Some New Technologies and Their Promise for the Life Sciences

THE LIFE SCIENCES PANEL
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This report on "Some New Technologies and Their Promise for the Life Sciences" was prepared at the request of the President's Science Advisory Committee. Because of its general interest for the scientific community at large, it is being released for publication.

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SOME NEW TECHNOLOGIES AND THEIR PROMISE FOR THE LIFE SCIENCES

PREAMBLE

During the past 100 years man has gained an astonishing understanding and control over the physical world, but he has made slower progress in controlling and understanding himself as an individual and as a member of society. But the means for improving the human condition are today more nearly within our grasp than ever before. Discovery of the principles of organization, communication, and control which underlie the life sciences will deepen our insight into the nature of men and their societies. The wise application of these insights should result in more comprehensive control of disease and hunger, more effective methods of education, and, by eliminating or channeling man's destructive impluses, more opportunities for the free development of individual personalities.

This appraisal has its roots in the fertile ground now being opened by the new technologies drawn in part from recent striking advances in the physical sciences and in almost equal measure from developments within the life sciences themselves. This report attempts to clarify the relations between some of the life sciences and technological change, and to evaluate their significance.

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Part I

THE IMPACT OF INFORMATION TECHNOLOGY ON THE LIFE SCIENCES

The digital computer epitomizes the new information technology in the range and diversity of information processing it makes possible and in the startling suddenness with which it has been thrust upon us. Its impact on the life sciences occurs in many places and in many guises: as traditional data analysis; as data processing of huge volumes of records; as networks for gathering primary data; as techniques for building responsive experimental arrangements; and as a basic theoretical tool in the simulation of complex systems.

Much of the impact is still only potential yet sufficient evidence is at hand to support the judgment that information technology will have an impact on the life sciences as significant as the technologies derived from thermodynamics did in an earlier period. It will do this, not by replacing other technologies, but by permeating them and becoming part of each attempt to advance the life sciences.

An understanding of the role of information technology requires some description of its basic nature and power. The digital computer is, in essence, a machine for following instructions. In the past, a machine merely responded to the setting of a switch or the position of a lever, but a computer responds to a language: this is the revolutionary development.

In processing information, the computer deals with a collection of specialized symbols that can be distinguished, compared, copied, remembered, and formed into expressions. What gives meaning to these symbols is the set of processing instructions. In principle, an astonishingly small set of primitive instructons suffices for information processing, but a typical computer can have scores of different instructions. In either case, the elementary built-in instructions can be concatenated into long sequences. Only a machine for processing information can obey a language and, conversely, only such a machine can form new instuctions for itself and thus change its mode of operation in intricate ways.

The capability of a computer is measured by the amount of information it can store, the number of basic instructions it can perform per second, and the reliability with which it operates. The first large commercial computer, which appeared in 1951, did about 4,000 additions per second and

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had 1,000 10-digit numbers stored and accessible at high speed. Today's biggest machine does about a million additions per second and has over 100,000 10-digit numbers accessible at high speed. Thus, in 10 years speed has been increased by a factor of 250, and memory by a factor of 100. Reliability has increased correspondingly, so that today's machines run with billions of operations between errors. Even without the further advances that are sure to come, machines are already powerful enough to bring about several revolutions in the application of information technology to the life sciences.

The figures quoted represent pure potential. For a computer to do sophisticated things it must have a sophisticated instructor. Fortunately, paralleling the increase in capacity there has been a growth of know-how in instructing the machine, or "programing." In areas of significance to the life sciences, an extraordinary range of numerical computations can be made with great facility: standard statistical analyses, matrix inversions, spectra and cross spectra, auto- and cross-correlation of time series, the numerical solution of ordinary and differential equations, and so on. Other operations have been carried out in a few experimental programs and will soon become routine: the recognition of fixed type fonts for direct input of printed material, the simulation of neural networks, and the extraction of meaningful data from background "noise." Speech recognition, inductive inference, and language translation are in exploratory stages.

The price paid for the general-purpose computer is the headache of writing sequences of tens of thousands of elementary instructions. The tedium involved in instructing computers has prompted the development of automatic programing procedures and languages whereby the machine assumes some of the burden of instructing itself. With numerical problems the results are often impressive. When it comes to the manipulation of more complex symbols the obstacles are of a more fundamental nature. What processes are useful in analytically manipulating linguistic expressions? in discovering proofs to theroems? in reasoning? As long as we are unable to formulate these problems effectively it is not easy to instruct the computer and still more difficult to instruct the machine to instruct itself.

The pressure to develop new instructions must come from potential users who have a clearly expressed need. Almost certainly, the most convenient programing for the life sciences will reflect some of the individualities of the language of biology—individualities that can be unearthed only by the life scientist in the course of actual programing and experimenting.

The need for effective and fairly rapid two-way communication with the machine is a major stumbling block. In all but a few instances today, 24 hours or more intervene between the gathering of experimental data and the retrieval of the results of their analysis. Such delays make impossible the

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adequate incorporation of the computer into experimentation. Either we must learn how to let many users have almost immediate access to a single large computer or we must supply each experimenter with a device of his own.

Many difficulties arise at the point of data generation. Original data must be converted and stored, too often in written form, and then must undergo yet another conversion (usually manual) to a form acceptable to the remotely located machine.

