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Ascertainment correction for a population tree via a pruning algorithm for likelihood computation

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Abstract

We present a method for correcting ascertainment-bias in a coalescent-based likelihood for population trees. Our method is computationally simple and fast. To correct for the bias we compute the probability of allele-counts conditioned on the locus being included. This conditional probability is simply the uncorrected likelihood divided by the inclusion probability. A modification of a pruning algorithm is introduced so that the inclusion probability can be computed with a single run of the algorithm. Our computation is exact and avoids Monte-Carlo based methods.

Keywords

phylogeny; population tree; pruning; ascertainment; likelihood

1 Introduction

Ascertainment is the process of selecting observational or experimental units for inclusion in a study. If these units are genetic single nucleotide polymorphism (SNP) loci, several considerations apply.

The SNPs with a small minor allele frequency provide little information for some genetic analyses (see, for example, Clayton [3]). Geneticists may therefore ascertain the sample so that each SNP locus has at least a few copies of the minor allele. Various SNP selection criteria exist in practice, with different criteria affecting the data differently. It is not uncommon for the selection process to use a complicated assortment of criteria. For example, the HapMap project ([4]) uses many pieces of information to identify SNPs (Clark et al. [2]).

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The ascertainment process distorts the allele frequency spectrum of the SNPs chosen for the study as well as the whole distribution of data outcomes. If the distortion of this distribution is not corrected for, an erroneous inference may result. For example, see, Clark et al. [2], for some illustrations of how ascertainment-bias can affect inference. Also, later in this article we illustrate how failure to correct for ascertainment-bias may introduce bias in the branch length estimates of population tree. Thus, correcting for the effect of ascertainment is a necessary part of a study involving SNP allele frequencies or counts.

Whereas no known analysis (including our method) can fully correct for ascertainment bias in a data collected using a highly complicated ascertainment strategy like HapMap (see, for example, Clark et al. [2]), using our method one will be able to correct for ascertainment-bias in data with where the ascertainment strategies are known and constant across the loci.

We implement a fast and simple method for correcting ascertainment bias when computing the likelihood of a population tree from SNP allele frequency spectra. The uncorrected likelihood is computed using the pruning algorithm of RoyChoudhury et al. [9].

To correct for the ascertainment bias we need to compute the probability of inclusion; that is, the sum of the probabilities of all outcomes that make up the ascertainment event (see, for example, Nielsen and Slatkin [7]). In the context of phenotypic data on pedigrees Elston [5] and Elston and Yelverton [6] used a pedigree peeling computation to obtain the probability of the ascertainment event. Analogously, in the case of population trees, we use the pruning algorithm of RoyChoudhury et al. [9], to compute the inclusion probability for several commonly used ascertainment strategies. The probability of sample allele counts falling within a specified set can be computed once only with a single application of the pruning algorithm. Thus our algorithm is computationally much faster than an approach which requires computation of the inclusion-probability for each SNP.

2 Theory and methods

As in RoyChoudhury et al. [9], we assume that loci are sufficiently far apart that the allele counts are independent and the loci have independent coalescent events. We will use the term “independent loci” to refer to such a set of loci. Consequently, the likelihood from L loci is the product of the likelihoods from each locus. Therefore, we only need to consider the computation of likelihood from a single locus. We also assume that each locus has two alleles, arbitrarily named ‘0’ and ‘1’.

As in RoyChoudhury et al. [9], the population-tree is specified by a set of parameters: the branch lengths, the tree-topology and a mutation parameter θ_0 at the root. (Note that, we denote the root as node 0.) The branch lengths are scaled units of generations. We assume, as in RoyChoudhury et al. [9], that the allele frequency spectrum at the root follows a symmetric Beta distribution with θ_0 as its sole parameter.

To describe the data and the related latent variables, we will use the notation of RoyChoudhury et. al [9] throughout this paper. For readers’ convenience, the notation is given in Table 1 and Figure 1. We term “a location just below a node, in the branch coming from the left (or right) side of the node x ”, to mean a time-point x' (on the left branch or the

right branch coming from the node), that is infinitesimally close to x (so that no coalescent event could have taken place between x and x').

