

Supplementary Appendix to “Combining Structural Equation Modeling with Genomic-Relatedness-Matrix Restricted Maximum Likelihood in OpenMx” by R. M. Kirkpatrick et al.

Derivatives of the Restricted Loglikelihood

Here, we show how the first and second derivatives of the restricted loglikelihood (which is used in REML analyses; Meyer & Smith, 1996) depend upon the first derivatives of the covariance matrix \mathbf{V} .

For ease of notation, we will consider derivatives with respect to two arbitrary parameters, θ_i and θ_j , and define:

$$\mathbf{A} \equiv \frac{\partial \mathbf{V}}{\partial \theta_i}$$

$$\mathbf{B} \equiv \frac{\partial \mathbf{V}}{\partial \theta_j}$$

The restricted loglikelihood is,

$$\ell = -0.5(\log|\mathbf{V}| + \log|\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X}| + \mathbf{y}^T \mathbf{P} \mathbf{y})$$

, where \mathbf{X} is the matrix of covariates, \mathbf{y} is the vector of phenotype scores, and

$$\mathbf{P} = \mathbf{V}^{-1} - \mathbf{V}^{-1} \mathbf{X} (\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X})^{-1} \mathbf{X}^T \mathbf{V}^{-1}$$

. Note that \mathbf{V} , and therefore \mathbf{P} , are functions of parameters, whereas \mathbf{X} and \mathbf{y} are not.

First, note that the derivative of \mathbf{V}^{-1} is

$$\frac{\partial \mathbf{V}^{-1}}{\partial \theta_i} = -\mathbf{V}^{-1} \frac{\partial \mathbf{V}}{\partial \theta_i} \mathbf{V}^{-1}$$

$$= -\mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1}$$

. The first derivative of the first term of the loglikelihood is

$$\frac{\partial \log|\mathbf{V}|}{\partial \theta_i} = \text{tr} \left(\mathbf{V}^{-1} \frac{\partial \mathbf{V}}{\partial \theta_i} \right)$$

$$= \text{tr}(\mathbf{V}^{-1} \mathbf{A})$$

. The first derivative of the second term is

$$\frac{\partial \log|\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X}|}{\partial \theta_i} = \text{tr} \left([\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X}]^{-1} \frac{\partial \mathbf{X}^T \mathbf{V}^{-1} \mathbf{X}}{\partial \theta_i} \right)$$

$$= \text{tr} \left([\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X}]^{-1} \mathbf{X}^T \frac{\partial \mathbf{V}^{-1}}{\partial \theta_i} \mathbf{X} \right)$$

$$= -\text{tr}([\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X}]^{-1} \mathbf{X}^T \mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1} \mathbf{X})$$

. The first derivative of the third term is cumbersome. First, we will let \mathbf{Q} denote a particular quadratic form in \mathbf{X} , specifically,

$$\mathbf{Q} = \mathbf{X}^T \mathbf{V}^{-1} \mathbf{X}$$

. Now, consider the following:

$$\frac{\partial \mathbf{Q}^{-1}}{\partial \theta_i} = -\mathbf{Q}^{-1} \frac{\partial \mathbf{X}^T \mathbf{V}^{-1} \mathbf{X}}{\partial \theta_i} \mathbf{Q}^{-1}$$

$$\begin{aligned}
&= -\mathbf{Q}^{-1}\mathbf{X}^T \frac{\partial \mathbf{V}^{-1}}{\partial \theta_i} \mathbf{X}\mathbf{Q}^{-1} \\
&= \mathbf{Q}^{-1}\mathbf{X}^T \mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1} \mathbf{X}\mathbf{Q}^{-1}
\end{aligned}$$

. Applying the Product Rule, we further have:

$$\begin{aligned}
\frac{\partial \mathbf{Q}^{-1}\mathbf{X}^T \mathbf{V}^{-1}}{\partial \theta_i} &= \mathbf{Q}^{-1} \frac{\partial \mathbf{X}^T \mathbf{V}^{-1}}{\partial \theta_i} + \frac{\partial \mathbf{Q}^{-1}}{\partial \theta_i} \mathbf{X}^T \mathbf{V}^{-1} \\
&= -\mathbf{Q}^{-1}\mathbf{X}^T \mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1} + \mathbf{Q}^{-1}\mathbf{X}^T \mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1} \mathbf{X}\mathbf{Q}^{-1} \mathbf{X}^T \mathbf{V}^{-1}
\end{aligned}$$

