Weill Cornell Medical College

DANIEL GARDNER, PH.D.
Professor of Physiology and Biophysics
Head, Laboratory of Neuroinformatics

Department of Physiology D-404
1300 York Avenue
New York, NY 10065–4805

Lab: 212 746-6373
Cell: 917 902-0654

dan@med.cornell.edu
dg458@columbia.edu

Welcome to Contemporary PBSB!

Version 12.0 of our core course is designed to prepare you for twenty-first century research in the function, analysis, modeling, and understanding of living systems at each of several scales, from the molecular through the cellular to the organ system and organism.

The course is modular: six semi-independent modules, each spanning several weeks, form a coherent whole. Within each module, multiscale and translational examples develop conceptual skills necessary to design meaningful experiments, derive insight from journal reports, work within the group structure now essential for contemporary research, and communicate new developments and related findings to today's peers and future students. Structural and developmental concepts are covered as they illuminate function.

Typical class sessions include in-depth lecture-conferences, computational analyses and/or models, and relevant illuminating articles from the literature. Several modules use new, active, teaching modalities that introduce and refine real-world skills for contemporary research. Each module is designed to give you some essentials that every PBSB student should know, and—importantly—offer examples and support toward enabling each of you to think about what is known, what isn't, and how to add to our scope of knowledge.

The course is also hybrid: in-person at Weill and Zoom-linked to Houston. Whether remote or local, each of you needs to *prepare* for each session by carefully reading any material sent to you in advance, *be present* at all sessions, and *participate* actively in class discussions.

The ***Fall*** term offers three modules covering essentials of PBSB, including an introduction to computational tools, as well as an independent study component (MOOCs or Books):
CPBSB 1: Membranes and cells (MAC) — concluding with a three-day immersion in unix.
CPBSB 2: Control and communication in bodies and brains (CCBB)
CPBSB 3: Protein function signaling and synthesis (PFSAS)

The ***Spring*** term opens with a special week (CPBSB++) on scientific presentations, then one module exploring a key organ system, and another applying computational tools to the genome and expression:
CPBSB 4: Action and mechanical work from biochemical energy (ΔG)
CPBSB 5: Introduction to Computational Systems Biology (CSB)
... and the course concludes with a synthesizing and bridging module:
CPBSB 6: Physiology of Systems and Diseases (SYS)
... that integrates lecture/conferences, problem-based learning sessions, and sequenced journal clubs to demonstrate how ideas and tools learned in the five preceding modules promote problem solving. Some weeks will have a translational focus on the underlying physiology, biophysics, or systems biology, whereas others will follow a major investigative thread through successive questions, techniques, and reports. This approach synthesizes journal club and PBL, understanding what questions are appropriate to ask, given existing techniques, and what questions require inventing or adopting new but feasible techniques.

On behalf of the dozens of PBSB faculty responsible for course design and implementation, welcome!

Daniel Gardner, Ph.D.

ReadMeFirst: how to prepare for our CPBSB course for 2023-2024

The Program asks each first-year PBSB student to devote time during the first year of study to our core course CPBSB: Contemporary Physiology, Biophysics, and Systems Biology. The course meets three days every week of the Fall and Spring terms, Monday, Wednesday, and Friday (excepting school holidays) from 1:00 to 3:00 PM. We meet in person, with only students at the Houston campus participating via Zoom. Here are some informative—reassuring—FAQ:

Why are we taking CPBSB?

CPBSB is not designed to give you the exact body of factual knowledge you need to begin your particular thesis project. No course could. Instead, our goal is help you develop the skills to do research. These are: to derive and pose questions that are interesting, significant, and answerable in finite time and with limited resources, to pick an appropriate preparation, to acquire sufficient data of the right kind to help answer the question, and to analyze, test, verify, organize, and present the findings clearly and convincingly. We want you to think, not just to manipulate symbols. If that were all, we would use ChatGPT. You're better than it is.

Each modality of CPBSB echoes some facet of the daily life of a researcher: lectures are like research seminars, discussions and student presentations are like lab meetings, journal clubs are like searching and reading the literature.

What do we need to do?

Each of you needs to *prepare* for each session by carefully reading any material sent to you in advance, be *present* at all sessions, and *participate* actively in class discussions.

We will not ask you to echo information provided by course Faculty, but we will engage you in discussion of important concepts, and encourage explorations, alternate views, questions, and even those useful remarks: 'I don't understand' or I don't really know'. Silence is not an option. You can look up a point in class by scanning PubMed for a reference, but please don't email, use social media, or check favorite web sites during class time.

