

Multivariate Twin Analysis

OpenMx 2012

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Copy Files

nl.dat

twinMulAceConNL_yours.R

twinMulAceConNL.R

Multivariate

- Saturated Model
 - equality of means/variances
- Genetic Models (ACE)
 - multivariate -> Cholesky Decomposition
 - Independent Pathway
 - Common Pathway

Data

- Dutch lab & questionnaire data
- MZ N=248
- DZ N=290

Practical Example

- Verbal IQ
- Performance IQ
- Educational Achievement
- Attention Problems
- Inattention
- Hyperactivity

Scientific Questions

- Are these measures influenced by the same genes (single common factor)?
- Is there more than one factor (intelligence factor - attention factor)?
- What is the structure of C and E?
- Contribution of A, C, E factors to

Cholesky Decomposition

- ‘Saturated’ Genetic Model

[a_1_1]	[a_1_2]	0	0	0	0
[a_2_1]	[a_2_2]	0	0	0	0
[a_3_1]	[a_3_2]	[a_3_3]	0	0	0
[a_4_1]	[a_4_2]	[a_4_3]	[a_4_4]	0	0
[a_5_1]	[a_5_2]	[a_5_3]	[a_5_4]	[a_5_5]	0
[a_6_1]	[a_6_2]	[a_6_3]	[a_6_4]	[a_6_5]	[a_6_6]

l :CholACE, matrix:c

[, 1]	[, 2]	[, 3]	[, 4]	[, 5]	[, 6]
[c_1_1]	0	0	0	0	0
[c_2_1]	[c_2_2]	0	0	0	0
[c_3_1]	[c_3_2]	[c_3_3]	0	0	0
[c_4_1]	[c_4_2]	[c_4_3]	[c_4_4]	0	0
[c_5_1]	[c_5_2]	[c_5_3]	[c_5_4]	[c_5_5]	0
[c_6_1]	[c_6_2]	[c_6_3]	[c_6_4]	[c_6_5]	[c_6_6]

l :CholACE, matrix:e

[, 1]	[, 2]	[, 3]	[, 4]	[, 5]	[, 6]
[e_1_1]	0	0	0	0	0
[e_2_1]	[e_2_2]	0	0	0	0
[e_3_1]	[e_3_2]	[e_3_3]	0	0	0
[e_4_1]	[e_4_2]	[e_4_3]	[e_4_4]	0	0
[e_5_1]	[e_5_2]	[e_5_3]	[e_5_4]	[e_5_5]	0
[e_6_1]	[e_6_2]	[e_6_3]	[e_6_4]	[e_6_5]	[e_6_6]

l :CholACE, matrix:Mean

[, 1]	[, 2]	[, 3]	[, 4]	[, 5]	[, 6]
-------	-------	-------	-------	-------	-------

Fit Statistics

	ep	-2LL	df	chi	df	p
Saturated	180	13015.57	4507	-	-	-
EqMV	144	13084.65	4543	69.07	36	0
CholACE	69	13232.02	4618	216.45	111	0

Matrix iSD %*% a

	stPathA1	stPathA2	stPathA3	stPathA4	stPathA5	stPathA6
	0.6533	0.0000	0.0000	0.0000	0.0000	0.0000
	0.5698	0.0001	0.0000	0.0000	0.0000	0.0000
Ach	0.6052	0.5426	0.0116	0.0000	0.0000	0.0000
tProb	-0.1967	-0.2979	0.7380	0.0685	0.0000	0.0000
tt	-0.2970	-0.5094	0.3565	0.3163	0.4079	0.0000
er	-0.1695	-0.2435	0.3988	0.6321	-0.4229	0.1733

"Matrix iSD %*% c"

	stPathC1	stPathC2	stPathC3	stPathC4	stPathC5	stPathC6
	0.5827	0.0000	0.0000	0.0000	0.0000	0.0000
	0.0955	0.5734	0.0000	0.0000	0.0000	0.0000
Ach	0.3965	0.1275	0.0001	0.0000	0.0000	0.0000
tProb	-0.0936	0.0603	0.0000	0.0001	0.0000	0.0000
tt	-0.0274	0.1024	0.0000	0.0000	0.0001	0.0000
er	0.0338	0.0312	0.0000	0.0000	0.0001	0.0001

"Matrix iSD %*% e"

	stPathE1	stPathE2	stPathE3	stPathE4	stPathE5	stPathE6
	0.4834	0.0000	0.0000	0.0000	0.0000	0.0000
	0.0074	0.5808	0.0000	0.0000	0.0000	0.0000
Ach	0.1347	-0.0289	0.3831	0.0000	0.0000	0.0000
tProb	-0.1011	-0.1050	-0.1386	0.5199	0.0000	0.0000
tt	-0.0832	-0.0926	-0.0869	0.2139	0.4228	0.0000
er	-0.0374	-0.0582	-0.0280	0.2076	0.0774	0.2961

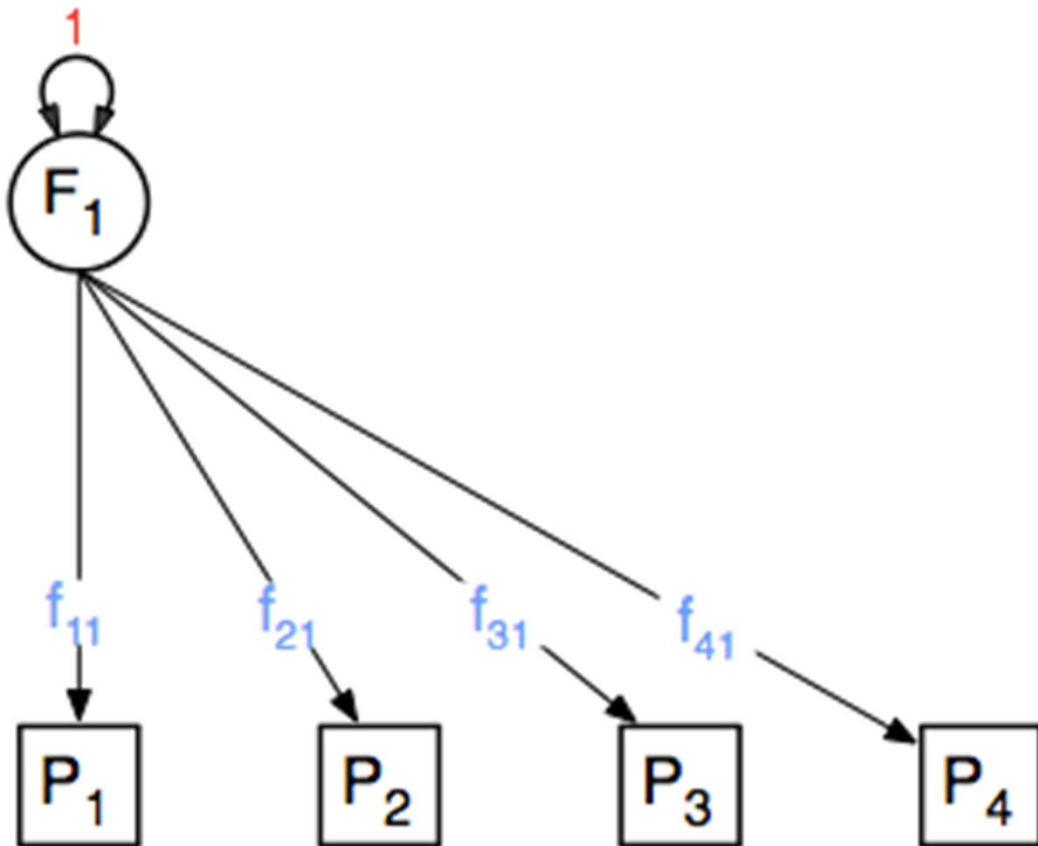
Fit Statistics

	ep	-2LL	df	chi	df	p
Saturated	180	13015.57	4507	-	-	-
EqMV	144	13084.65	4543	69.07	36	0
ACE Chol	69	13232.02	4618	-	-	-

