

MULTI-TYPE BIRTH-DEATH MODELS

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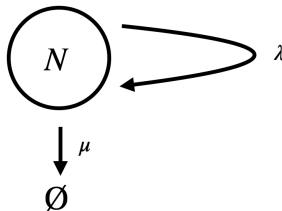
Day 3

- 1 FROM DISCRETE TRAIT ANALYSIS TO PHYLODYNAMICS
- 2 MULTI-TYPE BIRTH DEATH MODELS
- 3 SIMULATING MODELS IN R AND BEAST2

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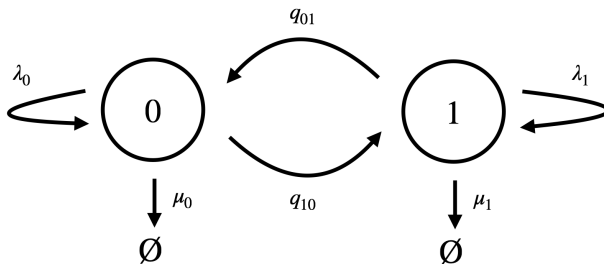
RECALL: BIRTH-DEATH MODELS AND BISSE MODELS



In the basic birth-death model, individual lineages can replicate or die

The parameter of this model is just $\theta = (\lambda, \mu)^T$, the replication/diversification rate, and the death/extinction rate

RECALL: BIRTH-DEATH MODELS AND BiSSE MODELS



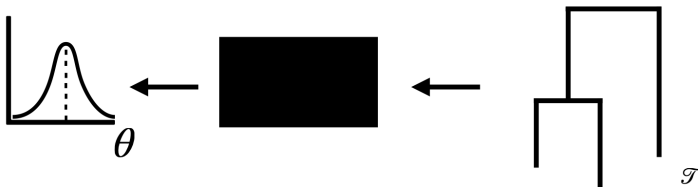
In the BiSSE model, trees \mathcal{T} depend on the parameters $\theta = (\lambda_0, \lambda_1, \mu_0, \mu_1, q_{01}, q_{10})^T$

WHAT FACTORS SHAPE TREES?



In the forward sense, parameters, θ , of these models dictate the types of trees we see (and because we are using biologically-grounded models, this isn't really that much of a "black box" framework)

HOW MUCH INFORMATION ABOUT PARAMETERS IS CONTAINED IN TREES?



On the other hand, the types of trees supported by our sequence data ought to contain some information about the parameters that created them (assuming the tree-generating model is appropriately specified)

PHYLODYNAMIC LIKELIHOOD

$$p(\theta, \mathbf{Q}, \mathbf{A} | \mathbf{s}, \mathbf{x}) \\ \propto \int_{\mathcal{T}} \sum_{\mathbf{u}, \mathbf{y}} p(\mathbf{s}, \mathbf{x}, \mathbf{u}, \mathbf{y} | \mathcal{T}) p(\mathcal{T} | \theta) p(\theta) p(\mathbf{Q}) p(\mathbf{A})$$

The general approach in BEAST2 is to adopt a Bayesian approach by supplying priors on the parameters of the tree-generating model, the sequence evolution model, and the character evolution model, and perform inference on the posterior distribution

PHYLODYNAMIC LIKELIHOOD

In BEAST2 parlance, models for tree generation such as the Yule and birth-death model are called “tree priors”

BiSSE models are sort of accommodated in BEAST2 as special cases of the more general multi-type birth death models, which we dive into in the next section

Another class of models are the **structured coalescent** models, which we will talk about this afternoon

multi-type birth death and structured coalescent models are the main two classes of phylodynamics models accommodated in BEAST2

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MULTI-TYPE BIRTH DEATH MODELS

Basic multi-type birth death model: each type can give birth to other types

- can ignore migration, or include it
- can include a sampling rate to produce heterochronous trees
- result: a character-mapped tree (just like BiSSE)

MULTI-TYPE BIRTH DEATH MODELS¹

λ_{ij} : rate at which individuals in i produce individuals in j

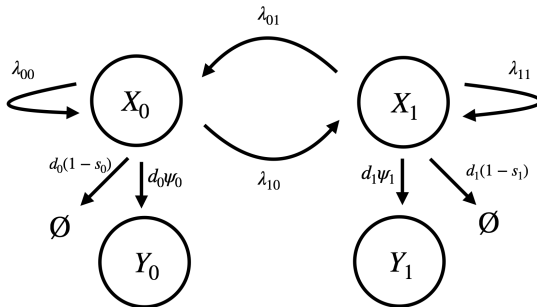
d_i : death rate of individuals in state i

s_i : probability of sampling upon death

This will produce a tree with sampled and unsampled individuals - only the sampled individuals are included in the final tree

¹Tanja Stadler and Sebastian Bonhoeffer. "Uncovering epidemiological dynamics in heterogeneous host populations using phylogenetic methods". In: *Philosophical Transactions of the Royal Society B: Biological Sciences* 368.1614 (2013), p. 20120198.

MULTI-TYPE BIRTH DEATH MODELS²



X_i unobserved, Y_i observed

²Tanja Stadler and Sebastian Bonhoeffer. "Uncovering epidemiological dynamics in heterogeneous host populations using phylogenetic methods". In: *Philosophical Transactions of the Royal Society B: Biological Sciences* 368.1614 (2013), p. 20120198.

