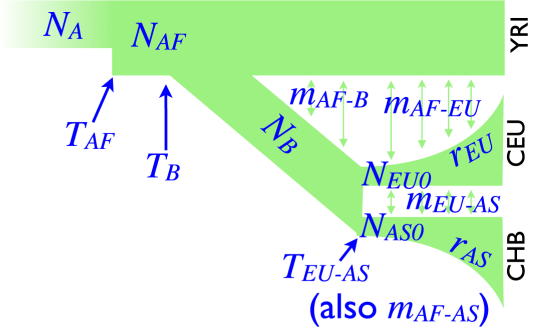
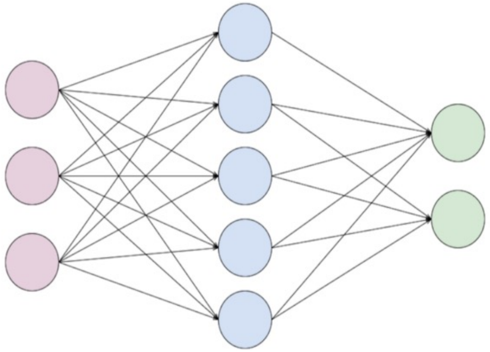
Computationally Efficient Demographic Inference with Supervised Machine Learning





Linh N. Tran, Connie Sun, Mathews Sajan, Ryan Gutenkunst
University of Arizona

SMBE everywhere GS2
July 12, 2022

THE UNIVERSITY OF ARIZONA

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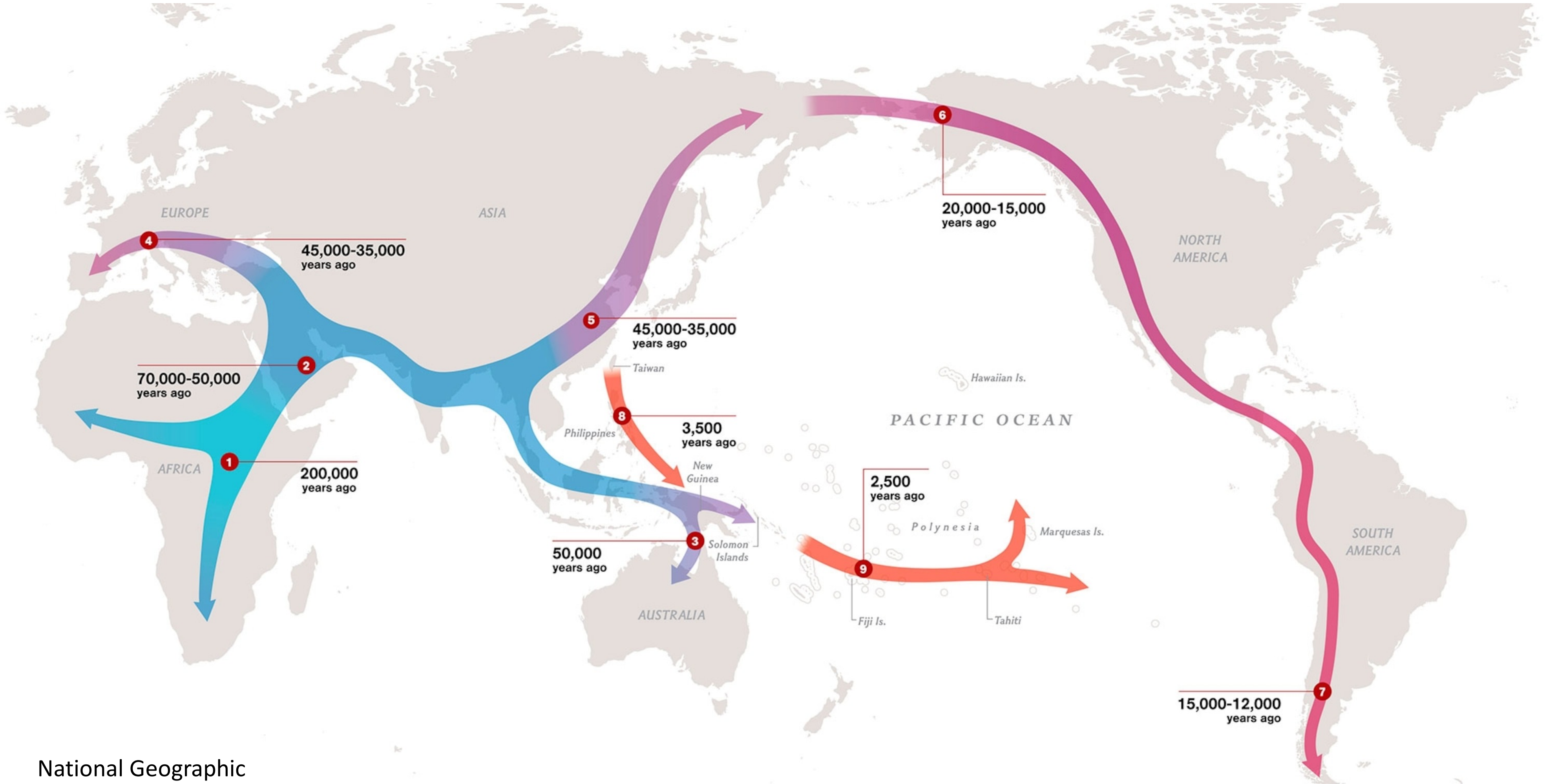
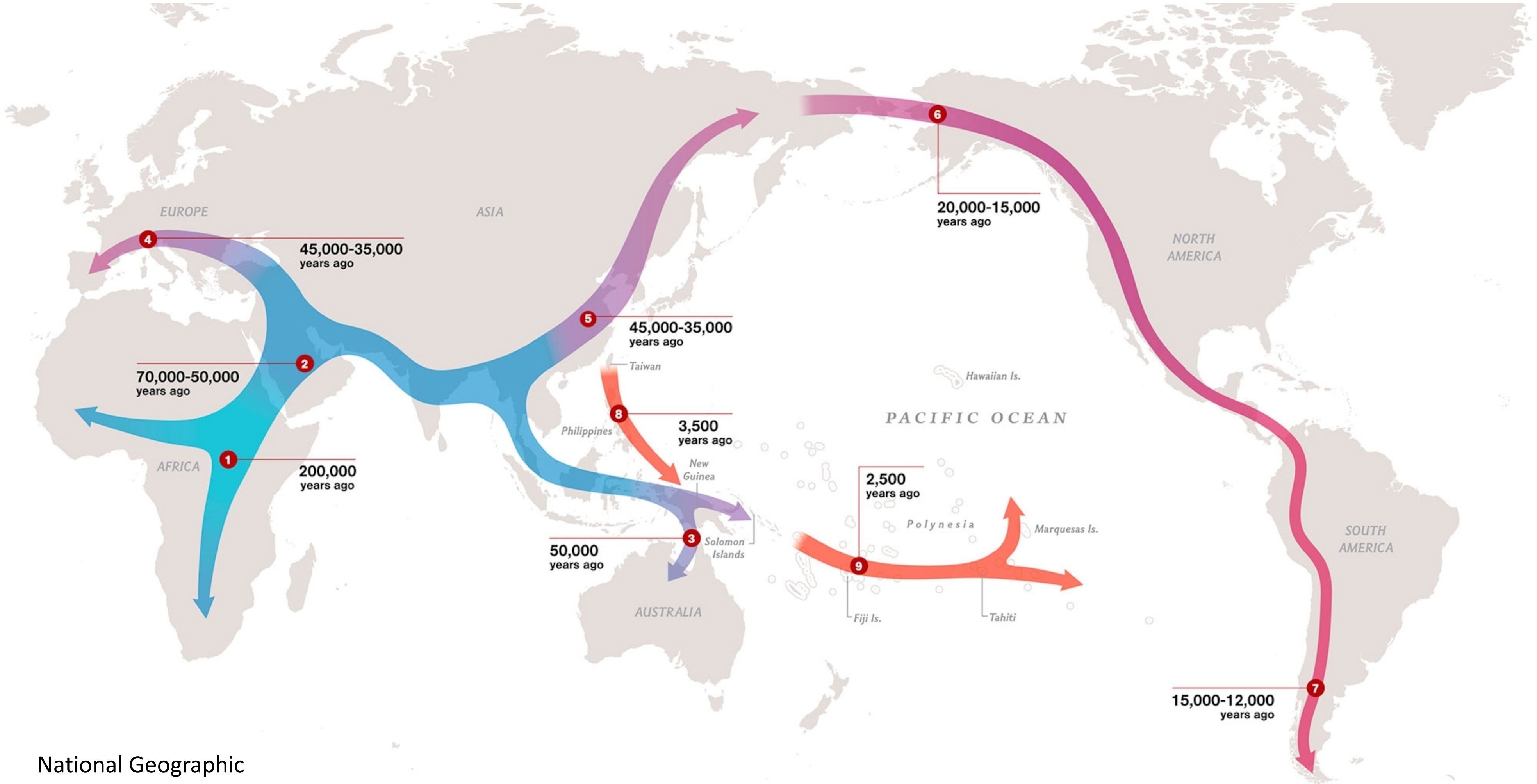
Demographic history inference



National Geographic

Demographic history inference – Motivation

- Understand population history: bottlenecks, gene flow, etc.



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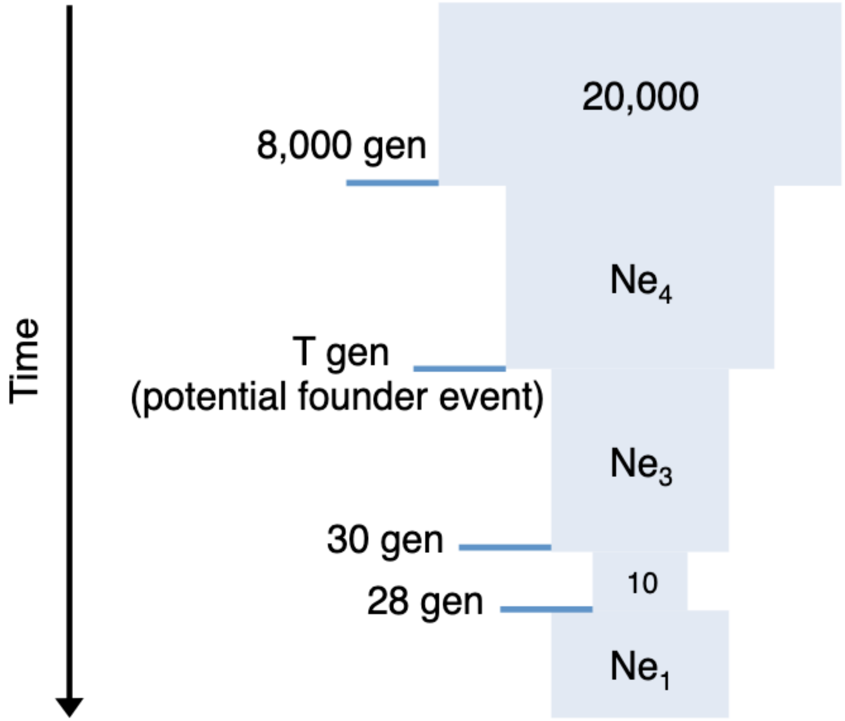
- Conservation: historical genetic diversity of endangered species

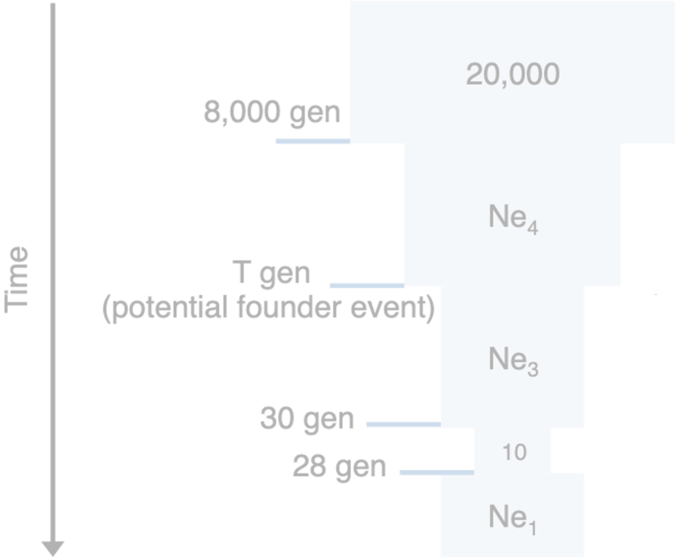


Robinson et al. (2016) *Current Biology*

Demographic history inference – Motivation

National Geographic

- Understand population history: bottlenecks, gene flow, etc.
- Conservation: historical genetic diversity of endangered species
- Selection: sets neutral background for detecting adaptation



