Using Topological Data Analysis to Study Glandular Architecture

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2 October 2016
TDA-Bio Workshop
Seattle, Washington

Joint Work With

- Carola Wenk (Tulane, CS)
- J. Quincy Brown (Tulane, BME)

[0]NSF DMS / NIH Planning Grant: 1557716 (MSU) and 1557750 (Tulane)

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- 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, harmone 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.

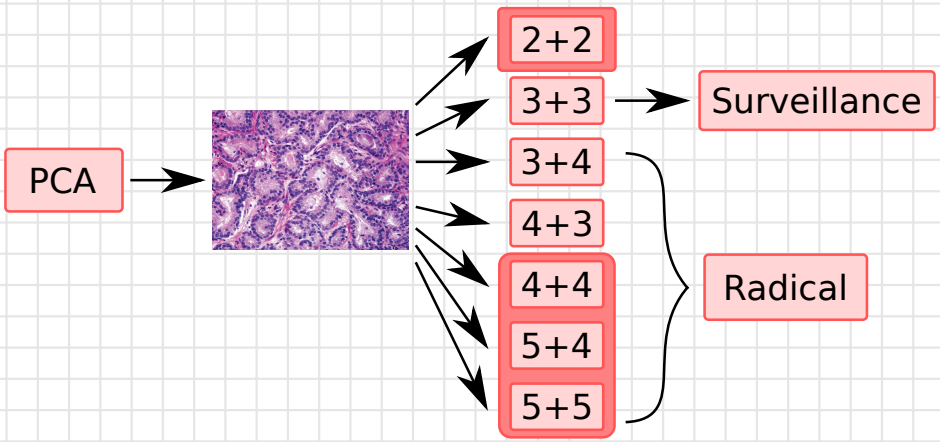
Prostate Cancer

Diagnosis

PCA

Prostate Cancer

Diagnosis



Prostate Cancer

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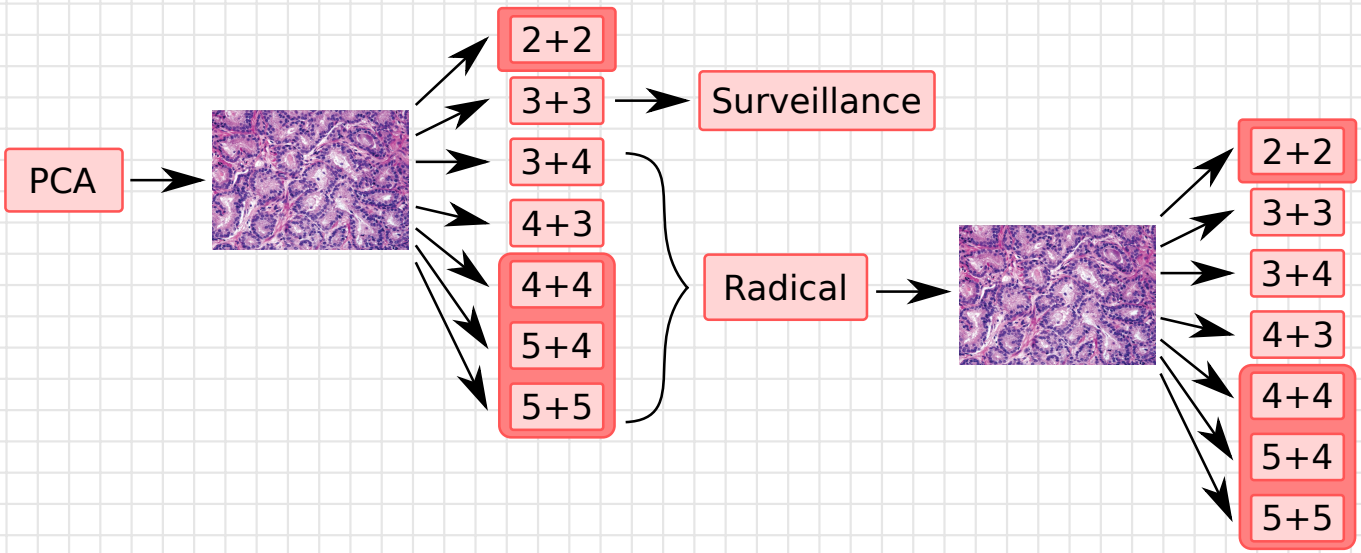
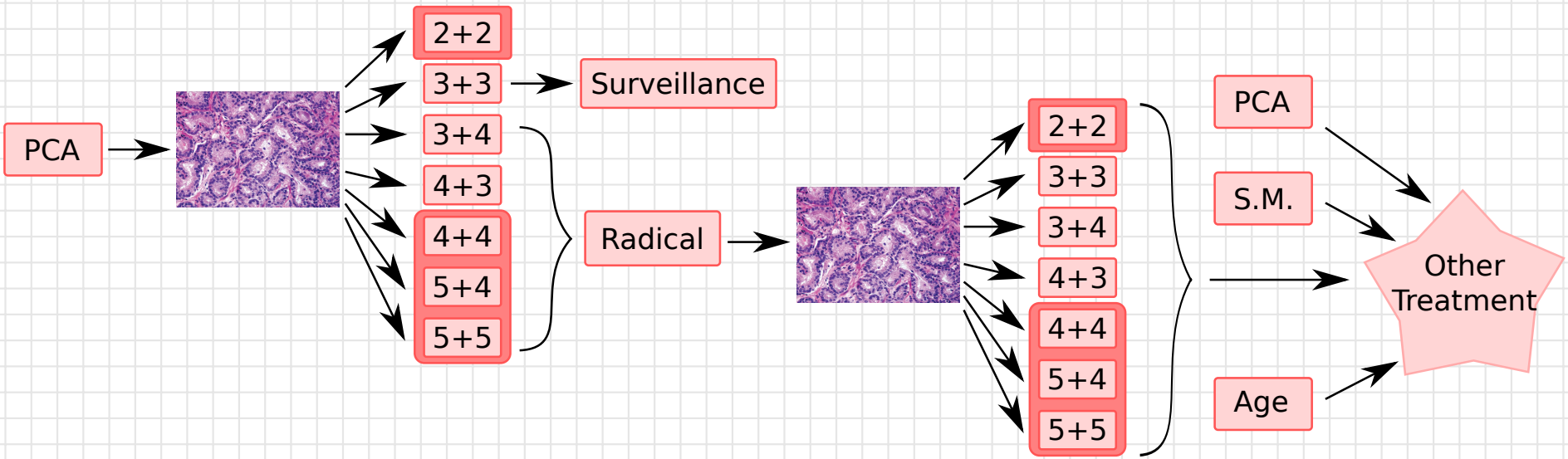


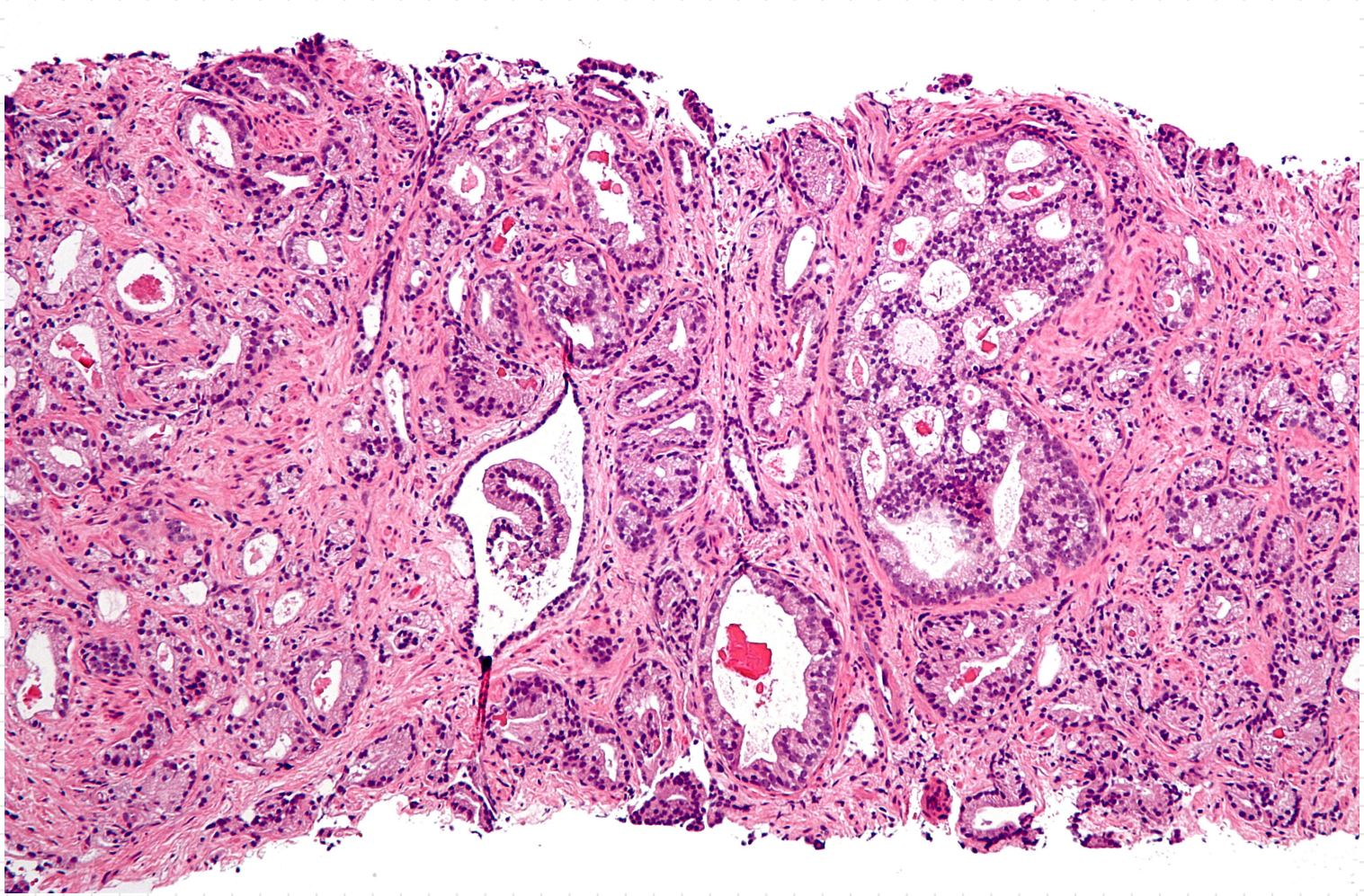
Prostate Cancer

Diagnosis

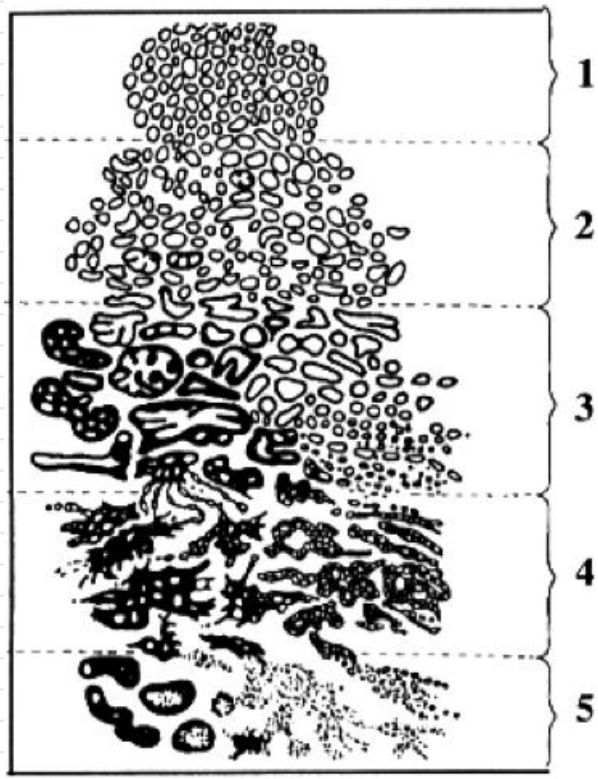


Biopsy and Prostectmy Slides

How to Describe Glandular Architecture



Gleason Grading



Grade 1: well-defined, nicely packed

Grade 2: larger, more tissue, less uniform

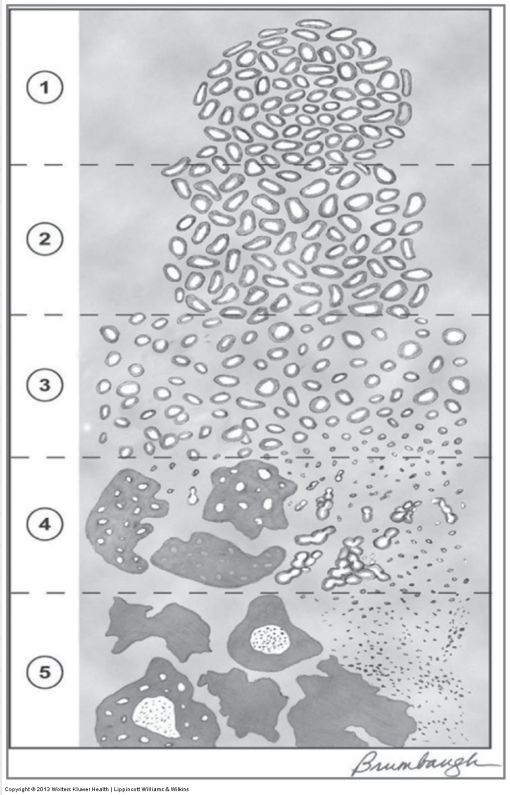
Grade 3: less defined glands, some cribriform

Grade 4: fused glands, open lumens

Grade 5: no glandular definition, sheets of cells

[0]Donald Gleason, 1966, image from *The Gleason Grading System: A Complete Guide for Pathologist and Clinicians* by Eppstein

Gleason Grading



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[0]2005 Consensus, image from *The Gleason Grading System: A Complete Guide for Pathologist and Clinicians* by Eppstein

Learning to Grade

The Gleason Grading System: A Complete Guide for Pathologists and Clinicians

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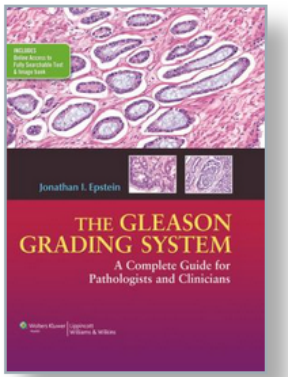

LARGER VIEW | GOOGLE PREVIEW

The Gleason Grading System

A COMPLETE GUIDE FOR PATHOLOGIST AND CLINICIANS

By Jonathan I. Epstein

Category: Medical, Pathology

Hardback | 9781451172829 | July 2012 | 224 pages

List Price: £129.00

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

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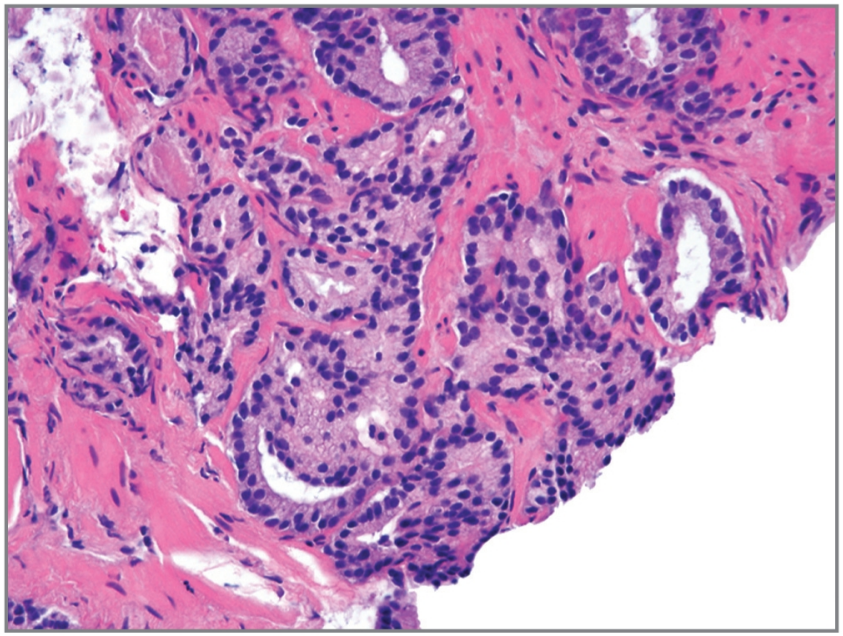
DESCRIPTION | REVIEWS (1) | SPECIFICATIONS

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.

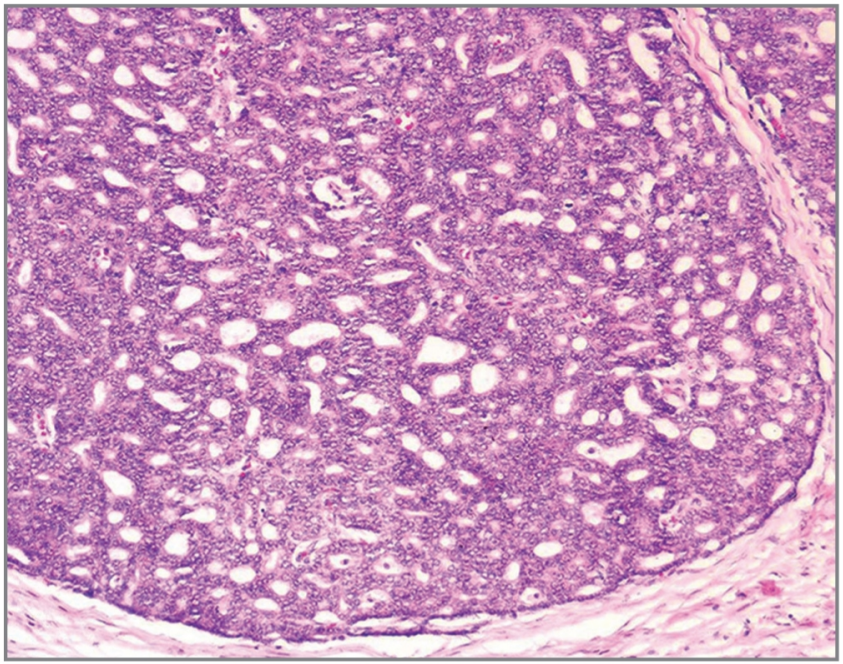
Gleason 4

Presence of fused glands.

