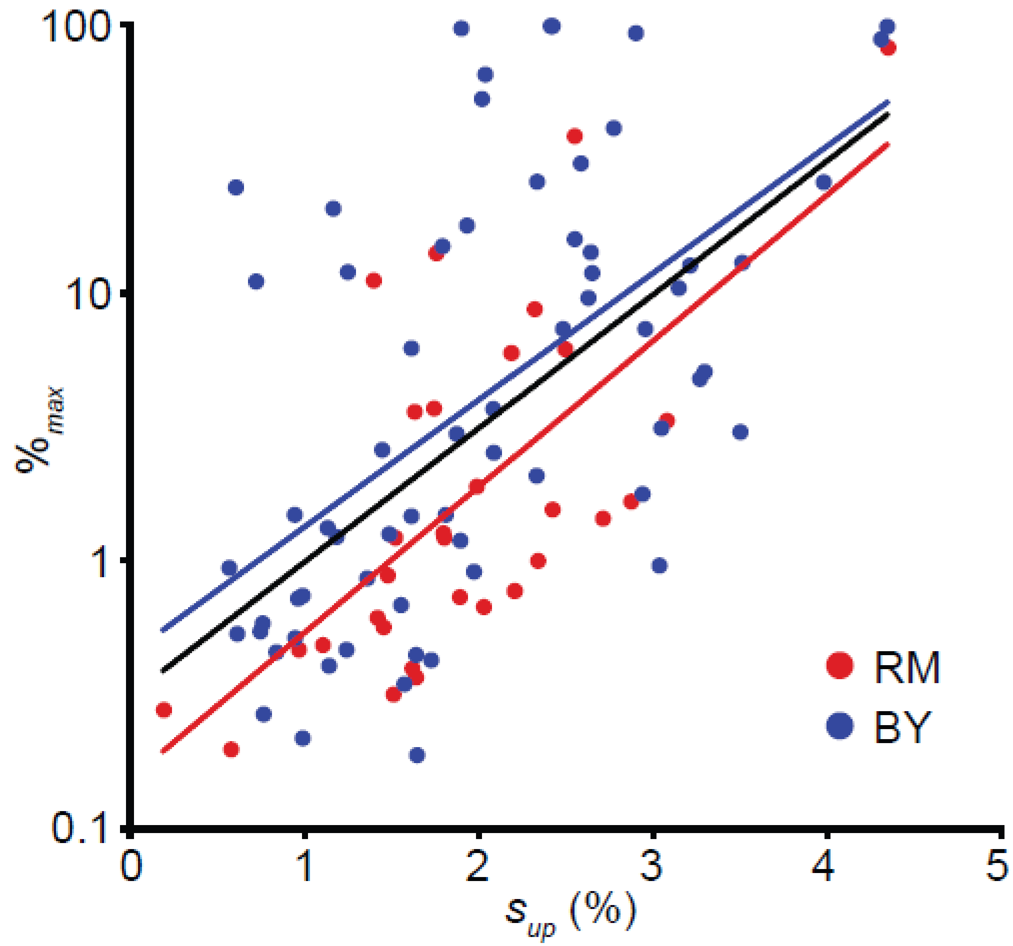




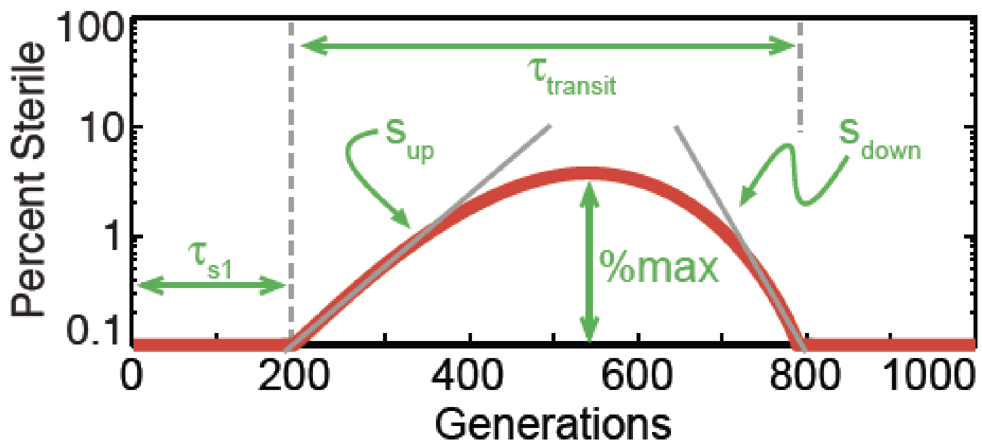


The best mutations are the luckiest



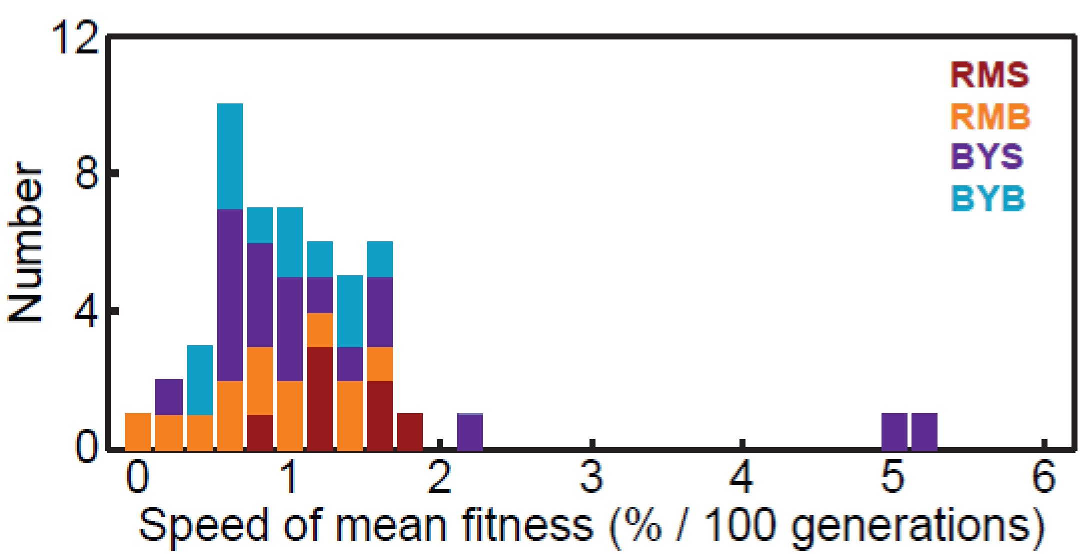


Rates of Fitness Increase

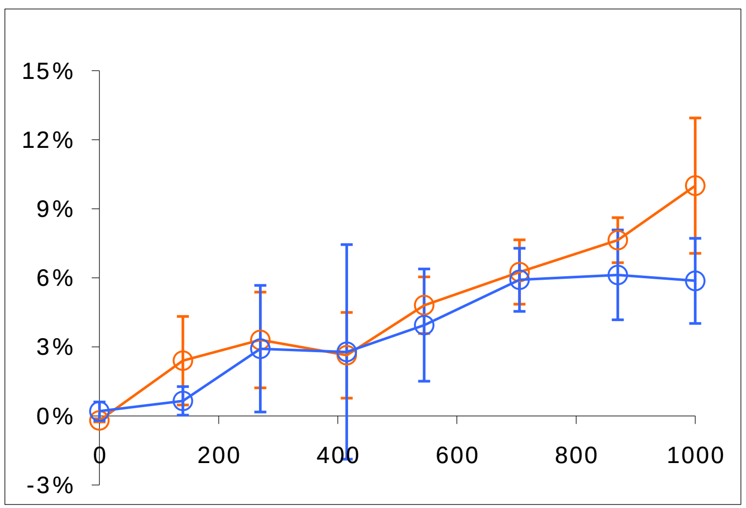


$\ln\left(\frac{\text{sterile}}{\text{nonsterile}}\right)$	$f(t)$	
Position of mean fitness	$\frac{d}{dt} f(t)$	s_{up} and s_{down}
Velocity of mean fitness	$\frac{d^2}{dt^2} f(t)$	$\frac{s_{up} + s_{down}}{\tau_{transit}}$
Acceleration of mean fitness	$\frac{d^3}{dt^3} f(t)$	$=0$ if $s_{up}=s_{down}$, $\neq 0$ if $s_{up} \neq s_{down}$

