Introduction to Multivariate Genetic Analysis

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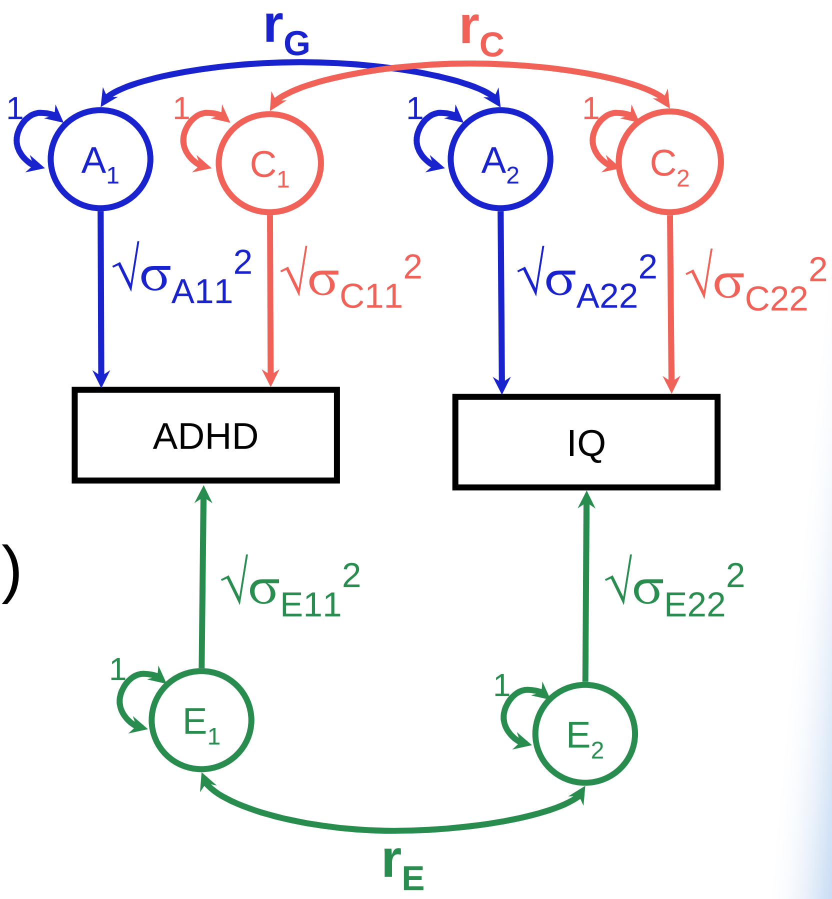
21st Twin and Family Methodology
Workshop, March 2008

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

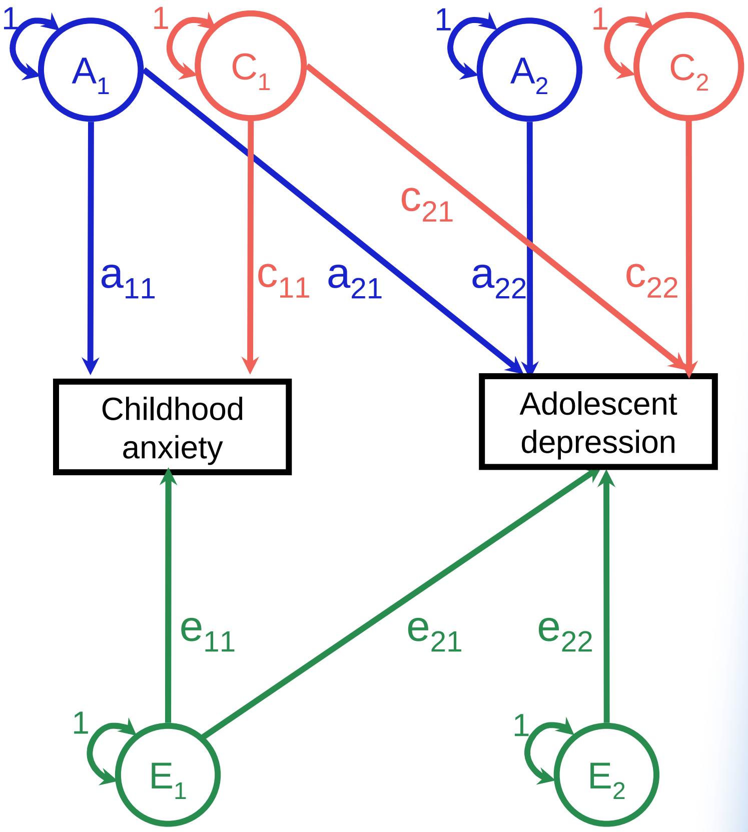
Example 1

- 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

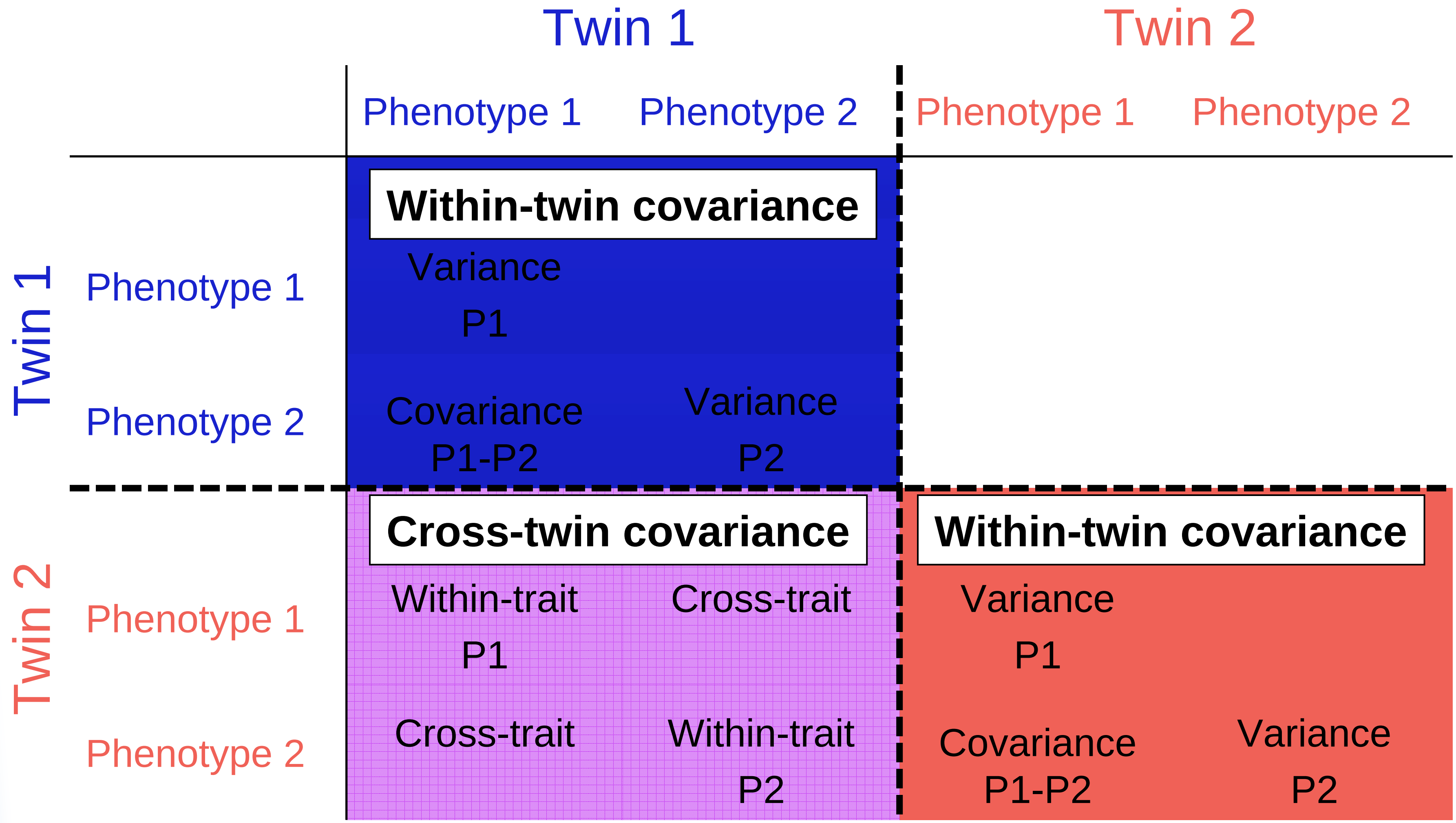
Observed Covariance Matrix

		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

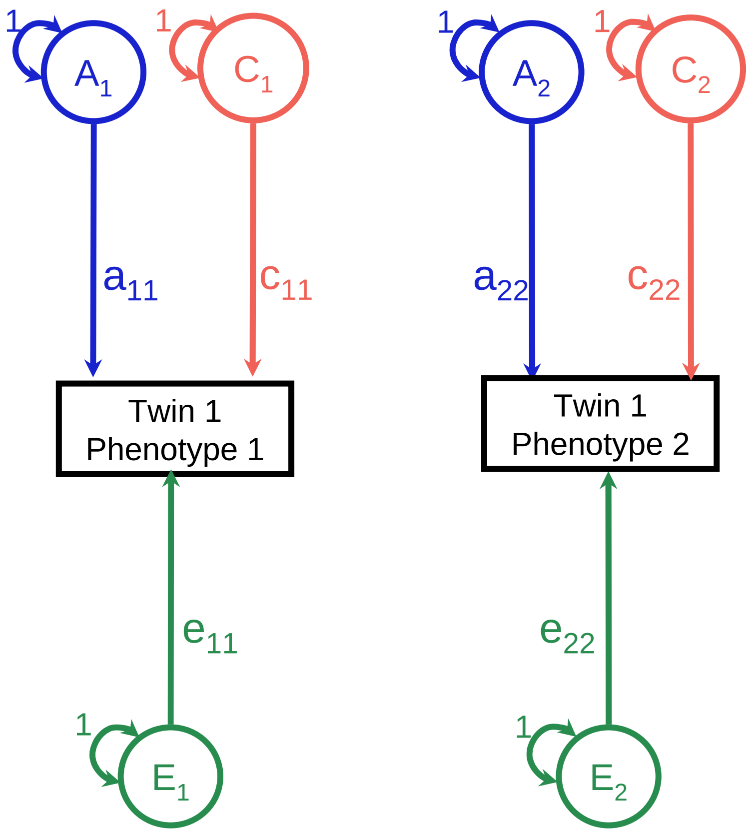
		Twin 1		Twin 2	
		Phenotype 1	Phenotype 2	Phenotype 1	Phenotype 2
Twin 1	Phenotype 1	**Within-twin covariance** Variance P1			
	Phenotype 2	Covariance P1-P2	Variance P2		
Twin 2	Phenotype 1	Within-trait P1	Cross-trait	**Within-twin covariance** Variance P1	
	Phenotype 2	Cross-trait	Within-trait P2	Covariance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

Observed Covariance Matrix

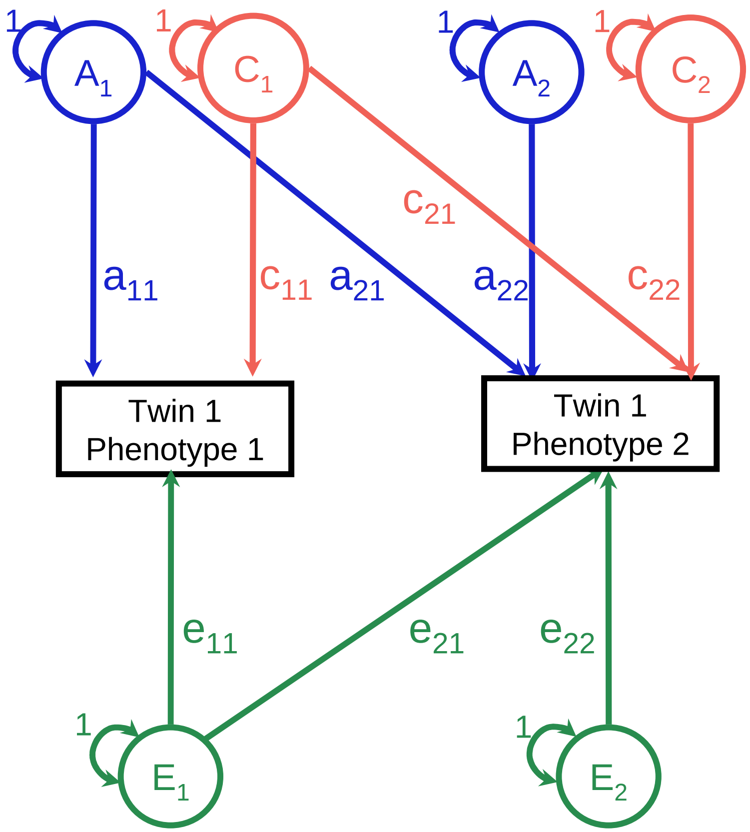


		Twin 1		Twin 2	
		Phenotype 1	Phenotype 2	Phenotype 1	Phenotype 2
Twin 1	Phenotype 1	**Within-twin covariance** Variance P1			
	Phenotype 2	Covariance P1-P2	Variance P2		
Twin 2	Phenotype 1	**Cross-twin covariance** Within-trait P1	Cross-trait	**Within-twin covariance** Variance P1	
	Phenotype 2	Cross-trait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

