The Coalescent Model

Florian Weber

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The Coalescent Model

coalescent = „zusammenwachsend“

Outline

- Population Genetics and the Wright-Fisher-model
- The Coalescent
- Non-constant population-sizes
- Further extensions
- Summary

Population Genetics

(Shamelessly stealing Alexis' slides)

- Study of polymorphisms in a population
  - What are the processes that introduce polymorphisms in the population?
  - If a polymorphism exists in a population, will it be there for ever?
  - Is there some process that removes polymorphisms from the population?
  - Do the polymorphisms exhibit patterns?
  - ...

Motivation

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- It can easily do calculations about the past
- It is very fast to compute
- Is can easily be extended to represent a more complex reality

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- Assuming an **infinite population size**, random mating, diploid population, no selection...
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- Infinity is weird... $0.3 \times \infty = \infty$
- ...and unrealistic

Wright-Fisher

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- The likelihood for an allele to prevail is equal to it's initial frequency

Wright-Fisher

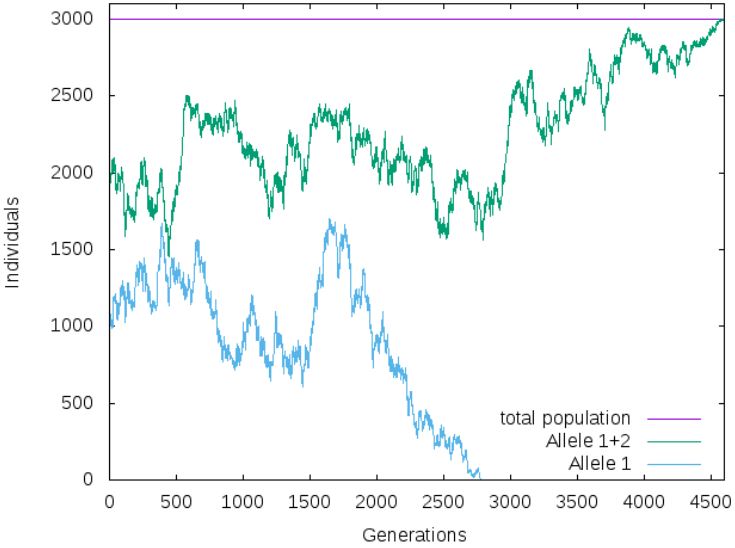

Figure 1: A simulation of three alleles under the model

Wright-Fisher (Individuals)

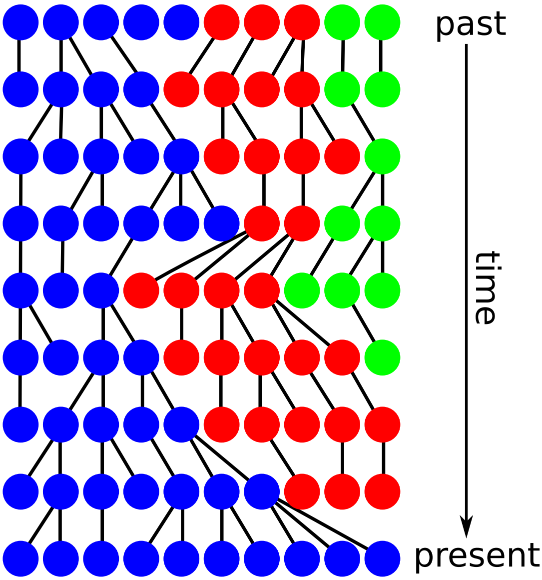

Figure 2: An evolutionary history in the model

Wright-Fisher (Individuals)

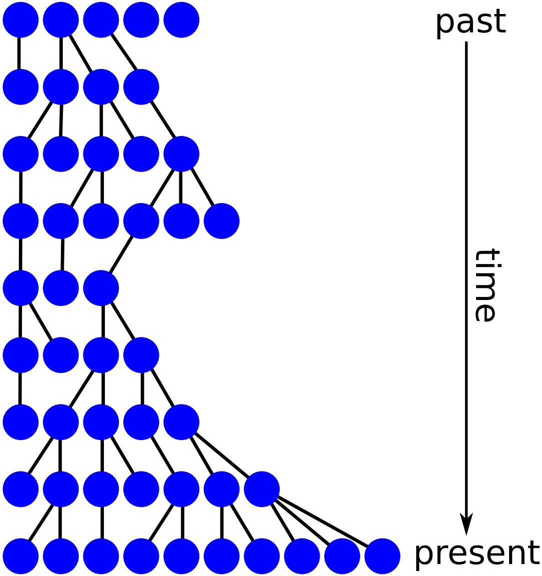

Figure 3: Extinct alleles removed

Wright-Fisher (Individuals)

