Duke Center for Statistical Genetics and Genomics

ASHG
VIRTUAL MEETING 2020
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Estimating ancestry from a population kinship matrix under arbitrary ancestral subpopulation structure

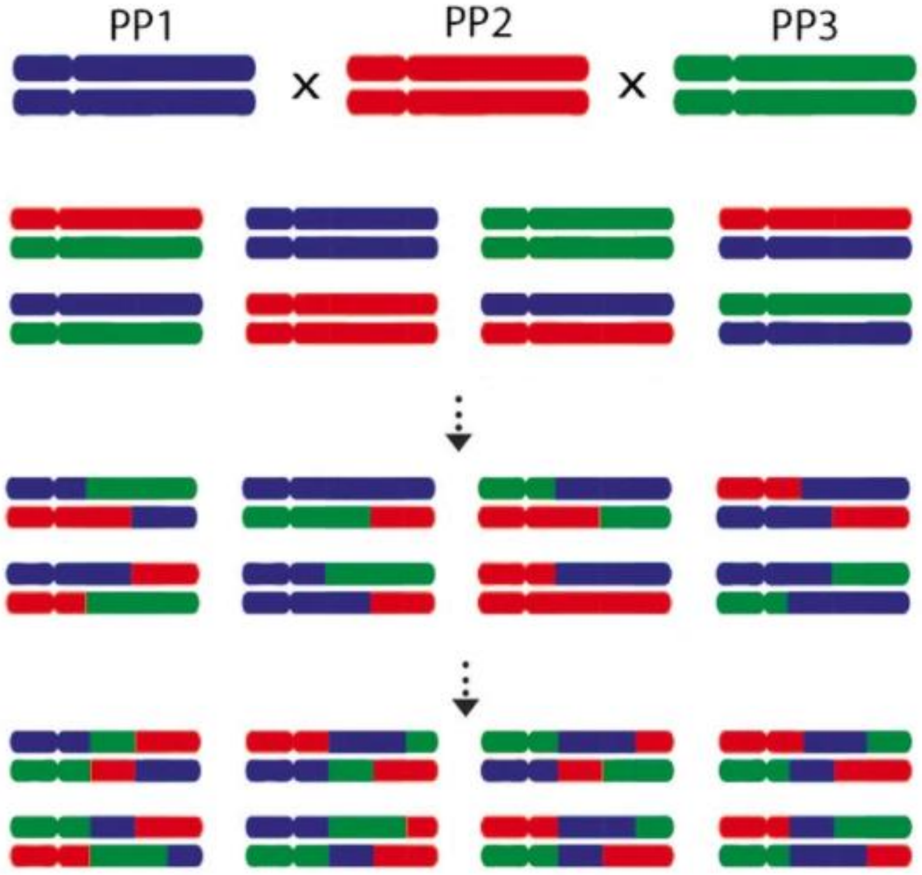
Amika Sood, Alejandro Ochoa
Duke University

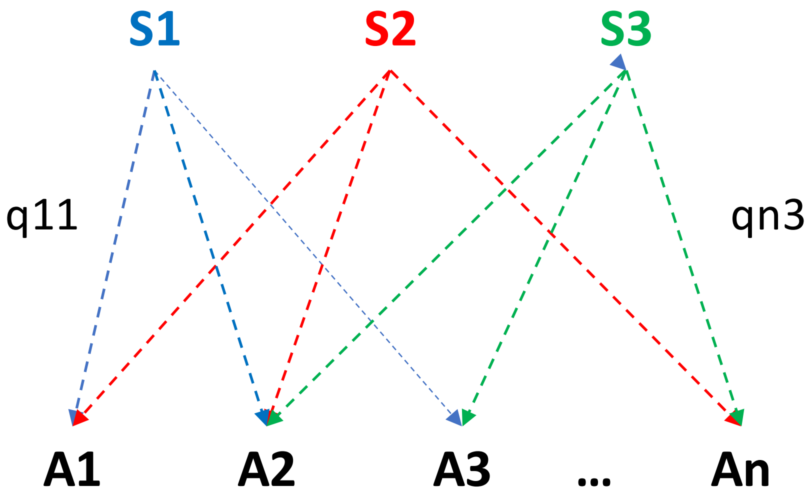
Disclosure Slide

Financial Disclosure for:
Amika Sood
Post-Doctoral Research Associate
Duke University

