**Source Code File**

# This is code to partition maternal genetic effects into pre- and postnatal effects from Hwang et al. (2021) Using adopted individuals to partition maternal genetic effects into prenatal and postnatal effects on offspring phenotypes

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# Input data: variance-covariance matrices between offspring phenotype and their own and their relatives' genotypes (or polygenic risk scores) from 7 different family structures.

#Fictitious data used in this example!

# Required R package: "OpenMx"

# Clear global environmental variables

rm(list=ls())

# Load the R package "OpenMx"

library(OpenMx)

# Read in a 4x4 variance-covariance matrix for G1: Biological Parent-offspring trios

# The diagonal contains the variances offspring genotype (Zo), maternal genotype (Zm), paternal genotype (Zp), and offspring phenotype (Y), and the off-diagonal contains their covariances.

group\_1 <- matrix(c(1.00, 0.00, 0.50, 0.25, 0.00, 1.00, 0.50, 0.15, 0.50, 0.50, 1.00, 0.25, 0.25, 0.15, 0.25, 1.00), nrow=4, byrow=TRUE) # This is where to read in the variance-covariance matrix

rownames(group\_1)<- c("Zm", "Zp", "Zo", "Y")

colnames(group\_1)<- c("Zm", "Zp", "Zo", "Y")

N\_G1 <- 1000 # This is the number of biological parent-offspring trios used to derive the variance-covariance matrix

# Read in a 3x3 variance-covariance matrix for G2: Mother-offspring pairs

group\_2 <- matrix(c(1.00, 0.50, 0.25, 0.50, 1.00, 0.25, 0.25, 0.25, 1.00), nrow=3, byrow=TRUE) # This is where to read in the variance-covariance matrix

rownames(group\_2)<- c("Zm", "Zo", "Y")

colnames(group\_2)<- c("Zm", "Zo", "Y")

N\_G2 <- 4000 # This is the number of biological Mother-offspring pairs used to derive the variance-covariance matrix

# Read in a 3x3 variance-covariance matrix for G3: Father-offspring pairs

group\_3 <- matrix(c(1.00, 0.50, 0.15, 0.50, 1.00, 0.25, 0.15, 0.25, 1.00), nrow=3, byrow=TRUE) # This is where to read in the variance-covariance matrix

rownames(group\_3)<- c("Zp", "Zo", "Y")

colnames(group\_3)<- c("Zp", "Zo", "Y")

N\_G3 <- 1800 # This is the number of Father-offspring pairs used to derive the variance-covariance matrix

# Read in a 2x2 variance-covariance matrix for G4: Singletons with Biological Parents

group\_4 <- matrix(c(1.00, 0.25, 0.25, 1.00), nrow=2, byrow=TRUE) # This is where to read in the variance-covariance matrix

rownames(group\_4)<- c("Zo", "Y")

colnames(group\_4)<- c("Zo", "Y")

N\_G4 <- 300000 # This is the number of Singletons with Biological Parents used to derive the variance-covariance matrix

# Read in a 2x2 variance-covariance matrix for G5: Singletons with Adoptive Parents

# Zo is adopted individual's genotype and Y is their phenotype

group\_5 <- matrix(c(1.00, 0.15, 0.15, 0.96), nrow=2, byrow=TRUE) # This is where to read in the variance-covariance matrix

rownames(group\_5)<- c("Zo", "Y")

colnames(group\_5)<- c("Zo", "Y")

N\_G5 <- 6000 # This is the number of Singletons with Adoptive Parents used to derive the variance-covariance matrix

# Read in a 3x3 variance-covariance matrix for G6: Adoptive Mother - Adopted Child Pairs

# Zo is adopted child's genotype. Zmf is adoptive mother's genotype. Y is adopted child's phenotype.

group\_6 <- matrix(c(1.00, 0.0, 0.15, 0.00, 1.0, 0.10, 0.15, 0.1, 0.96), nrow=3, byrow=TRUE) # This is where to read in the variance-covariance matrix

rownames(group\_6)<- c("Zo", "Zmf", "Y")

colnames(group\_6)<- c("Zo", "Zmf", "Y")

