

# Journal of Scientific & Industrial Research



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April 1967

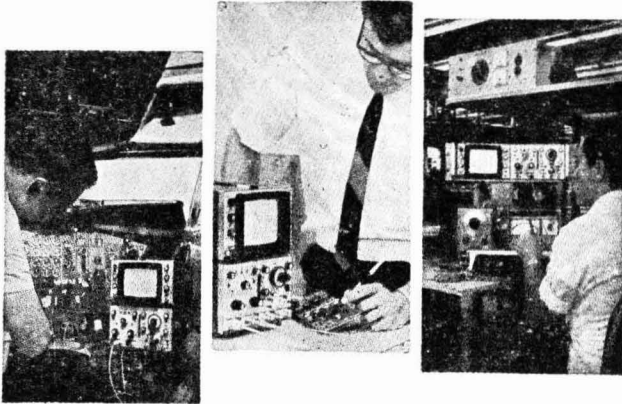
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# Journal of Scientific & Industrial Research

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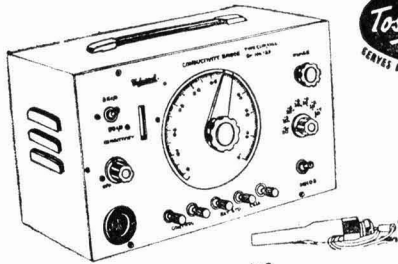
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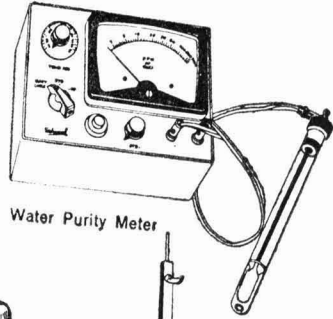
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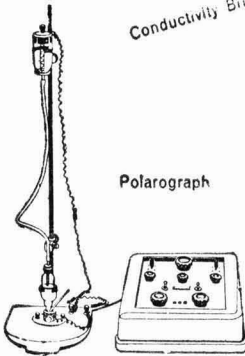
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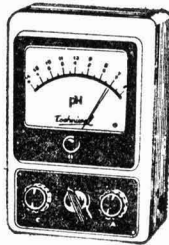
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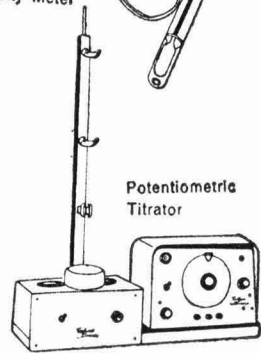
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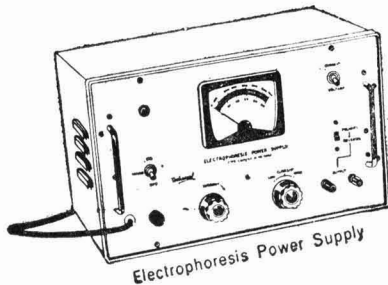
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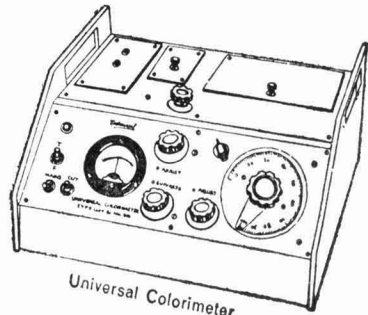
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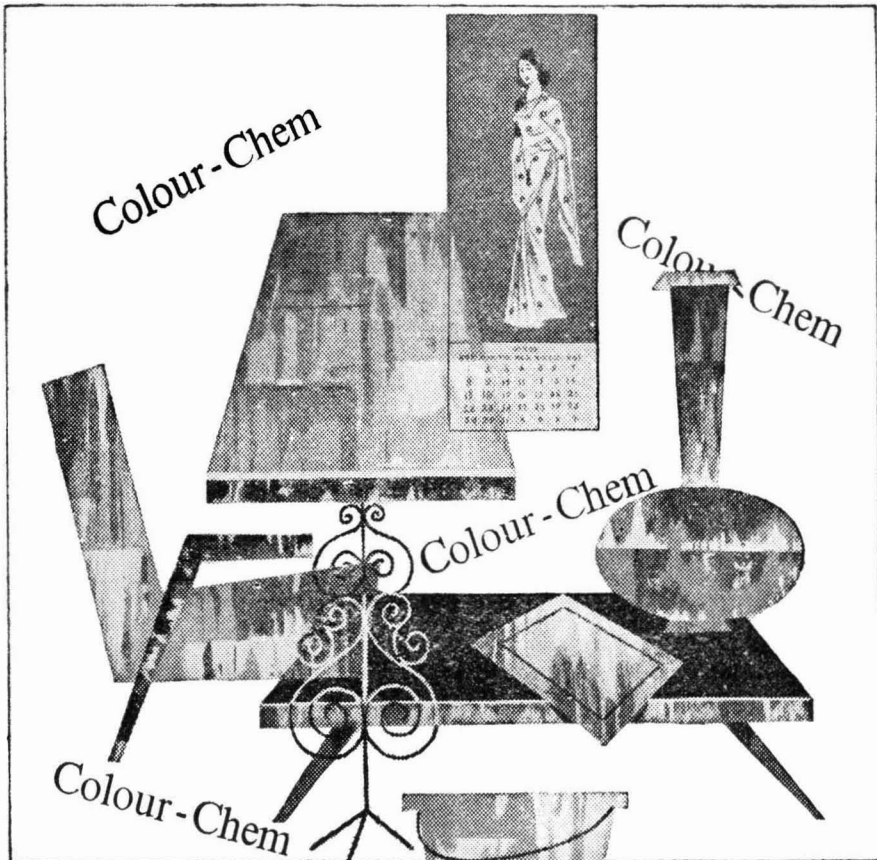
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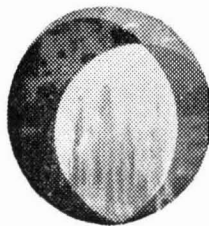
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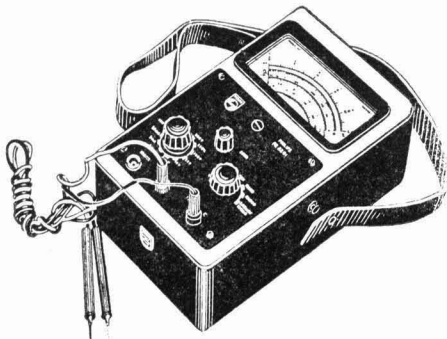
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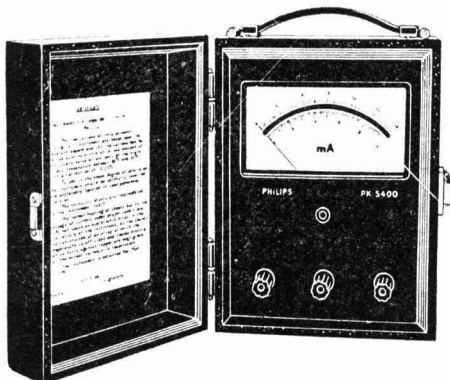
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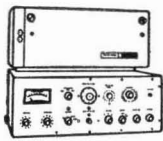
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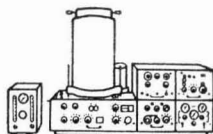
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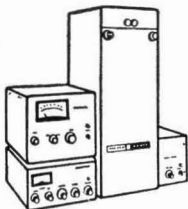
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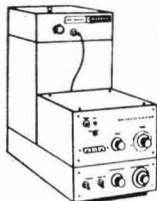
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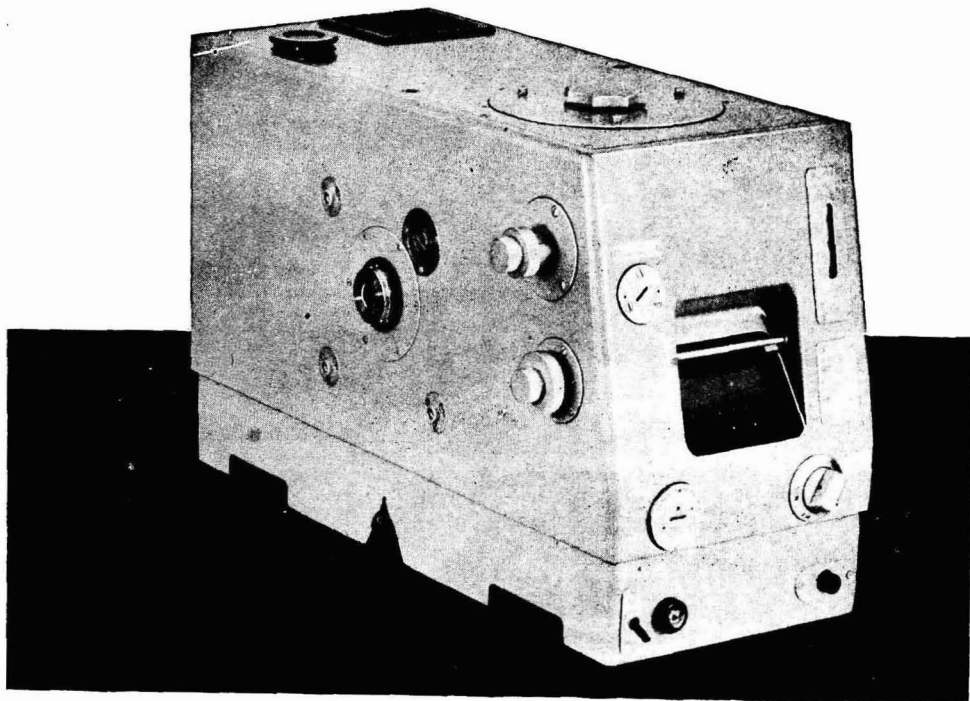
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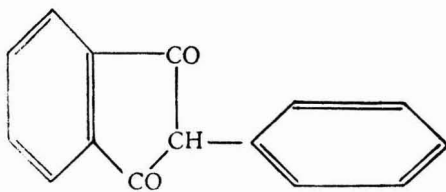
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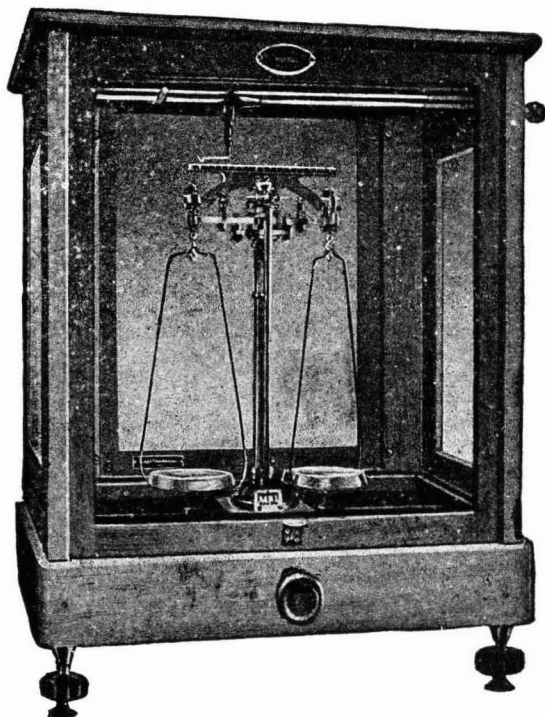
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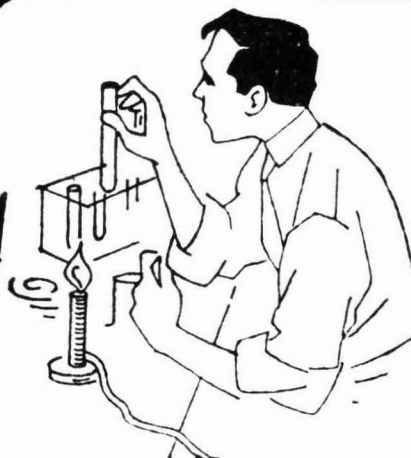
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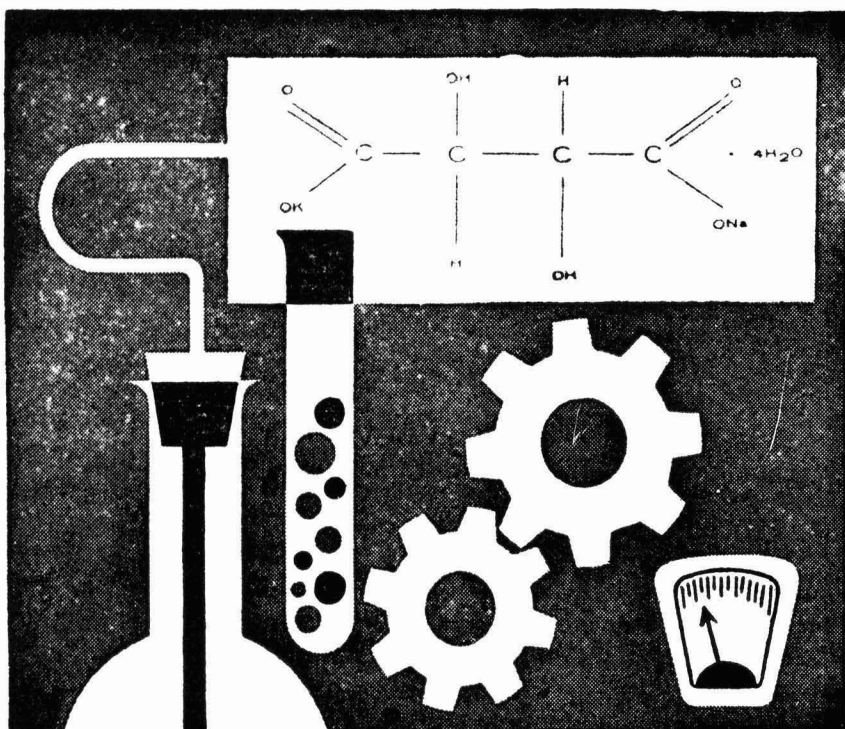


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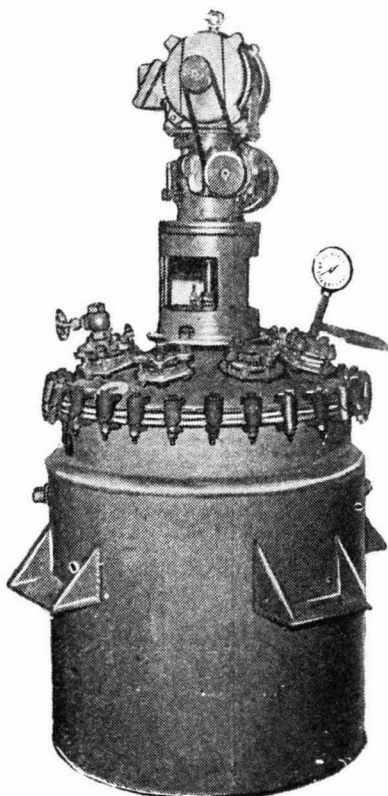
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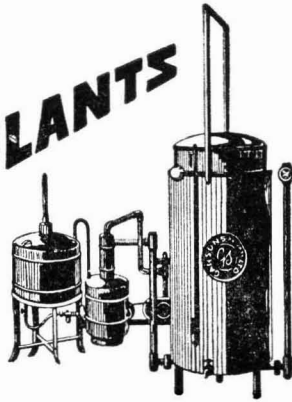
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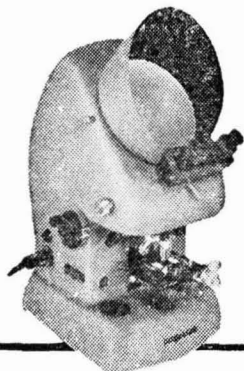
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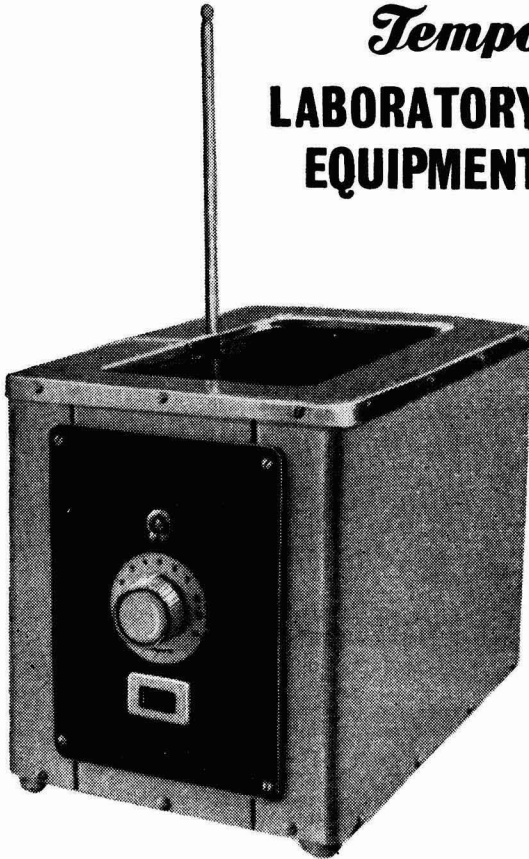
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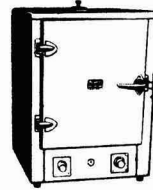
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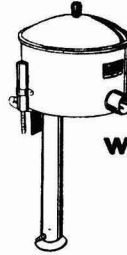
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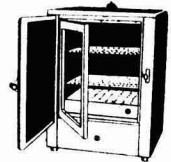
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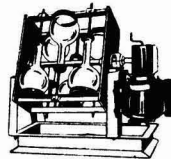
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# Current Topics

## Utilization of Second-hand Industrial Equipment

THE report of the Expert Group on Second-hand Equipment for Developing Countries\*, submitted to the Commissioner for Industrial Development, United Nations, has much interesting information, and deserves careful study by the developing countries. The report states that considerable quantities of second-hand equipment with potentialities for use in developing countries are generated in industrially advanced countries. For example, in USA, second-hand metal working equipment worth about \$ 500 million was generated in 1965, and the demand in developing countries was for equipment worth about \$ 1200 million. The report adds that the generation of second-hand equipment from industrially advanced countries will increase substantially in the foreseeable future.

Second-hand equipment is defined as that equipment which has been purchased by a potential user and resold at least once; it is not necessarily equipment which has been used is obsolete, or deteriorated. It can be classified as: (i) unused — equipment never installed for service, (ii) reconditioned — used equipment repaired and not used since, and (iii) as is — used equipment offered for sale as taken from service. The principal causes for the generation of such equipment in developed countries are: modernization, automation, closing of plants and mergers, government surpluses, obsolescence, physical deterioration, etc. Equipment falling within the first four classes is not obsolete, and could be of special interest to developing countries which have already made substantial industrial progress.

Advantages of second-hand equipment are: lower operating costs, shorter delivery period, suitability for small-scale operation, simpler maintenance, greater ease of manufacturing parts locally, less skill needed for operation, and a more flexible replacement policy. Disadvantages of such equipment are: shorter economic life, increased risk of obtaining unsound equipment and consequent breakdown, higher maintenance costs, lack of spares, lower ability to work to fine tolerances, lower product quality and increased spoilage, greater difficulty in locating the precise equipment, etc. Both the advantages and the disadvantages of second-hand equipment, the report points out, are debatable, but one definite advantage is that

such equipment can be acquired at a cost considerably lower than that of new equipment. Objections advanced by developing countries against the use of second-hand equipment are: it will slow down economic development because of obsolete technology; maintains technological gap between developing and developed countries; reduces productivity gains; and relegates the developing nations to a second-class status as economic powers. The report points out that while these objections are valid under some circumstances, under different conditions they can be altogether unfounded. For example, second-hand equipment generated as a result of switchover to large-scale operation is often suitable for use in developing countries. Or, technological innovation will make available in developed countries less costly raw material for some products requiring a changeover to a different type of production equipment. The machinery could, however, be still used to advantage in areas where the original raw material is abundant and cheap.

In selecting second-hand equipment for use in developing countries, it is the conditions in these countries and not those in developed countries that should be considered in determining its suitability. Great care is necessary in choosing the right type of technology in order to safeguard the interests of the developing countries. Correct and thorough identification of the equipment, by type or by industry sector, is essential, and should be done with the help of experts. Technical data about the equipment are essential before a selection can be made.

Difficulties in obtaining information and data regarding the technical and economic aspects of second-hand equipment are real. Also, the developing countries should be in a position to know their exact requirements. The report suggests the setting up of suitable agencies in developing countries to collect and catalogue data about the type of equipment needed. Similarly, in the developed countries, data on the type of equipment available must be collected and widely disseminated to the prospective users of the equipment. It is recommended that developing countries carry out periodic surveys to determine the possibilities of utilizing second-hand equipment in the implementation of their industrial programmes. The report also recommends that arrangements be made in developed countries for collecting and disseminating information on the availability of second-hand equipment, particularly complete plants, through suitable institutions and publications, so that the intending purchasers in developing countries can locate the desired equipment easily.

\*Report of the Expert Group on Second-hand Equipment for Developing Countries, 7-22 December 1965 (Centre for Industrial Development, United Nations, New York), 1966. Pp. 24. Price \$ 0.50.

# Symposium on Control & Computation in India

DWIJESH DUTTA MAJUMDAR

Secretary-Convener, Indian Society for Automation & Information Sciences, Calcutta

THE symposium, the second of its kind in India (the first one on automation and computation sciences in India was held at Bihar Institute of Technology, Sindri, during 22-23 February 1963) and sponsored jointly by the Indian Society for Automation & Information Sciences (ISAIS) and the Centre of Advanced Study (CAS) in Radiophysics and Electronics, was held at the Institute of Radiophysics and Electronics (IRPE), University of Calcutta, during 2-3 December 1966. The inaugural session started with a message from Dr Triguna Sen, President of ISAIS, followed by the presidential address by Dr J. N. Bhar, Director, CAS, both emphasizing the technical importance of such symposia.

Sixteen papers were presented at four sessions. Three papers were on numerical mathematics and programming, five on control systems engineering, two on coding theory, one on machine translation of languages, three on computer arithmetic logic, and three on threshold logic functions.

The papers in the group 'Numerical mathematics and programming' were: (1) A computer implemented calculus of change by Dr M. R. Lackner (Adviser on Information Processing of the Ford Foundation in India), (2) Pfaffian aggregate and network theorems by Prof. S. K. Mitra [Indian Statistical Institute (ISI)] and (3) Numerical solution of finite range Weiner-Hopf equation by Prof. F. A. Hinchey (New Mexico State University). The computer implemented calculus of change presents a finite state automaton and its behavioural description incorporates a change relationship which is a general dynamic logical operator. The calculus enables the deduction of a unique sequence of system descriptions from an original system description, and is of considerable importance in planning research. The change relationship has been exemplified with an implementation programme of IBM-1401 computer. In the paper by Prof. Hinchey, two numerical methods for solving certain integral equations using Weiner-Hopf technique and Mitra's approach were described.

The papers in the group 'Control systems engineering' were: (1) Approaches to the synthesis of first order controllers for second and higher order plants by Prof. U. S. Ganguli (Jadavpur University), (2) Partitioning in parametric plane and its applications in machine controllers by Dr L. M. Roy (Roorkee University), (3) Some developments in fast response magnetic amplifiers by Prof. B. K. Bose (Bengal Engineering College), (4) Some recent results on the Lurie problem of stability by Dr A. K. Mahalanobis (Roorkee University), and (5) Numerical solution of optimal control problems by Dr Sanjoy Mitra (Case Institute of Technology,

USA). While the first four papers dealt with the engineering design aspects of the respective problems, the paper by Dr Mitra presented digital computer solutions for some nonlinear optimal control problems, after summarizing the state of the art of numerical solution of optimal control problems.

In the group 'Coding theory and machine translation', there were two papers on coding theory, viz. (1) On the use of feedback coding in the nonlinear transformation of information signals by Dr J. Das (IIT, Kharagpur), and (2) A scheme for automatic human speech coding and recognition procedure by Dr Dwijesh Dutta Majumdar and Shri Asoke K. Dutta (ISI). Dr Das, after reviewing the existing methods for nonlinear transformation of the analogue information signals by various types of converters, discussed some new analogue-to-digital converters and compared their efficiencies. He concluded that the new feedback converters are more efficient than the equivalent direct converters. The paper by Dutta Majumdar and Dutta dealt with the construction of a digital code pattern from a human speech input suitable for the use of computers from which the full intelligence content can be extracted without any human intervention. The paper presented the major functions necessary in any pattern recognition system, along with the pertinent decision theory and the model for speech synthesis followed by a description of the design of the experimental circuits. The paper on 'Language data processing for machine translation' by Shri J. P. Roy Chowdhury and Shri S. Chakravarti (ISI) described how an apparatus of linguistic analysis can provide a tool for machine processing of language materials.

The papers in the group 'Computer arithmetic and logic functions' were: (1) A simple algorithm for digital division by Shri S. K. Nandi and Dr E. V. Krishnamurthy (ISI), and (2) On self-complementing  $A+B$  codes by Dr E. V. Krishnamurthy (ISI). In the first paper a simple and economical scheme for digital division was described. The second paper dealt with the problem of constructing a code for digits in radices from 2 to 10 with the properties of self-complementation and single error correction. The papers on logic theory were: (1) Synthesis of symmetric switching functions using threshold logic elements by Prof. P. K. Sinha Roy, (2) Testing and realization of threshold functions through classification of inequalities by Shri D. Sharma (IRPE) and (3) On the threshold order of Boolean functions by Shri T. Krishnan (ISI). The presentation of three papers on threshold logic elements by young researchers goes to show the awareness of the importance of this field.



# The Placenta—A Symposium

A. R. SHETH

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**A** SYMPOSIUM on The Placenta was held at the Cardiovascular and Thoracic Centre, Parel, Bombay, on 1 and 2 October 1966, under the joint auspices of the Indian Council of Medical Research, the Bombay Obstetrics & Gynaecology Society and the Indian Society for the Study of Reproduction. The symposium which formed a part of the 10th anniversary celebrations of the Reproductive Physiology Unit, Bombay, was organized by Dr (Mrs) Shanta S. Rao, Officer-in-Charge of the Unit and the Honorary Secretary of the Indian Society for the Study of Reproduction. Eleven papers were presented and discussed during the symposium.

In a paper on 'Immunological studies with human chorionic gonadotrophin', Shanta S. Rao and S. K. Shahani reported that human chorionic gonadotrophin (HCG) was antigenic in rabbits when injected along with adjuvants. It was demonstrated by them that HCG had three hormone specific antigens. Treatment of HCG with 30 per cent hydrogen peroxide and heating of HCG at 100°C. showed that the biological activity of HCG was contributed both by the FS-like principle and LH-like principle.

A paper on 'Hormone deficiency and foetal salvage' was presented by U. Krishna *et al.* They investigated whether substitution therapy by hormones could prevent reproductive loss in patients who reportedly have still births, premature deliveries and abortions. They found that 70 patients out of the 247 cases studied had progesterone deficiency as indicated by vaginal cytology. The authors reported a foetal salvage of 86 per cent when progesterone was substituted in the progesterone deficient patients. Out of the 15 patients showing chorionic gonadotrophin deficiency, 12 were treated with chorionic gonadotrophin and progesterone. The pregnancy could be salvaged in 10 such cases.

