The error in Bayesian phylogenetic reconstruction when speciation co-occurs

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Abstract

Keywords: computational biology, evolution, phylogenetics, Bayesian analysis, tree prior [RJCB: Have you already looked up for a target journal?] [GL: Honestly I have literally no idea how to select a good journal for this kind of article.] [RJCB: May I suggest we aim for Molecular Phylogenetics and Evolution, the same journal as the raket paper?]

1 Introduction

- There are many contemporary tools that provide the possibility to infer a phylogeny from genetic data (DNA, RNA, proteins). A popular Bayesian

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phylogenetic tool is called BEAST (Drummond & Rambaut 2007) and its cousin BEAST2 (Bouckaert *et al.* 2014).

- BEAST is very flexible, providing the user with the option to set up all possible phylogenetic priors (e.g. site/clock/speciation model).

- However, currently available priors can be not suitable to analyze some specific datasets. With this work we aim to test whether or not the implementation of a new prior model is beneficial to study a specific kind of diversification process.

- BEAST2 gives us the possibility to introduce new tree priors to infer phylogenies based on different assumptions on how the speciation process takes place.

- One of such speciation processes is the multiple birth hypothesis, a new model (described below) and thus currently absent in BEAST.

- The Multiple birth hypothesis can be useful to explain a phenomenon that has always puzzled evolutionary biologists: what are the drivers of the diversification processes for those phylogenies that show an impressive amount of speciation events in relatively short times? The (constant-rate) birth-death (BD) model embodies the common assumption that only a single speciation event can occur at any given time. The multiple-birth-death (MBD) model relaxes this assumption, allowing events in which large-scale environmental changes lead to a great number of species in relatively short time intervals. Such a hypothesis may be a better fit to describe the burst in systems like cichlid fish diversification in the African Great Lakes: Malawi, Tanganyika and Victoria (Janzen *et al.* 2016, Janzen *et al.* 2017).

- However, it may be that current BD tree priors are good enough at detecting such events, with a (preferred) lower level of complexity. If this is the case one should always be more keen to adopt the simplest model.

- Here we present our study with the aim of exploring when using a more complex MBD tree prior is warranted.

- We hypothesize that the error made today, using BD tree priors, increases with an increased number or stronger effect of multiple birth events. This is straightforward: without multiple birth events or such event having no effect, the MBD model falls back to a BD model. We expect larger errors when we deviate more from the BD model's assumptions. Additionally, we hypothesize MBD having a stronger effect if the normal speciation process is less pronounced. The more speciations are caused by the BD process, there are relatively less multiple-birth events. To put this hypothesis, H1, into an explicit equation, we expect the error made be correlated to the number of species created by the multiple-birth process over the total number of species created:

$$< e >= f\left(\frac{n_{taxa}^{MBD}}{n_{taxa}^{BD} + n_{taxa}^{MBD}}\right) \tag{1}$$

  Where $< e >$ denotes the expected error, f is a monotonously increasing function of unknown shape, n_{taxa}^{MBD} is the number of taxa created in multiple-birth events and n_{taxa}^{BD} is the number of taxa created by the standard BD speciation process.

- We have the hypothesis, H7, that there is no difference in inference errors if the MBD process generates many species in many modest MB events or few intense MB events.

H1: we expect the error made be correlated to the number of species created by the multiple-birth process over the total number of species created

error (nLTT statistic)
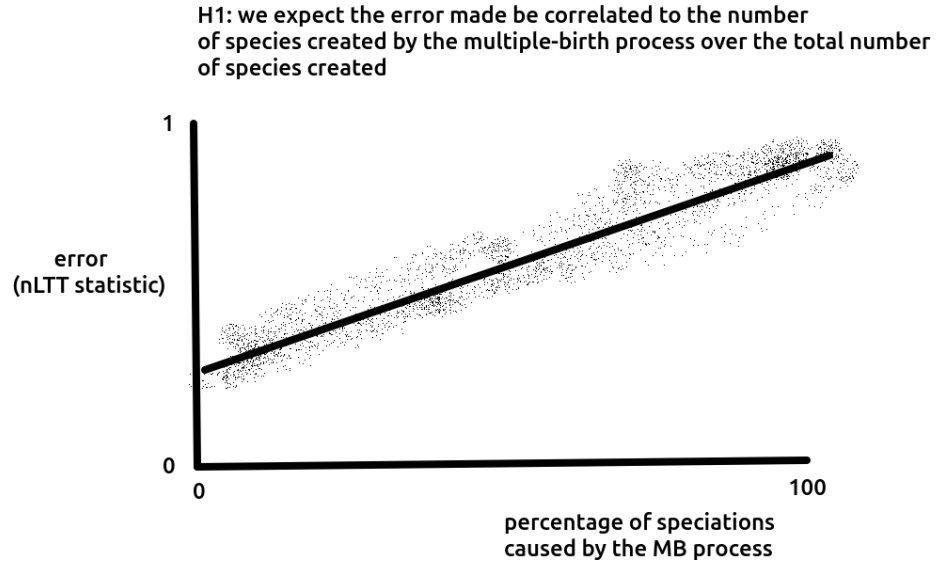
percentage of speciations caused by the MB process

