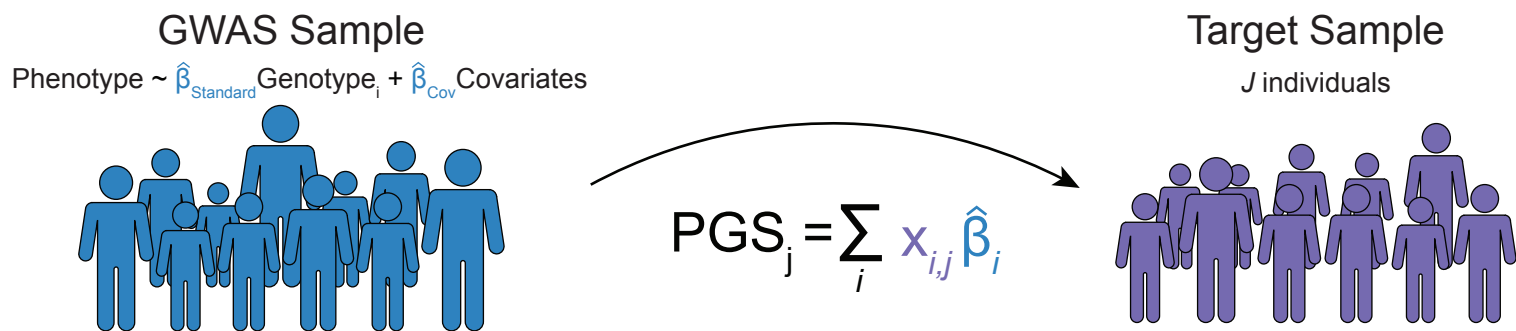


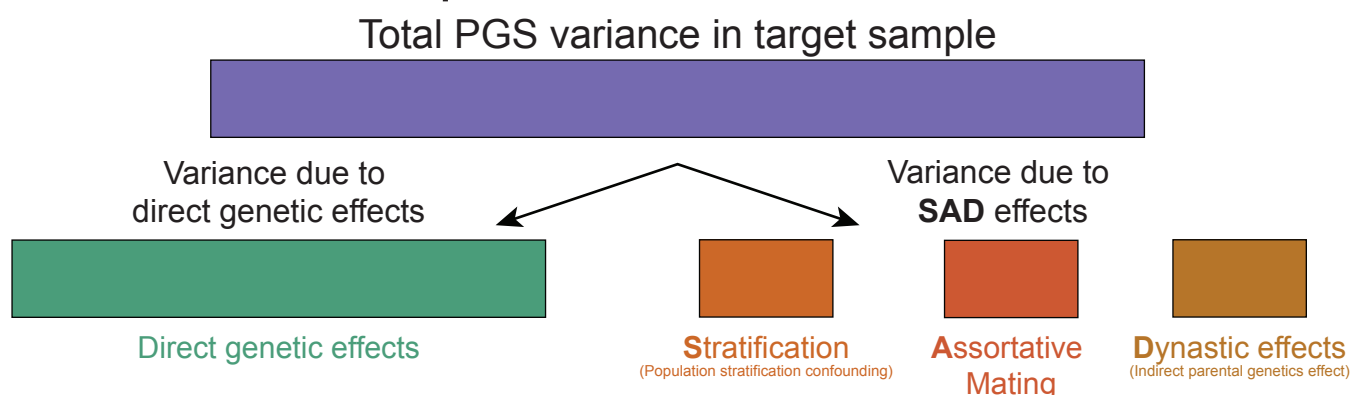
A

Standard PGS construction



B

Decomposition of PGS variance

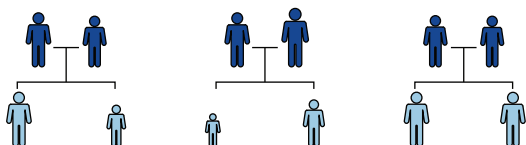


C

Effect estimates from a sibling GWAS framework are immune to SAD effects

Paired summary statistics from sibling and standard GWAS can isolate direct and SAD effects

$$\Delta \text{Phenotype} \sim \hat{\beta}_{\text{Sibling}} \Delta \text{Genotype}$$

