Factors Influencing accuracy of genomic selection with sequence Information

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Genomic selection, effective population size and sequence data

- Efficient genomic selection with sequence data - need QTN location and QTN variance (Fragomeni et al., 2017)
- GWAS developed mostly for human data – large effective population size (Ne=3000-10000)
- Farm populations have small Ne: 40 to 150
  - 5k to 15k independent chromosome segments (Stam, 1980; Pocrnic et al., 2016)
  - Each segment size 200k to 600k

- Questions
  - Does small effective population size affect GWAS?
  - What is Manhattan plot composed of?
  - Why small benefits of using sequence data for prediction?

Simulation study

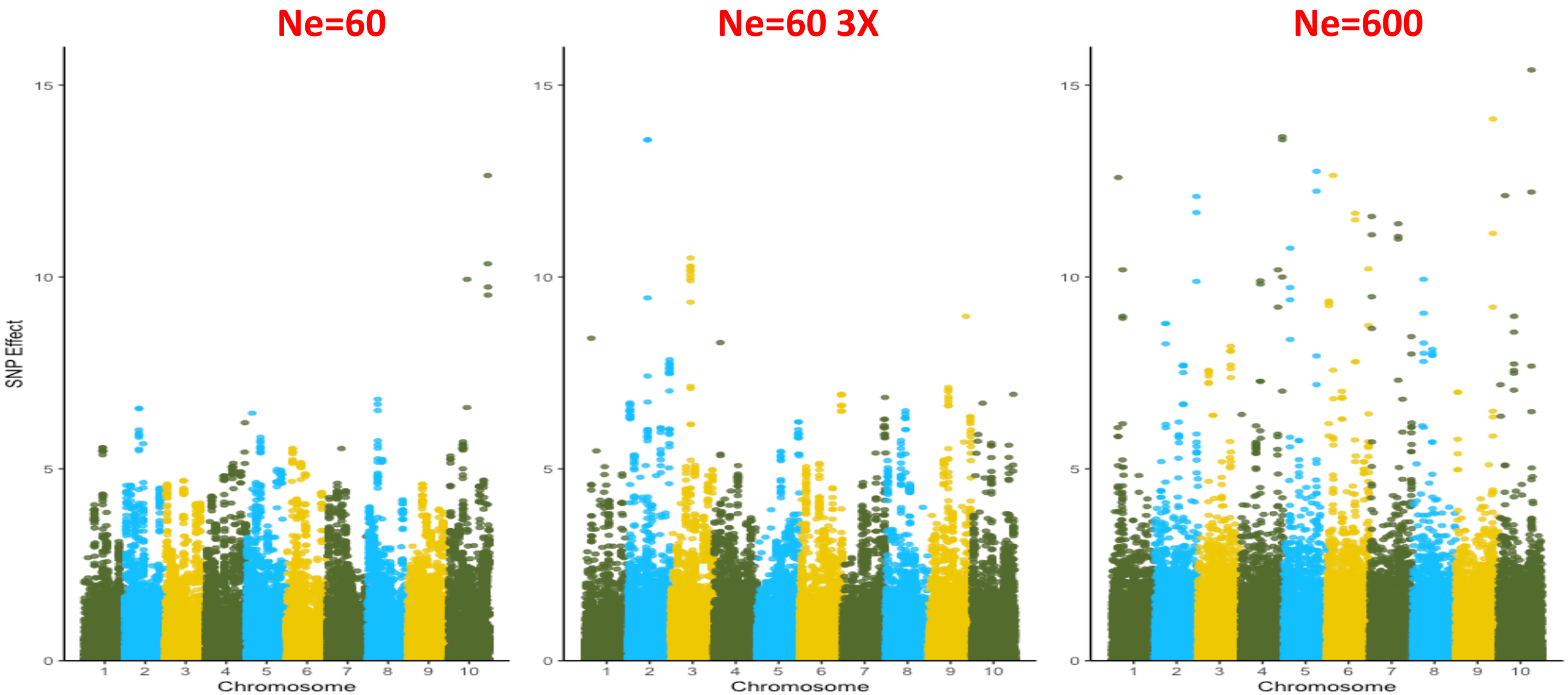
- AlphaSimR (Faux et al., 2016)

- 100 QTN with same effect and equally spaced
- 10 generations with 2000 animals in each
- Last 3 generations genotyped for 50k SNP – causative SNP included

