babette: BEAUti 2, BEAST2 and Tracer for R

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May 7, 2018

Summary

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- 1. In the field of phylogenetics, BEAST2 is one of the most widely used software tools. It comes with the graphical user interfaces BEAUti 2, DensiTree and Tracer, to create BEAST2 configuration files and to interpret BEAST2's output files. However, when many different alignments or model setups are required, a workflow of graphical user interfaces is cumbersome.
- 2. Here, we present a free, libre and open-source package, babette:

 'BEAUti 2, BEAST2 and Tracer for R', for the R programming language.

 babette creates BEAST2 input files, runs BEAST2 and parses its results,

 all from an R function call.
 - 3. We describe babette's usage and the novel functionality it provides compared to the original tools and we give some examples.
 - 4. As babette is designed to be of high quality and extendable, we conclude by describing the further development of the package.

Keywords: computational biology, evolution, phylogenetics, BEAST2, R

1 Introduction

Phylogenies are commonly used to explore evolutionary hypotheses. Not only can phylogenies show us how species (or other evolutionary units) are related to each other, but we can also estimate relevant parameters such as extinction and speciation rates from them. There are many phylogenetics tools available 27 to obtain an estimate of the phylogeny of a given set of species. BEAST2 (Bouckaert et al. 2014) is one of the most widely used ones. It uses a Bayesian statistical framework to estimate the joint posterior distribution of phylogenies and model parameters, from one or more DNA, RNA or amino acid alignments 31 (see figure 1 for an overview of the workflow). BEAST2 has a graphical and a command-line interface, that both need a 33 configuration file containing alignments and model parameters. BEAST2 is bundled with BEAUti 2 (Drummond et al. 2012) ('BEAUti' from now on), a desktop 35 application to create a BEAST2 configuration file. BEAUti has a user-friendly 36 graphical user interface, with helpful default settings. As such, BEAUti is an attractive alternative to manual and error-prone editing of BEAST2 configuration files. However, BEAUti cannot be called from a command-line script. This implies that when the user wants to explore the consequences of various settings, this must be done manually. This is the managable workflow when using a few alignments and doing a superficial analysis of sensitivity of the reconstructed tree to model settings. For exploring many trees (for instance from simulations) and for more thorough sensitivity analysis, one would like to loop through mul-45 tiple (simulated) alignments, nucleotide substitution models, clock models and tree priors. One such tool to replace BEAUti is BEASTmasteR (Matzke 2015), 47 which focuses on morphological traits and tip-dating, but also supports DNA data. BEASTmasteR, however, requires hundreds of lines of R code to setup the 50 BEAST2 model configuration and a Microsoft Excel file to specify alignment 51 files.

BEAST2 is also associated with Tracer (Rambaut & Drummond 2007) and
DensiTree (Bouckaert & Heled 2014). Both are desktop applications to analyze the output of BEAST2, each with a user-friendly graphical user interface. Tracer's purpose is to analyze the parameter estimates generated from a
BEAST2 run. It shows, among others, the effective sample size (ESS) and time
series ('the trace', hence the name) of each variable in the MCMC run. Both
ESS and trace are needed to assess the strength of the inference. DensiTree visualizes the phylogenies of a BEAST2 posterior, with many options to improve
the simultaneous display of many phylogenies.

However, for exploring the output of many BEAST2 runs, one would like a script to collect all parameters' ESSes, parameter traces and posterior phylogenies. There is no single package that offers a complete solution, but examples of R packages that offer a partial solution are rBEAST (Ratmann 2015) and RBeast (Faria & Suchard 2015). RBeast provides some plotting options and parsing of BEAST2 output files, but the plotting functions are too specific for general use. rBEAST was developed to test a particular biological hypothesis (Ratmann et al. 2016), and hence was not designed for general use.