. Again applying the Product Rule, we also have:

$$\begin{aligned}
\frac{\partial (\mathbf{V}^{-1}\mathbf{X})\mathbf{Q}^{-1}\mathbf{X}^T \mathbf{V}^{-1}}{\partial \theta_i} &= (\mathbf{V}^{-1}\mathbf{X}) \frac{\partial \mathbf{Q}^{-1}\mathbf{X}^T \mathbf{V}^{-1}}{\partial \theta_i} + \frac{\partial (\mathbf{V}^{-1}\mathbf{X})}{\partial \theta_i} \mathbf{Q}^{-1}\mathbf{X}^T \mathbf{V}^{-1} \\
&= (\mathbf{V}^{-1}\mathbf{X})(-\mathbf{Q}^{-1}\mathbf{X}^T \mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1} + \mathbf{Q}^{-1}\mathbf{X}^T \mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1} \mathbf{X}\mathbf{Q}^{-1} \mathbf{X}^T \mathbf{V}^{-1}) - \mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1} \mathbf{X}\mathbf{Q}^{-1} \mathbf{X}^T \mathbf{V}^{-1} \\
&= -\mathbf{V}^{-1} \mathbf{X}\mathbf{Q}^{-1} \mathbf{X}^T \mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1} + \mathbf{V}^{-1} \mathbf{X}\mathbf{Q}^{-1} \mathbf{X}^T \mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1} \mathbf{X}\mathbf{Q}^{-1} \mathbf{X}^T \mathbf{V}^{-1} \\
&\quad - \mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1} \mathbf{X}\mathbf{Q}^{-1} \mathbf{X}^T \mathbf{V}^{-1}
\end{aligned}$$

. Now, the derivative of \mathbf{P} :

$$\begin{aligned}
\frac{\partial \mathbf{P}}{\partial \theta_i} &= \frac{\partial \mathbf{V}^{-1}}{\partial \theta_i} - \frac{\partial (\mathbf{V}^{-1}\mathbf{X})\mathbf{Q}^{-1}\mathbf{X}^T \mathbf{V}^{-1}}{\partial \theta_i} \\
&= -\mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1} + \mathbf{V}^{-1} \mathbf{X}\mathbf{Q}^{-1} \mathbf{X}^T \mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1} - \mathbf{V}^{-1} \mathbf{X}\mathbf{Q}^{-1} \mathbf{X}^T \mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1} \mathbf{X}\mathbf{Q}^{-1} \mathbf{X}^T \mathbf{V}^{-1} \\
&\quad + \mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1} \mathbf{X}\mathbf{Q}^{-1} \mathbf{X}^T \mathbf{V}^{-1} \\
&= \mathbf{V}^{-1} \mathbf{X}\mathbf{Q}^{-1} \mathbf{X}^T \mathbf{V}^{-1} \mathbf{A} [\mathbf{V}^{-1} - \mathbf{V}^{-1} \mathbf{X}(\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X})^{-1} \mathbf{X}^T \mathbf{V}^{-1}] \\
&\quad - \mathbf{V}^{-1} \mathbf{A} [\mathbf{V}^{-1} - \mathbf{V}^{-1} \mathbf{X}(\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X})^{-1} \mathbf{X}^T \mathbf{V}^{-1}] \\
&= \mathbf{V}^{-1} \mathbf{X}\mathbf{Q}^{-1} \mathbf{X}^T \mathbf{V}^{-1} \mathbf{A} \mathbf{P} - \mathbf{V}^{-1} \mathbf{A} \mathbf{P} \\
&= -[\mathbf{V}^{-1} - \mathbf{V}^{-1} \mathbf{X}(\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X})^{-1} \mathbf{X}^T \mathbf{V}^{-1}] \mathbf{A} \mathbf{P} \\
&= -\mathbf{P} \mathbf{A} \mathbf{P}
\end{aligned}$$

Naturally,

$$\frac{\partial \mathbf{y}^T \mathbf{P} \mathbf{y}}{\partial \theta_i} = -\mathbf{y}^T \mathbf{P} \mathbf{A} \mathbf{P} \mathbf{y}$$

, which is the derivative of the third term of the loglikelihood.

Putting it all together,

$$\frac{\partial \ell}{\partial \theta_i} = -0.5 [\text{tr}(\mathbf{V}^{-1} \mathbf{A}) - \text{tr}([\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X}]^{-1} \mathbf{X}^T \mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1} \mathbf{X}) - \mathbf{y}^T \mathbf{P} \mathbf{A} \mathbf{P} \mathbf{y}]$$

. Because traces of a matrix product are invariant under cyclic permutations of the factors,

$$\text{tr}([\mathbf{X}^T \mathbf{V}^{-1} \mathbf{X}]^{-1} \mathbf{X}^T \mathbf{V}^{-1} \mathbf{A} \mathbf{V}^{-1} \mathbf{X}) = \text{tr}(\mathbf{V}^{-1} \mathbf{X}\mathbf{Q}^{-1} \mathbf{X}^T \mathbf{V}^{-1} \mathbf{A})$$

. Furthermore, the trace of a sum of square matrices is the sum of the traces. Therefore,

$$\begin{aligned}
\frac{\partial \ell}{\partial \theta_i} &= -0.5 [\text{tr}(\mathbf{V}^{-1} \mathbf{A} - \mathbf{V}^{-1} \mathbf{X}\mathbf{Q}^{-1} \mathbf{X}^T \mathbf{V}^{-1} \mathbf{A}) - \mathbf{y}^T \mathbf{P} \mathbf{A} \mathbf{P} \mathbf{y}] \\
&= -0.5 [\text{tr}(\mathbf{P} \mathbf{A}) - \mathbf{y}^T \mathbf{P} \mathbf{A} \mathbf{P} \mathbf{y}]
\end{aligned}$$

