

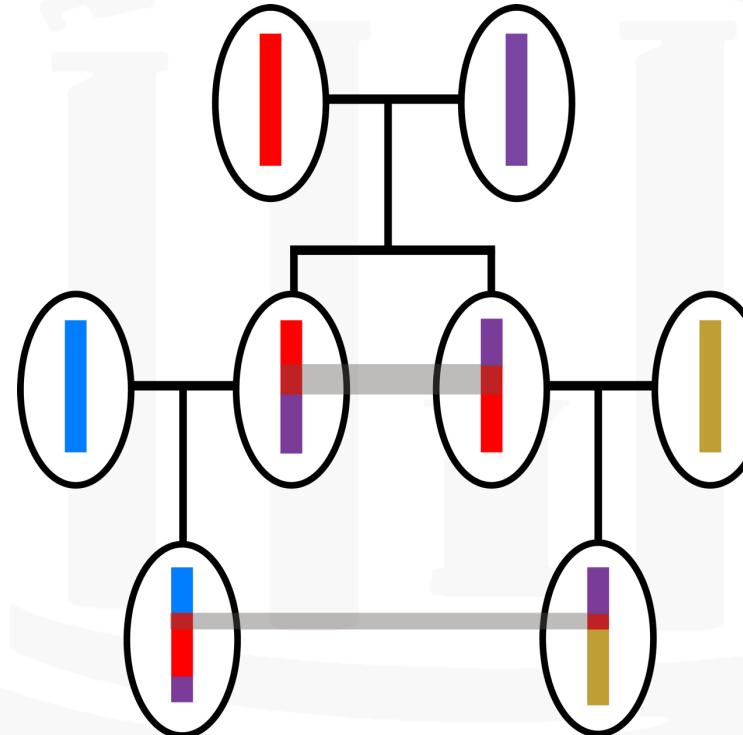
# **polyIBD: Inferring Identity by Descent in Complex, Polyclonal Infections**

Nicholas F. Brazeau,

Aimee R. Taylor, Steven R. Meshnick, Jonathan J. Juliano,  
Robert Verity

# Identity By Descent (IBD)

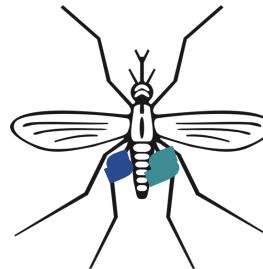
- Shared Segments
- Recombination
- Straightforward in simple scenarios



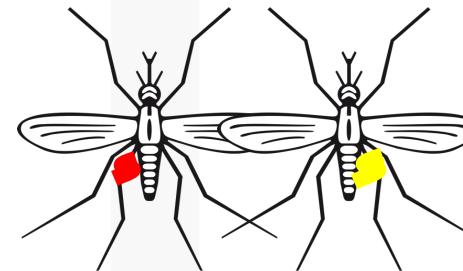
# Multiplicity of Infection (MOI)

aka Complexity of Infection

## Co-Transmission



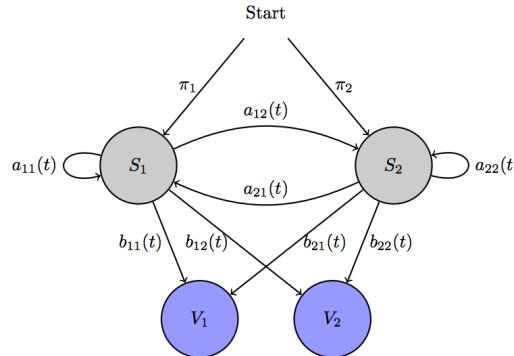
## Superinfection



Courtesy of OJ Watson

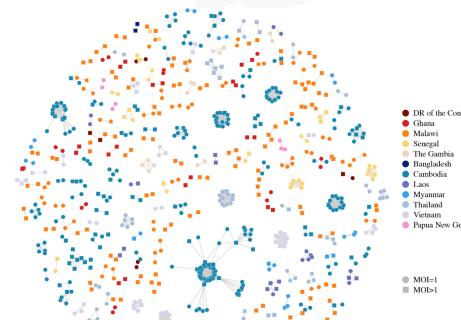
Wong W/Wirth D, Genome Med 2017  
Wong W/Wirth D, PLOS Bio 2018

# Hidden Markov Models for IBD



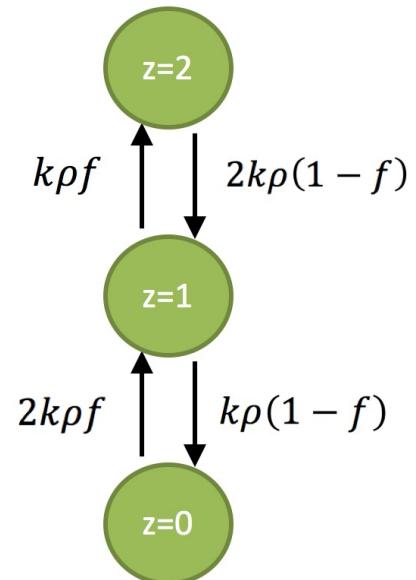
$$A(t) = \begin{pmatrix} 1 - \pi_2(1 - e^{-k\rho d_t}) & \pi_2(1 - e^{-k\rho d_t}) \\ \pi_1(1 - e^{-k\rho d_t}) & 1 - \pi_1(1 - e^{-k\rho d_t}) \end{pmatrix}$$

**hmmIBD**  
 Schaffner S & Taylor, A /Neafsey D,  
 Malar J, 2018



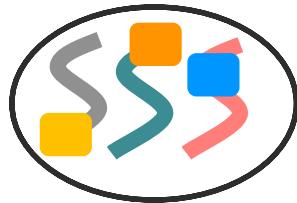
$$A = \begin{bmatrix} \omega_0 + \omega_1 e^{-\alpha t} & \omega_1(1 - e^{-\alpha t}) \\ \omega_0(1 - e^{-\alpha t}) & \omega_1 + \omega_0 e^{-\alpha t} \end{bmatrix}$$