Who will teach us?

Senior Faculty of Weill Cornell Medicine or Memorial Sloan-Kettering, each an experienced researcher in one or more of the very many areas that together comprise Physiology, Biophysics, and Systems Biology. Each member of the faculty is also dedicated to teaching as a professional activity, and regards participating in CPBSB as an opportunity, not an obligation.

What will CPBSB teach us?

A lot. But the course is not designed to cram a large body of facts into your heads. We have a different goal: to give you the skills to do research, whether wet-lab in-vitro, in-vivo, or computationally-based, and whether focused on bioinformatics, biophysics, or something transcending each of these. It's all computational: 21st century research is increasingly guided and informed by numerical, algorithmic, and analytic methods and models, often involving multi-dimensional or very large datasets. CPBSB highlights these. Even if your work will use analytic or modeling tools only incidentally, the concepts and vocabulary you acquire will enable you to combine forces with computational researchers with whom you collaborate.

To make the broad span of multidimensional concepts more readily understood, we divide the course into six modules, each with its own themes, style, and Faculty module director.

Module 1 stresses the importance of the membrane and of proteins—especially membrane proteins—to cell function and cell-cell communication. These ideas are so central that later modules will return over and over to the principles laid out in this module. This module also

introduces another theme that recurs throughout: living systems are information-processing entities, and molecules encode this information, process it, and act upon it.

Modules 2 and 4 each focus on an organ system essential to the function of organisms. For module 2 we examine the nervous system, the brain, and the information they acquire and process. Module 4 explores the heart and circulation, and here the focus is action and the control of action. Both modules stress the need to synthesize understanding across levels: events at the molecular level are critically important for proper structure and function of cells, assemblies, networks of cells, organs, and the whole body. Module 2 additionally emphasizes active learning: each student presents two short reports to colleagues, who are asked to critically review each effort.

Module 3 focuses on molecular mechanisms of cellular signaling, and the sub-cellular and cellular functions we call systems biology. An equal goal is to explore these using active modalities: both journal clubs and independent—but guided—work by students.

Module 5 further develops the informational theme introduced on module 1, focusing on how information in and derived from the genome enables the systems biology introduced in module 3. Importantly, this module gives students the ability to work with the many essential computational tools that read and build on sequencing and expression.

Module 6 ends the year of CPBSB and serves as a bridge to thesis work. Sequences of journal papers, dueling articles from the contemporary literature, papers that may or may not draw correct inferences from sets of data, and a problem-based active clinical/translational case each stretch the traditional classroom model to present real-world examples of skills essential for biomedical researchers.

Will there be homework?

Yes. Two kinds. First: many Faculty will send you slide sets, notes, or even transcripts several days in advance of a session. Your homework is to read these in advance of class, think about them, and formulate questions or mark points you don't understand. These should not just sit unread in your inbox until class begins. Second: journal articles from the reviewed biomedical literature ('papers') are important resources for most of the modules, and one goal of our course is to enable you to read the literature carefully, completely, critically, and inquisitively. Papers are similarly provided in advance of class sessions to give you the opportunity to read the works and come prepared for active discussion. Most papers are presented with only the briefest of introductions, and reading a paper in a new area can be hard, but this is how develops a skill all researchers need.

Will this be on the test?

Maybe. Some modules are graded by in-class performance, and some have take-home open-book exams at module end.

I've still got questions.

Faculty are accessible to students. Feel free to contact individual module directors or teachers for specific sessions (see schedule). For general questions, email Dr. Daniel Gardner at dan@med.cornell.edu

Contemporary PBSB: Cells, systems, and quantitative methods V12.0

Course content and organization are designed to prepare students for twenty-first century research in the function, analysis, modeling, and understanding of living systems at each of several scales, from the molecular through the cellular to the organ system and organism. Multiscale and translational examples develop conceptual skills necessary to design meaningful experiments, derive insight from journal reports, work within the group structure now essential for contemporary research, and communicate new developments and related findings to today's peers and future students. Structural and developmental concepts are covered as they illuminate function.

Each module consists of multiple weeks. Typical weeks for many modules include two in-depth lecture-conferences that combine careful presentation of core material with student participation, and conclude with either a computational analysis and/or model, or an illuminating article from the literature. Other modules introduce new instructional modalities and perspectives designed to instill skills essential for researchers, while providing insights into scales or approaches central to contemporary research.

