

A Bayesian model for hybrid vigor

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DNA and RNA

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Examples of gene
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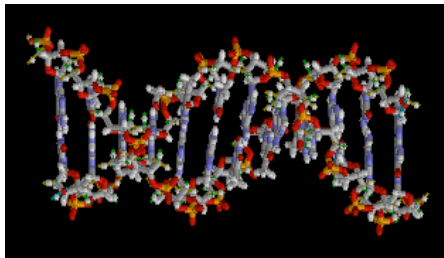
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DNA



```

... GTGCATCTGACTCCTGAGGAGAAG ...
... CACGTAGACTGAGGACTCCTCTTC ...

```

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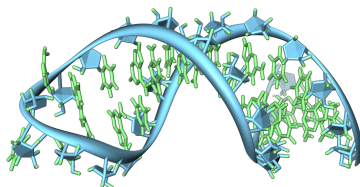
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RNA



... — GUGCAUCUGACUCCUGAGGAGAAG — ...

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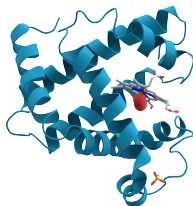
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Proteins



... — V — H — L — T — P — E — E — K — ...

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Central dogma: how organisms make proteins

... GTGCATCTGACTCCTGAGGAGAAG ...
 ... CACGTAGACTGAGGACTCCTCTTC ...

DNA

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Central dogma: how organisms make proteins



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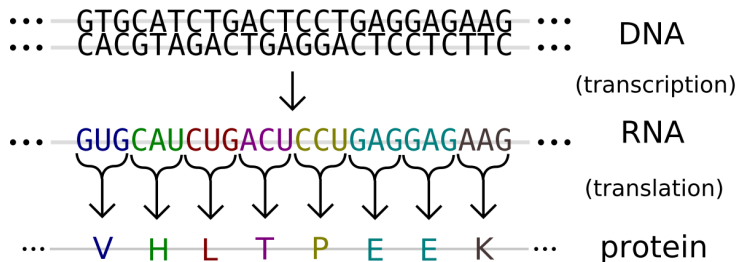
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Central dogma of genetics



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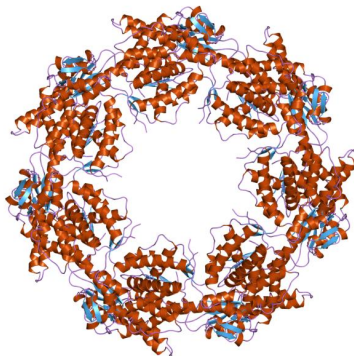
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HSP60

- ▶ HSP = heat shock protein.
- ▶ Prevent heat damage to other proteins.



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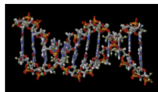
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Temperature spike triggers HSP60 production.

HSP60 Gene



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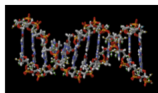
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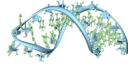
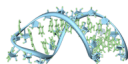
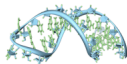
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Temperature spike causes HSP60 expression.

HSP60 Gene



HSP60 RNA



...

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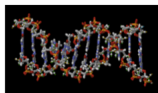
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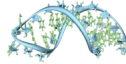
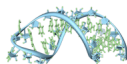
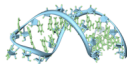
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Temperature spike causes HSP60 expression.

HSP60 Gene



HSP60 RNA



...

HSP60



...

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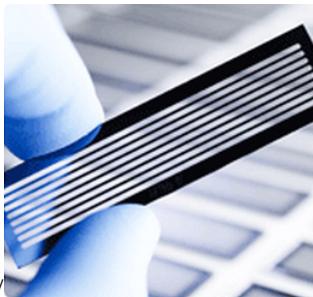
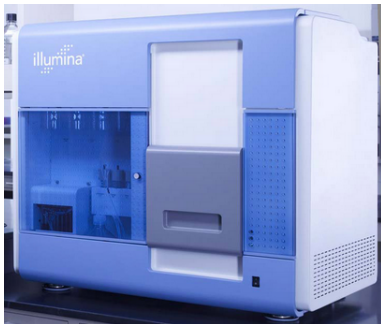
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RNA-seq

- ▶ RNA sequencing: measure gene expression using relative abundance of RNA.
- ▶ Illumina Genome Analyzer:



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RNA-seq data: counts of amplified RNA fragments

	Treatment 1			Treatment 2		Treatment 3	
Gene 1	100	225	0	70	279	300	106
Gene 2	0	1	1	50	501	2	7
Gene 3	3	4	2	700	900	0	0
Gene 4	893	400	760	5	5	1000	513
...
Gene 34897	10	13	6	819	761	902	912

- Goal: use RNA-seq to study hybrid vigor (heterosis).

