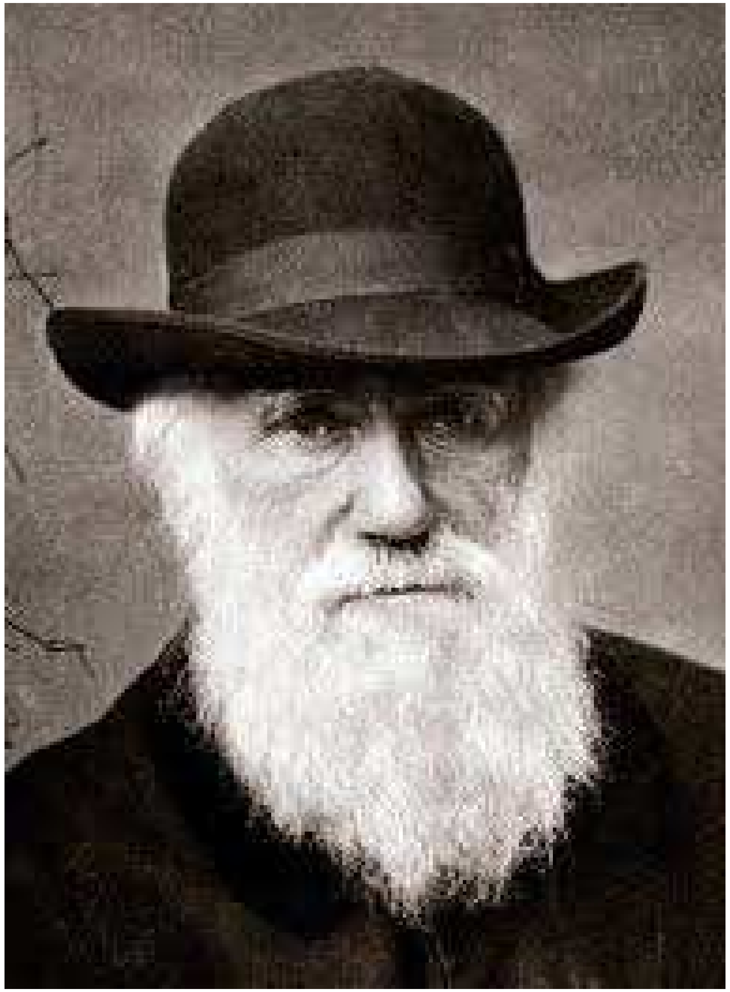
Adaptation in changing environments

Kavita Jain

J. Nehru Centre

Bangalore

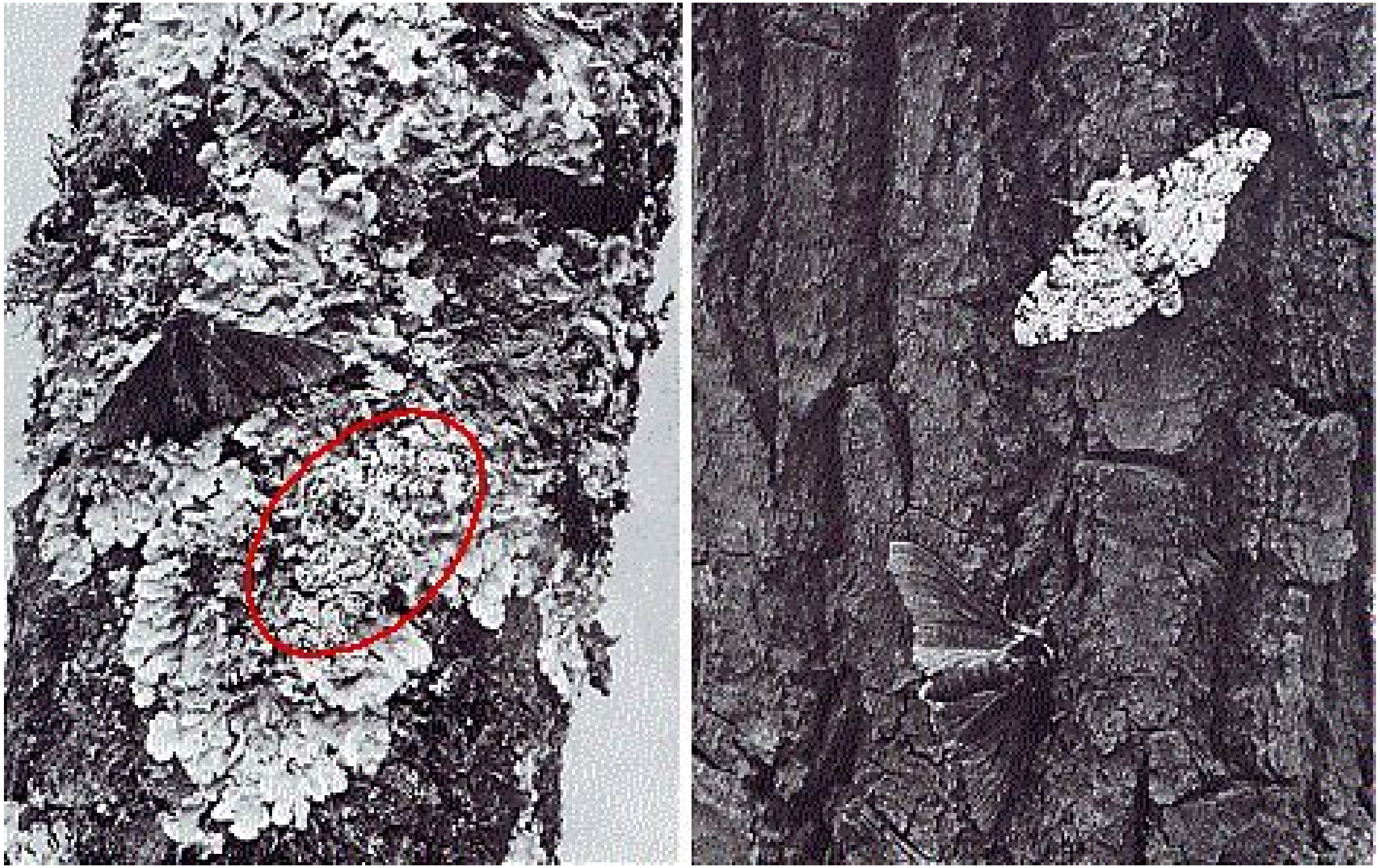
Glacial pace of evolution (Darwin 1859)



natural selection is ... scrutinizing ... the slightest [heritable] variations; rejecting that which is bad, preserving and adding up all that is good...

