

HIGH-VACUUM SHORT-PATH DISTILLATION—A REVIEW¹

K. C. D. HICKMAN

Laboratories of Distillation Products, Inc., Rochester, New York

Received September 13, 1943

CONTENTS

Part I

I. Introductory	51
II. Definitive	52
III. Historical	53
IV. Evolution and design of the high-vacuum surface still	59
A. The falling-film still	60
B. The centrifugal still	63
V. A comparison of film thickness	69
VI. The quiet distilland layer	73
VII. Relative still performance	74
A. Fractionation	75
B. Rate of distillation	75
C. Projective <i>vs.</i> equilibrant distillation	76
D. Partial condensation	77
E. Thermal balance in the molecular still	79
VIII. Contributory technique	80
A. Vacuum pumps	80
B. Pressure measurements	82
IX. Future and scope of short-path distillation	84

Part II

I. Applications of molecular distillation	84
II. Applications of the elimination-curve technique	95
III. Qualitative laboratory distillations	103
IV. Future of the method	103

I. INTRODUCTORY

This article traces the evolution of the short-path high-vacuum still with its growing technique and applications and attempts to offer a coherent story rather than a review of the whole field. The extended material is available in the bibliographies of Detwiler (23), in summaries by Burch (13), Fawcett (37), Burrows (16), Waterman (107), and again Detwiler (24), and in the rapidly expanding patent literature.²

The conditions for unobstructed distillation are simplicity itself, but they have led to an increasingly complicated and difficult practice. The process is no longer a new invention; it has become a self-contained technology, a school of

¹ Communication No. 54 from the Laboratories of Distillation Products, Inc. This article was completed in 1941, except for minor revisions.

² As we write, a compilation by D. D. Howat has appeared in *Chemical Age*, December, 1941-January, 1942.

thought. Three main branches have arisen, the Dutch under Waterman, the British inspired by Burch and Fawcett, and the American, first established at Kodak Park (52) and now transferred to Distillation Products, Inc. The European schools have summarized their technique; this paper stresses the methods of the Rochester group.

II. DEFINITIVE

Molecules are perpetually evaporating from liquids and solids. The number departing from the surface has been derived by Langmuir (80) from an equation introduced by Knudsen (77) which, in turn, was founded on the Maxwell-Boltzmann law:

$$n = \frac{ps}{\sqrt{2\pi MRT}} \quad (1)$$

when p , S , R , and T are the vapor pressure, the area, the gas constant, and the temperature, in appropriate units³. A square meter of platinum is unlikely to emit a molecule in many years. The same area of propyl phthalate loses about

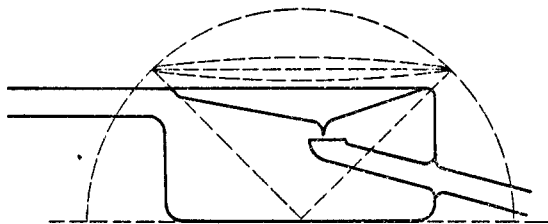


FIG. 1. Simple glass pot still showing cone of effective evaporation

2.5×10^{21} molecules or a cubic centimeter of liquid each second at 2 microns, which is approximately the vapor pressure of this substance at 25°C. Water ejects molecules so readily that the same relative quantity will evaporate even at the low temperature of dry ice. That water does not gasify spontaneously and propyl phthalate behaves as a fixed liquid is due to the surrounding atmosphere which knocks most of the molecules back into the surface. To secure active distillation, heat is used to increase the number and energy of evaporated molecules until they can drive away the obstructing gas and reach the condenser.

Distillation occurs at the lowest possible temperature when there is a complete absence of obstruction (mechanical obstacles or foreign gas), conditions typified by a drop of liquid evaporating freely into interstellar space. This ideal could be realized in the laboratory by placing a heated drop of liquid within a completely evacuated vessel with walls cooled sufficiently for every molecule striking them to condense. J. C. Hecker⁴ has simulated the arrangement by suspending the liquid in a spiral of electrically heated wire in an evacuated vessel. The liquid is held by surface tension and is free to evaporate in all directions not

³ Formulae in units useful to the chemist are given on page 75.

⁴ Patent applied for.

occupied by the wire. A simpler but less perfect interpretation of unobstructed evaporation is given by the laboratory pot still illustrated in figure 1. Liquid is heated in a shallow glass vessel connected with powerful vacuum pumps. Evaporation occurs without hindrance except by the sides of the vessel which prevent about half the molecules at any moment from condensing on the ceiling, whence they can be collected.

The process of free transfer under high vacuum from evaporator to condenser is known as *unobstructed-path* distillation; when the distance of transfer is comparable with the mean free path (75) of the vapor molecules in the residual gas, it is known as *molecular* distillation. The processes deserve attention because they are the simplest of all kinds of distillation; they occur at the lowest temperature and involve the least thermal decomposition. They make possible and therefore inevitable a revolution in the technology of one of the world's most plentiful raw materials,—the natural oils, fats, and waxes which hitherto have been considered undistillable.

III. HISTORICAL

The modern high-vacuum still has evolved gradually from the laboratory vacuum distillation train consisting of flask, condenser, receiver, manometer, and water ejector or mechanical pump. Chemists attempting to operate such apparatus at about 5 mm. of mercury found that further reduction of pressure in the receiver produced little increase in the rate of distillation or lowering in the readings of the thermometer placed in the neck of the flask (70). Minor variations in the design of the apparatus and in the supply of heat to the flask produced major alterations in the temperature and rate of distillation, a condition which resulted in elaborate instructions being issued to petroleum chemists for the standardization of distillation procedure. Substances of molecular weight above 300 could seldom be distilled, and a wide range of natural materials including heavy petroleum residues, vegetable and animal fats and their component fatty acids, and the natural waxes were all debarred from distillation. With improvement in vacuum technique it became appreciated that the bar to distillation was no longer the attainment of a sufficiently low pressure in the receiver but the resistance to the flow of vapor exerted by the neck and side arm of the distillation flask. The pressure of vapor in the flask was higher than the pressure in the receiver, causing decomposition and giving a false correlation between pressure and temperature, that is to say, the wrong boiling point. The state of affairs is illustrated in figure 2.

A quantitative key to the difficulties could have been found in the researches of M. Knudsen (76), who showed that the transfer of gases through tubes changes in kind and quantity at very low pressures. The transmission coefficient alters from one containing the viscosity of the gas and the fourth power of the diameter of the tubes, according to the laws of Poiseuille (84)

$$q = f \left[\frac{D^4}{\eta L} \right] \cdot p(p_2 - p_1) \quad (2)$$

to one containing the third power and independent of viscosity.

$$q = f \left[\frac{D^3}{L} \right] (p_2 - p) \quad (3)$$

The second equation is limited in its application by the double condition that the diameter of the tube must be small in comparison with the mean free path and with distances in which much change occurs in the density of the gas. There are end corrections which can be neglected only if the tubes are long. Although the volumetric transfer remains considerable, the weight of gases transported under high vacuum was found to decrease to extremely low levels. Thus, the newly introduced mechanical oil pumps would reduce the pressure to less than a

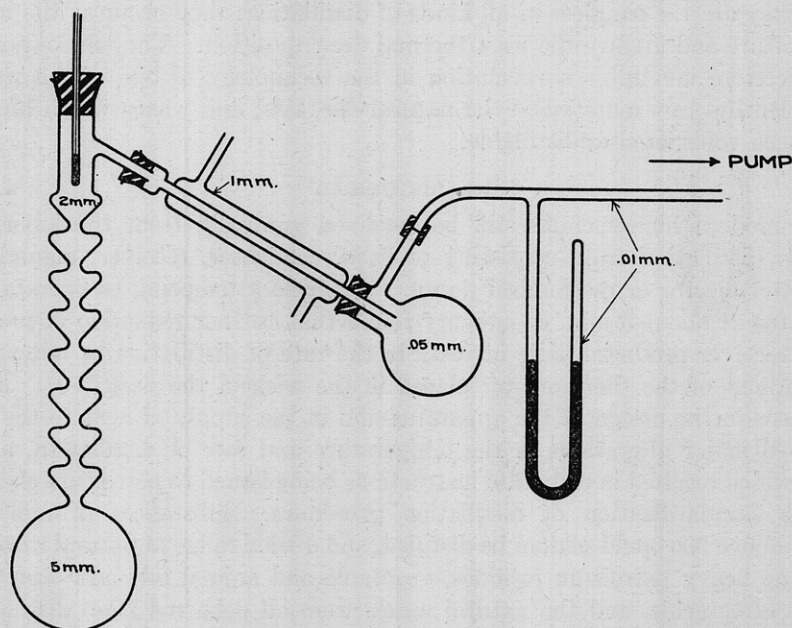


FIG. 2. Diagram of ordinary laboratory vacuum distillation apparatus showing probable pressures during distillation.

hundredth of a millimeter in the boiler of a laboratory vacuum distillation train, but the factor $(p_2 - p_1)$ in equation 2 representing the difference in pressure in the boiler and receiver became so small that the collection of distillate was prohibitively slow in apparatus of conventional design. Distillation done at these real pressures would take years and could be quickened only by (1) abandoning the low pressure and hence increasing the temperature and decomposition in the boiler, or (2) by redesigning the apparatus. It is this redesign of stills and the technique and consequences of their use which is the subject of this article.

The origins of open-path distillation stretch further back with each search of the literature. Detwiler's recent mimeographed abstracts (24) credit Krafft (79), Chevreul (21), and Caldwell and Hurtley (18) with being the first to harness

the x-ray vacuum to the laboratory still. Their methods remained unadopted by contemporary chemists, and it was not until the decade ending in 1920 that distillation equipment was designed with wide-necked flasks fitted with abnormally wide side arms (34) and much advantage was secured. (A recent version of the high-vacuum pot still (73) is shown in figure 3.) In the early 1920's German workers lowered into the distillation vessels condensers having trays (99)

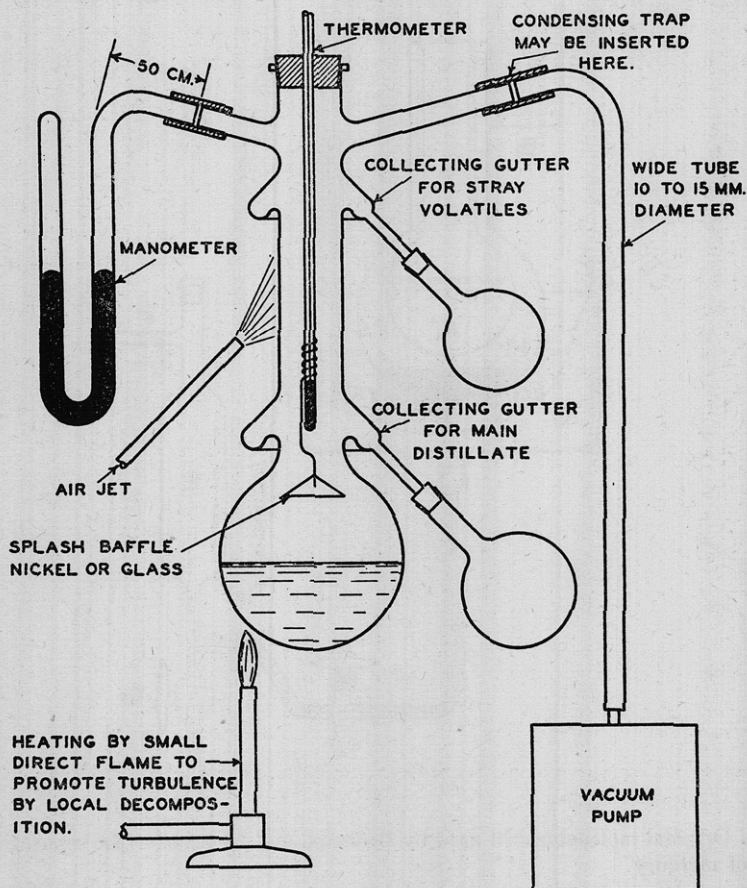


FIG. 3. High-vacuum pot still assembly

or umbrella-like lobes (103) to catch some distillate. The field was explored intensively by Waterman and coworkers (102) at Delft. About this time Brönsted and Hevesy, in order to separate the isotopes of mercury (10) by utilizing those distillation characteristics which depend on molecular weight as well as vapor pressure, produced a truly molecular still. A pool of mercury (figure 4) was allowed to evaporate slowly in high vacuum and condense upon the surface of a bulb cooled with liquid air and held just above the evaporating mercury. In the middle 1920's C. R. Burch (11) began experiments in high-

vacuum distillation. It is apparent that his experiments originated with an evaporative still and did not begin with study of conventional apparatus. Burch was one of the earliest if not the first worker to employ the Langmuir mercury condensation pump for producing the high vacuum in a still. Burch (12) examined the residue from petroleum refineries and demonstrated that he could distill a substantial proportion of this hitherto undistillable mixture. From vaseline he produced mobile liquid fractions of high molecular weights

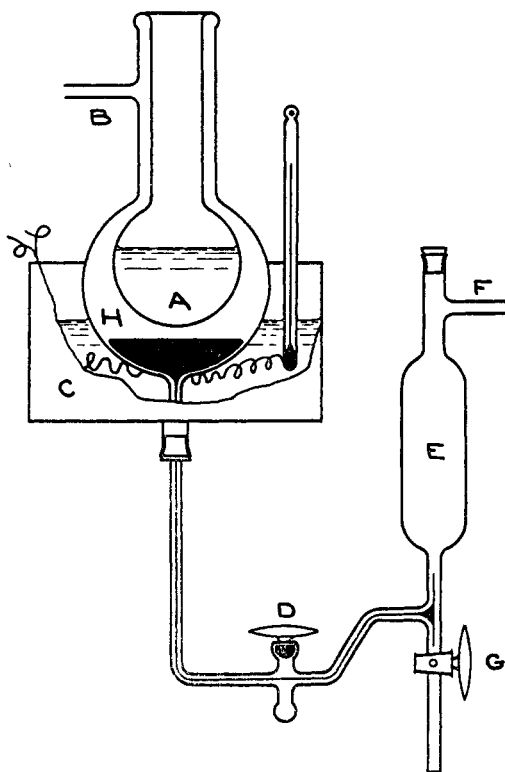


FIG. 4. Original molecular still used by Brönsted and Hevesy for the separation of the isotopes of mercury.

and exceedingly low vapor pressure. He introduced these as the first practical substitute for mercury to operate the Langmuir pump (81). In Langmuir's original patent (82) many liquids were mentioned for use in a diffusion pump, with mercury chosen as the most useful. Other inventors (72) suggested tin, potassium, sodium, etc., and even sulfuric acid as actuating liquids. Not only were Burch's hydrocarbons, now represented by the well-known Apiezon oils, the first serious substitute for mercury, but these oils and certain pure esters (5) devised for the same purpose have all but replaced mercury in high-vacuum pumps (51).