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High-parent heterosis: child's trait surpasses both parents

Parent 1



Parent 2



Child



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Low-parent heterosis: child's trait is weaker than in each parent

Parent 1



Parent 2



Child



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Mid-parent heterosis: child's trait is different than average of parents

Parent 1



Parent 2



Child



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High-parent heterosis in gene expression

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	Parent 1			Child		Parent 2	
Gene 1	100	225	0	70	279	300	106
Gene 2	0	1	1	50	501	2	7
Gene 3	3	4	2	700	900	0	0
Gene 4	893	400	760	5	5	1000	513
...
Gene 34897	10	13	6	819	761	902	912

Low-parent heterosis in gene expression

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$$y_{g,n} \stackrel{\text{ind}}{\sim} \text{Poisson}(y_{g,n} \mid \exp(c_n + \varepsilon_{g,n} + \mu(n, \phi_g, \alpha_g, \delta_g)))$$

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$$c_n \stackrel{\text{ind}}{\sim} N(c_n \mid 0, \sigma_c^2)$$

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$$c_n \stackrel{\text{ind}}{\sim} N(c_n \mid 0, \sigma_c^2)$$

$$\varepsilon_{g,n} \stackrel{\text{ind}}{\sim} N(\varepsilon_{g,n} \mid 0, \eta_g^2)$$

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$$\begin{aligned}
 y_{g,n} &\overset{\text{ind}}{\sim} \text{Poisson}(y_{g,n} \mid \exp(c_n + \varepsilon_{g,n} + \mu(n, \phi_g, \alpha_g, \delta_g))) \\
 c_n &\overset{\text{ind}}{\sim} \text{N}(c_n \mid 0, \sigma_c^2) \\
 \sigma_c &\sim \text{U}(\sigma_c \mid 0, \sigma_{c0}) \\
 \varepsilon_{g,n} &\overset{\text{ind}}{\sim} \text{N}(\varepsilon_{g,n} \mid 0, \eta_g^2)
 \end{aligned}$$

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$$y_{g,n} \stackrel{\text{ind}}{\sim} \text{Poisson}(y_{g,n} \mid \exp(c_n + \varepsilon_{g,n} + \mu(n, \phi_g, \alpha_g, \delta_g)))$$

$$c_n \stackrel{\text{ind}}{\sim} \text{N}(c_n \mid 0, \sigma_c^2)$$

$$\sigma_c \sim \text{U}(\sigma_c \mid 0, \sigma_{c0})$$

$$\varepsilon_{g,n} \stackrel{\text{ind}}{\sim} \text{N}(\varepsilon_{g,n} \mid 0, \eta_g^2)$$

$$\eta_g^2 \stackrel{\text{ind}}{\sim} \text{Inv-Gamma} \left(\eta_g^2 \mid \text{shape} = \frac{d}{2}, \text{rate} = \frac{d \cdot \tau^2}{2} \right)$$

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$$y_{g,n} \stackrel{\text{ind}}{\sim} \text{Poisson}(y_{g,n} \mid \exp(c_n + \varepsilon_{g,n} + \mu(n, \phi_g, \alpha_g, \delta_g)))$$

$$c_n \stackrel{\text{ind}}{\sim} \text{N}(c_n \mid 0, \sigma_c^2)$$

$$\sigma_c \sim \text{U}(\sigma_c \mid 0, \sigma_{c0})$$

$$\varepsilon_{g,n} \stackrel{\text{ind}}{\sim} \text{N}(\varepsilon_{g,n} \mid 0, \eta_g^2)$$

$$\eta_g^2 \stackrel{\text{ind}}{\sim} \text{Inv-Gamma} \left(\eta_g^2 \mid \text{shape} = \frac{d}{2}, \text{rate} = \frac{d \cdot \tau^2}{2} \right)$$

