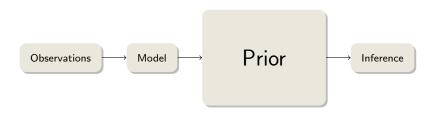


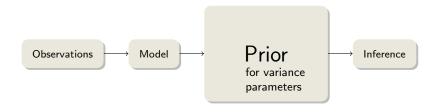
We consider *latent Gaussian models* where the linear predictor is Gaussian conditional on the model parameters



We consider *latent Gaussian models* where the linear predictor is Gaussian conditional on the model parameters



We consider *latent Gaussian models* where the linear predictor is Gaussian conditional on the model parameters



Note: We do not focus on fixed effects, and assign wide Gaussian priors

### Outline

- Motivating example: Wheat breeding
- Standard prior approach
- New approach: Hierarchical variance decomposition
- New method: Hierarchical decomposition prior framework
- New tool: R package makemyprior
- Neonatal mortality
- Discussion and summary

# Motivating example: Wheat breeding

- Purpose: More grain yield (weight of grain from each strain)
- How: Find which strains of wheat are genetically best
- Challenge: Separate environmental (residual) and genetic variation
- Observations: Grain yield y<sub>i</sub> (phenotype) and genetic markers

• Model: 
$$y_i = \mu + \underbrace{a_i + d_i + x_j}_{g_i} + \varepsilon_i$$
,  $i = 1, \dots, 100$ 

- $\begin{array}{l} \blacktriangleright \ \, \mu \sim \mathcal{N}(0, \sigma = 1000) \text{ (intercept)} \\ \blacktriangleright \ \, * \sim \mathcal{N}(\mathbf{0}, \sigma_*^2 V_*), \, \varepsilon_i \sim \mathcal{N}(0, \sigma_\varepsilon^2) \end{array}$
- ► Genetic = additive + nonadditive (= dominance + epistasis)
- Prior: Use information from a geneticist
- Inference: Stan through rstan
- See Hem et al. (2021)<sup>1</sup> for details

<sup>&</sup>lt;sup>1</sup>Ingeborg Gullikstad Hem et al. "Robust Modeling of Additive and Nonadditive Variation With Intuitive Inclusion of Expert Knowledge". In: Genetics 217.3 (2021), iyab002, DOI: 10.1093/genetics/iyab002.

Information from the geneticist

- 1. The broad-sense heritability  $(\frac{\sigma_g^2}{\sigma_g^2 + \sigma_e^2})$  is around 25%
- 2. Additive (a), dominance (d) and epistasis (x) account for most of, some of and a little of the genetic variance  $(\sigma_g^2)$

### Information from the geneticist

- 1. The broad-sense heritability  $(\frac{\sigma_g^2}{\sigma_g^2+\sigma_\epsilon^2})$  is around 25%
- 2. Additive (a), dominance (d) and epistasis (x) account for most of, some of and a little of the genetic variance  $(\sigma_g^2)$  85% 10% 5%

Information from the geneticist

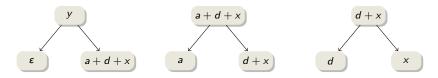
- 1. Total variation (y) is 25% genetic (a+d+x) and 75% environmental  $(\varepsilon)$  2. Genetic variation is 85% additive (a) and 15% nonadditive (d+x)
- 3. Nonadditive variation is 67% dominance (d) and 33% epistasis (x)

### Standard prior approach

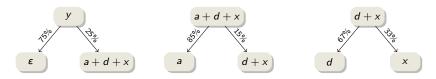
- 1. Total variation (y) is 25% genetic (a + d + x) and 75% environmental  $(\varepsilon)$
- 2. Genetic variation is 85% additive (  $\pmb{a}$  ) and 15% nonadditive (  $\pmb{d}+\pmb{x}$  )
- 3. Nonadditive variation is 67% dominance ( $\boldsymbol{d}$ ) and 33% epistasis ( $\boldsymbol{x}$ )
- Four variances:  $\sigma_{\varepsilon}^2$ ,  $\sigma_{a}^2$ ,  $\sigma_{d}^2$ ,  $\sigma_{x}^2$
- Independent variance priors (inverse gamma, half-Cauchy, penalized complexity prior<sup>2</sup>, ...)
- Prior info is not about the variances directly
- No information about magnitude

<sup>&</sup>lt;sup>2</sup>Daniel Simpson et al. "Penalising Model Component Complexity: A Principled, Practical Approach to Constructing Priors". In: Statistical Science 32.1 (2017), pp. 1–28.

