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Genomic selection

Modul no. 3: Animal Breeding

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Genomics and animal breeding

Genome - is the complete set of genetic information of an organism. In eukaryotic organisms, the genome is contained in a haploid set of chromosomes.

Post-2000 development of next-generation sequencing technologies -> ability to rapidly sequence entire genomes

Whole genome sequencing of major livestock species:

- Cattle, 2009, 2,7 Gbp (30 chromozomů/1n)
- Pig, 2009, 2,5 Gbp (19 chromozomů/1n)
- Chicken,2004, 1,05 Gbp (40 chromozomů/1n)

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Genetic variation in genomes

Short variants (mainly SNPs, indels) have been described in the genomes:

- Pig - 71 miliónů
- Cattle - 97 miliónů
- Sheep – 58 miliónů
- Chicken – 22 miliónů

- Genomic database ENSEMBL: http://www.ensembl.org/

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Genome-wide association and genomic selection in animal breeding

- Results from **genome-wide association studies (GWAS)** in farm animals and humans lead to the conclusion that the effect of an individual QTL complex trait is very small, and therefore a large number of QTLs need to be used to explain genetic variance in these traits.
- The gains from **MAS** programs are small from a small number of DNA markers to detect a limited number of QTL -> an alternative technology to use denser information using genomic **SNPs**, called **genomic selection (GS)**.
- GS uses a genome-wide panel of markers -> each QTL is in linkage disequilibrium with just one SNP. **Genomic breeding values are predicted as the sum of the effects of these SNPs across the genome.**

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Genomic selection - higher version of MAS

- **Genomic selection** is a form of marker-assisted selection in which genetic markers covering the whole genome are used so that all quantitative trait loci (QTL) are in **linkage disequilibrium (LD)** with at least one marker.
- This is possible by exploiting the large number of SNPs discovered by genome sequencing and new methods for genotyping large numbers of SNPs (DNA microarray)
  - SNP chips (60 tis., 700 tis. SNPs)
- The ideal method of estimating BV from genomic data is to **calculate the conditional average of the breeding value of a given animal genotype at each QTL (~ marker)**
- In practice, markers (SNPs) are used instead of QTL genotypes, but a more ideal method will be developed the closer we get to larger sequence and SNP data.
- **Genomic selection** refers to the use of a large number of genetic markers (such as SNPs) covering the entire genome to predict the genetic value of individuals (Meuwissen et al. **2001**).

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- **Genomic selection (GS)** – in the Czech Republic in dairy cattle

- Using knowledge of true genetic variability (mutations in or near genes) detectable by molecular genetic methods - genome-wide SNP markers

- **GS** – začlenění **matice genomických SNP markerů** do rovnic BLUP-AM (různé varianty; nutnost znát heritabilitu vlastnosti) a odhadnutí GEBV (**genomická OPH**)
- **GS** - incorporation of a **matrix of genomic SNP markers** into BLUP-AM equations (different variants; need to know trait heritability) and **estimation of GEBV** (genomic EBV)

  - **More efficient breeding (reduces costs, refines BV estimates, shortens generation intervals, reduces inbreeding)**

