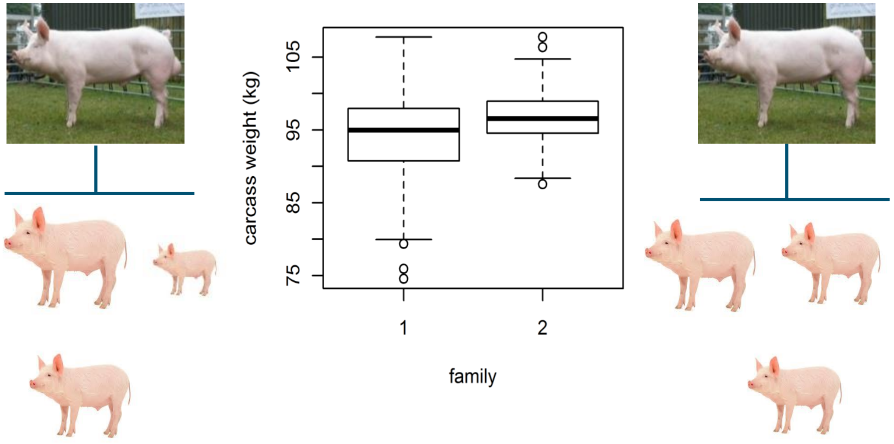
Quantitative genetics of environmental variance: analyses in livestock, aquaculture and natural populations

Dr Han Mulder



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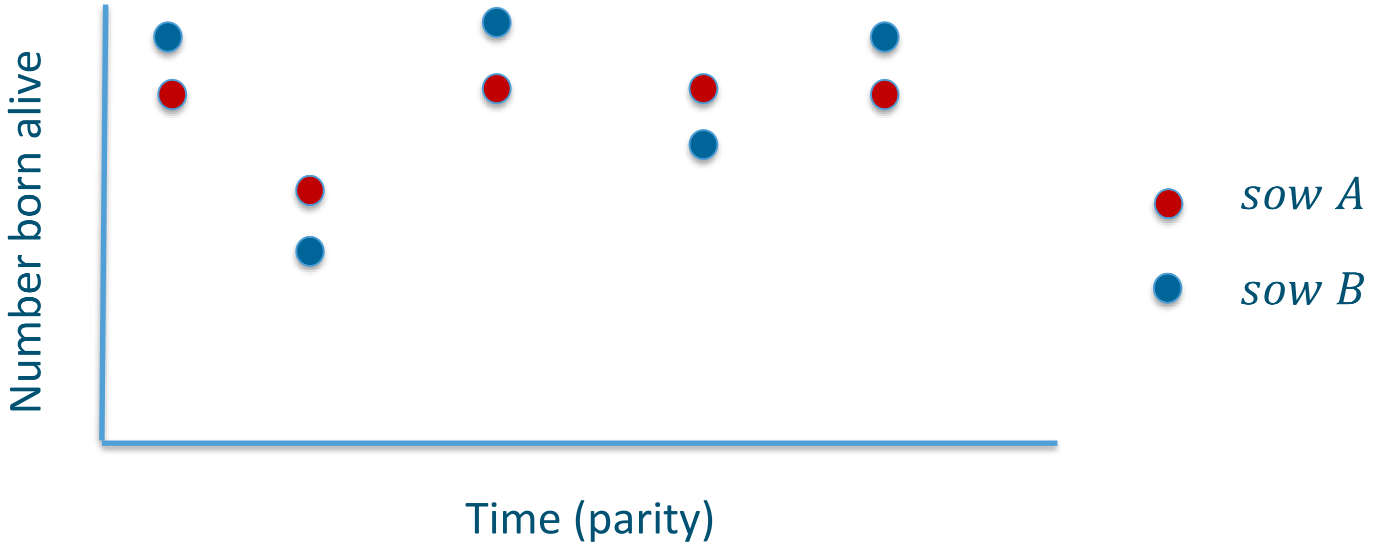
Animal Breeding and Genomics

What is genetic variation in Ve?

- Genetic variation in the size of the residual/environmental variance
- Observed as:
  - Differences in variances within individual with repeated observations
  - Differences in within-family variance

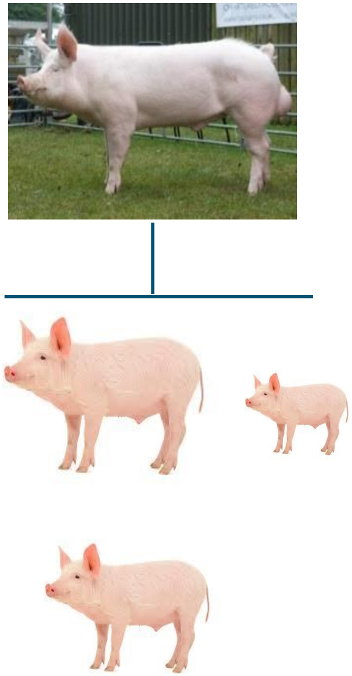
What is genetic variation in Ve?

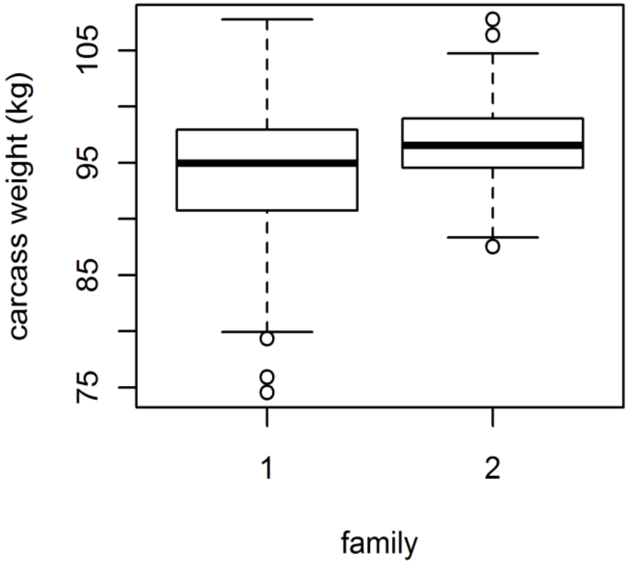
- Variation in repeated observations



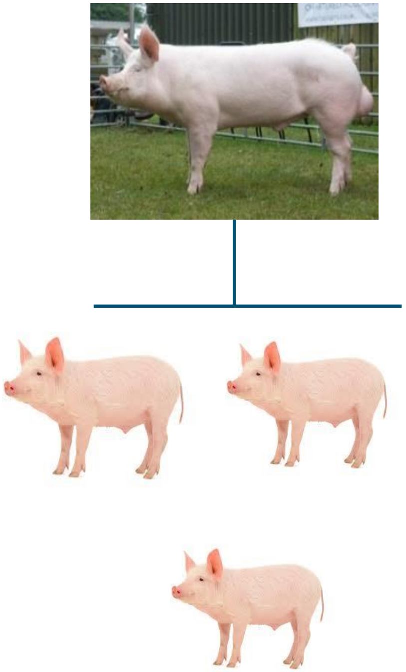
What is genetic variation in Ve?

