Generalizing Tree Probability Estimation via Bayesian Networks

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Abstract
Probability estimation is one of the fundamental tasks in statistics and machine learning. However, standard methods for probability estimation on discrete objects do not handle object structure in a satisfactory manner. In this paper, we derive a general Bayesian network formulation for probability estimation on leaf-labeled trees that enables flexible approximations which can generalize beyond observations. We show that efficient algorithms for learning Bayesian networks can be easily extended to probability estimation on this challenging structured space. Experiments on both synthetic and real data show that our methods greatly outperform the current practice of using the empirical distribution, as well as a previous effort for probability estimation on trees.

1 Introduction
Leaf-labeled trees, where labels are associated with the observed variables, are extensively used in probabilistic graphical models. A typical example is the phylogenetic leaf-labeled tree, which is the fundamental structure for modeling the evolutionary history of a family of genes [Felsenstein, 2003, Friedman et al., 2002]. Inferring a phylogenetic tree based on a set of DNA sequences under a probabilistic model of nucleotide substitutions has been one of the central problems in computational biology, with a wide range of applications from genomic epidemiology [Neher and Bedford, 2015] to conservation genetics [DeSalle and Amato, 2004]. To account for the phylogenetic uncertainty, Bayesian approaches are adopted [Huelsenbeck et al., 2001] and Markov chain Monte Carlo (MCMC) [Yang and Rannala, 1997, Mau et al., 1999, Huelsenbeck and Ronquist, 2001] is commonly used to sample from the posterior of phylogenetic trees. Posterior probabilities of phylogenetic trees are then typically estimated with simple sample relative frequencies (SRF), based on those MCMC samples.

While classical, this empirical approach is unsatisfactory for tree posterior estimation due to the combinatorially exploding size of tree space. Specifically, SRF does not support trees beyond observed samples, and is prone to unstable estimates for low-probability trees. As a result, reliable estimations using SRF usually require impractically large sample sizes. Previous work [Höhna and Drummond, 2012, Larget, 2013] attempted to remedy these problems by harnessing the similarity among trees and proposed several probability estimators using MCMC samples based on conditional independence of separated subtrees. Although these estimators do extend to unsampled trees, the conditional independence assumption therein is often too strong to provide accurate approximations for posteriors inferred from real data [Whidden and Matsen, 2015].

In this paper, we present a general framework for tree probability estimation given a collection of trees (e.g., MCMC samples) by introducing a novel structure called *subsplit Bayesian networks* (SBNs). This structure provides rich distributions over the entire tree space and hence differs from existing applications of Bayesian networks in phylogenetic inference [e.g. Strimmer and Moulton, 2000, Höhna et al., 2014] to compute tree likelihood. Moreover, SBNs relax the conditional clade independence assumption and allow easy adjustment for a variety of flexible dependence structures.
between subtrees. They also allow many efficient learning algorithms for Bayesian networks to be easily extended to tree probability estimation. Inspired by weight sharing used in convolutional neural networks [LeCun et al., 1998], we propose conditional probability sharing for learning SBNs, which greatly reduces the number of free parameters by exploiting the similarity of local structures among trees. Although initially proposed for rooted trees, we show that SBNs can be naturally generalized to unrooted trees, which leads to a missing data problem that can be efficiently solved through expectation maximization. Finally, we demonstrate that SBN estimators greatly outperform other tree probability estimators on both synthetic data and a benchmark of challenging phylogenetic posterior estimation problems. The SBN framework also works for general leaf-labeled trees, however for ease of presentation, we restrict to leaf-labeled bifurcating trees in this paper.

2 Background

A leaf-labeled bifurcating tree is a binary tree (rooted or unrooted) with labeled leaves (e.g., leaf nodes associated with observed variables or a set of labels); we refer to it as a tree for short. Recently, several probability estimators on tree spaces have been proposed that exploit the similarity of clades, a local structure of trees, to generalize beyond observed trees. Let \( \mathcal{X} = \{O_1, \ldots, O_N\} \) be a set of \( N \) labeled leaves. A clade \( X \) of \( \mathcal{X} \) is a nonempty subset of \( \mathcal{X} \). Given a rooted tree \( T \) on \( \mathcal{X} \), one can find its unique clade decomposition as follows. Start from the root, which has a trivial clade that contains all the leaves \( C_1 \). This clade first splits into two subclades \( C_2, C_3 \). The splitting process continues recursively onto each successive subclade until there are no subclades to split. Finally, we obtain a collection of nontrivial clades \( T_C \). As for the tree in Figure 1, \( T_C = \{C_2, C_3, C_4, C_5, C_6, C_7\} \). This way, \( T \) is represented uniquely as a set of clades \( T_C \). Therefore, distributions over the tree space can be specified as distributions over the space of sets of clades. Again, for Figure 1:

\[
p(T) = p(T_C) = p(C_2, C_3, C_4, C_5, C_6, C_7)
\]  

The clade decomposition representation enables distributions that reflect the similarity of trees through the local clade structure. However, a full parameterization of this approach over all rooted trees on \( \mathcal{X} \) using rules of conditional probability is intractable even for a moderate \( N \). Larget [2013], building on work of Höhna and Drummond [2012], introduced the Conditional Clade Distribution (CCD) which assumes that given the existence of an edge in a tree, clades that further refine opposite sides of the edge are independent. CCD greatly reduces the number of parameters. For example, (1) has the following CCD approximation

\[
p_{ccd}(T) = p(C_2, C_3)p(C_4, C_5|C_2)p(C_6|C_5)p(C_7|C_3)
\]

However, CCD also introduces strong bias which makes it insufficient to capture the complexity of inferred posterior distributions on real data (see Figure 5). In particular, certain clades may depend on their sisters. This motivates a more flexible set of approximate distributions.

