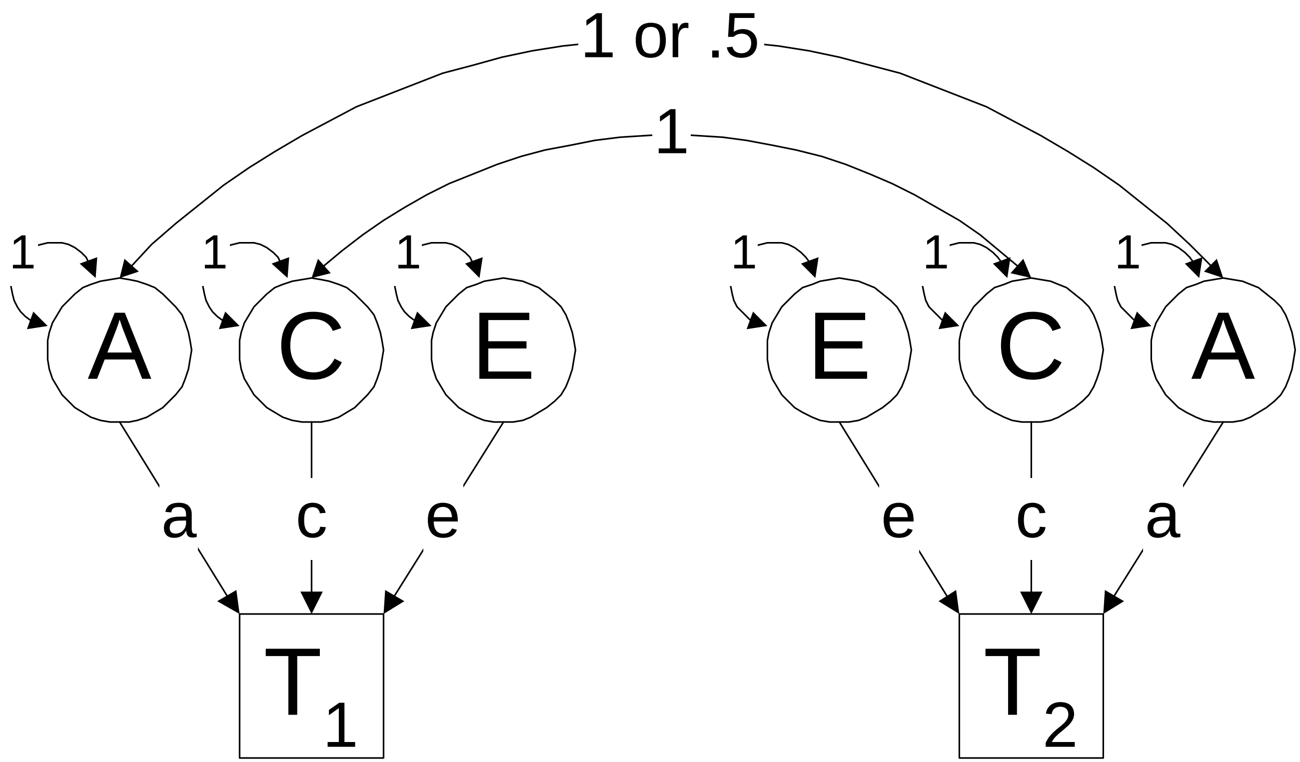
Bivariate analysis

Mx class 2004

Univariate ACE model



Expected Covariance Matrices

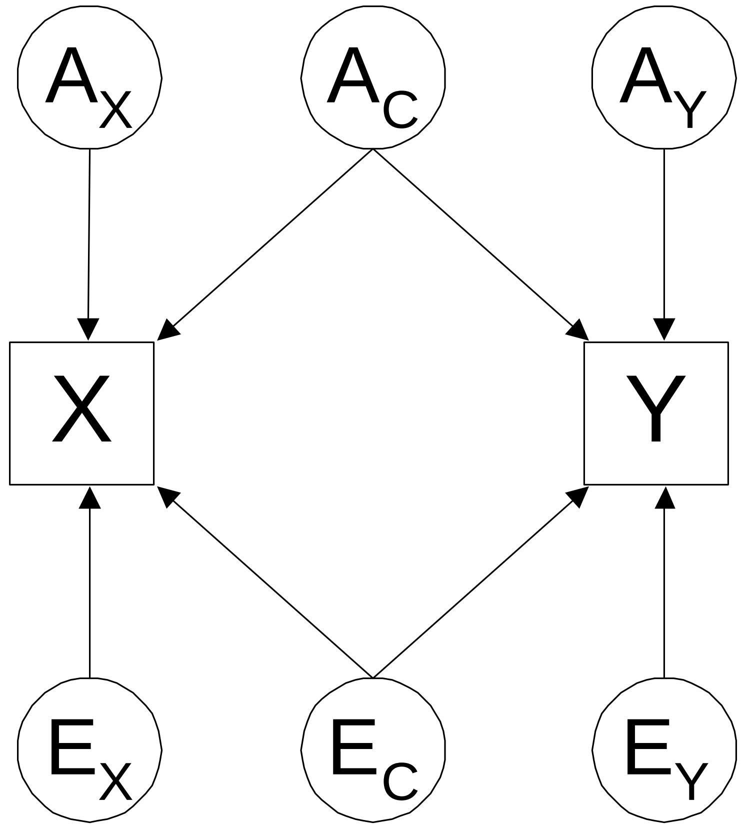
$$\Sigma\ MZ = \begin{bmatrix} a^2+c^2+e^2 & a^2+c^2 \\ a^2+c^2 & a^2+c^2+e^2 \end{bmatrix} \quad 2 \times 2$$

$$\Sigma\ DZ = \begin{bmatrix} a^2+c^2+e^2 & .5a^2+c^2 \\ .5a^2+c^2 & a^2+c^2+e^2 \end{bmatrix} \quad 2 \times 2$$

Bivariate Questions I

- Univariate Analysis: What are the contributions of additive genetic, dominance/shared environmental and unique environmental factors to the variance?
- Bivariate Analysis: What are the contributions of genetic and environmental factors to the covariance between two traits?

Two Traits



Bivariate Questions II

- Two or more traits can be correlated because they share common genes or common environmental influences
  - e.g. Are the same genetic/environmental factors influencing the traits?
- With twin data on multiple traits it is possible to partition the covariation into its genetic and environmental components
- Goal: to understand what factors make sets of variables correlate or co-vary