**isoRelate**  
 Henden L/Bahlo M,  
 PLOS Gen, 2018

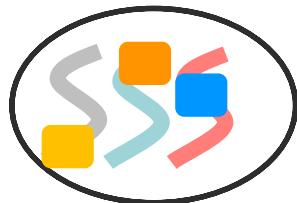


**polyIBD**  
 MCMC Multi-State HMM

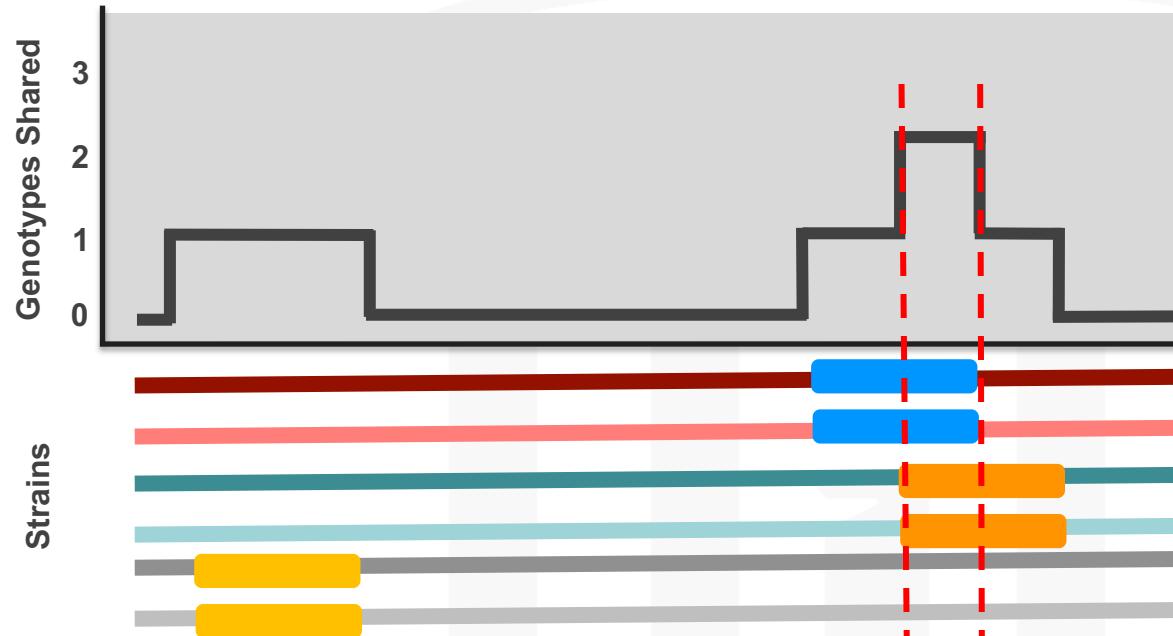
# polyIBD Model Framework



Sample 1



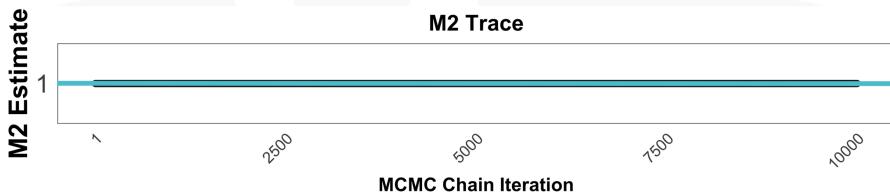
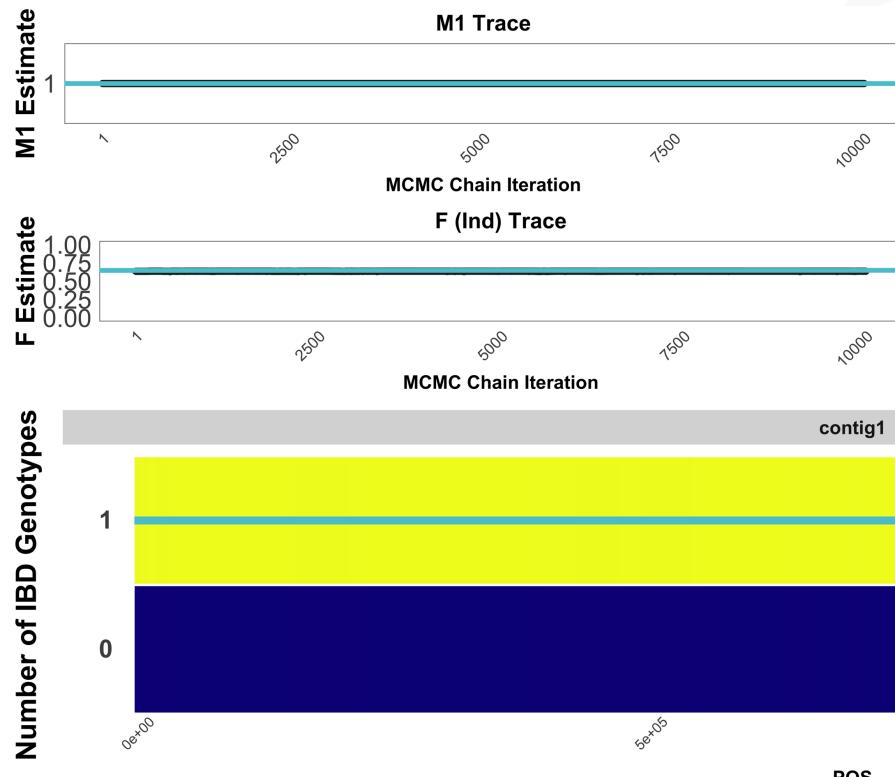
Sample 2



