Split Network Polytopes and Network Spaces

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Abstract. *Phylogenetics* begins with reconstructing biological family trees from genetic data. Nature, however, is not limited to *tree*-like histories. We have discovered new polytopes, metric spaces, and simplicial complexes which organize *phylogenetic networks*. Facet inequalities for our new family of network polytopes turn out to specialize to the solution of an older question: in the case of trees they correspond to facets of the Balanced Minimum Evolution polytopes (BME). We turned the results on the BME facets into a branch and cut algorithm, which shows initial success. Moreover, the space of phylogenetic trees dually embeds into the BME polytopes. Extending this result, we find a complex of faces within the subtour-elimination facets of the Symmetric Traveling Salesman polytope which is dual to a quotient complex in network space.

Keywords: polytopes, phylogenetics, trees, metric spaces

1 Introduction

A classical problem in computational biology is the inference of a phylogenetic tree from the aligned DNA sequences of n species. The most established tool used to build a phylogenetic tree from this data involves computing the maximum likelihood estimate for each of the $(2n - 5)!!$ possible trees with n leaves, where each leaf corresponds to a given species. Such a procedure is quite computationally expensive when there are more than a few species to consider. To circumvent this problem, we turn to distance-based methods: One can construct a distance between two species (perhaps via a model of mutation rates, using the probabilistic calculation pairwise on taxa.) Such information can be encoded by an $n \times n$ real symmetric, nonnegative matrix called a *dissimilarity matrix*, often given as a $\binom{n}{2}$-dimensional *distance vector* $\mathbf{d}$ with entries d_{ij} in lexicographic order. The classical phylogenetic problem is then to reconstruct a tree (possibly with weighted edges) that represents this matrix. We say that $\mathbf{d}_t$ is *additive* when the entries correspond perfectly to the summed edge values of a weighted tree t.

Oftentimes, however, dissimilarity matrices are not tree metrics, as data from sequence alignments often fails due to horizontal gene transfer, recombination, or gene duplication [13]. Indeed, assuming a tree model and applying phylogenetic inference tools on the data can be misleading [2]. In such cases, the underlying evolutionary relationships are better represented by a *split network*, a generalization of a tree in which

multiple parallel edges signify divergence; see Figure 1. From a biological context, network representations are important visualization tools at the beginning of data analysis, allowing researchers to see several hypothesized trees simultaneously, while looking for evidence of hybridization or reticulation.
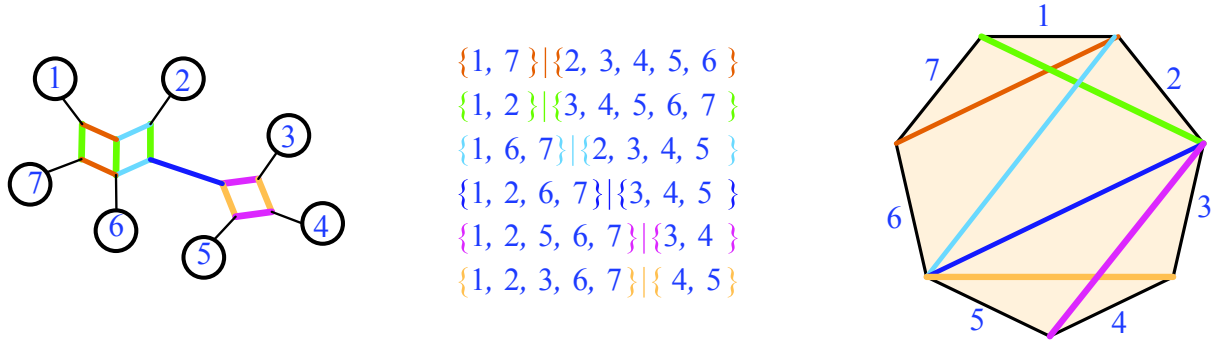

Figure 1: A split system, in the center, with its circular split network, and its polygonal representation. This network is externally refined, so no bridges can be added.