Family 1





Family 2



Difference in within-family variance

Contents

- Modelling genetic differences in Ve
- Heritability and genetic coefficient of variation for Ve
- Genetic parameters in different species
- Relationship plasticity and Ve
- Genetic architecture of Ve: GWAS
- Ve and competition between animals
- Ve and natural selection

Quantitative genetic model for Ve: The additive model

$$P_i = \mu + A + E = \mu + A_{m,i} + \chi\sqrt{\sigma_E^2 + A_{v,i}}$$

$$\begin{pmatrix} A_m \\ A_v \end{pmatrix} \sim N\left(\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \mathbf{G} \otimes \mathbf{A}\right) \qquad \mathbf{G} = \begin{bmatrix} \sigma^2_{A_m} & \mathrm{cov}_{A_{mv}} \\ \mathrm{cov}_{A_{mv}} & \sigma^2_{A_v} \end{bmatrix}$$

$$\chi \sim N(0,1)$$

$A_{m,i}$ = breeding value of i for mean
$A_{v,i}$ = breeding value of i for environmental variance

σ_E^2 = the mean environmental variance

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Quantitative genetic model for Ve: The exponential model

$$P_i = \mu + A + E = \mu + A_{m,i} + \chi \exp\left(\frac{\ln(\sigma_E^2) + A_{v,i}}{2}\right)$$

$$\begin{pmatrix} A_m \\ A_v \end{pmatrix} \sim N\left(\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \mathbf{G} \otimes \mathbf{A}\right) \qquad \mathbf{G} = \begin{bmatrix} \sigma^2_{A_m} & \mathrm{cov}_{A_{mv}} \\ \mathrm{cov}_{A_{mv}} & \sigma^2_{A_v} \end{bmatrix}$$

$$\chi \sim N(0,1)$$

$A_{m,i}$ = breeding value of i for mean
$A_{v,i}$ = breeding value of i for environmental variance

σ_E^2 = the mean environmental variance

Modelling the residual variance: Double hierarchical generalized linear model

- Model on the trait and on the residual variance

$$\begin{bmatrix}\mathbf{y}\\ \mathbf{y_v}\end{bmatrix}=\begin{bmatrix}\mathbf{X} & \mathbf{0}\\ \mathbf{0} & \mathbf{X_v}\end{bmatrix}\begin{bmatrix}\mathbf{b}\\ \mathbf{b_v}\end{bmatrix}+\begin{bmatrix}\mathbf{Z} & \mathbf{0}\\ \mathbf{0} & \mathbf{Z_v}\end{bmatrix}\begin{bmatrix}\mathbf{a}\\ \mathbf{a_v}\end{bmatrix}+\begin{bmatrix}\mathbf{W} & \mathbf{0}\\ \mathbf{0} & \mathbf{W_v}\end{bmatrix}\begin{bmatrix}\mathbf{pe}\\ \mathbf{pe_v}\end{bmatrix}+\begin{bmatrix}\mathbf{e}\\ \mathbf{e_v}\end{bmatrix}$$

- $\mathbf{y_v}$ uses the squared residual of $\mathbf{y}$
- $Ve = \exp(\mathbf{X_v b_v} + \mathbf{Z_v a_v} + \mathbf{W_v pe_v})$

- **Use genomic relationship matrix or H matrix is feasible**

Rönnegård et al., 2010. GSE 42:8
Felleki et al., 2012. Genet. Res. 94:307-317.

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Heritability of Ve

- In analogy of the normal heritability of the mean
- Regression of Av on P² (additive model)

$$h_v^2 = b_{A_V,P^2} = Cov(A_V, P^2)/Var(P^2)$$

$$h_v^2 = \sigma_{A_V}^2 / Var(P^2)$$

$$h_v^2 = \frac{\sigma_{A_V}^2}{2\sigma_P^4 + 3\sigma_{A_v}^2}$$

- Accuracy of EBV based on own performance = $\sqrt{h_v^2}$
- For exponential model: convert genetic variance to additive model

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Mulder et al. 2007; Genetics 175:1895-1910

Genetic coefficient of variation for Ve

- Genetic coefficient of variation: GCV = σ_a/μ
  - Evolvability (Houle, 1992, Genetics 130: 195)
  - For classical breeding traits: GCV ≈ 3 - 10%

- Application to heritable variance in the additive model
  - $\mu =$ mean environmental variance = Ve
  - $\sigma =$ genetic std in environmental variance = σ_{A_v}

- In exponential model: $GCV_{Ve} = \sigma_{A_v,exp}$

Mulder et al. 2007; Genetics 175:1895-1910

Genetic variance in Ve in pigs

Line	Trait	varav	GCV ve	h2v	Rg_mv
Large White	Piglet birth weight	0.04	0.19	0.01	0.62
Landrace	Piglet birth weight	0.04	0.21	0.01	0.55
Pietrain	Carcass weight	0.04	0.21	0.01	0.41
Large White	Total number born	0.03	0.17	0.01	0.49

Sell-Kubiak et al. 2015. J. Anim Sci. 93:900-911
Sell-Kubiak et al. 2015. J. Anim. Sci. 93:1471-1480
Sell-Kubiak et al. 2015. BMC Genomics 16:1049

Genetic variance in Ve dairy cattle

Trait	varav	GCV ve	h2v	Rg_mv
Milk NL	0.03	0.19	<0.01	-
Milk Sweden	0.05	0.22	0.01	0.63
SCS Sweden	0.05	0.21	0.01	-
SCS Robustmilk farms	0.08	0.28	0.01	-
milk Belgium	0.03	0.17	<0.01	-
SCS Belgium	0.03	0.16	<0.01	-
SFA Belgium	0.01	0.12	<0.01	-
UFA Belgium	0.02	0.12	<0.01	-
C18:1 cis-9 Belgium	0.02	0.12	<0.01	-

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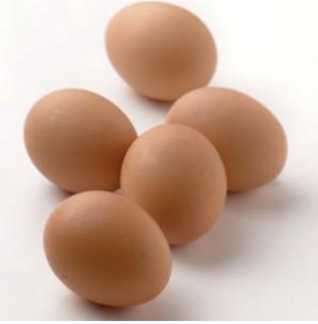
Mulder et al. 2013. J. Dairy Sci. 96:7306-7317.
Mulder et al. 2013. GSE 45:23.
Vandenplas et al., 2013. J. Dairy Sci. 96:5977-5990.