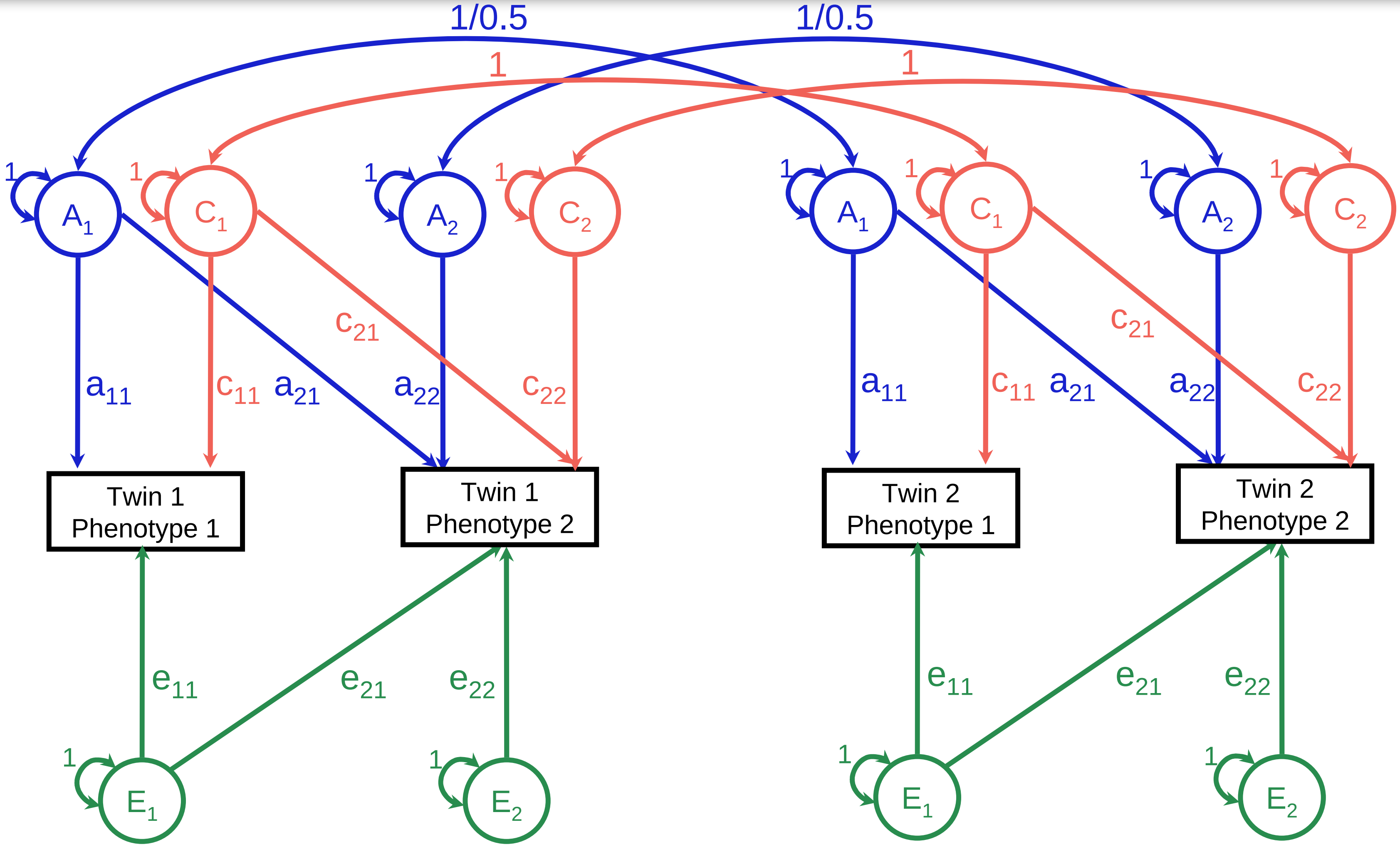
SEM: Cholesky Decomposition



SEM: Cholesky Decomposition



SEM: Cholesky Decomposition



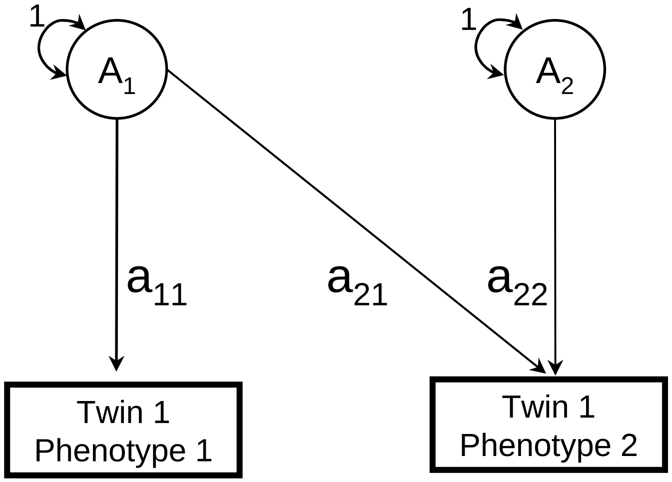
Why Fit This Model?

- 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 = X*X’
- Many other multivariate models possible
  - Depends on data and hypotheses of interest

Cholesky Decomposition

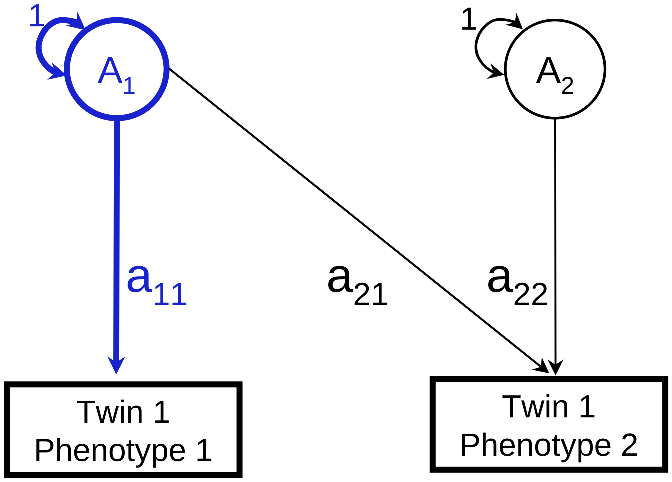
Path Tracing

Within-Twin Covariances (A)



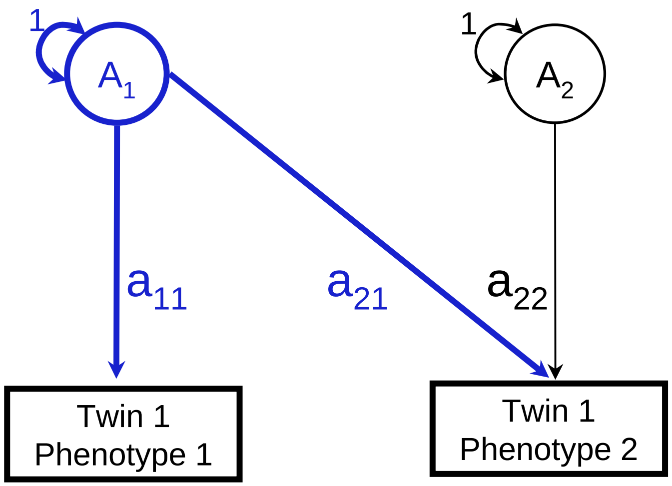
		Twin 1	
		Phenotype 1	Phenotype 2
Twin 1	Phenotype 1		
	Phenotype 2		

Within-Twin Covariances (A)



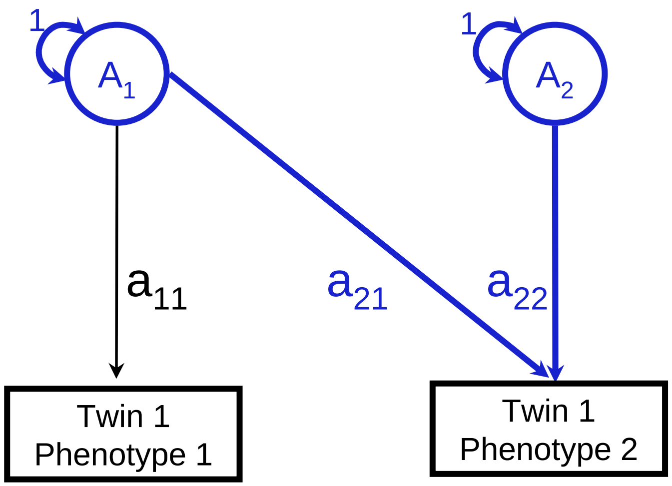
		Twin 1	
		Phenotype 1	Phenotype 2
Twin 1	Phenotype 1	a_{11}^2	
	Phenotype 2		

Within-Twin Covariances (A)



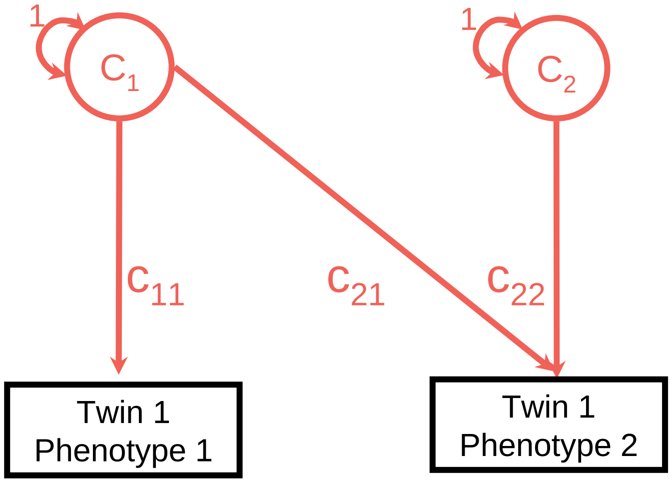
		Twin 1	
		Phenotype 1	Phenotype 2
Twin 1	Phenotype 1	a_{11}^2	
	Phenotype 2	$a_{11}a_{21}$	

Within-Twin Covariances (A)



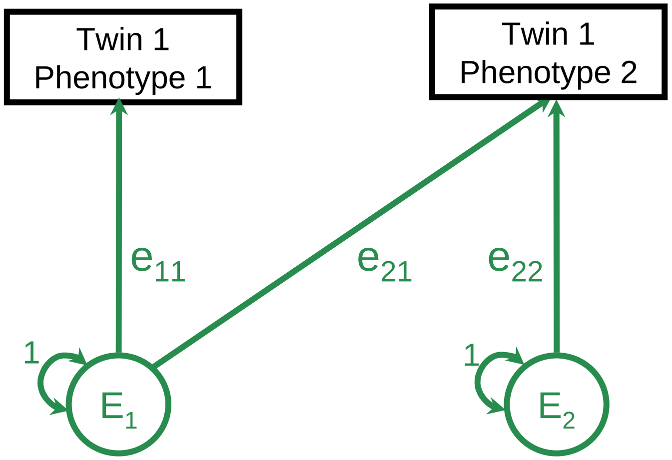
		Twin 1	
		Phenotype 1	Phenotype 2
Twin 1	Phenotype 1	a_{11}^2	
	Phenotype 2	$a_{11}a_{21}$	$a_{22}^2+a_{21}^2$

Within-Twin Covariances (C)



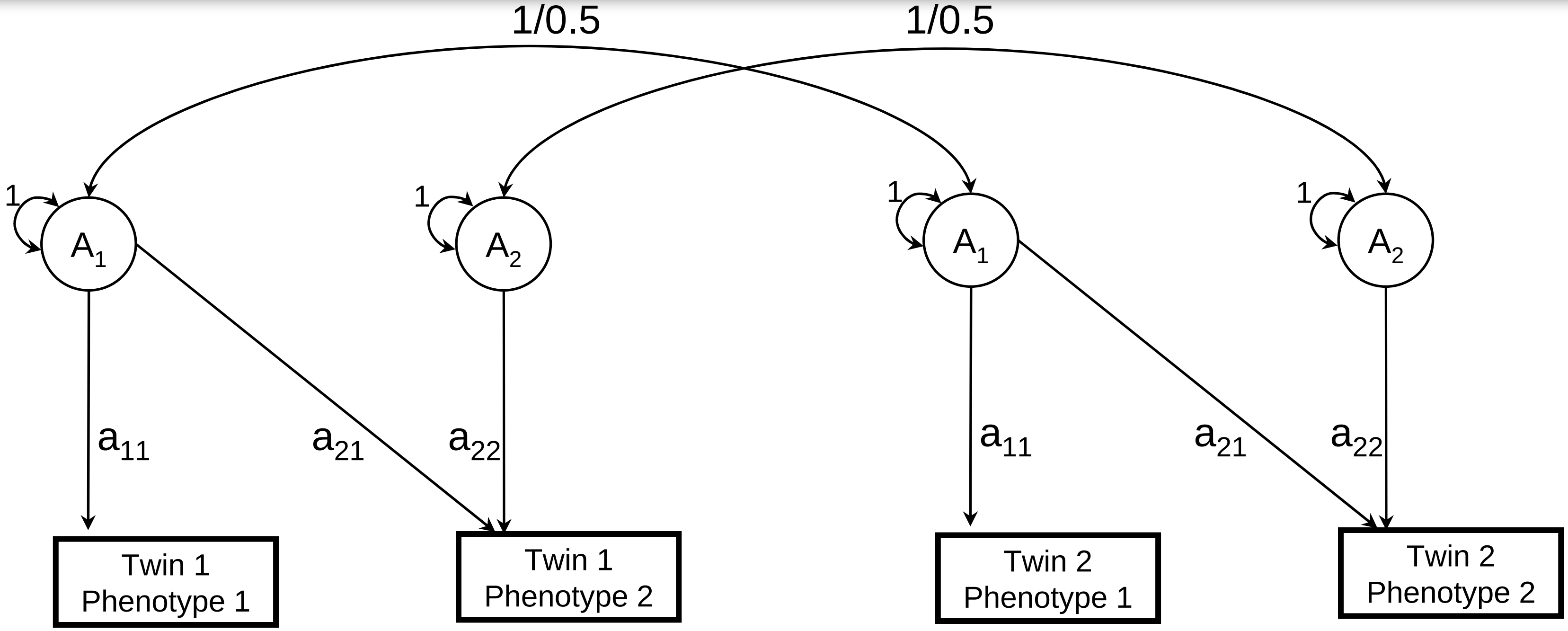
		Twin 1	
		Phenotype 1	Phenotype 2
Twin 1	Phenotype 1	$a_{11}^2+c_{11}^2$	
	Phenotype 2	$a_{11}a_{21}+c_{11}c_{21}$	$a_{22}^2+a_{21}^2+c_{22}^2+c_{21}^2$

Within-Twin Covariances (E)



