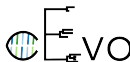


Taming the Beast Workshop

Priors and starting values

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June 28, 2016



Priors and starting values

Priors

Prior distribution

Tree prior

Substitution model prior

Clock prior

Parameter prior

Think twice

Starting values

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- ▶ Distribution of a parameter before the data is collected and analysed
- ▶ as opposed to POSTERIOR distribution which combines the information from the prior and the data


What is a prior?

- Using Bayes theorem, we can decompose the posterior:


$$P(\text{genetic sequences} | \text{genealogy} | \text{demographic model} | \text{substitution model} | \text{molecular clock model} | \text{genetic sequences}) = \frac{P(\text{genetic sequences} | \text{genealogy} | \text{demographic model} | \text{substitution model} | \text{molecular clock model}) P(\text{genealogy} | \text{demographic model} | \text{substitution model} | \text{molecular clock model}) P(\text{demographic model} | \text{substitution model} | \text{molecular clock model}) P(\text{substitution model} | \text{molecular clock model}) P(\text{molecular clock model})}{P(\text{genetic sequences})}$$




genetic
sequences




genealogy



demographic
model



substitution
model



molecular clock
model

Figure adapted from [du Plessis and Stadler, 2015]

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$$P(\text{genetic sequences} | \text{genealogy} | \text{demographic model} | \text{substitution model} | \text{molecular clock model}) = \underbrace{P(\text{genetic sequences} | \text{genealogy} | \text{demographic model} | \text{substitution model})}_{P(\text{genetic sequences} | \text{genealogy} | \text{demographic model} | \text{substitution model})} P(\text{genealogy} | \text{demographic model}) P(\text{demographic model}) P(\text{substitution model}) P(\text{molecular clock model})$$






 genetic sequences
  genealogy
  demographic model
  substitution model
  molecular clock model

Figure adapted from [du Plessis and Stadler, 2015]

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What is a prior?

- Using Bayes theorem, we can decompose the posterior:

$$P(\text{genetic sequences} | \text{genealogy}, \text{demographic model}, \text{substitution model}, \text{molecular clock model}) = \underbrace{P(\text{genealogy} | \text{genetic sequences})}_{P(\text{genetic sequences})} \underbrace{P(\text{demographic model} | \text{genealogy})}_{P(\text{genealogy})} \underbrace{P(\text{substitution model} | \text{demographic model})}_{P(\text{demographic model})} \underbrace{P(\text{molecular clock model} | \text{substitution model})}_{P(\text{substitution model})} \underbrace{P(\text{genetic sequences} | \text{molecular clock model})}_{P(\text{molecular clock model})}$$






 genetic sequences
  genealogy
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Figure adapted from [du Plessis and Stadler, 2015]

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- ▶ Allows us to include any information we have on the process, before looking at the data
 - ▶ Do not be afraid of using it in the inference
- ▶ Prior distribution does not have to, and is not expected to, be exactly the same as the posterior

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- ▶ Should not be and is not universal for all the analyses you will ever do in your research
- ▶ Should incorporate prior (before looking at the data) knowledge about the parameter/underlying process
 - ▶ use results of previous independent experiments
 - ▶ use other independent evidence
- ▶ Should not be too restrictive if prior knowledge/assumptions are weak
 - ▶ One can use diffuse priors
- ▶ May not be adjusted after the run, to give higher and higher posterior support

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- ▶ Is a choice of
 - ▶ model
 - ▶ tree-generating models, nucleotide/AA/codon substitution models, ...
- and of
 - ▶ distribution of plausible values for a parameter of interest
 - ▶ Uniform, Normal, Beta,...

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- ▶ Have to pick one from Coalescent or Birth-death process framework
- ▶ Have to put priors on parameters of the chosen model
 - ▶ e.g. growth-rate of the population, R_0 , extinction rate, ...

- ▶ The selection is big: JC69, HKY85, ..., GTR
- ▶ Use model which has been previously identified to be best for your type of data
 - ▶ e.g. HKY85
 - ▶ Prior for transition/transversion rate ratio (κ)
 - ▶ Prior for base frequencies
- ▶ To choose the best model
 - ▶ Use model comparison to choose the one best fitting the data
 - ▶ Use rjMCMC directly in BEAST2 to sample from the posterior distribution including different substitution models. The model where rjMCMC spends the most time (samples the most from), is the best fitting model.

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- ▶ Strict clock: all branches have the same clock rate
- ▶ Relaxed clock
 - ▶ Uncorrelated: branches have independent clock rate distributions
 - ▶ Correlated: child branch has clock rate distribution correlated to distribution of the parent branch

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- ▶ Can be fixed to a given value
(though this is generally not recommended)
- ▶ Can have upper and lower limits
 - ▶ If we know that any infected individual recovers after 5-10 days, we can set the distribution of infectious period to be e.g. min 4 days and max 11 days
- ▶ If specified by a parametric distribution, the parameters of this distribution can also be assigned a prior (hyperprior)
- ▶ You can visualise the distribution in BEAUti

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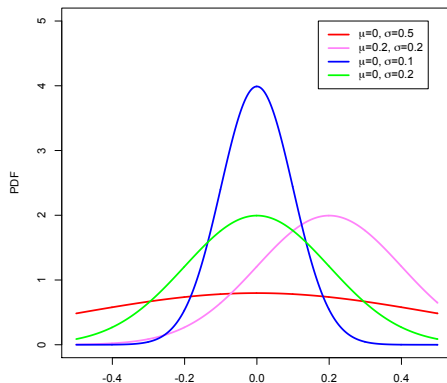
Clock prior

