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SCIENCE

CURRENT PROBLEMS IN RESEARCH

A Biologist Examines the Mind and Behavior

Many disciplines contribute to understanding human behavior, each with peculiar virtues and limitations.

Seymour S. Kety

I have given some thought to the question of whether, in an article such as this, it is better to present data or to discuss concepts, and have chosen to take the latter course. That is not entirely because the data are not so precise or so relevant as in some other fields; it is more because the knowledge of where to look, and how to look, and the meaning of what one finds may, in a field where the avenues to meaningful knowledge are uncertain or undiscovered, play a determining part in the productivity of men or movements.

It is no secret that psychiatry is such a field. There are well-ordered master plans in other branches of science, whose boulevards are already laid down, the trees pruned and the hedges clipped, and whose byways and alleys, even where they have not been broken through, have at least been indicated. In comparison with these, the territory of psychiatry is largely uncharted and unexplored, or spotted by primitive settlements trying to cut paths through the jungle between them. A creditable list of mental disorders have yielded their secrets to the pathologist or to the chemist, but the major psychoses taunt us today as they did the Hippocratic physicians.

It is easy to suppose, but difficult to demonstrate, that this state of affairs in psychiatry is to be ascribed to the ineptitude or indolence of its investigators, their lack of awareness of The Scientific Method, or their unwillingness to carry out research. A few direct encounters with some of the problems in the field are sufficient to convince one of the unparalleled intricacies of the nervous system and of the physical matrix which underlies behavior. If there is a more wonderfully complex structure in the universe, I do not know of it. One need not insist that psychiatry is not a branch of medicine to recognize that it is a superbly different one, nor deny the accomplishments and potentials of the physical sciences to recognize their limitations here.

Promise and Limitations of Biological Science

There are not many biological phenomena which tax the physicochemical complacency of the modern biochemist or biophysicist. The peculiar properties of protoplasm which formerly required the intervention of an *élan vital* seem almost comprehensible in terms of the versatilities of complex molecules; an understanding of the origin of life appears to have been made attainable through knowledge of viruses and bacteriophages which have filled the gulf between animate and inanimate matter, the deoxyribonucleic acid molecule appears capable of explaining genetic transmission, and concepts such as enzyme induction and biochemical specificity begin to provide models for the reduction of even the miracles of embryology to a self-determining series of physicochemical events.

Machines are being built or can be designed which will evaluate and discriminate, learn from experience, and adapt to changing situations. No matter how complex each segment of human behavior, an electronic circuit can be designed to duplicate it, so that even though the cost in resources and time would make such a construct unfeasible, the fact that physical models are conceivable does much to support what had previously been only a postulate of the mechanical basis of behavior.

The Problem of Consciousness

There remains one biological phenomenon, more central to psychiatry than to other fields, for which there is no valid physicochemical model and (or so it seems to me) little likelihood of developing one; this is the phenomenon of consciousness—the complex of present sensations and the memory of past experience which we call the mind.

When we look at the clear sky on a crisp autumn day, a remarkable sequence of physicochemical changes is set in motion, no less remarkable because it is commonplace. Today we can describe many of them, and we have every right to assume that some day we may be able to describe them all—from the light of a specific wavelength impinging on our retina, through the chemical and physical conversions there, to its emergence along the optic pathways as a series of specific signals in specific fibers. We shall trace these signals through the neuron pools in the

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great visual relay stations to certain portions of the visual cortex. We shall, I hope, someday be able to trace accompanying impulses through association pathways in the reticular system and in other areas of cortex, and if we are fortunate, we shall watch these ramifying impulses or their progeny converge in the motor centers of the brain in just the proper temporospatial arrangement to actuate the muscles which will say, "How blue the sky is today."

Where, pray, in that sequence is the sensation of blueness? It is neither wavelength, nor nerve impulse, nor spatial arrangement of impulses; it is not necessary to any of these processes and, though dependent on many of them, is explained or even described by none. It is richer and far more personal. One does not seem to get closer to its nature by increasing the complexity of its material counterpart —it is qualitatively and dimensionally different. As I indicated above, a machine can be built to perform any function that a man can perform in terms of behavior, computation, or discrimination. Shall we ever know, however, what components to add or what complexity of circuitry to introduce in order to make it *feel*?

These are not new thoughts, and they were not new to Aristotle or Plato, nor to Spinoza, Leibnitz, Berkeley, Hobbs, or Mach, nor to the other dozens of great minds which contemplated them. Modern students of the nervous system, with all their knowledge of the mechanisms which may underlie consciousness, have been unable to explain it any more than did the philosophers who preceded them; some (*1–4*) have, however, stated the problem quite cogently. Hughlings Jackson (*2*) wrote: "We cannot understand how any conceivable arrangement of any sort of matter can give us mental states of any kind. . . ." C. Judson Herrick (*2*) stated it more elegantly: ". . . awareness is an intrinsic psychobiological event, self centered and self contained. It is a product of a bodily mechanism, but it must not be identified with the mechanism that makes it. It has an identity which is distinctive and unique, an identity with qualities which cannot be described in terms of the temporospatial relations of the mechanism employed." Sir Russell Brain (*3*) has tried to come to grips with the problem by using the analogy of a pattern: "Not only are there twelve thousand million nerve cells out of which the patterns can be made, but nervous patterns exist in time, like a melody, as well as in space. If you look at a tapestry through a magnifying glass you will see the individual threads but not the pattern; if you stand away from it you will see the pattern but not the threads. My guess is that in the nervous system we are looking at the threads, while in the mind we perceive the patterns, and that one day we shall discover how the patterns are made of the threads." Fessard (*4*) very succinctly spots the difficulty: "Momentary distributions or patterns of excitatory or inhibitory state . . . has been proposed . . . as the basis for conscious experience; but what makes a pattern 'conscious' of its own patterning remains an irritating problem."

But science has faced other "irritating problems" without becoming paralyzed, and scientists have treated the problem of consciousness in one manner or another which is satisfying to them and permits them to get on with their work. There are the materialists and their psychological counterparts, the behaviorists, who solve the problem of explaining consciousness by ignoring it or denying that it exists. Their ritualistic avoidance of what they call "mentalisms" and their clumsy and inappropriate use of "behavior" in those instances when they could more meaningfully say "sensation," or "feeling," or "consciousness" make their approach less satisfying than it otherwise might be, but none can deny its usefulness.

