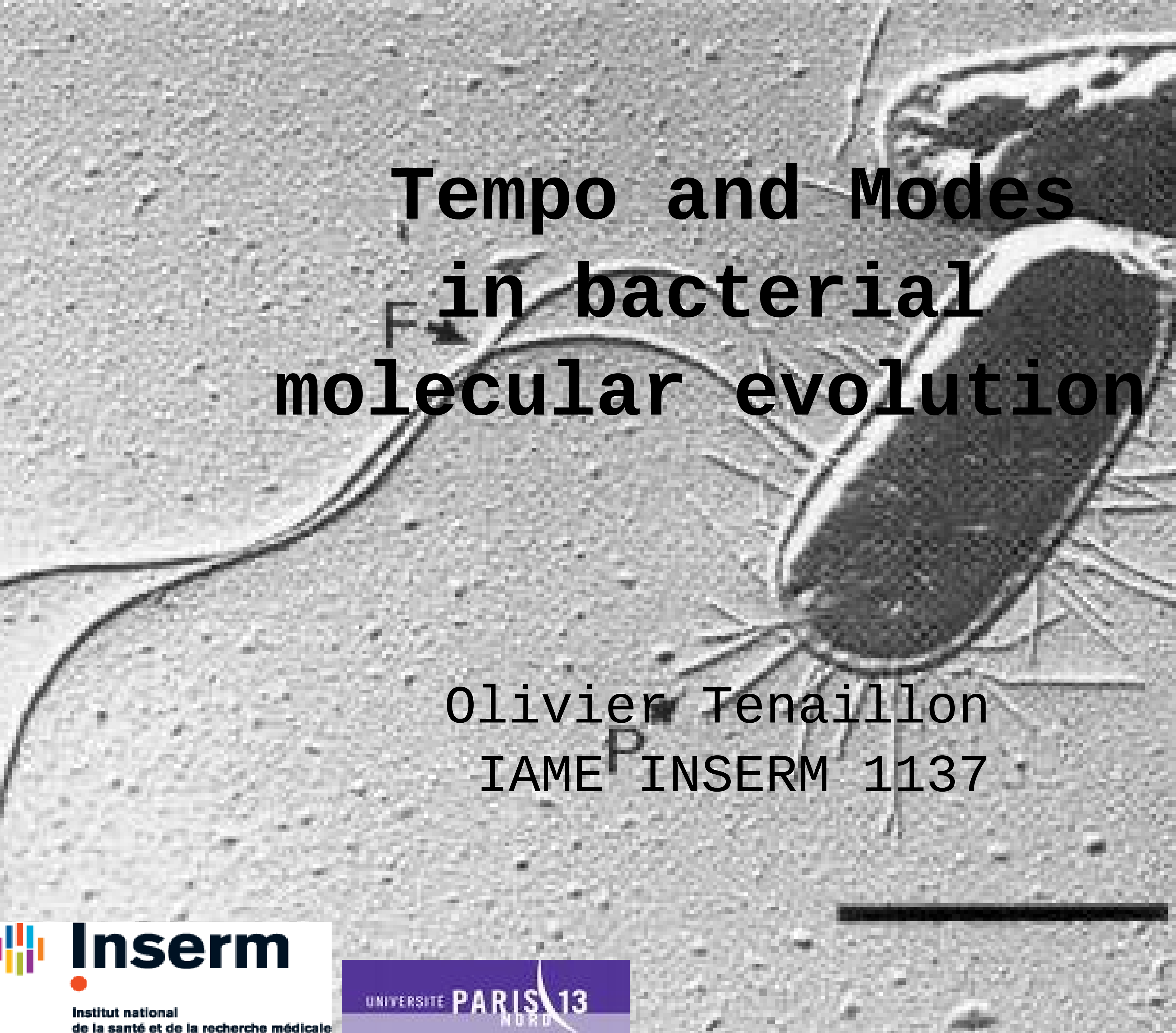

Tempo and Modes in bacterial molecular evolution

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erc

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  University Joseph Fourier Grenoble

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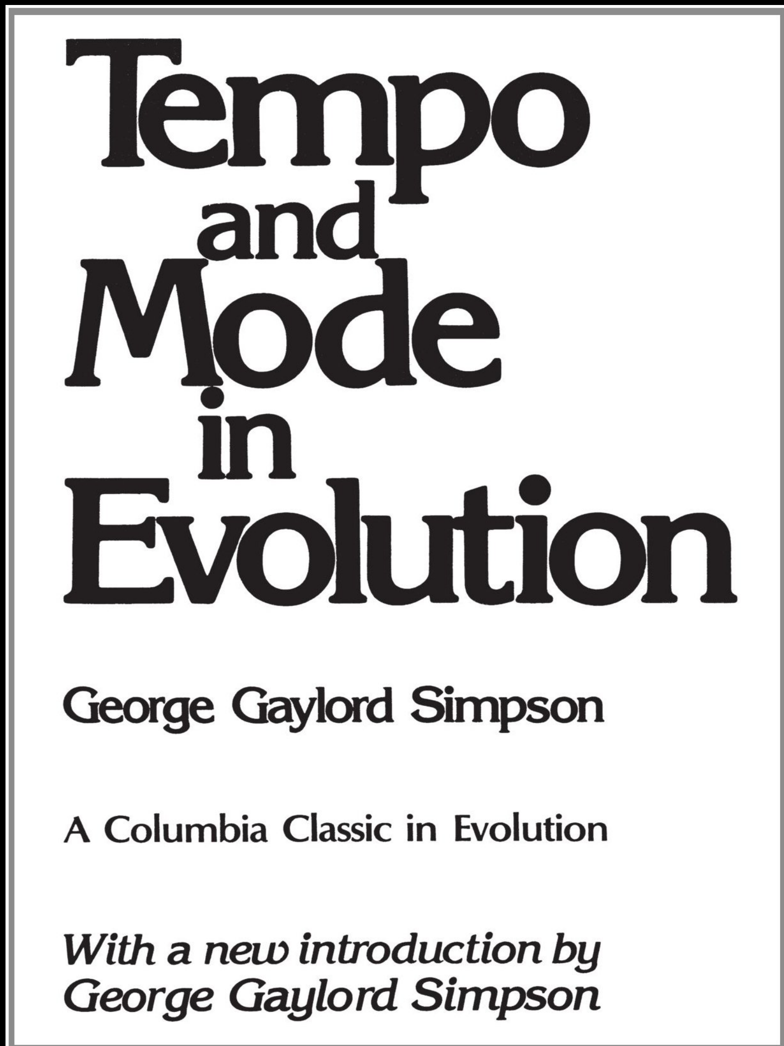
  University of Texas Austin