Here, we present babette: BEAUti 2, BEAST2 and Tracer for R, which creates BEAST2 (v.2.4.7) configuration files, runs BEAST2, and analyzes its results, all from an R function call. This will save time, tedious mouse clicking and reduces the chances of errors in such repetitive actions. The interface of babette mimics the tools it is based on. This familiarity helps both beginner and experienced BEAST2 users to make the step from those tools to babette. babette enables the creation of a single-script pipeline from sequence alignments to posterior analysis in R.

2 Description

babette is written in the R programming language (R Core Team 2013) and enables the full BEAST2 workflow from a single R function call, in a similar way to what subsequent usage of BEAUti, DensiTree and Tracer would produce. babette's main function is bbt_run, which configures BEAST2, runs it and 81 parses its output. bbt_run needs at least the name of a FASTA file containing a DNA alignment. The default settings for the other arguments of bbt_run are identical to BEAUti's and BEAST2's default settings. Per alignment, a site model, clock model and tree prior can be chosen. Multiple alignments can be 85 used, each with its own (unlinked) site model, clock model and tree prior. babette currently has 108 exported functions to set up a BEAST2 config-87 uration file. babette can currently handle the majority of BEAUti use cases. Because of BEAUti's high number of plugins, babette uses a software architecture that is designed to be extended. Furthermore, babette has 13 exported functions to run and help run BEAST2. One function is used to run BEAST2, another one installs BEAST2 to a default location. Finally, babette has 21 exported function to parse the BEAST2 output files and analyze the created posterior. babette gives the same ESSes and summary statistics as Tracer. The data is formatted such that it can easily be visualized using ggplot2 (for a trace, similar to Tracer) or phangorn (Schliep 2011) (for the phylogenies in a posterior, similar to DensiTree). 97 Currently, babette does not contain all functionality in BEAUti, BEAST2 and their many plug-ins, because these tools themselves also change in time. 99 babette currently works only on DNA data, because this is the most common 100 use case. Nevertheless, babette provides the majority of default tree priors and 101 supports the most important command-line arguments of BEAST2, provides the 102 core Tracer analysis options, and has the most basic subset of plotting options of 103

- DensiTree. Up till now, the babette features implemented are those requested
- by users. Further extension of babette will be based on future user requests.

3 Usage

```
babette can be installed easily from CRAN:
107
    install.packages("babette")
108
    For the most up-to-date version, one can download and install the package from
109
    babette's GitHub repository:
110
    devtools::install_github("richelbilderbeek/babette")
111
    To start using babette, load its functions in the global namespace first:
112
    library(babette)
113
    Because babette calls BEAST2, BEAST2 must be installed. This can be done
114
    from R, using:
115
    install_beast2()
116
    This will install BEAST2 to the default user data folder, but a different path
117
    can be specified as well. BEAUti, and likewise babette, needs at least a FASTA
118
    filename to produce a BEAST2 configuration file. In BEAUti, this is achieved
119
    by loading a FASTA file, then saving an output file using a common save file
    dialog. After this, BEAST2 needs to be applied to the created configuration
121
    file. It creates multiple files storing the posterior. These output files must be
    parsed by either Tracer or DensiTree. In babette, all this is achieved by:
123
    out <- bbt_run(fasta_filenames = "anthus_aco.fas")</pre>
124
```