By emphasizing the objective and measurable aspects of psychiatry and the behavioral sciences, they have demonstrated their kinship with medicine and the natural sciences and have brought into them considerable rigor at the price of just a little rigidity. But in denying the existence or the importance of mental states merely because they are difficult to measure or because they cannot be directly observed in others is needlessly to restrict the field of the mental sciences and to curtail the opportunities for the discovery of new relationships. The remarkable hallucinogenic properties of lysergic acid diethylamide (LSD) are barely hinted at in behavior, and the behavioral disturbances in schizophrenia are a mere fragment of the entire picture. Nature is an elusive quarry, and it is foolhardy to pursue her with one eye closed and one foot hobbled.

Then there are the idealists and the extremists among them—the solipsists, who are so struck with the fundamental and undeniable reality of consciousness that they are led to deny any other existence than their own sensations, for they cannot conceive of what the material world would be like aside from them. It is possible and valid to construct an astronomy with the earth central and stationary; Aristotle showed that it was possible, and Einstein's theories supported its validity.

In the same way, the doctrine that my own consciousness creates and determines the universe is pleasant, if pretentious, and quite unassailable. The real difficulty with egocentricity as with geocentricity is that it makes representation, comprehension, and prediction hopelessly complicated. The cosmogony, the physics, and the thermodynamics of a universe which is born each morning when I awake and annihilated when I fall asleep, which wobbles when I shake my head or have too much to drink, would make the complex equations of Ptolemaic astronomy a child's primer by comparison.

The glaring flaw in pure materialism and extreme idealism is that they are willing to entertain no inferences. And yet, science is born of inferences and thrives upon them. One may infer the existence of a universe of matter and energy outside of and quite independent of one's own consciousness and, by means of relatively simple generalizations called "laws of nature," render that universe and even consciousness itself more predictable and capable of description in parsimonious terms. One may also accept the direct and vivid testimony of the existence of one's own mental states and infer their existence in other beings similarly constructed.

Thus, one can acknowledge the existence of consciousness and of matter and energy without insisting that one must be reduced to the other. One can go further and study scientifically the relationships and correlations between them; one can without apology engage in a study of *psycho*pharmacology, first describing the effects of drugs not only on behavior but also on mental state and then attempting to elucidate their actions on the brain. One can, as Penfield (*5*) has done, study the particular sensations and mental states evoked from specific areas of the cortex; one can define a few of the correlates of sleep and attention in terms of the electroencephalogram, or, as Evarts (*6*) is doing, in the activity of single cortical neurons. One can seek the anatomical and pathological basis of coma and find that the regions essential for the maintenance of consciousness seem to lie in the brain stem. One can determine the metabolic requirements and the energy equivalence of consciousness.

This last function—the energy equivalent of consciousness—was vigorously speculated upon and pursued by the early materialists in the belief that its evaluation would somehow demonstrate that consciousness was a chemical process which adhered to the law of the conservation of matter and energy. Between 1945 and 1948, we were in the position of being able to make such measurements in conjunction with measurement of cerebral blood flow in normal, conscious young men (*7*). From these data the rate of energy utilization could be computed. Twenty watts provide the total power for the human brain—for all of its physicochemical processes, all of its thinking, all of its consciousness. What about the dependence of consciousness on the brain's power supply? If, as the result of circulatory insufficiency, substrate deficits, or derangements in metabolism, this continuous supply of energy becomes attenuated, consciousness begins to fail; the difference between full normal consciousness and the depths of coma is only a matter of seven or eight watts (*8*).

Now that we have an energy equivalent for thought (and it is a maximum figure, since the relevant processes may constitute only a small fraction of the total) I am not at all sure that this proves the physical nature of consciousness; what it does do, for me at least, is to demonstrate all the more what a remarkable mechanism the human brain is, which can correlate, discriminate, compute, effect behavior, and feel with such a trivial expenditure of energy.

By this time the biologist within me becomes impatient and says, "Enough of this prattle about consciousness, which I grant you exists, but which I can't dissect without losing it, and which I can never hope to understand. These are problems I worried about and resolved to my own satisfaction years ago (*9*). Let us talk about behavior, which is essentially nothing more than the contraction of muscles and the secretion of glands. That is the area which my physics and chemistry will someday understand quite completely."

The Mechanistic View of Life and Behavior

Most modern biologists enter their laboratories each day with an implicit assumption that the phenomena they are about to study are physical and chemical in nature and bound by the same laws which describe the behavior of matter and energy generally. This mechanistic treatment of life has had a long history, going back at least to Democritus. It was proclaimed heresy by the ecclesiasticism of the Middle Ages, to be reborn in the reaction of the Renaissance and nourished and invigorated by the materialism of the 18th century and beyond. But nowhere is the doctrine expressed more clearly than in the writings of Claude Bernard (*10*), the progenitor of modern physiology.

"In living bodies as in inorganic bodies, laws are immutable and the phenomena governed by these laws are bound to the conditions on which they exist by a necessary and absolute determinism . . . determinism in the conditions of vital phenomena should be one of the axioms of experimenting physicians. If they are thoroughly imbued with the truth of this principle, they will exclude all supernatural intervention from their explanations; they will have unshaken faith in the idea that fixed laws govern biological science. . . . Determinism thus becomes the foundation of all scientific progress and criticism."

Although I share this faith, I cannot avoid pointing out that it is in fact faith rather than proof which forms the basis of this Olympian generalization.

Of course, there have been arguments against mechanism, the most recent being based upon Heisenberg's principle of indeterminism, which rests upon our inability to study the motion of the tiny particles of which the world is constituted without disturbing them and harks back to Lucretius, who, with Epicurus, visualized atoms veering from their determined course "in uncertain position and indefinite time, by an amount so small as cannot be expressed . . . from which veering alone can come that freedom which is potent to subvert the bonds of fate, which alone need not follow the chain of cause on cause eternal" (*11*). These arguments seem quite inapplicable. Those of Lucretius were based on the purest speculation, and even the Heisenberg principle, which is based upon the cold experience of modern physics, seems irrelevant. No mechanist ever expected to tally the position and motion of every particle in the universe, and being assured that one cannot do so is not much of a shock. It would seem that the concepts of freedom and purpose in the universe should be based upon nobler stuff than the clumsiness of our instruments.

