Grapevine Breeding and Genetics – 17/07/2018

Genome-wide association study of a diverse grapevine panel to uncover the genetic architecture of numerous traits of interest

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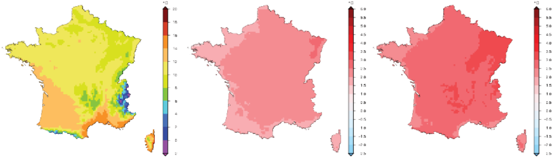
Multiple changes and challenges

Reduce pesticides

Adapt to climate change

ref. T° in 1970 pred. T° in 2055 pred. T° in 2085



ARPEGE model

Major questions to biologists:

1. how to phenotype the eco-physiological processes of interest?
2. what are their genetic architectures?
3. how to incorporate them into breeding programs?

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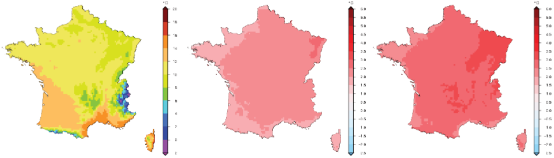

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2. **what are their genetic architectures?**
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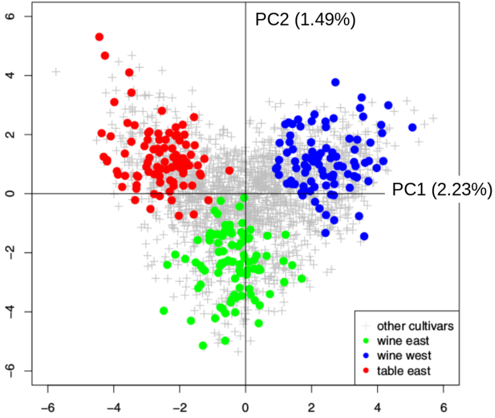
Diversity panel of *Vitis vinifera* L. from Domaine de Vassal

Beside bi-parental populations ⇒ 279 cultivars (weak structure)



Nicolas *et al.* (2016)

Field layout at Domaine du Chapitre

2009: overgraft on Marselan (control)

- 5 complete randomized blocks
- each genotype has 1 replicate per block

Intense phenotyping effort

2010-2012

- Traits: mean berry weight; mean bunch weight, length and compactness; pruning weight and number of woody shoots; malate, tartrate, shikimate; δ^{13}C
- Additional covariates: vigour, sanitary status
- No irrigation

2014-2015

- Traits: mean berry weight; δ^{13}C; β-damascenone and pDMS; polyphenols (Pinasseau *et al.*, 2017)
- Treatment: with or without irrigation

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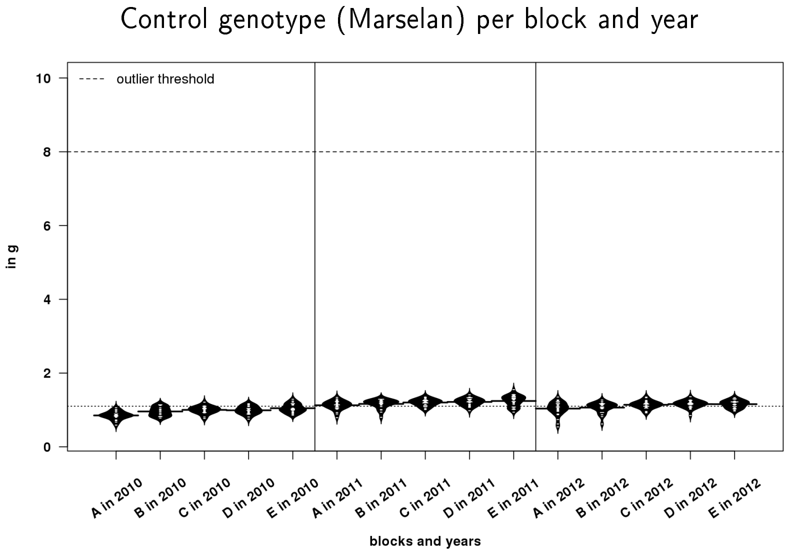
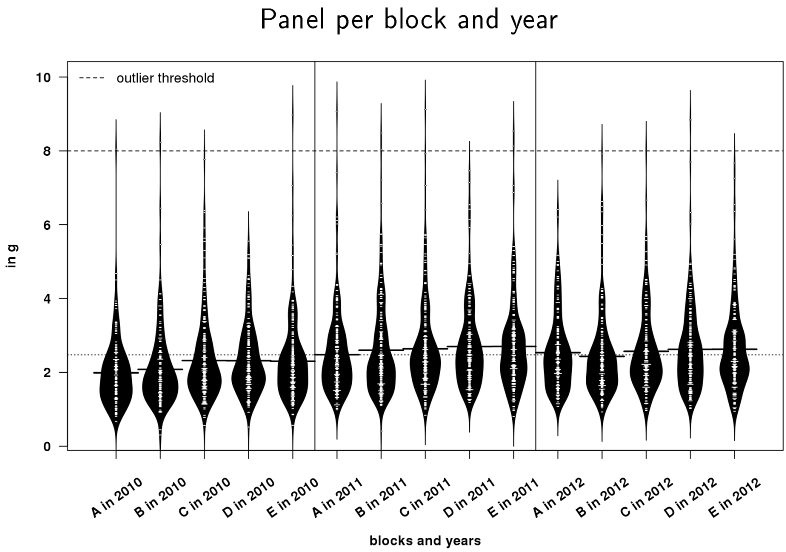
$\Rightarrow$ Focus on **mean berry weight** (2010-2012)