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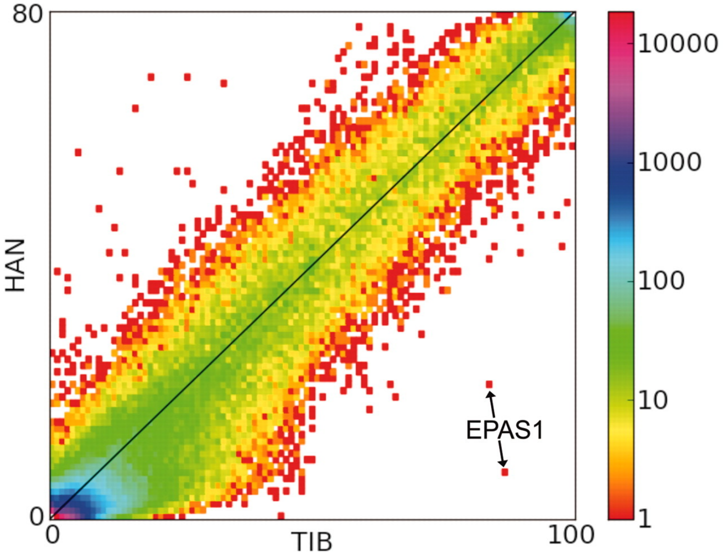

Yi et al. (2010) *Science*

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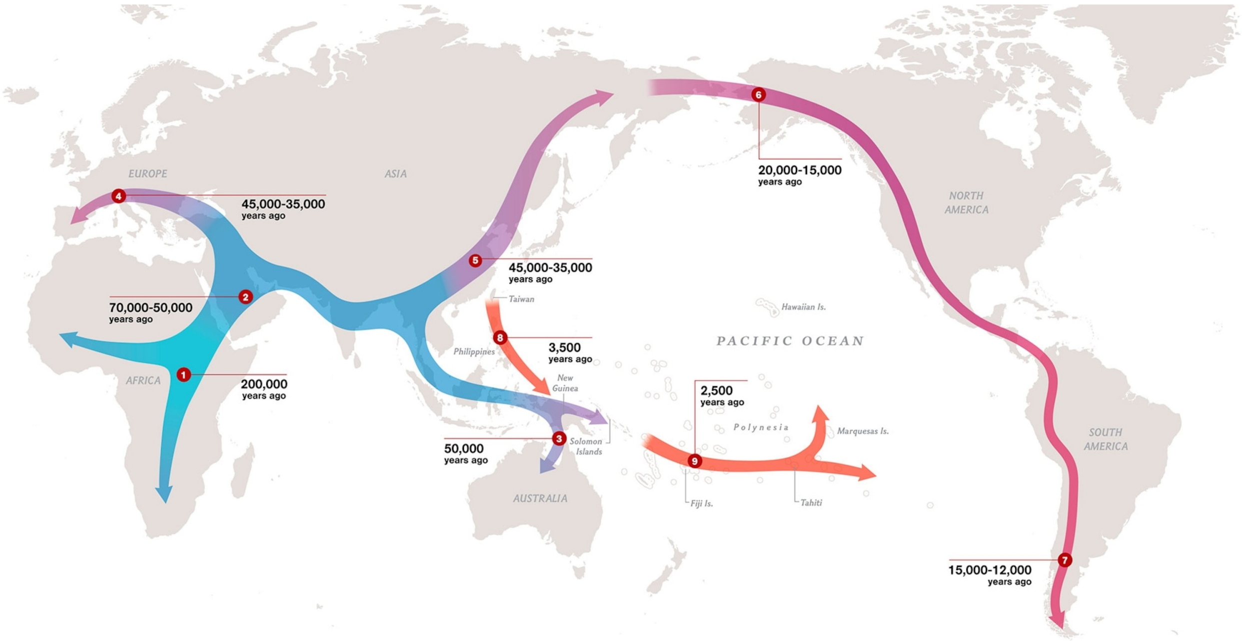

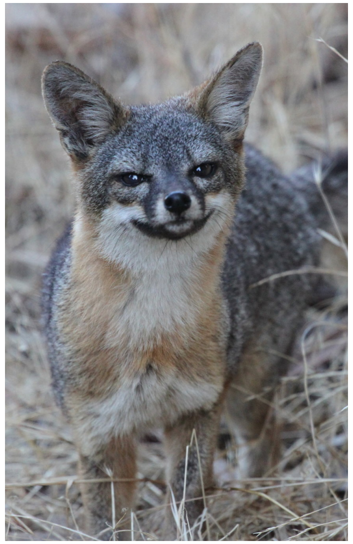

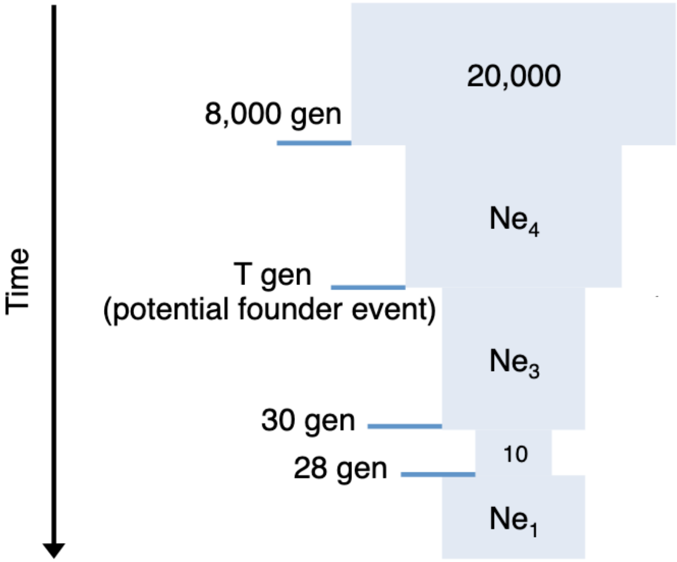

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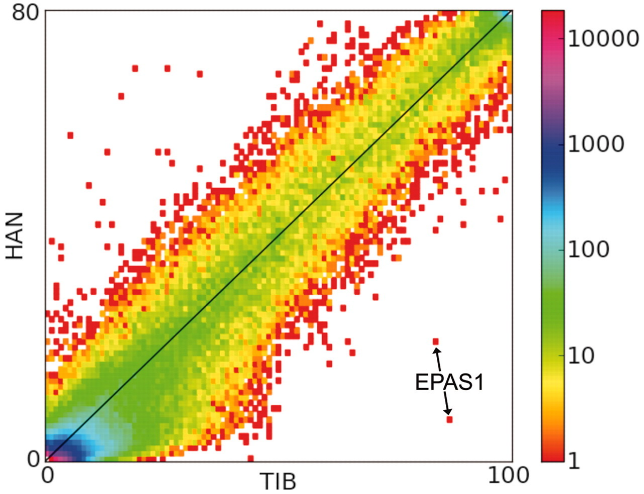

Yi et al. (2010) *Science*

Diffusion approximation for demographic inference (dadi)

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RESEARCH ARTICLE

Inferring the Joint Demographic History of Multiple Populations from Multidimensional SNP Frequency Data

Ryan N. Gutenkunst, Ryan D. Hernandez, Scott H. Williamson, Carlos D. Bustamante

Published: October 23, 2009 • https://doi.org/10.1371/journal.pgen.1000695

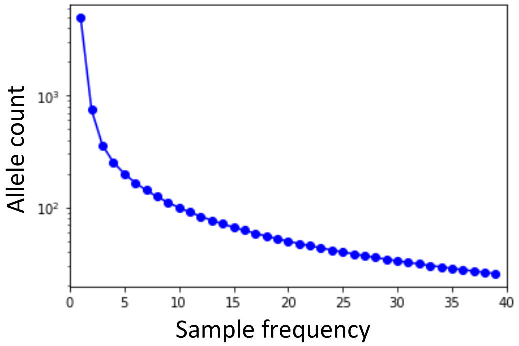
Groups

☆ dadi-user 391 members

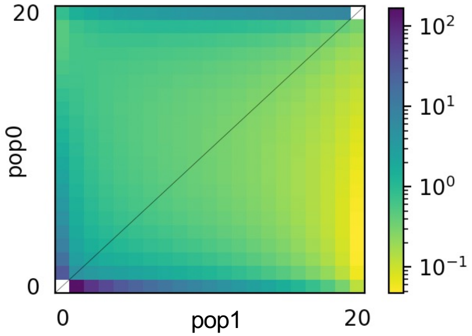
Diffusion approximation for demographic inference (dadi)

Data

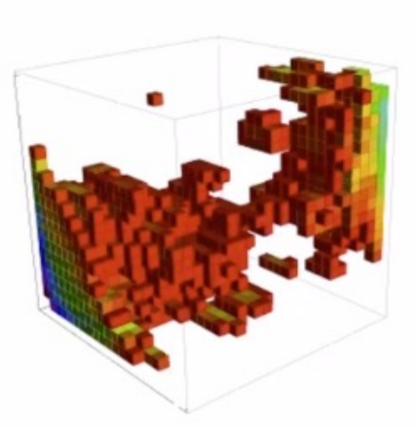
Data Summary



1D – 1 population



2D – 2 populations

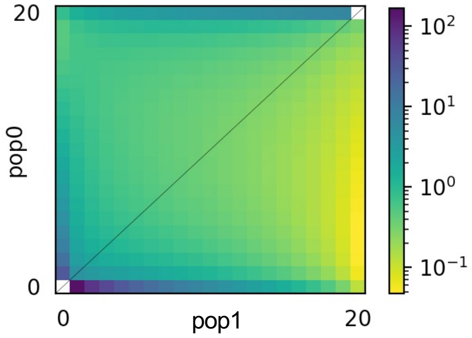


3D – 3 populations

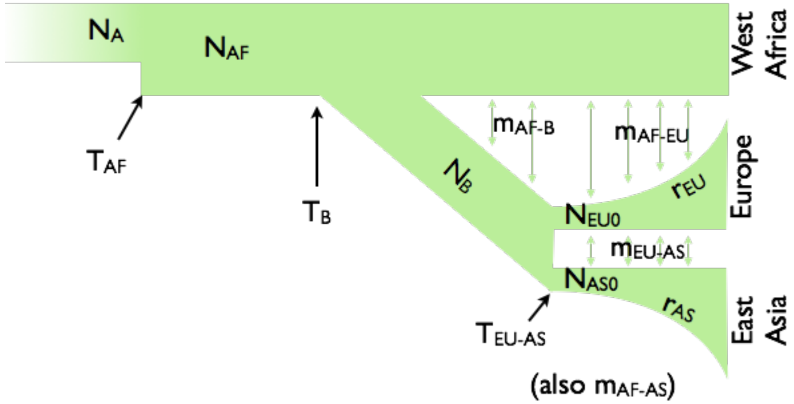
Diffusion approximation for demographic inference (dadi)

