Genetic simplex model: practical

Sanja Franic, Conor Dolan

Practical: estimate the genetic and environmental contributions to temporal stability and change in full-scale IQ measured at four time points (mean ages 5.5, 6.8, 9.7, 12.2, SDs .3, .19, .43, .24)

N = 562 twin pairs (261 MZ, 301 DZ)

```
> head(data)
  zyg IQ11 IQ21 IQ31 IQ41 IQ12 IQ22 IQ32 IQ42
1   1   NA   NA   NA  111   NA   NA   NA  114
2   1   NA   NA   78   NA   NA   NA   78   NA
3   1   NA   NA   78   NA   NA   NA   89   NA
4   1   NA   NA   78   84   NA   NA   88   94
5   1   NA   NA   79   80   NA   NA   95   87
6   1   NA   NA   79   85   NA   NA   82   78
```

The proportions of observed FSIQ data:
0.812, 0.295, 0.490, 0.828 (MZ twin 1)
0.812, 0.295, 0.490, 0.828 (MZ twin 2)
0.774, 0.379, 0.598, 0.797 (DZ twin1)
0.774, 0.379, 0.598, 0.797 (DZ twin 2)

Models

1) Saturated Model
   - estimate means (subject to twin1-twin2 equality constraints), variances and covariances

	IQ11	**IQ21**	**IQ31**	**IQ41**	**IQ12**	**IQ22**	**IQ32**	**IQ42**
IQ11	var1							
IQ21	cov21	var2						
IQ31	cov31	cov32	var3					
IQ41	cov41	cov42	cov43	var4				
IQ12	cov51	cov52	cov53	cov54	var5			
IQ22	cov61	cov62	cov63	cov64	cov65	var6		
IQ23	cov71	cov72	cov73	cov74	cov75	cov76	var7	
IQ24	cov81	cov82	cov83	cov84	cov85	cov86	cov87	var8

different over MZ & DZ

	IQ11	**IQ21**	**IQ31**	**IQ41**	**IQ12**	**IQ22**	**IQ32**	**IQ42**
mean	m1	m2	m3	m4	m1	m2	m3	m4

Models

1) Saturated Model
   - estimate means (subject to twin1-twin1 equality constraints), variances and covariances

	IQ11	**IQ21**	**IQ31**	**IQ41**	**IQ12**	**IQ22**	**IQ32**	**IQ42**
IQ11	var1							
IQ21	cov21	var2						
IQ31	cov31	cov32	var3					
IQ41	cov41	cov42	cov43	var4				
IQ12	cov51	cov52	cov53	cov54	var5			
IQ22	cov61	cov62	cov63	cov64	cov65	var6		
IQ23	cov71	cov72	cov73	cov74	cov75	cov76	var7	
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→ different over MZ & DZ

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mean	m1	m2	m3	m4	m1	m2	m3	m4

How many parameters?

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IQ24	cov81	cov82	cov83	cov84	cov85	cov86	cov87	var8

(8*(8-1)/2 + 8) * 2

different over MZ & DZ

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mean	m1	m2	m3	m4	m1	m2	m3	m4

How many parameters?

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4

How many parameters?

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How many parameters? 76

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(8*(8-1)/2 + 8) * 2

→ different over MZ & DZ

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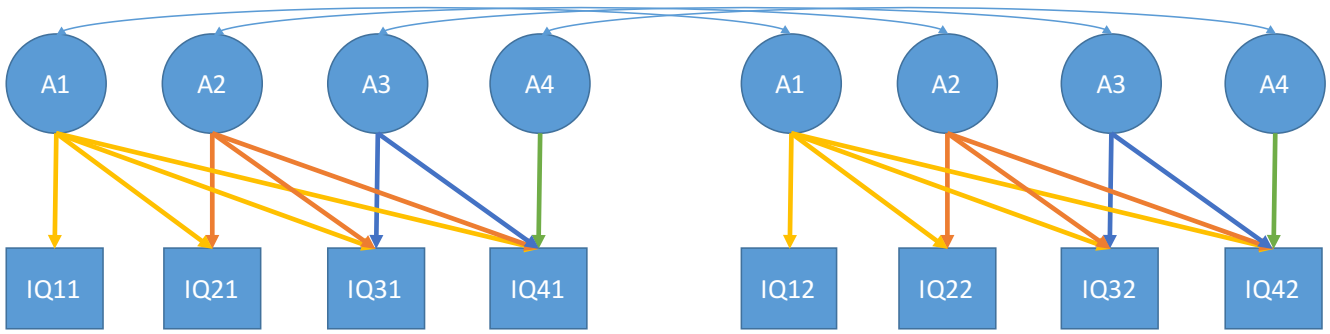
mean	m1	m2	m3	m4	m1	m2	m3	m4

