Independent Pathway Model: Genetic Correlation and Multivariate Models 3

Michael D. Hunter

School of Psychology
Georgia Institute of Technology

June 2, 2021

A Distinction

- Earlier: Not so theoretical models
  - Saturated Model
  - Fully Correlated Genetic Factors (Cholesky) Model
- Now: Theoretical models
  - Common Pathway Model
  - Independent Pathway Model

Scientific questions you can ask

- In *univariate* analyses: what are the contributions of additive genetic, dominance genetic, shared environmental, and unique environmental factors to the variance?
- In *multivariate* analyses: what are these contributions to the **covariance** between two or more traits?

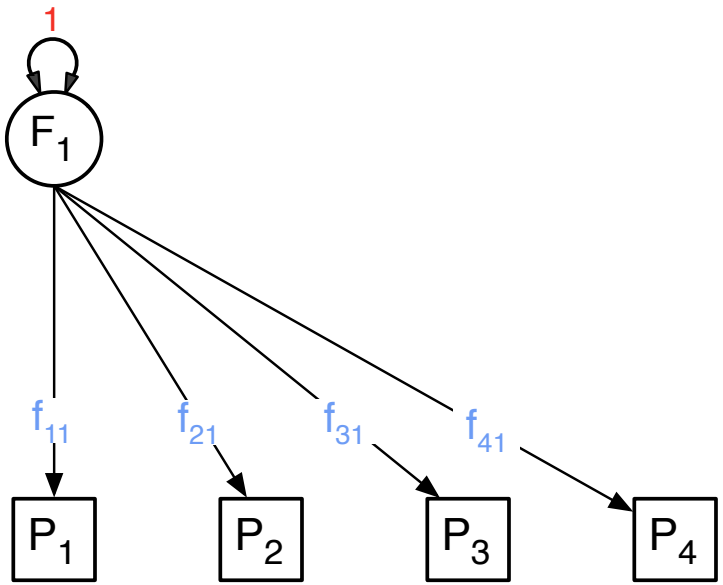
Georgia Tech

Genetic Factor Model

(Martin & Eaves, 1977)

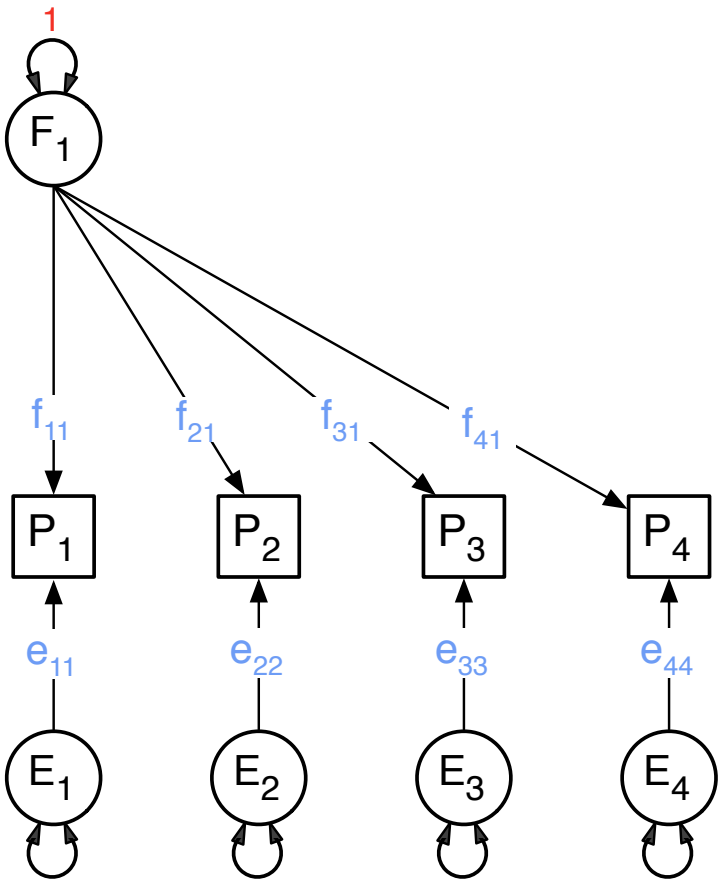
- Theoretical model
- Start with a biometric factor model
- Origin is more biometric than psychometric
- Allows different covariance structure across A, C, and E
- Create latent factors for A, C, E

