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LABELING OF CELL GRAPHS

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ABSTRACT. Several graph structures have been modeled to represent the tissue samples and studied with the help of graph theoretical tools. One of those models is Cell Graph whose vertices (nodes) are cells or cell clusters and an edge (link) is made between a pair of vertices with the assumption that has a biological foundation. Metrics that are derived from cell graph are helpful to comprehend the nature of tissue samples. To add flavor to this model, we try to impose the labeling technique into this concept. Graph labeling is an assignment of numbers to the vertices (or edges or both) of a graph subject to certain conditions. In this paper, we propose a method to construct cell graphs and introduce some labeling techniques to study the tissue properties mathematically.

1. INTRODUCTION

Numerous ways are available to study biological systems. One of the efficient ways is converting the respective biological system into a graphical structure. A graph G is an ordered pair $(V(G), E(G))$ where $V(G)$ is a finite non-empty set and $E(G)$ is a collection of unordered pairs of distinct elements of $V(G)$. Elements of $V(G)$ are called vertices (nodes) and that of $E(G)$ are called edges

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(links). We denote the number of vertices of G by $|V(G)|$ and the number of edges of G by $|E(G)|$. If $e = (u, v) \in E(G)$, we say that the edge $'e'$ joins the vertices u and v and denote the edge by $e = uv$. Several types of graphs have been modeled for man-made, social, and biological systems [2]. Among these, the biological networks are self-organizing structures. Some of them include neural networks, Protein-Protein Interaction networks, metabolic and biochemical networks, and regulatory networks [7]. In order to observe the interrelationship between the nodes of the biological networks, these networks are designed either as weighted graphs or bipartite graphs or directed graphs depending on their structure and these graphs play a vital role in the domain of Bioinformatics. Since the biological networks are complex and self-organizing systems, studying the properties of each node, like degree, clustering coefficient, etc., helps to muster the entire information of the network.

2. Graph Models for tissues

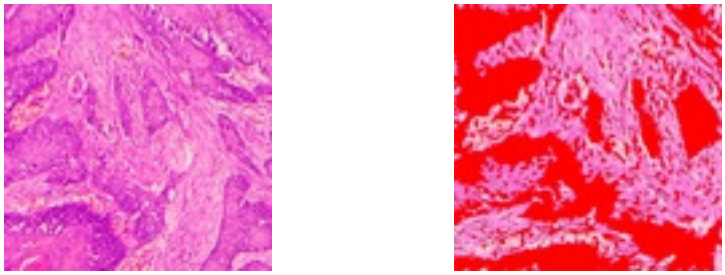
Similar to the network models, the conversion of tissue samples into several graph models has paved ways to acquire some profitable results in the study of tumors. These graph models have been constructed based on the location of cells or cell clusters [3, 4]. In 2004, Cigdem Demir et. al introduced the notion of cell graph [1,3] in order to classify the tissue samples of brain tumors. In a cell graph, cells or cell clusters of tissue are the nodes and an edge is defined between a pair of nodes (cell or cell clusters) based on an assumption that has a biological foundation. This graph model supports in distinguishing various tissues (healthy, inflamed and cancerous) despite their cellular density levels. Metrics such as average degree, average clustering coefficient, average eccentricity, etc., [5] are used to accomplish the task of classification. Later, cell graph model upgraded into another as Augmented cell graph (ACG) [4] in which nodes and edges are assigned weights (labels). Here, the size of the node u is assigned as the weight of the node u and the Euclidean distance between the pair (u, v) is assigned as the weight of the edge $e = uv$. Using average degree, average eccentricity, average node weight, etc., the ACGs are studied.

In Mathematics, the theory of Graph labeling was introduced by Rosa [9] in 1967. Following Rosa, many graph labeling methods were introduced. In this paper, we introduce methods to label the vertices of cell graphs on the basis of

the degrees and pixel values of the nodes. These vertex labels are used to assign Boolean labels to the edges. For standard graph theoretical terminology and notation we refer to [6].