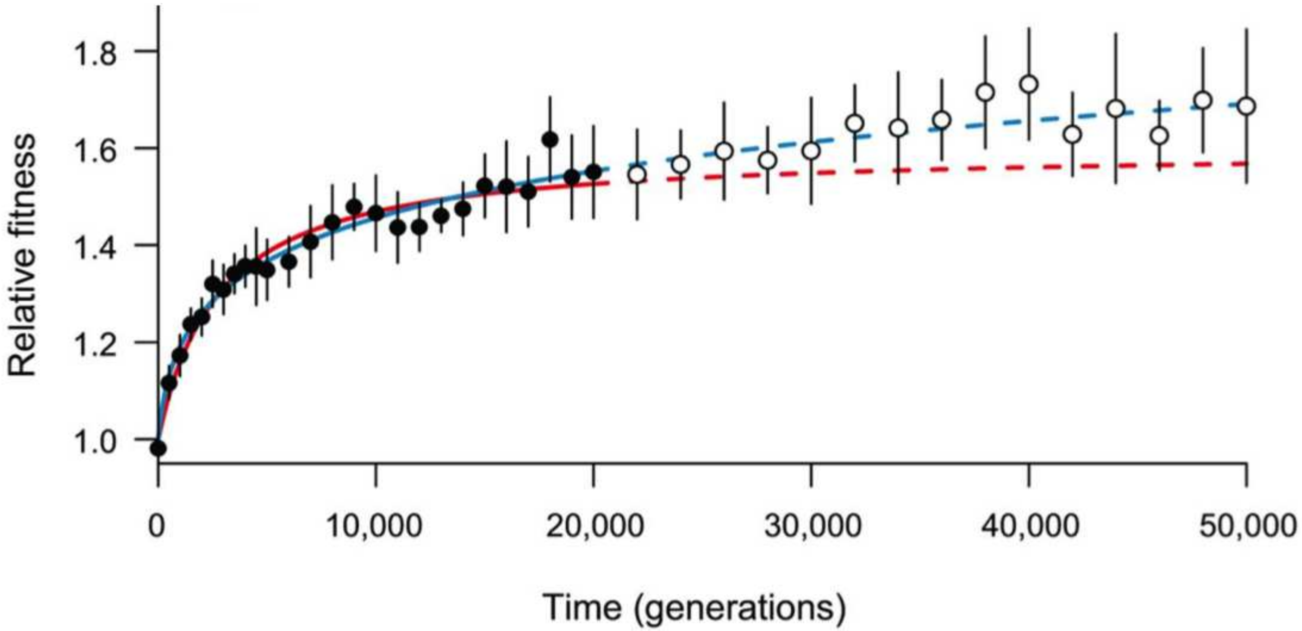
We see nothing of these slow changes in progress ... we only see that the forms of life are now different from what they formerly were.

The story of peppered moth (Kettlewell 1955; Cook & Saccheri 2013)



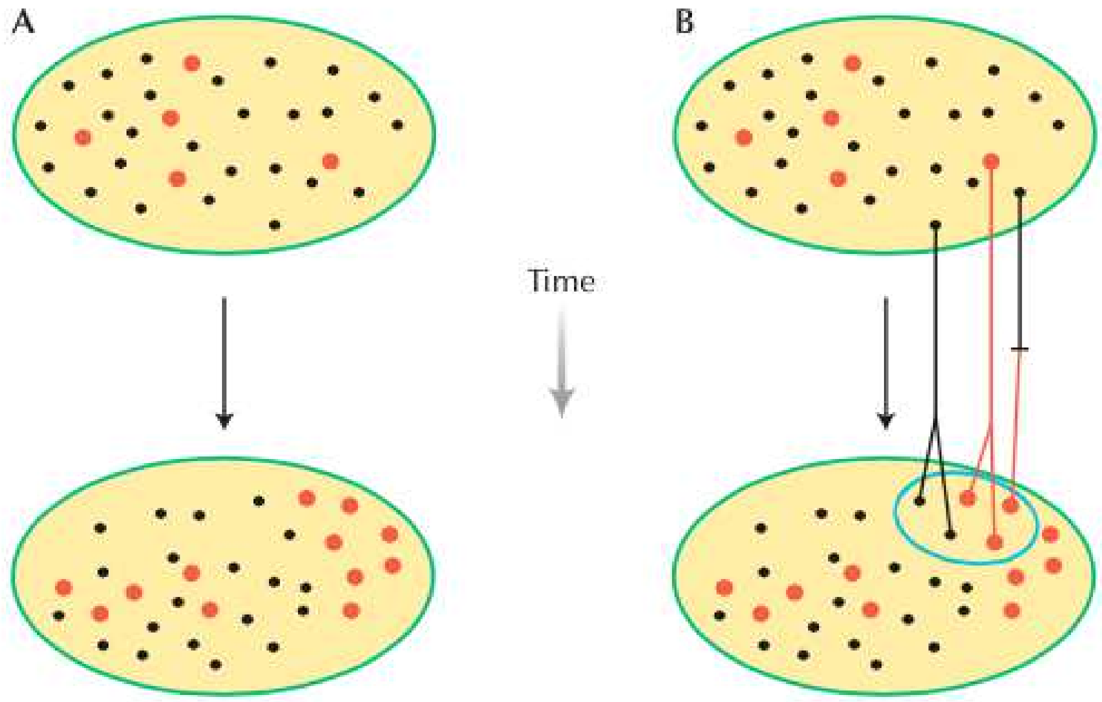
Rise and fall of the black-peppered moth in a span of 100 years

Long term microbial experiment (Lenski lab, 1988-)



Qualitative, verbal explanations → Quantitative modeling in evolution

Modeling in evolution



Predict the future

(classical pop gen)

Infer the past

(coalescent theory)

(*Evolution*, Barton et al.)

