Systems and Integrative Biology (SIB) Training Grant

An NIGMS Training Grant in Mathematical and Computational Biology

Formal Training Requirements

The goal of this training program is to support pre-doctoral students who seek a balanced and rigorous training in mathematics and biology/biomedicine with a special emphasis on research in mathematical modeling in biology or biomedicine. The early training includes formal course work, research rotations with participating faculty, and attendance and participation in seminar series.

Trainees are not expected to be already fully proficient in both biology and mathematics at the start of this program. However, it is expected that trainees are currently pursuing a graduate program in either a mathematical or biological discipline and already have a minimal level of undergraduate background in the other discipline (see the Trainee Selection Guidelines below). As summarized in the following sections, an aim of the didactic portion of this training program is for trainees to demonstrate a minimum of 20 quarter units of advanced courses in quantitative methods and 20 quarter units in biological sciences. Although the goal is graduate level competence in these areas, students can petition to have 8-10 units in each group satisfied by upper-division courses.

1. Trainees must develop with their advisor(s) a coherent plan for quantitative training that includes completion of five courses (total of 20 quarter units), with at least two courses from a series in Core Methodology and two from a series in Modeling Applications in Biology. The Core Methodology series covers basic modeling and computational techniques in the following areas: (1) deterministic modeling (2) stochastic modeling (3) statistical modeling (4) computation/algorithms/numerical methods (5) optimization and (6) other applied mathematics. Courses in the Modeling Applications in Biology series demonstrate the application of core methodologies to biological or medical research and have substantial mathematical and biological content and exposure to current research problems. The Appendix presents examples of suitable graduate courses in both series currently offered by a variety of mathematical, engineering, and natural science programs. These examples are not exhaustive, and the Executive Committee will review suggestions from participating faculty and update the lists on an annual basis. Moreover, in developing a plan for quantitative training, trainees may petition the Executive Committee to allow substitution of 8 of the 20 quarter units with upper division courses.

2. Trainees who are not already in a doctoral program in a biological or biomedical specialty must develop with their advisors a coherent plan for biological training that includes completion of at least 20 quarter units of upper division and graduate courses. At least half should be at the graduate level. The Executive Committee will maintain suggestions for coherent course sequences, including those already developed by Biomathematics for students interested in specialty training in Human Genetics, Microbiology Immunology and Molecular Genetics, Molecular Biology, Molecular Cellular and Integrative Physiology, the Neuroscience Interdepartmental Program, or EE Biol (Ecology and Evolutionary Biology). One notable example is the Graduate Programs
in Bioscience at UCLA, which offers a common first year curriculum for graduate students interested in research specialization in the molecular, cellular, and integrative life sciences.

3. To help prepare trainees for their dissertation research and professional development, trainees are required to go through at least one quarter per year of directed research in the laboratories of the participating faculty members. A special trainees seminar will be held at a suitable time in Winter Quarter in conjunction with a social gathering of trainees and participating faculty. Each trainee who has had a directed research experience will make an oral presentation of the results of that research, and participating faculty will provide commentary and feedback on the presentations. Trainees must also attend a seminar series on computational biology usually held Fall and Spring quarters. These requirements will give the trainees a broad perspective on how mathematical modeling is being applied in a variety of biological/medical areas and provide opportunities for trainees to establish personal contacts with active researchers in various fields. This exposure is especially helpful for those who do not yet have a research topic. The advisor or mentor for each trainee, of course, is expected to play an important role in guiding the trainee to select a topic that suits the trainee’s scientific interests and aptitude.

4. In addition, all trainees are required to take a class on ethics in biological/medical research, and a 4-year refresher (i.e., retake the same course or another ethics course after 4 years if the trainee has not obtained his/her doctoral degree by that time). Ethics course examples: Biomath M261 (offered fall quarter only), MIMG C234 (offered in spring quarter only), and Neuro 207 (spring quarter).

