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Accuracy of fine mapping methods on selected populations: a simulation study

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Purpose of the study

- Factors influencing LD
  - Mutation
  - Random drift
  - Selection

→ LD at larger distances in animal populations

→Sensitivity of the fine mapping methods to selection ?

Methods

	Regression	HapIM	Terwilliger	LDLA	Cluster
Accounting for LD through …	-	Decrease of LD with the distance		IBD probabilities	
Use of the pedigree	No	No		Yes	
Supposed origin of LD	-	Unique causal mutation		Initial population in LE	
Statistical method	Regression	Maximum likelihood		Variance components	Regression
Molecular information used	Single markers	Haplotypes of 2 markers		Haplotypes of 4 markers	

Clustering method

- Clustering applied on IBD probabilities (Meuwissen and Goddard, 2001)

- Previously shown that no constant threshold for optimal clustering (Ytournel *et al*, 2007)

  → choice of a fuzzy clustering algorithm

Simulated populations

Founder population

Random drift,

Random mating,

(sélection)

Last generation of the historical population

15 sire families with 100 descendants per sire

Data

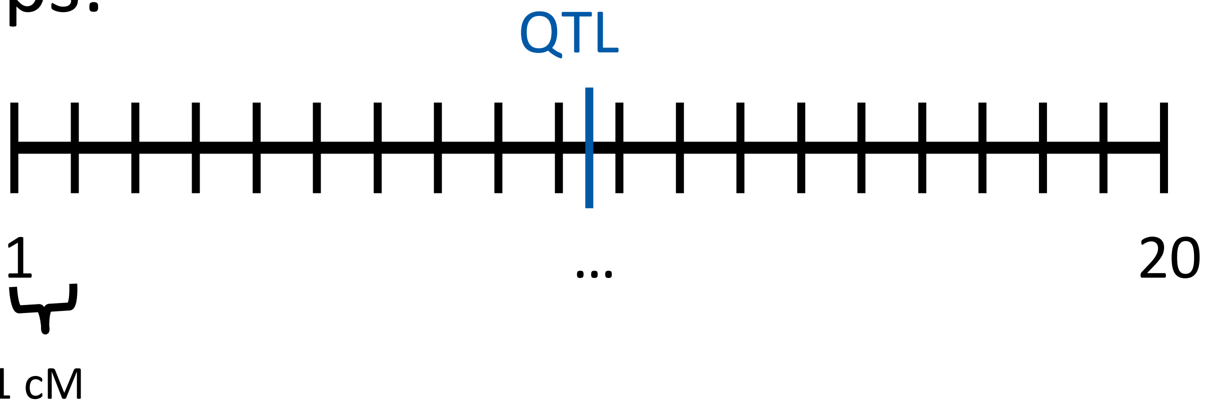
N=200

- 80 generations without selection
- 20 generations
    - without selection (No Selection, NS)
    - 80% of the individuals selected (Simple Selection, SS)
    - 80% of the individuals selected in the 10 first generations, then 50% (Double Selection, DS)

Genetic maps

- 2 maps:

- Sparse :



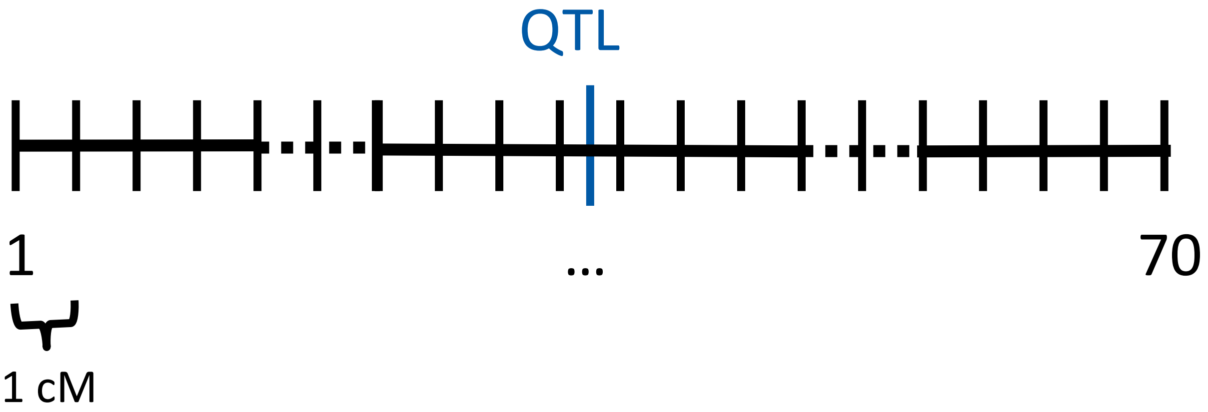
QTL

Locus 1 … 20

1 cM

5 alleles per locus

- Dense :