Basic evolutionary processes

- Natural selection
- Mutation
- Stochasticity (random genetic drift)
- Population structure (age-structured, spatially-structured, ...)

Due to interplay of these processes, how does allele frequency change?

Selection

- Suppose two variants (allele) of a gene: ○ and ●
- Simple model (Punnett/Norton 1915; Haldane 1924)

Allele	Fitness	Frequency
●	$1+s$	x
○	1	$1-x$

- Mutant can be beneficial ($s>0$), neutral ($s=0$), deleterious ($s<0$)
- Fitness can be measured in experiments, e.g., growth rate

(de Visser & Krug 2014; Fragata et al. 2019)

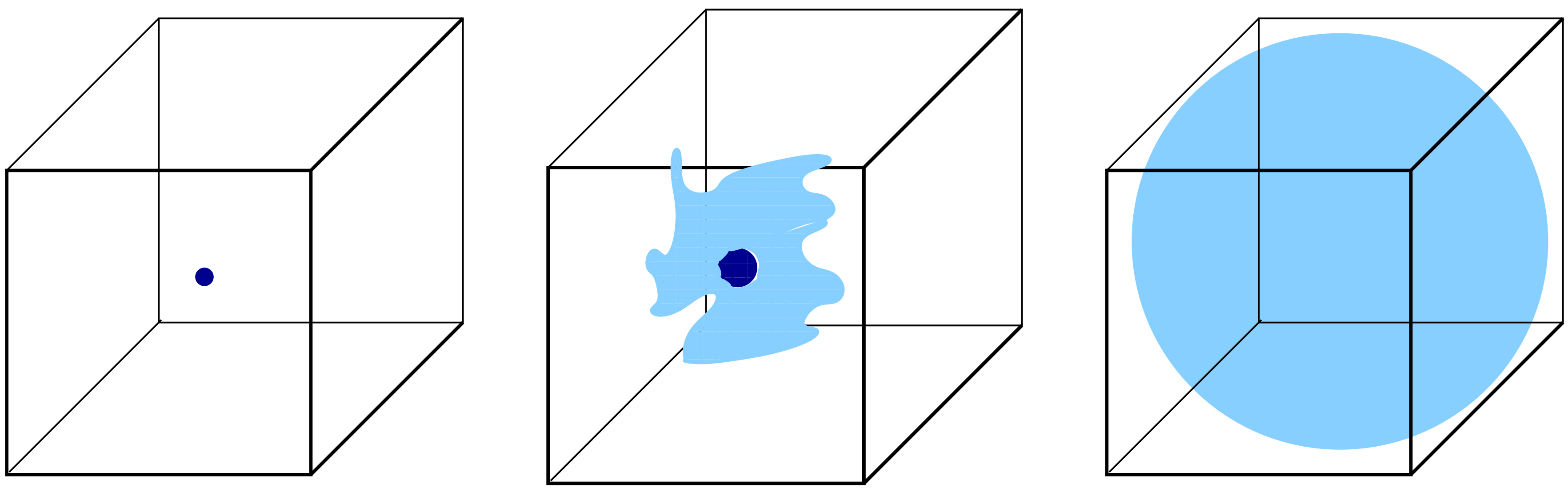
Mutation-selection balance

- Alleles can change: $\bullet \xrightarrow{\nu} \circ, \circ \xrightarrow{\mu} \bullet$

- Selection and mutation act in opposite manner

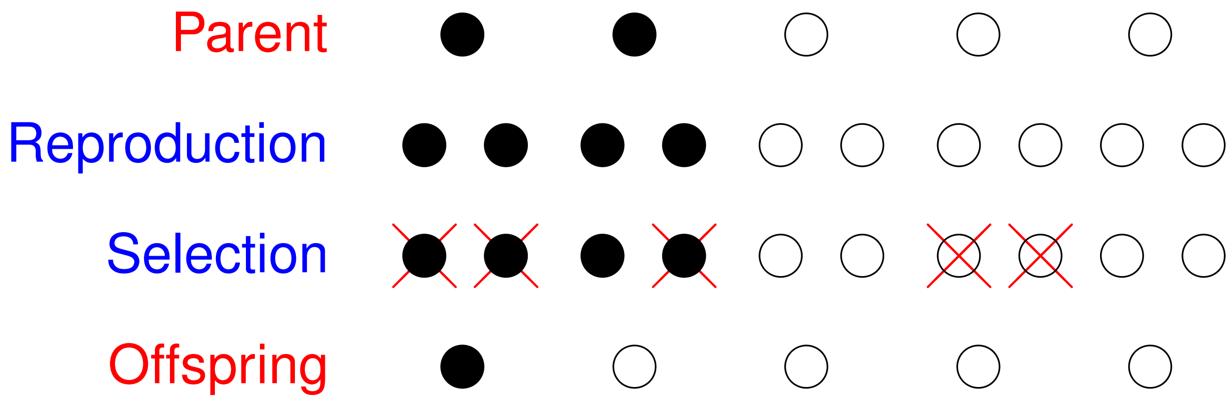
$\rightarrow$ Phase transitions can occur

(Eigen 1971; Peliti, Franz,... $\gtrsim$1995; review - Jain & Krug 2007)



Random genetic drift

Stochastic evolution because of finite resources (food...)