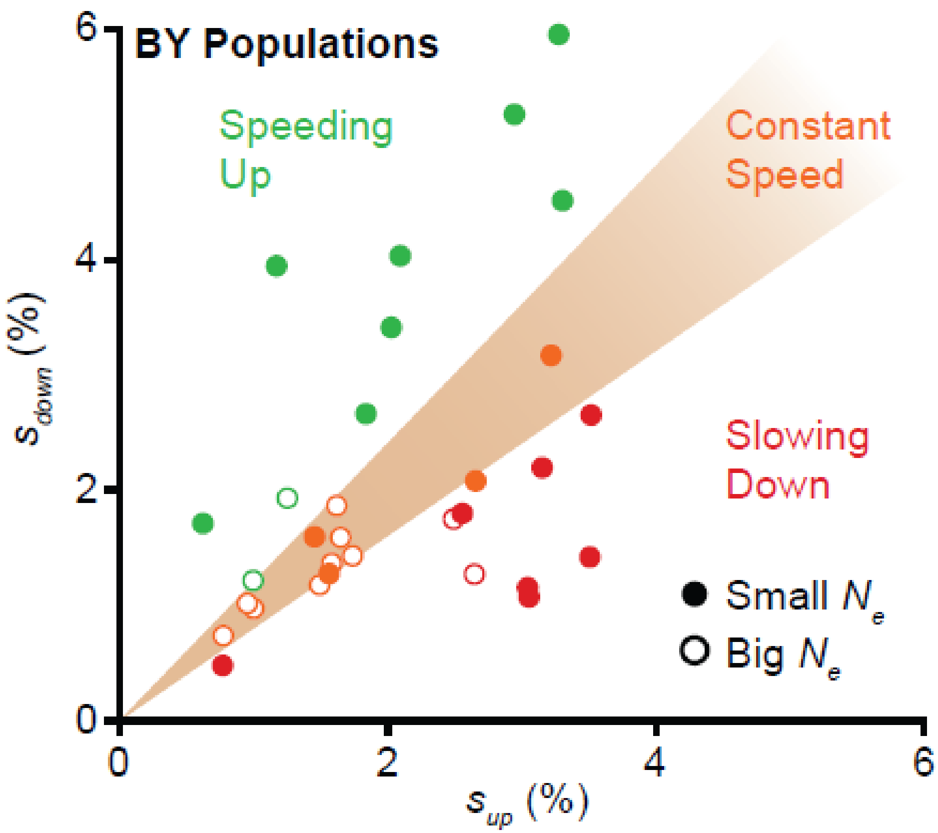
Inferred

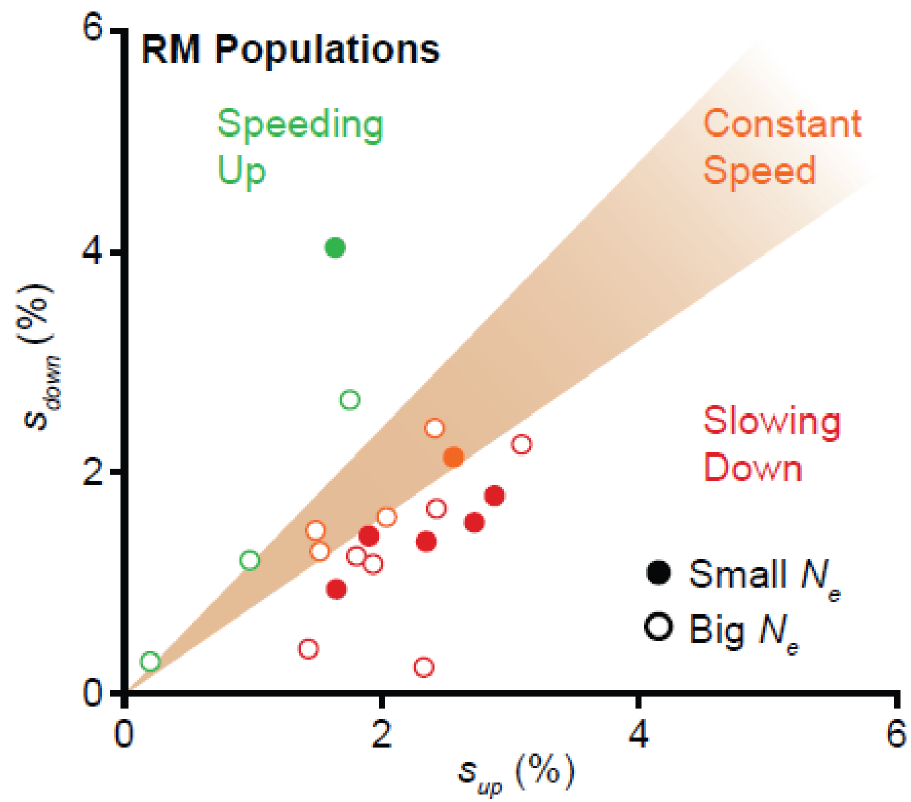


Measured

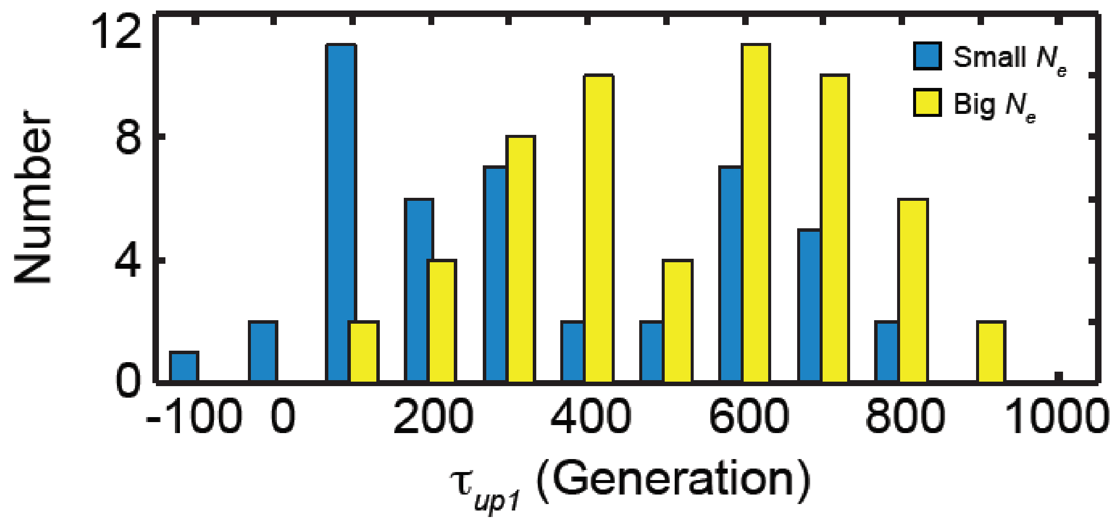


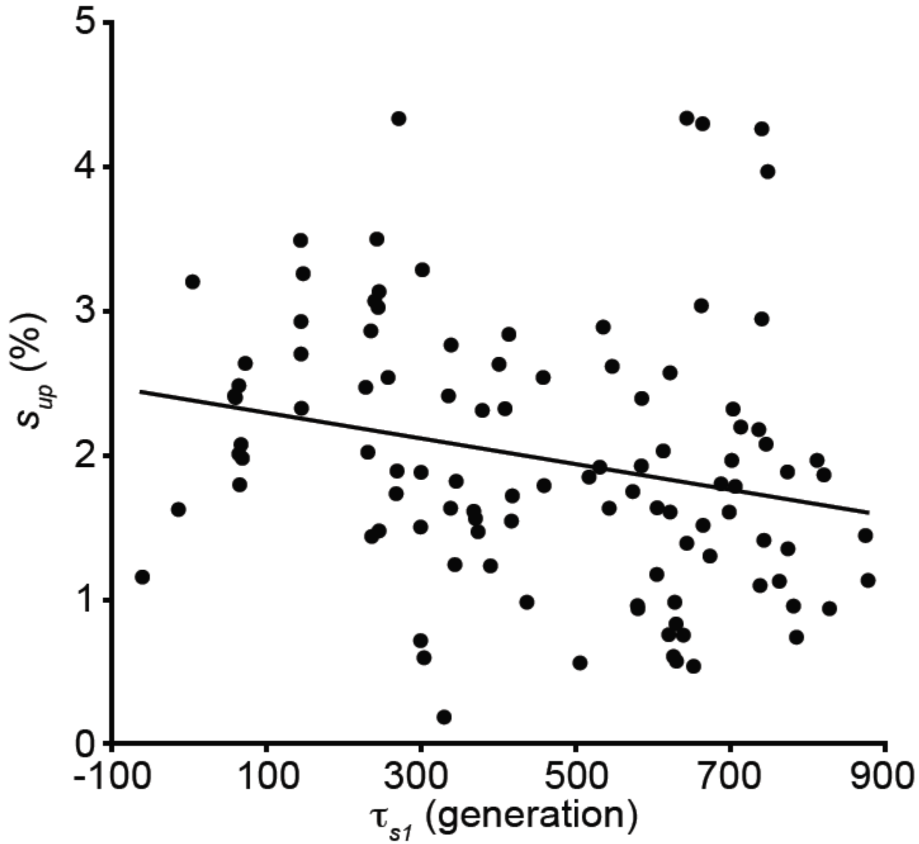
