

SOUTH DAKOTA ACADEMY OF SCIENCE PRESIDENTIAL ADDRESS

Science: The Search for Solutions

Stephen R. Metzner
University of South Dakota

The Academy has assembled again this year to discuss, investigate and consider the condition and progress of science in South Dakota. To most of the other citizens of the state, and, indeed, the United States, we are an unusual group. Scientists and those who are interested in science are suspect; we aren't interested in "normal" things that interest "normal" people. When I am introduced to someone for the first time, and they ask me what my profession is, they always look a little funny as I indicate that I am a chemist at the University of South Dakota.

They usually respond, "I took chemistry in high school or college, and I never did really understand what was going on." I usually mumble something to the effect that many people find chemistry difficult and quickly change the subject. What I would like to say, but have never had the courage to say, is: "Oh, that's too bad, but I know the tremendous strides they are making in educating the mentally handicapped these days."

Is it the mystery or the aura of science that discourages people from becoming involved with science or causes them to fear it? In the years to come, science and scientists will be more closely associated with society's problems, not its solutions. Perhaps we need to make more of an effort to explain to others what science is and why we enjoy what we do. The question then arises, what is it that science and scientists do? Let us consider then, very briefly, some of the things that we do, keeping in mind the words of Sir Peter Medawar (who won a Nobel Prize for his work in immunology) when he said, "What scientists do has never been the subject of a scientific inquiry. It is no use looking in scientific papers, for they do not merely conceal but actively misrepresent the reasoning that goes into the work they describe."

CURIOSITY AND THE NEED TO KNOW

At the beginning there is curiosity, and with curiosity, the joy and delight of discovery. A mathematician recently explained that his daughter, age eight, had just discovered, without his help, that some numbers are prime — that is numbers like 5 or 11 or 13 cannot be divided evenly by any other integer except by themselves and 1. She called them "unfair" numbers. When asked why she

called them unfair, she replied, "There is no way to share them out evenly." Had she attempted to divide 5 pieces of candy among friends? In any event, the child had experienced a moment of scientific perception — she had discovered something about the way things are.

Most children have an innate curiosity about their world; for some, this curiosity develops into a life long passion, while for others it dies or, at least fails to mature.

Harvard University physicist Sheldon Glasgow began his interest in eighth grade by asking his teacher, "Why is the Man in the Moon always looking at us?" As he says, "It turns out that not until you take a college level physics course do you really learn the answer." But the difference is that most people look at the moon, and wonder the same thing, and then forget about it. It turns out that some people can't let go. Medawar once described the feeling this way, "You must feel in yourself an acute discomfort at incomprehension."

Scientists don't believe that they think in ways that are too different from most other people. The difference, according to Philip Morrison, a physicist at MIT, is that scientists apply everyday methods to areas that most people never think about seriously or carefully.

Is it possible to stimulate this desire in another person? We can only communicate our view that in the bewildering variety of the world there is some underlying order and that this search can be stimulating, challenging and just plain fun.

Perhaps Albert Einstein best described it this way: "Out there is this huge world, which exists independently of us human beings and which stands before us like a great, eternal riddle, at least partially accessible to our inspection and thinking."

PATTERNS

We live by patterns. Intervals. Repetition. These patterns set up expectations; for when we observe a pattern we have already formed some idea of what comes next. Part of our search for solutions involves dealing with patterns and many discoveries come about when we recognize them.

Our recognition of pattern is so quick and so intricate it is almost impossible to explain. Study has shown that some elements of perception are built into the interconnections between eye and brain. Patterns have been recognized even as the signals are routed from the eye to the brain.

In the 1840s and 1850s, cholera arrived in England from India.

The disease is very nasty since the normal flow of fluid in the intestines is reversed, so that fluid moves from the blood and tissues into the intestine and is then lost in uncontrollable diarrhea. Death follows from dehydration.

