Statistics for phylogenetic time trees

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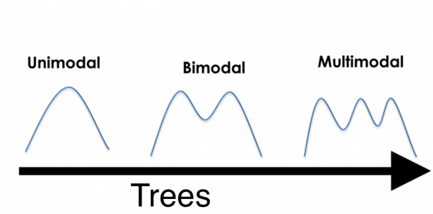
CHRISTCHURCH NEW ZEALAND

The goal



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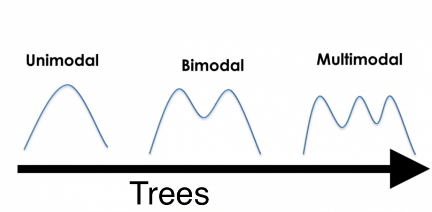


Bayesian Phylogenetic Inference via MCMC

- Key object of interest is often the rooted tree topology.
- **MCMC Output**: Sample of trees (typically thousands)
- Challenges in estimating mean and variance in treespace due to its high-dimensional, non-Euclidean nature.

Treespaces

τ-space

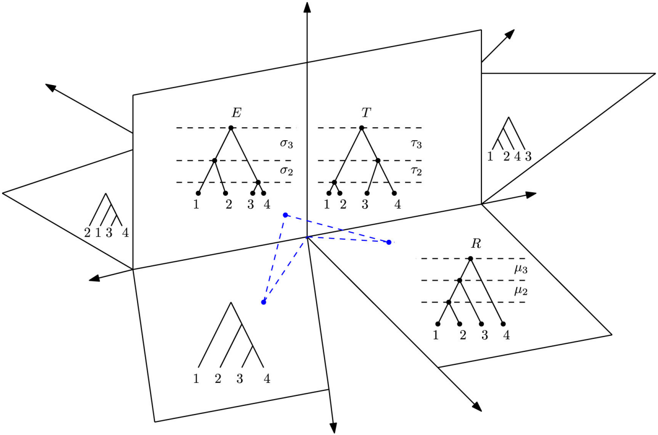


Figure: Three-dimensional projection of a part of τ space with 4 taxa.

The downfall of stratified spaces

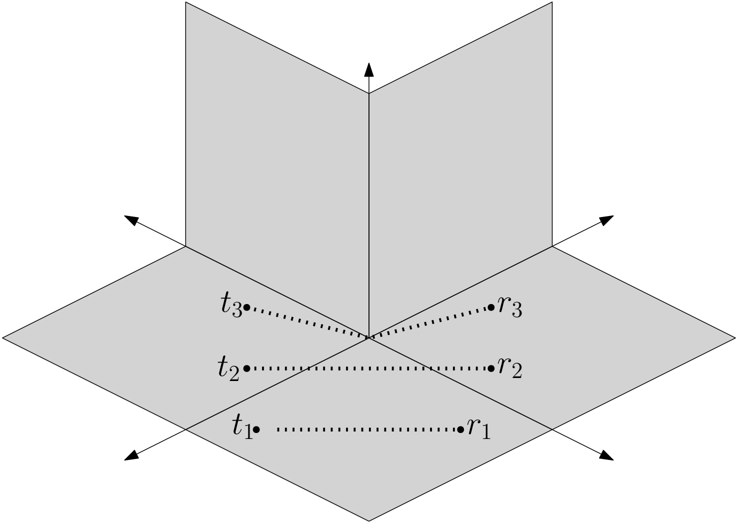
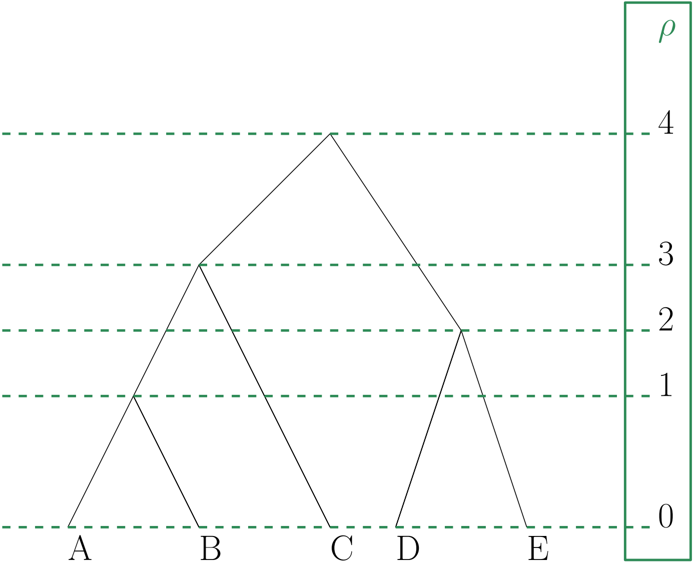