3 A Subsplit Bayesian Network Formulation

In addition to the clade decomposition representation, a rooted tree \( T \) can also be uniquely represented as a set of subsplits. Let \( \succ \) be a total order on clades (e.g., lexicographical order). A subsplit \( (Y, Z) \) of a clade \( X \) is an ordered pair of disjoint subclades of \( X \) such that \( Y \cup Z = X \) and \( Y \succ Z \). For example, the tree in Figure 1 corresponds to the following set of nontrivial subsplits

\[
T_S = \{(C_2, C_3), (C_4, C_5), \{O_3, O_5\}, \{O_6\}, \{O_7, O_8\}\}
\]

with lexicographical order on clades. Moreover, this set-of-subplits representation of trees inspires a natural probabilistic Bayesian network formulation as follows (Figure 2):

**Definition 1.** A subsplit Bayesian network (SBN) \( B_X \) on a leaf set \( \mathcal{X} \) of size \( N \) is a Bayesian network whose nodes take on subsplit values or singleton clade values of \( \mathcal{X} \) and: i) has depth \( N - 1 \) (the root counts as depth 1); ii) The root node takes on subsplits of the entire leaf set \( \mathcal{X} \); iii) contains a full and complete binary tree network \( B^*_X \) as a subnetwork.
We call the parent nodes in ("fake" split) until the whole network reaches depth 3. This approximation implicitly assumes that given the existence of a subsplit, subsplits that further refine opposite sides of this subsplit are independent. Note that CCD can be viewed as a simplification of the true splitting processes (e.g., \( T_{\text{full}} \)) of the trees while allowing singleton clades continue to split (the dashed gray nets) until depth of 3, both nets grow into the full and complete binary tree of depth 3.

Note that \( B_{X}^* \) itself is an SBN, the minimum SBN on \( X \). Moreover, \( B_{X}^* \) induces a natural indexing procedure for the nodes of all SBNs on \( X \): starting from the root node, which is denoted as \( S_1 \), for any \( i \), we denote the two children of \( S_i \) as \( S_{2i} \) and \( S_{2i+1} \), respectively, until a leaf node is reached. We call the parent nodes in \( B_{X}^* \) the natural parents.

**Definition 2.** We say a subsplit \( (Y, Z) \) is compatible with a clade \( X \) if \( Y \cup Z = X \). Moreover, a singleton clade \( \{W\} \) is said to be compatible with itself. With natural indexing, we say a full SBN assignment \( \{S_i = s_i \}_{i \geq 1} \) is compatible if for any interior node assignment \( s_i = (Y_i, Z_i) \) (or \( \{W_i\} \)), \( s_{2i} \), \( s_{2i+1} \) are compatible with \( Y_i \), \( Z_i \) (or \( \{W_i\} \)), respectively. Consider a parent-child pair in an SBN, \( S_i \) and \( S_{\pi_i} \), where \( \pi_i \) denotes the index set of the parent nodes of \( S_i \). We say an assignment \( S_i = s_i, S_{\pi_i} = s_{\pi_i} \) is compatible if it can be extended to a compatible assignment of the SBN.

**Lemma 1.** Given an SBN \( B_{X} \), each rooted tree \( T \) on \( X \) can be uniquely represented as a compatible assignment of \( B_{X} \).

A proof of Lemma 1 is provided in the Appendix. Unlike in phylogenies, nodes in SBNs take on subsplit (or singleton clade) values that represent the local topological structure of trees. By including the true splitting processes (e.g., \( T_{S} \)) of the trees while allowing singleton clades continue to split ("fake" split) until the whole network reaches depth \( N - 1 \) (see Figure 2), each SBN on \( X \) has a fixed structure which contains the full and complete binary tree as a subnetwork. Note that those fake splits are all deterministically assigned, which means the corresponding conditional probabilities are all one. Therefore, the estimated probabilities of rooted trees only depend on their true splitting processes. With SBNs, we can easily construct a family of flexible approximate distributions on the tree space. For example, using the minimum SBN, (1) can be estimated as

\[
p(C_2, C_3)p(C_4, C_5|C_2, C_3)p(C_6|C_4, C_5)p(C_7|C_2, C_3)
\]

This approximation implicitly assumes that given the existence of a subsplit, subsplits that further refine opposite sides of this subsplit are independent. Note that CCD can be viewed as a simplification where the conditional probabilities are further approximated as follows

\[
p(C_4, C_5|C_2, C_3) \approx p(C_4, C_5|C_2), \quad p(C_6|C_4, C_5) \approx p(C_6|C_5), \quad p(C_7|C_2, C_3) \approx p(C_7|C_3)
\]

By including the sister clades in the conditional subsplit probabilities, SBNs relax the conditional clade independence assumption made in CCD and allows for more flexible dependent structures between local components (e.g., subsplits in sister-clades). Moreover, one can add more complicated dependencies between nodes (e.g., dashed arrows in Figure 2(a)) and hence easily adjust SBN formulation to provide a wide range of flexible approximate distributions. For general SBNs, the estimated tree probabilities take the following form:

\[
p_{\text{SBN}}(T) = p(S_1) \prod_{i > 1} p(S_i|S_{\pi_i}). \tag{2}
\]

In addition to the superior flexibility, another benefit of the SBN formulation is that these approximate distributions are all naturally normalized if the conditional probability distributions (CPDs) are consistent, as defined next.
Definition 3. We say the conditional probability \( p(S_i | S_{\pi_i}) \) is consistent if \( p(S_i = s_i | S_{\pi_i} = s_{\pi_i}) = 0 \) for any incompatible assignment \( S_i = s_i, S_{\pi_i} = s_{\pi_i} \).

Proposition 1. If \( \forall i > 1, p(S_i | S_{\pi_i}) \) is consistent, then \( \sum_T p_{\text{sha}}(T) = 1 \).

With Lemma 1, the proof is standard and is given in the Appendix. Furthermore, the SBN formulation also allows us to easily extend many efficient algorithms for learning Bayesian networks to SBNs for tree probability estimation, as we see next.

