The Crossroads between Biology and Mathematics: The Scientific Method as the Basics of Scientific Literacy

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Biology is changing and becoming more quantitative. Research is creating new challenges that need to be addressed in education as well. New educational initiatives focus on combining laboratory procedures with mathematical skills, yet it seems that most curricula center on a single relationship between scientific knowledge and scientific method: that of the validity of knowledge claims, judged in terms of their consistency with data. Collecting data and obtaining results (however quantitative) are commonly part of science, but are not science itself. We envision that the operative use of the complete scientific method will play a critical role in providing the necessary underpinning for the integration of math and biology at various professional levels.

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D'Arcy Thompson began his book *On Growth and Form* (1917) by quoting Immanuel Kant: "…chemistry was a science, but not a Science…for that the criterion of true Science lay in its relation to mathematics." Thompson went on to explain how chemistry was elevated to the level of "Science," whereas biology had not yet reached that level. The search for universal quantitative laws of biology can be daunting, given the extraordinary complexity of biological systems (West and Brown 2004). Yet when such an interdisciplinary approach proves successful, it often provides a major breakthrough in biology (as was first exemplified by the discovery of the Mendelian laws of inheritance). We are now starting to understand that the amazing complexity and diversity of living organisms commonly stems from ultimately simple rules that can be explored by computational and mathematical means (Kauffman 1993). Although Thompson's attitude is widely present in the scientific culture today, we maintain that mathematics alone will not turn a field into science, but the application of the scientific method does. To illustrate this, we intend to show how mathematics, inquiry-based learning, and the application of a modern philosophy of science could produce pedagogy to better teach biology as a science. In this article, we define the "scientific method" as the sorts of things scientists do, and contrast this with the demonstrative methods more frequently used in current instruction.

Modern scientific advances have transformed the life sciences, but until recently they had little influence on undergraduate training, leaving an unprecedented gap between teaching and research (McComas 1998, Abell and Lederman 2007, Kerfeld and Simon 2007). In 2003, the National Research Council issued *BIO2010*, a report that suggested that biology should become more quantitative, an issue to be addressed both in research and education (NAP 2003). Biological researchers and educators today are closely collaborating with mathematicians and scientists from other fields. Even if tomorrow's biologists had a more extensive mathematical and computational background, a single person could not, in general, pursue all these fields in depth; thus, the formation of interdisciplinary collaborations continues to be essential in the pursuit of biology (Karsai and Knisley 2009).

These days, mathematics enters at every stage of science: in designing an experiment, seeking response patterns, and in the search for underlying mechanisms. The interdisciplinary approach is at the heart of many research areas, such as in genomics, where the size and complexity of the data sets and the scale of the problems require the joint expertise of computer scientists, statisticians, and biologists. However, while this type of collaboration is becoming more common in research, the real challenge seems to begin at the undergraduate level (Musante 2005), where we must train a workforce that is able to do collaborative work efficiently. According to major surveys, American students graduate from college

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poorly prepared to enter the math, science, and technology workforce (Stukus and Lennox 1995, NAP 2003, Abell and Lederman 2007). We argue that simply introducing more mathematics to biology majors will not solve this problem.

We believe that for mathematics to make sense in biology education, science should make sense first. The issue has two interrelated aspects, and we deal with them separately: They are the understanding of science and the understanding of mathematics for science (in this case, for biology).

Inquiry-based approach

Inquiry-based investigation is widely publicized as a basis of science instruction. The National Research Council's National Science Education Standards (1996) encourage teachers to focus on inquiry, where students are expected to formulate their own questions and devise ways to answer them. These are generally inductive activities that require students to work out their own procedures, collect their data, present and analyze those data, and derive conclusions from the results they obtain (DeBoer 1991). Because data collection and processing are quantitative ways to study biology, freshman inquiry-based labs are commonly the first venues where students study biology using statistics or simple math.