Figure: Geodesics and cone paths

The space of ranked trees



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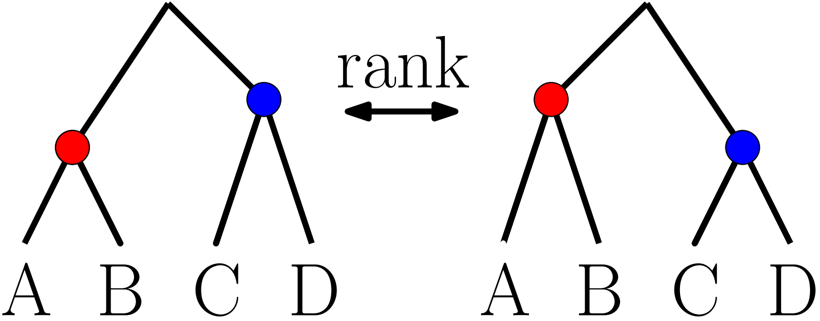

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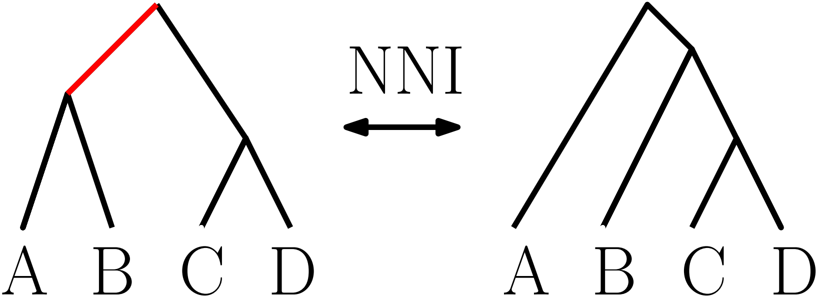

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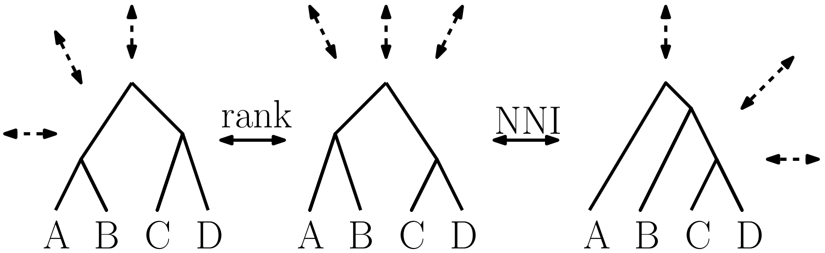

The RNNI graph

This graph is the **treespace** of ranked trees, **R**anked **N**earest **N**eighbour **I**nterchange space.

The shortest path problem

Induced distance

The minimal **number of rearrangement operations** to transform one tree into another

Equivalent: find a **path of minimal length** in the RNNI graph

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The minimal **number of rearrangement operations** to transform one tree into another

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Theorem

The **FindPath** algorithm computes a shortest path in RNNI, with time complexity $\mathbf{O}(\mathbf{n^2})$. [a]

[a] Collienne, Lena, and Alex Gavryushkin. "Computing nearest neighbour interchange distances between ranked phylogenetic trees." Journal of Mathematical Biology 82.1-2 (2021): 8.

