LNC: Graph Theory Rough Draft

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Name	Expertise	Contribution
Andy Cheon	BioE/bioinfo/programming	Glossary & Test Quesions
Tohma Judge	BioE	External Resources & Commentary
Steve Hoffman	Genetics/Biochem	Overview: Life Sciences
Zack Field	BioE/EECS	Overview: Math/CS/Engineering & Graph Theory papers

WHAT IS A GRAPH? (by everyone)

Graphs are composed of **nodes**(**vertices**) and edges. **Edges** connect vertices, and can have a **direction** and a **weight**. **Degree**, or **valency**, is the number of edges connected to a node. If direction is being used in the graph, count two separate degrees, one for away from the node and one for into the node. A **complete graph** has all its nodes connected by an edge to each other. They are noted as K_n, where n is the number of nodes. A **clique** is a set of vertices in a graph that forms a complete graph. A **hub** is a node connected to a large number of nodes.

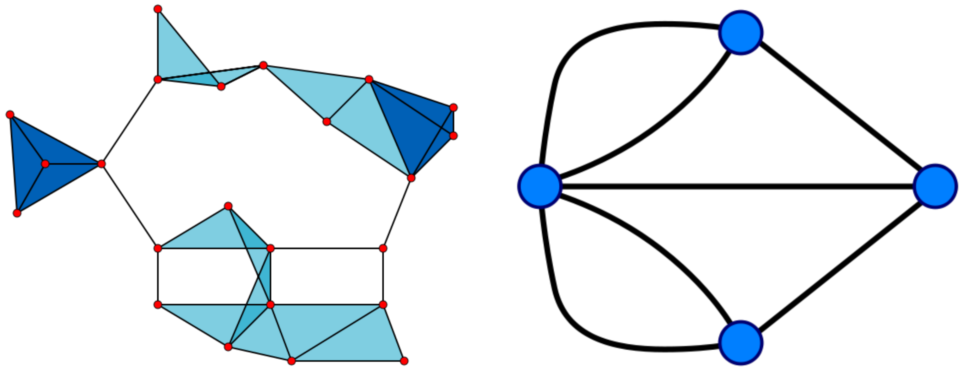


Figure 1: Examples of graphs

There are many everyday-life representations of graphs. Highways linking together cities, for example, are the edges of a directed graph. Vary the speed limit or the number of cars on each highway, and that graph becomes weighted.

OVERVIEW – MATH / CS / ENGINEERING

Graphs can be used wherever there is an interest in analyzing pairwise information. Graph theory is a mature field, and our understanding of the structure of, and information contained in, graphs is vast (although far from complete). As computational biologists we can use this accumulated knowledge of graphs to our advantage when analyzing data and attempting glean meaningful relationships within a dataset. A reliable strategy is to represent elements (objects) in your data as **vertices** and the relationships between them as **edges**. The ability to construct these graph relies on knowledge of biology, and intuition. This abstraction of relationships in data to a graph allows for formal analysis of the problem. After a graphical representation is formulated, the next step is to find some kind of structure (or particular element) within the graph (e.g. maximal clique, minimum pairwise distance, maximum flow). The graphical representation of your data will be based on the type of problem that you are trying to solve, and the structure you wish to find.

The complexity (difficulty) of your problem will follow from the structure or element that you are trying to uncover. An example (from lecture): The homology of proteins. We know that hierarchical clustering is used in conjunction with pairwise comparisons of proteins (by MDL or other methods). How could that problem be represented as a graph? We could start by placing the proteins at each of the **vertices**. The **edges** between each vertex would have a weight determined by pairwise alignment. This is an abstract enough definition of the problem that any decent general hierarchical clustering algorithm would return a hierarchy of clusters. If the pairwise alignment method is positively correlated with the homology of two proteins, then this hierarchy would be equivalent to a phylogenetic tree.

We can use hierarchical clustering as an example to see how the complexity of the problem relates to the structure or element that we wish to uncover. Each iteration of hierarchical clustering seeks to find the two elements that are most closely related (smallest weight edge). This means that for n vertices (proteins) we have to check n^2 edges (alignment scores) to find the smallest. Since one edge is removed with each iteration, our total running time is $O(n^3)$. Unfortunately, many of the interesting problems in graph theory, and (graph theoretic formulations of problems in biology) are not solvable in polynomial time. Many problems take exponential time in the size of their input: n âĂIJproteinsâĂİ $O(c^n), c > 1$ (i.e. NP-complete problems). If formulated in the right way, most problems in biology can be reduced to problems already discovered in the theory of graphs and related fields. It is up to computational biologists to provide the insight necessary to make these reductions.

