Nuclei Classification in Immunohistochemical Stainings for Tumor Microenvironment Analysis in Digital Pathology

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Tumor microenvironment (TME) is composed of the stromal cells surrounding cancer cells within a malignant tumor, including the immune system and the connective tissue. TME is being increasingly identified as an important factor in the dynamical behavior of a tumor. In histopathological imaging, the extraction of meaningful information describing the relationships between the tumor and its microenvironment relies on an accurate cell identification technique. In this work, we present an efficient approach for cell detection and classification from immunohistochemistry (IHC)-stained breast cancer tissue. The detected nuclei are classified in 3 types (cancer cells, fibroblasts and immune system cells) using Random Forest classifier based on morphologic, color and texture features.

Keywords: Nuclei Classification, Breast Cancer, Tumor Microenvironment, Immunohistochemistry.

Introduction

Tumor Microenvironment (TME):
• Cellular environment in which a tumor develops.

Characterization of heterotypic interactions from histopathology images:
◆ Cell detection and Classification
◆ Spatial Heterogeneity Analysis

Data:
• Breast cancer slides stained with Phospho-Histone-H3 (PHH3) : Immunohistochemistry marker of mitotic cells and Faenmatin counterstain
• 40 images (2000x2000 pixels) from 16 Whole Slide Images.
• 0.5µm/pixel resolution.

Method

Nuclei Segmentation

Nuclei Classification

Features Extraction

• 6 Geometric features
  - Area
  - Perimeter
  - Solidity
  - E Ellipticity
  - Roundness
  - Circularity

• 3 Color feature
  - Mean Blue Ratio

• 3 Morphological feature
  - 1 level of Gaussian Pyramid
  - RGB to Gray Contrast Adjustment
  - Altering Sequential Filter

• 4 Texture features
  - GLCM: Gray-Level Co-occurrence Matrix (Fisher) [1]
  - Frame: 100x100
  - 9-degree adjacency
  - 4 directions
  - Contrast, Correlation, Energy, Homogeneity

Random Forest Classifier (20 decision trees)

Nuclei Segmentation

Nuclei Classification

Results

Ground Truth Generation

10154 nuclei manually labelled:
• 3332 Cancer Cell Nuclei (−)
• 3516 Fibroblasts (−)
• 3306 Lymphocytes (−)

Quantitative & Qualitative Results

Example of nuclei segmentation and classification result

Confusion Matrix

Quantitative measures for nuclei classification [3]

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<th></th>
<th>Precision</th>
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Conclusion

• This work presents an efficient approach for nuclei classification in IHC-stained histopathology images.

• Texture, color, morphology and geometry of nuclei were studied to extract meaningful features.

• The proposed algorithm has been tested on a large dataset of nuclei that were manually labelled.

• Future works: This result represents a fundamental part of a broader study dedicated to tumor heterogeneity, focusing in particular on spatial distribution quantification of the tumor microenvironment using graph theory and sparse sets’ mathematical morphology.

References


Acknowledgement:
This study has been done with the support of the FUI project FlexMIN: Collaborative Digital Pathology - Funded by the Consolidated Interministerial Fund (FIS - Fonds d'Actions Interministérielles) French Ministry of Industry (MINES). We thank the team PathImage EA4656 BioTKLA from François Baclesse Center for providing the data set.