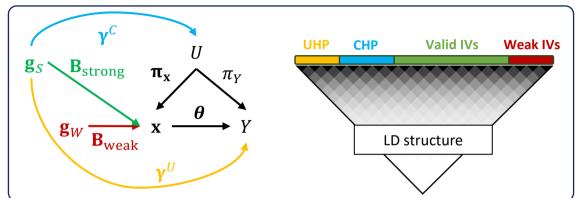
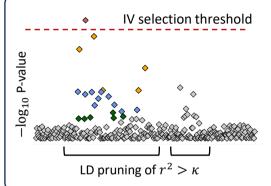
Exposure(s) and outcome GWAS

Overlapping GWAS samples $\begin{array}{c|cccc} X_1 & & & & \\ X_2 & & & & \\ X_p & & & & \\ \end{array}$

Causal model for exposure SNPs and outcome



Selection of IV Set



- Number of exposures
- GWAS sample sizes
- Exposure(s) GWASs overlap
- Exposure & outcome GWAS overlap

- Variance in \mathbf{x} explained by U
- Variance in Y explained by (\mathbf{x}, U)
- Phenotypic correlation in x
- Genetic correlation in x
- Variance in (\mathbf{x}, Y, U) explained by $(\mathbf{g}_S, \mathbf{g}_W)$

- Number of causal SNPs (g_i) 's)
- LD between SNPs in g
- Number of weak, UHP, & CHP SNPs
- Variance in ${\boldsymbol x}$ explained by:
 - Weak SNPs, UHP (γ^U) , CHP (γ^C)

Significance threshold for IV selection, based on test of:

$$H_{0i}$$
: $\beta_{i1} = \beta_{i2} = \cdots = \beta_{ip} = 0$

- Joint test of association
- LD r^2 pruning threshold: κ