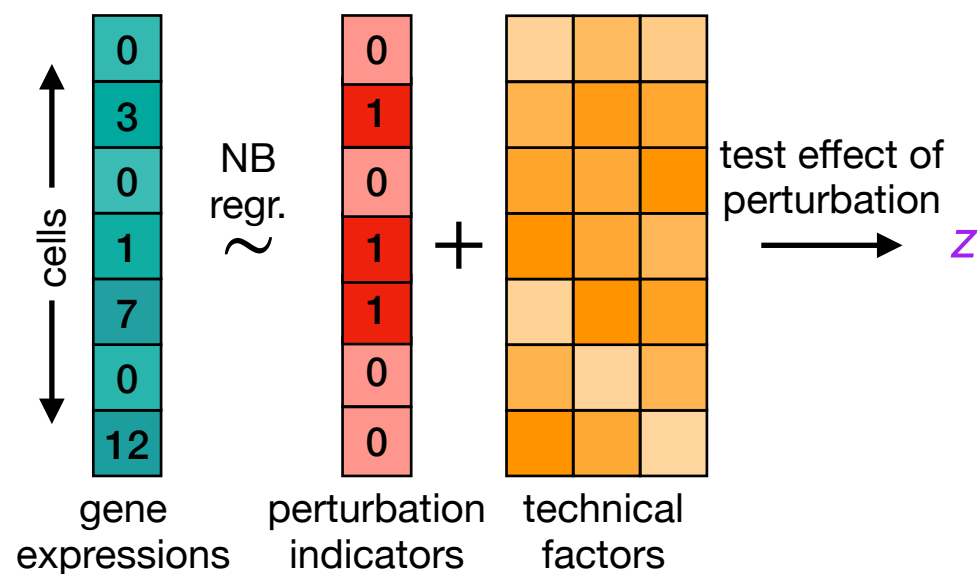


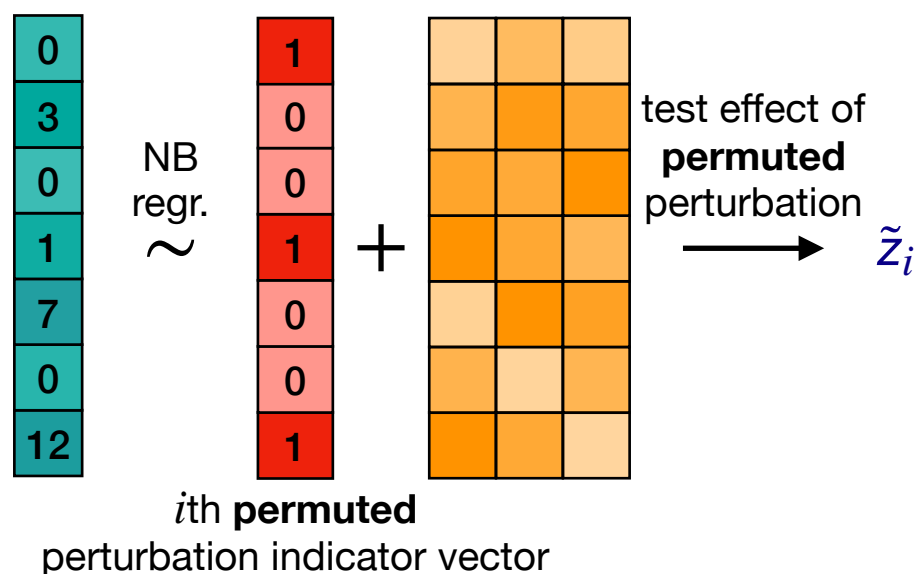
**a**

- ① Obtain z-score from NB regression of gene expression on perturbation indicator and technical factors

