Demographic inference based on Site frequency spectrum (SFS) – Part I

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CE3C – center for ecology, evolution and environmental changes

2018 WSPG Cesky Krumlov
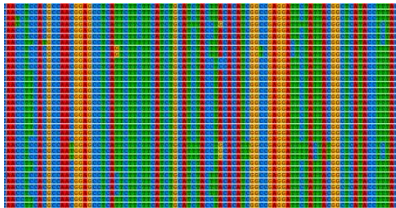22 Jan 2020

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Outline

Part I

- Modeling demographic history: Population trees vs gene trees

- The SFS and coalescent trees

- Fastsimcoal2 principles

Part II

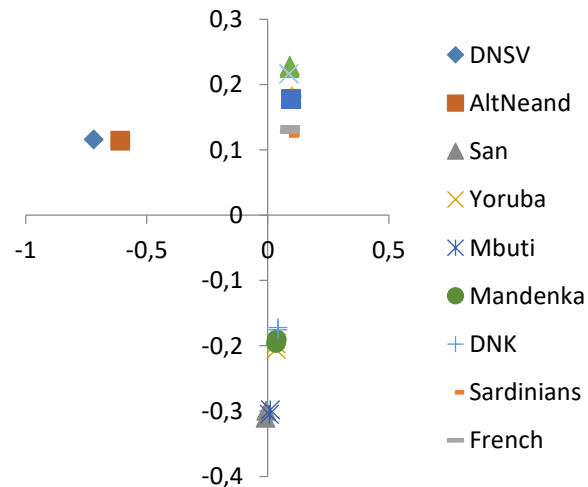- Example of applications to different problems and types of data

Connecting observed patterns to the evolutionary processes

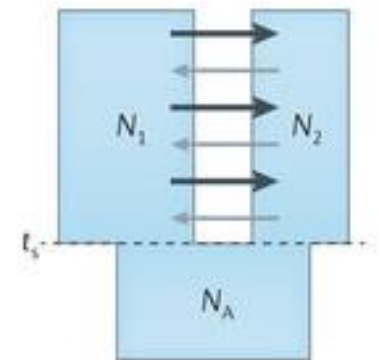**«Model-free» methods e.g. PCA**

Model-based methods
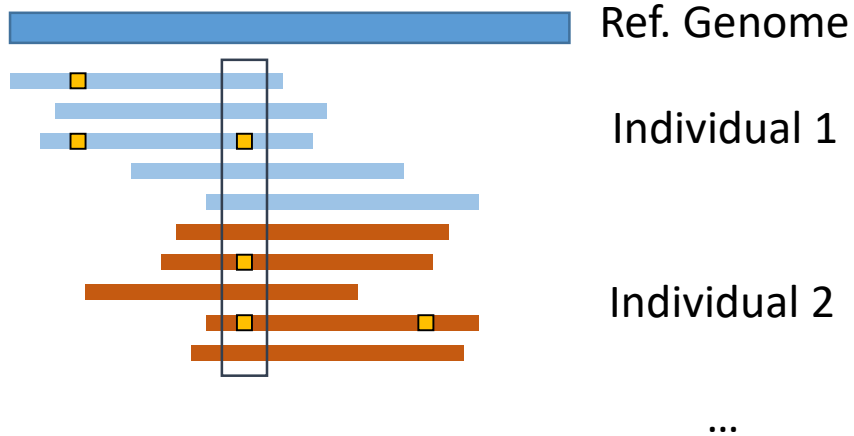
Genomic data

Evolutionary Processes:
- Demography
- Selection
- Mutation
- Recombination

Observed patterns

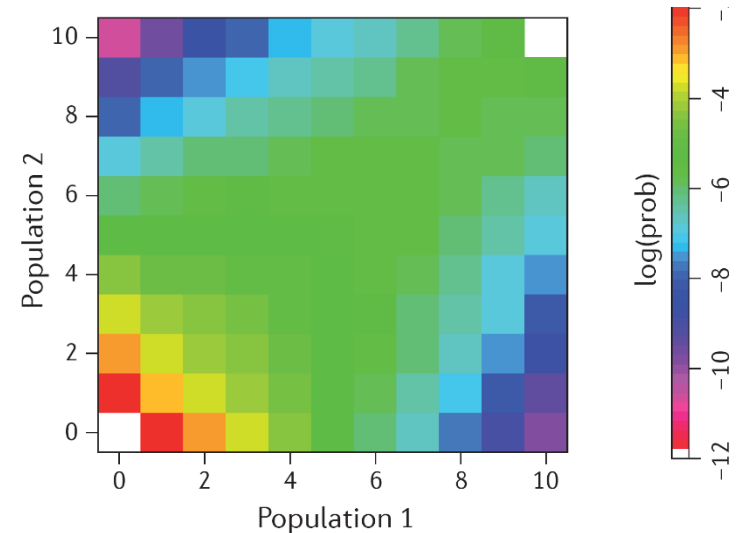# Genomic data with Next Generation Sequencing

Mapping

Ref. Genome

Individual 1

Individual 2

...

Genotypes

	SNP1	SNP2	SNP3	...	SNP *L*
Ind. 1	0	2	0	...	1
Ind. 2	0	0	1	...	2
Ind. 3	1	0	0	...	2
...	...	...	...	...	...
Ind. *n*	0	0	1	...	0

Site-frequency spectrum (SFS)

Information about:

- frequencies of variants
- linkage disequilibrium

Evolutionary forces affecting the history of populations

Demography

- Past effective population sizes
- Past migration rates

Selection

- Selective coefficient and type of selection (positive or negative)

Genomic processes

- Mutation rate
- Recombination rate

Demographic history of populations

Population tree

Past demographic events:

- Population split

- Migration events

- Changes in effective population sizes (expansions or bottlenecks)

- Temporal changes in migration rates and effective sizes
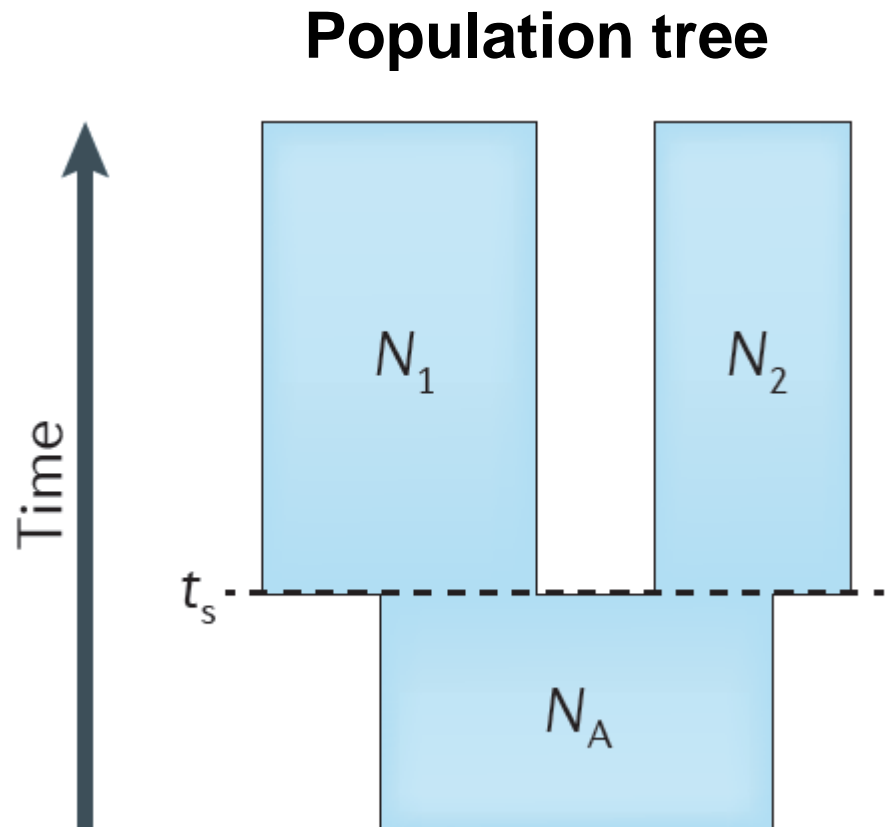
How to connect alleles with demographic history?
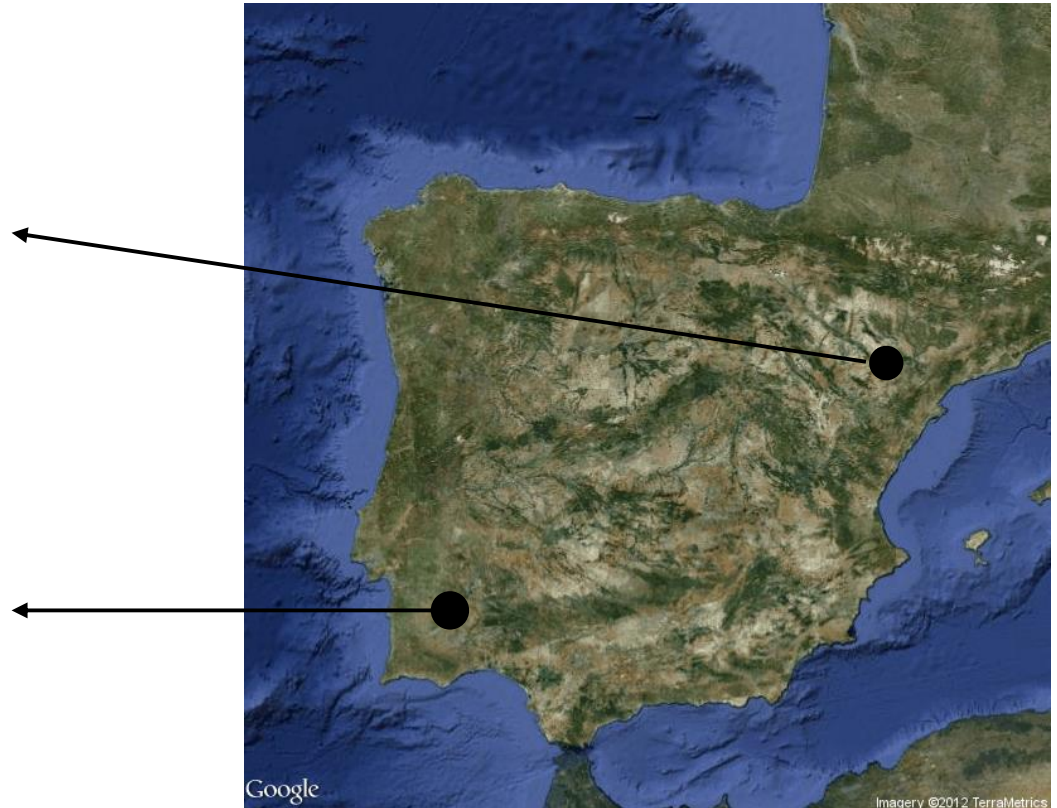
Sample site 1
ind1 AT**G**C – allele 1
ind2 AT**C**C – allele 2
ind3 AT**C**C – allele 2
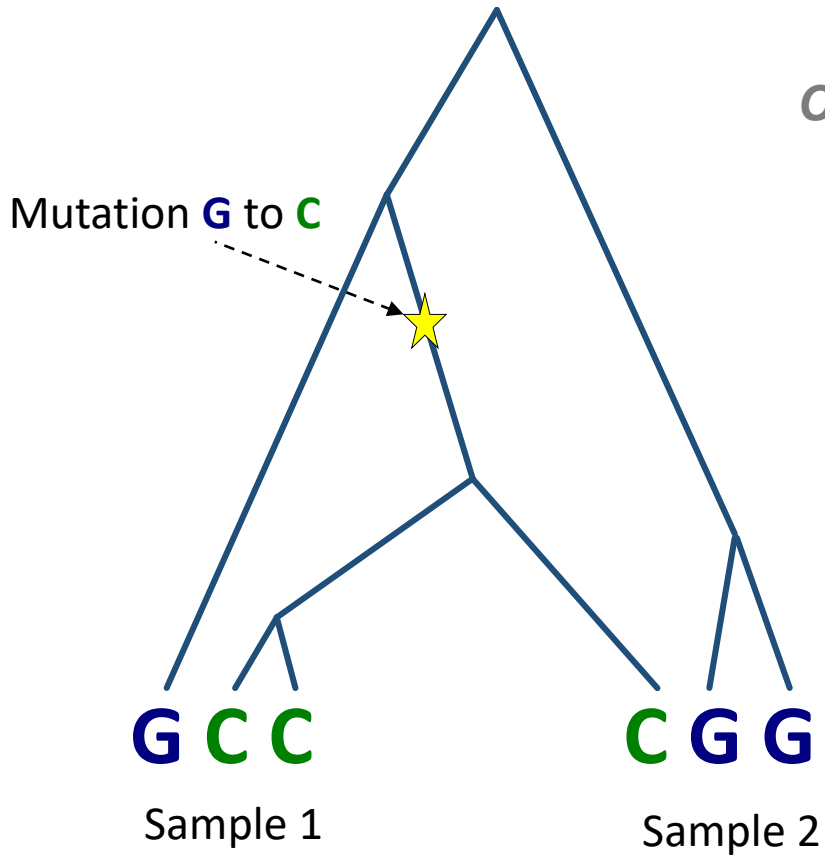
Sample site 2
ind1 AT**C**C – allele 2
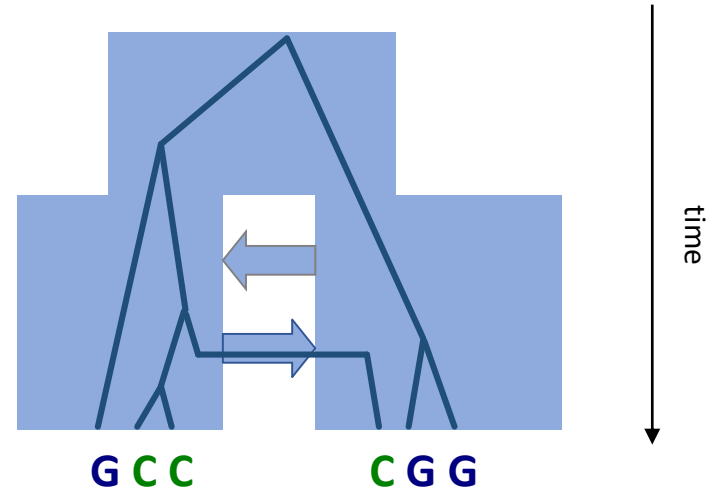ind2 AT**G**C – allele 1
ind3 AT**G**C – allele 1

Gene trees reflect the species history

Population tree with migration

Compatible

Mutation **G** to **C**

G C C
Sample 1

C G G
Sample 2

Gene trees reflect the species history

Mutation **G** to **C**

G C C
Sample 1

C G G
Sample 2

Population tree with migration

Compatible

time

G C C **C G G**
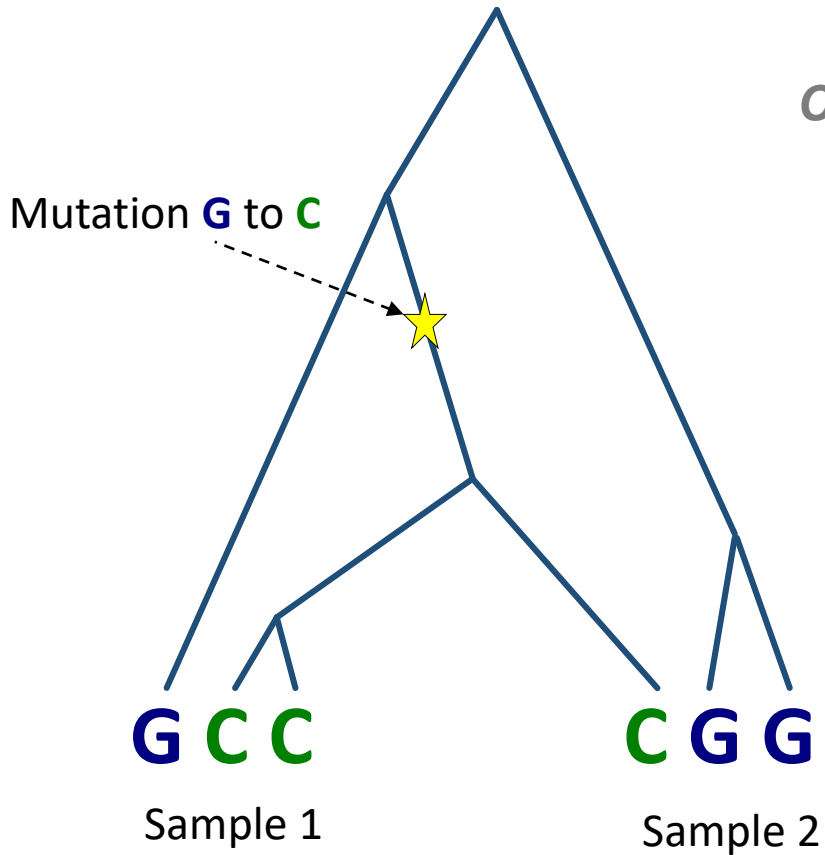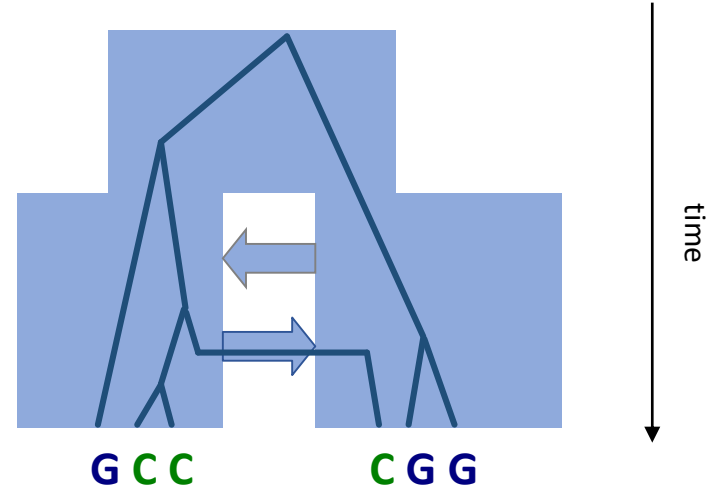
Population tree with no migration

Incompatible

time

G C C **C G G**
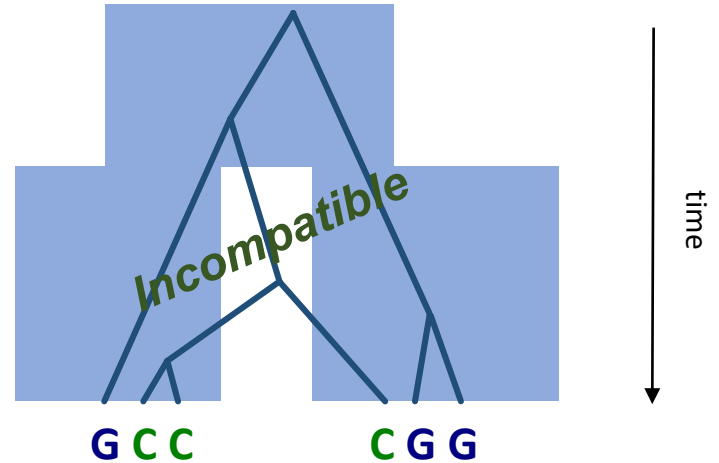
Gene trees within pedigrees

- **Gene trees** reflect the ancestral relationship of sampled gene copies

- For now, lets assume there is no mutations (**branch lengths do not reflect mutations in coalescent gene trees**!).

- Because of transmission of genes at each generation, at each position of the genome there is always a gene tree describing the relationship of gene copies in our sample.