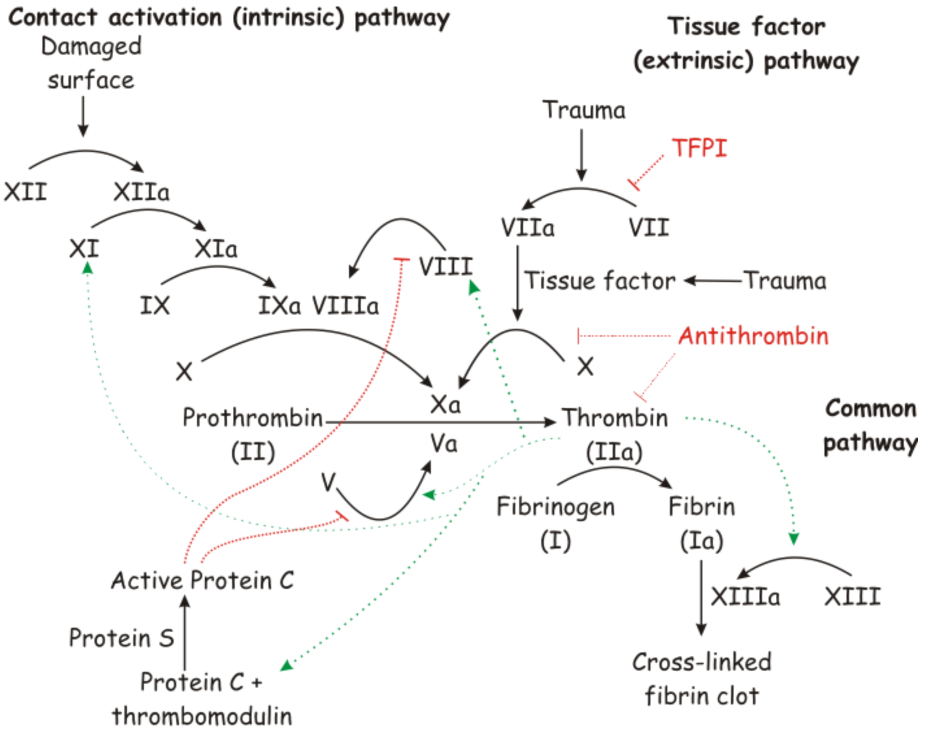


Figure 2: Graph representation of blood clotting process

OVERVIEW – LIFE SCIENCES

To familiarize individuals with graph theory with little computational background, this section will present the practical application of graphs in biology with examples. Graphs are fundamental in understanding in vivo interactions between molecules. Protein-protein interaction (PPI) networks, regulatory networks (GRNs) which contain information regarding gene expression, signal transduction networks, and multiple integrated metabolic pathways are examples requiring the use of graph theory. Any pathway you learned in biochemistry could be demonstrated by a graph.

Consider the following graphic that displays blood clotting in vivo induced by trauma:

This heavily regulated pathway involves a multitude of proteins activating (dotted lines with arrows) and inhibiting (dotted lines with flat line) others. Such interactions could be represented as edges on a graph, with the proteins represented as nodes. If we have a well-formed graph and consider that many problems in graph theory are well characterized, is there still be a need for biologists in computational biology? Absolutely. If you gave a computer scientist who has no background in basic principles of biology several protein sequences, they would not know what biochemical information is relevant in constructing a graph. In the context of PPI networks, knowing the interactions between proteins underscores the need for biologists in endeavors in computational biology. A computer could predict PPI networks but there could be false positives that predict interactions between proteins when there should not. Such a lack of an interaction could be demonstrated by a biologist in a laboratory.

GRAPH THEORY PAPERS

- (intro) Graph Theory introduction video
- (intro) Hierarchical Clustering Explanation
- (intermediate) Graph Theory and Networks in Biology
- (intermediate) Using graph theory to analyze biological networks
- (advanced) Berkeley's canonical algorithms text: "Algorithms" (recommend Ch. 3 Ch. 4)
- (advanced) (another) Graph theory text

COMMENTARY

Cs Foundations Short 2014 Slides 28-36

Graphs are composed of nodes(vertices) and edges. Edges connect vertices, and can have a direction and a weight. Degree, or Valency, is the number of edges connected to a node. If direction is being used in the graph, count two separate degrees, one for away from the node and one for into the node. A Complete Graph has all its nodes connected by an edge to each other. They are noted as Kn, where n is the number of nodes. A Clique is a set of vertices in a graph that forms a complete graph. A Hub is a node connected to a large number of nodes.

