

What could possibly go wrong?

Trouble shooting

Initialization Failure

One parameter does not mix

Many parameters do not
mix

Problem solving in general

Many things! But we will focus on the following three possibilities:



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- ▶ The chain runs, but one or more parameters mix slowly compared to the rest.



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Many things! But we will focus on the following three possibilities:

- ▶ MCMC chain fails to initialize.
- ▶ The chain runs, but one or more parameters mix slowly compared to the rest.
- ▶ The chain runs, but many parameters fail to mix adequately.



Problem 1: MCMC chain fails to initialize

Trouble-shooting
BEAST 2 Analyses

```
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Start likelihood: -Infinity after 10 initialisation attempts
P(posterior) = -Infinity (was -Infinity)
  P(prior) = -Infinity (was -Infinity)
    P(CoalescentConstant.t:seqs) = -73.84438811380579 (was -73.84438811380579)
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  P(treeLikelihood.seqs) = NaN (was NaN) **
Fatal exception: Could not find a proper state to initialise. Perhaps try another seed.
See http://www.beast2.org/2018/07/04/fatal-errors.html for other possible solutions.
java.lang.RuntimeException: Could not find a proper state to initialise. Perhaps try another seed.
See http://www.beast2.org/2018/07/04/fatal-errors.html for other possible solutions.
    at beast.core.MCMC.run(Unknown Source)
    at beast.app.BeastMCMC.run(Unknown Source)
    at beast.app.beastapp.BeastMain.<init>(Unknown Source)
    at beast.app.beastapp.BeastMain.main(Unknown Source)
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See http://www.beast2.org/2018/07/04/fatal-errors.html for other possible solutions.
java.lang.RuntimeException: An error was encountered. Terminating BEAST
    at beast.app.util.ErrorLogHandler.publish(Unknown Source)
    at java.logging/java.util.logging.Logger.log(Logger.java:979)
    at java.logging/java.util.logging.Logger.doLog(Logger.java:1006)
    at java.logging/java.util.logging.Logger.log(Logger.java:1029)
    at java.logging/java.util.logging.Logger.severe(Logger.java:1776)
    at beast.app.beastapp.BeastMain.<init>(Unknown Source)
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- Note that posterior of starting state is 0.

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- ▶ The likelihood is quoted as having a value of “NaN” (not a number) because this was never computed by BEAST: it stopped when encountering a zero in the prior.

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- ▶ Note that posterior of starting state is 0.
- ▶ Likewise the prior of the starting state is 0.
- ▶ The likelihood is quoted as having a value of “NaN” (not a number) because this was never computed by BEAST: it stopped when encountering a zero in the prior.
- ▶ The cause of the problem seems to be the 0 in the prior on the starting A→C transition rate.

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Problem 1: MCMC chain fails to initialize

Trouble-shooting
BEAST 2 Analyses

BEAUTi 2: Standard /Users/vaughant/teaching/bayesian-phylogenetics-course/classes/class2/analysis.xml

Partitions Tip Dates Site Model Clock Model Priors **MCMC**

Tree.t:seqs Coalescent Constant Population

clockRate.c:seqs Uniform initial = [0.1] [0.0,∞] substitution rate of partition c:seqs

popSize.t:seqs 1/X initial = [0.3] [0.0,∞] Coalescent population size parameter of partition t:seqs

rateAC.s:seqs Gamma initial = [0.0] [0.0,∞] GTR A-C substitution parameter of partition s:seqs

Alpha 0.05 ☐ estimate