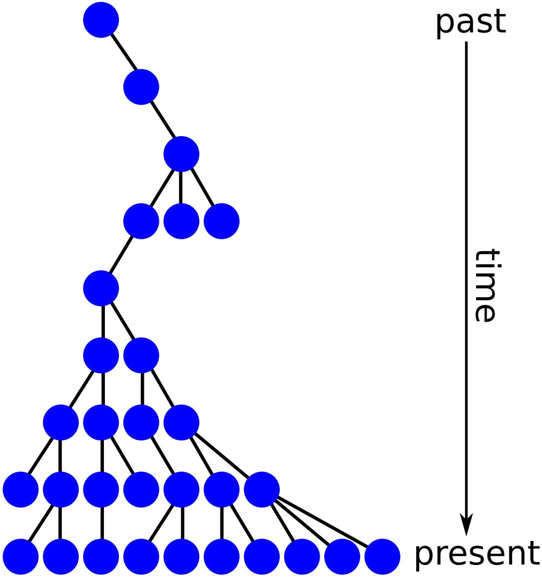

Figure 4: Surviving Tree

Wright-Fisher (MRCA)

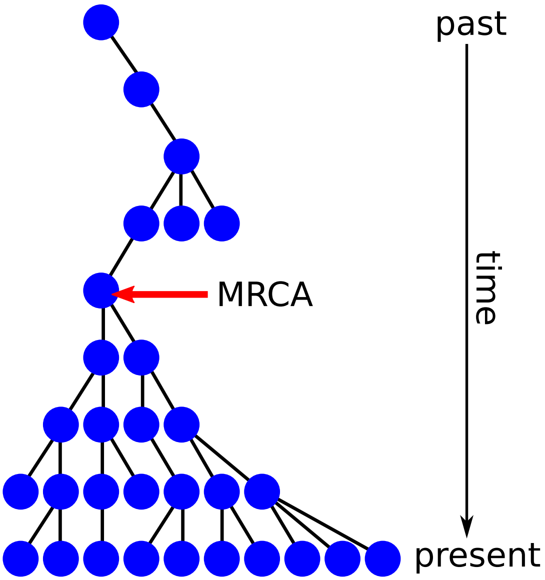

Figure 5: Most Recent Common Ancestor marked

Wright-Fisher (Coalescence-Events)

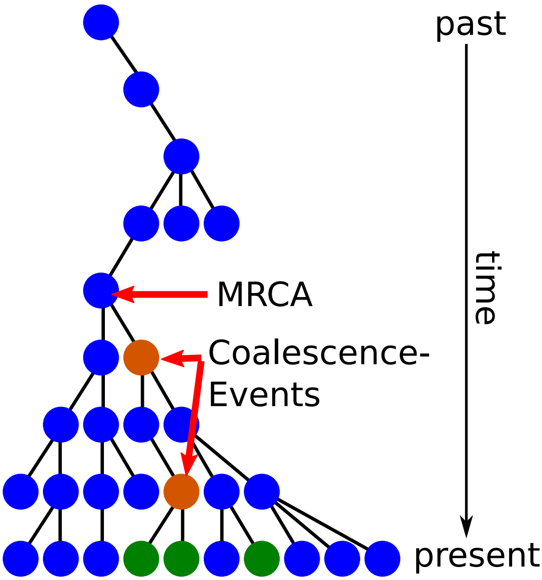

Figure 6: Coalescence-Events of the green individuals

The Coalescent Model

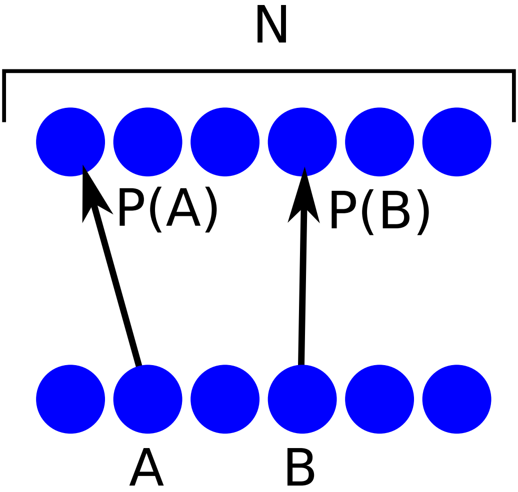

Figure 7: Two individuals and their parents

The Coalescent Model

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- In the previous t generations $1 - \left(\frac{N-1}{N}\right)^t$