N\_G6 <- 0 # This is the number of Adoptive Mother - Adopted Child Pairs used to derive the variance-covariance matrix

# Read in a 3x3 variance-covariance matrix for G7: Biological Mother - Adopted Child Pairs

# Zo is adopted child's genotype. Zmb is biological mother's genotype. Y is adopted child's phenotype.

group\_7 <- matrix(c(1.00, 0.50, 0.15, 0.50, 1.00, 0.15, 0.15, 0.15, 0.96), nrow=3, byrow=TRUE) # This is where to read in the variance-covariance matrix

rownames(group\_7)<- c("Zo", "Zmb", "Y")

colnames(group\_7)<- c("Zo", "Zmb", "Y")

N\_G7 <- 50 # This is the number of Biological Mother - Adopted Child Pairs used to derive the variance-covariance matrix

# Model parameters

V <- mxMatrix(type="Full", nrow=1, ncol=1, free=TRUE, values=1, label="v", name="V") #Variance of a SNP or a polygenic risk score

B\_OY <- mxMatrix(type="Full", nrow=1, ncol=1, free=TRUE, values=0, label="b\_oy", name="B\_OY") #Offspring genetic effect

B\_MY <- mxMatrix(type="Full", nrow=1, ncol=1, free=TRUE, values=0, label="b\_my", name="B\_MY") #Post-natal maternal genetic effect

B\_PY <- mxMatrix(type="Full", nrow=1, ncol=1, free=TRUE, values=0, label="b\_py", name="B\_PY") #Paternal genetic effect

G\_MY <- mxMatrix(type="Full", nrow=1, ncol=1, free=TRUE, values=0, label="g\_my", name="G\_MY") #Pre-natal maternal genetic effect

E1 <- mxMatrix(type="Full", nrow=1, ncol=1, free=TRUE, values=0.9, label="e1", name="E1") #Phenotypic error variance in biological families

E2 <- mxMatrix(type="Full", nrow=1, ncol=1, free=TRUE, values=0.9, label="e2", name="E2") #Phenotypic error variance in adopted families

R <- mxMatrix(type="Full", nrow=1, ncol=1, free=TRUE, values=0, label="rho", name="R") #Covariance between maternal and paternal genotypes

# Define elements of expected covariance matrix in terms of parameters

# G1 Parent offspring trios

c11\_G1 <- mxAlgebra(expression=V, name="C11\_G1")

c12\_G1 <- mxAlgebra(expression=R, name="C12\_G1")

c13\_G1 <- mxAlgebra(expression=0.5\*V+0.5\*R, name="C13\_G1")

c14\_G1 <- mxAlgebra(expression=(G\_MY + B\_MY)\*V + 0.5\*B\_OY\*V + B\_PY\*R + 0.5\*B\_OY\*R, name="C14\_G1")

c21\_G1 <- mxAlgebra(expression=R, name="C21\_G1")

c22\_G1 <- mxAlgebra(expression=V, name="C22\_G1")

c23\_G1 <- mxAlgebra(expression=0.5\*V+0.5\*R, name="C23\_G1")

c24\_G1 <- mxAlgebra(expression=B\_PY\*V + 0.5\*B\_OY\*V + (G\_MY+B\_MY)\*R + 0.5\*B\_OY\*R, name="C24\_G1")

c31\_G1 <- mxAlgebra(expression=0.5\*V+0.5\*R, name="C31\_G1")

c32\_G1 <- mxAlgebra(expression=0.5\*V+0.5\*R, name="C32\_G1")

c33\_G1 <- mxAlgebra(expression=V+0.5\*R, name="C33\_G1")

c34\_G1 <- mxAlgebra(expression=B\_OY\*(V+0.5\*R) + 0.5\*V\*(G\_MY + B\_MY) + 0.5\*V\*B\_PY + 0.5\*(G\_MY + B\_MY)\*R + 0.5\*B\_PY\*R, name="C34\_G1")

c41\_G1 <- mxAlgebra(expression=(G\_MY + B\_MY)\*V + 0.5\*B\_OY\*V + B\_PY\*R + 0.5\*B\_OY\*R, name="C41\_G1")

