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SCIENCE

Strong Inference

Certain systematic methods of scientific thinking may produce much more rapid progress than others.

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Scientists these days tend to keep up a polite fiction that all science is equal. Except for the work of the misguided opponent whose arguments we happen to be refuting at the time, we speak as though every scientist's field and methods of study are as good as every other scientist's and perhaps a little better. This keeps us all cordial when it comes to recommending each other for government grants.

But I think anyone who looks at the matter closely will agree that some fields of science are moving forward very much faster than others, perhaps by an order of magnitude, if numbers could be put on such estimates. The discoveries leap from the headlines - and they are real advances in complex and difficult subjects, like molecular biology and high-energy physics. As Alvin Weinberg says *(1)* "Hardly a month goes by without a stunning success in molecular biology being reported in the Proceedings of the National Academy of Sciences."

Why should there be such rapid advances in some fields and not in others? I think the usual explanations that we tend to think of - such as the tractability of the subject, or the quality or education of the men drawn into it, or the size of research contracts - are important but inadequate. I have begun to believe that the primary factor in scientific advance is an intellectual one. These rapidly moving fields are fields where a particular method of doing scientific research is systematically used and taught, an accumulative method of inductive inference that is so effective that I think it should be given the name of "strong inference." I believe it is important to examine this method, its use and history and rationale, and to see whether other groups and individuals might learn to adopt it profitably in their own scientific and intellectual work.

In its separate elements, strong inference is just the simple and old- fashioned method of inductive inference that goes back to Francis Bacon. The steps are familiar to every college student and are practiced, off and on, by every scientist. The difference comes in their systematic application. Strong inference consists of applying the following steps to every problem in science, formally and explicitly and regularly:

1. Devising alternative hypotheses;
2. Devising a crucial experiment (or several of them), with alternative possible outcomes, each of which will, as nearly is possible, exclude one or more of the hypotheses;
3. Carrying out the experiment so as to get a clean result;

4. Recycling the procedure, making subhypotheses or sequential hypotheses to refine the possibilities that remain, and so on.

It is like climbing a tree. At the first fork, we choose - or, in this case, "nature" or the experimental outcome chooses - to go to the right branch or the left; at the next fork, to go left or right; and so on. There are similar branch points in a "conditional computer program," where the next move depends on the result of the last calculation. And there is a "conditional inductive tree" or "logical tree" of this kind written out in detail in many first-year chemistry books, in the table of steps for qualitative analysis of an unknown sample, where the student is led through a real problem of consecutive inference: Add reagent A; if you get a red precipitate, it is subgroup alpha and you filter and add reagent B; if not, you add the other reagent. B; and so on.

On any new problem, of course, inductive inference is not as simple and certain as deduction, because it involves reaching out into the unknown. Steps 1 and 2 require intellectual inventions, which must be cleverly chosen so that hypothesis, experiment, outcome, and exclusion will be related in a rigorous syllogism; and the question of how to generate such inventions is one which has been extensively discussed elsewhere *(2, 3)*. What the formal schema reminds us to do is to try to make these inventions, to take the next step, to proceed to the next fork, without dawdling or getting tied up in irrelevancies.

It is clear why this makes for rapid and powerful progress. For exploring the unknown, there is no faster method; this is the minimum sequence of steps. Any conclusion that is not an exclusion is insecure and must be rechecked. Any delay in recycling to the next set of hypotheses is only a delay. Strong inference, and the logical tree it generates, are to inductive reasoning what the syllogism is to deductive reasoning in that it offers a regular method for reaching firm inductive conclusions one after the other as rapidly as possible.

"But what is so novel about this?" someone will say. This is *the* method of science and always has been, why give it a special name? The reason is that many of us have almost forgotten it. Science is now an everyday business. Equipment, calculations, lectures become ends in themselves. How many of us write down our alternatives and crucial experiments every day, focusing on the *exclusion* of a hypothesis? We may write our scientific papers so that it looks as if we had steps 1, 2, and 3 in mind all along. But in between, we do busywork. We become "method- oriented" rather than "problem-oriented." We say we prefer to "feel our way" toward generalizations. We fail to teach our students how to sharpen up their inductive inferences. And we do not realize the added power that the regular and explicit use of alternative hypothesis and sharp exclusion could give us at every step of our research.

