Introduction to Multivariate Genetic Analysis

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Aim and Rationale

Aim: to examine the source of factors that make traits correlate or co-vary

Rationale:

Traits may be correlated due to shared genetic factors (A) or shared environmental factors (C or E)

Can use information on multiple traits from twin pairs to partition covariation into genetic and environmental components
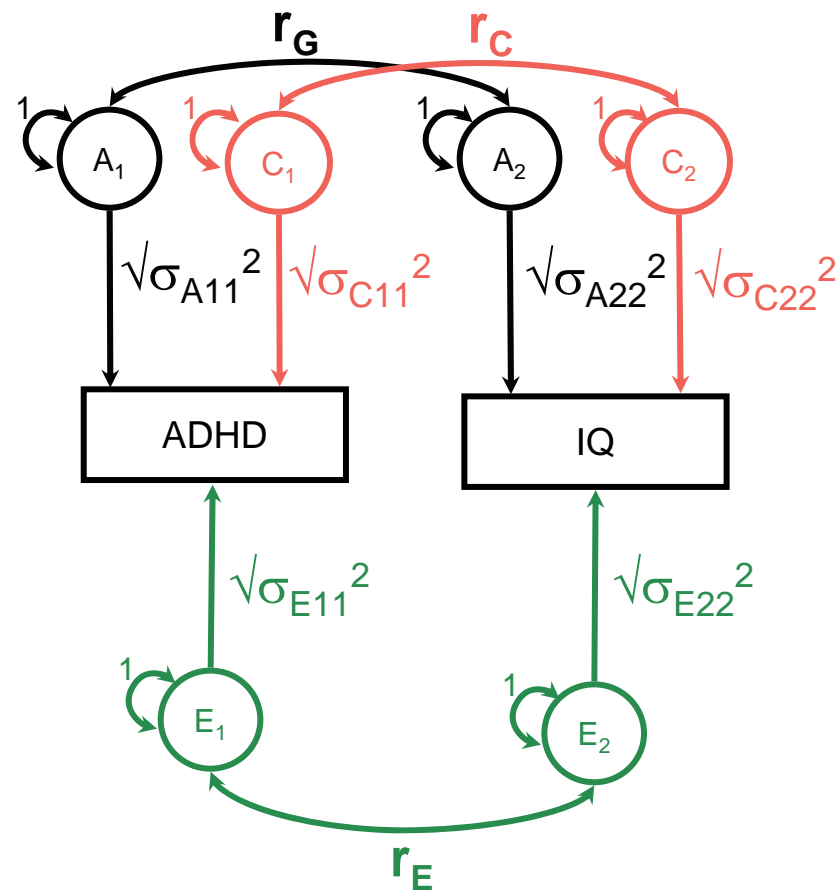
Example 1

Why do traits correlate/covary?

How can we explain the association?

Additive genetic factors (r_G)

Shared environment (r_C)

Non-shared environment (r_E)

Kuntsi et al. (2004) *Am J Med Genet B*, 124:41

Example 2

- Associations between phenotypes over time
  - Does anxiety in childhood lead to depression in adolescence?
- How can we explain the association?
  - Additive genetic factors (a_{21})
  - Shared environment (c_{21})
  - Non-shared environment (e_{21})
  - How much is not explained by prior anxiety?
- Rice et al. (2004) BMC Psychiatry 4:43
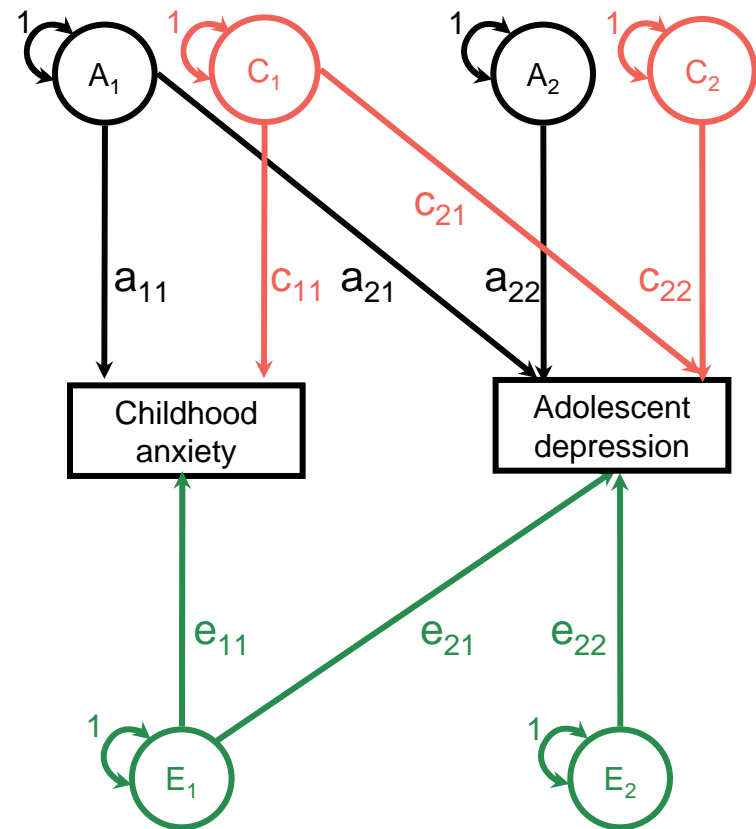
Sources of Information

- As an example: two traits measured in twin pairs
- Interested in:
  - Cross-trait covariance *within* individuals
  - Cross-trait covariance *between* twins
  - MZ:DZ ratio of cross-trait covariance between twins

Observed Covariance Matrix

		Twin 1		Twin 2	
		Phenotype 1	Phenotype 2	Phenotype 1	Phenotype 2
Twin 1	Phenotype 1	Variance P1			
	Phenotype 2	Covariance P1-P2	Variance P2		
Twin 2	Phenotype 1	Within-trait P1	Cross-trait	Variance P1	
	Phenotype 2	Cross-trait	Within-trait P2	Covariance P1-P2	Variance P2

Observed Covariance Matrix

		Twin 1		Twin 2	
		Phenotype 1	Phenotype 2	Phenotype 1	Phenotype 2
Twin 1	Phenotype 1	**Within-twin covariance** Variance P1			
	Phenotype 2	Covariance P1-P2	Variance P2		
Twin 2	Phenotype 1	Within-trait P1	Cross-trait	**Within-twin covariance** Variance P1	
	Phenotype 2	Cross-trait	Within-trait P2	Covariance P1-P2	Variance P2

Observed Covariance Matrix

|		Twin 1		Twin 2	
		Phenotype 1	Phenotype 2	Phenotype 1	Phenotype 2
Twin 1	Phenotype 1	**Within-twin covariance**			
		Variance P1			
	Phenotype 2	Covariance P1-P2	Variance P2		
Twin 2	Phenotype 1	**Cross-twin covariance**		**Within-twin covariance**	
		Within-trait P1	Cross-trait	Variance P1	
	Phenotype 2	Cross-trait	Within-trait P2	Covariance P1-P2	Variance P2

SEM: Cholesky Decomposition
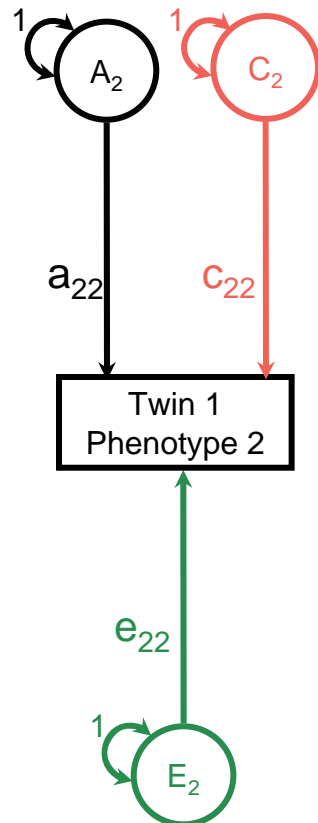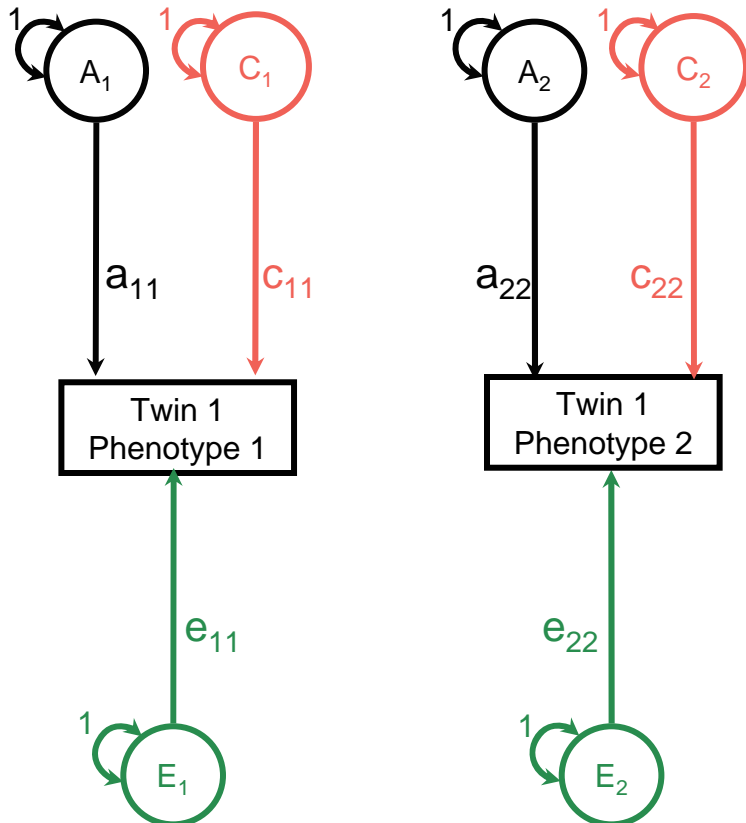
SEM: Cholesky Decomposition
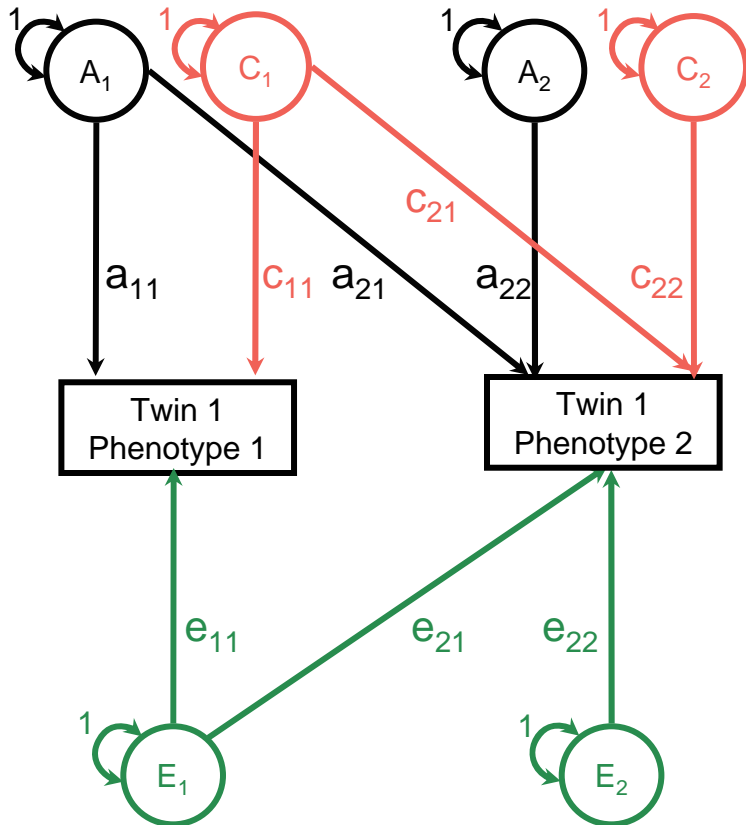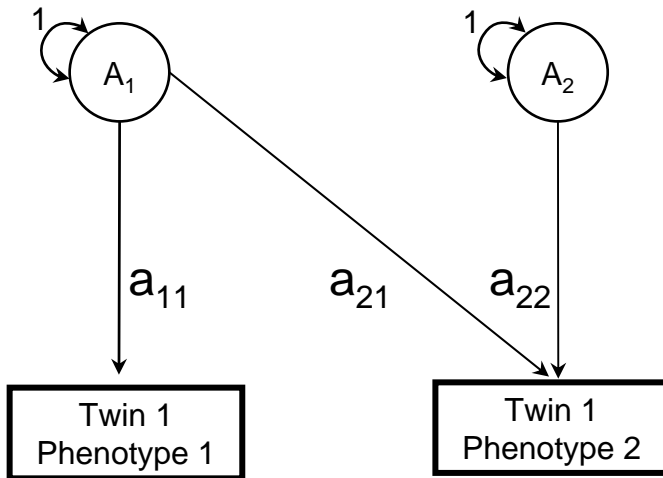
SEM: Cholesky Decomposition
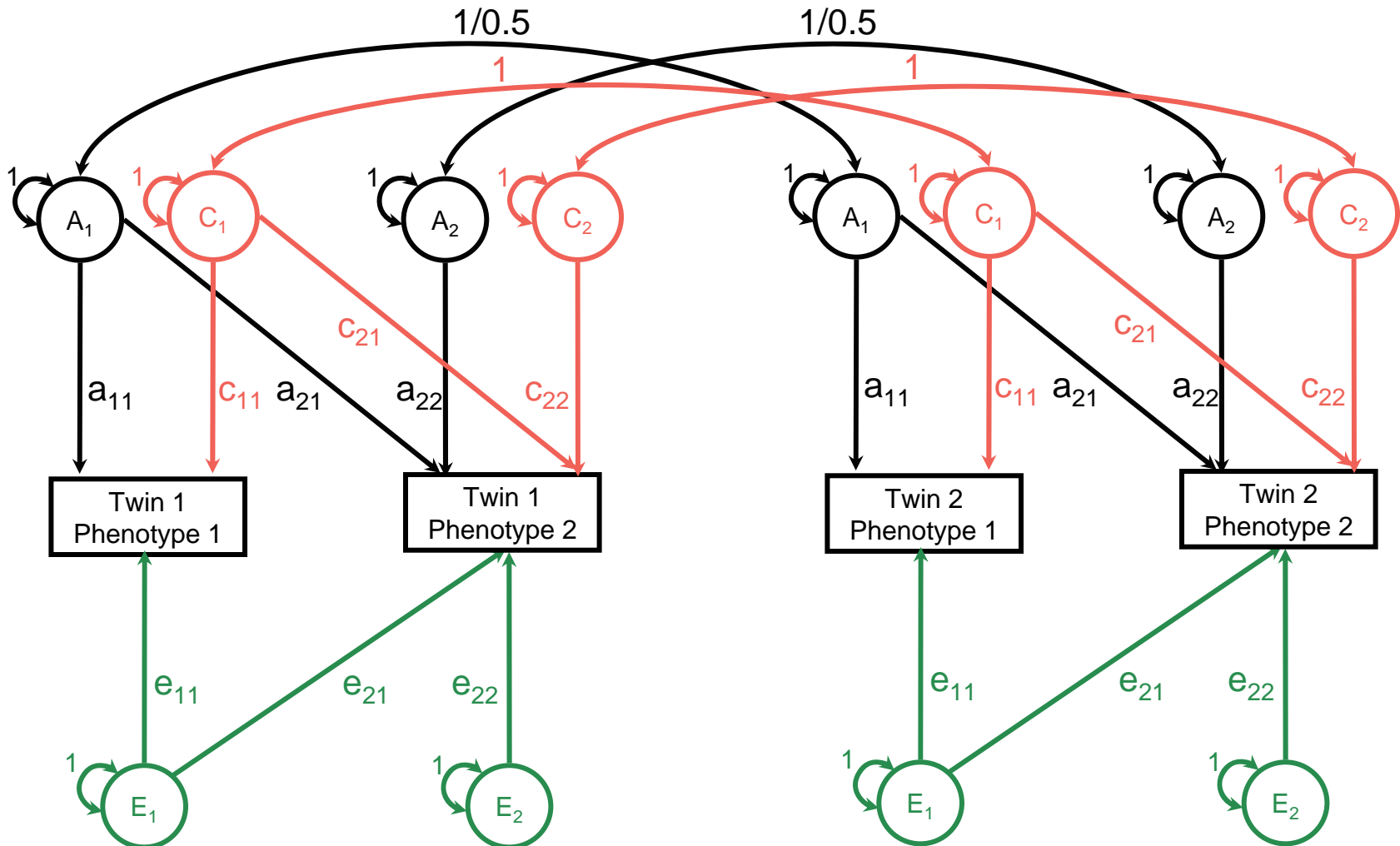
Why Fit This Model?