P. M. Naidu and S. Ramaswamy presented a paper on 'Cytology as an indicator of placental insufficiency'. They reported that the vaginal smear method is a very simple and sensitive indicator of placental insufficiency. Results obtained by this method were as reliable as any biochemical assay. Out of the 818 cases of toxæmia, surgical induction was carried out in 40. Among the above 40, in 30 cases induction by artificial rupture of membranes and syntocinon drip were indicated by cytology (At-term smears).

K. R. Laumas *et al.* presented a paper on 'Significance of estriol assays in pregnancy and the bio-synthesis of estrogens in normal placenta and from cases of placental insufficiency'. The authors have developed a short and precise method for the

estimation of estriol in the later months of pregnancy. According to these authors, the low values of estriol (2-3 mg./24 hr and below) indicated placental insufficiency. Further studies carried out with the microsomal fraction prepared from placenta of normal and placental insufficiency cases indicated that the conversion of precursors to estrogens was lower in the placental insufficiency cases.

M. Thangavelu and S. Varghese presented a paper on 'Trophoblastic tumours in Trivandrum'. They have reported a high incidence of trophoblastic tumours in Kerala. Histological studies were carried out with 395 trophoblastic tumours and were classified as: (1) benign vesicular mole, (2) invasive mole, and (3) choriocarcinoma. They found that hydatidiform mole is the commonest type preceding pregnancy in choriocarcinoma cases. High parity was postulated as a predisposing factor for the occurrence of the trophoblastic tumours.

A. Mehta and N. Wadia reported the various anatomical variations in seven hundred placenta studied in a paper on 'Microscopic study of placenta and clinical correlation to its anomalies'. A correlation between the placental anomalies and the outcome of the foetus was demonstrated.

The paper, 'A technique for the demonstration of the foetal placental circulation' by K. S. Adrianwala *et al.*, dealt with the standardization of the procedure for obtaining the cast of placental vessels. Fresh placenta were cleaned with a concentrated solution of saline and sodium citrate and then were filled with the specific 'Tiller'.

S. G. Daftary and E. J. Sequeira presented a paper on 'Soft tissue radiography in placental localization'. The authors have modified the radiographic technique for the localization of the site of placental attachment in the uterus. This technique was applied to study placental localization in 30 cases of antepartum haemorrhage.

T. R. Bhatena presented a paper on 'Management of troph-neoplasia'. A detailed protocol for the management of troph-neoplasia by chemotherapeutic drugs was described. He stressed the importance of various laboratory investigations to be carried out along with the treatment.

A paper on 'Pelvic arteriography in placental localization' was presented by N. S. Doshi *et al.* These authors have successfully used the technique of retrograde temoral angiography and visualization of placenta in 25 cases of antepartum haemorrhage.

The paper on 'Postpartum placental radiography' by S. D. Chaubal *et al.* dealt with the radiological studies carried out with 100 specimens of placenta in the immediate postpartum period. According to these authors, the method was very suitable to assess placental insufficiency.

# International Symposium on High Polymers

U. S. NANDI & SANTI R. PALIT

Indian Association for the Cultivation of Science, Jadavpur, Calcutta 32

THE symposium on macromolecular chemistry held under the auspices of the International Union of Pure & Applied Chemistry in Tokyo and Kyoto during 28-30 September and 3-4 October 1966 was attended by over 1500 delegates, about a third of them representing overseas delegates from 24 countries. Opening the symposium, the Chairman, Shinzo Ohya, said that there has been a tremendous growth in the field during the last few years, and particularly referred to its impact on Japan. He pointed out that the polymer science and industries in Japan have shown amazing development like an organic growth. This is also corroborated by the fact that the membership of the Society of Polymer Science, Japan has surged to 10,000, one-third of the total membership of the Chemical Society of Japan. This gives an indication of the pre-eminent position of polymer chemistry in the field of chemical science in Japan.

In the opening lecture, Prof. Herman Mark gave a masterly review of the present position of thermally stable polymers. Apart from the conventional polymers possessing high degree of crystallinity and crosslinking, he discussed a new class of polymers known as the rigid chain polymers, having high thermal stability. He described newer techniques of producing such polymers and elaborated the 'precursor method', in which a few bonds in the polymer are left open and after the final fabrication the open bonds are closed up to the desired extent. In addition, the technique of emulsion spinning to produce fibres of polymers like polyacrylonitrile, teflon, silica and even carbon was described.

The 19 general lectures and about 400 papers covered a wide range of aspects of macromolecular chemistry, including both academic work and fundamental studies on technically important processes.

Nine of the general lectures were devoted to solution properties, structure and configuration of high polymers. Flory and Huggins reviewed the various theories and their experimental correlation from the standpoint of thermodynamics and discussed the recent developments in the field. Configurational studies by nuclear magnetic resonance (NMR) spectroscopy and their application to the determination of the mechanism of vinyl polymerization were discussed by Bovey. Solution properties of high polymers were covered in the lectures delivered by Stockmeyer and Sadron. While the lecture by Stockmeyer covered the subject from the standpoint of dielectric dispersion, Sadron discussed the physico-chemical properties of high polymers. Scheraga discussed the configurational aspects of polypeptides and proteins. Keller and Takayanagi reviewed the field of crystallinity of polymers and discussed the recent results both in general and from the point of view of

dispersion behaviour of high polymers. Rheo-optical studies of morphology and deformation of crystalline polymers formed the subject of a lecture delivered by Stein. Three of the general lectures were concerned with the use of model substances in the field of polymers. Of these, Kern's lecture dealt with the model matrix reaction. Wichterle discussed the use of model substances as a tool in polymer science. The most exciting lecture was delivered by Overberger in which he discussed the introduction of polymers as model enzymatic compounds. He reviewed the present status of the subject and discussed the enzyme-like hydrolytic behaviour of polyimidazoles. The other lectures related to different aspects of polymerization processes. The most informative lecture in this group was on initiation and propagation processes given by Bamford. The field of photo-induced polymerization was elegantly reviewed by Weiss who also gave a detailed account of the use of triphenyl compounds as photo-initiators and their chemistry. The chemistry of polyamides was discussed by Schlak. Smets and Murahashi dealt with the chemistry and polymerization of arylidazoalkanes and vinyl alcohols respectively.

The 400 and odd papers presented fell under the following broad thematic groups: (1) Polymerization and chemical structure; (2) New polymerization processes and new polymers; (3) Photo- and radiation-induced polymerization; (4) Polymer reactions and graft polymerization; (5) Thermally stable polymers and related problems; (6) Physical characterization of polymers in solution; (7) Structure of polymer molecules and polymer systems; (8) Physical properties of solid polymers, polymer melts and concentrated polymer solutions; (9) Polymer behaviour of biologically important substances; (10) Natural polymers; and (11) Degradation of polymers.

The section on polymerization and chemical structure accounted for the maximum number of papers (over 80). The topics covered included radical, cationic, anionic, stereospecific and asymmetric polymerization. Some papers related to the polymerization of aldehydes, cyclic ethers and lactams. The formation and characteristics of phenol-urea and melamine-formaldehyde resins were also covered in this section, and the large number of papers presented indicated the still much alive fundamental and technological interest in these older lines of study.

About 200 papers were concerned with the physical characterization, physical properties and structure of polymers. The main topics covered include infrared, NMR, ESR and X-ray studies, chain conformation, equilibrium and non-equilibrium studies, as also rubber elasticity, viscoelastic and dielectric properties, molecular motion, mechanical, rheo-optical, physical, thermal and electrical

properties, glass transition, diffusion and surface phenomena and rheological properties of melts and concentrated solutions. As the papers presented and the discussions on rheological properties of polymers elicited a great deal of interest, a special informal session on the topic was arranged in Kyoto during the last two days of the symposium.

About 40 papers were presented at the section on new polymerization processes and new polymers. The papers were mainly devoted to new types of initiating reactions, applications of new initiators, such as sulphur dioxide, sulphur dioxide-pyridine, metal salts capable of forming complex with the monomer, etc., and the polymerization of substances like xylenes, phenols, amides, ethers, etc., which give rise to a new class of polymers.

Twenty-five papers were contributed to the section on photo- and radiation-induced polymerization, the main topics covered being photopolymerization and radiation-induced radical, ionic and graft polymerization. About 20 papers on graft polymerization by the more conventional polymer reactions were presented at a separate section. The papers elicited a great deal of lively discussion and, therefore, the discussions were carried over to a special two-day informal session led by Prof. Mark.

The remaining sections accounted for an average of ten papers per section. The poor response at some of the sections, for example, the section on

thermostable polymers, is indicative of the inherent difficulties met with during studies in these fields.

From the proceedings of the symposium it was evident that although the basic broad outlines of the polymerization processes were well understood, there are still many details to be filled in with respect to mechanism, kinetics, structural and configurational aspects, and grafting and solution properties of polymers. Factors affecting the stability, configurational sequence and the necessity for further theoretical studies of the polymerization processes were among several points raised by different speakers. Several interesting new techniques were discussed. The standard of the papers and discussions was high.

The papers will be published in the *Journal of Polymer Science (Part C)* and the lectures in the *Journal of Pure and Applied Chemistry*.

The symposium was most efficiently organized (the setting in Kyoto was almost a romantic extravaganza), a view unanimously subscribed to by all who attended the symposium, not to mention the fantastic banquets and dinners, formal or personal. Indeed, as remarked by one of the present reporters (S.R.P.) in the official banquet, the centre of gravity of polymer science and technology has shifted definitely to a considerable extent towards East, in which the overwhelming weightage has been lent by Japan.

## Chemical Dosimetry

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WITH the advent of several high energy radiation sources and because of their increased uses in various industrial and research laboratories there is a growing interest in finding a suitable standard dosimeter. Moreover, the incidence of nuclear explosions and man's survival in case of atomic warfare necessitate the importance of developing simple dosimeters for civil defence purposes. Although there are several methods of radiation dose measurements using several sophisticated physical instruments, chemical dosimeters have attracted a wide attention because of their ease of handling, simplicity of measurements and reproducibility of results.

A good dosimeter should be independent of intensity over a wide range and also independent of wavelength and slight changes in the temperature as well. Further, the response of the dosimeter should be proportional to dose, the extent of the radiation-induced reaction in the chemical dosimeter should be easily and accurately measurable and it should not be strongly dependent on the concentration of the reagent. And above all, the dosimeter should be simple, reproducible and insensitive to small amounts of impurities.

There is, at present, not a single dosimeter which conforms to all the above requirements and which can be used in all the ranges of doses. Several chemical systems have been studied and designed for the purpose of dosimetry, but amongst them only the Fricke dosimeter appears to be closest to the above requirements. In the discussions to follow, some of the salient features of the Fricke dosimeter will first be described and then we will restrict ourselves to various systems developed for low and high dose measurements.

### Fricke or Ferrous Sulphate Dosimeter

Fricke dosimeter is based on the radiation-induced oxidation of ferrous to ferric iron in aerated ferrous sulphate solution. That a solution of ferrous sulphate in 0.8N H<sub>2</sub>SO<sub>4</sub> can be used for X-ray dose measurements was first proposed by Fricke and Morse<sup>1</sup>. Later, several improvements have brought in greater versatility of the method. Dewhurst<sup>2</sup> first showed that when chloride ion is introduced in the system, it inhibits the oxidation of ferrous iron by certain organic impurities. Another contribution was made in 1952 by Hardwick<sup>3</sup> when he first demonstrated that the amount of ferric iron

formed by radiation-induced oxidation can be determined by direct reading of the absorbance at 305  $\mu$ .

The recommended procedure<sup>4</sup> for the dosimeter is to prepare a solution which is 0.0014M, 0.001M and 0.4M in FeSO<sub>4</sub>, NaCl and H<sub>2</sub>SO<sub>4</sub> respectively. The oxidized iron species formed as a result of irradiation is then usually measured through its absorption at 305  $\mu$ .

The Fricke dosimeter is useful in the range of about 4000-40,000 rads. The lower limit is, however, determined by the analytical method used. By using larger cells in the direct spectrophotometric method the Fricke dosimeter can be extended to still lower doses. Colorimetric measurement after extraction of the ferric thiocyanate complex<sup>5-7</sup> enables one to measure doses of about 100 rads with an accuracy of  $\pm 2$  per cent. Radioactive tracer methods<sup>5,6,8</sup> using <sup>59</sup>Fe has been applied either in the separation of Fe<sup>3+</sup> through extraction of the thiocyanate complex with isoamyl alcohol or in the isolation of Fe<sup>3+</sup> ion by zirconium phosphate ion exchanger; the relative error of the method is about  $\pm 5$  per cent for doses higher than 40 rads. Alternatively, ferrous iron can be estimated before and after irradiation by means of ferrous orthophenanthroline complex. The upper limit in the dose range is set by oxygen consumption in the system. A dose of  $4.2 \times 10^4$  rads is sufficient to use up all the O<sub>2</sub> in an air-saturated solution whilst  $2 \times 10^5$  rads is required if the dissolved air is displaced by pure oxygen. Recently, doses up to 10<sup>6</sup> rads have been measured by using deaerated ferrous sulphate solution [ $G(\text{Fe}^{3+})=8$ ] or by supplying oxygen to the dosimeter during irradiation<sup>9</sup>.

The absolute value of the yield of the Fricke or the aerated FeSO<sub>4</sub> dosimeter has been measured by several methods<sup>10</sup>. The usually accepted value for <sup>60</sup>Co  $\gamma$ -rays is  $G(\text{Fe}^{3+})=15.5$ .

Absolute yield values of the Fricke dosimeter when subjected to high energy (10-20 MeV.) electrons have been determined<sup>11</sup>. Possibility of utilizing it for high energy neutrons has also been studied<sup>12</sup> recently. A measurement of the yield of the Fricke dosimeter for 14.6 MeV. neutrons gave a value of  $G(\text{Fe}^{3+})=11.5 \pm 1.8$ . The possibility of utilizing it for in-pile dosimetry<sup>13</sup> of gamma radiations is yet to be evaluated.

The response of the dosimeter is independent of ferrous iron concentration<sup>14,15</sup> between  $5 \times 10^{-2}$  and  $10^{-4}M$ . The difficulty in using very low concentration arises from the fact that all the ferrous iron may be destroyed by the absorbed dose which may not be very large. However, a ferrous iron concentration of about  $10^{-3}M$  is generally used.

The dosimeter is also independent of H<sub>2</sub>SO<sub>4</sub> concentration<sup>16</sup> in the range 1.5 and 0.1N, and 0.8N H<sub>2</sub>SO<sub>4</sub> is, however, generally used since the time when it was first proposed by Fricke who actually considered that the electron density of this medium would approximate to that of the living cell.

The response of the dosimeter is independent of the dose rate<sup>17,18</sup> up to about  $10^7$ - $10^8$  rads/sec. but the yield decreases at higher dose rate. Anderson<sup>18</sup> gives a  $G$  value of  $11.4 \pm 0.5$  for the dose rates 2 to  $3 \times 10^9$  rads/sec. Practical limits<sup>19</sup> of

TABLE 1 -- VALUES OF  $G(\text{Fe}^{3+})$  AT DIFFERENT LET RADIATIONS

Radiation	LET (eV./A.)	$G(\text{Fe}^{3+})$	Ref.
<sup>60</sup> Co $\gamma$ -rays	0.034	15.5	19, 22
220 kV.P X-rays	0.27	15.0	19, 22
<sup>32</sup> P $\beta$ -particles	0.68	12.9	19, 23
1.99 MeV. protons	1.43	8.0	24
<sup>210</sup> Po $\alpha$ -particles	13.6	5.1	19, 25
<sup>235</sup> U fission fragments	440	3.0	7, 19

utility for the Fricke dosimeter are: (a) high LET (linear energy transfer), e.g. P<sub>0</sub>  $\alpha$ -particles — up to  $10^{20}$  eV.  $l^{-1} sec^{-1}$ ; and (b) low LET, e.g. X- or  $\gamma$ -rays — up to  $10^{26}$  eV.  $l^{-1} sec^{-1}$ .

As far as the effect of LET is concerned, the  $G(\text{Fe}^{3+})$  values depend upon the LET of the radiation and decrease with the increase of LET because the primary molecular product yields increase at the expense of the free radicals in the radiolysis of water when LET is increased. LET effects for doubly charged helium ions were studied by Schuler and Allen<sup>20</sup> and an empirical relationship between  $G(\text{Fe}^{3+})$  and LET was derived. Recently, Burke<sup>21</sup> has shown that for photons with energy in excess of 6 keV., the irradiation yield may be represented by the expression:  $G=15.61-15.43/E$  where  $E$  is the mean photon energy in keV. and  $G$  is the number of ferrous ions oxidized per 100 eV. of energy absorbed. Some values of  $G(\text{Fe}^{3+})$  for different types of radiations are given in Table 1.

Before we proceed to describe other chemical systems used as chemical dosimeter, mention must be made that within its limitations the Fricke dosimeter is convenient to use, reproducible<sup>22</sup> and it works well in the hands of even inexperienced personnel.

### Measurement of Doses below 1000 Rads

Measurement of doses smaller than 1000 rads is important because of its medical and biological interest. It is also useful for civil defence agencies during an atomic warfare. Although the Fricke dosimeter can be used for measuring such low doses employing suitable variations in the analytical technique<sup>21</sup>, use of chemical systems which are more sensitive to radiation is desirable.

Acid production from irradiation of chlorinated hydrocarbons has largely been used for low dose measurements<sup>27-30</sup>. The amount of acid produced may be determined by noting directly the changes in  $pH$  or through colour changes in a  $pH$  indicator dye. Simple acidometric titrations may also be employed.

Such systems apparently react with fairly long chain mechanism and are, therefore, susceptible to the presence of traces of impurities, variations in dose rate or temperature. Use of an optimal amount of a chain inhibitor may, however, reduce the effects due to undesirable factors of a chain process and yet preserve sufficient sensitivity to measure gamma radiation doses below 100 rads. Among several antioxidants such as alcohols, ketones, quinones, phenols, etc., resorcinol (0.1-1.0 per cent) provides



an excellent thermal stability and makes the system free from undesirable effects of dose rate preserving at the same time sufficient sensitivity ( $G$  values 37-75) to permit accurate dosimetry in the lower dose range.

Recently, a solid chemical dosimeter<sup>31</sup> with improved sensitivity to X-ray and stability to ultraviolet light has been described. In this system where chloroform is taken in paraffin base para-hydroxy azobenzene has been effectively used as a sensitizer and stabilizer.

The dosimeter using chlorinated hydrocarbons may be a two-phase or a single-phase system. The former is made from a chlorinated hydrocarbon overlaid with an aqueous indicator dye solution and the latter comprises an aqueous solution of a  $pH$  indicator dye saturated with a chlorinated hydrocarbon. Because of the high  $Z$  value of the two-phase system its response to radiation has a spectral dependence, whereas the single-phase system, which usually does not contain more than 5 per cent of chlorinated hydrocarbon and thus keeps the  $Z$  value similar to that of water, shows a relatively flat spectral dependence when exposed to radiations<sup>32</sup>.

The single-phase chlorinated hydrocarbon system has got greater sensitivity towards the fast neutrons than the two-phase systems, since the former has higher hydrogen content. Dosimeters made of tetrachloroethylene and carbon tetrachloride which are devoid of hydrogen have practically no sensitivity to fast neutrons but they are affected by X-rays. The chlorinated hydrocarbon dosimeters may thus be used to know the respective contribution in mixed neutron-gamma field<sup>33</sup>.

### Measurement of High Radiation Doses

Several systems have been described in the literature for using them as chemical dosimeter to measure high radiation doses. The Fricke dosimeter, as has already been pointed out, cannot be used for measurement of high doses under usual conditions because of prior consumption of oxygen in the system. The upper limit can, however, be extended to some extent by saturating the solution with pure  $O_2$  and increasing the  $FeSO_4$  concentration fivefold. Ceric sulphate dosimeter can be used in case of highly intense fields where the well-known Fricke dosimeter fails.

**Ceric sulphate** — The principle involved in using aerated ceric sulphate solution in 0.8N  $H_2SO_4$  as a chemical dosimeter consists in the reduction of ceric ion to cerous. The disappearance of  $Ce^{4+}$  due to absorption of radiation can be measured spectrophotometrically by its absorption<sup>34</sup> at 320  $m\mu$  or by taking recourse to standard analytical procedure by titration against Mohr's salt in presence of ferroin indicator<sup>35</sup>. The commonly accepted value<sup>36</sup> for  $G(-Ce^{4+})$  is  $2.50 \pm 0.026$ .

The usual range of utilizing ceric sulphate dosimeter is  $10^5$ - $10^7$  rads. Measurement of doses up to  $10^8$  rads has also been reported<sup>35</sup>, but the necessary increase in concentration of  $Ce^{4+}$  showed a tendency to change the  $G(-Ce^{4+})$  value. The yield in the ceric sulphate dosimetry has been reported<sup>36</sup> to be independent of dose rate up to about

$10^7$ - $10^8$  rads/sec. and independent of temperature from  $7^\circ$  to  $35^\circ C$ . The  $G$  value was found to be constant<sup>37</sup> in the range of ceric sulphate concentration of  $3 \times 10^{-3}$  to  $5 \times 10^{-2} M$ .

The ceric sulphate dosimeter, however, suffers from the drawback that it is very sensitive to traces of impurities leading to erratic and irreproducible  $G(-Ce^{4+})$  values. Recently,  $CuSO_4$  has been found to show some stabilizing influence; and it was observed that  $10^{-1} M$   $Cu^{2+}$  for  $10^{-3} M$  ceric solution can scavenge the minor impurities from ordinary distilled water<sup>38</sup>.

**Nitrous oxide** — The radiation-induced decomposition of nitrous oxide constitutes one of the most useful gaseous dosimeters<sup>19</sup> for high gamma dose range measurements in mixed or pure gamma fields. The overall reaction<sup>39</sup> of the system is:  $6N_2O = 5N_2 + O_2 + 2NO_2$ . The dosimeter is read out by freezing the undecomposed  $N_2O$  and the product  $NO_2$  with liquid nitrogen and then measuring the pressure of  $N_2 + O_2$  formed. At very high doses ( $3 \times 10^7$  to  $3 \times 10^9$  rads) the product  $NO_2$  is produced<sup>40</sup> in appreciable amounts and the extent of reaction can also be determined by measuring  $NO_2$  spectrophotometrically.

The dosimeter is independent of gas pressure<sup>41</sup> with nitrous oxide pressure above 500 mm. mercury and  $G(-N_2O) = 12$ , but at a lower pressure (70 mm. mercury) the results are inconsistent<sup>42</sup> and Johnson<sup>43</sup> found a very high yield as  $G(-N_2O) = 9.4 \times 10^4$  which indicates the presence of some chain reactions.

The nitrous oxide dosimeter has got the following important features: (a) it can be successfully utilized<sup>41,44</sup> in a very large dose range ( $5 \times 10^4$  to  $3 \times 10^9$  rads); (b) it is independent of dose rate and LET and also of temperature in the range  $-80^\circ$  to  $+200^\circ C$ ; (c) the cell diameter has got no influence on the  $N_2$  yield<sup>45</sup>  $G(N_2) = 11.4 \pm 0.8$ ; and (d) it has got its use in measuring gamma doses in mixed radiation fields since the maximum neutron response of the dosimeter is of the order of about 0.5 per cent.

**Oxalic acid** — The principle of the aqueous oxalic acid dosimeter<sup>46-49</sup> is based on the decomposition of oxalic acid induced by radiation energy absorbed in aqueous solution. The depletion in the concentration of oxalic acid as a result of radiation-induced decomposition is determined spectrophotometrically by measuring the concentration of oxalic acid before and after irradiation by means of cupribenzidine reagent at 246  $m\mu$ .  $G(-oxalic\ acid)$  was found<sup>50</sup> to be 4.9. The dosimeter is applicable up to a dose of  $1.6 \times 10^8$  rads. The lower limit is determined by the small concentration changes and the upper limit is set by the complete decomposition of the oxalic acid in the dosimeter. The concentration of oxalic acid is thus determined by the region of dose to be studied. The decomposition is linear with the absorbed dose up to about 30 per cent decomposition. For initial concentration of oxalic acid above 25  $mM/l$  there is no change in the  $G$  value. In general, 0.025-0.6  $M$  oxalic acid is used. The radiation-induced decomposition yield is not noticeably affected at dose rates up to  $10^{10}$  rads/sec. Irradiation temperature does not affect the radiation yield. The dosimeter is neither photosensitive nor sensitive

to impurities. It is very useful at high dose rates<sup>51,52</sup> and for large absorbed doses and in such region it can actually serve as a complement to the ceric sulphate dosimeter. Effect of high LET radiations<sup>53,54</sup> on the dosimeter has been studied, but, generally speaking, the LET dependence of oxalic acid decomposition yields is yet to be known.

The dosimeter is not made radioactive on irradiation with neutrons and since it can be used in high radiation fields, the oxalic acid dosimeter finds its useful application<sup>55</sup> in reactor dosimetry and with its aid the relative contribution of different radiation components in the reactor have been evaluated.

**Cyclohexane** — Production of hydrogen on irradiation of cyclohexane<sup>56-60</sup> constitutes one of the important chemical dosimeters for measurement in high dose range. The yield of hydrogen can be measured<sup>61</sup> through gas chromatography or by noting the increase in pressure by vacuum techniques<sup>62-64</sup>. The method is suitable in the region 0.5-5 Mrad with an accuracy<sup>61</sup> of  $\pm 5$  per cent. Measurement of doses as low as 0.05 Mrad can also be made with its aid. The effect of LET on the yield of hydrogen has been studied<sup>65-67</sup> and it was found that  $G(H_2)$  remained constant over wide limits of LET though the yields of other hydrogen deficient products are affected appreciably.

### Miscellaneous Systems

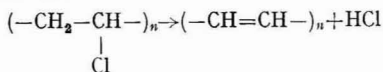
Among several other systems that have good prospects of their use in dosimetry, plastics have drawn the attention of several workers<sup>68-70</sup> since they are robust, inexpensive and easy to handle.

Clear perspex<sup>71</sup> absorbs strongly in the region of 290  $m\mu$  and when irradiated the optical density increases linearly with dose up to 3 Mrad and this forms the basis for its use in dosimetry. Perspex dosimeter is stable, does not change on storing whatever may be the environmental factors and it does not require special treatment before and after irradiation other than cutting and cleaning. Effects of temperature, dose rate, etc., are yet to be studied to make it more useful and versatile.

Commercial red perspex (Red 400) has also been tried for gamma dosimetry<sup>72</sup>. When it is irradiated in the dose range of 0.1-5 Mrad a characteristic absorption band having a peak at 620  $m\mu$  appears.

Use of simple polyethylene<sup>73</sup> has also been suggested for the purpose of dosimetry. If polyethylene is irradiated in an atmosphere containing  $O_2$  it increases in weight linearly with dose up to 50 Mrad and there occurs a parallel increase in the peroxide concentration and saponification index.

