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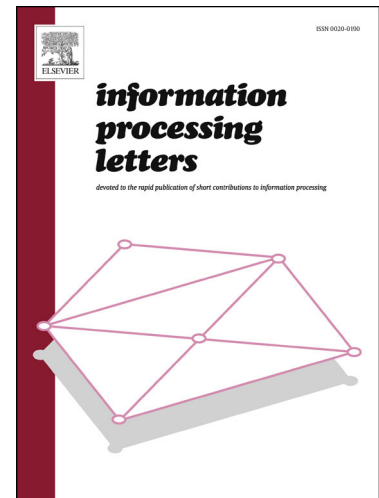
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Highlights

- Reconciliation spaces of phylogenetic trees are important in evolutionary biology.
- We introduce the median reconciliation for a subset reconciliation space.
- We show that it is a geometric median relative to edit-distance.
- We explain how the geometric median can be computed in polynomial time.
- The geometric median gives a new way to find a consensus reconciliation for a set.

Geometric medians in reconciliation spaces of phylogenetic trees

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Abstract

In evolutionary biology, it is common to study how various entities evolve together, for example, how parasites coevolve with their host, or genes with their species. Coevolution is commonly modelled by considering certain maps or *reconciliations* from one evolutionary tree P to another H, all of which induce the same map ϕ between the leaf-sets of P and H (corresponding to present-day associations). Recently, there has been much interest in studying spaces of reconciliations, which arise by defining some metric d on the set $\mathcal{R}(P, H, \phi)$ of all possible reconciliations between P and H.

In this paper, we study the following question: How do we compute a *geometric median* for a given subset Ψ of $\mathcal{R}(P, H, \phi)$ relative to d, i.e. an element $\psi_{med} \in \mathcal{R}(P, H, \phi)$ such that

$$\sum_{\psi' \in \Psi} d(\psi_{med}, \psi') \leq \sum_{\psi' \in \Psi} d(\psi, \psi')$$

holds for all $\psi \in \mathcal{R}(P, H, \phi)$? For a model where so-called host-switches or transfers are not allowed, and for a commonly used metric d called the *edit-distance*, we show that it is possible to compute a geometric median for a set Ψ in $\mathcal{R}(P, H, \phi)$ in polynomial time. We expect that this result could open up new directions for computing a consensus for a set of reconciliations.

Keywords: Reconciliation, Geometric median, Reconciliation space, Edit-distance, Consensus reconciliation

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1. Introduction

In phylogenetics, the reconciliation problem involves trying to find a map that reconciles one leaf-labelled evolutionary tree with another [12]. It has important applications in areas such as ecology and genomics, and arises in various situations. For example, biologists are interested in understanding how parasite and host species [7], genes and species [8], or species and habitats coevolve [13] (in what follows we shall use terminology for host-parasite

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relationships to keep things concrete).

More formally, a *phylogenetic tree T* is a rooted, binary tree (i.e. every vertex of T that is not the root or a leaf has indegree 1 and outdegree 2), which has root vertex ρ_T (with indegree 0 and outdegree 2). Given a *host-parasite triple* (P, H, ϕ), that is, two phylogenetic trees P and H (the parasite and the host tree, respectively), whose leaf-sets represent present-day species, and a map $\phi : L(P) \to L(H)$ between their leaf-sets (describing which parasite is currently on which host), a *reconciliation map* is a map $\psi : V(P) \to V(H)$ between their vertex sets which satisfies:

(i) The map ψ restricted to $L(P)$ equals ϕ.

(ii) If v is a vertex in the interior of P, then $\psi(v)$ is either strictly above or equal to $\psi(v')$, for any child v' of v.

We present an example of such a map in Figure 1. Note that various definitions have been proposed for reconciliation maps (see e.g. [8]). These model evolutionary processes including cospeciation (a host and parasite speciate together), duplication (a parasite speciates on a host), loss (a host speciates but not its parasite) and host-switches (e.g. a parasite switches to another host). In this paper, we are using the definition for a reconciliation map presented in [7, 14], with the added assumption that we do not allow host-switches.

