Measuring trait variation in unit of nucleotide changes to disentangle neutral and adaptive processes

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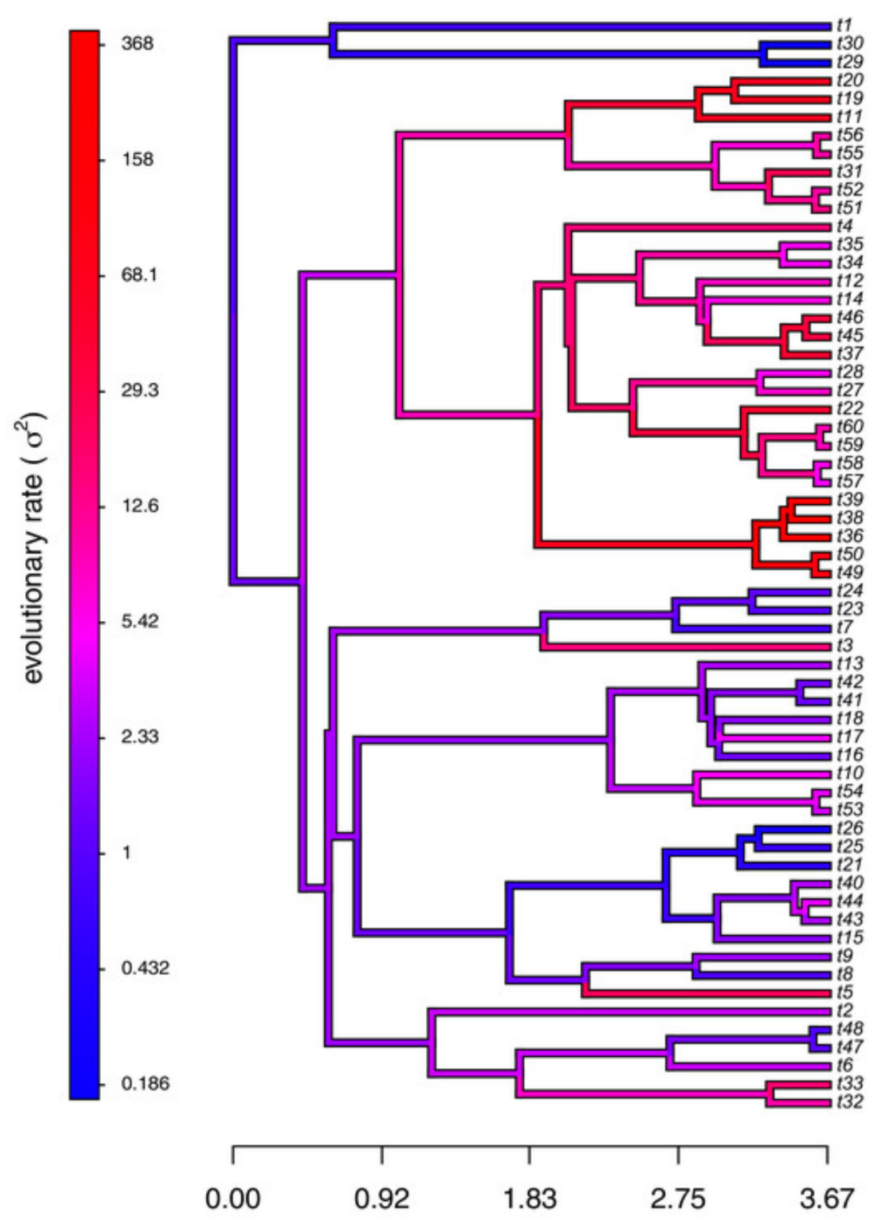
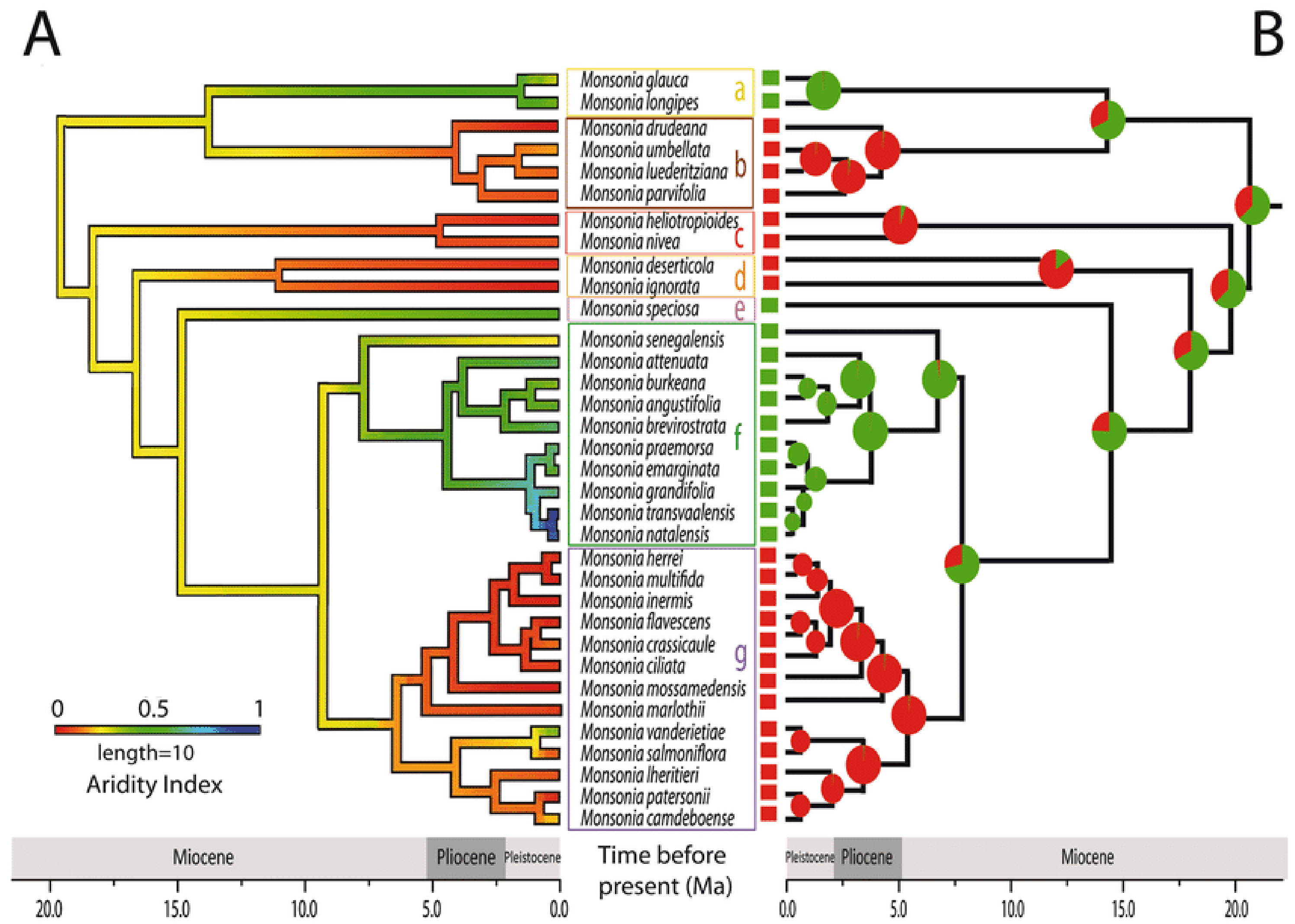
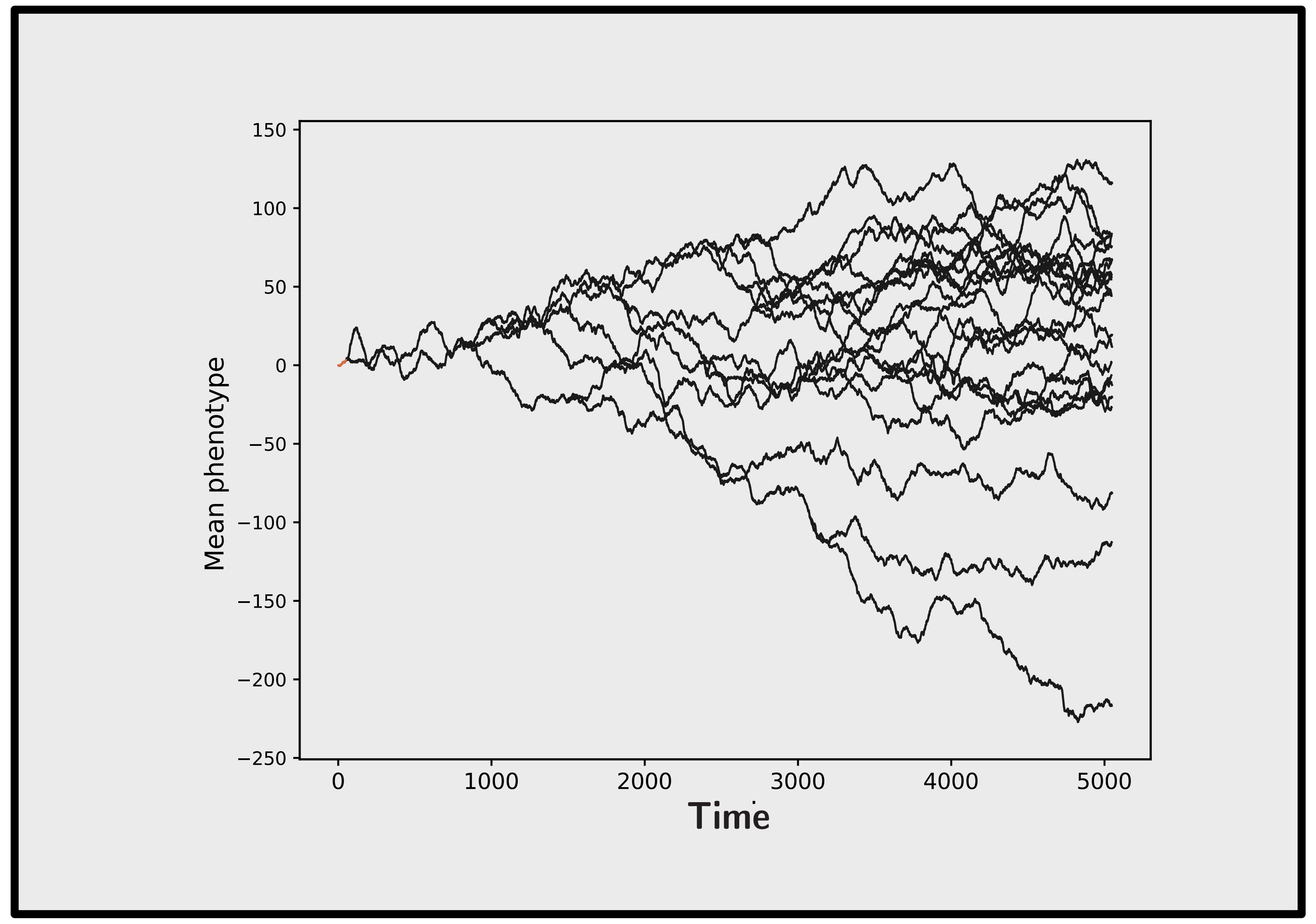
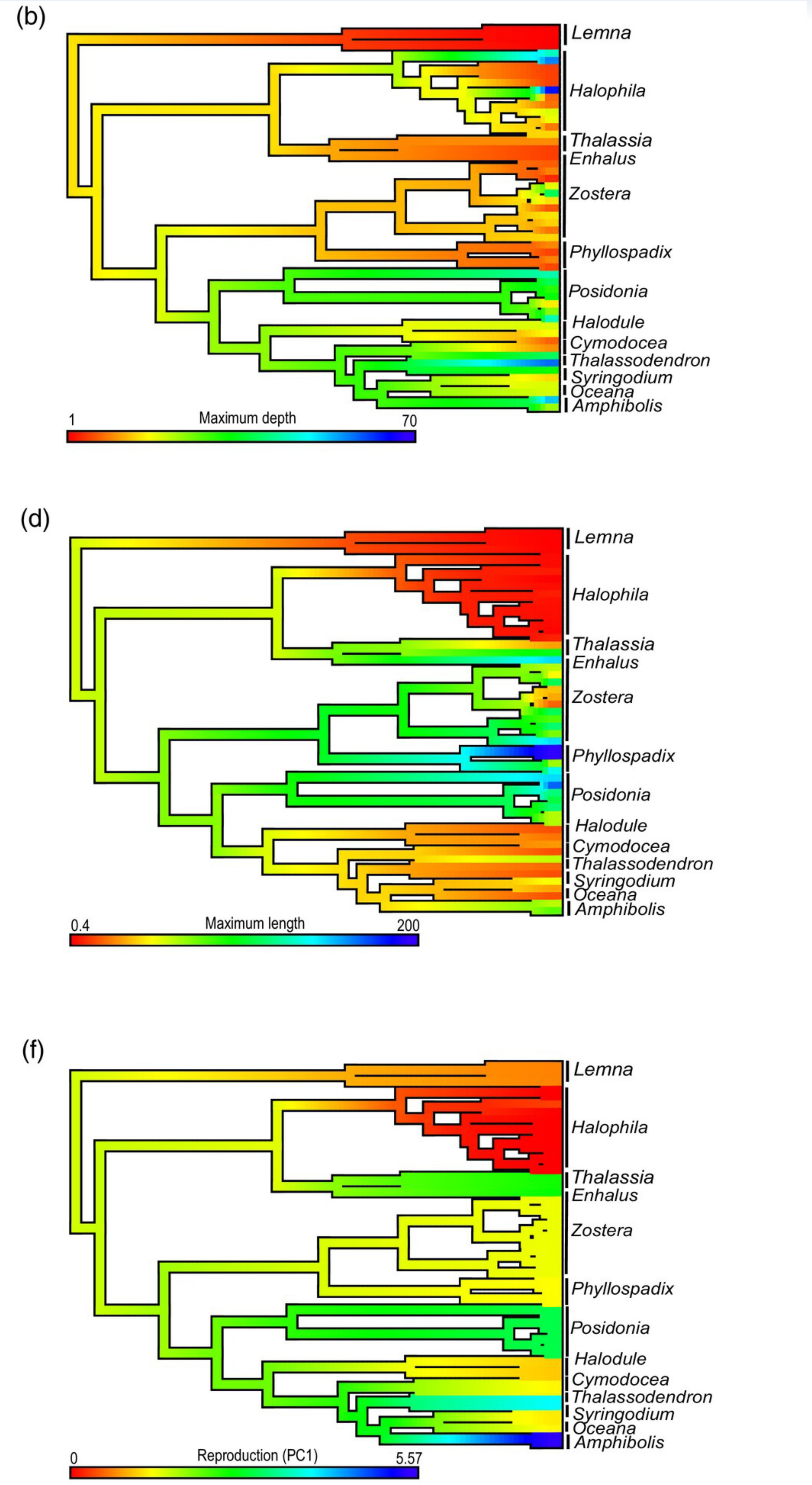
In which unit is measured trait variation?