Genetic variance in Ve laying hens



Trait	varav	GCV ve	h2v	Rg_mv
Egg color purebreds	0.08	0.28	0.01	-0.06
Egg color crossbreds	0.07	0.26	0.01	0.43

- Heritability of log-variance within-hen was 0.15
- Genetic correlation between Ve in purebred and crossbred was 0.70 (for eggcolor itself 0.86)

Mulder et al. 2016. GSE 48:39

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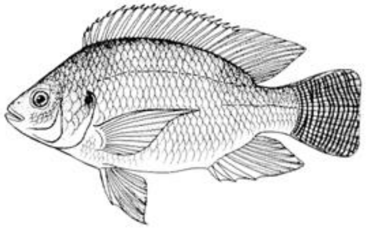
Genetic variance in Ve in Tilapia

	HW	**BC-HW**	**Length**	**Depth**	**Width**
σ^2_A	0.34 (0.07)	0.24 (0.05)	0.16 (0.04)	0.18 (0.04)	0.20 (0.05)
GCV, %	58	49	39	42	45

	HW	**BC-HW**	**Length**	**Depth**	**Width**
r_A	0.60 (0.09)	0.21 (0.14)	0.11 (0.16)	0.37 (0.13)	0.20 (0.15)

Marjanovic et al. 2016. GSE 48:41



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Genetic variance in Ve in salmon and rainbow trout

Trait	varav	GCV ve	h2v	Rg_mv
Harvest weight, rainbow trout, freshwater	0.04	0.21	0.01	0.30
Harvest weight, rainbow trout, seawater	0.04	0.19	0.01	0.79
Harvest weight salmon	0.23	0.48	0.04	0.95

Rainbow trout
Genetic correlation between freshwater and seawater:
Ve = 0.56
Harvest weight = 0.70

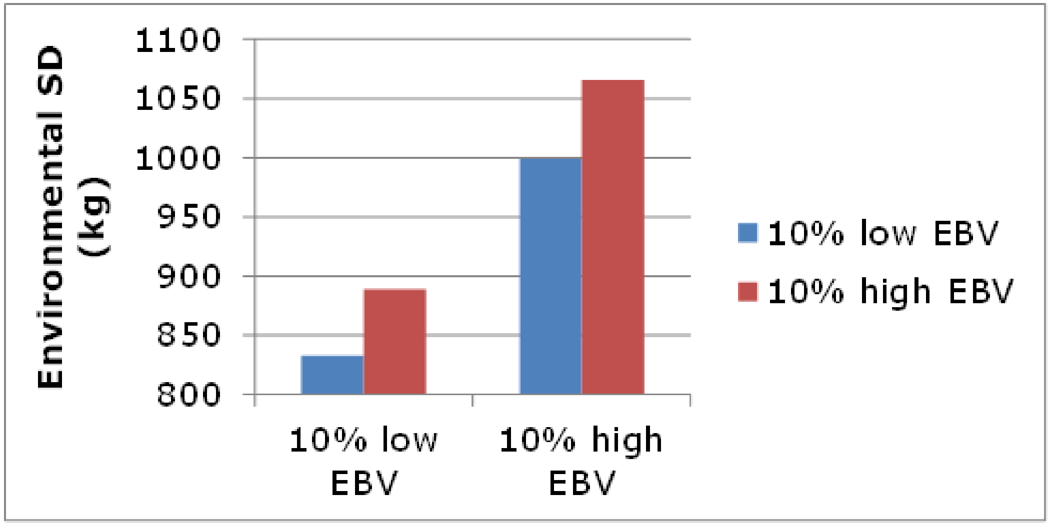
Sae-Lim et al., 2015; GSE 47:46
Sae-Lim et al., 2017; GSE 49:43

Plasticity (slope of RN) and Ve

- In cattle:
  - Genetic correlation for milk production: 0.77 (Mulder et al., 2013; GSE 45:23)
  - Genetic correlation for SCS: 0.78 (Wijga et al., 2013, PhD-thesis)

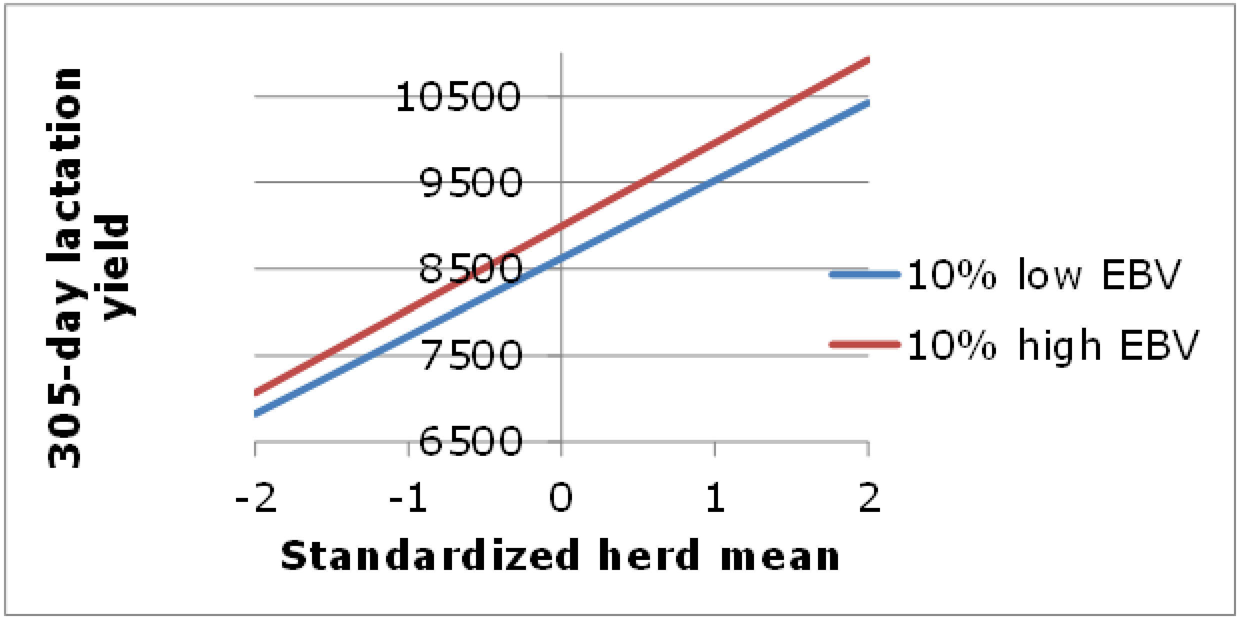
- Plasticity and Ve are likely to be positively correlated
  - Scaling effects
  - Common buffering of environmental perturbations, e.g. heat-shock proteins