$$d \sim \text{U}(d \mid 0, d_0)$$

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$$y_{g,n} \stackrel{\text{ind}}{\sim} \text{Poisson}(y_{g,n} \mid \exp(c_n + \varepsilon_{g,n} + \mu(n, \phi_g, \alpha_g, \delta_g)))$$

$$c_n \stackrel{\text{ind}}{\sim} \text{N}(c_n \mid 0, \sigma_c^2)$$

$$\sigma_c \sim \text{U}(\sigma_c \mid 0, \sigma_{c0})$$

$$\varepsilon_{g,n} \stackrel{\text{ind}}{\sim} \text{N}(\varepsilon_{g,n} \mid 0, \eta_g^2)$$

$$\eta_g^2 \stackrel{\text{ind}}{\sim} \text{Inv-Gamma} \left(\eta_g^2 \mid \text{shape} = \frac{d}{2}, \text{rate} = \frac{d \cdot \tau^2}{2} \right)$$

$$d \sim \text{U}(d \mid 0, d_0)$$

$$\tau^2 \sim \text{Gamma}(\tau^2 \mid \text{shape} = a_\tau, \text{rate} = b_\tau)$$

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$$y_{g,n} \stackrel{\text{ind}}{\sim} \text{Poisson}(y_{g,n} \mid \exp(c_n + \varepsilon_{g,n} + \mu(n, \phi_g, \alpha_g, \delta_g)))$$

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$$\mu(n, \phi_g, \alpha_g, \delta_g) = \begin{cases} \phi_g - \alpha_g & \text{sample } n \text{ from parent 1} \\ \phi_g + \delta_g & \text{sample } n \text{ from child} \\ \phi_g + \alpha_g & \text{sample } n \text{ from parent 3} \end{cases}$$

$$y_{g,n} \stackrel{\text{ind}}{\sim} \text{Poisson}(y_{g,n} \mid \exp(c_n + \varepsilon_{g,n} + \mu(n, \phi_g, \alpha_g, \delta_g)))$$

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$$\phi_g \stackrel{\text{ind}}{\sim} \text{N}(\phi_g \mid \theta_\phi, \sigma_\phi^2)$$

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$$\mu(n, \phi_g, \alpha_g, \delta_g) = \begin{cases} \phi_g - \alpha_g & \text{sample } n \text{ from parent 1} \\ \phi_g + \delta_g & \text{sample } n \text{ from child} \\ \phi_g + \alpha_g & \text{sample } n \text{ from parent 3} \end{cases}$$

$$y_{g,n} \stackrel{\text{ind}}{\sim} \text{Poisson}(y_{g,n} \mid \exp(c_n + \varepsilon_{g,n} + \mu(n, \phi_g, \alpha_g, \delta_g)))$$

$$\phi_g \stackrel{\text{ind}}{\sim} \text{N}(\phi_g \mid \theta_\phi, \sigma_\phi^2)$$

$$\alpha_g \stackrel{\text{ind}}{\sim} \pi_\alpha^{1-l(\alpha_g)} [(1 - \pi_\alpha) \text{N}(\alpha_g \mid \theta_\alpha, \sigma_\alpha^2)]^{l(\alpha_g)}$$

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$$y_{g,n} \stackrel{\text{ind}}{\sim} \text{Poisson}(y_{g,n} \mid \exp(c_n + \varepsilon_{g,n} + \mu(n, \phi_g, \alpha_g, \delta_g)))$$

$$\phi_g \stackrel{\text{ind}}{\sim} \text{N}(\phi_g \mid \theta_\phi, \sigma_\phi^2)$$

$$\alpha_g \stackrel{\text{ind}}{\sim} \pi_\alpha^{1-l(\alpha_g)} [(1 - \pi_\alpha) \text{N}(\alpha_g \mid \theta_\alpha, \sigma_\alpha^2)]^{l(\alpha_g)}$$

$$\delta_g \stackrel{\text{ind}}{\sim} \pi_\delta^{1-l(\delta_g)} [(1 - \pi_\delta) \text{N}(\delta_g \mid \theta_\delta, \sigma_\delta^2)]^{l(\delta_g)}$$

