INTRODUCTION

WHAT IS SCIENCE?

> *At one pole, the scientific culture really is a culture, not only in an intellectual but also in an anthropological sense… . Biologists more often than not will have a pretty hazy idea of contemporary physics; but there are common attitudes, common standards and patterns of behavior, common approaches and assumptions.*[1]
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> C.P. Snow, 1959

> *Philosophers cannot insulate themselves against science. Not only has it enlarged and transformed our vision of life and the universe enormously; it has also revolutionized the rules by which the intellect operates.*[2]
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> Claude Lévi-Strauss, 1991

In the span of one human lifetime, we have gone from ignorance about the nature of the genetic material to knowledge of how to edit any gene within it. In a previous life span, we went from defining the atom to splitting the atom, and entered the nuclear age. If the twentieth century was the era of physics, the twenty-first century will be the era of biology.

The idea for this book came from a meeting held at Cold Spring Harbor Laboratory on Long Island in New York in 2017 to celebrate the 100th anniversary of Francis Crick's birth. Listening to the talks, many of which focused on work done around and after the time of the discovery of the double helix in 1953, I was struck by the great difference in the way science was done then from how it is practiced now.

As Editor of *Cell* from 1974 to 1999, I saw a significant change in the atmosphere of science, with a transition from research performed principally by individual researchers to working in large groups with a team leader, from testing hypotheses to trawling for data, and from regarding science as an abstruse intellectual pursuit to viewing it with reference to its relevance to modern life. The question in my mind is how far these transitions have changed the very nature of science.

Science is founded on a unique proposition: that it is a self-verifying system in which everyone can play both sides of the game, as either researcher or reviewer. The two sides come together in the key unit of science, the research paper. This is the basic means by which scientists communicate with each other. Researchers write a paper when they feel they have enough data or new ideas to draw interesting conclusions. They submit the paper to a journal, which sends it out for review to two or more other researchers who are experts in the area. This is the much-vaunted system of peer review. On another occasion, roles might be reversed, and the authors of this paper might be reviewing one submitted by the experts who reviewed it. We'll come later to the questions of conflict of interest that can arise from playing dual roles.

The crucial feature of a research paper is that it should have enough information to enable others to reproduce the findings. Other researchers will probably not set out to reproduce a published paper directly, but they may well perform experiments based on its conclusions. If their experiments are inconsistent with the published work, sooner or later there will be experiments to repeat it, and this will lead ultimately to one set of experiments being accepted and one rejected. This is the self-correcting mechanism of science. Arguments about which reality is right are a standard part of the give and take of science.

A research paper is never an end: it is a means to the next paper. It may test a specific hypothesis or report the collection of a set of data, but it is in effect part of a work in progress, subject to reassessment as research continues. One problem with a wider public acceptance of science is that it requires some understanding of the subject and the techniques used in research. The need to master jargon and specialized techniques impedes a wider understanding.

Sociologist Robert Merton made a classic analysis of the value system of science in the 1940s, when he identified four features: communal activity builds on previous efforts (communality); results are independent of whoever makes the discovery (universalism); science is impartial with respect to whatever results emerge (disinterestedness); and science is subject to testing (organized skepticism). "Because of the practice of this ethos, the activity of the scientists is so productive and so different from the babbling and agitating of the ideologues and of the politicians," Merton said.[3]

Although this perhaps somewhat idealistic formulation has been attacked by later sociologists[4]—and it is, of course, the antithesis of postmodernist thinking—it captures the essence of why science represents a unique value system: it is based on facts that are tested objectively by each subsequent contribution. Applying this description, mathematics as well as physics, chemistry, and biology would qualify as science: social sciences are more questionable given the difficulties in establishing controls and verification.[5] Systems that appear to be scientific, but that are not based on hypotheses that can be tested, are (pejoratively) called pseudoscience.

