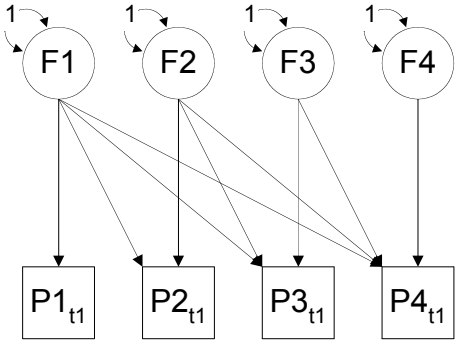
Longitudinal Analysis

HGEN619 class 2007

Longitudinal Questions

- Multivariate Analysis: What are the contributions of genetic and environmental factors to the covariance between more than two traits?
- Longitudinal Analysis: What are the contributions of genetic and environmental factors to the covariance between a trait measured on several occasions?

Phenotypic Cholesky



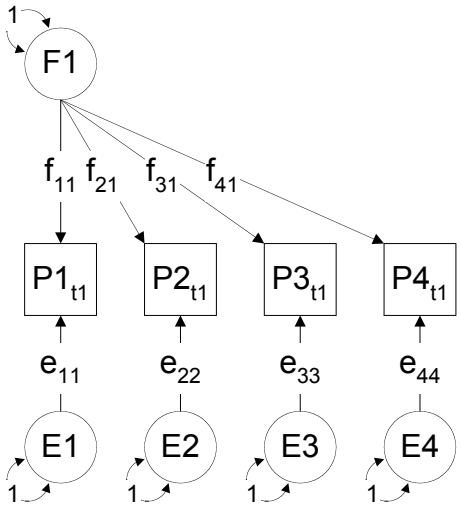
$$\begin{array}{c} \\ P1 \\ P2 \\ P3 \\ P4 \end{array} \begin{array}{c} \begin{array}{cccc} F1 & F2 & F3 & F4 \end{array} \\ \begin{bmatrix} f_{11} & 0 & 0 & 0 \\ f_{21} & f_{22} & 0 & 0 \\ f_{31} & f_{32} & f_{33} & 0 \\ f_{41} & f_{42} & f_{43} & f_{44} \end{bmatrix} \end{array}$$

Cholesky Decomposition

$$\begin{array}{c} \\ P1 \\ P2 \\ P3 \\ P4 \end{array} \begin{array}{c} \begin{array}{cccc} F1 & F2 & F3 & F4 \end{array} \\ \begin{bmatrix} f_{11} & 0 & 0 & 0 \\ f_{21} & f_{22} & 0 & 0 \\ f_{31} & f_{32} & f_{33} & 0 \\ f_{41} & f_{42} & f_{43} & f_{44} \end{bmatrix} \end{array} * \begin{bmatrix} f_{11} & f_{21} & f_{31} & f_{41} \\ 0 & f_{22} & f_{32} & f_{42} \\ 0 & 0 & f_{33} & f_{43} \\ 0 & 0 & 0 & f_{44} \end{bmatrix}$$

F * **F'**

Common Factor + Residuals



$$\mathbf{F} = \begin{array}{c} \\ P1 \\ P2 \\ P3 \\ P4 \end{array} \begin{array}{c} F1 \\ \begin{bmatrix} f_{11} \\ f_{21} \\ f_{31} \\ f_{41} \end{bmatrix} \end{array}$$

$$\mathbf{E} = \begin{array}{c} \\ P1 \\ P2 \\ P3 \\ P4 \end{array} \begin{array}{c} E1\ E2\ E3\ E4 \\ \begin{bmatrix} e_{11} & 0 & 0 & 0 \\ 0 & e_{22} & 0 & 0 \\ 0 & 0 & e_{33} & 0 \\ 0 & 0 & 0 & e_{44} \end{bmatrix} \end{array}$$

In Matrix Notation

$$\begin{array}{c} \\ P1 \\ P2 \\ P3 \\ P4 \end{array} \begin{array}{c} F1 \\ \begin{bmatrix} f_{11} \\ f_{21} \\ f_{31} \\ f_{41} \end{bmatrix} \end{array} * \begin{bmatrix} f_{11} & f_{21} & f_{31} & f_{41} \end{bmatrix}$$