Training Timetable

Trainees are expected to take courses required by their departments/programs concurrently with the ones required by this training program. They are expected to complete the curriculum requirements of the training program in 2 years, although up to an additional year may be requested by petition to complete the requirements under special circumstances, e.g., course series offered every other year or conflicts with requirements of the home department. Courses for the training program will naturally overlap with courses required by the department/program with which the trainee is affiliated, reducing the actual number of extra courses that the trainee will need to take. Moreover, the training program will help trainees to decide on research topics and carry out their dissertation research. Thus, the extra training time added to the regular time-to-degree from their home department is expected to be less than a year.

The emphasis of this training program will be on the early years of graduate training. After completing the curriculum requirements of the program, a trainee is expected to have decided on a dissertation research area, selected a laboratory or setting under which to do the work, and chosen a dissertation research mentor or co-mentors. At that time, no later than the end of the third year, the responsibility for the trainee’s financial support is expected to shift to the affiliated laboratory. Because theoretical research may not be performed in a traditional laboratory setting, students pursuing such research with limited access to funding can petition to apply for further extension of training grant support into their research dissertation years. The evaluation of all exceptions will be made on a case-by-case basis by the Executive Committee, taking into account the competitive basis for
evaluation of all new trainees and renewals.

**Trainee Selection**

Every student applying to the training program is asked to submit (1) GRE scores (2) transcripts covering his/her most recent academic degree or program involvement (3) a statement of purpose and research interests, and (4) letters of recommendation. For incoming students we will accept three letters of recommendation used for their application to a UCLA graduate program. For continuing students we expect two letters of recommendation, at least one of which is from their current faculty advisor or mentor.

In evaluating incoming students we are mindful of some ideal standards of undergraduate preparation for the dual areas of training required in this program. In mathematics these include exposure to multivariate calculus, linear algebra, ordinary differential equations, and probability and statistics. In biology we would expect to see a year long introduction to biological principles as well as a course in biochemistry/molecular biology. Evidence for successful performance in upper division courses in both areas is helpful for judging that timely completion of the formal requirements is likely. However, in our experience exceptional strengths in one area can balance deficits in the other.

**Monitoring and Evaluation**

As noted earlier, the progress and performance of each trainee is monitored closely by his/her advisor, with whom members of the Executive Committee will communicate at least quarterly. Yearly, the progress of each trainee will be reported (in writing and orally) to the Executive Committee, which determines whether progress is satisfactory, whether adjustment is needed, and whether support should be continued. The yearly evaluation and ranking of current trainees for renewal will be done competitively and at the same time as evaluation and ranking of new students for entry into the training program (see below). The competitive ranking of renewing students will also take into account their rate of progress. Students petitioning for exceptions, e.g., course work beyond the second year or continuation of support into the dissertation years, will have to show compelling cause as well as outstanding academic and research progress.
APPENDIX

Examples of Graduate Courses for Quantitative Training

Note: Trainees must develop with their advisor(s) a coherent plan for quantitative training that includes completion of five courses (total of 20 quarter units), with at least two courses in Core Methodology and two in Modeling Applications in Biology. The following examples are not exhaustive, and the Executive Committee will review suggestions from participating faculty and update the list on an annual basis. Trainees may petition the Executive Committee to allow substitution of 8 of the 20 quarter units with upper division courses.

Listings below include course descriptions taken from the 2014-15 General Catalog.

a) Core Methodology

(1) Deterministic Modeling

Biomath 201 - Deterministic Models in Biology

201. Deterministic Models in Biology. (4)
Lecture, three hours; laboratory, three hours. Preparation: knowledge of linear algebra and differential equations. Examination of conditions under which deterministic approaches can be employed and conditions where they may be expected to fail. Topics include compartmental analysis, enzyme kinetics, physiological control systems, and cellular/animal population models. S/U or letter grading.

