Identifiability of Models for Morphological Data

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I: Filtered models:

- Variants of standard Markov substitution models on trees where *only* non-constant, or *only* parsimony-informative patterns are observed

- Designed for phenotypic datasets — acquisition bias prevents appropriate sampling of non-informative character patterns

    Is a character recorded if all taxa show the same state?

    Is it recorded if only a single taxon shows a different state? if all taxa show unique states?

- Despite shortcomings of simple models for phenotypic datasets, statistical approaches such as ML, Bayesian inference might still be preferable to parsimony

- Model proposed by P. Lewis (2001) is "JC-like" but omits constant patterns

- Model of Ronquest–Hulsensebeck (2004?) is similar but omits parsimony-noninformative patterns;
used for combined analysis of sequence and morphological data by Nylander–Ronquest–Hulsenbeck–Nieves-Aldrey (2004)

- Growing use in literature for inference of trees and/or rates of gain/loss (e.g., intron gain/loss Csűrös et al., 2007)

For this talk, focus on

$\mathrm{GM2}_{\text{pars-inf}}$: 2-state General Markov model, with only parsimony-informative characters observed

Parameters: Tree, 2×2 Markov matrix on each edge,

arbitrary root distribution

$\mathrm{CFN}_{\text{pars-inf}}$: Cavender-Farris-Neyman model, with only parsimony-informative characters observed

Submodel of $\mathrm{GM2}_{\text{pars-inf}}$ with symmetric Markov matrics,

uniform root distribution

But results generalize to k-state models

II: Identifiability:

For a fixed model,

Given an exact distribution of site-patterns arising from the model

— infinite amounts of 'perfect' data —

can we determine all model parameters?

Identifiability is necessary for statistical consistency of inference

(Efficiency = good performance with finite amounts of data,

Robustness = good performance when model is wrong)

Tree identifiability: Failure

- Inference by parsimony for the CFN model (hence $\mathrm{CFN}_{\text{pars-inf}}$) on 4-taxa can be 'positively misleading' (Felsenstein 1978)
(This is *not* an identifiability statement)

- There are instances of non-identifiability of 4-taxon trees from only parsimony-informative CFN (Steel-Hendy-Penney 1993)

In fact, things are worse...

Theorem (AHR): Any strictly-positive distribution of parsimony-informative patterns on 4 taxa can arise on any of the three resolved tree topologies under a $\mathrm{CFN}_{\text{pars-inf}}$, $\mathrm{GM2}_{\text{pars-inf}}$, or k-state generalizations.

Identifiability of 4-taxon topologies fails completely.

ML, properly implemented, should return all tree topologies as equally likely.

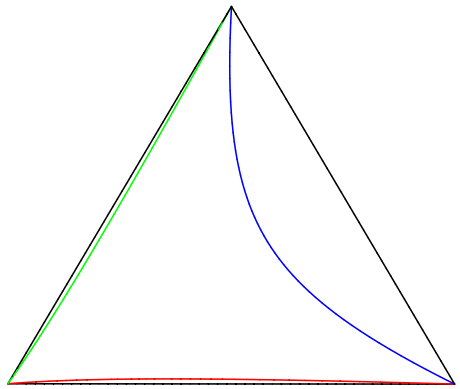
Aside:

For basic examples often given to motivate phylogenetic methods to students, consistent inference of a single tree is impossible by any method!

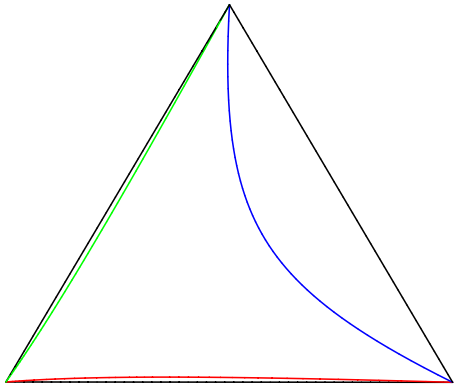
$$S_1 : ACTTA\ldots$$
$$S_2 : ACGGG\ldots$$
$$S_3 : GTTGG\ldots$$
$$S_4 : GTGGA\ldots$$

Sketch of proof:

For $T = ab|cd$, let $p_{xxyy}(s),\ p_{xyxy}(s),\ p_{xyyx}(s)$ be the expected frequencies of the 3 types of patterns. Represent the triple by points in the 2-d probability simplex



Then give an explicit loop in parameters space $\mathcal{S}$, which is mapped to the colored curves under the parameterization. (If certain edges have length 0, parameters map to corners; then find parameters that map to near the boundary.)



Since parameter space $S = \mathbb{R}^5$ is contractible, the image of the parameterization must include interior of curve (formal proof uses fundamental group, basic algebraic topology).

Loop depends on an $\epsilon > 0$, and as $\epsilon \to 0$, curves tend to boundary.

Thus full interior of simplex is in image of parameterization, for T, and hence other trees as well.