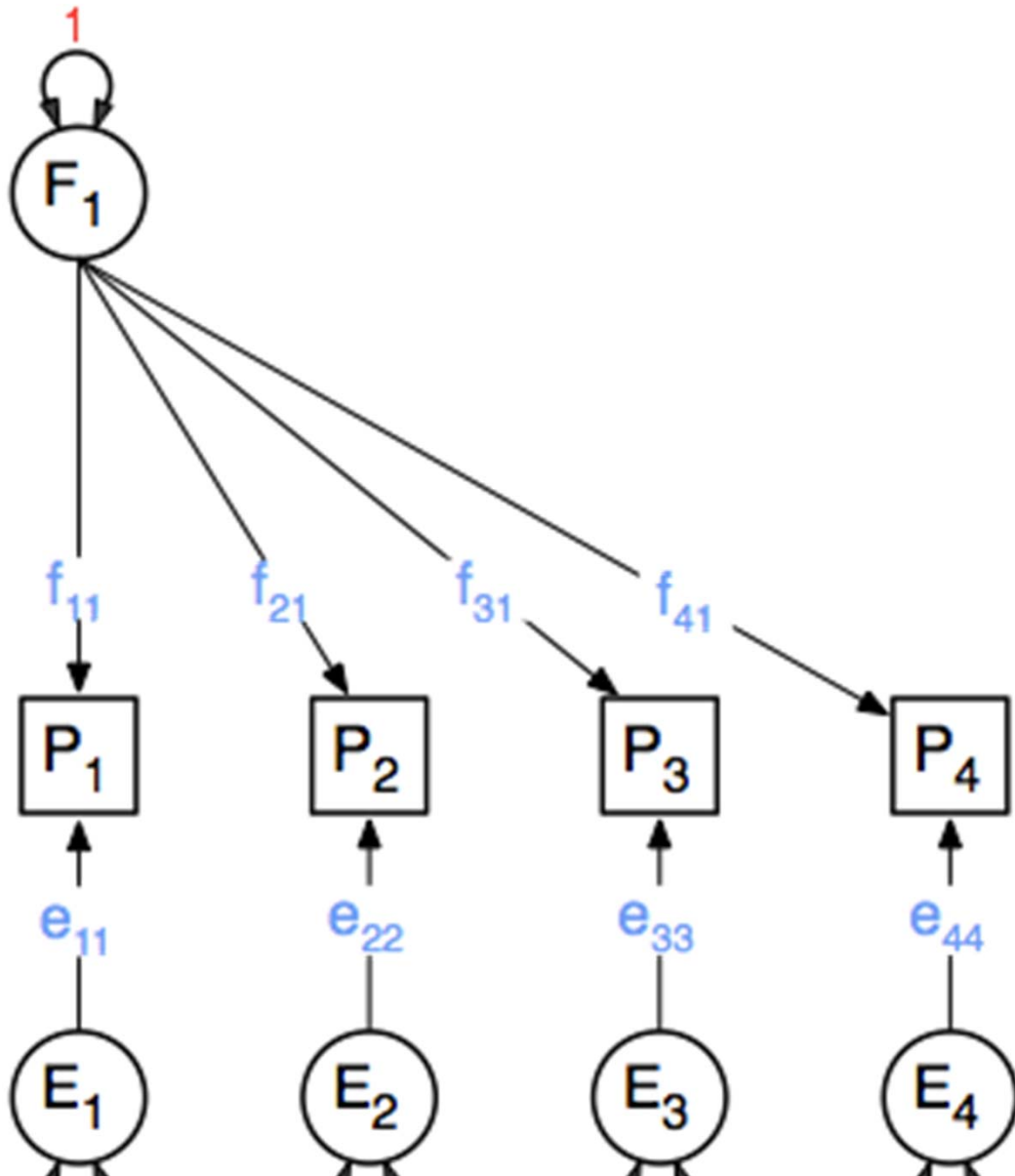
Theoretical Models

- Independent Pathway
- Common Pathway

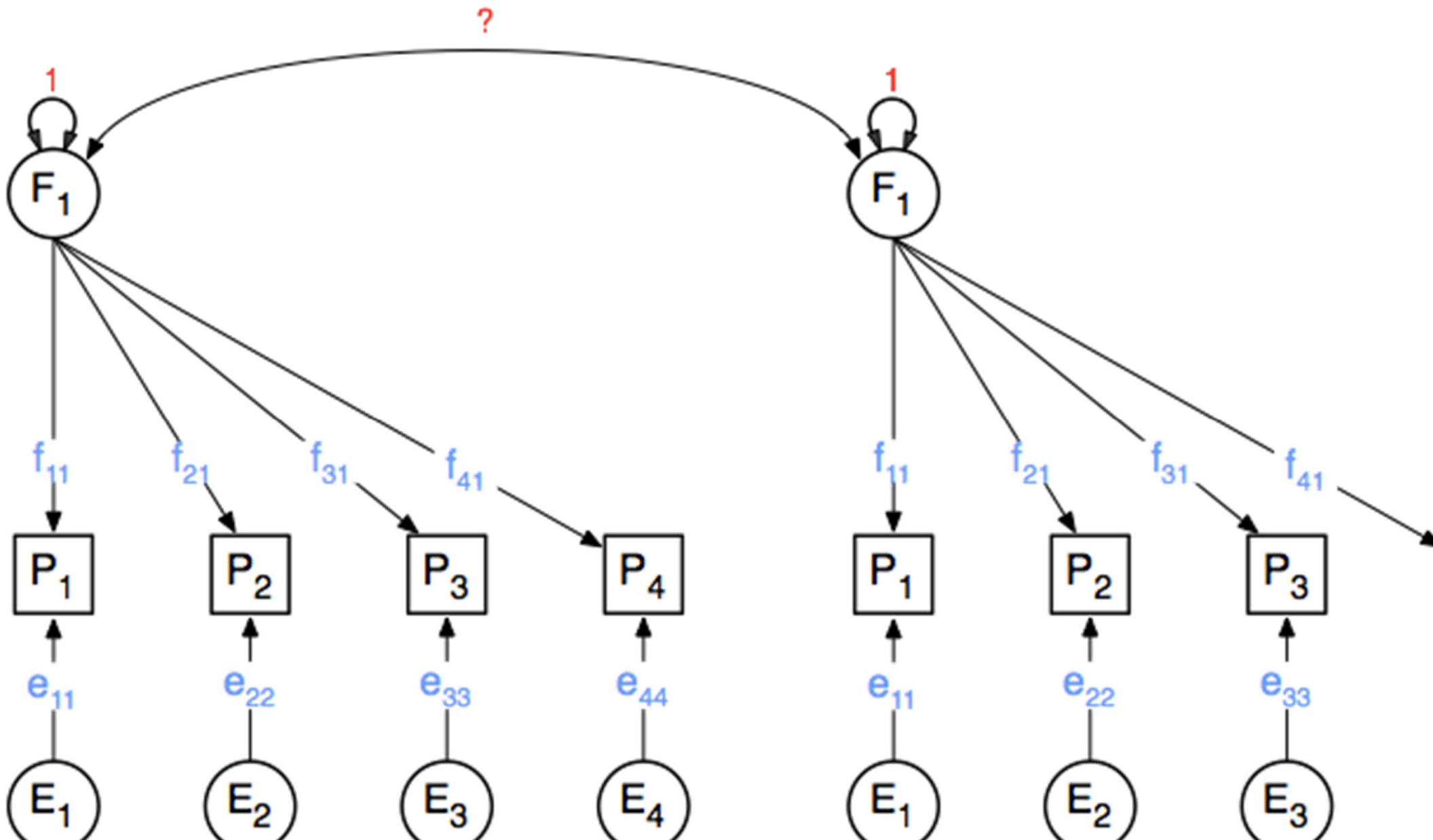
Common Factor



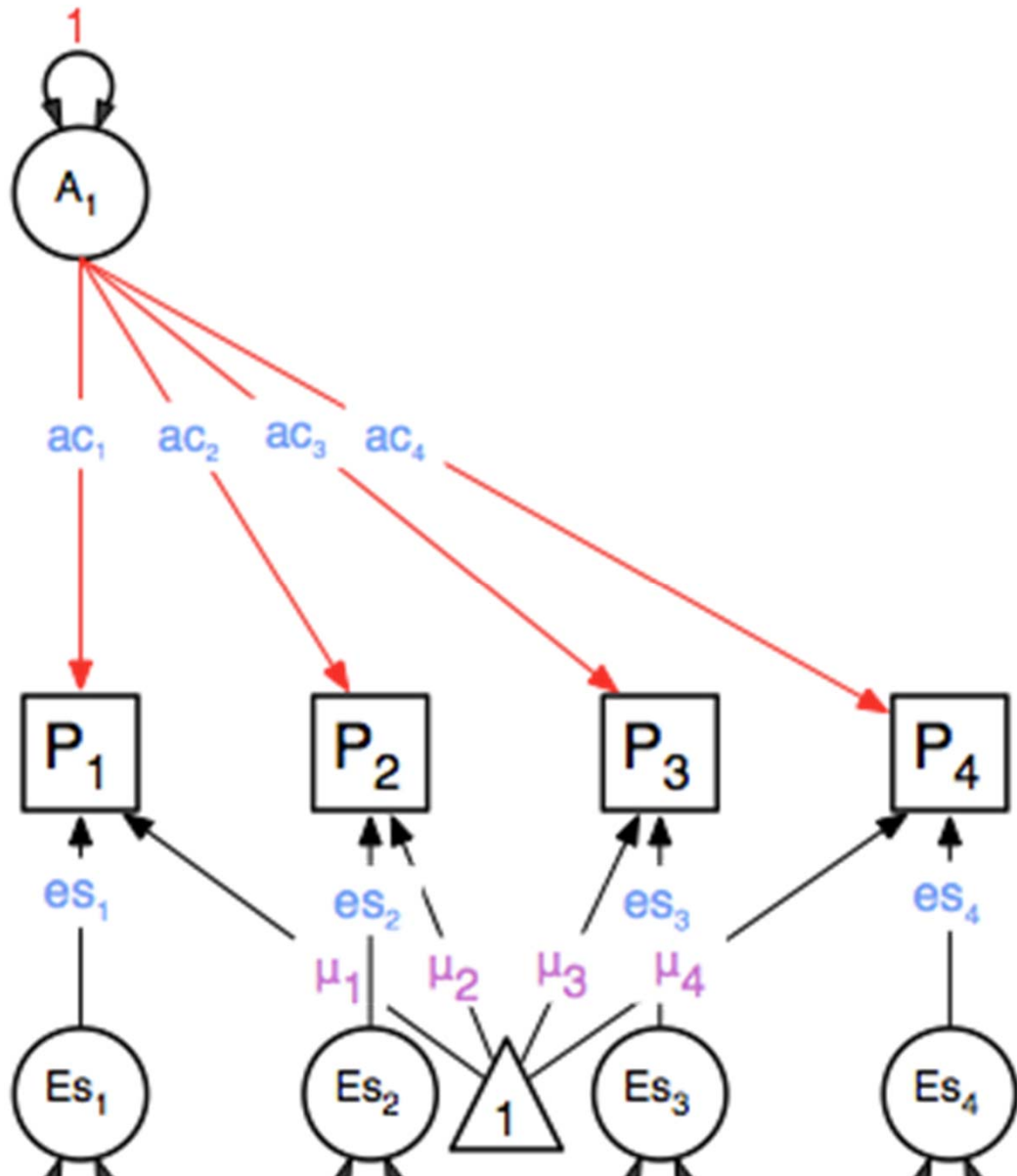
Residuals



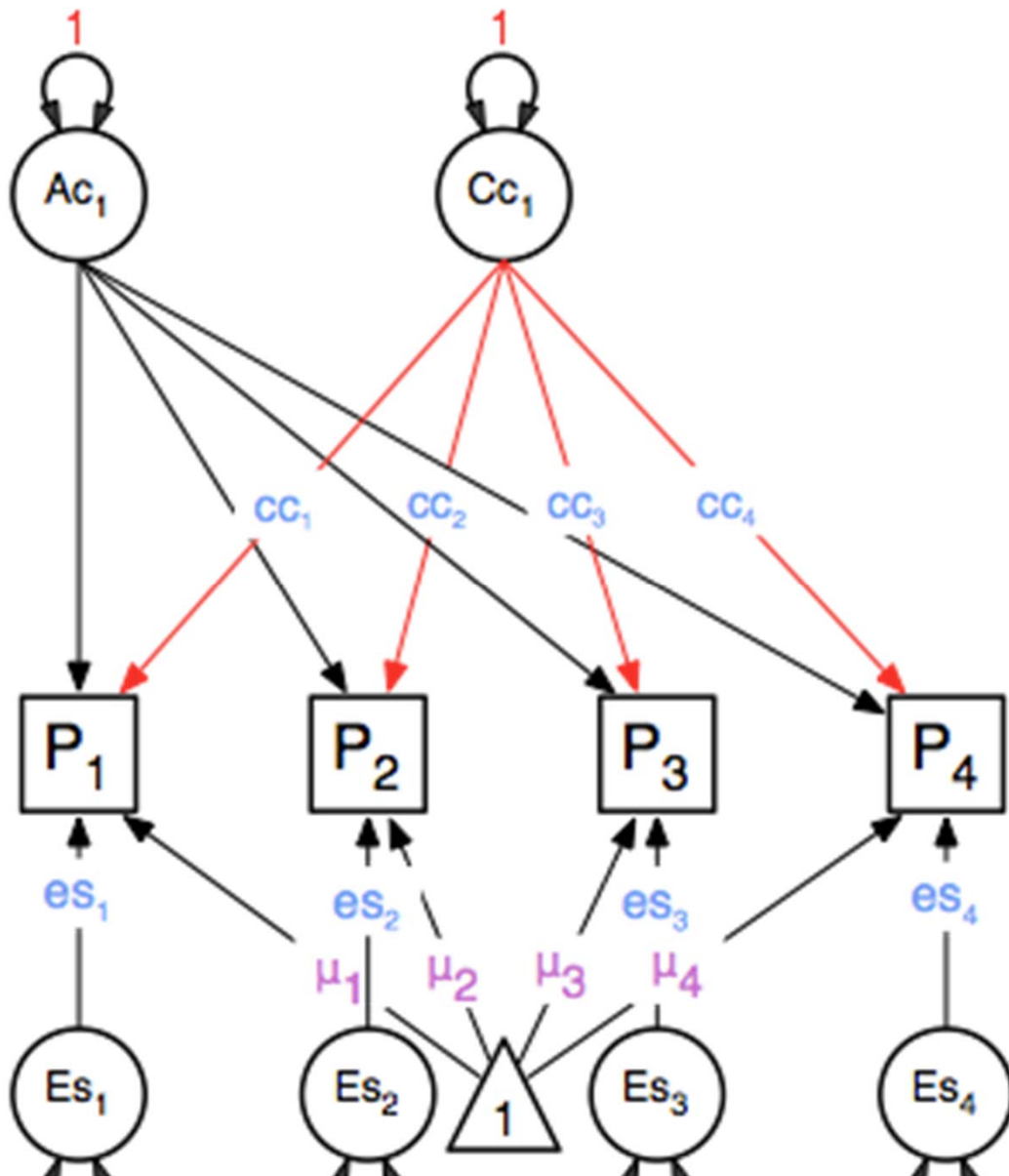
What about Twins



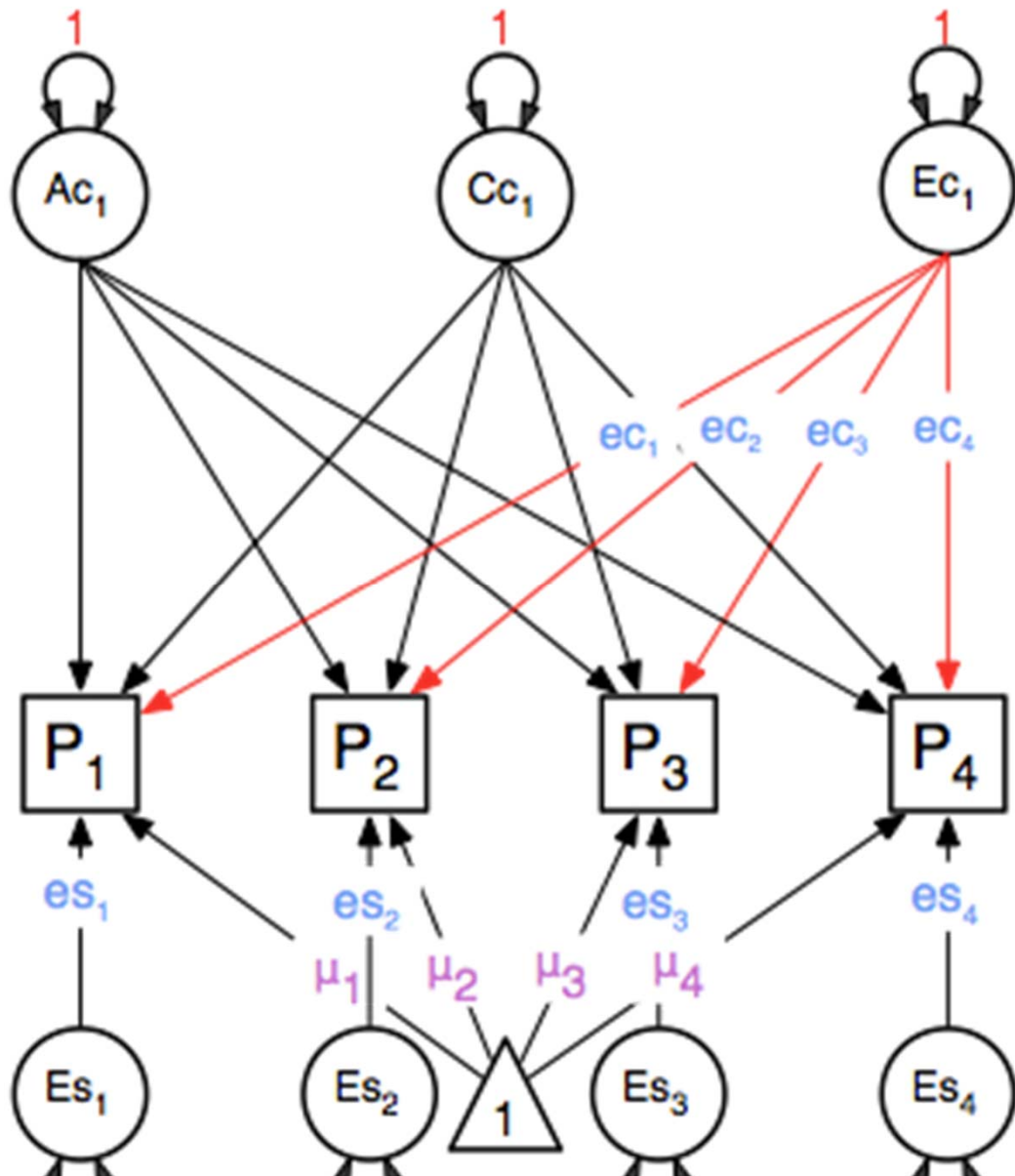
Common A Factor



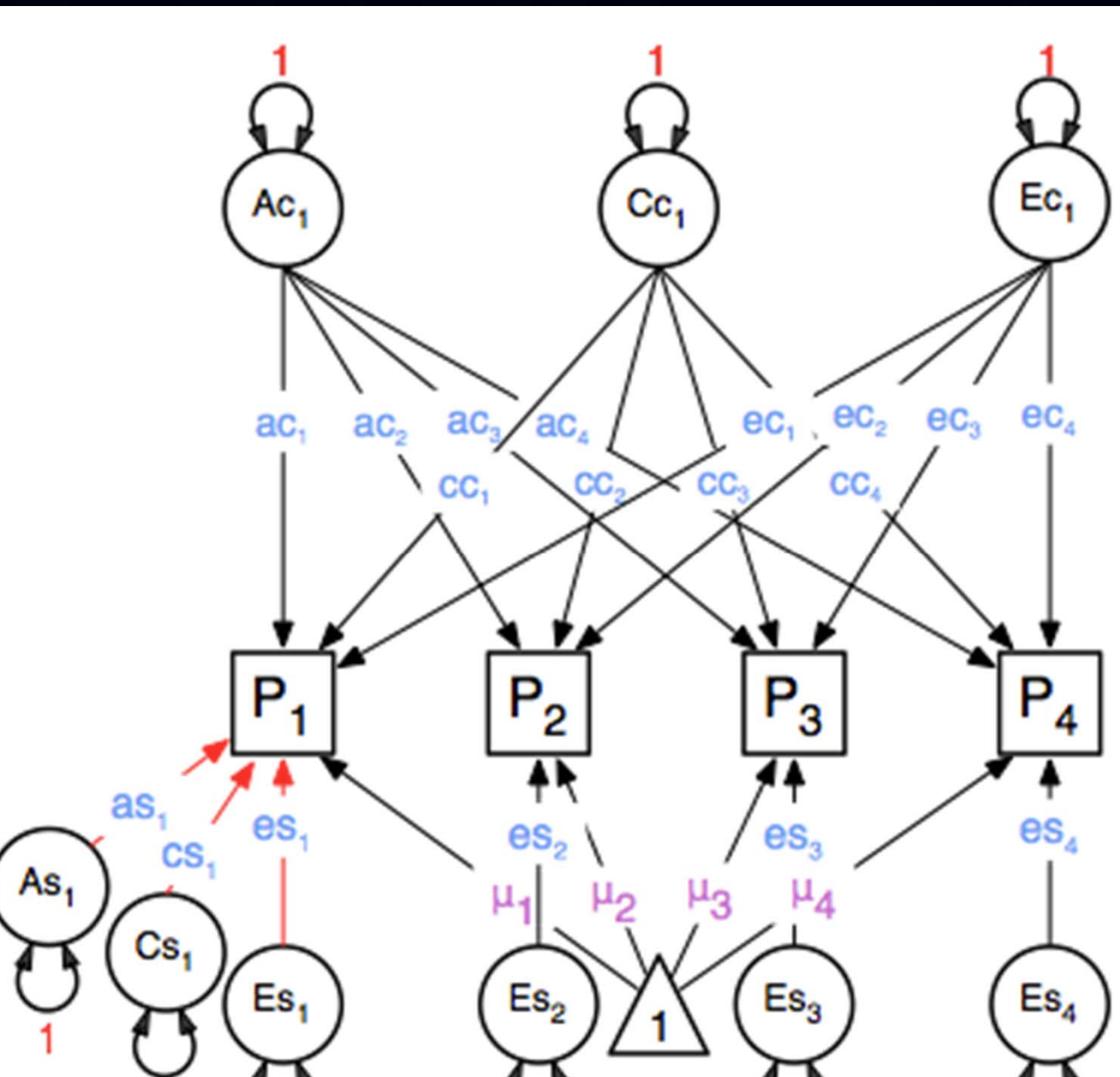
Common C Factor



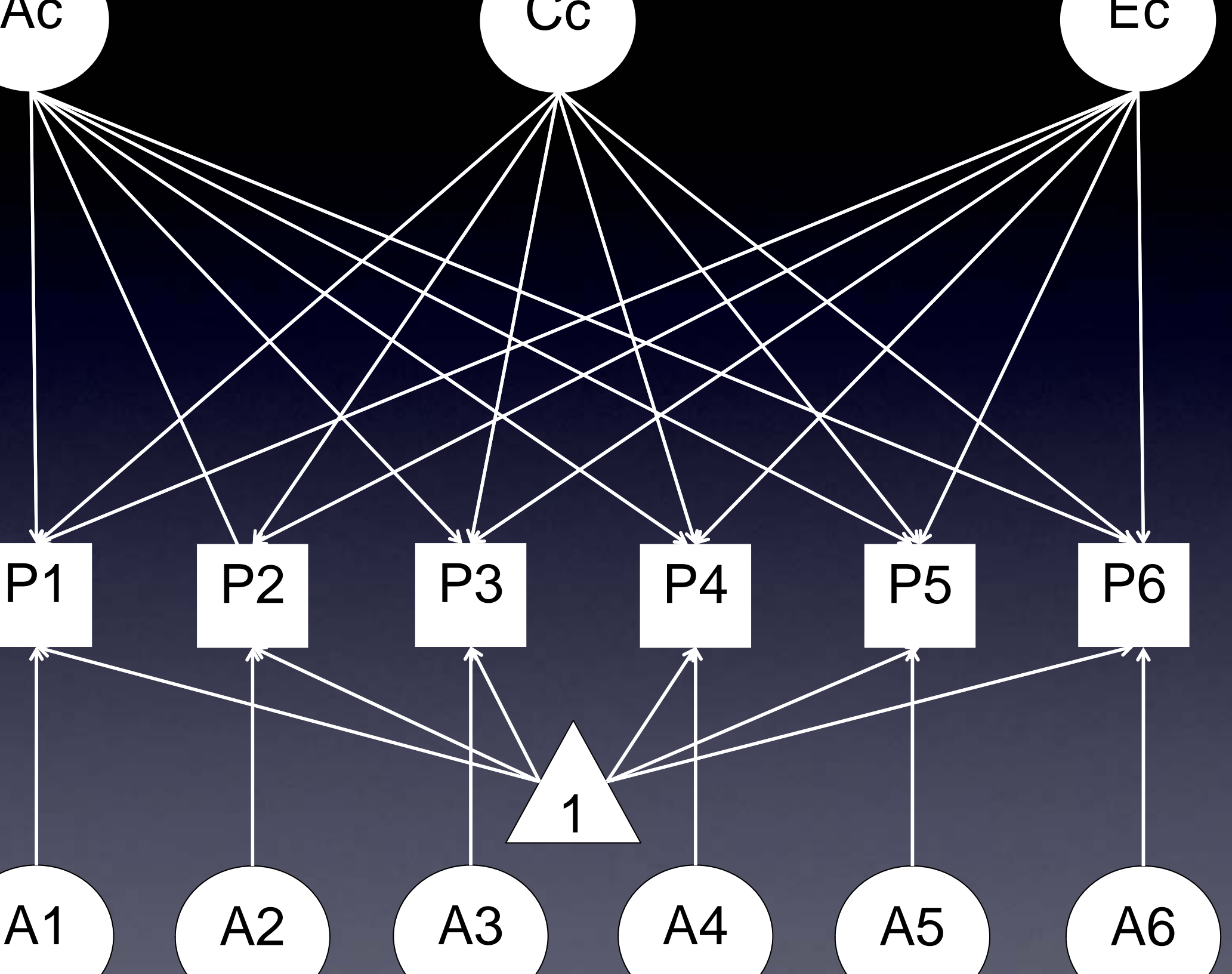
Common E Factor



ACE Specifics



Deconstructing the Independent Pathway Model

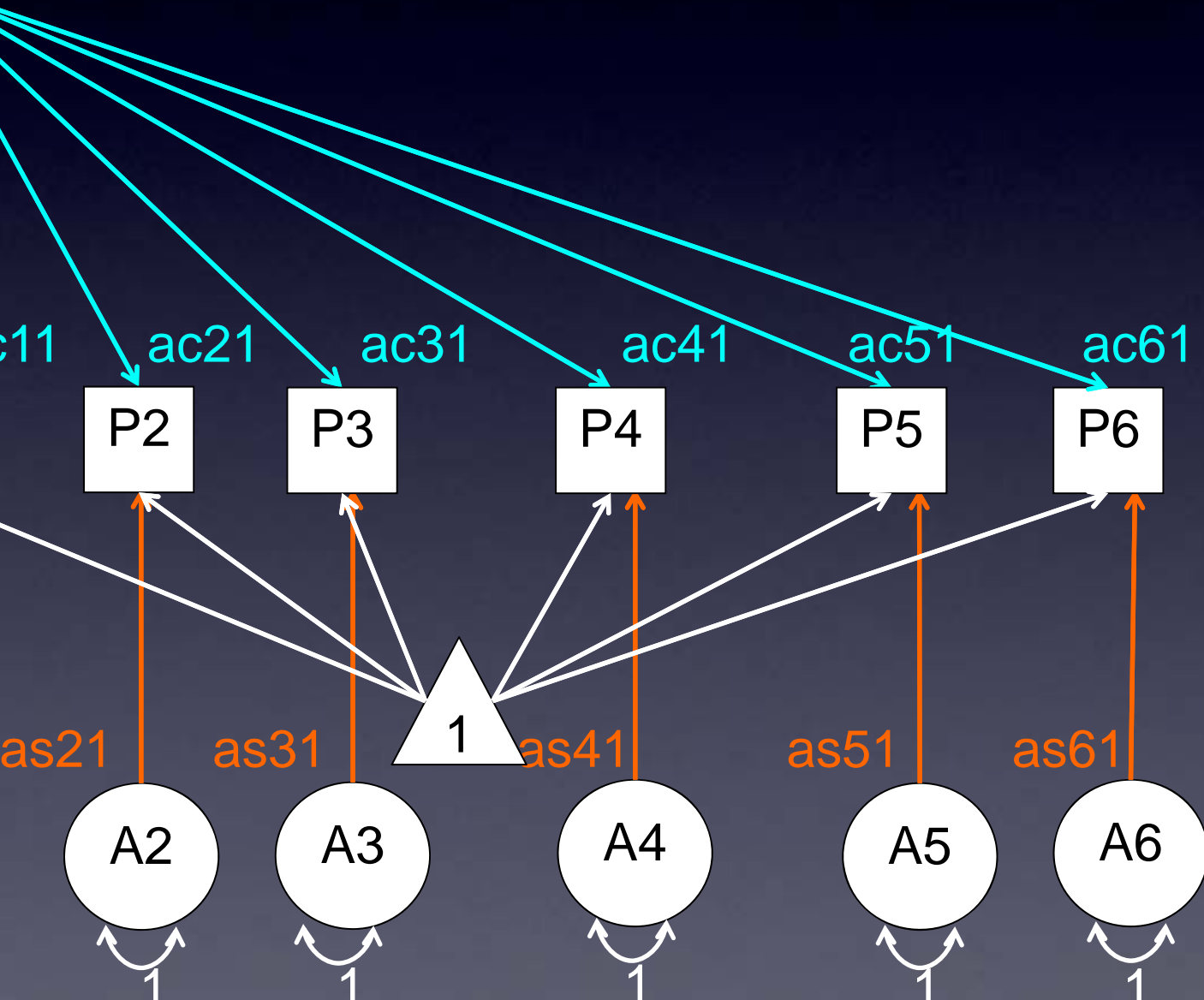


Factors

```
nv <- 6
```

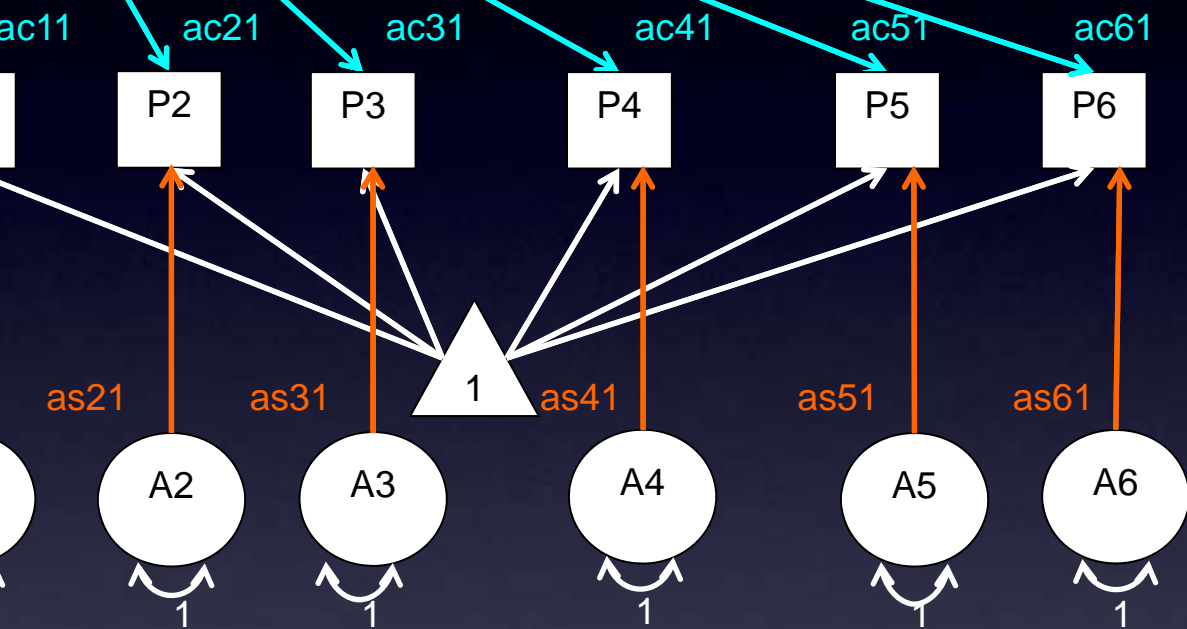
```
nf <- 1
```

```
pathAc <- mxMatrix(
  type="Full", nrow=nv,
  ncol=nf, free=TRUE,
  values=.6, labels=AcLabs,
  name="ac" )
```



```
pathAs <- mxMatrix(
  type="Diag", nrow=nv,
  ncol=nv, free=TRUE,
  values=4,
  labels=AsLabs,
  name="as" )
```

Six Specific Genetic Factors



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

```
[1,] "as_1_1" NA NA NA NA