In the summer of 1884, in a period of ten days, more than 500 people in London died of cholera. A London physician, John Snow, suspected that the disease was caused by water contaminated by sewage. He obtained a list of the people who died and found out where they got their water. Out of 77 cases he could verify, 59 had drawn their water from one particular public pump in Broad Street. In a nearby neighborhood, out of its 535 inhabitants, only 5 had died of cholera. All 5 had used water from the contaminated Broad Street pump rather than the one in their neighborhood. Snow found other deaths in London that could be traced to that neighborhood and finally persuaded the Board of Guardians to take the handle off the pump. The epidemic declined and soon stopped.

Five years later a similar cholera epidemic struck and Snow was able to do the same experiment again with house to house inquiries. By observing patterns, John Snow solved the problem of cholera transmission and founded the science of epidemiology.

Proteins are the most abundant biochemicals in human beings. They are the central substance for just about all biological processes. They control chemical reactions, transport substances, form muscle and connective tissue, fight disease organisms, etc. Proteins are composed of about 20 different amino acids, and the instructions telling how the body is to assemble these amino acids is carried by deoxyribonucleic acid (DNA).

The great biological mystery of the 1950s was how the instructions on the nucleic acids are translated into a sequence that is exactly the same for every molecule of a particular protein. Before this could be done, we needed to recognize the patterns on which the long protein molecules were built.

Linus Pauling, in 1948, solved the problem of protein structure. "The idea I had is this," he explained. "If you have a structure—and a second structure that is identical except for its position in space, the result is to rotate around an axis and translate along the axis. If you repeat this operation, you get a helix." In 1951, Pauling built a model—the alpha helix—that proved to be a structure often found in proteins. In 1953, James Watson and Francis Crick, using Pauling's approach, found the helix in the genetic material itself—the double helix of DNA.

One of the most dramatic perceptions of pattern in the history of science was Dmitri Mendeleev's creation of the periodic table

of elements. By the mid 1860s, about sixty different elements had been identified from hydrogen to uranium. Many chemists recognized that elements with widely different atomic weights were related. The English chemist, John Newlands, tried arranging the elements in order of increasing atomic weight. However, his arrangement had flaws. He failed to use the most reliable atomic weights for some of the elements and did not leave spaces for undiscovered elements. Mendeleev not only perceived the pattern, he imposed it—insisting in case after case that when the known facts of chemistry did not fit the pattern, the facts were at fault.

Mendeleev insisted that new atomic weight determinations be made and he left blank spaces where no known element fit the weight and properties he insisted should be there. One such blank space was below the element aluminum. In 1875 a French chemist, Lecoq de Boisbaudran, discovered a new element he named gallium. This element had the correct chemical properties but it was too light. Mendeleev wrote a brief paper insisting that this was his eka-aluminum. Boisbaudran objected and then remeasured its atomic weight. His original determination was wrong. Mendeleev predicted the properties of an element more accurately than the man who discovered it. The world of chemistry was astounded!

CHANCE

Tales of chance discovery pervade stories of scientific progress. "In the field of observation, chance favors only the prepared mind," observed Louis Pasteur.

Flies swarmed around the urine of a dog whose pancreas had been removed, and a lab assistant pointed them out. Sets of fresh frog's legs, strung on copper wire hanging near an iron support, twitched convulsively when the wind brushed them, and a physiologist thought that unusual. A photographic plate wrapped to keep out the light was put away with a small amount of a fluorescent powder. When developed, it was darkened when it shouldn't have been. A rabbit's ear was too warm, when a physiologist thought it should have been cold. Some chickens were inoculated with a culture of bacteria that was old. They got sick but recovered when they should have died. An animal that survived a large dose of the toxin from a sea anemone died after being given a much smaller dose two weeks later. A colony of green mold in a petri dish where staphylococci were growing, was surrounded by a circle of dead bacteria.

Of the seven incidents just described, all were a surprise. Each event led to an important discovery. Three of them led to Nobel Prizes while the others happened too early for such a prize. However, Lewis Thomas of the Sloan-Kettering Cancer Center

said recently, "I'm not as fond of the notion of chance discovery as I used to be. When you move away from speculating about a problem and start working on it, things happen. If you have your wits about you, you create the chance happenings." Was the discovery therefore inevitable; was the time just right to see opportunity in a chance observation? You be the judge on the seven.

