Mathematical Framework for Phylogenetic Birth-And-Death Models

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Abstract

A phylogenetic birth-and-death model is a probabilistic graphical model for a so-called phylogenetic profile, i.e., the size distribution for a homolog gene family at the terminal nodes of a phylogeny. Profile datasets are used in bioinformatics analyses for the inference of evolutionary trees, and of functional associations between gene families, as well as for the quantification of various processes guiding genome evolution. Here we describe the mathematical formalism for phylogenetic birth-and-death models. We also present an algorithm for computing the likelihood in a gain-loss-duplication model.

For background information on phylogenetic birth-and-death models, see [CM06] (preprint available under http://arxiv.org/abs/q-bio/0509037v1). Here we give a self-contained comprehensive review, concentrating on the mathematical results. We describe our new algorithm for a very general class of gain-loss-duplication models.

1 Introduction

A phylogenetic birth-and-death model formalizes the evolution of an organism-specific census variable along a phylogeny. The phylogeny is a rooted tree,

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i.e., a connected acyclic graph in which the edges are directed away from a special node designated as the tree root; the terminal nodes, or leaves, are bijectively labeled by the organisms. The model specifies edge lengths, as well as birth-and-death processes [Ros96, Ken49] acting on the edges. Let $\mathcal{E}(T)$ denote the set of edges, and let $\mathcal{V}(T)$ denote the node set of the tree. Populations of identical individuals evolve along the tree from the root towards the leaves by Galton-Watson processes. At non-leaf nodes of the tree, populations are instantaneously copied to evolve independently along the adjoining descendant edges. Let the random variable $\xi(x) \in \mathbb{N} = \{0, 1, 2, \ldots \}$ denote the population count at every node $x \in \mathcal{V}(T)$. Every edge $xy \in \mathcal{E}(T)$ is characterized by a loss rate $\mu_{xy}$, a duplication rate $\lambda_{xy}$ and a gain rate $\kappa_{xy}$.

If $(X(t): t \geq 0)$ is a linear birth-and-death process [Ken49, Tak62] with these rate parameters, then

$$P\{\xi(y) = m \mid \xi(x) = n\} = P\{X(t_{xy}) = m \mid X(0) = n\},$$

where $t_{xy} > 0$ is the edge length, which defines the time interval during which the birth-and-death process runs. The joint distribution of $(\xi(x): x \in \mathcal{V}(T))$ is determined by the phylogeny, the edge lengths and rates, along with the distribution at the root $\rho$, denoted as $\gamma(n) = P\{\xi(\rho) = n\}$. Specifically, for all set of node census values $(n_x: x \in \mathcal{V}(T))$,

$$P\{\forall x \in \mathcal{V}(T): \xi(x) = n_x\} = \gamma(n_\rho) \prod_{xy \in \mathcal{E}(T)} w_{xy}[n_y|n_x] \quad (1)$$

where $w_{xy}[m|n] = P\{X(t_{xy}) = m \mid X(0) = n\}$ denotes the transition probability on the edge $xy$ for the Markov process operating there.

It is assumed that one can observe the population counts at the terminal nodes (i.e., leaves), but not at the inner nodes of the phylogeny. Since individuals are considered identical, we are also ignorant of the ancestral relationships between individuals within and across populations. The population counts at the leaves form a phylogenetic profile. Our central problem is to compute the likelihood of a profile, i.e., the probability of the observed counts for fixed model parameters.

The transient distribution of linear birth-and-death processes is well-characterized [KM58, Ken49, Tak62], as shown in Table I. Table I precisely states the distribution of xenolog and inparalog group sizes.

The distribution of population counts can be obtained analytically from the constituent distributions of Table I as shown by the following lemma.
| Case | Condition | Transient distribution | Group |
|------|-----------|------------------------|-------|
| GLD  | $\kappa > 0, \lambda > 0$ | $\mathbb{P}\{X(t) = n | X(0) = 0\} = \text{NegativeBinomial}(n; \theta, q)$ | xenolog |
| GL   | $\kappa > 0, \lambda = 0$ | $\mathbb{P}\{X(t) = n | X(0) = 0\} = \text{Poisson}(n; r)$ | xenolog |
| DL   | $\kappa = 0, \lambda > 0$ | $\mathbb{P}\{X(t) = n | X(0) = 1\} = \text{ShiftedGeometric}(n; p, q)$ | inparalog |
| PL   | $\kappa = 0, \lambda = 0$ | $\mathbb{P}\{X(t) = n | X(0) = 1\} = \text{Bernoulli}(n; 1 - p)$ | inparalog |

Parameters:

$$\theta = \frac{\kappa}{\lambda}, \quad r = \frac{1 - e^{\mu t}}{\mu},$$

$$p = \frac{\mu - \mu e^{-(\mu - \lambda)t}}{\mu - \lambda e^{-(\mu - \lambda)t}} \quad \text{and} \quad q = \frac{\lambda - \lambda e^{-(\mu - \lambda)t}}{\mu - \lambda e^{-(\mu - \lambda)t}}$$

if $\lambda \neq \mu$,

$$p = q = \frac{\lambda t}{1 + \lambda t}$$

if $\lambda = \mu$.

