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Joint estimation of additive, dominance and residual polygenic variances using a female reference population

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Introduction

- German genomic evaluation is based on a bull reference population
  - 34,246 Holstein bulls with 41,726,604 daughters worldwide (EuroGenomics)

- New reference bulls have been highly genomically pre-selected
  - Possible bias of estimated SNP effects

- Novel traits are recorded on cows
  - Conventional evaluation of bulls available rather late

- German project **Kuh-L** to set up a female reference population
  - FBF (Umbrella organization of cattle breeding associations to coordinate and support joint research projects)
  - Univ. of MLU (Halle), Univ. of Kassel and
  - **vit**

Introduction and objective

- Daughter yield deviations (DYD) or deregressed proofs (DRP) as corrected phenotypes of bulls are used for routine genomic evaluations
- More and more female animals have being genotyped, genomic reference population may be changed to cows with own phenotypes. In the era of genomics phenotype is the king (Coffey, 2010, WCGALP Leipzig)
- Dominance effects can be estimated from cows' own phenotypes in addition to effects in genomic evaluation based on the bull reference population.
- Estimated dominance variance in dairy cattle were 20% (Sun et al., 2013) or 50% (Ertl et al., 2014) of total genetic variance
- Goal: Estimation of additive and dominance variances of SNP markers and residual polygenic variance for **Kuh-L** project in Germany

A genomic model with additive and dominance effects of SNP markers and a residual polygenic effect

$$\begin{bmatrix} X`X & X`Z_a & X`Z_p & X`Z_d \\ & Z_a^{\prime}Z_a + G^{-1}\lambda_1 & Z_a^{\prime}Z_p & Z_a^{\prime}Z_d \\ & & Z_p^{\prime}Z_p + A_{22}^{-1}\lambda_2 & Z_p^{\prime}Z_d \\ & & & Z_d^{\prime}Z_d + D^{-1}\lambda_3 \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{a} \\ \hat{p} \\ \hat{d} \end{bmatrix} = \begin{bmatrix} X`y \\ Z_a^{\prime}y \\ Z_p^{\prime}y \\ Z_d^{\prime}y \end{bmatrix}$$

y is dependent variable

$Z_a^{\prime}$, $Z_p^{\prime}$ und $Z_d^{\prime}$ are incidence matrices for add - SNP, add - RPG and Dom - SNP

$\lambda_1 = \sigma_e^2 \sigma_{DGV}^{-2}$, $\lambda_2 = \sigma_e^2 \sigma_{RPG}^{-2}$ und $\lambda_3 = \sigma_e^2 \sigma_{DOM}^{-2}$

$$A = \begin{bmatrix} A_{00} & A_{02} \\ A_{20} & A_{22} \end{bmatrix}$$

$$G = a * G_0 + b$$

$$G_0 = M_a^{\prime} M_a,\ M_a = (SNP - 2p_j)(2 \sum_{k=1}^{nSNP} p_k q_k)^{-\frac{1}{2}}, SNP = (0,1,2// \text{ for AA,AB,BB})$$

$$a = (avg\_offdiagA_{22} - avg\_diagA_{22})(avg\_offdiagG_0 - avg\_diagG_0)^{-1}$$

$$b = avg\_diagA_{22} - (a * avg\_diagG_0)$$

$$D = M_d^{\prime} M_d,\ M_d = (-2p_j^2 \text{ for AA, } 2p_j q_j \text{ for AB and } -2q_j^2 \text{ for BB})(2 \sum_{k=1}^{nSNP} p_k q_k)^{-1}$$

Genotype and phenotype data

- German Holstein genomic evaluation for April 2016
  - Number of all genotyped animals: 193,203
  - 640,588 animals in pedigree
  - 45,613 SNP markers used in genomic evaluation

- Genotyped young cows from German **Kuh-L** project: 20,000

- **Kuh-L** phenotypes (April 2016)
  - 12,239 genotyped cows with phenotypes of conformation traits
  - 11,785 cows with completed first lactation of production traits