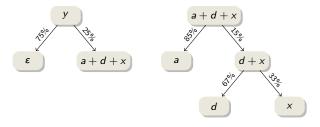
- 1. Total variation (y) is 25% genetic (a + d + x) and 75% environmental  $(\varepsilon)$
- 2. Genetic variation is 85% additive (a) and 15% nonadditive (d + x)
- 3. Nonadditive variation is 67% dominance ( $\boldsymbol{d}$ ) and 33% epistasis ( $\boldsymbol{x}$ )



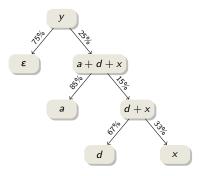
- 1. Total variation (y) is 25% genetic (a + d + x) and 75% environmental ( $\epsilon$ )
- 2. Genetic variation is 85% additive (a) and 15% nonadditive (d + x)
- 3. Nonadditive variation is 67% dominance ( $\boldsymbol{d}$ ) and 33% epistasis ( $\boldsymbol{x}$ )



- 1. Total variation (y) is 25% genetic (a + d + x) and 75% environmental  $(\varepsilon)$
- 2. Genetic variation is 85% additive (a) and 15% nonadditive (d + x)
- 3. Nonadditive variation is 67% dominance ( $\emph{d}$ ) and 33% epistasis ( $\emph{x}$ )

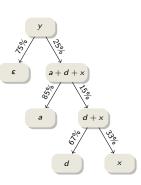


- 1. Total variation (y) is 25% genetic (a + d + x) and 75% environmental  $(\varepsilon)$
- 2. Genetic variation is 85% additive (a) and 15% nonadditive (d + x)
- 3. Nonadditive variation is 67% dominance ( $\emph{d}$ ) and 33% epistasis ( $\emph{x}$ )



# Hierarchical decomposition prior framework<sup>3</sup>

- Create joint prior for variance parameters from a prior tree
- Prior tree is based on the model structure and prior (expert) knowledge
- Assigning prior to the total latent variance (sum of variances)
  - Empirical data variation does not depend on model
  - Straight forward to add and remove model components
  - Any variance prior is possible, Jeffreys' prior useful for Gaussian data
- Assigning priors to splits in tree (representing variance partitions)
  - Ignorance through symmetric Dirichlet priors
  - Shrinkage through PC priors
- Keep fixed effects outside the HD prior framework



<sup>&</sup>lt;sup>3</sup>Geir-Arne Fuglstad et al. "Intuitive Joint Priors for Variance Parameters". In: *Bayesian Analysis* 15.4 (2020), pp. 1109–1137.

# Wheat breeding priors

#### Standard:

$$\sigma_{\varepsilon}^{2} \sim \pi(\mathsf{m} = V \cdot 0.75)$$

$$\sigma_{\sigma}^{2} \sim \pi(\mathsf{m} = V \cdot 0.25 \cdot 0.85)$$

$$\sigma_{d}^{2} \sim \pi(\mathsf{m} = V \cdot 0.25 \cdot 0.15 \cdot 0.67)$$

$$\sigma_{x}^{2} \sim \pi(\mathsf{m} = V \cdot 0.25 \cdot 0.15 \cdot 0.33)$$

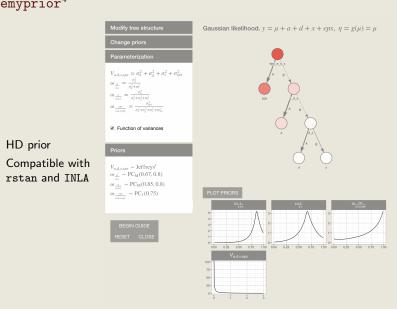
Must choose some V, and update all priors when changing model

#### Hierarchical:

$$V_{a+d+x+\epsilon} \sim ext{Jeffreys'}$$
  $\omega_{rac{g}{g+\epsilon}} \sim \pi( ext{m} = 0.25)$   $\omega_{rac{d}{d+x'}} \sim \pi( ext{m} = 0.85)$   $\omega_{rac{d}{d+x'}} \sim \pi( ext{m} = 0.67)$ 

## makemyprior<sup>4</sup>

HD prior

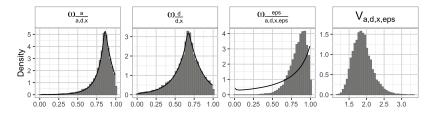


<sup>&</sup>lt;sup>4</sup>Ingeborg Gullikstad Hem, Geir-Arne Fuglstad, and Andrea Riebler. makemyprior: Intuitive Construction of Joint Priors for Variance Parameters in R. arXiv preprint arXiv:2105.09712v2 [stat.CO], 2022, https://CRAN.R-project.org/package=makemyprior