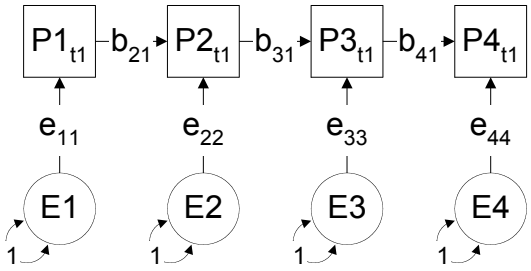
$$\mathbf{F} * \mathbf{F'}$$

$$\begin{array}{c} \\ P1 \\ P2 \\ P3 \\ P4 \end{array} \begin{array}{c} E1\ E2\ E3\ E4 \\ \begin{bmatrix} e_{11} & 0 & 0 & 0 \\ 0 & e_{22} & 0 & 0 \\ 0 & 0 & e_{33} & 0 \\ 0 & 0 & 0 & e_{44} \end{bmatrix} \end{array} * \begin{bmatrix} e_{11} & 0 & 0 & 0 \\ 0 & e_{22} & 0 & 0 \\ 0 & 0 & e_{33} & 0 \\ 0 & 0 & 0 & e_{44} \end{bmatrix}$$

$$\mathbf{E} * \mathbf{E'}$$

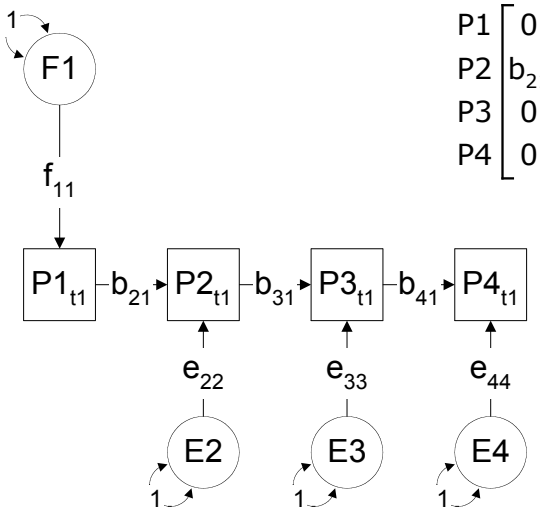
Simplex I

$$\mathbf{B} = \begin{array}{c} \\ P1 \\ P2 \\ P3 \\ P4 \end{array} \begin{array}{c} \begin{array}{cccc} P1 & P2 & P3 & P4 \end{array} \\ \begin{bmatrix} 0 & 0 & 0 & 0 \\ b_{21} & 0 & 0 & 0 \\ 0 & b_{32} & 0 & 0 \\ 0 & 0 & b_{43} & 0 \end{bmatrix} \end{array}$$



$$\mathbf{E} = \begin{array}{c} \\ P1 \\ P2 \\ P3 \\ P4 \end{array} \begin{array}{c} \begin{array}{cccc} E1 & E2 & E3 & E4 \end{array} \\ \begin{bmatrix} e_{11} & 0 & 0 & 0 \\ 0 & e_{22} & 0 & 0 \\ 0 & 0 & e_{33} & 0 \\ 0 & 0 & 0 & e_{44} \end{bmatrix} \end{array}$$

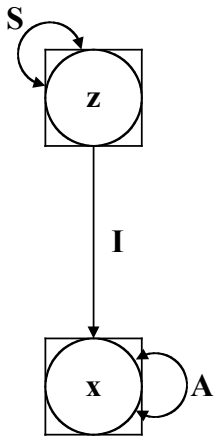
Simplex II



$$\mathbf{B} = \begin{array}{c} \\ P1 \\ P2 \\ P3 \\ P4 \end{array} \begin{array}{c} \begin{array}{cccc} P1 & P2 & P3 & P4 \end{array} \\ \begin{bmatrix} 0 & 0 & 0 & 0 \\ b_{21} & 0 & 0 & 0 \\ 0 & b_{32} & 0 & 0 \\ 0 & 0 & b_{43} & 0 \end{bmatrix} \end{array}$$

$$\mathbf{E} = \begin{array}{c} \\ P1 \\ P2 \\ P3 \\ P4 \end{array} \begin{array}{c} \begin{array}{cccc} E1 & E2 & E3 & E4 \end{array} \\ \begin{bmatrix} e_{11} & 0 & 0 & 0 \\ 0 & e_{22} & 0 & 0 \\ 0 & 0 & e_{33} & 0 \\ 0 & 0 & 0 & e_{44} \end{bmatrix} \end{array}$$

Reciprocal Causation



- multivariate path diagram
- **x** variables are caused by a set of independent variables, **z**
- **x** variables may cause each other, hence the unidirectional arrow from **x** to itself

$$x = Ax + Iz$$
$$= Ax + z$$

Model for X variables

$$x - Ax = z$$
$$(I - A)x = z$$
$$(I - A)^{-1}(I - A)x = (I - A)^{-1}z$$
$$x = (I - A)^{-1}z$$

$$xx' = (I - A)^{-1}z\,((I - A)^{-1}z)'$$
$$= (I - A)^{-1}zz'(I - A)^{-1'}$$
$$= (I - A)^{-1}S(I - A)^{-1'}$$

In Matrix Notation

$$\begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} - \begin{array}{c} \\ P1 \\ P2 \\ P3 \\ P4 \end{array} \begin{array}{c} \begin{array}{cccc} P1 & P2 & P3 & P4 \end{array} \\ \begin{bmatrix} 0 & 0 & 0 & 0 \\ b_{21} & 0 & 0 & 0 \\ 0 & b_{32} & 0 & 0 \\ 0 & 0 & b_{43} & 0 \end{bmatrix} \end{array}$$

