A Quarter Century in the Natural Sciences

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SPEAKING ROUGHLY, one may say that the 17th, 18th, and 19th centuries formed the period in which physical science learned how to analyze two-variable problems. During that 300 years, science developed the experimental and analytical techniques for handling problems in which one quantity—say, a gas pressure—depends primarily upon a second quantity—say, the volume of the gas. The essential character of these problems rests in the fact that, at least under a significant range of circumstances, the first quantity depends wholly upon the second quantity, and not upon a large number of other factors. Or in any event, and to be somewhat more precise, the behavior of the first quantity can be described with a useful degree of accuracy by taking into account only its dependence upon the second quantity, and by neglecting the minor influence of other factors.

These two-variable problems are essentially simple in structure, this simplicity resulting largely from the fact that the theories or the experiments need deal with only two quantities, changes in one of which cause changes in the other. The restriction to two variables, and in most cases to simple relations between the variables and their first and second derivatives, kept the theoretical system well within the then analytical and computational capacity of mathematics. Correspondingly, there could be simplicity in the experimental basis; and simplicity was a necessary condition for progress at that stage of development of science.

It turned out, moreover, that vast progress could be made in the physical sciences by theories and experiments of this essentially simple character. The physicists of this period could analyze how the intensity of light varies with the distance from the source; how the strength of a beam depends upon its dimensions or upon the physical properties of its material; how electric current is related to voltage or resistance; how gravitational attraction depends upon distance; how steam pressure is related to steam temperature; and hundreds of other such things. The resulting knowledge made possible great advances in our understanding and control of nature, great practical advances in technology. It was this kind of two-variable science which laid, over the period up to 1900, the foundations for our theories of light, of sound, of heat, and of electricity. It was this kind of two-variable science—or minor extensions of it to handle three or four variables—which brought us the telephone and the radio, the automobile and the airplane, the phonograph and the moving pictures, the turbine and the diesel engine, and the modern hydroelectric power plant.

The concurrent progress in biology and medicine was also impressive, but was of a different character. The significant problems of living organisms are seldom those in which one can rigidly maintain constant all but two variables. Living things are more likely to present situations in which a half-dozen, or even several dozen, quantities are all varying simultaneously and in subtly interconnected ways. And often they present situations in which some of the essentially important quantities are either non-

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quantitative, or have at any rate eluded identification or measurement up to the moment. Thus these biological and medical problems often involve the consideration of a most complicatedly organized whole.

Between the living world and the physical world, moreover, there is a critical distinction as regards dissectability. A watch spring can be taken out of a watch and its properties usefully studied apart from its normal setting. But if a heart be taken out of a live animal, then there is a great limitation on the range of useful studies which can be made.

It is not surprising that up to 1900 the life sciences were largely concerned with the necessary preliminary stages in the application of the scientific method—preliminary stages which involve collection, description, classification, and the observation of concurrent and apparently correlated effects. They had only made the brave beginnings of quantitative theories, and hardly even begun detailed explanations of the physical and chemical mechanisms underlying or making up biological events.

To sum up, physical science before 1900 was largely concerned with two-variable problems of simplicity; while the life sciences, in which these problems of simplicity are not so often significant, had not yet become highly quantitative or analytical in character.

Problems of Disorganized Complexity

Subsequent to 1900—and actually earlier, if we remember heroic pioneers such as Josiah Willard Gibbs—the physical sciences developed an attack on nature of an essentially and dramatically new kind. Rather than study problems which involved two variables or at most three or four, some imaginative minds went to the other extreme, and said: "Let us develop analytical methods which can deal with two billion variables." That is to say, the physical scientists (with the mathematicians often in the vanguard) developed powerful techniques of probability theory and of statistical mechanics which can deal with what we may call problems of disorganized complexity.

