Computational Pipeline for High-Throughput 3D Quantification of Cell States in Polymorphonuclear Neutrophils

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Reliable characterization of cell states, which encompass a cell's function, environment, and structure, is fundamental to comprehending healthy cell function and transition into diseased states. Development in microscopy and sequencing has created a massive influx of data; however, scalable pipelines to convert raw data into human-interpretable results remain absent. Neutrophils are an ideal model because their nuclei mature into morphologically distinct, multilobed structures. In these systems, 3D nuclear morphology serves as a robust phenotypic proxy for underlying molecular cell state identity. I hypothesize that cell states in neutrophils can be defined using morphological and spatial information extracted from 3D imaging data. The pipeline integrates preprocessing, segmentation, a custom extracted feature set, and unsupervised clustering to define cell states. Within the feature set, a novel recursive topological algorithm was created to automate 3D lobe counting, achieving 82% accuracy within one lobe and effectively capturing complex topology. Additionally, adaptive quantization was utilized to optimize texture feature calculations, reducing memory usage by 99% while preserving critical features. Unsupervised clustering of the resulting feature matrix successfully defined discrete neutrophil states. This project established a high-throughput computational pipeline to extract meaningful 3D morphological information from polymorphonuclear neutrophil imaging data. Ultimately, this pipeline bridges the gap between raw 3D microscopy and biologically interpretable cell states. This project, with the addition of time-series and sequencing data, linking physical cell states with genomic drivers, enables investigation of disease mechanisms and precise drug development.

Awards Won:
Third Award of $1,200