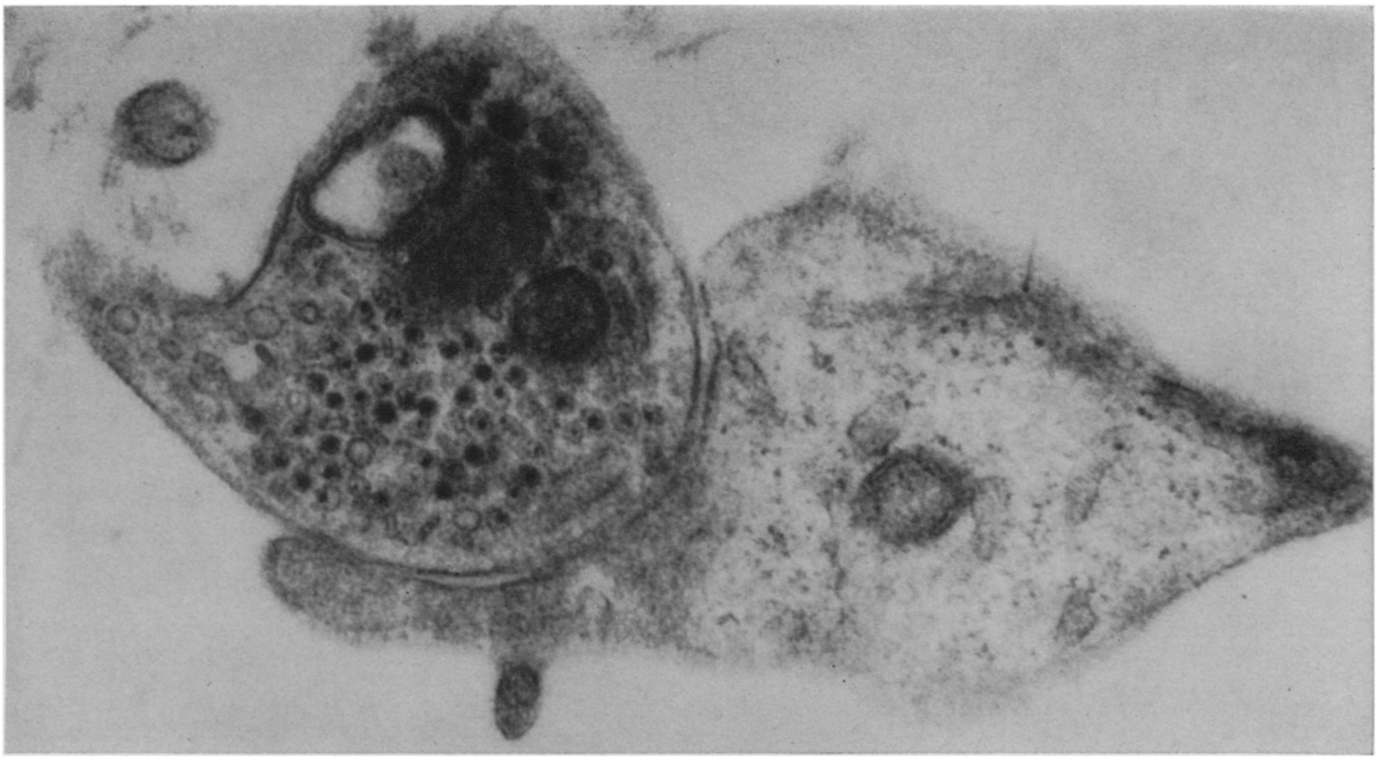


Form and function at work—the sympathetic nerve ending (left) is designed to fit snugly to the pineal gland.

Form and Function: Biological Key

Researchers are finding that experiments in vitro may interfere with understanding in vivo.

by Barbara J. Culliton

If an Egyptian had put even one round stone in the Great Pyramid, chances are King Cheops tomb would not still be standing. Every stone used to build this wonder of the ancient world was cut with the form of each piece designed according to its intended function.

One of the wonders of the modern world also relies on the intricate union of form and function. Biochemists attempting to take the components of life apart and fit them together again like stones in a magnificent monument are learning the pieces fit best when design and purpose match.

There has been a disturbing tendency among scientists to "mash up whole organs and examine their biochemical structures out of the body," one researcher said at the meeting of the American Association for the Advancement of Science. "Mixing kidney and liver in a test tube is silly," he said, because the body doesn't jumble things so, and what the body does is, after all, what scientists really want to know.

Scientists have been thinking in terms of a universality of living matter, a concept likening nature to a card player with only 52 cards. Dozens of games and innumerable hands may come from various combinations of hearts and spades, but in the end, it is merely a reshuffling of a given number of cards. This is "an extremely useful concept in biochemical speculation but one that has been carried too far," Dr. Bernard B. Brodie of the National Institutes of Health said. While the concept may be useful in studying cell physiology, more thorough knowledge of the way body chemistry works requires consideration of functional differences in various cells.

Universalists, for example, might take an enzyme from the adrenal gland of a frog and, having seen how it works, relate its behavior to man. The inadequacy of this kind of generalization lies in the fact that the adrenal glands in frog and man have different forms and therefore different functions. Enzymatic activity in man is influenced by the presence of the adrenal cortex covering the adrenal gland. In frogs there is no adrenal cortex, no additional layer of tissue through which enzymes must pass. Therefore, direct correlation between frog and man fails.

There are several convincing reasons for binding form to function in biochemical research, not the least of which is that life has done so.

