

# Dating with constraints

A detailed tutorial on McmcDate

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## Abstract

McmcDate can date a phylogenetic tree with constraints. That is, it can estimate the ages of ancestral nodes of phylogenetic trees with node age calibrations, node order constraints, and node braces. McmcDate is fast because it approximates the phylogenetic likelihood with a multivariate normal distribution.

Here, I briefly review the process of dating phylogenetic trees and provide an example dating analysis of a tree of eukaryotes. I use data from Strassert et al. (2021) who provide the alignment and node age calibrations from fossils. Moreover, I use node order constraints from two possible successions of plastid endosymbiosis events.

**This tutorial is a work in progress.**

## Contents

### 1 Definitions

We use the term (*rooted*) *tree* to denote a directed acyclic graph with node labels and branch lengths in which not more than one branch connects any two nodes. Usually, nodes correspond to (ancestral) species, and branch lengths to sequence distance or time. We use the term (*rooted*) *topology* to denote a (rooted) tree without information about branch lengths. We put the word *rooted* into parentheses, because it is sometimes omitted. The root of the tree or topology is the only node with all branches pointing away to other nodes. The root is the oldest node. Leaves are extant nodes with a single branch pointing towards them.

For a given topology, *dating the tree*<sup>1</sup> corresponds to finding branch lengths for this topology which are measured in absolute time units (for example, in Million years), and which describe the data in the *best* way. *Best* can mean different things, and we will carefully analyze what *best* means in our case. Sometimes, all we can do is date a tree with relative time units (Section ??).

Similarly, we use the term *unrooted tree* to denote an undirected acyclic graph with node labels and branch lengths in which not more than one branch

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<sup>1</sup>We should probably say *dating the topology* but this phrase is not used.

connects any two nodes. Finally, we use the term *unrooted topology* to denote an unrooted tree without information about branch lengths. We need unrooted trees and topologies because we will use reversible substitution models (for a review, see Yang 2006) to infer unrooted trees with branch lengths measured in expected number of substitutions. Reversible substitution models are unable to discriminate between the two directions in time.

## 2 Dating a tree

Dating a tree is difficult because we want to estimate branch lengths measured in absolute time units. However, an alignment only contains information about distances measured in expected number of substitutions. In particular, it does not contain information about the evolutionary rates nor about the actual elapsed absolute time units. For a given branch,

$$\begin{aligned} d [\text{expected number of substitutions}] &= \\ r [\text{expected number of substitutions per year}] \cdot t [\text{years}], \end{aligned} \tag{1}$$

where  $d$  is the branch length measured in expected number of substitutions,  $r$  is the evolutionary rate on this branch, and  $t$  is the branch length measured in absolute time units. The situation is severe because  $r$  and  $t$  are confounded. If we multiply  $t$  with a positive number  $c$  and divide  $r$  by the same positive number  $c$ , the distance  $d$  stays constant. Since the likelihood only depends on the distance  $d$  we can not discriminate between parameter tuples  $(t, r)$  and  $(t', r')$ , where

$$t' = t \cdot c, \tag{2}$$

$$r' = r/c, \tag{3}$$

for *any*  $c \in (0, \infty)$ ! This means we need auxiliary data to constrain the ages of at least some nodes. There are three forms of constraints from auxiliary data which are explained in the next sections: (a) node age calibrations, (b) node order constraints, and (c) node braces. Appendix ?? details the specifications about how auxiliary data is used with McmcDate.

### 2.1 Node age calibrations

We call constraints on the ages of internal nodes *node age calibrations*. Without node age calibrations, all dated trees are equally likely! Since most phylogenetic dating methods are Bayesian, and impose prior functions on all of their parameters, the values of the posterior function of different trees still differ in a deceiving way. However, in the absence of node age calibrations, the differences in the values of the posterior function are exclusively caused by the chosen prior functions, and not by the information we have obtained from the data.