But 4-taxon case is pathological...

For n taxa, there are exponentially many patterns, 2^n,

only linearly many of these are parsimony non-informative, $2n$,

so parsimony-informative data *should* retain most phylogenetic signal.

Tree identifiability:

Theorem (AHR): Suppose all Markov matrix parameters are non-singular and have all positive entries. Then topologies of n-taxon trees are identifiable for $\mathrm{GM2}_{\text{pars-inf}}$ (and hence $\mathrm{CFN}_{\text{pars-inf}}$) for $n \geq 8$.

Proof:

- Enough to identify all 4-taxon subtrees.
- For subtree relating taxa a_1, a_2, a_3, a_4, fix some choice of parsimony-informative pattern at all *other* taxa
- Consider only patterns extending this choice to $a_1, \ldots, a_4$.
- Observed frequencies of these extended patterns satisfy certain algebraic relationships (phylogenetic invariants) that depend on the 4-taxon topology.

(Invariants are inspired by the 4-point condition using a log-det distance – Cavender-Felsenstein, Steel)

Note: Identifiability of topologies for 5-, 6-, 7-taxon trees unknown.

Numerical parameter identifiability:

Suppose

- the tree topology is known,
- all Markov matrix parameters are non-singular, and
- some parsimony-informative pattern has positive probability of being observed

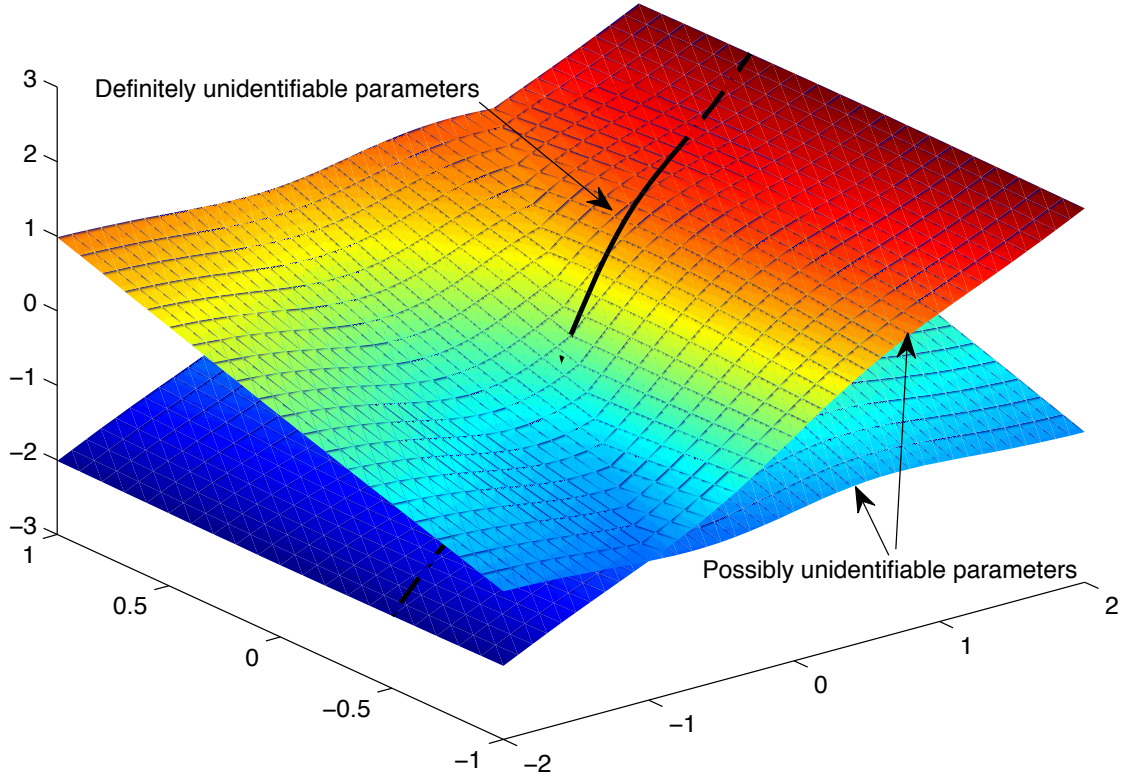
Theorem (AHR): For an n-taxon tree with $n \geq 7$, all numerical parameters of $\mathrm{GM2}_{\text{pars-inf}}$ are identifiable, up to 'label-swapping' at internal nodes. Hence numerical parameters of $\mathrm{CFN}_{\text{pars-inf}}$ are identifiable.

Theorem (AHR): For a 5-taxon tree generic numerical parameters of $\mathrm{GM2}_{\text{pars-inf}}$ are identifiable, up to 'label-swapping' at internal nodes.

However, there exists a subset of codimension 1 in the parameter space for which identifiability may fail.

Within this subset of potentially non-identifiable parameters, there is a smaller subset of codimension 2 in the full parameter space for which identifiability definitely fails.

