Towards an Automated Quantitative Diagnosis of Prostate Cancer

MONTANA STATE UNIVERSITY

PIs: B. Fasy, Q. Brown, C. Wenk Students: P. Lawson, C. Miller

Tulane University

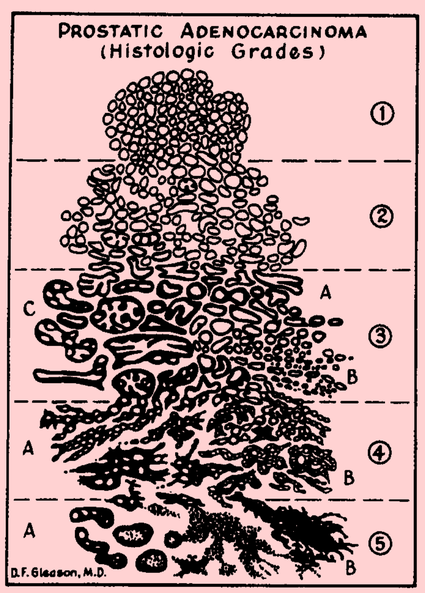
Overview

The widespread availability of whole slide digital pathology images, including the NCI Cancer Genome Atlas (TCGA), opens up new possibilities in the use of computational approaches for diagnosis, prognosis, and precision medicine. This project aims to discover new **quantitative image-based prognostic biomarkers** for prostate cancer, focusing on an investigation of novel concepts from **computational topology** applied to prostate cancer glandular architecture. The current standard for prostate cancer grading is the Gleason score, which is a subjective rating system based on an analysis of high-level tissue architecture and glandular shape and organization. However, Gleason scoring is variable between pathology reviewers, and may not capture all of the potentially prognostic information contained in glandular growth patterns.

In this project new topological descriptors will be developed that capture architectural features of prostate glands in pathology images. These descriptors can then be used to **aid pathologists** by providing quantitative, reproducible analogs to the traditional Gleason scores, and they may have independent prognostic value. In particular, the aim of this project is to demonstrate effectiveness of using computational methods based on tools from computational geometry and topology to **recognize and quantify** glandular architectural features.

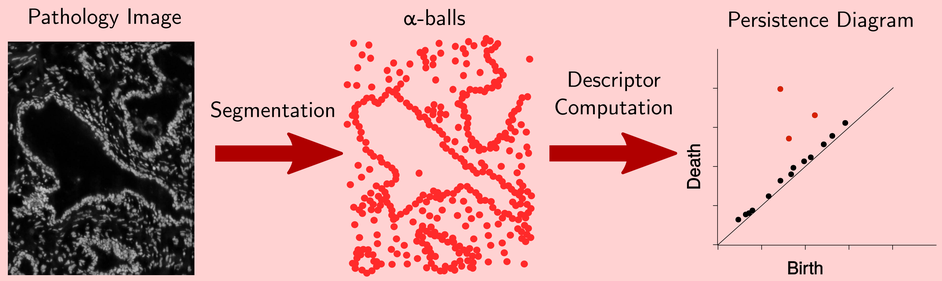
Gleason Score

An affirmative diagnosis of prostate cancer requires a trained pathologist who visually examines prepared slices of a prostate biopsy to determine malignancy, which is further graded using the Gleason grading system to assign a score. The Gleason score, originally developed by Donald Gleason in the 1960's is based on the **high-level tissue architectural patterns** or shapes of prostate carcinoma glands in hematoxylin-and-eosin (H&E) stained sections. Pathologists are trained to assign Gleason scores based on an illustration of Gleason patterns 1–5 in a standard drawing. An increased Gleason score is positively correlated with tumor size, surgical margin status, and pathologic stage, and it has proven useful in pre-treatment nomograms involving needle biopsy Gleason score, serum prostate specific antigen (PSA), and clinical stage. The Gleason score is thus used routinely in clinical prostate cancer management. and associated nomograms can be used to predict response to surgery or radiotherapy. Thus, while it is historically useful as a means for grading prostate cancer, and has shown value in prediction of treatment response, the Gleason score is inherently **subjective**, **poorly-reproducible** within and **variable** between pathology reviewers, and may not capture all of the potentially prognostic information contained in glandular growth patterns.



Topological Data Analysis (TDA)

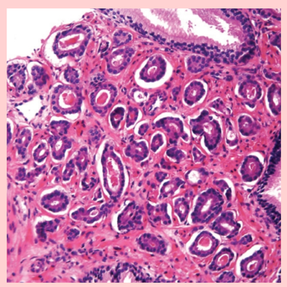
TDA refers to a collection of methods for finding topological structure in data. One such approach is persistent homology, a method for studying the homology at multiple scales simultaneously. Given a real-valued function f **persistent homology** describes how the topology of the lower level sets $\{x : f(x) \leq t\}$ changes as t increases from $-\infty$ to ∞. This information is encoded in the persistence diagram, a multiset of points in the plane, each corresponding to the birth and death of a homological feature that existed for some interval of t. Persistence homology can be used to capture the topology of a **set of nuclei** through studying the so-called α-filtration. In the example below the three red dots of the persistence diagram correspond to the three cycles formed by glands in the pathology image.