Probability distributions are 'continuous'

Comparing **probability distributions** in BHV and RNNI tree space on **one data set**. **x**-Axis displays **tree metric distance** (relative), **y**-axis displays **difference in probability** (relative)

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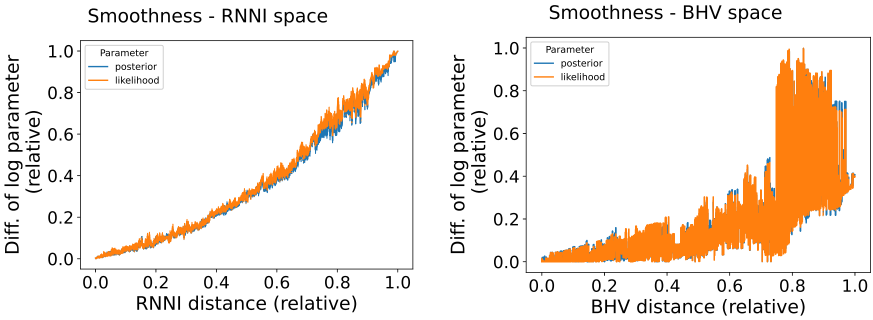
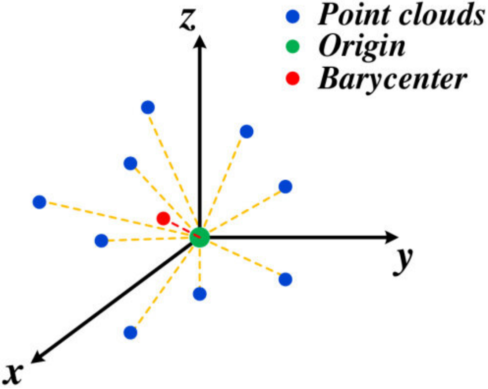


Mean tree

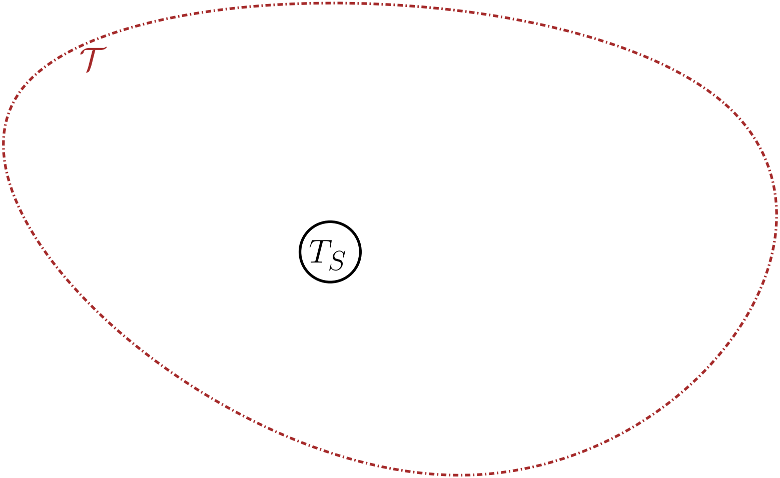
Geometric means



Fréchet variance

$Var(t)_{\mathcal{T}} = \sum_{t_i \in \mathcal{T}} d(t_i, t)^2$

The algorithm



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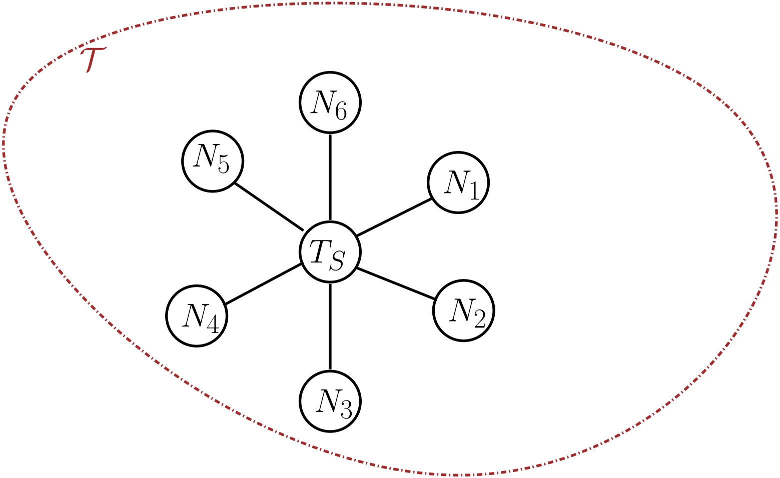