The difference between the average scientist's informal methods and the methods of the strong-inference users is somewhat like the difference between a gasoline engine that fires occasionally and one that fires in steady sequence. If our motorboat engines were as erratic as our deliberate intellectual efforts, most of us would not get home for supper.

Molecular Biology

The new molecular biology is a field where I think this systematic method of inference has become widespread and effective. It is a complex field, yet a succession of crucial experiments over the past decade has given us a surprisingly detailed understanding of hereditary mechanisms and the control of enzyme formation and protein synthesis.

The logical structure shows in every experiment. In 1953, James Watson and Francis Crick proposed that the DNA molecule - the "hereditary substance" in a cell - is a long two-stranded helical molecule *(4)*. This suggested a number of alternatives for crucial test. Do the two strands of the helix stay together when a cell divides, or do they separate? Matthew Meselson and Franklin Stahl used an ingenious isotope-density-labeling technique which showed that they separate *(5)*. Does the DNA helix always have two strands, or can it have three, as atomic models suggest? Alexander Rich showed it can have either, depending on the ionic concentration *(6)*. These are the kinds of experiments John Dalton would have liked, where the combining entities are not atoms but long macromolecular strands.

Or take a different sort of question: Is the "genetic map" - showing the statistical relationship of different genetic characteristics in recombination experiments - a one-dimensional map like the DNA molecule (that is, a linear map), as T. H. Morgan proposed in 1911, or does it have two-dimensional loops or branches? Seymour Benzer showed that his hundreds of fine micro-genetic experiments on bacteria would fit only the matrix for the one-dimensional case *(7)*.

But, of course, selected crucial experiments of this kind can be found in every field. The real difference in molecular biology is that formal inductive inference is so systematically practiced and taught. On any given morning at the Laboratory of Molecular Biology in Cambridge, England, the blackboards of Francis Crick or Sidney Brenner will commonly be found covered with logical trees. On the top line will be the hot new result just up from the laboratory or just in by letter or rumor. On the next line will be two or three alternative explanations, or a little list of "what he did wrong." Underneath will be a series of suggested experiments or controls that can reduce the number of possibilities. And so on. The tree grows during the day as one man or another comes in and argues about why one of the experiments wouldn't work, or how it should be changed.

The strong-inference attitude is evident just in the style and language in which the papers are written. For example, in analyzing theories of antibody formation, Joshua Lederberg *(8)* gives a list of nine propositions "subject to denial," discussing which ones would be "most vulnerable to experimental test."

The papers of the French leaders Francois Jacob and Jacques Monod are also celebrated for their high "logical density," with paragraph after paragraph of linked "inductive syllogisms." But the style is widespread. Start with the first paper in the *Journal of Molecular Biology* for 1964 *(9)*, and you immediately find: "Our conclusions . . . might be invalid if . . . (i). . .(ii). . . or (iii) . . . . We shall describe experiments which eliminate these alternatives." The average physicist or chemist or scientist in any field accustomed to less closely reasoned articles and less sharply stated inferences will find it a salutary experience to dip into that journal almost at random.

Resistance to Analytical Methodology

This analytical approach to biology has sometimes become almost a crusade because it arouses so much resistance in many scientists who have grown up in a more relaxed and diffuse tradition. At the 1958 Conference on Biophysics, at Boulder, there was a dramatic confrontation between the two points of view. Leo Szilard said: "The problems of how enzymes are induced, of how proteins are synthesized, of how antibodies are formed, are closer to solution than is generally believed. If you do stupid experiments, and finish one a year, it can take 50 years. But if you stop doing experiments for a little while and *think* how proteins can possibly be synthesized, there are only about 5 different ways, not 50! And it will take only a few experiments to distinguish these."

One of the young men added: "It is essentially the old question: How *small* and *elegant* an experiment can you perform?"

These comments upset a number of those present. An electron microscopist said. "Gentlemen, this is off the track. This is philosophy of science."

Szilard retorted. "I was not quarreling with third-rate scientists: I was quarreling with first-rate scientists."

A physical chemist hurriedly asked, "Are we going to take the official photograph before lunch or after lunch?"

