

Checking SNP and pedigree information of sibs for Mendelian inconsistencies

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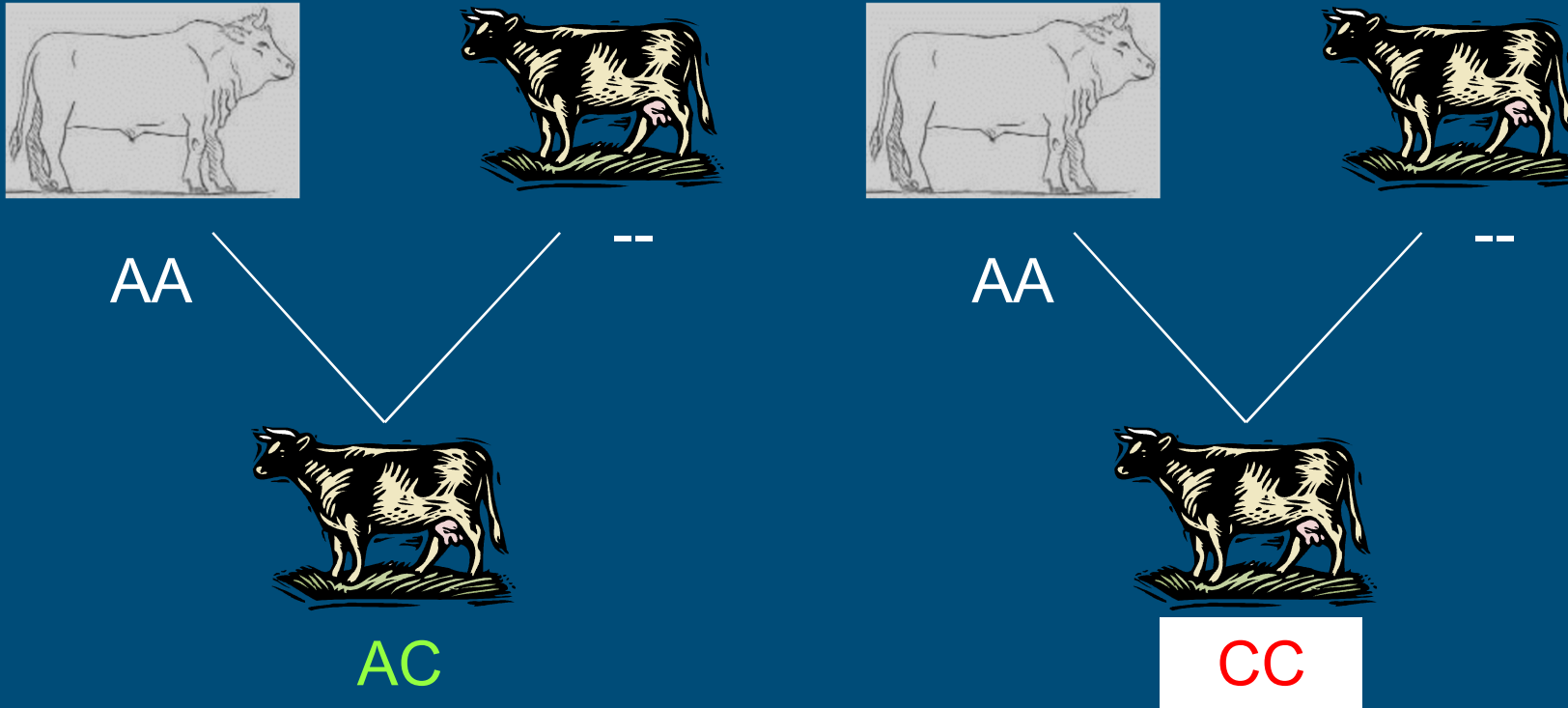