Environmental sensitivity (slope of RN) and Ve



Daughters of bulls with low variance have flatter slopes and a lower average milk yield

Correlated responses in level and slope



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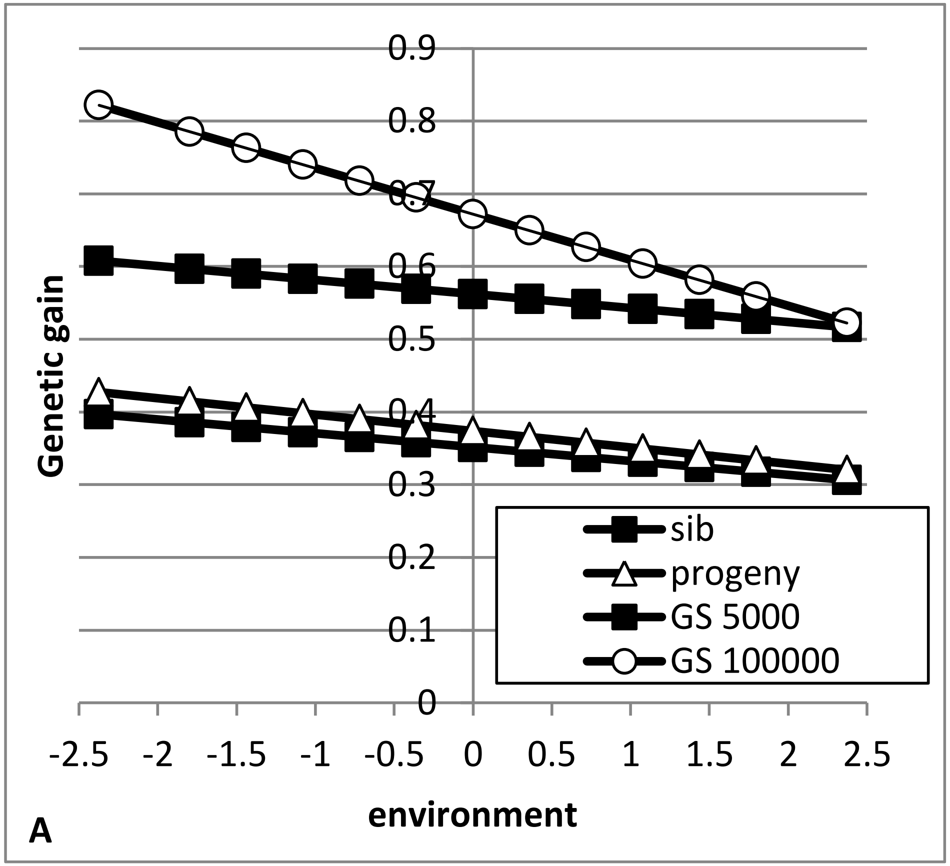
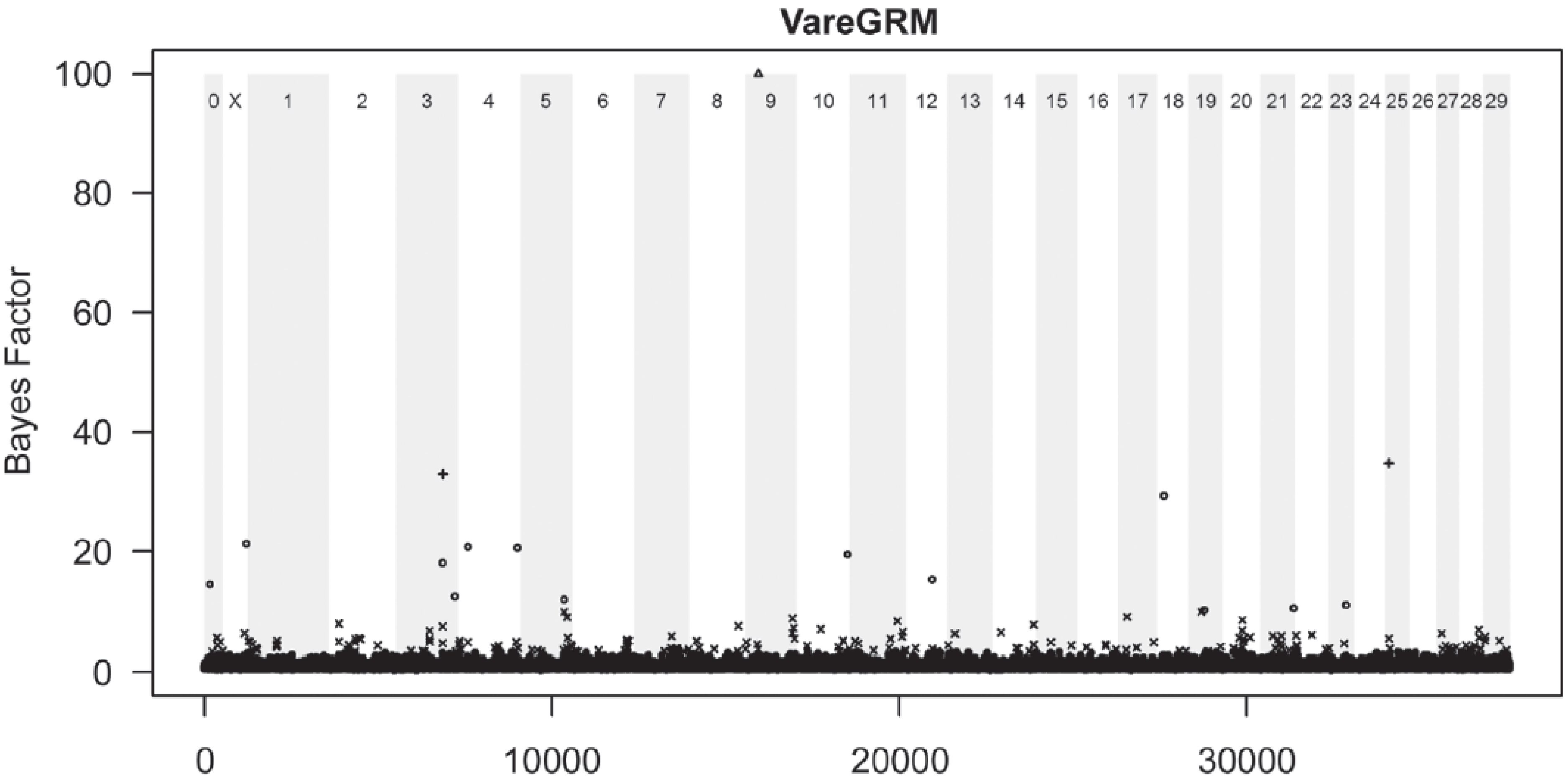
Genomic selection increases resilience exploiting GxE