Distributions:

\[
\text{NegativeBinomial}(n; \theta, q) = \begin{cases} (1 - q)^\theta & \text{if } n = 0 \\ \frac{\theta(\theta + 1)\cdots(\theta + n - 1)}{n!}(1 - q)^\theta q^n & \text{if } n > 0 \end{cases}
\]

\[
\text{ShiftedGeometric}(n; p, q) = \begin{cases} p & \text{if } n = 0; \\ (1 - p)(1 - q) & \text{if } n = 1 \\ (1 - p)(1 - q)q^{n-1} & \text{if } n > 1. \end{cases}
\]

\[
\text{Poisson}(n; r) = e^{-r} \frac{r^n}{n!}
\]

\[
\text{Bernoulli}(n; 1 - p) = \text{ShiftedGeometric}(n; p, 0) = \begin{cases} p & \text{if } n = 0 \\ 1 - p & \text{if } n = 1. \end{cases}
\]

Table 1: Transient behavior of linear birth-and-death processes with loss rate $\mu > 0$, gain rate $\kappa$ and duplication rate $\lambda$: gain-loss-duplication (GLD), gain-loss (GL), duplication-loss (DL) and pure-loss (PL) models. The last column of the table shows the relevant group for computing transition probabilities in a phylogenetic birth-and-death model. For the meaning of xenolog and inparalog groups, see the main text.
Lemma 1. Let \((\zeta_i: i = 1, 2, \ldots)\) be independent random variables that have identical, shifted geometric distributions with parameters \(p\) and \(q\). Let \(\eta\) be a discrete nonnegative random variable that is independent from \(\zeta_i\), with probability mass function \(P\{\eta = m\} = H(m)\). Define \(w[m|n] = P\{\eta + \sum_{i=1}^{n} \zeta_i = m\}\) for all \(m, n \geq 0\), and \(w^*[m|n] = P\{\eta + \sum_{i=1}^{n} \zeta_i = m; \forall \zeta_i > 0\}\) for all \(m \geq n \geq 0\). These values can be expressed recursively as follows.

\[
\begin{align*}
    w[m|0] & = H(m) \quad \{m \geq 0\} \quad (2a) \\
    w[0|n] & = p \cdot w[0|n-1] \quad \{n > 0\} \quad (2b) \\
    w[1|n] & = p \cdot w[1|n-1] + (1-p)(1-q) \cdot w[0|n-1] \quad \{n > 0\} \quad (2c) \\
    w[m|n] & = q \cdot w[m-1|n] + (1-p-q) \cdot w[m-1|n-1] \quad \{n > 0, m > 1\} \quad (2d) \\
    & + p \cdot w[m|n-1] \\
\end{align*}
\]

Furthermore,

\[
\begin{align*}
    w^*[m|0] & = H(m) \quad \{m \geq 0\} \quad (3a) \\
    w^*[n|n] & = (1-p)(1-q) \cdot w^*[n-1|n-1] \quad \{n > 0\} \quad (3b) \\
    w^*[m|n] & = q \cdot w^*[m-1|n] + (1-p)(1-q) \cdot w^*[m-1|n-1] \quad \{m > n > 0\} \quad (3c) \\
    & + (1-p-q) \cdot w^*[m-1|n-1] \\
\end{align*}
\]

For every edge \(xy\), Equation (2) provides the transition probabilities \(w_{xy}[m|n] = w[m|n]\) in (1), when \(p, q\) and \(H(m)\) are taken from Table 1 for the process operating on the edge \(xy\). Equation (3) is used below in our formulas.

2 Surviving lineages

A key factor in inferring the likelihood formulas is the probability that a given individual at a tree node \(x\) has no descendants at the leaves within the subtree rooted at \(x\). The corresponding extinction probability is denoted by \(D_x\). An individual at node \(x\) is referred to as surviving if it has at least one progeny at the leaves descending from \(x\). Let \(\Xi(x)\) denote the number of surviving individuals at each node \(x\). The distribution of \(\Xi(x)\) can be related to that of \(\xi(x)\) by

\[
P\{\Xi(x) = m\} = \sum_{i=0}^{\infty} \binom{m+i}{i} D_x^i (1-D_x)^m P\{\xi(x) = m+i\}. \quad (4)
\]
The next two lemmas characterize the number of surviving xenologs and inparalogs: they follow the same class of distributions as the total number of xenologs and inparalogs.

**Lemma 2.** For every edge \( xy \in E(T) \), let \( G_y(n) \) denote the probability that there are \( n \) surviving members within an inparalog group at \( y \). Then \( G_y(n) = \text{ShiftedGeometric}(n; p', q') \) with

\[
p' = \frac{p(1 - D_y) + (1 - q)D_y}{1 - qD_y} \quad \text{and} \quad q' = \frac{q(1 - D_y)}{1 - qD_y}.
\]

**Lemma 3.** For every edge \( xy \in E(T) \), let \( H_y(n) \) denote the probability that there are \( n \) xenologs at \( y \) that survive. If \( \lambda_{xy} = 0 \), then \( H_y(n) = \text{Poisson}(n; r') \) where \( r' = r(1 - D_y) \). If \( \lambda_{xy} > 0 \), then \( H_y(n) = \text{NegativeBinomial}(n; \theta, q') \).

In the formulas to follow, we use the probabilities \( w^*[m|n] \), which apply Lemma 1 to surviving populations on edge \( xy \): \( w^*[m|n] = w^*[m|n] \), where the latter is defined by Equation (3) with settings \( p \leftarrow p', q \leftarrow q', H(m) \leftarrow H_x(m) \) from Lemmas 2 and 3.

Lemma 2 provides the means to compute extinction probabilities in a postorder traversal of the phylogeny.

