Genetic Diversity in Changing Environment

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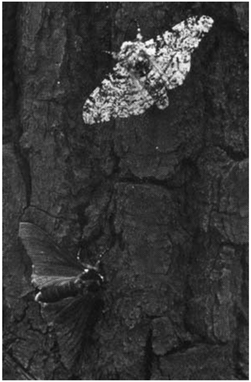
Why genetic diversity within population is important?

- Evolution requires diversity to act upon
- Loss of diversity increases the risk of extinction
- Potential for adaptation to the changing environment



(H.B.D Kettlewell, 1955)

What affects genetic diversity?

Increases Genetic variations:

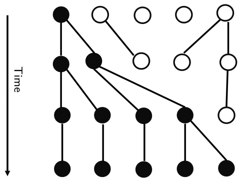
- Mutations : Random change in the DNA sequence
- Recombination : Mixing of the genetic material

Decreases Genetic variations :

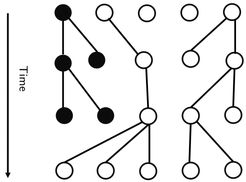
- Natural Selection : Better fit individual produces more offsprings
- Stochastic force : Sampling noise

Stochastic force

- Growth factor : ● $1 \pm s$ ○ 1
- Two absorbing states:



Mutant propagates

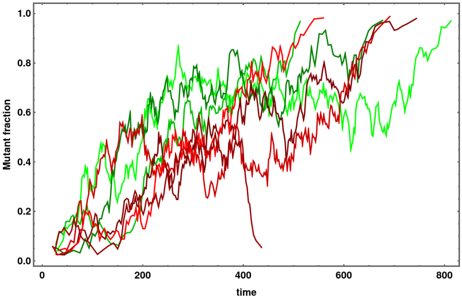


Mutant extincts eventually

- First passage probability?
- First passage time?

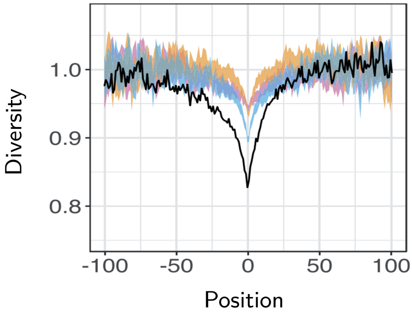
Static environment

- Beneficial and deleterious mutations have identical conditional mean first passage time (Maruyama & Kimura, 1974)
- $\bar{T}_c(s) = \bar{T}_c(-s)$
- Beneficial mutant $(1+s)$ hit boundary 1 sooner because of higher growth rate
- Deleterious mutant $(1-s)$ hit boundary 1 sooner to avoid extinction at late times



Reduction in genetic diversity

- Selective Sweep : Spread of a mutant in the entire population
- Similar diversity pattern are generated due to beneficial sweep and deleterious sweep(Johri et al. 2020)
- Can not distinguish between the two sweeps



Booker & Keightley, 2018

Motivation

- Natural environments are not static
- Examples: Global warming, less rainfall, shrinking of forest areas, seasonal change.
- Changing environment : $s(t)$ and $N(t)$
- Static environment vs slowly changing environment.
- Questions:

1. Effect of changing growth rate on the selective sweeps (Kaushik & Jain, 2021)

2. Joint effect of changing population size and changing growth rate on genetic diversity (Jain & Kaushik, 2022)

- In changing environment, time inhomogenous Markov process
- Probability distribution ($P(x, t|x_0, t_0)$) for a mutant obeys backward Fokker Planck equation:

$$-\frac{\partial P}{\partial t_0} = s(t_0)x_0(1-x_0)\frac{\partial P}{\partial x_0} + \frac{x_0(1-x_0)}{2N}\frac{\partial^2 P}{\partial {x_0}^2} \quad (1)$$

- Eventual first passage probability $P(x = 1, t \to \infty | x_0, t_0)$
- First passage probability is studied in detail for the changing environment. (Devi & Jain, 2020; Uecker & Hermisson, 2011)

