An overview of GWP in animals (and plants)

...

Evangelina López de Maturana & Oscar González-Recio

Something you need to carefully look at, or that may impair your GWP

Something to do, or that optimizes your GWP

Don’t. Discourage to use this.

Smart tip. Something that makes the trick.

Advanced. Something to dive in.

Challenges

What you need to know from this lecture

Basic concepts

Challenges

Interpret what a GWP implies

Genotyping strategies

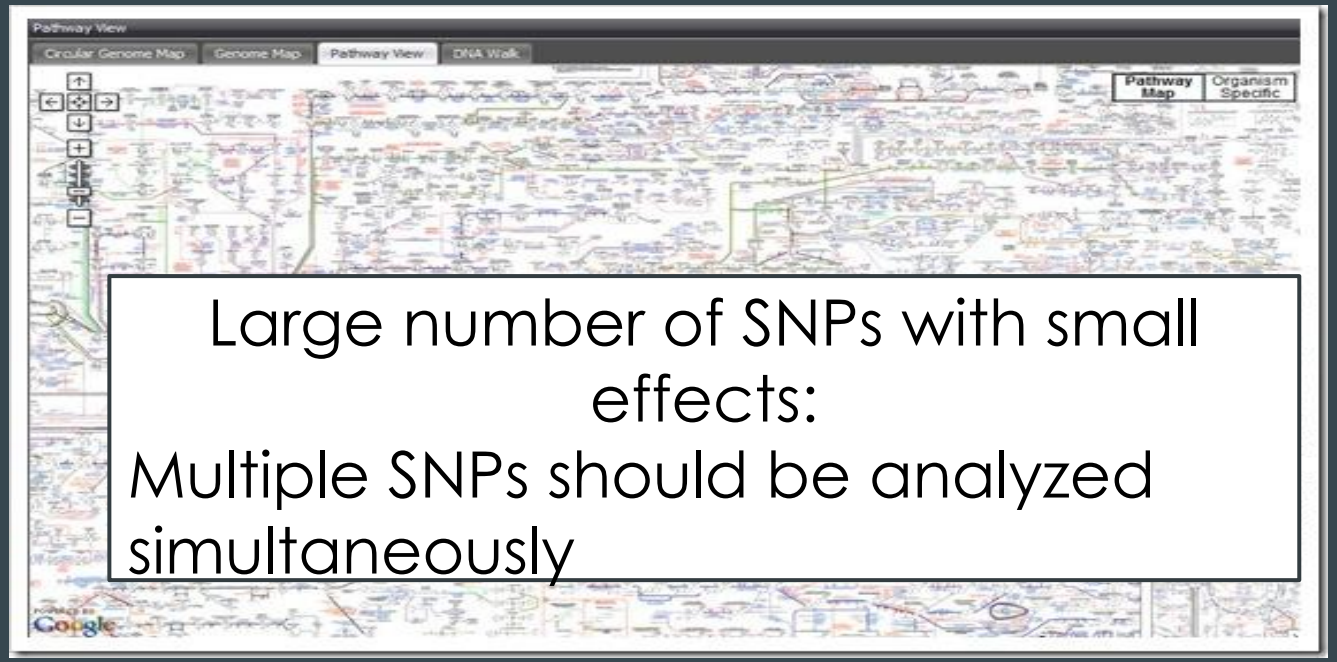
Phenotyping strategies

Objective of GWP in animals

1. Objective of GWP in animals

- Estimate breeding values using genomic markers (on high density)
  - To increase EBV reliability
  - To increase predictive accuracy
  - Lack of pedigree
- Rank animals for breeding purposes
- Predict phenotypes
  - Under a specific environments
  - GxE

2. Challenges of GWP

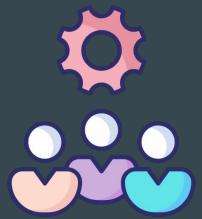


2. Challenges of GWP

- Need large populations with phenotypic and genomic data to train the statistical models
  - We are working with a statistical association
  - Need variability in genetic markers
  - Need phenotypic (**and** genetic) variation
  - Link marker effects to phenotypes
  - Large dimensionality problem

2. Challenges of GWP

- The phenotypic trait may be influenced (confounded) by environmental factors
- The trait may not follow a gaussian distribution
- Large or combined populations may
  - Have different phenotyping criteria
  - Have different genotyping/sequencing criteria (chip density, genotyping strategy, ...)



