Neutral evolution in a type space

Daniel Lawson
Bioinformatics and Statistics Scotland

Work with
Henrik Jeldtoft Jensen,
Imperial College London

Neutrality as a null model

- Neutrality is a "null model" for evolution...

- But provides a rich behaviour of its own.

- Accurate description requires description at individual level…

- Because a "species" is not always well defined.

- A distribution of types is a better representation.

The Neutral Model

- Assume that all individuals are 'equal'
    - Valid for Phenotypes that do not have function
    - Genotype not coding for protein synthesis (12% of Human DNA is variable! *Redon et al. Nature. doi:10.1038/nature05329*)
  - Each individual has the same probability to die (p_k), or give birth (p_b), in a time step
    - For simplicity, assume the total population (N) has reached equilibrium ($p_k = p_b$)

- Reproduction is asexual and imperfect – small changes can occur

A neutral evolution model

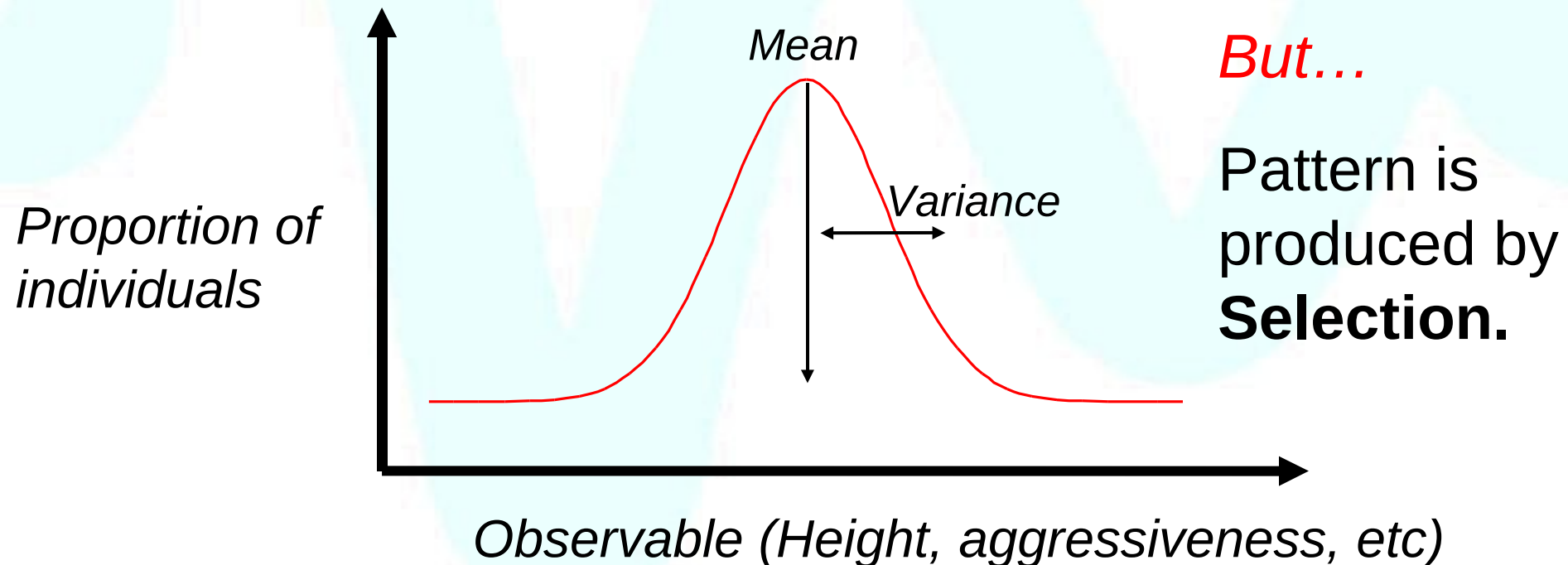- Consider N individuals each labeled by a type position:

TIMESTEP:

- Pick an individual (from N) and mark it to die.
- Pick an individual (from N) and copy it. With probability p_m Mutate to a similar type.
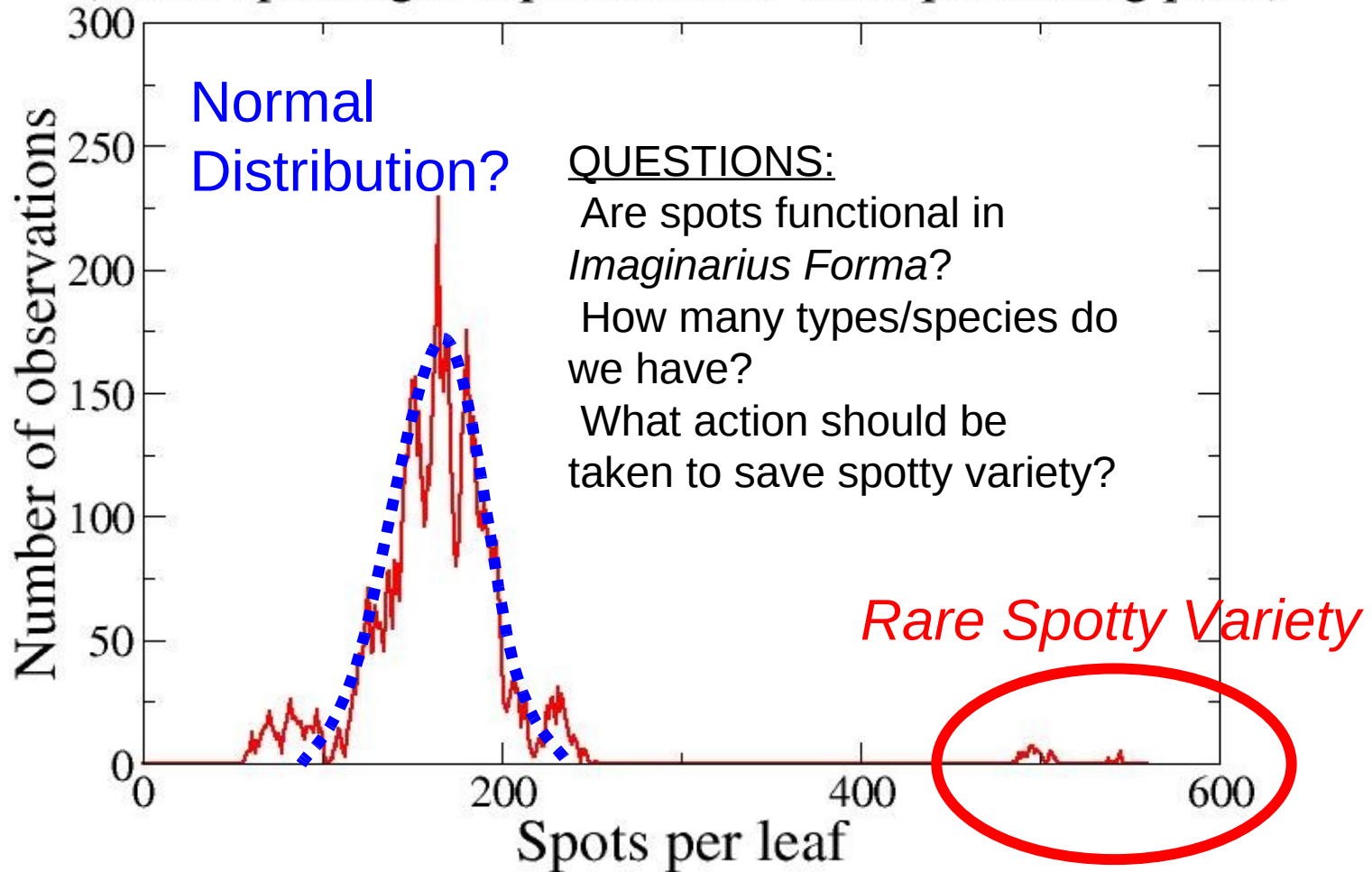- Kill the marked individual.
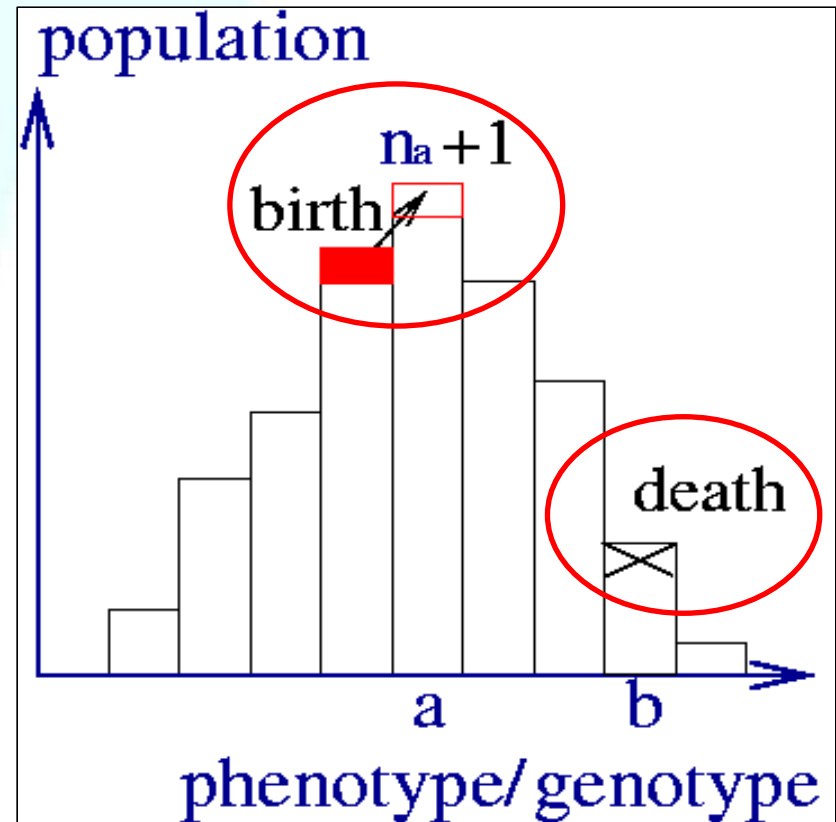
Phenotype Distribution

- Consider 1 dimensional case: mutations can be either to the left or to the right.
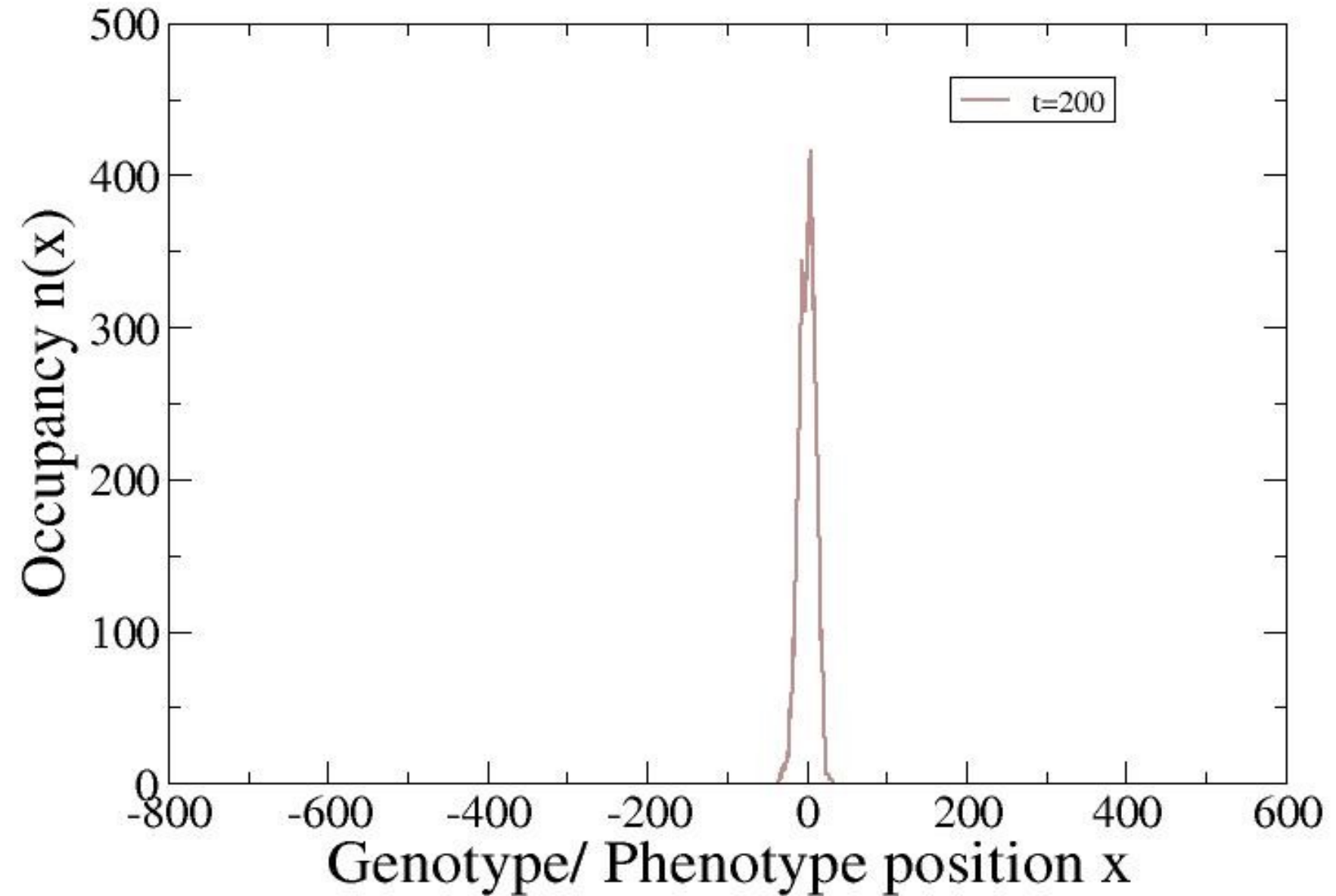
- Expected pattern is a Normal Distribution:

Mean

Variance

Proportion of individuals

But…

Pattern is produced by **Selection.**

Observable (Height, aggressiveness, etc)

Test Problem

Observations of number of spots per leaf of *Imaginarius Forma*
(Made up thought experiment for a self pollinating plant)

Normal
Distribution?

QUESTIONS:
 Are spots functional in
Imaginarius Forma?
 How many types/species do
we have?
 What action should be
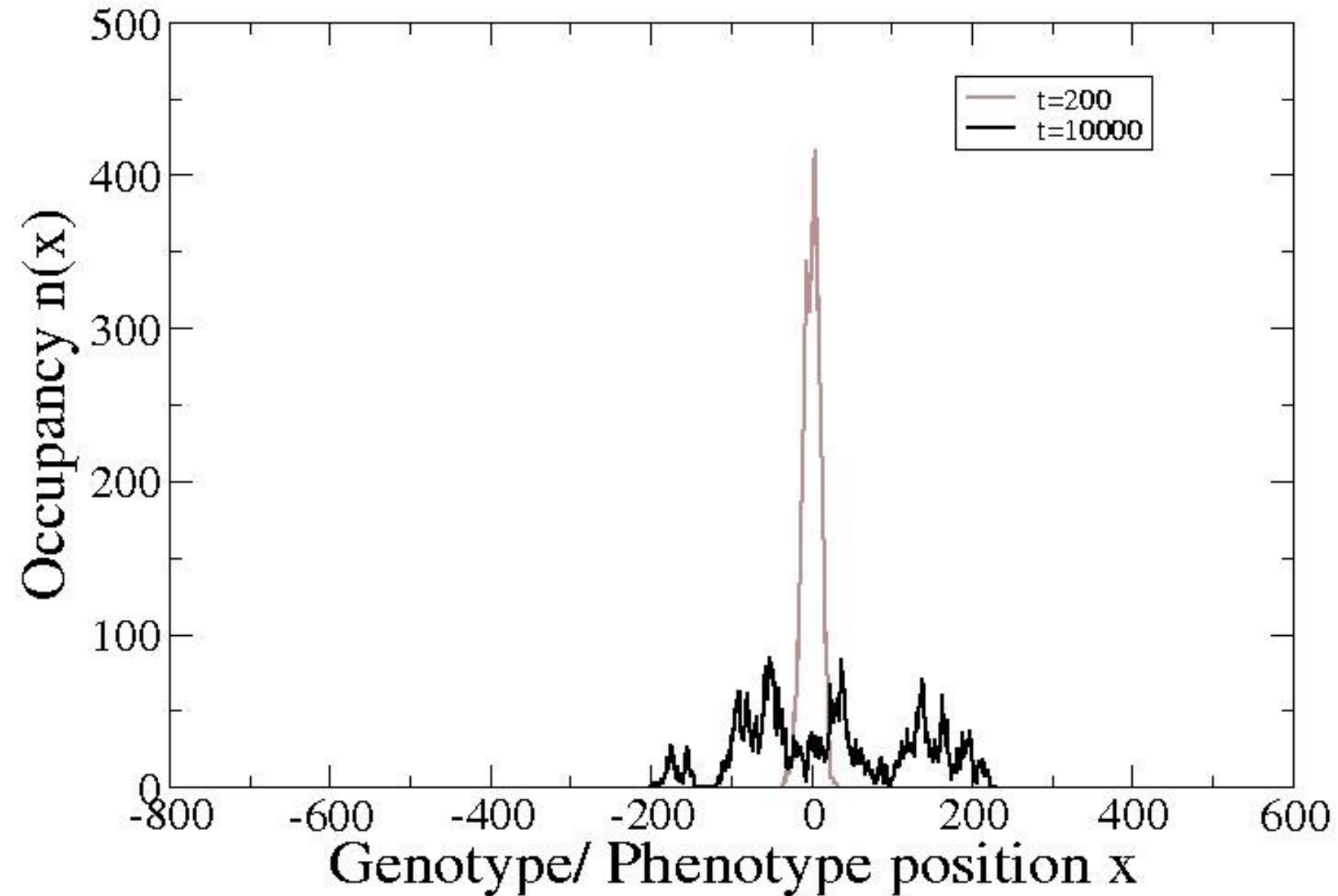taken to save spotty variety?

