BudJ–Cell Size Computation During the Cell Cycle

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Abstract
Coordination of cell growth and DNA replication is a universal mechanism that ensures size adaptation and homeostasis. Budding yeast cells, as most eukaryotic cells, exert this coordination essentially during G1, where a critical size is assumed to be attained. However, a molecular mechanism that acts as a "sizer" is yet to be uncovered. In order to tackle this problem, we decided to analyze cell growth kinetics during the cell cycle at a single-cell level by time–lapse microscopy. We have developed a specialized plugin for ImageJ that allows semi-automated computation of cell sizes from bright field images and, at the same time, provides with precise data of cell-cycle landmarks from fluorescence images. The algorithm first obtains a densitometric profile along a radial axis from a seed point within the cell (initially provided by the user) to establish the optical cell boundary. Then, all cell boundary pixels are iteratively defined by full rotation of the radial axis and a preliminary prolate object is fitted. Outliers are rigorously eliminated and missing boundary pixels are estimated by fitting ellipsoidal segments. Finally, different molecular and cellular events are analyzed from fluorescent distribution and levels within cell boundaries. Cell volumes obtained with BudJ are fully comparable to other methods that only produce data at a population level. With this tool, we have found that the critical size is set as a result of the individual growth potential by specific proteins of the network that controls entry into the cell cycle.

Keywords
Cell size, cell cycle, time-lapse analysis