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MASTER

FINAL REPORT

on

"RESOLUTION IN CHROMATOGRAPHY"

ATOMIC ENERGY COMMISSION

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J. CALVIN GIDDINGS--PRINCIPAL INVESTIGATOR

work carried out in the Department of Chemistry

RELEASED FOR ANNOUNCEMENT
IN NUCLEAR SCIENCE ABSTRACTS

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This document is the final report submitted under A. E. C. contract No. AT(11-1)-748, and is a summary of the major research accomplishments between April 1, 1959 and March 31, 1965. Throughout the six year period four major areas were extensively investigated and a number of experiments relating to each performed. These areas were:

1. Study of the basic chromatographic processes.
2. Investigation of the optimum parameters in chromatography.
3. The effects of temperature and temperature programming.
4. Preparative scale operation.

In each of the following sections these areas will be dealt with in detail with primary emphasis on the results achieved. For additional details the interim progress reports and the thirty-one technical publications resulting from this research may be consulted.

Study of the basic chromatographic processes. A complete interpretation of chromatographic results requires knowledge of the factors influencing both the migration parameter R , determining the time of appearance of a zone, and the plate height H , a parameter relating to the width of a zone. A number of complex kinetic processes were studied in detail and a method for finding the influence of each on the plate height was developed (2). This method, based on an assumption of near-equilibrium, makes possible the isolation of several effects such as large-molecule adsorption within the column, consecutive reactions such as adsorption and diffusion in the mobile and stationary phases, and other reactions such as decomposition, interconversion, and catalysis that may

effect of eddy diffusion on plate height was considerably less than previously predicted by other means.

Various partition mechanisms in gas chromatography were also extensively researched and with the aid of several models a number of expressions were derived for the roles of gas phase and liquid phase diffusion as rate controlling steps (9). Strongly related to partition phenomena are the thermodynamic states of the gas, liquid, and solid phases contained within the column (30). In the case of gas liquid chromatography an analysis of the complex distribution of the liquid phase was made resulting in the "General Combination Law," which can be applied directly to solve practical problems of micro-geometry in chromatographic column materials (22). The effects of packing uniformity and adsorption on plate height were also discussed.

In the case of gas solid chromatography a simplified model was used for a theoretical analysis of nonequilibrium (8) which eventually led to development of a rather complete theory of kinetic effects in adsorption chromatography for packed and capillary columns (25).

Due to a great number of published speculations, but no quantitative data, work was also initiated to measure vapor pressures of several stationary phases on solid supports in gas liquid chromatography and to determine the effect of liquid phase concentration on thermodynamic properties of the solvent (29). The results confirmed previous theoretical predictions from this laboratory that at most practical loadings the properties of the stationary phase liquid within the pores of the

of large diameter columns.

Progress in the research of optimum conditions for separation led to a mathematical formulation of a new function: "The separation per unit length" (7). It was shown that when minimized with respect to a number of operating parameters, this function provides a rapid means of estimating optimum conditions for separability.

Efforts were also concentrated on a theoretical study of the simultaneous reduction of temperature and liquid load in an attempt to extend the range and capabilities of gas chromatography (17). A mathematical treatment of liquid geometry was included in this study. The arguments and equations presented indicated that optimum conditions for separation could be best achieved with low load and low temperature columns.

The first extensive and thorough analysis of the significance of pressure drops in chromatography columns was attempted and completed, resulting in the conclusion, contrary to previous widespread beliefs, that pressure drop by itself has very little adverse effect on resolution (24).

The greatest effort expended in research on optimum conditions dealt with the problems of analysis speed in gas chromatography and in suggesting methods and instrumentation capable of greatly reducing analysis time. These studies were initiated during 1961 and were continued in 1963, 64, and 65. A number of equations resulting from theoretical studies were derived and used to show that for greatest separation speed in gas chromatography the column outlet should be held under vacuum

effect on plate height and retention is temperature. Its investigation assumed two courses: 1) the study of thermodynamic aspects of gas chromatography wherein a number of new standard states were defined and several previous misinterpretations were corrected; 2) an extensive theoretical investigation of programmed temperature gas chromatography (PTGC), a technique closely related to isothermal gas chromatography, but possessing a unique feature of controlled temperature rise. A theoretical analysis of retention times, retention temperatures, and changes in heating rate, column length, etc. in PTGC was presented and illustrated with several examples and calculations (6). The results led to a formulation of a new and more meaningful definition of plate height--one considerably different than its counterpart in iso-thermal gas chromatography, but more useful in predicting effects on separability unique to programmed temperature gas chromatography (10,16).