Rare Spotty Variety

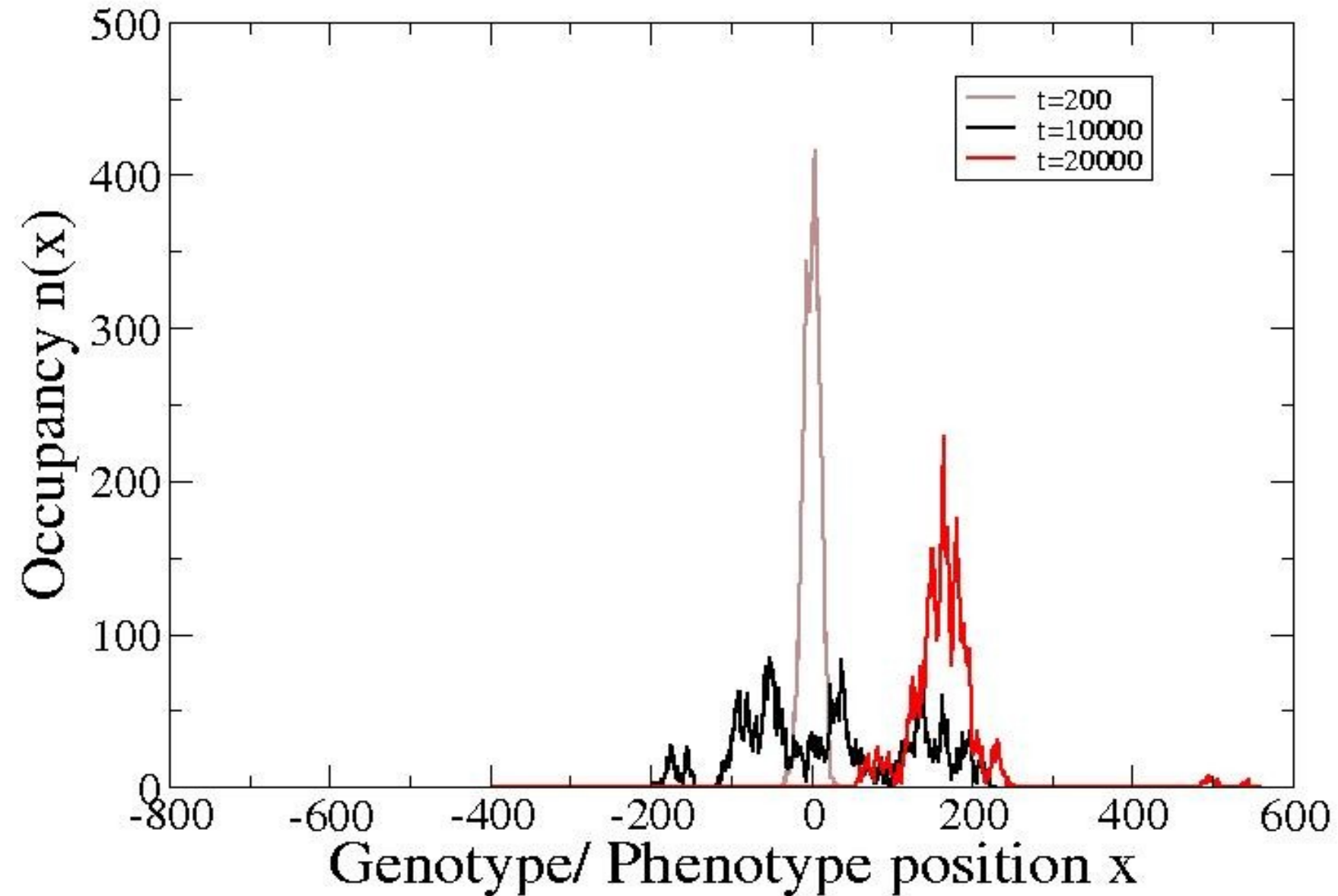# The behaviour of the neutral phenotype model

Evolution of 10000 individuals
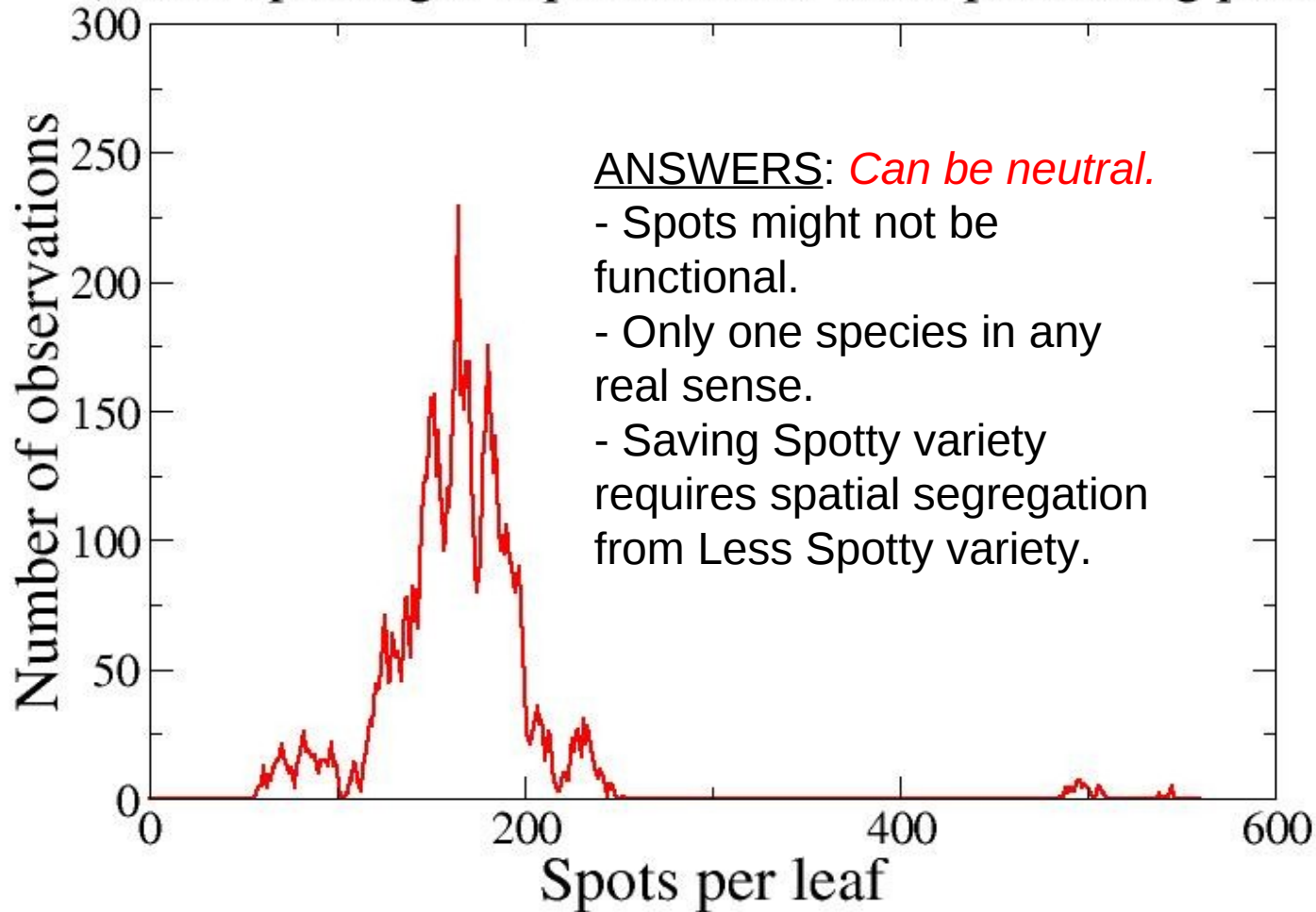
Evolution of 10000 individuals

Evolution of 10000 individuals

Test Problem

Observations of number of spots per leaf of *Imaginarius Forma*
(Made up thought experiment for a self pollinating plant)

ANSWERS: *Can be neutral.*
- Spots might not be functional.
- Only one species in any real sense.
- Saving Spotty variety requires spatial segregation from Less Spotty variety.

