

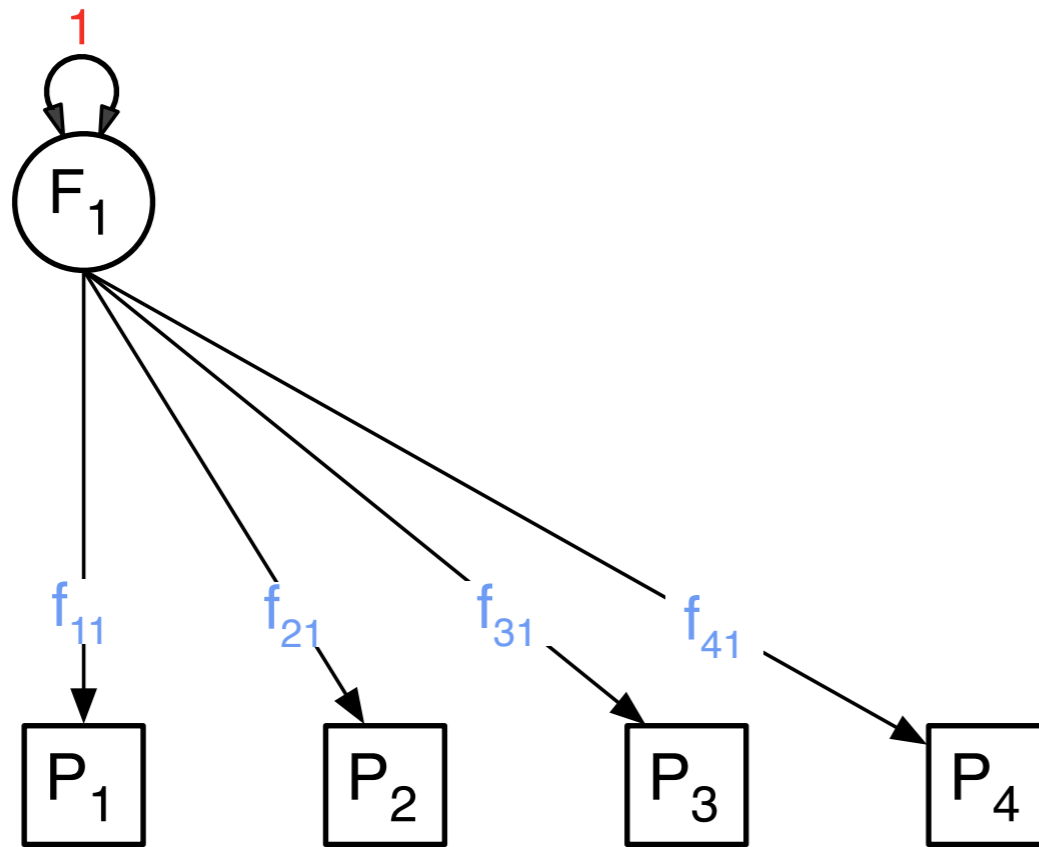
Multivariate Genetic Analysis

Hermine H. Maes, Meike Bartels, Elizabeth Prom-Wormley, Michel Nivard, Tim Bates & many others

Theoretical Models

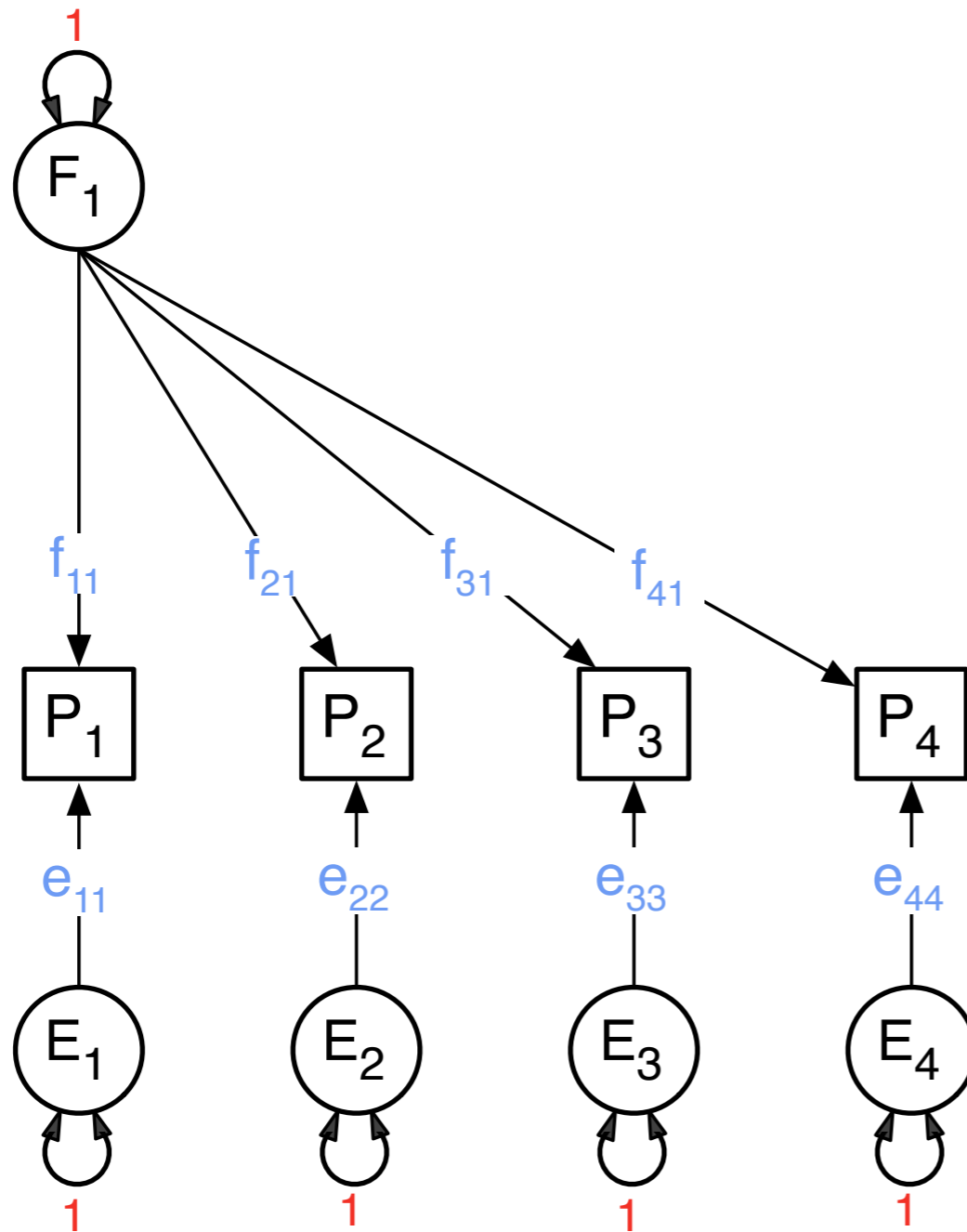
- Independent Pathway
- Common Pathway

Common Factor



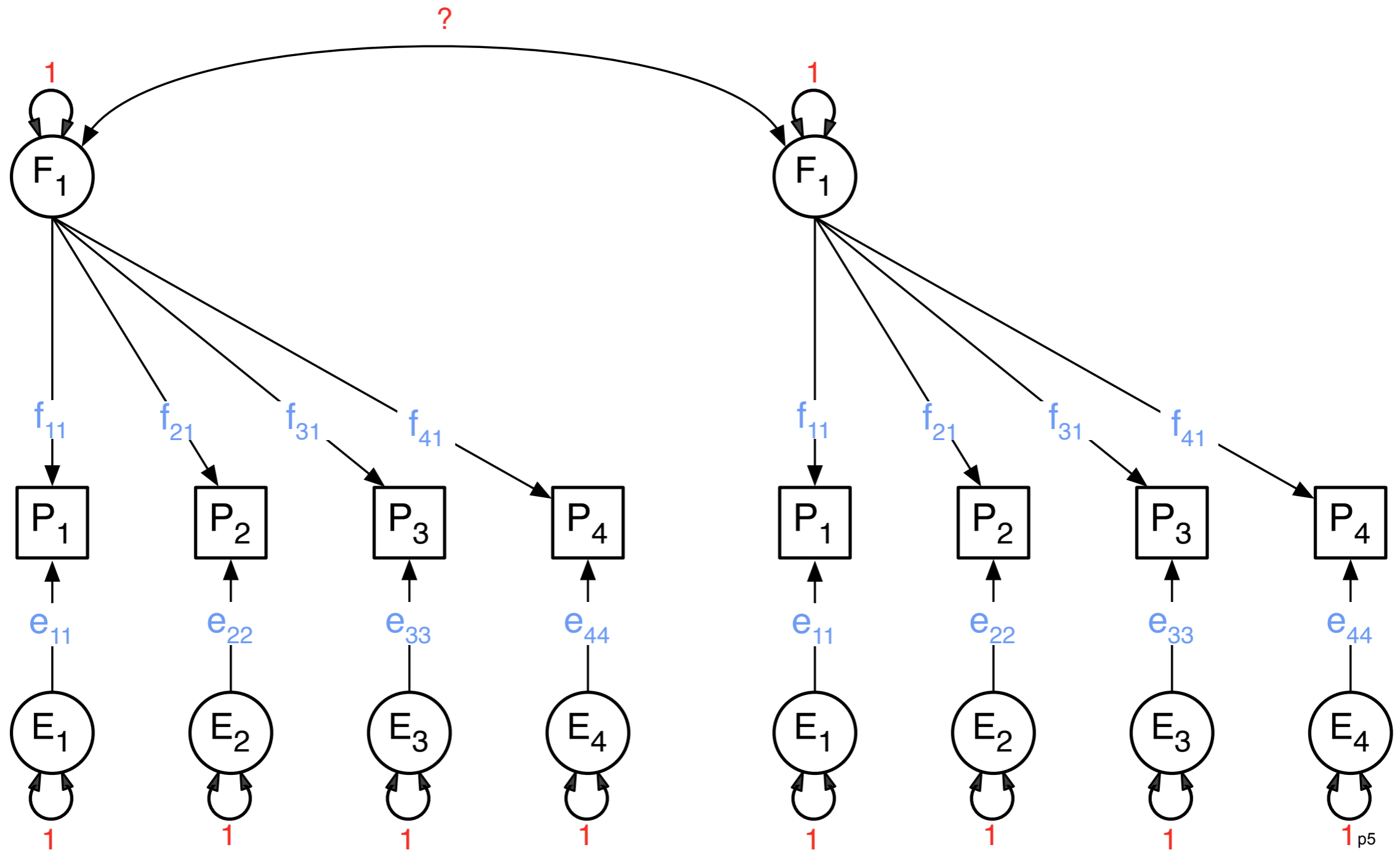
$$\begin{matrix} P_1 \\ P_2 \\ P_3 \\ P_4 \end{matrix} \begin{bmatrix} F_1 \\ f_{11} \\ f_{21} \\ f_{31} \\ f_{41} \end{bmatrix}$$