But this did not deflect the dispute. A distinguished cell biologist rose and said, "No two cells give the same properties. Biology is the science of heterogeneous systems." And he added privately. "You know there are *scientists*, and there are people in science who are just working with these over-simplified model systems - DNA chains and in vitro systems - who are not doing science at all. We need their auxiliary work: they build apparatus, they make minor studies, but they are not scientists."

To which Cy Levinthal replied: "Well, there are two kinds of biologists, those who are looking to see if there is one thing that can be understood and those who keep saying it is very complicated and that nothing can be understood. . . . You must study the *simplest* system you think has the properties you are interested in."

As they were leaving the meeting one man could be heard muttering, "What does Szilard expect me to do - shoot myself?"

Any criticism or challenge to consider changing our methods strikes of course at all our ego-defenses. But in this case the analytical method offers the possibility of such great increases in effectiveness that it is unfortunate that it cannot be regarded more often as a challenge to learning rather than as challenge to combat. Many of the recent triumphs in molecular biology have in fact been achieved on just such “oversimplified model systems,” very much along the analytical lines laid down in the 1958 discussion. They have not fallen to the kind of men who justify themselves by saying "No two cells are alike," regardless of how true that may ultimately be. The triumphs are in fact triumphs of a new way of thinking.

High-Energy Physics

This analytical thinking is rare, but it is by no means restricted to the new biology. High-energy physics is another field where the logic of exclusions is obvious, even in the newspaper accounts. For example, in the famous discovery of C. N. Yang and T. D. Lee, the question that was asked was: Do the fundamental particles conserve mirror-symmetry or "parity" in certain reactions, or do they not? The crucial experiments were suggested: within a few months they were done, and conservation of parity was found to be excluded. Richard Garwin, Leon Lederman and Marcel Weinrich did one of the crucial experiments. It was thought of one evening at suppertime; by midnight they had rearranged the apparatus for it; and by 4 a.m. they had picked up the predicted pulses showing the non conservation of parity *(10)*. The phenomena had just been waiting, so to speak, for the explicit formulation of the alternative hypotheses.

The theorists in this field take pride in trying to predict new properties or new particles explicitly enough so that if they are not found the theories will fall. As the biologist W. A. H. Rushton has said *(11)*, "A theory which cannot be mortally endangered cannot be alive." Murray Gell-Mann and Yuval Ne'eman recently used the particle grouping which they call "The Eightfold Way" to predict a missing particle, the Omega-Minus, which was. then looked for and found *(12)*. But one alternative branch of the theory would predict a particle with one-third the usual electronic charge, and it was not found in the experiments, so this branch must be rejected.

The logical tree is so much a part of high-energy physics that some stages of it are commonly built, in fact, into the electronic coincidence circuits that detect the particles and trigger the bubble-chamber photographs. Each kind of particle should give a different kind of pattern in the electronic counters, and the circuits can be set to exclude or include whatever types of events are desired. If the distinguishing criteria are sequential, they may even run through a complete logical tree in a microsecond or so. This electronic preliminary analysis, like human preliminary analysis of alternative outcomes, speeds up progress by sharpening the criteria. It eliminates hundreds of thousands of the irrelevant pictures that formerly had to be scanned, and when it is carried to its limit, a few output pulses, hours apart, may be enough to signal the existence of the antiproton or the fall of a theory.

I think the emphasis on strong inference in the two fields I have mentioned has been partly the result of personal leadership such as that of the classical geneticists in molecular biology, or of Szilard with his "Midwest Chowder and Bacteria Society at Chicago in 1948-50, or of Max Delbruck with his summer courses in phage genetics at

Cold Spring Harbor. But it is also partly due to the nature of the fields themselves. Biology, with its vast informational detail and complexity, is a "high-information" field, where years and decades can easily be wasted on the usual type of "low-information" observations or experiments if one does not think carefully in advance about what the most important and conclusive experiments would be. And in high-energy physics, both the "information flux" of particles from the new accelerators and the million-dollar costs of operation have forced a similar analytical approach. It pays to have a top-notch group debate every experiment ahead of time; and the habit spreads throughout the field.