[0]Image source: Eppstein, *The Gleason Grading System*

Glandular Architecture

Cribriform Pattern



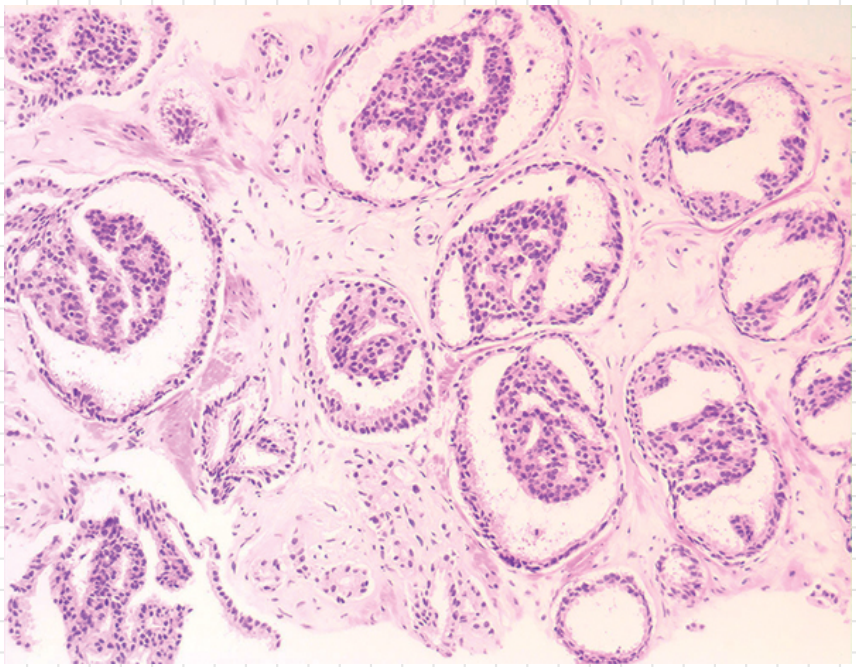
Gleason 4

A gland with numerous small holes.

[0]Image source: Eppstein, *The Gleason Grading System*

Glandular Architecture

Glomeruloid Structures



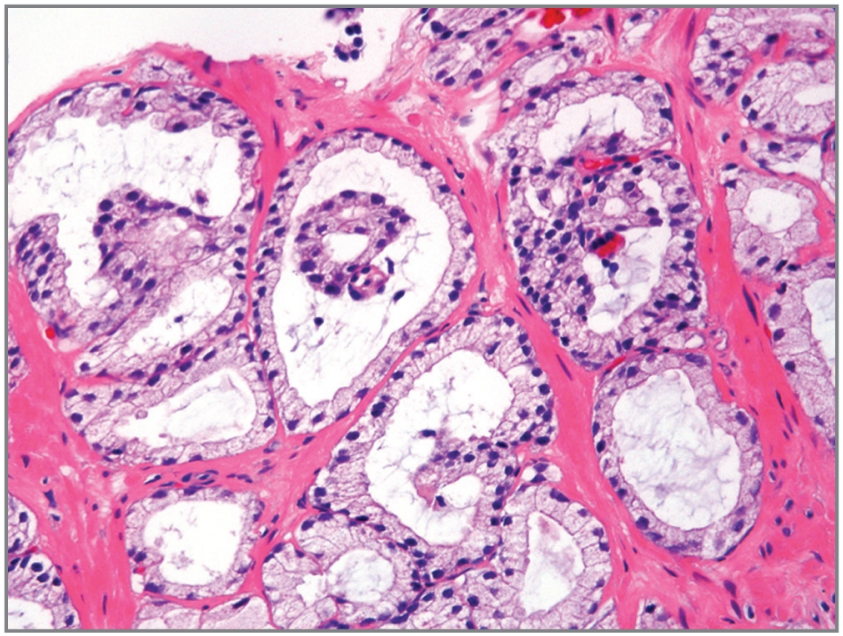
Gleason 3,4

Intraluminal cribriform, single point of attachment.

[0]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.

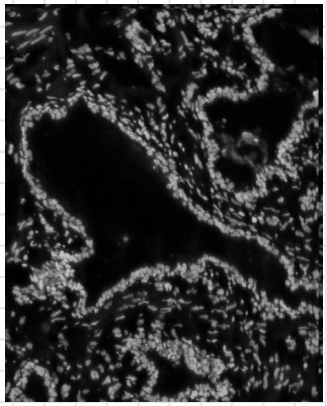
Gleason 4

Actual glumeroid pattern.

[0]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

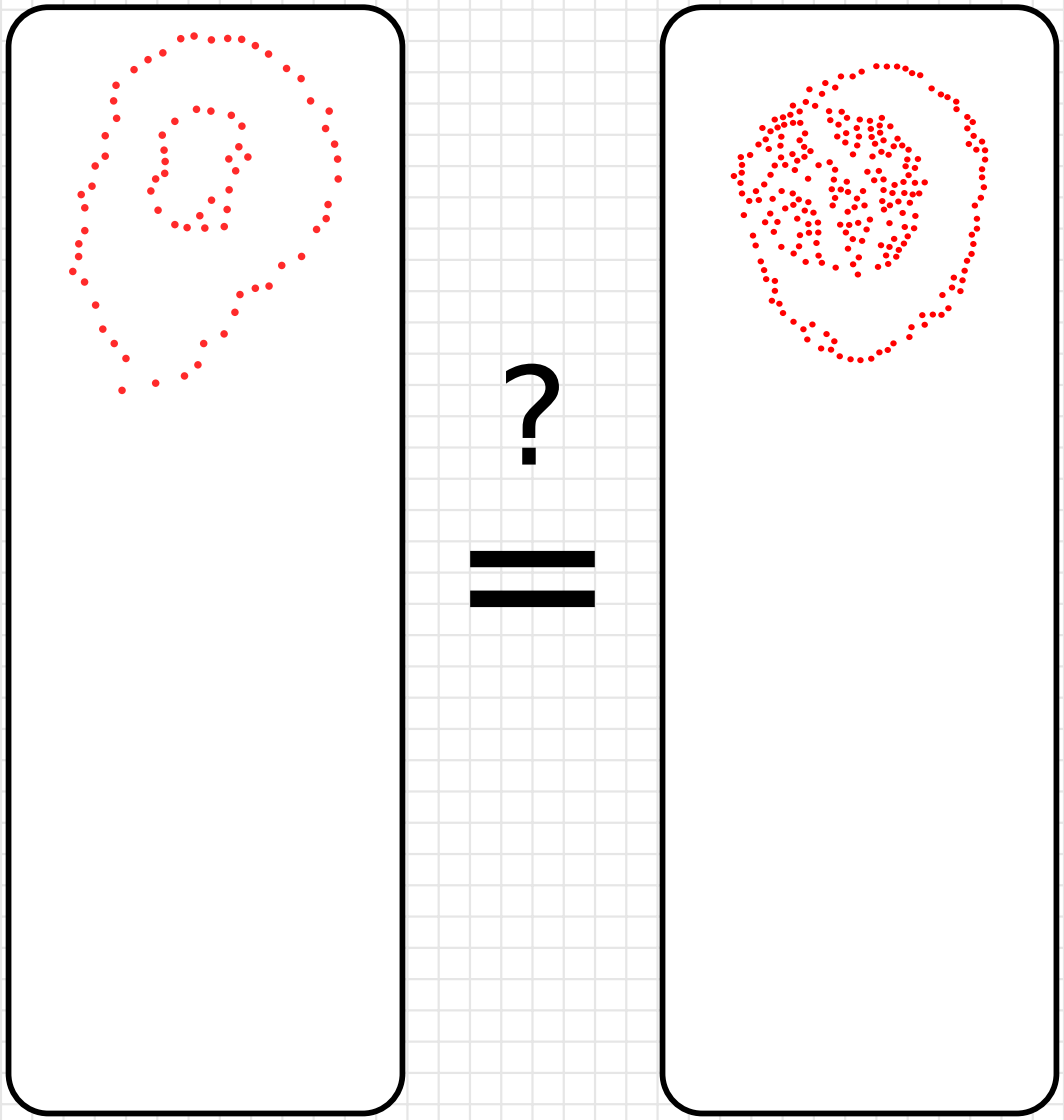
Irregularly separated glands.

Gleason 4

Poorly formed glands.

[0]Image source: Eppstein, *The Gleason Grading System*

Persistent Homology



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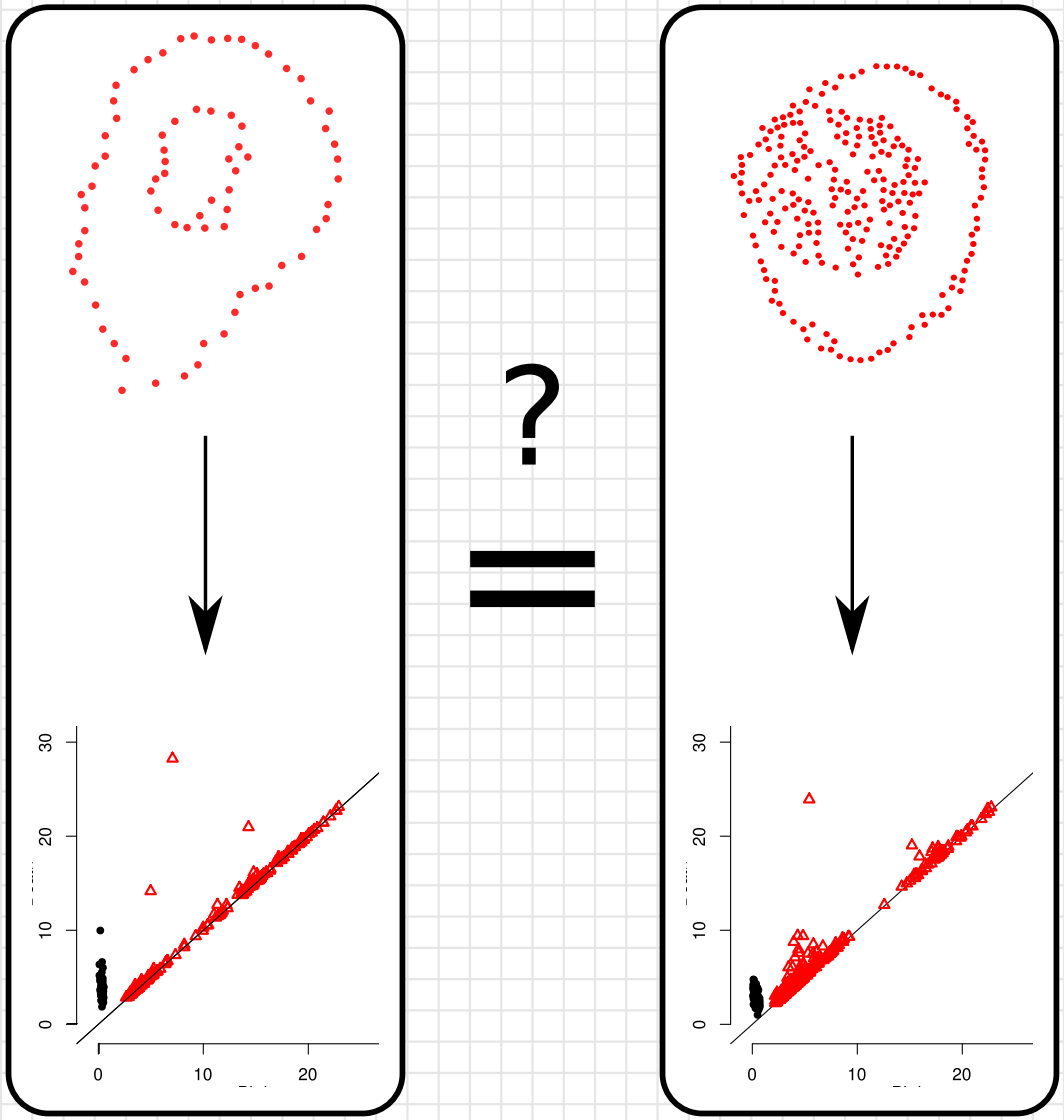
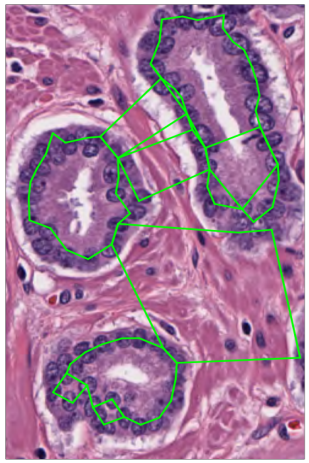


Quantifying the Process

TDA



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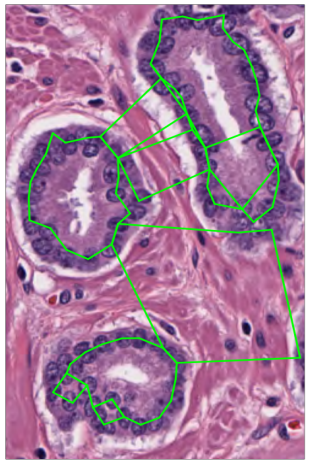

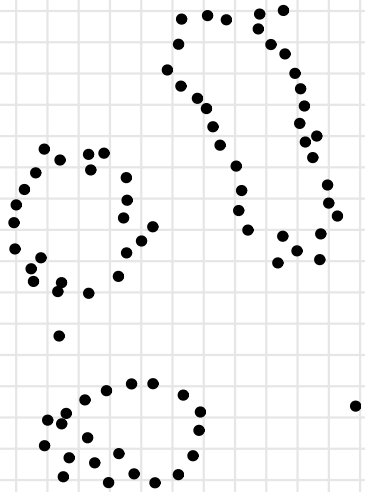

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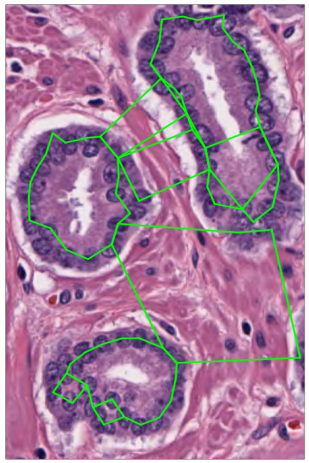

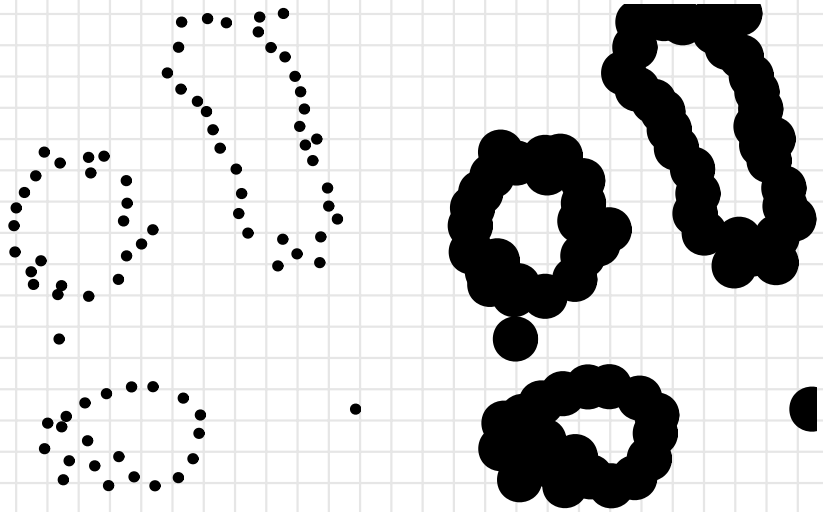

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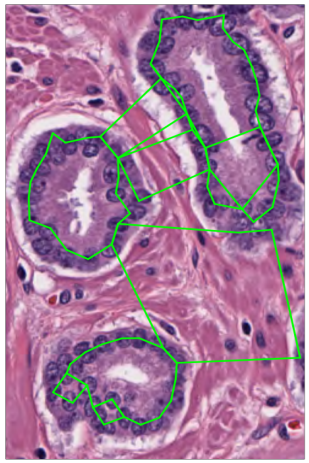

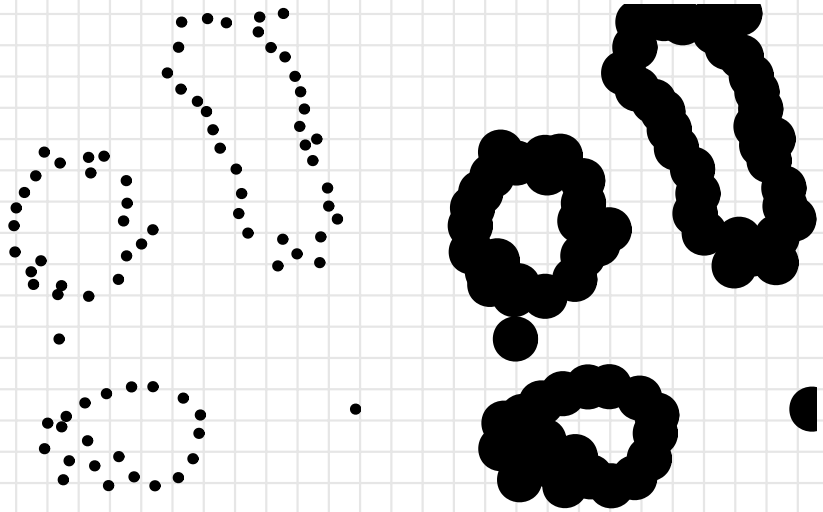

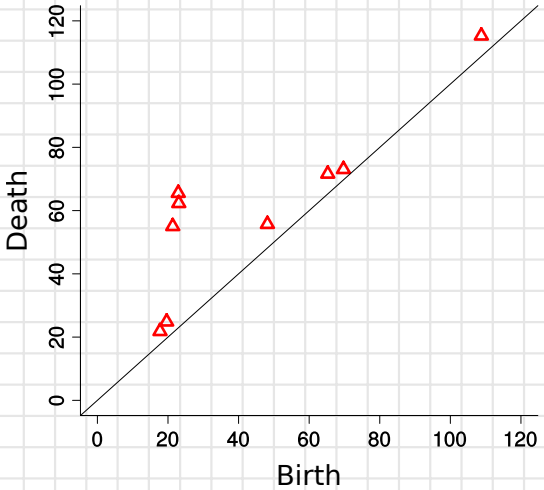

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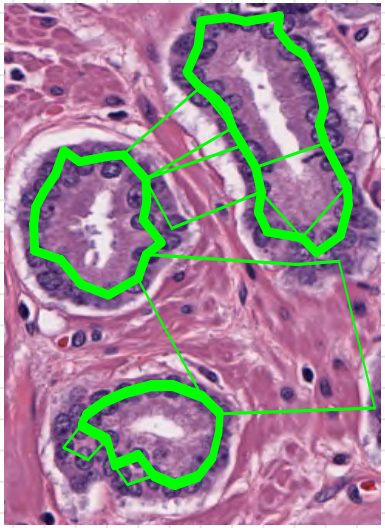

