Sparse Bayesian Group Factor Model for Feature Interactions in Multiple Count Tables Data

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Multivariate Count Data

- $\boldsymbol{y} \in \mathbb{N}^0 \Rightarrow$ represent the number of occurrences
- Various science fields: genomics (Schloissnig et al., 2013), epidemiology (Papoz, Balkau, and Lellouch, 1996), social sciences (Böhning, Dietz, and Schlattmann, 1997), and marketing (Ravishanker, Venkatesan, and Hu, 2016).
- Inferential goals: interactions among the features through covariance matrix
- Poisson distribution or negative binomial distribution

? Multivariate Poisson distribution or multivariate NB distribution

High-dimensional Count Data

- sample size n smaller than the number of variables J - ‘small n large J’ problem
- Banding sample covariance matrix or its Cholesky (Bickel and Levina, 2008b; Wu and Pourahmadi, 2003); thresholding with shrinkage (Bickel and Levina, 2008a; Rothman, Levina, and Zhu, 2009)
- Many regularization approaches but what about uncertainty?

⋆⋆ Bayesian model enters naturally

⇒ Latent continuous variables

⇒ Bayesian factor model (Bernardo et al., 2003)

Bayesian Factor model(Bernardo et al., 2003)

- Common latent factors without losing essential information

⋆⋆ the number of latent factors K smaller than dimension J

⋆⋆ the factor loadings matrix having a lot of zeros

- Spike-slab prior (Carvalho et al., 2008; Lucas et al., 2006);
  Heavy-tailed default prior (Ghosh and Dunson, 2009);
  Multiplicative gamma process shrinkage prior (Bhattacharya and Dunson, 2011)
  Dirichlet-Laplace prior (Bhattacharya et al., 2015).

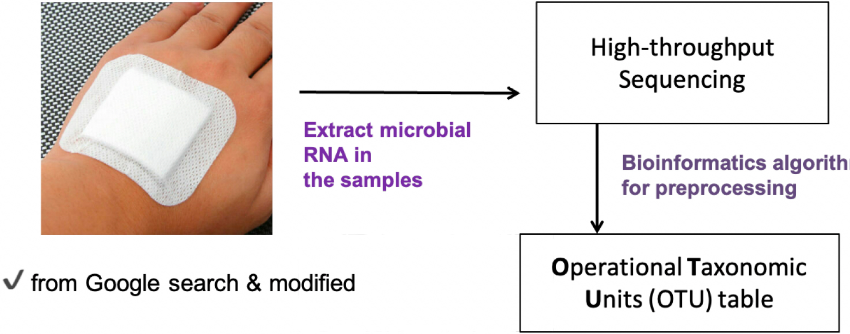
More Recent Development

- Group factor analysis (Klami et al., 2014; Virtanen et al., 2012)
- Multi-study factor analysis (De Vito et al., 2019)
- Perturbed factor analysis (Roy et al., 2021)
- Generalized factor models (Schiavon, Canale, and Dunson, 2022)

? high-dimensional multivariate count tables with added complexity

Microbiome Study

- High-throughput sequencing such as 16S rRNA gene sequencing is widely used in microbiome studies to profile microbial communities.



- Operational Taxonomic Units (OTUs) represent the information of microbial taxa.

Microbiome Count Data

subject	sample	OTU 1	OTU 2	OTU 3	$\cdots$	$\cdots$	OTU J	covariate
1	1	41	643	89	$\cdots$	0	1	x_1
1	2	0	56	24	$\cdots$	402	32	x_2
1	3	34	12	0	$\cdots$	28	17	x_3
$\vdots$	$\vdots$	$\vdots$	$\vdots$				$\vdots$	$\vdots$
S	N-2	410	601	305		106	509	x_{N-2}
S	N-1	0	0	10	$\cdots$	0	7	x_{N-1}
S	N	698	232	390	$\cdots$	131	987	x_N

Abundance changes with covariates

OTU interacts with each other

Additional Challenges

sample	OTU 1	OTU 2	OTU 3	⋯	⋯	OTU J	Total
1	41	643	89	⋯	104	1	841
2	0	56	24	⋯	10	32	908
3	34	89	0	⋯	762	17	3274
⋮	⋮	⋮				⋮	⋮
N-2	410	601	305		708	509	4210
N-1	0	0	10	⋯	0	7	590
N	698	232	390	⋯	545	987	6298

$$\frac{56}{908}$$

$$\frac{89}{3274}$$

- Compositionality; excess zeros; over-dispersion.

