LARGE-SCALE ANALYSIS OF SPATIOTEMPORAL ORGANELLAR NETWORK EVOLUTION

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We are designing and implementing a high-throughput, large-scale computational pipeline to detect changes in organellar morphology of cells. The framework will quantify changes in organellar shape, quantity, and spatial distribution over large sequences of Z-stack microscope images and digital videos, improving our understanding of cellular mechanisms as they respond to their environments. Any tagged subcellular component can be tracked. Our framework takes the novel approach of examining subcellular components as nodes in a social network. Characterizing ensembles of cellular machinery, such as labeled mitochondria or other organelles of interest, as networks allows our framework to study organellar evolution as a function of interconnectedness of cellular components. In addition to quantifying global information such as quantity and appearance, our framework's approach can also provide more detailed local feedback regarding how subsets of the organellar ensembles evolve. This framework will be scalable, employing "big data" paradigms to analyze large quantities of image data at very high resolutions. It will enable rapid quantitative analysis of organellar temporal evolution for extremely large data and provide detailed results at high statistical resolutions.

This current methodology will accurately characterize the spatio-temporal evolution of the organellar social networks in a large collection of time-lapse videos of human cells infected with pathogens, treated to toxins and chemicals or exposed to various environmental stimuli. [NOTES ON THE PROTOCOLS, CELL LINES, AND IMAGING TECHNIQUES USED]. Out initial image processing examined the temporal changes in distribution of spatial frequencies in infected cells as compared to healthy cells [1]. These statistics provided, in some sense, a quantitative representation of cellular morphology, and in turn captured the changes in that morphology as a response to the applied stimulus.

This can have a positive impact on efforts spanning multiple fields. The most immediate consequence will be genotype-phenotype associations and the efficient screening of large genomic libraries. By designing a scalable, open-source framework, extremely large assays can be collected and analyzed. The collaborators have access to a significant amount of established computing and imaging resources between their respective universities, ensuring a rapid influx of raw data that can be readily tested and deployed in a production setting. Besides contributing to our improved understanding of host cell interactions with various stimuli, practical applications could involve replacement of expensive animal studies and more rapid development of effective countermeasures.

[1] Simoncelli, E.P. and Olshausen, B.A., 2001. Natural image statistics and neural representation. *Annual review of neuroscience*, *24*(1), pp.1193-1216.