The molecular still of Burch's early experiments is shown in figure 5. An electrically heated tray was held within a glass vacuum-tight condenser which surrounded it entirely and was connected by a short wide tube to a condensation pump of diameter commensurate with the apparatus. In this simple assembly may be observed two of the cardinal points of a good molecular still: namely, that the condenser and evaporator shall be coëmbasive, without intervening obstruction, and that the pump and admittance of the connecting tubes shall be large. It is interesting to note in many of the more complicated (108) and otherwise more efficient stills (25) built later that these requirements have not at first been met. The pumps and connecting manifold may well be as big as the still, a generalization which follows from Knudsen's measurements of gas flow in high vacuum (76, 84). Burch's experiments were translated into an industrial high-vacuum technology which was expounded in British (14) and later American (15) patents, where natural molecular paths were equated to the design and dimensions of the apparatus through the kinetic theory of gases. The data

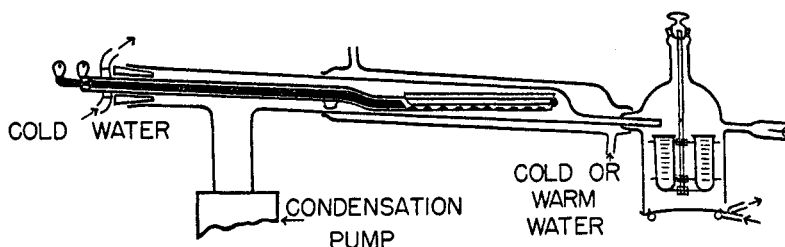


FIG. 5. Burch's flat-tray still first used to distill heavy petroleum residues

have indeed served as a textbook for later workers in the field. Burch's efforts were continued by a group of inventors (24), including Bancroft, Burrows, Fawcett, Sykes, Vigers and collaborators working in the laboratories of Metropolitan-Vickers Electrical Co., Ltd., and Imperial Chemical Industries, Limited. Whilst their endeavors were taking shape, Waterman with Elsbach, Oosterhof, van Vlodrop, and others at the University of Delft were progressing with the application of various pieces of high-vacuum equipment from the early distillation of cocoanut oil (105) to the study of drying oils (106). Although Waterman had at no time made the clear, sharp-cut statement of invention achieved by Burch, he and his school would appear to have done some of the earliest really high-vacuum distillation of natural oils (see, also, references 18, 21, and 79).

At about the time of these experiments a still was erected designed to produce some tons of heavy petroleum distillate daily (13), a development which was reflected in occasional short-path distillations done in American petroleum laboratories (109), although there is no record that the molecular still has reached commercial application in the petroleum industry either here or abroad. In America also three other groups were keenly interested in the high-vacuum

method. Carothers and Hill performed distillations and chemical reactions such as polymerization, with dehydration, in surface stills (19). Washburn at the Bureau of Standards made deductions of speed of distillation and degree of separation likely to be secured during the distillation of binary mixtures (101). The Kodak laboratories were the scene of experiments which had been started in 1928 on the distillation of plasticizers for motion picture film (49). The development of apparatus paralleled that of the German workers, beginning with low wide flasks (see figure 3) having vertical condensers and catchment rings, which were superseded by various kinds of pot stills (50, 69). A selection of pot stills designed by Kodak and other workers is given in figure 6.

In late 1930, a glass falling-film still was constructed in the author's laboratory and was used to repeat earlier experiments on the distillation of free vitamin D

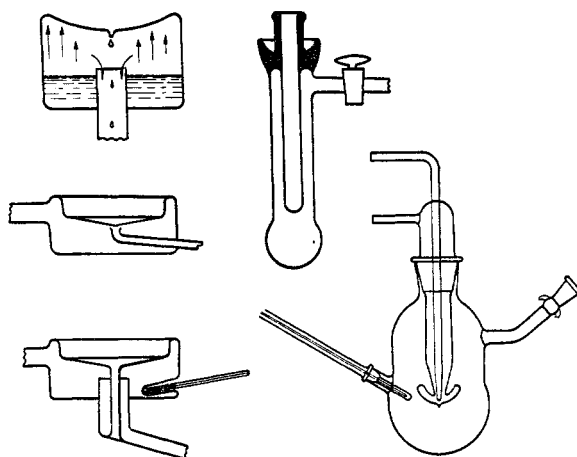


FIG. 6. Various glass pot stills

and esterified vitamin A from fish liver oils (59). Through the recommendation of M. H. Wodlinger the commercial possibilities of fish liver oil distillates came to interest General Mills, Inc., and in 1934 a joint project with the Eastman Kodak Company was launched to develop industrial short-path distillation. Concurrently in England, Carr and coworkers at British Drug Houses had commercialized the molecular purification of free vitamin A produced by the saponification of fish liver oils (20). A distillate secured by them in 1932 was by far the most potent preparation of vitamin A hitherto obtained and was then thought to represent the nearly pure product.

During the period from 1932-1936 Waterman (89, 104), and Fawcett *et al.* (41) severally explored the production of stand oils by the distillation of polymerized oils of high iodine value to remove the unpolymerized portion. The many important advances which resulted from this work have been abstracted by Detwiler (24), to whom the reader is referred. The work has been expanded by R. S. Morse (88) and successors at Distillation Products, Inc. Fawcett (36)

found that while most natural oils can be distilled in crude form, they are handled more readily if given a preliminary wet treatment to precipitate the proteins, phospholipides, glucosides, etc., which otherwise mar the hot columns.

Although the technology of short-path distillation was still far from complete, the question by 1935 had become not so much "how" as "what" to distill. The answer then was, "Valuable materials that can carry the cost of a partially developed process, extravagant in the use of apparatus and power." This criterion until recently has disposed of ventures into the petroleum and paint oil fields and left the concentration of the oil-soluble vitamins as the chief patron of the new art.

IV. EVOLUTION AND DESIGN OF THE HIGH-VACUUM SURFACE STILL

The short-path distillation of a constituent from a mixture occurs in four stages: (1) travel of the desired component from the body of the liquid to the surface; (2) distillation from the surface; (3) travel across the vapor gap; (4) condensation. Stages 2 and 3, which will be examined later, are readily facilitated by the proper temperature and vacuum, and stage 4 may be neglected because with substances which wet the condenser and with temperature differences contemplated in this article condensation is virtually complete. Stage 1, arrival at the surface, can become a limiting factor to such an extent that the design of the vacuum surface-still follows chiefly the requirements of the distilland layer.

Renewal of the surface occurs fairly rapidly under ebulliative distillation at normal pressures so that it is sometimes unnecessary to consider this factor in design. As the pressure falls and the molecular weight and viscosity of the distilland increase and as ebulliative distillation gives place to quiet surface evaporation, the bringing of the desired component to the surface becomes a major concern. A function of the highly efficient columns of the Podbielniak type is to delay exit of the vapors until all the chosen constituent has been evolved from the distilland. Under certain conditions this function is as important as sorting out the vapors after evaporation. In the evaporative still, surface renewal is at its slowest and there is no ready means for delaying the evaporation of unwanted constituents. It is imperative to keep the layer of distilland as thin as possible.

There is a second reason for a shallow distilland—decomposition. Thermal destruction can follow a number of courses, one of which terminates in explosion. More usually decomposition is a smooth function of temperature over a wide range, so that the loss of material is determined by temperature and the time of exposure. Therefore, although the establishment of molecular conditions surrounding the distilland may have reduced the *rate* of thermal destruction to an irreducible minimum, there remains almost unlimited scope for reducing actual destruction by diminishing the time of exposure. The need to renew the surface and the need to reduce decomposition both demand a flash-boiler which can operate with the thinnest film of distilland.

The first attempts to use thinner layers and better stirring than was feasible with pot stills were made by Burch and Bancroft (14), who allowed the distil-

land to wander through a series of trays, as in figure 7, supported within a cooled and evacuated cylinder. The evaporation from some of the trays was used to assist vacuum production and thus promote evaporation from other of the trays in a "self-pumping" still (see page 78). That this multiple arrangement gave better separations than a single tray showed that stirring had become an important factor.

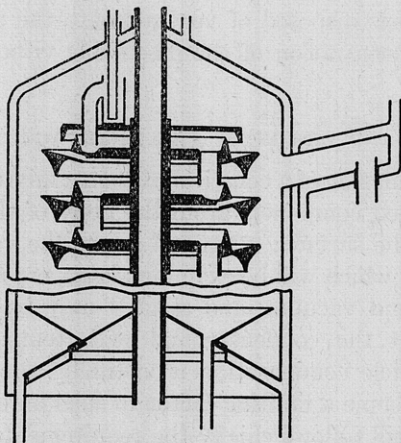


FIG. 7. Cascade tray still of Burch and Bancroft

A. *The falling-film still*

The next development was the falling-film still. The distilland is allowed to flow by gravity down a hot vertical surface on which it spreads in a layer generally 0.1–1.0 mm. thick according to viscosity and rate of feed. In figure 8 is shown the apparatus first used for separating vitamins A and D in the Kodak laboratory. This still is typical both as to virtues and faults of others (25, 104) described about this time. Since with minor alterations, such as increase in size of pumps and vacuum ducts, it embodies everything necessary for efficient laboratory distillation, a paragraph may be devoted to its description. The material to be distilled is admitted from reservoir A through a flow meter, sight glass, dropping pipet or other device, B, to a preheating tube, C, whence it enters the "explosion bulb," D, which bulb may be attached to the laboratory water pump or preferably to a single-stage mechanical pump at E. In the latter case a dry-ice trap may be interposed in the line. This is convenient when the preparation contains traces of solvents remaining from another operation. It is possible to allow the oil to enter the still directly, but it is preferable to provide another stage of degassing, F, which may be connected with the vacuum line servicing the condensation pump, G, attached to the main part of the still. The still itself consists of a central heated column, H, surrounded by a transparent condenser, K. The spent distilland flows into the reservoir, L, and the distillate into the receiver, M.

Much has been written concerning the best surface for spreading the distilland. Where moderate rates of flow—e.g., 0.15 cc. per square decimeter per second—are involved, glass or polished chromium-plated nickel is believed to be superior. With more rapid streams a spiral or knurled embossed pattern (56) helps to prevent the oil breaking into rivulets. Where the flow is extremely slow, a tenth to a hundredth of the amount mentioned above, a finely matted surface is favored by Detwiler (25) and coworkers. In the present case a spirally

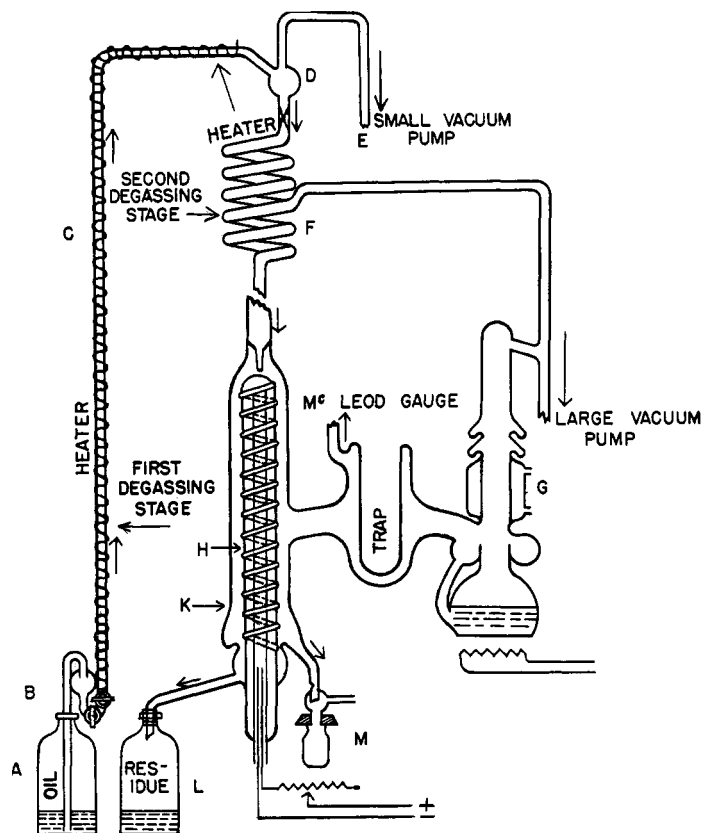


FIG. 8. Glass falling-film still first used to distill vitamins from fish liver oil

embossed glass column is shown. Admittedly much of the oil runs in a thicker stream around the spiral instead of flowing evenly over the surface. This tendency has been used to advantage in industrial apparatus by E. H. Payne (90). The temperature of the glass still can be maintained constant by using the vapor of a liquid of suitable boiling point, such as aniline or ethyl lactate. Liquids of considerably higher boiling point can be employed at lower pressures with a manostat which allows temperature control with some exactness (25). Another device is the electrically heated column where resistance winding replaces the heating fluid. The disadvantage of the electrical method is that the

temperature varies inversely with accidental variation of flow of distilland, whereas to maintain the distillation ratio it should vary superproportionately with the flow.