Even more, in order to limit the maximum ages of the nodes, we require at least one node age calibration with a maximum boundary. The closer in terms of absolute time units the calibrated node with a maximum boundary is to the root, the better. Ideally, we have a maximum age boundary for the root itself, but sometimes the root age boundaries are unknown. Section ?? provides details on how to add node age calibrations to your dating analysis with McmcDate.

I can not repeat this often enough: **Without proper node age calibrations**, and in particular, **without at least one maximum age boundary**, **dating a tree in absolute time units is impossible**. Without a single maximum node age boundary, we can still date the tree using branch lengths measured in *relative time units*. In particular, we achieve this by fixing the tree height to be 1.0. McmcDate automatically falls back to dating in relative time when no maximum node age boundary is found. If other programs date trees in absolute time units without a maximum age boundary, do not trust the results!

## 2.2 Node order constraints

Next to calibrating the absolute ages of nodes, we can also constrain the relative order of nodes on a tree. For example, due to external analyses, we may have detailed knowledge about a horizontal gene transfer. That is, we do know the exact donor and the recipient branches. In this case, a direct horizontal gene transfer can only happen, if these branches coexist for a period of time (Figure ??). If the branches do not coexist for a period of time but the recipient branch is younger than the donor branch, the horizontal gene transfer can still happen indirectly through multiple events. An indirect gene transfer requires an intermediate lineage carrying the gene. The intermediate lineage has either gone extinct (Szöllősi et al. 2013), has not been sampled, or has lost the gene. Gene transfers are impossible if the recipient branch is older than the donor branch.

For example, let the ages of the old and young nodes of the donor and recipient branches be  $DO$ ,  $DY$ ,  $RO$ , and  $RY$ , respectively. Then, a direct horizontal gene transfer provides us with two node order constraints,

$$DY < RO, \text{ and } DO > RY, \quad (4)$$

where  $<$  means *younger than* and  $>$  means *older than*. If we allow indirect gene transfers, we only get one node order constraint,

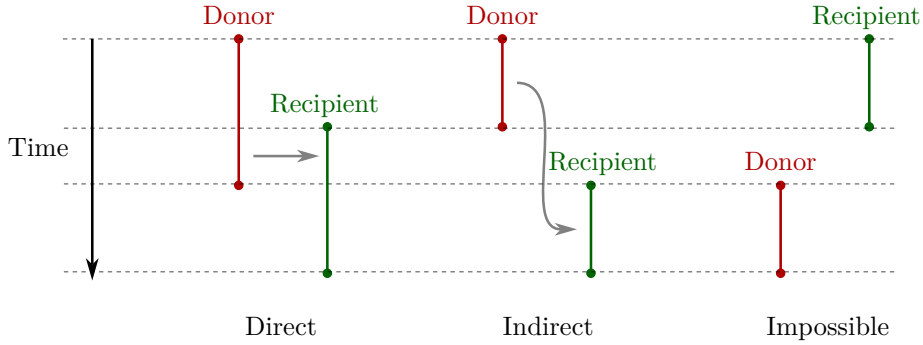
$$DO > RY. \quad (5)$$

The last constraint is enough to prohibit impossible gene transfers as depicted in Figure ??.

Sometimes, we do not know the exact donor branch but only that the donor branch must be part of a known subtree. However, we usually do know the recipient branch which is the stem of the subtree comprising the species which contain the horizontally transferred gene. In this case, the ancestral node of the stem of the donor subtree has to be older than the descending node of the recipient branch.

## 2.3 Node braces

Finally, sometimes we know that two or more nodes have the same age or similar ages. For example, when analyzing gene trees, an early gene duplication event may separate the gene tree into two subtrees. Subsequent speciation events may be observable on both subtrees, and the corresponding speciation nodes should have similar ages. In this tutorial we will not brace nodes but see Appendix ?? for the specifications.