We will here make two assumptions about \mathbf{A} and \mathbf{B} . First, we will assume that \mathbf{A} and \mathbf{B} are symmetric, that is, $\mathbf{A} = \mathbf{A}^T$ and $\mathbf{B} = \mathbf{B}^T$. Second, we will assume that $\frac{\partial \mathbf{A}}{\partial \theta_j} = \mathbf{0}$ and $\frac{\partial \mathbf{B}}{\partial \theta_j} = \mathbf{0}$. If the latter assumption is not true, then our result below for the second derivatives of the loglikelihood will not be exactly accurate, but may be a reasonable approximation in some cases.

We will now evaluate the second derivative of the loglikelihood:

$$\frac{\partial^2 \ell}{\partial \theta_i \partial \theta_j} = -0.5 \left[\frac{\partial \text{tr}(\mathbf{PA})}{\partial \theta_j} - \frac{\partial \mathbf{y}^T \mathbf{PAPy}}{\partial \theta_j} \right]$$

. The matrix trace is a linear operator, so

$$\frac{\partial \text{tr}(\mathbf{PA})}{\partial \theta_j} = \text{tr} \left(\frac{\partial \mathbf{PA}}{\partial \theta_j} \right)$$

, and since we assume that $\frac{\partial \mathbf{A}}{\partial \theta_j} = \mathbf{0}$,

$$\text{tr} \left(\frac{\partial \mathbf{PA}}{\partial \theta_j} \right) = -\text{tr}(\mathbf{PBPA})$$

. Note that $\mathbf{y}^T \mathbf{PAPy}$ evaluates to a scalar, and therefore, $\mathbf{y}^T \mathbf{PAPy} = \text{tr}(\mathbf{y}^T \mathbf{PAPy})$, and

$$\frac{\partial \text{tr}(\mathbf{y}^T \mathbf{PAPy})}{\partial \theta_j} = \text{tr} \left(\frac{\partial \mathbf{y}^T \mathbf{PAPy}}{\partial \theta_j} \right)$$

$$= \text{tr} \left(\mathbf{y}^T \mathbf{PA} \frac{\partial \mathbf{Py}}{\partial \theta_j} + \frac{\partial \mathbf{y}^T \mathbf{PA}}{\partial \theta_j} \mathbf{Py} \right)$$

$$= \text{tr}(-\mathbf{y}^T \mathbf{PAPBPpy} - \mathbf{y}^T \mathbf{PBPAPpy})$$

. Since the trace of a sum is the sum of the traces,

$$= -\text{tr}(\mathbf{y}^T \mathbf{PAPBPpy}) - \text{tr}(\mathbf{y}^T \mathbf{PBPAPpy})$$

. And, since the trace of a transpose equals the trace of the original matrix,

$$= -\text{tr}(\mathbf{y}^T \mathbf{PAPBPpy}) - \text{tr}([\mathbf{y}^T \mathbf{PAPBPpy}]^T)$$

, and since we assume that \mathbf{A} and \mathbf{B} are symmetric,

$$= -2\text{tr}(\mathbf{y}^T \mathbf{PAPBPpy})$$

Putting it all together,

$$\frac{\partial^2 \ell}{\partial \theta_i \partial \theta_j} = 0.5\text{tr}(\mathbf{PBPA}) + \text{tr}(\mathbf{y}^T \mathbf{PAPBPpy})$$

$$= 0.5\text{tr}(\mathbf{PBPA}) + \mathbf{y}^T \mathbf{PAPBPpy}$$

Worked Example of Analytic Derivatives

Here, we will consider the analytic derivatives of the \mathbf{V} matrix for an extension of the factor model described in the main text that also biometrically decomposes the unique-factor variances. This section also explains the analytic derivatives of \mathbf{V} used in script #2 in Table I, except that script is for 5 phenotypes instead of 3.

The present model has 10 free parameters: V_{AC} , the additive-genetic variance in the common factor; the 3 phenotypes' loadings onto the common factor, λ_1 , λ_2 , and λ_3 ; the 3 phenotypes' unique additive-genetic variance components, V_{A1} , V_{A2} , and V_{A3} ; and the 3 phenotypes' unique nonshared-environmental variance components, V_{E1} , V_{E2} , and V_{E3} . Let \mathbf{y} denote the vector of scores on the 3 phenotypes stacked on top of one another (i.e., "blocked by phenotype"). Let $\boldsymbol{\lambda}$ denote a column vector of the 3 factor loadings, i.e. $\boldsymbol{\lambda}^T = [\lambda_1 \quad \lambda_2 \quad \lambda_3]$. Let \mathbf{A} denote the $n \times n$

GRM, let \mathbf{I} denote an $n \times n$ identity matrix, and let $\mathbf{0}$ denote an $n \times n$ matrix of zeroes. The model does not include any covariates.