4 Learning Subsplit Bayesian Networks

4.1 Rooted Trees

Suppose we have a sample of rooted trees \( D = \{ T_k \}_{k=1}^{K} \) (e.g., from a phylogenetic MCMC run given DNA sequences). As before, each sampled tree can be represented as a collection of subsplits \( T_k = \{ S_i = s_{i,k}, \ i \geq 1, \ k = 1, \ldots, K \} \) and therefore has the following SBN likelihood

\[
L(T_k) = p(S_1 = s_{1,k}) \prod_{i > 1} p(S_i = s_{i,k} | S_{\pi_i} = s_{\pi_i,k}).
\]

Maximum Likelihood In this complete data scenario, we can simply use maximum likelihood to learn the parameters of SBNs. Denote the set of all observed subsplits of node \( S_i \) as \( C_i, i \geq 1 \) and the set of all observed subsplits of the parent nodes of \( S_i \) as \( C_{\pi_i}, i > 1 \). Assuming that trees are independently sampled, the complete data log-likelihood is

\[
\log L(D) = \sum_{k=1}^{K} \left( \log p(S_1 = s_{1,k}) + \sum_{i > 1} \log p(S_i = s_{i,k} | S_{\pi_i} = s_{\pi_i,k}) \right)
= \sum_{s_1 \in C_1} m_{s_1} \log p(S_1 = s_1) + \sum_{i > 1} \sum_{s_{i} \in C_i} m_{s_{i}, t_i} \log p(S_i = s_i | S_{\pi_i} = t_i)
\]

(3)

where \( m_{s_1} = \sum_{k=1}^{K} \mathbb{I}(s_{1,k} = s_1) \), \( m_{s_{i}, t_i} = \sum_{k=1}^{K} \mathbb{I}(s_{i,k} = s_i, s_{\pi_i,k} = t_i), \ i > 1 \) are the frequency counts of the root splits and parent-child subsplit pairs for each interior node respectively, and \( \mathbb{I}(\cdot) \) is the indicator function. The maximum likelihood estimates of CPDs have the following simple closed form expressions in terms of relative frequencies:

\[
p_{\text{ML}}^{\pi}(S_1 = s_1) = \frac{m_{s_1}}{\sum_{s \in C_1} m_s}, \quad p_{\text{ML}}^{\pi}(S_i = s_i | S_{\pi_i} = t_i) = \frac{m_{s_{i}, t_i}}{\sum_{s \in C_i} m_{s_{i}, t_i}}.
\]

Conditional Probability Sharing We can use the similarity of local structures to further reduce the number of SBN parameters and achieve better generalization, similar to weight sharing for convolutional nets. Indeed, different trees do share lots of local structures, such as subsplits and clades. As a result, the representations of the trees in an SBN could have the same parent-child subsplit pairs, taken by different nodes (see Figure 6 in the Appendix). Instead of assigning independent sets of parameters for those pairs at different locations, we can use one set of parameters for each of those shared pairs, regardless of their locations in SBNs. We call this specific setting of parameters in SBNs conditional probability sharing. Compared to standard Bayes nets, this index-free parameterization only needs CPDs for each observed parent-child subsplit pair, dramatically reducing the number of parameters in the model.

Now denote the set of all observed splits of \( S_1 \) as \( C_r \), and the set of all observed parent-child subsplit pairs as \( C_{\text{ch|pa}} \). The log-likelihood \( \log L(D) \) in (3) can be rewritten into

\[
\log L(D) = \sum_{s_1 \in C_r} m_{s_1} \log p(S_1 = s_1) + \sum_{s | t \in C_{\text{ch|pa}}} m_{s, t} \log p(s | t)
\]

where \( m_{s, t} = \sum_{k=1}^{K} \sum_{i > 1} \mathbb{I}(s_{i,k} = s, s_{\pi_i,k} = t) \) is the frequency count of the corresponding subsplit pair \( s | t \in C_{\text{ch|pa}} \). Similarly, we have the maximum likelihood estimates of the CPDs for those parent-child subsplit pairs:

\[
p_{\text{ML}}^{\pi}(s | t) = \frac{m_{s, t}}{\sum_{s \in C} m_{s, t}}, \quad s | t \in C_{\text{ch|pa}}.
\]

(4)

The main computation is devoted to the collection of the frequency counts \( m_{s_1} \) and \( m_{s, t} \) which requires iterating over all sampled trees and for each tree, looping over all the edges. Thus the overall computational complexity is \( O(KN) \).
where \( q \) is a probability distribution on \( S \). \( \sim \) means the SBN likelihood for unrooted trees can no longer be factorized. We, therefore, propose the following two algorithms to handle this challenge.

**Proposition 2.** Suppose that the conditional probability distributions \( p(S_i|S_{\pi_i}), \; i > 1 \) are consistent, then (5) is a probability distribution over unrooted trees (see a proof in the Appendix).

As before, assume that we have a sample of unrooted trees \( D^u = \{ T^u_k \}_{k=1}^K \). Each pair of the unrooted tree and rooting edge corresponds to a rooted tree that can be represented as: \( (T^u_k, e) = \{ S_i = s^e_{i,k}, \; i \geq 1 \}, \; e \in E(T^u_k), \; 1 \leq k \leq K \) where \( E(T^u_k) \) denotes the edges of \( T^u_k \) and \( s^e_{i,k} \) denotes all the resulting subsplits when \( T^u_k \) is rooted on edge \( e \). The SBN likelihood for the unrooted tree \( T^u_k \) is

\[
L(T^u_k) = \sum_{e \in E(T^u_k)} p(S_1 = s^e_{1,k}) \prod_{i>1} p(S_i = s^e_{i,k}|S_{\pi_i} = s^e_{\pi_i,k}).
\]

The lost information on the root node \( S_1 \) means the SBN likelihood for unrooted trees can no longer be factorized. We, therefore, propose the following two algorithms to handle this challenge.