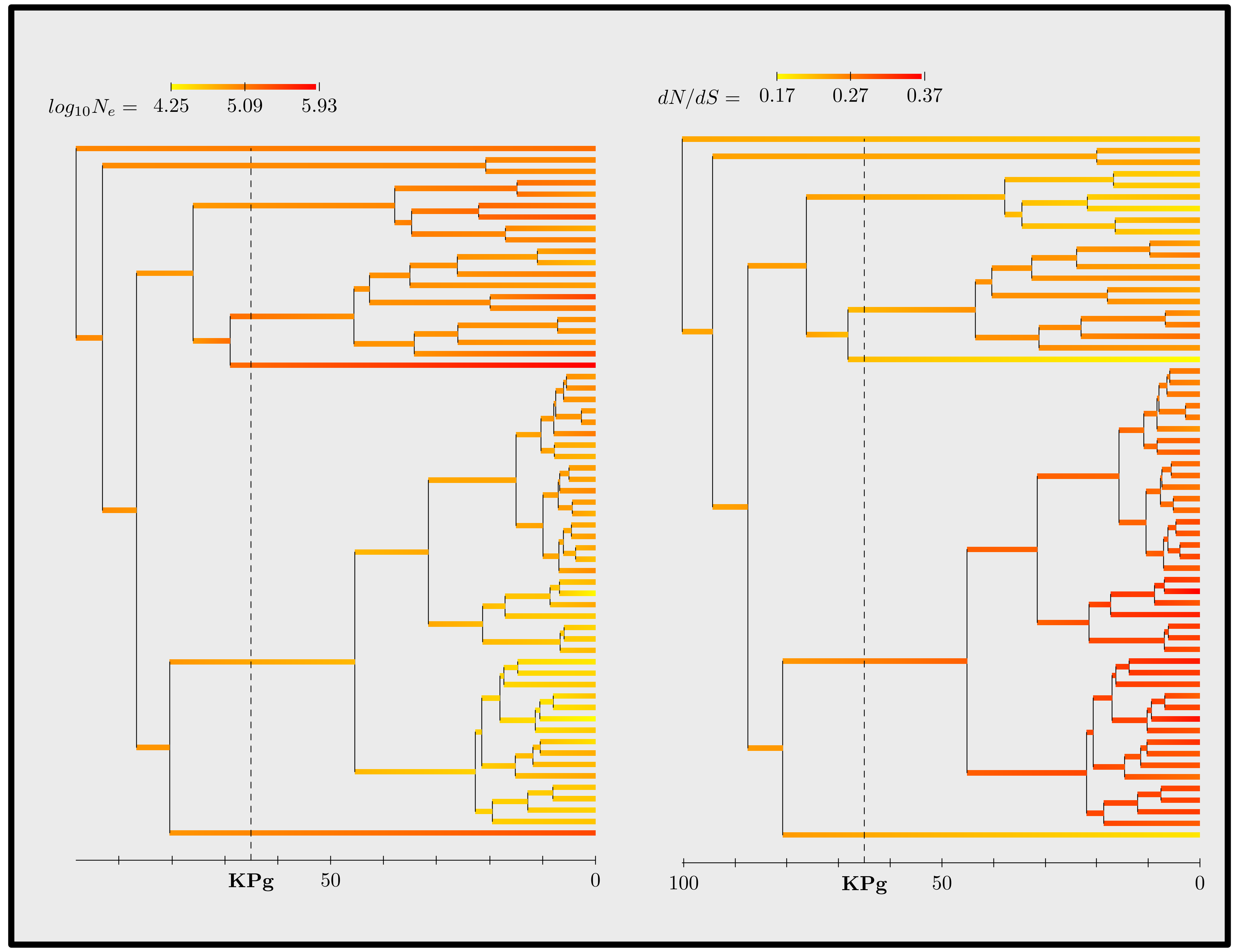
At the phylogenetic scale, in unit of time.

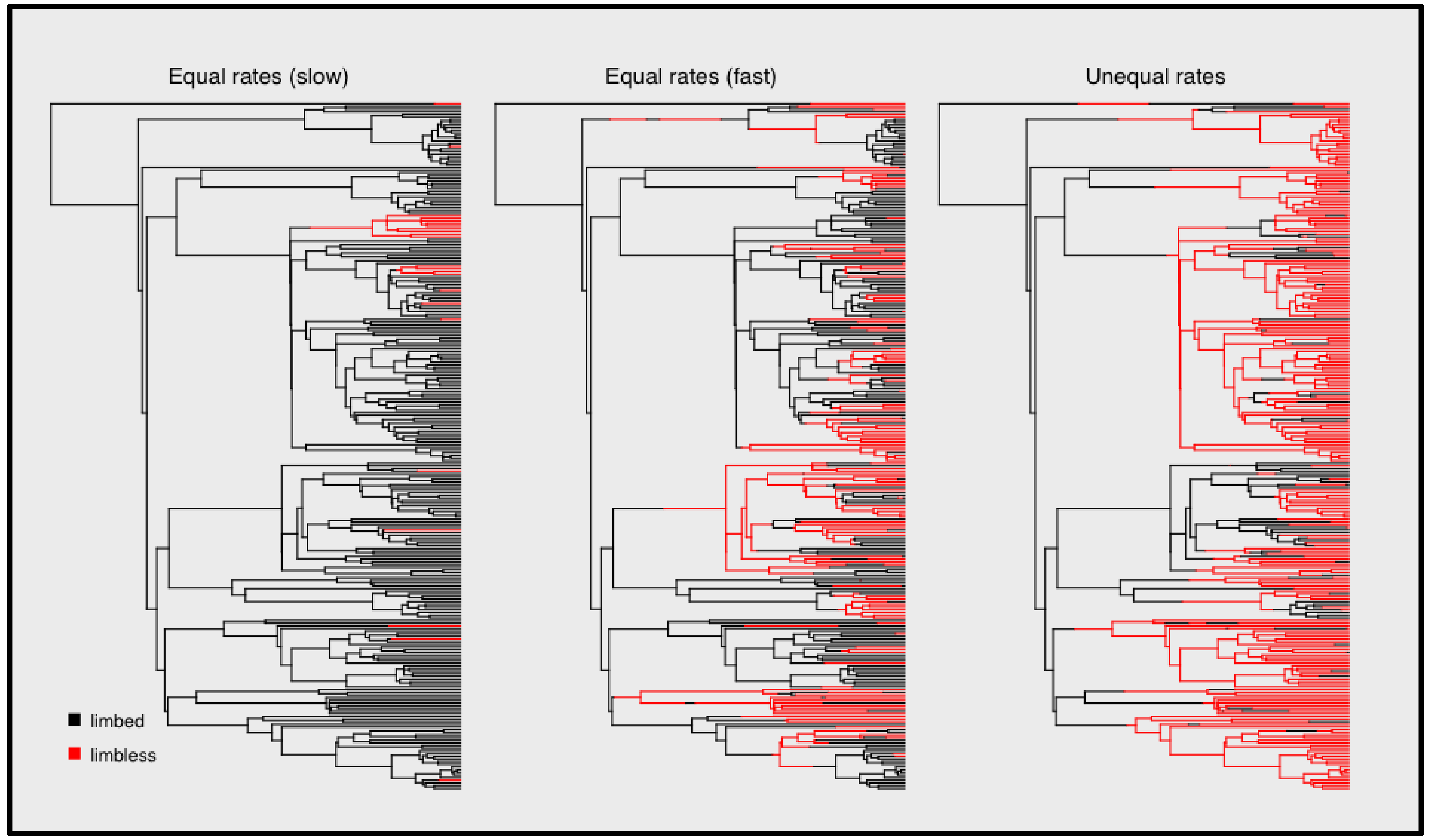






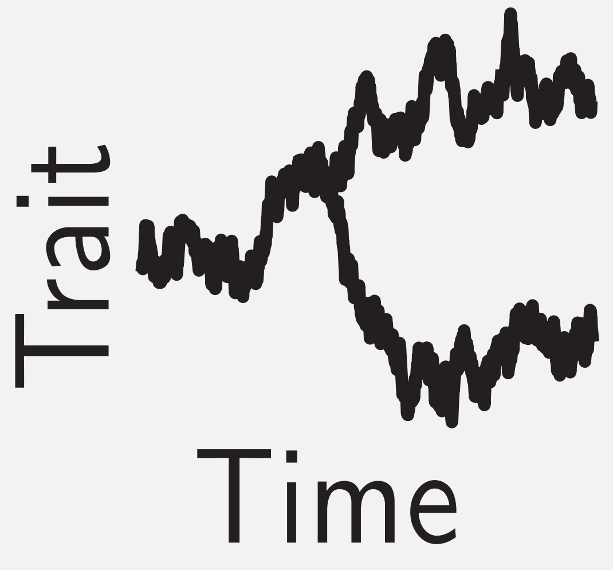






How to disentangle neutral and adaptive processes?

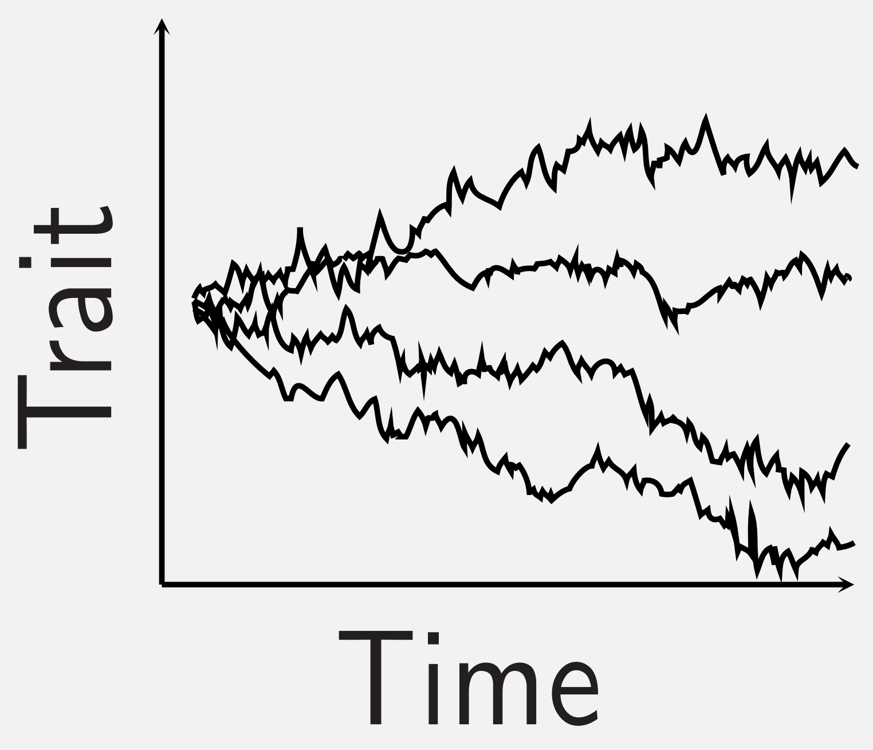
By fitting different models describing different evolutionary scenarios.

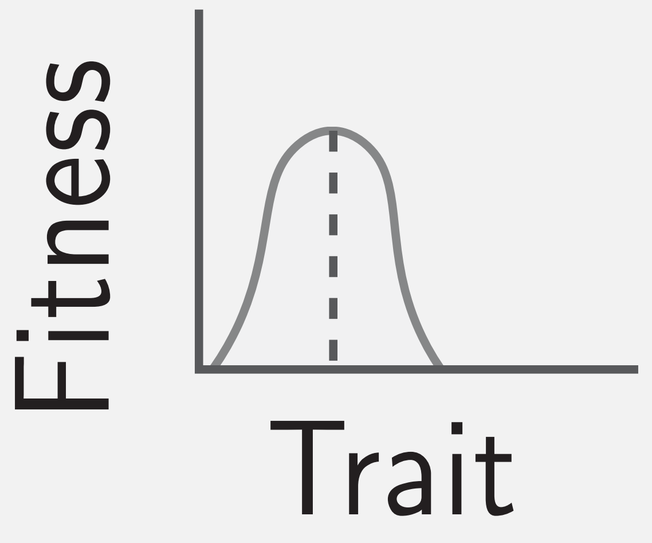


Neutral trait

Random walk of the trait.

