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A Vectorial Tree Distance Measure

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Abstract A vectorial distance measure for trees is presented. Given two trees, we align the trees from their centers outwards, starting from the root-branches, to make the next level as similar as possible. The algorithm is recursive; condition on the alignment of the root-branches we align the sub-branches, thereafter each alignment is conditioned on the previous one. We define a minimal alignment under a lexicographic order which follows the intuition that the differences between the two trees closer to their cores dominate their differences at a higher level. Given such a minimal alignment, the difference in the number of branches calculated at any level defines the entry of the distance vector at that level. We compare our algorithm to other well-known tree distance measures in the task of clustering sets of phylogenetic trees. We use the TreeSimGM simulator for generating stochastic phylogenetic trees. The vectorial tree distance can successfully separate symmetric from asymmetric trees, and hierarchical from non-hierarchical trees.

Key words: phylogenetic trees, alignment, tree distance measure

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I. INTRODUCTION AND MOTIVATIONS

A distance measure between two trees can be calculated based on several approaches. One can compare the two adjacency matrices by evaluating the eigenvalues or eigenvalue gaps [1]. Alternatively one can compare graph properties, such as centrality, density, etc. A well known distance measure is the Tree Edit Distance (TED), [2], [3], [4]. In the TED we look for the optimal set of editing actions (e.g., insertion, deletion) transforming one tree into the other. One can cut any of the two trees at any level, where an edge can be inserted. There are several distance measures for phylogenetic trees. Each phylogenetic tree comes with a set of labels (taxa) attributed to the leaves. In the Robinson-Foulds measure [5] two operations are defined, a contraction where an edge is deleted and the labels on the leaves are rearranged, and an inverse operation, a de-contraction where an edge is added, and a corresponding new partition of the labels is set. The minimal sequence of such operations leading one tree into the other defines the distance measure. In [6] a tanglegram is defined by comparing the two sets of labels, counting the minimal number of crossing of lines joining the corresponding labels. In [7] a score was computed to each pair of edges, based on the partition of labels defined by each edge, next an alignment of the trees was calculated to maximize the sum of scores. Recently, several software tools for the presentation of trees were suggested [8].

Another approach was suggested more recently, where one uses machine learning kernel methods to compare two trees. In kernel methods [9] [10] one maps the original data space into some feature space to compare two trees by computing their scalar ‘dot product’. The feature space could be of high dimension, however we can use the ‘kernel trick’ [11] to compute such dot products. Two trees are considered similar if their scalar product in the feature space is close to 1, and orthogonal or different if this product is 0. The question remains: which feature space is appropriate for the task? There are several families of known feature spaces for trees, making the following list of kernel methods:

- Convolutional Kernels, where kernels on the tree set are induced from kernels on subsets, such as subtrees [12] or subset trees [13] [14]. Similarly in [15] an approximate tree kernel was discussed in the context of NLP. Partial tree kernel were suggested by [16]. Elastic tree kernels were discussed in [17], Grammar Driven tree kernels [18], Semantic-Syntactic tree kernels in [19]. All of the above methods, being applied by a mapping into some feature space, lose some of the information. For example two trees could have several subset trees in common, however their differences are not accounted for. Adding several nodes while keeping the same number of subset trees in one of the trees may yield the same kernel ‘dot product’. The same applies to most of the kernel methods above. More flexible kernels like Elastic kernels or partial tree kernels are even worse in that sense, they allows the identification of edges that our Vectorial Tree Distance method presented here will not allow.
- Spectrum kernels [20] identify trees by searching for q-grams on the trees, these are patterns of predefined structure, possibly even labeled [21]. Q-grams are identified without respect to their position in the tree. Our VTD is highly dependent on the distance from the root.
- Fisher kernel is based on the generative stochastic model from which trees are drawn. Therefore different trees having the same statistical parameters are considered the same. Our VTD distance measure yields a distance between two specific trees.
- Self-Organizing Map of trees [9] [22] uses non-supervised learning by competitive networks, and is effectively a clustering method. It identifies trees in the same cluster and thereafter uses kernel methods. In that sense it could measure the similarity of clusters, but not of trees.

