

Common Pathway Model: Genetic Correlation and Multivariate Models 2

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June 1, 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

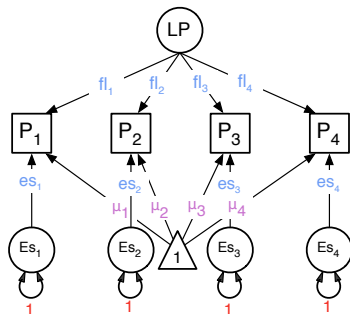
Scientific questions you can ask

- ▶ 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?

Common Pathway Model

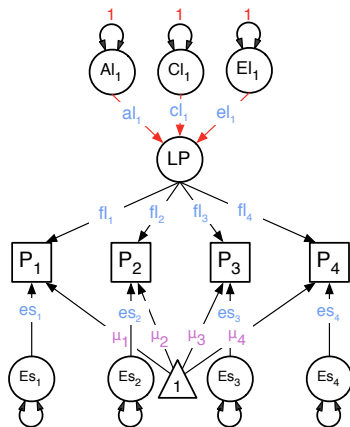
- ▶ Theoretical model
- ▶ Start with a phenotypic factor model
- ▶ Origin is more psychometric than biometric
- ▶ Fixes same covariance structure across A, C, and E
- ▶ Decompose the factor variance into A, C, E
- ▶ Decompose the residual variances into A, C, E

Factor Loadings



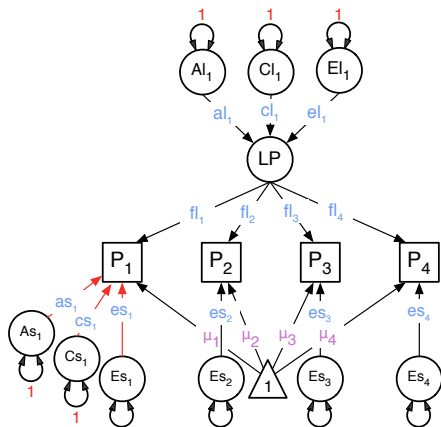
$$\begin{matrix} P_1 \\ P_2 \\ P_3 \\ P_4 \end{matrix} \begin{bmatrix} fl_{11} \\ fl_{21} \\ fl_{31} \\ fl_{41} \end{bmatrix}$$

Latent Phenotype ACE


 $[al_{11}]$
 $[cl_{11}]$
 $[el_{11}]$

$$\begin{matrix} P_1 \\ P_2 \\ P_3 \\ P_4 \end{matrix} \begin{bmatrix} fl_{11} \\ fl_{21} \\ fl_{31} \\ fl_{41} \end{bmatrix}$$

ACE Specifics



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

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

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

Common A Factors

Specific A Factors

$$\begin{array}{l}
 \text{object: pathFl} \\
 \text{matrix name: fl} \\
 \begin{bmatrix} fl_{11} \\ fl_{21} \\ fl_{31} \\ fl_{41} \end{bmatrix}
 \end{array}
 \times
 \begin{array}{l}
 \text{object: pathAl} \\
 \text{matrix name: al} \\
 [al_{11}]
 \end{array}
 \times
 \begin{array}{l}
 [al_{11}]
 \end{array}
 \times
 \begin{array}{l}
 [fl_{11} \quad fl_{21} \quad fl_{31} \quad fl_{41}]
 \end{array}
 =
 \begin{bmatrix}
 fl_{11}^2 al_{11}^2 & fl_{11} fl_{21} al_{11}^2 & fl_{11} fl_{31} al_{11}^2 & fl_{11} fl_{41} al_{11}^2 \\
 fl_{21} fl_{11} al_{11}^2 & fl_{21}^2 al_{11}^2 & fl_{21} fl_{31} al_{11}^2 & fl_{21} fl_{41} al_{11}^2 \\
 fl_{31} fl_{11} al_{11}^2 & fl_{31} fl_{21} al_{11}^2 & fl_{31}^2 al_{11}^2 & fl_{31} fl_{41} al_{11}^2 \\
 fl_{41} fl_{11} al_{11}^2 & fl_{41} fl_{21} al_{11}^2 & fl_{41} fl_{31} al_{11}^2 & fl_{41}^2 al_{11}^2
 \end{bmatrix}$$

