FINALLY FACING THE MIND

Robert Shulman

I have one story to tell about a conscious early step in my intellectual trajectory. It's one of my earliest memories. I was sitting in a school bus going to Far Rockaway High School in New York. Two boys behind me were talking about theater, poetry, actors, movies, and things like that. I turned around and said, "You guys know an awful lot. How come you know all this?" One of the boys was Howard Moss, who said, "Oh, we're intellectuals." I decided right then and there, at age fourteen, that I wanted to be an intellectual, and that's what I've been "doing" for many, many years.

Soon after that incident, I went to Columbia College on a wonderful scholarship. A friend of mine had the same scholarship a year ahead. He gave me the "great books" used in the first-year humanities course and I read them all, from Homer on, the year before I matriculated. I was hooked. My expectations for the course were raised even further by the good fortune of having Lionel Trilling as a teacher. We started reading and discussing under his guidance and things went very well. But then a little problem developed when Lionel announced a new method for the midterm exams. The questions were to be handed out in advance and we were to be prepared to answer all of them, without knowing which questions would be on the exam. I raised my hand

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Robert G. Shulman graduated from Far Rockaway High School in New York and matriculated at Columbia College in 1940, graduating with a B.A. in 1943. He was commissioned an ensign in the U.S. Navy in 1944. After the war he served as radar officer on the USS *Saratoga* and then as executive officer of the USS *Rio Grande*. Upon being discharged in 1946, he returned to Columbia for a Ph.D. in physical chemistry under the direction of Prof. Charles Townes. After a postdoctoral fellowship at Caltech and two years as head of semiconductor research at the Hughes Aircraft Company, in 1953 he went to the physical research department at Bell Telephone Laboratories in Murray Hill, N.J., where he started nuclear magnetic resonance (NMR) research on semiconductors, superconductors, and antiferromagnetics material. By chance this led to studies of biomolecules, starting with DNA. On a Guggenheim Fellowship in 1961, he simultaneously was a visiting professor of physics at the École Normale Supérieure in Paris and a research assistant at the Laboratory of Molecular Biology at Cambridge, where he worked with Francis Crick and Sidney Brenner on frame shifts of the genetic code. Returning in 1962 to Bell, he formed the Biophysics Research Department to use magnetic resonance, at first to study structural properties of macromolecules. Soon thereafter he developed methods to follow metabolism *in vivo,* first in microorganisms and eventually, after moving to Yale in 1979, in humans. At Yale he found that biophysics, as defined in his Department of Molecular Biophysics and Biochemistry, was restricted to molecular structure and molecular genetics, fields he had left behind, so he moved his lab to the Medical School, where he built the Magnetic Resonance Center (1984). He served as director of the Division of Biological Sciences (1981-87), was appointed Sterling Professor of Molecular Biophysics and Biochemistry in 1994, and was the first scientist appointed a fellow of the Whitney Humanities Center (1985-88 and 1996-98). There he learned the great value of literary criticism and philosophy for the conduct of scientific research. He taught that lesson to undergraduates in a course entitled "Issues in Science and the Humanities" from 2000 until 2002, when he retired. Since then he has been writing on philosophy and neuroscience. He is a member of the National Academy of Sciences and the Institute of Medicine.

and objected that it was intolerable to reward us for drudgery instead of creativity. I didn't want to be judged on that basis, I said.

When the time for the exam arrived, one of the questions was, "What did Montaigne and Shakespeare think about education?" I said, in one short sentence, that they both were very much in favor of it. I then quoted something from Montaigne and added, in one more sentence, that the Shakespeare plays we had read (*Henry IV*, parts 1and 2) were all about the education of Prince Hal. Lionel, later admitting it was a difficult decision, gave me a B plus, which in those days was a real grade, not an F under another name. We soon became very friendly. We played a lot of tennis and I went to his home often, for cucumber sandwiches and grown-up talk. For a long period we were close, although political differences during the Cold War drew us apart.

I had a great hero in Lionel. In his world, and that of Columbia generally in those days, what you thought of books and ideas was the stuff of life. It was a heady experience for a seventeen-year-old. But however excited I was by the prospect of entering western culture, I felt what I can only describe as a core of resistance to its attractions. In refusing to accept the changed midterm examination, I was, for an undergraduate, demanding an unusual degree of autonomy. In later life, recognizing Lionel's continual and explicit defense of the individual from the claims of a culture that he admired and appreciated to the limits of human perception, I began to understand how I had shared, naïvely and unknowingly, his concerns about the demands made upon the individual's essential uniqueness by that very culture. On the other hand, it was in the image of that culture, of the great books we read and the great discussions of them, that I was recreating myself. Perhaps it was my simultaneous resistance to the enculturing demands of the midterm exam and my wholehearted immersion in the course contents that prompted Lionel to befriend this young student.