**Lemma 4.** If \( x \) is a leaf, then \( D_x = 0 \). Otherwise, let \( x \) be the parent of \( x_1, x_2, \ldots, x_c \). Then \( D_x \) can be written as

\[
D_x = \prod_{j=1}^c G_{x_j}(0).
\]  

3 Conditional likelihoods

Let \( \mathcal{L}(T) \subset \mathcal{V}(T) \) denote the set of leaf nodes. A phylogenetic profile \( \Phi \) is a function \( \mathcal{L}(T) \mapsto \{0, 1, 2, \ldots\} \), which are the population counts observed at the leaves. Define the notation \( \Phi(\mathcal{L}') = (\Phi(x): x \in \mathcal{L}') \) for the partial profile within a subset \( \mathcal{L}' \subseteq \mathcal{L}(T) \). Similarly, let \( \xi(\mathcal{L}') = (\xi(x): x \in \mathcal{L}') \) denote the vector-valued random variable composed of individual population counts. The **likelihood** of \( \Phi \) is the probability

\[
L = \mathbb{P}\left\{ \xi(\mathcal{L}(T)) = \Phi \right\}.
\]
Let $T_x$ denote the subtree of $T$ rooted at node $x$. Define the survival count range $M_x$ for every node $x \in V(T)$ as $M_x = \sum_{y \in L(T_x)} \Phi(y)$. The survival count ranges are calculated in a postorder traversal, since

$$ M_x = \begin{cases} \Phi(x) & \text{if } x \text{ is a leaf} \\ \sum_{y \in \text{children}(x)} M_y & \text{otherwise.} \end{cases} $$

(7)

We compute the likelihood using conditional survival likelihoods defined as the probability of observing the partial profile within $T_x$ given the number of surviving individuals $\Xi(x)$:

$$ L_x[n] = P\{\xi(L(T_x)) = \Phi(L(T_x)) \mid \Xi(x) = n\}. $$

For $m > M_x$, $L_x[m] = 0$. For values $m = 0, 1, \ldots, M_x$, the conditional survival likelihoods can be computed recursively as shown in Theorem 5 below.

**Theorem 5.** If node $x$ is a leaf, then

$$ L_x[n] = \begin{cases} 0 & \text{if } n \neq \Phi(x); \\ 1 & \text{if } n = \Phi(x). \end{cases} $$

If $x$ is an inner node with children $x_1, \ldots, x_c$, then $L_x[n]$ can be expressed using $L_x[:i]$ and auxiliary values $A_i$ and $B_i$ for $i = 1, \ldots, c$ in the following manner. Let $w^*_x[m|s]$ denote the transition probability in Lemma 7 applied to surviving individuals at $x_i$, using the distributions $H_{x_i}(\cdot)$ from Lemma 5 and $G_{x_i}(\cdot)$ from Lemma 2. Let $M[j] = \sum_{i=1}^{c} M_{x_i}$ for all $j = 1, \ldots, c$ and $M[0] = 0$. Define also $D[j] = \prod_{i=1}^{j} G_{x_i}(0)$ and $D[0] = 1$. Auxiliary values $B_{i:t,s}$ are defined for all $i = 1, \ldots, c$, $t = 0, \ldots, M[i-1]$ and $s = 0, \ldots, M_{x_i}$ as follows.

$$ B_{i:0,s} = \sum_{m=0}^{M_{x_i}} w^*_x[m|s]L_x[m] \quad \{0 \leq s \leq M_{x_i}\} \quad (8a) $$

$$ B_{i:t,M_{x_i}} = G_{x_i}(0)B_{i:t-1,M_{x_i}} \quad \{0 < t \leq M[i-1]\} \quad (8b) $$

$$ B_{i:t,s} = B_{i:t-1,s+1} + G_{x_i}(0)B_{i:t-1,s} \quad \{0 \leq s < M_{x_i} \land 0 < t \leq M[i-1]\} \quad (8c) $$
For all $i = 1, \ldots, c$ and $n = 0, \ldots, M[i]$, define $A_{i,n}$ as

$$A_{1;n} = (1 - D[1])^{-n} B_{1;0,n};$$

$$A_{i;n} = (1 - D[i])^{-n} \sum_{0 \leq t \leq M[i-1]} \sum_{0 \leq s \leq M[i]} \binom{s}{i} B_{i-1,t} B_{i; t,s}, \quad (9b)$$

where $i > 1$ in (9b).

For all $n = 0, \ldots, M_x$, $L_x[n] = A_{c,n}$.

The complete likelihood is computed as

$$L = \sum_{m=0}^{M_\rho} L_\rho[m] \mathbb{P}\{\Xi(\rho) = m\}$$

$$= \sum_{m=0}^{M_\rho} L_\rho[m] \left( \sum_{i=0}^{\infty} \gamma(m + i) \binom{m + i}{i} D_\rho^i (1 - D_\rho)^m \right). \quad (10)$$

For some parametric distributions $\gamma$, the infinite sum in (10) can be replaced by a closed formula for $\mathbb{P}\{\Xi(\rho) = m\}$. Theorem 6 below considers the stationary distributions for gain-loss-duplication and gain-loss models.

**Theorem 6.** For negative binomial or Poisson population distribution at the root, the likelihood can be expressed as shown below.

1. If $\gamma(n) = \text{Poisson}(n; r)$, then

   $$\mathbb{P}\{\Xi(\rho) = m\} = \text{Poisson}(m; r')$$

   with $r' = r(1 - D_\rho)$. \quad (11a)

2. If $\gamma(n) = \text{NegativeBinomial}(n; \theta, q)$, then

   $$\mathbb{P}\{\Xi(\rho) = m\} = \text{NegativeBinomial}(m; \theta, q')$$

   with $q' = \frac{q(1-D_\rho)}{1-qD_\rho}$. \quad (11b)

3. If $\xi(\rho)$ has a Bernoulli distribution, i.e., if $\gamma(0) = 1 - \gamma(1) = 1 - p$, then

   $$L = L_\rho[0] + p(1 - D_\rho) (L_\rho[1] - L_\rho[0])$$

   (11c)
Consequently, the likelihood for a Poisson distribution at the root is computed as
\[
L = \sum_{m=0}^{M_\rho} L_\rho[m] \text{Poisson}(m; \Gamma(1 - D_\rho)),
\]  
(12)
where \( \Gamma \) is the mean family size at the root.

