

Population Genetics

Peerteaching KW24

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10. Juni 2024

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Population genetics aims to infer details of evolutionary processes based on the current population's genetic composition.

Subfield of Genetics

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Single Nucleotide Variant(SNV)

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A single-nucleotide variant (SNV) is a variation in a single nucleotide that occurs at a specific position in the genome. This may be rare or common in a population.

Single Nucleotide Polymorphism(SNP)

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A single-nucleotide polymorphism (SNP) is a SNV that occurs in a significant proportion (typically $> 1\%$) of a population.

Polymorphisms describe sites (nucleotide positions, etc.) that are variable within a species; divergence describes sites variable between species.

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$$r = \frac{s(T) - s(T_0)}{s(T_0)}$$

where $s(T)$ is the population size at time T and $s(T_0)$ the size of the initial population at time T_0 .

Alleles and ploidy

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An allele is the variant form of a given gene found at the same chromosomal location.

Ploidy is the number of sets of chromosomes in a cell and hence the number of possible alleles for genes.

Haploid and Diploid

Haploid Cells: Haploid cells have half the number of chromosomes (n) as diploid - germ cells Result of meiosis

Example: sperm and egg cells

Diploid Cells: Diploid cells contain two copies of each chromosome ($2n$) - somatic cells Result of mitosis

Example: skin cells

Haploid Reproduction Model

- Assume constant population size
- Each gene i in generation $t + 1$ is found by randomly choosing a predecessor gene g in generation t . This implies, that it is possible that one gene can have more than one offspring.
- Any gene in generation t not chosen “dies out”.

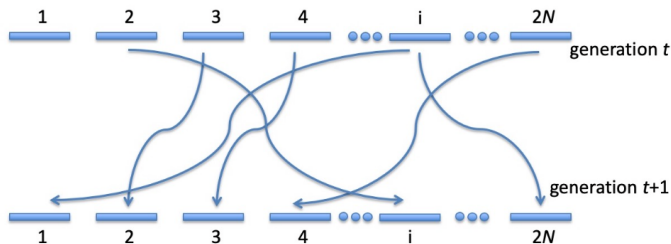


Abbildung: Haploid reproduction model

Diploid populations

Assumptions - Species has 2 Sexes, Male and Female.

Each individual has 2 copies of each gene, a gene is chosen for each parent with equal odds

In this model, each gene has one parent gene and each individual has two parents.

For large values of N , N_f and N_m , one can approximate the diploid model by the haploid model. Thus, we will only consider the haploid model.

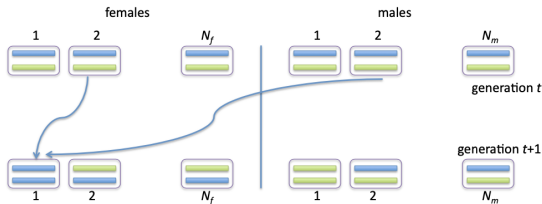


Abbildung: Diploid reproduction model

Haplotypes and Genotypes

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Haplotype: A haplotype is a sequence of an individual's genome that occurs together on one or two homologous copies of a chromosome.

Genotype: The two alleles at the same site on two homologous chromosomes form the genotype at that site. We denote that by 'P|Q', if 'P' and 'Q' are the alleles, respectively. Example

An individual has the two haplotypes

A T T G A C A T C

A C T G A C A C T

Then the genotype at the first site is A|A, at the second site T|C, and so on.

Task- Show the full genotype of the individual.

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Homozygous and Heterozygous

A site c is called homozygous if the genotype consists of two identical alleles at c . The site c is called heterozygous if the genotype consists of two different alleles at c .

Task- for an individual that has the two haplotypes

A T T G A C A T C

A C T G A C A C T

give the set of homozygous and heterozygous sites.

Calculating decendants

What is the probability of any gene i to have at least one decendant (It does not “die out”)?

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We look at the inverse probability, a gene has no decendants.

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Since the population keeps it size from generation to generation, the average number of decendants per gene is 1.

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No decendants: ($k = 0$)

$$\mathbb{P}_{\text{Poisson}}(X = 0) = e^{-1} \approx 0.37$$

At least one decendant:

$$1 - 0.37 \approx 0.63$$

Calculating decendants

Why is this useful?

What was the size of a population of 10 000 genes $t = 15$ generations ago?

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Calculating decendants

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So a population of 10 000 genes would have most likely evolved from just 10 genes over a course of 15 generations.

Calculating decendants

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$$10\,000 \cdot 0.63^{15} \approx 10$$

So a population of 10 000 genes would have most likely evolved from just 10 genes over a course of 15 generations.

This means we can now find out how many generations back there was just one individual (the most recent common ancestor of our whole population).