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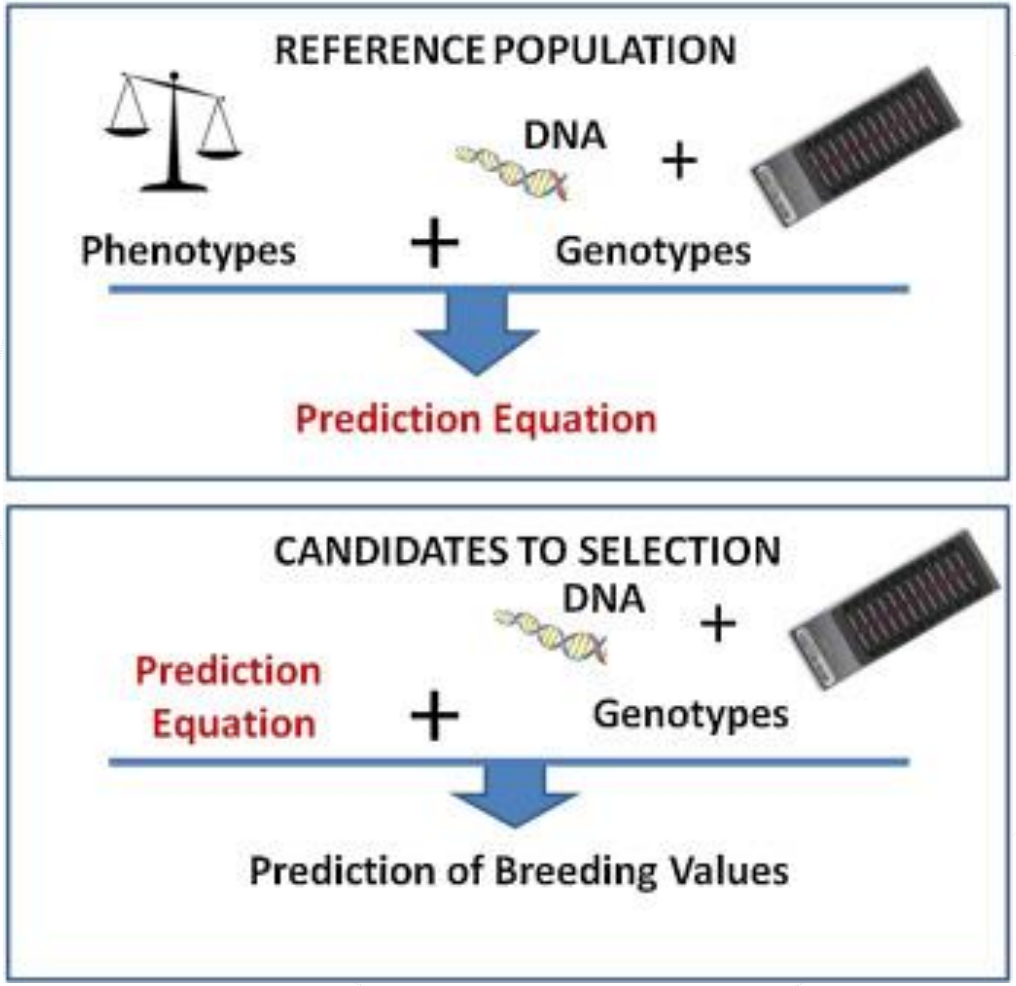
Comparison of traditional EBV estimation and genomic selection (GEBV)

- **Estimation of breeding value**
  - Estimated breeding value (EBV)
  - Additive genetic relationship matrix (A) -> **expected proportion** of genes shared between parents
  - Need to know relationships (pedigree data)
- **Estimation of genomic breeding value(~ genomic selection)**
  - Genomic estimation breeding value (GEBV)
  - Knowledge of genotypes of genetic markers (especially SNPs) -> genomic relationship matrix
    - elements of matrix -> estimates of the real proportion of the genome that two individuals share between their parents

Genomic selection system



https://doi.org/10.1016/j.crvi.2016.04.007

The prediction equation for estimating genomic PH is obtained from a reference population with phenotypes and SNP genotypes

The resulting prediction equation is used to evaluate candidate parents with only the genotypes

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GS - A paradigm shift in animal breeding - Next generation sequencing and genotyping technologies are revolutionizing animal breeding