In general, several algorithms have been developed to compute optimal and suboptimal reconciliations for a pair of trees relative to some predefined cost-function (cf. e.g. [8, 9]). When host-switches are not allowed (as in this paper), collections of
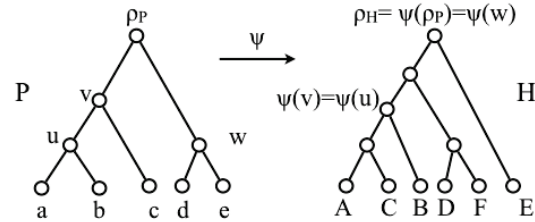

Figure 1: An example of a reconciliation map. Note that ϕ is given by $\phi(a) = A, \ldots, \phi(e) = E$.

suboptimal reconciliations can contain thousands of elements [9], and for more complex models (e.g. where host-switches are permitted), this can be the case even for collections of optimal reconciliations [7]. It is thus quite natural to consider properties of the set of all possible reconciliations endowed with some metric which also permits their comparison. These so-called *reconciliation spaces* are of growing importance in the literature [1, 3, 9, 10, 15] and permit quantitative analysis of the behavior of reconciliation maps.

In this paper, we are interested in the problem of computing geometric medians in reconciliation spaces. In general, for Y a finite set endowed with a metric D, and $Y' \subseteq Y$, an element $y^* \in Y$ is a *geometric median* for Y' in Y if

$$\sum_{y' \in Y'} D(y^*, y') = \min\{\sum_{y' \in Y'} D(y, y') : y \in Y\}.$$

Such elements are useful as they can act as an element which summarizes or forms a consensus for the set Y'. Within computational biology, geometric medians (and the closely related concept of *centroids*) have been used in phylogenetics to form a consensus tree for a set of phylogenetic trees [2], and in RNA secondary structure prediction to derive a consensus structure for a set of suboptimal

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RNA structures [6]. We therefore expect that being able to compute geometric medians in reconciliation spaces should be a useful addition to the theory of reconciliations (e.g. for computing a consensus of a collection of reconciliations).

We now summarize the contents of the rest of the paper. In the next section we present some preliminary definitions and results. This includes the definition of the edit-distance, a metric on the set $\mathcal{R}(P, H, \phi)$ of all reconciliation maps for a host-parasite triple (P, H, ϕ). Variants of this distance have been previously used to quantitatively analyse collections of reconciliations (cf. e.g. [9]). In Section 3, we present some basic observations concerning medians, which we then use in Section 4 to define the concept of a *median reconciliation* for a subset Ψ of $\mathcal{R}(P, H, \phi)$ (Theorem 2). In Section 5, we then show that a median reconciliation is in fact a geometric median for Ψ in $\mathcal{R}(P, H, \phi)$ relative to the edit-distance (Theorem 4). We also explain how to compute a geometric median in polynomial time, even though it should be noted that $\mathcal{R}(P, H, \phi)$ can be exponential in size (see e.g. [7, p.2]). We conclude in Section 6, with a brief discussion of some potential future directions.

2. Preliminaries

For a phylogenetic tree T, denote the set of interior vertices of T by $V^o(T) = V(T) - L(T)$, and the root by ρ_T. If $v \in V^o(T)$, we let $Ch(v)$ denote the set of children of v, and if $v \in V(T) - \{\rho_T\}$, we let $par(v)$ denote the parent of v in T.

We denote by $\succeq_T$ the partial order of $V(T)$ given by T. In case the context is clear, we just use $\succeq$. Also, we say for vertices $x, y \in V(T)$ with $x \succeq y$

that y is *below* x and that x is *above* y. Furthermore, we say that y is *strictly below* x if y is below x and $x \neq y$ and that x is *strictly above* y if x is above y and $x \neq y$. In that case, we also put $x \succ y$. If L is a subset of $L(T)$ of size at least two, we let $lca_T(L) = lca(L)$ denote the *least common ancestor* of the set L, that is, the lowest vertex in T which is above every element of L (with respect to the ordering $\succeq_T$). If $|L| = 1$, then we set $lca_T(L) = x$ where x is the unique element in L.

Now, let (P, H, ϕ) be a host-parasite triple. For $v \in V(P)$, we let

$$m(v) = lca_H(\{\phi(x) : x \in L(P) \text{ and } v \succeq_P x\}).$$

We also let $A(v)$ be the subset of $V(H)$ given by

$$A(v) = \{u \in V(H) : \rho_H \succeq u \succeq m(v)\}.$$

We now make some observations (cf. also [9]) – we prove only (R2) as the rest are straight-forward to check:

(R0) If $v \in V^o(P)$ and $v' \in Ch(v)$, then $m(v) \succeq m(v')$ and $A(v) \subseteq A(v')$.

(R1) If $\psi \in \mathcal{R}(P, H, \phi)$, $x \in L(P)$, $v \in V(P)$ and $v \succeq x$, then $\psi(v) \succeq \psi(x) = \phi(x)$.