- Richard Lenski
  Michigan State University

Tempo and mode in Evolution



Tempo and mode in Evolution

Tempo: evolutionary rates … their acceleration and deceleration…

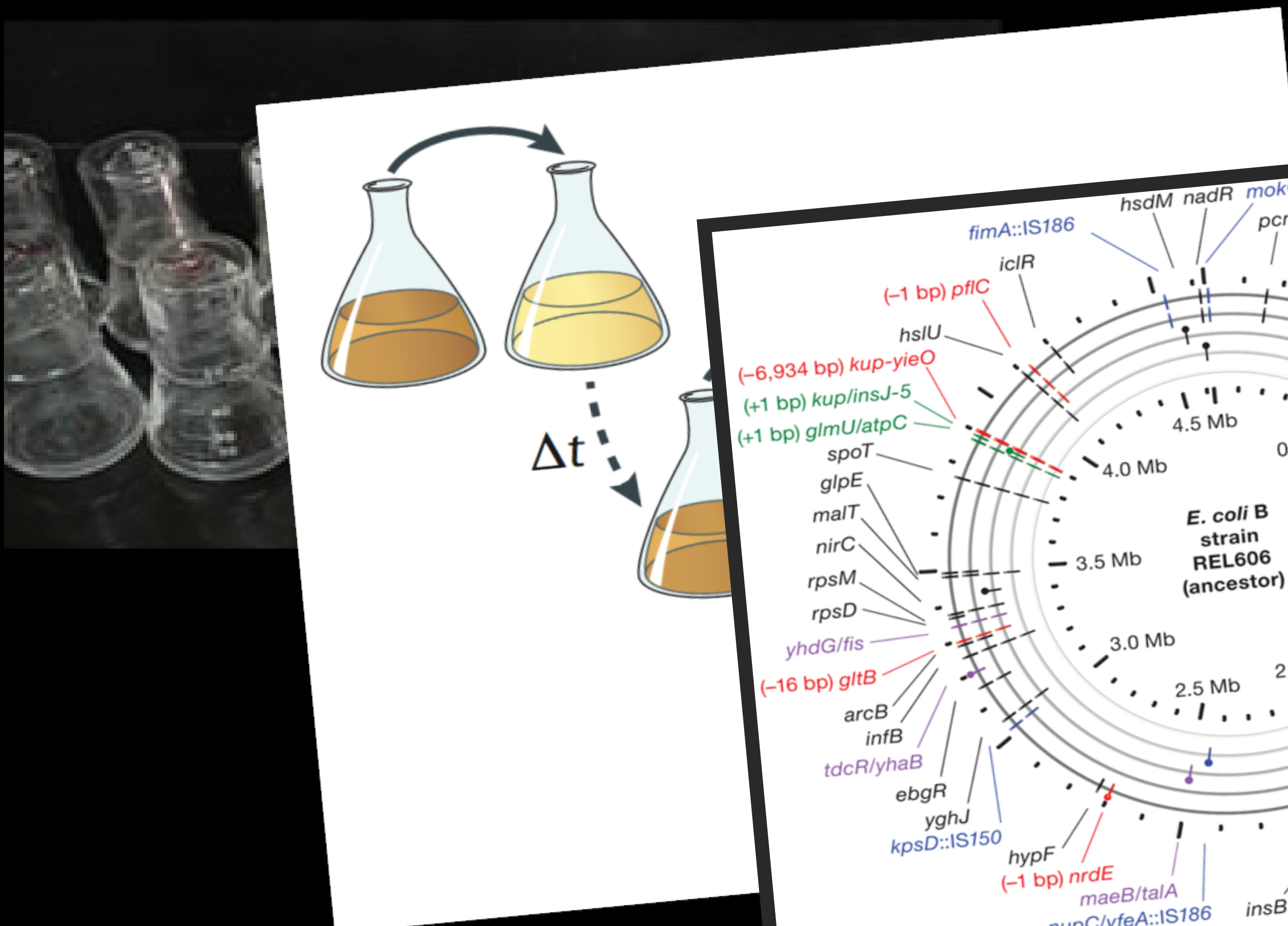
Tempo concerns rates

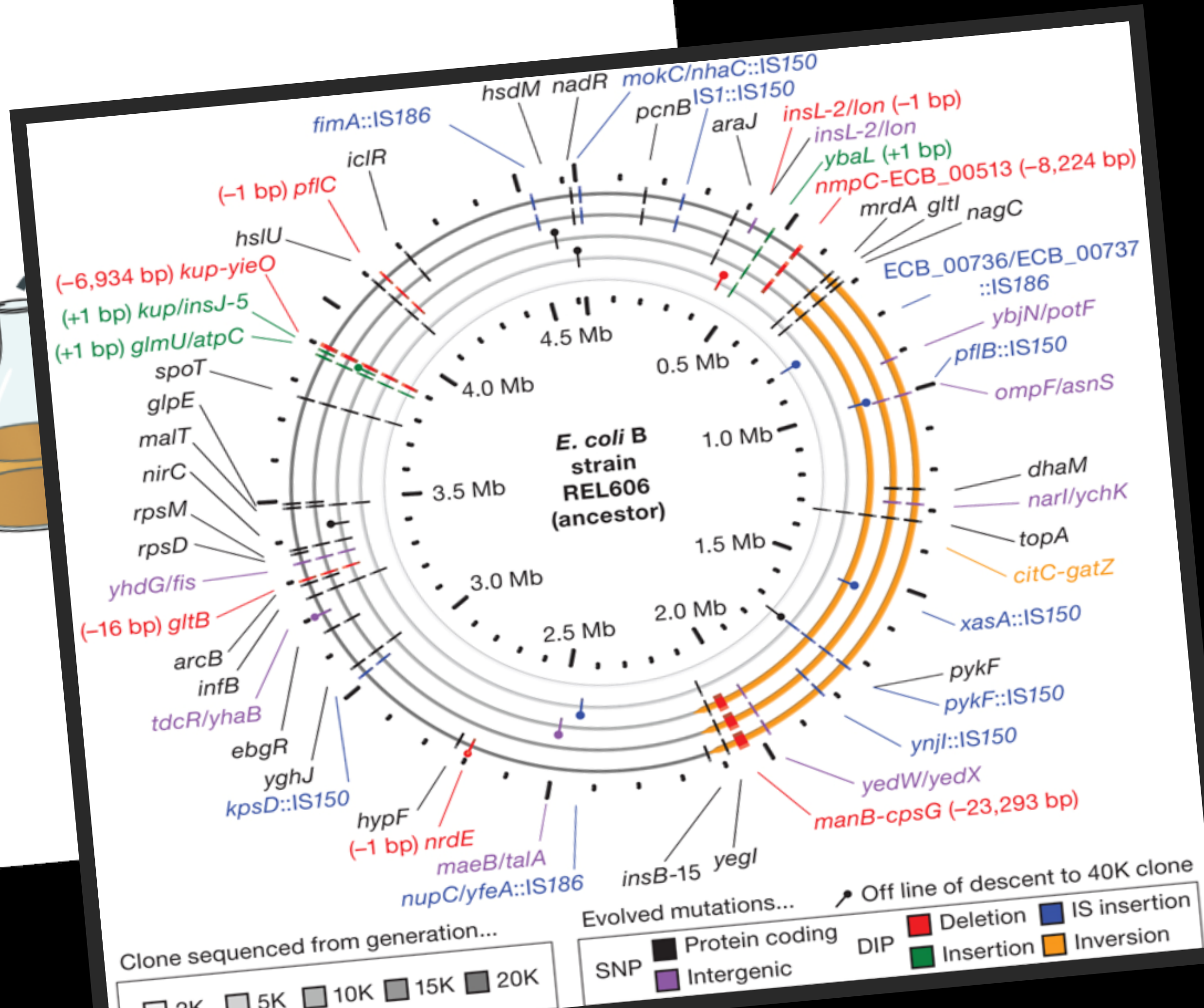
Mode: the study of the way, manner, **or pattern** of evolution, a study in which tempo is a basic factor, but which embraces considerably more than tempo

Mode concerns the underlying mechanisms and the global patterns of tempo

Evolution's tempo can impart information about its mode

tempo and mode in Bacterial evolution





Barrick et al *Nature* 2009

Forecasting evolution

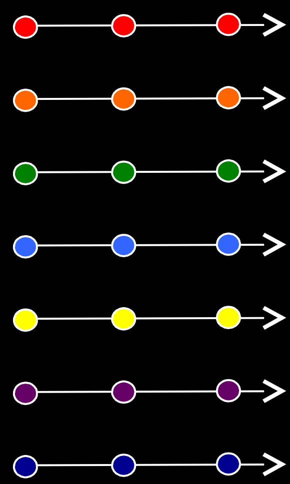
- Rates of fitness improvement
- Rates of mutation accumulation
- Which underlying patterns at the molecular level

Are there any rules
and simple explanatory models

Tempo of Fitness improvement

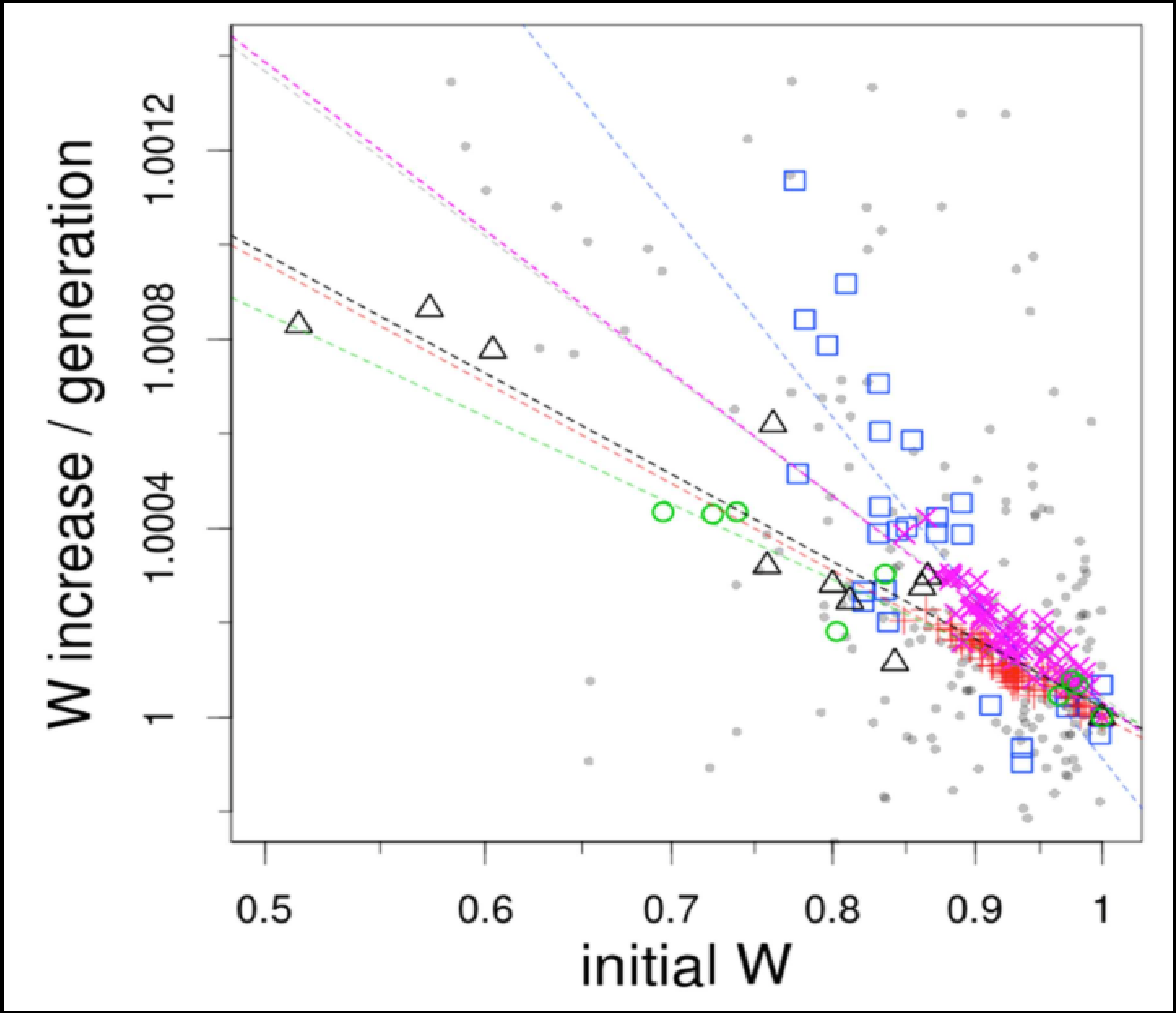
A short term approach

- Evolve several lineages with different initial fitness



Kryazhimskiy et al 2014,Perfeito et al 2014

Tempo: Rules of declining adaptability in fitness trajectories



Alejandro Couce

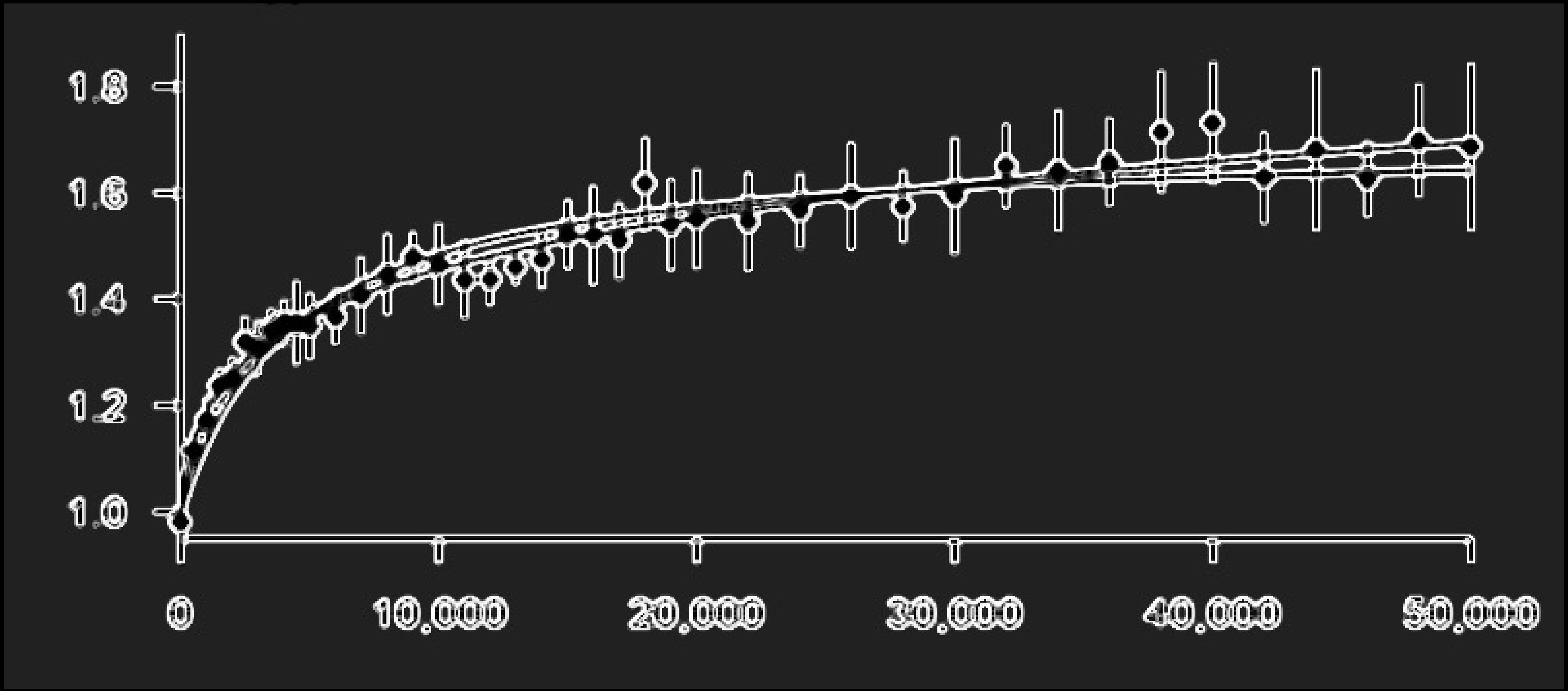
Couce & Tenaillon *Frontier in Genetics* 2015

A Long-term approach

- Mal-adapted strain,
- Long term 50000 generations

Wiser et al *Science* 2013

Consistant through time



Wiser et al *Science* 2013

Underlying models

- Many alternative models can lead to that pattern
  - No epistasis: exhaustion of beneficial mutation
  - Macroscopic epistasis without sign epistasis: beneficial mutations stay beneficial, but their effect decrease with adaptation
  - Macroscopic epistasis with sign epistasis: the fraction of beneficial mutations change with adaptation

Wiser et al 2013, Good Desai 2014, **Couce Tenaillon 2015**, McCandlish et al 2015