Figure 1: Hypothesis 1: we expect the error made be correlated to the number of species created by the multiple-birth process over the total number of species created

H7: there is no difference in inference errors if the MBD process generates many species in many modest MB events or few intense MB events

error (nLTT statistic)

High nu, low q

Low nu, high q
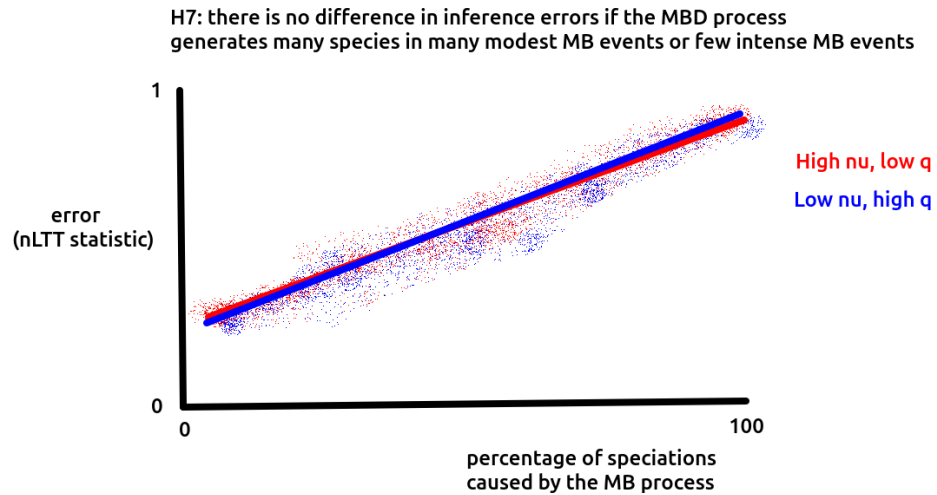
percentage of speciations caused by the MB process

Figure 2: Hypothesis 7: there is no difference in inference errors if the MBD process generates many species in many modest MB events or few intense MB events

66   • We have the hypothesis, H2, that the effect of extinction rates is neutral, as

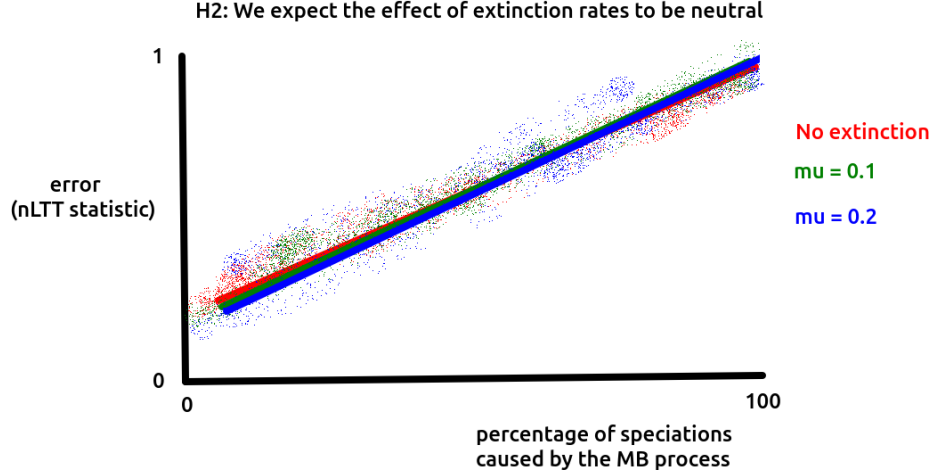67   extinctions will hit lineages created by both speciation processes equally.

Figure 3: Hypothesis 2: the effect of extinction rates is neutral

68   • Due to the proportionality of the term within f, we have the hypothesis,

69   H3, that the timing of a multiple birth event (be it close to the crown age

70   or close to the present) to have no effect. Compared to a late multiple

71   birth event, an early multiple birth event may have a longer-lasting effect

72   (as the next speciation event will be later), but it will create less new

73   species, as there are still fewer taxa.