(R2) If $\psi \in \mathcal{R}(P, H, \phi)$, then for all $v \in V(P)$ we have $\psi(v) \in A(v)$.

Proof. If $v \in L(P)$ then the statement clearly holds. Suppose now there exist some $v \in V^o(P)$, but $\psi(v) \notin A(v)$. Since $m(v) \in A(v)$, it suffices to consider the following two cases:

(i) $m(v) \succ \psi(v)$. Note that by (R1), $\psi(v) \succeq \phi(x)$ for every $x \in L(P)$ below v. Hence, $\psi(v) \succ lca_H(\{\phi(x) : x \in L(P) \text{ and } v \succeq_P x\}) = m(v)$, which is impossible.

(ii) $m(v)$ and $\psi(v)$ are not comparable via $\succeq_H$. Suppose $x \in L(P)$ is below v in P. By (R1), $\psi(v) \succeq \phi(x)$. But then $\phi(x)$ is not below $m(v)$ in H. This contradicts the definition of $m(v)$. ∎

(R3) By (R2), it follows that if $\psi, \psi' \in \mathcal{R}(P, H, \phi)$, then for all $v \in V(P)$, the vertices $\psi(v)$ and $\psi'(v)$ are comparable in H with respect to the ordering $\succeq_H$. In particular, it also follows that if $\{\psi_1, \ldots, \psi_l\} \subseteq \mathcal{R}(P, H, \phi)$, $l \geq 1$, then for all $v \in V(P)$, the ordering $\succeq_H$ induces a linear ordering on the set $\{\psi_1(v), \ldots, \psi_l(v)\}$.

To compute a geometric median for some subset of $\mathcal{R}(P, H, \phi)$, we need to define a metric on $\mathcal{R}(P, H, \phi)$. In this paper, we focus on the *edit-distance*, d_{edit}, since edit-distances are commonly used to compare reconciliations (see e.g. [9]).

The distance d_{edit} is defined as follows. Given $\psi \in \mathcal{R}(P, H, \phi)$ and $w \in V^o(P)$ with $\psi(w) \neq \rho_H$ and $\psi(w) \neq \psi(par(w))$ if $w \neq \rho_P$, we define a map ψ_w^{up} from $V(P)$ to $V(H)$ by setting $\psi_w^{up}(v) = par(\psi(v))$ if $v = w$ and $\psi_w^{up}(v) = \psi(v)$ if $v \in V(P) - \{w\}$. Moreover, given $\psi \in \mathcal{R}(P, H, \phi)$ and $w \in V^o(P)$ with $\psi(w) \succ m(w)$ and $\psi(w) \neq \psi(v')$ for all $v' \in Ch(w)$, we define a map ψ_w^{down} from $V(P)$ to $V(H)$ by setting $\psi_w^{down}(v)$ to be the (only) vertex in the set $A(w) \cap Ch(\psi(w))$ if $v = w$, and $\psi_w^{down}(v) = \psi(v)$ if $v \in V(P) - \{w\}$. Now, given $\psi, \psi' \in \mathcal{R}(P, H, \phi)$, we define $d_{edit}(\psi, \psi')$ to be the smallest number of up/down operations required to change ψ into ψ'. Note that this definition is closely related to the edit-distance defined in [9].

To prove our results concerning geometric medians, we will use an alternative description of the edit-distance which we now present. If $v, w \in$ $V(H)$, we let $d_H(v, w)$ be the length of the (undirected) path in H between v and w. Now, given $\psi, \psi' \in \mathcal{R}(P, H, \phi)$, we define the *path-distance* between ψ and ψ' by

$$d_{path}(\psi, \psi') = \sum_{v \in V(P)} d_H(\psi(v), \psi'(v)).$$

It is easy to check that d_{path} is a metric on $\mathcal{R}(P, H, \phi)$ (i.e. $d_{path}(\psi, \psi') = 0$ precisely when $\psi = \psi'$, it is symmetric meaning $d_{path}(\psi, \psi') = d_{path}(\psi', \psi)$, and it also satisfies the triangle inequality meaning $d_{path}(\psi, \psi'') \leq d_{path}(\psi, \psi') + d_{path}(\psi', \psi'')$, for all $\psi, \psi', \psi'' \in \mathcal{R}(P, H, \phi)$). We shall use the following result which is technically equivalent to [9, Theorem 2].

Theorem 1. *For all* $\psi, \psi' \in \mathcal{R}(P, H, \phi)$, $d_{edit}(\psi, \psi') = d_{path}(\psi, \psi')$. *In particular, since* d_{path} *is a metric on* $\mathcal{R}(P, H, \phi)$, *so is* d_{edit}.

