Conor Dolan
Biological psychology, VU, Amsterdam

Dirk Pelt
Biological psychology, VU, Amsterdam

28 slides 27 minutes

Multivariate twin models

- Section 1: from **uni**variate to **bi**variate (Dolan)
- Section 2: from **bi**variate to **multi**variate (Dolan)
- Section 3 : independent pathway model (IPM) a.k.a. biometric model (Pelt)
  - Recap multivariate model
  - The common factor model
- Section 4: the independent pathway model (continued) (Pelt)
- Section 5: the common pathway model (Dolan)

From univariate to bivariate to multivariate – First some notation

Notation	
Phenotype (variable)	Ph (Ph_1, Ph_2) or sensible ("IQ")
Latent variable - additive genetic	A
Latent variable - shared environmental	C
Latent variable - dominance	D
Latent variable - unshared environmental	E
variance of phenotype	var(Ph) or σ_{Ph}^2
variance of A (D, C,E)	var(A) or σ_A^2 (σ_D^2 σ_C^2 σ_E^2)
standard deviations (stdev)	sd(Ph) or σ_{Ph}; sd(A) or σ_A
Covariance matrix of p phenotypes (pxp symmetric matrix) - Phenotypic	Σ_{Ph} containing **p** variances and **((p-1)*p)/2** covariances
Covariance matrix of p phenotypes (pxp symmetric matrix) - A (D, C, E)	Σ_A (Σ_D, Σ_C, Σ_E)
Covariance and correlation between X and Y (off-diagonal element in Σ_{Ph})	cov(Ph_1,Ph_2) or $\sigma_{Ph1,Ph2}$ cor(Ph_1,Ph_2) or $\rho_{Ph1,Ph2}$ or $r_{Ph1,Ph2}$

Two ways of representing covariance.

cov	Ph_1	Ph_2
Ph_1	$\sigma_{Ph1}{}^2$	$\sigma_{Ph1,Ph2}$
Ph_2	$\sigma_{Ph1,Ph2}$	$\sigma_{Ph2}{}^2$

cov	Ph_1	Ph_2
Ph_1	$\sigma_{Ph1}{}^2$	$\sigma_{Ph1}{}^*\rho_{Ph1,Ph2}{}^*\sigma_{Ph2}$
Ph_2	$\sigma_{Ph1}{}^*\rho_{Ph1,Ph2}{}^*\sigma_{Ph2}$	$\sigma_{Ph2}{}^2$

cov	Ph_1	Ph_2
Ph_1	16	10
Ph_2	10	25

cor	Ph_1	Ph_2
Ph_1	$\sigma_{Ph1}{}^2/\sigma_{Ph1}{}^2$	$\{\sigma_{Ph1}{}^*\rho_{Ph1,Ph2}{}^*\sigma_{Ph2}\}\ /\{\sigma_{Ph1}{}^*\sigma_{Ph2}\}$
Ph_2	$\{\sigma_{Ph1}{}^*\rho_{Ph1,Ph2}{}^*\sigma_{Ph2}\}\ /\{\sigma_{Ph1}{}^*\sigma_{Ph2}\}$	$\sigma_{Ph2}{}^2/\sigma_{Ph2}{}^2$

cor	Ph_1	Ph_2
Ph_1	1	.5
Ph_2	.5	1

Two way of expressing a covariance (important!)

$\{\sigma_{Ph1}{}^*\rho_{Ph1,Ph2}{}^*\sigma_{Ph2}\} = \sigma_{Ph1,Ph2}$

(numerical: 4*.5*5) = 10

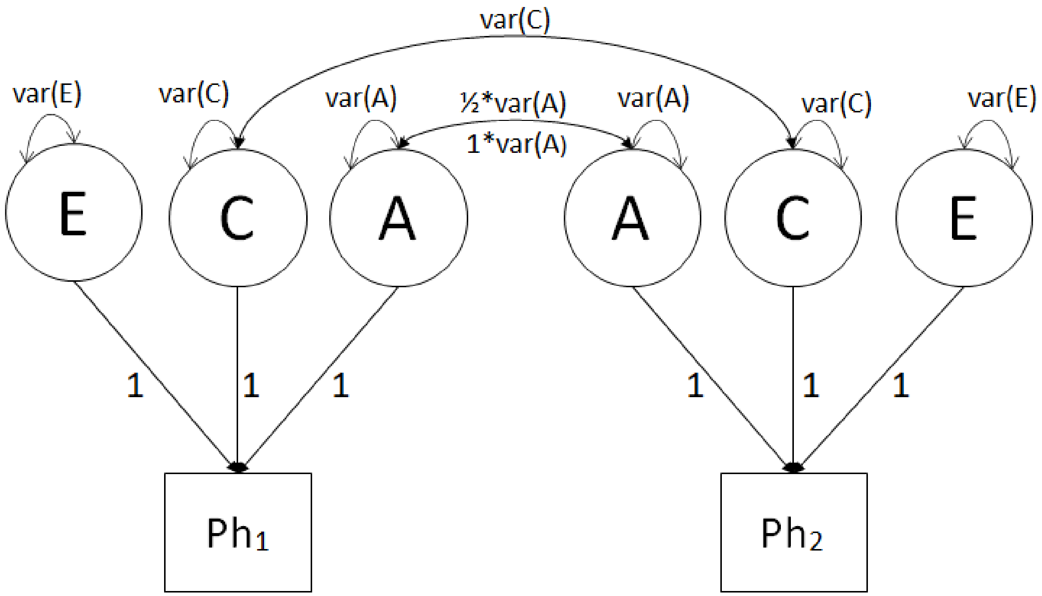
covariance

covariance = stdev*correlation*stdev

Univariate models

MODELING PHENOTYPIC COVARIANCE MATRICES USING ACE MODELS

Univariate ACE Model: *Variance components*



MZ twins phenotypic covariance matrix		
	MZ_1	MZ_2
MZ_1	var(A)+var(C)+var(E)	var(A) + var(C)
MZ_2	var(A) + var(C)	var(A)+var(C) +var(E)

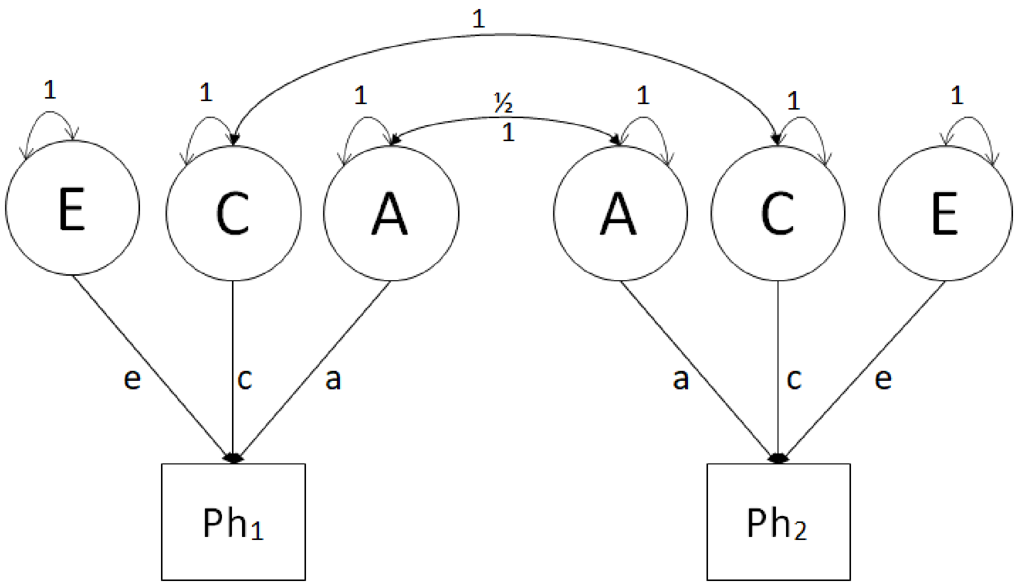
DZ twins phenotypic covariance matrix		
	DZ_1	DZ_2
DZ_1	var(A)+var(C)+var(E)	½var(A) + var(C)
DZ_2	½var(A) + var(C)	var(A)+var(C) +var(E)

Parameters of the model:
var(A), var(C), and var(E)

h^2 = var(A) / {var(A)+var(C)+var(E)}

alternative notation: $h^2 = \sigma_A^2 / \{\sigma_A^2 + \sigma_C^2 + \sigma_E^2\}$

Univariate ACE Model: *Path coefficients*



MZ twins phenotypic covariance matrix		
	MZ_1	MZ_2
MZ_1	$a^2+c^2+e^2$	a^2+c^2
MZ_2	a^2+c^2	$a^2+c^2+e^2$

DZ twins phenotypic covariance matrix		
	DZ_1	DZ_2
DZ_1	$a^2+c^2+e^2$	$½a^2+c^2$
DZ_2	$½a^2+c^2$	$a^2+c^2+e^2$

