# Biology 495 Seminar: Are Biological Systems Like Facebook? Understanding Interactions in Cells, Organisms, Ecosystems

#### Dr. Ann E. Stapleton

<u>Office phone</u>: (910) 962-7267 Email: <u>stapletona@uncw.edu</u> <u>Office location</u>: Friday Hall 2061 <u>Office hours</u>: Tuesday 3:30 to 5:30 PM, Thursday 3:30 to 5:30 PM and by advance appointment. You may drop by anytime; call first if you want to make sure I am in. The easiest way to reach me is by email from your uncw.edu email account. Note that UNCW provides desktop computers and *landlines* to faculty; this means that I will be able to contact to you during regular working hours when I am in my lab or office. I will return emails within two business days.

<u>Course objectives</u>: Mastery of speaking skills and research skills for professional scientific presentations [EBC1, EBC3] and knowledge of systems biology topics [EBC2]. You will:

1) Be able to select an appropriate topic of investigation or research and communicate the relationship between the topic and educational or career goals. [CAP1], [EBC 1] and [IL1]

2) Be aware of and use a range of information accessing skills and databases to find relevant research papers and literature related to this topic. [CAP1] and [IL2, IL3, IL5]

3) Independently read and comprehend primary research literature. [CAP1] and [IL1]

**4**) Be able to apply biological concepts, principles and theories in your research appropriately. **[CAP1] [EBC 2]** 

5) Accurately describe methods of investigation in the research you selected. [CAP1] and [IL3]

6) Critically analyzing and evaluate the scientific results of the research. [CAP1] and [IL3]

7) Assess the conclusions and implications of the research. [CAP1] and [IL3]

8) Present and discuss the findings and implications of your investigation clearly, coherently and succinctly to your peers. [CAP1], [EBC3] and [IL4]

9) Demonstrate ethical use of information sources in written and oral work. [IL5]

10) Be aware of the historical and/or social context and significance of scientific discoveries.

<u>Grading</u>: 70% of your grade will be computed from your two seminar presentations (30% first, 40% second). Your second talk will be graded on the extent of improvement from your first talk. The first talk will be 5 minutes with two slides, to introduce your main point. The second talk will be 15 minutes.

10% of your grade will be based on your completion of an outline of your talks, which will be critiqued by Professor Stapleton before your presentations.

5% of your grade will be your completion of a self-evaluation of your own video of your practice talks.

15% of your grade will be based on completion of thoughtful evaluations of other speakers and discussion participation as evaluated through CATME surveys.

Grades are straight percentage: 90% to 100% = A, 80% to 89% = B, 70% to 79% = C, 60% to 69% = D, below 60% = F.

#### Class Organization:

For the first few weeks, we will get familiar with the topics through instructor-led discussion on basic concepts from the assigned reading. The textbook chapters we will read at the beginning of this course are available as an e-book from Randall Library, <a href="http://libcat.uncw.edu/record=b2741112~S4">http://libcat.uncw.edu/record=b2741112~S4</a>, Principles of systems science [electronic resource] / George E. Mobus, Michael C. Kalton, Publisher New York, NY : Springer, [2014]. All other readings and handouts are available on blackboard. You will consult with the professor and work out a topic for your talks; you will need to make an appointment to do this outside of class time. You will be expected to use recent (2015 and later) scientific papers as a source of facts for your talk, and to create appropriate visuals to illustrate your points. Give the professor a copy of your slides the day you speak. Electronic devices may only be used during class for class-related purposes and must be used on silent mode and without earpieces.

Complete the online tutorial, found at http://www.kumc.edu/SAH/OTEd/jradel/Preparing\_talks/TalkStrt.html, and read the slightly irreverent but accurate advice here: <u>http://colinpurrington.com/tips/science-talks</u>. The required writing guide required for all biology majors (J. Pechenik, A Short Guide to Writing About Biology, 9<sup>th</sup> edition) has a very helpful chapter on searches (Chapter 2) and on preparing talks (Chapter 11), please read these chapters or the equivalent chapters in other editions.

Think about the best talk you have heard--what made it good? If you can, I recommend attending the Friday 3PM Biological Sciences seminars in Dobo 103.

All members of UNCW's community are expected to follow the academic Honor Code. Please read the UNCW Honor Code carefully (as covered in the UNCW Student Handbook).

Academic dishonesty in <u>any</u> form will not be tolerated in this class. Please be especially familiar with UNCW's position on plagiarism as outlined in the UNCW Student Handbook. Plagiarism is a form of academic dishonesty in which you take someone else's ideas and represent them as your own. Here are some examples of plagiarism:

a. You write about someone else's work and do not give them credit for it by referencing them.

b. You get facts from your textbook or some other reference material and do not reference that material.