The Coalescent Model

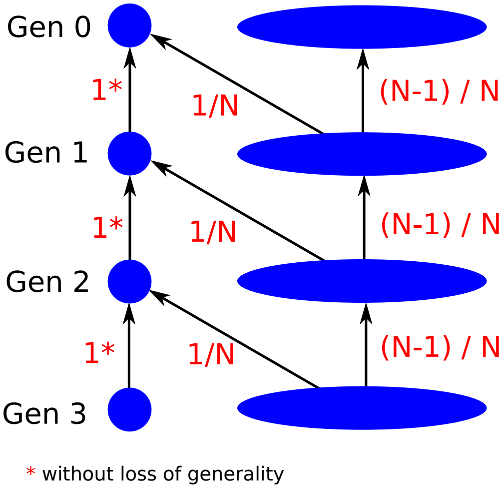

Figure 8: Likelihood of coalescence

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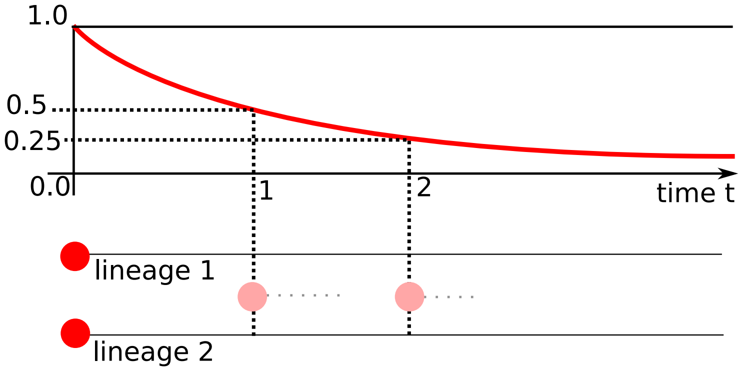
- Rescale: $\tau = \frac{t}{N}$:

$$\left(\frac{N-1}{N}\right)^{\lceil N\tau \rceil} \xrightarrow[N\to\infty]{} e^{-\tau}$$

The Coalescent Model

⇒ **The likelihood for two lineages to stay distinct over time is exponentially small!**



Moar Lineages!!

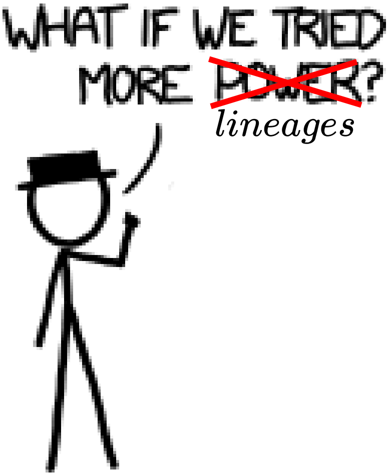


Figure 9: `http://what-if.xkcd.com/13/`

More Lineages

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- One generation, k lineages:

$$\frac{N-1}{N} \times \frac{N-2}{N} \times \cdots \times \frac{N-k+1}{N} = \prod_{i=1}^{k-1} \frac{N-i}{N}$$

More Lineages

- For some reason this is equal to:

$$\prod_{i=1}^{k-1} \frac{N-i}{N} = 1 - \frac{\binom{k}{2}}{N} + O\left(\frac{1}{N^2}\right) \approx 1 - \frac{\binom{k}{2}}{N}$$

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  - Therefore a coalescence-event is $\binom{k}{2}$-times as likely with k lineages than with 2

- **The number of coalescence-events grows quadratically with the number of lineages!**