This formulation is a fair account of the results of applying the scientific approach, but it does not take full account of, perhaps it even ignores, the human element. Aside from Merton, anthropologists may have largely, in fact almost entirely, misunderstood the functioning of science, but they are right in the principle that it is more than a methodology: it is a culture. Scientists take positions that are not always driven by objective views of the data; there are competition, ambition, petty rivalries, and from time to time even dishonesty. But science rises above these deficiencies because ultimately its self-correcting character means that data must triumph. Of course, science is a human endeavor, but the human ability to (mis)interpret the data is limited by the nature of the enterprise.

Each branch of science is admittedly a specialized discipline. It is not necessarily easy for scientists in one branch of specialization to understand the details of work in other branches. Making science intelligible to the nonscientist is a specialized task in itself. But my point is that understanding science, at any level beyond simply accepting its conclusions sight unseen, requires more than comprehending the details: it requires coming to grips with the scientific attitude, and understanding the limitations of the scientific process. Failure to do this results in failure to distinguish between science and pseudoscience.

Perhaps because the methodology of science is its own world, it is poorly understood by nonscientists. When he defined the difference between science and the humanities as *The Two Cultures* in the Rede Lecture at Cambridge University in 1959, C.P. Snow created a furor. He was ferociously attacked by the literary establishment for arguing that science was a driving intellectual force in society.

His most famous criticism was that so-called intellectuals are, in fact, illiterate about science. “I have been present at gatherings of people who … are thought highly educated and who have with considerable gusto been expressing their incredulity at the illiteracy of scientists… . I have asked the company how many of them could describe the Second Law of Thermodynamics. The response was cold: it was also negative. Yet I was asking something which is about the scientific equivalent of: have you read a work of Shakespeare’s?”[6]

This quotation came to epitomize the issue, to the extent that it was caricatured in a song in a musical performance on the London stage, which began, “The first law of thermodynamics, Heat is work and work is heat.”[7] Snow reinforced his position by saying later in his lecture, “Intellectuals, in particular literary intellectuals, are natural Luddites.”[8]

Perhaps the sharpest difference between science and the humanities is that nothing, but nothing, is immune from questioning in science, whereas outside of science, especially in what used to be regarded as traditional classical education, there were “givens” that could not be questioned. There had been little change in the traditional attitude since Matthew Arnold argued in an earlier Rede Lecture, in 1882, that “no one could be really educated unless they understood literature, particularly the literature of ancient Greece and Rome.” Certainly, there are “givens” in science, no better epitomized than in the Second Law of Thermodynamics, but they stand on a basis of objective data that can, in fact, be questioned at any time. There is no equivalent in the humanities, especially in the subjectivity of literary criticism—the source of the most vicious criticism of *The Two Cultures*.

Snow thought the problem of the two cultures was a consequence of the English educational system. Not only was there a gulf between science and the humanities, but it extended to a hierarchy within science. Certainly, when I went through the British school system, the brightest pupils were directed to Latin and Greek, the next group did physics and chemistry, and the bottom group did biology. This was already out of kilter with intellectual reality, and could scarcely have been a greater misreading of developments to come in the rest of the century. The Liberal Arts curriculum in American universities showed something of the same disdain for science, if not so stratified.

It is apparent today that incomprehension of science is a worldwide problem, but it does seem to be strongest in the Anglo-Saxon world, and perhaps at its peak in England. In typical English fashion, the educational system's response to C.P. Snow was not to educate arts graduates about science, but to take the view that supposedly illiterate scientists should be taught to write English, more or less the inverse of what was really needed. The situation has improved little in the following half-century.

Even today, on both sides of the Atlantic, although there is nominally greater acceptance of the idea that you cannot be truly educated unless you understand science, there is still a substantial proportion of the population for whom the concepts of science are impenetrable. (I suppose what seems to be an increasing number who are suspicious of science, or who utterly reject it, would be at the far extreme of that proportion.) When my first book on wine was nominated for the André Simon Award, at the award ceremony, the Chair of the committee described it by saying, "and it has graphs and things in it," with a tone of rising incredulity in her voice approaching a note of horror. I knew at once that I would not be awarded any prize. Yet surely innumeracy should be regarded as just as unacceptable as illiteracy.