Output is variably useful and appropriate. High-speed printers, which are enjoying a widespread vogue at present, can emit several full-size books per hour, but if our computer output is the product of very many minutes of printer time, the uncomfortable probability is that we are misusing the computer, or at least formulating our questions inefficiently. Other techniques of display are not so far advanced, most computers lacking even an adequate cathode-ray scope for producing and copying graphs.

These difficulties in communication and access are by no means incurable and are attracting much attention. For example, though no such system exists today, real progress can be expected from a proposed system involving small satellite computers that communicate intermittently with a large central computer. Another move toward solving these problems is to construct instruments for elementary processing, editing, and conversion of data. The fundamental point to be made is that the "new information technology" is not just a euphemism for the large high-speed digital computer. It implies the ability to construct processing devices in response to specific demands, and in combination with whatever other techniques are appropriate.

The life sciences are still relatively remote from the computer. Consistently, the barriers to use of the computer are the bother and infrequency of communicative encounters and the fact that most biological observations are not naturally adapted to the limited means of input and output now available. The basic need is for adaptation of the technology to the life scientist's unique requirements, such as programing systems that fit naturally the problems and concepts of biology, and advances that will permit the scientist and the machine to communicate back and forth while an experiment is in progress.

These advances will come about only from the pressures that arises as life scientists try to use new techniques in the course of actual experimentation and fieldwork. The state of the art can be traced directly to efforts of the various groups—physicists, statisticians, businessmen—who have needed information processing devices badly enough to grapple with the problems of using them. Experience in the life sciences cannot be different.

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Part II. LIFE SCIENCES TECHNOLOGIES: AREAS OF NEED AND PROMISE

There are many procedural differences between technologies in the life sciences and in the physical sciences. The simplicity and elegance the physicist expected to find and which often served as criteria for the "truth" of a generalization are usually foreign to the study of complex interacting systems. For the biologist, observation and recording are often more difficult and often more subjective.

While traditionally the physical sciences have been indispensable for dissecting life processes into their physical and chemical reactions, they have offered little to the biologist whose principal concern is what is most peculiar to life, the behavior of the animal as "a whole," and the phenomena of growth, differentiation, and evolution. Recent developments in information technology and in the various technologies developed by the life sciences themselves have begun to erase the earlier distinctions. More and more parameters of living systems are coming under the sort of precise observation and control that have long been the hallmark of investigation in the physical sciences. In the following section, attention is given to specific subject areas in which the new technologies offer special promise.

Health Record Systems

The application of computer technology to the recording, storage, and analysis of data collected in the course of observing and treating large numbers of ill people promises to advance our understanding of the cause, course, and control of disease. The need for a general-purpose health information technology stems in large part from increasingly rapid changes in the pattern of illness in the United States and from equally significant changes in the way medicine is practiced. The acute infectious diseases from which the patient either recovered or died have largely given place to chronic disorders which run an extremely variable course dependent on many factors both in the environment and within the patient himself. The varying degree of disability allows and sometimes requires the sufferer to participate in the constant internal migration which is such a striking feature of modern life. The result is that records of medical observations and therapeutic procedures are compiled over long periods of time and at many different places.

The bulk of the recorded material is further increased by the complexity of modern medical treatment. Scientific advance has made it possible and relevant to observe many more variations in the functioning of the body and has required the distribution of the medical task among numerous medical specialists and technicians.

As the public has recently seen, there is a pressing need for evaluating new ways of treating disease. Many current therapeutic procedures have far greater power than those available a decade or two ago, but this new power is two edged. For example, a wonderworking drug may on occasion produce illnesses and malformations far more serious than the condition it is supposed to cure. The recent history of the introduction of thalidomide is only an unusually dramatic example of what may happen when any effective compound comes into widespread use without the most careful sort of preliminary appraisals. Some unfortunate side effects will always be found, but their devastation could be kept to a minimum by devising careful methods of distribution to trained experimenters and more comprehensive methods of observation. The new information technologies would appear ideally suited to prompt recording, analyzing, and reporting of any untoward effects.

Within any sizable community there are numerous administrative organizations charged with providing health services. It is not uncommon for a single patient to be cared for by a large number of agencies in a single city, and workers in any one agency usually cannot find out about the activities of others; sometimes they even fail to learn that other agencies are active at all.

Modern data-processing techniques make it possible to assemble all the necessary information about all the patients in a given geographical or administrative area in one place with rapid access for all authorized health and welfare agencies. Such a system would produce an immediate and highly significant improvement in medical care with a simultaneous reduction in direct dollar costs of manual record processing and an even greater economy in professional time now wasted in duplicating tests and procedures.

Even greater benefits will accrue from the use of such a file as a source of information for research in epidemiology and on the natural history of disease within individuals. But the value of such material for research is critically dependent on the coverage and accuracy of the original data. Much of the information in existing hospital records is unfortunately gravely defective both in quantity and quality. Later on we will have something to say about the development of automatic methods of recording laboratory analyses and certain elements of the physical examination, but even these promising possibilities cannot compensate entirely for human error in the collection of the all-important data on the origin and early course of any given illness. Here, one can only urge that medical schools redouble their efforts to train physicians in accurate methods of observation and recording. It may also be pointed out that the existence of machine methods for data analysis should serve as a stimulus to everyone responsible for the original data collection, much as the invention of the motortruck has required the truckdriver to master skills and exhibit habits of sobriety which were largely unknown to coachmen and stagecoach drivers.