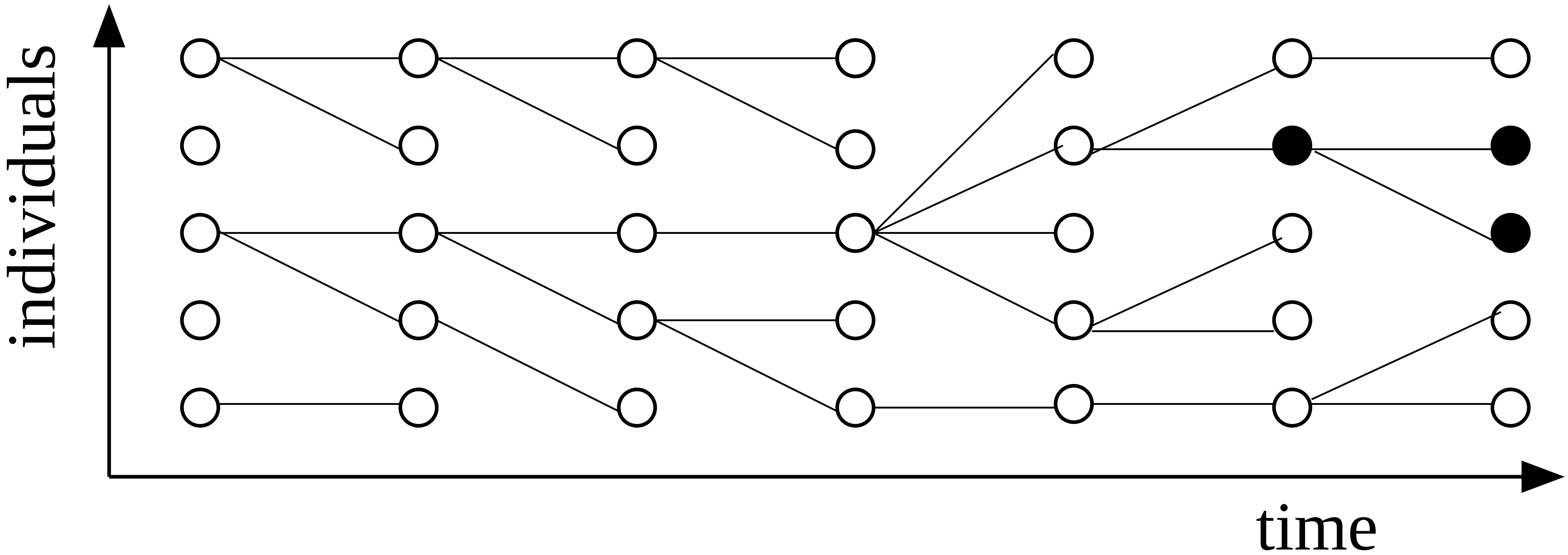


To maintain population size N, <u>sample</u> offspring with

$$\text{Prob} \propto \text{Fitness of parent}$$

“Ising model” of pop genetics: Wright-Fisher process

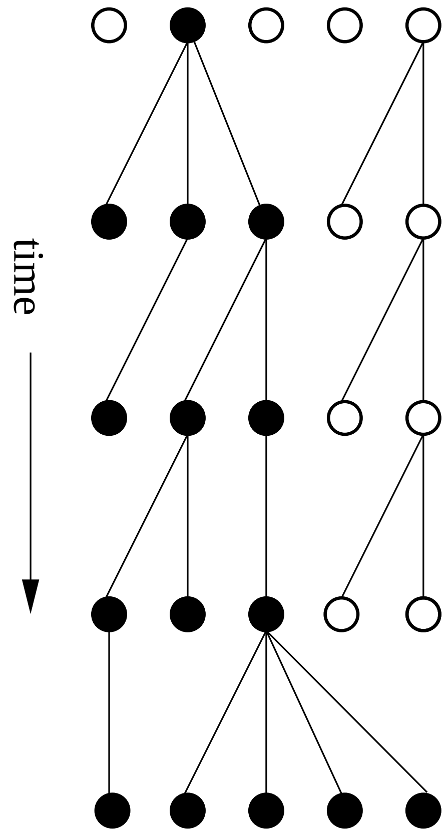
(Fisher 1922, Wright 1924)



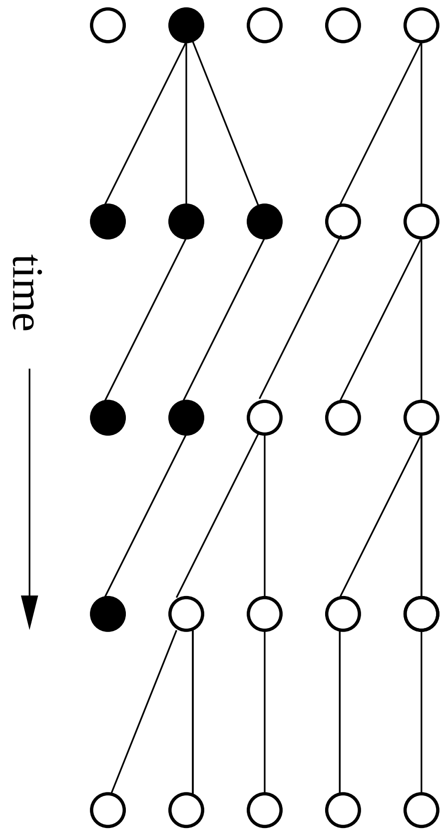
Rule: Choose a parent with prob $\propto$ parent’s fitness

First passage problem

Because mutation rates are low, ignore ● $\leftrightarrow$ ○ on time scales of interest