How many parameters? 76

Models

2) ACE Cholesky Model
   - depicting only A component to avoid clutter
   - means subject to same equality constraints as in the saturated model



$$\Sigma_{MZ} = \begin{matrix} \Sigma_A+\Sigma_C+\Sigma_E & \Sigma_A+\Sigma_C \\ \Sigma_A+\Sigma_C & \Sigma_A+\Sigma_C+\Sigma_E \end{matrix}$$

$$\Sigma_{DZ} = \begin{matrix} \Sigma_A+\Sigma_C+\Sigma_E & .5\Sigma_A+\Sigma_C \\ .5\Sigma_A+\Sigma_C & \Sigma_A+\Sigma_C+\Sigma_E \end{matrix}$$

Models

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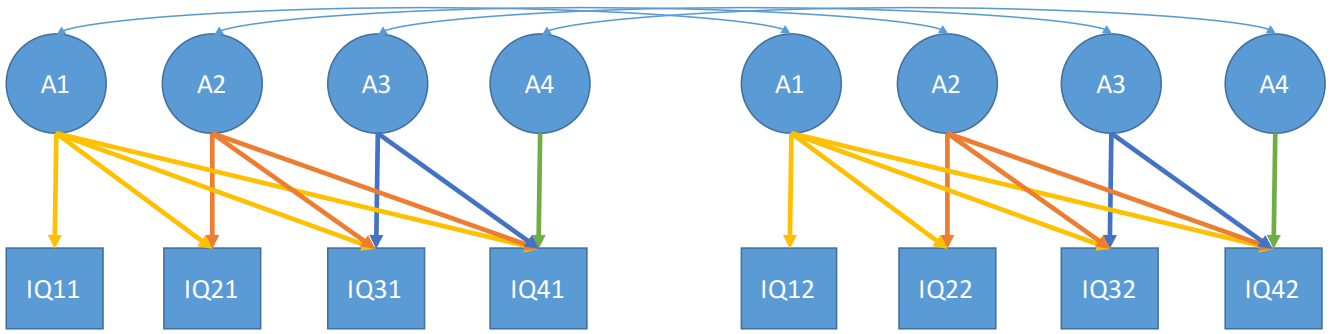

$$\Sigma_A = \Delta_A \Delta_A^t \qquad \Delta_A = \begin{matrix} \delta_{11} & 0 & 0 & 0 \\ \delta_{21} & \delta_{22} & 0 & 0 \\ \delta_{31} & \delta_{32} & \delta_{33} & 0 \\ \delta_{41} & \delta_{42} & \delta_{43} & \delta_{44} \end{matrix}$$

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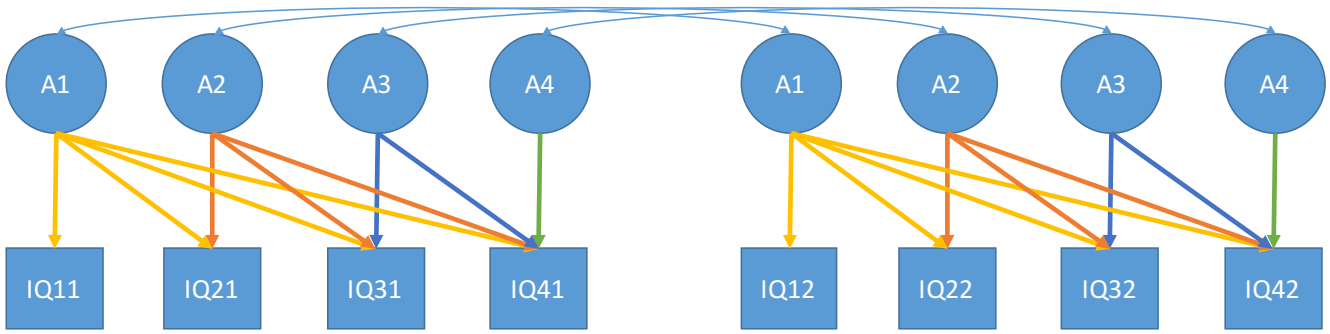
   - depicting only A component to avoid clutter
   - means subject to same equality constraints as in the saturated model



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How many parameters?

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   - depicting only A component to avoid clutter
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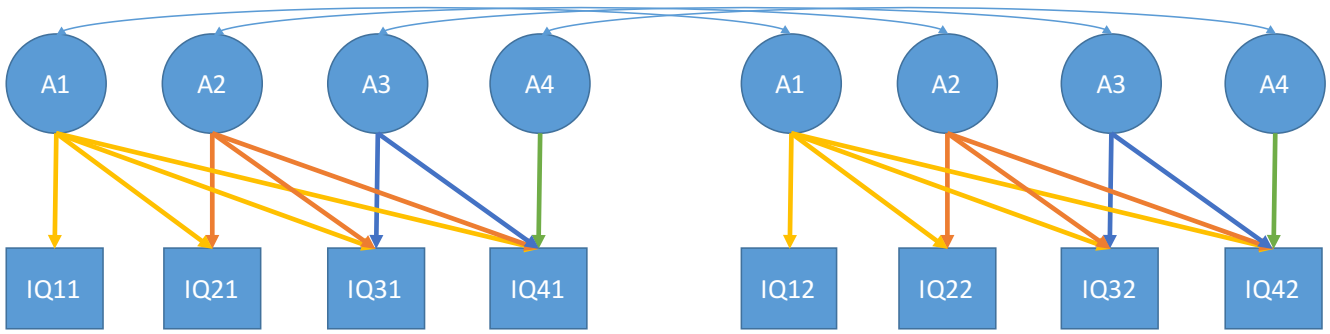

