

QTL mapping in humans

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Linkage vs association

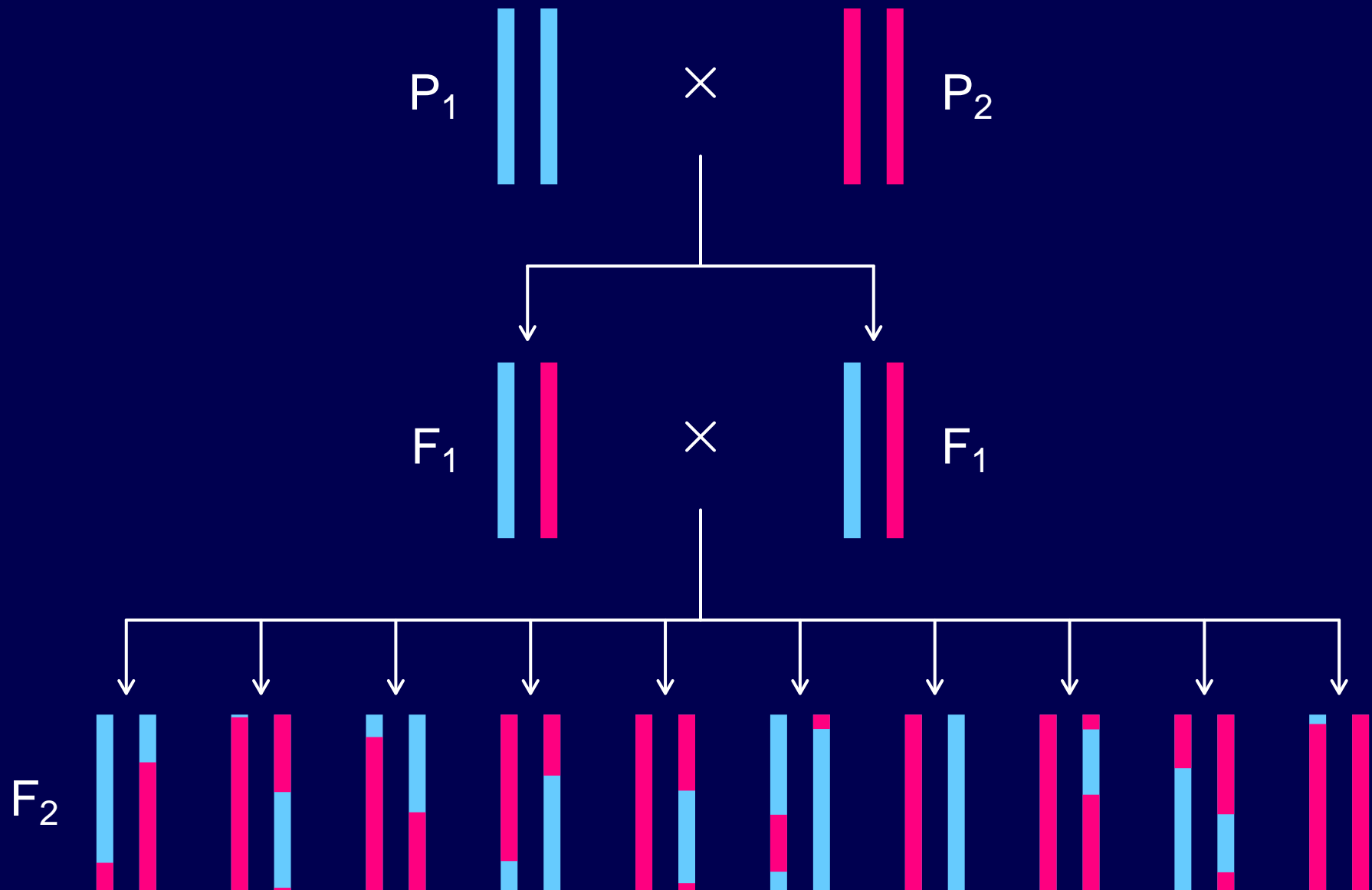
Advantages

- + If you find something, it is real
- + Power with limited genotyping
- + Numerous rare variants okay