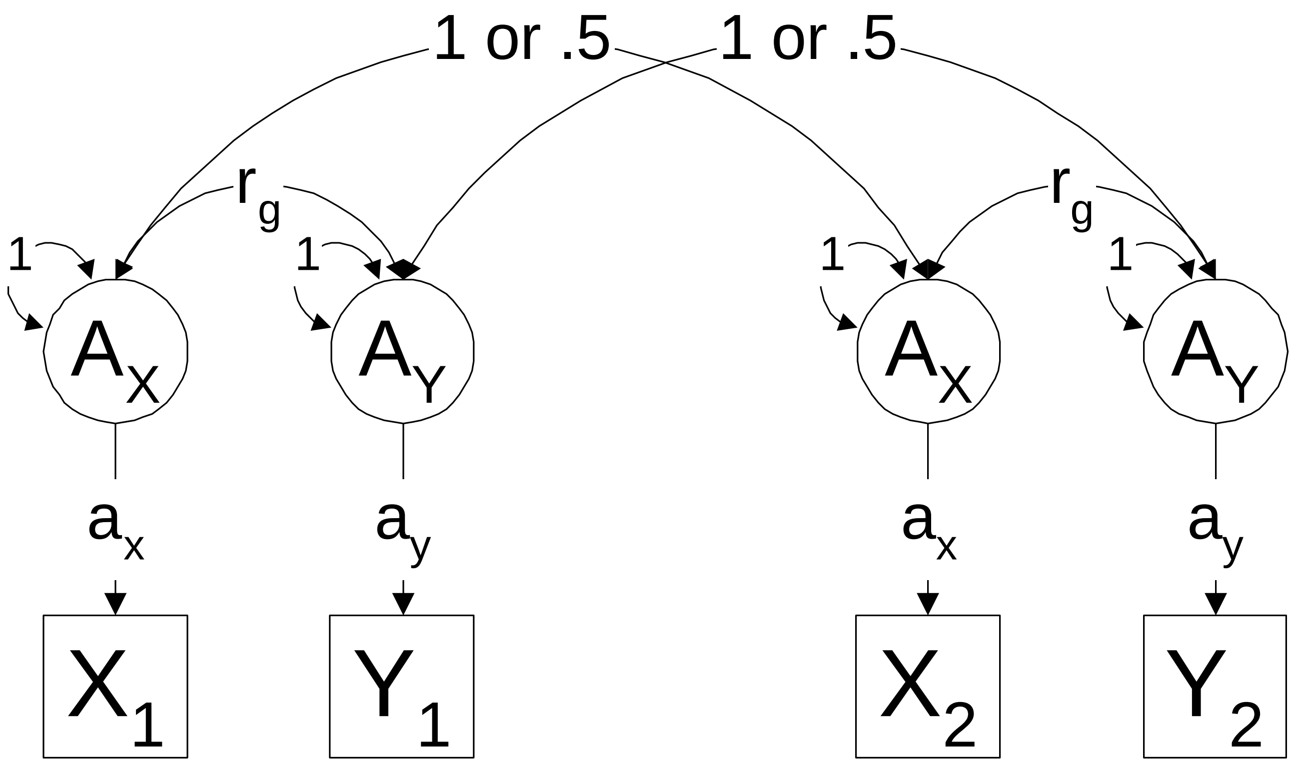
Bivariate Twin Data

		individual twin	
		within	between
trait	within	variance	twin covariance
	between	trait covariance	cross-trait twin covariance