2.1 The pruning algorithm

The pruning algorithm (RoyChoudhury et al. [9]) works by computing two arrays of conditional probabilities at each node. The arrays at each tip are computed from the data at the tip. Then the arrays at each non-tip node x are computed from the nodes directly below x (see Figures 1 and 2). Thus, the arrays for all the nodes are computed, moving upward node by node (see Figure 2). Eventually the arrays at the root are computed, and the likelihood is computed from these arrays.

Two arrays $A(x)$ and $B(x)$ are computed at each node x :

$$A(x) = \left(Pr(n_x = i), i = 1, 2, \dots, m_x^{(b)} \right),$$

where n_x is the number of lineages at node x and $m_x^{(b)}$ is the total number of gene copies sampled at or below node x ;

$$B(x) = \left(\left(Pr(s_x^{(b)} | n_x = i, r_x = j), j = 0, 1, 2, \dots, i \right), i = 1, 2, \dots, m_x^{(b)} \right), \quad (1)$$

where $S_x^{(b)}$ is all the data at or below node x and r_x is the allele-count (the count of '1' alleles) out of n_x lineages at node x . Thus,

$$A(x)_i = Pr(n_x = i); \quad B(x)_{ij} = Pr(s_x^{(b)} | n_x = i, r_x = j).$$

Two similar arrays ($A^{(L)}(x)$ and $B^{(L)}(x)$) are also computed for the point just below, and coming from the left side of node x :

$$A^{(L)}(x) = \left(Pr(n_x^{(L)} = i), i = 1, 2, \dots, m_x^{(b,L)} \right),$$

where $n_x^{(L)}$ is the number of lineages just below node x , in the branch coming from the left side of x and $m_x^{(b,L)}$ is the total number of gene copies sampled at or below the branch coming from the left side of node x ;

$$B^{(L)}(x) = \left(\left(Pr(s_x^{(b,L)} | n_x^{(L)} = i, r_x^{(L)} = j), j = 0, 1, 2, \dots, i \right), i = 1, 2, \dots, m_x^{(b,L)} \right), \quad (2)$$

where $s_x^{(b,L)}$ is all the data at or below the branch coming from the left side of node x and $r_x^{(L)}$ is the allele-count (out of $n_x^{(L)}$ lineages) just below node x , in the branch coming from the left side of x . Thus,

$$A^{(L)}(x)_i = Pr(n_x^{(L)} = i); \quad B^{(L)}(x)_{ij} = Pr(s_x^{(b,L)} | n_x^{(L)} = i, r_x^{(L)} = j).$$

The arrays $A^{(R)}(x)$ and $B^{(R)}(x)$ are similarly computed for each point just below, and coming from the right side of node x .

Consider a branch with nodes z and y at its top and bottom respectively. Without loss of generality, assume that the branch is on the left bottom side of z . “Step 1” in Figure 2 is the computation of the arrays $(A^{(L)}(z)$ and $B^{(L)}(z)$) at the top of the branch from the arrays $(A(y)$ and $B(y))$ at the bottom of the branch. In “Step 2” we combine the arrays of probabilities $(A^{(L)}(x)$, $B^{(L)}(x)$, $A^{(R)}(x)$ and $B^{(R)}(x)$) at the common top point x of the two branches and thus derive the arrays at x ($A(x)$, $B(x)$). In Appendix A we state the formulae used by RoyChoudhury et al. [9] for the computations of Steps 1 and 2.

Repeating Steps 1 and 2 (Figure 2), we eventually compute the arrays $A(0)$ and $B(0)$ at the root of the tree, and then the likelihood is computed as

$$L(\tau) = \sum_{i=1}^{m_0^{(b)}} \sum_{j=0}^i B(0)_{ij} A(0)_i \binom{i}{j} \left(\frac{\beta(j+\theta, i-j+\theta)}{\beta(\theta, \theta)} \right), \quad (3)$$

where τ is the vector containing all the branch lengths and $m_0^{(b)}$ is the total number of gene copies sampled below the root, equivalently, the total number of gene copies sampled in all the populations.