Let \mathbf{V} denote the variance of \mathbf{y} ,

$$\mathbf{V} = \boldsymbol{\lambda}\boldsymbol{\lambda}^T \otimes \text{var}(\mathbf{F}) + \text{var}(\mathbf{U})$$

, where \mathbf{F} is a random column vector of n common-factor scores, and \mathbf{U} is a random column vector of $3n$ unique-factor scores. The variance of \mathbf{U} is straightforward:

$$\text{var}(\mathbf{U}) = \begin{bmatrix} \mathbf{A}V_{A1} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{A}V_{A2} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{A}V_{A3} \end{bmatrix} + \begin{bmatrix} \mathbf{I}V_{E1} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{I}V_{E2} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{I}V_{E3} \end{bmatrix}$$

. The variance of \mathbf{F} is:

$$\text{var}(\mathbf{F}) = (\mathbf{A}V_{AC} + \mathbf{I}[1 - V_{AC}])$$

. The common variance in \mathbf{y} , $\boldsymbol{\lambda}\boldsymbol{\lambda}^T \otimes (\mathbf{A}V_{AC} + \mathbf{I}[1 - V_{AC}])$, can be expressed as

$$\begin{bmatrix} \lambda_1^2 & \lambda_1\lambda_2 & \lambda_1\lambda_3 \\ \lambda_2\lambda_1 & \lambda_2^2 & \lambda_2\lambda_3 \\ \lambda_3\lambda_1 & \lambda_3\lambda_2 & \lambda_3^2 \end{bmatrix} \otimes (\mathbf{A}V_{AC} + \mathbf{I}[1 - V_{AC}])$$

, or equivalently,

$$\begin{bmatrix} \mathbf{A}\lambda_1^2 & \mathbf{A}\lambda_1\lambda_2 & \mathbf{A}\lambda_1\lambda_3 \\ \mathbf{A}\lambda_2\lambda_1 & \mathbf{A}\lambda_2^2 & \mathbf{A}\lambda_2\lambda_3 \\ \mathbf{A}\lambda_3\lambda_1 & \mathbf{A}\lambda_3\lambda_2 & \mathbf{A}\lambda_3^2 \end{bmatrix} V_{AC} + \begin{bmatrix} \mathbf{I}\lambda_1^2 & \mathbf{I}\lambda_1\lambda_2 & \mathbf{I}\lambda_1\lambda_3 \\ \mathbf{I}\lambda_2\lambda_1 & \mathbf{I}\lambda_2^2 & \mathbf{I}\lambda_2\lambda_3 \\ \mathbf{I}\lambda_3\lambda_1 & \mathbf{I}\lambda_3\lambda_2 & \mathbf{I}\lambda_3^2 \end{bmatrix} (1 - V_{AC})$$

We now have the following first partial derivatives of \mathbf{V} . The derivatives with respect to the unique-factor variance components are quite simple:

$$\begin{aligned} \frac{\partial \mathbf{V}}{\partial V_{A1}} &= \begin{bmatrix} \mathbf{A} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} \end{bmatrix} \\ \frac{\partial \mathbf{V}}{\partial V_{A2}} &= \begin{bmatrix} \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{A} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} \end{bmatrix} \\ \frac{\partial \mathbf{V}}{\partial V_{A3}} &= \begin{bmatrix} \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{A} \end{bmatrix} \\ \frac{\partial \mathbf{V}}{\partial V_{E1}} &= \begin{bmatrix} \mathbf{I} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} \end{bmatrix} \\ \frac{\partial \mathbf{V}}{\partial V_{E2}} &= \begin{bmatrix} \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{I} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} \end{bmatrix} \\ \frac{\partial \mathbf{V}}{\partial V_{E3}} &= \begin{bmatrix} \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{I} \end{bmatrix} \end{aligned}$$

. The derivative of \mathbf{V} with respect to V_{AC} is,

$$\frac{\partial \mathbf{V}}{\partial V_{AC}} = \begin{bmatrix} \lambda_1^2 & \lambda_1\lambda_2 & \lambda_1\lambda_3 \\ \lambda_2\lambda_1 & \lambda_2^2 & \lambda_2\lambda_3 \\ \lambda_3\lambda_1 & \lambda_3\lambda_2 & \lambda_3^2 \end{bmatrix} \otimes (\mathbf{A} - \mathbf{I})$$

, or less compactly,

$$= \begin{bmatrix} \mathbf{A}\lambda_1^2 & \mathbf{A}\lambda_1\lambda_2 & \mathbf{A}\lambda_1\lambda_3 \\ \mathbf{A}\lambda_2\lambda_1 & \mathbf{A}\lambda_2^2 & \mathbf{A}\lambda_2\lambda_3 \\ \mathbf{A}\lambda_3\lambda_1 & \mathbf{A}\lambda_3\lambda_2 & \mathbf{A}\lambda_3^2 \end{bmatrix} - \begin{bmatrix} \mathbf{I}\lambda_1^2 & \mathbf{I}\lambda_1\lambda_2 & \mathbf{I}\lambda_1\lambda_3 \\ \mathbf{I}\lambda_2\lambda_1 & \mathbf{I}\lambda_2^2 & \mathbf{I}\lambda_2\lambda_3 \\ \mathbf{I}\lambda_3\lambda_1 & \mathbf{I}\lambda_3\lambda_2 & \mathbf{I}\lambda_3^2 \end{bmatrix}$$