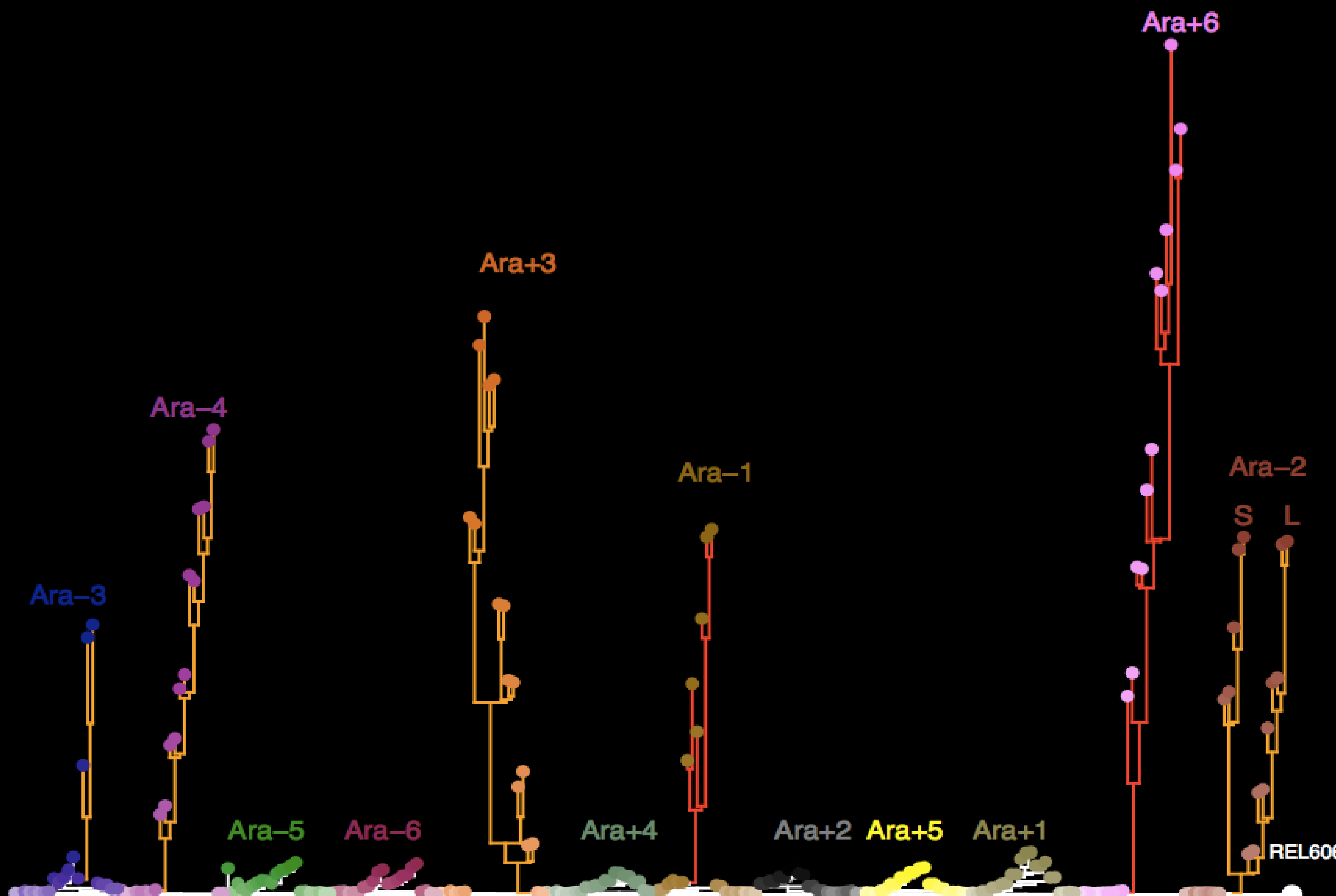
Tempo and mode in molecular evolution

A Long-term approach

- Mal-adapted strain,
- Long term 50000 generations
- Sequence 264 genomes

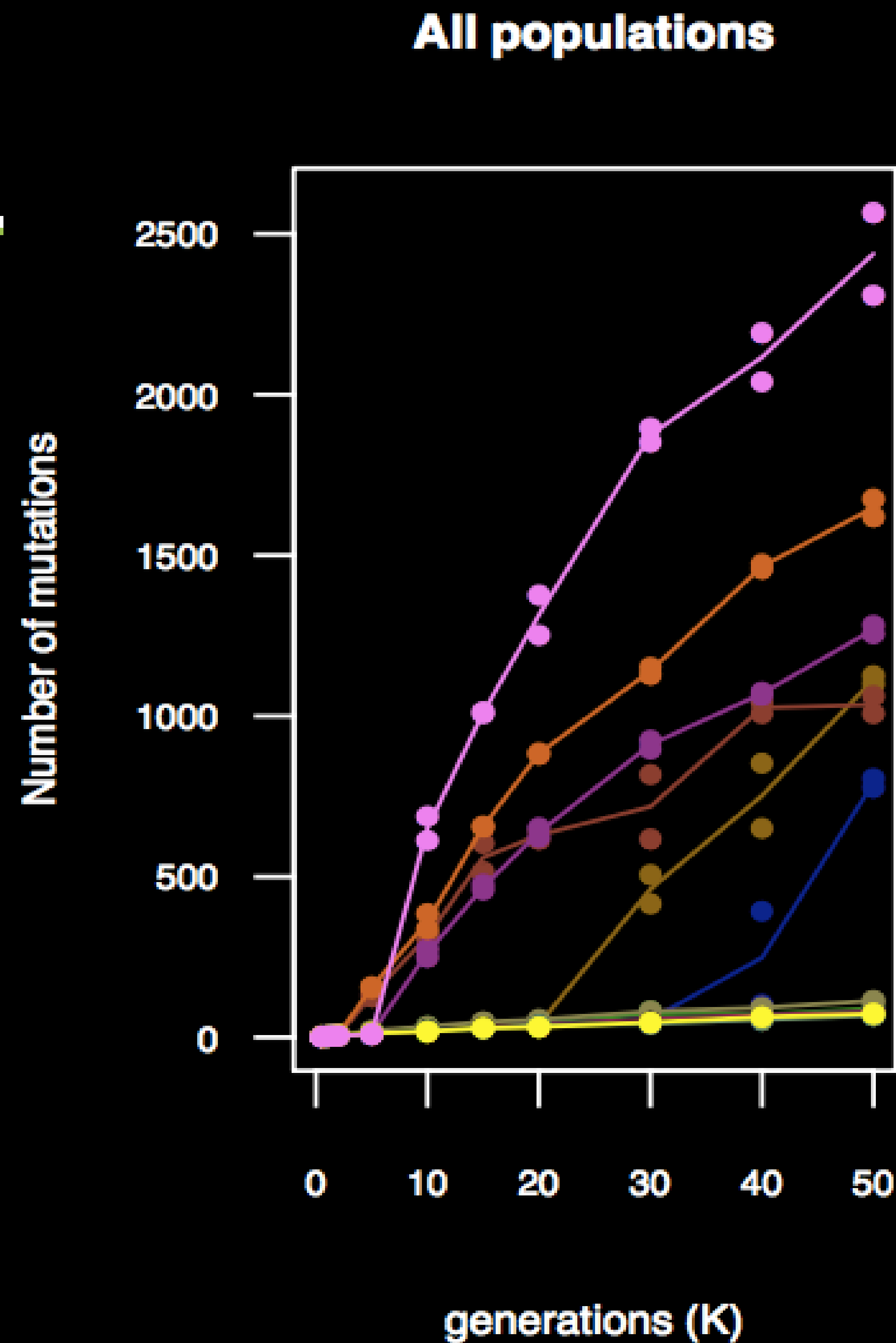
Wiser et al *Science* 2013

Phylogeny



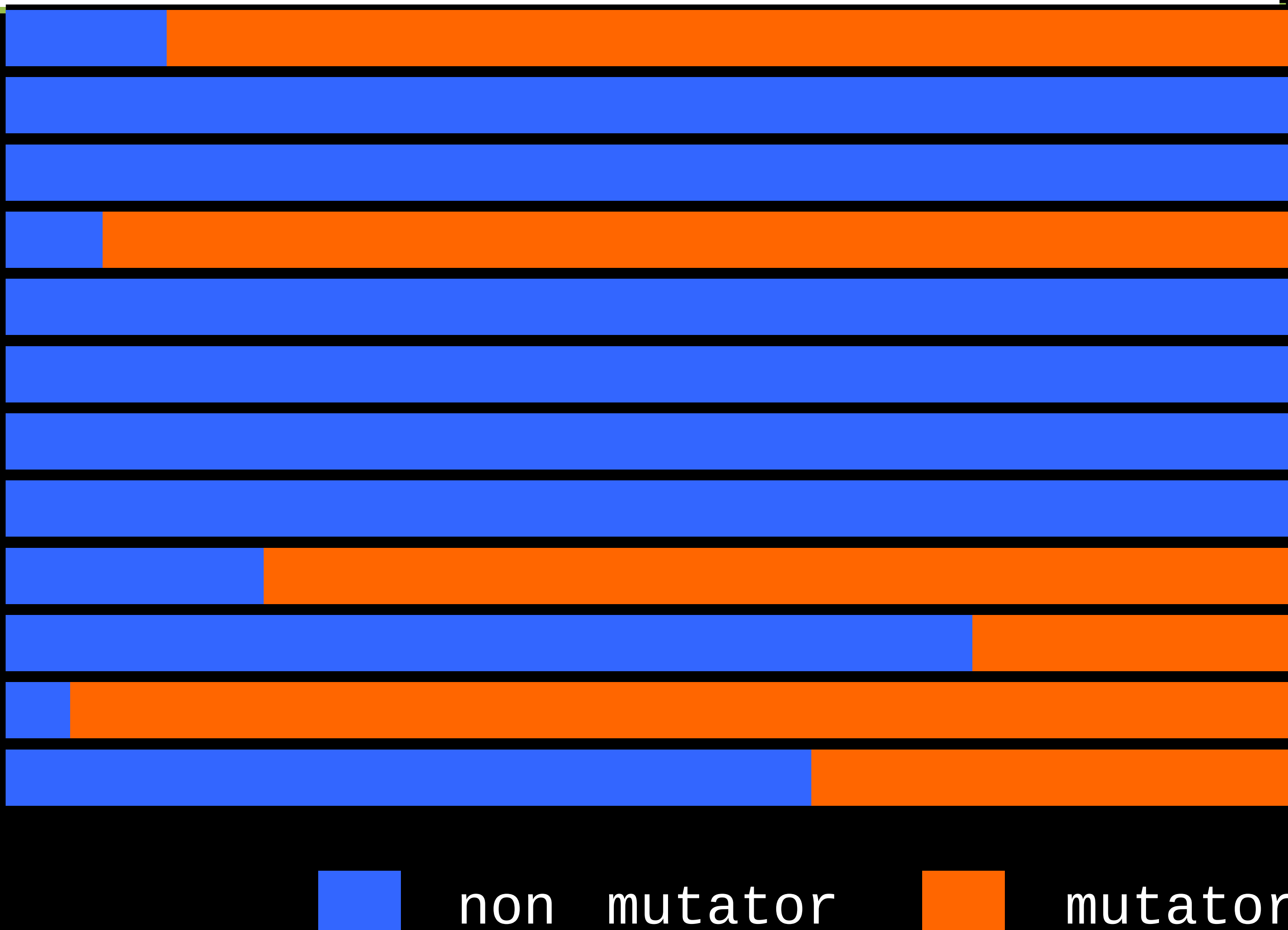
Ara+6
Ara+3
Ara–4
Ara–1
Ara–2
S
L
Ara–3
Ara–5
Ara–6
Ara+4
Ara+2
Ara+5
Ara+1
REL606

Mutators !

