Using Topological Data Analysis to Study Glandular Architecture

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TDA-Bio Workshop
Seattle, Washington
Joint Work With

- Carola Wenk (Tulane, CS)
- J. Quincy Brown (Tulane, BME)
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- J. Quincy Brown (Tulane, BME)
- Andrew Sholl (Tulane Med)
- John Sheppard (MSU, CS)
- Brian Summa (Tulane, CS)

NSF DMS / NIH Planning Grant: 1557716 (MSU) and 1557750 (Tulane)
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- John Sheppard (MSU, CS)
- Brian Summa (Tulane, CS)
- Pete Lawson (Tulane, BME)
- Eric Berry (MSU, Math)
- Sush Majhi (Tulane, Math)
- Alan Cleary (MSU, CS)
- Sawyer Payne (MSU, CS Undergrad)

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Prostate Cancer

The Question is *Will He Outlive It?*

- More than 225,000 cases per year (USA).
- One is seven men will be diagnosed.
- Treatments: surgery, chemo, radiation, hormone therapy.
- Either slowly-growing and benign or fast-growing and dangerous.
- Surgery / radiation benefits questionable for SG/B.
- Surgery / radiation side effects not desirable.
- ... therefore, active surveillance.
Prostate Cancer

Diagnosis
Prostate Cancer

Diagnosis

The Problem: Qualitative Diagnosis and Prognosis

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The Problem: Qualitative Diagnosis and Prognosis

Prostate Cancer

Diagnosis

Radical Surveillance

PCA

2+2
3+3
3+4
4+3
4+4
5+4
5+5

2+2
3+3
3+4
4+3
4+4
5+4
5+5
Prostate Cancer
Diagnosis
Biopsy and Prostatectomy Slides
How to Describe Glandular Architecture
Gleason Grading

Grade 1: well-defined, nicely packed
Grade 2: larger, more tissue, less uniform
Grade 3: less defined glands, some cribriform
Grade 4: fused glands, open lumens
Grade 5: no glandular definition, sheets of cells

Gleason Grading

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02005 Consensus, image from The Gleason Grading System: A Complete Guide for Pathologist and Clinicians by Eppstein
Learning to Grade

The Problem: Qualitative Diagnosis and Prognosis


By Jonathan I. Epstein
Category: Medical, Pathology

Hardback | 9781451172829 | July 2012 | 224 pages
List Price: £129.00

This price is valid for United Kingdom, change location to view local pricing and availability.

PRINTABLE VERSION

The Gleason Grading System: A Complete Guide for Pathologists and Clinicians provides exhaustive coverage of the updated Gleason Grading System, which deals not only with pathology but also with the associated clinical correlations and prognosis.

The Gleason Grading System is the most important prognostic marker of prostate cancer, which is critical to patient management and drives therapies across all disciplines dealing with prostate cancer. In addition to an extensive number of photographs, this book discusses in detail clinically related issues that are crucial for the urologist, radiotherapist, and oncologist to know, such as predicting upgrading and downgrading from needle biopsy to radical prostatectomy, risk of Gleason grading change over time, significance of tertiary grade patterns, and prognosis and implications related to various Gleason scores and different therapies. Images that were particularly difficult for contributing pathologists sent in for consultation are used in addition to classic examples, as these cases are the most informative in showing the difficulties with Gleason grading. This book is a valuable tool not only for surgical pathologists from the resident level to seasoned practitioners but also for urology residents, urologists, medical oncologists, and radiation oncologists.
Glandular Architecture

Discrete-vs-Fused Glands

Gleason 3
Discrete glands.

Gleason 4
Presence of fused glands.

Image source: Eppstein, *The Gleason Grading System*
Glandular Architecture

Cribriform Pattern

Gleason 4

A gland with numerous small holes.

Image source: Eppstein, *The Gleason Grading System*
Glandular Architecture

Glomeruloid Structures

Gleason 3,4
Intraluminal cribriform, single point of attachment.

Image source:
http://www.nature.com/modpathol/journal/v17/n3/fig_tab/3800050f9.html
Glandular Architecture

Telescoping Glands

**Gleason 3**
Telescoping (gland in gland) may mimic Glumeroid.

**Gleason 4**
Actual glumeroid pattern.

Image source: Eppstein, *The Gleason Grading System*
Glandular Architecture

Distribution of Glandular Shape and Size

Gleason 1
Uniform distribution of gland size. Round.

Gleason 3
Irregularly separated glands.

Gleason 4
Poorly formed glands.

Image source: Eppstein, The Gleason Grading System
Persistent Homology
Persistent Homology
Quantifying the Process

TDA

Methods: TDA

(Birth + Death)/2

20 40 60 80 100 120
Quantifying the Process

TDA
Quantifying the Process

TDA
Quantifying the Process

TDA
Quantifying the Process

Methods: TDA

TDA for Glandular Architecture

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Quantifying the Process

TDA
Quantifying the Process

TDA

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Methods: TDA

Functional and Vectorized Summaries

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[TDA Diagrams]

- Birth vs. Death plot
- (Birth + Death)/2 vs. (Birth + Death)/2 plot

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Aside: Hypothesis Testing

Upcoming Paper

The *Euler Characteristic* curve seems to be the most discriminating among the functional summaries when using the Hotelling Test\textsuperscript{a}.

\textsuperscript{a}Joint work with Jessi Cisewski, Wojciech Hellwing, Mark Lovell, Alessandro Rinaldo, Larry Wasserman, Mike Wu
Collaboration
Comparing Purely Graded Images

Initial Results

![Graph showing the results of comparing purely graded images.](image-url)
Analyzing DeBruijn Graphs
Joint work with Alan Cleary and Brendan Mumey

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TDA for Glandular Architecture
2 October 2016 19 / 22
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Other Problems:

Bubbles in DeBruijn Graphs

\(^0\text{Nature article: } De \text{ Novo Assembly and Genotyping of Variants using Colored De Bruijn Graphs by Iqbal, Caccamo, Turner, Flicek, McVean}\)
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\[ k = 3 \quad \rightarrow \quad k = 20 \]

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TDA R Package
Maintained by Fasy, Kim, and Maria

- Front-end to various TDA libraries
- Plotting Diagrams
- Landscapes, Silhouettes
- Statistical Techniques (including confidence sets)
- (Soon) Intensity Plots
Thank You!

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