Evolution under Delayed Selection Pressures

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Motivation

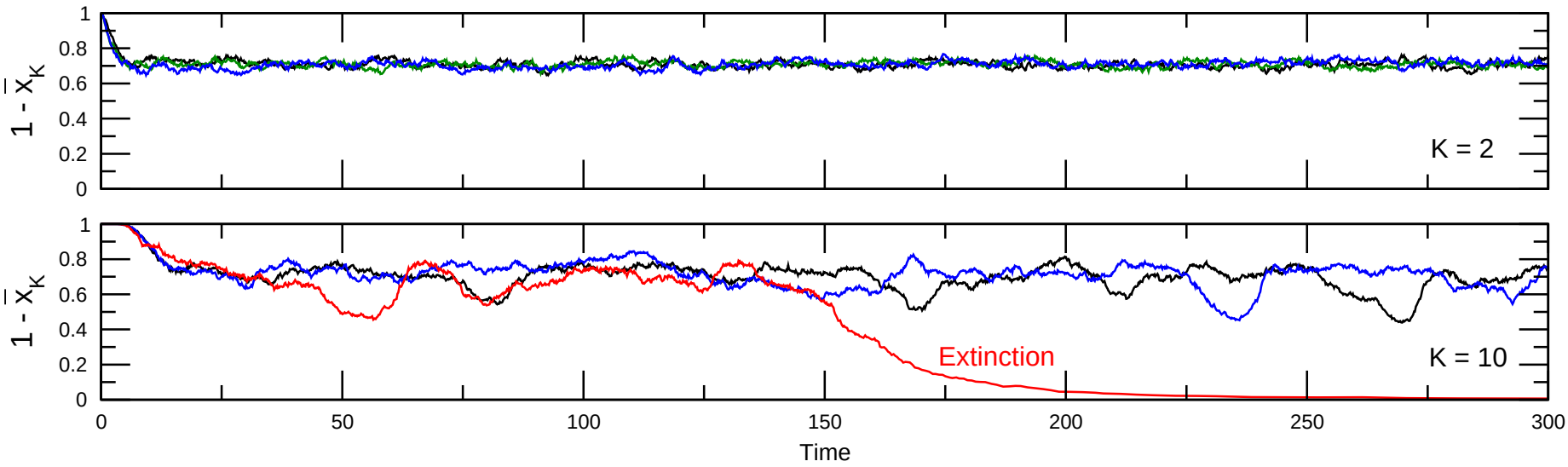
- Mice deficient for telomerase RNA (mTR-/-) are fertile and show initially little if any pathologies.
  However, they can breed only for about 6 generations, until their telomers are used up
- Monarch butterfly (*Danaus plexippus*):
  Migratory generation travels from the North East of the US to Mexico and overwinters.
  In the next year, several short-lived generations migrate back north
  Gene expression studies show massive difference between the generations

What happens is part of the genetic system is only sometime under stabilizing selection?