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$$y_{g,n} \stackrel{\text{ind}}{\sim} \text{Poisson}(y_{g,n} \mid \exp(c_n + \varepsilon_{g,n} + \mu(n, \phi_g, \alpha_g, \delta_g)))$$

$$\phi_g \stackrel{\text{ind}}{\sim} N(\phi_g \mid \theta_\phi, \sigma_\phi^2)$$

$$\theta_\phi \sim N(\theta_\phi \mid 0, \gamma_\phi^2)$$

$$\alpha_g \stackrel{\text{ind}}{\sim} \pi_\alpha^{1-l(\alpha_g)} [(1 - \pi_\alpha)N(\alpha_g \mid \theta_\alpha, \sigma_\alpha^2)]^{l(\alpha_g)}$$

$$\delta_g \stackrel{\text{ind}}{\sim} \pi_\delta^{1-l(\delta_g)} [(1 - \pi_\delta)N(\delta_g \mid \theta_\delta, \sigma_\delta^2)]^{l(\delta_g)}$$

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$$\mu(n, \phi_g, \alpha_g, \delta_g) = \begin{cases} \phi_g - \alpha_g & \text{sample } n \text{ from parent 1} \\ \phi_g + \delta_g & \text{sample } n \text{ from child} \\ \phi_g + \alpha_g & \text{sample } n \text{ from parent 3} \end{cases}$$

$$y_{g,n} \stackrel{\text{ind}}{\sim} \text{Poisson}(y_{g,n} \mid \exp(c_n + \varepsilon_{g,n} + \mu(n, \phi_g, \alpha_g, \delta_g)))$$

$$\phi_g \stackrel{\text{ind}}{\sim} \text{N}(\phi_g \mid \theta_\phi, \sigma_\phi^2)$$

$$\theta_\phi \sim \text{N}(\theta_\phi \mid 0, \gamma_\phi^2)$$

$$\alpha_g \stackrel{\text{ind}}{\sim} \pi_\alpha^{1-l(\alpha_g)} [(1 - \pi_\alpha) \text{N}(\alpha_g \mid \theta_\alpha, \sigma_\alpha^2)]^{l(\alpha_g)}$$

$$\theta_\alpha \sim \text{N}(\theta_\alpha \mid 0, \gamma_\alpha^2)$$

$$\delta_g \stackrel{\text{ind}}{\sim} \pi_\delta^{1-l(\delta_g)} [(1 - \pi_\delta) \text{N}(\delta_g \mid \theta_\delta, \sigma_\delta^2)]^{l(\delta_g)}$$

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$$\delta_g \stackrel{\text{ind}}{\sim} \pi_\delta^{1-l(\delta_g)} [(1 - \pi_\delta) \text{N}(\delta_g \mid \theta_\delta, \sigma_\delta^2)]^{l(\delta_g)}$$

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$$\theta_\phi \sim \text{N}(\theta_\phi \mid 0, \gamma_\phi^2)$$

$$\sigma_\phi \sim \text{U}(\sigma_\phi \mid 0, \sigma_{\phi 0})$$

$$\alpha_g \stackrel{\text{ind}}{\sim} \pi_\alpha^{1-I(\alpha_g)} [(1 - \pi_\alpha) \text{N}(\alpha_g \mid \theta_\alpha, \sigma_\alpha^2)]^{I(\alpha_g)}$$

$$\theta_\alpha \sim \text{N}(\theta_\alpha \mid 0, \gamma_\alpha^2)$$

$$\delta_g \stackrel{\text{ind}}{\sim} \pi_\delta^{1-I(\delta_g)} [(1 - \pi_\delta) \text{N}(\delta_g \mid \theta_\delta, \sigma_\delta^2)]^{I(\delta_g)}$$

$$\theta_\delta \sim \text{N}(\theta_\delta \mid 0, \gamma_\delta^2)$$

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$$\delta_g \stackrel{\text{ind}}{\sim} \pi_\delta^{1-I(\delta_g)} [(1 - \pi_\delta) \text{N}(\delta_g \mid \theta_\delta, \sigma_\delta^2)]^{I(\delta_g)}$$

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$$\theta_\delta \sim N(\theta_\delta \mid 0, \gamma_\delta^2)$$