In accordance with NC SL 2010-211, you are entitled to two excused absences for religious observances per academic year. You must inform me in writing the first week of class if you will be missing any classes due to religious observance and using one of the two permissible absences for the academic year. In addition, inform the Registrar the first week of class who will then confirm your intentions to miss class with the impacted course instructors. Any absence for religious purposes will be considered unexcused unless you submit the request in writing the first week to me and to the Registrar.

UNCW practices a zero tolerance policy for any kind of violent or harassing behavior. If you are experiencing an emergency of this type contact the police at 911 or UNCW CARE at 962-2273. Resources for individuals concerned with a violent or harassing situation can be located at http://www.uncw.edu/wsrc/crisis.html.

The course instructor is happy to make accommodations to those students with disabilities. Students should first contact the Office of Disability Services in Westside Hall (3746). After obtaining your referral from the Office of Disability Services, please contact the faculty in your course.

#### WEEKLY SCHEDULE

This schedule is subject to change; changes will be announced in class.

11 Jan In class: Discussion on syllabus led by professor, fill out CATME survey in class, make appointment with professor to discuss topic choice individually, write and turn in EBC1 prompt handout.

At home: list systems biology topics you are interested in and construct your topic assignment to turn in at the next class, reread syllabus, do talk tutorials online, read discussion prompt handout, read book chapters (available on the course blackboard page). The reading assignment is Mobus preface, Mobus Chapter 1.1, Mobus Chapter 1.2, 1.3, 1.4 and 1.5.

18 Jan In class: Discussion facilitated by professor, each team will lead discussion of two reading sections; team assignments will be made at the beginning of class and each team will have ten minutes to consult with each other on how they will lead their discussion. At the beginning of the class period turn in your talk topic area assignment.

At home: read Mobus Chapters 3 and 4, Meadows Chapter 1 and 2 (on Blackboard), finish your outline assignment to turn in at the next class meeting (first check that the professor has sent you an email approving your topic choice and scientific paper).

25 Jan Discussion of Mobus chapters 3 and 4, Meadows Chapter 1 and 2. Turn in the one-page outline of your talk at the beginning of the class period.

At home: Reading assignment Stapleton overview and InsightMaker modeling pdf (on Blackboard). Test your access to InsightMaker and plan to bring a laptop that can access the internet. You may work with your team to coordinate laptops/internet access. Begin preparing your short talk.

1 Feb In class: Discussion of reading, construct InsightMaker models in class. Your graded outline will be returned at the end of class. NOTE: please bring a laptop to class to access InsightMaker, each team will need individual access to the site. At home: Finish preparing your short talk.

8 Feb first six 5 min student talks: Write and turn in your peer and self review forms for each talk (these forms will be provided in class). Speaker list:

1 Feb second six 5 min student talks: turn in your peer and self review forms for each talk. Evaluations of the first set of talks will be handed back at the end of class. At home: Read Stapleton review of systems biology (on Blackboard). Speaker list:

8 Feb Discussion of reading, fill out CATME evaluation of team effectiveness. Evaluations of the second set of talks will be handed out at the end of class. Speakers for the next class will turn in their video evaluation form.

15 Feb two 15 min student talks, 3 min discussion. Speakers for the next class will turn in their video evaluation form. Speakers –

22 Feb two 15 min student talks, 3 min discussion. Speakers for the next class will turn in their video evaluation form. Speakers –

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22 Mar two 15 min student talks, 3 min discussion. Speakers for the next class will turn in their video evaluation form. Speakers –

5 Apr two 15 min student talks, 3 min discussion. Speakers for the next class will turn in their video evaluation form. Speakers –

12 Apr two 15 min student talks, 3 min discussion. Speakers -

#### How well you accomplished your Bio495 talk outline assignment

\_\_\_\_\_1) topic area listed

\_\_\_\_\_2) background information with headers and subheaders is logical order and arrangement

\_\_\_\_\_background includes all the areas listed in the tutorials and class handouts (what the study is about (species, system etc.), why the study is important, advantages of the approach used)

\_\_\_\_\_information about illustrations/graphics that will be needed to show the key background in a talk

\_\_\_\_\_3) main results of the article with headers and subheaders in a logical arrangement

\_\_\_\_\_explanation of which graphics/specific data would be needed to best explain the key results

\_\_\_\_\_statement on the key result/conclusion (either stated explicitly or listed as being needed)

\_\_\_\_\_4) At the end of the outline include the citations to the peer-reviewed articles from Web of Science or Pubmed that you used.

