Introduction to Multivariate Genetic Analysis

Meike Bartels & Lucia Colodro Conde

With thanks to

Hermine Maes, Elizabeth Prom-Wormley, and many others

NATURE AND NURTURE:
TWIN RESEARCH AND HUMAN GENETICS

SESSION 2: 18 JUL-1 AUG 2020 | 3 ECTS | ADVANCED BACHELOR/MASTER | €1150 | VU AMSTERDAM

VRIJE UNIVERSITEIT AMSTERDAM

SUMMER SCHOOL

GENES IN BEHAVIOUR AND HEALTH (RESEARCH MASTER)

EXPLORING GENE-ENVIRONMENT INTERPLAY ACROSS OUR LIFESPAN

WWW.VU.NL/GENES

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LOOKING FURTHER

Looking for a PhD or Postdoc?

PhD project:

Social Media Language and Wellbeing; Understanding the Exposome-Genome interplay

4-years, paid position

Postdoc project

A Comprehensive Framework for Well-being.

In this project we will use genomic, epigenomic, exposome, and well-being data and network approaches to understand the multi-layers interplay

3-years, paid position, 20-40% teaching

Introduction to Multivariate Genetic Analysis

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Research Questions

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, dominance/shared environmental, and environmental factors to the covariance between two traits?

Example 1

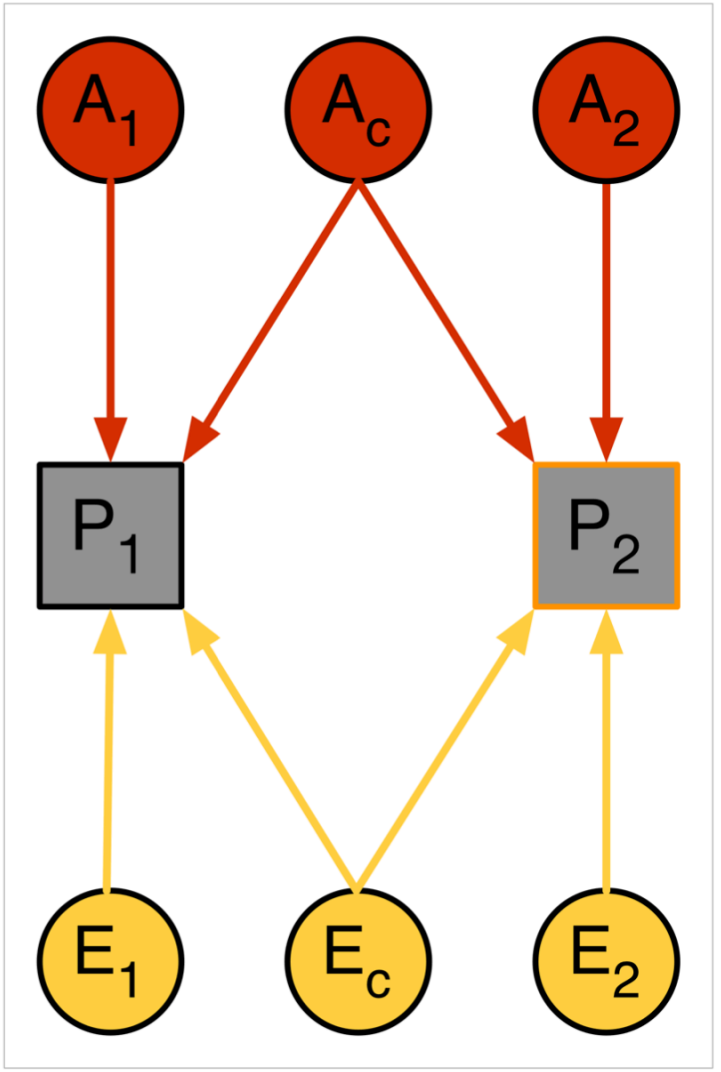
Why do traits correlate/covary?

How can we explain the association?

Shared Genes (r_G)

Shared shared environment (r_C)

Shared Non-shared environment (r_E)



Example 2

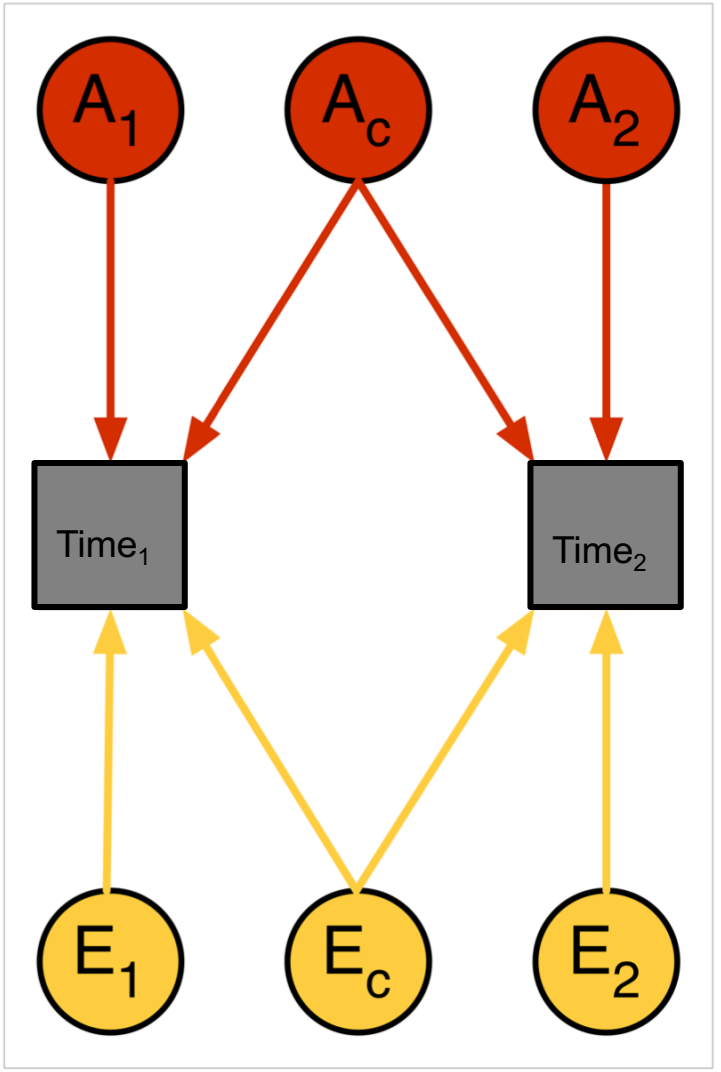
How do traits develop over time?

Does one trait in childhood lead to another trait in adolesence?

Shared/ Stable Genes (r_G)

Shared/ Stable shared environment (r_C)

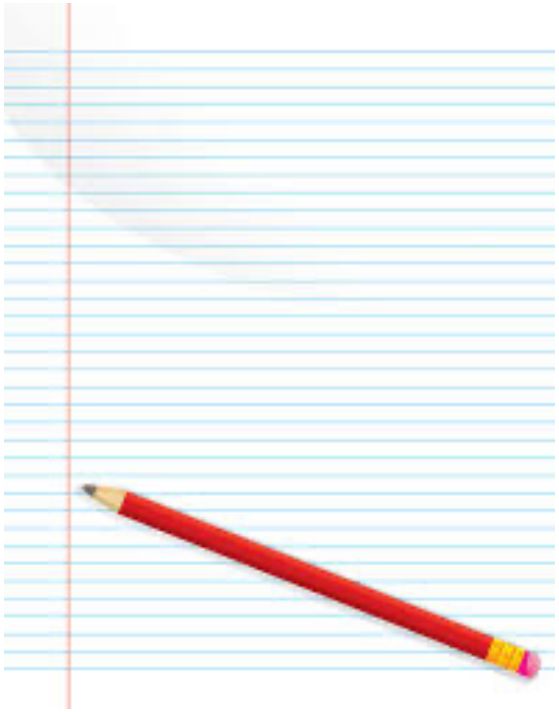
Shared/ Stable Non-shared environment (r_E)



