FBN

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FOR FARM ANIMAL BIOLOGY

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Posterior Probabilities of Genome-Wide Associations in Backcross Families

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WPPA

WPPA – Window Posterior Probability of Association

$\overline{m}$ - Vector of means of estimated posterior marker effects
$\hat{m}$ - Vector of estimated marker effects in one MCMC iteration

$\overline{sq} = {\Sigma_i \overline{m}_i^2}/{p}$ - Expected genetic variance reflected by markers (ignoring Linkage Disequilibrium)

Ratio: $q = \frac{observation\ in\ iteration\ t}{expected\ variance}$

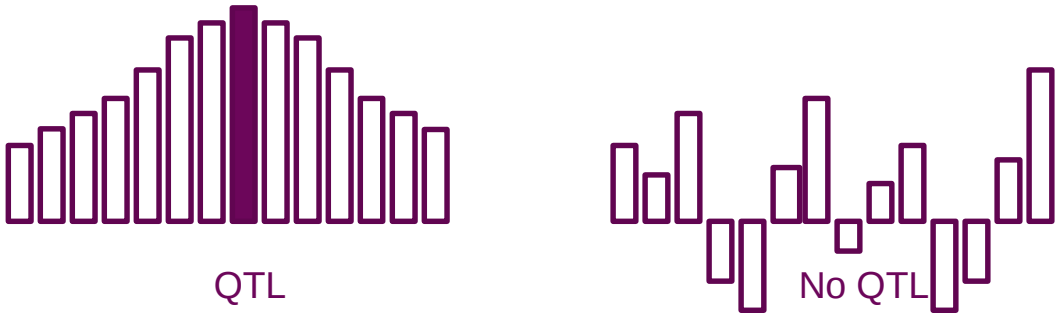
q is sampled
Posterior probabilities for q in a certain interval (window) is determined
$q > 1$ - Association

WPPA

Why windows?

Effect of a QTL is reflected by several adjacent markers jointly

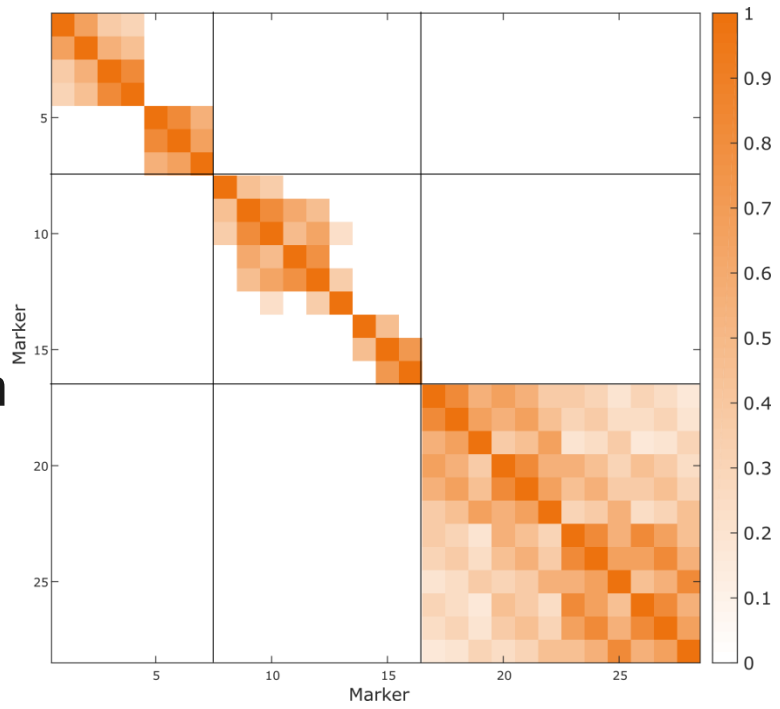
Marker effects



Windows reflect the effect of chromosome segments
No Linkage Disequilibrium – no covariance between markers is considered

