



BGSMath
BARCELONA GRADUATE SCHOOL OF MATHEMATICS

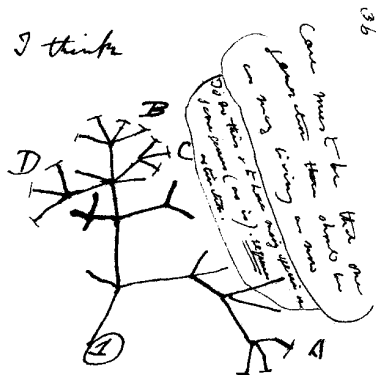
Semi-algebraic conditions for phylogenetic reconstruction

Marina Garrote-López

Seminari de Geometria Algebraica de Barcelona



Phylogenetics



Charles Darwin, 1859

Phylogenetics

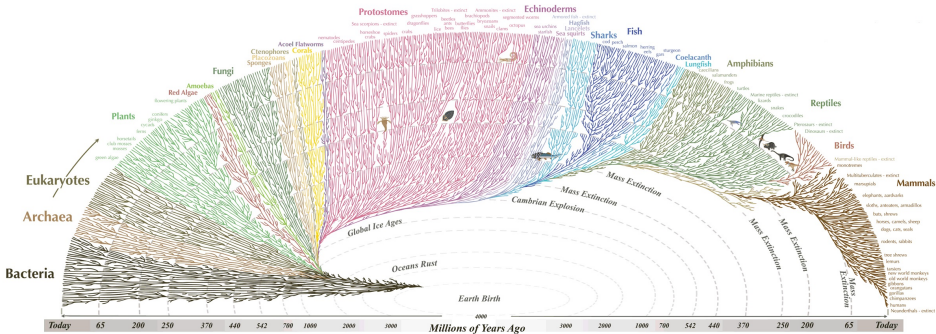




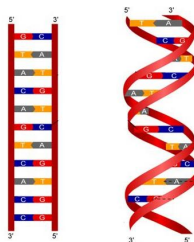
Table of contents

- 1 Modelling evolution
- 2 Phylogenetic varieties
- 3 Phylogenetic reconstruction methods
- 4 Stochastic phylogenetic regions
- 5 SAQ: Semi-algebraic quartet reconstruction method

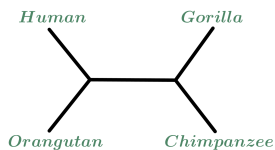
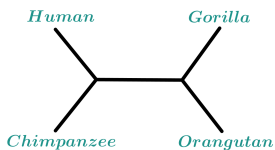
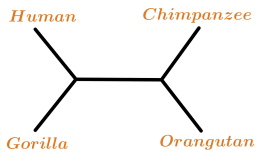
Phylogenetic reconstruction

Given an alignment of DNA sequences for some species,

<i>Gorilla</i>	AACTTCGAGGCTTACCGCTG
<i>Human</i>	AACGTCTATGCTCACCGATG
<i>Chimpanzee</i>	AAGGTCGATGCTCACCGATG
<i>Orangutan</i>	ATTGTGCGAACTCGTCGACC



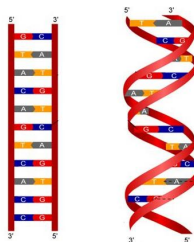
our goal is to reconstruct the topology of the phylogenetic tree that relates them.



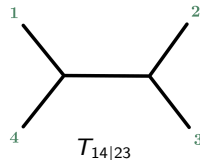
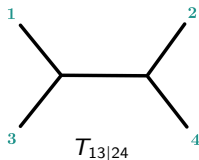
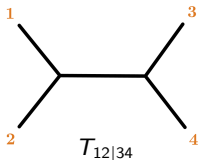
Phylogenetic reconstruction

Given an alignment of DNA sequences for some species,

<i>Gorilla</i>	AACTTCGAGGCTTACCGCTG
<i>Human</i>	AACGTCTATGCTCACCGATG
<i>Chimpanzee</i>	AAGGTCGATGCTCACCGATG
<i>Orangutan</i>	ATTGTGCAACTCGTCGACG

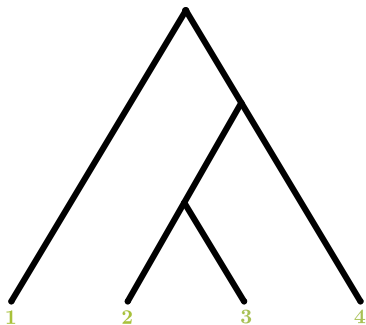


our goal is to reconstruct the topology of the phylogenetic tree that relates them.

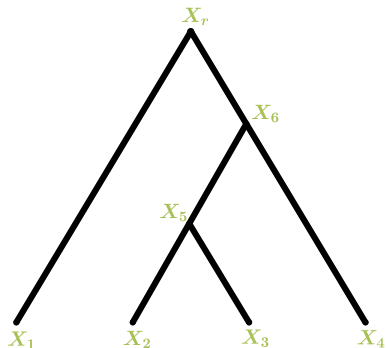




Modeling Evolution

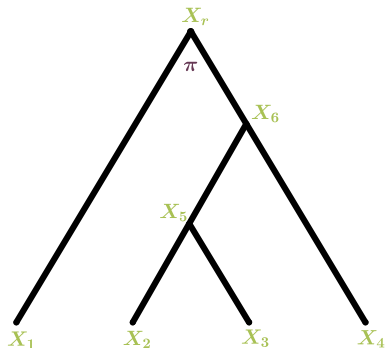


Modeling Evolution



Random variables at the nodes
 $X_i \in \mathcal{K} = \{A, C, G, T\}$

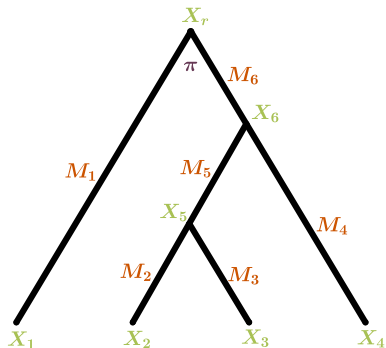
Modeling Evolution



Random variables at the nodes
 $X_i \in \mathcal{K} = \{A, C, G, T\}$

Distribution at the root
 $\pi = (\pi_A, \pi_C, \pi_G, \pi_T); \sum_{i \in \mathcal{K}} \pi_i = 1$

Modeling Evolution



Random variables at the nodes

$$X_i \in \mathcal{K} = \{A, C, G, T\}$$

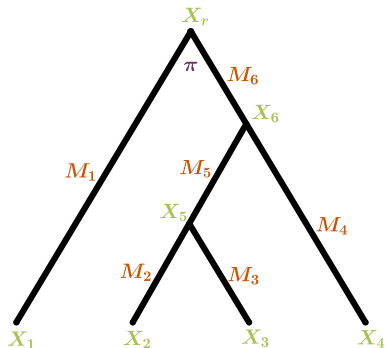
Distribution at the root

$$\pi = (\pi_A, \pi_C, \pi_G, \pi_T); \sum_{i \in \mathcal{K}} \pi_i = 1$$

Transition matrices at the edges

$$M_e = \begin{pmatrix} P(A \rightarrow A|e) & \dots & P(A \rightarrow T|e) \\ P(C \rightarrow A|e) & \dots & P(C \rightarrow T|e) \\ P(G \rightarrow A|e) & \dots & P(T \rightarrow G|e) \\ P(T \rightarrow A|e) & \dots & P(T \rightarrow T|e) \end{pmatrix}$$

Modeling Evolution



Random variables at the nodes
 $X_i \in \mathcal{K} = \{A, C, G, T\}$

Distribution at the root
 $\pi = (\pi_A, \pi_C, \pi_G, \pi_T); \sum_{i \in \mathcal{K}} \pi_i = 1$

Transition matrices at the edges

$$M_e = \begin{pmatrix} P(A \rightarrow A|e) & \dots & P(A \rightarrow T|e) \\ P(C \rightarrow A|e) & \dots & P(C \rightarrow T|e) \\ P(G \rightarrow A|e) & \dots & P(T \rightarrow G|e) \\ P(T \rightarrow A|e) & \dots & P(T \rightarrow T|e) \end{pmatrix}$$

A **transition matrix** is a square matrix with nonnegative entries and rows summing up to one.