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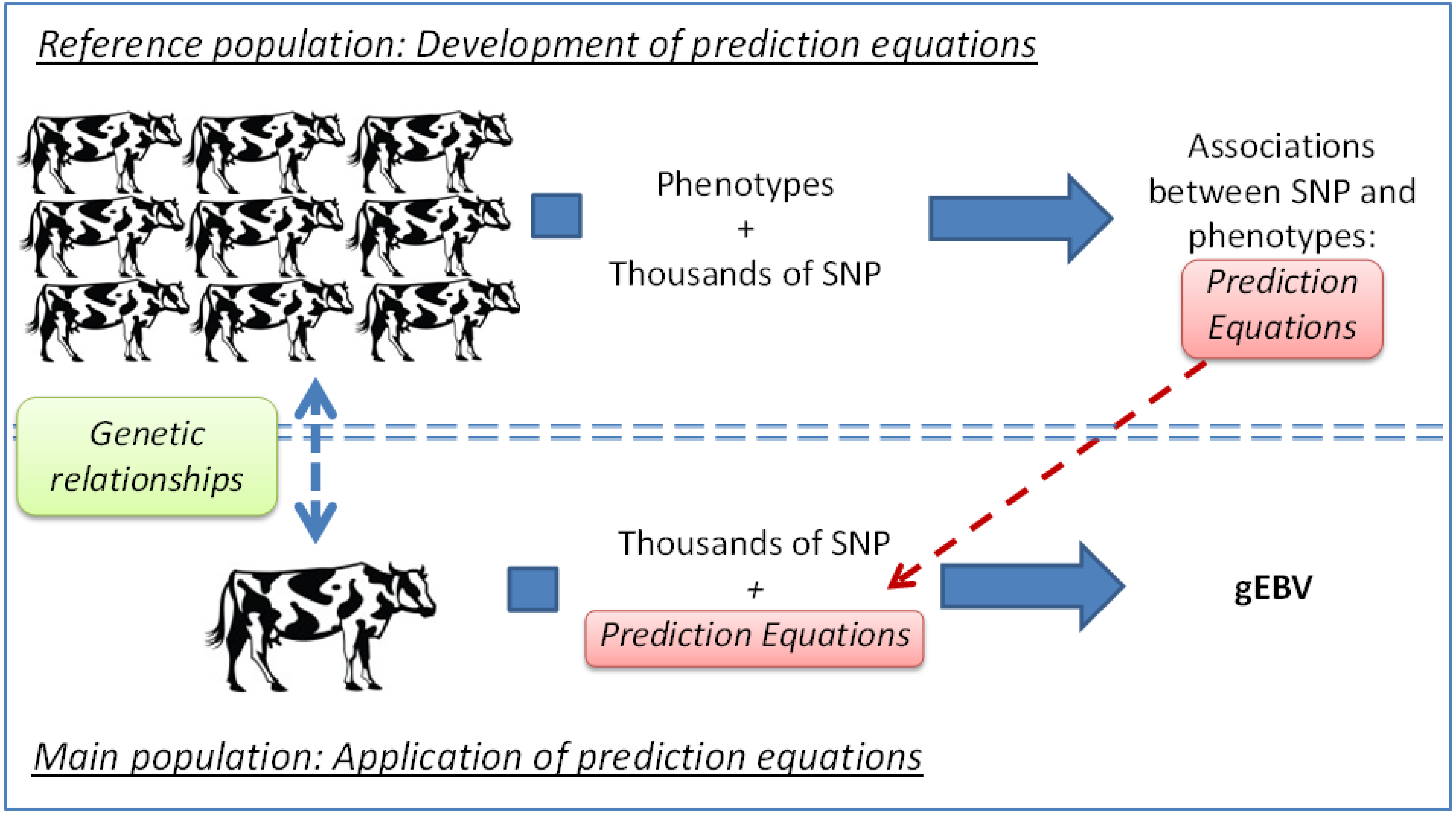

Reference population: Development of prediction equations

Phenotypes
+
Thousands of SNP

Associations between SNP and phenotypes:
Prediction Equations

Genetic relationships

Thousands of SNP
+
Prediction Equations

gEBV

Main population: Application of prediction equations

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Effects of GS

- **The accuracy** of statistical estimates of genomic breeding values is **high**
- **Shortening of the generation interval** (evaluation of the young and the embryo, without its own performance or the performance of its offspring)
- **Increasing genetic gain**
- **Reducing inbridging**
- Efficient breeding of traits with low heritability (meat quality, reproductive traits, disease resistance...), sex-linked traits

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The influence of technological advances in NGS and TGS

- Improvements in NGS technology and the development of TGS (third generation sequencing) - longer sequencing reads in less time
- -> more accurate identification of SNPs - increased detectability of their number and reduced false detection -> **increased number of informative markers**
- Reducing the cost of genome resequencing to a few hundred USD
- Estimating whole genome heritability to the nucleotide

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Conclusion

- Genomic selection has been very successful in cattle because it provides more genetic gain at a similar or lower cost.
- Genomic selection is a very recent innovation.
- Strong evolutions have started, including reduction in genotyping costs, phenotyping strategies for new traits, approaches for the creation or the replacement of reference populations, increase in robustness and persistency of genomic predictions using causal mutations identified from genome sequences, or genomic prediction of genetic × environment interactions.

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Thank you for your attention!

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