Graphs are useful for storing and analyzing interaction data, using programs such as Cytoscape. Examples of Graph usage given include a KEGG(Kyoto Encyclopedia of Genes and Genomes) pathway, where nodes represent substrates, while edges represent enzymatic reactions; Whole-Genome interactomes, where nodes represent Protein-Protein Interactions. Certain patterns become easy to spot when using graphs-a protein with many interactions will appear as the hub of a large network. Anything that can be represented as a node with connecting edges is graphical in nature. Some examples below

Example	Node represents	Edge represents
KEGG PAthway	Substrate	Enzymamtic Reactions
Whole-Genome Interactomes	Proteins	Protein-Protein interation (PPI)
Love Triangle	Person	Attraction (directed!)
Phylogenetic Trees	Species	Relation

EXTERNAL RESOURCES / LINKS

- "protein-protein interaction networks and biology–what's the connection?" hakes et al nature biotechnology 2008. Recommended by slide, unsure if this counts under third party or would go under assigned reading/recommended?

- A quick excerpt from a text on transportation networks, but clearly defines basic terms for graph theory. Graph Theory terms

- Review of Graph Theory in relation to proteomics. Covers terminology, biological terminology such as pathways and homology and their adaptation to graph data structure, Network properties such as clustering within a graph, describes random graphs, small networks, and scale free networks. The next section describes PPI data collection, and defines pathways. Lastly, it goes over properties of PPI networks constructed from said data and other notes for analysis. Should be noted that this is a fairly large paper, hitting nearly 61 pages. Unknown if this is too large for the LNC

- Presentation on graph theory's application to early genetic sequencing problems, goes over Euler theorem and it's application to sequencing by hybridization. Very good examples of graph theory being applied to problems that don't immediately appear to involve graphical information.

- Powerpoint going over graph theory, very clear description of the possible computational representations of a graph, as well as some applicable algorithms, such as dijkstra. Definitely nice for looking at graph theory from an entirely computation based perspective.

COMPREHENSION TEST QUESTIONS

1. Categorize the graph below as

   (a) directed or undirected

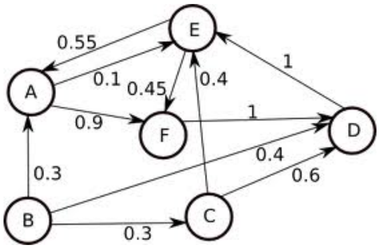
   (b) cyclic or acyclic

   (c) complete or incomplete

   (d) weighted or unweighted

   What are the shortest and longest paths from node A to node E?

   List any cliques you find.



2. What might the graph of a signaling pathway look like? Categorize the graph as you would in (1).

3. What might be some of the advantages and disadvantages of modeling biological systems with graphs?

GLOSSARY

Term	Definition	Notes/Comments	Related Words
acyclic graph	a graph where no possible cycles are present; i.e. following any path will not lead to a node that was already visited		opposite: cyclic graph
clique	a set of vertices in a graph that forms a complete graph		
complete graph	a graph that has all its nodes connected by an edge to each other		opposite: incomplete graph
cyclic graph	a graph where one or more possible cycles are present; i.e. following any path could lead to a node that was already visited		opposite: acyclic graph
directed graph	a graph in which edges have direction	Edges of a directed graph are represented with arrows	opposite: undirected graph
edge	a connection that links two vertices	may or may not be directional	
hub	a node connected to a large number of nodes		
incomplete graph	a graph that does not have all its nodes connected by an edge to each other		opposite: complete graph
indegree	the number of edges entering a vertex		opposite: outdegree
node	a point on a graph; may be connected to other nodes by edges or may be isolated		a.k.a. vertex
outdegree	the number of edges leaving a vertex		
undirected graph	a graph in which edges do not have direction		opposite: directed graph
valency	number of edges connected to a node		
vertex	a point on a graph; may be connected to other nodes by edges or may be isolated		a.k.a. node
weight	a level of "importance" or "heaviness" assigned to an edge e.g. distances of highways linking cities, or closeness between friends on a social network	a graph with weights is known as a weighted graph	