Residuals



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

What about Twins

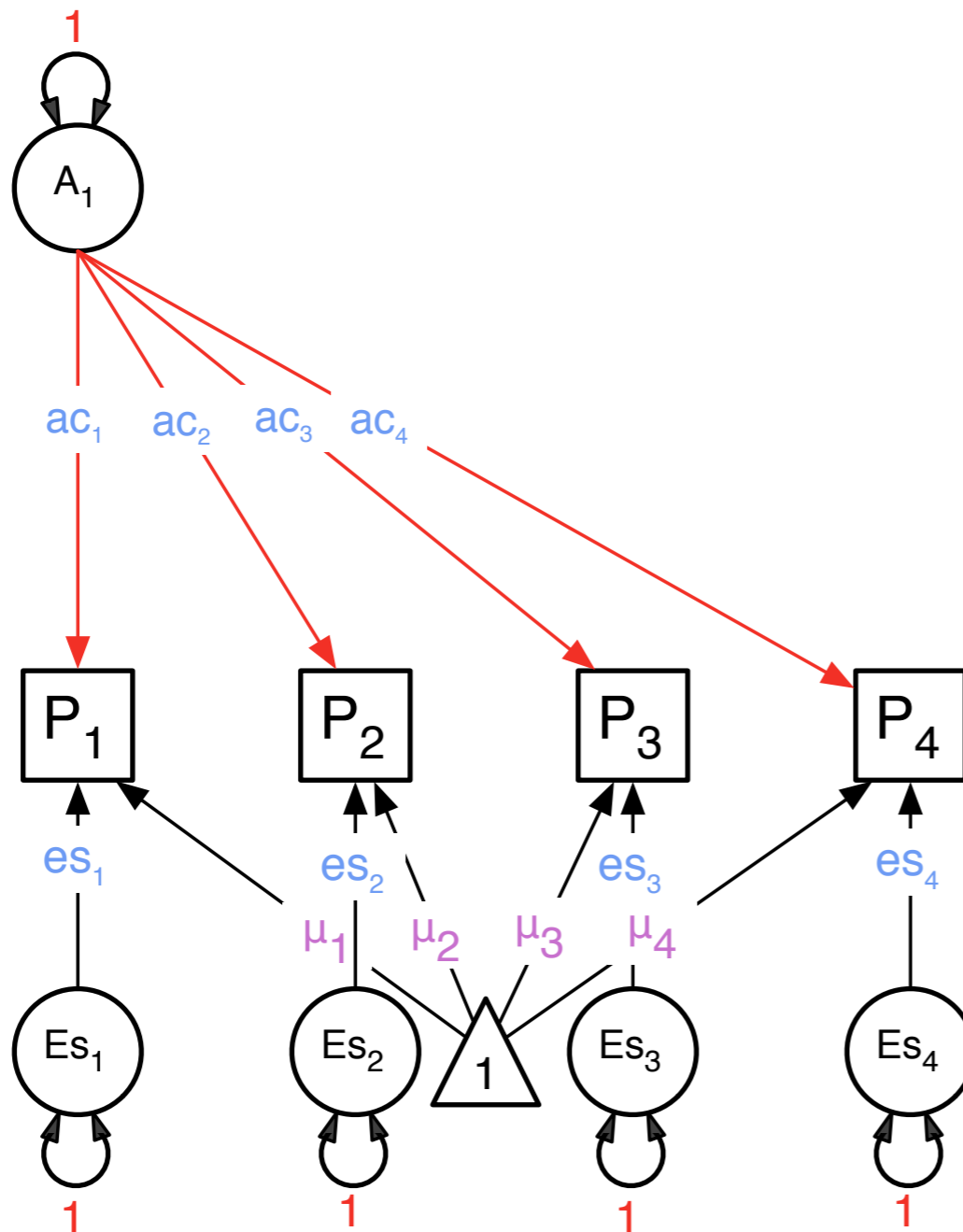


Common Factors Specifics

$$\begin{bmatrix} f_{11} \\ f_{21} \\ f_{31} \\ f_{41} \end{bmatrix} \times \begin{bmatrix} f_{11} & f_{21} & f_{31} & f_{41} \end{bmatrix} = \begin{bmatrix} f_{11}^2 & f_{11}f_{21} & f_{11}f_{31} & f_{11}f_{41} \\ f_{21}f_{11} & f_{21}^2 & f_{21}f_{31} & f_{21}f_{41} \\ f_{31}f_{11} & f_{31}f_{21} & f_{31}^2 & f_{31}f_{41} \\ f_{41}f_{11} & f_{41}f_{21} & f_{41}f_{31} & f_{41}^2 \end{bmatrix}$$

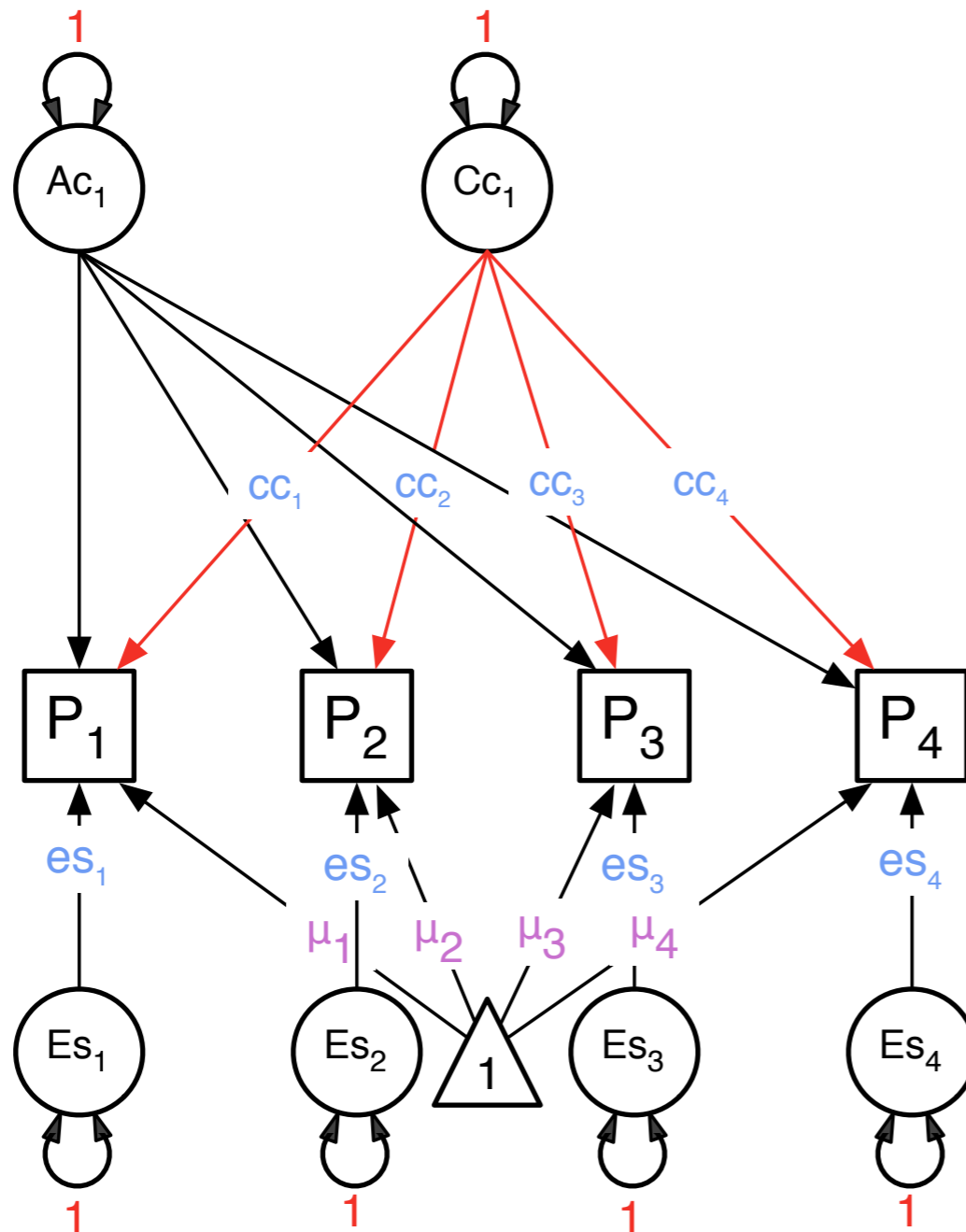
$$\begin{bmatrix} e_{11} & 0 & 0 & 0 \\ 0 & e_{22} & 0 & 0 \\ 0 & 0 & e_{33} & 0 \\ 0 & 0 & 0 & e_{44} \end{bmatrix} \times \begin{bmatrix} e_{11} & 0 & 0 & 0 \\ 0 & e_{22} & 0 & 0 \\ 0 & 0 & e_{33} & 0 \\ 0 & 0 & 0 & e_{44} \end{bmatrix} = \begin{bmatrix} e_{11}^2 & 0 & 0 & 0 \\ 0 & e_{22}^2 & 0 & 0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