. The derivative of \mathbf{V} with respect to the factor loadings are:

$$\frac{\partial \mathbf{V}}{\partial \lambda_1} = \begin{bmatrix} 2\lambda_1 & \lambda_2 & \lambda_3 \\ \lambda_2 & 0 & 0 \\ \lambda_3 & 0 & 0 \end{bmatrix} \otimes (\mathbf{A}V_{AC} + \mathbf{I}[1 - V_{AC}])$$

$$= \begin{bmatrix} \text{var}(\mathbf{F})2\lambda_1 & \text{var}(\mathbf{F})\lambda_2 & \text{var}(\mathbf{F})\lambda_3 \\ \text{var}(\mathbf{F})\lambda_2 & \mathbf{0} & \mathbf{0} \\ \text{var}(\mathbf{F})\lambda_3 & \mathbf{0} & \mathbf{0} \end{bmatrix}$$

$$\frac{\partial \mathbf{V}}{\partial \lambda_2} = \begin{bmatrix} 0 & \lambda_1 & 0 \\ \lambda_1 & 2\lambda_2 & \lambda_3 \\ 0 & \lambda_3 & 0 \end{bmatrix} \otimes (\mathbf{A}V_{AC} + \mathbf{I}[1 - V_{AC}])$$

$$= \begin{bmatrix} \mathbf{0} & \text{var}(\mathbf{F})\lambda_1 & \mathbf{0} \\ \text{var}(\mathbf{F})\lambda_1 & \text{var}(\mathbf{F})2\lambda_2 & \text{var}(\mathbf{F})\lambda_3 \\ \mathbf{0} & \text{var}(\mathbf{F})\lambda_3 & \mathbf{0} \end{bmatrix}$$

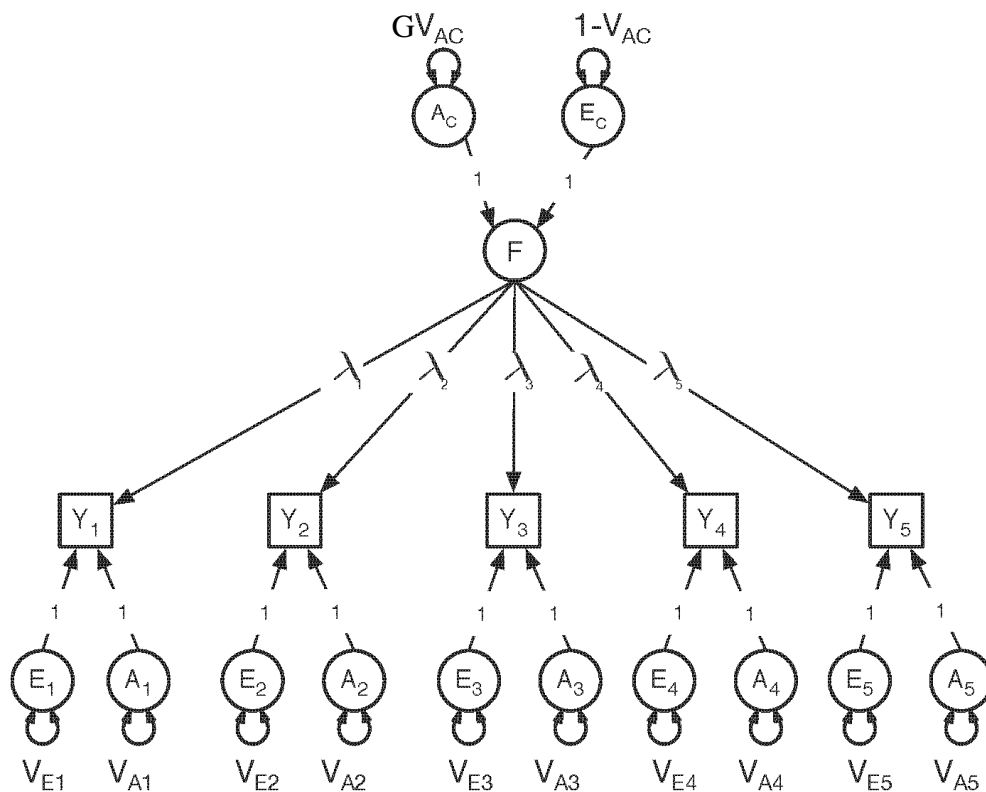
$$\frac{\partial \mathbf{V}}{\partial \lambda_3} = \begin{bmatrix} 0 & 0 & \lambda_1 \\ 0 & 0 & \lambda_2 \\ \lambda_1 & \lambda_2 & 2\lambda_3 \end{bmatrix} \otimes (\mathbf{A}V_{AC} + \mathbf{I}[1 - V_{AC}])$$

$$= \begin{bmatrix} \mathbf{0} & \mathbf{0} & \text{var}(\mathbf{F})\lambda_1 \\ \mathbf{0} & \mathbf{0} & \text{var}(\mathbf{F})\lambda_2 \\ \text{var}(\mathbf{F})\lambda_1 & \text{var}(\mathbf{F})\lambda_2 & \text{var}(\mathbf{F})2\lambda_3 \end{bmatrix}$$