Induction and Multiple Hypotheses

Historically, I think, there have been two main contributions to the development of a satisfactory strong-inference method. The first is that of Francis Bacon *(13)*. He wanted a “surer method” of “finding out nature” than either the logic-chopping or all-inclusive theories of the time or the laudable but crude attempts to make inductions “by simple enumeration.” He did not merely urge experiments as some suppose, he showed the fruitfulness of interconnecting theory and experiment so that the one checked the other. Of the many inductive procedures he suggested, the most important, I think, was the conditional inductive tree, which proceeded from alternative hypothesis (possible "causes," as he calls them), through crucial experiments ("Instances of the Fingerpost"), to exclusion of some alternatives and adoption of what is left ("establishing axioms"). His Instances of the Fingerpost are explicitly at the forks in the logical tree, the term being borrowed "from the fingerposts which are set up where roads part, to indicate the several directions."

Many of his crucial experiments proposed in Book II of *The New Organon* on are still fascinating. For example, in order to decide whether the weight of a body is, due to its “inherent nature” as some had said, or is due to the attraction of the earth, which would decrease with distance, he proposes comparing the rate of a pendulum clock and a spring clock and then lifting them from the earth to the top of a tall steeple. He concludes that if the pendulum clock on the steeple "goes more slowly than it did on account of the diminished virtue of its weights . . . we may take the attraction of the mass of the earth as the cause of weight."

Here was a method that could separate off the empty theories!

Bacon, said the inductive method could be learned by anybody, just like learning to “draw a straighter line or more perfect circle . . . with the help of a ruler or a pair of compasses.” “My way of discovering sciences goes far to level men's wit and leaves but little to individual excellence, because it performs everything by the surest rules and demonstrations.” Even occasional mistakes would not be fatal. "Truth will sooner come out from error than from confusion."

It is easy to see why young minds leaped to try it.

Nevertheless there is a difficulty with this method. As Bacon emphasizes, it is necessary to make "exclusions." He says, “The induction which is to be available for the discovery and demonstration of sciences and arts, must analyze nature by proper rejections and exclusions, and then, after a sufficient number of negatives come to a conclusion on the affirmative instances.” “[To man] it is granted only to proceed at first by negatives, and at last to end in affirmatives after exclusion has been exhausted."

Or, as the philosopher Karl Popper says today there is no such thing as proof in science - because some later alternative explanation may be as good or better - so that science advances only by disproofs. There is no point in making hypotheses that are not falsifiable because such hypotheses do not say anything, "it must be possible for all empirical scientific system to be refuted by experience" *(14)*.

The difficulty is that disproof is a hard doctrine. If you have a hypothesis and I have another hypthesis, evidently one of them must be eliminated. The scientist seems to have no choice but to be either soft-headed or disputatious. Perhaps this is why so many tend to resist the strong analytical approach and why some great scientists are so disputatious.

Fortunately, it seems to me, this difficulty can be removed by the use of a second great intellectual invention, the “method of multiple hypotheses,” which is what was needed to round out the Baconian scheme. This is a method that was put forward by T.C. Chamberlin *(15)*, a geologist at Chicago at the turn of the century, who is best known for his contribution to the Chamberlain-Moulton hypothesis of the origin of the solar system.

Chamberlin says our trouble is that when we make a single hypothesis, we become attached to it.

“The moment one has offered an original explanation for a phenomenon which seems satisfactory, that moment affection for his intellectual child springs into existence, and as the explanation grows into a definite theory his parental affections cluster about his offspring and it grows more and more dear to him. . . . There springs up also unwittingly a pressing of the theory to make it fit the facts and a pressing of the facts to make them fit the theory..."

“To avoid this grave danger, the method of multiple working hypotheses is urged. It differs from the simple working hypothesis in that it distributes the effort and divides the affections. . . . Each hypothesis suggests its own criteria, its own method of proof, its own method of developing the truth, and if a group of hypotheses encompass the subject on all sides, the total outcome of means and of methods is full and rich.”

Chamberlin thinks the method "leads to certain distinctive habits of mind” and is of prime value in education. "When faithfully followed for a sufficient time, it develops a mode of thought of its own kind which may be designated the habit of complex thought ....”

This charming paper deserves to be reprinted in some more accessible journal today, where it could be required reading for every graduate student - and for every professor.