Parameters of the model:
a, c, and e

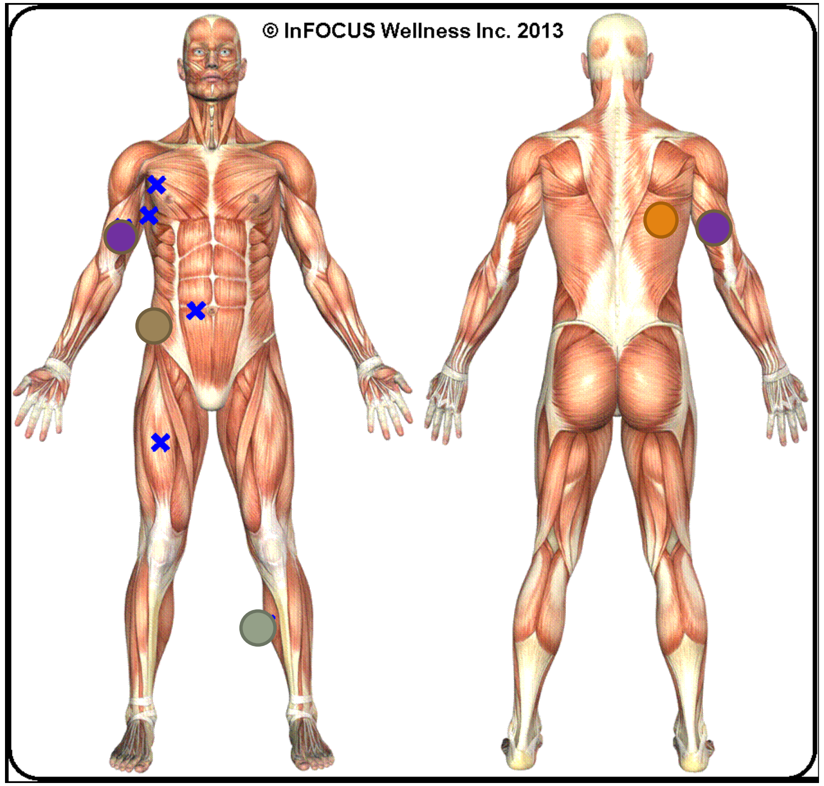
$h^2 = a^2 / (a^2+c^2+e^2)$

alt notation: $h^2 = \sigma_A^2 / \{\sigma_A^2 + \sigma_C^2 + \sigma_E^2\}$

From univariate to bivariate

MODELING ACE/ADE COVARIANCE MATRICES

Running example: skinfold data (*umx; Moskowitz, et al. 1999, https://pubmed.ncbi.nlm.nih.gov/10323623/*)

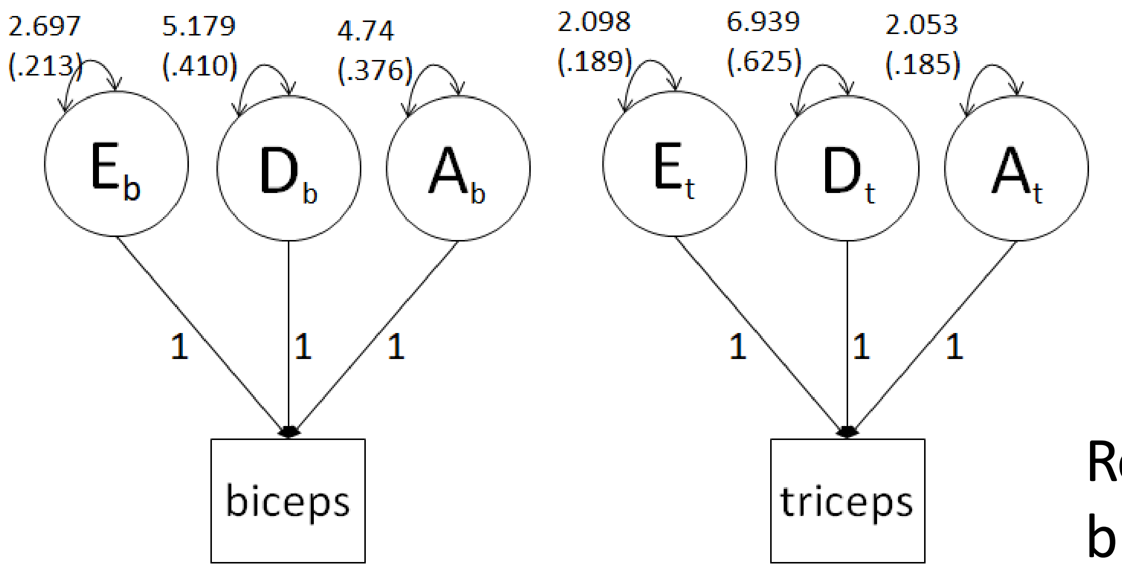


Skinfold Calipers - the measurement device

Skinfold measured at 5 loci:

Biceps and Triceps (purple ●), Calf (green ●), Subscapular (blue ●), Suprailiacal (orange ●).
us_skinfold_data available in the umx library (R library) (**x** are other standard locations)

From Univariate ADE Model to Bivariate ADE Model: biceps and triceps skinfold



Phenotypic covariance matrix (correlation)		
	Biceps	Triceps
Biceps	13.388	11.168 (.899)
Triceps	11.168 (.899)	11.537

Results of **univariate** ADE analysis (sex as covariate)

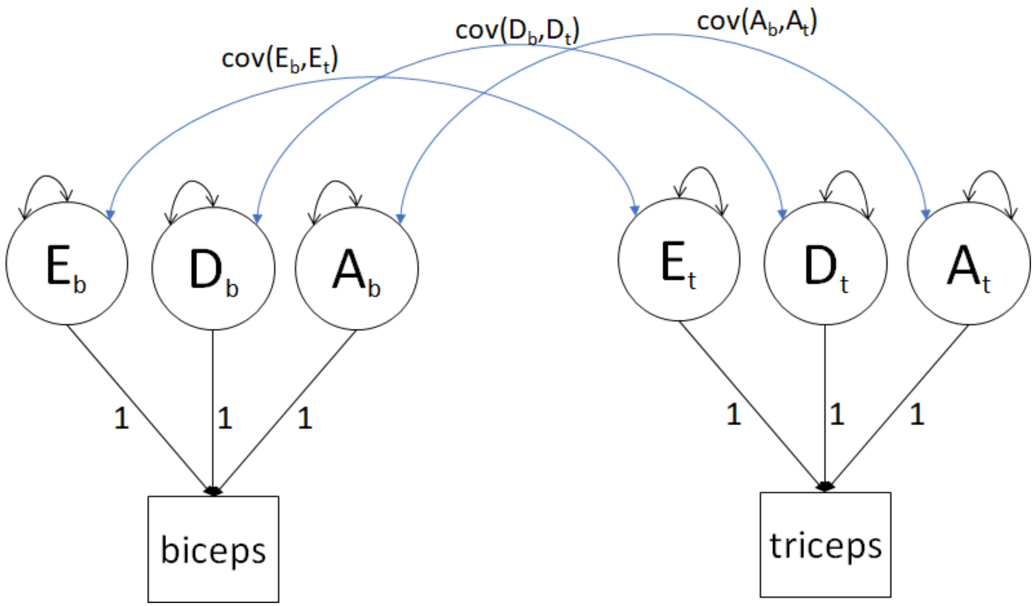
biceps: h^2_n = .376 & h^2_b = .376+.410= .786

triceps: h^2_n =.185 & h^2_b =.625+.185 = .811

So we know about the phenotypic variances.

But what about the covariance (11.168) and the correlation (.899)?

From decomposing variance to decomposing covariance matrices



Σ_{Ph}	biceps	triceps
biceps	σ_{bic}^2 13.388	$\sigma_{bic,tri}$ 11.168
triceps	$\sigma_{bic,tri}$ 11.168	σ_{tri}^2 11.537

Σ_{Ph}	biceps	triceps
biceps	$\sigma_{Ab}^2+\sigma_{Db}^2+\sigma_{Eb}^2$	$\sigma_{Ab,At}+\sigma_{Db,Dt}+\sigma_{Eb,Et}$
triceps	$\sigma_{Ab,At}+\sigma_{Db,Dt}+\sigma_{Eb,Et}$	$\sigma_{At}^2+\sigma_{Dt}^2+\sigma_{Et}^2$

univariate: $\sigma_{Ph}^2 = \sigma_A^2 + \sigma_D^2 + \sigma_E^2$ ← This is decomposition of one variance

bivariate: $\Sigma_{Ph} = \Sigma_A + \Sigma_D + \Sigma_E$ ← This is decomposition of two variances and one covariance

Deconstructing the phenotypic 2x2 covariance matrix (2 variances; 1 covariance)

bivariate: $\Sigma_{Ph} = \Sigma_A + \Sigma_D + \Sigma_E$

Σ_{Ph}	bic	tri
bic	σ_{bic}^2	$\sigma_{bic,tri}$
tri	$\sigma_{bic,tri}$	σ_{tri}^2

=

Σ_A	bic	tri
bic	σ_{Ab}^2	$\sigma_{Ab,At}$
tri	$\sigma_{Ab,At}$	σ_{At}^2

+

Σ_D	bic	tri
bic	σ_{Db}^2	$\sigma_{Db,Dt}$
tri	$\sigma_{Db,Dt}$	σ_{Dt}^2

+

Σ_E	bic	tri
bic	σ_{Eb}^2	$\sigma_{Eb,Et}$
tri	$\sigma_{Eb,Et}$	σ_{Et}^2

=

Σ_{Ph}	bic	tri
bic	$\sigma_{Ab}^2+\sigma_{Db}^2+\sigma_{Eb}^2$	$\sigma_{Ab,At}+\sigma_{Db,Dt}+\sigma_{Eb,Et}$
tri	$\sigma_{Ab,At}+\sigma_{Db,Dt}+\sigma_{Eb,Et}$	$\sigma_{At}^2+\sigma_{Dt}^2+\sigma_{Et}^2$

Covariance matrices of the twins - 2 phenotypes, 2 twins: 4x4 covariance matrices

Σ_{Ph} MZ	twin 1	twin 2
twin 1	$\Sigma_A + \Sigma_D + \Sigma_E$	$\Sigma_A + \Sigma_D$
twin 2	$\Sigma_A + \Sigma_D$	$\Sigma_A + \Sigma_D + \Sigma_E$

Σ_{Ph} DZ	twin 1	twin 2
twin 1	$\Sigma_A + \Sigma_D + \Sigma_E$	$½\Sigma_A + ¼\Sigma_D$
twin 2	$½\Sigma_A + ¼\Sigma_D$	$\Sigma_A + \Sigma_D + \Sigma_E$

...where...