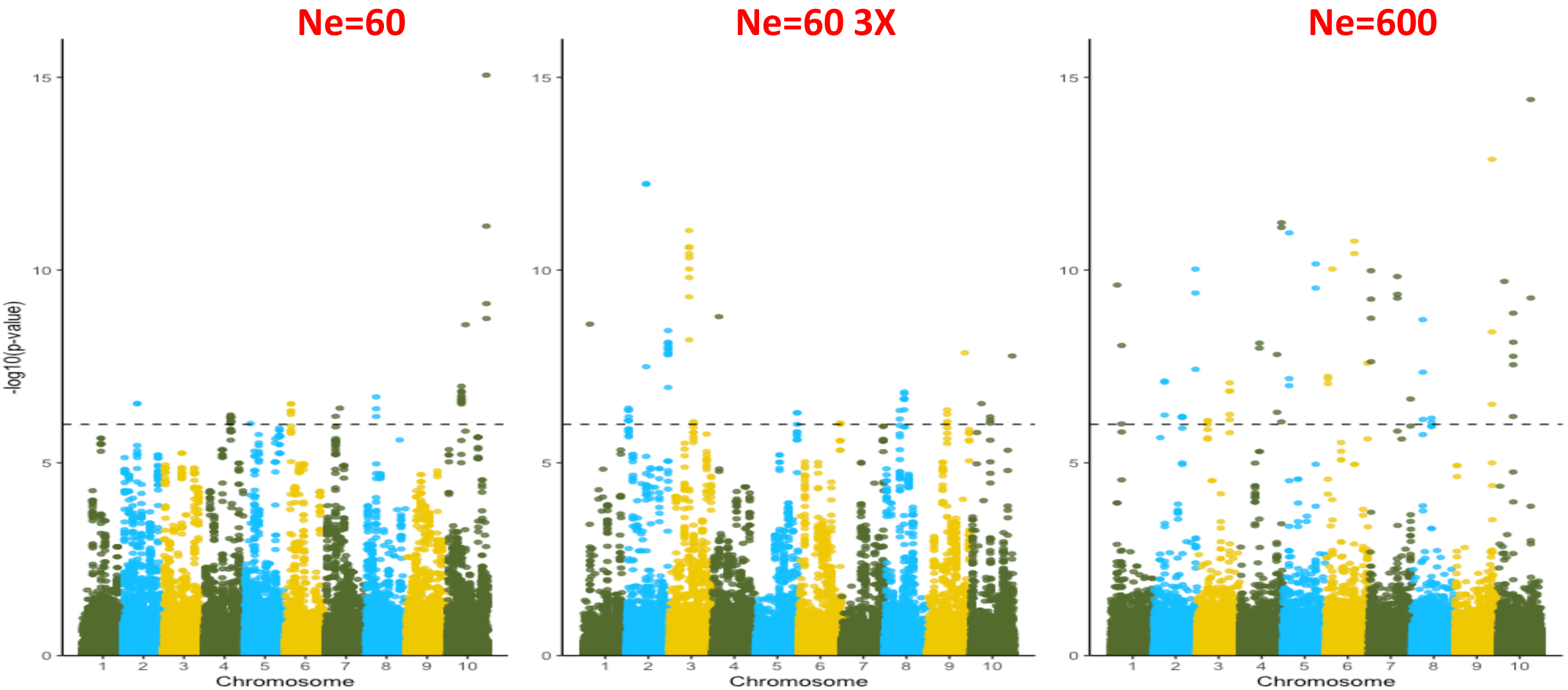
- 3 data sets
  - Ne=60
  - Ne=600
  - Ne=60_3x --3 times more data (6000 per generation)