## Return Summary Statistics

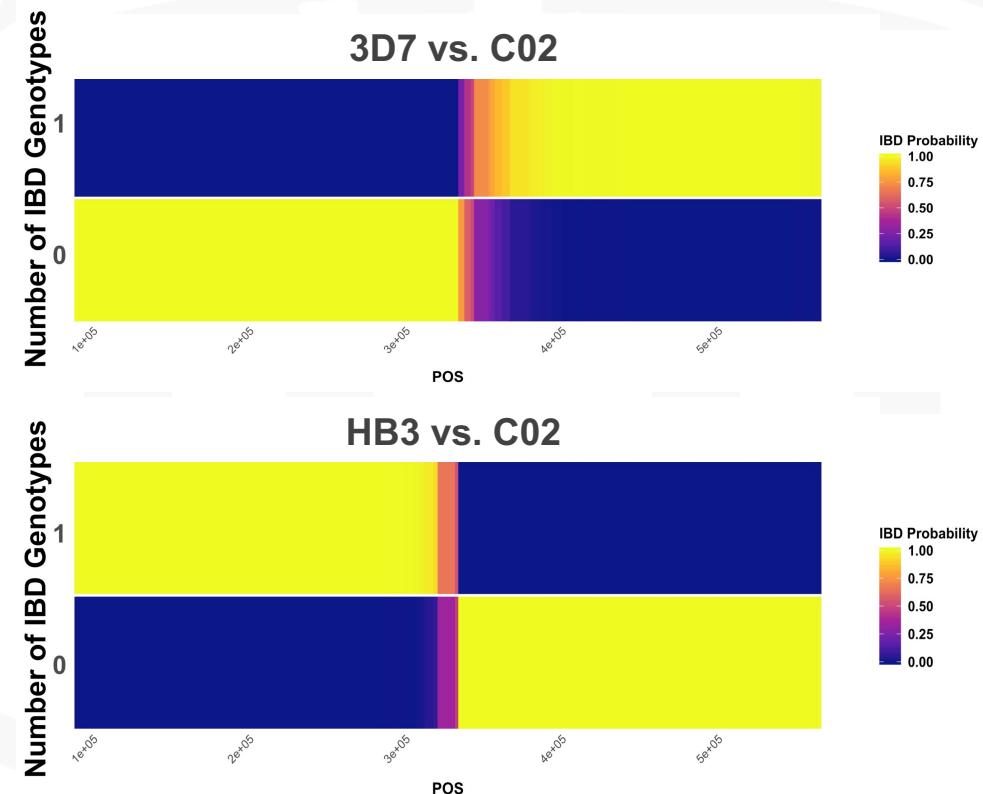
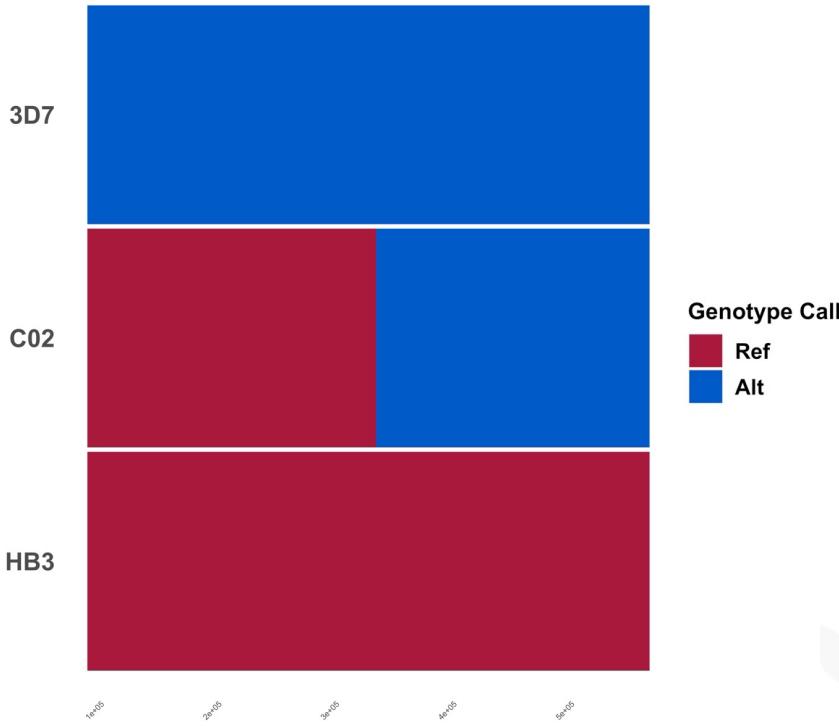
- MOI
- F-relatedness

# polyIBD Simulation

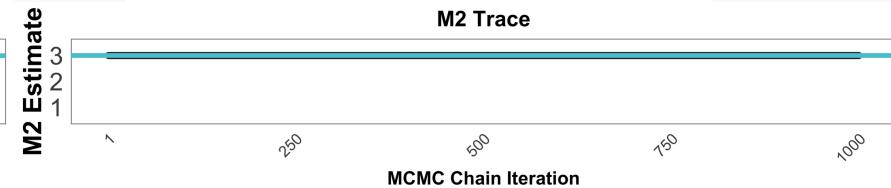
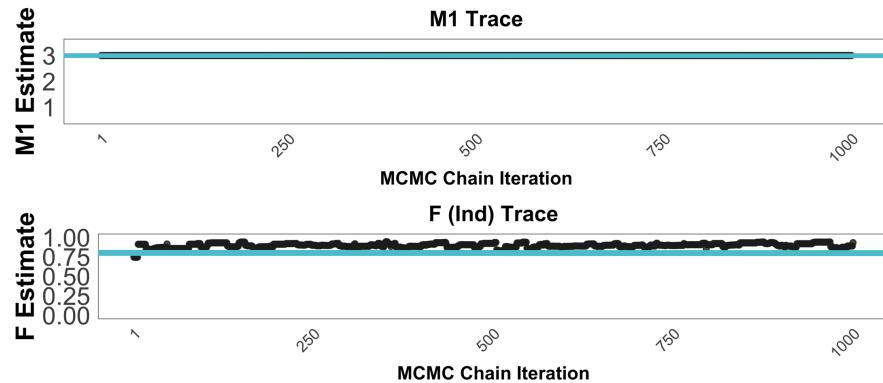


