Automated Mitosis Detection in Color and Multi-spectral High-Content Images in Histopathology: Application to Breast Cancer Grading

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Abstract of the proposed study

Digital pathology represents one of the major and challenging evolutions in modern medicine. Pathological exams constitute not only the gold standard in most of medical protocols, but also play a critical and legal role in the diagnosis process. Diagnosing a disease after manually analyzing numerous biopsy slides represents a labor-intensive work for pathologists. Thanks to the recent advances in digital histopathology, the recognition of histological tissue patterns in a high-content Whole Slide Image (WSI) has the potential to provide valuable assistance to the pathologist in his daily practice. Histopathological classification and grading of biopsy samples provide valuable prognostic information that could be used for diagnosis and treatment support. Nottingham grading system is the standard for breast cancer grading. It combines three criteria, namely tubule formation (also referenced as glandular architecture), nuclear atypia and mitotic count. Manual detection and counting of mitosis is tedious and subject to considerable inter- and intra-reader variations. The main goal of this dissertation is the development of a framework able to provide detection of mitosis on different types of scanners and multispectral microscope.

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The main contributions of this work are eight fold. First, we present a comprehensive review on state-of-the-art methodologies in nuclei detection, segmentation and classification restricted to two widely available types of image modalities: H&E (Hematoxylin Eosin) and IHC (Immunohistochemical). Second, we analyze the statistical and morphological information concerning mitotic cells on different color channels of various color models that improve the mitosis detection in color datasets (Aperio and Hamamatsu scanners). Third, we study oversampling methods to increase the number of instances of the minority class (mitosis) by interpolating between several minority class examples that lie together, which make classification more robust. Fourth, we propose three different methods for spectral bands selection including relative spectral absorption of different tissue components, spectral absorption of H&E stains and mRMR (minimum Redundancy Maximum Relevance) technique. Fifth, we compute multispectral spatial features containing pixel, texture and morphological information on selected spectral bands, which leverage discriminant information for mitosis classification on multispectral dataset. Sixth, we perform a comprehensive study on region and patch based features for mitosis classification. Seven, we perform an extensive investigation of classifiers and inference of the best one for mitosis classification. Eight, we propose an efficient and generic strategy to explore large images like WSI by combining computational geometry tools with a local signal measure of relevance in a dynamic sampling framework. The real time evaluation of these frameworks is done in MICO (COgnitive MIcroscopy, ANR TecSan project) platform prototyping initiative as shown in Figure 1.

We evaluate our proposed frameworks on MITOS contest dataset. According to the MITOS international benchmarking results, our multispectral framework (Figure 2) outperforms significantly among the top methods, according to the F-Measure. For the color framework (Figure 3), we thus manage to rank second during the contest, a promising result on the way on clinical routine use. Beside, our frameworks reach the same level of accuracy in mitosis detection on brightlight as multispectral datasets, an interesting complementary modality, able to reinforce combined quantitative assessment protocols in future innovative approaches.

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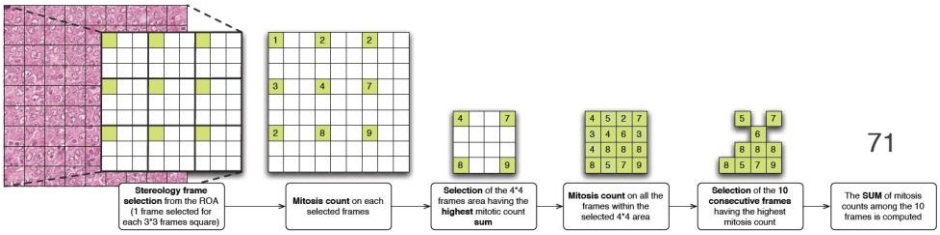

Figure 1. Stereology flow used for mitosis score over a ROI in MICO platform.

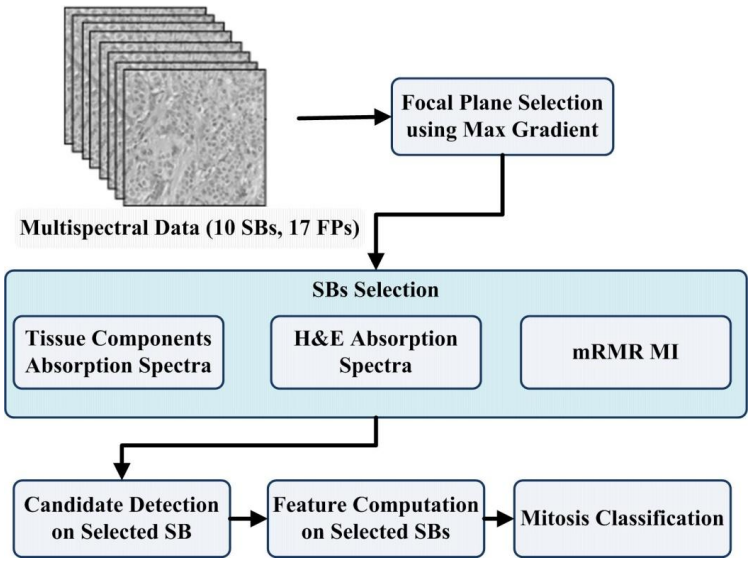

Figure 2. Mitosis Detection Framework for Multispectral Images.

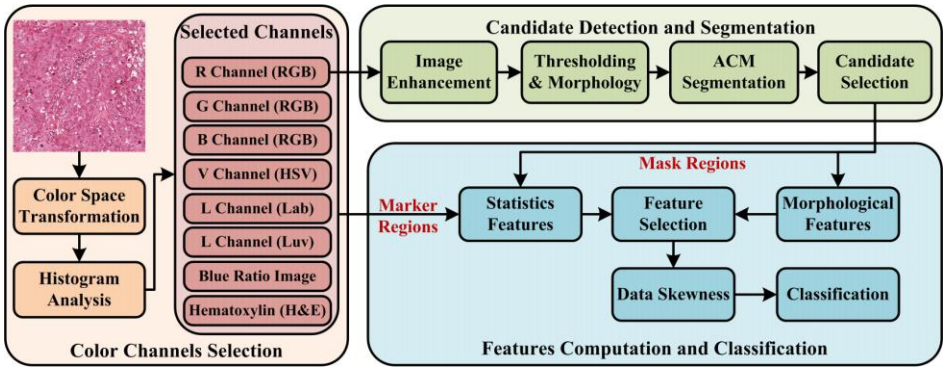

Figure 3. Mitosis Detection Framework for Color Images.

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