Detection of tumor cell spheroids from co-cultures using phase contrast images and machine learning approach

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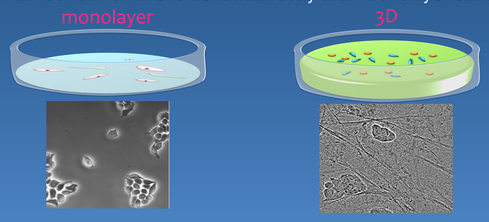
Phase Contrast (PC) Microscopy

The most commonly used label free microscopic method for visualising cells.

Suitable for thin monalayer (2D) samples

Convenient for long term living cell imaging.

For cancer research and drug discovery 3D model systems mimic the complexity of human tumour enviornment more accurately than monolayer cell cultures.



Motivation

There is a need for automated image analysis of 2D Phase Contrast Images of 3D cell co-cultures.

Proposal

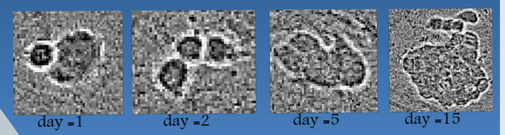
An automated method based on a learning framework on local features defined on superpixels for detecting particular cell type in PC images of 3D cell co-cultures.

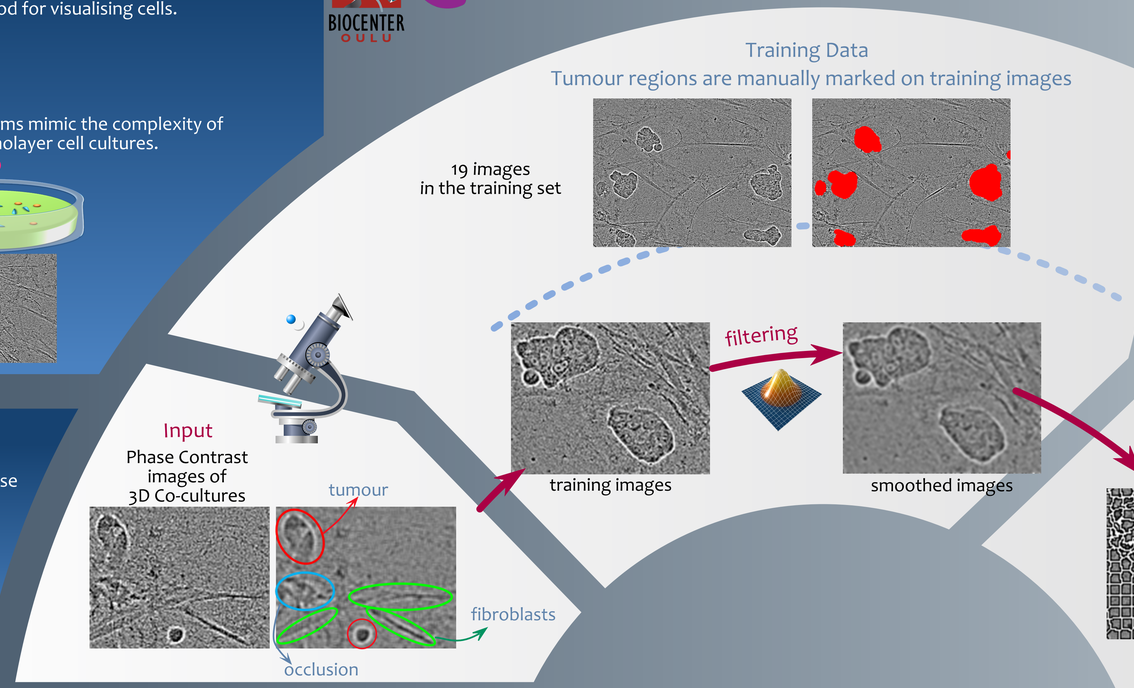
Dynamic Cell Morphology

The shape of cell spheroids vary in time due to proliferation of cancers cells and changes in their extracellular environment

Such variety in shapes prevent utilizing prior information about cell shape.

Depending on the intervals between imaging times, cancer cells within the spheroids can change their shapes thoroughly and/or change their positions relative to the previous time step.





