Text S2: Relationship between BF_{mean} and \(\Lambda_{\text{mean}}\)

Here we develop an expression for the relationship between the Bayes factor BF_{mean} and the likelihood ratio statistic \(\Lambda_{\text{mean}}\), under an additive model with \(d = 0\) and a fixed value of the prior variance of \(a\), \(\sigma_a\). (In the main paper we use a Bayes factor that averages over several values of \(\sigma_a\), and allows for some dominance, as in [1]. This is different from, though highly correlated with, the Bayes factor considered here.)

Under an additive model \((d = 0)\) the model (12) in the main text can be written as \(Y \sim N(\bar{X}\beta, 1/\tau)\), where \(\bar{X}\) is the \(n \times 2\) design matrix \((1, \bar{g})\) whose first column is all 1s, and second column contains the expected genotype values for each individual. Using the prior D2 from [1] the Bayes factor for the alternative \((a \neq 0)\) vs the null \((a = 0)\) is:

\[
BF_{\text{mean}} = \frac{(\alpha n)^{1/2}}{\det(\Omega)^{1/2}} \left( \frac{Y^t Y - Y^t \bar{X} \Omega^{-1} \bar{X}^t Y}{Y^t Y - n \bar{Y}^2} \right)^{-n/2}
\]

where for notational convenience we have written \(\alpha\) for \(\sigma_a^{-2}\), and \(\Omega = \begin{pmatrix} 0 & 0 \\ 0 & \alpha \end{pmatrix} + \bar{X}^t \bar{X}\). If we let \(V\) denote \(n\) times the sample variance of \(g\), \(V = (g^t g - n \bar{g}^2)\), then \(\det(\Omega) = n(\alpha + V)\), \(\det(\bar{X}^t \bar{X}) = nV\), and

\[
\Omega^{-1} = \frac{1}{\det(\Omega)} \left[ \det(\bar{X}^t \bar{X}) (\bar{X}^t \bar{X})^{-1} + \begin{pmatrix} 0 & 0 \\ 0 & \alpha \end{pmatrix} \right]
= \frac{V}{\alpha + V} \left[ (\bar{X}^t \bar{X})^{-1} + \begin{pmatrix} \alpha/nV & 0 \\ 0 & 0 \end{pmatrix} \right].
\]

Now let RSS_0 and RSS_1 denote the residual sum of squares for the maximum likelihood estimates under the null and alternative hypotheses:

\[
\begin{align*}
\text{RSS}_0 &= Y^t Y - n \bar{Y}^2 \\
\text{RSS}_1 &= Y^t Y - Y^t \bar{X} (\bar{X}^t \bar{X})^{-1} \bar{X}^t Y.
\end{align*}
\]

Taking the log of (1), and substituting, we obtain

\[
\log(BF_{\text{mean}}) = 0.5 \log[\alpha/(\alpha + V)] - (n/2) \log \frac{\alpha/(\alpha + V) \text{RSS}_0 + V/(\alpha + V) \text{RSS}_1}{\text{RSS}_0} \\
= 0.5 \log[\alpha/(\alpha + V)] - (n/2) \log \left[ 1 - \frac{V}{\alpha + V} \frac{\text{RSS}_0 - \text{RSS}_1}{\text{RSS}_0} \right].
\]
Note also that the log-likelihood ratio statistic is given by

\[ 2 \log \Lambda_{\text{mean}} = n \log \left[ \frac{\text{RSS}_0}{\text{RSS}_1} \right] = n \log \left[ 1 - \frac{\text{RSS}_0 - \text{RSS}_1}{\text{RSS}_1} \right]. \] (5)

Four observations come directly from these expressions for BF\(_{\text{mean}}\) and \(\Lambda_{\text{mean}}\):

- For fixed \(V\), both BF\(_{\text{mean}}\) and \(\Lambda_{\text{mean}}\) are monotone decreasing in \((\text{RSS}_0 - \text{RSS}_1)/\text{RSS}_1\). Hence, among SNPs with the same value of \(V\), BF\(_{\text{mean}}\) and \(\Lambda_{\text{mean}}\) will produce the same ranking of SNPs.

- If \(\alpha = kV\) (so that for each SNP the prior variance on \(a\) is chosen to be inversely proportional to the \(V\) for that SNP) then \(\log(BF_{\text{mean}})\) and \(\Lambda_{\text{mean}}\) produce the same ranking of SNPs.

- For fixed \(V\), if \((\text{RSS}_0 - \text{RSS}_1)/\text{RSS}_1\) is small (which it will be in our applications, where effect sizes are small), then both \(\log(BF_{\text{mean}})\) and \(\Lambda_{\text{mean}}\) are approximately linear in \((\text{RSS}_0 - \text{RSS}_1)/\text{RSS}_1\), because \(\log(1 - x) \approx -x\) when \(x\) small. This explains the approximately linear relationships evident in Figure 3 in the main text.

- For fixed \((\text{RSS}_0 - \text{RSS}_1)/\text{RSS}_0\), and fixed \(\alpha\), \(BF_{\text{mean}} \to 1\) as \(V \to 0\). Thus, compared with \(\Lambda_{\text{mean}}\), \(BF_{\text{mean}}\) down-weights SNPs with small \(V\).

**References**