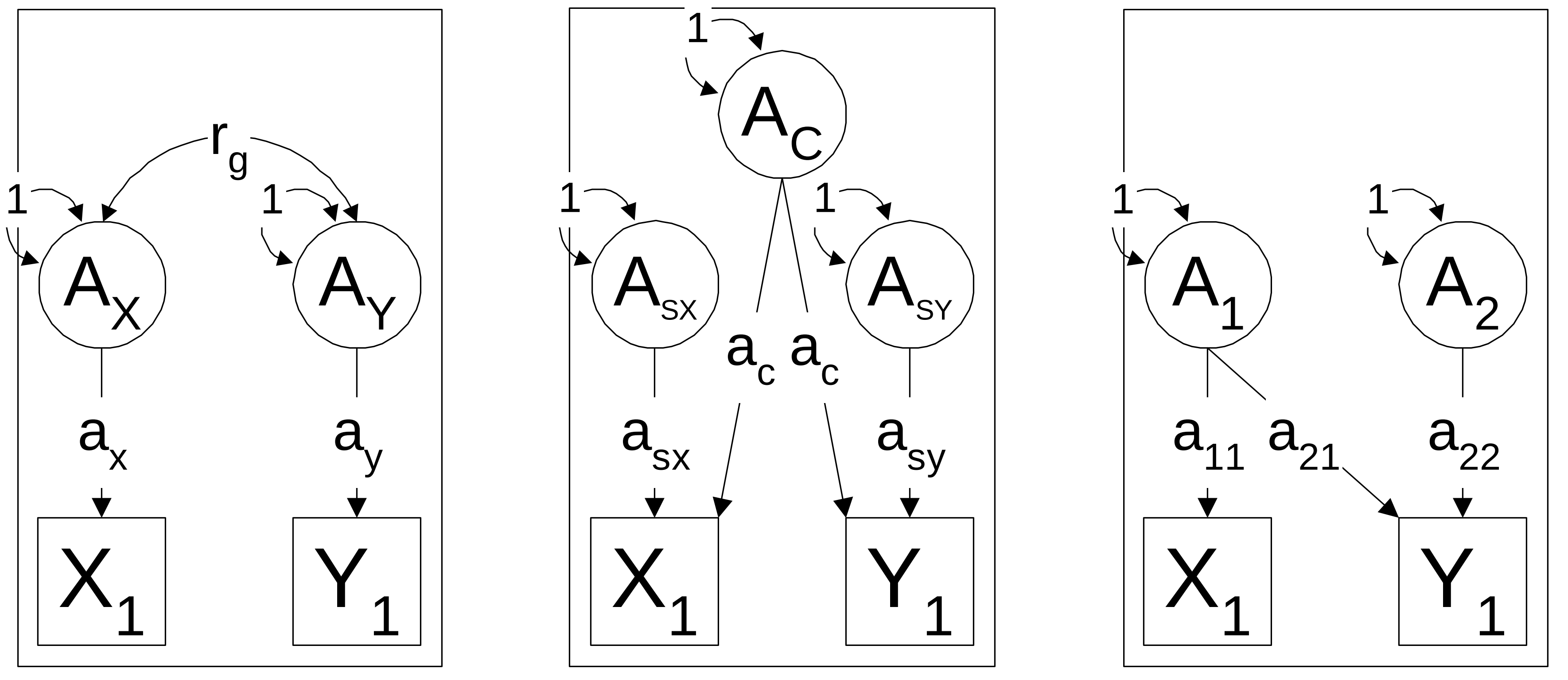
Bivariate Twin Covariance Matrix

	X_1	Y_1	X_2	Y_2
X_1	V_{X1}	C_{X1Y1}	C_{X1X2}	C_{X1Y2}
Y_1	C_{Y1X1}	V_{Y1}	C_{Y1X2}	C_{Y1Y2}
X_2	C_{X2X1}	C_{X2Y1}	V_{X2}	C_{X2Y2}
Y_2	C_{Y2X1}	C_{Y2Y1}	C_{Y2X2}	V_{Y2}