Bioengr M296A - Advanced Modeling Methodology for Dynamic Biomedical Systems

M296A. Advanced Modeling Methodology for Dynamic Biomedical Systems (4)
(Formerly numbered Biomedical Engineering M296B.) (Same as Biomathematics M270, Computer Science M296B, and Medicine M270D.) Lecture, four hours; outside study, eight hours. Requisite: course CM286 or M296A or Biomathematics 220. Estimation methodology and model parameter estimation algorithms for fitting dynamic system models to biomedical data. Model discrimination methods. Theory and algorithms for designing optimal experiments for developing and quantifying models, with special focus on optimal sampling schedule design for kinetic models. Exploration of PC software for model building and optimal experiment design via applications in physiology and pharmacology. Letter grading.


M280A. Linear Dynamic Systems. (4)
(Same as Electrical Engineering M240A and Mechanical and Aerospace Engineering M270A.) Lecture, four hours; outside study, eight hours. Requisite: Electrical Engineering 141 or Mechanical and Aerospace Engineering 171A. State-space description of linear time-invariant (LTI) and time-varying (LTV) systems in continuous and discrete time. Linear algebra concepts such as eigenvalues and eigenvectors, singular values, Cayley/Hamilton theorem, Jordan form; solution of state equations; stability, controllability, observability, realizability, and minimality. Stabilization design via state feedback and observers; separation principle. Connections with transfer function techniques. Letter grading.

Chem. Engineering 282A - Nonlinear Dynamic Systems

M282A. Nonlinear Dynamic Systems. (4)
(Same as Electrical Engineering M242A and Mechanical and Aerospace Engineering M272A.) Lecture, four hours; outside study, eight hours. Requisite: course M280A or Electrical Engineering M240A or Mechanical and Aerospace Engineering M270A. State-space techniques for studying solutions of time-invariant and time-varying nonlinear dynamic systems with emphasis on stability. Lyapunov theory (including converse theorems), invariance, center manifold theorem, input-to-state stability and small-gain theorem. Letter grading.

Computer Science 212A - Queueing Systems Theory

212A. Applied Ordinary Differential Equations. (4)

Math 266 A - Applied Ordinary Differential Equations

266A. Applied Ordinary Differential Equations. (4)

Math 266 B,C - Applied Partial Differential Equations

266B-266C. Applied Partial Differential Equations. (4-4)
Prerequisite: course 266A or consent of instructor. Classification of equations, classical potential theory, Dirichlet and Neumann problems. Green's functions, spectral theory of Laplace equation in bounded domains, first-order equations, wave equations, Cauchy problem, energy conservation, heat equation, fundamental solution, equations of fluid mechanics and magnetohydrodynamics.
Math 272A - Foundations of Continuum Mechanics

Math 272B - Mathematical Aspects of Fluid Mechanics

Math 273 - Optimization, Calculus of Variations, and Control Theory

Math 274A - Asymptotic Methods

Math 274B-274C - Perturbation Methods

Physics 215A - Statistical Physics
215A. Statistical Physics (4)

Physics 215B - Advanced Statistical Mechanics
215B. Advanced Statistical Mechanics. (4)

(2) Stochastic and Statistical Modeling

Biomath M203 - Stochastic Models in Biology
M203. Stochastic Models in Biology. (4)
(Same as Human Genetics M203.) Lecture, four hours. Requisite: Mathematics 170A or equivalent experience in probability. Mathematical description of biological relationships, with particular attention to areas where conditions for deterministic models are inadequate. Examples of stochastic models from genetics, physiology, ecology, and variety of other biological and medical disciplines. S/U or letter grading.

Biomath 204 - Biomedical Data Analysis
204. Biomedical Data Analysis. (4)
Lecture, four hours. Quantity and quality of observations have been greatly affected by present-day extensive use of computers. Problem-oriented study of latest methods in statistical data analysis and use of such arising in laboratory and clinical research. S/U or letter grading.