This last phrase calls for explanation. Consider first a simple illustration in order to get the flavor of the idea. The classical dynamics of the 19th century was well suited for analyzing and predicting the motion of a single ivory ball as it moves about on a billiard table. In fact, the relationship between positions of the ball and the times at which it reaches these positions forms a typical 19th century problem of simplicity. One can, but with a surprising increase in difficulty, analyze the motion of two or even of three balls on a billiard table. There has been, in fact, considerable study of the mechanics of the standard game of billiards. But as soon as one tries to analyze the motion of 10 or 15 balls on the table at once, as in pool, the problem becomes unmanageable, not because there is any theoretical difficulty, but just because the actual labor of dealing in specific detail with so many variables turns out to be impracticable.

Imagine, however, a large billiard table with millions of balls flying about on its surface, colliding with one another and with the side rails. The great surprise is that the problem now becomes easier: the methods of statistical mechanics are now applicable. One cannot trace the detailed history of one special ball, to be sure; but there can be answered with useful precision such important questions as: On the average how many balls per second hit a given stretch of rail? On the average how far does a ball move before it is hit by some other ball? On the average how many impacts per second does a ball experience?

Two paragraphs back it was stated that the new statistical methods were applicable to problems of disorganized complexity. How does the word "disorganized" apply to the large billiard table with the many balls? It applies because the balls are distributed, in their positions and motions, in a helter-skelter—that is to say, a disorganized—way. For example, the statistical methods would not apply if someone were to arrange the balls in a row parallel to one side rail of the table, and then start them all moving in precisely parallel paths perpendicular to the row in which they stand. Then the balls would never collide with each other nor with the end rails; and one would not have a situation of disorganized complexity.

We can see, from this illustration, what is meant by a problem of disorganized complexity. It is a problem in which the number of variables is very large, and one in which each of the many variables has a behavior which is individually erratic, and may be totally unknown. But in spite of this helter-skelter or unknown behavior of all the individual variables, the system as a whole possesses certain orderly and analyzable average properties.

A wide range of experience comes under this label of disorganized complexity. The method applies with increasing precision when the number of variables increases. It applies with entirely useful precision to the experience of a large telephone exchange, predicting the average frequency of calls, the probability of overlapping calls of the same number, and so forth. It makes possible the financial stability of a life insurance company. Although the company can have no knowledge whatsoever concerning the approaching death of any one individual, it has dependable knowledge of the average frequency with which deaths will occur.

This last point is interesting and important. Statistical techniques are not restricted to situations where the scientific theory of the individual events is very well known—as in the billiard example where there is a beautifully precise theory for the impact of one ball on another. This technique can also be applied to situations—like the insurance example—where the individual event is as shrouded in mystery as is the chain of complicated and unpredictable events which leads to the accidental death of a healthy man.

The examples of the telephone and insurance companies will suggest a whole array of practical applications of such statistical techniques. But they are in a sense unfortunate examples, for they tend to draw attention away from the more fundamental use which science makes of these new techniques. The motions of the atoms which form all matter, as well as the motions of the stars which form the universe, all come under the range of these new techniques. The fundamental laws of heredity are analyzed by them. The laws of thermodynamics, which describe basic and inevitable tendencies of all physical systems, are derived from statistical considerations. The whole structure of modern physics, our present concept of the nature of the physical universe and of the accessible experimental facts concerning it, rests on these statistical concepts. Indeed, the whole question of evidence, and the way in which knowledge can be inferred from evidence, is now recognized to depend on these same ideas. During the last years we have also come to realize that communication theory and information theory are similarly based upon statistical ideas. One is thus bound to say that probability notions are essential to any theory of knowledge itself.

Problems of Organized Complexity

And yet this statistical method of dealing with disorganized complexity, so powerful an advance over the earlier two-variable methods, leaves a great field untouched. One is tempted to oversimplify and say that scientific methodology went from one extreme to the other—from two variables to an astronomical number—and left untouched a great middle region. The importance of this middle region, moreover, does not depend primarily on the fact that the number of variables involved is moderate—large compared to two, but small compared to the number of atoms in a pinch of salt. The problems in this middle region will, in fact, often involve a considerable number of variables; but much more important than the mere number of variables is the fact that these variables are all interrelated. That is to say, the really important characteristic of the problems of this middle region which science has as yet little explored or conquered lies in the fact that these problems, as contrasted with the disorganized situations with which statistics can cope, show the essential feature of organization. We will therefore refer to this group of problems as those of organized complexity.

