TreePPL—a new DSL in Miking for Phylogenetics

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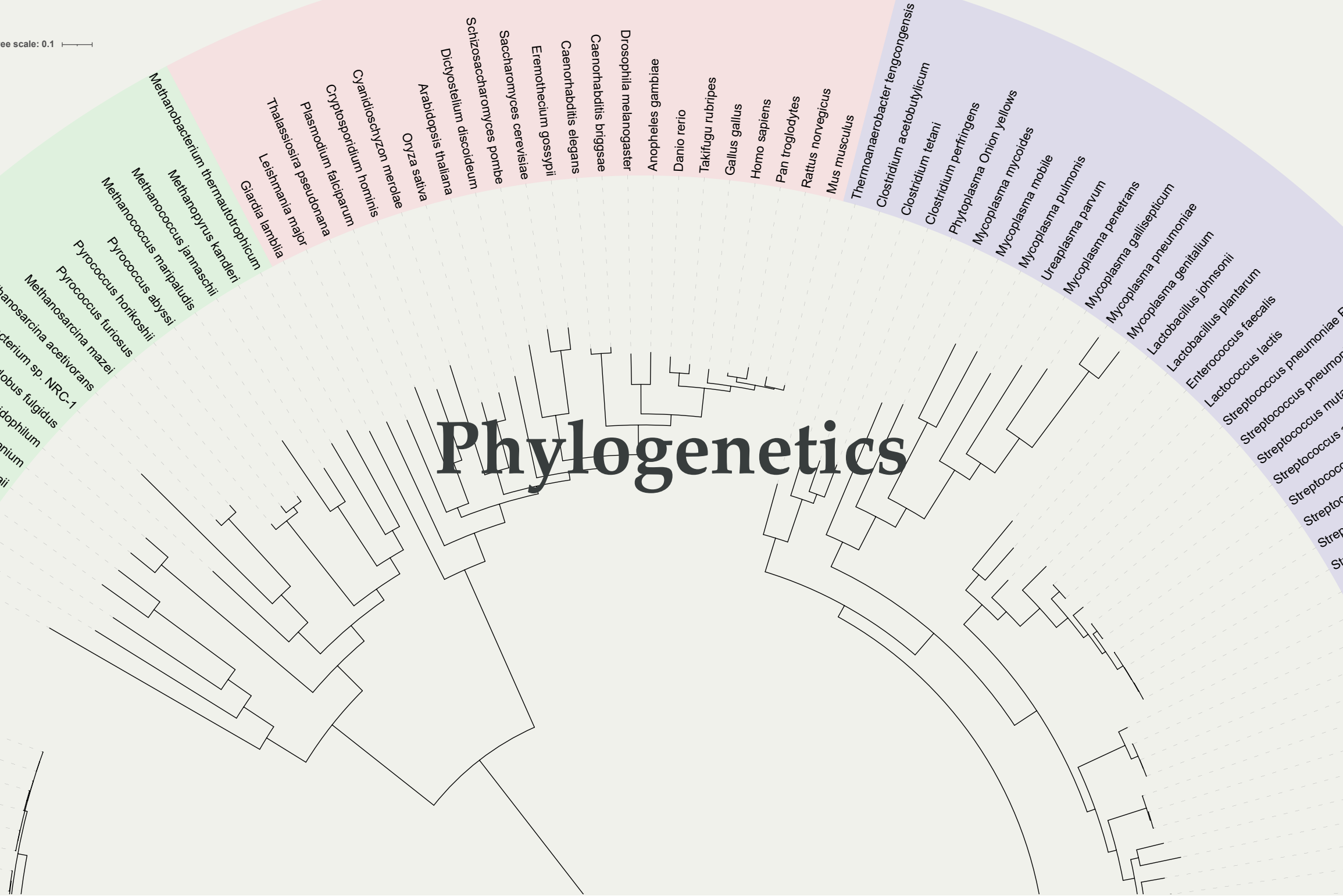
ee scale: 0.1
Methanobacterium thermautotrophicum
Methanopyrus kandleri
Methanococcus jannaschii
Methanococcus maripaludis
Pyrococcus abyssi
Pyrococcus horikoshii
Pyrococcus furiosus
Methanosarcina mazei
Methanosarcina acetivorans
hanosarcina acetivorans
cterium sp. NRC-1
lobus fulgidus
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anium
ali
Giardia lamblia
Leishmania major
Thalassiosira pseudonana
Plasmodium falciparum
Cryptosporidium hominis
Cyanidioschyzon merolae
Oryza sativa
Arabidopsis thaliana
Dictyostelium discoideum
Schizosaccharomyces pombe
Saccharomyces cerevisiae
Eremothecium gossypii