The importance of literature reemerged in my life many years later; when I came to the Whitney Humanities Center and Peter Brooks said to me, "What people don't realize is how serious the humanities are." My scientist colleagues generally regard the humanities as entertainment. Peter introduced me to Michael Holquist, and Michael and I started teaching an undergraduate course on literature and science. We recognized that how one thinks about literature is very serious, with consequences for the rest of life, especially science.

Soon after coming to Yale in 1979, I began to study the brain by nuclear magnetic resonance, or NMR. I've been in many different fields of science, and in the study of the brain, more than in any other field, scientific directions very rapidly become philosophical questions. What questions are you interested in? What mechanisms are you interested in explaining? What basis do you start from and what sort of findings do you consider significant? This is the realm of metaphysics, which calls into question your opinions about the intrinsic nature of the brain and mental activity. Understanding the mechanism of the brain is the realm of epistemology; it forces you to ask why you use a particular approach.

I think continually about the studies of the brain in terms of how you might approach them. Generally, of course, as with anything we do, we tackle the task with the shovel at hand. My own approach to the brain reflects a rather narrow view, one that is shared by a minority of brain researchers. Before I tell you about my particular approach, let me survey the more popular ways scientists study the brain. Nowadays, genetics is considered the key to finding out the truth about the organism and its behavior. So one way of studying the brain is to study the genes that make up the normal brain—how they help in the development of individuals' early learning processes and how they determine their actual behavior. The scientists who embrace this approach believe that certain genes, which may be differently expressed in different individuals, determine the behavior of the organism. That sounds perfectly reasonable, except that there's a very big gap between DNA molecules and behavior. So implicit in that kind of study is genetic determinism, a controversial position that has long been under attack, even by scientists who do not realize that they are, in fact, assuming the causal link between molecules and behavior. Many scientists recognize that the gap exists, but claim that while our present knowledge is too primitive to identify the deterministic connection, in the future such connections will be possible.

Evolutionary psychology offers another way of studying the brain. According to this approach, the brain controls certain patterns of behavior that have evolutionary survival value and therefore must be inheritable. Based on this series of assumptions, the evolutionary psychologists feel that they understand the brain itself.

The related field of cognitive psychology, which shares many assumptions about brain function with evolutionary psychology, is based on a computational theory of mind. Consider the physicist who says, "I know what the brain does: the brain handles information. I want to know how it handles that information. And since it handles information, it is like computers that also handle information. Therefore, I am going to try to explain the brain on the basis of its computer-like properties." Cognitive psychology assumes that the brain, like the computer, is completely rational and follows specific procedures. In this approach, the brain is asked to do a given task, which is chosen so as to include a mental activity such as memory. Then, by taking advantage of the wonderful techniques we have developed, it is hoped to see where the brain changes its activity as it performs this memory task. In so doing, it is hoped that not only will memory be localized in the brain, but the results will have justified the assumption that there was a generalized concept of memory that distinguished and identified it as a component of mental activity.

These studies are carried out by a majority of scientists who are studying the brain, in that large field of research called neuroscience. The scientific value of their studies, however, is diminished by the questionable assumptions that underlie them. Findings at these molecular levels are assumed to cause the organismic property, but until this connection is firmly established, the results must be considered uncertain. The new approaches resemble physics in their complicated apparatus and quantitative results, but the conclusions depend upon unproven assumptions and are no more valid than the assumptions. When reliable physical methods are at the service of personal values about the nature of memory and consciousness, then the conclusions drawn no longer have the certainty of physical science, and these new directions might better be described as "postmodern" science.

My own view of science predates genetic determinism: I depend upon physical science— that is, physics and certain fields of chemistry, such as thermodynamics, derived from physics— that offers a degree of certainty established by centuries of study. Needless to say, I don't believe in absolute certainty, but the consensual understanding of physics established by centuries of experimentation makes it a much more reliable approach than genetic determinism or evolutionary psychology. In the course of my life, I have studied many different materials—chemicals, semiconductors, superconductors, proteins, DNA molecules. In each case, I have proceeded from the known laws of physics, which explain quite well the properties of atoms in terms of their electrons and of molecules in terms of their atoms. When molecules become larger than three, four, five, six, or seven atoms, we begin to run out of reliability, so that functions of the large biomolecules—for example, proteins and nucleic acids—are no longer rigorously derivable. But there is a degree of certainty in small chemicals that is based upon physical science.