WPPA-R

- In certain types of populations linkage disequilibrium is large and wiedespread across chromosomes
- Such as in a backcross between inbred lines
- Covariance matrix $\boldsymbol{R}$ can be defined (Bonk et al., 2016)
- Reflects genetic distances between markers
- Linkage phase of markers in parents



WPPA-R

Matrix of thresholds
Example: 4 markers, equal distances of 0.01 M

$$\boldsymbol{R} = \begin{bmatrix} 1 & 0.98 & 0.96 & 0.94 \\ 0.98 & 1 & 0.98 & 0.96 \\ 0.96 & 0.98 & 1 & 0.98 \\ 0.94 & 0.96 & 0.98 & 1 \end{bmatrix}$$

$$\boldsymbol{T} = \boldsymbol{R}^0 \cdot \overline{cp} + \boldsymbol{I} \cdot \overline{sq} = \begin{bmatrix} 0 & 0.98 & 0.96 & 0.94 \\ 0.98 & 0 & 0.98 & 0.96 \\ 0.96 & 0.98 & 0 & 0.98 \\ 0.94 & 0.96 & 0.98 & 0 \end{bmatrix} \cdot \overline{cp} + \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \cdot \overline{sq}$$

$\overline{sq} = {\sum_i \bar{m}_i^2}/{p}$ (average genetic variance per marker)

$\overline{cp} = {\sum_i \sum_j \bar{m}_i \bar{m}_j}/{(p^2 - p)}$ (total covariance is equally distributed across all marker combinations)

WPPA-R

Matrix of threshold values for windows
Example: 3 markers in a window, 4 windows

$$\boldsymbol{K} = \begin{bmatrix} 1 & 1 & 0 & 0 \\ 1 & 1 & 1 & 0 \\ 0 & 1 & 1 & 1 \\ 0 & 0 & 1 & 1 \end{bmatrix}$$

$$\boldsymbol{T}_w = \boldsymbol{K}' \cdot \boldsymbol{T} \cdot \boldsymbol{K}$$

Matrix of expected variances and covariances of all defined windows and their combinations

WPPA-R

Observation in MCMC iteration t, estimated marker effects $\hat{m}_i$
Example: 3 markers in a window, 4 windows

$$\boldsymbol{K}_t = \begin{bmatrix} \hat{m}_1 & \hat{m}_1 & 0 & 0 \\ \hat{m}_2 & \hat{m}_2 & \hat{m}_2 & 0 \\ 0 & \hat{m}_3 & \hat{m}_3 & \hat{m}_3 \\ 0 & 0 & \hat{m}_4 & \hat{m}_4 \end{bmatrix}$$

$$\boldsymbol{T}_{wt} = \boldsymbol{K}_t' \cdot \boldsymbol{R} \cdot \boldsymbol{K}_t$$