[2,] NA "as_2_2" NA NA NA
[3,] NA NA "as_3_3" NA NA
[4,] NA NA NA "as_4_4" NA
[5,] NA NA NA NA "as_5_5"
[6,] NA NA NA NA NA "a
```



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

```
A1  
ac11  
ac21  
ac31  
ac41 %*% A1 P1 P2 P3 P4 P5  
ac51  
ac61
```

```
ac %*% t(ac)
```

```

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

```

A2	A3	A4	A5	A6		P1	P2	P3	P4	P5
0	0	0	0	0	A1	as11	0	0	0	0
as22	0	0	0	0	A2	0	as22	0	0	0
0	as33	0	0	0	A3	0	0	as33	0	0
0	0	as44	0	0	A4	0	0	0	as44	0
0	0	0	as55	0	A5	0	0	0	0	as55
0	0	0	0	as66	A6	0	0	0	0	0

as

%*%

t(as)

$ac \%^{*}\% t(ac) + as \%^{*}\% t(as), name="A")$

	A1	A2	A3	A4	A5	A6
P1	ac11 + as11	ac12	ac13	ac14	ac15	ac16
P2	ac21	ac22 + as22	ac23	ac24	ac25	ac26
P3	ac31	ac32	ac33 + as33	ac34	ac35	ac36
P4	ac41	ac42	ac43	ac44 + as44	ac45	ac46
P5	ac51	ac52	ac53	ac45	ac55 + as55	ac56
P6	ac61	ac62	ac63	ac64	ac65	ac66 + as66

6 x 6

Taking a Look at the A Variance/ Covariance Matrix

	[,1]	[,2]	[,3]	[,4]	[,5]	[,6]