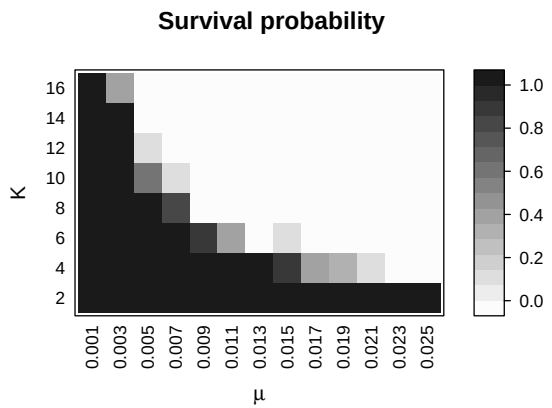
Simulation Model

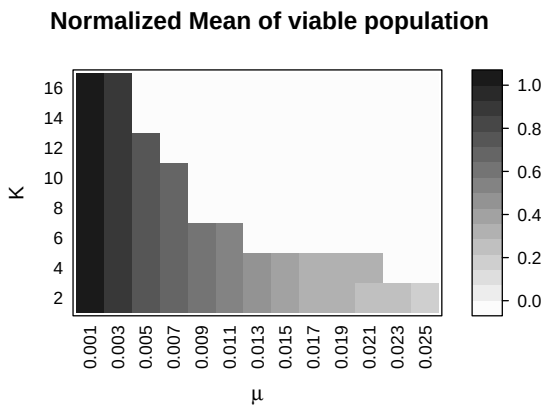
- Haploid population of N individual of chain length L.
- implemented as RNA sequences which have to fold into a target structure.
- correctly folded sequences have fitness 1 and full-length telomers
- incorrectly folded sequences have fitness 1 als long as their telomers have positive length. When these replicate, telemers are shortened by $1/K$.
- “damaged” lineages become infertile after K generations.