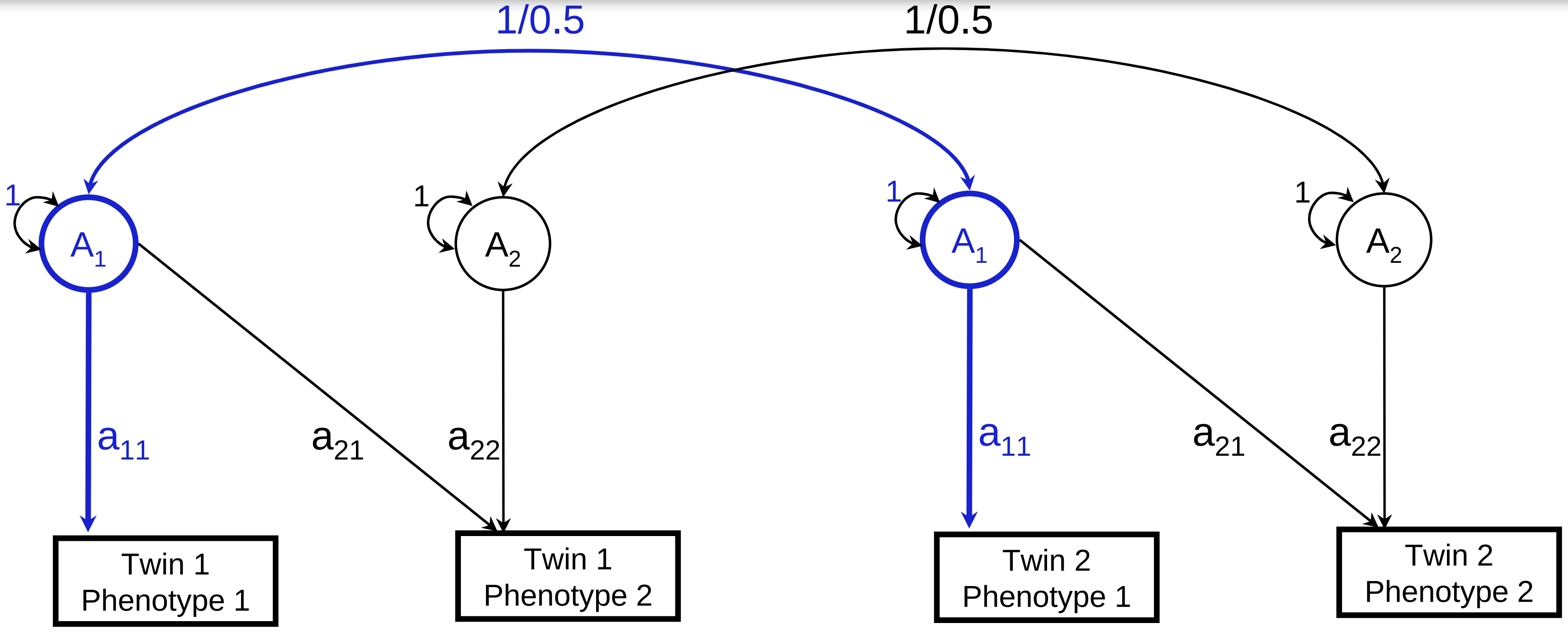
		Twin 1	
		Phenotype 1	Phenotype 2
Twin 1	Phenotype 1	$a_{11}^2+c_{11}^2+e_{11}^2$	
	Phenotype 2	$a_{11}a_{21}+c_{11}c_{21}+e_{11}e_{21}$	$a_{22}^2+a_{21}^2+c_{22}^2+c_{21}^2$ $+e_{22}^2+e_{21}^2$

Cross-Twin Covariances (A)



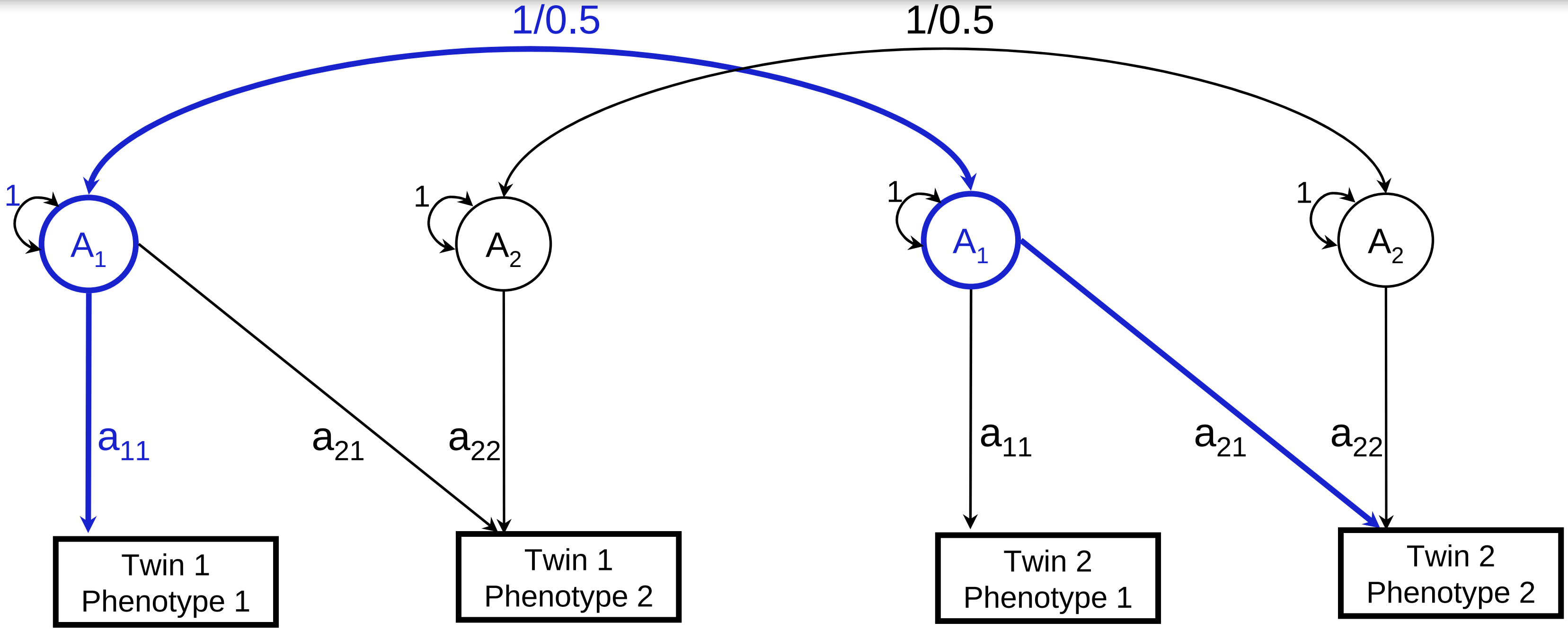
		Twin 1	
		Phenotype 1	Phenotype 2
Twin 2	Phenotype 1		
	Phenotype 2		

Cross-Twin Covariances (A)



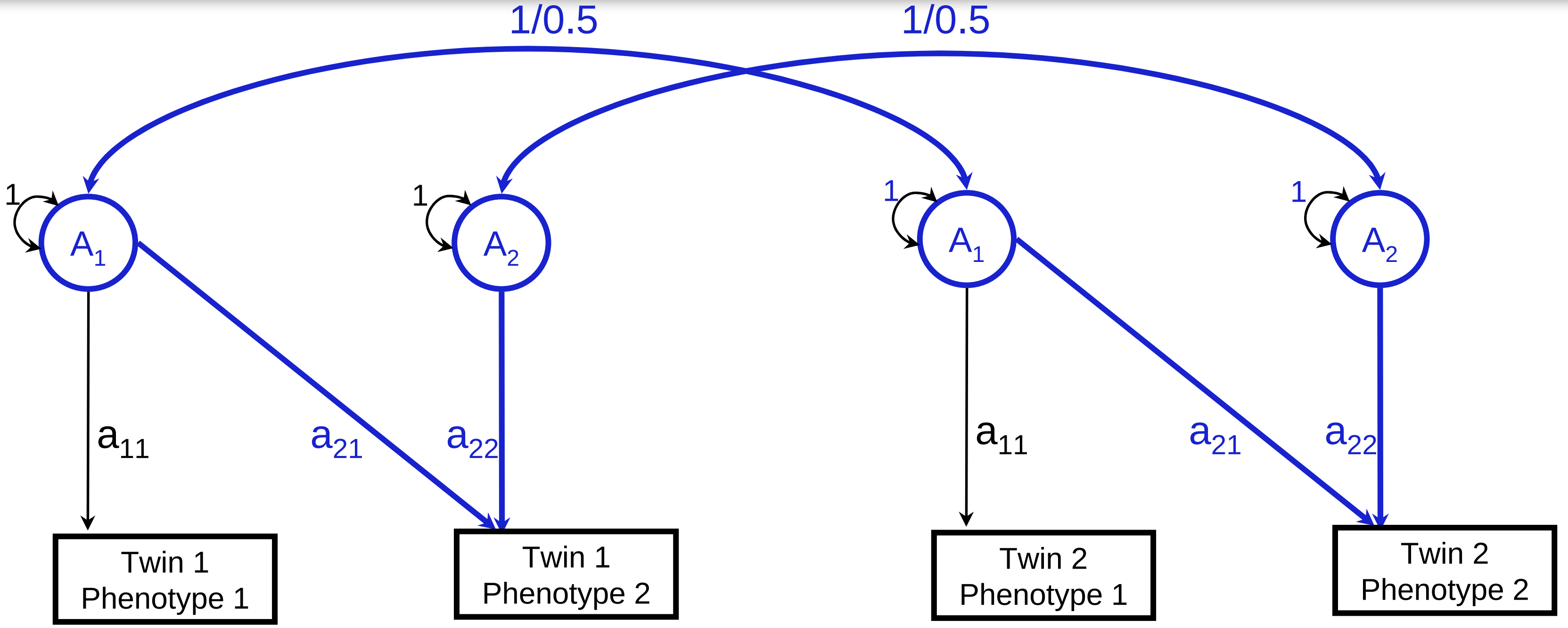
		Twin 1	
		Phenotype 1	Phenotype 2
Twin 2	Phenotype 1	$1/0.5a_{11}^2$	
	Phenotype 2		

Cross-Twin Covariances (A)



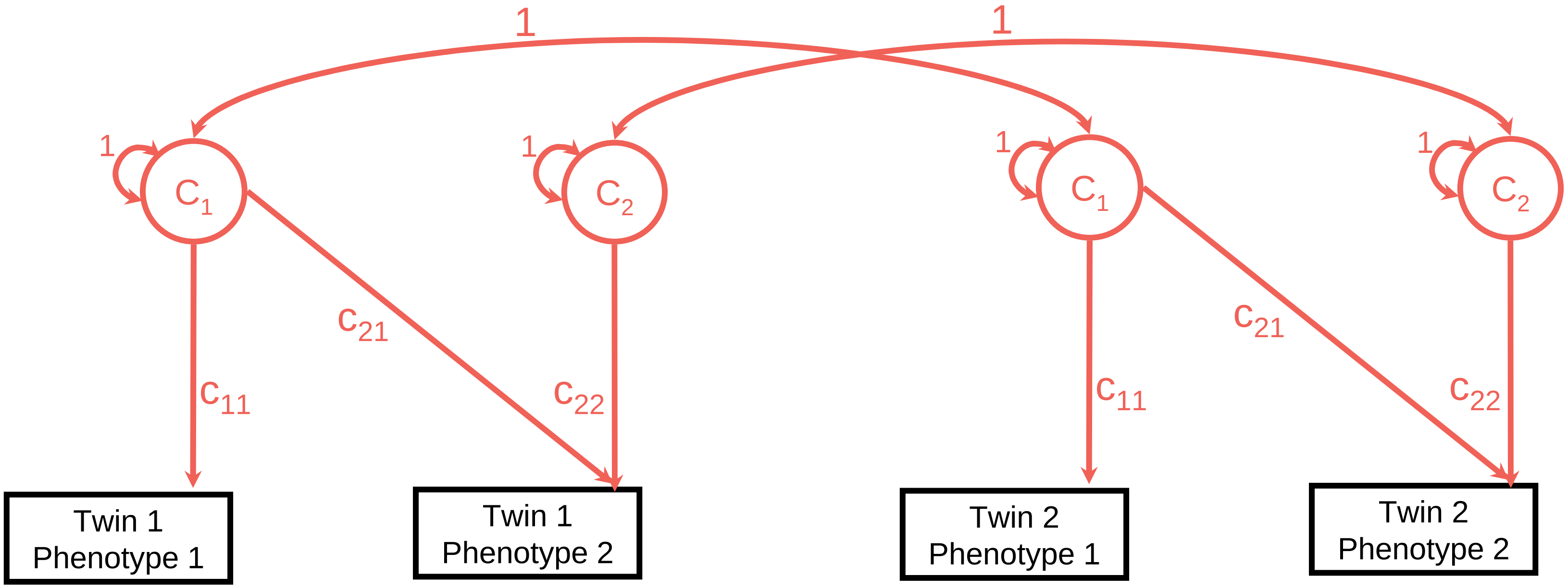
		Twin 1	
		Phenotype 1	Phenotype 2
Twin 2	Phenotype 1	$1/0.5a_{11}^2$	
	Phenotype 2	$1/0.5a_{11}a_{21}$	

Cross-Twin Covariances (A)



