

Feature *WWW.Life Sciences Education*

Math and Data Exploration

Dennis Liu

Howard Hughes Medical Institute, Chevy Chase, MD 20815

Biology is well suited for mathematical description, from the perfect geometry of viruses, to equations that describe the flux of ions across cellular membranes, to computationally intensive models for protein folding. For this short Web review, however, I'm going to focus on how mathematics helps us as biologists sort, evaluate, and draw conclusions about our data. Just as computer technology has revolutionized lab work, computers have revolutionized data analysis, in particular with a host of graphically driven methods for sorting, evaluating, and comparing data. The highly technical, often automated, and computationally driven biology of today makes it important to keep students aware of the importance of understanding the underlying mathematics. Computers might seem magical to students, but they only perform the calculations humans tell them to do.

Two independent, ongoing international assessment programs, Trends in International Mathematics and Science Study (TIMSS) and Program for International Student Assessment (PISA), are a perennial source of angst for those who care about education. Students in some wealthy nations, such as the United States, do not perform nearly as well as one might hope on these tests. Those interested in U.S. performance might find it educational to visit the National Center for Educational Statistics (NCES, U.S. Department of Education) website devoted to TIMSS at <http://nces.ed.gov/timss>. TIMSS testing takes place in fourth and eighth grade, so I invite you to “dare to compare” and see whether you are smarter than a fourth or eighth grader. The Dare to Compare section of the NCES website offers tests based on actual assessment items in the TIMSS tests for science and math (<http://nces.ed.gov/nceskids/eyk>; Figure 1). When you solve a problem incorrectly, you can see the reasoning for the correct answer and even compare your performance to the average performance in various U.S. regions (are you smarter than students in your region?).

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Address correspondence to: Dennis Liu (dliu@hhmi.org).

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Figure 1. The U.S. Department of Education Dare to Compare website offers sample tests from the TIMSS math and science test banks for fourth and eighth grades.

Dare to Compare is part of the NCES Kids' Zone (Figure 2) that also has a very nice feature on graphing that includes tutorials and interactive tools for creating graphs.

I took an eighth-grade sample math test, and I missed a question that required me to use a box and whisker plot. The box and whisker plot is in my son's eighth-grade curriculum but was not in mine because it was invented by John Tukey in 1977. My ignorance represents the attitude of many biologists toward math and statistics; if our own research or teaching doesn't require us to be conversant in a particular aspect, we ignore it. Fortunately, several sites offered ways for me to quickly learn this statistical representation. In the K–12 arena, Shodor, a nonprofit organization devoted to improving math and science education through simulation technology, has a wide variety of excellent math resources. Its “Interactivate” section is a great place to browse for interactive math learning tools (www.shodor).



Figure 2. The U.S. Department of Education Kids' Zone website has an excellent interactive graphing feature.

org/interactivate; Figure 3) and includes a box-plotting tool (www.shodor.org/interactivate/activities/BoxPlot) that allows you to enter data and generate box plots with various characteristics. Shodor provides several sample data sets to get you started, such as car mileage and ACT scores. Specific tabs provide support for learners and instructors. I also liked the box plot posting by Fabian Dill on The Information and Visualization blog (<http://informationandvisualization.de/blog/box-plot>). Dill starts out with a good straightforward description of the box plot and then gets into some interesting examples and elaborations. Others might prefer the very clear

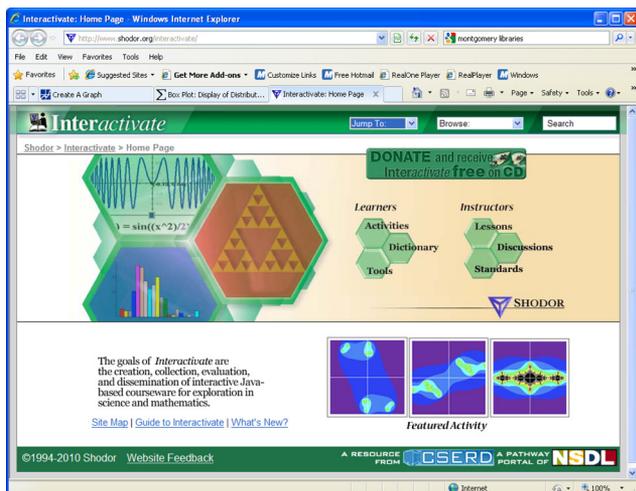


Figure 3. Shodor has an "interactivate" section on its website devoted to interactive simulations for supporting math learning.