Disadvantages

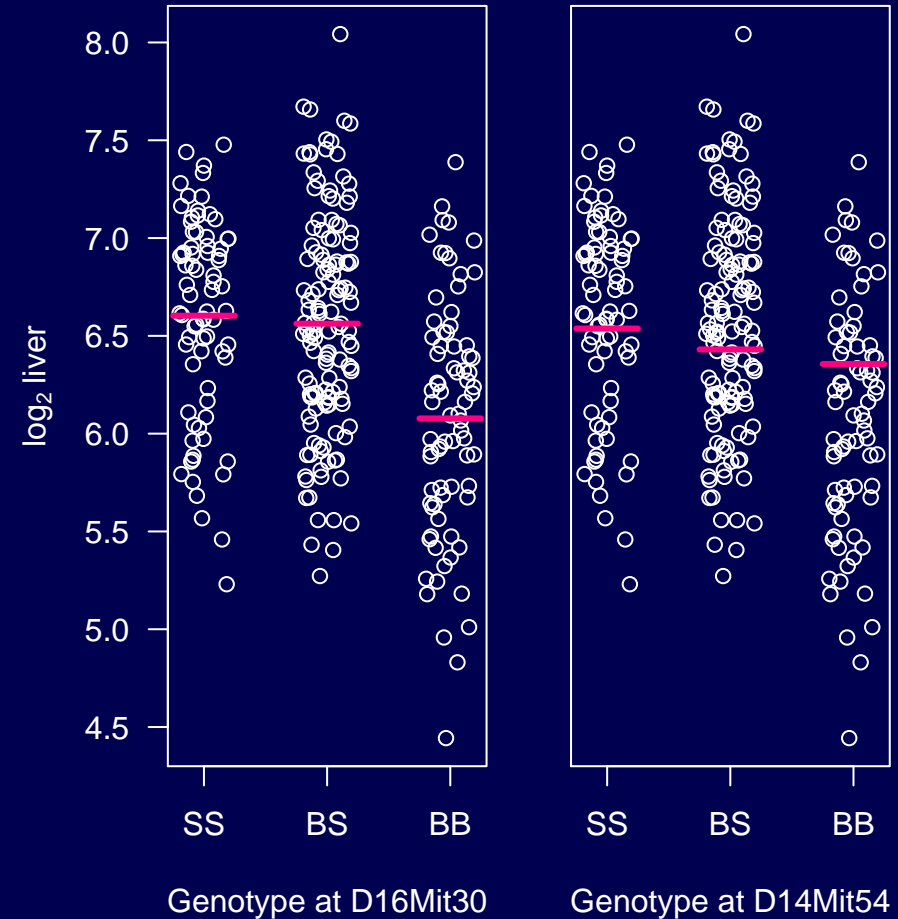
- Need families
- Lower power if common variant and lots of genotyping
- Low precision of localization

Intercross

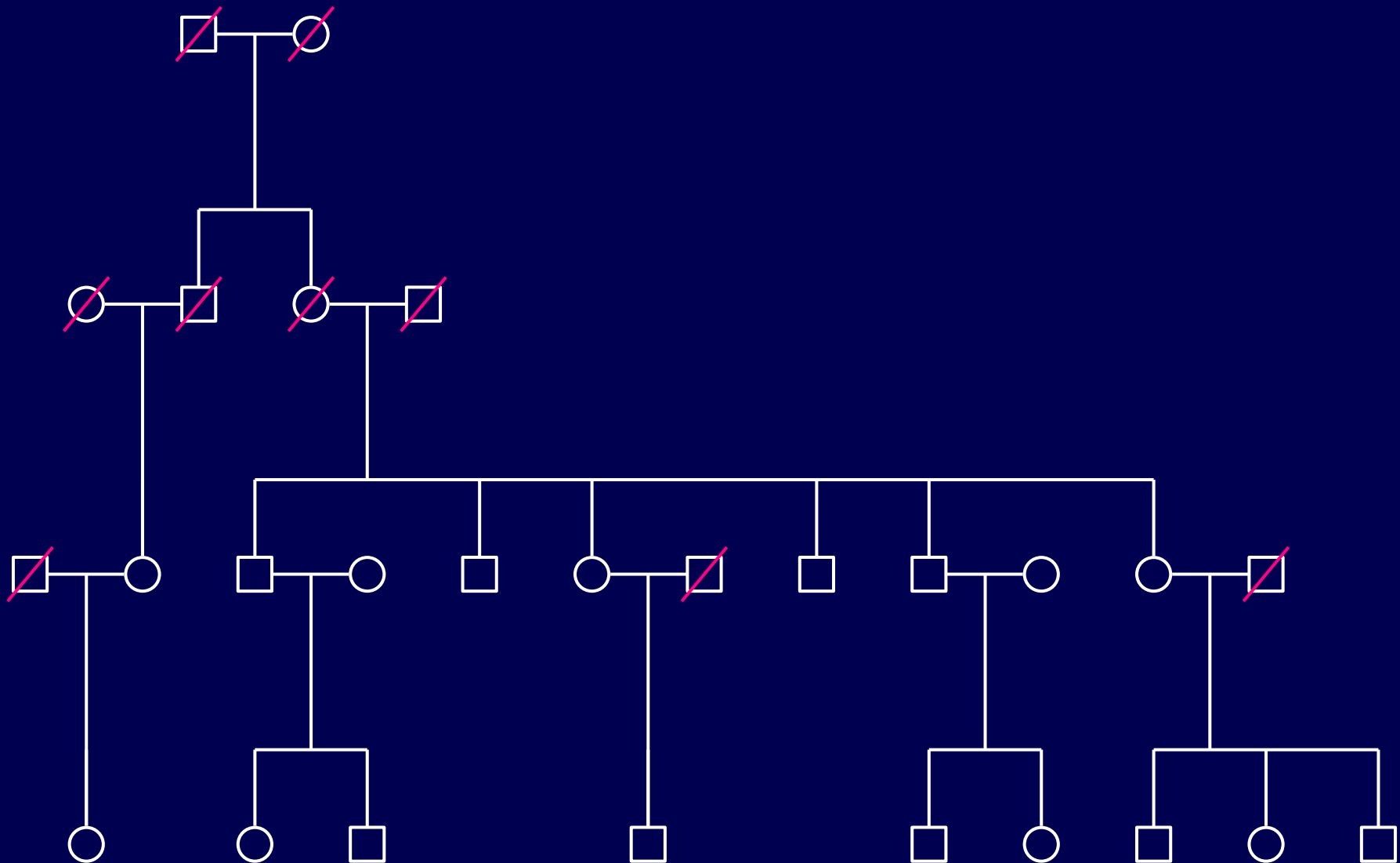


ANOVA at marker loci

- Split mice into groups according to genotype at a marker.
- Do a t-test / ANOVA.
- Repeat for each marker.