**Figure 1:** Direct, indirect and impossible horizontal gene transfers. A direct horizontal gene transfer happens between branches coexisting in time. An indirect horizontal gene transfer involves multiple events and an intermediate lineage. If the recipient branch is older than the donor branch, a horizontal gene transfer is impossible.

### 3 Pipeline

McmcDate is fast because it uses a clever way to approximate the phylogenetic likelihood similar to MCMCTree (Yang and Rannala 2005). MCMCTree approximates the surface of the phylogenetic likelihood using Taylor expansion (Reis and Yang 2011). That is, a prior analysis computes the maximum likelihood together with the gradient and the Hessian matrix which MCMCTree uses in a subsequent analysis to date the tree.

Here, we use a similar technique, albeit with a Bayesian method to estimate the posterior distribution of branch lengths measured in expected number substitutions. In particular, the pipeline for dating a tree with McmcDate is:

1. Prepare a multi sequence alignment and an unrooted topology.
2. For this alignment and unrooted topology, infer a distribution of unrooted trees with branch lengths measured in expected number of substitutions.
3. Find a rooted topology to date. Prepare auxiliary data such as node age calibrations or node order constraints.
4. Date the topology with McmcDate. In particular, infer a distribution of rooted trees with branch lengths measured in absolute time units. If the node age calibrations are insufficient, we can still use relative time units.

Steps 3 and 4 are fast, especially when compared to Step 2. Hence, we can conveniently amend parameters used in the actual dating analysis, or compute dated trees for different roots. The following section shows an example analysis and describes the steps of the pipeline in detail.

## 4 Example analysis

### 4.1 Step 1: Alignment and unrooted topology

We are going to date a topology of eukaryotes (Strassert et al. 2021). The full published data set contains three alignments:

1. The alignment with the highest number of taxa comprises 733 eukaryotes with 62723 amino acids.
2. The authors used the first alignment to infer a tree with IQ-TREE (Minh et al. 2020) so they can filter taxa in an informed way (for example, keep slow evolving taxa). The reduced data set comprises 136 operational taxonomic units with 73460 amino acids.
3. A small data set with 63 operational taxonomic units and 73460 amino acids for tree inference with Bayesian models.

Here, we focus on the second alignment with 136 taxa. We use shorter taxon names and I have converted the file from FASTA format to Phylip format which is required by Phylobayes (Lartillot et al. 2013). I provide the alignment `strassert-136taxa.phy` in the [data subfolder](#) of this tutorial:

```
1 data/strassert-136taxa.phy
```

For the phylogenetic inference in the next step, we also need an unrooted topology. I have unrooted the tree in Figure 3 in Strassert et al. (2021). Similar to the alignment, I provide the unrooted topology in the [data subfolder](#) of this tutorial:

```
1 data/strassert-136taxa.unrooted.tre
```

Please also see the [README](#) in the [data subfolder](#).

## 4.2 Step 2: Phylogenetic inference

Here, we use a Bayesian method to estimate the posterior distribution. In particular,

- Use Phylobayes (Lartillot et al. 2013).
- Decide on evolutionary model depending on the size of the data set and the computational requirements. Recommended models from preferred but slow and complex to fast and simple: GTR+CAT+G4, LG+CAT+G4, LG+EDM64+G4, LG+C60+G4, LG+G4.

We specify an evolutionary model with exchangeabilities EX, and across-site compositional heterogeneity model ASCH as EX+ASCH. All discussed evolutionary models used for simulations as well as inferences implicitly use discrete gamma rate heterogeneity with four components.

- GTR model (Tavaré 1986).
- CAT model (Lartillot and Philippe 2004).
- Gamma rate variation model (Yang 1993).
- LG model (Le and Gascuel 2008).
- EDM model (Schrempf et al. 2020).
- C60 model (Quang et al. 2008)

### 4.3 Step 3: Rooted topology and auxiliary data

Strassert et al. (2021) discuss one unrooted topology with two possible root positions. (1) The root separates amorphea from diaphoretickes and excavates (Figure 3 in Strassert et al. 2021), and (2) the root separates amorphea and excavates from diaphoretickes. Here, we choose option (1) which is the more plausible one.