Common Factor



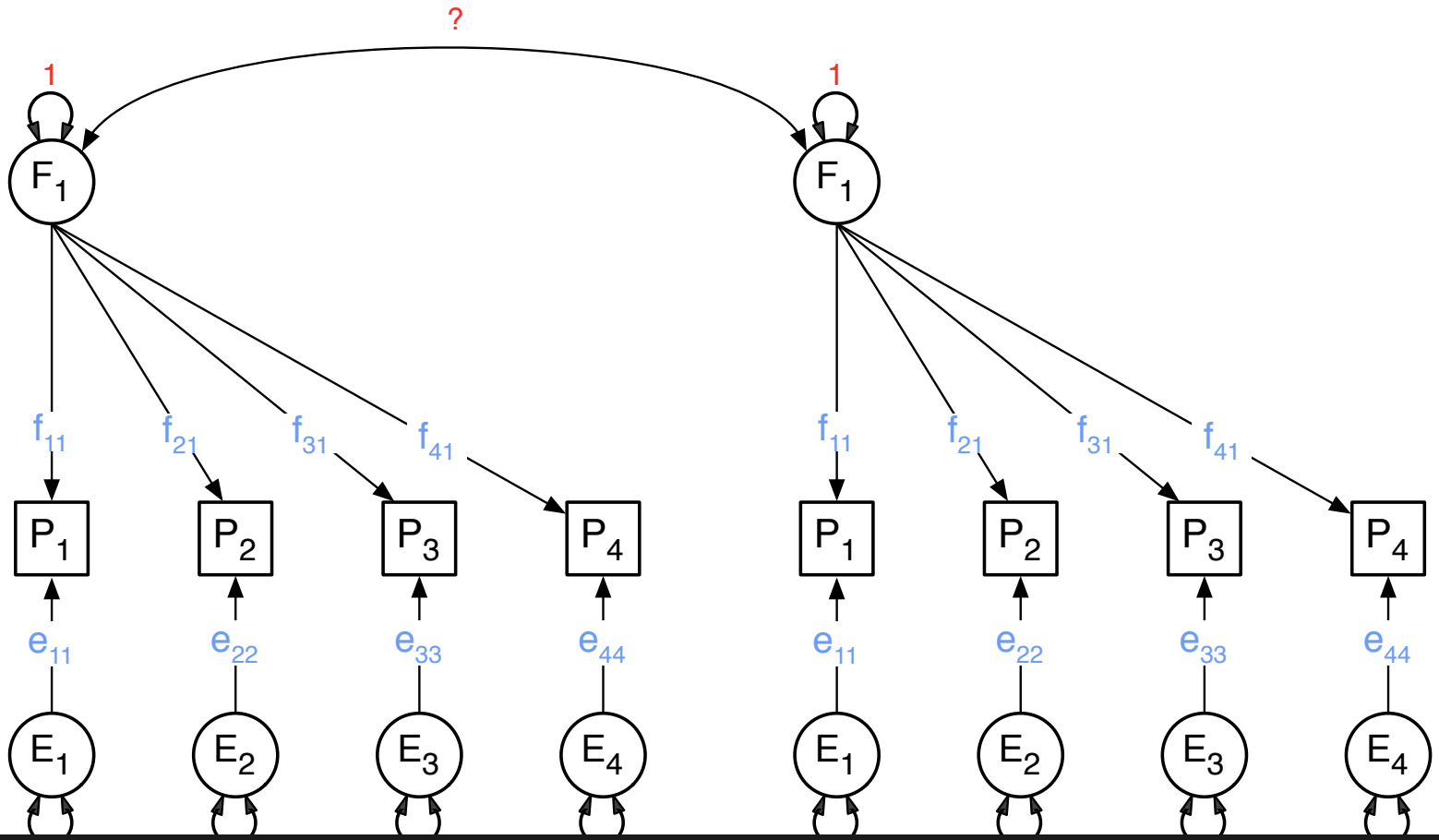
$$\begin{array}{c} \\ P_1 \\ P_2 \\ P_3 \\ P_4 \end{array} \begin{array}{c} F_1 \\ \left[\begin{array}{c} f_{11} \\ f_{21} \\ f_{31} \\ f_{41} \end{array}\right] \end{array}$$