2.2 Ascertainment Corrections

Each ascertainment strategy is characterized by a rejection set R which is a subset of the set of all possible allele-count matrices, as described below. Suppose that D_{i1} and D_{i2} are the numbers of ‘1’ and ‘0’ alleles (respectively) observed in population i and

$$\mathbf{D} = \begin{pmatrix} D_{11} & D_{12} \\ D_{21} & D_{22} \\ \dots & \dots \\ D_{P1} & D_{P2} \end{pmatrix},$$

the matrix of allele-counts from a locus l . For example, suppose we have three populations with 20 haploids from each population and the observed number of ‘1’ alleles are 16, 2 and 5 respectively from the three populations. (As in RoyChoudhury et al. [9], haploid is our sampling unit.) Then

$$\mathbf{D} = \begin{pmatrix} 16 & 4 \\ 2 & 18 \\ 5 & 15 \end{pmatrix}.$$

Let U be the set of all possible values $\mathbf{D}$ can take. Each ascertainment strategy is characterized by a rejection set R (which is a subset of U) as follows. If $\mathbf{D}$ falls into R , then l is excluded. The set R^C , which is the complement of R , is the acceptance set. If $\mathbf{D}$ falls into R^C , then l is included.

For an ascertainment based on the current sample, the corrected likelihood from a locus (given that it is included in the study) is

$$L(\tau|\mathbf{D}=\mathbf{d})=Pr(\mathbf{D}=\mathbf{d}|\mathbf{D} \in R^C)=\frac{Pr(\mathbf{D}=\mathbf{d})}{Pr(\mathbf{D} \in R^C)}, \quad (4)$$

where $Pr(\mathbf{D}=\mathbf{d})$ is the uncorrected likelihood. Suppose that an ascertainment is done based on a previous sample. Let the matrix of allele-counts in the previous sample be

$$\mathbf{D}^{(v)}=\begin{pmatrix} D_{11}^{(v)} & D_{12}^{(v)} \\ D_{21}^{(v)} & D_{22}^{(v)} \\ \vdots & \vdots \\ D_{p1}^{(v)} & D_{p2}^{(v)} \end{pmatrix},$$

where $D_{i1}^{(v)}$ and $D_{i2}^{(v)}$ are the numbers of '1' and '0' alleles (respectively) observed in population i in the previous sample. Then the correct likelihood is

$$\begin{aligned} L(\tau|\mathbf{D}=\mathbf{d}, \mathbf{D}^{(v)}=\mathbf{d}^{(v)}) &\propto Pr(\mathbf{D}+\mathbf{D}^{(v)}=\mathbf{d}+\mathbf{d}^{(v)}|\mathbf{D}^{(v)} \in R^C) \\ &= \frac{Pr(\mathbf{D}+\mathbf{D}^{(v)}=\mathbf{d}+\mathbf{d}^{(v)})}{Pr(\mathbf{D}^{(v)} \in R^C)}. \end{aligned} \quad (5)$$

Eq. 5 follows from the fact that

$$\frac{Pr(\mathbf{D}+\mathbf{D}^{(v)}=\mathbf{d}+\mathbf{d}^{(v)}|\mathbf{D}^{(v)} \in R^C)}{Pr(\mathbf{D}=\mathbf{d}, \mathbf{D}^{(v)}=\mathbf{d}^{(v)}|\mathbf{D}^{(v)} \in R^C)}$$

is free of τ , and thus the probability of observing allele-counts $\mathbf{d}$ and $\mathbf{d}^{(v)}$ in the two samples from P populations is a constant multiple (upto τ) of the probability of observing allele-counts $\mathbf{d} + \mathbf{d}^{(v)}$ in a combined sample. Another way of looking at it is that $Pr(\mathbf{D}=\mathbf{d}, \mathbf{D}^{(v)}=\mathbf{d}^{(v)}|\mathbf{D}+\mathbf{D}^{(v)}=\mathbf{d}+\mathbf{d}^{(v)})$ is free of τ and depends only on the sample sizes and allele counts, and thus it can be ignored while computing the likelihood.