c42\_G1 <- mxAlgebra(expression=B\_PY\*V + 0.5\*B\_OY\*V + (G\_MY+B\_MY)\*R + 0.5\*B\_OY\*R, name="C42\_G1")

c43\_G1 <- mxAlgebra(expression=B\_OY\*(V+0.5\*R) + 0.5\*V\*(G\_MY + B\_MY) + 0.5\*V\*B\_PY + 0.5\*(G\_MY+B\_MY)\*R + 0.5\*B\_PY\*R, name="C43\_G1")

c44\_G1 <- mxAlgebra(expression=B\_PY^2\*V + B\_OY^2\*(V+0.5\*R) + (G\_MY + B\_MY)^2\*V + B\_OY\*V\*(G\_MY + B\_MY) + B\_OY\*V\*B\_PY + E1 + 2\*B\_PY\*R\*(G\_MY+B\_MY) + B\_PY\*B\_OY\*R + B\_OY\*(G\_MY+B\_MY)\*R, name="C44\_G1")

# G2 Mother offspring pairs

c11\_G2 <- mxAlgebra(expression=V, name="C11\_G2")

c12\_G2 <- mxAlgebra(expression=0.5\*V+0.5\*R, name="C12\_G2")

c13\_G2 <- mxAlgebra(expression=(G\_MY + B\_MY)\*V + 0.5\*B\_OY\*V + B\_PY\*R + 0.5\*B\_OY\*R, name="C13\_G2")

c21\_G2 <- mxAlgebra(expression=0.5\*V+0.5\*R, name="C21\_G2")

c22\_G2 <- mxAlgebra(expression=V+0.5\*R, name="C22\_G2")

c23\_G2 <- mxAlgebra(expression=B\_OY\*(V+0.5\*R) + 0.5\*V\*(G\_MY + B\_MY) + 0.5\*V\*B\_PY + 0.5\*(G\_MY + B\_MY)\*R + 0.5\*B\_PY\*R, name="C23\_G2")

c31\_G2 <- mxAlgebra(expression=(G\_MY + B\_MY)\*V + 0.5\*B\_OY\*V + B\_PY\*R + 0.5\*B\_OY\*R, name="C31\_G2")

c32\_G2 <- mxAlgebra(expression=B\_OY\*(V+0.5\*R) + 0.5\*V\*(G\_MY + B\_MY) + 0.5\*V\*B\_PY + 0.5\*(G\_MY+B\_MY)\*R + 0.5\*B\_PY\*R, name="C32\_G2")

c33\_G2 <- mxAlgebra(expression=B\_PY^2\*V + B\_OY^2\*(V+0.5\*R) + (G\_MY + B\_MY)^2\*V + B\_OY\*V\*(G\_MY + B\_MY) + B\_OY\*V\*B\_PY + E1 + 2\*B\_PY\*R\*(G\_MY+B\_MY) + B\_PY\*B\_OY\*R + B\_OY\*(G\_MY+B\_MY)\*R, name="C33\_G2")

# G3 Father offspring pairs

c11\_G3 <- mxAlgebra(expression=V, name="C11\_G3")

c12\_G3 <- mxAlgebra(expression=0.5\*V+0.5\*R, name="C12\_G3")

c13\_G3 <- mxAlgebra(expression=B\_PY\*V + 0.5\*B\_OY\*V + (G\_MY+B\_MY)\*R + 0.5\*B\_OY\*R, name="C13\_G3")

c21\_G3 <- mxAlgebra(expression=0.5\*V+0.5\*R, name="C21\_G3")

c22\_G3 <- mxAlgebra(expression=V+0.5\*R, name="C22\_G3")

c23\_G3 <- mxAlgebra(expression=B\_OY\*(V+0.5\*R) + 0.5\*V\*(G\_MY + B\_MY) + 0.5\*V\*B\_PY + 0.5\*(G\_MY + B\_MY)\*R + 0.5\*B\_PY\*R, name="C23\_G3")

c31\_G3 <- mxAlgebra(expression=B\_PY\*V + 0.5\*B\_OY\*V + (G\_MY+B\_MY)\*R + 0.5\*B\_OY\*R, name="C31\_G3")