The algorithm presented here depends on the tree roots, and on the distance of the branches from the roots, therefore it is not allowed to swap nodes having different levels. This is the main reason why some of the above mentioned edit algorithms and their variants are different in principle [23]. Our algorithm resembles the tree alignment distance algorithm in [24] restricted to the case where all labels are the same, trees are unordered and having bounded degree, a trivial cost function is defined on the labels, and the output is a scalar function; moreover we do not allow the insertion of internal ‘space’ nodes, only new boundary nodes are allowed. The time complexity of [24] is of the order of $|T|^2$ where $|T|$ is the number of vertices. Our algorithm is more simplistic in the sense that it ignores all labels and therefore processes weaker information, however its time complexity is lower as we shall discuss later. Hence we trade information capacity with time complexity.

Intuitively, given two trees and their corresponding centers, we will say that the trees are similar if there is a mapping taking one tree into the other, which is covariant with respect to distances from the center and with respect

FIG. 1: The above trees look very different; however if one permutes the main branches, it becomes apparent that they differ only by two extra leaves on the right hand tree at the 4th level from the center.

to descendency. Covariance with respect to distance from the center means that for all R , a shell of radius R (from the center) of tree 1 is mapped into a shell of radius R of tree 2. Covariance with respect to descendency means that whenever branch a of tree 1 is mapped into branch a' of tree 2, the descendants of a are mapped into descendants of a' . If such a mapping exists we can say the two trees are similar, modulo a permutation or a naming of the branches.

Below we develop the above mentioned mapping and measure the residual difference after applying it. Originally two trees might look different, and only following the suggested mapping one can recognize their similarity. For example, consider the following two simple trees (figure 1), which seem different. However, if one permutes the main branches she will find that the only difference is two extra leaves on the right tree at the 4th level from the center.

Having recursively aligned two trees (see detailed description in section II), we define the Vectorial Tree Distance as:

the vector whose entries are the differences in the number of branches at each level.

Here is the algorithm in a nutshell (a detailed description is given in II). Suppose we are given two trees, each with its center point (the existence of such a point is well known, see [25]). We align the trees from their centers outwards, starting from their stumps. We attach an n -ary vector to each of the centers, where n is the number of branches in the stump, and each entry is the number of sub-branches, i.e. descendants of that branch, see fig. 2. For example, we attach the vector $(2,3,4,5)$ to node O since it has 4 branches: 2 sub-branches for node A , 3 for node B , 4 for node C , and 5 for node D . This ‘one step look ahead’ weighting method is similar to the one suggested by the ‘k-shell’ decomposition algorithm, see [26] and references therein. The ‘look-ahead’ method is defined as follows: Let O be the root of a tree, and $V(O) = (n_1, \dots, n_k)$ be the weight vector of O , where k is the outgoing degree of O , and n_k is the number of outgoing branches of the k -th branch of O (we do not count the edge between O and its k -th branch). Similarly we define the weight vector for any node, using the same direction, defined by the root. Next, we align the two stumps to minimize the L_1 difference of the vectors. This is the ‘weighted matching problem’ [27], and there can be several such matchings. This minimal L_1 difference will be the first entry of the VTD. Freezing this alignment we will force an alignment of the next level, i.e. their sub-branches. Thus if branch a in the first tree’s stump is paired with branch a' in the second tree, then the descendants of a will be aligned with the descendants of a' . For the current level we use the same look-ahead method and attach n -ary vectors to each node at distance 1 from the center (for example nodes A and A' in fig. 2), where n is the number of sub-branches for the corresponding branch, and the entries are the number of sub-sub-branches for each sub-branch; for example, we attach the vector $(3,2)$ to node A since it has 2 descending branches, one with 3 sub-branches, the other with 2 sub-branches. The set of all L_1 minimal distances at that level (the level of nodes A , B , C and D) defines an alignment of the sub-branches, and

FIG. 2: Simple example of trees' alignment

their sum will be the next entry of the VTD. This process is continued recursively. In case there is more than one minimal alignment at any level, the above process is continued with all those alignments in parallel.