If $\mathbf{d}^{(v)}$ is not available, then the corrected likelihood is

$$L(\tau|\mathbf{D}=\mathbf{d})=Pr(\mathbf{D}=\mathbf{d}|\mathbf{D}^{(v)} \in R^C)=\frac{Pr(\mathbf{D}=\mathbf{d}, \mathbf{D}^{(v)} \in R^C)}{Pr(\mathbf{D}^{(v)} \in R^C)} \propto \frac{Pr(\mathbf{D}+\mathbf{D}^{(v)} \in G)}{Pr(\mathbf{D}^{(v)} \in R^C)}, \quad (6)$$

where

$$G=\mathbf{d}+R^C=\{X:X=\mathbf{d}+Y, Y \in R^C\}.$$

Thus, the expressions for the corrected likelihoods in Eqs. (4), (5) and (6) involve probabilities of the allele-count matrices ($\mathbf{D}$ and $\mathbf{D}^{(v)}$) falling into a set. In the Eq. (4) the expression for the corrected likelihoods is the ratio between the probability of the allele count and the probability of the allele count falling into the acceptance set R^C . In the Eq. (5)

the expression for the corrected likelihoods is the joint probability of the current and the previous sample divided by the probability of the allele count (in the previous sample) falling into the acceptance set R^C . In the Eq. (6) the expression for the corrected likelihoods is the joint probability of the current sample and the event that the previous sample falls into the acceptance set R^C divided by the probability of the previous sample falling into R^C . An efficient way of computing the corrected likelihood is demonstrated in Subsection 2.3.

2.3 Probability of the allele-counts falling into a set

Claim—Consider a set

$$S = S_1 \times S_2 \times \dots \times S_P, \quad (7)$$

where S_i is a set of allele-counts at Population i at the tip of the tree; S is a set of the matrix of allele-counts. Then, if we substitute $B(x)_{ij}$, $B^{(L)}(x)_{ij}$ and $B^{(R)}(x)_{ij}$ (defined in Subsection 2.1) with

$$B(x)_{ij}^* = \sum_{s_x^{(b)} \in S_x^{(b)}} B(x)_{ij}, B^{(L)}(x)_{ij}^* = \sum_{s_x^{(b,L)} \in S_x^{(b,L)}} B^{(L)}(x)_{ij} \text{ and } B^{(R)}(x)_{ij}^* = \sum_{s_x^{(b,R)} \in S_x^{(b,R)}} B^{(R)}(x)_{ij}$$

(for each node x) in the pruning algorithm, then it would yield the probability of the allele-count matrix falling into S . Here

$$S_x^{(b)} = \prod_{i \in T_x} S_i; \quad S_x^{(b,L)} = \prod_{i \in T_x^{(L)}} S_i; \quad S_x^{(b,R)} = \prod_{i \in T_x^{(R)}} S_i;$$

T_x is the set of all tips at or below x ; $T_x^{(L)}$ and $T_x^{(R)}$ are the sets of all tips at or below the branch coming from the left and the right sides of x respectively.

We prove this in Appendix B by showing that the summations in the expression of $B(x)_{ij}^*$, $B^{(L)}(x)_{ij}^*$ and $B^{(R)}(x)_{ij}^*$ can be commuted through every step of the pruning algorithm. Note that $B(x)_{ij}^*$ is the array of probabilities (of the allele-count matrix at the tips falling into a given set) given the number of lineages and allele-counts at node x . $B^{(L)}(x)_{ij}^*$ and $B^{(R)}(x)_{ij}^*$ are the arrays of probabilities (of the allele-count matrix at the tips falling into a given set) given the number of lineages and allele-counts just below x at the left and right branch respectively. These are same as $B(x)_{ij}$, $B^{(L)}(x)_{ij}$ and $B^{(R)}(x)_{ij}$, except that they are probabilities of a set of allele counts rather than a single value of allele count.