Residuals

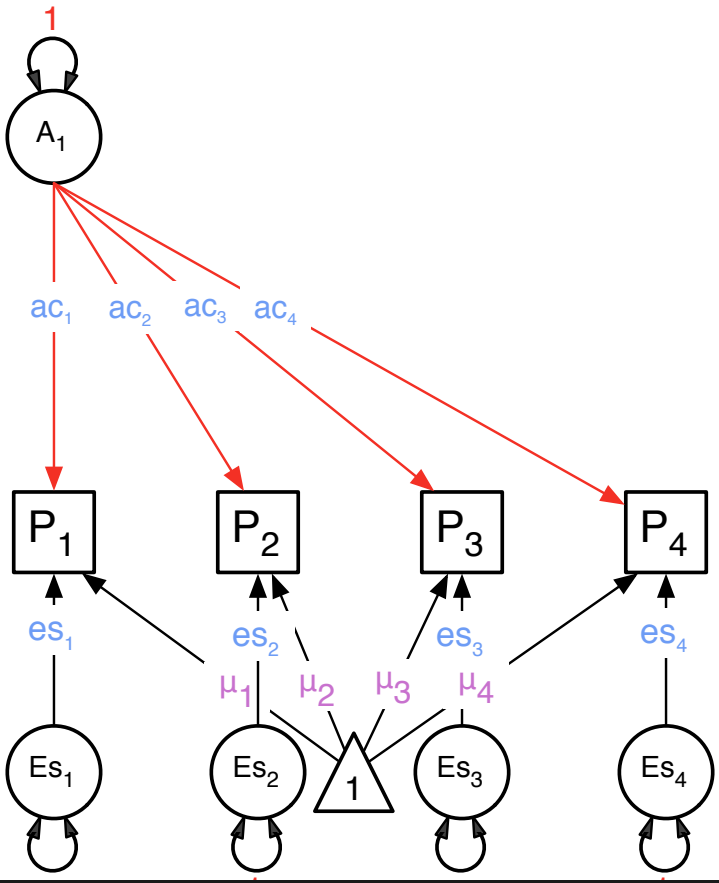


$$\begin{array}{c} P_1 \\ P_2 \\ P_3 \\ P_4 \end{array} \begin{bmatrix} e_{11} & 0 & 0 & 0 \\ 0 & e_{22} & 0 & 0 \\ 0 & 0 & e_{33} & 0 \\ 0 & 0 & 0 & e_{44} \end{bmatrix}$$