The industrial interpretation of the falling-film still has varied according as to whether the design is in the hands of chemists or of engineers. The chemist, wishing to obtain optimum conditions for the materials under treatment, has insisted on transparent apparatus in which the distribution on the column, the degree of separation, the amount of carbonization, etc. could be under constant surveillance. This has meant apparatus of low floor-space efficiency. The engineers have demanded all-metal construction with a grouping together of more than one distillation unit within a container. Burch and Bancroft's commercial stills for petroleum contained many flat trays in cascade or five or more cylindrical evaporators arranged side by side on a base-plate covered by a single removable tank. The flat-plate still (97) described by Burrows (16) used thick slabs of aluminum through which hot oil could be circulated to provide the heat for distillation. The distilland was distributed at the top of each slab and caused to flow down either side as evenly as possible, and a collection of N heated plates was sandwiched between $N + 1$ condensers within a vacuum tank. The advantages of such a compact design need no stressing; the disadvantages are lack of visibility and difficulty in cleaning. It is possible that this interleaved construction may find further application in the centrifugal still where many plates, mounted on one shaft (64), can be cleaned by their own motion during operation.

The stills which have survived in the author's laboratory are of a type that can be inspected continuously and dismantled when a defect develops, to be cleaned in the shortest possible time and put back into service. Our falling-film stills (52) have consisted, therefore, of little else than a series of vertical tubes standing on hollow metal bases which serve as connectors for the vacuum pumps, the columns being covered by bell jars as shown in figure 9. Cooling has been by air blast and heating by radiant heaters first introduced, we believe, by Fawcett. While this heat supply gives an admirably uniform allowance to each element of distilland when the latter is properly distributed, it places the entire assembly in unstable mechanical equilibrium. Let the oil "channel" ever so slightly, then the side receiving less oil becomes hotter and causes the column to expand vertically on this drier side, tipping the top of the column over to the wet side and aggravating the condition. The condition can, of course, be corrected with special alloys or compensating devices, but cost is an item.

Many schemes have been devised for distributing the oil evenly at the top of flat-plate and column stills. One group has favored a cascade divider (4) and another a dam of V-shaped serrations (52), but of all methods yet tried a rotating distributor appears to be the best (66). The oil having been distributed, it is necessary to prevent channelling during subsequent flow down the column. We have placed our faith in using designs embossed on the columns and placing a number of columns in series or series-parallel arrangement to redistribute the

distilland. Fawcett (39) has suggested redistribution from gutters placed at intervals around the column, a scheme which deserves more serious consideration.

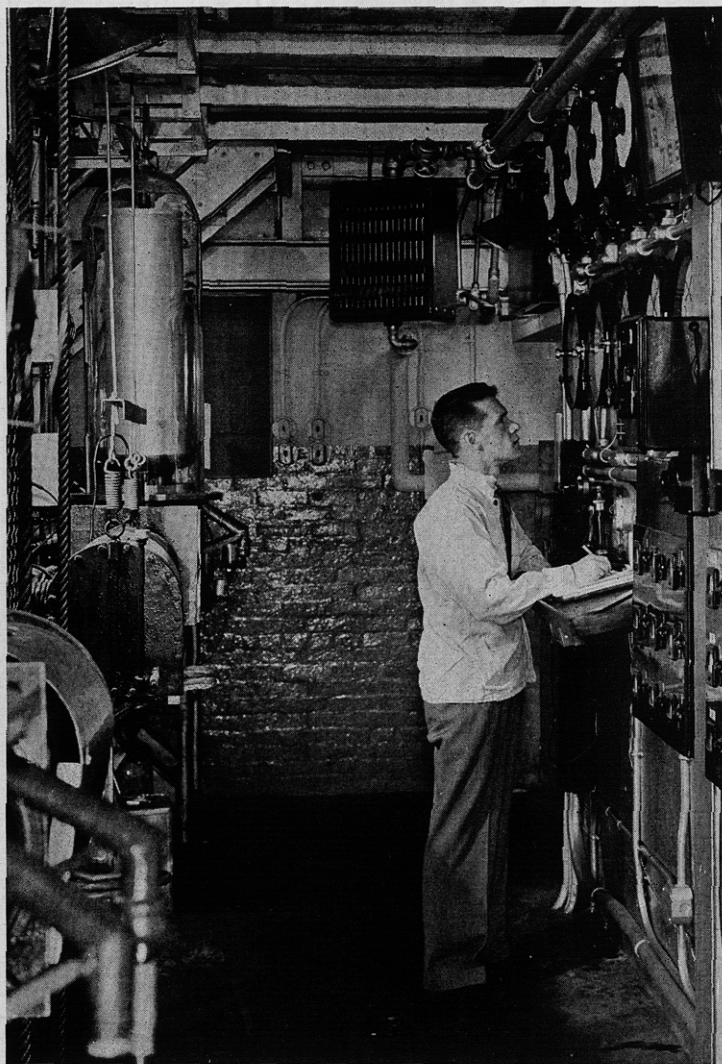


FIG. 9. Industrial falling-film still. Glass dome on the left covers the fifth evaporator in a succession of individual stills. The panels for controlling temperature and pressure are shown on the right.

B. The centrifugal still

From the rotary distributor it is a short step to the design of a completely rotating still (63). Here the inherently simple act of molecular distillation, itself the simplest variety of evaporation, reaches its simplest expression; a

frying pan is twirled in a completely empty chamber. We constructed a short-path centrifugal still in 1935 in the form of a deep cone spun from sheet aluminum. It was followed by a still shown in figure 10 (with condenser removed), having a stainless-steel rotor 7 in. in diameter turned to form a shallow cone with a deeper depression in the center. The plate was surrounded by a gutter to collect the oil which flew from the edge in a fine spray. The gutter being water-cooled, the distilland was maintained at the distillation temperature for a

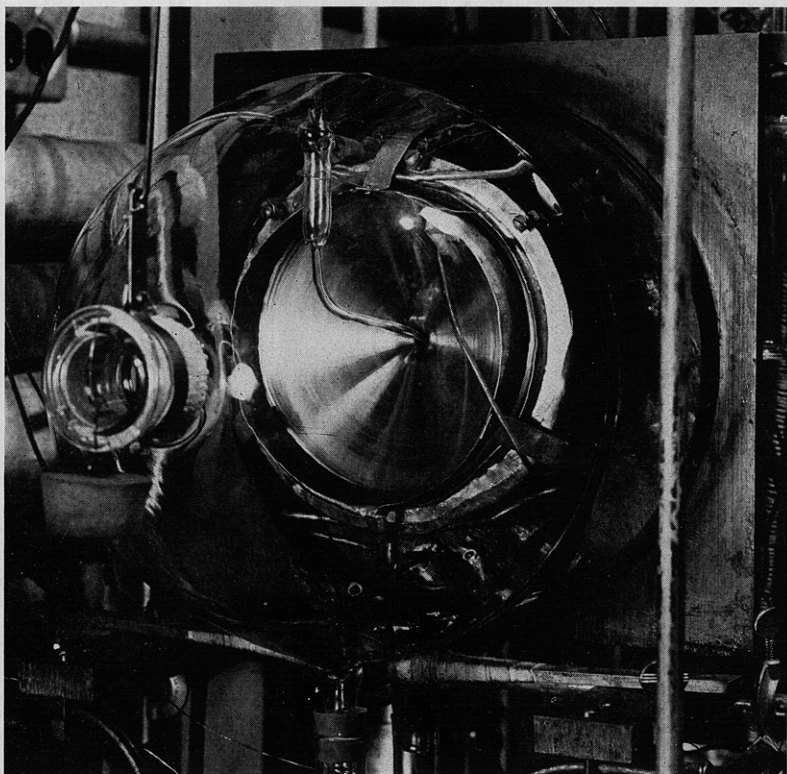


FIG. 10. Early centrifugal plate still. The oil is fed through the glass tube to the center of the plate whence it travels outwards towards the stationary, cooled collecting gutter. The condenser has been removed to give a better view of the evaporator.

small fraction of a second in a layer which was considerably thinner than had been secured with a falling-film still. The layer remained uniform in structure and the distilland advanced uniformly from center to the edge under trying conditions of temperature and variations of surface tension. A diagram showing the essential parts of a centrifugal still is given in figure 11. It was soon found that the cooled stationary gutter could be replaced by a rotating gutter and pick-up (61). Here the frying pan must be abandoned for a gramophone analogy, oil being fed to the center of the record and picked up at the periphery, an arrangement which is shown in figure 12. The distribution of charred material on

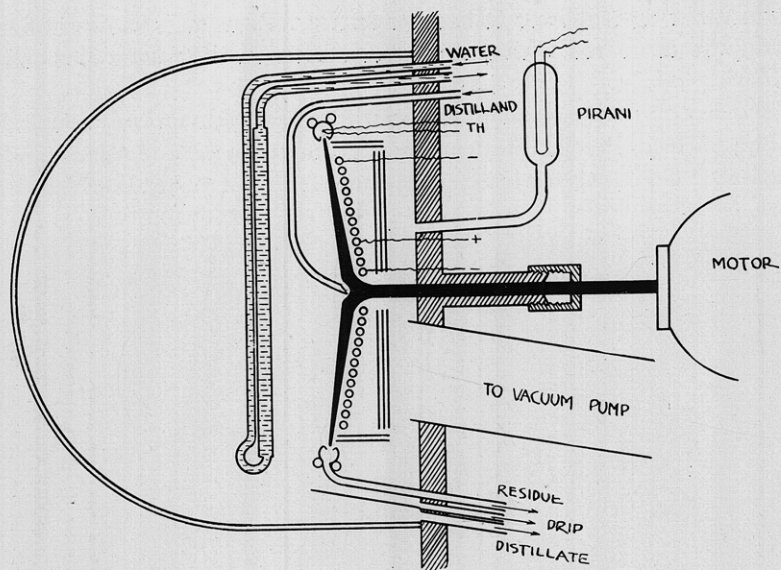


FIG. 11. Diagrammatic vertical section of centrifugal still

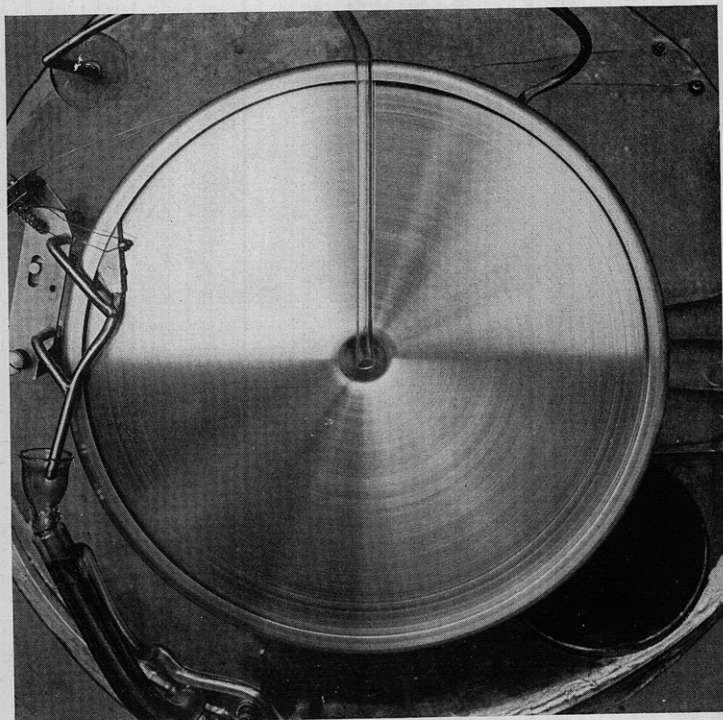


FIG. 12. Centrifugal plate with rotating collecting gutter and oil "pickup"

a still which has been allowed to become dirtier than usual is shown in figure 13, which may be compared with a similar condition on the falling-film column in figure 14.