Data

Data Summary



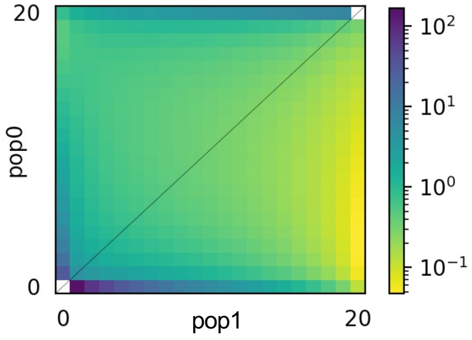
Input parameterized model

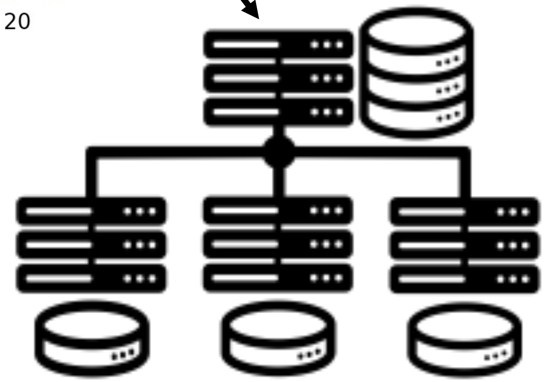


Diffusion approximation for demographic inference (dadi)

Data

Data Summary





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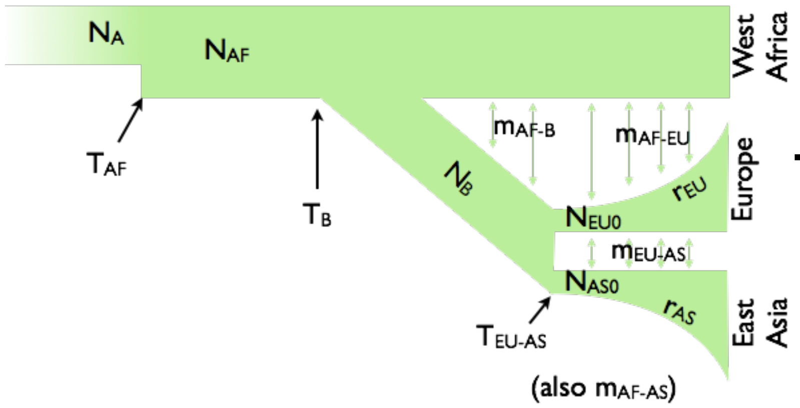
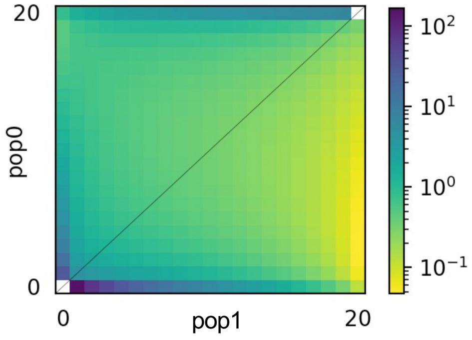


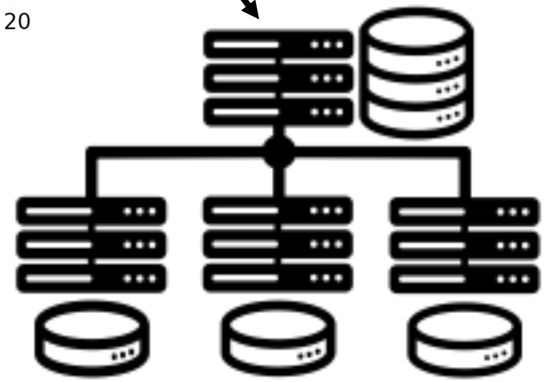
Likelihood Optimization

Diffusion approximation for demographic inference (dadi)

Data

Data Summary





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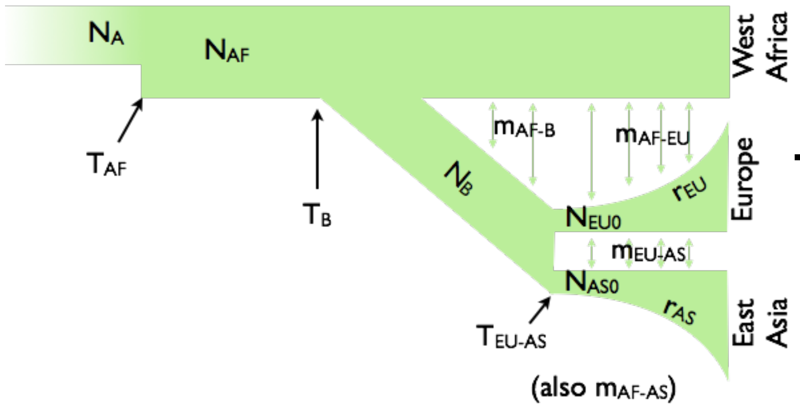
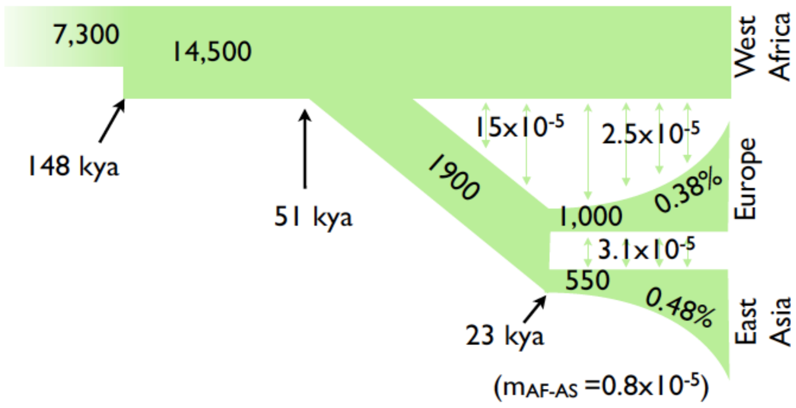
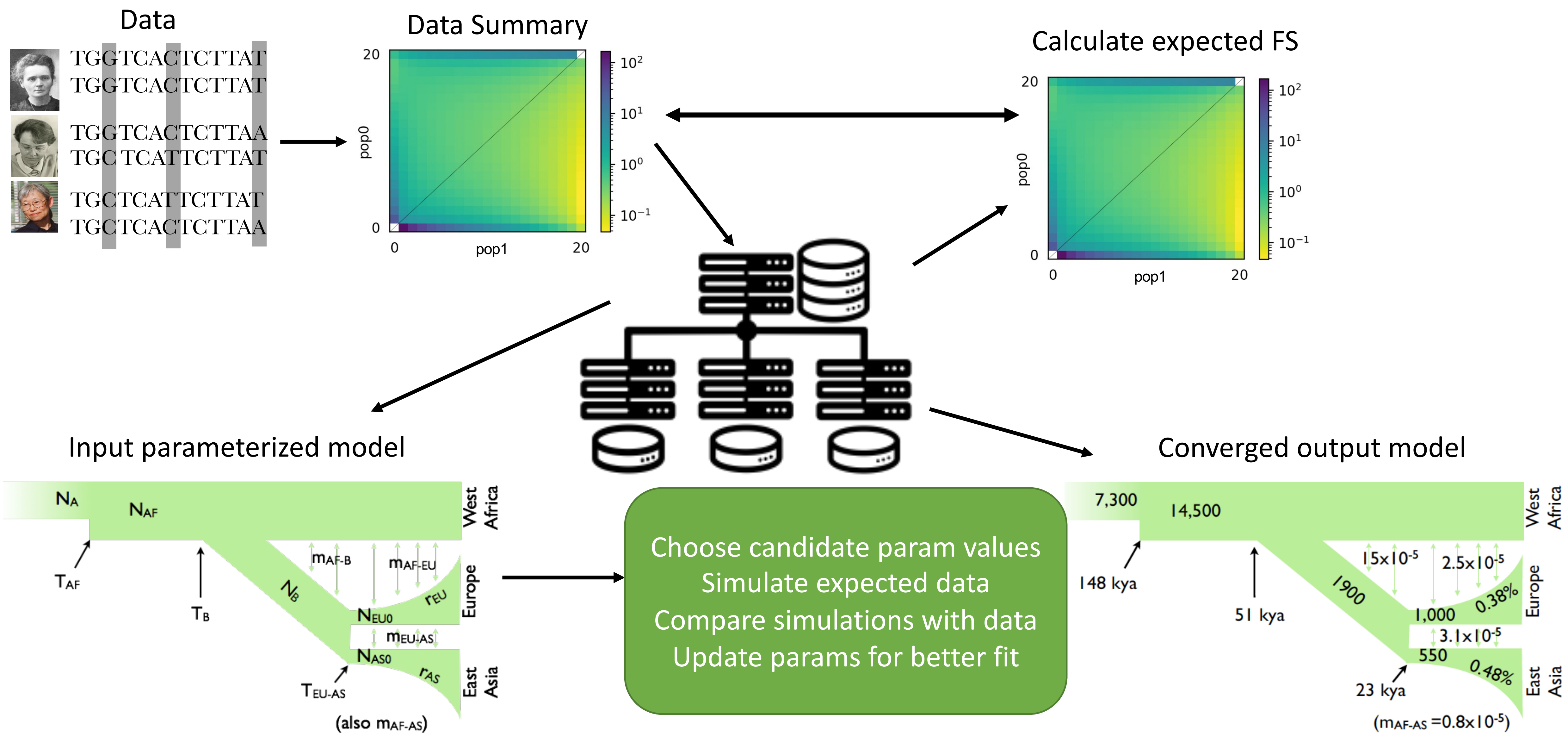


Likelihood Optimization

Converged output model



Diffusion approximation for demographic inference (dadi)



Diffusion approximation for demographic inference (dadi)

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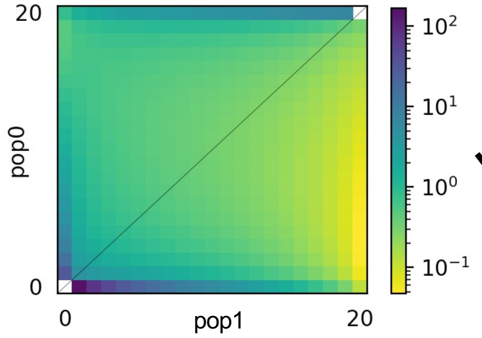
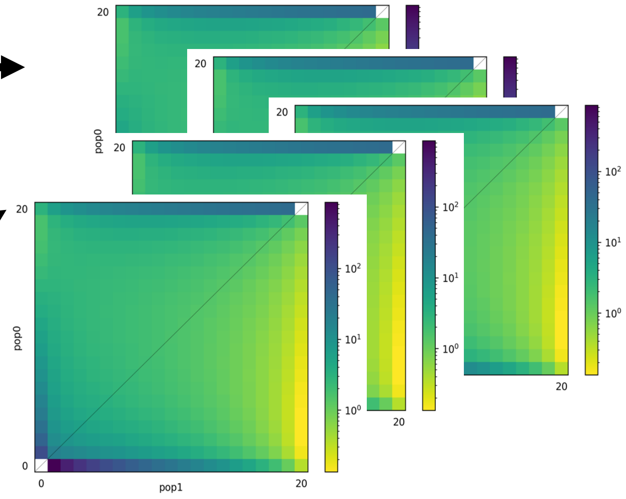
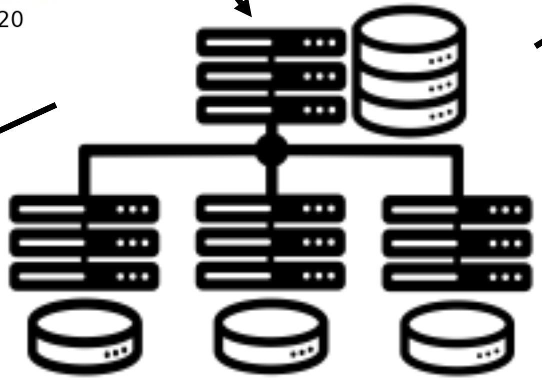
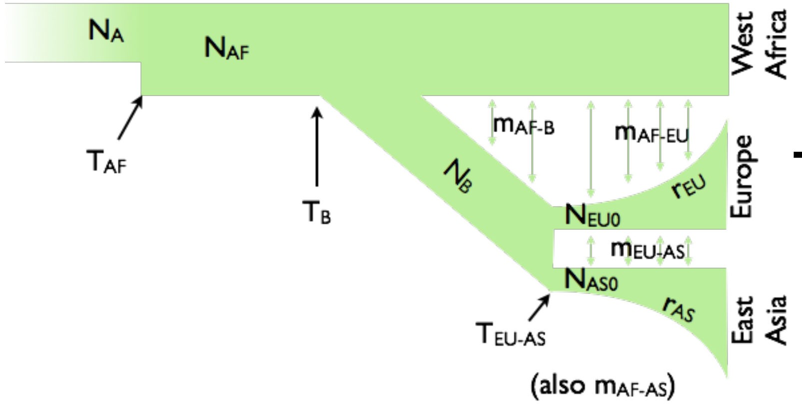


