Topological Data Analysis Applied to Pancreatic-Islet Architecture

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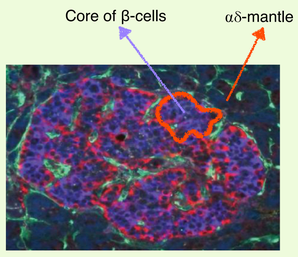
Introduction

- The arrangement of endocrine cells in islets affects paracrine signaling and islet function.
- Core-mantle hypothesis: non-β cells (α- and δ-cells) are adjacent to capillaries creating a mantle around a core of β-cells[2].

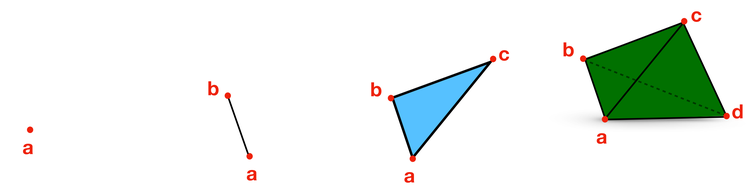


Source: D. Bosco[1], *Diabetes*, 59, 1201-1210 (2010)

- Disruption in putative biologically significant structural properties may affect normal function.
- To determine correlations between structural changes in the architecture and loss of healthy function, we extract topological features of spatial cellular arrangement in islets and compare them between normal and diseased states.

Topological Data Analysis (TDA)

- Represent cells as vertices and relate them with each other based on spatial proximity to define simplices.



- {a}
- 0-simplex, vertex
- dimension (dim) 0
- Faces: {}

- {a, b}
- 1-simplex, edge
- dim 1
- Faces: {a}, {b}

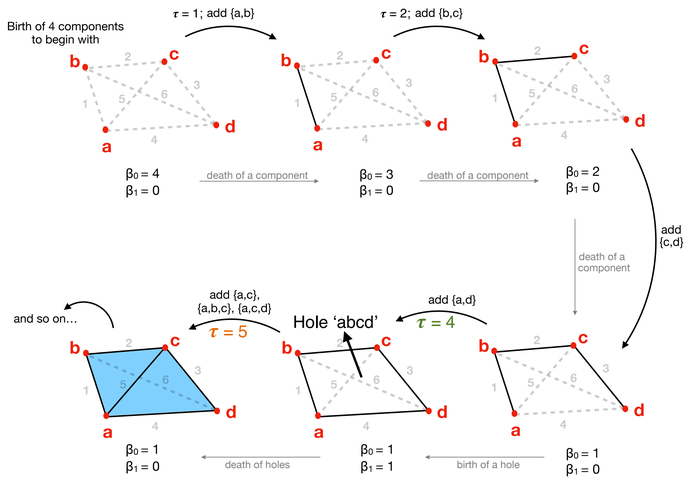
- {a, b, c}
- 2-simplex, triangle
- dim 2
- Faces: {a,b}, {b,c}, {c,a}, {a}, {b}, {c}

- {a, b, c, d}
- 3-simplex, tetrahedron
- dim 3
- Faces: All lower dimensional subsets of {a, b, c, d}

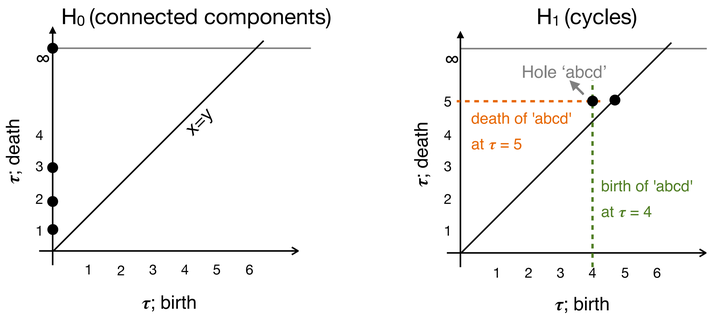
- TDA computes non-contractible structural properties of different dimensions: Homology groups (H_k)
  - The homology group H_0 corresponds to connected components, and the number of components is denoted by Betti number β_0.
  - H_1: cycles (hollow polygons); β_1 = #cycles
  - H_2: voids (hollow polyhedra); β_2 = #voids

Persistent Homology (PH)

- Topological features change as the scale of observation (threshold, τ) changes.



- PH evaluates the changes to the homology groups in the form of birth and death of topological features.
- These birth-death pairs give a multiscale view of the structure and can be summarized in persistence diagrams.

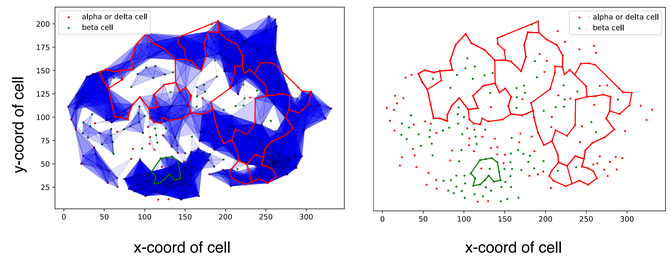


Pancreatic Islets

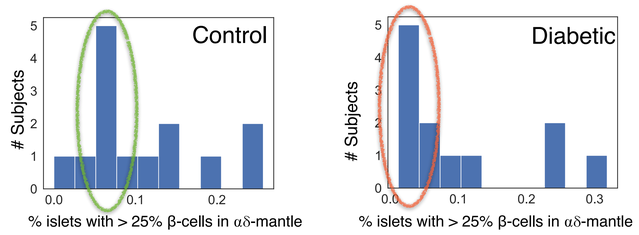
- Data: Images of 2-D slices of human islets; 13 Control and 12 Diabetic
- Relate similar cell-types based on spatial proximity, as defined by a threshold.
- Compute PH as the threshold changes from 0 to a maximum of 50 μm.
- Analyze the persistence diagrams within and between control and diabetic patients.
- *Can PH be used to find cores of β-cells surrounded by αδ-mantle?* Yes, we developed software to compute PH that can incorporate biological information a priori. Hence, biology drives the mathematical analysis. For this problem statement, we preserve αδ-cycles that contain β-cells.

Diabetes vs. Control

- Preliminary analysis does not show significant differences in the persistence diagrams.
- Finding cores of β-cells surrounded by αδ-mantle:



- Subject-wise differences — fraction of islets with at least 25% of β-cells surrounded by αδ-mantle:



- A larger number of diabetic subjects have a very small fraction of islets with at least 25% of β-cells surrounded by a αδ-mantle.

Conclusions

- We developed a software tool that computes PH such that it can incorporate biological information relevant to the data and the problem statement.
- We applied our tool to evaluate the number of β-cells surrounded by αδ-mantles in pancreatic islets from data for diabetic and non-diabetic groups.
- Our analysis showed that a higher number of subjects in the control group have a high proportion of islets with at least 25% of their β-cells surrounded by αδ-mantle.

Ongoing and Future Work

- We are analyzing and comparing the multiscale topological features computed by PH for control vs. diabetic groups.
- Using our tool we can determine 3-D structural features from spatial data, but availability of 3-D datasets is limited.

1. Bosco D, Armanet M, Morel P, et al. Unique arrangement of alpha- and beta-cells in human islets of Langerhans. Diabetes. 2010;59(5):1202–1210. doi:10.2337/db09-1177

2. Brereton MF, Vergari E, Zhang Q, Clark A. Alpha-, Delta- and PP-cells: Are They the Architectural Cornerstones of Islet Structure and Co-ordination?. *J Histochem Cytochem.* 2015;63(8):575–591. doi:10.1369/0022155415583535