- Covariance matrices must be positive definite

- If a matrix is positive definite, it can be decomposed into the product of a triangular matrix and its transpose:

  - ◆ $A = a*a^T$

- Many other multivariate models possible

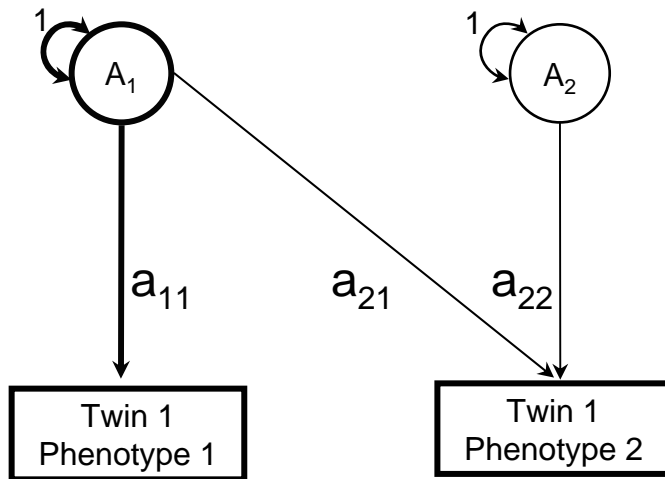 - ◆ Depends on data and hypotheses of interest

Cholesky Decomposition

Path Tracing

Within-Twin Covariances (A)

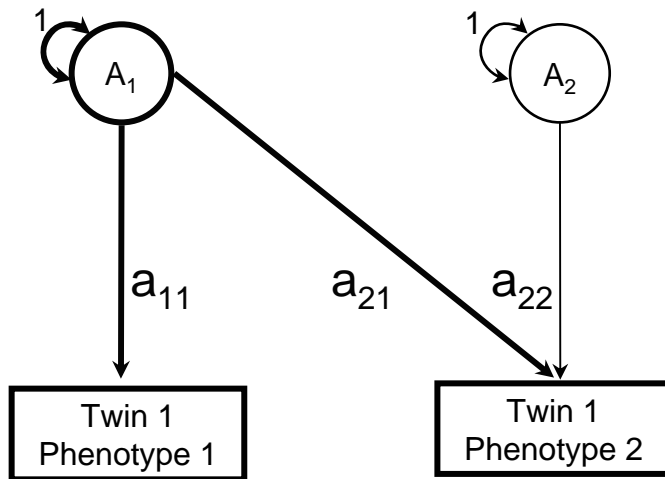| Twin 1		Phenotype 1	Phenotype 2
Twin 1	Phenotype 1		
	Phenotype 2		

Within-Twin Covariances (A)

Twin 1

		Phenotype 1	Phenotype 2
Twin 1	Phenotype 1	a_{11}^2	
	Phenotype 2		

Within-Twin Covariances (A)

Twin 1

	Phenotype 1	Phenotype 2
Phenotype 1	a_{11}^2	
Phenotype 2	$a_{11}a_{21}$	

Twin 1

Within-Twin Covariances (A)
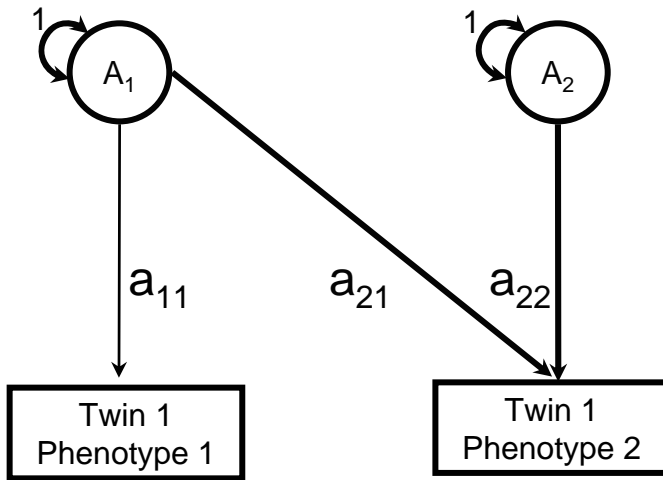
	Twin 1	
	Phenotype 1	Phenotype 2
Phenotype 1	a_{11}^2	
Phenotype 2	$a_{11}a_{21}$	$a_{22}^2 + a_{21}^2$

Within-Twin Covariances (C)
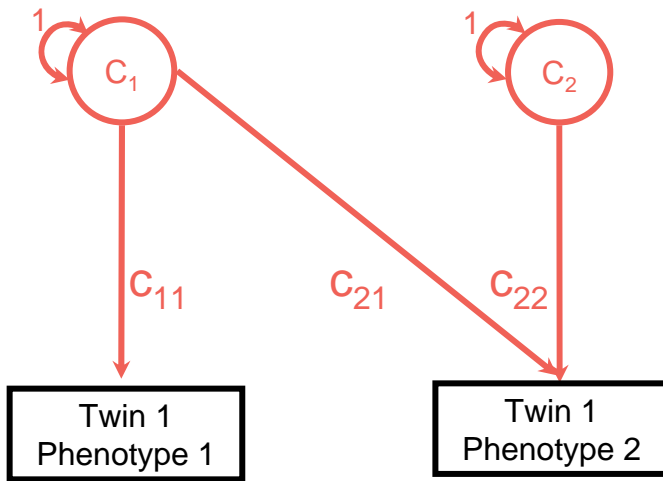
	Twin 1	
	Phenotype 1	Phenotype 2
Twin 1 Phenotype 1	$a_{11}^2 + c_{11}^2$	
Phenotype 2	$a_{11}a_{21} + c_{11}c_{21}$	$a_{22}^2 + a_{21}^2 + c_{22}^2 + c_{21}^2$

Diagram labels: 1, C_1, 1, C_2, c_{11}, c_{21}, c_{22}, Twin 1 Phenotype 1, Twin 1 Phenotype 2

Within-Twin Covariances (E)
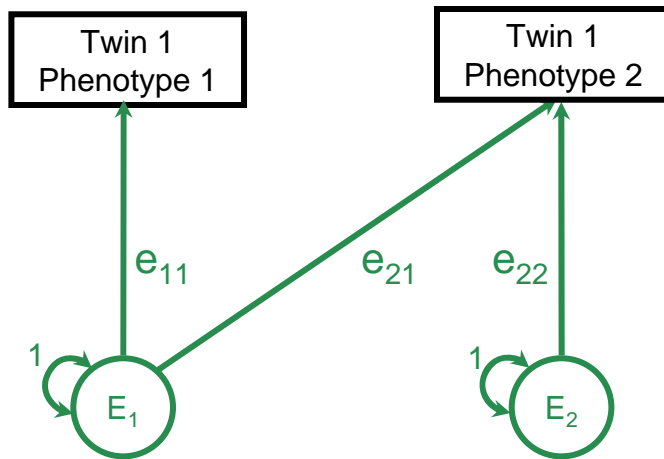
		Twin 1	
		Phenotype 1	Phenotype 2
Twin 1	Phenotype 1	$a_{11}^2 + c_{11}^2 + e_{11}^2$	
	Phenotype 2	$a_{11}a_{21} + c_{11}c_{21} + e_{11}e_{21}$	$a_{22}^2 + a_{21}^2 + c_{22}^2 + c_{21}^2 + e_{22}^2 + e_{21}^2$

Cross-Twin Covariances (A)

