teraction with the electron-transport system for pyridine nucleotide–linked substrates, and an additional site for succinate. The session on bacterial energetics was fittingly concluded by R. M. Hochster (Canada Department of Agriculture, Ottawa) with a discussion of some unsolved problems in this area. Major difficulties in assessing the efficiency of oxidative phosphorylation in microbial systems arise from high phosphatase activity and the existence of bypasses in the oxidative reactions.

The dynamics of carbohydrate metabolism in mammalian cells was discussed by G. R. Williams (University of Toronto) and E. Shrago (University of Wisconsin). By continuous monitoring of $C^{14}O_2$ released from carboxyl-labeled substrates by respiring liver mitochondria in vitro it was possible to calculate the rate constants for utilization of intermediates of the tricarboxylic acid cycle. The rate constant for fumaric acid was considerably greater than that for succinic acid, which suggests that succinic dehydrogenase is a limiting component of the cycle. Studies in vivo of enzymes in animals made diabetic by alloxan treatment revealed marked alterations in pathways of carbohydrate metabolism. The most dramatic change was the marked increase in activity of the soluble enzyme phosphoenolpyruvic acid carboxykinase in liver; since the increase was reversed by injection of insulin it would appear that this enzyme plays a key role in the endocrine regulation of gluconeogenesis.

Dissection of the mitochondrial oxidative phosphorylation process into its partial reactions was presented by C. L. Wadkins (Johns Hopkins University). A protein of low molecular weight which catalyses an exchange reaction between adenosine diphosphate and adenosine triphosphate may be extracted from liver mitochondria; simultaneously, the phosphorylation coupled to cytochrome *c* oxidation is abolished and may be restored by addition of the purified exchange enzyme to the depleted mitochondria. The exchange enzyme appears to correspond in its action and properties to the coupling factor III described by Green and co-workers. Kinetic studies indicate that ferro-cytochrome *c* combines at two sites on the exchange enzyme; interaction at one site is blocked by dinitrophenol, while azide or oligomycin A prevent combinations at both sites.

W. Chefurka (Agricultural Research Institute, London) presented comparative data on the lability of phosphorylation reactions in mammalian mitochondria and insect sarcosomes. The rapid aging of insect mitochondria is related to the rapid release of free fatty acids from mitochondrial lipids. The most sensitive indicator of the aging process is the adenosine triphosphate cleavage which occurs in the presence of dinitrophenol. The disappearance of the latter enzyme on aging may be reproduced in vitro by addition of fatty acid.

The symposium was thoroughly and efficiently organized by a local committee under the chairmanship of K. P. Strickland. Fortunately, the organization was not so rigid as to preclude free discussion of the stimulating data and ideas presented in the formal papers. Moreover, the speakers and participants widened their field of interest to take part in several interesting functions concerned with nutrition, digestion, and the products of fermentation. Plans are under way to publish the papers in the *Canadian Journal of Biochemistry*.

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Nerve as a Tissue

The biochemical and biophysical bases of brain functions are being increasingly studied and understood. In view of the rapid development of this field, the choice of "Nerve as a Tissue" as the subject of the fourth Lankenau conference on tissue, held 12–13 November 1964 in Philadelphia, was especially appropriate.

At the session on morphology, S. L. Palay (Harvard Medical School) discussed the way in which nerve cells and their processes are interconnected and, especially, the way in which the surrounding cells are related to the nerve cell. He showed that the glial fibers and glial processes are distributed throughout the neuropil of the system in a specific pattern. Palay suggested that the terminals within a single compartment of the glia arise from the same cell or from cells that have similar significance with respect to the postsynaptic element; the compartments of glia isolate the postsynaptic membrane from neighboring synapses which have a different significance with respect to the postsynaptic element. This Palay interpreted to mean that terminals lying within adjacent or neighboring compartments may be presumed to originate from different perikarya.

J. D. Robertson (Harvard Medical School and McLean Hospital) talked about intimate details of membrane structure, the relations between cells and membranes at their contact points, and the study of these relations by the use of x-ray diffraction techniques in conjunction with electron microscopy. G. D. Pappas (Columbia University) discussed ultrastructure of nerve cell membranes and problems of cell interaction and indicated the existence of a wide variety of interneural relations in the central nervous systems of vertebrates. Pappas discussed the various morphological criteria that have proved useful in correlating structure and function.

Eduardo De Robertis (Universidad de Buenos Aires) reviewed synaptic complexes and synaptic vesicles as structural and biochemical units of the central nervous system and described a technique of osmotic shock which permits isolation of synaptic vesicles from the nerve endings. He showed that synaptic vesicles are storage units for acetylcholine, norepinephrine, dopamine, and probably other transmitter substances in the brain.

David Nachmansohn (Columbia University), presiding over the biochemistry session, presented a paper on molecular forces which control bioelectric currents in membranes and concluded that the theory of neurohumoral transmission is no longer tenable. O. H. Lowry (Washington University School of Medicine) reviewed the chemistry of the nerve cell. R. J Rossiter (University of Western Ontario) discussed biosynthesis of phospholipids and sphingolipids in the nervous system, concluding that in brain and nerve, as in most other tissues, phospholipids and sphingolipids are formed *in situ* from appropriate smaller molecules; he pointed out that the brain of a young animal, taken at the time of rapid myelin deposition, serves as an excellent source of many of the enzymes responsible for the biosynthesis of complex lipids.