Sources of Information

- 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

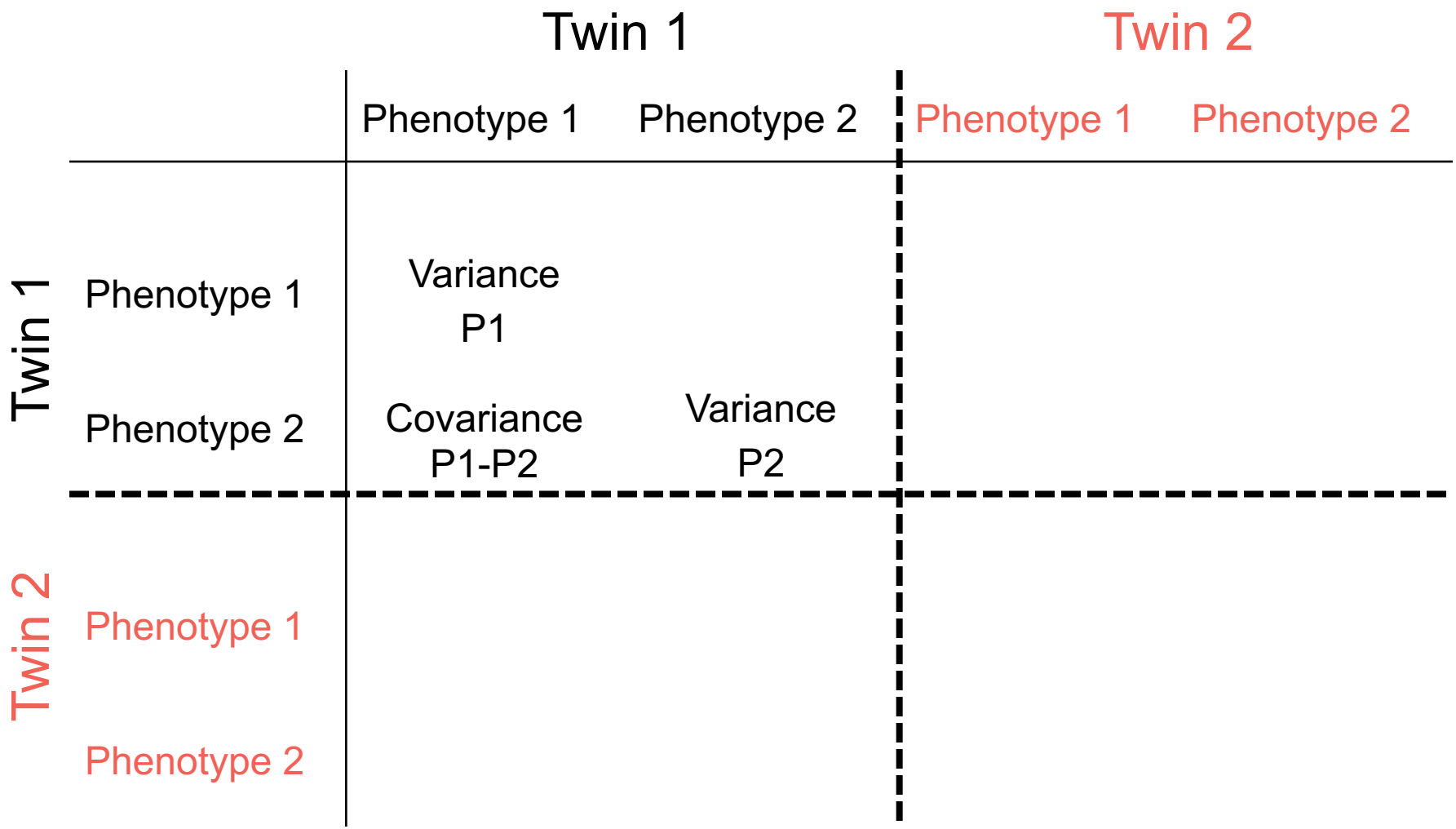
Paper and Pencil Exercise



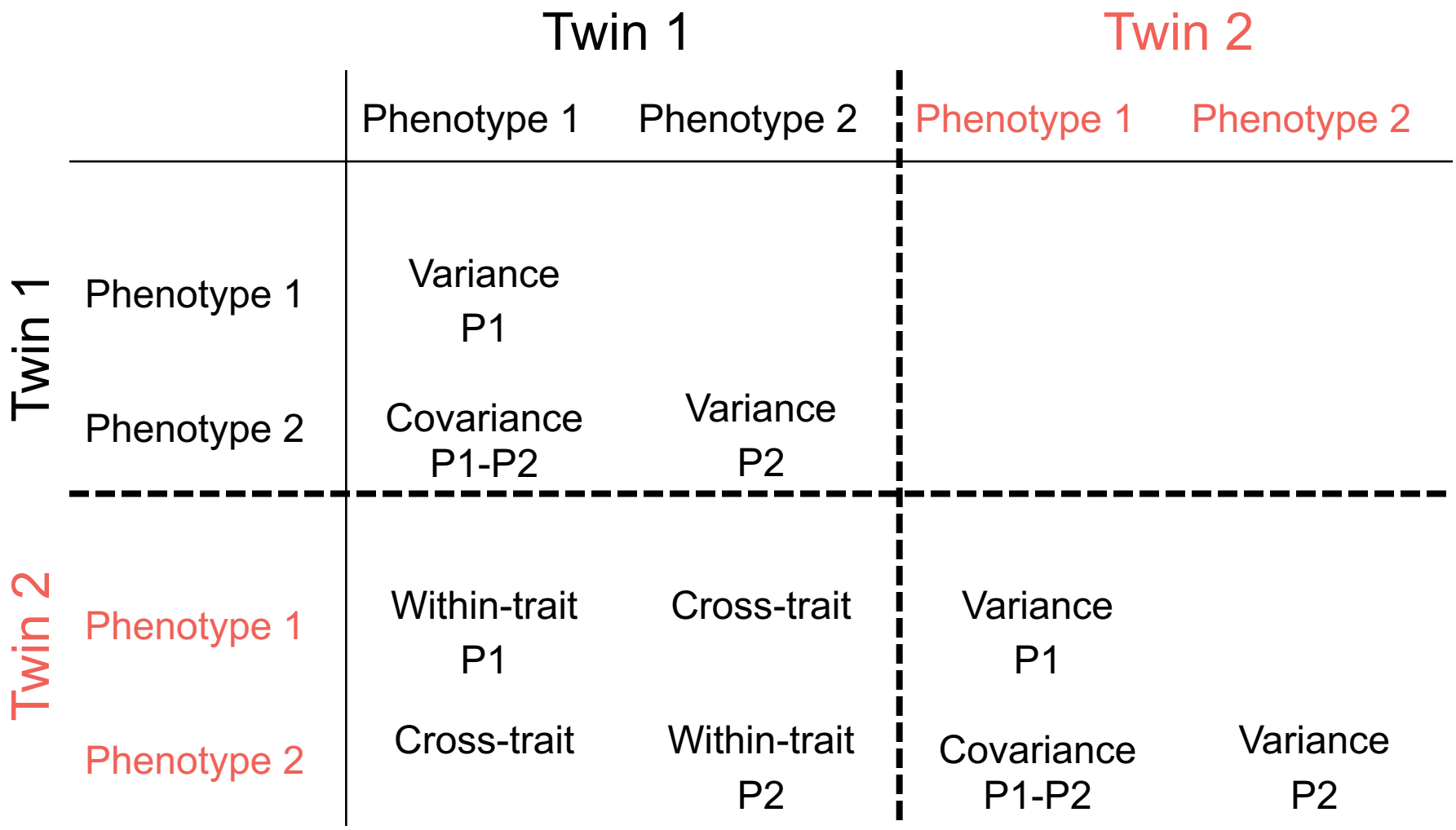
Observed Covariance Matrix- Univariate

	Twin 1	Twin 2
Twin 1	Variance T1	
Twin 2	Covariance T1-T2	Variance T2

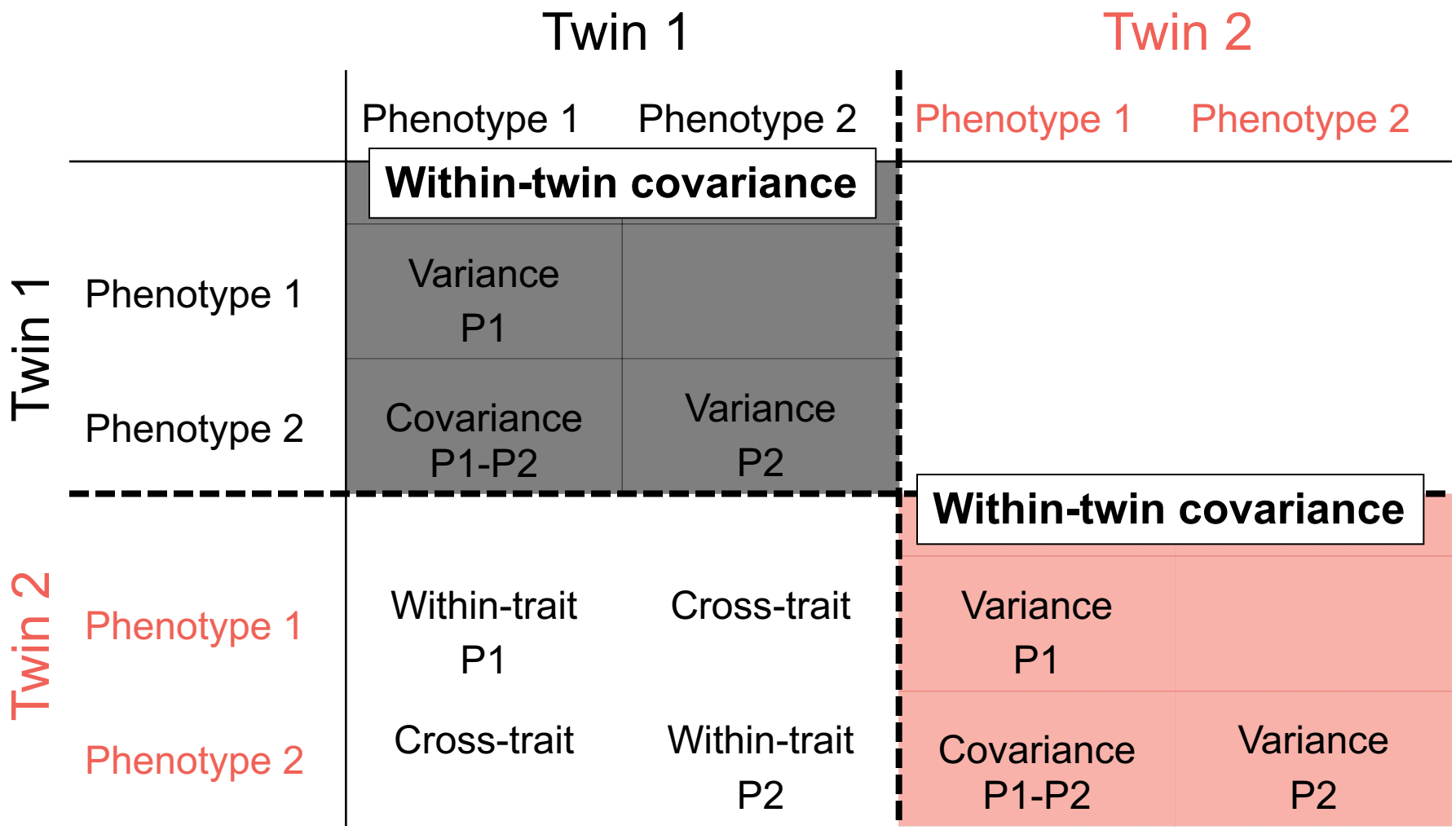
Observed Covariance Matrix- Bivariate



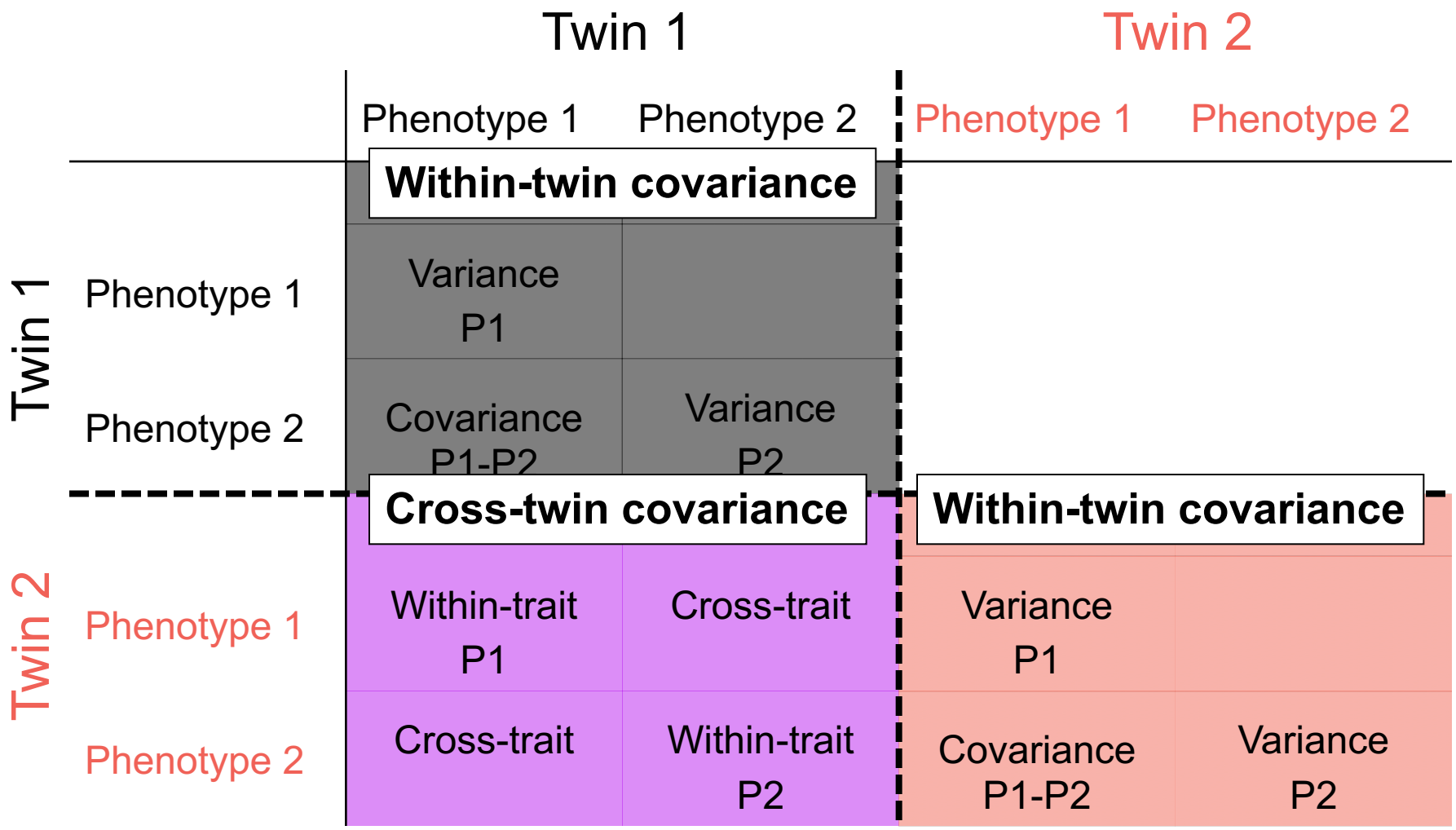
Observed Covariance Matrix



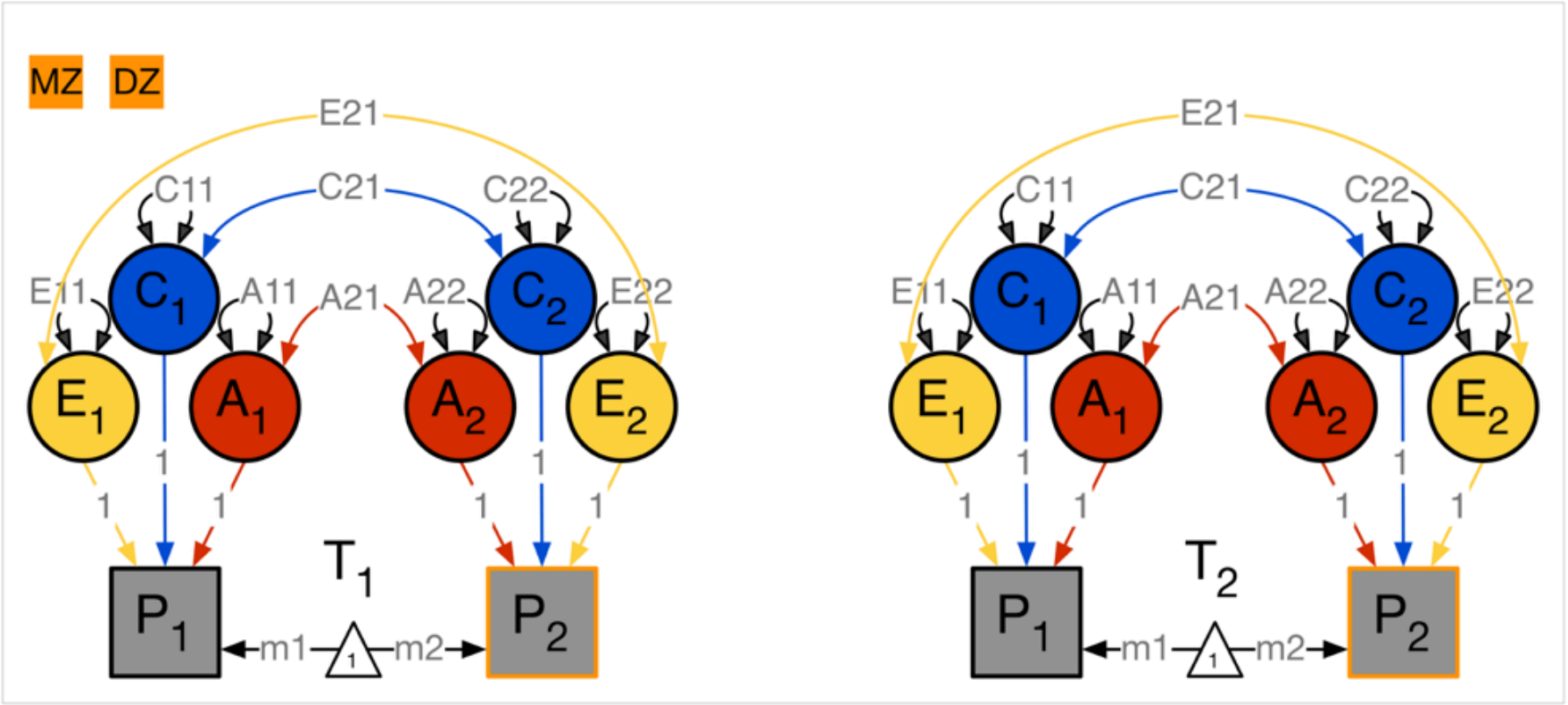
