$$Y_i = \sum_{t=1}^{q_2} \alpha_t E_{it} + \sum_{k=1}^{q_1} b_k C_{ik} + \sum_{j=1}^{p} \beta_j X_{ij} + \sum_{j=1}^{p} \eta_j \cancel{E_i} X_{ij} + \varepsilon_i$$

$\uparrow$ Env. $\quad \uparrow$ clinical $\quad \uparrow$ genes

$E_1 \quad E_2 \quad \ldots \quad E_{q_2}$

$X_1 \cdot (E_{11} \; E_{12} \; E_{13} \cdots E_{1q_2})$

$X_j(E_1, \cdots, E_{q_2})$

$i = 1, \cdots, n$

$$\Big(\underset{n\times 1}{X_1} (E_1, E_2, \cdots, E_{q_2})_{n\times q_2}, X_2(E_1, \cdots, E_{q_2})_{n\times q_2}, \cdots, X_p(E_1, \cdots, E_{q_2}) \Big)_{n\times (pq_2)}$$

$X = G_j. \quad j = 1, \cdots, p$

P1

$$Y = \underset{n\times q_2}{E} \cdot \underset{q_2\times 1}{\alpha} + \underset{n\times q_1}{C} \cdot \underset{q_1\times 1}{b} + \underset{n\times 1}{X} \underset{1\times 1}{\beta} + \underset{n\times q_2}{W} \cdot \underset{q_2\times 1}{\eta} + \varepsilon$$

$\alpha = (\alpha_1, \cdots, \alpha_{q_2})^T, \quad E = (E_1, \cdots, E_{q_2})$ (Env.)

$C = (C_1, \cdots, C_{q_1})$ (clinical). $\quad b = (b_1, \cdots, b_{q_1})^T$

$X = (X_1, \cdots, X_p)_{n\times p}$ (genes), $\quad \beta = (\beta_1, \cdots, \beta_p)^T_{p\times 1}$

$W_j = (\cancel{X_j} E_1, \cancel{X_j} E_2, \cdots, \cancel{X_j} E_{q_2})_{n\times q_2}. \quad \eta_j = (\eta_{j1}, \cdots, \eta_{jq_2})^T_{q_2\times 1}$

$W = (\underset{n\times q_2}{W_1}, \cdots, W_p)_{n\times pq_2}, \quad \eta = (\eta_1, \cdots, \eta_p)^T_{pq_2\times 1}$

$$W \cdot \eta = \Big(\underset{n\times 1}{X_1} (E_1, E_2, \cdots, E_{q_2})_{n\times q_2}, X_2(E_1, \cdots, E_{q_2}), \cdots, X_p(E_1, \cdots, E_{q_2}) \Big)_{n\times pq_2}$$

$W = (X E_1, X E_2, \cdots, X E_{q_2})_{n\times q_2} \qquad \beta_{1\times 1}. \quad X = G_j \; {}_{n\times 1}.$

$\eta = (\eta_1, \cdots, \eta_{q_2})^T_{q_2\times 1}$

$$\begin{pmatrix} X_1 E_{11} & \cdots & X_1 E_{1q_2} \\ X_2 E_{21} & \cdots & X_2 E_{2q_2} \\ \vdots & & \\ X_n E_{n1} & \cdots & X_n E_{nq_2} \end{pmatrix}_{n\times q_2} \begin{pmatrix} \eta_1 \\ \eta_2 \\ \vdots \\ \eta_{q_2} \end{pmatrix}_{q_2\times 1} \qquad X = \begin{pmatrix} X_1 \\ X_2 \\ \vdots \\ X_n \end{pmatrix}$$

