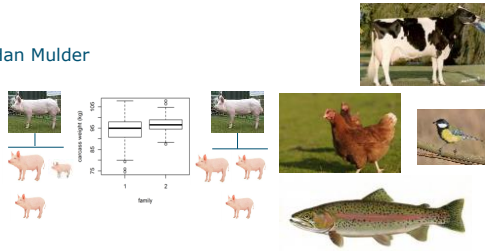


## Quantitative genetics and genomics of environmental variance in livestock and aquaculture

Dr Han Mulder



Animal Breeding and Genomics

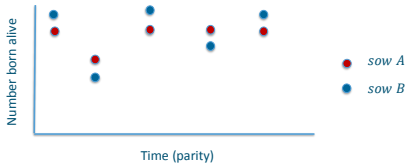
## What is genetic variation in $V_e$ ?

- 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

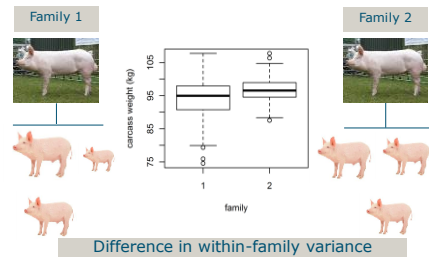


## What is genetic variation in $V_e$ ?

- Variation in repeated observations



## What is genetic variation in $V_e$ ?



## Contents

- Modelling genetic differences in  $V_e$
- Heritability and genetic coefficient of variation for  $V_e$
- Genetic parameters in different species
- Relationship plasticity and  $V_e$
- Genetic architecture of  $V_e$ : GWAS
- $V_e$  and natural selection
- Big data, resilience and  $V_e$



## Quantitative genetic model for $V_e$ : The additive model

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

$$\begin{pmatrix} A_m \\ A_v \end{pmatrix} \sim N \left( \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \mathbf{G} \otimes \mathbf{A} \right) \quad \mathbf{G} = \begin{bmatrix} \sigma_{A_m}^2 & \text{cov}_{A_m} \\ \text{cov}_{A_m} & \sigma_{A_v}^2 \end{bmatrix}$$

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

$A_{m,i}$  = breeding value of  $i$  for mean  
 $A_{v,i}$  = breeding value of  $i$  for environmental variance  
 $\sigma_E^2$  = the mean environmental variance




### Quantitative genetic model for Ve: The exponential model

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

$$\begin{pmatrix} A_m \\ A_v \end{pmatrix} \sim N\left(\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \mathbf{G} \otimes \mathbf{A}\right) \quad \mathbf{G} = \begin{bmatrix} \sigma_{A_m}^2 & \text{cov}_{A_m} \\ \text{cov}_{A_m} & \sigma_{A_v}^2 \end{bmatrix}$$

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

$A_{m,i}$  = breeding value of i for mean  
 $A_{v,i}$  = breeding value of i for environmental variance  
 $\sigma_e^2$  = the mean environmental variance




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### 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  $\mathbf{y}$
- $V_e = \exp(\mathbf{X}_v \mathbf{b}_v + \mathbf{Z}_v \mathbf{a}_v + \mathbf{W}_v \mathbf{pe}_v)$

**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.




### Heritability of Ve

- In analogy of the normal heritability of the mean
- Regression of  $A_v$  on  $P^2$  (additive model)
 
$$h_v^2 = b_{A_v, P^2} = \text{Cov}(A_v, P^2) / \text{Var}(P^2)$$

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


$$h_v^2 = \frac{\sigma_{A_v}^2}{2\sigma_p^4 + 3\sigma_{A_e}^2}$$
- Accuracy of EBV based on own performance =  $\sqrt{h_v^2}$
- For exponential model: convert genetic variance to additive model



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


### Genetic coefficient of variation for Ve

- Genetic coefficient of variation:  $GCV = \sigma_a / \mu$ 
  - Evolvability (Houle, 1992, Genetics 130: 195)
  - For classical breeding traits:  $GCV \approx 3 - 10\%$
- Application to heritable variance in the additive model
  - $\mu$  = mean environmental variance =  $V_e$
  - $\sigma$  = genetic std in environmental variance =  $\sigma_{A_v}$
- 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	-




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)




WAGENINGEN UNIVERSITY & RESEARCH Mulder et al. 2016. GSE 48:39 13

### Genetic variance in Ve in Tilapia


	HW	BC-HW	Length	Depth	Width
$\sigma_A^2$	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)




WAGENINGEN UNIVERSITY & RESEARCH Marjanovic et al. 2016. GSE 48:41 14

### 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



WAGENINGEN UNIVERSITY & RESEARCH Sae-Lim et al., 2015; GSE 47:46  
Sae-Lim et al., 2017; GSE 49:33 13

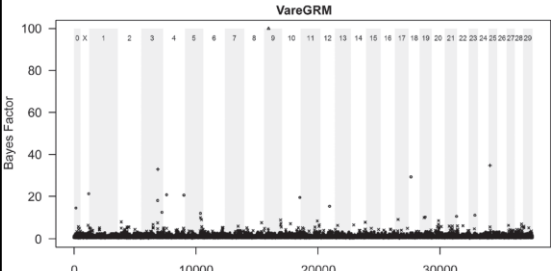
### Plasticity (slope of RN) and Ve

- 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



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### Genetic architecture of Ve: GWAS variability SCS in dairy cattle