I have nothing to disclose

Motivation

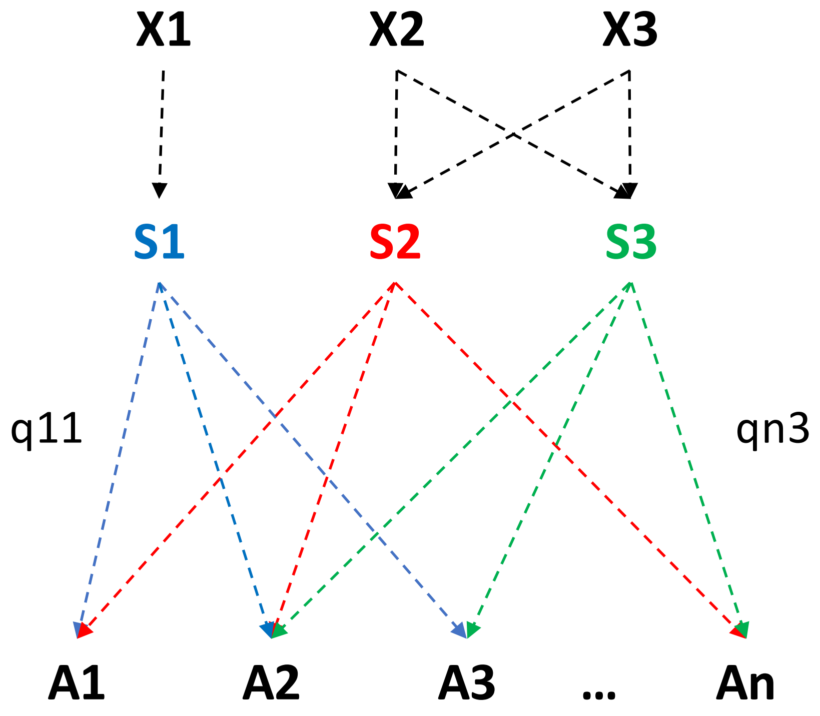




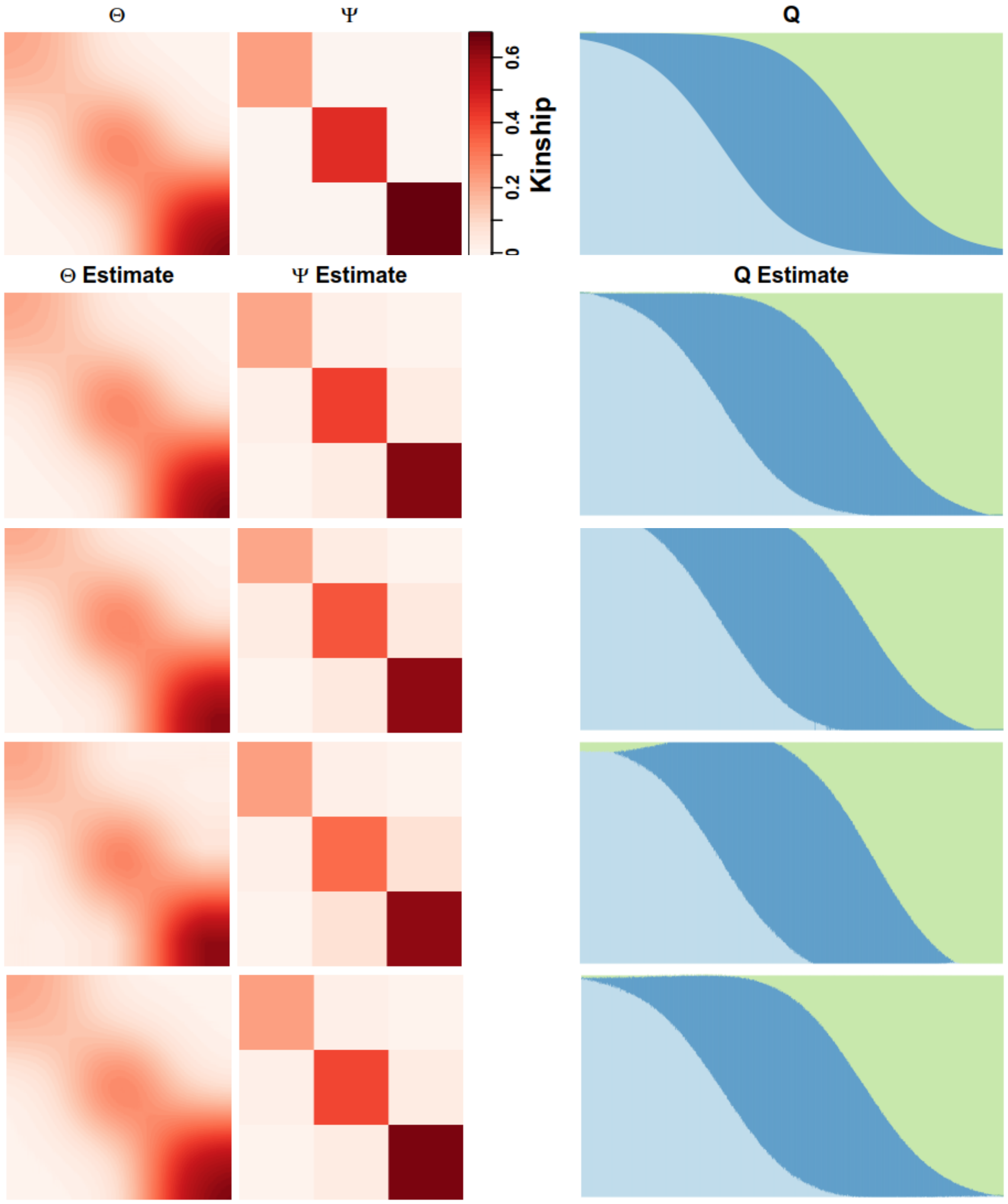
Soares-Souza, G., Borda, V., Kehdy, F. et al. Admixture, Genetics and Complex Diseases in Latin Americans and US Hispanics. Curr Genet Med Rep ***6,*** *208–223 (2018)*

Model and Data Generation

- $P \in R^{m \times k}$, $p_{ij} \in [0,1]$
- $Q \in R^{n \times k}$, $q_{ij} \geq 0, \sum_j q_{ij} = 1$
- $\pi = PQ^T$
- The coancestry matrix of P should equal the coancestry of the ancestral/intermediate subpopulations, Psi.