Caenorhabditis elegans
Caenorhabditis briggsae
Drosophila melanogaster
Anopheles gambiae
Danio rerio
Takifugu rubripes
Gallus gallus
Homo sapiens
Pan troglodytes
Rattus norvegicus
Mus musculus
Thermoanaerobacter tengcongensis
Clostridium acetobutylicum
Clostridium tetani
Clostridium perfringens
Phytoplasma Onion yellows
Mycoplasma mycoides
Mycoplasma mobile
Mycoplasma pulmonis
Ureaplasma parvum
Mycoplasma penetrans
Mycoplasma gallisepticum
Mycoplasma pneumoniae
Mycoplasma genitalium
Lactobacillus johnsonii
Lactobacillus plantarum
Enterococcus faecalis
Lactococcus lactis
Streptococcus pneumoniae
Streptococcus pneumo
Streptococcus muta
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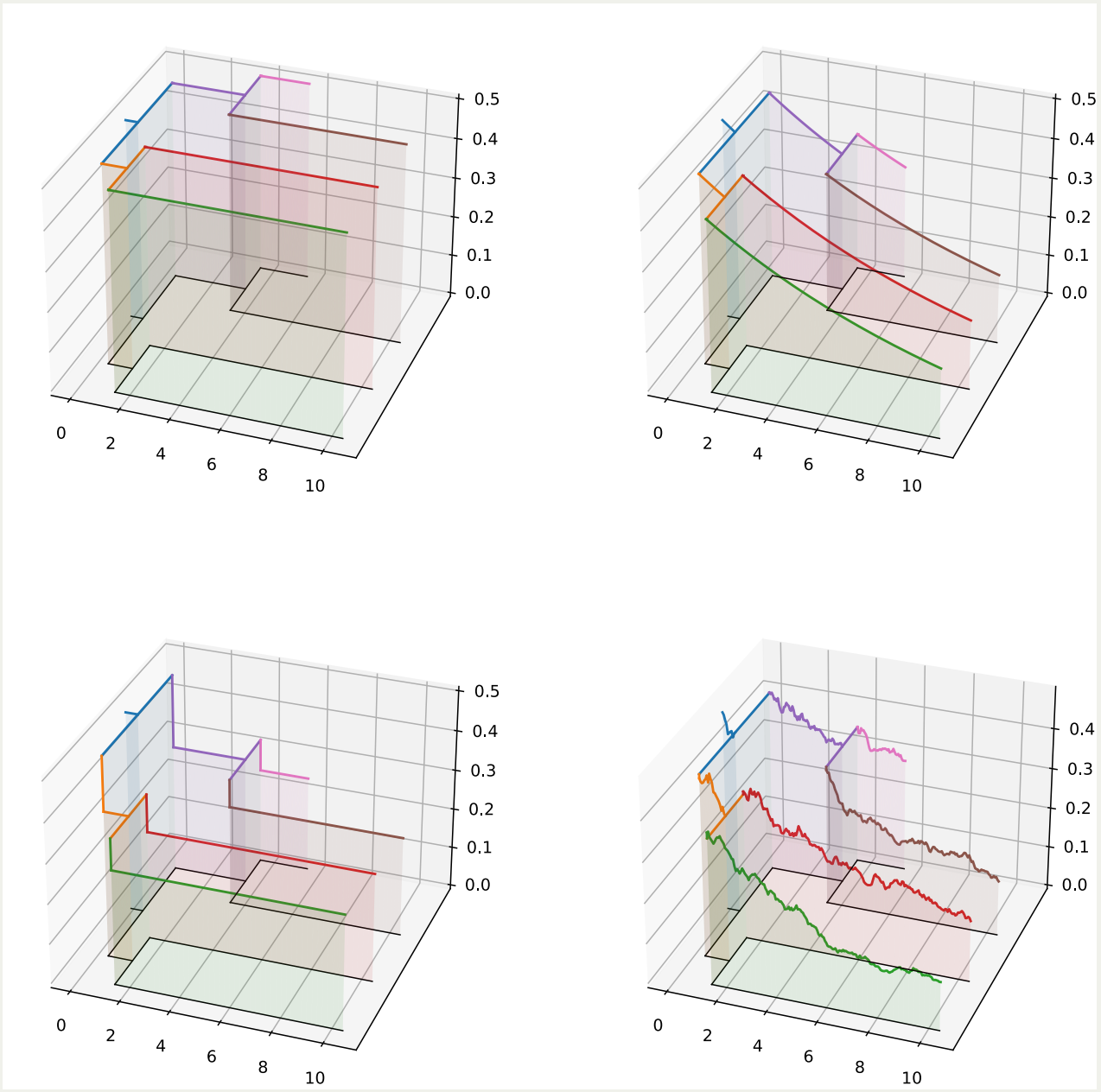
Phylogenetics

