GAS CHROMATOGRAPHY

An informal symposium organized by the Gas Chromatography Discussion Group of the Institute of Petroleum was held on April 7 at the Shell Centre, Waterloo, London, with Mr. C. S. G. Phillips in the chair. The symposium was preceded by the annual general meeting of the group followed by an introduction, on behalf of Shell, Ltd., by Lord Rothschild.

The first paper was given by Mr. J. C. Hawkes on "The Use of the Gas Density Meter for Process Monitoring and Control" in which he described the use of this detector for following the progress of vapour phase oxidation processes such as the production of maleic anhydride from benzene. Mr. Hawkes first listed the factors affecting the design of an instrument for applications of this sort. These were: (1) accuracy; (2) ease of calibration; (3) stability; (4) ease of maintenance; (5) facility for sample handling; (6) reliability; (7) provision of an output suitable for the control of the process. Passing on to a consideration of the detector itself, he said that the diameter of the orifice leading to the anemometer had an effect on the linearity of the detector. Enlargement of this orifice over a limited range increased both the linear range and the sensitivity. Increase of the carrier gas flow-rate through the cell, on the other hand, gave greater linear range without affecting the sensitivity, and by adjustment of these two parameters a detector having suitable characteristics could be obtained. A plot of gas flow-rate against thermocouple output rose sharply at first and then levelled out and, from a stability point of view, it was best to work in the level region where small changes in flow-rate would not affect the detector response. Other factors controlling the output of the detector were the nature and pressure of the carrier gas and its moisture content.

Mr. Hawkes next described a complete plant control system in which two density balances were utilized. The first of these was used alone as an on-stream detector to monitor continuously the input benzene concentration. In oxidation plants of this type the hydrocarbon reactant is carried through the system in a stream of air and this could be passed through the sample cell of the density balance to give a signal proportional to the benzene concentration. Process air from the same source, but containing no hydrocarbon, was used as reference gas, thus eliminating any response due to water in the carrier. The second detector was used with a column and sample loop to measure input hydrocarbon, output product and impurity concentrations. Use of a single chromatograph, with suitable valve system, for all these purposes avoided difficulties due to differences in sensitivity which might arise with more than one detector. Sample lines from the plant to the chromatograph were steam heated right up to the column oven. This was electrically heated with forced convection in order to achieve control to within 0·1° C with no temperature gradient. Pneumatically controlled solenoid valves were used for gas stream switching and these were normally automatically cam-operated by a programme unit. Results could be displayed on a recorder either as normal chromatograms or in compressed 'bar-graph' form. Concentrations were measured by peak height and, in order to obtain an accuracy within 0·1 per cent, it was necessary to maintain variables to within the following limits: gas flow-rate 0·3 c.c./min; oven temperature 0·1° C; gas pressure 0·4 mm; bridge current 0·002 amp. In order that sample switching and result presentation could be automatic it was also important that retention times of components did not vary by more than 1 sec. This required control of carrier flow-rate to within 1 c.c./min, column temperature within 0·3° C, and column pressure within 7 mm. Mr. Hawkes concluded by saying that he had had a number of instruments using density meters working for some time and had found this detector very satisfactory from the point of view of ease of calibration and stability. Other detectors, such as flame ionization, would, of course, give greater response, but for most of their applications the sensitivity of the density balance was quite adequate.

The second paper was given by Dr. C. S. F. Pine on the subject of "On-line p.p.m. Analysis by Gas Chromatography". He commenced by defining his field as that of direct measurement of substances present in vapour or liquid process streams at concentrations usually less than 100 p.p.m. Preconcentration techniques were generally unsuitable for on-line applications, but their use had become largely unnecessary due to the advent of ionization detectors.

On the use of in-line instruments by Imperial Chemical Industries, Ltd., Dr. Pine said that the first one had been installed in 1955 and used a katharometer detector for the determination of percentage amounts of mixed gaseous hydrocarbons. Their first p.p.m. instrument, installed in 1959, monitored hydrocarbons in oxygen over the range 0–3 p.p.m., sounding an alarm if the concentration rose above 2 p.p.m. This instrument used an argon ionization detector. Since this time instruments had been installed at the rate of about two per year, the earlier ones being home-made, but more recently some commercially produced instruments had also been used. The greatest advance in the development of in-line instruments during this time was the use of reliable automatic sampling valves for injection of liquids and gases. The type now widely employed was the linear movement sliding face valve developed by Imperial Chemical Industries, Ltd. Reasons for the spread of in-line instrumentation included its speed of analysis which was ideal for process control. Prevention of the formation of off-specification products had economic benefits in reducing the amount of repurification necessary. In the intermediate stages of production, on-line analysis detected impurities which might be undesirable or dangerous in later stages.