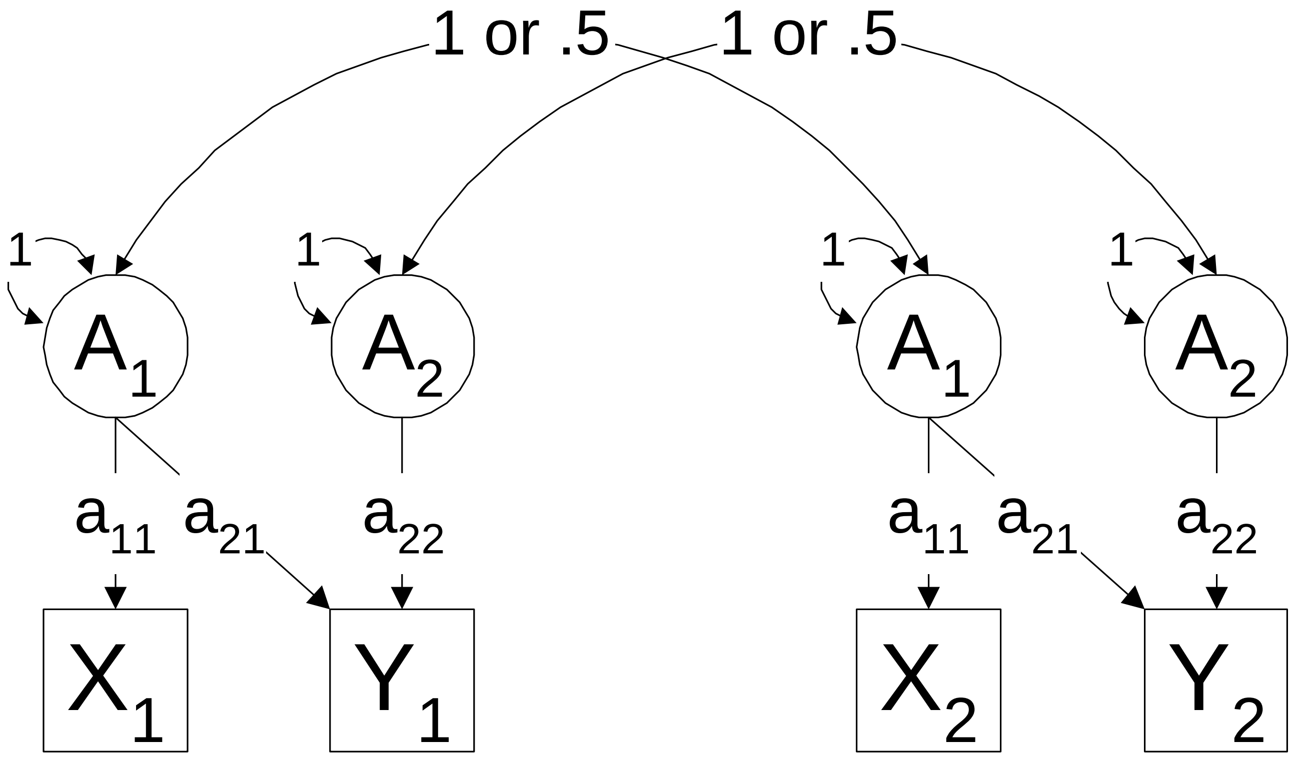
Genetic Correlation



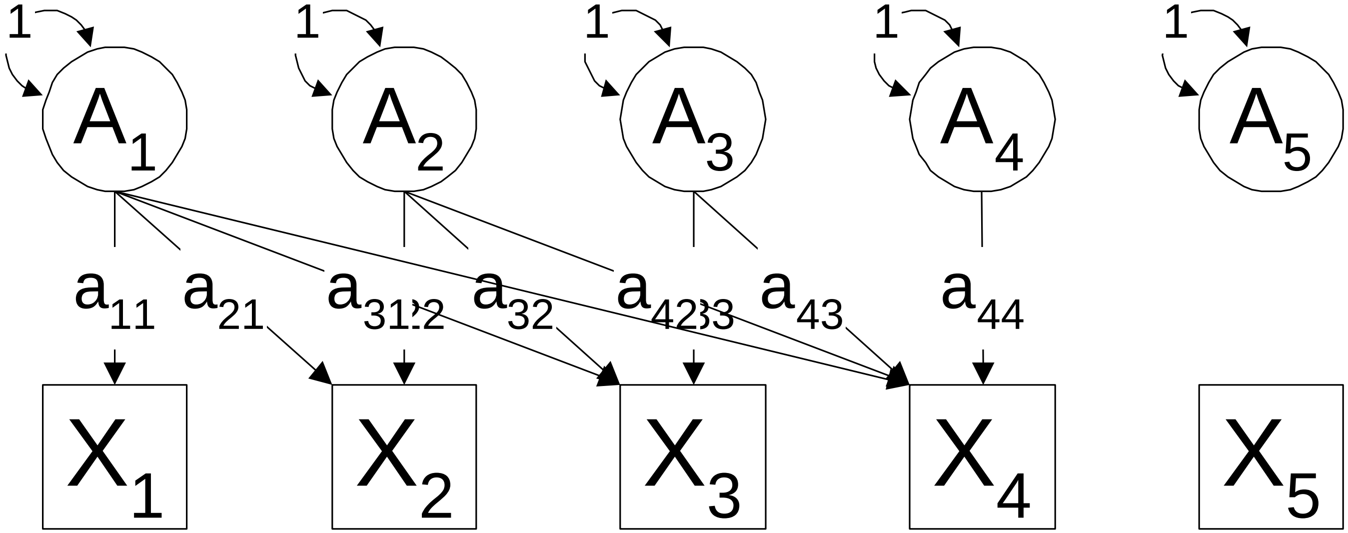
Alternative Representations



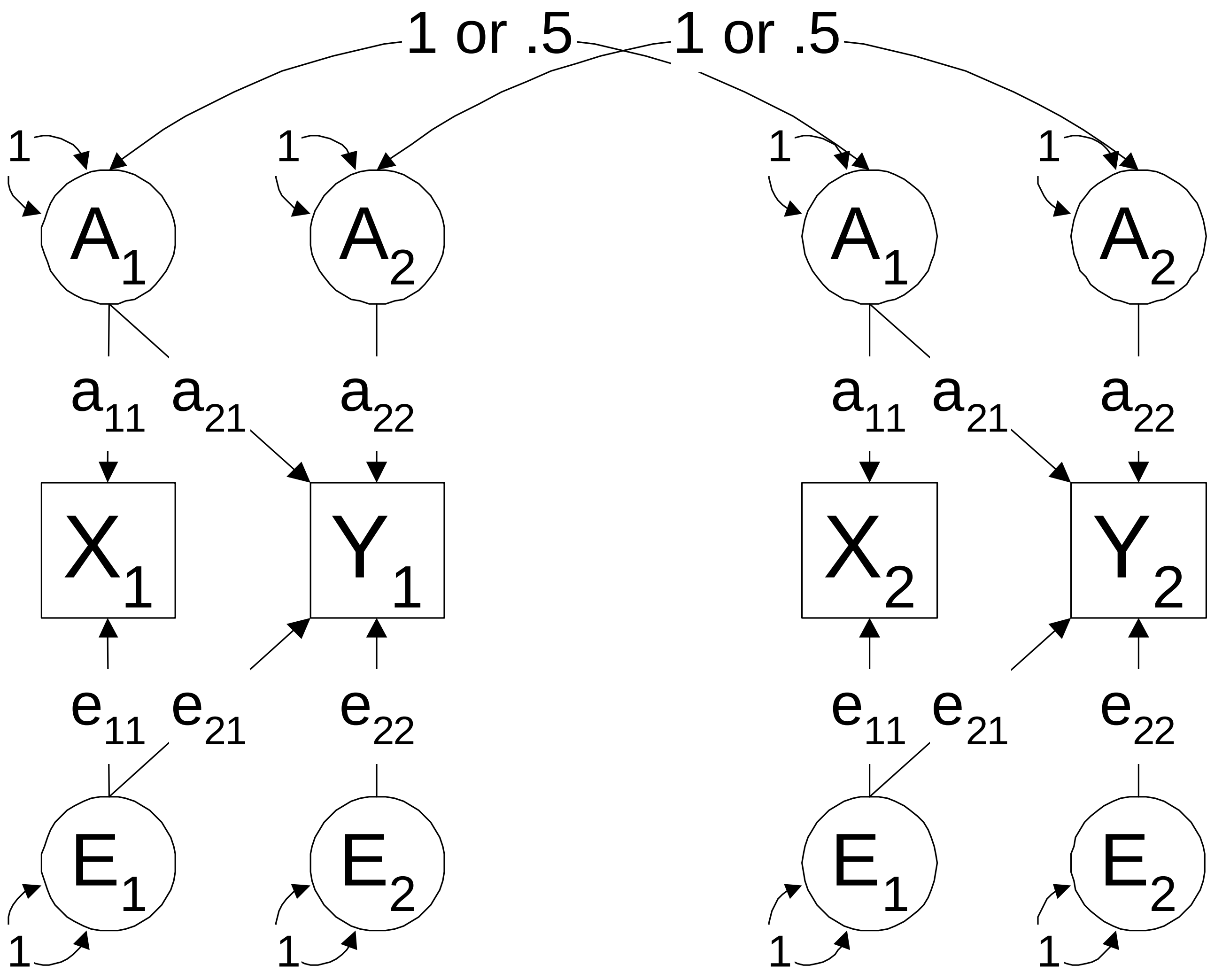
