

Genetic architecture of traits using multi-locus Genome Wide Association (GWA) mapping with GEMMA

https://visoca.github.io/popgenomworkshop-gwas_gemma

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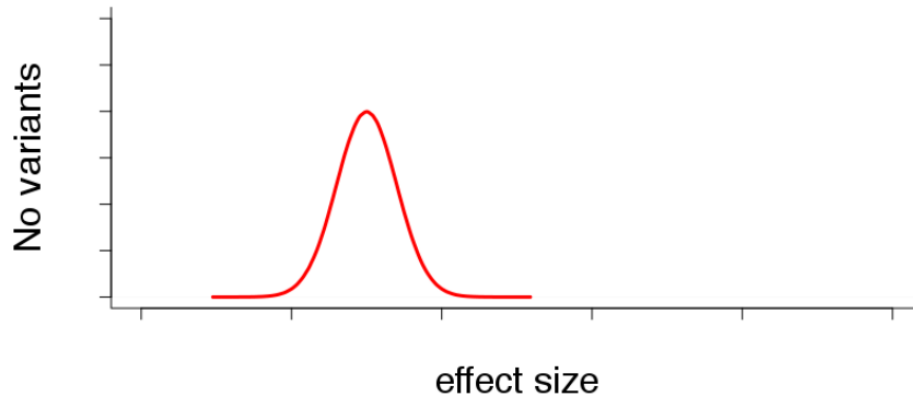


GWAS MULTI-SNP MODELS

Linear Mixed Model (LMM)

Assume polygenic basis:
all variants affect the phenotype

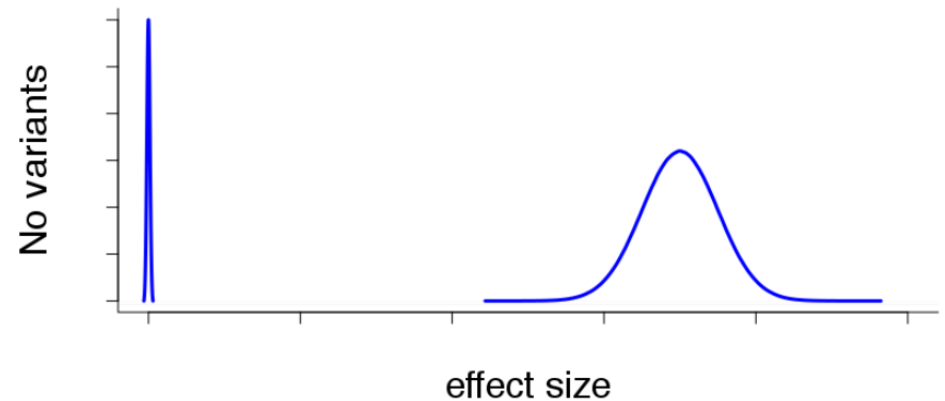
Effect sizes normally distributed



Bayesian Variable Selection Regression model (BVS)

Assume mono/oligogenic basis:
a small proportion of variants affect the phenotype

Effect sizes as mixture of point mass at 0 and normal distribution



GWAS MULTI-SNP MODELS

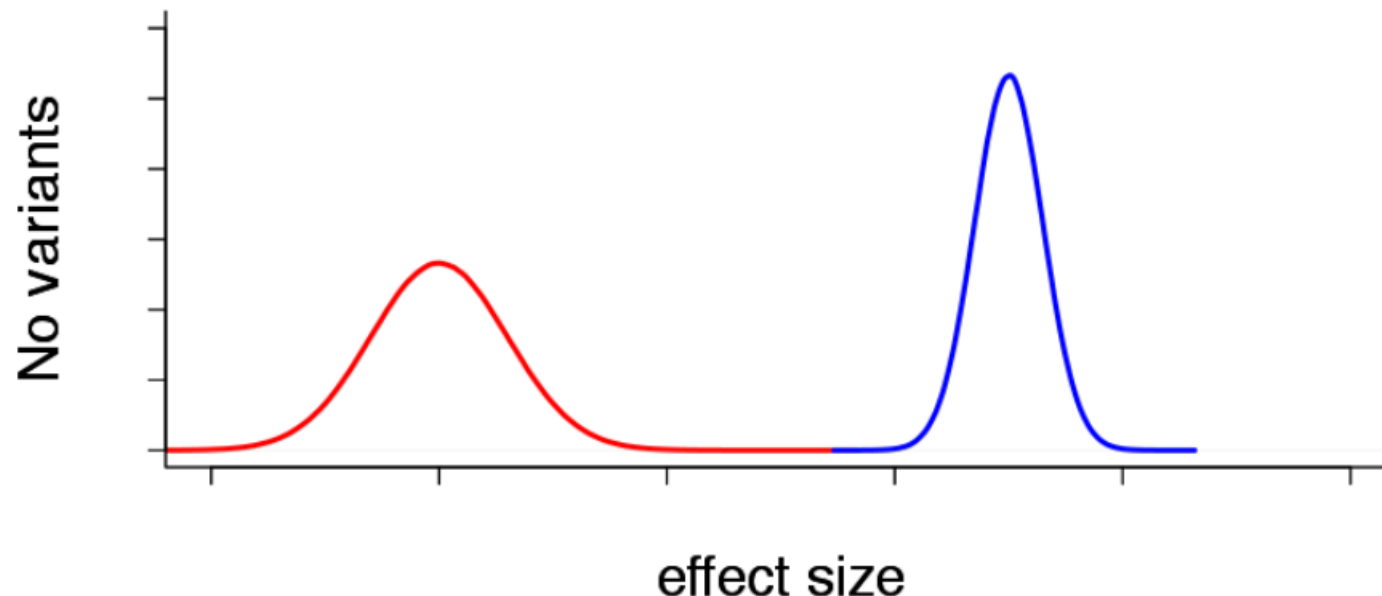
Hybrid general model: Bayesian Sparse Linear Mixed Model (BSLMM)

Mixture of polygenic (LMM) and mono/oligogenic basis (BVSR)

Two distribution of effect sizes:

- 1) small effect size of all variants (α)
- 2) additional large effect size of some variants (β)

effect size of a given variant = $\alpha_i + \beta_i$



GEMMA

Genome-wide Efficient Mixed Model Association

Three models:

- Univariate Linear Mixed Model (LMM)
- Multivariate Linear Mixed Model (mvLMM)
- **Bayesian-Sparse Linear Mixed Model (BSLMM)**

Manual – read it!

www.xzlab.org/software/GEMMAmanual.pdf

Publications

- Xiang Zhou and Matthew Stephens (2012). Genome-wide efficient mixed-model analysis for association studies. *Nature Genetics*. 44: 821–824. <http://goo.gl/pFb7Qy>
- Xiang Zhou and Matthew Stephens (2014). Efficient multivariate linear mixed model algorithms for genome-wide association studies. *Nature Methods*. 11(4): 407–409. <http://goo.gl/9pWM1Y>
- **Xiang Zhou, Peter Carbonetto and Matthew Stephens (2013). Polygenic modeling with Bayesian sparse linear mixed models. *PLoS Genetics*. 9(2): e1003264.**
<http://goo.gl/YStR2a>

Also, BSLMM accounts for sample relatedness and population stratification