



An information theory perspective on the balanced minimum evolution problem

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ABSTRACT

We show that the *Balanced Minimum Evolution Problem* (BMEP) is a cross-entropy minimization problem. This new perspective both extends the previous interpretations of the BMEP length function described in the literature and enables the identification of an efficiently computable family of lower bounds on the value of the optimal solution to the problem.

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1. Introduction

Consider a set $\Gamma = \{1, 2, \dots, n\}$ of $n \geq 3$ distinctly aligned molecular sequences (such as DNA, RNA, or codon sequences), hereafter referred to as *taxa*, and a $n \times n$ symmetric distance matrix \mathbf{D} whose generic entry d_{ij} – equal to zero on the main diagonal and strictly positive otherwise – represents a measure of the dissimilarity between the pair of taxa $i, j \in \Gamma$ (see Fig. 1). Then, the *Balanced Minimum Evolution Problem* (BMEP) consists in finding a *phylogeny* T of Γ , i.e., a pair constituted by (i) an unrooted binary tree having n leaves and (ii) a bijection between these leaves and the taxa in Γ , so as to minimize the following *length function*

$$L(T) = \sum_{i \in \Gamma} \sum_{j \in \Gamma \setminus \{i\}} \frac{d_{ij}}{2^{\tau_{ij}}}, \tag{1}$$

where τ_{ij} represents the *path-length* between taxa i and j , i.e., the number of edges belonging to the (unique) path in T connecting taxon i to taxon j [4,19] (see Fig. 2).

The BMEP is in general \mathcal{NP} -hard and inapproximable within c^n , for some positive constant $c > 1$, unless $\mathcal{P} = \mathcal{NP}$ [10]. The problem is instead polynomially solvable if the input distance matrix \mathbf{D} is *additive*, i.e., if its entries satisfy the following

Taxa	Sequence		
Taxon 1	A	A	A
Taxon 2	A	C	C
Taxon 3	C	G	C
Taxon 4	C	C	G
Taxon 5	G	A	G

$$= \mathbf{D}$$

Fig. 1. An example of a hypothetical set $\Gamma = \{1, 2, 3, 4, 5\}$ of five molecular sequences (or *taxa*) and the associated input distance matrix \mathbf{D} .

condition [13]:

$$d_{ij} + d_{kr} \leq \max\{d_{ik} + d_{jr}, d_{ir} + d_{jk}\} \quad \forall i, j, k, r \in \Gamma. \tag{2}$$

If the input distance matrix \mathbf{D} is just *metric*, i.e., if its entries satisfy the triangle inequality, then the optimal solution to the BMEP can be approximated within a factor of two [10].

The BMEP was introduced in the literature on molecular phylogenetics by Desper and Gascuel [7], based on an estimation model proposed by Pauplin [21] 20 years ago. Subsequently, the problem was the subject of extensive research efforts focused on the characterization of its statistical consistency [8,13,14], the study of its combinatorics [4–6,11,12,15,23], and the development of implicit enumeration algorithms [1,4,19] and heuristics [10,13,19] to tackle and solve its instances.

This article further adds to the above literature on the BMEP, by showing that, after an appropriate scaling of the input distance matrix \mathbf{D} , the BMEP is a *cross-entropy minimization problem* [2,16]. This new perspective extends the combinatorial interpretations of the BMEP length function proposed by Desper and Gascuel [8]

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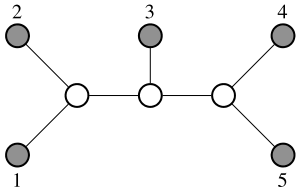


Fig. 2. An example of a phylogeny T for the set $\Gamma = \{1, 2, 3, 4, 5\}$ of Fig. 1. Each internal vertex of T has degree three (i.e., T is unrooted and binary) and each taxon in Γ is assigned precisely to a leaf of T . The topological distance between the pair of taxa 1 and 3, denoted as τ_{13} , is equal to four. Similarly, the topological distance between the pair of taxa 2 and 3, denoted as τ_{23} , is equal to three. T is provably optimal for the input distance matrix D shown in Fig. 1.

and Gascuel and Steel [14], by highlighting the presence of strong ties between the BMEP and information theory. Moreover, the scaling operation allows to define a family of lower bounds on the value of the optimal solution to the BMEP that is both efficiently computable and tight when \mathbf{D} is additive. Before discussing in detail these results, we introduce in the next section some notation and definitions that will prove useful throughout the article.