What about Twins

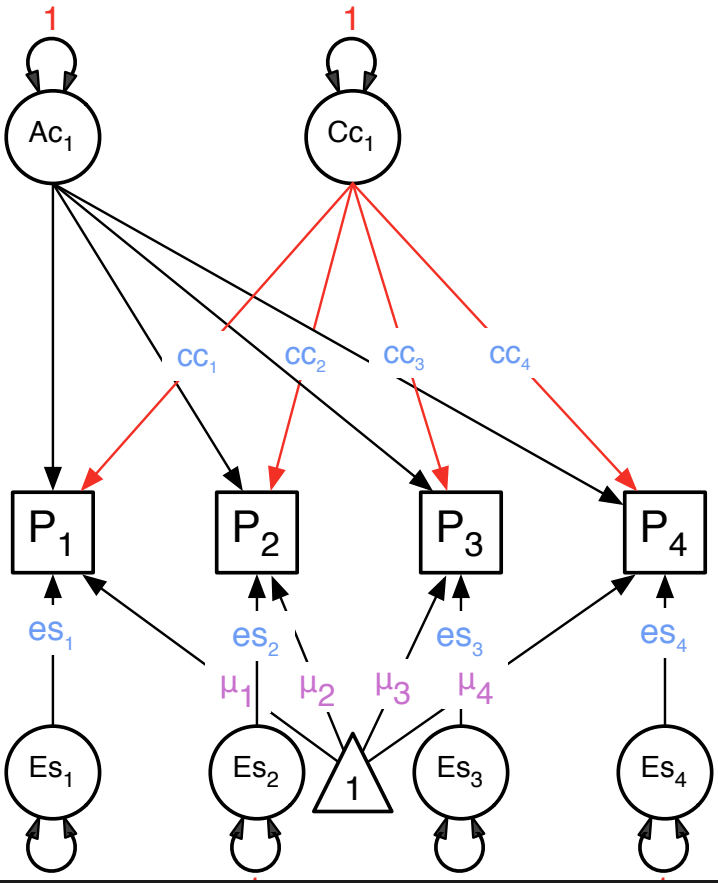


Common A Factor



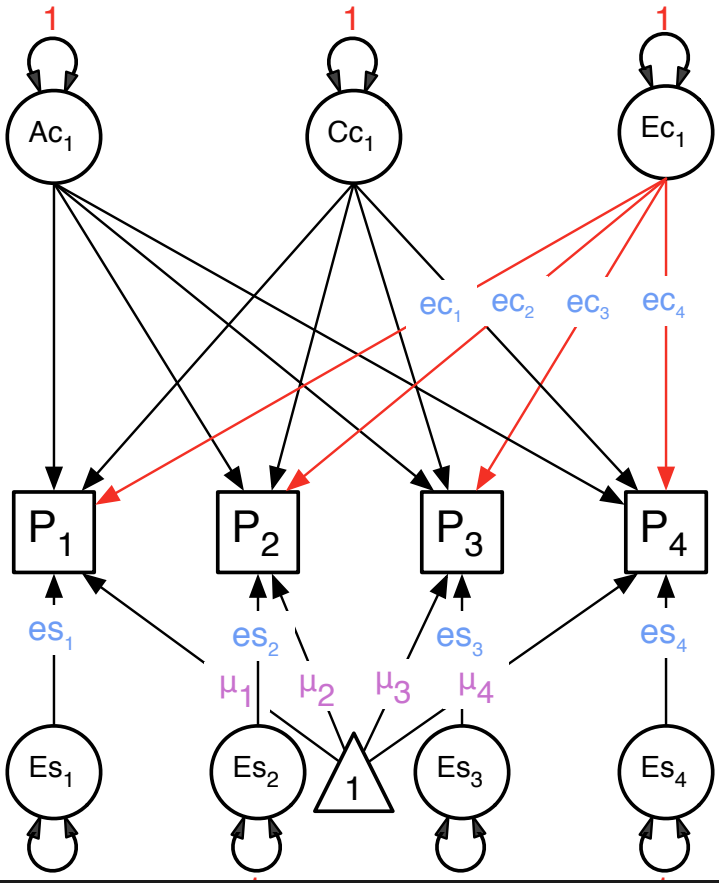
$$\begin{array}{c} \\ P_1 \\ P_2 \\ P_3 \\ P_4 \end{array} \begin{array}{c} A_1 \\ \begin{bmatrix} ac_{11} \\ ac_{21} \\ ac_{31} \\ ac_{41} \end{bmatrix} \end{array}$$

Common C Factor



$$
\begin{array}{c} \\ P_1 \\ P_2 \\ P_3 \\ P_4 \end{array}
\begin{array}{c} C_1 \\ \begin{bmatrix} cc_{11} \\ cc_{21} \\ cc_{31} \\ cc_{41} \end{bmatrix} \end{array}
$$

