QUANTIFYING LD DECAY BY QUANTILE REGRESSION A CASE STUDY

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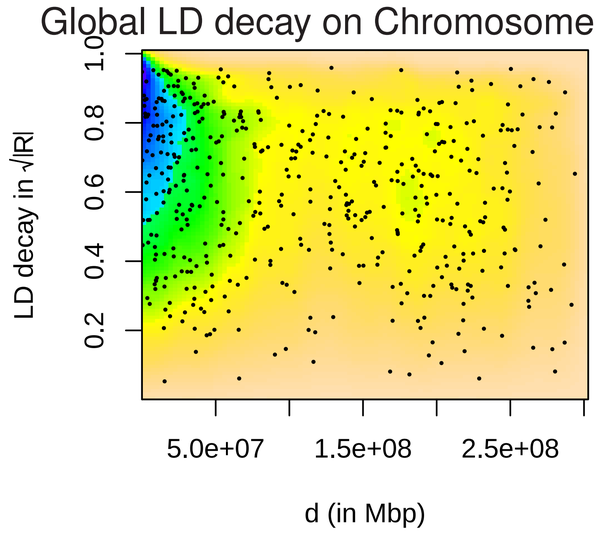
INTRODUCTION

- Genome-wide association studies: great tool for the localization of QTLs (quantitative trait loci) in plant and animal breeding programs.
- Investigation of the genetic relatedness (kinship matrix) required for powerful GWAS

  → Insight into LD between genetic markers necessary



- Find suitable set of independent markers
- Exploration of LD decay over the whole genome
- LD is commonly measured in terms of the squared Pearson correlation coefficient R^2 between pairs of genetic markers (HILL and ROBERTSON, 1968).

DATA AND VISUALIZATION

- Data from Maize population (FISCHER *et al.*, 2008), especially from Chromosome 1 with almost 5000 markers → more than 12 million pairwise comparisons
- For these large data: visualization is difficult in a scatterplot.
- Apply a scatterplot smoother (EILERS and GOEMAN, 2004)

  → computation of a two-dimensional histogram, smoothing of the counts and display with a color map
- In order to improve the quality of the fit and the visualization → use of $\sqrt{|R|}$ instead of Pearson's R^2.

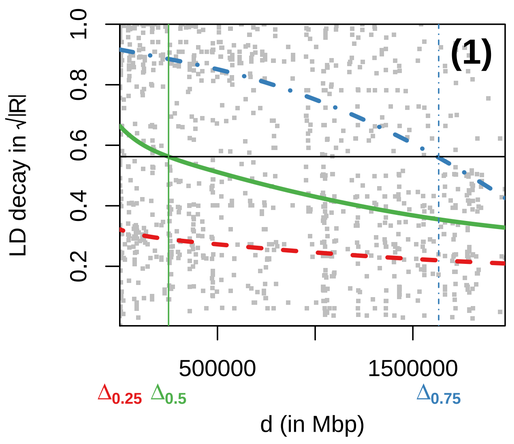
QUANTILE REGRESSION

- Using non-parametric quantile regression with a monotonicity constraint (BOLLAERTS *et al.*, 2006; MUGGEO *et al.*, 2013)
- Monotone decreasing curve is in line with biological assumptions.
- $\mu_\tau = s_\tau(d)$, μ_τ quantile function at percentile τ, d SNP distance between pairs of markers and $s_\tau(\cdot)$ smooth and unknown function
- $P-$splines for a smooth functional form, therefore:
  $\min \sum_k^K b_{k\tau} B_k(d)$ subject to $b_k < b_{k-1}$ for $k = 2, \ldots, K$, with $b_{k\tau}$ the coefficient of the B_k-th spline, K the dimension of the design matrix.

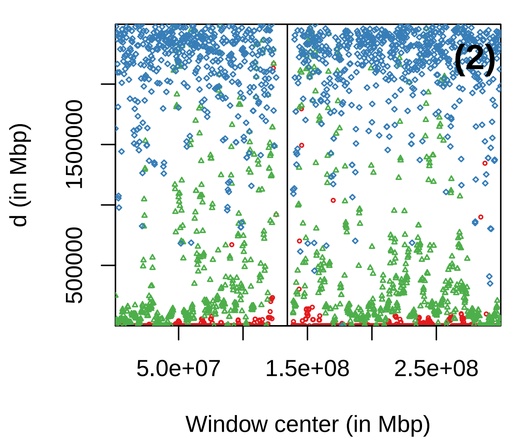
GLOBAL/LOCAL LD

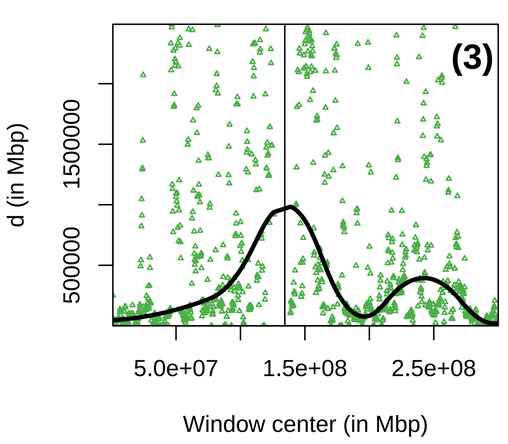
- Usually analysis focusses on the global LD decay (per chromosome) → general picture about the linkage desequilibrium and linkage between the markers
- Here: emphasis on local LD decay to get more insights on a smaller scale
  - Overlapping sliding windows of 2.5 Mbp → around 1000 windows on chromosome 1 with on average 2000 points per window
  - Fit a set of quantile curves to each of the windows (here $\tau = 0.25, 0.5, 075$)
  - Choose threshold T in terms of R^2 and collect the associated distances from whereon LD decay is lower than T

RESULTS



Some text





CONCLUSION AND DISCUSSION

- Case study of how to explore and quantify local LD decay patterns in Maize using quantile regression with monotonicity constraints for a first summary of the LD decay.
- Applying $P-$splines to smooth the median local LD decay → easy to interpret and inspect for the collaborating biologists
- In depth exploration of local LD decay (in comparison to global LD decay) leads to new insights.
- In addition to a good tool to quantify local LD decay → also an instrument in identifying problems with the underlying genotypic data that have previously been overlooked.
- Can serve as a diagnostic tool
  - Discovering of undercoverage through sliding windows with low sample sizes
  - Clustering of correlation values → unknown phenomenon in the data, adjustment in subsequent analysis

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