4 Algorithm

The algorithm we describe computes the likelihood of a phylogenetic profile for a given set of model parameters. Algorithm ComputeConditionals below proceeds by postorder (depth-first) traversals; the necessary variables are calculated from the leaves towards the root. The loop of Line 1 computes the transition probabilities \( w^*[-] \), extinction probabilities \( D[-] \) and survival count ranges \( M[-] \). The loop of Line 9 carries out the computations suggested by Theorem 5.

**Theorem 7.** Let \( T \) be a phylogeny with \( n \) nodes where every node has at most \( c^* \) children. Let \( h \) denote the tree height, i.e., the maximum number of edges from the root to a leaf. The ComputeConditionals algorithm computes the conditional survival likelihoods for a phylogenetic profile \( \Phi \) on \( T \) in \( O(M^2 h + c^*(Mh+n)) \) time, where \( M = M_\rho = \sum_x \Phi(x) \) is the total number of homologs.

If \( c^* \) is constant, then the running time bound of Theorem 7 is \( O(M^2 h+n) \). For almost all phylogenies in a Yule-Harding random model, \( h = O(\log n) \), so the typical running time is \( O(M^2 \log n) \). For all phylogenies, \( h \leq n - 1 \), which yields a \( O(M^2 n) \) worst-case bound.
ComputeConditionals

**Input:** phylogenetic profile $\Phi$

1. for each node $x \in V(T)$ in a postorder traversal do
2. Compute the sum of gene counts $M_x$ by (7).
3. Compute $D_x$ using (5).
4. if $x$ is not the root then let $y$ be the parent of $x$.
5. for $n = 0, \ldots, M_x$ do
6. for $m = 0, \ldots, M_x$ do
7. compute $w^*_y[x|m|n]$ using (3) with $H_x(\cdot)$ and $G_x(\cdot)$ from Lemmas 3 and 2.

9. for each node $x \in V(T)$ in a postorder traversal do
10. if $x$ is a leaf then for all $n \leftarrow 0, \ldots, \Phi(x)$ do set $L_x[n] \leftarrow \{n = \Phi(x)\}$
11. else
12. Let $x_1, \ldots, x_c$ be the children of $x$
13. Initialize $M[0] \leftarrow 0$ and $D[0] \leftarrow 1$
14. for $i \leftarrow 1, \ldots, c$ do
15. set $M[i] \leftarrow M[i - 1] + M_{x_i}$ and $D[i] \leftarrow D[i - 1] \cdot D_{x_i}$
16. for all $t \leftarrow 0, \ldots, M[i - 1]$ and $s \leftarrow 0, \ldots, M_{x_i}$ do
17. compute $B_{i;t,s}$ by Eqs. (8)
18. if $i = 1$ then for all $n \leftarrow 0, \ldots, M[i]$ do set $A_{1;n} \leftarrow (1 - D[1])^{-n}B_{1;0,n}$
19. else
20. for all $n \leftarrow 0, \ldots, M[i]$ do initialize $A_{i;n} \leftarrow 0$
21. for $t \leftarrow 0, \ldots, M[i - 1]$ and $s \leftarrow 0, \ldots, M_{x_i}$ do
22. set $A_{i;n} \leftarrow A_{i;n} + \text{Binomial}(s;n,D[i - 1])A_{i-1;t;B_{i;t,s}}$
23. for all $n \leftarrow 0, \ldots, M[i]$ do $A_{i;n} \leftarrow (1 - D[i])^{-n}A_{i;n}$
24. for all $n \leftarrow 0, \ldots, M_x$ do set $L_x[n] \leftarrow A_{i;n}$.

5 Mathematical proofs

*Proof of Lemma 1.* Equations (2a) and (3a) are immediate since

$$w[m|0] = w^*[m|0] = \mathbb{P}\{\eta = m\} = H(m).$$

By the independence of $\zeta_i$, for all $n > 0$,

$$w[0|n] = \mathbb{P}\{\eta + \sum_{i=1}^n \zeta_i = 0\} = w[0|n - 1]\mathbb{P}\{\zeta_n = 0\} = w[0|n - 1] \cdot p,$$
as in (2b).

Let \( G(n) = \text{ShiftedGeometric}(n; p, q) \) be the common probability mass function of \( \zeta_i \). For \( m, n > 0 \),

\[
 w[m|n] = \mathbb{P}\left\{ \eta + \sum_{i=1}^{n} \zeta_i = m \right\} = \sum_{k=0}^{m} \mathbb{P}\{\zeta_n = k\} \cdot \mathbb{P}\left\{ \eta + \sum_{i=1}^{n-1} \zeta_i = m - k \right\} = \sum_{k=0}^{m} G(k) \cdot w[m - k|n - 1]. \tag{13}
\]

For \( m = 1 \), (13) is tantamount to (2c), since \( G(0) = p \) and \( G(1) = (1 - p)(1 - q) \). For \( m > 1 \), (13) can be further rewritten using \( G(k) = qG(k - 1) \) for all \( k > 1 \):

\[
 w[m|n] = G(0) \cdot w[m|n - 1] + G(1) \cdot w[m - 1|n - 1] \\
+ \sum_{k=2}^{m} qG(k - 1) \cdot w[m - k|n - 1] \\
= p \cdot w[m|n - 1] + G(1) \cdot w[m - 1|n - 1] \\
+ q \sum_{k=1}^{m-1} G(k) \cdot w[m - 1 - k|n - 1] \\
= p \cdot w[m|n - 1] + G(1) \cdot w[m - 1|n - 1] \\
+ q \left( w[m - 1|n] - G(0) \cdot w[m - 1|n - 1] \right),
\]

which leads to the recursion of (2d) since \( G(1) - qG(0) = 1 - p - q \).