- Analyzes by ssGBLUP with p-value option

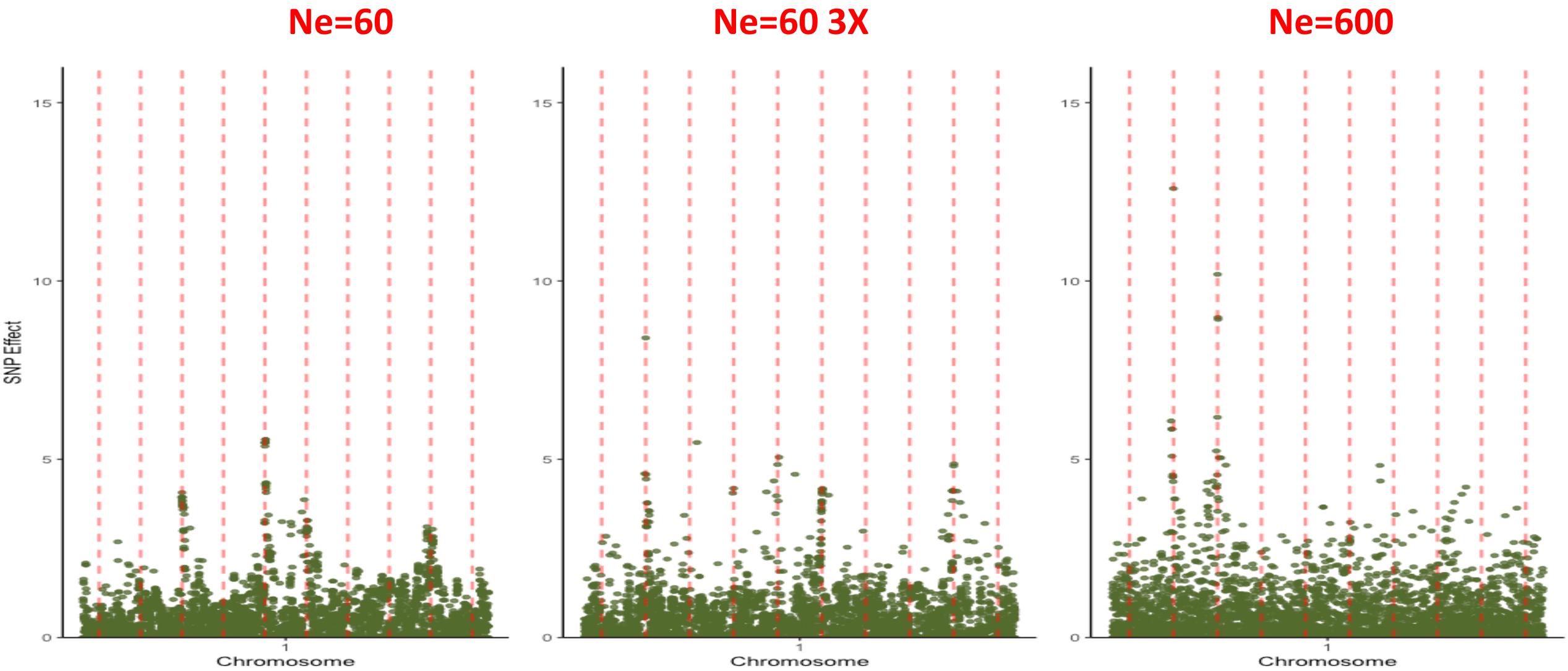
Manhattan plots for SNP effects



Manhattan plots for P-values

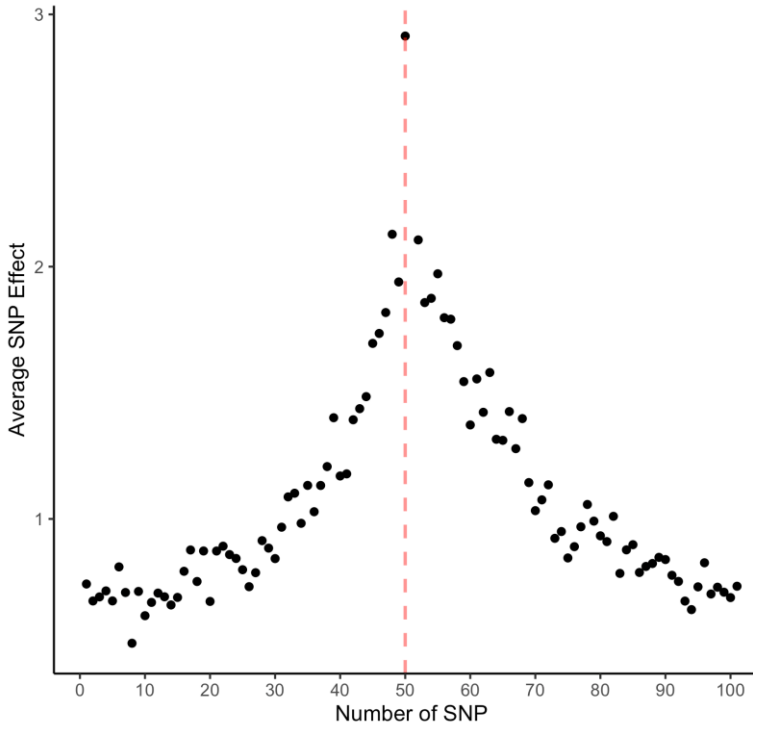


Manhattan plots for first chromosome

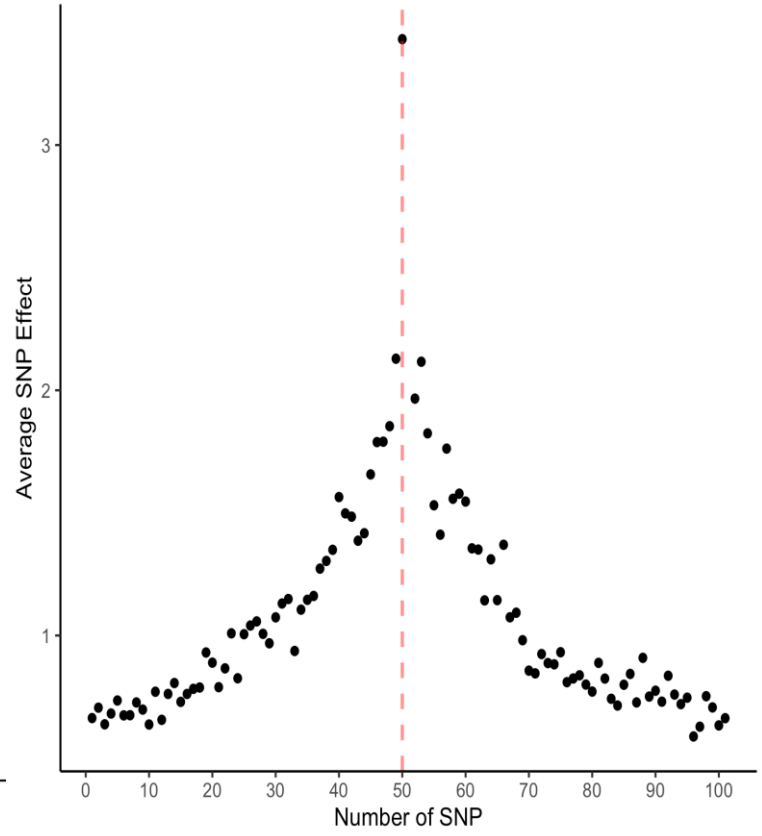


Plots averaged for all QTNs

