Partitioning the Sample Space on Five Taxa for the Neighbor Joining Algorithm

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Abstract

In this paper, we will analyze the behavior of the Neighbor Joining algorithm on five taxa and we will show that the partition of the sample (data) space for estimation of a tree topology with five taxa into subspaces, within each of which the Neighbor Joining algorithm returns the same tree topology. A key of our method to partition the sample space is the action of the symmetric group $S_5$ on the set of distance matrices by changing the labels of leaves. The method described in this paper can be generalized to trees with more than five taxa.

1 Introduction

The Neighbor Joining (NJ) algorithm is introduced by Saitou and Nei [1987] and it is widely used because of its accuracy and computational speed. A number of attempts have been made to understand the good results obtained with the Neighbor Joining algorithm, especially given the problems with the inference procedures used for estimating pairwise distances. For example, Bryant [2005] showed that the $Q$-criterion (defined in (Q) in Section 2.2) is in fact the unique selection criterion such that it is linear, permutation equivariant, and consistent, i.e. it correctly finds the tree corresponding to a tree metric and Gascuel and Steel [2006] showed a nice review of how the NJ algorithm works.

One of the most important questions to study the behavior of the NJ algorithm is to analyze its performance with pairwise distances that are not tree metrics, especially when all pairwise distances are estimated via the maximum likelihood estimation (MLE). The following theorem due to Atteson [1999] is one of the results to address this question:

Theorem 1.1. (Atteson [1999]) Neighbor-joining has $l_\infty$ radius $\frac{1}{2}$.

This means that if the distance estimates are at most half the minimal edge length of the tree away from their true value then the Neighbor Joining algorithm will reconstruct the correct tree. However, Levy et al. [2006] noted that Atteson’s criterion frequently fails to be satisfied even though the NJ algorithm returns the true tree topology. Recent work of Mihaescu et al. [2006] extended Atteson’s work. Mihaescu et al. [2006] showed that the NJ algorithm returns the true tree topology when it works locally for the quartets in the tree. This result gives another criterion when then NJ algorithm returns the correct tree topology and Atteson’s theorem is a special case of Mihaescu et al’s theorem. The results of Atteson [1999] and Mihaescu et al. [2006], however, depend on an input data and to analyze the performance of the NJ algorithm for any input data we need to study the sample space (the space of all possible distance matrices).

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Therefore, this justifies to study the sample space which is the subspace of the vector space \( \mathbb{R}^{\binom{n}{2}} \), where \( n \) is the number of taxa. In this paper, we will show the partition of the sample space for estimation of a tree topology with five taxa \( \{0, 1, 2, 3, 4\} \) into subspaces, within each of which the NJ algorithm returns the same tree topology. For five taxa, the sample space is the subspace \( \mathbb{R}^5 \) of the vector space \( \mathbb{R} \oplus \mathbb{R}^4 \oplus \mathbb{R}^5 \). Note that our method to partition the sample space into subspaces described in this paper can be generalized to trees with more than five taxa.

For every input distance matrix, the NJ algorithm returns a certain tree topology. It may happen that the minimum Q-criterion is taken by more than one pair of taxa at some step. In practice, the NJ algorithm will then have to choose one cherry in order to return a definite result, but for our analysis we assume that in those cases the NJ algorithm will return a set containing all tree topologies resulting from picking optimal cherries.

There are only finitely many tree topologies, and for every topology \( t \) we get a subset \( D_t \) of the sample space (input space) such that for all distance matrices in \( D_t \) one possible answer of the NJ algorithm is \( t \). We aim at describing these sets \( D_t \) and the relation between them.

It turns out that we can break up each \( D_t \) into easier subsets, by considering not only the topology returned by the NJ algorithm but also the order in which cherries are picked. Consider the tree in figure 1(a). There are two possible ways in which the NJ algorithm may reconstruct this tree, namely by first picking the cherry 1-0 or by first picking the cherry 4-3. The set of input distance matrices (vectors in \( \mathbb{R} \oplus \mathbb{R}^4 \oplus \mathbb{R}^5 \)) for which the NJ algorithm will pick exactly the same cherries in the same order then it turns out to be a cone, so it can easily be described by a set of halfspaces.