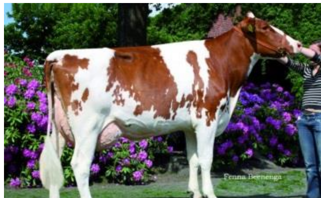


- Aim was to increase performance in low environments more than in high environments
- GS has 9-140% more gain than with sib testing
- GS has 10-114% more gain than progeny testing
- Large reference populations make changing slope of RN easier

Mulder, 2016. Front. Genet. 7:178

Genetic architecture of Ve: GWAS variability SCS in dairy cattle





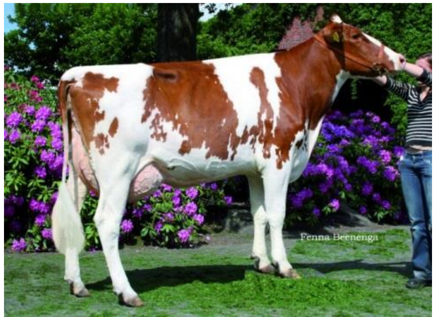
Mulder et al. 2013; JDS 96:7306–7317

Genetic architecture of Ve: GWAS variability SCS in dairy cattle

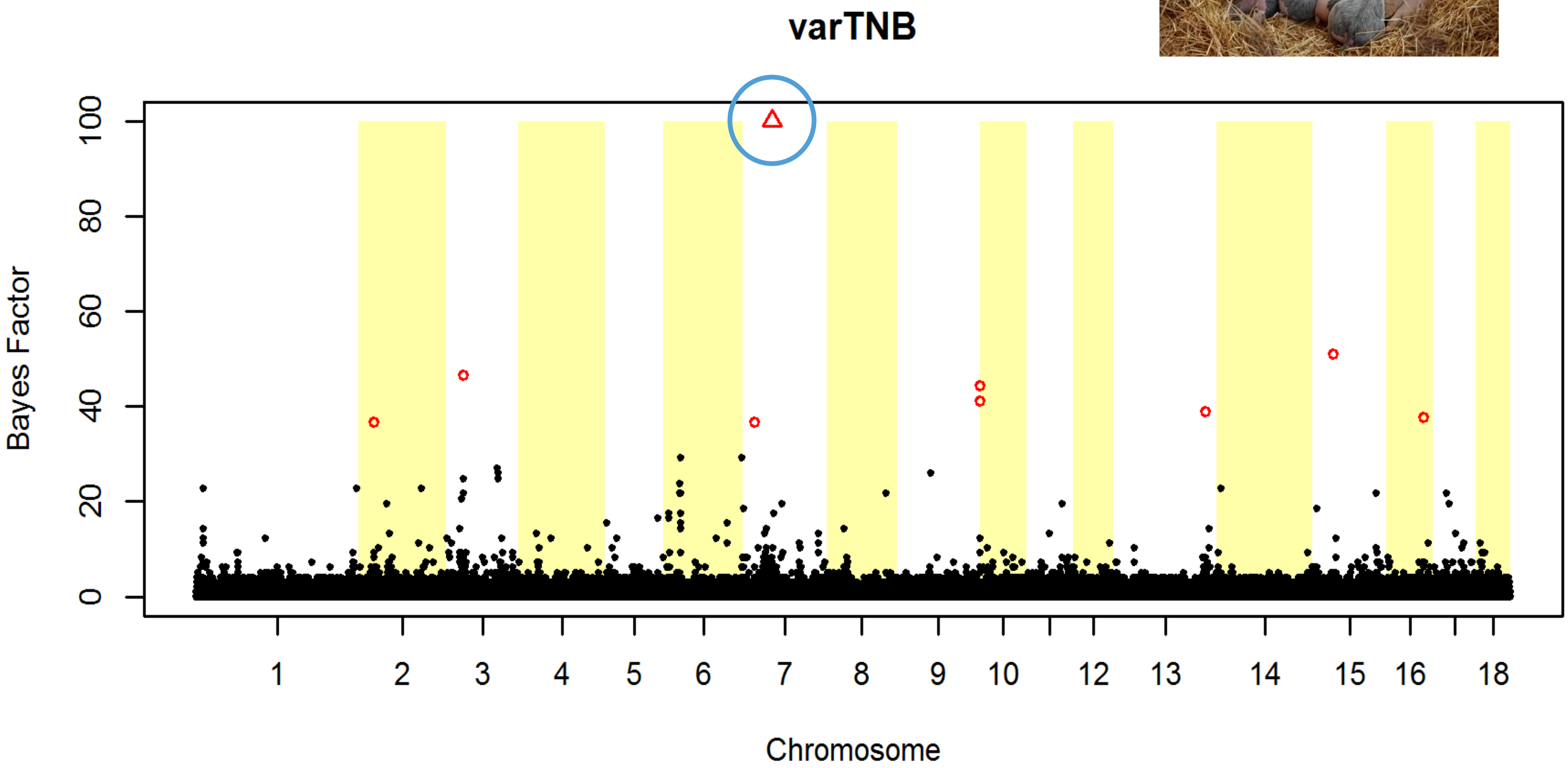
BTA	Most sign. SNP	Position (Mbp)	BF	Gen. var. expl. by SNP (%)
9	Hapmap31053-BTA-111664	27.02	134.7	3.5
25	Hapmap32191-BTC-019394	6.10	34.7	0.5
3	BTA-28541-no-rs	96.96	32.9	0.6

