

# The Human Side of Science



To the nonscientist, the world of research can seem intimidating, methodical, at times stogy, certainly esoteric, and maybe even boring. From the outside, science is a mystery of formulas, laboratories and robot-like experiments. These conceptions are often solidified in the impersonal style used to describe scientific methods and discoveries. The reality, however, is quite different.

Inspiration for an innovative idea may come from a casual discussion with a collaborator, a penetrating question from a student, a stimulating session at a scientific

meeting, a provocative published report or by reflection upon an unusual observation that “doesn’t quite fit.” Any of these and more can drive the scientific mind to the intellectual process that leads to discovery. Science is a human enterprise with most human dimensions. Whether through dedicated investigation, intuitive genius or simply blind luck, each scientific breakthrough is recognized and carried to fruition through *human* observation and intellect. Scientific methods, by necessity, are consistent and repetitive. Without precise routines, detailed searching and meticulous recording, human ideas could never be validated nor replicated; but it is the human spirit of

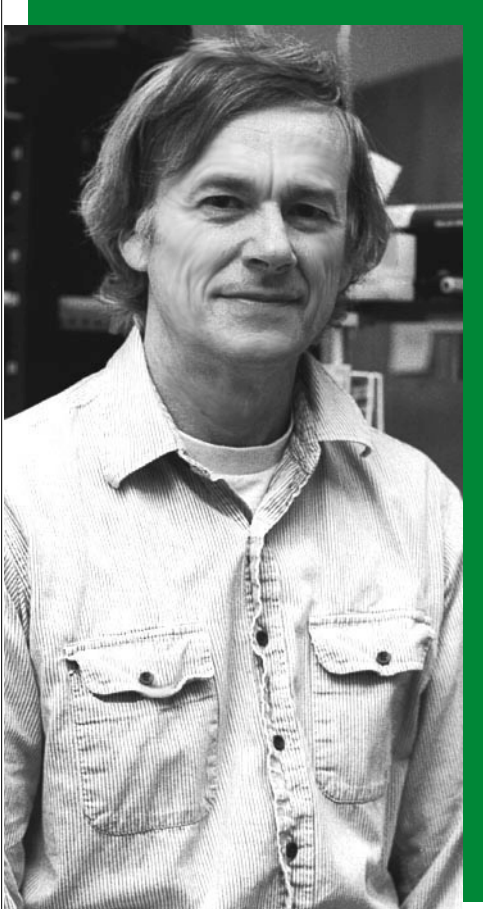
curiosity, the very human “need to know” that drives scientific progress. That element—the human conduit—provides the connection. Without the human ingredient stirred into the scientific formula, Mother Nature would go on, but she would offer no polio vaccines, no computer simulations, no DNA criminal evidence, not even canvas and paint for the great masterpieces of the world. Her bounty would remain a mystery. Every innovation the nonscientists enjoys in life would cease to exist. It is to this humanness we owe all modern progress, and it is for those among us who believe that the creative human impulse basic to discovery is worth exploring that we dedicate this forum: *The Human Side of Science.*

First in a Series:

## A Human Dimension in the Work of Ken Campbell

*There is No Truth,  
but Some Approaches Work Better than Others*

By Ken Campbell



In the late fall of 1981, I was enjoying some tremendous influences in my intellectual and professional life. Each week I met with graduate students for stimulating discussions of scientific methods and philosophy. Additionally, there was much excitement within the cardiac mechanics community about the scientific and clinical promise of describing the time course of change of the relationship between the pressure and volume within the heart’s left ventricle during a heart beat; and finally, a young Bryan Slinker was working with me to apply these pressure-volume concepts to predict the pumping activity of the heart during transient periods when the heart was responding to changes in arterial resistance.