Multiple Count Tables Data

Cross-domain interaction

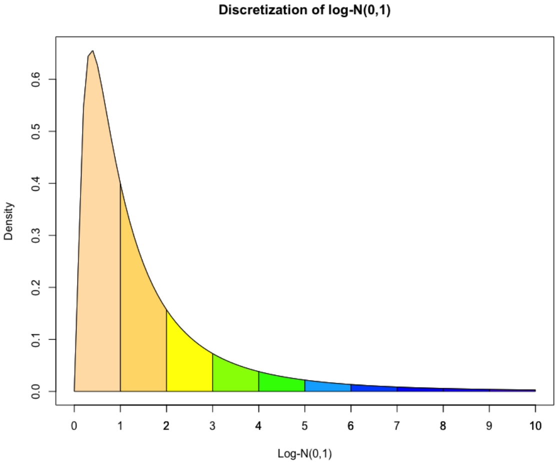
Domain 1 e.g., bacteria — **Within-domain interaction**

Domain 2 e.g., viruses — **Within-domain interaction**

subject	sample	OTU 1	OTU 2	OTU 3	⋯	OTU J_1	OTU 1	OTU 2	OTU 3	⋯	OTU J_2	covariate
1	*1*	41	643	89	⋯	1	53	79	43	⋯	83	x_1
1	*2*	0	56	24	⋯	32	120	87	42	⋯	20	x_2
1	*3*	34	12	0	⋯	17	34	0	209	⋯	73	x_3
⋮	⋮	⋮	⋮			⋮	⋮	⋮			⋮	⋮
S	*N-2*	410	601	305		509	98	158	47		92	x_{N-2}
S	*N-1*	0	0	10	⋯	7	101	934	0	⋯	82	x_{N-1}
S	*N*	698	232	390	⋯	987	389	920	0	⋯	372	x_N

Bayesian Rounded Kernel Model(Canale and Dunson, 2011)

- We propose to discretize a continuous multivariate log-normal distribution with fixed thresholds.



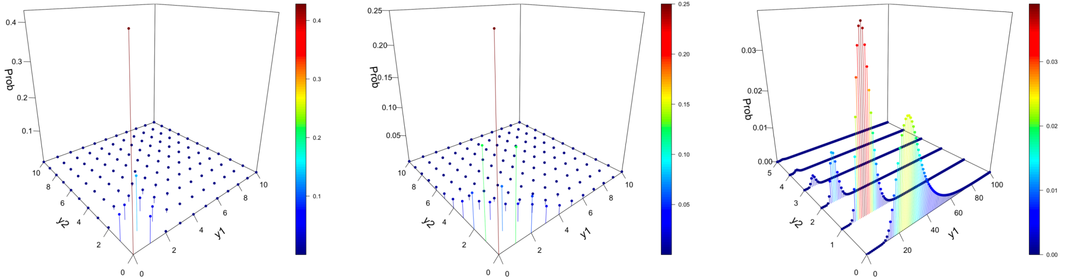
Sampling Distribution

- Sample index $i = 1, \cdots, N$, subject index $s_i = 1, \cdots, S$, group index $m = 1, \cdots, M$.
- Stack count vector from each group $\mathbf{Y}_{im}$ together as $\mathbf{Y}_i = (\mathbf{Y}_{i1}, \ldots, \mathbf{Y}_{iM})$,

$$\mathrm{P}(\mathbf{Y}_i = \mathbf{y}_i \mid \boldsymbol{\mu}_i, \Sigma) = \int_{A(\mathbf{y}_i)} \text{log-N}_J(\mathbf{y}^\star \mid \boldsymbol{\mu}_i, \Sigma) d\mathbf{y}^\star = \int_{\tilde{A}(\mathbf{y}_i)} \phi_J(\tilde{\mathbf{y}}^\star \mid \boldsymbol{\mu}_i, \Sigma) d\tilde{\mathbf{y}}^\star,$$

- where $A(\mathbf{y}_i) = \{\mathbf{y}^\star \mid y_{i1} \leq y_1^\star < y_{i1} + 1, \ldots, y_{iJ} \leq y_J^\star < y_{iJ} + 1\}$ and $\tilde{A}(\mathbf{y}_i) = \{\tilde{\mathbf{y}}^\star \mid \log(y_{i1}) \leq \tilde{y}_1^\star < \log(y_{i1} + 1), \ldots, \log(y_{iJ}) \leq \tilde{y}_J^\star < \log(y_{iJ} + 1)\}$.
- Moments of count distribution

Count distribution



(a) $\tilde{\boldsymbol{\mu}} = \begin{bmatrix} 0 \\ 0 \end{bmatrix}, \tilde{\Sigma} = \begin{bmatrix} 1 & 0.9 \\ 0.9 & 1 \end{bmatrix}$