Standardized procedures are a must

During the **experimental design** ✅ or data management procedures ⚠️

3. What information is necessary

- Phenotypes
- Genetic markers
- Environmental confounders

REFERENCE POPULATION

CANDIDATE POPULATION

- Genetic markers
- Environmental confounders (same ones as in the reference population)

Reference population

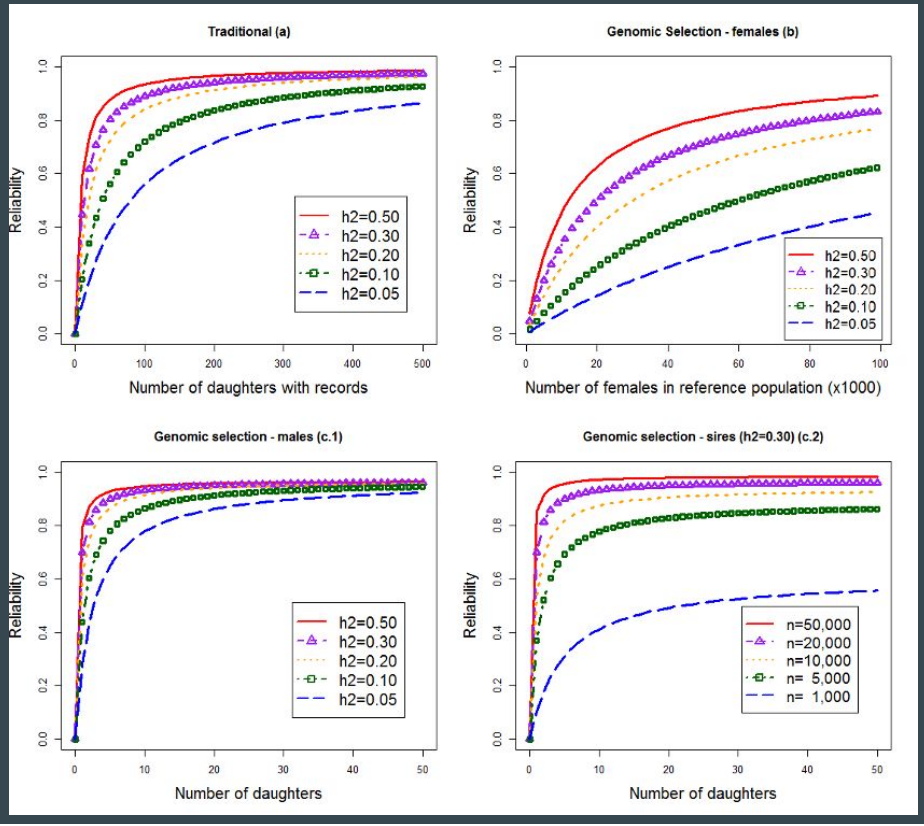
A Reference population is needed in Genome-wide prediction to train the statistical models

- Genotypes and phenotypes
- Statistical association between genotypes and phenotypes
  - Covariates
  - Genomic relationship
- Genomic predictions may be achieved in individuals without phenotype (but w/ genotypes) ←Candidate population

Strategies for phenotyping

Cost-benefit function

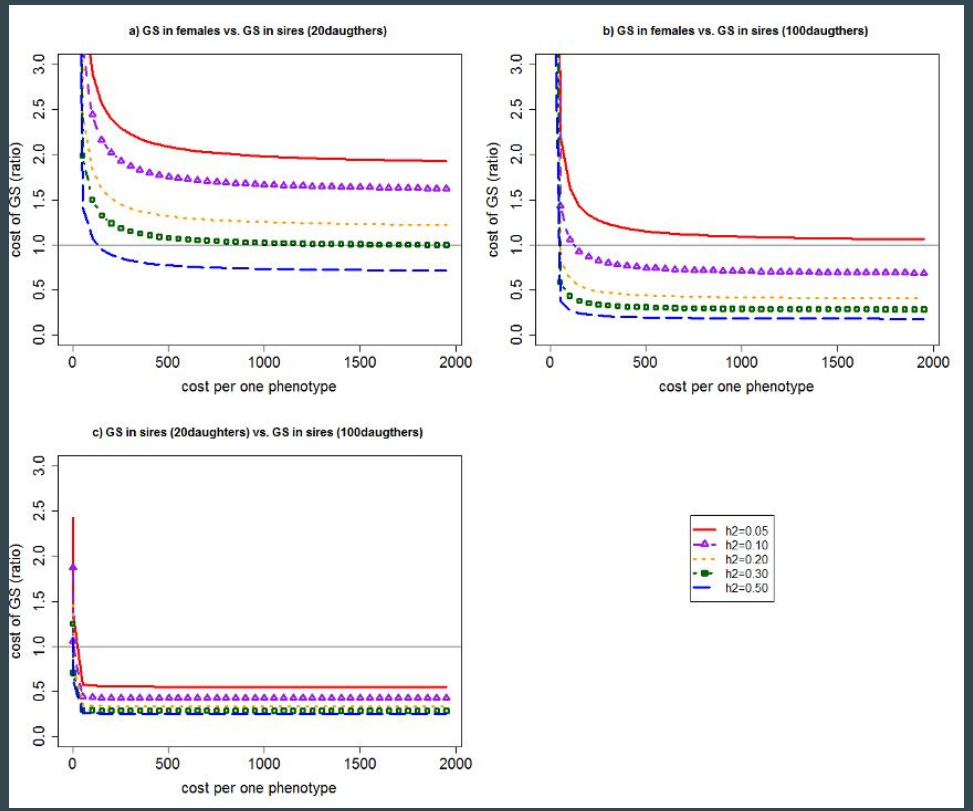
- How much phenotyping cost vs how much prediction accuracy is gained (trait dependent)