Epidemiology has usually been associated with the study of the spread of an infection through a population, the tracking down of the causative agent, the examination of the interplay of factors determining natural resistance, and the appraisal of preventive and therapeutic measures. Similar methodology is now being extended to noninfectious diseases, such as mental illness, arteriosclerosis, and cancer. Indeed, epidemiology has proved its value in drawing attention to possible causative agents in a number of important diseases. Most dramatic perhaps is the association of tobacco smoking with the current high incidence of coronary heart disease and of certain kinds of cancer. The statistical study of large numbers of cases may be essential in assessing the relative importance with which many variables appeal to be involved in the etiology and pathogenesis of chronic diseases.

Human genetics can be viewed as a special case of epidemiological study in which genetic material is the controlling variable. Except in the simplest cases, genetic epidemiology requires the accumulation of data for several generations on related individuals. Occasionally, important questions can be answered by analyzing data on normal individuals and their living relatives. One simple example is the determination of mutation rates by observing deviations from the expected inheritance of normal blood groups. An extensive study of this sort, which depends on the recording of the blood groups of mothers and their children, is underway in Italy.

The importance of improving our knowledge of human genetics is self-evident, not only because of problems of chronic illness but also because of the questions arising out of our ignorance of human mutation rates and the influence on them of radiation and other mutagenic agents.

The collection of demographic data on which epidemiological studies are based has long been recognized as an obligation of government. The recently established National Health Survey enlarges this obligation to meet modern requirements. But the Survey needs to enlist the cooperation of many groups outside Government to make its efforts better known and more effective. Even more comprehensive efforts—involving more agencies (the Census Bureau and the Social Security Agency, for instance) and more sophisticated technology, especially in obtaining and recording basic health data—will be necessary in order to realize the potential benefits of epidemiological studies.

Diagnosis and Prognosis

That computers might aid physicians in the diagnosis of difficult cases has occurred to many physical scientists familiar with the capacity and speed of these instruments. We think that efforts to explore this potential should be more widely and actively supported.

It must be remembered, however, that the practice of clinical medicine is a combination of components which are measurable with components which are intangible. Communication between the physician and patient is so beset by such intangibles and the interpretation of critical histories involving so many personal judgments that the use of machine methods in the management of individual patients is likely to remain limited in the foreseeable future.

Perhaps the most important clinical potentiality lies in the ability of data processing techniques to provide analyzed information in the natural history of diseases in relation to varying constitutional and environmental factors. Such analyses are especially important for the understanding and management of chronic conditions in which the diagnosis is not closely coupled to prognosis or an understanding of etiology.

The prognosis for multiple sclerosis, for example, varies from as little as 1 year to 30 or even 40 years. On the basis of current knowledge it appears likely that coronary heart disease probably does not stem from a single identifiable cause but is rather the outcome of a complex interaction between genetic constitution, diet, and habits of life.

In such conditions, the physician needs to know the long-term relationship between the individual variables he observes now and the future course of the illness. Particularly important is the ability to predict the changes in course that might be expected in response to any one of several different therapeutic regimes. Physicians have long realized that different patients with the same disease follow different courses and respond differently to a given therapy.

Conventional methods of recording and storing the relevant information for solving the problems of prognosis and therapy have been inadequate, but mechanical data-processing now provides the means for making complex analyses. The difficulties in designing a useful system should not be underestimated. The mere recording of the necessary data in processable form will tax the capacity of the largest available computers. Much more difficult will be the myriads of decisions about what to record and the devising of accurate methods for recording it. While all this is going on still other workers must produce analytic programs involving logical problems of the greatest challenge. Finally, and most formidable of all, there is the human problem of persuading practicing physicians to change procedures and habits of mind which have proven themselves over centuries.

It is likely that the larger the body of data accessible to the machine the more useful it will be. An integrated nationwide system should be the ultimate objective, but the task of designing such a system is too enormous to be grasped at once. The problem must be divided into a progression of limited objectives, the initial steps of which need to be clearly defined.

Automatic Recording of Elementary Health Data

The utility of data processing and retrieval for the purposes discussed is dependent on the accuracy of the information originally obtained, the form in which it is recorded, and its pertinence to some stated objective. Now that effective processing of health data is on its way to becoming a reality it is more important than ever to find ways of (1) reducing observer and instrument errors, (2) standardizing the recording of observations, and (3) establishing in advance the usefulness and appropriateness of the data to be recorded.

At present, progress in the methodology of data collection and recording is lagging behind progress in the machinery of data processing. Automatic recording can both reduce the cost of recording elementary data and improve its accuracy. Already in the pilot stage, for example, is a device for recording the electrocardiogram, expressing it in digital form, carrying out the usual set of measurements, and comparing the results with a set of standards to provide a complete analysis and diagnosis. Less far along in development is a machine for carrying out all the standard clinical chemical analyses on a single small sample of blood with greater reliability and at a lower cost than is attainable by standard procedures.