$\text{Cor}(y_1, y_2) = 0.835$

(b) $\tilde{\boldsymbol{\mu}} = \begin{bmatrix} 0 \\ 0 \end{bmatrix}, \tilde{\Sigma} = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$

$\text{Cor}(y_1, y_2) = 0$

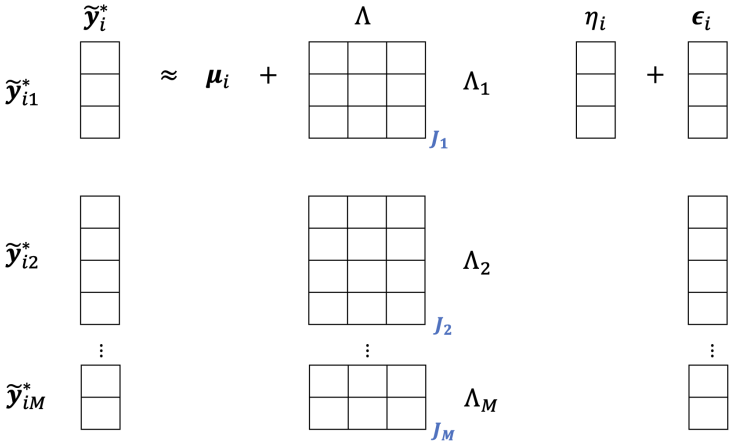
(c) $\tilde{\boldsymbol{\mu}} = \begin{bmatrix} 3 \\ 0 \end{bmatrix}, \tilde{\Sigma} = \begin{bmatrix} 0.5^2 & -0.9 \times 0.5^2 \\ -0.9 \times 0.5^2 & 0.5^2 \end{bmatrix}$

$\text{Cor}(y_1, y_2) = -0.643$

Figure: [Distribution of Counts of a Pair of OTUs] The joint distribution of counts of a pair of OTUs is computed for a rounded kernel method with bivariate log-normals, log-$N_2(\tilde{\boldsymbol{\mu}}, \tilde{\Sigma})$.

Covariance: Group Factor Model

Group factor model: extends traditional factor model to infer joint variability between two or more multivariate responses (Klami et al., 2014; Virtanen et al., 2012; Zhao et al., 2016).

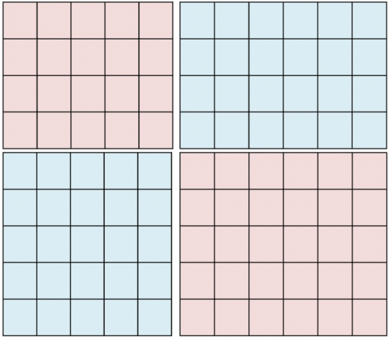


Covariance: Group Factor Model

$$\Sigma = \Lambda_{J\times K}\Lambda' + V,\ \Lambda = [\Lambda_1', \ldots, \Lambda_M']'$$

where $\Lambda_m = [\lambda_{mjk}]$ is a $J_m \times K$ matrix, and V is a J-dim diagonal matrix, with diagonal submatrices $V^{mm} = v_m^2 \mathbf{I}_{J_m}$.

$$\Sigma \approx \Lambda\Lambda' + V$$



$$\Sigma^{11} = \Lambda_1\Lambda_1' + v_1^2 \mathrm{I}_{J_1}$$

$$\Sigma^{21} = \Lambda_1\Lambda_2'$$

$$\Sigma^{12} = \Sigma^{21,\prime}$$

$$\Sigma^{22} = \Lambda_2\Lambda_2' + v_2^2 \mathrm{I}_{J_2}$$

Dirichlet-Horseshoe (Dir-HS) prior

- Construct a Dirichlet-Horseshoe (Dir-HS) prior for columns $\boldsymbol{\lambda}_k$ of Λ to efficiently induce joint sparsity;

★★ For each k, $k = 1, \ldots, K$,

$$\begin{aligned}
\lambda_{mjk} \mid \phi_{mjk}, \tau_k, \zeta_{mjk} &\overset{indep}{\sim} \mathrm{N}(0, \zeta_{mjk}^2 \phi_{mjk} \tau_k), \\
\zeta_{mjk} &\overset{iid}{\sim} \mathrm{C}^+(0, 1), \\
\boldsymbol{\phi}_k = (\phi_{11k}, \ldots, \phi_{MJ_Mk}) \mid a_\phi &\overset{iid}{\sim} \mathrm{Dir}(a_\phi, \ldots, a_\phi), \\
\tau_k \mid a_\tau, b_\tau &\overset{iid}{\sim} \mathrm{Ga}(a_\tau, b_\tau / J)
\end{aligned}$$