It seems to me that Chamberlin has hit on the explanation - and the cure - for many of our problems in the sciences. The conflict and exclusion of alternatives that is necessary to sharp inductive inference has been all too often a conflict between men, each with his single Ruling Theory. But whenever each man begins to have multiple working hypotheses, it becomes purely a conflict between ideas. It becomes much easier then for each of us to aim every day at conclusive disproofs - at *strong* inference - without either reluctance or combativeness. In fact, when there are multiple hypotheses, which are not anyone's "personal property," and when there are crucial experiments to test them, the daily life in the laboratory takes on an interest and excitement it never had, and the students can hardly wait to get to work to see how the detective story will come out. It seems to me that this is the reason for the development of those distinctive habits of mind and the "complex thought" that Chamberlin described, the reason for the sharpness, the excitement, the zeal, the teamwork - yes, even international teamwork - in molecular biology and high- energy physics today. What else could be so effective?

When multiple hypotheses become coupled to strong inference, the scientific search becomes an emotional powerhouse as well as an intellectual one.

Unfortunately, I think, there are other other areas of science today that are sick by comparison, because they have forgotten the necessity for alternative hypotheses and disproof. Each man has only one branch - or none - on the logical tree, and it twists at random without ever coming to the need for a crucial decision at any point. We can see from the external symptoms that there is something scientifically wrong. The Frozen Method, The Eternal Surveyor, The Never Finished, The Great Man With a Single Hypothcsis, The Little Club of Dependents, The Vendetta, The All-Encompassing Theory Which Can Never Be Falsified.

Some cynics tell a story, which may be apocryphal, about the theoretical chemist who explained to his class.

"And thus we see that the C-Cl bond is longer in the first compound than in the second because the percent of ionic character is smaller."

A voice from the back of the room said, "But Professor X, according to the Table, the C-CI bond is shorter in the first compound."

"Oh, is it?" said the professor, "Well, that's still easy to understand, because the double-bond character is higher in that compound."

To the extent that this kind of story is accurate, a "theory" of this sort is not a theory at all, because it does not exclude anything. It predicts everything, and therefore does not predict anything. It becomes simply a verbal formula which the graduate student repeats and believes because the professor has said it so often. This is not science, but faith; not theory, but theology. Whether it is hand-waving or number-waving, or equation-waving, a theory is not a theory unless it can be disproved. That is, unless it can be falsified by some possible experimental outcome.

In chemistry, the resonance theorists will of course suppose that I am criticizing *them*, while the molecular-orbital theorists will suppose I am criticizing *them*, but their actions - our actions, for I include myself among them - speak for themselves. A failure to agree for 30 years is public advertisement of a failure to disprove.

My purpose here, however, is not to call names but rather to say that we are all sinners, and that in every field and in every laboratory we need to try to formulate multiple alternative hypotheses sharp enough to be capable of disproof.

Systematic Applications

I think the work methods of a number of scientists have been testimony to the power of strong inference. Is success not due in many cases to systematic use of Bacon's "surest rules and demonstrations" as much as to rare and unattainable intellectual power? Faraday's famous diary *(16*), or Fermi's notebooks *(3, 17)*, show how these men believed in the effectiveness of daily steps in applying formal inductive methods to one problem after another.

Within 8 weeks after the discovery of x-rays, Roentgen had identified 17 of their major properties. Every student should read his first paper *(18)*. Each demonstration in it is a little jewel of inductive inference. How else could the proofs have gone so fast, except by a method of maximum effectiveness?

Organic chemistry has been the spiritual home of strong inference from the beginning. Do the bonds alternate in benzene or are they equivalent? If the first, there should be five disubstituted derivatives; if the second, three. And three it is *(19)*. This is a *strong*-inference test - not a matter of measurement - of whether there are grams or milligrams of the products, but a matter of logical alternatives. How else could the tetrahedral carbon atom or the hexagonal symmetry of benzene have been inferred 50 years before the inferences could be confirmed by x-ray and infrared measurement?

