**Title:**

Modelling the ordering of cell-cycle phase in single-cell RNA-seq data

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**Abstract:**

With the recent advances in single-cell RNA sequencing (scRNA-seq), we can profile cell-to-cell variation of transcriptional expression in different cell types, and investigate sources of variation in the cellular dynamics of unsynchronized cell populations. Cell cycle is a fundamental biological process inherent to living cells. Thus, understanding cell cycle states and their gene expression profiles are essential to single cell studies. We propose a model-based approach to recover cell-cycle order of the cells in unsynchronized cells using scRNA-seq data. The cell-cycle order depends on the gene-specific amplitude and frequency in one complete cell cycle, where each gene’s frequencies summed up to 1. Simulation case studies showed that our method outperforms principal component analysis (PCA) in recovering cell-cycle order under scenarios of moderately low to high amplitude-to-noise ratios. We also applied our model to 220 undifferentiated induced pluripotent stem cells. Results indicated that the recovered cell-cycle ordering was indeed driven by cell-cycle genes and regulators. Future work is required to model the heterogeneous of biological variation in different cell types.