In 1889, Joseph von Mering and Oscar Minkowski were studying the function of the digestive juices produced by the pancreas. They removed the pancreas from several dogs. One of the animal keepers noticed that flies were attracted to the urine of these dogs. But von Mering and Minkowski knew that flies swarm around the urine of diabetic patients. They had created diabetes experimentally. This was but the first step in the identification and eventually the treatment of the disease. Since von Mering and Minkowski were trained physiologists investigating the pancreas, was it inevitable that they would make the discovery they did?

Luigi Galvani was experimenting on nerves using frogs' legs. One day he threaded the legs on some copper wire, and hung them up in such a way that a circuit was made from the legs of the frog to a portion of the iron support through the copper. Wind blew the legs close enough to the iron to complete the circuit. When this happened, the legs jerked as a spark jumped from the iron to the legs. Galvani noticed and repeated his experiment successfully. However, he insisted that the muscles and nerves of the frog produced the spark. Alessandro Volta, a physicist, realized that it wasn't the animal but the junction of the two metals that produced the spark. With that chance observation, he built the first battery.

The chance happening with the photographic plates was preceded by another chance happening. Wilhelm Rontgen had fogged photographic plates by placing them near an electric discharge tube with which he was experimenting. A key placed on the plates left its shadow when they were developed. He called these strange new rays being given off by the discharge tube X-rays.

In Paris, Henri Becquerel was continuing his father's work with light. They had been working with a fluorescent compound, potassium uranyl sulfate. Becquerel was interested in Rontgen's discovery and decided to see if this compound gave off X-rays in addition to the visible fluorescent light. He placed the compound on top of some photographic plates he had wrapped in heavy, black paper and exposed it to sunlight. As expected, the plates were fogged when developed. Further experiments showed that the energy from the compound would penetrate aluminum and copper—something that only Rontgen's X-rays were known to do.

Then, the weather grew cloudy and he put the plates away with a little of the potassium uranyl sulfate lying on top. After several days he decided to develop the plates just to see if something might have been produced in the dark. The plates were heavily blackened; sunlight and fluorescence had nothing to do with it. Becquerel had discovered natural radioactivity. In 1903, Becquerel shared the Nobel Prize in physics with Marie and Pierre Curie.

French physiologist Claude Bernard was working with the transmission of nerve impulses. He correctly guessed that chemical changes along the nerve fibers caused the transmission of a nerve impulse. He thought that perhaps these chemical changes produced heat and could thus be detected. He cut the sympathetic nerve leading into one of a rabbit's ears, but left the other ear intact. He expected that the altered ear would be a few degrees cooler; instead, it grew 4 to 6 degrees warmer. What he had done was to cut the nerve that keeps the blood vessels more or less tensed—the ear was blushing. Bernard had discovered the vasopressor nervous system, which regulates blood pressure and the flow of blood through the flesh near the skin.

Louis Pasteur had been hired to help the French wine industry. It was losing millions of gallons of wine due to spoilage. Pasteur investigated the process of fermentation and souring and founded the science of bacteriology. From this discovery came the bacterial theory of disease. Pasteur turned to another costly problem in animal husbandry—fowl cholera. Pasteur or one of his assistants inoculated some chickens with a cholera culture from the wrong container—it was old. The chickens got sick, but then recovered. When injected with a fresh, virulent batch, the chickens didn't even get sick. Immunization had been known for almost a century. Edward Jenner had developed a vaccine for smallpox. But neither Jenner or any one else at the time knew how it worked. Pasteur realized that a weakened form of a bacteria may produce a mild illness from which recovery is possible with full immunity from the deadly form. Nobel Laureate Max Delbruck has called this the principle of limited sloppiness.