Common A Factor



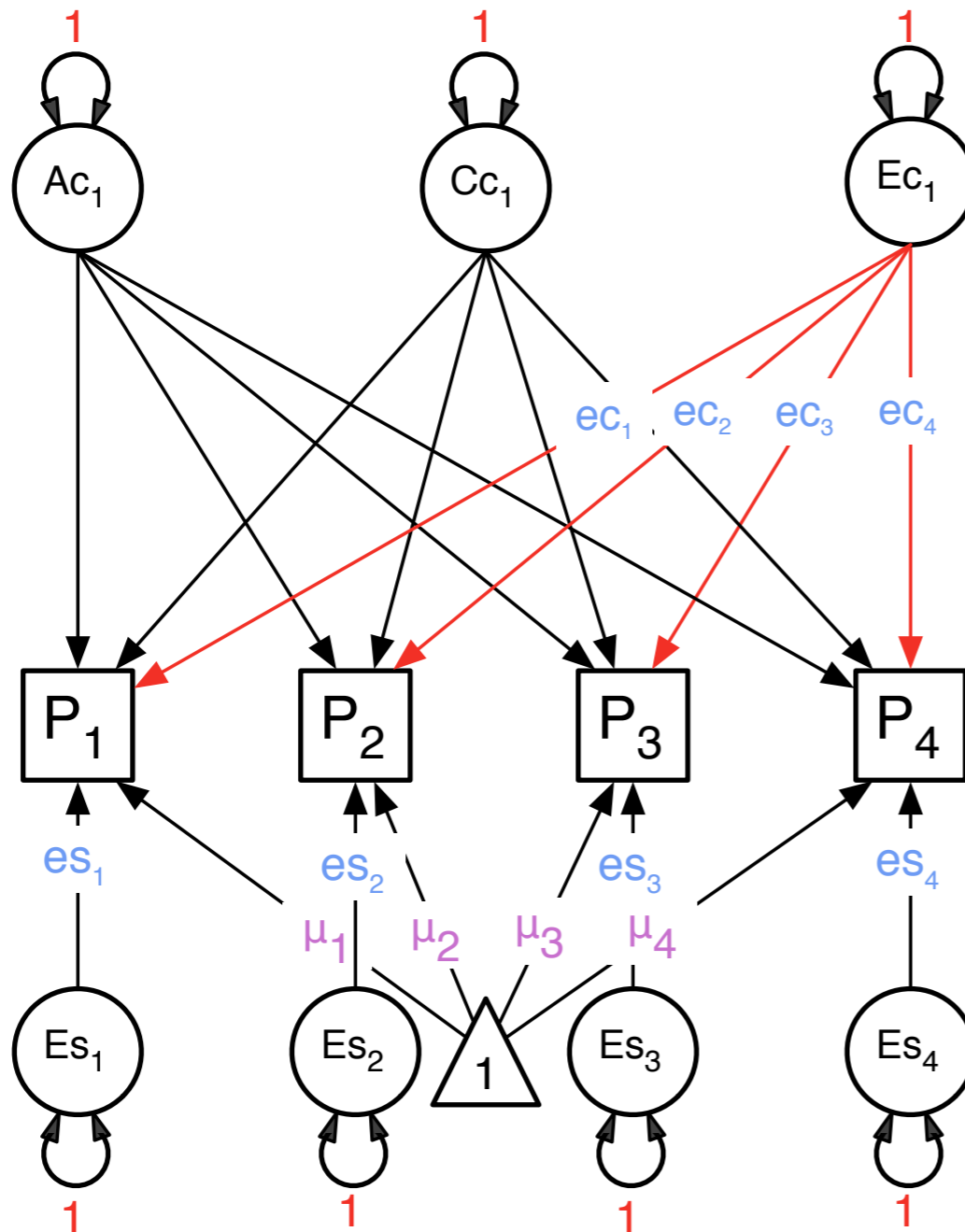
$$\begin{matrix} P_1 \\ P_2 \\ P_3 \\ P_4 \end{matrix} \begin{bmatrix} A_1 \\ ac_{11} \\ ac_{21} \\ ac_{31} \\ ac_{41} \end{bmatrix}$$

Common C Factor



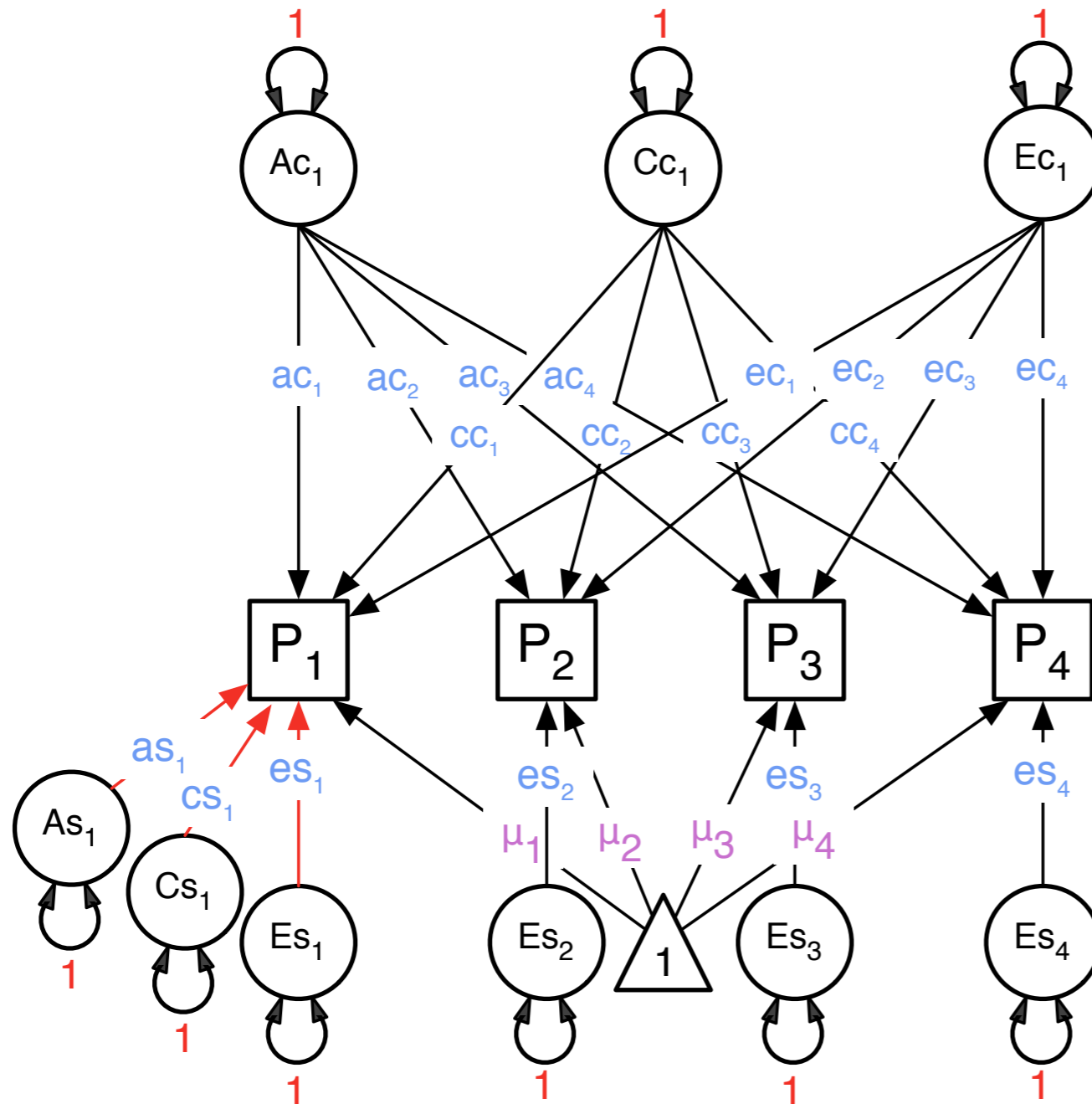
$$\begin{matrix} P_1 \\ P_2 \\ P_3 \\ P_4 \end{matrix} \begin{bmatrix} C_1 \\ cc_{11} \\ cc_{21} \\ cc_{31} \\ cc_{41} \end{bmatrix}$$

Common E Factor



$$\begin{matrix} P_1 \\ P_2 \\ P_3 \\ P_4 \end{matrix} \begin{bmatrix} E_1 \\ ec_{11} \\ ec_{21} \\ ec_{31} \\ ec_{41} \end{bmatrix}$$