Priors: $\beta,\ \eta,\ \alpha,\ b,\ \sigma^2,\ \tau^2_c,\ \tau^2_{ej},\ \lambda^2_c,\ \lambda^2_e$

$$y \mid - \sim N_n(\mu, \sigma^2 I_n), \qquad \mu = E(y)$$

$$\propto \frac{1}{(2\pi\sigma^2)^{\frac{n}{2}}} e^{-\frac{1}{2\sigma^2}\{(y-\mu)^T(y-\mu)\}}$$

$$\beta \mid \overset{\tau^2_c}{\cancel{\tau^2_{c1}, \cdots, \tau^2_{cp}}}, \sigma^2 \sim N_p(0_p, \overset{\sigma^2\tau^2_c}{\cancel{\sigma^2 D_\tau}}), \quad D_{\tau c} = \begin{pmatrix} \tau^2_{c1} & & \\ & \ddots & \\ & & \tau^2_{cp} \end{pmatrix}$$

$$\overset{\tau^2_c}{\cancel{\tau^2_{c1}, \cdots, \tau^2_{cp}}} \mid \lambda^2_c \sim \prod_{j=1}^{p} \frac{\lambda^2_c}{2} e^{-\frac{\lambda^2_c}{2}\tau^2_{cj}}$$

$$\left[\begin{array}{l} \beta_j \sim N(0, \sigma^2\tau^2_{cj}) \\ \tau^2_{cj} \sim \frac{\lambda^2_c}{2} \exp\{-\frac{\lambda^2_c}{2}\tau^2_{cj}\} \end{array}\right.$$

$$\alpha \sim N_{q_2}(0, \Sigma_{\alpha 0}), \qquad \sigma^2 \propto \frac{1}{\sigma^2}$$

$$D_{\tau e} = \begin{pmatrix} \tau^2_{e1} & & \\ & \ddots & \\ & & \tau^2_{eq_2} \end{pmatrix}$$

$$b \sim N_{q_1}(0, \Sigma_{b0}),$$

$$\eta_j \sim N(0, \sigma^2\tau^2_{ej}), \quad \tau^2_{ej} \sim \frac{\lambda^2_e}{2}\exp\{-\frac{\lambda^2_e}{2}\tau^2_{ej}\} \quad j=1,\cdots \cancel{p}\, q_2$$

$$\lambda^2_c \sim \text{gamma}(a_c, b_c), \quad \lambda^2_e \sim \text{gamma}(a_e, b_e)$$

full: $\pi(\sim \mid Y)$

$$\propto \underbrace{(\sigma^2)^{-\frac{n}{2}} \exp\{-\frac{1}{2\sigma^2}(y-\mu)^T(y-\mu)\}}_{y} \times \underbrace{\exp(-\frac{1}{2} b^T \Sigma^{-1}_{b0} b)}_{b} \times$$

$$\propto \underbrace{\exp(-\frac{1}{2}\alpha^T \Sigma^{-1}_{\alpha 0}\alpha)}_{\alpha} \times \underbrace{\prod_{j=1}^{p} \frac{1}{\sqrt{2\pi\sigma^2\tau^2_{cj}}} e^{-\frac{1}{2\sigma^2\tau^2_{cj}}\beta^2_j}}_{\beta} \times$$

$$\underbrace{\prod_{j=1}^{p} \frac{\lambda^2_c}{2} e^{-\frac{\lambda^2_c}{2}\tau^2_{cj}}}_{\tau^2_c} \cdot \underbrace{\left(\frac{1}{\sigma^2}\right)}_{\sigma^2} : \underbrace{(\lambda^2_c)^{a_c-1}\exp(-b_c\lambda^2_c)}_{\lambda^2_c} \times$$

$$\underbrace{\prod_{i=1}^{q_2} \frac{1}{\sqrt{2\pi\sigma^2\tau^2_{ei}}} e^{-\frac{1}{2\sigma^2\tau^2_{ei}}\eta^2_i}}_{\eta_i} \times \underbrace{\prod_{i=1}^{q_2}\frac{\lambda^2_e}{2}\exp\{-\frac{\lambda^2_e}{2}\tau^2_{ei}\}}_{\tau^2_{ej}} \times$$