One important tool in our analysis will be the action of the symmetric group \( S_5 \) on the set of distance matrices by changing the labels of leaves. Because there is only one unlabeled tree topology in the case of five taxa, any two labeled tree topologies can be mapped onto each other by changing leaf labels. Thus it suffices to analyze just one \( D_t \).

2 The Neighbor-Joining algorithm

2.1 Input data

The NJ algorithm is a distance based method which takes a distance matrix, a symmetric matrix \( (d_{ij})_{0 \leq i,j \leq n-1} \) with \( d_{ii} = 0 \) representing pairwise distances of a set of \( n \) taxa \( \{0, 1, \ldots, n-1\} \), as the input. Through this paper, we do not assume anything on an input data except it is symmetry and \( d_{ii} = 0 \). Because of symmetry, the input can be seen as a vector of dimension \( m := \binom{n}{2} = \frac{1}{2}n(n-1) \). We arrange the entries row-wise, so in the case \( n = 4 \) we get:

\[
\begin{pmatrix}
0 & d_0 & d_1 & d_2 \\
d_0 & 0 & d_2 & d_4 \\
d_1 & d_2 & 0 & d_5 \\
d_3 & d_4 & d_5 & 0
\end{pmatrix}.
\]

We denote row/column-indices by pairs of letters such as \( a, b, c, d \), while denoting single indices into the “flattened” vector by letters \( i, j, \ldots \). The two indexing methods are used simultaneously in the hope that no confusion will arise. Thus, in the four taxa example we have \( d_{0,1} = d_{1,0} = d_{5,0} \). In general, we get \( d_i = d_{a,b} = d_{b,a} \) with

\[a = \max \left\{ k \left| \frac{1}{2}k(k-1) \leq i \right. \right\} = \left\lfloor \frac{1}{2} \sqrt{\frac{1}{4} + 2i} \right\rfloor, \quad b = i - \frac{1}{2}(a-1)a, \]

\[d_{a,b} = \frac{d_{a,b} + d_{b,a}}{2} - \frac{1}{2}d_{a,b}.\]
and for $c > d$ we get
\[ d_{c,d} = d_{c(c-1)/2+d}. \]

### 2.2 The Q-Criterion

The NJ algorithm starts by computing the so-called Q-criterion or the cherry picking criterion, given by the formula
\[
q_{a,b} := (n - 2)d_{a,b} - \sum_{k=0}^{n-1} d_{a,k} - \sum_{k=0}^{n-1} d_{k,b}. \tag{Q}
\]

This is a key of the NJ algorithm to choose which pair of taxa is a neighbor.

**Theorem 2.1.** (Saitou and Nei [1987]; Studier and Keppler [1988]) Let $d_{a,b}$ for all pair of taxa \(\{a, b\}\) be the tree metric corresponding to the tree $T$. Then the pair $\{x, y\}$ which minimizes $q_{a,b}$ for all pair of taxa $\{a, b\}$ forms a neighbor.

