SIB LDSC

For SNP i, let $\hat{\theta}_i \sim \mathcal{N}(0, S_i + l_i V)$

Where

$$S_i = \frac{1}{M}\begin{bmatrix} \sigma_{i1}^2 & r_{is}\sigma_{i1}\sigma_{i2} \\ r_{is}\sigma_{i1}\sigma_{i2} & \sigma_{i2}^2 \end{bmatrix}$$

$$V = \frac{1}{M}\begin{bmatrix} v_1 & r\sqrt{v_1 v_2} \\ r\sqrt{v_1 v_2} & v_2 \end{bmatrix}$$

And l_i is the LD score for SNP i.

We drop the i subscript from now on.

Define $D := \sqrt{M}\begin{bmatrix} \frac{1}{\sigma_1} & 0 \\ 0 & \frac{1}{\sigma_2} \end{bmatrix}$

Let $z := D\hat{\theta}$

Then

$z \sim \mathcal{N}\left(0, \begin{bmatrix} 1 & r_s \\ r_s & 1 \end{bmatrix} + l \begin{bmatrix} \frac{v_1}{\sigma_1^2} & r\frac{\sqrt{v_1 v_2}}{\sigma_1\sigma_2} \\ r\frac{\sqrt{v_1 v_2}}{\sigma_1\sigma_2} & \frac{v_2}{\sigma_2^2} \end{bmatrix}\right)$

Let $\Sigma := \begin{bmatrix} 1 & r_s \\ r_s & 1 \end{bmatrix} + l \begin{bmatrix} \frac{v_1}{\sigma_1^2} & r\frac{\sqrt{v_1 v_2}}{\sigma_1\sigma_2} \\ r\frac{\sqrt{v_1 v_2}}{\sigma_1\sigma_2} & \frac{v_2}{\sigma_2^2} \end{bmatrix}$

Then we can define the log likelihood l as:

$$logll = -log(2\pi) - \frac{1}{2}|\Sigma| - \frac{1}{2}z'\Sigma^{-1}z$$

Let $T := z_1^2\left(1 + l\frac{v_2}{\sigma_2^2}\right) - 2\left(r_s + lr\frac{\sqrt{v_1 v_2}}{\sigma_1\sigma_2}\right)z_1 z_2 + z_2^2\left(1 + l\frac{v_1}{\sigma_1^2}\right)$

The gradient with respect to the parameters of interest are:

$$\frac{\partial l}{\partial v_1} = \frac{1}{|\Sigma|}\frac{\partial|\Sigma|}{\partial v_1} + \frac{1}{|\Sigma|}\left(\frac{\partial T}{\partial v_1} - \frac{T}{|\Sigma|}\frac{\partial|\Sigma|}{\partial v_1}\right)$$

Where $\frac{\partial|\Sigma|}{\partial v_1} = \frac{l}{\sigma_1^2}\left(1 + l\frac{v_2}{\sigma_2^2}\right) - \frac{rl}{\sigma_1\sigma_2}\left(r_s\sqrt{\frac{v_2}{v_1}} + l\frac{rv_2}{\sigma_1\sigma_2}\right)$

and $\frac{\partial T}{\partial v_1} = \frac{lz_2^2}{\sigma_1^2} - \frac{lrz_1z_2}{\sigma_1\sigma_2}\sqrt{\frac{v_2}{v_1}}$

$$\frac{\partial l}{\partial v_2} = \frac{1}{|\Sigma|}\frac{\partial|\Sigma|}{\partial v_2} + \frac{1}{|\Sigma|}\left(\frac{\partial T}{\partial v_2} - \frac{T}{|\Sigma|}\frac{\partial|\Sigma|}{\partial v_2}\right)$$

Where $\frac{\partial|\Sigma|}{\partial v_2} = \frac{l}{\sigma_2^2}\left(1 + l\frac{v_1}{\sigma_1^2}\right) - \frac{rl}{\sigma_1\sigma_2}\left(r_s\sqrt{\frac{v_1}{v_2}} + l\frac{rv_1}{\sigma_1\sigma_2}\right)$

and $\frac{\partial T}{\partial v_2} = \frac{lz_1^2}{\sigma_2^2} - \frac{lrz_1z_2}{\sigma_1\sigma_2}\sqrt{\frac{v_1}{v_2}}$

$$\frac{\partial l}{\partial r} = \frac{1}{|\Sigma|}\frac{\partial|\Sigma|}{\partial r} + \frac{1}{|\Sigma|}\left(\frac{\partial T}{\partial r} - \frac{T}{|\Sigma|}\frac{\partial|\Sigma|}{\partial r}\right)$$

Where $\frac{\partial|\Sigma|}{\partial r} = -2l\frac{\sqrt{v_1v_2}}{\sigma_1\sigma_2}\left(r_s + rl\frac{\sqrt{v_1v_2}}{\sigma_1\sigma_2}\right)$

and $\frac{\partial T}{\partial r} = -2l\frac{\sqrt{v_1v_2}}{\sigma_1\sigma_2}z_1z_2$