Observed Covariance Matrix



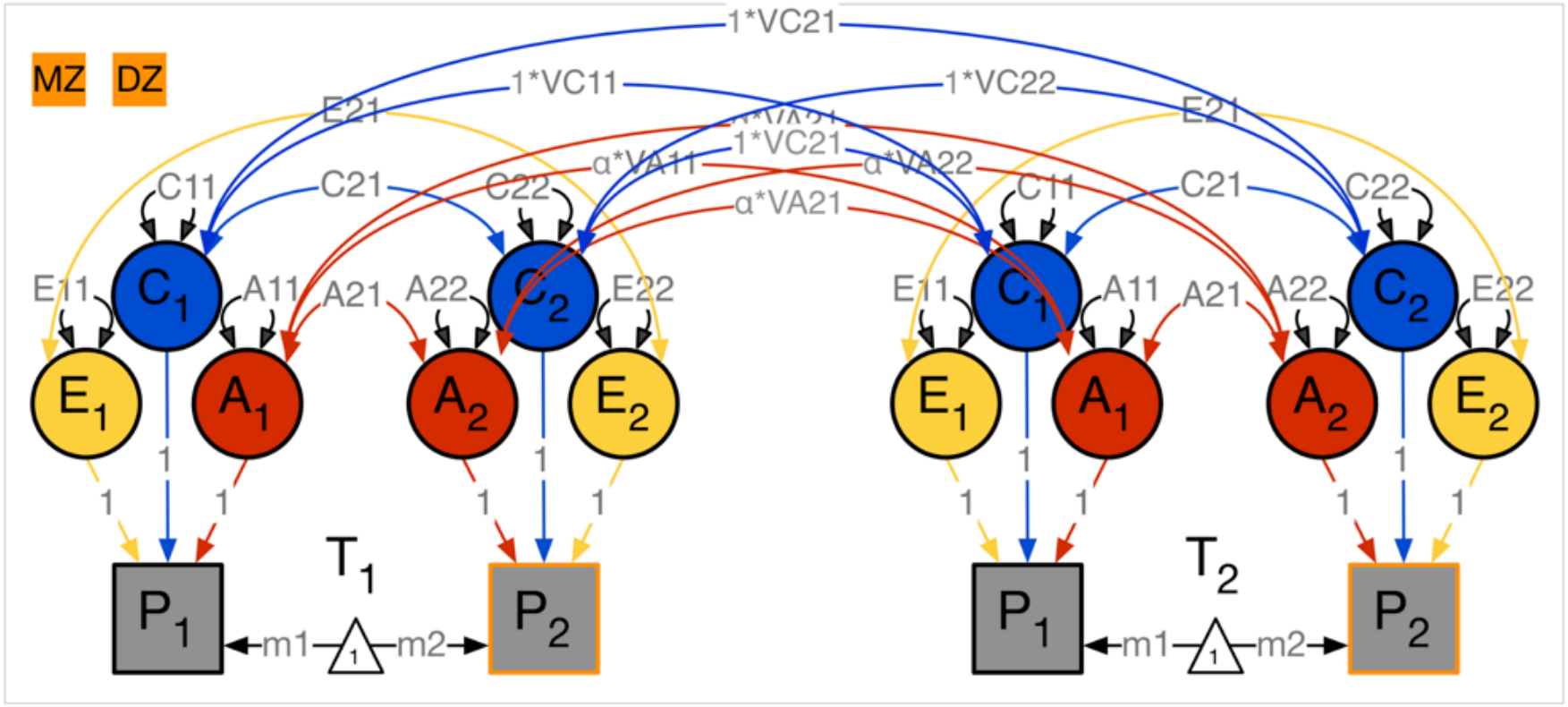
Observed Covariance Matrix



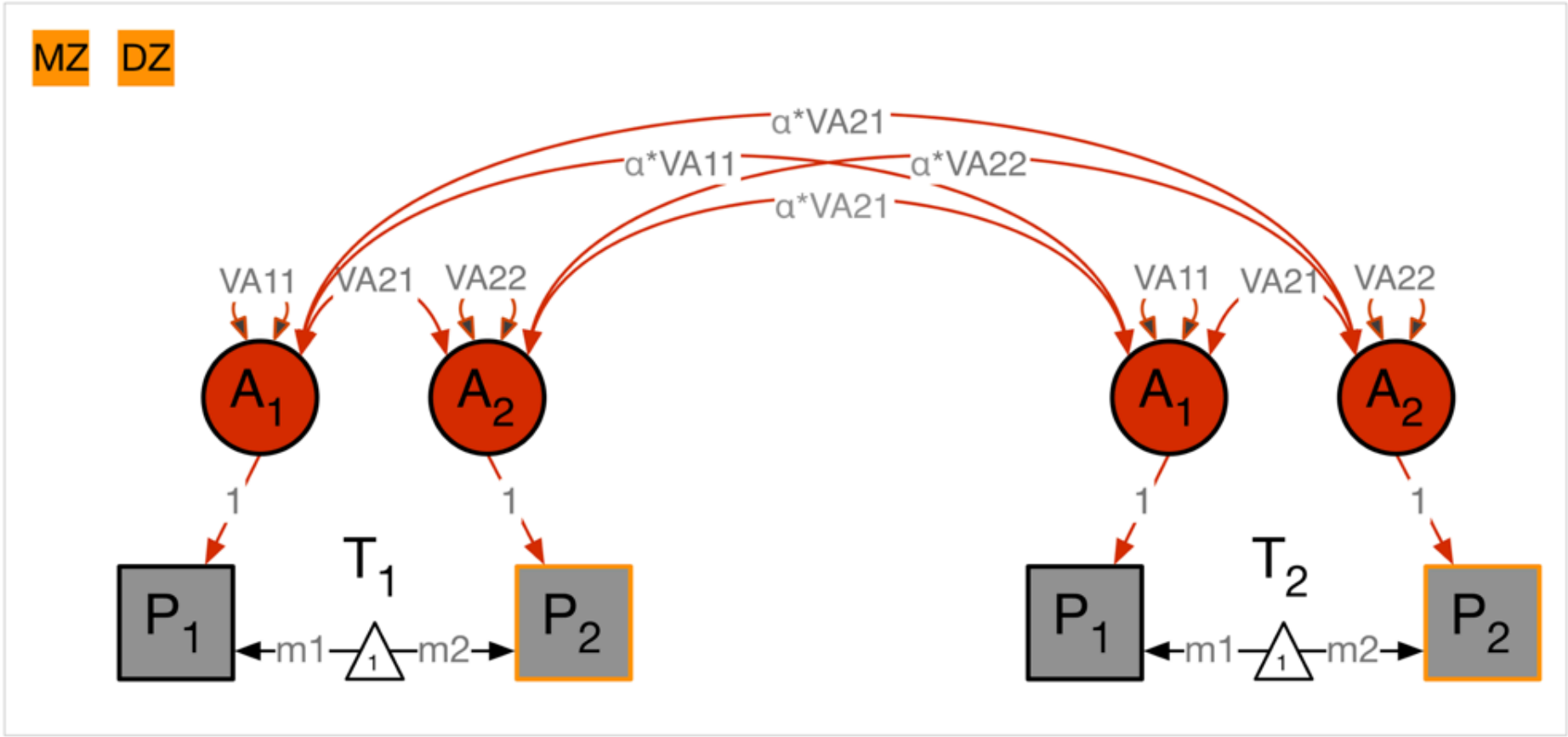
Within-Twin Covariance



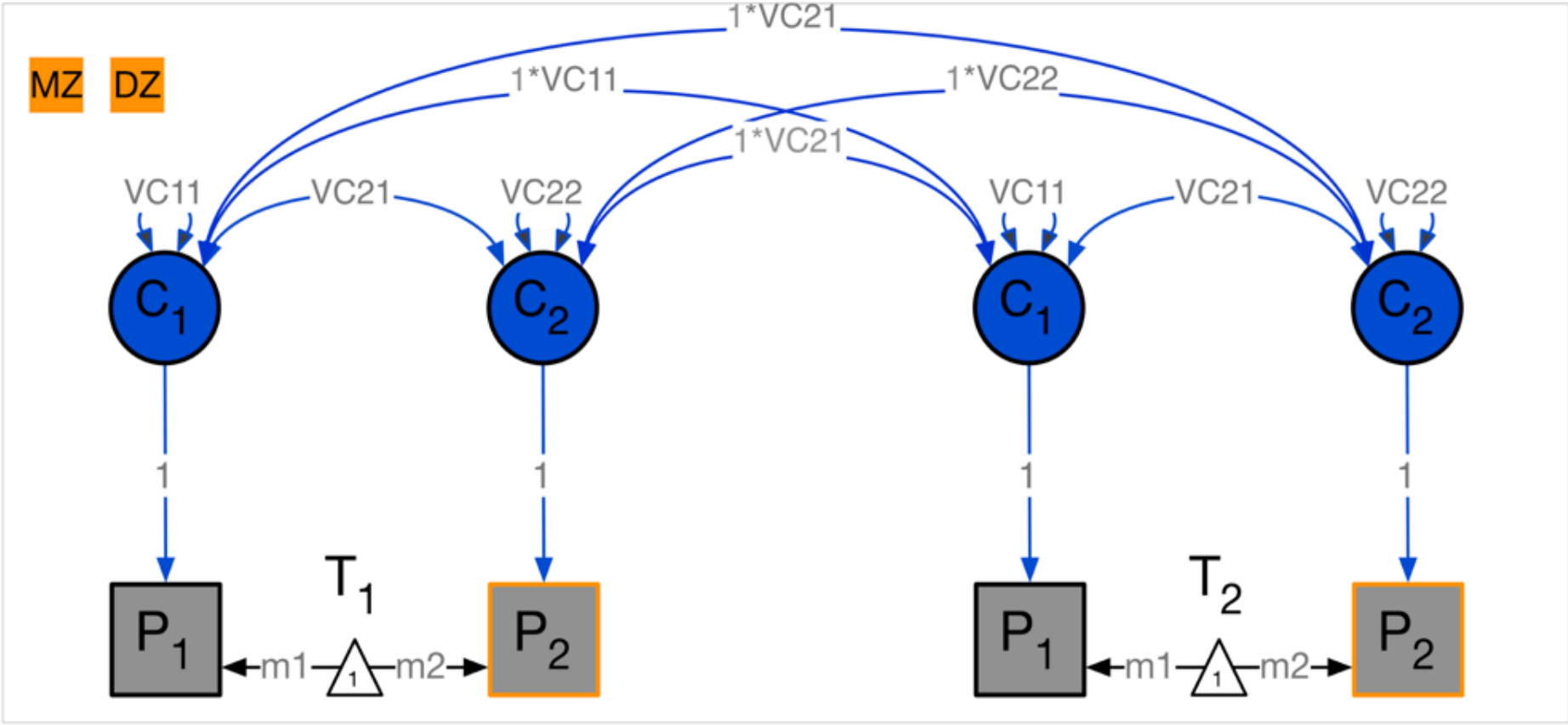
Cross-Twin Covariance



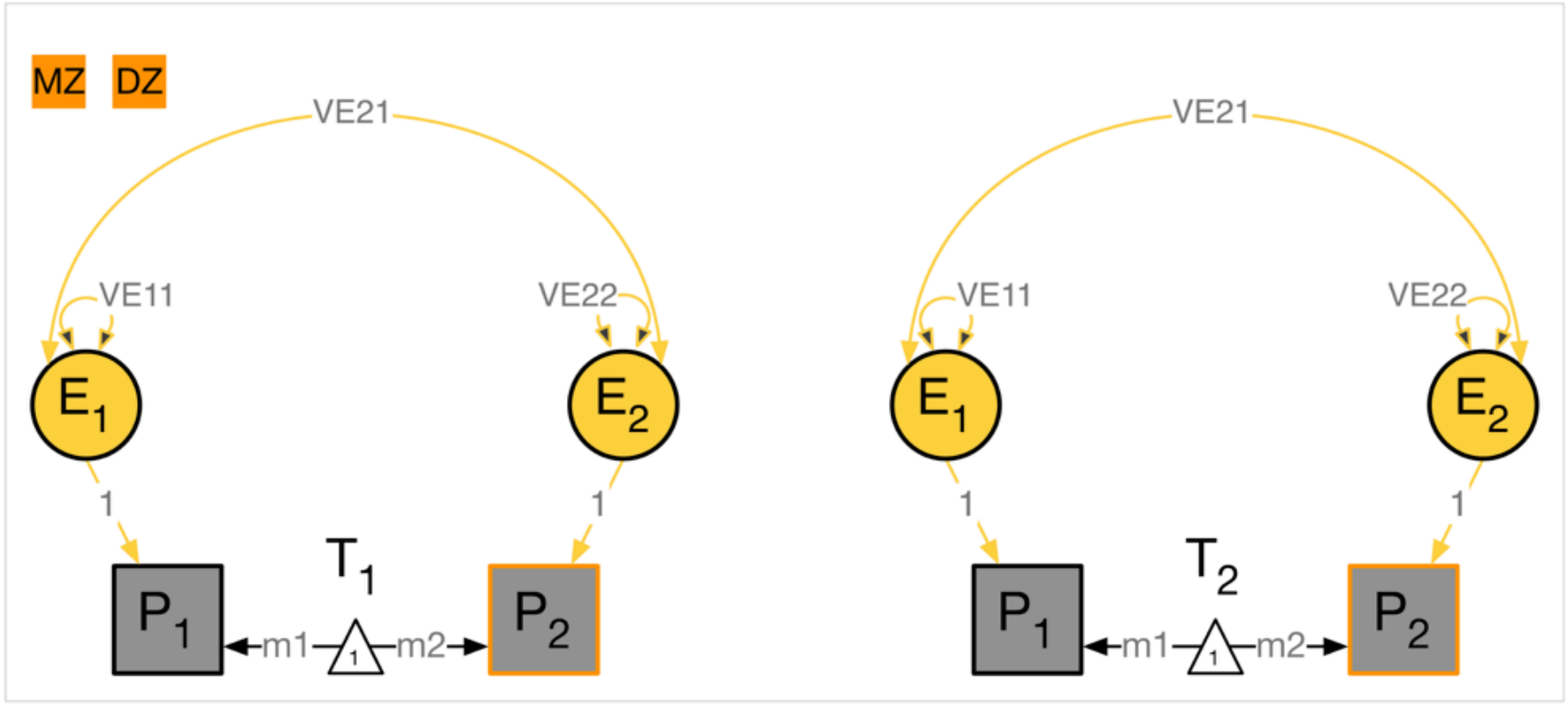
A Cross-Twin Covariance



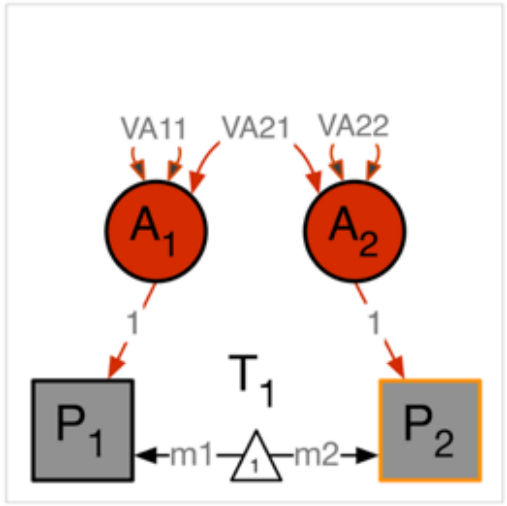
C Cross-Twin Covariance



E Cross-Twin Covariance



Bivariate within Twin Covariance Matrix

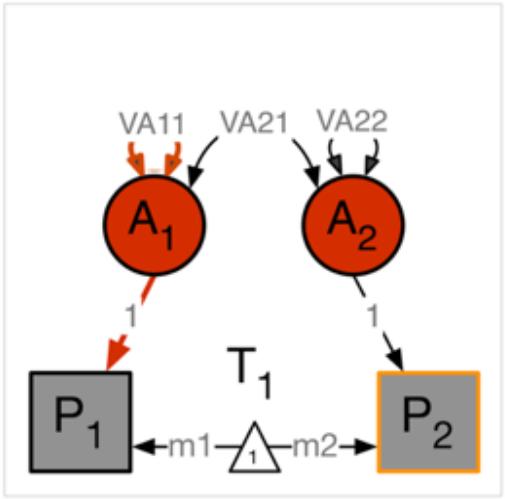


TWIN 1

TWIN 1

	$P1_{T1}$	$P2_{T1}$