Polyvinyl chloride (PVC) has long been used for dosimetry<sup>19</sup>. Polyene chains are coloured amber and this may be measured directly or alternatively a dye indicator such as methyl violet can be incorporated to measure the HCl formed on irradiation.



The PVC film has recently<sup>74</sup> been used for beta dosimetry by measuring colour changes at 370  $m\mu$ .

The films were made from various PVC powders and heat treated to stabilize the colour.

Conversion of liquid monomer to a solid polymer on irradiation can also provide the basis of its use in dosimetry<sup>75</sup>.

The use of polyacrylamide in dosimetry has more or less been studied in details<sup>76</sup>. It is useful in the range of about 50-7500 rads. The dosimeter consists of a dilute aqueous solution (0.078 per cent) of polyacrylamide and is based on the degradation of the polymer on absorption of radiation. The change in viscosity of the solution which is directly proportional to the dose received is measured with a micro viscometer. The dosimeter is stable over long periods of time before and after irradiation and, therefore, its exposure to intermittent doses of radiation are cumulative, the total dose being equal to the sum of the various exposures. This integration property coupled with the fact that the dosimeter can be read and returned for further exposure adds to its versatility as a long-range total dose monitor for ionizing radiation. The dosimeter was found to be dose rate independent up to a value of 2400 rads/hr and energy independent in the range of 39-1330 keV.

The polyacrylamide dosimeter may also find its application in radiation therapy as a monitor not only for the whole body irradiation but also for specific organs<sup>77</sup>.

Another system which has been proposed for the use as a dosimeter in the high dose range of 2-20 Mrads consists in the de-esterification of solutions of benzyl esters<sup>78</sup> on irradiation with high energy electrons. The organic acid produced is estimated and  $G$  values have been found to vary from 2.1 to 2.25.

Dosimeters using naphthalene-1- $T$  in aqueous solution were studied recently<sup>79</sup>. The hydrophilic compounds produced were analysed and the yield was found to be proportional to dose in the range 1-3000 rads. The dosimeter is also independent of dose rate between 3 and 50,000 rads/hr. Further study may find the naphthalene dosimeter useful in measuring low doses.

Studies are also being made to use ferrocene<sup>29</sup> in  $CCl_4$  solution as a convenient gamma dosimeter. Dosimeters using 2,6-dichloroindophenol<sup>80</sup> have been found to be useful for gamma dose measurement in the 0.5-30 krad range within the accuracy limits prevalent in industrial applications.

Convenient electrochemical dosimeters<sup>81,82</sup> for routine measurements have also been described where a redox system sensitive to radiation is used.

Liberation of  $NH_3$  from aqueous glycine solution on irradiation, the yield being proportional to dose over a large range, also serves the purpose of a dosimeter<sup>83</sup>. With concentrated aqueous glycine solution (71M) the dosimeter may be used for both  $\gamma$ -rays and fast neutrons in the range  $10^5$ - $10^8$  rads.

Aqueous nitrate solution on irradiation produces nitrite which can be easily estimated spectrophotometrically by reaction with sulphanilic acid and  $\alpha$ -naphthylamine. In case of aqueous  $NH_4NO_3$  solution<sup>84</sup> the nitrite formation has been found to be proportional to the absorbed dose over a wide range implying its use as a chemical dosimeter,



TABLE 2—CHARACTERISTICS OF SOME SYSTEMS STUDIED FOR CHEMICAL DOSIMETRY

Dosimeter	Chemical change measured and method of measurement	Dose range rad	Yield	Ref.
Fricke (ferrous sulphate)	$\text{Fe}^{2+} \rightarrow \text{Fe}^{3+}$ ; spectrophotometry, direct $\text{Fe}^{3+}$ titration	$4 \times 10^3$ – $4 \times 10^4$	$G(\text{Fe}^{3+}) = 15.5$	10
Ferrous + cupric sulphate	$\text{Fe}^{2+} \rightarrow \text{Fe}^{3+}$ ; spectrophotometry	$10^7$	$G(\text{Fe}^{3+}) = 0.66$ for $^{60}\text{Co}$ $\gamma$ -rays $G(-\text{oxalic acid}) = 4.9$	24, 89 90 49
Aqueous oxalic acid	Loss of oxalic acid; spectrophotometry	$1.6 \times 10^6$ – $1.6 \times 10^8$	$G(\text{H}_2) = 5.8$	61
Cyclohexane	Formation of gaseous product ( $\text{H}_2$ ); gas chromatography, pressure increase	$10^4$ – $10^8$	$G(-\text{Ce}^{4+}) = 2.5$	35, 36
Ceric sulphate	$\text{Ce}^{4+} \rightarrow \text{Ce}^{3+}$ ; spectrophotometry, direct titration	$10^4$ – $10^7$	$G = 0.446$ for $^{60}\text{Co}$ $\gamma$ -rays	91
Chromate	Decrease in extinction of acidic $\text{K}_2\text{Cr}_2\text{O}_7$	$10^4$ – $10^8$	$G(\text{NH}_3) = 1.48$ to 1.60	83
Aqueous glycine	Liberation of $\text{NH}_3$	$10^4$ – $10^8$	$G(\text{acid}) = 2.1$ to 2.25	78
Benzyl ester	De-esterification, production of organic acid	$2 \times 10^6$ – $3 \times 10^7$	—	92
Aqueous D(+)-maltose	Degradation of sugar; polarimetry	$2.5 \times 10^7$ – $10^8$	$G(-\text{N}_2\text{O}) = \sim 12$	41, 44
Nitrous oxide	$\text{N}_2\text{O} \rightarrow \text{N}_2, \text{O}_2, \text{NO}_2$ ; pressure increase over $10^7$ rads, colorimetry of $\text{NO}_2$	$5 \times 10^4$ – $3 \times 10^8$	$G(\text{HCl}) = \sim 26$	33, 93
Aqueous chloroform (single phase)	Formation of $\text{HCl}$ ; acid titration, pH measurement	$10^3$ – $4 \times 10^4$	$G(\text{HCl}) = 35$ to 90	33
Chloroform + water (two-phase) with inhibitor	Formation of $\text{HCl}$ ; titration, pH measurement, colorimetry	50–1000	—	31
Chloroform with paraffin base (solid)	Formation of $\text{HCl}$ ; pH measurement	to 5000	$G(-\text{quinine}) = 2.3$	94
Aqueous quinine sulphate	Fluorescence	10–1000	—	76
Polyacrylamide	Degradation of polymer to smaller molecules; viscosity	50–7500	$G(\text{H}_2\text{O}_2) = 1.22 \pm 0.07$ for $^{60}\text{Co}$ $\gamma$ -rays	88
Aerated water	Formation of $\text{H}_2\text{O}_2$ ; luminescence with spectrophotofluorimeter	30–3000	$G(\text{salicylic acid}) = \sim 2.3$	95–97
Calcium benzoate	Formation of salicylic acid; fluorescence	5–5000		

but the details are yet to be studied. Solid dosimeters showing colour changes on irradiation when halogenated hydrocarbon-azo dye system is distributed in paraffin base have been described<sup>85</sup>. Colourless derivatives of triphenyl methane dyes<sup>86</sup> such as stabilized forms of para-rosaniline nitriles showed special promise because of the high intensity of colour formed on irradiation, and its capability of being incorporated easily into a number of media. Sodium dimethyl arsenate and tris (hydroxymethyl) aminomethane have also shown special potential for gamma radiation dosimetry<sup>87</sup>. Dosimeter utilizing a very sensitive method for the determination of  $\text{H}_2\text{O}_2$  produced on irradiation of aerated water has been found to be useful in the range of 30–3000 rads<sup>88</sup>.  $\text{H}_2\text{O}_2$  is determined through the copper-catalysed chemiluminescent reaction between luminol and  $\text{H}_2\text{O}_2$ . The dosimeter is very simple and it is almost independent of LET, the initial yield of  $\text{H}_2\text{O}_2$  showing only about 15 per cent increase for an increase of LET from 0.02 to 14 eV./A.

Of all the methods described, the Fricke dosimeter seems, however, to be more popular because of its closeness in having the desirable characteristics to become an ideal dosimeter. Other methods that are receiving attention are yet to be studied in order to evaluate their versatility and easy manipulation. Still more methods will of course be added to those that are already known and a day may come when a chemical dosimeter may replace the present-day radiation monitoring devices since they are simple,

cheap and easy to handle. Desirable characteristics of some of the important and useful chemical dosimeters have been compiled in Table 2.

### Summary

A critical survey of the work done on chemical dosimetry till recent days has been made. The characteristics that make up an ideal dosimeter have been discussed. The scope and limitations of the most popular Fricke dosimeter have been discussed at length. Several other systems that are used or are being tried for both low and high dose measurements have been described. The prospects of various systems of being good dosimeters have been discussed and it has been assessed that chemical dosimeters may in future replace the present-day monitoring devices since they are simple, cheap and easy to handle.

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# Quality Control of Radiopharmaceuticals

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**T**HE term radiopharmaceuticals broadly signifies preparations of radioisotopes which are obtained after certain irradiated target materials are submitted to various chemical processes such as dissolution, oxidation-reduction, distillation, extraction, adsorption and desorption on ion-exchangers, and concentration. Some organic molecules in which certain atoms are exchanged by their radioisotopes or into which radioisotopes are substituted or added on or incorporated by biosynthesis are also grouped under this title.

Some commonly used radiopharmaceuticals have been included in the seventeenth revision of the *United States pharmacopoeia* (USP) and in the *British pharmacopoeia* 1963 and its *Addendum* 1964 (Table 1). It may, however, be noted that (1) though cyanocobalamin  $^{60}\text{Co}$  has been superseded by the vitamin labelled with  $^{57}\text{Co}$  and  $^{58}\text{Co}$ , the former is still official in the USP; (2) radiogold  $^{198}\text{Au}$  injection is official in the BP and though it was official in USP XVI it has now been dropped out of USP XVII 'as no longer meeting the requirements for listing'; and (3) only the USP has accorded recognition to Rose Bengal  $^{131}\text{I}$  and sodium iodo hippurate  $^{131}\text{I}$ . Even so the official recognition of some of the items appears to be belated. Table 1 also lists a number of other radiopharmaceuticals, which have not appeared in the above-mentioned pharmacopoeias, but which are routinely used in some measure in medical diagnosis. Besides these, there are several other radioactive labelled compounds used at present in the clinical field on an investigational basis.

TABLE 1 — RADIOPHARMACEUTICALS FOR CLINICAL DIAGNOSIS AND THERAPY

## ORAL PREPARATIONS

Aqueous solutions:  $\text{H}_3^{32}\text{PO}_4$ ;  $\text{Na}_2\text{H}^{32}\text{PO}_4$  (ref. 1),  $^{59}\text{FeCl}_2$ ; cyanocobalamin- $^{57}\text{Co}$  (ref. 1, 38); cyanocobalamin- $^{58}\text{Co}$  (ref. 38); cyanocobalamin- $^{60}\text{Co}$  (ref. 1);  $\text{Na}^{131}\text{I}$  (ref. 1, 2)

Oil solutions: Triolein- $^{131}\text{I}$ ; oleic acid ( $^{131}\text{I}$ )

Gelatin capsules:  $\text{Na}^{131}\text{I}$  (ref. 1)

Eluates from  
elution columns:  $^{99}\text{Mo}$  —  $^{99}\text{Tc}$ ;  $^{132}\text{Te}$  —  $^{132}\text{I}$

## PARENTERAL PREPARATIONS

Aqueous solutions:  $^{24}\text{NaCl}$ ;  $\text{Na}_2\text{H}^{32}\text{PO}_4$  (ref. 1, 2);  $\text{Cr}^{52}\text{PO}_4$  colloid;  $^{42}\text{KCl}$ ;  $^{51}\text{CrCl}_2$ ;  $\text{Na}_2^{51}\text{CrO}_4$  (ref. 2);  $^{59}\text{Fe}$ -citrate (ref. 38);  $\text{Na}^{82}\text{Br}$ ;  $\text{Na}^{131}\text{I}$  (ref. 1, 2);  $^{198}\text{Au}$ -colloid (ref. 38); bromosulphalein ( $^{131}\text{I}$ ); Congo red ( $^{131}\text{I}$ ); cholografin ( $^{131}\text{I}$ ); diodone ( $^{131}\text{I}$ ); Evans blue ( $^{131}\text{I}$ ); hippuran ( $^{131}\text{I}$ ) (ref. 1); synkavite ( $^{131}\text{I}$ ); Rose Bengal ( $^{131}\text{I}$ ) (ref. 1); human serum albumin ( $^{131}\text{I}$ ) (ref. 1, 38); neohydrin ( $^{203}\text{Tl}$ )

Solutions in propylene glycol: Diisopropyl fluorophosphate ( $^{32}\text{P}$ ); L-thyroxine ( $^{131}\text{I}$ )

Unlike the conventional pharmaceuticals the radiopharmaceuticals have to be looked upon as a special class of materials. Though they are employed for clinical diagnostic studies and therapeutic purposes, their distribution is highly restricted, and they are employed only in a few medical institutions. This is because their employment demands firstly the observance of strict regulations regarding the handling of radioactive materials and protection of personnel from radiation, and secondly the use of specialized equipment such as medical spectrometers for scanning. Another important distinction from the conventional pharmaceuticals is that they are produced in quantities rarely exceeding a couple of centilitres and they are used in small volumes within a short time of supply.

Conventional chemical and biological products destined for medical use are required to be tested appropriately before they are released for use. An exception to this rule is, however, to be found in the case of liquid BCG vaccine<sup>2</sup>, a biological preparation, which deteriorates rapidly and has, therefore, to be used even before the results of tests are known. The tests carried out on the product, however, serve as controls in the light of which the production methods are constantly reviewed. An analogous case is presented by a number of radiopharmaceutical preparations which, on account of their short half-life and the need to utilize them at a reasonably high specific activity, have to be supplied to the medical users even before the results of the tests are known.

The quality control carried out on the radiopharmaceuticals are considered under three aspects—physical, chemical and biological controls.

## Physical Control

Physical characteristics such as colour, density, melting point, boiling point, refractive index, optical rotation, etc., which are useful for the purpose of identification and sometimes as an index of purity of conventional pharmaceuticals, are neither easily nor always applicable to radiopharmaceuticals. Alternatively they are identified by their half-life, and by the radiations they emit. The assay for radioactive concentration is carried out by appropriate radiation measuring instruments. When the radiopharmaceuticals are in the form of colloids, particle size and distribution aspects are also examined.

The half-life of a radioisotope is measured by taking the count rate of a source with a Geiger-Müller counter or a scintillation counter over a suitable period. The value obtained should conform to the figures given in Table 2.

The radiations emitted by the radioisotopes are identified by examining the beta-ray absorption curve with a Geiger-Müller counter or the gamma-ray

spectrum with a gamma scintillation spectrometer. From an analysis of the absorption curve the maximum range is determined and from this the maximum beta-ray energy is calculated<sup>3</sup>. These values are given in Table 2 for some radioisotopes.

From the gamma-ray spectra the energies corresponding to the photopeaks are calculated and compared with the authentic values given in literature<sup>4</sup>. The prominent gamma radiations of a number of radioisotopes are given in Table 2.

The analysis of the beta-ray absorption curve and the gamma spectra are also helpful in detecting the presence of any radioactive contaminants.

The term radioactive concentration obviously means the amount of radioactive material in a solution. A knowledge of the actual amount is needed, for example, in the evaluation of target yields, and in the dispensing of radioisotopes particularly for medical purposes. The radioactive concentration is determined by methods relevant to the particular radioisotope depending on whether it emits hard or soft beta radiation, or beta and gamma radiation, or soft X-rays by electron capture. The primary methods<sup>5-7</sup> employed for the calibration and the secondary methods employed for routine measurements of the radioisotopes in a number of radiopharmaceuticals are listed in Table 2. With the help of calibrated solutions and sometimes standards obtained from the International Atomic Energy Agency (Vienna), efficiency factors are determined for the various radiation measuring instruments for subsequent routine secondary standardization.

Particle size, which considerably influences the biological properties of colloids, is examined periodically by electron microscopy on non-radioactive colloids<sup>8</sup> prepared under identical conditions.

### Chemical Control

Radiochemicals, like inactive chemicals, are required to be chemically pure, but besides this, two other aspects of purity come into consideration. They are concentration of the carrier element (or the stable isotopes of the radio-element under consideration), and the radiochemical purity. Owing to the radioactive decay and the effect of radiation on the substances, these aspects of purity change with time.

*Chemical purity* — The impurities in the processed solutions of the medical radioisotopes are mostly derived from the raw materials, and the reagents used in processing. These non-radioactive impurities or elements can be categorized as below from the physiological point of view<sup>9</sup>:

- (i) Essential elements —  
Bulk: Ca, Mg, Na, K, Cl, P, S  
Trace: Al, B, Co, Cu, Fe, Mn, Mo, V, Zn
- (ii) Non-essential elements —  
Non-toxic: Cr, Cs, Ni, Rb, Si, Sn, Sr  
Toxic: Ag, As, Ba, Be, Bi, Cd, Hg, Pb, Sb, Se, Te

Chemically, the presence of some physiologically harmless elements such as Al, Co, Cr or Fe is not desirable since they precipitate as insoluble hydroxides from neutral or slightly basic solutions. In turn these precipitates are likely to coprecipitate the radioisotope, for example, <sup>32</sup>P. Spectrographic analyses carried out on a number of processed solutions have shown that except for Na, B and Si the other elements are very much below 5 p.p.m. Since routine spectrographic analyses are not practicable, the presence of heavy metals, which are sometimes chemically incompatible or are physiologically toxic, is controlled by sulphide precipitation test. The heavy metals expressed as lead should not exceed 10 p.p.m.

TABLE 2 — PHYSICAL DATA ON SOME RADIOISOTOPES IN RADIOPHARMACEUTICALS

Radioisotope	Half-life	Radiations†			Max. range in aluminium mg./cm. <sup>2</sup>	Method of standardization	
		Beta	Gamma	EC %		Primary	Secondary
<sup>24</sup> Na	15h	1.39 (100)	1.37 (100), 2.75 (100)	—	620	ABC	DE
<sup>32</sup> P	14.2h	1.7 (100)	—	—	800	A	FG
<sup>42</sup> K	12.5h	2.0 (18), 3.6 (82)	1.5 (18)	—	1700	AB	DE
<sup>51</sup> Cr	27.8d	—	0.32 (8)	100	—	CH	DE
<sup>57</sup> Co	270d	—	0.122 (88), 0.136 (10)	100	—	—	—
<sup>58</sup> Co	71d	0.47* (15)	0.81 (100)	85	160	BCH	DE
<sup>60</sup> Co	5.27y	0.31 (100)	1.17 (100), 1.33 (100)	—	660	B	DE
<sup>69</sup> Fe	45d	0.27 (46), 0.46 (53)	1.10 (56), 1.29 (44)	—	140	BC	DE
<sup>82</sup> Br	36h	0.44 (100)	0.55 (75), 0.62 (42), etc.	—	143	ABC	DEF
<sup>99</sup> Tc	6h-2.1 × 10 <sup>5</sup> y	0.29 (100)	0.14 (99)	—	74	A	GI
<sup>131</sup> I	8d	0.33 (9), 0.61 (87)	0.36 (80), 0.64 (9), etc.	—	310	ABC	DEF
<sup>132</sup> I	2.26h	A No. of betas	0.67 (100), 0.78 (85), etc.	—	—	—	D
<sup>198</sup> Au	2.7d	0.96 (99)	0.41 (96)	—	600	ABC	DEF
<sup>197</sup> Hg(m)	24h	—	0.133 (31), 0.164 (4.4)	3	—	—	—
<sup>197</sup> Hg	65h	—	0.077 (20)	100	—	C	DE
<sup>203</sup> Hg	47d	0.21 (100)	0.28 (83)	—	47	BC	DEF

h, hours; d, days; y, years; EC, electron capture.

A, 4 pi beta counter; B, 4 pi beta-gamma coincidence counter; C, gamma spectrometer; D, gamma ionization chamber; E, well-type scintillation counter; F, absolute beta counting with end window Geiger-Müller counter; G, windowless 2 pi proportional counter; H, X-ray gamma coincidence counter; and I, liquid scintillation.

\*Positron. †Figures in parentheses represent MeV. %.

**Concentration of carrier element**—A knowledge of the actual amount of the carrier in a radioactive solution is necessary to quote the specific activity which is expressed in curies (or its submultiples) per milligram or millimole. The carrier concentration varies widely depending on whether the preparation is carrier-free, or of high or low specific activity. Sodium radioiodide ( $^{131}\text{I}$ ) and orthophosphoric acid ( $^{32}\text{P}$ ) solutions are essentially carrier-free and the concentration of the respective elements are far below the detection level of the most sensitive methods. Nevertheless spot tests are carried out on alumina impregnated (Gopal, N. G. S., unpublished data) or simple Whatman No. 3MM paper<sup>10</sup> (limit of detection 0.025  $\mu\text{g}$ ). High specific activity preparations are analysed by spectrophotometry (Table 3). Low specific activity solutions such as potassium chloride ( $^{42}\text{K}$ ) and sodium chloride ( $^{24}\text{Na}$ ) are estimated by suitable volumetric methods. Table 3 gives an idea of the carrier concentration of a number of typical solutions of medical radioisotopes, their estimation, and some spectrophotometric data.

**Radiochemical purity**—This term, which is not synonymous with chemical purity and radioactive purity, means the absence of other chemical forms of the radio-element than that stated. Different chemical forms can be expected to appear during processing and also as a result of storage. Polyphosphates may appear in orthophosphoric acid as a result of overheating. If elemental iodine were to be trapped in aqueous alkali free of any reducing agents iodate is formed in addition to iodide<sup>19</sup>. Carrier-free sodium iodide  $^{131}\text{I}$  in a solution free of reducing agents undergoes slow oxidation to iodate and iodine<sup>20</sup>. When organic compounds labelled with  $^{131}\text{I}$  are stored over extended periods there is a slow release of free iodide, which process is quickened by increase in  $\text{pH}$ <sup>21</sup>. When labelling a compound with a carrier-free radioisotope to obtain a product of high specific activity, it is likely that the impurities present are also labelled. This will result in a product containing a labelled impurity along with the desired labelled compound as in Rose Bengal (Table 4).

TABLE 3 — CARRIER CONCENTRATION IN RADIOPHARMACEUTICAL SOLUTIONS, THEIR ESTIMATION AND SOME SPECTROMETRIC DATA

Product	Carrier conc.		Method of estimation	$\lambda_{\text{max}}$ $\mu\mu$	1% $E_1$ cm.	Ref.
	Per mC.	Per ml.				
Sodium chloride ( $^{24}\text{Na}$ )	—	9 mg.	Volhard's	—	—	11
Orthophosphoric acid ( $^{32}\text{P}$ )	$\ll 0.1 \mu\text{g}$ . P	$< 1 \mu\text{g}$ . P	Spot test	—	—	*
Potassium chloride ( $^{42}\text{K}$ )	—	$< 40 \text{ mg}$ .	Volhard's	—	—	11
Sodium chromate ( $^{51}\text{Cr}$ )	$\ll 100 \mu\text{g}$ . Cr	$< 100 \mu\text{g}$ . Cr	Spectrophotometry	370 <sup>a</sup> 540 <sup>b</sup>	904 7000	12 13
Vitamin B <sub>12</sub> ( $^{58}\text{Co}$ )	$\ll 0.1 \text{ mg}$ .	—	Microbiological assay <sup>e</sup>	—	—	14
Ferric chloride ( $^{59}\text{Fe}$ )	$< 1 \mu\text{g}$ .	—	Spectrophotometry	504 <sup>d</sup>	1880	14
Sodium iodide ( $^{131}\text{I}$ )	$\ll 0.1 \mu\text{g}$ .	$\ll 1 \mu\text{g}$ .	Spot test	—	—	10
Bromsulphalein ( $^{131}\text{I}$ )	—	—	Spectrophotometry	580 <sup>e</sup>	800	15
Cholografin ( $^{131}\text{I}$ )	—	—	do	238 <sup>f</sup>	400	*
Diodrast ( $^{131}\text{I}$ )	—	—	do	290 <sup>g</sup>	201	†
Evans blue ( $^{131}\text{I}$ )	—	—	do	610 <sup>h</sup>	830	16
Hippuran ( $^{131}\text{I}$ )	—	—	do	445 <sup>i</sup>	212	*
Human serum albumin ( $^{131}\text{I}$ )	$< 20 \text{ mg}$ .	20 mg.	do	280 <sup>h</sup>	5.3	18
Rose Bengal (Merck) ( $^{131}\text{I}$ )	0.23-1.2 mg.	0.56-2.3 mg.	do	540 <sup>i</sup>	350 <sup>k</sup>	*
Rose Bengal extra (BDH) ( $^{131}\text{I}$ )	0.23-1.2 mg.	0.56-2.3 mg.	do	542 <sup>i</sup>	440 <sup>k</sup> (420) <sup>l</sup>	*
Rose Bengal (Kuhlmann) ( $^{131}\text{I}$ )	0.23-1.2 mg.	0.56-2.3 mg.	do	548 <sup>i</sup>	660 <sup>k</sup> (650) <sup>l</sup>	*
Colloidal gold ( $^{198}\text{Au}$ )	50-500 $\mu\text{g}$ .	3.5 mg.	do	530 <sup>m</sup> 315 <sup>n</sup>	254 270	* *

a, at pH 8.0; b, as diphenyl carbazide complex; c, assay organism: *Euglena gracilis* Z-strain; d, as ferrous-phenanthroline complex; e, in 0.05N NaOH; f, in 0.9 per cent NaCl; g, for the diethanolamine salt in water; h, in water; i, in pyridine-benzene sulphonyl chloride-chloroform (5:2:43 vol./vol.) (ref. 17); j, in 0.1M sodium acetate; k, values for raw product; l, values for acid precipitated product; m, 1:200 dilution with 3 per cent gelatin; and n, in 0.1N HCl.

\*Unpublished results from the Isotope Division, A.E.T. †Cohen, Y. & Prapart, P., private communication.

TABLE 4 — ACTIVITY DISTRIBUTION IN THE DIFFERENT COMPONENTS OF ROSE BENGAL LABELLED WITH  $^{131}\text{I}$

(Ascending paper chromatography on Whatman No. 1)

Product	Solvent	Batch No.	Age of solution days	$R_f$ (% of activity)					
				0	0.25	0.4	0.52*	0.62	0.80-0.85†
Rose Bengal ( $^{131}\text{I}$ ) (BDH)	5% ethanol, 0.84M, with reference to ammonia	A	6	—	0.1	0.3	31.8	30.2	14.6
		B	12	—	1.0	2.5	36.8	21.3	14.2
Rose Bengal ( $^{131}\text{I}$ ) (Kuhlmann)	10% ethanol, 0.84M, with reference to ammonia	C	11	1.9	3.2	1.8	55.4	19.3	11.0
		D	12	2.0	1.9	1.4	51.0	21.7	14.8
		E	19	1.8	2.7	1.6	53.4	17.6	19.8

\*Mauve-coloured zone of tetrachloro (P) tetraiodo (R) fluorescein. †Iodide zone.