Strategies for phenotyping

Cost-benefit function

- Cost of phenotype influences the genotyping strategy (parents vs individuals)



Strategies for phenotyping

Cost-benefit function

- Traits easy to measure
  - Use progeny tests and genotype parents
  - Establish a routine phenotype recording
- Traits difficult to measure and expensive
  - Use individual phenotype and record
  - Experimental conditions

⚠️(This rule of thumb may not work in human medicine, depending on the importance of the trait)

Strategies to obtain genetic marker information in populations

→Whole Genome Sequencing (WGS)

→Genotyping chips (SNPchips)

→Restriction site-associated DNA sequencing (RADseq)

→Genotype by low-pass sequencing (skim-Seq)

Strategies to obtain genetic marker information in populations

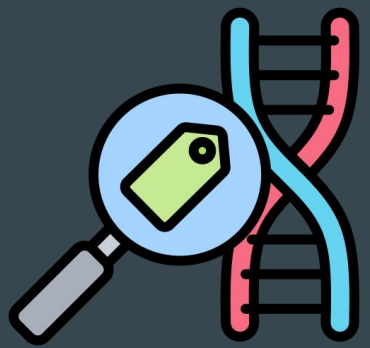
→Whole Genome Sequencing (WGS)

- Next generation sequencing
- Wide range of genetic variants (SNP, Indels, CNV, Structural Variants)
- High cost

Strategies to obtain genetic marker information in populations

→Genotyping arrays

- Most used / Widely implemented
- Large variety (species and densities)
- Most available from sequencing services /labs
- SNP + short indels
- Biallelic markers



Strategies to obtain genetic marker information in populations

→Genotyping arrays

Microarray
For Research Use Only
DNA

BovineHD DNA Analysis Kit

This comprehensive genome-wide bovine genotyping array kit features over 777,000 SNPs, and is compatible with any breed of beef or dairy cattle.

Microarray
For Research Use Only
DNA

BovineLD Genotyping BeadChip

Extend genomic selection to the entire herd with this expert-designed genotyping array featuring scalable content at an economical price.

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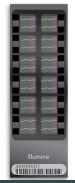
BovineSNP50 v3 DNA Analysis BeadChip

This BeadChip microarray provides high density multi-sample bovine genotyping for genome characterization of major dairy and beef cattle breed types.



OvineSNP50 DNA Analysis Kit

This sheep microarray features over 54,241 evenly spaced SNP probes for genome-wide association studies, genome-wide selection, and genetic merit determination.Read More...

The BeadChip was developed in collaboration with leading ovine researchers from AgResearch, Baylor UCSC, CSIRO, and the USDA as part of the International Sheep Genomics Consortium. It features over 54,241 evenly spaced probes that target single nucleotide polymorphisms (SNPs).

Microarray
For Research Use Only
DNA

GGP Equine Arrays 65k

Select desired breed traits and verify animal pedigree with the GeneSeek Genomic Profiler (GGP) equine microarray.

Microarray
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DNA

CanineHD Whole-Genome Genotyping BeadChip 170k

This array enables genotyping of any domestic dog breed, and offers ample SNP density for within-breed association and CNV studies.

GGP Porcine HD Array

This genome-wide porcine genotyping array is ideal for marker-assisted selection and prediction applications. Array content includes:

- 70,000 SNPs for all major porcine breeds
- Average marker spacing of ~42 kb
- 20 key causative mutations