Calculate many expected FS





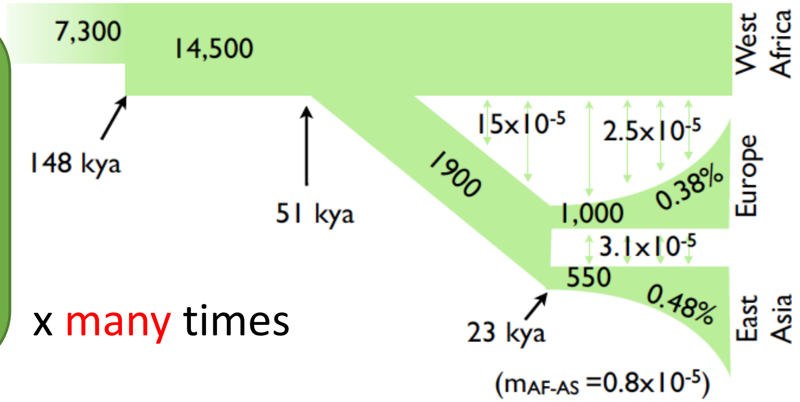
Input parameterized model



Choose candidate param values
Simulate expected data
Compare simulations with data
Update params for better fit

x many times

Converged output model



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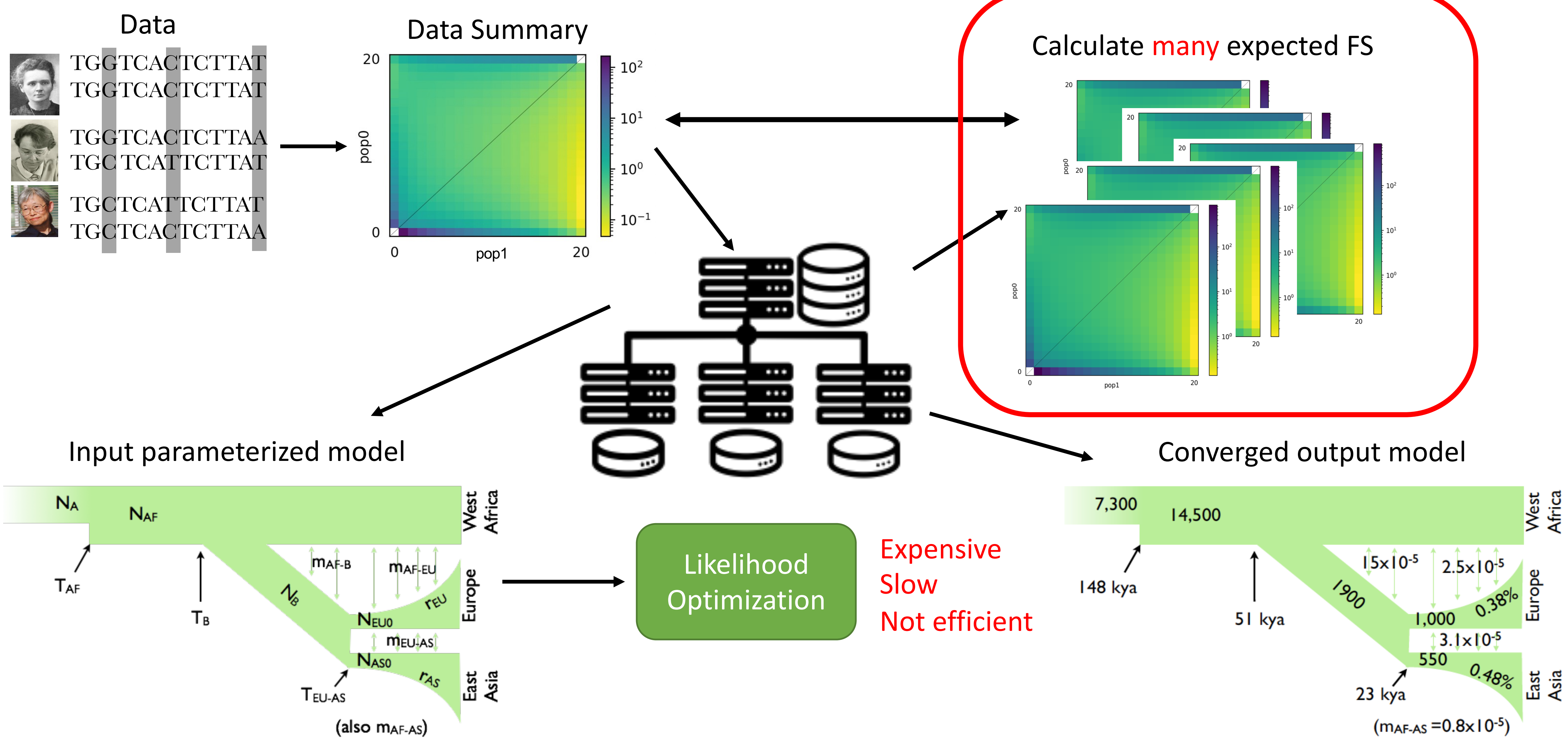

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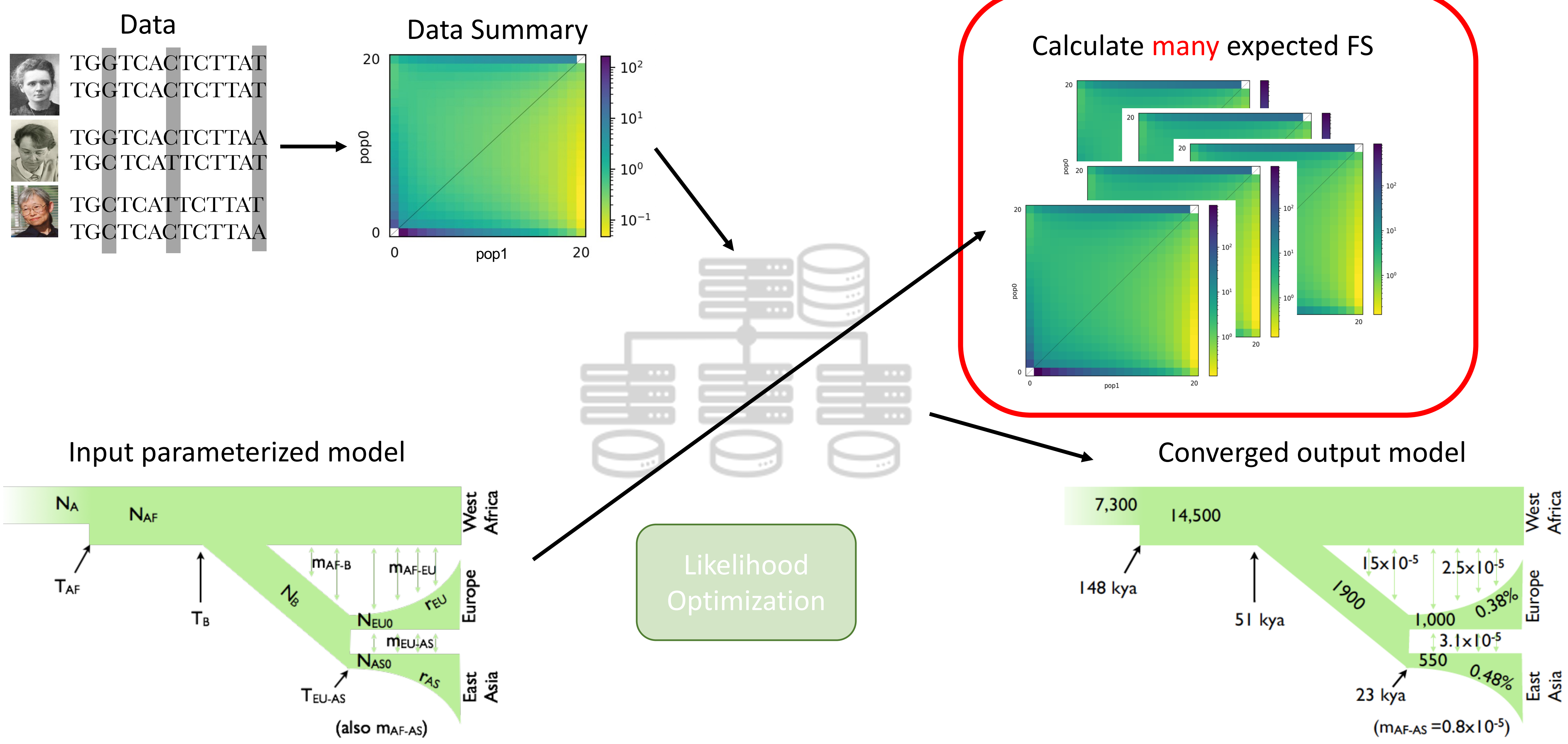

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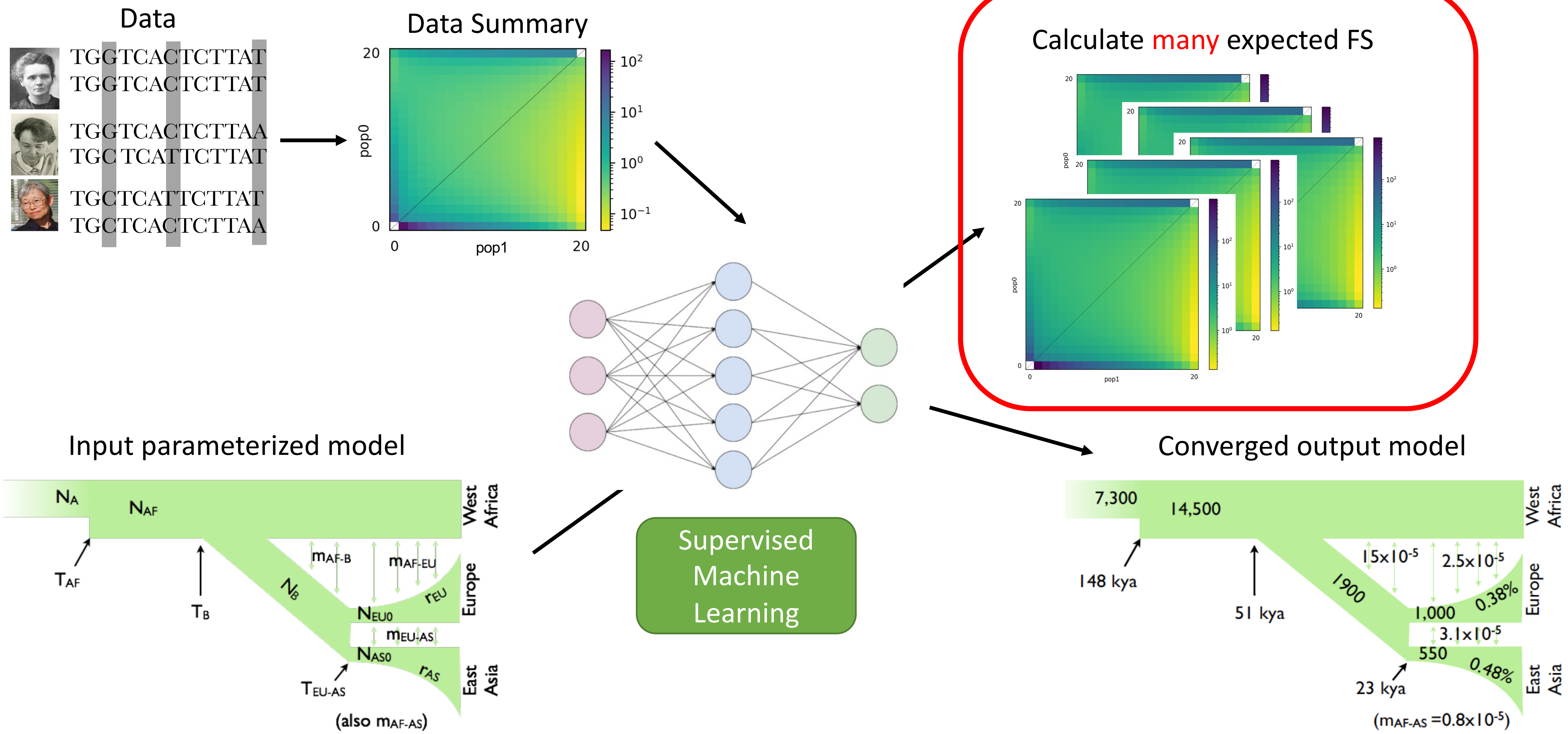