Supplementary References

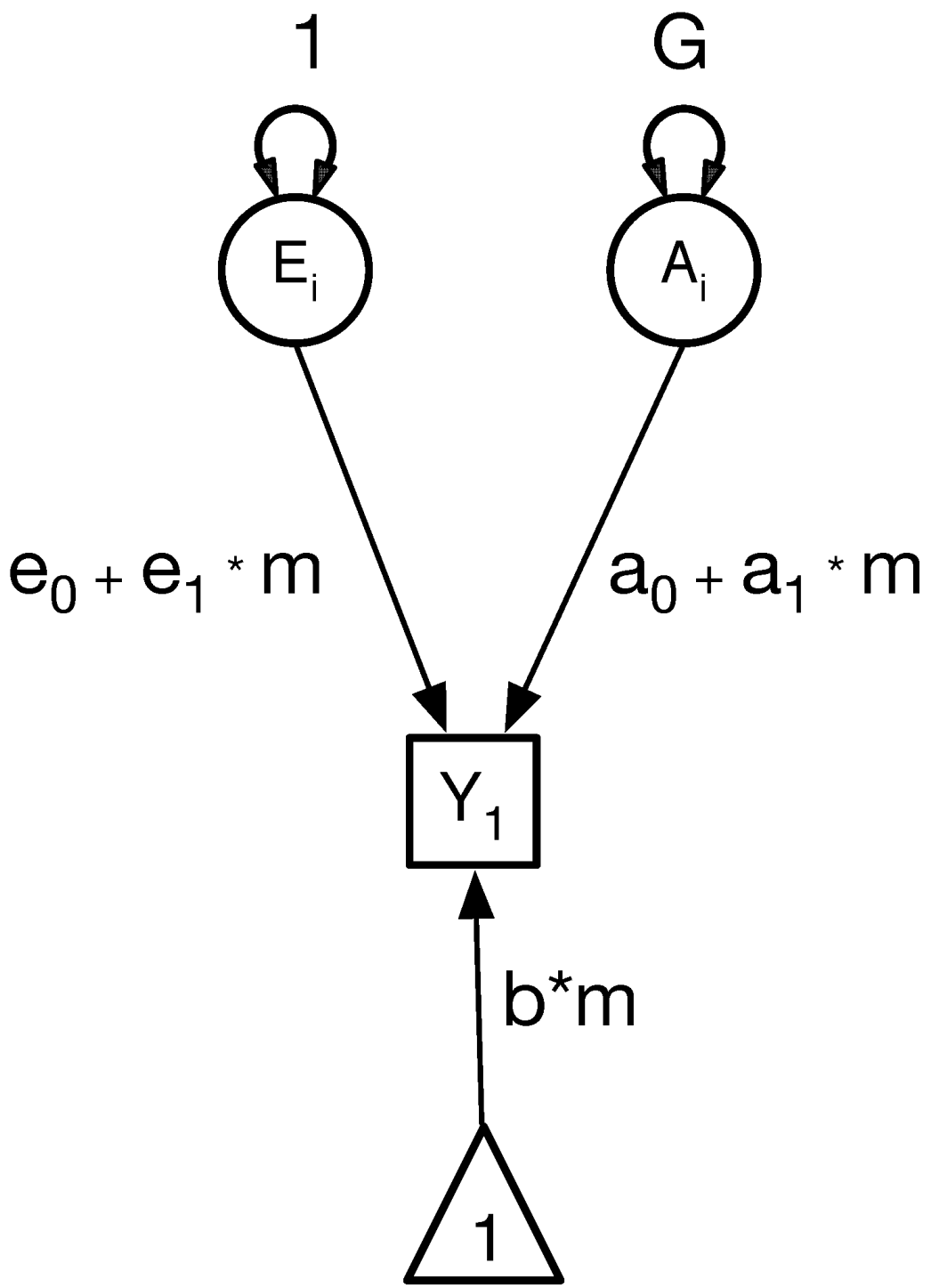
Meyer, K., & Smith, S.P. (1996). Restricted maximum likelihood estimation for animal models using derivatives of the likelihood. *Genetics Selection Evolution* 28: 23-49.

Figure S1. “Common-Pathway Model” (scripts #2 and #3 in Table I).