c32\_G3 <- mxAlgebra(expression=B\_OY\*(V+0.5\*R) + 0.5\*V\*(G\_MY + B\_MY) + 0.5\*V\*B\_PY + 0.5\*(G\_MY+B\_MY)\*R + 0.5\*B\_PY\*R, name="C32\_G3")

c33\_G3 <- mxAlgebra(expression=B\_PY^2\*V + B\_OY^2\*(V+0.5\*R) + (G\_MY + B\_MY)^2\*V + B\_OY\*V\*(G\_MY + B\_MY) + B\_OY\*V\*B\_PY + E1 + 2\*B\_PY\*R\*(G\_MY+B\_MY) + B\_PY\*B\_OY\*R + B\_OY\*(G\_MY+B\_MY)\*R, name="C33\_G3")

# G4 Singletons (biological)

c11\_G4 <- mxAlgebra(expression=V+0.5\*R, name="C11\_G4")

c12\_G4 <- mxAlgebra(expression=B\_OY\*(V+0.5\*R) + 0.5\*V\*(G\_MY + B\_MY) + 0.5\*V\*B\_PY + 0.5\*(G\_MY + B\_MY)\*R + 0.5\*B\_PY\*R, name="C12\_G4")

c21\_G4 <- mxAlgebra(expression=B\_OY\*(V+0.5\*R) + 0.5\*V\*(G\_MY + B\_MY) + 0.5\*V\*B\_PY + 0.5\*(G\_MY+B\_MY)\*R + 0.5\*B\_PY\*R, name="C21\_G4")

c22\_G4 <- mxAlgebra(expression=B\_PY^2\*V + B\_OY^2\*(V+0.5\*R) + (G\_MY + B\_MY)^2\*V + B\_OY\*V\*(G\_MY + B\_MY) + B\_OY\*V\*B\_PY + E1 + 2\*B\_PY\*R\*(G\_MY+B\_MY) + B\_PY\*B\_OY\*R + B\_OY\*(G\_MY+B\_MY)\*R, name="C22\_G4")

# G5 Singletons (adopted)

c11\_G5 <- mxAlgebra(expression=V+0.5\*R, name="C11\_G5")

c12\_G5 <- mxAlgebra(expression=B\_OY\*(V+0.5\*R) + 0.5\*V\*G\_MY + 0.5\*G\_MY\*R, name="C12\_G5")

c21\_G5 <- mxAlgebra(expression=B\_OY\*(V+0.5\*R) + 0.5\*V\*G\_MY + 0.5\*G\_MY\*R, name="C21\_G5")

c22\_G5 <- mxAlgebra(expression=B\_OY^2\*(V+0.5\*R) + G\_MY^2\*V + B\_MY^2\*V + B\_PY^2\*V + B\_OY\*V\*G\_MY + B\_OY\*G\_MY\*R + E2 + 2\*B\_MY\*B\_PY\*R, name="C22\_G5")

# G6 Foster Mother - Adopted Child Pairs

c11\_G6 <- mxAlgebra(expression=V+0.5\*R, name="C11\_G6")

c12\_G6 <- mxAlgebra(expression=0, name="C12\_G6")

c13\_G6 <- mxAlgebra(expression=B\_OY\*(V+0.5\*R) + 0.5\*V\*G\_MY + 0.5\*G\_MY\*R, name="C13\_G6")

c21\_G6 <- mxAlgebra(expression=0, name="C21\_G6")

c22\_G6 <- mxAlgebra(expression=V, name="C22\_G6")

c23\_G6 <- mxAlgebra(expression=B\_MY\*V, name="C23\_G6")

c31\_G6 <- mxAlgebra(expression=B\_OY\*(V+0.5\*R) + 0.5\*V\*G\_MY + 0.5\*G\_MY\*R, name="C31\_G6")

c32\_G6 <- mxAlgebra(expression=B\_MY\*V, name="C32\_G6")

c33\_G6 <- mxAlgebra(expression=B\_OY^2\*(V+0.5\*R) + G\_MY^2\*V + B\_MY^2\*V + B\_PY^2\*V + B\_OY\*V\*G\_MY + B\_OY\*G\_MY\*R + E2 + 2\*B\_MY\*B\_PY\*R, name="C33\_G6")