Σ_A	bic	tri
bic	σ_{Ab}^2	$\sigma_{Ab,At}$
tri	$\sigma_{Ab,At}$	σ_{At}^2

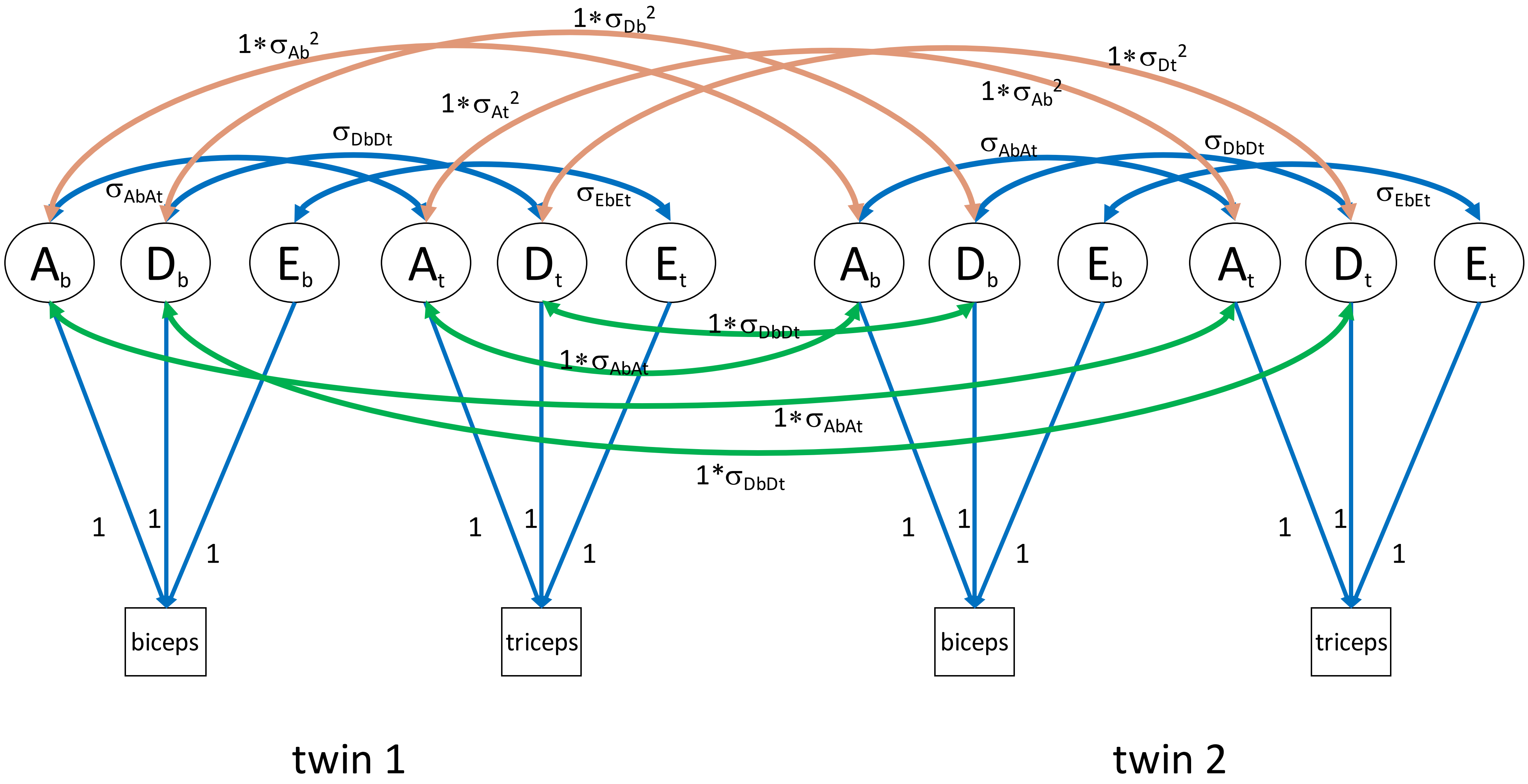
Σ_D	bic	tri
bic	σ_{Db}^2	$\sigma_{Db,Dt}$
tri	$\sigma_{Db,Dt}$	σ_{Dt}^2