$$\begin{array}{l}
 \begin{bmatrix} as_{11} & 0 & 0 & 0 \\ 0 & as_{22} & 0 & 0 \\ 0 & 0 & as_{33} & 0 \\ 0 & 0 & 0 & as_{44} \end{bmatrix}
 \end{array}
 \times
 \begin{array}{l}
 \begin{bmatrix} as_{11} & 0 & 0 & 0 \\ 0 & as_{22} & 0 & 0 \\ 0 & 0 & as_{33} & 0 \\ 0 & 0 & 0 & as_{44} \end{bmatrix}
 \end{array}
 =
 \begin{array}{l}
 \begin{bmatrix} as_{11}^2 & 0 & 0 & 0 \\ 0 & as_{22}^2 & 0 & 0 \\ 0 & 0 & as_{33}^2 & 0 \\ 0 & 0 & 0 & as_{44}^2 \end{bmatrix}
 \end{array}$$

$$\begin{array}{l}
 \text{object: pathAs} \\
 \text{matrix name: as}
 \end{array}$$

```

pathFl <- mxMatrix( type="Full", nrow=nv, ncol=nl, free=TRUE, values=.2,
  labels=labFull("fl",nv,nl), name="fl" )
pathAl <- mxMatrix( type="Lower", nrow=nl, ncol=nl, free=TRUE, values=.6,
  labels=labLower("al",nl), lbound=.00001, name="al" )
pathAs <- mxMatrix( type="Diag", nrow=nv, ncol=nv, free=TRUE, values=.5,
  labels=labDiag("as",nv), lbound=.00001, name="as" )
  
```


Total A Covariance

```
fl %%% (al %%% t(al))
```

$$\begin{bmatrix} fl_{11}^2 al_{11}^2 & fl_{11} fl_{21} al_{11}^2 & fl_{11} fl_{31} al_{11}^2 & fl_{11} fl_{41} al_{11}^2 \\ fl_{21} fl_{11} al_{11}^2 & fl_{21}^2 al_{11}^2 & fl_{21} fl_{31} al_{11}^2 & fl_{21} fl_{41} al_{11}^2 \\ fl_{31} fl_{11} al_{11}^2 & fl_{31} fl_{21} al_{11}^2 & fl_{31}^2 al_{11}^2 & fl_{31} fl_{41} al_{11}^2 \\ fl_{41} fl_{11} al_{11}^2 & fl_{41} fl_{21} al_{11}^2 & fl_{41} fl_{31} al_{11}^2 & fl_{41}^2 al_{11}^2 \end{bmatrix}$$

+

$$\begin{bmatrix} as_{11}^2 & 0 & 0 & 0 \\ 0 & as_{22}^2 & 0 & 0 \\ 0 & 0 & as_{33}^2 & 0 \\ 0 & 0 & 0 & as_{44}^2 \end{bmatrix}$$

```
as %%% t(as)
```

=

$$\begin{bmatrix} fl_{11}^2 al_{11}^2 + as_{11}^2 & fl_{11} fl_{21} al_{11}^2 & fl_{11} fl_{31} al_{11}^2 & fl_{11} fl_{41} al_{11}^2 \\ fl_{21} fl_{11} al_{11}^2 & fl_{21}^2 al_{11}^2 + as_{22}^2 & fl_{21} fl_{31} al_{11}^2 & fl_{21} fl_{41} al_{11}^2 \\ fl_{31} fl_{11} al_{11}^2 & fl_{31} fl_{21} al_{11}^2 & fl_{31}^2 al_{11}^2 + as_{33}^2 & fl_{31} fl_{41} al_{11}^2 \\ fl_{41} fl_{11} al_{11}^2 & fl_{41} fl_{21} al_{11}^2 & fl_{41} fl_{31} al_{11}^2 & fl_{41}^2 al_{11}^2 + as_{44}^2 \end{bmatrix}$$

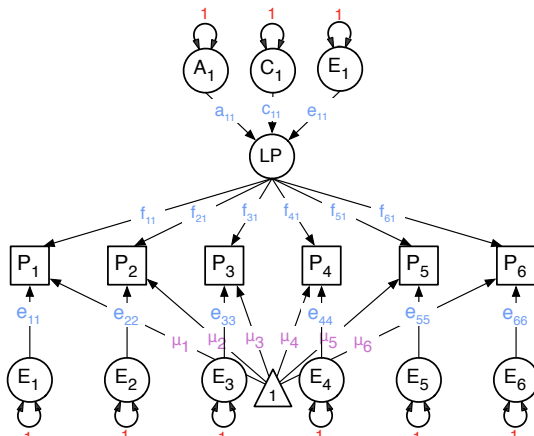
```
object: CovA  
matrix name:A
```

```
covA <- mxAlgebra( expression=fl %%% (al %%% t(al)) + as %%% t(as), name="A" )
```