2   Methods

2.1   Model

76   • Current phylogenetic tools assume that only a single speciation event can

77   occur at any given time. While this assumption is useful to construct

78   a wide variety of successful models (e.g Maddison *et al.* 2007, Valente

79   *et al.* 2015, Etienne *et al.* 2012, Etienne *et al.* 2014), they disallow for
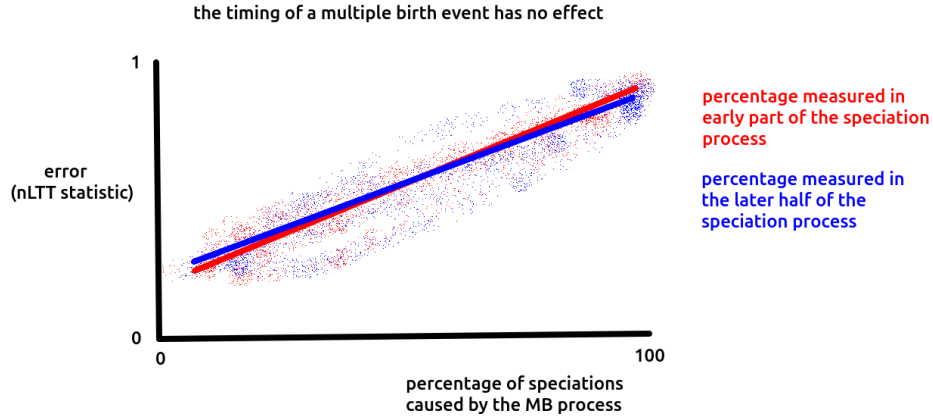
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Figure 4: Hypothesis 3: the timing of a multiple birth event has no effect.

environmental changes that trigger speciations in multiple clades at a same point in time.

- The (constant-rate) birth-death (BD) model embodies the common assumption that only a single speciation event can occur at any given time. The multiple-birth-death (MBD) model relaxes this assumption, allowing events in which large-scale environmental changes lead to a great number of species in relatively short time intervals. Such hypothesis can be useful to describe, for example, systems like cichlid fish diversification in the African Great Lakes: Malawi, Tanganyika and Victoria (Janzen *et al.* 2016, Janzen *et al.* 2017).

- In the MBD model, parameters λ and μ correspond, respectively, to the common per-species speciation and extinction rates present also in the standard BD model. Additionally, MBD relies on two additional parameters. Parameter ν is the rate at which an environmental change is triggered. When such event is triggered, all species present in the phylogeny at that moment have a probability q to speciate at that time, which is independent on λ. Polytomies are not allowed in such process as each

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species can speciate only once at the time.

• It is also possible to write down a likelihood function for such processes
as in Laudanno 2018.

2.2 Simulations

• To prove our hypothesis we simulate two twin datasets. All the simulations
are produced in continuous time, using the Doob-Gillespie algorithm.

• We start simulating $N_S = 1000$ MBD trees, with either 50, 100 and 200
taxa. We have the hypothesis H5, that the number of taxa does not have
an effect on the error being made, as there is no diversity dependency in
any of the processes. We have the hypothesis H6, that for a higher number
of taxa the variance in the error decreases, as more information is present
in the simulated phylogenies.
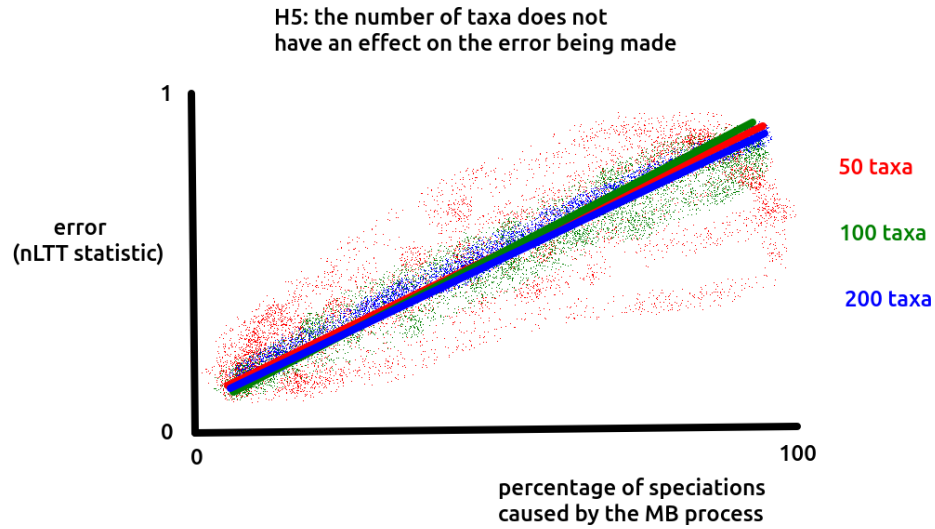

Figure 5: Hypothesis 5: the number of taxa does not have an effect on the error being made

