

# Overview

- PLIER model
  - Pathways used as prior
  - FDR thanks to cross-validation
  - Pathway eQTLs
- MultiPLIER
  - Work with small datasets

# PLIER model

## Pathway-level information extractor

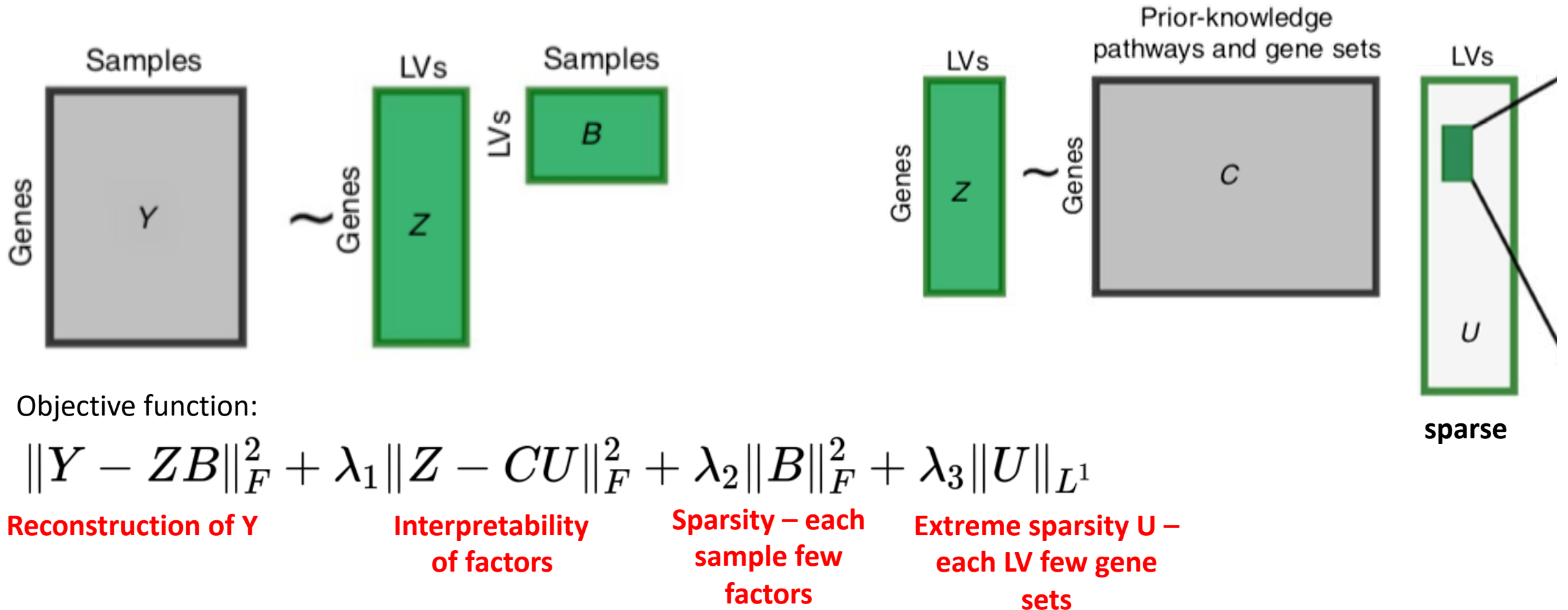
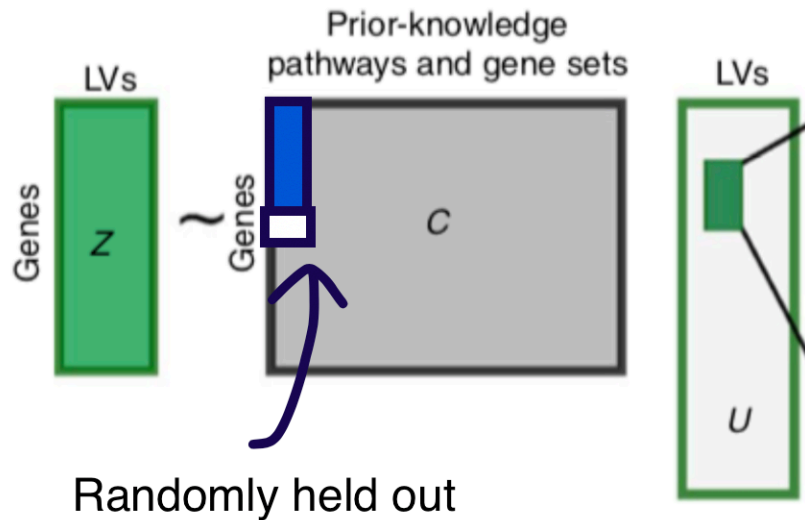