Ve of SCS seems rather polygenic

Mulder et al. 2013; JDS 96:7306–7317



Genetic architecture of Ve: GWAS variability litter size in pigs



Sell-Kubiak et al. 2015. BMC Genomics 16:1049

Genetic architecture of Ve: GWAS variability litter size in pigs

SSC	Most sign. SNP	Position (Mbp)	BF	Gen. var. expl. by SNP (%)
7	INRA0025193	43.76	167.2	0.50
7	ASGA0031511	17.47	36.6	0.06

Ve of litter size seems rather polygenic

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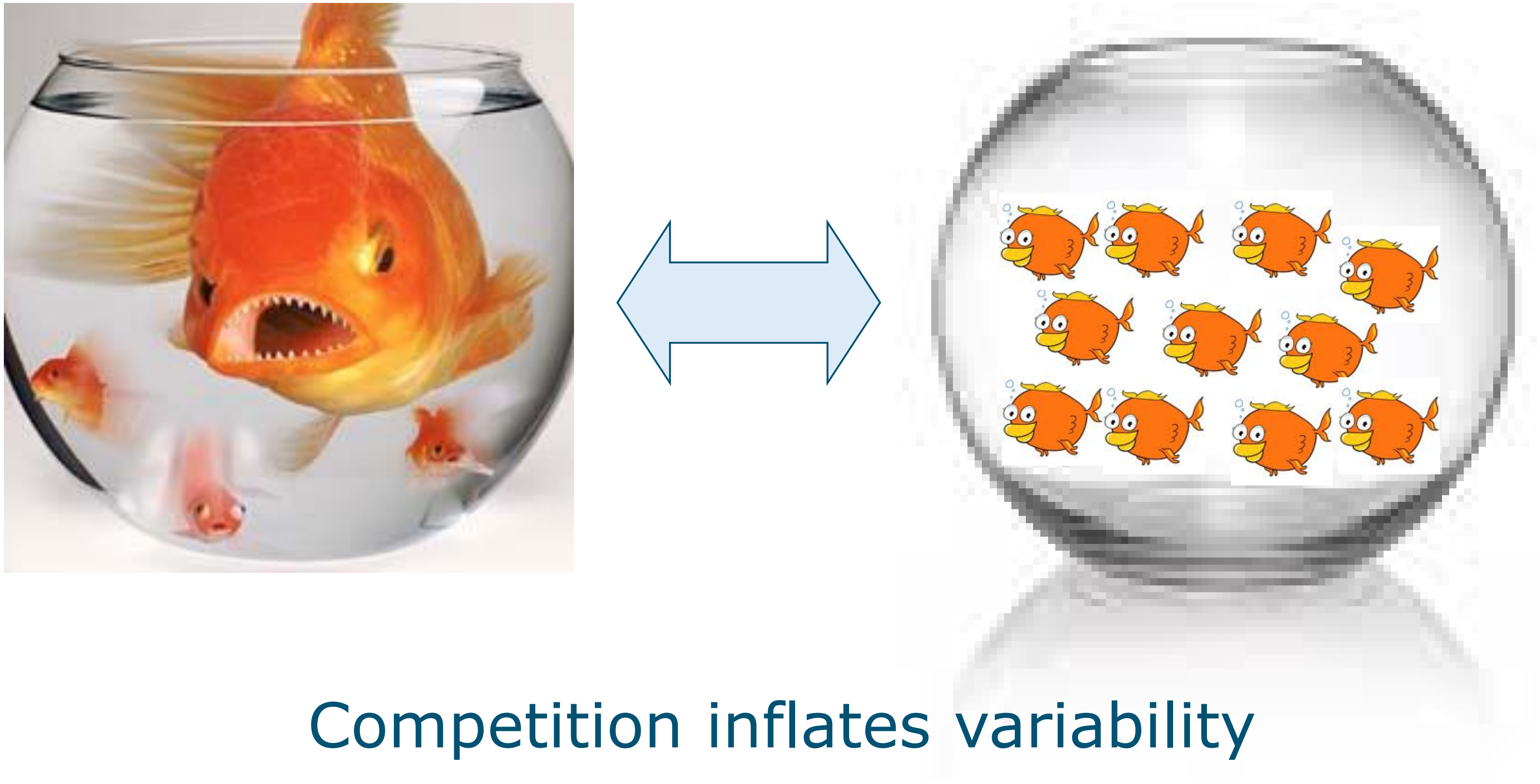
Sell-Kubiak et al., 2015. BMC Genomics 16:1049

Candidate genes Ve litter size

- Chromosome 7:
  - Cul7: expressed in embryonic, placental, and uterus tissues
  - HSPCB: buffering under stress
  - VEGFA: angiogenesis and vasculogenesis in the fetus
- Genome-wide associations for Ve can help in unraveling genetic architecture of response to environmental disturbances

Sell-Kubiak et al. 2015. BMC Genomics 16:1049

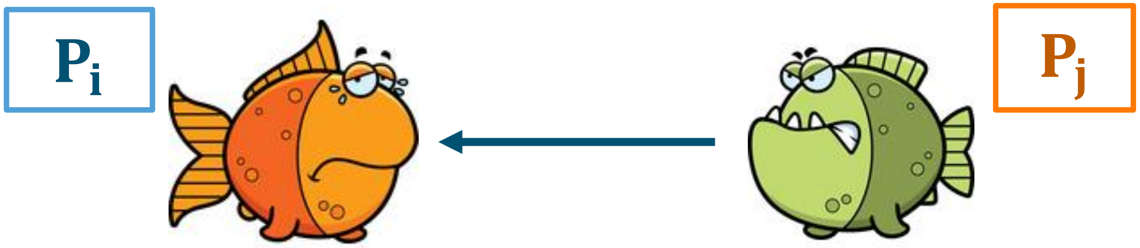
Ve and competition



Competition inflates variability

Theory

- Higher body weight gives competitive advantage
- Ordinary IGE models only model final phenotype
- We need to model the evolution of body weight over the life of the individuals
- Basic model involving interaction of two individuals