In this tutorial, we use 33 fossil calibrations compiled by Strassert et al.

- Node order calibrations (Yang and Rannala 2005).
- Relative node order constraints (Szöllösi et al. 2022).
- McmcDate can also brace nodes (Appendix ??).

Hello.

### 4.4 Step 4: Dating with McmcDate

- McmcDate is a Haskell program; Appendix ?? provides details about the internals of McmcDate.

## A Auxiliary data specifications

The specifications match McmcDate version 1.0.0.0 and may change between different versions of McmcDate.

### A.1 Node age calibrations

Node age calibrations can be provided in two ways:

- with comma separated value (CSV) files, or
- with Newick tree files (MCMCTree specification; see the documentation of MCMCTree; only L, U, and B are supported).

If the filename ends with `csv`, assume the calibrations are provided in CSV format. Otherwise, assume the calibrations are provided on a Newick tree. The CSV file has a header (see below), and one or more rows of the following format:

```
1 Name,LeafA,LeafB,YoungAge,YoungProbabilityMass,OldAge,OldProbabilityMass
```

In this case, the calibrated node is uniquely defined as the most recent common ancestor of `LeafA` and `LeafB`. The age of the node is calibrated between the lower (young) and upper (old) boundary. The probability mass describes the softness (or hardness) of a boundary. In other words, the probability mass describes the steepness of the decline of the prior function outside the calibration interval. In general, the larger the probability mass the softer the boundary. We specify probability masses with respect to a normalized time interval of size 1.0. That is, probability masses have to be strictly positive and strictly less than 1.0, which is the total probability mass in the unit interval.

I usually use values between 0.0001 (hard) and 0.03 (soft). If unsure, use probability masses of 0.025, which corresponds to 2.5 percent probability at each boundary or constraint. A probability mass close to 1.0 will correspond to a prior function too soft to have any effect. Note that this way of specifying boundary softness using relative values independent of the actual node ages differs from MCMCTree which uses absolute values (Yang and Rannala 2005). When using a Newick tree to specify node age calibrations, and when no probability masses are provided, a default value of 0.01 is used. This measure is in place to support the same input files as MCMCTree.

To specify one-sided node age calibrations, omit the other boundary and the corresponding probability mass. For example, the following file defines a node age calibration with a lower boundary at 1e6 time units (years in this case) with probability mass 0.025:

```
1 Name,LeafA,LeafB,YoungAge,YoungProbabilityMass,OldAge,OldProbabilityMass
2 Primates,Human,Chimpanzees,1e6,0.025,,
```

## A.2 Node order constraints

Node order constraints are provided using a comma separated value (CSV) file with a header (see below) and one or more rows of the following format:

```
1 Name,YoungerLeafA,YoungerLeafB,OlderLeafA,OlderLeafB,ProbabilityMass
```

The younger and older nodes are uniquely defined as the most recent common ancestors of YoungerLeafA and YoungerLeafB, as well as OlderLeafA and OlderLeafB, respectively. As described in the previous section about node age calibrations, the probability mass describes the softness (or hardness) of the constraint. For example, the following file defines a constraint where the ancestor of leaves A and B is younger than the ancestor of leaves C and D:

```
1 Name,YoungerLeafA,YoungerLeafB,OlderLeafA,OlderLeafB,ProbabilityMass
2 ExampleConstraint,A,B,C,D,0.025
```

McmcDate reports and removes redundant constraints such as constraints affecting nodes that are vertically related.

## A.3 Node braces

Node braces are provided using files in JavaScript object notation (JSON) format. Similar to node age calibrations and node order constraints, the braced nodes are specified using pairs of leaves. However, the softness (or hardness) of braces is defined in a different way. The reason is that more than two nodes can be braced, and so, there is no canonical way to describe the softness using probability mass. Rather, for a specific node brace, the differences between the node ages and the average age of all nodes in the particular node brace are normally distributed with the provided standard deviation.