Hence it is necessary to determine the extent of occurrence of the different species, which is examined by suitable techniques amongst which paper chromatography, paper electrophoresis, and ion-exchange chromatography stand out in their versatility. A summary of the methods used routinely in the laboratory for the control of the proposed solutions of medical radioisotopes is given in Tables 5-7.

**Biological Control**

Some of the processed solutions of the medical radioisotopes are used parenterally. At present, the biological controls carried out on such solutions consist of tests for pyrogens and/or for sterility, and tests for undue toxicity.

Tests for sterility are carried out on one vial by transferring 0.5-1 ml. of the radioactive solution into a tube containing 10 ml. of fluid thioglycollate<sup>34</sup>. These are respectively incubated at 31°C. for 7 days and at 24°C. for 10 days. Absence of any growth in these media indicates that the products are sterile. These tests are carried out either immediately, if the radioactive concentration permits, or after allowing for decay for a suitable period. In the case of the latter, the sterilizing conditions are also tested by autoclaving along with the radioactive parenteral solutions another vial containing an aqueous suspension of a spore bearing organism<sup>35</sup> such as *Bacillus subtilis*<sup>36</sup>. The suspension is later transferred to the two above-mentioned media. Absence

TABLE 5—CONTROL OF RADIOCHEMICAL PURITY—ASCENDING PAPER CHROMATOGRAPHY

Product	Paper	Solvent	Limit of radiochemical impurity	Ref.
Orthophosphoric acid ( <sup>32</sup> P)	A	F, G	<5 per cent non-orthophosphate activity*	—
Chromic phosphate ( <sup>32</sup> P)	A	F, G	<5 per cent orthophosphate activity*	—
Sodium iodide ( <sup>131</sup> I)	A	H	<5 per cent non-iodide activity	23
Diodone ( <sup>131</sup> I)	C or D	I	<5 per cent free-iodide activity*	24
Oleic acid ( <sup>131</sup> I)	E	J	<5 per cent free-iodide activity*	†
Rose Bengal ( <sup>131</sup> I)	C or D	I	<5 per cent free-iodide activity*	24
Rose Bengal ( <sup>131</sup> I)	A	K	For non-Rose Bengal components	†
Thyroxine ( <sup>131</sup> I)	C or D	I	<5 per cent free-iodide activity*	24
Thyroxine ( <sup>131</sup> I)	A	L	For other active thyronines	26
Triolein ( <sup>131</sup> I)	E	J	<5 per cent free-iodide activity*	†
Colloidal gold ( <sup>198</sup> Au)	A	M	<5 per cent free-gold activity*	28
Neohydrin ( <sup>203</sup> Hg)	B	N	For non-neohydrin components	†

Papers: A, Whatman No. 1; B, Whatman No. 3MM; C, Whatman No. AE30; D, Whatman No. DE20; E, S & S 2040, impregnated with silver chloride.

Solvents: F, isopropanol 75 ml., water 24.7 ml., trichloroacetic acid 5 g., 10 per cent ammonia 0.6 ml., pH 1.5-2 (ref. 22); G, absolute ethanol 30 ml., n-propanol 30 ml., water 37.5 ml., 10 per cent ammonia 2.5 ml. (ref. 22); H, methanol : water = 3 : 1; I, aqueous sodium citrate (0.25M); J, benzene : chloroform = 1 : 2 (ref. 25); K, aqueous sodium citrate, 2.5 per cent, with sodium hydroxide to adjust to pH 9-10; L, tert-amyl alcohol-2N ammonia (1:1); M, acetone 70 ml., water 20 ml., conc. HCl (sp. gr. 1.19) 10 ml. (ref. 27); and N, n-butanol-glacial acetic acid-water = 4 : 1 : 5 (ref. 29).

\*Tentative limits. †Unpublished data from the authors' laboratory (Isotope Division, AEET).

TABLE 6—CONTROL OF RADIOCHEMICAL PURITY—PAPER ELECTROPHORESIS

(Potential gradient: 8 V./cm.)

Product	Paper	Electrolyte	R <sub>m</sub>	Limit of radiochemical impurity	Ref.
Sodium chromate ( <sup>51</sup> Cr)	E	F	Cr(VI) 1, Cr(III) 0	<5 per cent Cr(III)	†
Chromic chloride ( <sup>51</sup> Cr)	E	F	do	<5 per cent Cr(VI)	†
Vitamin B <sub>12</sub> ( <sup>60</sup> Co)	B	H	Co(II) 1, B <sub>12</sub> 0	<5 per cent Co(II)	†
Sodium iodide ( <sup>131</sup> I)	B	G	I-1, IO <sub>3</sub> 0.7	<5 per cent non-iodide activity	†
Bromsulphalein ( <sup>131</sup> I)	B	G	I-1, BSI <sup>3</sup> 0.35	<5 per cent free-iodide activity	†
Cholografin ( <sup>131</sup> I)	B	G	I-1, Cholografin 0	do	†
Diodone ( <sup>131</sup> I)	A, D	{ I } { I-1, Diodone 0.35, 0.11*		do	24
Evans blue ( <sup>131</sup> I)	B	{ G } { I-1, Evans blue 0.05, 0.58*, 0.67*		do	†
Hippuran ( <sup>131</sup> I)	B	G	I-1, Hippuran 0.31	do	†
Oleic acid ( <sup>131</sup> I)	B	G	I-1, Oleic acid 0	do	†
Rose Bengal ( <sup>131</sup> I)	B	G	I-1, Rose Bengal 0	do	†
Rose Bengal ( <sup>131</sup> I)	A	I	I-1, Rose Bengal 0	do	24
Rose Bengal ( <sup>131</sup> I)	C or D	I	I-1, Rose Bengal 0	do	24
Human serum albumin ( <sup>131</sup> I)	†	B	G	I-1, Albumin 0	†
Thyroxine ( <sup>131</sup> I)	A, C or D	I	I-1, Thyroxine 0	do	24
Triolein ( <sup>131</sup> I)	B	G	I-1, Triolein 0	do	†
Colloidal gold ( <sup>198</sup> Au)	B	J	Au(III) 1, Au(0) 0	<5 per cent Au(III)	30
Neohydrin ( <sup>197</sup> Hg)	B	K	Hg(II) 1, Neohydrin 0.52	<5 per cent Hg(II)	†
Neohydrin ( <sup>203</sup> Hg)					

A, Whatman No. 1; B, Whatman No. 540; C, Whatman No. AE30; D, Whatman No. DE20; E, Glass fibre paper; F, 0.05M Na<sub>2</sub>HPO<sub>4</sub>, pH 9.0; G, 0.05M Na<sub>2</sub>HPO<sub>4</sub>-NaH<sub>2</sub>PO<sub>4</sub>, pH 6.5; H, 3N acetic acid; I, 0.025M sodium citrate; J, 0.075M Na<sub>2</sub>S<sub>2</sub>O<sub>5</sub>; and K, 0.1M NaCl.

\*Minor component. †Unpublished data from the authors' laboratory (Isotope Division, AEET).



TABLE 7 — CONTROL OF RADIOCHEMICAL PURITY — MISCELLANEOUS METHODS

Product	Method	Limit of radiochemical impurity	Ref.
Sodium chromate ( <sup>51</sup> Cr)	Chromatography on de-acidite FF (or its equivalent amberlite IRA-400 or Dowex-1)	<10 per cent Cr(III)	12
Vitamin B <sub>12</sub> ( <sup>58</sup> Co)	Chromatography on DEAE-cellulose (OH <sup>-</sup> ) and CM-cellulose (H <sup>+</sup> )	<10 per cent non-vitamin B <sub>12</sub> activity	31
do	Reverse isotope dilution analysis	do	32
do	Countercurrent distribution	do	33

TABLE 8 -- DOSES OF PROCESSED SOLUTIONS OF MEDICAL RADIOISOTOPES FOR PYROGEN TESTS

Product	Dose	Ref.
Gold colloid ( <sup>198</sup> Au)	A quantity equivalent to 10 mC. at the date and hour stated on the label and allowing the radioactivity to decay to not more than 100 μC. before injection	38
Sodium chloride ( <sup>24</sup> Na)	The radioactive concentration is allowed to fall to 100 μC./ml. and a quantity equivalent to 1 mC. at the date and hour stated on the label is injected into each rabbit*	—
Potassium chloride ( <sup>42</sup> K)	Same as above except that it is diluted with pyrogen-free normal saline to 0.3 per cent KCl concentration before injection*	—
Human serum albumin ( <sup>131</sup> I)	A quantity corresponding to not less than 10 μC. at the date and hour stated on the label per kg. of the rabbits' weight†. The quantity of solution required is diluted to 2 ml. with pyrogen-free normal saline before injection	39
Other <sup>131</sup> I labelled compounds and neohydrin labelled with <sup>197</sup> Hg(m) + <sup>197</sup> Hg or <sup>203</sup> Hg	do	—

\*Tentatively adopted doses.

†On a body weight basis this dose is 10 times proportionate to the single human dose recommended (50 μC.).

of growth in the media indicates that the sterilizing conditions are satisfactory, and that the radioactive solution can be assumed to be sterile. It must be noted, however, that on account of the short half-life of many of the radioisotopes and the need to utilize the products at a reasonably high specific activity, it is not always possible to await the final results of the sterility tests.

According to the *Drug Rules*, 1945 (ref. 37), pyrogen tests are to be carried out on solutions of substances administered parenterally in a volume of 10 ml. or more at a time. As it has already been pointed out the radiopharmaceuticals are employed mostly in small volumes (about 1 ml.) and very rarely exceeding 5 ml. Even so, as a measure of precaution pyrogen tests are carried out on a number of these products and the doses in which they are injected into the animals are given in Table 8. The products are considered to be free from pyrogens, if the total rise in temperature of 3 rabbits is less than 1.15°C. (ref. 40). The animals are not used over and over again since the radiotoxicity of the preparations may interfere with the test. They are normally allowed a rest period of 4-5 weeks between two successive tests. The problem is, however, under study.

Tests for undue toxicity<sup>41</sup> are carried out by injecting an aliquot (which is several times proportionate to the single human dose) of the stock solution into each of five mice, each weighing 20 g. If none of the mice dies within 24 hr, the products are considered safe for human use.

### Summary

Radiopharmaceutical preparations differ from the conventional pharmaceuticals, in that they

are radioactive. They require special methods of quality control which can be considered under three groups — physical, chemical and biological. The radioisotopes are identified as well as assayed by the radiations they emit. To guarantee the medical user a meaningful use of the radioisotopes, they are invariably checked for their radiochemical purity. Tests for pyrogens and for undue toxicity can be sometimes completed before their release. But results of tests for sterility are known only seven days after supply.

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## Recent Chemistry of Cyclobutadienes

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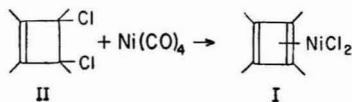
IN the quest for novel rings and highly strained molecules, cyclobutadiene occupies a prominent position and its history goes back at least six decades when the initial explorations to synthesize this molecule were made<sup>1,2</sup>. Earlier molecular orbital calculations which predicted unstable ground state triplet with zero delocalization energy provided considerable stimulus for synthetic effort on such derivatives<sup>3,4</sup>. Initial investigations to isolate cyclobutadiene derivatives proved anything but rewarding until a fresh approach to this problem was advanced by Longuet-Higgins and Orgel<sup>5</sup> who predicted the possibility of stabilization of cyclobutadiene through complexing with transition metals. Since then there has been tremendous activity in this direction which culminated recently in the synthesis of cyclobutadiene itself<sup>6</sup>. In view of the fact that summaries<sup>7-11</sup> of the earlier work in this area are available, only the highlights of this struggle and achievement are incorporated in the present survey. Benzocyclobutadienes and diphenylenes are not included in this article.

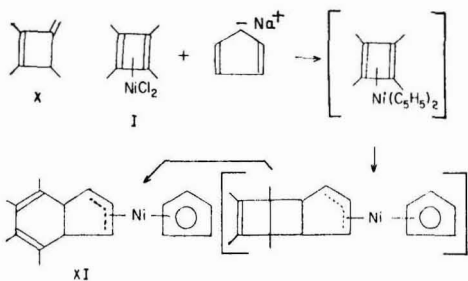
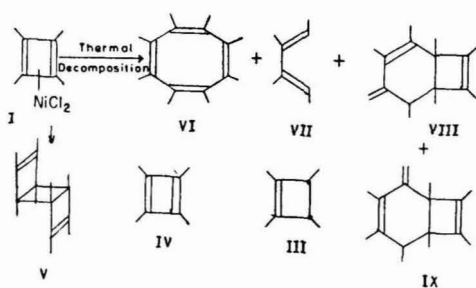
### Tetramethylcyclobutadiene Intermediates

Creige and Schröder<sup>12</sup> isolated the purple complex (I) by treating dichlorotetramethylcyclobutene (II) with nickel carbonyl. In the NMR spectrum, the complex (I) exhibited a singlet indicating the

equivalence of all the four methyl groups. On the basis of X-ray analysis, the structure (I) was conclusively established for the complex with the nickel atom situated above the centre of the four-membered ring<sup>13,14</sup>. Catalytic hydrogenation of the complex (I) yielded predominantly tetramethylcyclobutene (III). Attempts to liberate free tetramethylcyclobutadiene (IV) resulted only in dimerization<sup>9</sup>. The complex (I) on refluxing in water or in ethylene glycol<sup>9</sup> furnished *anti*-dimer (V) whereas thermal decomposition<sup>9</sup> *in vacuo* at 190°C. yielded octamethylcyclooctatetraene (VI), tetramethylbutadiene (VII), and a liquid dimer which may be a mixture of two hydrocarbons (VIII) and (IX).

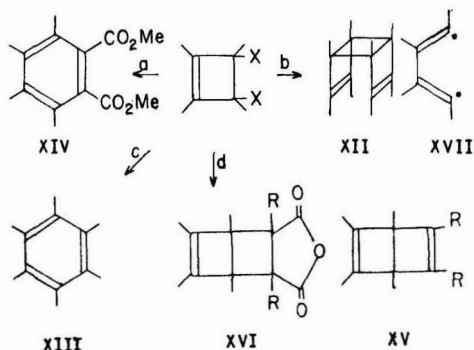
Triphenyl phosphine and phenanthroline add readily to the complex (I) forming weak bonds<sup>9</sup>. The phenanthroline complex on decomposition furnished a mixture of bicyclic derivatives (VIII) and (IX), methylenetetramethylcyclobutene (X) and the *anti*-dimer (V). Cyclopentadienyl sodium replaced the chlorine atoms in the complex (I) producing a red crystalline  $\pi$ -allyl- $\pi$ -cyclopentadienyl complex<sup>9</sup> (XI).





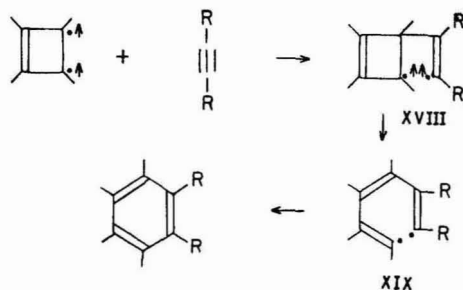
Employing dihalotetramethylcyclobutenes, several attempts have been made to liberate the corresponding cyclobutadiene (IV). On treating dichlorotetramethylcyclobutene (II) with sodium amalgam, the *syn*-dimer (XII) was obtained while with 2-butyne and acetylenedicarboxylate, hexamethylbenzene (XIII) and tetramethylphthalic ester (XIV) were isolated respectively<sup>15</sup> which can be formed either through Dewar benzene derivatives (XV, R = CH<sub>3</sub> or CO<sub>2</sub>CH<sub>3</sub>) or by direct addition to butadiene diradicals (XVII). Diiodotetramethylcyclobutene on shaking with silver or mercury in the presence of maleic anhydride and bromomaleic anhydride yielded the adducts (XVI) (R = H) and (XVI) (R = Br) respectively<sup>9,16</sup>.

It was suggested recently by van Tamelen<sup>17</sup> that Dewar benzene derivatives (XV) need not be the intermediates during the aforementioned trapping experiments since the incipient cyclobutadiene which



Reagents:

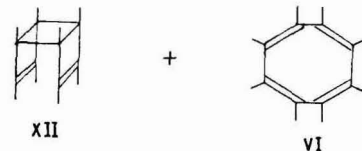
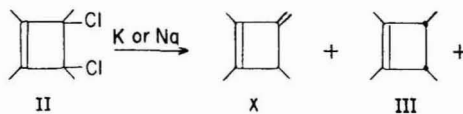
- (a) Zn-dimethyl acetylenedicarboxylate; (b) Na amalgam;  
(c) Zn-2-butyne; (d) Hg or Ag



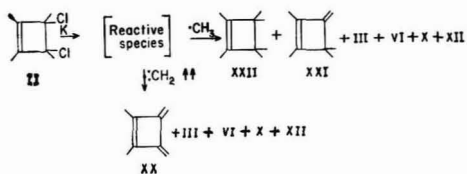
was supposed to exist as a ground state triplet could not directly produce the singlet Dewar benzene derivative and the energetic triplet Dewar benzene derivative if formed would undergo direct conversion to the product without the intermediacy of the ground state derivative. Furthermore, after the primary addition stage, the intermediate (XVIII) might undergo conversion to the open-chain diradical (XIX) and consequently it would not be essential to assume Dewar benzene intermediates<sup>17</sup> (XV).

Although it is probable that Dewar benzene derivatives are not intermediates in these reactions, van Tamelen's argument<sup>17</sup> is not germane to the situation since it depends on the assumption that cyclobutadiene exists in the ground state triplet contrary to the evidence recently obtained for the singlet ground state of cyclobutadiene (*vide infra*).

Skell and Petersen<sup>18</sup> treated dichlorotetramethylcyclobutene (II) with sodium or potassium vapour at 245-55°C. under a helium atmosphere and obtained the *syn*-dimer (XII), octamethylcyclooctatetraene (VI), 1-methylene-2,3,4-trimethylcyclobutene (X) and *cis*-tetramethylcyclobutene (III).



Disproportionation reaction of two triplet tetramethylcyclobutadiene molecules generated in the gas phase was thought to give rise to the methylenecyclobutene (X) whereas coupling reaction to the *syn*-dimer (XII). When a mixture of dichlorobutene (II) and dibromomethane was reacted with potassium vapour to study the interaction of the triplet methylene with the reactive intermediate, the major product was 1,2-dimethylene-3,4-dimethylcyclobutene (XX), the minor products being (XII), (VI), (X) and (III). In the presence of methyl radicals

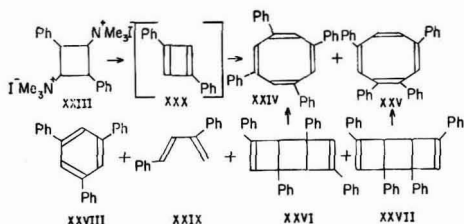


produced by interaction of methyl bromide with metal vapour, the reactive species furnished (XII), (VI), (X), (III), hexamethylcyclobutene (XXII) and 1-methylene-2,2,3,4-tetramethylcyclobutane (XXI).

From these data it was concluded that free tetramethylcyclobutadiene is liberated, and it should exist as a ground state triplet<sup>18</sup>. In view of the experimental conditions employed during these reactions, doubt was expressed as to the validity of this conclusion<sup>19</sup>.

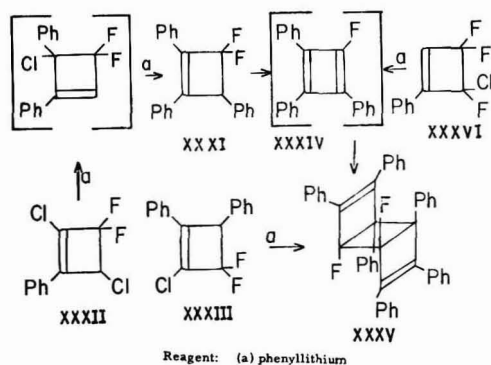
### 1,3-Diphenylcyclobutadiene Intermediates

White and Dunathan<sup>20</sup> reacted 1,3-diphenyl-2,4-bis(dimethylamino)-cyclobutane dimethiodide (XXIII) with potassium *tert*-butoxide in *tert*-butanol and isolated cyclooctatetraene derivatives (XXIV) and (XXV) among other products. In the presence of lithium diethylamide, the labile tricyclobutadiene intermediates (XXVI) and (XXVII) could be isolated which underwent isomerization to (XXIV) and (XXV) respectively. This sequence involves ephemeral diphenylcyclobutadiene (XXX) intermediate which undergoes spontaneous dimerization.

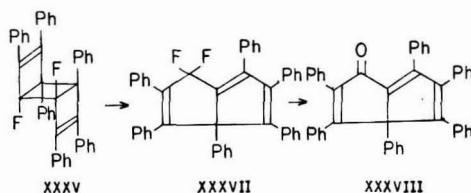


### Triphenylfluorocyclobutadiene Intermediates

The dimer (XXXV) was obtained via transient triphenylfluorocyclobutadiene (XXXIV) by treating 1,1-difluoro-2,4-dichloro-3-phenylcyclobutene (XXXII) with phenyl lithium or during related reactions<sup>21</sup>.



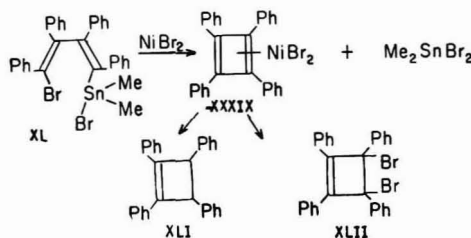
The dimer (XXXV) has a Raman band at 1656  $\text{cm}^{-1}$  and the ultraviolet maxima at 288 and 227  $\text{m}\mu$ . The PMR spectrum indicated a single resonance due to phenyl protons, and the fluorine spectrum exhibited a single peak. The dipole moment of the dimer in benzene was found to be  $2.15 \pm 0.08D$  quite in agreement with calculated values (1.56 and 2.2D). X-ray analysis had established conclusively the *anti*-tricyclo structure (XXXV) for the dimer<sup>22</sup>. On brief heating at 210-15°C., the dimer (XXXV) yielded a yellow solid which was tentatively assigned the structure (XXXVII). The fluorine spectrum of (XXXVII) indicated nonequivalence of the two fluorine atoms with  $J = 250$  c.p.s. Hydrolysis of (XXXVII) with sulphuric acid furnished a cyclopentenone (XXXVIII) as evidenced by an infrared band at 1710  $\text{cm}^{-1}$ .

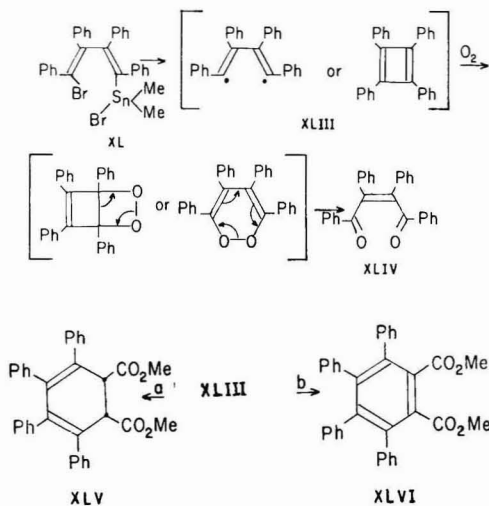


### Tetraphenylcyclobutadiene Intermediates

Freedman<sup>23,24</sup> obtained tetraphenylcyclobutadiene-nickel bromide complex (XXXIX) by heating 4-bromo-1,2,3,4-tetraphenyl-*cis,cis*-1,3-butadienyl dimethyl-tin bromide (XL) with nickel bromide suspension in triglyme. Mass spectral investigation of this complex (XXXIX) by Sharvit and Mandelbaum<sup>25</sup> revealed three major peaks at  $m/e$  712, 356 and 178 which correspond to dimeric tetraphenylcyclobutadiene, tetraphenylcyclobutadiene and a fragmentation product. Catalytic hydrogenation of the complex (XXXIX) afforded 1,2,3,4-tetraphenylcyclobutene<sup>23</sup> (XLI). In the presence of anhydrous pyridinium hydrobromide perbromide in methylene chloride, the complex (XXXIX) furnished the dibromobutene<sup>26,27</sup> (XLII). When the dibromide (XL) is decomposed in solution under oxygen atmosphere, *cis*-dibenzoylstilbene (XLIV) was isolated through the intermediate (XLIII) which also reacts with several dienophiles<sup>28</sup>. Thus, with dimethyl maleate and acetylenedicarboxylate, *cis*-dihydrophthalic ester (XLV) and 3,4,5,6-tetraphenylphthalate (XLVI) were formed respectively<sup>28</sup>.

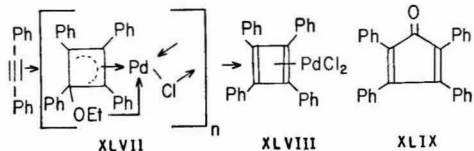
Diphenylacetylene either with palladium chloride<sup>29,30</sup> or bis(benzonitrile) palladium chloride<sup>31</sup> or sodium or ammonium chloropalladite<sup>32</sup> afforded a





Reagents: (a) dimethyl maleate; (b) dimethyl acetylenedicarboxylate

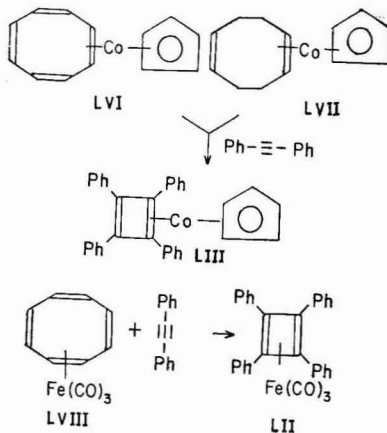
yellow complex<sup>33-35</sup> (XLVII) which on treatment with hydrogen chloride in ethanolic chloroform solution led to orange red tetraphenylcyclobutadiene-palladium chloride complex<sup>36,37</sup> (XLVIII). In



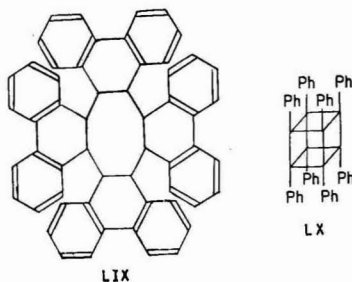
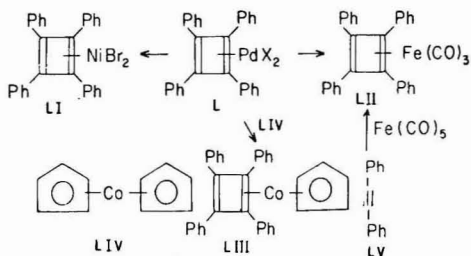
the mass spectrum (185°C.) of the palladium chloride complex (XLVIII) intense peaks at *m/e* 356 and 176 are present which correspond to tetraphenylcyclobutadiene (XLIII) and a decomposition product<sup>38</sup>. Similar peaks were also observed during the electron impact of tetracyclone (XLIX) at 300°C. which can liberate tetraphenylcyclobutadiene or the corresponding diradical (XLIII) with loss of carbon monoxide<sup>39</sup>. Maitlis and Games<sup>40</sup> have treated the palladium bromide complex (L, X = Br) with nickel tetracarbonyl and iron pentacarbonyl and obtained tetraphenylcyclobutadiene-nickel complex (LI) and tetraphenylcyclobutadiene-iron tricarbonyl (LII) which had been previously isolated during the reaction of diphenylacetylene with iron carbonyl<sup>41,42</sup>. Iron carbonyl pulls the loosely bound

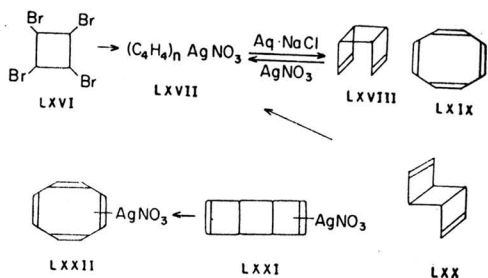
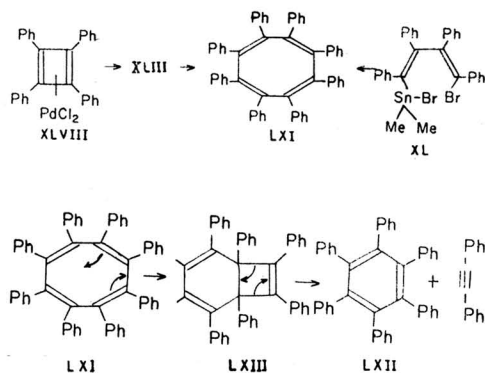
halogen atoms from the complex (L) leaving behind the free cyclobutadiene which on further reaction with metal carbonyl leads to the product<sup>40</sup> (LII).