Evolutionary models

Jukes Cantor Model

$$M_e = \begin{pmatrix} a_e & b_e & b_e & b_e \\ b_e & a_e & b_e & b_e \\ b_e & b_e & a_e & b_e \\ b_e & b_e & b_e & a_e \end{pmatrix},$$

where $3a_e + b_e = 1$.

Evolutionary models

Jukes Cantor Model

$$M_e = \begin{pmatrix} a_e & b_e & b_e & b_e \\ b_e & a_e & b_e & b_e \\ b_e & b_e & a_e & b_e \\ b_e & b_e & b_e & a_e \end{pmatrix},$$

where $3a_e + b_e = 1$.



Evolutionary models

Jukes Cantor Model

$$M_e = \begin{pmatrix} a_e & b_e & b_e & b_e \\ b_e & a_e & b_e & b_e \\ b_e & b_e & a_e & b_e \\ b_e & b_e & b_e & a_e \end{pmatrix},$$

where $3a_e + b_e = 1$.

Strand Symmetric Model

$$M_e = \begin{pmatrix} a_e & b_e & c_e & d_e \\ e_e & f_e & g_e & h_e \\ h_e & g_e & f_e & e_e \\ d_e & c_e & b_e & a_e \end{pmatrix},$$

where rows sum up to 1.

Evolutionary models

Jukes Cantor Model

$$M_e = \begin{pmatrix} a_e & b_e & b_e & b_e \\ b_e & a_e & b_e & b_e \\ b_e & b_e & a_e & b_e \\ b_e & b_e & b_e & a_e \end{pmatrix},$$

where $3a_e + b_e = 1$.

Strand Symmetric Model

$$M_e = \begin{pmatrix} a_e & b_e & c_e & d_e \\ e_e & f_e & g_e & h_e \\ h_e & g_e & f_e & e_e \\ d_e & c_e & b_e & a_e \end{pmatrix},$$

where rows sum up to 1.



=



=



Purines

=

Pyrimidines

Evolutionary models

Jukes Cantor Model

$$M_e = \begin{pmatrix} a_e & b_e & b_e & b_e \\ b_e & a_e & b_e & b_e \\ b_e & b_e & a_e & b_e \\ b_e & b_e & b_e & a_e \end{pmatrix},$$

where $3a_e + b_e = 1$.

Strand Symmetric Model

$$M_e = \begin{pmatrix} a_e & b_e & c_e & d_e \\ e_e & f_e & g_e & h_e \\ h_e & g_e & f_e & e_e \\ d_e & c_e & b_e & a_e \end{pmatrix},$$

where rows sum up to 1.

Kimura Model

$$M_e = \begin{pmatrix} a_e & b_e & c_e & d_e \\ b_e & a_e & d_e & c_e \\ c_e & d_e & a_e & b_e \\ d_e & c_e & b_e & a_e \end{pmatrix},$$

where $a_e + b_e + c_e + d_e = 1$.

Evolutionary models

Jukes Cantor Model

$$M_e = \begin{pmatrix} a_e & b_e & b_e & b_e \\ b_e & a_e & b_e & b_e \\ b_e & b_e & a_e & b_e \\ b_e & b_e & b_e & a_e \end{pmatrix},$$

where $3a_e + b_e = 1$.

Strand Symmetric Model

$$M_e = \begin{pmatrix} a_e & b_e & c_e & d_e \\ e_e & f_e & g_e & h_e \\ h_e & g_e & f_e & e_e \\ d_e & c_e & b_e & a_e \end{pmatrix},$$

where rows sum up to 1.

Kimura Model

$$M_e = \begin{pmatrix} a_e & b_e & c_e & d_e \\ b_e & a_e & d_e & c_e \\ c_e & d_e & a_e & b_e \\ d_e & c_e & b_e & a_e \end{pmatrix},$$

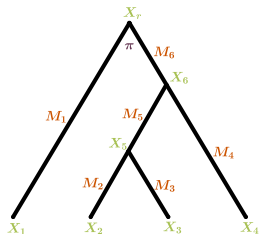
where $a_e + b_e + c_e + d_e = 1$.

General Markov Model

$$M_e = \begin{pmatrix} a_e & b_e & c_e & d_e \\ e_e & f_e & g_e & h_e \\ j_e & k_e & l_e & m_e \\ n_e & o_e & p_e & q_e \end{pmatrix},$$

where rows sum up to 1.

Joint distribution

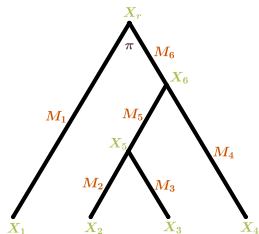


Definition

The **joint distribution** p_{s_1, \dots, s_n} at the leaves of a rooted phylogenetic tree T , which is the probability that the random variables X_1, \dots, X_n of the leaves take the states s_1, \dots, s_n

$$p_{s_1 \dots s_n} = \text{Prob}(X_1 = s_1, X_2 = s_2, \dots, X_n = s_n).$$

Joint distribution



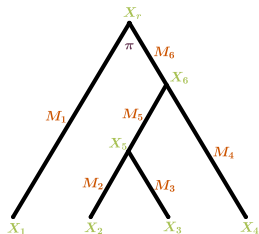
Definition

The **joint distribution** p_{s_1, \dots, s_n} at the leaves of a rooted phylogenetic tree T , which is the probability that the random variables X_1, \dots, X_n of the leaves take the states s_1, \dots, s_n

$$p_{s_1 \dots s_n} = \text{Prob}(X_1 = s_1, X_2 = s_2, \dots, X_n = s_n).$$

$$p_{X_1 \dots X_n} = \sum_{x_v, v \in \text{Int}(T)} \pi_{x_r} \prod_{e \in E(T)} M_e(x_{\text{pa}(e)}, x_{\text{ch}(e)}),$$

Joint distribution



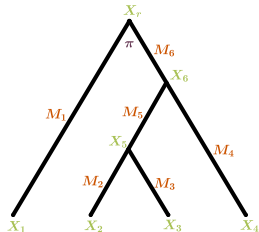
Definition

The **joint distribution** p_{s_1, \dots, s_n} at the leaves of a rooted phylogenetic tree T , which is the probability that the random variables X_1, \dots, X_n of the leaves take the states s_1, \dots, s_n

$$p_{s_1 \dots s_n} = \text{Prob}(X_1 = s_1, X_2 = s_2, \dots, X_n = s_n).$$

$$p_{A,T,C,C} = \sum_{x_r, x_5, x_6 \in \{A, C, G, T\}} \pi_{x_r} \cdot M_1(x_r, A) \cdot M_6(x_r, x_6) \cdot M_5(x_6, x_5) \cdot M_2(x_5, T) \cdot M_3(x_5, C) \cdot M_4(x_6, C)$$

Joint distribution



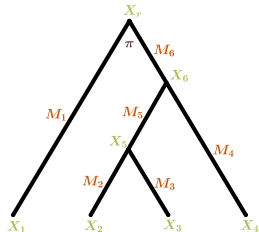
Definition

We denote by p_{s_1, \dots, s_n} the **joint distribution** at the leaves of a rooted phylogenetic tree T , which is the probability that the random variables X_1, \dots, X_n of the leaves take the states s_1, \dots, s_n

$$p_{s_1 \dots s_n} = \text{Prob}(X_1 = s_1, X_2 = s_2, \dots, X_n = s_n).$$

- The entries of the joint distribution at the leaves $p^T = (p_{s_1 \dots s_n})_{s_1, \dots, s_n}$ can be expressed as a **polynomial** in terms of the parameters of the model.

