Cell classification improvement by morphology and quantitative phase feature combination

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High content screening consists in acquiring a large number of samples to obtain statistically significant information on cell populations and their changes. Techniques for such studies include flow cytometry (and imaging flow cytometry), whole slide scanning and culture screening. One type of assay consists in detecting cell phenotype changes with time. Since changes can be tenuous, a large number of samples are required, making automatic data processing mandatory for such studies. Machine Learning techniques are powerful tools for mass data classification, well suited for high content screening assays. Cells are described by a large number of features which are combined to determine which class they belong to. The performance of such algorithms strongly relies on features selection.

Quantitative phase imaging (QPI) techniques are used in microscopy for label-free imaging of semi-transparent samples. Density or physical heterogeneities modify the local refractive index, which are revealed by optical path difference (OPD) or Quantitative Phase measurements. QPI is non-invasive (label-free), compatible with long time-lapse acquisition (no photo-bleaching) and other modalities (fluorescence, Raman, …). This is a good candidate for high content screening imaging.

The contribution of this paper is twofold. First, we show that adding quantitative phase features to standard morphology features greatly improves the performance of cell classification algorithms. Second we propose a supervised classification algorithm with features selection. This new algorithm provides weights for relevant features.

We use QuadriWave Lateral Shearing Interferometry as the QPI technique, available as a commercial product by PHASICS (SID4Bio, Phasics SA, Palaiseau, France). It can be implemented on a conventional microscope as a conventional camera and coupled to other modalities such as fluorescence. We built an imaging platform able to keep cells in growing conditions for several days. A fluorescence camera is also used for multimodality screening.
The principle of the experiment is to acquire a statistically large amount of data by screening different cell populations for 24h. After cell segmentation, we use Machine Learning techniques to classify them. Phase information is relevant as it allows classical morphological parameters determination (i.e. surface, perimeter, circularity…) but also quantitative measurements (i.e. density, mass, mass distribution…) on the segmented cells. Those biological features are then selected and used to process training and consequently cells classification.

We describe the use of a quantitative phase imaging technique associated with quantitative phase features and supervised classification as a diagnostic tool to differentiate between different cells populations or cells populations in different experimental conditions. Results on different populations treated or not with Staurosporine (STS), an apoptose inducer, will be shown.