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Dynamic analysis framework to detect cell division and cell death in live-cell imaging, using signal processing and machine learning

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The detection of cell division and cell death events in live-cell assays has the potential to produce robust metrics of drug pharmacodynamics and return a more comprehensive understanding of tumor cells responses to cancer therapeutic combinations. As cancer drugs may have complex and mixed effects on the biology of the cell, knowing precisely when cellular events occur in a live-cell experiment allows to study the relative contribution of different drug effects –such as cytotoxic or cytostatic, on a cell population. Yet, classical methods require dyes to measure cell viability as an end-point assay, where the proliferation rates can only be estimated when both viable and dead cells are labeled simultaneously –not to mention that the actual cell division events are often discarded due to analytical limitations.

Live-cell imaging is a promising cell-based assay to determine drug efficacies, however its main limitation remains the accuracy and depth of the analyses, to acquire automatic measures of the cellular response phenotype, making the understanding of drug action on cell populations difficult. In this work, we present a new algorithmic architecture integrating machine learning, image and signal processing methods to perform dynamic image analyses of single cell events in time-lapse microscopy experiments of drug pharmacological profiling. Our event detection method is based on a pattern detection approach on the polarized light entropy making, it free of any labeling step and exhibiting two distinct patterns for cell division and death events. Our analysis framework is an open source and adaptable workflow that automatically predicts cellular events (and their times) from each single cell trajectory, along with other classic cellular features of cell image analyses, as a promising solution in pharmacodynamics.

Keywords: single-cell, image analysis, cell signaling, cell dynamics, live-cell, machine learning, ... (with “single-cell” being the most important one).