Features

1. SIFT

-Histogram of gradient orientations
-Descriptors are computed at superpixel centers at a fixed scale: f_{sift}

2. Intensity Histograms

-Intensity values from pixels contained in a superpixels are extracted and represented with an n-bin histogram :$f_{intensity}$

3. Center Symmetric Local Binary Patterns

-Rotation invariant region descriptor.
-CS-LBP operator for N equally spaced pixels on a circle of radius R centered at point p_i:

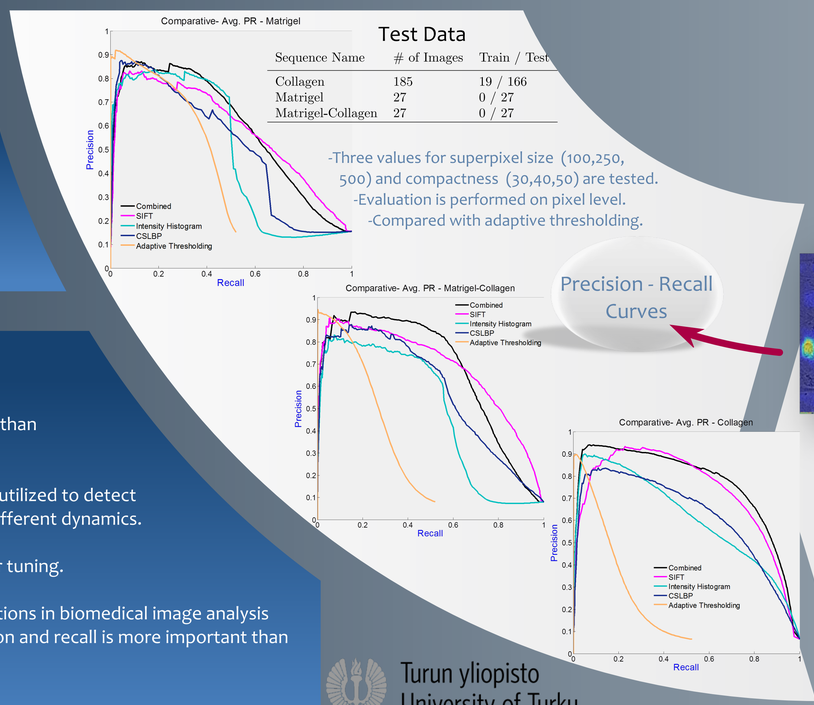
$$CS\text{-}LBP_{p_i} = \sum_{i=0}^{N/2-1} s(I_i - I_{i+N/2})2^i,$$

$$s(x) = \begin{cases} 1 & x > 0 \\ 0 & x < 0 \end{cases}, \quad I_i: \text{intensity at point } pi$$

-Histograms of CS-LBP labels over superpixels : $f_{cs\text{-}lbp}$

4. Composite Feature

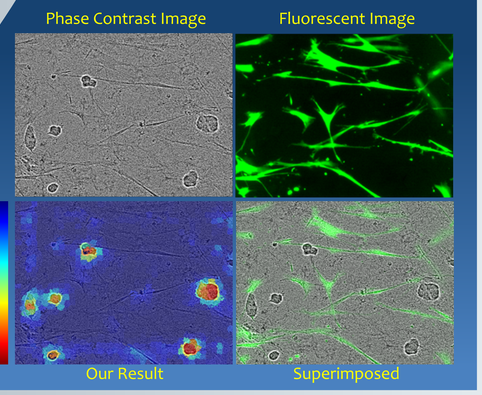
$f_{combined} = [\, f_{sift} \;\; f_{intensity} \;\; f_{cs\text{-}lbp} \,]$



Test Data

Sequence Name	# of Images	Train / Test
Collagen	185	19 / 166
Matrigel	27	0 / 27
Matrigel-Collagen	27	0 / 27

-Three values for superpixel size (100,250, 500) and compactness (30,40,50) are tested.
-Evaluation is performed on pixel level.
-Compared with adaptive thresholding.



Conclusion

Learning based detection approaches are better suited than blind segmentation methods

Learned features from single image sequence could be utilized to detect similar structures in other sequences that might have different dynamics.

Detection performance does not suffer from parameter tuning.

Proposed method can be employed in different applications in biomedical image analysis where obtaining approximate regions with high precision and recall is more important than extracting exact cell boundaries.

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