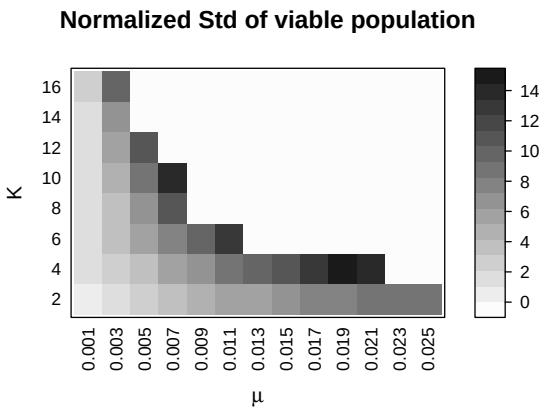
Stricter Error Threshold



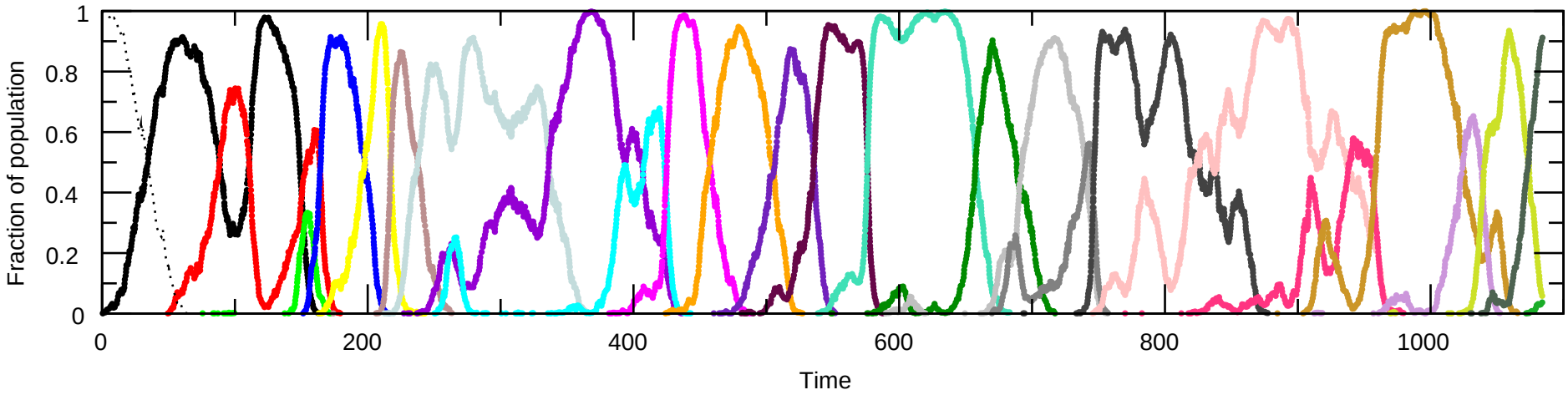
a



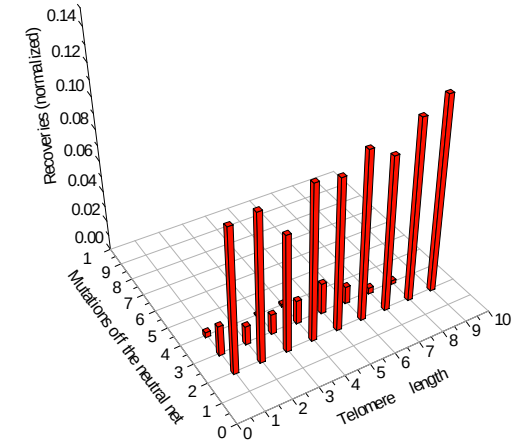


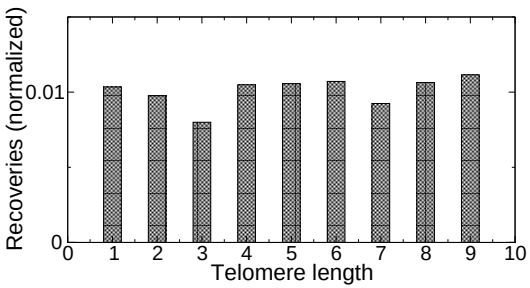


Damage and Repair

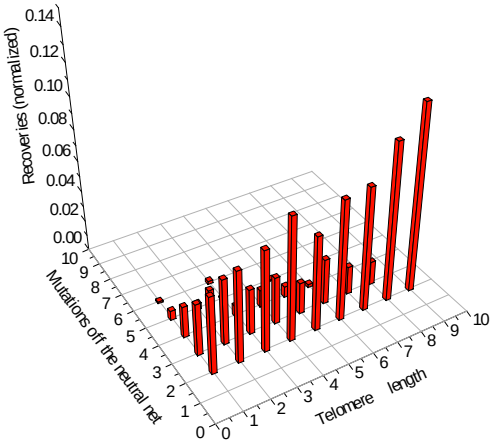


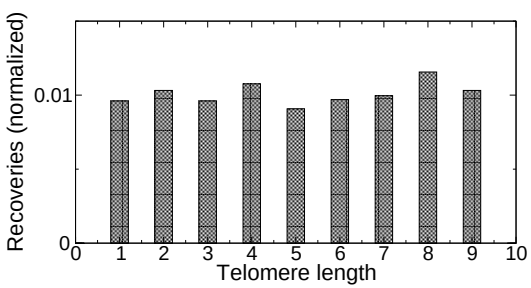