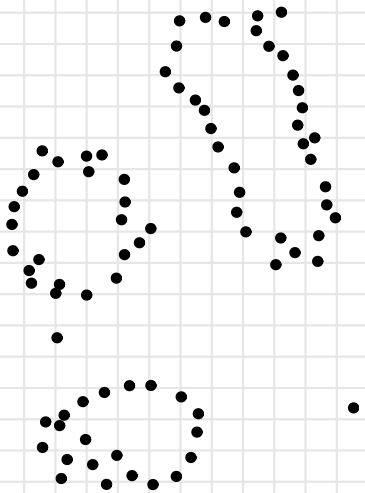

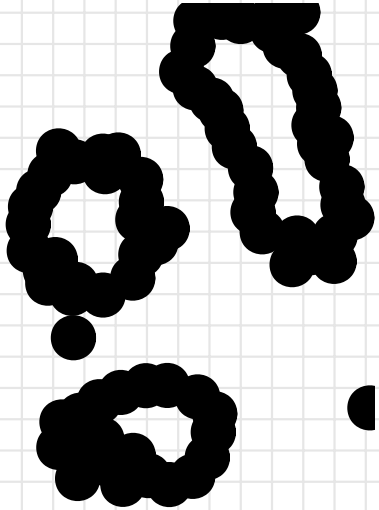

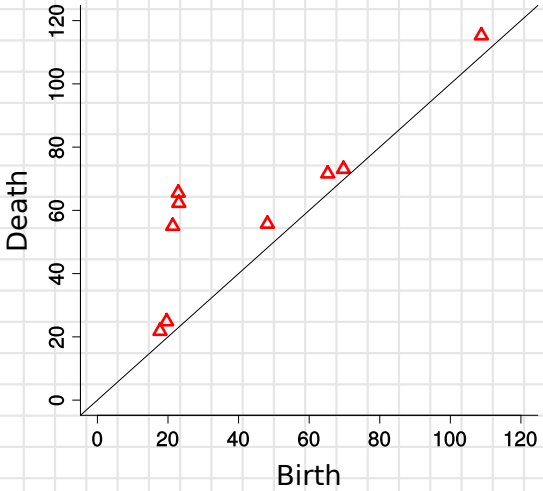

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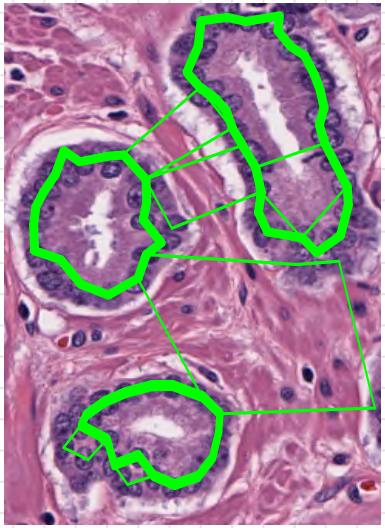

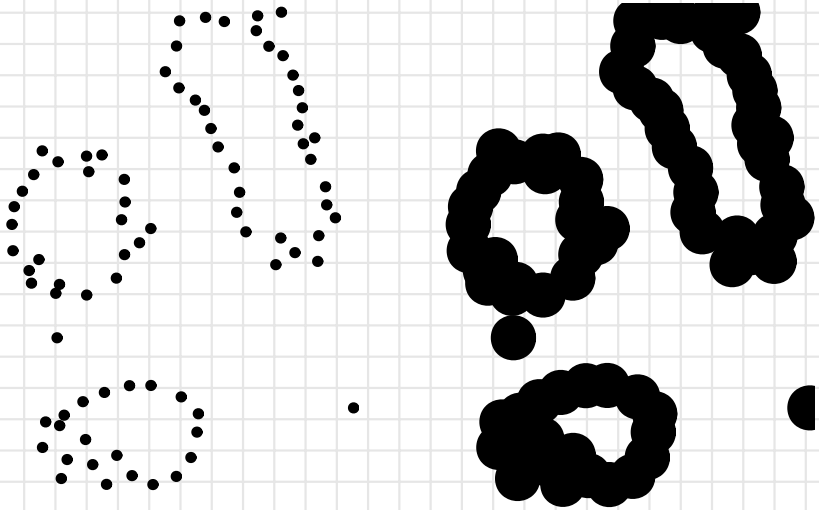

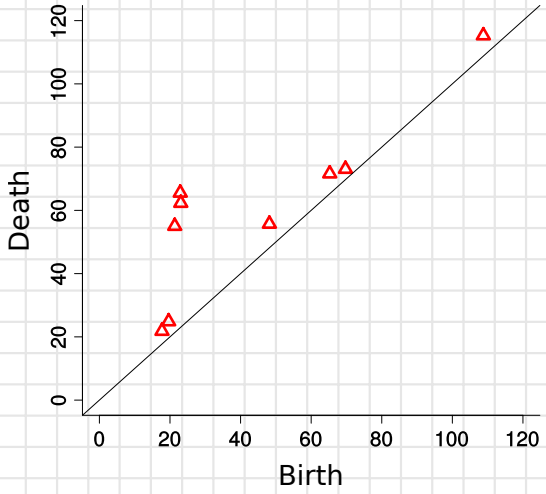

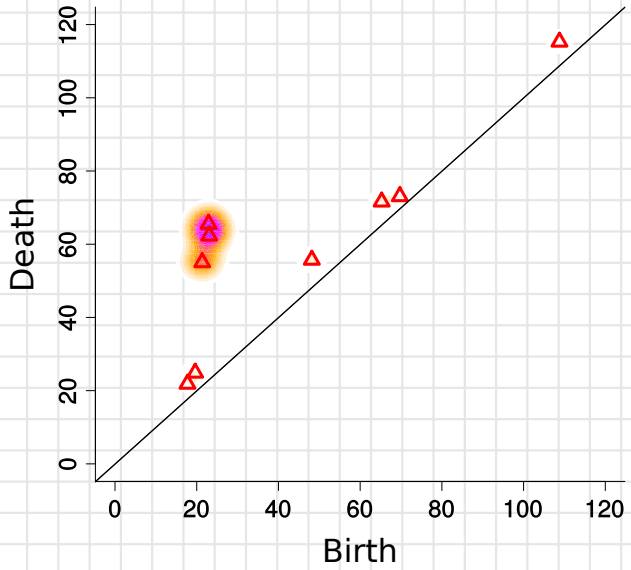

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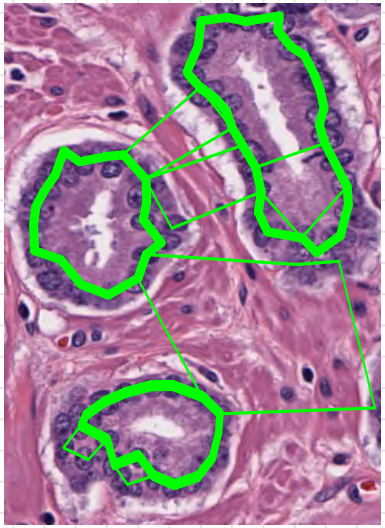
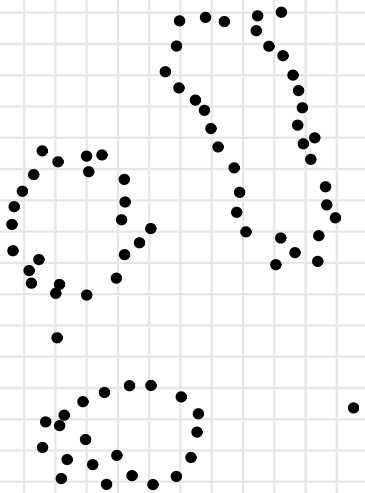
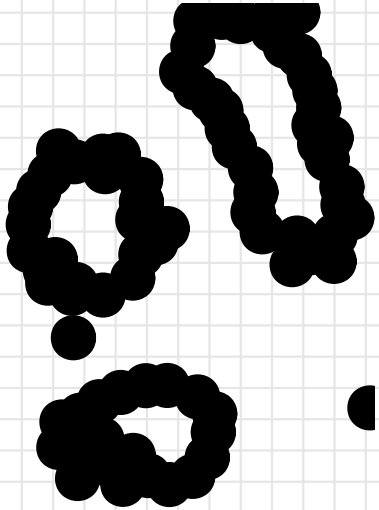
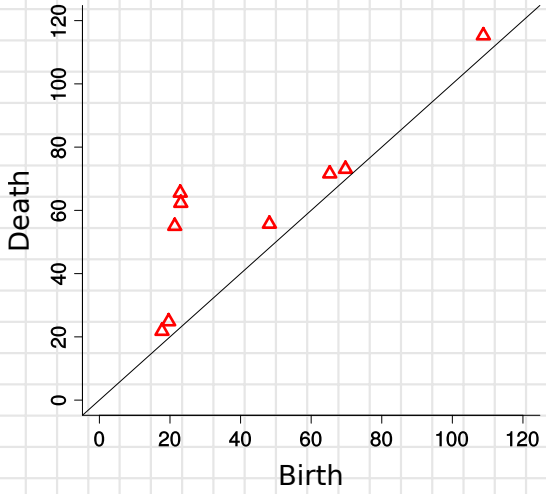
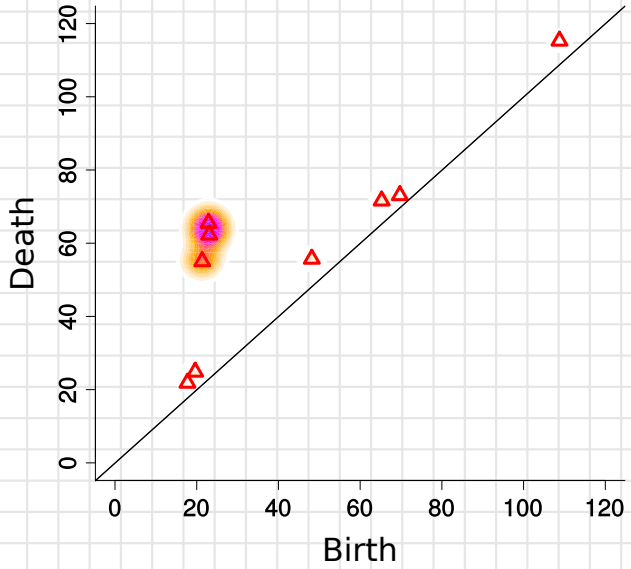
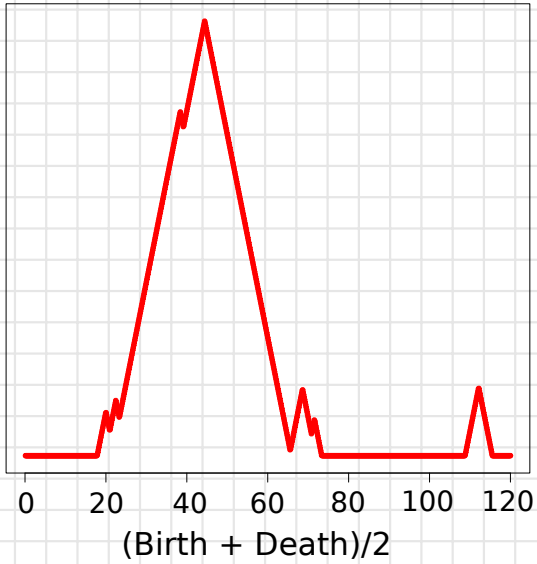