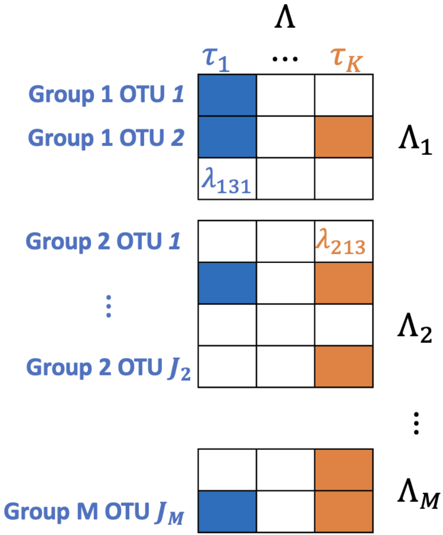
where $\mathrm{C}^+(0, 1)$ represents the half-Cauchy distribution for $\mathbb{R}_+$ with location and scale parameters 0 and 1.

Prior for Λ (contd)

$$\lambda_{mjk} \overset{indep}{\sim} \mathrm{N}(0, \zeta_{mjk}^2 \phi_{mjk} \tau_k)$$
$$\zeta_{mjk} \overset{iid}{\sim} \mathrm{C}^+(0, 1)$$
$$\Downarrow$$
$$\lambda_{mjk} \overset{indep}{\sim} \mathrm{HS}(\phi_{mjk} \tau_k)$$

with

$$\phi_k \overset{iid}{\sim} \mathrm{Dir}(a_\phi, \ldots, a_\phi)$$
$$\tau_k \overset{iid}{\sim} \mathrm{Ga}(a_\tau, b_\tau / J)$$



Dirichlet-Horseshor Prior

Theorem

Let $J = 2$. Assume $\phi_1 \sim Be(a_\phi, a_\phi)$ and let $\phi_2 = 1 - \phi_1$. Assume the Dir-HS distribution as a joint distribution for $\boldsymbol{\lambda} = (\lambda_1, \lambda_2) \in \mathrm{R}^2$ given τ. Without loss of generality, let $\tau = 1$. The marginal density $\Pi_{Dir\text{-}HS}(\lambda_1)$ of λ_1 satisfies: (a) $\lim_{\lambda_1 \to 0} \Pi_{Dir\text{-}HS}(\lambda_1) = \infty$. (b) For $\lambda_1 \neq 0$,

$$
\begin{aligned}
& 2^{2a_\phi - \frac{5}{2}} \pi^{-2} \frac{\Gamma^2(a_\phi + 1/2)}{\Gamma(2a_\phi + 1/2)} \frac{4}{\lambda_1^2} {}_3F_2\left(1, 1, a_\phi + 1/2; 2, 2a_\phi + 1/2; -\frac{4}{\lambda_1^2}\right) \\
& < \quad \Pi_{Dir\text{-}HS}(\lambda_1) \quad < \\
& 2^{2a_\phi - \frac{3}{2}} \pi^{-2} \frac{\Gamma^2(a_\phi + 1/2)}{\Gamma(2a_\phi + 1/2)} \frac{2}{\lambda_1^2} {}_3F_2\left(1, 1, a_\phi + 1/2; 2, 2a_\phi + 1/2; -\frac{2}{\lambda_1^2}\right),
\end{aligned}
$$

where ${}_pF_q$ is the generalized hypergeometric function, ${}_pF_q(\alpha_1, \ldots, \alpha_p; \beta_1, \ldots, \beta_q; x) = \sum_{t=0}^{\infty} \frac{(\alpha_1)_t \ldots (\alpha_p)_t}{(\beta_1)_t \ldots (\beta_q)_t} \frac{x^t}{t!}$.

Dirichlet-Horseshor Prior

Theorem

Especially when $a_\phi = \frac{1}{2}$,

$$\frac{1}{\sqrt{2\pi^5}}\left\{\sinh^{-1}(2/|\lambda_1|)\right\}^2 < \Pi_{Dir\text{-}HS}(\lambda_1) < \sqrt{\frac{2}{\pi^5}}\left\{\sinh^{-1}(\sqrt{2}/|\lambda_1|)\right\}^2$$

where the inverse hyperbolic sine function $\sinh^{-1}(x) = \log(x + \sqrt{x^2+1})$.