Phylogenetics discussion

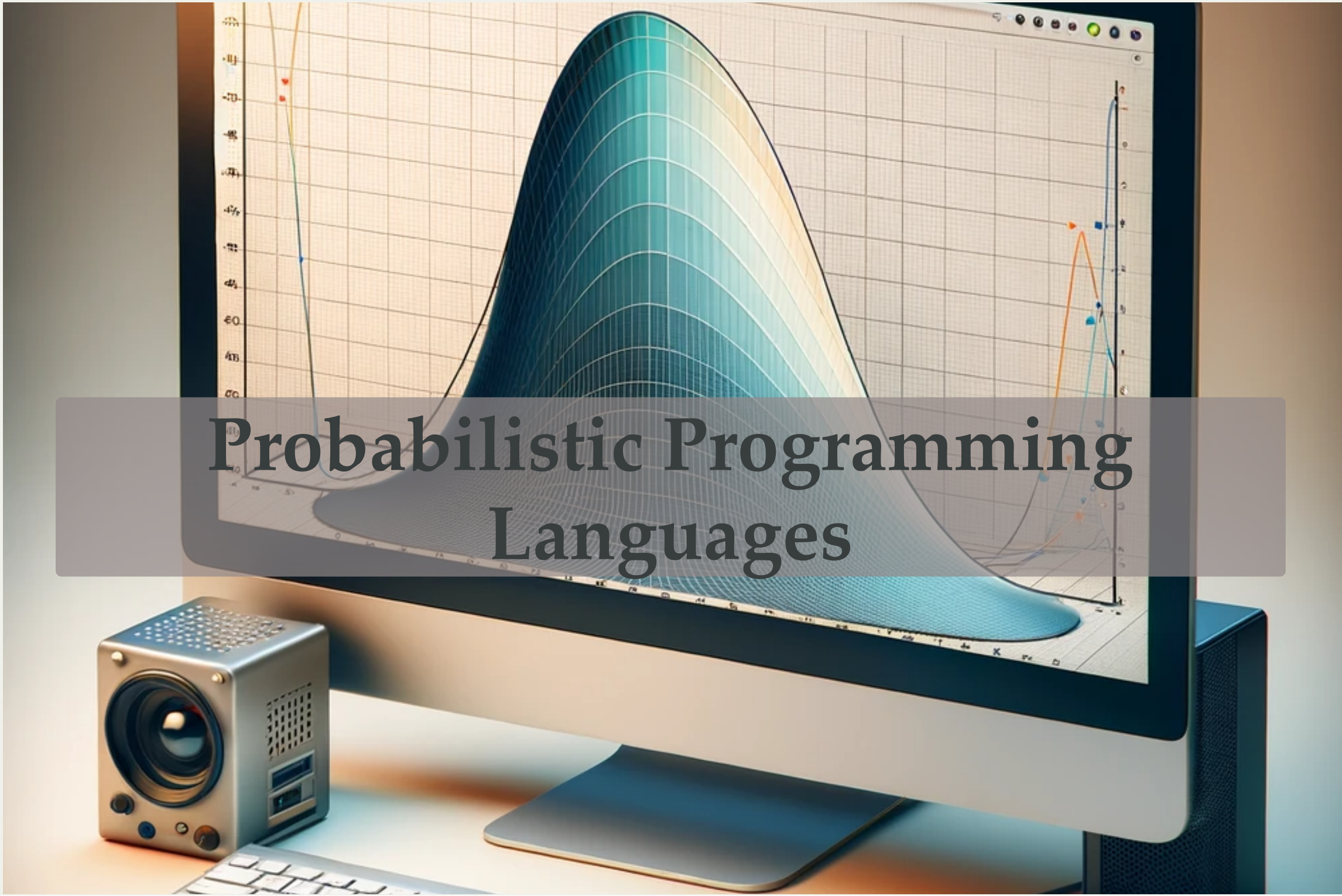
- Problems that phylogenetics deals with
  - Reconstructing phylogenetic trees
  - Using phylogenetic trees to understand evolution and ecology