Dr. Richard J. Wurtman, an endocrinologist at NIH and the Massachusetts Institute of Technology, had studied, for example, the pineal gland, the would-be eye at the back of the head. In lower vertebrates this organ has a photoreceptor like the retina. It is in fact, an eye and not a gland. It is stimulated by light and sends messages to the brain. Not so in man. The pineal gland has evolved to a state in which it has lost its photoreceptors and its direct line to the brain. Its form has changed; likewise its function. No longer directly affected by light, the gland lies at the end of a long, circuitous road over which nerve impulses in the brain, stimulated by light,

. . . Form and function

eventually reach the pineal via the sympathetic nerves. The pineal makes a hormone called melatonin which inhibits the activity of the ovaries and the pituitary and thyroid glands, but it is no longer an eye by either design or purpose.

"When the structure of an organ has changed radically with evolution, it seems reasonable to investigate whether these changes are involved in controlling the function of the organ," Dr. Wurtman said.

Form and function also hold the key to advances in drug therapy, locked in man's biological control systems wherein everything is dependent on everything else, Dr. Brodie said. We may not know, or ever learn, how certain cells work in a living man simply because we haven't the techniques for measuring all cellular activity in a living organism. However, Dr. Brodie said, in some cases we can and do know the specific action or behavioral pattern of a drug. Science can find its answers at the back door instead of the front. Most drugs used medicinally neither create nor destroy biochemical function; they merely alter its intensity. In other words, a medicinal drug of the right form can make the heart beat more rapidly or more slowly, but a medicinal drug will not alter its function and make it stop beating altogether. Therefore, if you know how a drug works and introduce it to a living system, you can tell something about the form and function of the system by seeing what it does under the influence of the drug.

Biological control systems are called transducers because they change one form of energy to another form. For example, a sympathetic nerve ending can be seen as a box with nerve impulses going in and the chemical noradrenalin coming out. Different drugs control the chemical in different known ways, so one can get at the root of the matter by injecting a drug into the box, so to speak, and find out how the biological control system behaved in its presence by studying the noradrenalin that is released. Thus, one can disclose the nature of the contents of that all important box without ever opening it.

Form and function showed themselves inextricably linked in other areas as well as these. Studies with chick embryos have revealed how in the developing eye the visual retina regulates the size and orientation of the lens which in turn decrees the growth of the cornea. The form of the lens is so important that if it is removed, a developing cornea regresses and disappears.

MOLECULAR MEMORY

Memory Still Elusive

Negative findings sometimes make good science.

An antibreakthrough in man's attempt to understand the way memory works was reported at the meeting of the American Association for the Advancement of Science.

Scientists trying to repeat experiments purporting to show that memory is based on certain molecular changes in the brain found that either the experiments did not repeat or that other explanations were possible. In science's enthusiasm over recent advances in breaking the genetic code, some have eagerly built a superstructure explaining the biochemical basis of memory. All this has been covered by a shadow of doubt.

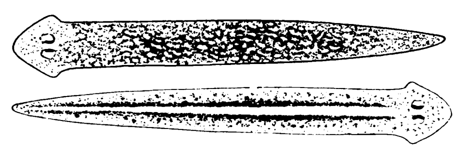
Learning and remembering are not necessarily contingent upon the synthesis of ribonucleic acid and protein, Dr. Samuel H. Barondes of Albert Einstein College of Medicine said.

Dr. Barondes used highly toxic antibiotics to test memory storage in mice. Large doses of the drugs that inhibit RNA and protein synthesis in the brain were injected directly into brain tissue. Inhibition of RNA synthesis was achieved, but none of the inhibiting drugs kept the mice from learning their way in a maze.

Three hours later, when they were tested to see if they still remembered what they had learned, the puromycin-injected mice had forgotten, but there is evidence that impairment of electrical activity in the brain rather than RNA inhibition may explain the effect.

"Long-term" memory, lasting one or more days, may be associated with protein synthesis in the brain according to some studies, but the "significance of these findings is presently uncertain," Dr. Barondes said, and the structure of memory remains elusive.

Among the experiments on which the molecular basis of memory theory is built is the famous experiment with flatworms or planaria. Flatworms were trained to perform a specific task. Then, for their pains, they were ground up and fed to another set of worms. And inexplicably—except by the molecular theory—they could perform the tasks their lunch had learned.



Smithsonian Institution

The RNA for lunch bunch.

RNA from the original worms provided the second group instant learning, it was hypothesized. But others were unable to duplicate the work.

BIOCHEMISTRY

Stress and the Brain

Brain chemistry is definitely affected by stress, isolation, noise and other environmental changes, the American Association for the Advancement of Science meeting was told.

Using mice and other animals, a symposium including a husband and wife team—Drs. Bruce and Annemarie Welch of the University of Tennessee and the Oak Ridge Institute for Environmental Studies—reported that the output of three compounds in the brain affects animal behavior and response. The amount of chemical substances regulates transmission of specific nerve impulses, and is linked to environment.

Dr. Bruce Welch said he hoped the animal research would lead to understanding mental illness. Chemical control of neurotransmission has been controversial, he admitted at a news conference, but the "weight of evidence" favors it, he said.

Dr. Annemarie Welch reported studies contrasting animals kept in isolation and those put into groups of 5 or 10 to a cage. By changing the animals back and forth the chemical effects were reversible. Metabolism changes rapidly in different environments, she said.

One of the tests conducted by Dr. Eugene Bliss of the University of Utah, consisted of a "combat situation" in which a submissive mouse was put into a cage with an aggressive mouse. After the meek mouse had been thoroughly frightened by an attack, its brain was examined for chemical compounds. In another test, electric shocks were given through the foot pads, and in still another test the animals were restrained up to 16 hours.

Dr. Bliss also tried sleep deprivation studies. An exhausted mouse on a pedestal surrounded by water became sleepy and would fall into the water because of the chemical change.