• From each MBD tree, a DNA sequence alignment is simulated. For each
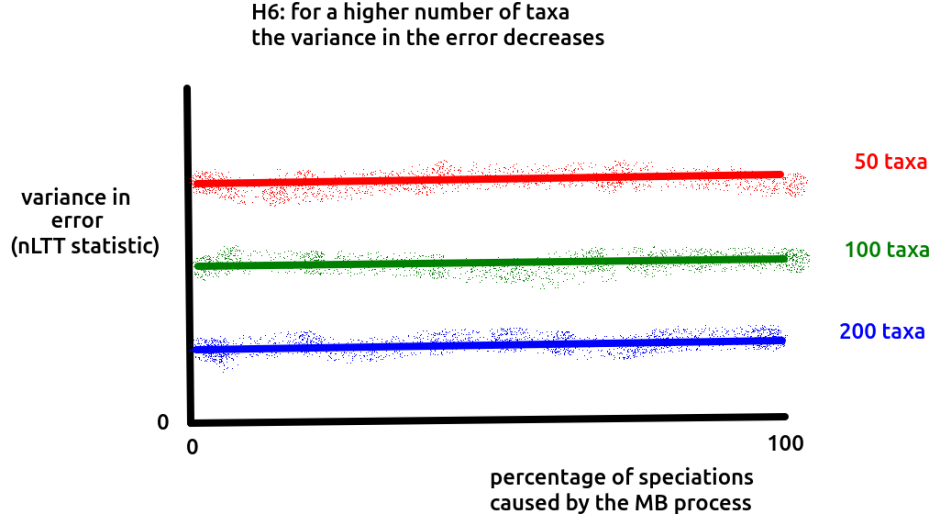
Figure 6: Hypothesis 6: for a higher number of taxa the variance in the error decreases

sequence alignment we then perform a Bayesian analysis to recover a poste-

rior distribution of trees, each composed of N_P phylogenies. Such analysis

is performed using the 'pirouette' package (Bilderbeek 2018) to call the

BEAST2 tool suite from R. We let the Bayesian analysis assume a BD

prior in both cases, to investigate the extent of the error we make under

this assumption.

- For each tree generated under the MBD model we aim to generate a "twin" tree under the BD model. With the word "twin" we denote a tree generated starting from the respective MBD tree, in order to perform a fair comparison with it. This operation has to be done, because we want to compare two trees that are generated by different processes. To do so we infer the parameters λ_{BD} and μ_{BD} from the MBD maximizing the likelihood under a BD model. To perform this operation we use the function "bd_ML" from the package "DDD" (Etienne *et al.* 2012).

- We then exploit such parameters to generate a BD tree using the func-

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¹²⁵ tion "`tess.sim.taxa.age`" from the package "TESS" (Hhna 2013). We

¹²⁶ simulate the tree in such a way the new tree has the same number of tips

¹²⁷ and the same crown age as the MBD tree. We furthermore require that

¹²⁸ the BD tree conserve the topology of the MBD tree. We have hypothesis

¹²⁹ H4 that, compared to the MBD trees, the error will be less in the BD

¹³⁰ twin tree. The difference between the errors made in MBD and twin BD

¹³¹ trees indicates the impact the MBD process has on the error we make in

¹³² inference using a contemporary BD prior.

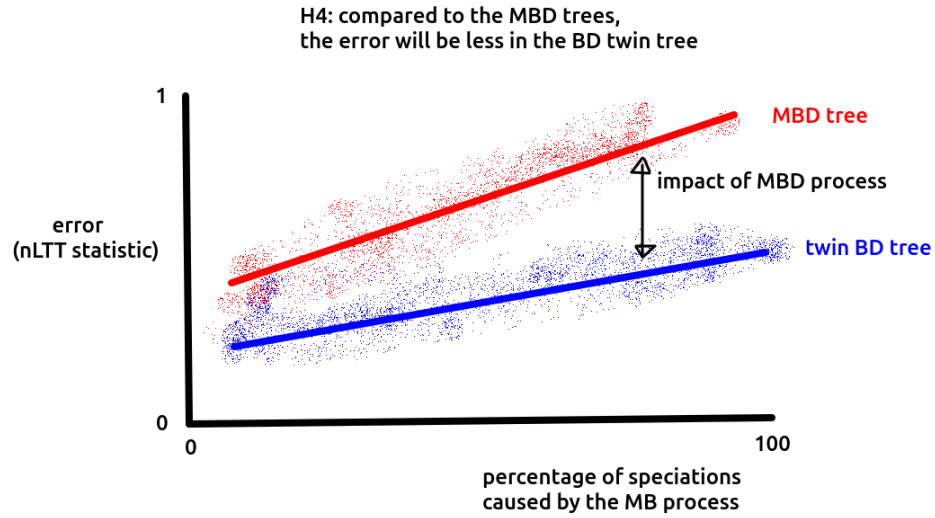Figure 7: Hypothesis 4: compared to the MBD trees, the error will be less in the BD twin tree

¹³³ We want the MBD and twin BD trees to contain the same amount of in-

¹³⁴ formation, i.e. the same number of DNA mutations and the same number

¹³⁵ of taxa at the present:

$$m_{MBD} = m_{BD} \tag{2}$$

¹³⁶ The expected number of mutations m of a phylogeny with crown age $-T$

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137 (with $T > 0$) in fact is given by [RJCB: So one of use likes '-T', the
138 other likes 'T'. How to resolve this?]

$$m = L \cdot \rho \cdot \int_0^T n(t) \ dt \tag{3}$$

139 where L is the number of DNA nucleotides, ρ is the per-site per-species
140 mutation rate and $n(t)$ the number of species at each time.