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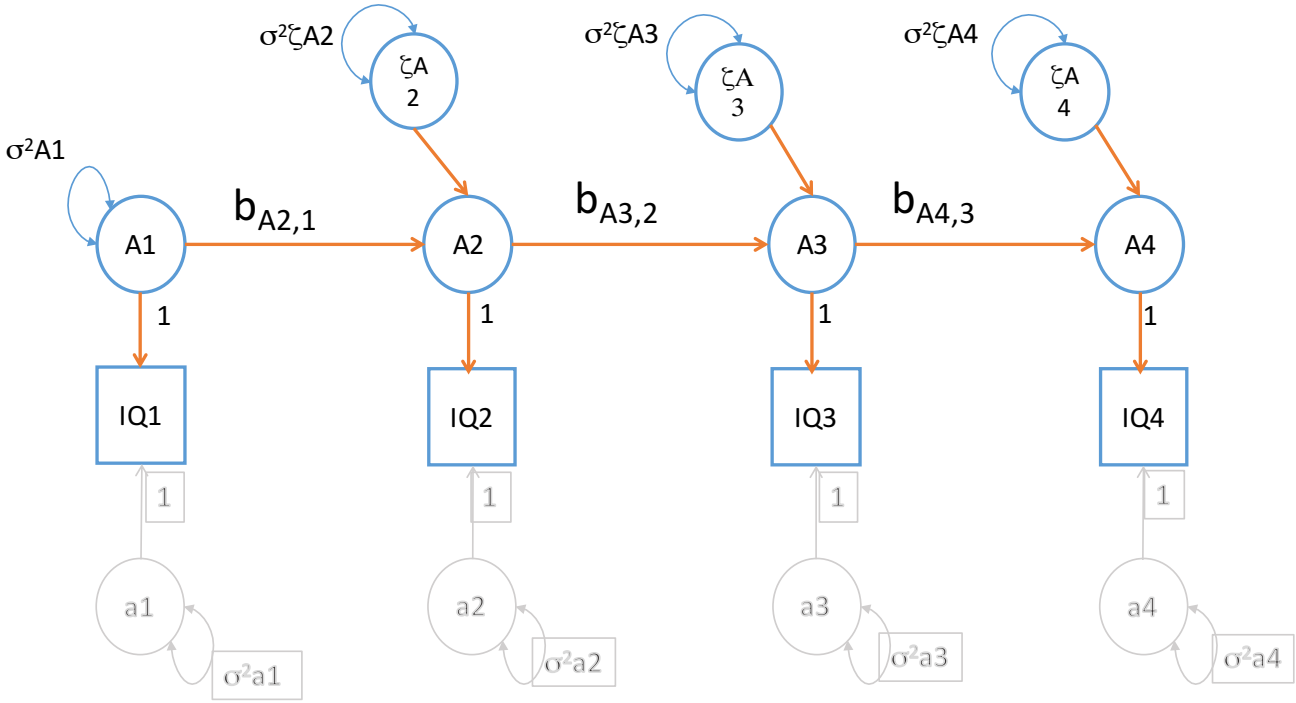
How many parameters? 34

Models

3) Simplex Model
- the genetic A simplex:
  3 + 4 = 7 parameters



$$\Sigma_{MZ} = \begin{matrix} \Sigma_A+\Sigma_C+\Sigma_E & \Sigma_A+\Sigma_C \\ \Sigma_A+\Sigma_C & \Sigma_A+\Sigma_C+\Sigma_E \end{matrix}$$

$$\Sigma_{DZ} = \begin{matrix} \Sigma_A+\Sigma_C+\Sigma_E & .5\Sigma_A+\Sigma_C \\ .5\Sigma_A+\Sigma_C & \Sigma_A+\Sigma_C+\Sigma_E \end{matrix}$$