The coalescent process

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“*to coalesce*”: grow together, to join, to fuse

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“to coalesce”: grow together, to join, to fuse

Definition (coalescent event)

If traversing the sequence-transmission paths backward in time, two sequence transmission paths intersect at some sequence, the paths coalesce at that intersection point. This is called a coalescent event.

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Basic idea

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Basic idea

- ▶ Start with present-day generation

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Basic idea

- ▶ Start with present-day generation
- ▶ Construct previous generations

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Basic idea

- ▶ Start with present-day generation
- ▶ Construct previous generations
- ▶ By randomly choosing parents in the previous generation

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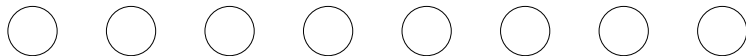
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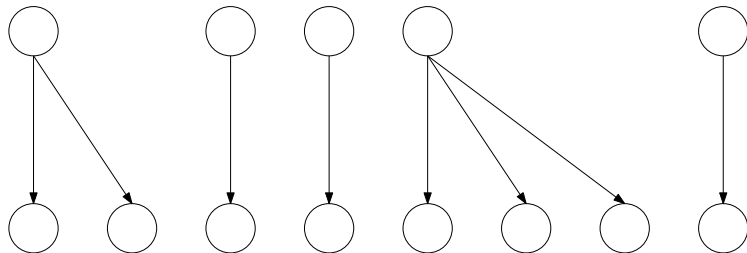
The coalescent process

Example



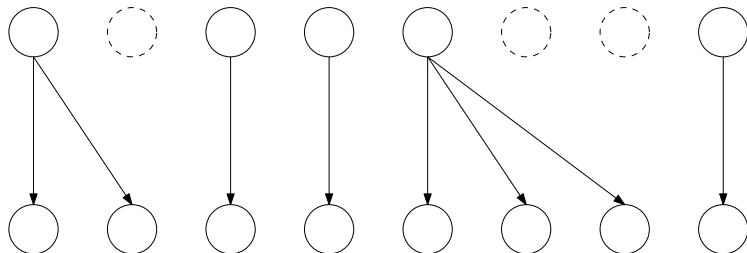
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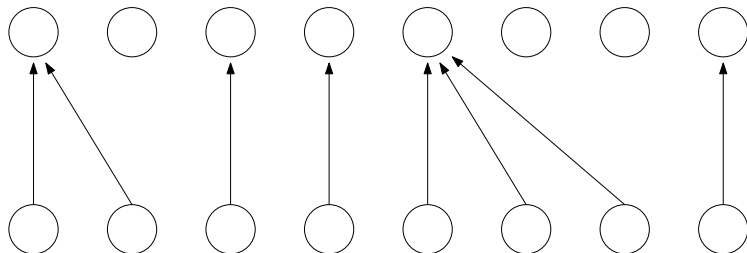
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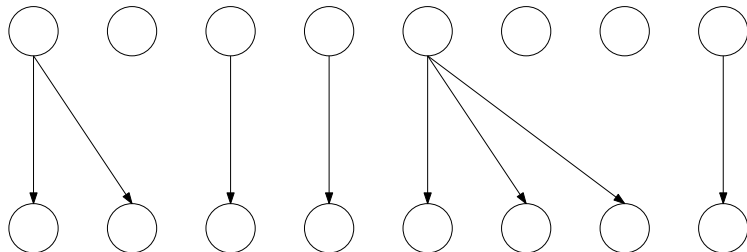
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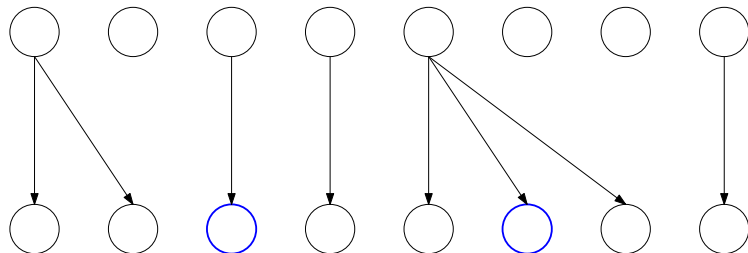
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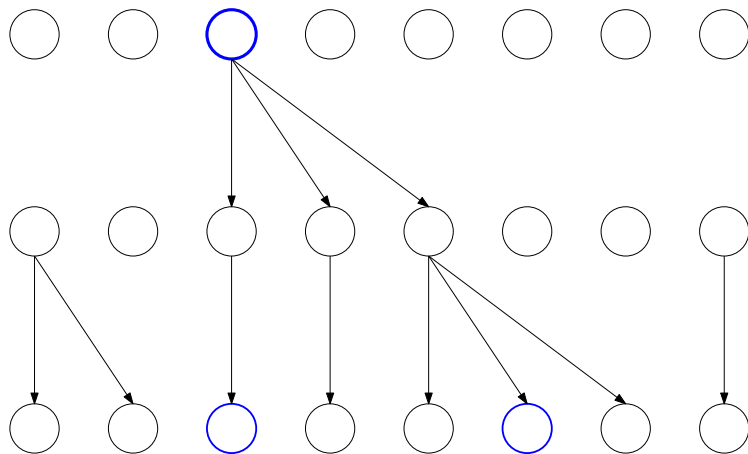
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The coalescent process

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Construct a tree based on estimated coalescent events.
Needs more content

Coalescence of 2 genes

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Considering a haploid model with n genes.