While it can not be said that the centrifugal still has entirely displaced the falling-film variety, it holds first interest at the moment. Perhaps the future will call for a cross between a centrifugal and a falling-film still in which the more

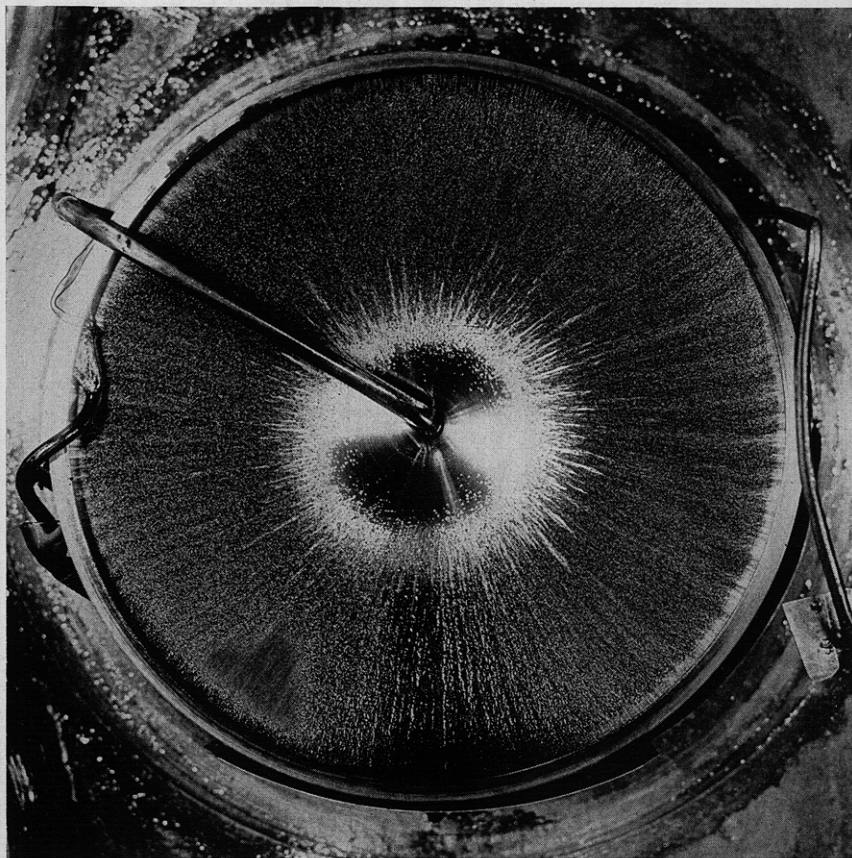


FIG. 13. Small centrifugal distillation plate after one week's continuous operation showing uniform distribution of charred deposit.

delicate constituents of an oil are removed on the rotating evaporator, which then distributes the stripped distilland to a stationary column for distillation of the glycerides. Although the temperature on the stationary column will be higher and the film thicker, the stripped glycerides can sometimes withstand this rougher treatment. Information concerning the early forms which multiplate centrifugal stills have taken industrially can be gleaned from figures 15 and 16, which depict batteries of small vertical plate and larger horizontal plate units used for the distillation of naturally occurring vitamins A and E.

There are some research aspects of the centrifugal still to which we may devote attention. At present the rate of spinning varies from a few hundred up to about 5000 R.P.M. There is little inherent reason why speeds approaching that of the ultracentrifuge should not be employed. Then if the liquid is ap-

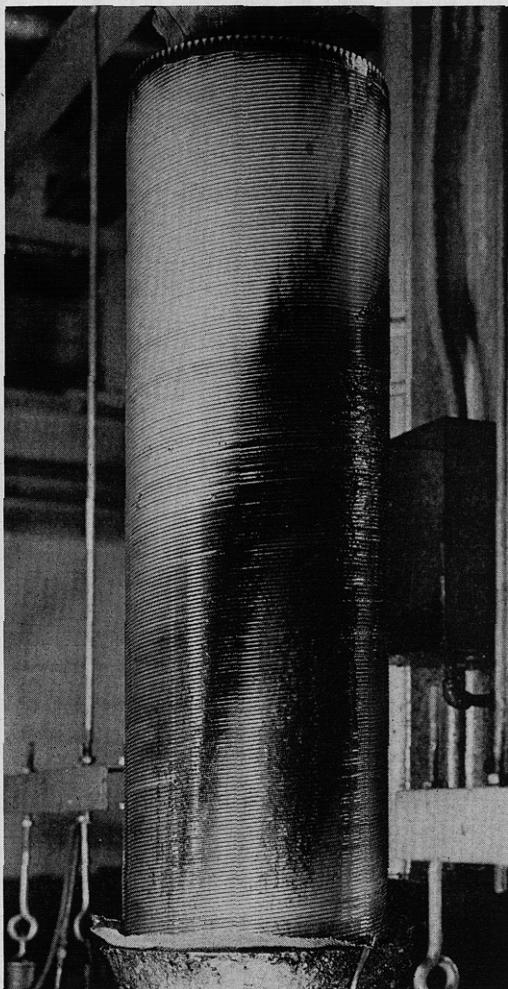


FIG. 14. Falling-film still showing unsymmetrical deposition of deposit after two days' operation.

plied to the center of a plate or cone, only the narrow periphery of which is heated to distillation temperature, travel of a thousandth of a second or less across the heated portions may be expected and it should be possible to distill, without harm, materials of very high molecular weight.

The centrifugal still and especially the rim type provide a better separation

than is possible from simple molecular distillation. The mixture of distillate molecules will leave the surface with average speeds proportioned according to

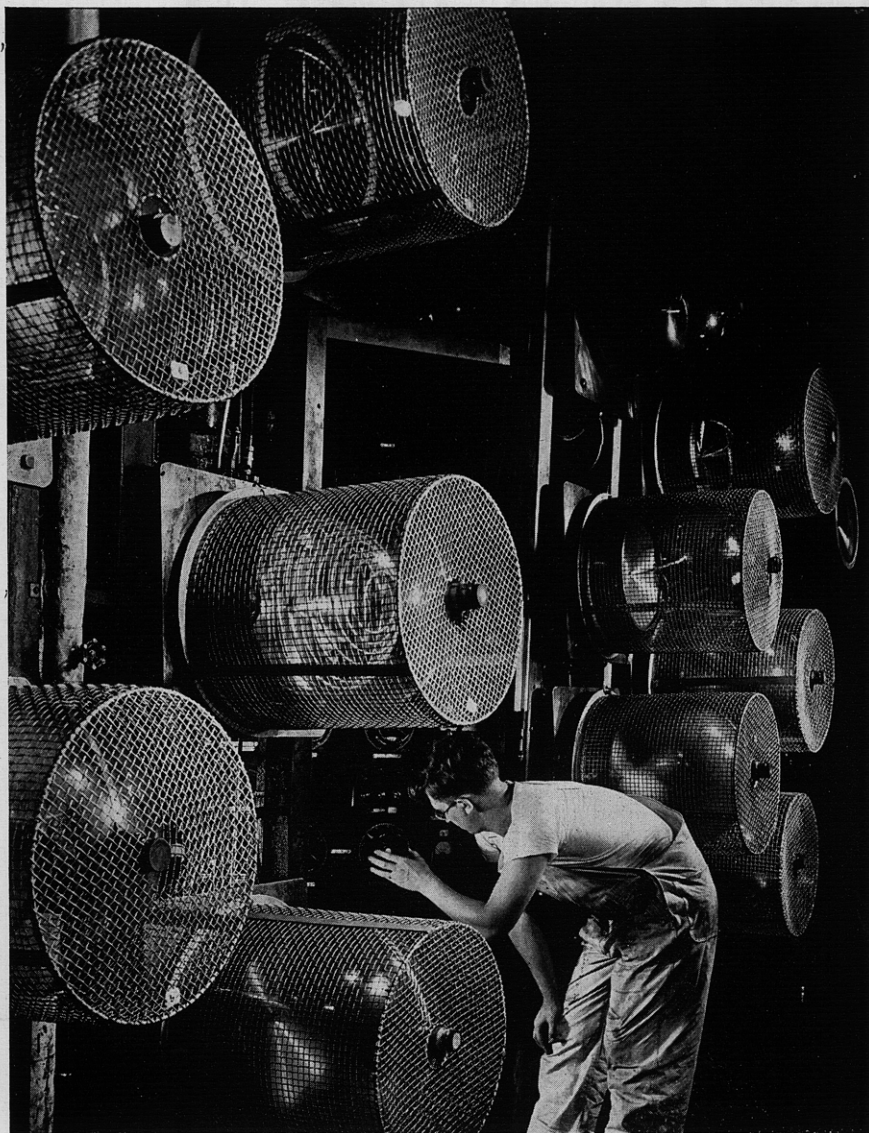


FIG. 15. Small industrial multiplate centrifugal still, with covers and condensers removed

the square root of the temperature and the molecular weights. But superimposed on this is another motion which is the tangential speed with which the molecules are flung from the rotating rim, and this will be the same for all the molecules. Now, in general, the heavy molecules will proceed further along

the *tangential path* during their passage under random motion than the small molecules will. But at the same time heavy molecules will be generated farther outward on the rim because they will evaporate later. So there will be a tendency for the more volatile materials to collect in an inner zone and the less volatile in an outer zone and this will give an improved separation. There is

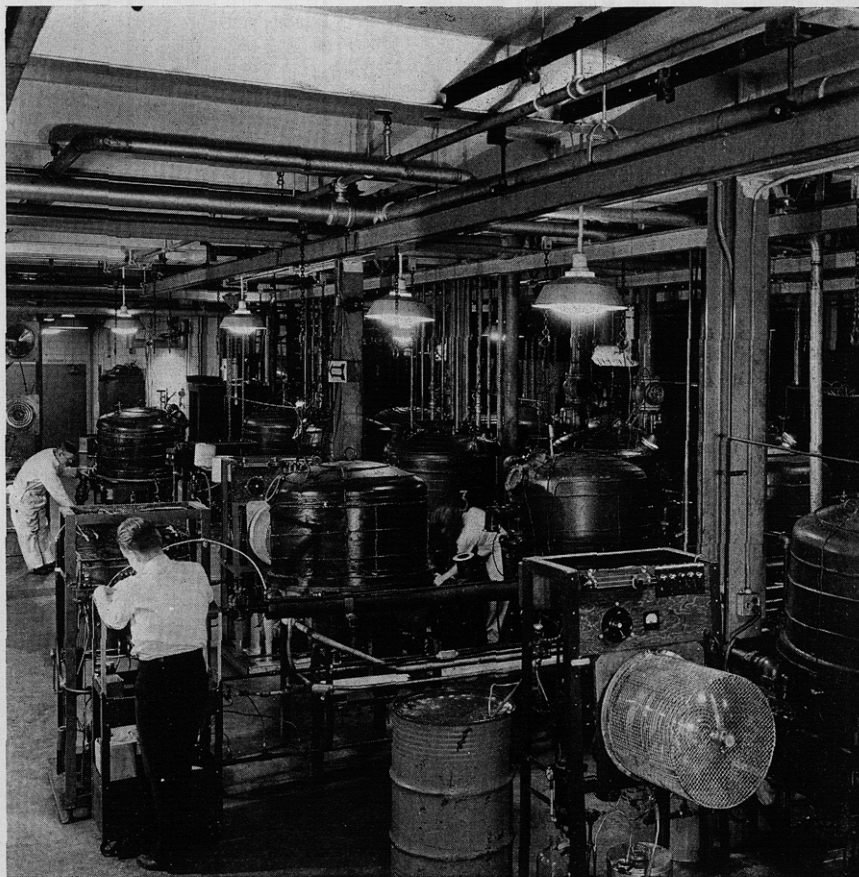


FIG. 16. Installation of larger industrial centrifugal stills; used chiefly for the separation of vitamin A ester concentrates from fish liver oils.

scope for considerable ingenuity in the design of stills in which the rotor is considered as the generator in the molecular-ray apparatus.

V. A COMPARISON OF FILM THICKNESS

The decrease in thickness of distilland, and thus time of exposure, which has come about during the transition from the pot still to the centrifugal is given in table 1. If we assume that a molecule of fat is approximately 5–25 Ångström units long and that a pool of distilland in a pot still is 5 cm. thick, then the dis-

TABLE 1
Transition from pot still to centrifugal still

APPROXIMATE DATE	STILL	APPROXIMATE* DISTILLAND THICKNESS	APPROXIMATE† MOLECULAR THICKNESS	APPROXIMATE TIME OF EXPOSURE
1922	Laboratory pot still (52, 82)	1-5 cm.	5×10^7	1-5 hr.
1928	Laboratory tray still (79)	0.1-1 cm.	5×10^6	5-60 min.
1935	Industrial falling-film still	1-3 mm.	5×10^5	2-10 min.
1930	Laboratory falling-film still	0.1-0.3 mm.	5×10^4	10-50 sec.
1940	Industrial centrifugal still	0.03-0.06 mm.	10,000	0.1-1 sec.
1936	Laboratory centrifugal still	0.01-0.02 mm.	3,000	0.04-0.08 sec.
1942	High-speed centrifugal rim still	0.001-0.005 mm.	400	0.001-0.005 sec.

* Assuming similar throughput for same unit area of all stills.

† Assuming that the molecule of glyceride fat has an effective diameter of 15 Å.

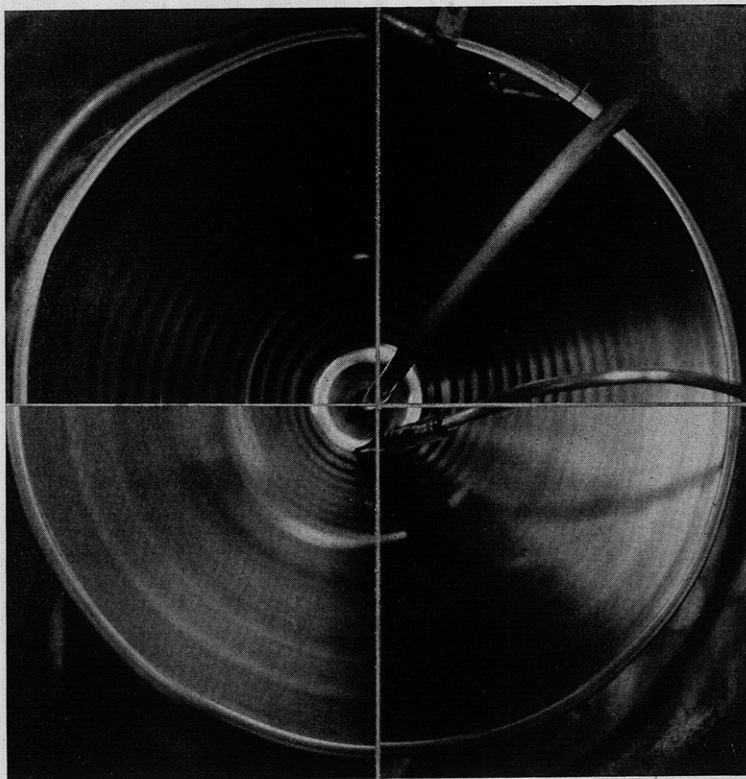


FIG. 17. Quarter sections of four photographs of centrifugal plate with small stream of dyed oil superimposed eccentrically on the main stream: upper left, 250 R.P.M.; upper right, 500 R.P.M.; lower right, 1500 R.P.M.; lower left, 3500 R.P.M.

tilland is some 2-10 million molecules deep. In the present stills the distilland averages 3000 molecules thick, but in the ultracentrifugal still of the future it need not be more than 25-500 molecules thick.