Cobaltocene (LIV) on reaction with the complex (L) furnished the ligand transferred complex<sup>40,43,44</sup> (LIII). Molybdenum and tungsten carbonyl complexes of cyclobutadiene were isolated in similar reactions<sup>45-50</sup>. Nakamura and Hagihara<sup>44,51</sup> obtained the complex (LIII) from cyclopentadienyl cobalt cyclooctatetraene (LVI) or cycloocta-1,5-diene complex (LVII) and diphenyl acetylene. The iron complex of cyclooctatetraene (LVIII) on heating with diphenyl acetylene at 190°C. led to the iron complex<sup>44</sup> of tetraphenylcyclobutadiene (LII).



Maitlis and Stone<sup>52</sup> as well as Cookson and Jones<sup>53</sup> obtained on treatment of the complex (XLVIII) with tertiary phosphine or pyrolysis a high melting dimer (m.p. 430°C.) which was first isolated by Freedman<sup>23</sup> by heating 4-bromo-1,2,3,4-tetraphenyl-*cis,cis*-1,3-butadienyl dimethyl-tin bromide (XL) at 150°C. and subsequently in several other reactions<sup>54-57</sup>. Earlier assignments of octaphenylcubane<sup>58</sup> (LX) or tetrabiphenylcyclooctane (LIX) structure<sup>53</sup> for this dimer were abandoned in favour of octaphenylcyclooctatetrene (LXI) on the basis of oxidation<sup>56,59</sup> and pyrolysis experiments<sup>38</sup> and conclusively through X-ray analysis<sup>59-61</sup>. Pyrolysis of the dimer (LXI) afforded diphenylacetylene and hexaphenylbenzene (LXII) probably through valency tautomerization to the bicycloderivative (LXIII) followed by cleavage<sup>38</sup>. Oxidation of the dimer

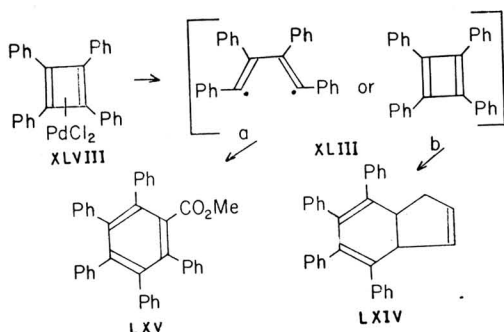




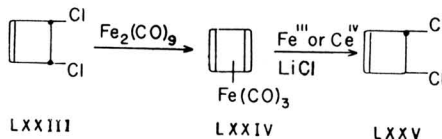
(LXI) with chromic acid furnished benzoic acid<sup>59</sup>, and *p*-nitrobenzoic acid with nitric acid<sup>56</sup>. The dimer (LXI) exhibited  $\lambda_{max}$  at 267 m $\mu$  and showed no  $-C=C-$  Raman band at a frequency higher than phenyl absorption (1605  $cm^{-1}$ ). Possibly the olefinic absorption in the Raman spectrum was concealed under the phenyl bands<sup>38</sup>. In the mass spectrum peak at *m/e* 712 corresponding to  $C_{56}H_{40}$  was observed<sup>38,59,62</sup>. The green solution produced by reaction of the palladium chloride complex (XLVIII) with tertiary phosphine in chloroform or benzene gave a strong ESR spectrum indicating the presence of paramagnetic species<sup>33</sup>. Similar coloured solutions were also observed during the decomposition of butadiene-tin bromide<sup>29</sup> (XL). When the complex (XLVIII) was decomposed<sup>33</sup> with triphenylphosphine in the presence of cyclopentadiene, the high melting dimer (LXI) was accompanied by the formation of the adduct (LXIV). Similar interception<sup>33</sup> of the intermediate (XLIII) with methyl phenylacetylenecarboxylate led to pentaphenylbenzoate (LXV).

presence of aqueous sodium chloride solution, the complex decomposed to *syn*-tricyclooctadiene (LXVIII) and cyclooctatetraene (LXIX). *syn*- and *anti*-tricyclooctadiene (LXVIII and LXX) yielded the same complex (LXVII, *n* = 1) on treatment with silver nitrate solution<sup>64</sup>. Recent NMR studies revealed<sup>65,66</sup> that the isolated complex (LXVII, *n* = 1) is not a monomer but should be best represented as a dimer (LXXI). The complex in a saturated solution of silver perchlorate in heavy water gave resonances at  $\tau$  2.74 and 5.83 which after a few hours disappeared and were replaced by a singlet at  $\tau$  2.9. *syn*-Tricyclooctadiene (LXVIII) showed in the NMR spectrum two peaks at  $\tau$  3.8 and 6.5 which were shifted to lower field in the complex (LXXI). The singlet at  $\tau$  2.9 observed<sup>65,66</sup> on standing may be due to slow decomposition of tricyclooctadiene complex (LXXI) to the cyclooctatetraene complex (LXXII). In fact, cyclooctatetraene (LXIX) with silver perchlorate in heavy water exhibited similar NMR behaviour and when small quantities of cyclooctatetraene (LXIX) was added to the solution of the decomposed *syn*-tricyclooctadiene complex (LXXI), only a single resonance at  $\tau$  2.9 appeared<sup>65</sup>.

The first cyclobutadiene complex of iron (LXXIV) was obtained by Emerson *et al.*<sup>67</sup> by the interaction of iron ennacarbonyl with *cis*-3,4-dichlorocyclobutene (LXXIII). It exhibited single resonance at  $\tau$  6.09 in the NMR spectrum<sup>67,68</sup> and had the infrared bands at 1985 and 2055  $cm^{-1}$ . In the mass



Reagents: (a) methyl phenylacetylenecarboxylate; (b) cyclopentadiene

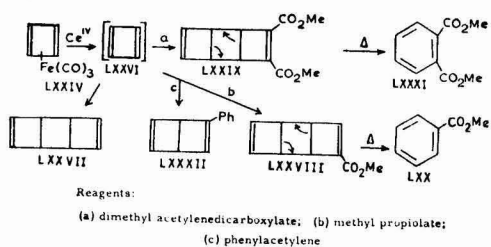


spectrum the parent peak at *m/e* 192 was observed and also peaks at *m/e* 164, 136 and 108 indicating the successive loss of carbonyl groups attached to iron<sup>67</sup>. In the presence of ferric chloride or ceric ammonium nitrate, an acetone solution of the complex (LXXIV) saturated with lithium chloride led to *trans*-3,4-dichlorocyclobutene<sup>67</sup> (LXXV). Decomposition of the complex (LXXIV) with ceric ammonium nitrate liberated free cyclobutadiene (LXXVI) which dimerized spontaneously in the absence of trapping agents to *syn*- and *anti*-tricyclooctadiene (LXXVII) in a 5:1 ratio but yielded Dewar benzene products in the presence of acetylenic

### Cyclobutadiene

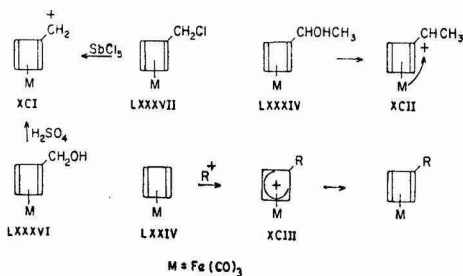
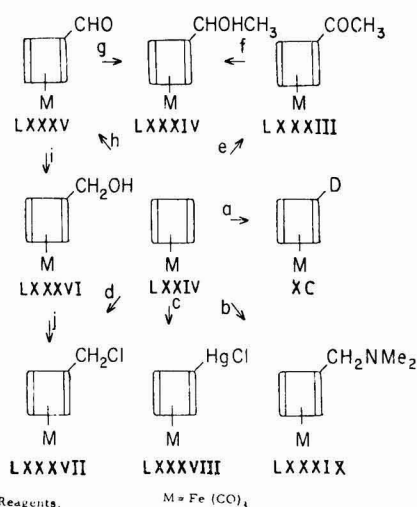
It was earlier reported<sup>63</sup> that through the action of lithium amalgam on 1,2,3,4-tetrabromocyclobutane (LXVI) followed by silver nitrate, a complex could be isolated which was assigned the monomeric structure (LXVII, *n* = 1). Subsequently, analogous palladium chloride, silver perchlorate and silver borofluoride complexes were isolated<sup>64</sup>. In the





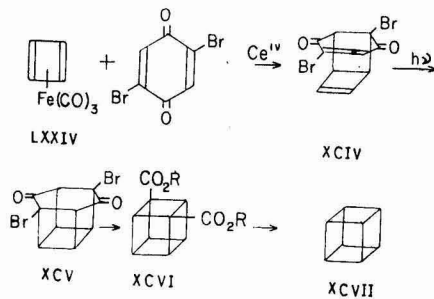
derivatives<sup>6</sup>. Thus, methyl propiolate and dimethyl acetylenedicarboxylate yielded (LXXVIII) and (LXXIX) which on pyrolysis gave the corresponding esters (LXXX) and (LXXXI) respectively<sup>6</sup>. Hemi-Dewar biphenyl (LXXXII) was formed during the decomposition of the complex (LXXIV) in the presence of phenyl acetylene<sup>69</sup>. The gases which were liberated from the decomposition of the complex (LXXIV) yielded methyl benzoate when heated with methyl propiolate proving conclusively the existence of free cyclobutadiene with a finite lifetime<sup>6</sup>.

The complex (LXXIV) is an aromatic system similar to ferrocene and undergoes a variety of electrophilic reactions<sup>70</sup>. Thus, with acetyl chloride and benzoyl chloride in the presence of aluminium chloride, the acetyl (LXXXIII) and benzoyl complexes were formed<sup>70</sup>. The acetyl complex (LXXXIII) on reduction gave an alcohol (LXXXIV) which was found to be identical with the product obtained on treating the formyl complex (LXXXV) with methylmagnesium bromide<sup>70</sup>. In the presence of formaldehyde and dimethyl amine, the dimethyl-amino complex (LXXXIX) was obtained and treatment with mercuric acetate and sodium chloride furnished the chloromercuri analogue<sup>70</sup> (LXXXVIII). Reaction with formaldehyde and hydrogen chloride led to the chloromethyl derivative (LXXXVII)



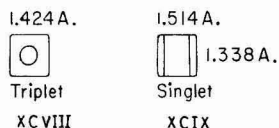
which was also obtained on reduction of the complex (LXXXV) with sodium borohydride followed by reaction with hydrogen chloride<sup>70</sup>. The chloromethyl complex (LXXXVII) on treatment with antimony pentachloride yielded hexachloroantimonate salt<sup>71</sup> (XCI). Similar cations (XCI) and (XCII) were also produced in sulphuric acid solution of the complexes (LXXXVI) and (LXXXIV). With trifluoroacetic acid, a deuterium atom was rapidly incorporated into the complex<sup>70</sup> (LXXIV). The electrophilic character of the complex (LXXIV) is probably due to the energetically economic process available through the intermediacy of the highly stable  $\pi$ -allyl-iron tricarbonyl cationic complex (XCIII) formed initially by the addition of electrophilic species R (ref. 70).

An interesting synthesis of cubane (XCVII) was effected from the *endo*-adduct (XCIV) obtained on decomposition of the complex (LXXIV) in the presence of 2,5-dibromobenzoquinone<sup>72</sup>.



### Ground State of Cyclobutadiene

A triplet ground state was predicted by several workers<sup>73-81</sup> for cyclobutadiene. On the other hand, SCF-MO (self-consistent field molecular orbital) calculations<sup>82,83</sup> recently made by Dewar and Gleicher<sup>84</sup> suggested that free cyclobutadiene should be more stable in the singlet state rather than in the triplet. A square geometry was indicated for the triplet cyclobutadiene (XCVIII) in the complexes and a rectangular shape with pure single and double bonds for the singlet (XCIX) in the free state<sup>84</sup>.

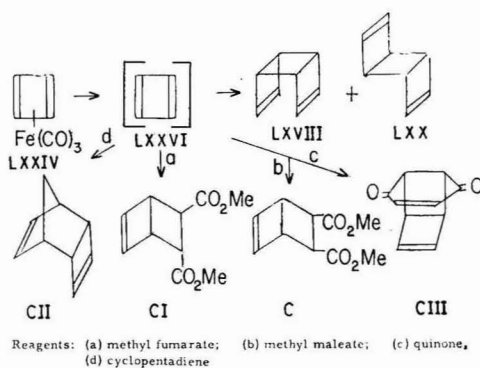




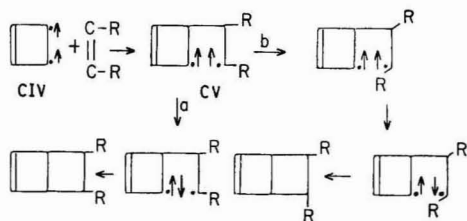
X-ray analysis of tetramethylcyclobutadiene-nickel chloride complex<sup>13,14</sup> (I) and tetraphenylcyclobutadiene-iron carbonyl complex<sup>42</sup> (LII) had indeed provided evidence for the square planar configuration of the cyclobutadiene moiety of the complexes. The calculated resonance energy is 0.8 kcal. and consequently it should, as observed, behave as a strained cyclic polyene for addition reactions<sup>84</sup>.

The earlier conclusions<sup>18</sup> that tetramethylcyclobutadiene should exist as a ground state triplet has been questioned since it is not certain whether free tetramethylcyclobutadiene is involved in the observed reactions<sup>19</sup>.

On decomposition of the iron complex of cyclobutadiene (LXXIV) by ceric ions with dimethyl maleate present in the reaction mixture, *endo*, *cis*-dicarbomethoxybicyclohexene (C) was obtained while in the presence of dimethyl fumarate, *trans*-dicarbomethoxybicyclohexene (CI) was formed<sup>19</sup>. Cyclopentadiene and quinone in similar experiments furnished only the *endo* adducts<sup>19</sup> (CII) and (CIII). When the liberated cyclobutadiene was allowed to dimerize *syn*- and *anti*-bicyclooctadienes (LXVIII) and (LXX) were formed in a 5:1 ratio<sup>19</sup>. The stereospecificity observed during these additions led Watts *et al.*<sup>19</sup> to assign ground singlet state for cyclobutadiene.



Although the singlet ground electronic state for free cyclobutadiene appears highly probable, the triplet form cannot be rigorously excluded from the present evidence. The observed stereospecificity during the addition reactions of cyclobutadiene is possible even in the case of triplet cyclobutadiene (CIV) if the rate of inversion of electron spin and bond formation is faster than rotation about the single bond in the diradical intermediate (CV) (path *a*)<sup>85-91</sup>.



## Summary

Earlier attempts to liberate cyclobutadiene derivatives from the metal complexes or otherwise resulted in dimerizations and side reactions of the corresponding cyclobutadiene intermediates. The synthesis of cyclobutadiene was finally accomplished through the isolation of the first iron-carbonyl complex of cyclobutadiene in 1965. Since then a gamut of reactions has been performed on free cyclobutadiene as well as the metal complexes and attractive routes have become available for the synthesis of molecules like Dewar benzene and cubane. The stereospecificity observed during the addition reactions of cyclobutadiene appears to indicate a singlet ground electronic state for it in concurrence with the conclusions reached through the recent SCF-MO calculations. The foregoing aspects of cyclobutadiene chemistry have been critically presented. In future, alternative routes to the synthesis of cyclobutenes may be forthcoming and this might open expedient routes to the synthesis of certain organic molecules with a sophisticated array.

## Acknowledgement

It is a pleasure to thank Prof. R. C. Cookson (Southampton, England) and Dr H. J. Ringold (Shrewsbury, Mass., USA) for helpful comments on the manuscript. Part of this article was written during a period of support by the American Cancer Society Grant T-185.

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# Scientific Research in India: An Analysis of Publications

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TO formulate or implement any programme in scientific and technological research and development, it is necessary to have sufficient data on resources in personnel, equipment, etc. Some surveys on the allocation of resources by different agencies in this field were conducted<sup>1,2</sup>. A beginning has also been made to survey research activity in specific fields as indicated by the research publications in the country<sup>3,4</sup>.

Scientific research is not like any produce from an industrial enterprise. Some areas of it defy any technique of evaluation, quantitative or qualitative. Publications are not the ends of research. However, the number of innovations developed by research efforts has to be related to the allotment of resources in men and materials. When research was merely an academic pursuit of a few men and women in universities, evaluations were not attempted. But in recent decades scientific and technological research has become part of industrial programme and the flow of funds has been ever increasing. A major part of the funds allotted is spent in applied research which aims at the development of new processes to reduce the costs or improve the quality of products already in production or create new devices which can replace the old with added advantage and help economic growth. Scientific research, unlike in the past, has become a social and economic necessity. Under these conditions evaluation of research activity becomes as much a necessity as in any other field of social activity.

Investments in scientific and technological research have to stand tests that are used in other fields of investment. It has been found so in several other countries. The investments in this social activity have been increasing since 1947. As shown in a report<sup>2</sup> the annual investments in India increased from Rs 55.75 millions in 1951 to 262.73 millions in 1959 and 840.65 millions in 1966. It is natural and reasonable to study the outcome of such increasing investments.

There are several studies made about the activities of individual organizations such as CSIR, ICAR and ICMR by Reviewing Committees and they made suggestions to improve the effectiveness of investments. It is felt, however, that if material necessary for such evaluations is prepared periodically on several aspects of scientific and industrial research, it should be possible for the Reviewing Committees or policy making bodies to analyse the existing conditions objectively and make more concrete suggestions to increase the effectiveness of scientific and industrial research. Publication of papers in technical journals is only one of the several activities of research workers, though it is a major output of those working in universities. Due to the lack of effective coordination, the research workers in other laboratories too themselves choose

the topics for investigation which tends to make publication of papers a major activity.

In recent years some studies have been carried out on the publications in technical journals. Price<sup>5</sup> and Shockley<sup>6</sup> used such analysis to study the dynamics of research activity. They are meant to understand the growth and working patterns of science and technology revealing the exponential growth, functioning of invisible colleges, etc. Such studies provide guidance in formulating policies as indicated by the measures recommended by the Council for Scientific Policy<sup>7</sup>, UK, to avoid 'catastrophic perturbations'.

In this study an attempt has been made to get the overall activity in research as indicated by publications in technical journals. The survey is confined to all the publications released in one year as abstracted in the *Indian Science Abstracts*. One year may not be a sufficiently representative period for a particular group of scientists or a particular institution, but for a country with several hundred laboratories and thousands of workers the fluctuation from one year to another, excluding regular changes, may not be significant. In a narrowly specialized branch the number in a particular year may show a significant variation if there are special conferences or symposia conducted. The number of papers alone is never a complete measure of the significance of research activity. It is necessary to evolve a method of reviewing research activity by studying thoroughly the papers in each specialized field. This study brings out the institutions where activity in research publication is considerable in any discipline of science and technology. This in turn may help to know our technical personnel resources, so that specific problems in those fields may be entrusted to the groups in the respective laboratories. Specialists are aware where researches in their fields are carried out actively, but scientist-administrators with responsibilities in broader fields have to depend upon personal knowledge or some ad hoc reports. Such studies also make available in an objective way the groups of institutions in various fields either to coordinate the efforts or to make alterations in stress. As stated by Seyfried<sup>8</sup>, the purpose of research evaluation is to guide future actions involving both business and research decisions, to help avoid or reduce wasted effort and keep research people on their toes, assuring them of management's interest in their activities.

## Source

The source material for this study is the *Indian Science Abstracts* published by the INSDOC. This abstracting journal was started in January 1965. In the first number the material that was available from publishers and distributors of technical journals in October 1964 was abstracted. Thereafter

the material available in succeeding months was abstracted in the respective numbers. This probably was not followed for the complete year and the journals received during one year from October 1964 to September 1965 were abstracted in thirteen numbers of the abstracting journal, i.e. twelve numbers of Vol. 1 (1965) and one number of Vol. 2 (1966).

This abstracting journal covers papers published in the Indian technical journals and in foreign journals if the work is carried out in India. If the papers originating abroad and published in Indian journals are omitted the rest is the outcome of work carried out in the universities and research laboratories in the country. Coverage of the papers published in foreign journals is carried out by scanning several of them and also by requesting the authors to send reprints to the INSDOC. It is claimed that 60-70 per cent of the papers in this category are covered. The coverage for the journals published in India is exhaustive, and in anyway not less than 98 per cent. Annual reports and technical reports from some organizations are also abstracted in the *Indian Science Abstracts*. The abstracts in each number are classified (UDC) and are arranged in that order. Patents accepted in India are included in the journal. Standards reports prepared by the Indian Standards Institution are also included. All the universities in India were requested to send copies or abstracts of these submitted for research degrees in science, engineering, medical, agricultural and technology faculties. In this field, coverage has not been satisfactory as the information was not received by the INSDOC. When the material submitted for research degrees is suitable for publication, in a condensed form, it is published as a research paper. For such reasons these items in the abstracts are omitted in the analysis. Information available from the Abstracts on patents is not sufficient to make any analysis. Generally, after a patent is accepted, if the invention is of research interest, the material is published in a technical journal. So these entries are also omitted for analysis. Similarly the Standards are not included in this analysis.

### Procedure

The information available in the citations of the papers as given in the Abstracts is coded. Volume number, serial number and classification number are noted as given. The number of authors for each paper is also noted. The journal in which the paper is published is given code number and recorded accordingly. The year of publication is also marked. Besides this information, the type of publication (research paper, short communication or letter to the editor, review paper, case report, etc.) and the language in which the original paper appears are coded. The reader may be cautioned here that sometimes the institution given in the entry is not the one at which the work is carried out but where the author is employed when the paper is published. The place of work has greater permanency and significance, and any credit that goes with the work that is carried out should go to the institution where it is carried out rather

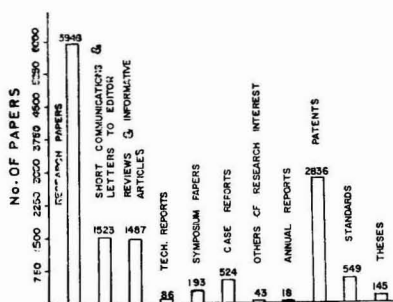


Fig. 1 — Number of papers abstracted in *Indian Science Abstracts* (1965)

than to the one where the author works afterwards. The credit due to the authors is anyway indicated, as the names of authors are included in citations. The analysis is carried out using a computer.

In Fig. 1 the numbers of different types of papers abstracted are given and the last four items are not included in the analysis. The number of papers published in Hindi and other Indian languages is negligible and they, generally, are not original research papers. Thus in this analysis this aspect is not studied and it will be discussed in another report devoted to the study of technical journals published in the country.

### Contributions by Different Institutions

The productivity of research papers in a particular laboratory depends upon the type of research carried out, basic, applied or development work, and the discipline. A general analysis of this nature is only a beginning to measure research publication activity.

The citations given are not identical in the Abstracts. Some journals do not give the name of the institution where the work is carried out. In such cases the publications are put under 'institution not known'. In the country there are nearly 2000 units where research is carried out. Many universities have a large number of research workers and every university has some research activity. There are about 3000 colleges affiliated to different universities and there are research workers in several of them. The affiliated colleges are not separately coded but all the research work carried out in the affiliated colleges and the university colleges is put under one head. Similarly, some research institutions or national laboratories have several research centres or field stations and for this analysis they are merged with the parent body. There are 68 universities and about 50 national laboratories either directly under the CSIR or partly financed by it, and 100 scientific and industrial development laboratories under different ministries in the centre and states, and some privately financed. Medical colleges are included in the universities to which they are affiliated. There are about 50 medical research laboratories, and medical practitioners in hospitals not attached to medical colleges

TABLE 1 — DISTRIBUTION OF RESEARCH PUBLICATIONS AND THEIR ORIGIN

Institution	Total No. of publications	Research papers	Letters to editor and short communications	Technical reports	Symposia and conference papers	Review and informative articles	Case reports	Others
Universities*	3816	2492	613	6	40	353	287	25
CSIR†	766	537	115	22	23	69	—	—
Medical laboratories and hospitals	1023	543	108	—	—	203	157	12
Agricultural laboratories	1187	764	291	4	1	123	4	—
Industrial and other laboratories‡	1545	957	277	43	88	177	3	—
Other institutions, individuals	1122	485	99	5	7	460	60	6
From abroad	345	170	20	6	34	102	13	—
Total	9804	5948	1523	86	193	1487	524	43

\*Including medical, engineering and agricultural colleges.

†Including research association laboratories supported by CSIR.