What makes an evening primrose open when it does? Why does salt water fail to satisfy thirst? Why is one chemical substance a poison when another, whose molecules have just the same atoms but assembled into a mirror-image pattern, is completely nontoxic? Why does the amount of manganese in the diet affect the maternal instinct of an animal? What is the description of aging in biochemical terms? What meaning is to be assigned to the question: Is a virus a living organism? What is a gene, and how does the original genetic constitution of a living organism express itself in the developed characteristics of the adult? What happens when previously normal cells suddenly start the uncontrolled growth we call cancer? Why can a salamander regenerate an amputated limb, whereas a man cannot? How does the DNA molecule reproduce itself, and just how does it store genetic information?

All these are certainly complex problems. But they are not problems of disorganized complexity, to which statistical methods hold the key. They are all problems which involve dealing simultaneously with a sizable number of factors which are interrelated into an organic whole. They are all, in the language here proposed, problems of organized complexity.

On what does the price of wheat depend? This too is a problem of organized complexity. A very substantial number of relevant variables is involved here, and they are all interrelated in complicated but nevertheless not in helter-skelter fashion.

How can we compare the social costs and the social gains to be expected from the continuation of atomic weapon testing? What are the total biological dangers involved in man's exposure to all sorts of radiations?

How can currency be wisely and effectively stabilized? To what extent is it safe to depend on the free interplay of such economic forces as supply and demand? Or to what extent must we employ systems of economic control to prevent the wide swings from prosperity to depression? These are also obviously complex problems, and they too involve analyzing systems which are organic wholes, with their parts all in close interrelation.

How can we explain the behavior pattern of an organized group of persons such as a labor union, or a group of manufacturers, or a racial minority? There are clearly many factors involved here, but it is equally obvious that here also we need something more than the mathematics of averages. Indeed if we only could, in the biological field, begin to learn how to deal with problems of organized complexity, then there might be opportunities to extend these new techniques, if only by helpful analogy, into vast areas of the behavioral and social sciences.

By the early thirties it was clear that science had generally effective tools and techniques for dealing with problems of simplicity, and problems of disorganized complexity. Advances falling under these broad categories continued to be highly important and highly desirable; but there was every basis for expecting that these advances would occur without the stimulation of special or additional financial support. Speaking in very broad terms, this meant that man's conquest of physical nature—so large a part of which comes under the two categories just stated—was certain to move forward and in fact with increasing momentum. But was the time ripe for stimulating advances in the more complex, more difficult, and in many ways more critical areas which, although involving many dissectable problems of the two simpler sorts, essentially involved problems of organized complexity? Was the time ripe for an accelerated and deeper attack upon the life sciences? . . .

Separating and Identifying

If biology presents, for the most part, problems of organized complexity, then one must expect any piece of living matter to contain a vast number of individual substances, all tangled together in an intimate interrelation. But this kind of complexity remains a mystery until one can, in some way, untangle the mess, separate out parts that are themselves homogeneous, and find out what these separate parts are. So separation is a basic procedure in attacking biological problems. . . .

That wise applied biologist, the gardener, preparing his potting soil, puts it through a screen to separate out the pebbles and the weed roots. Screening—or its finer form, filtration—has been useful to the sanitary engineer, and to the biologist also. But it illuminates the character of recent biological advances to remember that a quarter century ago the name "filterable virus" was used precisely to emphasize that one was dealing with an infective agent which would pass right through the filters which successfully screened out bacteria. At that time the virus particles remained unseen—now we take them apart and put them together again!

Thus first in our list of newer methods of separation we should note the improvements in the ancient procedure of screening. Modern science and technology now makes available cellulose ester filters of remarkable porosity (up to 80 or even 85 percent) with a range of carefully controlled pore sizes. One can have pores of five, or three, or one, or one-half of a ten-thousandth of a centimeter, to use with bacteria; or even pores as small as a millionth of a centimeter to use with viruses; and in all of these the variation in pore size need be only about 10 percent.

