# Chemistry 4000
# Modelling Biochemical Reaction Networks
# Fall 2010


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## Purpose of this document

This document describes the procedures by which this course will be conducted and evaluated. You are responsible for familiarizing yourself with this document and for seeking clarification from the instructor if anything is unclear to you. The procedures and deadlines enunciated in this document will not be altered without good reason. Any necessary changes or amendments to the procedures or deadlines will be announced via the class mailing list. I am willing to listen to requests for changes, particularly if they are made before the add/drop date (Sept. 14), but I reserve the right to decide whether changes are necessary or not.

## Course prerequisites

The prerequisites for this course are **Chemistry 2740**, or **Mathematics 3600**, or **Physics 2800**, or **Biochemistry 3100**.

## Textbook

*Computational Cell Biology*, edited by Fall, Marland, Wagner and Tyson (Springer, ISBN 0-387-95369-8)

## Software

XPPAUT version 5.99 or above, available from `http://www.math.pitt.edu/~bard/xpp/xpp.html`. You will need to install this software on a computer to which you have ready access. Installation instructions will be distributed separately. You will be given lessons on how to use this program in class.

## Email

Important information will frequently be communicated to the class via email. It is *your responsibility* to keep an eye on your email during the term. This includes making sure that you do not exceed your email quota. You can check your email account status at `https://www.uleth.ca/webtools/account_tools/acctstatus`.

## Office hours

I operate on an open-door basis: If I'm in, you are welcome to stop in to ask questions. You are also welcome to make appointments with me if you prefer.

## Grading scheme

| Evaluation type | Weight |
|---|---|
| Weekly assignments | 40% |
| Project | 55% |
| Participation during oral presentations | 5% |

Extensions or other accommodations for written work not submitted by the deadline will only be granted under exceptional circumstances. Weekly assignments submitted after the published deadline will normally earn a mark of zero. Project components submitted after their published deadlines will be penalized by 5% per day, with an automatic one-day minimum penalty.

In all written work submitted to me, spelling and grammar count. Please proofread your work carefully prior to submission.

## Plagiarism detection

Plagiarism is the use of someone else's ideas, words, or graphics without proper attribution, leaving the impression that these ideas, words or graphics are your own work. Whether intentional or not, plagiarism is a serious academic offense, and may result in severe sanctions, as outlined in the University Calendar.

It is my belief that, nowadays, most plagiarism is unintentional and results from writing some sentences about a topic immediately after reading about this topic, often with the source material still at hand. It's almost impossible to avoid writing using somebody else's words and structure at that point. The easiest way to avoid the plagiarism is to write in a "clean room" environment where you separate reading from writing:

- While you are reading, take notes in your own words in point form (no complete sentences), keeping track of the source from which each idea came.
- Think about how *you* think the ideas you have read about should be organized. Don't organize your paper the same way as some particular source you have read, since this is a form of plagiarism, too.
- Create an outline, still in point form, based on your plan.
- Now write the text, using your notes for details, and in particular citing the relevant sources as you go. Go back to the original source *only* to clarify a point and *only* after you have written some text (however crude) on the point in question.

In order to provide opportunities for you to learn what plagiarism is and how to avoid it, written components of your project (but not your weekly assignments) will be submitted through `turnitin.com`. This system will compare each of your submissions to billions of documents (web pages, published journal articles, previously submitted student papers, etc.) and generate an originality report. These reports highlight passages (often quite short) that look like passages in some of the source documents in `turnitin`'s database. Even in documents completely free of plagiarism, there are always some such passages. However, plagiarized documents generally show a pattern of extensive borrowing from a few sources that is usually easy to recognize.

What I like about `turnitin` is that it's a good teaching tool. I set it up so that you can resubmit assignments as often as you like until the deadline, and view your own originality reports. This means that, if you are inadvertently plagiarizing from one or more sources and don't wait until the last minute to submit an assignment, you have a chance to fix these problems. Ideally, if you were having problems understanding plagiarism or `turnitin`'s originality report, you would come talk to me.