‡Including research organizations of all ministries not covered by the above groups, private maintained laboratories, etc.

contribute articles to medical journals. Agricultural colleges are affiliated to agricultural or other universities and some have distinct entity due to development over many years. There are about 170 research institutions or centres of reasonable size to be counted individually. It appears that there are about 800 agricultural stations where research might be carried out. All those other than the 170 agriculture and veterinary research organizations coded are put under general heading for each state. Medical institutions, for which distinct entries are not made and which are not connected with universities, are coded under two heads for each state (private and government hospitals). Thus nearly 550 research organizations, many of them networks, are coded separately and the rest are coded under the state heads. Different stations under the Geological Survey of India, Botanical Survey of India, Zoological Survey of India, etc., are included under the respective organizations. Similarly meteorological observation stations are classified under one head of the Department of Meteorology. Several industries in private and public sector have research departments. All such are placed under two categories, private and public sector industrial units. In the absence of an authentic directory of research laboratories it is impossible to be able to give distinct numbers to each, and when several of them are going to occur once or a few times, it is not worth making distinct entries. When coding was being carried out it was not possible to visualize how frequently contributions would come from several not well-known units and there are a few institutions from where the contributions are about 10 in the year and were not given distinct numbers. The number of such organizations, however, is not more than 5.

There are some contributors whose residential addresses only are given. All such contributions were grouped along with 'other institutions'.

In Table 1 are recorded the general distribution of research publications and their origin. The papers contributed to conferences and symposia are often published afterwards as research papers

if the material is original. Similarly research results are published first as short communications or letters to the editor and afterwards with some additional data or with more critical discussion the materials are published as research papers. Technical reports meant for specific users are also published as research papers if the material contains original research results.

Thus the 9804 entries included in the analysis are not all original communications. Strictly, the original research publications are only those included under the heading 'research papers'. Review papers and informative articles too need not contain original research results. In medical and veterinary science journals several interesting case reports are published. These again cannot be considered as original results as the material is not out of the experiments conducted or of the investigations carried out in the laboratories. They, however, are of professional interest and can be materials of investigation for research workers. If all such publications are omitted there are only 5948 research papers abstracted in one year.

The seventeen organizations included in Table 2 account for 30 per cent of all publications and nearly 50 per cent of the papers contributed to foreign journals. In the last three columns the number of disciplines in which varying activity exists in each of these organizations is indicated.

Though the number of publications in basic and applied sciences is nearly equal, in a developing country research carried out in applied branches has more significance. In Table 3 are listed institutions from which more than 50 papers in applied sciences are published. Again, most of the publications in applied sciences are in medicine and agriculture. As pointed out earlier, it is misleading to take the figures as they appear; for example, in Table 3, 31 papers out of 63 from the Central Food Technological Research Institute, Mysore, are classified under medicine, as they are mainly on nutritional problems and could have come under food technology as well. From the University of Patna out of 64 papers published, 44 were in medicine.



TABLE 2 — INSTITUTIONS FROM WHICH MORE THAN 100 PAPERS WERE PUBLISHED DURING THE YEAR UNDER ANALYSIS

Institution	Total No.	No. in foreign journals	No. of disciplines in which contribution is		
			>10	10-5	<5
University of Calcutta*	279	50	8	3	1
Agra University	260	10	5	1	4
Indian Agricultural Research Institute	227	12	3	1	3
Banaras Hindu University	226	22	6	3	2
Delhi University	206	58	6	1	4
Indian Institute of Science	194	26	5	1	8
Rajasthan University	177	32	6	1	4
University of Madras†	174	16	4	3	5
University of Bombay	162	7	5	1	6
Punjab University	160	18	6	1	6
Andhra University	154	20	5	3	2
Atomic Energy Establishment	133	26	4	1	5
Kerala University	128	4	4	—	4
University of Allahabad	110	49	3	2	3
University of Lucknow	110	15	3	2	3
Tata Institute of Fundamental Research	107	63	2	—	4
Vikram University	107	2	3	1	5
All institutions	2914	430			

\*Excluding Saha Institute of Nuclear Physics.

†Excluding Agricultural College & Research Institute, Coimbatore.

In Table 4, data regarding number of disciplines in which research is carried out in the institutions are given. In industrialization, where development work is important, specialized institutions have to be organized with reasonable number of workers to pursue studies in that branch alone. The very fact that institutions are engaged in varied fields of research indicates that large-scale efforts for intensive research in specific fields are lacking. The numbers in parentheses in Table 4 are for universities alone out of the respective totals. Out of the 18 laboratories contributing more than 25 papers in one year in one discipline only 8 were in applied sciences, 4 in medicine, 2 in agriculture (Indian Veterinary Research Institute, Izatnagar, and Agricultural College & Research Institute, Coimbatore) and 2 in technology (leather and food). Out of the organizations contributing more than 25 papers in two disciplines, only one institution (Forest Research Institute) contributed them in applied sciences. Only from the Indian Institute of Science, Bangalore, and the Indian Agricultural Research Institute, New Delhi, more than 25 papers were contributed in several disciplines, basic and applied. Industrial research requires integration of scientific knowledge from different fields and so the teams have to be heterogeneous. Sometimes even after the efforts are oriented to specific needs, interesting results in the constituent fields may turn out and get published.

In Fig. 2 the cumulative number of publications from different number of institutions contributing papers, in the descending order, is shown. It is apparent that though there are a large number of research units in the country, the activity is serious only in a small number of them. Only 44 institutions

TABLE 3 — INSTITUTIONS FROM WHICH MORE THAN 50 PAPERS WERE CONTRIBUTED IN APPLIED SCIENCES

Institution	Total No.	Medicine	Engineering	Agriculture	Chemical Technology	Building Science and Manufacture
Indian Agricultural Research Institute	144	—	—	142	2	—
Agra University	142	102	4	35	—	1
University of Calcutta	141	96	18	20	7	—
University of Bombay	114	61	3	26	14	12
University of Madras	107	82	9	15	1	—
Banaras Hindu University	97	77	5	14	—	1
Kerala University	94	63	2	29	—	—
Calcutta School of Tropical Medicine	89	89	—	—	—	—
Indian Institute of Science	84	7	40	1	35	1
Vikram University	76	47	2	27	—	—
Rajasthan University	73	41	4	18	—	—
Punjabi University, Patiala	70	69	—	—	1	—
Forest Research Institute & College	68	1	4	29	—	34
Agricultural College & Research Institute	66	—	—	66	—	—
University of Delhi	59	55	—	3	1	—
Punjab University, Chandigarh	59	41	2	11	4	1
University of Lucknow	56	55	—	1	—	—
Central Food Technological Research Institute	55	31	—	2	22	—
Andhra University	52	30	9	6	7	—
All India Institute of Medical Sciences	51	51	—	—	—	—
University of Patna	51	44	1	6	—	—
Central Drug Research Institute	50	46	—	4	—	—

TABLE 4 — NUMBER OF ORGANIZATIONS CONTRIBUTING PAPERS IN DIFFERENT DISCIPLINES

No. of disciplines	No. of organizations in which contribution is			
	≥25	24-10	9-5	< 5
1	37 (19)	61 (23)	80 (36)	115 (18)
2	7 (5)	16 (11)	18 (12)	55 (12)
3	6 (5)	4 (4)	8 (5)	30 (12)
4	2 (1)	3 (3)	3 (3)	31 (21)
≥ 5	—	1 (1)	4 (4)	40 (29)

Figures in parentheses are for universities alone.

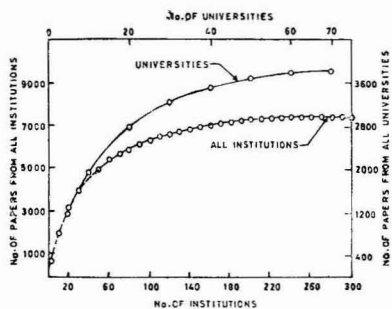


Fig. 2 — Cumulative contribution of papers from different institutions

contributed 50 per cent of all publications in the country and 12 of them more than 25 per cent. The second curve in the same figure is for similar distribution in universities alone. In universities, 8 (out of 68) account for 50 per cent of the publications. There are many research institutions in the country from which not a single paper was contributed during the year under review. It may be worth studying the per capita (per scientist) publication in different organizations. It is often the experience of individual scientists that where they work in teams of reasonable size, the per capita outcome is larger than when they have to work alone. Groups are more effective than individuals not only due to the cooperation necessary among themselves, but also several facilities required to carry on research can be provided effectively only when groups of optimum size are constituted. Good libraries cannot be provided when the units are small; workshop facilities too can be provided efficiently and economically only when the groups are of reasonable sizes. Grouping of research workers into optimum sizes brings considerable economy in administration also.

It would be further useful to study the productivity per scientist in scientific and technological laboratories in different fields throughout the country and to find out the optimum size. Such studies might have been conducted in advanced countries but depending upon the social conditions, administrative procedures, availability of research equipment in the market, the need for optimum utilization of the imported equipment and in terms

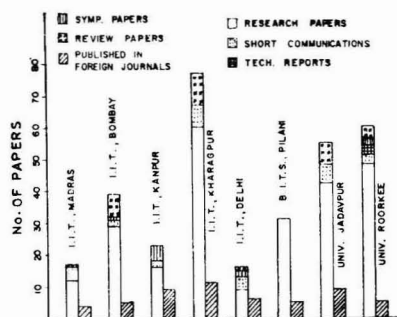


Fig. 3 — Breakup of publications from technological universities

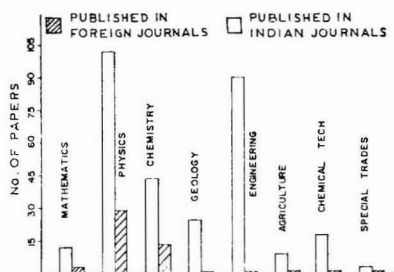


Fig. 4 — Discipline-wise breakup of publications from technological universities

of maintenance and utilization of library facilities peculiar to the conditions of the country, a systematic study and policy are necessary.

Though it is generally noticed that publication activity is high in universities, it does not equally apply to technological universities. The Indian Institutes of Technology were started to train engineer-scientists and conduct research in technology. The Birla Institute of Technology and Science has been upgraded to university level and there are Jadavpur University and Roorkee University for the same purpose. In Fig. 3 the breakup of technical publications from these universities is given. The figures indicated by the shorter columns are the numbers of papers published in foreign journals. The research publications from these universities are less, compared to the other universities. It is significantly so when the large number of qualified technologists and their salary scales are also taken into consideration.

In Fig. 4 the breakup of publications discipline-wise from these universities is given. Even from these institutions more than 60 per cent of the papers published were in basic sciences, mainly in physics (32 per cent). More than 50 per cent of all the papers published in foreign journals from these institutes are in physics alone.

### Subject-wise Distribution

In the formulation of national policies, distribution of resources subject-wise is more important than institution-wise. Coordination of research with



TABLE 5 -- DISCIPLINE-WISE BREAKUP OF ALL PUBLICATIONS

Discipline	Total No. of publications	No. of publications in foreign journals	No. originated abroad	Av. No. of authors	Research papers	Short commun. and letters to editor	Tech. reports	Symposia papers	Reviews and informative articles	Case reports	Others
General Science	5	--	--	1.00	2	--	--	--	3	--	--
Mathematics	237	53	14	1.19	204	29	--	2	2	--	--
Astronomy	37	12	1	1.37	21	7	3	--	6	--	--
Physics	838	282	16	1.76	552	144	21	95	26	--	--
Chemistry	1014	207	22	2.15	605	357	15	1	36	--	--
Geology and Meteorology	405	31	5	1.49	262	100	2	--	41	--	--
Palaeontology	70	1	4	1.37	41	26	--	--	3	--	--
Anthropology, Biochemistry, Microbiology, etc.	227	40	5	2.07	144	58	2	2	21	--	--
Botany	549	57	36	1.53	340	174	1	1	33	--	--
Zoology	497	50	22	1.58	312	167	--	--	18	--	--
Gen. Applied Sciences	2	--	--	1.00	2	--	--	--	--	--	--
Medical Sciences	2840	59	91	1.96	1488	149	10	2	661	492	38
Engineering and Technology	770	32	51	1.47	478	22	19	44	207	--	--
Agriculture, Forestry, Animal Sciences	1497	20	37	1.89	983	239	6	22	215	32	--
Management	33	--	2	1.39	21	--	--	--	12	--	--
Chemical Technology	444	35	25	2.05	290	38	7	3	101	--	5
Manufactures	279	9	9	1.90	168	11	--	20	80	--	--
Specialized trades	40	3	2	1.45	31	--	--	--	9	--	--
Others	20	--	3	1.36	4	2	--	1	13	--	--
Total	9804	891	345	1.82	5948	1523	86	193	1487	524	43

industrial development and agricultural requirements needs studies on research activities in these fields. Similar are the needs in respect of medical and health problems, whether the existing facilities are to be diverted or they should be further enhanced. Publication activity alone is no definite indication in many branches of industrial research, yet it may serve as a guide for further studies.

As classification numbers given for abstracts are included in coding, the data cards are arranged in that order and the following information in each subject is obtained: the total number of papers published and their types, papers published in foreign journals, number originating abroad, and the average number of authors per publication in each subject.

In Table 5, the above information is given for 19 broad subjects. In Figs. 5 and 6 and Chart 2 the breakups in three subjects, engineering, agriculture and physics, are given. Minute details in each subject are available, but it is considered unnecessary to include them in a general study like this. Publications are maximum in agriculture followed by medicine and chemistry.

In engineering under UDC number 621, several branches, such as material testing, nuclear technology, water power, electrical engineering, applied electrochemistry, electric and electromagnetic waves, electronics, telecommunication, engines, fluid containers, pumps, workshop practice, transmission systems and parts, material handling, mechanical attachments and fittings, machine tools, etc., are included. This is a wide field covering all branches of mechanical, electrical and electronics engineering. To give some detailed information, this group of papers is further analysed and the distribution of papers under eleven headings is given in Chart 1.

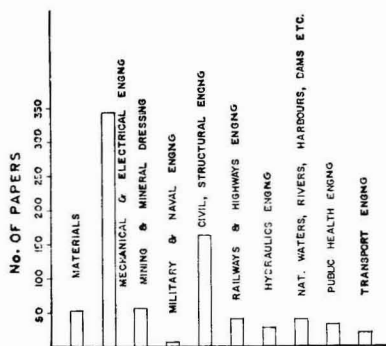


Fig. 5 — Breakup of papers in engineering

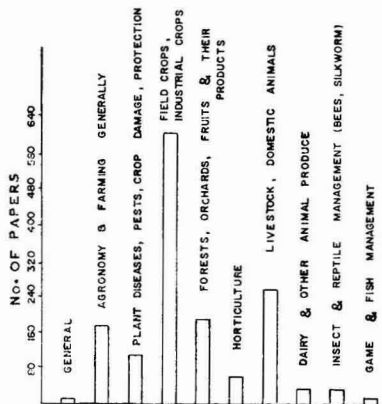


Fig. 6 — Breakup of papers in agriculture

Electrical and Mechanical Engineering  
343, 38 (204,13,16,-,110)

Machinery details 8 (6,-,-,2)	Mech. Engng and Nuclear Engines, Boilers 18 (3,2,7,-6)	Steam Power, Engines, Boilers 13 (5,-,-,8)	Water Power, Utilization 4 (3,-,-,1)	Electrical Engng 207 (14,1,8,7,-51)	Internal Com- bustion and other Special Engines 17 (9,-,-,8)	Pneumatic Energy, Machines, Refrigeration, Heat Pumps 6 (3,-,2,-1)	Fluid Distri- bution, Storage, Containers, Pipes, Pumps 6 (2,1,-,-,3)	Workshop Practice 32 (13,2,-,-,17)	Power Trans- mission, Materials Handling, Mech. Fixing Attachments, Intrication 18 (10,-,-,-,8)	Tools, Machine Tools, Machinery 14 (9,-,-,5)
Electrical Engng General 16 (12,-,-,4)	Power Generation, Supply, Control 64 (37,3,4,-20)	Electrical Lamps Nil (-,-,-,-)	Electric Traction 1 (-,-,-,1)	Appl. Elec. Chem., Cells, Batteries, etc. 19 (17,-,-,2)	Thermoelectricity, Electric Heating 1 (-,-,-,1)	Techniques of Electric and Electromagnetic Waves, Oscillators, Pulses 25 (18,1,-,-,6)	Electronics 40 (27,1,3,-,9)	Telecommu- nications 41 (30,3,-,-,8)		

Chart 1 — Distribution of publications in engineering — electrical and mechanical [The digits denote total number of publications, and number published abroad (bold). Those in parentheses denote research papers, short communications, technical reports, symposia papers and reviews respectively.]

Physics  
838, 282 (552,144,21,95,26)

Gen. Principles (Quan. and Rel. included) 24,16(21,3,-,-)	Mechanics 39, 8 (34,2,1,-,2)	Fluid Mech. 73, 16 (68,4,-,-,1)	Gas Mech. 34, 14 (20,8,2,3,1)	Vibrations, Acoustics, and Sound 22, 7 (11,4,6,-,1)	Optics 89, 17 (57,21,2,1,8)	Heat and Thermo- dynamics 49, 13 (38,9,-,-,2)	Electricity 37, 14 (30,6,-,1,-)	Mag. and Elec. Mag. 40, 16 (35,4,-,-,1)	Physical Nature of Matter 431, 161 (238,83,10,90,10)
Nuclear, Atomic and Molecular Phys. 309, 134 (148,63,7,86,5)		Properties and Structure of Molecular and Macromolecular Systems 65, 18 (46,9,1,4,5)		Mechanical Properties of Solids 57, 9 (44,11,2,-,-)					
Nuclear Physics (Theory, Measure- ments, Effects, etc.) 139, 55 (71,28,6,33,1)	Elementary Particles 71, 53 (40,18,-,12,1)	Nuclei (Forces, Model, etc.) 9, 8 (7,1,-,1,-)	Radioactivity and Decay 27, 6 (11,3,-,12,1)	Nuclear Reactions 8, - (3,1,1,3,-)	Physics of Single Atoms 20, 4 (5,2,-,12,1)	Physics of Single Molecules 35, 8 (11,10,-,13,1)			

Chart 2 — Distribution of publications in physics [The digits have same meaning as in Chart 1]

It is apparent from Chart 1 that the publication activity, excepting electrical engineering, is negligible in this group. Electrical engineering, including electronics, is again a broad subject; so further details are given for the 207 papers in this branch in the same chart. There is no publication activity in electric lamps, electric traction and thermoelectricity. In view of large investments by Railways in electric traction, possible use of solar energy and continued import of technology and materials for electric lamps, research and development work in these fields is very important. In view of the wide application of electronics in almost every industry, communications and scientific research, its growth and development is a primary necessity.

In physics more than 50 per cent of the publications are under 'physical nature of matter'. This branch includes nuclear physics, atomic physics, molecular physics, mechanical properties of materials, etc. In Chart 2, division of the 431 papers under the above heading is given. Nuclear, atomic and molecular physics is again a broad subject and to indicate the interest and activity of research workers in this field further details are given in the same chart. It is apparent that in all aspects of nuclear physics, there are groups engaged in research, unlike in engineering branches, though for development engineering branches are more urgent. It is of interest to note that 53 out of 58 papers in elementary particles contributed to journals were published in foreign journals; similarly 55 out of 99 in nuclear physics (theory, measurement, effect, etc.), all 8 on nuclei and 6 out of 14 on radioactivity were published in foreign journals.

Technical reports are published in reasonable number only from the Atomic Energy Establishment. More than 30 per cent of their total publications (41 out of 133) are technical reports. Among other institutions, National Aeronautical Laboratory published 11 technical reports (out of a total of 18). All the other institutions in the country published only 34 technical reports.

Similarly attendance and contribution of papers at symposia and conferences appear to be more in certain institutions. Tata Institute of Fundamental Research, Atomic Energy Establishment and the Indian Institute of Science contributed 23, 10 and 14 respectively (22, 7 and 7 per cent respectively of the total publications from each), out of 159 contributed by Indians. Atomic Energy Department organizes two symposia every year, one on high energy nuclear physics and another on low energy nuclear physics. Among the 40 such contributions from the universities, several might have been contributed to these two symposia only, as 90 papers out of 193 (34 were from abroad) enumerated under symposium papers, are in atomic and nuclear physics. From the subject analysis it appears that the proceedings of only three more symposia were abstracted during the year. They are in civil or structural engineering (30 papers), soil science (22), and textile engineering (20).

### Team Work

Scientific research, like other aspects of social activity, is undergoing several changes. The division

of scientific knowledge is one important aspect which has undergone such a change. A few decades back, mathematics, physics, chemistry, geology, botany, zoology, etc., were distinct branches of science. After considerable progress had been made in each branch, synthesis of these branches has been taking place. Industrial research itself is a synthesis of mathematics, physics and chemistry. Similarly agricultural science has made tremendous progress after several branches of knowledge have successfully combined. Due to this change it has become increasingly necessary to have teams instead of individual research workers.

It is pointed out by Price<sup>5</sup>, how multiple authorship of technical papers has been increasing in the past 50 years. Even in pure sciences, with increasing complexity of experimental techniques, the need for cooperative effort has become unavoidable. In a recent study Price and Beaver<sup>9</sup> observed that in a group of 533 papers in physics the average figure for multiple authorship was 2.32, while for papers in the same subject, abstracted in the *Indian Science Abstracts*, it is 1.76. In engineering subjects it is only rarely that one finds research papers contributed by single authors in foreign journals.

In Fig. 7, the breakup of publications with the number of authors is given. Maximum papers are still published in this country by single authors, while two-author papers are maximum in the world. Price<sup>5</sup> postulates that single-author papers will be extinct by 1980 in the scientific literature. It appears that dispersal of scientists in a vast number of small research units makes team work less practicable and individuals carry on research to fulfil their duty or in pursuance of individual taste. Institution-wise, only the Central Food Technological Research Institute has an average authorship (3.3) greater than 3. Even in the technological universities, where team work should be easy to organize, the average authorship is only 1.6.

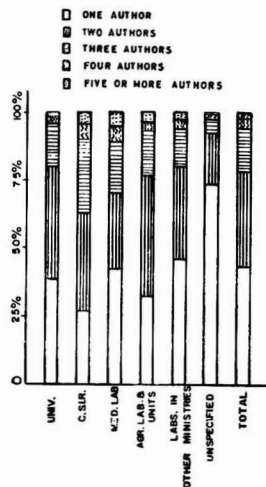


Fig. 7 — Multiplicity of authorship

This aspect requires some critical analysis and needs some radical policy changes to make research effective. It is a general practice in India to include the supervisor of the project, professor in university, department-head in other laboratories among the authors for which due acknowledgement would have been sufficient in advanced laboratories. If such inflations are also taken into consideration the average number of authors per paper appears so low that it is completely out of tune with the general trends in research and industrial research needs.

In Table 5, multiple authorship in various branches of basic and applied sciences is given. No marked difference in this respect between basic and applied branches is apparent. In another report<sup>4</sup> from this organization, this aspect has been studied in electronics engineering; 65 per cent of the papers published by the Indians were by single authors.

### Productivity of Publications

It is reported in a census survey<sup>10</sup> that there were about 400,000 scientists and technologists in 1961 of which 30 per cent postgraduates and 50 per cent agricultural graduates had research assignments. Each year 15 thousand engineers, 6 thousand medical graduates, 6 thousand agriculture graduates and 10 thousand M.Sc.'s in different branches of sciences are turned out from all the universities. As the number of scientists and technologists retiring from service is small compared to the number that is added, by 1964 the number of scientists and technologists with research assignments might have been more than 80,000.

Though for many of them research is a part-time activity, the equivalent whole-time research workers could be between 60,000 and 70,000. Taking all publications, it appears that productivity of publications is at the rate of one paper for 6-7 scientist-years effort. If one omits the repetitions that occur, such as first a paper being published in the proceedings of a symposium, and then being published in a science journal, or first a letter and afterwards a full paper being published, it requires 10-12 scientist-years to produce one paper.

If the exact number of scientists and technologists who published papers in one year is known, it would give some more information. As the author index to the first volume of the *Indian Science Abstracts* is not yet ready this aspect is not studied.

### Contributions to Foreign Journals

A considerable fraction of the papers by Indian scientists is published in foreign journals. In one year, 891 such publications are recorded in the *Indian Science Abstracts*. As the coverage in this group is expected to be 60-70 per cent only, it appears that about 1400 papers are published in foreign journals by the Indian scientists working in India. To the technical journals published in this country 345 papers are contributed by the research workers in other countries. Contributions to foreign journals are mainly in physics and chemistry, 282

and 207 respectively out of a total of 891. In applied sciences the number of papers published by Indian workers in foreign journals is nearly equal to the number of papers published in Indian journals by workers in foreign countries.

In some subjects like nuclear physics, the proportion of papers published in foreign journals is very high. Out of the 107 papers contributed by the Tata Institute of Fundamental Research during that year, 63 were published in foreign journals and 23 were contributed to symposia in the country. Thus only 21 were published in Indian journals. As shown in Chart 2, in certain branches major proportions of the papers are published in foreign journals. These aspects will be discussed further in another report devoted to a study of technical journals published in the country.

### Conclusions

The entries included in this analysis are diverse in nature. Papers published in certain journals serve the needs of factory engineers, field workers in agriculture, general practitioners in medicine, etc., while others provide material for research workers in laboratories. Papers from some journals are abstracted in international abstracting journals, while many are not. The research efforts required to report a 'case report' or a field experience are far different from those required to prepare an original paper in cytogenetics or statistical analysis. In this analysis no distinction has been made and hence this remains a general study. For any comparison, more homogeneous groups of papers are to be chosen. Citation index has to be studied to analyse material of original research interest.

In view of the large number of scientists and technologists engaged in research—60,000 to 70,000—with a bias for publication of papers, the number of publications appears very low. During the year under analysis nearly 40 per cent of all technical papers were contributed from universities. Each year about 1000 candidates take Ph.D. in science or M.D. degree and the total enrolment in the universities for research in science and technology is about 5000. The presence of so many research students working for degrees appears to be the main reason for a high proportion of the papers being published from universities. Further investigation into the authorship of the papers may provide useful information. However, degree incentive appears to have a dominant role in preparing material useful for publication.

Among the universities, there are marked differences in research activity. There are 70 universities of which 25 had been in existence since pre-independence years. There are 13 universities from which more than 100 publications were contributed during the year under analysis. They are neither the oldest nor have better financial grants than others. Research tradition cannot be thus explained by age or attractive salaries. There are more publications from the technology departments of some of the older universities than from the Indian Institutes of Technology, employing more qualified

technologists with better salaries. It has been estimated in a study<sup>11</sup> by the Institute of Applied Manpower Research that the expenditure per undergraduate student in Indian Institutes of Technology is five times that in the engineering colleges affiliated to universities after keeping reasonable component of expenditure apart for research and postgraduate teaching. It is necessary to investigate whether it is reasonable to start institutions with high ambitions or it is more fruitful to provide additional funds to selected centres already showing progress. Though it had been a recommendation of a committee headed by Sircar, 20 years back, in view of the experiences in its implementation such studies might be needed. The country, however, in 20 years of development should have entered a different phase which necessitates such studies. These studies need not be confined to technological subjects but could be extended to all sciences.

For industrial development, mathematics is as important as any subject of technology. There is no one institution in the country, universities included, contributing a dozen research papers in mathematics during one year under analysis, excepting the Indian Statistical Institute from which 26 papers in mathematics were contributed and of these 23 were in statistics. From institutions and universities throughout the country 223 papers in mathematics were published in one year. Though papers in mathematics are not as affluent as in several other subjects, in view of the need the activity appears to be too low.

