ASV proportions response $\mathbf{y}_i = (y_{i1}, \ldots, y_{ij}, \ldots, y_{ip})^T_{(np\times 1)} \sim \text{Dirichlet}(\alpha_{i1}, \ldots, \alpha_{ip})$

$$E(y_{ij}) = \mu_{ij} = \frac{\alpha_{ij}}{\alpha_{i1}}$$

where $\alpha_{i0} = \sum_{j=1}^{p} \alpha_{i0}$.

Indeces:

- Number of Samples: $i = 1, \ldots, n$.
- Number of OTUs: $j = 1, \ldots, p$
- Number of covariates, $k = 1, \ldots, q$

Define the design matrix $\mathbf{X}_{np\times(pq)}$ through the measurements for each sample $\mathbf{x}_i$ the $p$ rows for a given sample:

$$\mathbf{x}_i = \begin{pmatrix} x_{k=1} & \cdots & x_{k=q} & 0 & \cdots & 0 & 0 & \cdots & 0 \\ 0 & \cdots & 0 & x_1 & \cdots & x_q & 0 & \cdots & 0 \\ \vdots & & & & & & & & \\ 0 & \cdots & 0 & 0 & \cdots & 0 & x_1 & \cdots & x_q \end{pmatrix}_{p\times pq}$$

$$\boldsymbol{\beta} = \begin{pmatrix} \beta_{j=1,k=1} \\ \beta_{j=1,k=2} \\ \vdots \\ \beta_{j=1,k=q} \\ \beta_{j=2,k=1} \\ \beta_{j=2,k=2} \\ \vdots \\ \beta_{j=p,k=1} \\ \vdots \end{pmatrix}_{pq\times 1}$$

For notation, consider $\mathbf{x}_{ij}$ to denote the $j$th row of $\mathbf{x}_i$, but note that the nonzero values of each $\mathbf{x}_{ij}$ are the same for all $j$

Alternatively, if instead we consider $\mathbf{x}_i = (x_1, \ldots, x_q)^T$, define $\boldsymbol{\beta}_j = (\beta_{j,k=1}, \ldots, \beta_{j,k=q})^t$, and $\boldsymbol{\beta} = (\boldsymbol{\beta}_1^t, \ldots, \boldsymbol{\beta}_p^t)^t$

Link covarites to $\alpha$'s:

$$\log(\alpha_{ij_{1\times 1}}) = \mathbf{x_{ij_{1\times pq}}} \boldsymbol{\beta}_{pq\times 1}$$

and

$$\alpha_{ij} = e^{\mathbf{x_{ij}}\boldsymbol{\beta}}$$

Where only the corresponding $j$ elements of $\beta$ will have corresponding non-zero elements of $\mathbf{x}_{ij}$

If we use the alternate notation,

$$\log_{\alpha_{ij}} = \mathbf{x}_i^t \boldsymbol{\beta}_j, \text{ and } \alpha_{ij} = e^{\mathbf{x}_i^t \boldsymbol{\beta}_j}$$

The GEE equations are

$$\sum_{i=1}^{n}\left(\frac{\partial \boldsymbol{\mu}_i}{\partial \boldsymbol{\beta}}\right)^{t}_{pq\times p}\mathbf{V}^{-1}_{i_{p\times p}}(\mathbf{Y_i}-\boldsymbol{\mu}_i)_{p\times 1}=0$$