In parallel with these scheduled lectures, labs, and conferences, each PBSB student will also complete a Deep Independent Study Cycle. Students will select a MOOC or book by September and engage in deep self-study during the Fall, then present a short summary and review in the Spring term of CPBSB.

Days and times:	Mondays, Wednesdays and Fridays 1 to 3 PM Eastern ***except as noted!***
NYC Location:	SEMINAR STUDIO SUITE LC-504 in New York; Room WP5 in Houston
Zoom room:	937 6564 7836, passcode supplied separately
Course director:	Daniel Gardner, Ph.D.

Quarters I and II: PBSB.9000.01-Contemporary PBSB 1, 2, 3
16 weeks: August 21– December 8, 2023.
This is the first term of a one-year modular course required of all first-year students in the PBSB Program. The entire course or individual modules are open to students of other Programs with the permission of the course director; class limit 16 students.

CPBSB 1: Membranes and cells (MAC)
Five weeks August 21 – September 22, 2023; Daniel Gardner, Module director

This module introduces rigorous, essential fundamentals of membranes, cells, and membrane proteins. It also uses the relation between experimentally-derived data and mathematical and computational models and analyses as an introduction to how biophysicists think. Such a view is fundamental to understanding contemporary PBSB research, no matter the level, techniques, or system.

Week 1: Membranes and compartments

Monday, August 21:	Cell membranes, structure and function – Rusinova
Wednesday, August 23:	Compartments, electrolytes, and osmotic balance – Rusinova
Friday, August 25:	Membrane potentials – Rusinova

Week 2: Action potentials and intro to modeling

Monday, August 28:	Membrane potentials and action potentials – Gardner
Wednesday, August 30:	Hodgkin-Huxley models and beyond – Gardner
Friday, Sept 1:	Computational lab: Introduction to analysis of living systems (osmotic balance) – Krogh-Madsen

Week 3: Protein synthesis and function

Tuesday, Sept 5:	Journal Club – Gardner
Wednesday, Sept 6:	Protein structure/function and modification – Boudker
Friday, Sept. 8:	Computational lab: Hodgkin-Huxley modeling – Gardner, Victor

Week 4: Membrane protein structure and function
Monday, Sept. 11: Neuromuscular transmission – Gardner
Wednesday, Sept. 13: Membrane fusion – Dittman
Friday, Sept. 15: Channels, transporters, and pumps – Palmer

Monday, Sept. 18: Module evaluation/exam

Computational and algorithmic skills are essential for 21st Century biomedicine. Interposed between Modules 1 and 2, we interrupt and transfer control to a subroutine: a three-day immersion in UNIX™, the command line, and valuable tools and methods for the manipulation and analysis of text strings.

Intermodular Week 5: This does compute! (Course code HAL.9000)

Wednesday, Sept 20, 1–4 PM: File manipulation, introduction to editing – Skrabanek
Thursday, Sept 21, 1–4 PM Pattern matching, advanced editing – Skrabanek
Friday, Sept. 22, 1–4 PM: Shell scripting – Skrabanek

CPBSB 2: Control and communication in bodies and brains (CCBB)
Six weeks Wednesday, September 27 – November 3, 2022 Bernice Grafstein, Module director

CPBSB2 will give a working introduction to the concepts underlying the nervous system, and the ongoing study of it, with examples drawn from molecular, cellular, and systems levels. At the same time, it again uses student research and presentations, along with student critiques, as a principal modality, thus developing skills essential to contemporary research.

Week 6: The brain's networks and neurons
Wednesday, Sept. 27: Basic organization of the nervous system: structure, development, sensory coding – Grafstein
Friday, Sept. 29: Vision – retina to V1 – Grafstein

Week 7: Sensory transduction
Monday, Oct. 2: Computational lab: vision – Victor, Gardner
Wednesday, Oct. 4: Student presentations: Sensory organ transduction I – Grafstein
Friday, Oct. 6: Student presentations: Sensory organ transduction II – Grafstein

Week 8: Synapses; visual perception
Monday, Oct.9: CNS synapses and plasticity – Gardner
Wednesday, Oct. 11: Central visual pathways – Gardner
Friday, Oct. 13: Journal Club: Visual System – Gardner

Week 9: Brain and spinal cord organization; clinical correlates
Monday, Oct. 16: Cerebral cortex organization – Grafstein
Wednesday, Oct. 18: Spinal cord organization and reflex activity – Grafstein
Friday, Oct. 20: Pain – Grafstein