In practice, the construction of a split network from an arbitrary dissimilarity matrix tends to yield an overcomplicated system. Instead, a common heuristic is to chose a circular ordering compatible with most of the splits in order to produce a *circular split network*, adding the remaining splits at a later time [14]. Bryant and Moulton introduced the *neighbor-net* algorithm in 2004, equipped to construct such a circular split network from dissimilarity matrices satisfying the Kalamanson condition [2]. Neighbor-net is a greedy algorithm, but the circular split networks output by the algorithm are informative for exploring conflicting signals in data.

Applications of our new polytopes begin with linear programming. We have discovered a series of polytopes whose vertices are phylogenetic networks, filtering between the BME polytope and the STSP. We are using combinations of the simplex method, branch and bound, and cutting planes on these polytopes in order to choose precisely which network best fits the data. The discovery of large families of facets in every dimension allows us to attack the BME problem simply by making a series of modifications to existing STSP solvers.

2   Trees and Networks

We begin with the set $[n]$ used to number n taxa, species, or genes. A *(nontrivial) split* is a partition of $[n]$ into two parts, both with more than one element. A *split system* is a set of splits. Split systems may be drawn as connected graphs called *split networks* in which the degree-one nodes (leaves) are given the labels $1 \ldots n$, and nodes of higher

degree have no label. The interior (un-leafed) edges are drawn in sets of parallel edges which together represent a split: by cutting such a set of edges the graph separates into the parts of the split. See Figure 1. A split network can be interpreted as an (unrooted) phylogenetic network.

A *phylogenetic tree* is a circular split network whose splits form a tree. That is, a network for which each interior edge is a (nontrivial) *bridge*: cutting it disconnects the graph into two smaller graphs, called *clades*. A *circular* or *planar* split network is one whose graph may be drawn on the plane without edge crossings.

Definition. Let the *exterior degree* of a node of a circular split network in the plane be the number of incident edges which are adjacent to the the unbounded region of the plane. Recall that a cut node is one which would disconnect the graph if removed. An *externally refined* split network is one for which the exterior degree of any cut node must be 3.

An externally refined phylogenetic tree has non-leaf nodes that are all of degree three; this is usually referred to as a *binary* tree. We say a split system s' *refines* s when $s' \supset s$. In the network picture some splits of s' are collapsed (the parallel edges are assigned length zero) to achieve s. Note that an externally refined network can be a refinement of another externally refined network.

Definition. For each cycle c, the *incidence vector* $\mathbf{x}(c)$ has $\binom{n}{2}$ components. The component $x_{ij} = 1$ if i and j are adjacent in c, and $x_{ij} = 0$ if not. The $n(n-3)/2$-dimensional *Symmetric Traveling Salesman Polytope*, denoted as STSP(n), is the convex hull of these vectors. A cycle c is *consistent* with a circular split system s if a planar network of s may be drawn, such that the leaves lie on the exterior in the order given by c.

Examples of these vectors are calculated in Figure 2. STSP(4) is shown in Figure 3.

Remark. There exists a *dual polygonal representation* of a circular split network: Given a circular split system with a circular ordering c of the species, consider a regular n-gon, with the edges cyclically labeled according to c. For each split, draw a diagonal partitioning the appropriate edges; see Figure 1. Note that diagonals representing network-like edges are crossing and bridges are noncrossing. A *fully reticulated* split network is one with no bridges. When restricted to a given circular ordering these diagrams are known as the poset of *multitriangulations*, and it is an open conjecture that this poset is a polytope.

In order to analyze tree-like data, it is necessary not just to understand individual tree structures, but the relationships between them. Billera, Holmes, and Vogtmann laid the foundation for this process by constructing a geometric space BHV_n of such metric trees with n leaves. This space is contractible (in fact, a cone), formed by gluing $(2n-5)!!$ orthants $\mathbb{R}^{n-3}_{\geq 0}$, one for each type of labeled binary tree. As the weights go to zero, we get degenerate trees on the boundaries of the orthants, where two boundary faces are identified when they contain the same degenerate trees. The space BHV_n is not a manifold but a cone over a relatively singular simplicial complex.