At Yale over the past twenty-nine years, I have been studying by NMR methods what happens during life processes to the small molecules in the body—the metabolites. When you eat sugar, the body takes it first into the stomach and then into the intestines and the bloodstream. From the bloodstream the sugar passes into the brain (and muscle and tissues), where it undergoes chemical changes. Catalyzed by enzymes, sugar is converted to sugar phosphates and so on. Enzymes are big molecules, thousands of times bigger than the sugar metabolites. At the next level of complexity, macro-molecules are engaged in facilitating coupled chemical reactions. At this level, linked chemical changes are considered together as metabolism. In a central metabolic pathway, the sugars, serving as the fuel, are oxidized to provide the energy for forming ATP, which has the ability to transfer its energy around the body. ATP is like the currency of energy and delivers energy to different chemical reactions in different locations.

The laws of physics that help to explain solutions of small molecules, such as those found in the body, mostly derive from thermodynamics. Thermodynamics is not a Yale invention, of course, but it was put upon a coherent mathematical basis by Josiah Willard Gibbs at Yale more than a hundred years ago. Gibbs was a great scholar and a solitary scientific figure, in contrast to the team membership called for in science today. The first law of thermodynamics posits equality between the energy consumed in a reaction and the work that is done plus the heat dissipated. That's a very strong law. The work done in the brain is done by ATP and consists mainly of pumping ions—for example, sodium and potassium associated with neuronal firing. After a neuron fires, it sends neurotransmitters across a gap to the next neuron. The energy used in this process is provided by the consumption of ATP, which can be evaluated by measuring the oxidation of glucose. Hence, the amount of oxygen consumed by the brain measures the energy being consumed and the rate of neuronal firing measures the work done.

In the course of years, we have measured the energy used in the brain by means of the oxygen that is consumed. Our NMR methods look at the small but very important molecules in the brain, such as glutamate, glutamine, and gamma-aminobutyric acid (GABA), some of which measure the energy and all of which measure the work done by the signaling between neurons. We can follow those molecules by methods similar to the commonly known noninvasive magnetic resonance imaging (MRI) methods. Imaging provides a map of the distribution of the hydrogen nuclei in brain water. Basically, it tells you the density of the water—how much water there is in a particular space. When you come to a bone, for example, there is less water and hence a smaller signal. We're using similar techniques with noninvasive radio waves that are very easily transmitted through the skin and skull. Instead of measuring water molecules, we study the small chemical molecules like glutamate that support the neuronal signaling. We measure what these molecules are doing and where they are. We follow them in real time, in real people, under different circumstances, including sensory stimulation, dietary changes, and disease. We extend the results obtained by studying humans with similar studies of rats.

Our studies have led to the conclusion that the brain is very efficient in its use of energy. When we started our research, it was commonly thought that the brain uses only about 1 percent of its energy for functional tasks, with most energy used to repair damage or for simple maintenance. Our results, however, show that the brain uses something like 90 percent of its energy to support the processes by which neurons talk to each other, re-energizing the chemicals that do the talking and carry the message. This has led us to a very interesting insight into the popular functional imaging experiments being done nowadays to explain psychological concepts by brain activities. In these, the brain is assumed to act like a computer and people are given mental tasks to do while changes in different regions of the brain are monitored.

We've all seen pictures of different regions of the brain changing their activity during tasks, with different colors representing the degree of certainty that a given region really changed. Those signals locate a region of the brain that is doing something like memory. However, our results show that those signals commonly represent only a few percent of the energy change; the magnitude of the remaining 90 or so percent of the energy in those regions remains unchanged, but is nonetheless necessary for the task to be done. When the animal performs an objective task, brain activity does increase by a few percent, but a large majority of the activity needed for the task appears to be baseline energy, unchanged in the imaging experiment.

