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The Competitive World of the Pure Scientist

The quest for prestige can cause conflict between the goals of science and the goals of the scientist.

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The "pure scientist" is likely to be pictured as a person who devotes himself to the study of natural phenomena without regard to their possible practical or technological applications. Motivated by intellectual curiosity and immersed in his abstract work, he tends to be oblivious of the more mundane concerns of ordinary men. Although a few older scientists have become active in public affairs in recent years, the large majority who remain at work in their university laboratories lead peaceful lives, aloof from the competitive business practices or political manipulations of the outside world.

Stereotype versus Reality

There is some truth in this stereotyped portrait. But if a young student took its apparent serenity too seriously, he would be forced to revise his perspective very early in his scientific career. The work situation of the scientist is not just a quiet haven for scholarly activity, ideally suited to those of introverted temperament. The pure scientist, like the businessman or lawyer, works in a social setting, and like them, he is subject to appreciable social and competitive pressures. The institutional framework within which he functions is distinctive; it is basically the university system. Furthermore, his competition does not resolve primarily around money; there is no very direct relationship between the quality of the scientist's professional performance and the economic rewards he receives. But competition need not be confined to the acquisition of wealth or political power. It is, therefore, of particular interest to discover how intense competition can become in an area as remote as pure science. In recent years rapid expansion has occurred in many branches of science. More scientists are active in many fields, more laboratories (including some in industry and government) engage in pure research activities, and more dollars are spent on such research. While this expansion has given the scientist a more prominent social role, it has also intensified the competitive pressures under which he works.

A few examples will illustrate how such competition can manifest itself. I shall take these illustrations from the field of physics, because physics is a well-developed pure science and because this is the field with which I am most familiar. In this country research work in physics has traditionally been published in a bimonthly journal called the *Physical Review*. In addition to full-length research reports, this journal used to publish "Letters to the editor," short notes whereby scientists could briefly communicate important new developments. The time elapsed between submission of a manuscript and its appearance in print was approximately 5 months for a regular paper and 2 or 3 months for a "letter." But in a period of rapid growth and development the pressure to publish fast and to establish priority claims became sufficiently great to make the *Physical Review* appear an inordinately slow medium of communication. Three years ago, therefore, its editors decided to eliminate the "Letters" section and to found a separate bimonthly journal, the *Physical Review Letters*, devoted entirely to the fastest possible publication of short notes on important discoveries. The time between submission of a manuscript and its appearance in print has been reduced to as little as 4 weeks! Not only is the existence of such a journal a significant phenomenon in itself; it has also necessitated the formulation of new editorial policies. As a result, although editorials in scientific periodicals are ordinarily very rare, some illuminating examples have found their way into issues of the *Physical Review Letters*.

In one of these (*1*) the editor comments that a large number of manuscripts are submitted whose importance and meagre content are not adequate to justify publication in the *Letters*. He goes on to say: "When a 'hot' subject breaks there is a deluge of follow-up contributions. . . . With the rapid exploitation of new ideas, priority questions become serious problems. Possibly important technical applications often lurk in the background. . . ." After explaining that he feels compelled to reject as unworthy of publication more than 40 percent of the manuscripts received, he concludes: "We do not take kindly to attempts to pressure us into accepting letters by misrepresentation, gamesmanship, and jungle tactics, which we have experienced to some (fortunately small) extent."

From the foregoing comments it is apparent that scientists seem most eager to see their work appear in print as soon as practicable. But to achieve that purpose, even the *Letters* can appear unduly slow. Certainly, the daily press is even faster; and though it may be less

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suitable for erudite publication, it is more effective for publicity and no less effective for establishing priority. Consequently, there have been several instances in recent years when important discoveries in physics were first announced in the New York *Times*. This procedure is not, by traditional values of the scientific community, considered to be very ethical. Nor is it, as the *Letters* editor points out in another editorial, an activity to be confused with the well-developed public information and publicity activities carried out by his own office and by such agencies as the American Institute of Physics. The editor expresses himself quite forcefully (*2*): "As a matter of courtesy to fellow physicists, it is customary for authors to see to it that releases to the public do not occur before the article appears in the scientific journal. Scientific discoveries are not the proper subject for newspaper scoops, and all media of mass communication should have equal opportunity for simultaneous access to the information. In the future, we may reject papers whose main content has been published previously in the daily press."