$\Rightarrow a_\phi = \frac{1}{4}$, *lower bound* $\propto \frac{\sqrt[4]{x^2+4}}{\sqrt{|x|}} - 1$

$\Rightarrow a_\phi = 1$, *lower bound* $\propto \log(\frac{4}{x^2}+1) + x\arctan(\frac{2}{x}) - 2$

- Dir-HS has an infinite spike at 0
- $\lim_{\lambda_1\to\infty} \Pi_{\text{Dir-HS}}(\lambda_1) = O(\frac{1}{\lambda_1^2})$

Dir-HS prior

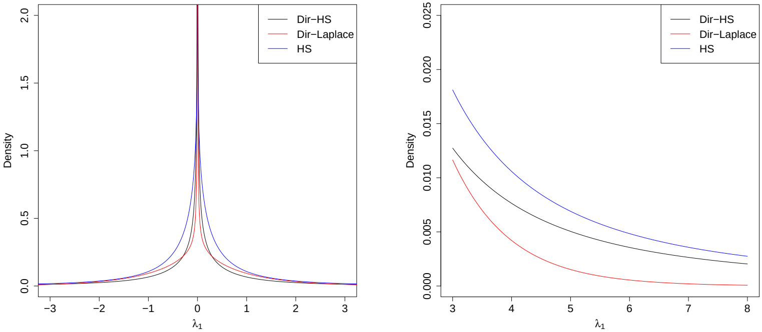


Figure: Marginal densities of λ_1 under $a_\phi = 1/20$.

- Dir-HS diverges faster than HS at 0 when $a_\phi = \frac{1}{4}, \frac{1}{2}$; the same rate when $a_\phi = \frac{3}{4}, 1$
- Dir-HS has a heavier tail than Dir-Laplace

Mean

- $$\mu_{imj} = r_{im} + \alpha_{s_i,mj} + \boldsymbol{\beta}'_{mj}\boldsymbol{x}_i$$

★★ r_{im}: sample scale factor for OTUs of group m in sample i.

Mean

subject	sample	OTU 1	OTU 2	⋯	OTU J_1	Total
1	1	μ_{imj}		⋯		5698
1	2			⋯		2312
1	3			⋯		9872
⋮	⋮		⋮		⋮	
S	N-2			⋯		598
S	N-1			⋯		532
S	N			⋯		2808

subject	sample	OTU 1	OTU 2	⋯	OTU J_2	Total
1	1			⋯		2102
1	2			⋯		743
1	3			⋯		3648
⋮	⋮		⋮		⋮	
S	N-2			⋯		2832
S	N-1			⋯		389
S	N			⋯		2231

r_{im}

Mean

- $$\mu_{imj} = r_{im} + \alpha_{s_i,mj} + \boldsymbol{\beta}'_{mj}\boldsymbol{x}_i$$

★★ r_{im}: sample scale factor for OTUs of group m in sample i.

$\Rightarrow$ Under log-N, $\text{Median}(y_{imj}) = \exp(\mu_{imj})$

$\frac{\text{Median}(y_{imj})}{\exp(r_{im})} = \exp(\alpha_{s_i,mj}) + \exp(\boldsymbol{\beta}'_{mj}\boldsymbol{x}_i)$

★★ $\alpha_{s_i,mj}$: normalized baseline abundance of OTU j belonging to group m for all samples from subject s_i.

Mean

subject	sample	OTU 1	OTU 2	⋯	OTU J_1	Total	OTU 1	OTU 2	⋯	OTU J_2	Total
1	1	μ_{imj}		⋯		5698			⋯		2102
1	2			⋯		2312			⋯		743
1	3			⋯		9872			⋯		3648
⋮	⋮		⋮		⋮			⋮		⋮	
S	N-2			⋯		598			⋯		2832
S	N-1			⋯		532			⋯		389
S	N			⋯		2808			⋯		2231

	r_{im}
$\alpha_{s_i,mj}$	

Mean

- Let

$$\mu_{imj} = r_{im} + \alpha_{s_i,mj} + \boldsymbol{\beta}'_{mj}\boldsymbol{x}_i$$

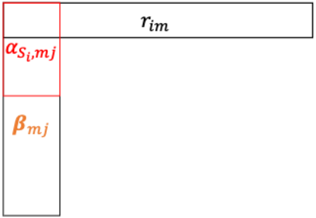
★★ r_{im}: sample scale factor for OTUs of group m in sample i.

★★ $\alpha_{s_i,mj}$: normalized baseline abundance of OTU j belonging to group m for all samples from subject s_i.

★★ $\boldsymbol{\beta}'_{mj}$: regression coefficients for OTU j of group m.

