Plague Phylodynamics and Phylogeography

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Keywords

- Plague
- Yersinia pestis
- Phylodynamics
- Phylogeography

Introduction

Plague has an impressively long and expansive history as a human pathogen. The earliest evidence of the plague bacterium Yersinia pestis comes from ancient DNA studies dating its emergence to at least the Neolithic [1,2]. Since then, Y. pestis has traveled extensively due to ever-expanding global trade networks [3] and the ability to infect a diverse array of mammalian hosts [4]. Few regions of the ancient and modern world remain untouched by this disease, as plague has an established presence on every continent except Oceania [5].

Accompanying this prolific global presence is unnervingly high mortality. The infamous medieval Black Death is estimated to have killed more than half of Europe's population [**???**]. This virulence can still be observed in the post-antibiotic era, where case fatality rates range from 22-71% [6]. As a result, plague maintains its status as a disease that is of vital importance to current public health initiatives.

The intriguingly high mortality that is repeatedly seen throughout history brings together diverse researchers with interests spanning the modern period, history, and even prehistory. This intersection has brought about novel insight to render what was once invisible, visible. For example, investigating the ecology of ancient rats [7] and reconstructing the genome of Black Death-era Y. pestis [**???**]. However, this breadth of research also reflects the observation that plague has traveled through immensely diverse populations, cultures, and landscapes. Thus it is unsurprising that any consensus on 'universal' disease dynamics or experiences are rare to uncover. For example, within China alone there are 11 natural plague foci, each characterized by distinct environmental factors, bacteriological properties, and host-vector interactions [8]. As a result, significant debate has emerged on topics such as the severity of past pandemics [9], their geographic origins [**???**], and the mechanisms of spread [**???**].

TO BE DONE:

- Introduce the genomic composition of Y. pestis and mechanism of evolution.
- Introduce the topics phylodynamics and phylogeography and what is known so far.
- Introduce the problem(s) and our objective(s).

Materials and Methods

Data Collection

Data Quality Criteria

Subsampled Datasets

Phylogenetic Reconstruction

Phylodynamics

Phylogeography

Results

Composition

Phylogeny

Divergence-scaled phylogeny of Y. pestis (Figure 1).

