Meetings

Magnetic Resonance in Biological Systems

Physical methods hold as much mystical fascination for the biologist disenchanted with the sterility of traditional biological techniques, as biology holds romantic lure for the physicist disenchanted with the drought of easily soluble problems in physics. It is therefore not surprising that the potentialities of magnetic resonance for resolving the problems of biology have aroused interest in both the exact and the descriptive sciences—ranging from solid state physics, through all branches of chemistry, to botany and medicine. At the first International Conference on Magnetic Resonance in Biological Systems, held at the American Academy of Arts and Sciences in Boston, Massachusetts, on 20–22 July 1964, the barely 10-year-old field had its moment of truth.

To allow an overall assessment of the current trends and state of knowledge and to take advantage of the common ground on rules of evidence, both branches of magnetic resonance spectroscopy—nuclear magnetic resonance (NMR) and electron spin resonance (ESR)—were represented. Some coherence of presentation was ensured by arranging the individual sessions according to subject—ion complexes, proteins and enzymes, photosynthesis, and so forth—rather than according to method.

In his opening remarks, C. H. Townes (M.I.T.) reminded the audience of the observation, all too frequently ignored by the champions of interdisciplinary research, that the limits of knowledge in a given discipline are determined much more by the relative intricacy of the subject matter than by the relative incompetence of the experts concerned. The subsequent program provided ample illustration. As the complexity of the observed system increased, the interpretability of the data decreased. Thus, where one could, with reasonable confidence, derive electron distributions from magnetic resonance measurements on simple molecules, the very origin of the signals observed on cells and tissues—not to speak of the changes in them—remained more often than not an open question.

In view of this fact, the contributions of magnetic resonance of interest to biology are perhaps best considered in three distinct categories: (i) structural studies of natural products, their complexes and free radicals; (ii) studies of molecular interactions and transformations in chemically defined systems of biological origin; and (iii) studies of events in crude cell fractions, whole cells, or tissues.

By far the largest number of reported contributions falls into the first category and only a few novel examples were discussed at the conference. Among the several noteworthy studies of metal ion complexes, reported by Vänngård (University of Goteborg), Blumberg (Bell Telephone Laboratories), Fujiwara (University of Tokyo), Klein (University of California) and others, was the structure determination of cobalt-ATP by a combination of NMR and ESR by R. G. Shulman and H. Sternlicht (Bell Telephone Laboratories). Using parameters measured from ESR spectra to calculate the proton and phosphorus relaxation rates observed by NMR, the authors obtained convincing evidence for the complexing of the metal with the terminal phosphate groups and some indication of chelation with the purine ring. G. Feher (U.C.S.D.) described the kinetics of the formation (first order) and decay (second order) of the photo-induced free radicals in porphyrins and suggested a meeting 2 years hence for presenting a structure determination. An elegant structure proof of the radiation center produced by exposure of thymine and DNA crystals to x-rays was advanced by J. Eisinger, P. Pershan, and R. G. Shulman (Bell Telephone Laboratories). By comparing the hyperfine splittings in the ESR spectra of deuterium-substituted thymine analogs, the conclusion was reached that in both instances the unpaired electron is first localized on the C(5) of thymine. The extensively documented discussion of the possible structure and kinetics of formation and decay of the chemically and enzymatically produced free radicals of chlorpromazine, given by L. H. Piette (Varian Associates), followed along similar lines. Two, now classical, series of structural studies—those of W. Gordy (Duke) on free radicals in amino acids and R. U. Lemieux (University of Alberta) on configuration and conformation of carbohydrates—were noted in the regrettable absence of their authors.

The second category of investigations was introduced by T. Vänngård and B. G. Malmström (University of Goteborg) who expanded on their well-known studies of ESR spectra of ceruloplasmin and fungal laccase. Their conclusion, based on the smallness of the ligand hyperfine splittings, is that the copper is bound to no more than two nitrogens. M. Cohn and H. Mildvan (University of Pennsylvania) discussed the use of NMR in the study of metal-activated enzymes and admirably demonstrated that with ingenuity in experimental design one can obtain conclusive evidence for the formation of ternary complexes between substrate, enzyme, and metal ion from a measurement as ambiguous as the relaxation rate of water protons. O. Jardetzky and J. J. Fischer (Harvard) introduced a new method for the determination of chemical groups involved in the formation of molecular complexes. The method is based on selective changes in the relaxation rates of NMR signals originating from different parts of the molecule and has been used to show that the phenyl moiety of penicillin is responsible for its binding to proteins and that the pyridine ring is the group stabilized by the binding of NAD to alcohol dehydrogenase. A. Kowalski reported the use of NMR contact shifts in oxidized cytochrome *c* to estimate rates of exchange between the oxidized and reduced forms, and H. J. C. Berendson (University of Groningen) proposed a model for a helical arrangement of water molecules in collagen fibers, which accounts for his broad-line NMR data.