2. Notation and background

We denote \mathcal{T} as the set of all of the possible $(2n - 5)!!$ phylogenies of a set Γ of n taxa [9] and, fixed a taxon $i \in \Gamma$, we define $\Gamma_i = \Gamma \setminus \{i\}$. Given a phylogeny $T \in \mathcal{T}$ and a taxon $i \in \Gamma$, we define $\sigma_{ij} = \tau_{ij} - 1$, for all $j \in \Gamma_i$, and we rewrite (1) as

$$L(T) = \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{d_{ij}}{2^{\tau_{ij}}} = \frac{1}{2} \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{d_{ij}}{2^{\sigma_{ij}}}; \tag{3}$$

we refer to the vector $\sigma_i = (\sigma_{i1}, \dots, \sigma_{i(i-1)}, \sigma_{i(i+1)}, \dots, \sigma_{in})$ as the *rooted path-length sequence of taxon $i \in \Gamma$* and we observe that its entries encode the lengths of the (unique) paths in T having origin in the (unique) internal vertex of T adjacent to i and destinations in the remaining $n - 1$ taxa in Γ_i . We refer to the set $\sigma = \{\sigma_i : i \in \Gamma\}$ as the *collection of path-length sequences associated to T* . Moreover, for each taxon $i \in \Gamma$ we denote Θ_i as the set of the path-length sequences σ_i induced by the phylogenies in \mathcal{T} . Finally, we denote Θ as the set of path-length sequence collections σ induced by the phylogenies in \mathcal{T} and we will write $\Theta^{[n]}$ whenever it will be necessary to specify that the set Θ refers to collections induced by phylogenies of n taxa. We observe that by construction there exists a bijection between the set \mathcal{T} and the set Θ . Hence, the problem of determining the phylogeny $T \in \mathcal{T}$ that minimizes (1) is equivalent to the problem of determining the corresponding collection $\sigma \in \Theta$ that minimizes the right-hand side of (3).

We recall that the sets Θ_i and Θ are characterized by specific equalities [4,5]. In particular, *Kraft's equality* states that for a fixed taxon $i \in \Gamma$, $\sigma_i \in \Theta_i$ if and only if

$$\sum_{j \in \Gamma_i} 2^{-\sigma_{ij}} = 1. \tag{4}$$

A second equality constrains each path-length sequence collection $\sigma \in \Theta$ to satisfy the following equation [5]:

$$\sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \sigma_{ij} 2^{-\sigma_{ij}} = 3n - 6. \tag{5}$$

We refer the reader interested in deepening the combinatorial meaning of these equalities to [4] and [5].

If not stated otherwise, we shall assume that any generic matrix mentioned in this article belongs to $\mathbb{R}^{n \times n}$, with $n = |\Gamma|$. We denote \mathbf{I} as the identity matrix. Moreover, given a square

matrix \mathbf{M} , we denote: $2^{-\mathbf{M}}$ as the square matrix obtained from \mathbf{M} by setting its generic entry m_{ij} to $2^{-m_{ij}}$, for all $i, j \in \Gamma$; and $\log_2(\mathbf{M})$ as the square matrix obtained from \mathbf{M} (in this case assumed positive) by setting its generic entry to $\log_2(m_{ij})$, for all $i, j \in \Gamma$. Given two matrices \mathbf{M} and $\tilde{\mathbf{M}}$, we say that they have the same *zero pattern* if

$$m_{ij} = 0 \iff \tilde{m}_{ij} = 0 \quad \forall i, j \in \Gamma. \tag{6}$$

We conclude this section by recalling some definitions from information theory that will be frequently used hereafter. Specifically, given two probability distributions $p = (p_1, \dots, p_n)$ and $q = (q_1, \dots, q_n)$, we define the *information entropy* associated to p , [22] as

$$\mathcal{H}(p) = - \sum_{j=1}^n p_j \log_2(p_j)$$

and the *cross-entropy* associated to p and q [2,16] as

$$\mathcal{H}(p, q) = - \sum_{j=1}^n p_j \log_2(q_j).$$

Finally, we recall that a common way to measure the distance between a pair of probability distributions p and q is given by the *Kullback–Leibler (KL) Divergence* [22], which is defined as

$$D_{KL}(p \parallel q) = \mathcal{H}(p, q) - \mathcal{H}(p). \tag{7}$$

3. The BMEP as a cross-entropy minimization problem

In this section we show that the BMEP is a cross-entropy minimization problem. Because this particular interpretation is enabled by an appropriated scaling of the input distance matrix \mathbf{D} , we will start by recalling first some definitions and results from matrix scaling theory. Specifically, we say that a square matrix having nonnegative entries is *doubly-stochastic* if each of its rows and columns sums to one. We also recall that if a square matrix \mathbf{M} has nonnegative entries then there exist – due to Sinkhorn's theorem [24] – two diagonal matrices, say Π_1 and Π_2 , such that $\Pi_1 \mathbf{M} \Pi_2$ is doubly-stochastic. When \mathbf{M} is also symmetric then Π_1 and Π_2 are unique, equal, characterized by positive entries, and computable in polynomial-time [3,17,18]. Then, in the light of these definitions and results, the following proposition holds:

Proposition 1. *Let \mathbf{D} be the input distance matrix of the BMEP. Then, there exists a unique scaling matrix $\Pi = \text{diag}(\pi_1, \dots, \pi_n)$, with $\pi_i > 0$ for all $i \in \Gamma$, such that the matrix $\mathbf{S} = \Pi(2^{-\mathbf{D}} - \mathbf{I})\Pi$ is doubly-stochastic and symmetric. Moreover, \mathbf{S} has the same zero pattern as $2^{-\mathbf{D}} - \mathbf{I}$.*