Diversification models on a phylogenetic tree

What can the users do?

- Methods of phylogenetics
  - Parsimony
  - Statistical methods: ML and Bayesian
- Software for phylogenetics
  - monolithic software: e.g. MrBayes, RAxML
  - extensible software: e.g. BEAST, BEAST2, RevBayes
- Write the model yourself
  - implement in a general-purpose language: e.g. C, Java, Python, or R
  - implement in a probabilistic programming language: e.g. WebPPL, Birch
  - implement in a phylogenic PPL: TreePPL


Probabilistic Programming
Languages

Bayes theorem

Let x be some observed data and θ be an unobserved parameter in whose value we are interested in in.

$$\overbrace{p(\theta|x)}^{\text{posterior distribution}} = \frac{\overbrace{p(x|\theta)}^{\substack{\text{data distribution/} \\ \text{likelihood}}} \overbrace{p(\theta)}^{\text{prior distribution}}}{\underbrace{p(x)}_{\text{normalizing constant}}}$$

Bayes theorem

Let x be some observed data and θ be an unobserved parameter in whose value we are interested in in.

observe/factor

data distribution/ likelihood

assume/sample

prior distribution

posterior distribution

$$\overbrace{p(\theta|x)} = \frac{\overbrace{p(x|\theta)}\ \overbrace{p(\theta)}}{\underbrace{p(x)}}$$