**Maximum Lower Bound Estimates** A simple strategy is to construct tractable lower bounds via variational approximations [Wainwright and Jordan, 2008]

\[
LB_q(T^u) := \sum_{S_1 \sim T^u} q(S_1) \left( \log \frac{p(S_1) \prod_{i>1} p(S_i|S_{\pi_i})}{q(S_1)} \right) \leq \log L(T^u)
\]

where \( q \) is a probability distribution on \( S_1 \sim T^u \). In particular, taking \( q \) to be uniform on the \( 2N - 3 \) tree edges together with conditional probability sharing gives the simple average (SA) lower bound of the data log-likelihood

\[
LB^{SA}(D^u) := \left( \sum_{s_1 \in C_1} m^u_{s_1} \log p(S_1 = s_1) \right) + \left( \sum_{s \in C_{ch|pa}} m^u_{s,t} \log p(s|t) \right) + K \log(2N - 3)
\]

\(^1\)The subspoints \( S_2, S_3, \ldots \) are well defined once the split in \( S_1 \) (or equivalently the root) is given.
Algorithm 1 Expectation Maximization for SBN

**Input:** Data $D^u = \{T^u_k\}_{k=1}^K$, regularization coeff $\alpha$.

Initialize $\hat{\tilde{p}}^{\text{EM},(0)}$ (e.g., via $\hat{p}^{\text{SA}}$) and $n = 0$. Set equivalent counts $\hat{m}_{n,s_1}^u, \hat{m}_{n,k,t}^u$ for regularization.

**repeat**

**E-step.** $\forall 1 \leq k \leq K$, compute $q_k^{(n)}(S_1) = \frac{p(T^u_k, S_1|\hat{\tilde{p}}^{\text{EM},(n)})}{\sum_{S_1 \sim T^u_k} p(T^u_k, S_1|\hat{\tilde{p}}^{\text{EM},(n)})}$

**M-step.** Compute the expected frequency counts with conditional probability sharing and update the CPDs by maximizing the regularized $Q$ score

$$
\hat{\tilde{p}}^{\text{EM},(n+1)}(S_1 = s_1) = \frac{\sum_{k=1}^K \sum_{s_1 \in C_r} \frac{1}{2N-3} l(s^e_1,k = s_1)}{\sum_{k=1}^K \sum_{s_1 \in C_r} \frac{1}{2N-3} \sum_{i>1} 0(s^e_1,k = s, s^e_{i,k} = t)},
$$

where

$$m_{n,s_1}^u = \sum_{k=1}^K \sum_{s_1 \in C_r} \frac{1}{2N-3} l(s^e_1,k = s_1), \quad m_{n,k,t}^u = \sum_{k=1}^K \sum_{s_1 \in C_r} \frac{1}{2N-3} \sum_{i>1} 0(s^e_1,k = s, s^e_{i,k} = t).$$

The maximum SA lower bound estimates are then

$$\hat{p}^{\text{SA}}(S_1 = s_1) = \frac{m_{n,s_1}^u}{\sum_{s \in C_r} m_{n,s}^u}, \quad s_1 \in C_r, \quad \hat{p}^{\text{SA}}(s|t) = \frac{m_{n,k,t}^u}{\sum_{s \in C_{ch|pa}} m_{n,s,t}^u}, \quad s|t \in C_{ch|pa}.$$  

**Expectation Maximization** The maximum lower bound approximations can be improved upon by adapting the variational distribution $q$, instead of using a fixed one. This, together with conditional probability sharing, leads to an extension of the expectation maximization (EM) algorithm for learning SBNs, which also allows us use of the Bayesian formulation. Specifically, at the E-step, an adaptive score is sufficient to improve the objective likelihood.

$$q_k^{(n)}(S_1) = p(S_1|T^u_k, \hat{\tilde{p}}^{\text{EM},(n)}), \quad k = 1, \ldots, K$$

given $\hat{p}^{\text{EM},(n)}$, the current estimate of the CPDs. The lower bound contains a constant term that only depends on the current estimates, and a score function for the CPDs $p$.

$$Q^{(n)}(D^u; p) = \sum_{k=1}^K Q^{(n)}(T^u_k; p) = \sum_{k=1}^K \sum_{S_1 \sim T^u_k} q_k^{(n)}(S_1) \left( \log p(S_1) + \sum_{i>1} \log p(S_i|S_{\pi_i}) \right)$$

which is then optimized at the M-step. This variational perspective of the EM algorithm was found and discussed by Neal and Hinton [1998]. The following theorem guarantees that maximizing (or improving) the $Q$ score is sufficient to improve the objective likelihood.

**Theorem 1.** Let $T^u$ be an unrooted tree. $\forall p,$

$$Q^{(n)}(T^u; p) - Q^{(n)}(T^u; \hat{\tilde{p}}^{\text{EM},(n)}) \leq \log L(T^u; p) - \log L(T^u; \hat{\tilde{p}}^{\text{EM},(n)}).$$

When data is insufficient or the number of parameters is large, the EM approach also easily incorporates regularization [Dempster et al., 1977]. Taking conjugate Dirichlet priors [Buntine, 1991], the regularized score function is

$$Q^{(n)}(D^u; \alpha \tilde{m}^u, \alpha \tilde{m}_{k,t}^u) = \sum_{s_1 \in C_r} \alpha \tilde{m}_{n,s_1}^u \log p(S_1 = s_1) + \sum_{s|t \in C_{ch|pa}} \alpha \tilde{m}_{n,s,t}^u \log p(s|t)$$

where $\tilde{m}_{n,s_1}, \tilde{m}_{n,k,t}$ are the equivalent sample counts and $\alpha$ is the global regularization coefficient. We then simply maximize the regularized score in the same manner as the M-step. Similarly, this guarantees that the regularized log-likelihood is increasing at each iteration. We summarize the EM approach in Algorithm 1. See more detailed derivation and proofs in the Appendix.
While all methods tend to perform worse as sample size $K$ and degree of diffusion $\beta$ increases and perform better as $K$ decreases. We compare algorithms performs consistently much better than CCD. Compared to SBN-SA, SBN-EM usually greatly improves the approximation with the price of additional computation. When the degree of

**Computational Complexity** Compared to those for rooted trees, the expected frequency counts $m_{s,t}^u, m_{s,t}^n, m_{s}^{u,(n)}, m_{s}^{n,(n)}$ for unrooted trees involves additional summation over all the edges. However, we can precompute all the accumulated sums of the root probabilities on the edges in a postorder tree traversal for each tree and the computation cost remains $O(KN)$. Each E-step in EM would in general cost $O(KN^2)$ time since for each tree, $O(N)$ probability estimations are required and each takes $O(N)$ time. Notice that most of the intermediate partial products involved in those SBN probability estimates are shared due to the structure of trees, we therefore use a two-pass algorithm, similar to the one used in [Schadt et al., 1998], that computes all SBN probability estimates for each tree within two loops over its edges. This reduces the computational complexity of each E-step to $O(KN)$. Overall, the computational complexities of maximum lower bound estimate and each EM iteration are both $O(KN)$, the same as CCD and SBNs for rooted trees. In practice, EM usually takes several iterations to converge and hence could be more expensive than other methods. However, the gain in approximation makes it a worthwhile trade-off (Table 1). We use the maximum SA lower bound algorithm (sbn-sa), the EM algorithm (sbn-em) and EM with regularization (sbn-em-\(\alpha\)) in the experiment section.