Cholesky Decomposition



More Variables



Bivariate AE Model



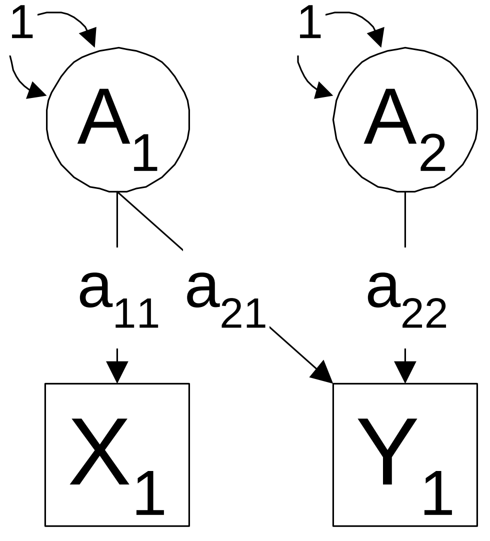
MZ Twin Covariance Matrix

	X_1	Y_1	X_2	Y_2
X_1	$a_{11}^2 + e_{11}^2$		a_{11}^2	
Y_1	$a_{21} * a_{11} + e_{21} * e_{11}$	$a_{22}^2 + a_{21}^2 + e_{22}^2 + e_{21}^2$	$a_{21} * a_{11}$	$a_{22}^2 + a_{21}^2$
X_2				
Y_2				