This conclusion—that the total brain energy is needed for a task, although only a small percentage changes when doing the task—brings us to the real problem of understanding the brain. Human brain activity embodies the dialectic between the subjective and the objective. This has led us to the hypothesis that the baseline activity represents activities needed to support the kind of subjective activity that we are not exploring when we give the person an objective test to do. Just think about it. Say I ask you to do the kind of complicated task that cognitive psychology presents, a task requiring numbers, retention, or manipulation. While doing that test, you're not supposed to be doing anything else, since any increments of brain activity are assigned to the identifiable task. Of course, you're in a large NMR magnet with a light shining in your eyes which presents instructions you must follow, your shoulders are beginning to hurt, you have to go to the bathroom, you're wondering about your mother, and so on. All of this is going on and everyone knows it; it's like the elephant in the room that no one talks about. However, after much experimentation disregarding these different degrees of unconscious activity, people begin to be susceptible to and accepting of the idea that there aren't important subjective activities going on.

From the perspective introduced by our studies, the increasingly popular cognitive experiments disregard most brain activity (by only mapping increments) and at the same time neglect the obviously significant parallel processes of subjective mentation that accompany any objective task. The argument against studying the neuroscience of the high baseline activity is that it has been too difficult, especially when compared with the ease of measuring incremental activity. Actually, the wonderful thing about science is that it's really mostly a question of wanting to do something. Philosophy determines the direction of science. We have so many well-developed experimental strengths that any number of experiments can be done. The choice depends upon philosophical disposition.

For several years, my laboratory has been conducting experiments designed to explore the baseline activity during an objectively defined task. We have studied this activity, looking for measurable aspects that correlate with the subjective. In simple experiments, we observe the somatosensory region of a rat's brain as its forepaw is stimulated with an electric shock. When the animal is deeply anesthetized, we get an imaging signal that is localized in that sensory region. We insert electrodes in that region and measure the firing rates of hundreds of individual neurons before and during the stimulus. At the level of deep anesthesia, increases in neuronal activity are confined to the somatosensory region and the animals, deeply anesthetized, are not responding to the sensory input. They don't feel anything. That's the object of anesthesia—to stop the animal from responding to the stimulus. And in this state the rest of the brain, outside the sensory input regions, is not changing its activity during stimulation. However, the pattern changes when we lighten the anesthesia, bringing the animal closer to an awakened state, so that it begins to feel the shock. When the animal begins to feel, the pattern of the firing includes interactions of firing of axonal connections between the neurons in this local sensory region and other parts of the brain. Those other parts of the brain are responding to the sensory. Thus, these detailed interactions are supporting the subjective responses aroused by the sensory stimulus — the responses of awareness that were inhibited by deep anesthesia.

This illustration shows that it is possible to study a particular kind of activity if the intent is there. If your philosophy says you cannot ignore the subjective (rather than saying it can be neglected, or assumed to be known), then you can do experiments that measure properties of human behavior that can be observed and correlated with physical measurements of neuronal activity. In other words, certain measurable aspects of awareness as measured by the anesthesiologists — can be connected with physical measurements of brain processes. Classical physics and well-established laws of thermodynamics can give us definite information about some observable neuronal properties which can be correlated with measurable degrees of awareness of the human.

In charting my scientific path, I never committed myself to anything that the scientific community had identified as an important quest. I have wanted to explore directions using scientific methods and to answer questions that seem interesting to me and, I hope, to other people. Of course, I very much enjoy any acceptance my ventures may find, but I have not been of a temperament to follow a research path because it was clearly intended to meet an established need.

There is a resonance with Oscar Wilde, whose essay "The Decay of Lying" wittily claimed that no one knows how to lie anymore. Oh, he says, there are routine lies, like those of politicians, and nearly everyone knows how to lie in this minor way. But they don't know how to lie in the great way, as when you express a personal vision that differs from what anybody else thinks. Art, Wilde says, is created by this kind of personal manifesto. And if it is truly Art, then life will eventually accept and imitate it, and it will become life. This is the power of intellectual innovation — that it ultimately, but not immediately, provides a base for power. Lionel Trilling knew that and, to the extent he spawned the neoconservatives, was disappointed by its fulfillment.

It has been my trajectory to have lived on this basis in science, with limited successes and many disappointments. In my lifetime, the great American society has allowed and supported basic scientific inquiries. It is rare to find such societal acceptance of self-expression, which often puts the individual in opposition to that society. Great resources have been placed by society at the use of individuals who do something that isn't obviously practical but has been the source of the transforming powers of science. Somehow this great society has had the resources to express its appreciation for an intellectual self-expression called pure research, whose self-indulgent yet altruistic depths I have been privileged to traverse. In payment, the present technological world has been created by collectives of such self-expression.