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

object: pathAc
matrix name: ac

$$\begin{bmatrix} ac_{11} \\ ac_{21} \\ ac_{31} \\ ac_{41} \end{bmatrix}$$

$$\times \begin{bmatrix} ac_{11} & ac_{21} & ac_{31} & ac_{41} \end{bmatrix}$$

$$= \begin{bmatrix} ac_{11}^2 & ac_{11}ac_{21} & ac_{11}ac_{31} & ac_{11}ac_{41} \\ ac_{21}ac_{11} & ac_{21}^2 & ac_{21}ac_{31} & ac_{21}ac_{41} \\ ac_{31}ac_{11} & ac_{31}ac_{21} & ac_{31}^2 & ac_{31}ac_{41} \\ ac_{41}ac_{11} & ac_{41}ac_{21} & ac_{41}ac_{31} & ac_{41}^2 \end{bmatrix}$$

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

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

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

object: pathAs
matrix name: as

```
pathAc <- mxMatrix( type="Full", nrow=nv, ncol=nf, free=TRUE, values=.6,
labels=labFull("ac",nv, nf), lbound=lbPa, name="ac" )
pathAs <- mxMatrix( type="Diag", nrow=nv, ncol=nv, free=TRUE, values=.5,
labels=labDiag("as",nv), lbound=.00001, name="as" )
```

Total A Covariance

$$\begin{array}{c}
 \text{ac \%*\% t(ac)} \\
 \left[\begin{array}{cccc}
 ac_{11}^2 & ac_{11}ac_{21} & ac_{11}ac_{31} & ac_{11}ac_{41} \\
 ac_{21}ac_{11} & ac_{21}^2 & ac_{21}ac_{31} & ac_{21}ac_{41} \\
 ac_{31}ac_{11} & ac_{31}ac_{21} & ac_{31}^2 & ac_{31}ac_{41} \\
 ac_{41}ac_{11} & ac_{41}ac_{21} & ac_{41}ac_{31} & ac_{41}^2
 \end{array} \right]
 \end{array}
 +
 \begin{array}{c}
 \text{as \%*\% t(as)} \\
 \left[\begin{array}{cccc}
 as_{11}^2 & 0 & 0 & 0 \\
 0 & as_{22}^2 & 0 & 0 \\
 0 & 0 & as_{33}^2 & 0 \\
 0 & 0 & 0 & as_{44}^2
 \end{array} \right]
 \end{array}
 =
 \begin{array}{c}
 \left[\begin{array}{cccc}
 ac_{11}^2 + as_{11}^2 & ac_{11}ac_{21} & ac_{11}ac_{31} & ac_{11}ac_{41} \\
 ac_{21}ac_{11} & ac_{21}^2 + as_{22}^2 & ac_{21}ac_{31} & ac_{21}ac_{41} \\
 ac_{31}ac_{11} & ac_{31}ac_{21} & ac_{31}^2 + as_{33}^2 & ac_{31}ac_{41} \\
 ac_{41}ac_{11} & ac_{41}ac_{21} & ac_{41}ac_{31} & ac_{41}^2 + as_{44}^2
 \end{array} \right] \\
 \text{object: CovA} \\
 \text{matrix name:A}
 \end{array}$$

```

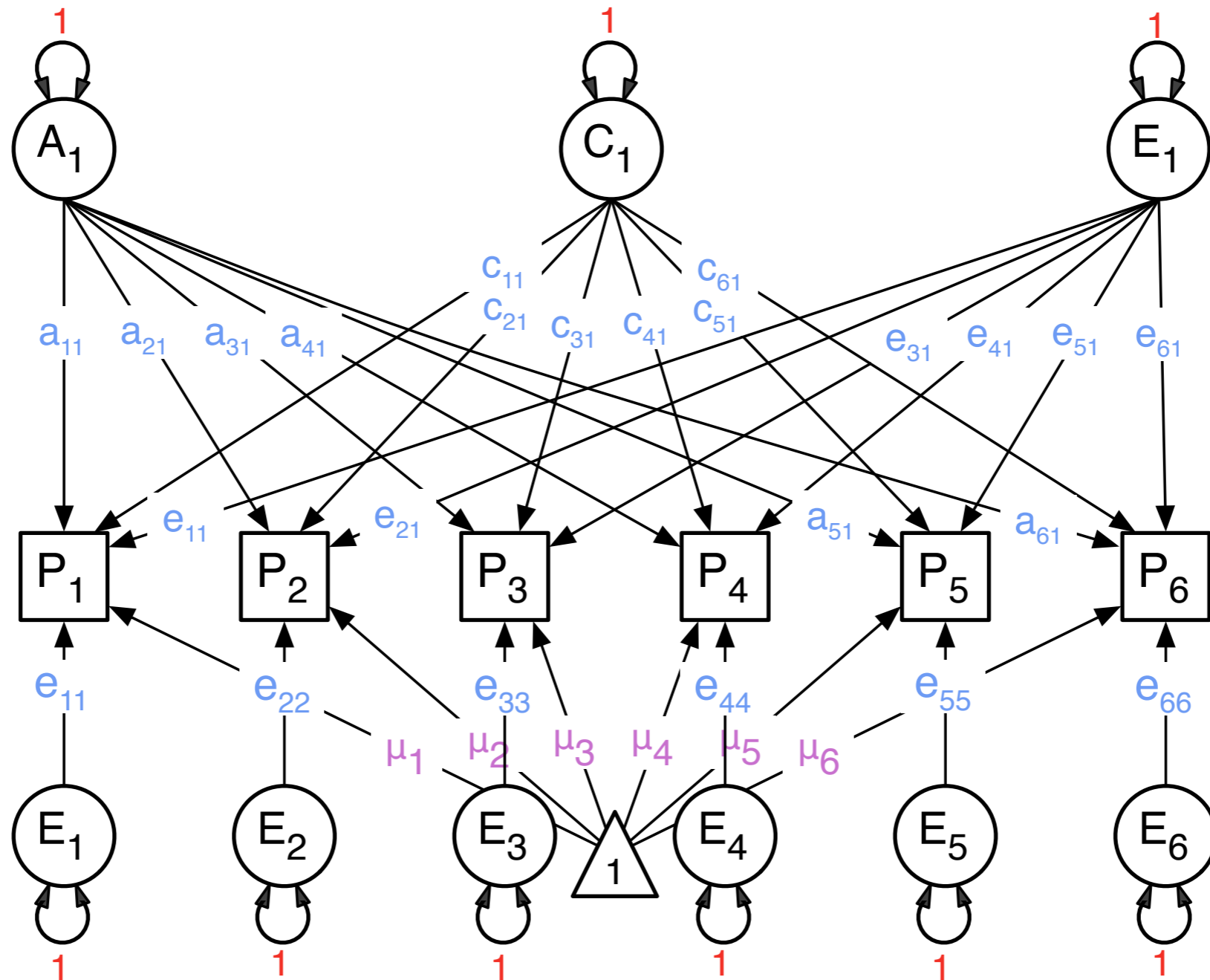
covA <- mxAlgebra( expression=ac \%*\% t(ac) + as \%*\% t(as), name="A" )

```

Independent Pathway Model

- Biometric model
- Different covariance structure for A, C and E

IP Model



Independent Pathway

Variance Component	a ²	c ²	e ²
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

Identification

- Be careful when adding common factors: total parameters per source of variance can not exceed $(nv*(nv+1))/2$
- For a common factor with only 2 indicators the two factor loadings on the latent factor need to be equated OR instead a correlation could be estimated between the residual factors (of the same source of variance) on the two indicators.

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 $nv \times nf$

specific factors of size $nv \times nv$ (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

Independent Pathway Specification

```
> parameterSpecifications(fitIP)
```

```
model:mulIPc, matrix:ac
```

```
      [,1]
[1,] [ac_1_1]
[2,] [ac_2_1]
[3,] [ac_3_1]
[4,] [ac_4_1]
[5,] [ac_5_1]
[6,] [ac_6_1]
```

```
model:mulIPc, matrix:as
```

```
      [,1] [,2] [,3] [,4] [,5] [,6]
[1,] [as_1_1] 0    0    0    0    0
[2,] 0        [as_2_2] 0    0    0    0
[3,] 0        0    [as_3_3] 0    0    0
[4,] 0        0    0    [as_4_4] 0    0
[5,] 0        0    0    0    [as_5_5] 0
[6,] 0        0    0    0    0    [as_6_6]
```

```
model:mulIPc, matrix:cc
```

```
      [,1]
[1,] [cc_1_1]
[2,] [cc_2_1]
[3,] [cc_3_1]
[4,] [cc_4_1]
[5,] [cc_5_1]
[6,] [cc_6_1]
```

```
model:mulIPc, matrix:cs
```

```
      [,1] [,2] [,3] [,4] [,5] [,6]
[1,] [cs_1_1] 0    0    0    0    0
[2,] 0        [cs_2_2] 0    0    0    0
[3,] 0        0    [cs_3_3] 0    0    0
[4,] 0        0    0    [cs_4_4] 0    0
[5,] 0        0    0    0    [cs_5_5] 0
[6,] 0        0    0    0    0    [cs_6_6]
```

```
model:mulIPc, matrix:ec
```

```
      [,1]
[1,] [ec_1_1]
[2,] [ec_2_1]
[3,] [ec_3_1]
[4,] [ec_4_1]
[5,] [ec_5_1]
[6,] [ec_6_1]
```

```
model:mulIPc, matrix:es
```

```
      [,1] [,2] [,3] [,4] [,5] [,6]
[1,] [es_1_1] 0    0    0    0    0
[2,] 0        [es_2_2] 0    0    0    0
[3,] 0        0    [es_3_3] 0    0    0
[4,] 0        0    0    [es_4_4] 0    0
[5,] 0        0    0    0    [es_5_5] 0
[6,] 0        0    0    0    0    [es_6_6]
```