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

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

Within-twin covariance

Cross-twin covariance

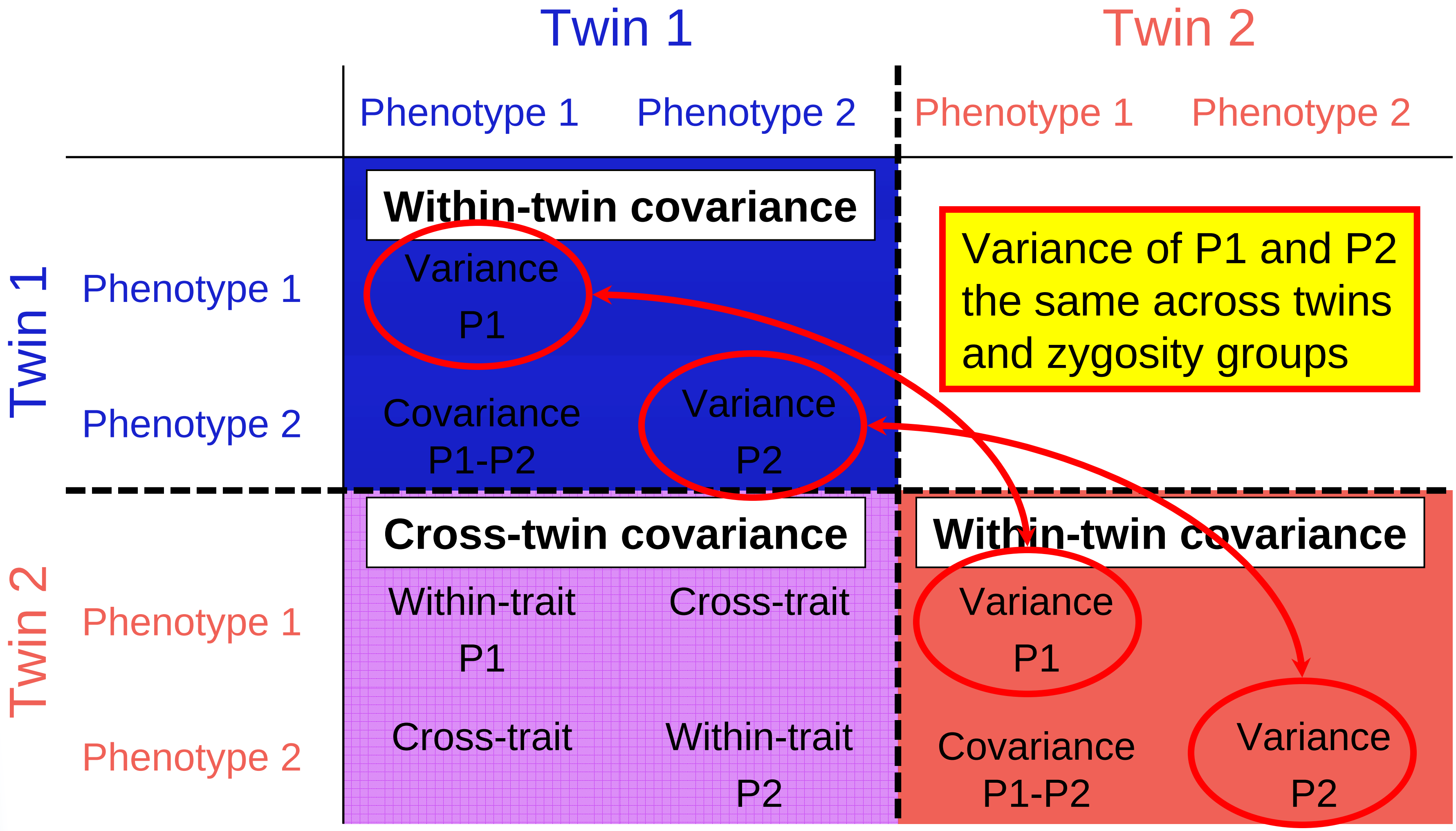
Within-twin covariance

		Twin 1		Twin 2	
		Phenotype 1	Phenotype 2	Phenotype 1	Phenotype 2
Twin 1	Phenotype 1	$a_{11}^2+c_{11}^2+e_{11}^2$			
	Phenotype 2	$a_{11}a_{21}+c_{11}c_{21}+e_{11}e_{21}$	$a_{22}^2+a_{21}^2+c_{22}^2+c_{21}^2+e_{22}^2+e_{21}^2$		
Twin 2	Phenotype 1	$1/.5a_{11}^2+c_{11}^2$		$a_{11}^2+c_{11}^2+e_{11}^2$	
	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
		Within-twin covariance			
Twin 1	Phenotype 1	Variance P1			
	Phenotype 2	Covariance P1-P2	Variance P2		
		Cross-twin covariance		**Within-twin covariance**	
Twin 2	Phenotype 1	Within-trait P1	Cross-trait	Variance P1	
	Phenotype 2	Cross-trait	Within-trait P2	Covariance P1-P2	Variance P2

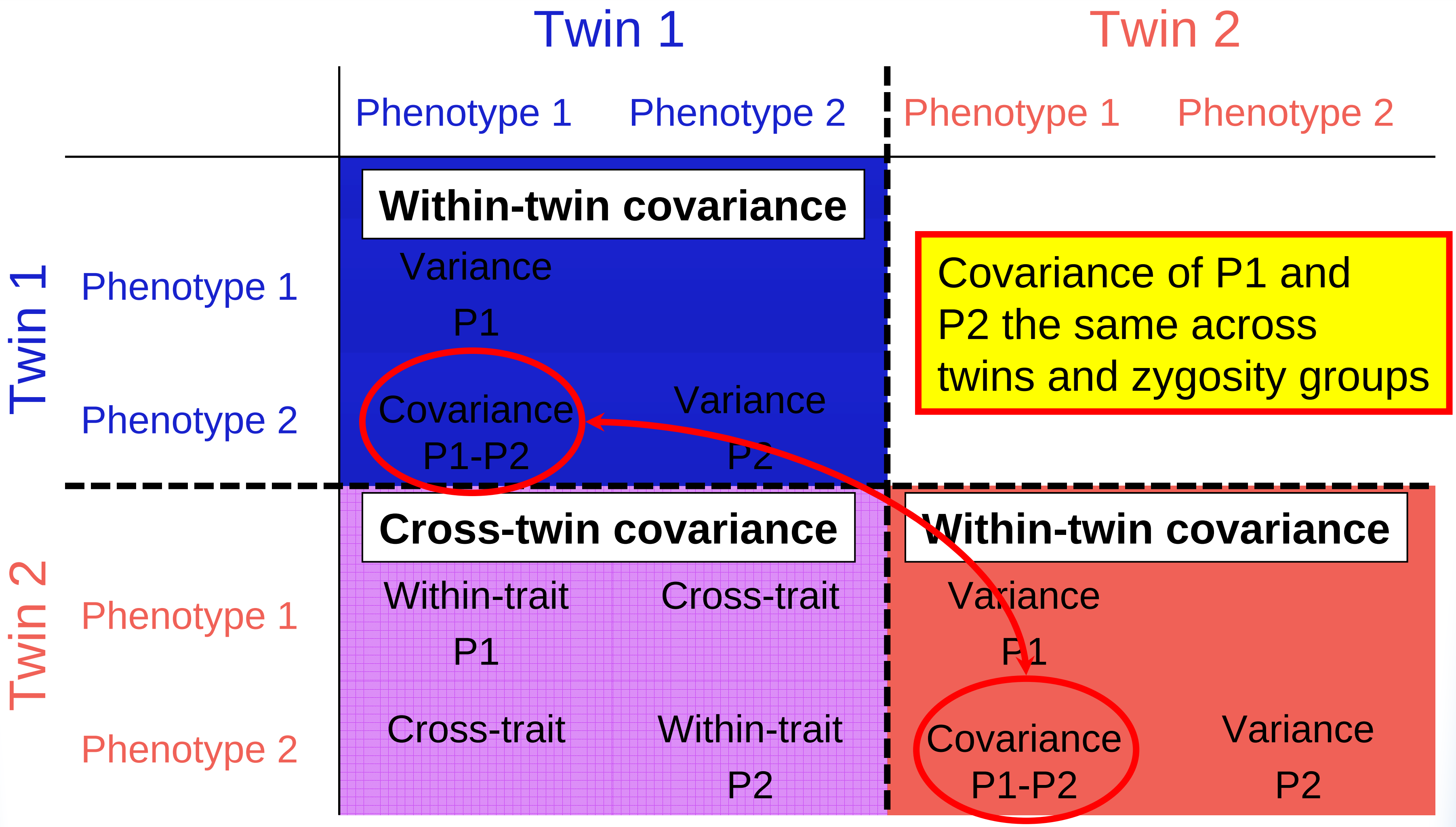
Predicted Model



		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

Variance of P1 and P2 the same across twins and zygosity groups

Predicted Model



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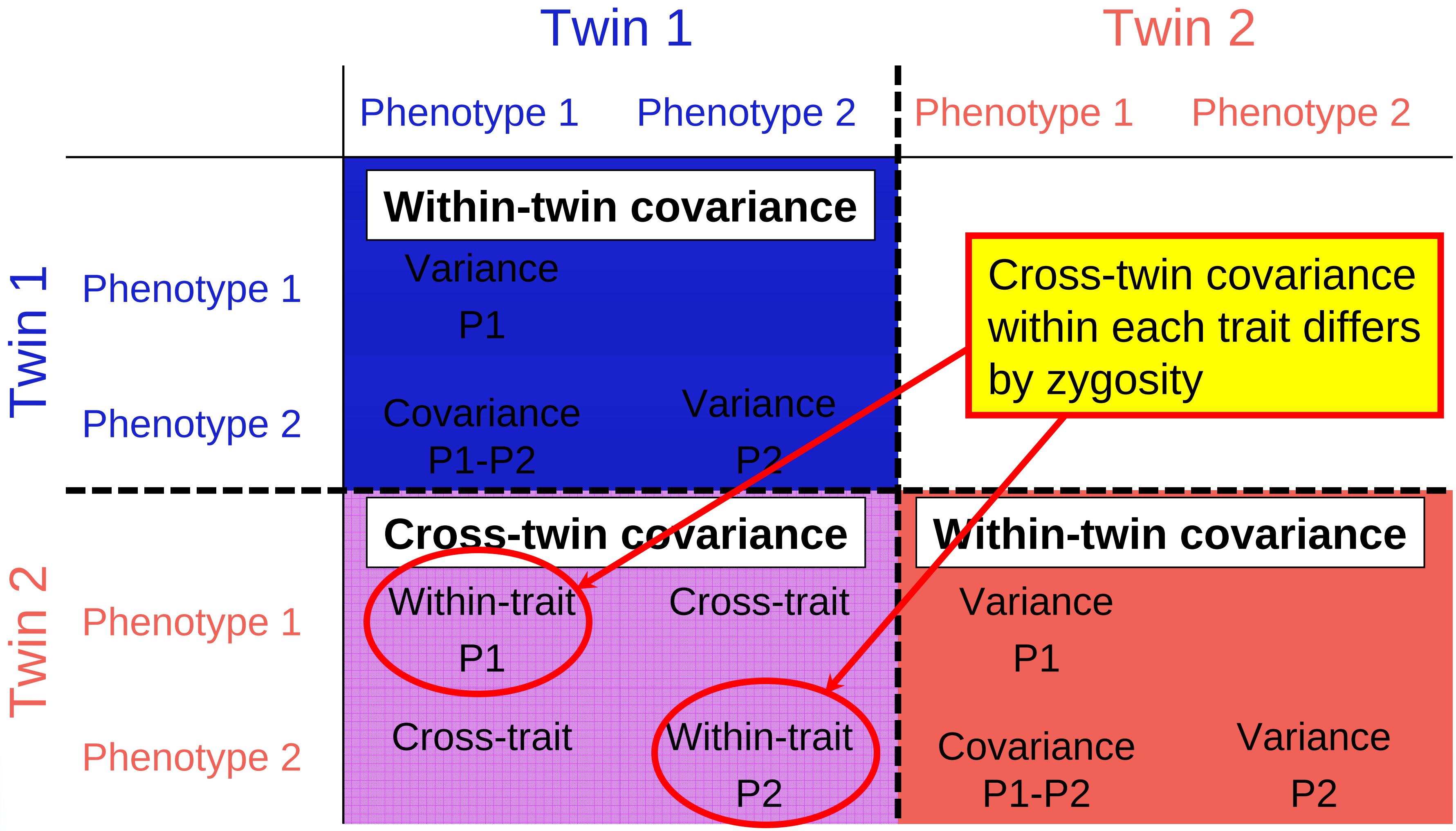
		Phenotype 1	Phenotype 2	Phenotype 1	Phenotype 2
Twin 1	Phenotype 1	**Within-twin covariance** Variance P1			
	Phenotype 2	Covariance P1-P2	Variance P2		
Twin 2	Phenotype 1	**Cross-twin covariance** Within-trait P1	Cross-trait	**Within-twin covariance** Variance P1	
	Phenotype 2	Cross-trait	Within-trait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

Covariance of P1 and P2 the same across twins and zygosity groups

Predicted Model



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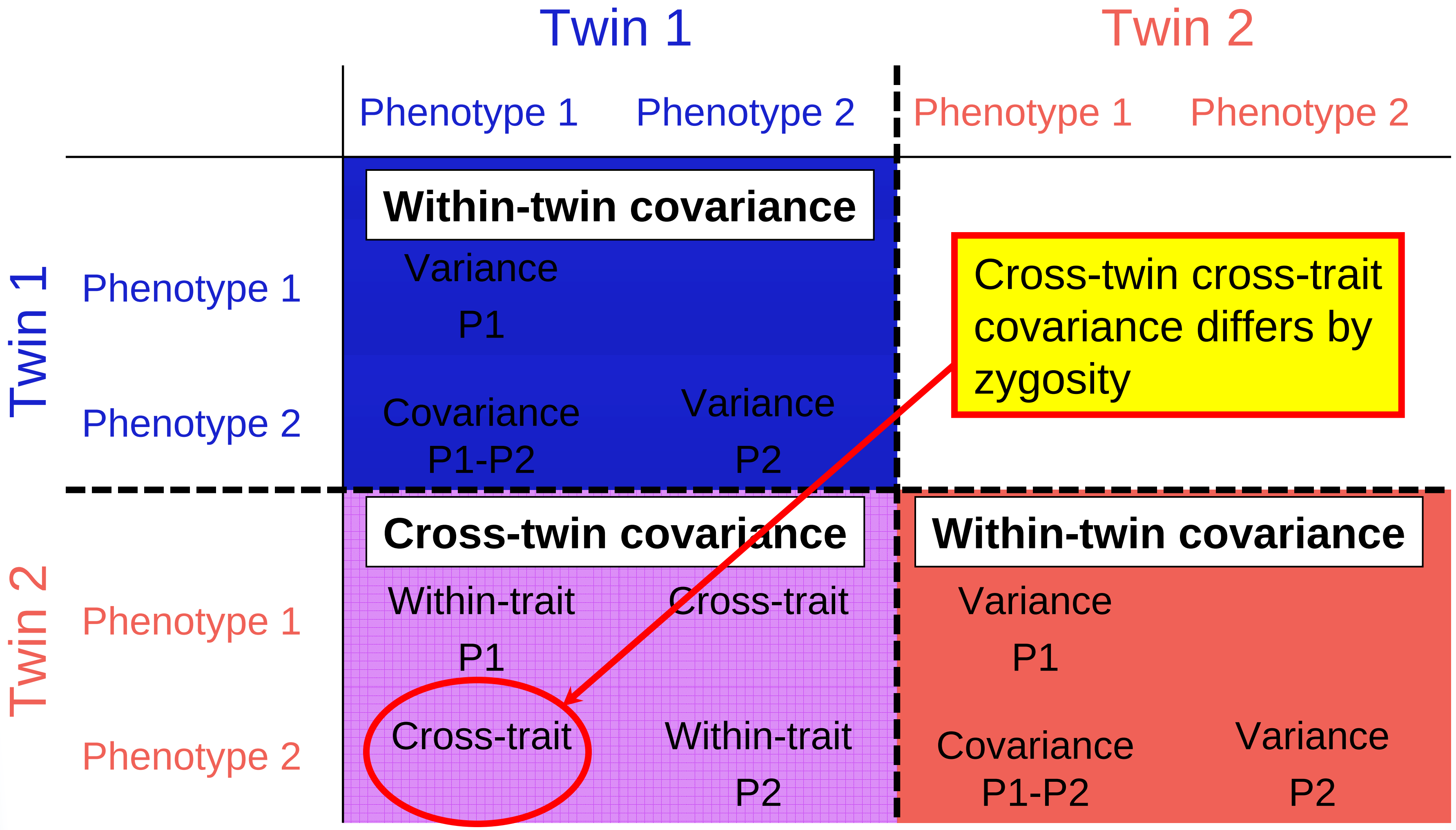
	Phenotype 2	Covariance P1-P2	Variance P2		
Twin 2	Phenotype 1	**Cross-twin covariance** Within-trait P1	Cross-trait	**Within-twin covariance** Variance P1	
	Phenotype 2	Cross-trait	Within-trait P2	Covariance P1-P2	Variance P2

