

Table 1: Summary of parameters, definitions, and priors/posteriors in the mediator and outcome submodels

Mediator Submodel		
Symbol	Definition / Role	Distribution / Prior
U_{ij}	Log relative abundance of the j th microbial feature for subject i .	$U_{ij} \mid \alpha_j, \phi_j, t_i, \theta_j, X_i, \sigma_U^2 \sim N\left(\alpha_j + \phi_j t_i + \sum_{p=1}^P \theta_{jp} X_{ip}, \sigma_U^2\right)$
α_j	Taxon-specific intercept for feature j .	$\alpha_j \sim N(0, \sigma_\alpha^2)$
ϕ_j	Effect of the treatment in the mediator model.	$\phi_j \mid \zeta_j, \sigma_j^2 \sim \zeta_j N(0, \sigma_j^2) + (1 - \zeta_j) \delta_0(\phi_j)$
θ_{jp}	Effect of covariate X_{ip} in the mediator model.	$\theta_{jp} \mid \eta_{jp}, \sigma_j^2 \sim \eta_{jp} N(0, \sigma_j^2) + (1 - \eta_{jp}) \delta_0(\theta_{jp})$
ζ_j	Inclusion indicator for ϕ_j (spike-and-slab).	$\zeta_j \sim \text{Beta-Bernoulli}(a_j, b_j)$
η_{jp}	Inclusion indicator for θ_{jp} (spike-and-slab).	$\eta_{jp} \sim \text{Beta-Bernoulli}(a_{jp}, b_{jp})$
σ_U^2	Error variance in the mediator model.	$\sigma_U^2 \sim \text{InvGamma}(a_0, b_0)$
Outcome Submodel		
Symbol	Definition / Role	Distribution / Prior
y_i	Observed outcome for subject i .	$y_i \mid \Delta, t_i, \kappa, X_i, \beta, U_i, \sigma_Y^2 \sim N\left(\Delta t_i + \sum_{p=1}^P \kappa_p X_{ip} + \sum_{j=1}^J \beta_j U_{ij}, \sigma_Y^2\right)$
Δ	Direct effect of treatment t_i on outcome y_i .	
κ_p	Effect of covariate X_{ip} on outcome y_i .	
β_j	Effect of microbial feature U_{ij} on outcome y_i .	The sum of selected microbial feature coefficients follows: $\sum_{j \in \gamma_\beta} \beta_j \sim N\left(0, \frac{p_{\gamma_\beta} \sigma^2}{1 + c^2 p_{\gamma_\beta}}\right).$
σ_Y^2	Error variance in the outcome model.	Also, the compositional constraint: $\sum_{j=1}^J \beta_j = 0$ applies. $\sigma_Y^2 \sim \text{InvGamma}(a_0^Y, b_0^Y)$
Additional Priors and Structures		
γ	Vector of selection indicators. $\gamma = (1, \gamma_\kappa, \gamma_\beta)$.	$P(\gamma) \propto \exp\left(a_\kappa^T \gamma_\kappa + b \gamma_\kappa^T \gamma_\kappa + a_\beta^T \gamma_\beta + \gamma_\beta^T Q_\beta \gamma_\beta\right)$

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Mediator Submodel (Continued)		
Symbol	Definition / Role	Distribution / Prior
Q_β	Inverse of phylogeny-induced correlation matrix C .	$Q_\beta = C^{-1}$. E.g. $c_{pq} = \exp(-2\rho d_{pq})$
T	Transformation matrix ensuring $\sum \beta_j = 0$.	$T'_\gamma T_\gamma$ is designed as a block matrix: $(T'_\gamma T_\gamma)^{-1} = \begin{bmatrix} I_{p_{\gamma\kappa}+1} & \mathbf{0} \\ \mathbf{0} & (T'_{\gamma_\beta} T_{\gamma_\beta})^{-1} \end{bmatrix},$ <p>where</p> $(T'_{\gamma_\beta} T_{\gamma_\beta})^{-1} = I_{p_{\gamma_\beta}} - \frac{c^2}{1 + c^2 p_{\gamma_\beta}} \mathbf{1}_{p_{\gamma_\beta}} \mathbf{1}'_{p_{\gamma_\beta}}.$
T_β	Specific transformation matrix for microbial feature constraints.	$T_\beta = (I_J \mid c \mathbf{1}_J^T)$, where large c enforces the sum-to-zero constraint.
\mathcal{M}_γ	\mathcal{M}_γ refers to the regression sub-model given the variable selection indicator vector γ .	
$\Delta, \kappa_\gamma, \beta_\gamma$	Coefficients (outcome submodel) under \mathcal{M}_γ ; z-prior form.	$\Delta, \kappa_\gamma, \beta_\gamma \mid M_\gamma, \sigma^2 \sim N(0, \sigma^2 (T_\gamma^T T_\gamma)^{-1})$