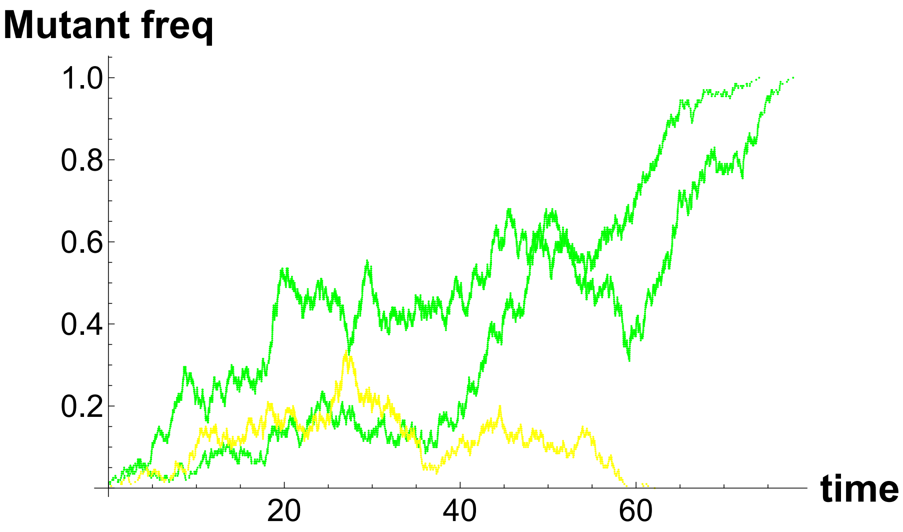


Mutant “fixes”

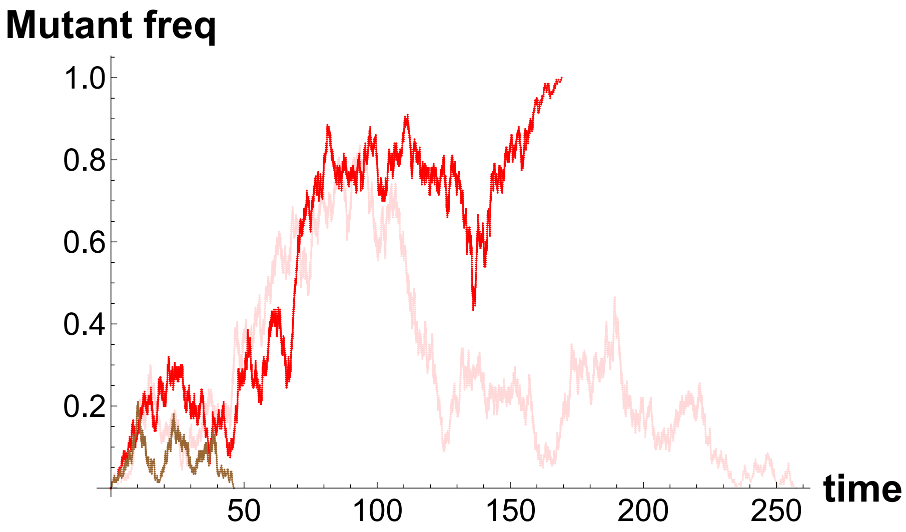


Mutant extinct

Stochastic trajectories in Wright-Fisher process



Beneficial mutant



Deleterious mutant

- Beneficial mutant can get lost
- Once reaches finite frequency, marches ahead

- Deleterious mutant can spread
- No such luck!

Basic questions

Today: Chance that an initially rare mutant spreads in the population?

(fixation probability)

How long does it take for the successful mutant to spread? (fixation time)

Put another way,

- Model with two absorbing boundaries
- First passage probability? First passage time?

Backward Fokker-Planck equation

- $P(x_0, 0|x, t) =$Prob(trajectories starting at x_0 terminate at a given x, t)

$$-\frac{\partial P}{\partial t_0} = D_1(x_0, t_0)\frac{\partial P}{\partial x_0} + D_2(x_0, t_0)\frac{\partial^2 P}{\partial x_0^2}$$

- For Wright-Fisher process with large populations and small selection,

$$-\frac{\partial P}{\partial t_0} = \underbrace{s(t_0)x_0(1-x_0)}_{\text{SELECTION}}\frac{\partial P}{\partial x_0} + \underbrace{\frac{x_0(1-x_0)}{N}}_{\text{GENETIC DRIFT}}\frac{\partial^2 P}{\partial x_0^2}$$

- Eventual probability of fixation, $P_{\text{fix}} \equiv P(x_0, t_0 | x = 1, t \to \infty)$

  - In constant environment, time-homogeneous Markov process

$$0 = s(t_0)x_0(1 - x_0)\frac{\partial P_{\text{fix}}}{\partial x_0} + \frac{x_0(1 - x_0)}{N}\frac{\partial^2 P_{\text{fix}}}{\partial x_0^2}$$

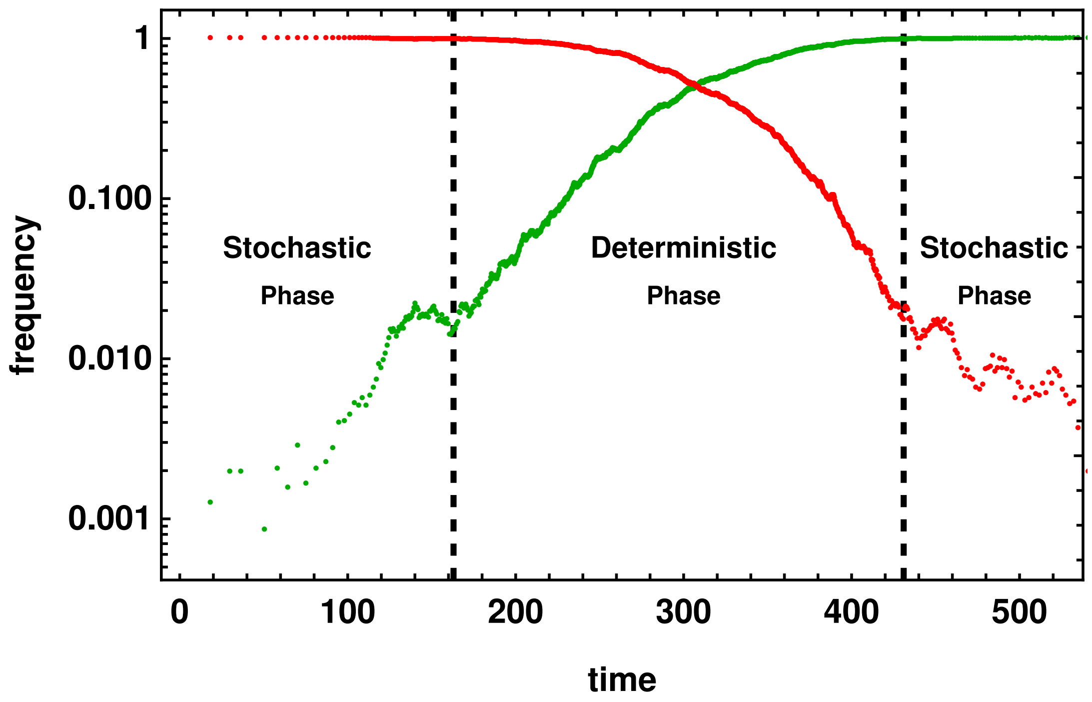
    Reduces to an ODE! (Kimura 1962)