- All individuals share the same pedigree, but gene trees can vary due to independent segregation and recombination
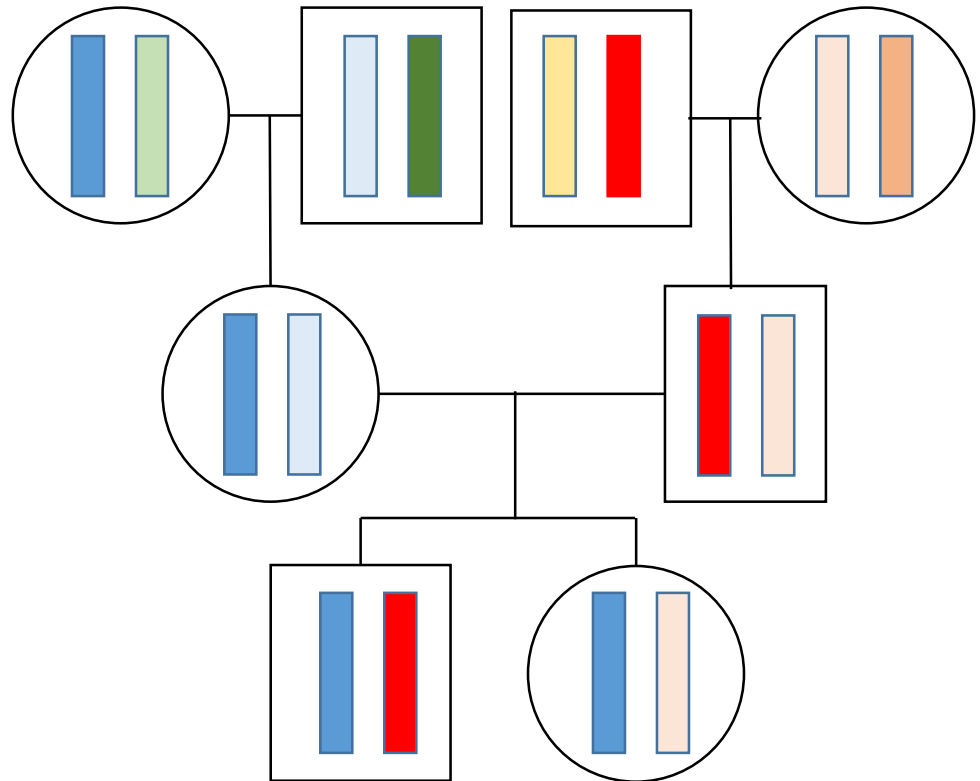
The same pedigree can lead to different gene trees across the genome
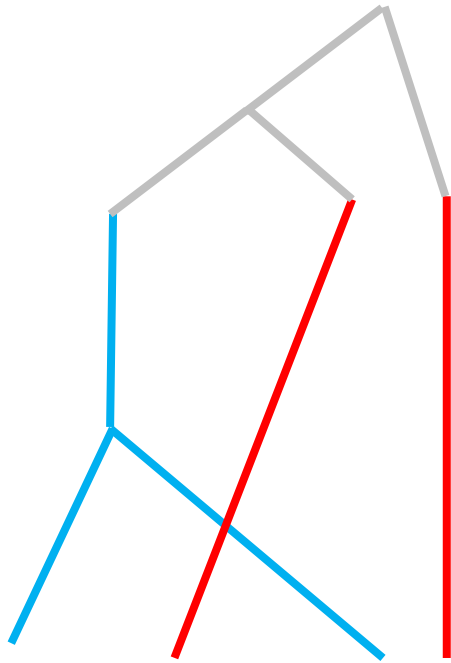
Gene tree of a sample of size n=4
(2 diploid individuals)
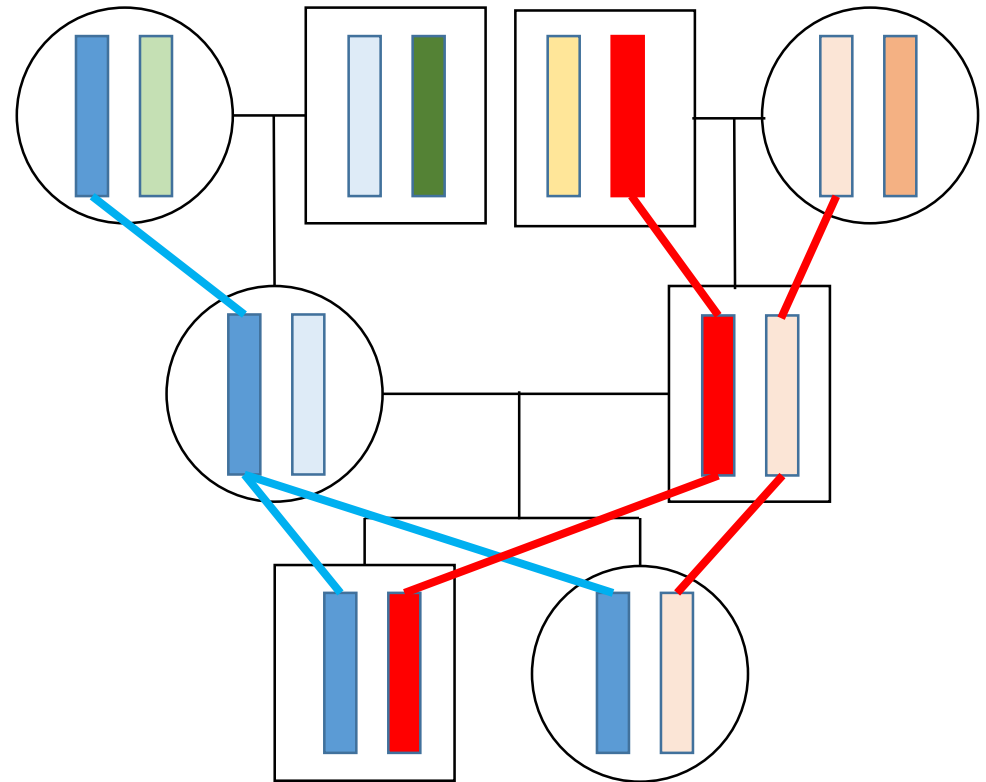
Chromosome 1

The same pedigree can lead to different gene trees across the genome
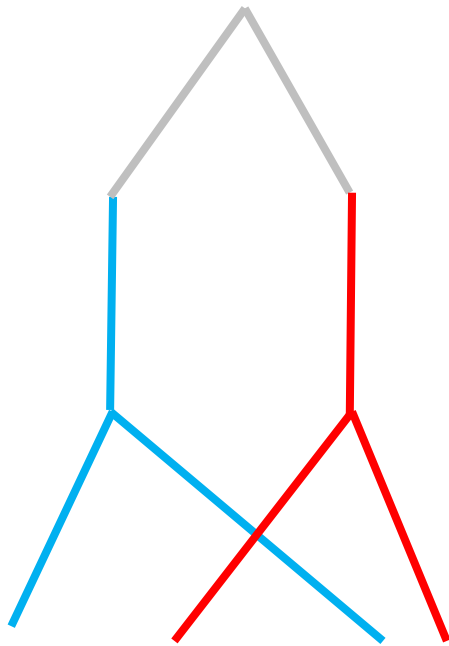
Gene tree of a sample of size n=4
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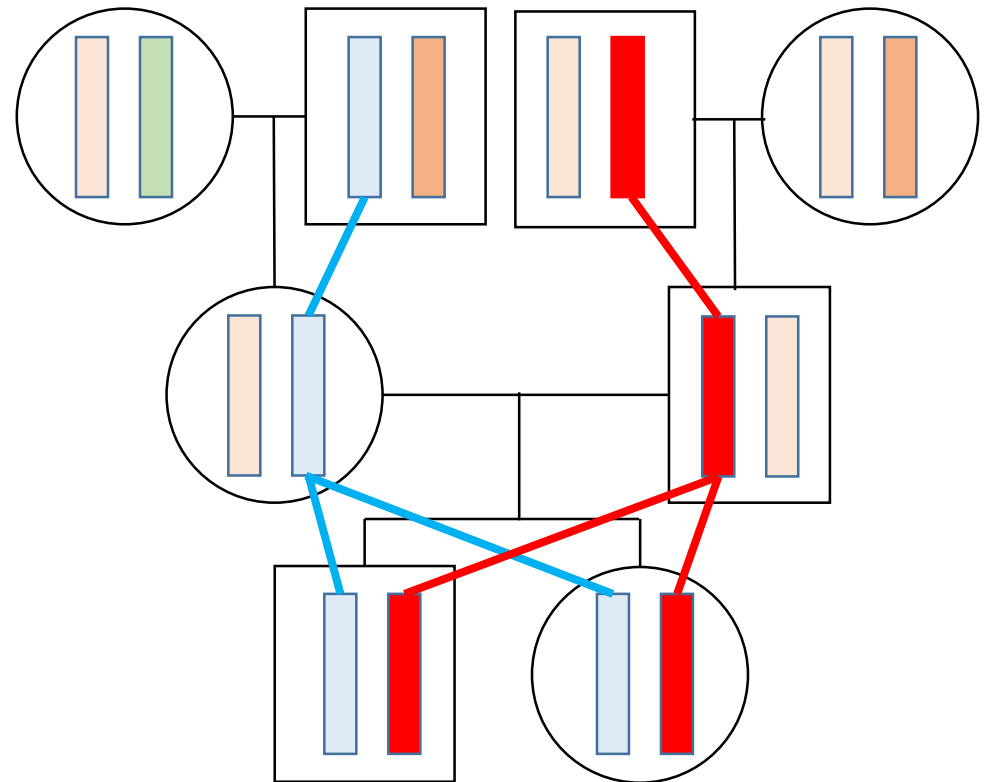
Chromosome 2

Gene trees and pedigrees

- Although we have the same pedigree, the gene trees at different loci will be different

- Ancestral chromosomes that did not contribute to our sample can be ignored

- With recombination, different regions of the chromosome will have different (correlated) gene trees

Gene trees and pedigrees
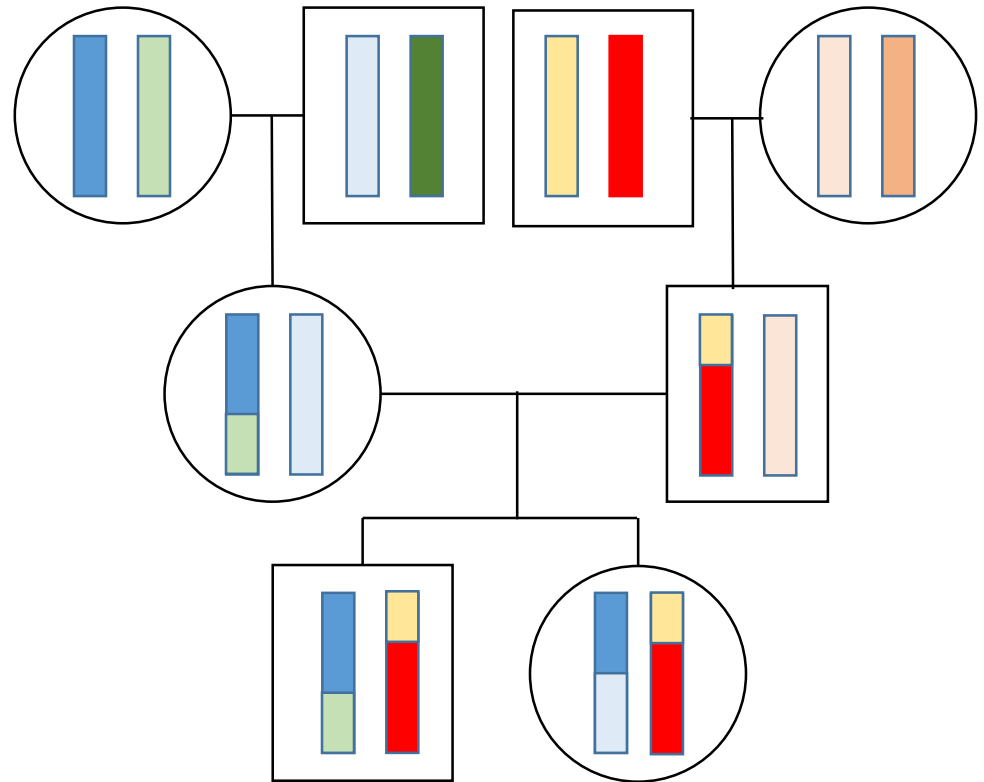
- Although we have the same pedigree, the gene trees at different loci will be different

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Gene tree 1

Gene tree 3

Gene tree 2

Gene tree 4

Gene trees vs. Population trees

Gene trees reflect the ancestral relationship of sampled gene copies.
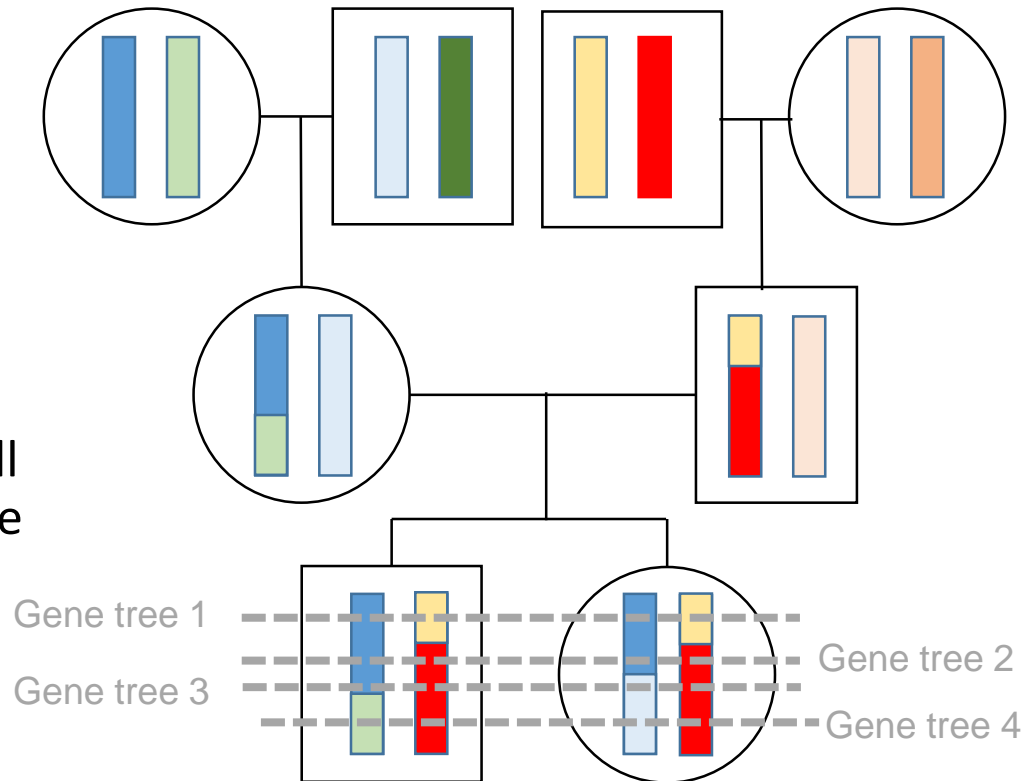
The relationship between populations is given by the **population tree**. As with pedigrees, the population tree reflects the relationship between populations that is shared by all individuals.

In phylogenetics it is usually assumed that the gene tree reflects the population/species tree.

However, in the time scale of population genetics, gene trees at a particular region of the genome (locus) can be very different from the population tree.

Time

A

T_1

(a)

T_2

(a)
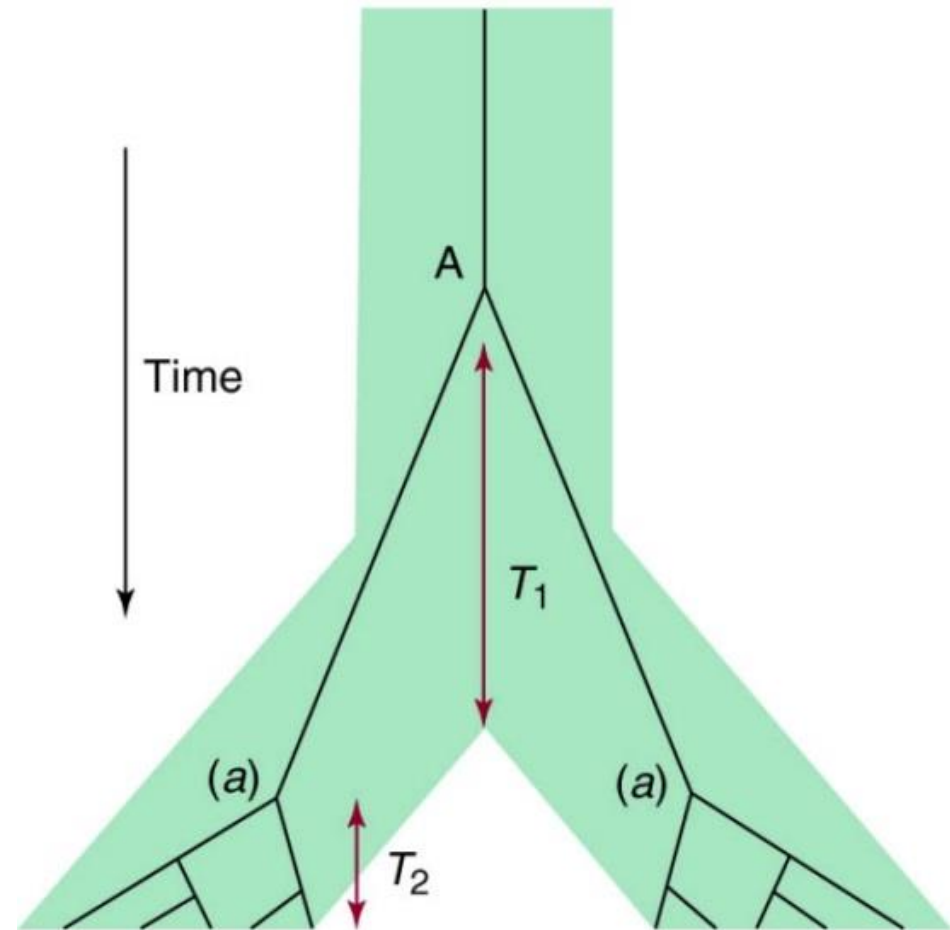
TRENDS in Ecology & Evolution

Nichols (2001) TREE

Forward in time vs backward in time

- Many results in population genetics come from studying how allele frequencies change forward in time

- But, when we look at samples from natural populations we want to know what happened in the past to explain what we see today

- **All sites in the genome have a gene tree describing the ancestral relationship of the lineages in a sample**

time
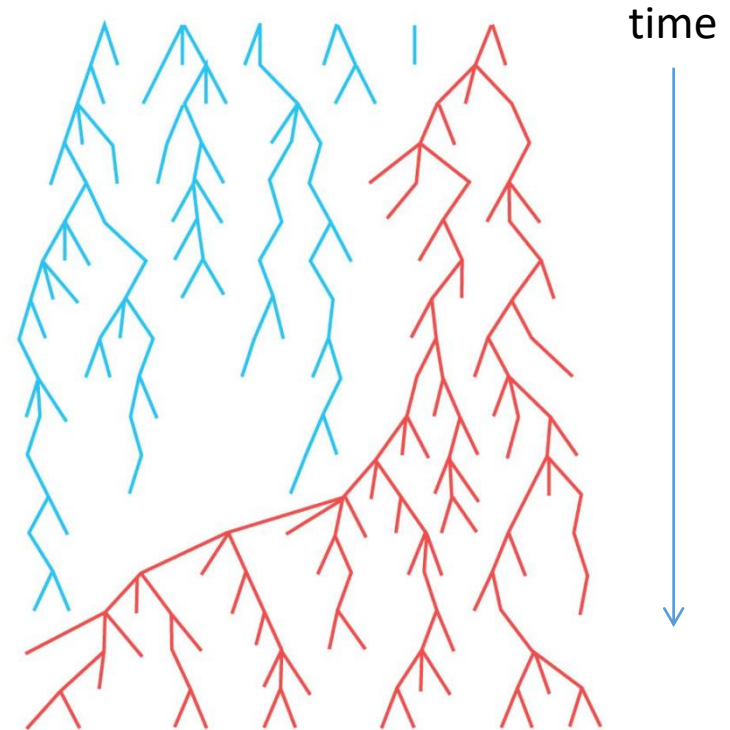
15.0, Genetic drift

Evolution © 2007 Cold Spring Harbor Laboratory Press

Reconstructing the demographic history from genomic data

Because of recombination, different regions of the genome can have different gene trees

Genome

- Demography is expected to affect the entire genome

- Natural selection acts on specific functional regions

time

All gene trees are consistent with the population tree. Independent gene trees can be seen as independent replicates of the same population tree.

Reconstructing the demographic history from genomic data

Because of recombination, different regions of the genome can have different gene trees
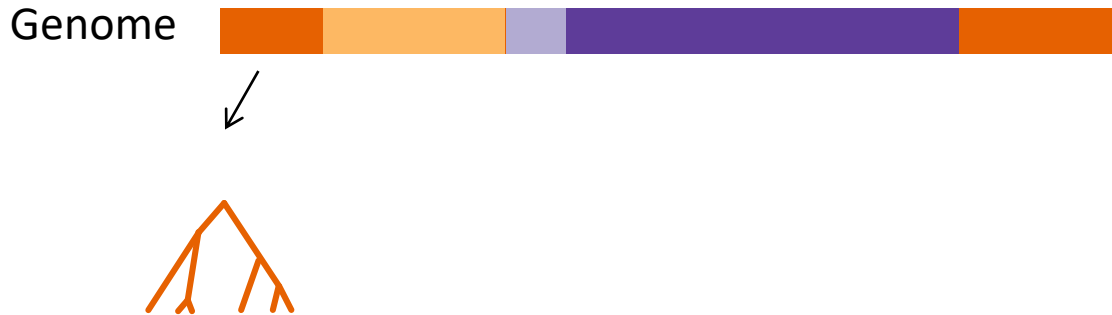
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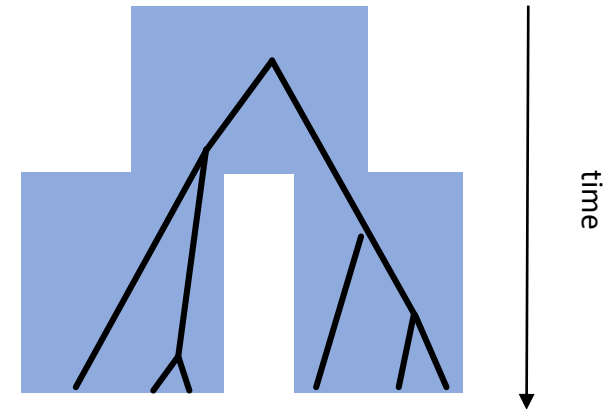
Reconstructing the demographic history from genomic data

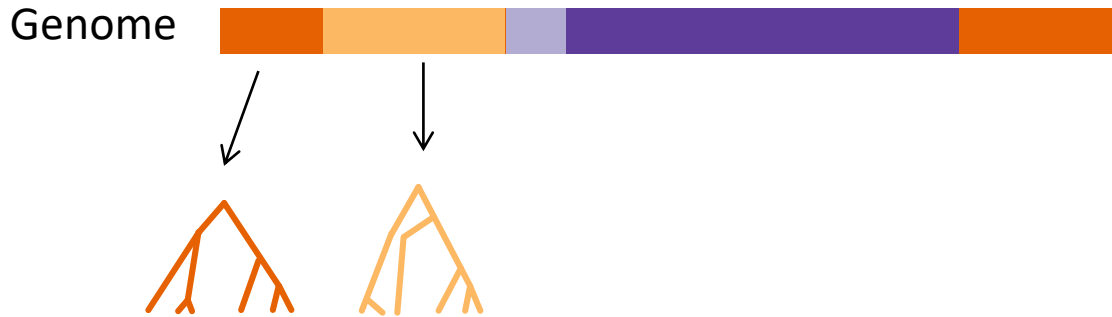Because of recombination, different regions of the genome can have different gene trees

Genome

- Demography is expected to affect the entire genome

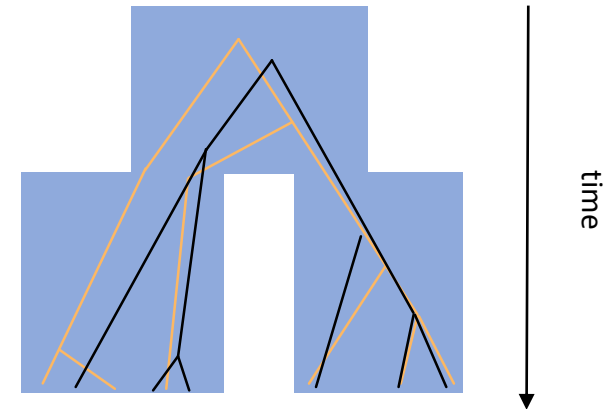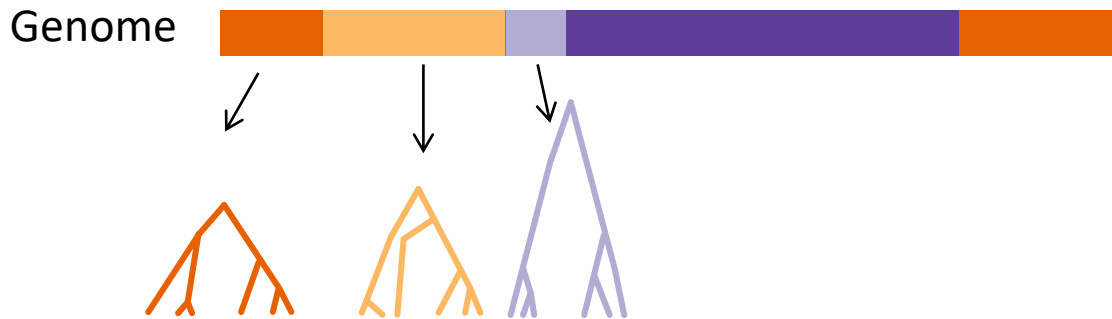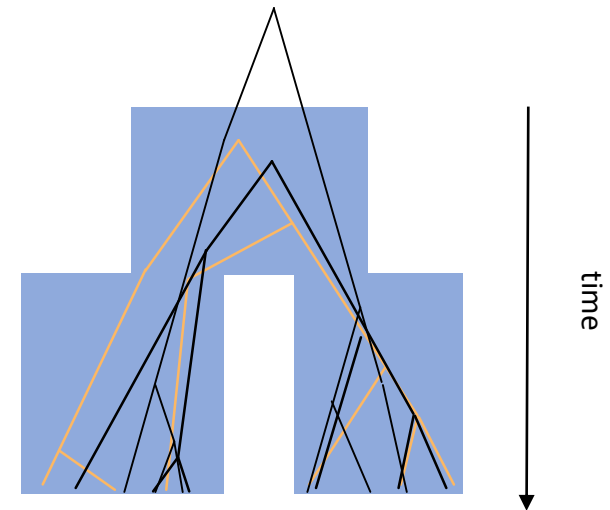- Natural selection acts on specific functional regions

time

All gene trees are consistent with the population tree. Independent gene trees can be seen as independent replicates of the same population tree.