Mean berry weight: exploratory analysis of phenotypes



Mean berry weight: exploratory analysis of phenotypes



Mean berry weight: exploratory analysis of phenotypes

Dual genotyping

- GrapeReSeq microarray (Illumina): 12k SNPs after QC
- GBS with ApeKI enzyme (Keygene): 120k SNPs after QC
- **Combined: 90k SNPs** with LD < 0.9 and MAF > 0.01

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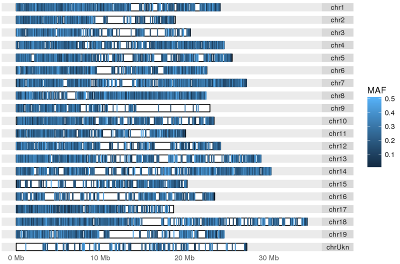
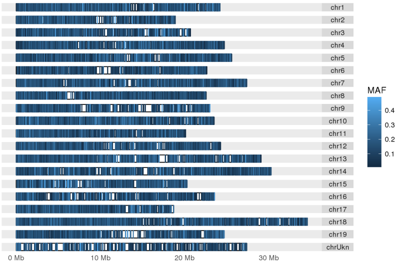
11k SNPs

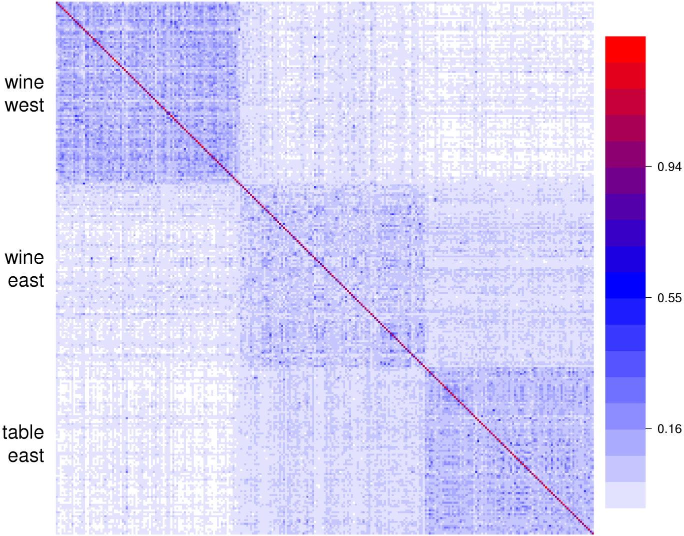


90k SNPs



$\Rightarrow$ **Densification** required to tag all/most causal polymorphisms

Kinship matrix from SNPs (additive genetic relationships)