Σ_E	bic	tri
bic	σ_{Eb}^2	$\sigma_{Eb,Et}$
tri	$\sigma_{Eb,Et}$	σ_{Et}^2

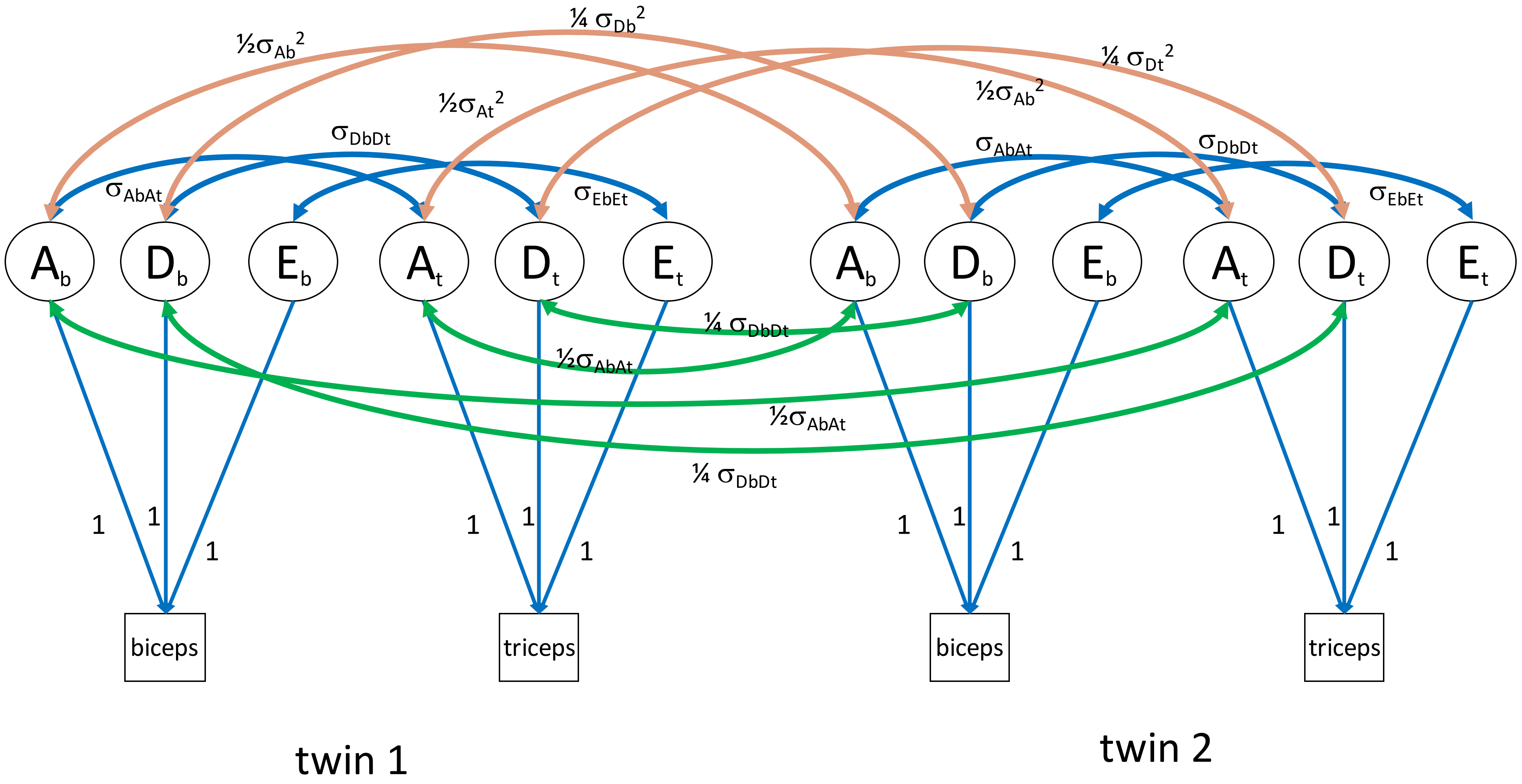
Σ_{Ph} of MZs and DZs are 4x4 matrices

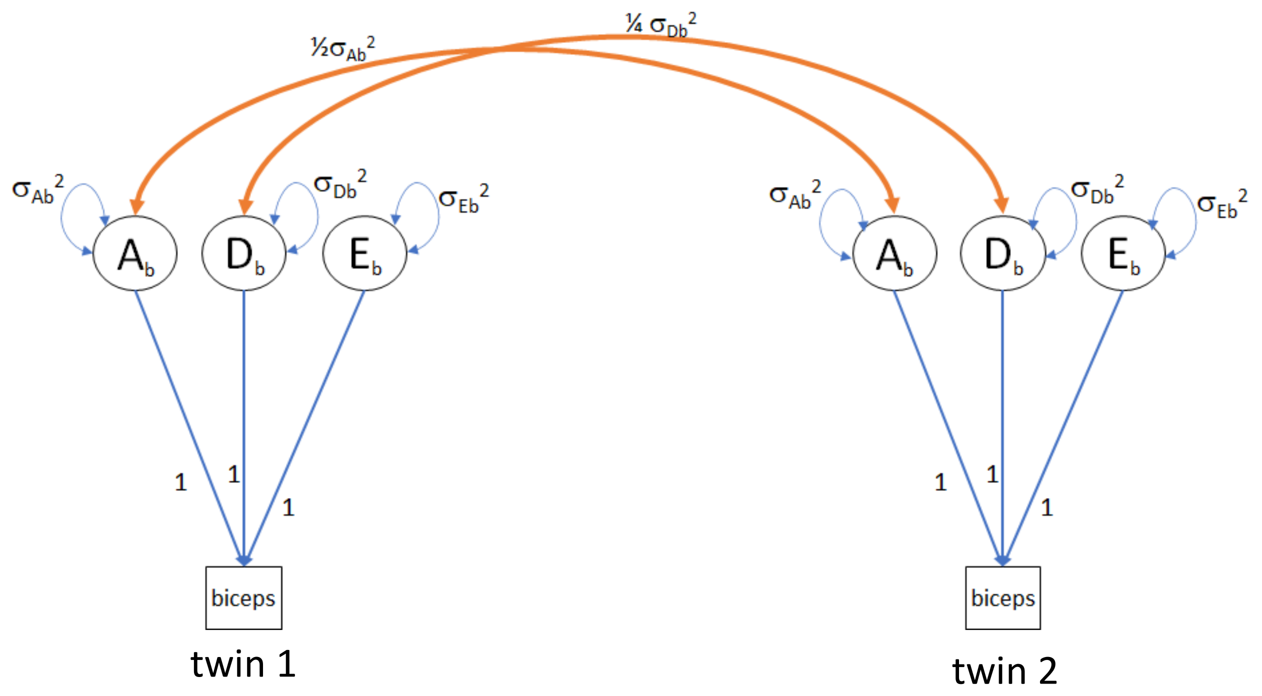
But Σ_A , Σ_D , and Σ_E are a 2x2 covariance matrices, p=2, i.e., a bivariate ADE model

Bivariate ADE model – two phenotypes – MZ twins



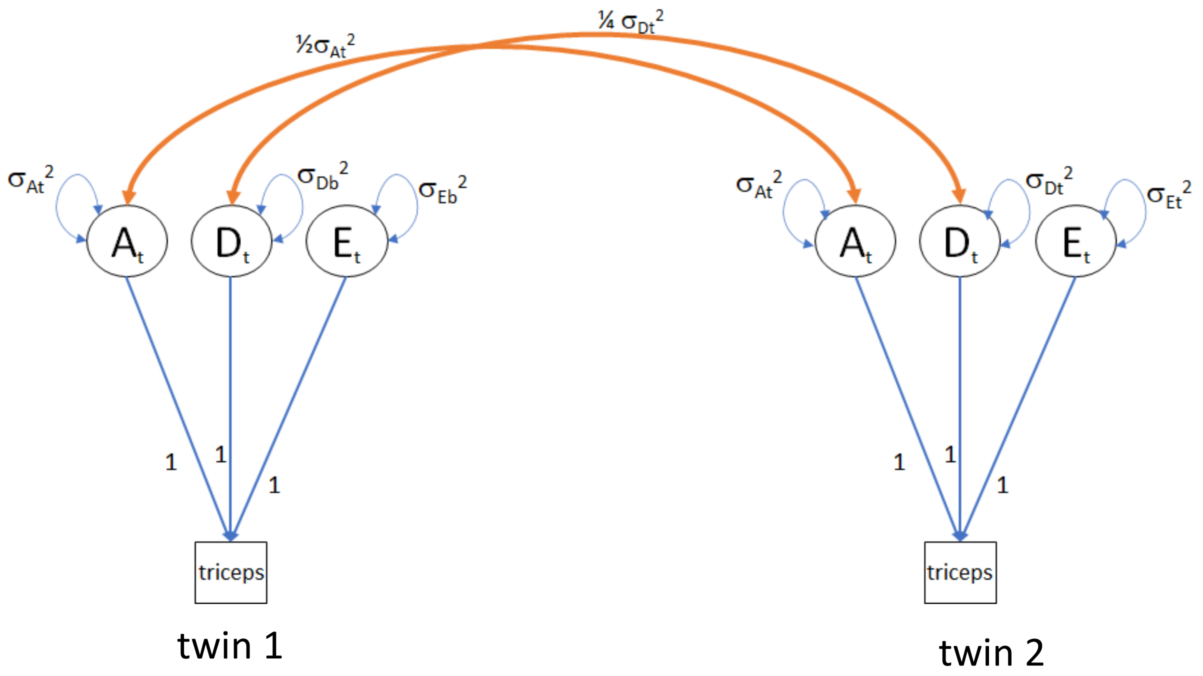
Bivariate ADE model – two phenotypes – DZ twins





Within trait (biceps)
Cross-twin

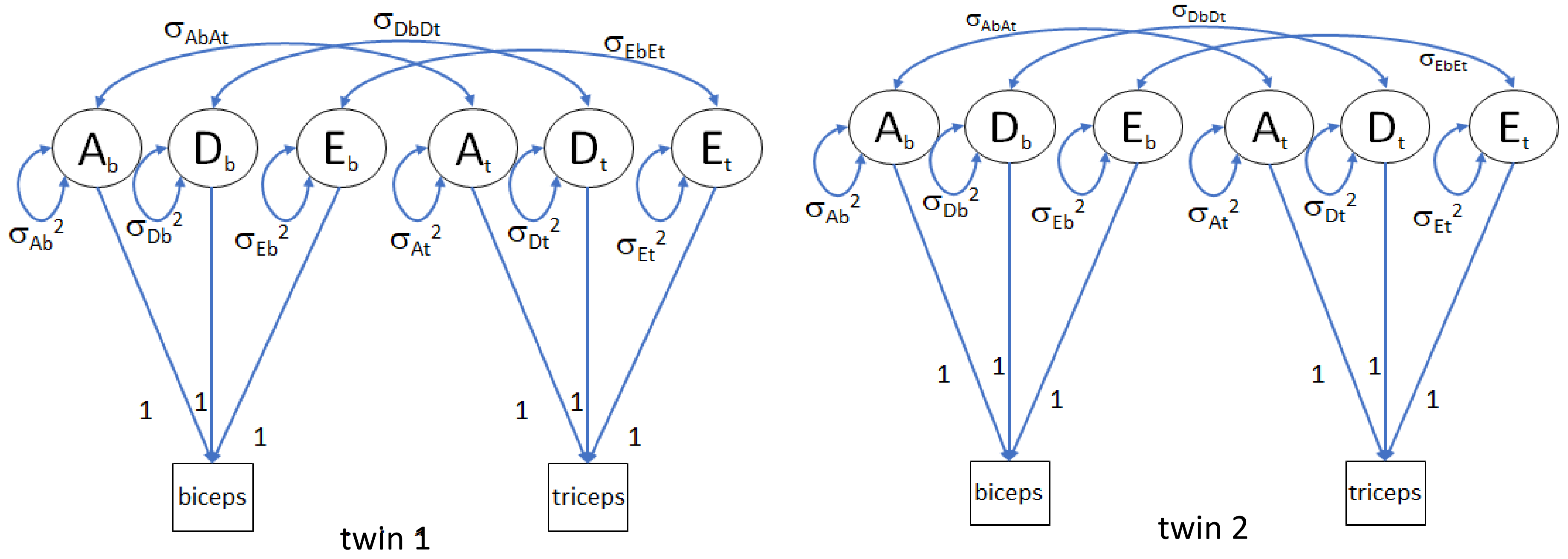
Σ_{Ph} (DZ)		Twin 1		Twin 2	
		bic1	tri1	bic2	tri2
Twin 1	bic1	$s_{Ab}^2 + s_{Db}^2 + s_{Eb}^2$		$½s_{Ab}^2 + ¼s_{Db}^2$	
	tri1				
Twin 2	bic2	$½s_{Ab}^2 + ¼s_{Db}^2$		$s_{Ab}^2 + s_{Db}^2 + s_{Eb}^2$	
	tri2				