Brownian process.

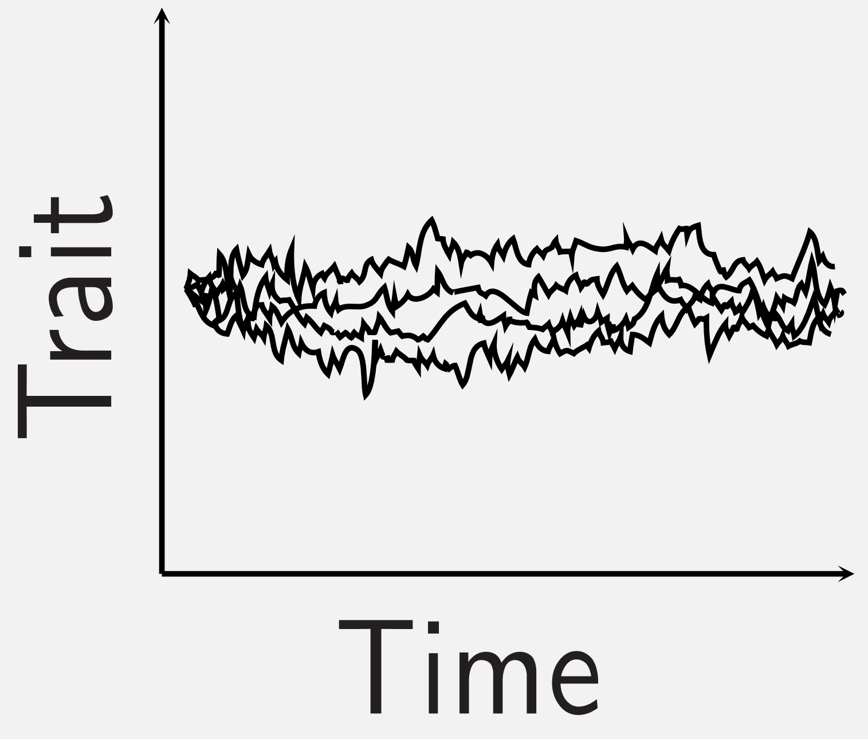


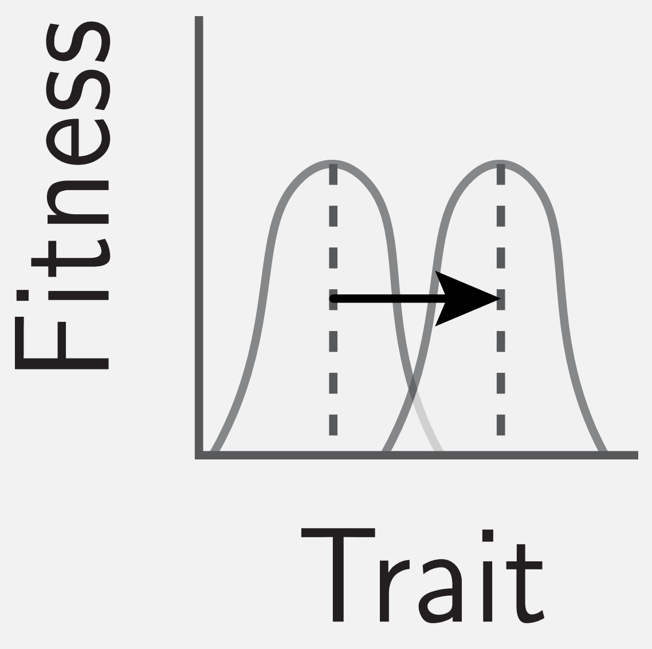


Stabilizing selection

An optimal value for the trait.

Ornstein-Uhlenbeck (OU) process.

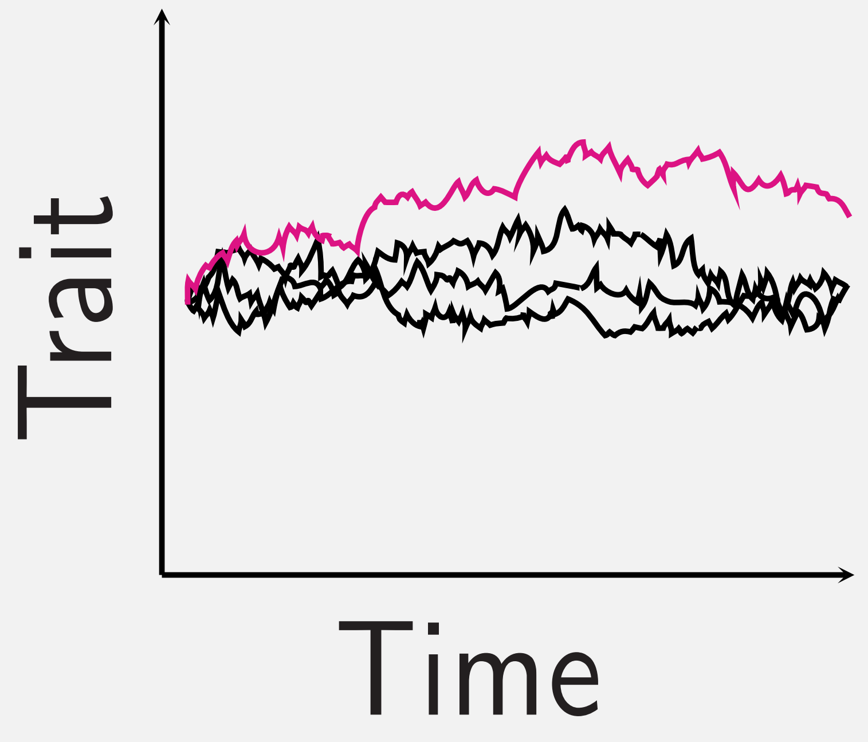




Changing optimum

Different optimal value for the trait, changing along the phylogeny.

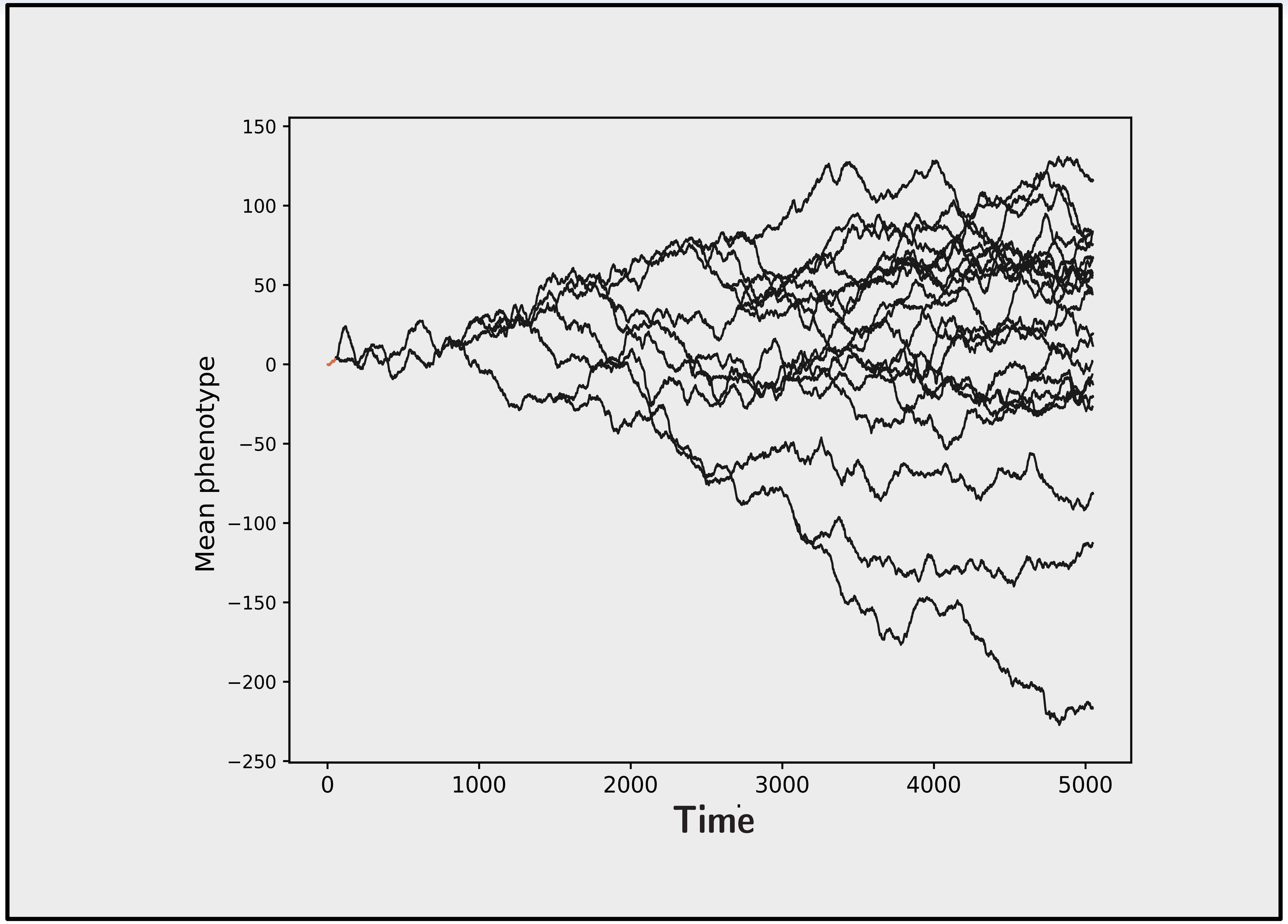
Shifted OU process.



Typically, the **best fit of a Brownian process** would conclude that the trait changes are due to **neutral evolution** or “genetic drift”.

But we have a problem.

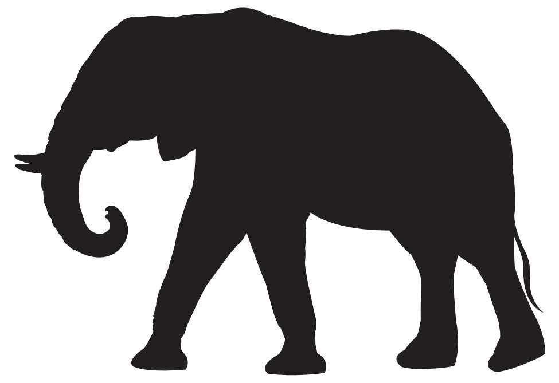
The best fit of a Brownian process is **NOT** a proof of neutral evolution.



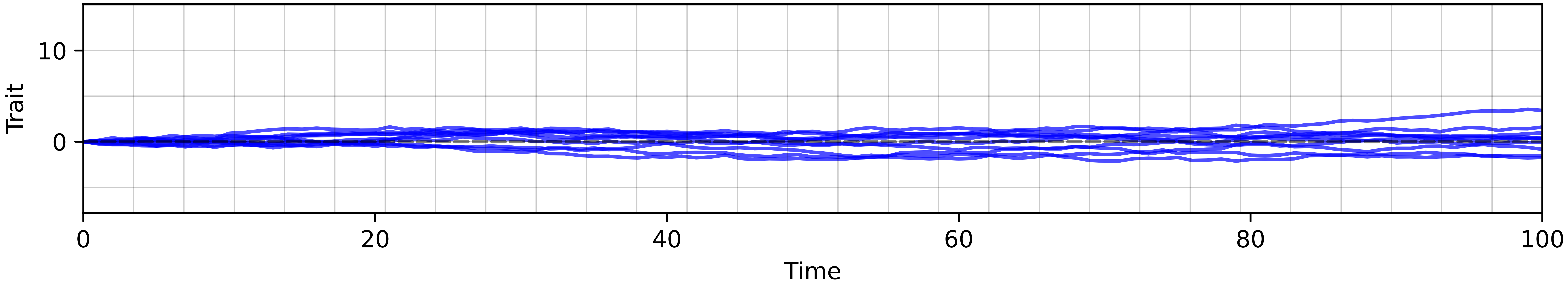
- A neutral trait will follow a Brownian process*. (*under some conditions).
- But a trait under a **constantly changing optimum** might follow a **Brownian process** too.

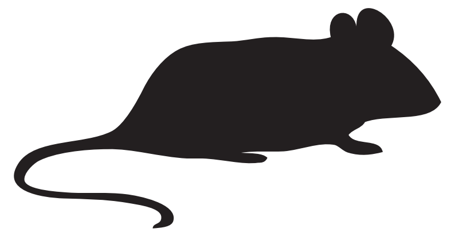
Is time the unit on which is measured the rate of a Brownian.

No, it is the number of generations (for a neutral trait).