1/0.5   1/0.5

A_1 A_2 A_1 A_2

a_{11} a_{21} a_{22} a_{11} a_{21} a_{22}

Twin 1 Phenotype 1   Twin 1 Phenotype 2   Twin 2 Phenotype 1   Twin 2 Phenotype 2
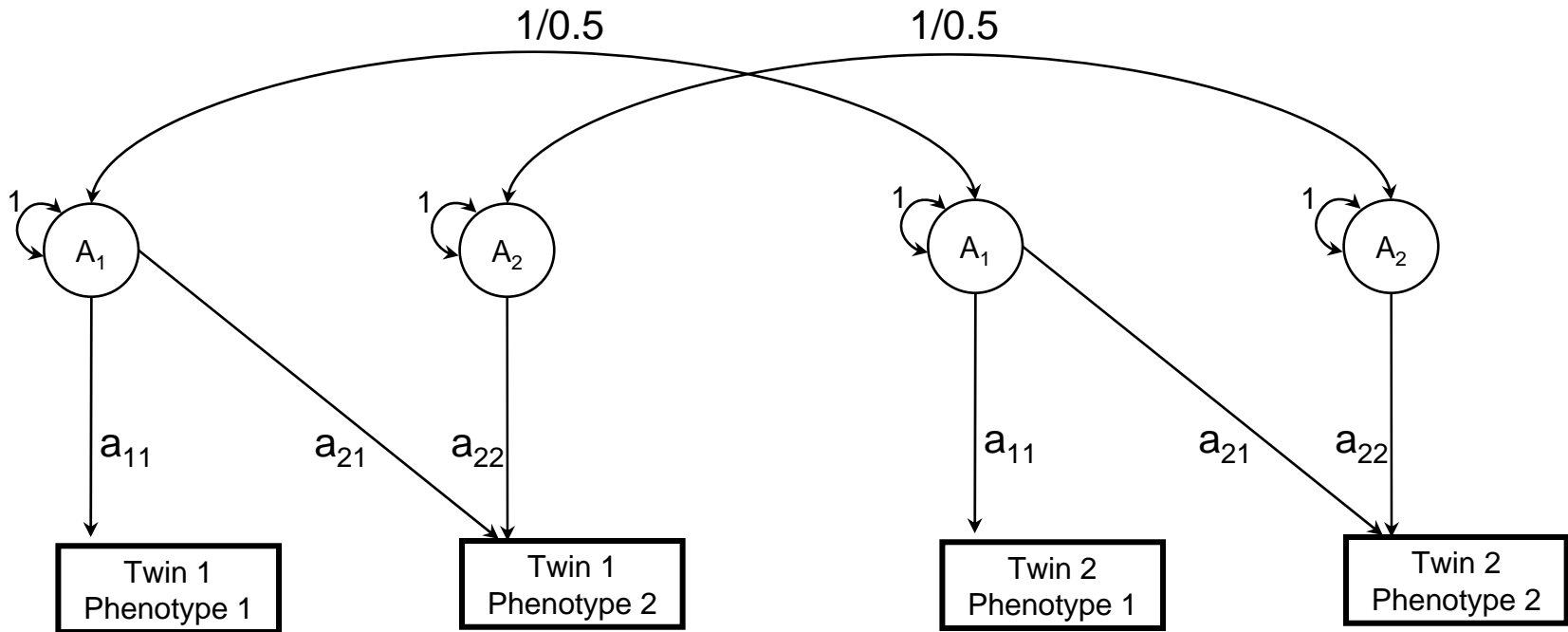
Twin 2	Twin 1		
	Phenotype 1		Phenotype 2
Phenotype 1			
Phenotype 2			

Cross-Twin Covariances (A)

	Twin 1	
	Phenotype 1	Phenotype 2
Phenotype 1	$1/0.5a_{11}^2$	
Phenotype 2		

Twin 2

Cross-Twin Covariances (A)
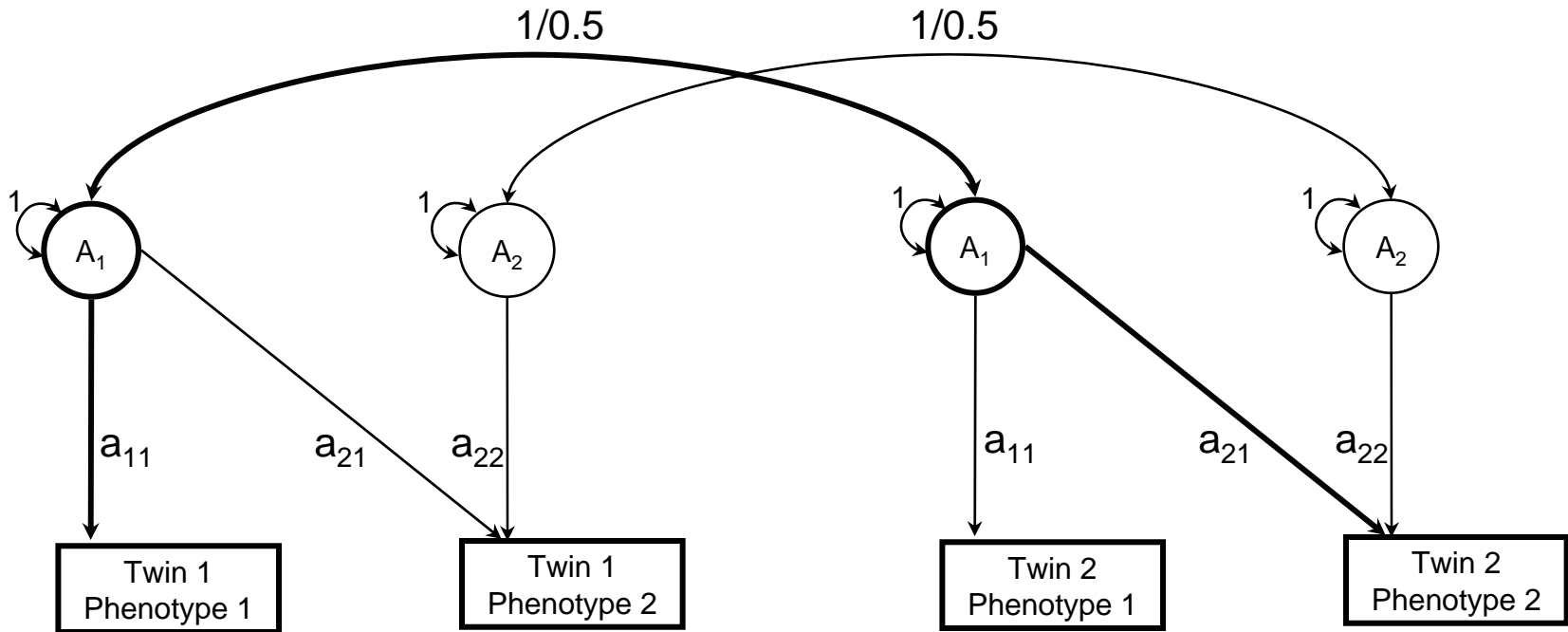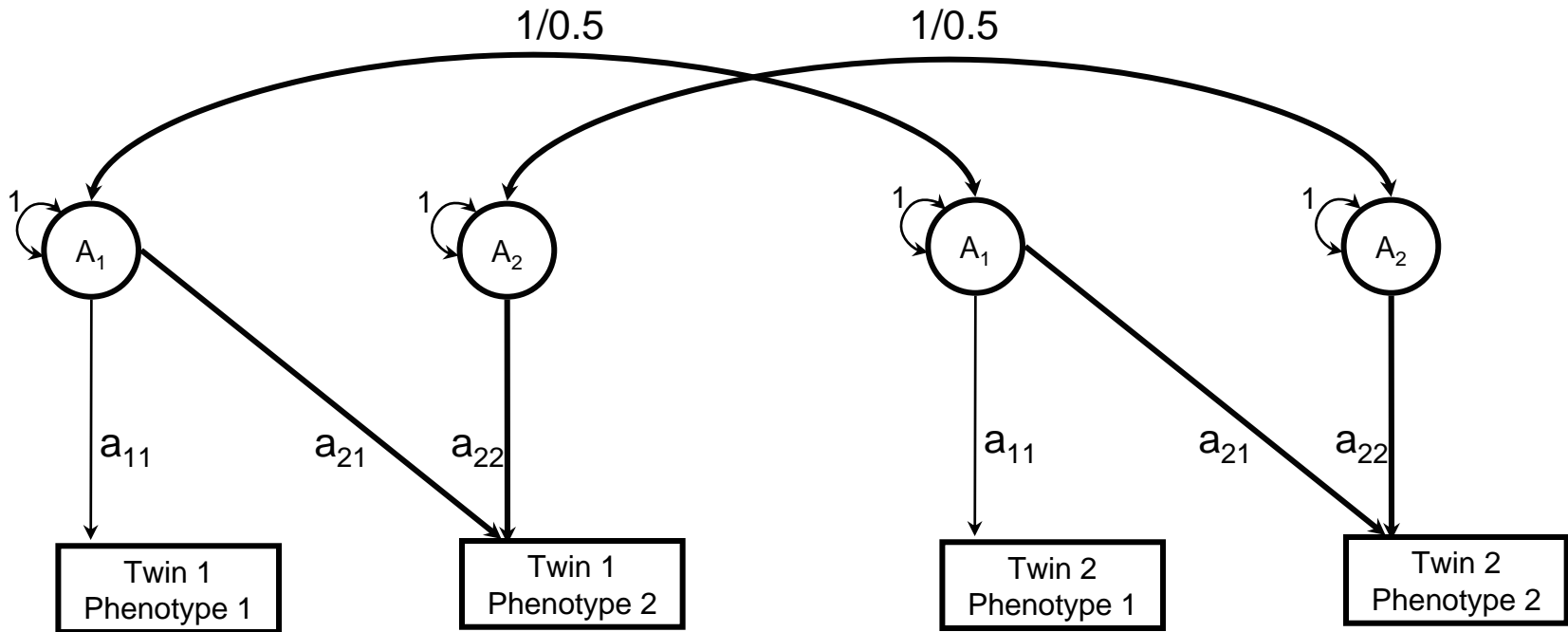
Cross-Twin Covariances (A)

	Twin 1	
	Phenotype 1	Phenotype 2
Phenotype 1	$1/0.5a_{11}^2$	
Phenotype 2	$1/0.5a_{11}a_{21}$	$1/0.5a_{22}^2 + 1/0.5a_{21}^2$

Twin 2

Cross-Twin Covariances (C)
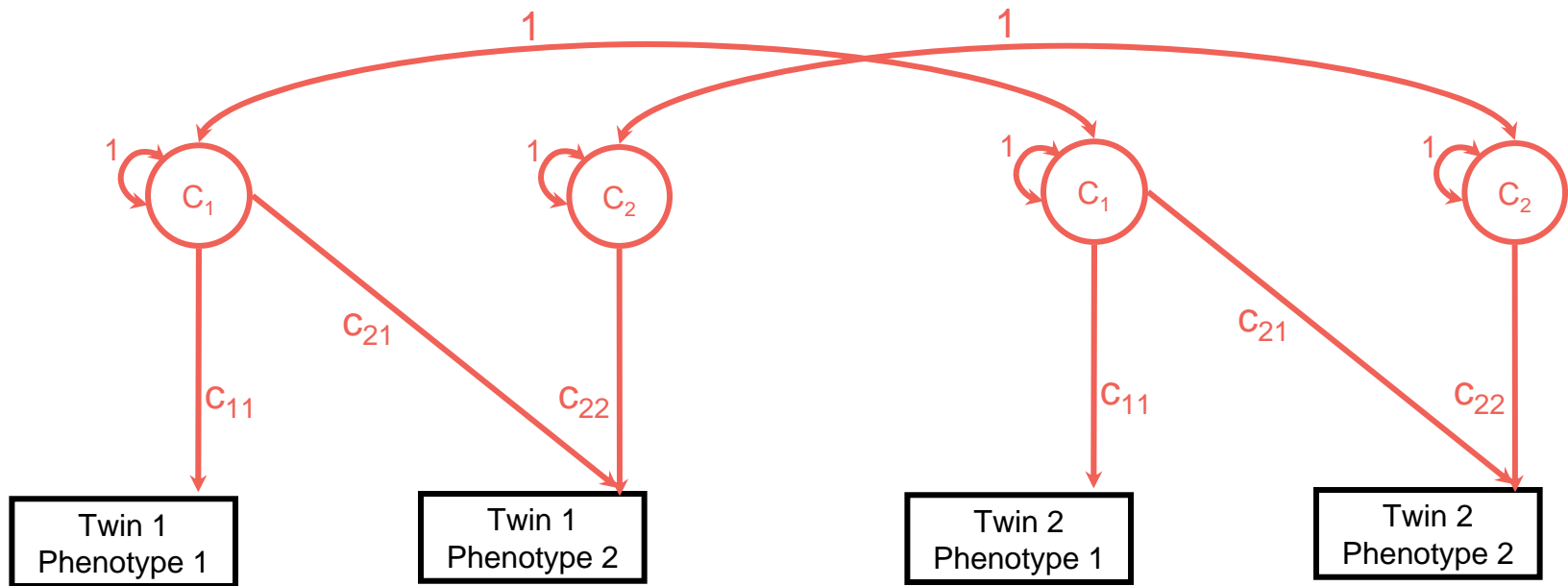
	Twin 1	
	Phenotype 1	Phenotype 2
Twin 2 Phenotype 1	$1/0.5a_{11}^2 + c_{11}^2$	
Phenotype 2	$1/0.5a_{11}a_{21} + c_{11}c_{21}$	$1/0.5a_{22}^2 + 1/0.5a_{21}^2 + c_{22}^2 + c_{21}^2$