For the nonmathematically inclined laboratory analyst or instrument operator an elementary theory of PTGC was developed. This theory made possible correlations of widely diverse separation problems and suggested that isothermal data may be used in predicting optimum parameters in routine PTGC experiments (10,19). With aid of the non-equilibrium theory for plate height calculations in chromatography, effects of zone compression and thermal lag were also investigated (16). In addition a new equation for the "significant temperature" was formulated to allow comparisons of the effectiveness of PTGC with iso-thermal techniques (19).

Preparative scale operation. Extension of gas chromatography as an

analytical tool to one useful for large scale preparative separations was the subject of considerable theoretical and experimental research which led to isolation of numerous sources of resolution loss in large columns and to the conceptual development of a unique large scale column (11). An initial theoretical study of scale-up effects, completed during 1962, showed that no less than ten factors were responsible for resolution loss when the column diameter was increased and that additional sources of loss, attributed to end effects, small diameter linkages, and multiple columns, may also be expected (20). An experimental program was initiated to verify some of these results and to provide further insight for the development of improved techniques (28).

An extensive theoretical investigation, based on the generalized non-equilibrium theory, was initiated in 1963 and led to an expression of zone spreading, or smearing, as a function of the velocity profile in the column cross section (21). For direct application to large scale gas chromatography a number of simple approximations to relate variations in retention within the column cross-section were also derived.

In addition an apparatus to study particle size distribution within large columns was assembled and numerous experiments, designed to correlate packing variations with velocity gradients, were performed (14). The results indicated that packing variations could be eliminated by several means, including one that is uniquely promising--a method wherein the annular space between two concentric cylinders is used to store the packing material.

To further aid experimental studies of large scale operation a 96 cubic foot constant temperature air box was constructed. This was used in conjunction with multi-channel detecting, amplifying, and recording equipment. This equipment makes possible the investigation of very large columns (up to 1 foot in diameter and 10 feet long) and promises to be a versatile tool for complex large scale experiments.

Initial studies, involving 2" diameter columns, have been completed and, in light of simple theoretical principles, interpreted to yield two significant conclusions (28): 1) many parameters relevant to preparative scale gas chromatography can be seen with this equipment and 2) the highly important "non-uniformity factor" can be quantitatively isolated and in fact is surprisingly close to a value predicted by a simple theoretical model. Similar experiments performed to date with a 4" diameter, 3 foot column have substantiated previous observations that packing uniformity within large scale columns is unpredictable at best.

SCIENTIFIC TRAINING

An indirect benefit of AEC support was the training of young scientists. Included in the latter are eight postdoctorals, four graduate students and three undergraduates, all of whom spent time with this project.

Included in the postdoctorals are Dr. George Stewart, now department chairman at Gonzaga University; Dr. Paul D. Schettler, a Yale graduate still doing postdoctoral work; Dr. Stephen Hawkes, now Assistant Professor of Chemistry at Brigham Young University; Dr. Keith Ensley, Assistant Professor of Chemistry, Montana College of Mineral Science and Technology; Dr. Gordon Jensen, now at United Technology Corporation, Santa Clara, California; Dr. Kanai Mallik, here again from India for additional work; Dr. D. W. Emerich, Professor of Chemistry at Mississippi State College; and Dr. H. Y. Chen, now working with an industrial firm in the East.

Graduate students who were trained in whole or part on this project are Dr. Spencer L. Seager, Assistant Professor of Chemistry at Weber State College; Dr. Marcus N. Myers, now doing postdoctoral work; Mr. Edward N. Fuller and Miss Margo Eikelburger.

Science undergraduates getting research training were Mr. Larry Stucki, now a graduate student at UCLA; Mr. Richard Robison, now a graduate student in Molecular Biology and Mr. Chris Russell.