I. Estimation of variance components (Conformation traits)

1. Original phenotypes as traits (Y)

➔Fixed effects:

classifier
herd-test-day
age at first calving
age class

➔ Random effects:

SNP substitution effect (Vitezica et al., 2013)
SNP dominance effect
additive residual polygenic effect (RPG)
residual

2. Corrected phenotypes (yield deviations, YD) from routine genetic evaluation

➔ only random effects

Results: Genetic parameter estimates for conformation trait Stature (Estimated with GCTA)

Yield deviations (YD) and phenotype (Y) as traits

(%)	σ^2_{ADD}	σ^2_{RPG}	σ^2_{DOM}	h^2	h^2_{ADD}	h^2_{RPG}	h^2_{DOM}	σ^2_e	AIC
ADD RPG DOM	77	21	2	0.54	0.42	0.11	0.01	4.21	36563
ADD RPG	79	21	-	0.53	0.42	0.11		4.30	36565
ADD DOM (Y)	98	-	2	0.45	0.45		0.01	4.93	36581
RPG DOM	-	94	6	0.53		0.50	0.03	4.44	38219
ADD				0.45	0.45			5.00	36582
RPG (Y)				0.50		0.50		4.73	38229
DOM				0.08			0.08	8.14	38976
ADD RPG DOM (YD)	73	25	2	0.50	0.36	0.13	0.01	3.78	-

ADD: Additive SNP effects RPG: Residual polygenic effect DOM: Dominance SNP effects

Results: Estimates of variance components for Stature (original phenotype) using ASReml

Sum of additive effects of SNP markers and residual polygenic effect

$G^{*}= \alpha *G+ (1- \alpha)*A_{22}$

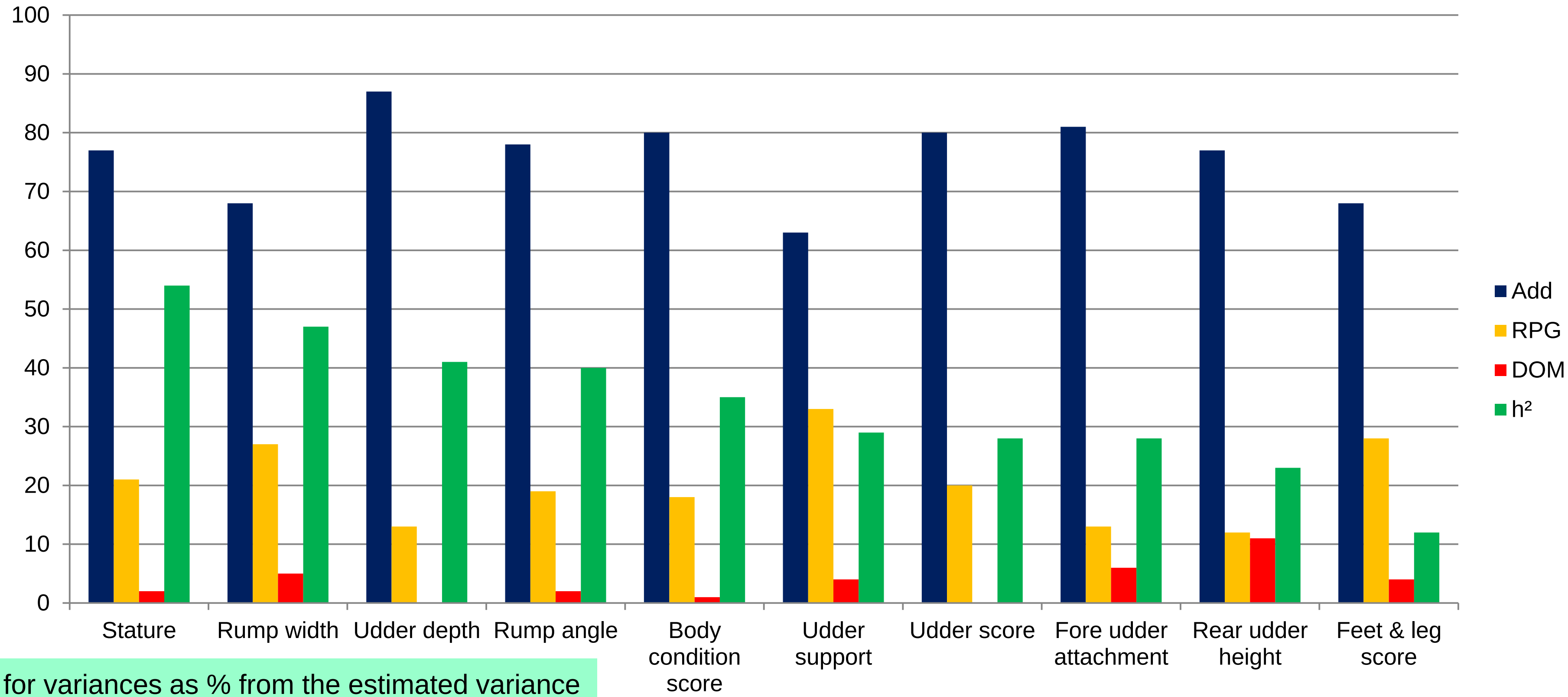
Alfa (α)*	$\sigma^2_{ADD+RPG}$	σ^2_e	σ^2_p	h²	AIC
1.00	4.04	5.13	9.17	0.44	36473
0.99	4.08	5.1	9.18	0.44	36471
0.95	4.23	4.98	9.21	0.46	36466
0.90	4.43	4.83	9.26	0.48	36461
0.80	**4.87**	**4.47**	**9.35**	**0.52**	**36456**
0.70	**5.4**	**4.06**	**9.46**	**0.57**	**36459**
0.60	6.06	3.56	9.62	0.63	36472

