The Wright-Fisher Model & Standard Coalescent

BIOL 1435

February 7, 2023

Overview

1. **Quiz Review**

2. **Wright Fisher Model**

3. **Standard Coalescent Model**

4. **Derivations**

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2. Wright Fisher Model
3. Standard Coalescent Model
4. Derivations

Segregating sites (S)

Definition

A segregating site is a site that is polymorphic in the data—i.e., there are multiple alleles observed.

Segregating sites (S)

$$\begin{bmatrix} 0 & 0 & 0 \\ 0 & 1 & 0 \\ 1 & 1 & 0 \\ 1 & 1 & 1 \end{bmatrix}$$

Segregating sites (S)

$$\begin{bmatrix} 0 & 0 & 0 \\ 0 & 1 & 0 \\ 1 & 1 & 0 \\ 1 & 1 & 1 \end{bmatrix} \rightarrow \begin{bmatrix} 0 \\ 1 \\ 1 \\ 0 \end{bmatrix} \rightarrow S = 2$$

Gene diversity (h & H)

Definition

Gene diversity is the probability that two random DNA sequences are different.

Equation

$$h = 1 - \left(p^2 + (1-p)^2\right) \tag{1}$$

Where p is the frequency of the derived/alternative allele at a given site.

$$H = \frac{1}{L}\sum_{j=1}^{L} h_j \tag{2}$$

Where h_j is the gene diversity for site j and L is to the total number of sites.

Gene diversity (h & H)

$$\begin{bmatrix} 0 & 1 & 1 & 0 \\ 1 & 1 & 1 & 0 \\ 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 \end{bmatrix}$$

Gene diversity $(h \,\&\, H)$

$$\begin{bmatrix} 0 & 1 & 1 & 0 \\ 1 & 1 & 1 & 0 \\ 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 \end{bmatrix} \rightarrow \begin{bmatrix} 1 - \left({}^{2^2}/_{4^2} + {}^{2^2}/_{4^2}\right) \\ 1 - \left({}^{3^2}/_{4^2} + {}^{1^2}/_{4^2}\right) \\ 1 - \left({}^{1^2}/_{4^2} + {}^{3^2}/_{4^2}\right) \\ 1 - \left({}^{2^2}/_{4^2} + {}^{2^2}/_{4^2}\right) \end{bmatrix}$$

Gene diversity (h & H)

$$\begin{bmatrix} 0 & 1 & 1 & 0 \\ 1 & 1 & 1 & 0 \\ 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 \end{bmatrix} \rightarrow \begin{bmatrix} 1 - \left({}^{2^2}\!/_{4^2} + {}^{2^2}\!/_{4^2} \right) \\ 1 - \left({}^{3^2}\!/_{4^2} + {}^{1^2}\!/_{4^2} \right) \\ 1 - \left({}^{1^2}\!/_{4^2} + {}^{3^2}\!/_{4^2} \right) \\ 1 - \left({}^{2^2}\!/_{4^2} + {}^{2^2}\!/_{4^2} \right) \end{bmatrix} \rightarrow h_j = \begin{bmatrix} {}^{8}\!/_{16} \\ {}^{6}\!/_{16} \\ {}^{6}\!/_{16} \\ {}^{8}\!/_{16} \end{bmatrix}$$

Gene diversity $(h \,\&\, H)$

$$\begin{bmatrix} 0 & 1 & 1 & 0 \\ 1 & 1 & 1 & 0 \\ 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 \end{bmatrix} \rightarrow \begin{bmatrix} 1 - \left({}^{2^2}\!/_{4^2} + {}^{2^2}\!/_{4^2}\right) \\ 1 - \left({}^{3^2}\!/_{4^2} + {}^{1^2}\!/_{4^2}\right) \\ 1 - \left({}^{1^2}\!/_{4^2} + {}^{3^2}\!/_{4^2}\right) \\ 1 - \left({}^{2^2}\!/_{4^2} + {}^{2^2}\!/_{4^2}\right) \end{bmatrix} \rightarrow h_j = \begin{bmatrix} {}^{8}\!/_{16} \\ {}^{6}\!/_{16} \\ {}^{6}\!/_{16} \\ {}^{8}\!/_{16} \end{bmatrix}$$

$$H = \frac{28}{16} \times \frac{1}{4} = \frac{7}{16}$$

Nucleotide diversity (Π & π)

Definition

Nucleotide diversity is the average number of pairwise differences between genotypes drawn from the same population.

Nucleotide diversity (Π & π)

Equation

$$\Pi = \sum_{i<j} k_{ij} \tag{3}$$

Where k_{ij} is the number of nucleotide differences between the i^{th} and j^{th} sample at a given site.

$$\pi = \frac{1}{\binom{n}{2}} \sum_{j=1}^{L} \Pi_j \tag{4}$$

Where Π_j is the nucleotide diversity for site j, L is to the total number of sites in the genotype matrix, and $\binom{n}{2}$ is number of of unique comparisons between n samples in the genotype matrix.