I would argue that in the half-century since Snow distinguished between the two cultures, the gap has if anything widened. There remain basic differences in comprehension, with the humanities failing to appreciate the sciences and vice versa, but, more to the point, there is a fundamental difference in attitudes toward knowledge. The humanities can be attractive because they admit a turbulence of ideas, with room to perpetuate completely contrasting views. But although there can, of course, be contrasting interpretations in science, and indeed arguments about the legitimacy of data, ultimately these give way to what scientists call objectivity, and those in the humanities might call the tyranny of data. That difference in attitude—the acceptance that ideas are subservient to facts—versus the view that all ideas can be legitimate, is a basic difference between scientists and nonscientists. A prime objective of this book is to explore how far that attitude is justified in science.

The “scientific attitude,” searching for objective truth, is the universal ideal of science. Whether physics, chemistry, or biology, science proceeds by obtaining data through controlled experiments that can be reproduced or challenged by others. However, biology is different in some important respects from physics or chemistry. Living organisms have an intrinsic variability that is different from the invariance of inorganic material. Molecular biology is the part of biology closest to physics or chemistry; experiments are performed in the controlled environment of test tubes (or their equivalents). The test tube contains only the components put there by the experimenters.

Experiments at the cellular level offer greater challenges to ensuring controlled conditions: an experiment performed with one cell type, for example, immediately raises the question of whether the results are valid for other cell types. Experiments with animals pose more questions of individual variation, and observations with humans often fall subject to problems with individuality. (This is why the extremes of psychology or social sciences have difficulty in being accepted as true sciences. It is hard to do a controlled experiment when every data point has a different basis.)

The use of *controls* is a distinctive feature of experimental science, and the reason why physics, chemistry, and (molecular) biology are regarded as “hard sciences.” The first thing you look at in assessing a paper in experimental science is whether it has adequate controls. In effect, this means comparing the experiment, in which the parameter of interest is changing, with a control in which that parameter is fixed. If this condition can’t be achieved, the experiment is not publishable. Practitioners of hard sciences harbor deep skepticism as to whether “soft sciences” (such as psychology or social sciences) should really be called sciences at all, largely because of the difficulty in establishing proper controls.

Biology has been an experimental science, practiced on a smaller scale than physics, in which experiments often need to be designed on a large scale to test theories. The practice of physics is divided between theoretical physicists and experimental physicists, but there is really no equivalent in biology, in which data rule the day and theory is not held in high esteem.

Physics has been occupied for decades by a search for a "theory of everything," and even though this might not be attainable, Nobel Prize–winning physicist Steve Weinberg could write a book entitled *Dreams of a Final Theory*.[9] Biology is more pragmatic. Since the discovery of the structure of the double helix and the breaking of the genetic code, advances in biology have been associated with ever-increasing amounts of data. Going into the twenty-first century, "big science" has invaded biology and brought its practice closer to that of physics.

Science has always been a rather self-contained system. Scientists accept, without thinking about it too much, that their mindset is different from the mindset of nonscientists. This means that some of the long-standing assumptions of science have rarely been questioned: that quality control is assured by the peer review system of asking other scientists to approve work before it is published; that including details of how experiments were performed makes it possible, in principle, to reproduce published work; that work is accurately reported and fraud or misrepresentation is rare; that science is intrinsically self-correcting because later work will show up errors in earlier work.

But the true scientific attitude should extend to questioning these internal assumptions. So I want to look at the validity of our long-standing assumptions about how science works, as well as to ask whether they remain true as we make a transition from science performed by small groups of individuals to science performed by large collaborative teams.