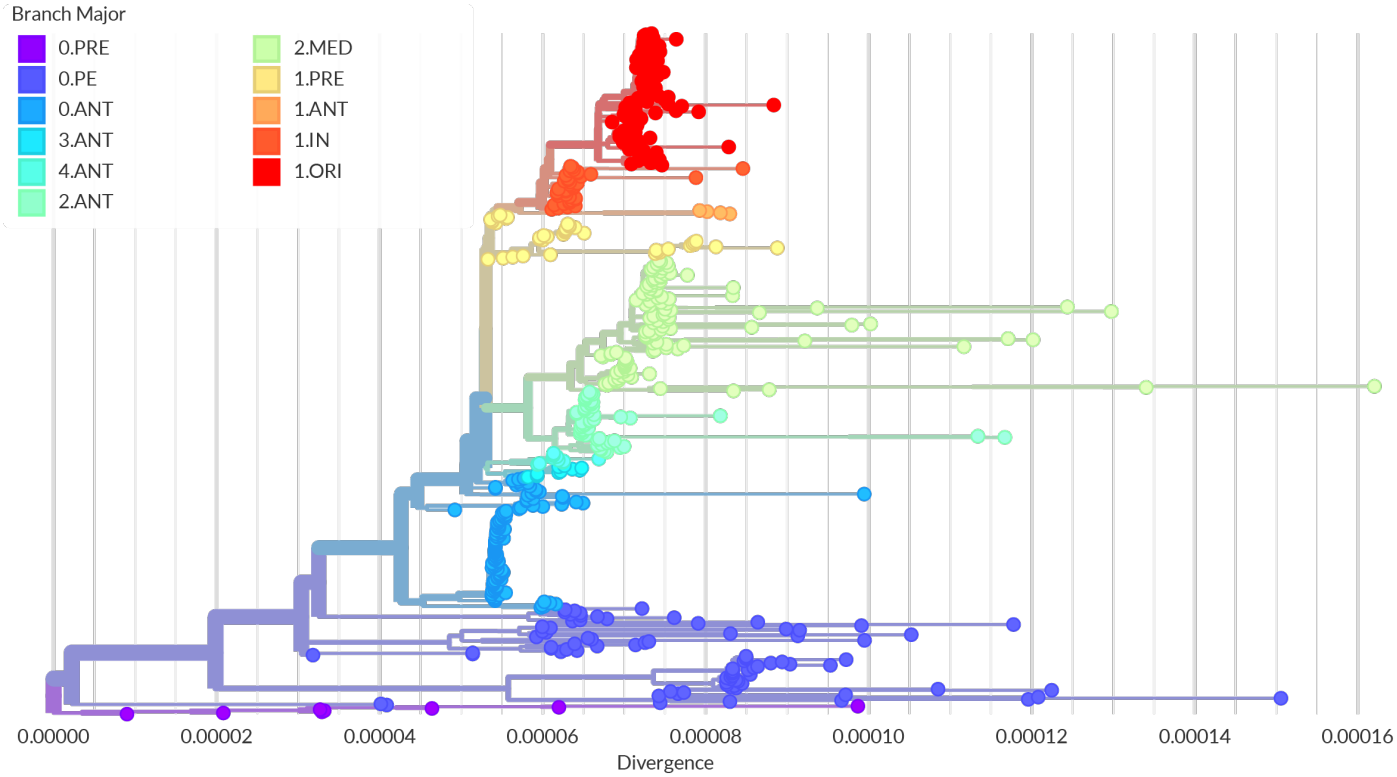

Figure 1: *Yersinia pestis* phylogeny. (Significant SVG editing required)|800

Phylodynamics

Molecular Clock

- *Y. pestis* has extreme rate variation.
- A Root to Tip Regression on collection date confirms this, as the Coefficient of Determination (R^2) is 0.09, revealing a poor fit to a simple linear model (Table 1).
- To some extent, this variation can be explained by examining the clades in isolation (Figure 2).
- Finding an appropriate evolutionary model is key to estimating historic events, like clade emergence (Figure 3).

Table 1: Temporal signal statistics by clade

Branch	Clade	Origin	R^2	p-value
all	all	Ancient, Modern	0.09	3.81E-14
0	0.PRE	Ancient	0.91	1.53E-04*
0	0.PE	Modern	0.01	2.25E-01
0	0.ANT4	Ancient	0.66	7.84E-04*
0	0.ANT	Modern	-0.01	7.35E-01
1	1.ANT	Modern	0.45	2.03E-01
1	1.IN	Modern	0.0	3.24E-01
1	1.ORI	Modern	0.04	1.32E-02*
1	1.PRE	Ancient	0.76	1.68E-13*
2	2.ANT	Modern	0.05	5.96E-02
2	2.MED	Modern	0.01	1.86E-01
3	3.ANT	Modern	-0.04	4.39E-01
4	4.ANT	Modern	-0.11	8.80E-01

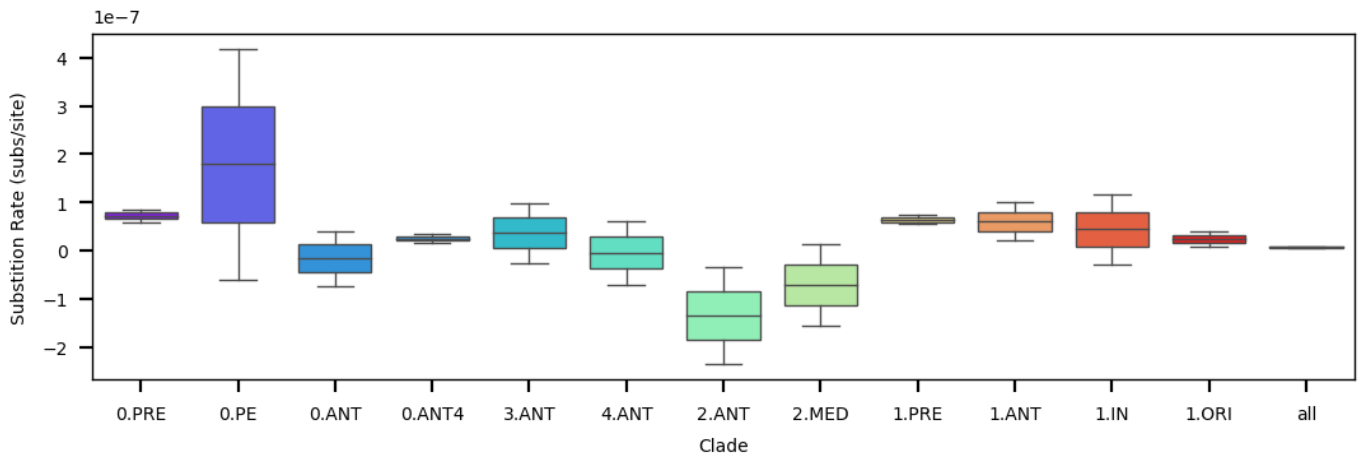

Figure 2: Rate variation by clade.

