cancer process. Jacquez then turned to the question of "dependent tumors" which require an endocrine factor to sustain them initially, but which thereafter become autonomous. The initiator is probably a virus and the endocrine dysfunction is a promoter. Jacquez concluded from the evidence accumulated from nuclear transplantation experiments that the basis for cancer is not exclusively genetic. He described the progression of cancer in terms of cell population genetics and ecology. The progression of the tumor involves cell growth, mutation, and selection. The selection mechanism usually favors the more malignant cell type and rarely leads to a cure of the tumor by regression.

Cornelius A. Tobias (University of California, Berkeley) described the role of ionizing radiation and environmental factors in the production of abnormal growth. A radiation lesion acts as an initiator in the presence of "goal-seeking" promoters that relate to homeostatic balance in the tissue. Tobias discussed the sequence of phenomena in the production of ribosomal RNA, the suppression mediated by transfer RNA, the presence of regulators and operators, and finally, the role of the operon in the genetic apparatus. He described a scheme in which the DNA and RNA mechanisms are involved in a feedback loop that is statistical in operation and has different levels of action. He then used this model to indicate where breakdowns might occur leading to pathological control mechanisms.

George E. Stapleton (U.S. Atomic Energy Commission, Washington, D.C.) pointed out that the effect of irradiation is twofold. First, it inhibits macromolecular synthesis, and secondly, the process of cell division is modified. Minimum effects depend upon the status of the cell metabolically at the time of irradiation. It has been shown that the resistance of the cell to radiation depends on the amount and class of ribosomes present in the cell when radiation occurs.

Howard I. Adler (Oak Ridge National Laboratory) described an interesting mutant of *E. coli* which had lost the capacity to divide following small doses of ionizing radiation. These bacteria grow to approximately 200 times their normal length, but in other respects their DNA-RNA mechanisms appear normal. Mating occurs between them, but no progeny results. They are anucleate and thus without DNA, but possess RNA and protein. These bacteria can be reverted to a normal type by back mutation.

Endocrine control of reproductive mechanisms at three organizational levels—the hypothalamus, the hypophysis, and the ovaries—was discussed by Charles W. Lloyd (Worcester Foundation for Experimental Biology, Massachusetts). He pointed out that corticotropin and gonadotropin may be different in the circulating state from their condition in the target organ. This difference apparently relates to the removal of protein that coats the substances in the circulating condition. Lloyd noted that the technique of radioimmune bioassay has shown that previously held views on the sequence of hormone levels in the menstrual cycle are not strictly correct. The breakdown and blockage of endocrine control mechanisms was discussed in relation to hypergonadism and to the regulation of fertility by oral contraceptives.

Eugene Roberts (City of Hope Medical Center, Duarte, California) presented a series of models for correlative thinking about brain, behavior, and biochemistry. The effect of puromycin injections on memory processes in goldfish was discussed by Bernard W. Agranoff (University of Michigan).

The conference, chaired by W. Ross Adey (UCLA), was organized under the auspices of the Interdisciplinary Communications Program of the New York Academy of Sciences (Dr. Frank Fremont-Smith, director) and was supported by the National Aeronautics and Space Administration and the Smithsonian Institution. An edited transcript of the proceedings is scheduled for publication before next year's meeting. Aspects of innate versus learned behavior and the temporal patterning of control mechanisms in these behavioral processes will be the subject of next year's conference.

DIANE M. RAMSEY
Douglas Aircraft Company, Newport Beach, California

Pi Complexes in Biological Systems

Pi-complexes have been implicated as intermediates in many chemical reactions and are involved in a number of important biological processes. To motivate interest and to demonstrate that π-interactions may well be the rule in biological systems and not the exceptions, the New York Academy of Sciences sponsored a discussion group that met on 28–29 March 1967 in New York City.

The opening sessions were devoted to a review of basic principles of π-interactions. The general theory of organic-organic π-complexes was summarized by S. P. McGlynn (Louisiana State University). Current theories of π-bonding in complexes of transition metals and organic compounds were covered by S. J. Lippard (Columbia University). Using the molecular orbital approach, with illustrations taken from various classes of organometallic complexes, he indicated that a major feature of these complexes is the "back-bonding" of accessible antibonding π-orbitals of the organic ligand which prevents the accumulation of an excess negative charge on the metal atom.

A. R. Lepley (Marshall University) discussed the electron-acceptor properties of indanetrione, a dehydration product of ninhydrin. This acceptor forms complexes with aromatic hydrocarbons and reacts with aldehydes, ketones, and amines via π-complex intermediates. Spectroscopic studies in various solvents yielded basic information concerning changes in transition energies and the nature of π-complexes. Evidence was presented for multiple complex formation.

Four papers on π-interactions in biological systems dealt with the question of the interaction of mutagenic and carcinogenic agents with nucleic acids. Isenberg (Oregon State University) discussed the solubilization of several aromatic hydrocarbons by DNA. Phenanthrene, pyrene, and benzo(*a*)-pyrene (but not coronene) are solubilized by DNA. The solubilization was ascribed to insertion of the hydrocarbon molecules between purine and pyrimidine base pairs of the nucleic acid and complex formation between the inserted hydrocarbons and the bases. In contrast to DNA, single-stranded polyadenylic acid did not solubilize these aromatic hydrocarbons.

The crystalline complexes formed by aromatic hydrocarbons or heterocyclics with purines are weak and dissociate in solution (B. L. Van Duuren, New York University Medical School). Both carcinogenic and noncarcinogenic hydrocarbons form such complexes. Also, both groups are solubilized by

nucleic acids. Such solubilization by nucleic acids might occur at denatured sections and not by intercalation. The binding of acridine orange dyes which contain bulky substituents to DNA was described. The spectroscopic patterns of the substituted dyes are similar to that of unsubstituted acridine orange. These molecules probably bind not by intercalation but by external electrostatic binding at phosphate sites and by hydrogen bonding.