Week 10: Using the brain—and modifying it
Monday, Oct. 23: Sensory-motor coordination – Grafstein
Wednesday, Oct. 25: Structural plasticity – Grafstein
Friday, Oct. 27: Memory and learning – Gardner

Week 11: Bringing it all together
Monday, Oct. 30: Computational approaches to Alzheimer disease – Zhao, de Leon
Wednesday, Nov. 1: Student presentations: Nervous system topics I – Grafstein
Friday, Nov. 3: Student presentations: Nervous system topics II – Grafstein

CPBSB 3: Protein function signaling and synthesis (PFSAS)
Five weeks November 6 – December 8, 2023; (with student proposals due December 14)
(note Thanksgiving break November 22 – 24)

Olga Boudker, Module director

The goal of our third Module is to combine lectures on quantitative aspects of cellular signaling with independent, but guided, work by students. Students will be working in pairs. At the end of the first week of the Module, each pair will be assigned one of three discussed papers. In addition, each pair will be assigned an advising Professor, who will provide guidance and one-on-one discussions throughout the module. Research papers will be provided to the students one week before the start of the Module and presented by the Faculty during the first week.

Week 12:	
Monday, Nov. 6:	Paper presentation 1 – Accardi
Wednesday, Nov 8:	Paper presentation 2 – Gregorio
Friday, Nov. 10:	Paper presentation 3 – Khelashvili
Week 13:	
Monday, Nov. 13:	Journal club 1 (Pairs 1, 2)/ Introduction to grant proposal writing – Boudker
Wednesday, Nov. 15	Journal club 2 (Pairs 3, 4)
Friday, Nov. 17:	Journal club 3 (Pairs 5, 6)
Week 14:	
Monday, Nov. 20:	One-on-one with advising Faculty, scheduled individually
Wednesday, Nov. 22:	***Thanksgiving break – no class***
Friday, Nov. 24:	***Thanksgiving break – no class***
Week 15:	
Monday, Nov. 27:	Student oral presentations of project Aims I (Pairs 1, 2, and 5)
Wednesday, Nov. 29:	Student oral presentations of project Aims II (Pairs 3 ,4, and 6)
Friday, Dec. 1:	no class
Week 16:	
Monday, Dec. 4:	Lab: Protein viewing and modeling I – Khelashvili
Wednesday, Dec. 6:	Lab: Protein viewing and modeling II – Khelashvili
Friday, Dec. 8:	Mock NIH study section (***Extended class***); *Final proposals due Friday, Dec. 15*

...and the Spring term begins on Wednesday, January 3, 2024 with:
CPBSB++: Presenting your science in a hybrid world

Contemporary PBSB: Cells, systems, and quantitative methods V12.1

Quarters III and IV: PBSB.9001.03-Contemporary PBSB 4-6
16 weeks January 3 (Wednesday) – April 26, 2024.

This is the second term of a one-year modular course required of all first-year students in the PBSB Program. The entire course or selected modules are open to students of other programs with the permission of the course director; class limit 20 students.

Each module consists of multiple weeks. Typical weeks for modules CPBSB 4 and 5 include two in-depth lecture-conferences that combine careful presentation of core material with student participation, and either a computational analysis and/or model, or a relevant illuminating article from the literature. The final module, CPBSB 6, introduces new instructional modalities and perspectives designed to instill skills essential for researchers.

Days and times:	Mondays, Wednesdays, and Fridays 1 to 3 PM
NYC Location:	SEMINAR STUDIO SUITE LC-504 in New York; Room WP5 in Houston
Zoom room:	937 6564 7836, passcode supplied separately
Course director:	Daniel Gardner, Ph.D.

CPBSB++: Presenting your science in a hybrid world
Week 1: Jan 3 – 5; Daniel Gardner and Bernice Grafstein

Wednesday, Jan. 3:	Preparing and presenting posters and their derivatives – Gardner
Friday, Jan. 5	Preparing good slides for hybrid talks – Grafstein and Gardner

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CPBSB 4: Action and mechanical work from biochemical energy (ΔG)
Five weeks January 8 – Feb 9; Daniel Gardner, Module director

Week 2: Skeletal and smooth muscle

Monday, Jan. 8:	Skeletal muscle contraction – Gardner
Wednesday, Jan. 10:	Smooth muscle contraction – Palmer
Friday, Jan 12:	Computer lab: Crossbridge dynamics – Krogh-Madsen