### Wheat breeding

```
formula <- y ~
  mc(a, model = "generic0", Cmatrix = Q.a, constr = TRUE) +
  mc(d, model = "generic0", Cmatrix = Q.d, constr = TRUE) +
  mc(x, model = "generic0", Cmatrix = Q.x, constr = TRUE)
prior <- make.prior(formula, wheat_data)

new.prior <- makemyprior.gui(prior)
res <- inference.stan(new.prior)</pre>
```



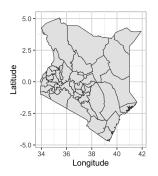
- ullet Without the prior knowledge, arepsilon and x are too hard to separate
- Standard approach leads to less stable inference than hierarchical approach
- Improved selection of genetically best individuals with the hierarchical approach

### Neonatal mortality in Kenya

- Observations: Number of live births  $b_{i,j}$  and neonatal<sup>5</sup> deaths  $y_{i,j}$  in cluster j in county i, urbanity indicator of cluster  $x_{i,i}$  (urban = 1)
- Model:

$$y_{i,j}|b_{i,j}, p_{i,j} \sim \text{Bin}(b_{i,j}, p_{i,j}), i = 1, ..., 47, j = 1, ..., m_i$$
  
 $\text{logit}(p_{i,j}) = \mu + x_{i,j}\beta + u_i + v_i + \nu_{i,j}$ 

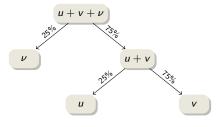
- ho  $\mu$ ,  $eta \sim \mathcal{N}(0, \sigma = 1000)$
- $v_i, v_{i,j} \sim N(0, \sigma_*^2),$  u is Besag effect with variance  $\sigma_*^2$
- Prior: Use spatial structure and avoid overfitting
- Inference: Stan using rstan



<sup>&</sup>lt;sup>5</sup>First 30 days of life

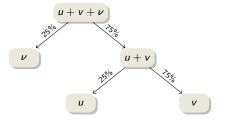
### Neonatal mortality

- Prefer coarser over finer effects (explain data at coarser level if possible)  $\implies u+v>\nu$
- Prefer unstructured over structured effects (reduce risk of estimating spurious effects) => v > u



### Neonatal mortality

- Prefer coarser over finer effects (explain data at coarser level if possible)  $\implies u + v > \nu$
- Prefer unstructured over structured effects (reduce risk of estimating spurious effects) => v > u

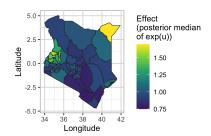


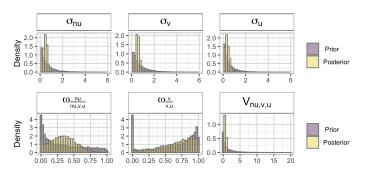
- PC priors for variance proportions with shrinkage to (u+v) and (v)
- PC prior for total variance, such that [0.1, 10] is a 90% credible interval for  $\exp(u_i + v_i + \nu_{i,j})$ : PC(3.35, 0.05)

### Neonatal mortality

formula <- y ~ urban + mc(nu) + mc(v) +
 mc(u, model = "besag", graph = graph.path,
 scale.model = TRUE)
prior <- make.prior(formula, neonatal.data,
 family = "binomial")</pre>

new\_prior <- makemyprior\_gui(prior)
res <- inference\_stan(new\_prior)</pre>





### Discussion and summary

- Non-variance parameters (such as a range) can be assigned independent priors
- Idea not restricted to PC and Dirichlet priors
- Can combine several prior trees
- Taking the model structure into account
- Visualization eases communication
- Prior knowledge can be incorporated at the level it applies to
- One, but not the only, way to construct priors
- Simple to explore options with makemyprior
- All priors are choices, make good ones



#### References I



Fuglstad, Geir-Arne et al. "Intuitive Joint Priors for Variance Parameters". In: Bayesian Analysis 15.4 (2020), pp. 1109-1137.



Hem, Ingeborg Gullikstad, Geir-Arne Fuglstad, and Andrea Riebler. makemyprior: Intuitive Construction of Joint Priors for Variance Parameters in R. arXiv preprint arXiv:2105.09712v2 [stat.CO]. 2022.



Hem, Ingeborg Gullikstad et al. "Robust Modeling of Additive and Nonadditive Variation With Intuitive Inclusion of Expert Knowledge". In: Genetics 217.3 (2021). iyab002. DOI: 10.1093/genetics/iyab002.



Simpson, Daniel et al. "Penalising Model Component Complexity: A Principled, Practical Approach to Constructing Priors". In: Statistical Science 32.1 (2017), pp. 1–28.