The disposition of the film on falling-film and centrifugal surfaces has been investigated by the use of heavily dyed oils. When an oil, colored so deeply blue that it appears black in a glass tube of 5-mm. bore, is allowed to flow over the surface of a smooth nickel column in a falling-film still, an even deep blue film results. However, after the application of vacuum and heat, the film collects into rivulets showing considerable variations in density. When the dyed oil is passed over the centrifugal surface, the distribution appears uniform

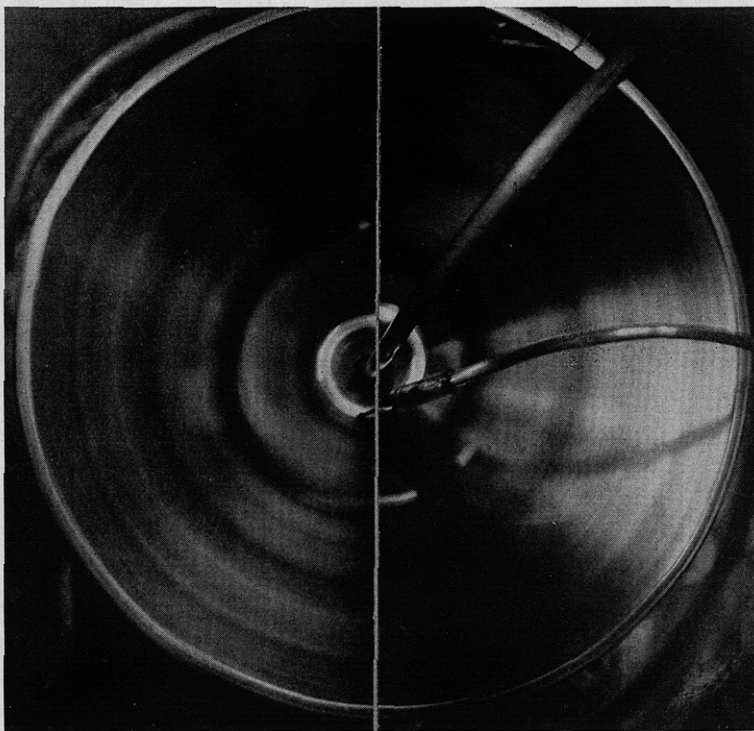


FIG. 17a. Two half-photographs of centrifugal plate with colorless oil flowing across surface and individual drops of dyed oil projected at $\frac{1}{4}$ -sec. intervals; left-hand section, 1500 R.P.M.; right-hand section, 3500 R.P.M.

under conditions so far investigated. The dyed oil has not been photographed above 150°C . because we do not yet have a sufficiently involatile dye of high solubility. The rate of progress down a vertical column when no distillation is occurring is uniform after the oil has attained the temperature of the column, which it does in the first few centimeters of travel, and thereafter the thickness remains constant also. The thickness over the centrifugal surface is not constant, because the oil is being spun thinner and thinner over an ever-widening circle. The progression has been investigated by measuring the reflection density of the oil film at the peak of the dye absorption curve. As an alternative method we have photographed an intermittent stream of colored and colorless

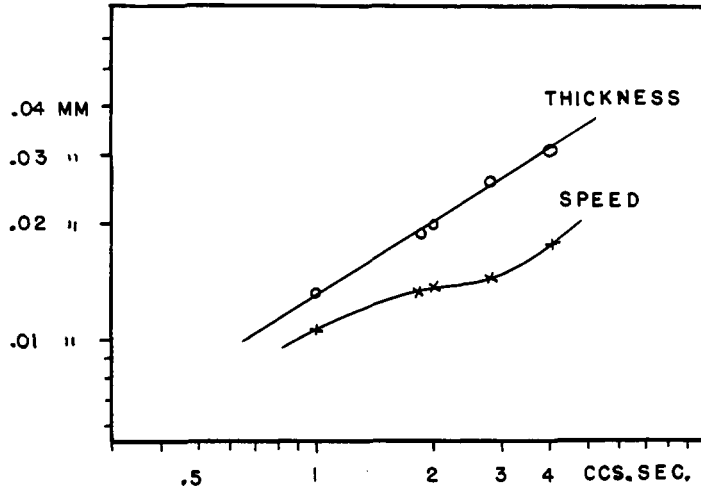


FIG. 18. Chart showing variation of thickness and rate of travel of oil across centrifugal plate with varying speeds of rotation. Measurements taken at 10 cm. from center.

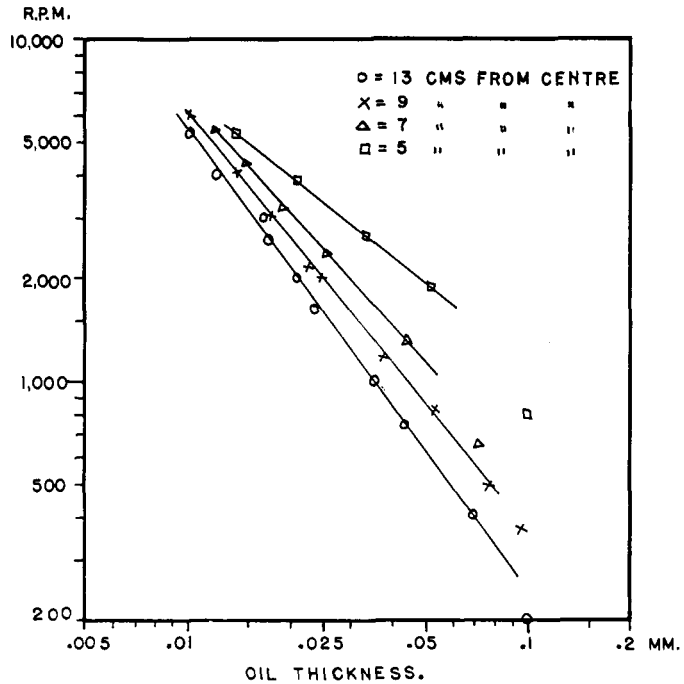


FIG. 19. Chart showing variations of thickness of oil with distance from center and rate of rotation of centrifugal evaporator.

oil fed to the center, in which case the color proceeds outwards in concentric rings. The flow of oil being stratified, an average speed must be interpreted as a faster travel over the outside surface and a slower travel, approaching zero,

against the plate. Since, however, diffusion is rapid compared with the rate of travel in such a thin film and turbulence may be present, we may still speak of the average progress of the film in the belief that this has a true physical meaning. We see from the photographs in figure 17 that the progression is nearly uniform from center to edge, with the thickness diminishing correspondingly with the distance from the center. The ratio of thickness of the oil film and its speed of progression at 100°C. and 3000 R.P.M. 10 cm. from the center of the plate to rate of feed is shown graphically in figure 18. The variation of thickness of film with distance from the center and speed of rotation is shown in figure 19. The logarithm of the speed of rotation is proportional to the inverse log of film thickness over a wide range.

$$\log \text{ R.P.M.} = R \left[\frac{1}{\log \theta} \right] \quad (4)$$

VI. THE QUIET DISTILLAND LAYER

Liquids have been classified as those which evaporate quietly in the molecular still and those which splash and bubble. The latter tendency, mentioned repeatedly (12) in the early literature (14, 15), has been referred to again recently (13). Our own observations suggest that, properly treated, few liquids need show this distressing behavior, which causes contamination of the distillate with distilland, often ruining a distillation. Among the causes of splashing may be listed: (1) imperfect degassing of the distilland (60); (2) fissures and cracks in the hot column or particles of dirt on the surface, all of which afford crevices for decomposition and evolution of gas and are points for detachment of distilland; (3) too rapid evaporation. A liquid evaporating into a vacuum at saturation pressure 5×10^{-3} , which is in the useful operating range, will develop a stream of vapor capable of lifting against gravity from a horizontal surface a layer of oil 0.075 mm. thick, assuming that the distilland is fifteen times lighter than mercury. The smallest pressure would detach the layer from a vertical falling-film or rotating plate were it not for surface tension and the whole range of properties comprised in "wetting." In addition to the evaporation pressure at the outside of the liquid film, there is the potential pressure on the inside against the hot column, which may be considerably higher during rapid distillation. The liquid separates from the column at a fissure or a particle of dirt and when once separated gathers into drops. The drops expose less surface and thus tend to return to the distilland, but they may be prevented from combining by the gas adsorbed to or emanating from the approaching surface. Droplets returning to the hot wet surface at glancing angles may be reflected many times before cohering. Detachment is minimized and reattachment facilitated when there is an external force pressing the liquid against the evaporator. The falling-film column should be a pyramid, broader at the base than at the top, and the centrifugal still should be conical, paraboloid, or cylindrical with the liquid flowing on the inner surface. If the approximate film thickness and speed of rotation are known, the minimum slope contour of the rotor can be calculated

and distillations can be done at high saturation pressures not previously contemplated (62).

VII. RELATIVE STILL PERFORMANCE

There are mechanical, thermal, and other limitations to the rate at which oil can be put across a surface still. Excessive throughput impairs the vacuum, overtaxes the heat transfer, and spoils the degree of separation. The ability to separate constituents from a mixed distilland is a fundamental property of a still. Classically, this would be investigated by measurement on distillates from a binary mixture. A method more in accordance with the technique from this laboratory is the examination of the shape of the elimination curve from a cyclic distillation. The generation of the curve is given in Part II, to which the reader is now referred.

The sharpness of separation can be expressed by the elimination coefficient ϵ , given by the ratio of the height to the area under the curve obtained when yield,

TABLE 2
Elimination coefficient with different stills

STILL	APPROXIMATE ELIMINATION COEFFICIENT	APPROXIMATE FRACTION SURVIVING		
		β -Carotene	Vitamin A palmitate*	Vitamin D palmitate*
		<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Wide-necked alembic flask (figure 2).....	0.7†	0	10-20	0
Pot still.....	0.6	20	80	0- 5
Falling-film still (laboratory).....	0.9	50	98	10-30
Centrifugal still (laboratory).....	1.1	90-95	100	75-98

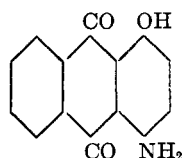
* Natural esters of C₁₆, C₁₈, C₂₀, and C₂₂ acids, C₁₈ predominating.

† With ebullition or mechanical stirring.

in successive fractions of a chosen constituent of a mixture, is plotted against temperature, in rigidly defined units.⁵ The optimum and limiting value for a very slow distillation of a polar dye from a polar oil⁶ is approximately $\epsilon = 1$. As the throughput is increased the coefficient decreases to 0.7-0.6, at which point vacuum impairment, splashing, and other factors begin to interfere. Distillations of fat-soluble vitamins from non-polar oils have been done with $\epsilon = 1.1-1.2$. Conditions which yield an elimination coefficient of 0.6 in the pot still and 0.7 in the falling-film still will often give $\epsilon = 1.1$ in the centrifugal. The survival of labile substances goes hand-in-hand with high ϵ values, as shown in table 2.

⁵ See page 87 *et seq.*

⁶ For instance, Celanthrene Red from glyceride constant-yield oil.



A. Fractionation

Separations better than are obtainable with a power of one theoretical plate can be secured by multiple distillation. When this enhanced separation is performed in one coördinated act, the term *fractionation* may be used. Fractionation by *feed-back* during passage of the distilland over a series of molecular stills has been covered by Fawcett (40) and Fraser (42). There are, however, so many other mechanical ways of inducing high-vacuum fractionation that a description of some of these must be left to a future paper.

B. Rate of distillation

Factors 2 and 3 (page 59),—namely, *distillation from the surface* and *travel across the vapor gap*,—will now be examined.

Two classes of molecules contribute to the pressure in a surface still—the residual gas and the distillate vapor. The pressures are referred to as *residual pressure* and *saturation pressure*. The mass, W , in grams evaporating per second per square centimeter of substance of molecular weight M , at absolute temperature T and saturation pressure P (in millimeters of mercury) or p (in microns of mercury), is

$$W = 5.83 \times 10^{-2} \cdot P \cdot \sqrt{\frac{M}{T}}$$

and

$$p = \frac{17,200 \cdot W}{\text{Area cm.}^2} \cdot \sqrt{\frac{T}{M}}$$

It so happens that $\sqrt{\frac{M}{T}}$ approximates unity. Thus, T for distillation at 1 micron varies from about 350°K. for palmitic and stearic acids to about 550°K. for tristearin and from 570 to 580°K. for castor oil and the harder waxes. The molecular weight varies from 284 for stearic acid to 850–950 for glyceride fat.