**Simulated Scenarios** To empirically explore the behavior of SBN algorithms relative to SRF and CCD, we first conduct experiments on a simulated setup. We choose a tractable but challenging tree space, the space of unrooted trees with 8 leaves, which contains 10395 unique trees. The trees are given an arbitrary order. To test the approximation performance on targets of different degrees of diffusion, we generate target distributions by drawing samples from the Dirichlet distributions $\text{Dir}(\beta \mathbf{1})$ of order 10395 with a variety of $\beta$s. The target distribution becomes more diffuse as $\beta$ increases. Simulated data sets are then obtained by sampling from the unrooted tree space according to these target distributions with different sample sizes $K$. The resulting probability estimation is challenging in that the target probabilities of the trees are assigned regardless of the similarity among them. For SBN-em-\(\alpha\), we adjust the regularization coefficient using $\alpha = \frac{50}{K}$ for different sample sizes $K$. Since the target distributions are known, we use KL divergence from the estimated distributions to the target distributions to measure the approximation accuracy of different methods. We vary $\beta$ and $K$ to control the difficulty of the learning task, and average over 10 independent runs for each configuration. Figure 4 shows the empirical approximation performance of different methods. We see that the learning rate of CCD slows down very quickly as the data size increases, implying that the conditional clade independence assumption could be too strong to provide flexible approximations. On the other hand, SBN-EM keeps learning efficiently from the data when more samples are available. While all methods tend to perform worse as $\beta$ increases and perform better as $K$ increases, SBN algorithms performs consistently much better than CCD. Compared to SBN-SA, SBN-EM usually greatly improves the approximation with the price of additional computation. When the degree of
We will compare various posterior estimates based on standard runs. For these standard runs, we perform an additional study on training data size, we collect the posterior samples every 100 iterations of these runs and discard the first 25% as burn-in for a total of 7.5 million posterior samples per data set. These extremely long “golden runs” form the ground truth to which we compare the results from each method.

Previous work [Whidden and Matsen, 2015] has observed that conditional clade independence does not hold in multimodal distributions. Figure 5 shows a comparison on a typical data set, DS1, that has such a “peaky” distribution. We see that CCD underestimates the probability of trees within the subpeak and overestimate the probability of trees between peaks. In contrast, \( \text{sbn-em-} \alpha \) gives much better performance than the others, showing that regularization indeed improves generalization.

### Table 1: Data sets used for phylogenetic posterior estimation, and approximation accuracy results of different methods across datasets. Sampled trees column shows the numbers of unique trees in the standard run samples. The results are averaged over 10 replicates.

| Data set | Reference | Tree size | Sampled trees | KL divergence to ground truth |
|----------|-----------|-----------|---------------|-------------------------------|
| DS1      | Hedges et al. [1990] | (27, 1949) | 5.84 x 10^12 | 1228 | 0.0155 | 0.6027 | 0.0687 | 0.0136 | 0.0130 |
| DS2      | Garey et al. [1996]  | (29, 2520) | 1.58 x 10^15 | 7   | **0.0122** | 0.0218 | 0.0218 | 0.0199 | 0.0128 |
| DS3      | Yang and Yoder [2003] | (36, 1812) | 4.39 x 10^10 | 43  | 0.5539 | 0.2074 | 0.1152 | 0.1243 | **0.0882** |
| DS4      | Henk et al. [2003] | (41, 1137) | 1.01 x 10^12 | 828 | 0.5322 | 0.1952 | 0.1021 | 0.0763 | **0.0637** |
| DS5      | Lakner et al. [2008] | (50, 378)  | 2.84 x 10^11 | 33752 | 11.5746 | 1.3272 | 0.8932 | 0.8599 | **0.8218** |
| DS6      | Zhang and Blackwell [2001] | (50, 1153) | 2.84 x 10^13 | 35407 | 10.0159 | 0.4526 | **0.2613** | 0.3016 | 0.2766 |
| DS7      | Yoder and Yang [2004] | (59, 1824) | 4.36 x 10^12 | 1125 | 1.2765 | 0.3292 | 0.2341 | 0.0483 | **0.0399** |
| DS8      | Rossman et al. [2001] | (64, 1088) | 1.04 x 10^13 | 3067 | 2.1653 | 0.4149 | 0.2212 | 0.1415 | **0.1236** |

When applied to a broad range of data sets, we find that SBNS consistently outperform other methods (Table 1). Due to its inability to generalize beyond observed samples, SRF is worse than generalizing probability estimators except for an exceedingly simple posterior with only 7 sampled trees (DS2). CCD is, again, comparatively much worse than SBN algorithms. With weak regularization, \( \text{sbn-em-} \alpha \) gives the best performance in most cases.

To illustrate the efficiency of the algorithms on training data size, we perform an additional study on DS1 with increasing sample sizes and summarize the results in the right panel of Figure 5. As before,
we see that CCD slows down quickly while SBN algorithms, especially fully-capable SBN estimators sbn-em and sbn-em-α, keep learning efficiently as the sample size increases. Moreover, SBN algorithms tend to provide much better approximation than SRF when fewer samples are available, which is important in practice where large samples are expensive to obtain.