As a pedagogical approach, of course, inquiry is full of merits, and inductive activities tend to bring undergraduates closer to understanding science (Kerfeld and Simons 2007). However, the integration of this approach into the curriculum commonly has flaws, and the true nature of inquiry is often forfeited in this process (Edwards 1997). Published research material is frequently too heavily structured and too complex for undergraduates, so instead of an original research project, preselected substitutes—so-called real-life problems—are investigated in the classroom, in a seriously canned manner. Understandably, there are common technical and logistic constraints (one of them is time), but the real danger is that technical difficulties in implementing an inquiry can change the whole pedagogy: Using scientific inquiry without first teaching the proper scientific method may generate a complete misunderstanding of how science works. Asking questions, collecting data, and obtaining an answer from the latter are parts of the scientific method, but do not wholly constitute the scientific method itself (Musante 2009).

Going a step further, it is true that the scientific method can be best learned through research (Roth 1995). So again, with right sentiment, many argue that getting undergraduates involved in research is important (McComas 1998). However, we argue that there is too much of a difference between engaging in research (such as a single project that continues for years) and doing "research projects" in the classroom. Many students are initially uninterested in science and some are actually afraid of it (Demers 2003). Many science majors are attracted to health professions but lack awareness of how science operates in general, or how this knowledge is important for their chosen career (Felzien and Cooper 2005).

Most undergraduates never meet anything close to real science, and are exposed to "research activities" in a classroom setting only. Simple investigation or inquiry, although called "research," is in reality not research at all (Ortez 1994, Mrosovsky 2006). Using the Google search engine and collecting (i.e., literally "researching") information into a report, or following a cookbook lab protocol are examples of "research" that in fact do not use the methods of science. By concentrating exclusively on such exercises, it is easy to lose focus of what real research is all about. Pedagogy should not give in to logistical problems. Attacking a smaller number of problems in greater depth could be a solution that is closer to real research. For example, Felzien and Cooper (2005) developed an "Introduction to Research" course in which students especially valued the assignments to write grant proposals. Students said this was the toughest task, but that it helped them most to understand the biological research process. Demers (2003) developed a well-rounded, student-driven, inquiry-directed course: It begins with epistemological definitions, discusses science and nonscience, investigates ethics, and develops critical thinking, all with an overview of the basic model of the scientific process. Then, students as a group are asked to apply their newly learned awareness to the discussion of selected research problems. In our opinion, these approaches provide better intellectual preparation to learn about how to do science than attacking different biological problems each week.

"A lab is where you do science" (Thornton 1972). This view is often heralded in the literature, but we disagree. Rather, it is in the investigative mind where we do science; the laboratory offers only an opportunity to test scientific hypotheses through predictions (the products of the mental process that constitutes science). By contrast, most science curricula tend to focus on a single relationship between scientific knowledge and scientific method: the validity of scientific knowledge claims, judged exclusively in terms of their consistency, with observable evidence (Hodson 1998). Most instructional laboratories incorporate only a few selected steps of inquiry even in hands-on experiments (Harker 1999). Harker argues that full participation in each step of the scientific method would be necessary instead, and he also presents a positive example from his microbial physiology course (Harker 1999; see box 1 for an example of our own approach to inquiry).

Scientific literacy doesn't necessarily call for deep understanding of difficult concepts such as the Nernst equations or the precise conditions of the Hardy-Weinberg equilibrium, but it does require a general understanding of basic scientific notions and the nature of scientific inquiry (Gross 2006). Becoming a successful researcher requires the learning of many skills. However, focusing on any special skill, whether quantitative or not (such as doing BLAST [basic local alignment search tool] searches for comparing genomes), will provide only the tools required by technicians, not scientists. To be a successful researcher, the most important skill to have is the self-sufficient use of the scientific method.

Box 1. Is body weight inherited or acquired? An example of the use of the scientific method in a freshman biology class.

At East Tennessee State University, we have developed a lab exercise that not only addresses the understanding of an important biological concept but also specifically fosters the use of a particular aspect of the scientific method, the testing of multiple hypotheses (Johnson et al. 2006).