Devadoss and Petti recently constructed a *geometric space* CSN_n of metric circular split networks with n labeled leaves [5]: A circular split network with n leaves has at most $\binom{n}{2} - n = n(n-3)/2$ splits compatible with a specific ordering. From a polygonal perspective, this is the maximal number of diagonals on an n-gon. Thus, the vector of interior edge lengths $(l_1, \ldots, l_{n(n-3)/2})$ specifies a point in the orthant $[0, \infty)^{n(n-3)/2}$, defining coordinate charts for the space of such networks. That is, to each point in this orthant, we associate the unique network which is combinatorially equivalent but with differing edge lengths, specified by the coordinates of that point.

The space of networks is assembled from $(n-1)!/2$ orthants, each of which corresponds to a unique circular ordering of the n species, up to rotation and reflection. As the interior edge lengths go to zero, we get degenerate networks representing the common boundary faces of these orthants. CSN(4) and BHV(4) are shown in Figure 3. The link of the origin $\mathfrak{S}_n$ of CSN_n is the union of the set of points in each orthant with internal edge lengths of networks that sum to 1.

Theorem 1. *[5] Network space $\mathfrak{S}_n$ is a connected simplicial complex of dim $(n(n-3)/2) - 1$, with one k-simplex for every labeled n-gon with $k + 1$ diagonals.*

Remark. Unlike the link of the origin of BHV_n, whose homotopy structure has been known for several decades, little is known about the topology of $\mathfrak{S}_n$. A partial key lies with the novel gluing of the chambers of $\mathfrak{S}_n$: we have recently shown that two chambers of $\mathfrak{S}_n$ can intersect along a face of *at most dimension* $\binom{n-2}{2} - 1$.

3   Polytopes

The Balanced Minimal Evolution Polytope BME(n) was first studied in 2008 [6]. We have recently found a simple description of its vertices as follows:

Definition. [8] For each given phylogenetic tree t with n leaves, the *vertex vector* $\mathbf{x}(t)$ has $\binom{n}{2}$ components $x_{ij}(t) = 2^{n-1-l(i,j)}$ where $l(i, j)$ is the number of nodes on the tree from leaf i to a different leaf j. The convex hull of all the $(2n-5)!!$ vertex vectors (for all binary trees t with n leaves), is the polytope BME(n), of dimension $\binom{n}{2} - n$.

We next define new families of polytopes by assigning vectors to each circular split network s. The vector $\mathbf{x}(s)$ is defined to be the sum of the vectors $\mathbf{x}(c)$ for all cycles c consistent with s. Thus the component $x_{ij}(s)$ is the number of circular orderings consistent with that system for which i and j are adjacent.[1] Note that these vectors agree with our previous $\mathbf{x}(t)$ when the split system is a tree t. Examples of these vectors are calculated in Figure 2.

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[1]Levy and Pachter [16], generalizing the work of Semple and Steel [18], define a coefficient η which takes values the components of our vector $\mathbf{x}(s)$.