Y = (I - B)~

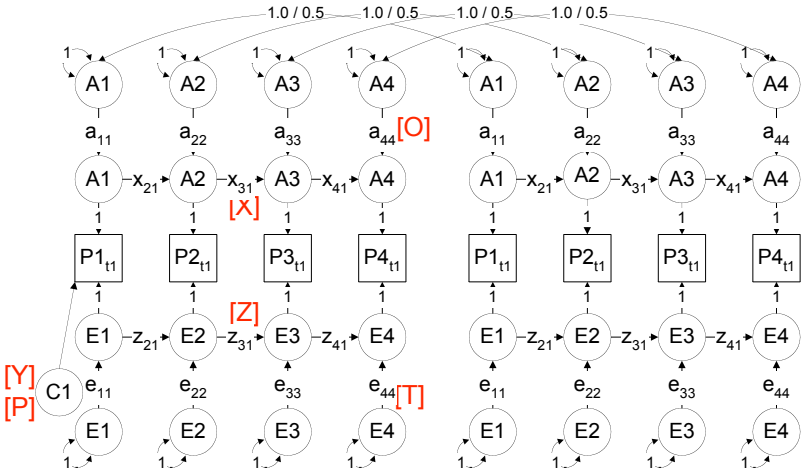
Simplex Expression

$$\begin{array}{c} \begin{array}{cccc} E1 & E2 & E3 & E4 \end{array} \\ \begin{bmatrix} e_{11} & 0 & 0 & 0 \\ 0 & e_{22} & 0 & 0 \\ 0 & 0 & e_{33} & 0 \\ 0 & 0 & 0 & e_{44} \end{bmatrix} \end{array} * \begin{bmatrix} e_{11} & 0 & 0 & 0 \\ 0 & e_{22} & 0 & 0 \\ 0 & 0 & e_{33} & 0 \\ 0 & 0 & 0 & e_{44} \end{bmatrix}$$

Y * E * E' * Y'

Y & E*E'

Simplex Model



Simplex Model I

```
G1: female model parameters
Calculation
 Begin Matrices;
  X Diag nvarm1 nvarm1 Free ! additive genetic transmission paths
  Y Diag nvarm1 nvarm1 Free ! common environmental transmission paths
  W Diag nvarm1 nvarm1 Fixed! dominance transmission paths
  Z Diag nvarm1 nvarm1 Free ! unique environmental transmission paths
  I Iden nvar nvar          ! identity matrix
  F Zero nvarm1 1           ! right column of zeros to fill out trans
  U Zero 1 nvar             ! top row of zeros to fill out trans
  O Diag nvar nvar Free     ! genetic specifics
  P Diag nvar nvar Free     ! common environmental specifics
  R Diag nvar nvar Fixed    ! dominance specifics
  T Diag nvar nvar Free     ! specific environmental specifics
  H Full 1 1
  Q Full 1 1
 End Matrices;
  Matrix H .5
  Matrix Q .25
```

Simplex Model II

```
Begin Algebra;
  G= (I-(U_X|F))~;
  K= (I-(U_Y|F))~;
  L= (I-(U_Z|F))~;
  J= (I-(U_W|F))~;
  A= G*O*O'*G';
  C= K*P*P'*K';
  E= L*T*T'*L';
  D= J*R*R'*J';
 End Algebra;
  Start .4 All
  Start .5 T 1 1 1 T 1 2 2 T 1 3 3 T 1 4 4 T 1 5 5
  Start 0 X 1 1 1 - X 1 nvarm1 nvarm1  Y 1 1 1 - Y 1 nvarm1 nvarm1
  Start 0 W 1 1 1 - W 1 nvarm1 nvarm1  Z 1 1 1 - Z 1 nvarm1 nvarm1
End
```

Simplex Model III

```
G4
Calculation
 Matrices = Group 1
  I Iden nvar nvar
 End Matrices;
 Begin Algebra;
  V= A+C+D+E ;
  S= \sqrt(I.(V)) ;
  M= \d2v(S~*O)_ \d2v(S~*P)_ \d2v(S~*R)_ \d2v(S~*T)_
     S~*(U_X|F)_ S~*(U_Y|F)_ S~*(U_W|F)_ S~*(U_Z|F);
 End Algebra;
End
```

Practical Example

- Dataset: US-CVT Study
- BMI
  - var1 = 11y
  - var2 = 12.5y
  - var3 = 14y
  - var4 = 15.5y
  - var5 = 17y
- N MZF: 108, DZF: 63

Summary

- Cholesky Decomposition
  - Saturated
- Independent Pathway Model
  - Common Factors
  - Residuals
- Simplex Model
  - Transmissions
  - Innovations