Geometry of Phylogenetic Inference

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References

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Hidden Markov Models

- *n* observed states $Y_1, \ldots, Y_n$, each taking ℓ possible values
- *n* hidden states $X_1, \ldots, X_n$, each taking k possible values
- conditional independence

$$\mathbb{P}(X_i | X_1, \ldots, X_{i-1}) = \mathbb{P}(X_i | X_{i-1})$$

$$\mathbb{P}(Y_i | X_1, \ldots, X_i, Y_1, \ldots, Y_{i-1}) = \mathbb{P}(Y_i | X_i)$$

- special case: all transitions $X_{i-1} \mapsto X_i$ same $k \times k$-stochastic matrix $P = (p_{ij})$; all transitions $X_i \mapsto Y_i$ same $k \times \ell$-stochastic matrix $T = (t_{ij})$

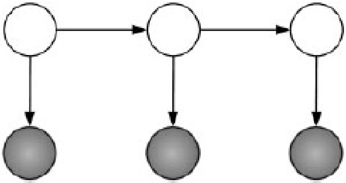
• a HMM described by the image of a polynomial map

$$\Phi : \mathbb{R}^{k(k+1)} \to \mathbb{R}^{\ell^n}$$

of degree $n-1$ bi-homogeneous in the coordinates p_{ij} and t_{ij}

• plus added positivity and normalization conditions (stochastic matrices and probability distributions)

• Example with $k=\ell=2$ and $n=3$, $\Phi=(\Phi_{ijk}):\mathbb{R}^8\to\mathbb{R}^8$



$$\begin{aligned}\Phi_{ijk} = \;& p_{00}p_{00}t_{0i}t_{0j}t_{0k} + p_{00}p_{01}t_{0i}t_{0j}t_{1k} + p_{01}p_{10}t_{0i}t_{1j}t_{0k} + p_{01}p_{11}t_{0i}t_{1j}t_{1k} \\ + \;& p_{10}p_{00}t_{1i}t_{0j}t_{0k} + p_{10}p_{01}t_{1i}t_{0j}t_{1k} + p_{11}p_{10}t_{1i}t_{1j}t_{0k} + p_{11}p_{11}t_{1i}t_{1j}t_{1k}\end{aligned}$$

• invariants of the HMM: polynomial functions on $\mathbb{R}^{\ell^n}$ that vanish on the image of Φ

• ideal $\mathcal{I}_\Phi$ generated by invariants? small k, ℓ, n Gröbner bases; larger computationally hard

Questions

• Viterbi sequence: find the most likely hidden data given observed data

• find all parameter values for a model that result in the same observed distribution

• find what parameter-independent relations hold between the observed probabilities $\mathbb{P}_{i_1,\ldots,i_n} = \Phi_{i_1,\ldots,i_n}$

Phylogenetic Algebraic Geometry

• $\mathcal{T}$ a rooted binary tree with n leaves (hence $2n-2$ edges)

• At each vertex a binary random variable (e.g. one of the syntactic parameters)

• Probability distribution at the root vertex $\pi = (p, 1-p)$

• Along each edge e transition matrix: stochastic matrix $P_e = (p_{ij}^{(e)})$ with $\sum_i p_{ij}^{(e)} = 1$

• these represent the probabilities that a mutation in the parameter happens along that edge

Model Parameters

• the random variables at the leaves of the tree are *observed*; the random variables at the interior nodes are *hidden* (assuming no direct knowledge of the "ancient languages" in the family)

• matrix entries of transition matrices P_e and probability π at root vertex are model parameters

• number of parameters $N = (2n-2)k^2 + k$
(binary variable $k = 2$)

Polynomial Map

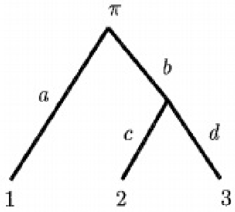
- at the n leaves there are $k^n = 2^n$ possible observations
- the probability of an observation at the leaves is a polynomial function of the parameters
- can view this as a complex polynomial

$$\Phi : \mathbb{C}^N \to \mathbb{C}^{2^n}$$

plus some (real) normalization conditions

- polytope $\Delta \subset \mathbb{R}_+^N \subset \mathbb{C}^N$ determined by the conditions $\pi_1 + \pi_2 = 1$ and $\sum_i p_{ij}^{(e)} = 1$ with $\pi_i \geq 0$ and $p_{ij}^{(e)} \geq 0$
- Φ should map Δ to a cube $\mathcal{I}^n$ in $\mathbb{C}^{2^n}$ where $[0,1] \simeq \mathcal{I} \subset \mathbb{C}^2$ is $\mathcal{I} = \{(p_1, p_2) \,|\, p_1 + p_2 = 1, p_i \geq 0\}$