Heritability is the proportion of phenotypic variance in a population that can be attributed to genetic differences among individuals rather than to environmental factors. The main steps we follow to introduce the concept are:

Stage 1: Turn the question ("Is weight/height inherited?") into a series hypotheses and predictions (HW denotes heritability of weight). Then, discuss the differences between statistical and scientific null hypotheses.

H_0: HW does not depend on the sex (it is not different for males and females)

H_A: HW depends on the sex (it is different for males and females)

Using logic (such as inductive and deductive reasoning) as a tool, testable claims (predictions) are derived from these hypotheses:

P_0: HW is not different for the two sexes

P_1: HW is smaller for males

P_2: HW is smaller for females

Note: We also create a similar hypothesis-prediction tree for the heritability of height. Our goal is to formulate at least one specific prediction derived from each hypothesis.

Stage 2: Experimental design.

What needs to be measured and how? What are the costs and benefits of different experimental approaches? A discussion is conducted and a plan is formulated for selecting basic data for the investigation, using the weight of parents at the time when their age was similar to that of the student today.

Stage 3: Data collection and processing.

We employ an online data collection form, previously developed for submitting data anonymously to a database. Data submission is homework and is voluntary. Data from several parallel classes and many years, accumulated in the database, are used for a regression analysis by the students. This requires the use of a preprogrammed Excel worksheet that contains explanations and instructions on how to process the data.

Stage 4: Evaluation of the results.

The results we obtained in a particular class are: male weight $h^2 = 86\%$ and female weight $h^2 = 57\%$ (Johnson et al. 2006).

We compare these results to our original hypotheses and predictions and conclude that the results supported P_2 (and did not support P_0 or P_1). We carry out the same steps for the heritability of height and reach similar conclusions. We compare our results to the professional literature (Brown et al. 2003) and discuss the differences in methodology and results.

Stage 5: Planning for the next step of investigation.

Now, we discuss possible reasons for the significant difference between males and females. We construct new testable hypotheses for further studies (e.g., how peer pressure may influence teenage girls and boys to control their weight differently, etc.).

Although this is one of the most difficult skills to acquire, university education tacitly expects students to pick it up on the fly, and it is also assumed that faculty mentoring will help this process. However, experience says otherwise. The scientific method is no trivial matter, and it appears that scientists are less interested in it than are philosophers (Salmon 1989, Norton 1998). Studies such as that by Lombrozo and colleagues (2006) indicate that students of various institutions carry several misconceptions about science and lack a sufficient understanding of how scientific views differ from everyday opinions or even religious claims.

The misrepresentation of science and the incorrect use of the scientific method has generated various myths and distorted views of science that are strongly rooted in the scientific mindset of the 1960s and early 1970s (Hodson 1998). For example, experiments are often thought to be decisive and universally essential for testing hypotheses, whereas in reality, no theory-independent experiments are possible; the method of data collection used in testing a given hypothesis and also the formulation of the hypothesis itself are dictated by the very theory under review (Hodson 1988). There is ample evidence that the current distorted image of science to which students are exposed is one of the major reasons many students turn away from science at an early age (Holton 1992). It is important to emphasize to students that every experiment is set up within a theoretical, procedural, and instrumental matrix, and it is this theoretical understanding that gives a purpose and a form to the experiments (Hodson 1998)—in short, that an experiment outside the matrix of the scientific method is junk. It is also imperative to demonstrate that alternative hypotheses can generate identical predictions, so there is no crucial experiment to decide between them, and that obtaining negative results and anomalous data is a natural feature of science. The challenge of science is exactly how to make progress despite these complexities and others. To face them, future researchers must be trained in a more targeted way.

At the level of the "big picture," such issues are commonly dealt with in the context of nature of science (NOS) discussions (McComas 1998, Abell and Lederman 2007). The NOS deals with an important, general overview of science education that we do not intend to address here. Instead, in the following sections, we hope to focus more concretely on the particular issue of why the quantitative approach is not identical to the scientific approach, and how mathematics and statistics can (and cannot) play an important role in teaching biology as science.