We realize that it was out of this kind of atmosphere that Pasteur came to the field of biology. Can anyone doubt that he brought with him a completely different method of reasoning? Every 2 or 3 years, he moved to one biological problem after another, from optical activity to the fermentation of beet sugar, to the "diseases" of wine and beer, to the disease of silk-worms, to the problem of "spontaneous generation," to the anthrax disease of sheep, to rabies. In each of these fields there were experts in Europe who knew a hundred times as much as Pasteur, yet each time he solved problems in a few months that they had not be able to solve. Obviously it was not encyclopedic knowledge that produced his success, and obviously it was not simply luck, when it was repeated over and over again; it can only have been the systematic power of a special method of exploration. Are bacteria falling in? Make the necks of the flasks S-shaped. Are bacteria sucked in by the partial vacuum? Put in a cotton plug. Week after week his crucial experiments build up the logical tree of exclusions. The drama of strong inference in molecular biology today is only a repetition of Pasteur's story.

The grand scientific syntheses, like those of Newton and Maxwell, are rare and individual achievements that stand outside any rule or method. Nevertheless it is interesting to note that several of the great synthesizers have also shown the strong- inference habit of thought in their other work, as Newton did in the inductive proofs of his *Opticks* and Maxwell did in his experimental proof that three and only three colors are needed in color vision.

A Yardstick of Effectiveness

I think the evident effectiveness of the systematic use of strong inference suddenly gives us a yardstick for thinking about the effectiveness of scientific methods in general. Surveys, taxonomy, design of equipment, systematic measurements and tables, theoretical computations - all have their proper and honored place, provided they are parts of a chain of precise induction of how nature works. Unfortunately, all too often they become ends in themselves, mere time-serving from the point of view of real scientific advance, a hypertrophied methodology that justifies itself as a lore of respectability.

We praise the "lifetime of study," but in dozens of cases, in every field, what was needed was not a lifetime but rather a few short months of weeks of analytical inductive inference. In any new area we should try, like Roentgen, to see how fast we can pass from the general survey to analytical inferences. We should try, like Pasteur, to see whether we can reach strong inferences that encyclopedism could not discern.

We speak piously of taking measurements and making small studies that will "add another brick to the temple of science." Most such bricks just lie around the brickyard *(20)*. Tables of constraints have their place and value, but the study of one spectrum after another, if not frequently re-evaluated, may become a substitute for thinking, a sad waste of intelligence in a research laboratory, and a mistraining whose crippling effects may last a lifetime.

To paraphrase an old saying. Beware of the man of one method or one instrument, either experimental or theoretical. He tends to become method-oriented rather than problem-oriented. The method-oriented man is shackled; the problem-oriented man is at least reaching freely toward that is most important. Strong inference redirects a man to problem-orientation, but it requires him to be willing repeatedly to put aside his last methods and teach himself new ones.

On the other hand, I think that anyone who asks the question about scientific effectivenss will also conclude that much of the mathematizing in physics and chemistry today is irrelevant if not misleading.

The great value of mathematical formulation is that when an experiment agrees with a calculation to five decimal places, a great many alternative hypotheses are pretty well excluded (though the Bohr theory and the Schrödinger theory both predict exactly the same Rydberg constant!). But when the fit is only to two decimal places, or one, it may be a trap for the unwary; it may be no better than any rule-of-thumb extrapolation, and some other kind of qualitative exclusion might be more rigorous for testing the assumptions and more important to scientific understanding than the quantitative fit.

I know that this is like saying that the emperor has no clothes. Today we preach that science is not science unless it is quantitative. We substitute correlations for causal studies, and physical equations for organic reasoning. Measurements and equations are supposed to sharpen thinking, but, in my observation, they more often tend to make the thinking noncausal and fuzzy. They tend to become the object of scientific manipulation instead of auxiliary tests of crucial inferences.

Many - perhaps most - of the great issues of science are qualitative, not quantitative, even in physics and chemistry. Equations and measurements are useful when and only when they are related to proof; but proof or disproof comes first and is in fact strongest when it is absolutely convincing without any quantitative measurement.

Or to say it another way, you can catch phenomena in a logical box or in a mathematical box. The logical box is coarse but strong. The mathematical box is fine-grained but flimsy. The mathematical box is a beautiful way of wrapping up a problem, but it will not hold the phenomena unless they have been caught in a logical box to begin with.