The proof for this theorem is very similar to that of [9, Theorem 2] – we include it in the Appendix for the sake of completeness.

3. Medians

Before moving on to computing geometric medians for reconciliations, we first collect together some basic observations concerning medians.

Given a multiset A of real numbers, we let $med(A)$ denote the *median of* A. This is a real number, and is the "middle" number of the set A when the elements are arranged in order of magnitude. If the cardinality of A is even, the median is taken to be the real number that is half-way between the two middlemost numbers.

Given a real number r, we now let $[r]$ denote the nearest integer to r in case there is only one,

and to be the largest integer that is nearest to r in case there are two nearest integers to r. For example, if $r = 0.5$ then $[r] = \max\{0, 1\} = 1$, if $r = 0.2$ then $[r] = 0$, and if $r = 0.7$ then $[r] = 1$. Given a multiset A of $m \geq 1$ integers, we define $zmed(A)$ to be $[med(A)]$. For example, if $A = \{1, 1, 2, 3, 4\}$ then $zmed(A) = 2$, and if $A = \{1, 1, 2, 3, 4, 5\}$ then $zmed(A) = 3$. Note that if $A = \{n_1, n_2, \ldots, n_m\}$, then we also denote $med(A)$ and $zmed(A)$ by $med(n_1, n_2, \ldots, n_m)$ and $zmed(n_1, n_2, \ldots, n_m)$, respectively. Also, if m is odd, then $zmed(A) = med(A)$.

We now list some useful facts concerning the above definitions.

(M0) Suppose that A is a multiset of real numbers. If $f : \mathbb{R} \to \mathbb{R}_{\geq 0}$ is the function given by setting

$$f(r) = \sum_{a \in A} |a - r|$$

for $r \in \mathbb{R}$, then $f(med(A)) \leq f(r)$ for all $r \in \mathbb{R}$.

Proof. This is a well-known fact concerning medians. Essentially it holds because, when r moves away from $med(A)$, then r moves away from at least as many elements of A as it approaches. Hence, f attains its minimum over all $r \in \mathbb{R}$ at $med(A)$. ∎

(M1) Suppose that A, B are two multisets of integers both containing $m \geq 1$ elements. Suppose that there exists an ordering $a_1, a_2, \ldots, a_m$ of the elements of A and an ordering $b_1, b_2, \ldots, b_m$ of the elements of B such that $a_i \geq b_i$ for all $1 \leq i \leq m$. Then $med(A) \geq med(B)$ and $zmed(A) \geq zmed(B)$.

Proof. If $med(A) \geq med(B)$, then clearly $zmed(A) \geq zmed(B)$.

To see that $med(A) \geq med(B)$, we consider the case where m is odd; the proof for m even is simi-

lar. Let $a_{i_1}, a_{i_2}, \ldots, a_{i_m}$ be an ordering of the elements of A such that $a_{i_1} \leq a_{i_2} \leq \cdots \leq a_{i_m}$. Then, $med(A) = a_{i_{\frac{m+1}{2}}}$ and, by assumption, at most $\frac{m+1}{2} - 1$ elements in B (namely, $b_{i_{\frac{m+1}{2}+1}}, \ldots, b_{i_m}$) can be greater than $med(A)$, since if $1 \leq j \leq \frac{m+1}{2}$, then $b_{i_j} \leq a_{i_j} \leq med(A)$. Hence, $med(B) = b_{i_{\frac{m+1}{2}}} \leq a_{i_{\frac{m+1}{2}}} = med(A)$. ∎

(M2) Suppose that A is a multiset of integers, and f is the function defined in (M0). Then $f(zmed(A)) = f(med(A))$, and so $f(zmed(A)) \leq f(r)$ for all $r \in \mathbb{R}$.

Proof. If A has an odd number of elements, we are done in view of (M0) since $zmed(A) = med(A)$.

Suppose A is even with cardinality m. If $zmed(A) = med(A)$ then we are done again in view of (M0). Assume now that $zmed(A) \neq med(A)$. Then $zmed(A)$ is of the form $[r]$ where $r = med(A) := \frac{z'}{2}$ for some $z' \in \mathbb{Z}$. Therefore, there exist two nearest integers z_1, z_2 to r that are both at distance $\frac{1}{2}$ from r. Assume without loss of generality that $z_1 > z_2$, so that $z_1 = r + \frac{1}{2}$, $z_2 = r - \frac{1}{2}$. Then $z_1 = zmed(A)$. But then for the function f in (M0), we clearly have $f(r') = f(med(A))$ for all $r' \in [z_2, z_1]$. Statement (M2) now follows immediately. ∎

4. Median reconciliations

In this section, we define a special type of reconciliation $\psi_{med} = \psi_{med}^{\Psi}$ that can be associated to any subset Ψ of $\mathcal{R}(P, H, \phi)$. In the next section, we prove that this is in actual fact a geometric median in the space $\mathcal{R}(P, H, \phi)$ endowed with the edit-distance.