The centrifuge, familiar to the dairyman who separates the cream from the milk by utilizing their difference in density, has been developed over the period under review into a most powerful tool for separating out the various component particles, differing in density, which are suspended in or go to make up a liquid. . . .

Ultracentrifuges are now produced in several places in the world. The most advanced American model, not very much larger than an old-fashioned upright piano in size, is an instrument of great precision and delicacy, which has been engineered to dependability even when used by nonspecialized operators.

Although the technique of high-speed whirling is quite different, being produced by a combination of electrical and magnetic effects, the mass spectrometer is in reality a close relative of the ultracentrifuge, separating and identifying the various atoms of different weights in a mixture. It has been used in studies of respiration, and is invaluable in connection with biological tracer experiments which utilize stable, rather than radioactive, isotopes. . . .

For two things to be separable from each other, they have to differ in some way, and this difference must be exploited as a sort of handle which permits the scientist to pick up the one and leave the other. Size is such a difference, and furnishes the handle for filtering methods. Density is such a difference, and furnishes the handle for centrifugation. But a difference which can be variously exploited, which is capable of very delicate discrimination, and which is related in a revealing way to the nature of the thing being separated, is furnished by electrical properties such as charge, distribution of electric charge, magnetic strength, and so forth.

One such method, useful both for identification and separating, is the modern procedure of electrophoresis. The basic principle is an old one, and is due to observations made in 1809 by the Russian physicist F. F. Reuss. But the modern development dates only from the mid-thirties, and is due very largely to the brilliant researches of the Swedish physical biochemist, Arne W. K. Tiselius.

If a conducting liquid, containing several or many kinds of permanently suspended colloidal particles, is located in a horizontal tube, and if an electrical potential difference is established between the two ends, then there is a voltage gradient at every point in the liquid that urges charged particles to drift in the liquid, the force being the larger, the larger their charge. By taking a suitable type of photograph at a suitable time one observes the whole range of kinds of particles, separated out in bunches like the slower and faster horses at the finish of a race. It will of course be recognized that this is a very crude description. In the course of years of experience and of instrumental development, electrophoresis has come to be a method of very great power and usefulness.

An extraordinarily useful and interesting set of procedures which involve identification, although normally not separation, depends upon the obvious fact that tiny experimental creatures such as bacteria or fungi are available in large, willing, and rapidly replenished numbers, and upon the further not at all obvious fact that they have chemical skills which no human chemist possesses.

If, for example, one studies a large number of micro-organisms (the red bread mold *Neurospora crassa* is a now classic example, although the method is only about 20 years old) some of these turn out to be mutant strains, this meaning that one of the creature's genes has become altered. According to the present view, certain genes are responsible for the possession by the organism of certain enzyme systems; and in some instances at least, one gene controls one enzyme. If this gene is altered, the mutant strain of the fungus would lack that particular enzyme.

Now this tiny and lowly creature, in order to live, carries out a great many chemical tasks.

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It can take a number of relatively simple chemical substances and link them together into some larger and more complex substance which it requires; or it can take large and complex material which is unusable in its complete form, and split it up into useful parts. Each one of these individual steps of joining or splitting is activated by one special enzyme. Whereas a human organic chemist can carry out multitudes of chemical reactions, an enzyme system (generally speaking) can carry out only one specific chemical operation. But it may be a job which no human chemist can do; and it is, moreover, easy to exploit the fact that each enzyme is such a specialist.

For suppose one has produced (by irradiating with X-rays, for example) a lot of mutant strains of *Neurospora*. Suppose these have been sorted out, and a strain isolated which cannot live unless the food furnished to it contains a supply of, say, the B vitamin thiamine, whereas the normal strains do not require thiamine since they possess an enzyme which is a specialist at making thiamine from other material.