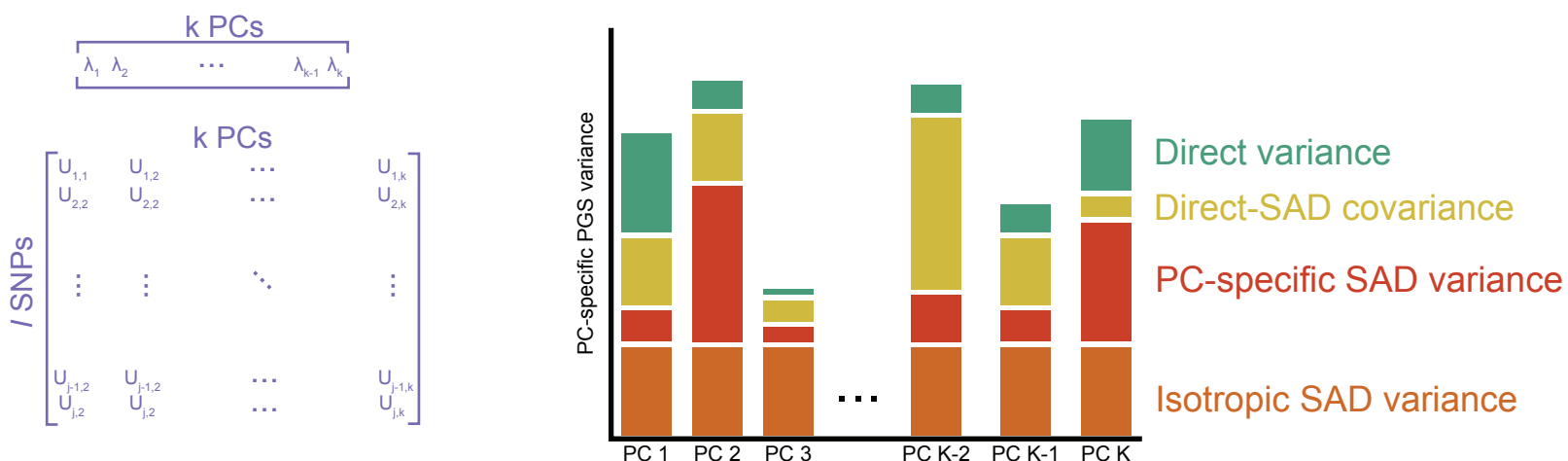


$$\beta_{\text{Direct}} = \hat{\beta}_{\text{Sibling}} - \epsilon_{\text{Sibling}}$$

$$\beta_{\text{SAD}} = (\hat{\beta}_{\text{GWAS}} - \hat{\beta}_{\text{Sibling}}) - \epsilon_{\text{GWAS}} - \epsilon_{\text{Sibling}}$$

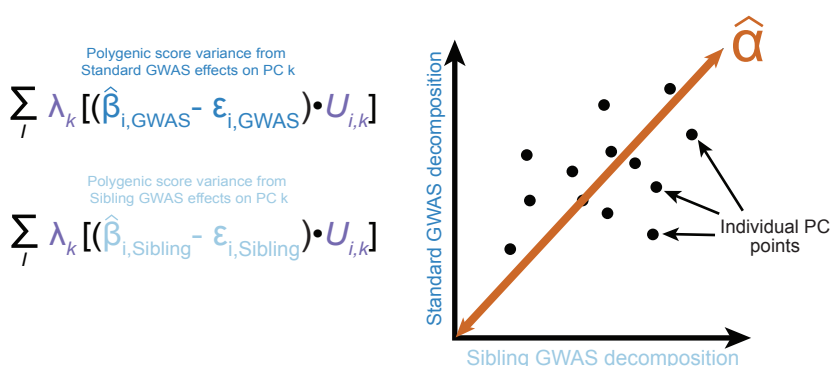
D

Eigenvalues (λ) and eigenvectors (U) from a PCA of the target sample genotypes can be used to estimate the isotropic inflation factor (α) across PCs and PC-specific effects



E

Estimation of Isotropic Inflation Factor (α)



F

Estimation of PC-specific variance

