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A more effective multiplicity of infection: incorporating within-host relatedness and genotyping error to obtain more accurate estimates of plasmodium within-host diversity and population allele frequencies

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Contact Information

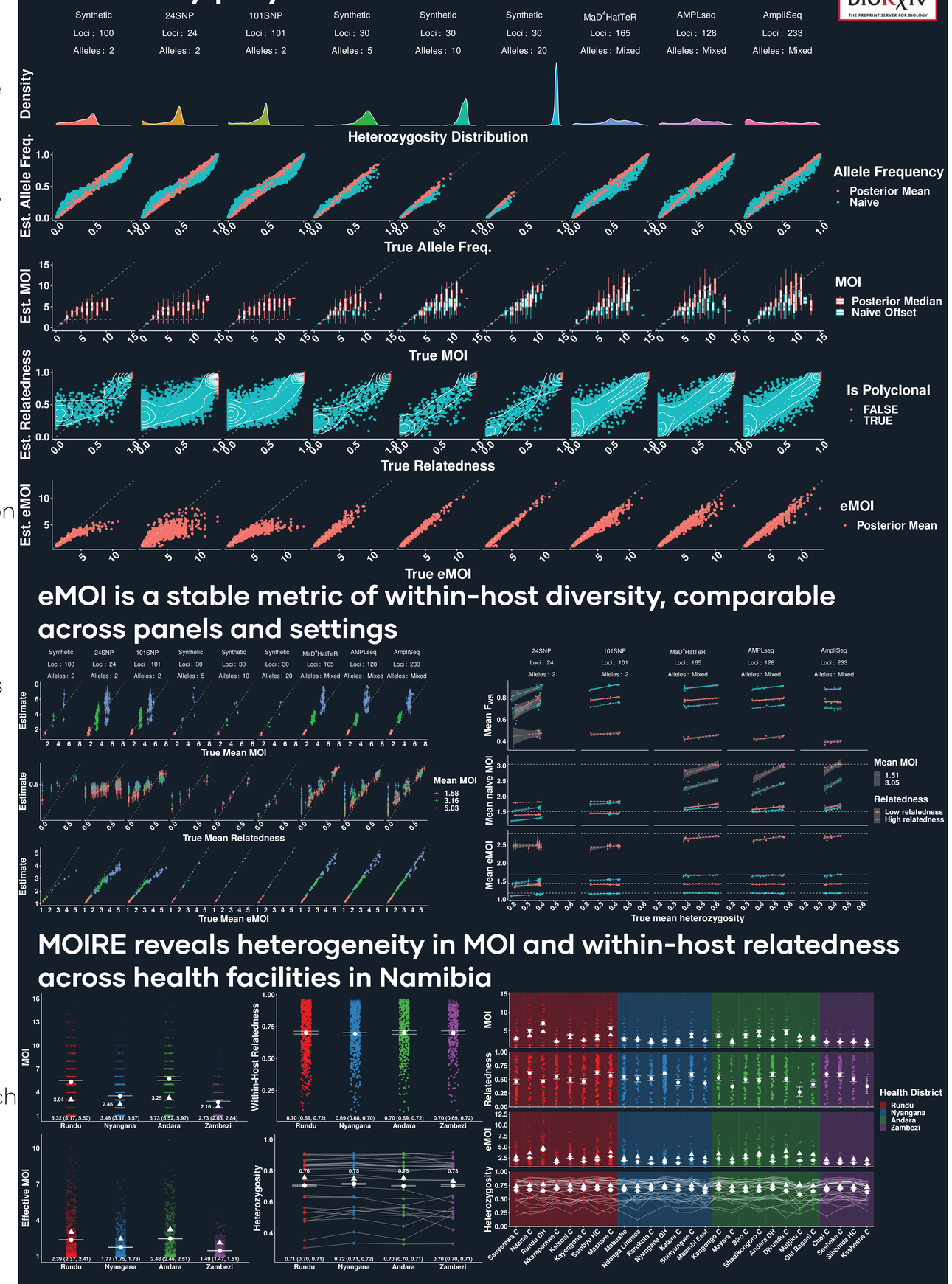
Motivation

- Malaria parasite genetic data can provide insight into parasite phenotypes, evolution, and transmission
- Estimating allele frequencies, multiplicity of infection (MOI), within-host relatedness is challenging, particularly in the presence of multiple related coinfecting strains
- Available methods often rely on SNPs and do not account for within-host relatedness

Methods

- Developed Bayesian approach (MOIRE) to **simultaneously estimate allele frequencies, MOI, and within-host relatedness** from noisy polyallelic data
- Method is flexible, **accomodating both polyallelic and SNP data**, making the method adaptable to diverse genotyping panels
- Identified new metric of within-host diversity, the **effective MOI (eMOI)**, which integrates sample MOI and within-host relatedness
- Implemented in R, available as an easy to install package at github.com/eppicenter/moire

MOIRE simultaneously recovers population allele frequencies, MOI and within-host relatedness from noisy polyallelic data



eMOI is a stable metric of within-host diversity, comparable across panels and settings

MOIRE reveals heterogeneity in MOI and within-host relatedness across health facilities in Namibia

Simulations

- Simulated data from synthetic as well as real world genotyping panels (SNP and microhaplotype based) to explore the potential performance of MOIRE
- Data was simulated with moderate levels of genotyping error, varying levels of within-host relatedness, and low, moderate, and high levels of mean MOI
- Data also simulated from different genetic backgrounds with identical MOI and within-host relatedness to explore impact of genotyping panel on metrics

Results

- MOIRE **accurately recovered allele frequencies** compared to naive empirical estimation that over estimates rare alleles and underestimates common alleles
- Diverse panels greatly improved the resolving power of MOIRE, allowing for **accurate estimation of MOI up to 7 strains**, as well as **accurately recovering within-host relatedness** at all levels
- **eMOI was recovered with high accuracy** under all conditions using polyallelic panels, and still performed well up to an eMOI of 4 when using SNP based panels
- eMOI as a metric of within-host diversity is **sensitive to shifting transmission dynamics** yet **insensitive to genotyping panel used**
- Application to data from Namibia reveals **heterogeneity in MOI and within-host relatedness**, suggesting **detectable differences in transmission** dynamics

Availability

moire

resources.eppicenter

eppicenter.github.io/moire

links.maxmurphy.dev/astmh2023

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