In the passages quoted, the editor of the official journal of American physicists makes some revealing comments about the behavior of his fellow scientists. What are some of the factors responsible for such behavior? Why should there be this exorbitant desire to publish and to do so ahead of others? The following discussion will focus attention on some of these questions in an attempt to clarify the conditions of modern science which contribute to this behavior. We shall first examine the great importance of prestige to the scientist. It will become apparent that the scientist carries out his work in a setting where he is extraordinarily dependent on the good opinion of others, and where his reputation becomes translated into many concrete consequences for him. Personal recognition thus assumes even more importance for the scientist than for most other people, and he competes persistently to achieve maximum prestige. I shall illustrate how this competition takes place and how it affects the manner in which scientific research is carried on. Finally, we shall ask how the existence of such competition serves to advance or impede scientific activity. This question will reveal the existence of some conflicts between these competitive pressures and scientific work proper. Throughout this discussion it should be borne in mind that the situation is not static and that the rapid expansion of science has made many of these problems more conspicuous than they were a few years ago.

Prestige and Success

The scientist is not different from others in his desire to be successful, but his definition of "success" has some distinctive features. The work of the pure scientist is abstract; it consists essentially only in gathering new data and formulating new concepts. To constitute scientific knowledge, these must be verifiable by other scientists and usable by them as the basis for further exploration. Thus, the very nature of scientific activity implies the need for recognition of the value of one's work by others in the field. Furthermore, success in such activities is not readily measurable in quantitative terms recognized by all. It does not revolve around tangible things such as amount of money earned or number of factories owned. Only other scientists in his field can understand the scientist's work and judge its merits. Indeed, throughout his life the scientist is dependent on the good opinion of significant other scientists for practically everything he does or hopes to attain. A review of the scientist's professional career will illustrate the truth of this statement.

While still in high school, the scientist-to-be becomes aware that competition and prestige will affect his future success. He must strive for good grades in order to be admitted to college and later to graduate school. He realizes the importance of attending a college of high reputation, not only because it will provide him with a better education but also because it will facilitate his later admission to a good graduate school. Finally, he must earn the good opinion of his teachers to secure the letters of recommendation which will help him enter college and gain scholarship grants or prizes.

After the student obtains his Ph.D. degree, his dependence on the good opinion of others is by no means ended. His first task is to find a suitable position. Characteristically, jobs in the better universities or in top industrial research laboratories are practically never advertised but are handled by personal communication between well-established scientists, who inquire informally whether their colleagues happen to know of some candidates for a given position or have an opening in their organization for a particular candidate. The job-seeking scientist is clearly in a more advantageous situation if he comes from a well-known institution and has been associated with a scientist of reputation. Invariably it is essential to him that there should be prominent scientists in the world who are willing to comment favorably upon the quality of his work. In most cases, before an appointment is decided upon, the hiring institution formally requests letters of recommendation concerning the candidate from several such prominent scientists. It is thus very important for the scientist to create, either through personal contact or through published work, a favorable impression among as many key scientists as possible.

Professional mobility of the scientist depends, therefore, in an essential way on the reputation he has acquired among prominent people in his field. This is true when he is securing his first job and true in his subsequent moves from one position to another. (In this connection it may be remarked that to move from an institution of high prestige to one of lower prestige is significantly easier than to move in the reverse direction.) Promotion to higher academic rank is subject to similar criteria. Again the university requests letters of recommendation from outside scientists and in some cases may appoint reviewing committees before deciding to promote someone to a tenure position. Even when the scientist has obtained a full professorship he has not reached the end of possible advancement based on his reputation. Within the academic hierarchy there are still some "name" professorships, or ultimately some administrative posts such as dean or university president. In these days of increasing importance of science in world affairs there are also potential opportunities in government—for example, advisory positions to the President or appointments to some such agency as the Atomic Energy Commission. Industrial organizations, as well, may offer key positions, such as the directorship of a research laboratory. Needless to say, the academic promotions which the scientist achieves carry with them increased financial rewards and, at the higher ranks, the security of a permanent position.

