Intersect Enrichment Model

$$y_{i,j}^{DEG} \sim Binomial(n_{i,j}^{DEG}, f(\pi_{i,j}^{DEG})) \tag{1.1}$$

$$y_{i,j}^{\neg DEG} \sim Binomial(n_{i,j}^{\neg DEG}, f(\pi_{i,j}^{\neg DEG})) \tag{1.2}$$

$$\pi_{i,j}^{DEG} = \pi_{i,j} + \frac{\alpha + \beta_i + \gamma_j + \epsilon_{i,j}}{2} \tag{1.3}$$

$$\pi_{i,j}^{\neg DEG} = \pi_{i,j} - \frac{\alpha + \beta_i + \gamma_j + \epsilon_{i,j}}{2} \tag{1.4}$$

$$\alpha \sim normal(0,1) \tag{1.5}$$

$$\beta_i \sim multi\text{-}normal(\vec{0}, \sigma_\beta^2 \Sigma_i) \tag{1.6}$$

$$\gamma_j \sim multi\text{-}normal(\vec{\mu_k}, \sigma_\gamma^2 \Sigma_j) \tag{1.7}$$

$$\epsilon_{i,j} \sim matrix\text{-}normal(0, \sigma_\epsilon \Sigma_i, \sigma_\epsilon \Sigma_j) \tag{1.8}$$

$$\mu_k \sim normal(0, \sigma_\mu) \tag{1.9}$$

$$\pi_{i,j} \sim matrix\text{-}normal(\eta_j, \sigma_\pi \Sigma_i, \sigma_\pi \Sigma_j) \tag{1.10}$$

$$\eta_j \sim multi\text{-}normal(\vec{\lambda_k}, \sigma_\eta^2 \Sigma_j) \tag{1.11}$$

$$\lambda_k \sim normal(\mu, \sigma_\lambda) \tag{1.12}$$

$$\mu \sim normal(0, 2) \tag{1.13}$$

$$\sigma_{\beta,\gamma,\epsilon,\mu,\pi,\eta,\lambda} \sim half\text{-}normal(0, 1) \tag{1.14}$$