Periods of high and low variation?



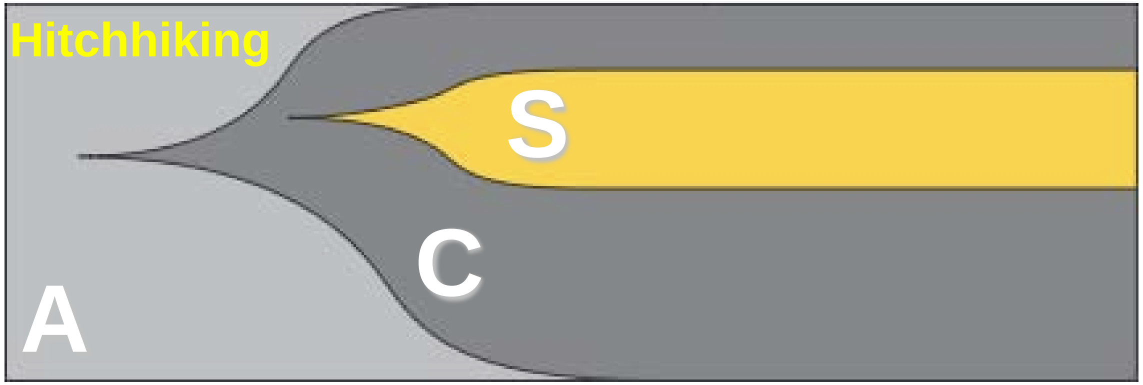


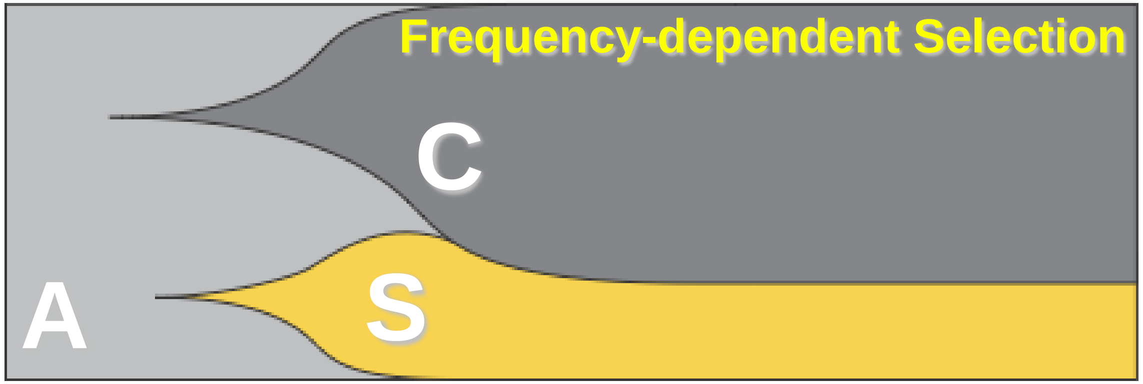
When did mutations occur?

