

Unmodeled GxE and r_{GE}

[Purcell, S. (2002). Variance components models for gene-environment interaction in twin analysis. *Twin Research*, 5(6), 554-571]

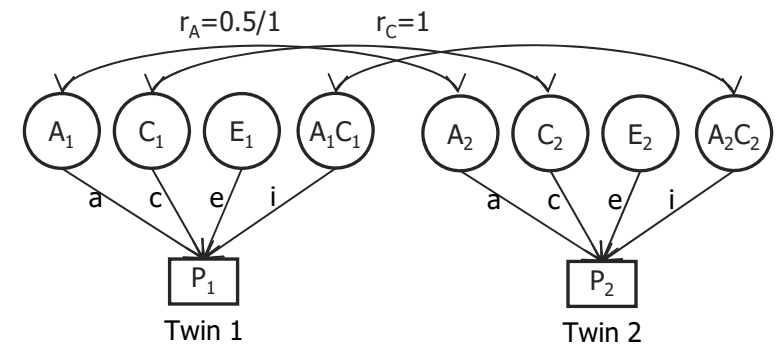
How do unmodeled GxE and r_{GE} bias parameter estimates in standard twin models?

E.g.: If the additive genotype (A) interacts with common environment (C; environmental influences that increase phenotypic similarity between family members), then the phenotypic value may be decomposed as follows:

$$P = aA + cC + iAC + eE,$$

and its expected variance is

$$V_p = a^2 + c^2 + i^2 + e^2$$



(assuming the variances of the latent variables are scaled to 1). The expected twin covariances are

$$\begin{aligned} \text{Cov}(P_1, P_2) &= a^2 \text{Cov}(A_1, A_2) + c^2 \text{Cov}(C_1, C_2) + e^2 \text{Cov}(E_1, E_2) + i^2 \text{Cov}(A_1 C_1, A_2 C_2) \\ &= a^2 + c^2 + i^2 \text{ for MZ twins} \\ &= a^2/2 + c^2 + i^2/2 \text{ for DZ twins} \end{aligned}$$

as $\text{Cov}(A_1, A_2)$ is 1 for MZ twins and 0.5 for DZ twins; $\text{Cov}(C_1, C_2)=1$ and $\text{Cov}(E_1, E_2)=0$ for all twins; also

$\text{Cov}(A_1 C_1, A_2 C_2) = \text{Cov}(A_1, A_2) \text{Cov}(C_1, C_2) = \text{Cov}(A_1, A_2)$. Similar covariance algebra can show that AxE interaction contributes to the E component.

Unmodeled GxE and r_{GE}

[Purcell, S. (2002). Variance components models for gene-environment interaction in twin analysis. *Twin Research*, 5(6), 554-571]

How do unmodeled GxE and r_{GE} bias parameter estimates in standard twin models?

If A is correlated with an environmental variable, say C, then the expected phenotypic variance is

$$V_P = a^2 + c^2 + 2ac * r_{AC} + e^2$$

and the expected twin covariances are

$$\begin{aligned} \text{Cov}(P_1, P_2) &= a^2 \text{Cov}(A_1, A_2) + c^2 \text{Cov}(C_1, C_2) + e^2 \text{Cov}(E_1, E_2) + \\ &\quad ac \text{Cov}(A_1, C_2) + ac \text{Cov}(A_2, C_1) \\ &= a^2 + c^2 + 2ac * r_{AC} \text{ for MZ twins} \\ &= a^2/2 + c^2 + 2ac * r_{AC} \text{ for DZ twins} \end{aligned}$$

as $\text{Cov}(A_1, C_2) = \text{Cov}(A_2, C_1) = r_{AC}$. Similarly, if A and E are non-independent then

$$\begin{aligned} \text{Cov}(P_1, P_2) &= a^2 + c^2 + 2ae * r_{AE} \text{ for MZ twins} \\ &= a^2/2 + c^2 + ae * r_{AE} \text{ for DZ twins} \end{aligned}$$

Thus: Interaction between A and C acts in the same way as A; interaction between A and E acts like E. Correlation between A and C acts like C; correlation between A and E acts like A.