# G7 Biological Mother - Adopted Child Pairs

c11\_G7 <- mxAlgebra(expression=V+0.5\*R, name="C11\_G7")

c12\_G7 <- mxAlgebra(expression=0.5\*V+0.5\*R, name="C12\_G7")

c13\_G7 <- mxAlgebra(expression=B\_OY\*(V+0.5\*R) + 0.5\*V\*G\_MY + 0.5\*G\_MY\*R, name="C13\_G7")

c21\_G7 <- mxAlgebra(expression=0.5\*V+0.5\*R, name="C21\_G7")

c22\_G7 <- mxAlgebra(expression=V, name="C22\_G7")

c23\_G7 <- mxAlgebra(expression=G\_MY\*V + 0.5\*B\_OY\*V + 0.5\*B\_OY\*R, name="C23\_G7")

c31\_G7 <- mxAlgebra(expression=B\_OY\*(V+0.5\*R) + 0.5\*V\*G\_MY + 0.5\*G\_MY\*R, name="C31\_G7")

c32\_G7 <- mxAlgebra(expression=G\_MY\*V + 0.5\*B\_OY\*V + 0.5\*B\_OY\*R, name="C32\_G7")

c33\_G7 <- mxAlgebra(expression=B\_OY^2\*(V+0.5\*R) + G\_MY^2\*V + B\_MY^2\*V + B\_PY^2\*V + B\_OY\*V\*G\_MY + B\_OY\*G\_MY\*R + E2 + 2\*B\_MY\*B\_PY\*R, name="C33\_G7")

# Expected covariance matrices

expCov\_G1 <- mxAlgebra( expression= rbind( cbind(C11\_G1, C12\_G1, C13\_G1, C14\_G1), cbind(C21\_G1, C22\_G1, C23\_G1, C24\_G1), cbind(C31\_G1, C32\_G1, C33\_G1, C34\_G1), cbind(C41\_G1, C42\_G1, C43\_G1, C44\_G1)), name="expCov\_G1")

expCov\_G2 <- mxAlgebra( expression= rbind( cbind(C11\_G2, C12\_G2, C13\_G2), cbind(C21\_G2, C22\_G2, C23\_G2), cbind(C31\_G2, C32\_G2, C33\_G2)), name="expCov\_G2")

expCov\_G3 <- mxAlgebra( expression= rbind( cbind(C11\_G3, C12\_G3, C13\_G3), cbind(C21\_G3, C22\_G3, C23\_G3), cbind(C31\_G3, C32\_G3, C33\_G3)), name="expCov\_G3")

expCov\_G4 <- mxAlgebra( expression= rbind( cbind(C11\_G4, C12\_G4), cbind(C21\_G4, C22\_G4)), name="expCov\_G4")

expCov\_G5 <- mxAlgebra( expression= rbind( cbind(C11\_G5, C12\_G5), cbind(C21\_G5, C22\_G5)), name="expCov\_G5")

expCov\_G6 <- mxAlgebra( expression= rbind( cbind(C11\_G6, C12\_G6, C13\_G6), cbind(C21\_G6, C22\_G6, C23\_G6), cbind(C31\_G6, C32\_G6, C33\_G6)), name="expCov\_G6")

expCov\_G7 <- mxAlgebra( expression= rbind( cbind(C11\_G7, C12\_G7, C13\_G7), cbind(C21\_G7, C22\_G7, C23\_G7), cbind(C31\_G7, C32\_G7, C33\_G7)), name="expCov\_G7")

# Create Data Objects for Multiple Groups

dataG1 <- mxData(observed=(group\_1), type="cov", numObs=N\_G1)

dataG2 <- mxData(observed=(group\_2), type="cov", numObs=N\_G2)

dataG3 <- mxData(observed=(group\_3), type="cov", numObs=N\_G3)

dataG4 <- mxData(observed=(group\_4), type="cov", numObs=N\_G4)

dataG5 <- mxData(observed=(group\_5), type="cov", numObs=N\_G5)

dataG6 <- mxData(observed=(group\_6), type="cov", numObs=N\_G6)

dataG7 <- mxData(observed=(group\_7), type="cov", numObs=N\_G7)

