Patrika

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58th Annual Meeting

At the invitation of the Physical Research Laboratory, Ahmedabad, the 58th Annual Meeting will be held at Ahmedabad from 6 to 9 November 1992.

The scientific programme will consist of two symposia, evening lectures and lecture presentations by new Fellows and Associates.

The first symposium will be the "J B S Haldane Centenary Symposium". The speakers are— Sahotra Sarkar on 'Haldane and the foundation of theoretical population genetics', J H Edwards on 'Haldane and the mutation rate', Partha Majumder on 'Formal genetics of complex disorders in man' and N V Joshi on 'Evolution when there are two or more conflicting interests: Some population genetic studies'. The second symposium is on "Interactive Processes in the Near-Earth Environment". The speakers are — A C Das on 'Solar wind magnetosphere interactions', T Chandrasekhar on 'Comets as probes of the interplanetary medium', V V Somayajulu on 'High latitude-low latitude ionosphere coupling', Y C Saxena on 'Laboratory simulation of ionosphere irregularities', G S Lakhina on 'Electrodynamic coupling between different regions of the atmosphere', R Sridharan on 'Ionosphere-thermosphere coupling', A Jayaraman on 'Middle atmosphere coupling processes' and Pranav Desai on 'Satellite remote sensing for atmospheric change studies'.

The evening lectures will be on "Some interesting problems in the development of ISRO satellites" by K Kasturirangan and "Gujarat through the ages" by S R Rao.

The following is the provisional list of lectures by Fellows and Associates.

R M Godbole, University of Bombay, Bombay, "Beamstrahlung and super colliders"

S R Wadia, TIFR, Bombay, "Black holes in string theory"

J Chandrasekhar, IISc., Bangalore, "Computational studies of organic reactivity"

E D Jemmis, University of Hyderabad, Hyderabad, "Three-membered rings and three-membered rings: Tips from boron"

Asis Datta, JNU, New Delhi, "A step towards developing transgenic plants with high nutritional quality"

S Dattagupta, JNU, New Delhi, "Dynamics of supercooled liquids"

S Ramasesha, IISc., Bangalore, "Correlated electronic structure of conjugated systems"

S R Shenoy, University of Hyderabad, Hyderabad, "Disorder parameter description of phase transitions"

A M Kayastha, BHU, Varanasi, "Studies on β-subunit of tryptophan synthase from *Salmonella typhimurium*"

J B Udgaonkar, TIFR, Bombay, "Protein folding: Studies on barstar"

J Gowrishankar, CCMB, Hyderabad, "How do organisms cope in environments of low water activity? Some answers from *Escherichia coli*"

P S Goel, ISRO Satellite Centre, Bangalore, "Attitude control of Indian satellites: Challenges met through innovations"

M Vidyasagar, Centre for Artificial Intelligence and Robotics, Bangalore, "Artificial neural networks: Some recent results"

Gomathy Gopinath, AIIMS, New Delhi, "Brain repair"

The business meeting of Fellows will be held on 8 November at 5.45 p.m. Visits to Lothal and the Space Application Centre will be organized on Sunday, 8 November.

All Fellows and Associates attending the Annual Meeting will be paid first class railway fare from their place of residence to Ahmedabad and back, in case they are unable to obtain travel support from other sources. Arrangements for the stay of the Fellows, Associates and other delegates will be taken care of by the organizers.

During the period of the Annual Meeting, the Editorial Boards of the Academy journals and Sectional Committees will also meet at Ahmedabad.

Associates – 1992

V G Gaikar, University of Bombay, Bombay — Chemical Engineering

A K Kshirsagar, Inter-University Centre for Astronomy and Astrophysics, Pune — String Theory

G Mandal, Tata Institute of Fundamental Research, Bombay — String Theory

N Mandal, Jadavpur University, Calcutta — Structural Geology

A Nangia, University of Hyderabad, Hyderabad — Bioorganic Chemistry

A J Parameswaran, Tata Institute of Fundamental Research, Bombay — Singularity Theory

K H Paranjape, Tata Institute of Fundamental Research, Bombay — Algebraic Geometry

A Patra, Indian Institute of Technology, Kharagpur — Computer Modelling

S Srikanth, National Metallurgical Laboratory, Jamshedpur — Thermodynamics of Alloys

In quest of magic bullets

Abstract of the lecture given by Sandip K Basu, National Institute of Immunology, New Delhi on "In quest of magic bullets: Site-specific drug delivery" at the Mid-Year Meeting of the Academy on 24 July 1992.