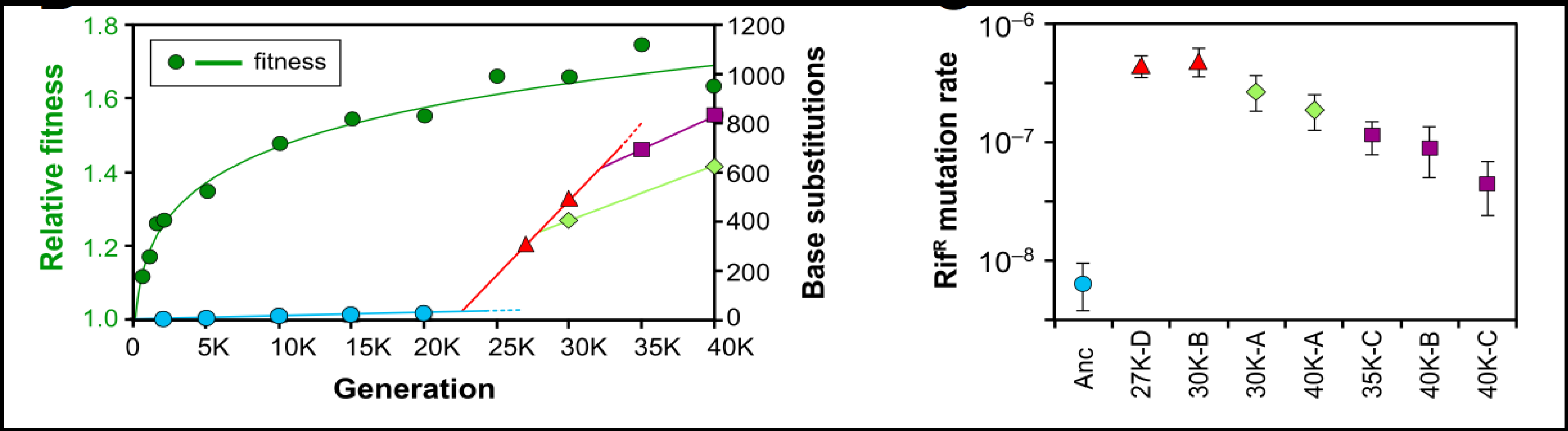


All populations
Number of mutations
2500
2000
1500
1000
500
0
0
10
20
30
40
50
generations (K)

Emergence of mutators

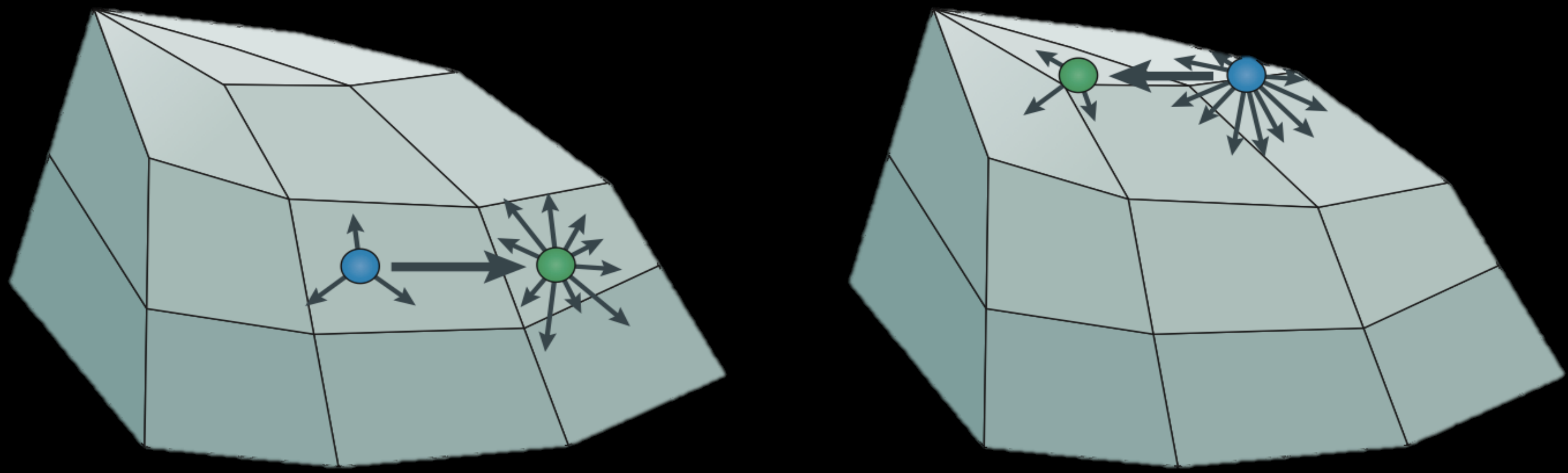


Mutation rate decays



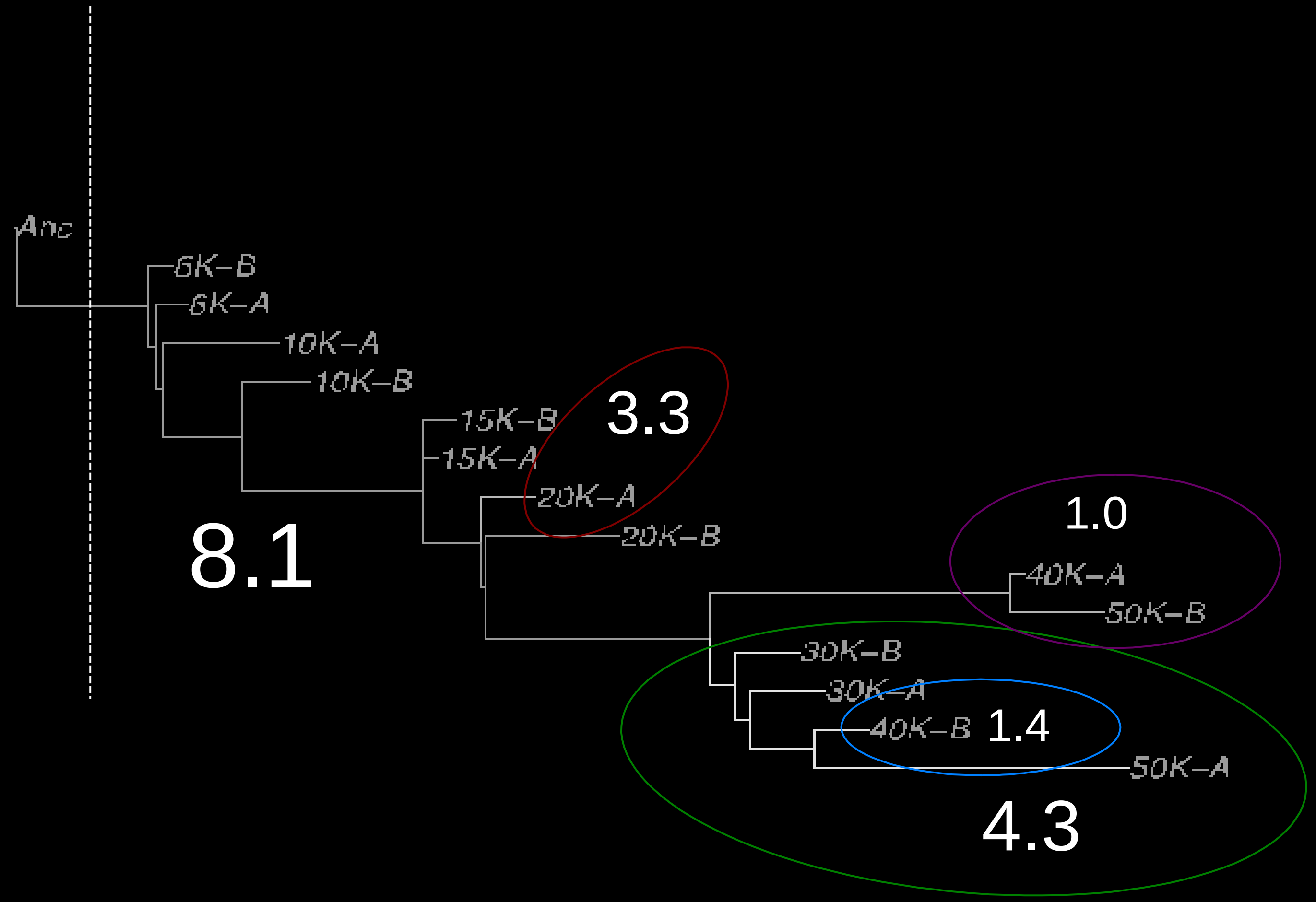
Wielgoss et al , PNAS 2013

Dynamics of mutation rate



Barrick & Lenski *Nature Review Genetics* 2013

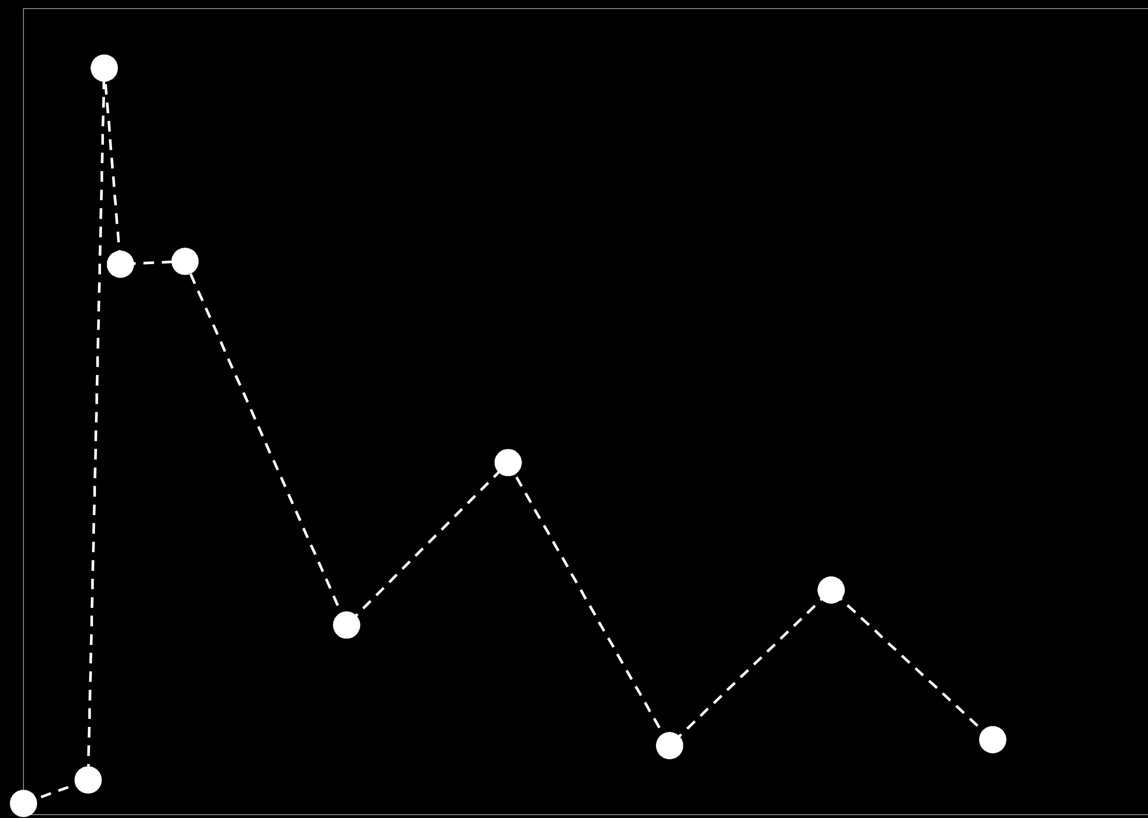
Decrease genomic in another population



genomic rate of AT->CG synonymous mutations per 100 generations

Viraphong et al in prep

The bumpy decay of mutation rate



Viraphong et al in prep

Fitness and mutations

Fitness of mutator lineages is slightly different from the one of non mutator

Yet

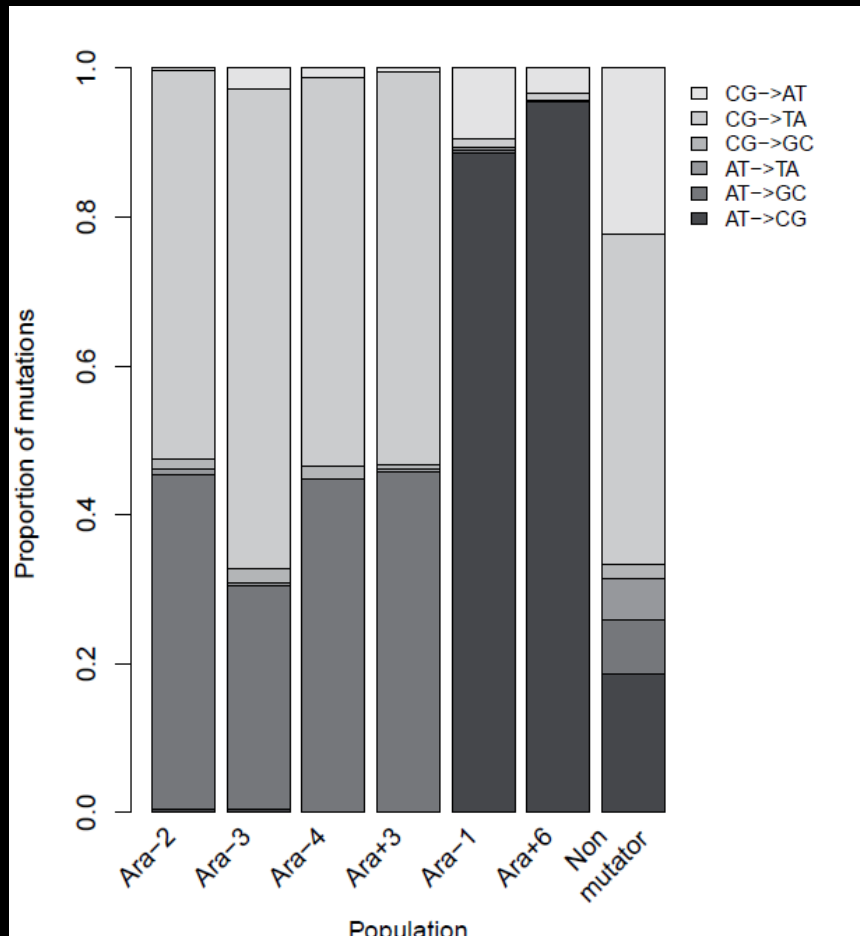
Very different tempo of mutation accumulation