Recovery Rates



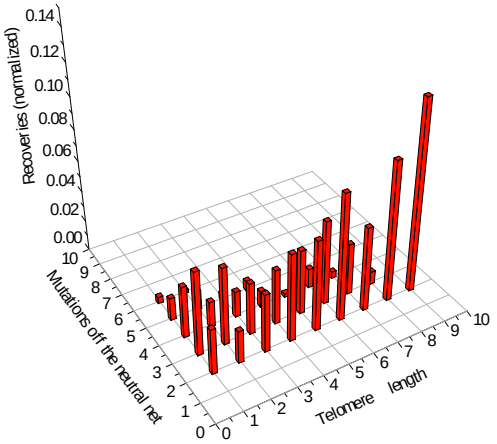


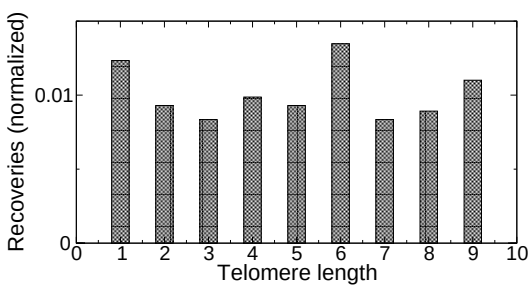
$\mu = 0.001$





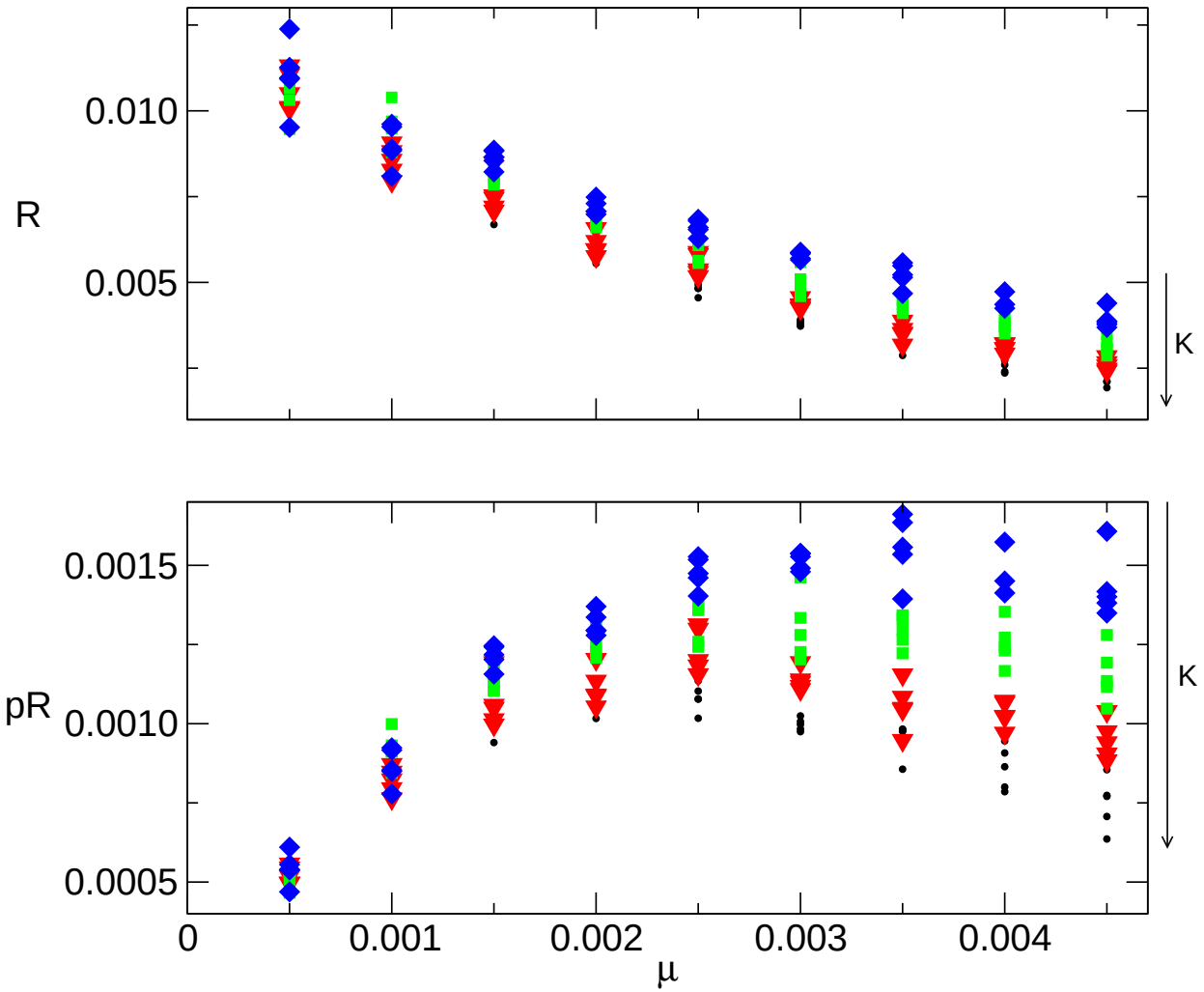
$\mu = 0,003$



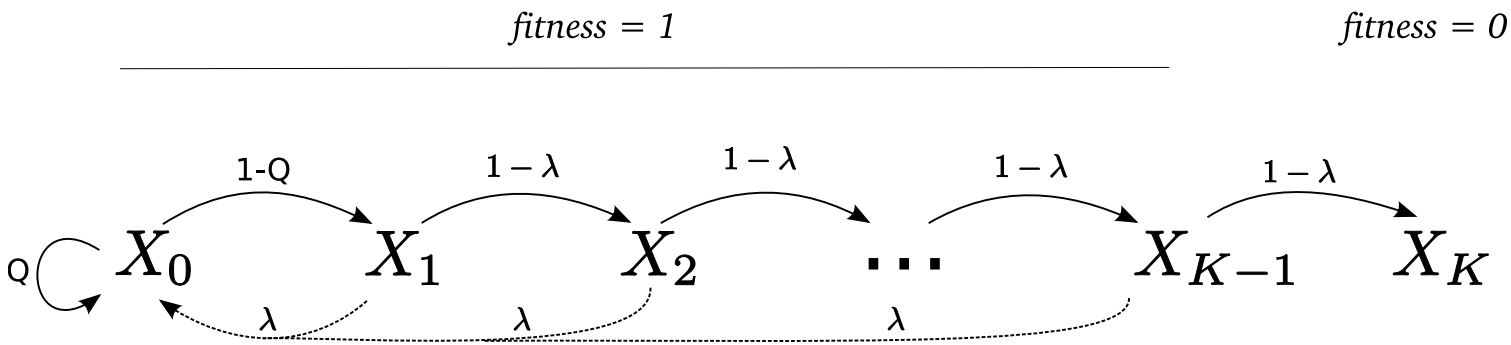


$\mu = 0.01$

Recovery Rates



Replication Kinetics