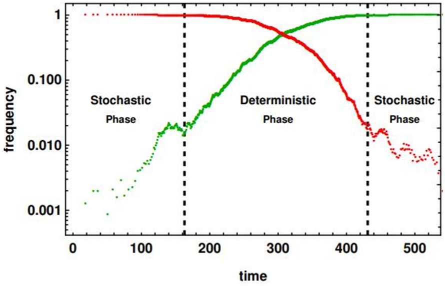
- Mean first passage time obeys time inhomogenous backward Fokker Planck equation:

$$-\frac{\partial \bar{T}}{\partial t_0} - P(x_0, t_0) = s(t_0)x_0(1-x_0)\frac{\partial \bar{T}}{\partial x_0} + \frac{x_0(1-x_0)}{2N}\frac{\partial^2 \bar{T}}{\partial {x_0}^2} \tag{2}$$

- Adiabatic approximation for slowly changing environment: $\bar{T} = \bar{T}_{static} + N\omega T_1$
- t_0 is the arrival time of the mutant and ω is environmental frequency

Method 2 : Semi Deterministic Approximation for Beneficial mutant

- Initially mutant evolves stochastically
- Fokker Planck equation is simplified to Feller equation ($x \to 0$)
- After escaping stochastic loss, mutant evolve deterministically
- First passage time distribution is obtained by matching the frequencies at the stochastic phase and deterministic phase boundaries

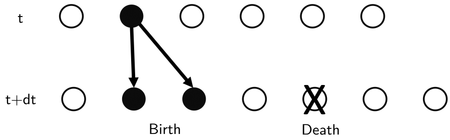


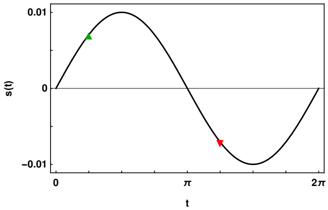
Martin & Lambert 2015

- Popuation with constant size N, growth rate varies periodically with time ($s(t)$)
- A mutant is chosen for reproduction with prob. $\propto (1 \pm s(t))$
- Another randomly chosen individual is killed
- Time dependent birth and death rates :

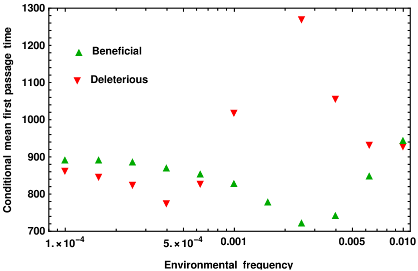
$$r_b(t) \propto (1 \pm s(t))\, i \left(1 - \frac{i}{N}\right)$$

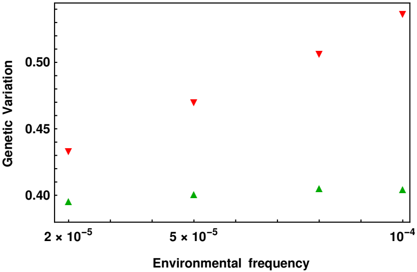
$$r_d(t) \propto (1) i \left(1 - \frac{i}{N}\right)$$





Results





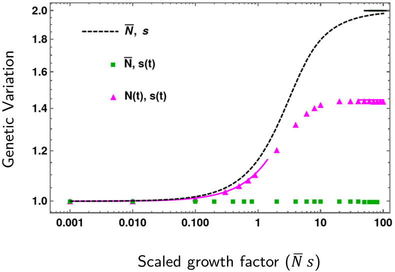
- No more Maruyama Kimura symmetry in changing environment $T_c(-s) \neq T_c(-s)$
- Deleterious sweeps are highly affected even in the slowly changing environment
- First passage probability : for deleterious and beneficial

$$(e^{-2N|s|}) \qquad\qquad (2s)$$

- Genetic variation can increase/decrease depending on the time of arrival of the mutant

Changing population size & Recurrent mutations

- On average neutral growth rate
- Population size changes periodically
- Recurrent mutations (arrival times of mutations are arbitrary)
- Multiple independent Birth Death processes
- Different diversity patterns even in the slowly changing environment compared to the static environment



Summary

- Maruyama Kimura symmetry is not preserved in changing environment
- Constant environment assumption is good for beneficial mutations
- Changing environment affects deleterious mutations strongly
- Even slowly changing environment can produce qualitatively different genetic diversity patterns
- Deleterious mutations are unlikely to spread, what happens when they get eliminated? (work in progress)