This code will create a (temporary) BEAST2 configuration file, from the FASTA file with name anthus_aco.fas (which is supplied with the package, from 126 (Van Els & Norambuena 2018)), using the same default settings as BEAUti,

```
which are, among others, a Jukes-Cantor site model, a strict clock, and a Yule
   birth tree prior. babette will then execute BEAST2 using that file, and parses
129
   the output. The returned data structure, named out, is a list of parameter
130
   estimates (called estimates), posterior phylogenies (called anthus_aco_trees,
131
   named after the alignment's name) and MCMC operator performance (operators).
132
    An example of using a different site model, clock model and tree prior is:
133
    out <- bbt_run(
134
      fasta_filenames = "anthus_aco.fas",
135
      site_models = create_hky_site_model(),
136
      clock_models = create_rln_clock_model(),
      tree_priors = create_bd_tree_prior()
138
   )
   This code uses an HKY site model, a relaxed log-normal clock model and a birth-
140
    death tree prior, each with their default settings in BEAUti. Table 1 shows an
141
    overview of all functions to create site models, clock models and tree priors. Note
    that the arguments' names site_models, clock_models and tree_priors are
143
    plural, as each of these can be (a list of) one or more elements. Each of these
    arguments must have the same number of elements, so that each alignment has
145
   its own site model, clock model and tree prior. An example of two alignments,
   each with its own site model, is:
147
    out <- bbt_run(
148
      fasta_filenames = c(
149
         "anthus_aco.fas",
150
         "anthus_nd2.fas"
151
      ),
152
      site_models = list(
153
         create_tn93_site_model(),
154
         create_gtr_site_model()
155
```

```
)
156
    )
157
    babette also uses the same default prior distributions as BEAUti for each of
158
    the site models, clock models and tree priors. For example, by default, a Yule
159
    tree prior assumes that the birth rate follows a uniform distribution, from minus
160
    infinity to plus infinity. One may prefer a different ddistribution instead. Here
161
    is an example how to specify an exponential distribution for the birth rate in a
162
    Yule tree prior in babette:
163
    out <- bbt_run(
      fasta_filenames = "anthus_aco.fas",
165
      tree_priors = create_yule_tree_prior(
166
         birth_rate_distr = create_exp_distr()
167
      )
168
    )
169
    In this same example, one may specify the initial shape parameters of the expo-
170
    nential distribution. In BEAST2's implementation, an exponential distribution
171
    has one shape parameter: its mean, which can be set to any value with BEAUti.
172
    To set the mean value of the exponential distribution to a fixed (non-estimated)
    value, do:
174
    out <- bbt_run(
175
      fasta_filenames = "anthus_aco.fas",
176
      tree_priors = create_yule_tree_prior(
177
         birth_rate_distr = create_exp_distr(
178
           mean = create_mean_param(
179
              value = 1.0,
180
              estimate = FALSE
181
           )
         )
```

```
)
184
    )
185
    babette also supports node dating. Like BEAUti, one can specify Most Recent
186
    Common Ancestor ('MRCA') priors. An MRCA prior allows to specify taxa
    having a common ancestor, including a distribution for the date of that ancestor.
188
    With babette, this is achieved as follows:
189
    out <- bbt_run(
190
      fasta_filenames = "anthus_aco.fas",
191
      mrca_priors = create_mrca_prior(
192
         taxa_names = sample(get_taxa_names("anthus_aco.fas"),
193
             size = 2),
194
         alignment_id = get_alignment_id("anthus_aco.fas"),
195
         is_monophyletic = TRUE,
196
        mrca_distr = create_normal_distr(
197
           mean = create_mean_param(value = 15.0, estimate =
198
               FALSE),
199
           sigma = create_sigma_param(value = 0.025, estimate =
200
               FALSE)
201
         )
      )
203
    )
    Instead of dating the ancestor of two random taxa, any subset of taxa can
205
    be selected, and multiple sets are allowed. babette allows for the same core
206
    functionality as Tracer to show the values of the parameter estimates sampled
207
    in the BEAST2 run. This is called the "trace" (hence the name). The start
208
    of the trace, called the "burn-in", is usually discarded, as an MCMC algorithm
209
    (such as used by BEAST2) first has to converge to its equilibrium and hence
210
    the parameter estimates are not representative. By default, Tracer discards the
```

```
first 10\% of all the parameter estimates. To remove a 20\% burn-in from all
    parameter estimates in babette, the following code can be used:
213
    traces <- remove_burn_ins(</pre>
214
       traces = out$estimates,
215
       burn_in_fraction = 0.2
216
    )
217
    Tracer shows the ESSes of each posterior's variables. These ESSes are important
218
    to determine the strength of the inference. As a rule of thumb, an ESS of 200 is
219
    acceptable for any parameter estimate. To calculate the effective sample sizes
    (of all estimated variables) in babette:
221
    esses <- calc_esses(
222
       traces = traces,
223
       sample_interval = 1000
224
225
    Tracer displays multiple summary statistics for each estimated variable: the
226
    mean and its standard error, standard deviation, variance, median, mode, geo-
227
    metric mean, 95\% highest posterior density interval, auto-correlation time and
228
    effective sample size. It displays these statistics per variable. In babette, these
229
    summary statistics are collected for all estimated parameters at once:
230
    sum_stats <- calc_summary_stats(</pre>
231
       traces = traces,
232
       sample_interval = 1000
233
    )
234
    babette allows for the same functionality as DensiTree. DensiTree displays the
    phylogenies in a posterior at the same time scale, drawn one over one another,
236
    allowing to see the uncertainty in topology and branch lengths. The posterior
```