Cross-twin covariance within each trait differs by zygosity

Predicted Model



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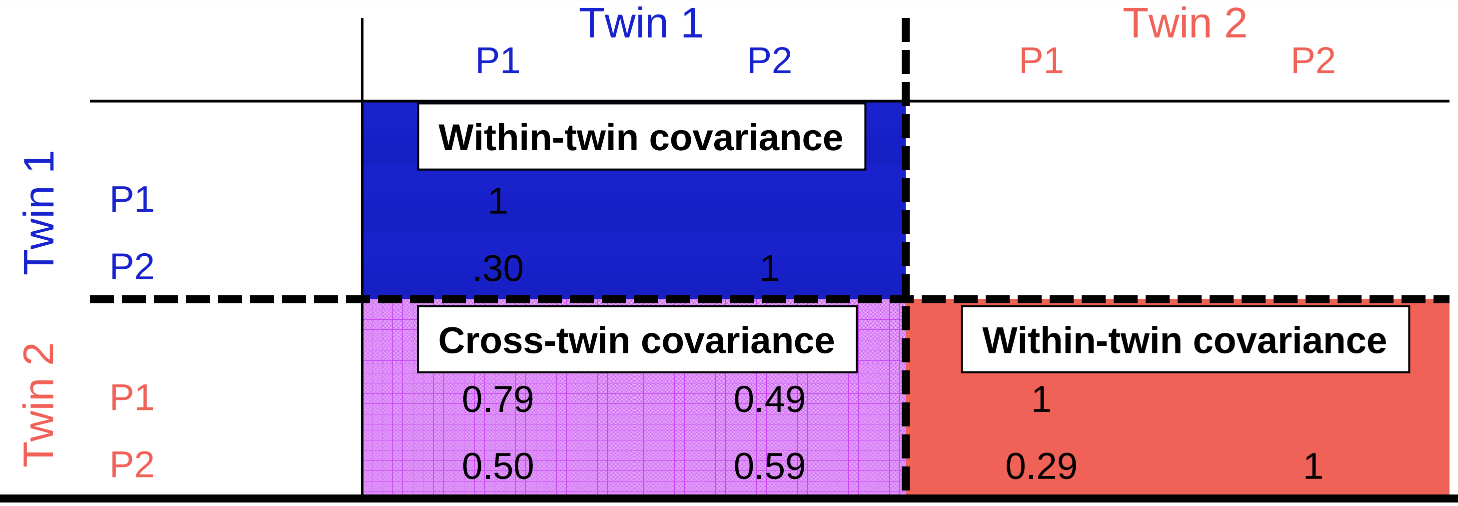
	Phenotype 2	Cross-trait	Within-trait P2	Covariance P1-P2	Variance P2

Cross-twin cross-trait covariance differs by zygosity

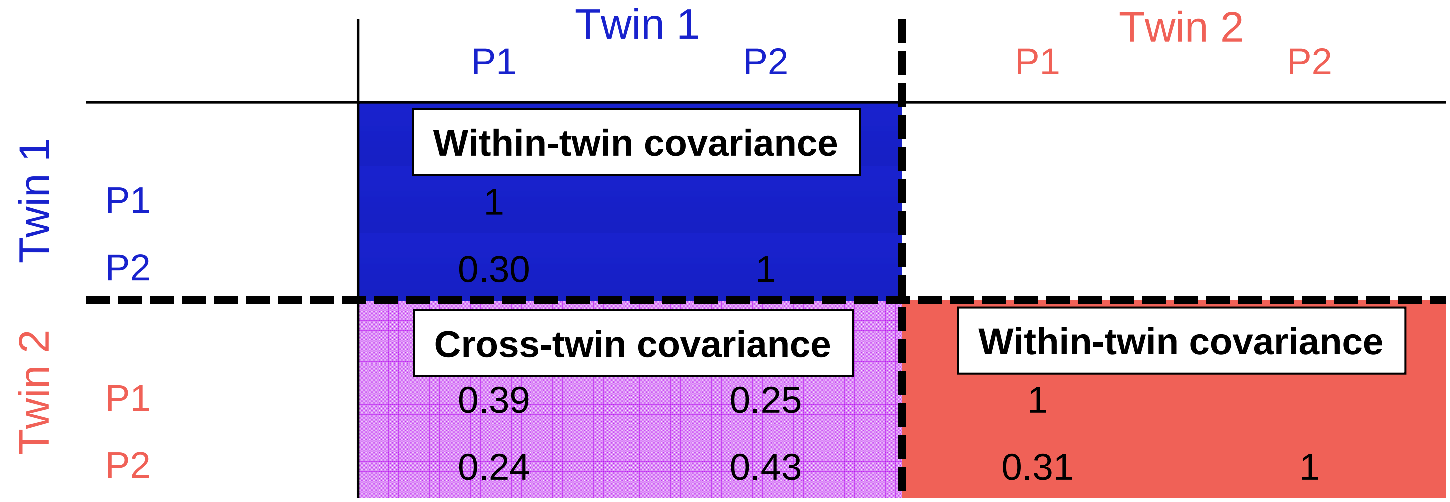
Example Covariance Matrix

MZ



		Twin 1 P1	Twin 1 P2	Twin 2 P1	Twin 2 P2
		Within-twin covariance			
Twin 1	P1	1			
	P2	.30	1		
		Cross-twin covariance		Within-twin covariance	
Twin 2	P1	0.79	0.49	1	
	P2	0.50	0.59	0.29	1

DZ



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Twin 1	P1	1			
	P2	0.30	1		
		Cross-twin covariance		Within-twin covariance	
Twin 2	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
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	P2	.30	1		
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Within-twin covariance

Cross-twin covariance

Within-twin covariance

DZ

		Twin 1		Twin 2	
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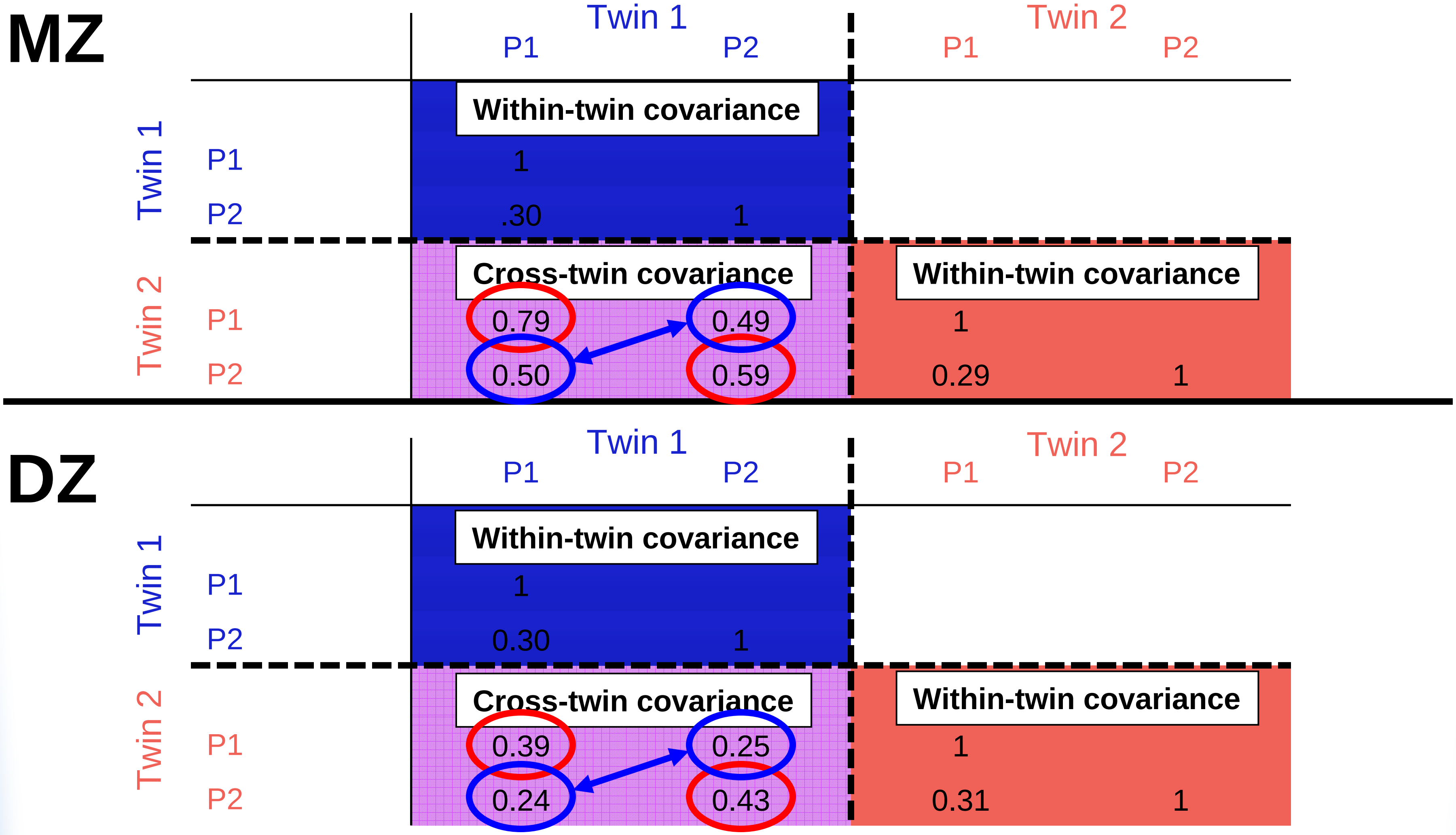
Within-twin covariance

Cross-twin covariance

Within-twin covariance

Example Covariance Matrix



MZ

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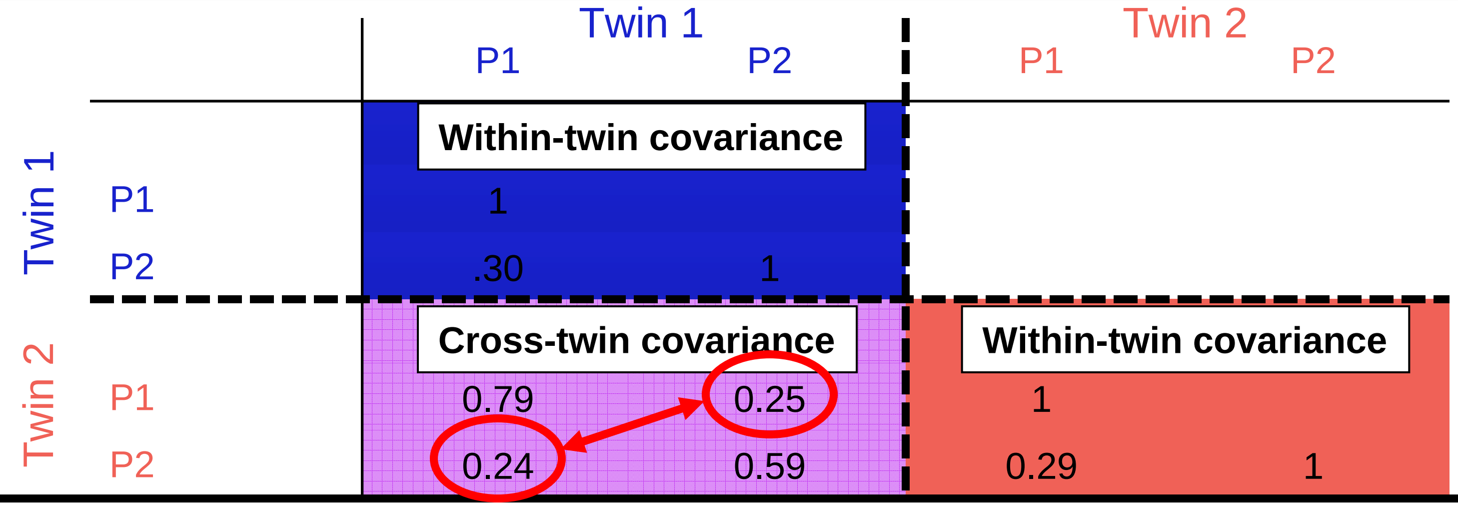
Example Covariance Matrix