Introduction

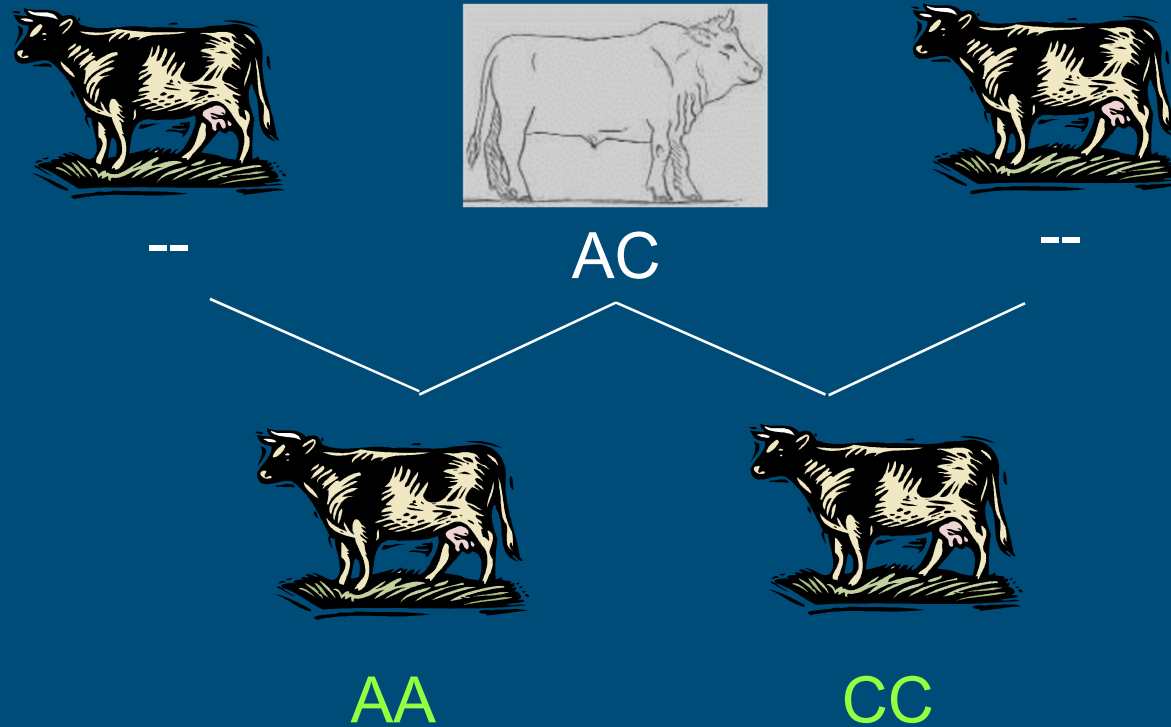
Mendelian Inconsistencies (MI):

- Identify animals with conflicting pedigree and SNP info
- Identified by counting loci with opposing homozygotes between 2 animals
- Identification is straightforward for parent-offspring pairs
 - Expected number of loci with opposing homozygotes = 0