The resulting matrix is again symmetric, and ignoring the diagonal entries we can see it as a vector of dimension $m$ just like the input data. Moreover, the Q-criterion is obtained from the input data by a linear transformation:
\[
q = A^{(n)}d,
\]
and the entries of the matrix $A^{(n)}$ are given by
\[
A_{ij}^{(n)} = A_{ab,cd}^{(n)} = \begin{cases} 
  n-4 & \text{if } i = j, \\
  -1 & \text{if } i \neq j \text{ and } \{a, b\} \cap \{c, d\} \neq \emptyset, \\
  0 & \text{else},
\end{cases}
\]  
\[\tag{1}
\]
where $a > b$ is the row/column-index equivalent to $i$ and likewise for $c > d$ and $j$. When no confusion arises about the number of taxa, we abbreviate $A^{(n)}$ to $A$. In the case of four taxa, we get
\[
A^{(4)} = \begin{pmatrix}
0 & -1 & -1 & -1 & -1 & 0 \\
-1 & 0 & -1 & -1 & 0 & -1 \\
-1 & -1 & 0 & 0 & -1 & -1 \\
-1 & 0 & -1 & -1 & 0 & -1 \\
0 & -1 & -1 & -1 & 0 & -1 \\
0 & -1 & -1 & -1 & 0 & -1
\end{pmatrix}.
\]

After computing the Q-criterion $q$, the NJ algorithm proceeds by finding the minimum entry of $q$, or, equivalently, the maximum entry of $-q$. The two nodes forming the chosen pair (there may be several pairs with minimal Q-criterion) are then joined ("cherry picking"), i.e. they are removed from the set of nodes and a new node is created. Suppose out of our $n$ taxa $\{0, \ldots, n-1\}$, the first cherry to be picked is $m-1$, so the taxa $n-2$ and $n-1$ are joined to form a new node, which we view as the new node number $n-2$. The reduced pairwise distance matrix is one row and one column shorter than the original one, and by our choice of which cherry we picked, only the entries in the rightmost column and bottom row differ from the original ones. Explicitly,
\[
d''_i = \begin{cases} 
  d_i & \text{for } 0 \leq i < \binom{n-2}{2} \\
  \frac{1}{2}(d_i + d_{i+(n-2)} - d_{m-1}) & \text{for } \binom{n-2}{2} \leq i < \binom{n-1}{2}
\end{cases}
\]
and we see that the reduced distance matrix depends linearly on the original one:

\[ d' = Rd, \]

with \( R = (r_{ij}) \in \mathbb{R}^{(m-n+1) \times m}, \) where

\[
r_{ij} = \begin{cases} 
1 & \text{for } 0 \leq i = j < \left( \frac{n-2}{2} \right) \\
1/2 & \text{for } \left( \frac{n-2}{2} \right) \leq i < \left( \frac{n-1}{2} \right), j = i \\
1/2 & \text{for } \left( \frac{n-2}{2} \right) \leq i < \left( \frac{n-1}{2} \right), j = i + n - 2 \\
-1/2 & \text{for } \left( \frac{n-2}{2} \right) \leq i < \left( \frac{n-1}{2} \right), j = m - 1 \\
0 & \text{else}
\end{cases}
\]

The process of picking cherries is repeated until there are only three taxa left, which are then joined to a single new node.

3 The cones \( C_{ab,c} \)

In the case of five taxa there is just one unlabeled tree topology (cf. figure 1) and there are 15 distinct labeled trees: We have five choices for the leaf which is not part of a cherry and then three choices how to group the remaining four leaves into two pairs. For each of these labeled topologies, there are two ways in which they might be reconstructed by the NJ algorithm: There are two pairs, any one of which might be chosen in the first step of the NJ algorithm.

![Figure 1](image) (a) A tree with five taxa (b) The same tree with all edges adjacent to leaves reduced to length zero. The remaining two edges have lengths \( \alpha \) and \( \beta \).

For distinct leaf labels \( a, b \) and \( c \in \{0, 1, 2, 3, 4\} \) we define \( C_{ab,c} \) to be the set of all input vectors for which the cherry \( a-b \) is picked in the first step and \( c \) remains as single node not part of a cherry after the second step. For example, the tree in figure 1(a) is the result for all vectors in \( C_{10,2} \cup C_{43,2} \). Since for each tree topology \( ((a, b), c, (d, e)) \) (this tree topology is written in the Newick format) for distinct taxa \( a, b, c, d, e \in \{0, 1, 2, 3, 4\} \), the NJ algorithm returns the same tree topology with any vector in the union of two cones \( C_{ab,c} \cup C_{de,c} \), there are 30 such cones in total, and we call the set of these cones \( \mathcal{C} \).