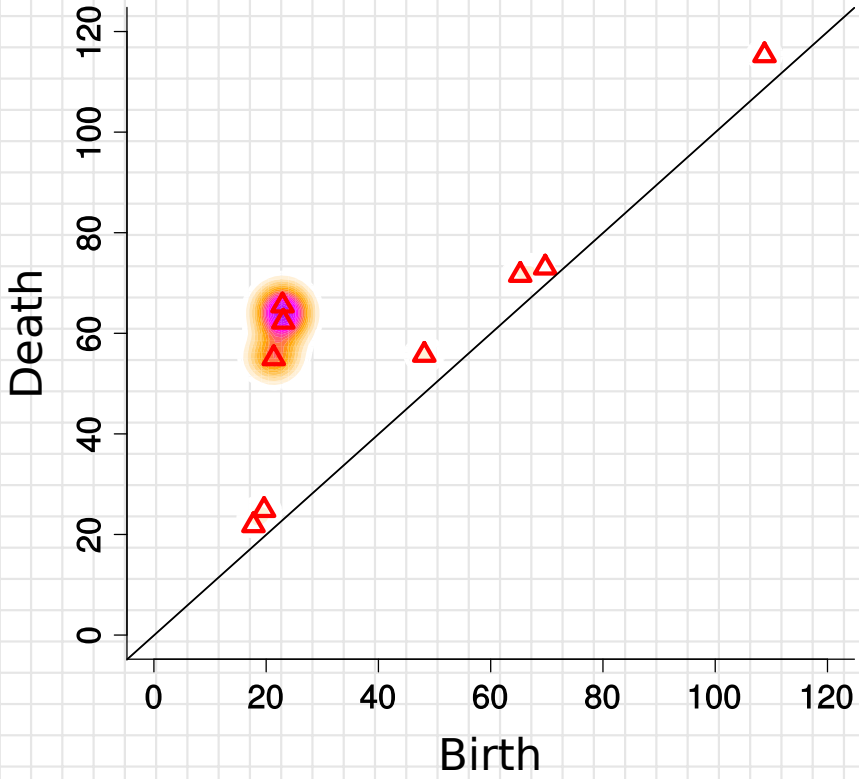


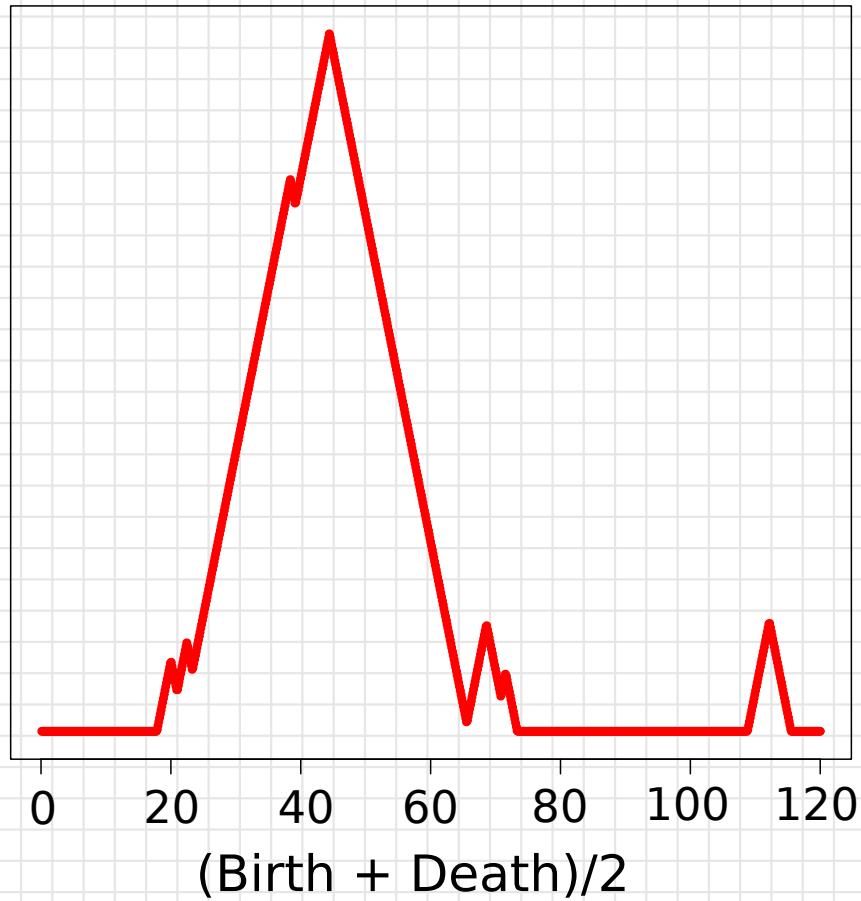






Functional and Vectorized Summaries





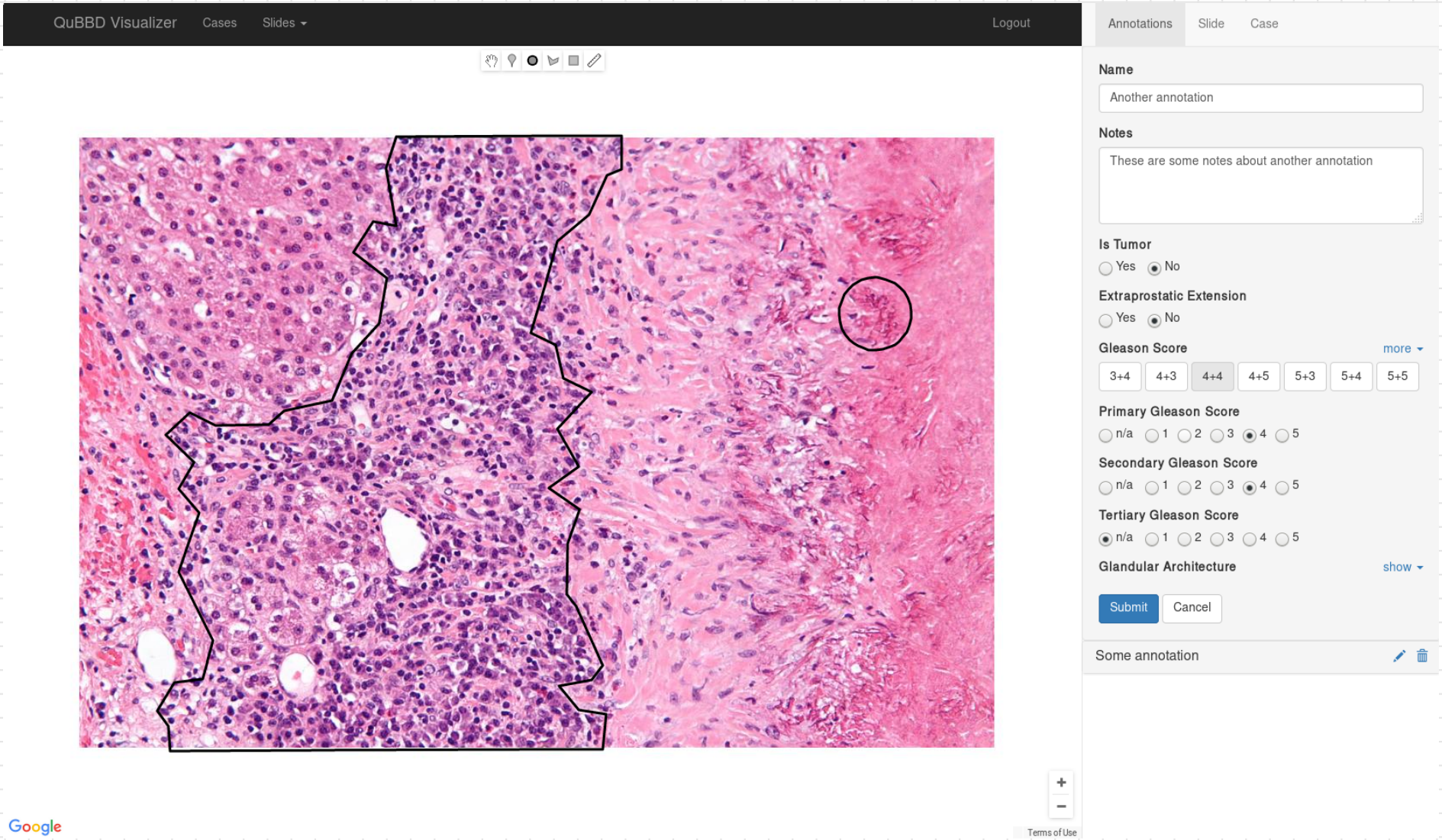
Aside: Hypothesis Testing

Upcoming Paper

The *Euler Characteristic* curve seems to be the most discriminating among the functional summaries when using the Hotelling Test[a].

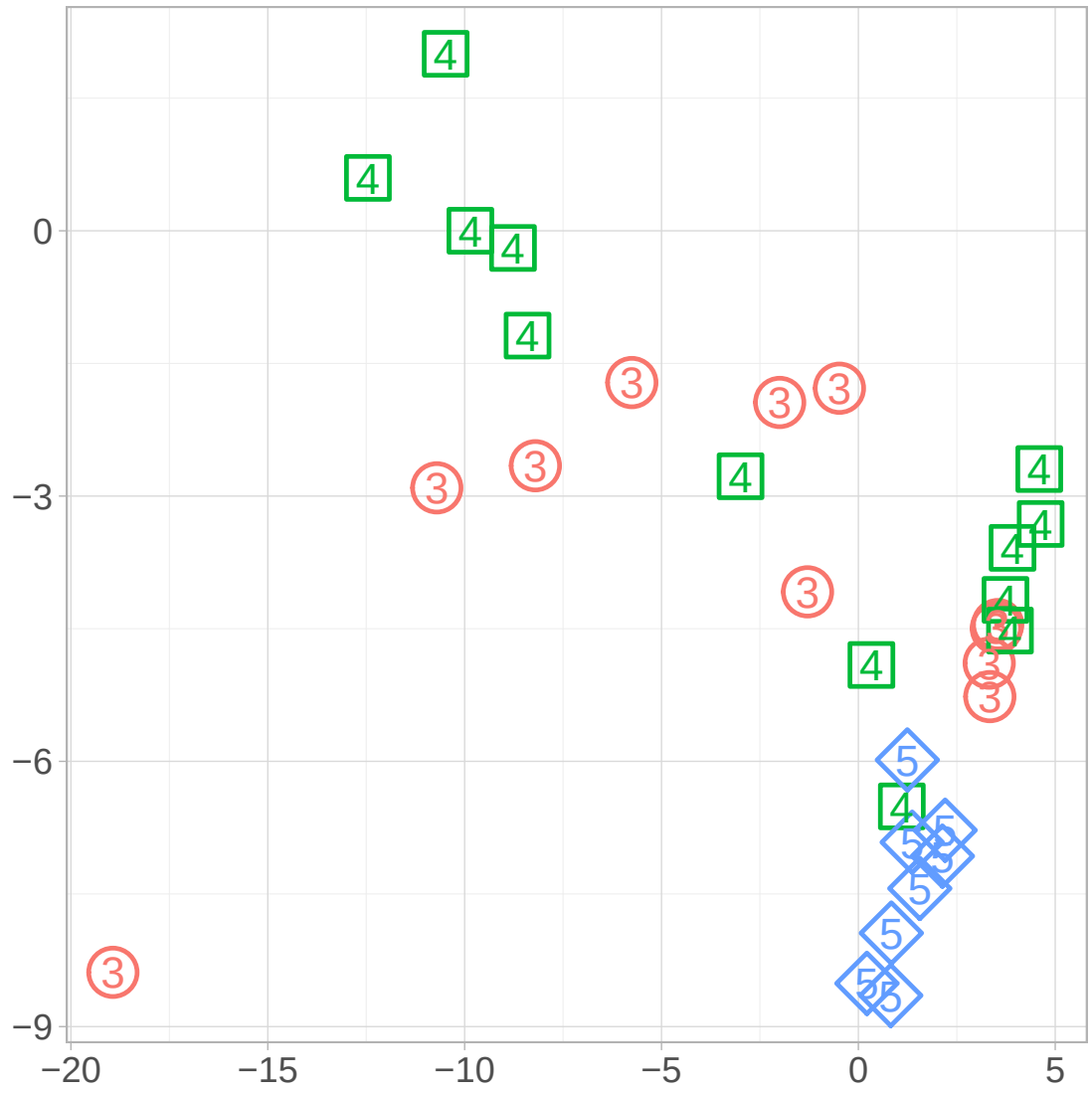
[a] Joint work with Jessi Cisewski, Wojciech Hellwing, Mark Lovell, Alessandro Rinaldo, Larry Wasserman, Mike Wu

Collaboration



Comparing Purely Graded Images

Initial Results



Analyzing DeBruijn Graphs

Joint work with Alan Cleary and Brendan Mumey

CTGAACAGCTAGCAGTAGTGTAGGG

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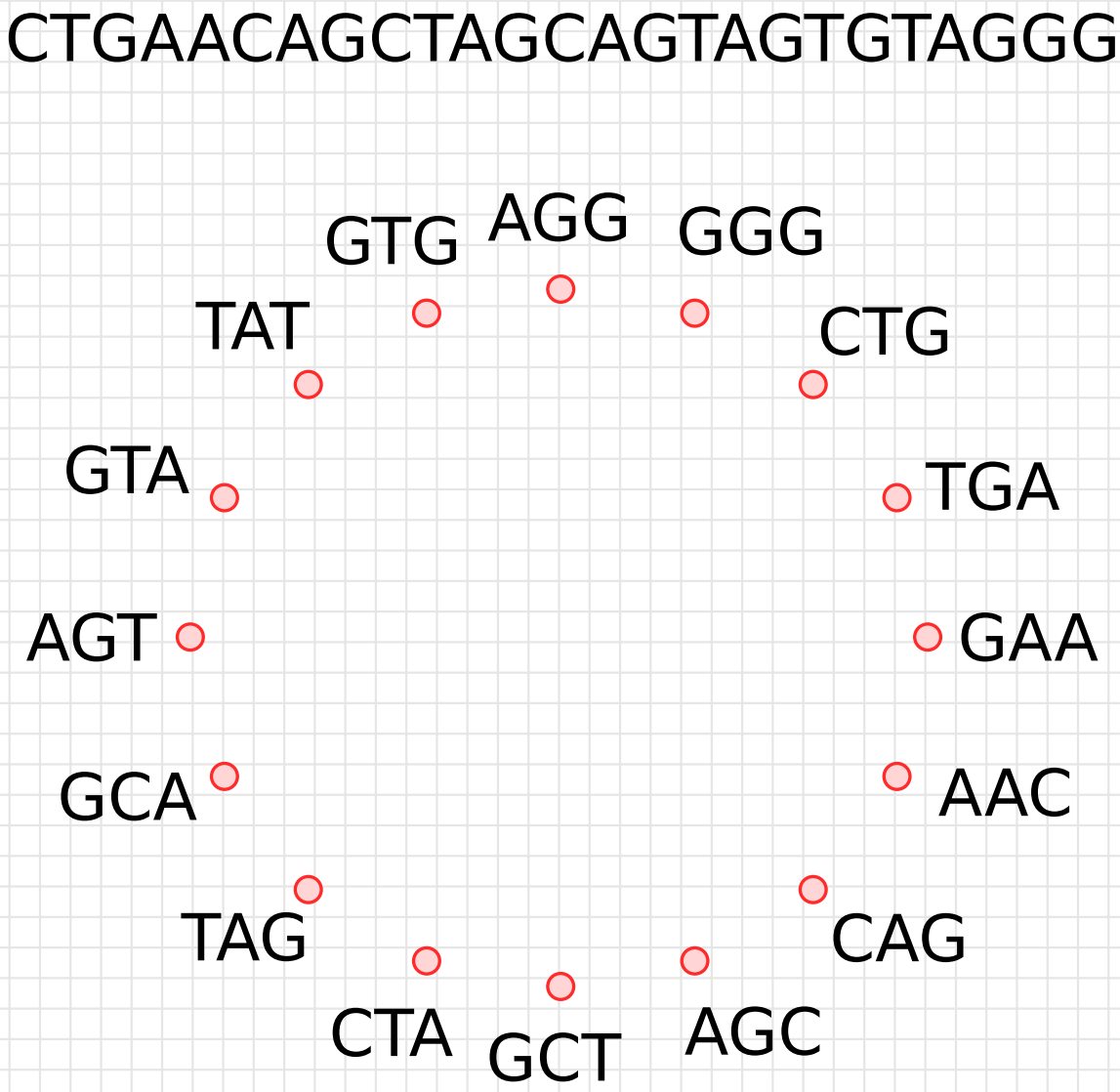

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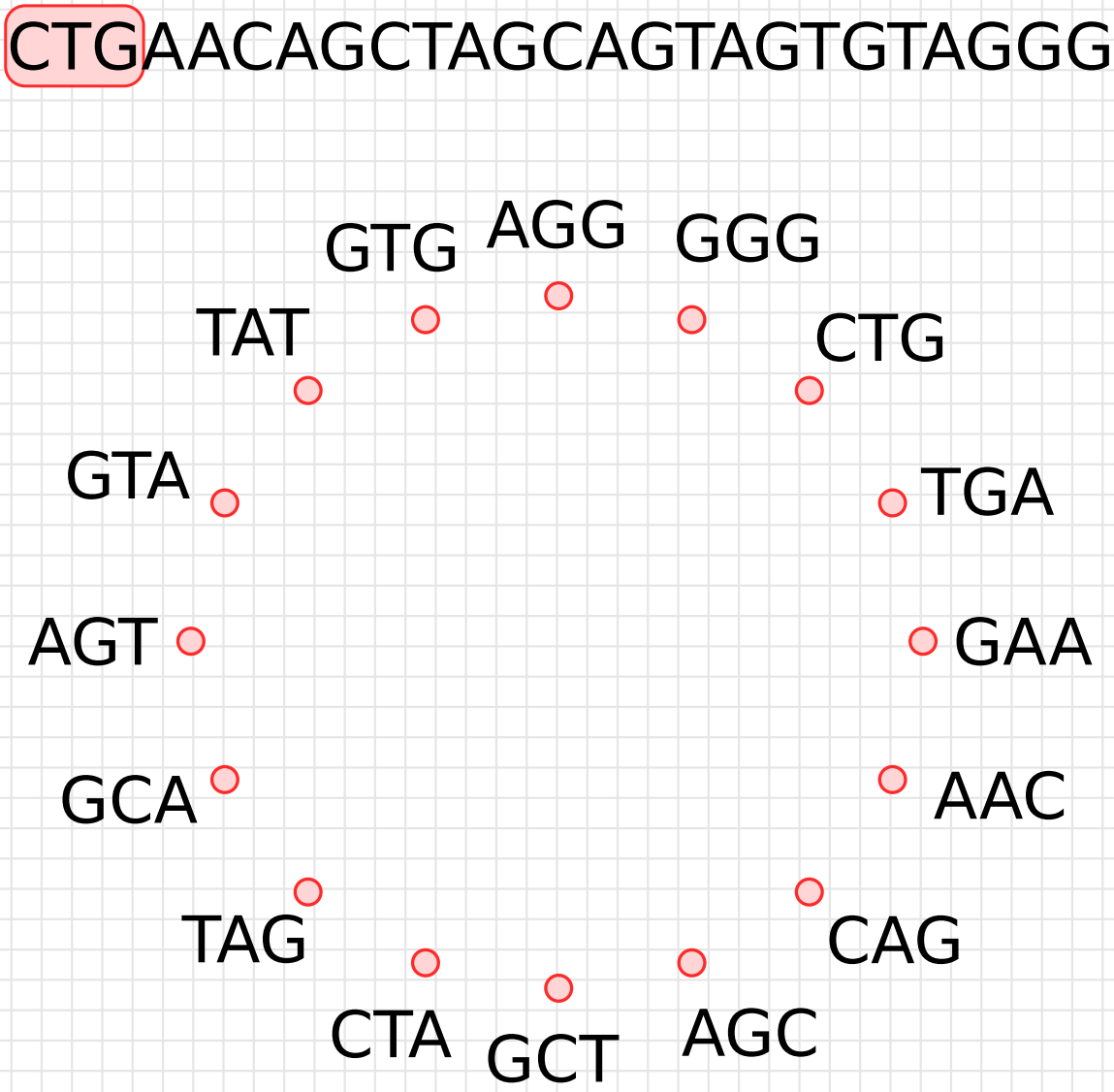

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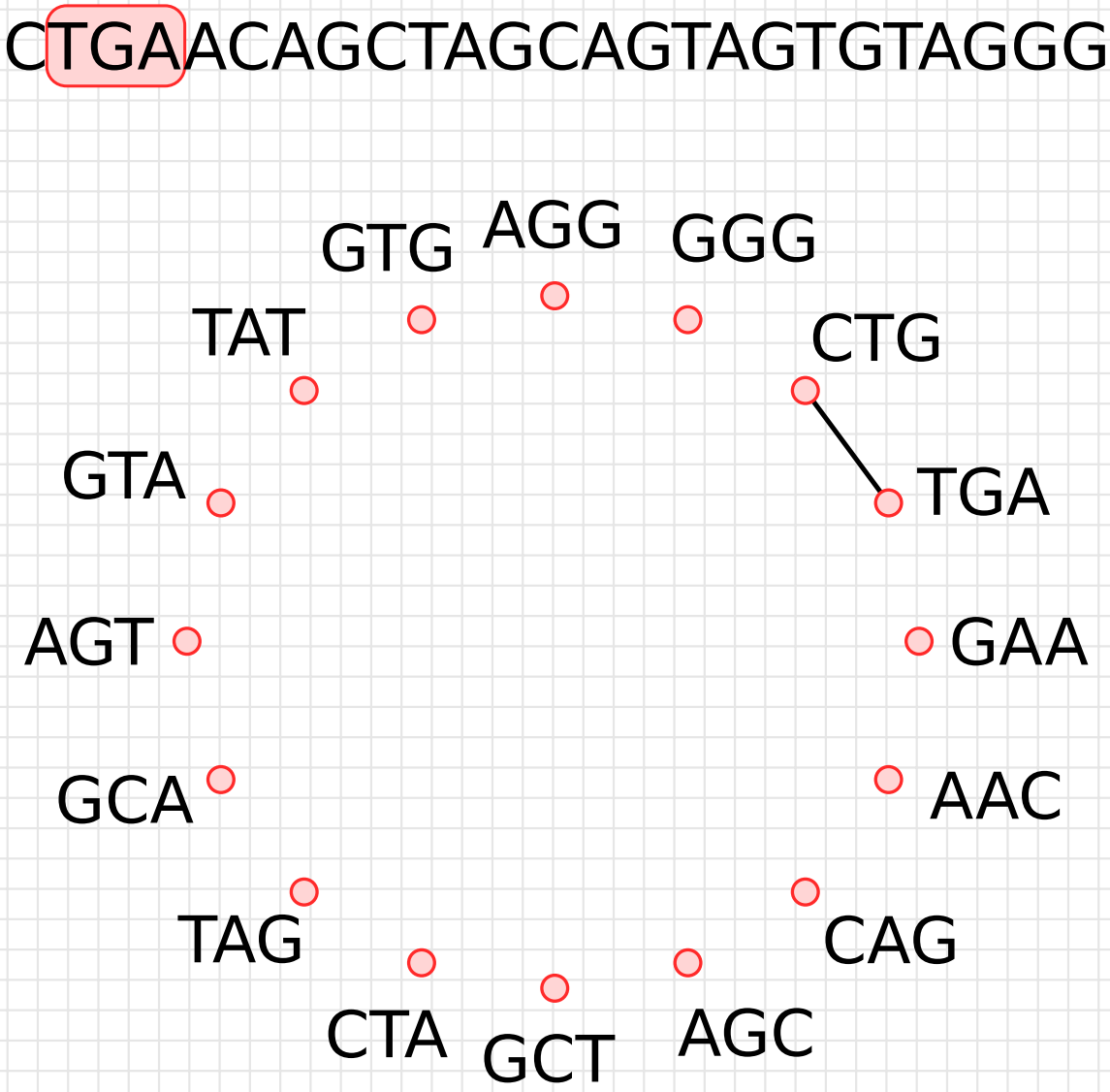