Equation (3b) follows from

\[
 w^*[n|n] = \mathbb{P}\left\{ \eta + \sum_{i=1}^{n} \zeta_i = n; \forall \zeta_i > 0 \right\} = \mathbb{P}\{\eta = 0\} \cdot \prod_{i=1}^{n} \mathbb{P}\{\zeta_i = 1\} = H(0)(G(1))^n.
\]
For \( m > n > 0 \),
\[
\begin{align*}
\mathcal{C}^* [m | n] &= \mathbb{P} \{ \eta + \sum_{i=1}^{n} \zeta_i = m; \zeta_i > 0 \} \\
&= \sum_{k=1}^{m-n+1} \mathbb{P} \{ \zeta_n = k \} \cdot \mathcal{C}^* [m - k | n - 1] \\
&= \sum_{k=1}^{m-n+1} G(k) \cdot \mathcal{C}^* [m - k | n - 1] \\
&= G(1) \cdot \mathcal{C}^* [m - 1 | n - 1] + \sum_{k=2}^{m-n+1} qG(k-1) \cdot \mathcal{C}^* [m - k | n - 1] \\
&= G(1) \cdot \mathcal{C}^* [m - 1 | n - 1] + q \cdot \mathcal{C}^* [m | n - 1],
\end{align*}
\]
as claimed in (3c).

\[ \square \]

Lemmas 2 and 3 rely on the following general result.

**Lemma 8.** Let \( \sigma \in \mathbb{R} \) be a fixed parameter, and let \( \{a_n\}_{n=0}^{\infty} \) and \( \{b_n\}_{n=0}^{\infty} \) be two number sequences related by the formula
\[
b_n = \sum_{i=0}^{\infty} \binom{n+i}{i} \sigma^i (1-\sigma)^n a_{n+i}.
\]
(We use the convention \( 0^0 = 1 \) in the formula when \( \sigma \in \{0,1\} \).) Let \( A(z) = \sum_n a_n z^n \) and \( B(z) = \sum_n b_n z^n \) denote the generating functions for the sequences. Then
\[
B(z) = A(\sigma + (1-\sigma)z)
\]

**Proof.** If \( \sigma = 0 \), then \( b_n = a_n \), and, thus (14b) holds. If \( \sigma = 1 \), then \( b_0 = \sum_{k=0}^{\infty} a_k \), and \( b_n = 0 \) for \( n > 0 \), which implies (14b). Otherwise,
\[
\begin{align*}
B(z) &= \sum_{n=0}^{\infty} z^n \sum_{m=0}^{\infty} a_m \binom{m}{n} \sigma^{m-n}(1-\sigma)^n \\
&= \sum_{m=0}^{\infty} a_m \sum_{n=0}^{\infty} z^n \binom{m}{n} \sigma^{m-n}(1-\sigma)^n \\
&= \sum_{m=0}^{\infty} a_m \left( \sigma + (1-\sigma)z \right)^m = A(\sigma + (1-\sigma)z),
\end{align*}
\]
as claimed.  \[ \square \]
Corollary 9. Let \( \{a_n\}_{n=0}^{\infty} \) and \( \{b_n\}_{n=0}^{\infty} \) be two probability mass functions for non-negative integer random variables, related as in (14a).

1. If \( a_n = \text{ShiftedGeometric}(n; p, q) \), then \( b_n = \text{ShiftedGeometric}(n; p', q') \) with
   \[
p' = \frac{p(1 - \sigma) + (1 - q)\sigma}{1 - q\sigma} \quad \text{and} \quad q' = \frac{q(1 - \sigma)}{1 - q\sigma}.
   \] (15)

2. If \( a_n = \text{NegativeBinomial}(n; \theta, q) \), then \( b_n = \text{Negativebinomial}(n; \theta, q') \), where \( q' \) is defined as in (15).

3. If \( a_n = \text{Poisson}(n; r) \), then \( b_n = \text{Poisson}(n; r') \) with \( r' = r(1 - \sigma) \).

Proof. The corollary follows for plugging into Lemma 8 the generating functions

\[
A(z) = \frac{p}{1 - qz}, \quad A(z) = \frac{(1-qz)^\theta}{1-qz}, \quad A(z) = e^{rz(z-1)}
\]

for the shifted geometric, negative binomial, and Poisson distributions, respectively.

Proof of Lemma 2. Let \( \zeta \) be the random variable that is the size of an inparalog group at node \( y \). In order to have \( n \) surviving inparalogs, there must be \( n + i \) inparalogs in total, out of which \( i \) do not survive, for some \( i \geq 0 \). Therefore,

\[
G_y(n) = \sum_{i=0}^{\infty} \mathbb{P}\{\zeta = n + i\} \binom{n + i}{i} D_y^i (1 - D_y)^n.
\]

By Table II \( \mathbb{P}\{\zeta = n\} = \text{ShiftedGeometric}(n; p, q) \) where the distribution parameters \( p \) and \( q \) are determined by the parameters of the birth-and-death process on the edge leading to \( y \) (\( q = 0 \) in the degenerate case where duplication rate is 0). The lemma thus follows from Corollary 9 with \( \sigma = D_y \).

Proof of Lemma 3. Let \( \eta \) be the random variable that is the size of the xenolog group at \( y \). In order to have \( n \) surviving xenologs, there must be \( n + i \) xenologs in total, out of which \( i \) do not survive, for some \( i \geq 0 \). Therefore,

\[
H_y(n) = \sum_{i=0}^{\infty} \mathbb{P}\{\eta = n + i\} \binom{n + i}{i} D_y^i (1 - D_y)^n.
\] (16)

By Table II if \( \lambda = 0 \), then \( \eta \) has a Poisson distribution with parameter \( r \); otherwise, \( \eta \) has a negative binomial distribution with parameters \( \theta \) and \( q \). In either case, the lemma follows from Corollary 9 after setting \( \sigma = D_y \).
Proof of Lemma 4. For leaves, the statement is trivial. When \( x \) is not a leaf, the lemma follows from the fact that survivals are independent between disjoint subtrees.