Common Pathway Model

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- ▶ Decompose the residual variances into A, C, E

CP Model



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

Common Pathway

Variance Component	a ²	c ²	e ²	
Common Factors	a ₁ 1 x 1	c ₁ 1 x 1	e ₁ 1 x 1	f ₁ nv x 1
Residual Factors	a _s nv x nv	c _s nv x nv	e _s nv x nv	



Constraint on Variance of Latent Phenotype

```

# Fit Common Pathway ACE Model
# -----
nl      <- 1

# Matrices ac, cc, and ec to store a, c, and e path coefficients for latent phenotype(s)
pathA1  <- mxMatrix( type="Lower", nrow=nl, ncol=nl, free=TRUE, values=.6, labels=labLower("a1",nl), lbound=.00001, name="a1" )
pathC1  <- mxMatrix( type="Lower", nrow=nl, ncol=nl, free=TRUE, values=.6, labels=labLower("c1",nl), lbound=.00001, name="c1" )
pathE1  <- mxMatrix( type="Lower", nrow=nl, ncol=nl, free=TRUE, values=.6, labels=labLower("e1",nl), lbound=.00001, name="e1" )

# Matrix and Algebra for constraint on variance of latent phenotype
covarLP <- mxAlgebra( expression=al %% t(al) + cl %% t(cl) + el %% t(el), name="CovarLP" )
varLP   <- mxAlgebra( expression=diag2vec(CovarLP), name="VarLP" )
unit    <- mxMatrix( type="Unit", nrow=nl, ncol=1, name="Unit" )
varLP1  <- mxConstraint( expression=VarLP == Unit, name="varLP1" )

# Matrix f for factor loadings on latent phenotype
pathF1  <- mxMatrix( type="Full", nrow=nv, ncol=nl, free=TRUE, values=.2, labels=labFull("f1",nv,nl), name="f1" )

# Matrices A, C, and E compute variance components
covA    <- mxAlgebra( expression=f1 %% (al %% t(al)) + as %% t(as), name="A" )
covC    <- mxAlgebra( expression=f1 %% (cl %% t(cl)) + cs %% t(cs), name="C" )
covE    <- mxAlgebra( expression=f1 %% (el %% t(el)) + es %% t(es), name="E" )

```

latent phenotype $n_f \times n_f$

$a^2 + c^2 + e^2 = 1$

factor loadings

factor loadings \times ace on LP
+ specifics



Fitting CP Model

```
# Create Model Objects for Multiple Groups
pars      <- list(meanG, matI, invSD,
                 pathA1, pathC1, pathE1, covarLP, varLP, unit, pathFL, pathAs, pathCs, pathEs, covA, covC, covE, covP)
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
modelCP   <- mxModel( "mulCPc", pars, varLP1, modelMZ, modelDZ, multi )
fitCP     <- mxRun(modelCP, intervals=F)
sumCP     <- summary( fitCP )
mxCompare( fitACE, fitCP )
parameterSpecifications(fitCP)

# Generate List of Parameter Estimates and Derived Quantities using formatOutputMatrices
matCPpaths <- c("al","cl","el") "iSD %*% fl","iSD %*% as","iSD %*% cs","iSD %*% es")
labCPpaths <- c("stPathAL","stPathCL","stPathEL","stPathFL","stPathAs","stPathCs","stPathEs")
formatOutputMatrices(fitCP, matCPpaths, labCPpaths, vars, 4)
```

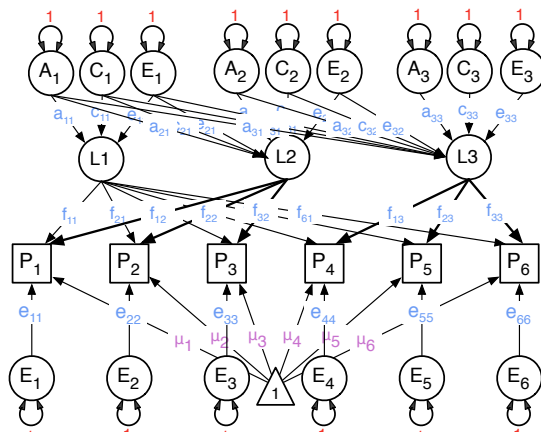
new objects

constraint object in combined model only

already standardized

Can you have multiple latent factors?

CP 3L 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?

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
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