$$\Sigma_A = (I-B_A)\,\Psi_A\,(I-B_A)^t + \Theta_A$$

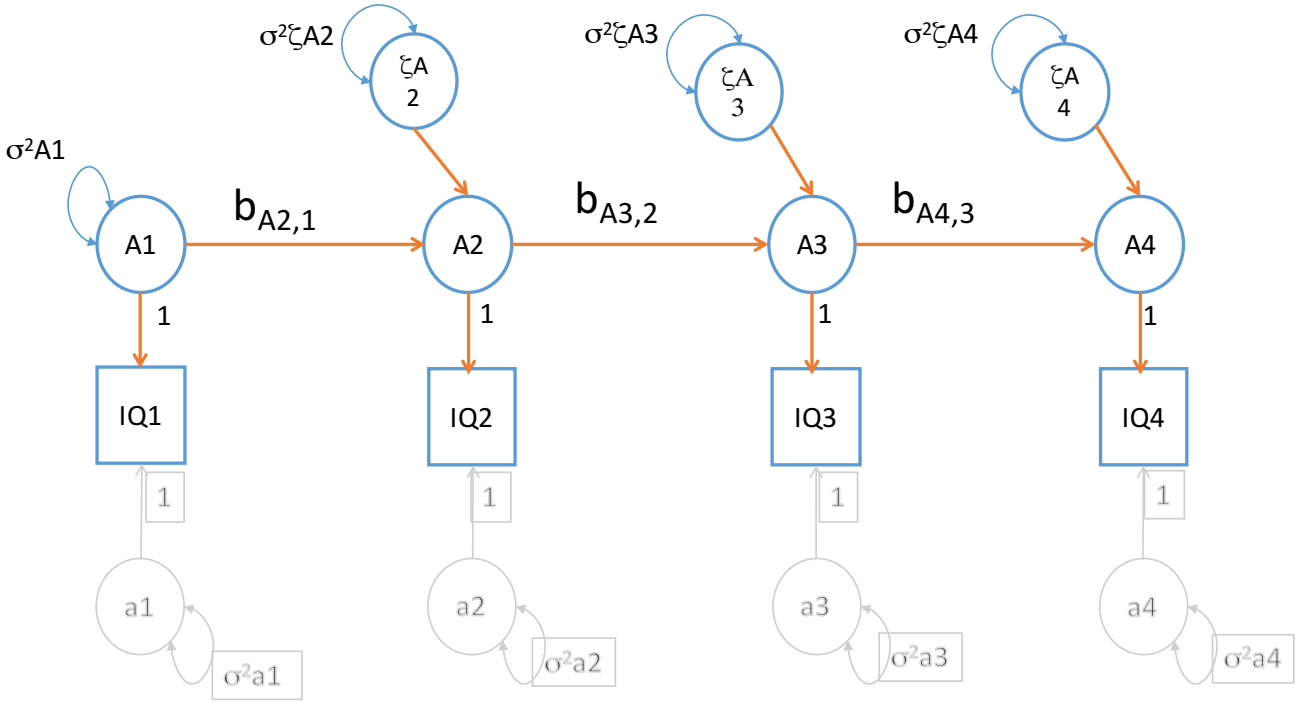
Models

3) Simplex Model

$$\Psi_A = \begin{bmatrix} \sigma^2_{\zeta 1} & 0 & 0 & 0 \\ 0 & \sigma^2_{\zeta 2} & 0 & 0 \\ 0 & 0 & \sigma^2_{\zeta 3} & 0 \\ 0 & 0 & 0 & \sigma^2_{\zeta 4} \end{bmatrix}$$

$$B_A = \begin{bmatrix} 0 & 0 & 0 & 0 \\ b_{A21} & 0 & 0 & 0 \\ 0 & b_{A32} & 0 & 0 \\ 0 & 0 & b_{A43} & 0 \end{bmatrix}$$

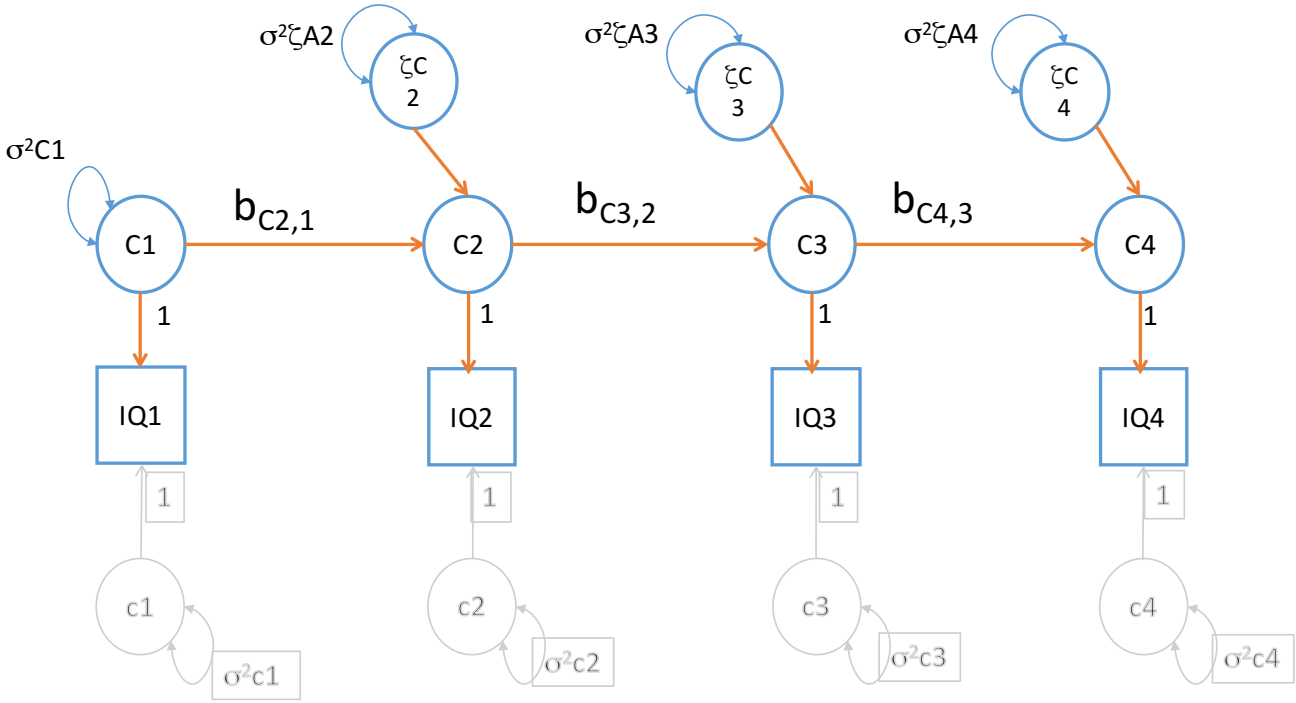
$$\Theta_A = \begin{bmatrix} \sigma^2_{a1} & 0 & 0 & 0 \\ 0 & \sigma^2_{a2} & 0 & 0 \\ 0 & 0 & \sigma^2_{a3} & 0 \\ 0 & 0 & 0 & \sigma^2_{a4} \end{bmatrix}$$