$\sqrt{\frac{M}{T}}$ varies from 0.9 to 1.3, the sterols having a factor of nearly unity. It is convenient to remember that at a saturation pressure of 1 micron (0.001 mm.), 1 square meter will evaporate approximately 0.5 g. of stearic or palmitic acid, 0.55 g. of sterols, and 0.75 g. of triglyceride fats or oil each second.

The rate of collection of distillate approaches the rate of evaporation only at zero residual pressure and a short unobstructed path. With wide gaps and substantial residual pressures few molecules will reach the condenser without collision and many will be returned to the distilland. Burch (British patent 303, 078 (see page 00)) predicts the fate of a mercury molecule in residual gas at 1 micron with distillation gaps of various widths, as shown in table 3, and hazards the guess that a distillation which is vigorous with a 2-cm. gap will be virtually stopped with ten times the gap. Experience teaches that distillation is less hindered by residual gas than is suggested by simple kinetic theory. The resi-

dual molecules are not an independent maze through which the vapor must wander, but a movable barrier readily disturbed by distillation. Transfer by diffusion is aided by convection currents impressed by the evaporating molecules, which induce a *draught* towards the condenser even when they are in the minority. When they are in the majority they drive all the residual gas towards the condenser and thence sideways to the edge of the gap. Under practical operating conditions (1–10 microns) there is a gradual increase in the rate of distillation as saturation overtakes residual pressure. The variation of rate of

TABLE 3
Fate of mercury molecules in residual gas at 1 micron with distillation gaps of various widths

DISTANCE BETWEEN EVAPORATOR AND CONDENSER	MULTIPLES OF MEAN FREE PATH	PROBABLE FRACTION OF MOLECULES MAKING JOURNEY WITHOUT COLLISION
<i>cm.</i>		<i>per cent</i>
1	0.25	77.5
2	0.5	60.1
20	5.0	0.005

TABLE 4
Variation of rate of distillation with pressure

PRESSURE OF RESIDUAL GAS (AIR)	RATE OF DISTILLATION PER SQUARE METER OF DISTILLAND SURFACE OF FALLING-FILM STILL (2-CM. GAP)		
	Saturation pressure of distilland (2-ethylhexyl phthalate or Octoil)		
	1 μ	3 μ	10 μ
μ	<i>grams per second</i>	<i>grams per second</i>	<i>grams per second</i>
0.3	0.6	1.85	6.4
4.0	0.46	1.59	5.7
7.0	0.38	1.37	5.2
10.0	0.32	1.18	4.6
15.0	0.25	0.95	3.8
25.0	0.21	0.70	2.1
50.0	0.12	0.40	1.67

distillation at three saturation pressures and varying residual pressure in a falling-film still is given in table 4.

c. Projective vs. equilibrant distillation

Under molecular conditions of direct transfer to the condenser, molecules do not reënter the distilland and there is no equilibrium between liquid and vapor. The quantity distilling is proportional to P/\sqrt{M} and the relative quantities of two or more constituents are

$$\frac{p_1}{\sqrt{M_1}}, \frac{p_2}{\sqrt{M_2}}, \dots, \frac{p_n}{\sqrt{M_n}}$$

In ordinary distillation, where the rate of escape of vapor is less than the rate of generation, molecules reënter the surface and produce approximate equilibrium between liquid and vapor phases. The quantities of constituents distilling are then proportional to their partial pressures, $p, p_2 \dots p_n$.

Molecular distillation will thus effect separation between substances of equal vapor pressure, providing the molecular weights are different. On the other hand, substances having

$$\frac{p_1}{\sqrt{M_1}} = \frac{p_2}{\sqrt{M_2}}$$

which are inseparable molecularly, can be separated if conditions of partial equilibrium can be tolerated at the necessarily higher temperature. A mixture can sometimes be resolved by distilling first under projective and then under equilibrant conditions.⁷

The unique kind of separation afforded by the molecular still was recognized by Brönsted and Hevesy (10) and has been featured by other writers (12, 13). It was early noted that the P/\sqrt{M} type of separations persisted at saturation pressures far exceeding the truly "molecular." The controlling factor would seem to be less the density of the advancing vapor, where collisions are of "the same sort," than the opposition offered to the vapor by hot mechanical obstructions or by residual gases which oppose collisions of "a different sort." The degree of equilibrium, therefore, is determined by the ratio of the rate of *reception* to the rate of generation of the vapor, and projective separation could be secured at extremely high saturation pressures if these could be generated without disruption of the distilland and if the vapor could escape and be absorbed without hindrance. Unobstructed-path distillation at high saturation pressure is feasible and commercially attractive in centrifugal apparatus (62). Conversely, more or less equilibrium distillation can be established even at the lowest saturation pressure by controlling the residual pressure or the temperature of the condenser, or both. By maintaining a relatively warm condenser, equilibrium distillations can be performed in the molecular still at the lowest temperatures compatible with the degree of obstruction.

D. Partial condensation

Partial condensation is a well-known aid to separation and is useful because it adds to the selective power exerted at the evaporating surface a second selection by the condenser. It can not be employed in the simple molecular still without banishing the very conditions under which the still was built to operate. In diagram A, figure 20, the solid arrows represent heavy molecules readily absorbed by the hot condenser, and the dotted arrows represent light molecules chiefly rejected. Neglecting the possible escape sideways to the pumps, the light molecules must return to the evaporator, enriching the distilland until so many can be thrust towards the condenser that the small proportion retained

⁷ The difference between the two kinds of distillation is small and its importance is apt to be exaggerated.

balances the input of the constituent to the still. Note that the steady composition of the distillate is the *same*⁸ as with a cooled condenser, but distillation is hindered both by the molecules uselessly cruising about the gap and by the number of false strikes before condensation—it is no longer a molecular distillation.

To utilize the advantages of a warm condenser the cruising light fraction must be allowed to escape, while the heavier molecules are condensed. This is done

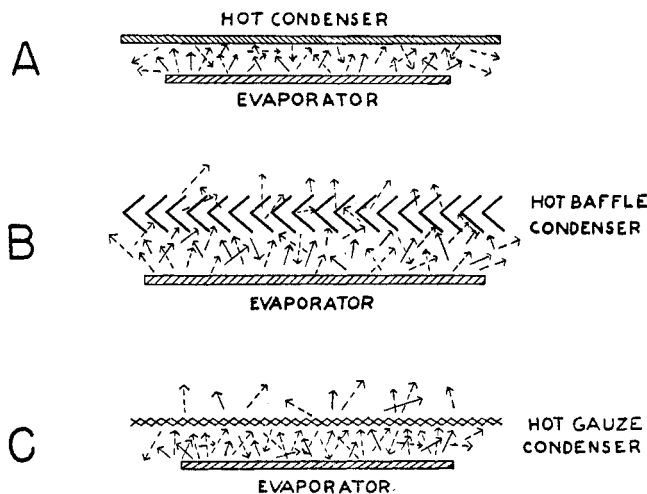


FIG. 20. Fractionation by partial condensation: A, with hot barrier; B, with barrier condenser; C, with semi-permeable film barrier.

TABLE 5

Typical losses during a molecular distillation of triglyceride fat

	FRACTION OF HEAT CONSUMED
	<i>per cent</i>
Conduction through body of still.....	6.2
Heating oil to distillation temperature.....	35.3
Radiation losses.....	54.1
Latent heat of distillation.....	2.0
Total accounted for.....	97.6

by a perforated construction (71) which may be open, as in B, figure 20, or closed by a film of condensate, as in the wire-mesh construction or C, figure 20. Here again distillation is partially unobstructed and partially equilibrant.

The idea of the self-pumping still has intrigued inventors from the first. In a multi-evaporator still, Burch (14) allowed the more volatile constituents of a mixture to provide the vacuum for the less volatile. Van Dijck (96) went further and grouped parts of distilling and evaporating plates so that the ma-

⁸ Except for the small change in *kind* produced by the approach to equilibrium condition.

jority of the inevitable collisions between evaporating molecules and residual gas is towards the exit to the pump.

These devices are a fundamental advance in design. When misapplied they involve a contradiction in terms, since they attempt to utilize collision to produce a vacuum in which there are no collisions,—the vacuum is to be lifted by its own bootstraps, so to speak. Recent self-pumping stills utilize the heat of condensation (65) and other spare energy to operate molecular or condensation pumps within the still. The value of a pump situated *within* the still appears to have been recognized first by Vigers (98).

E. Thermal balance in the molecular still

The molecular still has a naturally low thermal efficiency because the hot evaporator faces and is coextensive with the cooled condenser. Fawcett (38)

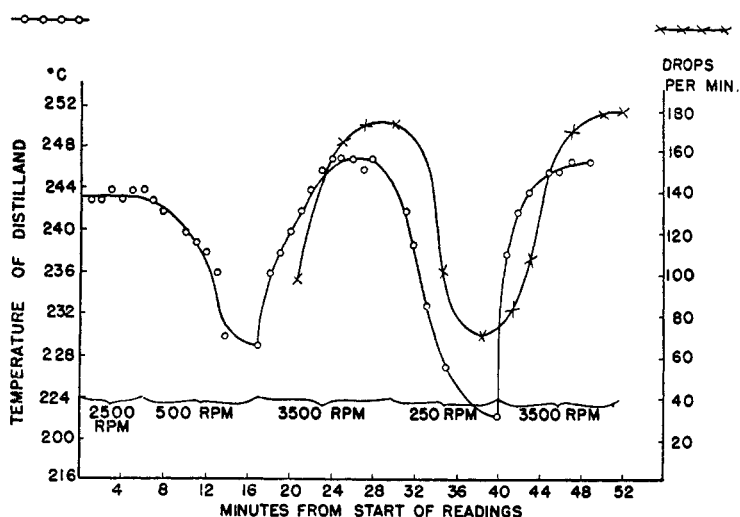


FIG. 21. Chart showing increase in temperature of distilland and rate of evaporation with increase in rate of rotation of evaporator.

has listed typical losses during a molecular distillation of triglyceride fat as shown in table 5.

Only about 2 per cent of the heat is actually used for the distillation, the rest being spent for contributory purposes. Of the fraction heating the oil some can be recovered by countercurrent flow, but this leaves radiation stealing an even greater share. Polished baffles (109) between condenser and evaporator have been proposed to reflect part of the heat, but these obstruct the path if hot and are inoperative if cold. The reason for the failure of a cold reflector is that the prime radiator of heat in the molecular still is not necessarily the hot distilling column, but is the oil on its surface. Glyceride oils are substantially opaque to radiation from bodies at 250–350°C. Even though the evaporator and condenser can be made of highly polished heat-reflecting metal, the hot oil on the

evaporator and the cold condensate on the condenser are the prime bodies emitting and receiving heat. The centrifugal still offers some hope for heat economy, because the distilland can be whirled so thin that it ceases to emit radiation. In a like manner the distillate can be whirled thin on an opposing condensing member, and if the base metals are maintained bright, little heat is emitted and that which is emitted is largely reflected whence it came. This effect has been measured in a number of ways, of which the most convincing is the increase in the rate of distillation with increase in speed of rotation of the distilling surface. This is shown in figure 21, where the history of a distillation done at constant heat input and varying rotational speeds is plotted graphically. A small part of the increase at high R.P.M. is due to increased convection in the vapor phase. We have not yet had the opportunity of repeating the measurements with a highly reflecting rotating condenser. It is evident that the use of *one* reflecting surface, either distilling or condensing, affords the greatest step in energy conservation, the second reflector effecting a minor saving.

VIII. CONTRIBUTORY TECHNIQUE

A. *Vacuum pumps*

The volumetric capacity of vacuum pumps required by a molecular still measured at the operating pressure (0.1–5 microns) is relatively enormous, many thousands of liters of gas having to be withdrawn for each liter of oil entering the distilling zone. There is no inherent reason why large mechanical pumps should not be devised to perform this evacuation efficiently but, as a matter of history, the larger molecular stills have been evacuated by Langmuir's condensation pumps. Early distillations were done with the mercury pump, but as apparatus increased in size—and particularly after Burch's introduction of the Apiezon oils—it was found more satisfactory to use organic liquids in the pump. One reason is the poisonous character of mercury; another is the tendency of the condensed mercury to become inextricably emulsified with the oily distillate withdrawn from the still by the pump.