The oldest argument against mechanism is the testimony of experience—we observe our will affecting our behavior in every moment of our waking lives. Against this the mechanist opposes a faith—but no demonstration—that the free choice was in fact an immutably determined event. Spinoza wrote (*12*), "Men think themselves free because they are conscious of their volitions and desires, but are ignorant of the causes by which they are led to wish and desire."

The modern mechanist can, moreover, correctly argue that no one has ventured to explain how a wish or desire in consciousness can move a muscle or activate a neuron. Clifford, who argued most convincingly for the reality of consciousness but also for its causal inefficacy, made this point (*13*): "the train of physical facts between the stimulus sent into . . . any one of our senses and the exertion which follows it and the train of physical facts which goes on in the train . . . these are perfectly complete physical trains and every step is fully accounted for by mechanical conditions. . . . If anybody says that the will influences matter, the statement is not untrue, it is nonsense. . . . It will be found excellent practice in the mental operations required by the doctrine to imagine a train, the forepart of which is an engine and three carriages linked with iron couplings, and the hindpart three other carriages linked with iron couplings: the bond between the two being made up of the feelings of amity subsisting between the stoker and the guard." And yet, even in classical Newtonian physics, we postulate and accept interactions for which there is no readily comprehensible model, explanation, or mechanism—for example, the gravitational "attraction" between two bodies across empty space.

Perhaps the most cogent argument

for a mechanistic concept of the universe, including animal and human behavior, is that it assumes and strives for predictability. And perhaps a need for predictability and a striving for it represent a primitive biological drive which the scientist in his laboratory shares with the young child or with the animal in the jungle, all of whom have learned that security in or mastery of their environments depends upon their ability to anticipate and predict its vicissitudes. Moreover, a mechanistic concept of the universe is heuristic. If productivity of a doctrine were the only proof necessary for its validity, the mechanistic concept would have been validated ten times over.

The mechanistic concept of behavior has sought and discovered a fascinating array of mechanisms which produce, determine, or modulate many aspects of behavior. The first two hundred years of the history of this search for a physiological basis of behavior was marked by a great debate over which was the organ of reason. The question appears to have been settled by the Hippocratic physicians who, around 400 B.C., wrote the final rebuttal of the Aristotelian notion that reason and feeling resided in the heart. I should like to quote their most succinct passage (*14*); even though it may have become quite familiar, its poetry and poignancy are nonetheless remarkable.

"And men should know that from nothing else but from the brain come joys, delights, laughter and jests, and sorrows, griefs, despondency and lamentations. And by this, in an especial manner, we acquire wisdom and knowledge, and see and hear and know what are foul and what are fair, what sweet and what unsavory. . . . And by the same organ we become mad and delirious and fears and terrors assail us, some by night and some by day, and dreams and untimely wanderings, and cares that are not suitable and ignorance of present circumstances, desuetude and unskillfulness. All these things we endure from the brain, when it is not healthy, but is more hot, more cold, more moist, or more dry than natural, or when it suffers any other preternatural and unusual affliction."

In the 23 centuries which have elapsed since those words were written, some progress has been made in postulating how the brain might perform certain of these functions and, to a more limited extent, in answering how in fact it does. Like the delusions of the paranoid psychotic, these designs for the brain have borrowed heavily from the technological developments of their times. We have seen first hydraulic, then mechanical, then crude electrical models of behavior. Cybernetics and computer and information theory, which in a sense emerged from efforts to understand the brain, have woven recently acquired anatomical and physiological information into a conceptual framework which electronics permits us to test in working models which perform useful functions.

Table 1. Cerebral oxygen consumption and mental state.

Condition	Cerebral oxygen consumption (% of normal)
Senile psychosis	82
Diabetic acidosis	82
Insulin hypoglycemia	79
Artificial hypothermia	67
Surgical anesthesia	64
Insulin coma	58
Diabetic coma	52
Alcoholic coma	49

Current Physiological Concepts of Behavior Mechanisms

Just as these electronic computers have tended to imitate the brain, so our concept of the nervous system has grown from what the computers have taught us. Instead of delineating a great sensory system and a great motor system feeding to and flowing from a massive memory and integrative system, one can view the nervous system as a decentralized organization of relatively autonomous functional units, each with its sensory, storage, and effector components and each with a built-in or acquired program.

Such systems could subserve practically all of our daily activities: standing, walking, shaving, driving our car, finding a parking space, pipetting, eating, playing the piano. A relatively small number, essential for immediate survival, such as breathing, sucking, and clasping, are probably laid down with the nervous system itself. Some are imprinted by early experience upon a genetically determined matrix, as exemplified in the lifelong positive tropism of the duckling for its mother but, equally, for any object which occupies its field of vision at a particular time after hatching. Some, such as sexual behavior, probably represent an acquired elaboration of an instinctive pattern. But many of the systems which mediate human behavior are experiential in origin, acquired by trial and error and by the persistence of the most successful or rewarding patterns.

Table 2. Cerebral oxygen consumption and mental state.

Condition	Cerebral oxygen consumption (% of normal or control)
Normal sleep	97
Schizophrenia	100
LSD psychosis	101
Mental arithmetic	102
Anxiety	118
Epinephrine infusion	122

There is remarkable economy in such a complex of semiautomatic sensory-motor programs to effect specific behavioral patterns. The cables actuating them can be relatively small, and the commands quite laconic, like "start; stop; slower; faster." These commands, in turn, can each be thought of as the result of a rigorous process of data reduction, whereby the tens of millions of impulses constantly pouring into the brain from all of the sensory receptors are sorted and compared against built-in or acquired master patterns to emerge as greatly condensed signals coded for destination and command or modulation.