Nucleotide diversity (Π & π)

$$\begin{bmatrix} 0 & 1 & 1 & 0 \\ 1 & 1 & 1 & 0 \\ 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 \end{bmatrix}$$

Nucleotide diversity (Π & π)

$$\begin{bmatrix} 0 & 1 & 1 & 0 \\ 1 & 1 & 1 & 0 \\ 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 \end{bmatrix} \rightarrow \begin{bmatrix} 2+1+1 \\ 1+1+1 \\ 3+0+0 \\ 2+1+1 \end{bmatrix} \rightarrow \Pi_j = \begin{bmatrix} 4 \\ 3 \\ 3 \\ 4 \end{bmatrix}$$

Nucleotide diversity (Π & π)

$$\begin{bmatrix} 0 & 1 & 1 & 0 \\ 1 & 1 & 1 & 0 \\ 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 \end{bmatrix} \rightarrow \begin{bmatrix} 2+1+1 \\ 1+1+1 \\ 3+0+0 \\ 2+1+1 \end{bmatrix} \rightarrow \Pi_j = \begin{bmatrix} 4 \\ 3 \\ 3 \\ 4 \end{bmatrix}$$

$$\pi = 14 \div \binom{4}{2} = 14 \div \frac{4(4-1)}{2} = \frac{14}{6}$$

Average nucleotide diversity in the presence of missing data (π_{pixy})

Equation

$$Numerator_{pixy} = \frac{1}{L_{called}} \sum_{j=1}^{L_{called}} \Pi_j \tag{5}$$

$$Denominator_{pixy} = \frac{1}{L_{called}} \sum_{j=1}^{L_{called}} \binom{n_{called}}{2}_j \tag{6}$$

$$\pi_{pixy} = \frac{Numerator_{pixy}}{Denominator_{pixy}} \tag{7}$$

Where Π_j is the nucleotide diversity among called genotypes for site j, L_{called} is to the total number of sites in the genotype matrix that have at least one called genotype, and $\binom{n_{called}}{2}_j$ is number of unique comparisons between n_{called} samples with genotype information at site j.

π_{pixy}

$$\begin{bmatrix} 0 & 0 & 0 & 0 & 1 \\ 1 & - & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 \\ 1 & - & - & 1 & 0 \\ 0 & 0 & - & 1 & 1 \end{bmatrix}$$

π_{pixy}

$$\begin{bmatrix} 0 & 0 & 0 & 0 & 1 \\ 1 & - & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 \\ 1 & - & - & 1 & 0 \\ 0 & 0 & - & 1 & 1 \end{bmatrix} \rightarrow \begin{bmatrix} 1+1+1+1 \\ 1+2+0 \\ 0+0+0+0 \\ 1+1 \\ 2+2+0 \end{bmatrix}$$

π_{pixy}

$$\begin{bmatrix} 0 & 0 & 0 & 0 & 1 \\ 1 & - & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 \\ 1 & - & - & 1 & 0 \\ 0 & 0 & - & 1 & 1 \end{bmatrix} \rightarrow \begin{bmatrix} 1+1+1+1 \\ 1+2+0 \\ 0+0+0+0 \\ 1+1 \\ 2+2+0 \end{bmatrix} \rightarrow \Pi_j = \begin{bmatrix} 4 \\ 3 \\ 0 \\ 2 \\ 4 \end{bmatrix}$$

π_{pixy}

$$\begin{bmatrix} 0 & 0 & 0 & 0 & 1 \\ 1 & - & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 \\ 1 & - & - & 1 & 0 \\ 0 & 0 & - & 1 & 1 \end{bmatrix} \rightarrow \begin{bmatrix} 1+1+1+1 \\ 1+2+0 \\ 0+0+0+0 \\ 1+1 \\ 2+2+0 \end{bmatrix} \rightarrow \Pi_j = \begin{bmatrix} 4 \\ 3 \\ 0 \\ 2 \\ 4 \end{bmatrix} \rightarrow \binom{n}{2}_j = \begin{bmatrix} 5C2 = 10 \\ 4C2 = 6 \\ 5C2 = 10 \\ 3C2 = 3 \\ 4C2 = 6 \end{bmatrix}$$

π_{pixy}

$$\begin{bmatrix} 0 & 0 & 0 & 0 & 1 \\ 1 & - & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 \\ 1 & - & - & 1 & 0 \\ 0 & 0 & - & 1 & 1 \end{bmatrix} \rightarrow \begin{bmatrix} 1+1+1+1 \\ 1+2+0 \\ 0+0+0+0 \\ 1+1 \\ 2+2+0 \end{bmatrix} \rightarrow \Pi_j = \begin{bmatrix} 4 \\ 3 \\ 0 \\ 2 \\ 4 \end{bmatrix} \rightarrow \binom{n}{2}_j = \begin{bmatrix} 5C2 = 10 \\ 4C2 = 6 \\ 5C2 = 10 \\ 3C2 = 3 \\ 4C2 = 6 \end{bmatrix}$$

$$Numerator_{pixy} = \frac{13}{5}$$

$$Denominator_{pixy} = \frac{35}{5}$$

$$\pi_{pixy} = \frac{13}{5} \div \frac{35}{5} = \frac{13}{35}$$

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Modeling evolution

Q: Why do we need to model evolution?