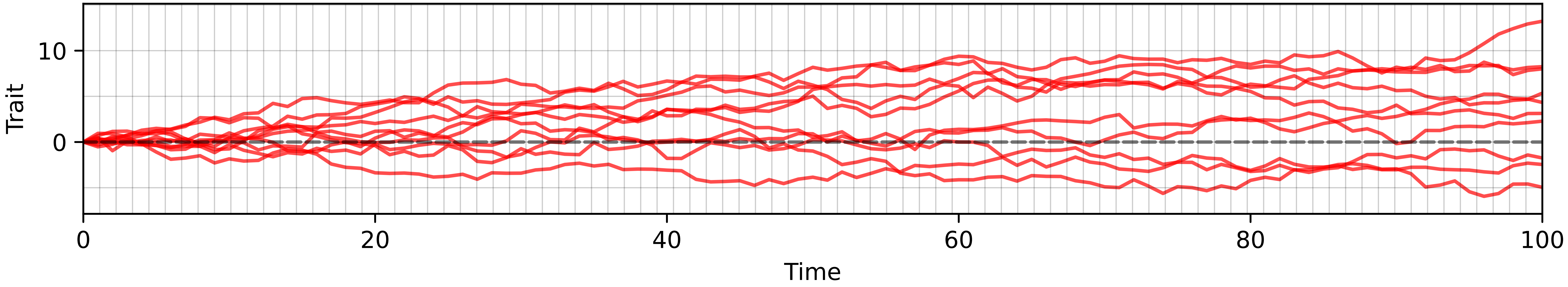


Long generation time.
Fewer generations.





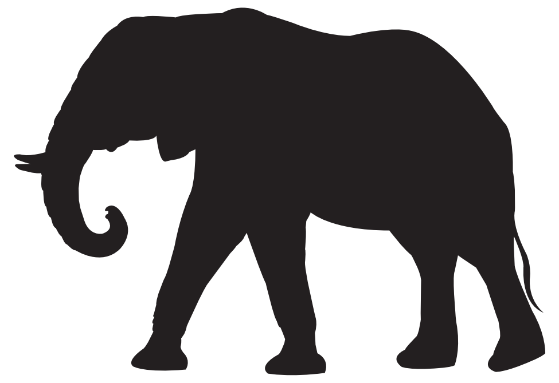
Short generation time.
More generations.



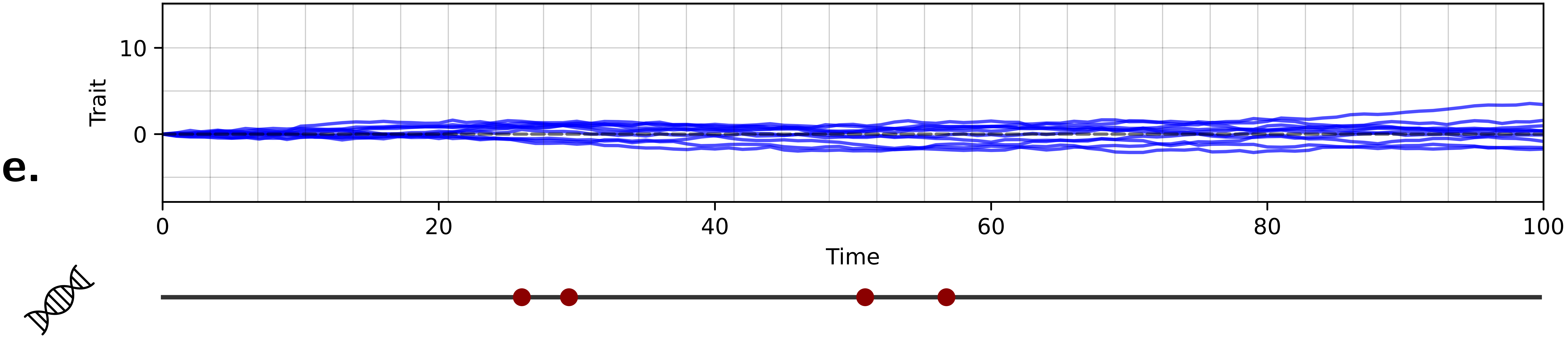
- A **neutral trait** will follow a Brownian process in unit of **generations**.

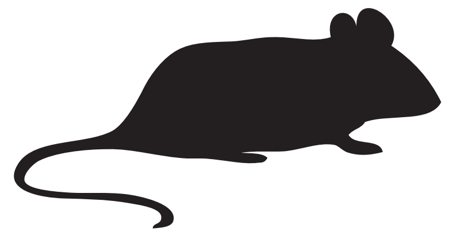
Is time the unit on which is measured the rate of a Brownian.

No, it is the number of generations (for a neutral trait).

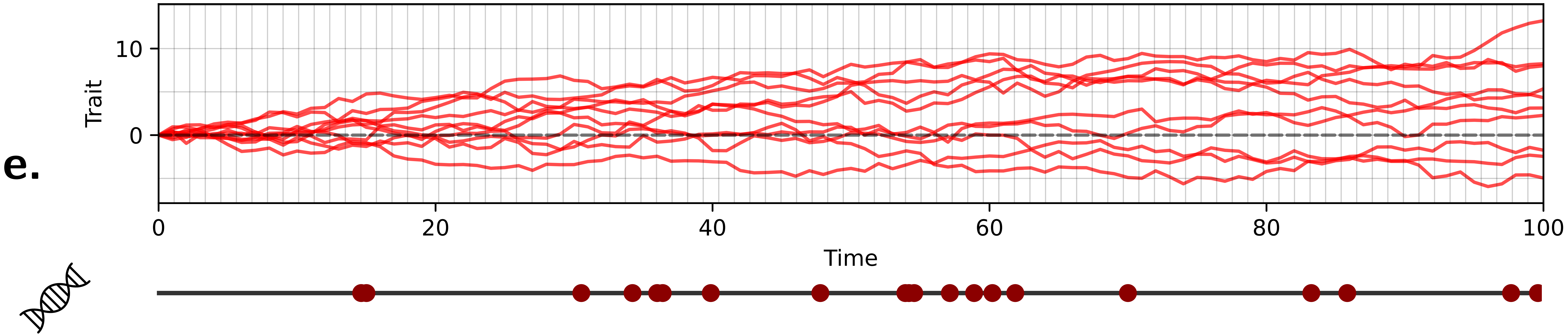


Long generation time.
Fewer generations.





Short generation time.
More generations.



- A **neutral trait** will follow a Brownian process in unit of **generations**.
- The **number of generations** is proportionnal to **sequence divergence** (🧬).

Can branch lenghts be proportionnal to the number of generations?

By using phylogram (number of substitutions) instead chronogram (time).

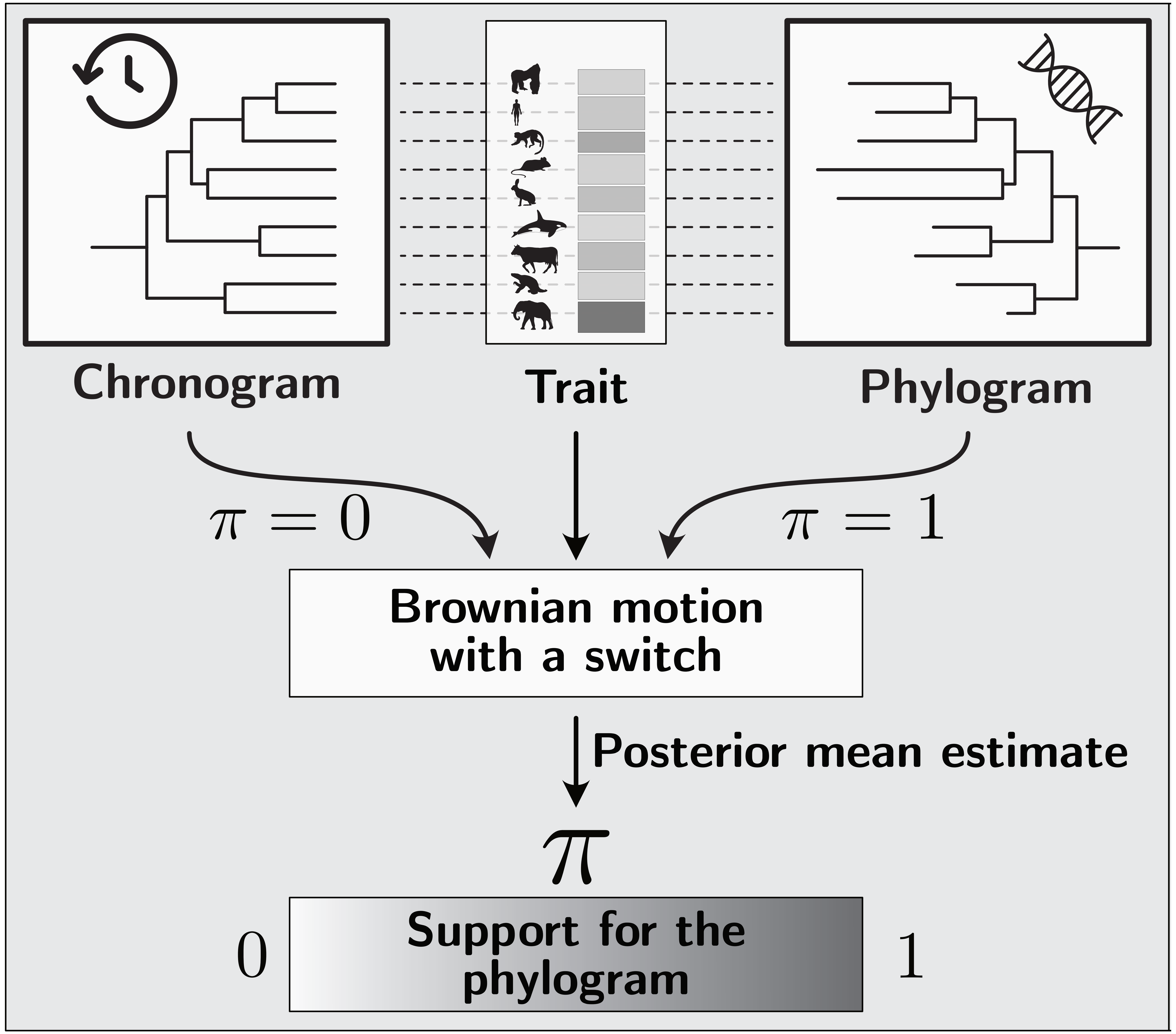
🕒: Chronogram in unit of time.

🧬: Phylogram in unit of expected substitutions per site.

A **neutral trait** will fit a Brownian process better a on a **phylogram** than on a chronogram.

Is a Brownian process best supported on a phylogram?

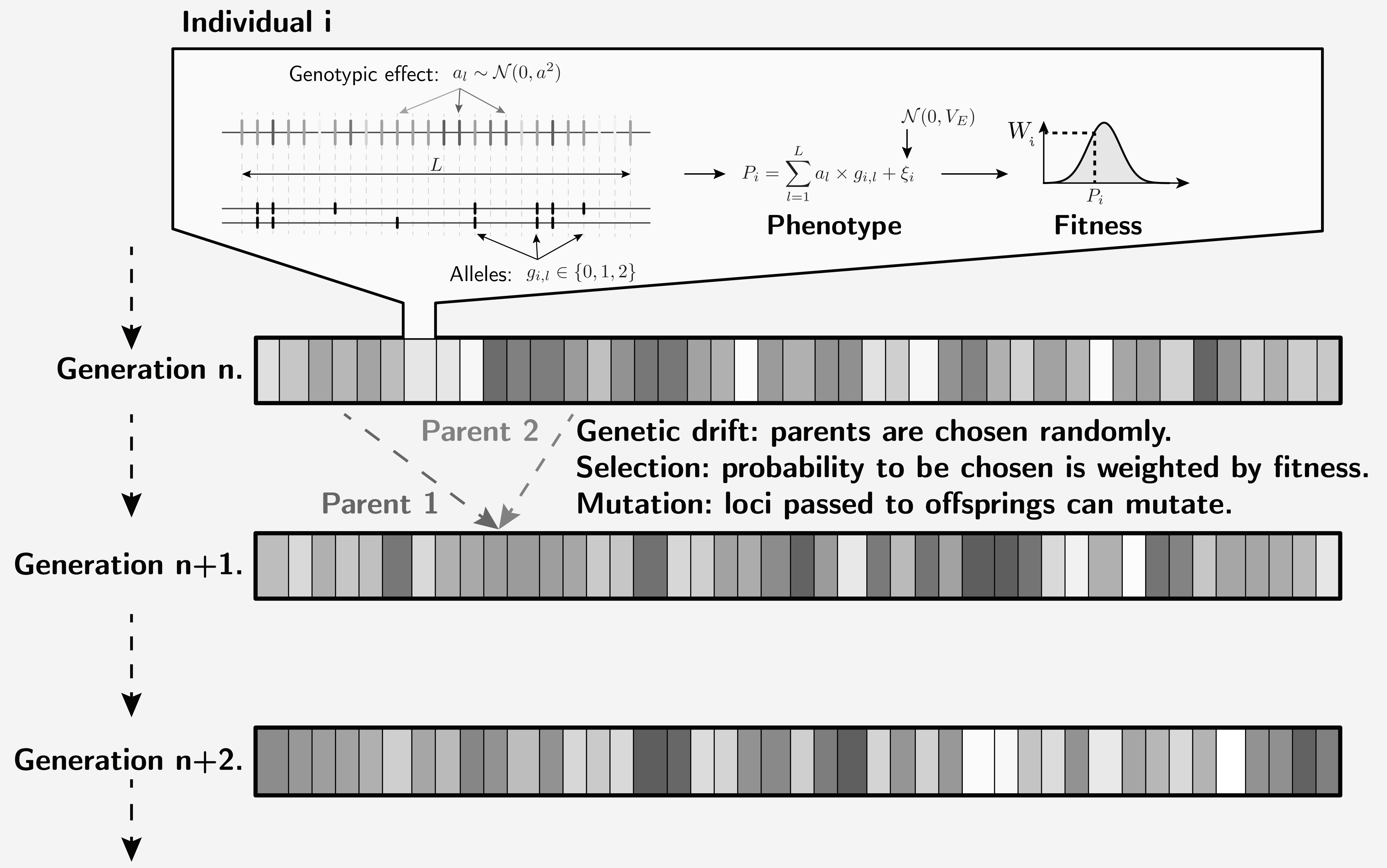
We can derive a model estimating the support for a phylogram.