Suppose $\Psi = \{\psi_1, \ldots, \psi_l\} \subseteq \mathcal{R}(P, H, \phi)$, $l \geq 1$.

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If $v \in V(P)$, then for $1 \leq i \leq l$, we let

$$n_i = d_H(m(v), \psi_i(v)).$$

We now define the map $\psi_{med} = \psi_{med}^{\Psi}$ from $V(P)$ to $V(H)$ by taking, for $v \in V(P)$, $\psi_{med}(v)$ to be an element $w \in A(v) \subseteq V(H)$ such that $d_H(m(v), w) = zmed(n_1, n_2, \ldots, n_l)$, for $v \in V(P)$. Note that such a w exists as $\psi_i(v) \in A(v)$ for all $1 \leq i \leq l$ by (R2), $zmed(n_1, n_2, \ldots, n_l)$ is an integer, and $zmed(n_1, n_2, \ldots, n_l) \leq d_H(\rho_H, m(v))$. We now show that ψ_{med} is a reconciliation.

Theorem 2. $\psi_{med} \in \mathcal{R}(P, H, \phi)$.

Proof. First note that ψ_{med} restricted to $L(P)$ is clearly equal to ϕ.

Suppose now that $v \in V^o(P)$ and that $v' \in Ch(v)$. We need to show that $\psi_{med}(v) \succeq \psi_{med}(v')$.

First note that since $\psi_i(v) \in A(v)$ for all $1 \leq i \leq l$, Property (R0) implies that $\{\psi_1(v), \ldots, \psi_l(v), \psi_1(v'), \ldots, \psi_l(v')\}$ is a subset of $A(v')$. Moreover, $\psi_i(v) \succeq \psi_i(v')$ for all $1 \leq i \leq l$ as each ψ_i is a reconciliation.

Now, let $n_i = d_H(m(v), \psi_i(v))$ and $n_i' = d_H(m(v'), \psi_i(v'))$ for all $1 \leq i \leq l$. Note that, by definition, $\psi_{med}(v)$ is equal to some $w \in A(v) \subseteq A(v')$ such that $d_H(m(v), w) = zmed(n_1, \ldots, n_l)$, and $\psi_{med}(v')$ is equal to some $w' \in A(v')$ such that $d_H(m(v'), w') = zmed(n_1', \ldots, n_l')$. For each $1 \leq i \leq l$, let

$$\begin{aligned} p_i &= n_i + d_H(m(v), m(v')) \\ &= d_H(\psi_i(v), m(v)) + d_H(m(v), m(v')) \\ &= d_H(\psi_i(v), m(v')) \end{aligned}$$

where the last equality holds in view of (R0). Hence, $d_H(m(v'), w) = zmed(p_1, \ldots, p_l)$. Moreover, since $\psi_i(v) \succeq \psi_i(v') \succeq m(v')$ for all $1 \leq i \leq l$,

it follows that $p_i \geq n_i'$. By definition and (M1), it follows that $d_H(m(v'), w) = zmed(p_1, \ldots, p_l) \geq zmed(n_1', \ldots, n_l') = d_H(m(v'), w')$. Hence, $\psi_{med}(v) \succeq \psi_{med}(v')$, as required. ∎

Remark: Using similar arguments, we can also define a "minimum reconciliation" for the set Ψ as follows. Let $\psi_{min} = \psi_{min}^{\Psi} : V(P) \to V(H)$ be given by taking $\psi_{min}(v)$ to be a lowest element in $\{\psi_1(v), \ldots, \psi_l(v)\}$ for $v \in V(P)$. Note that ψ_{min} is well-defined by (R3). Moreover, $\psi_{min} \in \mathcal{R}(P, H, \phi)$: Indeed, ψ_{min} restricted to $L(P)$ is clearly equal to ϕ. Moreover, if $v \in V^o(P)$, $v' \in Ch(v)$, then for $i, j \in \{1, \ldots, l\}$ such that $\psi_{min}(v) = \psi_i(v)$ and $\psi_{min}(v') = \psi_j(v')$, we have

$$\psi_{min}(v') = \psi_j(v') \preceq \psi_i(v') \preceq \psi_i(v) = \psi_{min}(v).$$

A similar approach can be used to define a "maximum reconciliation" for Ψ.