Predicted Model

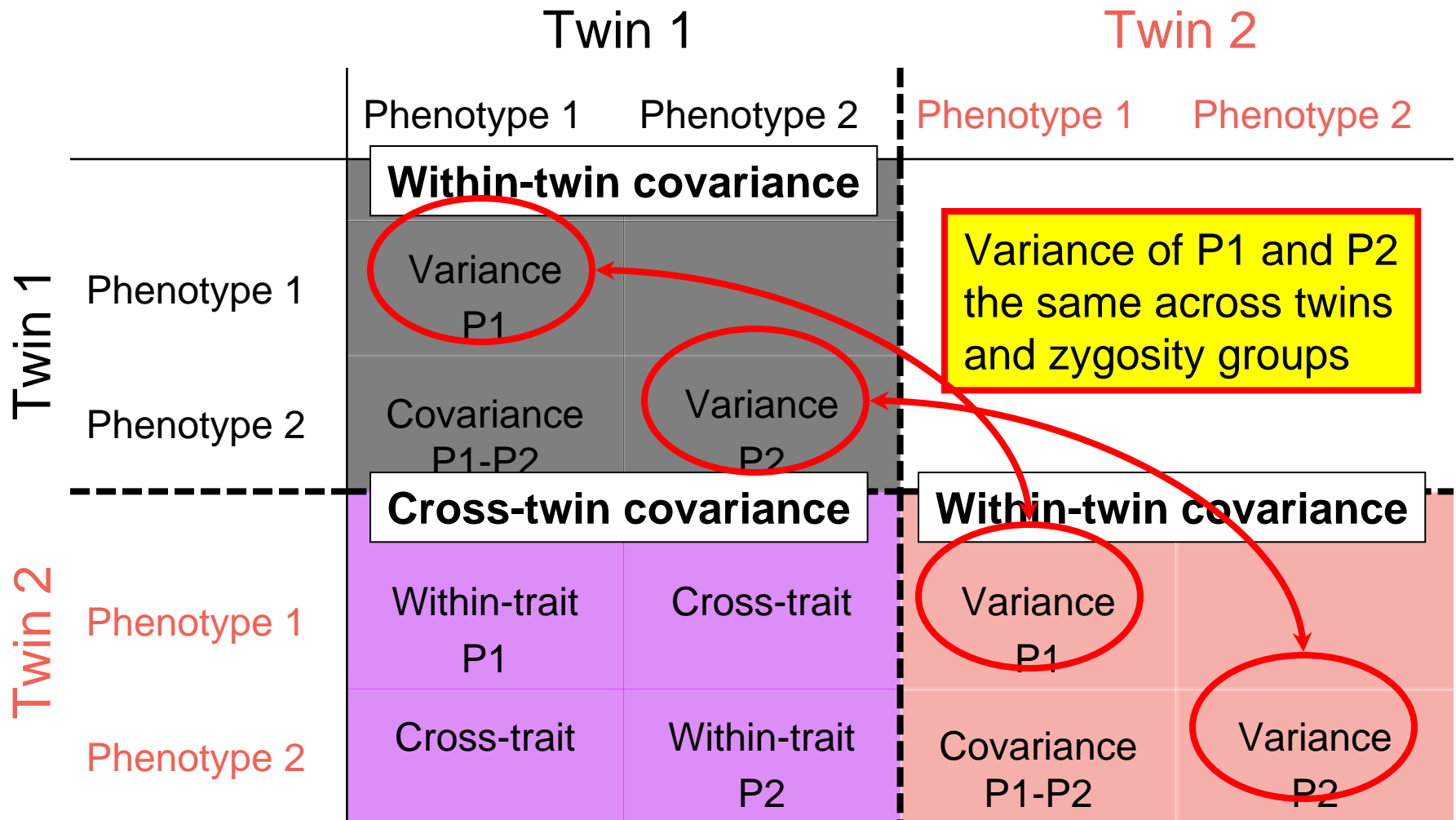|		Twin 1		Twin 2	
		Phenotype 1	Phenotype 2	Phenotype 1	Phenotype 2
Twin 1	Phenotype 1	**Within-twin covariance**			
		$a_{11}^2+c_{11}^2+e_{11}^2$			
	Phenotype 2	$a_{11}a_{21}+c_{11}c_{21}+e_{11}e_{21}$	$a_{22}^2+a_{21}^2+c_{22}^2+c_{21}^2+e_{22}^2+e_{21}^2$		
Twin 2	Phenotype 1	**Cross-twin covariance**		**Within-twin covariance**	
		$1/.5a_{11}^2+c_{11}^2$		$a_{11}^2+c_{11}^2+e_{11}^2$	
	Phenotype 2	$1/.5a_{11}a_{21}+c_{11}c_{21}$	$1/.5a_{22}^2+1/.5a_{21}^2+c_{22}^2+c_{21}^2$	$a_{11}a_{21}+c_{11}c_{21}+e_{11}e_{21}$	$a_{22}^2+a_{21}^2+c_{22}^2+c_{21}^2+e_{22}^2+e_{21}^2$

Predicted Model

		Twin 1		Twin 2	
		Phenotype 1	Phenotype 2	Phenotype 1	Phenotype 2
Twin 1	Phenotype 1	**Within-twin covariance** Variance P1			
	Phenotype 2	Covariance P1-P2	Variance P2		
Twin 2	Phenotype 1	**Cross-twin covariance** Within-trait P1	Cross-trait	**Within-twin covariance** Variance P1	
	Phenotype 2	Cross-trait	Within-trait P2	Covariance P1-P2	Variance P2

Predicted Model

Predicted Model

Predicted Model

Predicted Model

Example Covariance Matrix

MZ

		Twin 1		Twin 2	
		P1	P2	P1	P2
Twin 1	P1	1			
	P2				
Twin 2	P1	0.79	0.49	1	
	P2	0.50	0.59	0.29	1

Within-twin covariance

Cross-twin covariance

Within-twin covariance

DZ

		Twin 1		Twin 2	
		P1	P2	P1	P2
Twin 1	P1	1			
	P2				
Twin 2	P1	0.39	0.25	1	
	P2	0.24	0.43	0.31	1

Within-twin covariance

Cross-twin covariance

Within-twin covariance

Example Covariance Matrix

MZ

		Twin 1			Twin 2	
		P1	P2		P1	P2
Twin 1	P1	Within-twin covariance				
		1				
	P2					
Twin 2		Cross-twin covariance			Within-twin covariance	
	P1	0.79	0.49		1	
	P2	0.50	0.59		0.29	1

DZ

		Twin 1			Twin 2	
		P1	P2		P1	P2
Twin 1	P1	Within-twin covariance				
		1				
	P2					
Twin 2		Cross-twin covariance			Within-twin covariance	
	P1	0.39	0.25		1	
	P2	0.24	0.43		0.31	1

Example Covariance Matrix

MZ

		Twin 1			Twin 2	
		P1	P2		P1	P2
Twin 1	P1	1				
	P2					
Twin 2	P1	0.79	0.49		1	
	P2	0.50	0.59		0.29	1

Within-twin covariance

Cross-twin covariance

Within-twin covariance

DZ

		Twin 1			Twin 2	
		P1	P2		P1	P2
Twin 1	P1	1				
	P2					
Twin 2	P1	0.39	0.25		1	
	P2	0.24	0.43		0.31	1

Within-twin covariance

Cross-twin covariance

Within-twin covariance

Example Covariance Matrix

MZ

	Twin 1		Twin 2	
	P1	P2	P1	P2
Twin 1 P1	1			
Twin 1 P2				
Twin 2 P1	0.79	0.25	1	
Twin 2 P2	0.24	0.59	0.29	1

Within-twin covariance

Cross-twin covariance

Within-twin covariance

DZ

	Twin 1		Twin 2	
	P1	P2	P1	P2
Twin 1 P1	1			
Twin 1 P2				
Twin 2 P1	0.39	0.25	1	
Twin 2 P2	0.24	0.43	0.31	1

Within-twin covariance

Cross-twin covariance

Within-twin covariance

Example Covariance Matrix

MZ

		Twin 1			Twin 2	
		P1	P2		P1	P2
Twin 1	P1	Within-twin covariance				
		1				
	P2					
Twin 2		Cross-twin covariance			Within-twin covariance	
	P1	0.79	0.01		1	
	P2	0.01	0.59		0.29	1

DZ

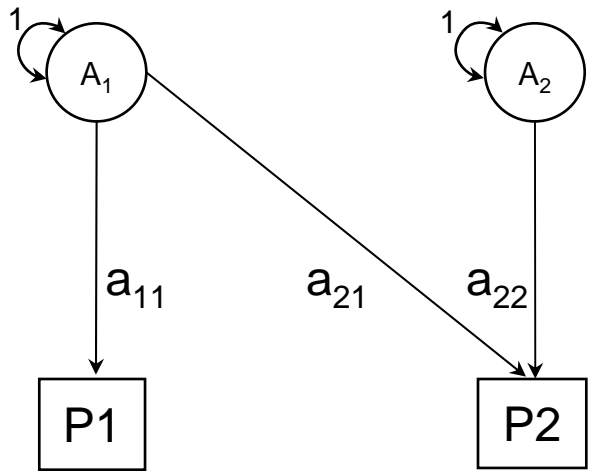|		Twin 1			Twin 2	
		P1	P2		P1	P2
Twin 1	P1	Within-twin covariance				
		1				
	P2					
Twin 2		Cross-twin covariance			Within-twin covariance	
	P1	0.39	0.01		1	
	P2	0.01	0.43		0.31	1

Summary

- Within-individual cross-trait covariance implies common aetiological influences

- Cross-twin cross-trait covariance implies common aetiological influences are familial

- Whether familial influences genetic or environmental shown by MZ:DZ ratio of cross-twin cross-trait covariances

Cholesky Decomposition Bivariate Genetic analyses
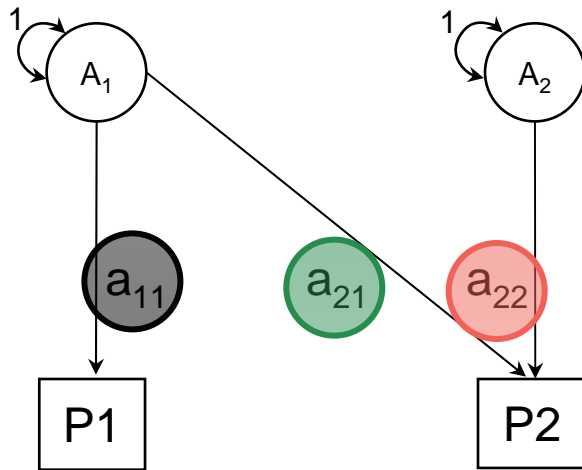
Specification in OpenMx

Within-Twin Covariance

Path Tracing:

$$\Sigma_A = \begin{bmatrix} a_{11}^2 & a_{11}a_{21} \\ a_{21}a_{11} & a_{21}^2 + a_{22}^2 \end{bmatrix}$$
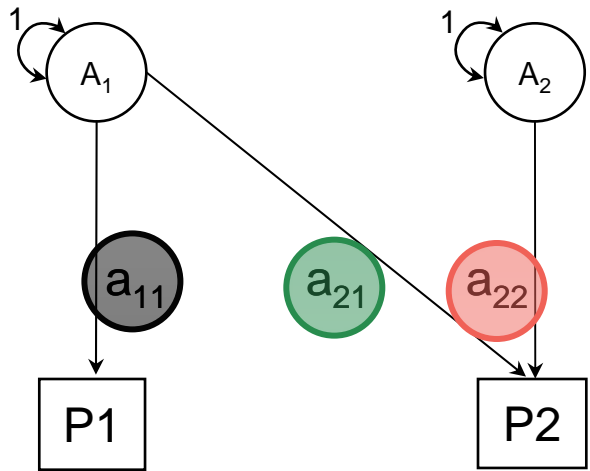
Within-Twin Covariance