Common E Factor

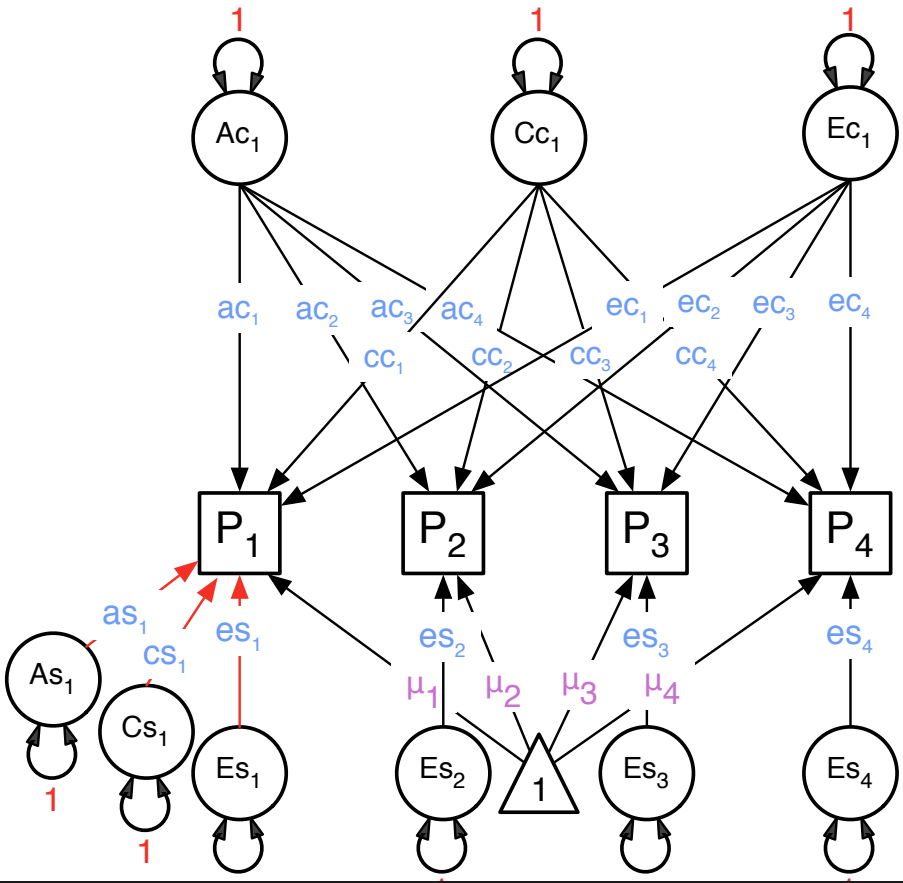


$$
\begin{array}{c} \\ P_1 \\ P_2 \\ P_3 \\ P_4 \end{array}
\begin{array}{c} E_1 \\ \left[\begin{array}{c} ec_{11} \\ ec_{21} \\ ec_{31} \\ ec_{41} \end{array}\right] \end{array}
$$

Independent Pathway Model

- Theoretical model
- Start with a biometric factor model
- Origin is more biometric than psychometric
- Allows different covariance structure across A, C, and E
- Create latent factors for *common* A, C, E components
- Decompose the residual variances into *specific* A, C, E components

ACE Specifics



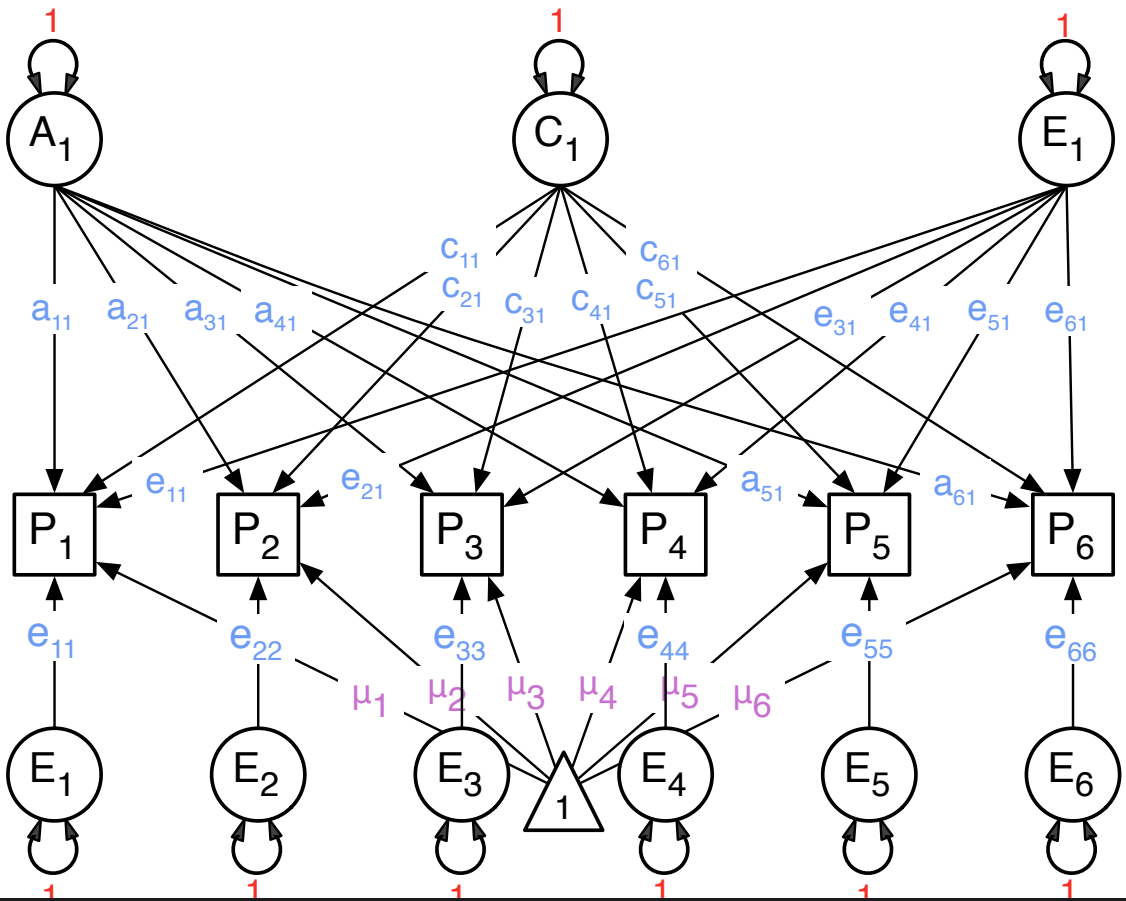
$$P \begin{bmatrix} P_1 \\ P_2 \\ P_3 \\ P_4 \end{bmatrix} \begin{bmatrix} es_{11} & 0 & 0 & 0 \\ 0 & es_{22} & 0 & 0 \\ 0 & 0 & es_{33} & 0 \\ 0 & 0 & 0 & es_{44} \end{bmatrix}$$