The following example defines two node braces constraining two and three nodes, respectively:

```

1  [
2    {
3      "braceDataName": "Brace1",
4      "braceDataNodes": [
5        [
6          "NodeXLeafA",
7          "NodeXLeafB"
8        ],
9        [
10         "NodeYLeafA",
11         "NodeYLeafB"
12       ]
13     ],
14     "braceDataStandardDeviation": 0.0001
15   },
16   {
17     "braceDataName": "Brace2",
18     "braceDataNodes": [
19       [
20         "NodeALeafA",
21         "NodeALeafB"
22       ],
23       [
24         "NodeBLeafA",
25         "NodeBLeafB"
26       ],
27       [
28         "NodeCLeafA",
29         "NodeCLeafB"
30       ]
31     ],
32     "braceDataStandardDeviation": 0.0001
33   }
34 ]

```

In this case, the braced nodes of the first node brace are uniquely defined as the most recent common ancestors of `NodeXLeafA` and `NodeXLeafB`, as well as `NodeYLeafA` and `NodeYLeafB`. The steepness of the brace prior function is defined using the standard deviation. This file defines hard node braces.

## B Internals

I have written `McmcDate` in Haskell. The Haskell programming language is versatile, interesting, and leads to more maintainable code with fewer bugs when compared to other programming languages. Nevertheless, the tooling support is sometimes sub-optimal. Before running `McmcDate` you need to compile the Haskell code. In most cases, the [wrapper script called `run`](#), which is used in this tutorial, does this for you in a reproducible way, and so there is no need for manual action. Sometimes, however, manual action may be required.

In this case, you need a rough understanding of the tools involved. There are two build tools commonly used with Haskell: `cabal-install`, and `Stack` with binaries `cabal`, and `stack`, respectively. I recommend using `cabal-install`, and the wrapper script uses `cabal-install` by default. If you want to use `Stack`, use the option `-s` like so: `run -s ...`. See also the output of `run -h`. In rare occasions you may want to clean your local build cache. You can do this by running `cabal clean` or `stack clean`; or more strictly, by deleting the `dist-newstyle` or



.stack-work directories in you working directories for cabal-install and Stack, respectively.

## B.1 Wrapper script

The wrapper script run tries to make a good compromise between usability and customizability. It exposes some, but not all functionality of McmcDate:

```
1 Usage: run [OPTIONS] RELAXED_MOLECULAR_CLOCK_MODEL LIKELIHOOD_SPECIFICATION COMMANDS
2
3 Prior options:
4 -b Activate braces
5 -c Activate calibrations
6 -k Activate constraints
7
8 Algorithm related options:
9 -i NAME Initialize state and cycle from previous analysis with NAME
10 -H Activate Hamiltonian proposal (slow, but great convergence)
11 -m Use Mc3 algorithm instead of Mhg
12
13 Other options:
14 -f FILE Use a different analysis configuration file (relative path)
15 -n SUFFIX Use an analysis suffix
16 -p Activate profiling
17 -s Use Haskell stack instead of cabal-install
18
19 Relaxed molecular clock model:
20 ug Uncorrelated gamma model
21 ul Uncorrelated log normal model
22 al Autocorrelated log normal model
23
24 Likelihood specification:
25 f Full covariance matrix
26 s Sparse covariance matrix
27 u Univariate approach
28 n No likelihood; use prior only
29
30 Available commands:
31 p Prepare analysis
32 r Run dating analysis
33 c Continue dating analysis
34 m Compute marginal likelihood
35
36 A configuration file "analysis.conf" is required.
37 For reference, see the sample configuration file.
```

If you need to adjust specific parameters or settings, you can (a) call the McmcDate executable directly, and, if this is not enough, (b) directly change parameters or functions in the code. In the following, I briefly explain both options.