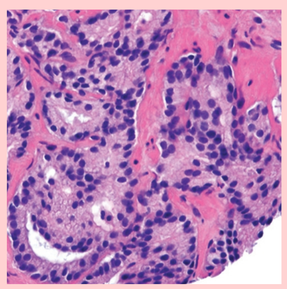
Descriptors for Biopsy Images

Trained pathologists use inter- and intra-glandular sizes, structures, and patterns to grade prostatic adenocarcinomas. These comprise architectural features, such as the size and shape of glands, density of glands, descrete versus fused glands, and the presence of telescoping glands. Additionally the infiltration of malignant neoplasia between benign glands and the presence of glomeruloid patterns serve as distinguishing features in the grading of prostatic adenocarcinoma. These architectural features are not quantitatively defined, resulting in imprecise methods for evaluating prostate cancer. We propose to **quantify** them **with topological and geometric descriptors**, with a focus on persistent homology-based descriptors. Glandular density can be decribed by the connectivity and higher order connectivity between glands. Understanding when these changes occcur will be captured by persistence diagrams. Quantitative descriptors can then be defined using these persistence diagrams, and these can be be used to generate an aggregate descriptor for a class of architecturally similar biopsy slides. In this manner the Gleason grade can be reproduced computationally.

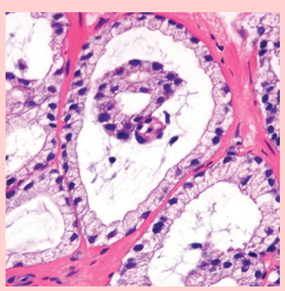
Discrete



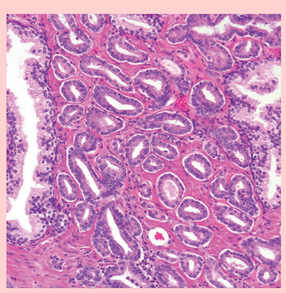
Fused



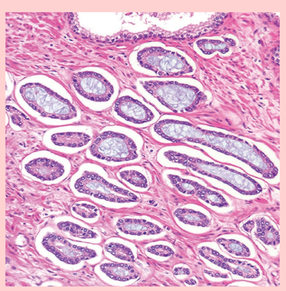
Telescoping



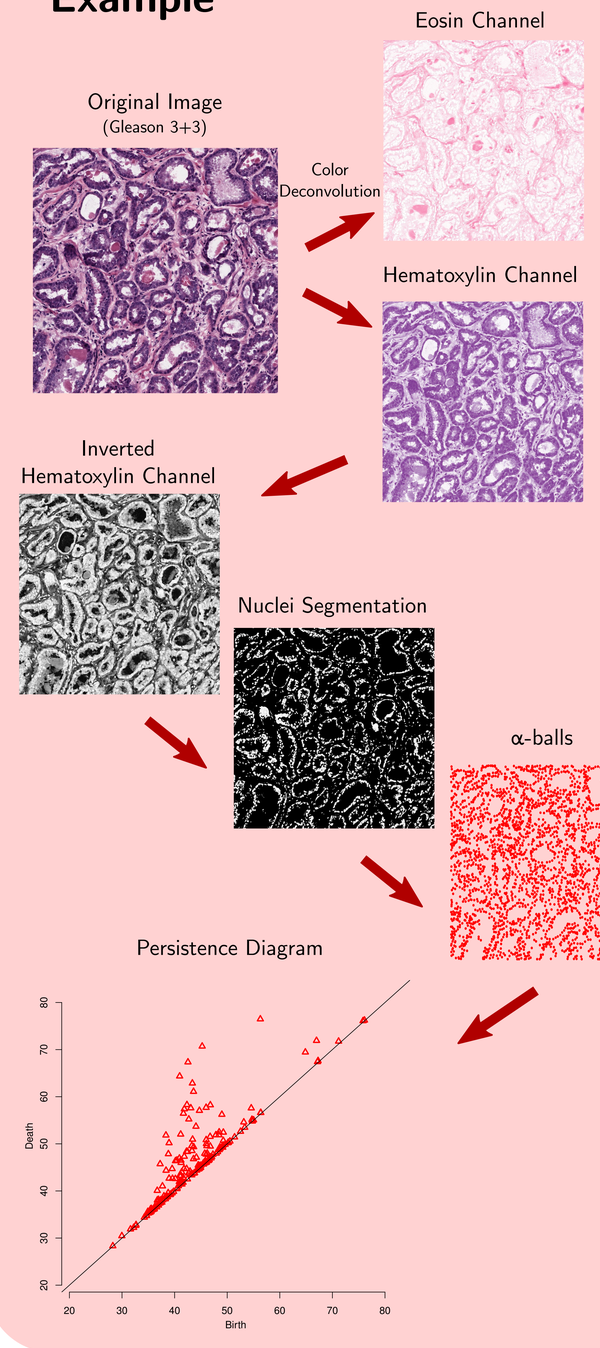
Infiltration



Glomeruloid



Example



Research reported in this poster was supported by the Division of Mathematical Sciences of the National Science Foundation under award number 1557750