Compare IP with Cholesky

```
> mxCompare( fitACE, fitIP )
```

base	ep	minus2LL	df	AIC	diffLL	diffdf	p
mu1ACEc	69	14362.137	5394	3574.1373	NA	NA	NA
mu1IPc	42	14449.871	5421	3607.8713	87.734027	27	2.4154318e-08

Standardized Estimates for fitIP

[1] "Matrix iSD %*% ac"

	stPathAc1
family	0.1455
happy	0.2472
life	0.2307
anxdep	-0.7073
somatic	-0.5972
social	-0.4640

[1] "Matrix iSD %*% as"

	stPathAs1	stPathAs2	stPathAs3	stPathAs4	stPathAs5	stPathAs6
family	0.4327	0.0000	0.0000	0.0000	0.0000	0.0000
happy	0.0000	0.1340	0.0000	0.0000	0.0000	0.0000
life	0.0000	0.0000	0.2051	0.0000	0.0000	0.0000
anxdep	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
somatic	0.0000	0.0000	0.0000	0.0000	0.1742	0.0000
social	0.0000	0.0000	0.0000	0.0000	0.0000	0.4839

[1] "Matrix iSD %*% cc"

	stPathCc1
family	-0.5533
happy	-0.4472
life	-0.4828
anxdep	0.2778
somatic	0.2023
social	0.2418

[1] "Matrix iSD %*% cs"

	stPathCs1	stPathCs2	stPathCs3	stPathCs4	stPathCs5	stPathCs6
family	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
happy	0.0000	0.1275	0.0000	0.0000	0.0000	0.0000
life	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
anxdep	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
somatic	0.0000	0.0000	0.0000	0.0000	0.3518	0.0000
social	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

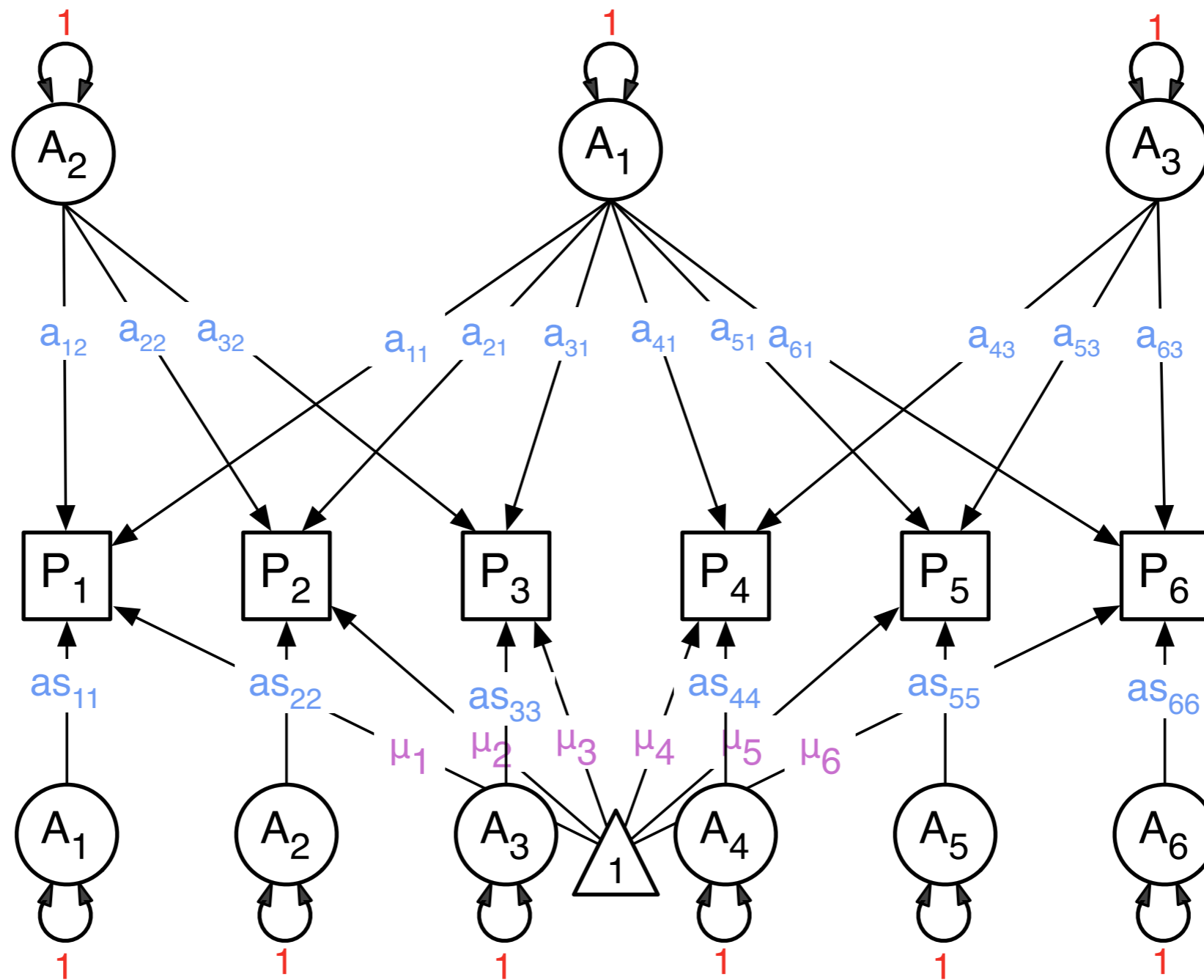
[1] "Matrix iSD %*% ec"

	stPathEc1
family	-0.1862
happy	-0.7594
life	-0.6250
anxdep	0.3511
somatic	0.0696
social	0.1002

[1] "Matrix iSD %*% es"

	stPathEs1	stPathEs2	stPathEs3	stPathEs4	stPathEs5	stPathEs6
family	0.6714	0.0000	0.0000	0.0000	0.0000	0.0000
happy	0.0000	0.3578	0.0000	0.0000	0.0000	0.0000
life	0.0000	0.0000	0.5300	0.0000	0.0000	0.0000
anxdep	0.0000	0.0000	0.0000	0.5470	0.0000	0.0000
somatic	0.0000	0.0000	0.0000	0.0000	0.6659	0.0000
social	0.0000	0.0000	0.0000	0.0000	0.0000	0.6943

IP3A Model : bi-factor model



Three Independent A Factors

```

# Fit 3A (1C 1E) Factor - Independent Pathway Model
# -----

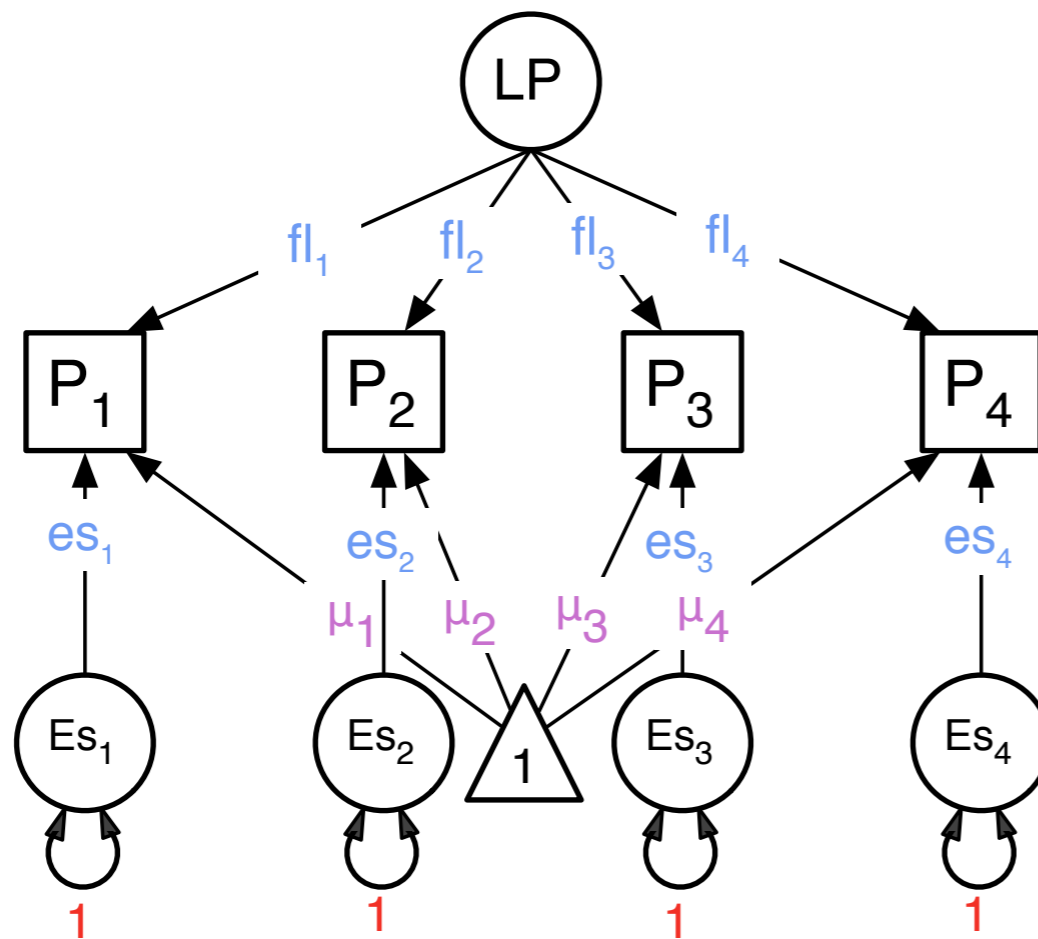
# Change Dimension of Additive Genetic Factor Matrix Ac
# Create Free and Values for 3 Additive Genetic Factors
#      free      values
#      A1  A2  A3      A1  A2  A3
# P1  T   T   F      P1  .5  .5  0
# P2  T   T   F      P2  .5  .5  0
# P3  T   T   F      P3  .5  .5  0
# P4  T   F   T      P4  .5  0  .5
# P5  T   F   T      P5  .5  0  .5
# P6  T   F   T      P6  .5  0  .5
nfA <- 3
frAc3 <- c(T,T,T,T,T,T, T,T,T,F,F,F, F,F,F,T,T,T)
svAc3 <- c(rep(.5,nv),rep(.5,3),rep(0,3),rep(0,3),rep(.5,3))
pathAc <- mxMatrix( type="Full", nrow=nv, ncol=nfA, free=frAc3, values=svAc3, labels=labFull("ac",nv,nfA), name="ac" )

# Create Model Objects, Build & Run Model
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 )
modelIP3A <- mxModel( "mulIP3Ac", pars, modelMZ, modelDZ, multi )
fitIP3A <- mxRun( modelIP3A )
mxCompare( fitACE, nested <- list(fitIP, fitIP3A) )
formatOutputMatrices(fitIP, matIPpaths, labIPpaths, vars, 4)