Performance of existing approaches



Independent ancestral populations

Admixture:
Model-based ancestry estimation

fastStructure :
Variational Bayesian framework

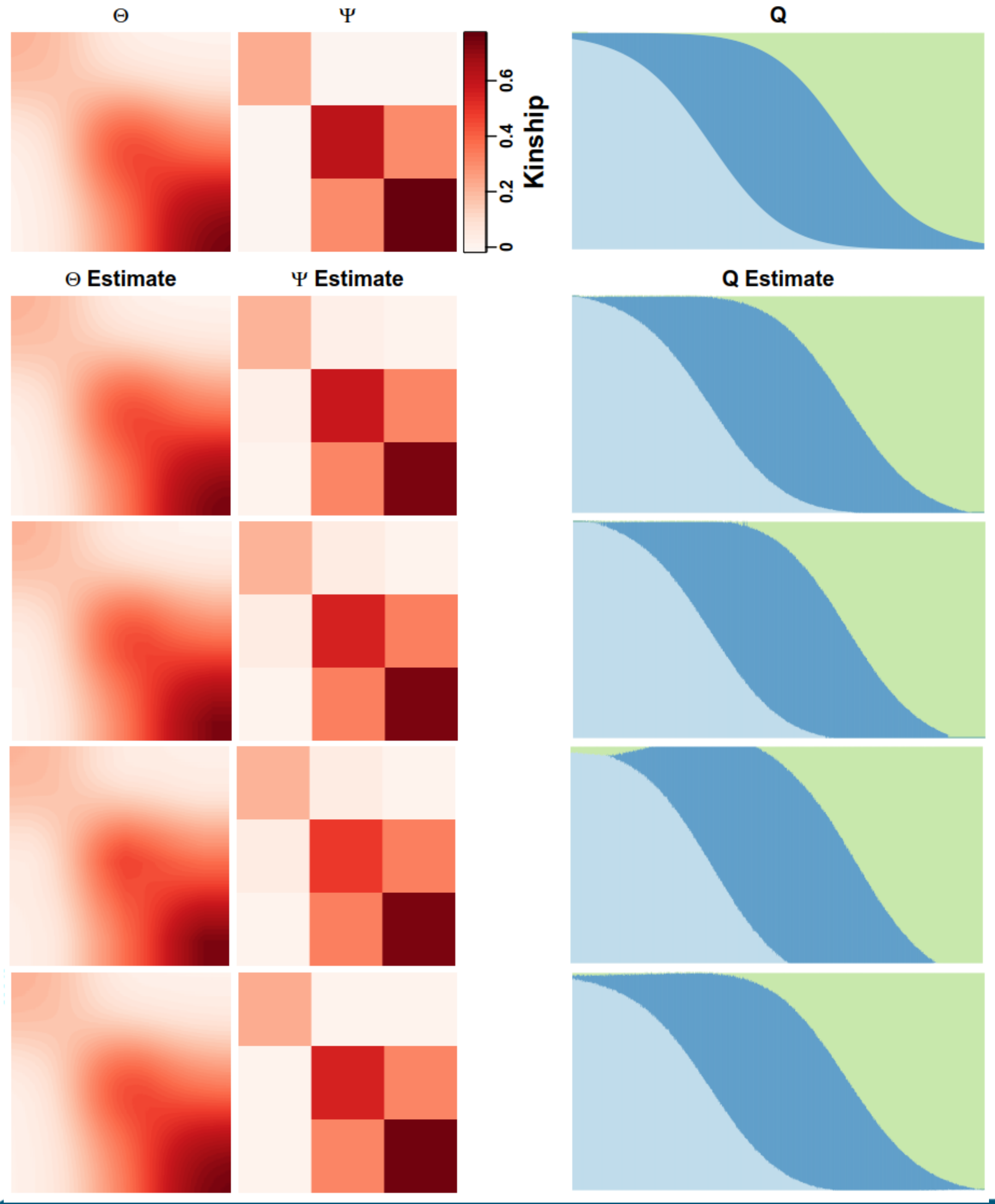
sNMF:
NMF and least-squares optimization

ALStructure:
PCA based method

- 1000 individuals
- 100, 000 loci
- 3 populations
- FST = 0.3

Performance of existing approaches

Correlated ancestral populations



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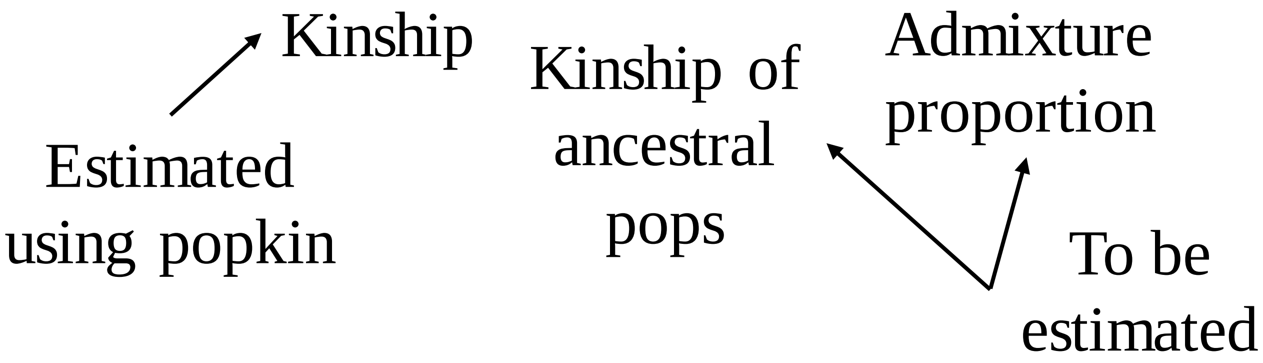
Optimization