These commands need not arise exclusively from the sensory systems; chemical changes arising from other regions of the body may operate at specific places to actuate appropriate sequences of behavior. Thus, dehydration sets off drinking by stimulation of specific osmoreceptors in the supraoptic nuclei of the hypothalamus, and certain of the sex steroids initiate appropriate sexual behavior in castrated animals when applied in infinitesimal amount directly to specific hypothalamic regions, and nowhere else. This study, reported only two years ago by Harris, Michael, and Scott (*15*), supports a remarkable speculation reached in 1905 by Freud (*16*): "We may now believe that in the interstitial tissues of the gonads special chemical substances are produced, which, when taken up in the blood stream, charge definite parts of the central nervous system with sexual tension."

There is a further economy in the multiple utilization of the same component in many circuits. A network with a finite number of interstices may still provide an almost infinite number of separate pathways, and as the young brain is known to do, provide such pathways even after large segments are cut away.

Many have speculated that the cerebral cortex represents a great network where much of this storage, comparison, and coding occurs. The studies of Penfield (*5*), who, by stimulation of the human cortex, is able to elicit crude sensations, or sometimes highly integrated memories of past experience, are compatible with such a function.

To this model of the nervous system there have been added, in recent years, the neurophysiological counterparts of attention and affect. The central reticular formation, rescued by Moruzzi and Magoun (*17*) from the neglect which comes of ignorance, has been shown to have important relationships to sleep and wakefulness. This longitudinal network of short-branched interlacing neurons which taps the sensory systems and feeds into the motor outputs of other structures is strategically placed to intervene in the automaticity of the functional systems of which I spoke above. By selective facilitation, or by the inhibition of irrelevant activity, it can, so to speak, focus attention on a particular channel of sensory input or program of motor activity for the purpose of making and reinforcing new pathways. It appears that the anatomical substrate of consciousness resides here more than in any other place in the brain, not only because this seems reasonable but also because unconsciousness is most frequently associated with damage here. This remarkable ability to prevent the intrusion into consciousness of information irrelevant to the task in hand, which is so characteristic of alertness, appears to be accomplished through the reticular system not only by action at adjacent relay stations but also by newly elucidated sensory feedback systems which suppress the unwanted information at the peripheral receptors (*18*).

A system capable of representing affect or emotion is emerging from the imaginative speculations of Papez, substantiated by the functional studies of MacLean and the anatomical evidence of Nauta (*19*). The limbic system, corresponding to the rhinencephalon or olfactory brain, is richly connected with the reticular system, the neocortex, and, by way of the hypothalamus, modulates the endocrine and autonomic nervous systems. Specific areas of the hypothalamus which effect the release of the various trophic hormones of the pituitary have recently been elicited (*20*). Most interesting are the experiments of Olds (*21*) and of others which suggest the presence of centers for reward as well as aversive centers in the brain. Animals with electrodes chronically implanted in various limbic areas and connected to a lever which, when pressed, will deliver a slight electrical stimulus will press the lever at extremely high rates, continuously for many hours. For the reward of stimulating these special areas, animals will run a maze or traverse an electrified grid with greater alacrity than will a hungry animal going after food. It is not unreasonable to suppose that such areas of affect enter into the sensory and motor programming circuits to facilitate or inhibit their establishment, and to compete for attention in terms of value to the animal.

Growth and Flourishing of Neurochemistry

While the physics of the nervous system was being studied so productively by the neurophysiologists, an interest in its chemistry was developing, but much more slowly. Though derided by many of the powerful chemists of his day, Thudichum began a monumental program of extraction, purification, and analysis of the major chemical components of nervous tissue (*22*).

The next generation of neurochemists, influenced by the emphasis on cell respiration among the general biochemists, examined the energy metabolism of brain as exemplified by thin slices of that organ in a nutrient bath. Despite the liberties which they took with the functional integrity of their preparations, they learned a great deal about how the brain differed metabolically from muscle and liver: that the brain was the seat of a high metabolic rate; that its respiratory quotient was close to unity, indicating that carbohydrate was its main substrate for oxidation. These observations were later confirmed and extended in vivo, first in animals and finally in man. The latter studies, although they were, perforce, limited to the brain as a whole, had the unique advantage that all of the special features which characterize the function of that organ, including thought and consciousness, were preserved and could be correlated with cerebral oxygen consumption in normal man and in a variety of diseases.

In Table 1 are presented some of the data of my associates and myself, as well as those of others, relating the over-all oxygen consumption of the brain to presumed mental state (*7, 23*). There is a rough progression downward in terms of the degree of interference with function, and it is clear that this interference with function is correlated with cerebral oxygen consumption. It is likely that these conditions have in common a primary interference with energy transfer in the brain, either through a circulatory embarrassment, which we know occurs in senile psychosis from concomitant cerebral blood flow measurement, or through some metabolic blockade, as with hypoglycemic, and possibly diabetic, coma, or by suppression of synaptic transfer of activity, as may occur in anesthesia. There is another condition, anxiety, whether endogenous or associated with epinephrine infusion, in which a significant increase in oxygen and energy utilization occurs (Table 2).

But to me, the most interesting information contained in Table 2 is the finding that in a large group of mental states markedly different from normal there is no significant deviation in cerebral oxygen consumption. On the basis of the studies in sleep we were able to rule out the theory which attributed this state to the piling up of an unknown narcotic substance and to confirm certain neurophysiological interpretations. From the studies in schizophrenia we concluded that it requires just as much oxygen to think an irra-

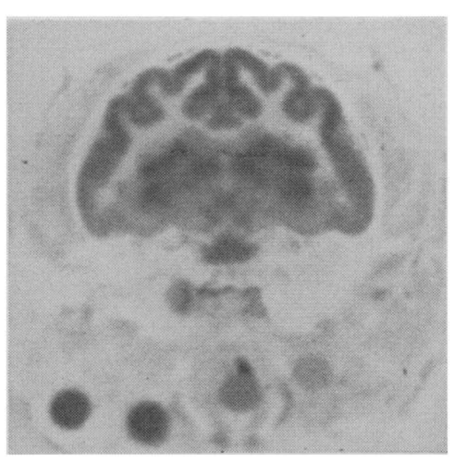

Fig. 1. Autoradiogram of a frozen section of the brain of a cat after exposure of the animal to a radioactive gas (CF_3I^{131}). There is a complex but roughly proportional relationship between photometric density and blood flow during life (as opposed to capillary blood volume) (*24*).

tional thought as to think a rational one. But we also derived some understanding along one of the dimensions in which the brain is unique. "For it is neither a pump nor a motor and its current counterparts seem to be instruments of computation and communication. In such an instrument, although a defective power supply will produce dysfunction, meaningfulness of content and accuracy are by no means always correlated with the power used" (*8*).

