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COMPUTATIONAL TOPOLOGY BASED QUANTIFICATION OF HEPATOCYTES NUCLEI IN LIPOPOLYSACCHARIDE-INDUCED LIVER INJURY IN MICE

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Introduction/ Background

Automated high resolution scanning microscopes digitize large sets of histological samples and access the anatomical features of cells and tissues from the mm range down to a resolution of .25mpp microns per pixel. The high quality of the scans allows for the collection of the quantitative morphotopological features of cells and tissues from different samples, which can be coupled to functional information through, e.g., concomitant immunostaining. The basis for robust and accurate quantification of structural and functional features is the segmentation of regions of interest (ROIs) which define different elements within the scans. Due to acquisition artifacts and the diversity and variance of possible targets, the characterization and segmentation of ROIs in histological samples is difficult and challenging. In recent years, computational algebraic topology, a field of mathematics, has established a robust and versatile way to obtain qualitative information from data. The most fundamental qualitative description of an object is given by the study of its topology, how the object is connected, how many holes it has, and of what type. That allows characterizing data sets according to their structure, increasing our understanding of their properties.

Aims

We propose a method for the robust segmentation of hepatocyte nuclei based on the principles of persistent homology, a tool of algebraic topology. We show the application of our technique in histopathological, whole slide images obtained from liver sections of lipopolysaccharide (LPS)-treated mice. The robustness is achieved by the introduction of persistent homology to characterize the hepatocyte nuclei. Its stability proves the usefulness of persistent homology; variations in the properties of the ROIs induce small changes in the resulting characterization. By means of this representation for the hepatocyte nuclei, the resulting segmentation is less sensitive to acquisition artifacts and natural variations of the images across batches of slides.

Methods

The sample space of this study consists of 856 cropped images of 616x616 pixels each, obtained from three specimens. Each image was fragmented into connected components at different scales. Persistent homology is used to study the inclusion relations between connected components. The outcome of such process is a persistence diagram that provides a low-dimensional projection of the image structure. From that representation, it is possible to use conventional statistical methods for segmenting hepatocyte nuclei. After the segmentation, we assess the performance in comparison to a gold standard segmentation validated by experts.

Results

The computational topology approach proposed successfully detected hepatocyte cells under several natural variations. We evaluated on a per-pixel basis how the segmentation performs on: i) all nuclei in the images,

ii) big round nuclei considered belonging to hepatocytes cells (accuracy 87.2%, recall 80.3%), and iii) nuclei regarded to non-parenchymal cells.