P_i

P_j

Model

Phenotype – focal individual

BV for growth

$$\mathbf{P_{t,i} = P_{t-1,i} + \mu_{GR} + A_{GR,i} + b_{ij}\left(P_{t-1,j} - P_{t-1,i}\right)}$$

Mean growth rate

Difference in body weight between **j** and **i**

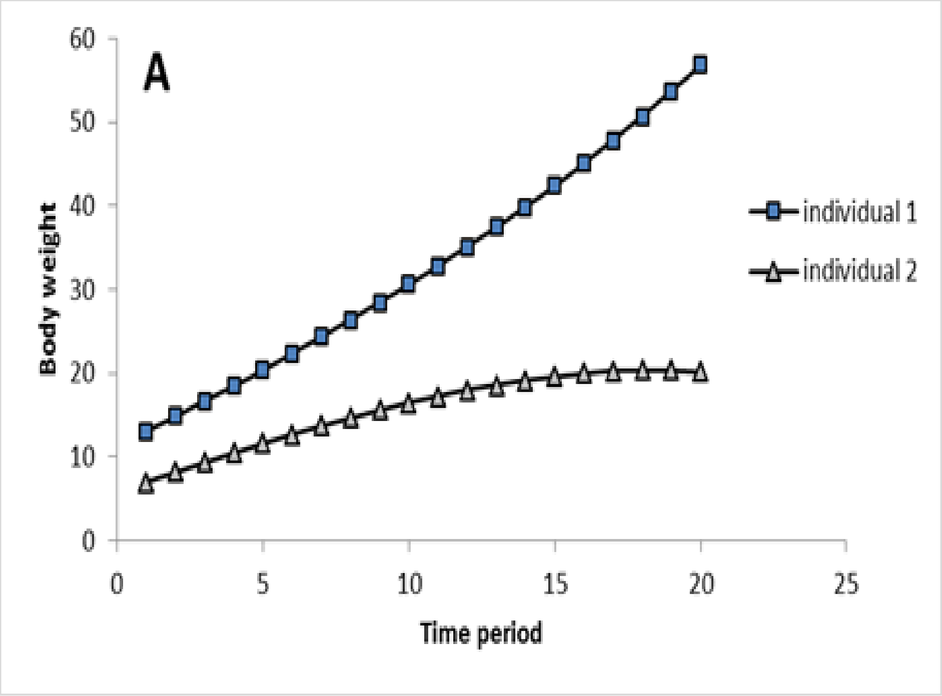
$$\mathbf{b_{ij} = \bar{b} + A_{D,i} + A_{S,j}}$$

Resistance to competition

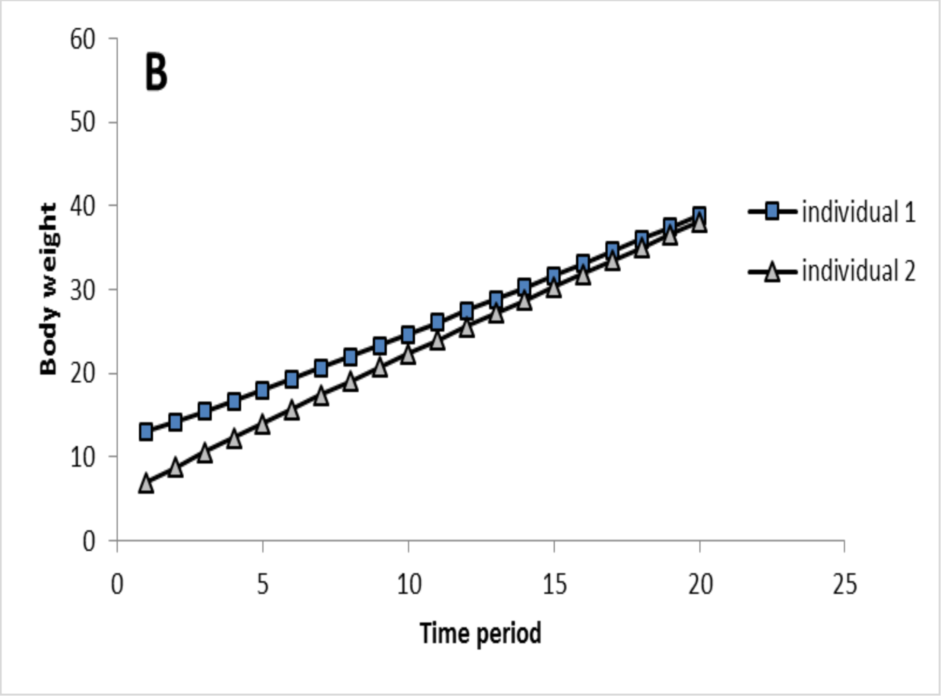
Cooperation effect

Competition vs cooperation

Competition



Cooperation



Competition leads to more variability; cooperation to less variability

Ve and natural selection

- Pedigreed natural population
- Fledging weight measured
- Fitness: number of recruits in next year