Here is the definition of our 'look-ahead' method: Let O be the root of a tree. Let $V(O) = (n_1, \dots, n_k)$ be the weight vector of O , where k is the outgoing degree of O , and n_k is the number of outgoing branches of the k -th branch of O . Implicit in the definition is a direction from the root O outwards (in computing n_k we do not count the edge between O and its k -th branch). Similarly we define the weight vector for any node, using the same direction, defined by the root. We can use a simple Breadth First Search to find the nodes' weights vector. When comparing two weight vectors, in case they have different lengths, we pad the shorter one by adding zeroes.

In the next section we present some definitions and preliminaries. In section II we elaborate on the algorithm along with detailed examples. In section III we compare our algorithm to other known methods in the task of clustering sets of phylogenetic trees generated by the TreeSimGM simulator [28], [29].

II. THE VECTORIAL TREE DISTANCE ALGORITHM

We start with some definitions and notations to be used later.

A. Definitions and preliminaries

Definition 1: An alignment of two trees: Given two trees Tr_1 and Tr_2 and their corresponding centers C_1 and C_2 , we will say that a mapping Al is an alignment of the trees if for every level R from both centers, Al maps the branches of one tree in that level to the branches of the other tree in the same level (with possible zero-padding into ghost branches), conditioned on the constraints that if branch a of tree Tr_1 is aligned with branch a' of Tr_2 , then all descendants of a will be aligned with all descendants of a' .

Definition 2: Minimal Alignment: Given two trees Tr_1 and Tr_2 and an alignment Al of the trees, we say that Al is minimal if for every level R , going over all possible alignments at level R , Al is such that the difference between the number of descendants of any two aligned branches, summed over all pairs of aligned branches in that level R is minimal.

Definition 3: Vectorial Tree Distance: Given two trees Tr_1 and Tr_2 and a minimal alignment Al , then the VTD of the two trees is the vector whose R -entry is the minimal difference given by the minimal alignment Al for the level R . We let D denotes the distance vector.

Note that the first two definitions above are recursive, namely, the constraints must be fulfilled for all levels R . At each level R , the sum of all minimal L_1 differences is the R entry of the distance vector.

In the following section, we elaborate on the algorithm. After describing the main steps of the procedure, we focus on the details via two specific examples. The MATLAB code implementation can be obtained from the authors.

B. Alignment and comparison

Given a pair of trees and center nodes we follow the trees from these nodes outwards. At **level 0** we simply compare the number of edges of the stumps. The difference is the 0-th entry of the distance vector. Suppose the left stump has m edges and the right stump has k edges, such that $m \geq k \geq 0$ (without loss of generality), then the **0-entry** of the distance vector is $m - k$. At **level 1**, there are several ways to align the m edges onto the k edges. We attach an n -ary vector to the center of each tree, where n is the number of branches in the corresponding stump, and each entry is the number of sub-branches, i.e. descendants of that branch, see examples below. The alignment problem is thus reduced to a 'weighted matching problem' [27]. We search for an alignment such that the L_1 norm distance between the two weight vectors is minimal. The minimal difference of weights will be the **1-entry** of the distance vector. It could be that more than one alignment has the same minimal difference; in that case, all such alignments are kept for the next step(s). At **level 2** we align the edges at distance 2 from the center, conditioned on the alignment(s) of the previous step. For that, we attach weight vectors to the nodes at level 1, looking ahead, the same way as above. At this stage we have several instances of the 'weighted matching problem', and we sum all L_1 norm distances at that level. The **1-entry** of the distance vector will be the minimum over all such sums of L_1 distances, going over all good (minimal) alignments of the previous level. This process is recursively continues until all nodes are exhausted. The following examples elaborate on the first few steps of the procedure.