5. Geometric medians

In this section, we show that for a subset Ψ of $\mathcal{R}(P, H, \phi)$ endowed with the edit-distance, the reconciliation ψ_{med}^{Ψ} is a geometric median for Ψ. This will follow immediately from the following observation concerning phylogenetic trees.

Observation 3. *Suppose that T is a phylogenetic tree and that $W = \{w_1, \ldots, w_l\} \subseteq V(T)$, $l \geq 1$, is a subset of the set of vertices of some path γ in T between ρ_T and some vertex $s \in V(T)$. Let $q_i = d_T(w_i, s)$, $1 \leq i \leq l$, and let u be a vertex in γ such that $d_T(u, s) = zmed(q_1, \ldots, q_l)$. Then for all $v' \in V(T)$,*

$$\sum_{w \in W} d_T(v', w) \geq \sum_{w \in W} d_T(u, w). \tag{1}$$

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Proof. Let $v' \in V(T)$. First, suppose that v' is a vertex in a path in T between ρ_T and some leaf of T that contains γ as a subpath.

Let $A = \{q_1, \ldots, q_l\}$, $\alpha = d_T(u, s)$ and $\beta = d_T(s, v')$ if v' is above or equal to s in T and $\beta = -d_T(s, v')$ if v is below s in T. Then, for the function f in (M0), we have $f(\beta) \geq f(zmed(A))$ in view of (M2). Hence, $\sum_{i=1}^l |\beta - q_i| \geq \sum_{i=1}^l |\alpha - q_i|$, from which the theorem follows.

Suppose now that v' is not of the above form. Then there must exist some vertex t in the path γ such that $t \succ v'$. Using the same argument as above for t instead of for v', it follows that

$$
\begin{aligned}
\sum_{w \in W} d_T(v', w) &= \sum_{w \in W} (d_T(w, t) + d_T(t, v')) \\
&= \sum_{w \in W} d_T(w, t) + |W| d_T(t, v') \\
&\geq \sum_{w \in W} d_T(u, w) + |W| d_T(t, v') \\
&\geq \sum_{w \in W} d_T(u, w).
\end{aligned}
$$

∎

Theorem 4. *Suppose that* $\Psi = \{\psi_1, \ldots, \psi_l\} \subseteq \mathcal{R}(P, H, \phi)$, $l \geq 1$. *Then* ψ_{med}^{Ψ} *is a geometric median for* Ψ *in the space* $\mathcal{R}(P, H, \phi)$ *endowed with the metric* $d_{edit}(= d_{path})$.

Proof. Suppose that $\psi \in \mathcal{R}(P, H, \phi)$. Then by (R2), for $v \in V(P)$, taking $w_i = \psi_i(v)$, $u = \psi_{med}(v)$, $s = m(v)$ and $v' = \psi(v)$ in Observation 3, we obtain

$$
\begin{aligned}
\sum_{i=1}^m d_{path}(\psi_{med}, \psi_i) &= \sum_{i=1}^l \sum_{v \in V(P)} d_H(\psi_{med}(v), \psi_i(v)) \\
&\leq \sum_{i=1}^l \sum_{v \in V(P)} d_H(\psi(v), \psi_i(v)) \\
&= \sum_{i=1}^l d_{path}(\psi, \psi_i).
\end{aligned}
$$

∎

Note that as a consequence of our results, a geometric median ψ_{med} can be computed for a set $\Psi \subseteq \mathcal{R}(P, H, \phi)$ in polynomial time. More specifically, the set of vertices $m(v)$, $v \in V(P)$, can be computed in a bottom-up fashion in $O(|L(P)|)$ time (see e.g. [8, p.393] for references concerning the computation of the so-called LCA mapping). Moreover, all of the distances $d_H(u, w)$ between any pair of vertices $u, v \in V(H)$ can be computed in $O(|V(H)|^2)$ time, from which the distances $d_H(m(v), \psi(v))$, $v \in V(P)$, $\psi \in \Psi$ can be derived. Finally, for each $m(v)$, $v \in V(P)$, the median of the multiset of integers $d_H(m(v), \psi(v))$, $\psi \in \Psi$, and hence $\psi_{med}(v)$ can be computed in $O(|\Psi|)$ time using, for example, a selection algorithm [5, Chapter 9.3].