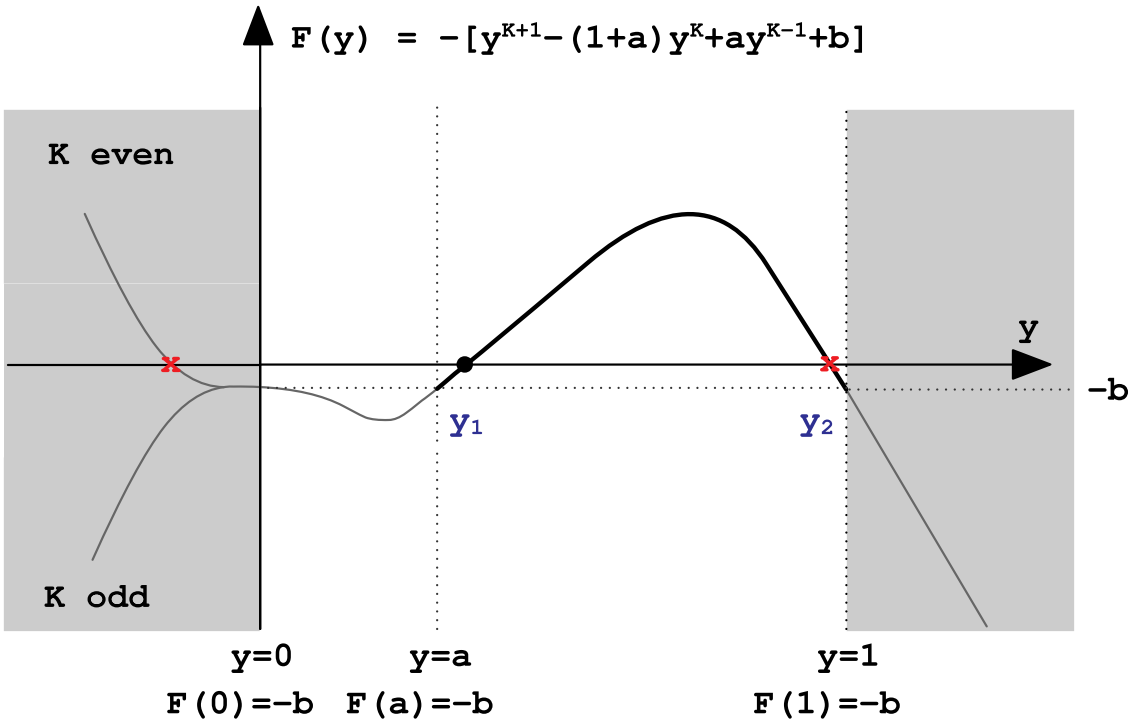


$$
\begin{aligned}
X_0 &\xrightarrow{Q} X_0 \\
X_0 &\xrightarrow{1-Q} X_1 \\
X_i &\xrightarrow{1-p} X_{i+1}, \quad i \in [1, K-1] \\
X_i &\xrightarrow{p(1-R)} X_{i+1}, \quad i \in [1, K-1] \\
X_i &\xrightarrow{pR} X_0, , \quad i \in [1, K-1]
\end{aligned}
$$