3.1 The shifting lemma

We first note that there is an \( n \)-dimensional linear subspace of \( \mathbb{R}^m \) which does not affect the outcome of the NJ algorithm (see [Mihaescu et al., 2006]). For a node \( a \) we define its shift vector \( s_a \) by

\[
(s_a)_{b,c} := \begin{cases} 
1 & \text{if } a \in \{b, c\} \\
0 & \text{else}
\end{cases}
\]
which represents a tree where the leaf $a$ has distance 1 from all other leaves and all other distances are zero. The Q-criterion of any such vector is $-2$ for all pairs, so adding any linear combination of shift vectors to an input vector does not change the relative values of the Q-criteria. Also, regardless of which pair of nodes we join, the reduced distance matrix of a shift vector is again a shift vector (of lower dimension), whose Q-criterion will also be constant. Thus, for any input vector $d$, the behavior of the NJ algorithm on $d$ will be the same as on $d + s$ if $s$ is any linear combination of shift vectors. We call the subspace generated by shift vectors $S$.

We note that the difference of any two shift vectors is in the kernel of $A$, and the sum of all shift vectors is the constant vector with all entries equal to $n$. If we fix a node $a$ then the set 
$$\{ s_a - s_b \mid b \neq a \}$$
is linearly independent.

### 3.2 Permuting leaf labels

Because there is only one unlabeled tree topology, we can map any labeled topology to any other labeled topology by only changing the labels of the leaves. Such a change of labels also permutes the entries of the distance matrix: For example, the result of swapping leaves 0 and 1 is the distance vector 
$$d' := (d_0, d_2, d_1, d_4, d_3, d_5, d_7, d_6, d_8, d_9)^T.$$

In this way, we get an action of the symmetric group $S_5$ on the input space $R^{10}$, and the permutation $\sigma \in S_5$ maps the cone $C_{ab,c}$ linearly to the cone $C_{\sigma(a)\sigma(b)\sigma(c)}$. Therefore any property of the cone $C_{ab,c}$ which is preserved by linear transformations must be the same for all cones in $C$, and it suffices to determine it for just one cone.

The action of $S_5$ on $R^{10}$ decomposes into irreducible representations by
$$\mathbb{R} \oplus \mathbb{R}^4 \oplus \mathbb{R}^5 = S \oplus W,$$
where the first summand is the subspace of all constant vectors and the second one is the kernel of $A^{(5)}$. The sum of these two subspaces is exactly the space $S$ generated by the shift vectors. The third summand, which we call $W$, is the orthogonal complement of $S$ and it is spanned by vectors $w_{ab,cd}$ in $W$ with
$$(w_{ab,cd})_{xy} := \begin{cases} 
1 & \text{if } xy = ab \text{ or } xy = cd \\
-1 & \text{if } xy = ac \text{ or } xy = bd \\
0 & \text{else}
\end{cases}$$

where $a$, $b$, $c$ and $d$ are pairwise distinct taxa in $\{0, 1, 2, 3, 4\}$ and $(w_{ab,cd})_{xy}$ is the $x$-$y$th coordinate of the vector $w_{ab,cd}$. One linearly independent subset of this is
$$w_1 := w_{01,34}, \quad w_2 := w_{12,40}, \quad w_3 := w_{23,01}, \quad w_4 := w_{34,12}, \quad w_5 := w_{40,23}.$$ 

Note that the 5-cycle $(01234)$ of leaf labels cyclically permutes these basis vectors, whereas the transposition $(01)$ acts via the matrix
$$T := \frac{1}{2} \begin{pmatrix} 
2 & 1 & 1 & 1 & 1 \\
0 & 1 & -1 & -1 & -1 \\
0 & -1 & 1 & -1 & -1 \\
0 & -1 & 1 & -1 & -1 \\
0 & -1 & 1 & -1 & 1
\end{pmatrix}.$$
Because a five-cycle and a transposition generate $S_5$, in principle this gives us complete information about the operation.