$$\begin{bmatrix} as_{11} & 0 & 0 & 0 \\ 0 & as_{22} & 0 & 0 \\ 0 & 0 & as_{33} & 0 \\ 0 & 0 & 0 & as_{44} \end{bmatrix}$$

$$\begin{bmatrix} cs_{11} & 0 & 0 & 0 \\ 0 & cs_{22} & 0 & 0 \\ 0 & 0 & cs_{33} & 0 \\ 0 & 0 & 0 & cs \end{bmatrix}$$

Note! For readabilty of the diagrams, we sometimes omit the residual variance decomposition.

IP Model


1
1
1
A1
C1
E1
c11
c21
c31
c41
c51
c61
a11
a21
a31
a41
e31
e41
e51
e61
e11
e21
a51
a61
P1
P2
P3
P4
P5
P6
e11
e22
e33
e44
e55
e66
μ1
μ2
μ3
μ4
μ5
μ6
E1
E2
E3
1
E4
E5
E6

Independent Pathway

Variance Component	a2	c2	e2
Common Factors	ac nv x 1	cc nv x 1	ec nv x 1
Residual Factors	as nv x nv	cs nv x nv	es nv x nv

Independent Pathway Model

Identification

- Be careful when adding common factors
- Total parameters per source of variance must be less than $nv * (nv + 1)/2$ for the number of phenotypes, nv
- For a single common factor with only 2 indicators, equate the 2 factor loadings
- Alternatively, remove the common factor and add a correlated residual
- If in doubt, try `mxCheckIdentification`
- When not identified, gives offending parameters

Georgia Tech

Independent Pathways

```
# Fit Independent Pathway ACE Model
# ------------------------------------------------------------------------------
nf         <- 1        # number of factors

# Matrices ac, cc, and ec to store a, c, and e path coefficients for common factors
pathAc     <- mxMatrix( type="Full", nrow=nv, ncol=nf, free=TRUE, values=.6, labels=labFull("ac",nv,nf), name="ac" )
pathCc     <- mxMatrix( type="Full", nrow=nv, ncol=nf, free=TRUE, values=.6, labels=labFull("cc",nv,nf), name="cc" )
pathEc     <- mxMatrix( type="Full", nrow=nv, ncol=nf, free=TRUE, values=.6, labels=labFull("ec",nv,nf), name="ec" )

# Matrices as, cs, and es to store a, c, and e path coefficients for specific factors
pathAs     <- mxMatrix( type="Diag", nrow=nv, ncol=nv, free=TRUE, values=4, labels=labDiag("as",nv), lbound=.00001, name="as" )
pathCs     <- mxMatrix( type="Diag", nrow=nv, ncol=nv, free=TRUE, values=4, labels=labDiag("cs",nv), lbound=.00001, name="cs" )
pathEs     <- mxMatrix( type="Diag", nrow=nv, ncol=nv, free=TRUE, values=5, labels=labDiag("es",nv), lbound=.00001, name="es" )

# Matrices A, C, and E compute variance components
covA       <- mxAlgebra( expression=ac %*% t(ac) + as %*% t(as), name="A" )
covC       <- mxAlgebra( expression=cc %*% t(cc) + cs %*% t(cs), name="C" )
covE       <- mxAlgebra( expression=ec %*% t(ec) + es %*% t(es), name="E" )
```