The principle of the condensation pump is well known but will be indicated here for the sake of completeness. Vapor issues from an orifice attached to a shallow boiler. The orifice may face upwards as in A, figure 22, but is generally turned downwards towards the boiler as in B. In any case the orifice or "jet" is surrounded by a water-cooled jacket, one end of which serves as the suction intake, while the other serves as the discharge lead. The pump is a secondary or "booster" device which requires a primary pump to bring the effluent up to atmospheric pressure. It is the function of the primary pump, which may be mechanical⁹ or a multi-stage steam ejector (57), to create a vacuum of 0.3–0.05 mm. into which the condensation pump is able to discharge. The vapor pump has an enormously greater volumetric capacity than the fore pump, but the mass of gas (PV), is identical for each of the two pumps in tandem. Indeed, the *re-*

⁹ Such as the well-known Cenco Hyvac or Megavac and the larger Kinney or Stokes pumps. Many other excellent makes are available.

serve mass capacity, or liter-micron-capacity as it has been called by the British group, must always be larger in the prime mover, which will otherwise be unable to handle the gas gathered and compressed by the condensation pump. An example will make this clear:

A condensation pump is required to handle 100 liters per second at 10^{-4}

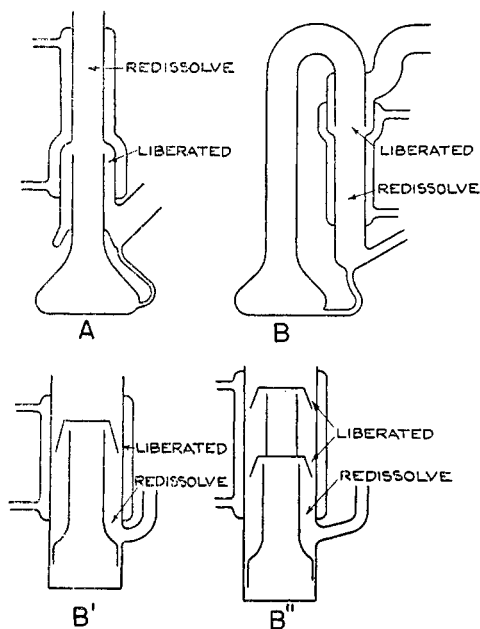


FIG. 22. Diagram illustrating contamination of condensation pumps

mm., which it will discharge into a mechanical fore pump at 0.1 mm. pressure. The volume of gas handled at higher pressure will be

$$\frac{100 \times 10^{-4}}{10^{-1}} \text{ liters} = 100 \text{ cc. per second}$$

This can be accommodated by the smallest laboratory mechanical oil pump. However, it will be necessary for the mechanical pump to handle larger quantities if the system is to begin operating within a reasonable time. Assuming that the condensation pump reaches its full speed at 5×10^{-3} mm., the capacity of the fore pump should be at least

$$\frac{100 \times 0.005}{0.1} = 5 \text{ liters per second}$$

Thus, in the interests of quick starting the vacuum prime mover may well have a capacity twenty to one hundred times that needed for ultimate maintenance.

In addition to a capacity for handling permanent gases, the pump attached to a molecular still should dispose of semivolatiles. Organic fluids

differ from mercury in that permanent gases are slightly soluble and vapors are extremely soluble in them and may form constant-boiling mixtures. The pump fluid, therefore, continually becomes contaminated (51) by the very materials which it should reject, and the speed of the pump diminishes correspondingly (see regions marked "liberated" and "redissolves" in figure 22). To overcome this, self-purifying pumps (17, 58, 86) have been devised which use a plurality of boilers in series, each boiler rejecting partially the impurities left over from the preceding boiler. In practice, three to four boilers (53) have proved sufficient for the industrial falling-film stills. With the continued growth of molecular distillation equipment it would appear that larger fractionating pumps must be devised or perhaps a complete purification plant will be added to pumps of more conventional design.

B. Pressure measurements

Two pressures only would seem to be of importance in the short-path still. One is the saturation pressure of the distillate vapor with which we have dealt previously; the other the pressure of residual gas. The pressure of residual gas is a measure of the equilibrium existing between leakage and decomposition on one hand and the sum of the "admittances" of the pumps and ducts on the other. The necessity for large ducts is indicated by the chart reproduced, as figure 23, by the courtesy of the General Electric Company Laboratory. For a fuller discussion of the problem of gas flow the reader is referred to the original work of Knudsen (76, 78) and the standard textbooks (75, 84), especially those of Dushman (27), Dunoyer (26), and Strong (94).

It is unnecessary to know the residual pressure unless this is harmfully high. It is the object of the distillation technologists to reduce the pressure to such a level that it is negligible. To do this it is imperative to use gauges which do not minimize the pressure in the still. Of the many gauges which are available, including the Pirani hot-wire, the ionization, the Knudsen, the oil manometer, and the McLeod, the latter is least suited for the purpose owing to its failure to register condensible vapors. The Pirani, in spite of criticism (37), remains our choice. The gauge requires constant checking for shift of zero point. It is advisable to have a number of instruments available so that those not in use can be returned to the calibration rack, where they are compared with a McLeod gauge which is operating properly upon residual air instead of vapors. The hot-wire gauge used in this manner becomes eminently satisfactory and has the merit that when it eventually fails it exaggerates the pressure in the still. The pressures which should obtain in the still are preferably less than 10^{-3} in laboratory stills and 5×10^{-4} in industrial stills.

Another gauge which is valuable is the tilted U-tube manometer filled with amyl phthalate (density = 1 at 25°C.). This is used as a double deflection instrument by placing one limb in connection with the vacuum to be measured, while the other is connected with a good reference vacuum. The connections to the two limbs are then reversed and the difference between the two readings—halved—yields the true pressure, compensated for the usual errors of the method.

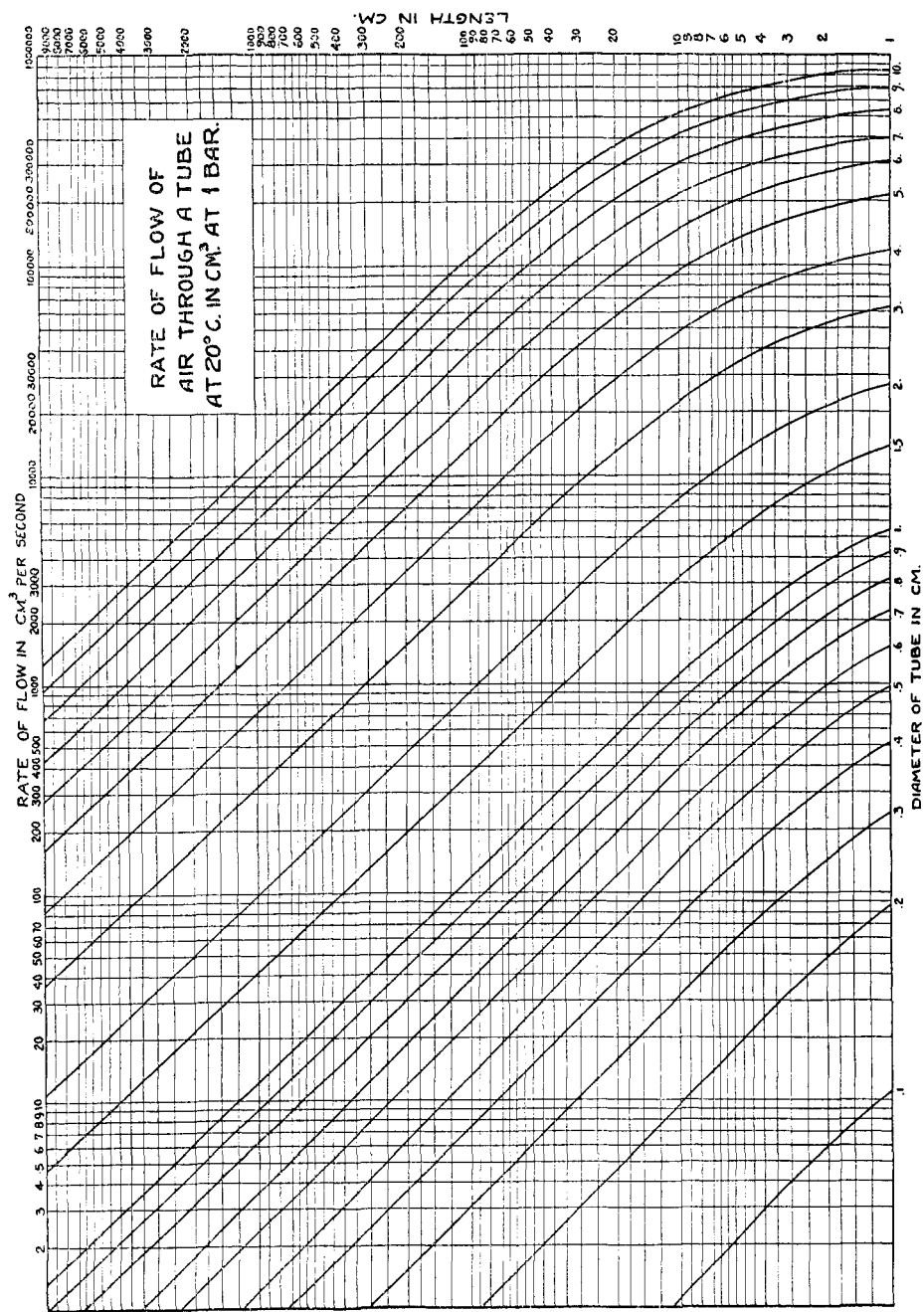


Fig. 23. Diagram showing variation in rate of flow of gases under high vacuum with variations of diameter and length of tube. (Courtesy of General Electric Company, Schenectady, N. Y.)

Absolute pressures down to 10 microns can be obtained which are useful in calibrating the Pirani instrument.

IX. FUTURE AND SCOPE OF SHORT-PATH DISTILLATION

Hitherto molecular distillation has succeeded industrially with valuable materials that can bear high process costs and with materials having constituents of such different volatilities that the poor separating power of the stills has been unimportant. Potent fish liver oils have been admirable candidates for distillation. Indeed, had it not been for the timely rise of the vitamin industry, short-path distillation might have languished in the limbo of forgotten inventions. The demand for vitamin A provided a use for the early stills, as well as funds and incentive for the development of larger more economical models.

Scientifically, the graduation of the molecular still from a capacity of a few drops to the present aggregate of about five million pounds annually represents the major developmental span. Industrially, the main period of development lies ahead. The natural oils and waxes which form one of the world's last great reservoirs of unprocessed organic raw material should be the source of a billion or more pounds of molecular distilland. From the heavy chemical industries plasticizers, plastics, resins, polymers, highly oxygenated glycols and sugar derivatives, rubber intermediates, synthetic lubricants, and petroleum residues head a long list of chemicals amenable to high-vacuum purification. No matter how complex the product, the last stage of synthesis generally involves the type reaction $A + B \rightarrow AB$, where A and B are intermediates of low or medium molecular weight and AB is of medium or high molecular weight. In either case A and B differ vastly in volatility from AB, so that excellent separations can be secured in a single passage through the short-path still. In some cases both reactant and product can be distilled in succeeding evaporators; in others the product can be stripped of reactants while itself remaining undistillable. In either event the excess of the original components can be returned to the reaction kettle to augment succeeding batches. At present they are wasted as a contaminant of the product, the properties of which are often impaired.

The future of the molecular still has sometimes been viewed with pessimism (13) because of high thermal requirements and ineffectiveness in separating the largest class of raw materials—the natural mixed triglycerides. However, there are ways of economizing in heat, as we have shown, and heat becomes cheaper each year. Indeed, the preëminent advantage of the molecular still in the oil refinery is that heat is the only contributory raw material needed. The separation of the mixed glycerides will probably wait upon the development of the *fractionating* wide-path still. In the meantime the stripping of vitamins, sterols, and volatiles from the natural oils may well occupy a decade of industrial development.

PART II

I. APPLICATIONS OF MOLECULAR DISTILLATION

The applications of the short-path still are as wide as the literature, which includes more than a hundred papers. Limitations both of space and of the

author's experience account for the emphasis which has been laid on the work of the Distillation Products laboratory in what follows.

Instructions for handling small quantities of oils, sterols (54), dyes, biologicals (55), and volatile solids have been given by McDonald (85) and others. Papers by McDonald, Almquist (2), Dam (22), and Carothers and Julian Hill (19), severally, are worthy of study. Whatever the conditions, the procedure is the

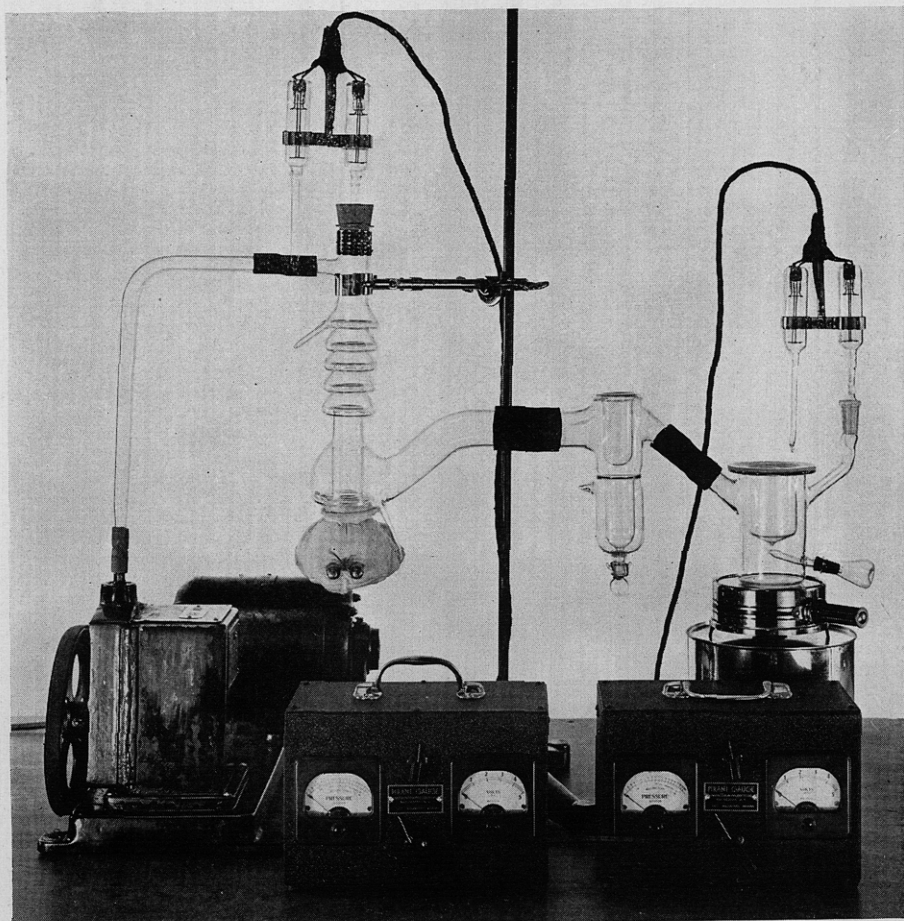


FIG. 24. Simple molecular pot still showing, from right to left, glass pot still with Pirani gauge, low-temperature trap, condensation pump, Pirani gauge for forepressure, mechanical vacuum pump.