3.3 The cone $C_{43,2}$

Since we can apply a permutation $\sigma \in S_5$, without loss of generality, we suppose that the first cherry to be picked is the cherry 9, which is the cherry with leaves 3 and 4. This is true for all input vectors $d$ which satisfy

$$(h_{9,i}, d) \geq 0 \text{ for } i = 0, \ldots, 8,$$

where the vector

$$h^{(n)}_{ij} := -A^{(n)}(e_i - e_j)$$

is perpendicular to the hyperplane of input vector for which cherries $i$ and $j$ have the same Q-criterion, pointing into the direction of vectors for which the Q-criterion of cherry $i$ is lower.

We let $r_1$, $r_2$ and $r_3$ be the first three rows of $-A^{(4)}R^{(5)}$. If $(r_1, d)$ is maximal then the second cherry to be picked is 0-1, leaving 2 as the non-cherry node, and similarly $r_2$ and $r_3$ lead to non-cherry nodes 1 and 0. This allows us to define the set of all input vectors $d$ for which the first picked cherry is 3-4 and the second one is 0-1:

$$C_{34,2} := \{d \mid (h_{9,i}, d) \geq 0 \text{ for } i = 0, \ldots, 8, \text{ and } (r_3 - r_1, d) \geq 0, (r_3 - r_2, d) \geq 0\}. \quad (2)$$

We have defined this set by 11 bounding hyperplanes. However, in fact, the resulting cone has only nine facets. A computation using polymake [Gawrilow and Joswig, 2000] reveals that the two hyperplanes $h_{9,1}$ and $h_{9,2}$ are no longer faces of the cone, while the other nine hyperplanes in (2) give exactly the facets of the cone.

3.4 The Rays of $C$

Again using polymake [Gawrilow and Joswig, 2000] we find that $C_{43,2}$ is the positive cone spanned by fourteen rays. The union of the orbits of these rays under the action of $S_5$ is a set of 82 vertices, which we call $R$. Each of the cones in $C$ is spanned by a certain subset with 14 vertices each of $R$.

The set $R$ has three orbits under the action of the symmetric group $S_5$. We characterize the rays in these orbits using the graphs in Figure 2. In these graphs, nodes which are connected by an edge form a pair with the minimum Q-criterion in the first step of the NJ algorithm, and the labels to each edge show which nodes are possible as the remaining unpaired node.

![Figure 2](image)

Figure 2: Graphs characterizing the rays in $R$. Here $a$, $b$, $c$, $d$ and $e$ are pairwise distinct labels between 0 and 4.

For each graph in figure 2 and each assignment of the five leaves 0, . . . , 4 to the variables $a$, . . . , $e$ we get a set $G$ of vectors which belong exactly to the cones indicated by the graph. By
what we have said in sections 3.1 and 3.2 the set $G$ has the form

$$G = \{ \alpha g + s \mid \alpha \geq 0 \text{ and } s \in S \},$$

where $S$ is the set of all shifting vectors in the sample space (which is the subspace in $\mathbb{R}^{10}$). Thus $G$ is described by a vector $g$ which is unique up to normalization by a positive constant.

We call this vector $g_{a b c d e}^{(a)}$, $g_{a b c d e}^{(b)}$ or $g_{a b c d e}^{(c)}$ depending on which graph it corresponds to.

Some of these graphs coincide for different choices of $a, \ldots, e$.

• The graphs in figure 2(a) are strings of four taxa. There are five ways to choose the four taxa, and $\frac{4!}{2} = 12$ ways in which to arrange them (reversing the order of the string does not matter). In total there are 60 rays of this type.