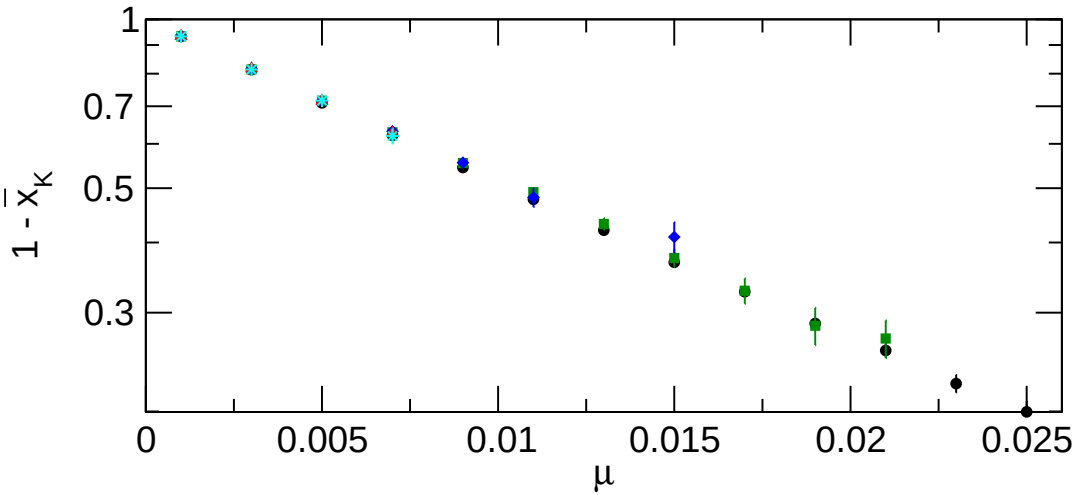
with $Q = [1-\mu(1-\nu)]^L$ and $p = 1-(1-\mu)^L$

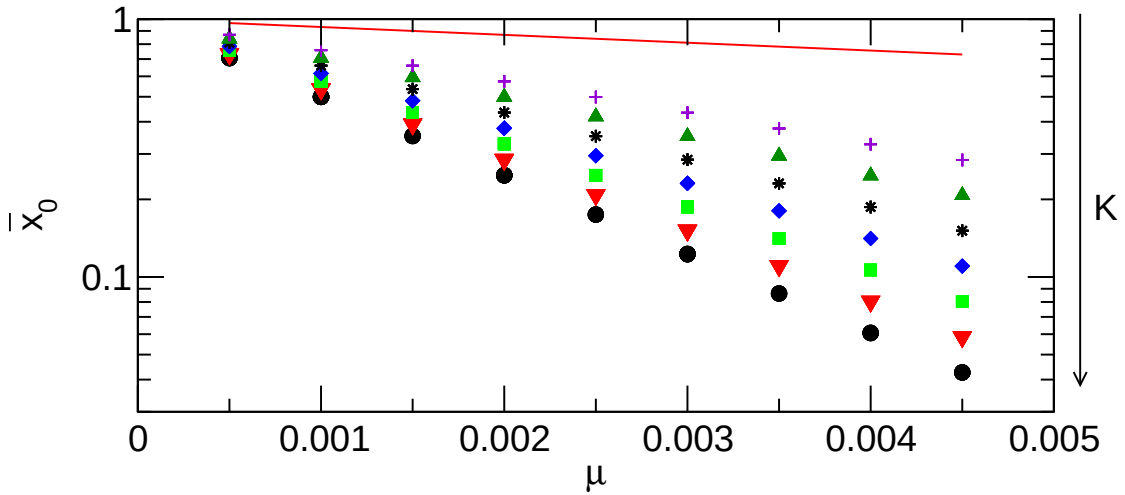
Equilibria

- Trivial equilibrium $\bar{x}_K = 1$, $\bar{x}_i = 0$ for $i \neq K$, $\Phi = 0$
- Non-trivial equilibrium