Path Tracing:

$$\Sigma_A = \begin{bmatrix} a_{11}^2 & a_{11}a_{21} \\ a_{21}a_{11} & a_{21}^2 + a_{22}^2 \end{bmatrix}$$

a Lower 2 x 2:

$$\begin{array}{cc} & \begin{array}{cc} a1 & a2 \end{array} \\ \begin{array}{c} P1 \\ P2 \end{array} & \begin{bmatrix} a_{11} & 0 \\ a_{21} & a_{22} \end{bmatrix} \end{array}$$

Within-Twin Covariance

Path Tracing:

$$\Sigma_A = \begin{bmatrix} a_{11}^2 & a_{11}a_{21} \\ a_{21}a_{11} & a_{21}^2 + a_{22}^2 \end{bmatrix}$$

a Lower 2 x 2:

$$\begin{array}{cc} & a1 \quad\quad a2 \\ \begin{array}{c} P1 \\ P2 \end{array} & \begin{bmatrix} a_{11} & 0 \\ a_{21} & a_{22} \end{bmatrix} \end{array}$$

$$\Sigma_A = a * a^T$$

$$\Sigma_A = a \% * \% t(a)$$

$$= \begin{bmatrix} a_{11} & 0 \\ a_{21} & a_{22} \end{bmatrix} * \begin{bmatrix} a_{11} & a_{21} \\ 0 & a_{22} \end{bmatrix}$$

$$= \begin{bmatrix} a_{11}^2 + 0 \times 0 & a_{11}a_{21} + 0 \times a_{22} \\ a_{21}a_{11} + 0 \times a_{22} & a_{21}^2 + a_{22}^2 \end{bmatrix}$$

Within-Twin Covariance

$$\Sigma_A = a * a^T$$

$$\Sigma_A = a\ \%*\%\ t(a)$$

$$= \begin{bmatrix} a_{11} & 0 \\ a_{21} & a_{22} \end{bmatrix} * \begin{bmatrix} a_{11} & a_{21} \\ 0 & a_{22} \end{bmatrix}$$

$$= \begin{bmatrix} a_{11}^2 + 0 \times 0 & a_{11}a_{21} + 0 \times a_{22} \\ a_{21}a_{11} + 0 \times a_{22} & a_{21}^2 + a_{22}^2 \end{bmatrix}$$

OpenMx

```
nv <- 2
..
mxMatrix ( type="Lower", nrow=nv, ncol=nv, free=TRUE, values=.6, name="a" ),
mxAlgebra( expression=a %*% t(a), name="A" ),
```

Total Within-Twin Covar.

$$\Sigma_A = \text{a \% *\% t(a)} = \begin{bmatrix} a_{11}^2 & a_{11}a_{21} \\ a_{21}a_{11} & a_{21}^2 + a_{22}^2 \end{bmatrix}$$

$$\Sigma_C = \text{c \% *\% t(c)} = \begin{bmatrix} c_{11}^2 & c_{11}c_{21} \\ c_{21}c_{11} & c_{21}^2 + c_{22}^2 \end{bmatrix}$$

$$\Sigma_E = \text{e \% *\% t(e)} = \begin{bmatrix} e_{11}^2 & e_{11}e_{21} \\ e_{21}e_{11} & e_{21}^2 + e_{22}^2 \end{bmatrix}$$

Using matrix addition, the total within-twin covariance for the phenotypes is defined as:

$$\Sigma_V = \Sigma_A + \Sigma_C + \Sigma_E$$

$$\Sigma_V = \begin{bmatrix} a_{11}^2 + c_{11}^2 + e_{11}^2 & a_{11}a_{21} + c_{11}c_{21} + e_{11}e_{21} \\ a_{21}a_{11} + c_{21}c_{11} + e_{11}e_{21} & a_{21}^2 + a_{22}^2 + c_{21}^2 + c_{22}^2 + e_{21}^2 + e_{22}^2 \end{bmatrix}$$

OpenMx Matrices & Algebra

```
multACEModel <- mxModel("multACE",      mxModel("ACE",
# Matrices a, c, and e to store a, c, and e path coefficients
mxMatrix( type="Lower", nrow=nv, ncol=nv, free=TRUE, values=.6, name="a" ),
mxMatrix( type="Lower", nrow=nv, ncol=nv, free=TRUE, values=.6, name="c" ),
mxMatrix( type="Lower", nrow=nv, ncol=nv, free=TRUE, values=.6, name="e" ),

# Matrices A, C, and E compute variance components        mxAlgebra(
expression=a %*% t(a), name="A" ),
mxAlgebra( expression=c %*% t(c), name="C" ),
mxAlgebra( expression=e %*% t(e), name="E" ),

# Algebra to compute total variances and standard deviations (diagonal only)
mxAlgebra( expression=A+C+E, name="V" ),
mxMatrix( type="Iden", nrow=nv, ncol=nv, name="I"),        mxAlgebra(
expression=solve(sqrt(I*V)), name="isd"),
```
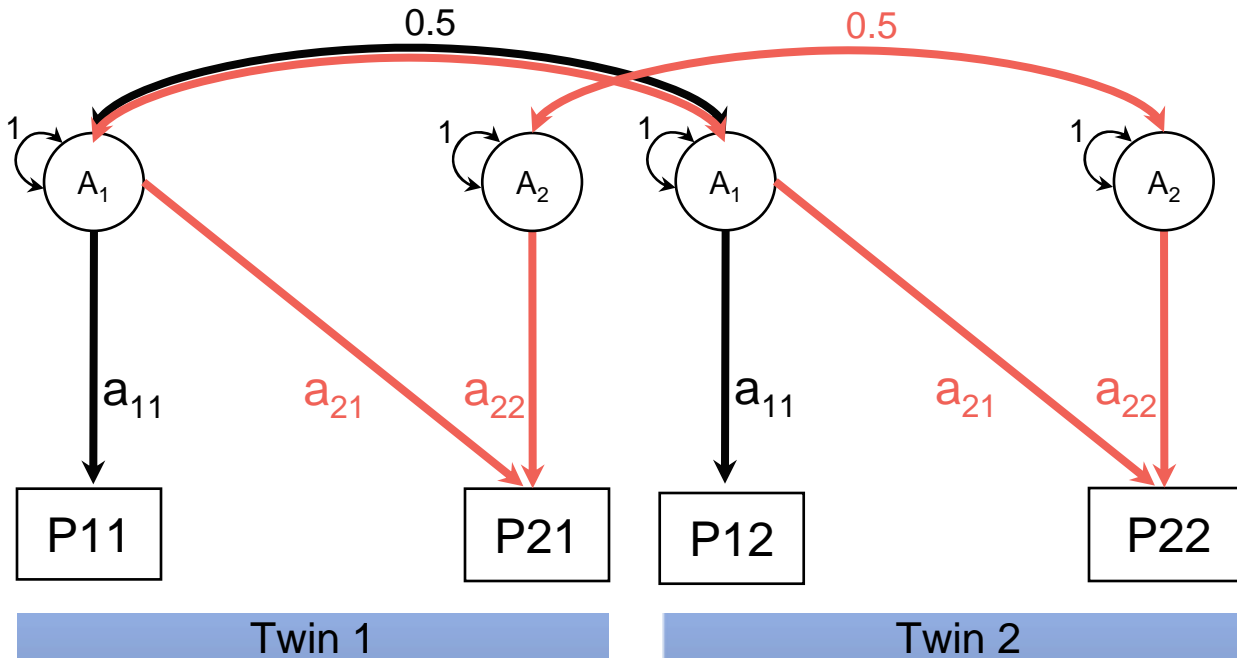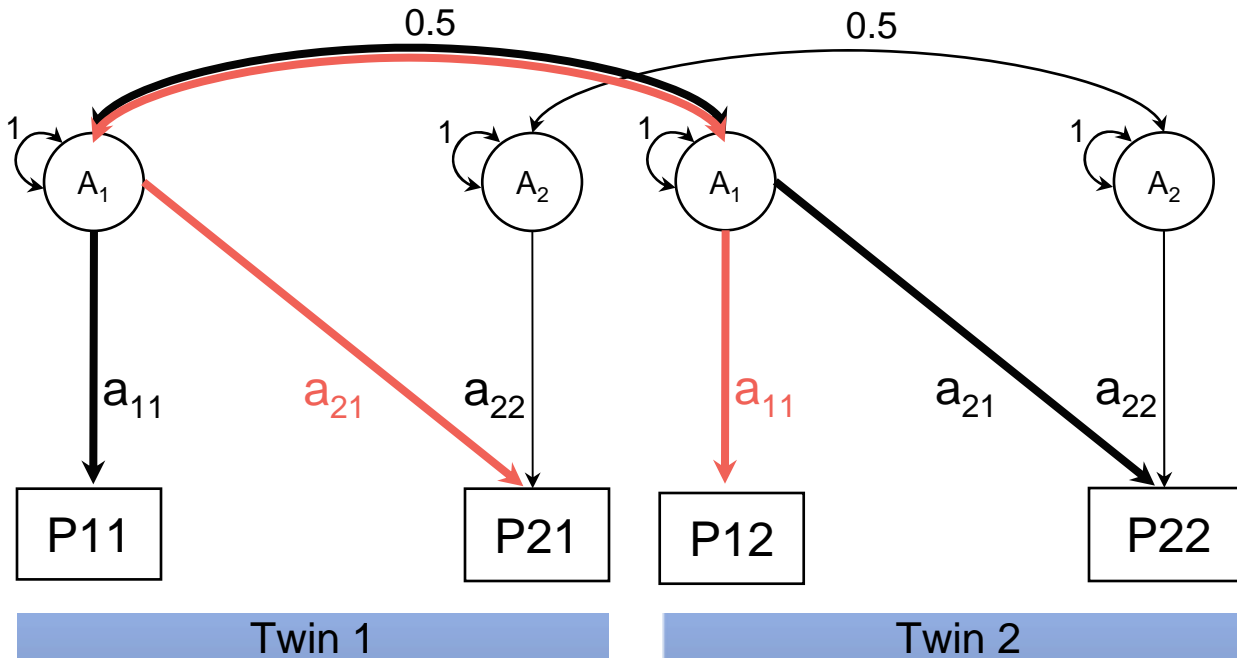
Cross-Twin Covariance (DZ)
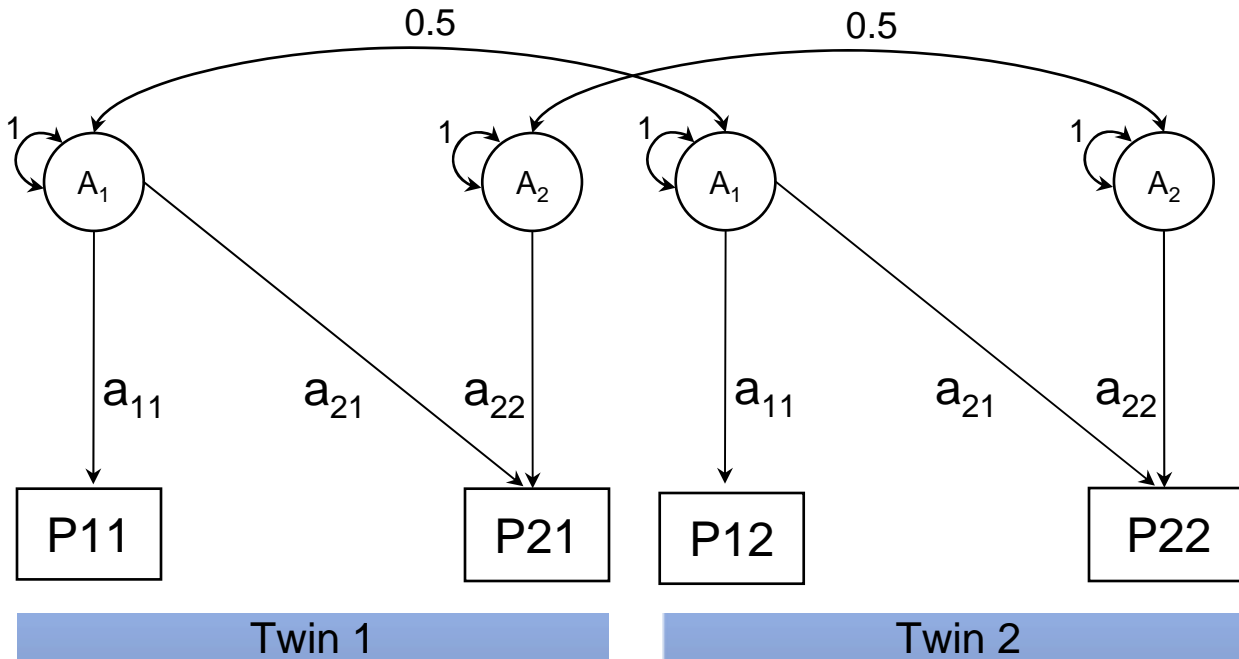
Cross-Twin Covariance (DZ)