# Create Expectation Objects for Multiple Groups

expG1 <- mxExpectationNormal( covariance="expCov\_G1", dimnames=c("Zm","Zp","Zo","Y") )

expG2 <- mxExpectationNormal( covariance="expCov\_G2", dimnames=c("Zm","Zo", "Y") )

expG3 <- mxExpectationNormal( covariance="expCov\_G3", dimnames=c("Zp","Zo","Y") )

expG4 <- mxExpectationNormal( covariance="expCov\_G4", dimnames=c("Zo","Y") )

expG5 <- mxExpectationNormal( covariance="expCov\_G5", dimnames=c("Zo","Y") )

expG6 <- mxExpectationNormal( covariance="expCov\_G6", dimnames=c("Zo","Zmf","Y") )

expG7 <- mxExpectationNormal( covariance="expCov\_G7", dimnames=c("Zo","Zmb","Y") )

funML <- mxFitFunctionML()

# Create Model Objects for Multiple Groups

pars <- list( V, B\_OY, B\_MY, B\_PY, G\_MY, E1, E2, R)

modelG1 <- mxModel( V, B\_OY, B\_MY, B\_PY, G\_MY, E1, R, c11\_G1, c12\_G1, c13\_G1, c14\_G1, c21\_G1, c22\_G1, c23\_G1, c24\_G1, c31\_G1, c32\_G1, c33\_G1, c34\_G1, c41\_G1, c42\_G1, c43\_G1, c44\_G1, expG1, expCov\_G1, dataG1, funML, name="G1" )

modelG2 <- mxModel( V, B\_OY, B\_MY, B\_PY, G\_MY, E1, R, c11\_G2, c12\_G2, c13\_G2, c21\_G2, c22\_G2, c23\_G2, c31\_G2, c32\_G2, c33\_G2, expG2, expCov\_G2, dataG2, funML, name="G2" )

modelG3 <- mxModel( V, B\_OY, B\_MY, B\_PY, G\_MY, E1, R, c11\_G3, c12\_G3, c13\_G3, c21\_G3, c22\_G3, c23\_G3, c31\_G3, c32\_G3, c33\_G3, expG3, expCov\_G3, dataG3, funML, name="G3" )

modelG4 <- mxModel( V, B\_OY, B\_MY, B\_PY, G\_MY, E1, R, c11\_G4, c12\_G4, c21\_G4, c22\_G4, expG4, expCov\_G4, dataG4, funML, name="G4" )

modelG5 <- mxModel( V, B\_OY, B\_MY, B\_PY, G\_MY, E2, R, c11\_G5, c12\_G5, c21\_G5, c22\_G5, expG5, expCov\_G5, dataG5, funML, name="G5" )

modelG6 <- mxModel( V, B\_OY, B\_MY, B\_PY, G\_MY, E2, R, c11\_G6, c12\_G6, c13\_G6, c21\_G6, c22\_G6, c23\_G6, c31\_G6, c32\_G6, c33\_G6, expG6, expCov\_G6, dataG6, funML, name="G6" )

modelG7 <- mxModel( V, B\_OY, B\_MY, B\_PY, G\_MY, E2, R, c11\_G7, c12\_G7, c13\_G7, c21\_G7, c22\_G7, c23\_G7, c31\_G7, c32\_G7, c33\_G7, expG7, expCov\_G7, dataG7, funML, name="G7" )

multi <- mxFitFunctionMultigroup( c("G1","G2","G3","G4","G5","G6","G7") )

modelFull <- mxModel( "Full\_Model", pars, modelG1, modelG2, modelG3, modelG4, modelG5, modelG6, modelG7, multi)

# RUN MODEL

fitFull <- mxRun( modelFull, intervals=F )

sumFull <- summary( fitFull )

sumFull

# v, variance of the SNP (polygenic risk score)

# B\_OY, offspring genetic effect

# b\_my, postnatal maternal genetic effect

# b\_py, paternal genetic effect

# g\_my, prenatal maternal genetic effect

# e1, error variance of biological children's phenotype

# e2, error variance of adopted children's phenotype

# rho, covariance between maternal and paternal genotypes