$$\Theta = Q\Psi Q^T$$



Kinship

Estimated using popkin

Kinship of ancestral pops

Admixture proportion

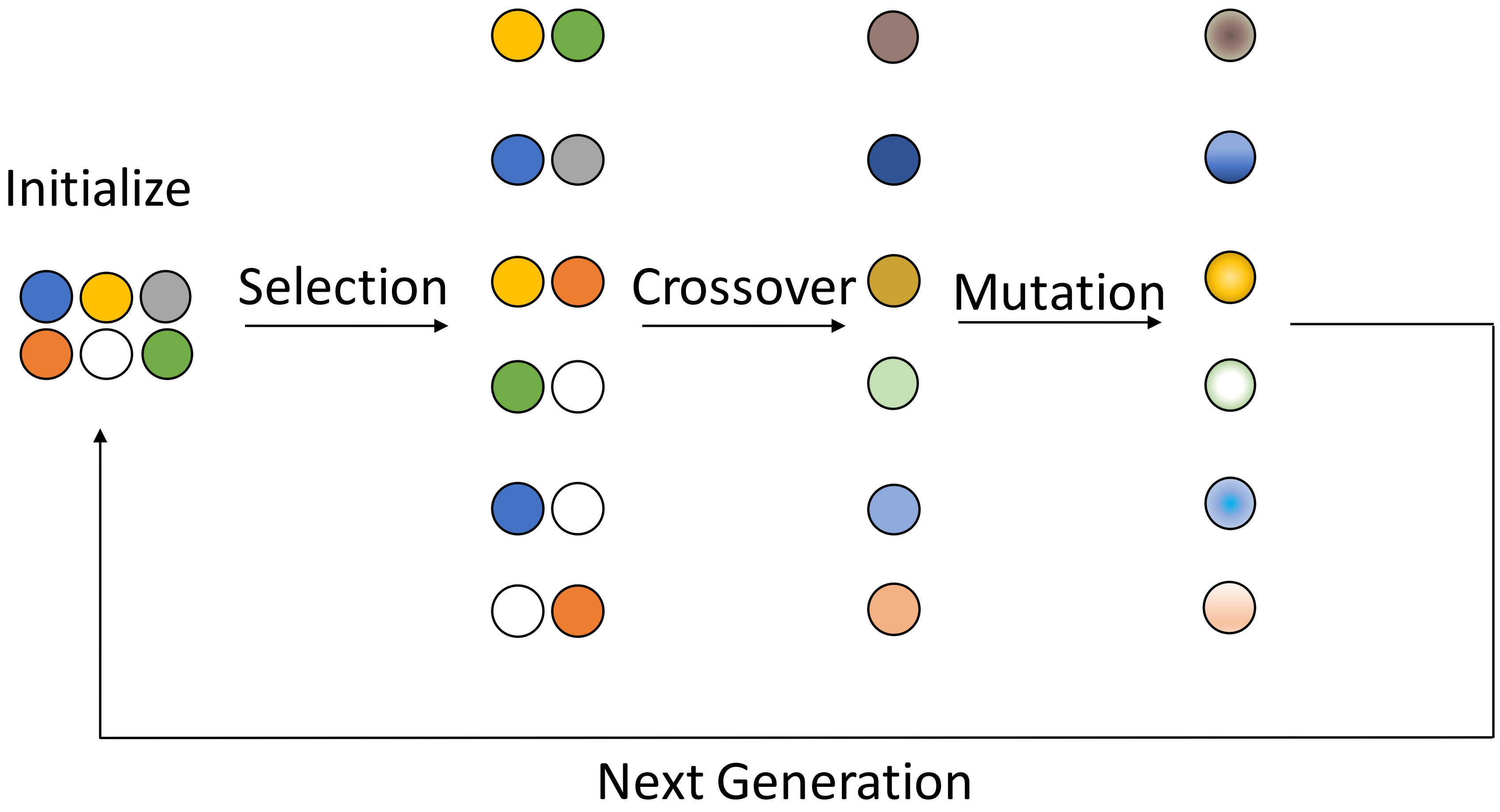
