Nanyang Technological University
Division of Physics and Applied Physics

Academic Year	2023/24	**Semester**	2
Course Coordinator	HAN Endao and Tanadet PIPATPOLKAI		
Course Code	PH3408/MH3401[1]		
Course Title	Signal and noise in biology		
Pre-requisites	MH1100 Calculus I and MH1101 Calculus II or MH1802 Calculus for the Sciences or BS1008 Biostatistics and MH1101 Calculus II		
No of AUs	3 AUs		
Contact Hours	Lectures: 2 hours (per week); Tutorial: 1 hour (per week)		
Proposal Date	21 August 2023		

Course Aims

At the interface between biology, physics, and engineering, there is a wild frontier waiting to be explored. Over recent years, an increasing number of researchers with math or physics backgrounds have developed interests in biology-related topics. Concurrently, biological research is becoming more quantitative, and data driven. The world needs a new generation of biologists equipped with skills in mathematical modeling, data processing, and coding. The aim of this course is to introduce quantitative biology using a diverse range of phenomena related to signal and noise in biological systems as examples. You will learn some basic yet essential mathematical techniques and discover how these tools further our understanding of biology and biophysics. If you are a physics or math major interested in biology but haven't been trained in it, this course is perfect for you. If you are a biology or engineering major with basic knowledge in calculus and statistics, this course is also ideal. Join us and position yourself at the forefront of a transformative movement toward interdisciplinary research.

Intended Learning Outcomes (ILO)

By the end of this course, you should be able to:

1. Apply fundamental concepts and techniques in statistics to describe various biological processes and solve problems in quantitative biology.
2. Describe the central dogma in biology and relevant properties of DNA, RNA, and proteins.
3. Distinguish Darwin and Lamarck's theories on mutation and their consequences.
4. Describe basic mechanism of kinetic proofreading.
5. Connect different phenomena related to stochastic gene expression.
6. Conclude that stochasticity is an important feature in biology.
7. Describe physics that govern bacterial motility.
8. Explain the physics principles behind molecule counting, chemotaxis, and development.
9. Apply simple differential equations and non-linear dynamics to model and describe biological systems.
10. Describe the mechanism that makes chemotaxis and other biological processes robust.
11. Describe all-or-none phenomena in biology.
12. Implement principles of information theory in biology.
13. Utilize efficient representation in biological contexts.

[1] Common course with PH3408

Course Content

Basic statistics, different distributions, and some of their applications in biology.
Basic knowledge in molecular biology.
Stochasticity in genetics

- Mutation: Darwin vs Lamarck
- Kinetic proofreading
- Stochastic gene expression

Molecule counting

- Motility and chemotaxis in bacteria
- Signals in development

Control

- Differential equations and non-linear dynamics
- Robustness of chemotaxis
- All-or-none phenomenon

Information and efficient representation

- Information theory
- Efficient representation

Assessment (includes both continuous and summative assessment)

Component	ILO Tested	Weighting	Team/Individual	Assessment Rubrics
1. Final Examination	All	50%	Individual	Point-based marking (not rubric-based)
2. Continuous Assessment 1 (CA1): Problem sets	*All*	25%	Individual	Point-based marking (not rubric-based)
3. CA2: Mid-term test	*1 to 7*	25%	Individual	Point-based marking (not rubric-based)
Total		100%		

Formative feedback

You will receive formative feedback through discussion within classes and tutorial lessons. Each homework will be scored and returned to you for review. Feedback is also given after the midterm on the common mistakes and level of difficulty of the problems. Discussions with me in person or via email are always welcome.

Learning and Teaching approach

Approach	How does this approach support you in achieving the learning outcomes?
Lectures	Learn the fundamental knowledge, principles, and techniques related to

	the topics listed above.
Problem solving (tutorial and lecture)	Develop competence in applying the principles and techniques learned to solve biology-related problems quantitatively.
Hands-on group coding session (during tutorial)	Write codes to solve biological problems. You are encouraged to work in groups and discuss with your classmates.

Reading and References

- Recommended papers on relevant topics.
- Biophysics: Searching for Principles by William Bialek, Princeton University Press, 2012. ISBN 978069113891.
- Physical Models of Living Systems (Second Edition) by Philip Nelson, Chiliagon Science, 2007. ISBN 978-1-7375402-4-3.
- Nonlinear Dynamics and Chaos by Steven H. Strogatz. Westview Press. ISBN 978-0738204536.
- Introduction to Molecular Biophysics (1st Edition) by Jack A. Tuszynski and Michal Kurzynski, CRC Press, 2020. ISBN 9780367578541.

Course Policies and Student Responsibilities

General
You are expected to attend all lectures punctually and take all scheduled assignments and tests by due dates. You are expected to take responsibility to follow up with course notes, assignments and course related announcements for lectures you have missed. You are expected to participate in all tutorial sessions.