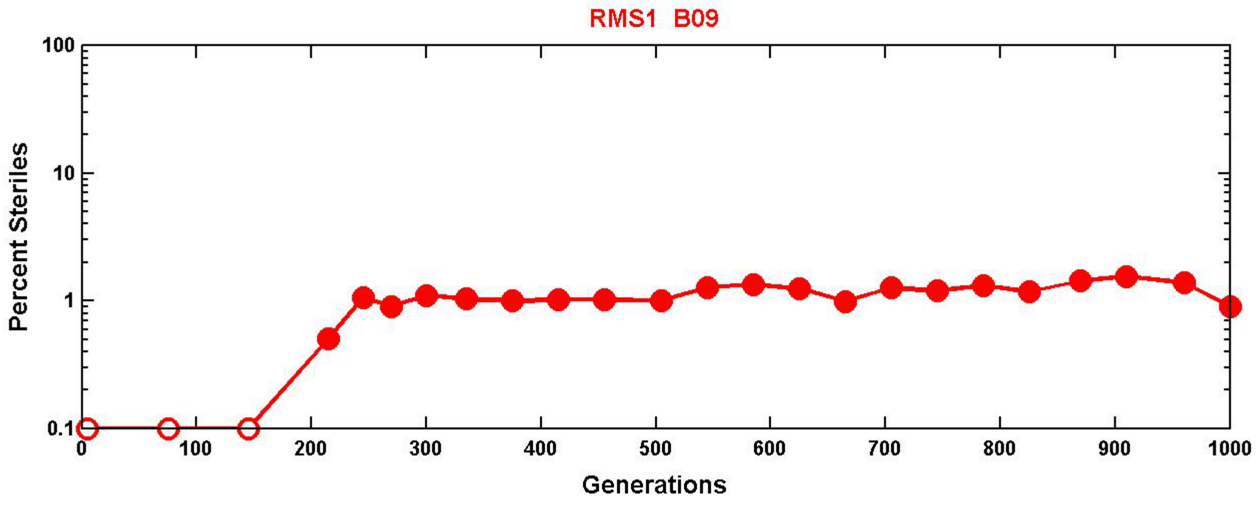




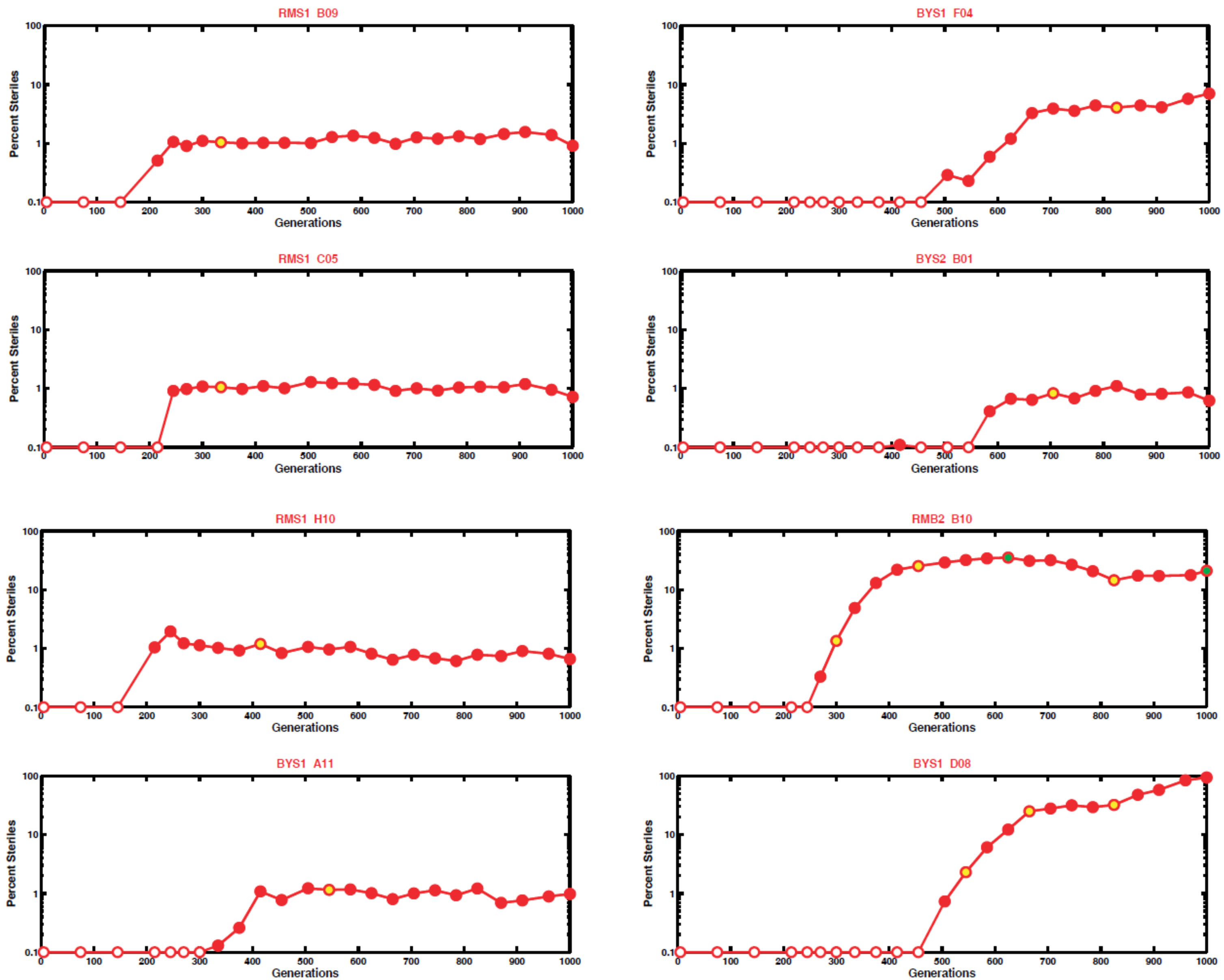
Steady Sterile Frequencies



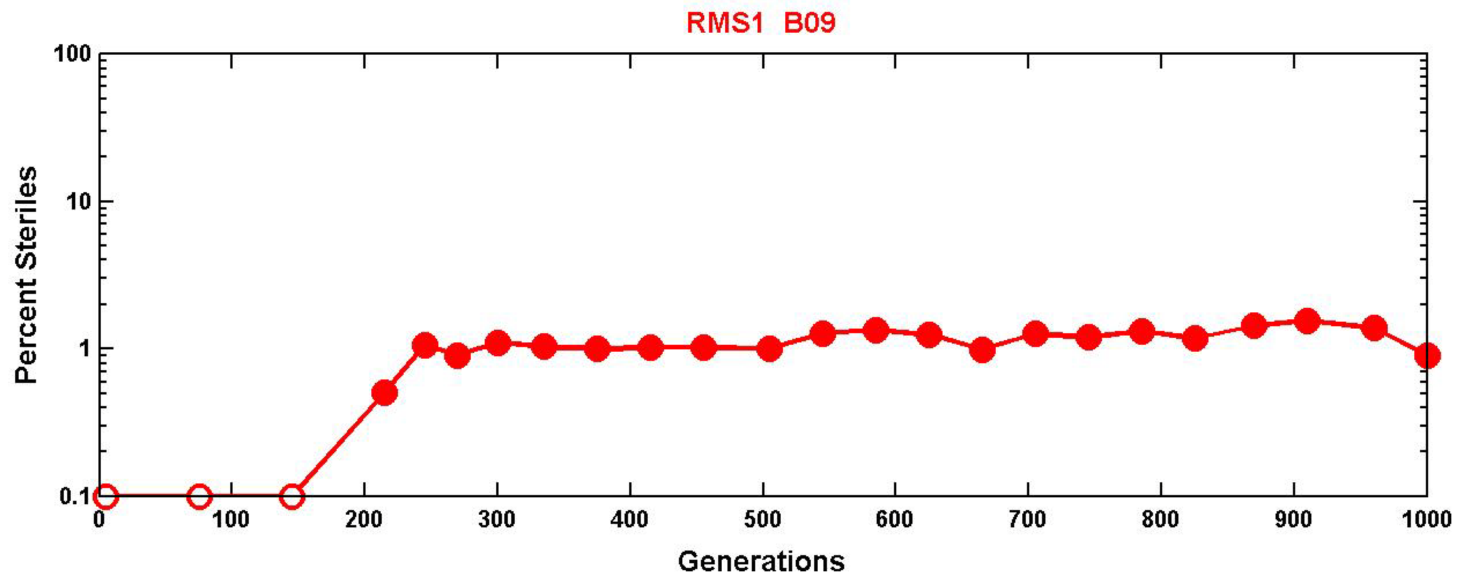


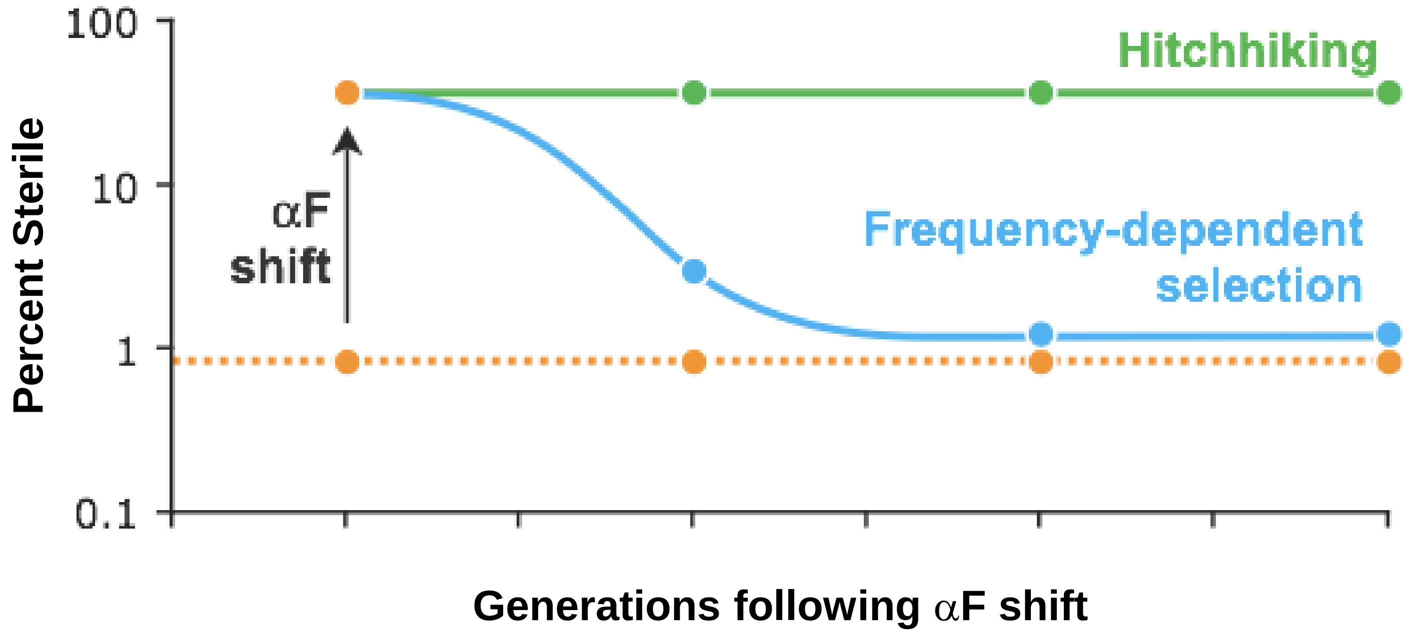


Steady Frequencies in ~2% of Cultures

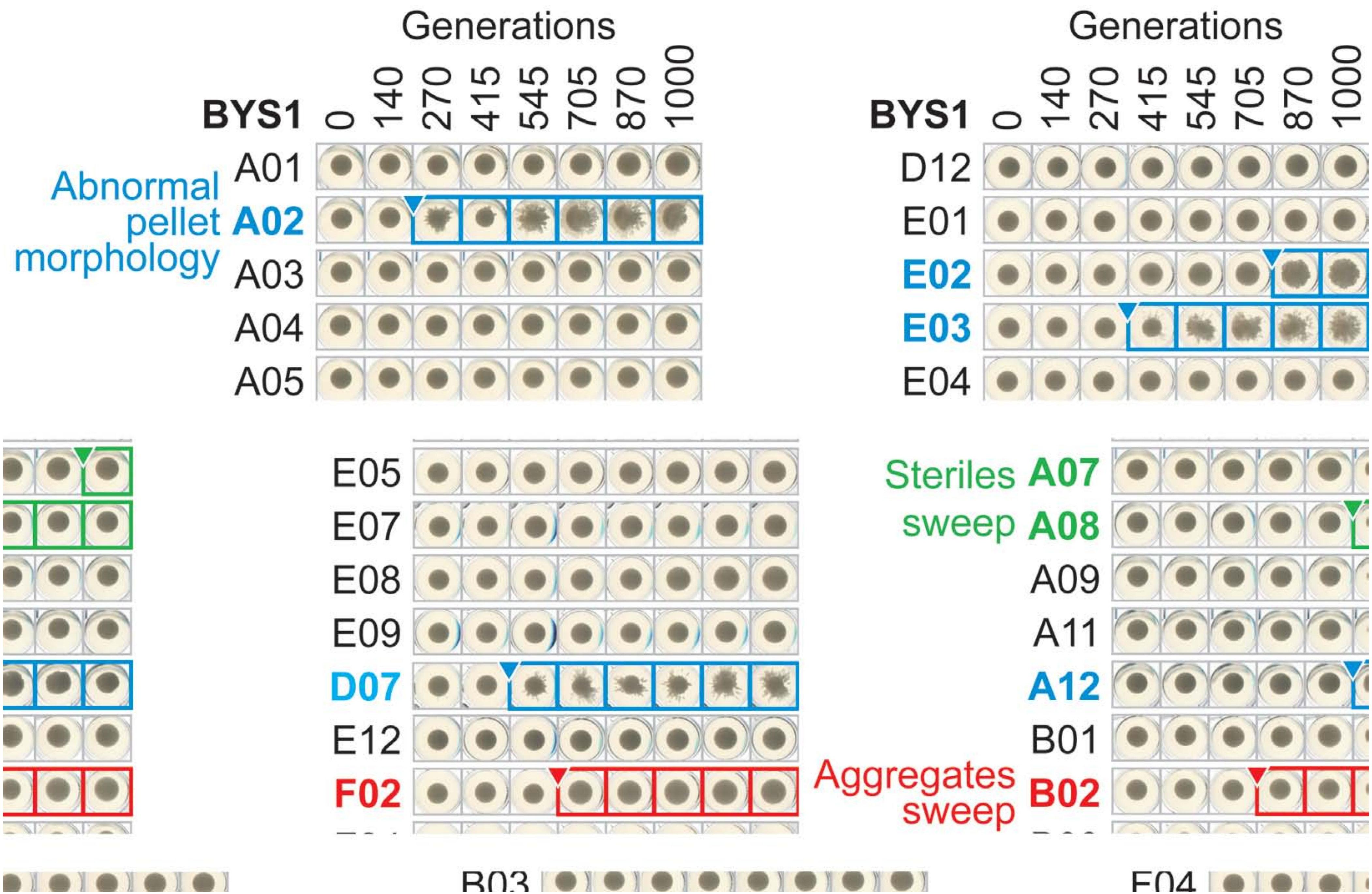


Decoding Steady Sterile Frequencies

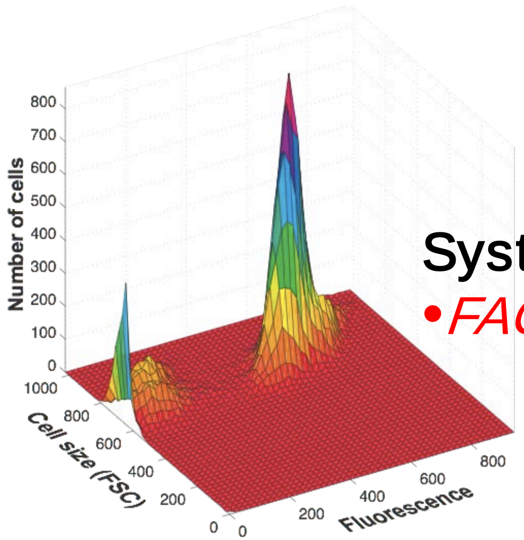




Other Observable Phenotypic Changes



Summary

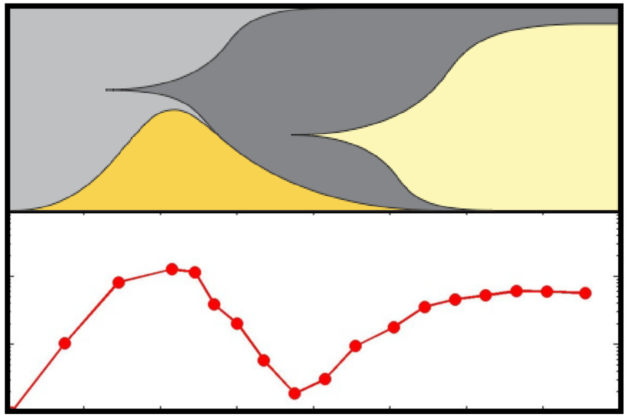