Proof of Theorem 5. The formulas are obtained by tracking survival within the lineages \( xx_i \) among the individuals at \( x \). Define the indicator variables \( X_{i,j} \) for each individual \( j = 1, \ldots, \xi(x) \) and lineage \( i = 1, \ldots, c \), taking the value 1 if and only if individual \( j \) has at least one surviving offspring at \( x_i \).

In order to work with the survivals, we introduce some auxiliary random variables that have the distributions of surviving xenologs and inparalogs. For every edge \( xx_i \), define the sequence of independent random variables \( \zeta_{ij} \) for each lineage \( i = 1, \ldots, c \), taking the value 1 with probability \( G_{x_i}(0) \), and the random variable \( \eta_i \) with distribution \( H_{x_i}(\cdot) \). Consequently,

\[
P\{ \Phi_i = \Phi(T_{x_i}) \} = \sum_{m=0}^{M_{x_i}} \left[ \sum_{j=1}^{s} \zeta_{ij} \right] \cdot \left[ \sum_{j=1}^{s} \eta_i + \sum_{j=1}^{s} \zeta_{ij} \right]
\]

where \( G_{x_i}(k) = \text{ShiftedGeometric}(k;p',q') \) with some \( p' \) and \( q' \).

Define the shorthand notation \( \Phi_i = \left\{ \xi(T_{x_i}) = \Phi(T_{x_i}) \right\} \) for observing the counts in the subtree rooted at \( x_i \). Let

\[
B_{i,t,s} = \mathbb{P}\left\{ \Phi_i; \sum_{j=1}^{s} X_{i,j} = s \mid \xi(x) = t + s \right\}.
\]

In other words, if there are \( t + s \) individuals at \( x \), then \( B_{i,t,s} \) is the probability that \( s \) selected individuals survive in the lineage \( xx_i \) and the given profile is observed in \( T_{x_i} \). By Lemma 1,

\[
B_{i,0,s} = \mathbb{P}\left\{ \Phi_i; \sum_{j=1}^{s} X_{i,j} = s \mid \xi(x) = s \right\}
\]

\[
= \sum_{m=0}^{M_{x_i}} \mathbb{P}\left\{ \sum_{j=1}^{s} X_{i,j} = m \mid \xi(x) = s \right\} \cdot \mathbb{P}\left\{ \sum_{j=1}^{s} X_{i,j} = s \mid \xi(x) = s \right\}
\]

\[
= \sum_{m} \mathbb{P}\left\{ \Phi_i \mid \xi(x) = m \right\} \cdot \mathbb{P}\left\{ \sum_{j=1}^{s} X_{i,j} = s \mid \xi(x) = s \right\}
\]

\[
= \sum_{m} \mathbb{P}\left\{ \Phi_i \mid \xi(x) = s \right\} \cdot \mathbb{P}\left\{ \sum_{j=1}^{s} \zeta_{ij} = m \mid \xi(x) = s \right\}
\]

\[
= \sum_{m} L_{x_i}[m] \cdot w_{x_i}^*[m,s]
\]
as shown in (8a). If \( t > 0 \), then

\[
B_{i;t,s} = \mathbb{P}\left\{ \Phi_i; X_{i,s+1} = 0; \sum_{j=1}^{s} X_{ij} = s \mid \xi(x) = t + s \right\}
\]

\[
+ \mathbb{P}\left\{ \Phi_i; X_{i,s+1} = 1; \sum_{j=1}^{s} X_{ij} = s \mid \xi(x) = t + s \right\}
\]

\[
= G_{x_i}(0) \cdot \mathbb{P}\left\{ \Phi_i; \sum_{j=1}^{s} X_{ij} = s \mid \xi(x) = t + s - 1 \right\}
\]

\[
+ \mathbb{P}\left\{ \Phi_i; \sum_{j=1}^{s+1} X_{ij} = s + 1 \mid \xi(x) = t + s \right\}
\]

\[
= G(0) \cdot B_{i;t-1,s} + B_{i;t-1,s+1},
\]

which is tantamount to (8c). Equation (8b) follows from the fact that \( B_{i;t,s} = 0 \) for \( s > M_{x_i} \).

For every \( i \), let \( Y_i \) denote the set of individuals at \( x \) that survive in at least one of the lineages \( x_1, \ldots, x_i \), i.e., \( Y_i = \left\{ j : \{ X_{1j} + \cdots + X_{ij} \neq 0 \} \right\} \).

Given the exchangeability of individuals, \( \mathbb{P}\{ \Phi_1; \ldots; \Phi_i \mid Y_i = Y \} \) is the same for all sets of the same size \(|Y| = n\). Let

\[
A_{i;n} = \mathbb{P}\{ \Phi_1; \ldots; \Phi_i \mid |Y_i| = n \}.
\]

In particular, \(|Y_{c|}\} = \Xi(x)\) and, thus, \( A_{c;n} = L_x[n] \).

