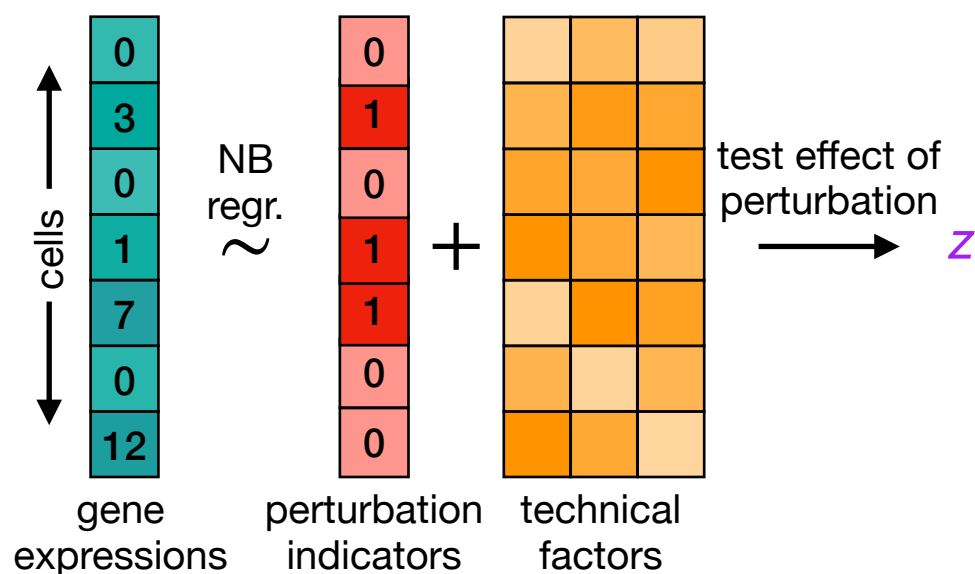


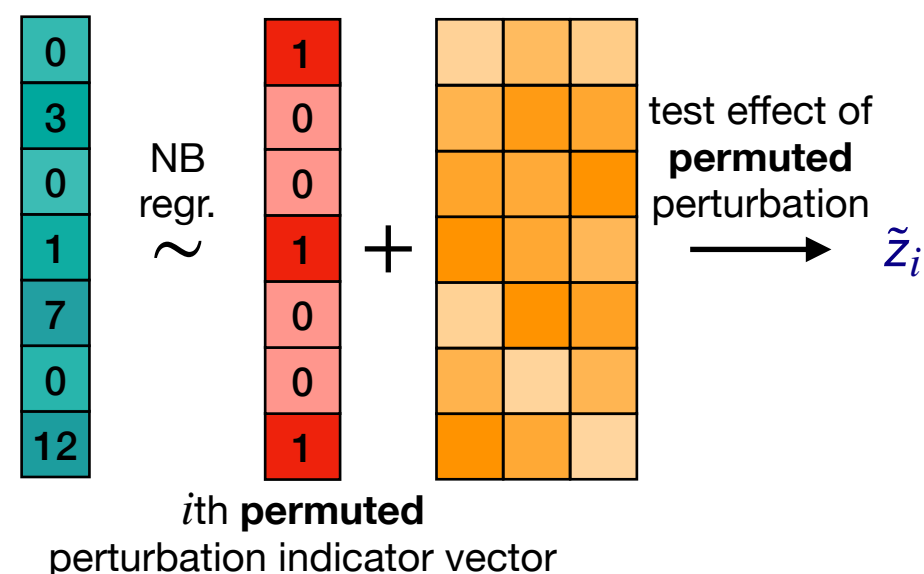
a

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

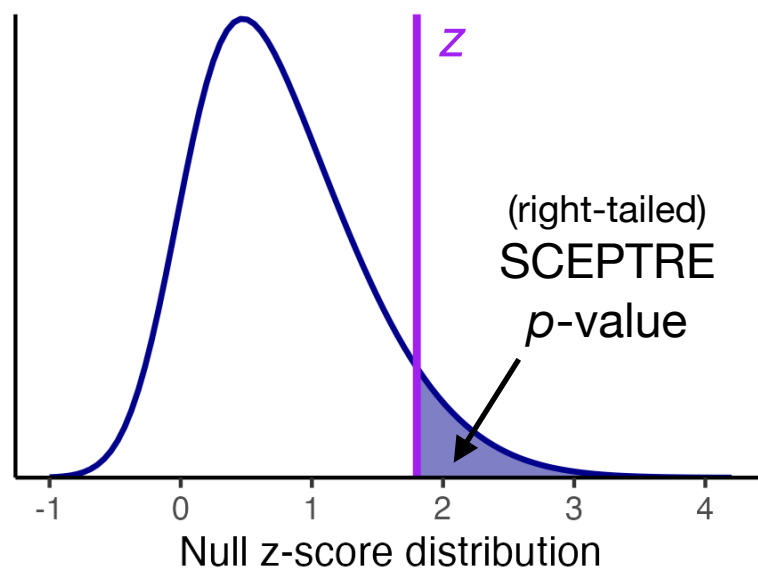


2