Modeling evolution

A: To assess departures from neutrality.

Assumptions of the Wright Fisher model

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- Panmictic population

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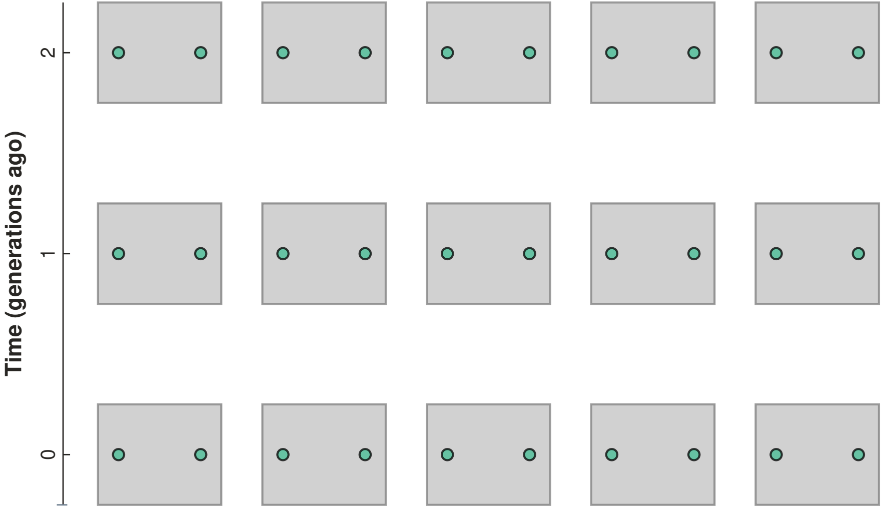
- Panmictic population
- Constant population size of N
- Total of $2N$ allele copies
- Discrete time process with non-overlapping generations
- All mutations are neutral

WF population ($N = 5$)

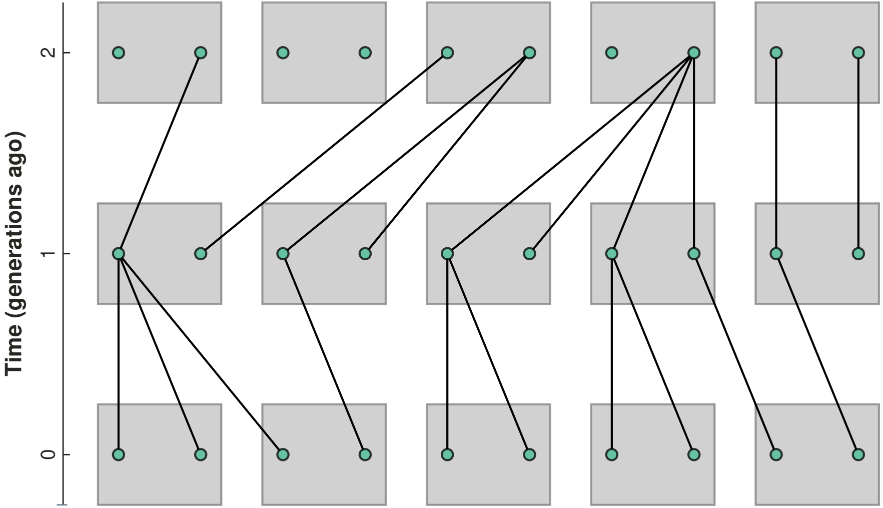


Simulating under the WF model

Simulating Reproduction

Sample with replacement an allelic copy (i) in the current generation (t) with a probability of $\frac{1}{2N}$ to produce an offspring in the next generation $(t+1)$, until there are $2N$ allelic copies in the next generation.