$P1_{T1}$	Variance $P1_{T1}$	Covariance $P1_{T1}P2_{T1}$
$P2_{T1}$	Covariance $P1_{T1}P2_{T1}$	Variance $P2_{T1}$

Bivariate within Twin Covariance Matrix

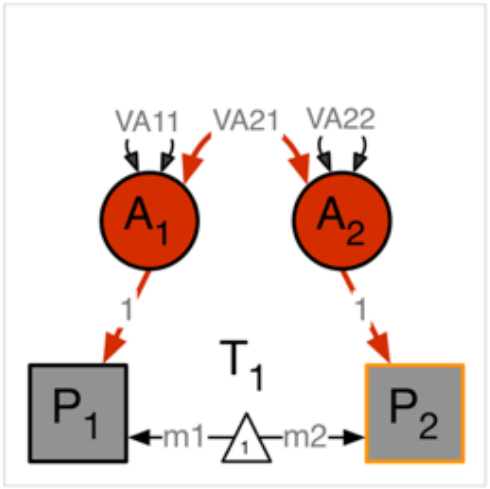


TWIN 1

TWIN 1

	$P1_{T1}$	$P2_{T1}$
$P1_{T1}$	VA11	Covariance $P1_{T1}P2_{T1}$
$P2_{T1}$	Covariance $P1_{T1}P2_{T1}$	Variance $P2_{T1}$

Bivariate within Twin Covariance Matrix

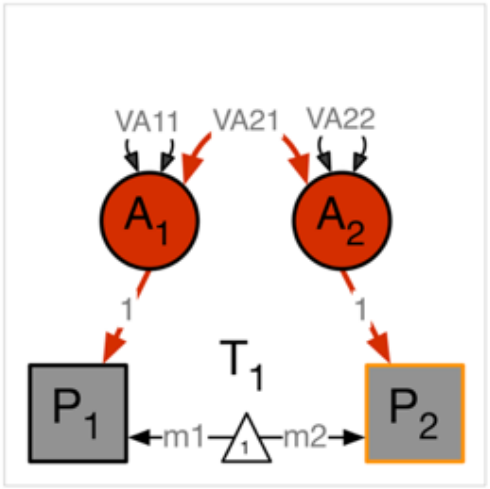


TWIN 1

TWIN 1

	$P1_{T1}$	$P2_{T1}$
$P1_{T1}$	VA11	Covariance $P1_{T1}P2_{T1}$