```

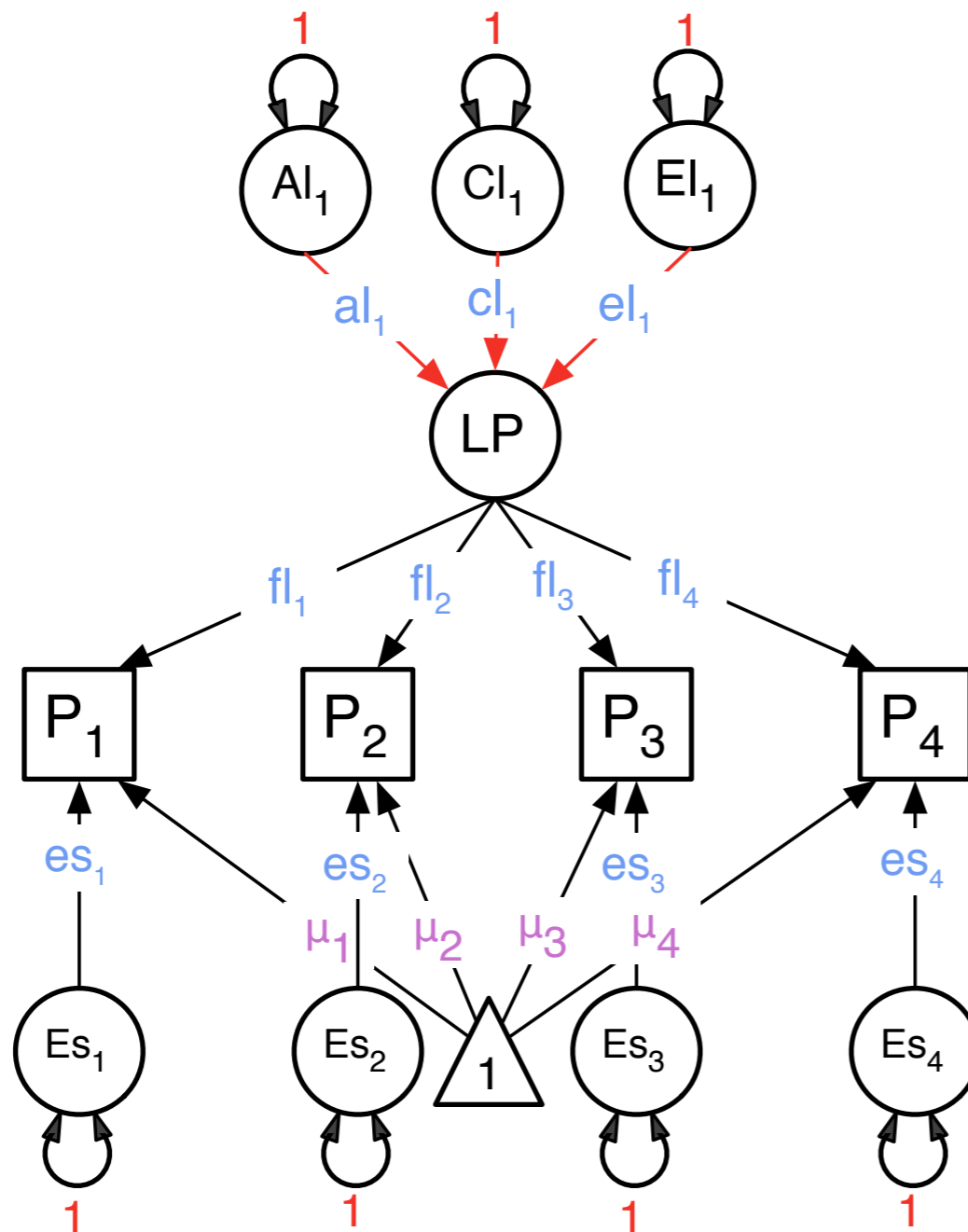
changing one matrix

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



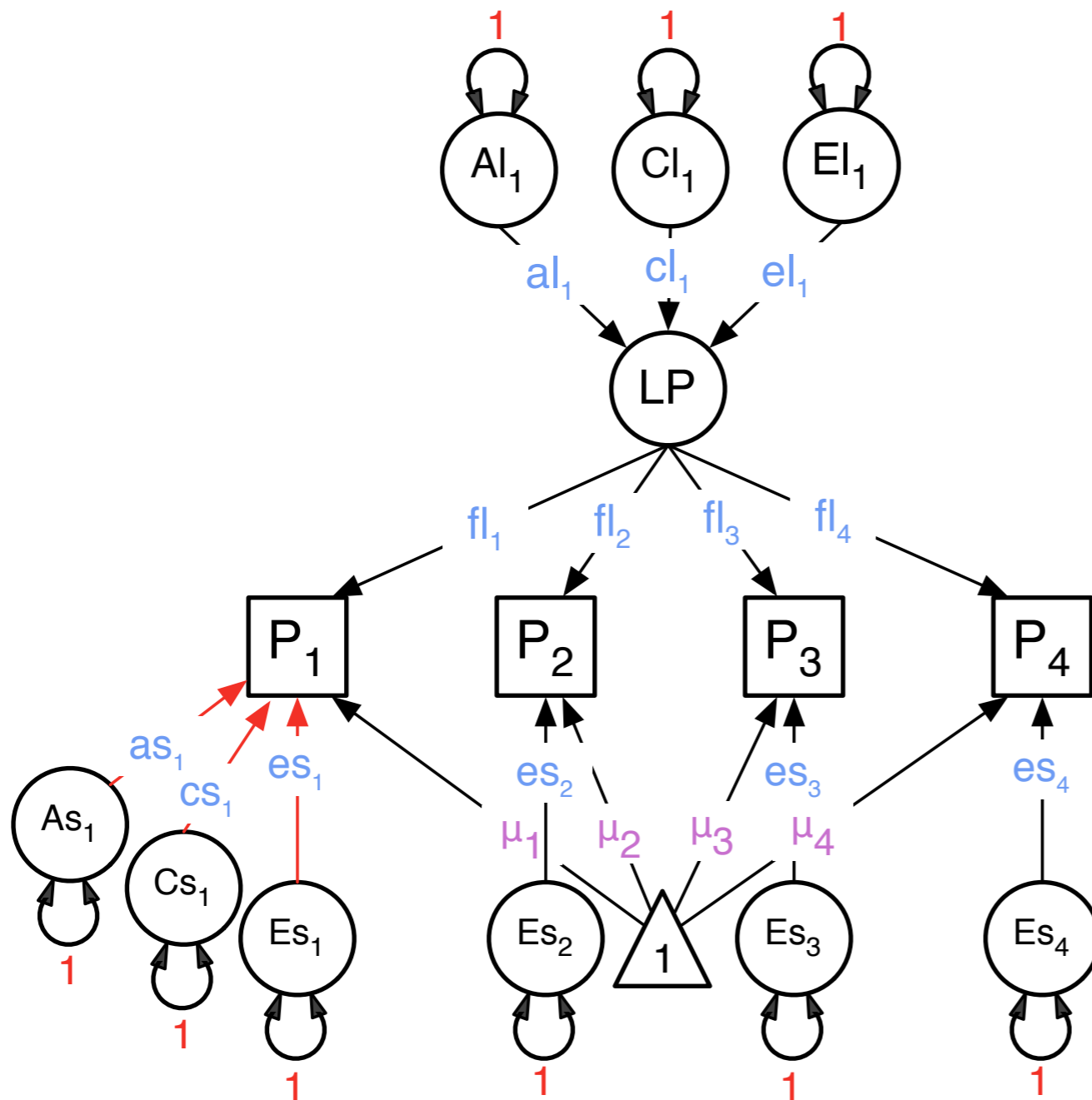
$$[al_{11}]$$

$$[cl_{11}]$$

$$[el_{11}]$$

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

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

object: pathFl
matrix name: fl

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

object: pathAl
matrix name: al

object: pathAs
matrix name: as

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

```
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

$$\begin{aligned}
 & \text{fl} \% \% (\text{al} \% \% \text{t}(\text{al})) \\
 & \begin{bmatrix} fl_{11}^2 al_{11}^2 & fl_{11} fl_{21} al_{11}^2 & fl_{11} fl_{31} al_{11}^2 & fl_{11} fl_{41} al_{11}^2 \\ fl_{21} fl_{11} al_{11}^2 & fl_{21}^2 al_{11}^2 & fl_{21} fl_{31} al_{11}^2 & fl_{21} fl_{41} al_{11}^2 \\ fl_{31} fl_{11} al_{11}^2 & fl_{31} fl_{21} al_{11}^2 & fl_{31}^2 al_{11}^2 & fl_{31} fl_{41} al_{11}^2 \\ fl_{41} fl_{11} al_{11}^2 & fl_{41} fl_{21} al_{11}^2 & fl_{41} fl_{31} al_{11}^2 & fl_{41}^2 al_{11}^2 \end{bmatrix} + \begin{bmatrix} as_{11}^2 & 0 & 0 & 0 \\ 0 & as_{22}^2 & 0 & 0 \\ 0 & 0 & as_{33}^2 & 0 \\ 0 & 0 & 0 & as_{44}^2 \end{bmatrix} = \begin{bmatrix} fl_{11}^2 al_{11}^2 + as_{11}^2 & fl_{11} fl_{21} al_{11}^2 & fl_{11} fl_{31} al_{11}^2 & fl_{11} fl_{41} al_{11}^2 \\ fl_{21} fl_{11} al_{11}^2 & fl_{21}^2 al_{11}^2 + as_{22}^2 & fl_{21} fl_{31} al_{11}^2 & fl_{21} fl_{41} al_{11}^2 \\ fl_{31} fl_{11} al_{11}^2 & fl_{31} fl_{21} al_{11}^2 & fl_{31}^2 al_{11}^2 + as_{33}^2 & fl_{31} fl_{41} al_{11}^2 \\ fl_{41} fl_{11} al_{11}^2 & fl_{41} fl_{21} al_{11}^2 & fl_{41} fl_{31} al_{11}^2 & fl_{41}^2 al_{11}^2 + as_{44}^2 \end{bmatrix} \\
 & \text{as} \% \% \text{t}(\text{as}) \\
 & \text{object: CovA} \\
 & \text{matrix name:A}
 \end{aligned}$$

```

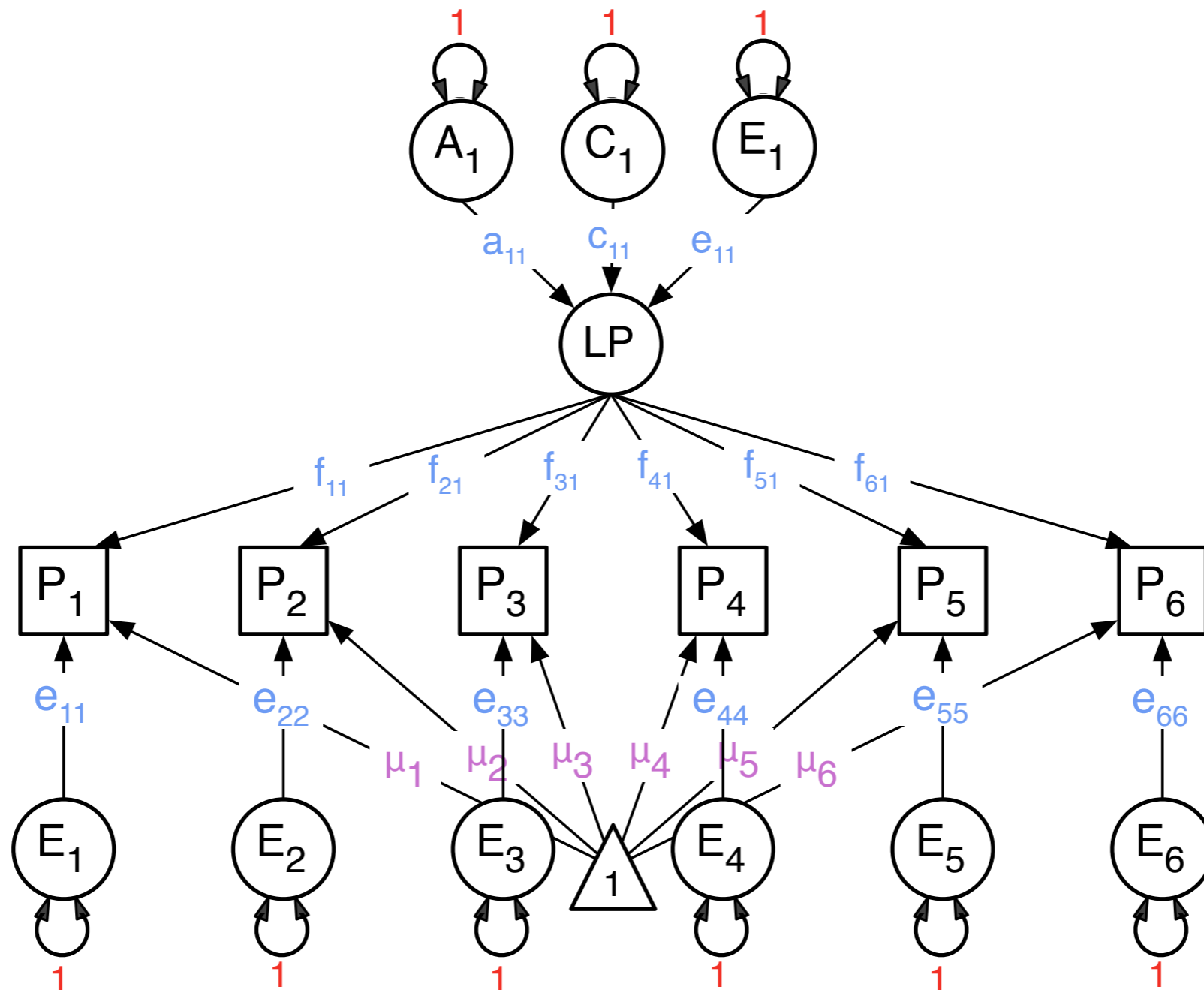
covA <- mxAlgebra( expression=fl %% (al %% t(al)) + as %% t(as), name="A" )