To carry on his work, the scientist needs money and adequate research facilities. Since World War II the financial expenditures required to perform the increasingly complex research of modern science have become so great that universities can provide only a very small fraction of the necessary funds. The remainder must come from outside sources—some of them private foundations but by far the greatest number government agencies such as the National Science Foundation, the Atomic Energy Commission, or the Office of Naval Research. On what basis do all these groups award their available funds to individual investigators? The usual procedure is to send the research proposal of the investigator to some prominent scientists for review. These scientists then make appropriate recommendations based on their evaluation of the specific proposal and their opinion of the merits of the scientist submitting it. The scientist today is thus increasingly dependent upon the reputation he has established among his colleagues to obtain the very means necessary for carrying out his work: funds for buying equipment and supplies and for paying the salaries of the personnel in his research group. In addition, the scientist's prestige helps him attract good and numerous students and postdoctoral fellows who can be of significant assistance in furthering his research program.

At times the scientist may be interested in obtaining a fellowship or grant —for example, a Guggenheim or National Science Foundation senior postdoctoral fellowship. Grants of this nature permit him to travel abroad for a year; or spend some time at a different university, where he can learn new techniques; or gain temporary relief from teaching duties to devote himself full time to his research. In applying for such a fellowship, the scientist will again be judged by some select prominent scientists, and once more his reputation among these scientists determines whether the award will be made to him.

The prestige acquired by the scientist very directly influences the likelihood of his nomination by fellow scientists for special honors or distinctions. Examples are the award of a Nobel prize or selection to membership in the National Academy of Sciences. Selection to serve as an officer of the national scientific organization is another recognition of distinction. The scientist's prestige may also lead to special invitations to attend scientific conferences as guest speaker or to join another university as visiting professor; finally, it may result in offers of remunerative consultantships in industry.

I think it is worth while, before leaving this discussion of the prestige system, to remark on a few of its peculiarities. One of these is the "positive feedback" involved—the fact that the possession of prestige tends to facilitate the acquisition of further prestige. For example, a person of prestige is likely to be affiliated with one of the better-known institutions, likely to obtain more funds to do effective research, and likely to attract better students—all of which circumstances, of course, tend to enhance his prestige even further. There is a similar relation between the prestige of individuals and the prestige of institutions. Institutions of good reputation can attract individuals of distinction whose presence, in turn, lends increased prestige to the institution.

Another feature of interest concerns the people who set the standards against which the individual scientist appraises himself and whose opinion determines his general reputation in the field. It is mainly the well-established scientists in the major universities of the world who set these standards. Since the institution with which the individual scientist is affiliated tends to evaluate him chiefly on the basis of his reputation, it becomes of greater concern to the individual to seek the good opinion of people on the national or international scene than to strive for accomplishments which attract only local attention. The scientist thus tends to have stronger loyalty to his field than to the specific institution of which he is a member. This is particularly true in the present days of expansion, when there is great mobility between different positions. The trend, in the major universities of this country, to minimize the importance attached to the teaching functions of the faculty reflects the situation. Teaching undergraduates is a local activity which may be appreciated by the students but does not serve to enhance the scientist's international prestige, on the basis of which the university will decide whether he is worthy of promotion. "Research and the training of graduate students are valued highly by the faculty; teaching, by contrast, is second-class. . . . It is a more usual, and probably a more realistic, view that time taken for teaching is time stolen from research, and that the road to academic heaven is paved with publications" (*3*).

