

Step	Description	TMM (edgeR)	RLE (DESeq2)
I	Pre-normalization by library size	$Y_{gkr} = \frac{X_{gkr}}{N_{kr}}$	
II	Reference sample, or <i>pseudo-reference sample</i> (DESeq2)	$Y_g^{\text{TMM}} = Y_{g11}$	$Y_g^{\text{RLE}} = \sqrt[KR]{\prod_{k=1}^K \prod_{r=1}^R X_{gkr}}$
III	Relative sizes of transcriptomes and reference sample, or <i>relative scaling factors</i> (edgeR), or <i>size factors</i> (DESeq2)	$\tau_{kr}^{\text{TMM}} = \frac{1}{\#\mathcal{G}_{kr}^*} \sum_{g \in \mathcal{G}_{kr}^*} \frac{Y_{gkr}}{Y_g^{\text{TMM}}}$ <p>where \mathcal{G}_{kr}^* represents the set of not trimmed genes</p>	$\tau_{kr}^{\text{RLE}} = \text{median}_g \left(\frac{X_{gkr}}{Y_g^{\text{RLE}}} \right)$
IV	<i>Relative scaling factors</i> adjusted to multiply to 1 (edgeR)	$\tilde{\tau}_{kr}^{\text{TMM}} = \frac{\tau_{kr}^{\text{TMM}}}{\bar{\tau}^{\text{TMM}}} \text{ where }$ $\bar{\tau}^{\text{TMM}} = \sqrt[KR]{\prod_{k=1}^K \prod_{r=1}^R \tau_{kr}^{\text{TMM}}}$	
V	Taking into account both the relative size and the library size, or <i>effective library size</i> (edgeR)	$e_{kr}^{\text{TMM}} = \tilde{\tau}_{kr}^{\text{TMM}} N_{kr}$	
VI	Normalization factors, or <i>relative normalization factors</i> (edgeR), or <i>size factors</i> (DESeq2)	$f_{kr}^{\text{TMM}} = \tilde{\tau}_{kr}^{\text{TMM}}$	$f_{kr}^{\text{RLE}} = \tau_{kr}^{\text{RLE}}$
VII	Normalization of counts, or <i>counts-per-million</i> (edgeR)	$Z_{gkr}^{\text{TMM}} = \frac{X_{gkr}}{e_{kr}^{\text{TMM}}} 10^6$	$Z_{gkr}^{\text{RLE}} = \frac{X_{gkr}}{f_{kr}^{\text{RLE}}}$