A possible way to identifying mixed infected samples

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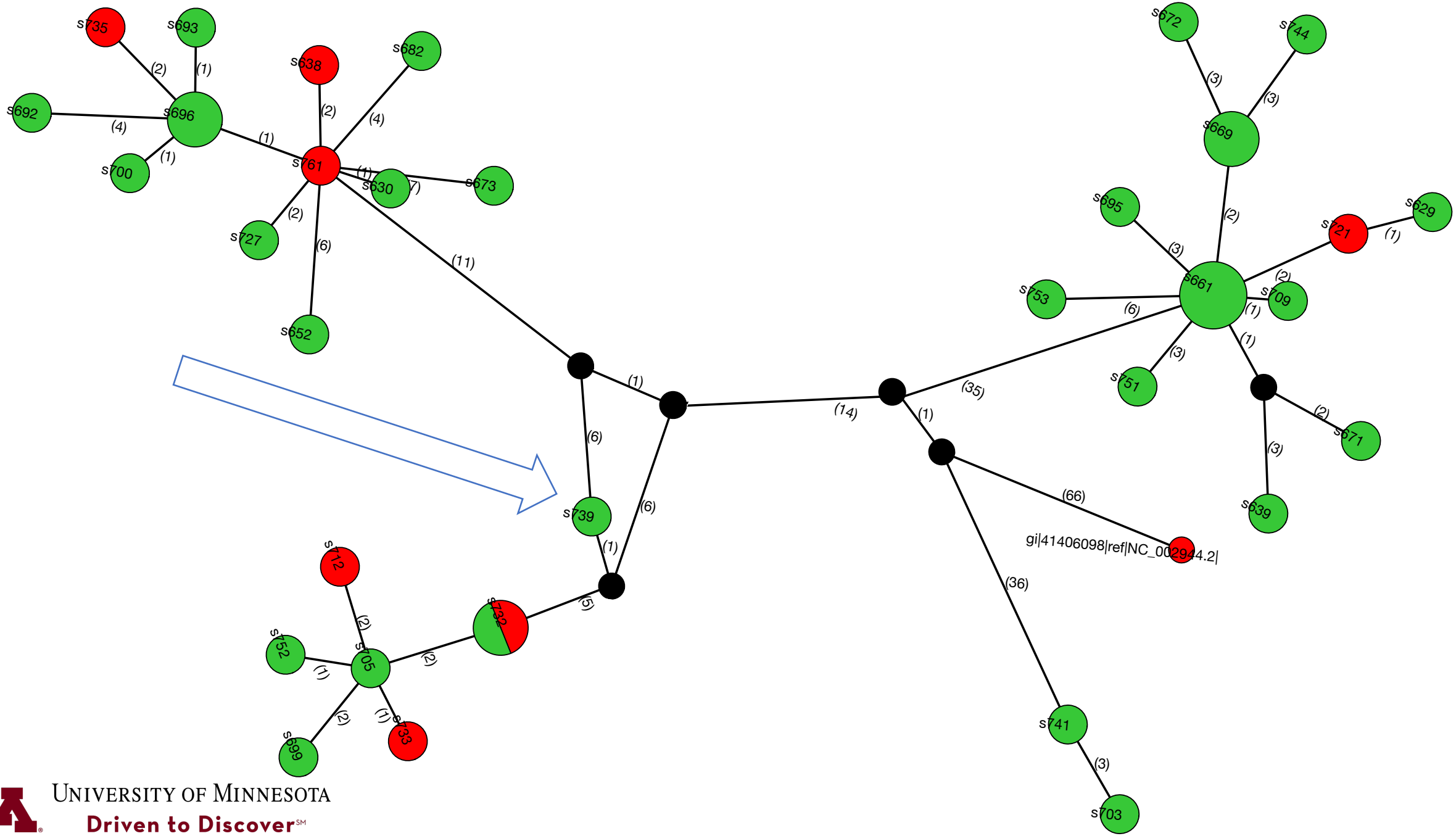
1. Multiple infections need to be identified

- Why do we care about multiple infections?
  - No recognition of mixture sample will result in wrong phylogenetic trees
  - Multiple infected individuals associated increased transmission intensity in the local environment. (Manske M, Miotto O, et al., 2012). Identifying those individuals maybe crucial to disease control.



