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- 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  $\tilde{z}_i$
  - 3 Fit smooth curve to null z-scores  $\tilde{z}_i$
  - 4 Obtain p-value by comparing original z-score  $z$  to fitted null distribution