GGP Porcine LD Array

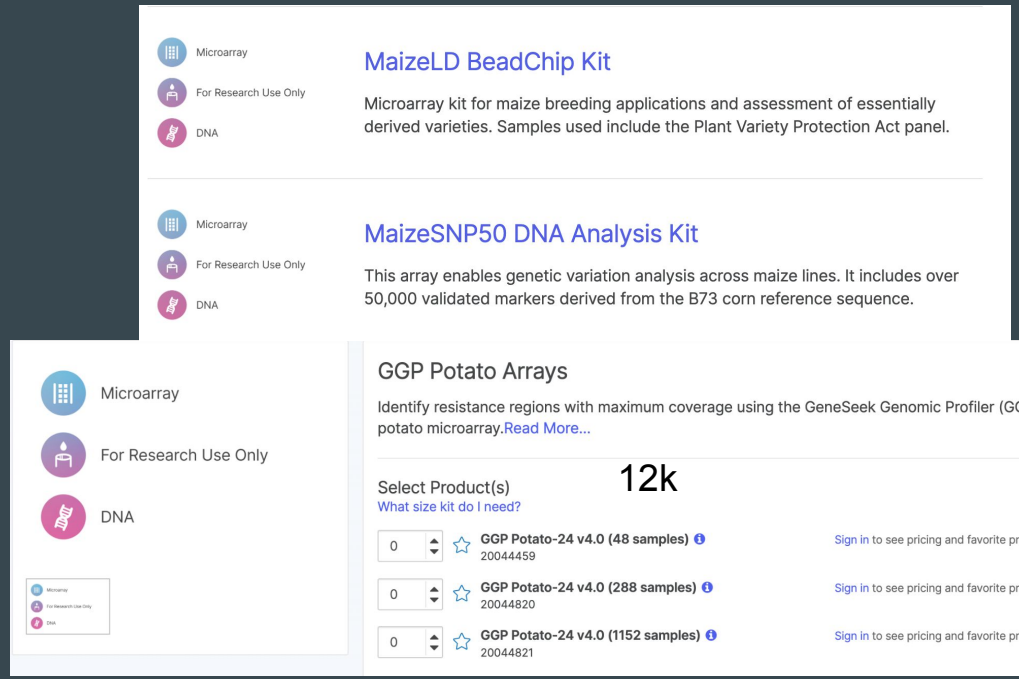
This array is designed for marker-assisted selection, Illumina PorcineSNP60 imputation, GGP Porcine HD imputation, and prediction applications. Array content includes:

- More than 10,000 SNPs for all major porcine breeds
- Average marker spacing of ~250 kb
- ~20 important causative mutations

Genome-wide prediction

Strategies to obtain genetic marker information in populations

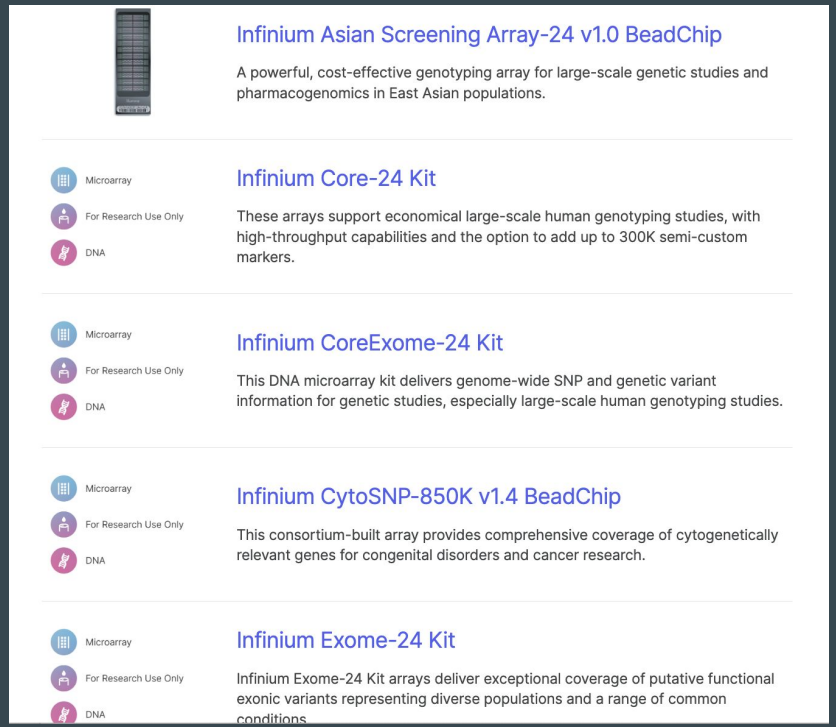
→Genotyping arrays



Genome-wide prediction

Strategies to obtain genetic marker information in populations

→Genotyping arrays



Infinium Asian Screening Array-24 v1.0 BeadChip

A powerful, cost-effective genotyping array for large-scale genetic studies and pharmacogenomics in East Asian populations.

Microarray
For Research Use Only
DNA

Infinium Core-24 Kit

These arrays support economical large-scale human genotyping studies, with high-throughput capabilities and the option to add up to 300K semi-custom markers.

Microarray
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Infinium CoreExome-24 Kit

This DNA microarray kit delivers genome-wide SNP and genetic variant information for genetic studies, especially large-scale human genotyping studies.