MZ



Within-twin covariance

Cross-twin covariance

Within-twin covariance

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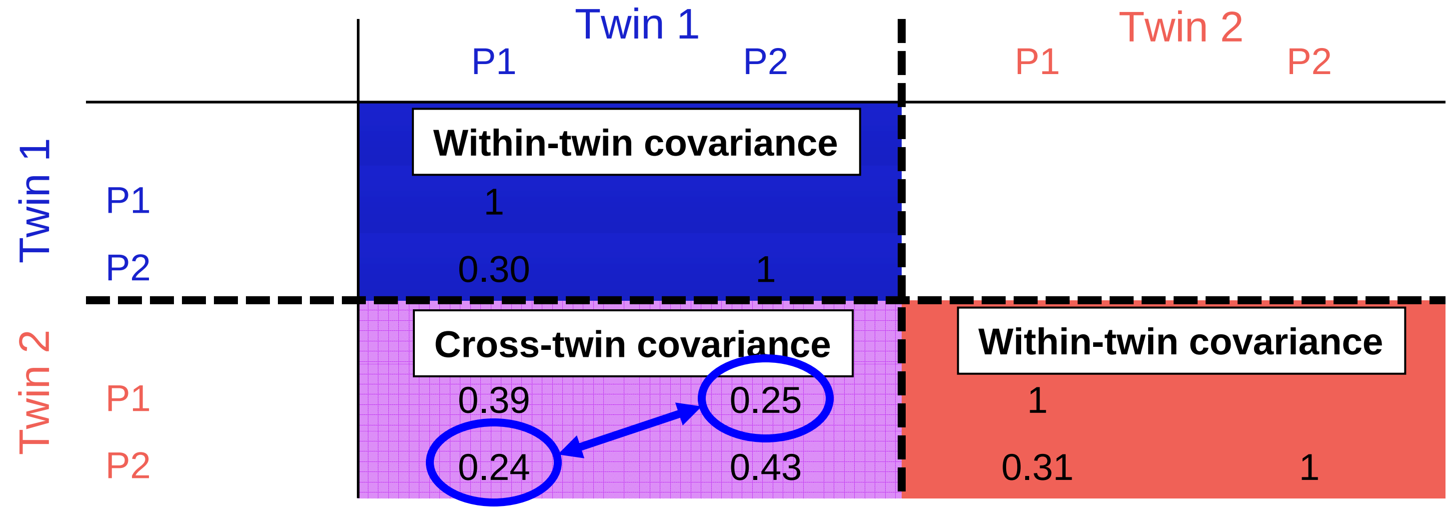
DZ



Within-twin covariance

Cross-twin covariance

Within-twin covariance

		Twin 1		Twin 2	
		P1	P2	P1	P2
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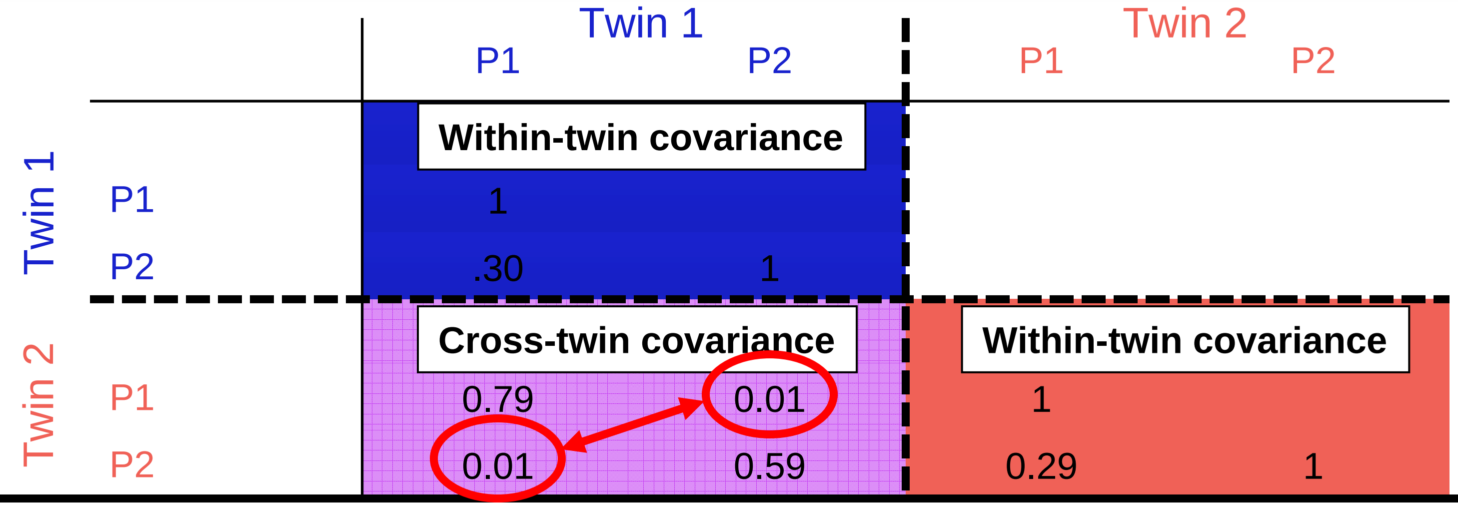
Example Covariance Matrix

MZ

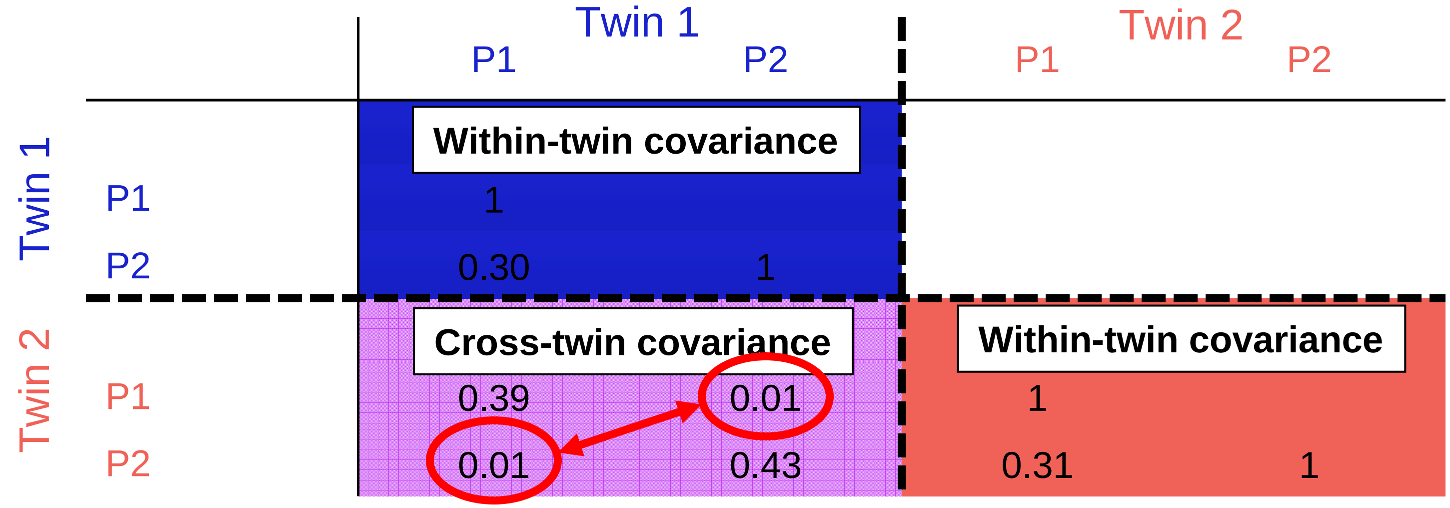

Within-twin covariance

Cross-twin covariance

Within-twin covariance

		Twin 1		Twin 2	
		P1	P2	P1	P2
Twin 1	P1	1			
	P2	.30	1		
Twin 2	P1	0.79	0.01	1	
	P2	0.01	0.59	0.29	1

DZ


Within-twin covariance

Cross-twin covariance

Within-twin covariance

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		P1	P2	P1	P2
Twin 1	P1	1			
	P2	0.30	1		
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	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

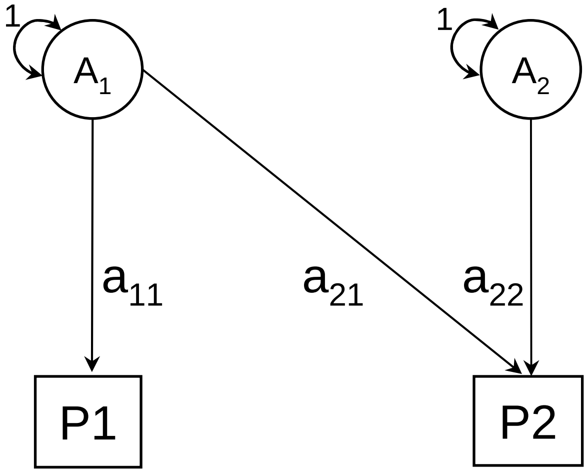
Cholesky Decomposition

Specification in Mx

Mx Parameter Matrices

```
#define nvar 2
Begin Matrices;
X lower nvar nvar free        ! Genetic coefficients
Y lower nvar nvar free        ! C coefficients
Z lower nvar nvar free        ! E coefficients
G Full 1 nvar free            ! Means
H Full 1 1 fix                ! 0.5 for DZ A covar
End Matrices;
Begin Algebra;
A=X*X’;                       ! A var/cov
C=Y*Y’;                       ! C var/cov
E=Z*Z’;                       ! E var/cov
P=A+C+E
End Algebra;
```

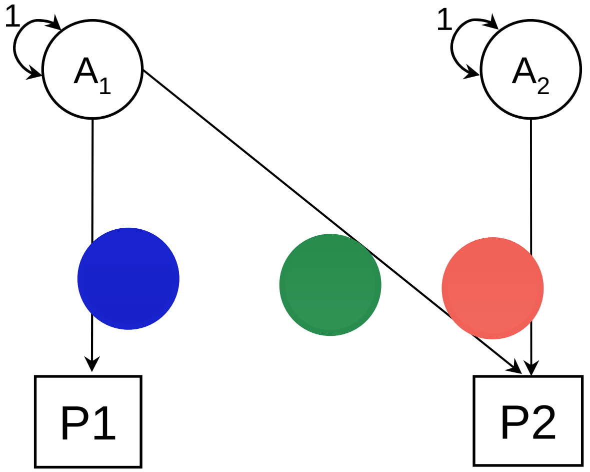
Within-Twin Covariance



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



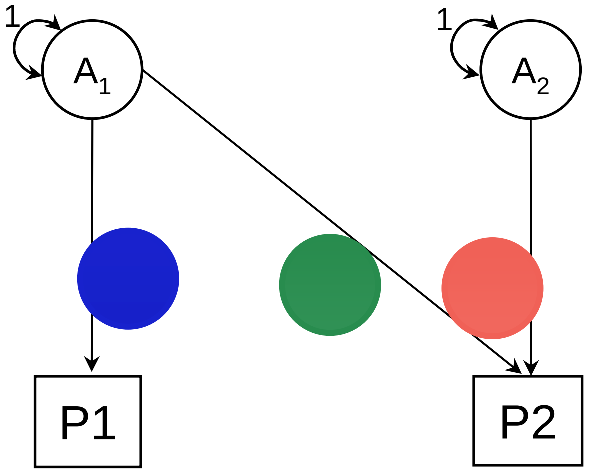
Path Tracing:

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

X Lower 2 x 2:

$$\begin{array}{c} \\ P1 \\ P2 \end{array} \begin{array}{c} \begin{array}{cc} A1 & A2 \end{array} \\ \begin{bmatrix} \blacksquare & 0 \\ a_{21} & a_{22} \end{bmatrix} \end{array}$$

Within-Twin Covariance



Path Tracing:

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

X Lower 2 x 2:

$$\begin{array}{c|cc} & \text{A1} & \text{A2} \\ \hline \text{P1} & \blacksquare & 0 \\ \text{P2} & a_{21} & a_{22} \end{array}$$

$$\begin{aligned} \Sigma_A &= \mathbf{X} * \mathbf{X}' \\ &= \begin{bmatrix} \blacksquare & 0 \\ a_{21} & a_{22} \end{bmatrix} * \begin{bmatrix} \blacksquare & a_{21} \\ 0 & a_{22} \end{bmatrix} \\ &= \begin{bmatrix} a_{11}^2 + 0 \times 0 & a_{11}a_{21} + 0 \times a_{22} \\ a_{21}a_{11} + 0 \times a_{22} & a_{21}^2 + a_{22}^2 \end{bmatrix} \end{aligned}$$

Total Within-Twin Covar.

$$\blacksquare \quad \Sigma_C = \mathbf{Y} * \mathbf{Y}' = \begin{bmatrix} c_{11}^2 & c_{11}c_{21} \\ c_{21}c_{11} & c_{21}^2 + c_{22}^2 \end{bmatrix}$$

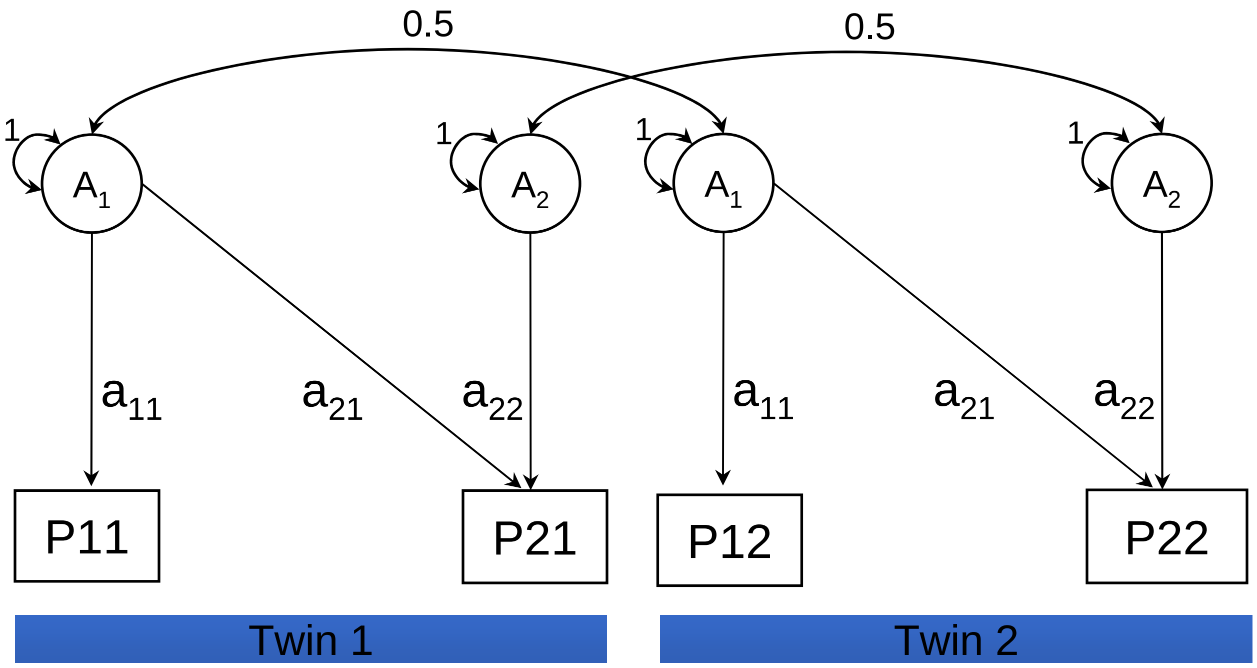
$$\Sigma_E = \mathbf{Z} * \mathbf{Z}' = \begin{bmatrix} e_{11}^2 & e_{11}e_{21} \\ e_{21}e_{11} & e_{21}^2 + e_{22}^2 \end{bmatrix}$$