Example



$$M_a = \begin{pmatrix} a_{00} & a_{01} \\ a_{10} & a_{11} \end{pmatrix} \qquad M_b = \begin{pmatrix} b_{00} & b_{01} \\ b_{10} & b_{11} \end{pmatrix}$$

$$M_c = \begin{pmatrix} c_{00} & c_{01} \\ c_{10} & c_{11} \end{pmatrix} \qquad M_d = \begin{pmatrix} d_{00} & d_{01} \\ d_{10} & d_{11} \end{pmatrix}.$$

$$\Phi_{ijk} = \pi_0 a_{0i} b_{00} c_{0j} d_{0k} + \pi_0 a_{0i} b_{01} c_{1j} d_{1k} + \pi_1 a_{1i} b_{10} c_{0j} d_{0k} + \pi_1 a_{1i} b_{11} c_{1j} d_{1k}$$

there are 8 such polynomials: $i, j, k \in \{0, 1\}$

- polynomial Φ is homogeneous in the parameters
- can view Φ as a map of projective spaces
- in the previous example

$$\Phi : \mathbb{C}^4 \times \mathbb{C}^4 \times \mathbb{C}^4 \times \mathbb{C}^4 \times \mathbb{C}^2 \to \mathbb{C}^8$$

$$\Phi : \mathbb{P}^3(\mathbb{C}) \times \mathbb{P}^3(\mathbb{C}) \times \mathbb{P}^3(\mathbb{C}) \times \mathbb{P}^3(\mathbb{C}) \times \mathbb{P}^1(\mathbb{C}) \to \mathbb{P}^7(\mathbb{C})$$

homogeneous with respect to each group of variables a, b, c, d, π

- the fibers of this morphism give all possible values of parameters (before imposing real normalization conditions) that give a certain probability at the leaves

Algebraic varieties occurring in these models

- Toric varieties (including Segre varieties and Veronese varieties)
- Determinantal varieties: the tree structure imposes rank constraints on matrices built starting from observed probabilities at the leaves
- Example: Segre embedding

$$\mathbb{P}^1 \times \mathbb{P}^1 \times \mathbb{P}^1 \times \mathbb{P}^1 \hookrightarrow \mathbb{P}^{15}$$

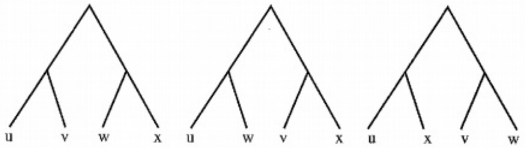
$$p_{ijkl} = u_i v_j w_k x_l \quad i, j, k, l \in \{0, 1\}$$

- Prime ideal defining this variety: generated by 2×2 minors of 4×4-matrices

$$\begin{pmatrix} p_{0000} & p_{0001} & p_{0010} & p_{0011} \\ p_{0100} & p_{0101} & p_{0110} & p_{0111} \\ p_{1000} & p_{1001} & p_{1010} & p_{1011} \\ p_{1100} & p_{1101} & p_{1110} & p_{1111} \end{pmatrix}, \begin{pmatrix} p_{0000} & p_{0001} & p_{0100} & p_{0101} \\ p_{0010} & p_{0011} & p_{0110} & p_{0111} \\ p_{1000} & p_{1001} & p_{1100} & p_{1101} \\ p_{1010} & p_{1011} & p_{1110} & p_{1111} \end{pmatrix},$$

$$\begin{pmatrix} p_{0000} & p_{0010} & p_{0100} & p_{0110} \\ p_{0001} & p_{0011} & p_{0101} & p_{0111} \\ p_{1000} & p_{1010} & p_{1100} & p_{1110} \\ p_{1001} & p_{1011} & p_{1101} & p_{1111} \end{pmatrix}.$$