and concise presentation on the Saint John's University website that also has a place for entering data sets into a box-plotting utility (www.physics.csbsju.edu/stats/box2.html). An interesting blog called Junk Chart, by charting maven Kaiser Fung, has a nice treatment of the box plot, including how effective these plots are for looking at the performance of S&P 500 stocks (http://junkcharts.typepad.com/junk_charts/boxplot). The box and whisker plot is particularly good at capturing the overall distribution of a data set and clearly showing outlier and potential outlier values.

Have I already spent too much time in a Junior High School mathematical backwater? Tukey did a lot more than just invent the box plot. His text *Exploratory Data Analysis* (EDA; Tukey, 1977) is full of ideas and inventions in addition to the box plot. Tukey is credited with revolutionizing statistical approaches to data and their graphical representations. Today, EDA isn't just an abbreviation for Tukey's book but shorthand for an important approach to data analysis. EDA is used extensively in DNA microarray experiments for example. EDA emphasizes generating hypotheses by looking at lots of data in many different ways, as opposed to more "traditional" statistical approaches for testing null hypotheses. The traditional and EDA approaches are complementary and not in opposition. The EDA approach fits particularly well with the massive data sets that are becoming more common with the growing prevalence of various high-throughput methods.

Microarrays have been an exciting research tool for two decades, but what I find so compelling about microarray experiments in the educational context is the broad range of topics and mathematical complexity that microarray experiments generate. The data raise issues such as raw numerical values (signal magnitude), simple ratios for comparing signals, standard data normalization and log transformations, and a large variety of data-sorting methods and algorithms. Malcolm Campbell (coincidentally the editor for this feature) has been a leading proponent of using DNA microarrays for undergraduate education. He cofounded the Genome Consortium for Active Teaching (GCAT; www.bio.davidson.edu/projects/gcat/gcat.html). It's hard to do justice to the many accomplishments and activities of GCAT in this short review (see Campbell *et al.*, 2007). You can learn a lot about DNA microarrays by visiting the GCAT website, including a section on Laurie Heyer's MAGIC Tool custom software for data analysis, codeveloped with students (www.bio.davidson.edu/projects/MAGIC/MAGIC.html).

The GCAT pages are full of useful information, but they are not what a media critic would call slick. Fortunately, Malcolm teamed up with collaborators at the University of North Carolina several years ago to develop a "MediaBook" on DNA microarrays that is slick enough to have won a Pirelli Prize in 2004 (<http://gcat.davidson.edu/Pirelli/index.htm>; Figure 4). The section on Data Interpretation covers every major aspect of analyzing array data, from creating heat map images to log transformation and hierarchical clustering of results. The entire MediaBook is beautifully done, with a very attractive design; superior explanatory graphics; and well written, if stiffly read, narration. If you are looking for a single place to start students on an exploration of DNA microarrays, look no further. The MediaBook



Figure 4. The Microarrays MediaBook is the best place on the Web for students to get an introduction to the data analysis methods used to interpret DNA microarray experiments.

includes interactive quizzes as well. But, of course, if you want to really engage students in the science of microarrays, you need to join GCAT and have your students do real experiments. For a taste of what it's like to work with array data without generating your own, you might visit the University of Barcelona website that presents a lab practical on analyzing microarray data (www.ub.es/stat/docencia/bioinformatica/microarrays/ADM/practicalMeV.htm).