Example 1: Consider the trees in figure 3. The **0-entry** of the distance vector $D(0) = 3 - 2 = 1$, which is the difference in the number of branches of the stumps. Attach the vector (2,3) to node O , corresponding to the two sub-branches stemming out of node A and 3 sub-branches stemming out of node B . Similarly we attach the vector (3,2,2) to node O' of the second tree. We fix the right tree and map the branches a and b of the left tree into the branches a' b' and c' of the right tree at level 1. There are 6 such mappings, each is denoted by a permutation of the weight vector (2,3,0) (while the vector (3,2,2) of the left tree fixed). The table in figure 4 show all possible mappings, where we zero-pad the vector at O i.e. $v(O) = (2, 3, 0)$, to allow permutations of two vectors with different sizes. The 3'rd column of the table includes the minimal L_1 differences, and the 4'th column gives the explicit mapping between the nodes. Observe that the 2'nd and 4'th mappings (see the second column of the table) both have L_1 minimal difference that equals 2. Therefore the 1'st entry of the distance vector $D(1) = 2$, and there are 2 minimal alignments at that level. How can we tell which of the two alignments is preferred? For that we will have to take a look at the next level alignments.

At the next level alignments we first attach vectors to the nodes at distance 1 from the centers; for the first tree we set $v(A) = (3, 3, 0)$ and $v(B) = (2, 2, 3)$, and for the second tree we set $v(A') = (2, 2, 3)$, $v(B') = (2, 3, 0)$ and $v(C') = (3, 4)$. Next we align the branches of level 2 conditioned on the two minimal alignments from the previous step. If we follow alignment number 2 of the first level (see the table in fig. 4), then b goes to a' and we have to align the descendants of b with the descendants of a' . Therefore, we have to match $v(B) = (2, 2, 3)$ with $v(A') = (2, 2, 3)$ which has 2 possible minimal matchings (where we permute the sub-branches with two leaves) with both L_1 difference

FIG. 3: Detailed alignment of two trees

equals 0. Similarly, since a goes to b' we have to match $v(A) = (3, 3)$ with $v(B') = (2, 3)$ which has 2 possible minimal matchings, and a minimal difference equals 1. To this L_1 difference at level 2 we have to add the number of (ghost) branches at level 2 which are the descendants of c' , i.e. 7. Therefore, if we follow the 2'nd alignment at level 1 we end with a sum of differences equals $0+1+7=8$ at level 2, which is the sum of 3 L_1 differences. Alternatively, if we follow the 4'th alignment at level 1 (4'th line on the table), we have to map b into a' , and therefore we have to match $v(B) = (2, 2, 3)$ with $v(A') = (2, 2, 3)$ which again has 2 possible minimal matchings and difference equals 0. Additionally, we map a into c' and therefore match $v(A) = (3, 3)$ with $v(C') = (3, 4)$, which has 2 possible minimal matchings with difference equals 1. To this L_1 difference we have to add the number of branches at level 2 which are the descendant of b' , i.e. 5. Therefore if we follow the 4'th alignment at level 1 we end with a difference of $0+1+5=6$. The 4'th alignment at the first level is therefore better and hence the 2'nd entry of the distance vector $D(2) = 6$. To summarize, the first 3 entries of the distance vector D are: $D = (1, 2, 6)$

In figure 5 we present the procedure describing the set of all mappings for the above example. An open circle denotes an alignment and a closed one denotes an alignment with minimal distance value. At the first level we had 6 possible alignments (see the table in figure 4), 2 were minimal with L_1 distance equals 2, and the other 4 with L_1 distance equals 4. At the second level we extend only the minimal alignments of the first level. To each minimal alignment of the first level we had 4 sub-alignments. The 2'nd alignment of the first level had 4 sub-alignments with L_1 distance 8, whereas the 4'th alignment of the first level had 4 sub-alignments with L_1 distance 6.

The following example is more complex, however we will not go into too much details, having in mind the previous example.