Why do we care about demographic history?

Demography affects the efficiency of natural selection

- Response to selection is different in small *vs* large populations, with *vs* without gene flow, etc.

Demographic history affects the genome-wide patterns

- It can be seen as a "null" model. Regions under selection are detected as outliers.

Between a pair of marine populations

Between marine and freshwater populations
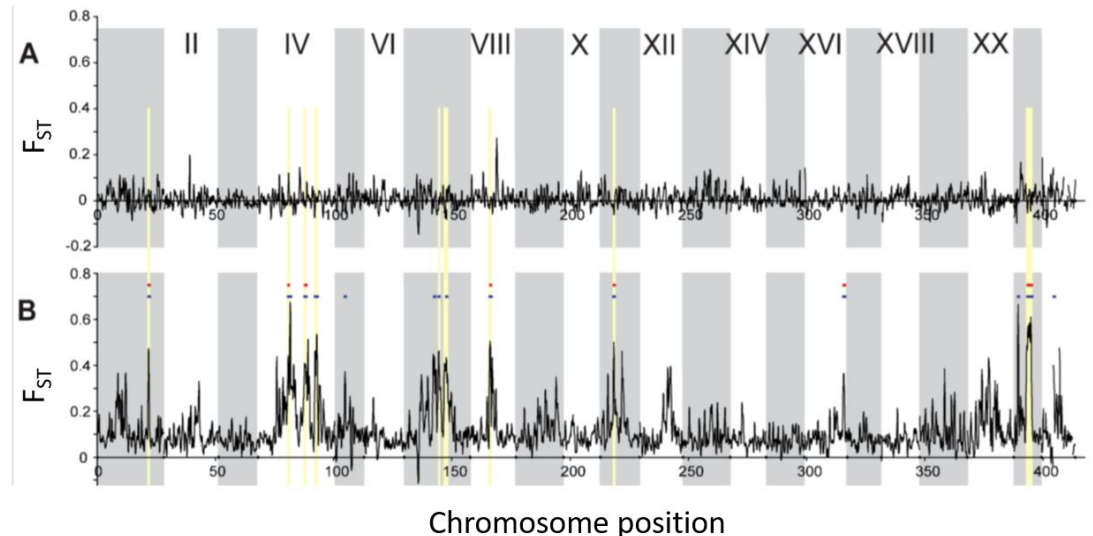
Chromosome position
Alternating white and grey indicate linkage groups (chromosomes)

Hohenlohe et al (2010) Plos Genetics

Coalescent Theory

Coalescent theory is a retrospective approach to population genetics that describes the ancestry of sampled of genes, as a function of an underlying model (demographic history).

Coalescent theory provides a model for the **evolutionary forces** (genetic drift, migration, mutation, recombination) and **the sampling process** that affect the observed data.

This process has been formalized by J.C. Kingman in a series of seminal papers published in 1982, and independently formalized by Hudson (1983) and Tajima (1983).

Intro to coalescent

- Coalescent theory provides a mathematical framework which describes the distribution of gene trees in populations

- However, while the tradition from phylogenetics is to estimate a tree and use the estimated tree to deduce evolutionary relationships, the population genetic tradition sees the tree as a random outcome of a population genetic process.

Random generalogies within and among populations

Time

X

T_3

H   C   G

TRENDS in Ecology & Evolution

Nichols (2001) TREE

Nature Reviews | Genetics

Rosenberg and Nordborg (2002) Nat. Rev. Genetics
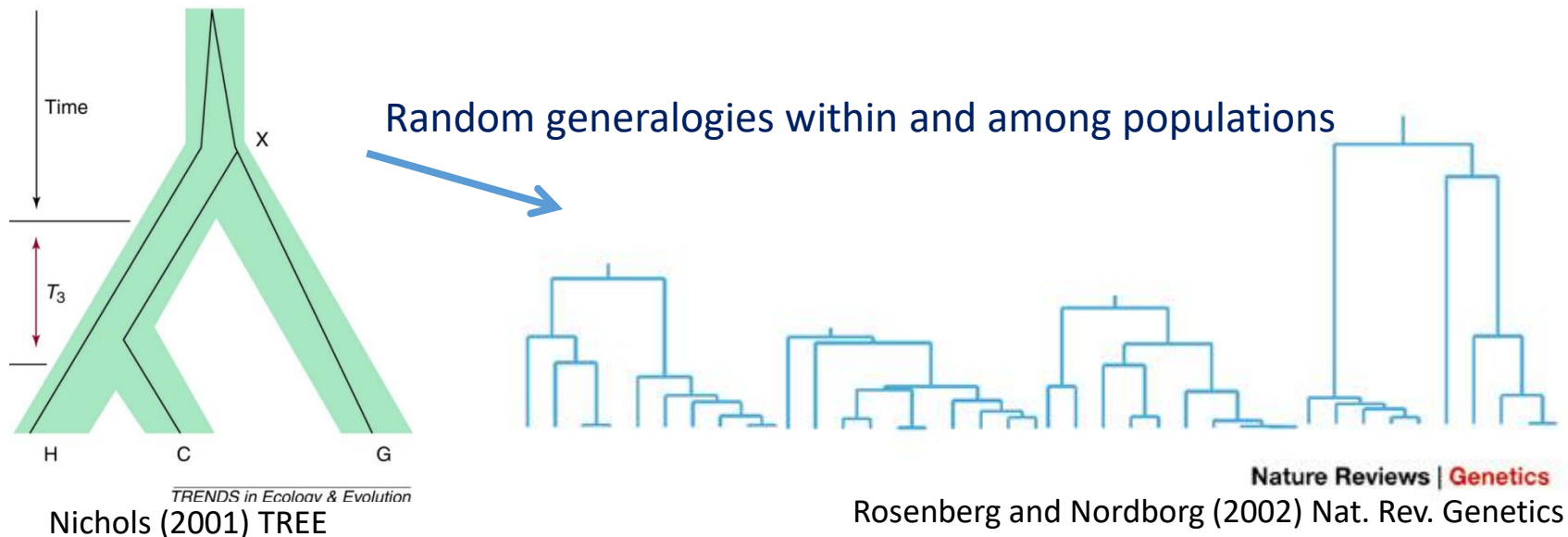
Coalescent backward process

Forward process   Fixation process   Coalescent process

MRCA

Past

Time

Present
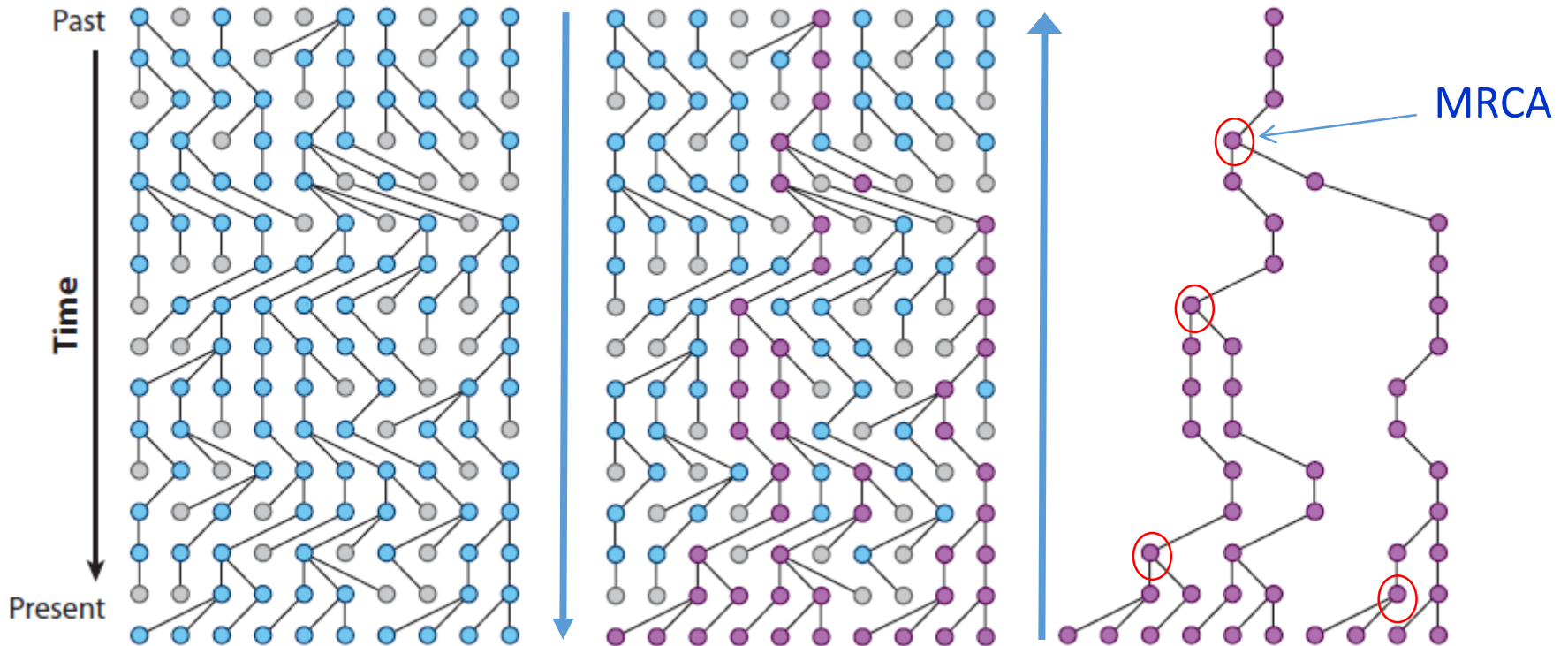
Legend:
○ Coalescent events

MRCA: Most Recent Common Ancestor

The principle of the coalescent theory

- For a given sample of individuals (gene copies or lineages) there is always a **gene tree** describing the ancestry of the sample.

- How many generations do we need to wait until they find an ancestor (i.e. a pair of lineages coalesce)?
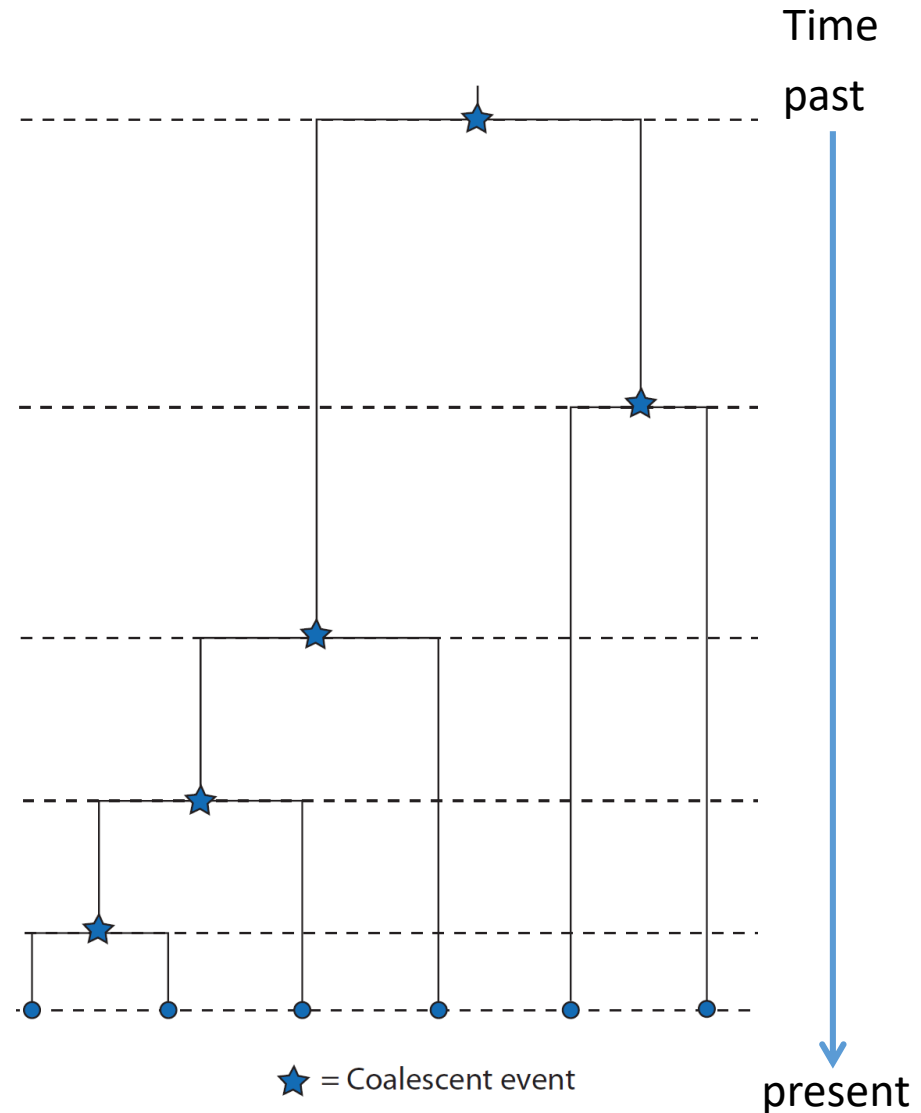
Time

past

present

★ = Coalescent event

Let's start simple: 2 lineages

In a population of N diploid individuals (2N gene copies)

In the 1st generation in the past:

t-1

t

present

Pr(coal)   = 1/2N
Pr(no coal) = 1-(1/2N)

Let's start simple: 2 lineages

In a population of N diploid individuals (2N gene copies)

In the 2nd generation in the past:

t-2

Pr(coal) = 1/2N
Pr(no coal) = 1-(1/2N)

t-1

No coalescent
Pr(no coal) = 1-(1/2N)

present   **t**
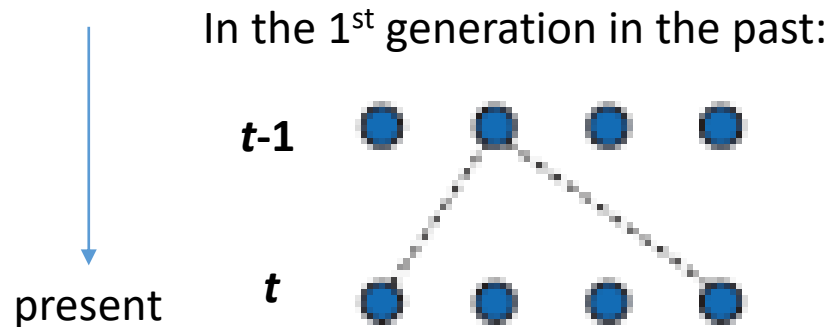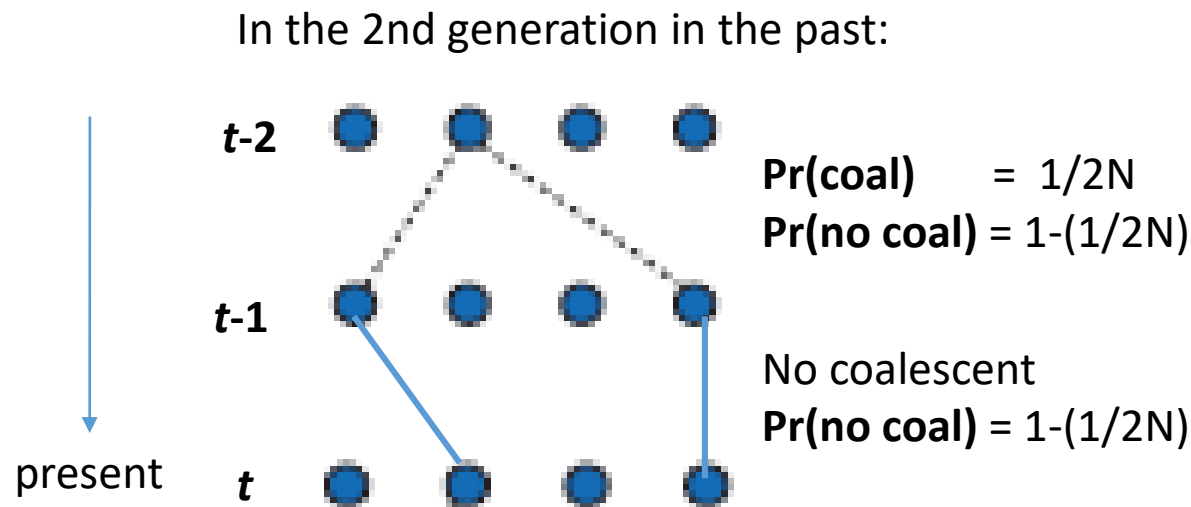
In the tth generation in the past the probabilities remain the same:

Pr(coal) = 1/2N
Pr(no coal) = 1-(1/2N)

Let's start simple: 2 lineages

In a population of N diploid individuals (2N gene copies)

t-2

Pr(coal)   = 1/2N
Pr(no coal) = 1-(1/2N)

t-1

No coalescent
Pr(no coal) = 1-(1/2N)

t
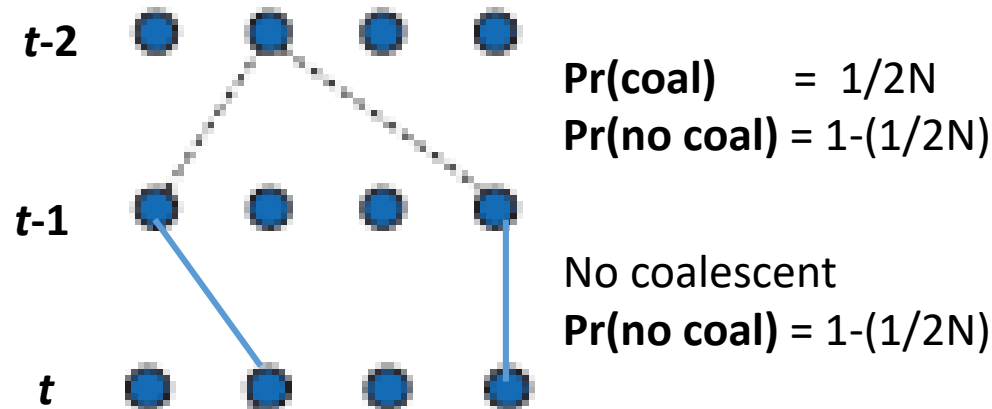
Hence, the probability of coalescent at generation *t* follows a geometric distribution, with probability of success (1/2N):

$$\Pr(\text{coal at generation } t\,) = \left(1 - \frac{1}{2N}\right)^{t-1} \frac{1}{2N}$$

Expected time of coalescent for two lineages

Lets say T_2 is the random variable describing the time (in generations) until two lineages coalesce

$$\Pr(\, T_2 = t\,) = \left(1 - \frac{1}{2N}\right)^{t-1} \frac{1}{2N}$$

T_2 follows a geometric distribution

with probability of success $p=(1/2N)$

Geometric distribution (N=5)

Probability of coalescent

generations into past

Expected time:

$$E[T_2]=(1/p) = 2N$$

(HUGE) Variance:

$$Var(T_2)=(1-p)/p^2 = 2N^2-2N$$
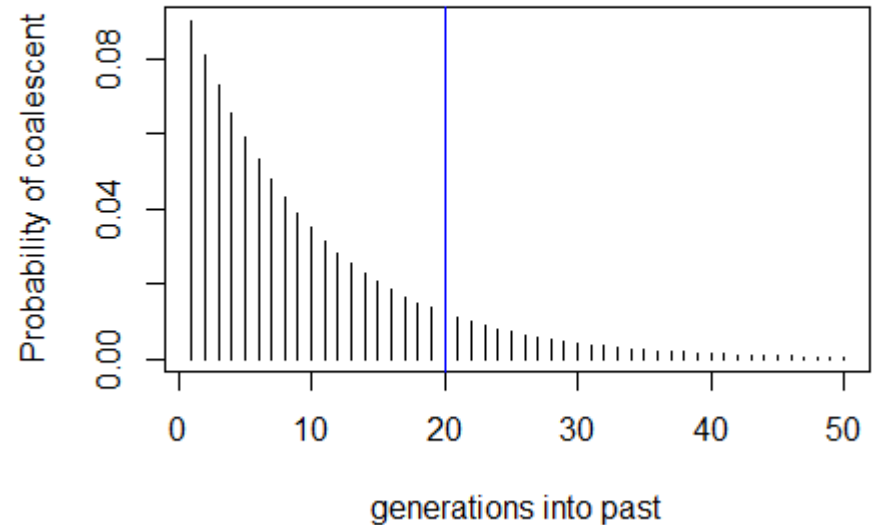
The expected time for the TMRCA of 2 lineages is 2N!