specific number of independent pathways by source of variance

common factors of size nv x nf

specific factors of size nv x nv (diagonal only

common factors + specifics

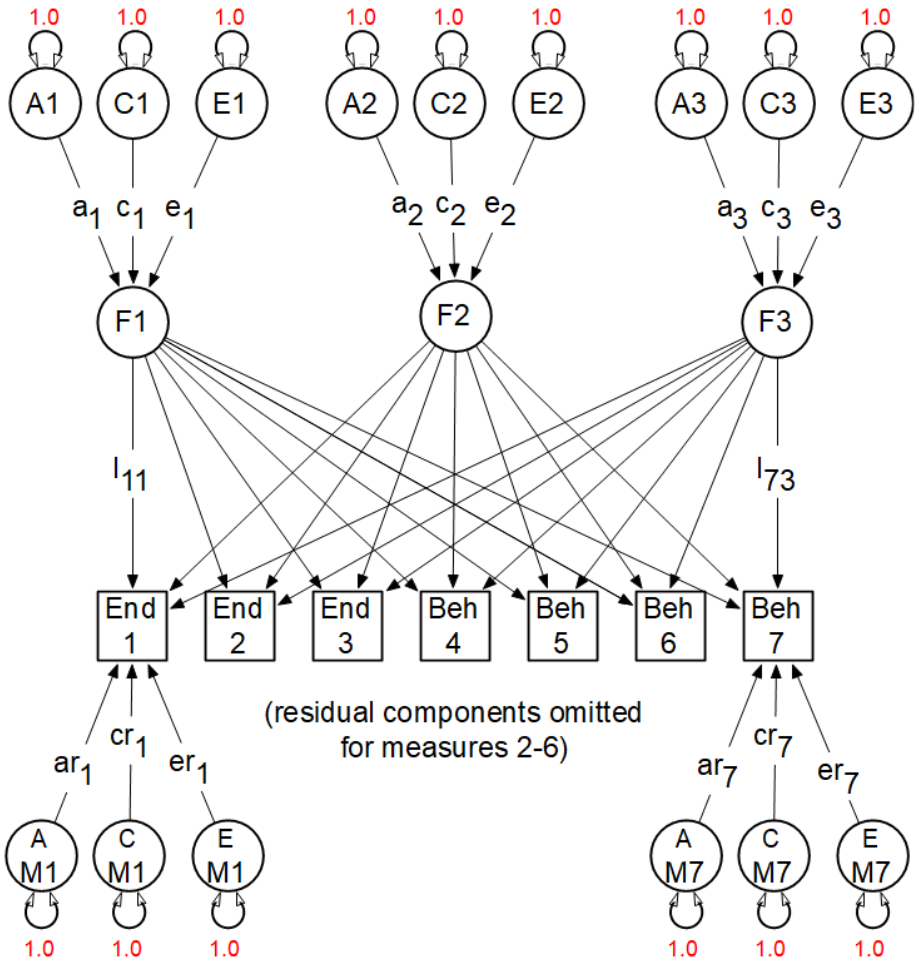
Fitting IP Model

```
# Create Model Objects for Multiple Groups
pars      <- list(meanG, matI, invSD,
                  pathAc, pathCc, pathEc, pathAs, pathCs, pathEs, covA, covC, covE, covP, corA, corC, corE)
modelMZ   <- mxModel( name="MZ", pars, covMZ, expCovMZ, dataMZ, expMZ, funML )
modelDZ   <- mxModel( name="DZ", pars, covDZ, expCovDZ, dataDZ, expDZ, funML )
multi     <- mxFitFunctionMultigroup( c("MZ","DZ") )

# Build & Run Model
modelIP   <- mxModel( "mulIPc", pars, modelMZ, modelDZ, multi )
fitIP     <- mxRun( modelIP, intervals=F )
sumIP     <- summary( fitIP )
mxCompare( fitACE, fitIP )
fitGofs(fitIP)

# Generate List
matIPpaths <- c("iSD %*% ac","iSD %*% cc","iSD %*% ec","iSD %*% as","iSD %*% cs","iSD %*% es")
labIPpaths <- c("stPathAc","stPathCc","stPathEc","stPathAs","stPathCs","stPathEs")
formatOutputMatrices(fitIP, matIPpaths, labIPpaths, vars, 4)
```