Example 2: In this example (see figure 2) the distance at **level 0** is 0 since both stumps have 4 branches. Next we attach the weight vector $(2, 3, 4, 5)$ to the center node O , and the weight vector $(3, 4, 5, 6)$ to the center node O' of the second tree. We now look at the set of all matches between the two weight vectors, having minimal L_1 sum. An optimal match would be to align a with a' , b with b' , c with c' , and d with d' . This would align the weights $(2, 3, 4, 5)$ with $(3, 4, 5, 6)$ having an overall distance equals 4. Therefore the first level distance coefficient is 4.

If we aligned a with a' at the first level we will have to align the descendants of a with the descendants of a' . We attach a 2-tuple weight vector to A , $(3, 2)$, and a 3-tuple weight vector to A' , $(3, 2, 3)$, and compute the minimal alignment between the two weight vectors. One of the branches of a' will be left non aligned (ghost) and all the descendants of that branch will add a corresponding difference at each of the next levels. Similarly we attach weight vectors to B and B' , C and C' , D and D' . For each of the above pairs we compute the minimal alignment. Finally, we sum all the above minimal L_1 differences to obtain the entry for the distance vector. In case both weight vectors have 0 entries (as in this example for B and B' , C and C' , and D and D'), we can pick any alignment and the L_1 difference will be 0.

No	Alignment	Difference	Explicit map
1	$\begin{array}{ccc} 3 & 2 & 2 \\ 2 & 3 & 0 \end{array}$	4	$\begin{array}{l} a \rightarrow a' \\ b \rightarrow b' \end{array}$
2	$\begin{array}{ccc} 3 & 2 & 2 \\ 3 & 2 & 0 \end{array}$	2	$\begin{array}{l} b \rightarrow a' \\ a \rightarrow b' \end{array}$
3	$\begin{array}{ccc} 3 & 2 & 2 \\ 2 & 0 & 3 \end{array}$	4	$\begin{array}{l} a \rightarrow a' \\ b \rightarrow c' \end{array}$
4	$\begin{array}{ccc} 3 & 2 & 2 \\ 3 & 0 & 2 \end{array}$	2	$\begin{array}{l} b \rightarrow a' \\ a \rightarrow c' \end{array}$
5	$\begin{array}{ccc} 3 & 2 & 2 \\ 0 & 2 & 3 \end{array}$	4	$\begin{array}{l} a \rightarrow b' \\ b \rightarrow c' \end{array}$
6	$\begin{array}{ccc} 3 & 2 & 2 \\ 0 & 3 & 2 \end{array}$	4	$\begin{array}{l} b \rightarrow b' \\ a \rightarrow c' \end{array}$

FIG. 4: First level matching table

FIG. 5: The set of possible mappings

At level 1 we could align the branches a with d' , b with a' , c with b' , and d with c' , i.e. $(2,3,4,5)$ with $(6,3,4,5)$, where the minimal L_1 distance also equals 4 as above. If we map a to d' we should align the descendants of a with the descendants of d' , therefore we should look at the 6-tuple weight vector for d' , and find its best match with the 2-tuple vector for a . We should also find the other minimal matches between the 3-tuple of b and the 3-tuple of a' , the 4-tuple of c and the 4-tuple of b' , and the 5-tuple of d and the 5-tuple of c' .

We will now compare the sum of L_1 differences of the 2'nd level we computed, conditioned on the first level alignment of $(2,3,4,5)$ with $(3,4,5,6)$, with the alternative sum of L_1 differences of the 2'nd level conditioned on the first level alignment of $(2,3,4,5)$ with $(6,3,4,5)$. In general, we will minimize the sum of L_1 differences of the 2'nd level going over all minimal alignments of the first level. It is easy to see that the VTD distance is $(0,4,3)$. We leave the rest of the details to the reader.

