BT 5240 — Computational Systems Biology
Jan–May 2020
Course Plan

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Lectures

Lectures/Labs:	**E slot**: Tue (11:00), Wed (10:00), Thu (08:00) and Fri (16:50), at CRC 203
Instructor:	Karthik Raman
Office:	BT-II 221
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Teaching Assistants:	Lavanya Raajaraam (bt17d401@smail / BT 516)
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Office hours:	By appointment
Course Materials:	https://home.iitm.ac.in/kraman/courses/2020-BT5240/
Piazza:	http://piazza.com/iitm.ac.in/spring2020/bt5240

Objectives

The main objective of the course is to introduce you to various aspects of mathematical modelling, in the particular context of biological systems. At the end of the course, it is expected that you will have a knowledge of important concepts related to the mathematical modelling of complex systems, especially metabolic networks, protein interaction networks and gene regulatory networks, and will be able to apply them to model the behaviour of biological systems as well as develop strategies for manipulating them.

Course contents

1. Introduction to Mathematical Modelling
2. Introduction to Static Networks
3. Reconstruction of Biological Networks/Databases and tools for systems biology
4. Dynamic Modelling of Biological Systems
    - Solving ODEs
    - Parameter Estimation
    - Dynamic Modelling: Boolean Networks
5. Real-world applications of modelling in pharmaceutical R&D (2 lectures by Dr. Rukmini Kumar from Vantage Research)

6. Modelling metabolic networks/Constraint-based analyses
    - Flux balance analysis
    - Elementary modes
    - Applications
7. Current/Advanced Topics in Systems Biology
    - Introduction to synthetic biology
    - Evolutionary systems biology: robustness and evolvability of complex biological systems
    - Perspectives and challenges in systems biology

Pre-requisites

There are no formal pre-requisites for the course, other than a keen interest in math and biology and the knowledge of a high-level programming language! If the non-biologists wish for a refresher in biology basics, I will be happy to point to material or have a separate lecture.

Coursework and grading

- Attendance to the lectures is required; late-comers will be marked absent
- Consistent performance will be key to a good grade
- Weightage (minor changes may happen):

Mid-semester exam	20%
Homework	25%
Project	35%
–Abstract	5%
–First Report	5%
–Presentation	10%
–Final Report	15%
End-semester exam	20%

For every hour spent in class, I expect you to spend at the least 2–3 hours outside of class on reading relevant and additional material/programming to understand the concepts. I also expect you to inculcate professionalism and maintain the highest level of integrity.

Important Dates

28th February	Mid-semester Exam
6th March	Project Abstract Due
20th March	Project First Report Due
18th April onwards	Project Final Report Due
18th April onwards	Project Presentation Due
8th May	End-semester Exam

Homework

There will be 3–4 assignments during the course. They will mostly involve programming in a high-level language such as MATLAB or Python. These languages are easy to pick up and I will give an adequate introduction to MATLAB during the course if requested. Please have a look at this page

(from Cosma Shalizi's blog), on minimal advice to under-graduates on programming: http://cscs.umich.edu/~crshalizi/weblog/593.html. All deadlines (homework/project) are usually at 5:00 pm on the date mentioned, unless instructed otherwise.

In the past, I have observed that the majority of the time put into the assignment goes towards installation of the required tools! The following are some really useful tools:

- MATLAB!
- MATLAB BGL — http://www.stanford.edu/~dgleich/programs/matlab_bgl/ — this library has a huge number of functions for network analysis
- Cytoscape — http://www.cytoscape.org/
- COBRA Toolbox — http://opencobra.sourceforge.net/
- SBTOOLBOX 2 — http://www.sbtoolbox2.org/

Exams

There will be only two exams during the course — a mid-semester exam on 28th February and the end-semester exam on 8th May.