Still in the early stages of my career, I was greatly influenced by my contact with giants in the field who had established themselves through many years of highly cited published work and keynote speaking experiences. From the laboratory of one of these influential scientists came convincing experimental evidence that if we could freeze time during the heart beat and hold the contraction process in a suspended state as we changed the volume in the left ventricle, we would see changes in pressure that were proportionate to changes made in volume. As a consequence, the defining characteristic of the pumping heart was the time-course of the changing slope of the pressure-volume relationship. An important element of this theory was that it didn’t matter what happened prior to any point in time, there would always be, at that time, a defined slope of the linear relationship between pressure and volume. That is, there was no history-dependence in the heart’s behavior. The new idea had been dubbed “time-varying elastance,” and it had captured the imaginations of a substantial number of leading investigators who were then extending it into all kinds of circumstances. To a young cardiovascular scientist, exploring and applying this idea was compelling.

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Bryan and I were attempting to use the time-varying elastance idea to describe the transient pumping behavior that took place over several heart beats. The problem was that we continued to be unsuccessful in collecting data that could be fit with a mathematical model based on the time-varying elastance concept. It was frustrating. We thought we were doing the experiments incorrectly and were not exerting sufficient controls. Bryan worked mightily to refine the experimental procedure and rejected data obtained from experiment after experiment because it was inconsistent with the current reigning idea of how the heart worked.

Luckily, however, Bryan and I were simultaneously engaged in a graduate student seminar where we were reading and discussing Thomas Kuhn's *The Structure of Scientific Revolutions*. Now, Kuhn's thesis was that science works by probing the limits of

reigning paradigms. Scientists accept a principle, a theory, or a set of ideas and devise experiments to see how far this idea can be used to explain all that may be observed experimentally. Ordinary science is the cumulative process by which these ideas are stretched to their limits. When the limits are found and the reigning ideas can no longer explain (or predict) what has been observed, an extraordinary scientific effort produces a completely new and often revolutionary set of ideas that provides an explanation for these previously unexplained findings. The reigning paradigm is shifted and new ideas replace the old. In this way science advances.

Thus, almost as a metaphor for the soon-to-emerge idea of punctuated biologic evolution, Kuhn proposed a theory of scientific evolution whereby there are long periods of gradual knowledge expansion nurtured by the practice of ordinary science and then, suddenly, a revolution in thinking where the old ideas are discarded and new ideas are adopted that result in rapid scientific advances. These revolutions are fueled by an extraordinary scientific event that is a complete departure from reigning paradigms (a metaphor for the environmental catastrophe that leads to extinction of species and their replacement with new species).

In the late evening hours of that day in November 1981, as we walked from the conference room where we had discussed scientific revolutions to the laboratory where we were unable to explain our data based on the current paradigm, I turned to Bryan and exclaimed, "Bryan, we have been throwing away all the good data and keeping just the bad. The problem is not with our experiment but with the time-varying elastance idea we have been using to predict our results. We have been locked into a reigning para-

digm and we have found its limits. We need to find a completely new idea."

Once free of the constraints of the reigning paradigm, Bryan quickly found a way to describe and predict his data. He soon obtained his Ph.D. and went on to pursue the path that has led him to where he is today, the highly-respected chair of our department of VCAPP.

### Retrospective

I spent several years after that evening with Bryan sniping at the time-varying elastance concept and showing its inadequacies as a predictor of cardiac blood pumping (Campbell, et al. *Am J Physiol*, 1986, 1989; *Circ Res*, 1990, 1991; *Am J Physiol* 1992, 1993). These days, few people take the time-varying elastance idea seriously and its use is mostly restricted to certain didactic exercises. However, it remains a frustration to me that I have not yet replaced the time-varying elastance idea with a new theory that is amendable to understanding by the serious cardiovascular scientist. I have only been able to offer an arcanum of mathematical expressions that have little meaning to the ordinary physiologist who is not strongly motivated to struggle with the inadequacies of outmoded ways of thinking.