Note that although we have considered only the sets of the form (7) in this section, the result also holds for any other set. This is because any set can be expressed as a disjoint union of the sets of the form (7). So, the probability of the whole set can be computed as the sum over probabilities of each disjoint set. Consider a three-population tree with sample size n at each population. If the rejection set

$$R = \{F_0^{(n)}, F_1^{(n)}\} \cup \{F_n^{(n)}, F_{n-1}^{(n)}\},$$

where

$$F_i^{(n)} = \begin{pmatrix} i & n-i \\ i & n-i \\ i & n-i \end{pmatrix}.$$

then

$$Pr(R) = Pr(\{F_0^{(n)}, F_1^{(n)}\}) + Pr(\{F_n^{(n)}, F_{n-1}^{(n)}\}).$$

3 Results

To test the performance of our method, we performed some simulation studies. In the first study, the data consist of allele-counts in 50 haploids from each of three different populations. We have simulated data for 50 independent SNP loci. Each SNP was required to meet the criterion that its minor allele is observed to have at least two copies in the sample collected from at least one population. Thus, the rejection set

$$R = \{\{F_0^{(n_1, n_2, n_3)}, F_1^{(n_1, n_2, n_3)}\}\} \cup \{\{F_{-0}^{(n_1, n_2, n_3)}, F_{-1}^{(n_1, n_2, n_3)}\}\},$$

where

$$F_i^{(n_1, n_2, n_3)} = \begin{pmatrix} i & n_1-i \\ i & n_2-i \\ i & n_3-i \end{pmatrix}$$

and

$$F_{-i}^{(n_1, n_2, n_3)} = \begin{pmatrix} n_1-i & i \\ n_2-i & i \\ n_3-i & i \end{pmatrix}.$$

The true tree is given in Figure 3(a). For the three possible tree-topologies the likelihood with no ascertainment-bias correction are given in Figure 3(b, c, & d). The likelihoods with the ascertainment-bias correction and the corresponding MLE branch lengths of three tree-topologies are given in Figure 3(e, f, & g). As we can see from the figure, the likelihood is maximized at the correct tree-topology in all cases. However, the MLE from the corrected likelihood has branch lengths that are larger and closer to the simulation truth. This is expected because the uncorrected likelihood takes the absence of extreme alleles as evidence of short branch lengths.

We have also tested our method for trees with four populations. We have considered a tree with four populations E, F, G and H. The common ancestor of E and F diverge from that of G and H at the root. Then E and F diverge and also G and H diverge. Thus, there are six branches in this tree. The length of each branch is 0.02. We have simulated 100 datasets from this tree, each with 8 haploids; for each haploid 1000 independent SNP loci are simulated. Assuming that we know the true tree-topology, we have estimated the branch lengths. The estimated biases are shown in Table 2. Using both a Wilcoxon signed-rank test and a paired t-test, we found the biases at each branch (represented as a column in Table 2) significantly different for correct vs. not corrected approach with p-values below 0.001 in all cases.

4 Discussion

The simulation studies indicate that as a result of not correcting for ascertainment-bias, it is possible to have significantly more bias in the branch lengths estimates for some data. Therefore, there is need for correcting for ascertainment-bias. In our examples, failure to correct for ascertainment did not affect the inference of the true tree topology.

We have introduced an efficient way of computing the probability of allele-count matrix falling in a set. We have thus improved the method of correcting for the ascertainment-bias in the pruning algorithm of RoyChoudhury et al. [9], making it faster and simpler.

Our approach is not equipped to deal with all possible ascertainment schemes. It is only designed to deal with schemes with known and deterministic ascertainment criteria. Our approach is designed for SNP data from independent loci.

Here we have used the pruning algorithm of RoyChoudhury et al. [9] to demonstrate our strategy. However, the idea of computing the probability of allele count falling into a set using pruning algorithm is more generally applicable. In particular, it is applicable to the method of Bryant et al. [1] which modifies the algorithm of RoyChoudhury et al. [9] to incorporate mutation, but keeps the structure of the algorithm and the use of the *A* and *B* arrays (defined in Subsection 2.1) unchanged. Our approach can also be applied to dependent loci using the composite likelihood approach of RoyChoudhury [8].

Our method of correcting for ascertainment-bias for likelihood of population trees can be applied to any data where the ascertainment strategies are well documented so that the rejection sets could be computed. In case different sets of loci in the data have different ascertainment strategies, the bias-corrected likelihood for each set may be computed separately by a separate set of runs of our method. The future applications of our method include sequence data where only some of the segregating SNPs may be selected for analysis from the whole sequence, and the ascertainment-bias correction will be needed to correct for the bias due to the selection process.