#### Self Evaluation of Practice Talk Video for Bio 495

1. How well did I cover the main talk sections of

main conclusion and background

experimental design

main result

restatement of answer to main question

what next

2. My main stylistic change to practice before my class talk should be (e.g. no 'um', no hands in pockets, etc):

3. What changes to illustrations will need to be made and practiced before my class presentation?

#### **TALK PEER EVALUATION BIO 495**

Speaker	 		
Evaluator	 	 	
Date			

Give suggestions for improvement in these areas. You will be evaluated on the quality of your suggestions and comments. This form will only be viewed by the instructor.

- 1. How could the speaker better give a 'roadmap' for the talk?
- 2. Write down one question that you'd like to ask the speaker during the question period after their talk.

4. Were there particularly bad or good illustrations? Explain and provide suggestions.

5. What is the most important change the speaker should make for their next presentation?

#### TALK EVALUATION BIO 495

Speaker	 	 
Evaluator _	 	 

Date\_\_\_\_

Give suggestions for improvement in these areas. You will be evaluated on the quality of your suggestions and comments.

1. How could the speaker better convey the main point of the research?

2. How well did the speaker do in following advice for designing and presenting short talks?

3. Were there particularly bad or good illustrations? Explain and provide suggestions.

4. What is the most important change the speaker should make for their next presentation?

Channeling David Banks...a short history of network analysis

Cycles and how they work

## 1. Some Background

Network science has no home. Many different fields have made important and completely distinct contributions to the underlying theory.

This talk will emphasize the work of sociologists, statisticians, and physicists. But this omits key ideas from:

- mathematicians, who developed graph theory, characteristic polynomials, hypergraphs, and tools such as the Laplacian spectrum of a graph;
- operations researchers, who developed the Ford-Fulkerson algorithm for network flows and Traveling Salesman methods for network traversal (i.e., Hamiltonian cycles);
- biochemists, who pioneered the use of feedback loops and compartmental modeling (e.g., for PK/PD metabolism);
- machine learners, who led the way in fitting dynamic models to very large and very complex data sets.

# 2 Sociology

Social networks, a major and popular strand of network science, began with work by Georg Simmel in the 1900s and was extended by Jacob Moreno in the 1930s.

Simmel introduced the concept of dyads and triads, emphasizing the fact that human behavior is not well-described in terms of individual choice, but rather needs explanation in terms of relationships among sets of people.

The term **Simmelian ties** refers to three-way relationships, and there is psychological evidence that this is how normative behaviors are enforced. ("God is watching" or "I'll tell Mom".)

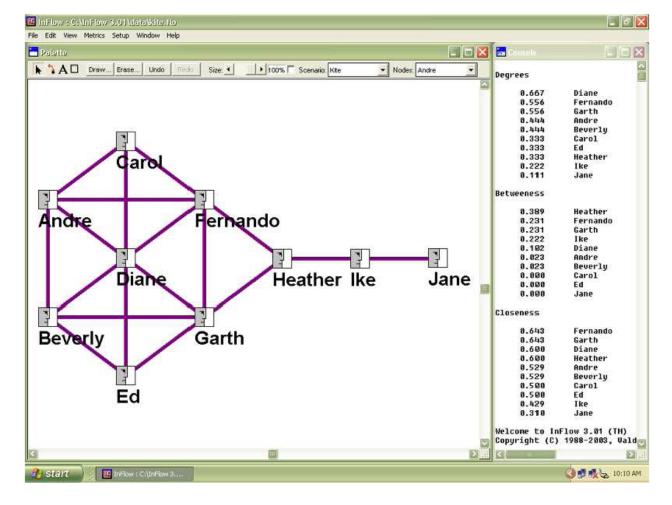
Moreno introduced the sociogram, which is the explicit representation of relationships among agents in terms of nodes and edges in a graph. This work led sociologists to develop theories of **social capital**, in which a web of favors and trust becomes an individual resource. The practical implication is that advancement through networking has become a favored business strategy.

A related concept is **centrality**, in which a node in a graph may be important becomes of its connectivity properties rather than any intrinsic merit. This is often described in terms of human social networks, where key information or resources might be accessed by someone who can link two parties, but it also arises in trade networks, international relations, and co-authorship patterns.