Can we test this model estimating the support for a phylogram?

Using simulations for the different evolutionary scenarios.

A: Wright-Fisher simulator for a trait



Genetic drift: parents are chosen randomly.
Selection: probability to be chosen is weighted by fitness.
Mutation: loci passed to offsprings can mutate.

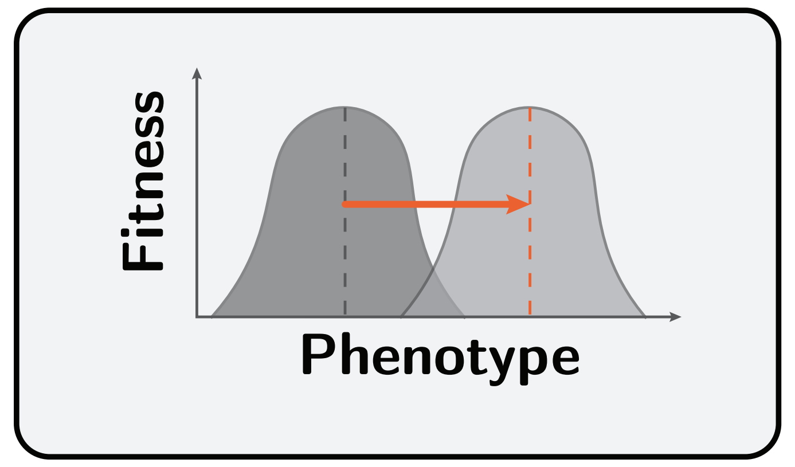
B: regime of selection

Neutral trait:

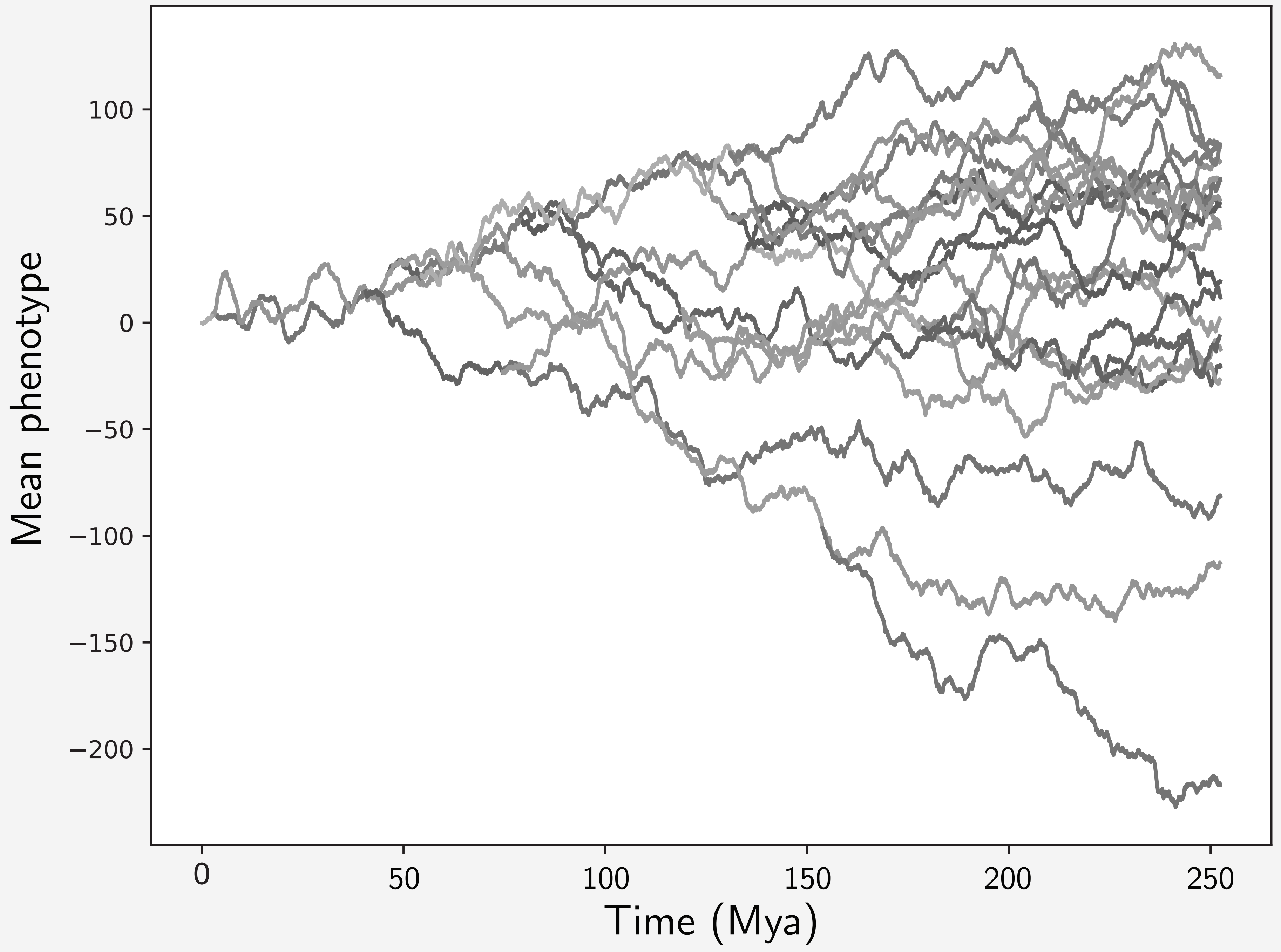
No fitness function.

Moving optimum or multiple optima:

An optimal value for the trait, changing along the phylogeny continuously, or a few times.

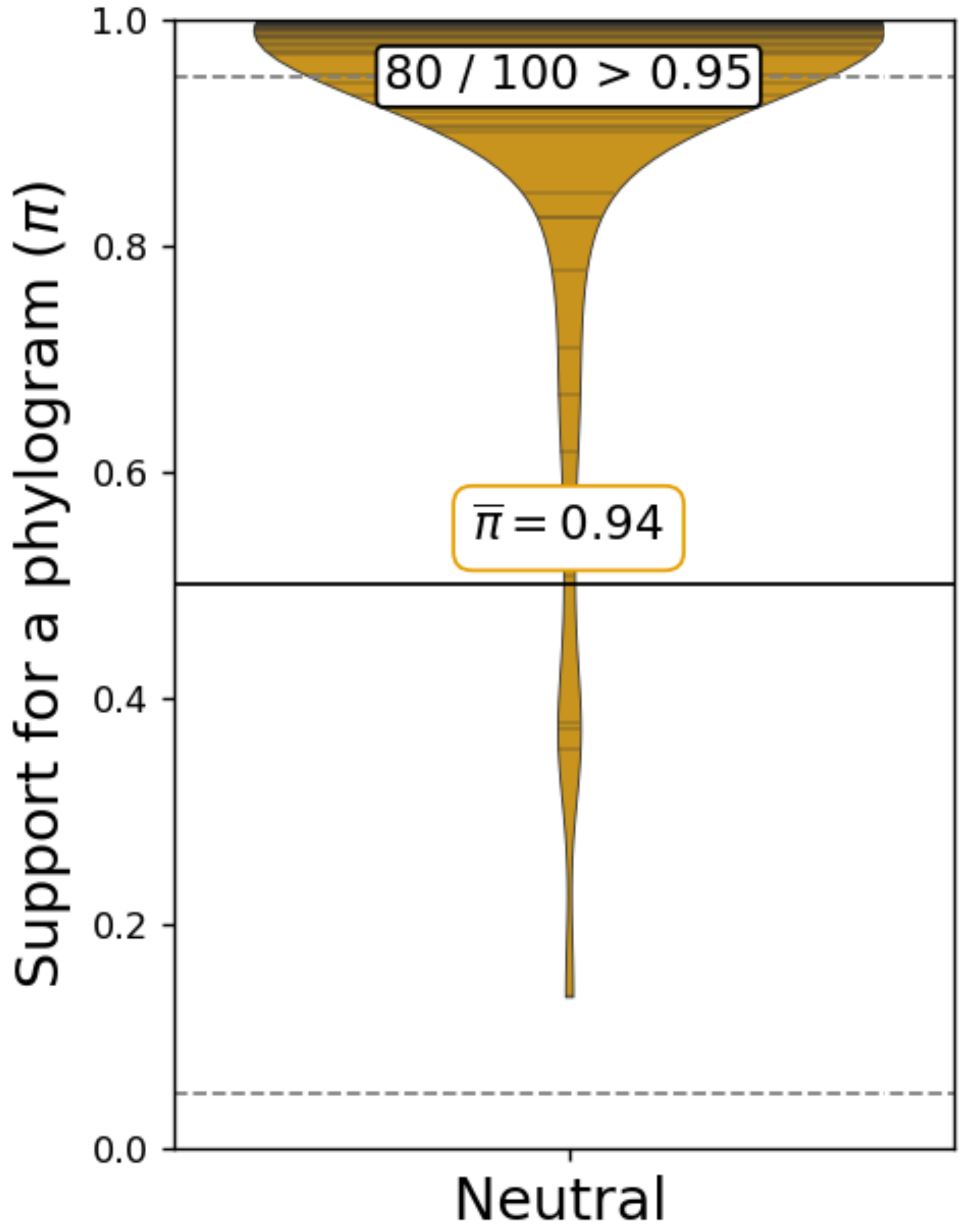


C: simulations along a phylogeny



Can the support for a phylogram be estimed?

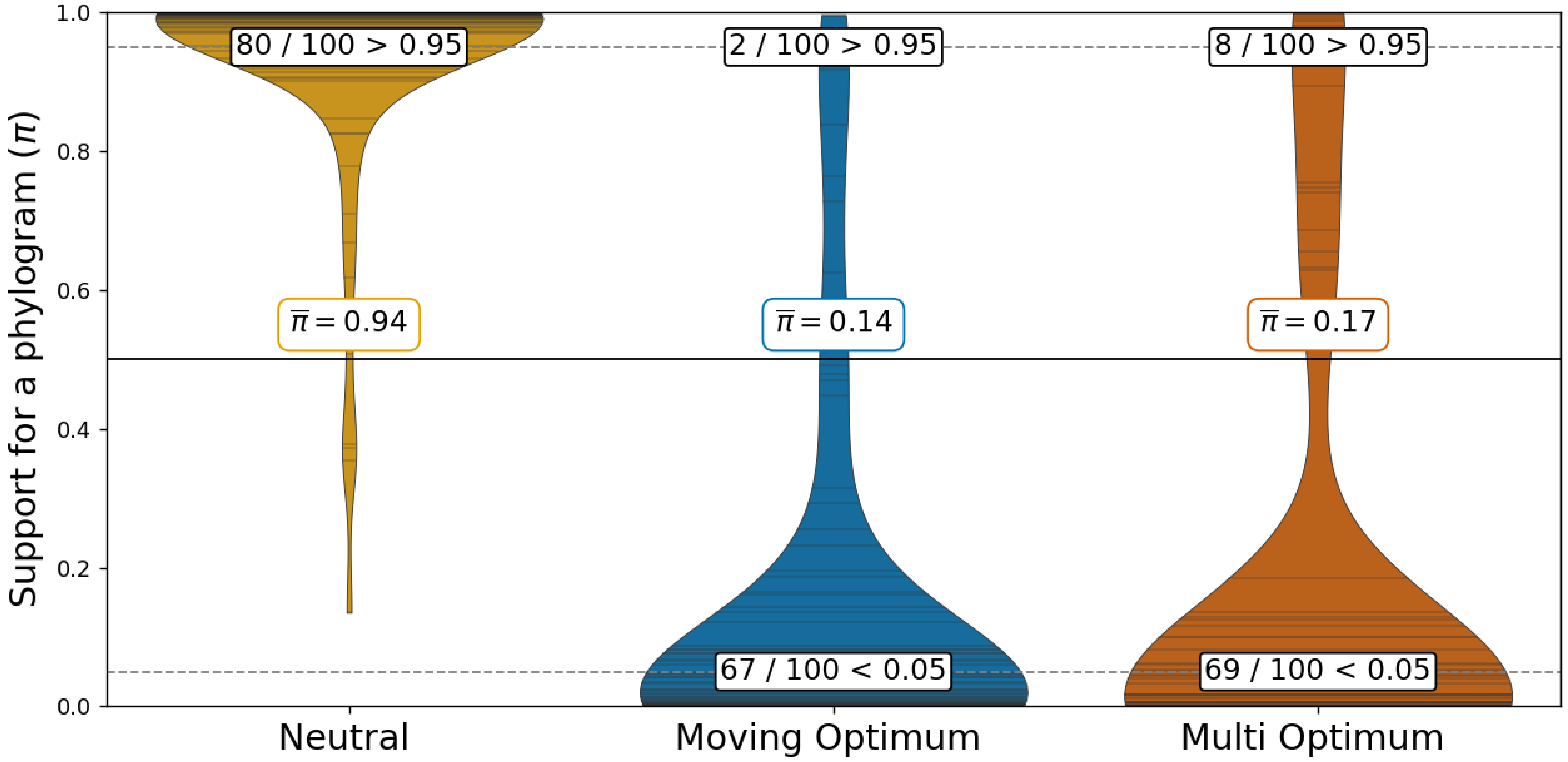
Yes, and it is high for trait simulated under neutral evolution.