[1,]	0.77	0.45	0.69	-0.59	-0.61	-0.37
[2,]	0.45	1.50	0.50	-0.43	-0.45	-0.27
[3,]	0.69	0.50	0.84	-0.65	-0.68	-0.41

```
model : IndACE, 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 : IndACE, 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 : IndACE, matrix:ec
      [, 1]
[1, ] [ec_1_1]
[2, ] [ec_2_1]
[3, ] [ec_3_1]
[4, ] [ec_4_1]
[5, ] [ec_5_1]
```

```
[as_1_1] 0 0 0 0 0
0 [as_2_2] 0 0 0 0
0 0 [as_3_3] 0 0 0
0 0 0 [as_4_4] 0 0
0 0 0 0 [as_5_5] 0
0 0 0 0 0 [as_6_6]
```

l : IndACE, matrix:cs

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

l : IndACE, matrix:es

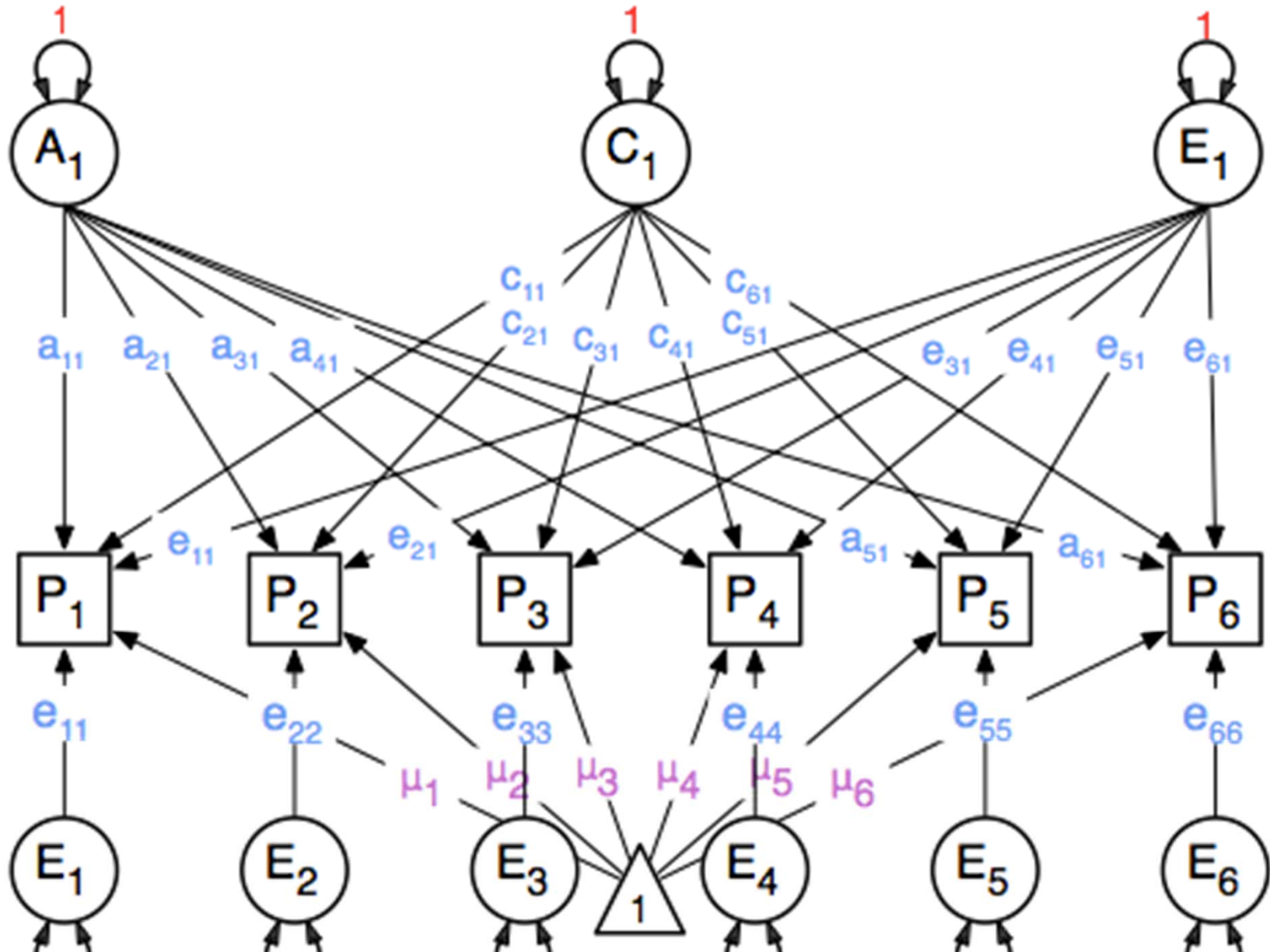
```
[, 1] [, 2] [, 3] [, 4] [, 5] [, 6]
[es_1_1] 0 0 0 0 0 0
0 [es_2_2] 0 0 0 0
0 0 [es_3_3] 0 0 0
0 0 0 [es_4_4] 0 0
0 0 0 0 [es_5_5] 0
0 0 0 0 0 [es_6_6]
```

l : IndACE, matrix:Mean

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 $nv \times 1$	cc $nv \times 1$	ec $nv \times 1$
Residual Factors	as $nv \times nv$	cs $nv \times nv$	es $nv \times nv$