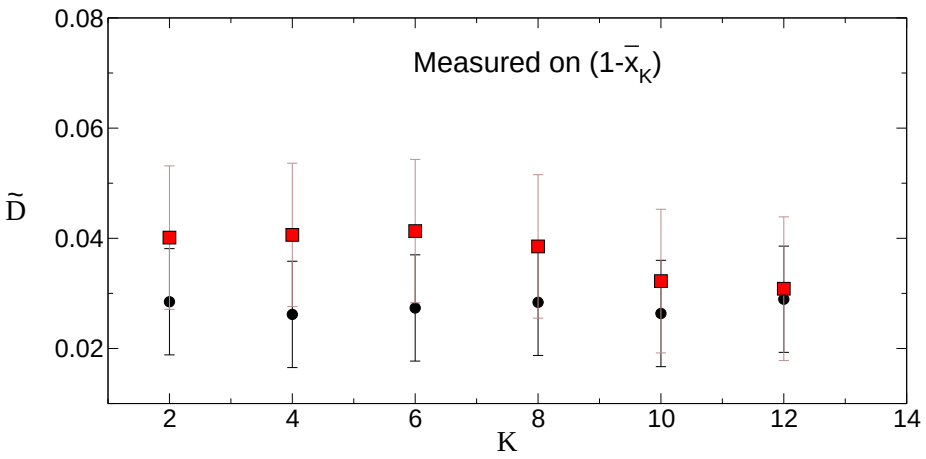


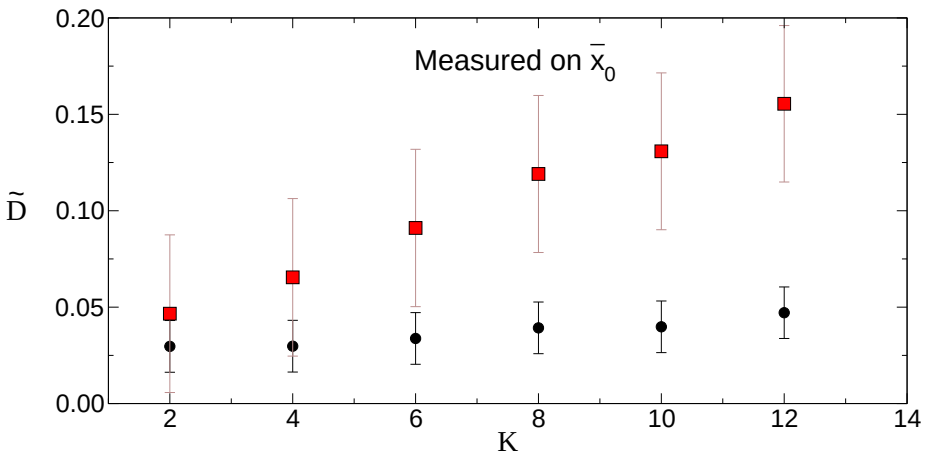
Equilibria


1
0.7
0.5
0.3
1 - $\bar{x}_K$
0
0.005
0.01
0.015
0.02
0.025
μ


1
0.1
$\bar{x}_0$
0
0.001
0.002
0.003
0.004
0.005
μ
K

Effect on Substitution Rates





l.h.s: Effective diffusion rate in sequence space for the entire population

r.h.s: Effective diffusion rate of undamaged subpopulation

Summary

- Delayed selection reduces the Error Treshold and increases extinction probability
- Ancestors of living undamaged individuals went through multiple cycles of damage and repair
- The effect of delayed selection on subsitution rates is very small.
  $\Longrightarrow$ may be a frequent phenomenon