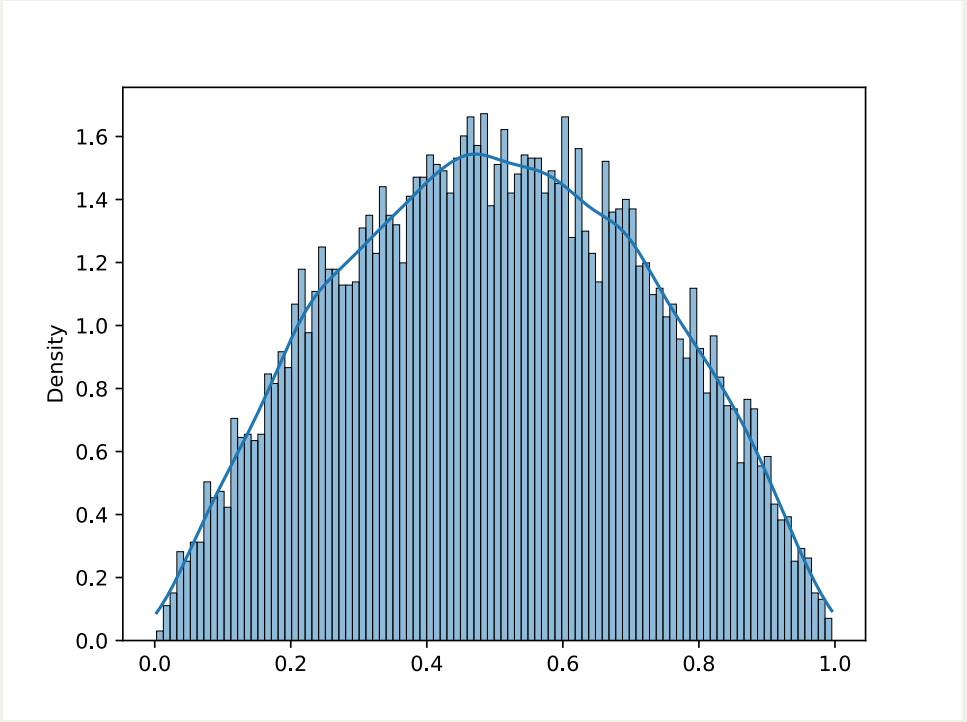
normalizing constant

Coin example

```
outcomes=[True, True, True, False, True, False, True, True, True, False,
    False, True, True, False, True, False, False, True, False, False]
```

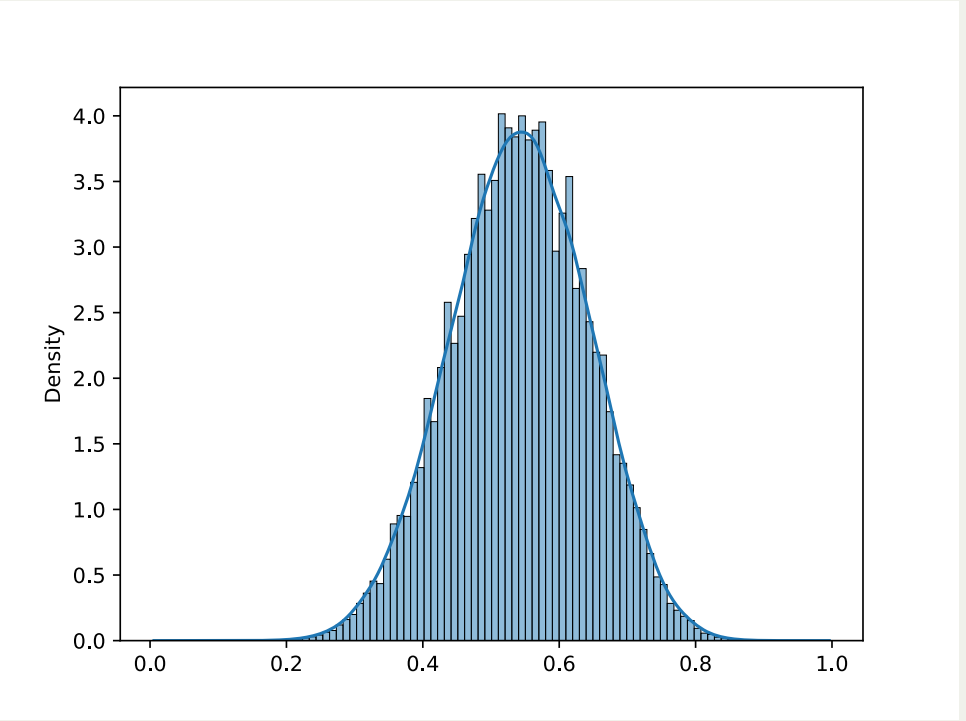
Define prior

```
assume p ~ Beta(2.0, 2.0);
```