Directionality Enrichment Model

$$y_{i,j} \sim Binomial(n_{i,j}, f(\pi_{i,j})) \tag{2.1}$$

$$\pi_{i,j} \sim normal(\vec{\mu_j}, \sigma_j) \tag{2.2}$$

$$\vec{\mu_j} \sim multi\text{-}normal(\vec{0}, SRS^T) \tag{2.3}$$

$$R = G_{SNP} \times \theta + I \times (1 - \theta) \tag{2.4}$$

$$\theta \sim Beta(1, 1) \tag{2.5}$$

$$diag(S) = \delta e^{\gamma_k} \tag{2.6}$$

$$\gamma_k \sim normal(0, \sigma_\gamma) \tag{2.7}$$

$$\sigma_j = \rho e^{\lambda_j} \tag{2.8}$$

$$\lambda_j \sim normal(0, \sigma_\lambda) \tag{2.9}$$

$$\rho, \delta \sim half\text{-}normal(0, 2) \tag{2.10}$$

$$\sigma_{\gamma,\lambda} \sim half\text{-}normal(0, 1) \tag{2.11}$$

Table 1: Intersect Enrichment Model Key

Symbol	Support	Interpretation
i	$\{1, 2, ..., 15\}$	tissue index
j	$\{1, 2, ..., 99\}$	trait index
k	$\{1, 2, ..., 12\}$	trait category index
$n_{i,j}^{DEG}$	$\mathbb{N}^0$	observed # of Differentially Expressed Genes (DEG) for tissue i and trait j
$n_{i,j}^{\neg DEG}$	$\mathbb{N}^0$	observed # of non-DEGs for tissue i and trait j
$y_{i,j}$	$\{1, 2, ..., n_{i,j}\}$	observed # of PrediXcan hits for tissue i and trait j
f		$f : \mathbb{R} \to (0, 1)$, logit function (maps log-odds to probabilities)
$\pi_{i,j}$	$\mathbb{R}$	mean log-odds of observing a PrediXcan hit for tissue i and trait j
α	$\mathbb{R}$	average difference in log-odds between DEGs and non-DEGs
β_i	$\mathbb{R}$	relative deviation to difference in log-odds between DEGs and non-DEGs for tissue i
γ_j	$\mathbb{R}$	relative deviation to difference in log-odds between DEGs and non-DEGs for trait j
μ_k	$\mathbb{R}$	relative deviation to difference in log-odds between DEGs and non-DEGs for trait category k
$\epsilon_{i,j}$	$\mathbb{R}$	relative deviation to difference in log-odds between DEGs and non-DEGs for trait $i \times$ tissue j
σ^*	$\mathbb{R}_{>0}$	various scale hyperparameters (for normal priors)
Σ_*		externally estimated correlation matrix
λ_k	$\mathbb{R}$	mean log-odds of observing a PrediXcan hit for trait in category k
η_j	$\mathbb{R}$	mean log-odds of observing a PrediXcan hit for trait j

Table 2: Directionality Enrichment Model Key

Symbol	Support	Interpretation
i	$\{1, 2, ..., 15\}$	tissue index
j	$\{1, 2, ..., 99\}$	trait index
k	$\{1, 2, ..., 12\}$	trait category index
$n_{i,j}$	$\mathbb{N}^0$	observed # of Differentially Expressed Genes (DEG) $\cap$ PrediXcan hits for tissue i and trait j
$y_{i,j}$	$\{1, 2, ..., n_{i,j}\}$	observed # of positive associations in the set of DEGs $\cap$ PrediXcan hits for tissue i and trait j
f		$f : \mathbb{R} \to (0, 1)$, logit function (maps log-odds to probabilities)
$\pi_{i,j}$	$\mathbb{R}$	mean log-odds of observing a positive association for tissue i and trait j
$\vec{\mu_j}$	$\mathbb{R}$	mean log-odds of observing a positive association for trait j
S	$\mathbb{R}_{>0}$	diagonal matrix of standard deviations of trait-wise log-odds enrichments in positive effects
R	Correlation Matrices	correlation matrix of mean positive association log-odds across traits
G	Correlation Matrices	externally estimated SNP correlation matrix across traits
I		$j \times j$ identity matrix
θ	$\in [0,1]$	weight proportion between G and I
δ	$\mathbb{R}_{>0}$	geometric average standard deviation of trait-wise enrichment in positive effects
γ_k	$\mathbb{R}$	multiplicative category deviation to δ for trait category k
ρ	$\mathbb{R}_{>0}$	geometric average standard deviation of tissue-wise enrichment in positive effects for a given trait
λ_j	$\mathbb{R}_{>0}$	multiplicative category deviation to ρ for trait j

Table 3: General Notation for Acronyms and Abbreviations

Symbol	Interpretation
MoTrPAC	Molecular Transducers of Physical Activity Consortium
EET	Endurance Exercise Training
F344	Fischer 344 Inbred Rats
GTEx	Genotype-Tissue Expression project
GWAS	Genome-Wide Association Study
GCTA	Genome-wide Complex Trait Analysis
TWAS	Transcriptome-Wide Association Study
LDSC	Linkage Disequilibrium Score Regression
SNP	Single Nucleotide Polymorphism
MESC	Mediated Expression Score Regression
eQTL	Expression Quantitative Trait Loci
h^2_{SNP}	narrow-sense heritability captured by variation at SNPs
8w_F1_M1	upregulated DEGs in both males and females after 8 weeks of training
8w_F-1_M-1	downregulated DEGs in both males and females after 8 weeks of training
IHW	Independent Hypothesis Weighting
BF%	Body Fat Percentage
ADRNL	Adrenals
BAT	Brown Adipose
COLON	Colon
CORTEX	Cortex
SKM-GN	Gastrocnemius
HEART	Heart
HIPPOC	Hippocampus
HYPOTH	Hypothalmus
KIDNEY	Kidney
LIVER	Liver
LUNG	Lung
BLOOD	Blood Rna
SMLINT	Small Intestine
SPLEEN	Spleen
SKM-VL	Vastus Lateralis
WAT-SC	White Adipose