Development of these promising methods and their extension to procedures for monitoring blood pressure and flow, the activities of the intestinal tract, skin temperature, and the electrical activity of the brain depend on collaboration between physicians, biologists, engineers, and mathematicians. The final section of this report makes specific recommendation for facilitating such cooperation. The emphasis here is on the importance of developing instrumentation as rapidly as possible to improve the quality and standardize the form of medical records for mechanical processing; to improve the quality and decrease the cost of medical care; and to extend scientific medicine to areas which now almost entirely lack the trained technicians to carry out laboratory studies in the old-fashioned way.

Biology of Behavior

Recent advances in the life sciences are establishing a base for understanding, predicting, and controlling the behavior of organisms. Progress is uneven, and the accumulated knowledge does not fit into a distinct pattern. Until recently, in fact, there has been little contact among the approaches made by several disciplines to the understanding of how and why animals behave as they do.

It is possible to discern a series of bridges between the tropisms of the biologist, the nerve impulses and reflexes of the physiologist, and the cognitions, perceptions, and memories of the psychologist. Somewhat to one side of this continuum, but by no means out of touch with it, is the develop-of getting one first-rate one has long been the plague of "interdisciplinary" programs.

Second, we recommend that existing graduate and postgraduate fellowships be administered in such a way as to encourage specialists in one field to acquire some experience, or possibly complete expertness, in another. The continuous type of support developed by the National Institutes of Health will be required.

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is needed. Under present rules and regulations such subcontracting is difficult to carry out effectively. Accordingly,

The Panel recommends that Government agencies responsible for support of the life sciences be encouraged to foresee needs for new types of instruments, and to support the development of such instruments both by direct contracts with industry and, where appropriate, by allowing grantee institutions to subcontract for such services.

Manpower and the Training of Scientists

Changes in traditional administrative arrangements, the provision of laboratory buildings, and so on, can provide a suitable environment for research, but the point of focus should always be the relatively small number of first-class human minds that will formulate the proper questions, develop the necessary apparatus, and manipulate the dials in the experiments. A question of first importance, then, is how to increase the number and quality of the scientists who can work comfortably and effectively in areas that require the synthesis of concepts and technologies derived from very diverse fields. Some few men will always be found who have mastered at least the elements of mathematics, physics, chemistry, and one or another of the special areas of the life sciences sufficiently to do the job of synthesis by themselves, but they will always be rare. Such individuals are capable of leaps into the future which provide the starting places for new sciences.

The Panel has two suggestions to encourage the development of personnel with the requisite capabilities.

First, we recommend a program of advance fellowships to enable certain individuals already thoroughly familiar with one discipline to be trained in another.

This program need not be a large one. Presumably, it could fit easily into the present fellowship programs of the National Science Foundation and the National Institutes of Health. Indeed, several such fellowships have already been given under existing arrangements. On the whole, it is probably wise to restrict such opportunities to individuals of outstanding quality. Anything less than the most careful selection presents the danger of attracting candidates who are failing to establish satisfactory careers in their original field and who nourish the hope that they will do better if they apply their partial mastery of one field to the problems of another. This effort to add two separate second-rate qualities together in the hope our universities in the development of modern research programs. The need is particularly critical for interdisciplinary groups, which have no departments to champion their needs. Contributions to building funds are at least as constructive and as much needed as are large research and training grants. Therefore:

We recommend increased flexibility in appropriations by Government agencies for construction and maintenance of university buildings for both teaching and research.

The Role of Industry

The panel sees two important roles for industry in the support of the life sciences. One is the development and sale of general- and special-purpose instruments. The other is research in areas closely related to the development of man-machine systems, such as large data-processing systems, or in areas that supplement the work in universities, institutes, and Government laboratories.

Under our system of private enterprise, the manufacture and distribution of standard scientific apparatus has been left almost entirely to private industrial establishments, while the design and development of new equipment is shared in a rather complicated way between industry and nonprofit research organizations. In general, industry is reluctant to embark on any project which does not promise to yield a return on investment within, at most, 5 years. The many relatively small companies that have recently grown up to exploit the development of new ideas, especially in the field of electronics, are, of course, strictly limited in their ability to support research with their own funds.

The Panel is convinced that both large and small industrial organizations have an important contribution to make toward the development of specialized apparatus for the new era in the life sciences. The policy adopted by the military services, of supporting necessary research on new equipment through contracts to industry, should be followed in the areas of life science equipment.

In some cases a particular new device can be easily foreseen to have a wide applicability—a machine for doing clinical biochemistry, for example. Contracts for the development of such items could appropriately be placed directly by a central agency such as the National Institutes of Health. In other instances involving the development of special-purpose instruments, the responsibility for initiating and supervising the work might better be delegated to a university department or research institute deeply engaged in the particular biological problem for the solution of which the new device

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salary, and tenure should be based on the individual's standing in his own field without regard for his professional competence in the nominal discipline represented by the department employing him. Ideally, personnel of this sort should be supported by the free funds of the university and not by outside grants.

The panel recognizes that many objections have been raised to contributions by the National Government to the free funds of universities. Nevertheless, in the belief that establishment of interdisciplinary appointments in certain areas of the life sciences is highly important to the national interest,

The panel recommends the use of Federal funds to support university appointments in such areas, with due provision for long-term support that would insure academic tenure where the latter is appropriate. As a possible, though perhaps less desirable, alternative, it suggests inclusion of such interdisciplinary positions in the present "career investigator" program of the National Institutes of Health.