Condition on data

```
for i in 1 to (length(outcomes)) {
    observe outcomes[i] ~
Bernoulli(p);
}
```



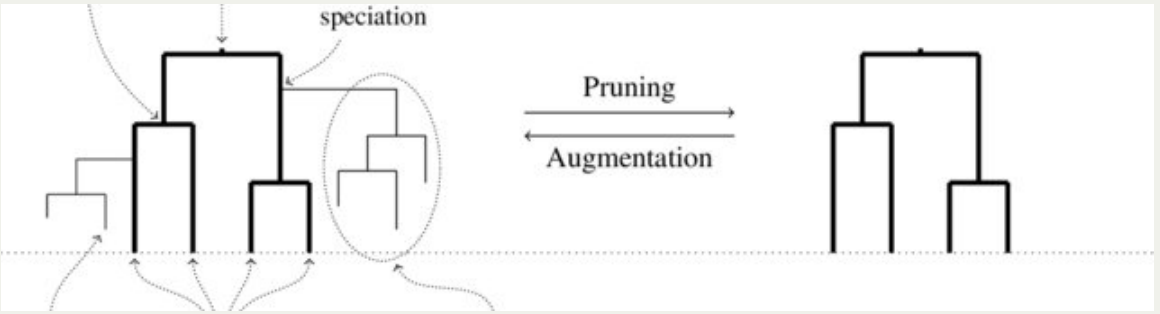
The complete coin example in TreePPL using Python as a wrapper.

```
source = """\
model function coin(outcomes: Bool[]): Real {
  assume p ~ Beta(2.0, 2.0);
  for i in 1 to (length(outcomes)) {
    observe outcomes[i] ~ Bernoulli(p);
  }
  return(p);
}
"""

with treeppl.Model(source=source, samples=10_000, method="is-lw") as coin:
    res = coin(
      outcomes=outcomes
    )
    sns.histplot(
        x=res.samples, weights=res.nweights, bins=100, stat="density", kde=
    )
    plt.show()
```

Universal PPLs

```
1  function simulateSubtree(time: Real, lambda: Real, mu: Real) {
2    assume waitingTime ~ Exponential(lambda + mu);
3    if waitingTime > time {
4      weight 0.0;
5      resample;
6    } else {
7      assume isSpeciation ~ Bernoulli(lambda / (lambda + mu));
8      if isSpeciation {
9        simulateSubtree(time - waitingTime, lambda, mu);
10       simulateSubtree(time - waitingTime, lambda, mu);
11     }
12   }
13 }
```



Simulating unobserved evolutionary lineages

TreePPL

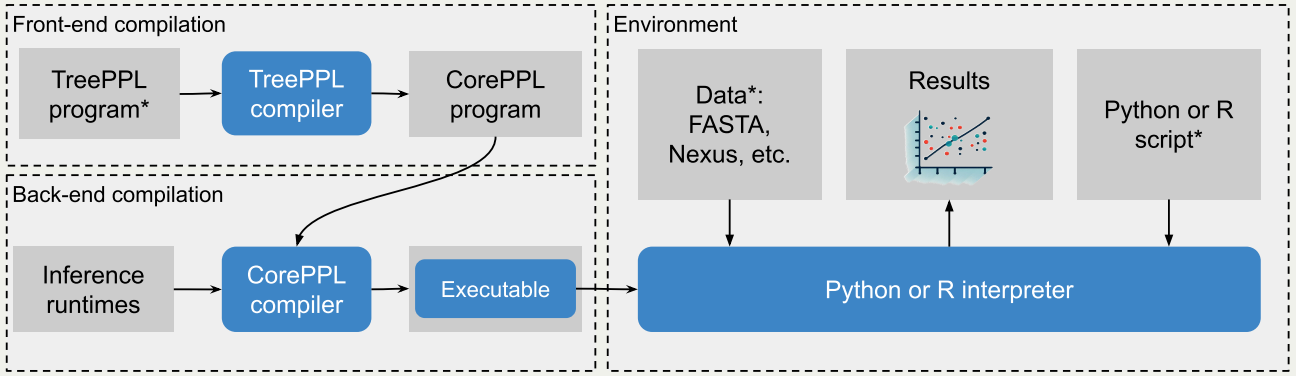
Phylogenetic Data
Supports natively the PhyJSON format for evolutoinary trees