141 The parameter we'll tune is ρ ... [RJCB: elaborate here :-)]

142 Since we cannot know $n_{BD}(t)$ before running simulations we need to re-
143 place it with a proxy. For this reason we will use the average number of
144 species in time according to the BD model. It's well known that this is
145 equal to [GL: insert proper citation]

$$< n_{BD} > (t) = n_0 \cdot e^{(\mu_{BD} - \lambda_{BD})t} \tag{4}$$

146 where $n_0 = n_{BD}(-T) = n_{MBD}(-T)$ is the initial number of species at
147 the crown age. From 2, 3 and 4 follows:

$$m_{MBD} = L \cdot \rho \cdot \int_0^T < n_{BD} > (t) \ dt = L \cdot \rho \cdot n_0 \cdot \left[\frac{e^{(\mu_{BD} - \lambda_{BD})T} - 1}{\mu_{BD} - \lambda_{BD}} \right] \tag{5}$$

148 If we set $\mu_{BD} = \mu_{MBD}$ and reverse this relation we can extrapolate the
149 value of λ_{BD} to use to generate BD trees.

150 • We explained how we set the parameters for each twin BD tree. Using
151 this rules we generate a BD dataset. We repeat the analysis, producing
152 alignments for each tree and subsequently using BEAST to produce a
153 posterior for each of them.

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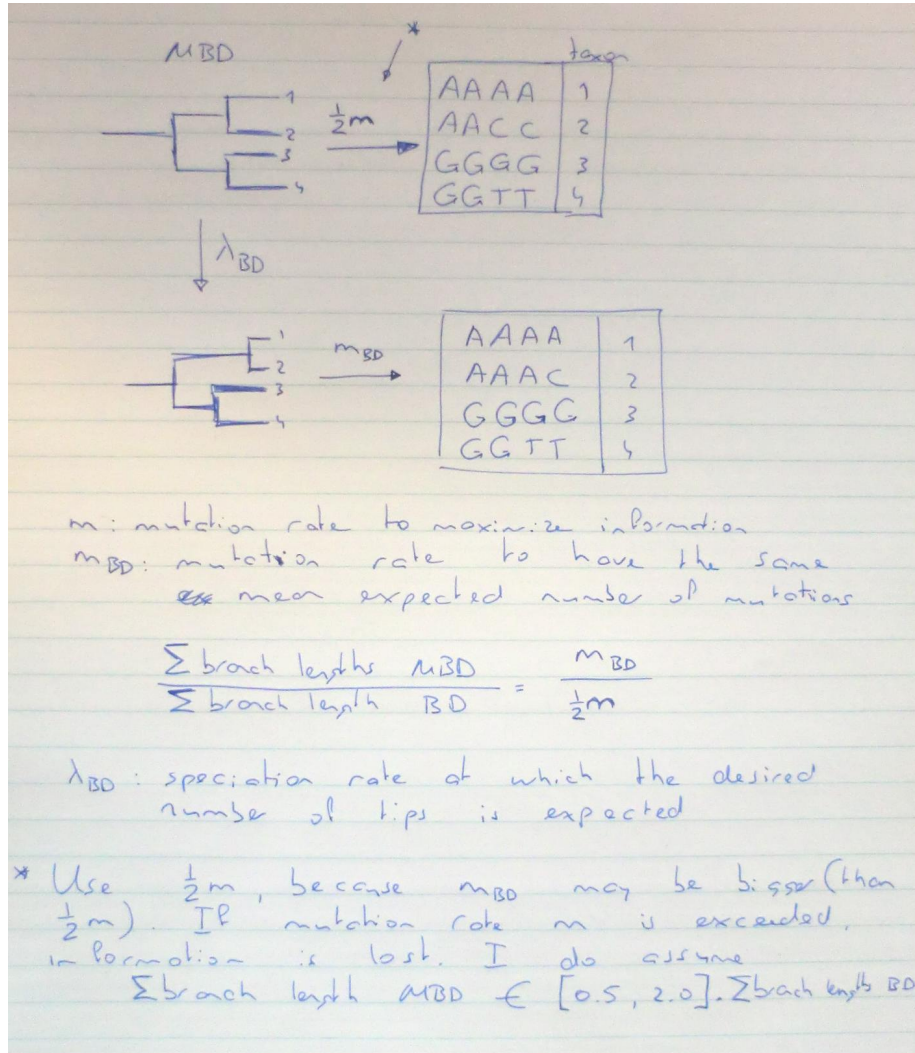
Figure 8: How to create twin trees and alignments. From a focal MBD tree, a twin tree is produced as such: (1) estimate the λ_{BD} to get the same expected number of tips, (2) simulate a BD tree with that amount of tips (discard trees with different number of tips), (3) estimate a mutation rate to get an alignment with the same expected number of mutations, (4) simulate alignments with that amount of mutations (discard those that don't, the picture shows an alignment that should be discarded)