Definition. The convex hull of all the vectors $\mathbf{x}(s)$ for s an externally refined circular network with n leaves and k bridges is the polytope BME(n,k).
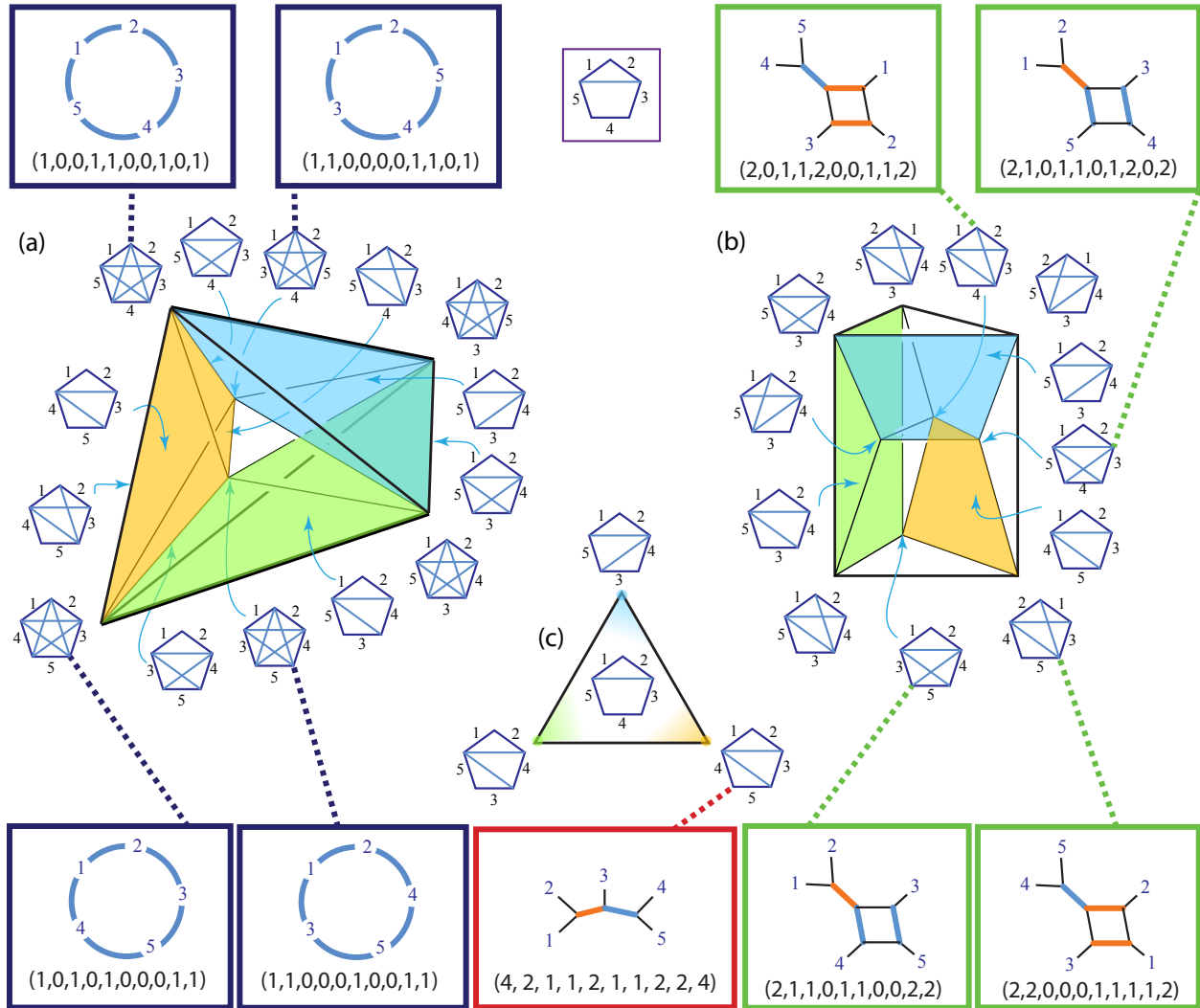

Figure 2: A facet (a) in STSP(5) , a facet (b) in BME(5,1), and a face (c) in BME(5).

Theorem 2. *The vertices of BME(n,k) are the vectors $\mathbf{x}(s)$ corresponding to the externally refined circular networks s with n leaves and k bridges. The dimension of BME(n,k) is $\binom{n}{2} - n$.*

Proof. To show that the vectors thus calculated are extreme in their convex hull, we use the fact that each is the sum of the vertices of the STSP which correspond to the cycles consistent with that network. Let $\mathbf{d}(s)$ be the distance vector whose i,j component is the path length between those leaves on s. Then the linear functional corresponding to the distance vector is: 1) simultaneously minimized at each of the vertices of the STSP, and