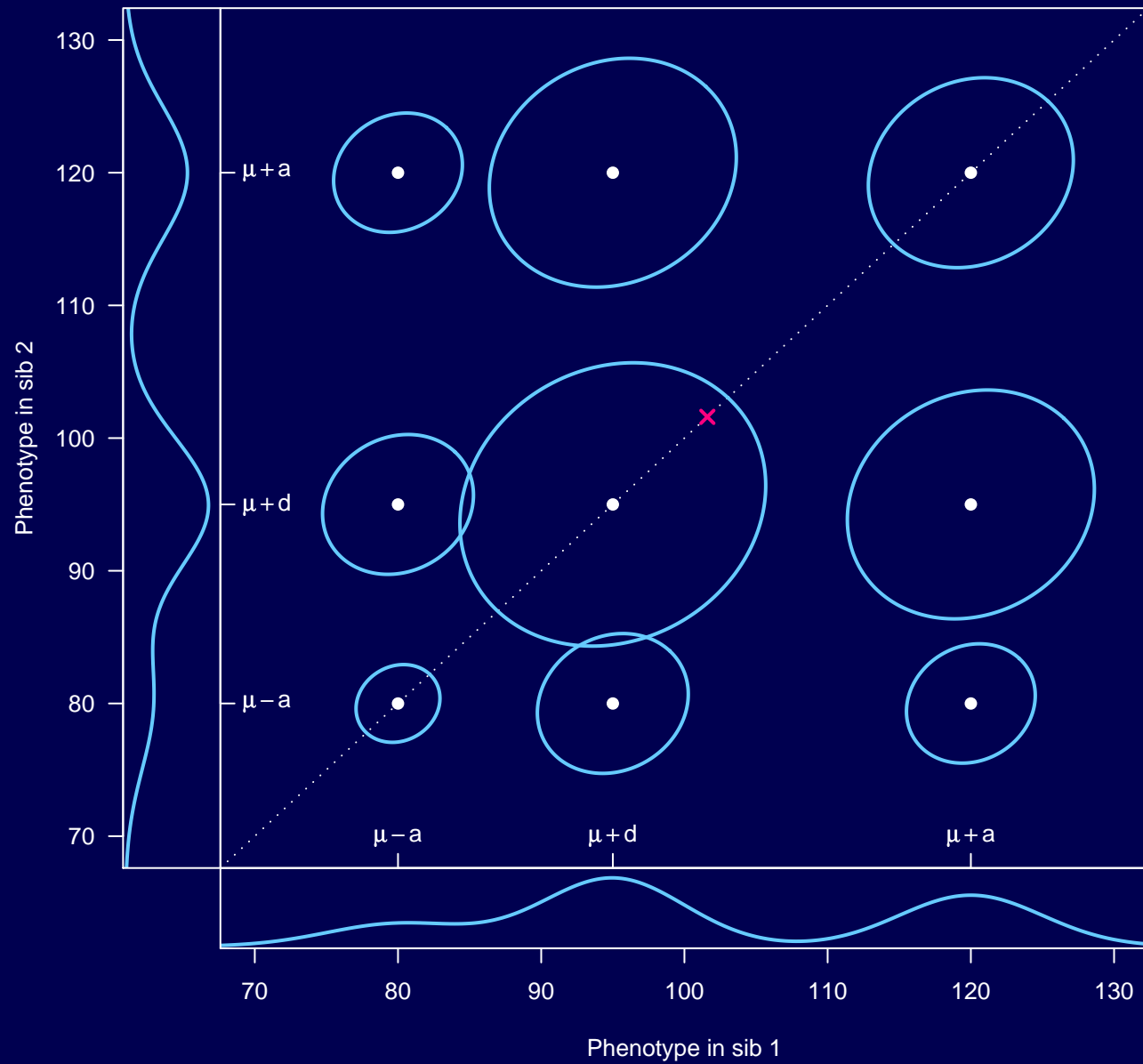
Human pedigree



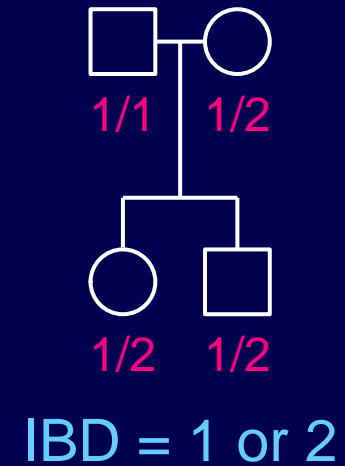
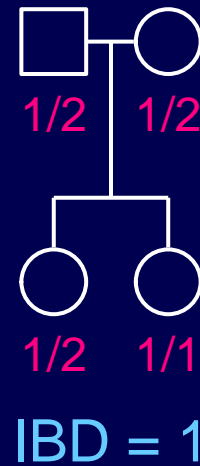
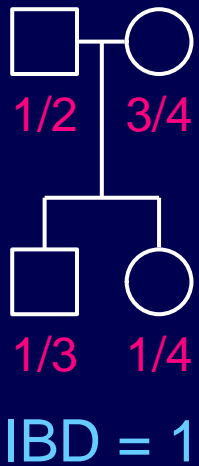
Humans vs mice