MOI Sample 1: 1  
MOI Sample 2: 1

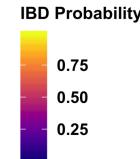
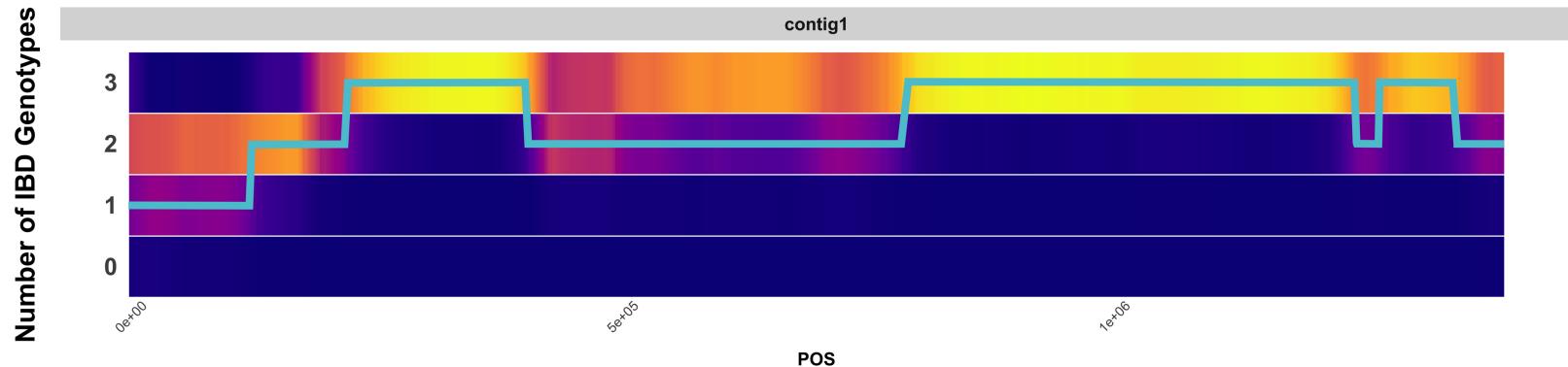
# polyIBD Validation – Pf Cross



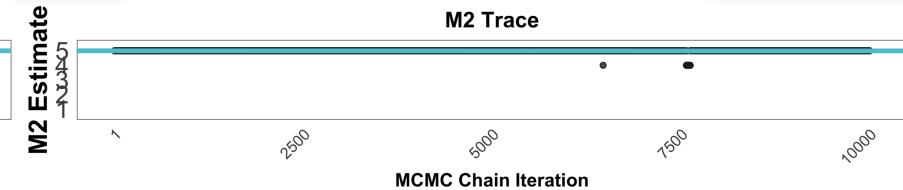
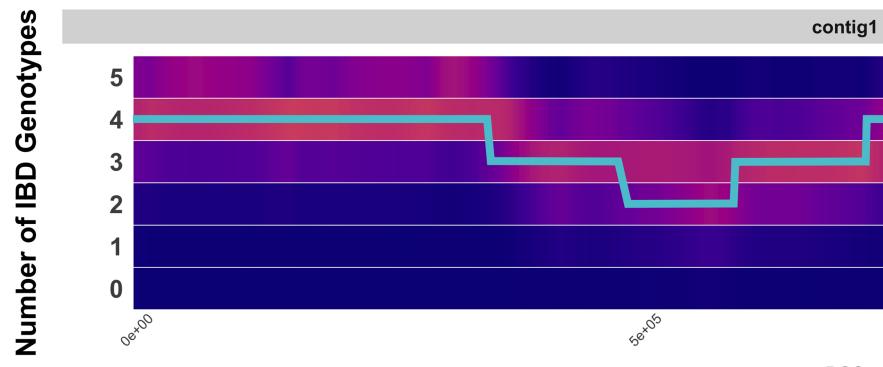
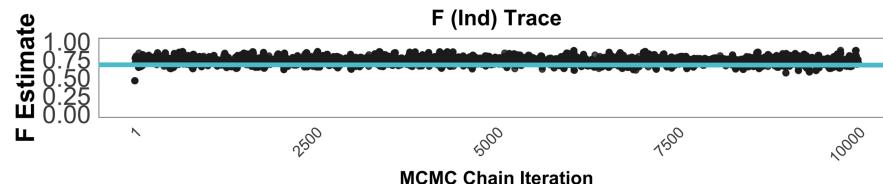
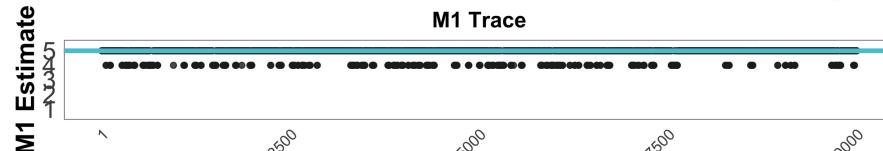
# polyIBD Simulation