Simplicity
Designed to meet the needs of computational biologists

Rich Model Library
Offers state-of-the art diversificati models as templates

Powerful Statistical Inference
Sequential Monte-Carlo (SMC) and Markov-chain Monte-Carlo (MCMC) inference

Architecture



Optimizations

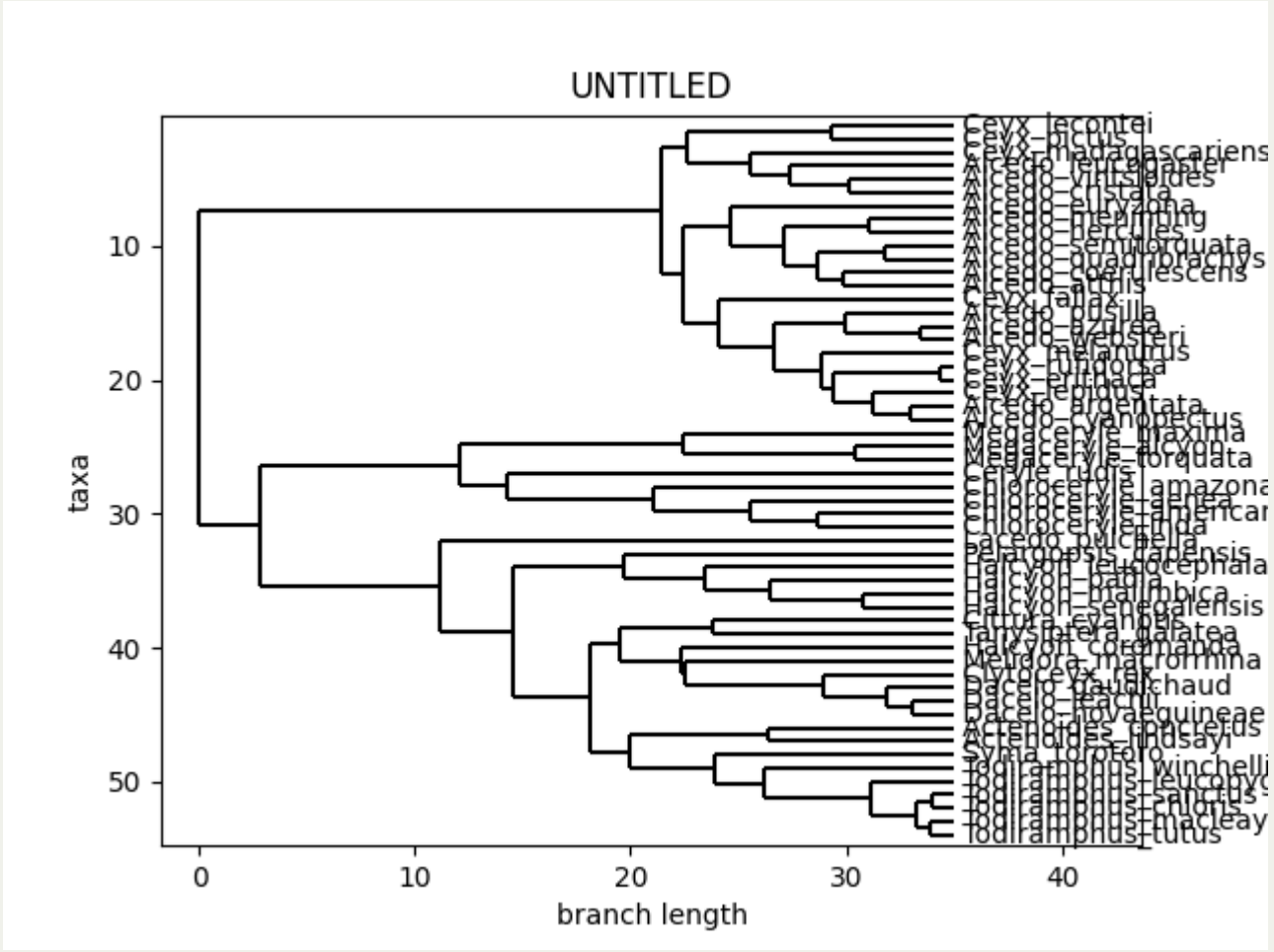
- Partial CPS transformation
- Automatic alignment
- (Delayed sampling/ conjugacy analysis)