In recent years neurochemistry has moved into the large and challenging area which lies between oxidation and the specialized functions of the brain, and into another dimension which distinguishes the brain from every other organ—its magnificent organization. Some of our own studies on cerebral blood flow and metabolism have also moved toward the regional differentiation of these functions (*24*). In Fig. 1 we see an autoradiogram of a cat's brain after brief exposure during life to a radioactive inert gas. The density of each area is a function of its cerebral blood flow, and from it the latter can be calculated. Since there is reason to believe that blood flow parallels metabolic demand, this gives us also an approximate map of the metabolic rates of the various parts of the brain during life. The differentiation, even on the basis of oxidative metabolism, is so marked that this figure is sometimes mistaken for a stained histological section.

But regional neurochemistry (*25*) has advanced far beyond oxidative metabolism. Lowry and his associates (*26*), by means of painstaking techniques by which it is possible to weigh individual neurons and analyze them for a variety of substrates and enzymes, are beginning to map the chemistry of the brain to its uttermost detail. In a number of laboratories a specific group of substances, the biogenic amines, have been demonstrated in relatively high concentrations and selectively distributed in the brain (*27*). The first of these to be studied was acetylcholine, and in recent years, in staccato fashion, we have learned about norepinephrine, histamine, γ-aminobutyric acid, and serotonin.

Scientists at the National Institutes of Health, such as Brodie, Udenfriend, Axelrod, and their respective associates, have contributed much to our understanding of the distribution, synthesis and degradation, and pharmacological interrelationships of these amines (*28*). The preferential distribution of some of them to the limbic system and the still crudely defined behavioral correlations of changes in their concentration in the brain suggest that they have important roles in behavior which remain to be defined. Udenfriend and his coworkers have shown that the enzyme for the synthesis of one of these amines, norepinephrine, exists in equal concentration in the caudate nucleus and in the adrenal medulla itself (*29*). It seems unlikely that these agents, pharmacologically active in other tissues, find themselves in the brain by sheer accident, and there is every reason to believe that neurochemistry, in association with precise psychological studies, will in the foreseeable future have a well-documented explanation of their presence in the brain.

The sensible and productive adolescence of neurochemistry portends a successful future, especially now that the earlier resistances of biochemistry to the field appear to be relaxing. That resistance was an interesting phenomenon and in marked contrast to the relationships of its parent discipline to neurophysiology. There were, of course, reasons for it.

The very origin of biochemistry from physiological chemistry—a handmaiden of clinical medicine—made it unduly defensive with respect to its interest in basic rather than applied research, forgetting all the while that biochemistry itself was an applied science, the application of chemistry to biology. But brain chemistry was looked upon as highly applied research—although I fail to see why the chemistry of neural transmission is less fundamental than the chemistry of fermentation or oxidation, or the chemistry of memory less interesting than chemical genetics. Then there was the doctrine of the "unity of biochemistry"—that all cells shared the same biochemical processes, so why gum up one's homogenizers with the mucky ointments of the brain when one could study bacteria. This doctrine, of course, emerged while biochemistry was preoccupied with the common mechanisms for energy production by cells—oxidation and phosphorylation—but it has always seemed to me like examining a tenement, the

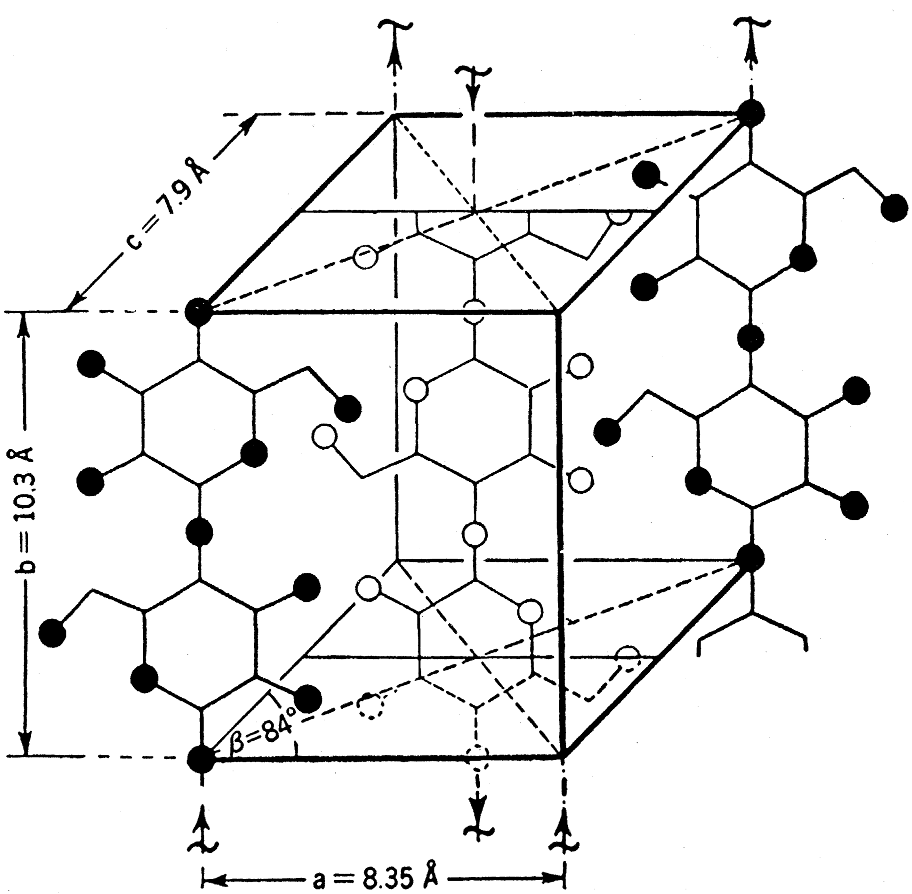

Fig. 2. A model of the molecular structure of cellulose. [Reproduced, with permission, from K. H. Meyer, *Natural and Synthetic High Polymers* (Interscience, New York, 1950), p. 304; copyright 1950 by Interscience Publishers, Inc., New York]

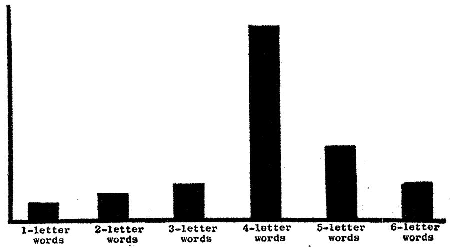

Fig. 3. Percentile frequency of words arranged according to their length in a particular book.