Week 3: Student reports on MOOCs and Books

Monday, Jan. 15:	No class; Presidents Day
Wednesday, Jan. 17:	Student presentations: reporting on MOOCs and books
Friday, Jan 19:	Student presentations: reporting on MOOCs and books

Week 4: Cardiac electrophysiology

Monday, Jan. 22:	Cardiac action potential – Krogh-Madsen
Wednesday, Jan. 24:	Cardiac ion channels – Pitt
Friday, Jan. 26:	Computer lab: Cardiac action potential – Krogh-Madsen

Week 5: Cardiovascular function and dysfunction

Monday, Jan. 29:	Heart and vasculature – Krogh-Madsen
Wednesday, Jan 31:	No class; Recruitment
Friday, Feb. 2:	Propagation, reentry, arrhythmias – Krogh-Madsen

Week 6: Cardiac disease models

Monday, Feb. 5:	Cardiac regeneration – Cao
Wednesday, Feb. 7	Clinical perspective: blood pressure control and hypertension – Pecker
Friday, Feb. 9:	Computer lab: Blood pressure and flow – Krogh-Madsen

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CPBSB 5: Introduction to computational systems biology (CSB)
Five weeks February 12 – March 24; Luce Skrabanek, Module director
(note Spring break February 26 - March 1)

Week 7: Intro to Next Gen Sequencing I

Monday, Feb. 12:	NGS basics: library prep, sequencing, raw read QC – Skrabanek
Wednesday, Feb 14:	NGS basics: short read alignment, read quantification – Skrabanek
Friday, Feb 16	Normalization, RNA-Seq differential gene expression analysis, experimental design – Skrabanek

Week 8: Intro to Next Gen Sequencing II

Monday, Feb 19	Presidents Day; no class
Wednesday, Feb 21:	ChIP-Seq peak calling – Skrabanek
Friday, Feb 23:	Clustering: PCA, t-SNE, UMAP – Skrabanek

(Spring break February 26 - March 1)

Week 9: Variants and their interpretation

Monday, Mar 4:	Coding and non-coding variants – Khurana
Wednesday, Mar 6:	Structural variants – Hajirasouliha
Friday, Mar 8	DNA Methylation – Betel

Week 10: Systems biology: single cells and networks

Monday, Mar 11:	Metabolomics – Krumsiek
Wednesday, Mar 13:	Integration of data from multiple sources, regulatory network construction [Journal Club] – Roskes
Friday, Mar 15	Single cell sequencing – Fansler

Week 11: Machine learning

Monday, Mar 18:	Classification and cross-validation – Krumsiek
Wednesday, Mar 20:	SVMs – Leslie
Friday, Mar 22:	Self-assessment – Skrabanek

CPBSB 6: Physiology of systems and diseases
Five weeks March 25 – April 26; Daniel Gardner, Module director
Weeks 12 to 16

Each week covers one major topic that links across scales to provide translational, longitudinal, or systemic synthesis.

Formats vary week to week, but include one or more of lecture/conferences, problem-based learning sessions, or journal clubs. Some weeks have a translational focus on the underlying physiology, biophysics, or systems biology, whereas others follow a major investigative thread through successive questions, techniques, and reports. This approach synthesizes lecture, discussion, journal club, and problem-based learning modalities. A major goal is understanding what questions are appropriate to ask, given existing techniques, and what questions require inventing or adopting new but feasible techniques. Each week additionally demonstrates how ideas and tools learned in the five preceding modules promote problem solving.

Week 12: Molecular timing for signal shaping

Monday, March 25:	Macroscopic timing at the synapse – Gardner
Wednesday, March 27:	Microscopic timing at the synapse – Gardner
Friday, March 29:	The invention of the electrophysiological microscope – Gardner

Week 13: A tour of the kidney, with a side trip to the pituitary
Monday, April 1; Wednesday, April 3; Friday, April 5 –Palmer

Week 14: Falsity and Inference

Monday, April 8:	Reproducibility – Gardner
Wednesday, April 10	Is the brain really doing that? How do we know? – Gardner
Friday, April 12:	More inference, then extra student reports on MOOCs and books

Week 15: Current controversy in biomedicine: what is the normal function of presenillin?

Monday, April 15:	Thesis – Accardi
Wednesday, April 17:	Antithesis – Accardi
Friday, April 19:	Surely not synthesis – Accardi

Week 16: Finale

Monday, April 22:	The Vision of Mr. I. – Gardner
Wednesday, April 24:	The Vision of Mr. I. (not Mr. II.) – Gardner
Friday, April 26:	CPBSB6 exam and module evaluation – entire company