Inference strategies

- Lightweight importance sampling
- Sequential Monte Carlo: Bootstrap Particle Filter,
- Sequential Monte Carlo: Alive particle filter
- Lightweight MCMC
- Trace MCMC
- Particle MCMC

Computer demo | Challenges

Write a program that infers the bifurcation rate λ and the extinction rate μ under the assumption that they are constant for a given binary evolutionary tree.


UNTITLED
taxa
branch length
0
10
20
30
40
50
Cevx_lecontei
Cevx_pictus
Cevx_madagascariens
Alcedo_cristata
Alcedo_euryzona
Alcedo_hercules
Alcedo_quadribrachys
Alcedo_coerulescens
Cevx_alcyon
Alcedo_azurea
Cevx_melanurus
Cevx_erithaca
Alcedo_argentata
Alcedo_cyanopectus
Megaceryle_maxima
Megaceryle_torquata
Chloroceryle_amazona
Chloroceryle_aenea
Chloroceryle_americana
Chloroceryle_inda
Lacedo_pulchella
Halcyon_leucocephala
Halcyon_badia
Halcyon_malimbica
Halcyon_senegalensis
Tanysiptera_galatea
Halcyon_coromanda
Melidora_macrorrhina
Dacelo_gaudichaud
Dacelo_leachii
Dacelo_novaeguineae
Actenoides_lindsayi
Syma_torotoro
Todiramphus_winchelli
Todiramphus_sanctus
Todiramphus_chloris
Todiramphus_macleayi
Todiramphus_tutus

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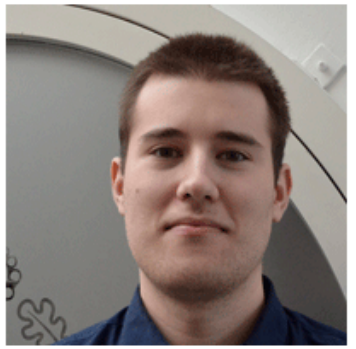

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Thank you

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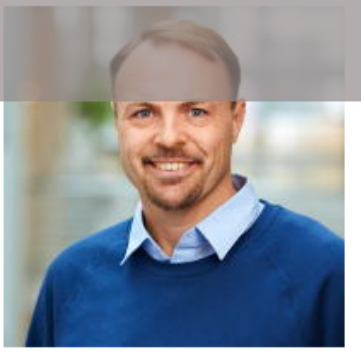

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- Slides have been designed using images from Flaticon.com as well DALL-E

Downloading

Project homepage: https://treeppl.org

Main repo: https://github.com/treeppl/treeppl

Python library: https://github.com/treeppl/treeppl-python

Paper:
https://www.biorxiv.org/content/10.1101/2023.10.10.561673v1

Citation:

```
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Viktor Senderov, Jan Kudlicka, Daniel Lundén, Viktor Palmkvist, Mariana P.
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```

Bonus material

Discussion of PPLs

- PPL semantics
  - Usual language: *input* → *output* + *side effects*
  - PPL: *each program trace describes a sample from a probability distribution*
- Advantages of PPLs
  - natural and generative way of encoding a posterior distribution
  - no need to implement inference
  - enables model comparison as estimation of normalizing constant possible