# Statistical inference of eQTL sharing among a high number of tissues

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This document describes the "type" model, an extension of the "config" model in details in the document "config_model.tex/pdf" available in the private repository paper-eQtlBma on GitHub.

## 1 Motivation

- *Most importantly, we assume that, given a type, the activity of an eQTL in tissue r is independent from its activity in other tissues*
- However, does this still allow us to exploit the shared effect among tissues? For example, in the **Likeilhood of the Whole Data Set pdf**, equation (5) and (6) show that the prior covariance matrix is indexed by configurations.

$$\boldsymbol{b}_{gp} | U_0 \sim \mathcal{N}_R(\mathbf{0}, U_0) \tag{1}$$

where, following Wen (2014), $U_0$ is parametrized as $(\Gamma_{gp}, \Delta_{gp})$:

$$p(U_0) = p(\Delta_{gp} | \Gamma_{gp}) \mathsf{P}(\Gamma_{gp}) \tag{2}$$

so that $\Gamma_{gp}$ is a binary matrix consisting of entry-wise non-zero indicators and is identical in size and layout to $U_0$, and $\Delta_{gp}$ is an indexed set of numerical values quantifying each non-zero entry in $\Gamma_{gp}$. The skeleton $\Gamma_{gp}$ has $\boldsymbol{\gamma}_{gp}$ on the diagonal. Each off-diagonal entry $\Gamma_{gp,ij}$ is equal to 1 has long as diagonal elements $\Gamma_{gp,ii}$ and $\Gamma_{gp,jj}$ are both equal to 1.

- Doesn't saying that given a type, the activity of an eQTL in tissue is independent from its activity in other tissues directly negate the covariance in effects?
- In the config model, given a configuration $\boldsymbol{\gamma}$,

$$b_{gpr} | \gamma_{gpr}, \bar{b}_{gp}, \phi \sim \gamma_{gpr} \mathcal{N}(\bar{b}_{gp}, \phi^2) + (1 - \gamma_{gpr}) \delta_0 \tag{3}$$

But here, according to Solution (1) of the document, The target distribution $\boldsymbol{b}|\boldsymbol{q}_k$ can thus be approximated by the $\mathcal{N}_R(0, U_k)$ where:

$$U_k = \begin{pmatrix} q_{k1}(\phi_l^2 + q_{k1}\omega_l^2) & \cdots & q_{k1}q_{kR}\omega_l^2 \\ \vdots & \ddots & \vdots \\ \cdots & \cdots & q_{kR}(\phi_l^2 + q_{kR}\omega_l^2) \end{pmatrix}$$

Since the fact that there are non-zero entries on the diagonal means that the convariance is non-zero and beta is a multivariate normal, doesn't b—q mean that the effects are *not independent conditional on type*? So are we always left with the BF conditional on q, or do we ever integrate out q?

I see in solution 2, we are effectively doing as in the supplement of the AOAS paper (i.e., equation A.6)

## 2 Question

In the type-based model, we use a latent indicator $K$-dimensional vector $\boldsymbol{t}_{gp}$ to denote the actual type. In case the SNP is not an eQTL,

$$\mathsf{P}(\boldsymbol{t}_{gp} = \boldsymbol{0} | v_{gp} = 0) = 1. \tag{4}$$

Otherwise, we assume the gene-SNP pair belongs to the $k$-th type with prior probability

$$\mathsf{P}(t_{gpk} = 1 | v_{gp} = 1) = \pi_k \tag{5}$$

with the constraints $\forall k \; \pi_k \geq 0$ and $\sum_k \pi_k = 1$. All column vectors $\boldsymbol{t}_{gp}$ for all $m_g$ SNPs are gathered into a $K \times m_g$ matrix $T_g$.

In the type-based model, we also index all tissues in which the eQTL is active via a latent indicator $R$-dimensional vector $\boldsymbol{\gamma}_{gp}$, which hence corresponds to its configuration. However, compare to the "config" model where $\boldsymbol{\gamma}_{gp}$ simply corresponds to the latent variable $\boldsymbol{c}_{gp}$ indexing the configuration, we now put a prior on $\boldsymbol{\gamma}_{gp}$. In case the SNP is not an eQTL,

$$\mathsf{P}(\boldsymbol{\gamma}_{gp} = \boldsymbol{0} | \boldsymbol{t}_{gp} = \boldsymbol{0}) = 1. \tag{6}$$

Otherwise, we assume the eQTL is active in the $r$-th tissue with prior probability depending on the type

$$\mathsf{P}(\gamma_{gpr} = 1 | t_{gpk} = 1) = q_{kr}, \tag{7}$$

for which we could also parametrize the $q_{kr}$ in terms of tissue-specific annotations, e.g. DNase peaks, and therefore have $q_{pkr}$. Joining the column vectors $\boldsymbol{\gamma}_{gp}$ for all $K$ types, we obtain a latent $R \times K$ matrix $\Gamma_{gp}$. All these matrices are gathered into $\boldsymbol{\Gamma}_g = (\Gamma_{g1}, \ldots, \Gamma_{gm_g})$. As a result, this bypasses the need for the $J$-dimensional vectors $\boldsymbol{c}_{gp}$ where $J = 2^R - 1$ and the corresponding prior probabilities (the $\eta_j$'s).

- I understand that the $K \times m_g$ matrix $T_g$ represents the identity of each SNP in the columns, so that the column sum is equal to 1 and the row sum is equal to the number of SNPs in the class.
- Furthermore, the $R \times K$ matrix $\Gamma_{gp}$ represents the tissue-specific patterns of expression for each class across tissues, such that the column sums will represent the number of tissues a SNP of type 'k' might be active and the rows reprsent the total number of types from which a tissue derives activity.
- However, since the matrix $\Gamma_{gp}$ is the same for all SNPs of a particular type, why is it necessary to stack the $\Gamma_{gp}$ into $\boldsymbol{\Gamma}_g$?