Clemson University
School of Mathematical & Statistical Sciences

Syllabus
MATH 9850-001, Algebraic Systems Biology (Fall 2024)
MWF 1:25–2:15pm, Martin Hall E-004

Instructor: Dr. Matthew Macauley

Course Description: It may come as a surprise to mathematicians and biologists alike when they first hear the term "*Algebraic Biology*." The reaction may be that of inquisitive curiosity, skepticism, or cynicism, as mathematicians have earned a reputation for occasionally making questionable abstractions and constructing frameworks that are perhaps too detached from reality to be more than just amusement. One reason is that abstract algebra is almost never taught in biology or biomathematics courses, nor are applications to biology usually presented in algebra courses. However, *linear algebra* plays a fundamental role in applied fields such as mathematical biology. Systems of linear equations arise both as models of natural phenomena and as approximations of nonlinear models. Similarly, it should not hard be to surmise that systems of *nonlinear* polynomials can also arise from biological problems. A natural setting to work with multivariate polynomials are commutative rings, and the branch of mathematics that involves solving systems of such polynomials is *algebraic geometry*. Polynomials arise in models of biological systems across a variety of frameworks, from classical differential equations, to Boolean networks, to statistical models in phylogenetics and genomics, to topics in neuroscience. Broadly speaking, *algebraic biology* is an umbrella term that encompasses a wide range of problems from mathematical biology where polynomials arise.

The primary focus of this course will be on discrete models of biological systems. If the state space is binary, then these are sometimes called *Boolean networks*. In general, any function over a finite field is a multivariate polynomial, which means that discrete models of this type can viewed as *algebraic models*, and analyzed using tools from computational algebra. The discrete framework is an alternative to the more classical modeling techniques involving differential equations. Both have their advantages and disadvantages, and we will learn about both of these. Additionally, it cannot be understated how many new mathematical research problems, that are interesting on their own right, arise out of the original application of algebra to biology.

Topics: There will be three main parts of this class, each of a different flavor, despite being intimately connected. If we get through this, we will explore additional topics, as time allows.

Part I: Biochemical reaction networks, gene regulation, and ODE models
- Biochemical reaction networks.
- Gene regulation by operons.
- Delay differential equation models.

Part II: Boolean models of molecular networks
- Basic Boolean models.
- Boolean models of operons.
- Advanced features in Boolean models.
- Reduction of Boolean models.

Part III: Algebraic models and methods
- Algebraic models and finite dynamical systems.
- Reverse engineering the wiring diagram.
- Reverse engineering the model space.

Target audience: There are no prerequisites for this course, and the target audience is mature (=at least at the advanced undergraduate level) students in mathematics, biological sciences, engineering, or physics. I will *not* assume that math students have any biological background, nor will I assume any mathematical background from students in biology. The goal is to create an inclusive course, where the *diversity of backgrounds is a strength*. Bringing together people from different scientific backgrounds to study interdisciplinary scientific problems and effectively communicate is difficult but essential. It is the hope of the instructor that this course will lead to networking between students from different departments with overlapping interests but different training, expertise, and academic footprints. Even just within the mathematical science, the content of this course can appeal to pure mathematicians with an interest in algebra, to applied and computational mathematicians and statisticians who don't know or care what a ring is.

Learning Outcomes: Upon successful completion of MATH 9850, students will be able to:

- Model a molecular network, such as an operon, with Boolean logic.
- Convert a Boolean models into a system of multivariate polynomials, and use techniques from computational algebra to analyze them.
- Use software, including Macaulay2, R, and GINSim, to analyze discrete models.
- Use pseudomonomials to reverse engineer a discrete model from partial data, to infer the possible interactions of the variables, or the reconstruct place fields in neuroscience.
- Build algebraic models that incorporate biological features such as time delays, dilution, degradation, and bistability.
- Model biochemical reaction networks with nonlinear differential equations, under the assumption of Michaelis–Menten kinetics, and interpret steady states using algebraic varieties.
- Use computational algebra to reduce a large state space while preserving key dynamical features, such as fixed points.
- Explore new research problems in the interface of algebraic geometry and biology.

Texts: There is no required book for this class. I will use a number of a books to draw materials from, all of which should be available online, such as:

- Raina Robeva and Terrell Hodge (eds.), *Mathematical Concepts and Methods in Modern Biology: using modern discrete models*, Academic Press, 2013.
- Raina Robeva (ed.), *Algebraic and Discrete Mathematical Methods for Modern Biology*, Academic Press, 2015.
- Raina Robeva and Matthew Macauley (eds.), *Algebraic and Combinatorial Computational Biology*, Academic Press, 2018.
- René Thomas and Thomas D'Ari, *Biological Feedback*, CRC Press, 2006.
- David A. Cox, John Little, and Donal O'Shea. *Ideals, Varieties, and Algorithms: An Introduction to Computational Algebraic Geometry and Commutative Algebra*, Springer, 2015 (4th edition).

