Centrality Measures on Vascular Networks

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Vascular Networks

Cancer cells require oxygen and other essential nutrients to survive. One method of obtaining nutrition is through osmosis. However, without a way to distribute nutrients tumor growth is severely limited and will begin to deteriorate on the inside. Consequently, some cancer tissues rely on a process called ***angiogenesis*** to create a system of blood vessels, called a vascular network, to circulate these nutrients needed for its survival.

Vascular network structure is critical to the understanding of how malignant cancer growth is spread and how it can be reduced.

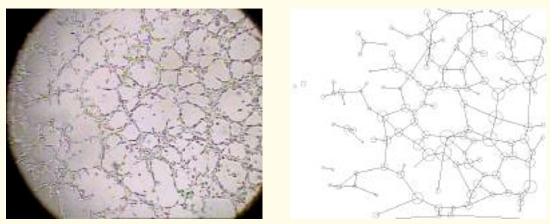


Figure 1: Sample vascular network and corresponding skeletonized graph.

Clinicians require a quantitative way to measure the effectiveness of various drug treatments. Identifying biologically significant patterns from within the vascular network structure is then of great necessity to the researcher.

Viewing these vascular networks as ***mathematical graphs*** we can identify important network "hubs," or highly connected vessel intersections, through looking at a variety of centrality measures.

Graph Connectivity

A mathematical graph consists of an *edge set*, E, and a *vertex set*, V. Vertices, or nodes, represent vessel intersections in our biological setting while edges represent the vessels themselves.

Graphs can be represented mathematically by an ***adjacency matrix***, which contains all the information about adjacent, or connected, nodes.

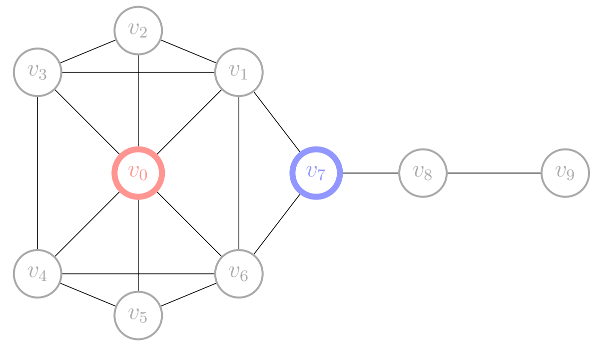
Definition: Adjacency Matrix The ijth entry of the $n \times n$ adjacency matrix A of a graph G is

$$A_{ij} = \begin{cases} 1 & \text{if } i \neq j \text{ and the } i\text{th and } j\text{th nodes are connected with an edge} \\ 0 & \textit{otherwise} \end{cases}$$

There are many ways to measure the structural properties of graphs. We chose to focus on ***point centralities*** to determine the relative importance of a single node in the graph.

The most basic centrality measure is ***degree***, which measures how many edges a node is connected.

How do you define *"importance"* in a network?



In Krackhardt's Kite, node v_0 has the highest eigenvector centrality value and node v_7 has the highest betweenness centrality value.

Adjacency matrices provide a way to mathematically represent graphs. We can use these matrices to compute a variety of centrality measures.

Betweenness Connectivity

Nodes strategically positioned between two clusters of a graph create a "bottleneck" for information flow. Such nodes are then assigned a high ***betweenness centrality*** score to represent their positional importance.

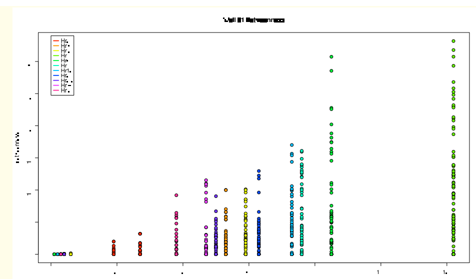


Figure 2: Betweenness vs Component Size

Let σ represent the number of shortest paths from some vertices $s, t \in V$. For vertex v, let $\sigma(v)$ denote the number of shortest paths between s and t that v lies on.

$$C_B(v) := \sum_{s \neq v \neq t \in V} \frac{\sigma_{st}(v)}{\sigma_{st}}$$

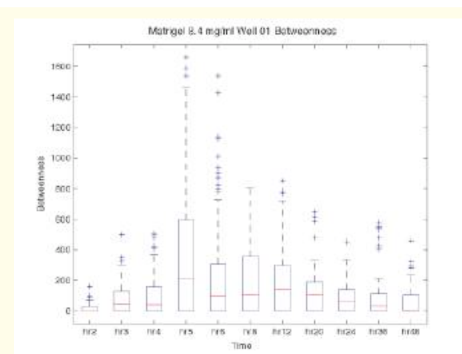


Figure 4: Betweenness vs Time (Hours)