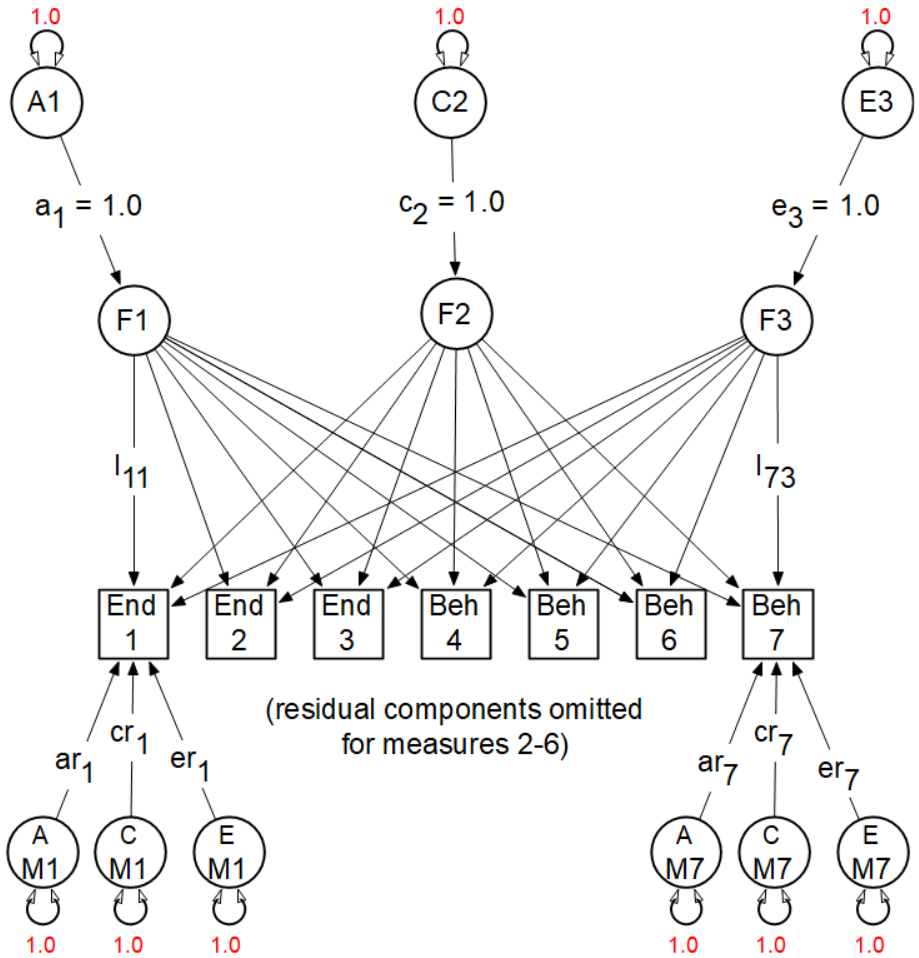
include all relevant matrices

fitted model, list of matrices (in quotes), list of labels (also in quotes), list of variable names, rounding value

Common Pathway



Independent Pathway



The independent pathway model is nested within the three factor common pathway model.

Scientific questions you can ask

- In *univariate* analyses: what are the contributions of additive genetic, dominance genetic, shared environmental, and unique environmental factors to the variance?
- In *multivariate* analyses: what are these contributions to the **covariance** between two or more traits?

Georgia Tech

Questions?

- Common Pathway
  - Can you test for a 1 factor vs a 2 factor vs a 3 factor CP?
  - Can you test for every common factor being A and C?
  - Can you test for every specific factor being only E?
  - Can you fit an ADE model?
- Independent Pathway
  - Can you test for a 1 factor vs a 2 factor vs a 3 factor IP?
  - Can you test for every A factor having the same loadings? What does that imply?
  - Can you test for every specific factor being only E?
  - Can you fit an ADE model?

Thank You

mhunter43@gatech.edu

Martin, N. G., & Eaves, L. J. (1977, Feb). The genetical analysis of covariance structure. *Heredity*, *38*(1), 79-95. doi: 10.1038/hdy.1977.9