BC571: Quantitative Biochemistry (Spring 2016) Syllabus

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Class: Tuesday & Thursday, 4/19–5/5   9AM – 10:50 AM (MRB 312)
Office Hours: By appointment

Description: This course is designed to provide students with the statistical and computational knowledge required to do basic mathematical analysis and curve fitting of data from biochemical and biophysical experiments. The course will have both theoretical and practical aspects and will focus on methods commonly encountered in various laboratories in the Department with students being able to bring their own data if desired.

On the theoretical side, the course will introduce the physical biochemistry concepts behind a number of common biochemical experiments, e.g. ligand binding, enzyme kinetics, and assembly of complexes, with a focus on experimental design and different methods for obtaining the data. On the practical side, the course will utilize Excel, Kaleidagraph, and simple scripting to efficiently import and process experimental data. Curve fitting analysis using standard and customized equations will be covered using Kaleidagraph with an emphasis on the determination and propagation of experimental errors and their use in weighted curve fitting.

Recommended Text: *An Introduction to Error Analysis* by John Taylor
                          University Science Books, 325 pages, $36.50

Optional Text: *Fitting Models to Biological Data Using Linear and Nonlinear Regression*
                By Harvey Motulsky & Arthur Christopoulos
                http://www.graphpad.com/prism/Prism.htm - Free demo download

Software: *Microsoft Excel* – available via CSU site license

                Kaleidagraph from Synergy software is available for Mac and Windows
                    - Academic cost is $120–$140 per copy (http://www.synergy.com)
                    - Several labs have program already
                    - Free 75-day trials of printing and saving *disabled* version

Grading: Traditional grading (A,B,C,…) based on problem sets (60%) that involve processing and analyzing experimental data and class participation (40%).

Lecture outline:
Classes will be split into theory and practical application halves

	Theory	Practical Application (DATA WANTED!)
1	Mean, median, quartiles, standard deviation, variance, standard error of the mean, and the Gaussian (normal) distribution	Excel tips and tricks; Calculating standard deviation and confidence intervals; Comparing data; Identifying outliers; Extracting data from images (data thief)
2	Error propagation: shifts, multiplicative factors, and sums; the general case; proof that error of N measurements $\sim 1/\sqrt{N}$	Error propagation calculator website; Verifying error propagation formulas; Basics of Kaleidagraph and comparison to Excel; Simulating data from fits to older data to plan new experiments
3	Fitting data (error analysis on a curve!): R vs R^2, $\chi 2$; Linear curve fitting theory and parameter estimate confidence intervals; Exponential fits; First-order binding (exponential decay)	Basics of Kaleidagraph curve-fitting; Linear fit to determine concentration; Image-based data analysis; Exponential fit to determine single molecule binding off rate; solution, pull-down, and gel-shift assays; SPR
4	Kinetics of enzyme turnover; Derivation of Michaelis-Menten equation; Kinetics of macromolecular complex formation; Hill coefficient and cooperativity	Choosing models: Ligand binding – single or multiple sites vs. "Hill" cooperativity Kinetics – single vs. double exponential, background corrections
5	Diffusion equation; reaction-diffusion kinetics; FRAP theory of reaction-diffusion	Choosing models for FRAP data: Two reactions vs. diffusion plus one reaction; two diffusion coefficients or one; multiple reactions
6	The binomial and Poisson distributions; Gaussian approximation to these distributions; Derivation of the Gaussian distribution	Examples of Poisson processes all around us; Application to stochastic gene expression (RNA FISH, RNA and protein per cell, ribosomes per polysome, ...)

Course Goals:

Theoretical:
- Understand the "Bell curve"
- Understand standard deviation and how it can be used to determine the consistency of data
- Understand why and how error propagates
- Understand the connection between error analysis and curve fitting
- Understand what a distribution is and the know the difference between the binomial, Gaussian, and Poisson distributions
- Understand the basis of models for ligand binding, enzyme kinetics, macromolecular assembly, and reaction-diffusion

Practical:
- Be able to properly report quantitative measurements
- Be able to fit 1D data to linear, polynomial, exponential, and general equations
- Become fluent in Excel and Kaleidograph to efficiently import, process, and interpret experimental data and better plan future experiments
- Be able to distinguish good and bad fits to distinguish (kinetic) models.
- Be able to generate publication worthy plots of data and data analysis

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Homework # 1:

1. **Student's cheating?** For homework, each student in a class of 35 measures the concentration of a protein. As a whole, the class finds the concentration is 0.8 ± 0.2 μM. The teacher notices that five students who are good friends and often work together obtained the following measurements: 0.78 μM, 0.82 μM, 0.81 μM, 0.80 μM, and 0.79 μM. Is this suspicious (i.e., does it suggest they cheated)? Why or why not?

2. **Working with the Normal Distribution.** A set of 500 measurements of the diameter of a Hela cell nucleus yields a value of d = 20 ± 0.5 μm (SEM). Assuming a normal distribution, calculate the average nuclear area A(d) = π (d/2)^2 using Wolfram Alpha. Verify with Excel by simulating 500 datapoints using the built-in Excel function NORM.INV(RAND(), MEAN, SD).

3. **Olve's assignment on Canvas**