$P2_{T1}$	VA21	Variance $P2_{T1}$

Bivariate within Twin Covariance Matrix

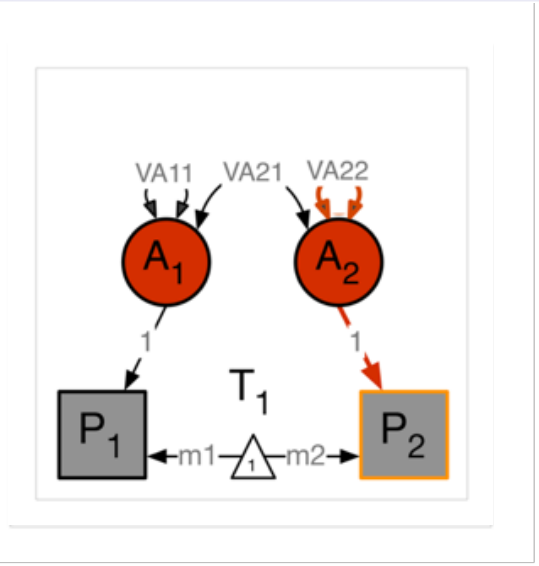


TWIN 1

TWIN 1

	$P1_{T1}$	$P2_{T1}$
$P1_{T1}$	VA11	VA21
$P2_{T1}$	VA21	Variance $P2_{T1}$

Bivariate within Twin Covariance Matrix



TWIN 1

TWIN 1

	$P1_{T1}$	$P2_{T1}$
$P1_{T1}$	VA11	VA21
$P2_{T1}$	VA21	VA22

Bivariate cross Twin Covariance Matrix

TWIN 1

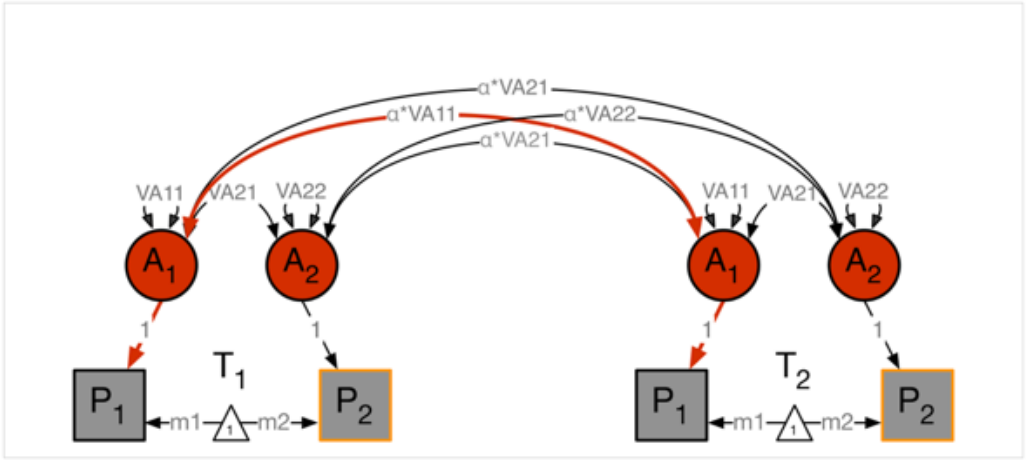
TWIN 1		$P1_{T1}$	$P2_{T1}$
	$P1_{T1}$	VA11 + VE11	VA21 + VE21
	$P2_{T1}$	VA21 + VE21	VA22 + VE22