Thus for example the string 0-1-2-3 refers to an input vector $g_{01234}^{(a)}$ which lies in the intersection of the five cones $C_{10,4}, C_{21,0}, C_{21,3}, C_{21,4}, C_{30,4}$ but not in any other cone. It is worth noting that this vector is a ray of the cones $C_{21,0}, C_{21,3}$ and $C_{21,4}$ but not of the cones $C_{10,4}$ and $C_{32,4}$, which is indicated by the dotted edges in figure 2. This implies that the cones in $C$ do not form a fan, and in particular no polytope in $\mathbb{R}^{10}$ can have $C$ as its normal fan.

• There are $\frac{4!}{2} = 12$ possibilities for the cycle graph in figure 2(b), each of which represents an input vector which forms a ray of ten of the cones in $C$.

• Finally, there are $\binom{5}{2} = 10$ graphs of type 2(c), because these are determined by the two nodes we choose for $a$ and $e$. Each of these corresponds to an input vector that forms a ray of twelve cones.

If we collect all those rays in $R$ which are rays of $C_{43,2}$ we get

• 6 rays of type (a):
  $$g_{03412}^{(a)}, g_{03421}^{(a)}, g_{13402}^{(a)}, g_{13420}^{(a)}, g_{23401}^{(a)}, g_{23410}^{(a)}$$

• 4 of type (b):
  $$g_{34201}^{(b)}, g_{34210}^{(b)}, g_{34012}^{(b)}, g_{34102}^{(b)}$$

• 4 of type (c):
  $$g_{34201}^{(c)}, g_{34210}^{(c)}, g_{34021}^{(c)}, g_{34120}^{(c)}$$

We call these vectors $g_1, \ldots, g_{14}$. Any vector $v \in C_{43,2}$ is a linear combination of these fourteen vectors with nonnegative linear coefficients, say

$$v = \sum_i \alpha_i g_i,$$

where we number the fourteen rays arbitrarily. By linearity, in both steps of the NJ algorithm, the Q-criteria are linear combinations of the Q-criteria for the $g_i$, using the same linear coefficients $\alpha_i$. Furthermore, because all of the vectors $g_i$ lie in $C_{43,2}$, in both steps of the NJ algorithm there is a pair of leaves such that the minimum of the Q-criteria is attained at this pair for all $g_i$, and therefore the minimum Q-criterion of the linear combination $\sum \alpha_i g_i$ is the linear combination of the minimum Q-criteria of the individual $g_i$. This minimum is attained
exactly by those pairs which have minimum Q-criterion in all $g_i$ with strictly positive linear coefficient $\alpha_i$, we get:

$$v \in C_{ab,c} \text{ iff } g_i \in C_{ab,c} \text{ for all } i \text{ with } \alpha_i > 0.$$ 

Therefore the rays in $R$ are the input vectors for which the NJ algorithm is least stable. We can give explicit descriptions of these vectors using the graphs in Figure 3. The graphs give the distance value assigned to each pair of leaves. For example, we get

$$g_{01234}^{(a)} = (-3, 5, -3, -1, 1, 1, 1, -1, 1, -1)^T.$$ 

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$$g_{01234}^{(a)} = (-3, 5, -3, -1, 1, 1, 1, -1, 1, -1)^T.$$ 

**Figure 3:** Graphs describing the vectors $g_{abcd}$ for each of the three types of graphs. Labels assigned to edges denote the distance assigned to the corresponding pair of leaves in the vector, and edges of the same type receive the same label.

### 3.5 The Cone of Tree Metrics

Suppose our input vector is a tree metric. By relabeling the tree and using the shifting lemma, we can reduce the tree to Figure 3(b), where all edges connecting to leaves have length zero. The edge-lengths $\alpha$ and $\beta$ determine the distance vector $v$ as follows:

$$v = \alpha(0, 1, 1, 1, 0, 1, 1, 0, 0, 0)^T + \beta(0, 0, 0, 1, 1, 1, 1, 1, 1, 0)^T =: \alpha a + \beta b.$$ 

If we assume these to be non-negative, we get a cone spanned by the two vectors $a$ and $b$. These satisfy

$$a \in C_{10,2} \cap C_{10,3} \cap C_{10,4}, \quad b \in C_{43,0} \cap C_{43,1} \cap C_{43,2} \quad \text{and} \quad \frac{1}{2}(a + b) \in C_{10,2} \cap C_{43,2},$$

and none of these vectors lies in any other cone.