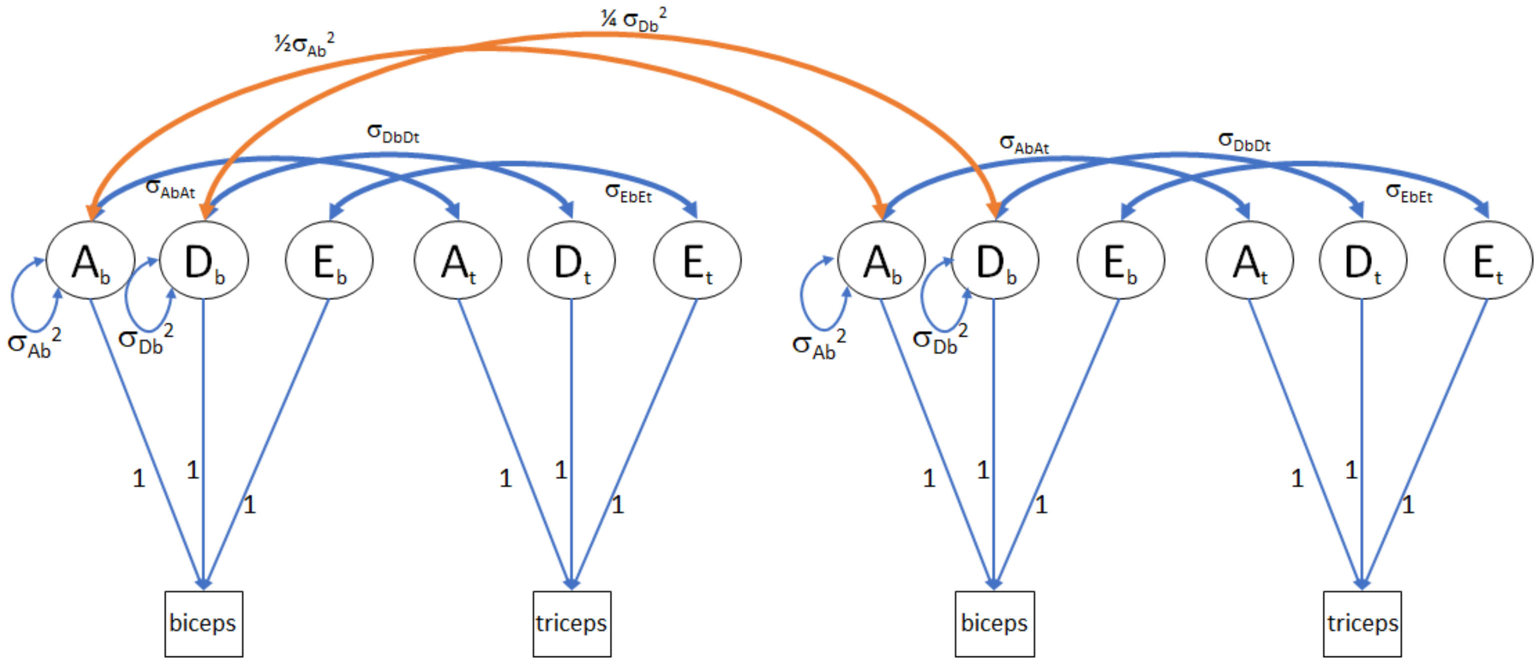
Within trait (triceps)
Cross-twin

Σ_{Ph} (DZ)		Twin 1		Twin 2	
		bic1	tri1	bic2	tri2
Twin 1	bic1	$s_{Ab}^2 + s_{Db}^2 + s_{Eb}^2$		$½s_{Ab}^2 + ¼s_{Db}^2$	
	tri1		$s_{At}^2 + s_{Dt}^2 + s_{Et}^2$		$½s_{At}^2 + ¼s_{Dt}^2$
Twin 2	bic2	$½s_{Ab}^2 + ¼s_{Db}^2$		$s_{Ab}^2 + s_{Db}^2 + s_{Eb}^2$	
	tri2		$½s_{At}^2 + ¼s_{Dt}^2$		$s_{At}^2 + s_{Dt}^2 + s_{Et}^2$

Cross-trait Within twin



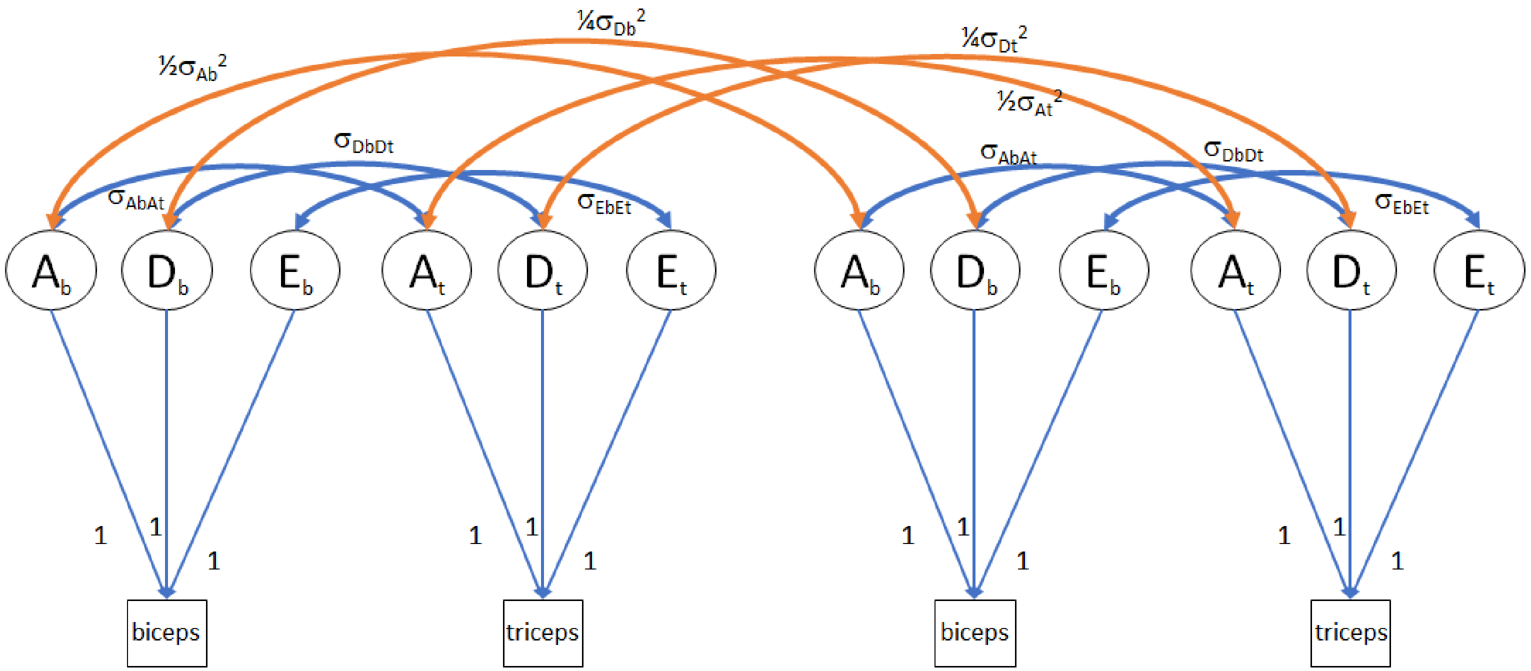
S_{Ph} (DZ)		Twin 1		Twin 2	
		bic1	tri1	bic2	tri2
Twin 1	bic1	$s_{Ab}^2 + s_{Db}^2 + s_{Eb}^2$	$s_{AbAt} + s_{DbDt} + s_{EbEt}$	$½s_{Ab}^2 + ¼s_{Db}^2$	
	tri1	$s_{AbAt} + s_{DbDt} + s_{EbEt}$	$s_{At}^2 + s_{Dt}^2 + s_{Et}^2$		$½s_{At}^2 + ¼s_{Dt}^2$
Twin 2	bic2	$½s_{Ab}^2 + ¼s_{Db}$		$s_{Ab}^2 + s_{Db}^2 + s_{Eb}^2$	$s_{AbAt} + s_{DbDt} + s_{EbEt}$
	tri2		$½s_{At}^2 + ¼s_{Dt}^2$	$s_{AbAt} + s_{DbDt} + s_{EbEt}$	$s_{At}^2 + s_{Dt}^2 + s_{Et}^2$