The number of small- to moderate-sized interdisciplinary groups that might deserve support in universities during the next 5 years is not known, but most of the Nation's universities and colleges, including separate medical and engineering schools, could justify support of a unit in at least one of the subject areas, and at least half might wish to support units in two or more areas. Such a program should start in a small way, and grow.

Many existing interdisciplinary groups will need expanded laboratory facilities sometime during the next 5 years, and new groups will require extensive facilities. All the universities in the country are hard pressed to provide new buildings for housing and instructing a rapidly expanding number of students. Demands for research space have increased at an even greater rate, in response to the ever-growing complexity of research activity and the forced draft provided by greatly expanded research grants from Government and other sources. Until recently the universities have been expected to finance such construction from their own resources. Funds for building purposes are now provided through the National Institutes of Health in modest amounts and in a more restrictive way through the National Science Foundation. The matching provisions required in the distribution of these funds frequently prevent their use where the need is greatest, and no provision is included for maintenance. In regard to the latter point, some of the institutions which have been most enterprising in trying to respond to the Nation's needs for new university buildings now find that their maintenance budgets have increased so much that they must sharply curtail their plans for future expansion.

We feel strongly that lack of adequate funds for the construction and maintenance of buildings is one of the principal financial problems facing

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computation center greatly superior to one designed from purely a priori considerations.

The third concern about independent centers is their effect on the next generation of research workers. It is often impossible for such organizations to develop sound graduate training programs of their own, and by their very existence they tend to draw some of the best teachers away from universities, and thus away from students.

The Role of the University

One of the most likely places for productive interdisciplinary research groups to grow is in the larger universities, where ordinarily most of the important disciplines are represented and where there are opportunities for contacts between men in different departments. Furthermore, a university is accustomed to supporting work directed at long-term objectives. Unfortunately, the classical structure of most universities is not well adapted for encouraging interdisciplinary studies. Specialists in one field who elect to work on problems originating in another department may find difficulty in maintaining academic status in either. Clearly, the support of such work requires administrative flexibility and inventiveness in the development of university policies that will provide the proper setting for research, new appointments in developing fields, and changing combinations of disciplines to attack new problems.

One mechanism for circumventing the departmental structure is the establishment of "university appointments" that carry academic tenure and all the usual perquisites but allow the individual to work outside his department. So far this procedure has been limited to a few top-level appointments in a handful of outstanding universities, but, to judge from the results, further experimentation is desirable. At present, however, few universities command the funds to provide this type of program on a substantial scale.

Another mechanism is to create new institutes or departments within universities. Such organizations could share many of the defects of independent institutions. If, as is usually the case, the institutes draw a substantial part of their support from outside the regular university budget, the members of such groups are frequently regarded, both by themselves and by other members of the faculty, as occupying a special status—a fact that defeats rather than encourages cooperative work. Further, overemphasis on the research function will lead to the neglect of teaching.

While these handicaps can be overcome by administrative foresight and adequate, long-term funds, it may often be easier and just as effective, in the promotion of interdisciplinary work, to encourage existing departments to add personnel with the necessary qualifications. In such cases, status, At present the various elements in this complex process are pursued in more or less complete isolation from one another and receive their financial support from entirely different sources.

> *We therefore recommend that serious attention be given to setting up a suitable administrative mechanism to encourage and finance coordinated research on the process of learning and the application of such knowledge to education.*

Interdisciplinary Institutes or Centers.

We take a conservative view of attempts to solve the problem of interdisciplinary research at one blow. We have heard many suggestions for embarking at once on the creation of large, relatively independent centers for biological computation, bioengineering, and the like. We favor an orderly growth in close relation to existing institutions. The ultimate size and composition should emerge as a result of natural evolution.

There are at least three reasons for this view. In the first place, productive associations among scientists usually result from internal pulls rather than from external pressures. Almost always the original contacts grow out of mutual interest in a problem whose general outline has already been defined by one or more members of the group. The cooperation of others is then elicited through discussion of the possibilities. A key element is the willingness of all participants to accept redefinition of the original problem in terms of the additional disciplines represented by the new arrivals. Interchanges of opinion and attitudes of this sort involve an intimacy and mutual trust that cannot be created quickly or by administrative fiat.

A second reason for caution is the fact that few people have satisfactorily thought through the proper functions of such institutes. We are reasonably clear about the sorts of objectives that the life sciences may reach in the next several decades, but we have little more than an impression of how they are going to get there. For example, it seems certain that histories can be taken and physical and laboratory examinations can be made on patients in such a way that the results can be fed into a computer which will predict the future course of the individual's illness in response to a variety of treatments and do this far more accurately than is possible now. But not a single element in this complex process is available now. Primary emphasis must be given to working out the individual steps, and very probably this initial stage should be carried out by relatively small units.