2.3 Measuring the inference error

• So far we have simulated two datasets of trees under the two models:
$\{T_i^{BD}\}_{i=1}^{N_S}$ and $\{T_i^{MBD}\}_{i=1}^{N_S}$. We used them to generate a dataset of align-
ments for each model: $\{X_i^{BD}\}_{i=1}^{N_S}$ and $\{X_i^{MBD}\}_{i=1}^{N_S}$. From each dataset we
produced a posterior distribution from a BD prior: $P_i(\theta|X_i^{BD}, BD)$ and
$P_i(\theta|X_i^{MBD}, BD)$. **[GL: 1) We might want to rename the models,**
e.g. BD = (0) and MBD = (1). These names with capital letters
are too big and ugly;] [RJCB: I would strongly prefer MBD
and BD, as I feel replacing the big ugly capital letters by short
pretty numbers hurts readability even more]

• To compare the results for the two models we measure the inference error
using the nLTT statistic between known/true tree and posterior/inferred
trees (Janzen 2015). To obtain such statistics the procedure is the follow-
ing:

- From each tree $T_{i,j}^M$ (with $j = 1, ..., N_S$) belonging to the posterior
$P_i(\theta|X_i^M, BD)$ and relative to the model M, we extrapolate the lineage-
through-time (LTT), in other words we measure the number of species as
a function of time $n_{i,j}(t)$. To allow a comparison we normalize dividing
by the maximum number of species of each tree, i.e. the number of tips
at the present $N_{i,j}(t) = \frac{n_{i,j}(t)}{n_{i,j}^{max}}$. We then define the nLTT measure as

$nLTT_{i,j} = \int_0^T |N_{i,j}(t) - N_{T_i}|dt$

[GL: I am running out of letters :(] [RJCB: Haha! I suggest to
use the same equation and symbols as equation 1 in the nLTT
article of Janzen, Hoehna and Etienne, 2015:]

$$\Delta nLTT = \int_0^1 |nLTT_1(t) - nLTT_2 t|dt$$

2.4 Model selection

We simulate alignments using the simplest nucleotide substitution model (JC69), the simplest clock model (strict). It is thus imminent to assume these models in our Bayesian inference. Nevertheless, the phylogeny the alignment was based on, could have followed either an MBD or BD tree model, where we in both cases assume a BD tree model. This will have an unknown effect on our inference: it may theoretically be that an MBD model generates (a tree that generates) an alignment in which a different site and/or clock model is favored.

We investigate this by measuring if the generative model (with the simplest nucleotide substitution and simplest clock model) is indeed selected to be the best fitting model. To be precise, we look at the model with the highest marginal likelihood (also called evidence MacKay & Mac Kay 2003), $f(D|M)$, which is the probability of the data D given model M. In the context of this research, D consists of the DNA alignment, and M is the combination of site, clock and tree models.

To estimate the marginal likelihood, we use an algorithm named nested sampling Skilling *et al.* 2006. Nested sampling is attractive to use in a phylogentic context, as it gives a good estimation, requires little tuning Russel *et al.* 2018. Nested sampling is available as a BEAST2 package and can be used by babette Bilderbeek & Etienne 2018.

The nested sampling algorithm stops its run when the marginal likelihood estimation error reaches below a certain tolerance. Similar to Russel *et al.* 2018, we use a (relative) error tolerance ϵ of 10^{-13}, 1 particle to explore the parameter space and 100 active points. To achieve the latter, we use the MCMC chain length L_c of 1M (as also used in the parameter estimates), and a sub-chain length L_{sc} of 10K.

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The models we use in our model comparison are the four combinations of two site models and two clock models. We use the JC69 site model, which is the (generative and) simplest model and GTR, the site model with most degrees of freedom. For the clock models, we use the strict clock model, which is the (generative and) simplest clock model, and the RLN clock model. [RJCB: Could also just be all site models and clock models = 8 models]

From these four marginal likelihood estimates, we calculate the weight of the generative model and plot this in figure 2. We do this for both the alignments derived from the MBD tree and the BD twin tree. We expect that the generative model has the heighest weight in both the MBD and BD alignments. We expect this weight to be higher in the BD alignments.

3   Results

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	Description	Value(s)
L_c	MCMC chain length	10^6
L_{sc}	MCMC sub-chain length	10^4
ϵ	relative error tolerance in marginal likelihood estimation	10^{-13}

Table 1: Overview of the simulation parameters.

Russel, P.M., Brewer, B.J., Klaere, S. & Bouckaert, R.R. (2018) Model selection and parameter inference in phylogenetics using nested sampling. *Systematic Biology*, p. syy050.