Within-traits

$$P11-P12 = 0.5a_{11}^2$$

$$P21-P22 = 0.5a_{22}^2+0.5a_{21}^2$$

Cross-Twin Covariance (DZ)
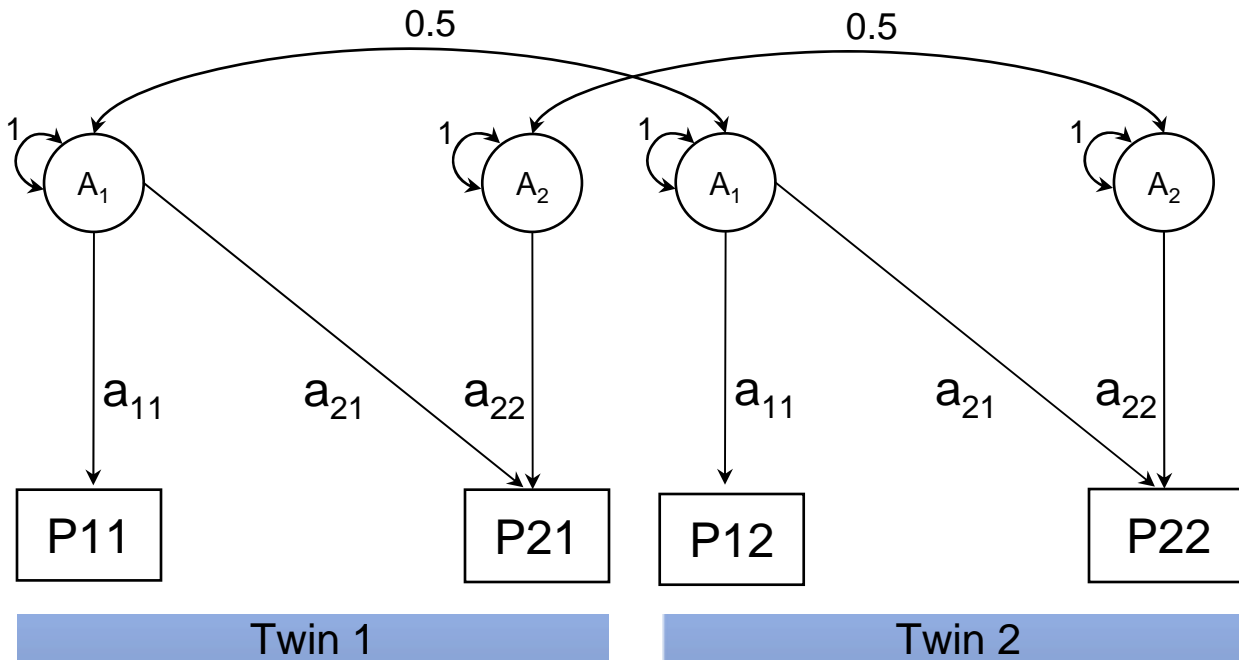

Path Tracing:

Within-traits
P11-P12 = $0.5a_{11}^2$
P21-P22 = $0.5a_{22}^2+0.5a_{21}^2$

Cross-traits
P11-P22 = $0.5a_{11}a_{21}$
P21-P12 = $0.5a_{21}a_{11}$

Additive Genetic Cross-Twin Covariance (DZ)

Path Tracing:

Within-traits
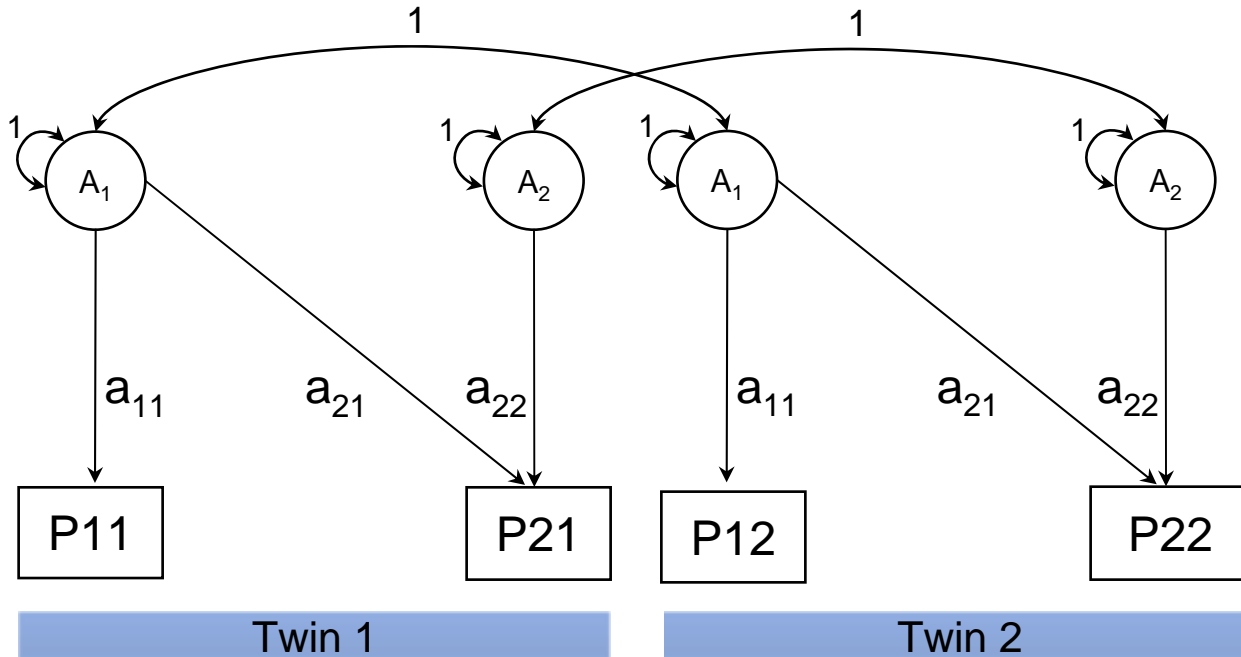P11-P12 = $0.5a_{11}^2$
P21-P22 = $0.5a_{22}^2 + 0.5a_{21}^2$

Cross-traits
P11-P22 = $0.5a_{11}a_{21}$
P21-P12 = $0.5a_{21}a_{11}$

$$0.5 \otimes \Sigma_A = 0.5 \% x \% (a \% * \% t(a)) = \begin{bmatrix} 0.5a_{11}^2 & 0.5a_{11}a_{21} \\ 0.5a_{21}a_{11} & 0.5(a_{21}^2 + a_{22}^2) \end{bmatrix}$$
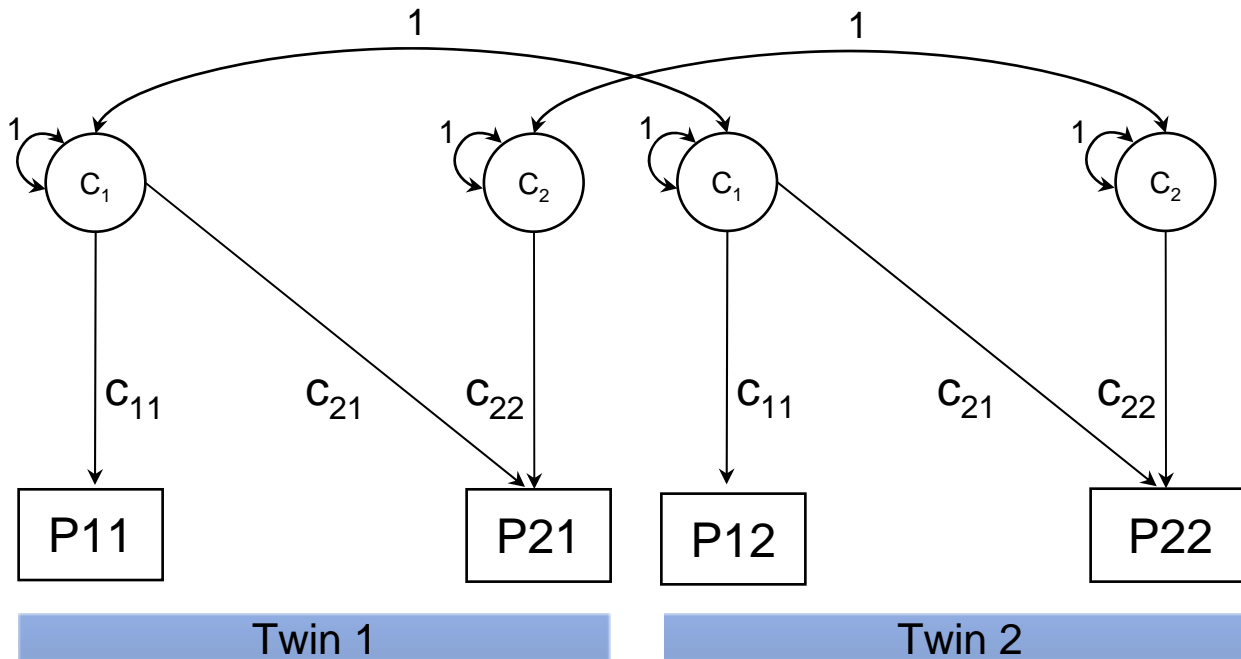
Additive Genetic Cross-Twin Covariance (MZ)

$$1 \otimes \Sigma_A = 1\% x\% (a\% * \% t(a)) = \begin{bmatrix} a_{11}^2 & a_{11}a_{21} \\ a_{21}a_{11} & (a_{21}^2 + a_{22}^2) \end{bmatrix}$$

Common Environment Cross-Twin Covariance

$$1 \otimes \Sigma_C = 1\% x\% (c\% * \% t(c)) = \begin{bmatrix} c_{11}^2 & c_{11}c_{21} \\ c_{21}c_{11} & (c_{21}^2 + c_{22}^2) \end{bmatrix}$$

Covariance Model for Twin Pairs

OpenMx

```
# Algebra for expected variance/covariance matrix in MZ          mxAlgebra(
expression= rbind  ( cbind(A+C+E , A+C),
                             cbind(A+C    , A+C+E)),
                             name="expCovMZ" ),


# Algebra for expected variance/covariance matrix in DZ, note use of 0.5,
converted to 1*1 matrix
mxAlgebra( expression= rbind  ( cbind(A+C+E , 0.5%x%A+C),
                             cbind(0.5%x%A+C , A+C+E)),
                             name="expCovDZ" )        ),
```
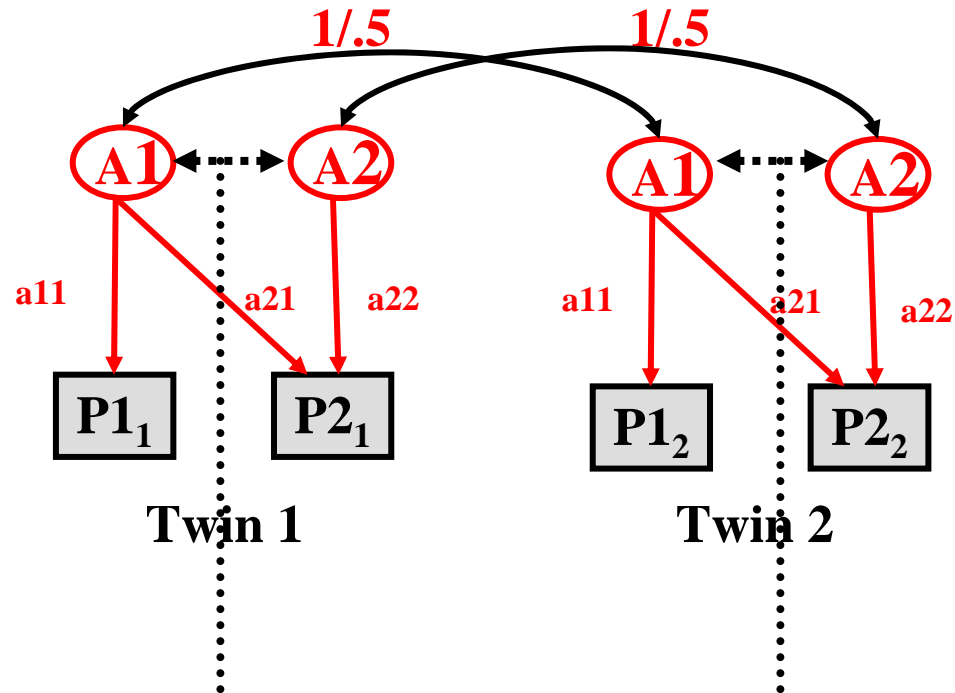
Obtaining Standardised Estimates