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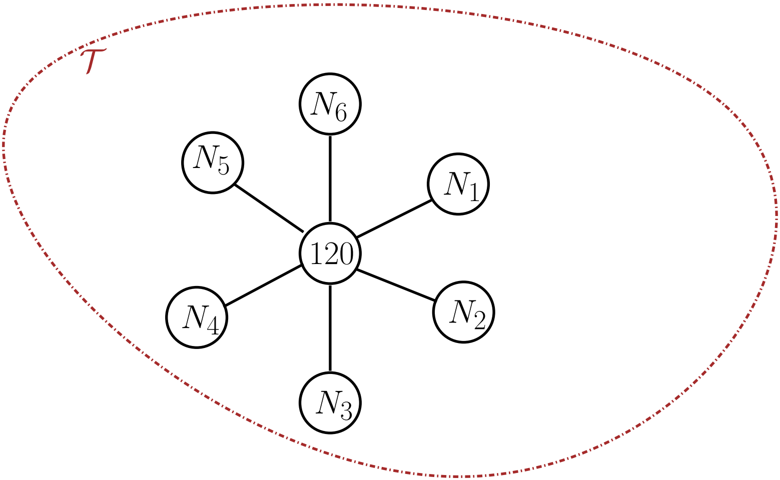

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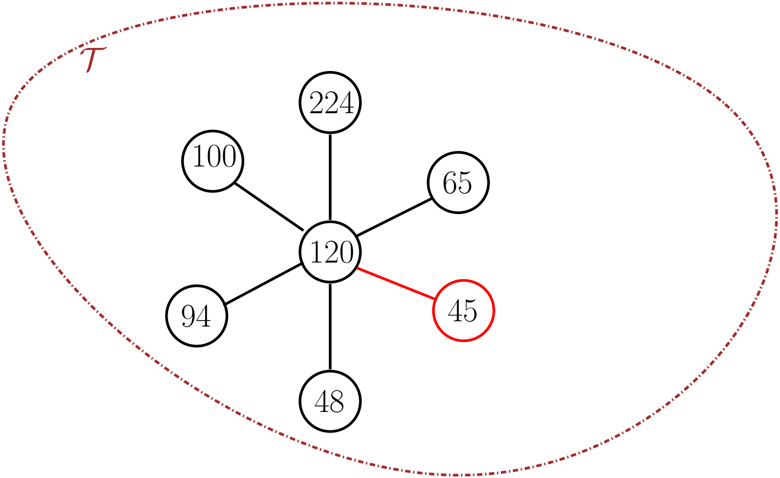

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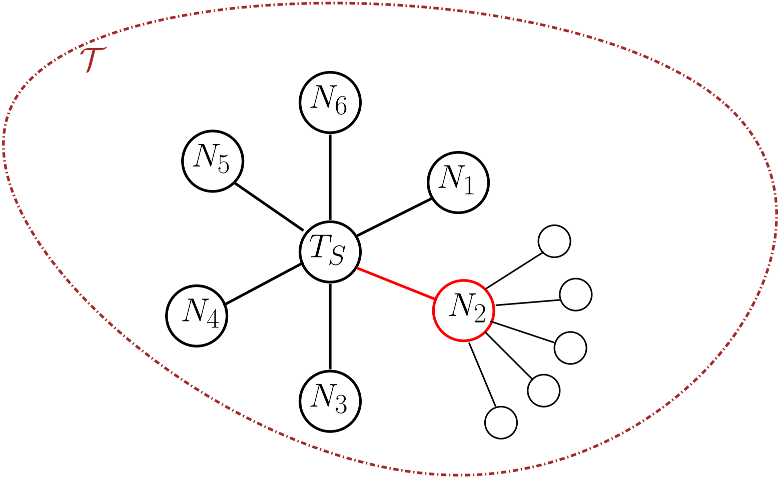

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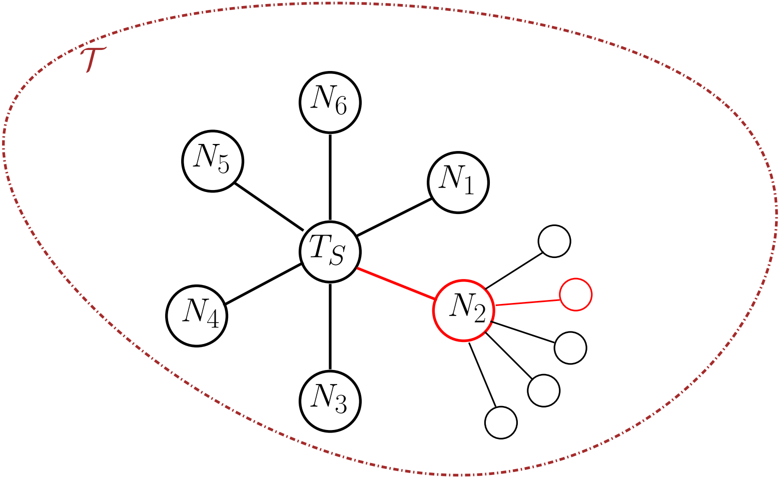

