Syllabus
ABE 591: Quantitative systems biology
Spring, 2010
CRN: 43739

Instructor:
David M. Umulis

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Class Meets: 9:00–10:15, ABE 301, Tuesday and Thursday

Description

Our major objective for this course is to study current problems in biology that are amenable to modeling, quantitative analysis, and systems biology approaches. The focus will be to understand current work on several aspects of embryo development, gene control networks, and signaling cascades and to identify the component processes and associated modeling/mathematical tools needed to address them. These include basic material on how to model chemical reactions, both deterministically and stochastically, how to formulate a model of gene control networks, and how to model signaling via morphogens. The course will also focus on problems of image analysis, FRAP, and population statistics for the quantification of fluorescent images. We expect the following student outcomes:

- Read and understand scientific papers that include coupled biological/mathematical analysis.
- Identify appropriate methods for quantitative image analysis (includes lab component/project).
- Communicate effectively between disciplines.

Prerequisite

One year of calculus or consent of instructor. Biology students: Background in biochemistry, molecular biology, development, genetics, or equivalent. Engineering and mathematics students: Background in physics or engineering with rudimentary understanding of thermodynamics, kinetics, or fluid mechanics.

Textbook

Every student will be required to maintain a 3-ring binder of class notes, handouts and other course relevant materials. (A single 3" binder will suffice). There is not an assigned textbook for the course. Keep an organized notebook as all exams will be completely open notes!

Academic honesty

All students are expected to perform with the highest academic integrity. Students are expected to abide by the Purdue University Code of Honor and Regulations regarding student conduct. The bottom line is DON'T CHEAT, and DON'T HELP OTHERS CHEAT. The source of the following two excerpts can be found at:

`http://www.purdue.edu/univregs/pages/stu_conduct/stu_regulations.html`

Part 5: Section II- Purdue University Code of Honor: "To foster a climate of trust and high standards of academic achievement, Purdue University is committed to cultivating academic integrity and expects students to exhibit the highest standards of honor in their scholastic endeavors. Academic integrity is essential to the success of Purdue Universitys mission. As members of the academic community, our foremost interest is toward achieving noble educational goals and our foremost responsibility is to ensure that academic honesty prevails."

Part 5: Section III Regulations Governing Student Conduct, Disciplinary Proceedings, and Appeals "Misconduct Subject to Disciplinary Penalties.The following actions constitute misconduct for which students may be subject to administrative action or disciplinary penalties. Dishonesty in connection with any University activity. Cheating, plagiarism, or knowingly furnishing false information to the University are examples of dishonesty. The commitment of the acts of cheating, lying, stealing, and deceit in any of their diverse forms (such as the use of ghost-written papers, the use of substitutes for taking examinations, the use of illegal cribs, plagiarism, and copying during examinations) is dishonest and must not be tolerated. Moreover, knowingly to aid and abet, directly or indirectly, other parties in committing dishonest acts is in itself dishonest. (University Senate Document 72-18, December 15, 1972)."

Campus emergency

Campus emergencies might include the following: classroom accidents, hazardous chemical releases/spills, fires, weather emergencies and natural disasters, violence, and pandemic. In the event of a major campus emergency, class will be cancelled and will only resume under notification by the instructor. In the event of a major campus emergency, course requirements, deadlines and grading percentages are subject to changes that may be necessitated by a revised semester calendar or other circumstances. Here are ways to get information about the course: Blackboard Vista, my phone (765-494-1223), or e-mail: (dumulis@purdue.edu).

Preliminary Grading Breakdown

The breakdown of the points for this class are as follows:

Team research project	50%
Research proposal	20%
Classroom participation	30%

We understand that individual students will have very different backgrounds coming into this course and instructors will take this into account by judging students based on their relative progress during the course.

Team project 50%

The majority of the grade is determined by the ability to work in a team environment on a quantitative biology project. Each team will be composed of at least one student with an engineering or math bias and one student with a bias towards biology, biochemistry and/or genetics. Projects will be selected by each team shortly after the beginning of the semester either by their own literature search or per instructor suggestion.

The specific tasks associated with the team project are as follows:

Project proposal	20%
Team member evaluations	10%
Progress report(s)	10% each
Project oral presentation	30%
Project final report	30%

Final research proposal 20%

Each member of the project teams will write a brief research proposal that includes *both* mathematics and biology questions for future work. Students are encouraged to discuss the research questions with each other but everyone must submit their own proposal.

Classroom participation 30%

A big portion of class will be discussion-based and participation accounts for 30% of the final grade. There will also be 3 paper review essays during the course and participation in the course wiki is required (more details later).

Course Schedule: NOTE THAT THIS CAN CHANGE AT ANY TIME PER INSTRUCTOR DISCRETION

Introduction and Background Material

Tu, Jan. 12: Introduction to embryology, patterning

Kitano H. Systems Biology: A Brief Overview. Science(2002) 295: 1662-1664

NOTE CARDS COMPLETED DURING CLASS

Th, Jan. 14: What are some issues that can be addressed by mathematical analysis?
Mass action kinetics, enzyme kinetics, transport processes.
Reeves GT, Muratov CB, Schupbach T, and Shvartsman SY. Quantitative Models of Developmental Pattern Formation. Dev. Cell(2006) 11: 289–300.

Tu, Jan. 19: Morphogen gradients I
Introduction to mathematical terminology, partial differential equations, transport processes.

Pattern formation in *Drosophila*

Th, Jan. 21: Morphogen gradients II
Lander A, Nie Q, and Wan YM. Do morphogen gradients arise by diffusion? Dev. Cell(2002) 2, 785–796.

Tu, Jan. 26: Bicoid, *in situ* hybridization, and immunostaining
Driever W, and C. Nüsslein-Volhard. The Bicoid protein determines position in the Drosophila embryo in a concentration-dependent manner. Cell(1998) 54: 95–104.