Sociologists also invented the idea of **triad completion** as a force in human relations. If Andy and Bob are friends, and Andy and Carl are friends, then there is a tendency for Bob and Carl to become friends. (But maybe not so much if Andy is replaced by Amy.)

These core ideas have been elaborated in many important ways. And sometimes these ideas (especially centrality) are useful in non-social networks.

Diane has degree centrality; she is highly connected. Heather has betweenness centrality; she links two communities. Garth and Fernando have closeness centrality, since they have short paths to everyone.



# 3. Physics

The physics community trigged a lot of the popular press attention to social networks. In particular, they established specific **small world** models and **power law** (or **scale-free**) models.

Small world theory has two (related) senses:

- the average shortest path length between two nodes is small;
- nodes tend to be part of densely connected cliques.

These properties are relative to an Erdös-Rényi network in which each possible edge is present or absent according to an independent coin toss with common p.

Power law models refer to the degree distribution, which describes the probability that a random node has k edges.

In large-world graphs, such as lattices, the average shortest path (ASP) tends to be large. But nodal clustering behavior can vary widely; some large-world graphs have many local edges (e.g., with lattices of cliques) and others do not.

There are many measures of clustering, but a standard one is the **global clustering coefficient** which is

# $C = \frac{3 \times \text{ number of triangles}}{\text{number of connected triples of nodes}}$

In Erdös-Rényi networks, both the ASP and the cluster measure tend to be small.

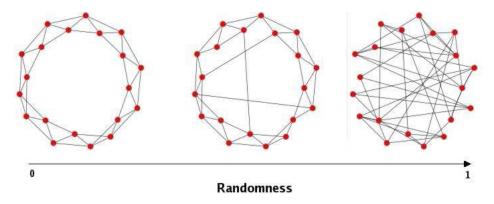
Watts and Strogatz (1998) wanted a model for networks that had short ASPs but tunable clustering. This is because real-world graphs (social relations, Internet pages, genetic regulation) tend to have small ASPs but large clustering measures.

Their beta model is an algorithm for generating a network on n nodes with mean degree k and cluster behavior controlled by a parameter  $\beta$ .

Arrange the n nodes in a circle. Then

- **1.** Connect each node to its k nearest neighbors along the circumference.
- 2. For each node, randomly reconnect its edges with probability  $\beta$ , where the new terminus is chosen uniformly from the n-1 other nodes.

Courtesy of Wikipedia, the following figure illustrates how a circular lattice graph changes as the *beta* model increases the probability of random connections.



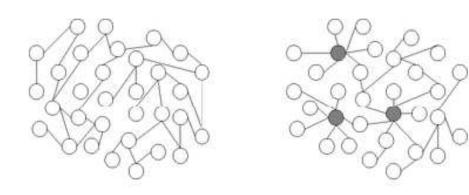
The beta model produces graphs in which all nodes have the same number of edges; the **degree** is constant. But real networks are inhomogeneous in degree, and the degree distribution is interesting.

One approach to inhomogeneous degree is the preferential attachment model (Barabási and Albert, 1999). Here the probability that a new edge is added to a node is proportional to the degree of that node (so the rich get richer). From a statistical standpoint, this relates to both Zipf's Law and the Chinese Restaurant Process.

The mathematics of preferential attachment imply that the degree distribution is (asymptotically) a power law, so

### ${\rm I\!P}[k] \propto k^{-\alpha}$

where, empirically, one usually sees  $2 \le \alpha \le 3$  for protein-protein interaction networks, neural networks, and Internet connectivity.



(a) Random network

(b) Scale-free network

The preferential attachment model has small world behavior, but does not produce networks with the strong clustering one often sees. Thus neither the beta model nor the preferential attachment model successfully capture all three of the small world, strong clustering, and power law phenomena that characterize most applications. Researchers are working to find tractable models that achieve all three.

In some cases (e.g., topic areas within the Wikipedia) one sees that degree distributions are more log-normal than scale free.

# 5. Dynamic Models

Dynamic models describe change in the nodes and edges of a network over time. My two favorite applications are:

- fitting a model to the evolution of the Wikipedia, where articles are nodes and hyperlinks are edges;
- predicting fission in baboon troops from information on kinship, agonism, genetics, grooming, agonism, and co-foraging.

The problems are quite different, and illustrate a range of issues.

Probably there are no broad models for dynamic networks; each analysis is idiosyncratic. But there are basic strategies that can be adapted to different situations (i.e., Markov chains, time series, EWMAs).