The growing importance of science has also led to a proliferation of industrial research laboratories. The oldest and most distinguished of these are active in pure research and are staffed by some very competent persons who might readily have joined a university had opportunities in industry not been available. These people are eager not to be considered inferior by the rest of the scientific community, despite their industrial affiliation. Hence, they adopt for themselves standards very similar to those prevalent in the universities and compete within the same prestige system. This also preserves their mobility and leaves open the road back into some university position. Since the pure scientist's reputation, irrespective of the particular institution to which he belongs, is determined by the same reference group of prominent scientists, there exists a common prestige system which cuts across purely organizational lines. Thus, more prestige may be attached to a good position at a major university than to one in an industrial laboratory, but a position in a top industrial or government laboratory carries more prestige than one in a smaller university.

Publishing "Fustest and Mostest"

Because the social context within which the scientist receives his training and does his research is one where the possession of prestige is highly rewarded, competition among scientists is largely directed toward the acquisition of prestige. The particular forms assumed by this competition are determined by the nature of the scientific discipline and the character of the institution where the scientist carries out his work. A scientist strives to do research which he considers important. But intrinsic satisfaction and interest are not his only reasons. This becomes apparent when one observes what happens if the scientist discovers that someone else has just published a conclusion which he was about to reach as a result of his own research. Almost invariably he feels upset by this occurrence, although the intrinsic interest of his work has certainly not been affected. The scientist wants his work to be not only interesting to himself but also important to others. He wants it to attract the maximum attention from other people, and in this quest priority is a crucial factor. An important discovery becomes intimately associated with the name of the scientist responsible for it. If somebody else makes this same discovery at about the same time, several names become attached to it and the contribution to his own prestige is correspondingly diluted. The chances of receiving a Nobel prize or a promotion are similarly decreased. Finally, if someone else succeeds in making this discovery a few months or weeks before he does, almost all of the scientist's efforts on the problem have come to naught. He may not even be able to publish his own results, since they may then represent only uninteresting duplication of work already in the scientific literature. Under the circumstances, it is not surprising if the scientist sometimes works at feverish speed under constant fear that he may be "scooped." Even a couple of weeks' delay can sometimes make a difference!

Being the first to make an important scientific contribution is, of course, only one way of obtaining recognition. For a scientist to be on the verge of making some discovery of far-reaching implications is relatively rare. Most of the time he is engaged in the less spectacular task of doing useful work leading gradually to increased knowledge. In this situation the most effective way to attract the continuing attention of other scientists is to publish as many papers as possible, to attend numerous scientific meetings, and to give many talks on one's research. The great emphasis on publishing copiously is exemplified by a motto familiar to all young faculty members—"publish or perish"— a phrase that well illustrates how the young scientist feels about the competitive pressures to which he is subject. Under the "up-or-out" rule, common in large universities, instructors and assistant professors are allowed only a fixed maximum number of years within their academic rank. If they are not promoted before the end of this time, their dismissal from the university is automatic. Whether or not an individual is promoted depends, of course, on the reputation he has achieved as a result of his publications.

Some of these competitive pressures have been familiar features of academic life for a long time. The expansion of scientific activity since World War II, has, however, significantly changed the conditions under which the scientist does his work. One consequence has been the emergence of new and intensified patterns of competition as the number of scientists at work in many areas has multiplied. Not only are more universities engaged in active research; more industry and government laboratories are also carrying out pure research of a type nearly indistinguishable from its academic counterpart. Many people in different institutions are thus likely to be working along fairly similar lines. Furthermore, the time lag between advances in basic science and the associated technological developments has become increasingly small. Sometimes new ideas or techniques arising in the work of the pure scientist may be such as to warrant patenting without further exploration. Even when potential technological applications are not immediately apparent, there are well-equipped industrial laboratories constantly poised to exploit all possible consequences of a basic advance. In addition, research has become an activity which involves the expenditure of large sums of money and which has come to attract attention even from the general public. Under these circumstances it is easy to understand why the scientist finds increasing difficulty in carrying out his work immune from outside pressures.