Proof. The matrix $2^{-\mathbf{D}} - \mathbf{I}$ is symmetric has zero-diagonal entries and strictly positive off-diagonal entries. Then, by *Brualdi's* theorems (see [3] and [17, Theorem 5.4]) there exists a unique scaling matrix Π having positive diagonal entries and such that $\mathbf{S} = \Pi(2^{-\mathbf{D}} - \mathbf{I})\Pi$ is symmetric, nonnegative and such that the sum of the entries of each row is equal to 1, i.e., such that \mathbf{S} is symmetric and doubly-stochastic. Moreover, Theorem 2 of [3] guarantees that \mathbf{S} has the same zero pattern as $2^{-\mathbf{D}} - \mathbf{I}$, so the statement follows. \square

Now, given the matrix $\mathbf{S} = \Pi(2^{-\mathbf{D}} - \mathbf{I})\Pi$, consider the matrix $\mathbf{S} + \mathbf{I}$, having as generic entry

$$s_{ij} = (\mathbf{S} + \mathbf{I})_{ij} = \begin{cases} 1 & \text{if } i = j \\ \pi_i \pi_j 2^{-d_{ij}} & \text{if } i \neq j \end{cases} \quad \forall i, j \in \Gamma. \tag{8}$$

Moreover, define $\hat{\mathbf{S}} = -\log_2(\mathbf{S} + \mathbf{I})$ as the matrix having as generic entry

$$\hat{s}_{ij} = \hat{\mathbf{S}}_{ij} = \begin{cases} 0 & \text{if } i = j \\ -\log_2(\pi_i) - \log_2(\pi_j) + d_{ij} & \text{if } i \neq j \end{cases} \quad \forall i, j \in \Gamma. \quad (9)$$

Finally, define the constant

$$K = \sum_{i \in \Gamma} \log_2(\pi_i). \quad (10)$$

Then, the following proposition holds:

Proposition 2. *The optimal solution to the BMEP does not change if one replaces the input distance matrix \mathbf{D} with its scaled version $\hat{\mathbf{S}}$, i.e.,*

$$\arg \min_{\sigma \in \Theta} \frac{1}{2} \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{d_{ij}}{2^{\sigma_{ij}}} = \arg \min_{\sigma \in \Theta} \frac{1}{2} \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{\hat{s}_{ij}}{2^{\sigma_{ij}}}.$$

Proof. For any fixed collection $\sigma \in \Theta$ we have that

$$\begin{aligned} \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{\hat{s}_{ij}}{2^{\sigma_{ij}}} &= \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{d_{ij}}{2^{\sigma_{ij}}} \\ &\quad - \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{\log_2(\pi_i)}{2^{\sigma_{ij}}} - \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{\log_2(\pi_j)}{2^{\sigma_{ij}}}, \end{aligned}$$

which in turn can be rewritten, in the light of (4) and (10), as

$$\begin{aligned} \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{\hat{s}_{ij}}{2^{\sigma_{ij}}} &= \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{d_{ij}}{2^{\sigma_{ij}}} - \sum_{i \in \Gamma} \log_2(\pi_i) - \sum_{j \in \Gamma} \log_2(\pi_j) \\ &= \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{d_{ij}}{2^{\sigma_{ij}}} - 2K. \end{aligned} \quad (11)$$

Because K is independent of the choice of the collection σ , the statement follows. \square

Eq. (11) paves the way for a precise information theory-based interpretation of the BMEP. Specifically, first note that in the light of Eq. (11) we can rewrite (1) as follows:

$$L(T) = \frac{1}{2} \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{d_{ij}}{2^{\sigma_{ij}}} = \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{\hat{s}_{ij}}{2^{\sigma_{ij}}} + K. \quad (12)$$

Now, for each $\sigma \in \Theta$, define $p_{ij}^\sigma = 2^{-\sigma_{ij}}$, for all distinct $i, j \in \Gamma$, and observe that they are strictly positive. Moreover, because $\sigma \in \Theta$, by Kraft's equality we also have that

$$\sum_{j \in \Gamma_i} 2^{-\sigma_{ij}} = \sum_{j \in \Gamma_i} p_{ij}^\sigma = 1,$$

for all $i \in \Gamma$. Hence, each vector $p_i^\sigma = \{p_{ij}^\sigma : j \in \Gamma_i\}$, $i \in \Gamma$, can be seen as a probability distribution over the underlying set Γ_i . Similarly, for all distinct $i, j \in \Gamma$, define $q_{ij} = 2^{-\hat{s}_{ij}}$, and observe that, by construction, these values are strictly positive and such that $\sum_{j \in \Gamma_i} q_{ij} = 1$. Hence, also each vector $q_i = \{q_{ij} : j \in \Gamma_i\}$, $i \in \Gamma$, can be seen as a probability distribution over the underlying set Γ_i . Then, given a scalar $\alpha \in [0, 1]$, we can rewrite (12) as follows:

$$\begin{aligned} L(T) &= \frac{1}{2} \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{d_{ij}}{2^{\sigma_{ij}}} = \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{\hat{s}_{ij}}{2^{\sigma_{ij}}} + K \\ &= \frac{1}{2} \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{\hat{s}_{ij} - \alpha \sigma_{ij}}{2^{\sigma_{ij}}} + \alpha \frac{1}{2} \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{\sigma_{ij}}{2^{\sigma_{ij}}} + K \\ &= \frac{1}{2} \sum_{i \in \Gamma} \left[- \sum_{j \in \Gamma_i} \frac{\log_2(2^{-\hat{s}_{ij}}) - \alpha \log_2(2^{-\sigma_{ij}})}{2^{\sigma_{ij}}} \right] \end{aligned}$$

$$+ \alpha \frac{1}{2} \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{\sigma_{ij}}{2^{\sigma_{ij}}} + K. \quad (13)$$

Then, in the light of Eq. (5) and by exploiting the definitions of p_{ij}^σ and q_{ij} , we can rewrite (13) as

$$L(T) = \frac{1}{2} \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} (-p_{ij}^\sigma \log_2(q_{ij}) + \alpha p_{ij}^\sigma \log_2(p_{ij}^\sigma)) + \alpha \frac{3n-6}{2} + K. \quad (14)$$

Now, observe that for each taxon $i \in \Gamma$

$$- \sum_{j \in \Gamma_i} p_{ij}^\sigma \log_2(p_{ij}^\sigma)$$

represents the entropy $\mathcal{H}(p_i^\sigma)$ associated to the probability distributions p_i^σ . Similarly,

$$- \sum_{j \in \Gamma_i} p_{ij}^\sigma \log_2(q_{ij})$$

represents the cross-entropy $\mathcal{H}(p_i^\sigma, q_i)$ associated to the probability distributions p_i^σ and q_i over the underlying set Γ_i . Then, (14) can be rewritten as

$$L(T) = \frac{1}{2} \sum_{i \in \Gamma} (\mathcal{H}(p_i^\sigma, q_i) - \alpha \mathcal{H}(p_i^\sigma)) + \alpha \frac{3n-6}{2} + K. \quad (15)$$

In particular, observe that if $\alpha = 0$ in (15), then solving the BMEP is equivalent to solving the following cross-entropy minimization problem:

$$L(T) = \frac{1}{2} \sum_{i \in \Gamma} \mathcal{H}(p_i^\sigma, q_i) + K. \quad (16)$$

Alternatively, if $\alpha = 1$ in (15), then solving the BMEP is equivalent to solving the following KL Divergence minimization problem:

$$\begin{aligned} L(T) &= \frac{1}{2} \sum_{i \in \Gamma} (\mathcal{H}(p_i^\sigma, q_i) - \mathcal{H}(p_i^\sigma)) + \frac{3n-6}{2} + K \\ &= \frac{1}{2} \sum_{i \in \Gamma} (D_{KL}(p_i^\sigma \parallel q_i)) + \frac{3n-6}{2} + K. \end{aligned} \quad (17)$$

4. On a family of lower bounds for the BMEP

In this section, we show that for any fixed scalar $\alpha \in [0, 1]$

$$LB(\alpha) = \frac{1}{2} \sum_{i \in \Gamma} \min_{\sigma_i \in \Theta_i} \sum_{j \in \Gamma_i} \frac{\hat{s}_{ij} - \alpha \sigma_{ij}}{2^{\sigma_{ij}}} + \alpha \frac{3n-6}{2} + K \quad (18)$$

provides a lower bound on the value of the optimal solution to the BMEP. Moreover, we also show that, for any fixed scalar $\alpha \in [0, 1]$, this lower bound can be efficiently computed.

We start by observing that the lower bound nature of (18) can be trivially derived by the following chain of equalities and inequalities:

$$\begin{aligned} \min_{T \in \mathcal{T}} L(T) &= \min_{\sigma \in \Theta} \frac{1}{2} \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{\hat{s}_{ij} - \alpha \sigma_{ij}}{2^{\sigma_{ij}}} + \alpha \frac{3n-6}{2} + K \\ &\geq \frac{1}{2} \sum_{i \in \Gamma} \min_{\sigma_i \in \Theta_i} \sum_{j \in \Gamma_i} \frac{\hat{s}_{ij} - \alpha \sigma_{ij}}{2^{\sigma_{ij}}} + \alpha \frac{3n-6}{2} + K = LB(\alpha). \end{aligned}$$