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Appendix

A Steps 1 and 2

Step 1 is derived as

$$A^{(L)}(z)_{i'} = \sum_{i=i'}^{m_y^{(b)}} Q_{ii'} A(y)_i, \quad (8)$$

$$Q_{ii'} = \left(\prod_{j=i'+1}^i \lambda_j \right) \sum_{j=i'}^i \frac{e^{-\lambda_j} \tau_{yz}}{\prod_{j'=i', j' \neq j}^i (\lambda_{j'} - \lambda_j)}, \quad \lambda_j = \frac{j(j-1)}{2},$$

$$B^{(L)}(z)_{ij} = \sum_{i'=i}^{m_y^{(b)}} \sum_{j'=0}^{i'} B(y)_{i'j'} \frac{\beta(j, i-j)}{\beta(j', i'-j')} \binom{i-i'}{j-j'} \frac{Q_{ii'} A(y)_i}{A^{(L)}(z)_{i'}}. \quad (9)$$

Step 2 is derived as

$$A(x)_i = \sum_{i'=0}^i A^{(L)}(x)_{i'} A^{(R)}(x)_{(i-i')}. \quad (10)$$

$$B(x)_{ij} = \sum_{i'=1}^{m_x^{(b,L)}} \sum_{j'=0}^{i'} \sum_{j''=0}^{i-i'} B^{(L)}(x)_{i'j'} B^{(R)}(x)_{(i-i')j''} \binom{j}{j'} \binom{i-j}{i'-j'} / \binom{i}{i'}. \quad (11)$$

Appendix

B Proof of the claim from Subsection 2.3

Claim

Consider a set

$$S = S_1 \times S_2 \times \dots \times S_p \quad (12)$$

where S_i is a set of allele-counts at Population i at the tip of the tree; S is a set of the matrix of allele-counts. Then, if we substitute $B(x)_{ij}$, $B^{(L)}(x)_{ij}$ and $B^{(R)}(x)_{ij}$ with

$$B(x)_{ij}^* = \sum_{s_x^{(b)} \in S_x^{(b)}} B(x)_{ij}, \quad B^{(L)}(x)_{ij}^* = \sum_{s_x^{(b,L)} \in S_x^{(b,L)}} B^{(L)}(x)_{ij} \text{ and } B^{(R)}(x)_{ij}^* = \sum_{s_x^{(b,R)} \in S_x^{(b,R)}} B^{(R)}(x)_{ij}$$

(for each node x) in the pruning algorithm, then it would yield the probability of the allele-count matrix falling into S . Here

$$S_x^{(b)} = \prod_{i \in T_x} S_i; \quad S_x^{(b,L)} = \prod_{i \in T_x^{(L)}} S_i; \quad S_x^{(b,R)} = \prod_{i \in T_x^{(R)}} S_i;$$

T_x is the set of all tips at or below x ; $T_x^{(L)}$ and $T_x^{(R)}$ are the sets of all tips at or below the branch coming from the left and the right sides of x respectively.

Proof

The array $B(x)$ is an indicator function of the data for each tip x . Next we will prove that the $B(x)^*$ arrays at non-tip nodes can be computed by Step 1 and Step 2.

As before, consider a branch with nodes z and y at its top and bottom respectively. Without loss of generality, assume that the branch is on the left bottom side of z . Using Eq. (9) and noting that $S_z^{(b,L)} = S_y^{(b)}$