phylogenies are stored as anthus_aco_trees in the object out, and can be

238

```
plotted as follows:
    plot_densitree(phylos = out$anthus_aco_trees)
240
   Instead of running the full pipeline, babette also allows to only create a BEAST2
241
    configuration file. To create a BEAST2 configuration file, with all settings to
   default, use:
243
    create_beast2_input_file(
244
      input_filenames = babette::get_babette_path("anthus_aco.
245
          fas"),
246
      output_filename = "beast2.xml"
247
   )
248
   This file can then be loaded and edited by BEAUti, run by BEAST2, or run by
   babette:
250
   run_beast2(
      input_filename = "beast2.xml",
252
      output_log_filename = "run.log",
253
      output_trees_filenames = "posterior.trees",
254
      output_state_filename = "final.xml.state"
255
   )
256
   run_beast2 is a function that only runs BEAST2, and does not parse the output
257
   files (unlike bbt_run). In the example above, we specify the names of the desired
   BEAST2 output files explicitly, and these will be created in the R working
259
    directory, after which they can be inspected with other tools, or used to continue
   a BEAST2 run. When the names of these files are not specified, both bbt_run
261
   and run_beast2 put these files in the default temporary folder (as obtained
   from temp.dir()) to keep the working directory clean of intermediate files.
263
```

4 babette resources

```
babette is free, libre and open source software available at http://github.
    com/richelbilderbeek/babette and is licensed under the GNU General Pub-
    lic License v3.0. babette uses the Travis CI (https://travis-ci.org) con-
267
    tinuous integration service, which is known to significantly increase the number
268
    of bugs exposed (Vasilescu et al. 2015) and increases the speed at which new
    features are added (Vasilescu et al. 2015). babette has a 100% code cover-
270
    age, which correlates with code quality (Horgan et al. 1994; Del Frate et al.
    1995). babette follows Hadley Wickham's style guide (Wickham 2015), which
272
    improves software quality (Fang 2001). babette depends on multiple packages,
273
    which are ape (Paradis et al. 2004), beautier (Bilderbeek 2018b), beastier
274
    (Bilderbeek 2018a), devtools (Wickham & Chang 2016), geiger (Harmon et al.
275
    2008), ggplot2 (Wickham 2009), knitr (Xie 2017), phangorn (Schliep 2011),
276
    rmarkdown (Allaire et al. 2017), seqinr (Charif & Lobry 2007), stringr (Wick-
277
    ham 2017), testit (Xie 2014) and tracerer (Bilderbeek 2018c). We tested
278
    babette to give a clean error message for incorrect input, by calling babette
279
    one million times with random or random sensible inputs, using a high perfor-
    mance computer cluster. The test scripts are supplied with babette.
281
       babette's development takes place on GitHub, https://github.com/richelbilderbeek/
    babette, which accommodates collaboration (Perez-Riverol et al. 2016) and im-
283
    proves transparency (Gorgolewski & Poldrack 2016). babette's GitHub facili-
284
    tates feature requests and has guidelines how to do so.
285
       babette's documentation is extensive. All functions are documented in the
286
    package's internal documentation. For quick use, each exported function shows
287
    a minimal example. For easy exploration, each exported function's documen-
288
    tation links to related functions. Additionally, babette has a vignette that
289
    demonstrates extensively how to use it. There is documentation on the GitHub
290
```

to get started, with a dozen examples of BEAUti screenshots with equivalent babette code. Finally, babette has tutorial videos that can be downloaded or viewed on YouTube, https://goo.gl/weKaaU.