The tentacles of a sea anemone are tipped with a poison. In 1900, Charles Richet, a physiologist at the University of Paris, was attempting to find the lethal dose of this toxin by injecting dogs with various doses. Some of the dogs that had been given doses too small to kill them were given another small dose several weeks later. To his surprise this second, smaller dose of the toxin killed the dogs in a few minutes. "At first," he later wrote, "I had enormous difficulty believing this." What he had observed was induced sensitization or anaphylaxis—the basis of all allergic reactions. He knew that some people were allergic to ragweed pollen or straw-

berries and that people had been killed by bee stings. He pursued the study to a Nobel Prize in 1913.

The most famous chance discovery of all was made at St. Mary's Hospital in London in 1928. Alexander Fleming, a bacteriologist, was looking for antibacterial agents. He was working with staphylococci, the organisms that cause boils and infect wounds. He was growing the bacteria in culture dishes. Since it was warm, he left the window open and a mold got started in one of the dishes. One day, Fleming noticed that all of the staph bacteria around the mold looked like they had melted. He preserved some of the new mold, cultured it and made a crude extract from it. He found that this extract was a killer of some bacteria but not of others. He named this active substance for the mold from which he had extracted it, penicillin. But what is more ironic is that the actual discovery of and proof of the action of the *Penicillium* mold was made some 75 years earlier by a twenty-two year old medical student named Duchesne. To qualify for the M.D. degree, he had to do research for a dissertation and chose to study the antagonism between molds and microbes. He produced the same results in his laboratory that Fleming observed by chance in his. Duchesne got his degree, joined the army, contracted tuberculosis and died in 1902. No one pursued his discovery. Some discoveries are premature — they appear at a time and place when they do not find acceptance and must wait for years or decades to be rediscovered.

MODELING

A model is a rehearsal for reality, a way of making a trial run that minimizes the penalties for error. By building a model, a scientist can reduce an object, or a theory to manageable form. Listen to a group of scientists talk about their work, no matter what the field, they talk about their models. They use "modeling" in many different ways, but they never mean something complete in every detail. Model-building, then, entails hazards, for something genuinely relevant may be omitted or it may be cluttered with irrelevant details. It is possible to create a model that is too simple or too complex to be of any use.

The first wind tunnel was built in 1871 by two British engineers who used it to study wing shapes. In 1901, the Wright Brothers built gliders in their bicycle shop in Dayton, Ohio and experimented with them along the Dunes of Kitty Hawk. Their first glider was unstable and hard to control, so they built their own small wind tunnel and tested different wing shapes and thicknesses. They learned from their models and, in 1903, flew the first engine powered airplane.

Not all modeling must be done with the hands. At the Jet Propulsion Laboratory in California, the computer modeled the flight of the unmanned spacecraft that successfully flew past Jupiter and Saturn. The computer model was accurate and the pictures that Voyager transmitted back to earth look much like the computer generated images.

A map is a kind of model but what one needs is one small enough and yet detailed enough to do the job. A sales manager uses a computer to create a map of the territory and the performance of the salesmen. The manager asks for a list of each item sold and the location in which it was sold — and the computer obligingly delivers a printout sixty inches thick.

The two most complex systems for which models are being constructed today are the weather and the economy. Difficulties in predicting the weather with accuracy are well known. It's laborious, yet not terribly difficult, to collect weather data and map it by computer. It's possible to see at what rate weather systems change, but how does one system interact with another and how do the rates of change themselves change? Yet, such a complex model is necessary or it will be of little use.

Economic models, too, require large amounts of data and much calculation time to compare trends. Yet, such models are required if we are to understand the cycles of inflation and depression that periodically sweep the world.

A model is not always just a stepping-stone; sometimes it can be a theory. In his attempt to determine protein structure, Linus Pauling constructed a very simple model. One day he was in bed with a cold. He had spent ten years building up a great quantity of fact about protein behavior and structural details and decided to spend some of his time in bed thinking about the problem. He drew the structure of a polypeptide chain on a piece of paper and began to fold the paper. He finally found out how to fold the paper so that the hydrogen atom on nitrogen just points toward an oxygen atom to form a helix. He and a colleague later built a three-dimensional model. "If you have a model," he said, "you know what the permissible structures are."