Solution

- Instead of a "species", use a conceptual model of a "peak":

- A Normal Distribution with <u>dynamic</u> mean μ and width w.

- Select death location x
- Select birth location y, mutated by 1 with probability P_m
- Remove individual from death location and place at birth location
- Update μ and w

Solution method

- Write down equations for:
  - Changes to the mean, $<d\mu>$, $<(d\mu)^2>$, …
  - Changes to the width, $<dw>$, $<(dw)^2>$, …
- Moment closure (rigorous in large N limit)
- Take continuous limit to obtain Stochastic Differential Equations
- Solve!

Solving for the width

Mutation distance

Generation time

$$d(w^2) = \left(p^* - \frac{2w^2}{N} \right) dT \quad + \frac{2w^2}{\sqrt{N}} dW$$

dW is Random, mean 0

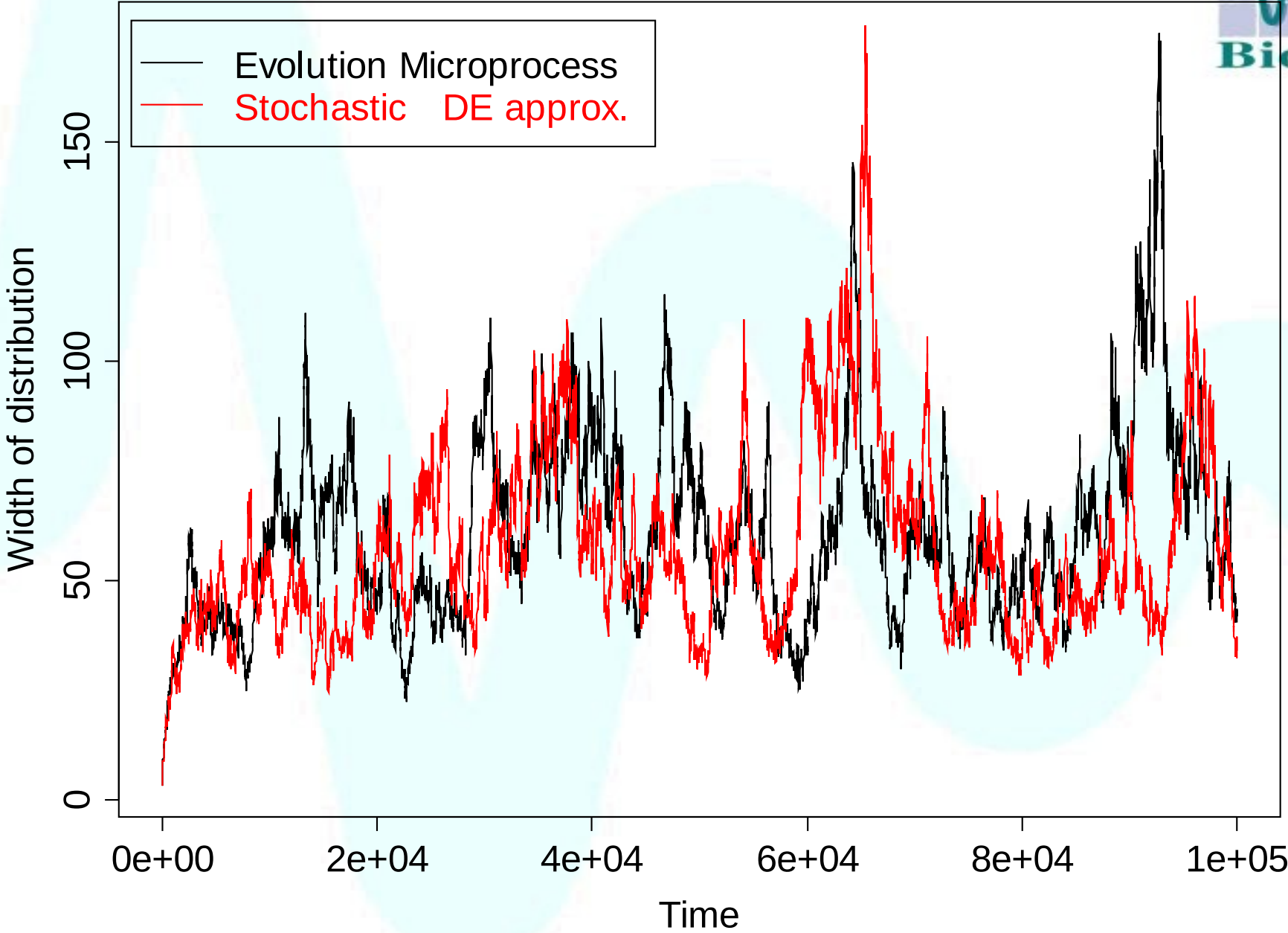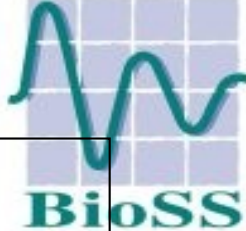Change in variance (in a timestep) = Deterministic part + Noise part

Solution at steady state:

$$p(w)dw = \frac{(Np_m)^2}{2w^5} e^{\frac{Np_m}{2w^2}} dw$$

Power-law decay at large w

Evolution in a 1D type space

The species concept

- Neutral clusters do form in type space but these are not stable in time

- Explicit distribution of types must instead be considered

- In neutrality, distribution is "effectively" a fluctuating normal distribution

- But really consists of many discrete clusters

Neutral evolution results

- Selection produces a stable peak, neutrality produces an *unstable* peak.

- Characteristic peak width, but large fluctuations *(multiple clusters).*

- Evolution speed *independent* of population size!

- *Evolution* is important for *Ecological* questions: *non-trivial* phenotype distributions are probable.

- The Genotype Distribution evolves similarly….