MULTI-TYPE BIRTH DEATH MODELS³

Much like BiSSE, we derive a backward equation for $D_{Ni}(t)$, the probability that we observe the tree below branch N (node N is at the tipward end of branch N), given that branch N is in state i at time t :

$$dN_i(t + \Delta t) = \left(1 - \left(\sum_j \lambda_{ij} + d_i \right) \Delta t \right) D_{Ni}(t) + 2 \sum_j \lambda_{ij} \Delta t E_j(t) D_{Ni}(t)$$

³Tanja Stadler and Sebastian Bonhoeffer. “Uncovering epidemiological dynamics in heterogeneous host populations using phylogenetic methods”. In: *Philosophical Transactions of the Royal Society B: Biological Sciences* 368.1614 (2013), p. 20120198.

MULTI-TYPE BIRTH DEATH MODELS⁴

Likewise, we have to track extinction probabilities,

$$\begin{aligned} dE_i(t + \Delta t) = & (1 - s_i) d_i \Delta t \\ & + \left(1 - \left(\sum_j \lambda_{ij} + d_i \right) \Delta t \right) E_i(t) \\ & + \sum_j \lambda_{ij} \Delta t E_i(t) E_j(t) \end{aligned}$$

Notice how $(1 - s_i)$ and d_i are multiplied in this equation

⁴Tanja Stadler and Sebastian Bonhoeffer. “Uncovering epidemiological dynamics in heterogeneous host populations using phylogenetic methods”. In: *Philosophical Transactions of the Royal Society B: Biological Sciences* 368.1614 (2013), p. 20120198.

MULTI-TYPE BIRTH DEATH MODELS⁵

Observations at tips supply initial conditions for our backward equations: the present is time 0, and because tips are sampled through time, we observe a tip at time τ in the past (time measured going into the past)

$$D_{Ni}(\tau) = d_i s_i$$

if the tip is in state i , and equals zero otherwise

Notice that s_i and d_i are always multiplying each other in the initial condition

⁵Tanja Stadler and Sebastian Bonhoeffer. "Uncovering epidemiological dynamics in heterogeneous host populations using phylogenetic methods". In: *Philosophical Transactions of the Royal Society B: Biological Sciences* 368.1614 (2013), p. 20120198.

MULTI-TYPE BIRTH DEATH MODELS⁶

Combining solutions on branches at ancestral nodes: let ancestral node A at time t connect to two branches, N and M
The solutions are combined in a more complicated expression than BiSSE:

$$D_{Ai}(t) = \sum_j (\lambda_{ij}(D_{Mi}(t)D_{Nj}(t) + D_{Mj}(t)D_{Ni}(t)))$$

⁶Tanja Stadler and Sebastian Bonhoeffer. "Uncovering epidemiological dynamics in heterogeneous host populations using phylogenetic methods". In: *Philosophical Transactions of the Royal Society B: Biological Sciences* 368.1614 (2013), p. 20120198.

MULTI-TYPE BIRTH DEATH MODELS⁷

At the root, at time t_0 , there is a collection of conditional likelihoods $D_{Ni}(t_0)$. Stadler and Bonhoeffer combine these in a similar manner as BiSSE, but they condition on observing one sampled individual,

$$\sum_i f_i \frac{D_{Ni}(t_0)}{1 - E_i(t_0)},$$

and they select f_i to be the expected fraction of lineages in state i under the demographic model

⁷Tanja Stadler and Sebastian Bonhoeffer. “Uncovering epidemiological dynamics in heterogeneous host populations using phylogenetic methods”. In: *Philosophical Transactions of the Royal Society B: Biological Sciences* 368.1614 (2013), p. 20120198.

EXTENDING MULTI-TYPE BIRTH DEATH MODELS

This model can be elaborated upon even further

- add migration
- can modify sampling to preserve lineages
- time-dependent rates (at least piece-wise constant with epochs)
- in BDMM-prime, it is possible to sample demographic trajectories alongside phylogenies⁸

⁸Timothy G Vaughan and Tanja Stadler. “Bayesian Phylodynamic Inference of Multitype Population Trajectories Using Genomic Data”. In: *Molecular Biology and Evolution* 42.6 (2025), msaf130.

SUMMARIZING MTBD

With the multi-type birth-death model, we have a way to simulate heterochronous trees, extending BiSSE-style models

These are incorporated in BEAST2, and allow us to sample phylogenetic trees in MCMC

limited functionality in R (but check out the TreeSim package)

SUMMARIZING MTBD

In a full MCMC analysis, we would

- 1 sample parameters of the MTBD model from a prior distribution
- 2 sample a tree from the MTBD model
- 3 calculate likelihood of MSA given the tree

In principle, step 2 could sample a tree that is (i) character-mapped, or (ii) has a particular configuration of internal node states

Recall that the BiSSE trees we simulated in R are character mapped. The same is true of MTBD trees

WHAT DO WE DO WITH A COLLECTION OF CHARACTER MAPPED TREES?

BEAST2 gives us a posterior sample of character-mapped trees arising from the MTBD model

(Actually, this is/can be true even if we are modeling trait change independently of demographics)

With ancestral character estimation, we saw that we could compute a joint or marginal reconstruction of ancestral states

This is not really feasible in an MCMC sampling scheme; actually, even a marginal reconstruction is hard to comprehend if trees have different topologies

HOW ARE POSTERIOR NODE PROBABILITIES CALCULATED?

We need to understand how posterior collections of trees are treated

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LIMITED SUPPORT IN R

These models are more computationally intensive than BiSSE or simpler birth-death/coalescent models without population structure

Our experience working with BiSSE models should help us bridge the gap

MTBD IN R

In R the following R package can simulate multi-type birth death models

- TreeSim

MTBD IN BEAST2

The following BEAST2 packages can simulate multi-type birth death models

- BDMM
- BDMM-prime