The pace of scientific and technological discovery has advanced rapidly over the past century in all fields of science, by any measure—number of scientists, number of published papers, number of new insights, and number of diseases that can be cured. Moore's "law," that the number of transistors in an integrated circuit doubles every decade, has held up well since it was proposed in 1965. Ray Kurzweil extends it in his argument that the Singularity is near (the point when computers can match human intelligence) to suggest that the rate of technological innovation now doubles every decade.[10]

Biology (at least in the sense of this book) is a more recent science than physics or chemistry and cannot claim to match that pace of technological advance. But in the time span covered by this book, the gaps between major discoveries have shortened, from four decades in the first half of the twentieth century to perhaps one decade at the end of the century. And the nature of discovery has shifted from the abstruse (what is the chemical basis of the genetic material) to the practical (how can we distinguish people by their DNA sequences). Molecular biology has made the transition from basic discoveries about living organisms to influencing daily life.

Changes in the concept of the gene are revealing about the nature of science as well as about the nature of the gene. The view of the gene as the sole unit of heredity dominated science until the concept of epigenetics introduced the idea that there might be other factors. Both epigenetics and the possibilities for gene editing created by the CRISPR technique have raised the question as to how far we are prisoners of our genes.

Should science be controlled—and, if so, how? Should scientists be completely free to tackle any problem, or are some techniques or experiments too dangerous or ethically questionable, so they should be subject to moratorium or permanent bans? The development of the CRISPR technique, rewarded by the most prestigious of all scientific prizes, the Nobel Prize, in 2020, raises a host of ethical questions going beyond science itself. But can there be an informed public debate without understanding of how science functions?

Increase in computing power has had a huge effect on all science. In increasing the pace of discovery, it raises the question of whether the traditional organization of science will be fit for purpose in the future. The recent extension from using mere algorithms into using artificial intelligence (AI) in research in biology calls into question whether the fundamental nature of research is about to change.

Although the issues I want to address are common to all areas of science, I approach them here through the prism of DNA. DNA is the thread of life both literally and metaphorically. If stretched out end to end, the DNA in one set of human chromosomes would be a very thin thread extending for about a meter; this is more than a million times the diameter of the cell that contains it. DNA is also the intellectual thread that holds together more than a century of scientific discovery, from Mendel to the latest results in molecular biology, from the concept that the gene is DNA to understanding inheritance, cancer, and evolution. In short, DNA is a unifying force in modern biology. The half-century following the discovery of the structure of DNA in 1953 saw an extraordinary flow of discoveries and surprises: can this continue?

This brings us back to the main question: what is science? At one point, I thought of calling this book *What Is Science?*, partly in homage to the book written by physicist Erwin Schrödinger in 1944, *What Is Life?*, which was so influential in persuading physicists and others to enter biology, inspiring the search to discover the physical basis for the genetic material.[11] That search led to the discovery of DNA: is it an exaggeration to say that our level of understanding of DNA is now so extensive as to become a dominant influence on human life? And DNA has become almost a catchphrase, with "it's in its DNA," meaning we have found the heart or quintessence of the matter. So this book is about the DNA of science: what science is, how it is practiced, and how that practice has been changing over the years.

Science depends on data, not on beliefs. I do not mean "belief" in any religious sense, but simply in the sense that even scientists may stick to ideas or hypotheses that are not actually in accordance with the data. One theme of this book is to show how ultimately data will triumph over mistaken beliefs.

I hold the view that science is intrinsically reductionist, but that leads us to ask what may be its limitations, not in the sense of questioning whether science can solve problems out of its sphere, but simply whether the reductionist approach can solve the ultimate scientific questions. This is as pressing a question now in biology as it has been in physics for the past half-century.

Almost a century later, I am not sure we are any closer to answering Schrödinger's question, *What Is Life?*, than when he posed it. Of course, Schrödinger meant it in a very precise sense: what is the nature of the hereditary material? With the immediate question of the genetic material resolved, biology can turn to beginnings and ends. So today we have progressed to asking the question in broader terms: how did life originate; and can we explain all functions of the organism, including human consciousness? It is a fair question whether these broader questions are answerable.