The coalescent process with **more than two lineages**
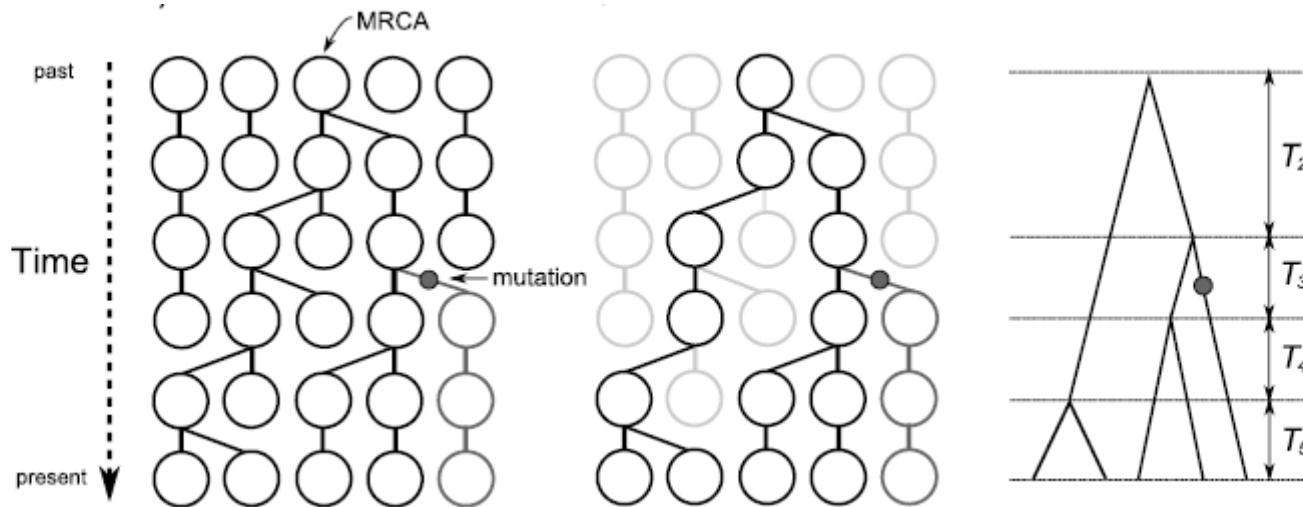
The coalescent process can thus be seen as a process going from n genes at the present time to a single gene sometimes in the past through a series of coalescent events. This last gene is said to be the **Most Recent Common Ancestor** (MRCA) of all genes of the sample.

$$n \rightarrow (n-1) \rightarrow (n-2) \rightarrow \cdots \rightarrow 2 \rightarrow 1\,(MRCA)$$

At each step the probability to pass from n gene lineages to n-1 lineages is $\quad p_n = \binom{n}{2}\dfrac{1}{2N}$

Each generation, we have the same probability p_n of having a coalescent event. The time to the next coalescent event T_n can thus be considered as the **waiting time** until we have a coalescent event, which is therefore **geometrically distributed** with mean

$$E(T_j) = \frac{1}{p_n} = \frac{4N}{n(n\text{-}1)}$$

Expected coalescent times in a constant size population

For a sample of *n* lineages the expected TMRCA is 4N

Continuous time (in 2N units)

Discrete time in generations

2.0 or 4*N*

$E(T_2) = \frac{2N}{1}$

1.3 or 2.6*N*

$E(T_3) = \frac{2N}{3}$

1.0 or 2*N*

$E(T_4) = \frac{2N}{6}$

0.6 or 1.2*N*

$E(T_5) = \frac{2N}{10}$

0.3 or 0.6*N*

$E(T_6) = \frac{2N}{15}$

Present time

★ = Coalescent event
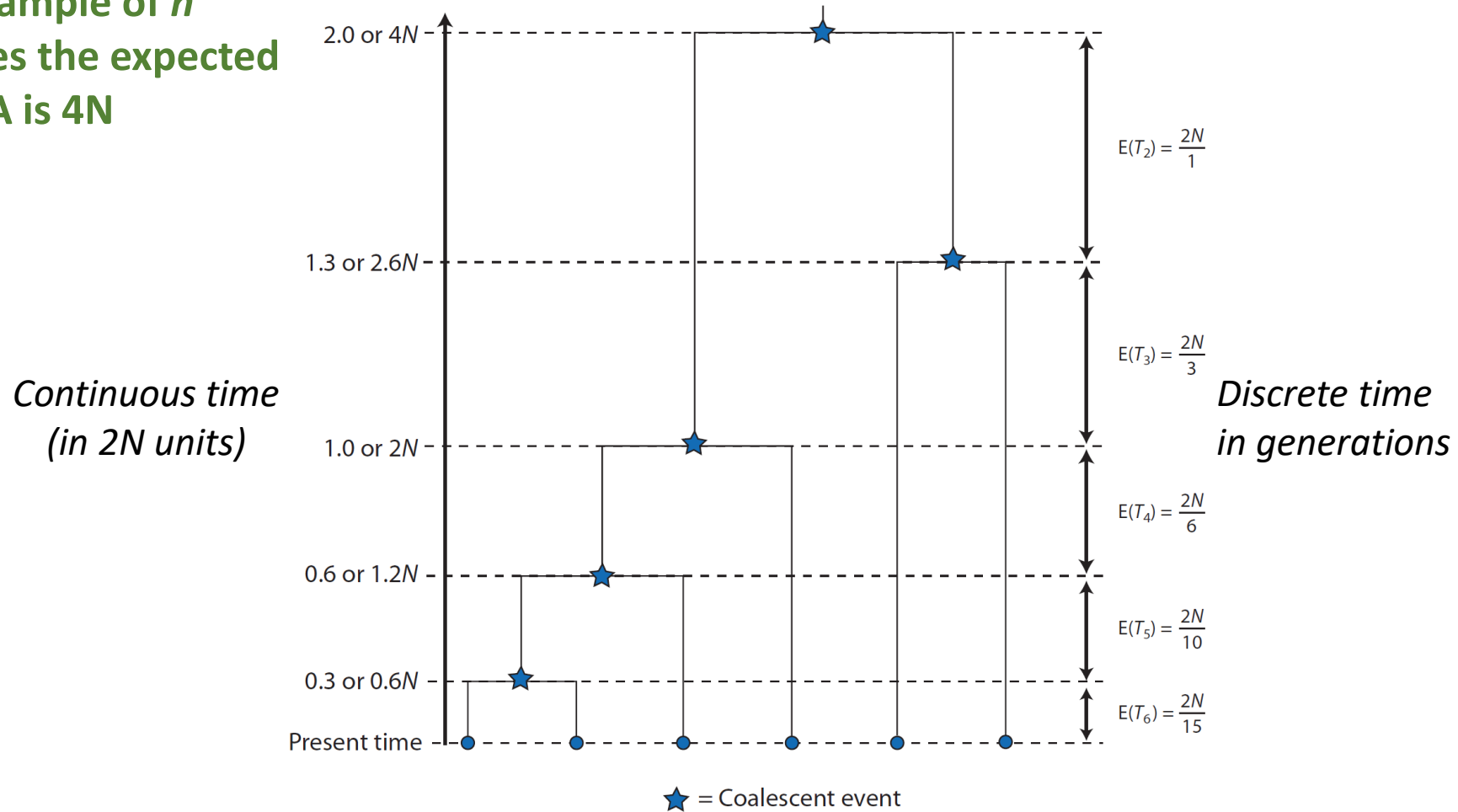
- What are the longest branches we expect in a stationary population?
- Do we expect the relative branch length to differ in large and small populations?

Expected times in a coalescent tree

We can draw a coalescent tree with branch lengths proportional to their expected values as

At each coalescent event, pick two lineages at random to coalesce

T_2 4N/2

T_3 4N/6

T_4 4N/12

T_5 4N/20

1   2   3   4   5
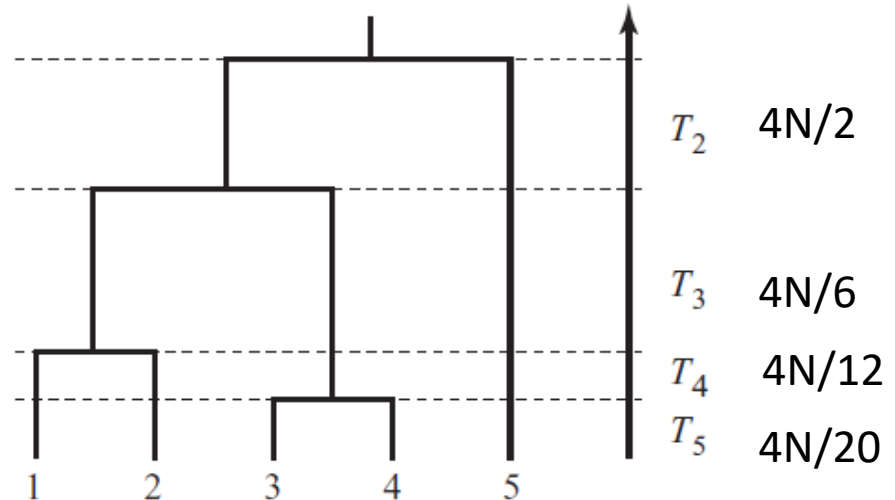
Note that:
1) The coalescent process only gives us times between successive coalescent events, but not the topology. Assuming that all individuals are equally fit, **a pair of lineage is chosen at random for each coalescent event.**
2) Coalescent times increase with decreasing number of lineages: we expect long internal branch length and small external branch lengths
3) There is an enormous variance in the coalescent process

The expected time is 4N, but there is a large variance
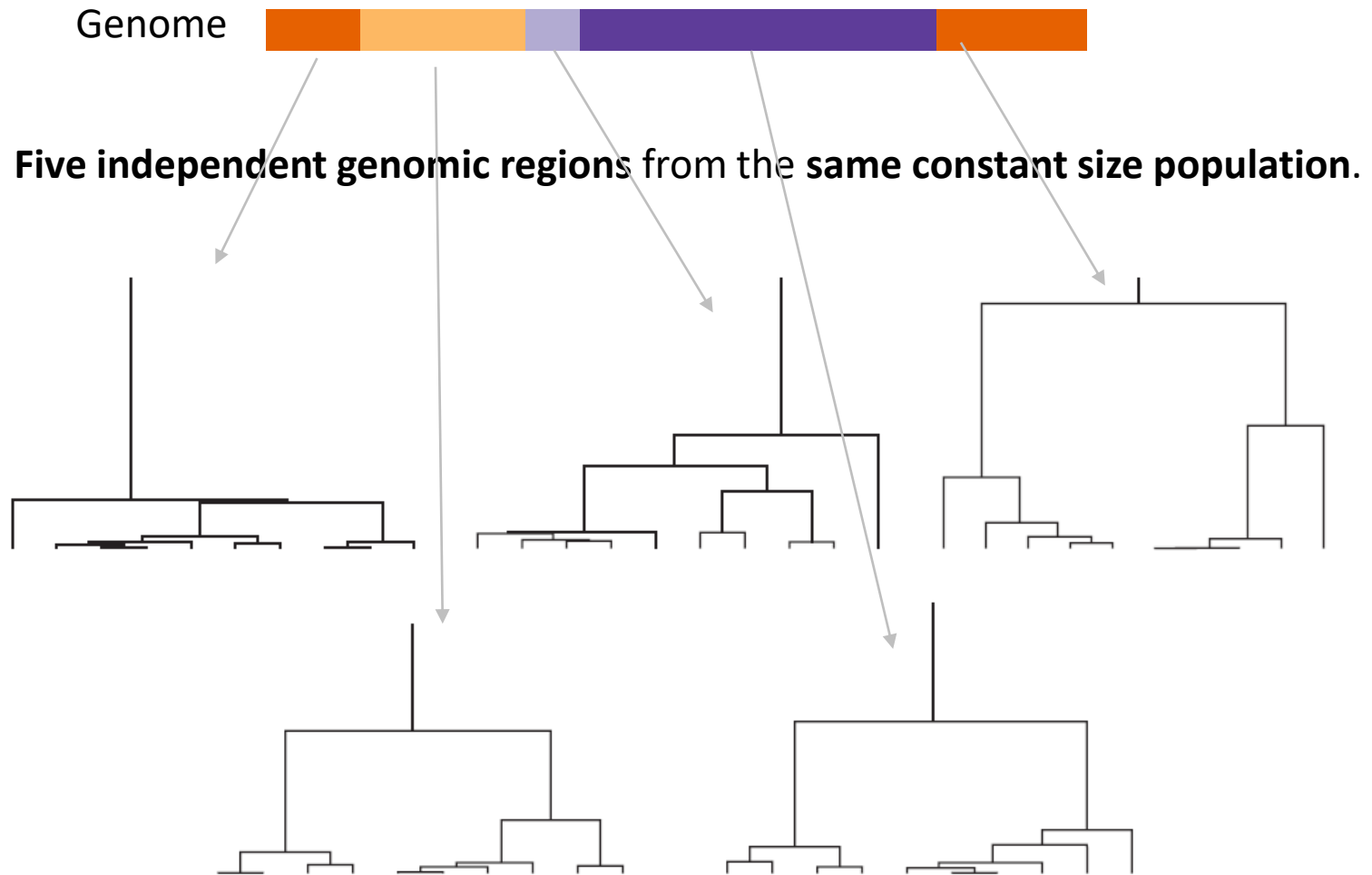
Figure 4.2 Five replicates of the coalescent process with constant population size for a sample of ten genes. Note the large variance in the time of the MRCA among replicates.

Hein et al (2004) Gene Genealogies, Variation and evolution

Gene trees in growing populations

Stationary Population

Expanding Population

With less lineages the longer the time intervals between coalescent events

Most coalescent occur in the ancestral population, when the size is smaller.

Long external branches
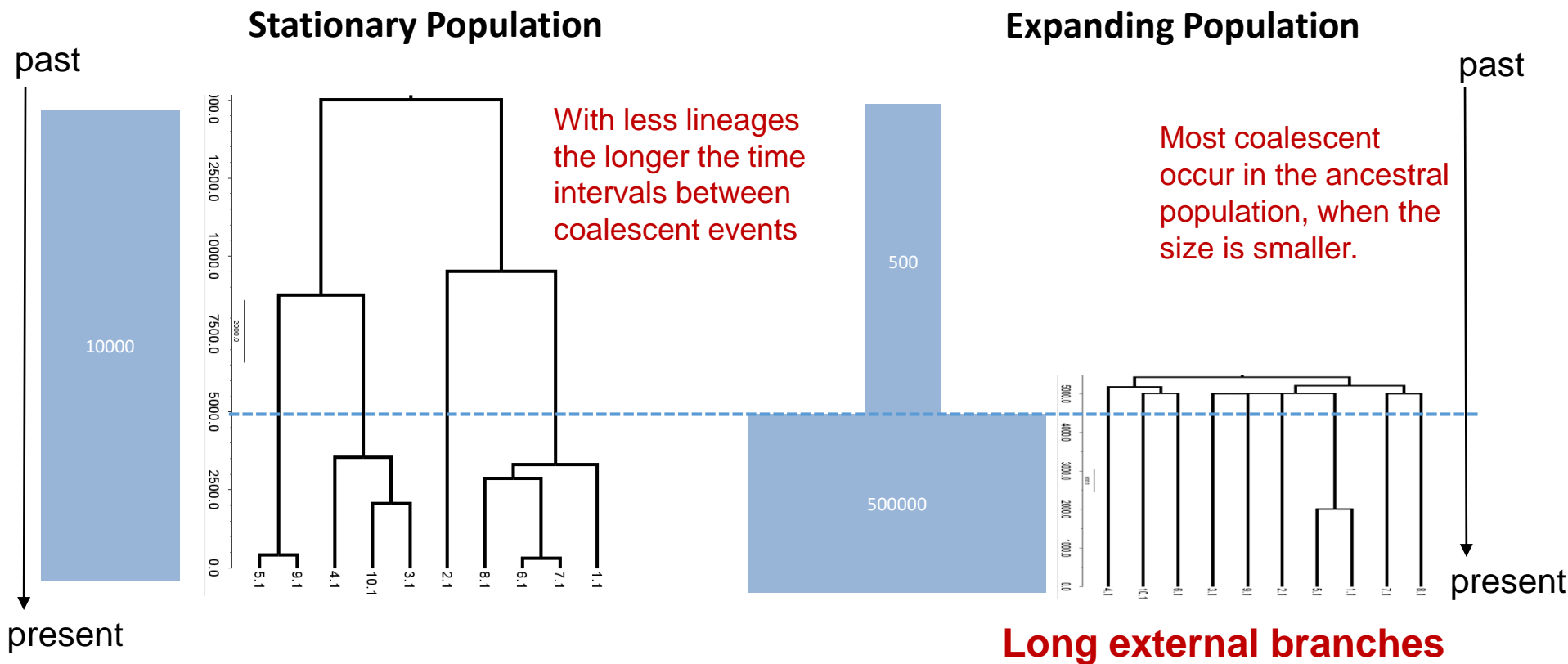
- Coalescent rate is larger in smaller populations, and so we expect smaller intervals between coalescent events in smaller populations

- Coalescent rate is lower with a lower number of lineages, and so we expected larger intervals between coalescent events as the number of lineages decrease

Stationary population
gene trees at five genome regions
(all share same population history!)

10000

Figure 4.2   Five replicates of the coalescent process with constant population size for a
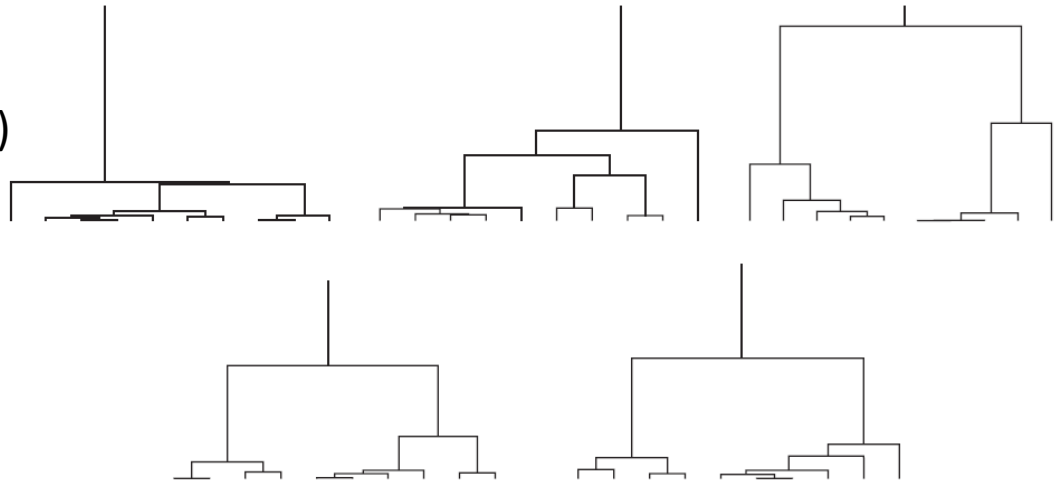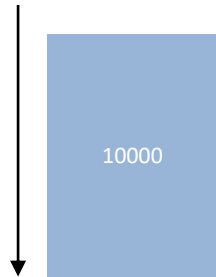sample of ten genes. Note the large variance in the time of the MRCA among replicates.

Expanding population
gene trees at five genome regions
(all share same population history!)

500

500000
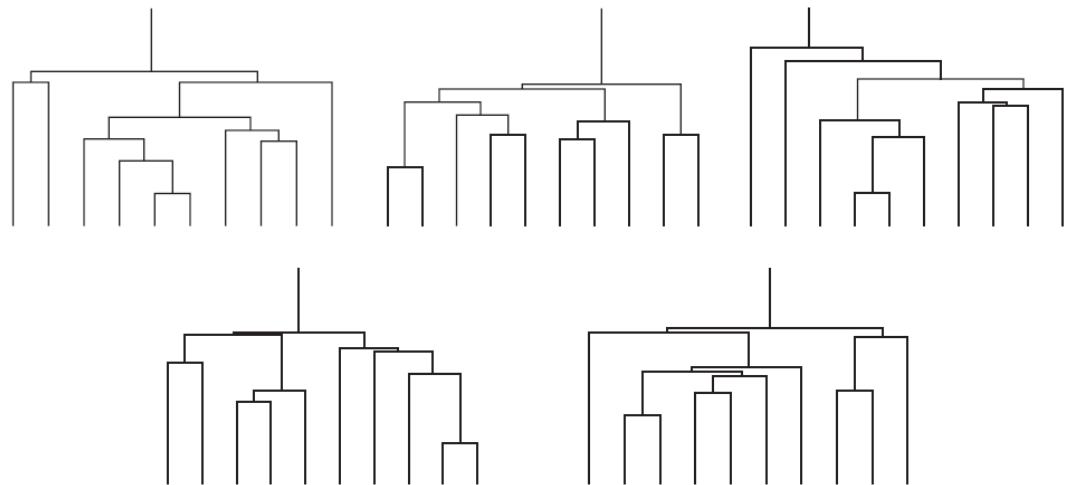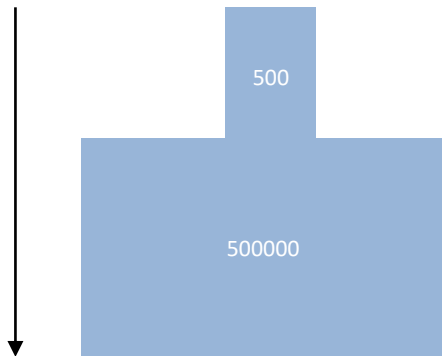
Figure 4.3   Five replicates of the coalescent with exponential growth, $\beta = 1000$, for a
sample of $n = 10$ genes. Note the smaller variance in the time until the MRCA compared
to the same quantity in Figure 4.2.

Hein et al (2004) Gene Genealogies, Variation and evolution

Gene trees for decreasing populations

Stationary Population

Bottleneck Population

past

past

With less lineages the longer the time intervals between coalescent events

Most coalescent events occur in recent times, when the size is smaller.