  - In changing environment, <u>time-inhomogeneous</u> Markov process

$$-\frac{\partial P_{\text{fix}}}{\partial t_0} = s(t_0)x_0(1 - x_0)\frac{\partial P_{\text{fix}}}{\partial x_0} + \frac{x_0(1 - x_0)}{N}\frac{\partial^2 P_{\text{fix}}}{\partial x_0^2}$$

    Have to deal with a PDE

Semi-deterministic approx for beneficial mutant (Desai & Fisher 2007)



Stochastic fluctn imp when

mutant/wildtype number is low

Once the frequency is finite,

mutant unlikely to get lost

- Deal with stochastic phase using branching-type process where lineages evolve <u>independently</u>
- Splice the stochastic and deterministic solutions

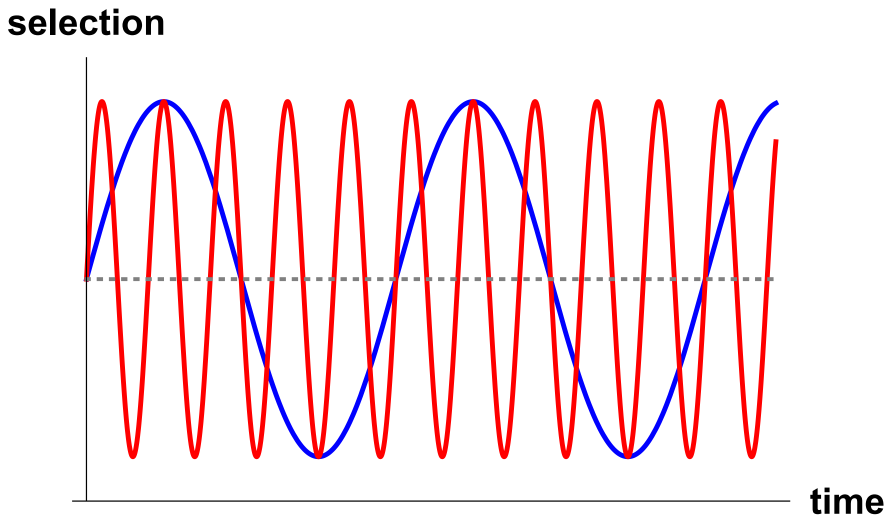
(Uecker & Hermisson 2011, Martin & Lambert 2015)

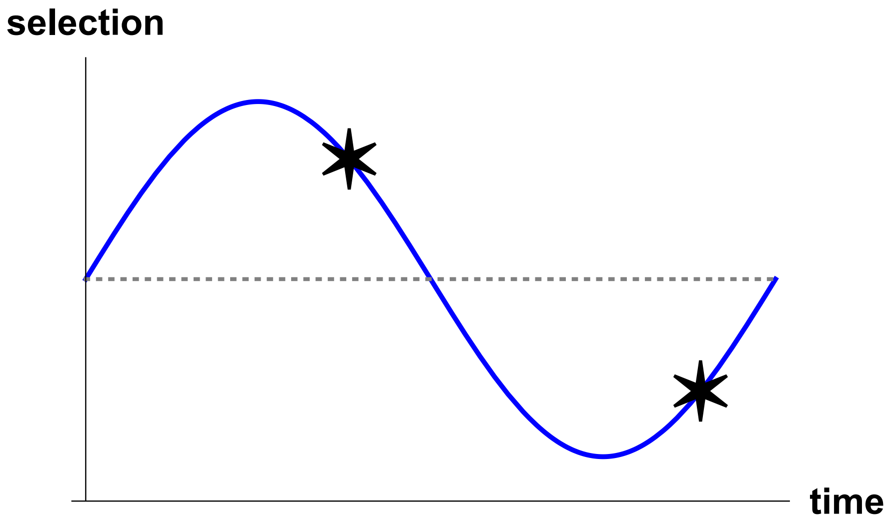
Specific model

Adaptation in periodically changing environment (Devi & Jain 2020)

Time-dependent growth rate due to seasonal cycle, drug cycling...