```

Common Pathway Model

- Psychometric model
- Same covariance structure for A, C and E

CP Model



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=a1 %**% t(a1) + c1 %**% t(c1) + e1 %**% t(e1), 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 %**% (a1 %**% t(a1)) + as %**% t(as), name="A" )
covC    <- mxAlgebra( expression=f1 %**% (c1 %**% t(c1)) + cs %**% t(cs), name="C" )
covE    <- mxAlgebra( expression=f1 %**% (e1 %**% t(e1)) + es %**% t(es), name="E" )

```

latent phenotype nf x nf

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

factor loadings

factor loadings x ace on LP
+ specifics

Fitting CP Model

```
# Create Model Objects for Multiple Groups
```

```
pars      <- list(meanG, matI, invSD,  
                 pathAl, pathCl, pathEl, 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") )
```

new objects

```
# Build & Run Model
```

```
modelCP   <- mxModel( "mulCPc", pars, varLP1, modelMZ, modelDZ, multi )  
fitCP     <- mxRun(modelCP, intervals=F )  
sumCP     <- summary( fitCP )  
mxCompare( fitACE, fitCP )  
parameterSpecifications(fitCP)
```

constraint object in combined model only

```
# 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)
```

already standardized

Common Pathway Specification

parameterSpecifications(fitCP)

model:mulCPc, matrix:a1

[,1]
[1,] [a1_1_1]

model:mulCPc, matrix:c1

[,1]
[1,] [c1_1_1]

model:mulCPc, matrix:e1

[,1]
[1,] [e1_1_1]

model:mulCPc, matrix:f1

[,1]
[1,] [f1_1_1]
[2,] [f1_2_1]
[3,] [f1_3_1]
[4,] [f1_4_1]
[5,] [f1_5_1]
[6,] [f1_6_1]

model:mulCPc, matrix:as

	[,1]	[,2]	[,3]	[,4]	[,5]	[,6]
[1,]	[as_1_1]	0	0	0	0	0
[2,]	0	[as_2_2]	0	0	0	0
[3,]	0	0	[as_3_3]	0	0	0
[4,]	0	0	0	[as_4_4]	0	0
[5,]	0	0	0	0	[as_5_5]	0
[6,]	0	0	0	0	0	[as_6_6]

model:mulCPc, matrix:cs

	[,1]	[,2]	[,3]	[,4]	[,5]	[,6]
[1,]	[cs_1_1]	0	0	0	0	0
[2,]	0	[cs_2_2]	0	0	0	0
[3,]	0	0	[cs_3_3]	0	0	0
[4,]	0	0	0	[cs_4_4]	0	0
[5,]	0	0	0	0	[cs_5_5]	0
[6,]	0	0	0	0	0	[cs_6_6]

