Meetings

New Perspectives in Biology

A notable symposium on new perspectives in biology was held at the Weizmann Institute of Science, Rehovoth, Israel, 10–17 June 1963 to celebrate the inauguration of the Ullmann Institute of Life Sciences. Biologists, biochemists, and biophysicists from Europe, the United States, and Israel presented papers on the present state and future prospects of many fundamental problems in biology and carried on informal discussions for a week.

We may recall briefly the history of the Weizmann Institute. Its forerunner, the Daniel Sieff Research Institute, was dedicated in 1934, and formally opened by Chaim Weizmann, who played an active role in its development. Expansion of the Sieff Institute was conceived in 1944, when a group of Weizmann's friends wished to honor his 70th birthday, and the Weizmann Institute was formally dedicated by Weizmann in November 1949. It has since grown to comprise 18 research units, and its activities range from applied mathematics and theoretical chemical physics to genetics and cell biology. The Ullmann Institute of Life Sciences, which was dedicated at the beginning of the symposium on 10 June, is the newest institute. It was donated by Siegfried and Irma Ullmann of New York and will comprise research units of biochemistry, biophysics, virology, and genetics.

Jacques Monod (Pasteur Institute) delivered the opening lecture of the symposium on the role of allosteric effects in the control of cellular metabolism. These involve the transmission of inhibiting, or sometimes of activating, effects from one region of an enzyme molecule to another. The inhibiting agent represents generally the final product of a metabolic pathway whereas the enzyme catalyzes the initial reaction in that same pathway. The profound biological significance of these mechanisms is clear; Monod and his colleagues, J. P. Changeux and F. Jacob, have recently provided an admirable review [*J. Mol. Biol.* **6**, 306 (1963)].

The following morning session was devoted to proteins, beginning with a survey of important trends in current protein research by J. T. Edsall (Harvard), followed by a discussion by J. C. Kendrew (Cambridge) of the detailed structural features of myoglobin and hemoglobin, their implications for protein structure in general, and the prospects and difficulties of further explorations of protein structure by x-ray crystallography. H. Neurath (University of Washington) dealt with the structure and function of proteolytic enzymes, and particularly with the recent remarkable findings in his laboratory involving the activation of pancreatic procarboxypeptidase to give at least two distinct active enzymes.

In the afternoon session E. Katchalski (Weizmann Institute) surveyed his work on synthetic polyamino acids and their many applications in biology, including the induction, in "prolineless" mutants of *Escherichia coli*, of an enzyme, proline iminopeptidase, that digests polyproline; the growing of "whiskers" of polyamino acid side chains on the amino groups of natural proteins; the stabilization of enzymes by binding them to water-insoluble carriers; and the use of polypeptidyl derivatives of aminoacyl compounds of soluble ribonucleic acids to pick out the molecules of sRNA that are specific for particular amino acids. F. A. Lipmann (Rockefeller Institute) gave a thoughtful and searching discussion of the problems of protein biosynthesis. F. Lynen (Munich) considered the coordination of metabolic processes by multienzyme complexes, with definite morphological structure, but at a far simpler level than that of the mitochondrion. The protein components possess both catalytic sites and binding sites that hold the components of the complex together. The pyruvate dehydrogenase system [Koike, Reed, and Carroll, *J. Biol. Chem.* **238**, 30 (1963)] and the multienzyme complex concerned with converting malonyl coenzyme A to higher fatty acids—the latter has been studied intensively in Lynen's laboratory—are outstanding examples of such systems.

On the following day all participants in the symposium journeyed to Jerusalem, where a morning session was held at the Hebrew University, in one of the buildings of the beautiful new campus on Givat Ram. Paul Doty (Harvard) discussed his work, and that of others, on hybrid molecule formation in nucleic acids, and George Klein (Stockholm) considered fundamental problems in the genetic aspects of neoplasia. The afternoon was spent in visiting Jerusalem and its surroundings in Israel, and in the evening the President of Israel gave a most delightful and informal reception for the whole group.

In Rehovoth again, the symposium continued the next day with discussion of nucleic acids. Erwin Chargaff (Columbia University) presented, with clarity and elegance, the problem of nucleotide sequences in nucleic acids, and his own approach to the problem by the use of reagents that selectively attack the purine or the pyrimidine rings —the latter offering far the more difficult chemical problem. David Elson (Weizmann Institute) considered the structure of ribosomes, with particular reference to certain enzymes found in ribosomes. When 70S ribosomes dissociate into 50 and 30S components, at very low concentration of magnesium ion (Mg^{++}), ribonuclease is found exclusively in the 30S component. Deoxyribonuclease is found in neither, but passes into solution, the process being reversible, whereas β-galactosidase is found in both components and does not leave the ribosomes when they dissociate. He described how transfer (soluble) ribonucleic acid can be obtained from ribosomes exposed to high salt concentration. Alfred Gierer (Tübingen) discussed the mechanism of protein synthesis in reticulocytes, with particular emphasis on the role of polyribosomes, the great importance of which has become manifest only during the last year or so, as a result of work in his and several other laboratories. Severo Ochoa (New York University) discussed the present state of work on the genetic coding problem—a subject so widely known that I omit further comment on it here, in spite of its supreme importance. C. B. Anfinsen (Na-

tional Institutes of Health, Bethesda) considered the problems involved in predicting three-dimensional structure of proteins from the amino acid sequence. There is strong experimental evidence from his work on ribonuclease and other proteins, that, given the sequence, the peptide chain will fold spontaneously into the correct steric structure, but the problems of predicting this structure are formidable.