Joint distribution



Definition

We denote by p_{s_1, \dots, s_n} the **joint distribution** at the leaves of a rooted phylogenetic tree T , which is the probability that the random variables X_1, \dots, X_n of the leaves take the states s_1, \dots, s_n

$$p_{s_1 \dots s_n} = \text{Prob}(X_1 = s_1, X_2 = s_2, \dots, X_n = s_n).$$

- The entries of the joint distribution at the leaves $p^T = (p_{s_1 \dots s_n}^T)_{s_1, \dots, s_n}$ can be expressed as a **polynomial** in terms of the parameters of the model.
- We can estimate p^T easily (by the relative frequencies in an alignment) but **NOT** the parameters.

Phylogenetic variety

Definition

For fixed tree T and model \mathcal{M} , fixed the position of the root r we use φ_T to denote the **parametrization map**,

$$\begin{aligned} \varphi_T : \mathbb{R}^d &\longrightarrow \mathbb{R}^{4^n} \\ (\pi, \{M_e\}_{e \in E(T)}) &\longmapsto P = (p_{x_1, x_1, \dots, x_1}, p_{x_1, x_1, \dots, x_2}, \dots, p_{x_n, x_n, \dots, x_n}) \end{aligned}$$

Phylogenetic variety

Definition

For fixed tree T and model \mathcal{M} , fixed the position of the root r we use φ_T to denote the **parametrization map**,

$$\begin{aligned} \varphi_T : \mathbb{R}^d &\longrightarrow \mathbb{R}^{4^n} \\ (\pi, \{M_e\}_{e \in E(T)}) &\longmapsto P = (p_{x_1, x_1, \dots, x_1}, p_{x_1, x_1, \dots, x_2}, \dots, p_{x_n, x_n, \dots, x_n}) \end{aligned}$$

The **phylogenetic algebraic variety** associated to a tree T and a model \mathcal{M} is

$$\mathcal{V}_T = \overline{\text{Im } \varphi_T}.$$

$I_T = I(\mathcal{V}_T)$ is the **phylogenetic ideal** of T and \mathcal{M} .

Phylogenetic variety

Definition

For fixed tree T and model \mathcal{M} , fixed the position of the root r we use φ_T to denote the **parametrization map**,

$$\begin{aligned} \varphi_T : \mathbb{R}^d &\longrightarrow \mathbb{R}^{4^n} \\ (\pi, \{M_e\}_{e \in E(T)}) &\mapsto P = (p_{x_1, x_1, \dots, x_1}, p_{x_1, x_1, \dots, x_2}, \dots, p_{x_n, x_n, \dots, x_n}) \end{aligned}$$

The **phylogenetic algebraic variety** associated to a tree T and a model \mathcal{M} is

$$\mathcal{V}_T = \overline{\text{Im } \varphi_T}.$$

$I_T = I(\mathcal{V}_T)$ is the **phylogenetic ideal** of T and \mathcal{M} .

Polynomials $f \in I_T$ are called **phylogenetic invariants** of T .

Phylogenetic variety

Definition

For fixed tree T and model \mathcal{M} , fixed the position of the root r we use φ_T to denote the **parametrization map**,

$$\begin{aligned} \varphi_T : \mathbb{R}^d &\longrightarrow \mathbb{R}^{4^n} \\ (\pi, \{M_e\}_{e \in E(T)}) &\longmapsto P = (p_{x_1, x_1, \dots, x_1}, p_{x_1, x_1, \dots, x_2}, \dots, p_{x_n, x_n, \dots, x_n}) \end{aligned}$$

The **phylogenetic algebraic variety** associated to a tree T and a model \mathcal{M} is

$$\mathcal{V}_T = \overline{\text{Im } \varphi_T}.$$

$I_T = I(\mathcal{V}_T)$ is the **phylogenetic ideal** of T and \mathcal{M} .

Polynomials $f \in I_T$ are called **phylogenetic invariants** of T .

Polynomials $f \in I_T$ and $f \notin I_{T'}$, with $T \neq T'$ are the **topology invariants** of T .



Using algebraic varieties in phylogenetics

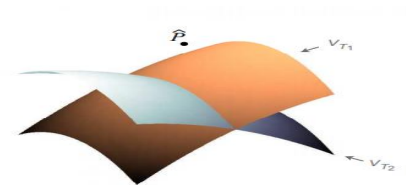
- An alignment produces a point $\hat{p} = (p_{AA\dots A}, p_{AA\dots C}, \dots, p_{TT\dots T})$ in \mathbb{R}^{4^n} .

Using algebraic varieties in phylogenetics

- An alignment produces a point $\hat{p} = (p_{AA\dots A}, p_{AA\dots C}, \dots, p_{TT\dots T})$ in \mathbb{R}^{4^n} .
- \hat{p} should be *close* to \mathcal{V}_{T_0} (if the tree T_0 and model \mathcal{M} fit the data).

Using algebraic varieties in phylogenetics

- An alignment produces a point $\hat{p} = (p_{AA\dots A}, p_{AA\dots C}, \dots, p_{TT\dots T})$ in \mathbb{R}^{4^n} .
- \hat{p} should be *close* to \mathcal{V}_{T_0} (if the tree T_0 and model \mathcal{M} fit the data).
- **Tree topology reconstruction using algebraic geometry.** For each possible topology T , evaluate elements of $I(\mathcal{V}_T)$ at \hat{p} : the polynomials of $I(\mathcal{V}_{T_0})$ should be ≈ 0 when evaluated at \hat{p} .





Problem: computation of invariants

Computational algebra softwares fail to compute the ideal for ≥ 4 species!

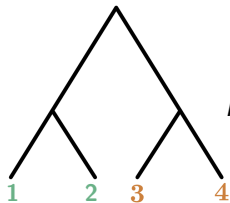


Problem: computation of invariants

Computational algebra softwares fail to compute the ideal for ≥ 4 species!