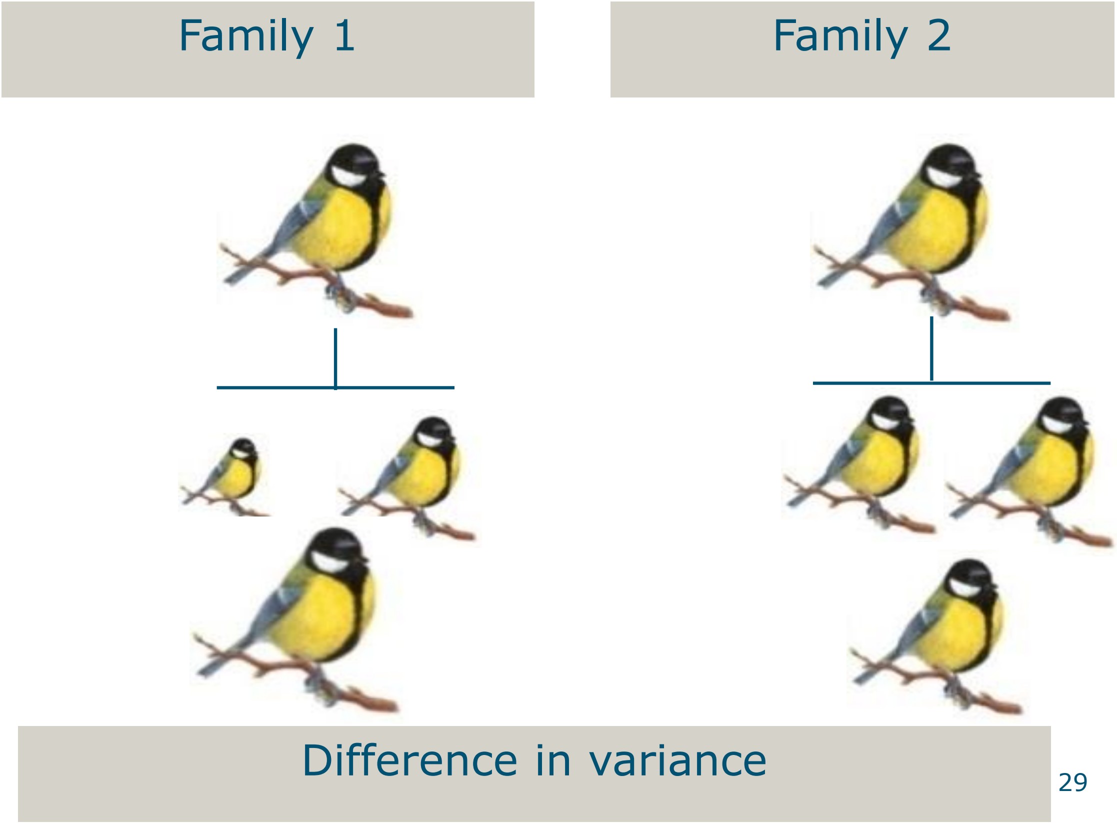
Mulder et al. 2016; Evolution 70:2004-2016

Genetic variance in within-nest variability of fledging weight of Great Tit

Genetic coefficient of variation: 25%

Heritability: 0.005

Rg_mv: 0.10

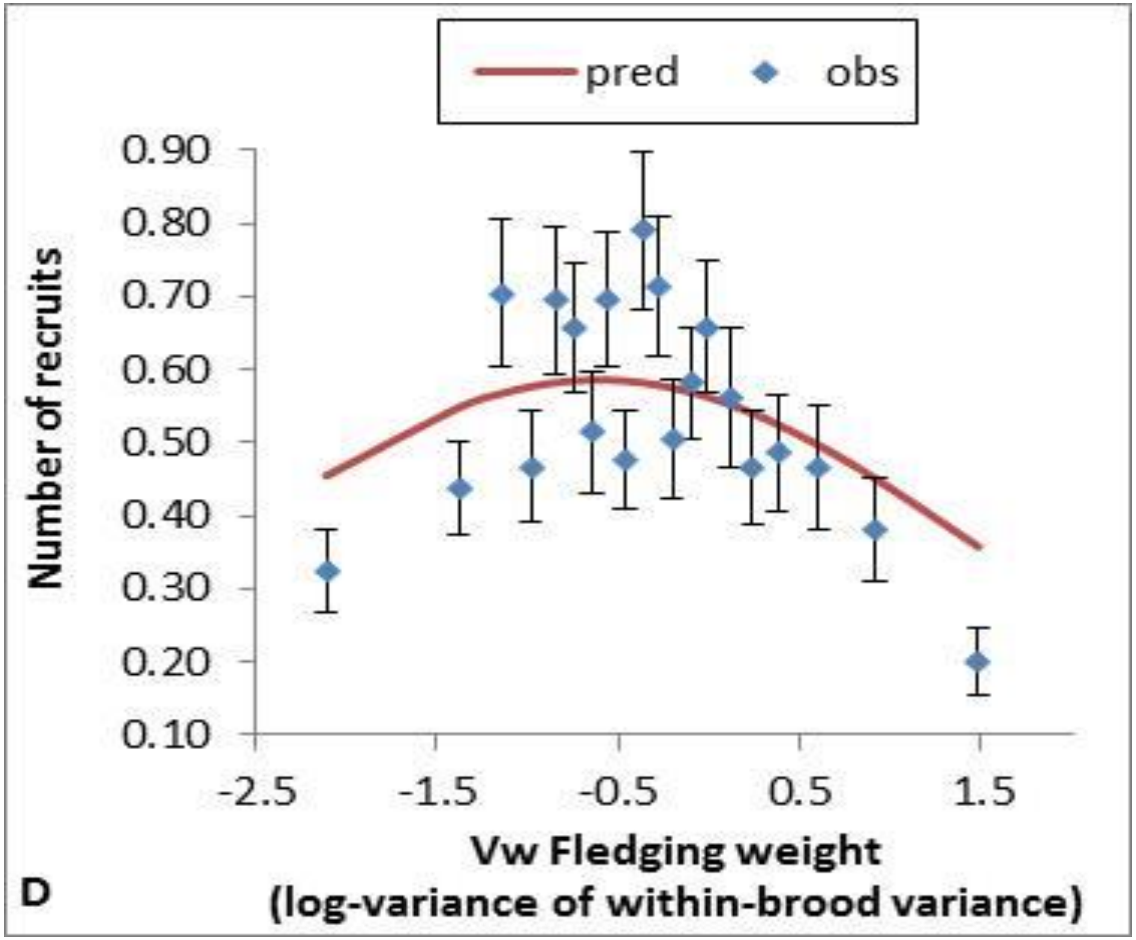


Family 1

Family 2

Difference in variance

Evolution of within-nest variability: evidence for stabilizing selection



I like some variation in my chicks, but not too much

Summary

- Heritability of Ve is low but GCV is high
  - Partly scaling effects are picked up
- Ve and plasticity have partly the same genetic background
- Ve seems highly polygenic; some genes related directly to the trait, but some also related to buffering stress
- Competition may lead to hidden genetic variation in Ve due to IGE
- Evidence for stabilizing selection on Ve in a natural population of Great tit

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CRV

HENDRIX GENETICS

Topigs Norsvin
PROGRESS IN PIGS

Summary

- Heritability of micro-environmental sensitivity/uniformity is low but GCV is high
    - Partly scaling effects are picked up
- Ve and plasticity have partly the same genetic background
- Ve seems highly polygenic; some genes related directly to the trait, but some also related to buffering stress
- Competition may lead to hidden genetic variation in Ve due to IGE
- Evidence for stabilizing selection on Ve in a natural population of Great tit

Food for thought

- Genomic selection has great potential in aquaculture to exploit GxE and genetic variation in Ve to increase
    - Harvest weight and its uniformity
    - Increase survival
    - Adaptation to different environments
    - Resilience to environmental disturbances