It's appropriate that the MediaBook, as an educational tool, very effectively uses graphics to teach about DNA microarrays, because today's state-of-the-art data analysis tools feature powerful graphics capabilities as well. One of the most popular tools for microarray experiments as well as other large data sets is R, an open-access statistical software package (www.r-project.org; Figure 5). The R project provides users with a complete package of computing environment, language, and graphing tools in a suite that is flexible enough to serve the needs of diverse researchers. R is not as easy to learn as standard desktop software, but a variety of tutorials are available to help (e.g., see <http://mercury.bio.uaf.edu/mercury/R/R.html>). By the way, although the MediaBook does not feature any box plots, the modest graphing method is extensively used in DNA microarray experiments for early quality-control stages of data processing. The box plot is particularly useful for comparing replicate data sets, and for identifying outliers, which can be associated with key findings or the result of experimental errors. Raphael Gottardos' presentations at the 2008 Canadian Bioinformatics Workshops provide a good overview of the EDA approach and the use of R (www.bioinformatics.ca/workshops/2008/course-content). Scroll down to Essential Statistics in Biology and look at Module 1 as a PDF or PowerPoint file. Gottardos' lab at The Clinical Research Institute of Montreal and the University of British Columbia focuses on computational biology, especially for high-throughput genomic analysis (www.rglab.org).

There are at least two other important software packages that should be mentioned in connection with data analysis, MATLAB and Mathematica. MATLAB is a product of The MathWorks (Natick, MA) and enjoys wide use in academic and industrial research settings (www.mathworks.com/products/matlab). MATLAB began as a numerical computing language but has grown to include symbolic computing capabilities and more sophisticated graphing features. Mathematica is the mainline product of Wolfram Research (Champaign, IL), founded by physicist, mathematician, entrepreneur, and computational guru Stephen Wolfram. The best portal into the Wolfram world provides a list and description of his many different websites (www.wolfram.com/webresources.html). Wolfram declares that his various insights into computing forced him to invent, not a new science, but "a new kind of science," the title of his book and a website (www.wolframscience.com). The central tenant of Wolfram's science is that natural laws are digital, and very simple programming rules are the basis for complex natural systems. He is particularly fond of showing simple "cellular automata" programs that illustrate the complex patterns that can arise from many iterations of a simple set of interactions. You can get a taste of his style and ideas by viewing his 20-minute talk on the TED website (www.ted.com/talks/lang/eng/stephen_wolfram_computing_a_theory_of_everything.html). A hallmark of Wolfram Research products is outstanding graphic capabilities, and the demonstrations website is the best place to get a sample (<http://demonstrations.wolfram.com>). For example, search for "turbulence," an important factor in many real biological systems, and you will find 13 interesting demonstrations. To use the interactive demonstrations, you will have to download the free Mathematica Player. Wolfram calls his latest project WolframAlpha and describes it as an attempt to make all knowledge computable (www.wolframalpha.com). I think of WolframAlpha as "Ask Jeeves" (www.ask.com), where Jeeves is a robot butler who always answers your questions with data instead of sentences. Interestingly, when I tried to

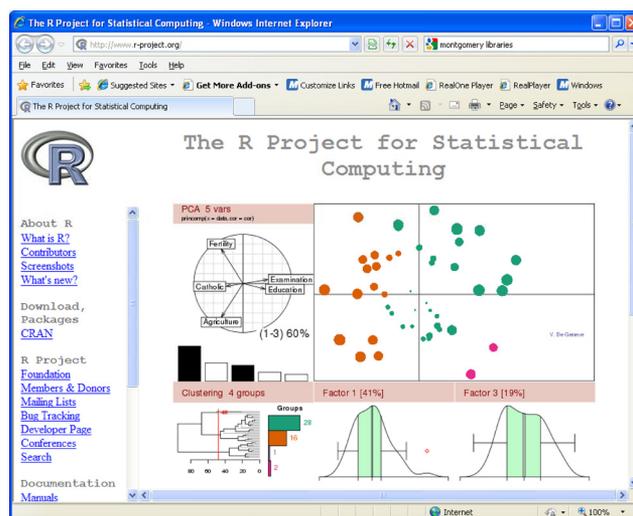


Figure 5. The R Project for Statistical Computing is an open source package for data analysis and a favorite of EDA aficionados.