There are many research publications in nuclear physics, plasma physics, lasers, etc., which are modern subjects in advanced countries, but are rather fashionable in a developing country. This might be due to the large number of scientists trained in advanced countries in the subjects of their personal choice instead of being directed by the needs in the country. The brain drain talked of so much these days is intimately linked up with this aspect.

The scientists and technologists engaged in research are widely scattered in a large number of small units (Fig. 2). It is not feasible to provide costly equipment if the teams are small and the budgets for the units are small. Auxiliary facilities, such as workshops and libraries, cannot be provided for small groups and if at any small unit these facilities are provided the optimum utilization will be lacking. Administrative machinery has to be any way provided and a greater proportion of expenditure will be spent for this than in bigger units. The number of publications from the small units is so small that there are several hundred units contributing one each or no paper at all in a year. Regrouping of small units into larger ones and utilization of savings from administrative and auxiliary facilities for better research equipment may prove more effective. It is estimated that expenditure per scientist in laboratory equipment and other facilities for research activity is very low in India<sup>2</sup>. This needs consideration, since several expensive items of research equipment are not used to the optimum level. The equipment should be used to the maximum extent before it becomes

obsolete, which happens in a relatively short time. The necessity is obvious for organization of laboratories, by which scientists requiring a particular expensive equipment are brought together at one place so that the facilities are available to a greater number of them. It is a policy matter which requires consideration whether research units in a country can be organized on the basis of equipment. Scientists and technologists often choose places of work upon social convenience, independent of their training and laboratory facilities. Sometimes expensive items are imported but sanctioned posts in laboratories are few. It is particularly difficult to provide equipment for those who got training abroad. It is not economically feasible to provide the desired equipment at each place a trained person chooses to work. Even advanced nations cannot afford to equip laboratories according to only the needs of individual scientists. Scientists move to the places where the equipment is available and where groups of scientists are engaged in the fields of their choice. It is worth preparing an inventory of expensive imported research equipment items and the use they are put to. Wherever the items are not put to optimum use, it may be necessary to evolve a policy by which scientists at other places who are in need of such equipment are shifted or vice versa. From several institutions with certain costly items of equipment there were no papers published during the year under consideration utilizing that equipment.

One important feature of science and technology in this age is, along with narrow specialization, considerable horizontal integration that is taking place. Use of science for industrialization depends upon the number of ways in which different bits of knowledge can be combined. Different permutations and combinations of the physical, chemical, biological and engineering principles give rise to the development of new processes for industrial exploitation. To be able to integrate the different branches of science, cooperative efforts are necessary on a larger scale than they exist at present. Distribution of papers with different number of authors is only one aspect of it. Very often even when two or three authors contribute a paper jointly they are all from one discipline, with the same specialization. There are more deep-rooted reasons for the lack of interdisciplinary approach in research in this country. Compartmentalization of departments, restricting appointments in each faculty to those with degrees in that faculty, etc., lead to isolation of different branches with very adverse effects on industrial research. There is a well-equipped department in an important engineering branch with 8 professors and more than 50 assistant professors and lecturers contributing hardly any publication in one year. In the appointments to senior posts, basic degrees are sufficient qualification and research experience or ability does not get sufficient attention.

In this study no special efforts are made to compare the trends and intensity of research with those in other countries. The trends are and have to be peculiar to each country depending upon its state of development and resources. It is difficult



to get similar data for another similar country and it is misleading to compare with any for which data are available, which generally is an industrially advanced country.

Though experienced scientists and technologists are aware of the conditions conducive to active scientific research, it is necessary to give concrete shape to such ideas by studying the existing conditions in different organizations and find out what differences exactly make staff at an institution more productive than at another. As long as these matters remain subjective views of individuals, however eminent, it becomes difficult to make the suggestions explicit and expect them to be implemented. In a democratic set-up, such as ours, what appears obvious for some, requires proof for several others. Even in a group of people which appears very homogeneous in one aspect there is diversity when a solution for a specific problem is required. This type of studies may provide objective data to evolve policies to make scientific and technological research more effective.

The author takes the opportunity to express his thanks to Prof. G. S. Ramaswamy, Director, Structural Engineering Research Centre, for readily making available computer facilities. He also thanks Shri R. N. Bhargava who prepared computer programmes, and Shri D. K. Bhatnagar and Miss Kavita Chachra for their assistance in computation work.

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## Seminar on Mathematical Sciences

The Council of Scientific & Industrial Research constituted in April 1966 a preparatory committee for arranging a seminar on mathematical sciences to be attended by top mathematical scientists in India and some Indian mathematicians from abroad.

The seminar was held at the Indian Institute of Science, Bangalore, during 27-29 September 1966. The participants included pure mathematicians, applied mathematicians, theoretical physicists, mathematical statisticians, astrophysicists, geophysicists and specialists in numerical analysis and computer science. As many as eighteen persons participated in the seminar. Prof. Shreeram Abhayankar of Purdue University was the only pure mathematician to participate from outside India.

Prof. S. Dhawan, Director, Indian Institute of Science, welcomed the participants. In the plenary session of the seminar, important issues were brought to focus against the background of the general agenda prepared for the seminar by the preparatory committee. The remaining sessions of the seminar were devoted to the discussion of these issues.

The proceedings of the seminar including the general recommendations for raising the standard of mathematical education in the country, proposal for constituting a national committee for mathematics and mathematical sciences and the subject of national institutes of higher learning and an appendix giving the programme, list of participants, addresses at the opening session and messages have been published in the form of a 24-page brochure.



# REVIEWS

THE PRINCIPLES OF ELECTROMAGNETIC THEORY AND OF RELATIVITY by Marie-Antoinette Tonnelat; translated from the French by Arthur J. Knodel (D. Reidal Publishing Co., Dardrecht), 1966. Pp. xii+475. Price 70 fr.

The book under review is the English translation of the original French edition entitled *Les principes de la théorie électromagnétique et la relativité*, first published in 1959. The author has published several papers on relativity and gravitation and also another book in 1965 entitled *Les théories unitaires de l'électromagnétisme et la gravitation*. The aim of the present book is to explain the principles of the classical and relativistic theories of electromagnetic and gravitational fields and the gradual development of these ideas.

The book is divided into four parts. Part I (Chapters I-IV) deals with the principles of electrostatics, magnetostatics, electromagnetism, Maxwell and Lorentz theory of the electron. Part II (Chapters V-X), forming the major part of the book, deals with the principles of special relativity. The four-dimensional formalism of special relativity, relativistic kinematics, relativistic dynamics of a point mass, relativistic dynamics of continuous media, covariant form of Maxwell's theory, Mie's theory and the theory of Max Born and Infeld, experimental verification of the consequences of special relativity are the main topics discussed here. The author has attempted to give some historical development of the subject of the theory of special relativity, putting emphasis on the logical course in the development of the theories. In this attempt the presentation, particularly in Chapter V, has degenerated into mere cataloguing of references to earlier work. Part III (Chapters XI-XIII) deals with general relativity (theory of gravitation). The equivalence principle, the introduction of the non-Euclidian universe, Einstein's law of gravitation, Schwarzschild's solution of the field equations are some of the topics discussed here. Chapter XIII on unified theory of electromagnetism and gravitation is written in general terms and is mostly speculative. The last two chapters (XIV and XV) of Part IV form a mathematical supplement dealing with tensor calculus. Each chapter contains a set of interesting problems and useful notes. The bibliography and the subject index at the end are meagre. The book is commendable as a reference book and it is hoped that it will be widely used and appreciated.

T. VENKATARAYUDU

GENERAL AND INORGANIC CHEMISTRY FOR UNIVERSITY STUDENTS by J. R. Partington (Macmillan & Co. Ltd, London), Fourth Edition, 1966. Pp. xxiii+926. Price 72s.

This excellent textbook has been highly popular from the time it was first published in 1946. Intended for pupils in higher forms at school and for degree and honours students in universities,

the book deals with general and physical chemistry in the first part and with inorganic chemistry in the second. A large amount of material is presented in a concise and intelligible manner without unduly increasing the size of the book.

The present (fourth) edition incorporates a number of additions and alterations designed to bring it up to date. New material includes accounts of molecular orbital and ligand field theory and description of many new compounds. Physical properties of substances have been revised in the light of new knowledge. Many references to recent publications and several new illustrations enhance the usefulness of the book.

The use of symbols has not been uniform in a couple of instances. The practice of lettering new pages A, B, etc., is also a little annoying. These will no doubt be rectified in a subsequent edition. The general get-up and illustrations are, as in previous editions, good. The book presents virtually all the inorganic chemistry a degree student requires and it can unhesitatingly be recommended to him.

S. R. MOHANTY

KINETIC METHODS OF ANALYSIS by K. B. Yatsimirskii (Pergamon Press Ltd, Oxford), 1966. Pp. xvi+155. Price 50s.

The book under review has appeared at a time when the analytical chemist is looking around for more and more sensitive and selective methods of analysis for trace constituents. After a brisk introduction to general physico-chemical methods of analysis, the book gets divided into six chapters. The first one, dealing with the theoretical basis of kinetic methods, is followed by experimental methods of studying the kinetics of chemical reactions, and determination of the amount of analysed substances on the basis of kinetic data. The fourth chapter discusses the types of reactions which can be used in kinetic methods of analysis; the fifth, the study of complex formation with the aid of kinetic methods; and finally the sixth, covering 64 of the 157 pages, lists a number of kinetic methods of determining individual elements and ions. At the end of the book is given a complete table of kinetic methods for the determination of elements and ions.

The overall presentation of matter is crisp and well conceived. Specially on the experimental side, there are clear warnings for the over-enthusiasts about the limitations of each approach and the different practical problems, even though at times these get lost in the discussions of the methods themselves. The presentation at times is confusing as, for example, when the author tries to explain the concept of indicator reaction. The oxidation of iodide in acid medium by hydrogen peroxide, which is catalysed by cupric ions, is considered an indicator reaction for this ion, since its concentration is determined by the rate of this reaction. But when he considers the oxidation of thiosulphate

by ferric ion as an indicator reaction for the latter ion, one starts wondering about the definition and how such a reaction can have the high sensitivity which kinetic methods are claimed to have. However, a little later, when the same reaction, which is catalysed by copper ion, is considered an indicator for this ion, the definition becomes clear again. Similarly, the term 'induction periods' is used under two contexts in pages 4 and 16. It is hoped that these defects would be rectified in subsequent editions.

Right from the beginning the author tries to drive home the high sensitivity and selectivity of kinetic methods. On going through Chapter VI and the final table, one finds that many elements can be determined at concentration levels of  $10^{-2}$  to  $10^{-3}$   $\mu\text{g./ml.}$  and, in a few cases, even down to  $10^{-6}$  to  $10^{-8}$   $\mu\text{g./ml.}$  However, when it comes to selectivity one gets the feeling that there is a tendency to overstate the case of kinetic methods.

The main contribution of the book is that it serves the useful purpose of focusing the interest of analytical chemists, who are generally taught to look for rapid reactions, on the usefulness of kinetic aspects of chemical reactions.

M. SHANKAR DASS

TECHNIQUES IN FLAME PHOTOMETRIC ANALYSIS by N. S. Polue'ktov (D. Van Nostrand Co. Inc., New York), 1966. Pp. xvi+219. Price \$ 4.95

Flame photometry, a simple form of emission spectral analysis, has gained prominence in recent years as a rapid analysis method, particularly for the alkali and alkaline earth metals.

Chapter 1 gives a brief description of the underlying principles of flame photometry with reference to the emission of elements in flame, characteristics of flames, relation between emission intensity and concentration of elements in solution. The effect of solution composition on emission intensity of an element in flame is also discussed.

Chapter 2 deals with the various photometers and flame spectrophotometers. The factors affecting the sensitivity and accuracy of the method are discussed in Chapter 3, while the details of the measurement procedure are given in Chapter 4.

The last section, viz. 'Techniques for determining elements in various materials', is the most useful section for analytical chemists in general and practising analysts in particular. In this section, detailed procedures are given for the determination of alkali and alkaline earth metals in natural and industrial products. The analyses of gallium, indium, thallium, iron, manganese, chromium, and lead are also discussed. In the last chapter, a few special techniques are given.

The book thus gives a survey of the principles and applications of flame photometry. The specific section on procedures is the highlight of the book. As expected, the book is heavily biased on Russian work. The work by non-Russian scientists has not been given the credit due to it. The bibliography section at the end of the book has not done much justice to non-Russian work. Quite a few references (Nos. 29, 33, 115, 121 and 244) are incomplete. In spite of these shortcomings, the English transla-

tion of the Russian book is a welcome addition to literature for the analytical chemists.

A. K. DE

REFRACTORY TRANSITION METAL COMPOUNDS by G. V. Samsonov; translated by G. B. Gurr & D. J. Parker (Academic Press Inc., New York), 1964. Pp. viii+220. Price \$ 9.00

Refractory compounds have attained new significance recently because of their great technological importance. This book is a collection of articles on transition metal refractory compounds, including those presented in the seminar on 'Physical properties and electron structure of compounds of transition metals' held in USSR. An account is given of the Russian work on the physical properties, electrical behaviour, crystal structures, etc., of borides, silicides, carbides and nitrides of transition metals by X-ray and NMR techniques; some theoretical treatment is also included. As a collection of articles, this book has some drawbacks, but it would be helpful to those interested in this important field.

A.G.

EUTECTIC ALLOY SOLIDIFICATION by G. A. Chadwick (Progress in Materials Science, Vol. 12, No. 12, 1963); edited by Bruce Chalmers (Pergamon Press Ltd, Oxford), 1963. Pp. 84. Price 25s.

This is a review article on eutectic alloys classified on the basis of their microstructure, namely lamellar, spiral and discontinuous types, with special emphasis on the growth and nucleation process, the theory of the growth of alloys, effect of impurities on the microstructure, etc., of the lamellar type of alloys.

The article is well written and would be useful for specialists as well as to physicists and chemists interested in the subject. The cost of the booklet is rather high.

A.G.

FUNDAMENTALS OF RADIOBIOLOGY: Vol. 5, by Z. M. Bacq & P. Alexander (Pergamon Press Ltd, Oxford, and English Language Book Society, London), 1966. Pp. xii+562. Price 24s.

The rapid advances in the safe development of nuclear energy and the many diagnostic and therapeutic applications of varied radiological techniques have necessitated an integration of physics, biochemistry, cytology, genetics and general biology into radiobiology, which is now a science on its own right. The volume of research on radiation effects is now so great that it is scarcely possible to survey the entire field of radiobiology in a book of this size. Nevertheless, the present authors have done an excellent job of attempting this task. The fundamental aspects of the subject have been dealt with in sufficient detail with information on the overall effects of radiation, such as genetic and biochemical lesions, neuro-endocrine and pathological reactions and lethal action.

Studies with unicellular organisms like bacteria, yeast cells or isolated mammalian cells in tissue culture have yielded enormous information which helps us to understand what happens in complicated multi-cellular organisms. There is, however, no

reason to expect that one and the same mechanism applies to all cellular effects. Qualitative and quantitative differences suggest that there could be a variety of injury processes. Yet, it is in the nature of science to look for unification and the authors develop a working hypothesis which relies on one type of initial lesion capable of varied expression. This is the action of radiation on the cytoskeleton or membranes and surfaces within the cell and, more especially, the lysosomes with consequent release of many hydrolytic enzymes.

Until there is a more complete elucidation of the many biochemical processes and their regulation in normal living cells as well as on aspects of radiation biology, such as differential sensitivity of various types of cells and the relationship of damage or of repair mechanisms to level of biological organization, it will not be possible to pinpoint any primary effect of radiation. Again, since we know that many chemicals as well as other metabolic disturbances can provoke lesions indistinguishable from those produced by radiation, it becomes necessary to consider that these effects are the result of a complex interplay of different factors in a living system which react to changes brought about in its environment. One does wonder, therefore, when going through the chapter on biochemical mechanisms, if the authors have not overemphasized the enzyme-release hypothesis with only a cursory treatment of damage to the DNA structure and other radiobiological effects.

Although this English Language Book Society edition has been released in 1966, the book is only a reprint of the second and, in many respects, completely rewritten edition, published in 1961. In their postscript, the authors have expressed the fear that the enormous rate of progress may necessitate a revision of the text before long. This has indeed come true. While the book could still be a useful compilation at the present time, it can greatly benefit by revision of several chapters and by amplification in particular of the topics on radiation repair, radiation sensitivity and the effects of radiation on several aspects of nucleic acid metabolism.

A. SREENIVASAN

APPLICATION OF FRACTURE TOUGHNESS PARAMETERS TO STRUCTURAL METALS: Vol. 31, edited by H. D. Greenberg (Gordon & Breach Science Publishers, New York), 1966. Pp. x+406. Price \$ 10.50 (paper); \$ 24.95 (cloth)

This publication contains ten papers presented at the symposium sponsored by the Structural Materials Technical Committee of AIME. This symposium was held at the Fall meeting of the AIME in Philadelphia during 1964.

The papers cover the application of fracture mechanics in selecting materials for structural applications. The opening paper by Prof. Parker provides an excellent background on the theory of fracture processes. A refreshing feature of this article is the application of the Griffith approach for studying the behaviour of notched bars and plates. Such a useful but fundamental approach has not hitherto been attempted while discussing the various processes in fracture mechanics. In

the second article, Brothers and Yukawa discuss different fracture test methods in vogue today. A concise summary of test procedures employing transition temperature criteria (TTC) is presented in this article.

Critical thickness concept (CTC) in designing structural components is discussed in the next article by Katz and Abbot. Examples of this approach in evaluating structural failures in rocket motor cases have been discussed. The next two articles also describe practical applications in designing fracture-safe structures for large cylindrical pressure vessels (Bates and Greenberg) and deep-diving submarine hulls (Huber and Goode).

The last five papers describe researches aimed at a basic understanding of the metallurgical factors governing fracture toughness. An important observation, namely that principal metallurgical factors that increase toughness of the matrix are deleterious for the weld-metal strengthening, emerges from an excellent article on the fracture toughness of 18 Ni mar-ageing welds (Superstein *et al.*). The other papers in this section deal with the effects of chemical composition on the fracture toughness of aluminium alloys (Piper *et al.*), the optimum microstructure for the fracture toughness in a high strength steel (Trozzo and Pellissier) and the effects of fabrication history and the mode of testing on the fracture characteristics of ultra-high strength steel (Bucher *et al.*). The concluding paper by Banerjee *et al.* discusses the fracture toughness of extra-workhardened type 301 stainless steel and cryogenic temperatures.

Since most of the papers presented have been selected from a large number of papers submitted, it is hardly necessary to emphasize the high standard of the material contained in this volume. However, in the reviewer's opinion, some attention could have been devoted to the problem of micro-cracks, as it is increasingly realized that this is just but an initial step in the formation and subsequent propagation of macro-cracks. Another omission is on fracture-toughness properties of materials subject to stress-corrosion cracking. Be this as it may, the publication of this volume is timely and it should prove a valuable source of information to those engaged in research on the subjects concerned or in their industrial application.

V. S. ARUNACHALAM

PORTLAND CEMENT TECHNOLOGY by J. C. Witt (Chemical Publishing Co. Inc., New York), 1966. Pp. xiii+346. Price \$ 16.50

The present revised edition is very timely inasmuch as it not only documents and discusses the important technological advances made during the last two decades but also presents a much wider spectrum of the technology. This has made the book an enlarged volume of 24 chapters and 346 pages.

After a short and pertinent introduction in Chapter 1, landmarks in the history of Portland cement are described in the second chapter. Raw materials and their proportioning are discussed in the next two chapters. Proportioning problems are well illustrated with typical cases and a calculation form for the proportioning of materials has

been proposed. Chapters 5 and 6 deal with preparing raw mix and fuels. Proportioning of raw mix on blending system has been reviewed critically.

Clinkering, the most important step in cement manufacture, has been dealt with in Chapter 7 under the heads of the development of rotary kiln, design of the modern kilns and auxiliary equipment of draft fans, seal rings, feeders, chain systems, dust collectors, etc. Because of its importance, the output of a rotary kiln or its dimensions for a desired output should have been discussed in greater detail and objectively enough to provide guidance. The kiln functions and kiln operations, however, are adequately dealt with. Chapter 8 gives facts and figures on power and describes conditions favourable for the provision of waste-heat boilers. The subject of grinding of clinker is very well dealt with in Chapter 9.

Valuable suggestions are given on plant location, preconstruction work, selection of equipment, distribution of principal raw materials handling equipment, etc., in the chapter on plant design. This, together with the chapter on experimental engineering, a new branch of great importance, will be of great interest to those in cement industry. The information on automatic control of kilns is objectively discussed. The nature of cement has been dealt with in the light of modern knowledge on cement minerals and their hydration. Properties and ASTM specifications of cement have also been given. Chapters 16 and 17 on the non-aqueous liquid process and the counter cyclone clinkerer are based on the author's original work and present new approach of great promise in the years to come. The advantages of the processes have been discussed in the light of merits and demerits of the current manufacturing processes of vertical kiln, and the dry and wet process rotary kiln.

Chapters 19 and 21 deal with concrete technology and are of interest to engineers, architects and building material technologists. Specifications for ready-mixed concrete have also been given. The chapter on some concrete accomplishment is interesting to read and that on Iris Color Process (Chapter 23) presents very interesting and valuable ideas on a concrete of colour—a development of the near future. The last chapter gives valuable general information and bibliography. This book caters for the interests of students, cement and concrete technologists, engineers and architects and machinery manufacturers and in this the author has achieved his objective.

S. K. CHOPRA

#### PUBLICATIONS RECEIVED

RETICLES IN ELECTRO-OPTICAL DEVICES: Vol. 1 (International Series of Monographs in Infrared Science and Technology), by Lucien M. Biberman

- (Pergamon Press Ltd, Oxford), 1966. Pp. x+177. Price 45s.
- FOUNDATIONS SUBJECTED TO VIBRATIONS, annotated bibliography compiled by Shamsheer Prakash & D. C. Gupta (School of Research & Training in Earthquake Engineering, Roorkee), 1966. Pp. 43. Price Rs 5.00; \$ 1.00
- LA DIFFUSION DANS LES SOLIDES by Y. Adda & J. Philibert (Institut National des sciences et Techniques nucléaires, Saclay), Vol. 1: 1966. Pp. xvii+666; Vol. 2: 1966. Pp. xvii+667-1268. Price 212 fr. (both)
- MACHINE DEVICES AND INSTRUMENTATION edited by Nicholas P. Chironis (McGraw-Hill Book Co. Inc., New York), 1966. Pp. vii+359. Price \$ 10.00
- MODERN OPTICAL ENGINEERING by Warren J. Smith (McGraw-Hill Book Co. Inc., New York), 1966. Pp. xii+476. Price \$ 15.00
- ANTIFERTILITY COMPOUNDS IN THE MALE AND FEMALE by Harold Jackson (Charles C. Thomas, Publishers, Springfield), 1966. Pp. xvii+214. Price \$ 8.75
- USEFUL PLANTS OF BRAZIL by Walter B. Mors & Carlos T. Rizzini (Holden Day Inc., San Francisco), 1966. Pp. xiii+166. Price \$ 11.00
- STATE VECTOR SPACES WITH INDEFINITE METRIC IN QUANTUM FIELD THEORY by K. L. Nagy (Akadémiai Kiadó, Budapest), 1966. Pp. x+131. Price \$ 4.20
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- CHEMICAL EQUILIBRIUM by Allen J. Bard (Harper & Row Publishers, New York), 1966. Pp. xi+202. Price Rs 22.88
- ACOUSTICS: DESIGN AND PRACTICE, Vol. 1, by R. L. Suri (Asia Publishing House, Bombay), 1966. Pp. xxviii+539. Price Rs 50.00
- ANNUAL REPORTS IN MEDICINAL CHEMISTRY, 1965, by Cornelius K. Cain (Academic Press Inc., New York), 1966. Pp. ix+342. Price \$ 7.50



The existence of a new kind of molecule which had been predicted theoretically in certain semiconductors has been experimentally proved to exist in silicon at the Bell Telephone Laboratories. Known as the 'excitonic molecule', this stable entity is built up of two electrons and two holes. Even though it is usual to designate both electrons and holes as 'particles' responsible for conduction in semiconductors, holes cannot be strictly considered to be a 'particle', being essentially just the positive charged 'receptacles' into which electrons can fall. The excitonic molecule discovered in silicon can be also considered as made up of two excitons. Considered in this way, the concept indicates connection between the exciton and the hypothetical positronium molecule postulated in 1946, but not yet found. According to theoretical postulation, the positronium molecule would contain an electron and a positron in a stable configuration.

In the experiments conducted at the Bell Telephone Laboratories, excess of electrons and holes were produced by illuminating a silicon crystal with strong light. Infrared spectrometric studies of the emitted radiation on the far side of the crystal showed strong lines which could be explained only as due to the recombination of the excitonic molecule, a process in which the two combined exciton pairs breaking into one exciton, a normal electron and a hole and a photon. Excitons can exist independently in a crystal and travel through its lattice. Being electrically neutral they cannot conduct current. The experiments also showed that two excitons can combine to form the new stable molecule [*Phys. Rev. Lett.*, **17** (1966), 860].

### A new synthesis of large rings

A new synthetic route to large ring compounds has been developed involving the reaction of cycloalkynes such as cyclodecyne and 1,8-cyclotetradecadiyne with butadiene in the presence of catalysts containing zerovalent nickel.

Cyclodecyne on reaction with butadiene gives 4,5-oligomethylene-*cis*-1,*cis*-4,*trans*-7-cyclodecatrienes in high yields which through a series of reactions like hydrogenation, oxidation and Wolff-Kischner reaction, give rise to compounds containing large rings, many of them previously unknown. Cyclotetradecadiyne on reaction with butadiene yields bicyclo- and isomeric tricyclic hydrocarbons. The structures of the compounds isolated were characterized by IR, NMR and mass spectral data. Some of the Raman bands characteristic of the tetra-substituted double bonds in a few new large ring compounds synthesized were in unexpectedly high wavelengths — 1630-1640  $\text{cm}^{-1}$  [*Angew. Chem. internat. Edn.*, **5** (1966), 961].

### Apparatus for analytical disc electrophoresis

A modified apparatus for disc electrophoresis in which all the electrophoresis tubes are sealed into a glass plate to form a single unit thereby considerably simplifying the preparation and running of the acrylamide gels has been developed by Drs K. J. Catt and Barbara Moffat of the Department of Medicine, Prince Henry's Hospital, Melbourne.

The apparatus differs from the original design in the construction of the upper buffer vessel. This vessel, with its rubber grommets and individually inserted glass tubes, is replaced by an all-glass vessel consisting of two parts. The upper part is simply a vertical glass tube 80 mm. high  $\times$  85 mm. diam., the lower end of which is flanged and ground flat. The lower part is a circular glass plate 110 mm. diam.  $\times$  4 mm. thickness. The upper surface of this plate is ground flat, and around its periphery are 12 holes of 9 mm. diam., evenly spaced around a circle of 80 mm. diam. Into each of these holes is sealed, by epoxy resin, a glass electrophoresis tube 80 mm. long  $\times$  5 mm. internal diam. The lower surfaces of these tubes are

ground flat, so that all tubes are of identical length.