Can mathematics help students better understand biology?

Is focused quantitative training in biology a solution? Virtually all educators agree that our goal should be to develop students' capacity for critical thinking and problem solving (Gross 2004, Abell and Lederman 2007). As a pioneering example, the University of Tennessee implemented a process called "multiple routes to quantitative literacy" (*www.tiem.utk.edu/bioed/*), in which quantitative topics were introduced to general biology courses, and math courses were redesigned to provide more varied and informative topics for students of the life sciences (Gross 2004). Including biological data and biology-loaded topics in math courses and quantitative training in biology courses has become a successful and applauded recent trend, with many more recent examples, but there has been no comparable success in integrating calculus and statistics with biology at the freshman level (Karsai and Knisley 2009).

May (2004) pointed out some of the dangers practicing biologists face when attempting to use computational methods without a good understanding of the underlying mathematics; there is a similar danger when mathematicians try to do research in biology. The interdisciplinary bridge between biology and chemistry, or biology and physics, has been smoother. Such projects may require collaborations from scientists with different backgrounds, yet they all use the same approach, or "language," housed within the scientific method they share. The interaction of mathematics with science has never been smooth (exemplified by the difference between Baconian and Cartesian science and the resulting fight between empiricism and rationalism in the 17th and 18th centuries). We believe this is because mathematics and science have significantly different roots and approaches. Mathematics is a language that develops its own internal structure through proving theorems. Mathematics and statistics do not use the methods of the empirical sciences. Understanding science is a first step in clarifying this; understanding the role of mathematics in science is a second.

Sometimes things get mixed up. For example, the testing of scientific or statistical hypotheses, although they may sound very similar, are in effect profoundly different activities, mainly because of the different epistemological groundwork involved. Their differences can generate confusion, especially in inquiry-based labs or when biological examples are used in math classes. Students commonly fail to understand the distinction between a scientific hypothesis and a statistical hypothesis (Maret and Ziemba 1997). In short, in math, the acceptance of a hypothesis implies that our conjecture is true by itself or within a well-calculated degree of certainty. By contrast, in science, the certainty obtained when a hypothesis is confirmed (its predictions "come out true") is very different in quality: A positive outcome merely indicates that the available evidence is not *against* the hypothesis. To say more than that, we would need to compare predictions from various alternative hypotheses.

There are further issues to consider here. Hypothetico-deductivism, often taught as the "right way" to do science, maintains that the task of scientific theories is to explain and predict facts about observed data. We rarely explain to students that such empirical adequacy is insufficient by itself, or that consistency with data and the validity of a hypothesis do not grant "truth" status to a theory. This important matter is sometimes overlooked even by some scientists, who as individuals fight fervently for their pet theories (Mitroff and Mason 1974). In reality, consistency with data signifies that the theory *may* be correct, but numerous other theories may also apply (a classic source is Duhem 1962).

Next, a failure to draw a distinction between data and phenomena is particularly deceptive (Haig 1996). In science, it is phenomena and not the bare data that we want to decipher. Haig (1996) asserts: "Phenomena are relatively stable, recurrent general features of the world that we seek to explain…. Data, by contrast, are idiosyncratic to particular investigative contexts. They are not as stable and general as phenomena." Data are important, of course, because they serve as evidence for the phenomena. When we want to render phenomena from data, we often employ some kind of data-processing methods such as provided by statistical tools. However, we should be aware that these methods help detection, but not explanation (Haig 1996, Maret and Ziemba 1997). Therefore, implementing statistics in biology courses without understanding the scientific method actually misrepresents how science works. Paradoxically, this danger is even higher when a statistical course uses genuine biological data, because although the students obtain the vital statistical skills, the lively essence of the scientific knowledge process is easy to miss, since data are taken at face value, and are taken as "given."