What I am saying is that, in numerous areas that we call science, we have come to like our habitual ways, and our studies that can be continued indefinitely. We measure, we define, we compute, we analyze, but we do not exclude. And this is not the way to use our minds most effectively or to make the fastest progress in solving scientific questions.

Of course it is easy - and all too common - for one scientist to call the others unscientific. My point is not that my particular conclusions here are necessarily correct, but that we have long needed some absolute standard of possible scientific effectiveness by which to measure how well we are succeeding in various areas - a standard that many could agree on and one that would be undistorted by the scientific pressures and fashions of the times and the vested interests and busywork that they develop. It is not public evaluation I am interested in so much as a private measure by which to compare one's own scientific performance with what it might be. I believe that strong inference provides this kind of standard of what the maximum possible scientific effectiveness could be - as well as a recipe for reaching it.

Aids to Strong Inference

How can we learn the method and teach it? It is not difficult. The most important thing is to keep in mind that this kind of thinking is not a lucky knack but a system that *can* be taught and learned. The molecular biologists today are living proof of it. The second thing is to be explicit and formal and regular about it, to devote a half hour or an hour to analytical thinking every day, writing out the logical tree and the alternatives and crucial experiments explicitly in a permanent notebook. I have discussed elsewhere *(3)* the value of Fermi's notebook method, the effect it had on his colleagues and students, and the testimony that it "can be adopted by anyone with profit."

It is true that it takes great courtesy to teach the method, especially to one's peers - or their students. The strong-inference point of view is so resolutely critical of methods of work and values in science that any attempt to compare specific cases is likely to sound but smug and destructive. Mainly one should try to teach it by example and by exhorting to self-analysis and self-improvement only in general terms, as I am doing here.

But I will mention one severe but useful private test - a touchstone of strong inference - that removes the necessity for third-person criticism, because it is a test that anyone can learn to carry with him for use as needed. It is our old friend the Baconian "exclusion," but I call it "The Question." Obviously it should be applied as much to one's own thinking as to others'. It consists of asking in your own mind, on hearing any scientific explanation or theory put forward, "But sir, what experiment could *dis*prove your hypothesis?"; or, on hearing a scientific experiment described, "But sir, what hypothesis does your experiment *dis*prove?"

This goes straight to the heart of the matter. It forces everyone to refocus on the central question of whether there is or is not a testable scientific step forward.

If such a question were asked aloud, many a supposedly great scientist would sputter and turn livid and would want to throw the questioner out, as a hostile witness! Such a man is less than he appears, for he is obviously not accustomed to think in terms of alternative hypotheses and crucial experiments for himself; and one might also wonder about the state of science in the field he is in. But who knows - he question might educate him, and his field too!

On the other hand, I think that throughout most of molecular biology and nuclear physics the response to The Question would be to outline immediately not one but several tests to disprove the hypothesis - and it would turn out that the speaker already had two or three graduate students working on them!

I almost think that government agencies could make use of this kind of touchstone. It is not true that all science is equal; or that we cannot justly compare the effectiveness of scientists by any method other than a mutual-recommendation system. The man to watch, the man to put your money on, is not the man who wants to make "a survey" or a "more detailed study" but the man with the notebook, the man with the alternative hypotheses and the crucial experiments, the man who knows how to answer your Question of disproof and is already working on it.

There are some really hard problems, some high-information problems, ahead of us in several fields, problems of photosynthesis, of cellular organization, of the molecular structure and organization of the nervous system not to mention some of our social and international problems. It seems to me that the method of most rapid progress in such complex areas, the most effective way of using our brains, is going to be to set down explicitly at each step just what the question is, and what all the alternatives are, and then to set up crucial experiments to try to disprove some. Problems of this complexity, if they can be solved at all, can be solved only by men generating and excluding possibilities with maximum effectiveness, to obtain a high degree of information per unit time - men willing to work a little bit at thinking.

When whole groups of us begin to concentrate like that, I believe we may see the molecular-biology phenomenon repeated over and over again, with order-of-magnitude increases in the rate of scientific understanding in almost every field.

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[1] The author is professor of biophysics and physics at the University of Chicago, Chicago, Ill. This is the text of an address given before the Division of Physical Chemistry of the American Chemical Society in September 1963, under the title "The New Baconians."

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