3D feature extraction for segmented nuclei in large light microscopy datasets.

[1]Rob Serafin, [2]Karl Gilmore, [3]Nels Schimek
[1]Department of Mechanical Engineering, [2]Department of Chemical Engineering, [3]Department of Chemistry

CHEMICAL ENGINEERING
UNIVERSITY of WASHINGTON

Background

Alterations in nuclear morphologies are almost ubiquitous across cancer species[1]. Many studies have demonstrated that 2D nuclear features can drastically enhance risk stratification for patient outcomes[2-4]. While 2D analysis of nuclear features has led to novel insights on disease progression the prognostic value of 3D nuclear features remains unexplored. With the invention of high-throughput volumetric microscopy techniques, such as light sheet microscopy, and efficient deep-learning based segmentation algorithms, analysis of 3D nuclear features in cancerous tissues is now possible.

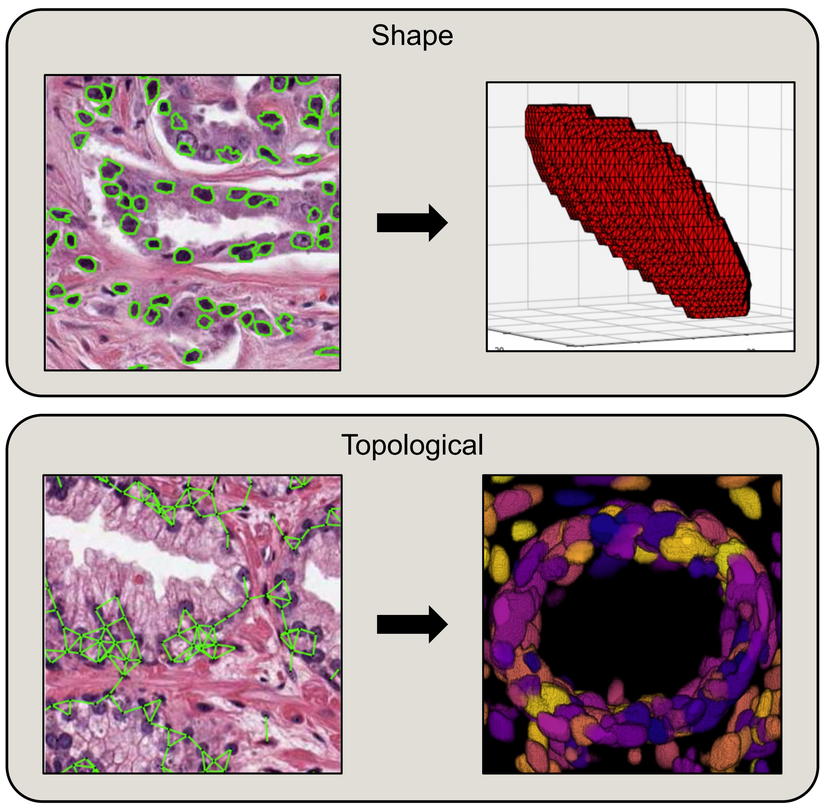

Figure 1. Examples of 2D nuclear features with demonstrated prognostic value and analogous 3D features.

The goal of this project is to develop a pipeline which can efficiently analyze segmented 3D images of nuclei. The aims of this project were:

1) Investigate available packages which could extract 3D features from segmented images.

2) Identify a set of 3D features for analysis and develop a full workflow to quantify these 3D features in large image data.

Methods

The primary packages used in this project were the measure and morphology modules from skimage, and the spatial module from scipy. The remove_small_objects method from morphology was used to clean the data and remove segmentation errors. 3D shape features were extracted into a pandas DataFrame using the regionprops_table method from skimage measure. Additional statistical features of shape descriptors were extracted using scipy stats. Next, the centroids of each nucleus in the segmented image were used to construct graphs which quantify spatial relationships between nearby nuclei. Graphs were constructed using the Delaunay and Voronoi methods from the spatial module in scipy. Additionally, we developed a few methods to visualize the results and optimize a curve fit using matplotlib and scipy.

Results

With the methods described above we were able to extract 3D analogs of 2D features with previously established prognostic significance. In total we extracted 43 shape-based, topological, and statistical features from 3D images of segmented nuclei, described in **Table 1**. Shape based features such as solidity and extent enabled detection of both over- and under-segmentation errors which occur with any segmentation algorithm. Which will hopefully improve downstream analysis. Statistical descriptors added 24 additional quantitative measures of 3D shape and topological features.

Shape

- Nuclear volume (mean, SD, skewness, kurtosis)
- Spherical equivalent diameter (mean, SD, skewness, kurtosis)
- Convex hull volume (mean, SD, skewness, kurtosis)
- Major/minor axis length
- Centroids
- Inertia tensor & eigen values
- Solidity (object volume/convex hull volume)
- Extent (object volume/bbox volume)

Topological

- Voronoi diagram
  - Tessellation volume – (avg, SD, min/max, skewness, kurtosis)
  - Tessellation area - (avg, SD, min/max, skewness, kurtosis)
- Delaunay triangulation
  - Triangle volume – (avg, SD, min/max, skewness, kurtosis)
  - Triangle area - (avg, SD, min/max, skewness, kurtosis)

Table 1. Features of segmented nuclei extracted in this workflow. Statistical metrics such as skewness and kurtosis enabled us to further quantify relevant feature distributions within 3D images.

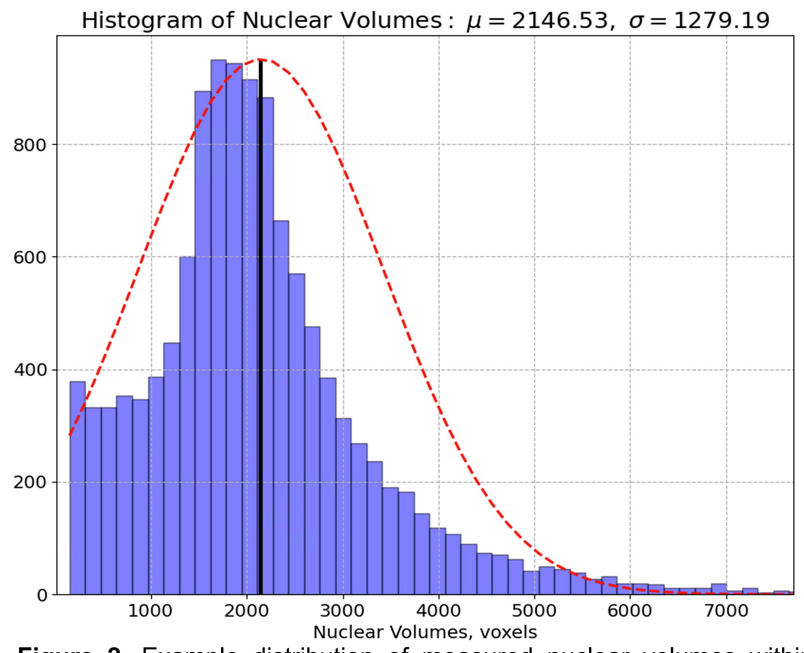

Figure 2. Example distribution of measured nuclear volumes within a segmented image.

Future work

In the future, this workflow will be used to explore the role of 3D nuclear features in predicting prostate cancer patient outcomes. A machine learning classifier will be trained to identify which of the 43 extracted features hold the greatest prognostic significance, and ultimately predict patient outcomes such as disease recurrence post curative surgery. Additionally, this kind of approach could be used to potentially predict the most appropriate course of treatment.

References and Acknowledgements

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