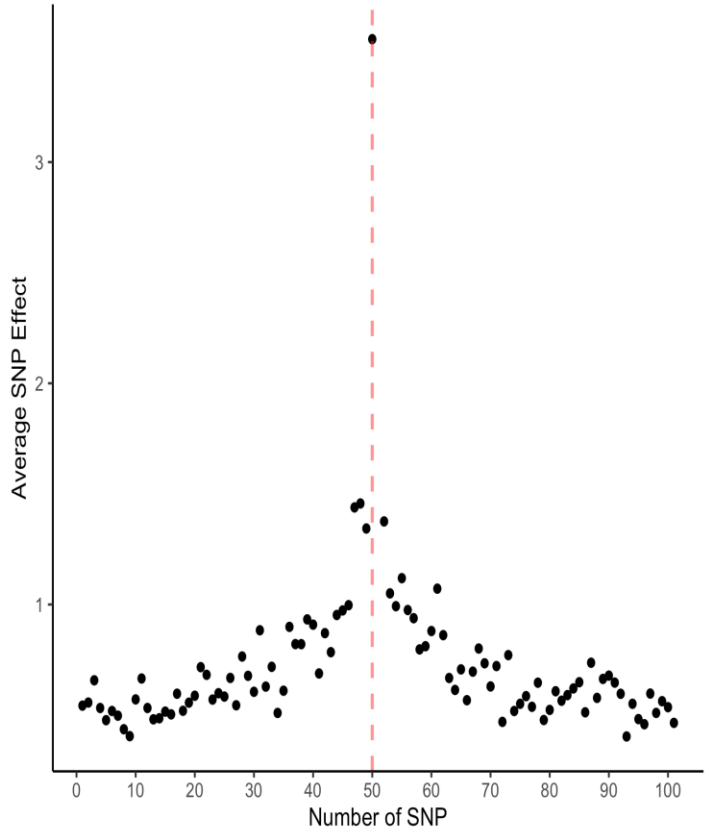
Ne=60



Ne=60 3X



Ne=600

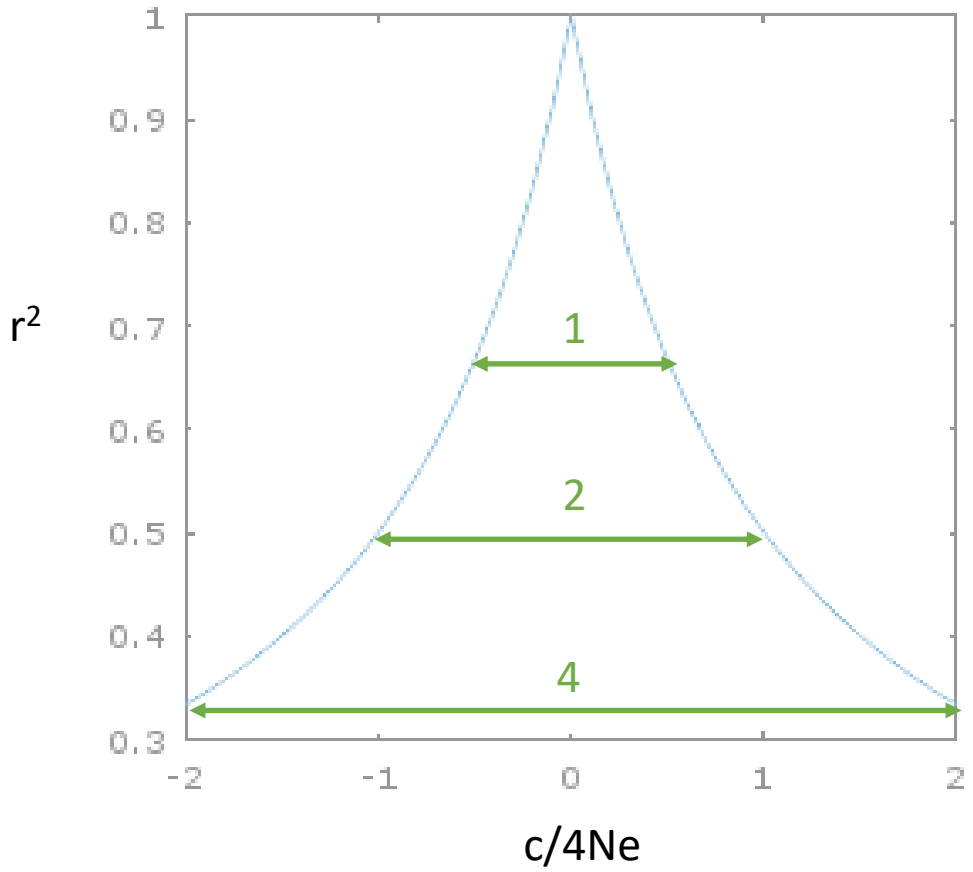


Pairwise linkage disequilibrium (r^2)

$E(r^2)=1/(4\ c\ Ne\ +1)$ Sved (1971)

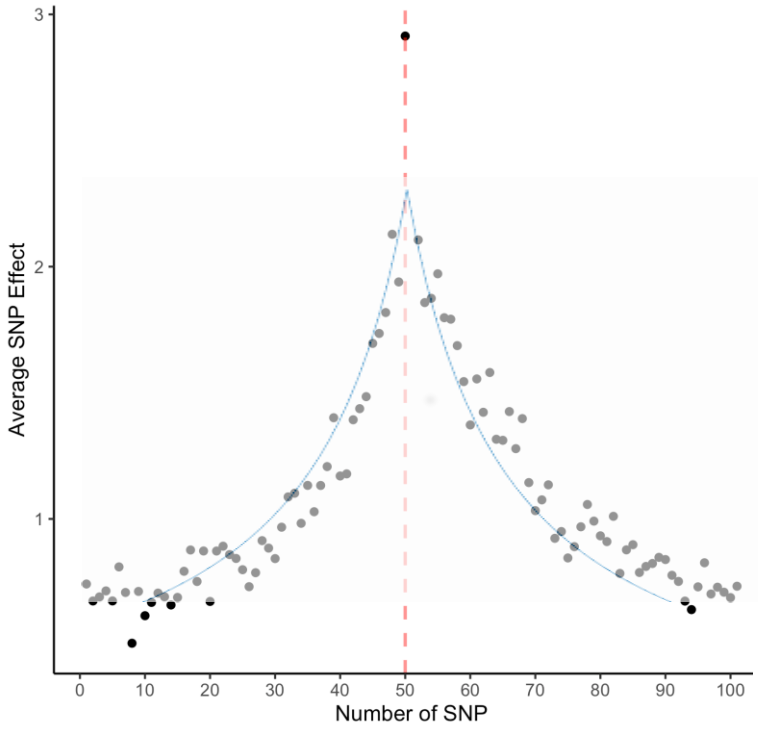
c – distance between genes
Ne – effective population size

One Stam segment - (1/4Ne Morgan)