Beta 10.0 ☐ estimate

Mode ShapeScale

Offset 0.0

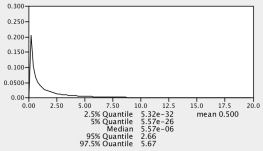
rateAG.s:seqs Gamma initial = [1.0] [0.0,∞] GTR A-G substitution parameter of partition s:seqs

rateAT.s:seqs Gamma initial = [1.0] [0.0,∞] GTR A-T substitution parameter of partition s:seqs

rateCG.s:seqs Gamma initial = [1.0] [0.0,∞] GTR C-G substitution parameter of partition s:seqs

rateGT.s:seqs Gamma initial = [1.0] [0.0,∞] GTR G-T substitution parameter of partition s:seqs

+ Add Prior



	mean	0.500
2.5% Quantile	5.32e-32	
5% Quantile	5.57e-26	
Median	5.57e-06	
95% Quantile	2.66	
97.5% Quantile	5.67	

Trouble shooting

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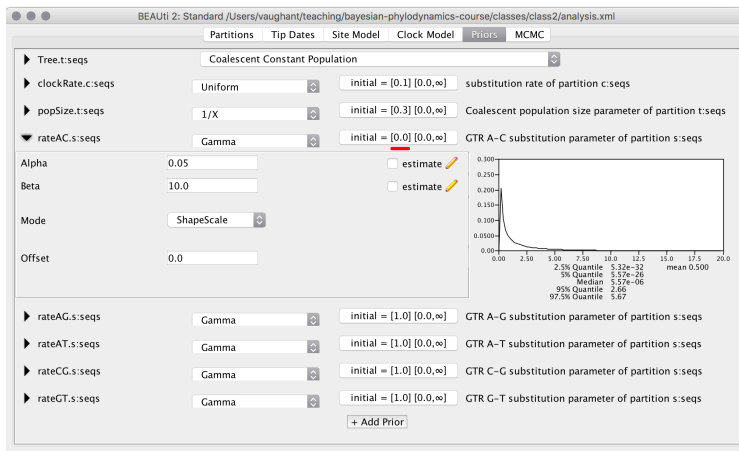
Many parameters do not mix

Problem solving in general



Problem 1: MCMC chain fails to initialize

Trouble-shooting
BEAST 2 Analyses



Trouble shooting

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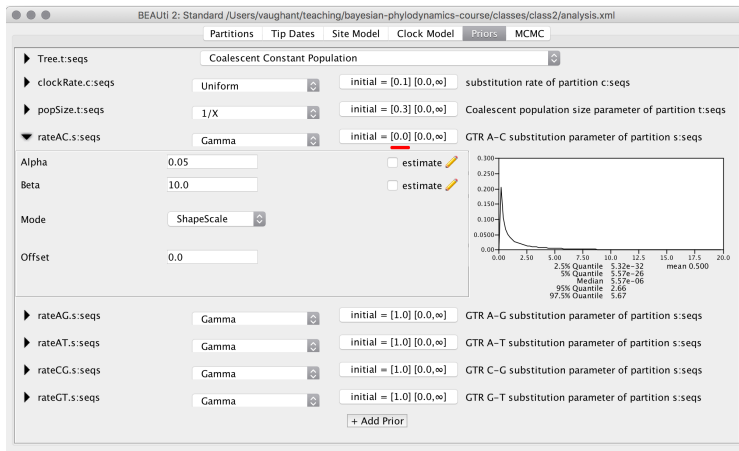
Problem solving in general

- Problem is that A→C rate is initially zero, while the prior on A→C excludes zero.



Problem 1: MCMC chain fails to initialize

Trouble-shooting
BEAST 2 Analyses



Trouble shooting

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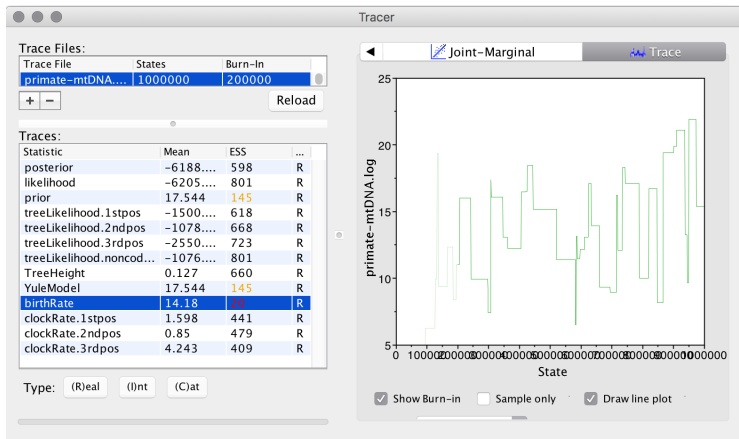
Problem solving in general

- Problem is that A→C rate is initially zero, while the prior on A→C excludes zero.
- Fix is to change the starting value (proper solution in this particular situation) or to modify the prior to allow the starting value.



Problem 2: One parameter mixes slowly

Trouble-shooting
BEAST 2 Analyses



Trouble shooting

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Problem solving in general

- Tracer output of run shows the birth rate parameter is mixing much slower than the others.



Why might MCMC mix poorly?

- Mixing rate refers to how quickly (in terms of computation time) it takes the algorithm to explore the space of possible parameter values and trees.

Trouble shooting

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Problem solving in general



Why might MCMC mix poorly?

- ▶ Mixing rate refers to how quickly (in terms of computation time) it takes the algorithm to explore the space of possible parameter values and trees.
- ▶ ESS (effective sample size) provides an *estimate* of how thoroughly the state space has been explored. (I.e. large ESS = good.)

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- ▶ Mixing rate is determined by the combination of the posterior distribution (function of the data) and the random walk strategy used to explore the state space.

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- ▶ Mixing rate is determined by the combination of the posterior distribution (function of the data) and the random walk strategy used to explore the state space.
- ▶ Random walk strategy defined by a series of “operators” that modify the state (parameter values or trees). Operator “weights” determine how frequently a given operator is used.

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- ▶ Mixing rate is determined by the combination of the posterior distribution (function of the data) and the random walk strategy used to explore the state space.
- ▶ Random walk strategy defined by a series of “operators” that modify the state (parameter values or trees). Operator “weights” determine how frequently a given operator is used.
- ▶ A single slow-mixing parameter may be the result of the operator responsible for adjusting that value having a weight which is too low.

Trouble shooting

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Problem solving in general