This thiamine-requiring mutant strain (which incidentally breeds true so that it can be maintained in the laboratory) is now ready to go to work for the scientist. If he has a sample of mixed-up material, and wants to know whether or not it contains thiamine, he merely introduces the sample into a thiamine-lacking food supply and offers it to the mutant strain. If the fungus prospers, then the mess contained thiamine; otherwise, not.

A single example of this sort is likely to sound like a tour de force; but actually there are numerous and highly useful ramifications of this general technique. The chemist has, for example, isolated and purified enzymes; and he can then himself use one of these to split some large and complex molecule, confident that the precise inanimate specialist he is using is carrying out the operation in just that one place, in the whole structure of the molecule, where it is known to be able to operate. . . .

Before closing this section on separating and identifying we must pay tribute to one of the most dramatic successes of this period—the development of chromatography. This is in fact a kind of screening procedure, so that in a very broad sense we return to the topic which started this section. But the screening, here, does not depend on size.

Just over 50 years ago a young Russian botanist, Michael Tswett, found a way of separating out the various pigments of a green leaf. He packed a fine, white powder (usually calcium carbonate) into a vertical glass tube, poured into the top of the tube a petroleum ether extract obtained from mashed-up green leaves, and let this complex mixture seep down into and through the tube. The marvel was that various components of the pigmented mixture—components of different shades of yellow, orange, orange-green, and so forth—separated out and produced, on the previously pure white column, a Roman stripe pattern of various shades and colors, each layer of the striped pattern having a sharp boundary. The whole core of the tube could then be pressed out and sliced up into the various layers, from which the separated-out fractions (in this case the various types of chlorophyll pigment) could be dissolved. Subsequent evaporation produces the material in crystalline form—the chemist's hallmark of purity.

This amazing discovery was used only a few times between 1906 and the beginning date of this review; but chromatography, in its present greatly improved forms, is now one of the most powerful tools in the hands of the chemically minded biologist. It promptly turned out that this method of separation, almost mysterious in its simplicity and its ability to deal with complex mixtures which defy ordinary chemical means, was not restricted to colored dyes, but could be used for a wide range of materials. It can be used not only for liquids or dissolved solids but also for gases, and this rather recent extension of the method has proved specially valuable. It is so gentle a procedure, chemically speaking, that it can handle very unstable and elusive substances, this being a great advantage to the biologist.

Extremely clever automatic devices have been developed to collect the various fractions of a complex mixture as they drip out, one after another, from the bottom of a Tswett column.

British workers, 14 years ago, perfected a simplified method. A drop of the mixture to be separated is put on one corner of a vertically suspended sheet of special filter paper, and the adjoining horizontal edge of the paper is placed in contact with a suitable solute. As the solute spreads out, like moisture spreading in a sheet of blotting paper, the soluble fractions of the drop mixture move in the dampened paper (just as the fractions move in the dampened column of the original method), coming to rest in different places to form a vertical line of spots. The separation of the spots occurs because of the fact that the different fractions move with differing speeds. The sheet is then turned through 90°, and the then horizontal edge next to the line of spots is brought into contact with a second solute. Again the solute spreads, and the soluble fractions of the mixture move, again at varying speeds, coming to rest in a pattern which now extends over the entire sheet of paper. The paper, after it is dried, is then sprayed with some chemical that makes visible (colored) the various spots, or the paper is viewed by ultraviolet light; and the net result is a two-dimensional set of colored spots which visually exhibits the recipe of the original mixture, telling just what constituents it contained.

In a brilliant modification, developed by Melvin Calvin, a complex mixture containing certain molecules labeled with radioactive atoms is separated by the two-dimensional paper method, and the dried chromatogram is then placed in contact with X-ray film, for 2 weeks or so. The radioactive spots affect the film, and, so to speak, "take their own picture."

The method can be used with as little as a fraction of a milligram of material, and tricks have been developed which make possible not only separation and identification, but also measurement of the amount of each constituent. . . .

New Ways to See

Even more spectacular than the new ways to separate are the developments which give the biologist new ways of seeing; and among these the most obvious and also one of the most important is to be found in the modern improvements in microscopy. . . .