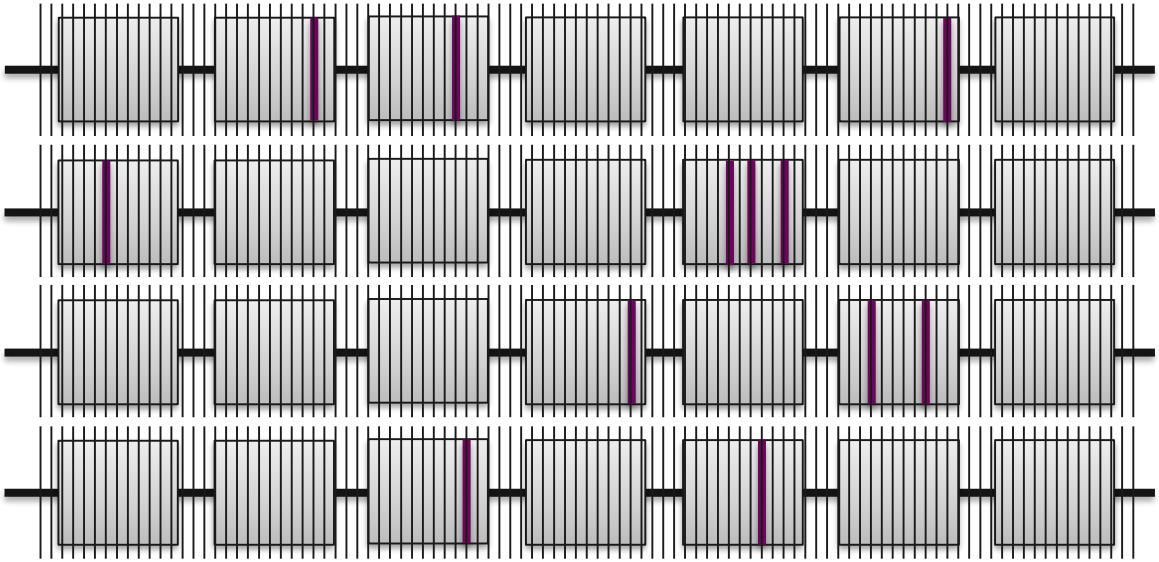
Matrix of observed variances and covariances of all defined windows and their combinations