To be estimated

$$F = \|Q\Psi Q^T - \Theta\|^2$$

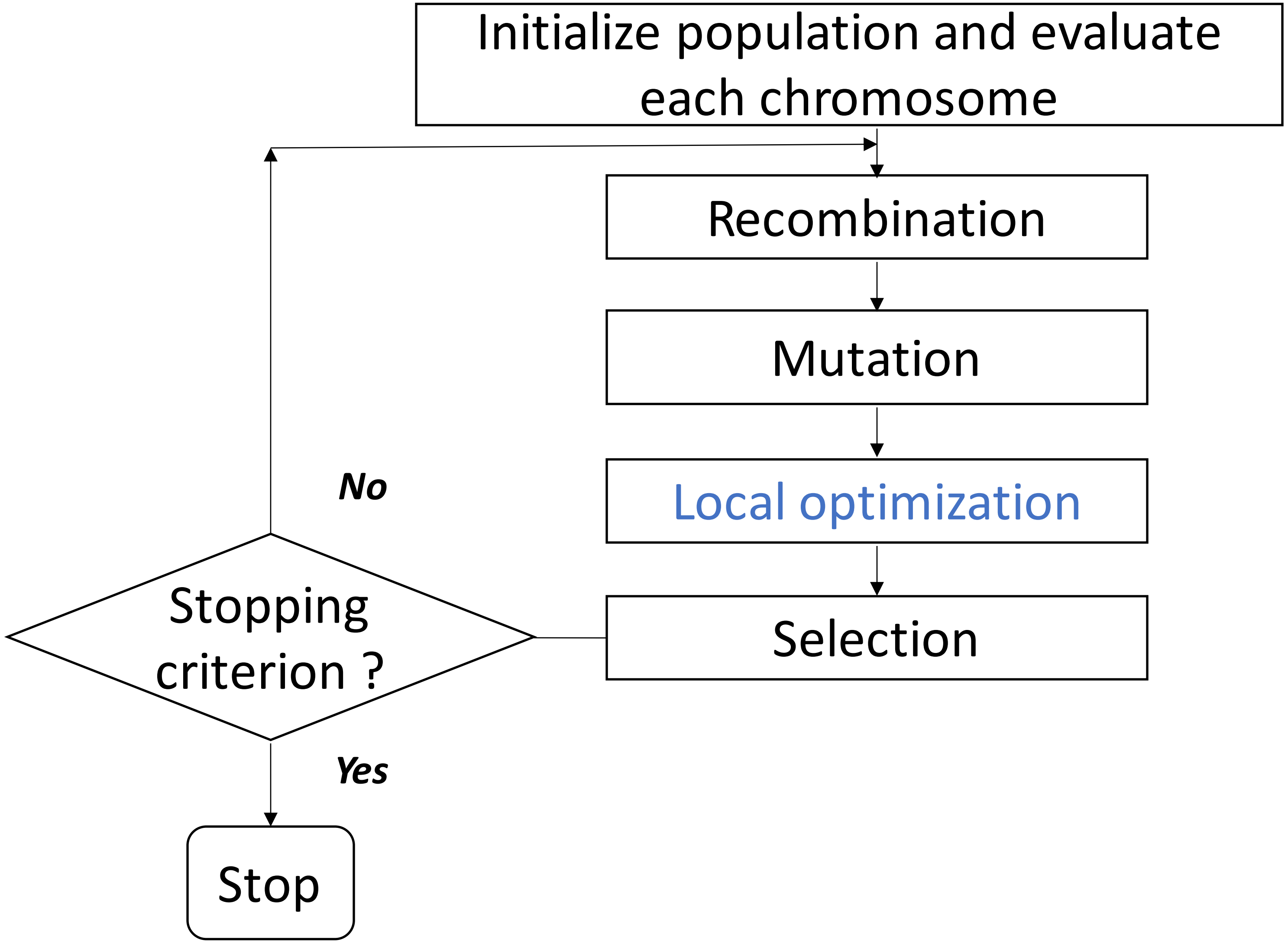
- Multiple minima problem,
- Factorization is not unique.