The complete upper buffer vessel is assembled simply by placing a smear of silicone grease around the opposing ground surfaces of the flange and glass plate, then pressing the two parts firmly together. The assembled vessel is supported by an annular plastic ring which, in turn, sits on a lower polythene buffer vessel containing a central stainless steel electrode. A plastic top, which covers the upper buffer vessel, carries a central platinum wire electrode, and is machined with an annular slot to fit the rim of the upper buffer vessel.

The use of this unit has been found to considerably simplify the procedure of analytical electrophoresis, especially when large number of samples (e.g. column fractions) have to be handled. The only maintenance required for the apparatus is the occasional renewal of the epoxy resin used to cement the tubes of the destaining apparatus into place [*Aust. J. exp. Biol. Med.*, **44** (1966), 597].

### New method of ring expansion

A new method of three-membered ring opening and one carbon ring enlargement has been described by R. C. De Selms [*Tetrahedron Lett.*, **18** (1966), 1965]. The procedure is free from the limitations of competing side reactions and difficulties in preparation of starting materials, which are generally encountered with the normal methods of three-membered ring expansion. Using the method of Hagemeyer and Hull, readily available ketones have been converted to the enol esters which are then converted to acetoxydichlorocyclopropanes in 25-50 per cent yield by reacting with dichlorocarbonene. The cyclopropanes on treatment with a slight excess of lithium aluminium hydride in ether, at room temperature, give good yields of the ring expanded  $\alpha$ -haloalkenyl carbionols. Simple distillations at reduced pressure give analytically

pure products. The reaction probably proceeds via a transient union or some complexed equivalent.

### Separation of enantiomers

A method for the resolution of enantiomers by gas liquid chromatography on an optically active stationary phase, hitherto not yielding fruitful results has been reported [*Tetrahedron Lett.*, (No. 10) (1966), 1009]. The unsuccessful methods reported in the literature so far have used packed columns for separation. To improve the efficiency of separation, capillary columns of pyrex glass (0.25 mm. diam., 50-100 m. length) have now been used. After cleaning with different solvents, the capillaries were coated with 20 per cent ether solution of optically active N-TFA 1-isoleucine lauryl ester by the plug method, and other N-TFA  $\alpha$ -amine esters, viz. N-TFA alanine esters of ethanol, *n*-propanol, isopropanol, *n*-butanol were taken as solvents. The capillaries were dried and conditioned overnight while raising the temperature gradually to 80°C. The samples were injected in ether solution (0.3-0.6  $\mu$ l.) with a split ratio of 100:1. The temperature of the injector and the column were maintained at 90° and 210°C.; and the nitrogen pressure at 20 p.s.i. N-TFA alanine esters of ethanol, *n*-propanol, isopropanol, *n*-butanol and 2-butanol and N-TFA valine and leucine esters of 2-butanol have been unambiguously separated using column 100 m. long. All these compounds have also been checked for purity by chromatography on a capillary column coated with an inactive phase. Compounds with one asymmetric centre give one peak on the inactive phase and two on the active phase, while those with two asymmetric carbons give two and four peaks respectively. The steric factors of the alcoholic chain have been found to influence the resolution of the enantiomers N-TFA alanine esters.

### Slagceram, a new construction material

Slagceram, a new constructional material developed at the laboratories of the British Iron & Steel Research Association, is based on

the use of blast furnace slag. The production is based on controlled crystallization of slag-based glass. Slagceram is likely to find use in the manufacture of a variety of road and building materials, including kerbstones, paving flags, floor tiles, roof tiles, and slates, guttering, drain pipes, stair treads, tunnel living, sea defences, building blocks, wall panels, non-skid road surfaces, etc.

One of the full scale production processes envisaged on the basis of pilot plant studies involves the following stages: adjustment of slag composition to give a glass suitable for crystallization; shaping of the glass into the final product; and a two-stage heat treatment of the article to convert it into slagceram. Thirty parts of silica in the form of pure sand is added to 100 parts of slag (preferably delivered in the molten state direct from the furnace), in addition to the nucleating agents. The melting and mixing of the components to give a homogeneous melt can be performed in the conventional glass making furnaces, with suitable modifications for producing turbulence. The casting and shaping processes used in the glass industry would, with suitable modifications to take into account the differences of properties between slagceram and ordinary glasses (the quicker rate of cooling and sharp change in viscosity with temperature in the case of slagceram), be suitable for slagceram. For heat treatment, the continuous annealing furnaces, with provisions to give the required temperatures of 650-750°C. for nucleus formation and 900-1100°C. for crystallization for several hours, might be used. To go beyond the limited range of colours, obtained by the adjustment of various conditions, vitreous enamelling combined with heat treatment can be used [*Chemistry Ind.*, 42 (1966), 1745].

### Low density refractories

A novel method of producing low density, high heat resistant, inorganic refractories using aromatic, unsaturated polyester resins as the foamable polymer system has been reported [*Ind. Engng Chem. (Prod. Res. Develop.)*, 5 (No. 3) (1966), 282].

Alumina and silica refractories have been produced by foaming the oxides in a variety of unsaturated polyester and aromatic resins (polyester, ureaformaldehyde, epoxy, urethane, resole and phenolic), and firing the foamed objects up to 1900°C. As the normal foaming systems do not develop enough gel strength to prevent collapse during rise when heavily loaded with inorganic fillers, modified techniques, catalysts and blowing agents have been developed. A typical alumina refractory using unsaturated polyester resins as the foamable polymer system, was produced as follows: To a base mixture, consisting of polyester, alumina, sodium bicarbonate, cellulose acetate butyrate and styrene, a mixture of cobalt octoate, maleic anhydride and water was added. Before pouring the mixture into a mould, methyl ethyl ketone peroxide was added. Foaming, resulting from the liberation of CO<sub>2</sub> formed by the reaction of maleic anhydride with water and sodium bicarbonate occurred within 4 min. and setting within 22 min. The resulting foamed object had a density of about 35 lb./cu. ft. All the cured foams containing about 60 per cent by weight refractory fillers have been subjected to temperatures up to 1100-1650°C. in conventional kilns. During firing, the organic material vanishes, leaving a carbon structure behind.

It has been observed that of the resulting charred foam structures, the unsaturated polyester derived chars show higher compressive strength as well as toughness. This has been explained through the kinetics of the thermal degradation of the unsaturated polyesters.

### *Acta Chimica Sinica* and *Acta Mechanica Sinica*

A complete cover-to-cover English translation of *Acta Chimica Sinica*, the bimonthly Chinese journal of chemistry, has been made available by the Consultants Bureau Division of the Plenum Publishing Corp., New York. The English translation, edited by Prof. Ju Chin Chu of the Polytechnic Institute of Brooklyn, commences with the first issue of Volume 32, 1966. The



third issue of this volume carries four articles reporting the total synthesis of insulin achieved by members of the Institute of Organic Chemistry and Biochemistry of Academia Sinica and the Department of Chemistry at Peking University.

A cover-to-cover English translation of *Acta Mechanica Sinica*, the Chinese journal of mechanics and applied mathematics, is also being published from December 1966 by the Consultants Bureau, New York.

### Indian Institute of Science, Bangalore

The annual report of the Institute for the year 1964-65 gives a summary of the teaching and research activities of the various departments. Three hundred and eighty-four contributions — 211 in pure sciences and 173 in engineering, were published during the year. Summer schools in biochemistry, molecular physics and nuclear spectroscopy were held.

A number of projects in the fields of solid state chemistry and gas reactions have been pursued at the Department of Inorganic and Physical Chemistry. The structures of a variety of carbonates of rare earths have been investigated by X-ray diffraction, infrared and magnetic susceptibility methods. Differential thermal analysis has been employed for the study of the decomposition of these compounds. During kinetic studies on the adsorption of CO-H<sub>2</sub> gas mixtures on iron, preferential adsorption of hydrogen has been observed at higher temperatures. During studies on sulphur compounds, chloramine-T was found to oxidize some of the compounds produced by the reaction of anhydrous hydrogen iodide with sulphur halogen compounds, giving sulphuric acid.

X-ray studies on cobalt alloys electrodeposited from the pyrophosphate bath have shown the existence of solid solutions in the case of Co-Fe, Co-Cu and Co-Fe-Ni and different phases in Co-Zn. The pyrophosphate bath has been found suitable for the electrodeposition of Co-Ni-W alloys.

Among studies in progress in the Department of Organic Chem-

istry are the syntheses of steroids (oestrone, *d,l*-testosterone, azaxsteroids) and terpenoids (vetivone, nepetalactone, jatansone and acarenone).

In the Department of Biochemistry, a new member of the siderochrome class of compounds containing S-N-hydroxy ornithine, ornithine and  $\beta$ -methyl glutamic acid has been isolated from cobalt-toxic cultures of *N. crassa*. This compound has been found to be more potent than inorganic iron at the level of incorporation into the cell for heme synthesis. Cow and buffalo caseins have been found to be similar though not identical in their amino acid compositions. Cow casein on digestion with pepsin gave a gel like material containing five major peptides. A new reagent, 2,4-dinitro anilino-N-phenyl isothiocyanate, has been synthesized and shown to react with twenty amino acids giving nearly quantitative yield of highly coloured crystalline phenyl thiohydrates. The reagent has also been shown to react quantitatively with synthetic peptides to yield coloured PTC-peptides.

It has been found that vitamin A acid is more active than the acetate or alcohol in supporting the growth of vitamin A deficient rats. Besides being easily absorbed, the acid is also readily formed inside the animal body. It has been demonstrated that almost all of the cholesterol ether hydrolysate of the mucosal cells are present in the brush border of the cells; during the adsorption of the cholesterol, the brush border hydrolyses the dietary cholesterol esters, and transfers the de-esterified sterol into the mucosal cells where it is slowly re-esterified.

The presence of a potent inhibitor of follicle stimulating hormone in the urine of monkeys has been shown for the first time. The inhibitor, a non-dialysable heat-labile protein, has no effect on luteinizing hormone.

Studies conducted in the Fermentation Technology Laboratory on the nutritional requirements of *Arthrobaacter* species isolated from soil, sewage and activated sludge have helped in formulating an improved system of classification of this group of bacteria. A method using potassium tellurite as the bacteriostic agent in the

culture media has been developed for the isolation of yeasts from sewage, sludge and other habitats.

Studies on biosynthesis of nucleic acid purines in *M. tuberculosis* in progress in the Pharmacology Laboratory have shown that in this organism, formate is not an efficient precursor for the carbon atoms 2 and 8 of the purine ring; instead they are efficiently derived from the  $\beta$ -carbon of serine and also from the  $\alpha$ -carbon of glycine.

The major areas of investigation in the Department of Physics were Raman and IR spectroscopy, structure analysis by X-rays, nuclear and paramagnetic resonance, semiconductors, lattice dynamics, ferroelectricity, molecular spectroscopy, mass spectrometry and nuclear geology, computers and nuclear instrumentation, and crystal elasticity.

The Raman spectra of glycine and its addition compounds, ferroelectric crystals 'GASH' and lithium hydrozinium sulphate, sodium zinc sulphate tetrahydrate, hydroxylamine hydrochloride and acetonitrile have been investigated. In the field of molecular spectroscopy, more refined values of vibrational constants, based on the twenty new bands of the (A-X) system of BiF, have been reported.

X-ray studies on the double salt (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>·3NH<sub>4</sub>NO<sub>3</sub> have shown that it has a distinct crystal structure, different from those of its constituents. Other compounds whose structures have been determined by X-ray analyses included borazole, dimethyl sulphoxide and antipyrine.

Based on NMR analyses, a possible hydrogen bonding scheme in MnSO<sub>4</sub>·4H<sub>2</sub>O crystal has been suggested. In the field of semiconductors, point contact diodes have been made from purified crystals of germanium and aluminium antimonide, their reverse and forward turnover characteristics have been investigated to establish their thermal origin. The preparation of pure silicon tetrachloride has been successfully undertaken for use in the preparation of semiconductor grade silicon and for epitaxial growth studies.

Based on theoretical work on the lattice dynamics of caesium

chloride structures, a slightly modified model taking into account the short-range interactions and Coulomb interactions between ions has been suggested. Using Blackion's root sampling method with this model, the frequency distribution in caesium iodide has been worked out.

In the Department of Metallurgical Engineering the preparation of spherical powders of tin, by carbothermic reduction of stannic oxide in nitrogen, using excess of carbon has been investigated. It has been observed that particle size depends on the temperature of reduction and the amount of excess of carbon used. From preliminary investigations it has been observed that copper-5 per cent magnesia sinter powder compacts resist high temperature oxidation better than pure copper compacts even at 1000°C. The effect of adding alkali and alkaline earth metals, on the mechanical and structural properties of copper-bismuth alloys is under investigation.

A static 3-step distance relay has been built in the Department of Electrical Engineering, based on static components (transistors, zener diodes and thyristors); the relay provides ideal protection for long heavily loaded transmission lines against all types of defects. A test bench, which can simulate accurately the appropriate power system conditions and any type of single or multiple fault, has been developed for protective gear testing. During studies on adoptive control systems, a solution involving the use of delays has been obtained for the basic problem of obtaining the gradient of the performance index in parameter space in the case of linear system whose configuration is entirely unknown.

#### Announcement

■ A Conference on Water Desalination will be held during November 1967 at the Central Salt & Marine Chemicals Research Institute, Bhavnagar. The Director of the Institute has invited intending participants to suggest topics for discussion at the conference.

#### FORTHCOMING INTERNATIONAL SCIENTIFIC CONFERENCES, 1967

Date	Conference	Place
15-19 May	International Conference on Essential Oils: Production in Developing Countries	London
22-27 May	Fifth International Television Symposium	Montreux, Switz.
6-10 June	Tenth International Gas Conference	Hamburg
6-12 June	International Conference on Soil Water	Prague
12-14 June	International Communications Conference	Minneapolis
12-16 June	Eighth International Conference on Hot Dip Galvanizing	London
12-17 June	International Symposium on Radiation Dose Measurements	Stockholm
12-17 June	Symposium on the Chemistry and Internal Structure of Synthetic High Polymers (IUPAC)	Louvian, Belg.
12-19 June	Second International Conference on Solid Compounds of Transition Elements	Enschede, Neth.
19-23 June	Thirteenth International Spectroscopy Colloquium	Ottawa
19 June to 2 July	Tenth International Conference on Cosmic Rays	Calgary or Banff, Canada
25 June to 2 July	Fourth International Congress on the Application of Mathematics in Engineering	Weimar
26 June to 1 July	Fifth International Congress of Chemotherapy	Vienna
June	International Conference on Chemical and Radiological Safety	USA
June	International Conference on the Physics Problem in Thermal Reactor Design	London
June	International Symposium on Fluidization	Findhoven
June or July	International Conference on Nuclear Structure	Dubna, USSR
3-8 July	Fourth International Measurement Congress	Warsaw
10-12 July	International Symposium on Naturally Occurring Phosphoric Esters	Newcastle-upon-Tyne
10-15 July	Fifth International Mining Congress	Moscow
17-19 July	International Symposium on Corrins	Nottingham
17-23 July	Fifth International Conference on the Physics of Electronic and Atomic Collisions	Leningrad
18-23 July	First International Conference on Laser Applications	Paris
21-31 July	Eighth International Space Science Symposium	London
24-28 July	Fourth International Conference on Carbohydrate Chemistry	Kingston, Canada
24-29 July	Fourth International Fluorine Symposium	Estes Part, Colo.
25-27 July	International Symposium on Solution Properties of Natural Polymers	Edinburgh
July	Second International Symposium on Photochemistry	Enschede, Neth.
7-12 August	Fourteenth International Spectroscopy Colloquium	Debrecen, Hungary
14-18 August	Fourteenth International Symposium in Microscopy	Cambridge
19-25 August	Seventh International Congress of Biochemistry	Tokyo
20-25 August	Sixth International Biometric Conference	Sydney
27 August to 2 September	Eighth International Conference on Ionization Phenomena in Gases	Vienna
27 August to 3 September	Twenty-fourth Conference, International Union on Pure & Applied Chemistry	Prague
30 August to 6 September	Sixth International Congress of Plant Protection	Vienna
30 August to 7 September	Twelfth International Congress on Refrigeration	Madrid
August	Seventh International Conference on Medical Electronics and Biological Engineering	Stockholm
August	Third International Symposium on Organometallic Chemistry	Munich
August-September	Eighth International Embryological Conference	Bern

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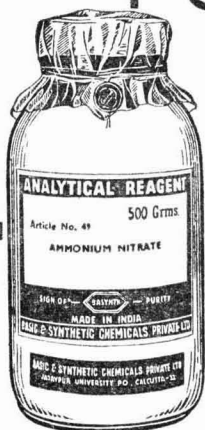
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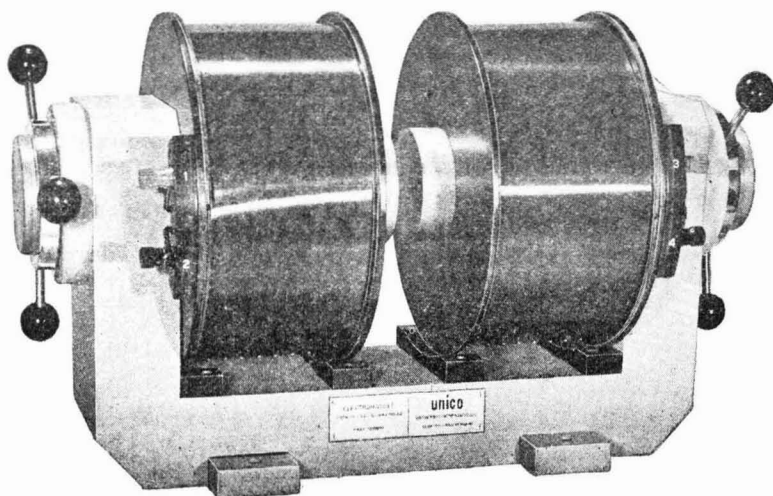
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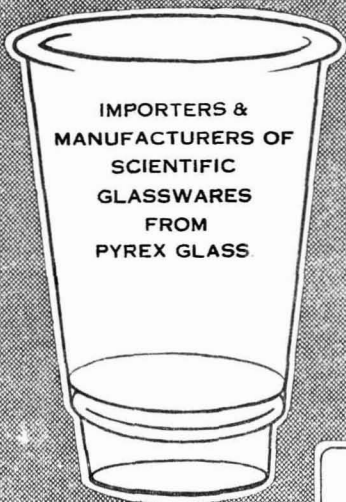
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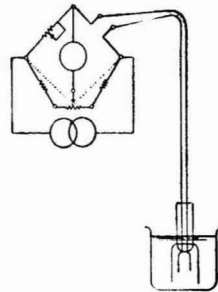
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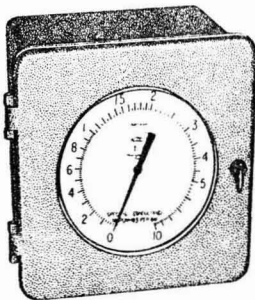
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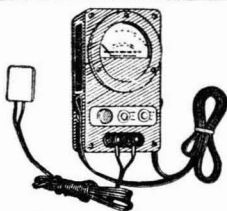
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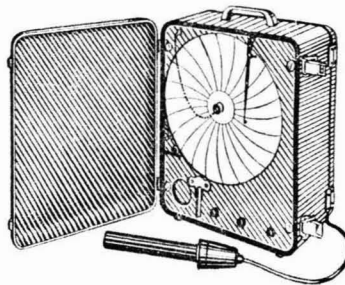
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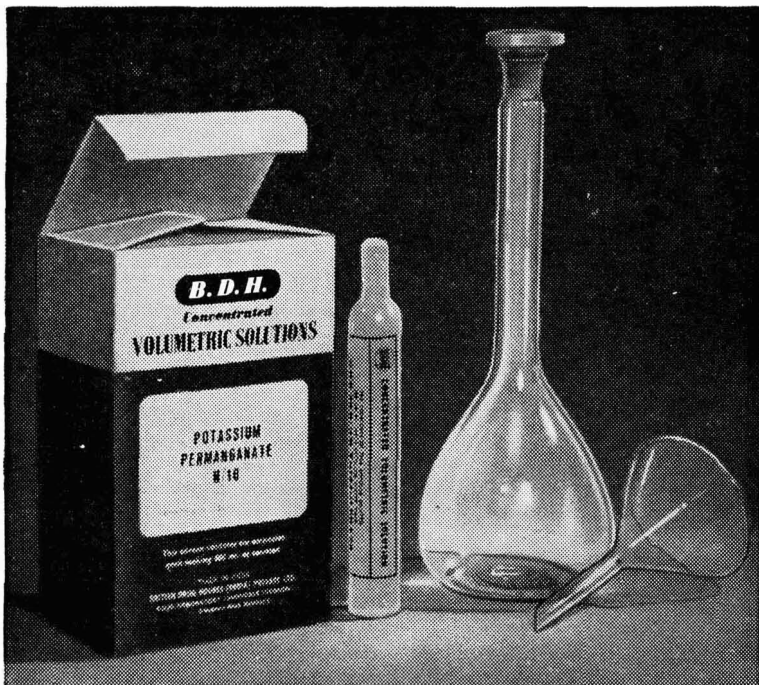
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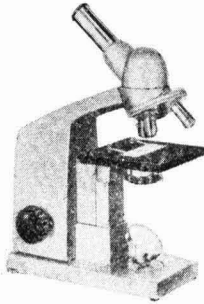
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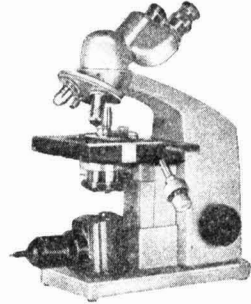
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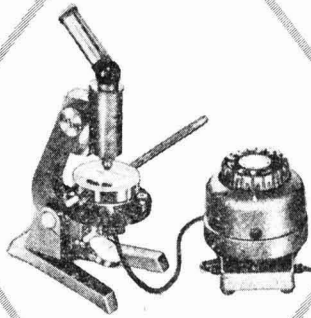
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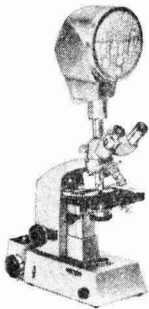
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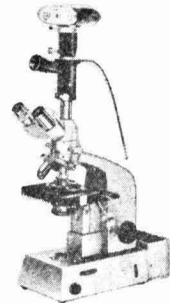
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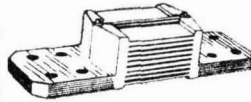
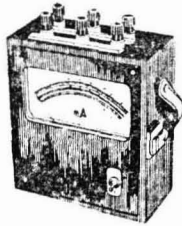
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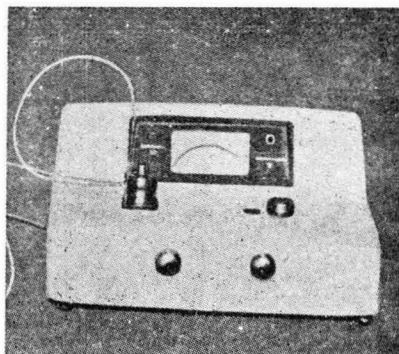
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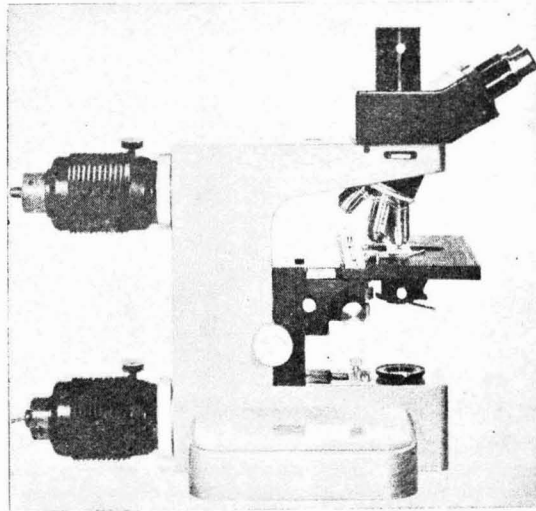
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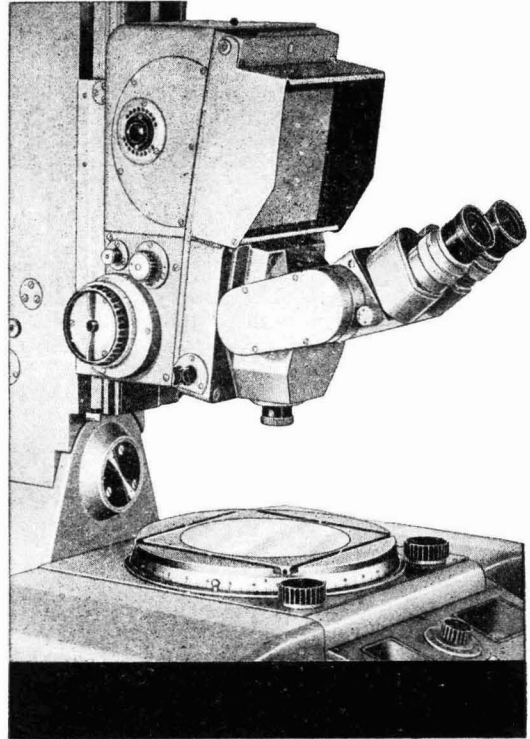
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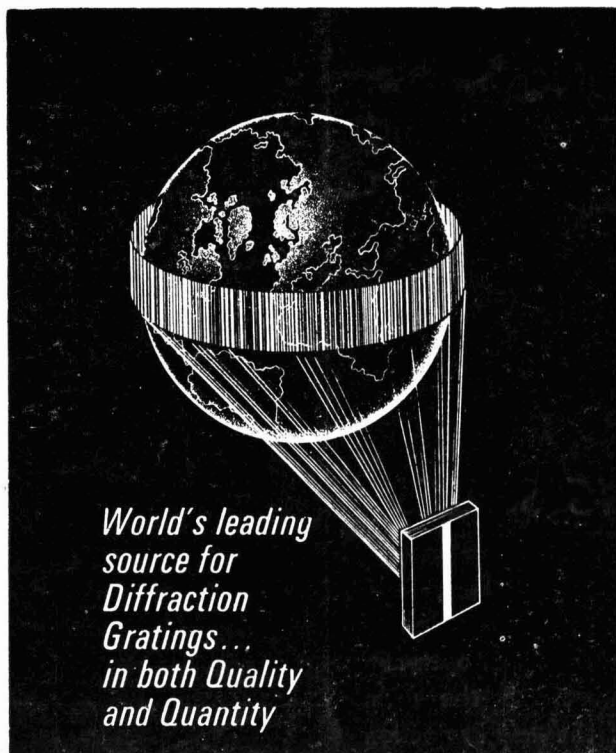
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