MOI Sample 1: 3  
MOI Sample 2: 3

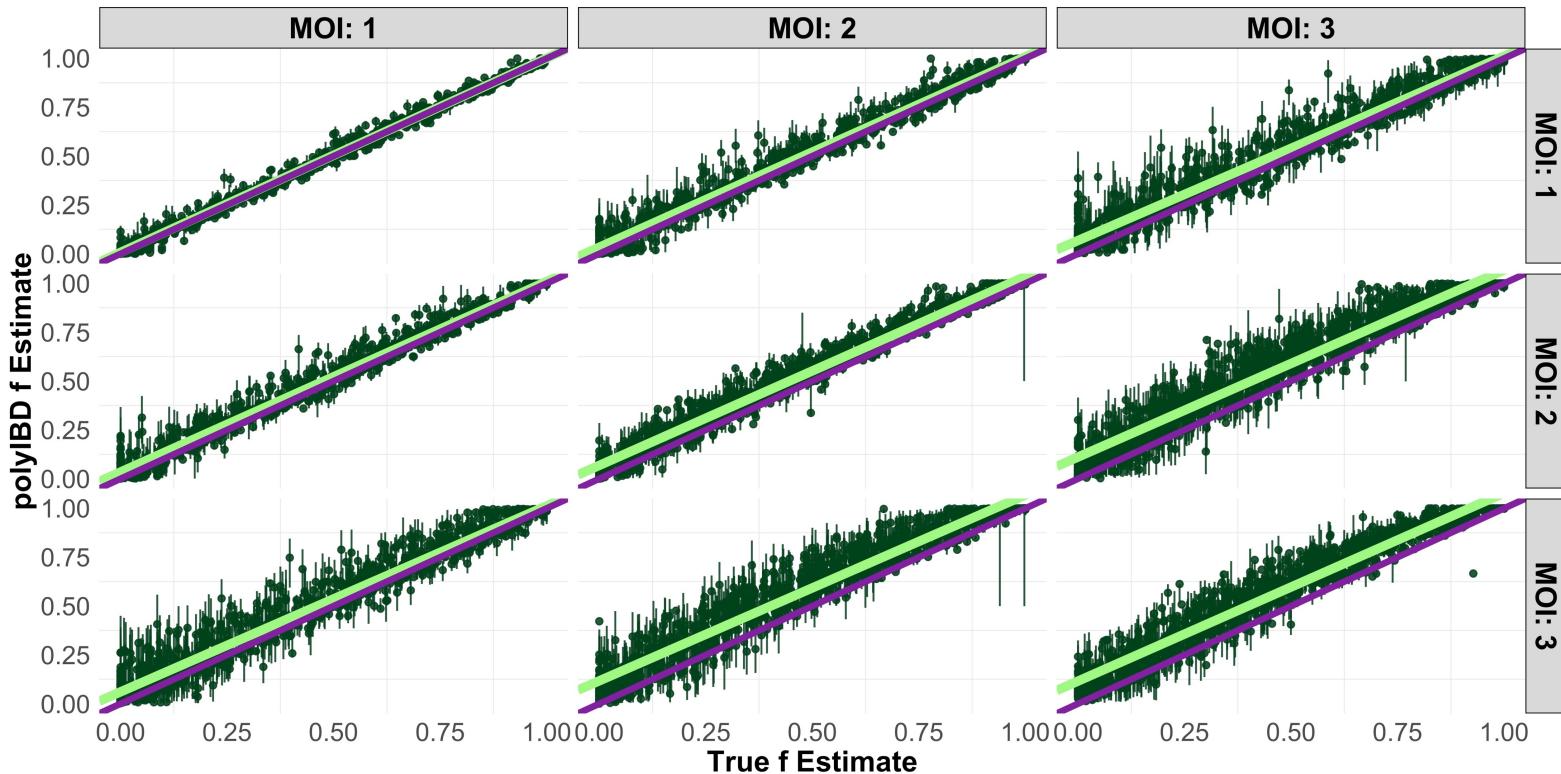


# polyIBD Simulation

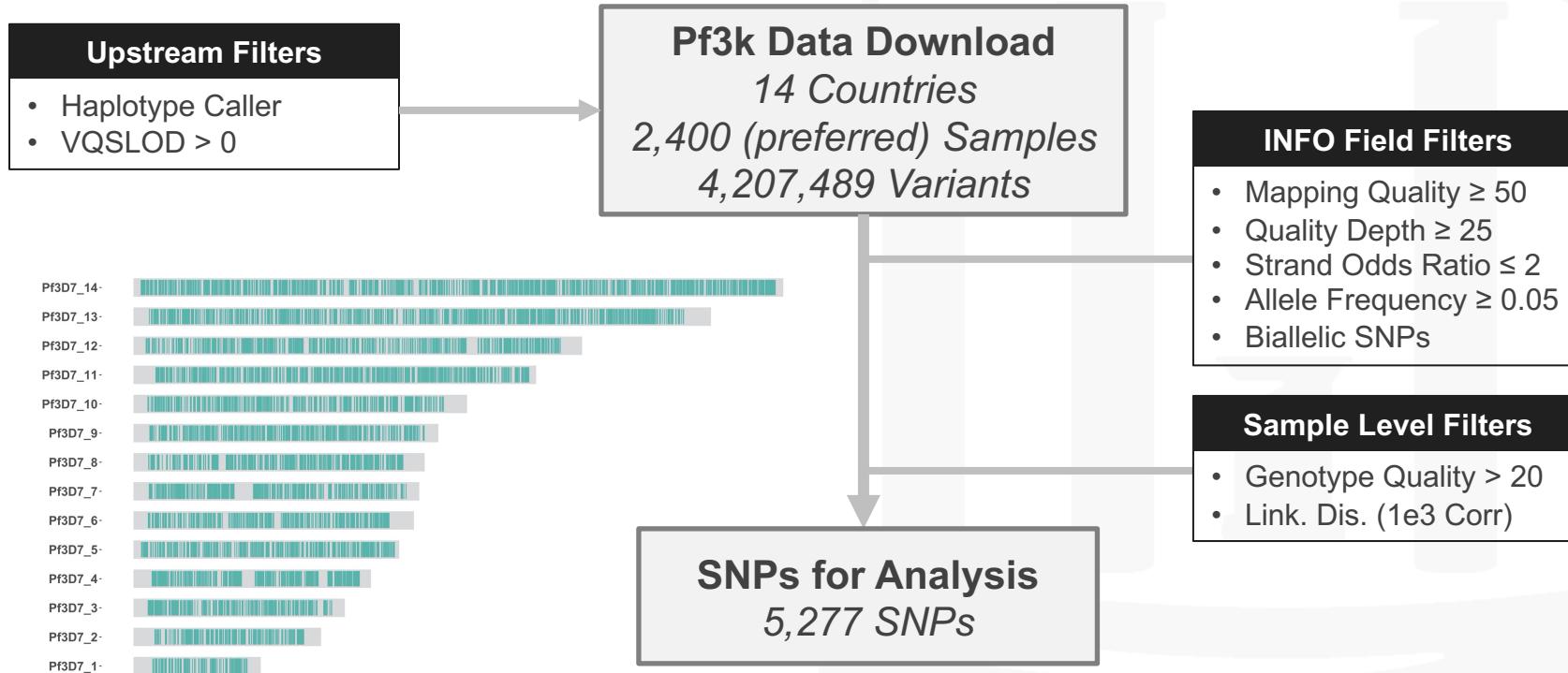


MOI Sample 1: 5  
MOI Sample 2: 5

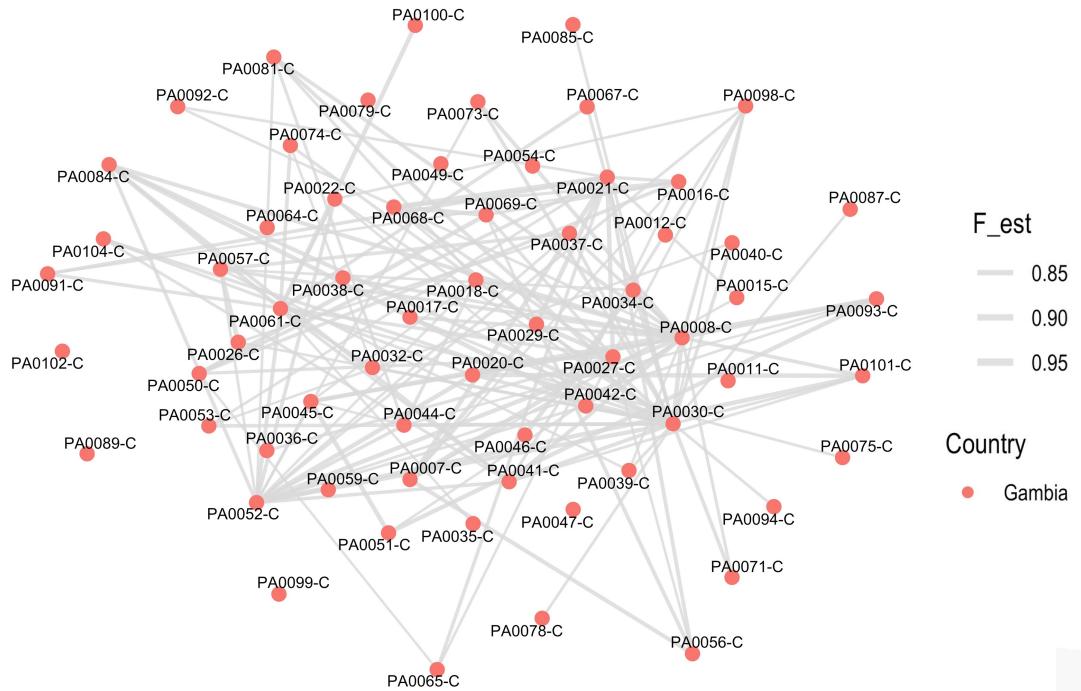
# polyIBD Power for “f”



# polyIBD Pf3k Filters



# polyIBD Pf3k Preliminary



- High degree of sharing
  - Preliminary run

# polyIBD Under Development

- Power/Lower-limit of Detection
  - » SNPs needed to infer relatedness (K-generations)
- Within sample heterozygosity ( $F_{ws}$ )