Statistical analysis of phenotypic data

$$\boldsymbol{y} = X\boldsymbol{\beta} + Z\boldsymbol{g} + \boldsymbol{\epsilon} \text{ with } \boldsymbol{g} \sim \mathcal{N}(\mathbf{0}, \sigma_g^2 \, \text{Id}); \boldsymbol{\epsilon} \sim \mathcal{N}(\mathbf{0}, \sigma^2 \, \text{Id})$$

- $\boldsymbol{y}$: phenotypic observations
- $\boldsymbol{\beta}$: effects of known factors, modeled as "fixed"
- $\boldsymbol{g}$: total genotypic values, modeled as "random"
- $\boldsymbol{\epsilon}$: errors
- $H^2 = \frac{\sigma_g^2}{\sigma_g^2 + (\sigma^2 / \#rep)}$: broad-sense heritability (of means)

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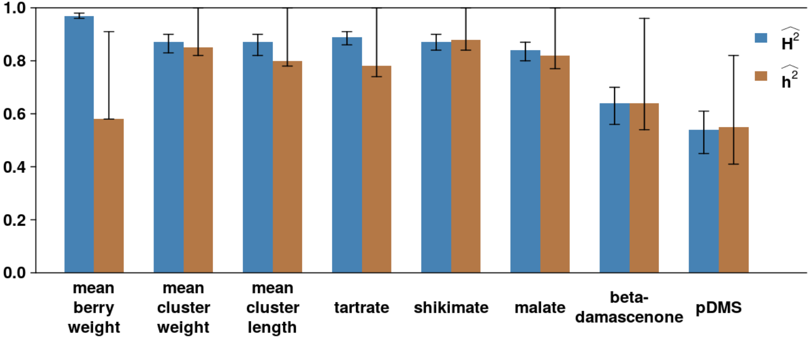
$$\boldsymbol{y} = X\boldsymbol{\beta} + Z\boldsymbol{a} + \boldsymbol{\epsilon'} \text{ with } \boldsymbol{a} \sim \mathcal{N}(\mathbf{0}, \sigma_a^2 \, A); \boldsymbol{\epsilon} \sim \mathcal{N}(\mathbf{0}, \sigma'^2 \,\text{Id})$$

- A: kinship matrix of additive genetic relationships
- $\boldsymbol{a}$: additive genotypic values (a.k.a. *breeding values*)
- $h^2 = \frac{\sigma_a^2}{\sigma_g^2 + (\sigma^2 / \#rep)}$: narrow-sense heritability (of means)

Estimation of heritabilities

H^2: higher, better $\rightarrow$ $\boldsymbol{g}$ well approximated by its BLUP

h^2: higher, better $\rightarrow$ σ_a^2 large enough for selection purposes



Statistical analysis of genotypic values

SNP-by-SNP: *ad hoc*

$$\text{BLUP}(\boldsymbol{g}) = \mathbf{1}\mu + \boldsymbol{m}_p \beta_p + \boldsymbol{u} + \epsilon$$

- β_p: effect of the p^{th} SNP $\rightarrow$ **test if** $\beta_p = 0$
- $\boldsymbol{u}$: polygenic effect with kinship matrix $K \propto MM^T$

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Multi-SNP: explicit modelling of the genetic architecture

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Multi-SNP: explicit modelling of the genetic architecture

$$\text{BLUP}(\boldsymbol{g}) = \mathbf{1}\mu + M\boldsymbol{\beta} + \boldsymbol{\epsilon}$$

- fully polygenic: all $\beta_p \neq 0$
- major QTLs only: few $\beta_p \neq 0$ and all others $= 0$
- hybrid: all $\beta_p \neq 0$ and few $\tilde{\beta}_p \neq 0$

Estimation of hybrid genetic architectures

PVE: proportion of variance of total genotypic values explained by the polygenic component *and* the major QTL effects