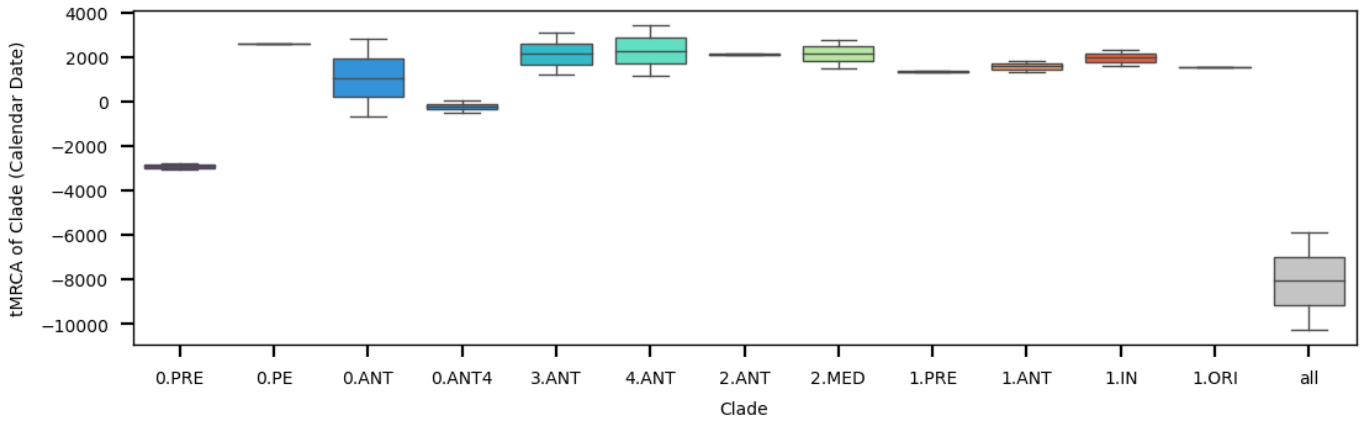

Figure 3: tMRCA by clade.

Relaxing the Clock

- Relaxed clock MCMC runs produce a high Coefficient of Variation indicating a relaxed model is favored over a strict model (Figure 4). However, these runs do not converge, suggesting there is too much rate variation to confidently estimate key parameters such as the mean Substitution Rate or tMRCA.