Let us now provide the general formulation of the process in terms of ‘Dynamic-Programming’:

Let $\vec{X} = (x_1, \dots, x_k)$, $\vec{Y} = (y_1, \dots, y_k)$,

$$L_1(\vec{X}, \vec{Y}) = \sum_{i=1}^k |x_i - y_i|; \quad (1)$$

define

$$M(\vec{X}, \vec{Y}) = \min_{\sigma \in \text{Sym}(k)} L_1(\sigma(\vec{X}), \vec{Y}) \quad (2)$$

where $\text{Sym}(k)$ is the Symmetric group on k elements. Let

$$M_\sigma(\vec{X}, \vec{Y}) = \arg_{\sigma}(\min_{\sigma \in \text{Sym}(k)} L_1(\sigma(\vec{X}), \vec{Y})) \quad (3)$$

denote the set of permutations in $\text{Sym}(k)$ satisfying the above minimum. In case the two vectors are not of the same length we pad the shorter one with zeroes.

Let $D = D_{(O, O')}$ be the tree distance vector computed from the two centers outwards; O for tree 1, O' for tree 2. Given a root O , let $V(O) = (n_1, \dots, n_k)$ be the weight vector for node O , where k is the degree of O and n_k the number of sub-branches of O that are branches of the k -th branch of O . Let $V_k(O)$ denotes the k -th weight n_k and $V^k(O)$ the corresponding node. Then $D_{V(O)^k, V(O')^j}$ is the tree distance vector for the two subtrees stemming outwards of vertices $V(O)^k$ and $V(O')^j$. Let z be a predetermined length of the measurement vector D . The vectorial tree distance can be computed by the following recursive process:

The zero coordinate (level) of $D = D_{(O, O')}$ satisfies:

$$D_{(O, O')}(0) = M(V(O), V(O')) \quad (4)$$

and the $(1, \dots, z)$ coordinates (levels) satisfy:

$$\begin{aligned} D_{(O, O')}(1, \dots, z) = & \\ = \text{lexmin}_{\sigma \in M_\sigma(V(O), V(O'))} & \left\{ D_{V(O)^1, V(O')^{\sigma(1)}} + \right. \\ & + D_{V(O)^2, V(O')^{\sigma(2)}} \\ & \left. \dots + D_{V(O)^k, V(O')^{\sigma(k)}} \right\} \end{aligned} \quad (5)$$

Namely, to compute the distance vector from any two root points, we look-ahead to the neighboring vertices, having computed the distance vectors for the corresponding pairs of sub-trees (paired by one minimal alignment of the root branches), we sum the vectors point-wise. We now compute the minimal sum under the lexicographic order, going over all minimal alignments of the root branches. To compute $D_{V(O)^i, V(O')^{\sigma(i)}}$ we need to re-use the above formula with $V(O)^i$ and $V(O')^{\sigma(i)}$ as the new roots.

III. CLUSTERING OF SIMULATED PHYLOGENETIC TREES - COMPARING VTD TO OTHER METHODS

In this section we demonstrate our VTD measure on the problem of clustering families of phylogenetic trees generated by the TreeSimGM package [28], [29]. TreeSimGM, is an r-package simulation tool for generating stochastic phylogenetic trees under a general Bellman and Harris model [30]. The package allows the user to specify any desired probability distribution for the waiting times until speciation and extinction. Trees generated by the TreeSimGM have basic and simple parameters and can be considered as representing possible natural trees. We also compared our VTD with known tree distance measures; Robinson Foulds [36], SPR distance [37], KF distance [38], and path distance [39]. We took 3 families of 60 trees each. On each family we tested a different property. We used k-means algorithms ($k=2$) on the distance matrices to cluster each family according to the property tested. For the VTD measure we built a k-means algorithm anew, denoted vectorial k-means (VKM). This variant defers from standard k-means in the following aspects. First, the cluster-center in the VKM is a representative tree chosen to be the closest to all other members (trees) of the cluster. Although this 'closeness' measure can be obtained in many ways, for our analysis we simply used the root-mean-square of the VTD between pairs of trees. Second, the association stage, i.e. tree-to-cluster assignment is also done in the vector sense, i.e., the cluster chosen for each tree is obtained by calculating the VTD to any of the clusters' representatives and selecting the one with the minimal root mean square. This process is repeated iteratively.