- More than two alleles
- Don't know QTL genotypes
- Unknown phase
- Parents may be homozygous
- Markers not fully informative
- Varying environment

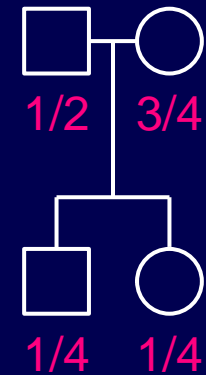
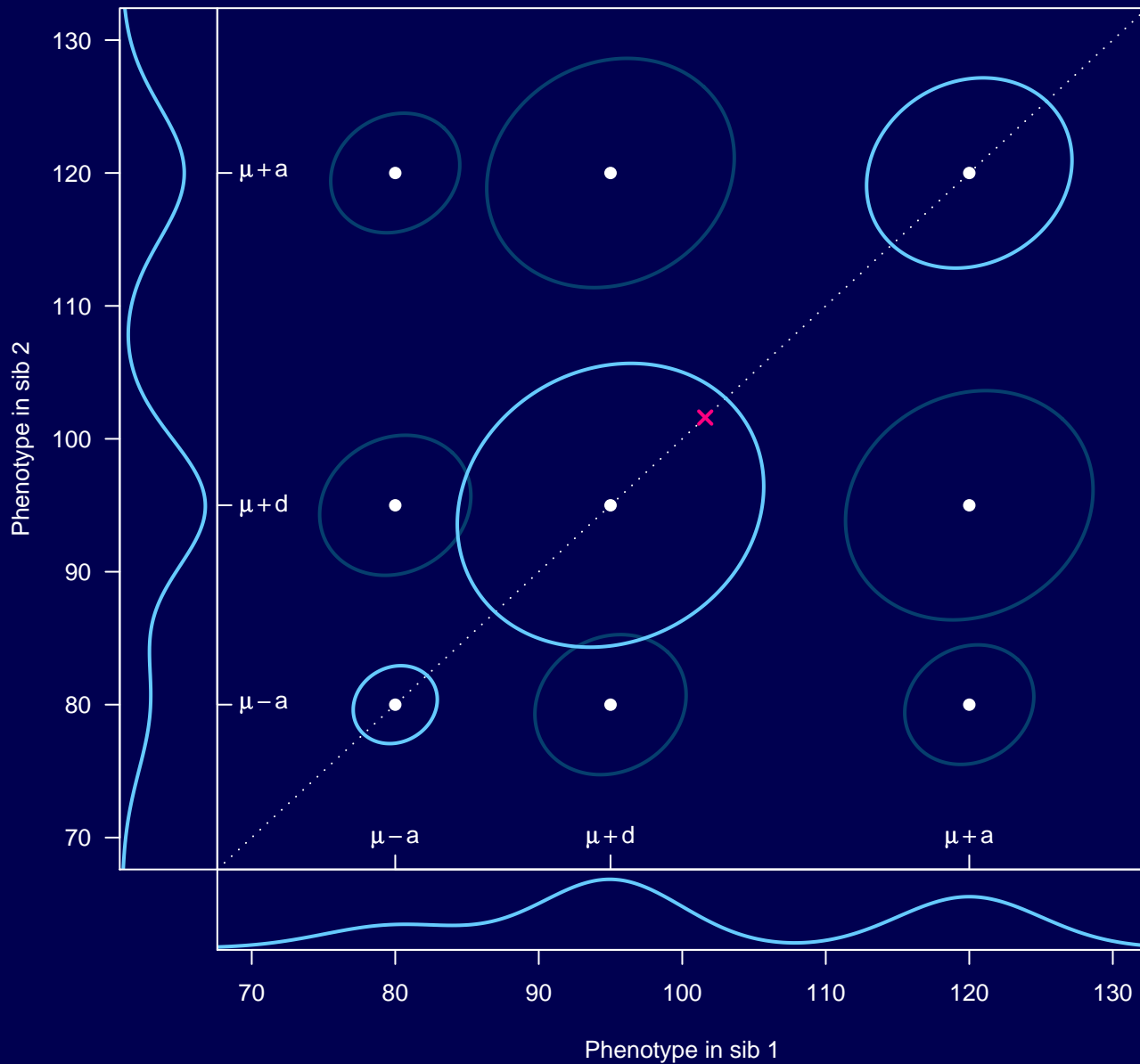
Diallelic QTL