$$\Sigma_A = (I-B_A)\,\Psi_A\,(I-B_A)^t + \Theta_A$$

Models

3) Simplex Model
- the genetic C simplex:
  3 + 4 = 7 parameters



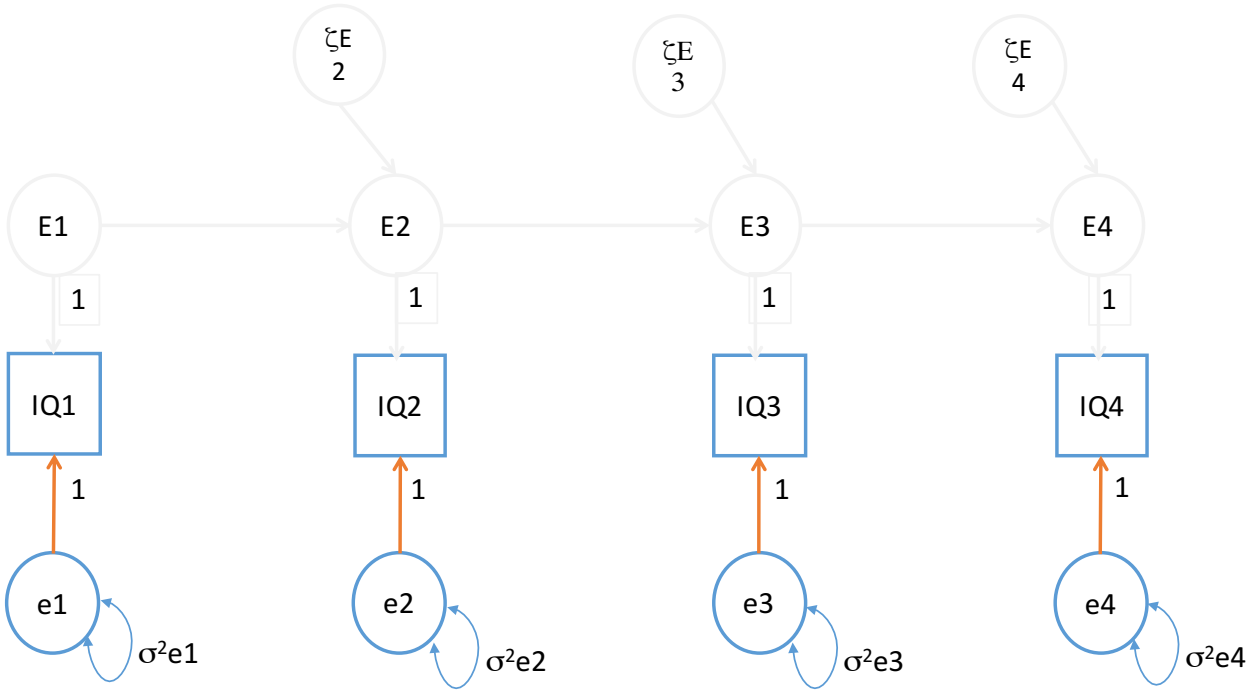
$$\Sigma_{MZ} = \begin{matrix} \Sigma_A+\Sigma_C+\Sigma_E & \Sigma_A+\Sigma_C \\ \Sigma_A+\Sigma_C & \Sigma_A+\Sigma_C+\Sigma_E \end{matrix}$$

$$\Sigma_{DZ} = \begin{matrix} \Sigma_A+\Sigma_C+\Sigma_E & .5\Sigma_A+\Sigma_C \\ .5\Sigma_A+\Sigma_C & \Sigma_A+\Sigma_C+\Sigma_E \end{matrix}$$

$$\Sigma_C = (I-B_C)\,\Psi_C\,(I-B_C)^t + \Theta_C$$

Models

3) Simplex Model
- the genetic E model:
  4 parameters



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$$\Sigma_E = \Theta_E$$

Practical:

faculty/sanja/2016/Simplex/Practical/simplexPractical.R

Saturated model:

Rmz

[1,] 1.000 0.650 0.523 0.409 0.769 0.510 0.482 0.455
[2,] 0.650 1.000 0.748 0.608 0.655 0.696 0.665 0.582
[3,] 0.523 0.748 1.000 0.775 0.609 0.745 0.840 0.757
[4,] 0.409 0.608 0.775 1.000 0.549 0.723 0.747 0.799
[5,] 0.769 0.655 0.609 0.549 1.000 0.572 0.550 0.613
[6,] 0.510 0.696 0.745 0.723 0.572 1.000 0.782 0.658
[7,] 0.482 0.665 0.840 0.747 0.550 0.782 1.000 0.760
[8,] 0.455 0.582 0.757 0.799 0.613 0.658 0.760 1.000

Rdz

[1,] 1.000 0.603 0.475 0.471 0.641 0.397 0.201 0.248
[2,] 0.603 1.000 0.661 0.673 0.298 0.481 0.317 0.396
[3,] 0.475 0.661 1.000 0.737 0.283 0.374 0.483 0.469
[4,] 0.471 0.673 0.737 1.000 0.258 0.346 0.368 0.501
[5,] 0.641 0.298 0.283 0.258 1.000 0.481 0.361 0.345
[6,] 0.397 0.481 0.374 0.346 0.481 1.000 0.627 0.635
[7,] 0.201 0.317 0.483 0.368 0.361 0.627 1.000 0.707
[8,] 0.248 0.396 0.469 0.501 0.345 0.635 0.707 1.000

5.5y	6.8y	9.7y	12.2y	
0.769	0.696	0.840	0.799	MZ FSIQ correlation (FIML estimates)
0.641	0.481	0.483	0.501	DZ FSIQ correlation (FIML estimates)

ACE Cholesky model:

RA_est

5.5y	6.8y	9.7y	12.2y
1.000	0.939	0.909	0.802
0.939	1.000	0.997	0.959
0.909	0.997	1.000	0.978
0.802	0.959	0.978	1.000

RC_est

5.5y	6.8y	9.7y	12.2y
1.000	0.610	0.295	0.388
0.610	1.000	0.609	0.651
0.295	0.609	1.000	0.767
0.388	0.651	0.767	1.000

RE_est

5.5y	6.8y	9.7y	12.2y
1.000	0.107	-.057	0.020
0.107	1.000	0.233	0.150
-.057	0.233	1.000	0.126
0.020	0.150	0.126	1.000

Simplex model:

Ψ_A

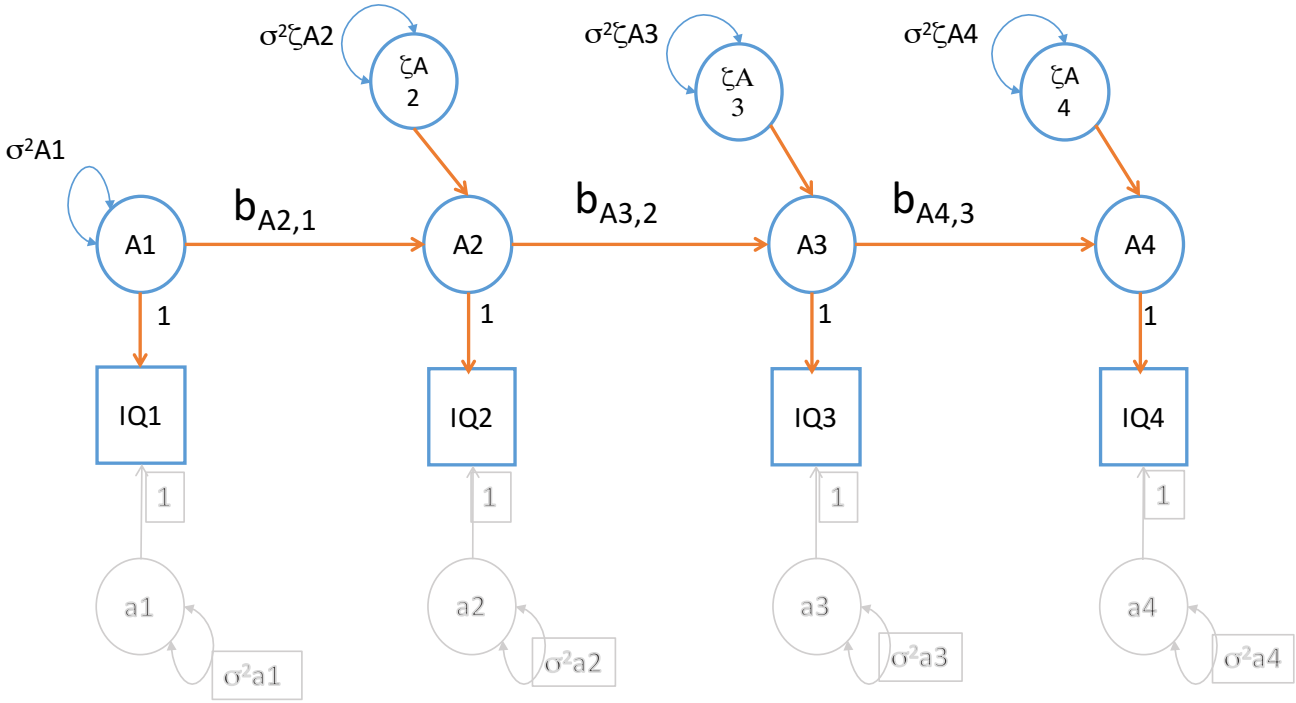
[1,]	62.926	0.000	0	0
[2,]	0.000	32.775	0	0
[3,]	0.000	0.000	0	0
[4,]	0.000	0.000	0	0