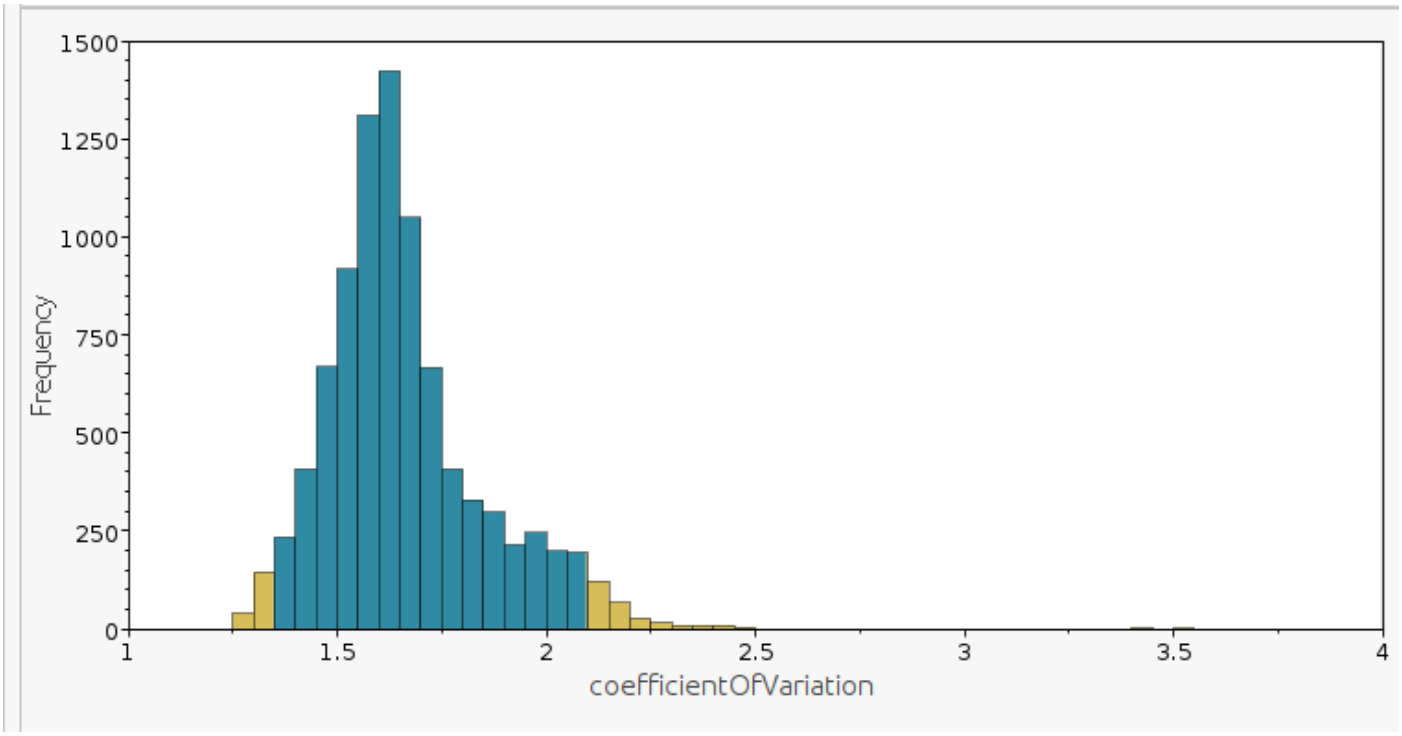

Figure 4: Coefficient of variation.

- A strict clock and relaxed clock have overlapping distributions with similar peaks for the Tree Height (blue: strict, green: relaxed) (Figure 5).