Rapid publication of results and questions of priority assume, therefore, great importance; nor is the need for a journal such as *Physical Review Letters* too surprising. No longer does a scientist study a topic at some length before publishing his findings in a paper or monograph. Instead, he tries to publish a note on a subject as soon as he obtains any result worth mentioning—and occasionally even before. The threat of someone else's getting there first is too great. At times a scientist may publish just a proposal for an experiment, merely pointing out that such an experiment might be interesting and feasible. To obtain preliminary experimental results before publishing anything may take too much time—time during which the scientist might "get scooped" by someone else. For similar reasons scientists may be led to engage in various practices which the editor of *Physical Review Letters* finds reason to discuss. In his words (*4*), there is the "author who uses the *Letters* merely to announce a later paper and whose Letter is incomprehensible by itself"; the "author who submits many Letters hoping that statistics rather than quality will cause one to be accepted"; or the "author who tries to sneak a Letter in to 'scoop' a competitor who has already submitted an Article."

The emergence of rapidly changing "fashionable areas" of scientific activity is still another consequence of the expansion of science. In a highly developed discipline such as physics, genuinely new ideas or unexpected breakthroughs are not really very common. When such a discovery does occur, many people are eager to drop more routine work in order to explore the potentially important consequences of the new development. Present conditions are also such as to permit a substantial number of scientists to shift their field of research quite rapidly. One reason is that the major university and industrial laboratories provide the flexibility of a large variety of experimental facilities and adequate manpower resources. Moreover, since work is often proceeding along similar lines in a number of different laboratories, scientists active in areas related to the discovery are in a particularly good position to turn their attention to an investigation of its consequences. Every new discovery, therefore, results in a burst of intense and very competitive activity. In physics there ensues a profusion of "Letters," until the editor decides that the subject has become sufficiently old to be routine. Since so many people concentrate their efforts in one area, the road from the novel to the routine is often traveled in a few months.

The preceding discussion illustrates the increasingly important role played in modern science by large-scale research organizations. This is true not only in industrial and government laboratories but also in the universities, where specialized research institutes have become quite common. Here the scientist is usually a member of some group organized around a particular project or a special research facility, such as a high-energy accelerator, and work is often done jointly by several people. An experiment was recently reported in a "Letter" by no less than 24 coauthors! Working under these conditions is appreciably different from the individualistic endeavors prevalent 10 or 20 years ago, and the scientist must compete in some novel ways. He must establish an individual reputation even though he works as a member of a larger group. He also has to compete in a setting which tends to be organized along hierarchical lines, where scientists in the top positions determine policy and the direction of research. Finally, many members of research institutes constitute a "secondary faculty" of research associates. They do not teach or belong to a department, nor do they have permanent positions. If they hope to gain the security of a tenure position they must strive for sufficient eminence to be appointed to regular academic rank.

Conflicting Values

After this description of the existing conditions in pure science, let us consider some of the consequences of competition in this area. This competition certainly affects the functioning of scientific research in several beneficial ways. The prestige system helps to maintain high standards of accomplishment which reflect the collective judgment of important scientists and are therefore fairly uniform throughout the world. Prestige accrues predominantly to those whose discoveries prove fruitful as a basis for further work by other scientists. Specific areas of activity in science thus become fashionable not just because they are novel and different but because they are likely to lead to scientific contributions of permanent value. Even when current fashion leads to duplication of work by different investigators, the resulting critical checking of results may occasionally help in avoiding mistakes and oversights. Competition under these conditions encourages continuing active exploration as well as rapid and thorough exploitation of all new discoveries. Research institutions have become well adapted to carry out these functions. Not only are they well equipped and staffed but they are capable of using their resources with considerable flexibility.

On the other hand, the competitive atmosphere has results which are less desirable. It subjects the individual scientist to appreciable strains, thus increasing further the demands made upon him by an already rigorous scientific discipline. But apart from such psychological effects, there are possible deleterious consequences affecting his research activity itself. These are usually the result of conflicts between the requirements of the scientific work proper and the pressures of competition. To the individual scientists they may appear as conflicts between the values inherent in science and more selfish personal values.