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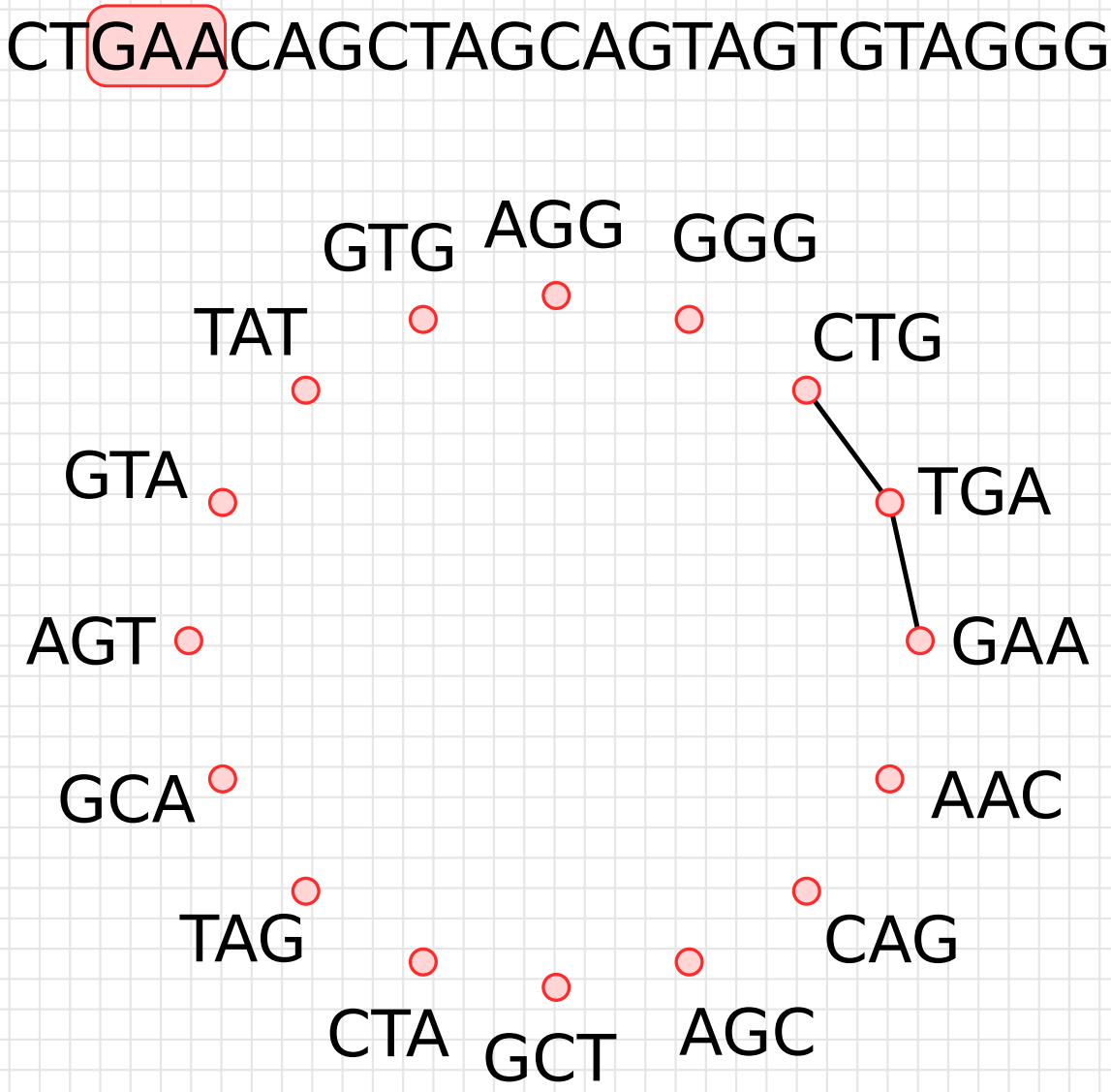
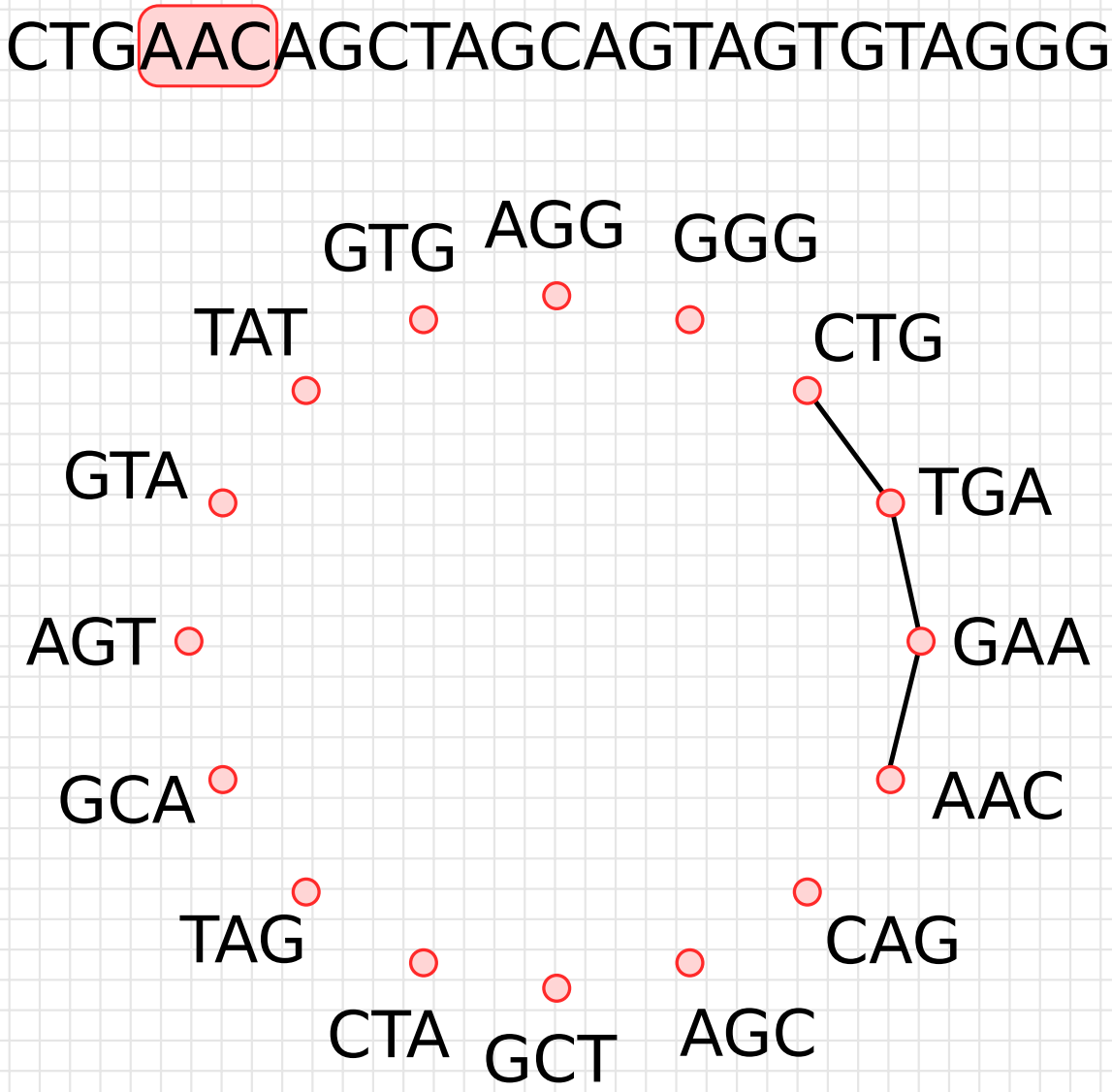


Analyzing DeBruijn Graphs

Joint work with Alan Cleary and Brendan Mumey



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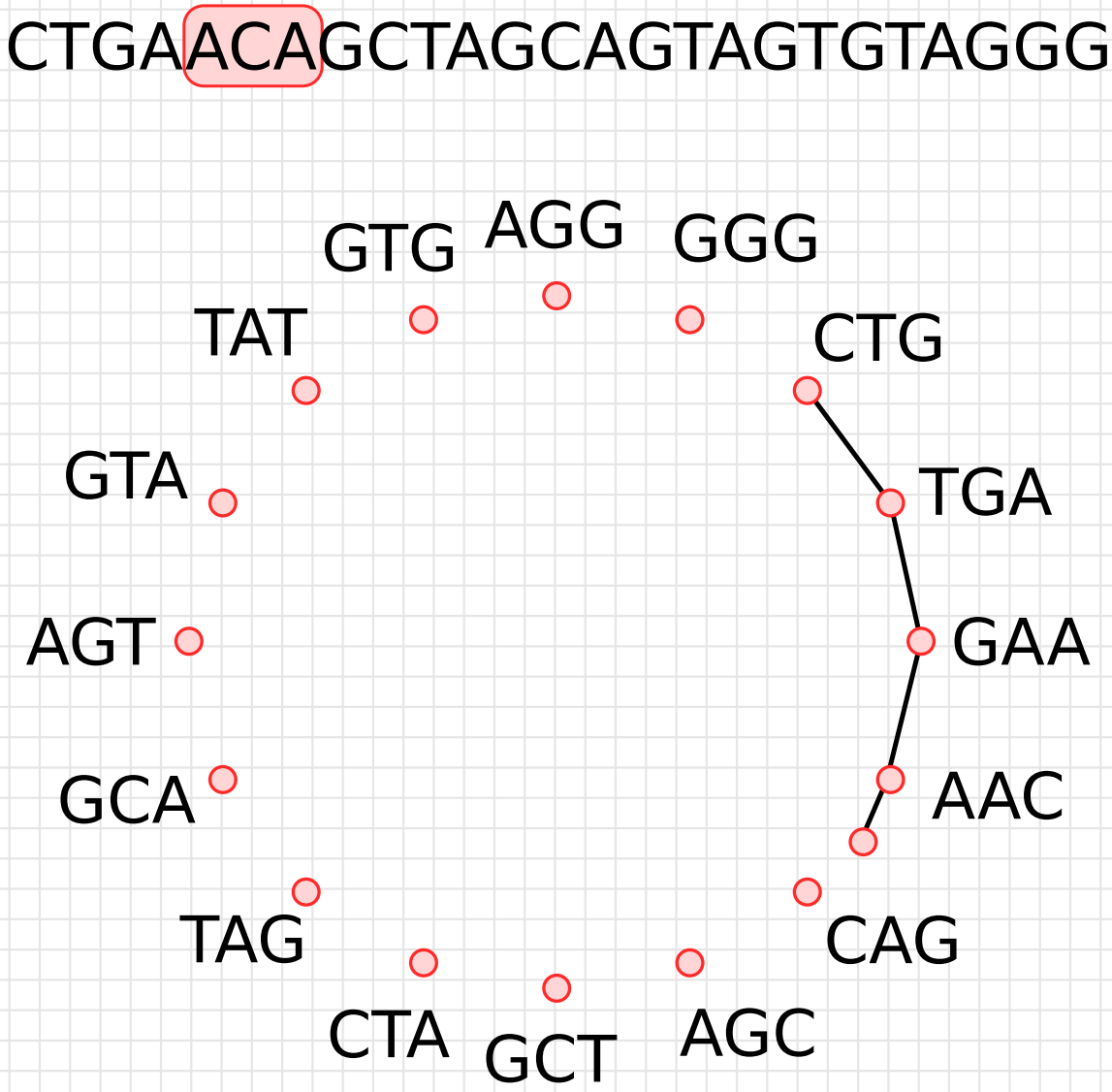

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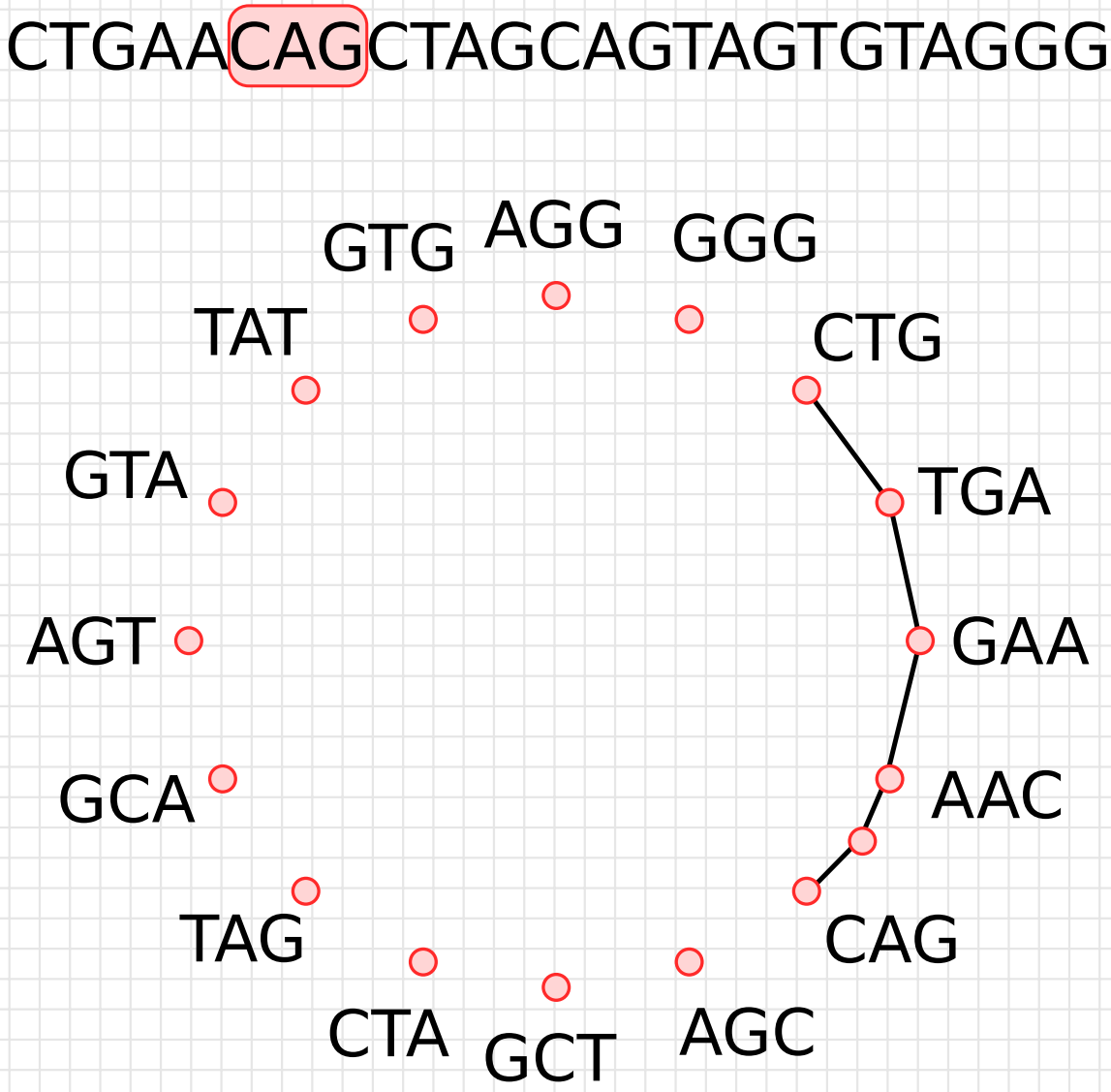

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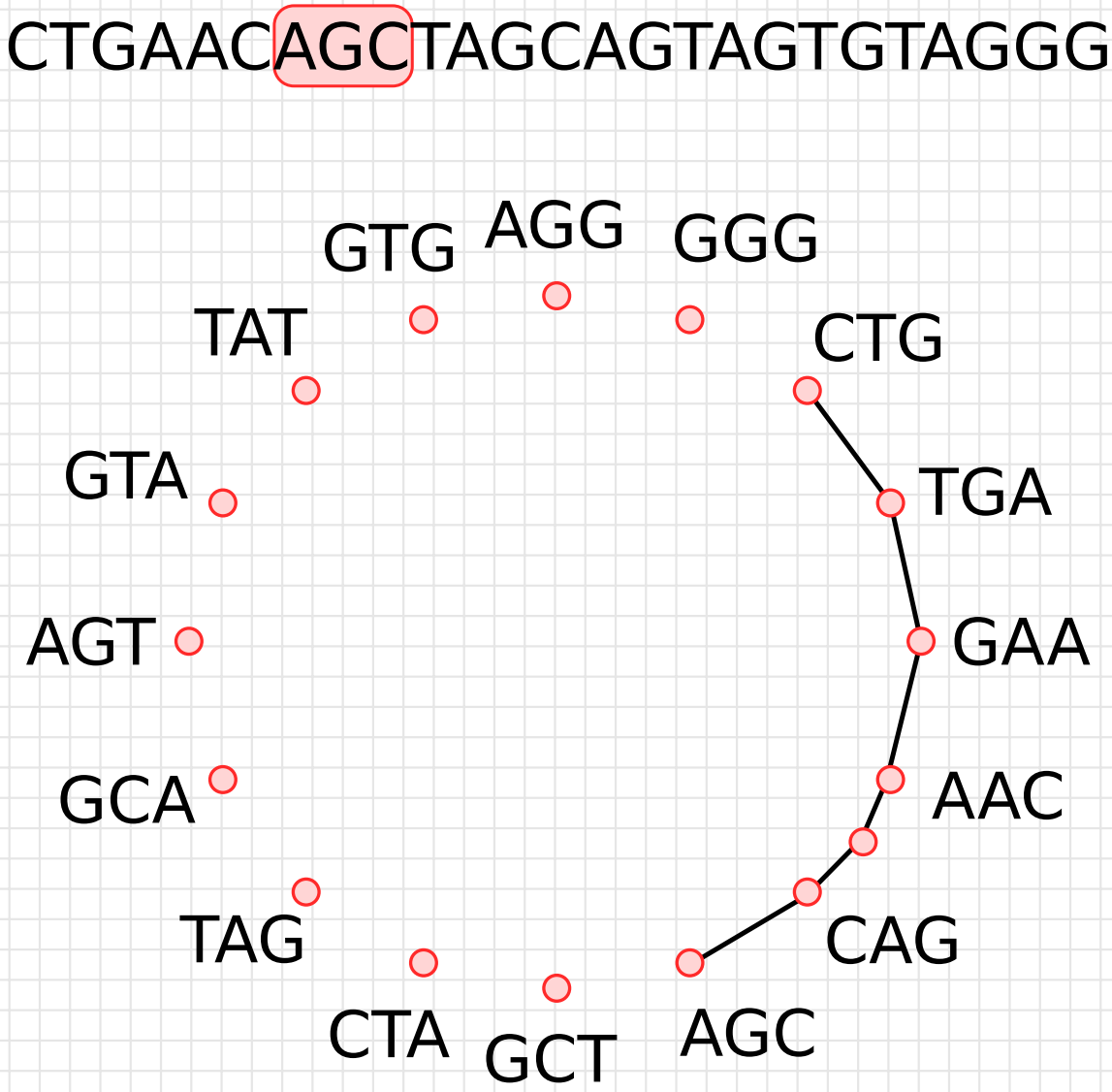