Simulation

„Mouse“ genome

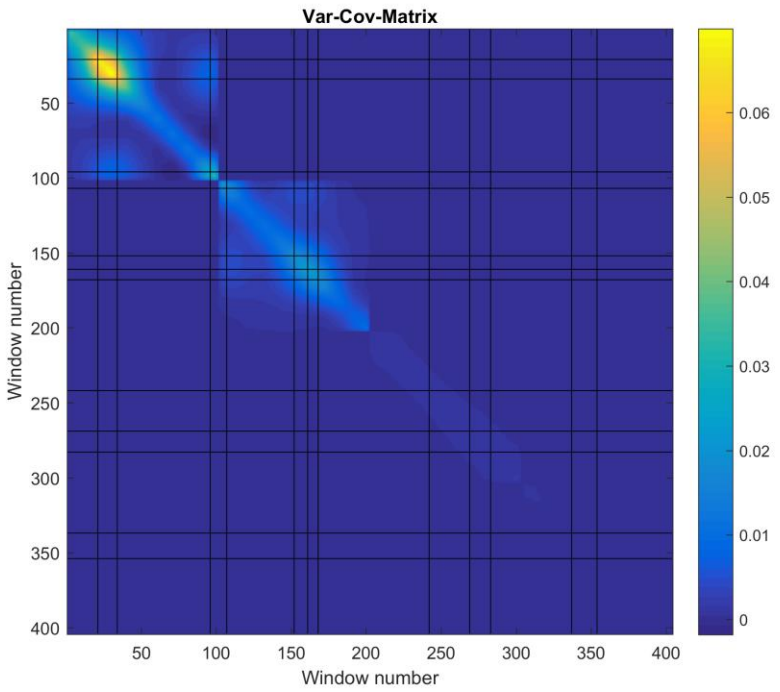
20 chromosomes

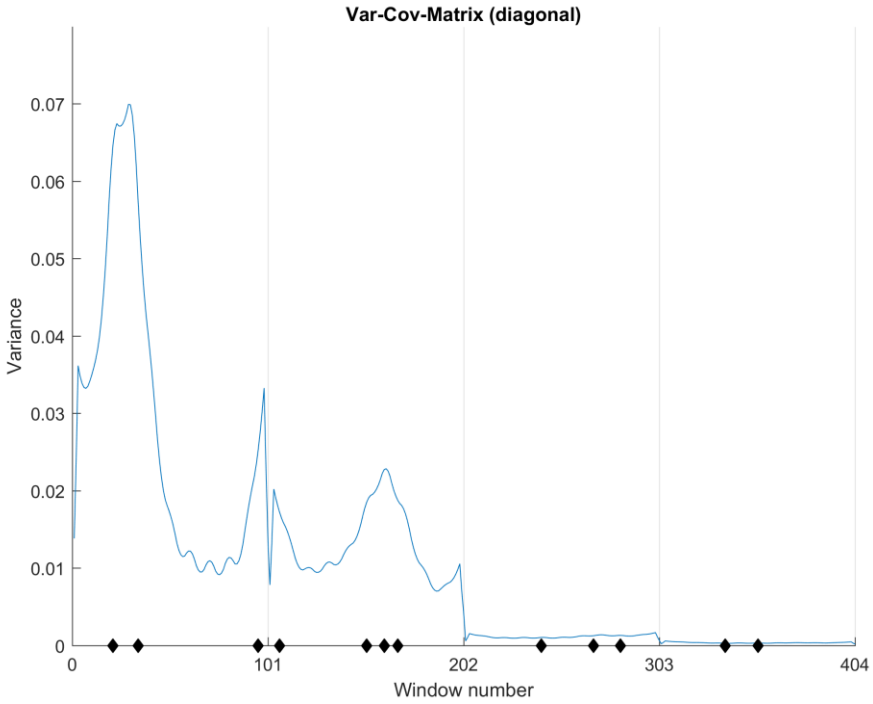
Length of 1 M
101 equally spaced markers
12 QTLs
Heritabilities $h^2 \in \{0.17,\ 0.29,\ 0.70\}$
200 experiments



Simulation $h^2 = 0.17$

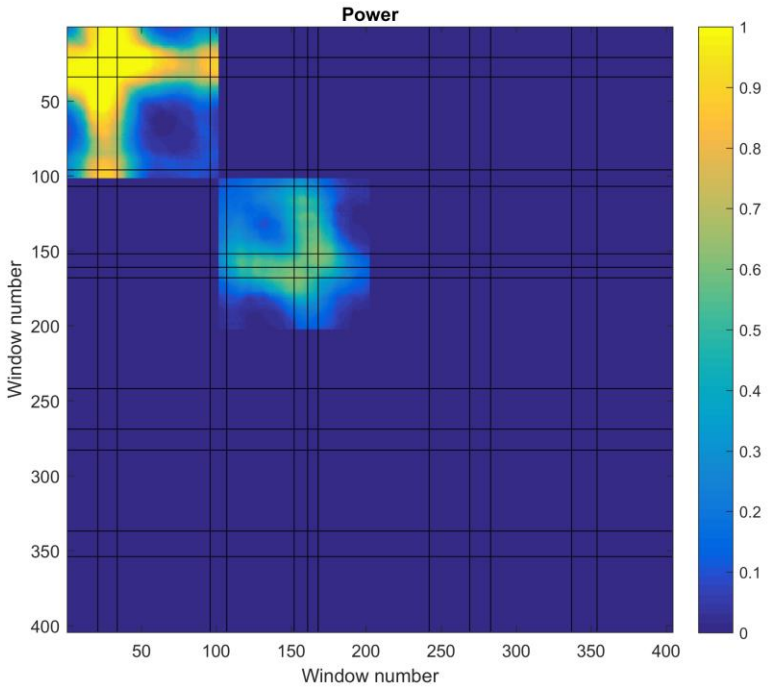
Mean (over all repetitions) estimated variances and covariances