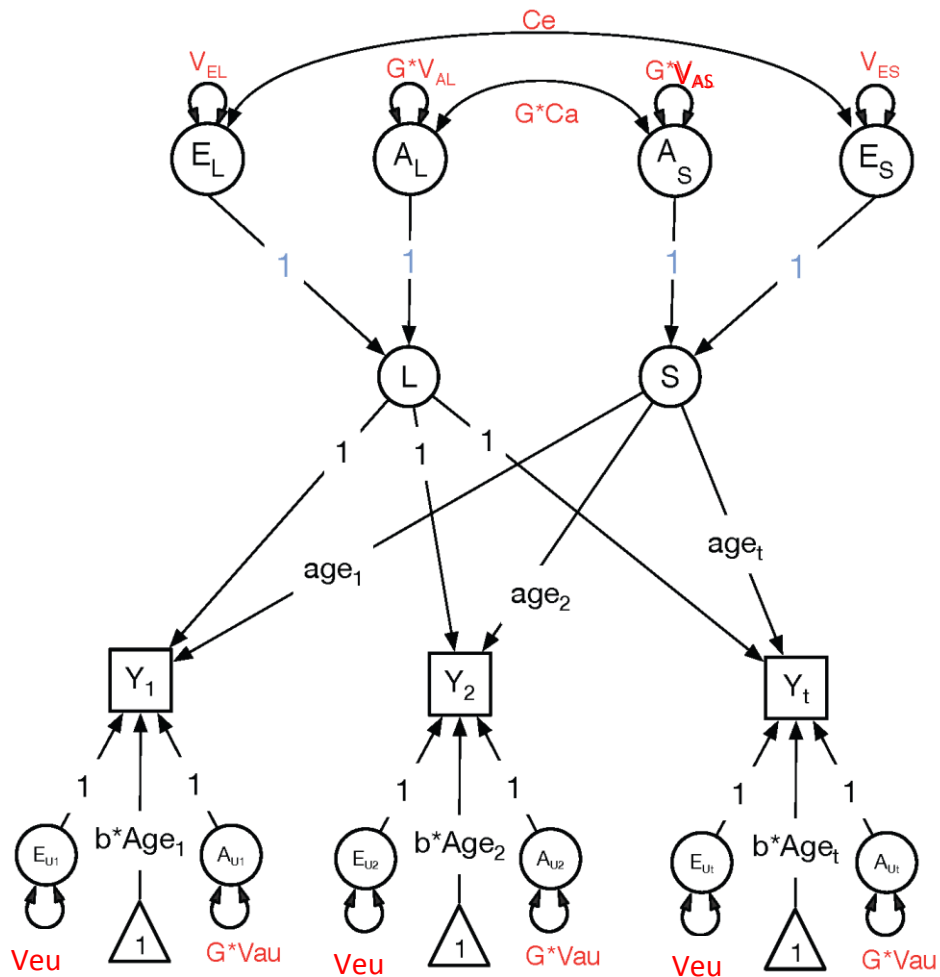
The λ s are factor loadings, V_{AC} is the heritability of the common factor, the V_{A_i} s are unique additive-genetic variance components, the V_{E_i} s are unique nonshared-environmental variance components, and G is the given individual's diagonal GRM element. The scale of the common factor is identified by defining its nonshared-environmental variance to be $1 - V_{AC}$.

Figure S2. “Biometric Moderation Model” (scripts #6 and #7 in Table I).