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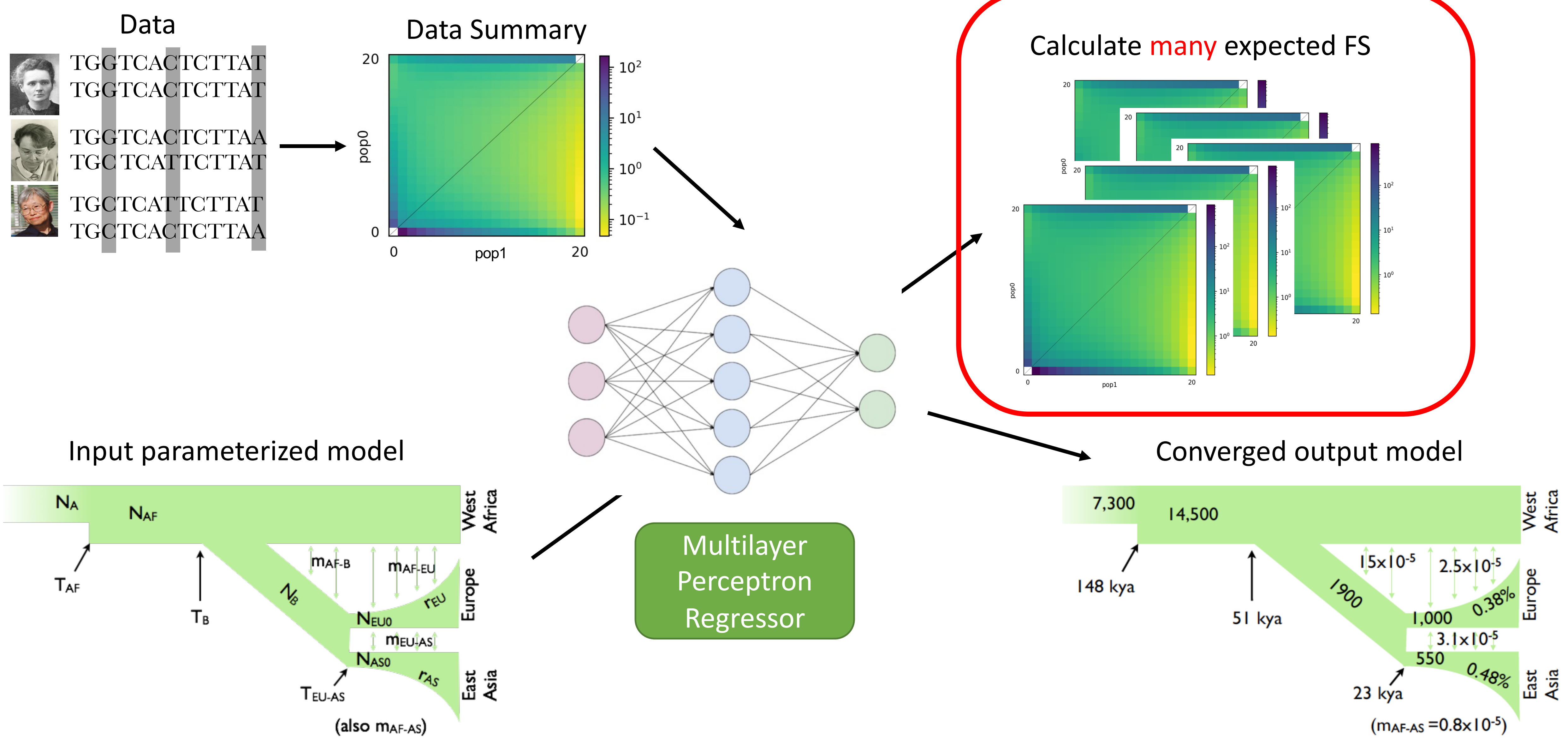
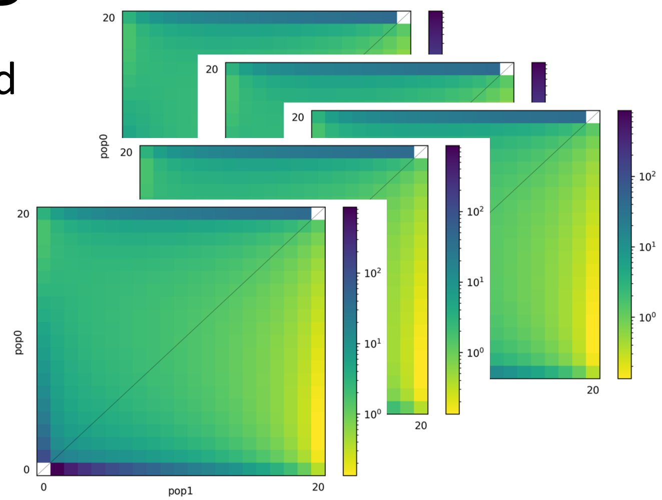


dadi-machine learning workflow

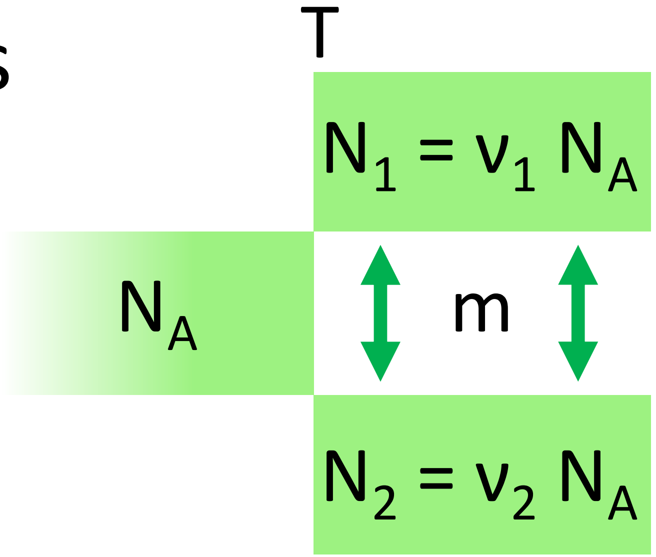
Training data

dadi-simulated spectra (1000)



Labels

parameter values



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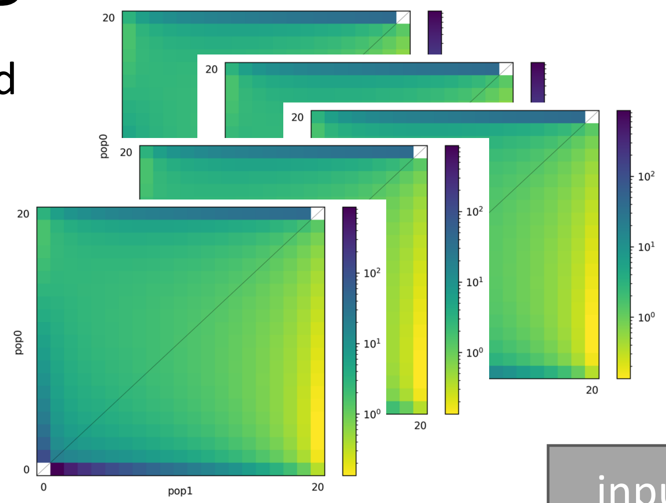

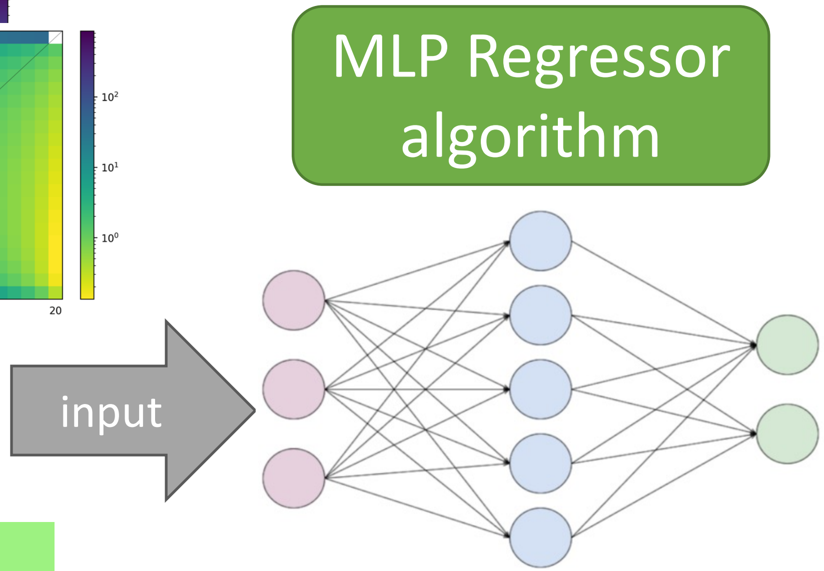

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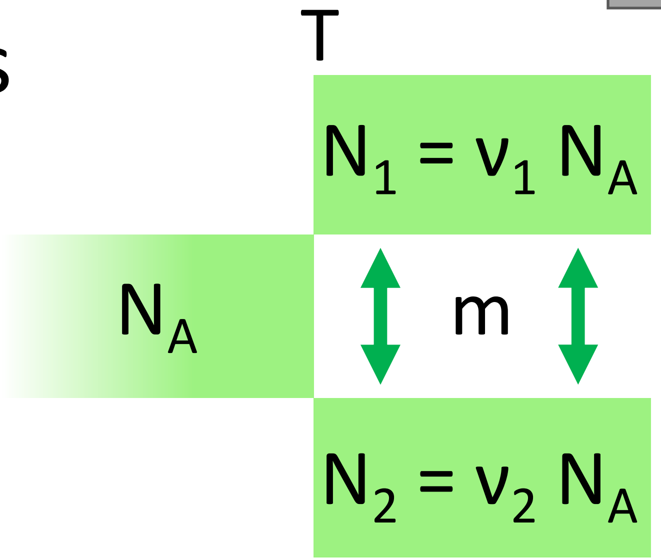

Learns:
Finds pattern of association

dadi-machine learning workflow

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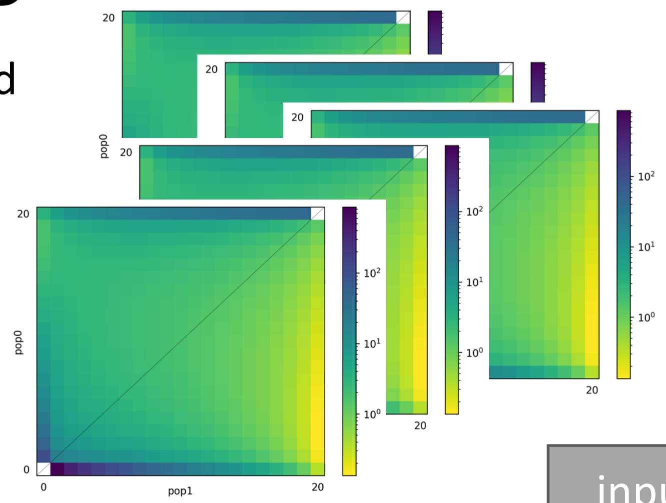
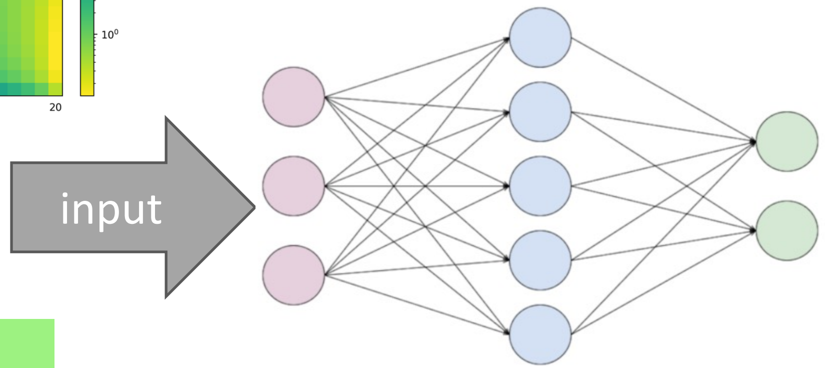