Discussing the ways in which on-line chromatographs differ from their laboratory counterparts, Dr. Pine listed the following characteristics of control instruments: (*a*) fixed volume samples are used so that the recorder trace can be calibrated in terms of peak height; (*b*) multiple columns with switching and by-pass valves are used to reduce analysis time to a minimum; (*c*) column materials must be stable over a period of at least 12 months; (*d*) electrical circuits are arranged to show only signals from components of interest; (*e*) attenuators are used to adjust the scale range for each component and the recorder is usually started and stopped to give compact 'bar-graph' presentation; (*f*) programming units perform all the repetitive operations, thus necessitating stability of peak elution times; (*g*) lay-out and housing of the units are designed for easy sample handling and to comply with factory safety regulations; (*h*) on-line chromatographs must be designed to operate for long periods with a minimum of maintenance.

On-line p.p.m. analysis could be applied to most organic substances boiling below 300° C, but analysis of permanent gases was not practicable at the moment due to lack of a

satisfactory detector. Concerning the problem of sample injection, Dr. Pine said that satisfactory sliding valves were now available from W. G. Pye, Ltd. With samples in the 1–20 μl. range the valve had sufficient heat capacity to act as an efficient flash vaporizer. Realizable peak height reproducibility was within about 1·5 per cent although the actual volumetric reproducibility of the valve was known to be better than 0·1 per cent in 5 μl. Failure of the sample to evaporate as a compact plug, among other factors, was thought to be responsible for this discrepancy. It would be preferable to work always with vapour samples, but if these were condensable complications arose with accurate pressure and temperature control. The sliding valves were also used, connected in a different manner, for other functions such as back-flushing and column switching. Difficulties often arose in the choice of a suitable stationary phase and in some cases multiple columns using different stationary phases were necessary. The greatest trouble usually arose from the large tailing peak due to the major constituent. If this was the last substance to be eluted time could often be saved by back-flushing it from the column after all the impurities had gone through. When some impurities followed the major constituent and were contaminated by its tail the position was more difficult. The best solution found was to collect the eluent over the period when it contained the impurities and to re-chromatograph this material on another column. The impurity peaks were then often completely resolved from that due to the now much reduced amount of major constituent. Preparation of columns for on-line p.p.m. work required that great care be taken to ensure as complete a removal as possible of volatile impurities and residual solvent. All the columns in present use were of the packed type as capillary columns had been found to lack sufficient long-term stability. In setting up these analysers all carrier gas pipework required to be thoroughly degreased and then baked out *in situ*, sometimes for some weeks, until contamination was reduced to a very low level.

Surveying the present position, Dr. Pine put forward a plea to manufacturers to provide more equipment for this field at a reasonable cost. Application engineering, normally supplied by the manufacturer, might well be left for at least the larger users to provide for themselves with consequent reduction in purchase price. The position was, he said, improving at least so far as American and Continental manufacturers were concerned. He concluded his paper by suggesting that future development might be aimed at increasing speeds of analysis, improving liquid handling techniques, collecting and publishing adequate retention data and developing linear and stable detectors which would extend the applicability of this field of gas chromatography.

Owing to the absence of Mr. J. Mawson, the paper on "Some General Aspects of Process Control with G.L.C. Analysers" could not be given, and it was left for Dr. H. J. Noebels of Beckman Instruments to put forward the view of the manufacturers in a contribution entitled "Applications of Industrial Gas Chromatographs to Process Monitoring and Control". He said that they had considerable experience in this field and that analysis of their instruments sold over the past year showed that 1 in 4 were equipped for continuous control of plant. The first chromatographs of this type were made in 1957, and since then about 2,000 instruments of all manufacturers had moved into the process field. Some six months ago Beckman produced an instrument which incorporated some new and important features. A major difference between process and laboratory instruments was that the latter were controlled by a competent operator who could take into account a number of factors such as varying base-lines. Control instruments, on the other hand, had to work completely alone practically continuously with perhaps, at the most, 2-h maintenance per month. The instrument must therefore be exact, automatic, dependable and capable of providing as short an analysis time as possible.