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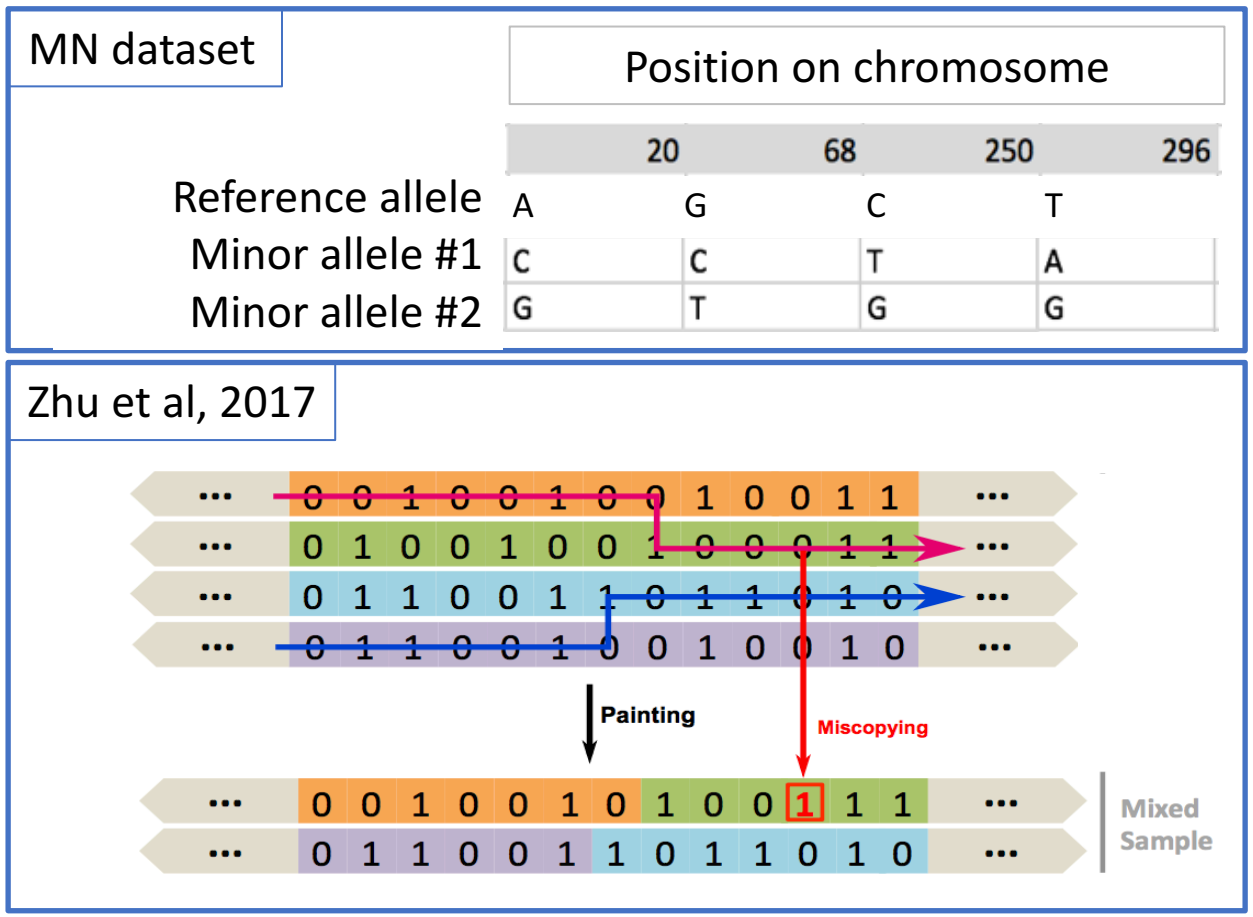
2. Definitions of multiple infections

- From WGS data, how to tell if the animal has multiple infection?
  1) [Biology]
     Heterozygous loci:
     - when a loci that has multiple alternative alleles. (not suitable for single-colony isolates)
  2) [Transmission]
     Patterns/Haplotypes:
     - when a sequence (sample) shares haplotypes/ evolutionary path with other sequences.