$$\underbrace{(\lambda^2_e)^{a_e-1}\exp(-b_e\lambda^2_e)}_{\lambda^2_e}$$

$$\mu_{(-\alpha)} = E(y) - E\alpha$$

$$\bullet\ \alpha|- \propto \exp\left\{-\frac{1}{2\sigma^2}(y-\mu_{(-\alpha)}-E\alpha)^T\cdot(y-\mu_{(-\alpha)}-E\alpha) - \frac{1}{2}\alpha^T\Sigma_{\alpha_0}^{-1}\alpha\right\}$$

$$\propto \exp\left\{-\frac{1}{2}\left\{\alpha^T\Sigma_{\alpha_0}^{-1}\alpha + \alpha^T\frac{1}{\sigma^2}E^TE\alpha - 2\frac{1}{\sigma^2}(y-\mu_{(-\alpha)})^TE\alpha\right\}\right\}$$

$$= \exp\left\{-\frac{1}{2}\left\{\alpha^T\left(\Sigma_{\alpha_0}^{-1}+\frac{1}{\sigma^2}E^TE\right)\alpha - 2\frac{1}{\sigma^2}(y-\mu_{(-\alpha)})^TE\alpha\right\}\right\}$$

$$\Sigma_\alpha = \left(\Sigma_{\alpha_0}^{-1}+\frac{1}{\sigma^2}E^TE\right)^{-1}, \quad \mu_\alpha = \Sigma_\alpha\cdot\Big(\frac{1}{\sigma^2}\underbrace{(y-\mu_{(-\alpha)})}_{n\times1}{}^T_{1\times n}\cdot\underbrace{E}_{n\times q_2}\Big)^T_{1\times q_2}$$

$$\sim N(\mu_\alpha, \Sigma_\alpha)$$

Similarly,

$$\bullet\ b|- \propto \exp\left\{-\frac{1}{2\sigma^2}(y-\mu_{(-b)}-Cb)^T(y-\mu_{(-b)}-Cb) - \frac{1}{2}b^T\Sigma_{b_0}^{-1}b\right\}$$

$$\Sigma_b = \left(\Sigma_{b_0}^{-1}+\frac{1}{\sigma^2}C^TC\right)^{-1}, \quad \mu_b = \Sigma_b\cdot\left(\frac{1}{\sigma^2}(y-\mu_{(-b)})^T\cdot C\right)^T$$

$$\sim N(\mu_b, \Sigma_b) \qquad \mu_{(-b)} = E(y) - Cb$$

$$\frac{1}{2\sigma^2}\cdot\frac{\beta^2}{\tau_c^2}$$

$$\bullet\ \beta|- \propto \exp\left\{-\frac{1}{2\sigma^2}(y-\mu_{(-\beta)}-X\beta)^T(y-\mu_{(-\beta)}-X\beta) - \frac{1}{2\sigma^2}\cancel{\beta^TD_{\tau c}^{-1}\beta}\right\}$$

$$\cancel{D_{\tau c} = \begin{pmatrix}\tau_{c1}^2 & & \\ & \ddots & \\ & & \tau_{cp}^2\end{pmatrix}}$$

$$\mu_{(-\beta)} = E(y) - X\beta$$

$$\sim \overset{N}{\cancel{MVN}}(\mu_\beta, \sigma^2\Sigma_\beta), \quad \bullet\ \mu_\beta = \Sigma_\beta X^T(Y-\mu_{(-\beta)})$$

$$\bullet\ \Sigma_\beta = \left(X^TX + \overset{\frac{1}{\tau_c^2}}{\cancel{D_{\tau c}^{-1}}}\right)^{-1}$$

$$\bullet\ \sigma^2|- \propto (\sigma^2)^{-\frac{n}{2}}\cdot(\sigma^2)^{-1}\cdot(\sigma^2)^{-\frac{1}{2}}\cdot(\sigma^2)^{-\frac{q_2}{2}}\cdot$$

$$\exp\left\{-\frac{1}{2\sigma^2}\left[(y-\mu)^T(y-\mu) + \beta^TD_{\tau c}^{-1}\beta + \eta^TD_{\tau e}^{-1}\eta\right]\right\}$$

$$= (\sigma^2)^{-\frac{n+1+q_2}{2}-1}\exp\left\{-\frac{1}{2\sigma^2}\left[(y-\mu)^T(y-\mu) + \beta^TD_{\tau c}^{-1}\beta + \eta^TD_{\tau e}^{-1}\eta\right]\right\}$$

$$\sim \text{inv. Gamma}\left(\frac{n+1+q_2}{2}, \frac{1}{2}\left[(y-\mu)^T(y-\mu) + \underset{\frac{\beta^2}{\tau_c^2}}{\cancel{\beta^TD_{\tau c}^{-1}\beta}} + \eta^TD_{\tau e}^{-1}\eta\right]\right)$$