Trained MLP Regressor



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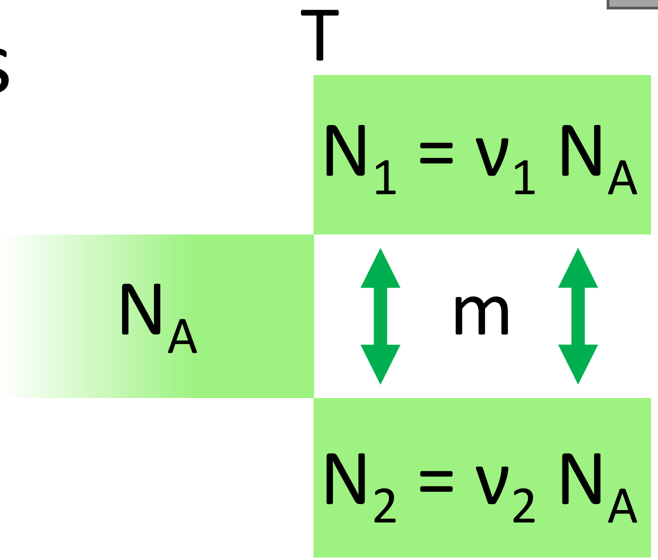

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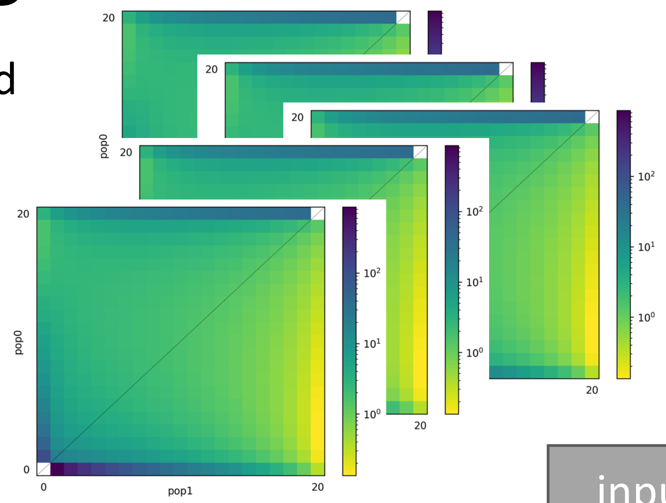

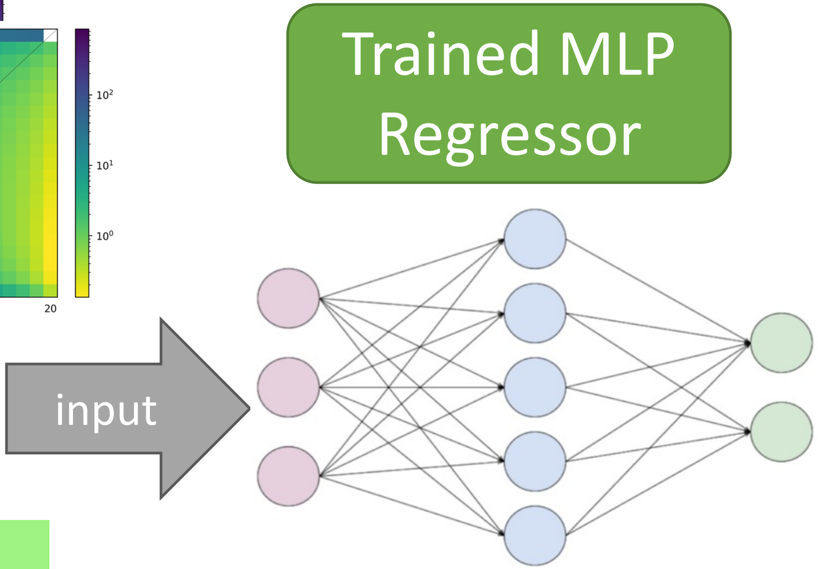

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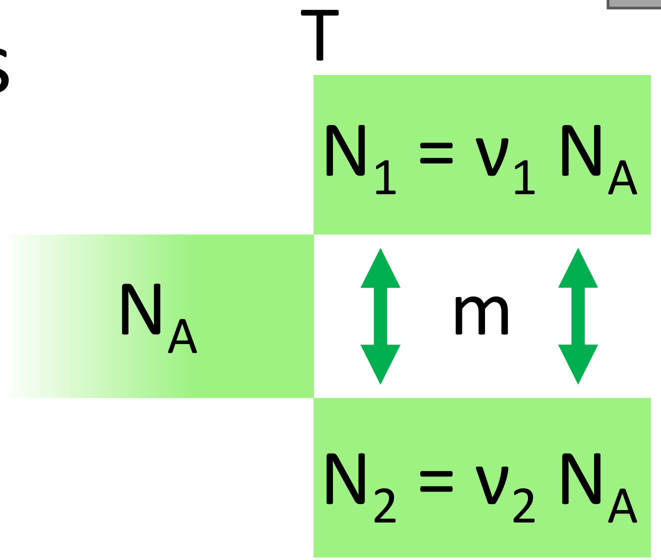

Strength of frequency spectra simulation with dadi:

- Faster and less expensive than coalescent simulations
- Organism-agnostic and transferability

Weakness:

- Ignores linkage

dadi-machine learning workflow

Training data

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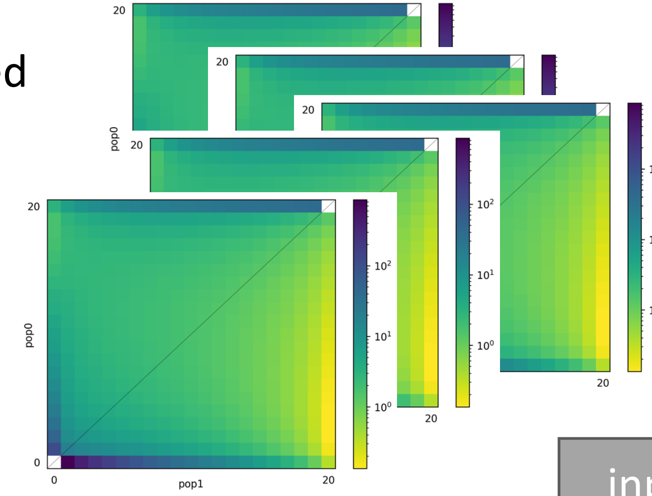
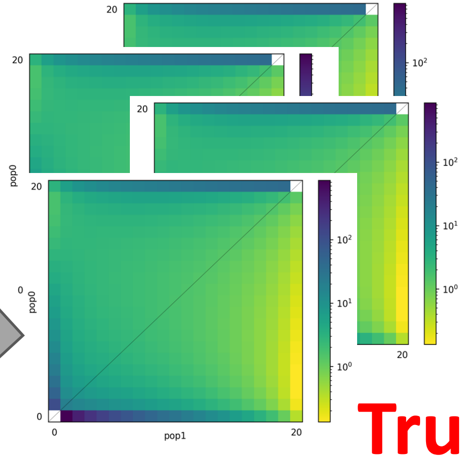
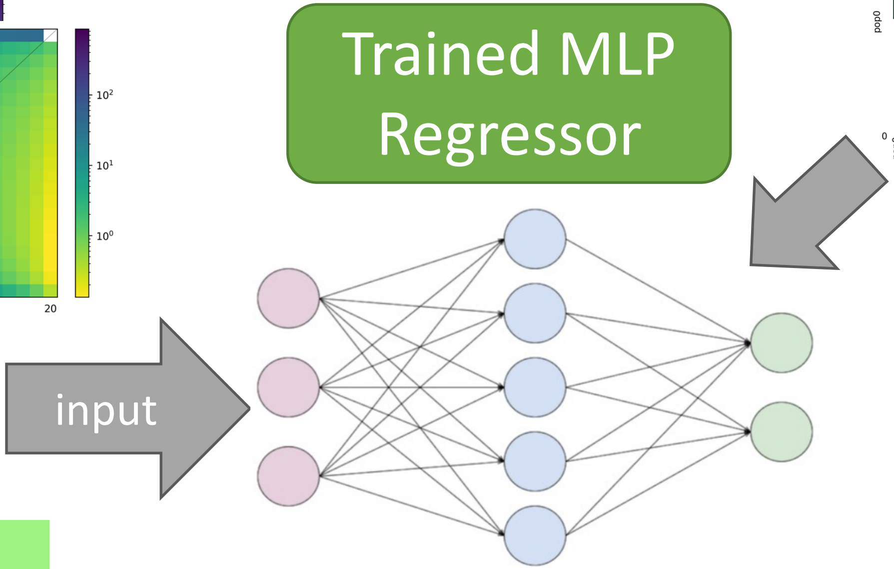


Test data



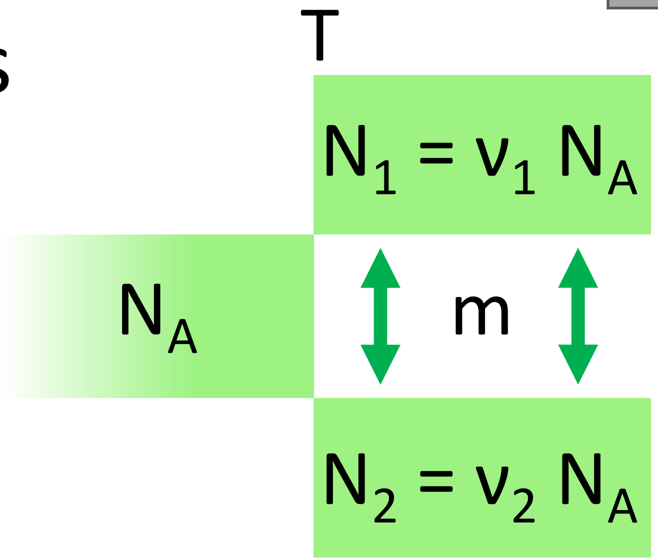
dadi- and msprime-simulated spectra (100-200)



True params: set aside for comparison

Labels

parameter values



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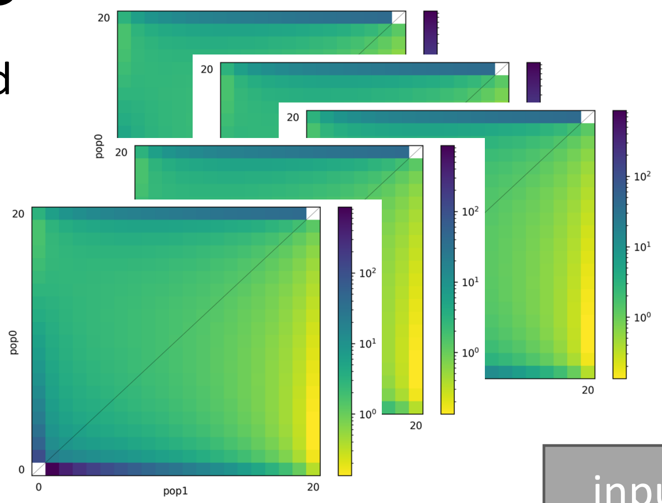