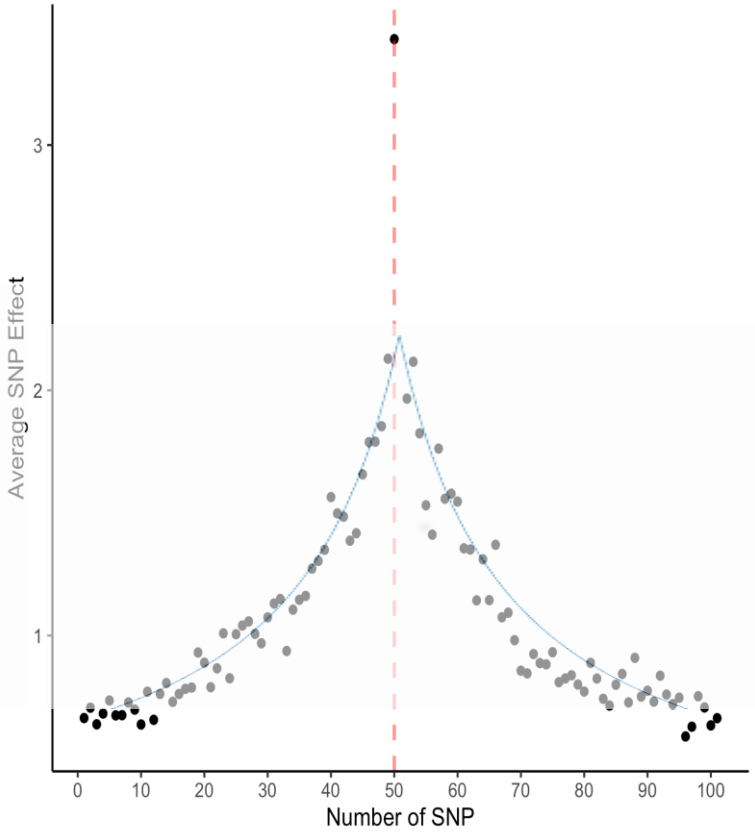


LD fitting….

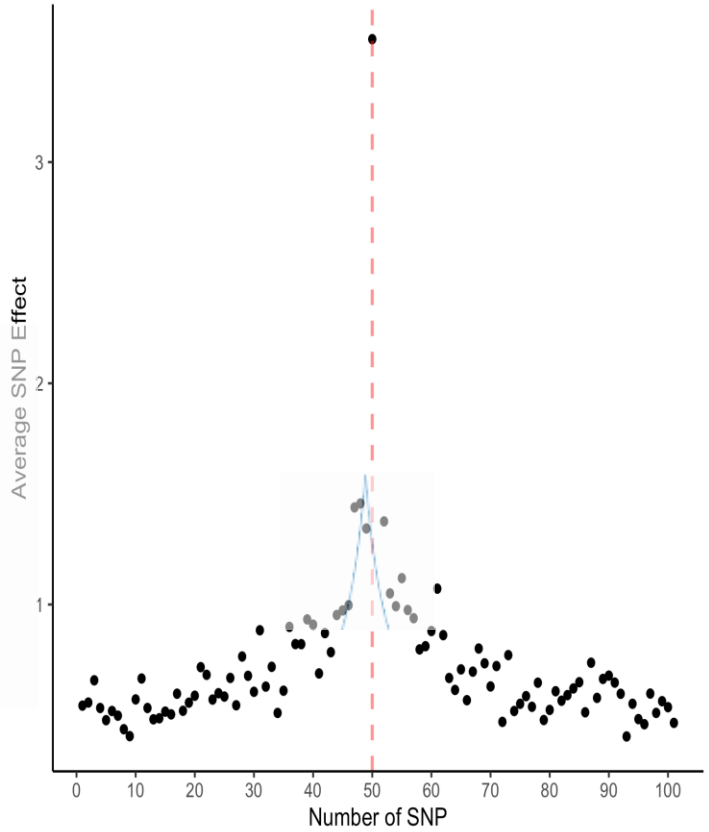
Ne=60



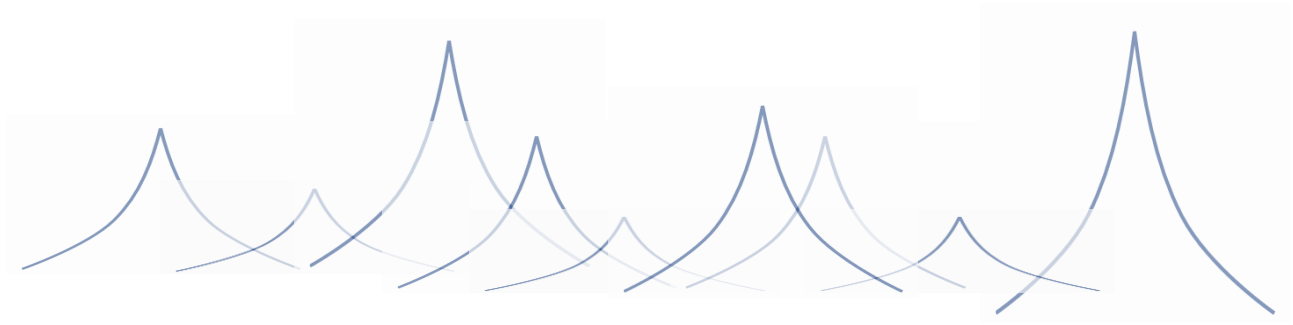
Ne=60 3X



Ne=600



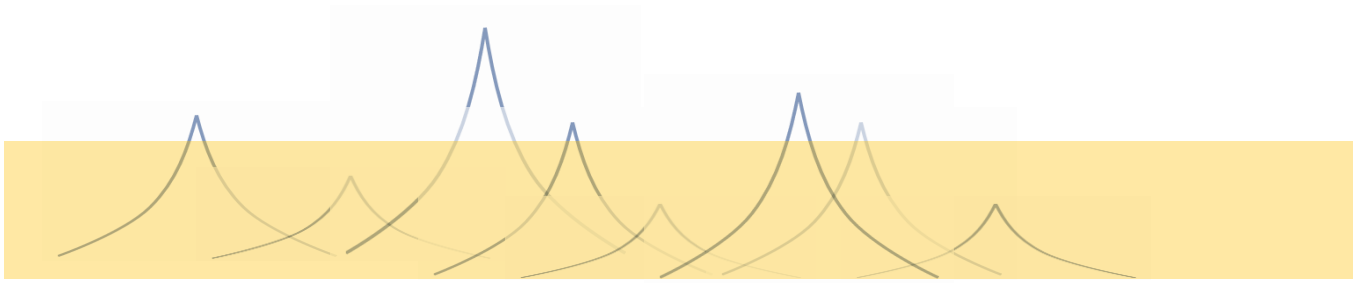
What is Manhattan plot composed of?