²⁹⁴ 5 Citation of babette

Scientists using babette in a published paper can cite this article, and/or cite
the babette package directly. To obtain this citation from within an R script,
use:

> citation("babette")

²⁹⁹ 6 Acknowledgements

Thanks to Yacine Ben Chehida and Paul van Els for supplying their BEAST2 300 use cases. Thanks again to Paul van Els for sharing his FASTA files for use 301 by this package. Thanks to Leonel Herrera-Alsina, Raphael Scherrer and Gio-302 vanni Laudanno for their comments on this package and article. Thanks to 303 Huw Ogilvie and one anonymous reviewer for reviewing this article. Thanks to rOpenSci, and especially Noam Ross and Guangchuang Yu for reviewing the 305 package's source code. We would like to thank the Center for Information Technology of the University of Groningen for their support and for providing access 307 to the Peregrine high performance computing cluster. We thank the Netherlands Organization for Scientific Research (NWO) for financial support through 309 a VICI grant awarded to RSE.

7 Authors' contributions

- 312 RJCB and RSE conceived the idea for the package. RJCB created and tested
- the package, and wrote the first draft of the manuscript. RSE contributed
- 314 substantially to revisions.

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- tion in R. R package version 1.17.

Name	Description
bbt_run	Run BEAST2
create_gtr_site_model	Create a GTR site model
create_hky_site_model	Create an HKY site model
create_jc69_site_model	Create a Jukes-Cantor site model
create_tn93_site_model	Create a TN93 site model
create_rln_clock_model	Create a relaxed log-normal clock model
create_strict_clock_model	Create a strict clock model
create_bd_tree_prior	Create a birth-death tree prior
create_cbs_tree_prior	Create a coalescent Bayesian skyline tree prior
create_ccp_tree_prior	Create a coalescent constant-population tree prior
create_cep_tree_prior	Create a coalescent exponential-population tree prior
create_yule_tree_prior	Create a Yule tree prior
create_beta_distr	Create a beta distribution
create_exp_distr	Create an exponential distribution
create_gamma_distr	Create a gamma distribution
create_inv_gamma_distr	Create an inverse gamma distribution
create_laplace_distr	Create a Laplace distribution
create_log_normal_distr	Create a log-normal distribution
create_normal_distr	Create a normal distribution
create_one_div_x_distr	Create a 1/X distribution
create_poisson_distr	Create a Poisson distribution
create_uniform_distr	Create a uniform distribution

Table 1: babette's main functions

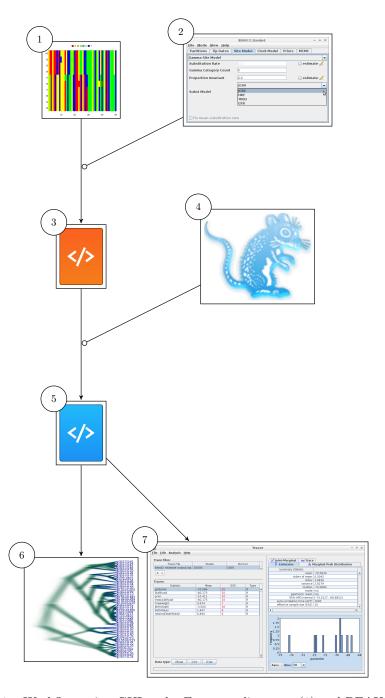


Figure 1: Workflow using GUI tools. From an alignment (1) and BEAUti (2), a BEAST2 configuration file (3) is created. BEAST2 (4) uses that file to infer a posterior, storing it in multiple files (5). These results are visualized using DensiTree (6) and Tracer (7). babette allows for the same workflow, all from an R function call.