There should be some contact among these units, but their association should be loose enough to allow each one considerable choice of method and direction. As solutions are reached, the need for new and more complex associations will become clearer and may lead to establishment of a medical and much planning. A few pilot studies are already underway, but they lack adequate financing and proper coordination with one another . Many of the relevant administrative groups that must ultimately be brought into the plan are scarcely aware of the possibilities. At present, the development even of pilot studies is in danger of falling between two stools. Research panels tend to brush them off as "not research," and public health groups dismiss them as insufficiently related to practice.

We recommend the establishment of a special standing committee or panel, located within the Department of Health, Education, and Welfare, to guide the development of a general-purpose health record system. This committee should broadly represent both the research and practical aspects of this problem, keep in close touch with new developments, acquaint the relevant agencies with the possibilities as they arise, and recommend allocation of funds for an orderly development of the new field.

Such a group would be primarily concerned with encouragement and support of agencies outside the Federal Government, but it should maintain close relationship with a similar panel, perhaps set up under the Federal Council for Science and Technology, to coordinate the efforts of Government agencies, the Department of Defense, the Veterans' Administration, and the United States Public Health Service, with responsibilities for the medical care of large numbers of people.

In the near future the sums needed should not be very large in comparison with the total spent on health, care, and research (perhaps a few million dollars per year). Much larger amounts will be necessary, particularly for capital equipment, as the system moves from the pilot phase to the stage of practical operation. Maintenance and operational costs, however, will be considerably less than those incurred by the increasingly inadequate pencil-paper, filing-cabinet, messenger-boy system we have at present.

Research on Learning and the Effectiveness of Education

The devising and applying of new technologies to education holds great promise. To realize this promise, much more research and development is needed. Research in the basic processes of learning should be brought more closely in touch with development of new classroom methods. Specialists in the content of the disciplines to be imparted must be brought into close cooperation with those who are primarily concerned with teaching, especially at the elementary and secondary level. Particularly important, perhaps, is the development of much better methods than we have now for evaluating the actual results of different teaching methods in practical classroom situations.

Our major recommendation is simple:

That the evolution of the life sciences toward increased involvement with the new technologies be recognized and its course facilitated.

We would first draw attention to the importance of providing support for planning and feasibility studies. Such studies might be at any one of several levels—the planning of a university unit for a computation center to be used in solving specified life sciences problems, the consideration of alternate designs for a major piece of apparatus, or the formulation of an interdisciplinary group.

Although most institutions have one or more persons versed in one or another facet of such problems, any new venture will require skills not available locally. Planning grants should provide, among other things, for the expenses of visiting consultants and for some of the local group to visit other institutions. Too often, private foundations and Government agencies have been reluctant to make grants for planning or feasibility studies on the grounds that these do not fall within the definition of "research" under which such groups are supposed to operate. This attitude led the late Alan Gregg to remark that it is usually easier to get a million dollars with which to do something than $10,000 with which to find out what would be worth doing. We recommend that advisory groups and research administrators be encouraged to support planning and feasibility studies, to be carried out by full-time teams of scientists and engineers. These projects could be implemented through appropriate grants or contracts to universities, private research groups, or industry.

Since so much of the promised technological revolution in the life sciences seems to depend on appropriate exploitation of computer techniques, we have given special thought to ways and means of giving both the present and the oncoming generation of biologists a "fingertip" familiarity with these new devices . We strongly endorse the plans of the National Science Foundation to make appropriate facilities available on a generous scale, and we recommend that the program be enlarged to include those liberal arts colleges with an interest in developing the ability to utilize computers effectively for educational purposes.

Health Records

In the health sciences, a general-purpose record system would serve to improve the quality, the planning, and administration of health services; to help in evaluation of comparative therapies; and to forward research on epidemiology and human genetics, and problems of diagnosis and especially on the natural-history of disease.

The development of such a system on a countrywide basis is a long-term objective that can only be reached after experimentation on a limited scale

Among contemporary stressful environments the space capsule commands overwhelming topical interest. The capsule constitutes, as the submarine did and still does, a special instance of the everyday problem of adapting machines to men, and vice versa. Considerable progress has been made in designing levers, dials, and other displays to fit human sensory and motor capacities and in training men in the new skills required by new machines. Man finds it difficult to make the adjustments required by the incessant transfer to machines of what were regarded as peculiarly human skills and capacities.

Massive technological change affects, however, not only man's interaction with his machines, but also the reciprocal relations between man and the world of men in which he lives. Automation and the concomitant pressures demand that we employ our best available techniques for analyzing the changing human condition and that we dare experiment—albeit under proper safeguards—in order to preserve human worth and dignity. We can hardly expect to attain this conservative goal unless we are willing to reexamine traditional value systems and to rethink and even redesign the functioning of human communities.

Part III. PLANNING AND IMPLEMENTATION

The preceding sections have outlined several areas in the life sciences which promise important advances. If society is to make the most of the benefits of scientific knowledge, it must take a conscious responsibility for the ordering of these advances. More effort must be made to foresee the results of new technologies before they burst upon us unannounced. More effort must also be made to develop new kinds of knowledge so that the new technologies can be better fitted to society's needs and purposes.

The subjects we have selected as illustrative examples involve close cooperation by individual scientists representing different disciplines. We feel that such cooperation is both desirable and urgent. While the necessary cooperative effort can scarcely be forced, neither can it be expected to arise fortuitously.