- Also relevant for sexual populations in explicit physical space

Reference

Lawson and Jensen:
*"**Neutral Evolution as Diffusion in phenotype space: reproduction with mutation but without selection**"*
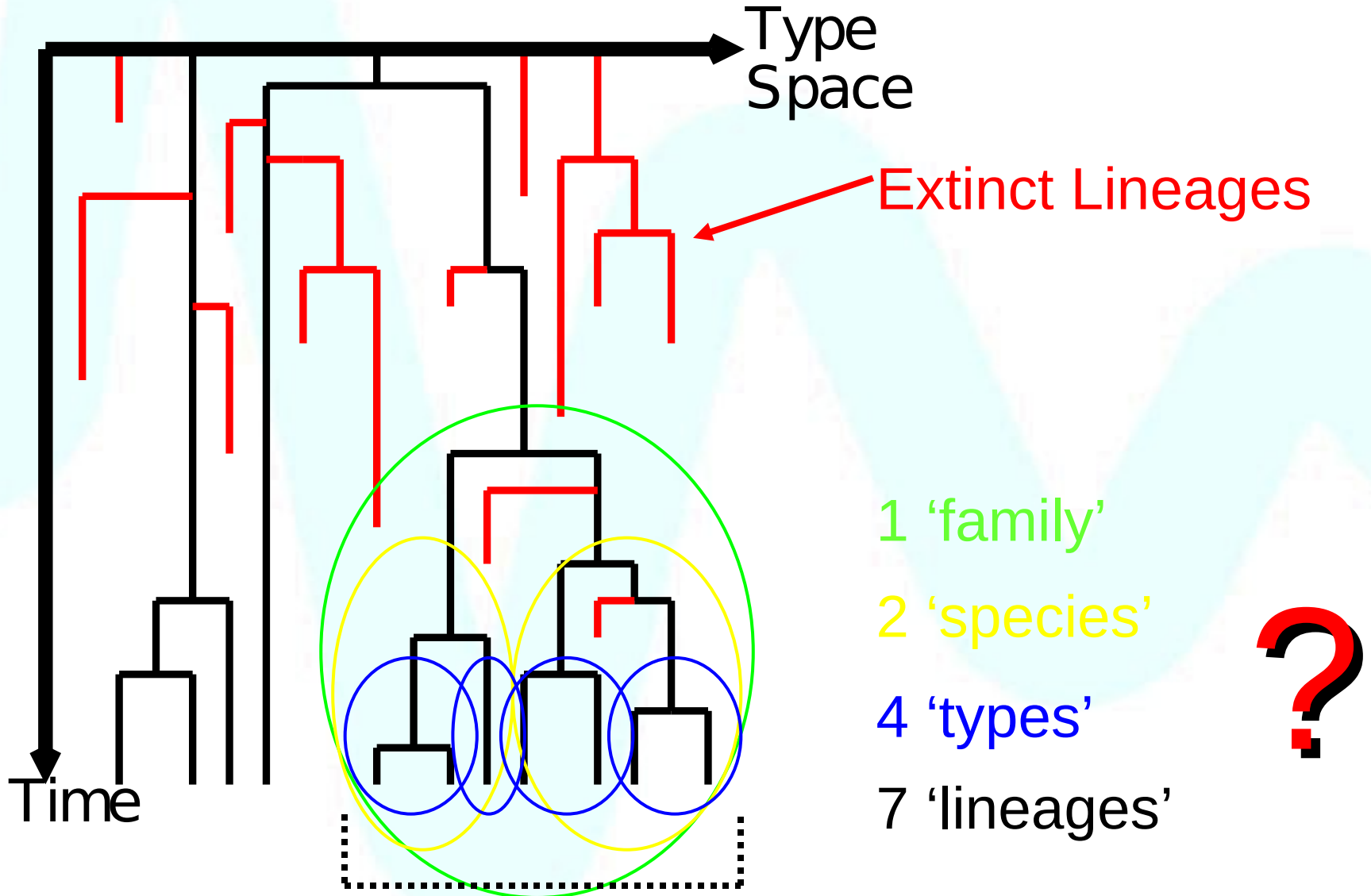*Physics Review Letters, March 07 (**98**, 098102)*
www.arxiv.org/abs/q-bio/0609009

Thank you for your attention!

Cut material

The Lineage

Type Space

Extinct Lineages

1 'family'

2 'species'

4 'types'

7 'lineages'

Time

?

The Lineage (2)

- If mutations occur at random on an "infinite length" genotype:

- All mutations are 'away'. Equivalent to analysing the lineage.

- Reference: B. Derrida and L. Peliti, Bull. Math. Biol. **53**, 355 (1991).

- Question: Is considering a Type - *a "unit" of similar individuals* - useful for understanding diversity?

Diversity measures

- Measured diversity depends on diversity measure:

  - Species Richness:

  $$D_{Raw} = \sum_i 1$$

  Sum over species i

  - Simpson Diversity:

  $$S_S = 1 - \sum_i p_i^{\,2}$$

  $$D_S = \frac{1}{1 - S_S}$$

  Proportion of species i from total population N
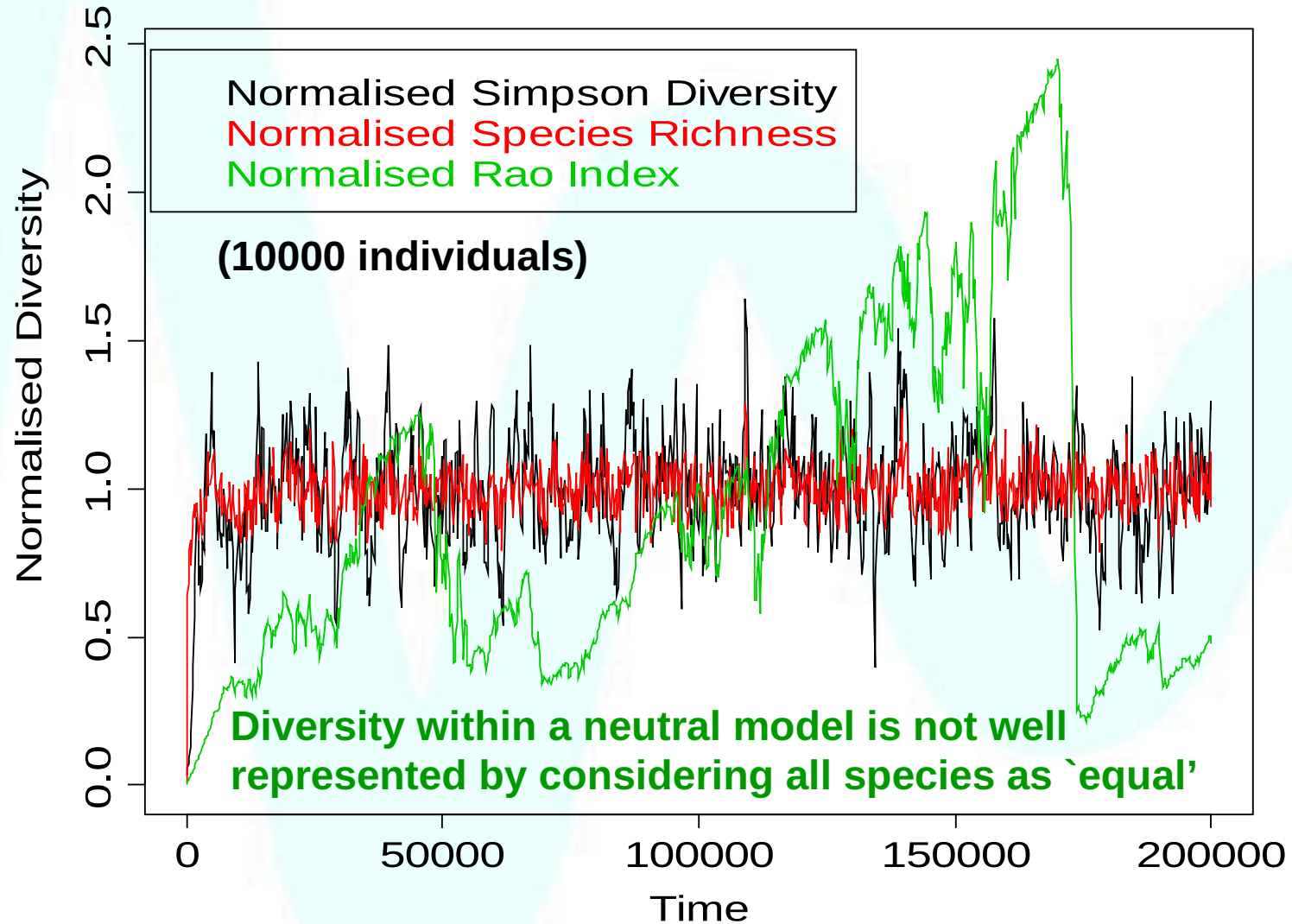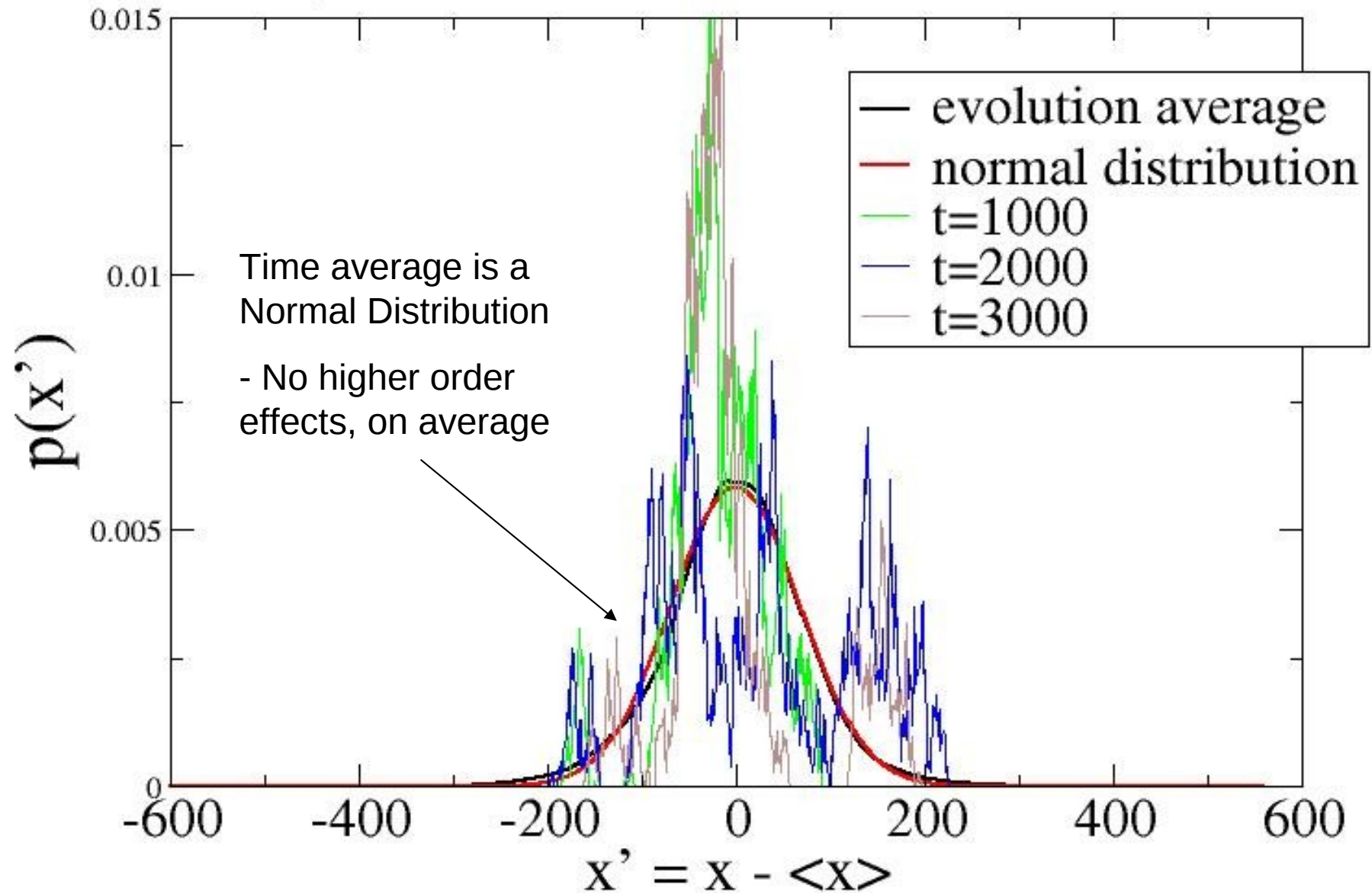
  - Rao Index:

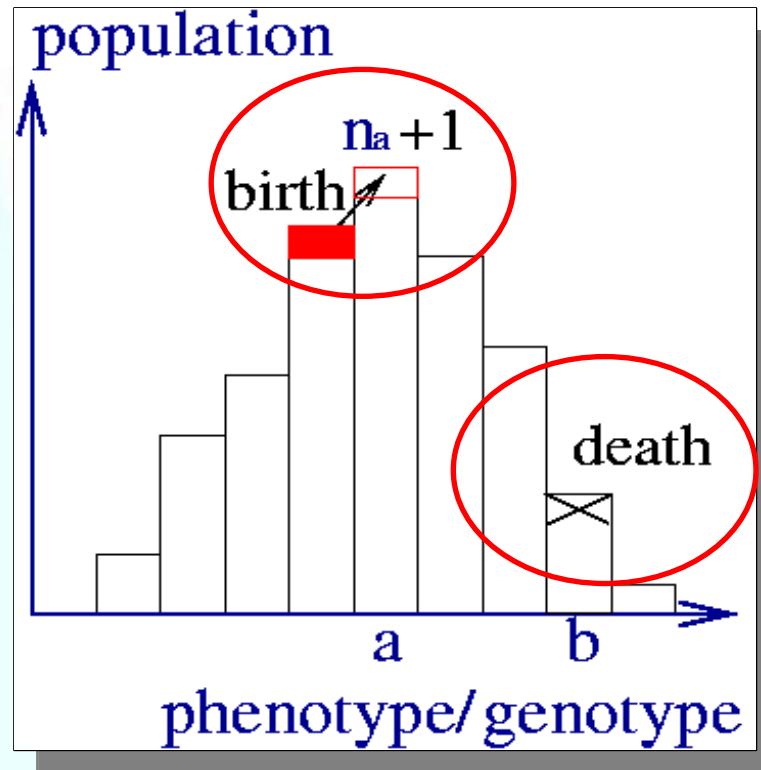 $$D_{Rau} = \sum_{i,j} d_{ij} p_i p_j$$

  "Difference" between types

Diversity of asexual lineages

Time average distribution of evolution process around the mean

compared with a normal distribution at same standard deviation (N=10000)

Time average is a
Normal Distribution

- No higher order
effects, on average

Legend:
— evolution average
— normal distribution
— t=1000
— t=2000
— t=3000

Y-axis: p(x')

X-axis: x' = x - ⟨x⟩

Solution: first try (1)

$$p_b(a) = \frac{n_a}{N}(1 - p_m) + \frac{p_m}{2}\frac{n_{a+1} + n_{a-1}}{N}$$

$$p_k(a) = \frac{n_a}{N}$$

Solution: first try (2)

- Consider average behaviour:

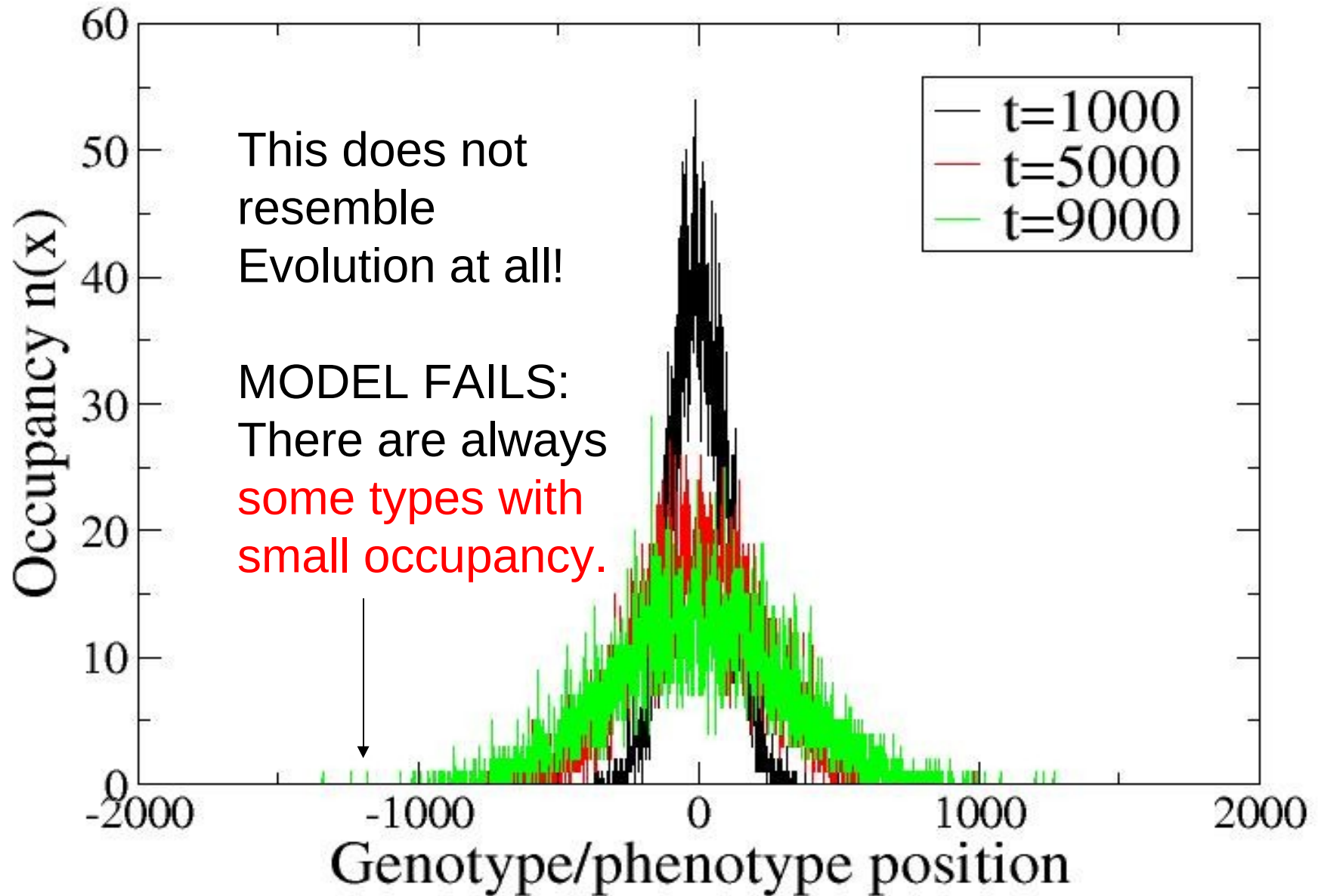$$\langle n_a(t+1) - n_a(t) \rangle = p_b(a) - p_k(a)$$

  – Expect this to be valid when N large?

- This becomes:

$$\langle n_a(t+1) - n_a(t) \rangle = \frac{p_m}{2N}\left[n_{a+1}(t) + n_{a-1}(t) - 2n_a(t) \right]$$

- This is just the diffusion of N particles!

Diffusion of 10000 particles

This does not resemble Evolution at all!

MODEL FAILS: There are always some types with small occupancy.

Legend: t=1000, t=5000, t=9000

Defining Asexual Diversity

- We want the "number" of different species or types

- Requires definition of species:

    - *Biological Species Concept?*
    - *Phenotypically distinct?*
    - *Genotypic Species Concept?*

HOWEVER:

- "Species" don't exist – though individuals cluster in type space

- Instead examine the similarity between types