MI – Parent-offspring pair

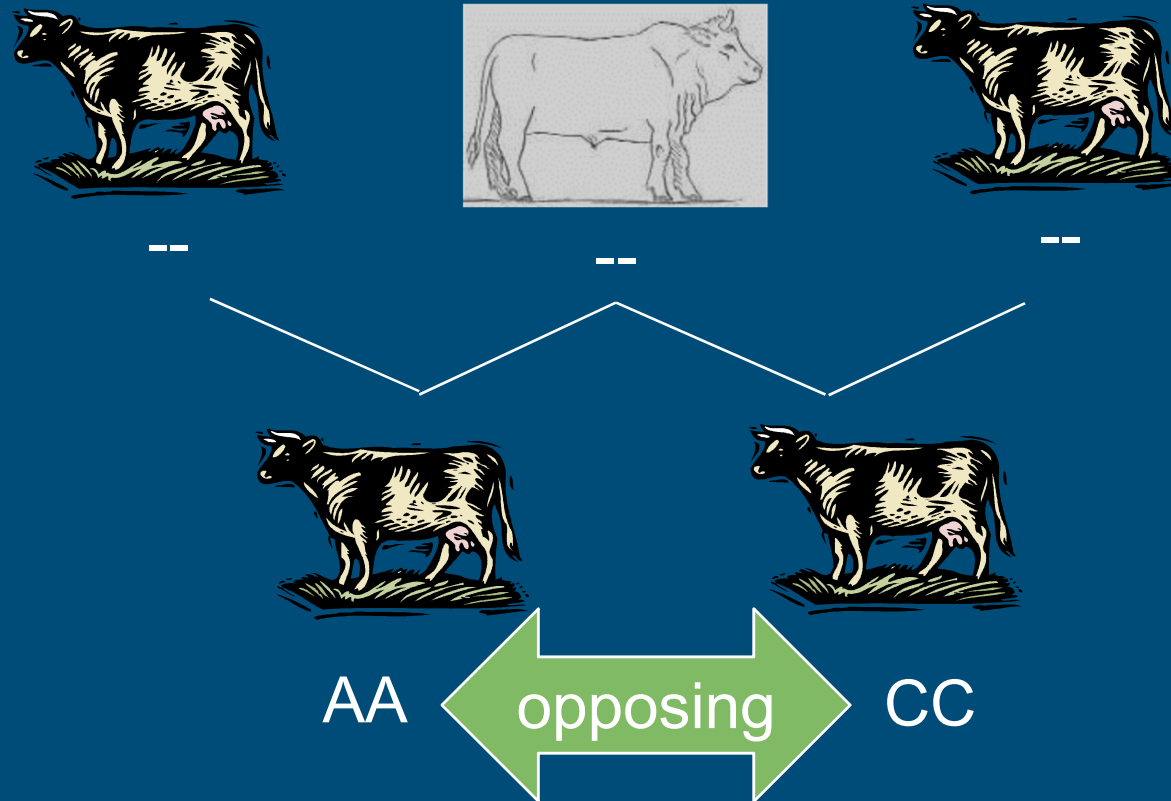


MI – Paternal half sib pair (dams not genotyped)



What if we don't know the sires genotype?

MI – Paternal half sib pair (parents not genotyped)

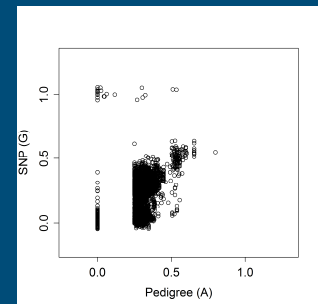
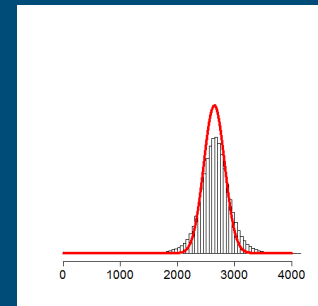


What is the expected number of opposing homozygote loci for a pair of sibs?

Objective

Develop tests to detect MI between sibs, based on:

- Realized number of opposing homozygote SNP loci
- Comparing pedigree and SNP based relationships between sibs



Two tests developed for sibs - algorithms

■ SIBCOUNT

- Count SNP with opposing homozygotes per sib pair

■ SIBREL

- Compare A (pedigree) with G (SNP) relationships per sib pair

In both tests:

- Define empirical thresholds to declare conflicts
- Iteratively remove animals that cause most MI

Identify animals causing MI – approach taken

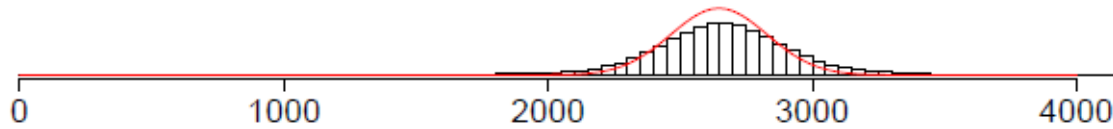
- Detect MI for parent-offspring pairs
 - Parent-offspring pairs were defined based on pedigree or SNP
- Run SIBCOUNT or SIBREL
- Type I & II error rates for SIB tests were derived by permuting part of the ‘cleaned up’ data

RobustMilk genotype data

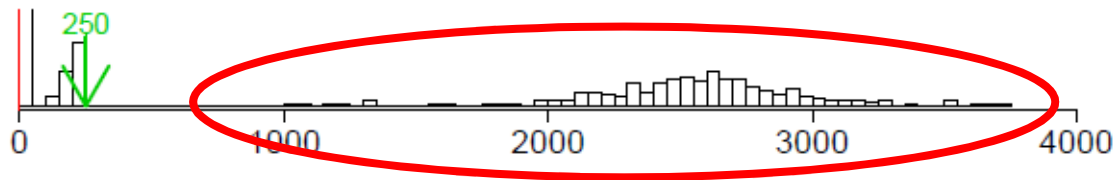
- 2,078 cows and 211 bulls; 36,884 SNP loci
 - Cows from research herds in NL, UK, Ireland & Sweden
- 891 genotyped mother – daughter pairs
- 1,448 genotyped father – daughter pairs
- 508 genotyped animals without genotyped parent