QTNs

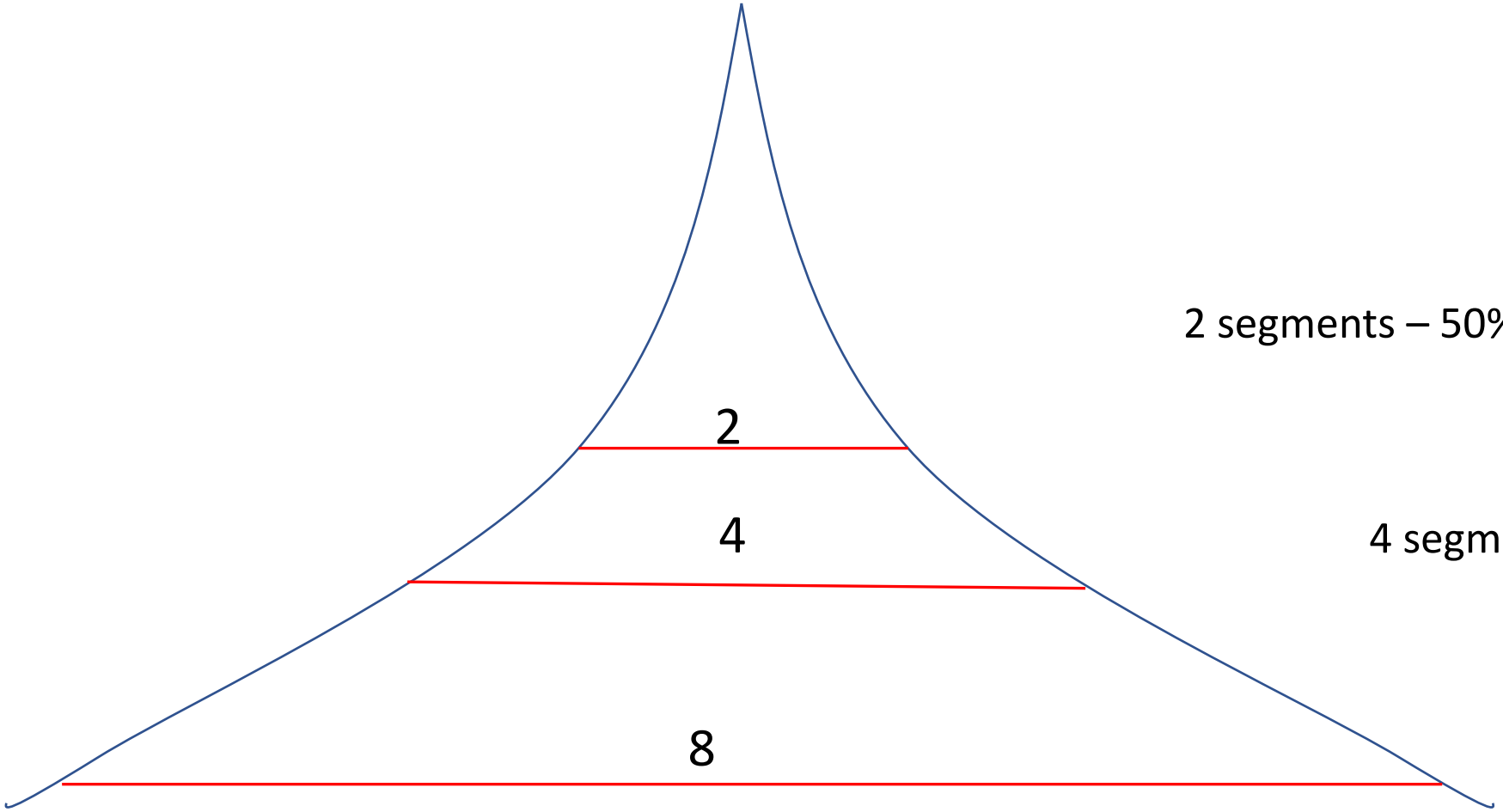
Relationships

Noise



Composite plot

Proportion of QTN variance explained by different number of segments

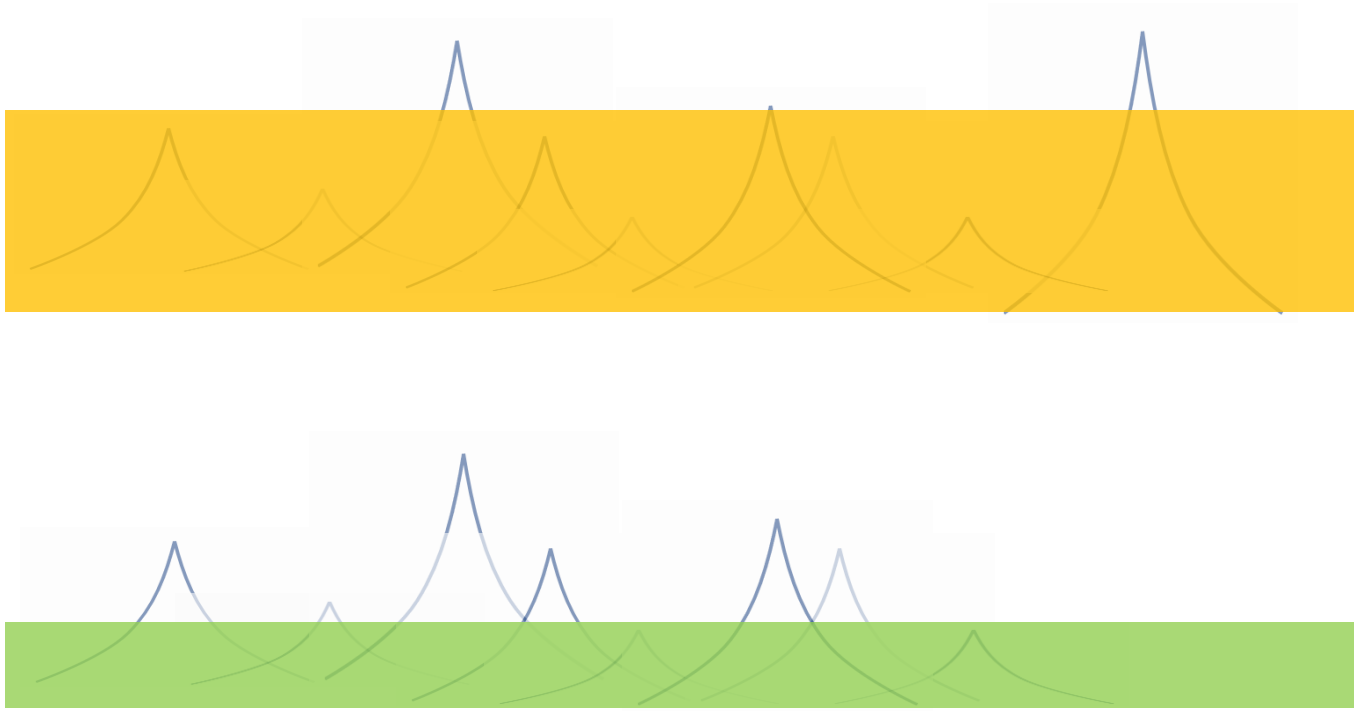


2 segments – 50% QTN variance

4 segments – 66% QTN variance

8 segments – 80% QTN variance

Size of data

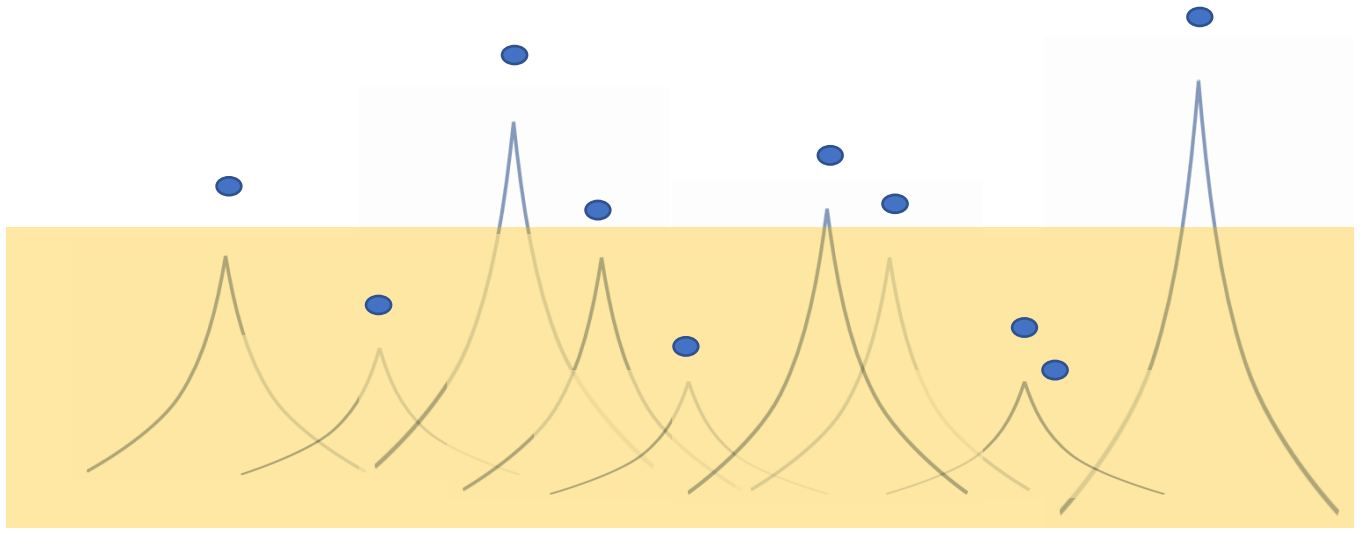


Small data

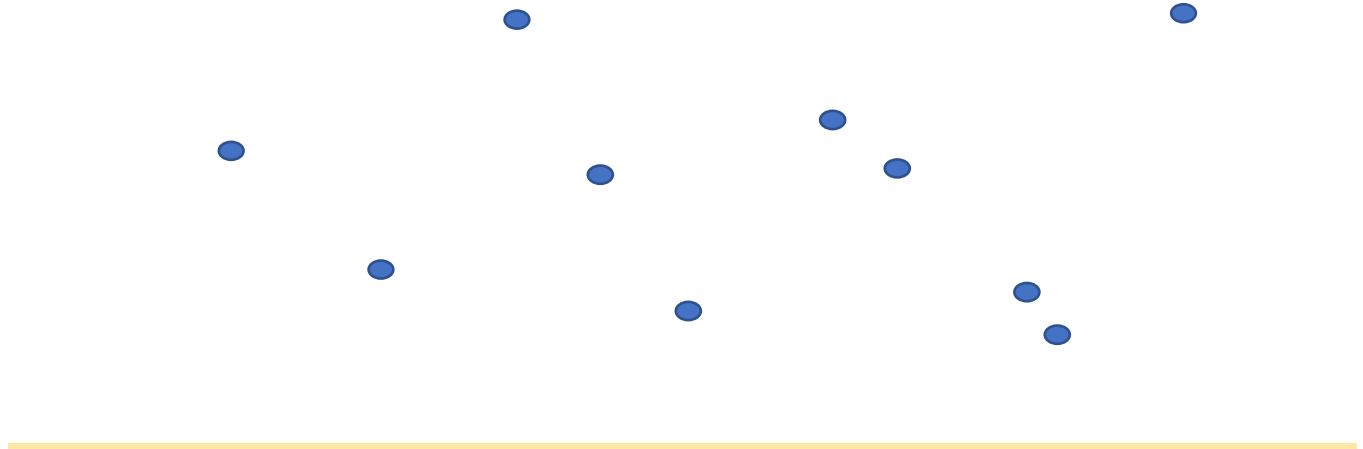
Large data