The limitation of the ordinary light microscope can be relieved somewhat by using ultraviolet light, since it has a wavelength about half that of ordinary visible light. In the mid-thirties the uv microscope was being perfected, especially by Swedish workers, and it did reveal details about twice as fine as those which could be studied previously.

But the great advance in resolution—which is the technical term for the capacity of a seeing device to discriminate fine detail—came from the development of the electron microscope. Utilizing the fact that electrons behave like light of wavelength less than one-thousandth that of ordinary light, instruments have been developed which can handle detail down to a ten-millionth of a centimeter. This whole instrumental development has occurred over the period here under review. . . .

Since that time the "e. m." has become such a generally useful and standard device that it goes by this familiar nickname; and the present pattern of use is not a single instrument for a university, but often two or more for a department. Only a few years ago a resolution of 50 Å (an Ångstrom is one hundred-millionth of a centimeter) was considered excellent, and there was in the whole world only one manufacturer of electron microscopes. Now these devices are made not only in the United States but also in England, Holland, Germany, and Japan. It is understood that the Japanese instrument is now guaranteed to give a resolution of 10 Å, this being at the level of size which begins to deal directly with the largest molecules. This resolution is also achieved, under optimum circumstances, with other makes of instruments. . . .

There are still further variants such as the reflecting microscope; fluorescent microscopy; the "flying-spot" microscope which can scan living material with ultraviolet light, pausing such a short time at any one place that the specimen is not killed; and the linking up of microscopy with the picture tube of television, so as to obtain a large image that can be seen by many persons at once. . . .

Still more indirect ways of "seeing" have been developed in recent years. One of these is the method of X-ray and electron diffraction. Suppose that every person who goes through the main concourse, upper level, of Grand Central Station in New York City carries a lighted candle; and suppose that a large camera, located in the ceiling and pointed toward the floor, records the path of each one of these spots of light but shows nothing else. If the exposure were kept up until many hundreds of persons—light tracks on the film—had passed through, then by studying this film one could deduce that in the center of this great concourse is a special impenetrable region, whose size and shape would become more and more definite as more and more light tracks were photographed. Certain light spots would go up to this region, and then start off in other directions. Other light spots would veer around this region; but none would go through this region. Gradually, as the evidence accumulated, a person who has never been in Grand Central Station, who has seen only these photographs of light tracks, would begin to "see" the size and shape of the information booth in the center of the concourse.

In a way which is only very roughly similar, a scientist can take an unknown structure built out of atoms, pass through this structure a very large number of light particles (X-rays) or electrons, make a photograph which shows the pattern in which the light particles or electrons emerge, and then in a very complicated, very tedious, most ingenious way, he begins to get ideas about the details of the structure through which the light particles or electrons have passed. He has a much harder job than our cameraman in Grand Central. He does not have a picture of the lights going through the structure, but only the pattern in which they emerge; and he is dealing with a three-dimensional structure which may easily contain thousands of atoms, each of which must be located. He cannot, by any rigorous and straightforward way, calculate what that structure is. He can only get hunches of what it might be; and then rigorously calculate what effect this assumed structure would have on a lot of light particles passing through. Only by an incredible miracle would the first hunch turn out right; so there must be months or even years of trial and error. The organic chemist, the biochemist, and the physical chemist help him a great deal, telling him how many of what kinds of atoms he is dealing with, discouraging certain guesses which they know to be unlikely, suggesting certain guesses which their chemical knowledge makes probable. And out of all of this, with skill and art and patience, with inspired guess and with laborious check calculations, using all the aid that can be furnished by modern computing devices, comes an eventual knowledge of the detailed arrangement of the atoms which make up the structure which has been under study.

The culmination of this is a three-dimensional drawing of the structure. The X-ray diffraction or the electron diffraction expert has succeeded in "seeing" the structure—but in how indirect and sophisticated a sense! . . .