National Gallery of Art, and the White House, finding a furnace in the basement of each, and, without bothering to see what went on upstairs, declaring that they were all the same.

In a way this early provincialism served a useful purpose and perhaps contributed to the rich and rapid development of the field, and now that a point of diminishing returns appears to have been reached in the cataloging of enzymes and pathways of intermediary metabolism, biochemistry is moving upstairs, and the chemistry of differentiation and of genetics, chemical embryology, and even neurochemistry are becoming attractive areas. One can see a bright future in the study of the chemical processes in neural transmission—a work which has already begun; in the chemistry of memory, where interesting and heuristic hypotheses are being developed, centered on the coding possibilities which the protein molecule offers; in questions like neural specificity—how nerve fibers or neurons find their proper peripheral and central connections even when transplanted to unlikely places; and in the whole range of chemical processes in affect and behavior. For such work the biochemist will have to become interested in neurophysiology, in neuroanatomy, and in the behavioral sciences, and there is every indication that many are willing to do so.

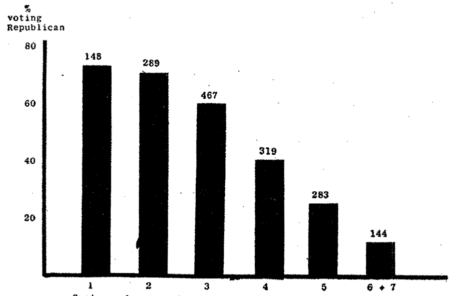

Fig. 4. Relationship between a socioenvironmental index and voting behavior. The figures above each bar represent total number in the sample. [From Lazarsfeld, Berelson, and Gaudet (*30*)]

So the sciences of biochemistry and biophysics have an assured and secure future in the study of the brain (and they were hardly waiting for me to point that out!). And if our assumption of the mechanistic nature of life and of behavior is correct, and man is nothing more than the most magnificent physicochemical engine which has ever been constructed, but an engine nevertheless, is it not obvious then that he or at least his behavior ought someday to be explained completely by physics and chemistry? If we believe that, and many do, then do not physics and chemistry and their sister biological sciences become the *real* sciences of behavior; while disciplines or bodies of knowledge and techniques like psychology, sociology, and psychoanalysis become merely empirical, descriptive, and derivative, to be tolerated as a sort of first-aid manual—what to do until the biophysicist or the biochemist arrives?

I should like to answer this question in the form of a parable; it is entitled "The True Nature of a Book."

The True Nature of a Book

Let us imagine a community with inhabitants who are of high intelligence and quite civilized except that they have never seen a book and have developed other means for the transmission of knowledge. One day a million books appear in their midst, an event which arouses so much curiosity and consternation that they decide to establish a scientific institute to study them. They set up this institute by disciplines and establish a policy that each scientist may examine these objects only with the tools and techniques and concepts of his discipline.

The first laboratory to be organized is the Laboratory of Anatomy. There the workers study these strange objects for a while, and their conclusion reads like this: "The specimen is a roughly rectangular block of material, covered ventrally and dorsally with two coarse, fibrous, encapsulated laminae approximately 3 millimeters thick. Between these lie several hundred white lamellae a fraction of a millimeter thick, all fastened at one end and mobile at the other. On closer inspection, these are found to contain a large number of black surface markings arranged in linear groupings in a highly complex manner."

By that time the chemists have appeared on the scene. The first chemist to get hold of a specimen burns it, and satisfies himself that it obeys the law of the conservation of matter and is therefore in his province; he may even compute the energy release per gram on complete oxidation. Next comes the analytical chemist, who discovers first its elementary composition but later breaks it down less completely into pure compounds; he also reports traces of elementary carbon, "which are probably impurities." Before I forget to mention it, one day a chemist accidentally drops a colored solution on one of the pages and by serendipity discovers paper chromatography, which lies around for 25 years before someone figures out what to do with it.

Then there are the biochemists, who slice the book and mince it and, best of all, homogenize it (because on the slices and the mince they can still see those black contaminants, while the homogenate can be centrifuged to remove them, permitting them to work with a Pure System). But all of these chemists have an uncomfortable feeling that though what they are doing is important, the real answers will come from the fellow down the hall who has just arrived and is still polishing his bright and expensive equipment—the molecular biologist.

With the self-confidence which comes from the adulation of the less fundamental sciences, he is anxious to begin work on the book he has selected because someone has told him that it is biased and distorted. Having hung a sign over his door which reads, "No twisted book without a twisted molecule," he proceeds to search for the molecule. By repeated extraction, centrifugation and ultracentrifugation, electrophoresis, hydrolysis, and repolymerization he finally isolates a pure substance, free of the carbon particles, and—what is even better—a macromolecule, and a twisted one at that. Figure 2 represents his version of the fundamental nature of the book, which many will recognize as a current hypothesis of the structure of cellulose.

Simultaneously, the physiologists have been attacking the subject. Unlike the biochemists, they have read the report from the anatomists and proceed to study and speculate upon why and how the pages are attached on one

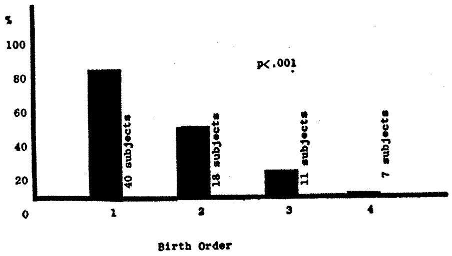

Fig. 5. Relationship between birth order and affiliative tendency under stress. [From S. Schachter (*31*)]

side. They study the movement of the pages as the book is riffled and derive complex equations to describe it. Then a biophysicist discovers that in an appropriate electrostatic field the graphite deposits produce discontinuities in potential. Fine microelectrodes are developed to pick these up, and amplifiers and oscilloscopes to display them. The biophysicists discover by sticking these electrodes into the book in various places that those which do not break off will pick up signals, some of which are reproducible. They develop thousands of tracings of these signals and call in the cyberneticist to help uncode them. The signals are recorded on miles of magnetic tape and fed into huge computers. Excitement mounts when, in a particular region extending over a few millimeters in a certain book, one of them discovers on a particular day that, for a few minutes before he damaged the source of the signals, a tremendously complex pattern appeared which was reproducible but incomprehensible. This pattern is fed into the data reducers and the computers, which can generate and test thousands of hypotheses per minute. Finally, the electric typewriter begins to print; a meaning has been found in that complex pattern—it reads "THE."