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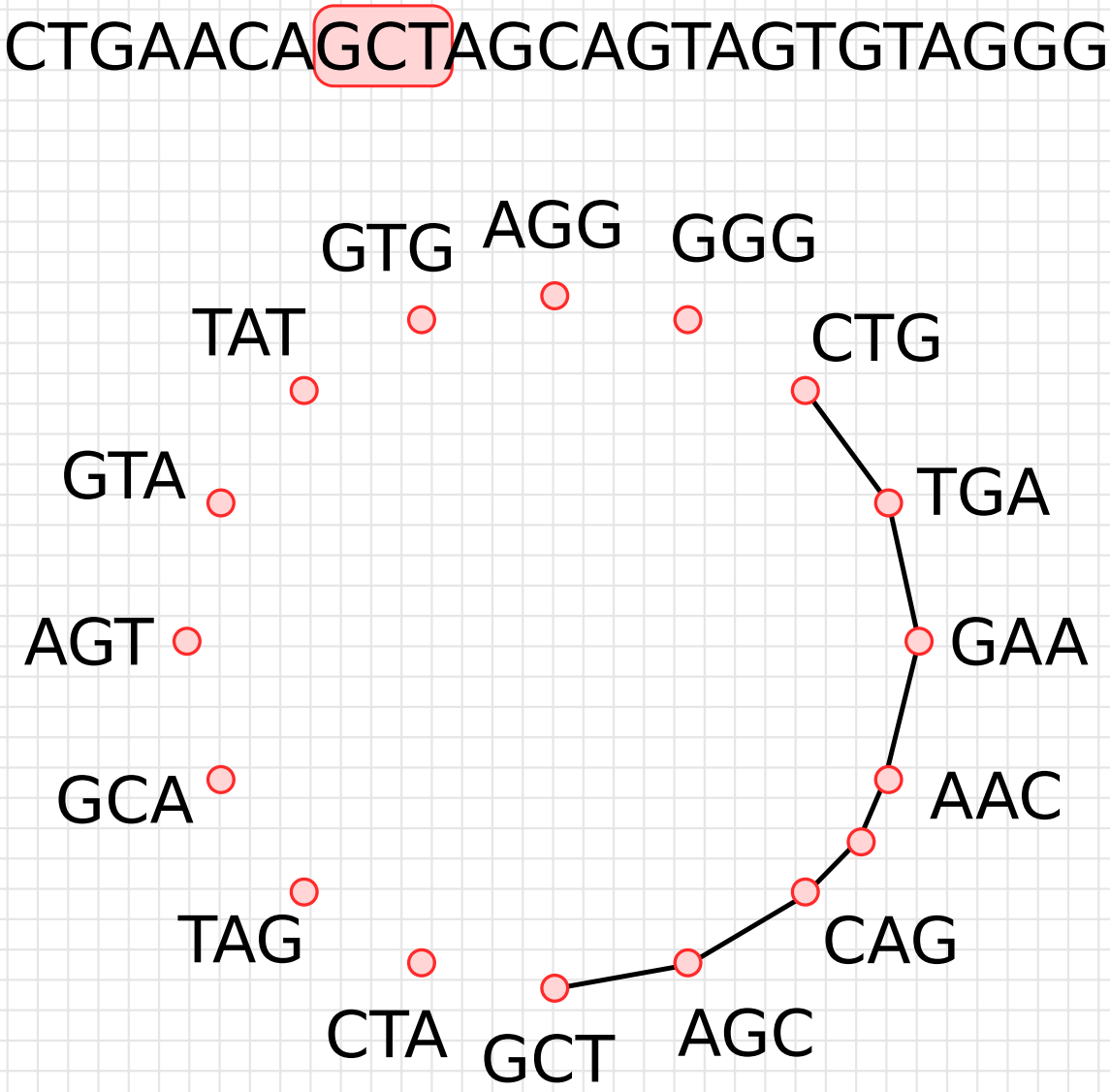

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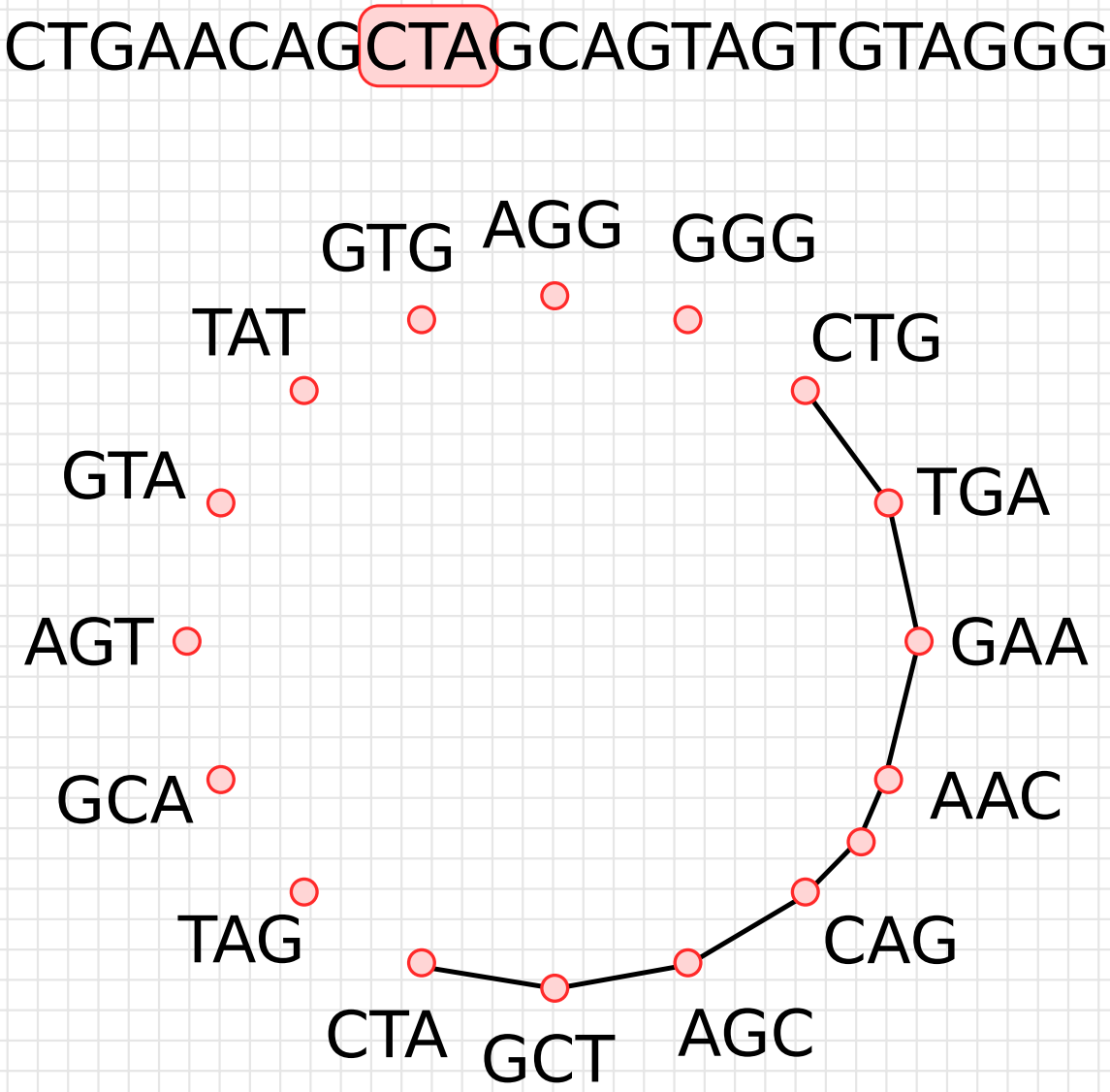

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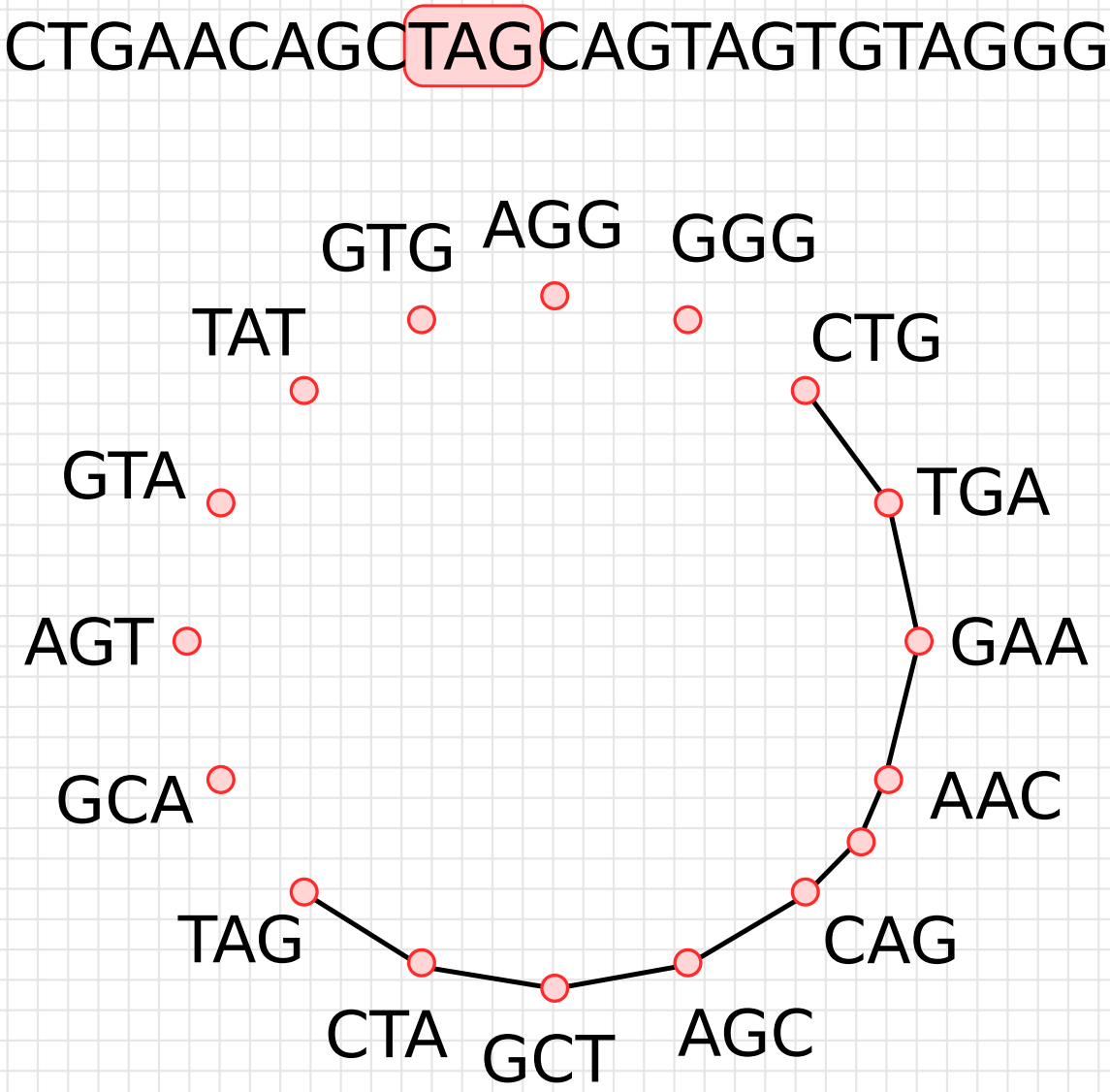

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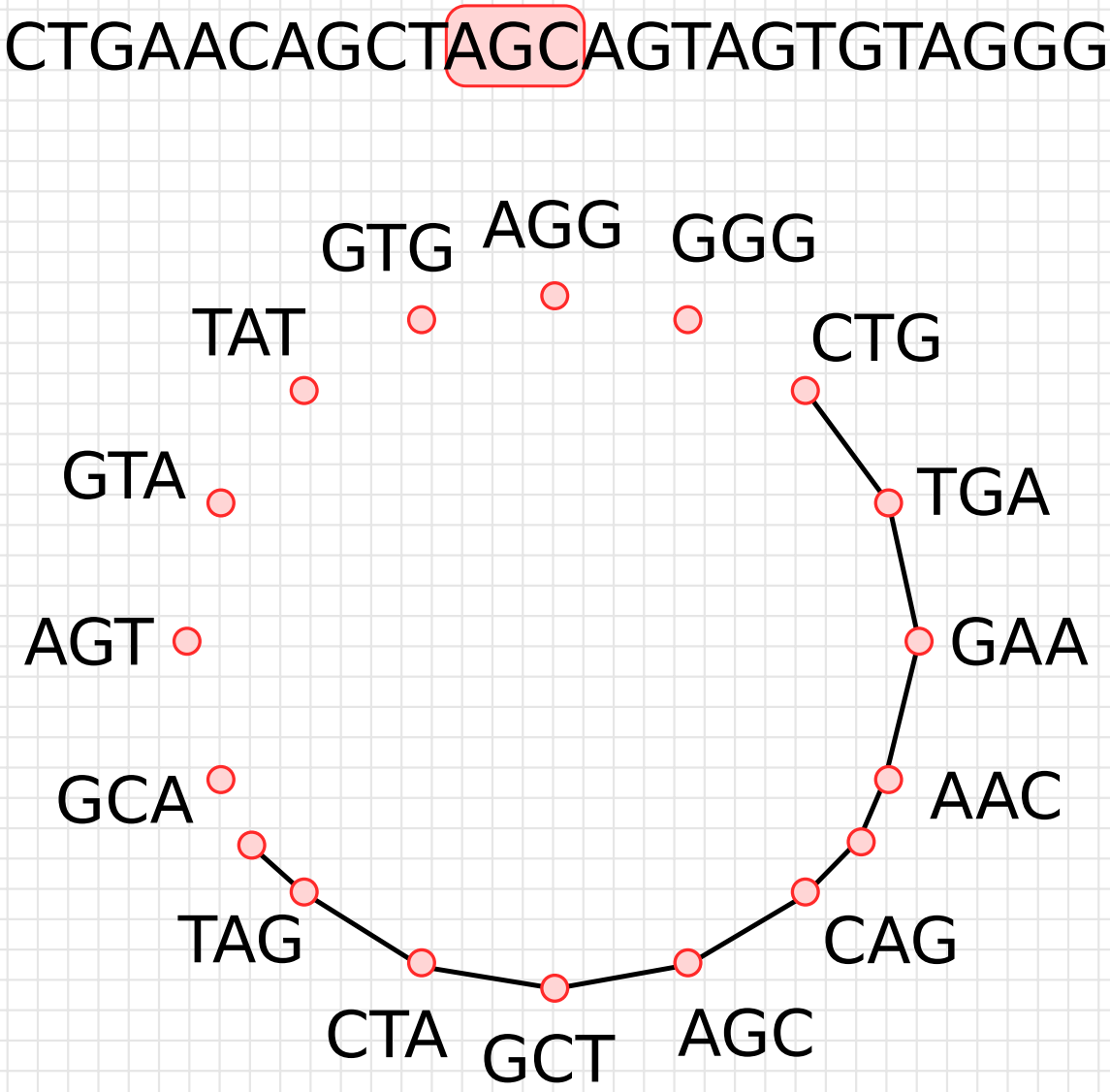