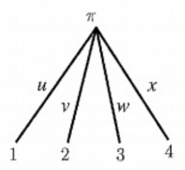
corresponding to



Secant variety of the Segre variety

- X nine-dimensional subvariety of $\mathbb{P}^{15}$ given by al $2 \times 2 \times 2 \times 2$-tensors of rank at most 2

$$p_{ijkl} = \pi_0 u_{0i} v_{0j} w_{0k} x_{0l} + \pi_1 u_{1i} v_{1j} w_{1k} w_{1l}$$

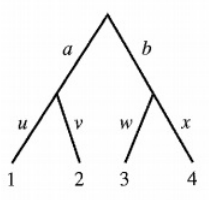


- Ideal generated by all 3×3-minors of previous matrices

$$X = X_{(12)(34)} \cap X_{(13)(24)} \cap X_{(14)(23)}$$

Determinantal variety

• each determinantal variety corresponds to a Markov model on one of the binary trees: $X_{(12)(34)}$ is defined by



$$\begin{aligned} p_{ijkl} = & \pi_0(a_{00}u_{0i}v_{0j} + a_{01}u_{1i}v_{1j})(b_{00}w_{0k}x_{0l} + b_{01}w_{1k}x_{1l}) \\ + & \pi_1(a_{10}u_{0i}v_{0j} + a_{10}u_{1i}v_{1j})(b_{10}w_{0k}x_{0l} + b_{11}w_{1k}x_{1l}) \end{aligned}$$

this corresponds to vanishing of all 3×3-minors in first matrix

• stratification of $\mathbb{P}^{2^n-1}$ by phylogenetic models X

Special case: Jukes-Cantor model

• special case where all the edge matrices P_e have the form

$$P_e = \begin{pmatrix} p_0 & p_1 \\ p_1 & p_0 \end{pmatrix}$$

• it is known that in this case an explicit change of coordinates describes it as a toric variety.

General Idea of Phylogenetic Algebraic Geometry

• generators of the ideal defining the complex variety = phylogenetic invariants

• which phylogenetic invariants suffice to distinguish between different Markov models?

• parameter inference from tropicalization of the algebraic variety

Tropical Semiring

• min-plus (or tropical) semiring $\mathbb{T} = \mathbb{R} \cup \{\infty\}$, with operations $\oplus$ and $\odot$ given by

$$x \oplus y = \min\{x, y\},$$

with ∞ the identity element for $\oplus$ and with

$$x \odot y = x + y,$$

with 0 the identity element for $\odot$

• operations $\oplus$ and $\odot$ satisfy associativity and commutativity and distributivity of the product $\odot$ over the sum $\oplus$

• addition is no longer invertible and is idemponent
$x \oplus x = \min\{x, x\} = x$

Tropical polynomials

- function $\phi : \mathbb{R}^n \to \mathbb{R}$ of the form

$$\phi(x_1, \ldots, x_n) = \oplus_{j=1}^{m} a_j \odot x_1^{k_{j1}} \odot \cdots \odot x_n^{k_{jn}}$$

$$\begin{aligned} = \min\{ \quad & a_1 + k_{11}x_1 + \cdots + k_{1n}x_n, \\ & a_2 + k_{21}x_1 + \cdots + k_{2n}x_n, \\ & \ldots \\ & a_m + k_{m1}x_1 + \cdots + k_{mn}x_n \ \}. \end{aligned}$$

- tropicalization: algebraic varieties become piecewise linear spaces
- can recover information about a variety from its tropicalization

• in the previous HMM example with $n = 3$ and $k = \ell = 2$ the tropicalization of the polynomials Φ_{ijk}

$$\begin{aligned} \Phi_{ijk} = & \quad p_{00}p_{00}t_{0i}t_{0j}t_{0k} + p_{00}p_{01}t_{0i}t_{0j}t_{1k} + p_{01}p_{10}t_{0i}t_{1j}t_{0k} + p_{01}p_{11}t_{0i}t_{1j}t_{1k} \\ + & \quad p_{10}p_{00}t_{1i}t_{0j}t_{0k} + p_{10}p_{01}t_{1i}t_{0j}t_{1k} + p_{11}p_{10}t_{1i}t_{1j}t_{0k} + p_{11}p_{11}t_{1i}t_{1j}t_{1k} \end{aligned}$$