By this time the behavioral scientists have been admitted to the institute and begin to study the problem. They are a strange lot. Some of them have read the reports of the anatomists, the chemists, and the physiologists, but many of them don't seem to care. Most will admit, if pressed, that the book is material in nature, that it obeys material laws, that it and its contents are nothing more than a highly specialized arrangement of chemical substances. But they don't slice the book, and they don't purify its chemical components—in fact, they seem to feel that it is improper to do so. Instead, they ask questions peculiar to their disciplines and look in the book for the answers. The first one likes to count, so he counts the number of letters in the words and comes up with a frequency distribution of the words by their length (Fig. 3). He finds a preponderance of four-letter words, forms a hypothesis that the book is a modern novel, and ventures a prediction that it will be a best seller and also banned by the Postmaster General. Then he looks for particular words and counts them and confirms the hypothesis. His colleagues join him, asking other general questions and finding their answers in the content of the book. They learn a great deal about classes of books, how they differ from one another, and what their effects are on the community. Although the behavioral scientist has learned much about the nature of books—infinitely more, in certain areas, than the physical scientist—his techniques falter in the area of the individual book, its characteristics, and his ability to make entirely reliable predictions about it. If it is important to learn something about the individual book, then there is need for a technique which can read it completely. Such a technique has not yet appeared, but some progress has been made in its development.

Finally, the book is brought in desperation to the psychoanalyst in the hope that he will be able to read it. That he does not do precisely, but instead asks the author to select portions and read them while he listens. Of course, the author is biased and reads what he wants to read, or, if there is "good transference," those passages which he thinks the analyst would like to hear. And the analyst himself doesn't always hear with equal acuity but, depending on his school or on his preconceived notions, is deaf to greater or lesser portions of the data.

Nonetheless, this anecdotal, biased, and selected patchwork may be the closest approximation which we have to the rich and almost inexhaustible fund of information which reposes in the individual human brain and, to a significant extent, determines individual behavior. Like all scientific methodologies this one was not born perfect and complete, and there are increasing numbers of analysts who recognize that. Many of the unavoidable biases in the data may not be all bad. To deal with all of the stored information would be impossible; some selection is clearly necessary, and there is some chance that the selection which the subject employs may have some relationship to the actual weightings of the data in his affect and behavior. Furthermore, this particular technique has been largely employed for therapeutic purposes, and clinical therapy in other branches of medicine has not always been characterized by the strictest adherence to scientific methodolo-

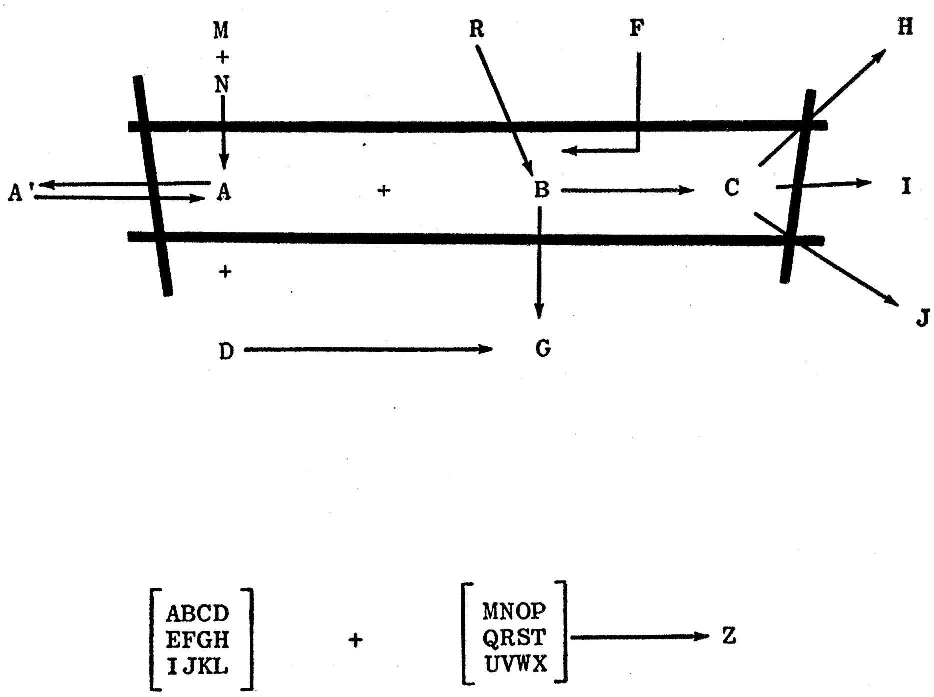

Fig. 6. Models of problems typical of those encountered (top) in biochemistry and (bottom) in human behavior.

gies. There is increasing recognition of its unique values and limitations as an instrument of research, and its critical use in that connection by trained and qualified observers is a worth-while goal toward which perceptible progress is being made.

The Hierarchy of the Scientific Disciplines

If I seem to have attached increasing values to the disciplines as I have enumerated them, I have done so only to counteract a hierarchical tendency in the opposite direction which I fear exists today. There are no higher or lower, better or worse, disciplines except with respect to their relevance to particular problems.

In the case of the brain, the biological disciplines have made and will continue to make remarkable progress toward understanding its structure, its metabolism, its functional interrelationships, and the mechanisms which underlie behavior, and they have solved or will solve those mental disorders which are primarily the result of disturbances there. But in the area of information, content, and experience, stored as it is in the complex interrelationships of 13 billion neurons, biology is extremely pretentious if it thinks that it can unravel them by means of its tools. There will, no doubt, some day be a biochemistry or a biophysics of memory—but not of memories.