For example, Kimura 3-parameter with 4 species is a toric variety with 8002 generators like,

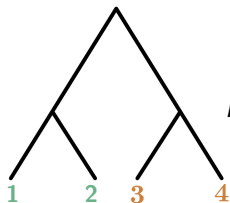
Flattening



$$Flatt_{12|34}(P) =$$

$$\begin{array}{l}
 AA \\
 AC \\
 AG \\
 \vdots \\
 TT
 \end{array}
 \left(
 \begin{array}{ccccc}
 AA & AC & AG & \dots & TT \\
 p_{AAAA} & p_{AAAC} & p_{AAAG} & \dots & p_{AATT} \\
 p_{ACAA} & p_{ACAC} & p_{ACAG} & \dots & p_{ACTT} \\
 p_{AGAA} & p_{AGAC} & p_{AGAG} & \dots & p_{AGTT} \\
 \vdots & \vdots & \vdots & \ddots & \vdots \\
 p_{TTAA} & p_{TTAC} & p_{TTAG} & \dots & p_{TTTT}
 \end{array}
 \right)$$

Flattening



$$Flatt_{12|34}(P) = \begin{matrix} AA \\ AC \\ AG \\ \vdots \\ TT \end{matrix} \begin{pmatrix} AA & AC & AG & \dots & TT \\ p_{AAAA} & p_{AAAC} & p_{AAAG} & \dots & p_{AAAT} \\ p_{ACAA} & p_{ACAC} & p_{ACAG} & \dots & p_{ACTT} \\ p_{AGAA} & p_{AGAC} & p_{AGAG} & \dots & p_{AGTT} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ p_{TTAA} & p_{TTAC} & p_{TTAG} & \dots & p_{TTTT} \end{pmatrix}$$

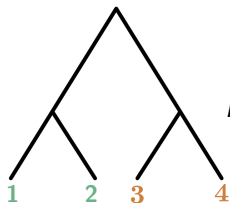
Theorem [Allman – Rhodes]

Let $P = \varphi_T(\pi, \{M_e\}_{e \in E(T)})$ where $T = T_{12|34}$. Then

$$\text{rank}(Flatt_{12|34}(P)) \leq 4.$$

$Flatt_{13|24}(P)$ and $Flatt_{14|23}(P)$ have rank 16 for generic P .

Flattening



$$Flatt_{12|34}(P) = \begin{matrix} AA \\ AC \\ AG \\ \vdots \\ TT \end{matrix} \begin{pmatrix} p_{AAAA} & p_{AAAC} & p_{AAAG} & \dots & p_{AAAT} \\ p_{ACAA} & p_{ACAC} & p_{ACAG} & \dots & p_{ACTT} \\ p_{AGAA} & p_{AGAC} & p_{AGAG} & \dots & p_{AGTT} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ p_{TTAA} & p_{TTAC} & p_{TTAG} & \dots & p_{TTTT} \end{pmatrix}$$

Theorem [Allman – Rhodes]

Let $P = \varphi_T(\pi, \{M_e\}_{e \in E(T)})$ where $T = T_{12|34}$. Then

$$\text{rank}(Flatt_{12|34}(P)) \leq 4.$$

$Flatt_{13|24}(P)$ and $Flatt_{14|23}(P)$ have rank 16 for generic P .

Therefore 5×5 minors of $Flatt_{12|34}(P)$ are **topology invariants**.

Algebraic phylogenetic reconstruction methods

The distance of an $m \times n$ matrix M to the set

$$\mathcal{R}_k = \{m \times n \text{ matrices of rank } \leq k\}$$

can be computed easily by,

Eckart-Young Theorem

$$d_k(M) = d_F(M, \mathcal{R}_k) = \sqrt{\sum_{i \geq k+1} \sigma_i^2},$$

where σ_i are the singular values of M .

Algebraic phylogenetic reconstruction methods

The distance of an $m \times n$ matrix M to the set

$$\mathcal{R}_k = \{m \times n \text{ matrices of rank } \leq k\}$$

can be computed easily by,

Eckart-Young Theorem

$$d_k(M) = d_F(M, \mathcal{R}_k) = \sqrt{\sum_{i \geq k+1} \sigma_i^2},$$

where σ_i are the singular values of M .

Phylogenetic reconstruction methods

Compute $d_4(Flat_{A|B}(P))$ for the tree possible bipartitions. The lower the score is, the more it is likely that the bipartition comes from an edge of T.

Stochastic phylogenetic regions

Definition

The **stochastic phylogenetic regions** is defined as

$$\mathcal{V}_T^+ = \{P \in \mathcal{V}_T \mid P = \varphi_T(s) \text{ and } s \in S \subset [0, 1]^d\},$$

is the subset of \mathcal{V}_T that contains distributions arising from stochastic parameters.

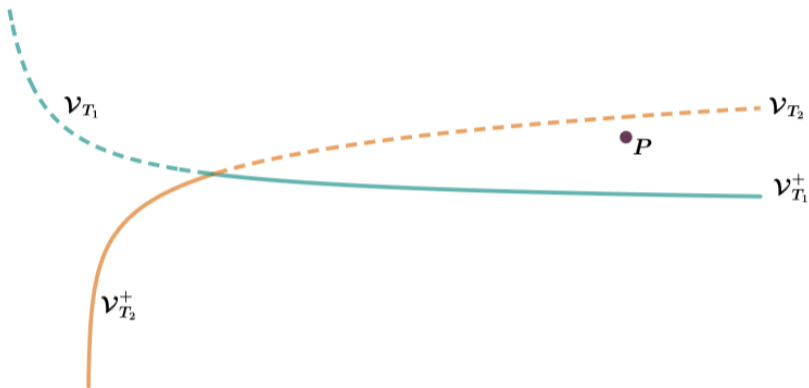
Stochastic Parameters

A vector π is stochastic iff its entries are non-negative and $\sum \pi_i = 1$.

A matrix is stochastic iff its entries are non-negative and

$$\sum_j M_e(i, j) = 1, \forall i, e$$

Could the stochastic varieties be useful for phylogenetic reconstruction?





Computing the distance to a Phylogenetic variety

Let $P = (p_1, \dots, p_{4^n}) \in \Delta^{4^n-1}$ be a distribution. We want to compute the distance of P to \mathcal{V}_T^+ ,

$$d(P, \mathcal{V}_T^+) = \min_{Q \in \mathcal{V}_T^+} d(P, Q)$$

Computing the distance to a Phylogenetic variety

Let $P = (p_1, \dots, p_{4^n}) \in \Delta^{4^n-1}$ be a distribution. We want to compute the distance of P to \mathcal{V}_T^+ ,

$$d(P, \mathcal{V}_T^+) = \min_{Q \in \mathcal{V}_T^+} d(P, Q)$$

Since $Q \in \mathcal{V}_T^+$, we can write $Q = \varphi_T(x)$ with stochastic parameters $x \in \mathbb{R}^d$. Denote by $\Omega \subset \mathbb{R}^d$ the domain of stochastic parameters. Let

$$f_P(x) := d(P, \varphi_T(x)) = \sum_i^{4^n} (p_i - \varphi_i(x))^2.$$

Computing the distance to a Phylogenetic variety

Let $P = (p_1, \dots, p_{4^n}) \in \Delta^{4^n-1}$ be a distribution. We want to compute the distance of P to \mathcal{V}_T^+ ,

$$d(P, \mathcal{V}_T^+) = \min_{Q \in \mathcal{V}_T^+} d(P, Q)$$

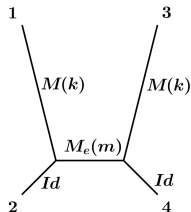
Since $Q \in \mathcal{V}_T^+$, we can write $Q = \varphi_T(x)$ with stochastic parameters $x \in \mathbb{R}^d$. Denote by $\Omega \subset \mathbb{R}^d$ the domain of stochastic parameters. Let

$$f_P(x) := d(P, \varphi_T(x)) = \sum_i^{4^n} (p_i - \varphi_i(x))^2.$$

If $P^+ = \varphi_T(x^*) \in \mathcal{V}_T^+$ is such that $d(P, P^+) = d(P, \mathcal{V}_T^+)$ then

- $(P - P^+) \perp T_P \mathcal{V}_T$, i.e. x^* is a critical point of $f_P(x)$
- x^* is not a critical point of $f_P(x)$ but $P^+ \in \partial\Omega$

Long branch attraction for JC model

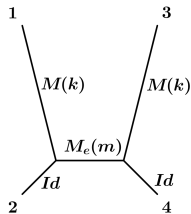


Let $P = \varphi_{12|34}(M, Id, M, Id, M_e)$.