B_A

[1,]	0.000	0.000	0.000	0
[2,]	1.191	0.000	0.000	0
[3,]	0.000	1.058	0.000	0
[4,]	0.000	0.000	0.913	0

Θ_A (fixed)

[1,]	0	0	0	0
[2,]	0	0	0	0
[3,]	0	0	0	0
[4,]	0	0	0	0



$$\Sigma_A = (I-B_A)\,\Psi_A\,(I-B_A)^t + \Theta_A$$

Simplex model:

Ψ_C

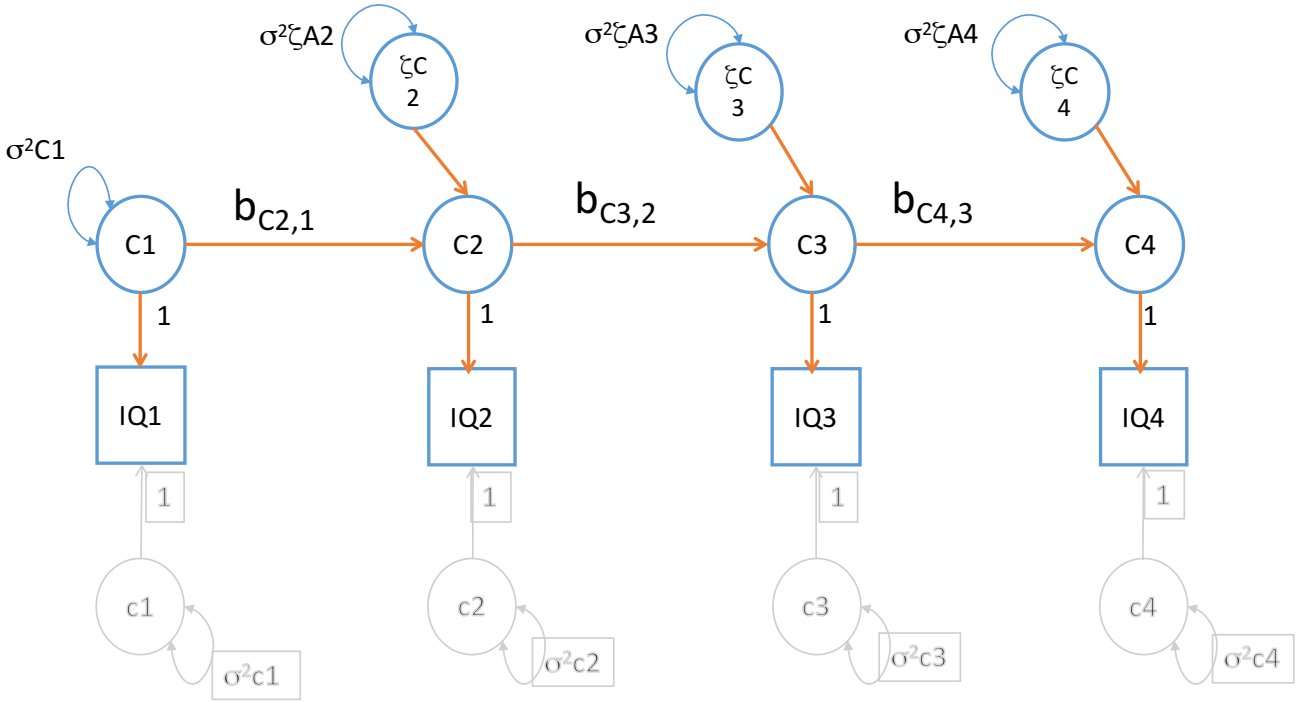
[1,]	103.218	0.000	0.00	0.000
[2,]	0.000	15.587	0.00	0.000
[3,]	0.000	0.000	38.31	0.000
[4,]	0.000	0.000	0.00	23.119

B_C

[1,]	0.000	0.000	0.000	0
[2,]	0.468	0.000	0.000	0
[3,]	0.000	0.614	0.000	0
[4,]	0.000	0.000	0.691	0

Θ_C (fixed)

[1,]	0	0	0	0
[2,]	0	0	0	0
[3,]	0	0	0	0
[4,]	0	0	0	0



$$\Sigma_C = (I-B_C)\,\Psi_C\,(I-B_C)^t + \Theta_C$$

Simplex model:

Ψ_E (fixed)

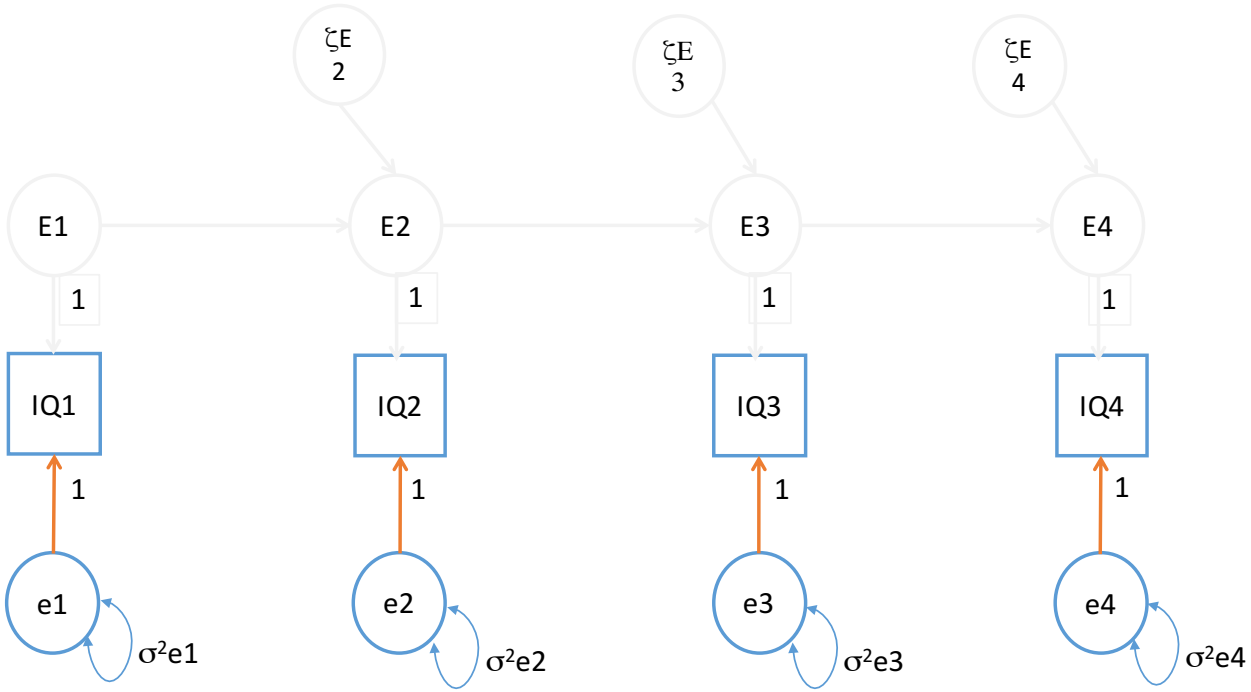
[1,]	0	0	0	0
[2,]	0	0	0	0
[3,]	0	0	0	0
[4,]	0	0	0	0

B_E (fixed)

[1,]	0	0	0	0
[2,]	0	0	0	0
[3,]	0	0	0	0
[4,]	0	0	0	0

Θ_E

[1,]	48.95	0.000	0.000	0.000
[2,]	0.00	56.691	0.000	0.000
[3,]	0.00	0.000	44.331	0.000
[4,]	0.00	0.000	0.000	44.897



$$\Sigma_E = \Theta_E$$

Simplex model:

Standardized variance components

	5.5y	6.8y	9.7y	12.2y	
h2	0.293	0.562	0.584	0.550	Increasing
c2	0.480	0.176	0.226	0.233	Decreasing
e2	0.228	0.261	0.190	0.217	About constant

Simplex model:

```
> round(SA_est/Sph_est,3)
[1,] 0.293 0.608 0.728 0.779
[2,] 0.608 0.562 0.846 0.879
[3,] 0.728 0.846 0.584 0.774
[4,] 0.779 0.879 0.774 0.550

> round(SC_est/Sph_est,3)
[1,] 0.480 0.392 0.272 0.221
[2,] 0.392 0.176 0.154 0.121
[3,] 0.272 0.154 0.226 0.226
[4,] 0.221 0.121 0.226 0.233

> round(SE_est/Sph_est,3)
[1,] 0.228 0.000 0.00 0.000
[2,] 0.000 0.261 0.00 0.000
[3,] 0.000 0.000 0.19 0.000
[4,] 0.000 0.000 0.00 0.217
```

Phenotypic covariance between age 9.7 and 12.2 equals 123.271

Contributions of A to 123.271 is 77.4%
Contributions of A to 123.271 is 22.6%
Contributions of E to 123.271 is 0%

Conclude?

Standardized variance components

	5.5y	6.8y	9.7y	12.2y	
h2	0.293	0.562	0.584	0.550	Increasing
c2	0.480	0.176	0.226	0.233	Decreasing
e2	0.228	0.261	0.190	0.217	About constant