6. Discussion

In this paper, we have described how to find a geometric median for a set of reconciliations within the space of all reconciliations endowed with the path-distance (or, equivalently, the edit-distance). It would be of interest to understand properties of a geometric median. For example, reconciliations are usually assigned some cost (see e.g. [9]), and it could be interesting to understand how the cost of the geometric median of a set of reconciliations is related to the costs of each of the reconciliations in the set. Also, we have focused on the edit-distance. However, it should be possible to define alternative metrics on collections of reconciliations, and to potentially derive geometric medians relative to these metrics.

In another direction, as stated in the introduction, we considered one of the simplest models for

reconciling trees. There are more complex models which allow the inclusion of additional evolutionary processes (such as host-switches or, in the case of gene-species reconciliation, lateral gene transfer) [14], and it would be of interest to see whether geometric medians can also be derived for these models. This could be useful since such models can generate multiple optimal solutions [7]. However, it could also be quite complicated as in our proofs we heavily relied on properties of the median of a set of points in the real line, and for the more complex reconciliation models it is not clear that such arguments can be applied.

Finally, in general the geometric median can be regarded as a consensus for a set of reconciliations. It would be interesting to find other methods for defining a consensus reconciliation and to understand how these are related to the geometric median (e.g. we could try to define a centroid reconciliation for a set which, roughly speaking, would correspond to the center of mass for the set).

7. Appendix: Proof of Theorem 1

The theorem immediately follows from the last of the following sequence of observations.

(Up) If $\psi \in \mathcal{R}(P, H, \phi)$ and $w \in V^o(P)$ with $\psi(w) \neq \rho_H$ and $\psi(w) \neq \psi(par(w))$ if $w \neq \rho_P$, then $\psi_w^{up} \in \mathcal{R}(P, H, \phi)$.

Proof. This follows immediately, since if $v \in V(P) - (\{par(w)\} \cup Ch(w))$ then $\psi_w^{up}(v) = \psi(v)$. If $v \in Ch(w)$, then

$$\psi_w^{up}(w) = par(\psi(w)) \succ \psi(w) \succeq \psi(v) = \psi_w^{up}(v)$$

and if $v = par(w)$ then $\psi_w^{up}(v) = \psi(v) = \psi(par(w)) \succeq par(\psi(w)) = \psi_w^{up}(w)$. ∎

(Down) If $\psi \in \mathcal{R}(P, H, \phi)$ and $w \in V^o(P)$ with $\psi(w) \succ m(w)$ and $\psi(w) \neq \psi(v')$ for all $v' \in Ch(w)$, then $\psi_w^{down} \in \mathcal{R}(P, H, \phi)$.

Proof. Since $\psi(w) \neq m(w)$, it follows that $\psi_w^{down}(w) \in A(w)$. Moreover, since $\psi(w) \neq \psi(v')$ for all $v' \in Ch(w)$ and, by (R0), $A(v) \subseteq A(v')$ holds for all such v', we have $\psi_w^{down}(w) \succeq \psi(v') = \psi_w^{down}(v')$, for all $v' \in Ch(w)$. Since $\psi_w^{down}(x) = \psi(x) = \phi(x)$ holds for all $x \in L(P)$, it follows that $\psi_w^{down} \in \mathcal{R}(P, H, \phi)$. ∎

(E) Given $\psi, \psi' \in \mathcal{R}(P, H, \phi)$ distinct, there exists a sequence $(w_1, t_1), (w_2, t_2), \ldots, (w_p, t_p)$ with $w_i \in V^o(P)$ and $t_i \in \{up, down\}$, for all $1 \leq i \leq p = d_{path}(\psi, \psi')$, such that ψ' is the map obtained by successively applying up/down operations according to the pairs (w_i, t_i), $1 \leq i \leq p$, starting with the map ψ. Moreover, no shorter sequence of operations exists for transforming ψ into ψ'.

Proof. By the assumption on ψ and ψ' and (R3), we may assume without loss of generality that there exists some $w \in V^o(P)$ such that $\psi'(w) \succ \psi(w)$. Then either $\psi'(w) = \rho_H$ or we may assume without loss of generality that w is such that, for all $w' \in V(P)$ strictly above w, we have that $\psi(w') = \psi'(w')$. Hence, $\psi(w) \neq \psi(par(w))$. Starting with the map ψ, it is straightforward to check using (Up) that in either case we can apply a sequence of $d_H(\psi(w), \psi'(w))$ operations of the form (w, up) to obtain a new map $\psi'' \in \mathcal{R}(P, H, \phi)$ with $\psi''(w) = \psi'(w)$ and $\psi''(v) = \psi(v)$ if $v \in V(P) - \{w\}$. If there still exist vertices $w' \in V(P) - \{w\}$ such that $\psi'(w') \succ \psi(w')$, then we repeat this process until we obtain a map $\psi^* \in \mathcal{R}(P, H, \phi)$ with the property that $\psi^*(v) \succeq \psi'(v)$ holds for all $v \in V(P)$.