Here are the details followed by a table of the results:

a) Symmetric trees vs. asymmetric trees - A set of 60 trees was generated. A sub-set of 30 was generated by a symmetric process, the other by a asymmetric generator. We used the same taxa 10 for all trees to allow the comparison with classical tree distance measures. In all trees a Weibull(3,0.1) was used as the waitsp (waiting time for speciation) distribution and an $\exp(0)$ as the waitext (waiting time for extinction) distribution.

b) Hierarchical vs. non-hierarchical trees - A set of 60 trees was generated. A sub-set of 30 was generated by an hierarchical process, the other by a non-hierarchical generator. To construct hierarchical trees we used Weibull(4,0.1) as the waitesp distribution, and Weibull(1,0.1) for the non-hierarchical case. Otherwise all trees had taxa 15 and waitext distribution of $\exp(0)$. All trees were asymmetrically generated.

c) Trees of different taxa - in this case the classical measures are harder to use for measuring the distance between trees. We demonstrated the fact that the VTD measure can easily separate between different speciation parameters. We compared trees having waitsp distribution $\exp(0.5)$, with trees having waitsp of $\exp(0.2)$. Otherwise all trees had waitext distribution of $\exp(0.3)$. All trees were asymmetrically generated with the same age parameter, sim.age equals 10.

The table in figure 6 summarizes the details of the experiments. The table in figure 7 summarizes the details of the results. In separating symmetric vs. asymmetric trees the VTD measure showed better results than the RF and path distance measures. In separating hierarchical vs. non-hierarchical trees the VTD measure showed better results than all the above methods. The VTD distance could also well separate trees having different waitsp (exponential) distributions with different taxa.

IV. DISCUSSION

In this manuscript we present a new vector distance measure for a pair of trees, denoted VTD. The distance vector is calculated following an alignment process of the trees, applied from a given pair of center points outwards. We describe the algorithm in details.

To compare the VTD to other well known tree distance measures we simulated several families of phylogenetic trees using the TreeSimGM r-package. In separating symmetric vs. asymmetric trees the VTD measure showed better results than the RF or path distance measure, and in separating hierarchical vs. non-hierarchical trees it was found

	Number of simulations	Waitsp distribution	Waitext distribution	taxa	symmetry
a1	30	Weibull(3,0.1)	exp(0)	10	Asymmetric
a2	30	Weibull(3,0.1)	exp(0)	10	Symmetric
b1	30	Weibull(4,0.1)	exp(0)	15	Asymmetric
b2	30	Weibull(1,0.1)	exp(0)	15	Asymmetric
c1	30	exp(0.5)	exp(0.3)	sim.age = 10	Asymmetric
c2	30	exp(0.2)	exp(0.3)	sim.age = 10	Asymmetric

FIG. 6: Details of TreeSimGM simulations .

	RF		KF		Path		SPR		VTD	
a	56.6%	43.3%	96.6%	3.3%	76.6%	23.3%	96.6%	3.3%	86.6%	13.3%
	3.3%	96.6	3.3%	96.6	3.3%	96.6	3.3%	96.6	6.6%	93.3%
b	70%	30%	60%	40%	100%	0%	100%	0%	96.6%	3.3%
	46.6%	53.3%	0%	100%	26.6%	73.3%	30%	70%	3.3%	96.6%
c									100%	0%
									0%	100%

FIG. 7: Confusion matrices for the above experiments.

better than the RF, KF, Path, or SPR distance measure.

Some remarks concerning computational complexity. We assume the degree of each vertex in both trees is bounded by some integer k . At each vertex we compute a weighted matching on two k -dimensional integer vectors. The ‘weighted matching problem’ is known to have polynomial complexity (in k) [27]. Furthermore, finding **all** minimal solutions to the weighted matching problem is also polynomial (in k) [33]. Denote by $|M(k)|$ the complexity of finding all minimal matchings of two k dimensional integer vectors, let $\#M(k)$ be the number of such minimal alignments. Consider now the process of alignment, going from the center outwards. At each level, and for each alignment we compute the matching between the nodes aligned. Therefore the complexity will be the product of $|M(k)|$ by the number of vertices at that level by the number of alignments at that level. Multiple equivalent alignments at any level

could have been originated at a previous level, or could have been originated at that level by equivalent matchings. For random trees multiple alignments from both sources are rare. We can therefore characterize the tree of alignments described in figure 5. Having all that in mind it is easy to see that for random trees the complexity of the VTD is $O(|M(k)||V|)$ where $|V|$ is the number of vertices (maximal). The exact proof is left for future research.