Mutation numbers are not telling us the underlying model

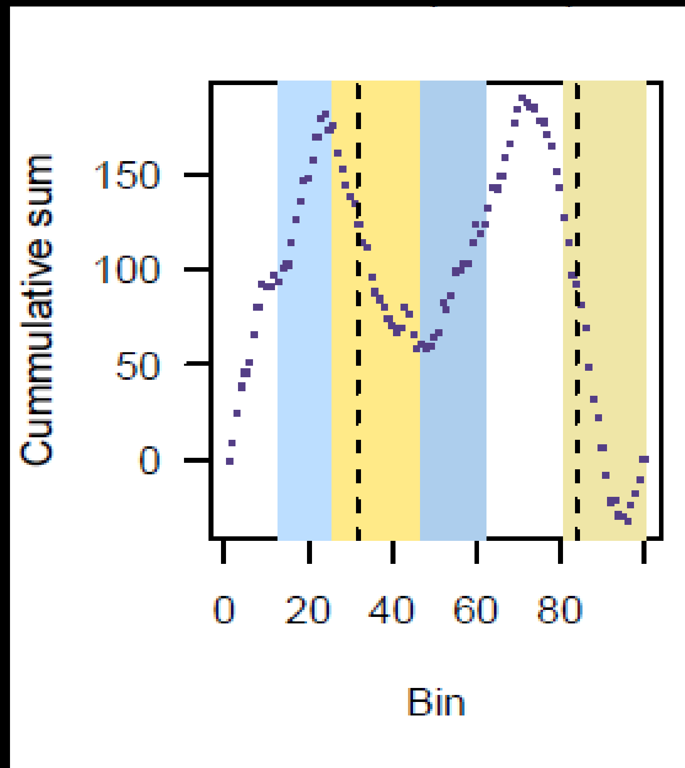
Tempo and mode in molecular evolution:

mutators and mutations

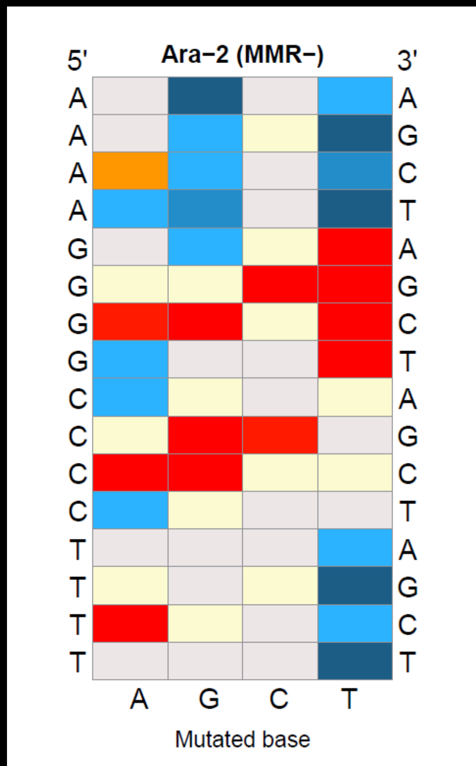
Impact of the mutators on mutations

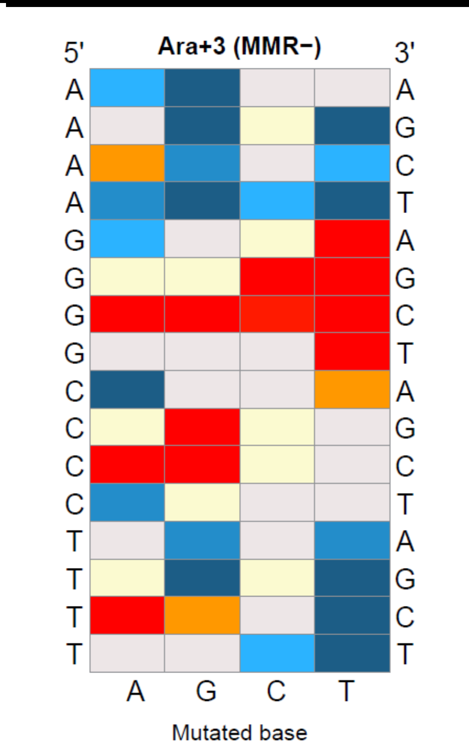


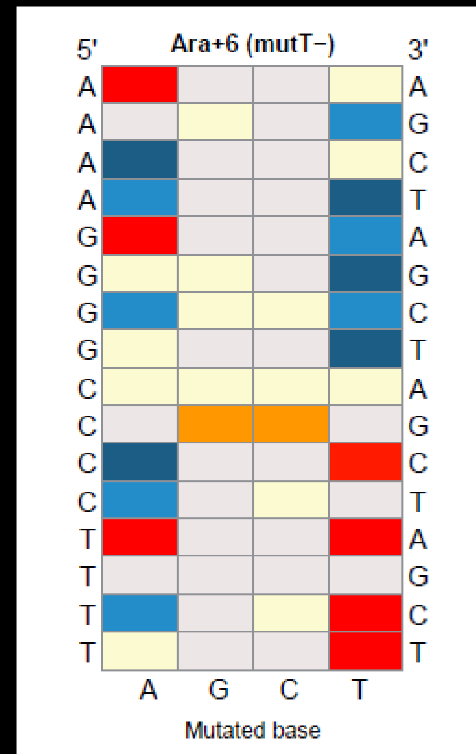
Some non-random organisation on MMR-



Some local biases, similar to MA

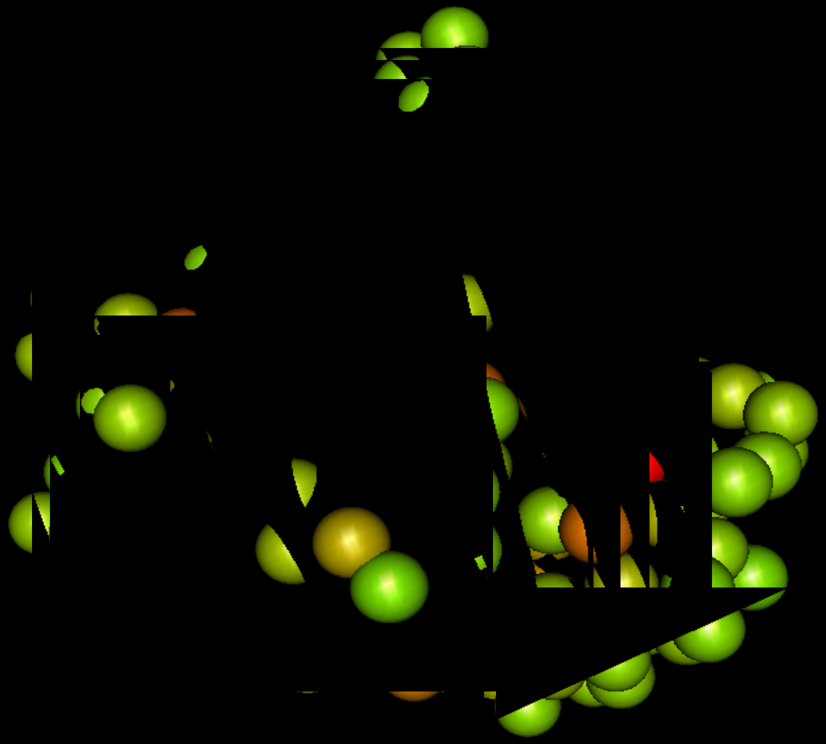






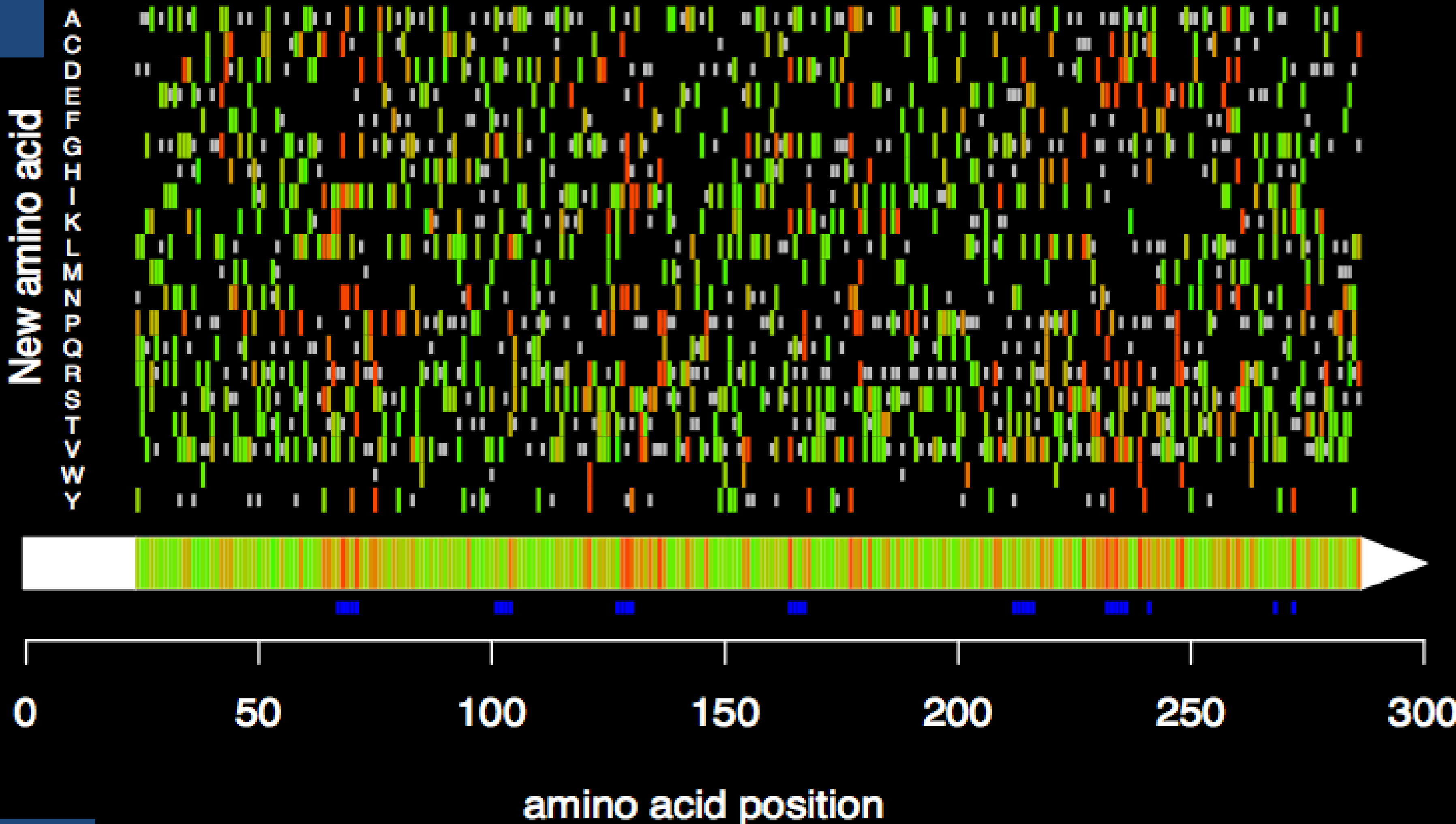
Focussing on a single gene

What are the molecular determinants of that distribution

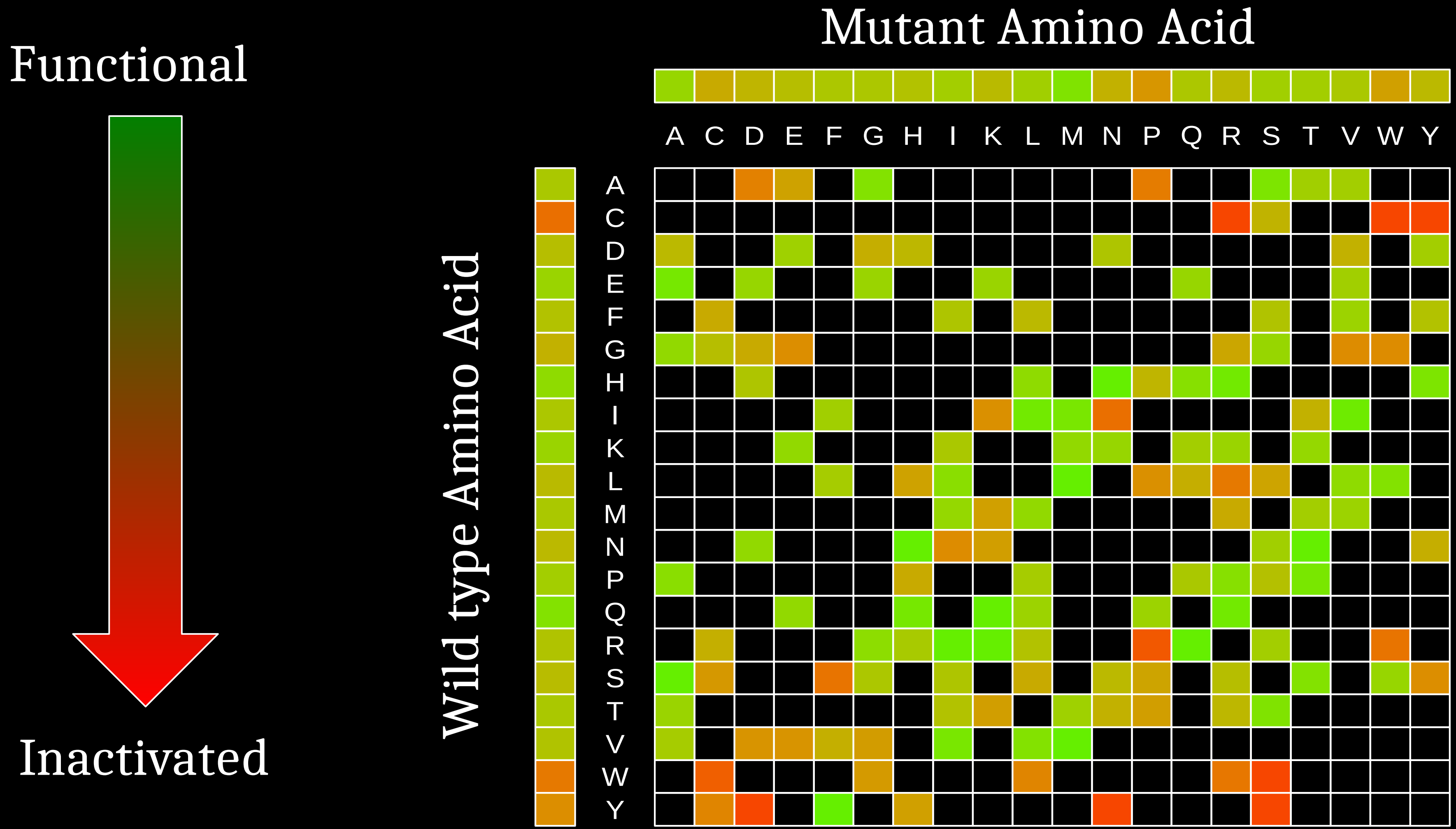


Jacquier et al, PNAS 2013

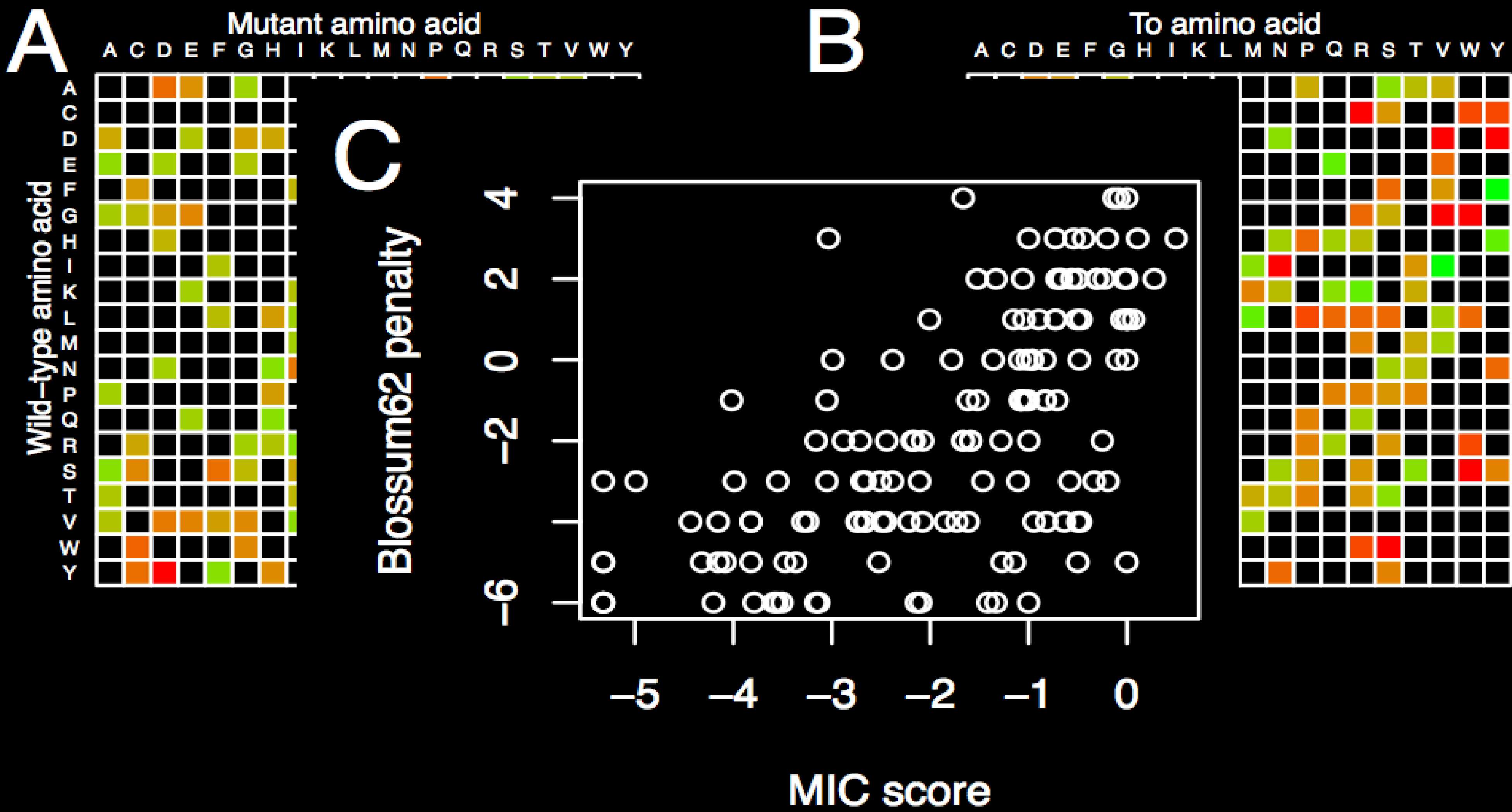
A large database



Determinants: Type of mutation



Blossum62


A
Mutant amino acid
A C D E F G H I K L M N P Q R S T V W Y
Wild-type amino acid
A C D E F G H I K L M N P Q R S T V W Y
B
To amino acid
A C D E F G H I K L M N P Q R S T V W Y
C
Blossum62 penalty
4
2
0
−2
−6
−5
−4
−3
−2
−1
0
MIC score

In the case of mutators: Biases stronger than selection?

Despite the presence of selection patterns are consistant with mutation accumulation results

