Phylogenetics

SPAGETI: Stabilizing Phylogenetic Assessment with Gene Evolutionary Tree Indices

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Abstract

The standard approach to estimate species trees is to align a selected set of genes, concatenate the alignments and then estimate a consensus tree. However, individual genes contain differing levels of evolutionary information, either supporting or conflicting with the consensus. Based on individual gene evolutionary tree, a recent study has demonstrated that this approach may result in incorrect solutions and developed the internode certainty (IC) heuristic for estimating the confidence of splits made on the consensus tree. Although an improvement, this heuristic neglects the differing rates of molecular evolution in individual genes. Here I develop an improved version of this method such that each gene is proportionally weighted based on its overall signal and specifically with the imbalanced signal for each node represented with gene tree.

Introduction

Proposed on 1983, bootstrap and its theory for assessing the reliability of a phylogenetic tree is still being argued (Felsenstein, 1983). Despite nonrealistic assumptions of the method, such as independence of the residues, the method is still commonly being used as a measure of reliability of the phylogenetic tree. Nowadays method has been applied also to consensus trees estimated from concatenated alignments of genes. In this case, use of bootstrap induces a bias due to the fact that bootstrap samples from a large amount of sites always produce very similar trees (Salichos and Rokas, 2013). As a result, bootstrap will falsely give high confidence values for consensus trees from concatenated gene alignments, even if the tree itself is incorrect. One of the alternatives as a measure of nodes certainty of a consensus tree is the use of internode certainty (IC) proposed by Salichos and Rokas (2013) and Salichos et al. (2013). This sounds appealing since it is making its judgment of the nodes placements based on the topology of the gene trees. While still as a generalization of this method, Salichos et al. (2013) tries to gather even more information from the gene trees, the information related to the molecular clock of each gene is neglected and one focus is only placed on the bipartitions deduced from the gene trees. One immediate improvement would be to integrated this information and tune up the values of nodes certainty. There are at least two conceivable source of information that could be exploited to make such improvement. First, one can look at the genes molecular clock and correspondingly weight the genes that bear more evolutionary information, higher in their analysis. And second, it is crucial to integrate the evolutionary distance of two clades caused by a specific bipartition, as long as one is concerned with an index that relies on the gene trees. Here I propose a feasible method to take such information into account and provide a theory that is needed to support our method.

Bipartition indices

Being concerned with a measure of reliability over a consensus tree, in specific on the node placements, one can focus on each gene tree. Efforts has been made to address this issue in different ways. For example Salichos and Rokas (2013) proposed a gene-support frequency (GSF) as well as internode certainty (IC) that relies on the bipartition observed on the topology of each gene tree for a specific determined node on the consensus tree. Given the maximum number of the internodes of a consensus tree $L$, each internode $o_k \in O, k = 1, \ldots, L$ will result on a bipartition
The ratio of the number of the genes that exhibit the same type of bipartition, \( m_s \), to the total number of the genes, \( m \), will account for the GSF. On the other hand, we will look for the most frequent conflicting bipartition \( m_{f1} \), as well. Then form a proper probabilistic measure over 1 = \( p_s + p_{f1} \) with \( p_s = \frac{m_s}{m} \) and \( p_{f1} = \frac{m_{f1}}{m} \) and apply the modified version of the Shannon’s notion of entropy as:

\[
IC = 1 + p_s \log_2(p_s) + p_{f1} \log_2(p_{f1}).
\]

The conflicting bipartition is defined as the bipartition that has at least one conflicting bipartition \( m_{f1} \), and of course we are not confined to one form. Sukul et al. \(2013\) has extended this definition of IC to a more generalized form that is not only restricted to the most frequent conflicting bipartition but all, resulting in ICA,

\[
ICA = 1 + p_s \log_2(p_s) + \sum_{i=2}^{c} p_{f1,i} \log_2(p_{f1,i}).
\]

where \( c \) is the maximum number of conflicting bipartitions that has the overall frequency of \( 0.05 \) or more. This cut-off value is imposed as a trade-off between accuracy and computational expense. We further note that in this case the proper probabilistic measure is 1 = \( p_s + p_{f1} + \ldots + p_{f_c} \). Also note the parabolic shape of the above formulas where it takes it minimum zero when the \( p_s = p_{f1} = p_{f2} = \ldots = p_{f_c} \). In IC and ICA, respectively. Sukul et al. \(2013\) propose negative signs for the rare cases when \( p_s < p_{f1} \).