E. Reich (Rockefeller University) discussed the formation of complexes between actinomycin and DNA. The selective substitution or elimination of functional groups of guanine in DNA indicates that the amino group at the 2-position of guanine is an indispensable component of the actinomycin binding site in DNA. Modified DNA-like polymers containing A-T (adenine-thymine) base pairs which also have an amino group at the position corresponding to the location of the amino group of guanine were synthesized, and this kind of polymer also interacts with actinomycin. The resulting complexes resemble in every way those formed between actinomycin and DNA. It was concluded that a purine 2-amino group in a narrow groove of DNA determines the binding of actinomycin.

P. O. Ts'o (Johns Hopkins University) summarized his studies on the association of purine and pyrimidine nucleosides in aqueous solution. Nuclear magnetic resonance studies show that the nucleosides associate by vertical stacking that results in partial overlap of the nitrogen bases. Ts'o also examined the interaction of purine bases with nucleic acids and showed that there are specific interactions, such as that between adenosine and polyuridylic acid. These interactions were ascribed to hydrophobic forces, but hydrogen bonding also appears to play some role. Ts'o also considered the problem of the interaction between carcinogenic hydrocarbons such as benzo(*a*)pyrene and nucleic acids. Evidence was presented indicating that the carcinogen binds to single-stranded and helical polyadenylic acid and to deoxyribonucleic acid. These conclusions were reached on the basis of sucrose-gradient electrophoresis and small shifts in the ultraviolet absorption spectra of benzo(*a*)pyrene to longer wavelength. These observations support the notion that aromatic hydrocarbons bind to nucleic acids by insertion between base pairs of the nucleic acid, possibly at an interrupted or locally disordered region of the double helix.

R. Rein (State University of New York at Buffalo) presented a critical analysis of the approximations made in the quantum-mechanical calculation of stacking energies of DNA base pairs. The method involving the polarizability of the monopole bond gave values which agree better than those obtained by semiempirically calculated methods. The approximation is good not only for calculation of stacking energies for base pairs in DNA, but perhaps for π-conjugated systems in general.

Four papers on π-complexes of metals and bioorganic compounds were presented. W. Kornicker and B. L. Vallee (Harvard University) have examined the interaction of proteins with well-defined metal π-complexes, such as the metallocene sandwich complexes. The lipophilic nature of the metal π-complex permitted entry into the protein in regions that are inaccessible to simple metal ions. The properties of π-complexes of transition metals and organic compounds offer other advantages for study.

The important biological role of copper is recognized, but the precise chemical nature of copper-protein remains unclear. J. Harris and K. Ritchie (Barrow Neurological Institute and Arizona State University) presented a model of copper-protein oxidative activity with a system obtained from the interaction of copper (II) and tricyanoaminopropene. The latter, with an imine-enamine structure, can undergo π-π or n-π transitions (or both) and then reacts specifically with copper in the presence of oxygen. Identical fluorescence complexes result from the interaction of tricyanoaminopropene and protein-bound copper as found in ceruloplasmin and cytochrome oxidase. Various substrates of copper-proteins, such as aminophenols and reduced cytochrome *c*, also react rapidly with copper (II) and tricyanoaminopropene or the already formed complex. From this fact, a model was developed which paralleled the behavior of cytochrome oxidase. W. S. Caughey (Johns Hopkins University) presented experimental and theoretical data showing the contributions of π-interactions to structure-function relationships of heme proteins as well as simpler metalloporphyrins. Theoretical calculations, magnetic susceptibilities, and Mössbauer parameters for oxygenated myoglobins and hemoglobins indicated π-bonding between oxygen (acceptor) and iron (II) (donor). The π-bonding between axial ligands and iron is important in the interaction between carbon monoxide and porphyrins. The effect of peripheral substituents as related to the nature of interaction of porphyrin with protein or solvent environment was discussed.

The nature of the carbon-cobalt bond in cobalamins (B_{12} coenzymes) was discussed by L. L. Ingraham (University of California, Davis). The special properties of the π-electron system of the corrin ring was examined by a modified Wolfberg-Helmholtz calculation.

The action of antibiotics on oxidative phosphorylation was reviewed by R. Guillory (Cornell University). The probability of π-interaction as a basis for antibiotic inhibition of oxidation or phosphorylation was discussed on the basis of the aromatic properties of two classes of antibiotics. In the case of actinomycin A, a possible interaction between π-electrons of the aromatic ring and nonheme iron of mitochondria cytochrome could account for its observed effects. Data were presented on the effect of an uncharacterized antibiotic (DIO-9) on oxidative phosphorylation. The aromatic character and grossly similar behavior to the classical uncoupler, 2,4-dinitrophenol, suggests possible π-interaction. However, DIO-9 has activity which makes it distinct from that of 2,4-dinitrophenol and actinomycin A.

The evening speaker was A. Szent-Györgyi, who reviewed his work on charge-transfer phenomena and on cell growth.

The conference was more than a communication of research findings. There was concern for the need to encourage biological investigators to make use of principles and methods of coordination chemistry. The term "prospectives" was not chosen arbitrarily but was significantly related to the sponsorship by the New York Academy of Sciences in its sesquicentennial year.

JOSEPH HARRIS
Barrow Neurological Institute, Phoenix, Arizona, and *Arizona State University, Tempe*
MINORU TSUTSUI
Department of Chemistry, New York University, Bronx
BENJAMIN L. VAN DUUREN
Institute of Environmental Medicine, New York University School of Medicine, New York