Toxic side effects resulting from the administration of therapeutic agents often complicate successful therapy in a number of diseases. These adverse side reactions possibly arise due to the fact that at therapeutically effective concentrations in the blood, the non-target cells in the body are also exposed to the cytotoxic effects of the drugs. It is probable that such side effects could be minimized if a modality of delivering drugs could be worked out which would: (i) minimize uptake of the drugs by non-target cells, (ii) selectively deliver the drug only to the target cells at relatively low concentration in the blood, and (iii) ensure efficient intracellular availability of the drug. As macrophages are affected in a large number of viral, bacterial, fungal, protozoal, metabolic and neoplastic diseases, we have demonstrated the feasibility of a novel approach for delivering drugs selectively to these cells. For this purpose, we have exploited the exquisite cell-type specificity and high efficiency of the process of receptor-mediated endocytosis of macromolecules. Our approach consists of chemical coupling of an appropriate drug to a carrier molecule, *viz.* maleylated bovine serum albumin (MBSA) which is recognized by receptors present exclusively on cells of macrophage lineage. We have shown that such drug conjugates bind with high affinity to the receptors on macrophage surface leading to rapid internalization and subsequent degradation of the ligand in the lysosomes releasing a pharmacologically active form of the drug. So far we have tested the efficacy of this approach in cell culture and/or animal models of macrophage-associated disorders of protozoal (leishmaniasis), bacterial (tuberculosis) and neoplastic etiology. In all three instances examined, the conjugated drug was nearly 100-fold as effective as the free drug. These results indicate that the receptor-mediated modality of delivering drugs to macrophages could contribute to greater therapeutic efficacy and minimization of toxic side effects of drugs used in the management of intracellular infections as well as neoplastic diseases. MBSA-mediated delivery of various agents provides a generalized tool for manipulating the metabolic activity of macrophages for a variety of purposes as well as for reduction of toxicities of various chemotherapeutic agents.

Obituaries

Daniel Bovet was born on March 23, 1907 at Neuchatel, Switzerland as the son of a professor of pedagogy. He studied at the University of Geneva, receiving the "license" (a degree intermediate between the baccalaureate and the doctorate) in 1927 and a DSc in Zoology and Comparative Anatomy in 1929. He accepted a position as assistant in the Laboratory of Therapeutic Chemistry at the Pasteur Institute in Paris that year and was appointed as Director in 1936. He left this post in 1947 to become Chief of the Laboratory of Therapeutic Chemistry at the Instituto Superiore di Sanita in Rome. In 1964 he became Professor of Pharmacology at the University of Sassari, and in 1971, Professor of Psychobiology at the University of Rome. From 1969 to 1975 he was also the Director of the Laboratory of Psychobiology and Psychopharmacology at the Consiglio Nazionale delle Richerche in Rome. He was elected a Member of the Accademia Nazionale dei XL (1949), the Accademia Nazionale dei Lincei (1958), the American Academy of Arts and Sciences (1960), and the Royal Society of London (1962) and the Academy in 1967.

While conducting research in therapeutic chemistry, Bovet observed organic compounds that proved effective as muscle relaxants (used to supplement light general anaesthesia during surgery) and antihistamines (useful in alleviating the effects of allergies). In recognition of his discoveries relating to synthetic compounds that inhibit the action of certain body substances, and especially their action on the vascular system and the skeletal muscles, Bovet was awarded the 1957 Nobel Prize for Medicine or Physiology.

Following the first observations by Griffith and Cullen concerning the muscle relaxant properties of curare in surgery, Bovet worked to develop a synthetic curare. He proceeded to synthesize molecules chemically related to the chosen models and to prepare relatively simple derivatives with analogous properties. In this way, Bovet synthesized more than 400 compounds that simulated the effects of the natural product in varying degrees. One of these compounds, succinylcholine, came closest to duplicating the activity of curare, and clinical tests showed it to be an effective substitute. This made it possible to use succinylcholine as a muscle relaxant whose effective dosages could be determined with precision. By its use, the surgeon is able to produce complete muscle relaxation with only light anaesthesia, thus avoiding some detrimental effects of deep anaesthesia.