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$$\theta_\alpha \sim N(\theta_\alpha \mid 0, \gamma_\alpha^2)$$

$$\sigma_\alpha \sim U(\sigma_\alpha \mid 0, \sigma_{\alpha 0})$$

$$\pi_\alpha \sim \text{Beta}(\pi_\alpha \mid a_\alpha, b_\alpha)$$

$$\delta_g \stackrel{\text{ind}}{\sim} \pi_\delta^{1-I(\delta_g)} [(1 - \pi_\delta)N(\delta_g \mid \theta_\delta, \sigma_\delta^2)]^{I(\delta_g)}$$

$$\theta_\delta \sim N(\theta_\delta \mid 0, \gamma_\delta^2)$$

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$$\sigma_\delta \sim \text{U}(\sigma_\delta \mid 0, \sigma_{\delta 0})$$

$$\pi_\delta \sim \text{Beta}(\pi_\delta \mid a_\delta, b_\delta)$$

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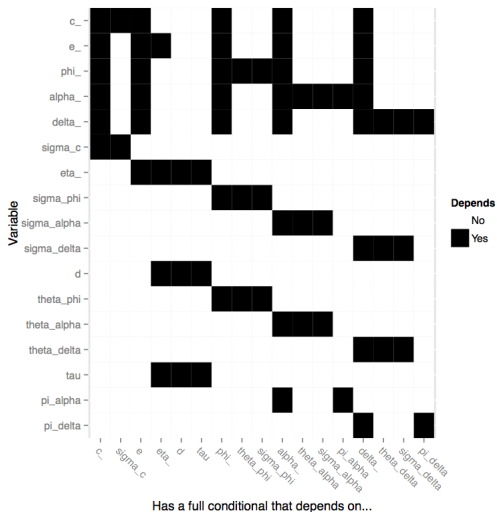
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Partition parameters by conditional independence.



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Use these partitions as Gibbs steps.

$$y_{g,n} \stackrel{\text{ind}}{\sim} \text{Poisson}(y_{g,n} \mid \exp(c_n + \varepsilon_{g,n} + \mu(n, \phi_g, \alpha_g, \delta_g)))$$

- From the appropriate full conditional distributions, sample the following:

1. c_1, \dots, c_N

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- From the appropriate full conditional distributions, sample the following:

1. c_1, \dots, c_N
2. $\tau, \pi_\alpha, \pi_\delta$

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- From the appropriate full conditional distributions, sample the following:

1. c_1, \dots, c_N
2. $\tau, \pi_\alpha, \pi_\delta$
3. $d, \theta_\phi, \theta_\alpha, \theta_\delta$

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- From the appropriate full conditional distributions, sample the following:

1. c_1, \dots, c_N
2. $\tau, \pi_\alpha, \pi_\delta$
3. $d, \theta_\phi, \theta_\alpha, \theta_\delta$
4. $\sigma_c, \sigma_\phi, \sigma_\alpha, \sigma_\delta, \eta_1^2, \dots, \eta_G^2$

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- From the appropriate full conditional distributions, sample the following:

1. c_1, \dots, c_N
2. $\tau, \pi_\alpha, \pi_\delta$
3. $d, \theta_\phi, \theta_\alpha, \theta_\delta$
4. $\sigma_c, \sigma_\phi, \sigma_\alpha, \sigma_\delta, \eta_1^2, \dots, \eta_G^2$
5. $\varepsilon_{1,1}, \varepsilon_{1,2}, \dots, \varepsilon_{1,N}, \varepsilon_{2,N}, \dots, \varepsilon_{G,N}$

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1. c_1, \dots, c_N
2. $\tau, \pi_\alpha, \pi_\delta$
3. $d, \theta_\phi, \theta_\alpha, \theta_\delta$
4. $\sigma_c, \sigma_\phi, \sigma_\alpha, \sigma_\delta, \eta_1^2, \dots, \eta_G^2$
5. $\varepsilon_{1,1}, \varepsilon_{1,2}, \dots, \varepsilon_{1,N}, \varepsilon_{2,N}, \dots, \varepsilon_{G,N}$
6. ϕ_1, \dots, ϕ_G

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- From the appropriate full conditional distributions, sample the following:

1. c_1, \dots, c_N
2. $\tau, \pi_\alpha, \pi_\delta$
3. $d, \theta_\phi, \theta_\alpha, \theta_\delta$
4. $\sigma_c, \sigma_\phi, \sigma_\alpha, \sigma_\delta, \eta_1^2, \dots, \eta_G^2$
5. $\varepsilon_{1,1}, \varepsilon_{1,2}, \dots, \varepsilon_{1,N}, \varepsilon_{2,N}, \dots, \varepsilon_{G,N}$
6. ϕ_1, \dots, ϕ_G
7. $\alpha_1, \dots, \alpha_G$