Absenteeism
If you are sick and unable to attend your class / Mid-terms, you have to:
1. Send an email to the instructor regarding the absence.
2. Submit the Medical Certificate* or official letter of excuse to administrator.
3. Request for a make-up mid-term and attend the assigned make-up mid-term.

* The medical certificate mentioned above should be issued in Singapore by a medical practitioner registered with the Singapore Medical Association.

Academic Integrity

Good academic work depends on honesty and ethical behaviour. The quality of your work as a student relies on adhering to the principles of academic integrity and to the NTU Honour Code, a set of values shared by the whole university community. Truth, Trust and Justice are at the core of NTU's shared values.

As a student, it is important that you recognize your responsibilities in understanding and applying the principles of academic integrity in all the work you do at NTU. Not knowing what is involved in maintaining academic integrity does not excuse academic dishonesty. You need to actively equip yourself with strategies to avoid all forms of academic dishonesty, including plagiarism, academic fraud, collusion and cheating. If you are uncertain of the definitions of any of these terms, you should go to the academic integrity website for more information.

On the use of technological tools (such as Generative AI tools), different courses / assignments have different intended learning outcomes. Students should refer to the specific assignment instructions on their use and requirements and/or consult your instructors on how you can use these tools to help your learning.

Consult your instructor(s) if you need any clarification about the requirements of academic integrity in the course.

Course Instructors

Instructor	Office Location	Phone	Email
HAN Endao	SPMS PAP-03-09	6513 8494	endao.han@ntu.edu.sg
Tanadet PIPATPOLKAI	SPMS PAP-04-26	9396 6722	tanadet.pipatpolkai@ntu.edu.sg

Planned Weekly Schedule

Week	Topic	ILO	Readings/ Activities
1	Introduction	1	Lecture notes and paper: • Crick, F. 1970. Central Dogma of Molecular Biology. Nature 227, 561–563.
2	Statistics	1	Lecture notes. Assignment 1.
3	Mutation: Darwin vs. Lamarck	2	Lecture notes and paper: • Luria SE, Delbruck M. 1943. Mutations of bacteria from virus sensitivity to virus resistance. Genetics 28:491-511. • Jablonka E, Lamb MJ, Avital E. 1998. 'Lamarckian' mechanisms in Darwinian evolution. Trends Ecol. Evol. 13(5):206-10 • Holmes CM, Ghafari M, Abbas A, Saravanan V, Nemenman I. 2017. Luria-Delbrück, revisited: the classic experiment does not rule out Lamarckian evolution. Phys. Biol. 21;14(5):055004. Tutorial 1.
4	Kinetic proofreading	3	Lecture notes and paper: • Hopfield JJ. 1974. Kinetic proofreading: a new mechanism for reducing errors in biosynthetic processes requiring high specificity. PNAS 71:4135-9

			• Zaher HS, Green R. Fidelity at the molecular level: lessons from protein synthesis. Cell. 2009 Feb 20;136(4):746-62. • Demeshkina, N., Jenner, L., Westhof, E. et al. A new understanding of the decoding principle on the ribosome. Nature 484, 256–259 (2012).
5	Stochastic gene expression	4, 5	Lecture notes and papers: • Santillán M, Mackey MC. 2008. Quantitative approaches to the study of bistability in the lac operon of Escherichia coli. J R Soc Interface. 5 Suppl 1(Suppl 1):S29-39. • Elowitz MB, Levine AJ, Siggia ED, Swain PS. 2002. Stochastic gene expression in a single cell. Science 297: 1183-6. • Yu J et al. 2006. Probing Gene Expression in Live Cells, One Protein Molecule at a Time. Science 311:1600-3. Assignment 2.
6	Motility and chemotaxis in bacteria	6, 7	Lecture notes and paper: • Purcell EM. 1977. Life at low Reynolds number. American Journal of Physics 45, 3–11. Tutorial 2.
7	Chemotaxis and signals in development	7	Lecture notes. Assignment 3.
8	Mid-term test	1 - 7	Tutorial 3.
9	Differential equations and non-linear dynamics	8	Lecture notes.
10	Robustness	9	Lecture notes and paper: • Alon U et al. 1999. Robustness in bacterial chemotaxis. Nature 397:168-71. Assignment 4.
11	All-or-none phenomenon	10	Lecture notes and paper: • Novick A, Wiener M. 1957. Enzyme induction as an all-or-none phenomenon PNAS 43:553-66. Tutorial 4.
12	Information theory	11	Lecture notes. Assignment 5.
13	Efficient representation	12	Lecture notes and paper: • Laughlin SB. 1981. A simple coding procedure enhances a neuron's information capacity. Z. Naturforsch. 36:910-12. Tutorial 5.