10000

500000

500

present

present

Long internal branches
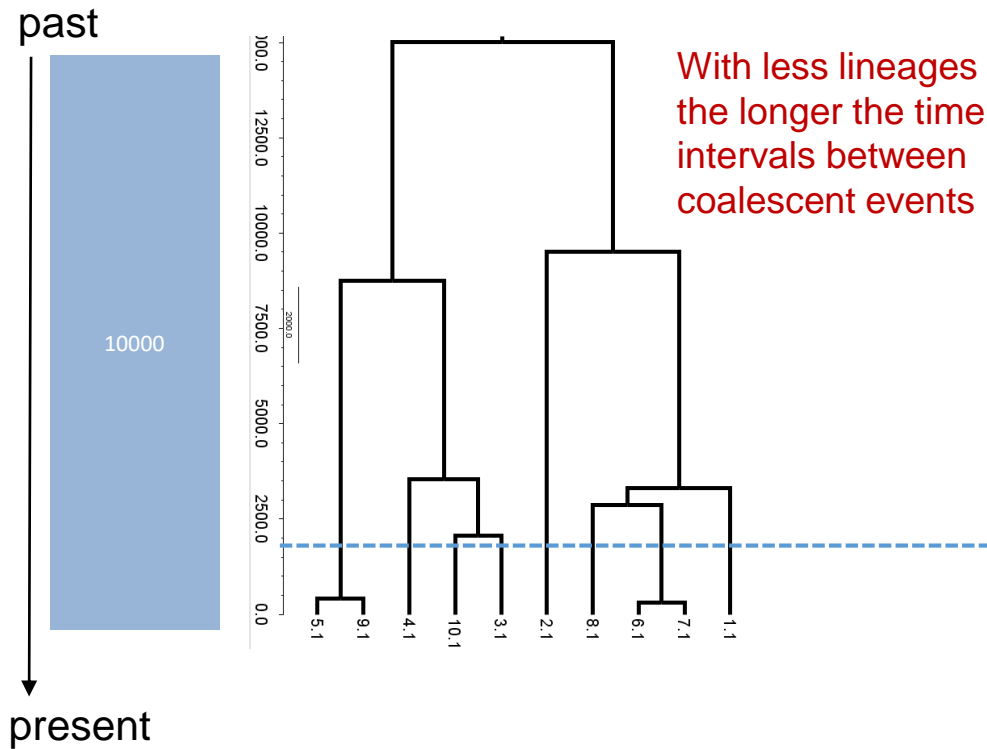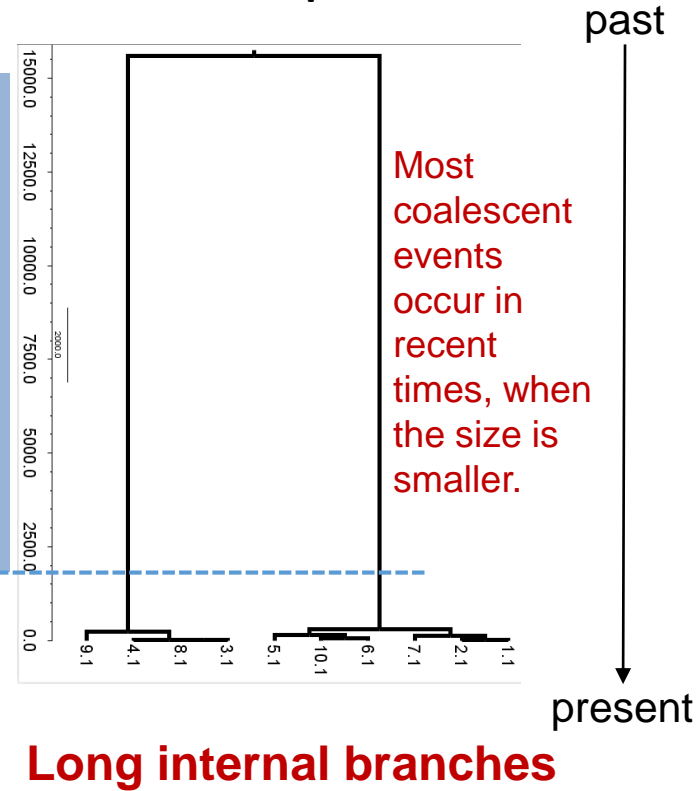
- If we could observed directly the gene trees, we could easily reconstruct the population tree and the demographic history.

- But we do not observe gene trees…

- We can still learn about gene trees from the observed mutations and the allele frequencies in samples

Adding neutral mutations

The shape of neutral coalescent trees only depend on the population demography, and not on the mutational process. Assuming that all alleles have the same fitness, the mutational process can be modeled as an independent process superimposed on a realized coalescent tree.
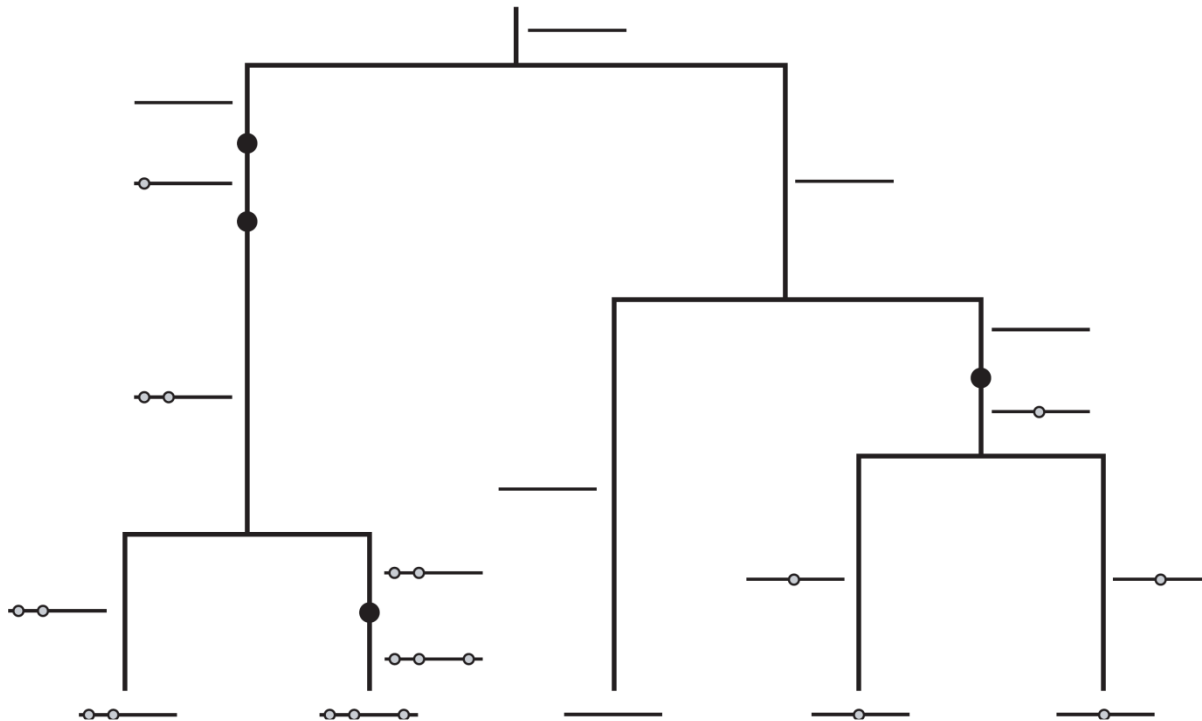

Mutations just accumulate along the branches of the tree according to a **Poisson process** with rate $\lambda_i = \mu t_i$ for the *i*-th branch of length t_i. The Poisson process is stochastic but it should be immediately **obvious that long branches will carry more mutations than short branches**

Hein et al (2004) Gene Genealogies, Variation and evolution

We expect less diversity in a bottlenecked population

- Mutations accumulate along the branches.
- The longer a given branch the more likely it becomes that a mutation have happened on it.

Stationary Population

Bottleneck Population

past

present

Mutations shared by 5 descendents

Mutations only found in one descendent (Singletons)

Mutations shared by 4 descendents

Mutations shared by 6 descendents

Most individuals share the same mutations
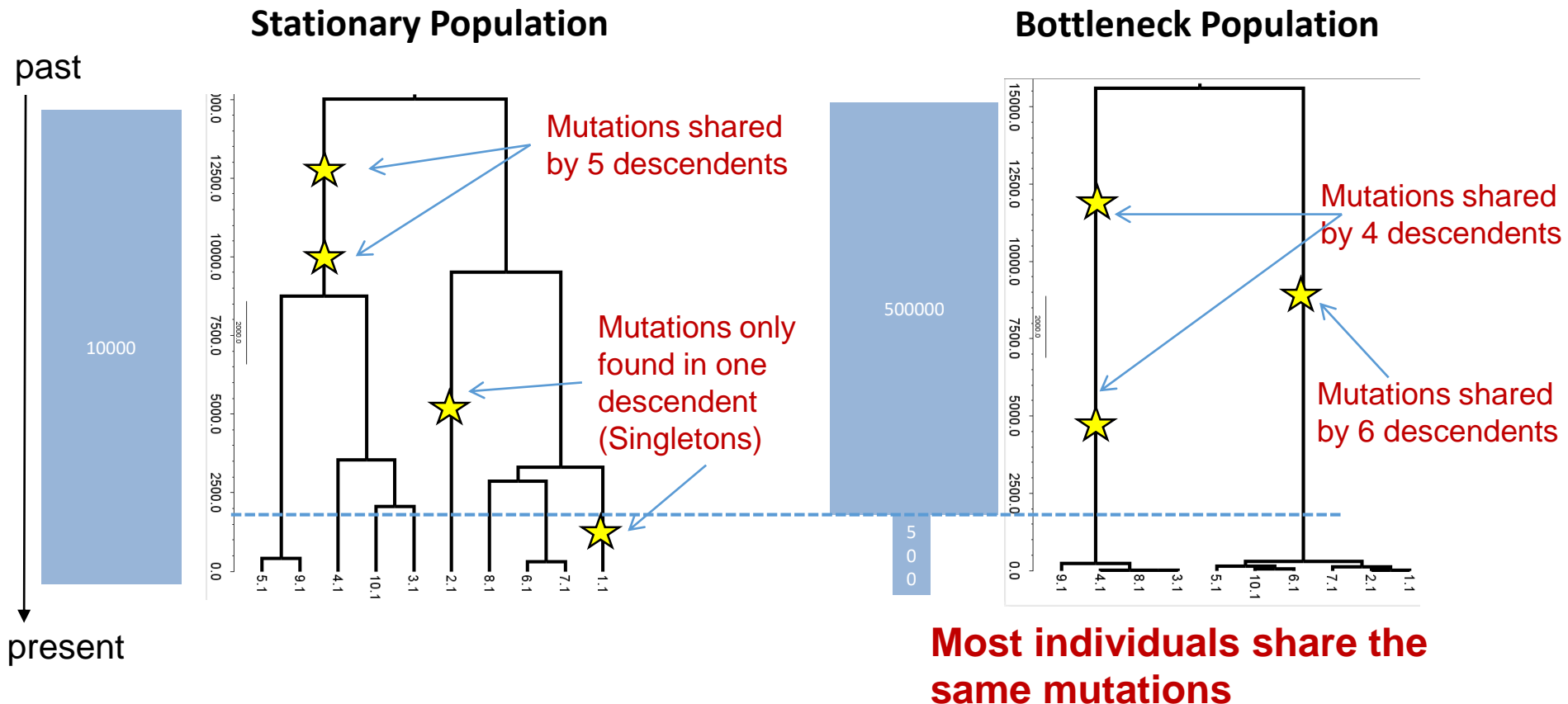
We expect less diversity in a bottlenecked population

Stationary Population

Expanding Population

past

present

Mutations shared by 5 descendents

Mutations only found in one descendent (singletons)
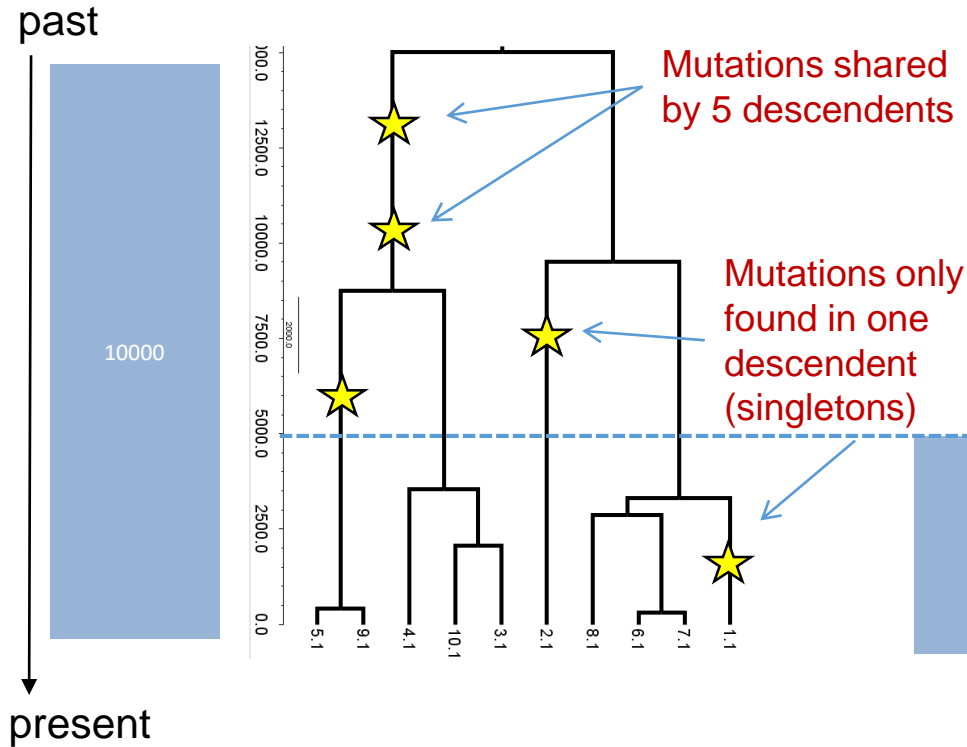
In an expanding population, most mutations are only found in a single lineage - SINGLETONS
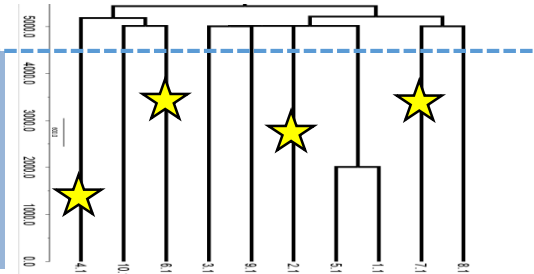
10000

500

500000

Site frequency spectrum (SFS)

- The SFS summarizes efficiently genome-wide data

- Assuming a single population – 1Dimensional SFS

Outgroup   ATACCG...
Individual 1 ATACCG...
Individual 2 ATTCGG...
Individual 3 ATACGG...

Data

?

Observed SFS

Site frequency spectrum (SFS)

↓

Outgroup ATACCG…
Individual 1 ATACCG…
Individual 2 ATTCGG…
Individual 3 ATACGG…

Data

- The SFS summarizes efficiently genome-wide data

- Assuming a single population – 1Dimensional SFS

Observed SFS

Frequency of derived allele

Site frequency spectrum (SFS)

↓

Outgroup   ATACCG…
Individual 1 ATACCG…
Individual 2 ATTCGG…
Individual 3 ATACGG…

Data

- The SFS summarizes efficiently genome-wide data

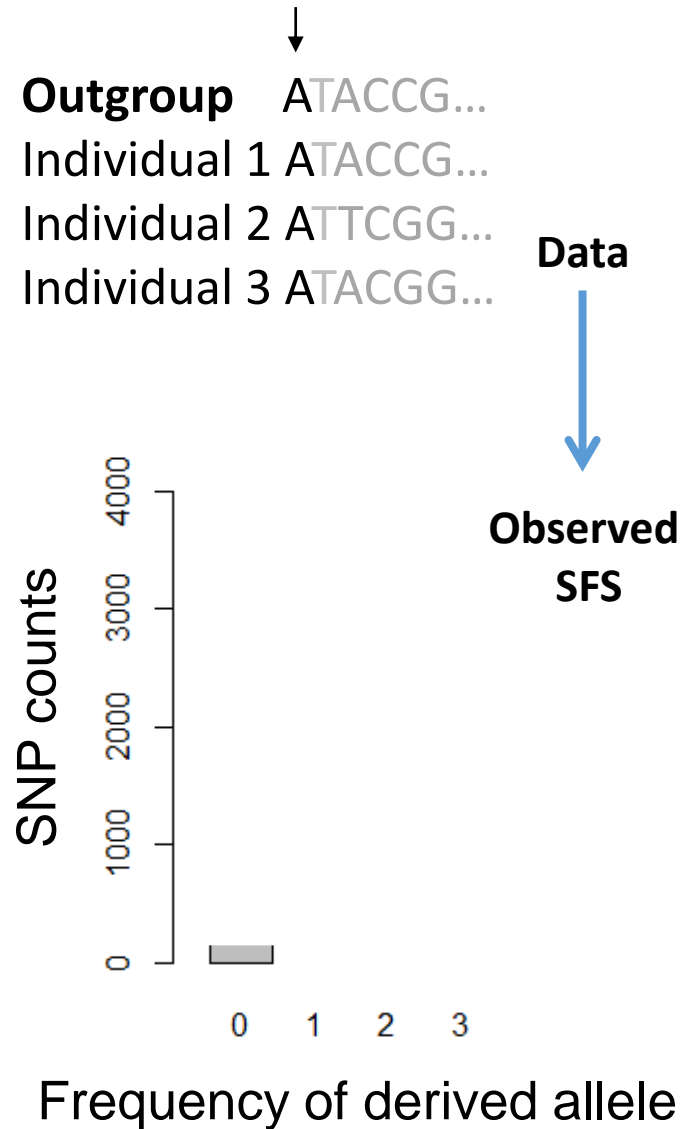- Assuming a single population – 1Dimensional SFS
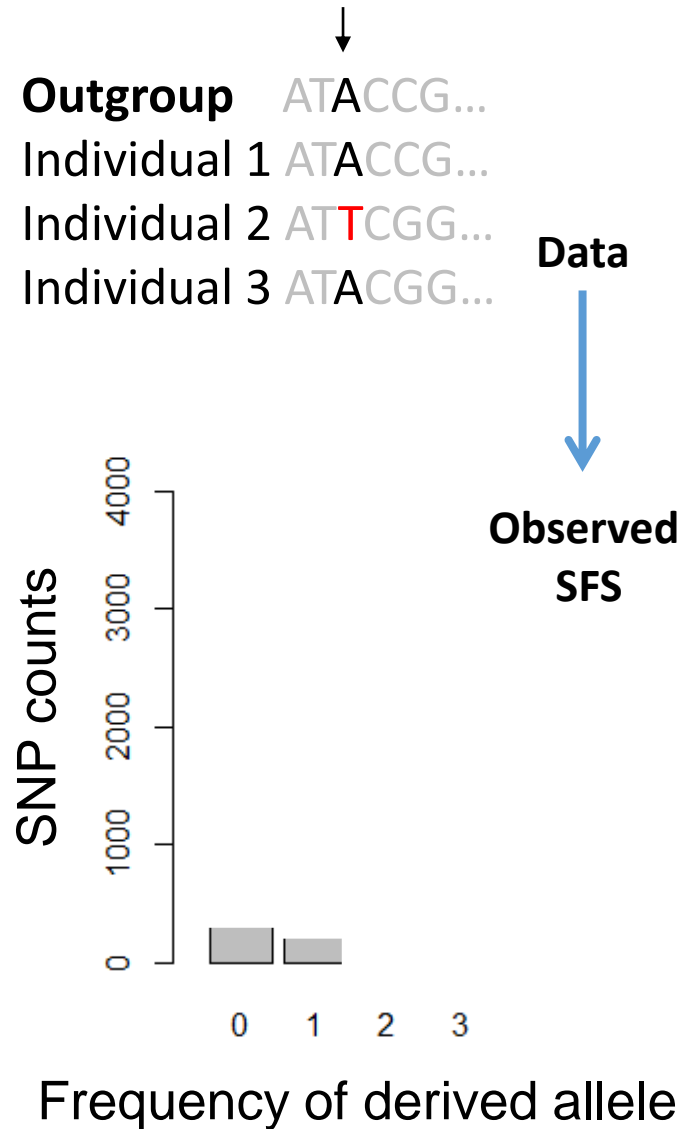
Observed SFS

Frequency of derived allele

Site frequency spectrum (SFS)

- The SFS summarizes efficiently genome-wide data

- Assuming a single population – 1Dimensional SFS

The SFS ignores information about linkage. It is best suited for the study of many unlinked (or recombining) DNA sequences.

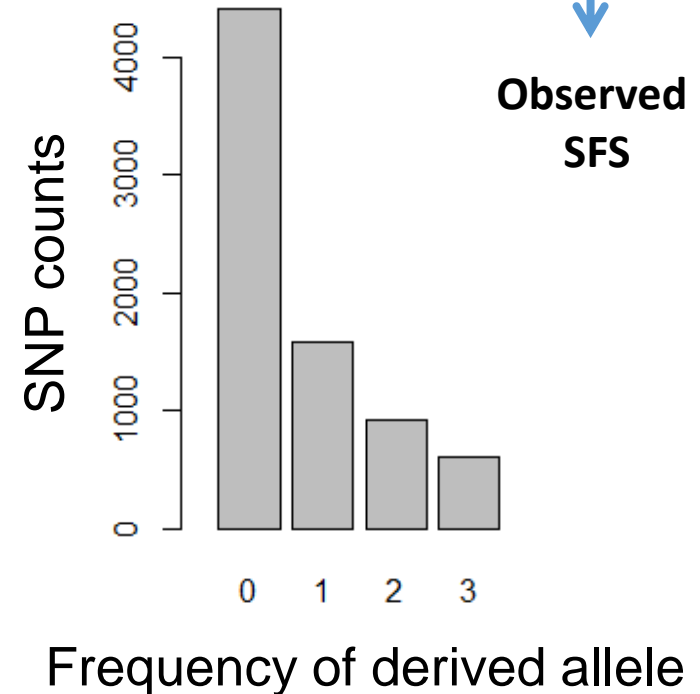In a stationary population, the expected SFS relative frequencies are given by:

$$E(\xi_i) = \frac{\theta}{i}$$

Fu and Li, 1993

Outgroup ATACCG…
Individual 1 ATACCG…
Individual 2 ATTCGG…
Individual 3 ATACGG…

Data

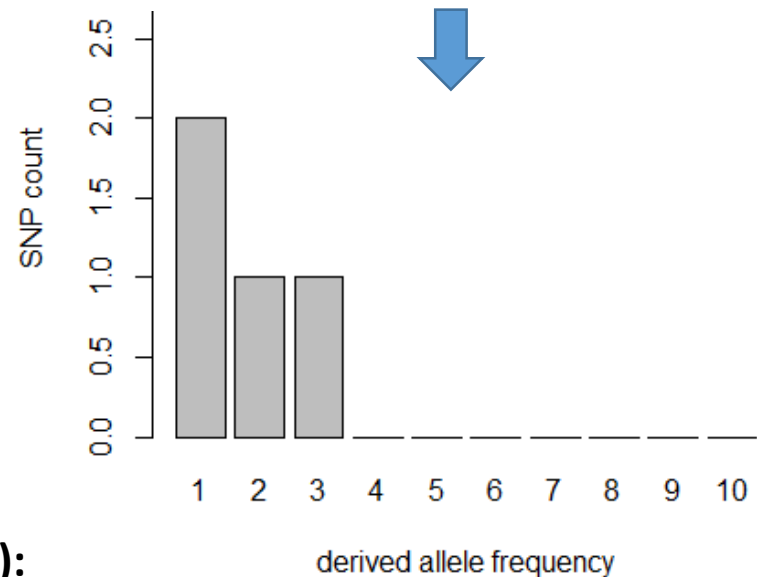**Observed SFS**

SNP counts

Frequency of derived allele

We can obtain the SFS from genotype call data

Genotypes:

- 0 homozygote for reference allele

- 1 heterozygote

- 2 homozygote for alternative allele

This can be done if we have enough depth of coverage (>10x)

	SNP1	SNP2	SNP3	SNP4
Individual 1	0	2	0	1
Individual 2	0	0	1	0
Individual 3	1	0	0	0
Individual 4	0	1	0	0
Individual 5	0	0	1	0

Observed SFS is a vector (1 dimensional SFS):

Frequency	0	1	2	3	4	5	6	7	8	9	10
SNP count	0	2	1	1	0	0	0	0	0	0	0

SFS from genotype call data

Even if we have millions of SNPs we can summarize the genomic data to 10 numbers with the SFS!