Fit Statistics

	ep	-2LL	df	chi	df	p
Saturated	180	13015.57	4507	-	-	-
EqMV	144	13084.65	4543	69.07	36	0
CholACE	69	13232.02	4618	-	-	-
IndACE	42	13297.49	4645	65.47	27	0

```
| "Matrix iSD %*% ac"  
  stPathAc1  
Q      -0.6131  
Q      -0.3481  
Ach    -0.7855  
tProb  0.5749  
att    0.6569  
per    0.4177
```

```
| "Matrix iSD %*% cc"  
  stPathCc1  
Q      -0.4891  
Q      -0.4067  
Ach    -0.4090  
tProb -0.2553  
att    -0.1717  
per    -0.2312
```

```
| "Matrix iSD %*% ec"  
  stPathEc1  
Q      -0.0207  
Q      -0.0985  
Ach    -0.0595  
tProb  0.5595  
att    0.3708
```

[1] "Matrix iSD %*% as"

	stPathAs1	stPathAs2	stPathAs3	stPathAs4	stPathAs5	stPathAs6
/IQ	0.3013	0.0000	0.0000	0.0000	0.0000	0.0000
PIQ	0.0000	0.6554	0.0000	0.0000	0.0000	0.0000
EdAch	0.0000	0.0000	0.2458	0.0000	0.0000	0.0000
AttProb	0.0000	0.0000	0.0000	0.4418	0.0000	0.0000
natt	0.0000	0.0000	0.0000	0.0000	0.4949	0.0000
lyper	0.0000	0.0000	0.0000	0.0000	0.0000	0.7599

[1] "Matrix iSD %*% cs"

	stPathCs1	stPathCs2	stPathCs3	stPathCs4	stPathCs5	stPathCs6
/IQ	0.2813	0.0000	0.0000	0.0000	0.0000	0.0000
PIQ	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
EdAch	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
AttProb	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
natt	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
lyper	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

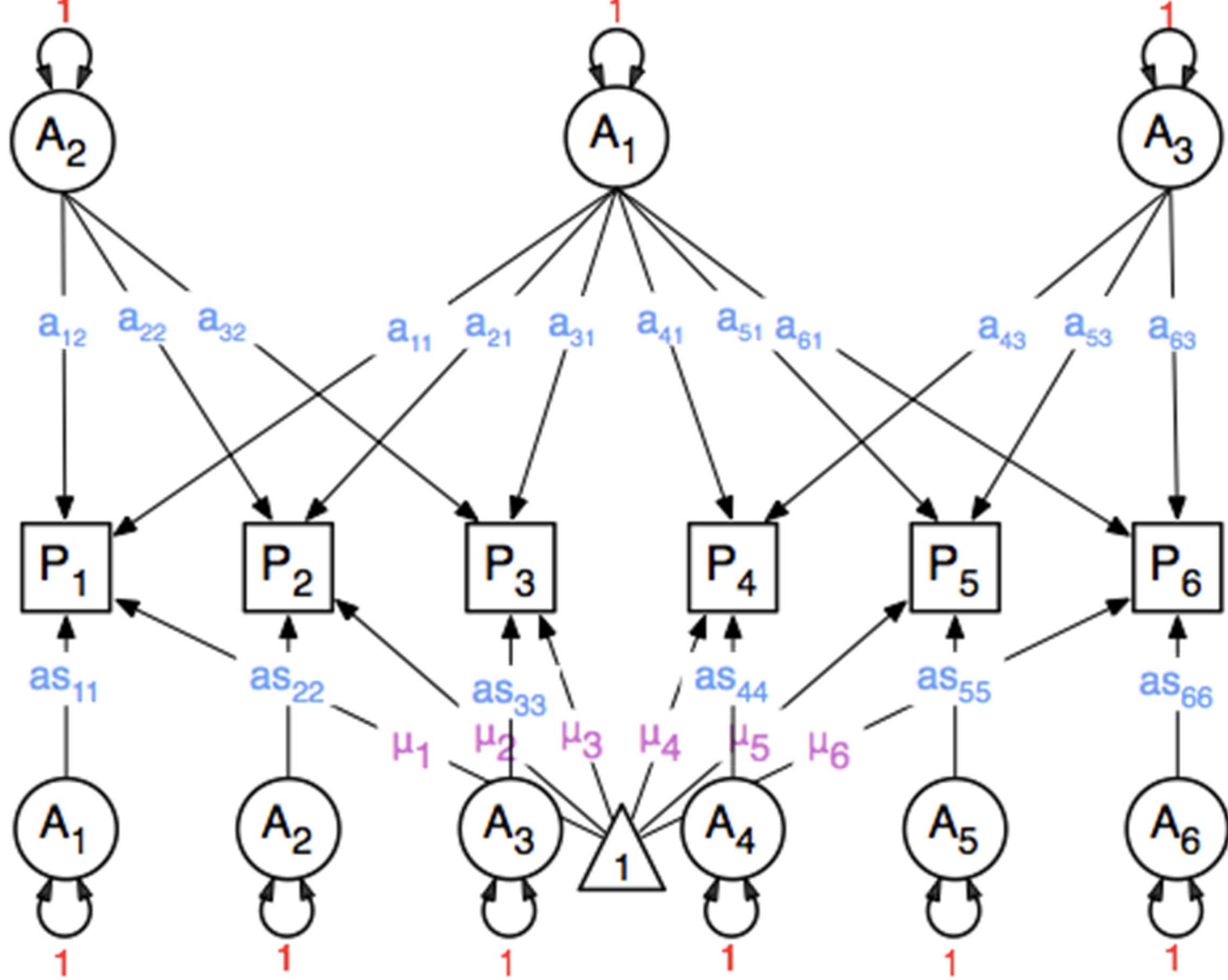
[1] "Matrix iSD %*% es"

	stPathEs1	stPathEs2	stPathEs3	stPathEs4	stPathEs5	stPathEs6
/IQ	0.4632	0.0000	0.0000	0.0000	0.0000	0.0000
PIQ	0.0000	0.5236	0.0000	0.0000	0.0000	0.0000
EdAch	0.0000	0.0000	0.3896	0.0000	0.0000	0.0000
AttProb	0.0000	0.0000	0.0000	0.3099	0.0000	0.0000
natt	0.0000	0.0000	0.0000	0.0000	0.3957	0.0000

Theory

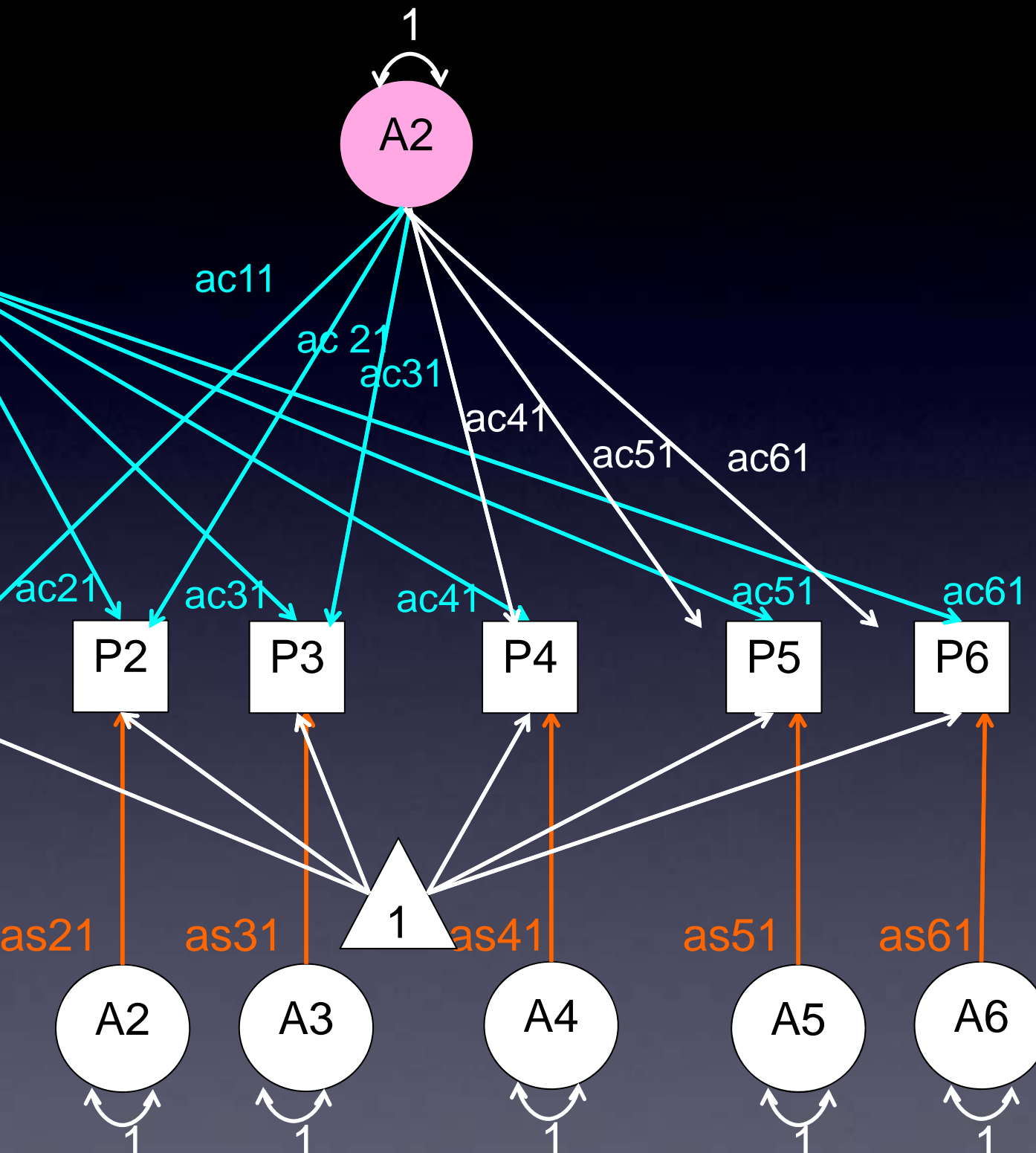
- Intelligence Factor
- Attention Problem Factor

- General Factor?