Proposition [Casanellas – Fernández-Sánchez – G-L]

If M_e has negative off-diagonal entries and M is stochastic then $P^+ = \varphi_{12|34}(\tilde{M}, Id, \tilde{M}, Id, Id)$ is a local minimum of the distance function $d(P, \mathcal{V}_T^+)$.

Long branch attraction for JC model



Let $P = \varphi_{12|34}(M, Id, M, Id, M_e)$.

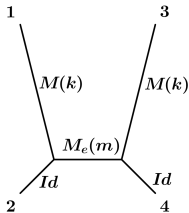
Proposition [Casanellas – Fernández-Sánchez – G-L]

If M_e has negative off-diagonal entries and M is stochastic then $P^+ = \varphi_{12|34}(\tilde{M}, Id, \tilde{M}, Id, Id)$ is a local minimum of the distance function $d(P, \mathcal{V}_T^+)$.

Conjecture: Global minimum

$$d(P, \mathcal{V}_T^+) = d(P, P^+).$$

Long branch attraction for JC model



Let $P = \varphi_{12|34}(M, Id, M, Id, M_e)$.

Proposition [Casanellas – Fernández-Sánchez – G-L]

If M_e has negative off-diagonal entries and M is stochastic then $P^+ = \varphi_{12|34}(\tilde{M}, Id, \tilde{M}, Id, Id)$ is a local minimum of the distance function $d(P, \mathcal{V}_T^+)$.

Conjecture: Global minimum

$$d(P, \mathcal{V}_T^+) = d(P, P^+).$$

Theorem [Casanellas – Fernández-Sánchez – G-L]

Let $P_0 = \varphi_{12|34}(M, Id, M, Id, M_e)$ such that $d(P_0, \mathcal{V}_T^+) = d(P_0, P^+)$ then, for any P close enough to P_0 we have

$$d(P, \mathcal{V}_T^+) \geq d(P, \mathcal{V}_{T_2}^+).$$

Computing the distance to a Phylogenetic variety

Lemma [Draisma – Horobet – Ottaviani – Sturmfels – Thomas]

For general $P \in \mathbb{C}^{4^n}$ the number of critical points of f_P on the manifold $\mathcal{V} \setminus \mathcal{V}_{sing}$ is finite and is called the **Euclidean Distance degree** of \mathcal{V} .

Computing the distance to a Phylogenetic variety

Lemma [Draisma – Horobet – Ottaviani – Sturmfels – Thomas]

For general $P \in \mathbb{C}^{4^n}$ the number of critical points of f_P on the manifold $\mathcal{V} \setminus \mathcal{V}_{sing}$ is finite and is called the **Euclidean Distance degree** of \mathcal{V} .

Computations difficulties

ED degree for the Jukes Cantor model on 4-leaf trees is 290.

- > 2.5 months with *Macaluy2*.
- ≈ 2.5 hours with *Magma*.

Numerical Algebraic Geometry Only PHCpack founds the 290 solutions.

The computations were performed on a machine with 10 Dual Core Intel(R) Xeon(R) Silver 64 Processor 4114 (2.20 GHz, 13.75M Cache) equipped with 256 GB RAM running Ubuntu 18.04.2.

Computing the distance to a Phylogenetic variety

Lemma [Draisma – Horobet – Ottaviani – Sturmfels – Thomas]

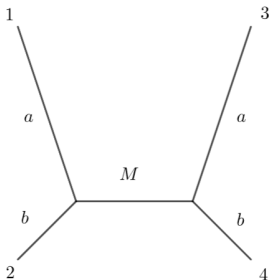
For general $P \in \mathbb{C}^{4^n}$ the number of critical points of f_P on the manifold $\mathcal{V} \setminus \mathcal{V}_{sing}$ is finite and is called the **Euclidean Distance degree** of \mathcal{V} .

Algorithm

1. Compute the Euclidean distance degree d for the variety \mathcal{V}_T .
2. Compute the d critical points x such that $\nabla f(x) = 0$ and $x \in \Omega$.
3. Compute the critical points $\nabla f = 0$ at the boundaries $\partial\Omega$.
4. Choose point with the lowest value when evaluated at f .

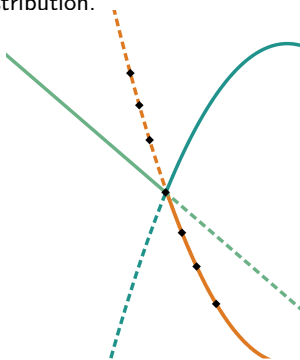
Simulations

- We took trees with branch lengths a and b at the exterior edges. M is a JC matrix with eigenvalue $m \in [0.94, 1.06]$.
- For each set of parameters we considered 100 data points, each corresponding to 10000 independent samples from the corresponding multinomial distribution.

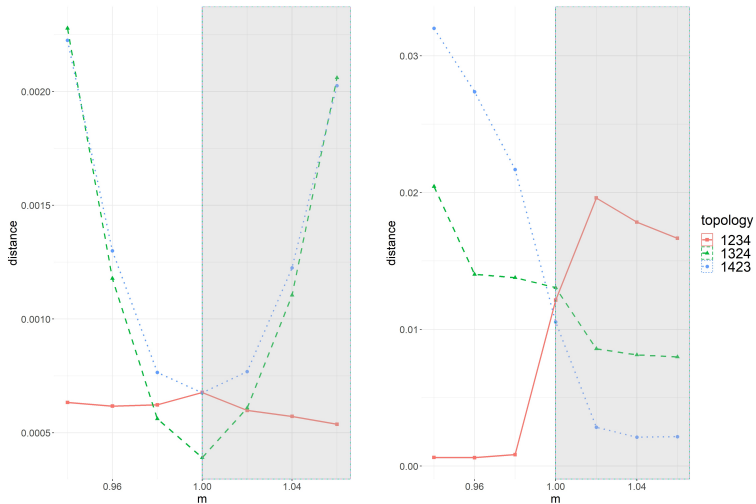


Simulations

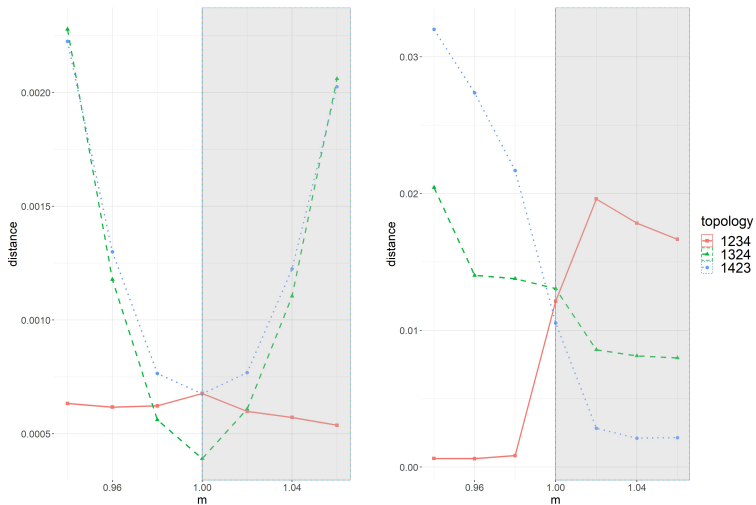
- We took trees with branch lengths a and b at the exterior edges. M is a JC matrix with eigenvalue $m \in [0.94, 1.06]$.
- For each set of parameters we considered 100 data points, each corresponding to 10000 independent samples from the corresponding multinomial distribution.