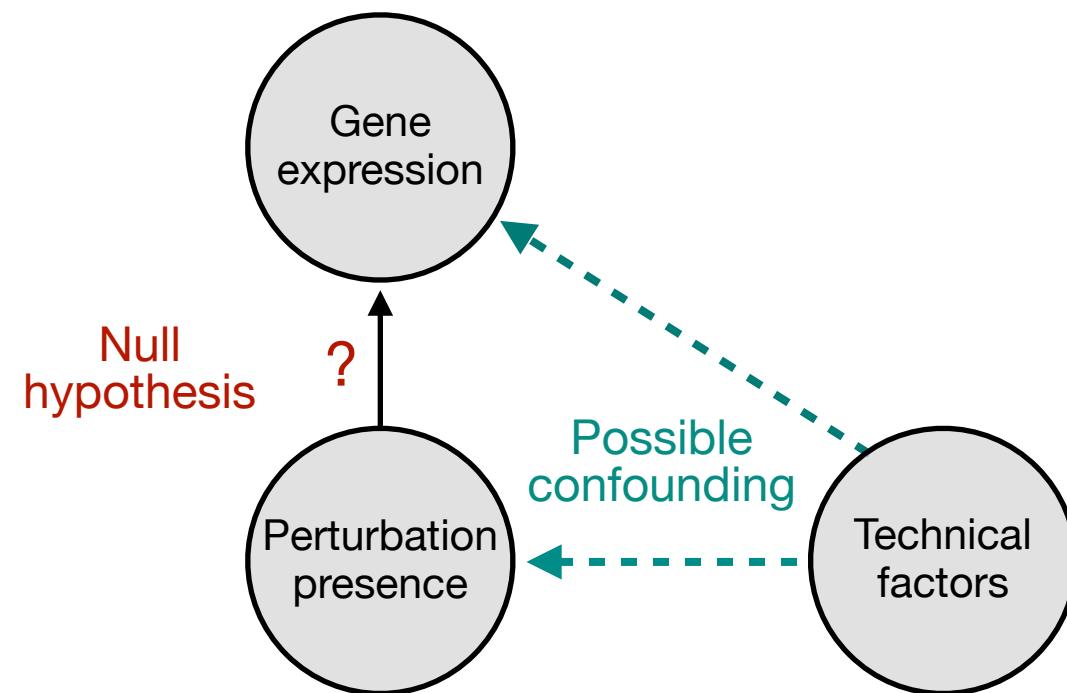


②

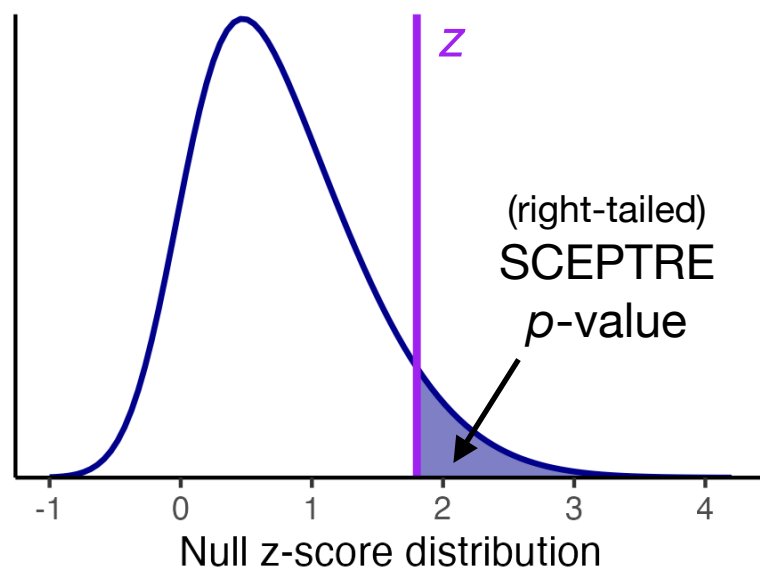
- For  $i = 1, \dots, M$ :  
Permute perturbation indicator and rerun NB regression to obtain null z-score  $\tilde{z}_i$

**b**

Relationships among variables in the analysis

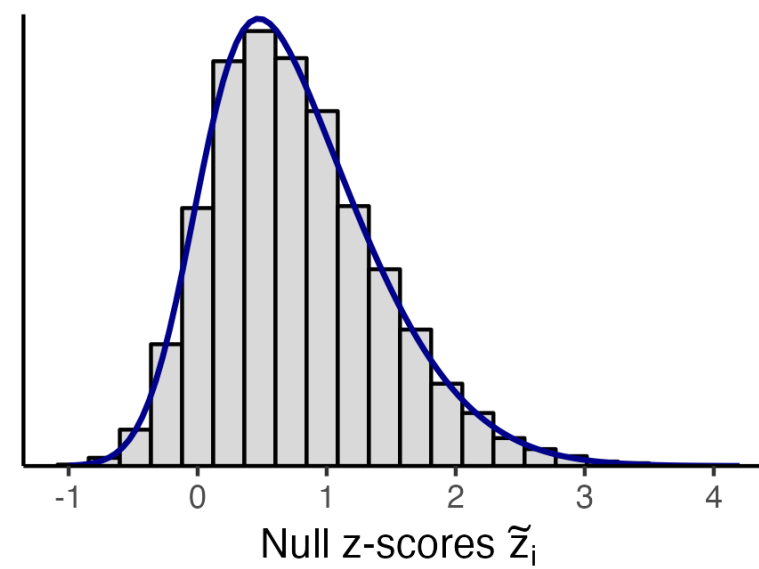


- ④ Obtain p-value by comparing original z-score  $z$  to fitted null distribution



③

- Fit smooth curve to null z-scores  $\tilde{z}_i$

**c**