$$\begin{aligned} B^{(L)}(z)^*_{ij} &= \sum_{s_z^{(b,L)} \in S_z^{(b,L)}} Pr(s_z^{(b,L)} | n_x^{(L)} = i, r_x^{(L)} = j) \\ &= \sum_{s_z^{(b,L)} \in S_z^{(b,L)}} \sum_{i'=i}^{m_y^{(b)}} \sum_{j'=j}^{i'} B(y)^*_{i'j'} \frac{\beta(j, i-j)}{\beta(j', i'-j')} \binom{i-i'}{j-j'} \frac{Q_{i',i} A(y)_i}{A^{(L)}(z)_{i'}} \\ &= \sum_{s_z^{(b,L)} \in S_z^{(b,L)}} \sum_{i'=i}^{m_y^{(b)}} \sum_{j'=j}^{i'} Pr(s_y^{(b)} | n_y = i', r_y = j') \frac{\beta(j, i-j)}{\beta(j', i'-j')} \binom{i-i'}{j-j'} \frac{Q_{i',i} A(y)_i}{A^{(L)}(z)_{i'}} \\ &= \sum_{i'=i}^{m_y^{(b)}} \sum_{j'=j}^{i'} \frac{\beta(j, i-j)}{\beta(j', i'-j')} \binom{i-i'}{j-j'} \frac{Q_{i',i} A(y)_i}{A^{(L)}(z)_{i'}} \sum_{s_z^{(b,L)} \in S_z^{(b,L)}} Pr(s_y^{(b)} | n_y = i', r_y = j') \\ &= \sum_{i'=i}^{m_y^{(b)}} \sum_{j'=j}^{i'} \frac{\beta(j, i-j)}{\beta(j', i'-j')} \binom{i-i'}{j-j'} \frac{Q_{i',i} A(y)_i}{A^{(L)}(z)_{i'}} \sum_{s_y^{(b)} \in S_y^{(b)}} Pr(s_y^{(b)} | n_y = i', r_y = j') \\ &= \sum_{i'=i}^{m_y^{(b)}} \sum_{j'=j}^{i'} B(y)^*_{i'j'} \frac{\beta(j, i-j)}{\beta(j', i'-j')} \binom{i-i'}{j-j'} \frac{Q_{i',i} A(y)_i}{A^{(L)}(z)_{i'}}. \end{aligned}$$

Thus the same equation as in Step 1 can be used to compute $B^{(L)}(z)^*_{ij}$ from $B(y)^*_{i'j'}$. The array $B^{(R)}(z)^*$ can be similarly computed from the bottom point of the branch coming from the right side.

Using (11) and noting the fact $S_x^{(b)} = S_x^{(b,L)} \times S_x^{(b,R)}$

$$\begin{aligned}
B(x)_{ij}^* &= \sum_{s_x^{(b)} \in S_x^{(b)}} Pr(s_x^{(b)} | n_x=i, r_x=j) \\
&= \sum_{s_x^{(b,L)} \in S_x^{(b,L)}} \sum_{s_x^{(b,R)} \in S_x^{(b,R)}} Pr((S_x^{(b,L)}, S_x^{(b,R)}) | n_x=i, r_x=j) \\
&= \sum_{s_x^{(b,L)} \in S_x^{(b,L)}} \sum_{s_x^{(b,R)} \in S_x^{(b,R)}} \sum_{i'=1}^{m_x^{(b,L)}} \sum_{j'=0}^{i-i'} \sum_{j''=0}^{i-i'-j'} B^{(L)}(x)_{i'j'}^* B^{(R)}(x)_{(i-i')j''} \binom{j}{j'} \binom{i-j}{i'-j'} / \binom{i}{i'} \\
&= \sum_{s_x^{(b,L)} \in S_x^{(b,L)}} \sum_{s_x^{(b,R)} \in S_x^{(b,R)}} \sum_{i'=1}^{m_x^{(b,L)}} \sum_{j'=0}^{i-i'} \sum_{j''=0}^{i-i'-j'} \binom{j}{j'} \binom{i-j}{i'-j'} / \binom{i}{i'} \\
&\quad \times Pr(S_x^{(b,L)} | n_x^{(L)}=i', r_x^{(L)}=j') Pr(s_x^{(b,R)} | n_x^{(R)}=i-i', r_x^{(R)}=j'') \\
&= \sum_{i'=1}^{m_x^{(b,L)}} \sum_{j'=0}^{i-i'} \sum_{j''=0}^{i-i'-j'} \binom{j}{j'} \binom{i-j}{i'-j'} / \binom{i}{i'} \\
&\quad \times \sum_{s_x^{(b,L)} \in S_x^{(b,L)}} Pr(S_x^{(b,L)} | n_x^{(L)}=i', r_x^{(L)}=j') \\
&\quad \times \sum_{s_x^{(b,R)} \in S_x^{(b,R)}} Pr(s_x^{(b,R)} | n_x^{(R)}=i-i', r_x^{(R)}=j'') \\
&= \sum_{i'=1}^{m_x^{(b,L)}} \sum_{j'=0}^{i-i'} \sum_{j''=0}^{i-i'-j'} B^{(L)}(x)_{i'j'}^* B^{(R)}(x)_{(i-i')j''}^* \binom{j}{j'} \binom{i-j}{i'-j'} / \binom{i}{i'}.
\end{aligned}$$