Cross-trait
Within twin +

Within trait (biceps)
Cross-twin

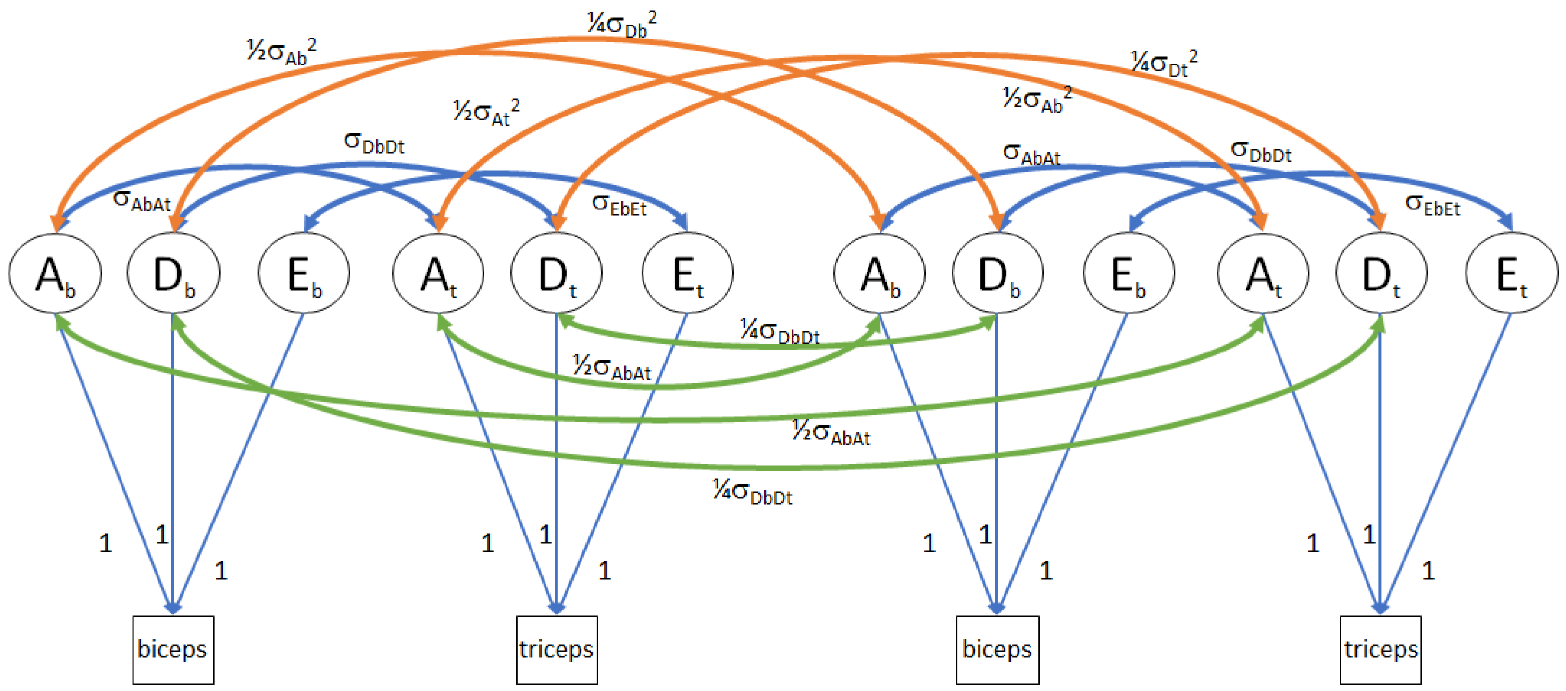
S_{Ph} (DZ)		Twin 1		Twin 2	
		bic1	tri1	bic2	tri2
Twin 1	bic1	$s_{Ab}^2 + s_{Db}^2 + s_{Eb}^2$	$s_{AbAt} + s_{DbDt} + s_{EbEt}$	$½s_{Ab}^2 + ¼s_{Db}^2$	
	tri1	$s_{AbAt} + s_{DbDt} + s_{EbEt}$	$s_{At}^2 + s_{Dt}^2 + s_{Et}^2$		$½s_{At}^2 + ¼s_{Dt}^2$
Twin 2	bic2	$½s_{Ab}^2 + ¼s_{Db}^2$		$s_{Ab}^2 + s_{Db}^2 + s_{Eb}^2$	$s_{AbAt} + s_{DbDt} + s_{EbEt}$
	tri2		$½s_{At}^2 + ¼s_{Dt}^2$	$s_{AbAt} + s_{DbDt} + s_{EbEt}$	$s_{At}^2 + s_{Dt}^2 + s_{Et}^2$



Cross-trait
Within twin +

Within trait (biceps + triceps)
Cross-twin

S_{Ph} (DZ)		Twin 1		Twin 2	
		bic1	tri1	bic2	tri2
Twin 1	bic1	$s_{Ab}^2 + s_{Db}^2 + s_{Eb}^2$	$s_{AbAt} + s_{DbDt} + s_{EbEt}$	$½s_{Ab}^2 + ¼s_{Db}^2$	
	tri1	$s_{AbAt} + s_{DbDt} + s_{EbEt}$	$s_{At}^2 + s_{Dt}^2 + s_{Et}^2$		$½s_{At}^2 + ¼s_{Dt}^2$
Twin 2	bic2	$½s_{Ab}^2 + ¼s_{Db}^2$		$s_{Ab}^2 + s_{Db}^2 + s_{Eb}^2$	$s_{AbAt} + s_{DbDt} + s_{EbEt}$
	tri2		$½s_{At}^2 + ¼s_{Dt}^2$	$s_{AbAt} + s_{DbDt} + s_{EbEt}$	$s_{At}^2 + s_{Dt}^2 + s_{Et}^2$



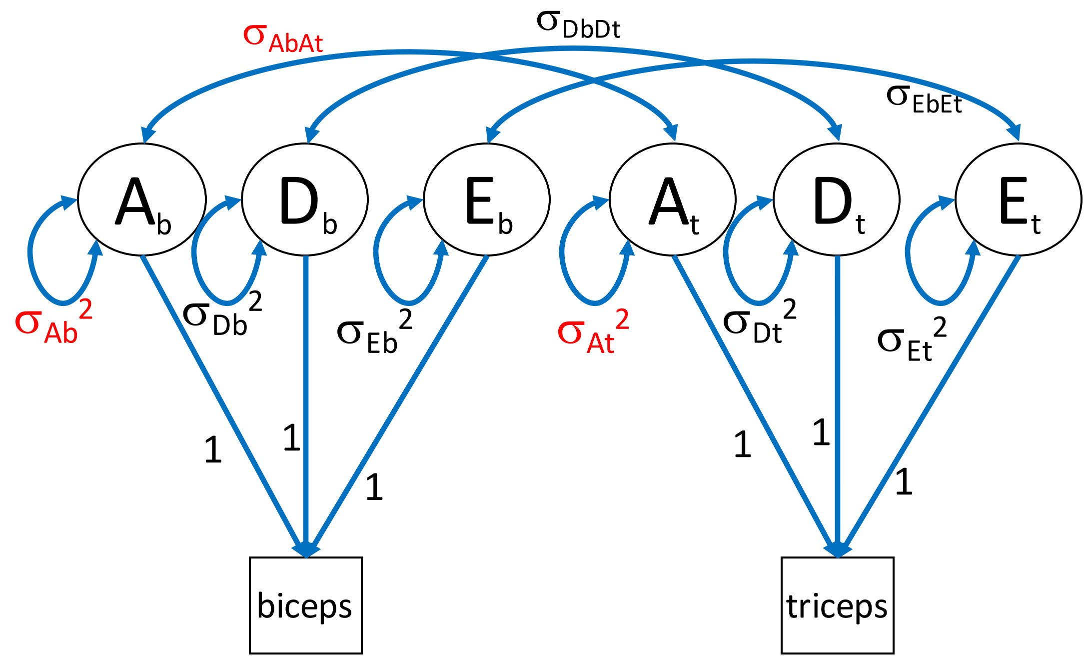
Cross-trait
Within twin +

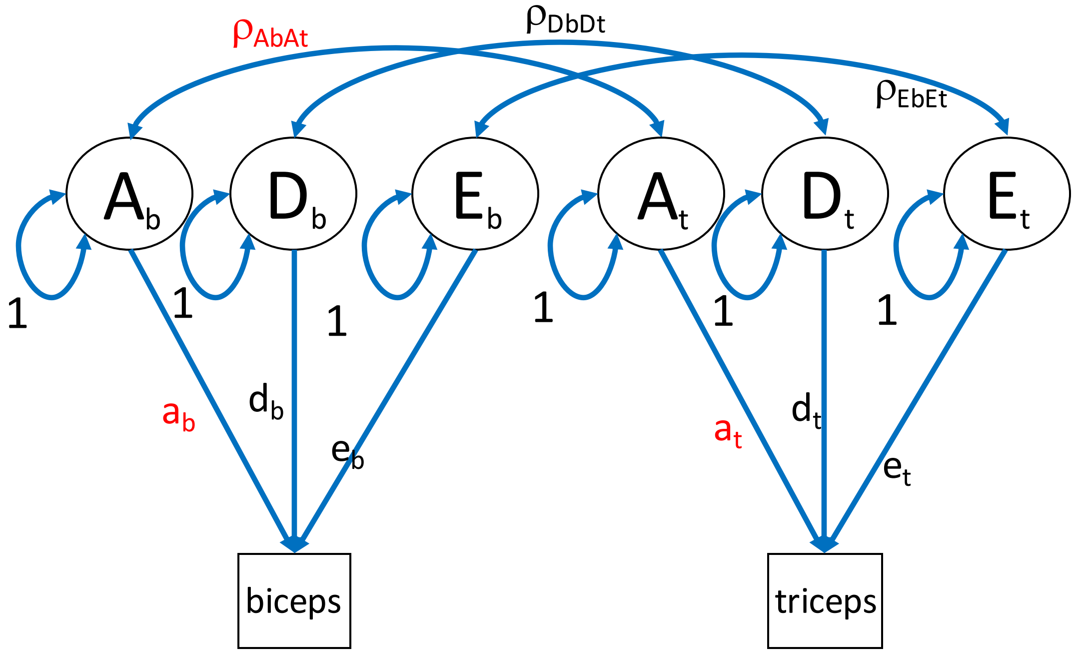
Within trait (biceps + triceps)
Cross-twin

Cross-trait
Cross-twin

S_{Ph} (DZ)		Twin 1		Twin 2	
		bic1	tri1	bic2	tri2
Twin 1	bic1	$s_{Ab}^2 + s_{Db}^2 + s_{Eb}^2$	$s_{AbAt} + s_{DbDt} + s_{EbEt}$	$½s_{Ab}^2 + ¼s_{Db}^2$	$½s_{AbAt} + ¼s_{DbDt}$
	tri1	$s_{AbAt} + s_{DbDt} + s_{EbEt}$	$s_{At}^2 + s_{Dt}^2 + s_{Et}^2$	$½s_{AbAt} + ¼s_{DbDt}$	$½s_{At}^2 + ¼s_{Dt}^2$
Twin 2	bic2	$½s_{Ab}^2 + ¼s_{Db}^2$	$½s_{AbAt} + ¼s_{DbDt}$	$s_{Ab}^2 + s_{Db}^2 + s_{Eb}^2$	$s_{AbAt} + s_{DbDt} + s_{EbEt}$
	tri2	$½s_{AbAt} + ¼s_{DbDt}$	$½s_{At}^2 + ¼s_{Dt}^2$	$s_{AbAt} + s_{DbDt} + s_{EbEt}$	$s_{At}^2 + s_{Dt}^2 + s_{Et}^2$

variance components vs. path coefficients





Σ_A	biceps	triceps
biceps	$\sigma_{Ab}{}^2$	σ_{AbAt}
triceps	$\sigma_{Ab,At}$	$\sigma_{At}{}^2$