Simulations $a = 0.5$ & $b = 0.5$



Simulations $a = 0.75$ & $b = 0.1$



Stochastic conditions for the General Markov Model

Theorem [Allman – Rhodes – Taylor]

Let $P = \varphi_{\mathcal{T}}(\pi, \{M_e\}_{e \in E(\mathcal{T})})$ be a 4-tensor that arises from nonsingular real parameters for $GM(\kappa)$ model on $T_{12|34}$. If the marginalizations $P_{+...}$ and $P_{...+}$ arise from stochastic parameters and, moreover, the $\kappa^2 \times \kappa^2$ matrix

$$\text{Flatt}_{13|24}(P *_2 (\text{adj}(P_{+..+}^T) P_{+..+}^T) *_3 (\text{adj}(P_{.++}) P_{.++}))$$

is positive semidefinite, then P arises from stochastic parameters.

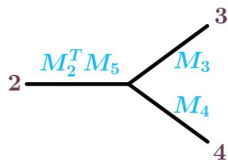
Stochastic conditions for the General Markov Model

Theorem [Allman – Rhodes – Taylor]

Let $P = \varphi_{\mathcal{T}}(\pi, \{M_e\}_{e \in E(\mathcal{T})})$ be a 4-tensor that arises from nonsingular real parameters for $GM(\kappa)$ model on $T_{12|34}$. If the marginalizations $P_{+...}$ and $P_{...+}$ arise from stochastic parameters and, moreover, the $\kappa^2 \times \kappa^2$ matrix

$$Flatt_{13|24}(P *_2 (adj(P_{+.+.}^T) P_{+.+.}^T) *_3 (adj(P_{.+.}) P_{.+.}))$$

is positive semidefinite, then P arises from stochastic parameters.



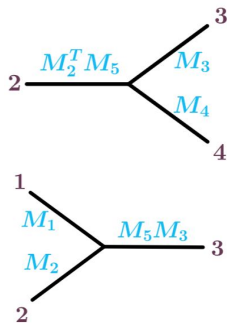
Stochastic conditions for the General Markov Model

Theorem [Allman – Rhodes – Taylor]

Let $P = \varphi_{\mathcal{T}}(\pi, \{M_e\}_{e \in E(\mathcal{T})})$ be a 4-tensor that arises from nonsingular real parameters for $GM(\kappa)$ model on $T_{12|34}$. If the marginalizations $P_{+...}$ and $P_{...+}$ arise from stochastic parameters and, moreover, the $\kappa^2 \times \kappa^2$ matrix

$$Flatt_{13|24}(P *_2 (adj(P_{+.+.}^T) P_{+.+.}^T) *_3 (adj(P_{.++}) P_{.++}))$$

is positive semidefinite, then P arises from stochastic parameters.



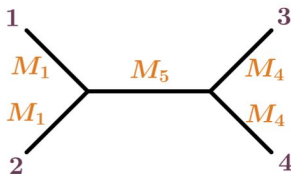
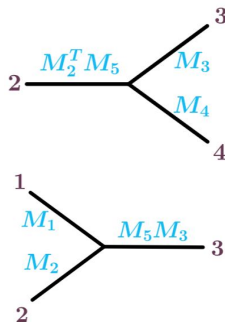
Stochastic conditions for the General Markov Model

Theorem [Allman – Rhodes – Taylor]

Let $P = \varphi_T(\pi, \{M_e\}_{e \in E(T)})$ be a 4-tensor that arises from nonsingular real parameters for $GM(\kappa)$ model on $T_{12|34}$. If the marginalizations $P_{+...}$ and $P_{...+}$ arise from stochastic parameters and, moreover, the $\kappa^2 \times \kappa^2$ matrix

$$Flatt_{13|24}(P *_2 (adj(P_{+..+}^T) P_{+..+}^T) *_3 (adj(P_{...+}) P_{...+}))$$

is positive semidefinite, then P arises from stochastic parameters.



Stochastic conditions for the General Markov Model

Theorem (Casanelas, Fernández-Sánchez, G-L)

Let $P = \varphi_{\mathcal{T}}(\pi, \{M_e\}_{e \in E(\mathcal{T})})$ be a 4-tensor for $GM(\kappa)$ model on $T_{12|34}$. Let \tilde{P} be constructed as in the previous theorem. Then,

$$Flat_{13|24}(\tilde{P}) = Flat_{14|23}(\tilde{P}),$$

and

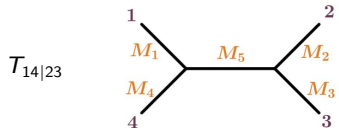
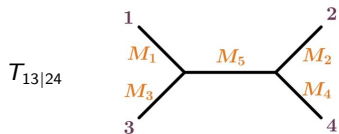
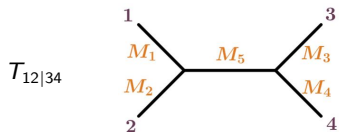
$$Flatt_{12|34}(\tilde{P}) \neq Flatt_{13|24}(\tilde{P}).$$

In particular

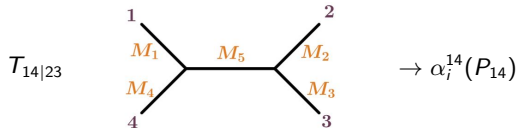
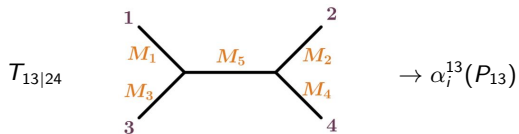
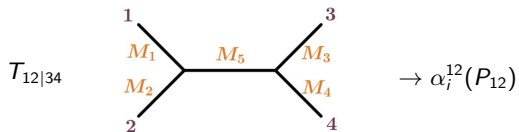
$$\begin{aligned} & \det(P_{+..+})\det(P_{.+..+})Flatt_{13|24}(P *_2 (\text{adj}(P_{+..+}^T)P_{.+..+}^T)) *_3 (\text{adj}(P_{.+..+})P_{+..+})) \\ &= \det(P_{+..+})\det(P_{.+..+})Flatt_{14|23}(P *_2 (\text{adj}(P_{+..+}^T)P_{.+..+}^T)) *_3 (\text{adj}(P_{.+..+})P_{+..+})) \end{aligned}$$

gives rise to 256 topology invariants of degree 17.