Are we able to fit a
second factor?

Six Specific Genetic Factors



```
nfAc <- 2
```

```
AcLabs <-
paste("ac", 1:nv, rep(1:nv),
      , each=nv), sep="_"
pathAc <- mxMatrix(
type="Full", nrow=
ncol=nfAc,
free=c(T,T,T,T,T,T,
,F),
values=c(rep(.5, nv
,3), rep(0,3)),
labels=AcLabs,
name="ac" )
```


Previous Model into New Model and change name

```
IC_1E_Model <- mxModel( IndAceFit, name="Ind2Ace" )
```

Dimension of Additive Genetic Factor Matrix Ac

2

Labels for all Factor Loadings in Ac

```
Ac2Labs <- paste("ac", 1:nv, rep(1:nfAc, each=nv), sep="_")
```

Free and Values for 2 Additive Genetic Factors

```
Ac2Free values
```

```
  A2      A1  A2
```

```
T  T      P1  .5  .5
```

```
T  T      P2  .5  .5
```

```
T  T      P3  .5  .5
```

```
T  F      P4  .5  0
```

```
T  F      P5  .5  0
```

```
T  F      P6  .5  0
```

```
Ac2Free <- c(T, T, T, T, T, T, T, T, T, F, F, F)
```

```
Ac2Values <- c(rep(.5, nv), rep(.5, 3), rep(0, 3))
```

```
Ac2Path <- mxMatrix( type="Full", nrow=nv, ncol=nfAc,
  Ac2Free, values=Ac2Values, labels=Ac2Labs, name="ac" )
```

Replace Old matrix named 'ac' by Newly Created Object 'pathAc'

to be done in every MxModel in which it appears (MZ, DZ and overall)

```
IC_1E_Model$MZ$ac <- pathAc
```

```
IC_1E_Model$DZ$ac <- pathAc
```

```
model: Ind2Ace, matrix: ac
      [, 1]      [, 2]
[1, ] [ac_1_1] [ac_1_2]
[2, ] [ac_2_1] [ac_2_2]
[3, ] [ac_3_1] [ac_3_2]
[4, ] [ac_4_1] 0
[5, ] [ac_5_1] 0
[6, ] [ac_6_1] 0
```

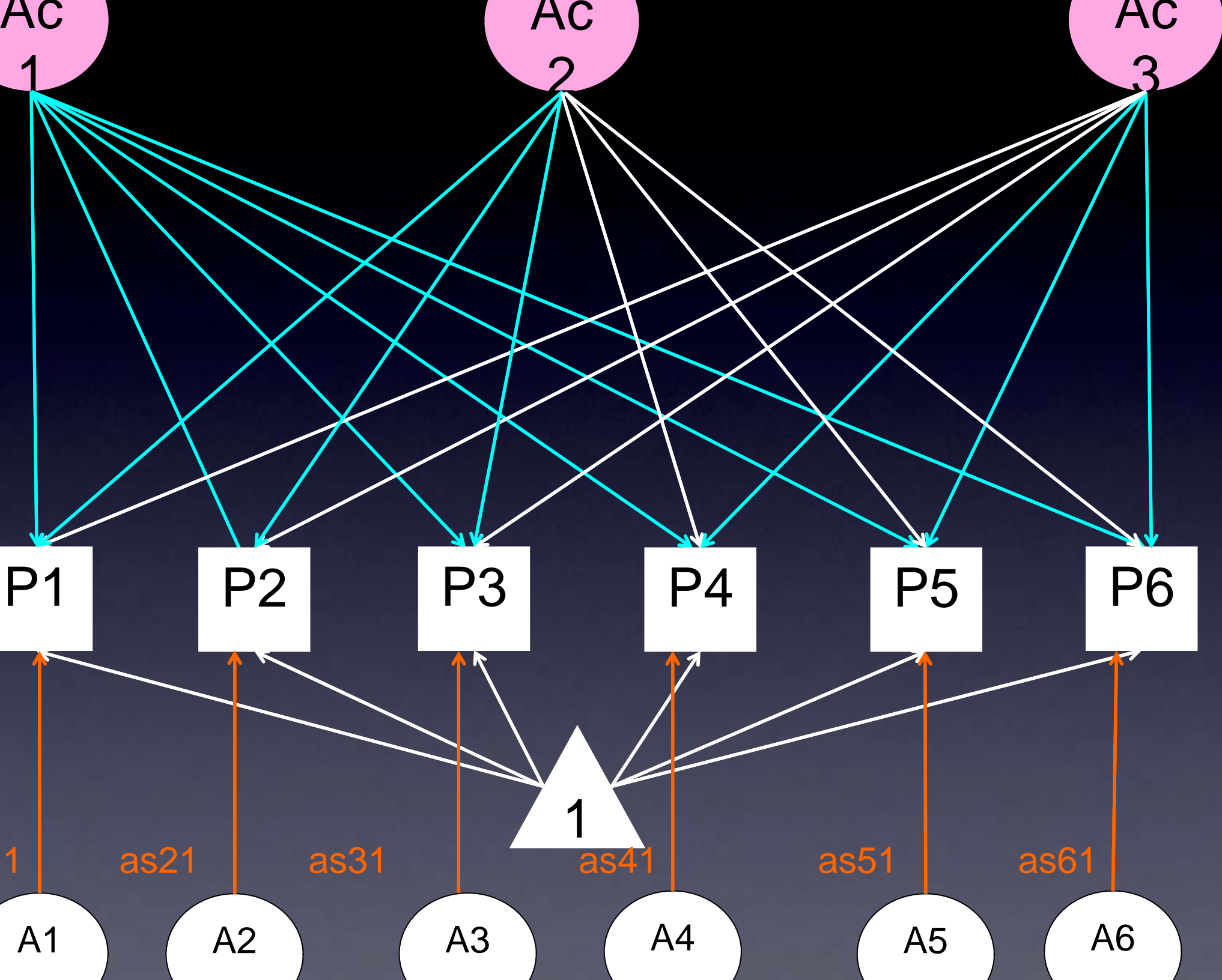
```
model: Ind2Ace, matrix: cc
      [, 1]
[1, ] [cc_1_1]
[2, ] [cc_2_1]
[3, ] [cc_3_1]
[4, ] [cc_4_1]
[5, ] [cc_5_1]
[6, ] [cc_6_1]
```

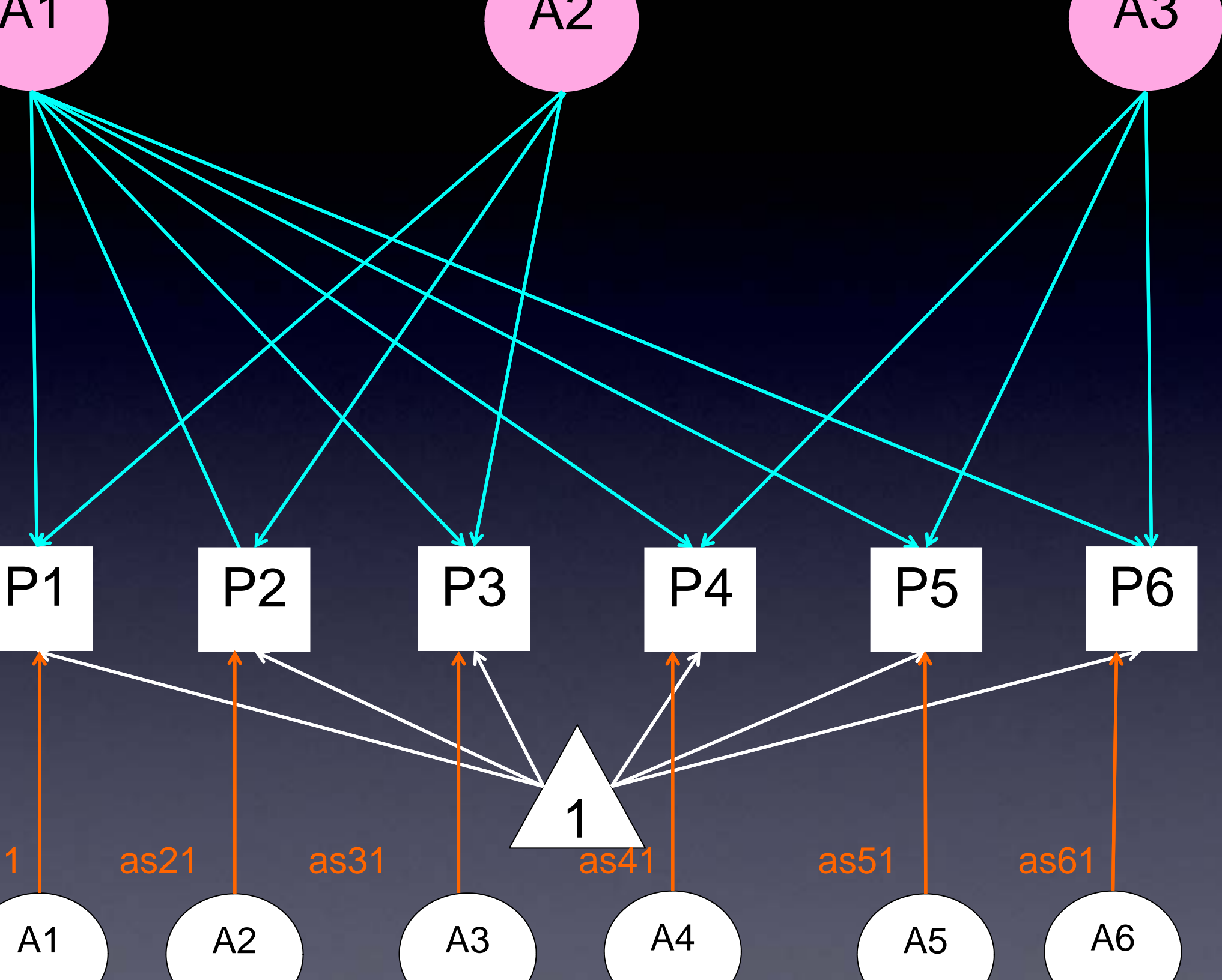
```
model: Ind2Ace, matrix: ec
      [, 1]
[1, ] [ec_1_1]
[2, ] [ec_2_1]
[3, ] [ec_3_1]
[4, ] [ec_4_1]
[5, ] [ec_5_1]
[6, ] [ec_6_1]
```

Fit Statistics

	ep	-2LL	df	chi	df	p
Saturated	180	13015.57	4507	-	-	-
EqMV	144	13084.65	4543	69.07	36	0
CholACE	69	13232.02	4618	-	-	-
IndACE	42	13297.49	4645	65.47	27	0
nd_2A_1C_1E	45	13261.75	4642	29.73	24	0.1

What about a third
factor?





Your Turn

- Add a third genetic factor loading on Attention Problem measures (AttProb, Inatt & Hyper)
- Does it further improve the fit of the model?
- How much of the variance is accounted for by different factors?