THEORY AND PREDICTION

Scientific theories give shelter and shape to our visions of the world. In the scientific search for solutions, what qualities of the mind are required? Joshua Lederberg, a Nobel geneticist, answered the question this way, "I don't think there is one logic for science and another for the common sense world. If there were, we would be in real trouble. I think that the ability to move from one level

of reasoning to another and not get stuck in between is important. You have to be able to fantasize but then shift from one frame of reference to another. When I think of a DNA molecule, I think of it as a rope. I know, for example, that if I pull on the ends it will break somewhere in the middle. Then I have to jump to a different level and say, "I know that it isn't quite like that, but can I predict where the DNA molecule will break, knowing that it isn't quite like that rope?"

A model takes on the quality of a theory when its inventor extracts from the raw data the things that are believed to be fundamental and puts them together in new ways thereby generating predictions that were not understood before. Paul A. M. Dirac, who predicted the existence of antimatter, suggested in his Nobel lecture that theories compel belief because they bind diverse consequences together. A theory is self supporting because of the connections it makes. Scientific knowledge eventually becomes a web or network of laws, models, theories, formulas, hypotheses, interpretations, etc., which are so closely woven together that they become stronger than any single element. This framework concept of scientific understanding explains why it is so difficult to describe a "scientific method" as though it could ever be reduced to a serial process or why descriptions by historians or philosophers are so remote from most scientists' own experiences.

It is this interconnection that protects science against error and fraud. Once a new discovery is made, the process of connecting the new to the old begins. The new must "fit" or it will be discarded. In pseudoscience theories are fabricated to explain known facts, a theory should lead to predictions that cannot, at the moment, be verified. In fact, predictions force the growth of theories.

The best example of this is the man who persuaded Isaac Newton to publish his theory of gravitation and the calculations of the elliptical orbits of the planets. The man was Edmund Halley and the results of his use of the theory and the resulting return of a comet named after him is well known.

Another spectacular example of prediction came from Einstein's Special Theory of Relativity. One consequence of that theory was that not only matter but light should be affected by gravity. The verification of this idea took place on May 29, 1919 on a ship in the south Atlantic Ocean. Astronomers took photographs of a portion of the sky during a total eclipse and compared the photograph to the same region of the sky while the sun was not there. Measurements showed that the light from 5 stars that had passed near the sun had been displaced by the sun's gravitational field.

The success of the physical sciences has acted as a lure for other areas. Social scientists have long been struggling to turn the mathematics of the physical sciences to their own use. The first difficulty is that the parameters of human behavior are more elusive, but it is also true that the social sciences are more like hybrids, requiring some of the methods of the physical sciences and also the scholarship of the historian or philosopher.

Here, too, the biological sciences are not able to use the mathematical model of the physical scientist. Some more physical aspects such as the X-ray analysis of a protein molecule or the electrical transmission of nerve impulses may lend themselves to mathematical calculation but the predictions must often have a less formal theoretical base.

Yet some predictions in biology have been spectacular. One good example was the understanding of blood circulation by William Harvey, a seventeenth century English physician. He worked before the microscope, before anesthesia made experimentation possible, and before it was acceptable to use a human corpse. Harvey had to explain that the arteries carried only blood, not air or bile or other substances. He had to establish the heart as an active pump and to impose a one-way flow from the heart to the lungs and back and from the heart through the body and back. Others would verify what Harvey postulated. What he saw was the unifying pattern in what had been a confused jumble of facts.

Well, our time grows short. We have other, more important business in these next few hours and days. I hope my wanderings have started you thinking about how we might promote science among the nonscientist and how we might use science itself to attract students into it. Let me leave you with a challenge for next year — I would like to see each of you bring one more person with you than you brought this year. Just one — interested, lukewarm or even a little hostile. Maybe some of the magic that we see in science will rub off, and, even if we don't draw anyone into a scientific career, we may impart some of the excitement that we all find in the search for solutions.

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