- higher → better to predict genotyping values

PGE: proportion of PVE explained *only* by major QTL effects

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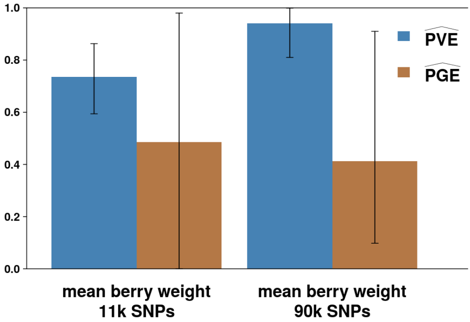
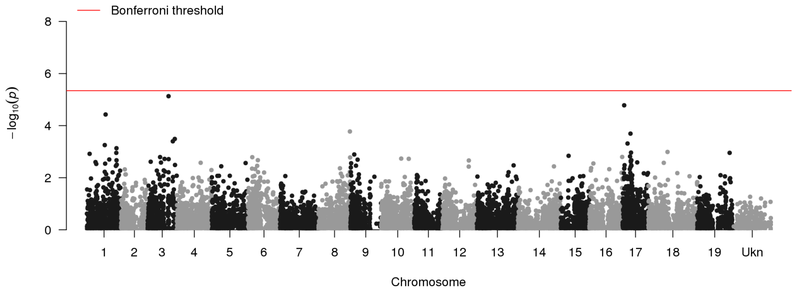


trait	#SNPs	*med*(#QTLs)
mbw	11k	31 [0,169]
mbw	90k	14 [2,115]

- importance of genotyping densification
- large amount of genetic variance from polygenic component

Mean berry weight: SNP-by-SNP versus multi-SNP

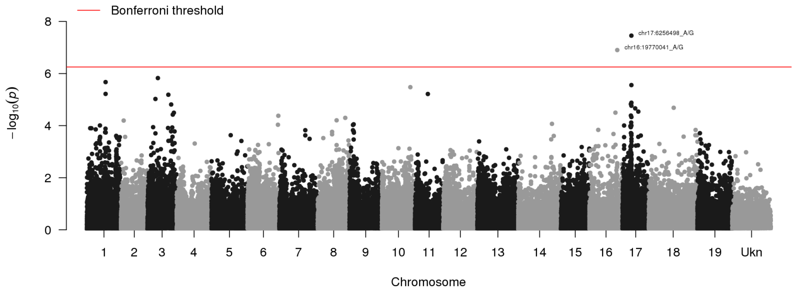
SNP-by-SNP with 11k SNPs



⇒ **genotyping not dense enough**

Mean berry weight: SNP-by-SNP versus multi-SNP

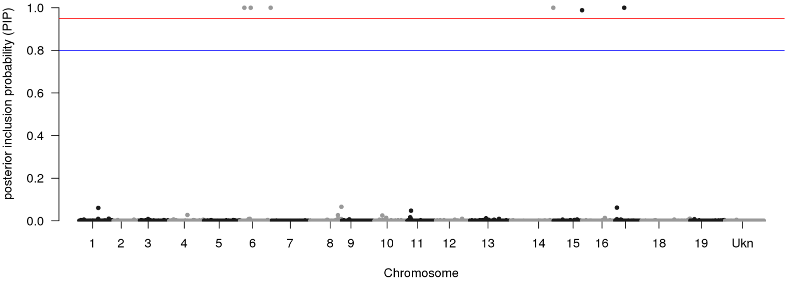
SNP-by-SNP with 90k SNPs



⇒ **dense enough to find two significant SNPs**

Mean berry weight: SNP-by-SNP versus multi-SNP

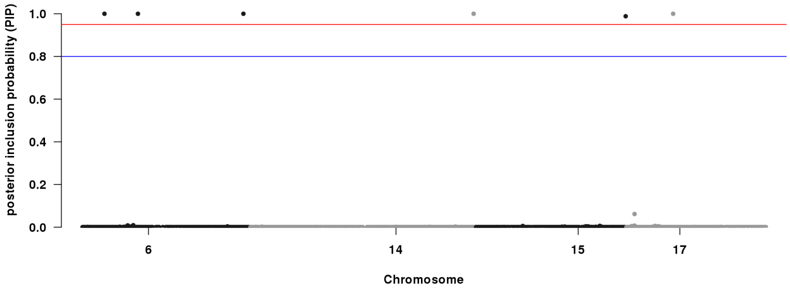
Multi-SNP (major QTLs only) with 90k SNPs