Fortunately, the basic mechanisms for the support of science in our country have been developed from a broad base. The young physical, biological, or behavioral scientist is receiving a sound education. The amazing advances within individual disciplines attest to the validity of this, but also make us impatient as it is clear that even more rapid advances could be made in areas of critical importance to our national welfare. We need to find a workable approach to the solution of problems requiring contributions of more than a single discipline.

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ments may well lead to disillusionment and a reaction that will block later acceptance of effective programs.

Admittedly, teaching devices can only contribute to a part of the educational process; how large a part no one can tell. They are emphasized because of their apparent effectiveness in certain circumstances, and even more because the method grows out of a large body of carefully controlled biological experiments on learning. Time-honored educational techniques and such recent innovations as movies, filmstrips, and television rest on a much less firm experimental base. Indeed, it is embarrassing to discover how little reliable information there is about the relative effectiveness of any teaching methods as employed in actual classroom situations. Much more research is needed both on the basic nature of human learning and on the practical problems of teaching.

Problems of Special Environments

Classical ecology has given us qualitative descriptions of the way in which living organisms exchange water, oxygen, carbon dioxide, and a number of other inorganic elements with the environment and of the means by which some species adjust their numbers to the existing means of support. Much is known about competition between species, the effects of crowding on fertility, dynamics, and cellular ecology, but quantitative work is in its infancy. A few workers have begun to apply modern instrumentation to the study of homogeneous groups of cells in tissue culture to control the composition of the substratum and the physical characteristics of the environment. The scattered results suggest that extension of these precisely controlled observations can tell us much about how cells interact with one another, differentiate in order to perform specialized functions, and form themselves into organ systems. As a byproduct, artificial cultivation of unicellular organisms has provided highly sensitive methods for assaying certain essential food elements in very dilute solutions.

Far too little is known about the interaction in complex mixed communities such as those that occupy an isolated arm of the sea. A given species may at one time contribute essential food elements for consumption by other members of the community, or it may at another time protect its living space by excreting a specific antibiotic. Since the number of species is very large, the permutations and combinations run far beyond conventional methods of analysis. Examination of such systems is important, not only because of their intrinsic theoretical interest, but also because of the possibility of increasing the production of food substances and biological products useful to man. New technologies should permit continuous monitoring and control of isolated environments. Once the significant parameters are defined, ecological studies should prove amenable to computer simulation techniques.

now possible to devise precisely defined situations in which experimental animals or, in some cases, human subjects can be made to produce new behavior patterns with a high degree of precision and at quite unprecedented speeds.

Beginning with such simple cases as the training of a rat to press a lever in order to gain the "reward" of a small bit of food, methods have been devised for manipulating the total environmental situation in such a way as to produce behavioral repertoires of great complexity. Technological advances in the analysis of behavior under total and continuous environmental control have had rather dramatic consequences. Behavior can be more accurately shaped and maintained for longer periods of time than was possible with conventional techniques. More complex situations can be established, and with considerably less time and effort. For example, a recent experimental report describes a sustained performance of two monkeys under complex conditions of choice and discrimination on a 1-hour-work, 1-hour-rest schedule 24 hours a day for approximately 2 years. The increased experimental control afforded by these advances in behavioral technology has made it possible to analyze the complex interactions between two or more organisms.

The concepts and principles of this type of experimental analysis of behavior are stated in terms of environmental variables. By confining itself to objective variables, such an analysis maintains the closest possible relations with other experimental sciences dealing with the same variables.

Teaching Machines and Programs

Techniques for continuous shaping of behavior by reinforcement are now used to teach human beings. They appear to facilitate the learning process and to save teaching time. The most obvious place for such methods is in the learning of factual material; for example, the multiplication table or certain routine industrial operations. Less obvious, but apparently quite real, is their effectiveness in imparting certain kinds of theoretical knowledge.

It is scarcely necessary to emphasize the importance of any method for improving teaching effectiveness. The most advanced countries are seriously short of capable teachers. The newly emerging nations are straining national budgets to provide perhaps a third, maybe as much as a half, of their children with teachers who themselves have scarcely mastered the elements of reading, writing, and arithmetic.

It is not surprising that any promising innovation in method is grasped with enthusiasm. Nevertheless, the construction of an effective teaching program demands painstaking effort and close cooperation by experts in the theory of the method, and scholars thoroughly familiar with the subject. Materials prepared and distributed without regard for these critical require-

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scribing the changes in operational terms have been opened—some precise enough to guide the synthetic chemist in the production of new compounds with more of the desirable and fewer of the undesirable effects.

The new substances are powerful tools for analyzing the function of the nervous system and promise much for the control of certain forms of mental illness. It appears, however, that much recent work has been undertaken in the search for quick results, while too little has been directed toward more fundamental understanding. In addition, behavioral techniques for measuring more exactly, in animals and men, the changes produced by these drugs, need to be improved.

Genetic Background of Behavior

Although much "common sense" observation and a good deal of scattered scientific analysis point to the importance of genetic factors in the determination of behavior, this field of study continues to lack cohesiveness and vigor. Here and there a psychiatrist has studied the family trees of patients with mental illness, a psychologist has developed a strain of highly aggressive or unusually shy mice, or a biologist has observed the assortment of behavioral characteristics in different strains of dogs. Some penetrating studies have been made by workers interested in the interaction of inborn and environmental factors in the development of reproductive and migratory behavior in birds. Much of this study has been carried out by zoologists in relative isolation from investigators interested in behavior. Interestingly, much of the financial support for the work on animal orientation and migration has come from the military services because of their concern with navigation.