WF population ($N = 5$)



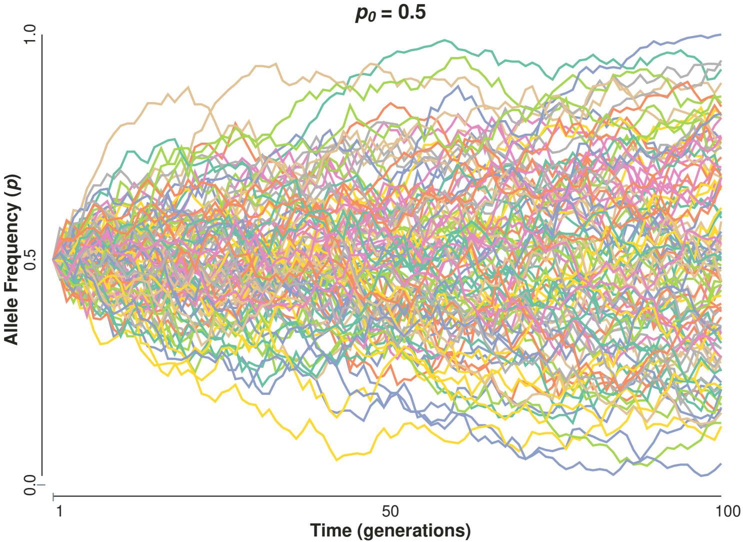
WF model & genetic drift

Definition

$$Pr(j) = \binom{2N}{j} \left(\frac{j}{2N}\right)^{j} \left(\frac{2N-j}{2N}\right)^{2N-j} \tag{8}$$

Where j represents the number of allelic copies of a particular allele.

WF model & genetic drift



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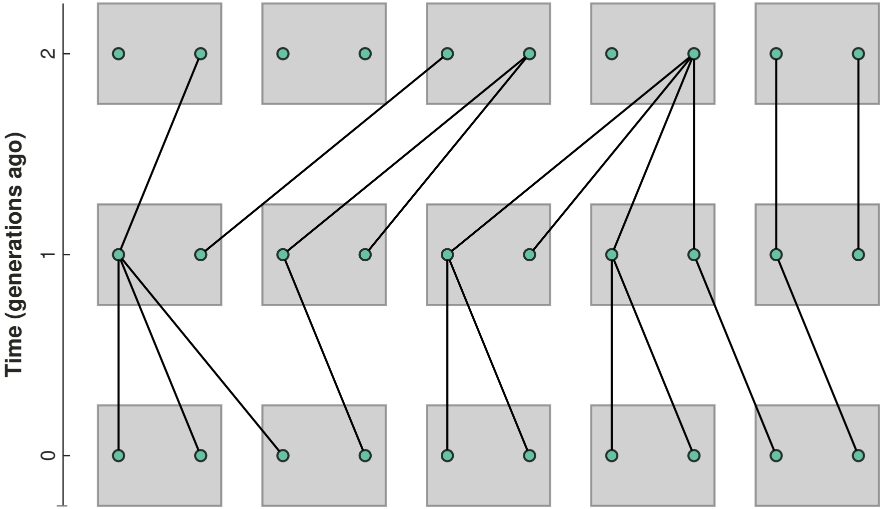
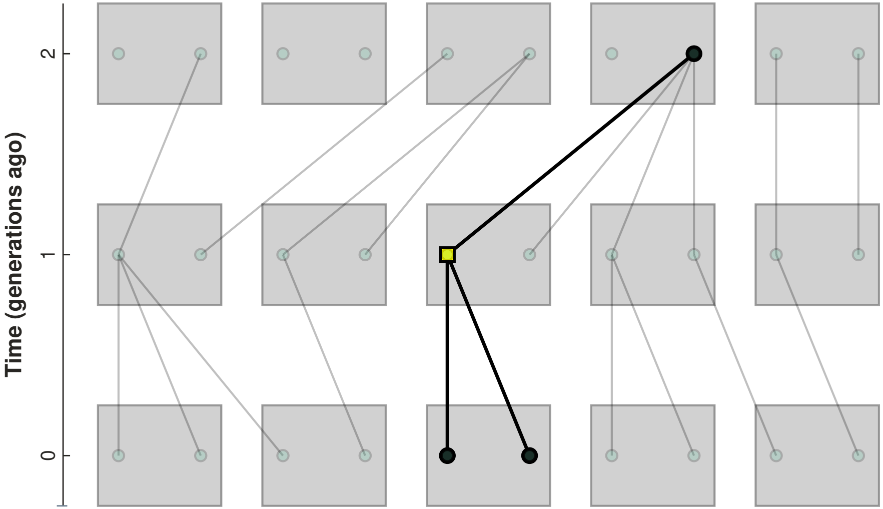
The standard coalescent



Finding the same parent = coalescence



Pr(two lineages coalesce in the previous generation)

Example

$$\begin{aligned} Pr(COAL \text{ in the previous generation}) &= \#\text{ of possible parents} \\ &\quad \times Pr(\text{two lineages pick the same parent}) \end{aligned} \tag{9}$$

where $2N = 10$

Pr(two lineages coalesce in the previous generation)