- **Support for phylogram** is high if the trait is **neutrally evolving**.

Can the support for a chronogram be estimed?

Yes, and it is high for trait under selection.



- **Support for phylogram** is high if the trait is **neutrally evolving**.
- **Support for chronogram** is high if the trait is **tracking a changing optimum**.

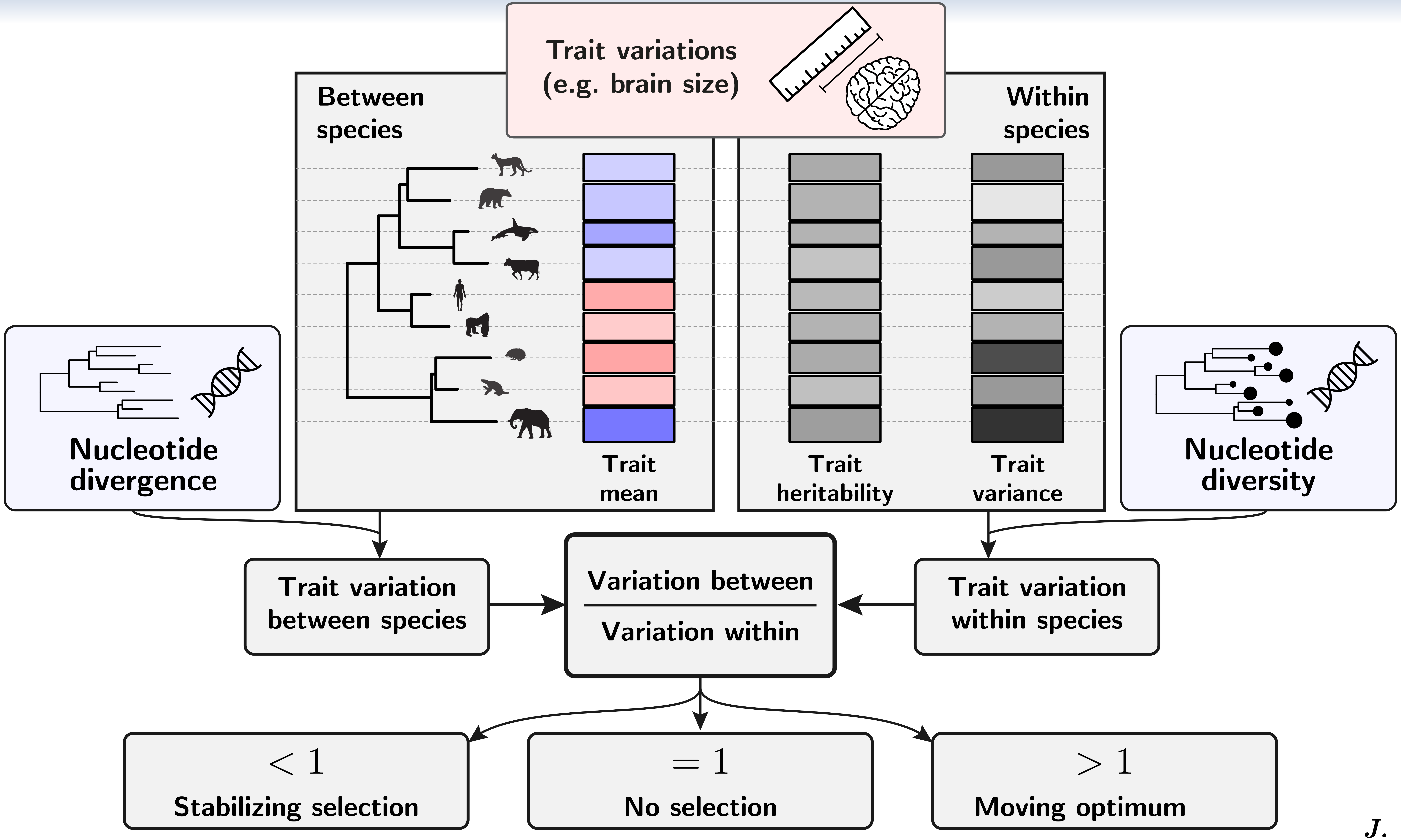
revbayes

Measuring morphological variation in unit of nucleotide changes to disentangle neutral and adaptive processes

- Changes of a trait tracking a changing optimum is better supported on a chronogram (🕓).
- Changes of a neutral trait is better supported on a phylogram (🧬).
- If one **claims that a trait is neutrally evolving**, this should be assessed by comparing the **support for a phylogram** (🧬) **over a chronogram** (🕓).
- Can we do better and use both between and within species variation?

Can we derive a neutrality index using between and within species variation?

By normalising trait variation using nucleotide changes.



Trait variations (e.g. brain size)

Between species

Within species

Trait mean

Trait heritability

Trait variance

Nucleotide divergence

Nucleotide diversity

Trait variation between species

Trait variation within species

$$\frac{\text{Variation between}}{\text{Variation within}}$$

< 1
Stabilizing selection

$= 1$
No selection

> 1
Moving optimum

Latrille *et al.*
J. Evol. Biol., 2024

How to derive formally a neutrality index?

Similar to dN/dS ratio, or Qst-Fst, but for a trait at the phylogenetic scale.

Within species variation:

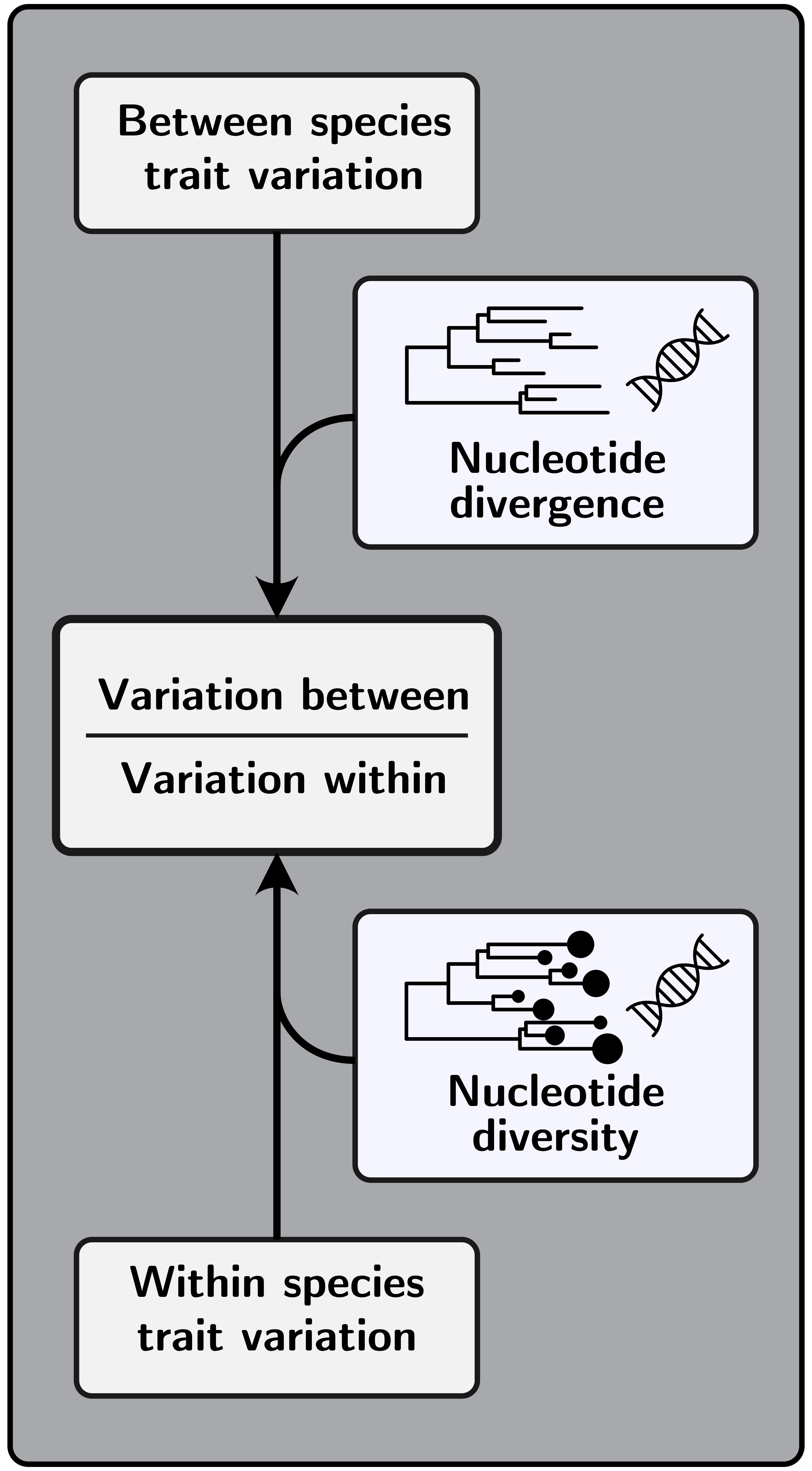
- V_P: phenotypic variance.
- h^2: heritability for the trait.
- π: mutations per site between two haplotypes.

Between species variation:

- $\text{cov}\left(\bar{P}_i, \bar{P}_j\right)$: covariance in mean trait value between a pair of species.
- d: shared nucleotide divergence between a pair of species.

$$\begin{cases} \sigma^2_{\text{W}} \overset{\text{def}}{=} \dfrac{V_P \cdot h^2}{\pi} = \dfrac{\cancel{4N_{\text{e}}} \cdot \cancel{\mu} \cdot \sigma^2_{\text{M}}}{\cancel{4N_{\text{e}}} \cdot \cancel{\mu}} = \sigma^2_{\text{M}}, \\ \sigma^2_{\text{B}} \overset{\text{def}}{=} \dfrac{\text{cov}\left(\bar{P}_i, \bar{P}_j\right)}{4d} = \dfrac{\cancel{4t} \cdot \cancel{\mu} \cdot \sigma^2_{\text{M}}}{\cancel{4t} \cdot \cancel{q}} = \sigma^2_{\text{M}}. \end{cases} \implies \boldsymbol{\sigma^2_{\text{B}} / \sigma^2_{\text{W}} = 1}.$$

- μ: mutation rate per generation.
- q: substitution rate per generation.
- N_{e}: effective population size.
- σ^2_{M}: effect on the trait per mutation.



Latrille *et al.* (*J. Evol. Biol.*, 2024)

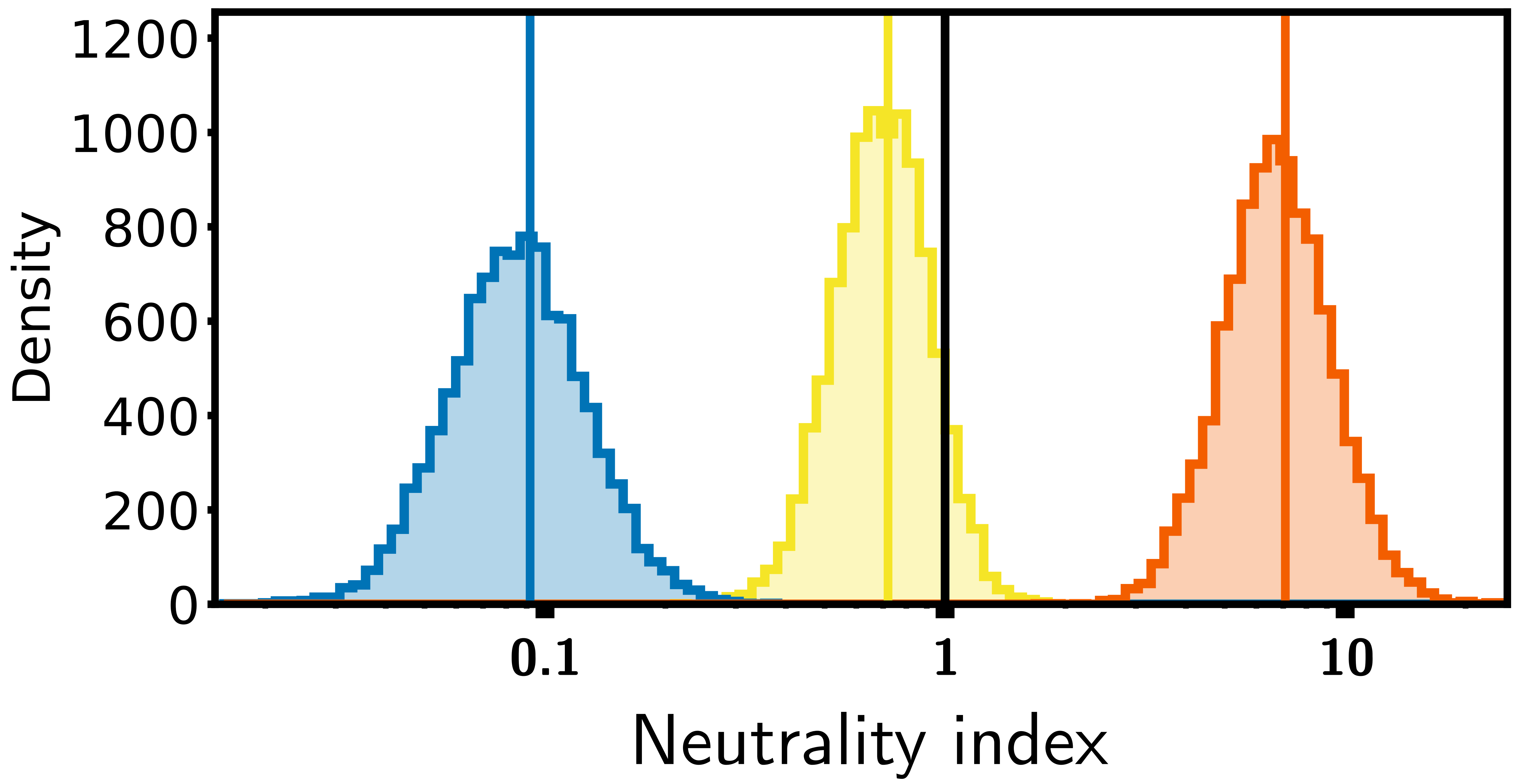
Can we test such neutrality index?

