A Mathematical Modeling on Breast Cancer Tissues using Graph Theory

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Abstract

Cancer is a major health problem in the world. Early diagnosis of breast cancer is curable. The diagnosis and staging prognosis is based on histopathological examination. Mathematical modeling interprets with real life problem. The study was focused on breast cancer. Breast tissue modeling is constructed by a cell - graph taken from tissue image. Consequence of the study was to qualify how the cells are distributed over the tissue

Keywords: Kongsberg Bridge; Breast Tissues; Hierarchical Cell-Graphs; node segmentation.

1. Introduction

A model is a set of mathematical equation that provides an adequate description of a physical system. Mathematical modeling essentially consists of translating real world problems which may be physical, chemical, biological, social, and economic or any other setting into mathematical problems solving the mathematical problems and interpreting these solutions in the language of the real world.

The origin of graph theory started with the problem of Kongsberg Bridge, in 1735. This problem lead to the concept of Eulerian Graph. Euler studied the problem of Konigsberg bridge and constructed a structure to solve the problem called Eulerian graph [14]. In 1840, A.F. Mobius gave the idea of complete graph and bipartite graph and Kuratowski proved that they are planar by means of recreational problems. The concept of tree, a connected graph without cycle was implemented by Gustav Kirchhoff in 1845, and he employed graph theoretical ideas in the calculations of currents in electrical networks are circuits [12].

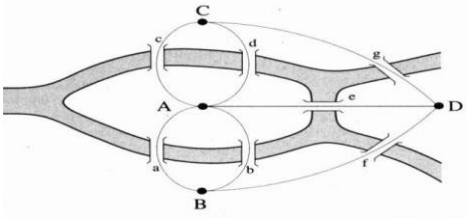


Figure 1: Kongsberg Bridge

Cancer is a major health problem in the world. There are several different stages in the growth of cancer before it becomes so large that causes the patient to die or reduces permanently their quality of life. Various types of cancer are there, here the model was done with breast tissue. Breast tissue modeling is constructed by a graph of cells taken from tissue image. After

interpreting the graph, it helps to qualify how the cells are distributed over the tissue.

2. Microscopic Example of Removed Human Breast

Breast cancer is the most common cancer. Early diagnosis of breast cancer is curable. The diagnosis and staging was prognosis is based on histopathological examination. It is developed from epithelial cells that develop neoplasia in breast tissue and so have carcinoma. The below image shows about the Microscopic images of tissue samples surgically removed from Human breast tissues:

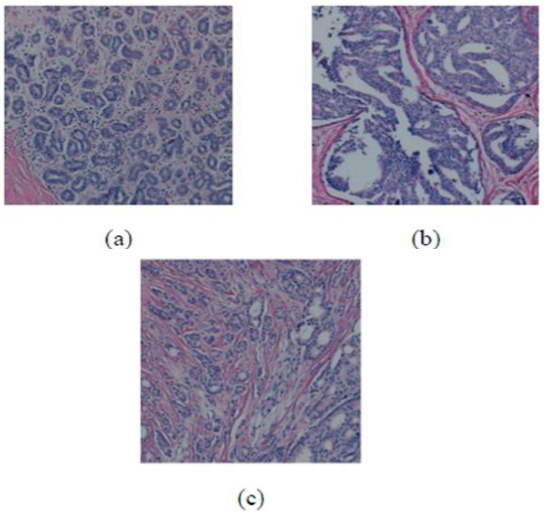


Figure 2: (a) A benign tissue example, (b) An in-situ tissue(c) An invasive tissue

2.1 Image Segmentation:

In order to form graphs for the cells, first have to segment the cells in tissue images. K means algorithm, which clusters the pixels of images according to their RGB values into clustering vectors, gave satisfactory results for breast tissue images[13]. The clustering vectors are estimated as to minimize the following error function E, $E = K, Xj = 1, Xn \in Sj\ (xn - \mu j)2,$ where μ_j is the center of j^{th} cluster and x_n's are the intensity values of the images[15].

2.2 Node Identification:

The next step is to translate the class information to node information. The segmentation produces pixels that constitute a cell but still the boundaries of the cells are not available [8]. Placed a grid on the resulting images of segmentation, each grid entry was calculated and the probability of bringing a cell as the ratio of cell pixels to the total number of pixels in the grid.

Then we applied thresholding to decide whether this grid entry is a cell or not. For a grid entry, the probability is computed as the average of the values of the pixels located in this particular grid entry [11]. Then, the grid entries with a probability greater than a threshold are identified as the nodes of the cell-graph

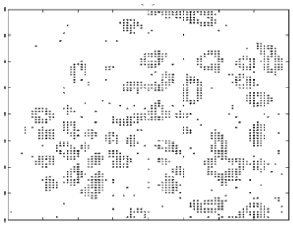


Figure 3: Nodes of tissue cells

2.3 Cell-Graph Generation:

A graph is represented by a cell-graph $G = (V, E)$ is an undirected and unweighted graph without loops, with V and E being the nodes and edges of the cell-graph G[4]. Next, determine the node set V by identifying the cell clusters in the image and then establish the edges between the nodes in V [6]. Three different kinds of cell-graphs captured the pairwise distance relationship between the nodes[12].