2) uniquely minimized at the vertex $\mathbf{x}(s)$. For the dimension we use the following: for each leaf $j = 1, \ldots, n$ these vertices $\mathbf{x}(s)$ satisfy $\sum_{i=1, i \neq j}^{n} x_{ij} = 2^{k+1}$, where k is the number of *bridges* (non-crossing diagonals) in the diagram.   □

Corollary 3. *Restricting BME(n,k) to the phylogenetic trees, where $k = n - 3$, recovers the polytopes BME(n). Restricting BME(n,k) to the fully reticulated networks, where $k = 0$, turns out to recover STSP(n).*

Theorem 4. *Every circular split network s with k bridges corresponds to a face of each BME(n, j) polytope for $j \leq k$. That face has vertices all the j-bridge networks s' which externally refine s.*

Proof. Again let $\mathbf{d}(s)$ be the distance vector whose i, j component is the path length between those leaves on s. Then the linear functional corresponding to that distance vector is simultaneously minimized at each of the j-bridge networks s' which externally refine s. This time the reason is that $\mathbf{d}(s)$ is equivalent to a distance vector $\mathbf{d}(s')$ in which some splits are given the zero length instead of length 1.   □

We have found that all of the known facets of BME(n) have analogues in BME(n, k) for small n. For large n we also see the following:

Theorem 5. *Any nontrivial split of $[n]$ corresponds to a facet of BME(n,k), for all $k \leq n - 4$.*

Proof. We use the fact that any sum of exactly m vectors from a facet of a polytope will lie in an affine space of the same dimension as that facet. Thus any subset of those sums of m vectors each will have a convex hull of smaller or equal dimension than the original facet. We have that a split corresponds to a facet of STSP(n)=BME$(n, 0)$ and also to a facet of BME$(n, n - 3)$= BME(n) (except in the case of cherries; where we need BME$(n, n - 4)$). The vertices of the split-face in BME(n, k) are all vectors formed by summing sets of 2^k vertex vectors of STSP(n) from the facet corresponding to that split. Since the dimension cannot increase at any step, it must remain constant at $\binom{n}{2} - n - 1$.   □

Example. Figure 2(a) shows a subtour elimination facet of STSP(5) = BME(5,0), corresponding to the split $s = \{\{1, 2\}, \{3, 4, 5\}\}$. Split networks label subfaces of this facet. Figure 2(b) shows the corresponding split facet of BME(5,1), in which the vertices are nine networks with a single bridge that each refine s. Figure 2(c) shows the face of BME(5) corresponding to the same split. Summing either of the horizontal or vertical pairs of vectors shown in (a) gives the four vectors shown in (b). Summing all four vectors in (a) gives the vector shown in (c).

Remark. For a general network s with bridge number k, embedded in each polytope BME(n, j) for $k > j > 0$ is a collection of networks which resolve to our given network s. Each of these new networks correspond to a distinct face in STSP(n). Those faces link up to make an interesting complex, as shown by the shaded subfaces in Figure 2. The topology of these complexes in general is an open question.

4   Facets of BME(*n*)

Until our recent work, only certain of the low-dimensional faces of BME(*n*) were known–
the *clade faces* as described in [12]. Now, we have discovered exponentially large collec-
tions of (maximum dimensional) facets for all *n* [8]. In the following list we introduce
our new facets, and present evidence supporting a conjecture: faces of the BME(n) arise
as vertex collections corresponding to binary trees which display any maximal compat-
ible subset of the splits of a given circular network. These collections of trees have a
biological application. The binary trees which display any maximal compatible subset
of the splits of a given network are known as the fully resolved trees allowed by the
network. The number of these for a given network on *n* leaves, divided by the number
of binary phylogenetic trees possible with *n* leaves, gives us the cladistic information
content (CIC) of the tree as defined in [11].

1. Any split of $[n]$ with both parts larger than 3 corresponds to a facet of BME(n), with
   vertices all the trees displaying that split. These vertices constitute the cladistic
   information content collection (CICC) of that split. The number of these facets
   grows like 2^n.

