

# Genesis of *Biochemistry: A Problems Approach*

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When I began teaching as a young assistant professor at Caltech in 1966, my assignment was to take over the undergraduate biochemistry course taught for many years by Henry Borsook, who was about to retire. Students dreaded this course. Henry insisted on teaching it at 8 AM, and his approach was largely rote learning—I remember how he used to call bleary-eyed students to the board to draw the structures of amino acids from memory. Having delighted in biochemistry during my graduate training at Stanford, I was determined to put some life and intellectual challenge into the subject but was not sure how to go about it. I began by moving the course to a more civilized hour, which gained me some quick popularity but did not address the real problem. I knew I could get students excited about the emerging science of molecular biology, but what about the more classical aspects? Biochemistry in the 1950s had been largely a descriptive science, based on the cataloging of biomolecules by natural products chemists and characterization of metabolic reactions by enzymologists and physiological chemists. Generally, the subject was still taught that way in the mid-1960s. Students were asked to learn a bewildering array of structures and metabolic pathways, without much discussion about the roles they played in the overall function of a cell and why they might have evolved to their present forms.

Two sources of inspiration helped to steer me in a favorable direction. The first was Al Lehninger's remarkable little book *Bioenergetics* (Lehninger, 1965). It was the first coherent explanation and rationalization of energy metabolism in terms of simple thermodynamics and cell function that I had encountered, and it demonstrated how metabolism could be taught as an intellectually challenging discipline, with clear relevance to biological function and evolution. I became excited about introducing these ideas to students. The second source was the writings of a few renegade educators who were challenging the standard ways of teaching young children. I first encountered them in thinking about the education of our own kids, who were beginning elementary school. It was a time of heady ideas for changing many things, and education was high on the list. John Holt in *How Children Fail* (1964) and

*How Children Learn* (1967), Nat Hentoff in *Our Children are Dying* (1966), Jonathan Kozol in *Death at an Early Age* (1967), and others were pointing out the inadequacies of passive learning. In its place, they were advocating student-centered teaching, open classrooms, and more active involvement of students in their own education. These writers, at the time considered radicals, articulated most of the ideas about how real learning takes place that have since been tested and documented by academic educational researchers since the mid-1960s (summarized, for example, in the National Research Council report entitled *How People Learn*, 1999). The ideas of these iconoclasts were refreshing and inspiring, and they argued convincingly that most real learning must be active and experiential, through doing rather than just listening to lectures and reading books.

There was no laboratory associated with my course, so laboratory simulations and problems seemed like the next best thing. As the course matured over the next few years, it attracted creative colleagues who shared my interests in biochemistry and how best to teach it. John Wilson, one of my first graduate students, became a teaching assistant in the course and developed an unusual knack for creating challenging and instructive problems. Sharon Long, one of the first women undergraduates at Caltech, took the course as a junior and was recruited to be a teaching assistant in her senior year. When Lee Hood joined the Caltech faculty in 1968, we expanded the course to include new topics such as immunology and molecular evolution, and he and I shared the lecturing. At one point, I organized an informal seminar with a few other interested students to read and discuss differing views, from B.F. Skinner to Carl Rogers, on what a teacher can actually do to promote learning, besides simply transmitting information. In the course, we experimented with simulated laboratory exercises, of the same sort that can now be done much more effectively with good software programs—we used index cards to provide the results of experiments proposed by the students in working through a research question. Another card game, Krebs Cycle Poker, helped students to master the citric acid cycle (do not bet on your apparent straight unless you are sure about all the intermediates). And, we gradually accumulated a substantial number of problems related to all aspects of the course, problems that required the students to think analytically and quantitatively, integrating the material in ways beyond those we had discussed in class.

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It was John Wilson's initiative that ultimately led to the problems becoming a book. When his pitch to an editor at W.A. Benjamin (the publishers of Lehninger's *Bioenergetics* and Watson's *Molecular Biology of the Gene*) elicited some interest, we recruited Bob Benbow, another Caltech graduate student who had served as a teaching assistant, to be a co-author and began to make plans. Our initial idea was simply to take the collection of problems and answers we had and publish them in some sort of a binder for use as a supplement to existing textbooks. However, as we got into the project, we realized we wanted to do more. The comprehensive biochemistry texts used in most courses were becoming thicker and more intimidating for students with each new edition. Might it not be useful to write a short book that briefly summarized the most essential concepts in each area, and then expanded them with a series of problems? And answers—we soon realized that much of the teaching value of the book could come from detailed explanations of the answers to problems that students had already wrestled with.

So that is what we did, and *Biochemistry: A Problems Approach* was published in 1974 (Wood *et al.*, 1974). We prefaced the book with an "ancient Chinese proverb" (I do not in fact know if it is either), which seemed to encapsulate our rationale:

I hear, and I forget.  
I read, and I remember.  
I do, and I understand.

In the preface we wrote, "Listening to lectures, reading, and memorizing factual information are important components of learning, but confronting experimental data and solving concrete problems lead to a deeper working understanding that cannot be acquired passively."

Of course we realized we had not invented anything new in general. Physics and chemistry, and biology, genetics, had always been taught using problems as effective learning tools. But at the time it was unusual for biochemistry. The book became widely used and was translated into several languages. A second edition, improved and expanded, was published in 1981 (we were particularly proud of the new computer-generated triptychs of molecular structures and our directions for how to visualize them three-dimensionally without a viewer: wall-eyed or cross-eyed, take your choice). When I was teaching a course on *Caenorhabditis elegans* genetics in Shanghai in 1987, some of the Chinese students brought their copies into class for me to sign. But unfortunately, that was as far as it went. During the 1980s, the four authors moved in different directions, both geographically and professionally, and although the book is still used in a few places (as we know from our continuing two-figure royalty checks), it never progressed to further editions.

How much of an influence this book had in spreading the problems approach to other areas I do not know, but problem-based learning subsequently became widely used in medical training (the case studies approach) and many other disciplines, and it has become an accepted general teaching paradigm at the secondary and college levels (see, for example, Allen, 1997).

In rereading our 1974 preface, I was interested to find the statement, "The challenge of the future will be to comprehend, as completely as possible at the molecular level, the more complex systems we call organisms. To do so, we must understand not only the internal chemistry of cells, but also the chemistry of communication between them." That is the direction my own career took, working to understand animal development through genetics and molecular biology. As a result of the recent explosion of knowledge in this area, the field of developmental biology has become, from the standpoint of students, discouragingly similar to early 1960s biochemistry: an intimidating array of ligands, pathways, signaling components, and transcription factors, all referred to by confusing acronyms that must be memorized and regurgitated on exams. The time seems ripe for a problems approach here as well.

Meanwhile Sharon Long, now a distinguished plant molecular biologist, has recently become Dean of Humanities and Sciences at Stanford, and is still deeply involved in educational issues. Whether or not there is any causal relationship, an unusually high proportion of her Caltech '73 classmates who took the biochemistry course also went on to high-level positions in academic biology. And John Wilson, among his other endeavors as a Professor of Biochemistry and Molecular Biology at Baylor College of Medicine, is still creating challenging problems—watch for *Molecular Biology of the Cell: A Problems Approach*, coming soon!

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