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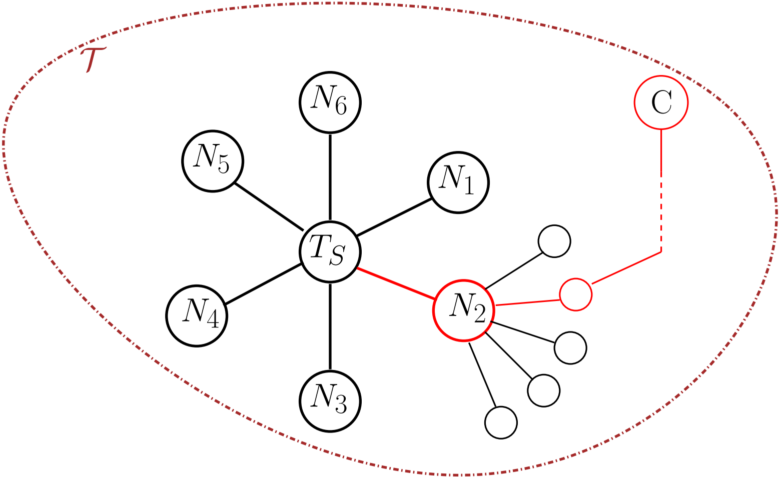
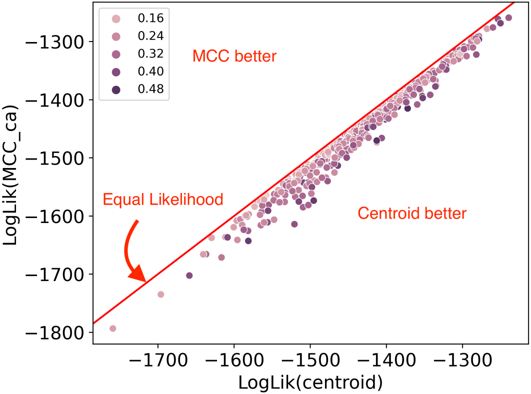


Comparing Likelihood to MCC



MCC

Maximum Clade Credibility Tree from treeannotator (BEAST).

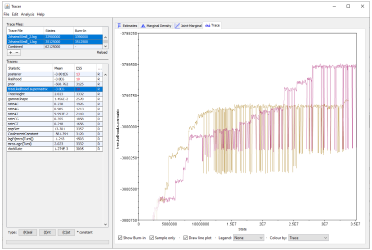
Convergence Assessment

Convergence

- Sampling from the stationary distribution

→ Parameter trace no trend

- **E**ffective **S**ample **S**ize at least 200 (rule of thumb)

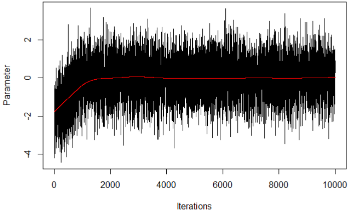


Trace File	States	Burn-In
2chains50mil_2.log	33900000	3390000
2chains50mil_1.log	35125000	3512500
Combined	62125000	-

Statistic	Mean	ESS	...
posterior	-3.801E6	13	R
likelihood	-3.8E6	10	R
prior	-568.762	3125	R
treeLikelihood.supermatrix	-3.8E6	10	R
TreeHeight	2.023	3332	R
gammaShape	1.456E-2	2570	R
rateAC	0.238	1926	R
rateAG	0.985	1213	R
rateAT	9.993E-2	2110	R
rateCG	0.355	1858	R
rateGT	0.248	1656	R
popSize	13.301	3357	R
CoalescentConstant	-561.394	3120	R
logP(mrca(Tursi))	-1.243	4503	R
mrca.age(Tursi)	2.023	3332	R
clockRate	1.274E-3	3095	R