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- Parameters: mean $\mu \in \mathbb{R}$, standard deviation $\sigma > 0$
- Range of values: $(-\infty, \infty)$

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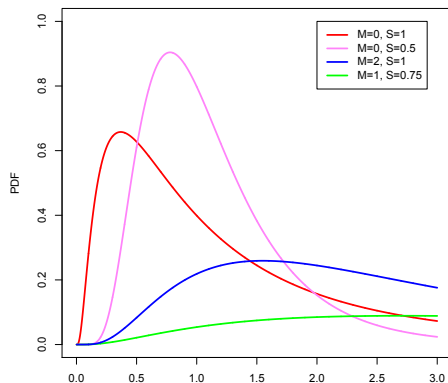
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- Parameters: mean $M \in \mathbb{R}$, standard deviation $S > 0$
- Range of values: $[0, \infty)$
- Long tail, always positive

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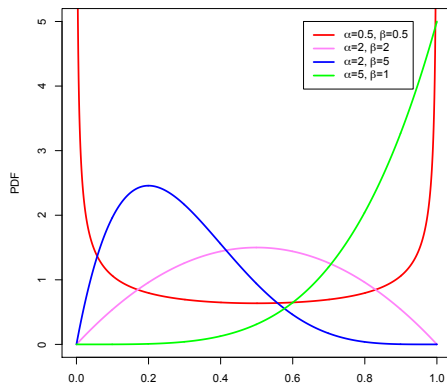
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- Parameters: shape $\alpha > 0$, shape $\beta > 0$
- Range of values: $[0,1]$
- Good for e.g. sampling probability prior

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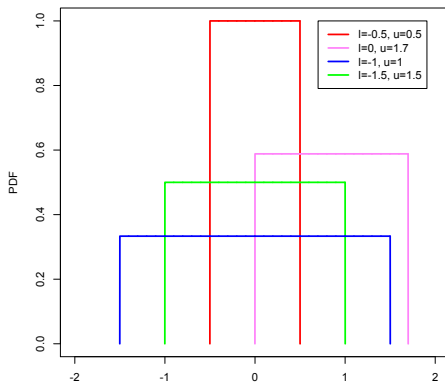
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Examples - Uniform distribution



- Parameters: lower, upper bound
- Range of values: $(-\infty, \infty)$

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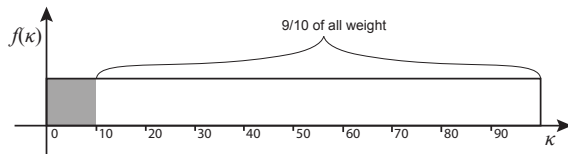
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Is uniform distribution a non-informative prior?

- Not really

- Imagine setting a $\text{Uniform}(0, 100)$ prior for the transition/transversion rate ratio (κ). You also know that the most likely values for κ are between 0 and 10. But you now put 9/10 of the weight to values > 10 .



- In fact there is nothing such as an non-informative prior
- If little or no information on the parameter is available, use diffuse priors
- Try to avoid $\text{Uniform}(-\infty, \infty)$ or $\text{Uniform}(0, \infty)$

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- ▶ Sometimes the prior distribution is such that the sum or the integral of the prior values does not converge, this is called an IMPROPER prior
- ▶ Examples
 - ▶ $1/x$
 - ▶ $\text{Uniform}(-\infty, \infty)$

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Are my priors what I set them to be?

- ▶ Not always
 - ▶ Induced priors may change the picture, i.e. if the parameters interact, the marginal prior distribution for each individual parameter may be different from the originally specified prior
- ▶ Use sampling from the prior, to see what your 'real' prior is

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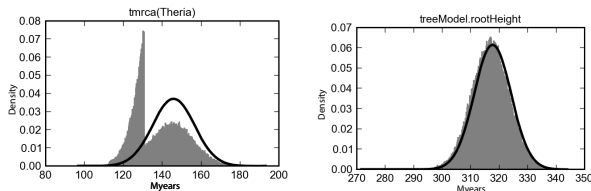


Figure adapted from [Heled and Drummond, 2012]

The marginal prior distributions that result from the multiplicative construction (gray) versus calibration densities (black line) specified for the calibrated nodes.

- ▶ Use all the prior knowledge you have to choose models and set appropriate parameter priors
- ▶ Sample from the prior distribution before using your data to check you really have the priors you want
- ▶ Check your posterior distribution against the prior

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- ▶ In practice, it is important to evaluate the impact of the prior on the posterior in a Bayesian robustness analysis
- ▶ Ideally, the posterior should be dominated by your data, such that the choice of the prior has little influence on the result
- ▶ If this is not the case, the choice of prior is very important, and should be reported

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- ▶ Are just starting values
- ▶ Have to be within the prior distribution, and its upper and lower limits, you chose for the parameter
- ▶ Use your best guess
 - ▶ BEAST2 attempts 10 times at most (can be changed) to initialize the run, but if the starting values are unreasonable, the runs may keep failing
- ▶ Start from different starting values to make sure the chains converge to the same distribution

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- du Plessis, L. and Stadler, T. (2015). Getting to the root of epidemic spread with phylodynamic analysis of genomic data. *Trends in microbiology*, 23(7):383–386.
- Heled, J. and Drummond, A. J. (2012). Calibrated tree priors for relaxed phylogenetics and divergence time estimation. *Systematic Biology*, 61(1):138–149.

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