The size of the SFS depends on the number of sampled individuals.
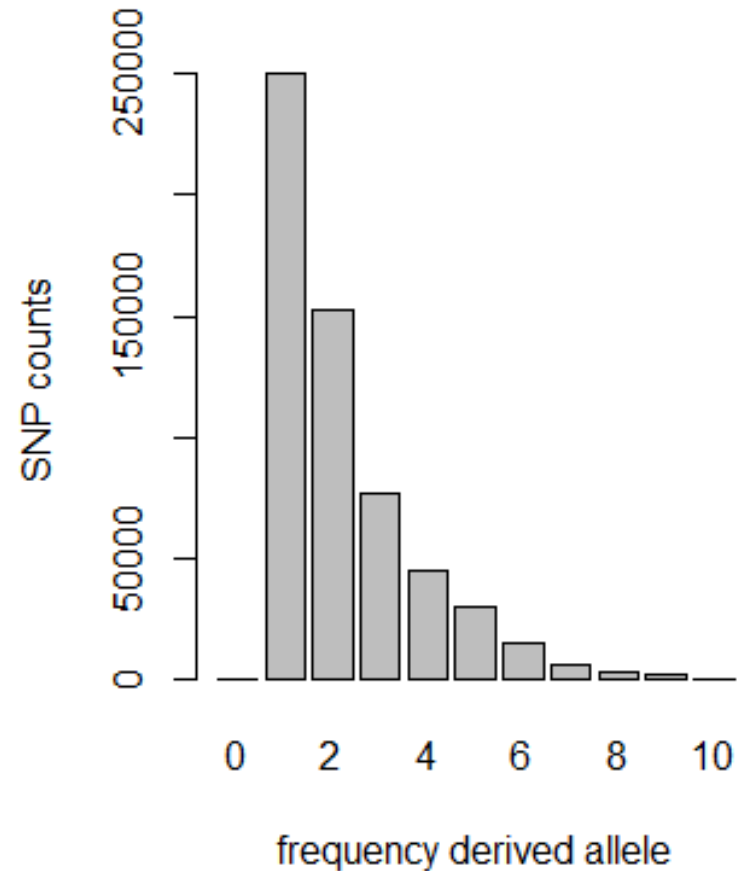
Observed SFS is a vector (1 dimensional SFS):

Frequency	0	1	2	3	4	5	6	7	8	9	10
SNP count	0	250,032	152,300	76,504	45,362	30,210	15,329	5,642	3,524	2,123	0

Coalescent and the SFS

- A recent population growth following a bottleneck leads to gene trees with long external branches

- Very few mutations in the internal branches

- Most mutations in long external branches are only found in one lineage, resulting in an excess of singletons

past

Internal branches

External branches

present

Count SNPs

6
5
4
3
2
1

1 2 3 4 5 6
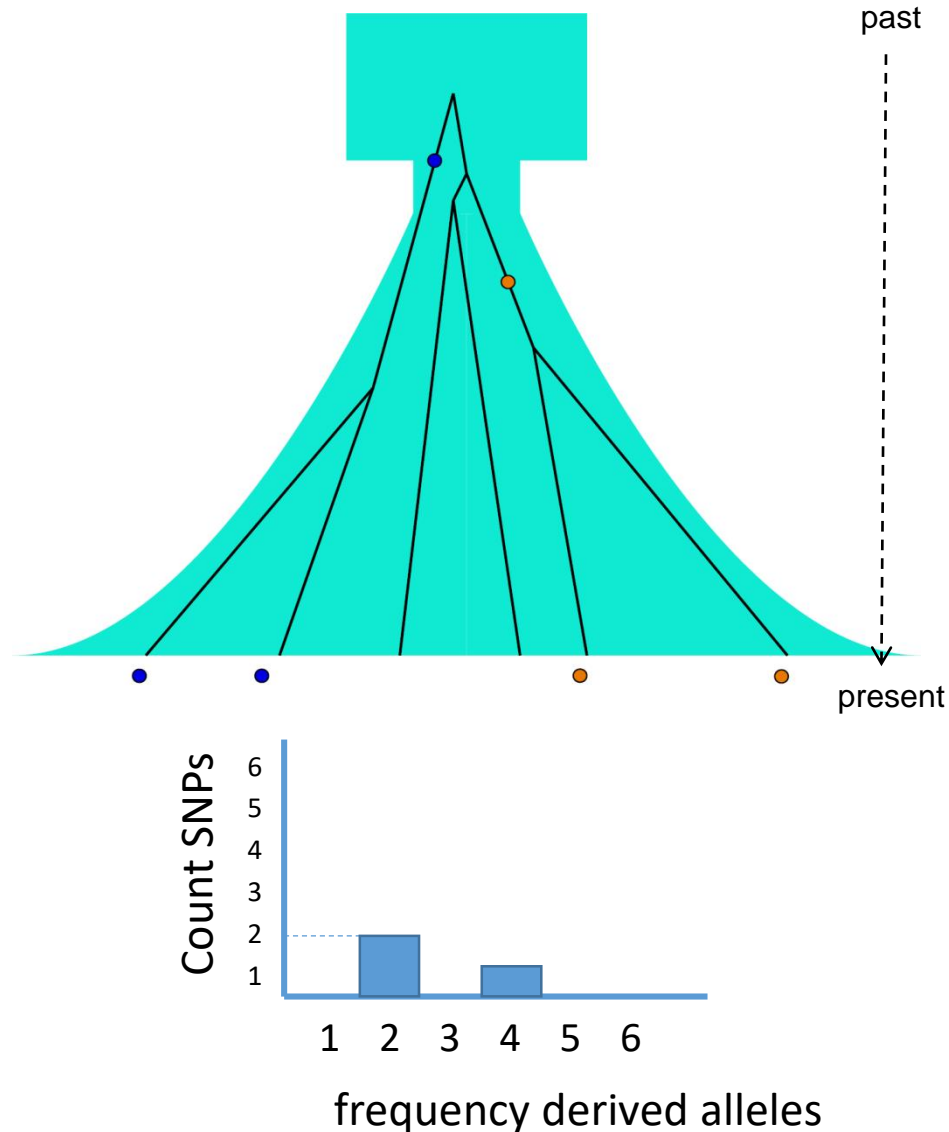
frequency derived alleles
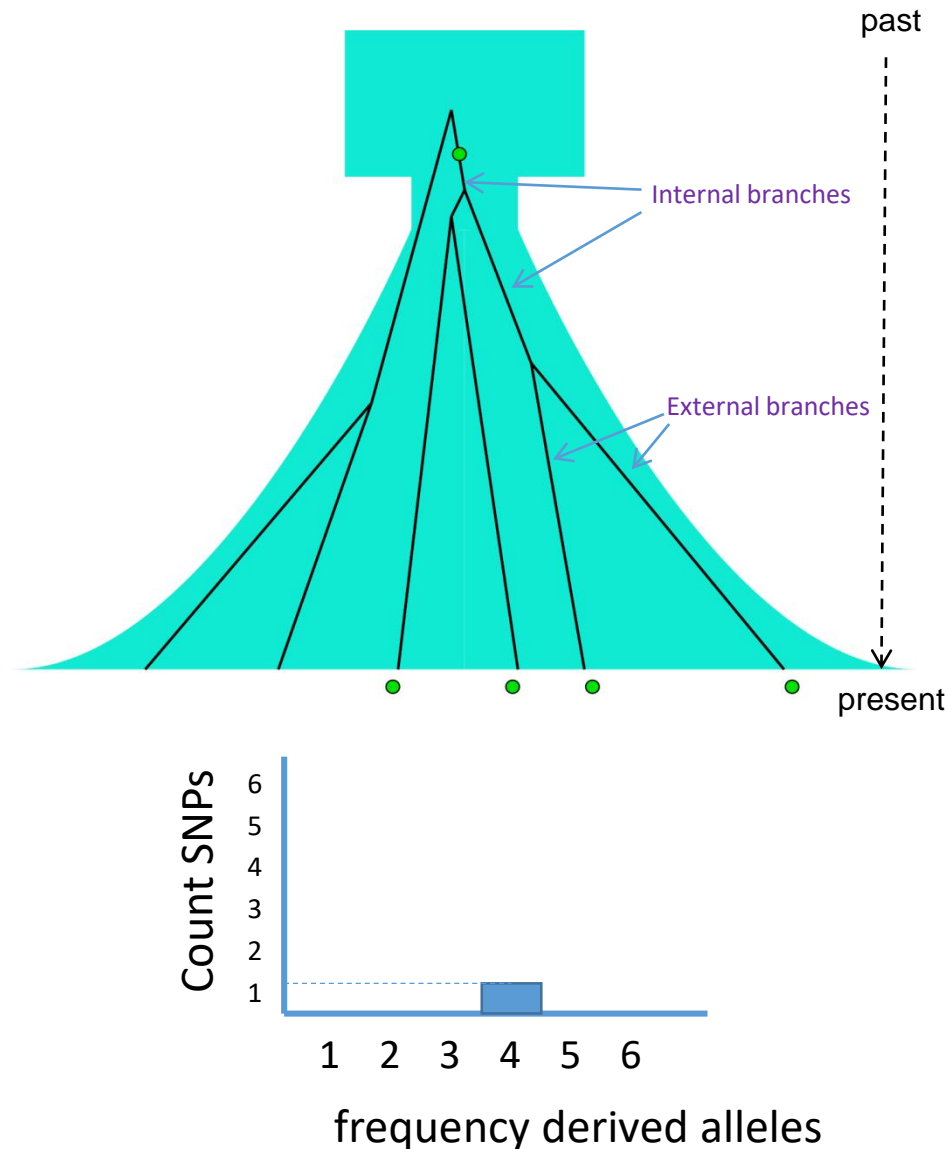
Coalescent and the SFS

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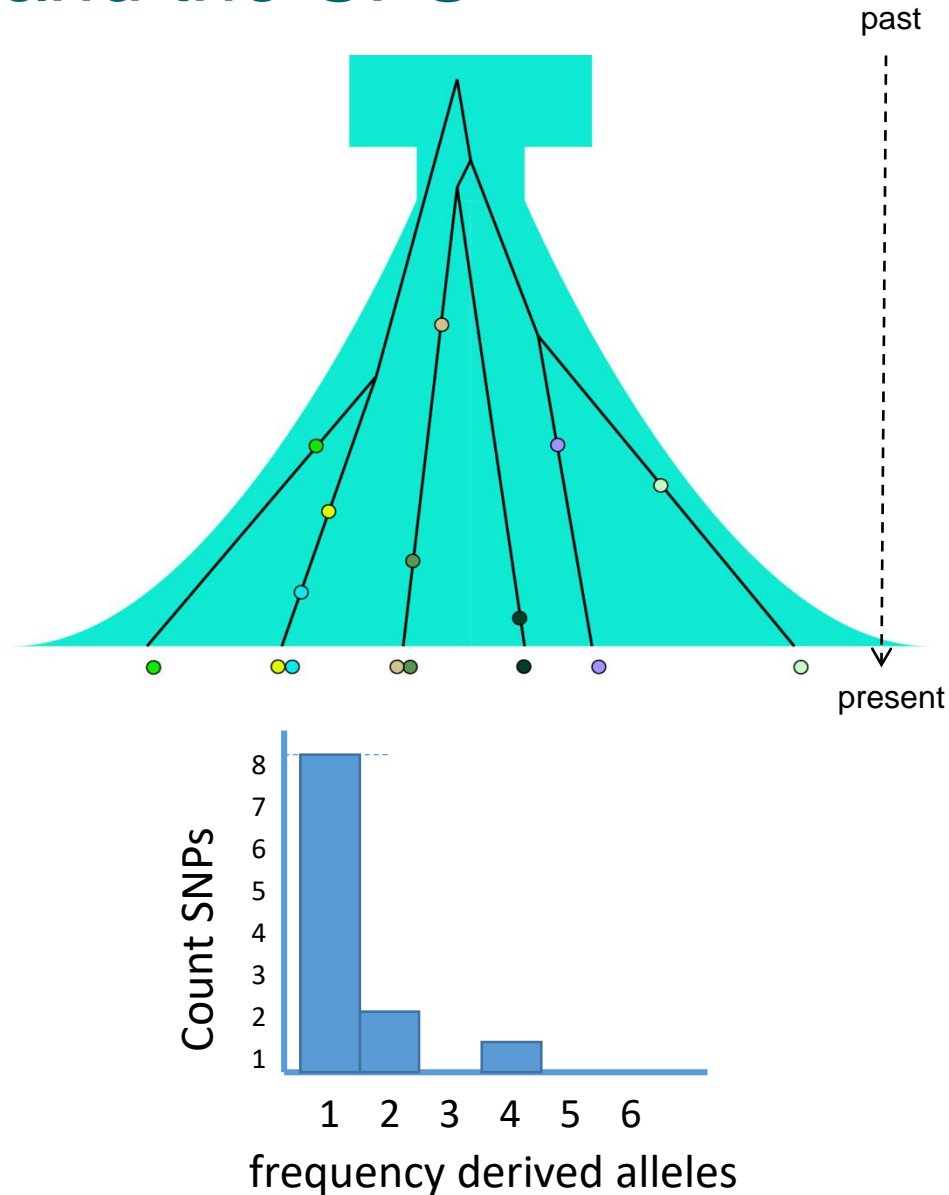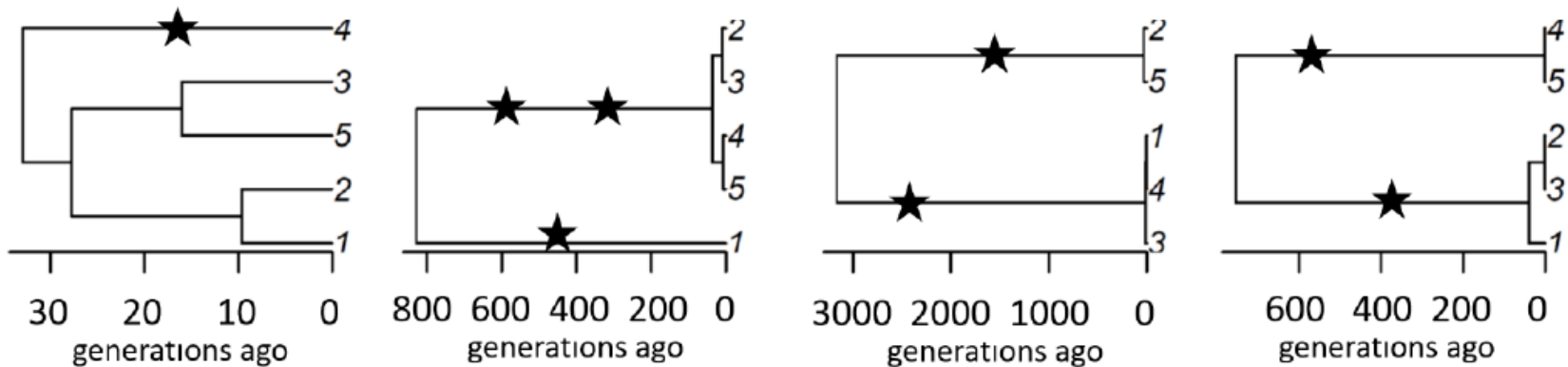
Coalescent and the SFS

- A recent population growth following a bottleneck leads to gene trees with long external branches

- Very few mutations in the internal branches

- Most mutations in long external branches are only found in one lineage, resulting in an excess of singletons

Coalescent gene trees at multiple independent sites and the SFS

- The SFS is summed across loci
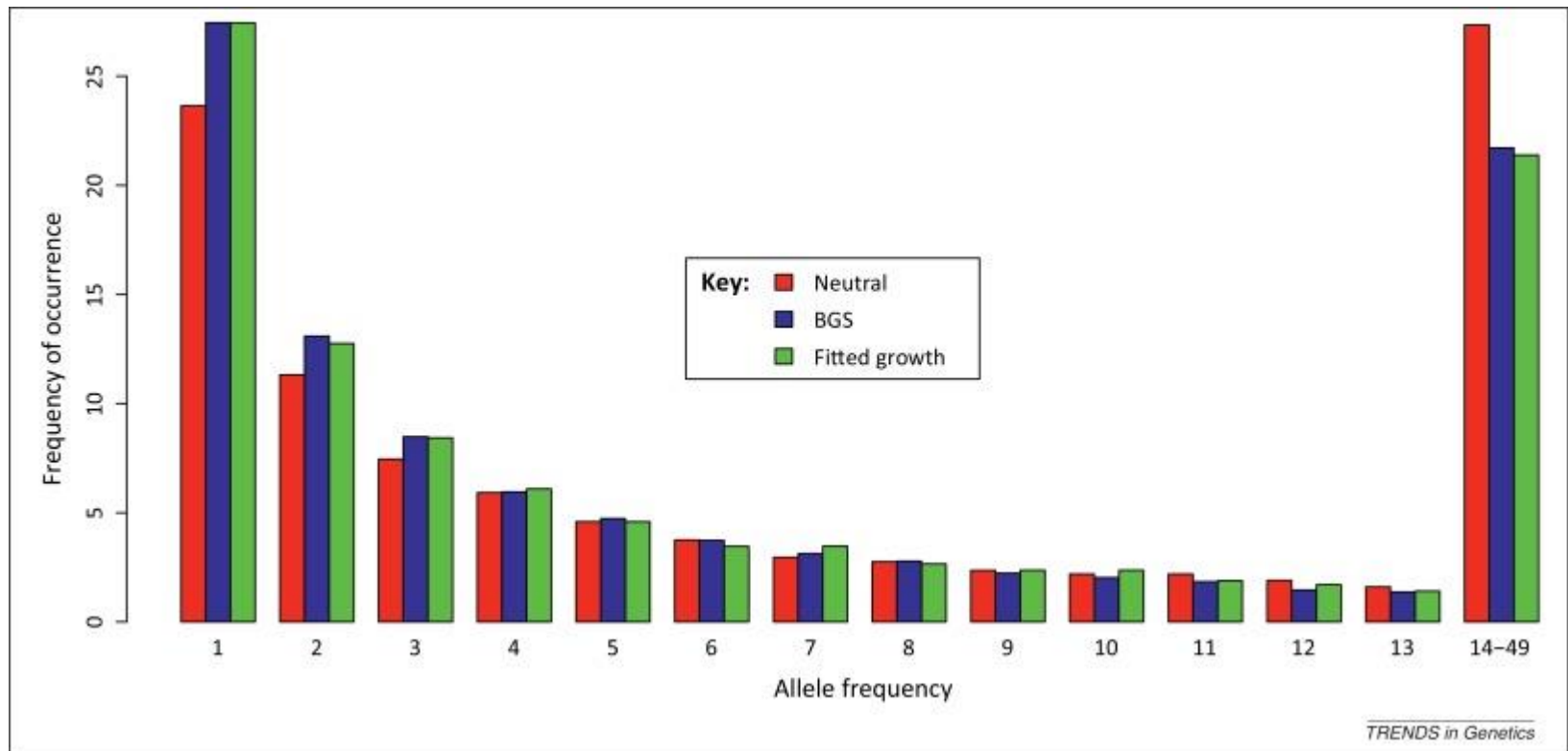
- Independent loci can have different gene trees, and different mutations and allele frequencies

- But, assuming neutrality, all sites in the genome reflect the population tree and the demographic history