Fig 1, PLIER (Mao et al. 2019)

# PLIER: Calculating uncertainty of pathway associations



- 1) Hold out random 1/5 of genes from each pathway
- 2) Find latent variable (LV) with non-zero value for the pathway
- 3) Count false positives/negatives

	Predicted positive – in LV	Predicted negative – not in LV
Positive – In pathway (held out)	True positive	False negative
Negative – Not in pathway	False positive	True negative

# PLIER: Pathway eQTLs

Gene-level eQTL

SNP



Change in expression of gene A

$$E_A$$

Pathway-level eQTL

SNP

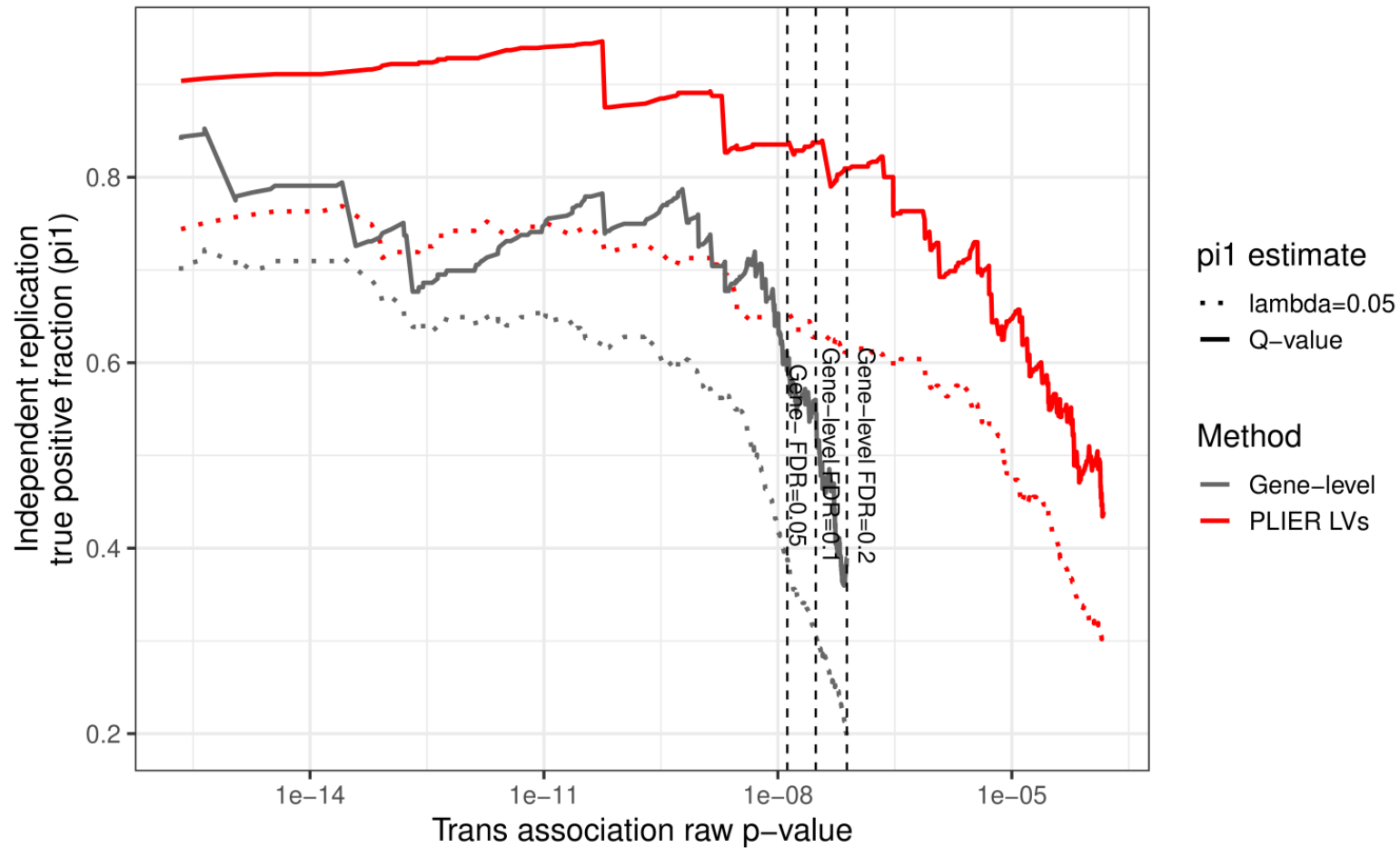


Change in latent variable (linear combination of expression of multiple genes)