Representing Vascular Network Components

As vascular networks slowly converge and connect over time, many images will contain multiple connected components. This poses a problem for computing point centrality scores since they rely on a single connected graph.

$$A = \begin{pmatrix} 0&1&1&1&1&1&1&0&0&0 \\ 1&0&1&1&0&0&1&1&0&0 \\ 1&1&0&1&0&0&0&0&0&0 \\ 1&1&1&0&1&0&0&0&0&0 \\ 1&0&0&1&0&1&1&0&0&0 \\ 1&0&0&0&1&0&1&0&0&0 \\ 1&1&0&0&1&1&0&1&0&0 \\ 0&1&0&0&0&0&1&0&1&0 \\ 0&0&0&0&0&0&0&1&0&1 \\ 0&0&0&0&0&0&0&0&1&0 \end{pmatrix}$$

The adjacency matrix of each vascular image is run through a computer program which separates the matrix into individual matrices for each connected component.

Eigenvector Centrality

Highly connected nodes that are connected to other highly connected nodes have a high ***eigenvector centrality*** score.

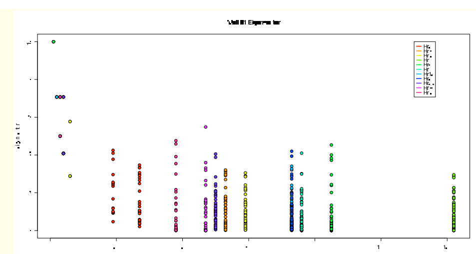


Figure 3: Eigenvector vs Component Size

Eigenvector centrality is derived from the vector equation $Ax = \lambda x$ using the largest eigenvalue of the adjacency matrix to apply a weight to "popular" nodes.

$$C_\lambda := \sum_{j=1}^{n} a_{ij} C_\lambda(v_j)$$

We viewed eigenvector centrality as a more representative replacement for a typical degree measurement.

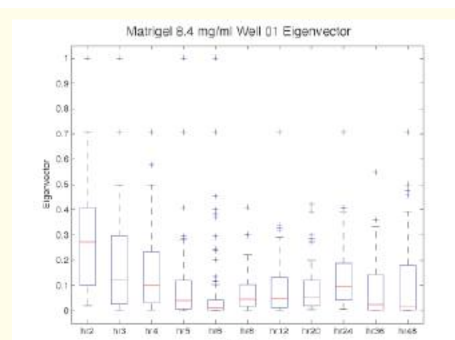
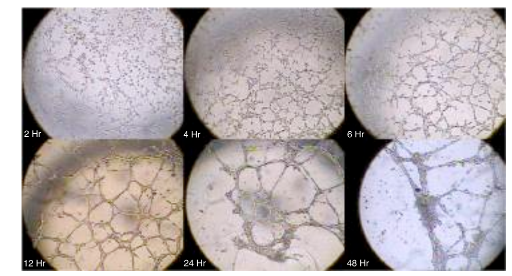


Figure 5: Eigenvector vs Time (Hours)

Results & Discussion

Endothelial cells are responsible for vascular growth. Early in network formation you can observe the migration of cells forming small, disjoint networks which join together to form a single connected network. The structural measures of networks formed by Human Umbilical Vein Endothelial Cells (HUVEC) suggest the highest growth during the first 12 to 20 hours and followed by a reversal of network growth.



Vascular network formation is characterized by many disconnected components which later fuse together to create a single connected component.

For each image in a time series of vascular network formation, we computed over a dozen different centrality measures. A previous student showed that some basic structural measurements reflected biologically significant patterns of structural organization. We aimed to identify analogous patterns in point centrality measurements.

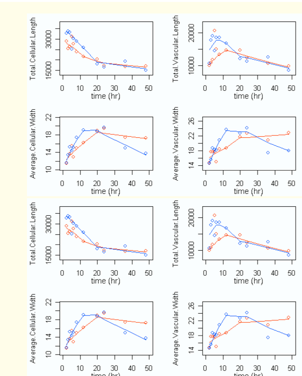


Figure 6: Vascular structural measurements.

Patterns shown in Figures 2 and 3 (as well as Figures 4 and 5) suggest that betweenness and eigenvector centralities may reflect biological structure of the vascular network.

Betweenness obtains its highest values around 5 hours when the network has remodeled itself into one component. The nodes responsible for joining two components of the network would thus have a high betweenness score. Eigenvector centrality provided the greatest mathematical interest but its biological significance is still not well known.

Acknowledgments

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