⇒ **more power to find six SNPs tagging putative QTLs**

Mean berry weight: SNP-by-SNP versus multi-SNP

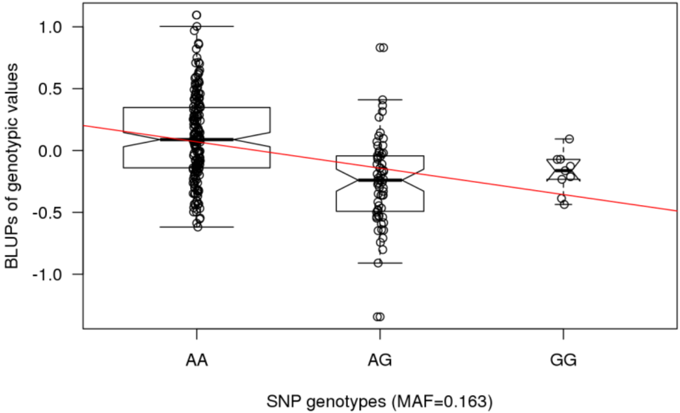
Focus on the selected SNPs



- $\widehat{\text{PVE}} = 0.668 \quad [\,0.613, \, 0.735\,]$
- need to define QTLs around selected SNPs

Mean berry weight: selected SNPs

SNP #1 at ≈ 6.3 Mb on chr17 (overlap known QTLs)

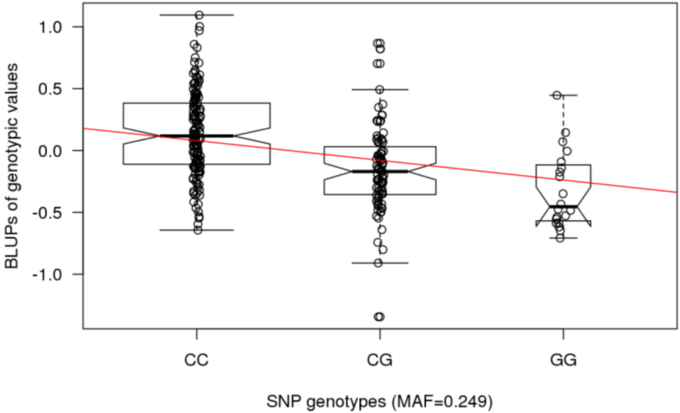


$\Pr(\widehat{\beta_p \neq 0}) = 1$; $\widehat{\text{PVE}}_p = 0.094$; $\widehat{\beta}_p = -0.213$; $\text{CI}_{95\%} = [-0.263, -0.163]$

location: coding of `Vitvi17g00537`, (-)-isopiperitenol/(-)-carveol dehydrogenase, mitochondrial

Mean berry weight: selected SNPs

SNP #2 at ≈ 29.9 Mb on chr14



$\text{Pr}(\widehat{\beta_p \neq 0}) = 0.999$; $\widehat{\text{PVE}}_p = 0.074$; $\widehat{\beta}_p = -0.159$; $\text{CI}_{95\%} = [-0.202, -0.117]$

location: promoter of `Vitvi14g02008`, uncharacterized

Prospects with the panel

Phenotyping:

- improved phenotyping of berry physiology (poster 49); tolerance to pathogens (poster 57)
- phenotyping in multiple sites and greenhouses to study GxE

Genotyping:

- capture-based sequencing of GBS-defined SNPs
- search for traces of selection

Modeling:

- genomic prediction to speed-up selection (poster 82)
- multi-pop/-trait statistical analysis (ongoing work)

Take-home message

With **dense** genotyping and **multi-SNP** models,
the **diversity panel** of *V. vinifera* L.
from INRA Montpellier
allows estimating the **genetic architecture** of
numerous traits of interest,
to help design efficient **breeding** strategies.

- diversity panel: virus-free and available
- data and reproducible analyzes: available upon publication
- contact: Agnès Doligez (`agnes.doligez@inra.fr`)

Acknowledgments

- DAAV team from the UMR AGAP
- Vassal-Montpellier grapevine biological resources center
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- AGAP genotyping platform (notably P. Mournet)
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