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idx	n_{taxa}	f^{MB}_{taxa}	μ	MB regime	n_ν evts	q	λ
1	50	0	0	many modest	8	1 / 8	derive
2	50	0	0	intermediate	4	1 / 4	derive
3	50	0	0	few intense	2	1 / 2	derive
4	50	0	0.1	many modest	8	1 / 8	derive
5	50	0	0.1	intermediate	4	1 / 4	derive
6	50	0	0.1	few intense	2	1 / 2	derive
7	50	0	0.2	many modest	8	1 / 8	derive
8	50	0	0.2	intermediate	4	1 / 4	derive
9	50	0	0.2	few intense	2	1 / 2	derive
10	50	0	0.2	many modest	8	1 / 8	derive
11	50	0.25	0	intermediate	4	1 / 4	derive
12	50	0.25	0	few intense	2	1 / 2	derive
13	50	0.25	0	many modest	8	1 / 8	derive
14	50	0.25	0.1	intermediate	4	1 / 4	derive
15	50	0.25	0.1	few intense	2	1 / 2	derive
16	50	0.25	0.1	many modest	8	1 / 8	derive
17	50	0.25	0.2	intermediate	4	1 / 4	derive
18	50	0.25	0.2	few intense	2	1 / 2	derive
19	50	0.25	0.2	many modest	8	1 / 8	derive
20	50	0.25	0.2	intermediate	4	1 / 4	derive
21	50	0.5	0	few intense	2	1 / 2	derive
22	50	0.5	0	many modest	8	1 / 8	derive
23	50	0.5	0	intermediate	4	1 / 4	derive
24	50	0.5	0.1	few intense	2	1 / 2	derive
25	50	0.5	0.1	many modest	8	1 / 8	derive
26	50	0.5	0.1	intermediate	4	1 / 4	derive
27	50	0.5	0.2	few intense	2	1 / 2	derive
28	50	0.5	0.2	many modest	8	1 / 8	derive
29	50	0.5	0.2	intermediate	4	1 / 4	derive
30	50	0.5	0.2	few intense	2	1 / 2	derive
31	50	0.75	0	many modest	8	1 / 8	derive
32	50	0.75	0	intermediate	4	1 / 4	derive
33	50	0.75	0	few intense	2	1 / 2	derive
34	50	0.75	0.1	many modest	8	1 / 8	derive
35	50	0.75	0.1	intermediate	4	1 / 4	derive
36	50	0.75	0.1	few intense	2	1 / 2	derive
37	50	0.75	0.2	many modest	8	1 / 8	derive
38	50	0.75	0.2	intermediate	4	1 / 4	derive
39	50	0.75	0.2	few intense	2	1 / 2	derive
40	50	0.75	0.2	many modest	8	1 / 8	derive
41	50	1	0	intermediate	4	1 / 4	0
42	50	1	0	few intense	2	1 / 2	0
43	50	1	0	many modest	8	1 / 8	0
44	50	1	0.1	intermediate	4	1 / 4	0
45	50	1	0.1	few intense	2	1 / 2	0
46	50	1	0.1	many modest	8	1 / 8	0
47	50	1	0.2	intermediate	4	1 / 4	0
48	50	1	0.2	few intense	2	1 / 2	0
49	50	1	0.2	many modest	8	1 / 8	0
50	50	1	0.2	intermediate	4	1 / 4	0

Table 2: Overview of the MBD parameters 1/3.

idx	n_{taxa}	f_{taxa}^{MB}	μ	MB regime	n_ν evts	q	λ
51	100	0	0	few intense	2	1 / 2	derive
52	100	0	0	many modest	8	1 / 8	derive
53	100	0	0	intermediate	4	1 / 4	derive
54	100	0	0.1	few intense	2	1 / 2	derive
55	100	0	0.1	many modest	8	1 / 8	derive
56	100	0	0.1	intermediate	4	1 / 4	derive
57	100	0	0.2	few intense	2	1 / 2	derive
58	100	0	0.2	many modest	8	1 / 8	derive
59	100	0	0.2	intermediate	4	1 / 4	derive
60	100	0	0.2	few intense	2	1 / 2	derive
61	100	0.25	0	many modest	8	1 / 8	derive
62	100	0.25	0	intermediate	4	1 / 4	derive
63	100	0.25	0	few intense	2	1 / 2	derive
64	100	0.25	0.1	many modest	8	1 / 8	derive
65	100	0.25	0.1	intermediate	4	1 / 4	derive
66	100	0.25	0.1	few intense	2	1 / 2	derive
67	100	0.25	0.2	many modest	8	1 / 8	derive
68	100	0.25	0.2	intermediate	4	1 / 4	derive
69	100	0.25	0.2	few intense	2	1 / 2	derive
70	100	0.25	0.2	many modest	8	1 / 8	derive
71	100	0.5	0	intermediate	4	1 / 4	derive
72	100	0.5	0	few intense	2	1 / 2	derive
73	100	0.5	0	many modest	8	1 / 8	derive
74	100	0.5	0.1	intermediate	4	1 / 4	derive
75	100	0.5	0.1	few intense	2	1 / 2	derive
76	100	0.5	0.1	many modest	8	1 / 8	derive
77	100	0.5	0.2	intermediate	4	1 / 4	derive
78	100	0.5	0.2	few intense	2	1 / 2	derive
79	100	0.5	0.2	many modest	8	1 / 8	derive
80	100	0.5	0.2	intermediate	4	1 / 4	derive
81	100	0.75	0	few intense	2	1 / 2	derive
82	100	0.75	0	many modest	8	1 / 8	derive
83	100	0.75	0	intermediate	4	1 / 4	derive
84	100	0.75	0.1	few intense	2	1 / 2	derive
85	100	0.75	0.1	many modest	8	1 / 8	derive
86	100	0.75	0.1	intermediate	4	1 / 4	derive
87	100	0.75	0.2	few intense	2	1 / 2	derive
88	100	0.75	0.2	many modest	8	1 / 8	derive
89	100	0.75	0.2	intermediate	4	1 / 4	derive
90	100	0.75	0.2	few intense	2	1 / 2	derive
91	100	1	0	many modest	8	1 / 8	0
92	100	1	0	intermediate	4	1 / 4	0
93	100	1	0	few intense	2	1 / 2	0
94	100	1	0.1	many modest	8	1 / 8	0
95	100	1	0.1	intermediate	4	1 / 4	0
96	100	1	0.1	few intense	2	1 / 2	0
97	100	1	0.2	many modest	8	1 / 8	0
98	100	1	0.2	intermediate	4	1 / 4	0
99	100	1	0.2	few intense	2	1 / 2	0
100	200	1	0.2	many modest	8	1 / 8	0