Fit Statistics

	ep	-2LL	df	chi	df	p
Saturated	180	13015.57	4507	-	-	-
EqMV	144	13084.65	4543	69.07	36	0
CholACE	69	13232.02	4618	-	-	-
IndACE	42	13297.49	4645	65.47	27	0
Ind_2A_1C_1E	45	13261.75	4642	29.73	24	0.1
Ind_3A_1C_1E	48	13242.40	4639	10.38	21	0.9


```
rix iSD %*% ac
stPathAc1 stPathAc2 stPathAc3
0.3087 0.5740 0.0000
0.1113 0.4504 0.0000
0.5613 0.5608 0.0000
-0.5277 0.0000 0.5966
-0.8466 0.0000 0.0930
-0.3581 0.0000 0.4311
```

```
rix iSD %*% cc"
stPathCc1
-0.4671
-0.2615
-0.3784
0.0559
-0.0374
-0.0356
```

```
rix iSD %*% ec"
stPathEc1
-0.1027
-0.1639
-0.1198
0.4424
0.3272
0.2674
```

matrix iSD %*% as

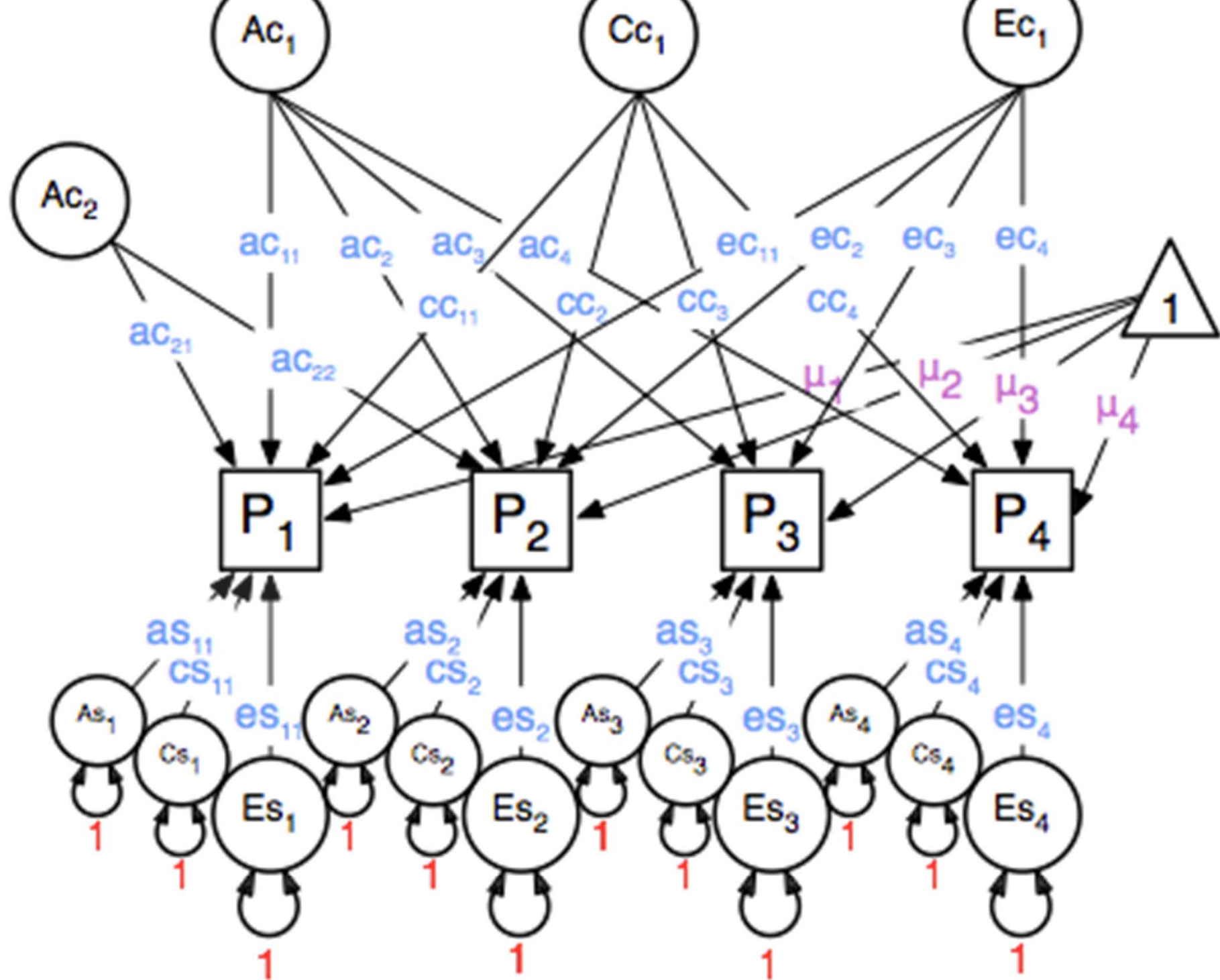
stPathAs1	stPathAs2	stPathAs3	stPathAs4	stPathAs5	stPathAs6
0.1610	0.0000	0.0000	0.0000	0.0000	0.0000
0.0000	0.5908	0.0000	0.0000	0.0000	0.0000
0.0000	0.0000	0.2555	0.0000	0.0000	0.0000
0.0000	0.0000	0.0000	0.2327	0.0000	0.0000
0.0000	0.0000	0.0000	0.0000	0.1538	0.0000
0.0000	0.0000	0.0000	0.0000	0.0000	0.7365

matrix iSD %*% cs

stPathCs1	stPathCs2	stPathCs3	stPathCs4	stPathCs5	stPathCs6
0.3340	0.0000	0.0000	0.0000	0.0000	0.0000
0.0000	0.2726	0.0000	0.0000	0.0000	0.0000
0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

matrix iSD %*% es

stPathEs1	stPathEs2	stPathEs3	stPathEs4	stPathEs5	stPathEs6
0.4572	0.0000	0.0000	0.0000	0.0000	0.0000
0.0000	0.5160	0.0000	0.0000	0.0000	0.0000
0.0000	0.0000	0.3844	0.0000	0.0000	0.0000
0.0000	0.0000	0.0000	0.3357	0.0000	0.0000
0.0000	0.0000	0.0000	0.0000	0.3774	0.0000
0.0000	0.0000	0.0000	0.0000	0.0000	0.2658

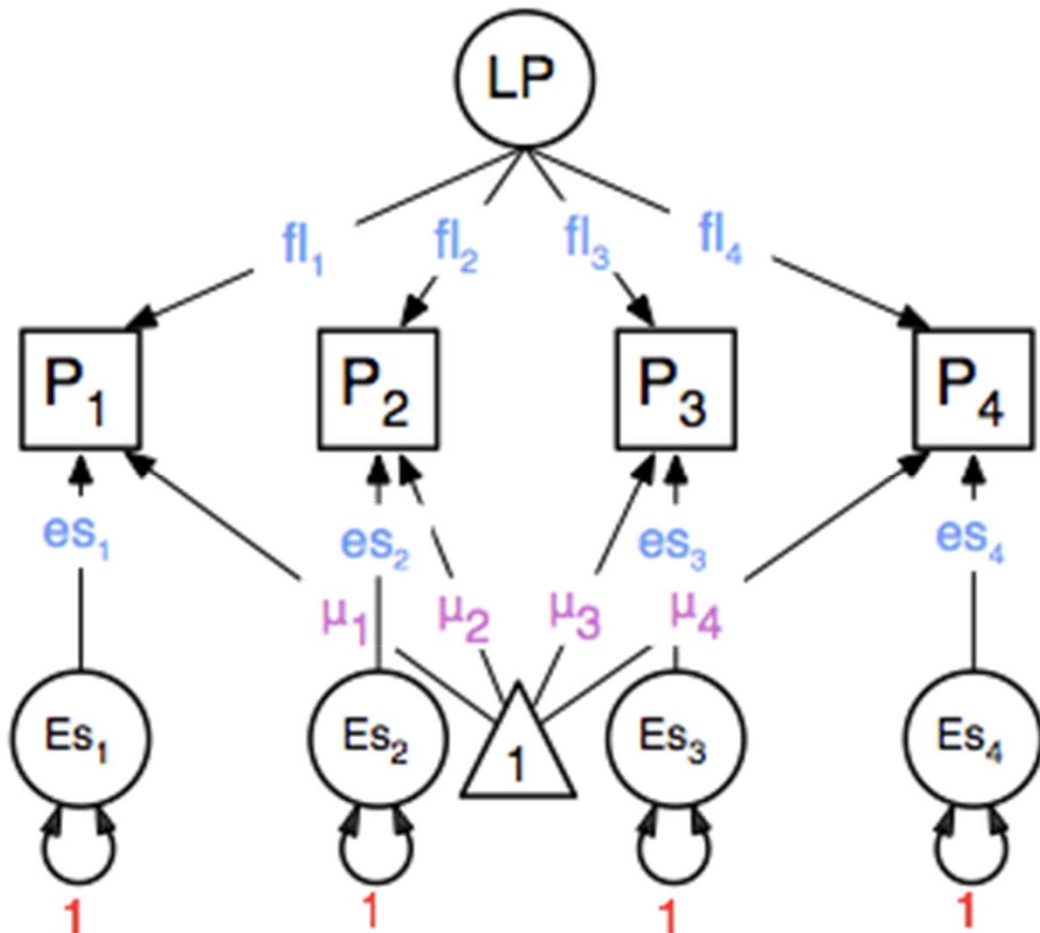


$$\text{var}P_1 = ac_{11}^2 + cc_{11}^2 + ec_{11}^2 + as_{11}^2 + cs_{11}^2 + es_{11}^2 + ac_{21}^2 +$$

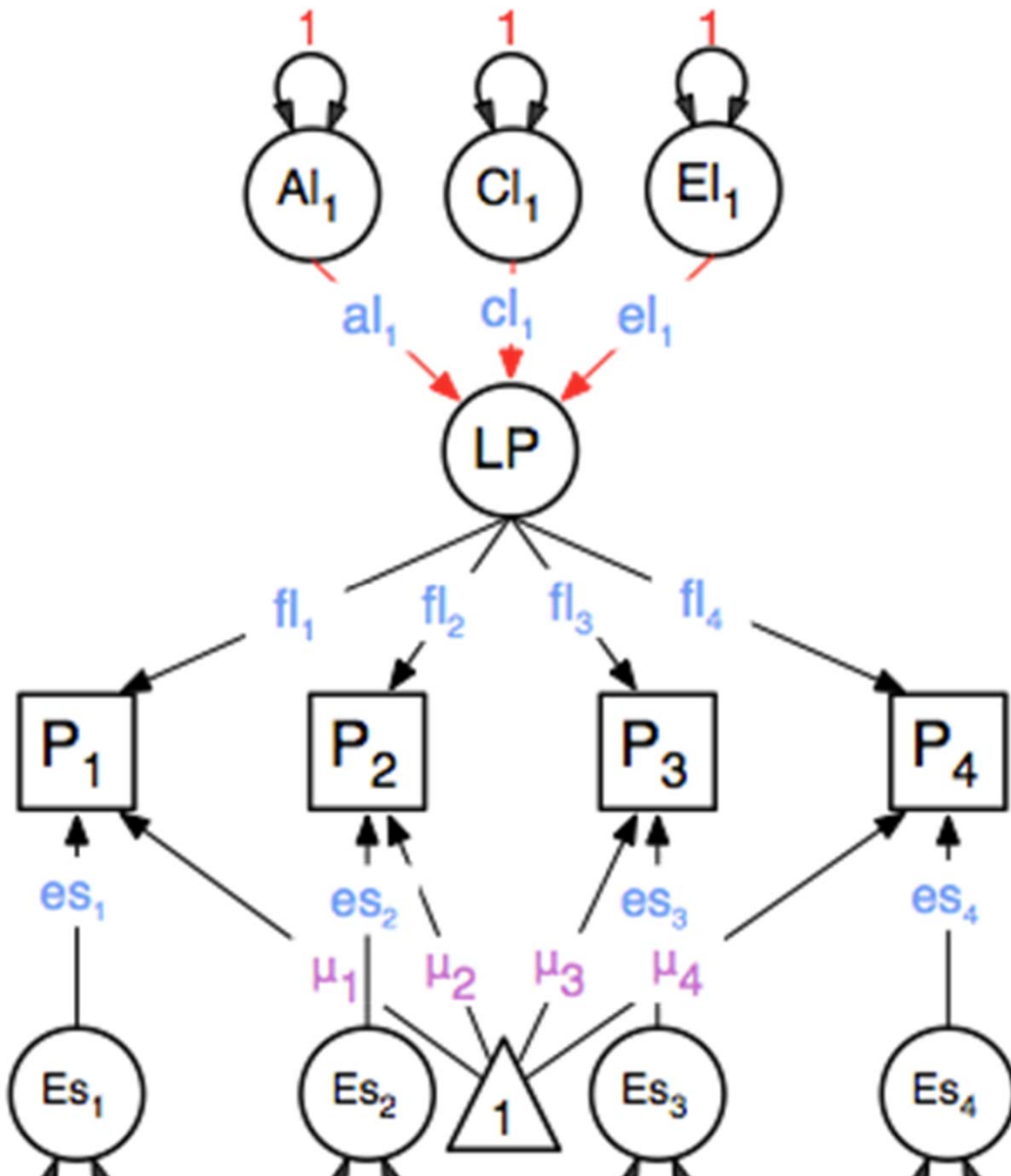
Identification

- 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.