Th, Jan. 28: Robustness of morphogen gradients
Houchmandzadeh B, Wieschaus E, and Leibler S. Establishment of developmental precision and proportions in the early *Drosophila* embryo. Nature(2002) 415, 798–802.
Aegerter-Wilmsen T, Aegerter CM, and Bisseling T. Model for the robust establishment of precise proportions in the early *Drosophila* embyro. J. Theor. Biol.(2005) 234, 13–19.

Tu, Feb. 2: Robustness of morphogen gradients continued
TEAM PROJECT PROPOSAL DUE

Th, Feb. 4: Scale invariance of the Bicoid gradient
Gregor T, Bialek B, de Ruyter van Steveninck RR, Tank DW, and Wieschaus EF. Diffusion and scaling during early embryonic pattern formation. PNAS(2005) 102: 18403–18407.

Tu, Feb. 9: Scale invariance of the Bicoid gradient continued
Gregor T, Wieschaus EF, McGregor AP, Bialek W and Tank D W. Stability and nuclear dynamics of the bicoid morphogen gradient.Cell (2007) 130: 141–152.

Th, Feb. 11: Introduction to Matlab and Image Processing

Tu, Feb. 16: Image normalization and analysis continued

Th, Feb. 18: Image normalization and analysis continued

Tu, Feb. 23: Gap genes
Lebrecht D, Foehr M, Smith E, Lopes FJP, Vanario-Alonso CE, Reinitz J, Burz DS and Hanes SD. Bicoid cooperative DNA binding is critical for embryonic patterning in Drosophila. Proc Nat Acad Sci USA(2005), 102: 13176–13181.
Jaeger J, Surkova S, Blagov M, Janssens H, Kosman D, Kozlov KN, Manu, Myasnikova E, Vanario-Alonso CE, Samsonova M, Sharp DH and Reinitz J. Dynamic control of positional information in the early Drosophila blastoderm. Nature(2004) 430: 368–371.

Th, Feb. 25: Dorsal/Ventral patterning background
Levine M, and Davidson EH. Gene Regulatory Networks Special Feature: Gene regulatory

networks for development. PNAS(2005) 102: 4936–4942.
Zinzen RP, Senger S, Levine M, and Papatsenko P. Computational Models for Neurogenic Gene Expression in the *Drosophila* Embryo. Current Biology(2006) 16: 1358–1365.
TEAM PROGRESS REPORT DUE

Tu, Mar. 2: Dorsal surface patterning by BMPs; Gal4-UAS
Raftery L, Sutherland DJ. Gradients and thresholds: BMP response gradients unveiled in *Drosophila* embryos. Trends Genet.(2003) 19: 701–708.
Eldar A, Dorfman R, Weiss D, Ashe H, Shilo BZ and Barkai N. Robustness of the BMP Morphogen Gradient in Drosophila embryonic patterning. Nature(2002) 419: 304–308.

Th, Mar. 4: Robustness of the BMP morphogen gradient.
Mizutani CM, Nie Q, Wan FY, Zhang YT, Vilmos P, Sousa-Neves R, Bier E, Marsh JL and Lander AD. Formation of the BMP activity gradient in the Drosophila embryo. Dev. Cell(2005) 8: 915–924.
Shimmi O, Umulis DM, Othmer HG, and O'Connor MB. 2005. Facilitated transport of a Dpp/Scw heterodimer by Sog/Tsg leads to robust patterning of the Drosophila blastoderm embryo. Cell(2005) 120:873–86.

Tu, Mar. 9: Robustness of the BMP morphogen gradient?
Wang YC, and Ferguson EL. Spatial bistability of Dpp-receptor interactions during Drosophila dorsal-ventral patterning. Nature(2005) 434: 229–234.
Umulis DM, Serpe M, O'Connor MB, and Othmer HG. Robust, bistable patterning of the dorsal surface of the Drosophila embryo. PNAS(2006) 103: 11613–11618.

Th, Mar. 11: Review

Tu, Mar. 16: Spring break- no class

Th, Mar. 18: Spring break- no class

Tu, Mar. 23: Comsol multiphysics training

Th, Mar. 25: Comsol multiphysics training

Tu, Mar. 30: Comsol multiphysics training

Th, Apr. 1: Comsol multiphysics training
TEAM PROGRESS REPORT DUE

Left/Right asymmetry in vertebrates

Tu, Apr. 6: Left/Right asymmetry background
Hirokawa N, Tanaka Y, Okada Y, and Takeda S. Nodal flow and the generation of left-right asymmetry. Cell(2006) 125: 33–45.

Th, Apr. 8: Background on fluid mechanics
Basic concepts of fluid mechanics.

Tu, Apr. 13: Nodal flow

Okada Y, Takeda S, Tanaka Y, Izpisa Belmonte JC, and Hirokawa N. Mechanism of Nodal Flow: A Conserved Symmetry Breaking Event in Left-Right Axis Determination. Cell(2005) 121: 633–644.

Th, Apr. 15: Robustness of nodal flow

Nakamura T, Mine N, Nakaguchi E, Mochizuki A, Yamamoto M, Yashiro K, Meno C, and Hamada H. Generation of Robust Left-Right Asymmetry in the Mouse Embryo Requires a Self-Enhancement and Lateral-Inhibition System. Dev. Cell(2006) 11: 495–504.

Tu, Apr. 20: Stochastic gene expression papers TBD

Th, Apr. 22: Stochastic gene expression papers TBD

Tu, Apr. 27: Project presentations

PROJECT FINAL REPORT DUE.

Th, Apr. 29: Project presentations

Note

Also, this schedule is subject to change at the instructors' discretion.