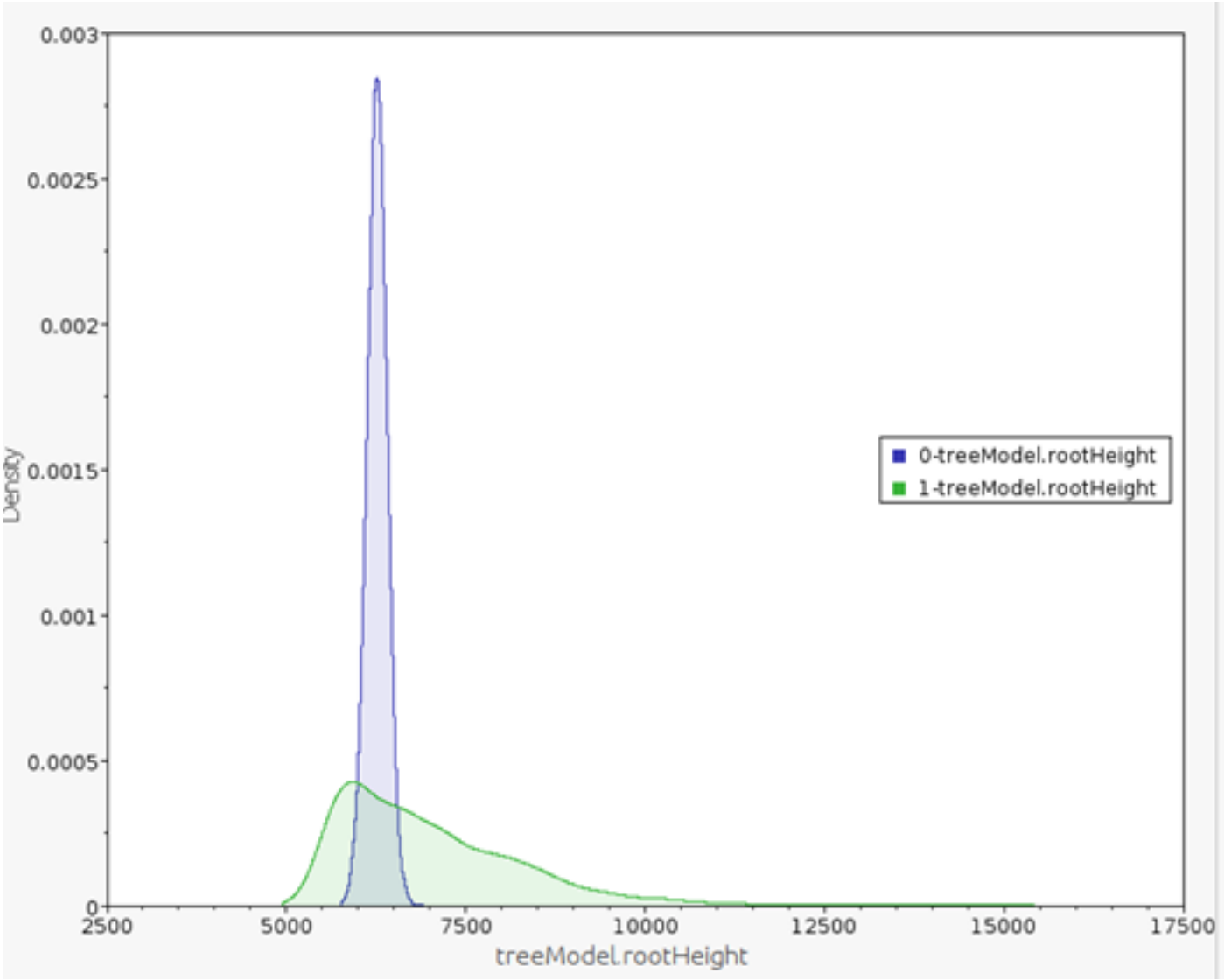

Figure 5: Tree height comparison.

- When estimating a Substitution Rate for all of *Y. pestis*, a [[Clock Model|strict clock]] and relaxed clock produce different estimates (green: strict, orange: relaxed) (Figure 6).