Bivariate cross Twin Covariance Matr

TWIN 1

TWIN 2	$P1_{T1}$	$P2_{T1}$
$P1_{T2}$	Within-Trait $P1_{T1}P1_{T2}$	Cross-Trait $P1_{T1}P2_{T2}$
$P2_{T2}$	Cross-Trait $P2_{T1}P1_{T2}$	Within-Trait $P2_{T1}P2_{T2}$

Bivariate cross Twin Covariance Matr

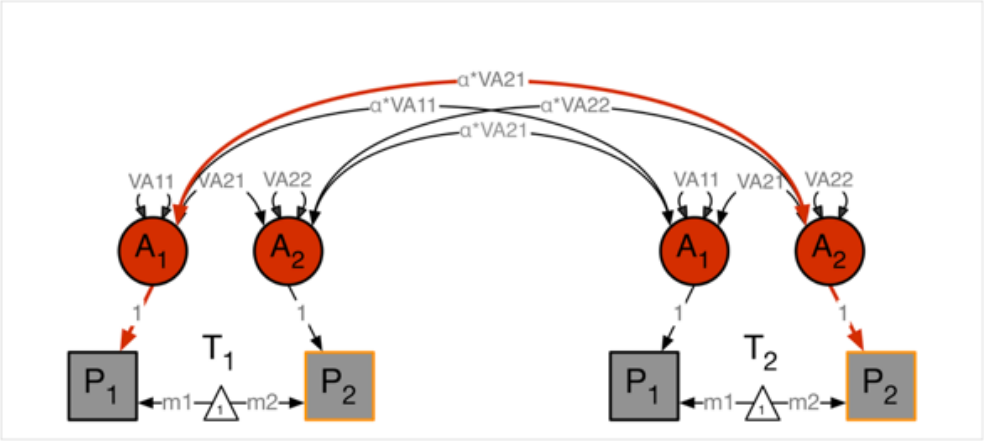


TWIN 1

TWIN 2

	$P1_{T1}$	$P2_{T1}$
$P1_{T2}$	1/0.5 * VA11	Cross-Trait $P1_{T1}P2_{T2}$
$P2_{T2}$	Cross-Trait $P2_{T1}P1_{T2}$	Within-Trait $P2_{T1}P2_{T2}$

Bivariate cross Twin Covariance Matr

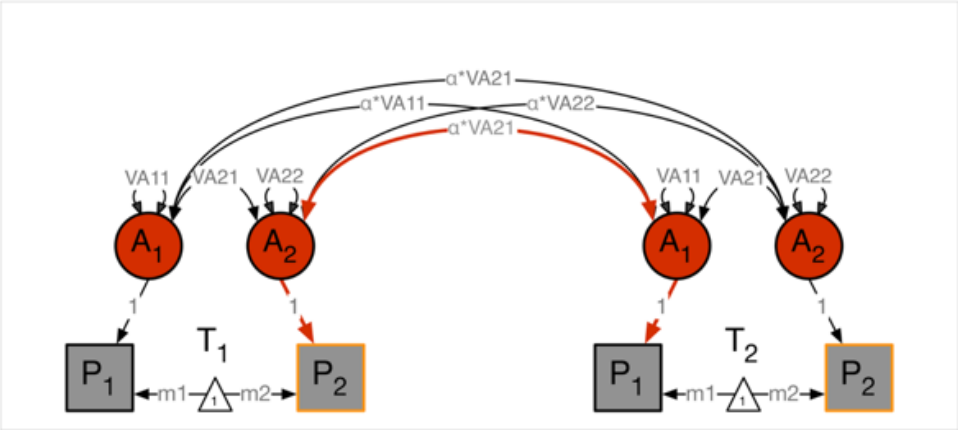


TWIN 1

TWIN 2

	$P1_{T1}$	$P2_{T1}$
$P1_{T2}$	1/0.5 * VA11	Cross-Trait $P1_{T1}P2_{T2}$
$P2_{T2}$	1/0.5 * VA21	Within-Trait $P2_{T1}P2_{T2}$

Bivariate cross Twin Covariance Matr

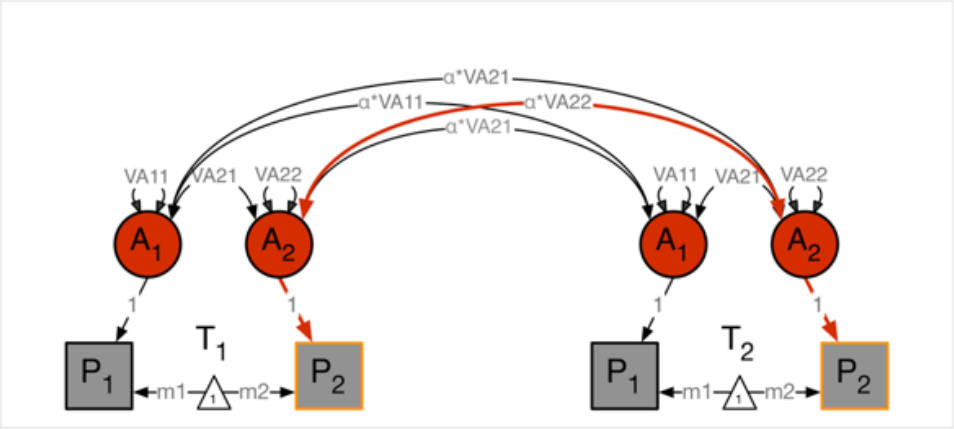


TWIN 1

TWIN 2

	$P1_{T1}$	$P2_{T1}$
$P1_{T2}$	1/0.5 * VA11	1/0.5 * VA21
$P2_{T2}$	1/0.5 * VA21	Within-Trait $P2_{T1}P2_{T2}$

Bivariate cross Twin Covariance Matr



TWIN 1

TWIN 2

	$P1_{T1}$	$P2_{T1}$
$P1_{T2}$	1/0.5 * VA11	1/0.5 * VA21
$P2_{T2}$	1/0.5 * VA21	1/0.5 * VA22

Predicted Twin Covariance Matrix

		twin 1		twin 2	
		$P1_{T1}$	$P2_{T1}$	$P1_{T2}$	$P2_{T2}$
twin 1	$P1_{T1}$	VA11 +VC11 +VE11	VA21 +VC21 +VE21	1/0.5 * VA11 +VC11	1/0.5 * VA21 +VC21
	$P2_{T1}$	VA21 +VC21 +VE21	VA22 +VC22 +VE22	1/0.5 * VA21 +VC21	1/0.5 *VA22 +VC22
twin 2	$P1_{T2}$	1/0.5 * VA11 +VC11	1/0.5 * VA21 +VC21	VA11 +VC11 +VE11	VA21 +VC21 +VE21
	$P2_{T2}$	1/0.5 * VA21 +VC21	1/0.5 *VA22 +VC22	VA21 +VC21 +VE21	VA22 +VC22 +VE22