Assumed Alfa for estimation (percentage of additive SNP variance from total genetic variance)

Results: Comparison variance component estimates with ASReml and GCTA (Conformation traits)

Trait	ASReml				GCTA					
	Assumed Alfa(%)	$\sigma^2_{ADD+RPG}$	σ^2_{e}	AIC	σ^2_{ADD}	σ^2_{RPG}	σ^2_{DOM}	σ^2_{e}	AIC	Estimated Alfa(%)
Stature	70-80	4.88	4.47	36456	3.87	1.06	0.09	4.2	36568	77
Chest width	70-80	0.41	1.22	18126	0.32	0.11	0.03	1.17	18109	70
Angularity	60-70	3.36	7.14	39567	2.29	1.22	0.10	6.84	39684	63
Rump width	70-80	0.82	1.01	18309	0.58	0.23	0.04	0.97	18312	68

Results: Percentages of additive and dominance variances of SNP markers and residual polygenic variances and estimated broad-sense heritabilities



SE for variances as % from the estimated variance

SE_DOM >40%, SE_RPG 25 - 50%,

SE_Add 4-22% and SE_h^2 5-20%

II: Variance component estimates for milk production traits and somatic cell score

- Scenario 1: Test-day yield between DIM 150 and 200 (milk, fat, protein and somatic cell score)

  ➔ Fixed effects: DIM, herd-test-date and age at first calving

  ➔ Random effects: additive and dominance effects of SNP markers, residual polygenic effects (RPG) and residual effect

- Scenario 2: 305-day first lactation yields: milk, fat, protein and average of SCS

