

# Deviation from HWE

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GE02: day 1 part 4

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# Overview

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- Genotyping error
- Wahlund's effect
- Inbreeding

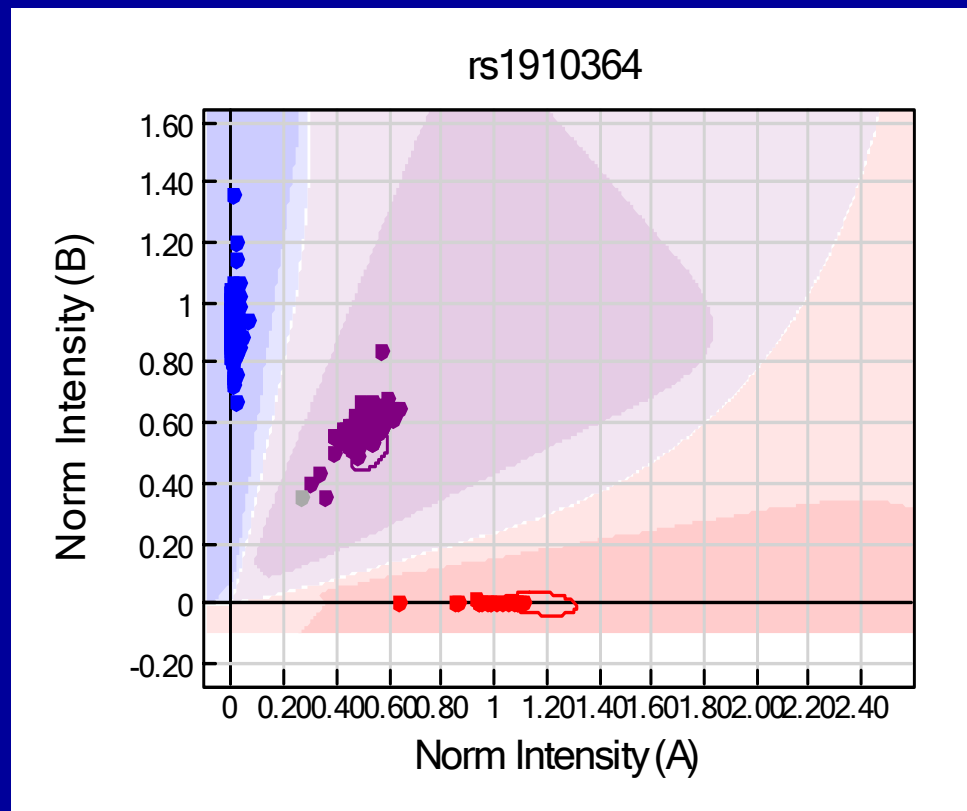
# Why HWE may be violated?

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- **Genotyping or calling error**
- Samples come from different populations
- Non-random mating (e.g. inbreeding)
- Selection
- Mutation

# Genotyping

- Single Nucleotide Polymorphisms (SNPs)
- Two alleles, e.g. A/G, or T/C, etc
- Blue and Red probes marking the alleles