Many behavioral scientists are preoccupied with the role of environment if not actually prejudiced against the consideration of genetic elements in the determination of complex behavior. The field as a whole is in need of more cooperative studies involving techniques drawn from all the relevant disciplines.

Learning

One of the most characteristic and at the same time most puzzling capacities of higher organisms is their ability to elaborate new patterns of adaptive behavior in response to outside stimuli. During the present century many investigators have sought to elucidate this capacity in a series of specialized experimental situations. Depending in part on the experimental procedures employed and in part on the school of thought represented by the experimenter, the results have been described in terms of memory, learning, or conditioned reflexes.

Although the mechanism of the process still largely eludes us, each school of thought has contributed considerably to an understanding of the conditions under which "learnings" occur. The overall result is that it is generated by the normal brain. Computer techniques are quite capable of solving the problems of analysis and correlation posed by such data, but in most instances produce their results several days after the original experiment has been completed. What the physiologist needs is equipment designed to meet his requirements for analyzed data in time to allow him to alter his procedures during the course of a single experiment. Development of such apparatus has proceeded far enough to demonstrate that ultimate success is within the reach of existing technology.

No matter how refined our methods for gathering and analyzing neurophysiological data become, they now seem unlikely to result in mathematical formulas for behavior similar to those that "explain" the physical world. But such data should provide the raw material for advanced simulation techniques. Indeed, some of the most intellectually stimulating work going on at present seeks to explore the processes of man's own mind. There are several approaches. One can try to find out the actual processes a man uses to solve a problem or compose a poem and then simulate those particular processes, judging one's success by direct comparison of the results. One can also examine other processes, such as the recognition of visual or auditory patterns, and try to construct a process that will produce the same results. Even when they are successful in reproducing the result of a given form of mental activity, such simulations provide no assurance that the intervening processes are the same in simulator and simulated. Nevertheless, such work should prove a rich source of hypotheses for understanding processes that, until now, have remained discouragingly obscure. Conversely, the probability is worth noting that, as the neurophysiologist learns more about the neural networks involved in perception, learning, and memory, he may provide useful suggestions to those interested in designing computers to perform ever more difficult and complex tasks. To a large extent, this two-way interaction will require that the languages used by the different fields of science coincide to a much greater degree than they do now. The dialog is being aided by the digital computer, but there is a long way to go.

Neuropharmacology

Man has sought for centuries to alter his feelings and capabilities by the ingestion of alcohol, opium, or caffeine, but only recently has it become possible to describe behavioral effects precisely enough for controlled experimentation. This development coincides with the production of a range of new substances by synthetic chemistry. We can now identify classes of compounds that allay or induce anxiety, increase or decrease depression, induce or delay sleep, and produce confusions of thought closely analogous to those that occur in psychotic breakdown. Admittedly, however, instruments for measuring such phenomena are primitive. Promising leads de-

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ment of methods for studying the genetic and environmental determinants of social interactions in insects, birds, and mammals.

Since another panel* has provided an account of the behavioral sciences as a whole, we have limited ourselves to considering new technologies, many of which have been developed specifically for the solution of specialized problems.

For the first time there is reason to suppose that the process of simulation will play a role in the future development of biology analogous to the role that mathematical analysis has had in modern physics. In the physical sciences, mathematics provides conceptual models of great generality, utility, and elegance. Similar formulations are rarely applicable to biological phenomena determined as they are by large sets of interdependent variables. When provided with a suitable program, the computer may be used to model such complex systems and to deliver detailed data on the probable effects of proposed alterations in the value of the several variables that compose the system. Already the use of simulation has been explored in systems ranging from nerve cells to economic models and, as the accessibility of computers increases, simulation should become a major theoretical tool throughout the life sciences.

The first three subjects considered here—neurophysiology, neuropharmacology, and the genetics of behavior—are primarily concerned with the characteristics of the organism and provide an understanding of behavior in terms of the intrinsic properties of the behaving system. The second group is concerned with behavior in terms of input-output analysis and gives less emphasis to events within the organism.

Classical neurophysiology has built up a useful body of knowledge about the routine functions of the nervous system. Much is known about the characteristics of the nerve impulse, the distribution of different classes of sensory information within the nervous system, and the patterns of motor responses elicited by simple stimuli. An exciting recent development is the means for studying the neurological correlates of complex adaptive behavior—the recognition of patterns of stimuli, the learning of new responses, and the storage of learned material in memory. This development has involved the invention of methods for sampling neural activity by implanting arrays of very small electrodes deep within the brain and simultaneously displaying the electrical signs of such activity from many different locations. Such experiments result in an embarrassingly large number of records. Each signal must be laboriously measured and compared by hand and eye. In many cases significant evoked activity is obscured by the large number of apparently random signals continuously

*"Strengthening the Behavioral Sciences and Improving Their Use," report to the President's Science Advisory Committee, dated Feb. 20, 1962, published in Science magazine, Apr. 20, 1962, vol. 136, No. 3512.