M270. Optimal Parameter Estimation and Experiment Design for Biomedical Systems. (4)
(Same as Biomedical Engineering M296B, Computer Science M296B, and Medicine M270D.) Lecture, four hours; outside study, eight hours. Requisite: course 220 or Computer Science M296A. Estimation methodology and model parameter estimation algorithms for fitting dynamic system models to biomedical data. Model discrimination methods. Theory and algorithms for designing optimal experiments for developing and quantifying models, with special focus on optimal sampling schedule design for kinetic models. Exploration of PC software for model building and optimal experiment design via applications in physiology and pharmacology. Letter grading.

Statistics 200 A,B - Statistical Theory
200A. Applied Probability. (4)
Lecture, three hours. Requisite: course 100A or Mathematics 170A. Limited to graduate statistics students. Simulation, renewal theory, martingale, and selected topics from queueing, reliability, speech recognition, computational biology, mathematical finance, epidemiology. S/U or letter grading.

200B. Theoretical Statistics (4)
Lecture, three hours. Sufficiency, exponential families, least squares, maximum likelihood estimation, Bayesian estimation, Fisher information, Cramér-Rao inequality, Stein's estimate, empirical Bayes, shrinkage and penalty, confidence intervals. Likelihood ratio test, p-value, false discovery, nonparametrics, semi-parametrics, model selection, dimension reduction. S/U or letter grading.

Statistics M230 - Statistical Computing
(Same as Biomathematics M280 and Biostatistics M280.) Lecture, three hours. Requisites: course 100C, Mathematics 115A. Introduction to theory and design of statistical programs: computing methods for linear and nonlinear regression, dealing with constraints, robust estimation, and general maximum likelihood methods. Letter grading.

(3) Computation/Algorithms/Numerical Methods

Chemistry C226A - Computational Methods for Chemists
C226A. Computational Methods for Chemists. (4)
Lecture, four hours; laboratory, four hours. Preparation: programming experience in either BASIC, Fortran, C++, Java, or Pascal. Requisites: courses 110A, 113A, Mathematics 33B. Theoretical, numerical, and programming tools for constructing new chemical applications, including simple force fields and resulting statistical mechanics for simple molecules, simple ab-initio methods for organic molecules and nanotubes, and classical dynamics and spectroscopy. Concurrently scheduled with course C126A. S/U or letter grading.

Computer Science 280AP – Algorithms
280A-280P. Algorithms. (4 each)
Lecture, four hours; outside study, eight hours. Requisite: course 180. Background in discrete mathematics helpful. Theoretically sound techniques for dealing with NP-Hard problems. Inability to solve these problems efficiently means algorithmic techniques are based on approximation — finding solution that is near to best possible in efficient running time. Coverage of approximation techniques for number of different problems, with algorithm design techniques that include primal-dual method, linear program rounding, greedy algorithms, and local search. Letter grading.

Math 269 A,B,C – Advanced Numerical Analysis
269A-269B-269C. Advanced Numerical Analysis. (4-4-4)

(4) Optimization

Biomath 210 - Optimization Methods in Biology
210. Optimization Methods in Biology. (4)
Lecture, four hours. Preparation: undergraduate mathematical analysis and linear algebra; familiarity with programming language such as Fortran or C. Modern computational biology relies heavily on finite-dimensional optimization. Survey of theory and numerical methods for discrete and continuous optimization, with applications from genetics, medical imaging, pharmacokinetics, and statistics. S/U or letter grading.

Chem. Engineering M280C - Optimal Control
M280C. Optimal Control. (4)
(Same as Electrical Engineering M240C and Mechanical and Aerospace Engineering M270C.) Lecture, four hours; outside study, eight hours. Requisite: Electrical Engineering 240B or Mechanical and Aerospace Engineering 270B. Applications of variational methods, Pontryagin maximum principle, Hamilton/Jacobi/Bellman equation (dynamic programming) to optimal control of dynamic systems modeled by nonlinear ordinary differential equations. Letter grading.