Problem 2: One parameter mixes slowly

BEAUti 2: Standard /Users/vaughant/Downloads/primates.xml

Partitions	Tip Dates	Site Model	Clock Model	Priors	Operators	MCMC
▶ Scale: <u>birthRate.t:tree</u>	Scales birth rate of Yule prior for partition.t:tree				0.01	
▶ Scale: Tree.t:tree	Scales all internal nodes for tree.t:tree				3.0	
▶ Scale: Tree.t:tree	Scales root node for tree.t:tree				3.0	
▶ Uniform: Tree.t:tree	Draws new internal node heights uniformly for tree.t:tree				30.0	
▶ Subtree Slide: Tree.t:tree	Performs subtree slide rearrangement of tree.t:tree				15.0	
▶ Exchange: Tree.t:tree	Narrow exchange performs local rearrangement of tree.t:tree				15.0	
▶ Exchange: Tree.t:tree	Wide exchange performs global rearrangement of tree.t:tree				3.0	
▶ Wilson Balding: Tree.t:tree	Performs Wilson-Balding global rearrangement of tree.t:tree				3.0	
▶ Scale: clockRate.c:3rdpos	Scale substitution rate of partition c:3rdpos				3.0	
▶ Scale: clockRate.c:1stpos	Scale substitution rate of partition c:1stpos				3.0	
▶ Scale: clockRate.c:2ndpos	Scale substitution rate of partition c:2ndpos				3.0	
▶ Up Down: clockRate.c:2ndpos Tree.t:tree	Scale up substitution rate c:2ndpos and scale down tree t:(\$n)				3.0	
▶ Up Down: clockRate.c:1stpos Tree.t:tree	Scale up substitution rate c:1stpos and scale down tree t:(\$n)				3.0	
▶ Up Down: clockRate.c:3rdpos Tree.t:tree	Scale up substitution rate c:3rdpos and scale down tree t:(\$n)				3.0	

- ▶ Operator corresponding to birth rate parameter has a very low weight.
- ▶ Increasing this weight solves the mixing problem.

Trouble shooting

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Trouble-shooting BEAST 2 Analyses

Initialization Failure

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Problem solving in general



Problem 3: Many parameters mix slowly

- Check burn-in percentage in tracer.

Trouble shooting

Initialization Failure

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Problem 3: Many parameters mix slowly

Trouble-shooting BEAST 2 Analyses

- ▶ Check burn-in percentage in tracer.
- ▶ In general, if an analysis is not mixing well there is not much you can do besides run the analysis longer.

Trouble shooting

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Problem 3: Many parameters mix slowly

- ▶ Check burn-in percentage in tracer.
- ▶ In general, if an analysis is not mixing well there is not much you can do besides run the analysis longer.
- ▶ A very good idea is to run multiple chains (i.e. multiple independent analyses).
 - ▶ This way, once you are happy that each chain is independently sampling the same posterior, you can combine the results to get sufficient ESS.
 - ▶ Results can be combined using the LogCombiner utility that comes with BEAST.
 - ▶ **ONLY** combine the results if each of the independent chains has “converged”.

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Problem 3: Many parameters mix slowly

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 - ▶ This way, once you are happy that each chain is independently sampling the same posterior, you can combine the results to get sufficient ESS.
 - ▶ Results can be combined using the LogCombiner utility that comes with BEAST.
 - ▶ ONLY combine the results if each of the independent chains has “converged”.
- ▶ Note that you can resume completed chains to extend the analysis. (Select the “resume” option in the BEAST start dialog box.)

Trouble shooting

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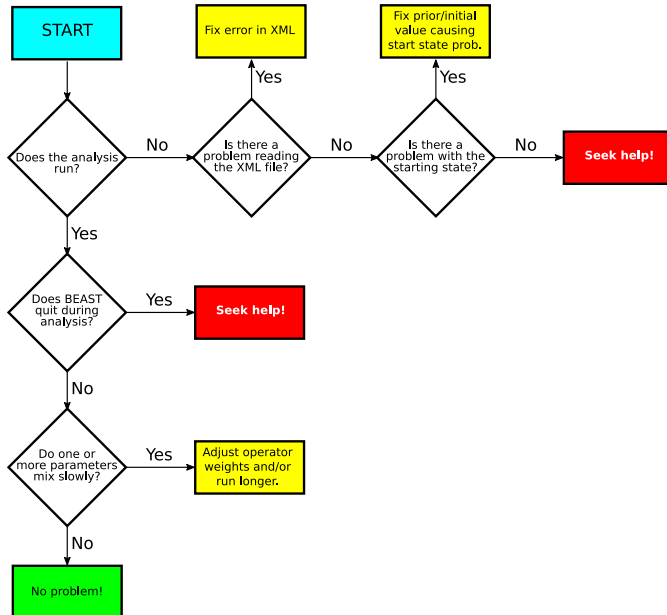
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General problem-solving flow chart



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