Mean

subject	sample	OTU 1	OTU 2	⋯	OTU J_1	Total	OTU 1	OTU 2	⋯	OTU J_2	Total
1	1	μ_{imj}		⋯		5698			⋯		2102
1	2			⋯		2312			⋯		743
1	3			⋯		9872			⋯		3648
⋮	⋮		⋮		⋮			⋮		⋮	
S	N-2			⋯		598			⋯		2832
S	N-1			⋯		532			⋯		389
S	N			⋯		2808			⋯		2231



Under log-N,

$$\text{Median}(y^*_{imj}) = \exp(r_{im} + \alpha_{S_i,mj} + \beta'_{mj}\, x_i)$$

Mean prior

- A mean-constrained prior with a mixture of mixture of normals on r_{im} and $\alpha_{s_i mj}$: (Li et al., 2017; Shuler et al., 2021)

$$r_{im} \overset{indep}{\sim} \sum_{l=1}^{\infty} \psi^r_{ml} \left\{ \omega^r_{ml} \mathrm{N}(\xi^r_{ml}, u_r^2) + (1-\omega^r_{ml}) \mathrm{N}\left(\frac{\nu^r_m - \omega^r_{ml}\xi^r_{ml}}{1-\omega^r_{ml}}, u_r^2 \right) \right\}$$

- Normalized baseline abundance of OTU j of group m in samples taken from subject s_i:

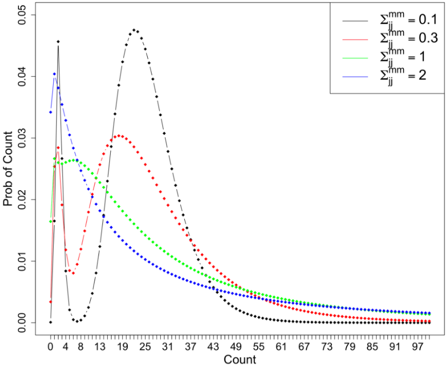
$$\begin{aligned}
\boldsymbol{\alpha}_{s_i} \mid G &\overset{iid}{\sim} G(\boldsymbol{\alpha}), \qquad s_i \in \{1, \ldots, S\}. \\
G(\boldsymbol{\alpha}) &= \prod_{m=1}^{M} \prod_{j=1}^{J_m} G_{mj}(\alpha_{mj}) \\
&= \prod_{m=1}^{M} \prod_{j=1}^{J_m} \left[\sum_{l=1}^{\infty} \psi^{\alpha}_{ml} \left\{ \omega^{\alpha}_{ml} \delta_{\xi^{\alpha}_{mjl}} + (1-\omega^{\alpha}_{ml}) \delta_{\left(\frac{\nu^{\alpha}_{mj} - \omega_{ml}\xi^{\alpha}_{mjl}}{1-\omega^{\alpha}_{ml}} \right)} \right\} \right]
\end{aligned}$$

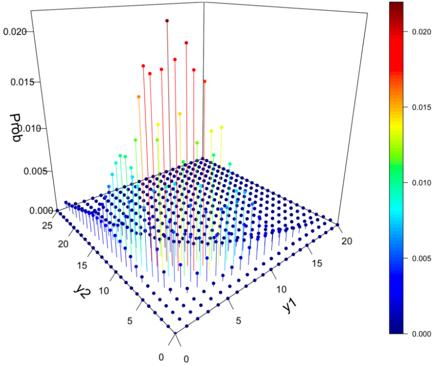
- location $\xi \overset{iid}{\sim}$ N, inner weights $\omega \overset{iid}{\sim}$ Be, outer weights $\psi \sim$ a stick-breaking process

Model for the Mean (contd)

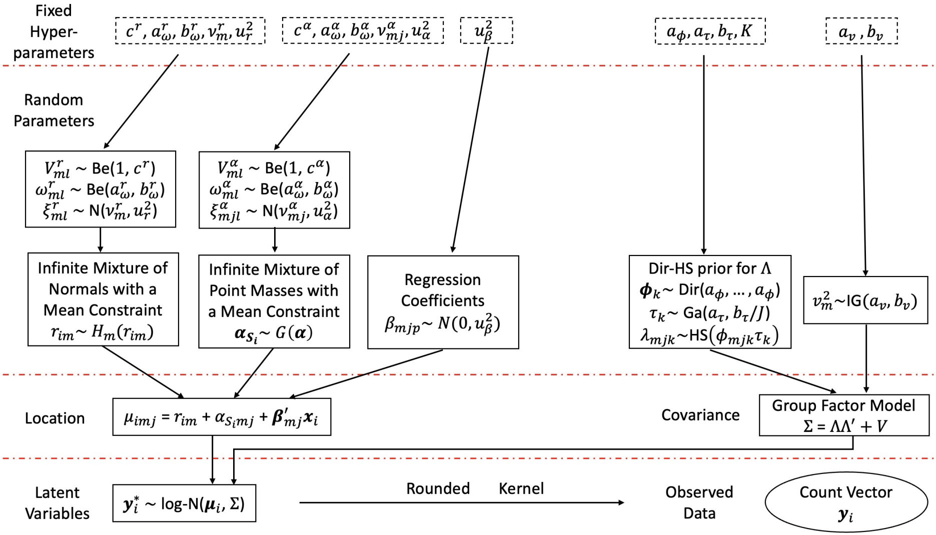
- For sample i from subject s_i, we assume