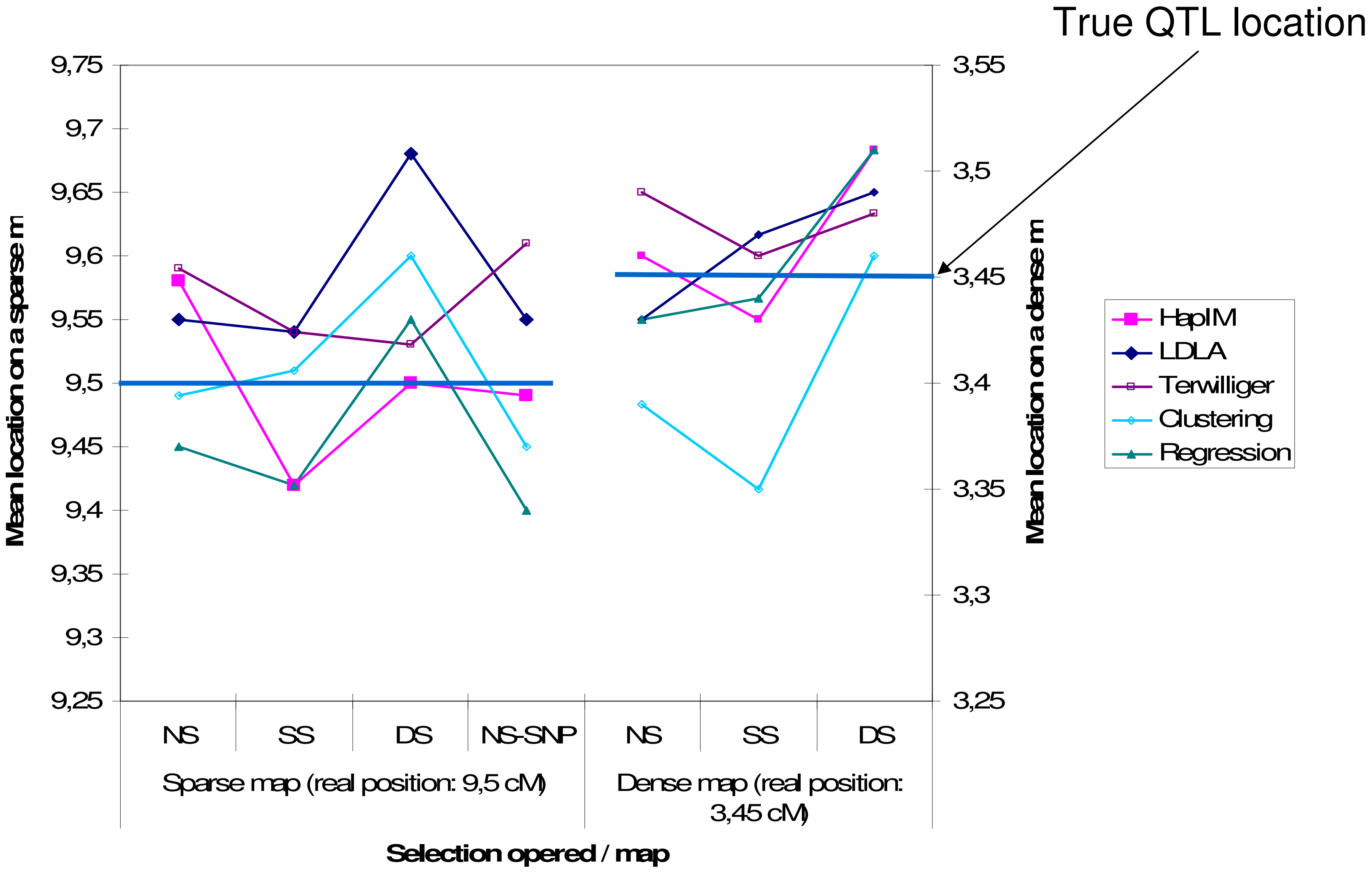
QTL

Locus 1 … 70

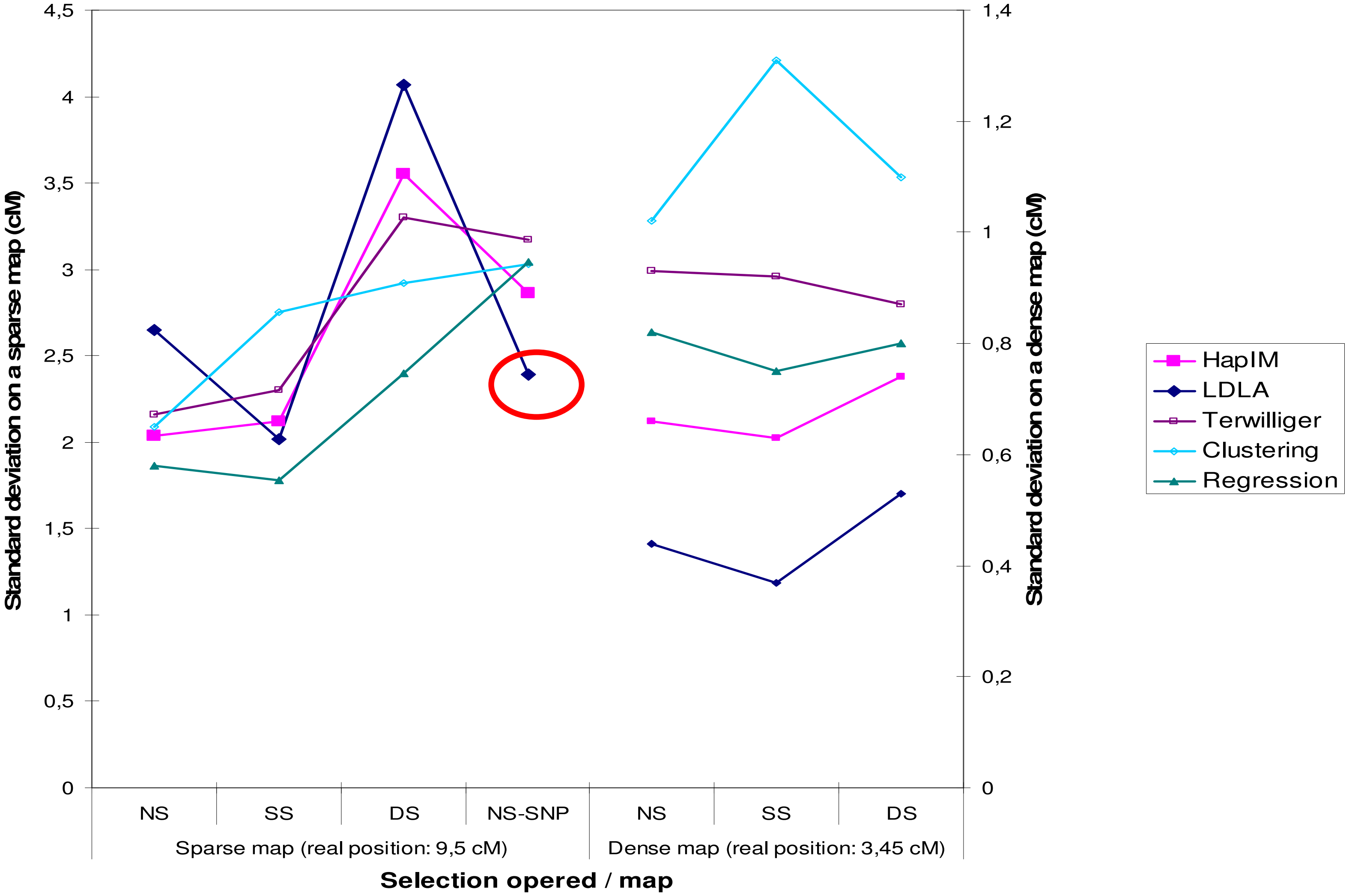
0,1 cM

2 alleles par locus

Results: mean location



Results: standard deviations



Discussion

- On average, QTL correctly detected

- No effect if “light“ selection
- But 10 generations of “strong“ selection → deleterious impact through increase of variability of the location detected

Discussion

- Regression on single markers = best on sparse map covered by multi-allelic markers

- But LDLA method = best when SNP are used, whatever the map density

- This Clustering does not have the qualities of full LDLA

Thank you
for your attention