Similar problems occur also when mathematics (calculus, for example) is integrated into biology and math takes over the course. If the course changes track, concentrating on mathematical tractability and skill training instead of scientific meaning, it will not progress in the same way that a typical science course would; that is, through the study of alternative hypotheses or learning about historical shifts of scientific paradigms. For example, the well-known Lotka-Volterra predator-prey model generates regular oscillations in population size. The model is typically considered one of the most important mathematical equations in biology (Jungck 1997), although the system is known to be mathematically unstable against modifications, spatial variations, and stochasticity, and is therefore unlikely to be biologically relevant (Murray 2002). Beyond doubt, the Lotka-Volterra equations provided very important inspirations to ecology and other fields of science, such as complexity science. However, there are virtually no biological data that fit the predictions of this model. The biggest problem, nevertheless, is not the lack of such predictive value but the biologically unacceptable assumptions behind the model. The Lotka-Volterra model is on the basis of assumptions that do not hold in biology, such as aggregated food resources. In engineering and the computational sciences, trusted master models (such as the Hamiltonian or Maxwell equations) are available, and the question is how to best exploit them. A similar approach is misinformative in biology, where such master models are not present, and analysis is subordinate to discovery—an integral part of the knowledge process. Even well-known constructs such as the Lotka-Volterra model cannot be used as master equations: Tweaking and twisting them to give better predictions, as in engineering problems, does not present as much new insight as dealing with the phenomena and trying to build better models.

We think that the problems mentioned above are rooted in the epistemological differences between the fields of mathematics and biology, and that these differences need to be exposed. In mathematics, theories are laid out explicitly and in advance, as in the theory of equations or the theory of complex variables. Results are obtained analytically; that is, by proving properties. The model's description is typically complete and the standard of correctness is mathematical proof. Biology obtains results in a very different way. Here, just as everywhere in science, the basic mental construct takes the form of a hypothesis. Hypotheses cannot be proven or disproven, only supported or unsupported through tests of their predictions. Theoretical and computational models (in the same way as laboratory experiments or observations) can serve as additional tools to test the predictions of a hypothesis and to perform limited experiments in the sense of "what if" scenarios. Besides, in biological investigations, simulations are often preferred to formal models, because their assumptions can be more realistic (e.g., for prey-predation interaction, local models typical in simulations can be favored over aggregate models typical in equations). Models in biology are seldom proved mathematically; instead, model predictions are compared with natural findings, and sensitivity analyses check how the model varies with a few selected parameters.

In other words, instead of looking for a complete proof, the biologist marshals evidence to present the claim of a hypothesis beyond reasonable doubt. A hypothesis that is well supported and whose alternatives do not receive superior evidential support may eventually become a theory. For example, evolution is a successful theory, but there is no way to prove that the theory of evolution is correct in a mathematical sense; however, the scientific method does not require that. Focusing on formalism, truth, and proof thus misinforms students about science.

Philosophy of science, modeling, and simulations

Clarifying science, and clarifying the role of math in science, are important steps. But there may be more to come. Modeling and simulation might offer a farther step forward, while bearing on the former two. To see how, consider that Hodson (1988) urged us to change our traditional view: "In the old stereotyped school curriculum view of science, scientific knowledge exists 'out there' and scientists carefully, systematically and exhaustively collect information that reveals it." The hypothetico-deductive method is still heralded as the main model for science, and other approaches such as the grounded theory (Glaser and Strauss 1967) are not even mentioned, although they have been around for decades. "Logico-deductive theorizing," as Glaser and Strauss (1967) pointed out, exaggerates the significance of theory testing (which is not concerned with the theory's origin or development, only with its validation) and denies the role of inductive reasoning. However, in reality, most hypotheses and theories tend to be underdeveloped, and as a consequence researchers usually submit "low-content" theories to early empirical testing (Haig 1996). The presupposition of the hypothetico-deductive method, that theories arise in a full-blown form, should be shifted to a more dynamic perspective on theory construction, in which a theory becomes an ever-developing entity, interwoven with data and hypotheses.

