Cellular Component Specific Growth studied by

Phase Imaging with Computational Specificity (PICS)

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Fluorescence microscopy is a widely used technique in cell biology as it provides the specific required to study cellular structures. However, the chemical and photo-toxicity that comes with fluorescence may reduce the cell viability greatly. In the recent years, Quantitative phase imaging (QPI) [1], with its capability to image transparent samples without any stains at multiple temporal scales, has emerged as an important imaging method for biomedical research. Here we propose phase imaging with computational specificity, an AI-enhanced QPI technique that may potentially replace fluorescence tags by utilizing deep learning to provide required specificity directly from phase images.

The training data for PICS is generated automatically using QPI methods like spatial light interference microscopy (SLIM) [2] and gradient light interference microscopy (GLIM) [3]. The phase images and the fluorescence images are generated and registered simultaneously. We train our model to approximate the mapping from phase images to fluorescence images. Our model architecture is adapted from the U-Net [4], with the addition of batch normalization and a great reduction in number of parameters. PICS can work with different cell types (e.g. SW480, SW620 and CHO) and different fluorophores (e.g. DAPI and DIL). With its accuracy, PICS allows us to estimate the growth rate of nuclei and cytoplasm from unstained cell samples.

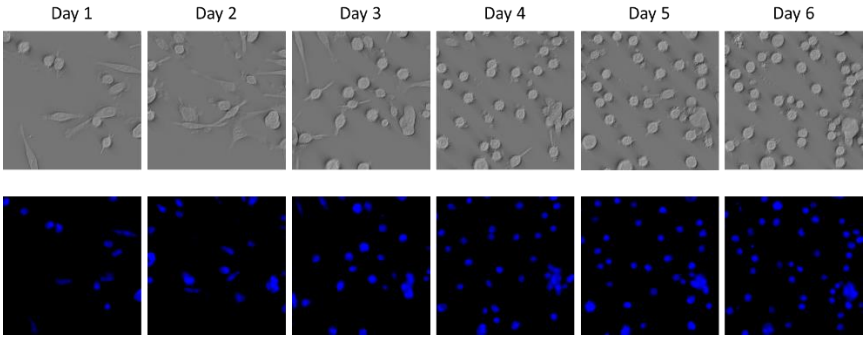

Figure 1 PICS-DAPI (label-free) applied on time-lapse imaging of unstained SW cells

[1] G. Popescu, *Quantitative phase imaging of cells and tissues*. McGraw Hill Professional, 2011.

[2] Z. Wang *et al.*, "Spatial light interference microscopy (SLIM)," *Optics Express,* vol. 19, no. 2, pp. 1016-1026, 2011/01/17 2011.

[3] T. H. Nguyen, M. E. Kandel, M. Rubessa, M. B. Wheeler, and G. Popescu, "Gradient light interference microscopy for 3D imaging of unlabeled specimens," *Nat Commun,* vol. 8, no. 1, p. 210, Aug 8 2017.

[4] O. Ronneberger, P. Fischer, and T. Brox, "U-net: Convolutional networks for biomedical image segmentation," in *International Conference on Medical image computing and computer-assisted intervention*, 2015, pp. 234-241: Springer.