MN dataset

	Position on chromosome			
	20	68	250	296
Reference allele	A	G	C	T
Minor allele #1	C	C	T	A
Minor allele #2	G	T	G	G



3. A quick way to screening for mixture samples using allele frequency plots

RESEARCH ARTICLE

Inferring Strain Mixture within Clinical *Plasmodium falciparum* Isolates from Genomic Sequence Data

John D. O'Brien[1]*, Zamin Iqbal[2], Jason Wendler[3], Lucas Amenga-Etego[2,4]

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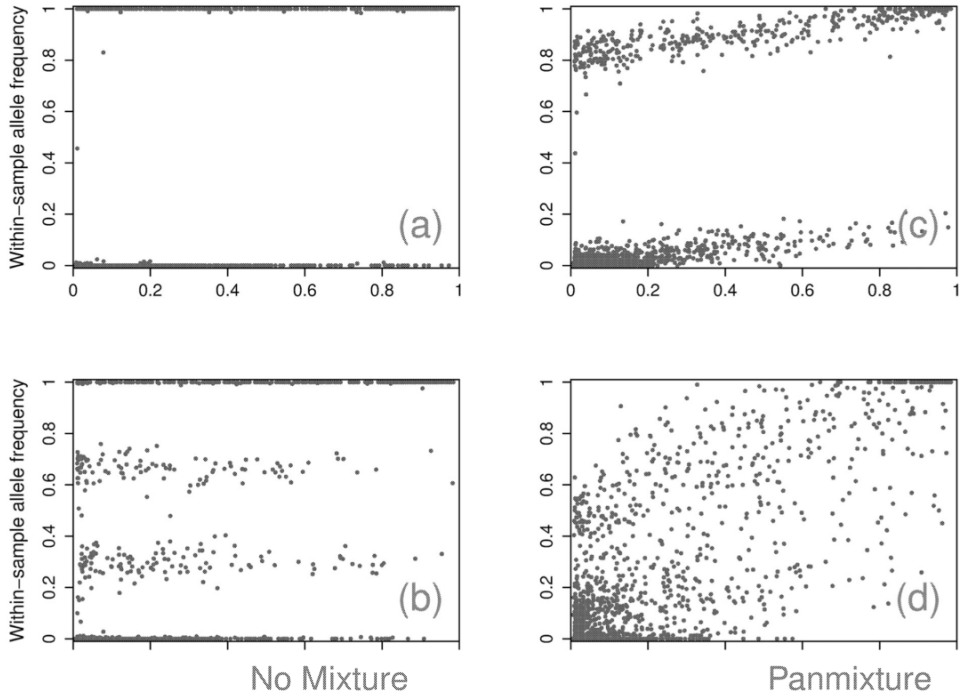
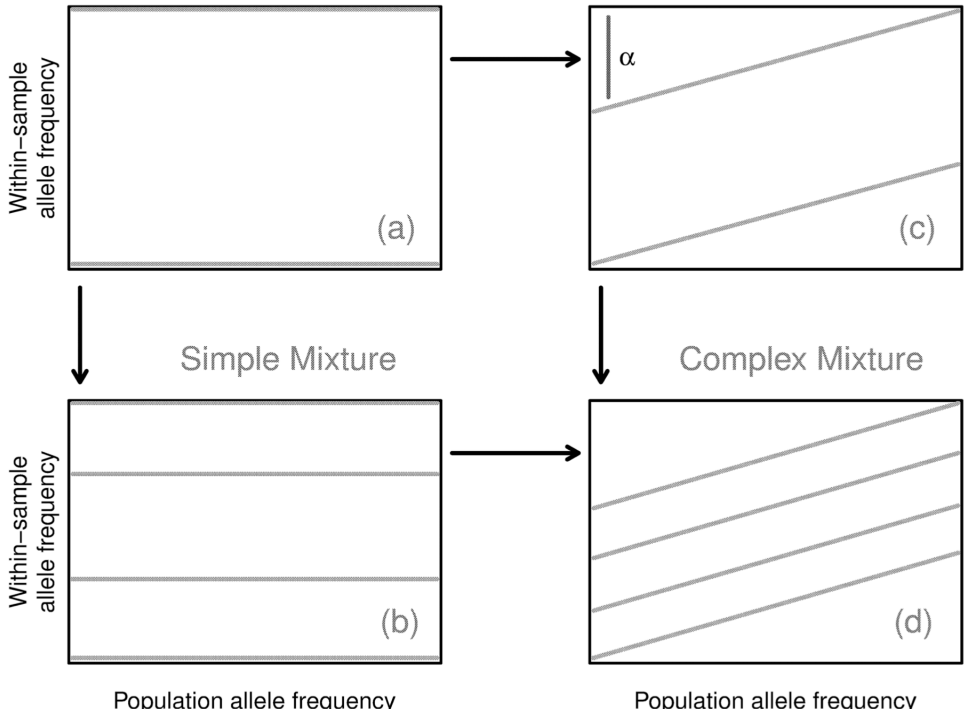
PLOS COMPUTATIONAL BIOLOGY