- What can we say about the demographic events that lead to this SFS?
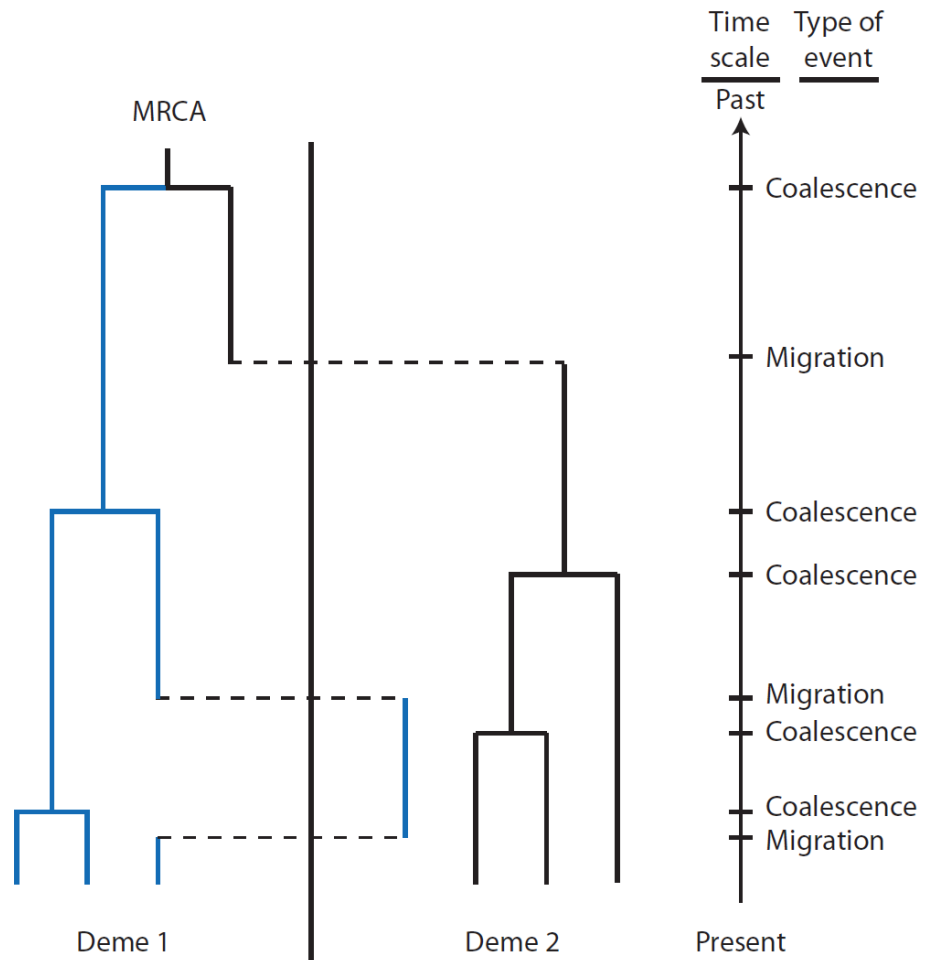   - Bottleneck, expansion, constant size population?
    - Time of event?
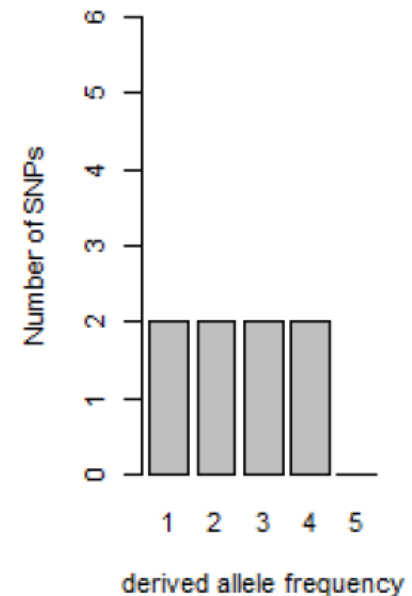
SFS depends on past demography
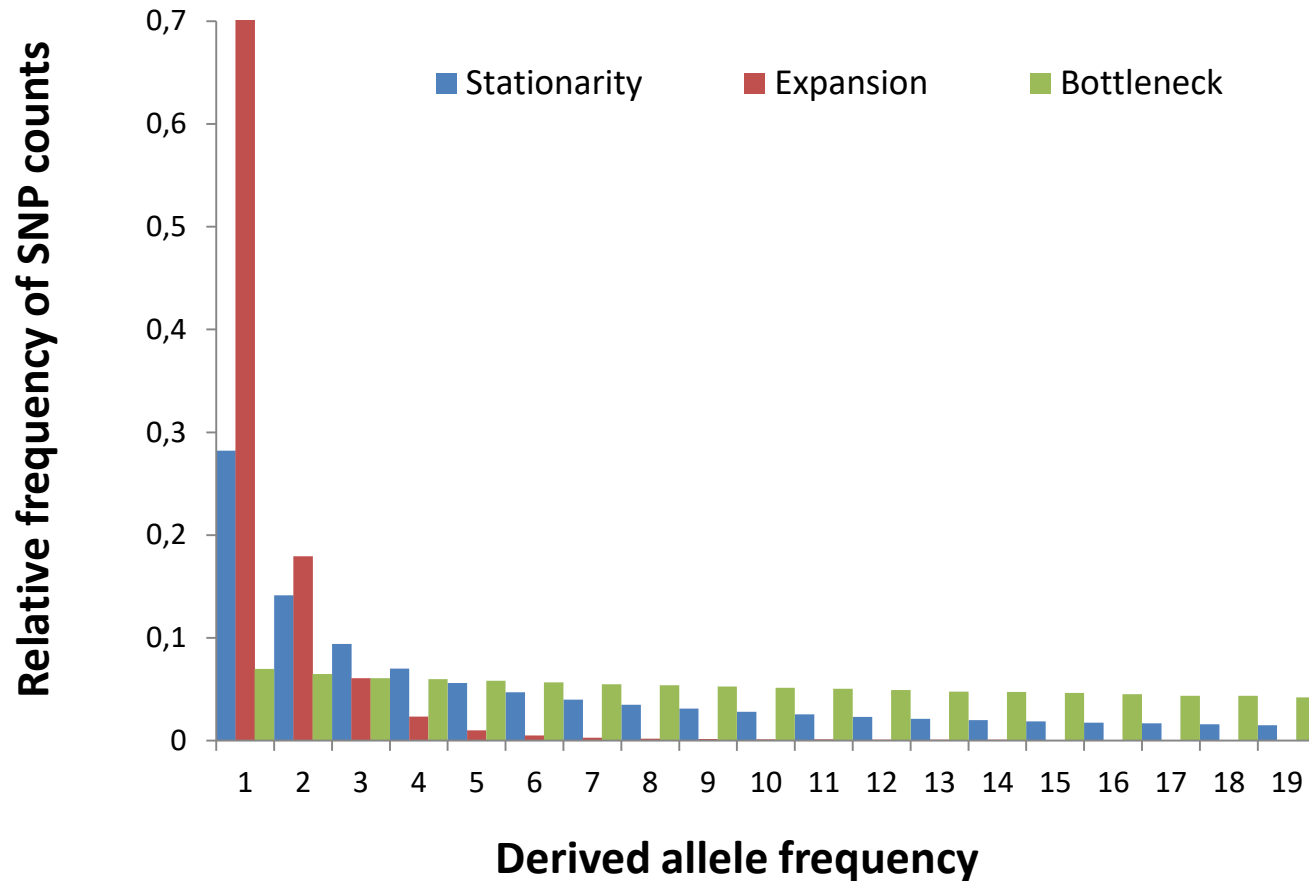
Natural selection also affects the SFS

Background selection (BGS) leads to patterns similar to population expansion.

Bank et al (2014) Trends in Genetics

Population structure

Migration events can be incorporated into gene trees.

Migration from Pop 2 to Pop 1, leads to lineages moving from Pop 1 to pop 2 backward in time.

At each generation, the probability of immigration into population 1 from population 2 is given by:

Pr(migrate) = $n_1 * m$

Where n_1 is the number of lineages in population 1, and m is the immigration rate.

Site frequency spectrum from multiple populations (joint SFS)

- For a pair of populations – 2D SFS
  - Count the SNPs have a frequency of the derived allele of i in population 1, and of j in population 2

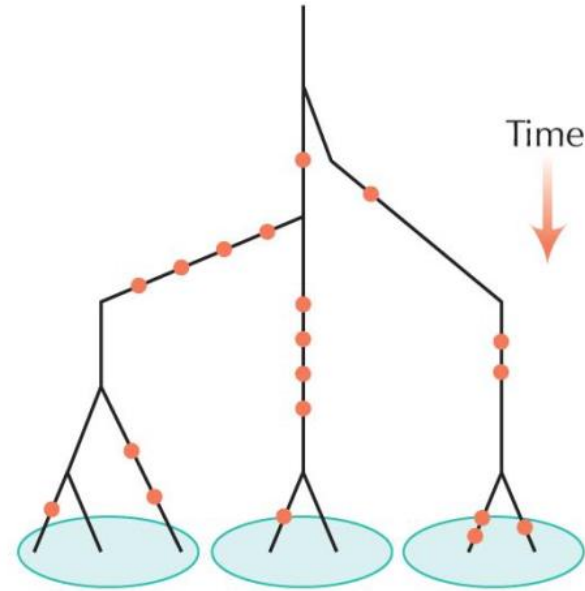- We can extend this to 3D SFS, 4D SFS, etc.
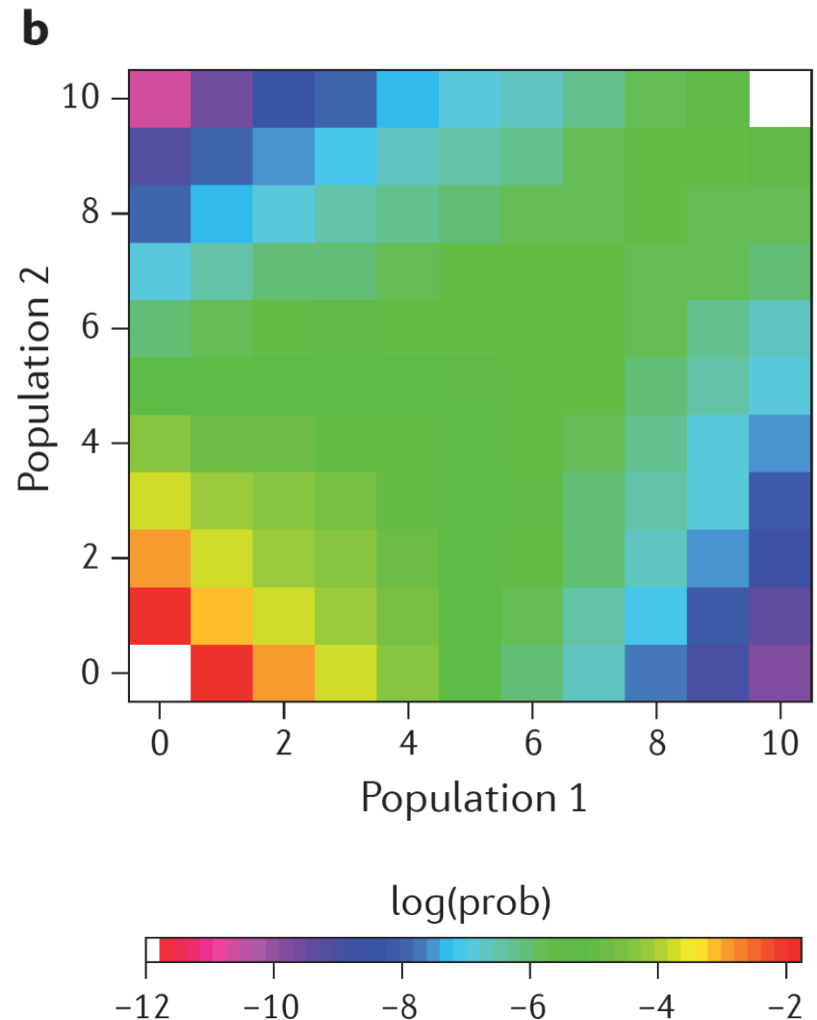
F_{ST} in terms of coalescent times

$$F_{ST} = (f - f_w)/f$$

Where:

f is the average coalescent time among populations

f_w is the average coalescent time within populations

FIGURE 16.13. Wright's F_{ST} is related to the mean coalescence time between pairs of genes within demes, compared with the mean coalescence time between randomly chosen pairs: $F_{ST} = (\overline{T} - T_w)/\overline{T}$. These coalescence times, and hence F_{ST}, can be estimated from the number of mutations that separate each pair of genes (assuming the infinite sites model; see p. 424). In this example, seven genes are sampled from three demes; mutations are indicated by *red circles*. On average, there are 8.1 differences between pairs of genes sampled at random compared with 2.0 differences between genes within the same deme. Hence, F_{ST} is estimated to be $(8.1 - 2.0)/8.1 = 0.753$.
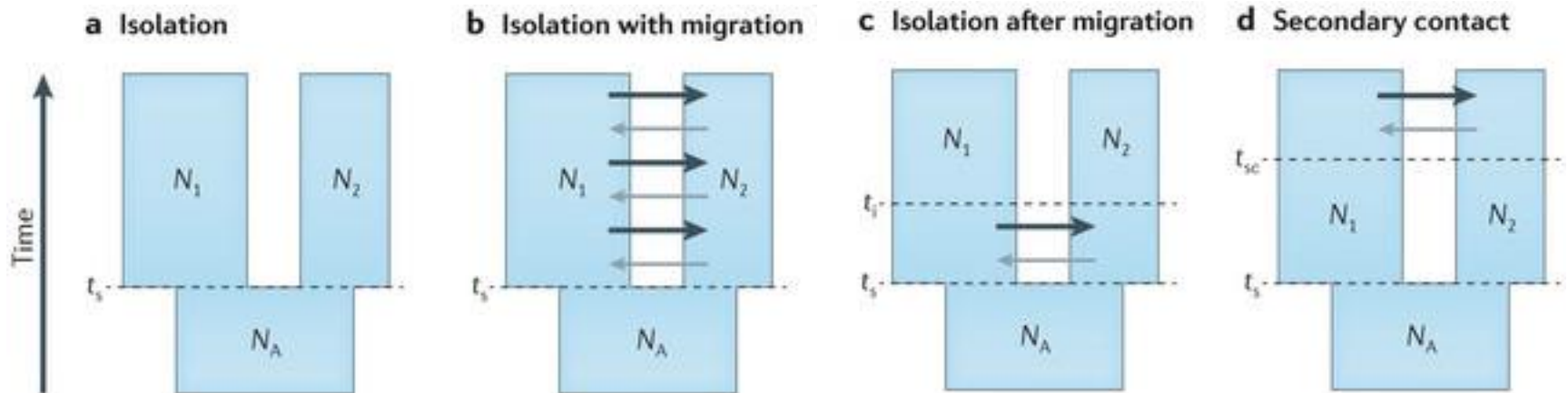
Derived vs Minor allele frequency spectrum

- So far, we have assumed that the allele frequency is the number of sequences with the derived allele frequency (unfolded SFS). We need information (outgroup) to determine the ancestral/derived state.

- If we do not have that information, we can work with the minor allele frequency (folded SFS). In this case, the allele with a lower frequency is treated as the reference.

# Model based inference

- What is the model that best fits the data?
- What are the most likely parameters of each model?

a Isolation

b Isolation with migration

c Isolation after migration

d Secondary contact

Sousa and Hey (2013) Nat. Rev. Gen.

# A model is represented by a population tree that reflects the past evolutionary history

Parameters:

Demography

- Population split times
- Migration rates
- Effective population sizes
- Temporal changes in migration rates and effective sizes

Selection

- Selective coefficient and type of selection (positive or negative)

Genomic processes

- Mutation rate
- Recombination rate

Population tree

Time

t_s

N_1

N_2

N_A
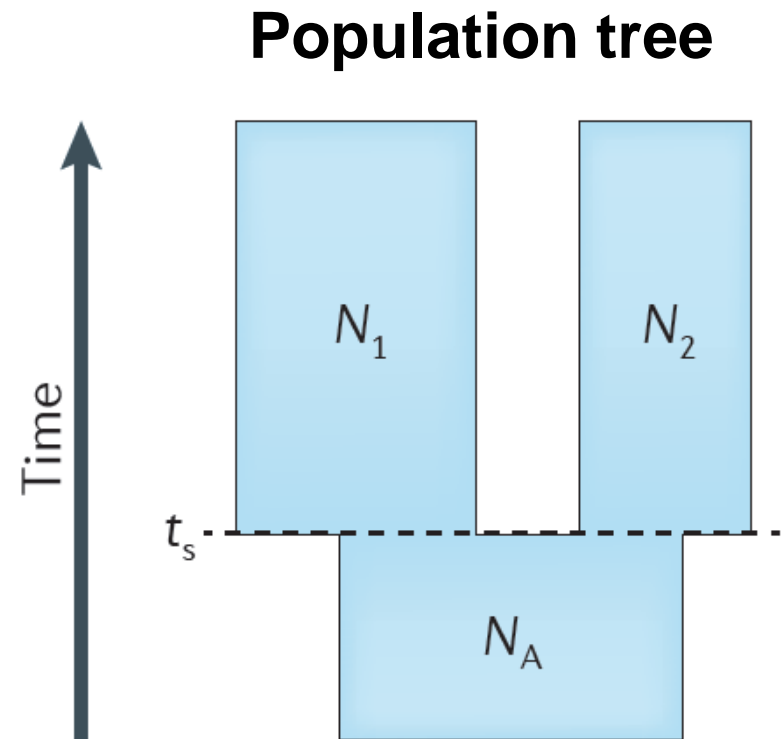
Site frequency spectrum (SFS)

The SFS contains information about the demographic history of populations

Sousa and Hey (2013) Nat. Rev. Genet.

Inferring the demographic history from the SFS

Genomic Data
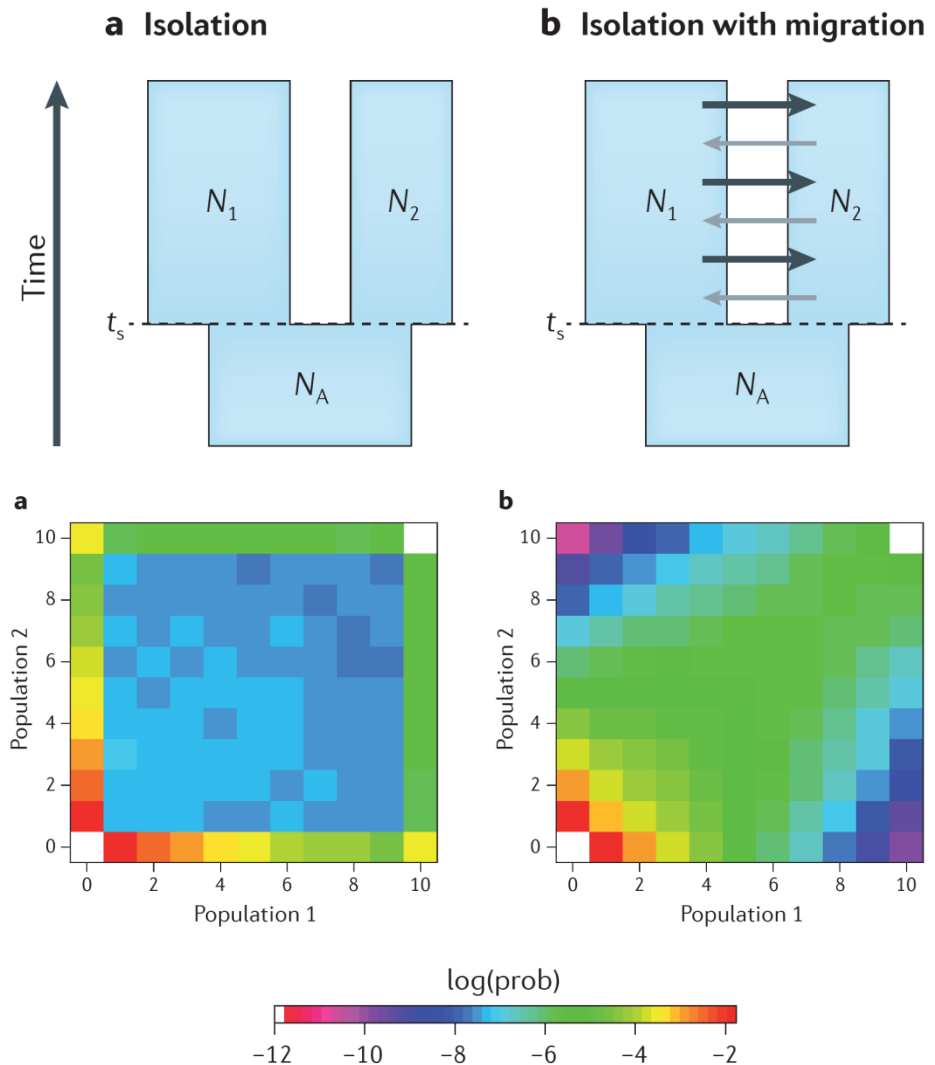
Model

Parameters:
- Time of split
- Migration rates
- Effective sizes
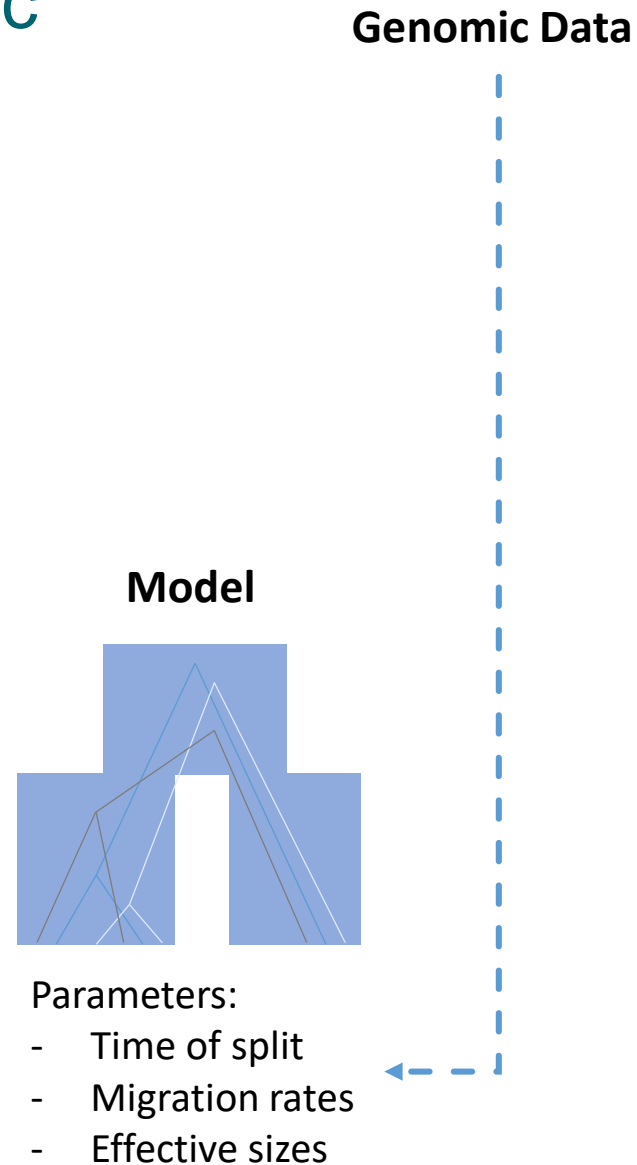
Inferring the demographic history from the SFS

- The likelihood is easily computed based on the expected SFS under a given model

- There are different ways to obtain the expected SFS
  - Diffusion (forward in time)
  - Coalescent (backward in time)

Genomic Data

Observed SFS

Likelihood

Model

Parameters:
- Time of split
- Migration rates
- Effective sizes

Expected SFS

Excoffier et al. (2013) *PloS Genetics*
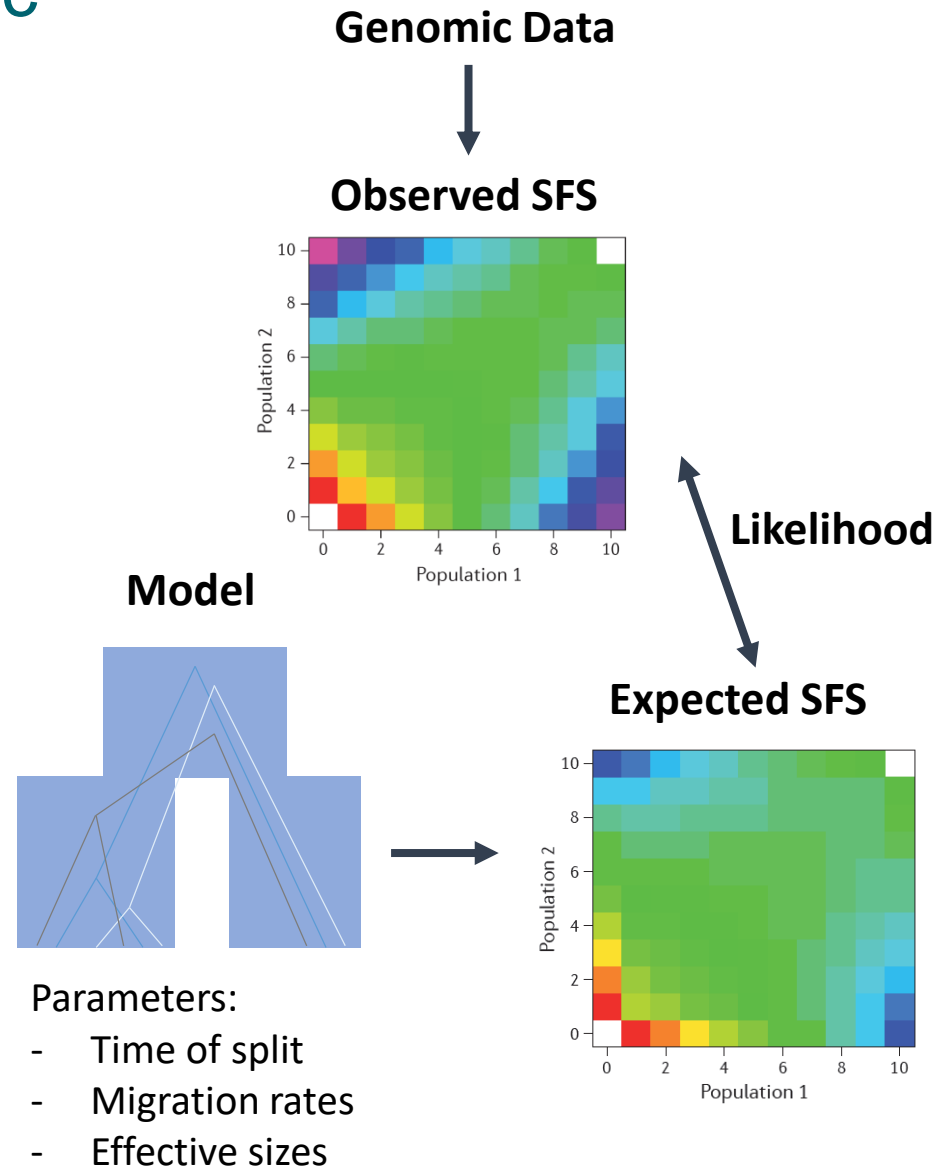
Framework for demographic inference

"Truth"
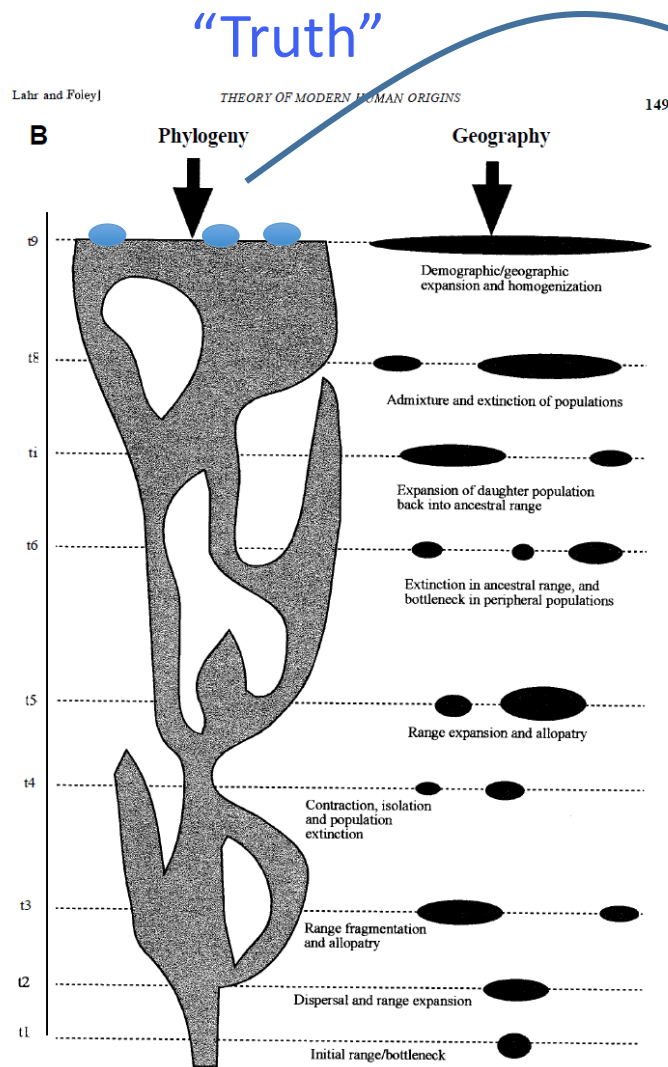
Lahr and Foley, 1994

Sample genomic data

What generated the data?
Test specific hypotheses.