☑ Show Burn-in ☑ Sample only ☑ Draw line plot Legend: None Colour by: Trace

Figure: Not converged



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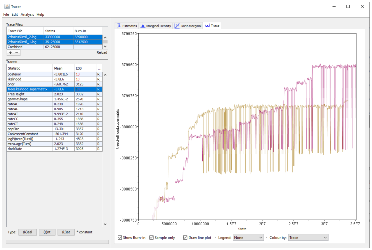

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Type: (R)eal (I)nt (C)at * constant

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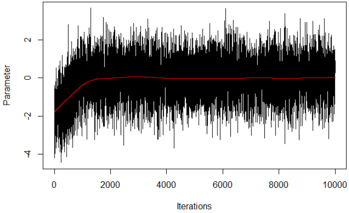
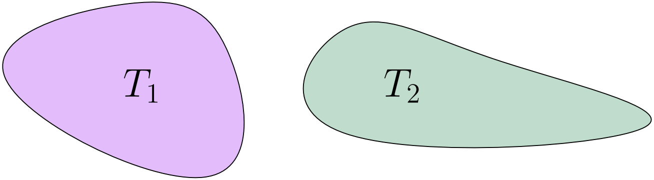


Figure: Converged

Do two sets have the same underlying distribution?

independently sampled sets of trees



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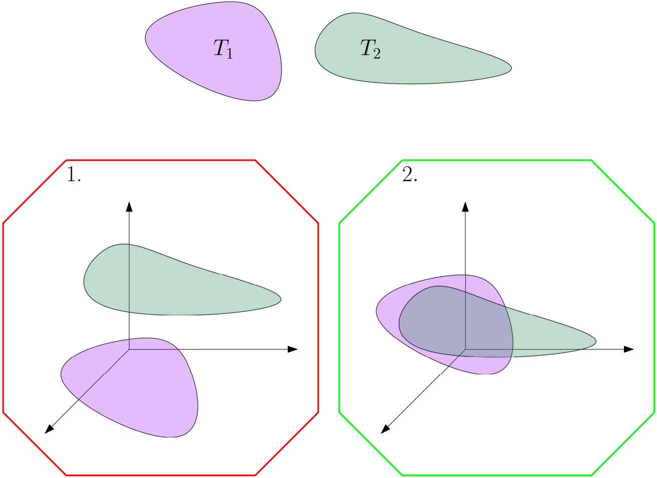
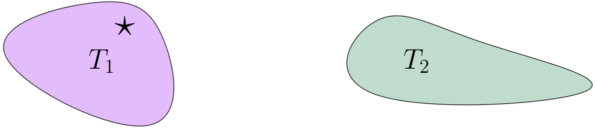
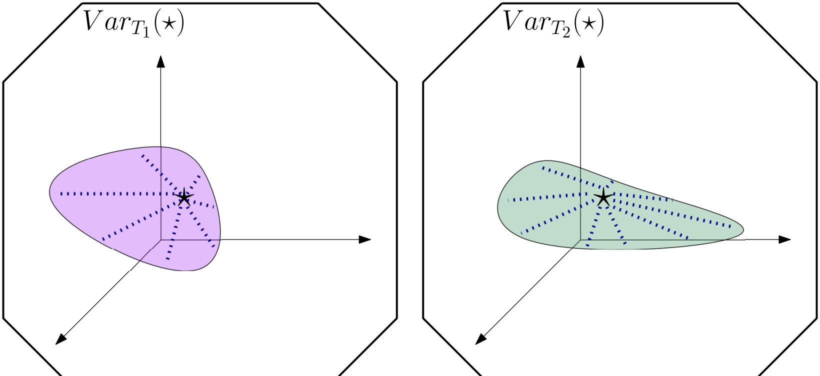