WAGENINGEN UNIVERSITY & RESEARCH Mulder et al. 2013; JDS 96:7306-7317 13

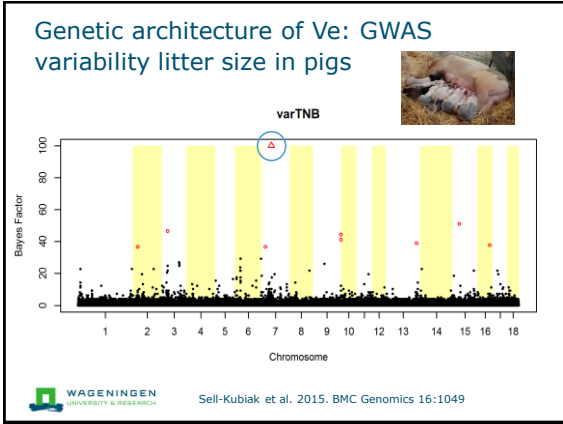
### Genetic architecture of Ve: GWAS variability SCS in dairy cattle

BTA	Most sign. SNP	Position (Mbp)	BF	Gen. var. expl. by SNP (%)
9	Hapmap31053-BTA-111664	27.02	134.7	3.5
	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



WAGENINGEN UNIVERSITY & RESEARCH Mulder et al. 2013; JDS 96:7306-7317 13



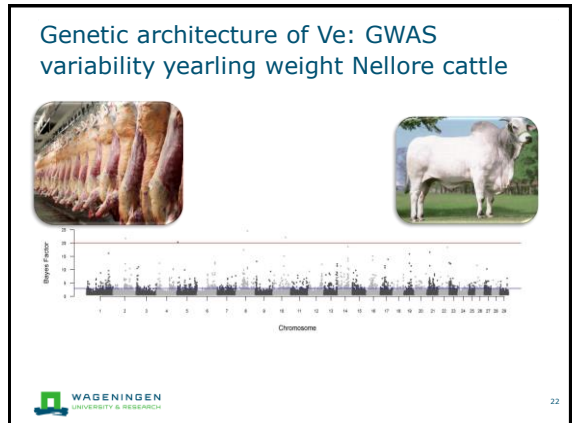
### Genetic architecture of Ve: GWAS variability litter size in pigs

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

WAGENINGEN UNIVERSITY & RESEARCH  
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
- WAGENINGEN UNIVERSITY & RESEARCH  
Sell-Kubiak et al. 2015. BMC Genomics 16:1049



### Candidate genes variability yearling weight

Table 1. SNPs with a strong association (BF > 20) with uniformity of YW

Chromosome	Position	BF	% Var	Candidate Genes
8	67465702	24.51	1.35	<b>LPL, SLC18A1, ATP6V1B2</b>
10	74342168	22.11	1.16	<b>HIF1A</b>
2	73421284	21.75	1.08	<b>GLI2</b>
5	5383239	20.32	0.93	<b>BBS10, OSBPL8</b>

- Potential biological candidate genes:
  - Metabolism
  - Stress response/Adaptation

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- ### Ve and natural selection
- Pedigreed natural population
  - Fledging weight measured
  - Fitness: number of recruits in next year
- 
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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

Mulder et al. 2016; Evolution 70:2004-2016 25

### Evolution of within-nest variability: evidence for stabilizing selection

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

Mulder et al. 2016; Evolution 70:2004-2016 26

### Big data, resilience and Ve

■ Daily milk yield from AMS

Elgersma et al. 2018; J. Dairy Sci. ahead of print  
doi: 10.3168/jds.2017-13270 27

### Genetic correlations with health and longevity

	Udder health	Claw health	Ketosis	Longevity
Drop average	-0.09	-0.03	-0.20	-0.08
Drop regression	-0.10	0.15	-0.15	0.10
LNvar	-0.36	-0.07	-0.52	-0.30
Milk	-0.12	-0.06	-0.25	-0.02

Elgersma et al. 2018; J. Dairy Sci. ahead of print  
doi: 10.3168/jds.2017-13270 28

### Opportunities to use macro- and micro-environmental sensitivity to breed robust and resilient animals

DOI: 10.1111/ajg.12303

EDITORIAL

WILEY Animal Breeding and Genetics

#### Is GxE a burden or a blessing? Opportunities for genomic selection and big data

Genomic selection and genomic prediction have been widely adopted in many livestock breeding programmes, including some fish schemes. Genomic prediction increases the accuracy of breeding values, especially for lowly heritable traits and traits that are difficult to measure. Genotype-by-environment interaction (GxE) is often seen as a burden

When the reference populations of cross-bred animals are made of animals raised in a wide range of environments, genomic selection for improved cross-bred performance is more efficient than with traditional selection relying on pedigree information. Such multi-environment reference populations could be easily combined with

Mulder, 2017; J. Anim. Breed. Genet. 134: 435-436 29

### 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
- Evidence for stabilizing selection on Ve in a natural population of Great tit
- Big data offer great opportunities to use heritable variation in Ve to increase resilience

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## Summary

- Heritability of  $V_e$  is low but GCV is high
  - Partly scaling effects are picked up
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- $V_e$  seems highly polygenic; some genes related directly to the trait, but some also related to buffering stress
- Evidence for stabilizing selection on  $V_e$  in a natural population of Great tit
- Big data offer great opportunities to use heritable variation in  $V_e$  to increase resilience