is given by

$$\tau_{ijk} = \min\{u_{h_1 h_2} + u_{h_2 h_3} + v_{h_1 i} + v_{h_2 j} + v_{h_3 k} \,|\, (h_1, h_2, h_3) \in \{0,1\}^3\}$$

where $u_{ab} = -\log(p_{ab})$ and $v_{ab} = -\log(t_{ab})$

• Viterbi sequence: (h_1, h_2, h_3) realizing mimimum, given observed (i, j, k) is the Viterbi sequence of hidden data

Newton polytope

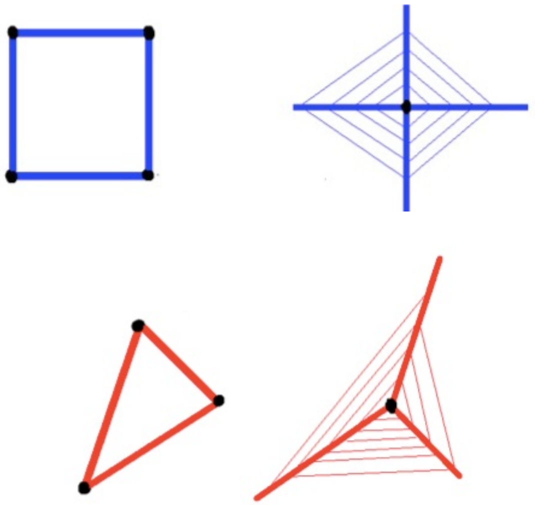
- polynomial $f = \sum_{\omega \in \mathbb{Z}^n} a_\omega x^\omega$ with $x^\omega = x_1^{\omega_1} \cdots x_n^{\omega_n}$
- Newton polytope

$$\mathcal{N}(f) = \text{Convex Hull}\{\omega \in \mathbb{Z}^n \,|\, a_\omega \neq 0\} \subset \mathbb{R}^n$$

- $\mathcal{N}(f+g) = \mathcal{N}(f) \cup \mathcal{N}(g)$ and $\mathcal{N}(f \cdot g) = \mathcal{N}(f) + \mathcal{N}(g)$ (Minkowski sum of polytopes $\mathcal{P} + \mathcal{Q} = \{x + y \,|\, x \in \mathcal{P}, y \in \mathcal{Q}\}$
- normal fan $\mathcal{C}(\mathcal{N}(f))$: normal cones of all faces $\mathcal{C}_F(\mathcal{N}(f))$

$$\mathcal{C}_F(\mathcal{N}(f)) = \{w \in \mathbb{R}^n \,|\, F = F_w(\mathcal{N}(f))\}$$

$$F_w(\mathcal{N}(f)) = \{x \in \mathcal{N}(f) \,|\, (x-y) \cdot w \leq 0 \;\forall y \in \mathcal{N}(f)\}$$



• the set of parameters $U = (u_{ab})$, $V = (v_{ab})$ in tropicalization τ_{ijk} of Φ_{ijk} that determine the Viterbi sequence (h_1, h_2, h_3) is the normal cone to a vertex of the Newton polygon $\mathcal{N}(\Phi_{ijk})$

• given observed data (i, j, k) and hidden data (h_1, h_2, h_3) the normal cones of $\mathcal{N}(\Phi_{ijk})$ give all parameter values for which (h_1, h_2, h_3) is the most likely explanation for the observed (i, j, k)

• domains of linearity of the piecewise linear tropical τ_{ijk} are the cones in the normal fan $\mathcal{C}_F(\mathcal{N}(\Phi_{ijk}))$; each maximal cone corresponds to one set of hidden data (h_1, h_2, h_3) maximizing probability

$$\tau_{ijk} = -\log \mathbb{P}((X_1, X_2, X_3) = (h_1, h_2, h_3) \,|\, (Y_1, Y_2, Y_3) = (i, j, k))$$

• each vertex of the Newton polygon $\mathcal{N}(\Phi_{ijk})$ determines an inference function: $(i, j, k) \mapsto (h_1, h_2, h_3)$ that realize min τ_{ijk}