Deciding the complexity of computing (18) for a fixed scalar $\alpha \in [0, 1]$ is however a less trivial task. In order to address it, we introduce some notation and definitions that will prove useful throughout the remainder of the article. Specifically, given a vector $x \in \mathbb{R}_{0+}^n$, we define $sort(x)$ as the vector obtained from x by sorting its entries in non-decreasing order. For example, if $x = (8, 6, 7, 9)$, then $sort(x) = (6, 7, 8, 9)$. We also

denote $\pi(x)$ as a permutation of x . Given a n -dimensional vector $d_i \in \mathbb{R}^n$ and a scalar $\alpha \in [0, 1]$, we define d_i^α as the $(n-1)$ -dimensional vector $d_i^\alpha = (d_{i1}, \dots, d_{i(n-2)}, (d_{i(n-1)} + d_{in})/2 - \alpha) \in \mathbb{R}^{n-1}$. Given a path-length sequence $\sigma_i \in \Theta_i^{[n-1]}$, we define $\sigma^+(\sigma_i) = (\sigma_{i1}, \dots, \sigma_{i(n-1)}, \sigma_{in-1} + 1, \sigma_{in-1} + 1)$, $\Theta_i^{s[n]} = \{\text{sort}(\sigma_i) : \sigma_i \in \Theta_i^{[n]}\}$ and $\Theta_i^{+[n]} = \{\sigma^+(\sigma_i) : \sigma_i \in \Theta_i^{[n-1]}\}$. Finally, given a n -dimensional non-negative vector $d_i = (d_{i1}, \dots, d_{i(i-1)}, 0, d_{i(i+1)}, \dots, d_{i(n-2)}, d_{i(n-1)}, d_{in}) \in \mathbb{R}^n$ we consider the function $f_n^\alpha : \Theta_i^{[n]} \times \mathbb{R}^n \rightarrow \mathbb{R}$, defined as

$$f_n^\alpha(\sigma_i, d_i) = \sum_{j=1, j \neq i}^n (d_{ij} - \alpha \sigma_{ij}) / 2^{\sigma_{ij}},$$

and we define the following auxiliary problem:

$$\min_{\sigma_i \in \Theta_i^{[n]}} f_n^\alpha(\sigma_i, d_i). \tag{19}$$

Then, we observe that deciding the complexity of computing (18) for a fixed scalar $\alpha \in [0, 1]$ is equivalent to deciding the complexity of the auxiliary problem (19), for any $n = |\Gamma|$ and for a given row d_i of matrix (9), $i \in \Gamma$. Moreover, in the light of the above notation and definitions, we observe that the following proposition holds:

Proposition 3.

1. For any permutation π and path-length sequence $\sigma_i \in \Theta_i^{[n]}$, it holds that $\pi(\sigma_i) \in \Theta_i^{[n]}$ and $\text{sort}(\sigma_i) \in \Theta_i^{[n]}$.
2. For any permutation π , path-length sequence $\sigma_i \in \Theta_i^{[n]}$ and vector $d_i \in \mathbb{R}^n$, it holds that $f_n^\alpha(\sigma_i, d_i) = f_n^\alpha(\pi(\sigma_i), \pi(d_i))$.
3. For any path-length sequence $\sigma_i \in \Theta_i^{[n-1]}$, it holds that $\sigma^+(\sigma_i) \in \Theta_i^{[n]}$.
4. $\Theta_i^{[n]} \supset \Theta_i^{+[n]} \supset \Theta_i^{s[n]}$.

Proof.

1. Recall that an integer vector ξ_i belongs to $\Theta_i^{[n]}$ if and only if it satisfies the Kraft's equality (4). Because σ_i satisfies (4) then, by the commutative property of summation, any of its permutations, hence also $\text{sort}(\sigma_i)$, satisfies (4).
2. This property trivially follows by observing that $f_n^\alpha(\pi(\sigma_i), \pi(d_i))$ can be obtained by commutating the terms of the summation that defines $f_n^\alpha(\sigma_i, d_i)$.
3. This property follows again from Kraft's equality (4). Specifically, as σ_i satisfies (4) then also $\sigma^+(\sigma_i)$ satisfies (4). The first $n - 3$ terms of the two summations are identical; the last term of (4), when computed for σ_i , is equal to $2^{-\sigma_{in-1}}$, which in turn is equal to the sum of the last two terms of (4), i.e., $2^{-(\sigma_{in-1}+1)} + 2^{-(\sigma_{in-1}+1)}$, when computed for $\sigma^+(\sigma_i)$.
4. The first set inclusion $\Theta_i^{[n]} \supset \Theta_i^{+[n]}$, is implied by 3. The second set inclusion $\Theta_i^{+[n]} \supset \Theta_i^{s[n]}$ derives from Theorem 3.1 in [20]. Specifically, this theorem guarantees that, given $\sigma_i \in \Theta_i^{[n]}$, the last two entries of $\tilde{\sigma}_i = \text{sort}(\sigma_i)$ are equal, i.e., $\tilde{\sigma}_{in-1} = \tilde{\sigma}_{in}$. Hence, we can derive from $\tilde{\sigma}_i$ the integer vector $\xi_i = (\tilde{\sigma}_{i1}, \dots, \tilde{\sigma}_{in-2}, \tilde{\sigma}_{in-1} - 1) \in \Theta_i^{[n-1]}$. Indeed, ξ_i satisfies Kraft's equality (4) as $\text{sort}(\sigma_i)$ satisfies (4) and $2^{-(\tilde{\sigma}_{in-1}-1)} = 2^{-\tilde{\sigma}_{in-1}} + 2^{-\tilde{\sigma}_{in}}$. Then, the inclusion $\Theta_i^{+[n]} \supset \Theta_i^{s[n]}$ follows as $\text{sort}(\sigma_i) = \sigma^+(\xi_i)$. \square

Proposition 4. The auxiliary problem (19) can be solved in $O(n \log(n))$ time.