$$\mathbf{y}_i^\star \mid \boldsymbol{r}_i, \boldsymbol{\alpha}_{s_i}, \boldsymbol{\beta}, \Sigma \overset{indep}{\sim} \int \text{log-N}_J(\boldsymbol{r}_i + \boldsymbol{\alpha}_{s_i} + \boldsymbol{\beta}\mathbf{x}_i, \Sigma) dG(\alpha)$$





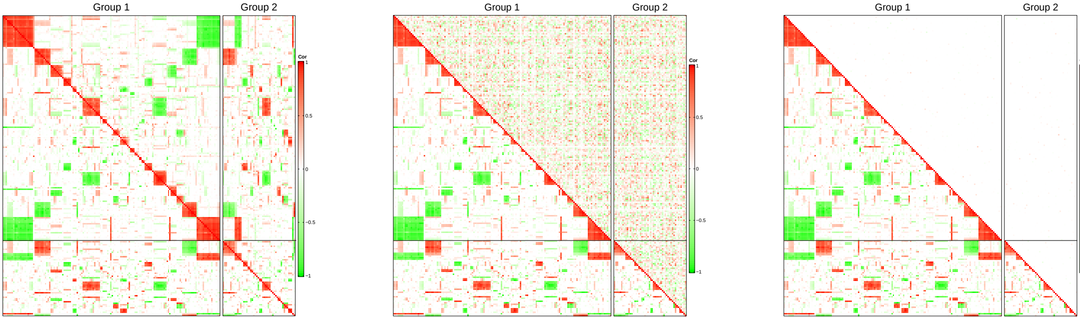
Sp-BGFM Model



Simulation Studies

- $M = 2$ groups, $N = 20$ samples, $J_1 = 150$, $J_2 = 50$ OTUs, baseline abundance level: -5, N(4, 1), N(10, 1)
- Sim 1: $\lambda_{mjk}^{\mathrm{tr}} \sim \mathrm{N}(0, 1) \pm 1$
- Sim 2,3 vine method ((Lewandowski, Kurowicka, and Joe, 2009) random correlation w & w/o covariates
- Sim 4 multinomial distribution without any associations
- Sim 5 SpiecEasi(Kurtz et al., 2015) without cross-domain association

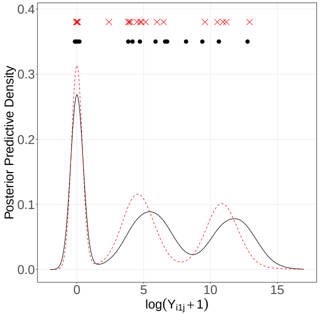
Simulation 2



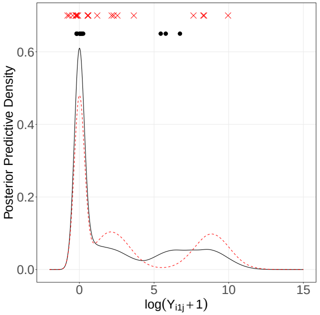
(a) Sp-BGFM (b) MOFA(Argelaguet et al., 2018) (c) SPIEC-EASI

Figure: [Simulation 2] The upper right and lower left triangles of a heatmap illustrate estimates $\hat{\rho}_{jj'}^{mm'}$ of correlations and their truth, respectively. The horizontal and vertical lines are to divide the groups. The estimates in panels (a)-(c) are from Sp-BGFM, MOFA and SPIEC-EASI, respectively.