I will also likely use recent papers and other sources, as appropriate.

Useful websites:

Course webpage: `http://www.math.clemson.edu/~macaule/classes/f24_math9850/`

Macaulay2: `http://www2.macaulay2.com/Macaulay2/`

GINsim (Gene Interaction Network simulation) `http://ginsim.org/`

Cyclone: open source package for simulation and analysis of finite dynamical systems.
`https://github.com/discretedynamics/cyclone/`

Posit (formerly RStudio) `https://posit.co/download/rstudio-desktop/`

Canvas: `https://www.clemson.edu/canvas/`

Overleaf: `http://www.overleaf.com/`

Schedule: This course will be conducted in-person. However, they may be times when I am unavailable, either due to illness or travel. In this case, class will be held over Zoom.

Homework: This is a topics course, and will be significantly less work-intensive than a regular graduate prelim course. There will be light homework, to make sure that students keep up with the material beyond just attending lecture. Even in a topics class, there is no substitute for problem solving. *Submitted assignments must be typeset with LaTeX.* Working together is encouraged, but everyone must do their own work, and *collaborators must be cited.*

Project: Students will choose a special topic to give a short presentation on, and a short high-level written summary, much like the AMS Notices "*What is... ?*" long-running column. This will allow students to explore topics that they might be interested in, which we are not covering in lecture.

Exams: There will be one midterm exam during the semester. The purpose is mostly to encourage everyone to keep up with the basic ideas of the material. I will proctor the midterm over Zoom. You must provide consent to having the meeting recorded.

Grading: Final grades will be calculated as follows:

Homework	30%
Midterm	20%
Project	20%
Participation	20%
Quizzes	10%

I will begin with the default assumption that final grades will correspond to the following ranges:

$$\text{A} \geq 90\% > \text{A–} \geq 85\% > \text{B+} \geq 80\% > \text{B} \geq 75\% > \text{B–} \geq 70\% > \text{C+} \geq 65\% > \text{C} \geq 60\% > \text{C–} \geq 50.$$

I may lower these cutoff, but will not raise them. For example, the bottom end of the B range might be lower than 75%, but the top end will *not* by higher than 80%.

Communication Strategy: Email (**macaule@clemson.edu**) is the best way to reach me. I will check it several times a day, six days a week. (I frequently don't check email on Saturdays.)

If you send me an email and do not get a reply by the time you go to bed, please re-send it, as that is my mistake. Just click "Reply" and "Send"; no need to explain.

Students are responsible for checking their Clemson email regularly, as that address will be the one subscribed to the class email list. I encourage all of us to be on a first-name basis.

I will be in my office most weekdays, and my office phone is 656-1838. This is a good way to reach me, on a moment's notice, if needed, but please send email instead of a leaving a voicemail.

Office hours: I will be available for office hours over Zoom several days a week at 7pm. I am also in my physical office every day; students are welcome to drop by.

Required technology:

A computer and reliable internet connection.

A free Zoom account.

A smartphone scanning app. There are many free apps, such as CamScanner or Adobe Scan. If you do not have a smartphone, a traditional scanner will suffice, but a smartphone app is preferred.

Access to a program that runs LaTeX. I recommend `overleaf.com`.

Zoom Info: Please turn your camera on for all Zoom meetings, whether they are remote classes and/or office hours.

There will be one common Zoom URL for all remote classes, and another for all Office Hours, which may also be attended by my other class. These URLs will be emailed to the class list. I am also available to meet by appointment, if desired. In that case, email me and include block(s) of time in which you are available. Please let me know in advance if you want any meeting to be private, like if you want to discuss your grade. In that case, I will use a different Zoom meeting.

If I do not show up by the beginning of class, check your email. If you have not heard anything from me 10 minutes into class, you may assume that class has been canceled.

Key Dates

Aug 21 (Wed)	Classes begin
Aug 27 (Wed)	Last day to register or add a class
Sep 2 (Mon)	Labor Day holiday; no class
Sep 4 (Wed)	Last day to drop a class or withdraw from the University without a **W** grade
Oct 28 (Wed)	Last day to drop a class or withdraw from the University without final grades
Oct 14–15 (M–Tu)	Fall break
Nov 27–29 (W–F)	Thanksgiving break break
Dec 6 (Fri)	Last day of class
Dec 13 (Fri)	Project presentations (final exam block), 3:00–5:30pm

"No exceptions": In any class syllabus, no matter how they are worded, policies and phrases like "no exceptions", "no make-ups", etc. are *never* actually what they sound, and this is especially true this semester. Things happen, from natural disasters (hurricanes, tornadoes), to human disasters (9/11, school shootings), to personal and family tragedies, to health emergencies (COVID, auto accidents, hospitalizations). This does not mean that any exception or extension will be granted, but I will do my best to be reasonable, fair, and accommodating.