2.3.1 Simple cell-graphs:

In simple cell-graphs we set a link between two nodes if the Euclidean distance is less than a threshold [16]. The Euclidean distance between two cells is given by

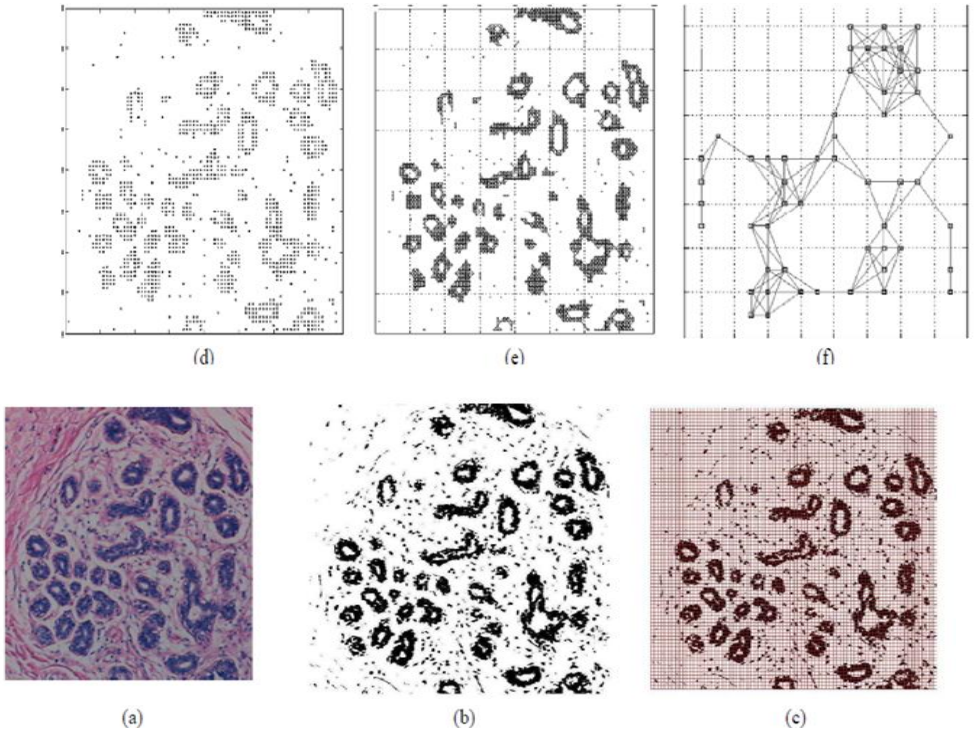


Figure: 4

(a) Original
(b) tissue image is opened in RGB space.
(c) The result of K-means segmentation, black points is part of cells and white points are treated as background.
(d) The application of grid and thresholding to the resulting segmentation. Appling a thresholding will get rid of the noise in the segmentation and the center of grid entries will be used as the locations of cells.
(e) The overall result of node identification.
(f) Simple cell-graphs are formed based on the location information of the cells.
(g) A bigger grid is applied to the image to capture the cell clusters.

Each grid entry is then thresholded to get the clusters [10]. After cluster identification, hierarchical graphs are built on cluster cells using $d\,(u,v) = \sqrt{(u_{x-}v_x)^2} + (u_{y-}v_y)^2$, where *UX* and *UY* are *X* and *Y* coordinates of node U respectively[5]. These graphs form a relation between nodes if they are close to each other.

2.3.2 Probabilistic Cell-Graphs:

The probabilistic model is a more general version of simple cell-graphs. In this model a link between two nodes was formed with a certain probability which is given by $P(u,v) = d(u,v) - \alpha$, for nodes *u* and *v* [2]. As the distance between nodes increasing, the probability of linking them decreases.

2.3.3 Hierarchical Cell-Graphs:

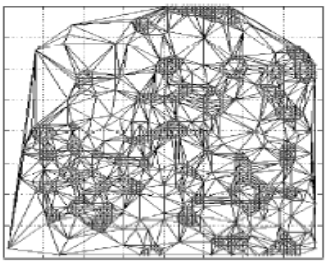
Simple and probabilistic Cell-Graphs capture the global distribution of the cells

and were particularly useful for brain tissue images[9]. However, there is architectural difference between the brain and breast tissues. Breast tissues have lobular architecture whereas brain tissues do not have it [7]. For breast tissues, the pair-wise relationship of cells within the same gland as well as different glands are therefore important [3]. To capture the lobular architecture of the breast tissues, a hierarchical representation of the tissues is needed. A hierarchical graphs similar to cell-graphs was formed. After the node identification step (cells) of the graphs, the cluster (lobes) of the tissues was found, by placing a grid on top of these cells. After obtaining the probability values for each grid entry, a threshold value and considered the grid entries with a probability greater than this threshold as a cluster. Finally formed graphs of these clusters.

3. Delaunay Triangulation:

In order to quantify the spatial distribution of nuclei, Voronoi diagrams, Delaunay triangulations are proposed. On a tissue image, the Voronoi diagram constitutes convex polygons for each nucleus. For a particular nucleus, every point in its polygon is closer to itself than to another nucleus in the tissue [1]. The dual graph of the Voronic diagram is the Delaunay triangulation. In this approach, a Delaunay triangulation on cell-clusters was in node identification step and evaluates the metrics for these graphs. The choice of the parameter for graph generations affects the learning ratio significantly

(a)



(b)

Figure 5 (a) The voronic cells of the tissues. (b) The dual of the voronic diagram

4. Conclusion:

In the work the enhanced modeling is the cell-graph approach and classification of breast tissue samples which has a lobular/glandular architecture, thus differ from brain tissues significantly in architecture. To capture this difference we introduce hierarchical graphs and obtain the best learning ratio compared to the other techniques which is 81.8%. Cell-graphs enable us to identify and compute a rich set of features that represent the two dimensional structure information of breast tissues. The feature sets are input to a support vector machine for classification of benign, invasive and noninvasive (ductal carcinoma in situ) cancerous tissues. A computational comparison of the approach related to work in the literature shows that hierarchical cell-graphs are much more accurate for breast tissues. However, the accuracy can be improved further by increasing the data

size and by improving the image segmentation.

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