More Lineages

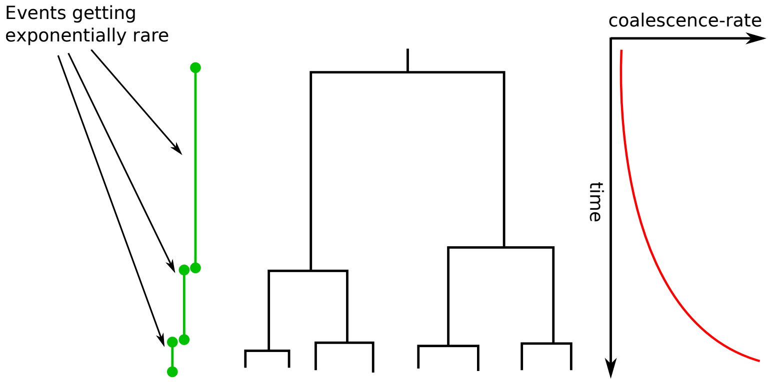

Figure 10: More lineages = faster coalscence

Properties

- Few deep furcations

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- Likelihood: Everything is possible but maybe unlikely
- Calculation is backward in times (Wright-Fisher: forward)
- Efficient: no calculation per individual or for extinct lineages

Non-constant population-sizes

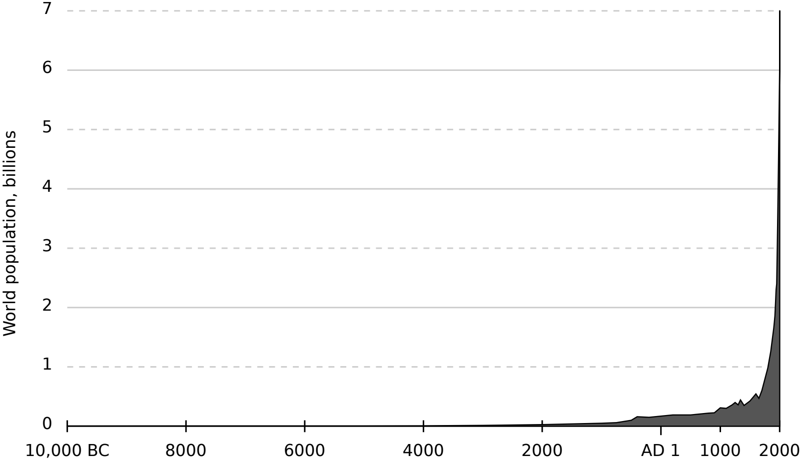

Figure 11: Wordpopulation - not very constant [Wikimedia]

Non-constant population-sizes

- Non-constant, but known population-size
- Coalescence is more likely in small populations
- $\Rightarrow$ Coalescence-rate changes over time

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- Simply rescale time.

Rescaling Time

- Before: t Generations corresponded to t/N units of coalescence-time
- Now: t Generations correspond to

  $$\sum_{i=1}^{t} \frac{1}{N_i}$$

  units of coalescence-time
- Note: for a constant population both formulas are equal

Rescaling Time - Example

- 5 Generations, with on average 5 individuals:

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- For non-constant $\{4, 4, 5, 6, 6\}$ individuals:

$$\tau = \sum_{i=1}^{t} \frac{1}{N_i} = \frac{1}{4} + \frac{1}{4} + \frac{1}{5} + \frac{1}{6} + \frac{1}{6} = \frac{31}{30}$$

note the lesser influence of the larger generations

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  note the lesser influence of the larger generations