Chem. Engineering 284A - Optimization in Vector Spaces
284A. Optimization in Vector Spaces. (4)

(5) Other Applied Mathematics

Electrical Engr. 211 A – Digital Image Processing
211A. Digital Image Processing I. (4)
Lecture, three hours; laboratory, four hours; outside study, five hours. Preparation: computer programming experience. Requisite: course 113. Fundamentals of digital image processing theory and techniques. Topics include two-dimensional linear system theory, image transforms, and enhancement. Concepts covered in lecture applied in computer laboratory assignments. Letter grading.

Math 274 A,B,C – Asymptotic Methods; Perturbation Methods
274A. Asymptotic Methods (4)

274B. Perturbation Methods (4)
Lecture, three hours. Prerequisite: course 266A or equivalent. Boundary layer theory, matched asymptotic expansions, WKBJ theory. Problems with several time scales: Poincaré method, averaging techniques, multiple-scale analysis. Application to eigenvalue problems, nonlinear oscillations, wave propagation, and bifurcation problems. Examples from various fields of science and engineering.
b) Modeling Applications in Biology

Biomath 202 – Structure, Function, and Evolution of Biological Systems
Lecture, four hours. Preparation: knowledge of calculus, differential equations, and partial differential equations. Introduction to concepts, equations, and approximations that describe structure and function of biological systems, evolutionary principles, and network design and dynamics. Topics include cancer initiation and progression, gene expression, epistasis, response to fluctuating environments, network structure, and functional traits. S/U or letter grading.

Biomath 206 - Introduction to Mathematical Oncology
206. Introduction to Mathematical Oncology. (4)
Lecture, four hours; computer laboratory, two hours. Preparation: ordinary partial differential equations, one computer programming course. Deterministic and stochastic modeling of cell metabolism, colony growth, and responses to radio-, chemo- and immunotherapeutic agents applied to carcinogenesis, therapy, emergence of resistance to therapy. Simulation, optimization methods introduced. Current literature review. S/U or letter grading.

Biomath 207A - Theoretical Genetic Modeling
M207A. Theoretical Genetic Modeling. (4)
(Same as Biostatistics M237 and Human Genetics M207A.) Lecture, three hours; discussion, one hour. Requisites: Mathematics 115A, 131A, Statistics 100B. Mathematical models in statistical genetics. Topics include population genetics, genetic epidemiology, gene mapping, design of genetics experiments, DNA sequence analysis, and molecular phylogeny. S/U or letter grading.

Biomath 207B - Applied Genetic Modeling
M207B. Applied Genetic Modeling. (4)
Same as Biostatistics M237 and Human Genetics M207B.) Lecture, three hours; laboratory, one hour. Requisites: Biostatistics 110A, 110B. Methods of computer-oriented human genetic analysis. Topics include statistical methodology underlying genetic analysis of both quantitative and qualitative complex traits. Laboratory for hands-on computer analysis of genetic data; laboratory reports required. Course complements M207A; students may take either and are encouraged to take both. S/U or letter grading.

Biomath 208 (A or B) - Modeling in Neurobiology
208A. Modeling in Neurobiology for Mathematicians. (4)
Lecture, four hours; laboratory, two hours. Preparation: introductory ordinary partial differential equations, programming experience. Introduction to electrochemical bases for nerve function and mathematical and computational methods for studying this, appropriate for physicists, engineers, and mathematicians. Survey of current leading research areas and software systems. S/U or letter grading.

Biomath 209 - Mechanisms and Modeling in Bioanalytical Assays
209. Mechanisms and Modeling in Bioanalytical Assays. (4)
Lecture, three hours. Preparation: knowledge of basic physical chemistry and ordinary differential equations. Recommended requisite: course 201. Review of basic physical mechanisms and mathematical analyses used in common bioanalytical assays. Topics include chromatography, electrophoresis, blotting, DNA sequencing, PCR, SELEX, ChIP-seqencing, FACS, FAP, and FISH. S/U or letter grading.