Most algorithms for the alignment of pairs of trees have higher time complexity of the order of $O(|V_1||V_2|)$ (see Table 1 in [2]), however these algorithms align trees with labels. Our algorithm is more simplistic in the sense that it ignores all labels and therefore processes weaker information, however its time complexity is lower.

Our algorithm can be used to gain some insights in several areas, such as game theory, decision-making processes, genetics, communication networks and more. For example in the area of decision making, assuming it is possible to map the decision processes into trees. Then one can define a distance measure between two such processes, each may occur in different organizations, or situations. This could also be applied in crisis management cases where complex scenarios can be mapped into a corresponding tree and further analyzed against other scenarios or use cases.

In immunology, currently it is possible to obtain the repertoire sequencing of various immune cells, e.g. B/C cells [34], [35] from peripheral blood. This means that different subjects, or even the same subject at different time points, exhibit different repertoires. One of the major hurdles is to infer useful insights from this vast information. We suggest that applying the vector distance measure, it is possible to compare repertoires after they have been mapped to their network representation.

V. BIBLIOGRAPHY

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Author Contribution statement

A.P. and B.T. wrote the algorithm, wrote the main manuscript text and prepared figures 1-7. A.P. and B.T. reviewed the manuscript and prepared the submission.

Competing Interest statement

The authors declare no competing interests.

Figures

Figure 1

The above trees look very different; however if one permutes the main branches, it becomes apparent that they differ only by two extra leaves on the right hand tree at the 4th level from the center.

Figure 2

Simple example of trees' alignment

Figure 3

Detailed alignment of two trees

No	Alignment	Difference	Explicit map
1	<div> <div>322</div> <div>230</div> </div>	4	$a \rightarrow a'$ $b \rightarrow b'$
2	<div> <div>322</div> <div>320</div> </div>	2	$b \rightarrow a'$ $a \rightarrow b'$
3	<div> <div>322</div> <div>203</div> </div>	4	$a \rightarrow a'$ $b \rightarrow c'$
4	<div> <div>322</div> <div>302</div> </div>	2	$b \rightarrow a'$ $a \rightarrow c'$
5	<div> <div>322</div> <div>023</div> </div>	4	$a \rightarrow b'$ $b \rightarrow c'$
6	<div> <div>322</div> <div>032</div> </div>	4	$b \rightarrow b'$ $a \rightarrow c'$

Figure 4

First level matching table

Figure 5

The set of possible mappings

	Number of simulations	Waitsp distribution	Waitext distribution	taxa	symmetry
a1	30	Weibull(3,0.1)	exp(0)	10	Asymmetric
a2	30	Weibull(3,0.1)	exp(0)	10	Symmetric
b1	30	Weibull(4,0.1)	exp(0)	15	Asymmetric
b2	30	Weibull(1,0.1)	exp(0)	15	Asymmetric
c1	30	exp(0.5)	exp(0.3)	sim.age = 10	Asymmetric
c2	30	exp(0.2)	exp(0.3)	sim.age = 10	Asymmetric

Figure 6

Details of TreeSimGM simulations

	RF		KF		Path		SPR		VTD	
a	56.6%	43.3%	96.6%	3.3%	76.6%	23.3%	96.6%	3.3%	86.6%	13.3%
	3.3%	96.6	3.3%	96.6	3.3%	96.6	3.3%	96.6	6.6%	93.3%
b	70%	30%	60%	40%	100%	0%	100%	0%	96.6%	3.3%
	46.6%	53.3%	0%	100%	26.6%	73.3%	30%	70%	3.3%	96.6%
c									100%	0%
									0%	100%

Figure 7

Confusion matrices for the above experiments.