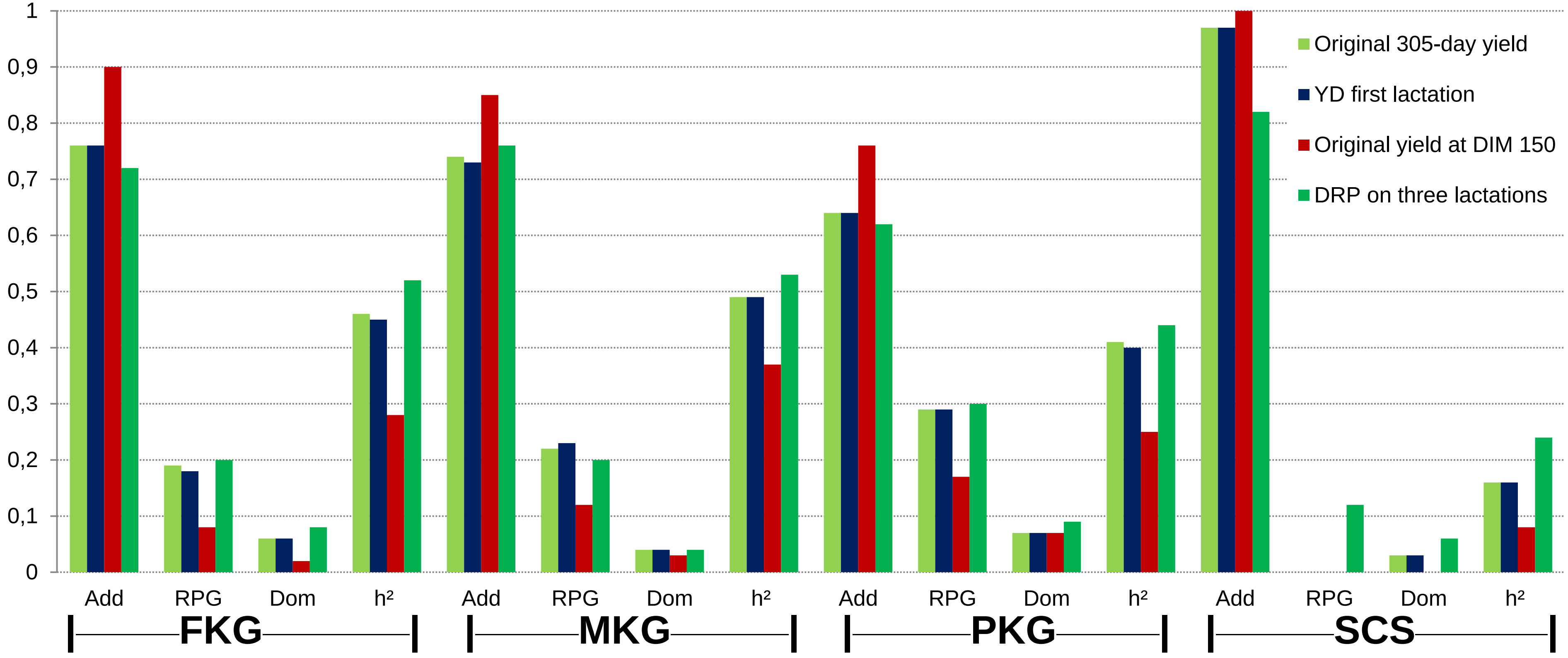
  ➔ Fixed effekts: herd-year-season, age at first calving

  ➔ Random effects: additive and dominance effects of SNP markers, residual polygenic effects (RPG) and residual effect