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

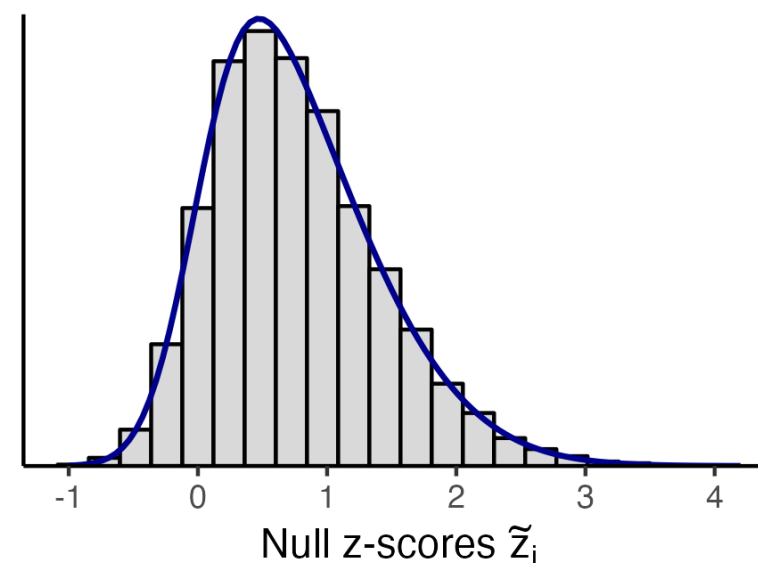
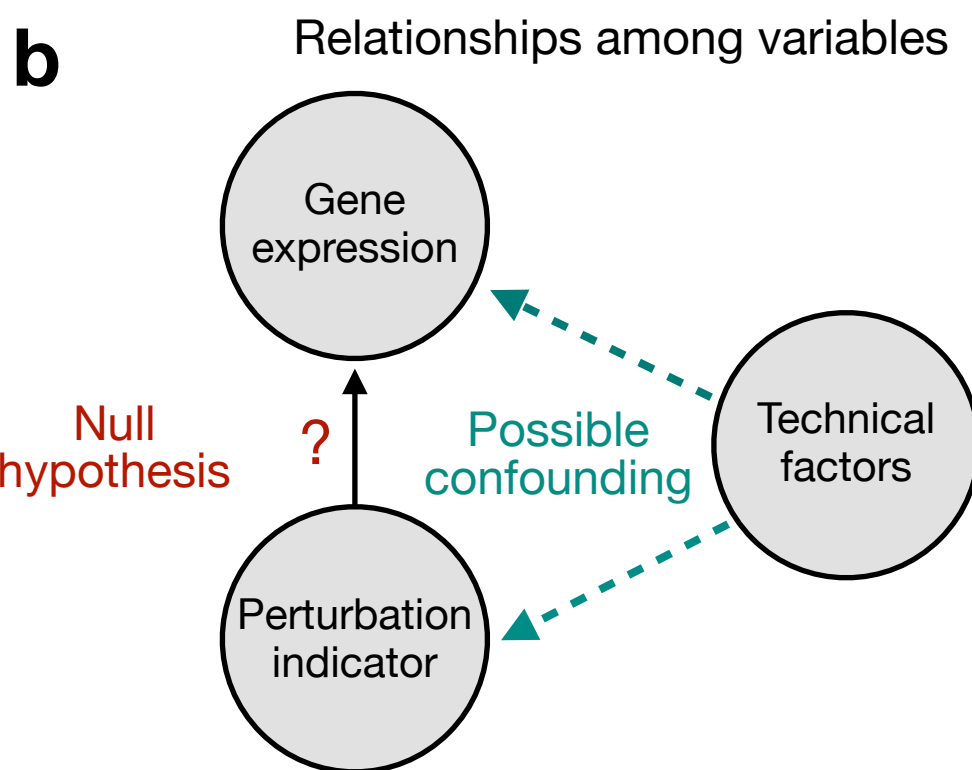
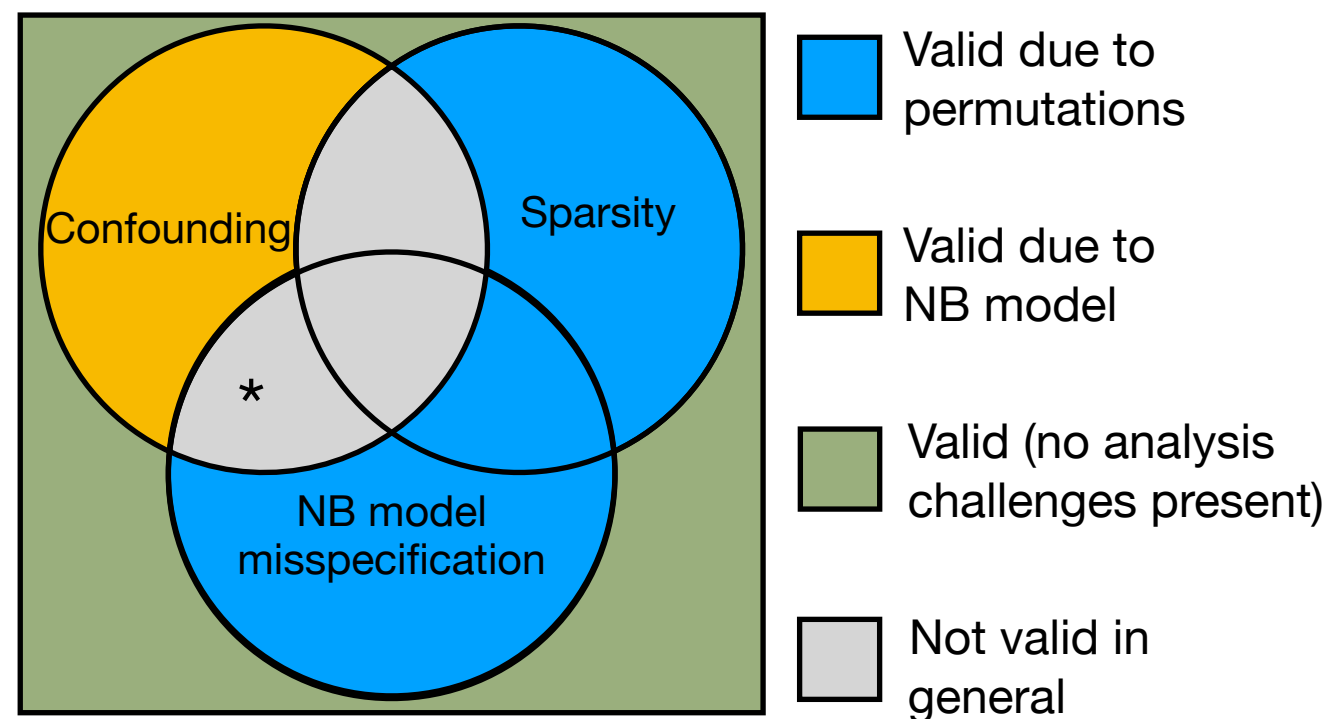


- 4 Obtain p-value by comparing original z-score z to fitted null distribution



3

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

**b****c**

* Still valid if only NB dispersion is misspecified.