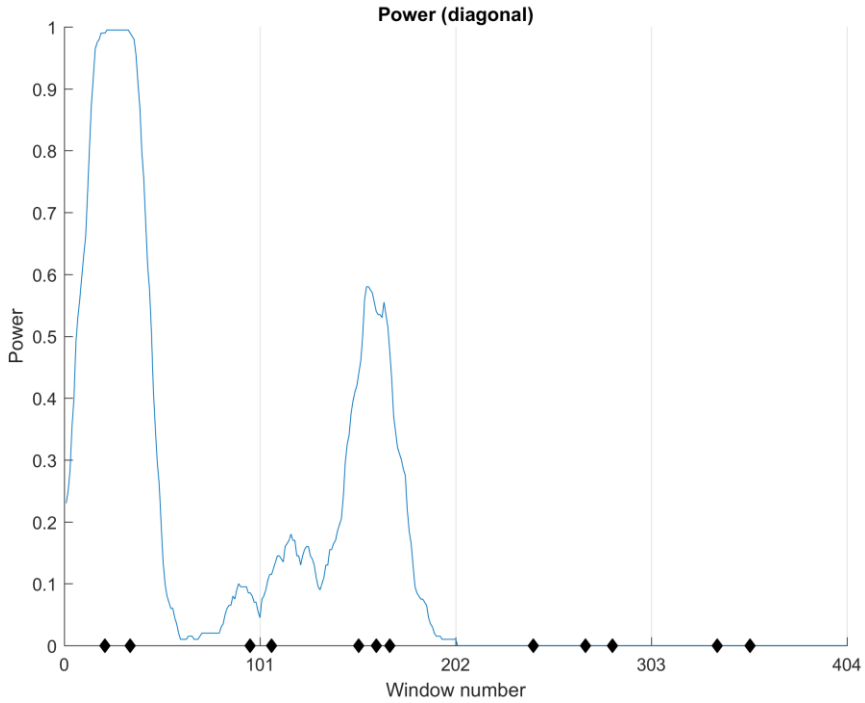




Simulation $h^2 = 0.17$

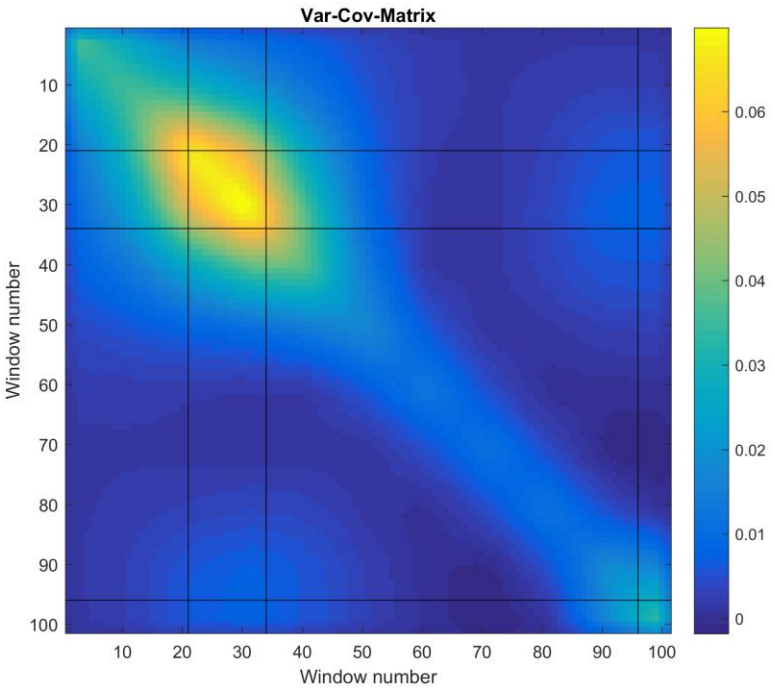
Mean (over all repetitions) posterior probabilities to exceed the threshold („Power“)