Example

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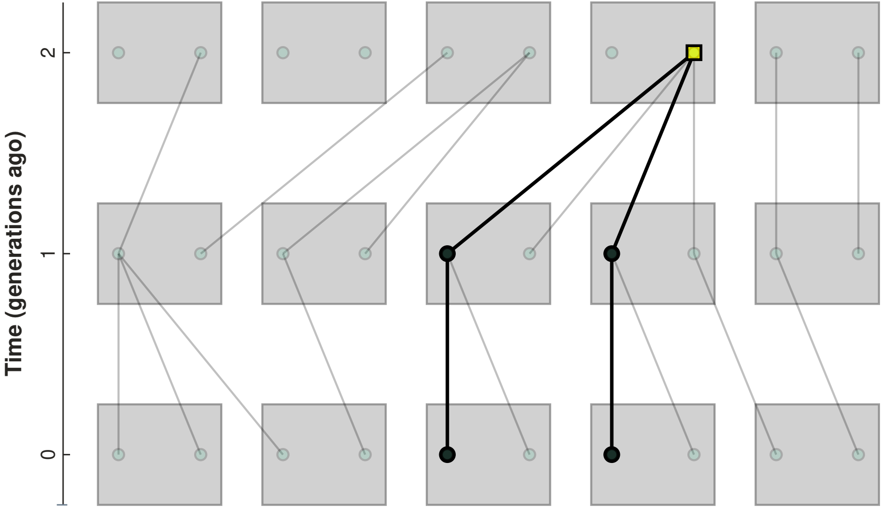
$$\text{where } 2N = 10$$

$$Pr(\mathit{COAL\ in\ the\ previous\ generation}) = 10 \times \frac{1}{10} \times \frac{1}{10} = \frac{1}{2N} \tag{10}$$

Parent $\neq$ Most Recent Common Ancestor (MRCA)



Pr(two lineages coalesce two generations ago)

Example

$$\begin{aligned} Pr(COAL\ two\ generations\ ago) &= Pr(no\ COAL\ at\ generation\ one) \\ &\quad \times Pr(COAL\ at\ generation\ two) \end{aligned} \tag{11}$$

where $2N = 10$

Pr(two lineages coalesce two generations ago)

Example

$$\begin{aligned} Pr(COAL\ two\ generations\ ago) &= Pr(no\ COAL\ at\ generation\ one) \\ &\times Pr(COAL\ at\ generation\ two) \end{aligned} \tag{11}$$

where $2N = 10$

$$Pr(COAL\ two\ generations\ ago) = \left(1 - \frac{1}{10}\right) \times \frac{1}{10} = \left(1 - \frac{1}{2N}\right) \times \frac{1}{2N} \tag{12}$$

Coalescence times for two lineages

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Example

$$Pr(COAL\ at\ generation\ t) = \left(1 - \frac{1}{2N}\right)^{t-1} \times \frac{1}{2N} \tag{13}$$

Coalescence times for two lineages

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Given that $T_2 \sim Geo\,(p)$ where $p = \frac{1}{2N}$ the expected time to coalescence for two lineages is:

Coalescence times for two lineages

Example

$$Pr(COAL\ at\ generation\ t) = \left(1 - \frac{1}{2N}\right)^{t-1} \times \frac{1}{2N} \tag{13}$$

Given that $T_2 \sim Geo\left(p\right)$ where $p = \frac{1}{2N}$ the expected time to coalescence for two lineages is:

$$\mathbb{E}\left(T_2\right) = \frac{1}{p} = 2N \tag{14}$$

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Waiting times until the first coalescent event

Definition

$$Pr(T_i = t) = \left(1 - \frac{\binom{i}{2}}{2N}\right)^{t-1} \times \frac{\binom{i}{2}}{2N} \tag{15}$$

Where $T_i \sim Geo\left(\binom{i}{2}/2N\right)$ thus...

Waiting times until the first coalescent event

Definition

$$Pr(T_i = t) = \left(1 - \frac{\binom{i}{2}}{2N}\right)^{t-1} \times \frac{\binom{i}{2}}{2N} \tag{15}$$

Where $T_i \sim Geo\left(\binom{i}{2}/2N\right)$ thus...

$$\mathbb{E}\left(T_i\right) = \frac{2N}{\binom{i}{2}} \tag{16}$$

Time until the first coalescent event (T_i)

Example

$$\mathbb{E}\left(T_2\right)$$

$$\mathbb{E}\left(T_3\right)$$

$$\mathbb{E}\left(T_4\right)$$

$$\mathbb{E}\left(T_5\right)$$

Time until the first coalescent event (T_i)