Microarray
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DNA

Infinium CytoSNP-850K v1.4 BeadChip

This consortium-built array provides comprehensive coverage of cytogenetically relevant genes for congenital disorders and cancer research.

Microarray
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DNA

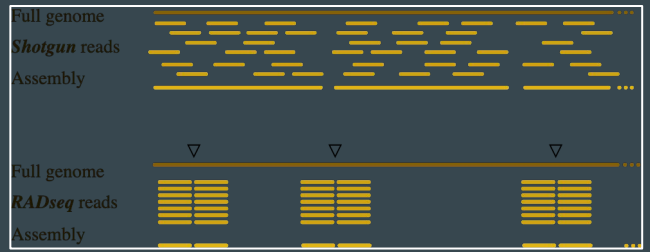
Infinium Exome-24 Kit

Infinium Exome-24 Kit arrays deliver exceptional coverage of putative functional exonic variants representing diverse populations and a range of common conditions

Strategies to obtain genetic marker information in populations

→Restriction site-associated DNA sequencing (RADseq)

- Uses NGS
- Requires specific library preparation with specific restriction enzymes
- Most effective in organisms with well-characterized reference genomes
- Cost-effective and medium-throughput



Strategies to obtain genetic marker information in populations

→Restriction site-associated DNA sequencing (RADseq)

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Hiroto Yamashita, Tomoki Uchida, Yasuno Tanaka, Hideyuki Katai, Atsushi J. Nagano, Akio Morita & Takashi Ikka ✉

Scientific Reports **10**, Article number: 17480 (2020) | Cite this article

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Restriction site-associated DNA sequencing technologies as an alternative to low-density SNP chips for genomic selection: a simulation study in layer chickens

Florian Herry, Frédéric Hérault, Frédéric Lecerf, Laëtitia Lagoutte, Mathilde Doublet, David Picard-Druet, Philippe Bardou, Amandine Varenne, Thierry Burlot, Pascale Le Roy & Sophie Allais ✉

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Genome-wide prediction

Strategies to obtain genetic marker information in populations

→Restriction site-associated DNA sequencing (RADseq)

Highly dependent on the restriction enzyme

GEBV correlation <0.50 with HD SNP arrays
(probably missing important regions)

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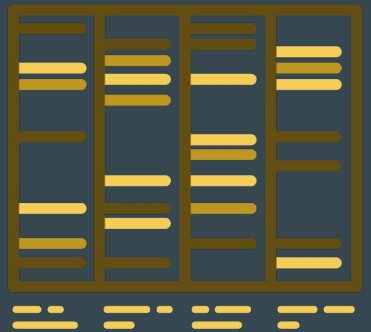
Table 6 Pearson correlations between true "Full_HD" GEBVs and imputed HD GEBVs based on ancestry for the 67 G1 breeders, according to each enzyme used for egg weight (EW), eggshell colour (ESC), eggshell strength (ESS) and albumen height (AH).

	Number of SNPs	EW	ESC	ESS	AH
EcoRI	1,797	0.3774	0.2962	0.3420	0.4261
TaqI	4,126	0.4476	0.2453	0.3906	0.4478
TaqI_PstI	11,193	0.4740	0.2442	0.3869	0.4684
AvaII	12,453	0.4681	0.2430	0.3859	0.4794
PstI	14,390	0.4664	0.2450	0.3953	0.4689
HD SNP chip	300,028	0.4713	0.2460	0.3940	0.4802

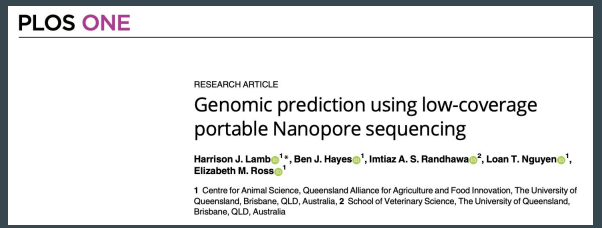
The line HD SNP chip corresponds to the Pearson correlation between true "Full_HD" GEBVs and true HD GEBVs based on ancestry for the 67 G1 breeders.

Strategies to obtain genetic marker information in populations



→Genotype by low-pass sequencing (Skim-Seq)

- Low cost
- Non targeted sequencing (needs imputation)
- NGS (Illumina or ONT)
- Minimum coverage ranges between 0.5x and 4x depending on population and sequencing method

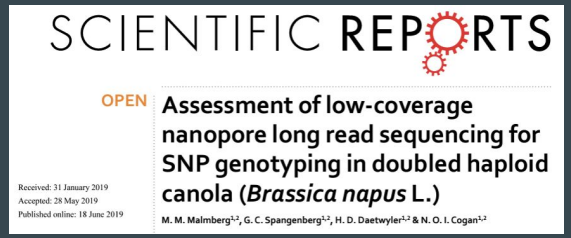

PLOS ONE

RESEARCH ARTICLE

Genomic prediction using low-coverage portable Nanopore sequencing

Harrison J. Lamb[1]*, Ben J. Hayes[1], Imtiaz A. S. Randhawa[2], Loan T. Nguyen[1], Elizabeth M. Ross[1]