Correlated Factors Solution
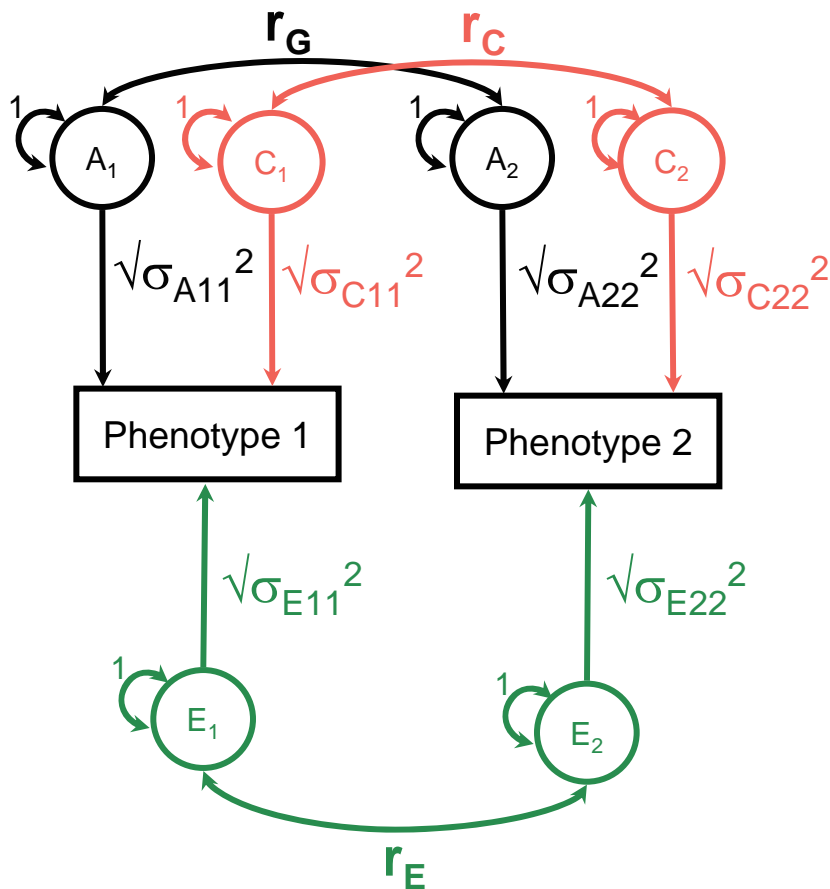
- Each variable decomposed into genetic/environmental components
- Correlations across variables estimated
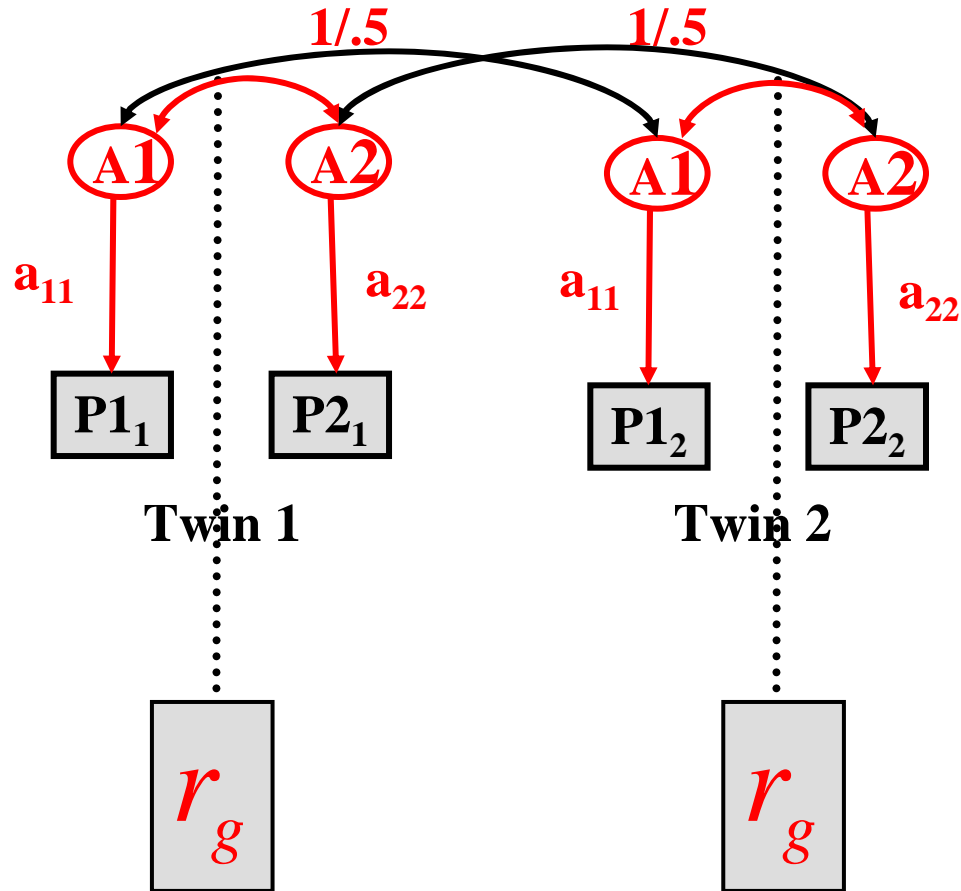- Results from Cholesky can be converted to this model

Genetic correlation

Standardized drawing or correlated factors solution

Standardized solution

- A correlation coefficient is a standardized covariance that lies between -1 and 1 so that it is easier to interpret

- It is calculated by dividing the covariance by the square root of the product of the variances of the two variables

Covariance to Correlation

$$r_{12} = \frac{\sigma_{12}^2}{\sqrt{\sigma_{11}^2 \times \sigma_{22}^2}} = \frac{1}{\sqrt{\sigma_{11}^2}} * \sigma_{12}^2 * \frac{1}{\sqrt{\sigma_{22}^2}}$$

Using matrix algebra notation:

$$\begin{bmatrix} 1 & r_{12} \\ r_{21} & 1 \end{bmatrix} = \begin{bmatrix} \frac{1}{\sqrt{\sigma_{11}^2}} & 0 \\ 0 & \frac{1}{\sqrt{\sigma_{22}^2}} \end{bmatrix} * \begin{bmatrix} \sigma_{11}^2 & \sigma_{12}^2 \\ \sigma_{21}^2 & \sigma_{22}^2 \end{bmatrix} * \begin{bmatrix} \frac{1}{\sqrt{\sigma_{11}^2}} & 0 \\ 0 & \frac{1}{\sqrt{\sigma_{22}^2}} \end{bmatrix}$$

Genetic Correlations

$$\Sigma_A = \begin{bmatrix} a_{11}^2 & a_{11}a_{21} \\ a_{21}a_{11} & a_{21}^2 + a_{22}^2 \end{bmatrix}$$

$$= \begin{bmatrix} \sigma_{A_{11}}^2 & \sigma_{A_{12}}^2 \\ \sigma_{A_{21}}^2 & \sigma_{A_{22}}^2 \end{bmatrix}$$

$$\begin{bmatrix} 1 & r_G \\ r_G & 1 \end{bmatrix} = \begin{bmatrix} \frac{1}{\sqrt{\sigma_{A_{11}}^2}} & 0 \\ 0 & \frac{1}{\sqrt{\sigma_{A_{22}}^2}} \end{bmatrix} * \begin{bmatrix} \sigma_{A_{11}}^2 & \sigma_{A_{12}}^2 \\ \sigma_{A_{21}}^2 & \sigma_{A_{22}}^2 \end{bmatrix} * \begin{bmatrix} \frac{1}{\sqrt{\sigma_{A_{11}}^2}} & 0 \\ 0 & \frac{1}{\sqrt{\sigma_{A_{22}}^2}} \end{bmatrix}$$

Specification in OpenMx

$$\begin{bmatrix} 1 & r_G \\ r_G & 1 \end{bmatrix} = \begin{bmatrix} \frac{1}{\sqrt{\sigma^2_{A_{11}}}} & 0 \\ 0 & \frac{1}{\sqrt{\sigma^2_{A_{22}}}} \end{bmatrix} * \begin{bmatrix} \sigma^2_{A_{11}} & \sigma^2_{A_{12}} \\ \sigma^2_{A_{21}} & \sigma^2_{A_{22}} \end{bmatrix} * \begin{bmatrix} \frac{1}{\sqrt{\sigma^2_{A_{11}}}} & 0 \\ 0 & \frac{1}{\sqrt{\sigma^2_{A_{22}}}} \end{bmatrix}$$

$$= \sqrt{(I \bullet A)}^{-1} * A * \sqrt{(I \bullet A)}^{-1}$$

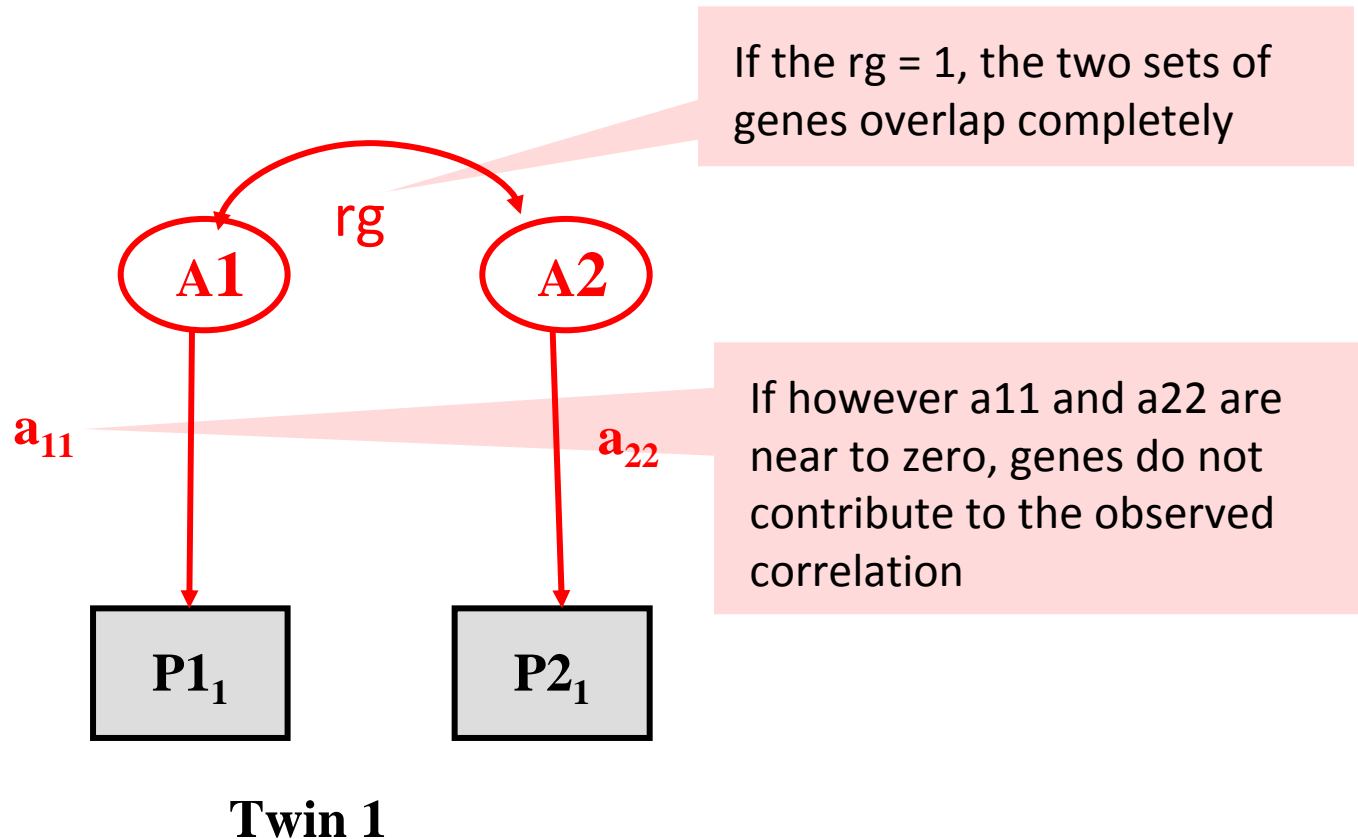Where **I** is an identity matrix: $\begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$

and **I.A** = $\begin{bmatrix} \sigma^2_{A_{11}} & 0 \\ 0 & \sigma^2_{A_{22}} \end{bmatrix}$

OpenMx

```
solve(sqrt(ACE.I*ACE.A)) %*% ACE.A %*% solve(sqrt(ACE.I*ACE.A))
```

# Genetic correlation & contribution to observed correlation

If the rg = 1, the two sets of genes overlap completely

If however a11 and a22 are near to zero, genes do not contribute to the observed correlation

The contribution to the observed correlation is a function of both heritabilities and the rg

Interpreting Results

- High genetic correlation = large overlap in genetic effects on the two phenotypes

- Does it mean that the phenotypic correlation between the traits is largely due to genetic effects?