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$$\mathbb{P}(\mathcal{Q},\mathcal{P},\mathcal{W},\alpha,v,K|\mathcal{D}_i) \propto \mathbb{P}(\mathcal{D}_i|\mathcal{Q},\mathcal{P},v,K)\cdot\mathbb{P}(\mathcal{Q}|\mathcal{P},v,K,\mathcal{W},\alpha)\cdot \mathbb{P}(\mathcal{P})\cdot\mathbb{P}(v)\cdot\mathbb{P}(\mathcal{W}|K)\cdot\mathbb{P}(K)\cdot\mathbb{P}(\alpha).$$

Table 1. Parameters and definitions for the model and its description.

Parameter	Definition
N	Number of samples
M	Number of SNPs
K	Number of strains
$i = 1, \cdots, N$	Index for samples
$j = 1, \cdots, M$	Index for SNPs
$r = 1, \cdots 2^K$	Index for bands / strain mixtures
p_j	(Non-reference) allele frequency for SNP j
$\mathcal{P} = [p_j]$	The PLAF for all SNPs
$\mathcal{Q} = [q_{ij}]$	Within-sample allele frequency for SNP j in sample i
α	Degree of panmixia within a sample, panmixia coefficient
$\mathcal{S} = [s_1, \cdots, s_K]$	Strains in a sample
$\mathcal{W} = [w_1, \cdots, w_K]$	Strain proportions in a sample
λ_r	Band proportions within sample
v	Variation parameter for Beta-binomial
WSAF	Within-sample allele frequency
PLAF	Population-level allele frequency