Course project

The main purpose of this project is to acquaint you with serious modelling. This will be in teams of two. In this project, you will have to:

- Propose a problem
- Define the corresponding system
- Formulate a mathematical model
- Attempt to validate it
- Refine the model
- Write a report explaining everything you did

What I expect essentially is that you will implement a reasonably challenging model, which has already been proposed in literature, and add a couple of improvements of your own. If you can build something from the scratch, that would be fantastic! This will be valuable hands-on experience in modelling/systems biology. The project will be for the duration of **seven weeks (8th March – 20th April)**, with the following schedule:

- 6th March: Problem statement due (300–400 word abstract). Please discuss with me beforehand, so that we can finalise the problem statement by this time. This is a very critical step of the project!
- 20th March: Project report 1 due (2 page write-up on the work done so far, challenges etc.)
- 18th April onwards: Final project report (8 page formal technical report) due, along with presentations

All abstracts/reports must be diligently formatted as per IFAC standards (commonly used in many 'control' conferences): see http://www.ifac-control.org/events/author-guide

Academic integrity

While you can take help from your colleagues on homework, *copying* is not permitted. Copying from anywhere, including the Web is not allowed. Offenders will be penalised letter grades. For example, you can ask your friends for hints if you are stuck, but at no point should you take a look at their code itself. I would much rather that you come to me if you are stuck. Note that I take copying extremely

seriously, and will not show any mercy.

The Institute guidelines (which I consider lenient) may be found here: http://academic.iitm.ac.in/sites/default/files/Graded_punishments.pdf. You must not carry your mobile phone/e-book reader to the exam desk, even if they have been switched off.

Tentative schedule

Week	Date	Day	Lecture #	Lab #	Topic
1	14-Jan-20	Tue	0		Introduction/Administrivia
1	15-Jan-20	Wed			Holiday – Pongal/MakaraSankranti
1	17-Jan-20	Fri	1		Introduction to Mathematical Modelling
1	17-Jan-20	Fri	2		Introduction to Mathematical Modelling
2	21-Jan-20	Tue		1	Introduction to MATLAB
2	22-Jan-20	Wed	3		The Practice of Mathematical Modelling
2	24-Jan-20	Fri	4		Introduction to Graph Theory
2	24-Jan-20	Fri		2	MATLAB continued
3	28-Jan-20	Tue	5		Representation of Biological Networks; SBML/SBGN
3	29-Jan-20	Wed	6		Network Biology: Structure of Biological Networks
3	31-Jan-20	Fri		3	Introduction to Network Biology
3	31-Jan-20	Fri		4	Network Biology (Cytoscape)
4	4-Feb-20	Tue	7		Network Topologies/Models
4	5-Feb-20	Wed	8		Community Detection/Network Motifs
4	7-Feb-20	Fri	9		Network Perturbations
4	7-Feb-20	Fri		5	Network Biology (Topologies)
5	11-Feb-20	Tue	10		Network Biology Applications
5	12-Feb-20	Wed	11		Reconstruction of Gene networks/Protein interaction networks
5	14-Feb-20	Fri	12		Reconstruction of signalling networks and metabolic networks
5	14-Feb-20	Fri		6	Network Perturbations
6	18-Feb-20	Tue	13		Introduction to Dynamic Modelling
6	19-Feb-20	Wed	14		Modelling Enzyme Kinetics/Solving ODEs
6	21-Feb-20	Fri	15		Parameter Estimation: Intro/Optimisation
6	21-Feb-20	Fri		7	Solving ODEs/Parameter Estimation with MATLAB
7	25-Feb-20	Tue	16		Parameter Estimation: Algorithms
7	26-Feb-20	Wed		8	Parameter Estimation with MATLAB
7	28-Feb-20	Fri			**Mid-semester Exam, 5:00 pm - 7:00 pm**
8	3-Mar-20	Tue	17		Parameter Estimation: Algorithms/Diagnostics; **Mid-term course feedback due**
8	4-Mar-20	Wed	18		Discrete Dynamic Models: Boolean Networks
8	6-Mar-20	Fri	19		Introduction to Constraint-based Modelling
8	6-Mar-20	Fri		9	Boolean Networks; **Project Abstract Due**
9	10-Mar-20	Tue			No class – Non-instructional day—Holi
9	11-Mar-20	Wed	20		Introduction to Constraint-based Modelling: FBA/FVA/Understanding FBA
9	13-Mar-20	Fri	21		Constraint-based Analyses of Metabolic Networks: MoMA/ROOM; **Mid-sem Discussion**