We normalize to $\alpha + \beta = 1$, and because of symmetry we may assume that $\alpha \geq \beta$, or equivalently $\alpha \geq \frac{1}{2}$. Then we can write $v$ as

$$v = \alpha a + (1 - \alpha)b$$

$$= \left(\alpha - \frac{1}{2}\right) a + (1 - \alpha)b'$$

Because both $a$ and $b'$ are in the convex set $C_{10,2}$, the convex linear combination $v$ is also in $C_{10,2}$, proving correctness of the NJ algorithm for five taxa.

We can also compute the $\ell_2$ distance of $v$ from the faces of the cone $C_{10,2}$. There are 9 hyperplanes defining $C_{10,2}$, but we may ignore one of them, which defines the common facet
with $C_{43,2}$. For any hyperplane $H$ such that $a$ and $b'$ lie on the same side of $H$, the distance $d(v, H)$ between $H$ and $v$ is given by

$$d(v, H) = \left(\alpha - \frac{1}{2}\right) d(a, H) + (1 - \alpha) d(b', H),$$

and taking the minimum of this over the eight remaining faces of $C_{10,2}$ we obtain

$$d(v, (C_{10,2} \cap C_{43,2})^c) = \frac{1 - \alpha}{\sqrt{3}},$$

where $(C_{10,2} \cap C_{43,2})^c$ is the complement of $C_{10,2} \cap C_{43,2}$. If we divide this by the length $\beta = 1 - \alpha$ of the smaller of the two interior edges, we get an $\ell_2$-radius of $1/\sqrt{3} \approx 0.577$. Note that because our method relies on orthogonal projections, we get $\ell_2$ bounds instead of $\ell_\infty$ bounds.

## 4 Simulation results

In this section we will analyze how the tree metric for a tree and pairwise distances estimated via the maximum likelihood estimation locate in the partition of the sample space. Particularly, we analyze subtrees of the two parameter family of trees described by [Ota and Li, 2000]. These are trees for which the NJ algorithm has difficulty in resolving the correct topology. In order to understand how they locate to each other, we simulated 10,000 data sets on each of the two tree shapes, $T_1$ and $T_2$ (Figure 4) at the edge length ratio, $a/b = 0.03/0.42$ for sequences of length 500BP under the Jukes-Cantor model [Jukes and Cantor, 1969]. We also repeated the runs with the Kimura 2-parameter model [Kimura, 1980]. They are the cases (on eight taxa) in [Ota and Li, 2000] that the NJ algorithm had most difficulties in their simulation study (also the same as in [Levy et al., 2006]). Each set of 5 sequences are generated via *evolver* from PAML package [Yang, 1997] under the given model. *evolver* generates a set of sequences given the model and tree topology using the birth-and-death process. For each set of 5 sequences, we compute first pairwise distances via the heuristic MLE method using a software *fastDNAml* [Olsen et al., 1994]. To compute cones, we used MAPLE and polymake.

![Figure 4: $T_1$ and $T_2$ tree models which are subtrees of the tree models in [Ota and Li, 2000].](image-url)
To study how far each set of pairwise distances estimated via the maximum likelihood estimation (which is a vector \( y \) in \( \mathbb{R}^5 \)) locates from the cone, where the additive tree metric lies, in the sample space, we calculated the \( \ell_2 \)-distance between the cone and a vector \( y \).