Example

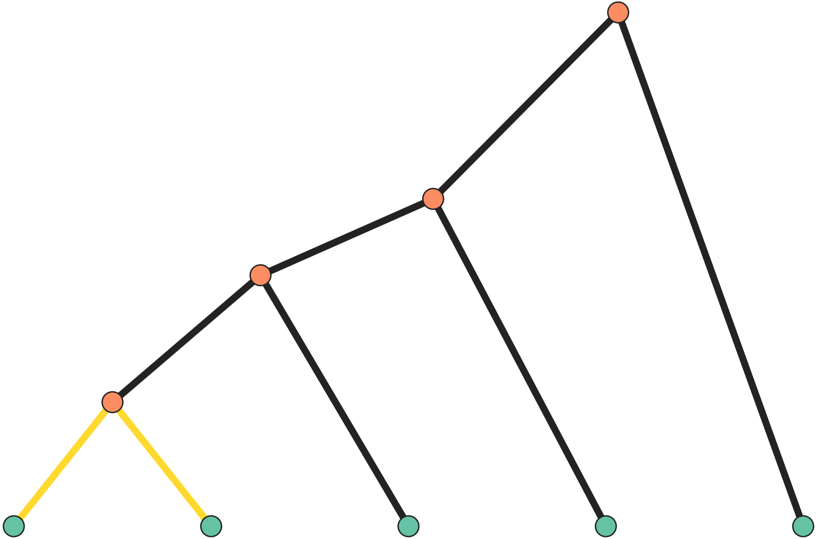
$$\mathbb{E}(T_2) = 2N$$

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

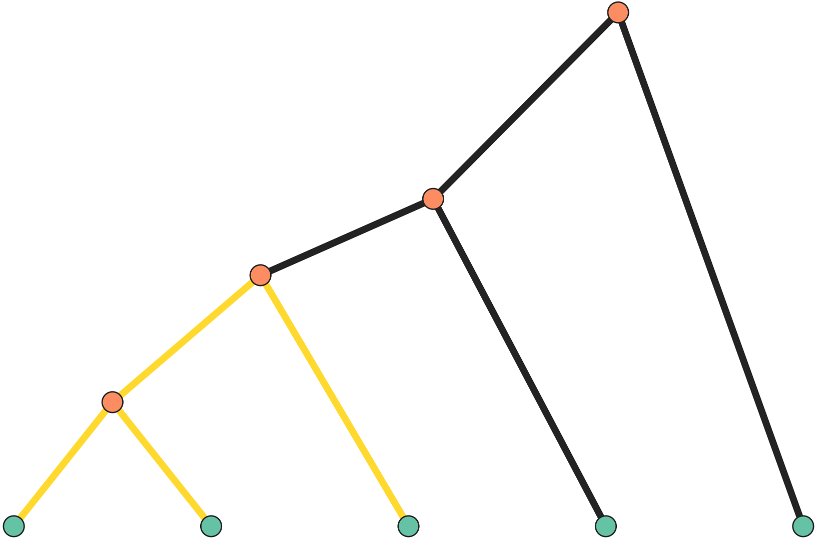
$$\mathbb{E}(T_4) = \frac{2N}{6}$$

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

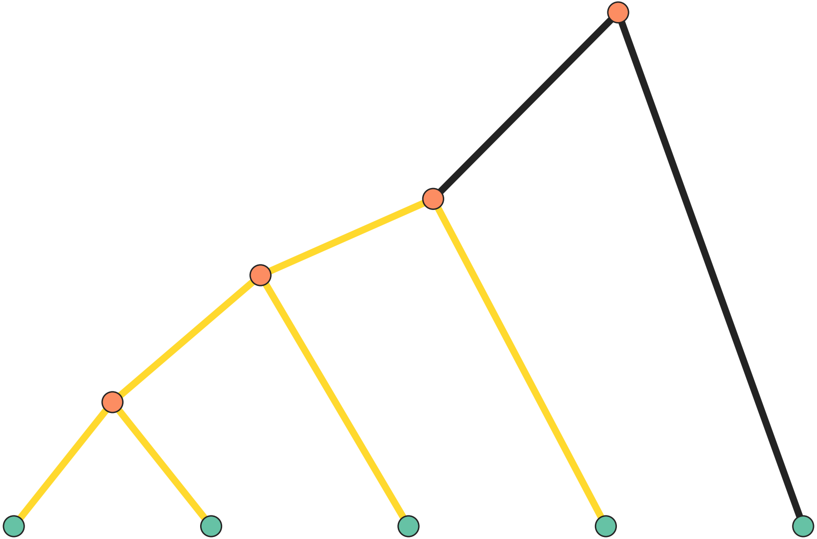
T_5



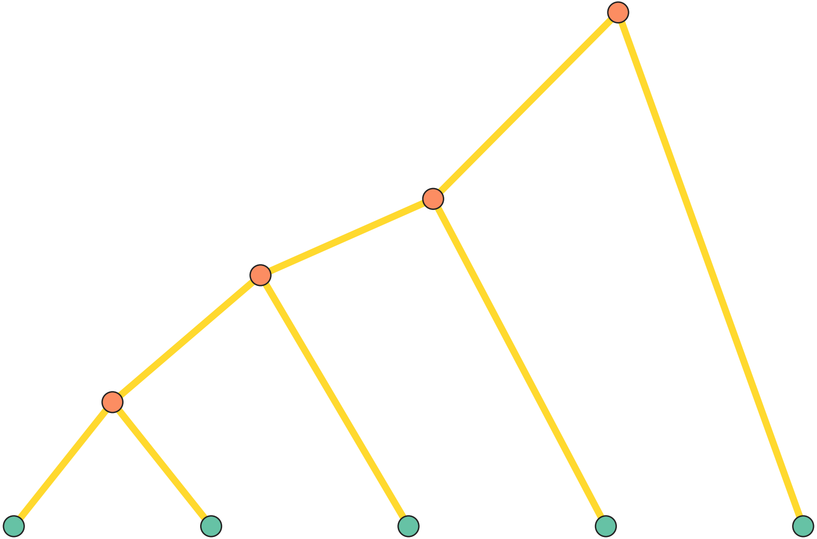
T_4



T_3



T_2



Time to most recent common ancestor (T_{MRCA})

Definition

$$T_{MRCA} \sum_{i=2}^{n} T_i \tag{17}$$

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Definition

$$T_{MRCA} \sum_{i=2}^{n} T_i \tag{17}$$

$$\mathbb{E}\left(T_{MRCA}\right) = \sum_{i=2}^{n} \mathbb{E}\left(T_i\right) \tag{18}$$

Time to most recent common ancestor (T_{MRCA})

Example

What is the the $\mathbb{E}\left(T_{MRCA}\right)$ for a five lineages?

Time to most recent common ancestor (T_{MRCA})

Example

What is the the $\mathbb{E}\left(T_{MRCA}\right)$ for a five lineages?

$$\mathbb{E}\left(T_{MRCA}\right) = \sum_{i=2}^{n} \mathbb{E}\left(T_i\right) = 2N + \frac{2N}{3} + \frac{2N}{6} + \frac{2N}{10}$$