An intriguing report by H. Beinert (University of Wisconsin) dealt with the sequence of intramolecular electron transport in metal-flavoproteins. The sequence was derived from a very detailed study of the kinetics of appearance and decay of ESR signals attributable to flavin, molybdenum, and iron. A direct interaction between the flavin semiquinone and the metal ions was suggested by saturation experiments. A potential use of NMR in the study of helix-coil transitions of nucleic acids and polynucleotides was discussed by C. C. McDonald, W. D. Phillips (Du Pont), and S. Penman (M.I.T.).

The third category of studies—the biological applications *sensu proprio* of at least ESR (comparable applications of NMR are virtually nonexistent)—was surveyed by B. Commoner (Washington University), who also gave an illustration of ESR as a diagnostic tool for differentiating medical from surgical jaundice. Among the several interesting reports which followed—notably those of E. Weaver (Stanford), R. Ruby (University of California), and A. Ehrenberg (Nobel Institute)—there emerged a disquieting lack of consensus concerning the significance of the observations. Despite the masterful exercise of the art of chairmanship by M. Kamen (U.C.S.D.) and B. Chance (University of Pennsylvania), the discussion often became heated and left one wondering whether the abundance of enthusiasm and technical know-how displayed by the ever-increasing number of pioneers in this area is really sufficient to cope with the very real handicap posed by the lack of uniquely identifying characteristics in most of the signals observed. A ray of hope for dispelling the reigning uncertainty was offered by H. Beinert, whose isotopic substitution experiments with Fe^{57} suggest that the heretofore unidentified signal at $g = 1.94$, frequently reported in biological materials, is indeed due to iron.

As N. Davidson (Caltech) pointed out in closing the last session, one may or may not agree with Thurber's dictum that it is better to ask some of the questions than to know all the answers, but one must acknowledge that some parts of the field have raised many questions with no answers in sight. Somewhat paradoxically, in view of the wave of popularity for biological applications of ESR, as compared with NMR, the latter emerges as contributing the proportionally larger share of generally applicable answers. The former continues to rely heavily on technical tours de force, hope, and promise. The meeting left little doubt that both branches of magnetic resonance spectroscopy are established as powerful tools for the study of molecular structure and molecular interactions even in rather complex, but chemically well characterized, systems. Beyond that, one treads the treacherous ground between the hope of dramatic discovery and the danger of having a vast investment of skill, labor, and funds rewarded by rather inconsequential observations. It is encouraging to observe, however, that the pure joy of a new adventure, which has dominated the field in its first years, is more and more tempered by careful consideration as to whether the questions one is asking are indeed answerable, or, for that matter, worth asking.

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Estuaries

Inshore and estuarine waters are of importance to man for various reasons, including their value as a source of food and recreation. However, with the continuing and extensive development of coastal areas it has become evident that our fundamental knowledge of the estuarine and coastal environments is not keeping pace with the need to resolve the practical problems evolving from their intensive exploitation.

The increasing need for a more comprehensive understanding of estuaries and adjoining waters and the lack of an adequate mechanism to foster an exchange of ideas concerning estuarine research stimulated the development of the Conference on Estuaries—the first one ever held on this subject—which took place on Jekyll Island, Georgia, during the period 31 March–4 April 1964. Its objectives were (i) to provide an opportunity for an interdisciplinary exchange of ideas between individuals and groups active in estuarine research; (ii) to critically summarize the status of knowledge relating to the natural characteristics of estuaries; and (iii) to delineate the direction of current research efforts in the estuarine environment.

The program was organized in a series of plenary sessions interspersed with 15 concurrent symposia; participants were selected to provide coverage of present knowledge of estuarine phenomena, as well as current research activities. There were nearly 90 invited participants and observers, including representatives from Mexico, Germany, the Netherlands, England, France, Australia, Denmark, Nigeria, Canada, Spain, the Republic of South Africa, Norway, Portugal, Italy, and New Zealand. Approximately 500 registrants and about 50 nonregistrants were in attendance at the conference. Six manufacturers displayed a wide variety of their newest equipment designed for estuarine research.

The topics treated by the papers were extremely broad and included the origin of estuaries, circulation, sediment transport and sedimentation, sediment geochemistry, instrumentation, physiology of estuarine animals, fisheries, plankton, benthos, microbiology, nutrients, organic detritus, pollution, and related subjects.

In a symposium on geomorphology and coastal processes arranged by James A. Steers, the transient nature of estuaries was discussed. Examples were taken mainly from Great Britain, because the island has numerous estuaries of various types with records that assist in understanding the changes that have taken place in estuaries during the last 4000 years. Axel Schou presented information on estuarine conditions along the North Sea coast of Denmark. Since 1931, this area has been studied in detail as an integral part of research as a base for reclamation projects. The regional characteristics of Australian estuaries were reviewed by J. N. Jennings in terms of major dynamic factors: river regimes, wave conditions, tidal ranges, vegetation effects, dune formation, and neotectonism. The question of the origin of sediments in estuaries was discussed by Andre Guilcher. Early Dutch investigations suggested that estuarine mud was derived from the sea. However, studies in other areas have demonstrated that estuarine muds may originate from tidal erosion of deposits covering the lower parts of the slope or from inland sources. These differences can be ascribed to contrast in supply of sediments by rivers and in hydrological structure of estuaries.

The processes and nature of estuarine sedimentation were the subject of