PUBLICATIONS

1. "Influence of Pressure Gradients on Resolution in Gas Chromatography," G. H. Stewart, S. L. Seager, and J. C. Giddings, Anal. Chem., 31, 1738 (1959).
2. "Nonequilibrium Kinetics and Chromatography," J. C. Giddings, J. Chem. Phys., 31 1462 (1959).
3. "Kinetic Processes and Zone Diffusion in Chromatography," J. C. Giddings, J. Chromatog., 3, 443 (1960).
4. "Plate Height in Gas Chromatography," J. C. Giddings, S. L. Seager, L. R. Stucki and G. H. Stewart, Anal. Chem., 32, 867 (1960).
5. "Coiled Columns and Resolution in Gas Chromatography," J. C. Giddings, J. Chromatog., 3, 520 (1960).
6. "Retention Times in Programmed Temperature Gas Chromatography," J. C. Giddings, J. Chromatog., 4, 11 (1960).
7. "Optimum Conditions for Separation in Gas Chromatography," J. C. Giddings, Anal. Chem., 32, 1707 (1960).
8. "Theoretical Basis for Kinetic Effects in Gas-Solid Chromatography," J. C. Giddings, Nature, 188, 847 (1960).
9. "Lateral Diffusion and Local Nonequilibrium in Gas Chromatography," J. C. Giddings, J. Chromatog., 5, 61 (1961).
10. "Theory of Programmed Temperature Gas Chromatography: The Prediction of Optimum Parameters," J. C. Giddings, Gas Chromatography 1962, Academic Press Inc., New York, New York.
11. "Theoretical Basis for a Continuous, Large-Capacity Gas Chromatographic Apparatus," J. C. Giddings, Anal. Chem., 34, 37 (1962).
12. "The Role of Pressure Gradients in Obtaining Minimum Time in Gas Chromatography," J. C. Giddings, Nature, 191, 1291 (1961).
13. "Theory of Minimum Time Operation in Gas Chromatography," J. C. Giddings, Anal. Chem., 34, 314 (1962).
14. "Particle Size Nonuniformity in Large Scale Columns," J. C. Giddings and E. N. Fuller, J. Chromatog., 7, 255 (1962).
15. "Failure of the Eddy Diffusion Concept of Gas Chromatography," J. C. Giddings and R. A. Robison, Anal. Chem., 34, 885 (1962).

16. "Plate Height Theory of Programmed Temperature Gas Chromatography," J. C. Giddings, Anal. Chem., 34, 722 (1962).
17. "Theoretical Investigation of Low Liquid Load and Low Temperature Operation in Gas Chromatography," J. C. Giddings, Anal. Chim. Acta., 27, 207 (1962).
18. "Comparison of Theoretical and Experimental Efficiencies in Glass Bead GC Columns," J. C. Giddings, K. L. Mallik, M. Eikelburger, Anal. Chem., 34, 1026 (1962).
19. "Elementary Theory of Programmed Temperature Gas Chromatography," J. C. Giddings, J. Chem. Ed., 39, 569 (1962).
20. "Principles of Column Performance in Large Scale Gas Chromatography," J. C. Giddings, J. Gas Chromatog., 1, 1, 12 (1963).
21. "Generalized Nonequilibrium Theory of Plate Height in Large-Scale Gas Chromatography," J. C. Giddings, J. Gas Chromatog. 1, 4, 38 (1963).
22. "General Combination Law for C Terms in Gas Chromatography," J. C. Giddings, J. of Phys. Chem., 68, 184 (1964).
23. "Evidence on the Nature of Eddy Diffusion in Gas Chromatography from Inert (Non-Sorbing) Column Data," J. C. Giddings, Anal. Chem., 35, 1338 (1963).
24. "Role of Column Pressure Drop in Gas Chromatographic Resolution," J. C. Giddings, Anal. Chem., 36, 741 (1964).
25. "Theory of Gas-Solid Chromatography: Potential for Analytical Use and the Study of Surface Kinetics," J. C. Giddings, Anal. Chem., 36, 1170 (1964).
26. "Measurement and Interpretation of the C Terms of Gas Chromatography," J. C. Giddings and P. D. Schettler, Anal. Chem., 36, 1483 (1964).
27. "Comparison of the Theoretical Limit of Separating Speed in Gas and Liquid Chromatography," J. C. Giddings, Anal. Chem., 37, 60 (1965).
28. "Experimental Verification of Plate-Height Abnormalities in Preparative-Scale GC," J. C. Giddings, G. E. Jensen, J. Gas Chromatog., 2, 290 (1964).

29. "Vapor Pressure of Stationary Phases over Gas Chromatographic Supports," Stephen J. Hawkes and J. C. Giddings, Anal. Chem., 36, 2229 (1964).
30. "Thermodynamic Pitfalls in Gas Chromatography," M. R. James, J. C. Giddings, and R. A. Keller, J. Gas Chromatog., 3, 57 (1965).
31. "Evidence on the Effect of Column-to-Particle Diameter Ratio in Gas Chromatography," P. D. Schettler, C. P. Russell, J. C. Giddings, Anal. Chem., 37, 609 (1965).