2. A *cherry* is a clade with two leaves. For each intersecting pair of cherries $\{a, b\}, \{b, c\}$,
   there is a facet of BME(n) whose vertices correspond to trees having either cherry.
   The facet inequality is $x_{ab} + x_{bc} - x_{ac} \leq 2^{n-3}$. These vertices constitute the CICC
   corresponding to a certain network in CSN$_n$.

3. For each pair of leaves $\{i, j\}$, the caterpillar trees with that pair fixed at opposite
   ends constitute the vertices of a facet. These bound BME(n) from below: $x_{ij} \geq 1$.

5   Duality

We have discovered that the facet structure of BME(n) has a direct relationship to the
quotient structure of BHV$_n$. Let $\mathcal{L}(\text{BME}(n))$ be the poset of faces of the BME polytopes.
Let $\mathcal{L}(\text{BHV}_n)$ be the poset of cells of BHV$_n$. Both these posets are ordered by inclusion.
We have the following:

Theorem 6. *There exists a poset injection: $f : \mathcal{L}(BHV_n) \to \mathcal{L}(BME(n)^\Delta)$. In particular the
$(2n - 5)!!$ top-dimensional cells of BHV$_n$ map to the $(2n - 5)!!$ vertices of BME(n).*

Specifically, any (non-binary) phylogenetic tree *t* corresponds to a face $f(t)$ of BME(n)
which contains the vertices corresponding to binary trees that refine *t*. For an example
see the triangular face in Example 1(b). Further, these faces are ordered by inclusion
exactly opposite the inclusion in BHV$_n$. For each (non-binary) *t*, there is a distance vector

$\mathbf{d}(t)$ for which the product $\mathbf{d}(t) \cdot \mathbf{x}(t')$ is minimized simultaneously by the set of *binary* phylogenetic trees t' which refine t. In particular, for any tree t', we have

$$\sum_{i<j} d_{ij}(t) \, x_{ij}(t') \ \geq \ 2^{(n-2)}|E(t)| \,,$$

where $E(t)$ is the set of edges of t. This inequality is precisely an equality if and only if the tree t' is a refinement of t. Thus the distance vector is the normal to the face. The map thus described is an injective poset map from BHV_n to faces in $\mathrm{BME}(n)$, ordered by reverse inclusion (the polar ordering); see Figure 3.
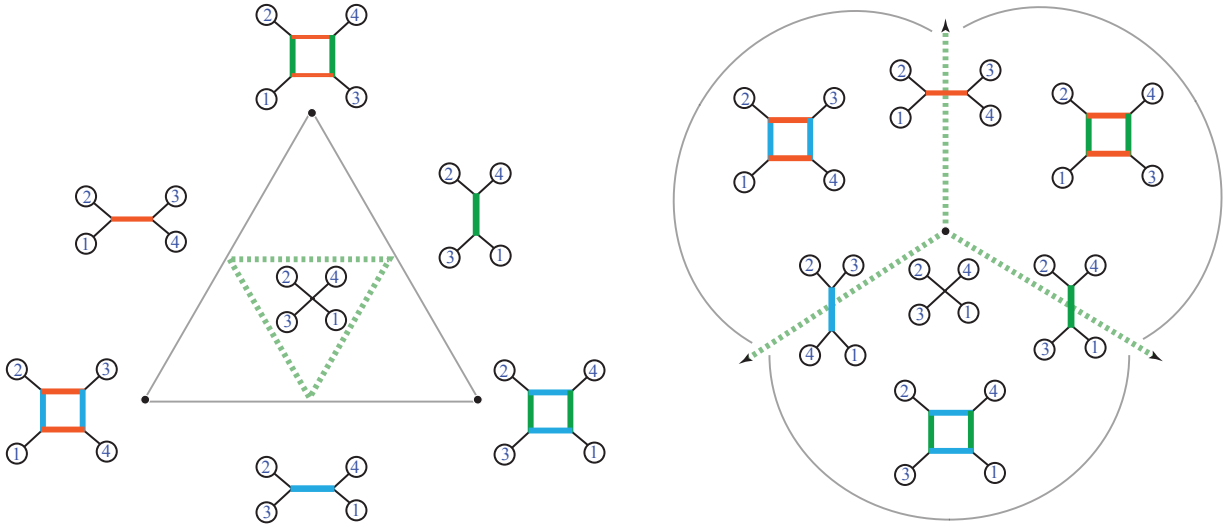

Figure 3: STSP(4) = BME(4,0) on the left is dual to CSN(4) on the right. BME(4) = BME(4,1) is dual to BHV(4); these are the restrictions to trees.

