**Picture1.emf**

Multi-instance based feature descriptor of a tissue image: automatic extraction of lumen areas and profiling of surrounding regions by means of a progressively expanding set of neighborhood sampling rings.

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*Abstract*: Automated tissue image analysis aims to develop algorithms for a variety of histological applications. This has important implications in the diagnostic grading of cancer such as in breast and prostate tissue, as well as in the quantification of prognostic and predictive biomarkers that may help assess the risk of recurrence and the responsiveness of tumors to endocrine therapy.

In this thesis, we use pattern recognition and image analysis techniques to solve several problems relating to histopathology and immunohistochemistry applications. In particular, we present a new method for the detection and localization of tissue microarray cores in an automated manner and compare it against conventional approaches.

We also present an unsupervised method for color decomposition based on modeling the image formation process while taking into account acquisition noise. The method is unsupervised and is able to overcome the limitation of specifying absorption spectra for the stains that require separation. This is done by estimating reference colors through fitting a Gaussian mixture model trained using expectation-maximization.

Another important factor in histopathology is the choice of stain, though it often goes unnoticed. Stain color combinations determine the extent of overlap between chromaticity clusters in color space, and this intrinsic overlap sets a main limitation on the performance of classification methods, regardless of their nature or complexity. In this thesis, we present a framework for optimizing the selection of histological stains in a manner that is aligned with the final objective of automation, rather than visual analysis.

Immunohistochemistry can facilitate the quantification of biomarkers such as estrogen, progesterone, and the human epidermal growth factor 2 receptors, in addition to Ki-67 proteins that are associated with cell growth and proliferation. As an application, we propose a method for the identification of paired antibodies based on correlating probability maps of immunostaining patterns across adjacent tissue sections.

Finally, we present a new feature descriptor for characterizing glandular structure and tissue architecture, which form an important component of Gleason and tubule-based Elston grading. The method is based on defining shape-preserving, neighborhood annuli around lumen regions

and gathering quantitative and spatial data concerning the various tissue-types.