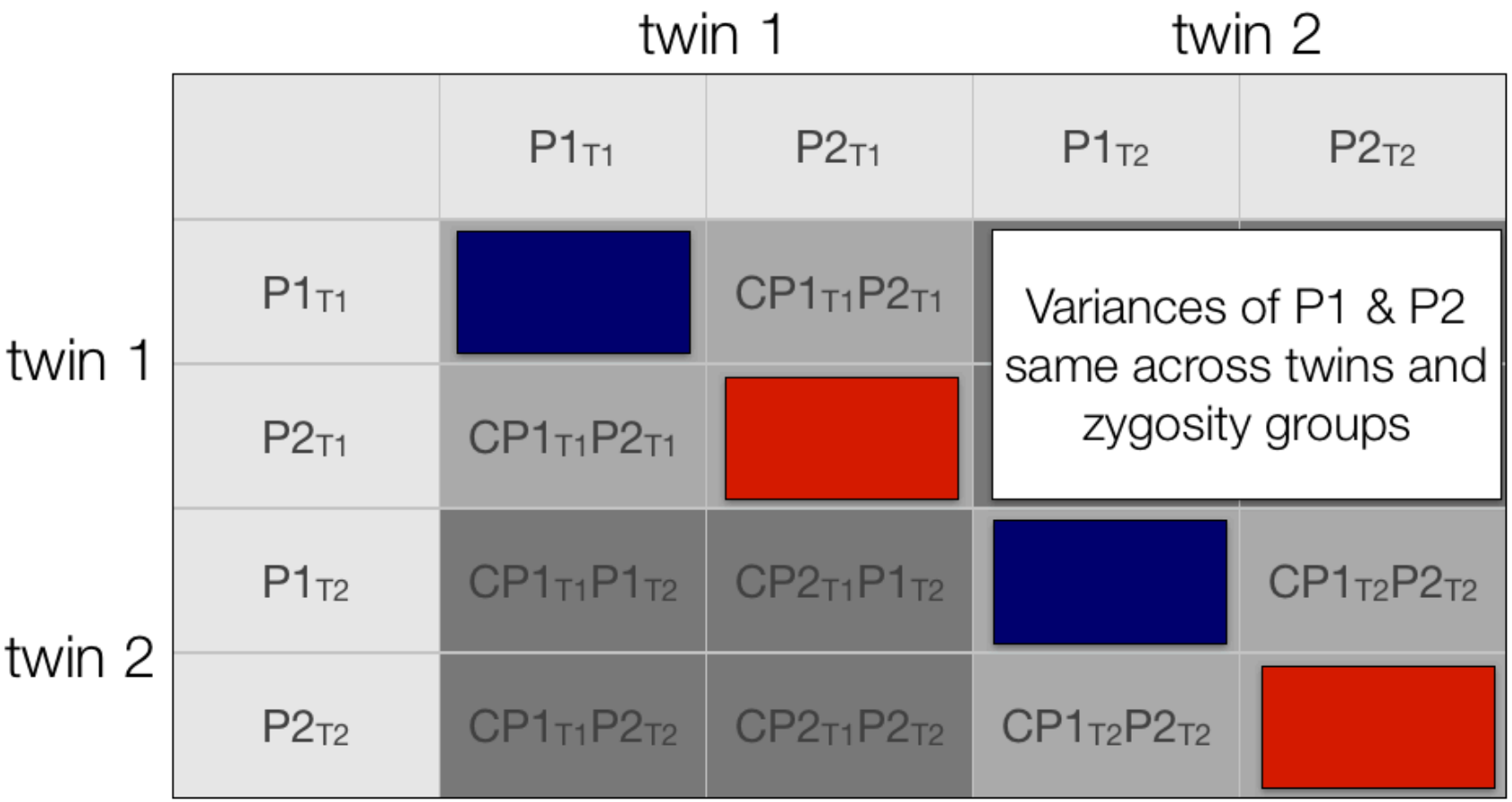
Predicted MZ Twin Covariance Matrix

		twin 1		twin 2	
		$P1_{T1}$	$P2_{T1}$	$P1_{T2}$	$P2_{T2}$
twin 1	$P1_{T1}$	VA11 +VC11 +VE11	VA21 +VC21 +VE21	VA11 +VC11	VA21 +VC21
	$P2_{T1}$	VA21 +VC21 +VE21	VA22 +VC22 +VE22	VA21 +VC21	VA22 +VC22
twin 2	$P1_{T2}$	VA11 +VC11	VA21 +VC21	VA11 +VC11 +VE11	VA21 +VC21 +VE21
	$P2_{T2}$	VA21 +VC21	VA22 +VC22	VA21 +VC21 +VE21	VA22 +VC22 +VE22

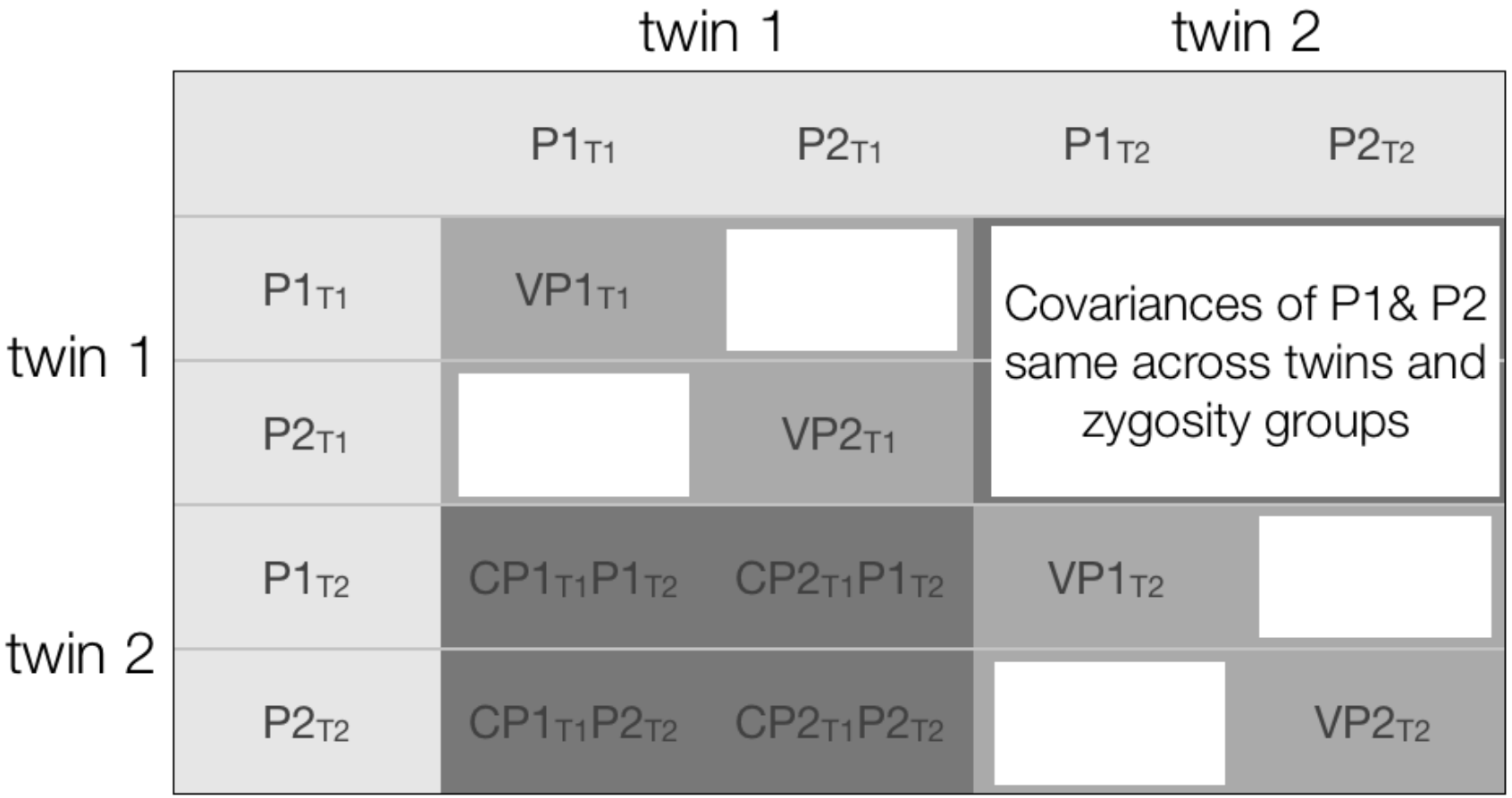
Predicted DZ Twin Covariance Matrix

		twin 1		twin 2	
		$P1_{T1}$	$P2_{T1}$	$P1_{T2}$	$P2_{T2}$
twin 1	$P1_{T1}$	VA11 +VC11 +VE11	VA21 +VC21 +VE21	0.5 * VA11 +VC11	0.5 * VA21 +VC21
	$P2_{T1}$	VA21 +VC21 +VE21	VA22 +VC22 +VE22	0.5 * VA21 +VC21	0.5 *VA22 +VC22
twin 2	$P1_{T2}$	0.5 * VA11 +VC11	0.5 * VA21 +VC21	VA11 +VC11 +VE11	VA21 +VC21 +VE21
	$P2_{T2}$	0.5 * VA21 +VC21	0.5 *VA22 +VC22	VA21 +VC21 +VE21	VA22 +VC22 +VE22

