Label-free Identification of Cell Cycle using

Phase Imaging with Computational Specificity (PICS)

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Quantitative phase imaging (QPI) [1], with its capability to image transparent samples, has emerged as an important imaging method for biomedical research. However, due to its label-free nature, QPI lacks specificity and thus faces limitations in complex cellular systems. Here we propose phase imaging with computational specificity (PICS), a new AI-enhanced imaging approach that advances QPI by utilizing deep learning for specificity. Our approach facilitates the study of individual cell behavior and cellular dry mass change across different phases of the cell cycle by generating Fluorescence Ubiquitin Cell Cycle Indicator (FUCCI) [2], a widely used technique that helps visualize the cell cycle behavior, directly from phase images.

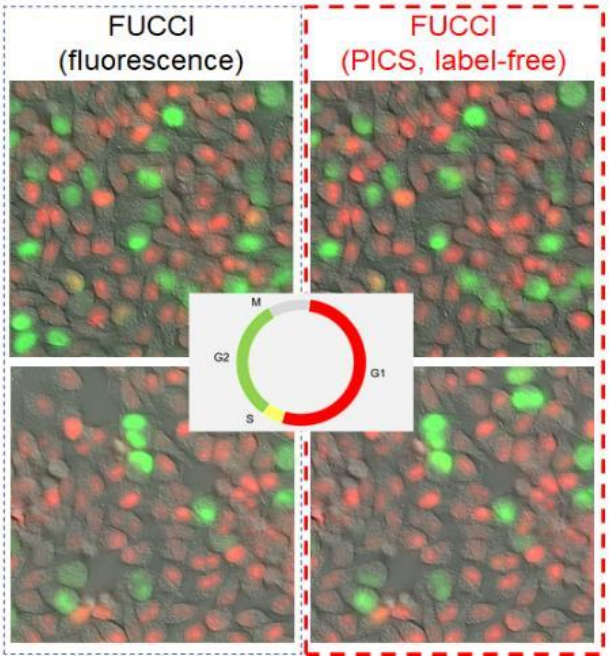

Figure 1. QPI images (grey background) and overlaid FUCCI channel (left) and inferred PICS channel (right). Cell cycle phases colors: Red – G1, Green - S and G2 phases, Yellow - G1/S

We performed time-lapse imaging on HeLa cells tagged with FUCCI. With gradient light interference microscopy [3], fluorescence images and phase images can be acquired and registered simultaneously. We then performed training on these automatically generated phase-fluorescence image pairs. Our model, CycNet, was adapted from the U-Net architecture [4] with a great reduction in the number of parameters. The model achieved satisfying accuracy, with an average PSNR of over 30, on both the training data and test data.

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