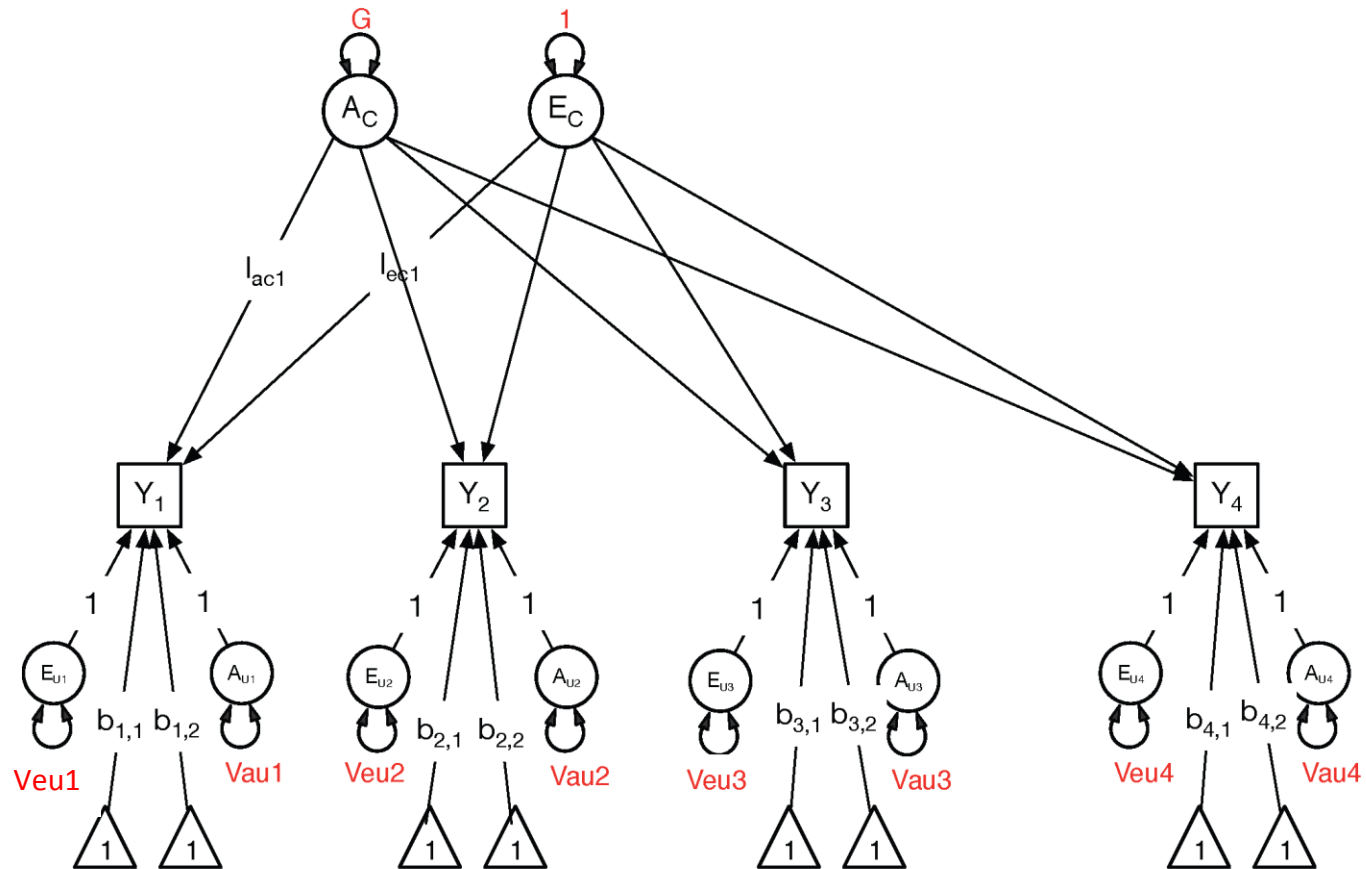
In this model, the moderator, m , is treated as exogenous. a_0 and a_1 are respectively the unmoderated and moderated additive-genetic path coefficients, e_0 and e_1 are respectively the unmoderated and moderated nonshared-environmental path coefficients, $b * m$ represents the main effect of the moderator, and G is the given individual’s diagonal GRM element.

Figure S3. “Latent-Growth Curve Model” (scripts #11 and #12 in Table I).



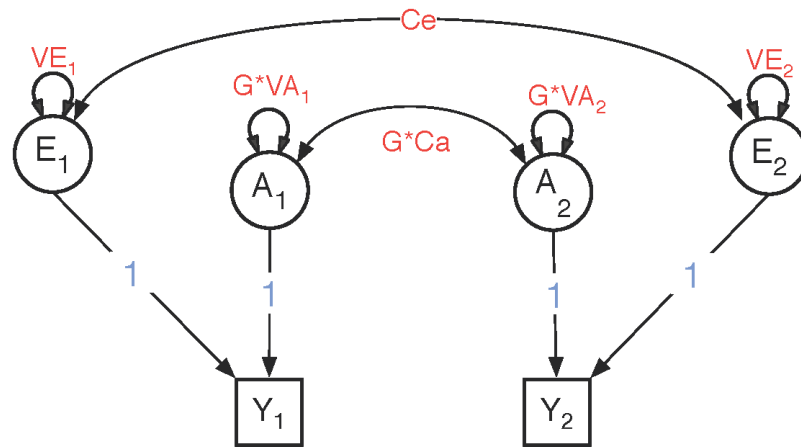
This diagram depicts timepoints 1, 2, and t ; scripts #11 and #12 have $t=5$ timepoints. In this model, age at timepoint is the time metric. G is the given individual’s diagonal GRM element, V_{AL} is additive-genetic latent-intercept variance, V_{EL} is nonshared-environmental latent-intercept variance, V_{AS} is additive-genetic latent-slope variance, V_{ES} is nonshared-environmental latent-slope variance, C_a is additive-genetic intercept-slope covariance, C_e is nonshared-environmental intercept-slope covariance, V_{au} is additive-genetic residual variance, and V_{eu} is nonshared-environmental residual variance.

Figure S4. “Independent-Pathway Model” (scripts #13 and #14 in Table I).



G is the given individual's diagonal GRM element. Phenotype Y_i 's loading onto the additive-genetic and nonshared-environmental common factors are respectively denoted by l_{aci} and l_{eci} (only depicted for Y_1). Phenotype Y_i 's additive-genetic and nonshared-environmental unique-factor variances are respectively denoted by V_{au_i} and V_{eu_i} .

Figure S5. “Saturated Diphenotype Model” (script #4 in Table I)



G is the given individual's diagonal GRM element. V_{A_1} and V_{A_2} are the additive-genetic variances of Y_1 and Y_2 , respectively, whereas V_{E_1} and V_{E_2} are likewise their respective nonshared-environmental variances. C_a and C_e are the two phenotypes' additive-genetic and nonshared-environmental covariances.