Prior to beginning his work with curare, Bovet had developed the first antihistaminic compound. Histamine, which is found in all body tissues, was believed to be the causative agent in producing allergy symptoms. Every body tissue reacts to histamine in some way, and excessive amounts intensify reactions to the point where discomfort sets in. When introduced by means other than adsorption through the intestine, histamine is extremely toxic, indicating that it is undoubtedly present in the body in a nontoxic combination, probably with a protein.

Bovet realized that relief from allergy symptoms would probably require a mechanism that could interfere with the production of free histamine from this combined form. In collaboration with A.M. Staub, he considered the similarities among histamine, adrenaline, and acetylcholine. He then began to investigate substances that demonstrated a specific antagonism for histamine, comparable to that shown by sympatholitics and parasympatholitics for adrenaline and acetylcholine, respectively. In 1937 he succeeded in producing the first antihistamine, thymoxydiethylamine, which was too toxic to be used clinically. However, thymoxydiethylamine served as the basis for the derivation of almost all subsequent antihistamines. Thus, Bovet's research led to the development in the 1950s of new antihistaminic drugs, which have proved to be of use in relieving the symptoms associated with such allergies as hay fever, hives and poison oak.

Bovet's earlier work was concerned with the development of sulfa drugs. Soon after its discovery in 1935, the orange-red dye sulfamyldiaminobenzene was found to have chemotherapeutic properties by the German biochemist Gerhard Domagk. Since this dye was found to be effective against streptococci in the human body but ineffective when added to laboratory cultures, Bovet theorized that the complex organic dye was broken down in the body to simpler compounds that worked against the streptococci. He therefore proceeded to reduce it to its component compounds. One of these, sulfanilamide, proved to be effective against streptococci both in the body and in cultures. With this evidence to support his premise, Bovet began to synthesize derivatives of sulfanilamide in an effort to discover even more therapeutic compounds. He found that the majority of the superior derivatives had the common feature of a complex organic group in the place of a hydrogen atom in the sulfonamide group, SO_2NH_2. Although this finding led to the preparation of numerous derivatives, only a few had both the high antibacterial actvity and the low toxicity to human beings to permit their

use in chemotherapy. Sulfanilamide and its derivatives are of value in combating many types of bacterial infections.

In addition to his chemotherapeutic work with sulfa drugs, Bovet studied the ataraxics, or tranquilizers, and the oxytocii, substances that resemble exytoxin (hormone regulating uterine contraction during childbirth) in activity.

Bovet was the author of several books, among them *Curare and Curare-like Agents*, with F. Bovet-Nitti and G.R. Marini-Betolo (1959), and *Controlling Drugs*, with R.H. Blum and J. Moore (1974).

He passed away in Rome on 7 April 1992.

Madhavarao Ranibennur Raghavendra Rao was born on 24 May 1924. He had his early education at the Central College, Bangalore from where he obtained a B.Sc. (Hons) Degree in Chemistry in 1944, after which he worked at the Indian Institute of Science for a period of 6 years taking AIISc and M.Sc. degrees. He obtained his Ph.D. degree from the University of Illinois at Champaign-Urbana in 1955.

After his return from the US, he joined the Central Drug Research Institute, Lucknow and later the National Chemical Laboratory, Pune, where he worked for 12 years. At Pune he organized work in the area of microbial biochemistry, enzymology, intermediary metabolism and fermentation biochemistry. His important contributions at NCL, Pune centred around the metabolism of organic acids and he worked on enzymes like aconitase, aconitate isomerase, citraconase and tricaballylate dehydrogenase. In 1969, he joined the Central Food Technological Research Institute (CFTRI), Mysore and was Head of the Department of Biochemistry and Applied Nutrition for the next 15 years.