This discovery allows us to define a projection from Kapranov's *permutoassociahedron* $\mathcal{K}P_n$ to a complex of the $\mathrm{BME}(n)$ polytope, taking faces to faces and preserving the partial order of faces. This polytope $\mathcal{K}P_n$ can be viewed as a polyhedral and combinatorial analog of both tree spaces BHV_n and the real moduli space of curves $\overline{\mathcal{M}}_{0,n}(\mathbb{R})$ The polytope $\mathcal{K}P_n$ blends two classical polyotopes: the *associahedron* (measuring tree structures) and the permutohedron (measuring permutations of leaves). The details of the map from $\mathcal{K}P_n$ to $\mathrm{BME}(n)$ are given in [9].

We have extended this discovery of duality to the space of networks CSN_n. In the following, the projection f defined on networks is the same map f as just described when restricted to trees.

Theorem 7. *The polytope STSP(n) has a complex of subfaces which is the dual image of a*

projection f from CSN$_n$. The $(n-1)!/2$ orthants of CSN$_n$ map to the vertices of STSP(n). The networks with a single split map to the the sub-tour elimination facets of STSP(n).

Equivalently, we could say f projects network space onto a complex in the *fan* of the STSP. This theorem is illustrated in Figures 2 and 3. A network s maps to the face $f(s)$ of STSP(n) whose vertices are cycles consistent with s. We conjecture that f is a Galois connection of posets.

6   Algorithms and Operads

The *balanced minimum evolution* method reconstructs phylogenetic trees by minimizing the total tree length. This method is *statistically consistent* in that as the dissimilarity matrix approaches the zero-noise accuracy of an additive metric, the BME output approaches that tree's true topology.

   The BME tree for an arbitrary positive vector **d** is the binary tree t that minimizes $\mathbf{d} \cdot \mathbf{x}(t)$ for all binary trees with n leaves,[2] this *objective value* dot product being the least variance estimate of tree-length [4]. With our discovery of large collections of facet inequalities comes the opportunity to solve the BME problem directly as a linear program over a polytope.

   If we take all the split-faces of the BME polytope, including the cherries and caterpillar facets, the resulting intersection of half-spaces becomes a bounded polytope (appearing inside the $\binom{n}{2}$-cube). We can then add the intersecting-cherry facets and other split-network facets and note that this new polytope envelopes the BME polytope by restricting to a known subset of the latter polytope's facets. The advantage of considering this *relaxed BME polytope* is that it shares many of the same vertices, often allowing linear programming over the relaxation to work just as well as linear programming over BME(n). Our algorithm, POLYSPLIT, is outlined below:

 (i) The input is the number n and a distance vector **d**. The matrix of inequalities $A(n)$ is constructed for the relaxed BME polytope. We initially run the simplex method over $A(n)$.

 (ii) A valid result must have coordinates all powers of 2. If the current result is not valid, we recursively perform *Branch and Bound* on the powers of 2, choosing the coordinate to branch on based on the current entry's greatest distance from the nearest powers of 2.

 (iii) When coordinates of a potential solution approach the value 2^{n-3} of a cherry, we may fix that value. This effectively pushes the problem into a face of the polytope.

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[2] If the dissimilarity matrix comes from a tree matrix, this dot product is simply a scaled sum of all the edge lengths, a sum which is known as the *tree length*.