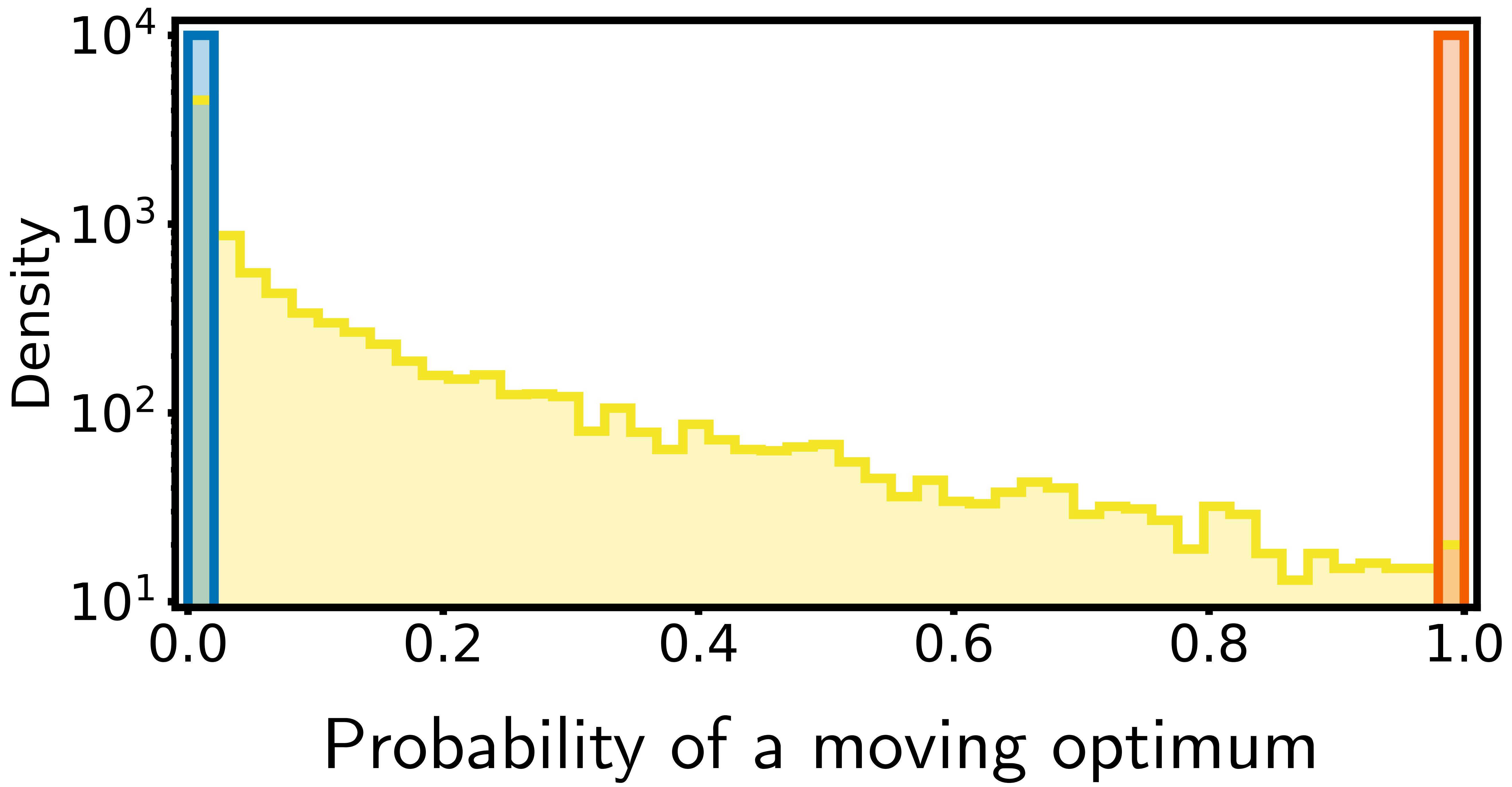
Using simulation under different evolutionary scenarios.

🟦 **Stabilizing selection**
An optimal value for the trait.

🟨 **Neutral trait**
No fitness function.

🟧 **Moving optimum**
An optimal value for the trait, changing randomly.





- A neutrality index disentangling neutral and adaptive processes acting on trait.

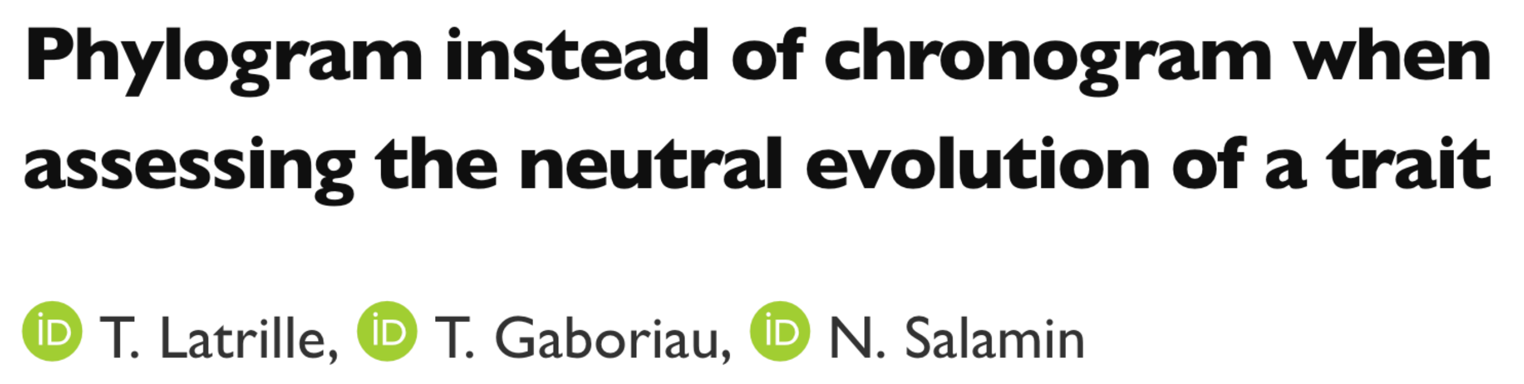
Latrille *et al.* (*J. Evol. Biol.*, 2024)

Nucleotide changes allow disentangling neutral and adaptive processes by contrasting trait variation:

- in unit **of nucleotide divergence** instead of **time.**
- at the between species level (**divergence**) and within species (**diversity**).

Théo Gaboriau
Nicolas Salamin

Computational Phylogenetics Group



Phylogram instead of chronogram when assessing the neutral evolution of a trait

T. Latrille, T. Gaboriau, N. Salamin

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Detecting diversifying selection for a trait from within and between-species genotypes and phenotypes

T Latrille, M Bastian, T Gaboriau, N Salamin

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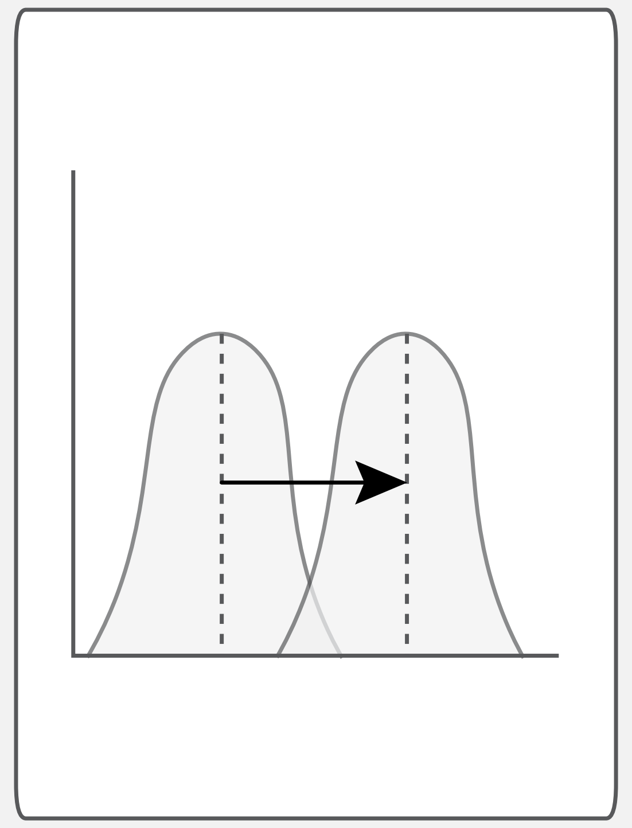
What is the expected rate of evolution for a neutral trait?

Can we derive a test of selection

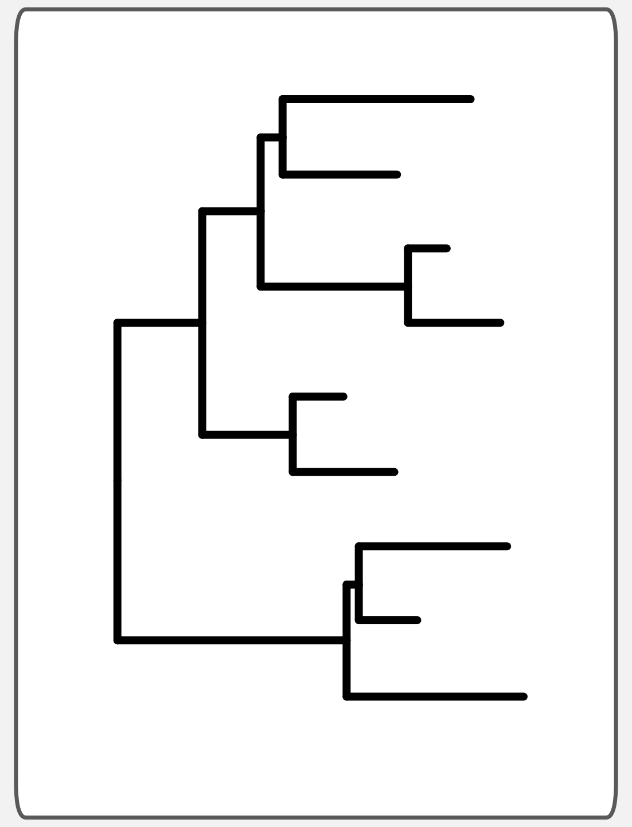
Quantitative-genetics across populations.

→ How to adapt Q_{ST}-F_{ST} methods across species?



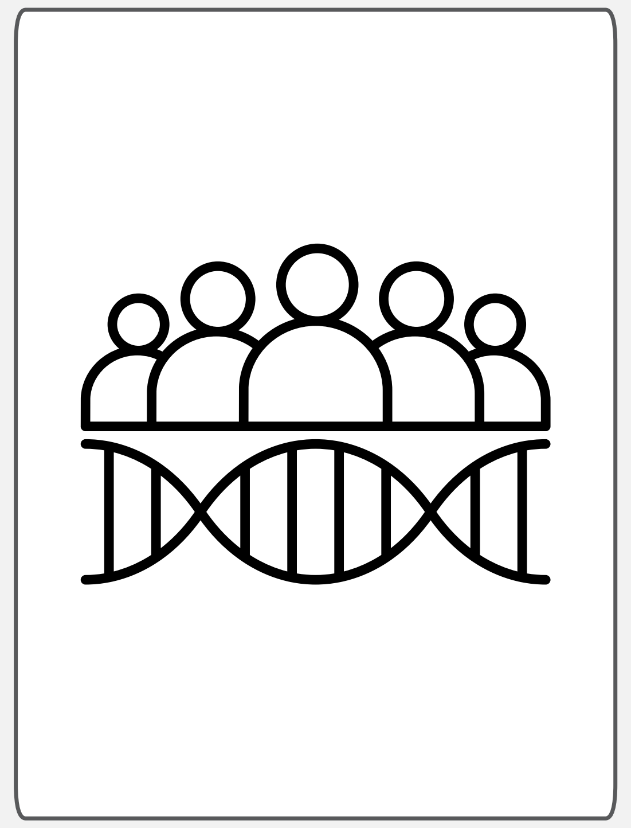
Phylogenetic DNA evolution.