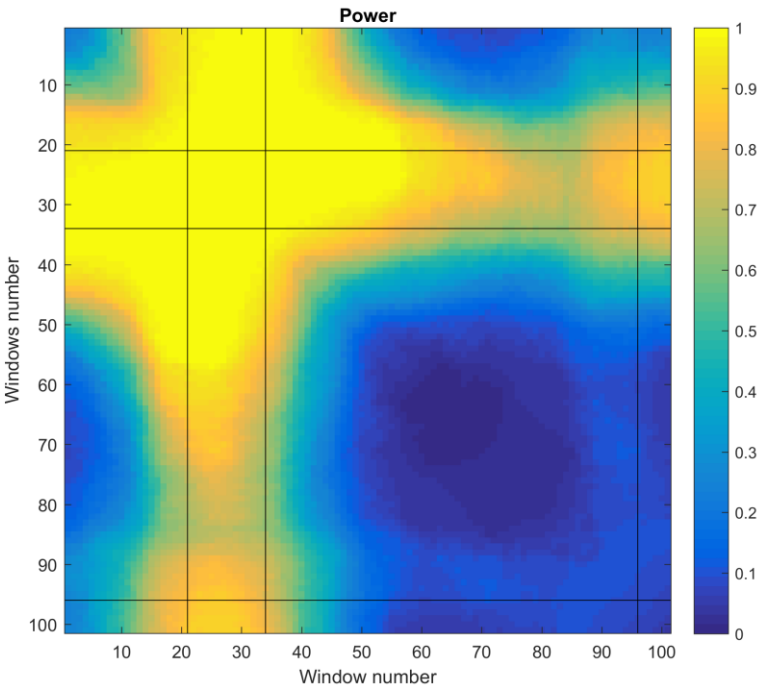


Simulation $h^2 = 0.17$

Estimated variances and covariances



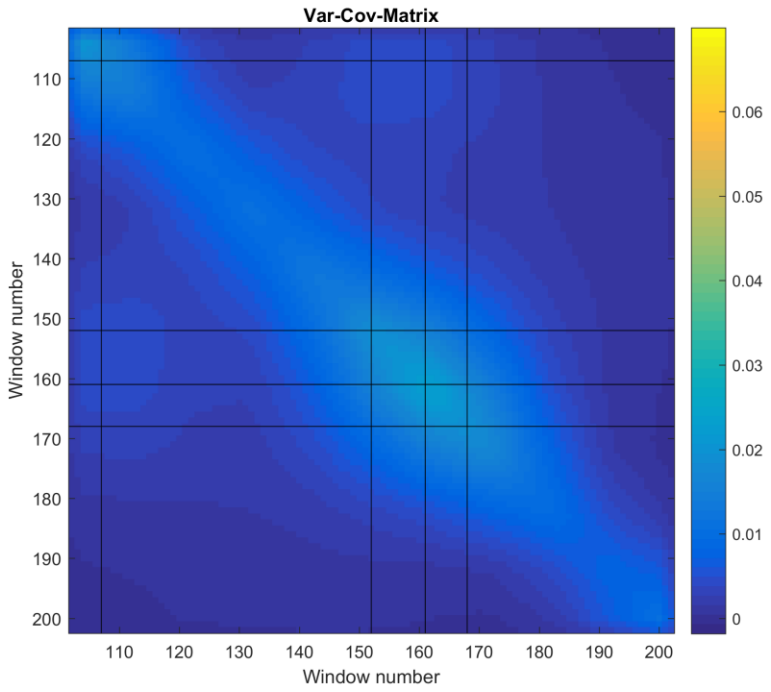
Posterior probabilities



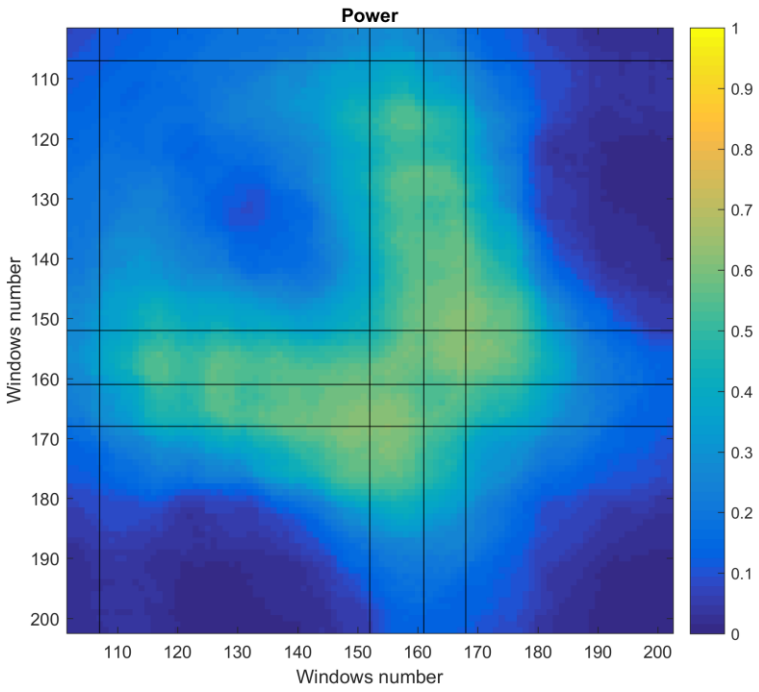
First chromosome: 3 marker effects: 2.0, 2.0, 1.0

Simulation $h^2 = 0.17$

Estimated variances and covariances



Posterior probabilities



Second chromosome: 4 marker effects: 1.0, 1.0, 0.5, 1.0

Simulation $h^2 = 0.17$

scenario			Max. Power Chr. 1 (3 marker effects: 2.0, 2.0, 1.0)			Max. Power Chr. 2 (4 marker effects: 1.0, 1.0, 0.5, 1.0)		
Nr.	h^2	cM	IN	IB_{1_w}	DB_{1_w}	IN	IB_{1_w}	DB_{1_w}
1	0.17	5	0.07	0.98	1.00	0.02	0.39	0.67
2	0.17	1	0.01	0.66	1.00	0.01	0.16	0.58
4	0.29	5	0.23	1.00	1.00	0.03	0.73	0.94
5	0.29	1	0.02	0.92	1.00	0.01	0.38	0.87
7	0.70	5	0.98	1.00	1.00	0.37	1.0	1.0
8	0.70	1	0.15	1.00	1.00	0.03	0.95	1.0

Simulation $h^2 = 0.17$

scenario			Max. Power Chr. 1 (3 marker effects: 2.0, 2.0, 1.0)			Max. Power Chr. 2 (4 marker effects: 1.0, 1.0, 0.5, 1.0)		
Nr.	h^2	cM	IN	IB_{1_w}	DB_{1_w}	IN	IB_{1_w}	DB_{1_w}
1	0.17	5	0.07	0.98	1.00	0.02	0.39	0.67
2	0.17	1	0.01	0.66	1.00	0.01	0.16	0.58
4	0.29	5	0.23	1.00	1.00	0.03	0.73	0.94
5	0.29	1	0.02	0.92	1.00	0.01	0.38	0.87
7	0.70	5	0.98	1.00	1.00	0.37	1.0	1.0
8	0.70	1	0.15	1.00	1.00	0.03	0.95	1.0

Conclusions and Outlook

- Different methods can be analysed and compared with the same calculations

- Three methods are known:
  1. Inferences drawn of posterior probabilities of marker effects
  2. WPPA
  3. WPPA-R

- Better visualisation of the representation of the genetic architecture with WPPA and WPPA-R

- Covariances help with the analysis of this architectures

Thank you for your attention!

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Literature:

- **Bonk S.**, Reichelt M., Teuscher F., Segelke D., Reinsch N. (2016): *Mendelian sampling covariability of marker effects and genetic values.* Genet Sel Evol 48: 36

- **Fernando R.L.**, Toosi A., Garrick D.J., Dekkers J.C.M. (2014) Application of Whole-Genome Prediction Methods for Genome-Wide Association Studies: a Bayesian Approach. Proceedings of the 10th World Congress of Genetics Applied to Livestock Production, 17-22 August, Vancouver, BC, Canada, 201

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