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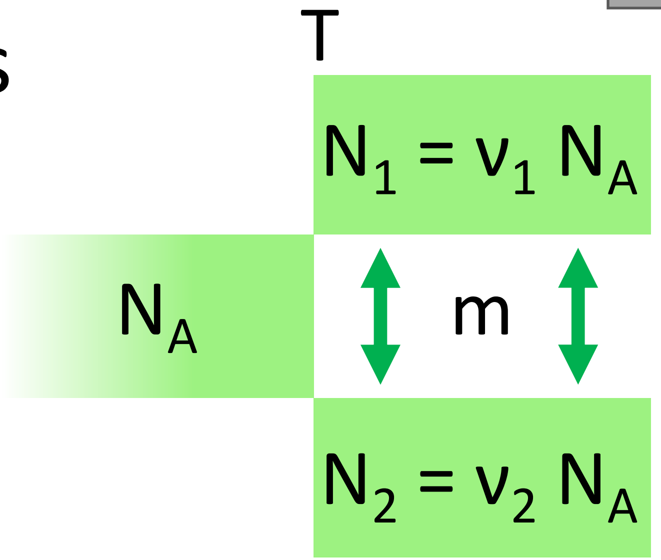

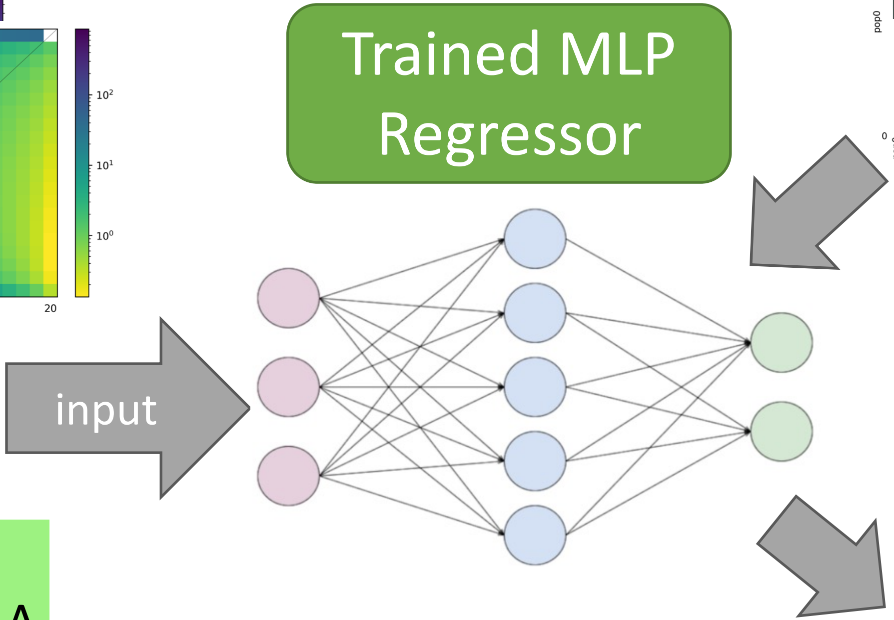

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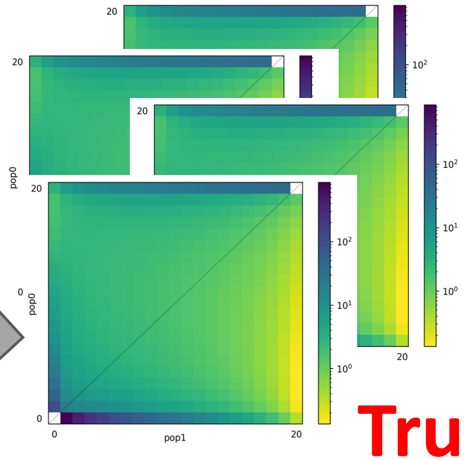


dadi- and msprime-simulated spectra (100-200)

True params: set aside for comparison

Prediction

param values for each test spectrum

Predict :

$\nu_1 = 0.1$

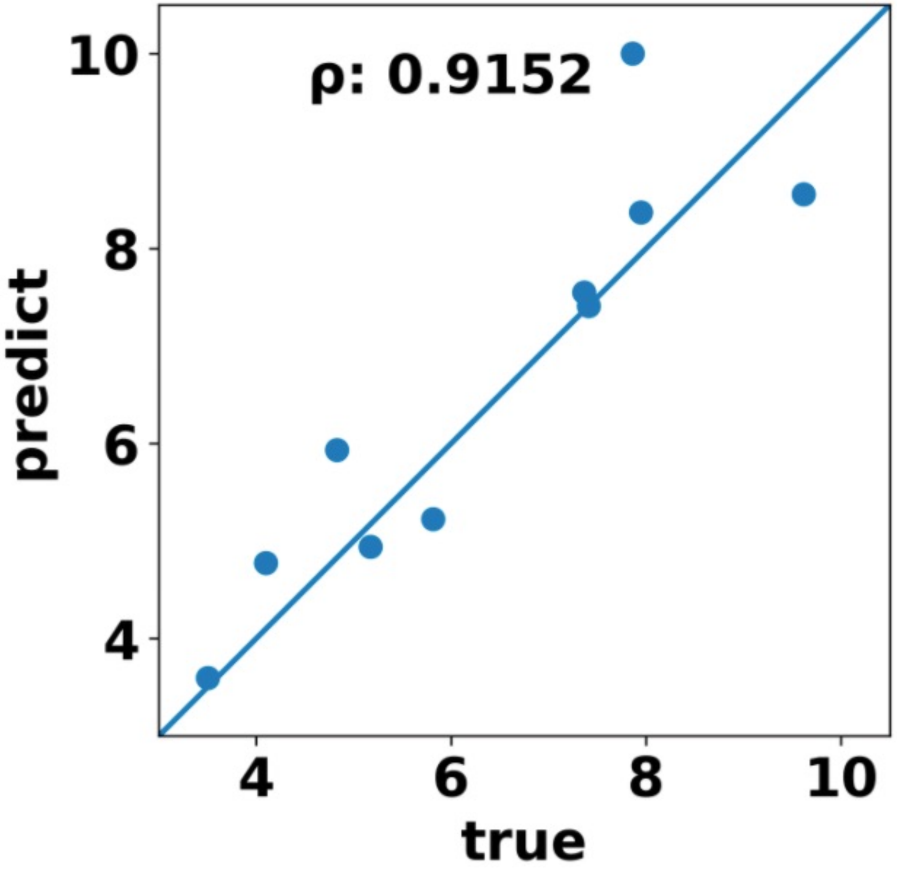
$\nu_2 = 0.5$

$T = 1.3$

$m = 5$

Testing and validation

Prediction accuracy



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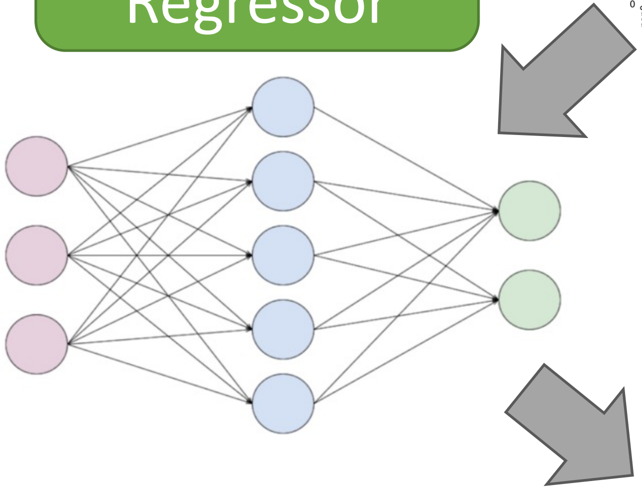

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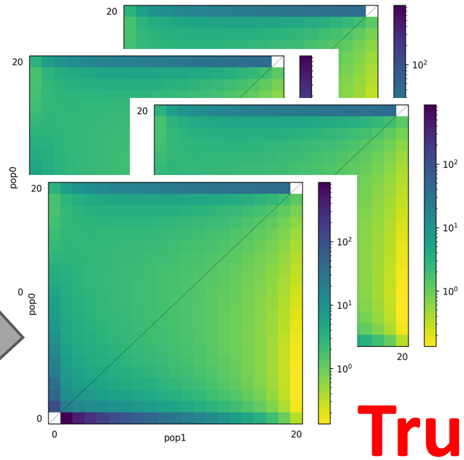

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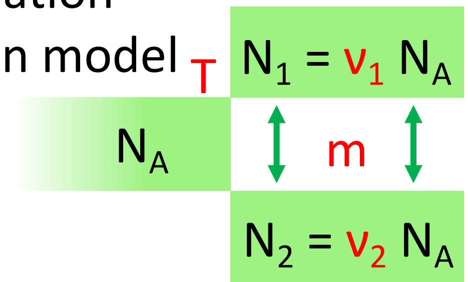
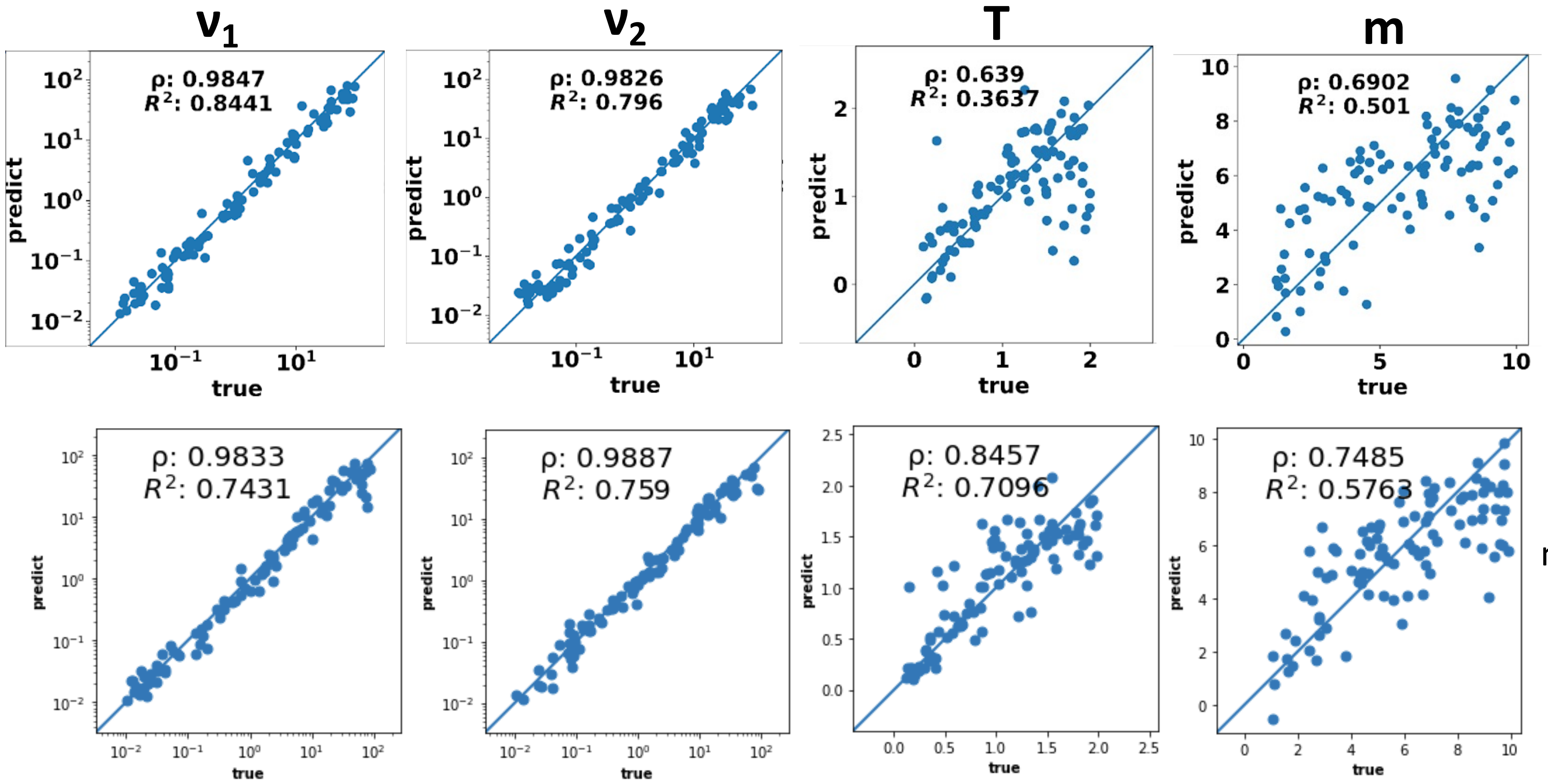
Results – prediction accuracy