Gelman Rubin diagnostic for trees



$\star$ = new sample in T_1

⋯ = RNNI distance



Gelman Rubin diagnostic for trees

Potential scale reduction factor

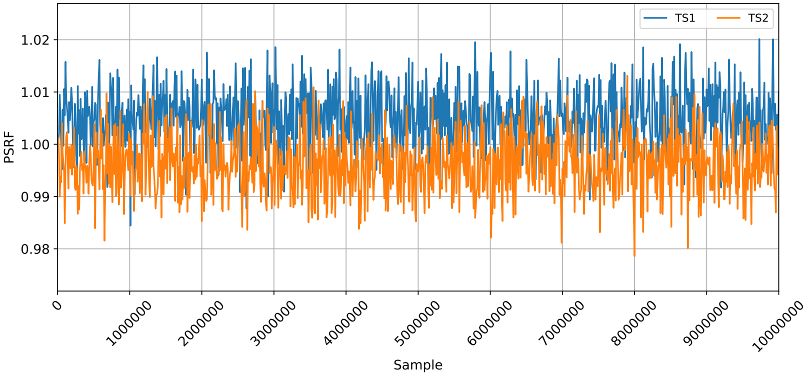
$$PSRF(t|\mathcal{T}_1, \mathcal{T}_2) = \sqrt{\frac{Var(t)_{\mathcal{T}_2}}{Var(t)_{\mathcal{T}_1}}}, t \in \mathcal{T}_1$$ [a]

[a] Inference from Iterative Simulation Using Multiple Sequences, A. Gelman and D. Rubin

Fréchet variance (normalized)

$$Var(t)_{\mathcal{T}} = \frac{\Sigma_{t_i \in \mathcal{T}} d(t_i, t)^2}{|\mathcal{T}|}$$

Gelman Rubin diagnostic for trees



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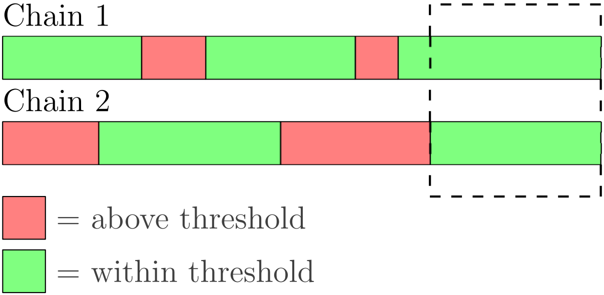

Further assessment of overlap

- **E**ffective **S**ample **S**ize at least 200 (rule of thumb)
- Further downstream analysis: Summarizing/ computing a mean tree

Results on DS1-DS11

		mean - 0.05						mean - 0.02						mean - 0.01					
	ESS-threshold	C1	C2	C3	C4	C5	C6	C1	C2	C3	C4	C5	C6	C1	C2	C3	C4	C5	C6
DS1	200	0	0	1	1	1	1	0	0	0	1	1	1	0	0	0	0	1	1
	500	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0
DS2	200	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
	500	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0	1	0	1
DS3	200	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	500	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
DS4	200	0	1	1	1	1	1	0	0	0	1	1	1	0	0	0	0	0	0
	500	0	0	0	0	1	1	0	0	0	0	0	1	0	0	0	0	0	0
DS5	200	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1
	500	1	0	1	1	1	1	0	0	1	1	1	1	0	0	1	1	0	1
DS6	200	1	1	0	1	1	1	0	0	0	0	1	1	0	0	0	0	0	1
	500	0	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0
DS7	200	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	500	1	1	1	1	1	1	0	0	1	1	1	1	0	0	0	0	0	1
DS8	200	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
	500	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
DS9	200	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	500	0	1	1	1	1	1	0	0	1	1	1	1	0	0	1	1	1	1
DS10	200	1	1	1	1	1	1	0	0	1	1	1	1	0	0	1	1	1	1
	500	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DS11	200	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	500	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Orange cell = convergence, Blue cell = non-convergence

Conclusion

Summary and Outlook

- Developed a mean tree within the RNNI treespace

→ Theoretical foundation is still an open problem

- Convergence assessment of samples of trees

→ Multimodal distributions?

→ Advanced characterization of tree distributions

Conclusion

Software

- BEAST2 package: ASM
  `https://github.com/rbouckaert/asm`
- Python package: tetres
  `https://github.com/bioDS/tetres`

References

- Lars Berling; Lena Collienne; Alex Gavryushkin, Estimating the mean in the space of ranked phylogenetic trees, Bioinformatics (2024)
- Lars Berling; Remco Bouckaert; Alex Gavryushkin, An Automated Convergence Diagnostic for Phylogenetic MCMC Analyses, IEEE/ACM TCBB (2024)