The last point became even more important when, as sometimes occurred, 5 min was taken for the sample to travel from its point of extraction from the plant stream to the analyser. A process instrument, Dr. Noebels said, must handle complicated streams and often was required to produce results expressed in a number of different ways. It might, for example, be required to estimate C_3, C_4 and C_5 compounds separately but to give a combined figure for C_6–C_{10} compounds. For this reason a considerable amount of stream switching was necessary. The valves utilized for this purpose were similar in design to those described by Dr. Pine and, when used for sample injection, had a lower limit of 1 μl. 'Teflon' was used in their construction for applications below 225° C, and they could be used at pressures of up to 350 lb./in.^{2}. Two types of detector were normally used: (1) four-element katharometer having a sensitivity such that full-scale deflexion was obtained with 50 p.p.m. of acetylene in ethylene; (2) flame ionization detector giving full-scale deflexion for 1 p.p.m. of acetylene in ethylene. Difficulty had been experienced in introducing flame detectors for plant control particularly in refineries, but their high dynamic range made them of great value for process monitoring applications. Dr. Noebels said that it was desirable to keep the number of controls on the front of the instrument as small as possible. Those which required occasional adjustment were mounted inside the case and pre-set, while repetitive operations such as gas flow switching, attenuation adjustment, etc., were carried out by a programme unit. This was normally of the type using magnetic tape but could be replaced by a cam-operated unit for those operators who desired a visual indication of the progress of the control cycle. Columns were heated by circulation of pre-heated air and required to have a life of at least six months with only a very slow change in retention times.

Eight basic column configurations were used: (1) single column; (2) single column with back-flush; (3) single column with back-flush and stripping: this elutes light compounds individually and the heavier ones as a group; (4) dual column: low boiling materials go through to a second column while high boiling compounds are detected after the first; (5) dual column with back-flush; (6) dual column with back-flush and stripping; (7) heart cut column: this was similar to the system described by Dr. Pine for chopping out a portion of the tail of a major peak; (8) 'flip-flop' column. This system comprised three similar sections designated the pre-splitter, storage and regrouping columns which were connected in series in the order given. It could be used for recombining a number of peaks when it was desired to estimate these together. Thus a sample containing substances eluting normally in the order *A*, *B*, *C*, *D*, etc., could be put on the column and allowed to run for a calculated time such that it was known that substance *B* had just entered the regrouping section. At this time fractions *C*, *D* and *E* could be at various points in the centre storage section, and if the flow through this part of the column were now reversed they would pass from it to the regrouping section in the reverse order (*E*, *D*, *C*). Fractions *A* and *B* would therefore emerge normally as separate peaks, but *C*, *D* and *E*, having the same distance to travel to the end of the column as they had each already travelled from the start, would recombine and would emerge as a single peak.

On presentation of results, Dr. Noebels said that 'bar-graph' readings were often insufficient and that a steady-state signal was useful for conversion to a pneumatic output for control of the plant. Such a signal could be obtained by amplification of the detector output and storage in capacitors, one for each component. Of actual analysis, 90 per cent was accomplished by peak height measurements, but integration was sometimes necessary. Features which made the gas chromatograph an ideal

instrument for plant applications were its great speed (three components could be estimated in less than 1 min) and its high sensitivity. Applications had included such things as: (1) estimation of 0–50 p.p.m. of acetylene in benzene; (2) control of phthalic anhydride production; (3) determination of hydrochloric acid, chlorine and phosgene from 'Fluolube' on 'Teflon'; (4) determination of hydrogen in water in the range 0–5 p.p.m.; this estimation could be carried out in 5 min on a 50-μl. sample; (5) heart cut analysis of ethylene; (6) cascade control of distillation columns. He concluded by saying that generally a pay-off time of one year could be considered a good application of instrumentation.

C. D'Oyly-Watkins

PLACE OF BIOCHEMISTRY IN THE NEW UNIVERSITIES

At the Middlesex Hospital Medical School on April 16, the Biochemical Society held an evening discussion on "The Place of Biochemistry in the New Universities", a topic which aroused considerable interest and not a little feeling. In framing the discussion it had been agreed not to limit it strictly to the new universities but to include all universities in which biochemistry had only recently been introduced or was about to be taught.