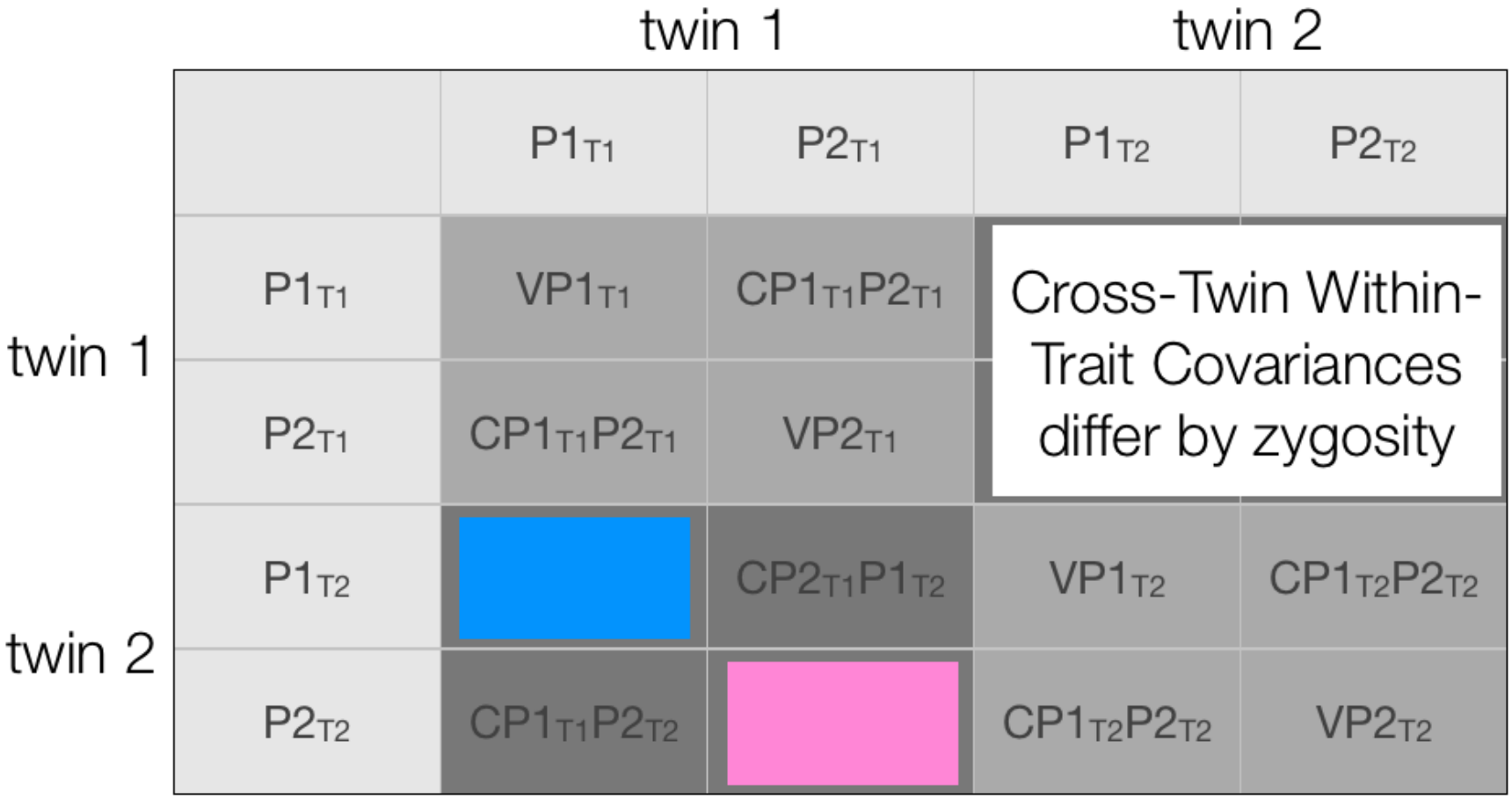
Bivariate Twin Covariance Matrix



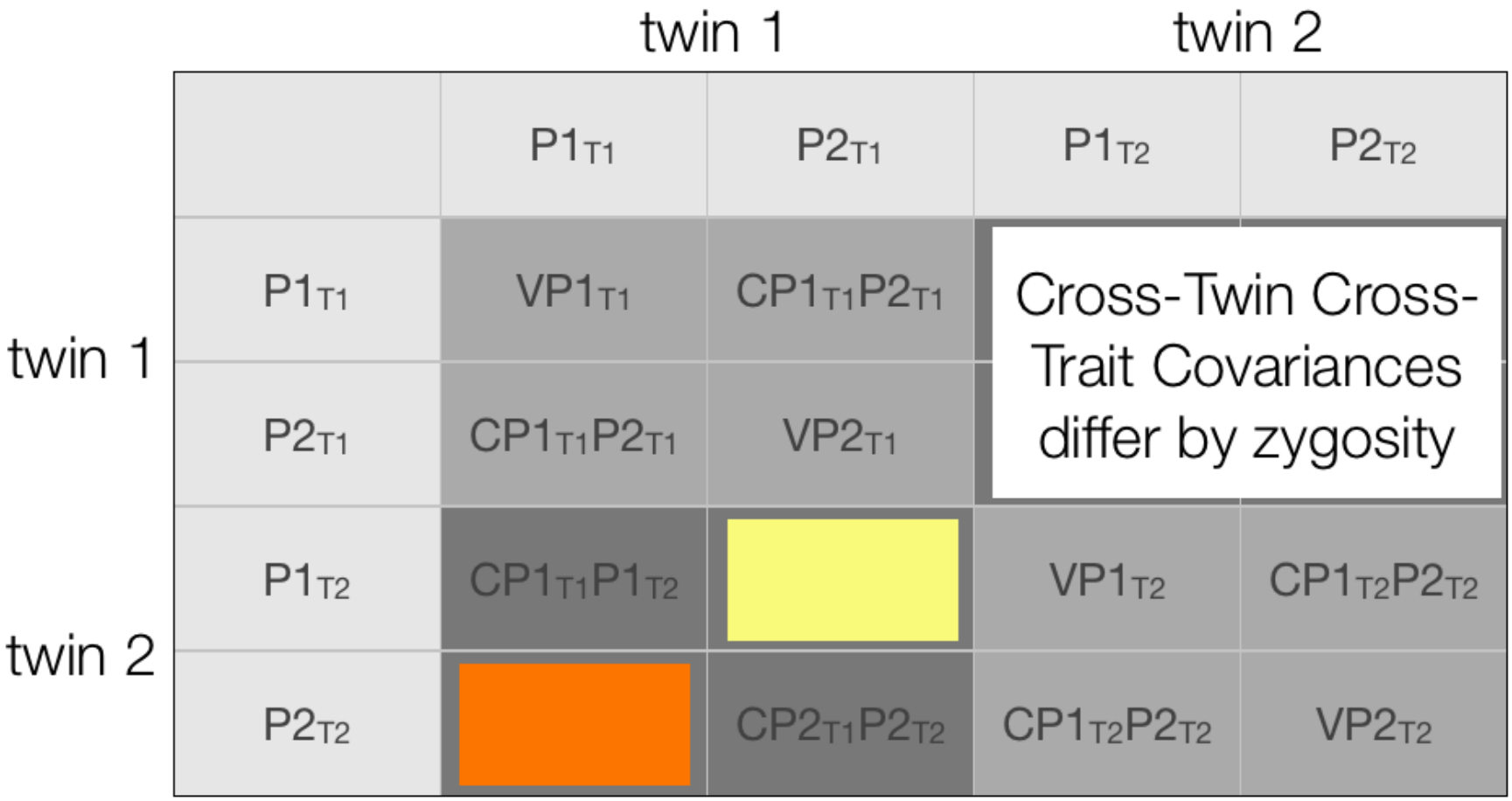
Bivariate Twin Covariance Matrix



Bivariate Twin Covariance Matrix



Bivariate Twin Covariance Matrix



Bivariate MZ Twin Covariance Matrix

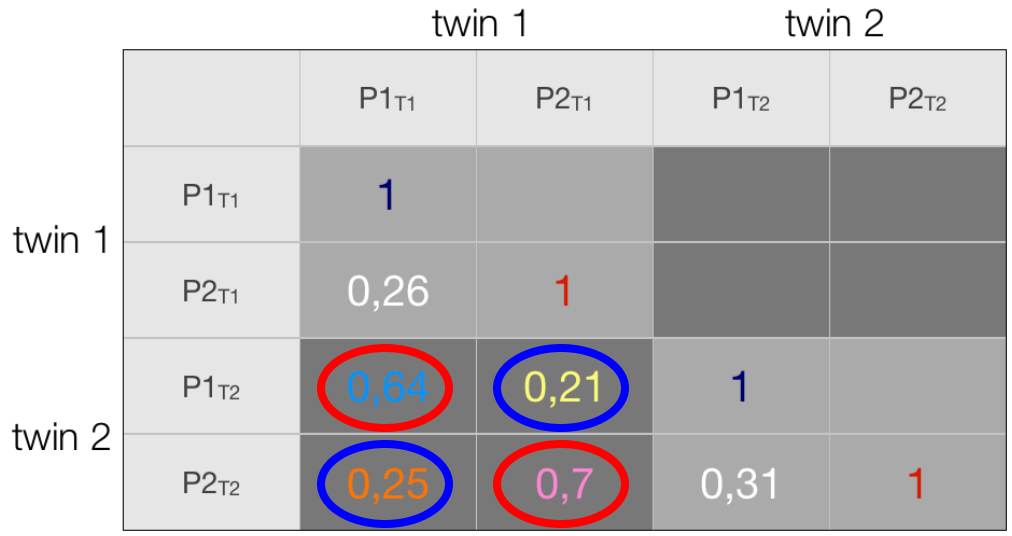
		twin 1		twin 2	
		$P1_{T1}$	$P2_{T1}$	$P1_{T2}$	$P2_{T2}$
twin 1	$P1_{T1}$	1			
	$P2_{T1}$	0,26	1		
twin 2	$P1_{T2}$	0,64	0,21	1	
	$P2_{T2}$	0,25	0,7	0,31	1

Bivariate DZ Twin Covariance Matrix

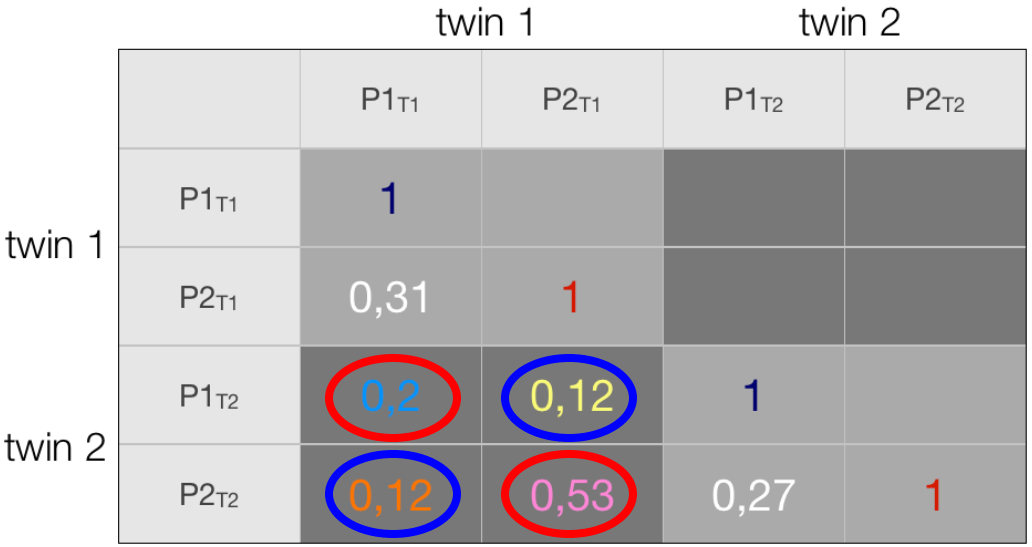
		twin 1		twin 2	
		$P1_{T1}$	$P2_{T1}$	$P1_{T2}$	$P2_{T2}$
twin 1	$P1_{T1}$	1			
	$P2_{T1}$	0,31	1		
twin 2	$P1_{T2}$	0,2	0,12	1	
	$P2_{T2}$	0,12	0,53	0,27	1

Bivariate Twin Covariance Matrix

MZ



DZ



Summary

- Within-individual cross-trait covariance implies common aetiological influences
- Cross-twin cross-trait covariance implies common aetiological influences are familial
- Whether familial influences are genetic or environmental shown by MZ:DZ ratio of cross-twin cross-trait covariances