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If $\psi^* = \psi'$, then Property (E) follows. Assume that $\psi^* \neq \psi'$. Then there must exist some $v \in V(P)$ such that $\psi^*(v) \succ \psi'(v)$. Out of all those $v \in V(P)$ with $\psi^*(v) \succ \psi'(v)$, choose a vertex w such that $d_P(w, \rho_P)$ is maximal. We can then transform ψ^* into a new map in $\mathcal{R}(P, H, \phi)$ by using a sequence of operations of the form $(w, down)$. To see this, note first that $\psi^*(w) \succ \psi'(w) \succeq m(w)$. Next, note that there cannot exist some $v' \in Ch(w)$ such that $\psi^*(v') = \psi^*(w)$ as otherwise the choice of w implies $\psi^*(w) = \psi^*(v') = \psi'(v') \preceq \psi'(w) \prec \psi^*(w)$ which is impossible. Since $\psi^* \in \mathcal{R}(P, H, \phi)$, it follows by (Down) that $(\psi^*)_w^{down} \in \mathcal{R}(P, H, \phi)$. If we repeat this process $d_H(\psi^*(w), \psi'(w))$ times, we eventually obtain a map that agrees with ψ' on w and is equal to $\psi^*(v)$ for all $v \in V(P) - \{w\}$. Repeating this process as many times as necessary, we eventually obtain the map ψ'.

To obtain ψ' from ψ, we used $d_{path}(\psi, \psi')$ operations. Moreover, we clearly need at least this number of operations. ∎

[1] M. Bansal, E. Alm, M. Kellis, Reconciliations revisited: handling multiple optima when reconciling with duplication, transfer, and loss, J. Comp. Bio. 20(10) (2013) 738–754.

[2] L. Billera, S. Holmes, K. Vogtmann, Geometry of the space of phylogenetic trees, Adv. in App. Math. 27 (2001) 733–767.

[3] Y. Chan, V. Ranwez, C. Scornavacca, Exploring the space of gene/species reconciliations with transfers, J. Math. Biol. 71 (2015) 1179–1209.

[4] M. A. Charleston, Jungles: a new solution to the host/parasite phylogeny reconciliation problem, Math. Biosci., 149(2) (1998) 191–223.

[5] T. Cormen, Introduction to algorithms, MIT press, 2009.

[6] Y. Ding, C. Chan, C. Lawrence, RNA secondary structure prediction by centroids in a Boltzmann ensemble, RNA, 11 (2005) 1157–116.

[7] B. Donati, C. Baudet, B. Sinaimeri, P. Crescenzi, M. F. Sagot, EUCALYPT: Efficient tree reconciliation enumerator, Alg Mol. Biol. 10(1) (2015) 3.

[8] J. P. Doyon, V. Ranwez, V. Daubin, V. Berry, Models, algorithms and programs for phylogeny reconciliation, Brief. Bioinform. 12(5) (2011) 392–400.

[9] J. Doyon, C. Chauve, S. Hamel, Space of gene/species tree reconciliations and parsimonious models, J. Comp. Biol. 16(10) (2009) 1399–1418.

[10] J. Doyon, S. Hamel, C. Chauve, An efficient method for exploring the space of gene tree/species tree reconciliations in a probabilistic framework, IEEE/ACM Trans. Comp. Bio. Bioinf. 9(1) (2012) 26–39.

[11] C. A. R. Hoare, Algorithm 65: Find, Comm. ACM., 4(7) (1961) 321–322.

[12] R. Page, Maps between trees and cladistic analysis of historical associations among genes, organisms, and areas, Sys. Bio. 43(1) (1994) 58–77.

[13] D. Rosen, Vicariant patterns and historical explanation in biogeography, Syst. Biol. 27(2) (1978) 159–88.

[14] A. Tofigh, M. Hallett, J. Lagergren, Simultaneous identification of duplications and lateral gene transfers, IEEE/ACM Trans. Comp. Bio. Bioinf. 8(2) (2011) 517–535.

[15] T. Wu, L. Zhang, Structural properties of the reconciliation space and their applications in enumerating nearly-optimal reconciliations between a gene tree and a species tree, BMC Bioinf. (2011) 12(Suppl 9):S7.

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