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- From the appropriate full conditional distributions, sample the following:

1. c_1, \dots, c_N
2. $\tau, \pi_\alpha, \pi_\delta$
3. $d, \theta_\phi, \theta_\alpha, \theta_\delta$
4. $\sigma_c, \sigma_\phi, \sigma_\alpha, \sigma_\delta, \eta_1^2, \dots, \eta_G^2$
5. $\varepsilon_{1,1}, \varepsilon_{1,2}, \dots, \varepsilon_{1,N}, \varepsilon_{2,N}, \dots, \varepsilon_{G,N}$
6. ϕ_1, \dots, ϕ_G
7. $\alpha_1, \dots, \alpha_G$
8. $\delta_1, \dots, \delta_G$

- and then repeat.

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$$\mu(n, \phi_g, \alpha_g, \delta_g) = \begin{cases} \phi_g - \alpha_g & \text{sample } n \text{ from parent 1} \\ \phi_g + \delta_g & \text{sample } n \text{ from child} \\ \phi_g + \alpha_g & \text{sample } n \text{ from parent 3} \end{cases}$$

$$y_{g,n} \stackrel{\text{ind}}{\sim} \text{Poisson}(y_{g,n} \mid \exp(c_n + \varepsilon_{g,n} + \mu(n, \phi_g, \alpha_g, \delta_g)))$$

$$I(\delta_g^{(i)} > |\alpha_g^{(i)}|)$$

$$I(\delta_g^{(i)} < -|\alpha_g^{(i)}|)$$

$$I(\delta_g^{(i)} \neq 0)$$

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Consider one chain with M iterations.

$$I(\delta_g^{(i)} > |\alpha_g^{(i)}|)$$

$$I(\delta_g^{(i)} < -|\alpha_g^{(i)}|)$$

$$I(\delta_g^{(i)} \neq 0)$$

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Consider one chain with M iterations.

$$P(\text{high-parent heterosis in gene } g) \approx \frac{1}{M} \sum_{i=1}^M I(\delta_g^{(i)} > |\alpha_g^{(i)}|)$$

$$I(\delta_g^{(i)} < -|\alpha_g^{(i)}|)$$

$$I(\delta_g^{(i)} \neq 0)$$

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$$y_{g,n} \stackrel{\text{ind}}{\sim} \text{Poisson}(y_{g,n} \mid \exp(c_n + \varepsilon_{g,n} + \mu(n, \phi_g, \alpha_g, \delta_g)))$$

Consider one chain with M iterations.

$$P(\text{high-parent heterosis in gene } g) \approx \frac{1}{M} \sum_{i=1}^M I(\delta_g^{(i)} > |\alpha_g^{(i)}|)$$

$$P(\text{low-parent heterosis in gene } g) \approx \frac{1}{M} \sum_{i=1}^M I(\delta_g^{(i)} < -|\alpha_g^{(i)}|)$$

$$I(\delta_g^{(i)} \neq 0)$$

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$$P(\text{high-parent heterosis in gene } g) \approx \frac{1}{M} \sum_{i=1}^M I(\delta_g^{(i)} > |\alpha_g^{(i)}|)$$

$$P(\text{low-parent heterosis in gene } g) \approx \frac{1}{M} \sum_{i=1}^M I(\delta_g^{(i)} < -|\alpha_g^{(i)}|)$$

$$P(\text{mid-parent heterosis in gene } g) \approx \frac{1}{M} \sum_{i=1}^M I(\delta_g^{(i)} \neq 0)$$

Tons of opportunity for GPU parallelism across genes!

$$y_{g,n} \stackrel{\text{ind}}{\sim} \text{Poisson}(y_{g,n} \mid \exp(c_n + \varepsilon_{g,n} + \mu(n, \phi_g, \alpha_g, \delta_g)))$$

- ▶ Sample in parallel:

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- c_n 's
- τ, d

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- $\theta_\phi, \theta_\alpha, \theta_\delta$

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- $\theta_\phi, \theta_\alpha, \theta_\delta$
- $\sigma_\phi, \sigma_\alpha, \sigma_\delta, \sigma_c$

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- ▶ Time for a demo...

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