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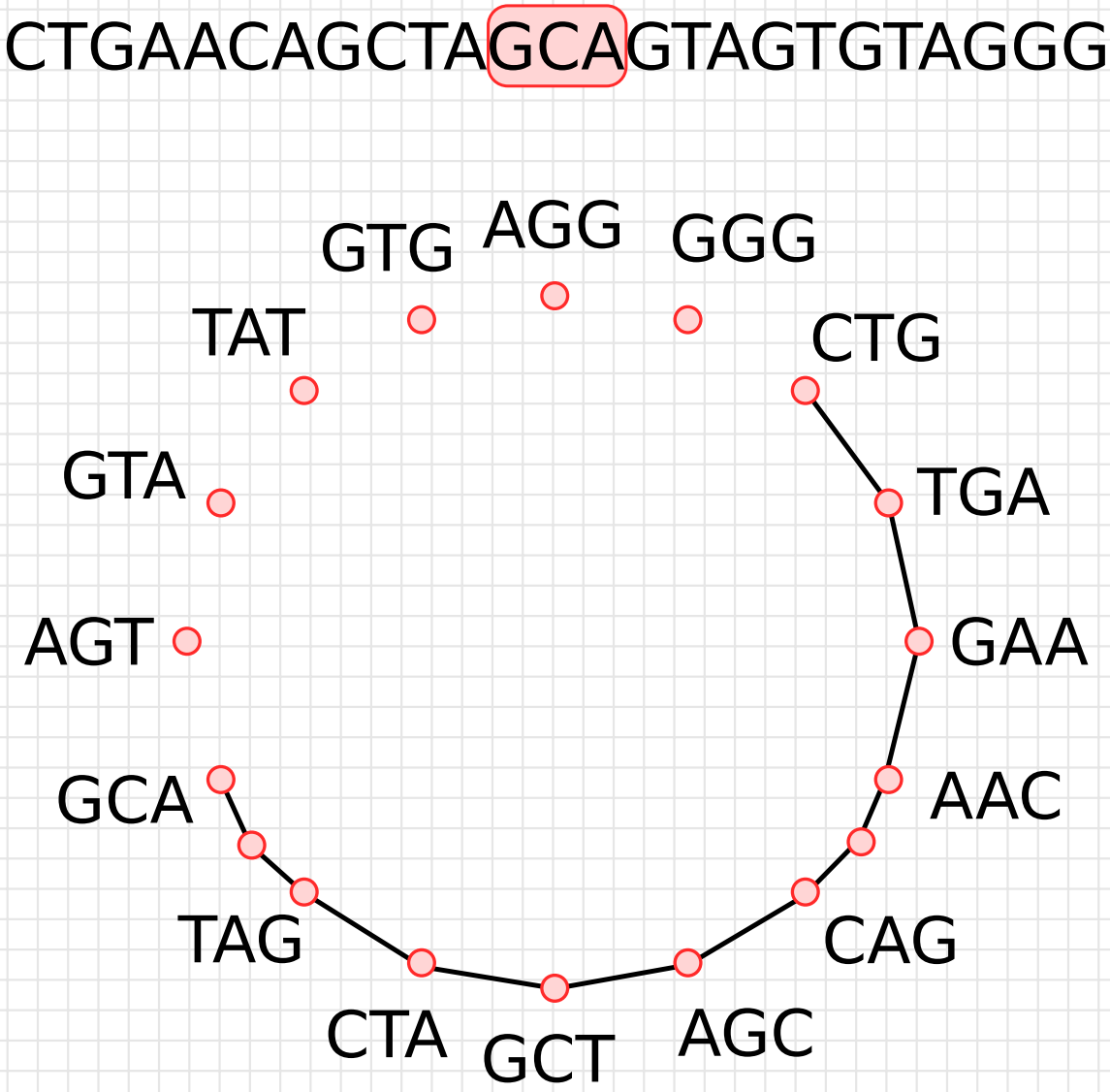

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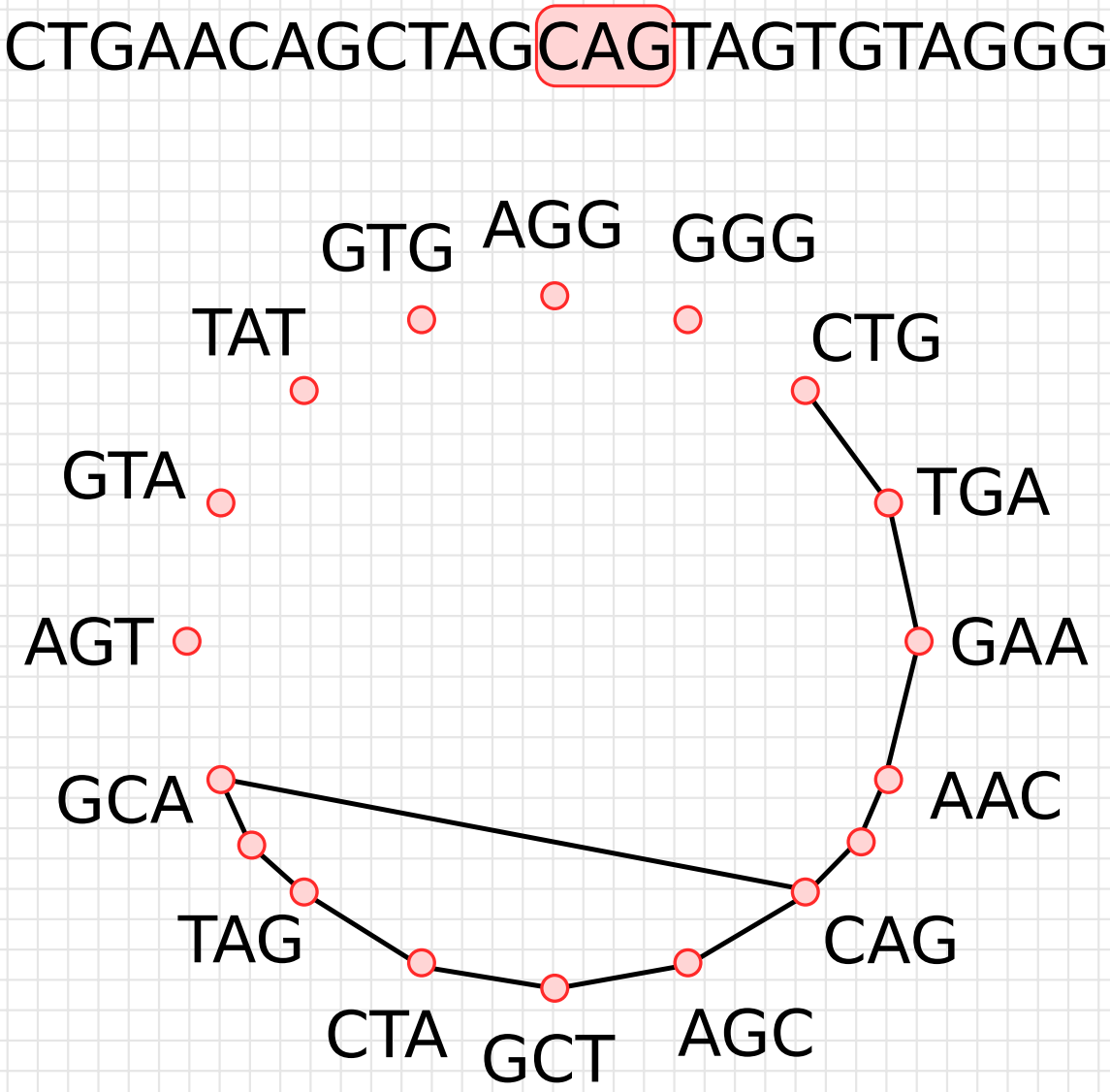

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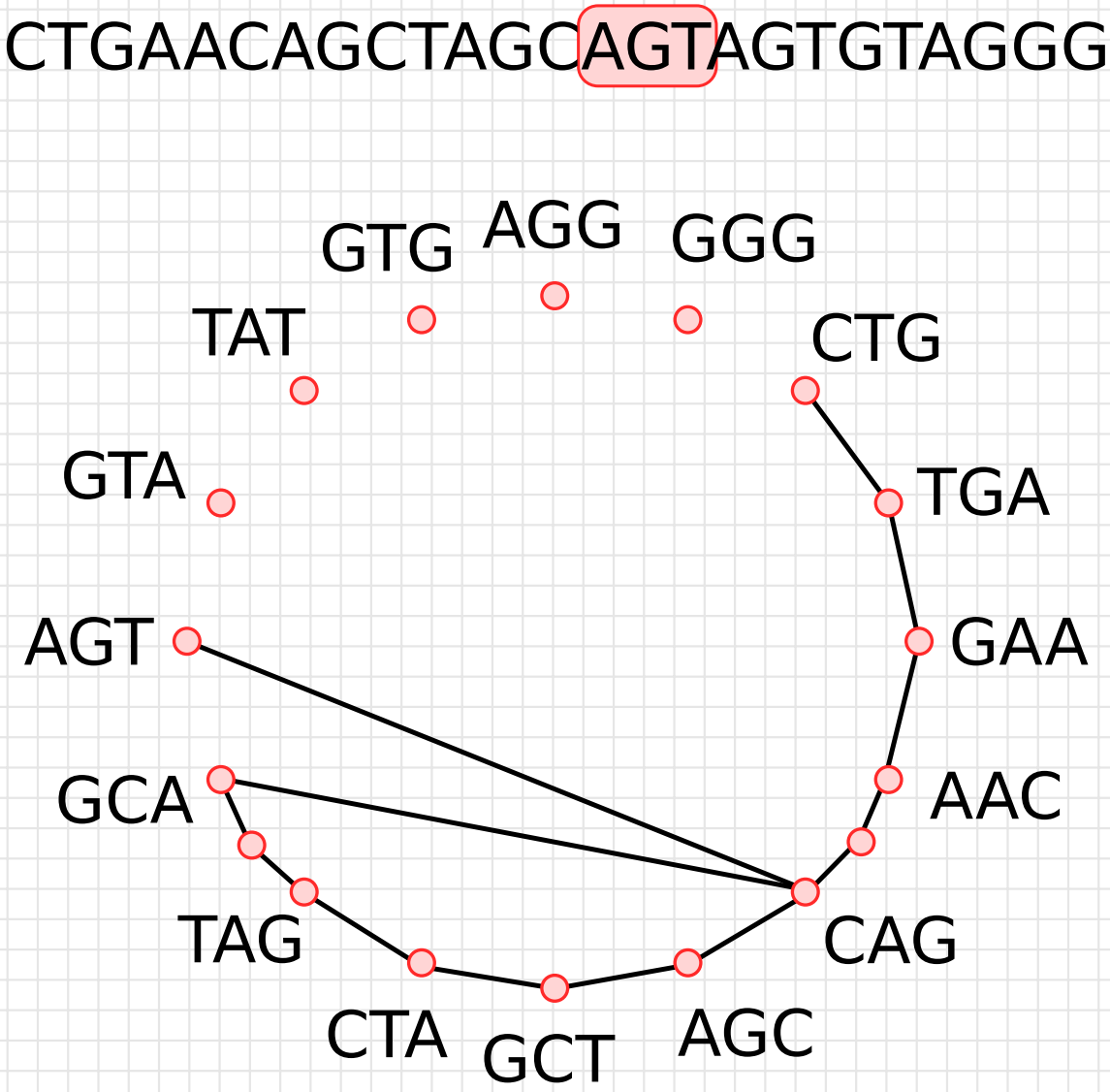

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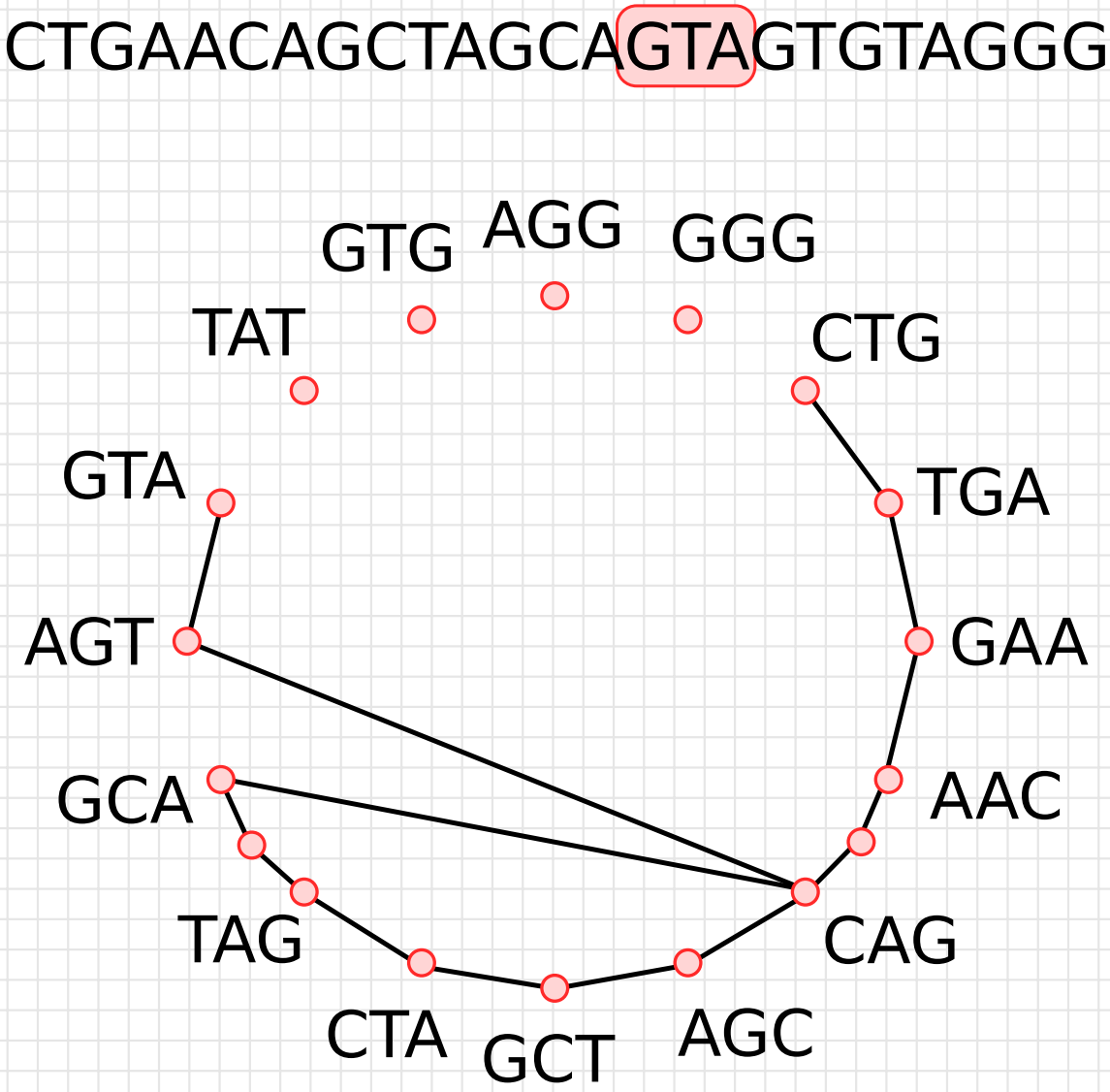

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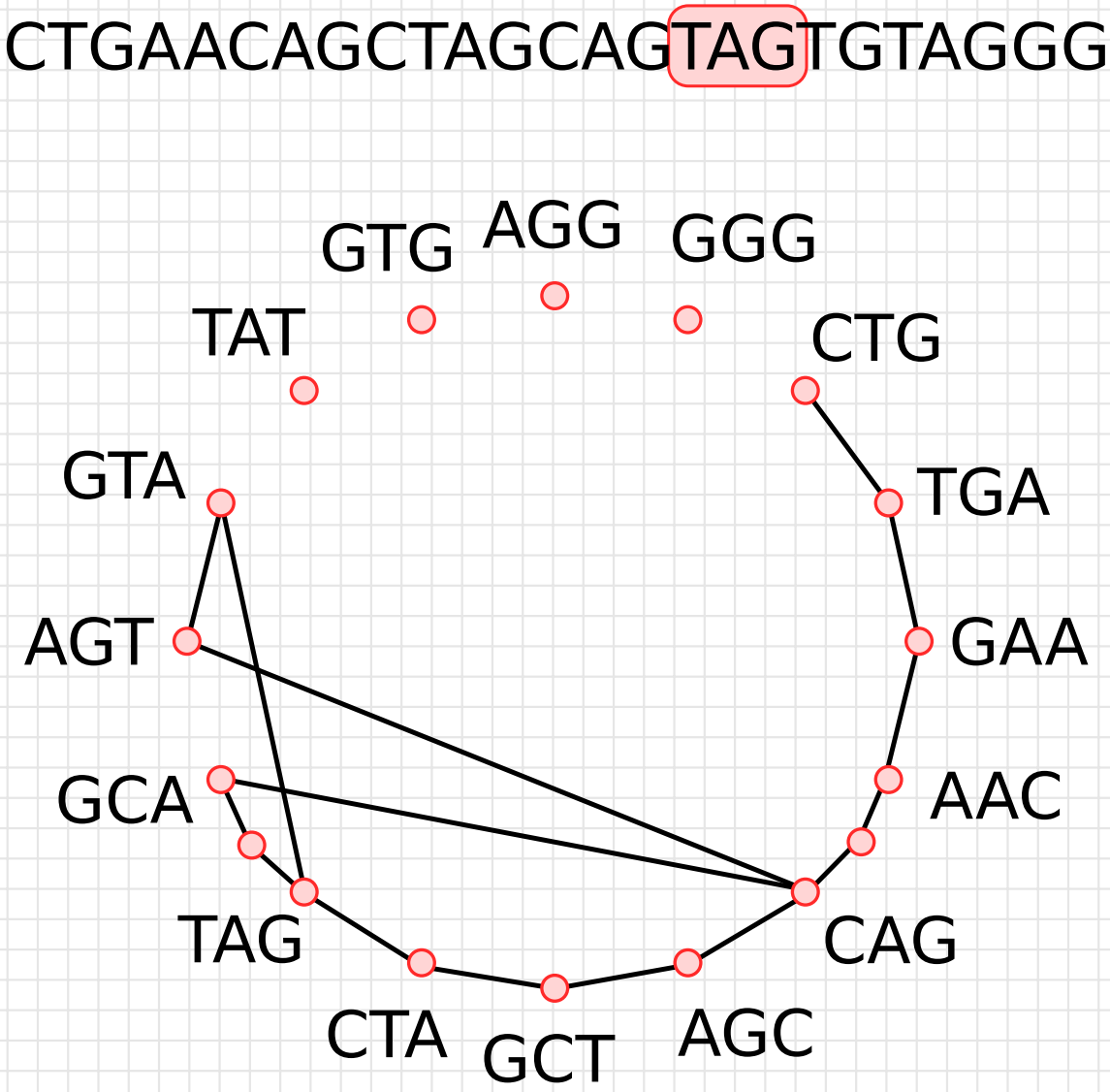