Biomath M211 – Mathematical and Statistical Phylogenetics
M211. Mathematical and Statistical Phylogenetics. (4)
(Same as Biostatistics M239 and Human Genetics M211.) Lecture, three hours; laboratory, one hour. Requisites: Biostatistics 110A, 110B, Mathematics 170A. Theoretical models in molecular evolution, with focus on phylogenetic techniques. Topics include evolutionary tree reconstruction methods, studies of viral evolution, phylogeography, and coalescent approaches. Examples from evolutionary biology and medicine. Laboratory for hands-on computer analysis of sequence data. S/U or letter grading.

Biomath 213 – Modeling Vascular Networks
213. Modeling Vascular Networks. (4)
Lecture, four hours. Recommended preparation: calculus, differential equations, complex analysis, elementary knowledge of partial differential equations. Introduction to equations that describe fluid flow dynamics and branching, and hierarchal networks to provide survey of models for structure and flow of vascular systems. Vascular systems are nearly ubiquitous in nature, occurring across animals, plants, and other organisms. Coverage of applications to tumor growth and angiogenesis, sleep, allometric scaling, and other phenomena. S/U or letter grading.

Biomath 220 – Kinetic and Steady State Models in Pharmacology & Physiology
220. Kinetic and Steady State Models in Pharmacology and Physiology. (4)
Biomath M230 - Computed Tomography: Theory and Applications
Same as Biomathematics M230. Lecture, four hours. Computed tomography is three-dimensional imaging technique being widely used in radiology and is becoming active research area in biomedicine. Basic principles of computed tomography (CT), various reconstruction algorithms, special characteristics of CT, physics in CT, and various biomedical applications. S/U or letter grading.

Biomath/Physics M243 – Condensed Matter Physics of the Cell
(As same as Physics M243L.) Seminar, four hours. Designed for graduate students. Basic paradigms of condensed matter physics and applications to biophysical modeling. S/U or letter grading.

Bioengineering M296D - Introduction to Computational Cardiology
M296D. Introduction to Computational Cardiology. (4)
(Formerly numbered Biomedical Engineering M296D.) (Same as Computer Science M296D.) Lecture, four hours; outside study, eight hours. Requisite: course CM186. Introduction to mathematical modeling and computer simulation of cardiac electrophysiological process. Ionic models of action potential (AP). Theory of AP propagation in one-dimensional and two-dimensional cardiac tissue. Simulation on sequential and parallel supercomputers, choice of numerical algorithms, to optimize accuracy and to provide computational stability. Letter grading.

Biomed. Physics 210 - Computer Vision in Medical Imaging
210. Computer Vision in Medical Imaging. (4)
Lecture, three hours; discussion, one hour. Recommended requisites: Mathematics 155, Program in Computing 10A. Study of image segmentation, feature extraction, object recognition, classification, and visualization with biomedical applications. Topics include region-growing, edge detection, mathematical morphology, clustering, neural networks, and volume rendering in lectures, case studies, and programming projects. S/U or letter grading.

Molecular & Medical Pharmacology M248 – Introduction to Biological Imaging
M248. Introduction to Biological Imaging. (4)
(As same as Bioengineering M248 and Biomedical Physics M248.) Lecture, three hours; laboratory, one hour; outside study, seven hours. Exploration of role of biological imaging in modern biology and medicine, including imaging physics, instrumentation, image processing, and applications of imaging for range of modalities. Practical experience provided through series of imaging laboratories. Letter grading.

Ecology and Evolutionary Biology C219 – Mathematical Ecology
C219A. Mathematical and Computational Modeling in Ecology (4)
(Formerly numbered C219.) Lecture, three hours; discussion, one hour. Enforced requisite: Mathematics 3B or 31A. Recommended: courses 100, 122, Life Sciences 1, Mathematics 3C. Introduction to modeling dynamics of ecological systems, including formulation and analysis of mathematical models, basic techniques of scientific programming, probability and stochastic modeling, and methods to relate models to data. Examples from ecology but techniques and principles applicable throughout life and physical sciences. Concurrently scheduled with course C119A. S/U or letter grading.