Week	Date	Day	Lecture #	Lab #	Topic
9	13-Mar-20	Fri		10	Constraint-based Analyses of Metabolic Networks
10	17-Mar-20	Tue	22		Constraint-based Analyses of Metabolic Networks: Other approaches
10	18-Mar-20	Wed	23		Elementary Modes
10	20-Mar-20	Fri	24		Perturbations to Metabolic Networks: Knock-outs
10	20-Mar-20	Fri		11	Constraint-based Analyses of Metabolic Networks; **Project 1st Report Due**
11	24-Mar-20	Tue	25		Perturbations to Metabolic Networks: Synthetic Lethals
11	23-Mar-20	Mon	26		Perturbations to Metabolic Networks: Over-expression/Regulation; **Wednesday timetable**
11	24-Mar-20	Tue	27		Applications of Constraint-based Analyses and Limitations
11	25-Mar-20	Wed	28		Modelling Microbial Communities
11	27-Mar-20	Fri		12	Constraint-based Analyses of Metabolic Networks: Over-expression/Synthetic Lethals
11	27-Mar-20	Fri		13	Constraint-based Analyses of Metabolic Networks: Over-expression/Synthetic Lethals
12	31-Mar-20	Tue	29		Introduction to Synthetic Biology
12	1-Apr-20	Wed	30		Design Principles of Biological Networks
12	3-Apr-20	Fri	31		Robustness in Biological Systems
12	3-Apr-20	Fri		14	FSEOF etc.
13	7-Apr-20	Tue		15	Introduction to Synthetic Biology; **(Venue: BT Seminar Hall)**
13	8-Apr-20	Wed	32		Robustness and Evolvability
13	10-Apr-20	Fri			Holiday – Good Friday
14	14-Apr-20	Tue		16	Buffer Lab
14	15-Apr-20	Wed	33		Robustness and Evolvability
14	16-Apr-20	Thu	34		Robustness and Evolvability; **Tuesday timetable**
14	17-Apr-20	Fri	35		Buffer classes
14	17-Apr-20	Fri	36		Buffer classes
14	18-Apr-20	Sat			**Project Final Report Due**; **Project Presentations: All Day**
15	21-Apr-20	Tue	37		Project Presentations
15	22-Apr-20	Wed	38		Project Presentations
15	24-Apr-20	Fri	39		Project Presentations
15	24-Apr-20	Fri	40		*Informal class: Q & A*
17	8-May-20	Fri			**End Semester Examination**

Feedback

Any suggestions for improvement are welcome at any time. A mid-term feedback will happen on 6th March 2019. The final feedback will happen during the TCF/registration week.

Reading

Books

- Raman K (2021) *An Introduction to Computational Systems Biology*. CRC Press, 1/e.
- Voit E (2012) *A First Course in Systems Biology*. Garland Science, 1/e. ISBN 0815344678
- Klipp E (2009) *Systems biology : a textbook*. Wiley-VCH, 1/e. ISBN 9783527318742
- Newman MEJ (2011) *Networks : an introduction*. Oxford Univ. Press. ISBN 9780199206650

Papers

Some major overview papers are listed below. There are many more interesting and relevant papers, which are available from http://www.citeulike.org/group/17566 and will also be on the course website.

- Hartwell LH, Hopfield JJ, Leibler S, and Murray AW (1999) From molecular to modular cell biology. *Nature* **402**(6761 Suppl):C47–C52. doi: 10.1038/35011540
- Barabasi AL and Oltvai ZN (2004) Network biology: understanding the cell's functional organization. *Nature Reviews Genetics* **5**(2):101–113. doi: 10.1038/nrg1272
- Papin JA, Hunter T, Palsson BO, and Subramaniam S (2005) Reconstruction of cellular signalling networks and analysis of their properties. *Nat Rev Mol Cell Biol* **6**(2):99–111. doi: 10.1038/nrm1570
- Jaqaman K and Danuser G (2006) Linking data to models: data regression. *Nat Rev Mol Cell Biol* **7**(11):813–819. doi: 10.1038/nrm2030
- Lewis NE, Nagarajan H, and Palsson BO (2012) Constraining the metabolic genotype–phenotype relationship using a phylogeny of *in silico* methods. *Nat Rev Micro* **10**(4):291–305. doi: 10.1038/nrmicro2737
- Karlebach G and Shamir R (2008) Modelling and analysis of gene regulatory networks. *Nature Reviews Molecular Cell Biology* **9**(10):770–780. doi: 10.1038/nrm2503
- Endy D (2005) Foundations for engineering biology. *Nature* **438**(7067):449–453. doi: 10.1038/nature04342

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