Thus, the same equation as in Step 2 can be used to compute $B(x)^*$ from $B^{(L)}(x)^*$ and $B^{(R)}(x)^*$ as well. Repeating Steps 1 and 2 (Figure 2) we can eventually compute the arrays at the root ($A(0)$ and $B(0)^*$). Then, using a equation similar to Eq. (3) we find the probability of the allele-count matrix falling into S from $A(0)$ and $B(0)^*$.

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Figure 1.
Structure of an evolutionary tree

Figure 2.

The pruning algorithm works by computing two arrays of conditional probabilities at each node. The arrays at each tip are computed from the data at the tip. Then the arrays at each non-tip node are computed from the nodes directly below it. Thus, the arrays for all the nodes are computed, moving upward node by node and eventually the arrays at the root are computed.

Figure 3.

The result from the simulation study: (a) is the true tree; (b)-(d): three possible tree-topologies estimated from the data not corrected for ascertainment-bias; (e)-(g): three possible tree-topologies estimated from the data corrected for ascertainment-bias. In both corrected and not-corrected cases, the likelihood is maximized at the correct tree-topology ((e) and (b)) respectively. However, the branch-length estimates have less bias when corrected for ascertainment-bias.

Table 1

Notation: see also Figure 1

n_x	number of lineages at node x ; $n_x \geq 1$
r_x	allele-count (the count of '1' alleles) out of n_x lineages at node x ; $0 \leq r_x \leq n_x$
$s_x^{(b)}$	all the data at or below node x
$s_x^{(a)}$	all the data that are not at or below node x
$m_x^{(b)}$	total number of gene copies sampled at or below node x ; $m_x^{(b)} \geq n_x$
$m_x^{(a)}$	total number of gene copies sampled that are not at or below node x
$n_x^{(L)}$	number of lineages just below node x , in the branch coming from the left side of x ; $n_x \geq n_x^{(L)} \geq 1$
$r_x^{(L)}$	allele-count (out of $n_x^{(L)}$ lineages) just below node x , in the branch coming from the left side of x ; $r_x^{(L)} \leq r_x$
$s_x^{(b,L)}$	all the data at or below the branch coming from the left side of node x
$s_x^{(a,L)}$	all the data that are not at or below the branch coming from the left side of node x
$m_x^{(b,L)}$	total number of gene copies sampled at or below the branch coming from the left side of node x ; $m_x^{(b,L)} \geq n_x^{(L)}$
$m_x^{(a,L)}$	total number of gene copies sampled that are not at or below the branch coming from the left side of node x
$n_x^{(R)}$	number of lineages just below node x , in the branch coming from the right side of x ; $n_x \geq n_x^{(R)} \geq 1$
$r_x^{(R)}$	allele-count (out of $n_x^{(R)}$ lineages) just below node x , in the branch coming from the right side of x ; $r_x^{(R)} \leq r_x$
$s_x^{(b,R)}$	all the data at or below the branch coming from the right side of node x
$s_x^{(a,R)}$	all the data that are not at or below the branch coming from the right side of node x
$m_x^{(b,R)}$	total number of gene copies sampled at or below the branch coming from the right side of node x ; $m_x^{(b,R)} \geq n_x^{(R)}$
$m_x^{(a,R)}$	total number of gene copies sampled that are not at or below the branch coming from the right side of node x

Table 2

Estimated bias for the four-population tree

	E branch	F branch	G branch	H branch	E-F branch	G-H branch
Not corrected	-0.011	-0.003	-0.010	-0.008	-0.017	-0.022
Corrected	-0.001	0.002	-0.001	-0.003	-0.003	0.005