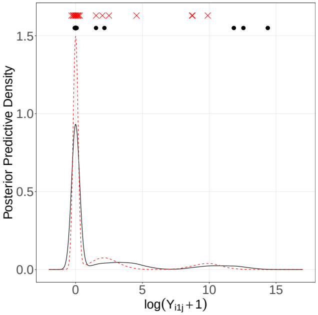
Posterior Predictive Checking



(a) Group 1 OTU 12



(e) Group 1 OTU 32

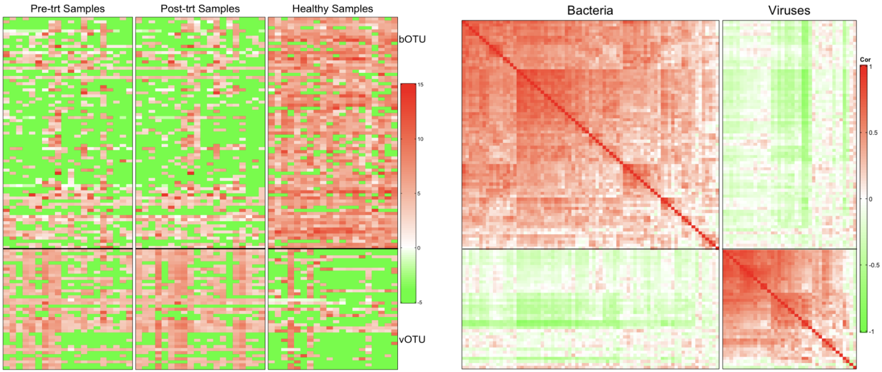


(f) Group 2 OTU 11

Multi-domain Skin Microbiome Data Analysis

- $S = 20$ patients at wound care clinic
- Three samples: pre- and post-treatment, and a control site on the healthy skin

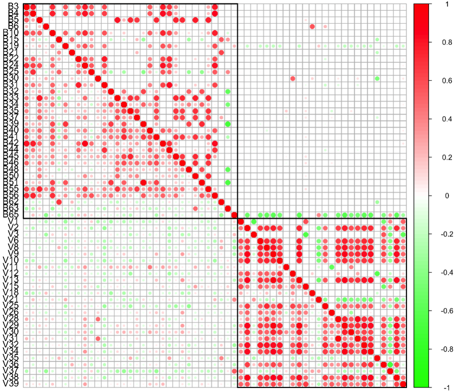
$\Rightarrow$ $N = 60$ samples from $S = 20$ subjects with a categorical covariate



(a) Log-transformed normalized OTU counts

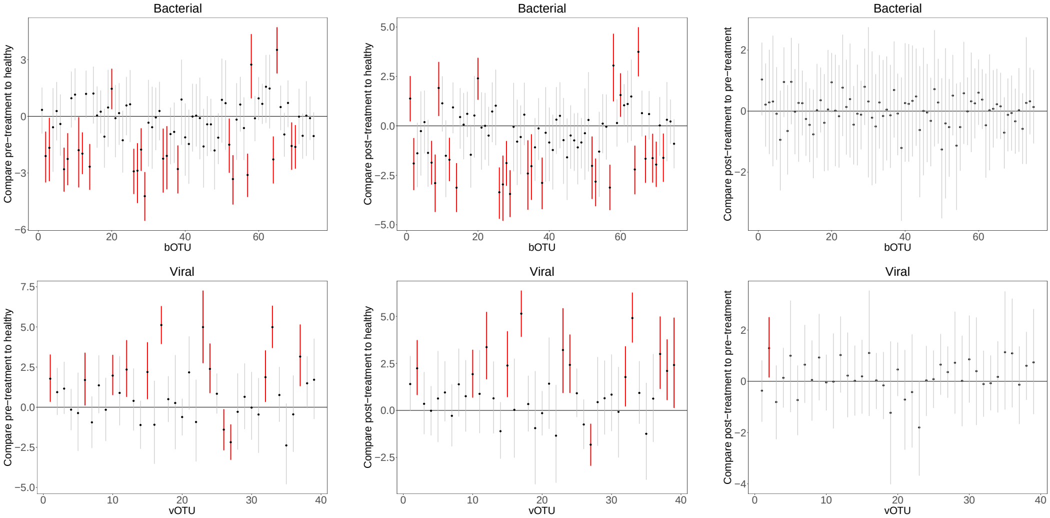
(b) Empirical correlation estimates

Multi-domain skin microbiome data



- bOTU 65(Staphylococcus aureus), a prominent skin pathogen
- *Pseudomonas* (b 59) and *Pseudomonas* phage (v 18) $\hat{\rho} = 0.38$

$\hat{\beta}_{mjp} - \hat{\beta}_{mjp'}$



Ongoing and future work

- Heteroskedasticity $\Sigma(x_i)$
- Longitudinal microbiome analysis
- Future work: tree-evolving count tables

Selected Reference

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