One such conflict is that of reflection versus production. The scientist may desire to take some time to think and speculate; he may want to get a fresh point of view by reading about developments outside his special field and to discover suggestive analogies worth pursuing; or he may be tempted to undertake an experiment sufficiently novel in character for him to be uncertain about its ultimate feasibility. Activities of this kind are potentially fruitful precisely because they focus attention upon lines of investigation off the beaten track. But, by the same token, they are also risky, since in many cases they may lead to no results at all. In order to make his reputation with a steady stream of publications, it is safer for the scientist to work along more conventional and familiar lines, where he has greater assurance of obtaining results. Young scientists are in a particularly vulnerable situation. Since they must establish their reputation in a relatively short period of time to achieve a permanent academic position, undertaking risky projects during this period is dangerous. Interesting in this connection are instances where a fundamental discovery is made by someone in a small laboratory in an out-of-the-way place. As soon as the result is published, many big laboratories employ their superior facilities to exploit the consequences of the discovery so effectively that the scientist originally responsible for it finds it difficult to compete with them. People in the big laboratories had available, of course, all the resources necessary to make the original discovery themselves, but they used them less imaginatively. Organizations well adapted to the exploitation of a field in which the direction of approach has become clear are not necessarily the best for stimulating exploration of the genuinely unknown.

A further conflict, which may lead to slipshod work when competitive pressures are pronounced, is that of careful versus fast work. Another *Letters* editorial describes the dilemma succinctly (*5*). "One of our most ticklish problems concerns the large number of contributions that pour into our office when a 'hot' subject breaks and many groups initiate related work. . . Because of the rapid development, and the intense competition, we have found it necessary to relax our standards and accept some papers that present new ideas without full analysis, relatively crude experiments that indicate how one can obtain valuable results by more careful and complete work, etc.—in short, papers which under less hot conditions would be returned to authors with the recommendation that further work be done before publication. . . . Such incomplete papers have been accepted reluctantly since we realize that thereby we penalize some physicists who, working along the same lines, want to do a more complete job before publishing."

Another conflict is that of communication versus secrecy. It is intrinsic in scientific activity that knowledge and ideas are common property, to be shared and used by all scientists. But if scientist *A* has an interesting idea and describes it to scientist *B*, the latter may exploit it before scientist *A* himself can do so. It may then be better for *A* not to disclose his ideas before they are published and before his claim to priority is safely established. Closely related to this conflict is that of cooperation versus rivalry. Should scientist *A* tell scientist *B* about some new technique he has developed if *B* may use it in his own work to compete more effectively against *A*? Lack of full communication can, of course, slow down scientific progress. A significant amount of energy is diverted from struggling with the subject matter of science to fighting other people in the field.

There exist other conflicts, such as that between research and teaching. But instead of elaborating further, I might better give a specific example illustrating how the pursuit of a purely scientific problem can give rise to the competitive pressures described. A few years ago Mössbauer, a young German physicist, discovered that the radiation emitted by certain atomic nuclei in solids is characterized by an exceedingly well defined frequency. This observation suggested to several people, in particular to two scientists, *X* and *Y* (*6*), that such nuclei might be used as extremely accurate clocks well suited for checking a consequence of Einstein's general theory of relativity. This theory predicts that the rates of two identical clocks should be minutely different if they are located at different heights in a gravitational field. Both *X* and *Y* undertook to check this prediction experimentally. Scientist *X*, however, first published a "Letter" outlining his proposal for the experiment, long before he was ready to obtain actual data. A few weeks later, again before either *X* or *Y* had published any preliminary results in the scientific literature, the front page of the New York *Times* carried a picture of scientist *X*, together with an article describing the experiment he was undertaking. When *X* discussed his experiment at a scientific meeting 6 weeks later he reported reluctantly that, despite hard work at great speed, he had not yet been able to reach any conclusions. At the same meeting *Y* announced that he had successfully carried out the experiment and obtained results in agreement with the theory; shortly thereafter *Y* published his findings. It was not until some 2 months later that *X*, in a "Letter," was able to report his own experiment, which also confirmed the theoretical expectation. He pointed out, however, the necessity of controlling the temperature of the experiment quite carefully to avoid introducing large extraneous effects; indeed, since *Y* had not taken such precautions, his findings lacked significance. In this instance an important experiment was performed in a short time and ultimately in a reliable way. But the example shows vividly the actual circumstances under which the experiment was carried out—the announcement of an experiment before it was undertaken, the newspaper publicity, the hurried activity of two scientists working under pressure to be the first to publish—and the lack of sufficiently careful work which may result from these conditions.