Since \( A_{i;n} \) is the same for all values of \( \xi(x) \geq n \), and \( \Phi_1 \) is determined solely by survival in lineage \( xx_1 \),

\[
B_{1;0,n} = \mathbb{P}\left\{ \Phi_1; \sum_{j=1}^{n} X_{i,j} = n \mid \xi(x) = n \right\}
\]

\[
= \mathbb{P}\left\{ \sum_{j=1}^{n} X_{i,j} = n \mid \xi(x) = n \right\} \cdot \mathbb{P}\{ \Phi_1 \mid \sum_{j=1}^{n} X_{i,j} = n; \xi(x) = n \}
\]

\[
= (1 - D[1])^n \mathbb{P}\{ \Phi_1 \mid |Y_1| = n \} = (1 - D[1])^n A_{1;n},
\]

implying (9a).
By a similar reasoning for \( i > 1 \),

\[
\mathbb{P}\{\Phi_1; \ldots; \Phi_i; |Y_i| = n \mid \xi(x) = n\} = \mathbb{P}\{|Y_i| = n \mid \xi(x) = n\} \cdot \mathbb{P}\{\Phi_1; \ldots; \Phi_i \mid |Y_i| = n; \xi(x) = n\}.
\]

(17)

Let \( X_i \) denote the set of individuals that survive in the lineage \( xx_i \): \( X_i = \{ j : X_{i,j} \neq 0 \} \). We rewrite the left-hand side of (17) by conditioning on the set of individuals that survive in lineage \( xx_i \) but not in the lineages \( xx_1, \ldots, xx_{i-1} \).

\[
\mathbb{P}\{\Phi_1; \ldots; \Phi_i; |Y_i| = n \mid \xi(x) = n\} = \sum_{S \in 2^{[n]}} B_{i,t,s} A_{i-1,t} \mathbb{P}\{|Y_{i-1}| = t \mid \xi(x) = n\}.
\]

Combining this latter equality with (17) leads to (9b).

**Proof of Theorem 6.** By (4), Lemma 8 with \( \sigma = D_x \) shows the relationship between the generating functions for the distributions of \( \xi(x) \) and \( \Xi(x) \). The theorem considers the case when \( x \) is the root and Corollary 9 applies to \( \gamma(n) = \mathbb{P}\{ \xi(x) = n\} \).

**Proof of Theorem 7.** By Theorem 5, the algorithm correctly computes the conditional survival likelihoods. Let \( T \) be the phylogeny with root \( \rho \) and \( n \) nodes. In order to prove the running time result, consider first the loop of Line 1. Lines 2–5 take \( O(1) \) time for each \( x \in \mathcal{V}(T) \). Line 8 is executed \( (M_x + 1)^2 \) times for every non-root \( x \). If \( x \) is an inner node with children \( x_1, x_2, \ldots, x_c \), then \( M_x = \sum_{j=1}^c M_{x_j} \). Consequently,

\[
\sum_{j=1}^c (M_{x_j} + 1)^2 \leq (M_x + 1)^2 + (c - 1). \tag{18}
\]
Now, consider the tree levels $V_0, V_h$, where $V_0 = \{\rho\}$, and for all $i = 1, \ldots, h$, $V_i$ consists of all the children of nodes in $V_{i-1}$. In other words, $V_i$ is the set of nodes that are reached through $i$ edges from the root. By (18),
\[
\sum_{y \in V_i} (M_y + 1)^2 \leq |V_i| - |V_{i-1}| + \sum_{x \in V_{i-1}} (M_x + 1)^2.
\]
for all $i > 0$. Therefore,
\[
\sum_{y \in V_i} (M_y + 1)^2 \leq \left(|V_i| - 1\right) + (M_\rho + 1)^2
\]
(19)
So,
\[
\sum_{x \in V(T) \setminus \{\rho\}} (M_x + 1)^2 = \sum_{i=1}^{h} \sum_{x \in V_i} (M_x + 1)^2
\]
\[
\leq n - 1 - h + h (M_\rho + 1)^2
\]
\[
= O(n + hM^2).
\]
Therefore, executing Line 8 through all iterations takes $O(M^2h + n)$ time. In order to bound the loop’s running time in Line 9, consider the $B_{i,t,s}$ and $A_{i,n}$ values that are needed for a given node $x$ with children $x_1, \ldots, x_c$. By (8a), computing all $B_{i,0,s}$ values takes $O((M_{x_i} + 1)^2)$ time. Every $B_{i,t,s}$ with $t > 0$ and $A_{i,n}$ is calculated in $O(1)$ time. Using the bound $M[i] \leq M_x$, iteration $i$ of the loop in Line 15 takes $O((M_x + 1)(M_{x_i} + 1))$ time. By summing for $i = 1, \ldots, c$, we get that for node $x$ with $c_x$ children, the loop of Line 9 takes $O((M_x + 1)(M_x + c_x))$ time (since $\sum_i(M_{x_i} + 1) = M_x + c$). Now, $(M_x + 1)(M_x + c_x) = (M_x + 1)(M_x + 1 + c - 1)$, and
\[
\sum_{x \in V(T)} (M_x + 1)(c_x - 1) = \sum_{i=0}^{h} \sum_{x \in V_i} (M_x + 1)(c_x - 1)
\]
\[
\leq \left(\max x c_x - 1\right) \sum_{i=0}^{h} \sum_{x \in V_i} (M_x + 1)
\]
\[
\leq (c^* - 1)(M_\rho(h + 1) + n).
\]
By our previous discussions,
\[
\sum_{x \in V(T)} (M_x + 1)(M_x + c_x) \leq n - 1 - h + h (M_\rho + 1)^2 + (c^* - 1)(M_\rho(h + 1) + n)
\]
\[
= O(M^2h + c^*(Mh + n)).
\]
So, the loop of Line 9 takes \( O(M^2 h + M h c^*) \) time, which leads to the Theorem’s claim when combined with the bound on the loop’s running time in Line 11.