Note that \( \mathcal{D} \) will give a value for each internode on the consensus tree. Upon gathering all of these values for all the internodes and adding them together, the tree certainty (TC), will be obtained as, \( TC = \sum_{k=1}^{L} IC_k \).

Furthermore, the definition of ICA based on \( \mathcal{D} \) has been proposed as the counterpart of TC, \( TCA = \sum_{k=1}^{L} IC_k A_k \). These two stand as the comparative values between different consensus trees. In the following section I describe the model that integrates the genetic information laid in the gene trees and their underlying distance matrices. This integration, will be in two layers based on the gene tree topology. In the first scenario the mean of each gene tree distance matrix would be a weighting scale of each gene on the major scale. The second case on the other hand, accounts for the mean of each gene tree distance matrix would be a weighting scale of each gene tree topology. This integration, will be in two layers based on the gene tree topology. In the first scenario the mean of each gene tree distance matrix would be a weighting scale of each gene on the major scale. The second case on the other hand, accounts for the mean of each gene tree distance matrix would be a weighting scale of each gene tree topology. This integration, will be in two layers based on the gene tree topology.

Moreover, by looking closer at bipartitions, we can infer more evolutionary information. The previous model is distinguishing between supporting and conflicting bipartitions and even has a concern on different types of bipartitions observed but still neglecting the different forms of the trees within each of these classes of bipartitions. It is indeed the case that all the supporting bipartitions are not equally supportive nor all the conflicting ones equally contracting. To amend this situation we focus on the sub-topology of each gene tree governed with a specific bipartition as two mutually distinct sub trees. This in turn will cause a bipartition on the underlying distance matrix of that tree with corresponding mean values of their lower triangle values. For the jth gene we refer to \((c_j^f, c_j^p, t_j^f, t_j^p, m_j^f, m_j^p)\), and \(\mu_j, \nu_j\), as the bipartitions incurred on corresponding tree, distance matrix, and mean values, respectively. With setting the distance between two means of a specific bipartition as \(d_{ji} = |\mu_j^f - \nu_j^p|\) we can form the interaction ratio as \(\tau_j = d_{j1}/\mu_j\). This value shows the mixed effect of overall gene signal that encompasses both the gene importance per se and its underlying structure imposed by a specific bipartition. Replacing the \(\mu_j, \nu_j\) with \(\sigma_j = \sum_{i=1}^{c} \nu_i\) and \(\sigma_{f1} = \sum_{i=1}^{c} \nu_i\) will make this minor treatment effective in calculating \(\mathcal{D}\) and \(\mathcal{D}\) and correspondingly the values of IR and IRA.

### Gene signals

Suppose that we have the set of species \(S = \{s_1, s_2, \ldots, s_n\}\), and the ith, \(i = 1, \ldots, n\), species having a set of genes \(G_i = \{g_{i1}, g_{i2}, \ldots, g_{im_i}\}\). For simplicity let’s consider \(m_1 = m_2 = \ldots = m_i\), while \(j = 1, \ldots, m_i\) is prevailing the genes for species. This will result in a complete matrix of genes \(G = \{g_j\}\). Furthermore let \(T = \{T_1, \ldots, T_m\}\) and \(D = \{D_1, \ldots, D_m\}\) denote the set of gene trees and distance matrices related to each of the genes, respectively. Furthermore let \(N = \{n_1, \ldots, n_m\}\) be the vector of scalar means of corresponding lower triangle matrices of \(D\).