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• $\tau_{cj}^2 \mid - \;\propto\; \frac{1}{\sqrt{2\pi\sigma^2\tau_{cj}^2}} \cdot e^{-\frac{1}{2\sigma^2\tau_{cj}^2}\beta_j^2} \cdot e^{-\frac{\lambda_c^2}{2}\tau_{cj}^2}$

~~$j=1,\dots,p$~~

$1/\tau_c^2 \sim$ inv. Gaussian $\left(\underbrace{\sqrt{\frac{\sigma^2}{\beta_j^2}\lambda_c^2}}_{\text{mean}},\ \underbrace{\lambda_c^2}_{\text{scale}}\right)$

• $\tau_{ei}^2 \mid - \;\propto\; \frac{1}{\sqrt{2\pi\sigma^2\tau_{ei}^2}} \cdot e^{-\frac{1}{2\sigma^2\tau_{ei}^2}\eta_i^2} \cdot e^{-\frac{\lambda_e^2}{2}\tau_{ei}^2}$

$1/\tau_{ei}^2 \sim$ inv. Gaussian $\left(\sqrt{\frac{\sigma^2}{\eta_i^2}\lambda_e^2},\ \lambda_e^2\right)$ $\quad i=1,\dots,q_2$

• $\lambda_c^2 \mid - \;\propto\; \prod_{j=1} \frac{\lambda_c^2}{2} e^{-\frac{\lambda_c^2}{2}\tau_{cj}^2} \cdot (\lambda_c^2)^{a_c-1} \cdot e^{-b_c\lambda_c^2}$

$\propto (\lambda_c^2)^{1+a_c-1} \exp\left(-\lambda_c^2\left(\sum\frac{\tau_{cj}^2}{2} + b_c\right)\right)$

$\sim$ Gamma $\left(a_c+1,\ \cancel{\frac{1}{2}\sum_{j=1}\tau_{cj}^2 + b_c}\ \ \frac{1}{2}\tau_c^2 + b_c\right)$

• $\lambda_e^2 \mid - \;\propto\; \prod_{i=1}^{q_2} \frac{\lambda_e^2}{2} \exp\left\{-\frac{\lambda_e^2}{2}\tau_{ei}^2\right\} \cdot (\lambda_e^2)^{a_e-1} \exp(-b_e\lambda_e^2)$

$\propto (\lambda_e^2)^{q_2+a_e-1} \exp\left\{-\lambda_e^2\left(\frac{\sum\tau_{ei}^2}{2} + b_e\right)\right\}$

$\sim$ Gamma $\left(a_e+q_2,\ \frac{1}{2}\sum_{i=1}^{q_2}\tau_{ei}^2 + b_e\right)$

• $\eta \mid - \;\propto\; \exp\left\{-\frac{1}{2\sigma^2}(y-\mu_{(-\eta)}-W\eta)^T(y-\mu_{(-\eta)}-W\eta) - \frac{1}{2\sigma^2}\eta^T D_{\tau e}^{-1}\eta\right\}$

$\mu_{(-\eta)} = E(y) - W\eta$

$D_{\tau e} = \left(\tau_{e1}^2 \ \cdots\ \tau_{eq_2}^2\right)$

$\sim MVN(\mu_\eta, \sigma^2\Sigma_\eta)$ • $\mu_\eta = \Sigma_\eta W^T(Y-\mu_{(-\eta)})$

• $\Sigma_\eta = (W^TW + D_{\tau e}^{-1})^{-1}$