These remarks have by no means exhausted the ways, either unknown in 1932 or at least greatly refined since then, which enable the present-day scientist to "see" the revealing details, down to the molecular or even atomic scale, of the structures which are important to the biologists. The very recent methods of nuclear paramagnetic resonance and electron spin resonance are in essence spectroscopic procedures; but have the great advantage to the biologist that information can be obtained about the free radicals in wet biological material.

The labeling of compounds with radioactive isotopes enables the scientist to trace them as they move about in a biological system, sometimes actually by hearing them as they produce clicks in a counter, and sometimes by "seeing" them as they register their positions on a photographic film through autoradiography. In a somewhat similar way it is possible to stain antibodies with a chemical which fluoresces when ultraviolet light impinges, thus making the antibodies visible through photography. Seeing, incidentally, has been greatly improved by the development of photographic emulsions of great speed, finer grain, and sensitivities to various forms of energy which do not directly affect the human eye but which are made humanly visible by the photochemical reactions in the emulsion. The way in which light is scattered by particles of various sizes, shapes, and electrical properties has been most usefully exploited to enable us to "see" these sizes and shapes. And modern electronic techniques have been used to intensify weak optical images, such as might be produced in the X-ray of a difficult region, to reveal otherwise invisible detail.

A great many of the newer tools of the biologist come under the headings we have already considered, of separation, identification, and seeing; but there are additional ways in which the chemist, the physicist, the engineer, and the mathematician are aiding in the exploration and analysis of living matter.

The more modern aspects of this service began less than 40 years ago when Pregl developed methods for the microchemistry of organic compounds. These classical microchemical methods are able to accept a bit of matter only a millimeter in dimension and only a thousandth of a gram in weight, and determine the sorts and amounts of the individual chemical compounds it contains. But under the demands of present-day biology (and also through the work of the chemists who are associated with atomic and nuclear researches, and who also have to deal with very small amounts of material) it is possible to carry out limited chemical analyses of samples which measure not a millimeter, but a tenth or even a thousandth of a millimeter, and whose weight is not a thousandth of a gram, but a millionth of a gram. Indeed some sort of estimates of chemical composition can be made on samples even smaller than this. . . .

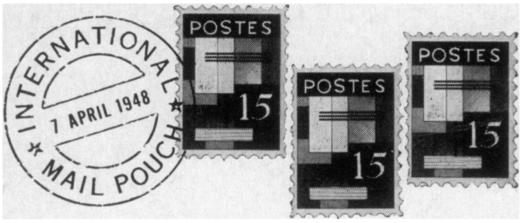
It is of the most characteristic significance, relative to the movements in modern biology, that in many instances the underlying facts are now being successfully explored at the submicroscopic scale of molecular and even atomic dimensions. Biological ultrastructure has become a recognized and rich field. For several years now a term has been used, seriously and in an operational sense, which in 1932 would have been used only with imagination and hope—molecular biology.

A great deal of the information about biological material at this new scale of smallness consists of knowledge about structure. This knowledge has to a great extent been made possible by the procedures and instruments which have been reviewed in the preceding sections. The organic chemists interested in natural products, the physical chemists interested in macromolecules, the specialists in X-ray and electron diffraction, the micro- and submicroanatomists, the molecular biologists, the ultramicroscopic cytologists, the physiologists and biophysicists concerned with life at the smallest scale, the electron microscopist, and many others have all played essential and often interlinked roles in developing the new knowledge about the ultrastructure of living material. . . .

For centuries it has been considered that physical nature is orderly, that it is subject to discoverable laws, and that it may be brought under a considerable degree of control through the study of its problems of simplicity and its problems of disorganized complexity. But it has not only been recognized that the phenomena of life present problems of organized complexity; it has also been considered by many that these phenomena of life are, in some dark and foreboding way, irrational. Indeed, some have gone even further, and have believed that vital phenomena are not only inaccessible to scientific investigation, but are improper and impious objects of any such attempt. This is an old attitude, which centuries ago forced the Italian anatomists to steal corpses in order to carry out their studies.