Having the consensus phylogenetic tree \(T\), the aim is to attach a value to each node as a measure of reliability of that node’s correct placement on that tree.

### Genes weighting: Major treatment

In the definition of \(\mathcal{D}\), we can integrate the information of the molecular clock of a gene into account; those genes that have more evolutionary signals be weighted more in the analysis. One index reflecting such information is embedded in \(\mu_j\), such that the higher this value the more evolutionary information is expected to be contained in gene \(g_j\). So one natural update in the values of GSF and ICA will be the weighting each genes by this corresponding values and update the probability measure accordingly. With this regard, we can form the weighted gene support (WGS) as \(\sum_{i=1}^{c} \mu_i\), where \(s\) is the set of all the genes supporting the specific bipartition. Furthermore, with defining \(\sigma_s = \sum_{i=s}^{c} \mu_i\) and \(\sigma_{f1} = \sum_{i=1}^{c} \mu_i\), the counterparts of the \(p_s\) and \(p_{f1}\) for the IC can be updated as,

\[
\pi_s = \frac{\sigma_s}{\sigma_s + \sigma_{f1}}, \quad \pi_{f1} = \frac{\sigma_{f1}}{\sigma_s + \sigma_{f1}}
\]

and for the ICA as,

\[
\pi_s = \frac{\sigma_s}{\sigma_s + \sum_{j=1}^{c} \sigma_{fj}}, \quad \pi_{fj} = \frac{\sigma_{fj}}{\sigma_s + \sum_{j=1}^{c} \sigma_{fj}}.
\]

These two will result in intermediate reliability (IR) and for all (IRA) indices as follow:

\[
IR = 1 + \pi_s \log_2(\pi_s) + \pi_{f1} \log_2(\pi_{f1}).
\]

\[
IRA = 1 + \pi_s \log_2(\pi_s) + \sum_{j=1}^{c} \pi_{fj} \log_2(\pi_{fj}).
\]

### Bipartitions weighting: Minor treatment

Moreover, by looking closer at bipartitions, we can infer more evolutionary information. The previous model is distinguishing between supporting and conflicting bipartitions and even has a concern on different types of bipartitions observed but still neglecting the different forms of the trees within each of these classes of bipartitions. It is indeed the case that all the supporting bipartitions are not equally supportive nor all the conflicting ones equally contracting. To amend this situation we focus on the sub-topology of each gene tree governed with a specific bipartition as two mutually distinct sub trees. This in turn will cause a bipartition on the underlying distance matrix of that tree with corresponding mean values of their lower triangle values. For the jth gene we refer to \((c_j^f, c_j^p, t_j^f, t_j^p, m_j^f, m_j^p)\), and \(\mu_j, \nu_j\), as the bipartitions incurred on corresponding tree, distance matrix, and mean values, respectively. With setting the distance between two means of a specific bipartition as \(d_{ji} = |\mu_j^f - \nu_j^p|\) we can form the interaction ratio as \(\tau_j = d_{j1}/\mu_j\). This value shows the mixed effect of overall gene signal that encompasses both the gene importance per se and its underlying structure imposed by a specific bipartition. Replacing the \(\mu_j, \nu_j\) with \(\sigma_j = \sum_{i=1}^{c} \nu_i\) and \(\sigma_{f1} = \sum_{i=1}^{c} \nu_i\) will make this minor treatment effective in calculating \(\mathcal{D}\) and \(\mathcal{D}\) and correspondingly the values of IR and IRA.

### Tree reliability (TR) and adopted IR

Evidently now with the availability of the IR and IRA values one can talk about tree reliability for the case of only most prevalent conflicting bipartition or many as \(TR = \sum_{j=1}^{c} IR_j\), and \(TRA = \sum_{j=1}^{c} IRA_j\), respectively. Furthermore, since the interaction ratio \(\nu_j\) could be well close to zero in scenarios that either the gene is bearing weak signal or the partitioned clades are not distinctive, one can use the exponential of this value to ensure the minimum role of an observed bipartition.

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