SIBCOUNT

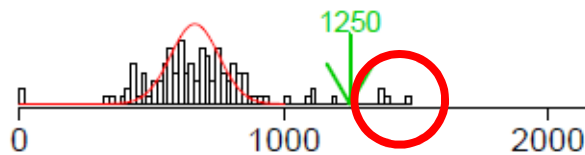
A. - Unrelated animals



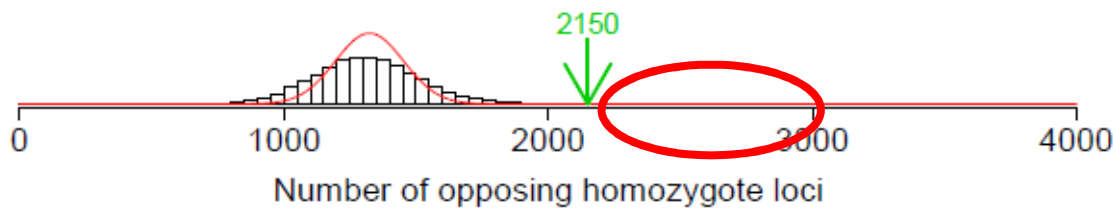
B. - Parent-offspring



C. - Full sibs



D. - Half sibs

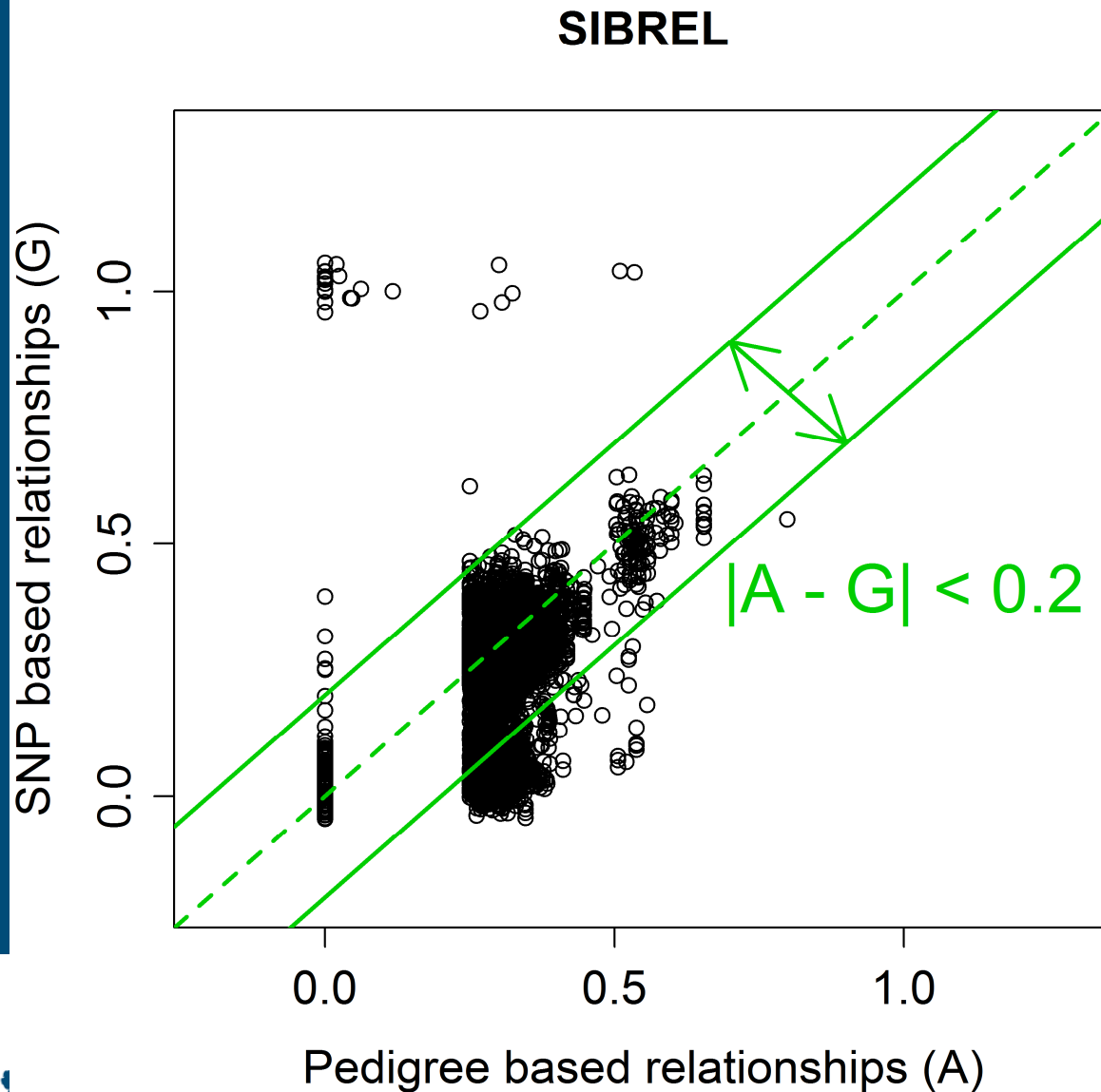


Distributions of number of opposing homozygote loci:

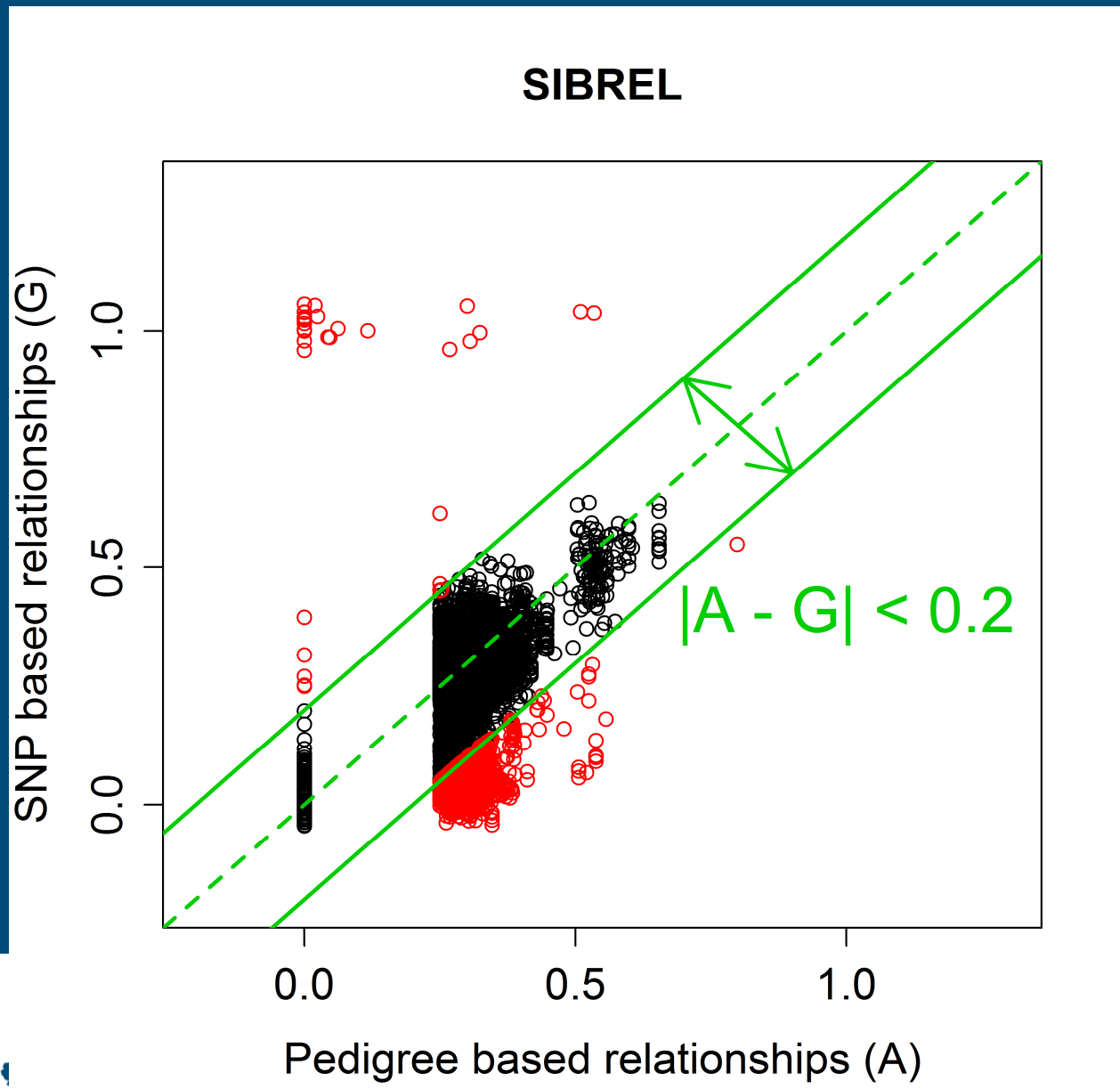
- Observed (histogram)
- Expected (allele frequencies)
- Thresholds (empirical)

Mendelian inconsistencies!

SIBREL: relationships & thresholds



SIBREL: relationships & thresholds



Results

Removed animals:

- 223 based on parent-offspring inconsistencies
- 31 (34) based on SIBCOUNT (SIBREL)

After permuting 10% of the data:

- Incorrectly deleted animals (Type I error)
 - Equally low for SIBCOUNT & SIBREL (~ 0.5%)
- Incorrectly non-deleted animals (Type II error)
 - SIBCOUNT (5.2%) << SIBREL (9.8%)

Conclusions

- SIBCOUNT was better able to identify animals causing MI
 - Lower Type II error rate
- Test for opposing homozygotes is:
 - Powerful tool to detect MI between sib pairs
 - Easy to implement



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