## B.2 Direct invocation of McmcDate

Use the build tool of your choice (see above) to directly run McmcDate. For example, with cabal-install:

```
1 cabal run mcmc-date-run -- -h
```

```
1 Up to date
2 mcmc-date; version 1.0.0.0
3
4 Usage: mcmc-date-run COMMAND
5
6   Date a phylogenetic tree using calibrations and constraints
7
8 Available options:
9   -h,--help           Show this help text
10
11 Available commands:
12   prepare             Prepare data
13   run                 Run MCMC sampler
14   continue            Continue MCMC sampler
15   marginal-likelihood Calculate marginal likelihood
```

The help shows that McmcDate exposes four sub-commands. For example, to get help about how to run a new analysis:

```
1 cabal run mcmc-date-run -- run -h
```

```
1 Up to date
2 Usage: mcmc-date-run run --analysis-name NAME [--preparation-name NAME]
3           [--calibrations "SPEC FILE" (mind the quotes)]
4           [--ignore-problematic-calibrations]
5           [--constraints FILE] [--ignore-problematic-constraints]
6           [--braces FILE] [--init-from-save ANALYSIS_NAME]
7           [--profile] [--hamiltonian] --likelihood-spec ARG
8           --relaxed-molecular-clock ARG [--seed NUMBER] [--mc3]
9
10   Run MCMC sampler
11
12 Available options:
13   --analysis-name NAME      Analysis name
14   --preparation-name NAME   Preparation name
15   --calibrations "SPEC FILE" (mind the quotes)
16                             Specify calibrations (SPEC is either csv or tree)
17   --ignore-problematic-calibrations
18                             Ignore and use problematic calibrations
19   --constraints FILE        File name specifying constraints
20   --ignore-problematic-constraints
21                             Ignore and drop problematic constraints
22   --braces FILE             File name specifying braces
23   --init-from-save ANALYSIS_NAME
24                             Reuse state and proposal tuning parameters from a
25                             previous run; if successful, also reduce burn in
26   --profile                  Activate profiling
27   --hamiltonian              Activate Hamiltonian proposal
28   --likelihood-spec ARG      Likelihood specification (see below).
29   --relaxed-molecular-clock ARG
30                             Relaxed molecular clock model (see below).
31   --seed NUMBER              Set the seed (default: unset, random).
32   --mc3                      Use MC3 instead of MHG algorithm
33   -h,--help                  Show this help text
34
35 Relaxed molecular clock model:
```

```

36 - UncorrelatedGamma
37 - UncorrelatedLogNormal
38 - AutocorrelatedLogNormal
39 Likelihood specification:
40 - FullMultivariateNormal
41 - SparseMultivariateNormal PENALTY (usually 0.1)
42 - UnivariateNormal

```

Hence, an example command line is:

```

1 cabal run -- mcmc-date-run run \
2   --analysis-name example \
3   --calibrations "csv calibrations.csv" \
4   --constraints "constraints.csv" \
5   --relaxed-molecular-clock "UncorrelatedLogNormal" \
6   --likelihood-spec "SparseMultivariateNormal 0.1"

```

Get help about how to continue an analysis with:

```

1 cabal run mcmc-date-run -- continue -h

```

Consequently, continue the above example analysis with:

```

1 cabal run -- mcmc-date-run continue \
2   --analysis-name example \
3   --calibrations "csv calibrations.csv" \
4   --constraints "constraints.csv" \
5   --relaxed-molecular-clock "UncorrelatedLogNormal" \
6   --likelihood-spec "SparseMultivariateNormal 0.1"

```

The commands are verbose. In my experience, detailed specification of the parameters and settings on the command line involves more investment in the beginning, but reduces the number of bogus analyses in the end.