Even during the magnificent progress made in the last century by the medical sciences, there continued the attitude that certain gross and relatively simple disorders of man were analyzable and curable; but that man as a conceiving, childbearing, thinking, remembering, behaving, growing, and finally dying organism presented problems that were in large part outside the range of rational analysis. The last quarter century has seen a considerable reversal of this view.

We can be well satisfied if this Program in Experimental Biology of The Rockefeller Foundation has helped in a small way to demonstrate that the living world, in its most intimate details, exhibits discoverable rationality and orderly beauty; and that the tools of science are just as effective here as they have proved to be in the purely physical world. Indeed one no longer wishes to insist that man is alien to the universe in which he exists. It involves no belittlement of his higher self to recognize that his body is brother to the molecule and the star.



Carabao Cart to Tractor

Many municipal public health officers in the Philippines are beset with complaints about uncollected and spilled refuse, odors from rotting garbage, flies and rodents near open dumping areas, and smoke from refuse burning at dumps. The complaints stem from improper storage of refuse at collection points, obsolete vehicles or lack of vehicles, and faulty disposal methods.

Cities which have won prizes during National Clean-up Week, observed annually for the last several years, are those which have developed effective and sanitary refuse disposal. Baguio started incinerating refuse a number of years ago and in 1959 began using sanitary landfills to get rid of excess waste and reclaim land. The city of Cavite contracted for the task, after competitive bidding, and now enjoys daily collection service at half the former cost.

To encourage other municipalities, the International Cooperation Administration is providing technical and commodity assistance to demonstrate how refuse can be disposed of successfully and economically. To augment their present 15-year-old equipment, each of two small cities has been given a 10-cubic yard compacting type truck and a crawler-tractor with bucket loader and dozer blade to operate a sanitary landfill. To qualify for the assistance the communities had to provide sufficient refuse receptacles, make collection service systematic, and pass the ordinances necessary to improve their sanitation services. In three smaller communities without organized collections or only carabao carts, small 3-wheel vehicles of Japanese manufacture are being tried. They are successful when loads are light and the streets are narrow.

Composting as a method of disposal has attracted interest, particularly in agricultural areas where chemical and organic fertilizers, imported from Japan, are used. In Manila, a pilot composting plant designed to handle 10 tons of raw refuse a day has been completed with local funds and technical assistance from WHO and ICA. Visitors came from many parts of the country to see it even before it was put into daily operation.

In Dagupan and Cabanatuan, cities of 32,000 and 47,000 population, respectively, two composting plants that will process 25 tons of refuse daily are being built in 1960 and 1961. ICA is supplying each plant with $35,000 worth of mechanical equipment not available locally. The cities are acquiring the land, supplying labor and construction materials, and will finance the costs of operations and maintenance.

Both cities are near farm areas. If the product can be marketed for 11 Filipino pesos per ton, the operation will be self-supporting and the mechanical equipment amortized over a 7-year period. If these two subsidized operations prove economically feasible, private firms are prepared to build similar plants for a number of other municipalities.

—Lloyd Florio, M.D., *chief, health division, U.S. Operations Mission, Republic of the Philippines.*

Along the Maroni

Eradication of malaria is particularly difficult along the Maroni River, the border between Surinam and French Guiana. Spraying in the bush hinterland has not sufficed. Indian dwellings in the area have no sidewalls, and mosquitoes are never found on the roofs or ceilings. After feeding, the vector supposedly leaves the shelter and is not exposed to insecticide. Also, the Indians often leave their villages for periods up to a year to visit tribes in Brazil, and Bush Negroes along the river may stay for months at a time at hidden farm plots far from their villages. Some have five or six widely scattered houses, but only one is known and sprayed.

WHO malaria workers in Surinam and workers from the Pasteur Institute in French Guiana met in St. Laurent early in 1960 to coordinate the campaign along the river and the islands. They agreed to intensify efforts to locate hidden dwellings so that spraying may approach 100 percent coverage in Surinam, where the campaign is in the attack phase. In French Guiana, where malaria has been greatly reduced in 10 years, the surveillance phase has been reached.

—Saul Ruby, M.D., *chief public health officer, U.S. Operations Mission, Surinam.*