1 Centre for Animal Science, Queensland Alliance for Agriculture and Food Innovation, The University of Queensland, Brisbane, QLD, Australia, 2 School of Veterinary Science, The University of Queensland, Brisbane, QLD, Australia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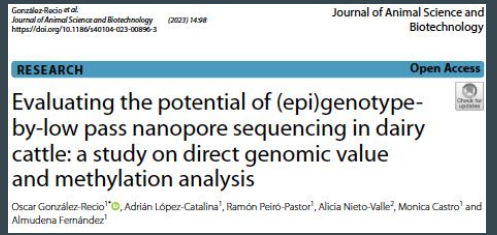
Assessment of low-coverage nanopore long read sequencing for SNP genotyping in doubled haploid canola (*Brassica napus* L.)

Received: 31 January 2019
Accepted: 28 May 2019
Published online: 18 June 2019

M. M. Malmberg[1,2], G. C. Spangenberg[1,2], H. D. Daetwyler[1,2] & N. O. I. Cogan[1,2]


González-Recio et al. Journal of Animal Science and Biotechnology (2023) 14:98
https://doi.org/10.1186/s40104-023-00896-3

Journal of Animal Science and Biotechnology

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Evaluating the potential of (epi)genotype-by-low pass nanopore sequencing in dairy cattle: a study on direct genomic value and methylation analysis

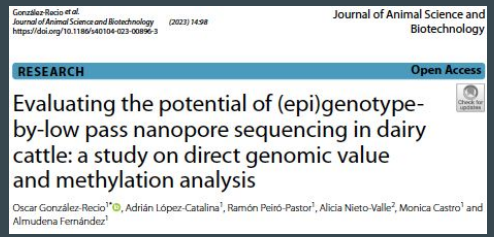
Oscar González-Recio[1*], Adrián López-Catalina[1], Ramón Peiró-Pastor[1], Alicia Nieto-Valle[2], Monica Castro[1] and Almudena Fernández[1]

Strategies to obtain genetic marker information in populations

→Genotype by low-pass sequencing (Skim-Seq)

Imputation accuracy improves with

sequencing depth →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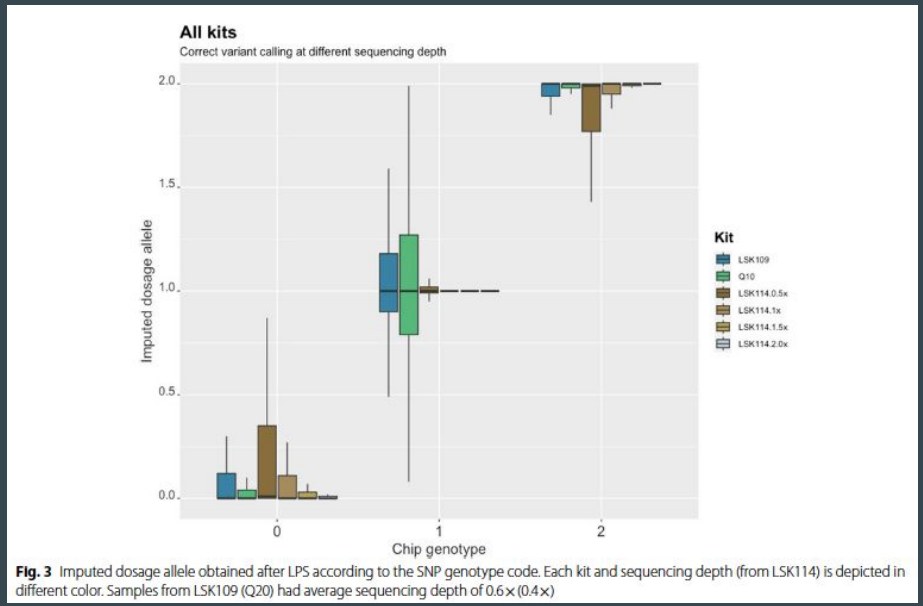

Fig. 3 Imputed dosage allele obtained after LPS according to the SNP genotype code. Each kit and sequencing depth (from LSK114) is depicted in different color. Samples from LSK109 (Q20) had average sequencing depth of 0.6× (0.4×)

Strategies to obtain genetic marker information in populations

→Genotype by low-pass sequencing (Skim-Seq)