Σ_A	biceps	triceps
biceps	$a_b{}^2$	$a_b * \rho_{AbAt} * a_t$
triceps	$a_b * \rho_{AbAt} * a_t$	$a_t{}^2$

A covariance (A): $a_b * \rho_{AbAt} * a_t$; standard deviations: a_b and a_t; correlation: ρ_{AbAt}

Bivariate ADE model: example

MODELING ACE/ADE COVARIANCE MATRICES

S MZ (N=214)

	bic_T1	tri_T1	bic_T2	tri_T2
bic_T1	12.478	10.379	9.571	8.586
tri_T1	10.379	10.604	8.103	8.503
bic_T2	9.571	8.103	11.845	9.894
tri_T2	8.586	8.503	9.894	10.447

S DZ (N=181)

	bic_T1	tri_T1	bic_T2	tri_T2
bic_T1	15.376	13.228	4.635	3.349
tri_T1	13.228	13.848	3.792	3.334
bic_T2	4.635	3.792	13.256	10.641
tri_T2	3.349	3.334	10.641	10.855

R MZ (N=214)

	bic_T1	tri_T1	bic_T2	tri_T2
bic_T1	1.000	0.902	0.787	0.752
tri_T1	0.902	1.000	0.723	0.808
bic_T2	0.787	0.723	1.000	0.889
tri_T2	0.752	0.808	0.889	1.000

R DMZ (N=181)

	bic_T1	tri_T1	bic_T2	tri_T2
bic_T1	1.000	0.907	0.325	0.259
tri_T1	0.907	1.000	0.280	0.272
bic_T2	0.325	0.280	1.000	0.887
tri_T2	0.259	0.272	0.887	1.000

Σ_{Ph} MZ	twin 1	twin 2
twin 1	$\Sigma_A + \Sigma_D + \Sigma_E$	$\Sigma_A + \Sigma_D$
twin 2	$\Sigma_A + \Sigma_D$	$\Sigma_A + \Sigma_D + \Sigma_E$

Σ_{Ph} DZ	twin 1	twin 2
twin 1	$\Sigma_A + \Sigma_D + \Sigma_E$	$\frac{1}{2}\Sigma_A + \frac{1}{4}\Sigma_D$
twin 2	$\frac{1}{2}\Sigma_A + \frac{1}{4}\Sigma_D$	$\Sigma_A + \Sigma_D + \Sigma_E$

Bivariate model: variance components

Σ_{Ph}	biceps	triceps
biceps	σ_b^2	$\sigma_{b,t}$
triceps	$\sigma_{b,t}$	σ_t^2

Σ_A	biceps	triceps
biceps	σ_{Ab}^2	σ_{AbAt}
triceps	$\sigma_{Ab,At}$	σ_{At}^2

Σ_D	biceps	triceps
biceps	σ_{Db}^2	σ_{DbDt}
triceps	$\sigma_{Db,Dt}$	σ_{Dt}^2

Σ_E	biceps	triceps
biceps	σ_{Eb}^2	σ_{EbEt}
triceps	$\sigma_{Eb,Et}$	σ_{Et}^2

Σ_{Ph}	biceps	triceps
biceps	12.620	10.572
triceps	10.572	11.091

Σ_A	biceps	triceps
biceps	4.729	2.783
triceps	2.783	2.069

Σ_D	biceps	triceps
biceps	5.188	5.913
triceps	5.913	6.923

Σ_E	biceps	triceps
biceps	2.703	1.876
triceps	1.876	2.099

Decomposition of **phenotypic covariance**
cov(biceps, triceps) = 10.572
cov(biceps, triceps) = 2.783 (A) + 5.913 (D) + 1.876 (E)

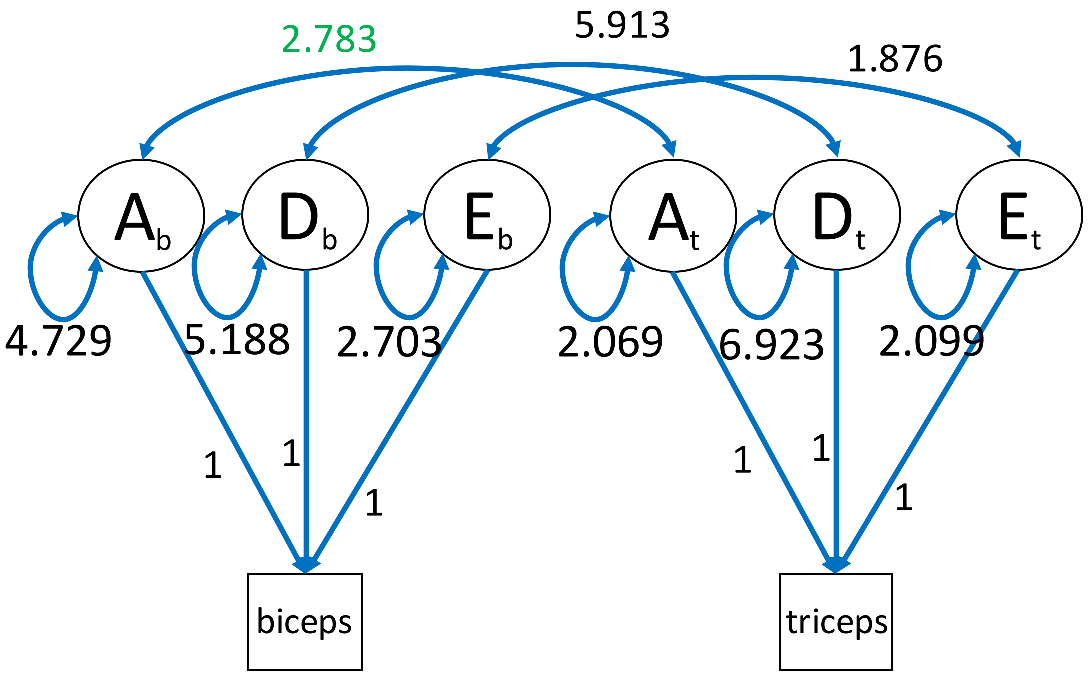
remember slide 3? $\sigma_{Ph1,Ph2} = \{\sigma_{Ph1} * \rho_{Ph1,Ph2} * \sigma_{Ph2}\}$

2.783 = √4.729*0.889* √ 2.069 (A)
5.913 = √ 5.188*0.987* √ 6.923 (D)
1.876 = √ 2.703*0.787* 2 √.099 (E)

Proportions:
A: 2.783/10.572 = .263 (26.3%)
D: 5.913/10.572 = .559 (55.9%)
E: 1.876/10.572 = .177 (17.7%)

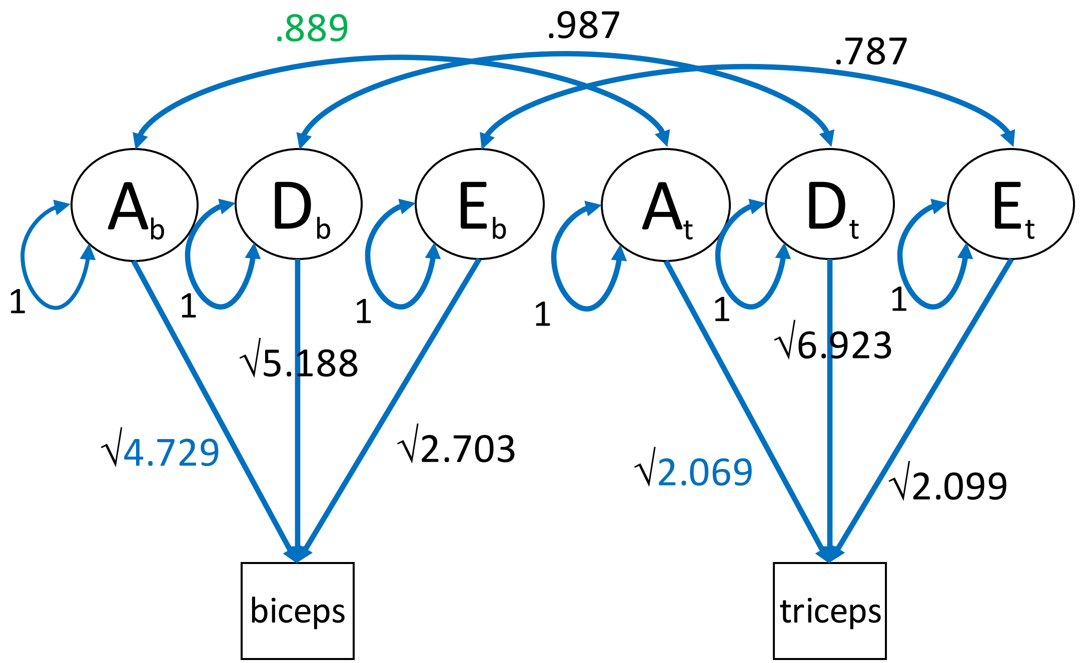
Q: what is .263?
A: The contribution of A to the phenotypic covariance expressed as a proportion of the phenotypic variance