→ How to a derive a d_N/d_S ratio but for a trait instead of protein coding DNA sequences?



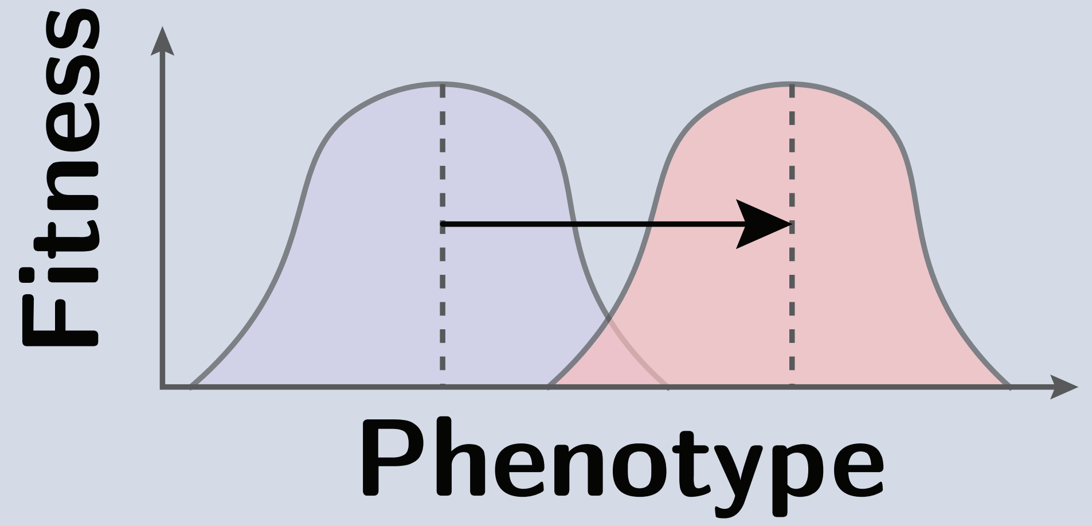
Contrast polymorphism & divergence.

→ How to adapt McDonald & Kreitman test ($d_N/d_S>p_N/p_S$) for trait changes along a phylogeny?

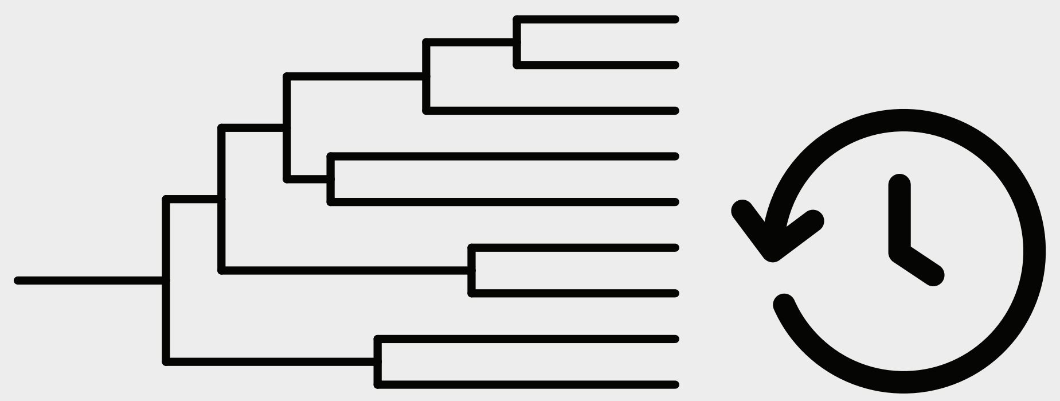


Simulation

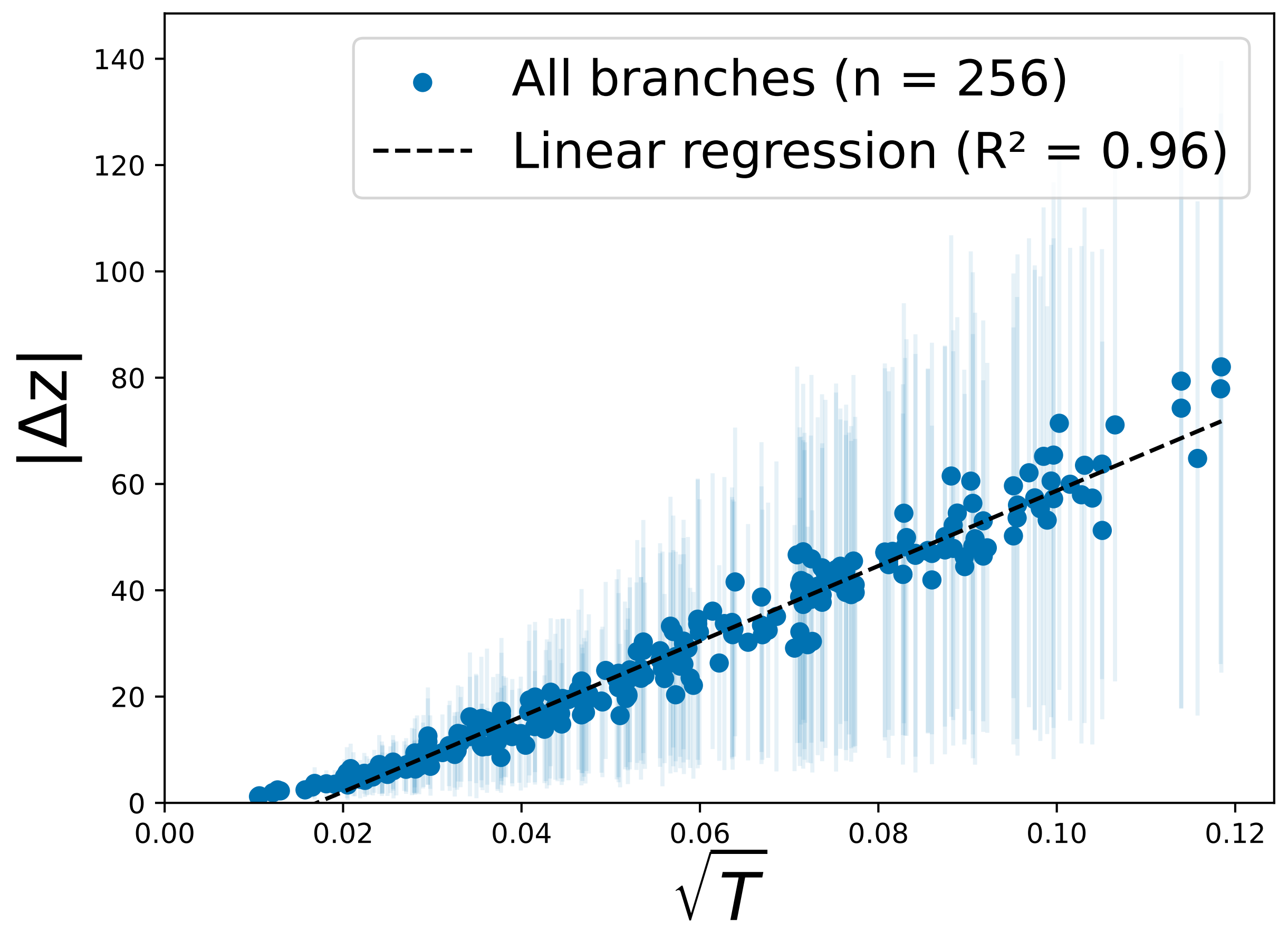
Tree

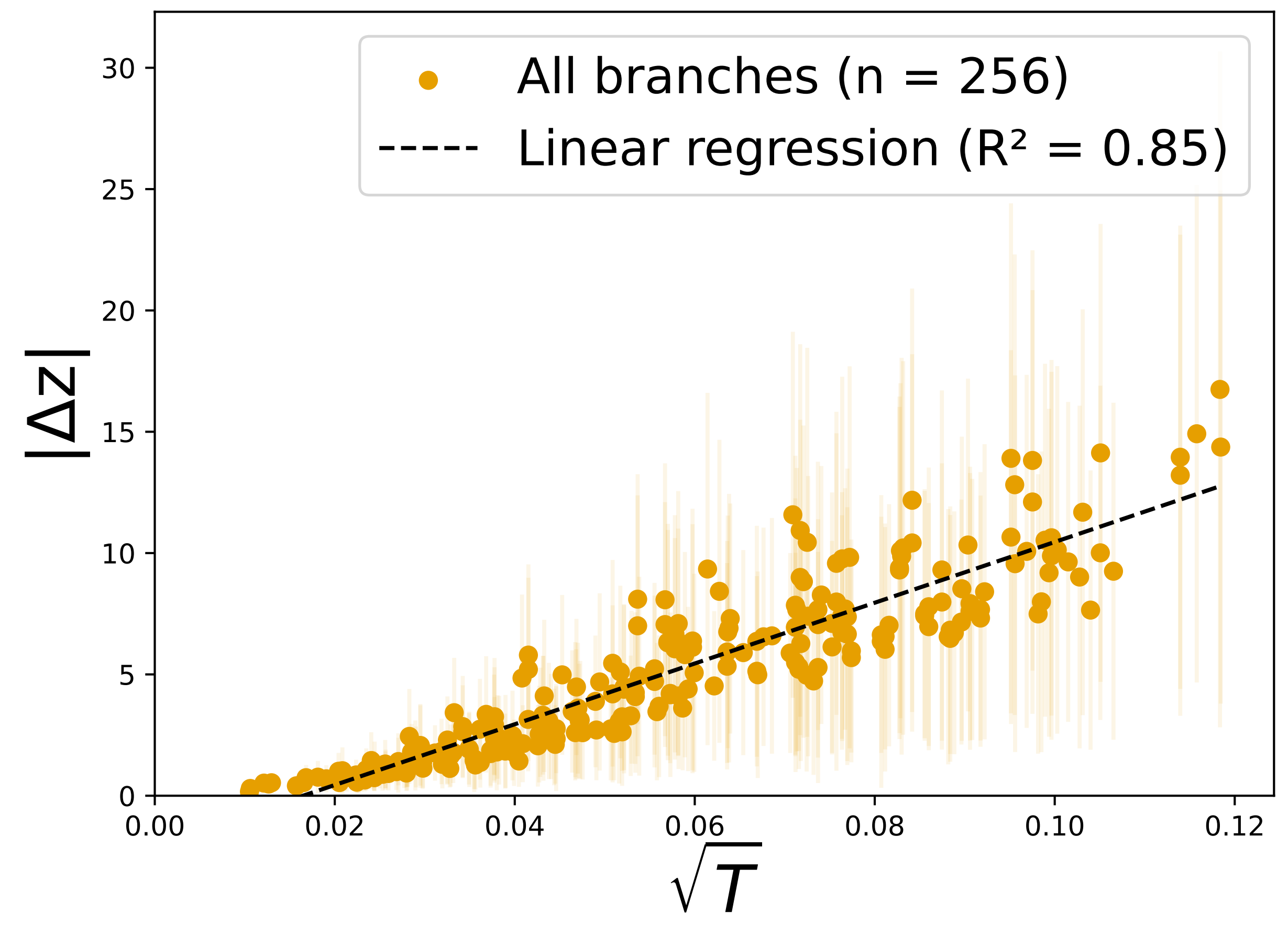


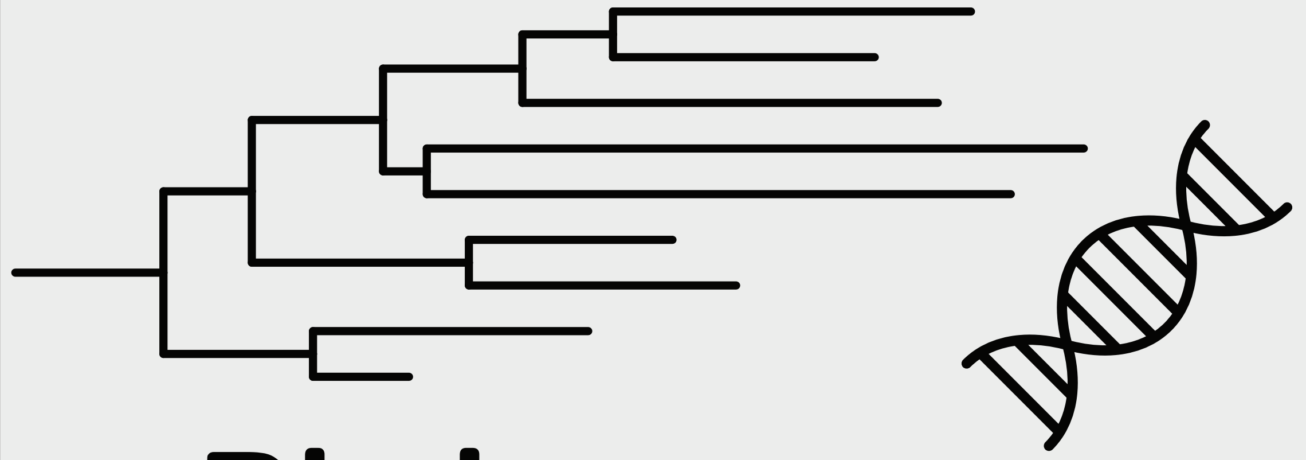
Neutral trait encoded by many loci



Chronogram







Phylogram