High correlation (>0.98) with latest technology

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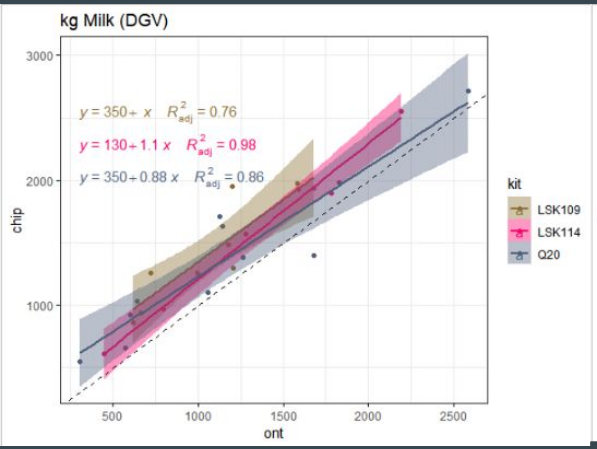
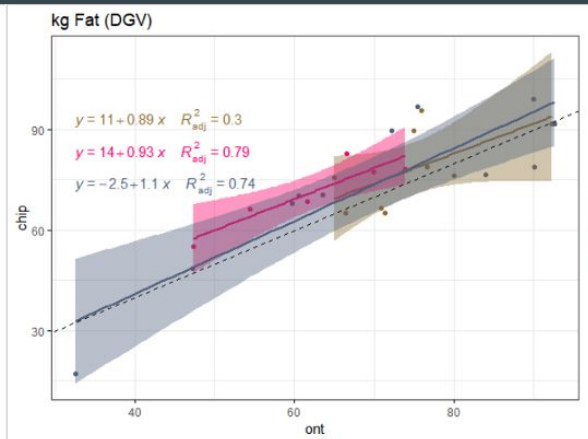
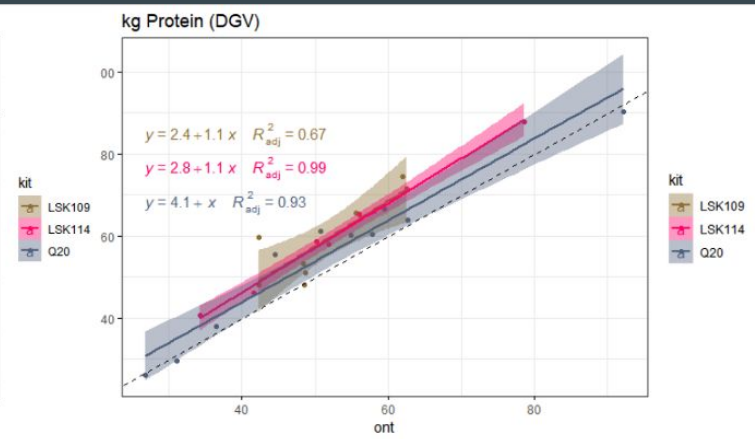






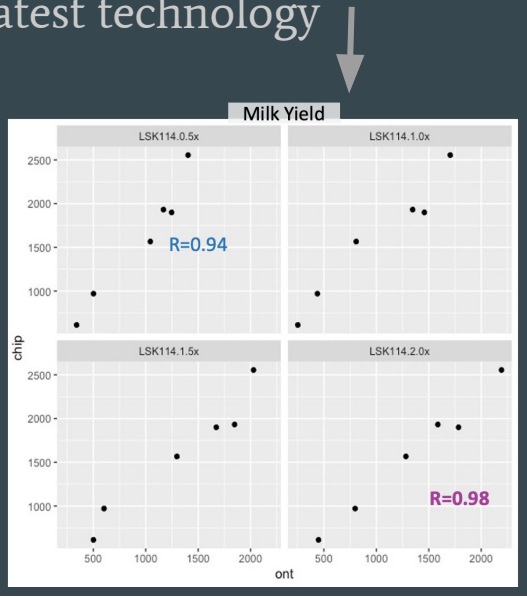
Genome-wide prediction

Strategies to obtain genetic marker information in populations

→Genotype by low-pass sequencing (Skim-Seq)

High correlation (>0.98) with latest technology

and seq-depth>2x.