Only the person who submitted an assignment (you) and the instructor (me) can view your submissions to `turnitin` and the corresponding originality report. Thus, your privacy is protected. **Note that your submissions will be added to `turnitin`'s database** to prevent future plagiarism of your work. This database is not directly visible to users of the system. In particular, student papers are not visible, even when they generate a "hit" in `turnitin`. The only information given to users in these cases is the originating university. No personal information about the original author is divulged, nor is the original paper accessible, although the overlapping passage is highlighted. There is a mechanism for anonymously contacting the instructor of the original course to request permission to view the paper. I would not release permission without contacting the original author (you, the student), so permission to use your intellectual property, beyond simply flagging overlaps with submitted papers, remains with you. To my mind, there are no serious privacy or intellectual property issues with `turnitin`. However, I do understand that some people have concerns about the archiving of their work by `turnitin.com`, so if you object to this, please discuss your concerns with me as soon as possible.

You must understand that `turnitin` is not a panacea. There are a few things that you should bear in mind:

- It cannot detect all forms of plagiarism, so a clean originality report is not certification of non-plagiarism. It is still your responsibility to educate yourself about plagiarism and to avoid it. I will deal with cases of plagiarism, if any surface, according to University policies, as enunciated in the current Calendar. If you are not sure what plagiarism is, I strongly urge you to read the Office of Research Integrity's guide on this subject, available at `http://ori.hhs.gov/education/products/plagiarism`.
- The originality report for a first submission is generated very quickly (within the hour). If you resubmit an assignment, subsequent originality reports can take up to 24 hours to appear. (This is necessary so that they can flush your original submission out of their database prior to generating a new originality report. Otherwise, we would get a useless report showing that your resubmission is very similar to your original submission.) Keep this in mind if you intend to go through several rounds of submission and want to view your originality reports prior to the final submission deadline. (It is not necessary for your final originality report to be generated by the submission deadline for an assignment, so you can submit assignments up to the last minute, even if you had previously submitted a version to `turnitin`.)

The class ID and enrollment password as well as instructions for using `turnitin` will be distributed by email after the add/drop date for this term.

## Weekly assignments

Assignment deadlines will be printed on the assignments, which will be available as hard copy in class, or on the course web site. As a rule, assignments will be released on Fridays and due by 4:00 p.m. the following Friday. All assignments should be typed and may either be submitted in printed form or electronically (by email). Acceptable electronic formats (in no particular order): Word, pdf, LaTeX. Other formats may be acceptable, but check with me first.

While I expect that you will talk to each other and to me about the assignments, each assignment must be the product of your own work. My advice, in order to avoid misunderstandings and charges of plagiarism, is not to take written notes of any kind when talking to fellow students about an assignment, and not to exchange files.

## Project

The objective of your project will be to demonstrate mastery of the techniques developed in class by studying a previously published model of a biochemical network. Your study need not be greatly original, but it should show some ability to go beyond the published results, either by exploring an issue not fully studied in the source literature (e.g. looking at what happens when you change some of the rate or equilibrium constants in the model, or looking at a stochastic version of a deterministic model), or by extending the model in some way (e.g. adding a reaction not considered by the original authors). Your work will culminate in a report and in a short oral presentation.

The project will have the following components:

| Component | Weight | Deadline |
|---|---|---|
| Selection of problem | 5% | October 15, 4:00 p.m. |
| Preliminary report | 10% | November 12, 4:00 p.m. |
| Final report | 30% | December 9, 11:59 p.m. |
| Oral presentation | 10% | TBA |
| Total: | 55% | |

**Selection of problem:** The goal of this assignment is to make sure that you are proposing to do something reasonable (not too little, not too difficult, etc.). You will need to choose a published model of a biochemical system and to decide (roughly) what you intend to do with it. You must submit a **two-page double-spaced** document that

- describes the general problem area and why it's interesting;
- describes briefly what the previously published model had accomplished; and
- indicates the work you intend to carry out.

There should be at least one reference (the paper you intend to use as a basis for your work). If you include more references than that, they can go onto a third page.