6 Likelihood correction for absent profiles

Suppose that profiles are restricted to the condition that \( \{ \Phi(x) > 0 \} \) must hold for at least one terminal node \( x \). The corresponding likelihoods

\[
L_1 = \mathbb{P}\left\{ \forall x \in \mathcal{L}(T): \xi(x) = \Phi(x) \mid \xi(x) > 0 \text{ for at least one leaf} \right\}
\]

are obtained from the full likelihood by employing a correction that involves the probability of the condition [Fel92]. Namely,

\[
L_1 = \frac{L}{\mathbb{P}\{ \xi(x) > 0 \text{ for at least one leaf} \}} = \frac{L}{1 - \mathbb{P}\{ \xi(x) = 0 \text{ for all leaves } x \}}.
\]

The probability that \( \xi(x) = 0 \) at all the leaves is the likelihood of the all-0 profile \( \Phi_0 = (0, \ldots, 0) \). By Theorem 5, \( L_\rho[0] = \prod_{xy \in E(T)} H_y(0) \) for the profile \( \Phi_0 \). Combined with (12), we have the correction formula

\[
L_1 = \frac{L}{1 - p_0}
\]

with

\[
p_0 = \left( \prod_{xy \in E(T)} H_y(0) \right) \cdot \exp\left( \Gamma(1 - D_\rho) \right),
\]

for \( \gamma(n) = \text{Poisson}(n; \Gamma) \).

7 Inferring family sizes at ancestors and counting lineage-specific events

Given a profile \( \Phi \), the posterior probabilities for gene family size at node \( x \) are computed by using the conditional survival likelihoods \( L_x[n] \) and likelihoods of some relevant profiles on truncated phylogenies. In order to compute the gene content at node \( x \), for example, consider the profile \( \Phi_{x:m} \) for all \( m \) that applies to a phylogeny obtained by pruning the edges below \( x \), that is, \( \Phi_{x:m}(y) = \Phi(y) \) for \( y \not\in T_x \) and \( \Phi_{x:m}(x) = m \). Let \( L_{x:m} \) denote the likelihood
of \( \Phi_{x,m} \) on the pruned tree. Then

\[
P\left\{ \xi(x) = m \ \bigg| \ \xi(\mathcal{L}(T)) = \Phi \right\} = \frac{L_{x:m} \sum_{n=0}^{m} \binom{m}{n} (D_x)^{m-n} (1 - D_x)^n L_x[n]}{L}
\]

gives the posterior probability that the family had \( m \) homologs at node \( x \).

The number of families present at node \( x \), denoted by \( N_x \), is inferred as a posterior mean value by summing posterior probabilities:

\[
N_x = \sum_{i=1}^{n} P\left\{ \xi(x) > 0 \ \bigg| \ \xi(\mathcal{L}(T)) = \Phi_i \right\} + \frac{n \cdot p_0}{1 - p_0} P\left\{ \xi(x) > 0 \ \bigg| \ \xi(\mathcal{L}(T)) = \Phi_0 \right\}, \tag{21}
\]

where \( \Phi_i: i = 1, \ldots, n \) are the profiles in the data set and \( p_0 \) is the likelihood of the all-0 profile \( \Phi_0 \) from (20). Notice that the formula includes the absent all-0 profiles; there are \( np_0 \) such profiles by expectation.

For each edge \( xy \), the posterior probabilities for gain, loss, expansion and contraction are:

\[
P\{\text{gain}(xy)\} = P\{\xi(x) = 0, \xi(y) > 0\} = P\{\xi(x) = 0\} - P\{\xi(x) = 0, \xi(y) = 0\}
\]

\[
P\{\text{loss}(xy)\} = P\{\xi(x) > 0, \xi(y) = 0\} = P\{\xi(y) = 0\} - P\{\xi(x) = 0, \xi(y) = 0\}
\]

\[
P\{\text{expansion}(xy)\} = P\{\xi(x) = 1, \xi(y) > 1\} = P\{\xi(x) = 1\} - P\{\xi(x) = 1, \xi(y) = 0\} - P\{\xi(x) = 1, \xi(y) = 1\}
\]

\[
P\{\text{contraction}(xy)\} = P\{\xi(x) > 1, \xi(y) = 1\} = P\{\xi(y) = 1\} - P\{\xi(x) = 0, \xi(y) = 1\} - P\{\xi(x) = 1, \xi(y) = 1\},
\]

where all probabilities are conditioned on the observation of the phylogenetic profile \( \{\xi(\mathcal{L}(T)) = \Phi\} \). Expected numbers for gains, losses, expansions and contractions on each edge \( xy \) are computed by formulas analogous to (21).

Posterior probabilities of the general form \( P\left\{ \xi(x) = n, \xi(y) = m \ \bigg| \ \xi(\mathcal{L}(T)) = \Phi \right\} \), characterizing lineage-specific family size changes on edge \( xy \), can also be computed by using survival likelihoods on truncated phylogenies.
In particular, we decompose the events as

\[ P\{\xi(x) = n, \xi(y) = m, \xi(\mathcal{L}(T)) = \Phi\} = I \times II \times III \]

\[ = P\{\xi(x) = n, \xi(\mathcal{L}(T) \setminus \mathcal{L}(T_x)) = \Phi(\mathcal{L}(T) \setminus \mathcal{L}(T_x))\} \times P\{\xi(y) = m, \xi(\mathcal{L}(T_y)) = \Phi(\mathcal{L}(T_y)) \mid \xi(x) = n\} \times P\{\xi(\mathcal{L}(T_x) \setminus \mathcal{L}(T_y)) = \Phi(\mathcal{L}(T_x) \setminus \mathcal{L}(T_y)) \mid \xi(x) = n\}, \tag{22} \]

where the second factor can be written as

\[ P\{\xi(y) = m, \xi(\mathcal{L}(T_y)) = \Phi(\mathcal{L}(T_y)) \mid \xi(x) = n\} = P\{\xi(y) = m \mid \xi(x) = n\} \sum_{k=0}^{m} \binom{m}{k} (D_y)^{m-k} (1 - D_y)^k L_y[k]. \]

Figure 1 illustrates the decomposition of the phylogeny into three parts, corresponding to the three factors in (22).
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