When doing research, we often do not possess actual knowledge of the causal mechanisms that we abductively probe. Constructing models by analogy, drawing on mechanisms we already know, helps researchers construct new theories. Reality is commonly simulated in a concrete visual image, such as a stock-and-flow model, where the causal mechanisms are drawn from the domain of previous experience in other disciplines. Biology in particular uses many mechanical and electric circuit analogs. This kind of "abductive explanatory inferentialism" suggests that the theory of the scientific method is centrally concerned with generating theories in a "backward" sense. The approach is also very close to how scientists generate models and work with them in practice, in terms of what philosophers have come to call "inference to the best explanation" (Harman 1965).

We can safely predict that the strongest effect of math on biology and biology education will be the extensive use of models and simulations, as has happened in other fields of science (Clement and Rea-Ramirez 2008). Since 1998, studies using models have increased more than fourfold in scientific literature (Keeling and Rohani 2007). Statistics continues to have an important role in providing tools for testing predictions and constructing statistical descriptions, but on the other hand, the role of mathematical and computational modeling becomes ever stronger and will infuse biology in all phases, from hypothesis abduction to the testing of alternative "what if" scenarios. Although more formal models (e.g., differential equations) will continue to inspire quantitative thinking, we foresee that their roles will be increasingly augmented and partly replaced by simulations. Computer simulations can be used as effective tools for collaborative research and education as well, and many biology researchers and students can access these tools today without extensive special mathematical training. Collaboration between a mathematician and a biologist through a simulation platform can help a project stay focused as a genuinely scientific enterprise that uses the full power of the scientific method. In such a system, the biologist can keep track of biological assumptions, and the mathematician can help the biologist avoid using naive math, thus inspiring the biologist to understand the importance of embedded assumptions (such as the assumptions about distributions, randomness, and so on; Brent 2004, May 2004).

We believe that simulation platforms using individual-based approaches especially will provide excellent educational tools for biology. Today, integrated platforms and information systems such as Visual Cell, the Virtual Physiological Human, and others provide templates where data, models, simulations, theories, mechanisms, and qualitative and quantitative knowledge are represented in a uniform and transparent fashion that makes it easy to experiment, form, and evaluate models and alternative hypotheses (see Sauro 2003 for earlier examples). This integration is highly instructive as it suggests a style for doing science by merging several aspects of the scientific method into a uniform representational system while perhaps also serving as a useful template for science education. Although some of these integrated research tools are not easily accessible to all students, many open-source or commercial software platforms exist already (e.g., Netlogo, or Starlogo TNG for agent-based modeling, and Sage and Vensim for mathematical modeling). Using these accessible simulation platforms, we managed to successfully engage freshman biology students with minimal math skills both in classroom exercises and in interdisciplinary research that involved strong mathematical components (Johnson et al. 2009).

Math and mathematics education can also gain from the infusion of biology, and modeling or simulation can be of help there, too. There is already a long list of mathematics problems that have arisen from biological studies, ranging from the age structure of stable populations to qualitative calculus, which applies formalism to incomplete information (Kuipers 1994). The teaching of the concept of "rate of change" has traditionally been founded in analytical geometry, focusing on parabolas and ballistics. In biology, new bases can be found for the same concepts, such as muscle tension or proprioception in locomotion (Brent 2004). We hope that new areas at the crossroads of biology and math will soon develop to a level where biologists can use them intuitively and they can also be incorporated into education. To make it useful for science and the scientist, an integrated or infused curriculum should be based on a solid understanding of the scientific method. We envision that successful programs in research and education in the United States and worldwide will promulgate the scientific method to stress that biology *is* science, and at the same time stimulate the use of common simulation platforms to enhance collaboration between mathematicians and biologists in their efforts to generate, test, and analyze alternative hypotheses—and to educate a skilled workforce.

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