$$Q' = QR$$
$$\Psi' = R^{-1}\Psi(R^{-1})^T$$

Genetic Algorithm



Memetic Algorithm



Initialize population and evaluate each chromosome

Recombination

Mutation

Local optimization

Selection

Stopping criterion ?

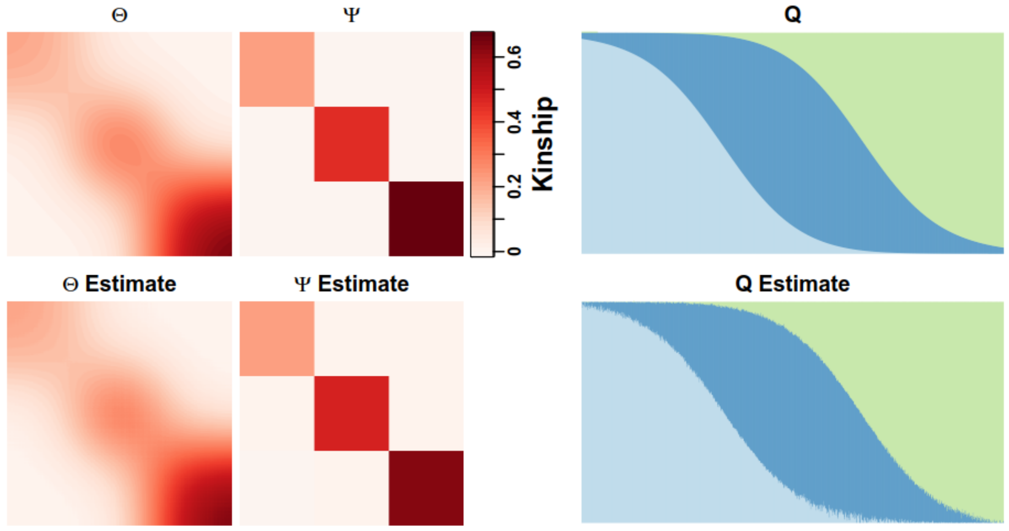
No

Yes

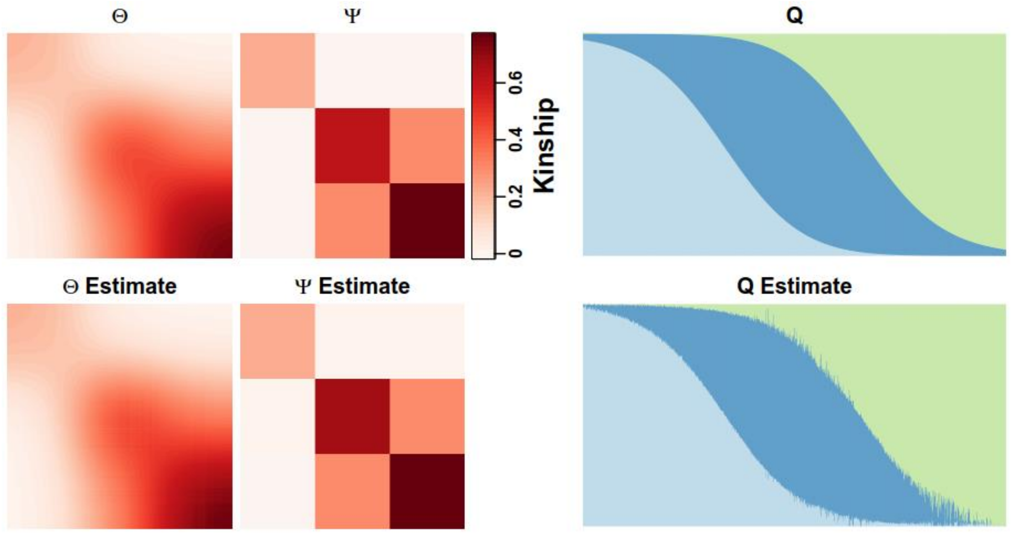
Stop

Memetic Algorithm

Independent ancestral populations

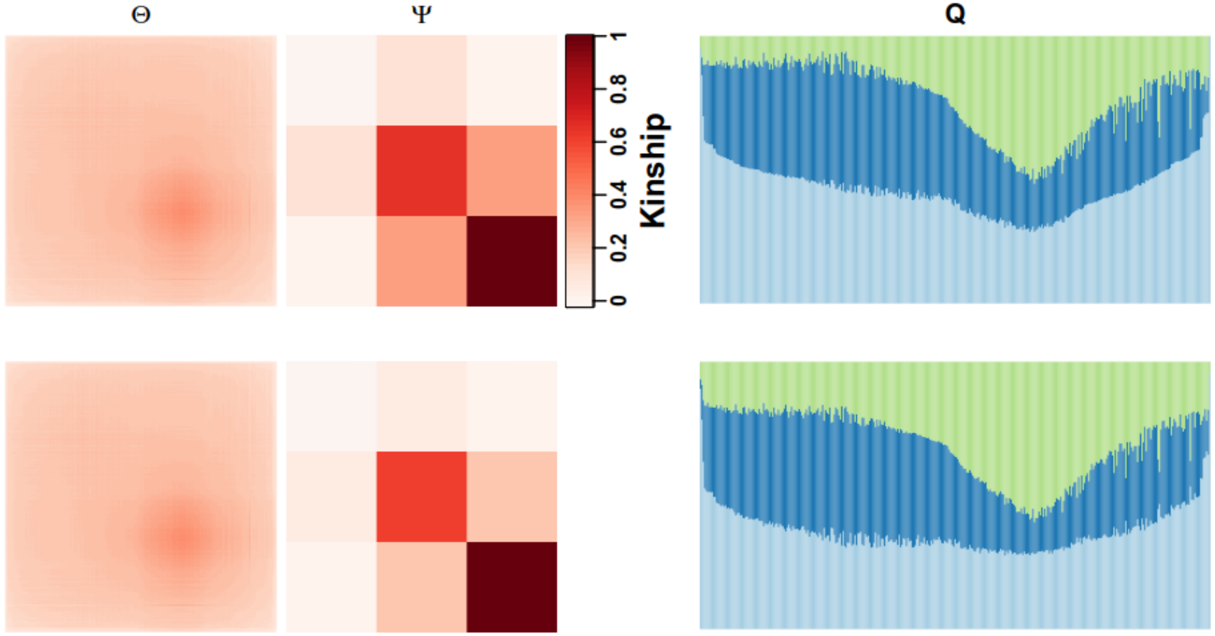


Correlated ancestral populations



- 1000 individuals,
- 100, 000 loci, and
- 3 subpopulations

Hispanic individuals in the 1000 Genomes Project



Admixture

Memetic Algorithm

6.7 million high-frequency SNPs

347 individuals

Conclusion and Next steps

- First likelihood free approach to jointly estimate admixture and kinship between ancestral subpopulations without bias.
- Estimated from a kinship matrix only.
- Not dependent on the number of loci, therefore run time is only dependent on the number of individuals and populations.

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