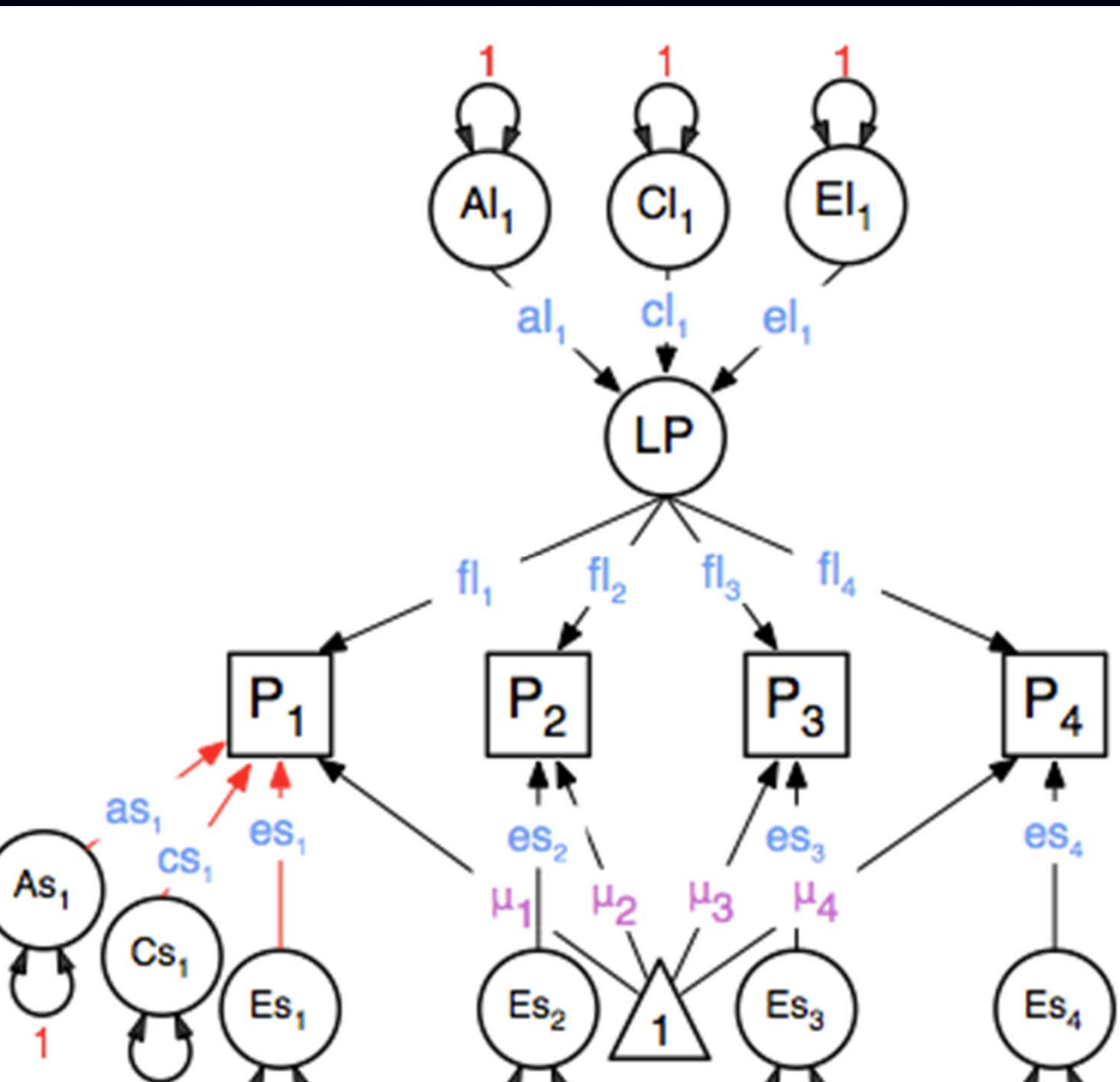
Factor Loadings



Role of Latchin Phenotype



ACE Specifics



```
> parameterSpecifications (ComAceFit)
```

```
model:ComACE, matrix:a1
```

```
    [, 1]  
[1, ] [a1_1_1]
```

```
model:ComACE, matrix:c1
```

```
    [, 1]  
[1, ] [c1_1_1]
```

```
model:ComACE, matrix:e1
```

```
    [, 1]  
[1, ] [e1_1_1]
```

```
model:ComACE, matrix:f1
```

```
    [, 1]  
[1, ] [f_1_1]  
[2, ] [f_2_1]  
[3, ] [f_3_1]  
[4, ] [f_4_1]  
[5, ] [f_5_1]  
[6, ] [f_6_1]
```



```
[as_1_1] 0 0 0 0 0
0 [as_2_2] 0 0 0 0
0 0 [as_3_3] 0 0 0
0 0 0 [as_4_4] 0 0
0 0 0 0 [as_5_5] 0
0 0 0 0 0 [as_6_6]
```

l : ComACE, matrix:cs

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

l : ComACE, matrix:es

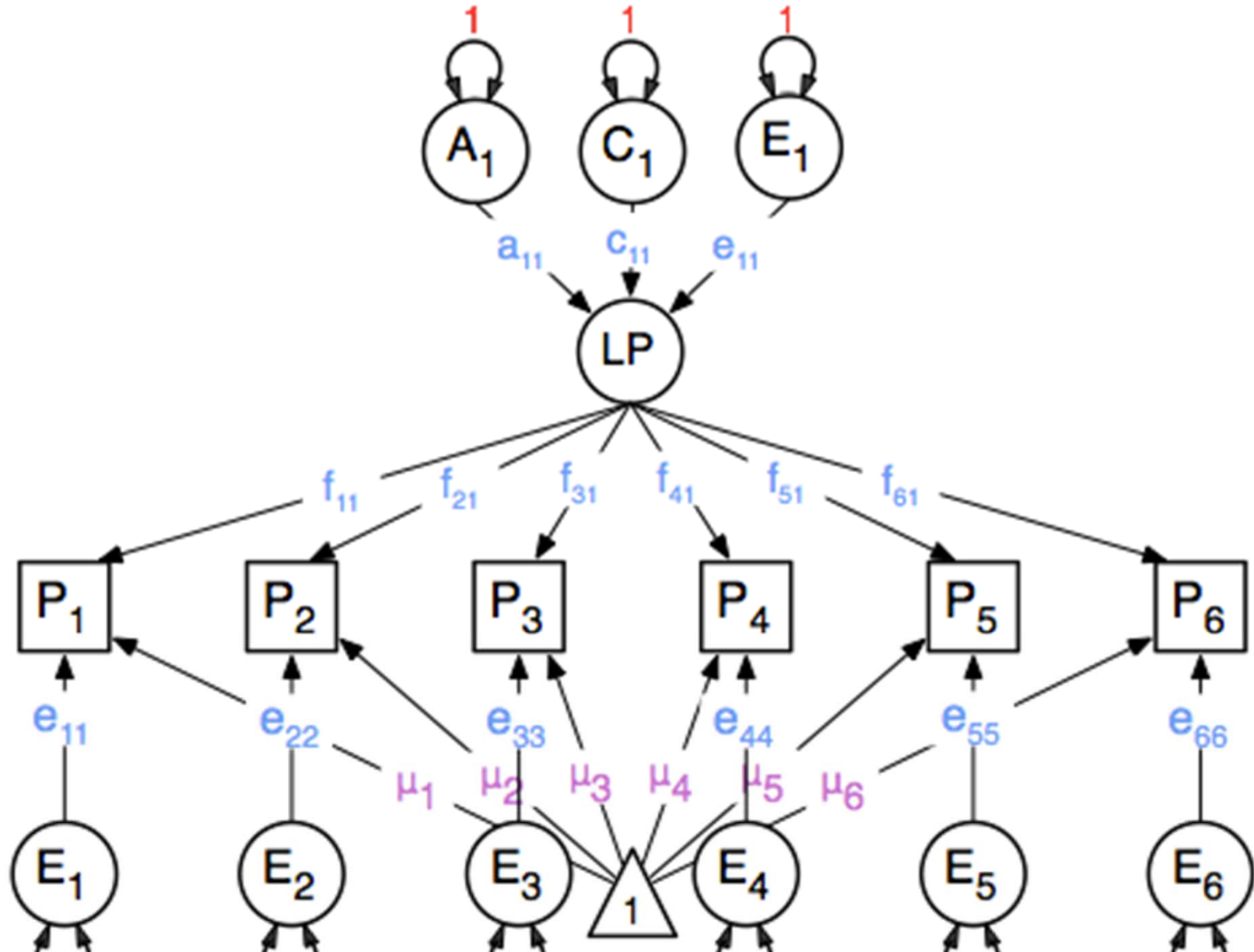
```
[, 1] [, 2] [, 3] [, 4] [, 5] [, 6]
[es_1_1] 0 0 0 0 0 0
0 [es_2_2] 0 0 0 0
0 0 [es_3_3] 0 0 0
0 0 0 [es_4_4] 0 0
0 0 0 0 [es_5_5] 0
0 0 0 0 0 [es_6_6]
```

l : ComACE, matrix:Mean

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 1×1	c_1 1×1	e_1 1×1	f_1 $n_v \times 1$
Residual Factors	a_s $n_v \times n_v$	c_s $n_v \times n_v$	e_s $n_v \times n_v$	

Fit Statistics

	ep	-2LL	df	chi	df	p
Saturated	180	13015.57	4507	-	-	-
EqMV	144	13084.65	4543	69.07	36	0
CholACE	69	13232.02	4618	-	-	-
IndACE	42	13297.49	4645	65.47	27	0
Ind_2A_1C_1E	45	13261.75	4642	29.73	24	0.1
Ind_3A_1C_1E	48	13242.40	4639	10.38	21	0.9
ComAce	33	13620.02	4655	388	37	0

formatOutputMatrices (ComAceFit, ACEpathMatricesLP, ACEpathLabelsLP, Vars

"Matrix a1"

stPathA11

0.9173

"Matrix c1"

stPathC11

0.0001

"Matrix e1"

stPathE11

0.3982

formatOutputMatrices (ComAceFit, ACEpathMatricesFL, ACEpathLabelsFL, Vars

"Matrix iSD %*% fl"

stPathF11

-0.5267

-0.3720

-0.6790

prob 0.6901

t 0.7772

r 0.5786

Fit Statistics

	me	a	c	e					E
ACE Chol	6	21	21	21					C
	me	ac	cc	ec		as	cs	es	E
1A1C1E IP	6	6	6	6		6	6	6	4
2A1C1E IP	6	9	6	6		6	6	6	4
3A1C1E IP	6	12	6	6		6	6	6	4
	me	al	cl	el	fl	as	cs	es	E
1LP CP	6	1	1	1	6	6	6	6	3