Proof. We prove the proposition by recursion. Specifically, for $n = 4$, the proposition holds as the set $\Theta_i^{[4]}$ reduces to $\{(1, 2, 2)\}$,

hence $\sigma_i = (1, 2, 2)$ trivially is the optimal solution to the auxiliary problem (19).

Now, fixed an integer $n > 4$, denote $\tilde{\sigma}_i = \text{sort}(\sigma_i)$, $\tilde{d}_i = \text{sort}(d_i)$, and observe that, for any given path-length sequence $\sigma_i \in \Theta_i^{[n]}$, the following relationship holds:

$$\begin{aligned} f_n^\alpha(\sigma_i, d_i) &= \sum_{j=1, j \neq i}^n \frac{d_{ij}}{2^{\sigma_{ij}}} - \alpha \sum_{j=1, j \neq i}^n \frac{\sigma_{ij}}{2^{\sigma_{ij}}} \\ &\geq \sum_{j=1, j \neq i}^n \frac{\tilde{d}_{ij}}{2^{\tilde{\sigma}_{ij}}} - \alpha \sum_{j=1, j \neq i}^n \frac{\tilde{\sigma}_{ij}}{2^{\tilde{\sigma}_{ij}}} \\ &= f_n^\alpha(\text{sort}(\sigma_i), \text{sort}(d_i)). \end{aligned} \tag{20}$$

Indeed, we have that

$$\sum_{j=1, j \neq i}^n \sigma_{ij} 2^{-\sigma_{ij}} = \sum_{j=1, j \neq i}^n \tilde{\sigma}_{ij} 2^{-\tilde{\sigma}_{ij}},$$

moreover, we also have that

$$\sum_{j=1, j \neq i}^n d_{ij} 2^{-\sigma_{ij}} \geq \sum_{j=1, j \neq i}^n \tilde{d}_{ij} 2^{-\tilde{\sigma}_{ij}}$$

as $d_{ip} < d_{iq}$ and $\sigma_{ip} \geq \sigma_{iq}$, for $1 \leq p < q \leq n$, imply $d_{ip} 2^{-\sigma_{ip}} + d_{iq} 2^{-\sigma_{iq}} > d_{ip} 2^{-\sigma_{iq}} + d_{iq} 2^{-\sigma_{ip}}$. We also note that, for any given vectors $d_i \in \mathbb{R}^n$ and $\sigma_i \in \Theta_i^{[n-1]}$, it holds that

$$\begin{aligned} f_n^\alpha(\sigma^+(\sigma_i), d_i) - f_{n-1}^\alpha(\sigma_i, d_i^\alpha) &= \frac{d_{i(n-1)} - \alpha(\sigma_{i(n-1)} + 1)}{2^{\sigma_{i(n-1)}+1}} \\ &+ \frac{d_{in} - \alpha(\sigma_{i(n-1)} + 1)}{2^{\sigma_{i(n-1)}+1}} - \frac{\left(\frac{d_{n-1} + d_n}{2} - \alpha\right) - \alpha \sigma_{i(n-1)}}{2^{\sigma_{i(n-1)}}} = 0. \end{aligned} \tag{21}$$

Next, we observe that, for a given vector d_i , the following chain of inequalities holds

$$\begin{aligned} \min_{\sigma_i \in \Theta_i^{[n]}} f_n^\alpha(\sigma_i, d_i) &= \min_{\sigma_i \in \Theta_i^{[n]}} f_n^\alpha(\sigma_i, \text{sort}(d_i)) \\ &\leq \min_{\sigma_i^+ \in \Theta_i^{+[n]}} f_n^\alpha(\sigma_i^+, \text{sort}(d_i)) \\ &\leq \min_{\tilde{\sigma}_i \in \Theta_i^{s[n]}} f_n^\alpha(\tilde{\sigma}_i, \text{sort}(d_i)) \\ &\leq \min_{\sigma_i \in \Theta_i^{[n-1]}} f_n^\alpha(\sigma_i, d_i) \end{aligned} \tag{22}$$

where the first equality is implied by Properties 1 and 2 in Proposition 3 and the next two inequalities are implied by 4 of the same proposition. Finally, the last inequality is implied by (20). In turn, inequalities (22) and (21) imply that

$$\begin{aligned} \min_{\sigma_i \in \Theta_i^{[n]}} f_n^\alpha(\sigma_i, d_i) &= \min_{\sigma_i^+ \in \Theta_i^{+[n]}} f_n^\alpha(\sigma_i^+, \text{sort}(d_i)) \\ &= \min_{\sigma_i \in \Theta_i^{[n-1]}} f_{n-1}^\alpha(\sigma_i, \text{sort}(d_i)^\alpha). \end{aligned} \tag{23}$$