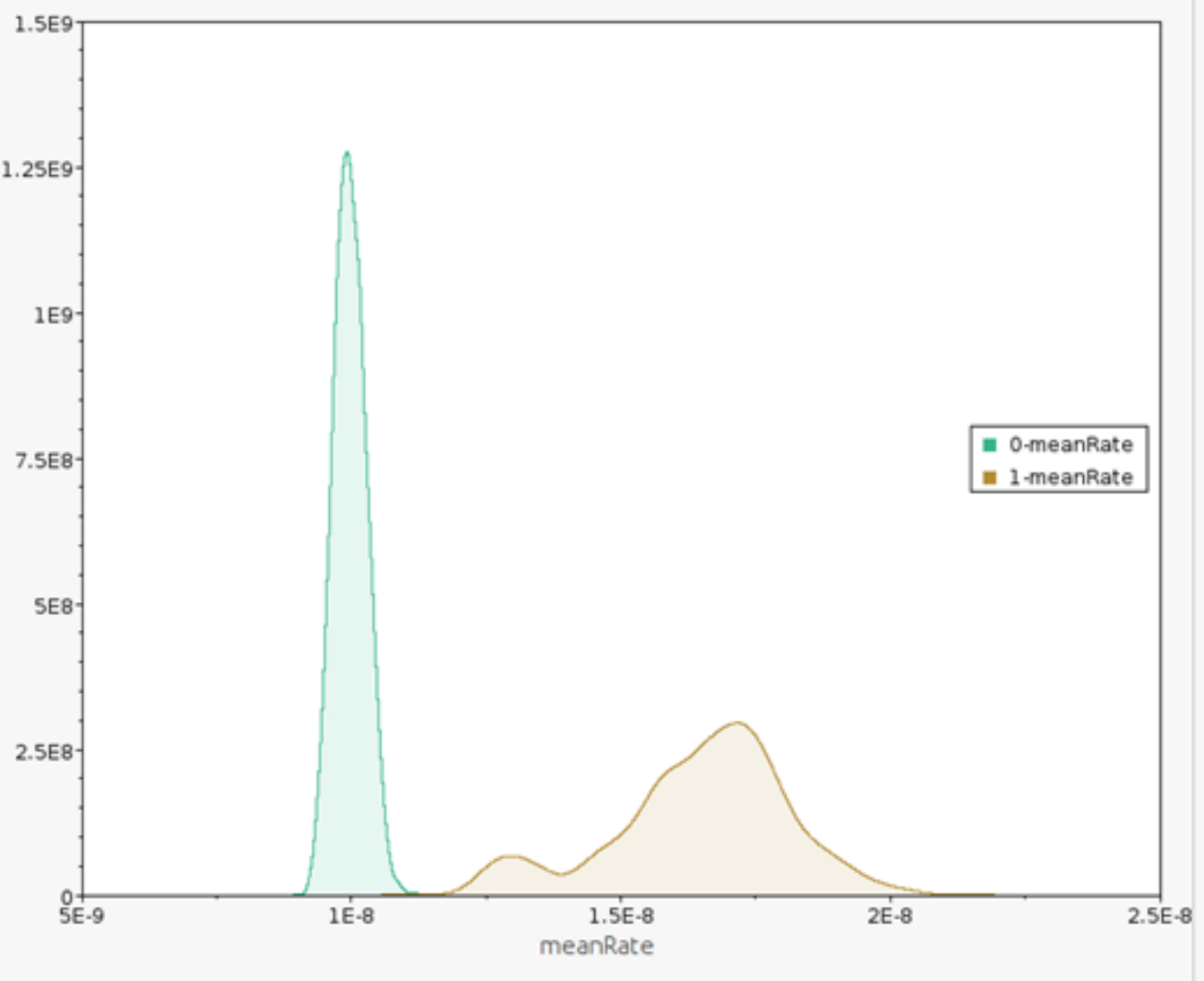

Figure 6: Substitution rate comparison.

- There doesn't appear to be clustering of rates. Branches with high rates are next to those with low rates (Figure 7).

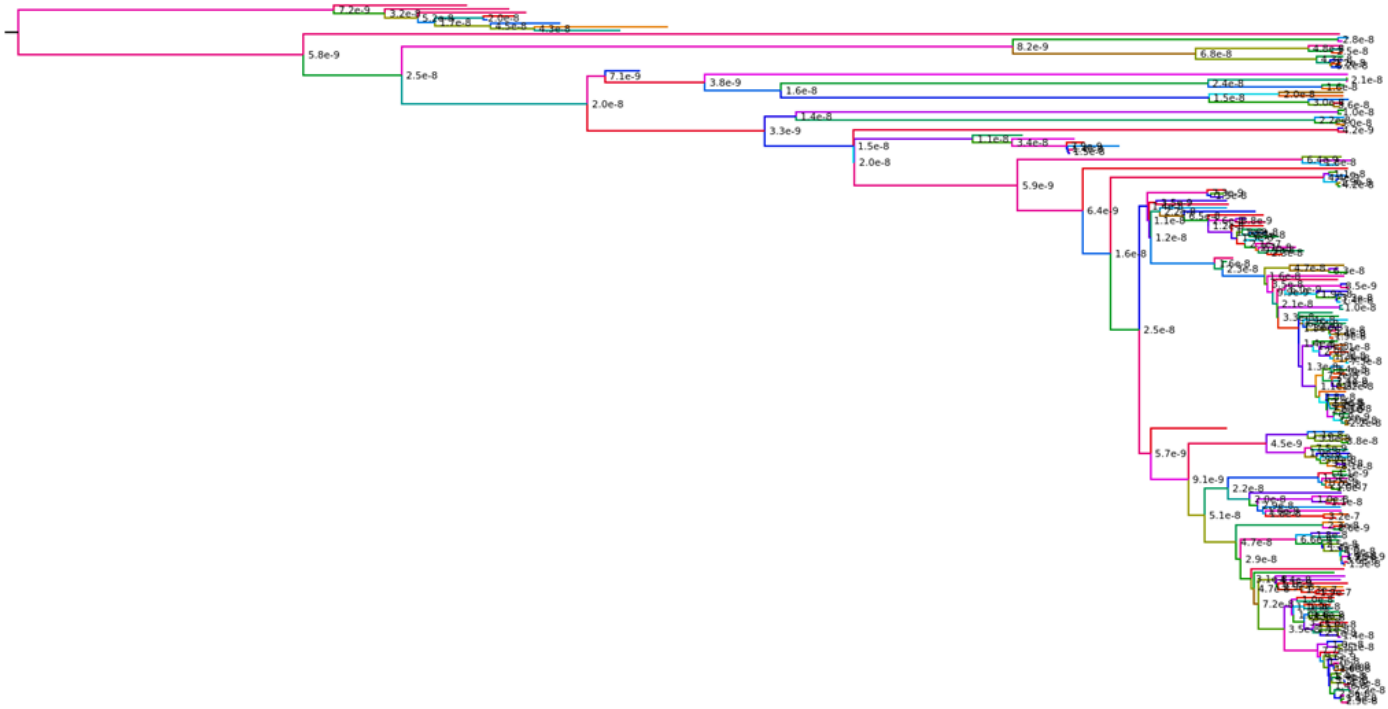

Figure 7: Time tree colored by rate.

Discussion

Conclusion

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