Time to most recent common ancestor (T_{MRCA})

Definition

$$\mathbb{E}\left(T_{MRCA}\right) = \sum_{i=2}^{n} \mathbb{E}\left(T_i\right) = \sum_{i=2}^{n} \frac{2N}{\binom{i}{2}}$$

Time to most recent common ancestor (T_{MRCA})

Definition

$$\mathbb{E}\left(T_{MRCA}\right) = \sum_{i=2}^{n} \mathbb{E}\left(T_i\right) = \sum_{i=2}^{n} \frac{2N}{\binom{i}{2}}$$

$$\mathbb{E}\left(T_{MRCA}\right) = \sum_{i=2}^{n} \mathbb{E}\left(T_i\right) = \sum_{i=2}^{n} \frac{2N}{\binom{i}{2}} = 2N \sum_{i=2}^{n} \frac{2}{i\left(i-1\right)} = 4N \sum_{i=2}^{n} \left(\frac{1}{i-1} - \frac{1}{i}\right)$$

Time to most recent common ancestor (T_{MRCA})

Definition

$$\mathbb{E}\left(T_{MRCA}\right) = \sum_{i=2}^{n} \mathbb{E}\left(T_i\right) = \sum_{i=2}^{n} \frac{2N}{\binom{i}{2}}$$

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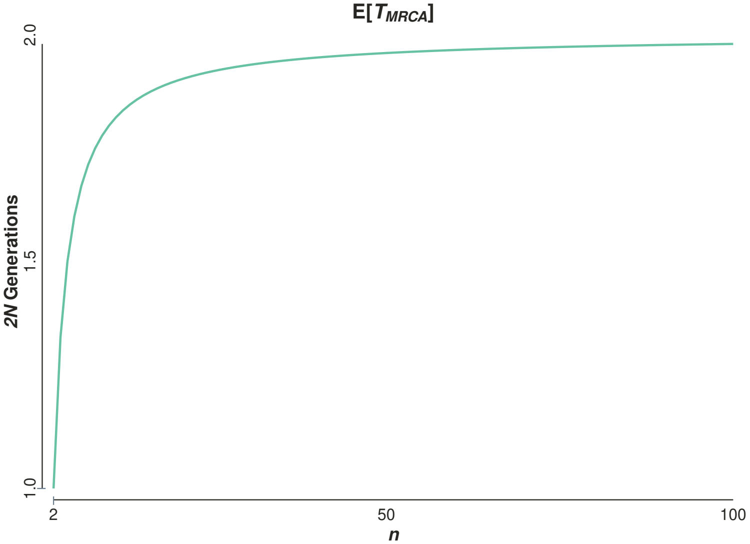
$$\mathbb{E}\left(T_{MRCA}\right) = 4N\left(1 - \frac{1}{n}\right) \tag{19}$$

Behavior of $\mathbb{E}\left[T_{MRCA}\right]$



Total tree height (T_{tot})