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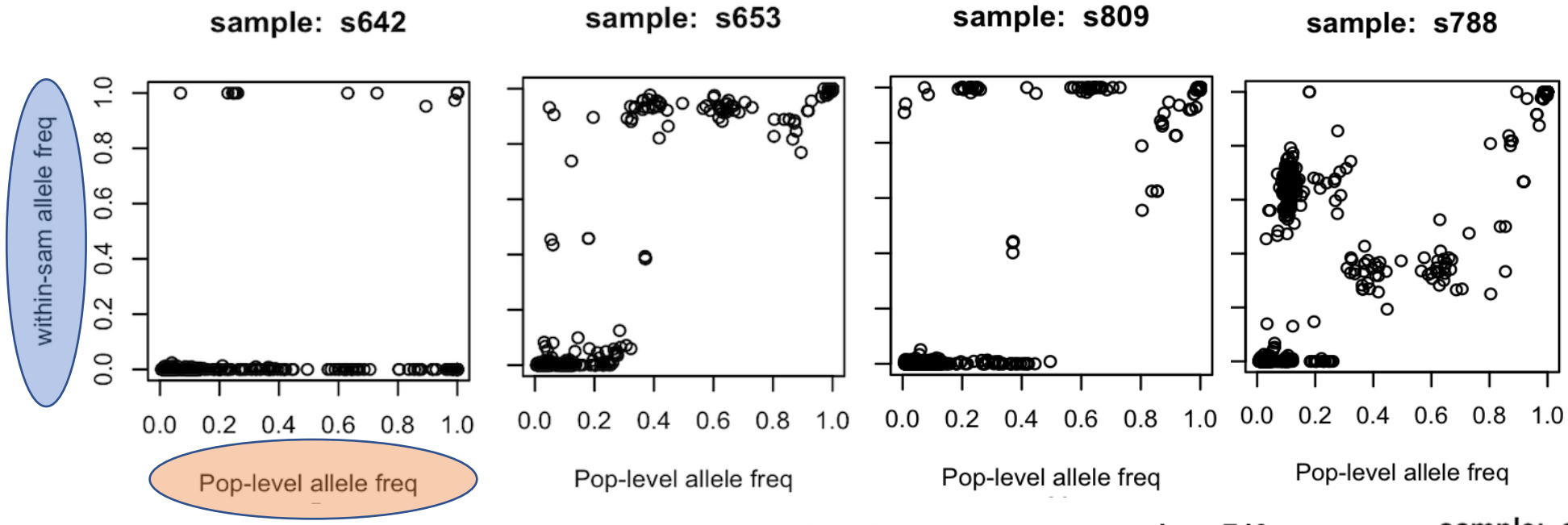
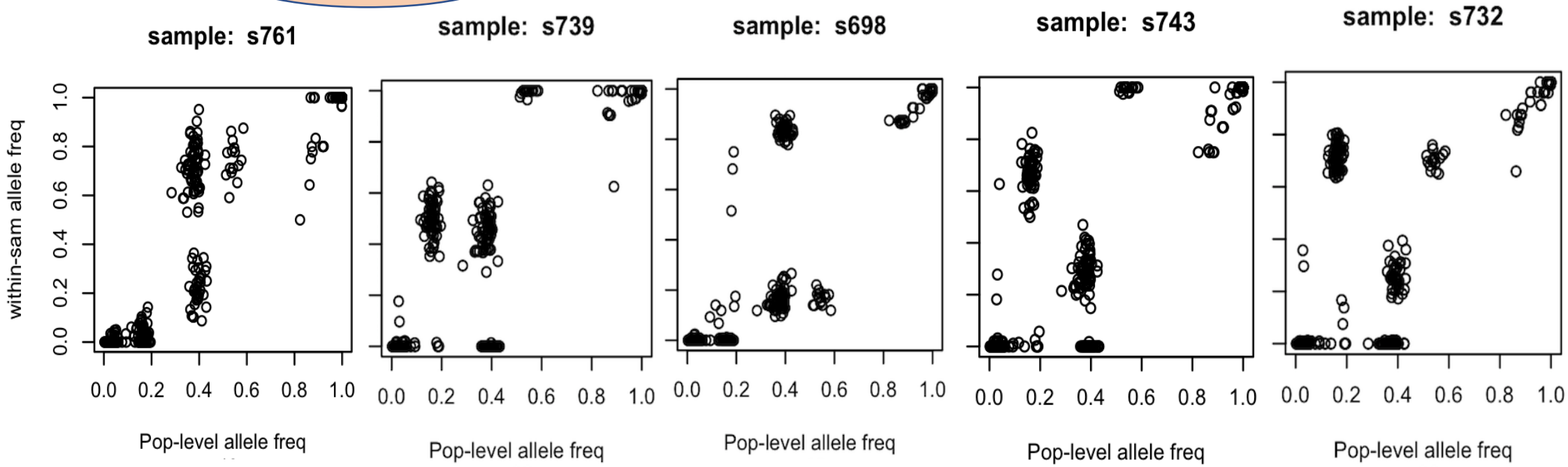

sample: s642
sample: s653
sample: s809
sample: s788
within-sam allele freq
Pop-level allele freq
0.0
0.2
0.4
0.6
0.8
1.0

S farm


sample: s761
sample: s739
sample: s698
sample: s743
sample: s732
within-sam allele freq
Pop-level allele freq
0.0
0.2
0.4
0.6
0.8
1.0

Q farm