No correlation with any of the matrices

Fitness and mutations

Fitness of mutator lineages is slightly different from the one of non mutator

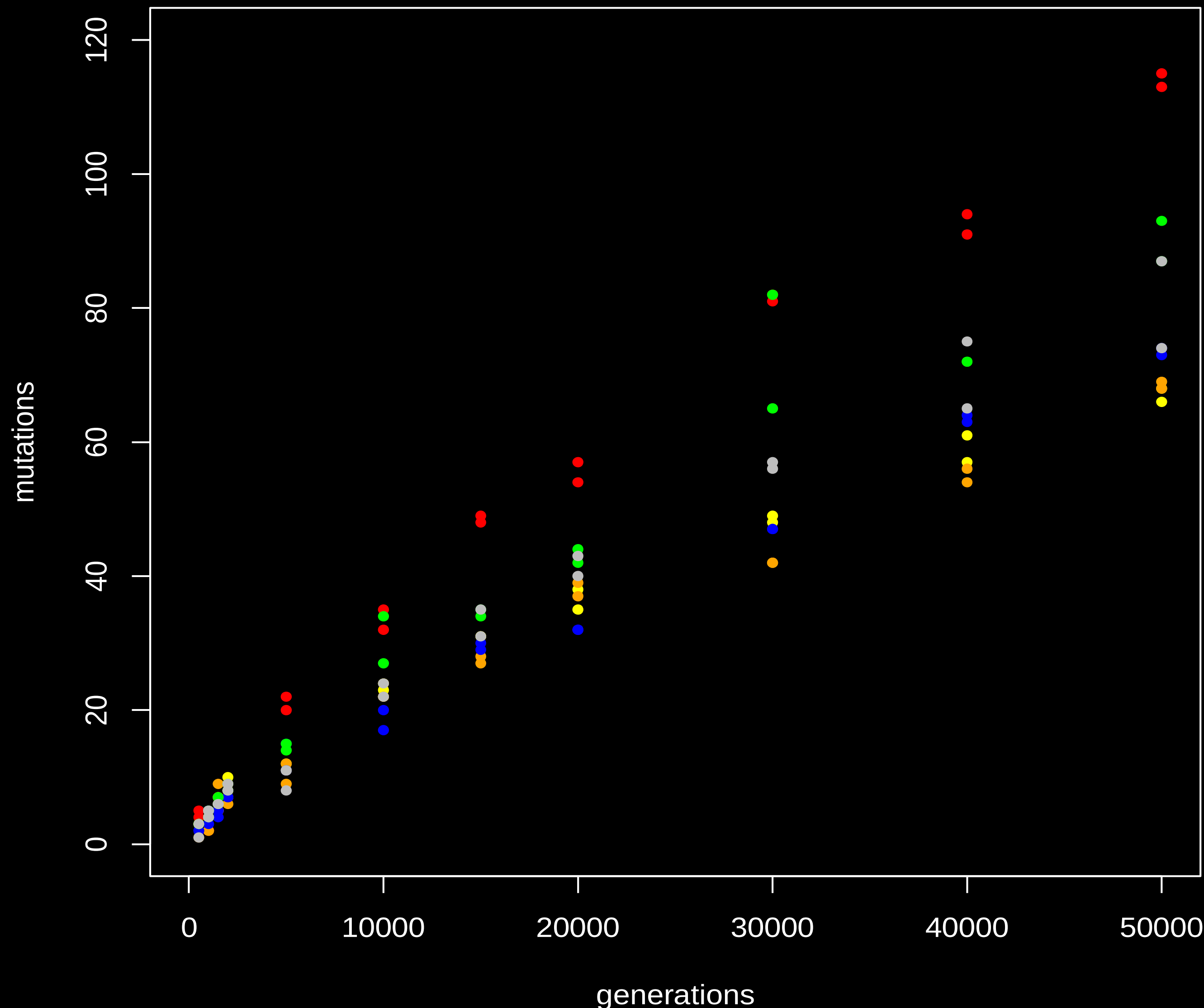
Yet

Very different tempo of mutation accumulation

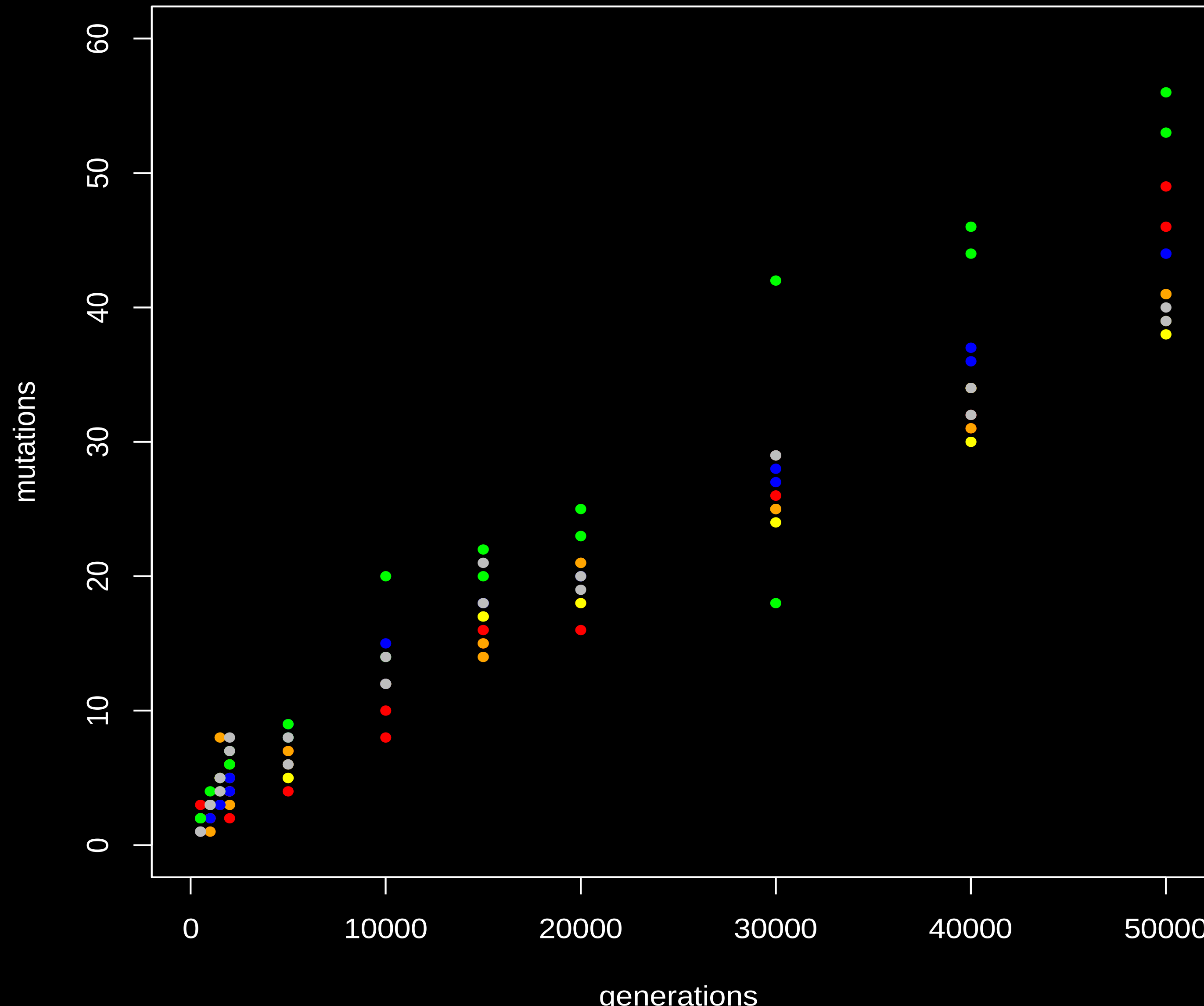
Mutation numbers are not telling us the underlying model