Hans Weil-Malherbe (St. Elizabeth's Hospital, Washington, D. C.) spoke on storage and metabolism of neurotransmitters, and Eugene Roberts (City of Hope Medical Center, Duarte, Calif.)

presented a theory for the synapse as a biochemical self-organizing cybernetic unit. Roberts concluded that according to the best data presently available it is not necessary to postulate actual production and storage of chemical memory records or stimulus-directed syntheses of special "memory" molecules. During the discussion period there was a vigorous exchange of views between Nachmansohn and the audience.

The chairman of the session on the physiology and pharmacology of the nerve cell, G. B. Koelle (University of Pennsylvania), briefly summarized the two earlier sessions and reviewed evidence supporting the theory of neurohumoral transmission, thus setting the stage for discussion of nerve functions. R. D. Keynes (Institute of Animal Physiology, Cambridge, England) reported on his studies of the thermodynamics of nerve and of the electric organ in fish; he discussed theories of the causes of temperature changes in the nerve which are associated with single impulses and of temperature changes in electric organs. W. L. Nastuk (Columbia University) discussed the action of certain quaternary ammonium compounds in neuromuscular transmission. D. R. Curtis (John Curtin School of Medical Research, Canberra) comprehensively reviewed synaptic transmission in the central nervous system and its pharmacology, including central inhibition, the role of acetylcholine as a central transmitter, and the possibility that amino acids present in central nervous tissue are also transmitters. K. S. Cole (National Institute of Neurological Diseases and Blindness) reviewed the nerve impulse, pointing out that an impulse is conducted along a nerve fiber by a rise of the membrane potential and an inflow of sodium ions. Recovery follows, with a loss of potassium ions and a return of the potential to the original resting level. Cole also pointed out that it now seems probable that the membrane is a bimolecular layer, but that the processes by which ions move across it and produce an impulse are entirely unknown and most proposed theoretical and experimental models for a nerve membrane are not able to explain important observed facts.

At the session on the pathophysiology of nerve tissue, Frederic Bremer (University of Brussels) spoke on "The tissue and the organ." A. A. Ward (University of Washington, Seattle) presented conclusive evidence that neurons in the epileptogenic focus are characterized by autonomous hyperactivity, confirming Jackson's hypothesis that they are in a hyperphysiologic state. His data suggest that such neurons are at least partially denervated. Ward pointed out that there is a body of evidence supporting the idea that denervation of excitable membrane is associated with autonomous hyperactivity and suggested that one of the proximate causes of the autonomous hyperactivity may well be a reduction of resting membrane potential of dendrites or soma, or of both.

D. Elmqvist (University of Lund, Sweden) reported on his studies of neuromuscular transmission in patients suffering from myasthenia gravis; the work was done in vitro with intracellular electrodes. The amplitudes of the miniature endplate potentials and of the quanta in the endplate potentials were found to be small, but the frequencies, as well as the number of quantal components, of the miniature endplate potentials were normal. The sensitivity of the postsynaptic membrane to carbachol and decamethonium was the same in the muscle of myasthenic patients as in that of controls. Elmqvist concluded that in myasthenia there is a deficiency in the amount of acetylcholine in the quanta released from the motor nerve terminals.

R. B. Richter (University of Chicago) presented a general commentary on research accomplishments which have most profoundly influenced the practice of clinical neurology. He anticipated that knowledge of brain as a tissue will provide definitive explanations of the pathogenesis of many degenerative neurological diseases which are currently merely surmised to be inborn errors of metabolism. "It is even possible," he said, "that much more occult disorders such as schizophrenia will be shown to have their specific histo- or cytometabolic substrates."

At the conference dinner Sir John Eccles spoke on the strategy of neurophysiologic research in a most informative and stimulating manner. He pointed out that it is not scientifically disgraceful to have one's hypothesis falsified, saying, "We will advance in scientific understanding by the experimental rejection of erroneous hypotheses, so that the way is cleared for new conceptual developments." He emphasized the importance of choosing very carefully the best sites for experimental investigation and warned against "running in a groove." Eccles recommended breaking off now and then from detailed scientific work "to lift one's eyes to scan distant horizons" and underlined the value of personal communications and free exchange of ideas with constructive criticism. "I would suggest that if your theories are attacked, that is really a compliment," he said; "It shows that they are worthwhile and a challenge to criticism. How much worse it is to have them ignored!"

The proceedings, including discussions, will be published by Harper & Row, New York.

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Nuclear Activation Analysis

What appears to be a major breakthrough in the field of small neutron generators was announced at the conference on recent advances in activation analysis held in Glasgow, Scotland, 27–28 August 1964. Whereas simple sealed-tube sources of 14-Mev neutrons available heretofore have had an output range of only about 10^7 to 10^8 neutrons per second, a new British system has a neutron output of 10^{10} per second.

C. H. Gill (Elliott Electronic Tubes, Ltd.) described the new tube. Operating with a mixed deuteron-triton beam of 1 to 2 ma and an accelerating potential of 110 kv, the tube maintains 14-Mev neutron output rates of 10^{10} per second or more for at least 100 hours and possibly for as long as 500 hours; the target can then be replaced at a reasonable cost. According to P. D. Lomer (Services Electronics Research Laboratory), the tube can be switched on and off at will and rapidly reaches a steady output rate. A thin film of erbium metal (tritiated) on a simple metal backing is used as the target. The lifetime of the tube appears to be limited primarily by target sputtering. A similar 10-ma current tube, which may give about 10^{11} neutrons per second, is under development; this tube would rank in output with the larger, more expensive, pumped, gas-input 14-Mev neutron generators now in wide use, especially in the United States.

An advanced, high-precision activation-analysis system for quantitative determination of oxygen in metals and