Special Accommodations: Clemson University values the diversity of our student body as a strength and a critical component of our dynamic community. Students with disabilities or temporary injuries/conditions may require accommodations due to barriers in the structure of facilities, course design, technology used for curricular purposes, or other campus resources. Students who experience a barrier to full access to a class should let the instructor know, and make an appointment to meet with a staff member in Student Accessibility Services as soon as possible. You can make an appointment by calling 864-656-6848 or by emailing studentaccess@lists.clemson.edu. Students who receive Academic Access Letters are strongly encouraged to request, obtain and present these

to their instructors as early in the semester as possible so that accommodations can be made in a timely manner. It is the student's responsibility to follow this process each semester. You can access further information here: `http://www.clemson.edu/campus-life/campus-services/sds/`.

COVID-19: Most of the following will not apply to our online class, but I am required to include it. While on campus, face coverings are required in all buildings and classrooms. Face coverings are also required in outdoor spaces where physical distance cannot be guaranteed. Please be familiar with the additional information on the Healthy Clemson website (`https://www.clemson.edu/coronavirus/index.html`), such as the use of disinfectant wipes for in-person classes.

If a student does not have a face covering or refuses to wear an approved face covering without valid documented accommodation, *I will ask the student to leave the academic space and will report the student's actions to the Office of Community & Ethical Standards as a violation of the Student Code of Conduct*. If the student's actions disrupt the class to the extent that an immediate response is needed, I may call the Clemson University Police Department at 656-2222.

Mental health: Your mental health is important to me, and I am always available to talk. Please don't hesitate to reach out. We're in this together, and *all* of us are struggling in some regards, myself included.

Title IX Policy: Clemson University is committed to a policy of equal opportunity for all persons and does not discriminate on the basis of race, color, religion, sex, sexual orientation, gender, pregnancy, national origin, age, disability, veteran's status, genetic information or protected activity (e.g., opposition to prohibited discrimination or participation in any complaint process, etc.) in employment, educational programs and activities, admissions and financial aid. This includes a prohibition against sexual harassment and sexual violence as mandated by Title IX of the Education Amendments of 1972.

The University is committed to combating sexual discrimination including sexual harassment and sexual violence. As a result, you should know that University faculty and staff members who work directly with students are required to report any instances of sexual harassment and sexual violence, to the University's Title IX Coordinator. What this means is that as your professor, I am required to report any incidents of sexual harassment, sexual violence or misconduct, stalking, domestic and/or relationship violence that are directly reported to me, or of which I am somehow made aware.

There are two important exceptions to this requirement about which you should be aware:

Confidential Resources and facilitators of sexual awareness programs such as "Take Back the Night and Aspire to be Well" when acting in those capacities, are not required to report incidents of sexual discrimination.

Another important exception to the reporting requirement exists for academic work. Disclosures about sexual harassment, sexual violence, stalking, domestic and/or relationship violence that are shared as part of an academic project, a research project, classroom discussion, or course assignment, are not required to be disclosed to the University's Title IX Coordinator.

This policy is at `http://www.clemson.edu/campus-life/campus-services/access/title-ix/`. Alesia Smith is the Executive Director for Equity Compliance and the Title IX Coordinator. Her office is at 223 Holtzendorff Hall, phone number is 864.656.3181, and email address is alesias@clemson.edu.

Academic Integrity: As members of the Clemson University community, we have inherited Thomas Green Clemson's vision of this institution as a 'high seminary of learning'. Fundamental to this vision is a mutual commitment to truthfulness, honor, and responsibility, without which we cannot earn the trust and respect of others. Furthermore, we recognize that academic dishonesty detracts from the value of a Clemson degree. Therefore, we shall not tolerate lying, cheating, or stealing in any form.

Copyright Statement: Some of the materials in this course are possibly copyrighted. They are intended for use only by students registered and enrolled in this course and only for instructional activities associated with and for the duration of the course. They may not be retained in another medium or disseminated further. They are provided in compliance with the provisions of the Teach Act. Refer to the Use of Copyrighted Materials and "Fair Use Guidelines" policy on the Clemson University website for additional information: `http://clemson.libguides.com/copyright`.