6 Conclusion

We have proposed a general framework for tree probability estimation based on subsplit Bayesian networks. SBNs allow us to exploit the similarity among trees to provide a wide range of flexible probability estimators that generalize beyond observations. Moreover, they also allow many efficient Bayesian network learning algorithms to be extended to tree probability estimation with ease. We report promising numerical results demonstrating the importance of being both flexible and generalizing when estimating probabilities on trees. Although we present SBNs in the context of leaf-labeled bifurcating trees, it can be easily adapted for general leaf-labeled trees by allowing partitions other than subsplits (bipartitions) of the clades in parent nodes. We leave for future work investigating the performance of more complicated SBNs for general trees and further applications of SBNs to other probabilistic learning problems in tree spaces, such as designing more efficient tree proposals for MCMC transition kernels and providing flexible and tractable distributions for variational inference.

References

W. Buntine. Theory refinement on Bayesian networks. In B. D’Ambrosio, P. Smets, and P. Bonissone, editors, Proceedings of the 7th Conference on Uncertainty in Artificial Intelligence, pages 52–60. Morgan Kaufmann, 1991.

A. P. Dempster, N. M. Laird, and D. B. Rubin. Maximum likelihood from incomplete data via the EM algorithm. Journal of the Royal Statistical Society Series B, 39:1–38, 1977.

Rob DeSalle and George Amato. The expansion of conservation genetics. Nat. Rev. Genet., 5(9): 702–712, September 2004. ISSN 1471-0056. doi: 10.1038/nrg1425. URL http://dx.doi.org/10.1038/nrg1425.

J. Felsenstein. Inferring Phylogenies. Sinauer Associates, 2nd edition, 2003.

N. Friedman, M. Ninio, I. Pe’er, and T. Pupko. A structural EM algorithm for phylogenetic inference. Journal of Computational Biology, 9(2):331–353, 2002.

J. R. Garey, T. J. Near, M. R. Nonnemacher, and S. A. Nadler. Molecular evidence for Acanthocephala as a subtaxon of Rotifera. Mol. Evol., 43:287–292, 1996.

S. B. Hedges, K. D. Moberg, and L. R. Maxson. Tetrapod phylogeny inferred from 18S and 28S ribosomal RNA sequences and review of the evidence for amniote relationships. Mol. Biol. Evol., 7:607–633, 1990.

D. A. Henk, A. Weir, and M. Blackwell. Laboulbeniopsis termitarius, an ectoparasite of termites newly recognized as a member of the Laboulbeniomyces. Mycologia, 95:561–564, 2003.

S. Höhna, T. A. Heath, B. Boussau, M. J. Landis, F. Ronquist, and J. P. Huelsenbeck. Probabilistic graphical model representation in phylogenetics. Syst. Biol., 63:753–771, 2014.

Sebastian Höhna and Alexei J. Drummond. Guided tree topology proposals for bayesian phylogenetic inference. Syst. Biol., 61(1):1–11, January 2012. ISSN 1063-5157. doi: 10.1093/sysbio/syr074. URL http://dx.doi.org/10.1093/sysbio/syr074.

J. P. Huelsenbeck and F. Ronquist. MrBayes: Bayesian inference of phylogeny. Bioinformatics, 17: 754–755, 2001.

J. P. Huelsenbeck, F. Ronquist, R. Nielsen, and J. P. Bollback. Bayesian inference of phylogeny and its impact on evolutionary biology. Science, 294:2310–2314, 2001.

T. H. Jukes and C. R. Cantor. Evolution of protein molecules. In H. N. Munro, editor, Mammalian protein metabolism, III, pages 21–132, New York, 1969. Academic Press.
C. Lakner, P. van der Mark, J. P. Huelsenbeck, and B. Larget and F. Ronquist. Efficiency of Markov chain Monte Carlo tree proposals in Bayesian phylogenetics. *Syst. Biol.*, 57:86–103, 2008.

Bret Larget. The estimation of tree posterior probabilities using conditional clade probability distributions. *Syst. Biol.*, 62(4):501–511, July 2013. ISSN 1063-5157. doi: 10.1093/sysbio/syt014. URL http://dx.doi.org/10.1093/sysbio/syt014.

Y. LeCun, L. Bottou, Y. Bengio, and P. Haffner. Gradient based learning applied to document recognition. *Proceedings of the IEEE*, 86(11):2278–2324, 1998.

B. Mau, M. Newton, and B. Larget. Bayesian phylogenetic inference via Markov chain Monte Carlo methods. *Biometrics*, 55:1–12, 1999.

R. M. Neal and G. E. Hinton. A view of the em algorithm that justifies incremental, sparse, and other variants. *Learning in Graphical Models*, 89:355–368, 1998.

Richard A Neher and Trevor Bedford. nextflu: Real-time tracking of seasonal influenza virus evolution in humans. *Bioinformatics*, June 2015. ISSN 1367-4803, 1367-4811. doi: 10.1093/bioinformatics/btv381. URL http://dx.doi.org/10.1093/bioinformatics/btv381.

F. Ronquist, M. Teslenko, P. van der Mark, D. L. Ayres, A. Darling, S. Hohna, B. Larget, L. Liu, M. A. Shchard, and J. P. Huelsenbeck. MrBayes 3.2: efficient Bayesian phylogenetic inference and model choice across a large model space. *Syst. Biol.*, 61:539–542, 2012.

A. Y. Rossman, J. M. Mckemy, R. A. Pardo-Schultheiss, and H. J. Schroers. Molecular studies of the Bionectriaceae using large subunit rDNA sequences. *Mycologia*, 93:100–110, 2001.

Eric E. Schadt, Janet S. Sinsheimer, and Kenneth Lange. Computational advances in maximum likelihood methods for molecular phylogeny. *Genome Res.*, 8:222–233, 1998. doi: 10.1101/gr.8.3.222.

K. Strimmer and V. Moulton. Likelihood analysis of phylogenetic networks using directed graphical models. *Molecular biology and evolution*, 17:875–881, 2000.

M. J. Wainwright and M. I. Jordan. Graphical models, exponential families, and variational inference. *Foundations and Trends in Maching Learning*, 1(1-2):1–305, 2008.