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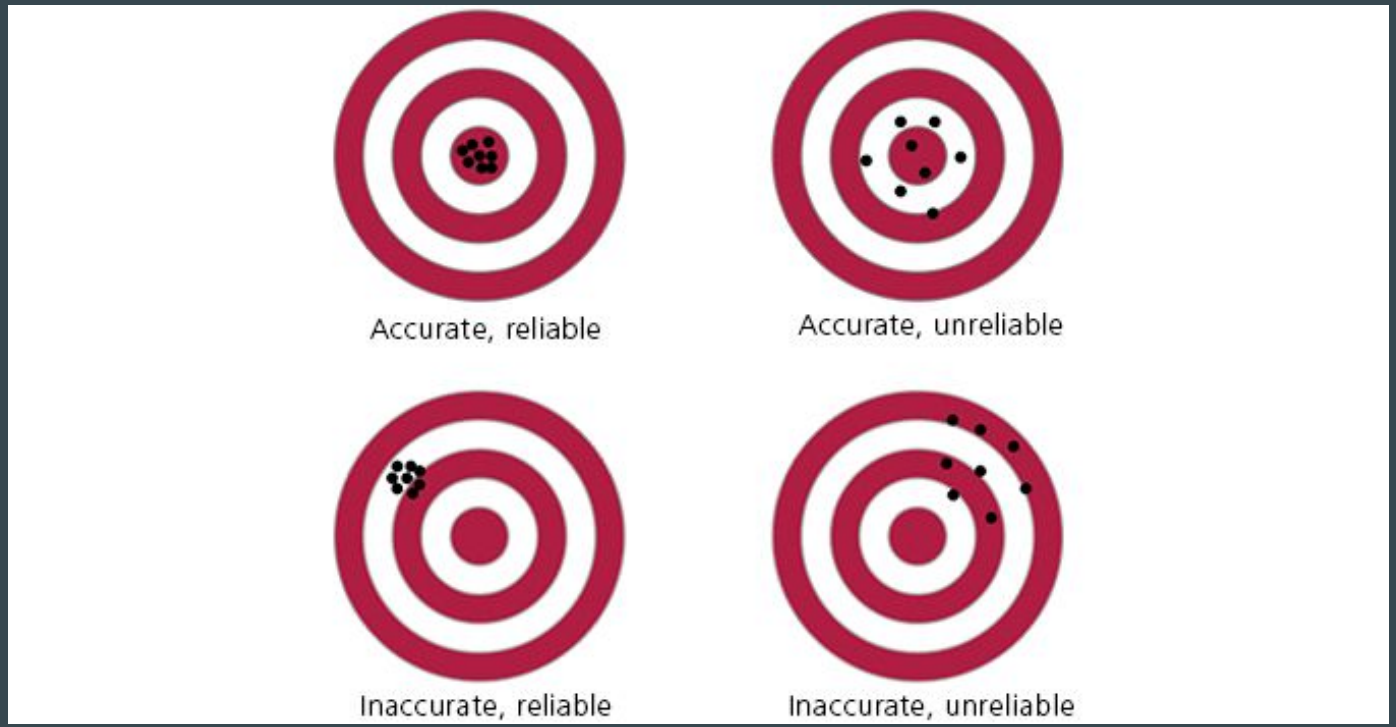
4. Is my prediction reliable? And accurate?



4. Is my prediction reliable? And accurate?

Reliability

Refers to the consistency of the EGBV over time (with addition of new information)

⚠️ An animal may have high EGBV reliability but still inaccurate (wrong model, consistent preferential treatment, systematic environmental confounders, ...)

4. Is my prediction reliable? And accurate?

Reliability

$$R^2(\hat{a}_i) = 1 - \frac{Var(a_i - \hat{a}_i)}{Var(a_i)},$$

$Var(a_i - \hat{a}_i)$ Can be calculated through:

- approximation methods from the coefficient matrix when using a frequentist approach
- Posterior distribution of the estimated Genomic Breeding Value

4. Is my prediction reliable? And accurate?

Accuracy

Refers to how close a measurement is to the real value

✅ This should be our aim

Predict the future (yet-to-be observed data)

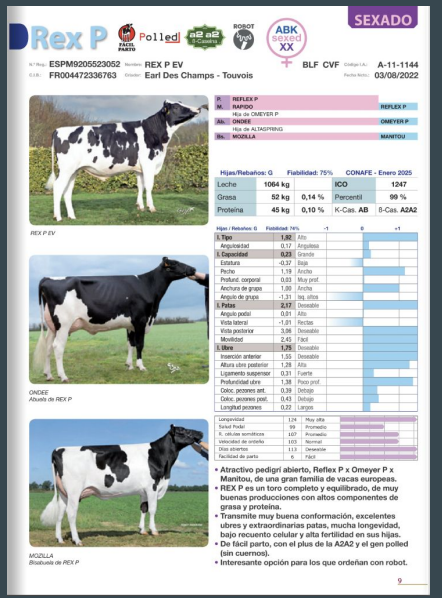
Cross-validation strategies (with known outputs, as pretending to predict the future)

5. Then what?

Prediction-based decisions (e.g. culling)

Rank candidates (and reference) as parents of next generation

Design matings based on selection criteria (or breeding goals)



RECAP

Assume gaussian distribution on phenotypes (... subsequently residuals)

Why variance is important

Inference is different from prediction.

Genetic architecture challenge

How to establish a reference population: Phenotyping strategies & Genotyping strategies