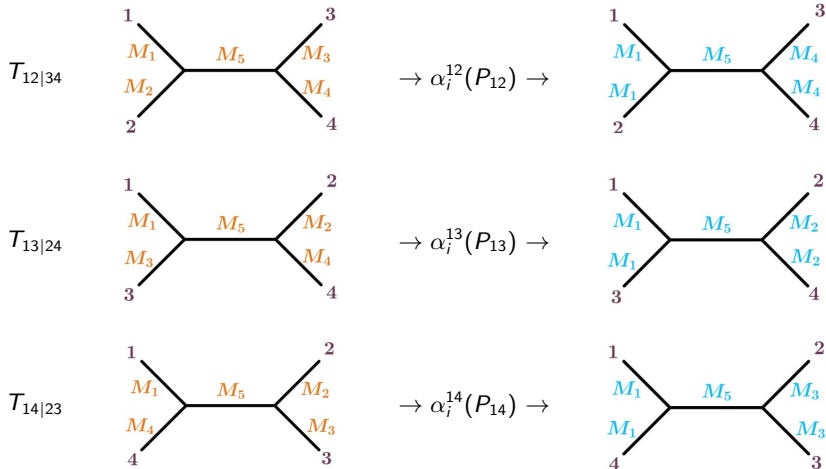
\mathcal{T} Leaf-transformations



\mathcal{T} Leaf-transformations

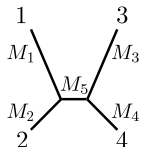


\mathcal{T} Leaf-transformations

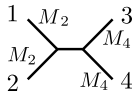
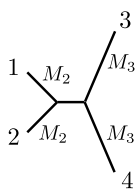
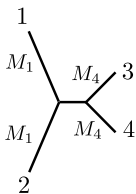
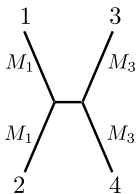


12|34 Leaf-transformations

Original tree T

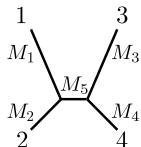


Resulting trees associated with the 12|34 leaf-transformations on the (theoretical) distribution from T

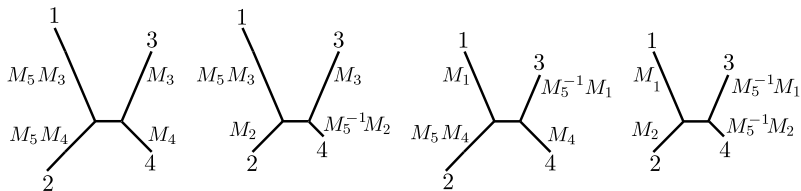


13|24 Leaf-transformations

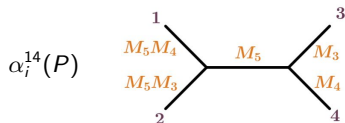
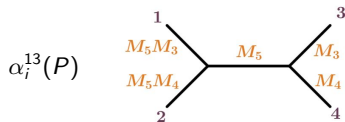
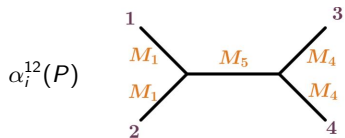
Original tree T



Resulting trees associated with some 13|24 leaf-transformations on the (theoretical) distribution from T

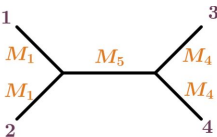


Leaf-transformations on distributions of $T = 12|34$



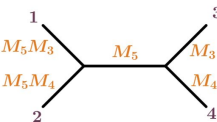
Leaf-transformations on distributions of $T = 12|34$

$\alpha_i^{12}(P)$



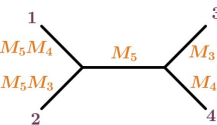
$$\Rightarrow \begin{cases} \text{Flatt}_{12|34}(\alpha_i^{12}(P)) & \rightarrow \text{rank} \leq 4 \checkmark \\ \text{Flatt}_{13|24}(\alpha_i^{12}(P)) & \rightarrow \text{rank} \leq 4 \times \\ \text{Flatt}_{14|23}(\alpha_i^{12}(P)) & \rightarrow \text{rank} \leq 4 \times \end{cases}$$

$\alpha_i^{13}(P)$



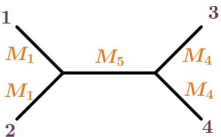
$$\Rightarrow \begin{cases} \text{Flatt}_{13|24}(\alpha_i^{13}(P)) & \rightarrow \text{rank} \leq 4 \times \\ \text{Flatt}_{12|34}(\alpha_i^{13}(P)) & \rightarrow \text{rank} \leq 4 \checkmark \\ \text{Flatt}_{14|32}(\alpha_i^{13}(P)) & \rightarrow \text{rank} \leq 4 \times \end{cases}$$

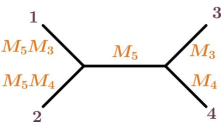
$\alpha_i^{14}(P)$

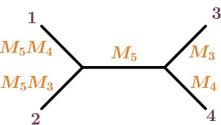


$$\Rightarrow \begin{cases} \text{Flatt}_{14|23}(\alpha_i^{14}(P)) & \rightarrow \text{rank} \leq 4 \times \\ \text{Flatt}_{12|43}(\alpha_i^{14}(P)) & \rightarrow \text{rank} \leq 4 \checkmark \\ \text{Flatt}_{13|42}(\alpha_i^{14}(P)) & \rightarrow \text{rank} \leq 4 \times \end{cases}$$

Leaf-transformations on distributions of $T = 12|34$

$\alpha_i^{12}(P)$

 $\Rightarrow \begin{cases} \text{Flatt}_{12|34}(\alpha_i^{12}(P)) \rightarrow \text{PSD } \times \\ \text{Flatt}_{13|24}(\alpha_i^{12}(P)) \rightarrow \text{PSD } \checkmark \\ \text{Flatt}_{14|23}(\alpha_i^{12}(P)) \rightarrow \text{PSD } \checkmark \end{cases}$

$\alpha_i^{13}(P)$

 $\Rightarrow \begin{cases} \text{Flatt}_{13|24}(\alpha_i^{13}(P)) \rightarrow \text{PSD } \times \\ \text{Flatt}_{12|34}(\alpha_i^{13}(P)) \rightarrow \text{PSD } \times \\ \text{Flatt}_{14|32}(\alpha_i^{13}(P)) \rightarrow \text{PSD } \times \end{cases}$

$\alpha_i^{14}(P)$

 $\Rightarrow \begin{cases} \text{Flatt}_{14|23}(\alpha_i^{14}(P)) \rightarrow \text{PSD } \times \\ \text{Flatt}_{12|43}(\alpha_i^{14}(P)) \rightarrow \text{PSD } \times \\ \text{Flatt}_{13|42}(\alpha_i^{14}(P)) \rightarrow \text{PSD } \times \end{cases}$



SAQ: semi-algebraic quartet reconstruction method

Theorem [Casanellas – Fernández-Sánchez – G-L]

The rank of the *psd* approximation of a real matrix M is less than or equal to $\text{rank}(M)$.

SAQ: semi-algebraic quartet reconstruction method

Theorem [Casanellas – Fernández-Sánchez – G-L]

The rank of the *psd* approximation of a real matrix M is less than or equal to $\text{rank}(M)$.

Lemma [Casanellas – Fernández-Sánchez – G-L]

Let P be the theoretical distribution from a 3-parameter Kimura process on the quartet tree $T = 12|34$. Then, the rank of the *psd* approximation of the flattening matrix $\text{Flat}_{T'}(\alpha^{T'}(P))$ is greater than 4 for $T' \neq T$.