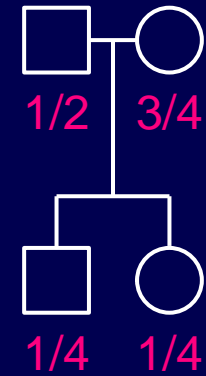
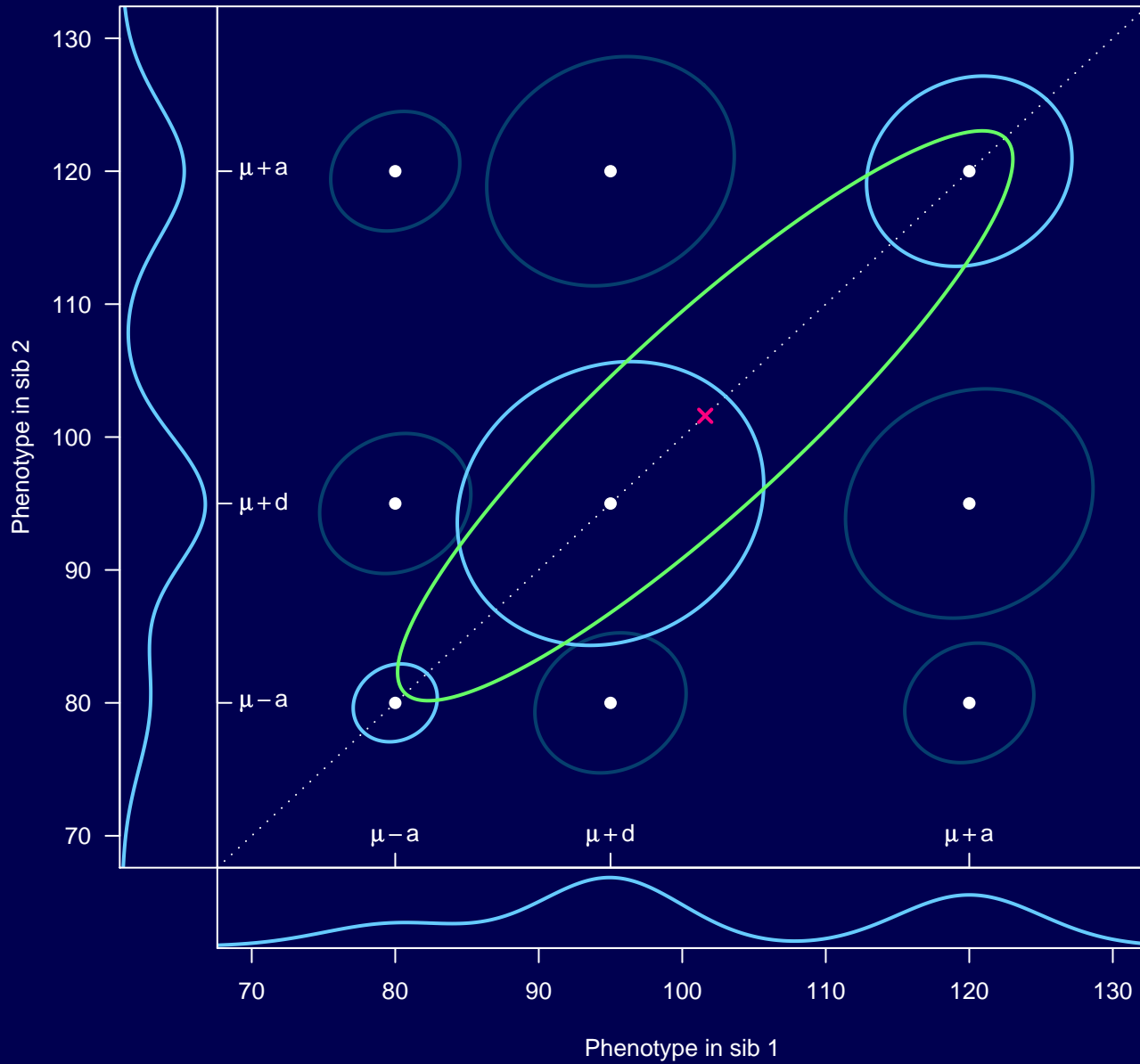
Identity by descent