Definition

$$T_{tot} \sum_{i=2}^{n} i \times T_i \tag{20}$$

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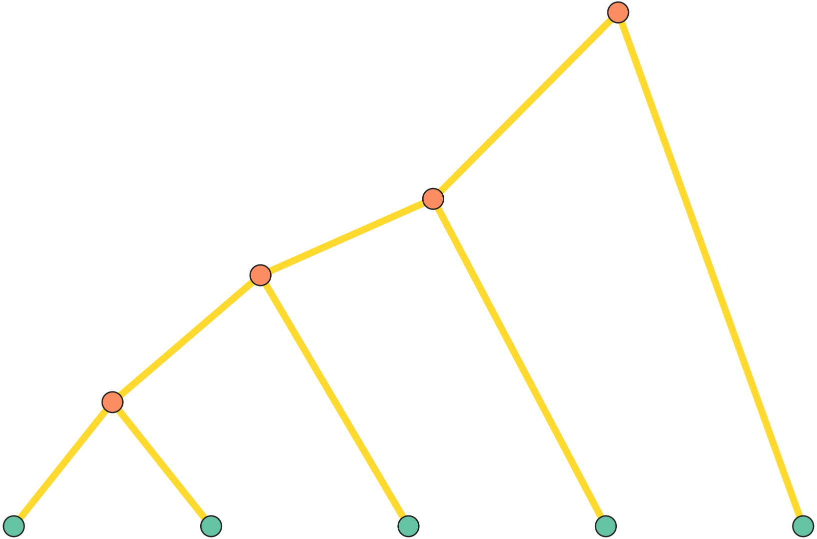
$$\mathbb{E}\left(T_{tot}\right) = \sum_{i=2}^{n} i \times \mathbb{E}\left(T_i\right) \tag{21}$$

T_{tot}



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Example

What is the the $\mathbb{E}\left(T_{tot}\right)$ for a five lineages?

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What is the the $\mathbb{E}\left(T_{tot}\right)$ for a five lineages?

$$\mathbb{E}\left(T_{tot}\right) = \sum_{i=2}^{n} i \times \mathbb{E}\left(T_i\right) = (2 \times 2N) + \left(3 \times \frac{2N}{3}\right) + \left(4 \times \frac{2N}{6}\right) + \left(5 \times \frac{2N}{10}\right)$$

Total tree height (T_{tot})

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$$\mathbb{E}\left(T_{tot}\right) = \sum_{i=2}^{n} i \times \mathbb{E}\left(T_i\right) = \sum_{i=2}^{n} i \times \frac{2N}{\binom{i}{2}} = 2N \sum_{i=2}^{n} \frac{2i}{i\left(i-1\right)} = 4N \sum_{i=2}^{n} \frac{1}{i-1}$$

Total tree height (T_{tot})

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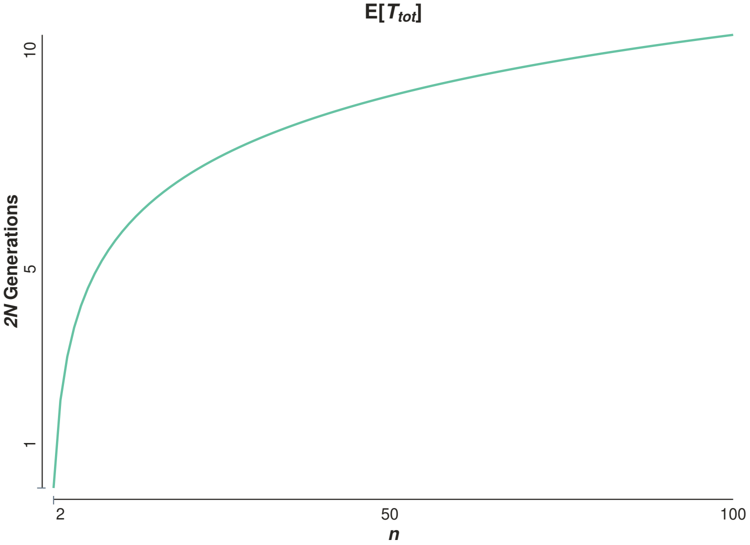
$$\mathbb{E}\left(T_{tot}\right) = \sum_{i=2}^{n} i \times \mathbb{E}\left(T_i\right)$$

$$\mathbb{E}\left(T_{tot}\right) = \sum_{i=2}^{n} i \times \mathbb{E}\left(T_i\right) = \sum_{i=2}^{n} i \times \frac{2N}{\binom{i}{2}} = 2N \sum_{i=2}^{n} \frac{2i}{i\left(i-1\right)} = 4N \sum_{i=2}^{n} \frac{1}{i-1}$$

$$\mathbb{E}\left(T_{tot}\right) = 4N \sum_{i=1}^{n-1} \frac{1}{i}$$

Behavior of $\mathbb{E}\left[T_{tot}\right]$


E[T_{tot}]
2N Generations
n