If GWAS by sliding window, optimal size 4-8 Stam segments
1-2 Mb cattle, 3-6 Mb pigs and chicken

+ QTN in the data

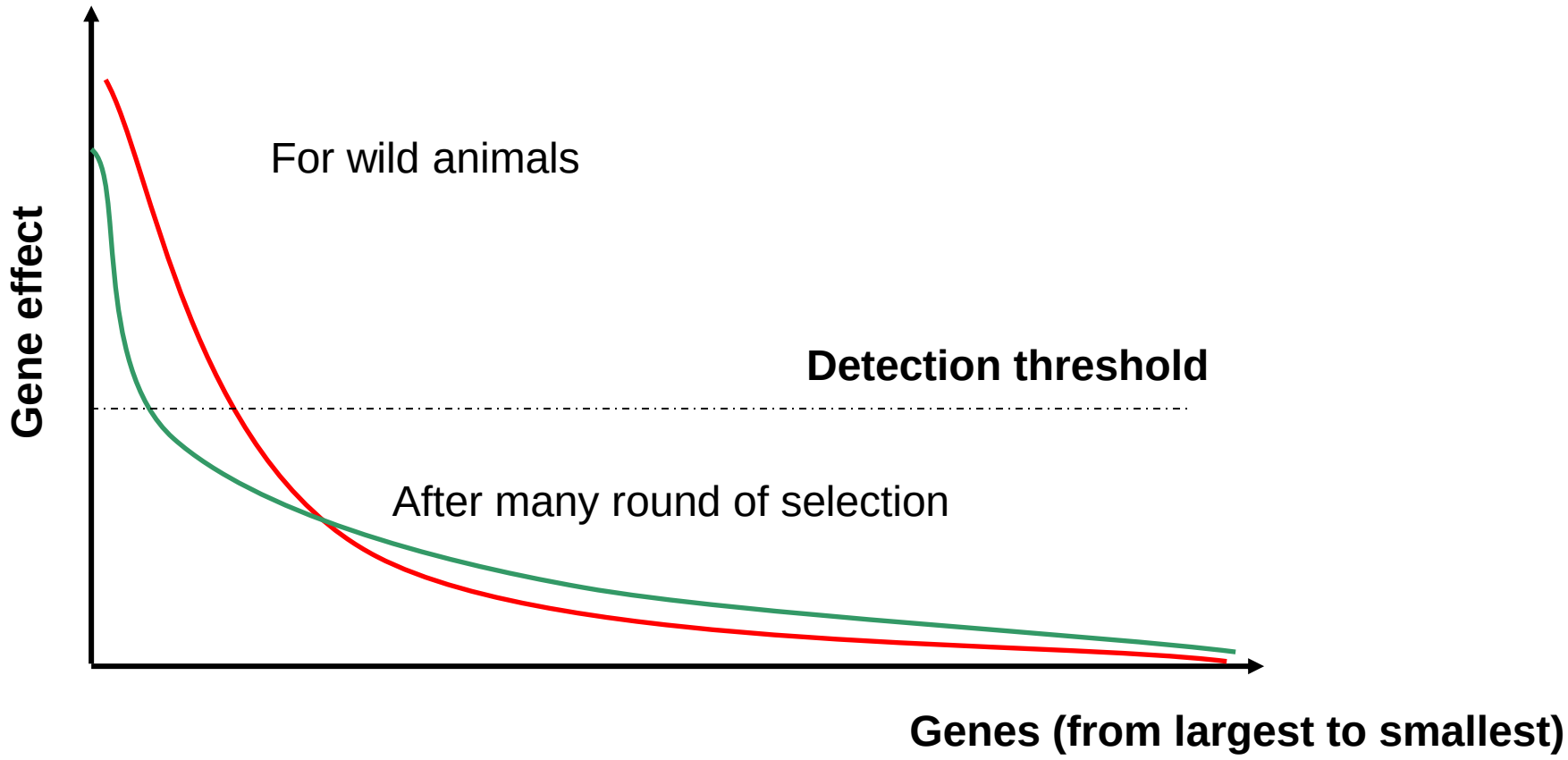


All SNP including QTN unweighted



QTN properly weighted

Distribution of QTL effects



Other factors

- Bayesian methods pick up large signals due to QTL, relationships and noise
  - If small signals undetected, probably large signals inflated

- Large signals without LD curves due to imputation errors (Li Ma, personal communication)

Conclusions

- QTN profile wide with small effective population size
  - Optimal window size 4 to 8 segments
  - About 1-2 Mb at Ne=100
- Sharp peak for QTN
- Large signals in GWAS due to QTN, relationships and noise and imputation
- Most QTNs probably below detection limit

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Acknowledgements

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