# Acknowledgements



Imperial College  
London



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- Alison Regan

UNC MD-PhD Program

Harvard T.  
Chan School of  
Public Health

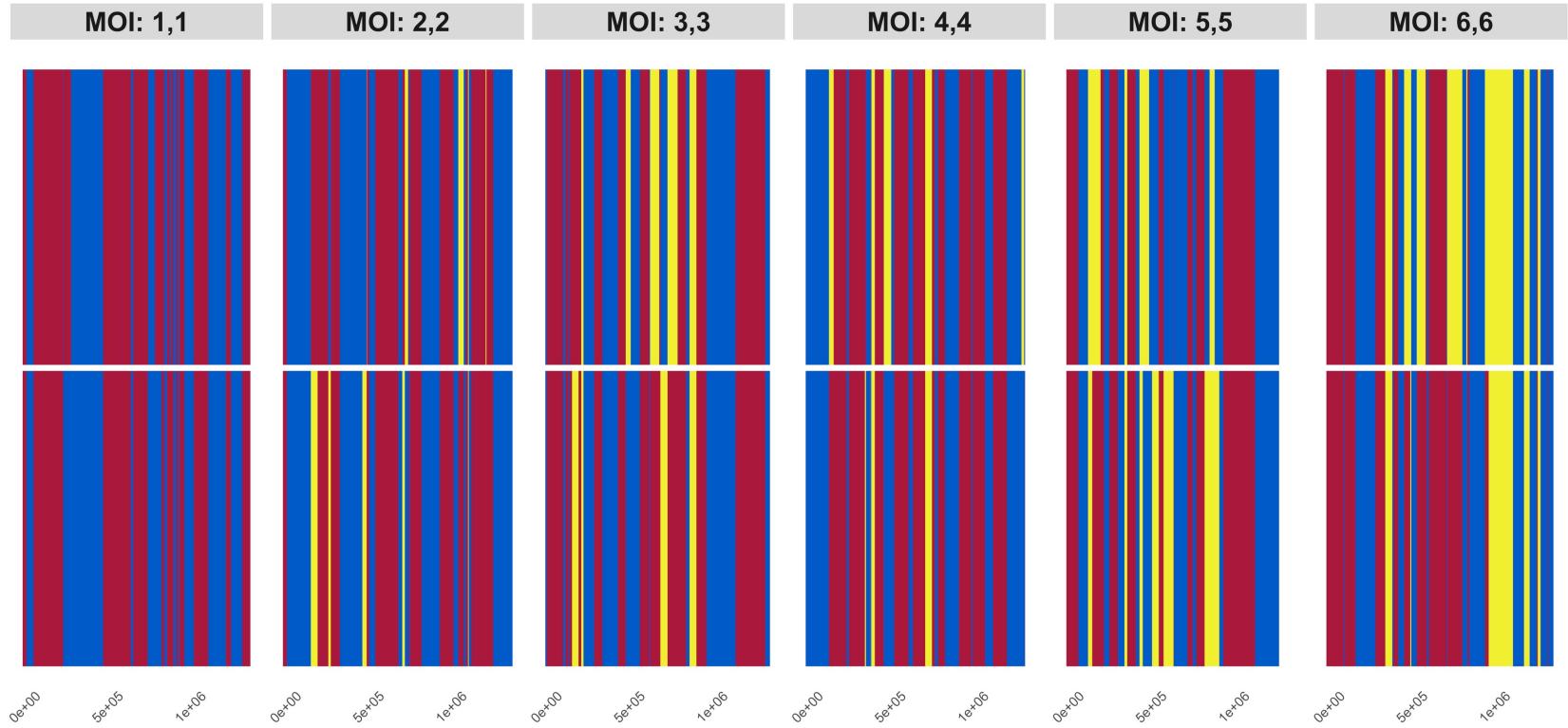
Our thanks to the MalariaGEN Consortium for data generated by the Pf3k  
and Pf Cross Project

# Questions?

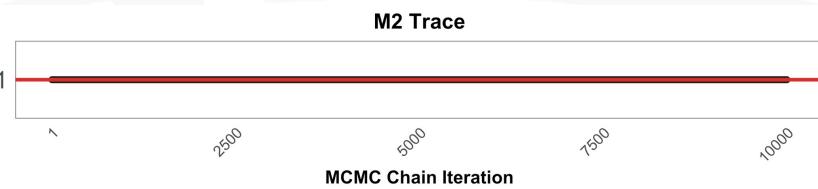
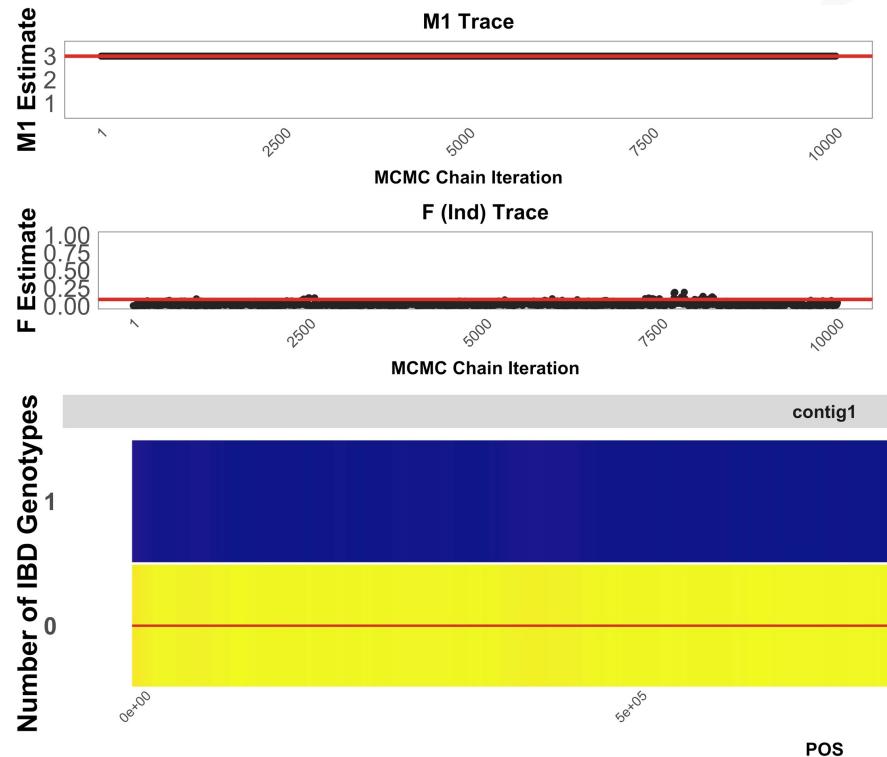
# polyIBD Use Case

- Simulations for SNP density
- MOI > 2 to infer relatedness
- Sparse WGS data with low coverage (proportions unreliable)