SAQ: semi-algebraic quartet reconstruction method

SAQ method

Let P be a data point obtained from an alignment, then the score for $T = 12|34$ is:

$$s_{12|34}^i := \frac{\min \{ \delta_4 (\text{psd} (\text{Flatt}_{13|24} (\alpha_i^{12}(P)))) , \delta_4 (\text{psd} (\text{Flatt}_{14|23} (\alpha_i^{12}(P)))) \}}{\delta_4 (\text{psd} (\text{Flatt}_{12|34} (\alpha_i^{12}(P))))}$$

SAQ: semi-algebraic quartet reconstruction method

SAQ method

Let P be a data point obtained from an alignment, then the score for $T = 12|34$ is:

$$s_{12|34}^i := \frac{\min \{ \delta_4 (\text{psd} (\text{Flatt}_{13|24} (\alpha_i^{12}(P)))) , \delta_4 (\text{psd} (\text{Flatt}_{14|23} (\alpha_i^{12}(P)))) \}}{\delta_4 (\text{psd} (\text{Flatt}_{12|34} (\alpha_i^{12}(P))))}$$

$$\text{and } s_{12|34} := \text{mean}_i \{ s_{12|34}^i \}$$

SAQ: semi-algebraic quartet reconstruction method

SAQ method

Let P be a data point obtained from an alignment, then the score for $T = 12|34$ is:

$$s_{12|34}^i := \frac{\min \{ \delta_4 (\text{psd} (\text{Flatt}_{13|24} (\alpha_i^{12}(P)))) , \delta_4 (\text{psd} (\text{Flatt}_{14|23} (\alpha_i^{12}(P)))) \}}{\delta_4 (\text{psd} (\text{Flatt}_{12|34} (\alpha_i^{12}(P))))}$$

$$\text{and } s_{12|34} := \text{mean}_i \{ s_{12|34}^i \}$$

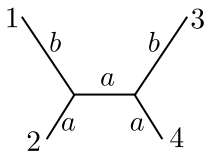
$$\text{SAQ}(P) := \frac{1}{s_{12|34}(P) + s_{13|24}(P) + s_{14|23}(P)} (s_{12|34}(P), s_{13|24}(P), s_{14|23}(P)).$$

If $Q \in \mathbb{R}^{256}$ is a distribution that tends to P generated on the tree $12|34$ with generic stochastic parameters, then

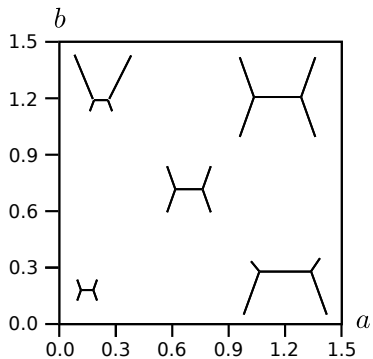
$$\lim_{Q \rightarrow P} \text{SAQ}(Q) = \text{SAQ}(P) = (1, 0, 0).$$

Simulations: Tree Space

a)

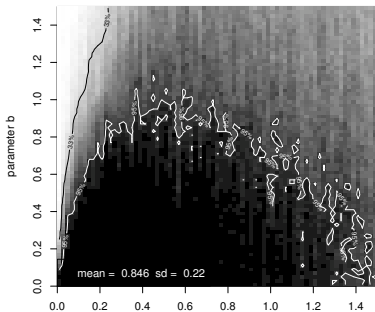


b)

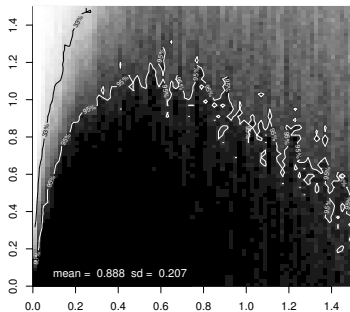


Simulations: Tree Space

GM; length 500 bp



GM; length 1 000 bp

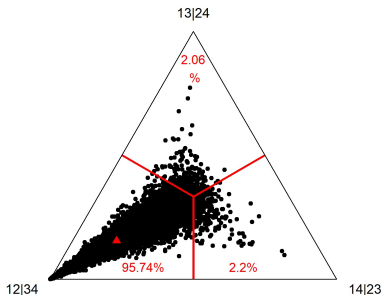


base pairs	SAQ	Erik+2	NJ	ML
500	84.6	72.4	72.5	72.1
1 000	88.8	80.3	79.7	73.6

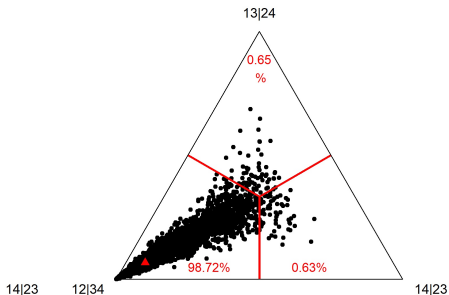
Simulations: Random branch lengths

A total of 10 000 alignments are considered, obtained from 4-taxa trees with random branch lengths uniformly distributed in the interval $(0,1)$, and generated according to the General Markov substitution model.

GM: branch length $(0,1)$; length 1 000 bp

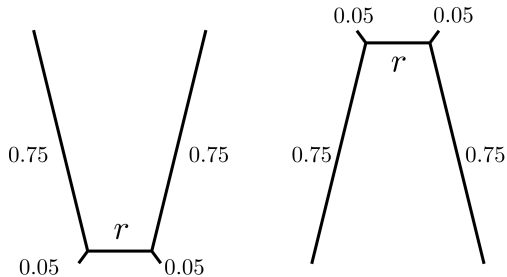


GM: branch length $(0,1)$; length 10 000 bp

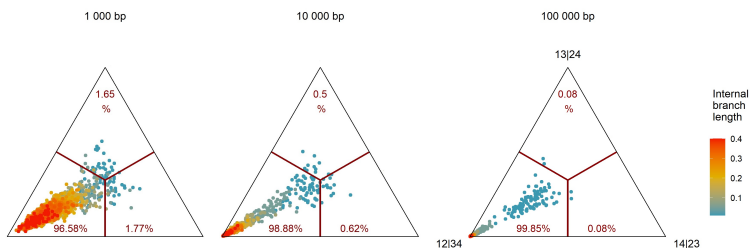


Simulations: Mixture models

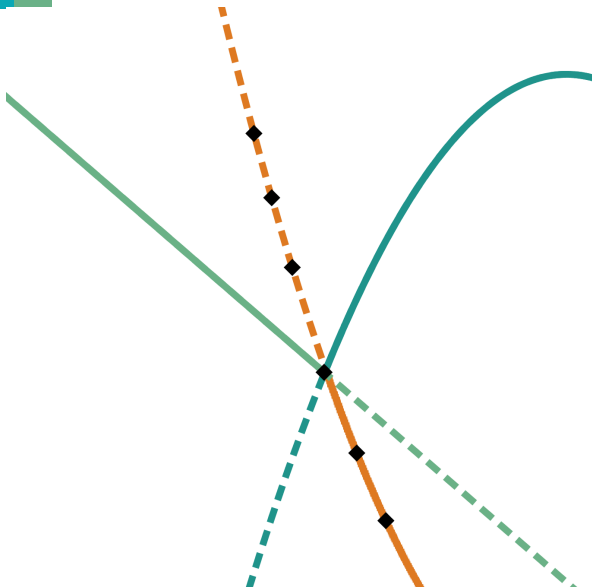
Mixture data



Simulations: Mixture models



internal branch length	0.01	0.05	0.1	0.2	0.3
SAQ	37	83	96	100	100
Erik+2 (2)	12	35	60	86	96
MP	0	2	19	76	99
ML(GTR+2 Γ)	0	4	14	77	95





Thanks for
your attention!