System for monitoring sterile mutants in a population

- *FACS-based method sensitive to low-frequency events*

Propagated ~600 cultures through 1000 generations

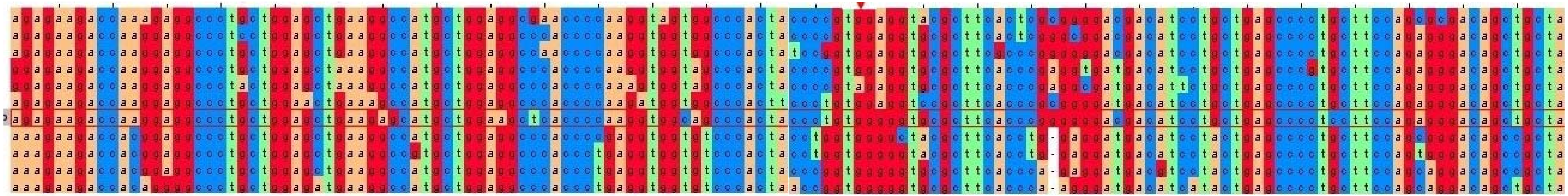
- *Followed the emergence and fate of sterile mutations*
- *Total of almost 600,000 population-generations*
- *Frequency-dependence and aggregates to be investigated*

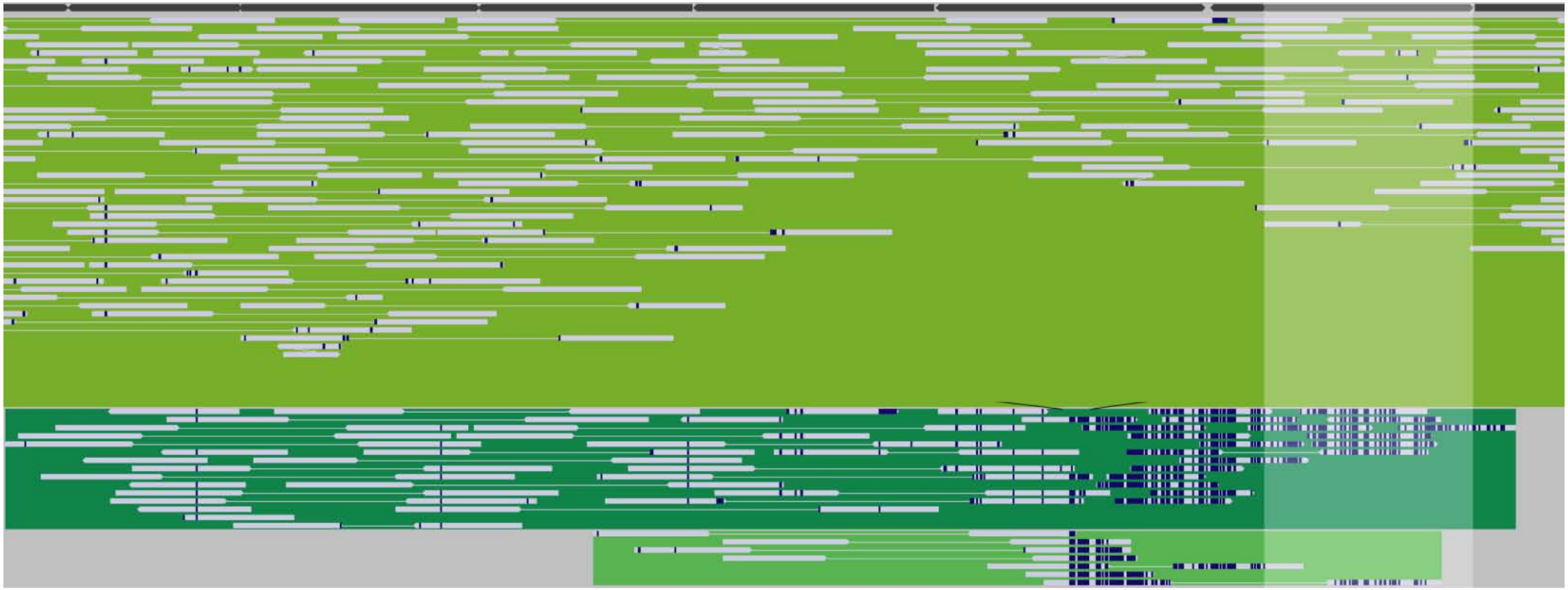


Visualized the dynamics of beneficial mutations

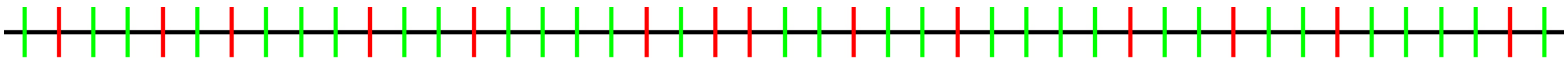
- *Infer the presence of competing mutations*
- *Information about the rate and fitness effects of beneficial mutations*

Selection and the Shape of Genetic Diversity





The simplest null model involving purifying selection



Neutral mutation rate U_n

Deleterious mutation rate U_d

Population size N

Selection strength s

What do we expect sequence data to look like?

What are we looking for?

Acknowledgements

Technical Help:
Tina DeCoste
Donna Storton
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Christian Daly
Claire Reardon

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Fei Li
Sebastian Akle

Theory:
Aleksandra Walczak
Joshua Plotkin
Lauren Nicolaisen
Daniel Fisher

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JSMF
Milton Fund
(Your ad here)