(iv) For $n > 11$, we need to dynamically use the $\sim 2^n$ split facets. That is, we begin by further relaxing BME(n) to just the intersecting cherry and caterpillar facets. If the initial solution fails to satisfy a split inequality, we add that split facet as a *cutting plane* and repeat.

We have shown that for an n-leaved binary phylogenetic tree, if the number of cherries is at least $n/4$, the tree represents a vertex in the BME polytope that is also a vertex of our relaxation [9]. For $n \leq 11$, the tree represents a vertex of the relaxation regardless of the number of cherries. For BME(5), for instance, there are 15 vertices and 52 facets. The relaxed version in 5D has all the same facets minus 12 of them, so 40, and it turns out to possess exactly the same vertices plus 12 new ones! Therefore, if the BME objective value is optimized at a valid tree vertex of the relaxation, it is also optimized in the BME polytope. More importantly, the binary phylogenetic trees for any n all lie on the boundary of several facets of the relaxation, which are also facets of the BME polytope.

Our approach takes advantage of a self-similar *operadic* structure of BME(n). Phylogenetic trees form an operad, as shown in [1], using the basic operation of grafting. The clade-faces of the BME polytope are themselves smaller-dimensional BME polytopes, and the inclusion of a clade-face in BME(n) corresponds to all the ways of grafting those clades to the leaves of any binary tree. Thus the composition in the phylogenetic operad is mirrored by inclusion of faces in the polytope.

Furthermore, each of the smaller BME polytopes included as faces of a larger one can also be approximated in turn by smaller versions of our relaxation. Taking full advantage of the operadic structure would mean recursively solving the corresponding linear programs in the smaller and smaller included faces. Our current algorithm approximates this approach by recursively fixing components that represent cherries.

7   Results and Future Directions

The most frequently used method for distance-based phylogeny reconstruction is *Neighbor Joining* (NJ), developed in [17], a greedy algorithm for finding the balanced minimal evolution tree [10]. Unfortunately, NJ is shown to lose accuracy quickly as taxa (leaves) increases [7]: for eight taxa, the theoretical accuracy is between 69% and 72% for trees with more than two cherries, but drops to 62% for caterpillar trees, with the conjecture that the accuracy will continue to drop quickly, especially for caterpillar trees with more taxa. The best current published *improvement* on Neighbor Joining is the algorithm known as FASTME and FASTME2.0, shown to improve on NJ by between 3.5% and 7% for 24 taxa, and as much as 21.3% for 96 taxa. [3, 15]. Our algorithm POLYSPLIT experimentally shows 100% accuracy up to 11 taxa, even including noise.

Next we plan to use our new two-parameter family of polytopes to take phylogenetic reconstruction to the next level, attacking the grand challenge of finding the true split

network for a general dissimilarity matrix. The following facts will be the foundation of the effort. We say that $\mathbf{d}_s$ obeys *Kalmanson* conditions when the entries correspond perfectly to the summed edge values of a circular weighted network *s*.

Theorem 8. *For any Kalmanson distance vector $\mathbf{d}_s$ its dot product is minimized simultaneously at the vertices of the STSP(n) = BME(n,0) which correspond to the cycles with which s is consistent.*

Corollary 9. *If s has $j \geq k$ bridges then $\mathbf{d}_s$ will be simultaneously minimized at the vertices of BME(n,k) which correspond to the split networks that refine s. Summing those vertices (as vectors) yields the coordinate vector of the vertex of BME(n,j) which uniquely characterizes the split network s.*

Remark. If a distance vector is uniquely minimized at bridge number *k*, there will also be a unique minimum answer at bridge number $k + 1$, but the latter will be an approximation to the true network.

Thus the new polytopes will allow fine-tuning of the phylogenetic network search, so that the result shows exactly the right amount of hybridization, lateral gene transfer, and uncertainty of descent. For noisy data, one can produce phylogenetic networks at multiple levels: from the tree to increasingly complicated split systems all the way up to the cyclic ordering which represents the maximum complexity of zero bridges. Precise answers give confidence in the result, while for noisy data an optional range of answers allows the biologist to select based on phenotypes or other factors.

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