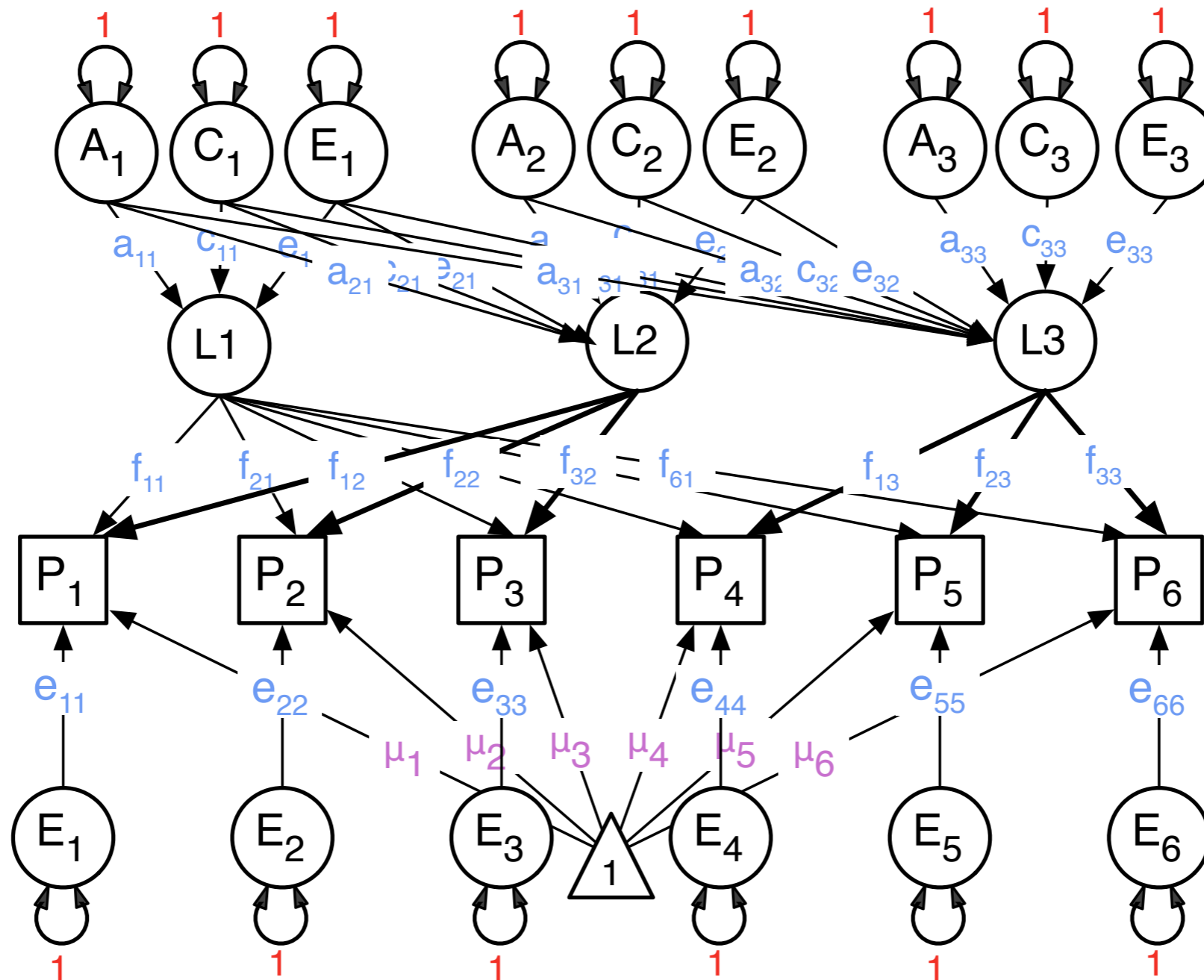
model:mulCPc, matrix:es

	[,1]	[,2]	[,3]	[,4]	[,5]	[,6]
[1,]	[es_1_1]	0	0	0	0	0
[2,]	0	[es_2_2]	0	0	0	0
[3,]	0	0	[es_3_3]	0	0	0
[4,]	0	0	0	[es_4_4]	0	0
[5,]	0	0	0	0	[es_5_5]	0
[6,]	0	0	0	0	0	[es_6_6]

Standardized Estimates for fitCP

		[1] "Matrix iSD %*% as"					
		stPathAs1	stPathAs2	stPathAs3	stPathAs4	stPathAs5	stPathAs6
	family	0.5565	0.0000	0.0000	0.0000	0.0000	0.0000
	happy	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	life	0.0000	0.0000	0.1387	0.0000	0.0000	0.0000
	anxdep	0.0000	0.0000	0.0000	0.1707	0.0000	0.0000
[1] "Matrix aI"	somatic	0.0000	0.0000	0.0000	0.0000	0.5050	0.0000
stPathA11	social	0.0000	0.0000	0.0000	0.0000	0.0000	0.5837
LP1		0.7208					
		[1] "Matrix iSD %*% cs"					
		stPathCs1	stPathCs2	stPathCs3	stPathCs4	stPathCs5	stPathCs6
	family	0.1541	0.0000	0.0000	0.0000	0.0000	0.0000
	happy	0.0000	0.1247	0.0000	0.0000	0.0000	0.0000
	life	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	anxdep	0.0000	0.0000	0.0000	0.3818	0.0000	0.0000
[1] "Matrix cI"	somatic	0.0000	0.0000	0.0000	0.0000	0.3063	0.0000
stPathC11	social	0.0000	0.0000	0.0000	0.0000	0.0000	0.1828
LP1		0.3267					
		[1] "Matrix iSD %*% es"					
		stPathEs1	stPathEs2	stPathEs3	stPathEs4	stPathEs5	stPathEs6
	family	0.6627	0.0000	0.0000	0.0000	0.0000	0.0000
	happy	0.0000	0.4979	0.0000	0.0000	0.0000	0.0000
	life	0.0000	0.0000	0.5511	0.0000	0.0000	0.0000
	anxdep	0.0000	0.0000	0.0000	0.6010	0.0000	0.0000
[1] "Matrix iSD %*% fI"	somatic	0.0000	0.0000	0.0000	0.0000	0.6997	0.0000
stPathF11	social	0.0000	0.0000	0.0000	0.0000	0.0000	0.6915
family		0.4768					
happy		0.8582					
life		0.8228					
anxdep		-0.6811					
somatic		-0.4018					
social		-0.3843					

CP 3L Model



Standardized Estimates for fitCP3L

[1] "Matrix a1"				[1] "Matrix iSD %*% as"						
	stPathA11	stPathA12	stPathA13		stPathAs1	stPathAs2	stPathAs3	stPathAs4	stPathAs5	stPathAs6
LP1	0.4446	0.0000	0.0000	family	0.3909	0.0000	0.0000	0.0000	0.0000	0.0000
LP2	0.2956	0.3004	0.0000	happy	0.0000	0.1881	0.0000	0.0000	0.0000	0.0000
LP3	0.4062	0.3409	0.0187	life	0.0000	0.0000	0.1949	0.0000	0.0000	0.0000
				anxdep	0.0000	0.0000	0.0000	0.0092	0.0000	0.0000
				somatic	0.0000	0.0000	0.0000	0.0000	0.4129	0.0000
				social	0.0000	0.0000	0.0000	0.0000	0.0000	0.5237
[1] "Matrix c1"				[1] "Matrix iSD %*% cs"						
	stPathC11	stPathC12	stPathC13		stPathCs1	stPathCs2	stPathCs3	stPathCs4	stPathCs5	stPathCs6
LP1	0.4294	0.0000	0.0000	family	0.0196	0.0000	0.0000	0.0000	0.0000	0.0000
LP2	0.1407	-0.0021	0.0000	happy	0.0000	0.0371	0.0000	0.0000	0.0000	0.0000
LP3	0.1023	0.2202	0.1211	life	0.0000	0.0000	0.0174	0.0000	0.0000	0.0000
				anxdep	0.0000	0.0000	0.0000	0.0177	0.0000	0.0000
				somatic	0.0000	0.0000	0.0000	0.0000	0.2750	0.0000
				social	0.0000	0.0000	0.0000	0.0000	0.0000	0.0125
[1] "Matrix e1"				[1] "Matrix iSD %*% es"						
	stPathE11	stPathE12	stPathE13		stPathEs1	stPathEs2	stPathEs3	stPathEs4	stPathEs5	stPathEs6
LP1	0.7860	0.0000	0.0000	family	0.6502	0.0000	0.0000	0.0000	0.0000	0.0000
LP2	0.8910	0.0935	0.0000	happy	0.0000	0.3222	0.0000	0.0000	0.0000	0.0000
LP3	0.7331	-0.0190	0.3272	life	0.0000	0.0000	0.5422	0.0000	0.0000	0.0000
				anxdep	0.0000	0.0000	0.0000	0.3670	0.0000	0.0000
				somatic	0.0000	0.0000	0.0000	0.0000	0.6213	0.0000
				social	0.0000	0.0000	0.0000	0.0000	0.0000	0.6820
[1] "Matrix iSD %*% f1"				[1] "Matrix iSD %*% es"						
	stPathF11	stPathF12	stPathF13		stPathEs1	stPathEs2	stPathEs3	stPathEs4	stPathEs5	stPathEs6
family	-1.4243	1.3720	0.0000	family	0.6502	0.0000	0.0000	0.0000	0.0000	0.0000
happy	-1.1893	1.8167	0.0000	happy	0.0000	0.3222	0.0000	0.0000	0.0000	0.0000
life	-1.2577	1.7095	0.0000	life	0.0000	0.0000	0.5422	0.0000	0.0000	0.0000
anxdep	0.9893	0.0000	-1.5090	anxdep	0.0000	0.0000	0.0000	0.3670	0.0000	0.0000
somatic	0.8554	0.0000	-1.0095	somatic	0.0000	0.0000	0.0000	0.0000	0.6213	0.0000
social	0.6964	0.0000	-0.8516	social	0.0000	0.0000	0.0000	0.0000	0.0000	0.6820

Compare IPs & CPs with Cholesky

```
> mxCompare( fitACE, fitIP )
```

base	ep	minus2LL	df	AIC	diffLL	diffdf	p
mulACEc	69	14362.137	5394	3574.1373	NA	NA	NA
mulIPc	42	14449.871	5421	3607.8713	87.734027	27	2.4154318e-08
mulIP3Ac	48	14423.010	5415	3593.0100	60.872650	21	9.4141500e-06
mulIP0Cc	36	14439.733	5427	3585.7332	77.595881	33	1.8718979e-05
mulIP3Ec	54	14381.308	5409	3563.3076	19.170256	15	2.0612213e-01
mulCPc	33	14713.003	5431	3851.0029	350.865628	37	8.9554069e-53
mulCP3Lc	54	14394.178	5412	3570.1782	32.040945	18	2.1743094e-02