You must submit this document through `turnitin.com`. I will be happy to comment on drafts of this document before you submit your final version to be graded. If you want to benefit from this option, submit your draft to `turnitin.com` and send me an email to ask me to look at it. The same process would apply if you are concerned about your `turnitin` originality report. The final date for submitting a draft for comment is October 11.

The model you will study should be a model of a biochemical system and should take one of the following forms:

- a set of ordinary or delay differential equations, or
- a stochastic model, typically simulated using the Gillespie stochastic simulation algorithm.

Models of these types are now routinely found in many journals. If you have a particular area of interest, you can find models by doing a search on one of the Library's databases (Web of Science, Medline, etc.) using keywords appropriate to your interests and the word "model". Alternatively, you can browse specialist journals in theoretical biology and closely related areas such as *Biophysical Chemistry*, *BMC Systems Biology*, *Bulletin of Mathematical Biology*, *Computational Biology and Chemistry*, *IET Systems Biology*, *Journal of Biological Systems*, *Journal of Mathematical Biology*, *Journal of Theoretical Biology*, *Mathematical Biosciences*, *Mathematical Biosciences and Engineering*, *Mathematical Medicine and Biology*, *PLoS Computational Biology*, or *Theoretical Biology and Medical Modelling*, to name just a few. I will be more than happy to discuss potential topics with you before you commit anything to paper.

**Important note:** If you have previous or current experience in modeling (summer work, undergraduate thesis or independent study, etc.), you **may not** work on problems in the same area for your class project. You are however welcome to tie your modeling work in with past or current *experimental* work.

**Preliminary report:** Think of this as a report of your findings to, say, your lab boss. You should explain the model, what you have done, and show your results (preferably in graphical form). Make sure to include all equations and any parameters necessary to reproduce your results. Parameters should preferably be given in the figure captions or in tables since it's often hard to find parameters given in the text when you need them. References should be given where appropriate, but since there won't be a full discussion, there may not be many beyond the paper that inspired your study.

This assignment will give me a chance to provide some feedback on the amount and quality of work you have completed prior to your presentation and completion of your final report. I will also provide feedback on the presentation of your results (whether you are showing the right graphs to prove your point, etc.). It will be graded, so I expect your best effort, but if there are problems, we can catch them here and hopefully improve the quality of your final report.

Your report should be double spaced to leave me room for comments. Other than that, I don't require any particular format for the preliminary report, but you may want to think about the formatting requirements for the final report when composing this document.

Evaluation criteria for this assignment:

| Criterion | Weight |
|---|---|
| Completeness of report | 40% |
| Writing (logic, language) | 20% |
| Graphs, tables | 20% |
| Results (sufficiency, correctness) | 20% |

Note that there is less weight given to the results in this part of the evaluation so that, if you misunderstood what was expected or if there is some other problem (e.g. incorrect results), you can make it up in your final report.

You will submit your preliminary report through `turnitin.com`. I am willing to comment on drafts of your preliminary report submitted to `turnitin` up to November 5. If you want me to look at a draft, send me an email after uploading the document.

In addition to your report, you are required to send me your `xppaut` input file(s) by email to facilitate verification of your results.

**Final report:** Your final report should be formatted like a complete scientific paper, with an introduction, a section describing the model and computational methods used, results, discussion and conclusions. (Results and discussion can be combined if you prefer to write your paper that way.) Your references should be formatted as for the journal *BioSystems* (`http://www.elsevier.com/wps/find/journaldescription.cws_home/506017/authorinstructions`) and cited in text by the author-date method.

To label the axes of graphs and table headings, I prefer the following style: Suppose that we have some speeds, $v$, with the following values: $\{0.89 \times 10^8\,\mathrm{m/s}, 1.01 \times 10^8\,\mathrm{m/s}, 1.22 \times 10^8\,\mathrm{m/s}, 1.89 \times 10^8\,\mathrm{m/s}\}$. The corresponding table column heading or graph axis would be labeled $v/10^8\,\mathrm{m\,s^{-1}}$. The actual values entered in the table or plotted would then be $\{0.89, 1.01, 1.22, 1.89\}$. Note the use of division to take out both common factors and units from the quantities to be tabulated or plotted. Also note the use of exponents in the units rather than a solidus (/) to avoid ambiguity.