Suppose we have a cone \( C \) defined by hyperplanes \( n_1, \ldots, n_r \), i.e.

\[
C = \{ x \mid (n_i, x) \geq 0 \text{ for } i = 1, \ldots, r \},
\]

and we want to find a closest point in \( C \) from some given point \( v \). Because \( C \) is convex, for \( \ell_2 \)-norm there is only one such point, which we call \( u \). If \( v \in C \) then \( u = v \) and we are done. If not, there is at least one \( n_i \) with \( (n_i, v) < 0 \), and \( u \) must satisfy \( (n_i, u) = 0 \).

Now the problem reduces to a lower dimensional problem of the same kind: We project \( v \) orthogonally into the hyperplane \( H \) defined by \( (n_i, x) = 0 \) and call the new vector \( \tilde{v} \). Also, \( C \cap H \) is a facet of \( C \), and in particular a cone, so proceed by finding the closest point in this cone from \( \tilde{v} \).

We say an input vector (distance matrix) is \textit{correctly classified} if the vector locates in one of the cones where the vector representation of the tree metric (noiseless input) lies. We say an input vector is \textit{incorrectly classified} if the vector locates in the complement of the cones where the vector representation of the tree metric lies. For input vectors (distance matrices) which are correctly classified by the NJ algorithm, we compute the minimum distance to any cone giving a different tree topology. This distance gives a measure of robustness or confidence in the result, with bigger distances meaning greater reliability. The results are plotted in the left half of Figure 5 and in Figure 6. Note that the distance of the noiseless input, i.e. the tree metric from the tree we used for generating the data samples, gives an indication of what order of magnitude to expect with these values.

![Distances of correctly classified vectors from closest misclassified vector](image1)

![Distances of misclassified input vectors from closest correctly classified vector](image2)

**Figure 5**: Distances of correctly (left) and incorrectly (right) classified input vectors from the closest incorrectly/correctly classified vector.

| # of cases | T1 JC | T2 JC | T1 Kimura | T2 Kimura |
|------------|-------|-------|-----------|-----------|
| Mean       | 3.581 | 6.441 | 3.795     | 4.467     |
| Variance   | 0.0221| 0.0421| 0.0415    | 0.0629    |

**Figure 6**: Mean and variance of the distances of correctly classified vectors from the nearest misclassified vector.
For input vectors to which the NJ algorithm answers with a tree topology different from the correct tree topology, we compute the distances to the two cones for which the correct answer is given and take the minimum of the two. The bigger this distance is, the further we are off. The results are shown in the right half of Figure 5 and in Figure 7.

|         | JC     | Kimura2 |
|---------|--------|---------|
|         | T1     | T2      | T1     | T2      |
| # of cases | 6,419  | 3,559   | 6,205  | 5,533   |
| Mean    | 0.0594 | 0.0331  | 0.0951 | 0.0761  |
| Variance| 0.0203 | 7.39 \cdot 10^{-4} | 0.0411 | 3.481 \cdot 10^{-3} |

Figure 7: Mean and variance of the distances of misclassified vectors to the nearest correctly classified vector.

From our results in Figure 6 and Figure 7, one notices that the NJ algorithm returns the correct tree more often with T2 than with T1. These results are consistent with the results in [Gascuel and Steel, 2006; Mihaescu et al., 2006]. Note that any possible quartet in T1 has a smaller (or equal) length of its internal edge than in T2 (see Figure 4). Gascuel and Steel [2006] defined this measure as neighborliness. Mihaescu et al. [2006] showed that the NJ algorithm returns the correct tree if it works correctly locally for the quartets in the tree. The neighborliness of a quartet is one of the most important factors to reconstruct the quartet correctly, i.e., the shorter it is the more difficult the NJ algorithm returns the correct quartet. Also Figure 5 shows that most of the input vectors lie around the border lines of cones, including the noiseless input vector (the tree metric). This shows that the tree models T1 and T2 are difficult for the NJ algorithms to reconstruct the correct trees. All source codes for these simulations described in this paper will be available at authors’ websites.
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