$$s(t) = \bar{s} + \sigma \sin(\omega t)$$

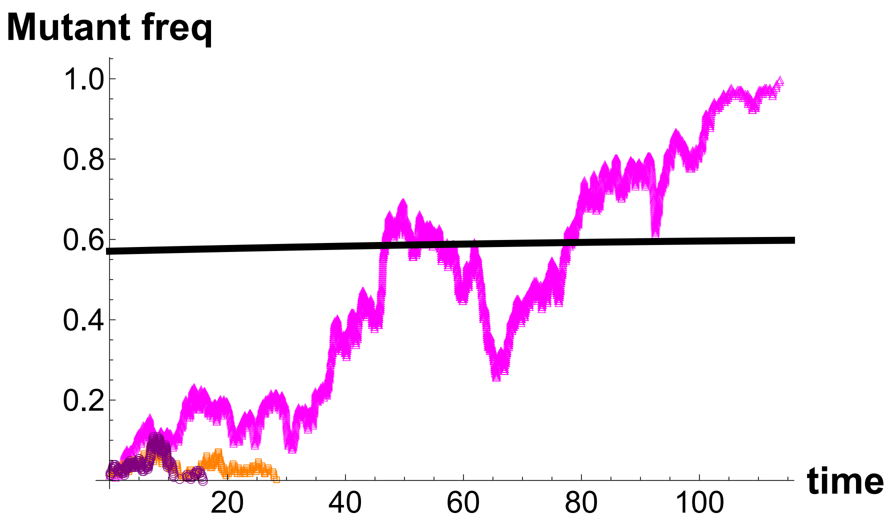


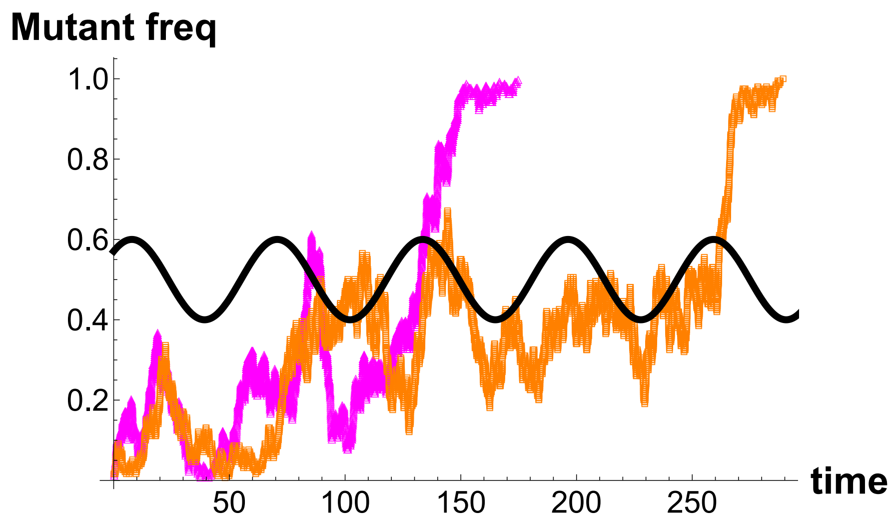


Effect of rate of environmental change (ω)?

Does time of arrival matter? (time-inhomogeneous equation)

Qualitative picture





$$T_{\text{env}} \gg T_{\text{fix}}$$

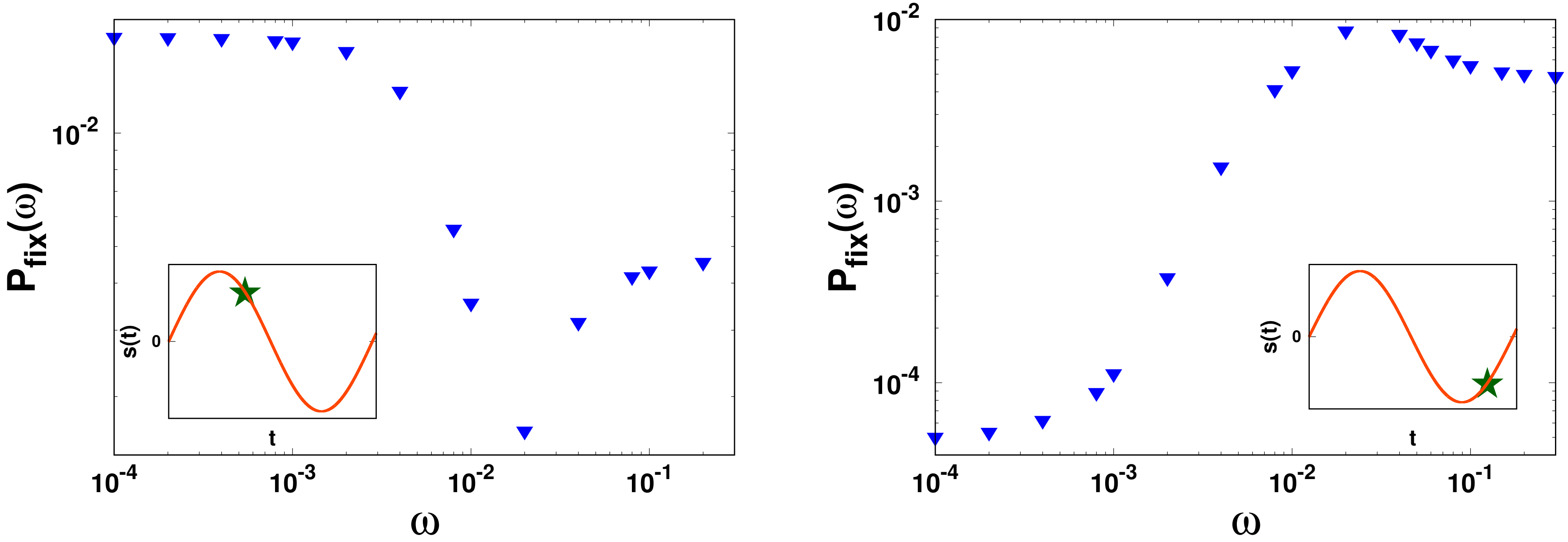
- Almost static environ
- Arrival time obviously imp