$$z_1 E_1 + z_2 E_2 + \dots + z_g E_g$$

**Pathway-level eQTLs were more reproducible than gene-level eQTLs**

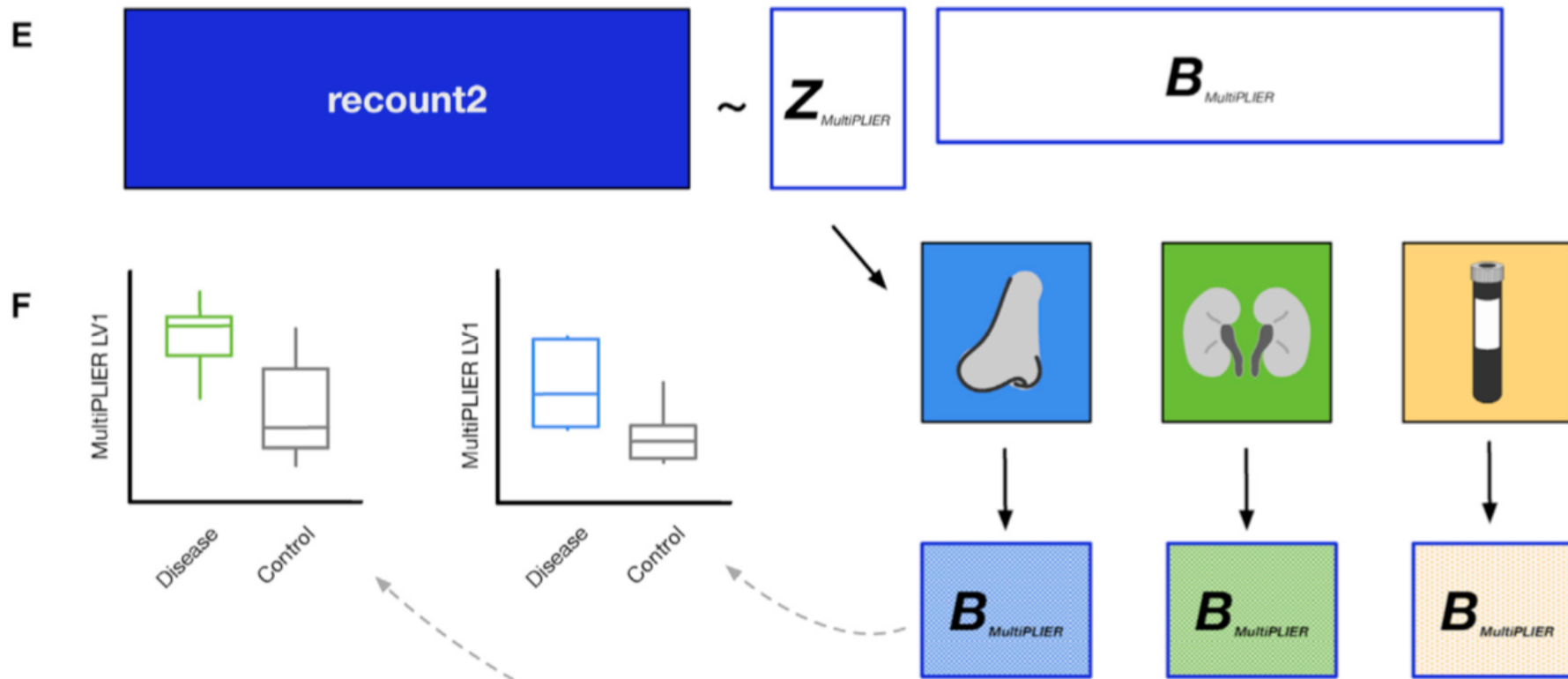
# Pathway-level eQTLs were more reproducible than gene-level eQTLs



Supplementary Figure 4, (Mao et al., 2019)

# MultiPLIER for small datasets

Learn good interpretable factors on big dataset



Apply to smaller datasets

Fig 1, MultiPLIER (Taroni et al., 2019)