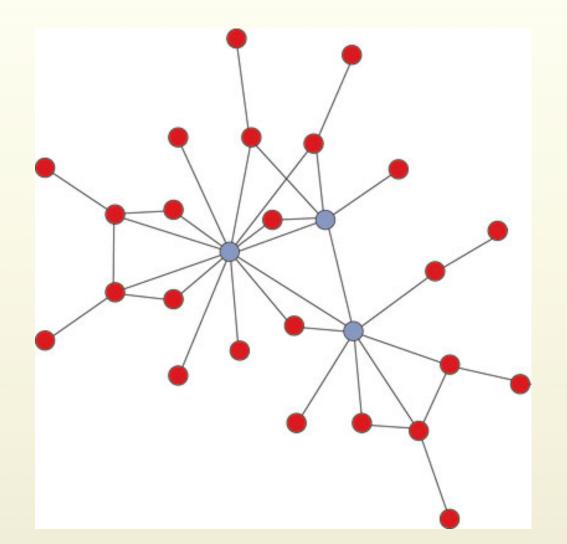
# 6. Conclusions

Network models are hot new science. The field is unsettled, and the combination of tools from multiple disciplines is still being worked out.

Key ingredients include logistic regression models to predict link probabilities from covariates, feedback mechanisms, and fits with cluster structure, prescribed degree distributions, and small world features.

We talked about static models, but that's misleading. In most cases one may observe a single time point and try to model it, but the model used would depend on whether this is a mature or new network.

Latent space ideas have become very popular—they provide automatic cliquing, good visuals, and are often interpretable. But models for change in latent space are still being built.



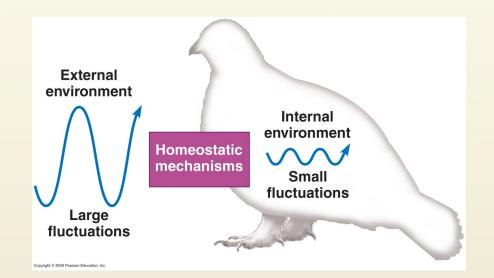
# Beyond nodes and edges: when the type of edge matters

Feedforward and feedback—amplifying and dampening the system flow

# Stampede or riot

# Homeostasis in animals

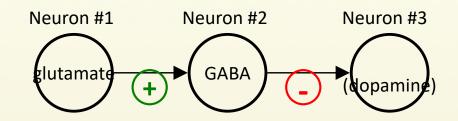




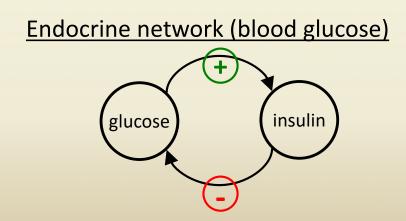
# Is this a balancing feedback loop?

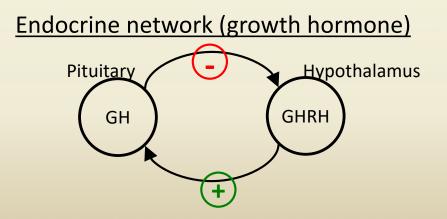
# Network that does not result in homeostasis:

Neuronal network (neurons in series)

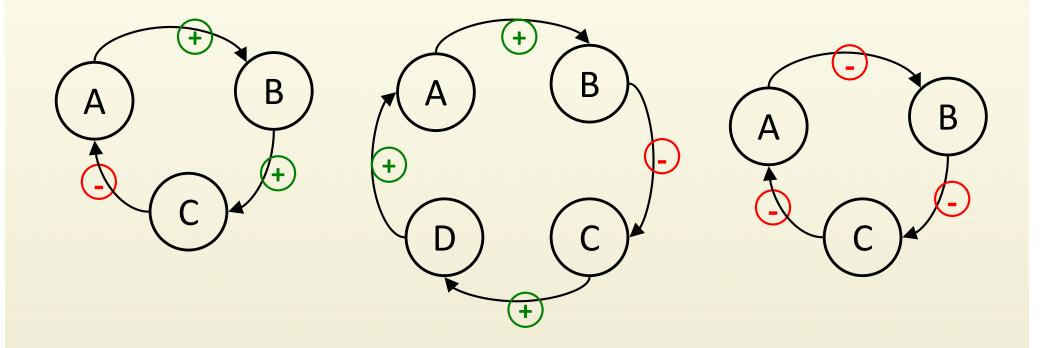


# Networks that do result in homeostasis:





# What do these networks do?



If there is an odd number of repressive/negative arrows, the system has negative feedback.

# Does Facebook have balancing feedback loops?

Is biology like Facebook?