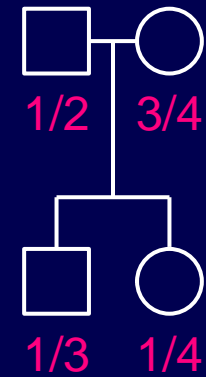
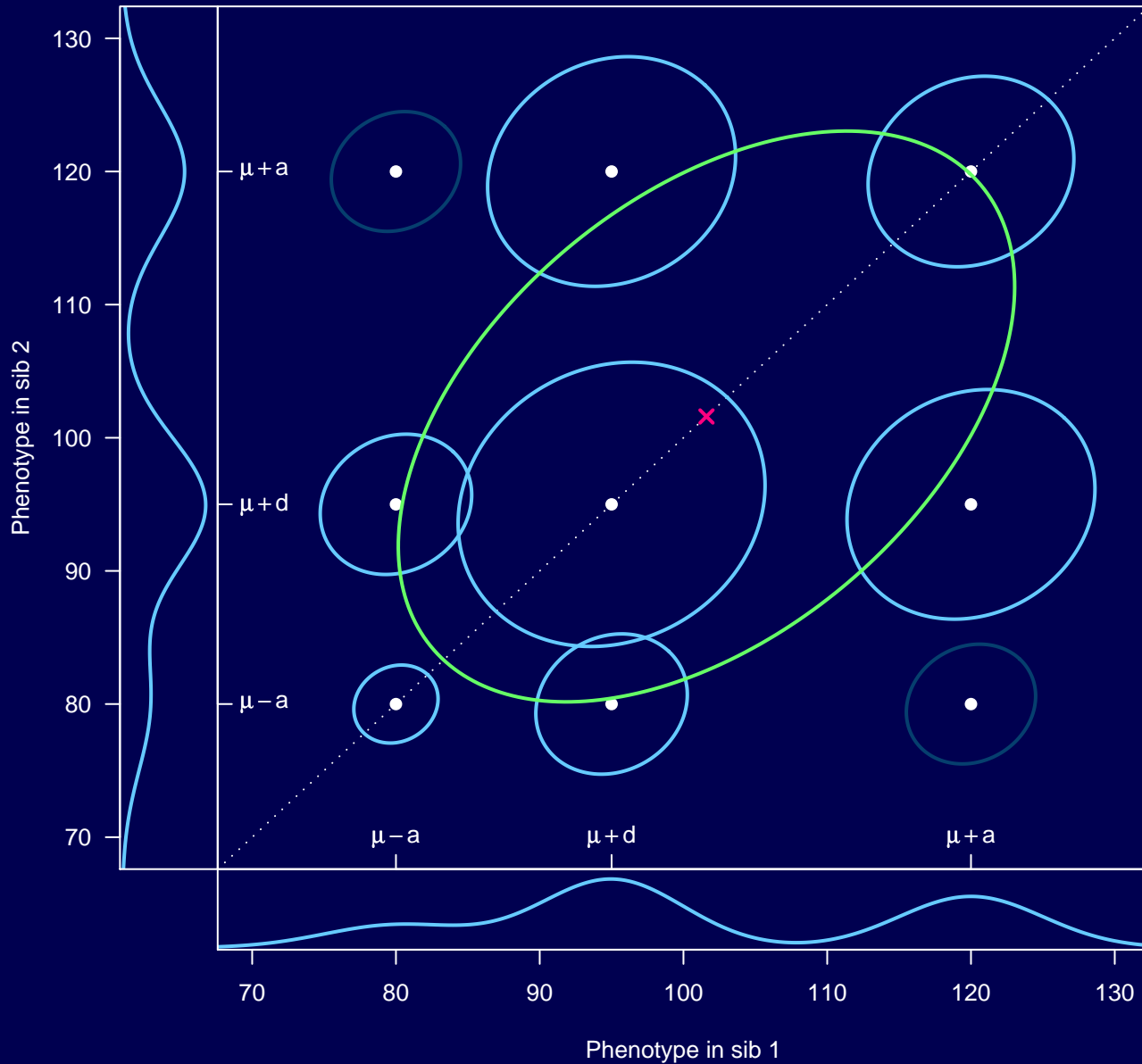
IBD = 2