Cartoon of parameter space for 5-taxon trees:

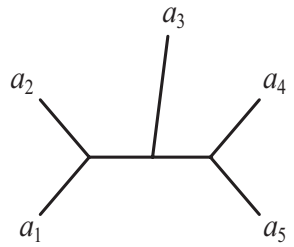


Specializing to $\mathrm{CFN}_{\text{pars-inf}}$, generic parameters are identifiable.

However, the potentially non-identifiable parameters for 5-taxon trees include those from ultrametric (molecular clock) trees!

Sketch of method of proof of identifiabilty of numerical parameters:
We use

Theorem (AR, 2008): For the 2-state General Markov model on a 5-taxon binary tree as shown, let $\{0, 1\}$ denote the set of character states. Let $p_{i_1 i_2 i_3 i_4 i_5}$ denote the joint probability of observing state i_j in the sequence at leaf a_j, $j = 1, \ldots, 5$.



Then the ideal of phylogenetic invariants for this model are generated by the 3×3 minors of the following two matrices:

$$\begin{pmatrix} p_{00000} & p_{00001} & p_{00010} & p_{00011} & p_{00100} & p_{00101} & p_{00110} & p_{00111} \\ p_{01000} & p_{01001} & p_{01010} & p_{01011} & p_{01100} & p_{01101} & p_{01110} & p_{01111} \\ p_{10000} & p_{10001} & p_{10010} & p_{10011} & p_{10100} & p_{10101} & p_{10110} & p_{10111} \\ p_{11000} & p_{11001} & p_{11010} & p_{11011} & p_{11100} & p_{11101} & p_{11110} & p_{11111} \end{pmatrix}$$

and

$$\begin{pmatrix} p_{00000} & p_{00001} & p_{00010} & p_{00011} \\ p_{00100} & p_{00101} & p_{00110} & p_{00111} \\ p_{01000} & p_{01001} & p_{01010} & p_{01011} \\ p_{01100} & p_{01101} & p_{01110} & p_{01111} \\ p_{10000} & p_{10001} & p_{10010} & p_{10011} \\ p_{10100} & p_{10101} & p_{10110} & p_{10111} \\ p_{11000} & p_{11001} & p_{11010} & p_{11011} \\ p_{11100} & p_{11101} & p_{11110} & p_{11111} \end{pmatrix}.$$

If we have only probabilities q of patterns conditioned on parsimony-informativeness, then we know only *some* of these entries, but rescaled by an unknown factor.

$$\begin{pmatrix} \mathbf{q}_{00000} & \mathbf{q}_{00001} & \mathbf{q}_{00010} & q_{00011} & \mathbf{q}_{00100} & q_{00101} & q_{00110} & q_{00111} \\ \mathbf{q}_{01000} & q_{01001} & q_{01010} & q_{01011} & q_{01100} & q_{01101} & q_{01110} & \mathbf{q}_{01111} \\ \mathbf{q}_{10000} & q_{10001} & q_{10010} & q_{10011} & q_{10100} & q_{10101} & q_{10110} & \mathbf{q}_{10111} \\ q_{11000} & q_{11001} & q_{11010} & \mathbf{q}_{11011} & q_{11100} & \mathbf{q}_{11101} & \mathbf{q}_{11110} & \mathbf{q}_{11111} \end{pmatrix}$$

Red entries are unknown; 3×3 minors must still be zero.

Judicious choices of 3×3 minors allows for determination of unknown entries, provided certain 2×2 minors don't vanish. E.g.,

$$\begin{vmatrix} q_{01001} & q_{01010} & q_{01011} \\ q_{10001} & q_{10010} & q_{10011} \\ q_{11001} & q_{11010} & \mathbf{q}_{11011} \end{vmatrix} = 0,$$

Expanding the determinant in cofactors by the last column we have

$$q_{01011} \begin{vmatrix} q_{10001} & q_{10010} \\ q_{11001} & q_{11010} \end{vmatrix} - q_{10011} \begin{vmatrix} q_{01001} & q_{01010} \\ q_{11001} & q_{11010} \end{vmatrix} + \mathbf{q}_{11011} \begin{vmatrix} q_{01001} & q_{01010} \\ q_{10001} & q_{10010} \end{vmatrix} = 0$$

Thus provided

$$\begin{vmatrix} q_{01001} & q_{01010} \\ q_{10001} & q_{10010} \end{vmatrix} \neq 0$$

we can determine $\mathbf{q}_{11011}$ from other $q_{\mathbf{i}}$ where $\mathbf{i} \in S$.

For 5-taxon trees, enough 2×2 minors may be zero to defeat this approach, but still gives understanding of potential non-identifiability.

For trees with at least 7 taxa, enough 2×2 minors must be non-zero to determine all unknown entries.

Determining scaling factor is easy – sum of $p_{\mathbf{i}}$ is 1.