- **A generation with twice the size, will get halve the coalescence-time**

Rescaling Time - Exponential Growth

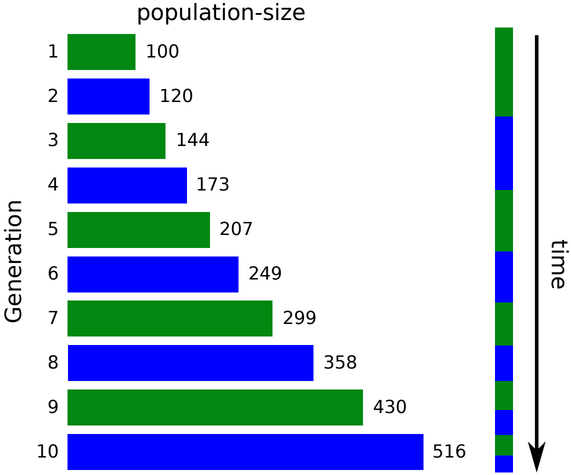

Figure 12: Exponentially growing population versus coalescence-time

Rescaling Time - Exponential Growth

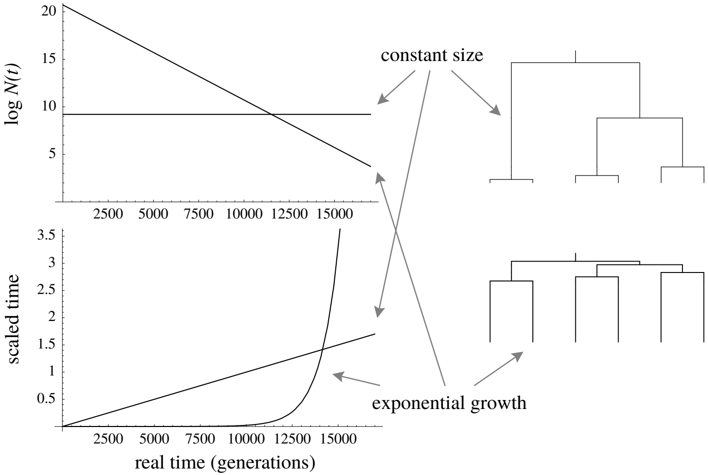

Figure 13: Exponentially growing and constant opulations. Note the reverse time-scale! [Nordborg]

Rescaling Time - Applicability

- Approximation converges against theory for growing N
- Close enough for most purposes

Further Extensions

- Separated Populations
- Diploid Populations
- Males and Females
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Wright-Fisher:

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Coalescent:

Assuming non-overlapping generations...

An actual example

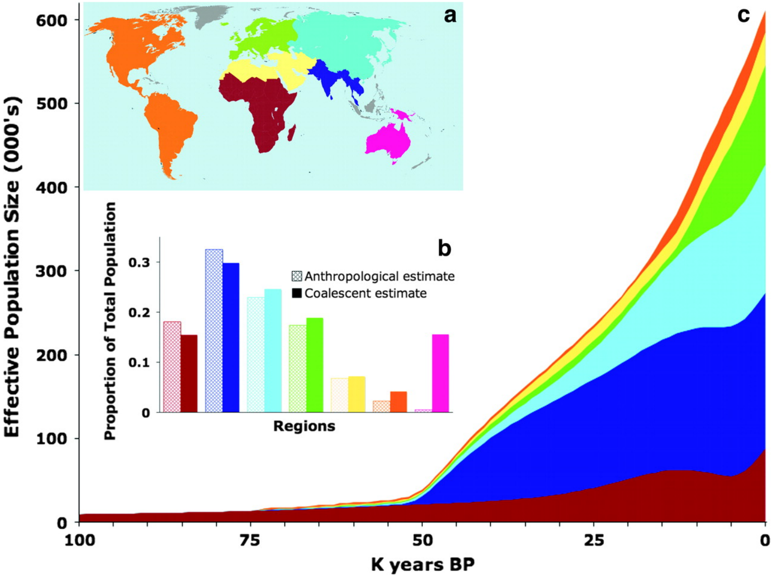

Figure 14: Coalescent vs. Anthropological Estimates [Atkinson et al.]

Software

Software that uses the coalescent model[1]:
BEAST, COAL, CoaSim, DIYABC, DendroPy, GeneRecon, genetree, GENOME, IBDSim, IMa, Lamarc, Migraine, Migrate, MaCS, ms & msHOT, msms, Recodon and NetRecodon, SARG, simcoal2, TreesimJ

[1] Source: `https://en.wikipedia.org/wiki/Coalescent_theory`

Summary

- The coalescent is the Wright-Fisher-model plus math
- Coalescent-events are, with exponential likelihood, relatively recent
- The more lineages there are, the more coalescence-events occur
- Non-Constant populations can be simulated by rescaling time
- The simulated time for a generation is anti-proportional to it's size

References

Content

- Magnus Nordborg, “Coalescent Theory”, March 2000

Software-list

- `en.wikipedia.org/wiki/Coalescent_theory`

Images

- Fig. 09: Randal Munroe: `what-if.xkcd.com/13/`
- Fig. 11: El T: `commons.wikimedia.org/wiki/File:Population_curve.svg`
- Fig. 13: Magnus Nordborg: “Coalescent Theory”, 2000
- Fig. 14: Atkinson et al.: “mtDNA variation predicts population size in humans and reveals a major Southern Asian chapter in human prehistory”, 2008