Take the question of voting Republican or Democratic in a particular election. All of the experience and the biases and the motivation for doing one or the other are stored in the physical chemistry of the brain, but these cannot be reached by physics or chemistry. There are other, more appropriate, techniques for that. Figure 4 depicts a correlation with voting behavior of an index based on only a few factors in the experience of individuals: economic level, religion, and urban versus rural abode (*30*). In Fig. 5 the tendency of individuals to want to be together or alone in an anxious situation is correlated with a single factor, birth order, and a surprisingly large segment of the variance is defined (*31*). Information like that is obtained without attempting to get to the fundamental physiological basis of the tendency; in fact, it would be lost if we were to try.

In Fig. 6 I have attempted to represent two kinds of problems which face scientists. One (Fig. 6, top) seems deceptively complex but is relatively simple, since by four cuts one can rule out all but the relevant variables and study a fundamental process: *A* plus *B* yields *C*. That is the kind of problem to which biochemistry has frequently addressed itself and which it has solved so successfully.

But even in biochemistry, that approach is not the one always and uniquely adapted to yield truth, as DeWitt Stetten (*32*) has so keenly pointed out: "Which of these many levels of disorganization is then to be recommended? The answer to this question is that unequivocal results as to what is happening in the intact mammal cannot be gleaned from studies conducted at any one level. Each level, considered separately, has led to unsatisfactory conclusions. We know of reactions catalyzed by isolated enzymes for which no counterpart in the intact animal has been discovered. We know of over-all conversions observed in the intact animal which have thus far defied study at subcellular levels and for which no enzymes have been unearthed. It is improper to hold that any one approach is in all cases superior to all others. Selection of level of disorganization, often in fact determined by the skills or prejudices of the individual investigator, should be based upon the nature of the specific question which is being asked." If this is true for metabolism, how much more true is it for behavior?

In Fig. 6 (bottom) one sees a representation, deceptively simple but actually terribly complex, of what happens in behavior—say, an interaction between a candidate, or the impression of a candidate, and a voter that results in a vote. *A*, *B*, *C*, and *D* are certain obvious characteristics — the candidate's party, his stand, his age, among others. *M*, *N*, *O*, and *P* are obvious characteristics of the voter—his economic class, his religion, his income, and so forth. All the other factors (and there are many) represented by the other letters, and many more which are unrepresented, are the idiosyncratic ones—the candidate's smile, how he parts his hair, how the voter feels toward his father, what books he has read, what people he has met, to list a few. The net reaction is the resultant of *all* of these and is quite a different one for each case, even though the outcome is restricted to a choice between *Y* and *Z*. It is the problem of the sciences of behavior to develop techniques for the study of multivariant processes without reducing them to simpler ones which do not ask or answer the particular question. Let us hope that such techniques will continue to be developed and be intelligently used, for much depends upon them.

It has most certainly not been my intention to deny the tremendous importance and the major contributions which biochemistry and biophysics and the biological sciences generally have achieved within our lifetime. I have merely wanted to point out that we do not always get closer to the truth as we slice and homogenize and isolate—that what we gain in precision and in the rigorous control of variables we sometimes lose in relevance to normal function, and that, in the case of certain diseases or problems, the fundamental process may often be lost in the cutting. A Heifitz and a Rubinstein playing different sonatas at the same time will produce a cacophony which the most exhaustive study of either individually would never have revealed, and a truer picture of the nervous system and behavior will emerge only from its study by a variety of disciplines and techniques, each with its own virtues and its own peculiar limitations (*8*).

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Recent Statistical Studies in Astronomy

The nature of the galaxies and the birth-death process among comets are revealed in statistical studies.

Thornton Page

There have been many advances in statistical astronomy since Herschel first reasoned from the concentration of stars in the Milky Way that the sun must be located in a disk-shaped system of stars now called the Milky Way galaxy. Later studies of the distances and motions of stars have proved well suited to statistical analysis, and more recently the analogous studies of galaxies have been added to this list. It was therefore appropriate that a portion of the Fourth Berkeley Symposium on Mathematical Statistics and Probability, held at the University of California from 20 June to 29 July, 1960, should be devoted to recent applications of statistics in astronomy. The problems discussed were in the fields of radio astronomy, dynamics, and cosmology, and they concerned both the most massive and the least massive of astronomical bodies: galaxies and comets.

Distances of Cosmic Radio Sources

The most recent additions to the variety of celestial objects studied by astronomers are the strong sources of radio waves from outside the earth. When radio telescopes first came into use it was found that much of the cosmic radio emission comes from our Milky Way galaxy, or from objects belonging to it, such as the Crab nebula (a cloud of turbulent gas remaining from the explosion of a star several centuries ago) or the sun itself. However, there are about 100 small regions of apparently empty sky from which strong radio signals are also coming—signals which could not at first be identified with any visible object but which are now known to be from extragalactic sources located far outside our galaxy. Two questions then arose: How far away are these extragalactic radio sources, and, if we built even more powerful radio telescopes, how many more such sources would be detected?

R. Minkowski of the Mount Wilson and Palomar Observatories, Carnegie Institution of Washington, and California Institute of Technology has identified many of the extragalactic radio sources with distant galaxies found on photographs taken with the 200-inch telescope and other large optical instruments. Over the past five years he has obtained a sufficient number of these identifications to study the radio sources statistically.

Since the radio observations themselves offer no direct evidence of the distance of the source, Minkowski obtained optical spectra of 17 of the faint galaxies identified with the nearer radio sources; from these he measured the red shift or apparent velocity of recession, and from the Hubble law (that the red shift is proportional to distance) computed distances ranging from 30 million to 3000 million light years. Though they appear faint, these radio-emitting galaxies have an average optical brightness 25 billion times that of the sun and 3 or 4 times that of a normal galaxy, when the distance is taken into account. In the same manner, their individual outputs of radio power can be determined; these are as large as 5×10^{32} watts per cycle per second at a radio frequency of 158 megacycles per second.

Comparing the numbers of radio sources found in surveys of over half the sky with data from comparable

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