For two present day genes i and j , when did they coalesce?

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Considering a haploid model with n genes.

For two present day genes i and j , when did they coalesce?

We want to know two things:

Coalescence of 2 genes

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Considering a haploid model with n genes.

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We want to know two things:

1. When did the two genes coalesce?

Coalescence of 2 genes

Considering a haploid model with n genes.

For two present day genes i and j , when did they coalesce?

We want to know two things:

1. When did the two genes coalesce?
→ Who is their common ancestor

Coalescence of 2 genes

Considering a haploid model with n genes.

For two present day genes i and j , when did they coalesce?

We want to know two things:

1. When did the two genes coalesce?
→ Who is their common ancestor
2. How long is the waiting time until the two genes coalesced?

Coalescence of 2 genes

Considering a haploid model with n genes.

For two present day genes i and j , when did they coalesce?

We want to know two things:

1. When did the two genes coalesce?
→ Who is their common ancestor
2. How long is the waiting time until the two genes coalesced?
→ How many generations back is their common ancestor?

Coalescence of 2 genes

When did the two genes coalesce?

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Coalescence of 2 genes

When did the two genes coalesce?

We select a random ancestor for each individual:

Coalescence of 2 genes

When did the two genes coalesce?

We select a random ancestor for each individual:
Probability to select the right ancestor of i is 1, since there are no requirements.

Coalescence of 2 genes

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Coalescence of 2 genes

When did the two genes coalesce?

We select a random ancestor for each individual:

Probability to select the right ancestor of i is 1, since there are no requirements.

Probability to select the right ancestor of j is

$$P(T_2 = 1) = \frac{1}{n}$$

since we need to "hit" the ancestor we've chosen for i .

Coalescence of 2 genes

How long is the waiting time until the two genes coalesced?

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Coalescence of 2 genes

How long is the waiting time until the two genes coalesced?

What is the Probability that the common ancestor is in Generation t ?

Coalescence of 2 genes

How long is the waiting time until the two genes coalesced?

What is the Probability that the common ancestor is in
Generation t ?
($n - 1$ failures following one success)

$$P(T_2 = t) =$$

Coalescence of 2 genes

How long is the waiting time until the two genes coalesced?

What is the Probability that the common ancestor is in Generation t ?
($n - 1$ failures following one success)

$$P(T_2 = t) = \left(1 - \frac{1}{n}\right)^{n-1}$$

Coalescence of 2 genes

How long is the waiting time until the two genes coalesced?

What is the Probability that the common ancestor is in Generation t ?
($n - 1$ failures following one success)

$$P(T_2 = t) = \left(1 - \frac{1}{n}\right)^{n-1} \cdot \left(\frac{1}{n}\right)$$

Coalescence of 2 genes

Exercise

Let's assume $n = 50$

What is the probability that two genes coalesce exactly 5 generations in the past?

$$P(T_2 = 5) =$$

Coalescence of 2 genes

Exercise

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Let's assume $n = 50$

What is the probability that two genes coalesce exactly 5 generations in the past?

$$P(T_2 = 5) = \left(1 - \frac{1}{50}\right)^{5-1} \cdot \frac{1}{50} \approx 0.01845 = 1.845\%$$

Coalescence of 2 genes

Exercise

Let's assume $n = 50$

What is the probability that it takes them at least 5 generations to coalesce?

$$P(T_2 > 5) =$$

Coalescence of 2 genes

Exercise

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Let's assume $n = 50$

What is the probability that it takes them at least 5 generations to coalesce?

$$P(T_2 > 5) = \left(1 - \frac{1}{50}\right)^{5-1} \approx 0.92237 = 92.237\%$$

Most recent common ancestor(MRCA)

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**Most recent
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How many generations back is the most recent common ancestor (MRCA) of two present-day genes?

Wright Fisher Model

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Key assumptions of the Wright-Fisher model:

1. Discrete and non overlapping generations.
2. Constant population size.
3. Haploid individuals
4. All individuals are equally fit.
5. The population has no geographic or social structure
6. No recombinations of genes (or sequences)