### B.3 Understanding the Haskell code

At the core of McmcDate are two libraries I have authored: [mcmc](#), a general purpose Markov chain Monte Carlo (MCMC) sampler with advanced algorithms; and [elynx-tree](#), a library for handling trees.

Additionally, I have separated McmcDate into two parts. Part (a) is the executable `mcmc-date-run` with modules specifying the state space, the prior and likelihood functions, the proposals, and MCMC-specific settings such as the number of burn-in and normal iterations. These modules are in the subfolder [app](#) of the McmcDate repository. Part (b) is a library containing prior functions and proposals specific to phylogenetic trees. I will not provide details for the library part here, but feel free to contact me for specific questions if you want. In general, you can access detailed help by rendering and opening the documentation directly contained in the source files:

```

1 cabal haddock mcmc-date

```

```

1 Build profile: -w ghc-9.2.4 -01
2 In order, the following will be built (use -v for more details):
3 - mcmc-date-1.0.0.0 (lib) (ephemeral targets)
4 Preprocessing library for mcmc-date-1.0.0.0..
5 Running Haddock on library for mcmc-date-1.0.0.0..
6 100% ( 4 / 4) in 'Mcmc.Tree.Import'
7 100% ( 16 / 16) in 'Mcmc.Tree.Types'
8 100% ( 2 / 2) in 'Mcmc.Tree.Prior.Branch'
9 100% ( 10 / 10) in 'Mcmc.Tree.Prior.Branch.RelaxedClock'
10 100% ( 6 / 6) in 'Mcmc.Tree.Prior.BirthDeath'
11 100% ( 3 / 3) in 'Mcmc.Tree.Monitor'
12 100% ( 11 / 11) in 'Mcmc.Tree.Lens'
13 100% ( 18 / 18) in 'Mcmc.Tree.Prior.Node.Constraint'
14 100% ( 20 / 20) in 'Mcmc.Tree.Prior.Node.Calibration'
15 100% ( 2 / 2) in 'Mcmc.Tree.Prior.Node.CalibrationFromTree'
16 100% ( 12 / 12) in 'Mcmc.Tree.Prior.Node.Brace'
17 100% ( 2 / 2) in 'Mcmc.Tree.Prior.Node.Combined'
18 100% ( 12 / 12) in 'Mcmc.Tree.Proposal.Unconstrained'
19 100% ( 7 / 7) in 'Mcmc.Tree.Proposal.Ultrametric'
20 100% ( 7 / 7) in 'Mcmc.Tree.Proposal.Contrary'
21 100% ( 3 / 3) in 'Mcmc.Tree.Proposal.Brace'
22 100% ( 22 / 22) in 'Mcmc.Tree'
23 Documentation created:
24 /home/dominik/Shared/haskell/mcmc-date/dist-newstyle/build/x86_64-linux/ghc-9.2.4/ ...

```

In my case, the documentation in HTML format is then available at

`${SUBSTITUTE_ABOVE_PATH}/mcmc-date-1.0.0.0/doc/html/mcmc-date/index.html`

which, I am sure, you can remember easily. Did I already say that Haskell tooling has room for improvements?

Now, back to the application part (a), which will most likely be more important for you. In particular, you may want to have a look at the modules

**Definitions** Contains proposals and monitors, as well as MCMC-specific settings. If you want to change the number of burn-in iterations, or the number of total iterations, have a look and change this file.

**State** Defines the state space. If you really want to understand what is going on, this should be your starting point. The documentation is detailed, and explains the separation of the time tree and rate tree objects, as well as the birth and death prior.

The other more important modules are:

**Main** Contains functions to prepare the data, as well as to run and continue the analysis. This module also contains helper functions to calculate the marginal likelihood.

**Probability** Defines the prior and likelihood functions. This module is important, if you want to tweak the prior.

The less important modules are:

**Hamiltonian** Hamiltonian proposal.

**Monitor** Prior specific monitoring functions.

**Options** Handle command line options.

**Tools** Miscellaneous tools.

## References

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