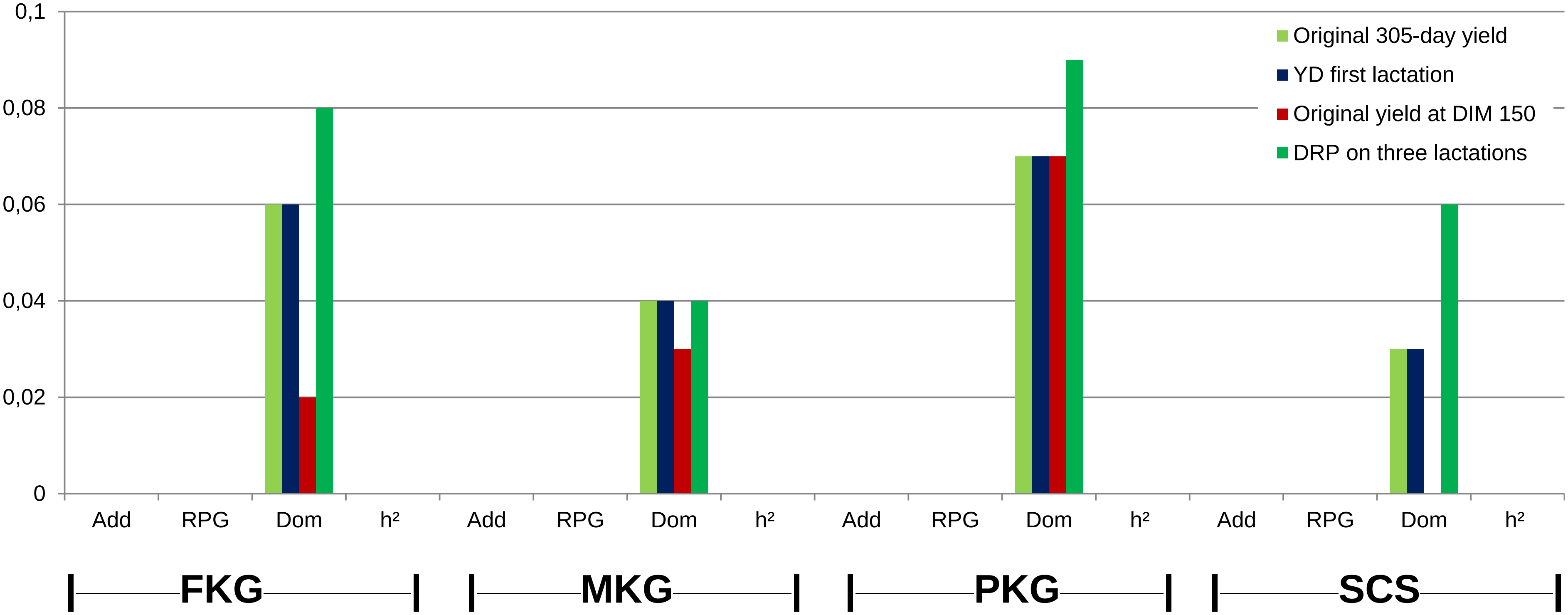
- Scenario 3: Yield deviation (YD): only the random effects fitted

- Scenario 4: Deregressed EBV (DRP): only the random effects fitted

Results: Percentages of additive and dominance variances of SNP markers and residual polygenic variances and heritability estimates



Results: Percentages of additive and dominance variances of SNP markers and residual polygenic variances and heritability estimates