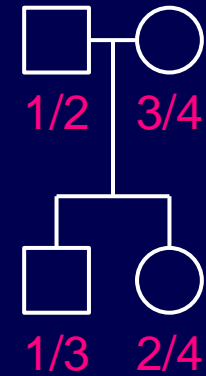
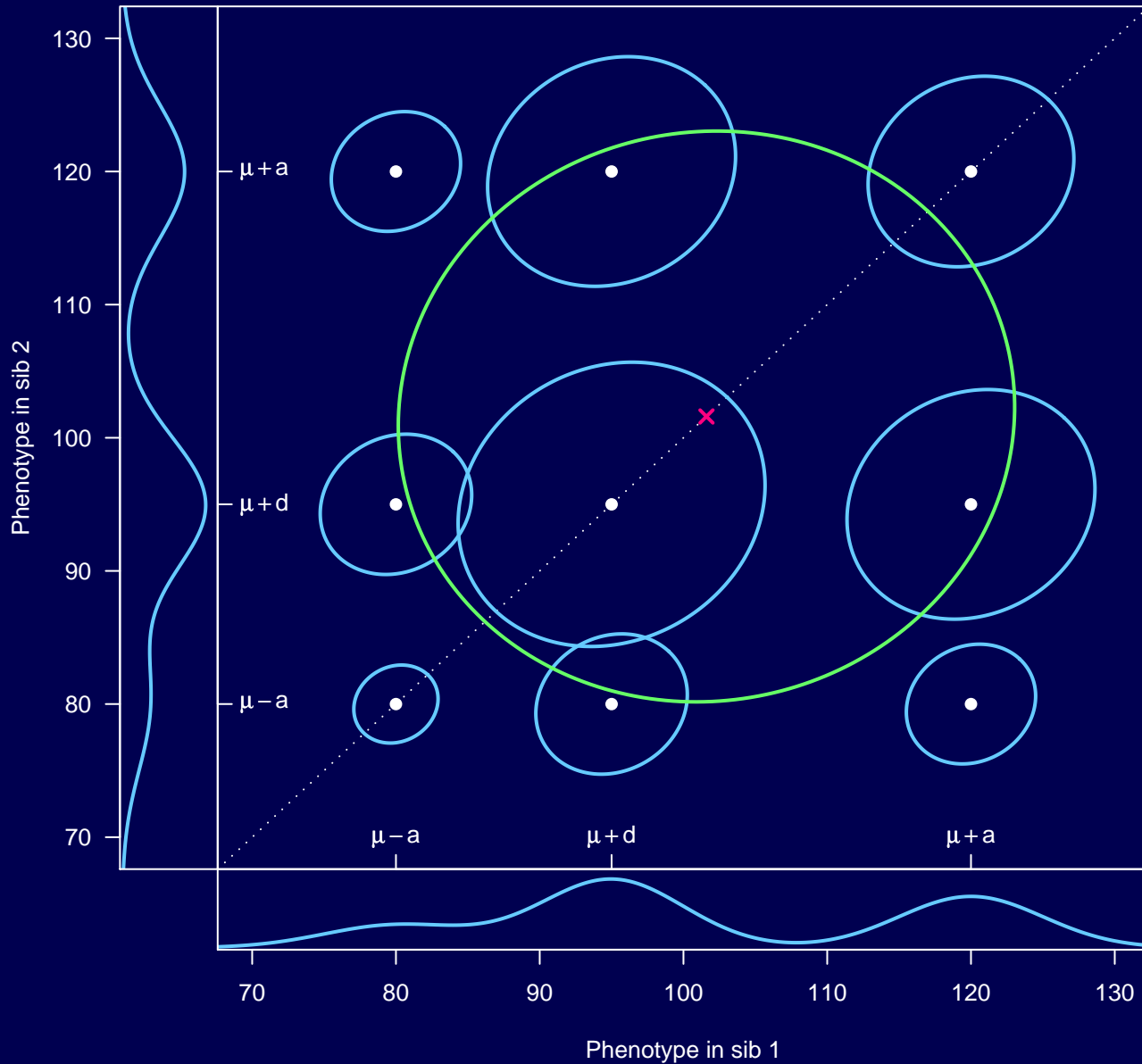
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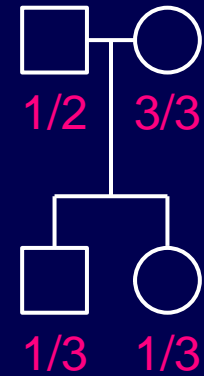
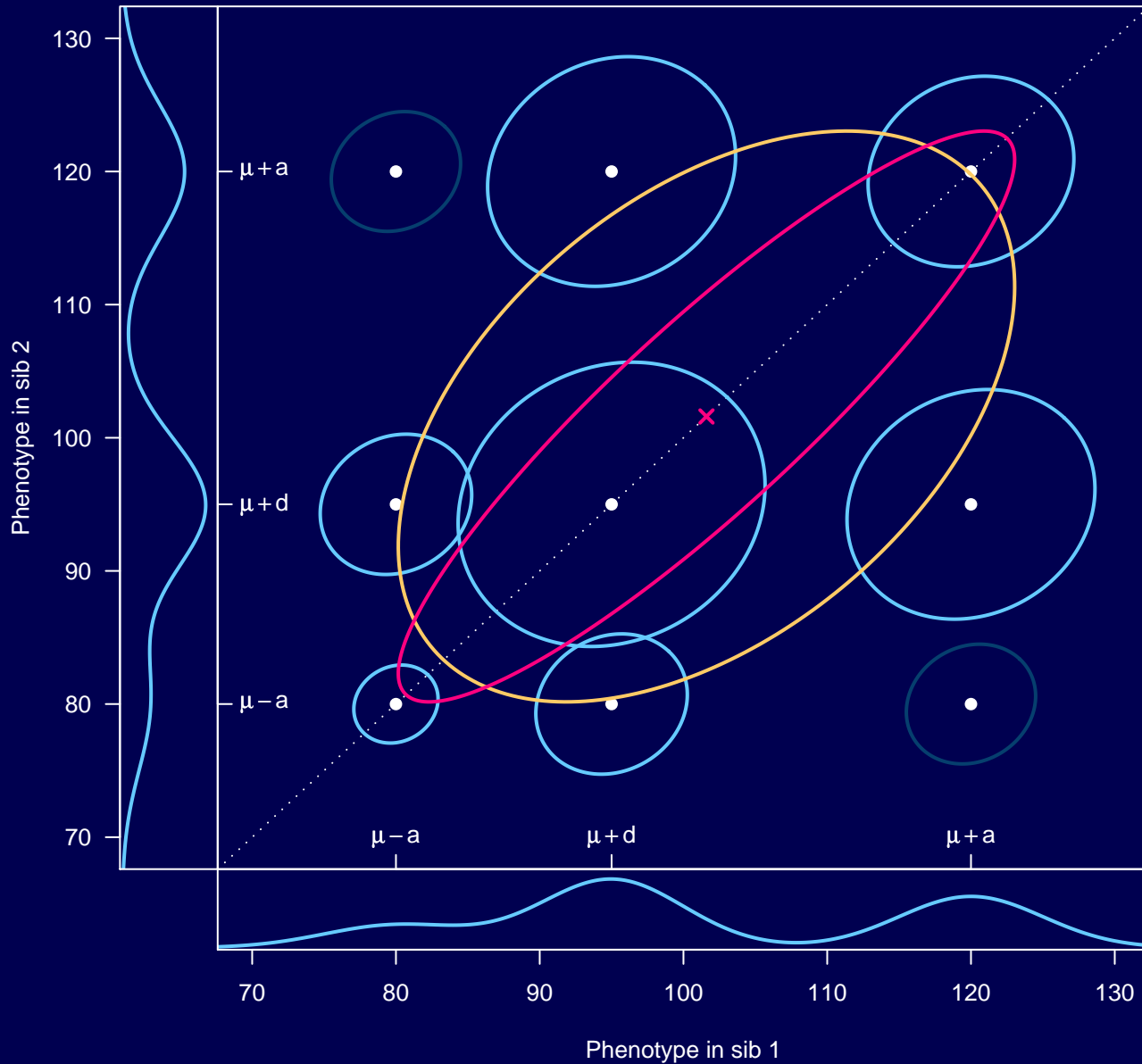
IBD = 1