  - **No:** the substantive importance of a particular r_G depends the value of the correlation **and** the value of the $\sqrt{\sigma_A^2}$ paths i.e. importance is also determined by the heritability of each phenotype

Example
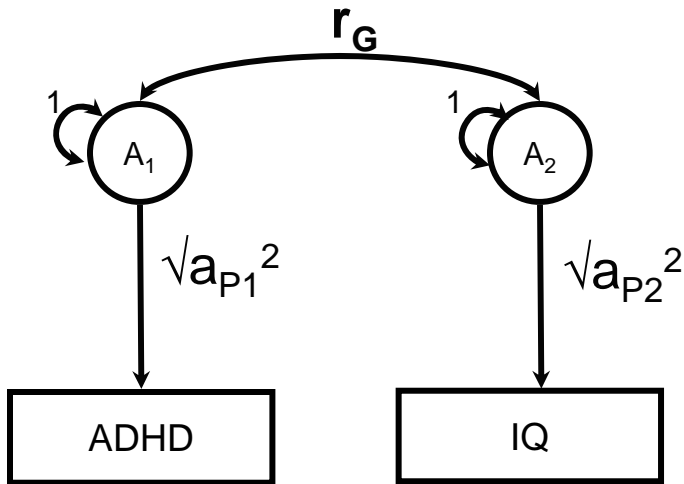
Proportion of r_P due to additive genetic factors:

$$\left(\sqrt{a_x^2} * r_g * \sqrt{a_y^2}\right)\Big/ r_p$$

Heritability of ADHD

Genetic correlation between ADHD and IQ

Heritability of IQ

Phenotypic corr. ADHD & IQ

Proportion of pheno.corr. Due to genetic factors

$$\left(\sqrt{0.63} * -0.525 * \sqrt{0.33}\right)/ -0.29 = 0.8357$$

Standardised Results

```
ACEcovMatrices <-
c("ACE.A","ACE.C","ACE.E","ACE.V","ACE.A/ACE.V","ACE.C/ACE.V","ACE.E/ACE.V")
ACEcovLabels < c("covComp_A","covComp_C","covComp_E","Var",
"stCovComp_A","stCovComp_C","stCovComp_E")formatOutputMatrices(multACEFit,ACEcovMatrices,ACEcovLabels, Vars, 4)
```

```
[1] "Matrix ACE.A/ACE.V"
    stCovComp_A1 stCovComp_A2
LP1 0.2491       0.4784
LP2 0.4784       0.2673
```

$$\begin{pmatrix} h_{P1}^2 & A_{COV} \\ A_{COV} & h_{P2}^2 \end{pmatrix}$$

Proportion of the phenotypic correlation due to genetic effects

```
[1] "Matrix ACE.C/ACE.V"
    stCovComp_C1 stCovComp_C2
LP1 0.2441       0.2417
LP2 0.2417       0.0292
```

$$\begin{pmatrix} c_{P1}^2 & C_{COV} \\ C_{COV} & c_{P2}^2 \end{pmatrix}$$

Proportion of the phenotypic correlation due to shared environmental effects

```
[1] "Matrix ACE.E/ACE.V"
    stCovComp_E1 stCovComp_E2
LP1 0.5069       0.2799
LP2 0.2799       0.7035
```

$$\begin{pmatrix} e_{P1}^2 & E_{COV} \\ E_{COV} & e_{P2}^2 \end{pmatrix}$$

Proportion of the phenotypic correlation due to unshared environmental effects

Interpretation of Correlations

Consider two traits with a phenotypic correlation of 0.40 :

$h^2_{P1} = 0.7$ and $h^2_{P2} = 0.6$ with $r_G = .3$

- Correlation due to additive genetic effects = **?**
- Proportion of phenotypic correlation attributable to additive genetic effects = **?**

$h^2_{P1} = 0.2$ and $h^2_{P2} = 0.3$ with $r_G = 0.8$

- Correlation due to additive genetic effects = **?**
- Proportion of phenotypic correlation attributable to additive genetic effects = **?**

Correlation due to A: $\sqrt{h^2_{P1}} * r_G * \sqrt{h^2_{P2}}$

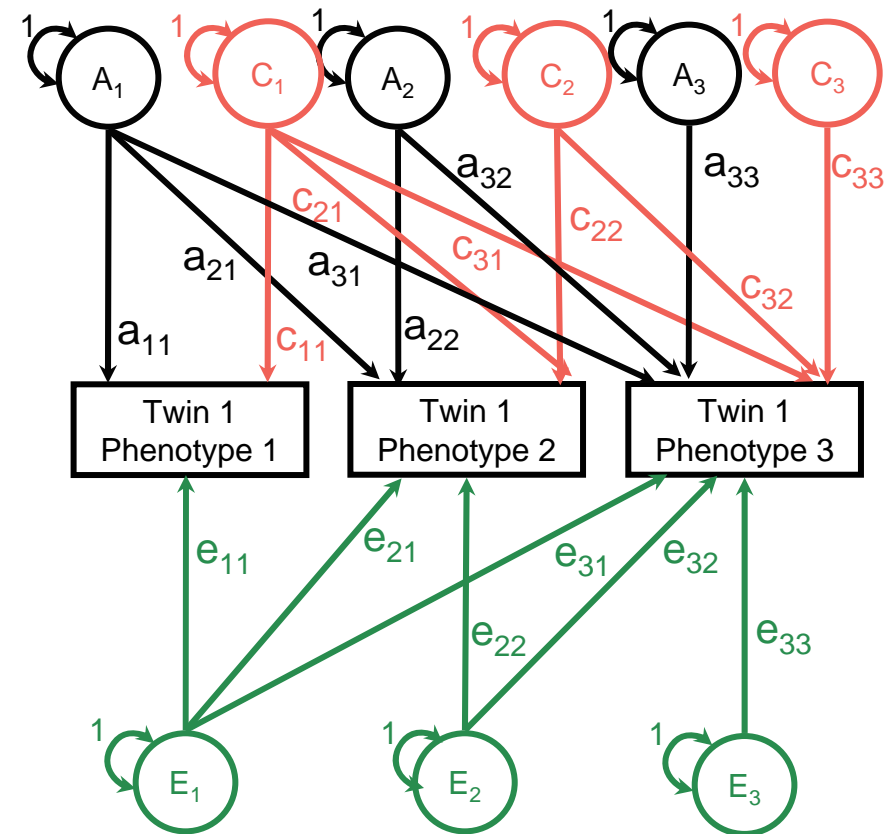Divide by r_P to find proportion of phenotypic correlation.

Summary

- Genetic correlation (r_g) is the correlation between two latent genetic factors

- The proportion of the genetic factors to the observed correlation is a function of the r_g and the heritabilities of the two traits
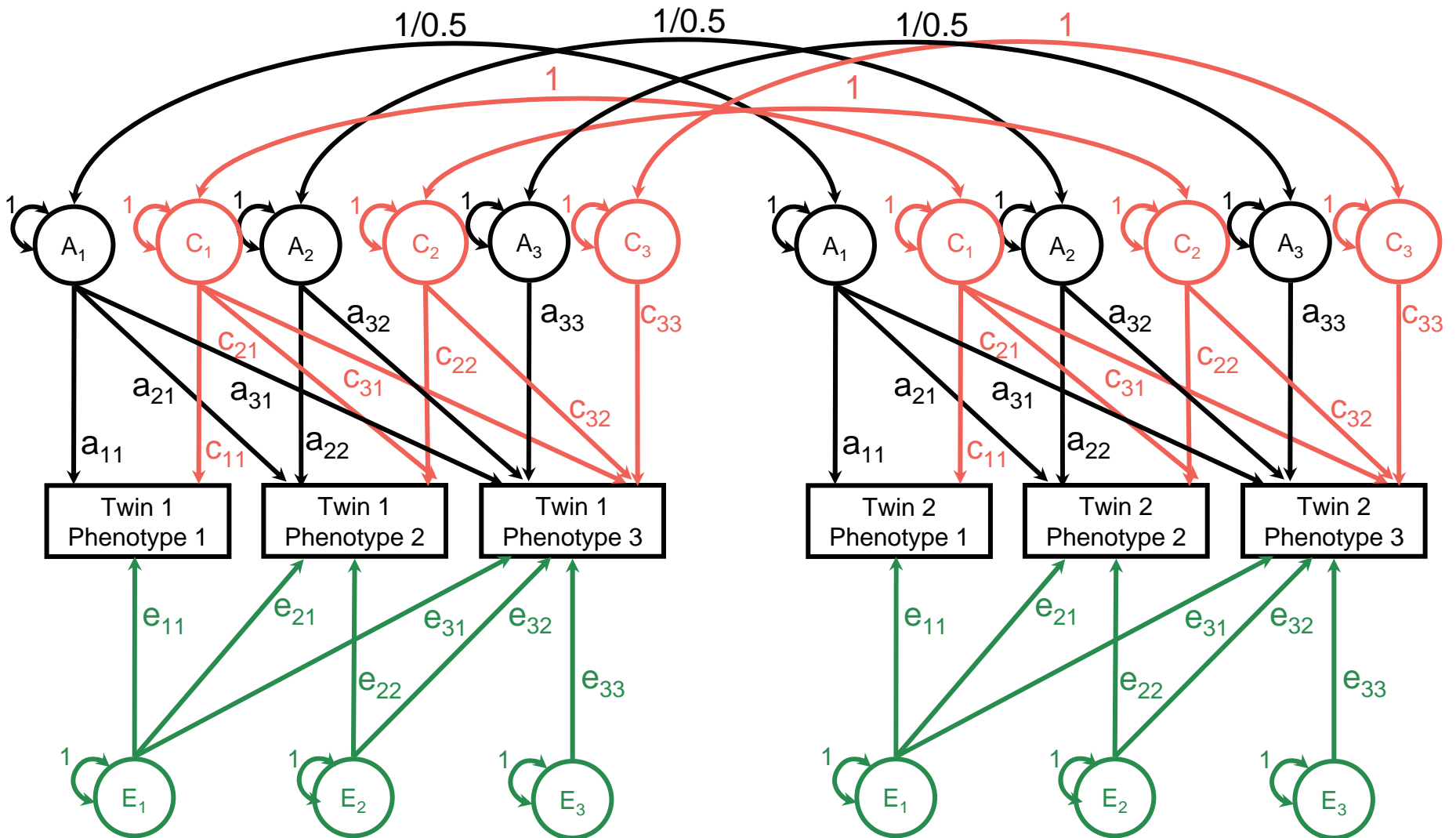
More Variables…

More Variables…

Expanded Matrices

a Lower 3 x 3 $\longrightarrow$ $\begin{bmatrix} a_{11} & 0 & 0 \\ a_{21} & a_{22} & 0 \\ a_{31} & a_{32} & a_{33} \end{bmatrix}$

c Lower 3 x 3 $\longrightarrow$ $\begin{bmatrix} c_{11} & 0 & 0 \\ c_{21} & c_{22} & 0 \\ c_{31} & c_{32} & c_{33} \end{bmatrix}$

e Lower 3 x 3 $\longrightarrow$ $\begin{bmatrix} e_{11} & 0 & 0 \\ e_{21} & e_{22} & 0 \\ e_{31} & e_{32} & e_{33} \end{bmatrix}$

OpenMx Parameter Matrices


```
Vars <- c('varx', 'vary', 'varz')

nv <- 3

multACEModel <- mxModel("multACE",    mxModel("ACE",
# Matrices a, c, and e to store a, c, and e path coefficients
mxMatrix( type="Lower", nrow=nv, ncol=nv, free=TRUE, values=.6, name="a" ),
mxMatrix( type="Lower", nrow=nv, ncol=nv, free=TRUE, values=.6, name="c" ),
mxMatrix( type="Lower", nrow=nv, ncol=nv, free=TRUE, values=.6, name="e" ),
```

Lunch

- After lunch: practical bivariate and trivariate genetic analysis