Variance components



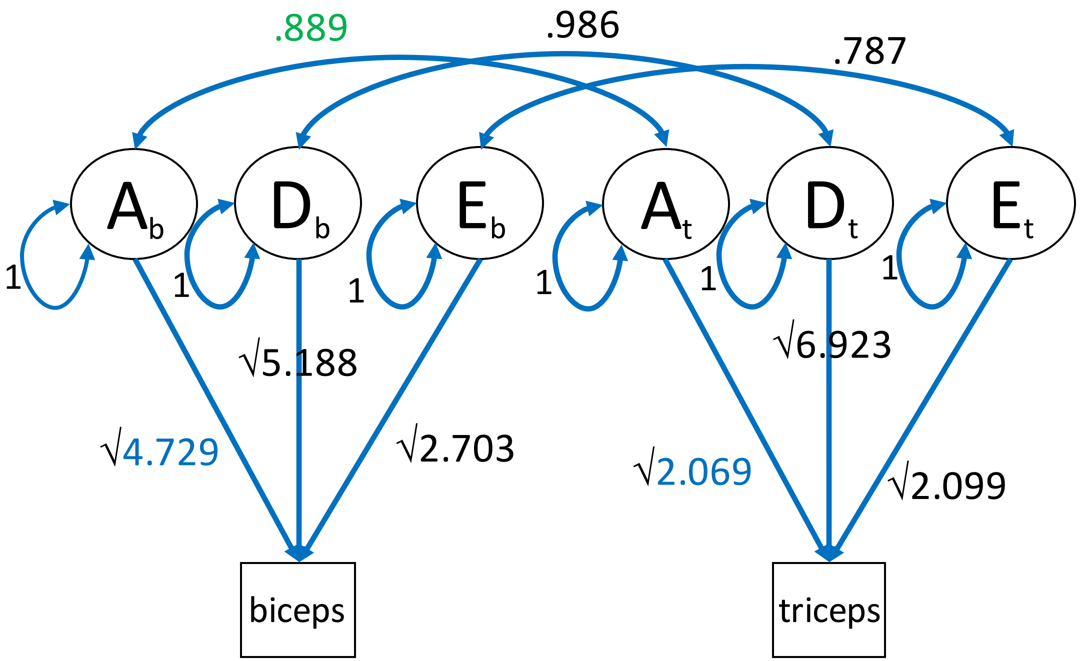
Σ_A	biceps	triceps
biceps	σ_{Ab}^2	σ_{AbAt}
triceps	$\sigma_{Ab,At}$	σ_{At}^2

Path coefficients

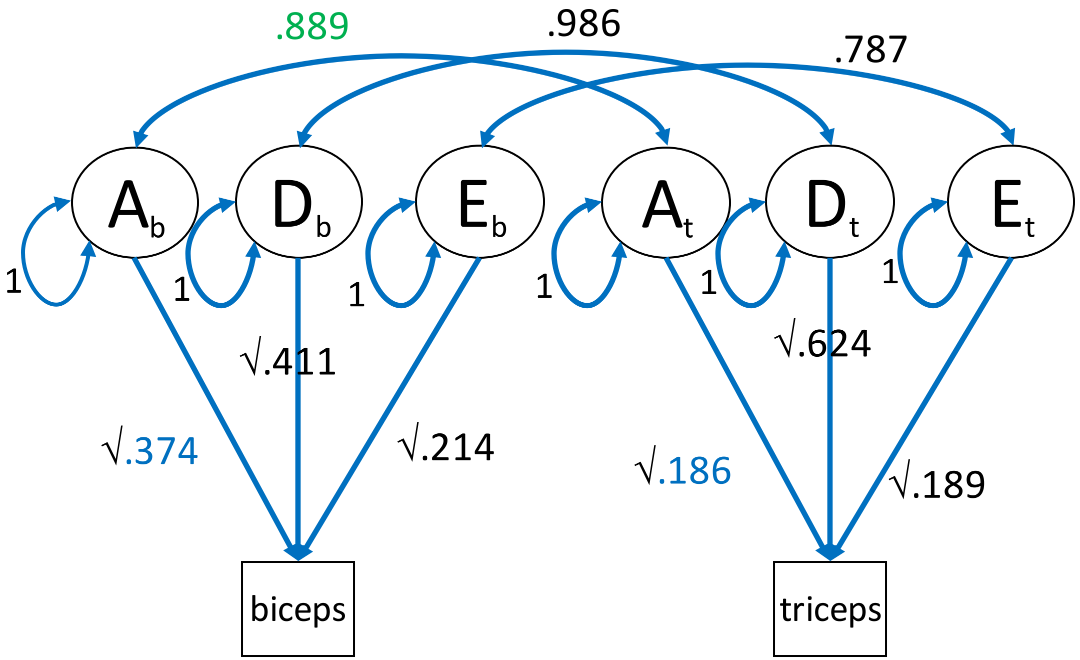


Σ_A	biceps	triceps
biceps	a_b^2	$a_b \rho_{Ab,At} a_t$
triceps	$a_b \rho_{Ab,At} a_t$	a_t^2

Bivariate model: path coefficients

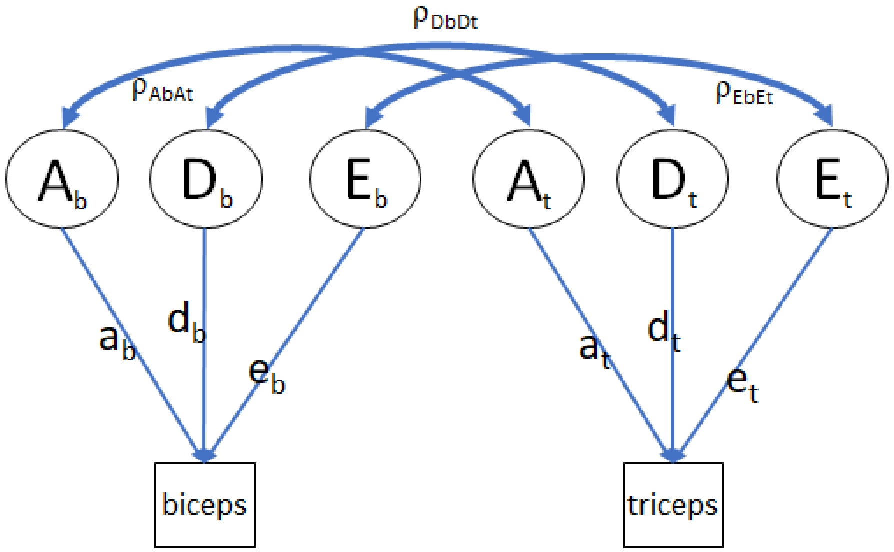


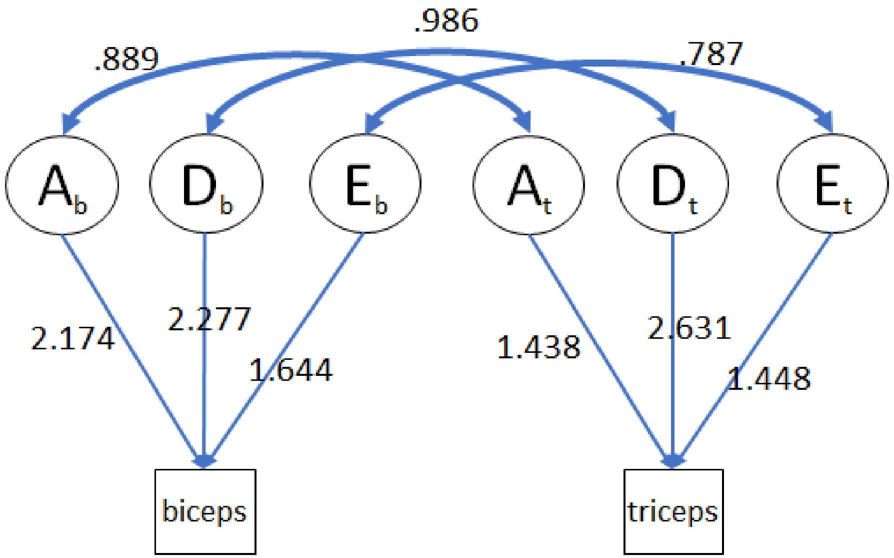
Phenotypes not standardized,
A,D,E standardized



Completely standardized
Phenotypes standardized, A,D,E standardized

.374 = 4.729 / (4.729+5.188+2.703) = A_b
.411= 5.188/ (4.729+5.188+2.703) = D_b
.214 = 2.703 / (4.729+5.188+2.703) = E_b





Question 1: Suppose $\rho_{Ab,At}$ is large (say .889), does that mean that the contribution of A factors to the phenotypic covariance is large?

Σ_A	biceps	triceps
biceps	a_b^2	$a_b\rho_{Ab,At}a_t$
triceps	$a_b\rho_{Ab,At}a_t$	a_t^2

Question 2: Why can we not estimate $\rho_{Ab,At}$ accurately, if a_b or a_t are relatively small?

E.g., suppose that A_b accounts for 3% of the biceps variance and A_t accounts for 40% of the triceps variance...

remember if $a_t^2 = 0$, $\rho_{Ab,At} = 0$