Chris Whidden and Frederick A Matsen, IV. Quantifying MCMC exploration of phylogenetic tree space. *Syst. Biol.*, 64(3):472–491, May 2015. ISSN 1063-5157, 1076-836X. doi: 10.1093/sysbio/syv006. URL http://dx.doi.org/10.1093/sysbio/syv006.

Z. Yang and B. Rannala. Bayesian phylogenetic inference using DNA sequences: a Markov chain Monte Carlo method. *Mol. Biol. Evol.*, 14:717–724, 1997.

Z. Yang and A. D. Yoder. Comparison of likelihood and Bayesian methods for estimating divergence times using multiple gene loci and calibration points, with application to a radiation of cute-looking mouse lemur species. *Syst. Biol.*, 52:705–716, 2003.

A. D. Yoder and Z. Yang. Divergence data for Malagasy lemurs estimated from multiple gene loci: geological and evolutionary context. *Mol. Ecol.*, 13:757–773, 2004.

N. Zhang and M. Blackwell. Molecular phylogeny of dogwood anthracnose fungus (Discula destructiva) and the Diaporthales. *Mycologia*, 93:355–365, 2001.

A Proof of Lemma 1

Proof. It suffices to prove the lemma for the minimum SBN $B^*_X$. For any rooted tree $T$, with natural indexing, a compatible assignment is easy to obtain by following the splitting process and satisfying the compatibility requirement defined in Definition 2. Moreover, the depth of the splitting process is at most $N - 1$, where $N$ is the size of $X$. To show this, consider the maximum size of clades, $d_i$, in the $i$-th level of the process. The first level is for the root split, and $d_1 \leq N - 1$ since the subclades need to be proper subset of $X$. For each $i > 1$, if $d_i > 1$, the splitting process continues and the
maximum size of clades in the next level is at most \(d_i - 1\), that is \(d_{i+1} \leq d_i - 1\). Note that the split process ends when \(d_i = 1\), its depth therefore is at most \(N - 1\). The whole process is deterministic, so each rooted tree can be uniquely represented as a compatible assignment of \(B^*_X\). On the other hand, given a compatible assignment, we can simply remove all fake splits. The remaining net corresponds to the true splitting process of a rooted tree, which then can be simply restored.

\[\square\]

**B Proof of Proposition 1**

**Proof.** Denote the set of all SBN assignments as \(A\). For any assignment \(a = \{S_i = s_i^a\}_{i \geq 1}\), we have

\[p_{sbn}(a) = p(S_1 = s_1^a) \prod_{i > 1} p(S_i = s_i^a | S_{\pi_i} = s_{\pi_i}^a) > 0 \Rightarrow a \text{ is compatible.} \tag{7}\]

As a Bayesian network,

\[\sum_{a \in A} p_{sbn}(a) = \sum_{s_1} p(S_1 = s_1) \prod_{i > 1} \sum_{s_i} p(S_i = s_i | S_{\pi_i} = s_{\pi_i}) = 1.\]

By Lemma 1,

\[\sum_T p_{sbn}(T) = \sum_{a \sim \text{compatible}} p_{sbn}(a) = \sum_{a \in A} p_{sbn}(a) = 1.\]

\[\square\]

**C Figure for Shared Parent-child Subsplit Pairs in SBNs**

![Figure 6: Subsplit pairs shared among different nodes in SBNs. Top panels show the rooted trees that share the same local parent-child subsplit pair \((B, C), D\). Bottom panels are their corresponding representations in SBNs. Just like in the trees, the same pair could appear at multiple locations in SBNs.]

**D Proof of Proposition 2**

**Proof.**

\[\sum_{T^u} p_{sbn}(T^u) = \sum_{T^u} \sum_{S_1 \sim T^u} p(S_1) \prod_{i > 1} p(S_i | S_{\pi_i})\]

\[= \sum_{T} p_{sbn}(T) = 1.\]
The second equality is due to the one-to-one correspondence between rooted trees and unrooted trees with specific rooting edges (compatible splits):

\[ T \xrightarrow{T \cup \pi} (T^u, S_1), \quad S_1 \sim T^u. \]

\[ \square \]

### E On Expectation Maximization for SBNs

Using the conditional probabilities of the missing root node, we can construct the following adaptive lower bound

\[
LB^{(n)}(T^u; p) = \sum_{S_1 \sim T^u} p(S_1|T^u, \hat{p}^{EM,(n)}) \log \left( \frac{p(S_1) \prod_{i>1} p(S_i|S_{\pi_i})}{p(S_1|T^u, \hat{p}^{EM,(n)})} \right) \leq \log L(T^u; p). \tag{8}
\]

The above adaptive lower bound \( LB^{(n)}(T^u; p) \) contains a constant term that only depends on the current estimates, and another term that is the expected complete log-likelihood with respect to the conditional distribution of \( S_1 \) given \( T^u \) and the current estimates:

\[
Q^{(n)}(T^u; p) = \sum_{S_1 \sim T^u} p(S_1|T^u, \hat{p}^{EM,(n)}) \left( \log p(S_1) + \sum_{i>1} \log p(S_i|S_{\pi_i}) \right). \tag{9}
\]

Summing (9) over \( T^u \in D^u \) together with conditional probability sharing, we get the complete data score function

\[
Q^{(n)}(D^u; p) = \sum_{k=1}^K Q^{(n)}(T^u_k; p)
= \sum_{k=1}^K \sum_{e \in E(T^u_k)} q^{(n)}(S_1 = s_{1,k}^e) \left( \log p(S_1 = s_{1,k}^e) + \sum_{i>1} \log p(S_i = s_{i,k}^e|S_{\pi_i} = s_{\pi_i,k}^e) \right)
= \sum_{s_1 \in C_r} \bar{m}^{u,(n)}_{s_1} \log p(S_1 = s_1) + \sum_{s \in t \in C_{ch|pa}} \bar{m}^{u,(n)}_{s,t} \log p(s|t) \tag{10}
\]

where

\[
\bar{m}^{u,(n)}_{s_1} = \sum_{k=1}^K \sum_{e \in E(T^u_k)} q^{(n)}(S_1 = s_{1,k}^e) \log(s_{1,k}^e = s_1)
\]

and

\[
\bar{m}^{u,(n)}_{s,t} = \sum_{k=1}^K \sum_{e \in E(T^u_k)} q^{(n)}(S_1 = s_{1,k}^e) \sum_{i>1} \log(s_{i,k}^e = s, s_{\pi_i,k}^e = t)
\]

are the expected frequency counts.