3. Construction of Cell graphs

In this section, we discuss a novel method of constructing cell graphs. To execute this, we used foot cancer tissue samples (Figure 1(A)) and observed each sample under a magnification of $400\times$. The following steps are involved in the construction:



(A) Tissue sample (B) Processed tissue sample

FIGURE 1

(i) **Node Identification:**
Since we consider cells (or cell clusters) as nodes, we implement Watershed Algorithm to distinguish cells (or cell clusters) from its background. As a result, the cells (or cell clusters) are obtained as segments (Figure 1(B)). Now, except the overlapping segments, fix a pixel (a, b) on all the segments and establish these pixels as nodes of the cell graph. We observe that every node of a cell graph is of the form $u = (a, b)$ where (a, b) is the pixel representing the vertex u (a and b are integers).

(ii) **Edge Assignment:**
The probabilistic edge assignment between two nodes u and v is done using "mutually visible neighbors"(MVN) method [8]. Here, if a node v is visible from u, (i.e)., there is no node in the line segment joining u and v, then we declare that u and v are adjacent.

Note 1. *The cell graph thus constructed is connected and hamiltonian [6].*

4. Labeling of cell graphs

Let $G = (V, E)$ be a simple, connected cell graph, where $V = V(G)$ and $E = E(G)$ denote the node set and the edge set of G respectively. We define the following labeling methods:

(i) **Degree - (0,1) Labeling**

Degree of a vertex v, denoted $d(v)$, is the number of edges incident with v. We label the vertices and edges based on the degree of the vertices of G. Define a function $f_d : V(G) \cup E(G) \longrightarrow \{0, 1, 2, \ldots, |V(G)| - 1\}$ as follows:

$f_d(v) = d(v) \; \forall \; v \in V(G)$ and

$$f_d(e = uv) = \begin{cases} 1 & \text{if } \gcd(f_d(u), f_d(v)) = 1 \\ 0 & \text{if } \gcd(f_d(u), f_d(v)) > 1. \end{cases}$$

The mapping f_d is called *degree - $(0, 1)$ labeling* of the cell graph G.

(ii) **Pixel - (0,1) Labeling**

Let $v = (a, b)$ where (a, b) denotes the pixel representing the vertex v. Define a function $f_p : V(G) \cup E(G) \longrightarrow \mathbb{Z}^+ \cup \{0\}$ as follows:

$f_p(v) = |a - b|$ and

$$f_p(e = uv) = \begin{cases} 1 & \text{if } \gcd(f_p(u), f_p(v)) = 1 \\ 0 & \text{if } \gcd(f_p(u), f_p(v)) > 1. \end{cases}$$

The mapping f_p is called *pixel - $(0, 1)$ labeling* of the cell graph G.

Note 2. *f_d and f_p need not be bijective.*

Notation 1. *The spanning subgraph of G which consists of the edges of G that receive the label 0 under degree - $(0, 1)$ labeling, together with all vertices of G, is denoted by M_d.*

Notation 2. *The spanning subgraph of G which consists of the edges of G that receive the label 1 under degree - $(0, 1)$ labeling, together with all vertices of G, is denoted by N_d.*

Notation 3. *The spanning subgraph of G which consists of the edges of G that receive the label 0 under pixel - $(0, 1)$ labeling, together with all vertices of G, is denoted by M_p.*

Notation 4. *The spanning subgraph of G which consists of the edges of G that receive the label 1 under pixel - $(0,1)$ labeling, together with all vertices of G, is denoted by N_p.*

5. Experimental Results

We applied the above discussed labeling techniques on several cell graphs that are constructed through MVN method and observed the following properties which are common to all cell graphs:

1. $d_{M_d}(v) + d_{N_d}(v) = d_G(v) \ \forall \ v \in V(G)$ and $d_{M_p}(v) + d_{N_p}(v) = d_G(v) \ \forall \ v \in V(G)$.
2. If u and v are adjacent in M_d, then they are not adjacent in N_d and vice versa. Therefore $E(M_d) \cap E(N_d) = \phi$ and $E(M_d) \cup E(N_d) = E(G)$. The same holds good for M_p and N_p.
3. If $f_d(v)$'s are all distinct primes, then $E(M_d) = \phi$. In this case, $E(N_d) = E(G)$. The same holds good for f_p.
4. If G is a regular graph in which $\delta(G) = \Delta(G)$ and greater than 1, then $E(N_d) = \phi$ and therefore $E(M_d) = E(G)$. If $G \cong K_n$ and $n > 2$, then $\gcd(f_d(u), f_d(v)) = n - 1$, then $E(N_d) = \phi$. Thus $E(M_d) = E(G)$. In particular, if $n = 2$, then $G \cong K_2$ which implies that $E(M_d) = \phi$ and therefore $E(N_d) = E(G)$. The same holds good for $E(M_p)$ and $E(N_p)$.
5. Some vertices of G have same degree and therefore $f_d(u) = f_d(v)$ for atleast one pair (u, v).
6. $E(M_d) \neq \phi$ and $E(N_d) \neq \phi$
7. $|E(M_d)| \neq |E(N_d)|$
8. N_d is connected whereas M_d is disconnected.
9. $E(M_p) \neq \phi$ and $E(N_p) \neq \phi$
10. $|E(M_p)| \neq |E(N_p)|$
11. N_p is connected whereas M_p is disconnected.
12. In general, pixel difference $|a - b|$ need not be distinct. However, for the cell graphs constructed, all the pixel difference values are distinct and therefore $f_p(u) \neq f_p(v)$ for any pair (u, v).
13. $E(M_d) \cap E(M_p) = \phi$ if and only if $f_d(e) \neq f_p(e) \forall e \in E(M_d)$ and $E(M_p)$. Similarly, $E(N_d) \cap E(N_p) = \phi$ if and only if $f_d(e) \neq f_p(e) \forall e \in E(N_d)$ and

$E(N_p)$. In this case, $E(M_d) = E(N_p)$ and M_d is isomorphic to N_p and $E(M_p) = E(N_d)$ and M_p is isomorphic to N_d. Also, $E(M_d) \cup E(M_p) = E(G)$ and $E(N_d) \cup E(N_p) = E(G)$.

14. $E(M_d) \cap E(M_p) \neq \phi$ and $E(N_d) \cap E(N_p) \neq \phi$.
15. $|E(M_d) \cap E(M_p)| < |E(N_d) \cap E(N_p)|$.
16. Also, the subgraph induced by the edges lying in the intersection of the two graphs, N_d and N_p, is connected, (i.e)., the subgraph induced by $E(N_d) \cap E(N_p)$ is connected whereas the subgraph induced by $E(M_d) \cap E(M_p)$ is disconnected with considerable number of isolated vertices.

On the basis of the results attained above we conclude that the edges of the two subgraphs, N_d and N_p are alone sufficient for further study. The subgraph induced by the edges which are common to two spanning subgraphs need not be connected. However, in our study we observe that the subgraph induced by the edges common to N_d and N_p is connected and the vertices have degree greater than or equal to 2 and therefore the subgraph induced by $E(N_d) \cap E(N_p)$ becomes a significant component of the cancer tissue. Thus considering the spanning subgraph induced by $E(N_d) \cap E(N_p)$ for further study will reduce the complexity of the graph considerably.

6. Conclusion

In this paper, we introduced a method of constructing cell graphs for tissue samples and a novel perspective to analyze cell graphs in terms of graph labeling. This concept revealed the similarities among spanning subgraphs induced by the labelings. These Boolean valued labeling methods pave the way to identify the core component of cancer tissues.

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