At CFTRI, he contributed significantly in the area of enzymes used in the food industry: lipases and lipoxygenases or rice bran, pectolytic enzymes and glucoamylases from Aspergilli and polyphenol oxidases from tea leaves and mango peel. He was responsible for the initial work on the carbohydrates from groundnut and millets like ragi etc. He built an active group on food carbohydrates at CFTRI and nurtured its development. This is one of the few centres in our country where work on carbohydrates is exclusively carried out.

He was a member of the Nutritional Society of India, the Association of Food Scientists and Technologists, of the Guha Research Conference, of the National Committee for the International Union of Biochemistry and of the Advisory Council of the Indian Jute Industries' Research Association and the Society of Biological Chemists, of which he was also President for one term. He was elected a Fellow of the Academy in 1978. He was given the M. Sreenivasaya award of the Society of Biological Chemists of India in 1956.

He passed away at Mysore on 9 June 1992.

Kollagunta Gopalaiyer Ramanathan was born at Bombay in 1920. After obtaining his B.A. degree in Mathematics from Osmania University and an M.A. degree from the University of Madras, he worked for some time as a research scholar at Madras, coming into contact with the genial Rev. Fr. Racine, as well as with eminent mathematicians like Vaidyanathaswamy and Vijayaraghavan. He also taught for a while, before proceeding to Princeton for further studies at the Institute for Advanced Study, where he came under the influence of the great mathematician Carl L. Siegel, while functioning as Assistant to Prof. Hermann Weyl. Soon after obtaining his Ph.D. degree from Princeton University with Prof. Emil Artin as his guide, he returned to India in 1951 to work with K. Chandrasekharan at the Tata Institute of Fundamental Research, Bombay in their magnificent efforts for the steady evolution of the School of Mathematics at TIFR into an enviable centre for mathematical research. With his remarkable expertise and all-consuming passion for number theory, he built up the Number Theory School at TIFR. His polished and meticulously delivered lectures, reinforced by informal discussions, unfolded for many a budding scholar enthralling vistas of the exciting mathematical world of Fermat, Euler, Lagrange, Gauss, Abel, Jacobi, Dirichlet, Kummer, Galois, Eisenstein, Kronecker, Riemann, Dedekind, Minkowski, Siegel, Hilbert, Hecke, Artin, Weil, Chevalley etc. His abiding enthusiasm for the propagation of good mathematics and the spread of wholesome mathematical culture has been mainly instrumental in the moulding and flowering of several fine mathematicians and for the betterment of teaching of mathematics and its further pursuit in many of our universities.

The earlier papers of Prof. Ramanathan deal, for the most part, with congruence properties of some arithmetical functions, Ramanujan's trigonometric sums and certain identities of Ramanujan type. Following Siegel's famous work on quadratic forms and Humbert's reduction theory, he studied in two of his papers the properties of unit groups of quadratic and hermitian forms over algebraic number fields such as their finite generation or volume co-finiteness. In a paper in *Acta Arithmetica*, 1959, he used a general formula of Siegel's concerning

lattice points in symmetric bounded convex Euclidean domains to obtain a formula for the discriminant of a division algebra, yielding, as a nice sequence, the Hasse-Brauer local-global splitting theorem for the case of quaternion algebras over the rationals.

In an ensuing series of papers, he made a systematic study of the equivalence of and representation by quadratic forms over division algebras with involution and of the unit groups and theta series associated with such quadratic forms, as a prelude to an analytic theory (on the lines of Siegel's fundamental papers on the analytic theory of quadratic forms) for this general set-up. (The famous *Acta Mathematica* papers of Weil in this context appeared later during 1964-65.) Using the foregoing results of his own, along with certain methods of Siegel and some theorems due to Selberg and Borel, he solved in his important paper (in *Göttingen Nachrichten*, 1963) the problem of constructing infinitely many classes of mutually incommensurable discrete groups of the first kind in classical semi-simple groups. This was followed in 1964, by a beautiful paper wherein he settled the question of maximality of discrete subgroups of arithmetically defined classical groups, generalizing certain results of Hecke and Maass. He has also done interesting work establishing the 'dense' nature of the set of values at integral algebraic arguments of 'irrational indefinite' quadratic forms representing zero non-trivially (over an algebraic number field), generalizing an earlier result of Oppenheim, whose well-known conjecture on the values of irrational indefinite quadratic forms at integral arguments, was settled only recently by Margulis using various ideas and techniques from Ergodic Theory, Lie Groups, Algebraic Groups etc.