two-population
split-migration model



MLPR

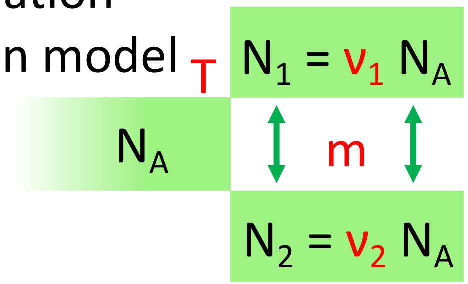


dadi-simulated
data sets

msprime-simulated
data sets

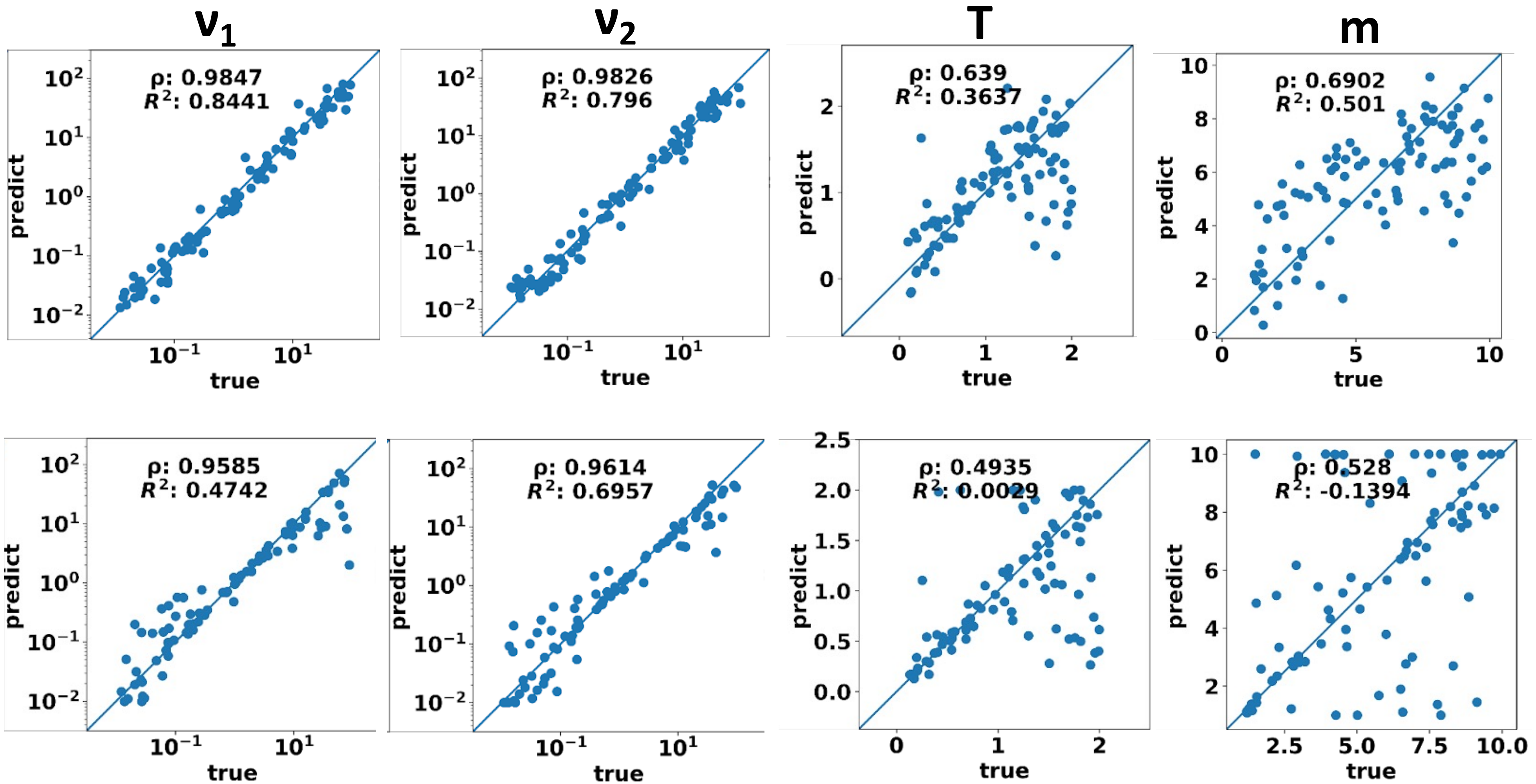
Results – prediction accuracy

two-population
split-migration model



MLPR

dadi

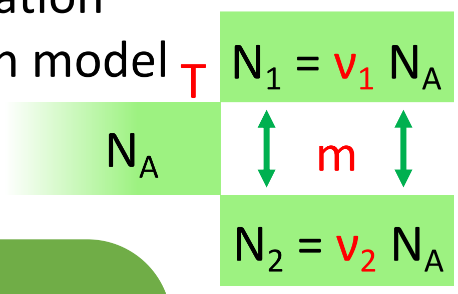


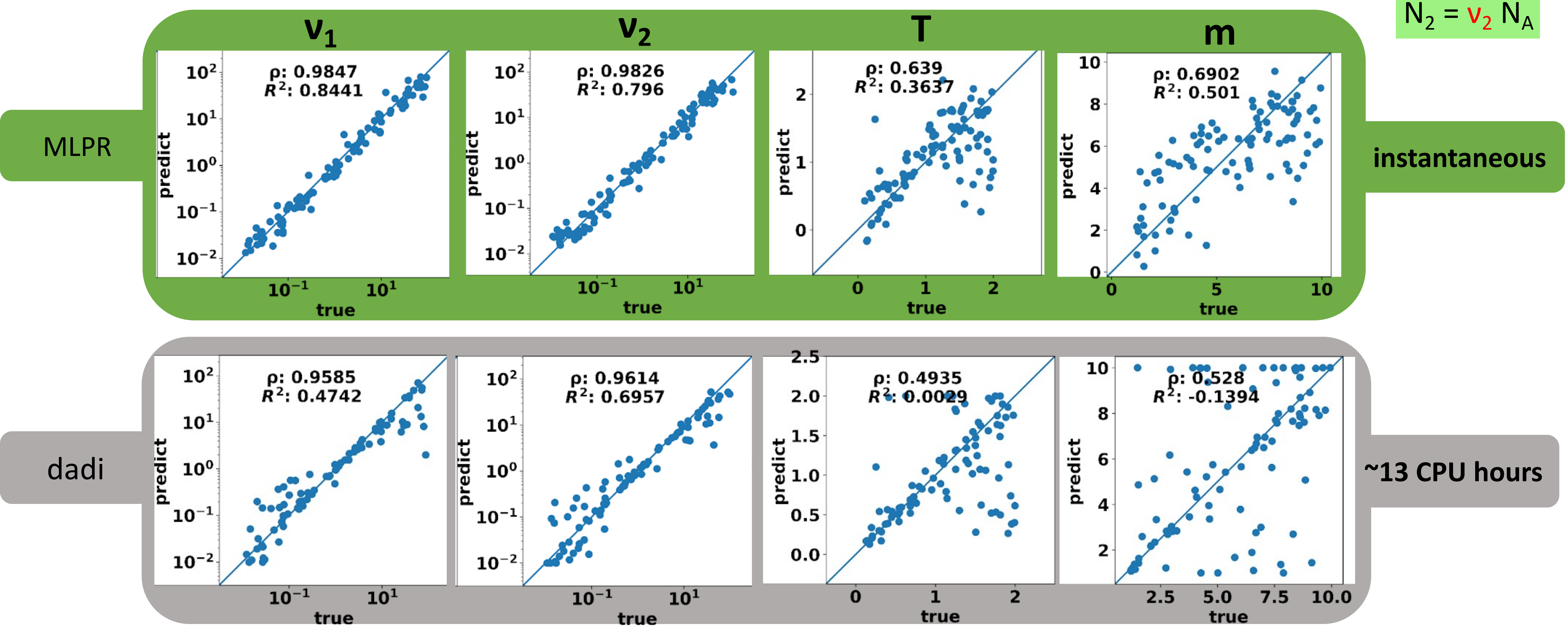
dadi-simulated data sets

dadi-simulated data sets

Results – prediction accuracy and computational efficiency

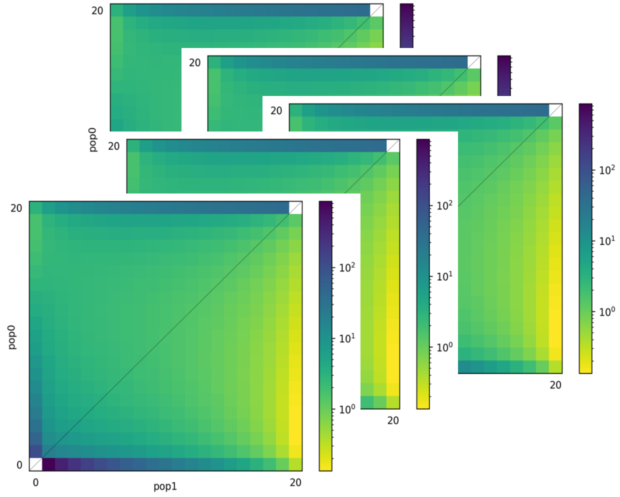
two-population split-migration model

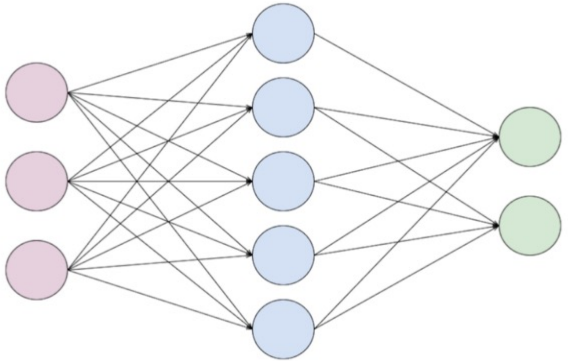


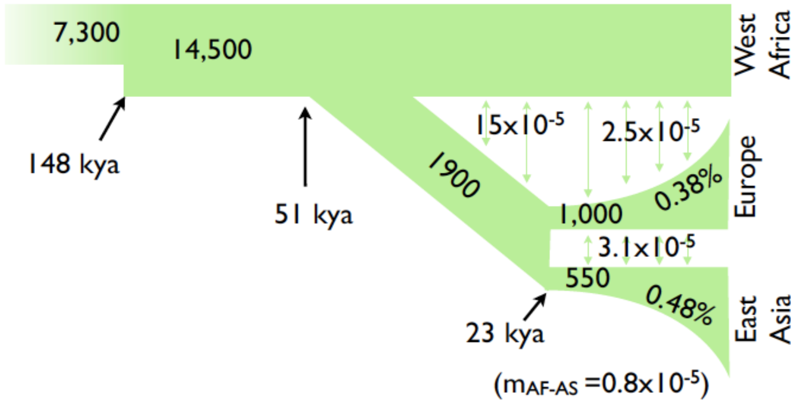


Summary

- Machine learning approach to improve the computational efficiency of a widely used likelihood-based demographic inference method
- Comparable accuracy with significantly reduced computational cost & complexity
- Robust to test simulations generated with linkage
- Accompanying uncertainty quantification method that provides prediction intervals
- Trained MLPRs for frequently used demographic models and workflow will be distributed







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