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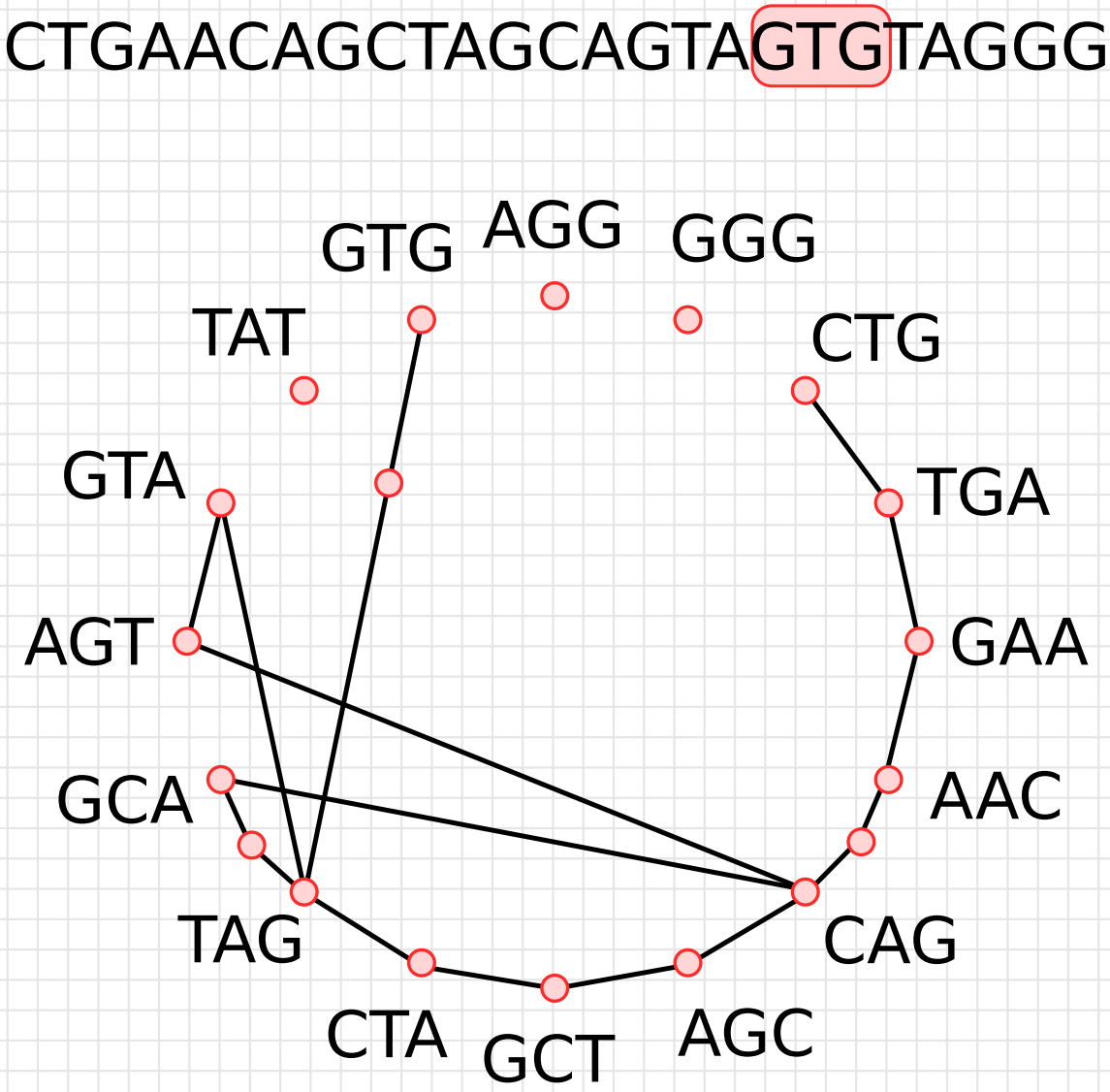

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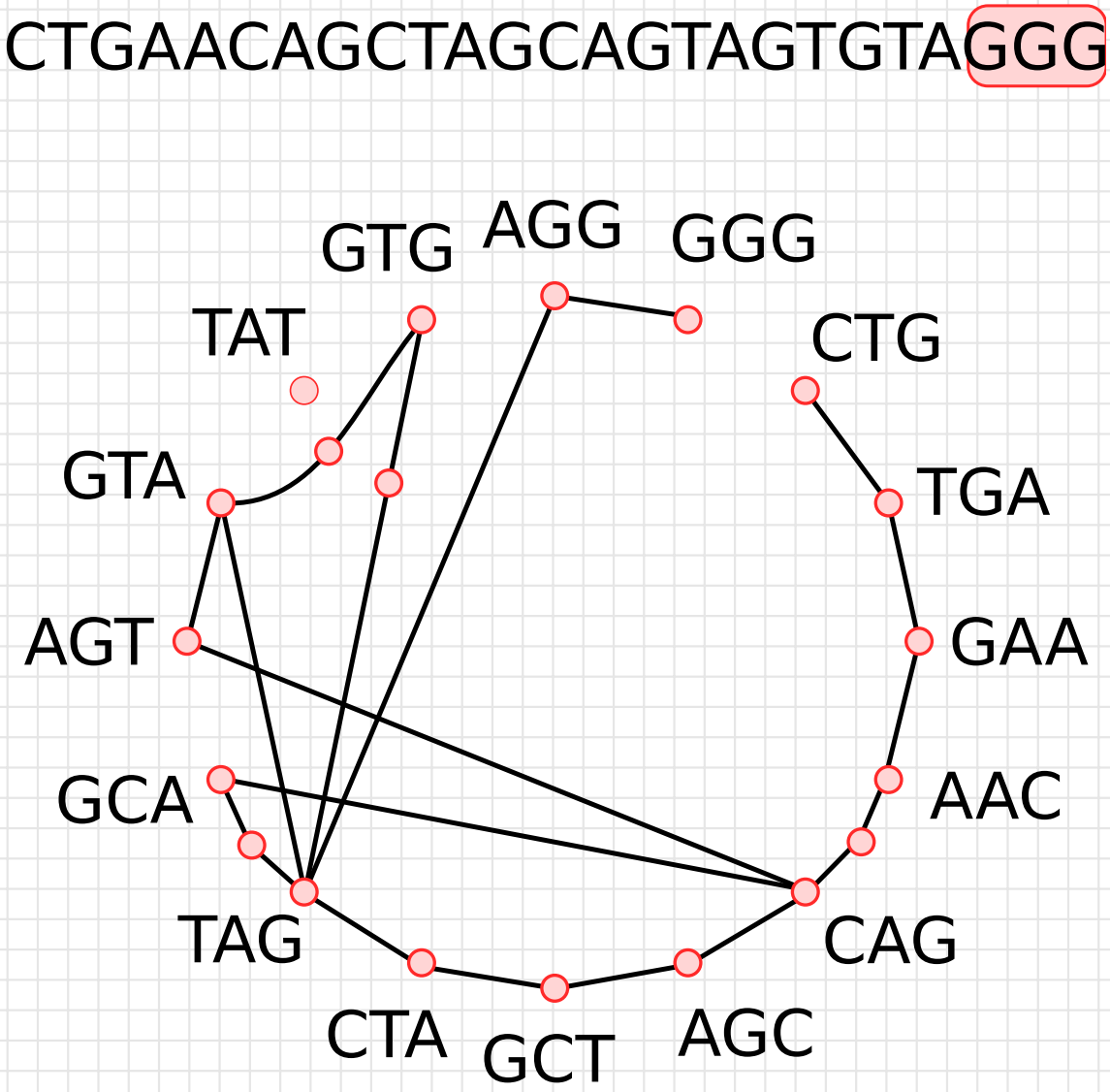

Bubbles in DeBruijn Graphs

[0]Nature article: *De Novo Assembly and Genotyping of Variants using Colored De Bruijn Graphs* by Iqbal, Caccamo, Turner, Flicek, McVean

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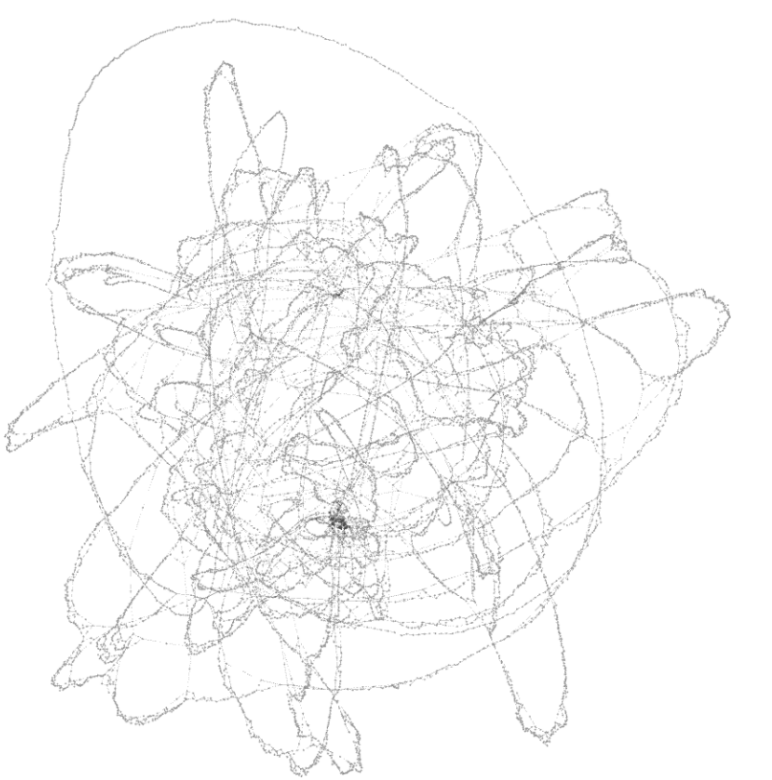

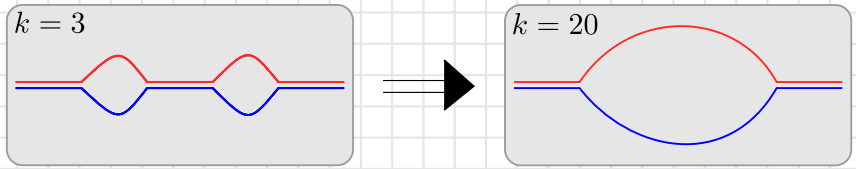

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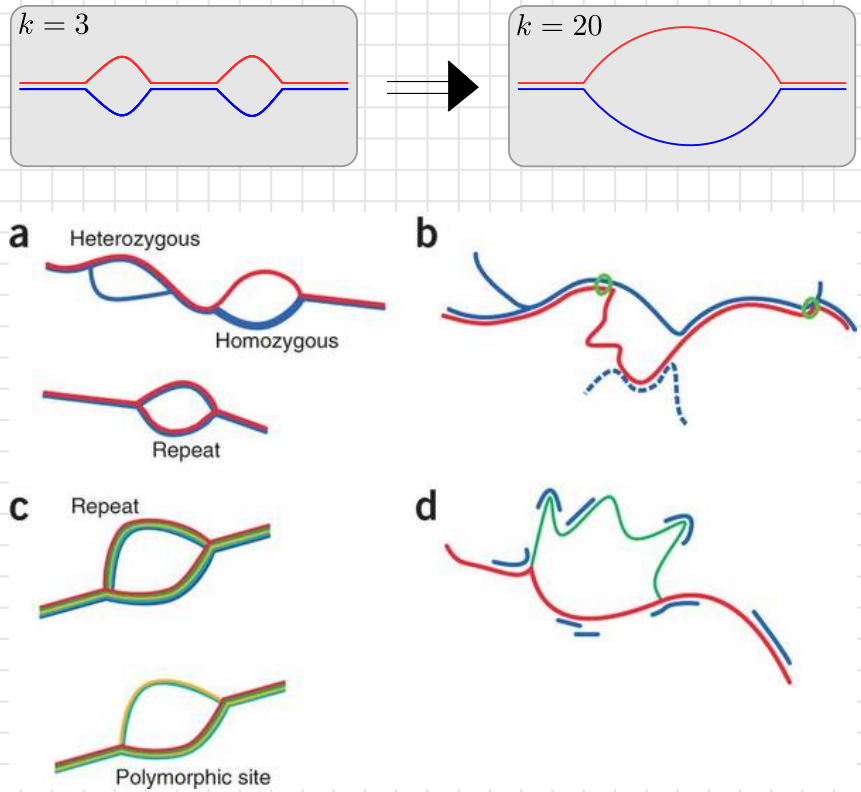

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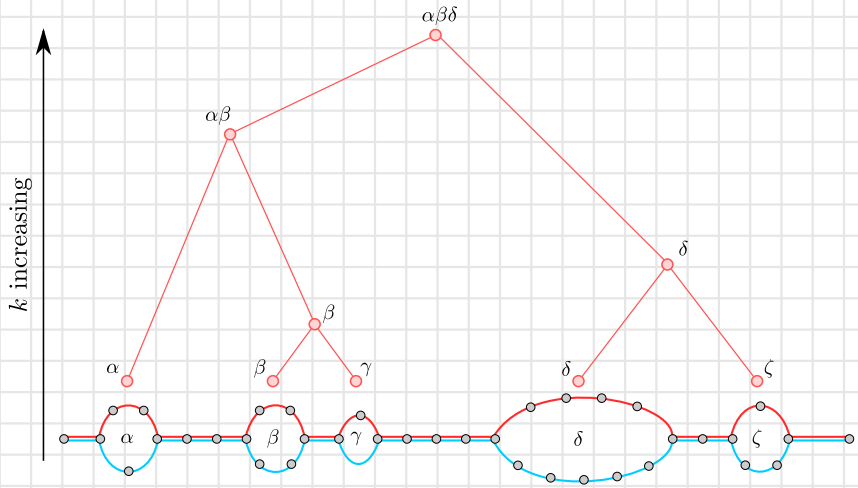

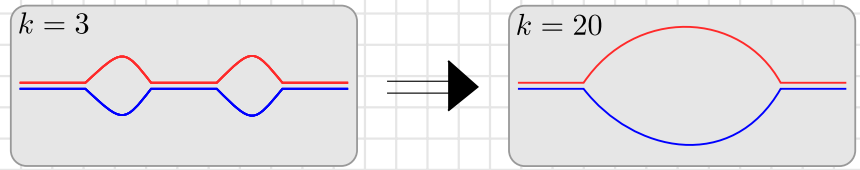

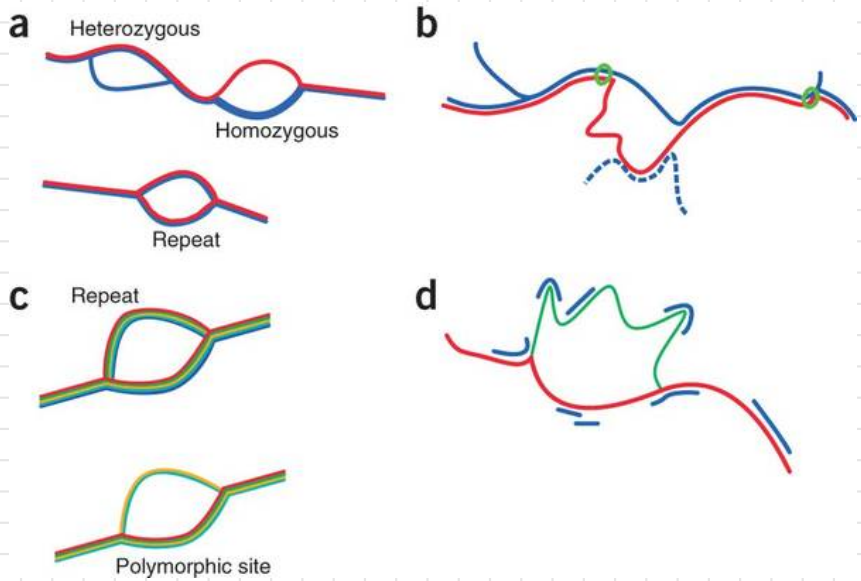

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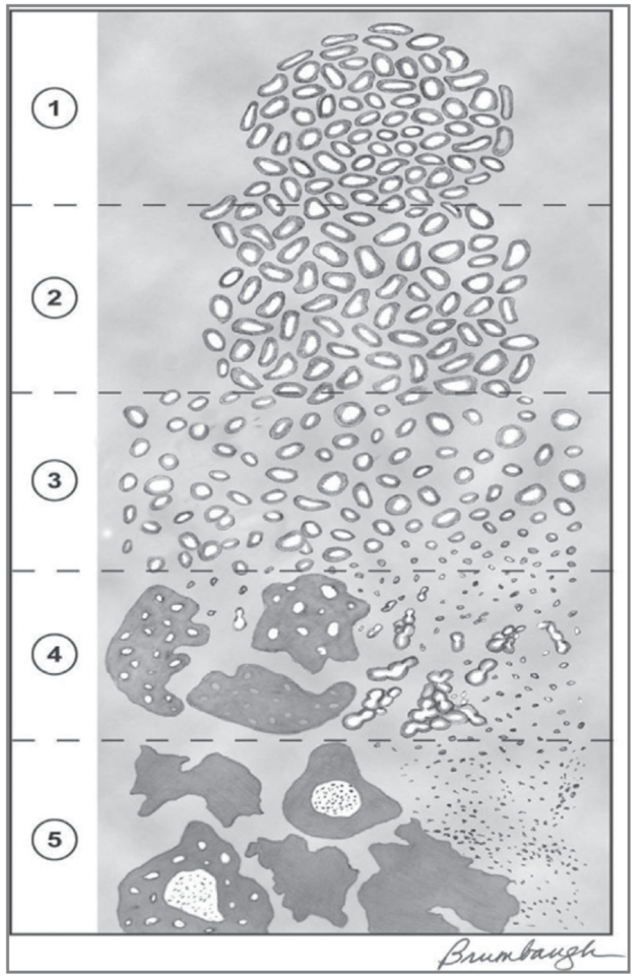
TDA R Package

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!

Contact: brittany@fasy.us



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