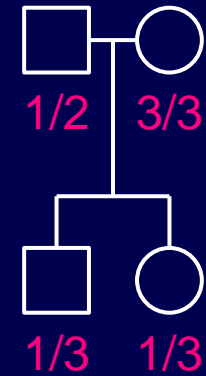
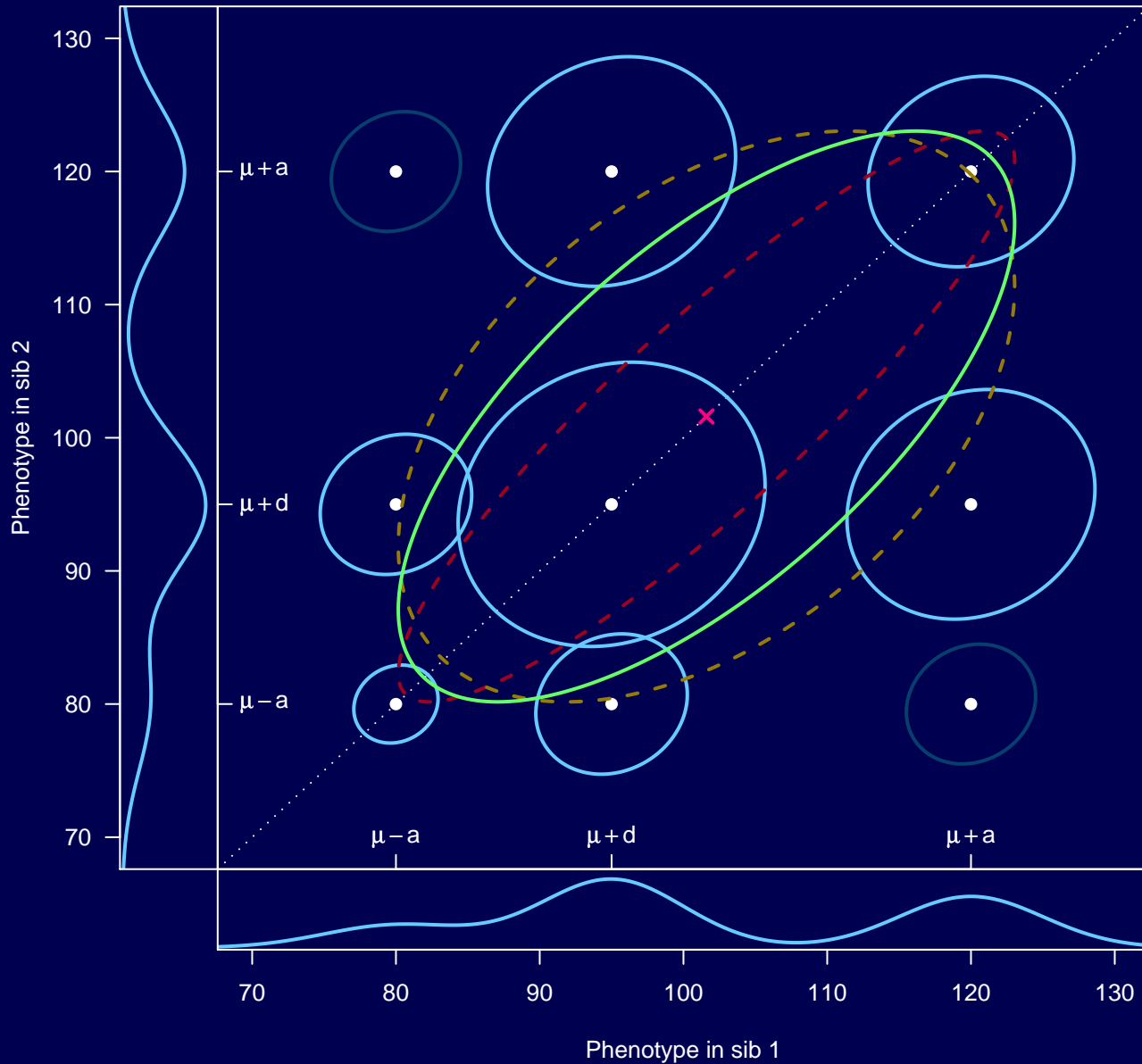
IBD = 0



IBD = 1 or 2



IBD = 1 or 2



Challenges

- Non-normality
- Genetic heterogeneity
- Environmental covariates
- Multiple QTL
- Multiple phenotypes
- Complex ascertainment
- Precision of mapping