Your report will be evaluated by the following criteria:

| Criterion | Weight |
|---|---|
| Presentation (completeness, formatting, language, graphs, etc.) | 40% |
| Results | 40% |
| Discussion and conclusions | 20% |

Note the heavier emphasis on results in this evaluation. If you also consider the weighting of this report relative to other project components, you will realize that this will be the main point at which your results will be evaluated for the purpose of computing your final course grade. By now, you will have had lots of feedback on what is expected, so there should be no surprises. Also note the separate evaluation of the discussion and conclusions of your study. In your final report, I expect a thorough discussion of what your results mean (in terms of the biochemical problem the model is intended to illuminate), of what questions are still open, and of what further modeling and experimental work could be used to answer these questions. A good discussion will have both parts that are detailed discussions of individual results (e.g. of a particular graph or table), and integrative elements that consider all of your results together.

In addition to your report, you are required to send me your `xppaut` input file(s) by email to facilitate verification of your results.

**Oral presentation:** The oral presentations will be held in the last two weeks (or so) of term. Undergraduate oral presentations will be of a duration of **10 minutes**, with an additional 5 minutes set aside for questions and changeover from one student to another.

Oral presentations will be evaluated as follows:

| Criterion | Weight |
|---|---|
| Content and organization | 40% |
| Visual aids | 20% |
| Delivery | 30% |
| Ability to answer questions | 10% |

## Participation during oral presentations

You are required to attend all oral presentations unless you have a valid, verifiable reason such as a medical problem. You are also expected to participate by asking questions during the question periods which will

follow each presentation. It is of course understood that not all students will be able to ask questions in the limited time we have following any given presentation. I will be looking for an average level of participation when setting this part of your course mark.

## A rough roadmap for the course

OK, so what is this course going to be about? The purpose of this course is to introduce you to *some* of the methods used to model and analyze models of biochemical (and, by extension, chemical) reaction networks. We will likely not study any topics in great depth, adopting a survey approach instead. This will allow us to discuss, at least briefly, a couple of very modern topics, namely delay-differential equation models and stochastic models.

My intention is for this course to be accessible to a wide audience, including both undergraduate and graduate students, from a variety of majors. The consequence of teaching a course like this is that everyone will have something to learn, but that almost everyone will also run into topics they know well. Hopefully, the number of classes in which you learn something new will outnumber the number of classes in which we're just repeating stuff you already know.

Since this is the first time I have taught this course, I don't have a detailed, lecture-by-lecture plan laid out. The following is therefore just a rough road map of where we are likely to go. Depending on how things evolve and on your interests, we may deviate from this path in one way or another over the term. Please let me know at any time during the term if you think there are topics I should include or if there are topics on which you want more depth of coverage. I may not be able to satisfy all wants, but I will certainly take your suggestions into account. Note also that I may not cover topics in exactly the order presented here, particularly if I feel the need to rearrange some material in order to provide background for student projects. Finally, while the list below consists primarily of theoretical topics, rest assured that I intend to take a very practical, hands-on approach to the subject, hence the requirement that you get yourself a copy of `xppaut`.

You will probably have at least a vague idea of what most of the stuff in the outline below means, except perhaps for the material relating to stochastic systems. "Stochastic" means roughly the same thing as "random". For a variety of reasons, individual reactive events in reactions occur randomly. We can observe this randomness in experiments involving only small numbers of molecules. You can probably imagine the relevance of such systems to biology, so I'll leave it at that for now.

Here is the road map:

1. Kinds of models of biochemical systems and what they are good for
2. Preliminaries: brief overviews of cell biology and biochemistry, differential equations, chemical kinetics
3. Differential equation models of biochemical networks
    - Introduction to `xppaut`
    - Numerical integration methods
    - Alternative modeling approaches and their consequences
    - Types of behavior and their biological significance
4. Delay-differential equations and genetic regulation
5. Some key statistical ideas
6. Stochastic systems
    - Master equation
    - Stochastic simulations
    - Ways in which stochastic systems are different from differential equation models
    - Biological consequences of stochasticity