DZ Twin Covariance Matrix

	X_1	Y_1	X_2	Y_2
X_1	$a_{11}^2 + e_{11}^2$		$.5a_{11}^2$	
Y_1	$a_{21}*a_{11}+$ $e_{21}*e_{11}$	$a_{22}^2+a_{21}^2+$ $e_{22}^2+e_{21}^2$	$.5a_{21}*a_{11}$	$.5a_{22}^2+$ $.5a_{21}^2$
X_2				
Y_2				

Within-Twin Covariances [Mx]



X Lower 2 2

	A_1	A_2
X_1	a_{11}	0
Y_1	a_{21}	a_{22}

A=X*X'

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

Within-Twin Covariances

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

$$\Sigma E = \begin{bmatrix} e_{11}^2 & e_{11}*e_{21} \\ e_{21}*e_{11} & e_{22}^2+e_{21}^2 \end{bmatrix}$$

$$\Sigma P = \Sigma A + \Sigma E = \begin{bmatrix} a_{11}^2 + e_{11}^2 & a_{11}*a_{21} + e_{11}*e_{21} \\ a_{21}*a_{11} + e_{21}*e_{11} & a_{22}^2+a_{21}^2 + e_{22}^2+e_{21}^2 \end{bmatrix}$$

Cross-Twin Covariances

MZ $\Sigma A = \begin{bmatrix} a_{11}^2 & a_{11}*a_{21} \\ a_{21}*a_{11} & a_{22}^2+a_{21}^2 \end{bmatrix}$

DZ $.5@\Sigma A = \begin{bmatrix} .5a_{11}^2 & .5a_{11}*a_{21} \\ .5a_{21}*a_{11} & .5a_{22}^2+.5a_{21}^2 \end{bmatrix}$

Cross-Trait Covariances

- Within-twin cross-trait covariances imply common etiological influences
- Cross-twin cross-trait covariances imply familial common etiological influences
- MZ/DZ ratio of cross-twin cross-trait covariances reflects whether common etiological influences are genetic or environmental

Univariate Expected Covariances

Σ MZ =

$a^2+c^2+e^2$	a^2+c^2
a^2+c^2	$a^2+c^2+e^2$

2 x 2

Σ DZ =

$a^2+c^2+e^2$	$.5a^2+c^2$
$.5a^2+c^2$	$a^2+c^2+e^2$

2 x 2

Univariate Expected Covariances II

$$\Sigma\ MZ = \begin{bmatrix} \Sigma A+\Sigma C+\Sigma C & \Sigma A+\Sigma C \\ \Sigma A+\Sigma C & \Sigma A+\Sigma C+\Sigma C \end{bmatrix} \quad 2 \times 2$$

$$\Sigma\ DZ = \begin{bmatrix} \Sigma A+\Sigma C+\Sigma C & .5@\Sigma A+\Sigma C \\ .5@\Sigma A+\Sigma C & \Sigma A+\Sigma C+\Sigma C \end{bmatrix} \quad 2 \times 2$$

Bivariate Expected Covariances

Σ MZ =

ΣA+ΣC+ΣC	ΣA+ΣC
ΣA+ΣC	ΣA+ΣC+ΣC

4 x 4

Σ DZ =

ΣA+ΣC+ΣC	.5@ΣA+ΣC
.5@ΣA+ΣC	ΣA+ΣC+ΣC

4 x 4

Practical Example I

- Dataset: MCV-CVT Study
- 1983-1993
- BMI, skinfolds (bic,tri,calf,sil,ssc)
- Longitudinal: 11 years
- N MZFY: 107, DZF: 60

Practical Example II

- Dataset: NL MRI Study
- 1990's
- Working Memory, Gray & White Matter

- N MZFY: 68, DZF: 21