Then, solving

$$\min_{\sigma_i \in \Theta_i^{[n]}} f_n^\alpha(\sigma_i, d_i)$$

reduces to solving

$$\min_{\sigma_i \in \Theta_i^{[4]}} f_4^\alpha(\sigma_i, d_i(4))$$

by recursively applying (23) and the following definition

$$\begin{aligned} d_i(k-1) &= \text{sort}(d_i(k))^\alpha \quad \text{for } k = n, \dots, 5 \\ d_i(n) &= d_i. \end{aligned} \tag{24}$$

The value of

$$\min_{\sigma_i \in \Theta_i^{[4]}} f_4^\alpha(\sigma_i, d_i(4))$$

can be determined in $O(1)$ as the set $\Theta_i^{[4]}$ consists of the single element $(1, 2, 2)$. The vector $d_i(4)$ can instead be computed in $O(n \log(n))$ time. Specifically, for $k = n$, computing $d_i(n - 1) = \text{sort}(d_i(n))^\alpha$ requires $O(n \log(n))$ time as we have to sort d_i in $O(n \log(n))$ time and determine $d_{i_{n-1}}(n - 1)$ in $O(1)$ time. For $k < n$, computing $d_i(k - 1) = \text{sort}(d_i(k))^\alpha$ requires $O(\log(n))$ time because we can sort $d_i(k)$ in $O(\log(n))$ time as only its last entry $d_{ik}(k)$ is possibly not already ordered. Thus, the statement follows. \square

In the next example we show how the recursion (24) works.

Example 1. Consider an instance of the auxiliary problem (19) associated to the eight-dimensional vector $d_i = (0, 1, 3, 3, 4, 4, 4, 4)$, $i = 1$, and the scalar $\alpha = 1$. By Proposition 4, the optimal solution to

$$\min_{\sigma_i \in \Theta_i^{[8]}} f_8^\alpha(\sigma_i, d_i)$$

can be computed by applying the recursion (24) to $d_i(8) = d_i$ until $k = 3$. This process gives rise to the following sequence of vectors:

$$\begin{aligned} \text{sort}(d_i(8)) &= (0, 1, 3, 3, 4, 4, 4, 4) &\Rightarrow d_i(7) &= (0, 1, 3, 3, 4, 4, 3) \\ \Rightarrow \text{sort}(d_i(7)) &= (0, 1, 3, 3, 3, 4, 4) &\Rightarrow d_i(6) &= (0, 1, 3, 3, 3, 3) \\ \Rightarrow \text{sort}(d_i(6)) &= (0, 1, 3, 3, 3, 3) &\Rightarrow d_i(5) &= (0, 1, 3, 3, 2) \\ \Rightarrow \text{sort}(d_i(5)) &= (0, 1, 2, 3, 3) &\Rightarrow d_i(4) &= (0, 1, 2, 2). \end{aligned}$$

As $(1, 2, 2) = \arg \min \{f_4^\alpha(\sigma_i, d_i(4)) : \sigma_i \in \Theta_i^A\}$, the base case of the recursion returns zero. Now, let π_k be the permutation used to map $\text{sort}(d_i(k))$ to $d_i(k)$. Then, we know from Eq. (23) that the corresponding optimal solution $\hat{\sigma}(k)$ is given by $\pi_k(\sigma^+(\hat{\sigma}(k - 1)))$. Thus, the recursion returns the following sequences:

$$\begin{aligned} \hat{\sigma}(4) &= (1, 2, 2) &\Rightarrow \sigma^+(\hat{\sigma}(4)) &= (1, 2, 3, 3) \\ \Rightarrow \hat{\sigma}(5) &= (1, 3, 3, 2) &\Rightarrow \sigma^+(\hat{\sigma}(5)) &= (1, 3, 3, 3, 3) \\ \Rightarrow \hat{\sigma}(6) &= (1, 3, 3, 3, 3) &\Rightarrow \sigma^+(\hat{\sigma}(6)) &= (1, 3, 3, 3, 4, 4) \\ \Rightarrow \hat{\sigma}(7) &= (1, 3, 3, 4, 4, 3) &\Rightarrow \sigma^+(\hat{\sigma}(7)) &= (1, 3, 3, 4, 4, 4, 4). \end{aligned}$$

5. On the tightness of the $LB(\alpha)$ bounds

In this section we study the tightness of the lower bounds $LB(\alpha)$. Before proceeding, we recall some definitions and results from the literature that will be frequently used hereafter. Specifically, we say that \mathbf{D} is *uniform* if all of its non-diagonal entries are equal. We also recall that if the matrix \mathbf{D} is *additive* then there exists a phylogeny $\hat{T} \in \mathcal{T}$ that fits \mathbf{D} [9], or equivalently, there exists a collection $\hat{\sigma} \in \Theta$ such that $d_{ij} = \hat{\sigma}_{ij}$, for all distinct $i, j \in \Gamma$. Finally, with a little abuse of notation, we say that $\hat{\mathbf{S}}$ is uniform or additive whenever the corresponding matrix \mathbf{D} is uniform or additive, respectively, and we write $\hat{\mathbf{S}}^U$ or $\hat{\mathbf{S}}^A$ to distinguish the two respective cases. Then, the following proposition holds:

Proposition 5. *Let \mathbf{D} be the input distance matrix of the BMEP. If \mathbf{D} is uniform, then the lower bound $LB(0)$ is tight. Alternatively, if \mathbf{D} is additive, then the lower bound $LB(1)$ is tight.*

Proof. If the input distance matrix \mathbf{D} is uniform, then $d_{ij} = d$ for all distinct $i, j \in \Gamma$. This fact implies: (i) that the non-diagonal entries of the matrix $\hat{\mathbf{S}}^U$ are equal to $\log_2(n - 1)$; (ii) that

$$K = \frac{n(d - \log_2(n - 1))}{2};$$

Table 1

A comparison of the (normalized values of the) lower bounds $LB(0)$ and $LB(1)$ for random uniform or additive matrices $\hat{\mathbf{S}}$ having increasing values of n .

n	$\hat{\mathbf{S}}^U$		$\hat{\mathbf{S}}^A$	
	$LB(0)/n$	$LB(1)/n$	$LB(0)/n$	$LB(1)/n$
10	1.5850	1.2225	1.0918	1.2000
11	1.6610	1.2632	1.1158	1.2273
12	1.7297	1.2922	1.1250	1.2500
13	1.7925	1.3117	1.1440	1.2692
14	1.8502	1.3234	1.1374	1.2857
15	1.9037	1.3287	1.1607	1.3000
25	2.2925	1.4225	1.1356	1.3800
50	2.8074	1.4817	1.1576	1.4400
100	3.3147	1.5112	1.1342	1.4700

and (iii) that

$$\min_{T \in \mathcal{T}} L(T) = \min_{2^{-\sigma} \in 2^{-\Theta}} \frac{1}{2} \sum_{i \in \Gamma} \sum_{j \in \Gamma \setminus \{i\}} \frac{d_{ij}}{2^{\sigma_{ij}}} = \frac{d}{2} \sum_{i \in \Gamma} \sum_{j \in \Gamma \setminus \{i\}} \frac{1}{2^{\sigma_{ij}}} = \frac{nd}{2}.$$

Now, observe that (18) attains the value $nd/2$ for $\alpha = 0$. Specifically, in this situation we get

$$LB(0) = \sum_{i \in \Gamma} \min_{\sigma_i \in \Theta_i} \frac{1}{2} \sum_{j \in \Gamma_i} \frac{\log_2(n - 1)}{2^{\sigma_{ij}}} + K = \frac{nd}{2},$$

thus the statement follows. Now suppose that the input distance matrix \mathbf{D} is additive and let $\hat{\sigma} = \{\hat{\sigma}_i, i \in \Gamma\} \in \Theta$ be the collection induced by the phylogeny $\hat{T} \in \mathcal{T}$ that fits \mathbf{D} . Because the additivity hypothesis is equivalent to saying that $\hat{\mathbf{S}}_{ij}^A = \hat{\sigma}_{ij}$, for all distinct $i, j \in \Gamma$, we have that

$$\begin{aligned} \min_{2^{-\sigma} \in 2^{-\Theta}} \sum_{i \in \Gamma} D_{KL}(p_i^\sigma \parallel q_i) &= \sum_{i \in \Gamma} \min_{\sigma_i \in \Theta_i} D_{KL}(p_i^\sigma \parallel q_i) \\ &= \sum_{i \in \Gamma} D_{KL}(p_i^{\hat{\sigma}} \parallel q_i) = 0. \end{aligned}$$

Then, the statement trivially follows once again by observing that

$$\begin{aligned} \min_{2^{-\sigma} \in 2^{-\Theta}} \frac{1}{2} \sum_{i \in \Gamma} \sum_{j \in \Gamma_i} \frac{d_{ij}}{2^{\sigma_{ij}}} &= \min_{2^{-\sigma} \in 2^{-\Theta}} \frac{1}{2} \sum_{i \in \Gamma} D_{KL}(p_i^\sigma \parallel q_i) + \frac{3n - 6}{2} + K \\ &= \frac{1}{2} \left(\sum_{i \in \Gamma} \min_{\sigma_i \in \Theta_i} D_{KL}(p_i^\sigma \parallel q_i) \right) + \frac{3n - 6}{2} + K \\ &= \frac{3n - 6}{2} + K = LB(1). \quad \square \end{aligned}$$

Table 1 provides a computational confirmation of the above proposition, by showing a comparison of the normalized values of the lower bounds $LB(0)$ and $LB(1)$ for random uniform or additive matrices $\hat{\mathbf{S}}$ having increasing values of n . The table shows that if $\hat{\mathbf{S}}$ is uniform then $LB(0) \geq LB(1)$. Vice versa, if $\hat{\mathbf{S}}$ is additive then $LB(0) \leq LB(1)$.

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