QB 829, *Introduction to Physical, Mathematical, and Computational Methods*

QB 829, *Introduction to Physical, Mathematical, and Computational Methods* (3 credits) is offered to biologists in the QB program. Students receive hands-on training in existing physical, chemical, mathematical, and statistical techniques—particularly those implemented in software—rather than training in how to develop new techniques. Students should be able to apply methods in research, understand them in papers and seminars, and foster collaborations with other faculty. Using user-friendly software packages, the students need not be able to derive the equations or write the programs themselves; rather, they focus on understanding what the methods can do, how to choose and run the programs, how to interpret their results in a valid fashion, and how to assess the strengths and weaknesses of the method.

The QB 829 course focuses on seven major topics (see syllabus below). Students explore each topic using examples from biology, including approaches such as kinetic modeling of metabolic pathways; Markov models of species populations; phase diagrams of phospholipid bilayers; thermodynamic parameters of protein folding transitions; and modulation of solution conditions to favor or disfavor folding, assembly, and ligand binding. The course consists of two 50-min lectures per week plus one student recitation, during which students present their solutions to weekly homework assignments. The homework consists almost entirely of problems to be worked in groups of 2-3 by computational modeling. Two mid-term exams and one final, as well as online LON-CAPA quizzes test the students' conceptual understanding and critical assessment of the method and results—students should also be able to identify the quantitative method(s) that best answer the biological questions posed. A LON-CAPA quiz at the start of the course tests the students' basic math aptitudes.

Table 2. Syllabus of the Spring 2009 QB 829 course.

Module 1: **Basic statistics**	Discrete vs. continuous variables; 1D distributions; error bars vs. confidence limits; error propagation; statistical significance; 2D (and higher) distributions; principal component analysis; covariance; distribution comparisons; hierarchical clustering algorithms
Module 2: **Statistical correlation, curve fitting**	2D rank correlation; linear correlation; χ^2 distribution; ordinate and abscissa errors; fitting to sums of exponentials; over- and under-fitting; two-state transition; X-ray refinement and self-bias; NMR structure solutions; parsimony and ensembles of solutions
Module 3: **Diffusion,** **Protein size estimates**	Composition of statistical variables; central limit theorem; diffusion, translational and rotational; Einstein relation; diffusion constants and analytical ultracentrifugation; gel filtration, SDS page, light scattering, fluorescence
Module 4: **Matrix methods; computational efficiency**	Matrices and linear problems; Markov processes; mass spectra; single value decomposition; structural superposition; algorithms and computational efficiency: $O(N)$, $O(N^2)$, $O(N \log N)$
Module 5: **Kinetics**	Soluble kinetic models: receptor-ligand interactions; steady-state and rapid equilibrium approximations; computational solutions and fitting data to kinetic models; metabolic network modeling
Module 6: **Equilibrium; thermo/statistical mechanics**	Equilibrium; balancing of kinetic rates; time/ensemble averages; equipartition theorem; Boltzmann factor; different ensembles; entropy; chemical potential, free energy G in kinetic terms; transition state; Arrhenius' kinetic law; Nernst potential; action potentials, redox potentials; osmotic pressure; molecular machines
Module 7: **Noise, noise reduction, filtering**	Fourier transforms; real and reciprocal (time/frequency); signal to noise; sources of noise (Poisson); types of noise; noise reduction by phase-sensitive and correlation methods; optimal filters of known spectrum