While much more could be said about the differing patterns of competition in various sciences and about the rapid changes taking place in many of these disciplines, my aim has not been to treat the topic exhaustively. It is sufficient if the perspectives of the outside observer have been broadened, to make him aware that the scientist is not just somebody concerned with new ideas and techniques, but that he carries out his work in a human, and sometimes all too human, context.

References and Notes

1. S. Pasternack, *Phys. Rev. Letters* **4**, 109 (1960).
2. S. A. Goudsmit, *ibid.* **4**, 1 (1960).
3. *Science* **134**, 159 (1961).
4. S. A. Goudsmit, *Phys. Rev. Letters* **6**, 587 (1961).
5. ——, *ibid.* **4**, 395 (1960).
6. R. V. Pound and J. P. Schiffer.

Chemical Factors Controlling Nerve Activity

Analysis reveals the underlying chemical system that generates the currents responsible for nerve impulses.

David Nachmansohn

One of the characteristic features of living cells is their high potassium ion (K^+) concentration in contrast to the low K^+ concentration in the outer environment. The reverse is true for the sodium ion (Na^+) concentration. However, only conducting cells, nerve fibers, and muscle fibers make use of these concentration gradients for generating the electric currents which propagate impulses. These currents are carried by ions. During activity, Na^+ moves into the interior, and this movement is followed by an outflow of an equivalent amount of K^+ (*1*). There is a strong and rapid rise of sodium conductance and an equally rapid return to the initial stage. Subsequently, potassium conductance, already high in the resting state, increases but slightly, and the changes are relatively slow (*2*). These facts raise immediately the fundamental question: What is the special mechanism which enables conducting cells to use ionic concentration gradients, the source of electromotive force, for the generation of electricity?

It is difficult to see how electricity in a fluid system such as the living cell can be generated without chemical reactions. Conducting cells must be endowed with a special chemical system controlling the movements of ions in a specific way. Any doubt as to the chemical nature of this process has been removed by the recent heat-production measurements of A. V. Hill and his associates (*3*). They found that the initial heat can be separated into two phases: a strong positive heat, coinciding with electrical activity, followed by a negative heat during recovery. The conducting membrane is only 50 to 100 angstroms thick. Per gram of active material, the positive heat amounts to about 3 millicalories. This is about the same amount of heat as that produced per gram of muscle during a twitch.

What is the chemical reaction? About 30 years ago, acetylcholine was linked to a special phase of nerve activity. It was assumed to be released from nerve endings and to act as a neurohumoral transmitter on the effector cell, nerve or muscle. The observations were based on classical methods of pharmacology. However, the idea of a special mechanism at nerve endings which is basically different from that in axons was opposed by many electrophysiologists. The facts were not questioned, but the interpretation was. A new approach appeared imperative.

The rapid development of biochemistry, especially the spectacular rise of protein and enzyme chemistry during the last few decades, has provided powerful tools for analyzing cellular function in terms of physics and chemistry. An approach with biochemical methods was initiated 25 years ago. The enzymes effecting hydrolysis and the formation of acetylcholine were analyzed, the sequence of energy transformations was established, and a number of chemical reactions were correlated with physical events. Central to these studies have always been the proteins and enzymes, especially those linked specifically to the action of acetylcholine. They have been isolated and purified from the

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