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

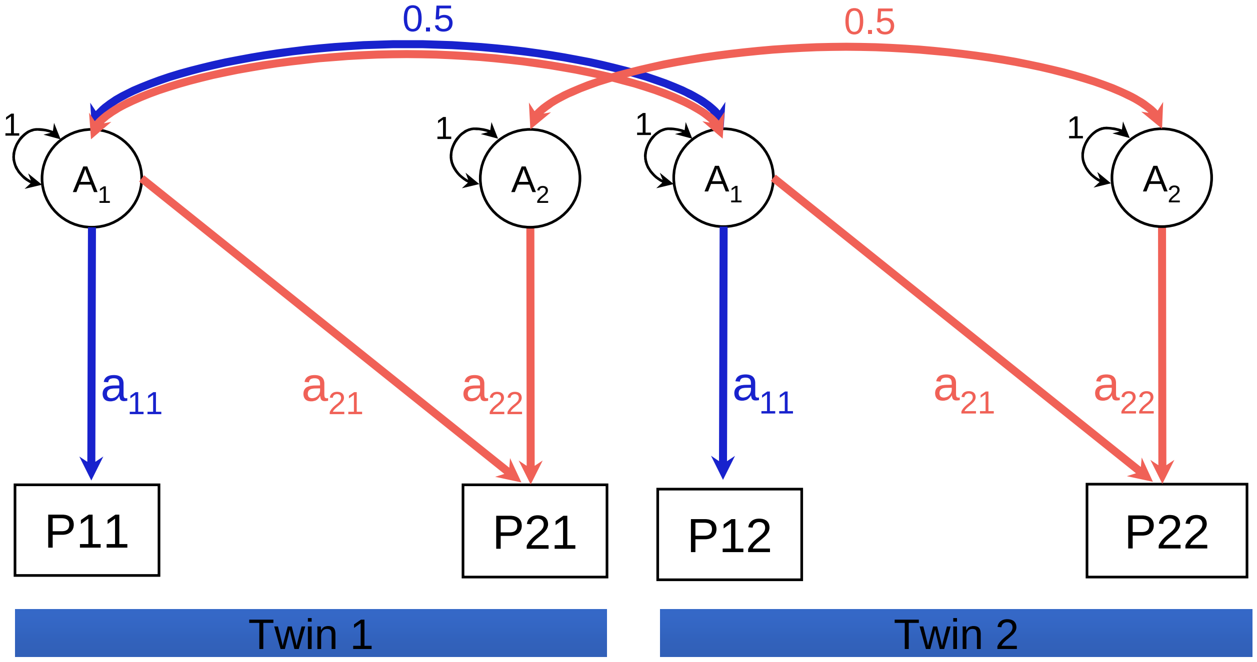
$$\Sigma_P = \blacksquare + \Sigma_C + \Sigma_E$$

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

Cross-Twin Covariance (DZ)



Cross-Twin Covariance (DZ)

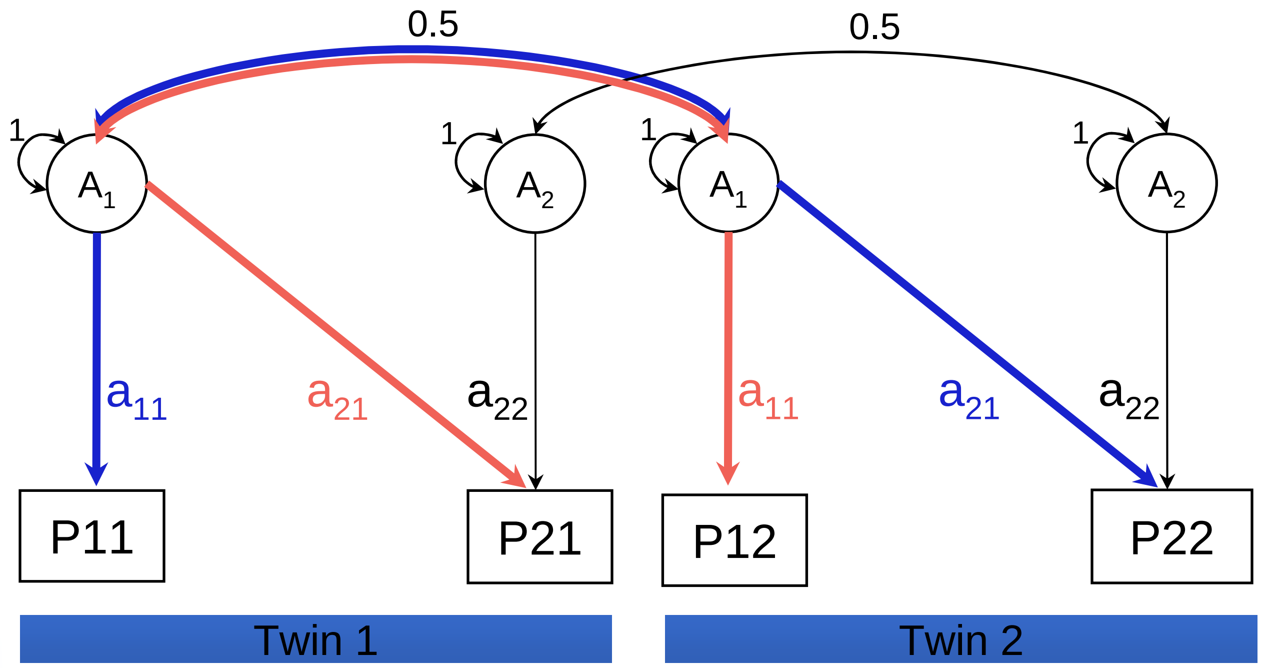


Within-traits

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

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

Cross-Twin Covariance (DZ)



Path Tracing:

Within-traits

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

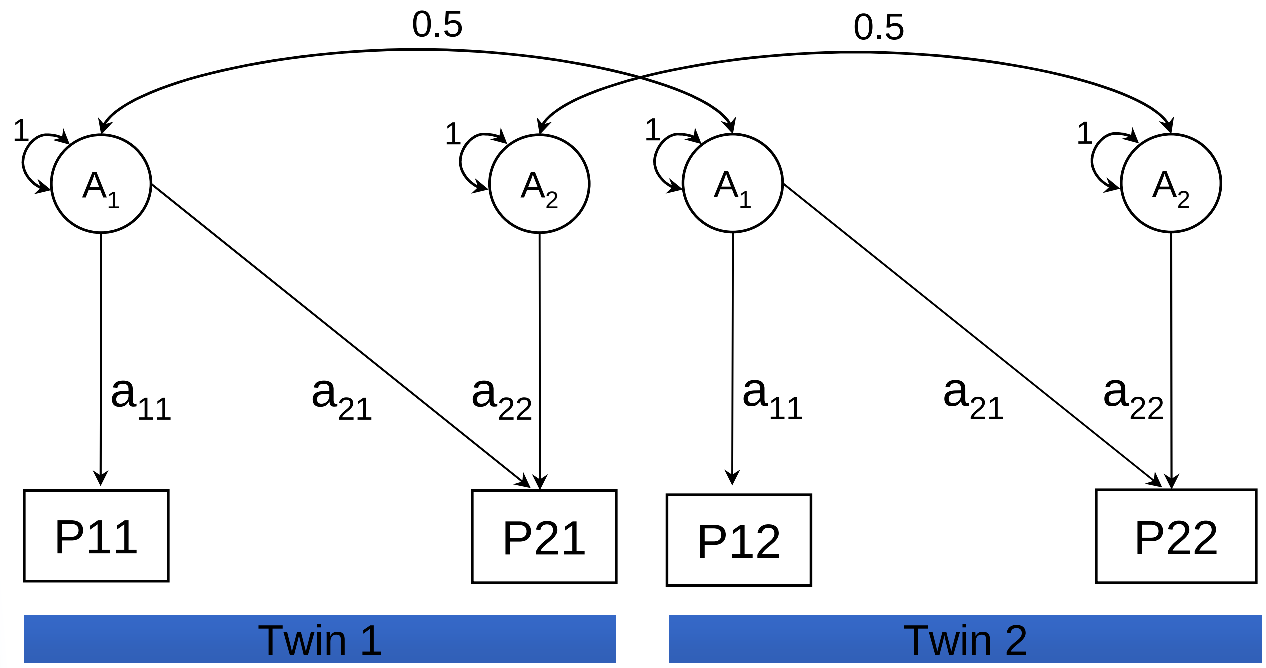
$P21\text{-}P22 = 0.5a_{22}^2+0.5a_{21}^2$

Cross-traits

$P11\text{-}P22 = 0.5a_{11}a_{21}$

$P21\text{-}P12 = 0.5a_{21}a_{11}$

Additive Genetic Cross-Twin Covariance (DZ)



Path Tracing:

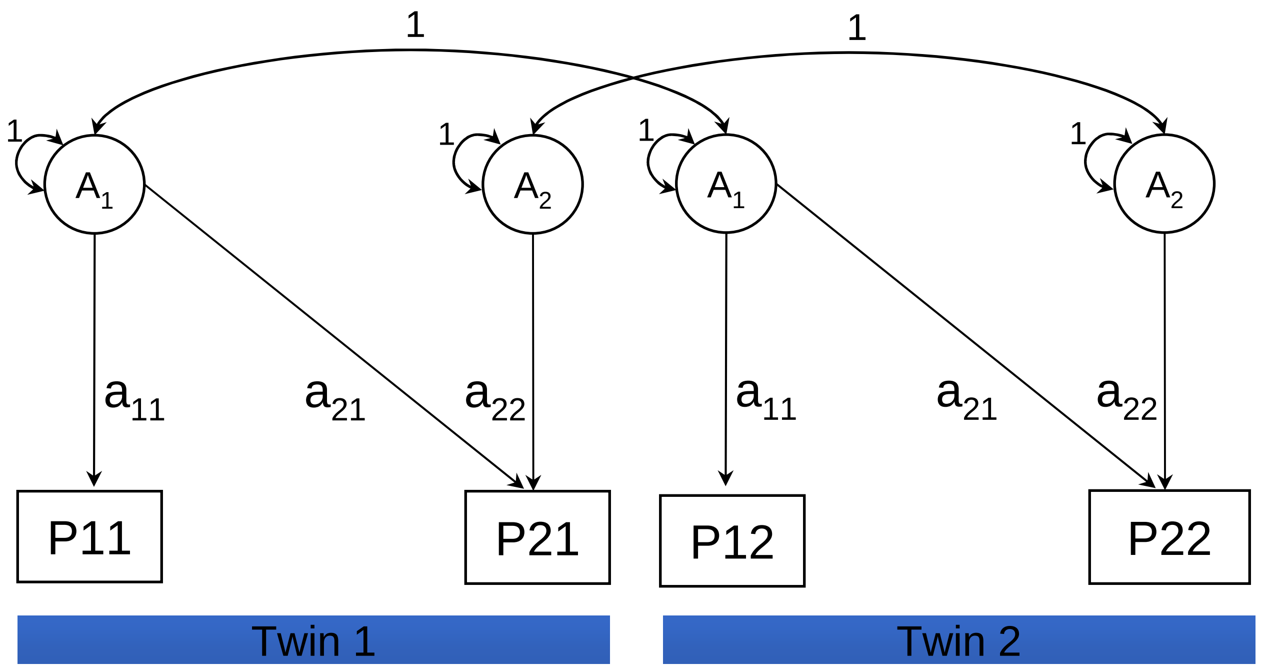
Within-traits
P11-P12 =
P21-P22 = $0.5a_{22}^2+0.5a_{21}^2$

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

$$0.5 \otimes \Sigma_A = 0.5 \otimes \mathbf{X} * \mathbf{X}' = \begin{bmatrix} & 0.5a_{11}a_{21} \\ 0.5a_{21}a_{11} & 0.5(a_{21}^2 + a_{22}^2) \end{bmatrix}$$

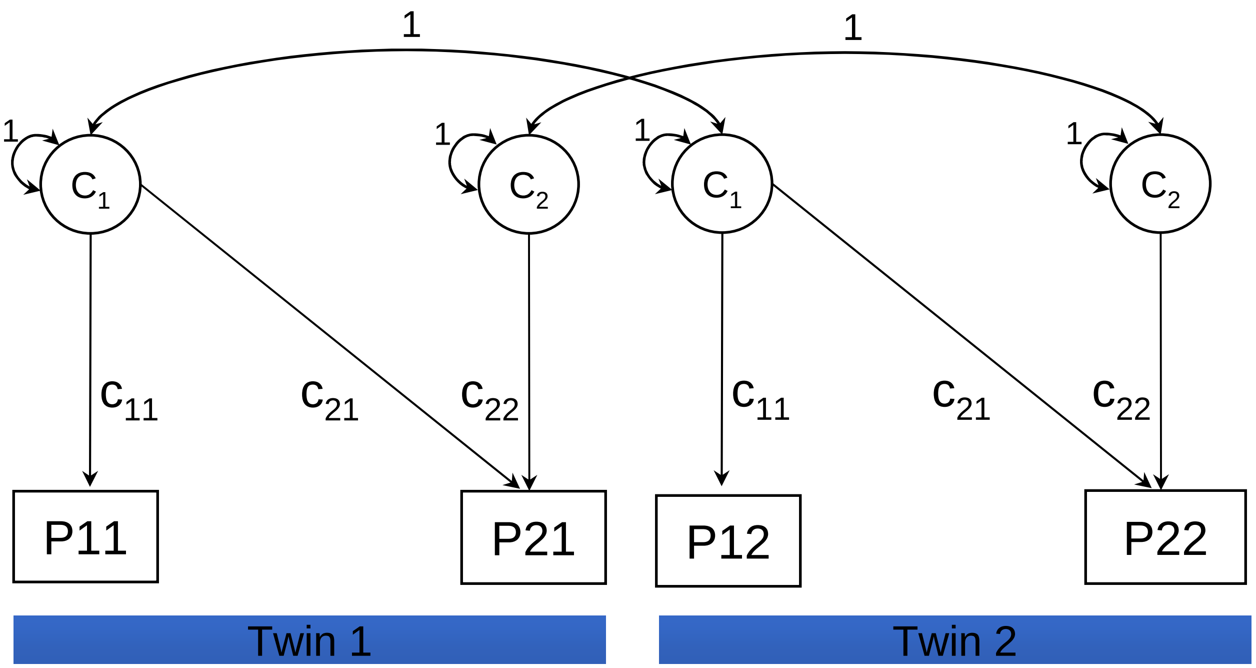
N.B. in Mx ⊗ = @

Additive Genetic Cross-Twin Covariance (MZ)



$$1 \otimes \Sigma_A = 1 \otimes \mathbf{X} * \mathbf{X}' = \begin{bmatrix} a_{11}^2 & a_{11}a_{21} \\ a_{21}a_{11} & (a_{21}^2 + a_{22}^2) \end{bmatrix}$$