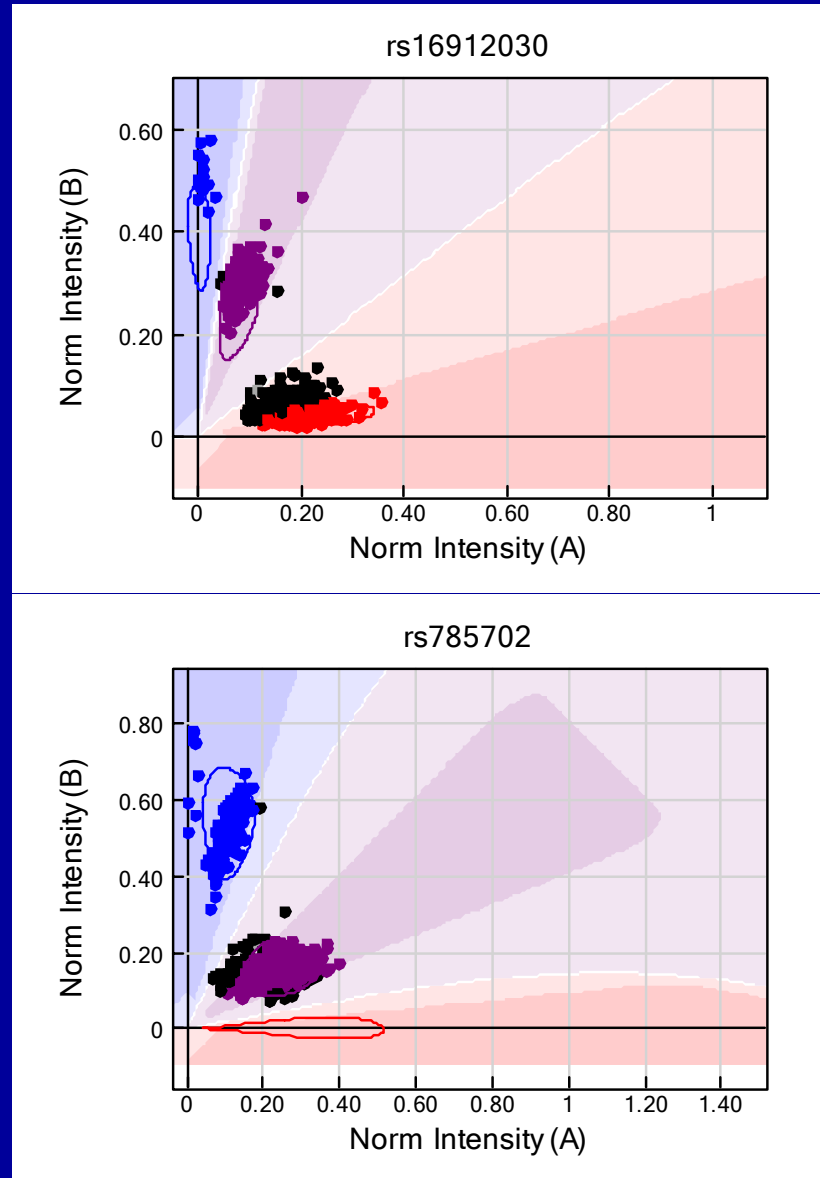
# Genotyping errors

## Differential calling

- Percent of “no-calls” (missing) depends on the genotype

## Classification errors

- Genotypes are called wrongly



# Problem

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- A/G polymorphism with  $q = P(G) = 0.15$
- SNP is in HWE
- 40% of "AA" are NOT called
- What will be genotypic distribution?

# Solution

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- $P(A) = 1 - P(G) = 0.85$
- Under HWE
  - $P(GG) \sim 0.02$
  - $P(AG) \sim 0.26$
  - $P(AA) \sim 0.72$
- Total proportion called
  - $1 - P(\text{not called}) = 1 - 0.4 \times 0.72 = 0.71$
- Among these:
  - $P(GG \text{ among called}) = 0.02/0.71 \sim 0.03$
  - $P(AG \text{ among called}) = 0.26/0.71 \sim 0.36$
  - $P(AA \text{ among called}) = 0.6 \times 0.72/0.71 \sim 0.61$

# Mixture of populations (Whalund's effect)

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- Study sample
  - 50% are Europeans with allele frequency 0.2
  - 50% are Japanese with allele frequency 0.9
- Both populations are in HWE
  
- Question:
  - What will be genotypic distribution in the mixed population?
  - What would be expected under HWE?



# Solutions: Wahlund's effect

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	AA	Aa	aa
Pop1	0.64	0.32	0.04
Pop2	0.01	0.18	0.81
1:1 Mixture	0.325	0.25	0.425

- In mixed population
  - $P(a) = 0.425 + 0.25/2 = 0.55$
- Expected under HWE:

	AA	Aa	aa
Expected	0.20	0.50	0.30

- Mixture usually leads to heterozygote deficiency

# Inbreeding

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- **Inbreeding** is breeding between relatives
  - Limited population size
  - Biological reasons (e.g. self-pollination)
  - Cultural reasons (e.g. systematic marriages to cousins)
- A genotype is called **autozygous** (or homozygous by descent) if it contains two alleles, which are copies of exactly the same ancestral allele
- **Coefficient of inbreeding**,  $F$ , is probability that a genotype is autozygous

# Inbreeding leads to deviation from HWE

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Inbreeding  $\Rightarrow$

Autozygosity (identity-by-descent)  $\Rightarrow$

Excess homozygosity (identity-by-state)

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	Genotype		
	AA	Aa	aa
No inbreeding	$p^2$	$2pq$	$q^2$
Inbreeding	$p^2 + pqF$	$2pq(1-F)$	$q^2 + pqF$

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