Define demographic scenarios
Models

Estimation of demographic parameters

"All models are wrong but some are useful"
George Box

Estimating the SFS from the coalescent

The probability of a SFS entry *i* can be estimated under a specific model *θ* from its expected coalescent tree as (Nielsen 2000)

$$p_i = \frac{E(t_i \mid \theta)}{E(T \mid \theta)}$$

Where t_i is the total length of all branches directly leading to i terminal nodes, and T is the total tree length.

It gives the relative probability that if a mutation occurs on one of these b_i branches, it will be observed *i* times in the sample

This is true under the infinite sites model. No more than 1 mutation per site, back mutations not allowed!
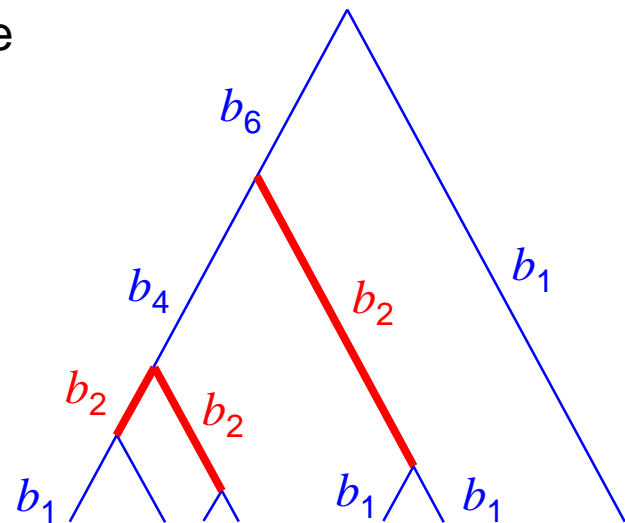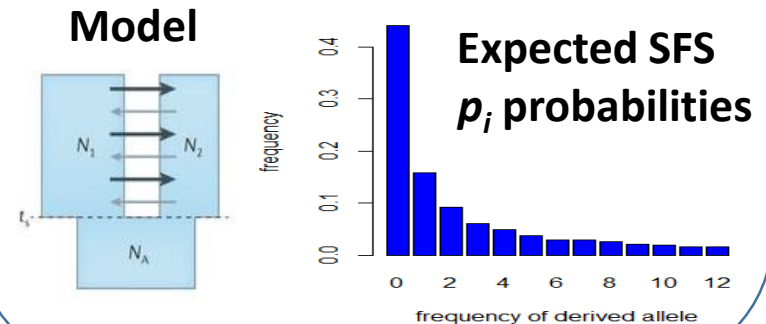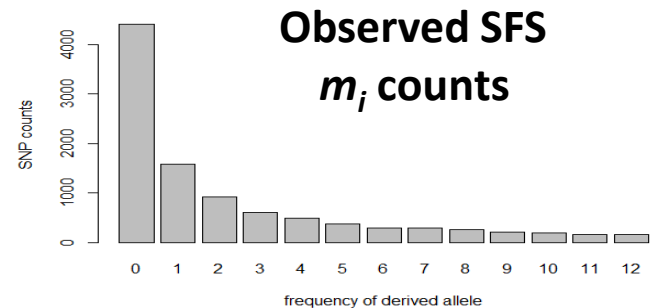
Composite likelihood

Even though we can have linked sites, we assume that all sites are independent. Given S polymorphic sites (SNPs) out of L sites (Adams and Hudson, 2004) the composite likelihood is:

$$CL = \Pr(X \mid \theta) \propto P_0^{L-S}(1-P_0)^S \prod_{i=1}^{n-1} \hat{p}_i^{m_i}$$

probability of no mutation on the tree

probability of at least one mutation in the tree

These probabilities depend:
- Number of monomorphic sites
- A fixed and mutation rate

3 ingredientes for likelihood

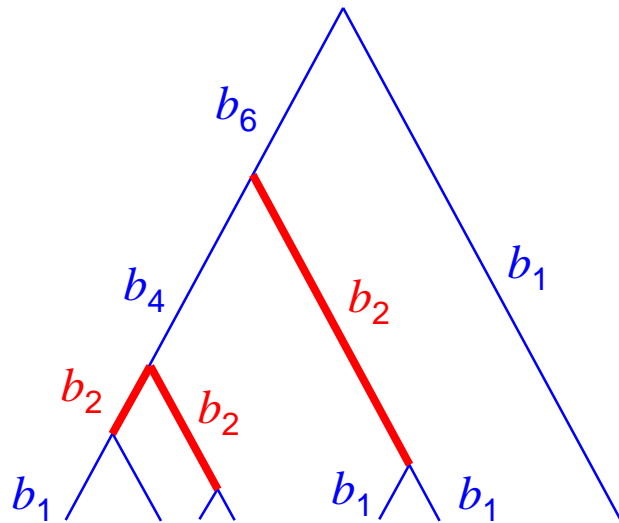**Observed SFS**
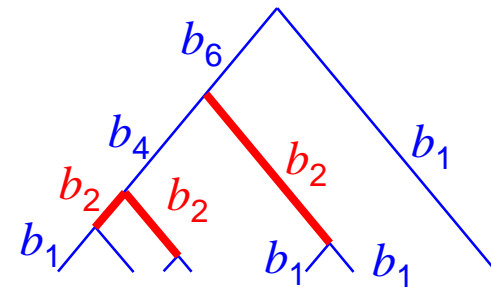**m_i counts**

SNP counts — frequency of derived allele

Model

Expected SFS
p_i probabilities

frequency of derived allele

Composite likehood

Everything is relative

T_L = total branch length

Frequency	0	1	2	3	4	5	6	7
SNP probability p_i	0	$\text{Sum}(b_1)/T_L$	$\text{Sum}(b_2)/T_L$	$\text{Sum}(b_3)/T_L$	$\text{Sum}(b_4)/T_L$	$\text{Sum}(b_5)/T_L$	$\text{Sum}(b_6)/T_L$	0

- The same expected SFS can be obtained in a large or small tree

- We need a mutation rate and the number of monomorphic sites to distinguish among the two!

Methods based on the SFS

Different ways to obtain the expected SFS p_i under different demographic models

- Coalescent-based
  - Multiple populations
    Fastsimcoal2 (Excoffier et al 2013 PLoS Genetics)
    Momi (Kamm et al 2015) and Momi 2
    Rarecoal (Schiffels et al 2016 Nat Genetics)
  - Single population
    Stairway plot (Liu and Fu, 2015 Nat Genetics)
- Diffusion-based
    Dadi (Gutenkunst et al 2009 PLoS Genetics)
    Multipop (Lukic and Hey 2012 Genetics)
    Jouganous et al (2017) Genetics

fastsimcoal2 program

- Fastsimcoal2 can estimate parameters from the SFS using coalescent simulations

- Maximum (composite) likelihood method

- Uses a conditional expectation (CEM) maximization algorithm to find parameter combinations that maximize the likelihood

- **It approximate the expected SFS** by performing coalescent simulations (>50,000)

Estimating the SFS and likelihoods with coalescent simulations

This probability p_i can then be estimated on the basis of Z simulations as

$$\hat{p}_i = \frac{\sum\limits_{j}^{Z} \sum\limits_{k \in \Phi_i} b_{kj}}{\sum\limits_{j}^{Z} T_j}$$ where b_{kj} is the length of the k-th compatible branch in simulation j.

These probabilities can then be used to compute the composite likelihood of a

given model as (Adams and Hudson, 2004)

$$CL = \Pr(X \mid \theta) \propto P_0^{L-S} (1 - P_0)^S \prod_{i=1}^{n-1} \hat{p}_i^{m_i}$$

where X is the SFS in a population sample of size n, S is the number of

polymorphic sites, L is the length of the studied sequence,

and P_0 is the probability of no mutation on the tree

# Approximating the expected SFS with coalescent simulations

Increasing the number of simulations improves the approximation of the expected SFS

B   **T=0.1 - Expected vs. Fastsimcoal SFS**
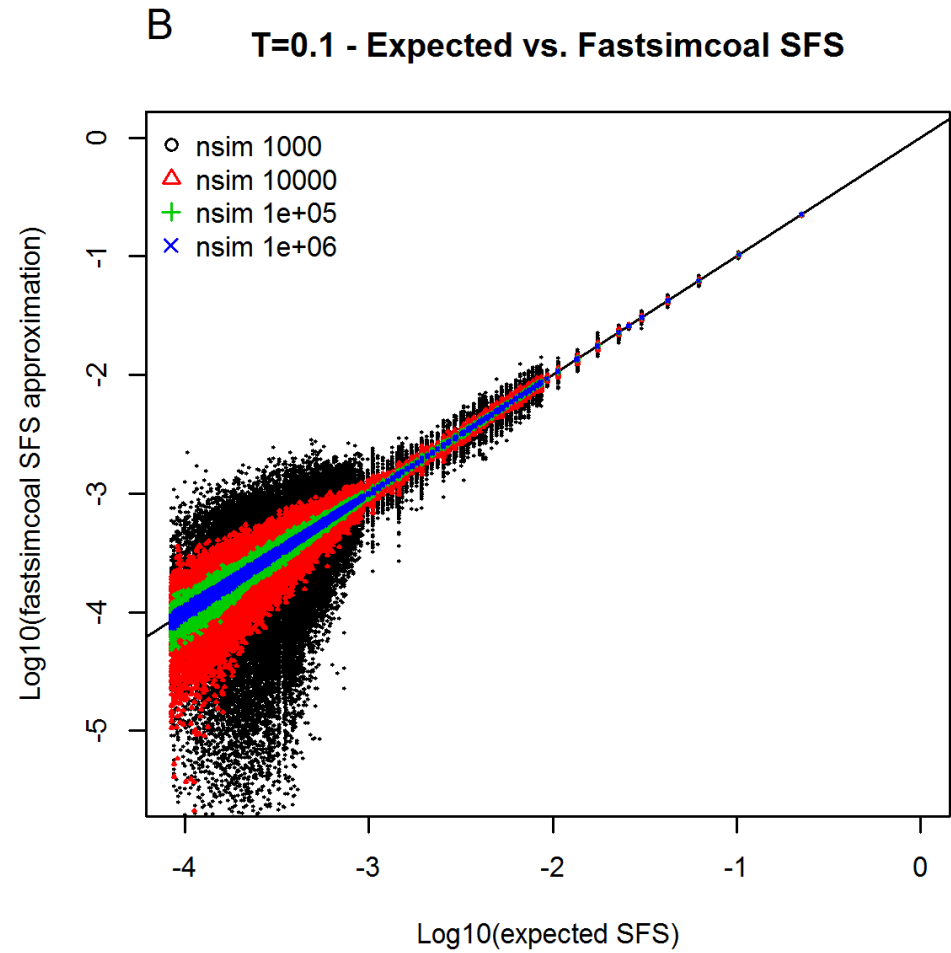
Properties of composite likelihoods

This composite likelihood (CL) is not a proper likelihood due to the non-independence of allele frequencies at linked sites.

- CL is maximized for the same parameters as full likelihood
- Can be used for parameter estimation
- Confidence intervals cannot be estimated from likelihood profile, need to bootstrap
- CL surface might be more complex than likelihood surface, and thus more difficult to explore and get the global maximum
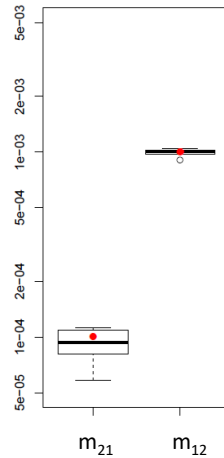- CL ignores information on linkage disequilibrium (recombination) between sites
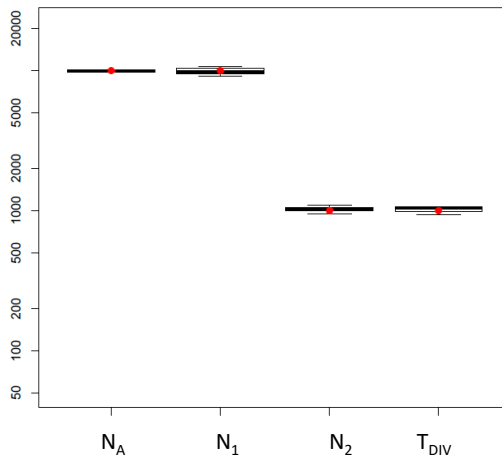

— Composite likelihood
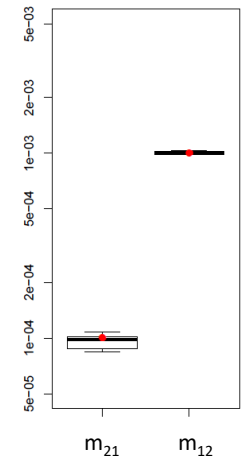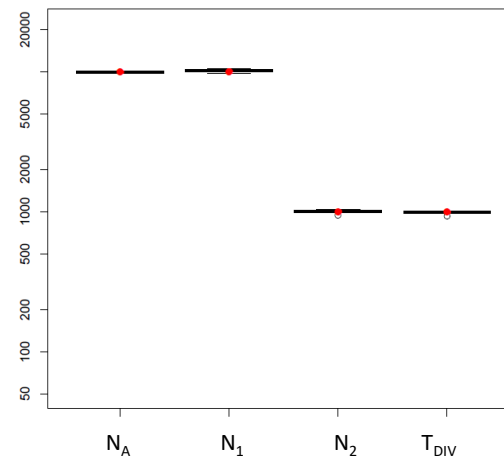— "correct" likelihood

log10(Likelihood)

Effective size (Ne)
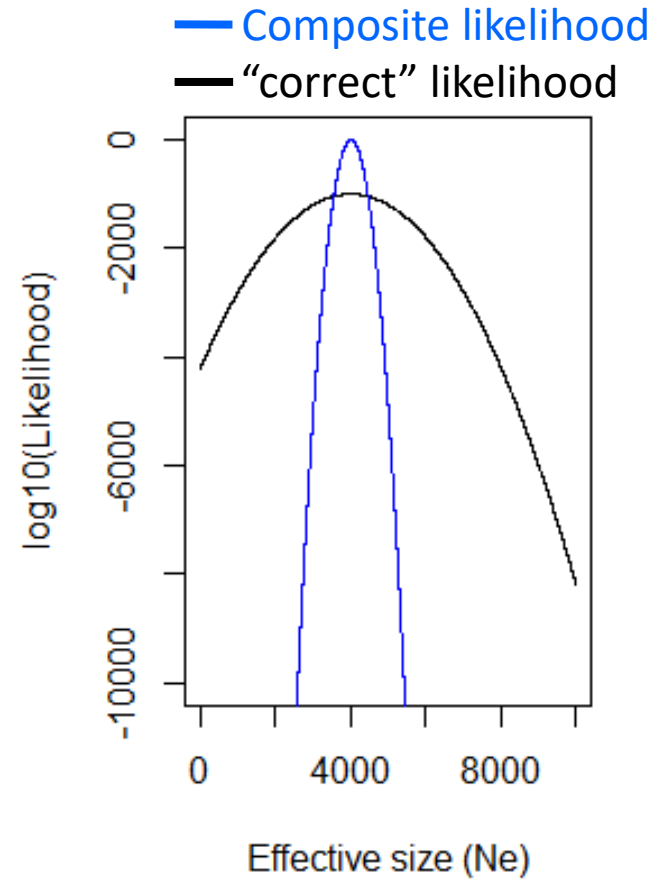
Comparisons of approaches

Simulation of 20 Mb data
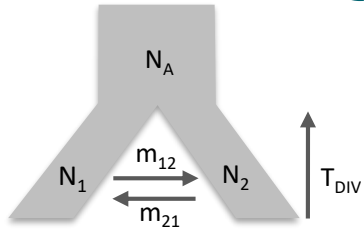
fastsimcoal2

$\partial a \partial i$

Protocol for parameter estimation

1. **Get the observed SFS**:
    *   derived SFS (DAF or unfolded SFS), when the ancestral state is known;
    *   minor allele frequency SFS (MAF or folded SFS) when the ancestral state is unknown

2. Define the **demographic model**

3. **Estimate the parameters** – repeat 50-100 runs, and selecting the run with maximum likelihood

4. **Bootstrap** to obtain confidence intervals for each parameter – bootstrap 10-100 datasets, by repeating a few runs for each dataset
    *   For datasets with linked sites use block-bootstrap, diving the genome into blocks

Potential problems

- Maximization of the CL is not trivial (precision of the approximation and convergence problems)

- Need to repeat estimations to find maximum CL

- Needs genomic data (several Mb), difficult to have gene-specific estimates

- Next-generation sequencing data must have high coverage (>10x) to correctly estimate SFS

Problems with estimation of demographic parameters from SFS
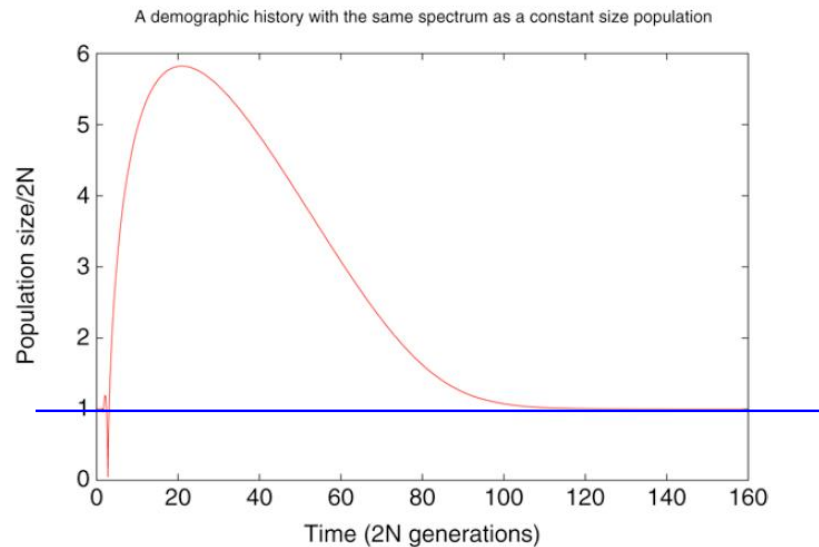
Can one learn history from the allelic spectrum?

Simon Myers[a], Charles Fefferman[b], Nick Patterson[a,*]

[a] *Broad Institute of MIT and Harvard, 7 Cambridge Center, Cambridge MA 02142, United States*
[b] *Deptartment of Mathematics, Fine Hall, Washington Road, Princeton, NJ 08544, United States*

A demographic history with the same spectrum as a constant size population

On the decidability of population size histories from finite allele frequency spectra

Soheil Baharian, Simon Gravel

Geometry of the Sample Frequency Spectrum and the Perils of Demographic Inference

Zvi Rosen, Anand Bhaskar, Sebastien Roch and Yun S. Song

Fundamental limits on the accuracy of demographic inference based on the sample frequency spectrum

Jonathan Terhorst and Yun S. Song

Acknowledgements

c^M_PG

Laurent Excoffier

FNS NF
FONDS NATIONAL SUISSE
SCHWEIZERISCHER NATIONALFONDS
FONDO NAZIONALE SVIZZERO
SWISS NATIONAL SCIENCE FOUNDATION

u^b

b
UNIVERSITÄT
BERN

SIB
Swiss Institute of
Bioinformatics

Thank you!

cE3c
centre for ecology, evolution
and environmental changes

FCT
Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR

^FC Ciências
ULisboa

UID/BIA/00329/2015-2018
UID/BIA/00329/2019
CEECIND/02391/2017

MARIE CURIE ACTIONS

MCSA 2018-2020:
MAPgenome
(N.799729)