Where $\boldsymbol{V}_i = A_i^{\frac{1}{2}}R_iA_i^{\frac{1}{2}}$
Then,

$$\begin{aligned}
\left(\frac{\partial \boldsymbol{\mu}_i}{\partial \boldsymbol{\beta}}\right)^{t} &= \left(\frac{\partial}{\partial \boldsymbol{\beta}}\frac{\boldsymbol{\alpha}_i}{\alpha_{i0}}\right)^{t} \\
&= \left(\frac{\partial}{\partial \boldsymbol{\beta}}\frac{e^{\mathbf{x}_i\boldsymbol{\beta}}}{\sum_{j=1}^{p}e^{\mathbf{x_{ij}}\boldsymbol{\beta}}}\right)^{t} \\
&= \begin{pmatrix}
\frac{\partial}{\partial\boldsymbol{\beta}_1}\frac{e^{\mathbf{x}_i^T\boldsymbol{\beta}_1}}{\sum_{j=1}^{p}e^{\mathbf{x_i}^T\boldsymbol{\beta}_j}} & \cdots & \frac{\partial}{\partial\boldsymbol{\beta}_1}\frac{e^{\mathbf{x}_i^T\boldsymbol{\beta}_p}}{\sum_{j=1}^{p}e^{\mathbf{x}_i^T\boldsymbol{\beta}_j}} \\
\vdots & \ddots & \vdots \\
\frac{\partial}{\partial\boldsymbol{\beta}_p}\frac{e^{\mathbf{x}_i^T\boldsymbol{\beta}_1}}{\sum_{j=1}^{p}e^{\mathbf{x}_i^T\boldsymbol{\beta}_j}} & \cdots & \frac{\partial}{\partial\boldsymbol{\beta}_p}\frac{e^{\mathbf{x}_i^T\boldsymbol{\beta}_p}}{\sum_{j=1}^{p}e^{\mathbf{x}_i^T\boldsymbol{\beta}_j}}
\end{pmatrix} \\
&= \frac{1}{\alpha_{i0}^2}\begin{pmatrix}
x_1\alpha_1\alpha_0-\alpha_1x_1\alpha_1 & -\alpha_2x_1\alpha_1 & \cdots & -\alpha_px_1\alpha_1 \\
x_2\alpha_1\alpha_0-\alpha_1x_2\alpha_1 & -\alpha_2x_2\alpha_1 & \cdots & -\alpha_px_2\alpha_1 \\
\vdots & \vdots & \ddots & \vdots \\
x_q\alpha_1\alpha_0-\alpha_1x_q\alpha_1 & -\alpha_2x_q\alpha_1 & \cdots & \vdots \\
-\alpha_1x_1\alpha_2 & x_1\alpha_2\alpha_0-\alpha_2x_2\alpha_2 & & \\
\vdots & \vdots & \ddots & \vdots \\
-\alpha_1x_q\alpha_p & \cdots & & x_q\alpha_p\alpha_0-\alpha_px_p\alpha_p
\end{pmatrix}_{pq\times p} \\
&= \frac{1}{a_{i0}}\begin{pmatrix}
x_1\alpha_1 & 0 & \cdots & 0 \\
x_2\alpha_1 & 0 & \cdots & 0 \\
\vdots & \vdots & \ddots & \vdots \\
x_q\alpha_1 & 0 & \cdots & 0 \\
0 & x_1\alpha_2 & \cdots & 0 \\
0 & x_2\alpha_2 & \cdots & 0 \\
\vdots & \vdots & \ddots & \vdots \\
0 & 0 & \cdots & x_1\alpha_p
\end{pmatrix} - \frac{1}{\alpha_{i0}^2}\begin{pmatrix}
\alpha_1^2x_1 & \alpha_1\alpha_2x_1 & \cdots & \alpha_1\alpha_px_1 \\
\alpha_1^2x_2 & \alpha_1\alpha_2x_2 & \cdots & \alpha_1\alpha_px_2 \\
\vdots & \vdots & \ddots & \vdots \\
\alpha_1^2x_q & \alpha_1\alpha_2x_q & \cdots & \alpha_1\alpha_px_q \\
\alpha_1\alpha_2x_1 & \alpha_2^2x_1 & \cdots & \alpha_2\alpha_px_1 \\
\alpha_1\alpha_2x_2 & \alpha_2^2x_2 & \cdots & \alpha_2\alpha_px_2 \\
\vdots & \vdots & \ddots & \vdots \\
\alpha_1\alpha_px_q & \alpha_2\alpha_px_q & \cdots & \alpha_p^2x_q
\end{pmatrix} \\
&= \frac{1}{\alpha_{i0}}[I_p\otimes\mathbf{x}_i]diag(\boldsymbol{\alpha}_i) - \frac{1}{\alpha_{i0}^2}\boldsymbol{\alpha}_i\boldsymbol{\alpha}_i^t\otimes\mathbf{x}_i
\end{aligned}$$