A.

Condition 1

mRNA1, mRNA2, …

RPF1, RPF2, …

Normalization across conditions

Condition 2

mRNA1, mRNA2, …

RPF1, RPF2, …

Normalization across mRNA and RPF

Negative Binomial models

mRNA: $k_{gi} = NB(\mu_{gi}(mRNA), \alpha_g)$
RPF: $k_{gi} = NB(\mu_{gi}(RPF), \alpha_g)$

Condition 1: $k_{gi} = NB(\mu_{gi}(C1), \alpha_g)$
Condition 2: $k_{gi} = NB(\mu_{gi}(C2), \alpha_g)$

log2 fold change (log2FC)

log2 Ratio (log2R)

Translational Difference

$$log2FC(RPF) - log2FC(mRNA)$$

$$log2R(C2) - log2R(C1)$$

B. *Estimation of the probability distribution, for log2FC and log2R*

$$\beta_{PDF} = \arg\max \sum_i \log(f_{NB}(K_{gi}; \mu_{gi}(\beta_g); \alpha_g) + f_N(\vec{\beta}|0, \sigma))$$

Crossing two probability distributions

log2FC(RPF)

log2FC(mRNA)

Joint probability

small   large

log2R(C2)

log2R(C1)

P-value - - - - - -> *Compare* <- - - - - - P-value

Final P-value