Mutation accumulation in non mutator populations

In non mutator populations

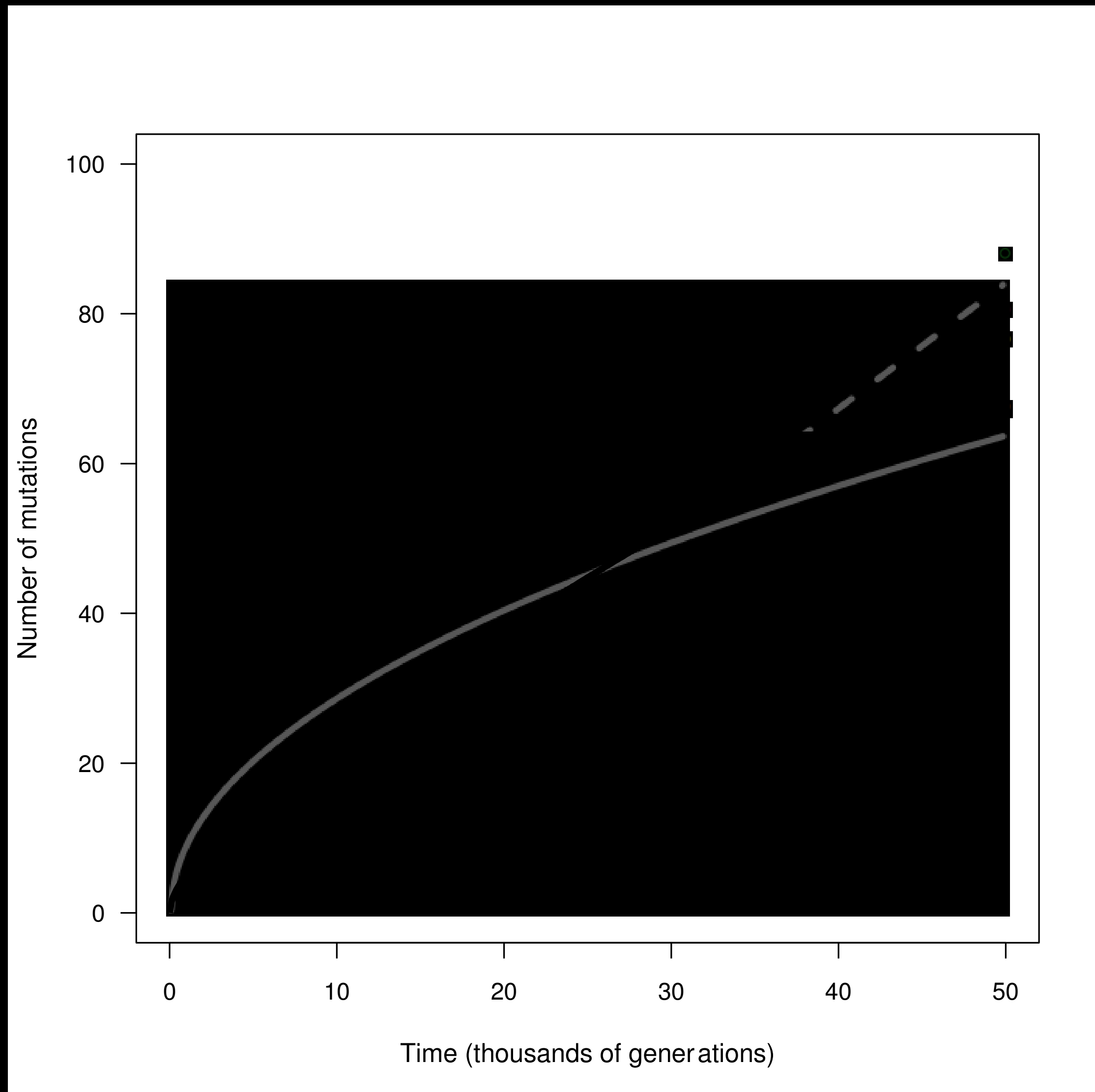


More similar in point mutations

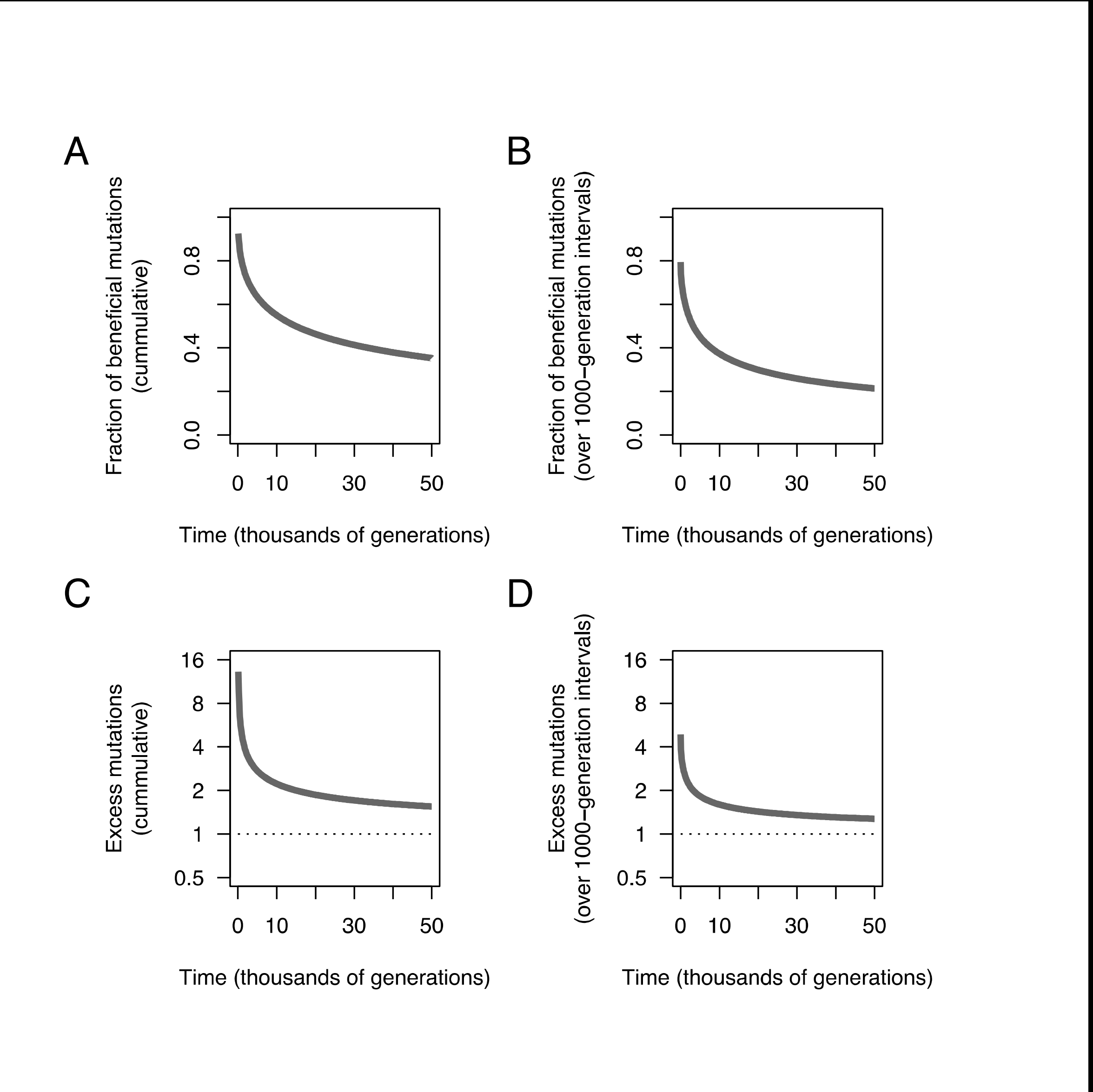


What fraction of beneficials

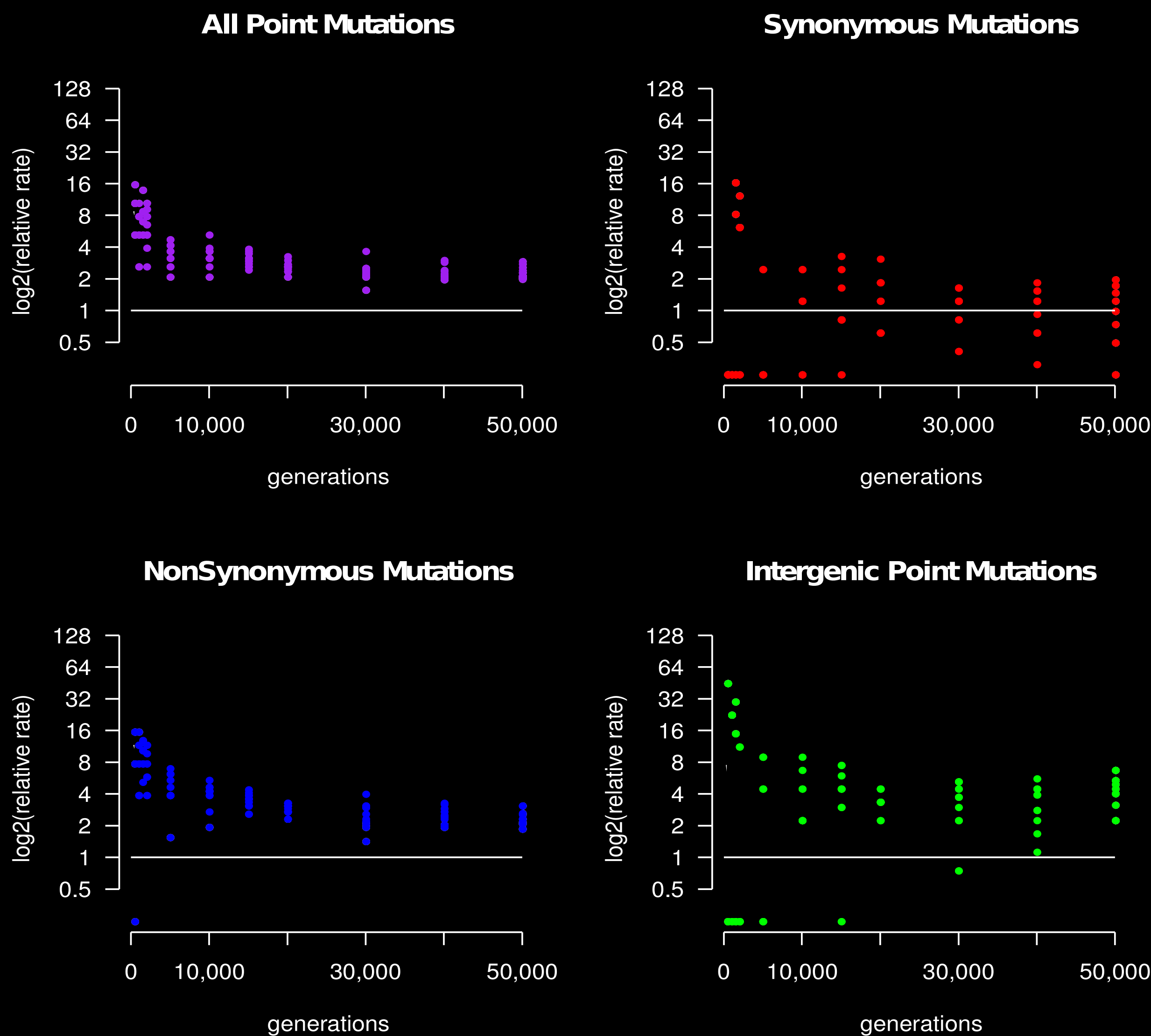
A combination of square root and linear



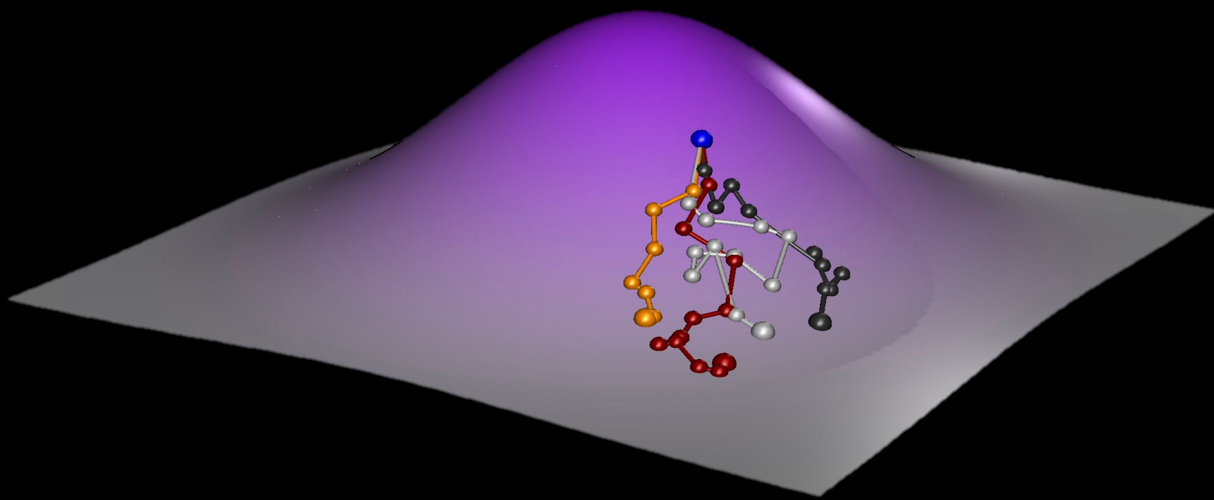
Predict a large fraction of beneficial



What fraction of beneficial

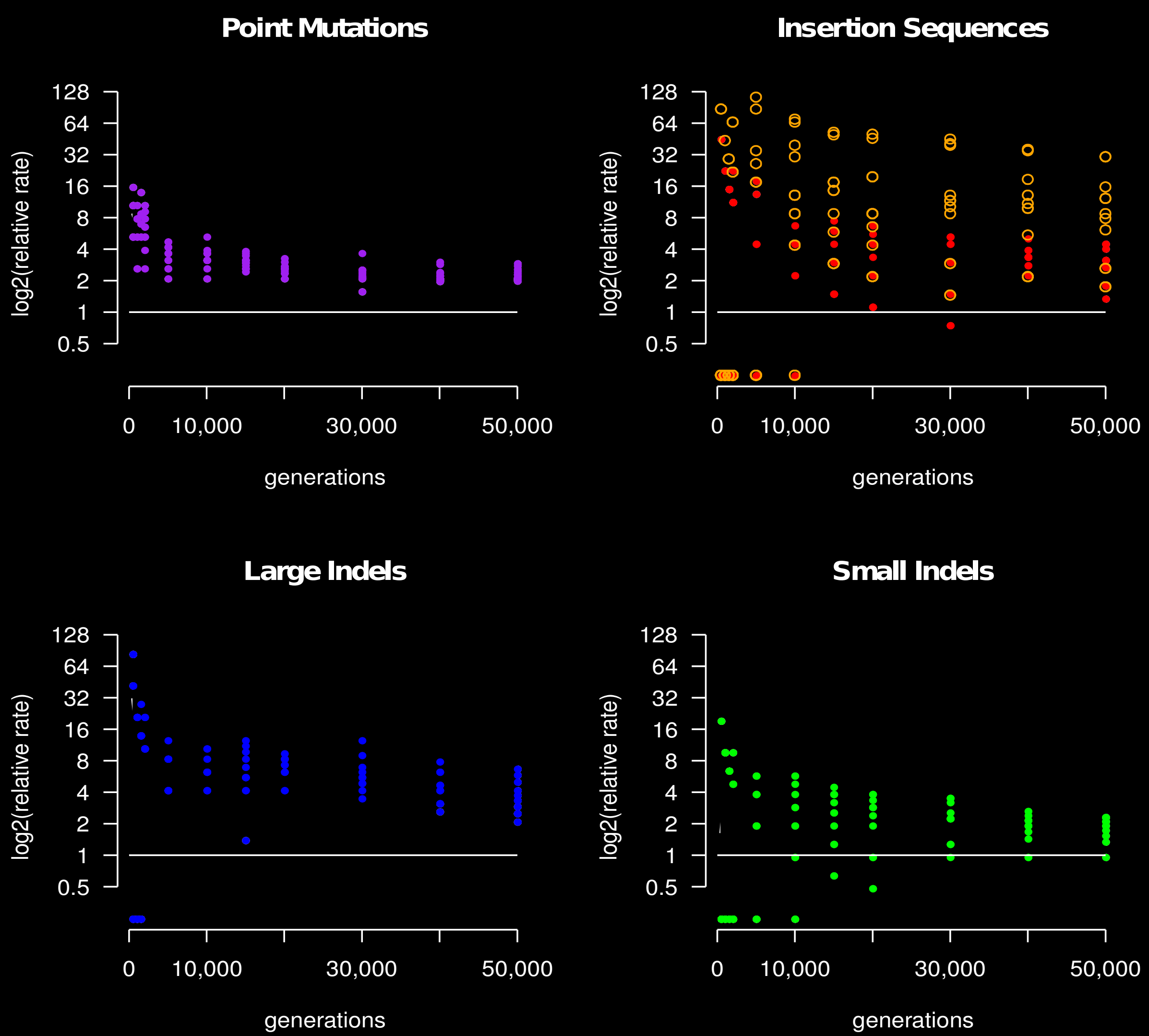


Use Mutation Accumulation



Long et al *Nature Review Genetics* 2015

A excess of beneficial even after 50K



Tempo of mutations

Fast mutation accumulation decrease to a linear accumulation

Still a sustained fraction of beneficial mutations despite a lower fitness improvement

Several models may still fit both mutation accumulation and fitness trajectories

Conclusion

Forecasting evolution

- Fitness trajectories appear higly predictable with a global rule of declining adaptability
- Many models can produce that shape
- Mutation trajectory are not sufficient
- Benefical mutation trajectory may be better
- Convergence adds another layer of complexity
- Simple models do not match easily all tempos, more complex forms of epistasis may have to be included

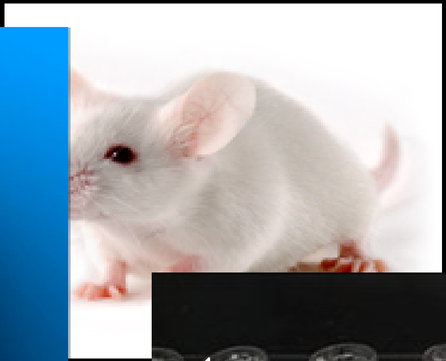
An adaptationist view

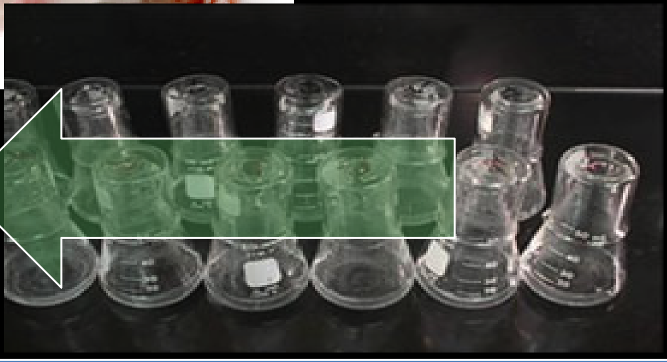
A large fraction of mutations
are the product of selection
even after 50000 generations
more draft than drift

is it general?
what is specific:

-artificial
-boringly stable
-no sex

Conclusion





Rate … on

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