He was actively interested in the study of the published and unpublished work of Srinivasa Ramanujan, expounding, elucidating and extending Ramanujan's beautiful work on singular values of certain modular functions, Rogers-Ramanujan continued fractions and hypergeometric series. Since the mathematicians in the West had already made tremendous advances in respect of many aspects of Ramanujan's unpublished work, it was only natural that he urged many of his colleagues in India to take seriously to this fascinating domain, even if such activity might be cold-shouldered by 'peers' from within. Actually, during the last few months of his life when his right arm was virtually disabled due to Parkinson's disease, he continued to work preparing a "Monograph on Continued Fractions" with their two aspects — one relating to the hypergeometric series and the other to the basic hypergeometric series.

Realizing the need to establish a good school in applications of mathematics, he mooted in 1975 the idea of a joint TIFR-IISc programme to be operated at Bangalore on the campus of the Indian Institute of Science. This programme has now come of age, thanks to his efforts and vision, with the emergence of a viable group of competent mathematicians specializing in Differential Equations and Numerical Analysis.

He was elected a Fellow of the Academy in 1974. He was a Founder-Fellow of the Maharashtrian Academy of Sciences, President of the Indian Mathematical Society and Life-President of the Bombay Mathematics Colloquium. He was a member of the editorial board for *Acta Arithmetica* for nearly three decades. He was a recipient of many national awards — the Shanti Swarup Bhatnagar Prize, the Jawaharlal Nehru Fellowship, the Homi Bhabha Medal and Padma Bhushan.

His interests in English, Telugu and Tamil literature with his unfailing knack for pulling out apt quotations, were just as remarkable as his erudition in music. He shunned publicity as much as he abhorred those who craved for power and ephemeral glory through the media; those who happened to know him somewhat closely, could not have failed to note his simplicity and inner humility.

He passed away at Bombay on 10 May 1992, leaving behind his wife and two sons and countless friends, admirers and former colleagues to mourn his loss.

Kasi Sreenivasan was born on 10 July 1899. He obtained his B.Sc. degree from the University of Mysore in June 1920 and joined the Indian Institute of Science in the Department of Electrical Technology for his higher studies. He was awarded the certificate of Proficiency in Electrical Technology in July 1926 and Associateship in the Electrical Technology in March 1927. From October 1927 to December 1930, he continued his studies as a J N Tata Scholar in UK, at the Marconi College of Wireless Communication, Radio Research Station, Slough, BBC Engineering Department and the British Post Office. During February–July 1930, he also served as Radio Engineer in Les Laboratories Standard, Paris, France.

He was appointed Assistant Professor of Electrical Communication Engineering in the Department of Electrical Technology, Indian Institute of Science in April 1932, which post he held until February 1945. During this period, he conducted studies and research in radio broadcasting techniques and architectural acoustics. In February 1945, he was appointed

as Professor of Telecommunication Engineering at the College of Engineering, Guindy, Madras. During his three-year tenure, he was responsible for the planning and implementation of the academic programme in telecommunication engineering. In June 1948, he returned to the Institute as Professor and Head of the Department of Electrical Communication Engineering, which position he held until July 1959 during which period he also served as Acting Director of the Institute from August 1955 to March 1957. During this period, he laid a strong foundation for electrical communication engineering education and research at the Institute and many innovative courses, training programme and other activities were introduced by him.

After his retirement from the Institute, he served as Director, Madras Institute of Technology from April 1960 to November 1971.

He was one of the founders of the Institution of Electronics and Telecommunication Engineers (India), of which he was the President during 1956-57, and a distinguished Fellow (1980). He was also a Fellow of the Institution of Electrical Engineers, London (1942), a Senior Member of the Institute of Electrical and Electronics Engineers, New York (1943). He was elected a Fellow of the Academy in 1943. He passed away at Bangalore on 17 August 1992 after a brief illness leaving his many students, friends and colleagues to mourn his loss. In his passing away the Electronics and Telecommunication fraternity has lost an educationist par excellence and a great human being.

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