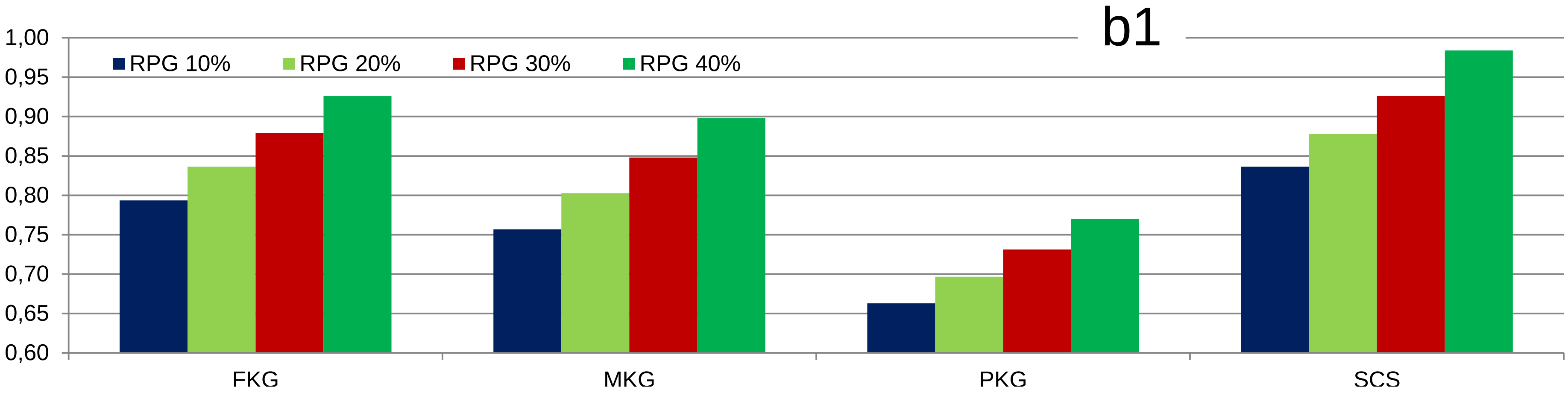
Data for genomic validation

- Phenotype: lactation yield deviations (LYD)
  - 11,785 cows with at least 7 test-day records in first lactation to be included in reference population
  - Traits: milk, fat, protein and SCS
- Validation: 750 bulls with own phenotype, born between 2009 und 2010

  (DYD only available from bulls with daughters in Germany)
- Residual polygenic effect (10, 20, 30 and 40% of total genetic variance)
- Dominance variance (5% of genetic variance)

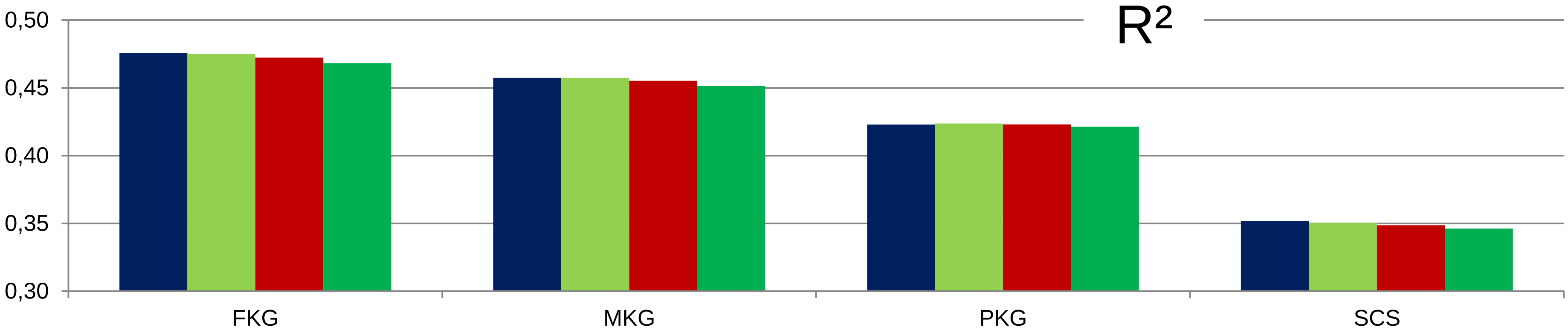
Result: genomic validation

$$DYD = b_0 + b_1 * GEBV$$



28% of ref. cows are daughters of validation bulls

145 from 750 validation bulls are sires of ref-cows



Conclusions

- SNP additive and dominance effects can be jointly estimated with residual polygenic effect

- Dominance variance of SNP markers
  - For milk production traits < 10% of total genetic variance
  - For conformation traits between 0 and 10%

- Estimated residual polygenic variances higher than currently used
  - For milk production traits: 15% to 30% of total genetic variance
  - For conformation traits: 12% to 33% of total genetic variance

- Optimal residual polygenic variances determined from the validation study were similar to the estimated RPG variances

- Dominance effects of SNP markers can be accurately estimated and may be included in genomic prediction

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