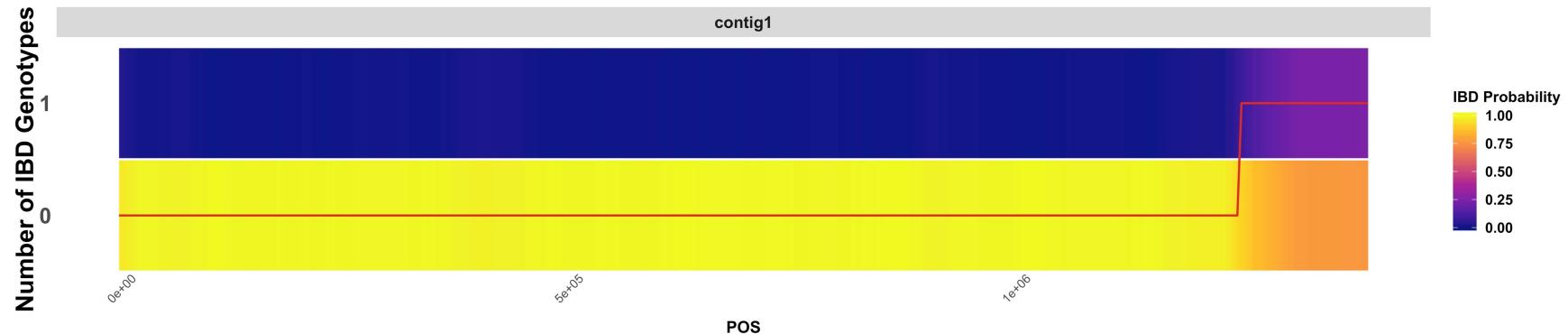
# Identifying Regions of IBD



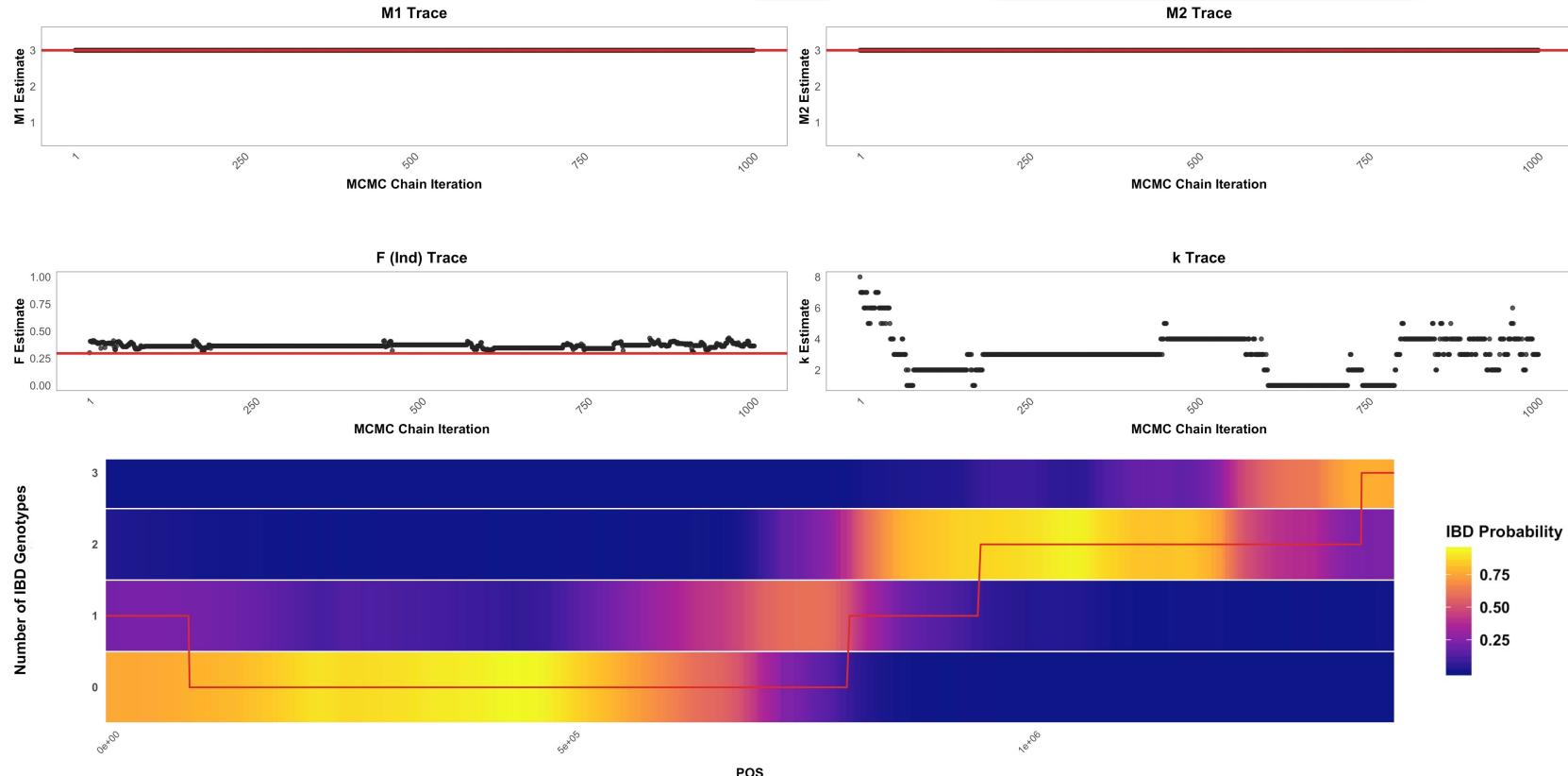
# polyIBD Simulation



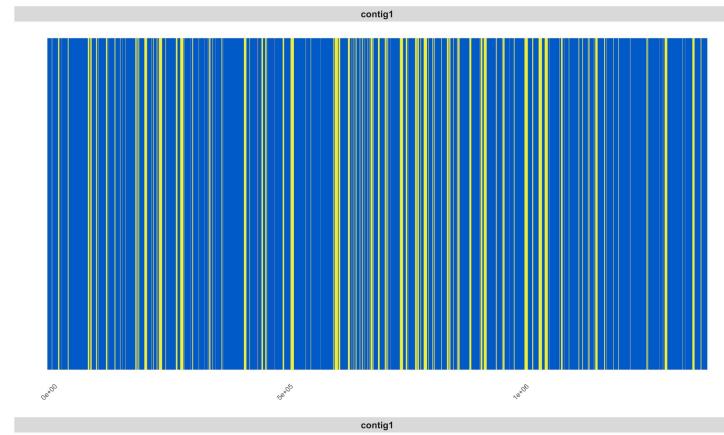
MOI Sample 1: 3  
MOI Sample 2: 1



# polyIBD Simulation -- MOIs of 3



# polyIBD Simulation



Support

- Concord
- Discord
- Het