Table 3: Overview of the MBD parameters 2/3.

idx	n_{taxa}	f_{taxa}^{MB}	μ	MB regime	n_ν evts	q	λ
101	200	0	0	intermediate	4	1 / 4	derive
102	200	0	0	few intense	2	1 / 2	derive
103	200	0	0	many modest	8	1 / 8	derive
104	200	0	0.1	intermediate	4	1 / 4	derive
105	200	0	0.1	few intense	2	1 / 2	derive
106	200	0	0.1	many modest	8	1 / 8	derive
107	200	0	0.2	intermediate	4	1 / 4	derive
108	200	0	0.2	few intense	2	1 / 2	derive
109	200	0	0.2	many modest	8	1 / 8	derive
110	200	0	0.2	intermediate	4	1 / 4	derive
111	200	0.25	0	few intense	2	1 / 2	derive
112	200	0.25	0	many modest	8	1 / 8	derive
113	200	0.25	0	intermediate	4	1 / 4	derive
114	200	0.25	0.1	few intense	2	1 / 2	derive
115	200	0.25	0.1	many modest	8	1 / 8	derive
116	200	0.25	0.1	intermediate	4	1 / 4	derive
117	200	0.25	0.2	few intense	2	1 / 2	derive
118	200	0.25	0.2	many modest	8	1 / 8	derive
119	200	0.25	0.2	intermediate	4	1 / 4	derive
120	200	0.25	0.2	few intense	2	1 / 2	derive
121	200	0.5	0	many modest	8	1 / 8	derive
122	200	0.5	0	intermediate	4	1 / 4	derive
123	200	0.5	0	few intense	2	1 / 2	derive
124	200	0.5	0.1	many modest	8	1 / 8	derive
125	200	0.5	0.1	intermediate	4	1 / 4	derive
126	200	0.5	0.1	few intense	2	1 / 2	derive
127	200	0.5	0.2	many modest	8	1 / 8	derive
128	200	0.5	0.2	intermediate	4	1 / 4	derive
129	200	0.5	0.2	few intense	2	1 / 2	derive
130	200	0.5	0.2	many modest	8	1 / 8	derive
131	200	0.75	0	intermediate	4	1 / 4	derive
132	200	0.75	0	few intense	2	1 / 2	derive
133	200	0.75	0	many modest	8	1 / 8	derive
134	200	0.75	0.1	intermediate	4	1 / 4	derive
135	200	0.75	0.1	few intense	2	1 / 2	derive
136	200	0.75	0.1	many modest	8	1 / 8	derive
137	200	0.75	0.2	intermediate	4	1 / 4	derive
138	200	0.75	0.2	few intense	2	1 / 2	derive
139	200	0.75	0.2	many modest	8	1 / 8	derive
140	200	0.75	0.2	intermediate	4	1 / 4	derive
141	200	1	0	few intense	2	1 / 2	0
142	200	1	0	many modest	8	1 / 8	0
143	200	1	0	intermediate	4	1 / 4	0
144	200	1	0.1	few intense	2	1 / 2	0
145	200	1	0.1	many modest	8	1 / 8	0
146	200	1	0.1	intermediate	4	1 / 4	0
147	200	1	0.2	few intense	2	1 / 2	0
148	200	1	0.2	many modest	8	1 / 8	0
149	200	1	0.2	intermediate	4	1 / 4	0
150	200	1	0.2	few intense	2	1 / 2	0

Table 4: Overview of the MBD parameters 3/3.