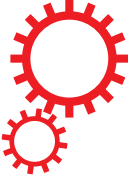


# SCIENTIFIC REPORTS



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## Multiparameter mechanical and morphometric screening of cells

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Received: 22 October 2015

Accepted: 01 November 2016

Published: 02 December 2016

We introduce a label-free method to rapidly phenotype and classify cells purely based on physical properties. We extract 15 biophysical parameters from cells as they deform in a microfluidic stretching flow field via high-speed microscopy and apply machine-learning approaches to discriminate different cell types and states. When employing the full 15 dimensional dataset, the technique robustly classifies individual cells based on their pluripotency, with accuracy above 95%. Rheological and morphological properties of cells while deforming were critical for this classification. We also show the application of this method in accurate classifying cells based on their viability, drug screening and detecting populations of malignant cells in mixed samples. We show that some of the extracted parameters are not linearly independent, and in fact we reach maximum classification accuracy by using only a subset of parameters. However, the informative subsets could vary depending on cell types in the sample. This work shows the utility of an assay purely based on intrinsic biophysical properties of cells to identify changes in cell state. In addition to a label-free alternative to flow cytometry in certain applications, this work, also can provide novel intracellular metrics that would not be feasible with labeled approaches (i.e. flow cytometry).

Intrinsic physical properties of cells that reflect underlying molecular structure are indicators of cell state associated with a number of processes including cancer progression, stem cell differentiation, and drug response<sup>1–3</sup>. Nuclear and cytoplasmic structure or morphology have been one of the main tools for histological detection and classification of cells. The most common method to quantitatively measure cell morphology is flow cytometry, which uses light scattering and fluorescence to measure cell size, shape, and internal structure. However, flow cytometry is a label-based method, which requires the use of fluorescent dyes or antibodies to label cells. This work introduces a label-free method to rapidly phenotype and classify cells purely based on physical properties. We extract 15 biophysical parameters from cells as they deform in a microfluidic stretching flow field via high-speed microscopy and apply machine-learning approaches to discriminate different cell types and states. When employing the full 15 dimensional dataset, the technique robustly classifies individual cells based on their pluripotency, with accuracy above 95%. Rheological and morphological properties of cells while deforming were critical for this classification. We also show the application of this method in accurate classifying cells based on their viability, drug screening and detecting populations of malignant cells in mixed samples. We show that some of the extracted parameters are not linearly independent, and in fact we reach maximum classification accuracy by using only a subset of parameters. However, the informative subsets could vary depending on cell types in the sample. This work shows the utility of an assay purely based on intrinsic biophysical properties of cells to identify changes in cell state. In addition to a label-free alternative to flow cytometry in certain applications, this work, also can provide novel intracellular metrics that would not be feasible with labeled approaches (i.e. flow cytometry).