$$T_{\text{env}} \ll T_{\text{fix}}$$

- Sensitive to average environ
- Must survive at short times

$\longrightarrow$ Time-inhomogeneity is imp at all frequencies

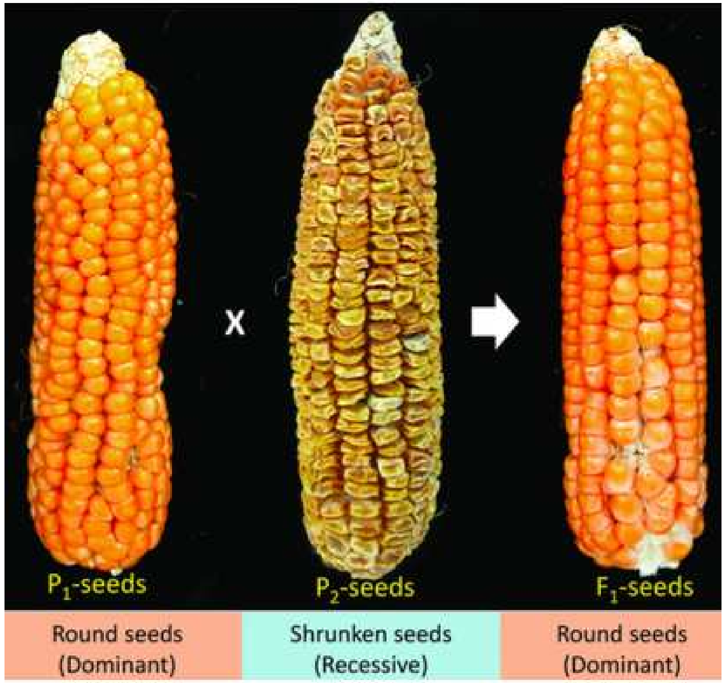
Fixation probability in changing environments



$$P_{\text{fix}} = \begin{cases} P_{\text{fix}}(\text{static}) + \omega \cos(\omega t_0) & , \ \omega \ll \omega_r \\ P_{\text{fix}}(\text{avg environ}) \left(1 + \frac{h\sigma \cos(\omega t_0)}{\omega}\right) & , \omega \gg \omega_r \end{cases}$$

where resonance frequency, ω_r is growth rate (or inverse pop size)

Impact of dominance (Mendel 1865)



(Hossain et al. 2019)

One type only: Dominant/Recessive

$$h = 1/0$$

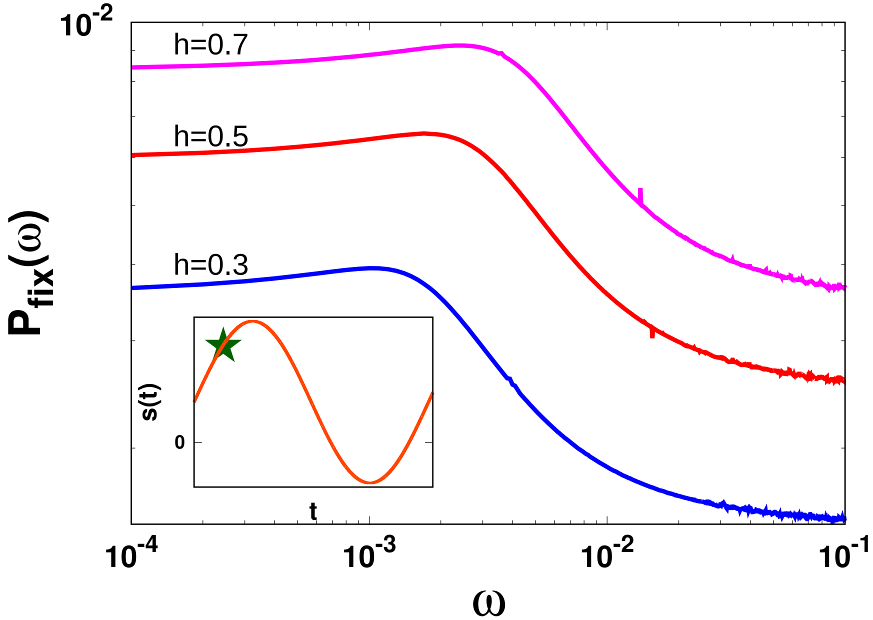
Both types: Intermediate dominance

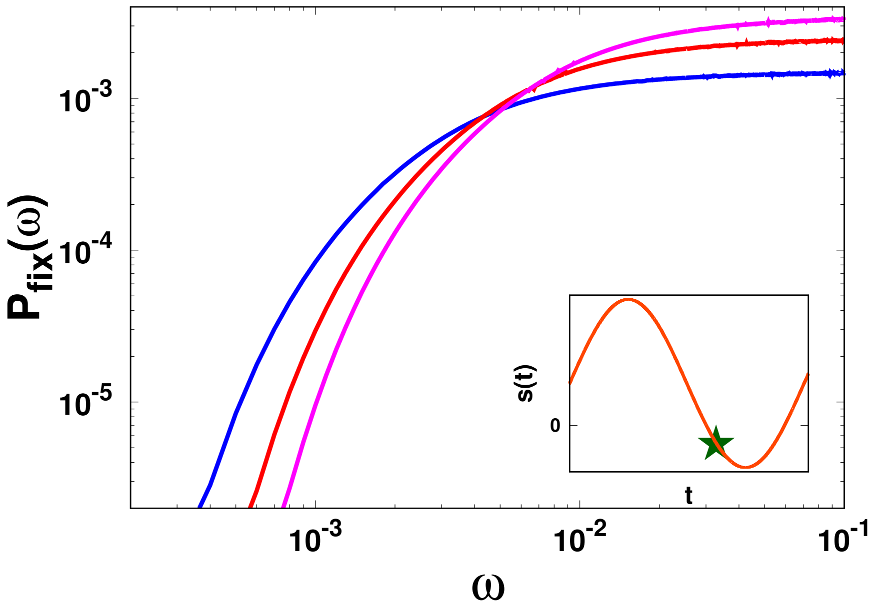
$$0 < h < 1$$

Haldane's sieve (Haldane 1927, Turner 1981)

Dominant beneficial mutants have higher fixation prob than recessives

$\longrightarrow$ infer direction of evolution (dominants are younger)





Haldane's sieve does not always operate in changing environments

(Devi & Jain 2020)

Summary

- Discussed a stochastic model of biological evolution
- In a periodically changing environment,
  - chances of survival can be substantially different from that in static environment
  - Haldane's sieve does not always operate
- Fixation time in changing environments? (Kaushik & Jain, in prep)