Sir Rudolph Peters took the chair and, in the course of his opening remarks, pointed out that nowadays many aspects of biochemistry masqueraded under other titles. The new term 'molecular biology' had been introduced by Astbury and was, perhaps, valuable for getting money, but the claim that biochemistry only dealt with small molecules was just not true—we had always dealt with substances like proteins. With the present ramifications of biochemistry it was especially pertinent to discuss its role in the new universities.

Prof. R. A. Morton (Liverpool), under the title of "Biochemistry—Past and Present", traced the development of biochemistry with special reference to universities where the subject is now firmly established. The first department of biochemistry in Great Britain was founded at Liverpool in 1906, the inspiration of the department and of biochemistry in general at that time being derived from work on vitamins and nutrition. This and other departments were first set up in faculties of medicine, for it was from this direction that the need for teaching and research first arose. Very few honours courses in science faculties were started before 1939, but since the War the number of such courses had multiplied rapidly so that to-day most recruits to the subject have been trained as biochemists.

Over the years, the courses for medical, dental and veterinary students have changed and continue to do so. Although in the teaching, applications are not forgotten, they are subordinated to the need to expound the basic principles of biochemistry so that, for example, the clinical aspects of the subject come later from specialists.

Prof. Morton stressed that the biochemist should be competent in chemistry but must also have biological training and insight. Much had been achieved in the past, and no doubt would be in the future, by those who had detected, isolated and determined the structure of metabolites. Theories, for example, of photosynthesis or oxidative phosphorylation could be elegant even with an incomplete roll-call, but truer theories follow a full muster of the molecular species engaged—whether in biosynthesis or enzymatic mechanisms.

Biochemistry is now a central part of many curricula in biology. The sharp boundaries between sciences have gone; trespassing invokes only a shrug and territories are 'invaded' without apology. Chemistry, biochemistry and microbiology interpenetrate, and terms like genetics, biochemical pharmacology, neurobiochemistry and biochemical systematics all point to unification within diversity. This calls for psychological readjustment and reconstruction of teaching, organization and administration, on a scale easier to realize in a new university than an established one. There must be flexibility, perhaps, especially in M.Sc. courses. Prof. Morton emphasized that there is, however, a hard core of biochemistry which cannot safely be watered down.

In a period of expansion the penury of the past was easily forgotten, but it may be more difficult to sustain the peculiar excellence which raises university studies above the trivial.

In the subsequent discussion, Prof. J. N. Davidson (Glasgow) pointed out that biochemistry has tended always to suffer from being a hybrid subject. It grew up under the wing of physiology in most universities (occasionally under pathology) and only within recent years has begun to lead an adult independent life as a scientific discipline in its own right, rather than merely as a subdivision of some other subject. However, there are now disturbing trends. The chemists, who used to despise it, are now beginning to realize its importance and are tending to say that biochemistry should certainly be developed in all universities, but only as part of the chemistry department.

The biologists are belatedly taking an interest in biochemistry and are tending to follow the same unfortunate course as the chemists. By showing less interest in taxonomy and ecology and a greater interest in cell biology, they have realized that they cannot go very far in any biological discipline without biochemical help and they are therefore tending to say biochemistry must certainly be developed, but only as a part of a biological department.

Prof. Davidson went on to say that he was all in favour of breaking down barriers between sciences and of having the utmost collaboration between representatives of different disciplines, but was utterly opposed to the trend that biochemists may develop into mere laboratory assistants helping 'big brother biologist' to solve his problems.

Prof. E. A. Dawes (Hull) then presented the results of a survey he had made on present and future developments in Britain with particular reference to the place of biochemistry in the development of biological sciences in the new universities. There are seven new universities in England of which five have either planned or already initiated biological studies, and a sixth has it under active consideration. In Scotland, at the new University of Strathclyde, existing biology departments of the Glasgow Royal College of Science and Technology are to become part of a School of Biological Sciences, housed together in a separate new building and offering honours degrees in biochemistry, food science, biology, microbiology and general biological sciences.

The development of biological sciences in the new English universities has, without exception, followed the suggestion of the *ad hoc* Committee of the Royal Society (*Ann. Rep. Advisory Council on Scientific Policy, 1961–62*, H.M.S.O., 1963) that multi-professorial departments be created and under the one roof a variety of different biological disciplines be represented. East Anglia, at present, is the only school to have started teaching along these lines; Sussex and York both commence