

# Supplementary Methods

## Modeling expression ranks for noise-tolerant differential expression analysis of scRNA-seq data

Krishan Gupta<sup>1</sup>, Manan Lalit<sup>2</sup>, Aditya Biswas<sup>3</sup>, Chad D. Sanada<sup>4</sup>, Cassandra Greene<sup>4</sup>, Kyle Hukari<sup>4</sup>, Ujjwal Maulik<sup>5</sup>, Sanghamitra Bandyopadhyay<sup>6</sup>, Naveen Ramalingam<sup>4</sup>, Gaurav Ahuja<sup>7</sup>, Abhik Ghosh<sup>8\*</sup>, Debarka Sengupta<sup>1,7,9,10\*</sup>

<sup>1</sup> Department of Computer Science and Engineering, Indraprastha Institute of Information Technology, Delhi 110020, India, <sup>2</sup> Max Planck Institute of Molecular Cell Biology and Genetics, Dresden 01307, Germany, <sup>3</sup> Microsoft India Pvt. Ltd., Hyderabad, Telangana 500032, India, <sup>4</sup> Fluidigm Corporation, 2 Tower Place, Suite 2000, South San Francisco, CA 94080, USA <sup>5</sup> Department of Computer Science, Jadavpur University, Kolkata, West Bengal 700032, India, <sup>6</sup> Machine Intelligence Unit, Indian Statistical Institute, Kolkata 700108, India, <sup>7</sup> Department of Computational Biology, Indraprastha Institute of Information Technology, Delhi 110020, India, <sup>8</sup> Interdisciplinary Statistical Research Unit, Indian Statistical Institute, Kolkata 700108, India <sup>9</sup> Centre for Artificial Intelligence, Indraprastha Institute of Information Technology, Delhi 110020, India, <sup>10</sup> Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Australia.

---

\*To whom correspondence should be addressed. Tel: +91 11 2690 7446; Email: debarka@iiitd.ac.in  
Correspondence may also be addressed to Abhik Ghosh. Tel: +91 33 2575 2307; Email: abhik.ghosh@isical.ac.in

## Derivation of the Fisher Information Matrix

Note that, for our DGBD model with likelihood function given by Eq (2) of the main paper, we have

$$\begin{aligned}\frac{\partial^2 \log L}{\partial a^2} &= \left(\sum_{r=1}^N y_r\right) \frac{\partial^2 \log(A)}{\partial a^2} \\ \frac{\partial^2 \log L}{\partial b^2} &= \left(\sum_{r=1}^N y_r\right) \frac{\partial^2 \log(A)}{\partial b^2} \\ \frac{\partial^2 \log L}{\partial a \partial b} &= \left(\sum_{r=1}^N y_r\right) \frac{\partial^2 \log(A)}{\partial a \partial b}\end{aligned}\tag{1}$$

So in order to evaluate the above mentioned double derivatives, the first order derivative  $\frac{\partial \log A}{\partial a}$  and  $\frac{\partial \log A}{\partial b}$  are determined as follows:

$$\begin{aligned}\log A &= -\log \left( \sum_{r=1}^N \frac{(N+1-r)^b}{r^a} \right) \\ \frac{\partial \log A}{\partial a} &= \frac{1}{\left( \sum_{r=1}^N \frac{(N+1-r)^b}{r^a} \right)} \times \sum_{r=1}^N \frac{(N+1-r)^b \log r}{r^a} \\ \frac{\partial \log A}{\partial b} &= \frac{-1}{\left( \sum_{r=1}^N \frac{(N+1-r)^b}{r^a} \right)} \times \sum_{r=1}^N \frac{(N+1-r)^b \log(N+1-r)}{r^a}\end{aligned}\tag{2}$$

Re-writing Equation 2 in a more succinct form in the Equation 3 below, we get

$$\frac{\partial \log A}{\partial a} = \frac{u_{1,0}}{u_{0,0}} \quad \text{and} \quad \frac{\partial \log A}{\partial b} = -\frac{u_{0,1}}{u_{0,0}}\tag{3}$$

where  $u_{i,j}$ s are as defined in the main paper. Evaluating the partial derivatives of  $u_{1,0}$ ,  $u_{0,0}$  and  $u_{0,1}$  with

respect to  $a$  and  $b$ , in the Equation 4:

$$\begin{aligned}
\frac{\partial u_{1,0}}{\partial a} &= -\sum_{r=1}^{r=N} \frac{(N+1-r)^b (\log r)^2}{r^a} \\
\frac{\partial u_{1,0}}{\partial b} &= \sum_{r=1}^{r=N} \frac{(N+1-r)^b [\log r] [\log(N+1-r)]}{r^a} \\
\frac{\partial u_{0,0}}{\partial a} &= -\sum_{r=1}^{r=N} \frac{(N+1-r)^b \log r}{r^a} \\
\frac{\partial u_{0,0}}{\partial b} &= \sum_{r=1}^{r=N} \frac{(N+1-r)^b \log(N+1-r)}{r^a} \\
\frac{\partial u_{0,1}}{\partial a} &= \sum_{r=1}^{r=N} \frac{(N+1-r)^b [\log r] [\log(N+1-r)]}{r^a} \\
\frac{\partial u_{0,1}}{\partial b} &= -\sum_{r=1}^{r=N} \frac{(N+1-r)^b [\log(N+1-r)]^2}{r^a}
\end{aligned} \tag{4}$$

In a compact form, these can be written more generally, for any  $i, j = 0, 1$ , as

$$\frac{\partial u_{i,j}}{\partial a} = -u_{i+1,j}, \quad \frac{\partial u_{i,j}}{\partial b} = u_{i,j+1}. \tag{5}$$

Substituting the above expressions in the formula for Fisher information matrix in Eq (3) of the main paper, we get its simplified form for computation within our ROSeq.