That evening, in Tel Aviv, E. B. Chain (Rome) gave a dramatic and very interesting lecture on the newly developed penicillins, which have so significantly enlarged the therapeutic uses of penicillin.

The symposium then turned to problems of development and differentiation. E. Kellenberger (Geneva) reported on the use of facultative lethal mutants for the investigations on the assembly (morphogenesis) of phage particles. These mutants are distributed all over the genetic map, so that they affect numerous genes: eight genes affect the formation of the phage head. Mutants in some genes produce abnormal assembly of subunits, as for example into long tubes, the "polyheads." The subunits are not self-assembling, but need supplementary information (morphogenetic principles) to be shaped correctly. The micrographs of "polysheath," however, suggest that the subunits of the tailsheath are of the self-assembling type. Leo Sachs (Weizmann Institute) considered problems of cell differentiation and the immune mechanism. Lymphoid cell precursors, in tissue culture, can form essentially pure cultures of either mast cells or antibody-producing cells, provided a suitable layer of other cell types is present in the medium. Lymphoid precursors from lymph nodes of a rat, exposed to mouse cells, differentiate to give cells releasing antibodies, which destroy the mouse cells; that is, this is a heterograft reaction in vitro. Both Sachs and, independently, Dulbecco have studied the transformation of normal into tumor cells by the polyoma virus, and the virus acts directly on the cells to induce the change. Michael Feldman (Weizmann Institute) considered the role of the thymus in promoting antibody formation in the adult organism, making use of the histocompatibility antigens which are determined by the Y-chromosome of male animals. Transfer of such antigens from a male to a female of the same species, in a tissue graft, leads to rejection of the graft by the female, due to an anti-Y immune response. Some tumors induced in males cannot grow when transplanted into females because they evoke a similar response. However, animals previously irradiated with x-rays fail to develop the immune response until after several weeks, and the tumor in the female continues to grow. If the animal has been thymectomized, the immune mechanism does not recover at all after x-radiation; grafting a thymus back into such animals, however, does lead to recovery of the immune response. This recovery is an inductive effect of the thymus; it is not due to production of immunologically competent cells by the thymus itself.

H. H. Weber (Heidelberg) discussed the role of adenosine triphosphate (ATP) in the active transport of ions, with special reference to the work of W. Hasselbach in his institute on the vesicles of the sarcoplasmic reticulum, which accumulate calcium ions. There is a very close correlation between the Ca^{++} ions transported and the ATP hydrolyzed (2 Ca^{++} per ATP). He concludes that the ATP denotes an energy-rich bond to phosphorylate a carrier in the membrane, and that the phosphorylated carrier has an affinity for Ca^{++} ion several hundred times as great as the unphosphorylated carrier. David Nachmansohn (Columbia University) considered chemical control of movements of ions across conducting membranes, with special reference to nerve and electric organs. Hugo Theorell (Stockholm) set forth, with beautiful clarity, his recent work on complexes of liver alcohol dehydrogenase with coenzymes and inhibitors or substrates.

The last session was devoted to immunochemistry. Michael Heidelberger (Rutgers University) described his recent work on the immunological properties of the capsular material of pneumococci of various types. The structure of the carbohydrates in these capsules is now becoming known in far more detail than ever before—in type SV, for example, recent work of Barker in Birmingham, on material supplied by Heidelberger, has identified N-acetyl-L-fucosamine and N-acetyl-6-deoxytalosamine, among other constituents. These two sugars were never before known in natural products. The chemical identification of antigens by immunochemical techniques is now being greatly refined, and in many cases furnishes a short cut to determination of the structure of the antigen. Michael Sela (Weizmann Institute) described his researches on the development of

polyamino acids and their derivatives as synthetic antigens. One good antigen can be made from polylysine by first growing alanyl chains on the amino groups of the lysyl side chains and then attaching tyrosyl chains to the alanyl chains. If the attachments are made in reverse order—first tyrosine, then alanine—the resulting product is not antigenic. The tyrosyl groups must be on the outside to make a good antigen. The optical specificity of the amino acids is important—compounds made from combinations of D-amino acids are generally nonantigenic, even when the corresponding L-compounds are strongly antigenic. Sela's recent work has shown that electric charge is not necessary for antigenicity. He and a colleague have recently synthesized a water-soluble, uncharged polymer that is strongly antigenic. [M. Sela and S. Fuchs, *Biochim. Biophys. Acta* **74**, 797 (1963)]. When galactose is attached to a synthetic polymer, the galactose grouping becomes a powerful antigenic determinant. Immunological tolerance may be established to synthetic antigens, as shown by experiments on new-born rabbits. The aim of all these researches is to throw light on the nature of the immune mechanisms found in living organisms; the synthetic chemicals are merely a means to this end.

J. C. Kendrew concluded the final session with brief, graceful, and humorous comments on some of the major points of the symposium.

One nonscientific interlude deserves mention. Midway in the week, we left Rehovoth for a 2-day trip along the coast to Caesarea, Haifa, and Acre, then to the Galilee mountains and the Lake of Galilee. We stopped overnight at a kibbutz which, in addition to the usual farming and other community activities, ran a small and very pleasant hotel for visitors. That evening all of us had the opportunity to talk with members of the kibbutz and learn directly about their way of life, its values and its problems. We returned with renewed zest to the scientific conference after this fascinating interlude. In addition to this thoughtfully arranged pause in the symposium, all of us will remember the warm and generous hospitality of our Israeli hosts, during and after the conference, which combined with the high level of the scientific discourse at the meetings to make this a most memorable occasion.

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