Common Environment Cross-Twin Covariance



$$1 \otimes \Sigma_C = 1 \otimes \mathbf{Y} * \mathbf{Y}' = \left[\begin{array}{cc} c_{11}^2 & c_{11}c_{21} \\ c_{21}c_{11} & (c_{21}^2 + c_{22}^2) \end{array} \right]$$

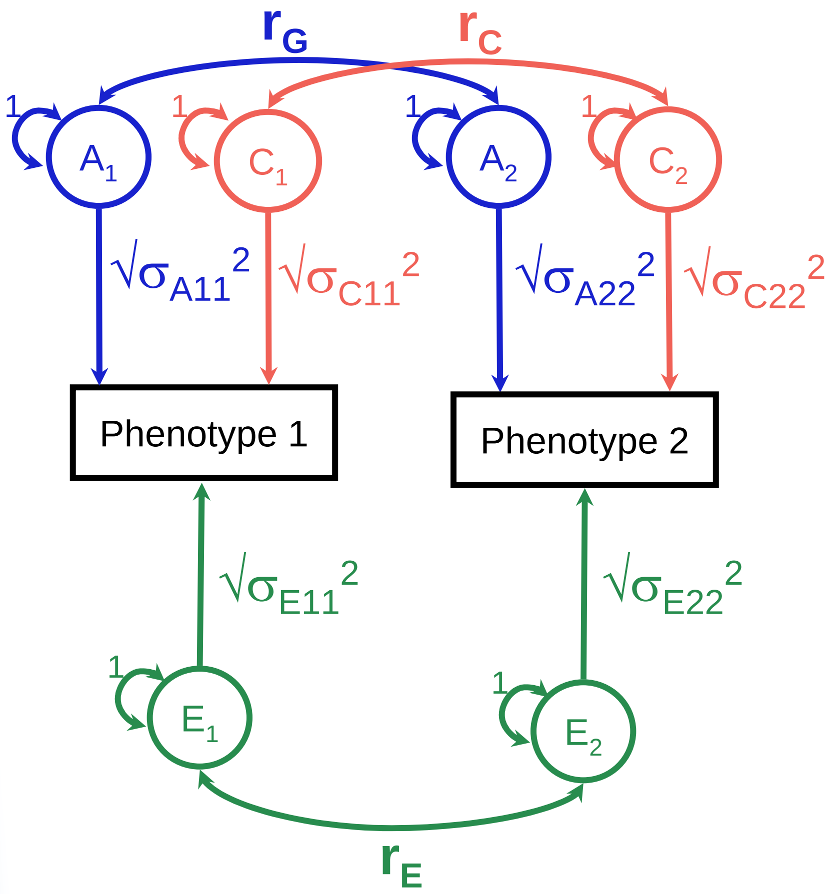
Covariance Model for Twin Pairs

- MZ:
  ```
  Covariance    A+C+E | A+C_
                A+C   | A+C+E /
  ```
- DZ:
  ```
  Covariance    A+C+E | H@A+C_
                H@A+C | A+C+E /
  ```

```
N.B. H Full 1 1 Fixed = 0.5
```

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

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

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

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

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

Specification in Mx

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

1. Matrix function in Mx: **R** = \stnd(**A**);
2. **R** = \sqrt(**I.A**)~ * **A** * \sqrt(**I.A**)~;

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

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

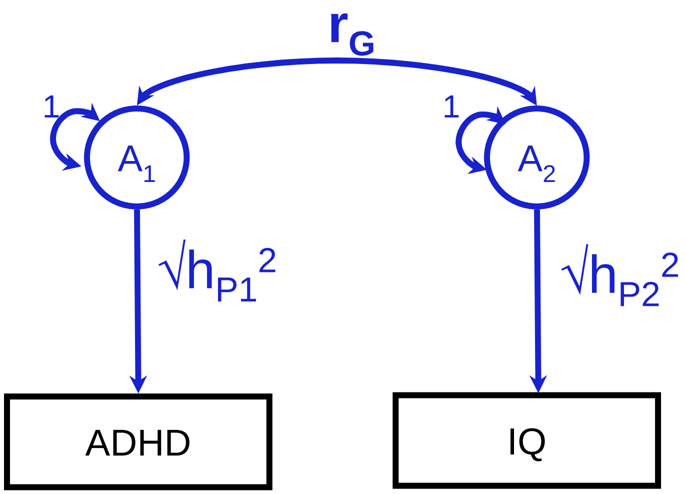
Interpreting Results

- 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

N.B. $\sqrt{h_{P1}{}^2} = \sqrt{\sigma_{A11}{}^2}$



Proportion of r_P due to additive genetic factors:

$$(\sqrt{h^2_{P1}} * r_G * \sqrt{h^2_{P2}})/r_P$$

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

Standardised Results

-
  ```
  Begin algebra;
  K = A%P|C%P|E%P;
  End algebra;
  ```

  % is the Mx operator for element division

$$\mathbf{K} = \left[\; \text{[redacted]} \quad \begin{matrix} c^2_{P1} & C_{COV} \\ C_{COV} & c^2_{P2} \end{matrix} \quad \begin{matrix} e^2_{P1} & E_{COV} \\ E_{COV} & e^2_{P2} \end{matrix} \;\right]$$

Proportion of the phenotypic correlation due to genetic effects

Example Mx Output

- Matrix K:
  - Additive Genetic Component of ADHD = 63%, for IQ = 33%
  - % of covariance between ADHD and IQ due to A = 84%

```
Matrix K Estimates [A%P|C%P|E%P]
              1         2         3         4         5         6
 1      0.6286    0.8360    0.0000    0.0000    0.3714    0.1640
 2      0.8360    0.3338    0.0000    0.3666    0.1640    0.2996

[S=\STND(P)]                                 [R=\STND(A)]
              1         2                                  1         2
 1      1.0000   -0.2865                      1      1.0000   -0.2865
 2     -0.2865    1.0000                      2     -0.5248    1.0000
```

Phenotypic correlation

Genetic correlation

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 = **?**

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 $r_G = .3$

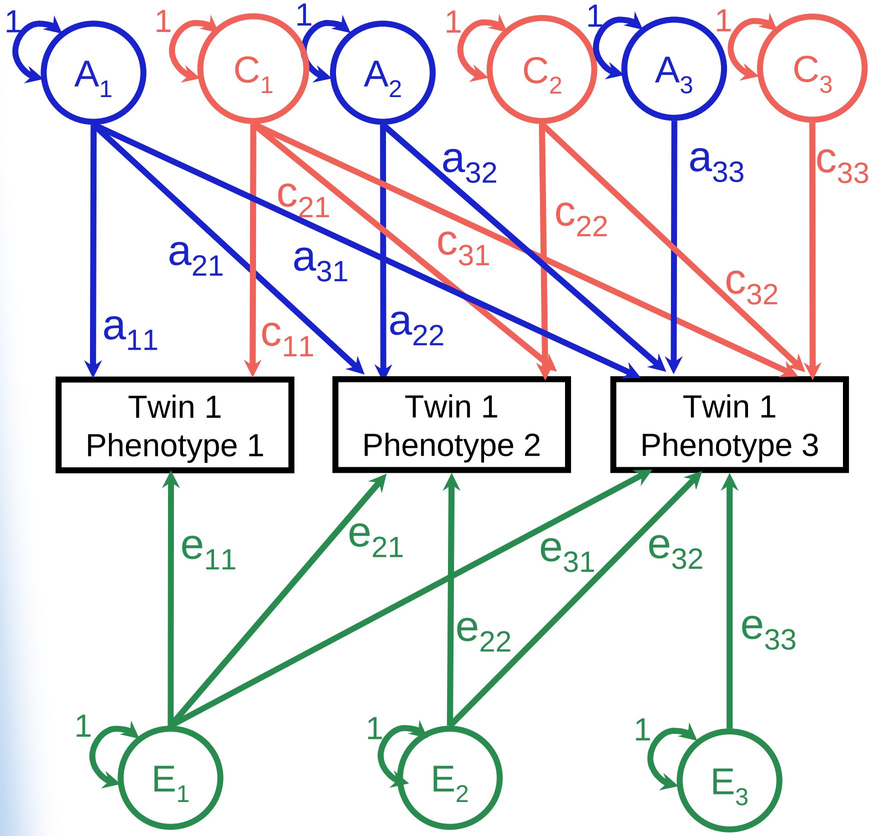
- Correlation due to additive genetic effects = **0.19**
- Proportion of phenotypic correlation attributable to additive genetic effects = **0.49**

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

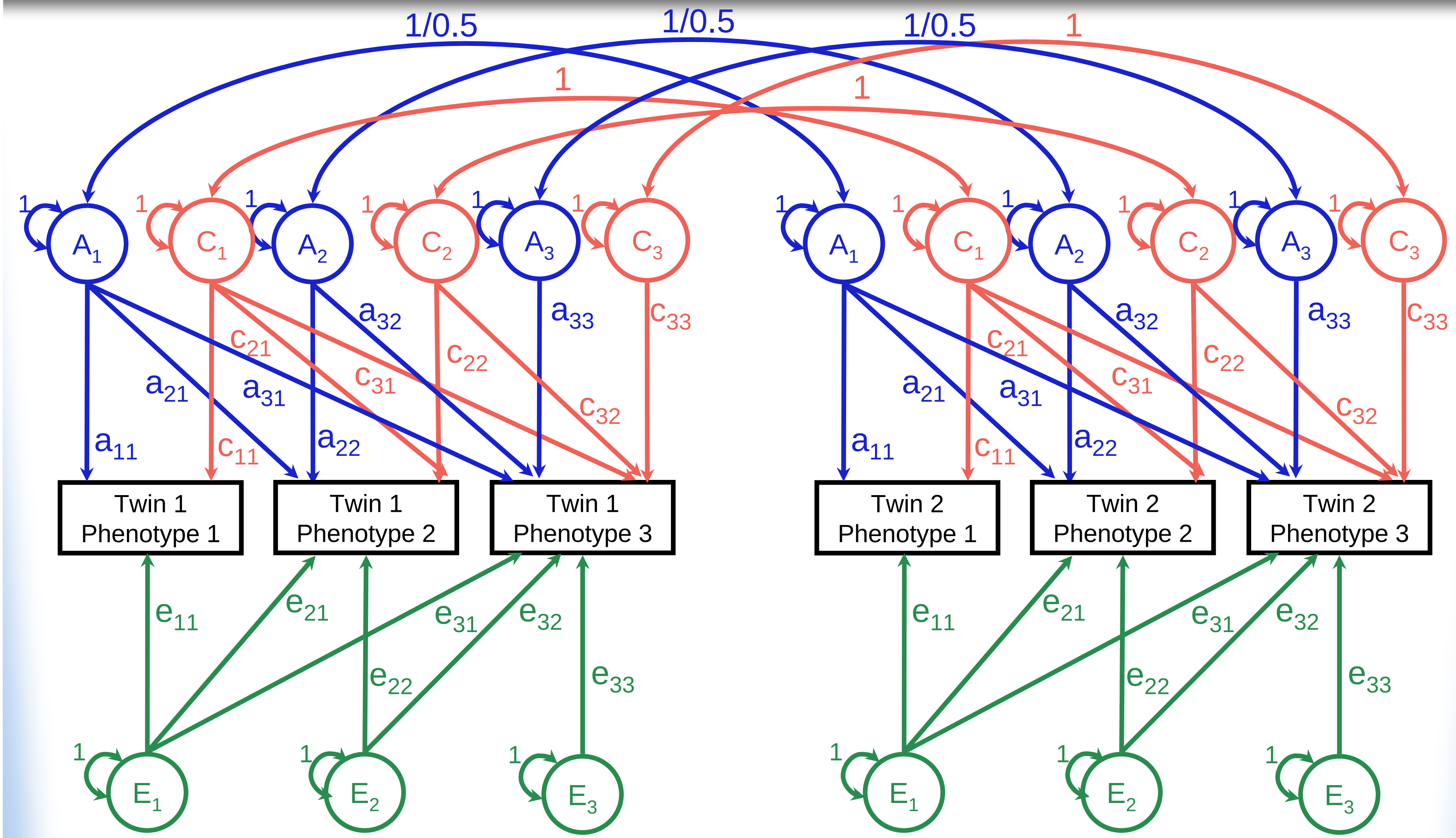
- Correlation due to additive genetic effects = **0.20**
- Proportion of phenotypic correlation attributable to additive genetic effects = **0.49**

Weakly heritable traits can still have a large portion of their correlation attributable to genetic effects.

More Variables…



More Variables…



Mx Parameter Matrices

```
#define nvar 3
Begin Matrices;
X lower nvar nvar free          ! Genetic coefficients
Y lower nvar nvar free          ! C coefficients
Z lower nvar nvar free          ! E coefficients
G Full 1 nvar free              ! Means
H Full 1 1 fix                  ! 0.5 for DZ A covar
End Matrices;
Begin Algebra;
A=X*X';                         ! Gen var/cov
C=Y*Y';                         ! C var/cov
E=Z*Z';                         ! E var/cov
P=A+C+E
End Algebra;
```

Expanded Matrices

X Lower 3 x 3 →

$$\begin{bmatrix} a_{11} & 0 & 0 \\ a_{21} & a_{22} & 0 \\ a_{31} & a_{32} & a_{33} \end{bmatrix}$$

Y Lower 3 x 3 →

$$\begin{bmatrix} c_{11} & 0 & 0 \\ c_{21} & c_{22} & 0 \\ c_{31} & c_{32} & c_{33} \end{bmatrix}$$

Z Lower 3 x 3 →

$$\begin{bmatrix} e_{11} & 0 & 0 \\ e_{21} & e_{22} & 0 \\ e_{31} & e_{32} & e_{33} \end{bmatrix}$$