#### E.1 Proof of Theorem 1

**Proof.**

\[
Q^{(n)}(T^u; p) - Q^{(n)}(T^u; \hat{p}^{EM,(n)}) = LB^{(n)}(T^u; p) - LB^{(n)}(T^u; \hat{p}^{EM,(n)}) \leq \log L(T^u; p) - \log L(T^u; \hat{p}^{EM,(n)})
\]
With Theorem 1, it is clear that

\[ Q(n)(D^u; p) - Q(n)(D^u; \hat{p}_{\text{EM}}(n)) \leq \log L(D^u; p) - \log L(D^u; \hat{p}_{\text{EM}}(n)). \]

As before, the maximum estimates of \( Q(n) \) have closed form expressions which lead to the following updating formula for the CFDs at the M-step

\[ \hat{p}_{\text{EM},(n+1)}(S_1 = s_1) = \frac{\overline{m}_{s_1}^{u,(n)}}{\sum_{s \in \mathcal{C}_r} \overline{m}_{s}^{u,(n)}} = \frac{\overline{m}_{s_1}^{u,(n)}}{K}, \quad s_1 \in \mathcal{C}_r \]

\[ \hat{p}_{\text{EM},(n+1)}(s|t) = \frac{\overline{m}_{s,t}^{u,(n)}}{\sum_{s} \overline{m}_{s,t}^{u,(n)}}, \quad s|t \in \mathcal{C}_{\text{ch}|\text{pa}}. \]

\[ \hat{p}(p | S_1 = s_1) = \alpha S_1 + 1, \quad \hat{p}(p | s|t) = \alpha S_1 + 1, \quad s|t \in \mathcal{C}_{\text{ch}|\text{pa}}. \]

where \( \alpha_{s_1} > 0, \alpha_{s,t} > 0 \) are some hyper-parameters. The regularized score function, therefore, takes the following form

\[ Q^{R,(n)}(D^u; p) = Q(n)(D^u; p) + \sum_{s_1 \in \mathcal{C}_r} \alpha_{s_1} \log p(S_1 = s_1) + \sum_{s|t \in \mathcal{C}_{\text{ch}|\text{pa}}} \alpha_{s,t} \log p(s|t) \]

\[ = \sum_{s_1 \in \mathcal{C}_r} (\overline{m}_{s_1}^{u,(n)} + \alpha_{s_1}) \log p(S_1 = s_1) + \sum_{s|t \in \mathcal{C}_{\text{ch}|\text{pa}}} (\overline{m}_{s,t}^{u,(n)} + \alpha_{s,t}) \log p(s|t). \]

One can adapt the hyper-parameters according to this decomposition as follows

\[ \alpha_{s_1} = \alpha \cdot \overline{m}_{s_1}^{u}, \quad \alpha_{s,t} = \alpha \cdot \overline{m}_{s,t}^{u}, \]

where \( \alpha \) is the global regularization coefficient that balances the effect of the data on the estimates in comparison to the prior, and \( \overline{m}_{s_1}^{u}, \overline{m}_{s,t}^{u} \) are the equivalent sample counts for the root splits and parent-child subsplit pairs that distribute the regularization across the CFDs. In practice, one can simply use the the sample frequency counts as equivalent sample counts as we did in our experiments.

**Remark:** The choice of hyper-parameter setting is not throughly studied and what we do here is some modification from the common practice in Bayesian estimation for learning Bayesian networks; see Buntine [1991] for more details.

Theorem 1 also implies that maximizing (or improving) the regularized Q score is sufficient to improve the regularized log-likelihood. Denote the regularization term as

\[ R(p) = \sum_{s_1 \in \mathcal{C}_r} \alpha \overline{m}_{s_1}^{u} \log p(S_1 = s_1) + \sum_{s|t \in \mathcal{C}_{\text{ch}|\text{pa}}} \alpha \overline{m}_{s,t}^{u} \log p(s|t) \]
we have
\[ Q^{R,(n)}(D^u; p) - Q^{R,(n)}(D^u; \hat{p}^{EM,(n)}) = Q^{(n)}(D^u; p) - Q^{(n)}(D^u; \hat{p}^{EM,(n)}) + R(p) - R(\hat{p}^{EM,(n)}) \leq \log L(D^u; p) + R(p) - (\log L(D^u; \hat{p}^{EM,(n)}) + R(\hat{p}^{EM,(n)})) \].

Similarly, the regularized score \( Q^{R,(n)} \) can be maximized in the same manner as \( Q^{(n)} \)

\[ \hat{p}^{EM,(n+1)}(S_1 = s_1) = \frac{\overline{m}_{s_1}^{u,(n)} + \alpha \overline{\tilde{m}}_{s_1}^{u}}{\sum_{s_1 \in S}(\overline{m}_{s_1}^{u,(n)} + \alpha \overline{\tilde{m}}_{s_1}^{u})} = \frac{\overline{m}_{s_1}^{u,(n)} + \alpha \overline{\tilde{m}}_{s_1}^{u}}{K + \alpha \sum_{s_1 \in S} \overline{\tilde{m}}_{s_1}^{u}}, \quad s_1 \in C_r \tag{14} \]

\[ \hat{p}^{EM,(n+1)}(s|t) = \frac{\overline{m}_{s,t}^{u,(n)} + \alpha \overline{\tilde{m}}_{s,t}^{u}}{\sum_{s}(\overline{m}_{s,t}^{u,(n)} + \alpha \overline{\tilde{m}}_{s,t}^{u})}, \quad s|t \in C_{chpa} \tag{15} \]