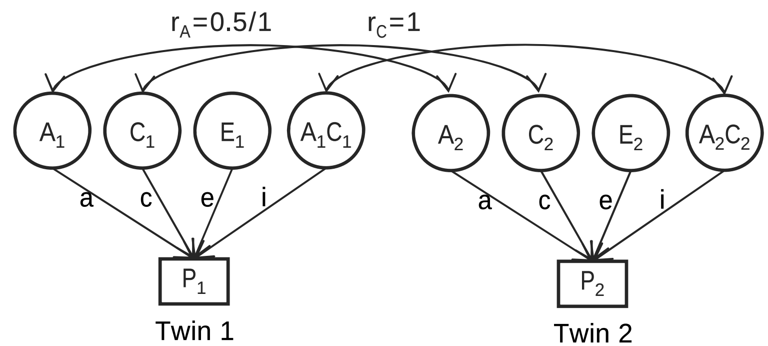
Unmodeled GxE and r_{GE} [Purcell, S. (2002). Variance components models for gene-environment interaction in twin analysis. Twin Research, 5(6), 554-571.]

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

$Cov(P_1,P_2) = a^2Cov(A_1, A_2) + c^2Cov(C_1, C_2) + e^2Cov(E_1, E_2) + i^2Cov(A_1C_1, A_2C_2)$

$= a^2 + c^2 + i^2$ for MZ twins

$= a^2/2 + c^2 + i^2/2$ for DZ twins

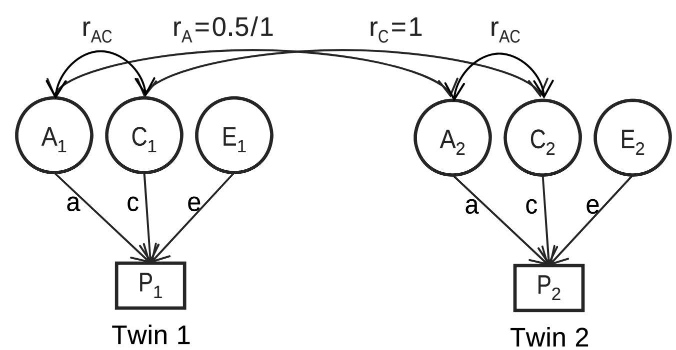
as $Cov(A_1, A_2)$ is 1 for MZ twins and 0.5 for DZ twins; $Cov(C_1,C_2)=1$ and $Cov(E_1, E_2)=0$ for all twins; also $Cov(A_1C_1,A_2C_2)=Cov(A_1, A_2)Cov(C_1, C_2)=Cov(A_1, A_2)$. Similar covariance algebra can show that AxE interaction contributes to the E component.

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

$Cov(P_1,P_2) = a^2Cov(A_1, A_2) + c^2Cov(C_1, C_2) + e^2Cov(E_1, E_2) +$
$acCov(A_1, C_2) + acCov(A_2, C_1)$
$= a^2 + c^2 + 2ac * rAC$ for MZ twins
$= a^2/2 + c^2 + 2ac * rAC$ for DZ twins

as $Cov(A_1, C_2) = Cov(A_2, C_1) = rAC$. Similarly, if A and E are non-independent then

$Cov(P_1, P_2) = a^2 + c^2 + 2ae * rAE$ forMZ twins
$= a^2/2 + c^2 + ae \times rAE$ for DZ twins

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.