While I strove to replace the old paradigm with a new one, a real scientific revolution took place in a totally different arena. Ideas and techniques for studying the molecular foundations of physiology developed and captured the imagination of most cardiovascular scientists. These scientists lost interest in better characterizations of cardiac pumping and moved on to new molecular-genetic approaches and understanding. Frankly, it is good that they did because new discoveries based on enhanced understanding of molecular and cellular processes have greatly improved our view of mechanisms responsible for cardiac function. These new discoveries give promise for better treatments for heart diseases. Although I continued to probe the limits of the old ideas, it ended up that I played no role in the revolution that changed the thinking and mode of work of the modern cardiovascular scientist.

Despite not leading to a revolutionary scientific discovery, my revelation was instrumental in shaping my personal world view. Since that evening in 1981, I have come to discover for myself that Fick's Law of diffusion is not a law at all but only an approximation that gives reasonable descriptions and predictions of diffusional flux in the presence of a concentration gradient. Also, Michaelis-Menten enzyme kinetics are known by physical chemists to be derived from crude approximations that don't really represent actual events in an enzymatically catalyzed chemical reaction. This notwithstanding, a good many experimental biologists would be without some of their most useful tools if they no longer could use standard methods for treating diffusion based on Fick's Law or no longer could use  $V_{max}$ ,  $K_m$ , or the Lineweaver-Burk plot from Michaelis-Menten kinetics.

**“While I strove to replace the old paradigm with a new one, a real scientific revolution took place...”**

Even more profound was the realization that chemical reactions in solution are probably poor representations of how analogous reactions transpire in a cell with an aqueous phase that is highly compartmented and limited by the cell's protein content. Free access by bio-molecules to binding sites via diffusion in solution is probably an experimental fiction. Nonetheless, solution biochemistry is the backbone of much of what has been documented as scientific fact and much of what is done in biologic science even today. Those of us who teach from widely accepted textbooks often cringe at the content, not because of factual error, which is easily corrected, but because of representation of current understanding based on questionable ideas. We teach this material because, over the limited range of experiences that our students will encounter the subject, the textbook presentation will suffice and no further elaboration is necessary. The truth of the matter is really not that important to these student's lives.

### ***Epilogue***

I no longer believe that science is a search for truth. I believe that it is a search for facts (confidence in repeated observation rather than essential reality being the measure of acceptance of fact) embedded in mental constructs that more-or-less work either for explanation or for application. From this standpoint, I view all of science as an artifice; that is, an entity of our own making. As such, it should be judged, as are all artifacts, by how well it works. The issue of truth really has no bearing on this measure.

This opinion made it difficult for me to function as a scientist as my philosophy is very apparent in my writings and many scientific reviewers find it objectionable. I needed a different identity. These days, I call myself a bioengineer.

I find comfort in the expectation that an engineer is not concerned with the truth of the matter, only with how well things work. An engineer is given a situation and asked to make it better. I see the world of scientific knowledge as a situation in which much of that knowledge is poorly integrated into workable constructs. This limits its application. The situation can be made better by construction of models (in the most general sense) that enable knowledge to be utilized in engineering design practices.

For instance, there is a formidable accumulation of knowledge about spinal level neuromuscular control. In fact, many neuroscientists would believe that the book on this subject is nearly complete. Maybe so, but if one were asked to reconstruct the behavior of this system, even in the nonmaterial, virtual world of the computer, we would, collectively, have a tough time doing so. If we could accomplish this, animations of animal movement would be more realistic (Disney just spent more than \$200 million dollars making the animated movie "Dinosaur" and this state-of-the-art computer animation of animal movement is clearly lacking in realism) and limb prostheses would function better. More must be done with that knowledge to make it more useful.

Rather than add the last paragraph to nearly completed volumes of physiologic knowledge, I prefer to spend my time making this knowledge accessible to those who would use it for practical engineering purposes. These days I couch what I do in terms of design rather than discovery.

In summary, an epiphanous event in the fall of 1981 led to a personal revelation wherein I discovered what it was I actually do. The world of science did not benefit, but I did. I take satisfaction in having made this personal discovery and am content with my new identity.