same; the substance is placed in the still, a residual pressure of 10 microns or less is established, heat is applied, and a *number of fractions* is collected. A photograph of a simple assembly of apparatus is shown in figure 24. A more ambitious installation of many small stills, treated as permanent laboratory fixtures, has just been described by Riegel, Beiswanger, and Lanzl (92). The photographs reproduced as figure 24a are by the courtesy of these authors. The degree of separation of constituents is poor, generally less than a single theoretical "plate,"

and there is no sharply defined boiling point to guide the operator, who is thus hampered in selecting the best temperature range for collecting fractions. This

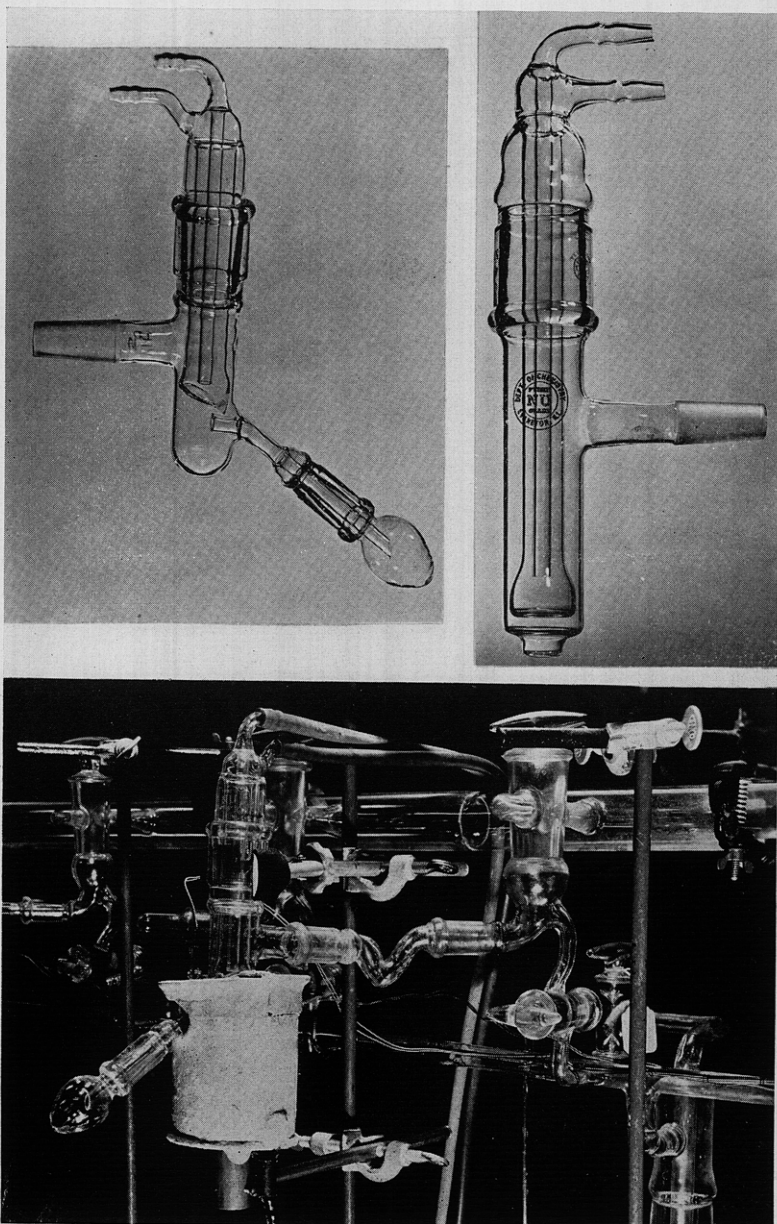


FIG. 24a. Installation of miniature molecular stills after Riegel *et al.* (photographs by courtesy of the authors).

indefiniteness has hindered the wide adoption of molecular distillation in the organic laboratory.

The boiling point of a substance is the temperature at which the pressure of the vapor overcomes that of the surrounding gas. In the molecular still there is no surrounding gas and hence no boiling point, distillation occurring in some degree whenever there is a difference of temperature between evaporator and condenser. Increase in the absolute temperature and in the difference increases the rate of evaporation, but there is no abrupt transition for observation and record. The problem has been to provide a practical substitute for the boiling point.

It was early noted that the change in concentration of a constituent in a sequence of fractions lay on a smooth curve having a well-defined maximum. At low temperatures little of the constituent would collect, but as the temperature was advanced, distillation of the constituent would increase, reaching a maximum only to fall again in later fractions as the distilland became impoverished. It appeared probable that each substance in a mixture would come to maximum yield in fixed relative order which would be unaffected by changes in the absolute rate of distillation. Then, by determining the position of the *elimination maximum*, that is, the fraction richest in any one constituent, it should be possible to predict which of the other fractions contained the greatest yields of accompanying substances. The observed constituent would be referred to as the distillation pilot (52). Volatile dyes were an obvious choice as visible pilots.

Many of the valuable constituents of natural mixtures are present in traces only. Free fatty acids, vitamins, sterols, and hormones are contained in large relative volumes of non-volatile fat. When these are treated in the molecular still the minor constituents collect as a mist on the condenser, from which they can not be removed without interrupting distillation. It was found convenient to add to the distilland a mixture of volatile oils which would distill with the minor constituents and give them sufficient volume to flow from the apparatus without interrupting distillation. The distilland was thus doctored with a pilot dye and a *controlled-yield oil* (6), so that all the significant fractions should have approximately similar bulk and be subject to about the same drainage errors. N. Embree (28) pointed out that if the time for collecting each fraction were kept constant and the temperature raised by uniform increments, the distillation curves would be accurately reproducible and could be employed without pilot dyes. This has proved to be the case and the method of the *elimination curve*, figure 25, has become pivotal for our researches with the molecular still. As a practical matter the pilot technique has been retained, extremely accurate comparisons between the elimination curves of pilot dyes and the accompanying substances being realized. Indeed, relative elimination maxima can be determined in the range 100–200°C. with a precision of $\pm 1^\circ\text{C}$., which compares satisfactorily with ordinary boiling-point measurements.

The elimination technique does not require special apparatus, but it makes heavy demands on the operator who with clock and thermometer must give the distillation undivided attention until the last fraction has been collected.

At present the most convenient type of apparatus for these analytical distillations is a circulating batch still. The falling-film cyclic still has been described many times (52, 54), and a photograph of it (figure 26) is included here merely

for completeness. The distilland is circulated over a small vertical column at a constant rate, and fractions are removed periodically as the temperature is allowed to rise. The still accommodates from 50 to 500 cc. of distilland. A larger model holding 15 liters and equipped with a centrifugal evaporator is shown in figure 27. A later version (figure 28), built and largely designed by F. R. Kraselt, embodies automatic means for advancing the temperature and collecting distillates. The operator places the mixture of distilland, constant-yield oil, and pilot dye in the reservoir, A, arranges fifty matched test tubes in the rotating nest, B, replaces the glass dome, C, and starts the operating clock, D. About 4 hr. later the clock has shut off the pump and heaters, after which the dome may be lifted and the test tubes removed for analysis. A still is under construction

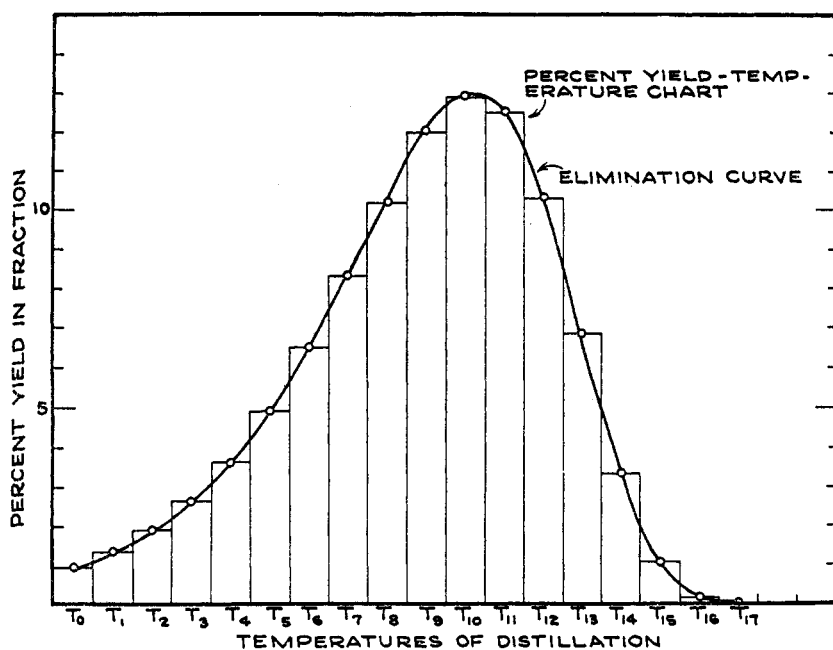


FIG. 25. Theoretical elimination curve, after Ebbree

which will present a series of individual condensers to the evaporator, thus obviating the need for constant-yield oil. An excellent analytical still of simple construction which can dispense with constant-yield oil has recently been described by Quackenbush and Steenbock (91). Concentric evaporators and condensers are employed, but the latter are on the *inside*, providing a smaller draining surface which, if necessary, can be *wiped* clean. The temperature of the evaporator is accurately controlled by vapor heating.

The elimination technique provides essentially practical information—how substances can be separated from the mixtures in which they occur. Consider the simple case of oleic and stearic acids. From their relative vapor pressures *unmixed* it could be deduced, according to Fawcett (37), that a half-and-half

mixture after a single distillation which removed a quarter of the bulk would give a distillate having the composition 68 per cent oleic acid and 32 per cent stearic acid. But this does not take into account the effect of each acid on the vapor pressure of the other, so that a practical distillation gives the quite different ratio 36 per cent oleic acid and 64 per cent stearic acid, *which could not readily*

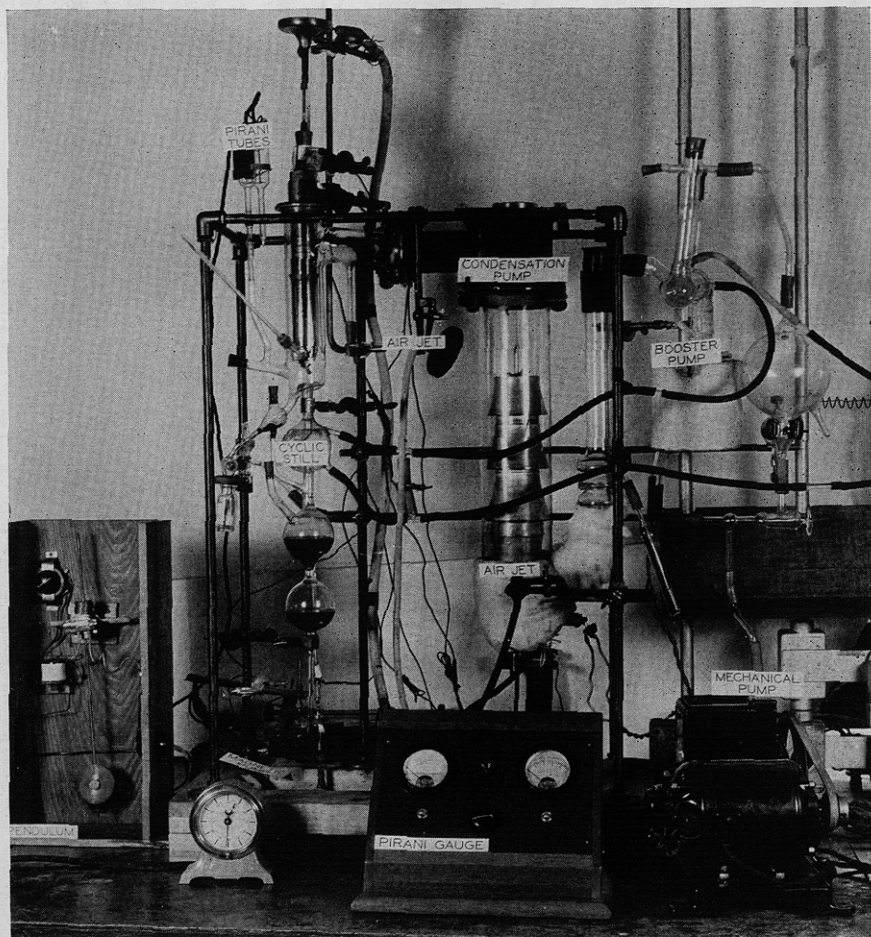


FIG. 26. Cyclic molecular still assembly

have been predicted. It is unlikely that anyone would attempt to separate these pure acids by distillation, crystallization being a better method. But it might well be desirable to distill traces of the two acids separately from a rancid oil. By plotting the elimination curves one can learn at a glance how to conduct a simpler type of distillation to secure the best separation.¹⁰

¹⁰ Our argument, in effect, recommends a practical determination instead of a theoretical approach based on related data. Of course, Fawcett also made the practical measurement, thus furnishing the text for this paragraph. The stress laid on the elimination technique is a plea for a systematized experimental approach which will yield readily recognizable data.

The elimination-curve theory takes into consideration only the mole concentration of the constituents. There are, in addition, their relative affinities for the distilland and for one another,—all those forces vaguely referred to as “asso-

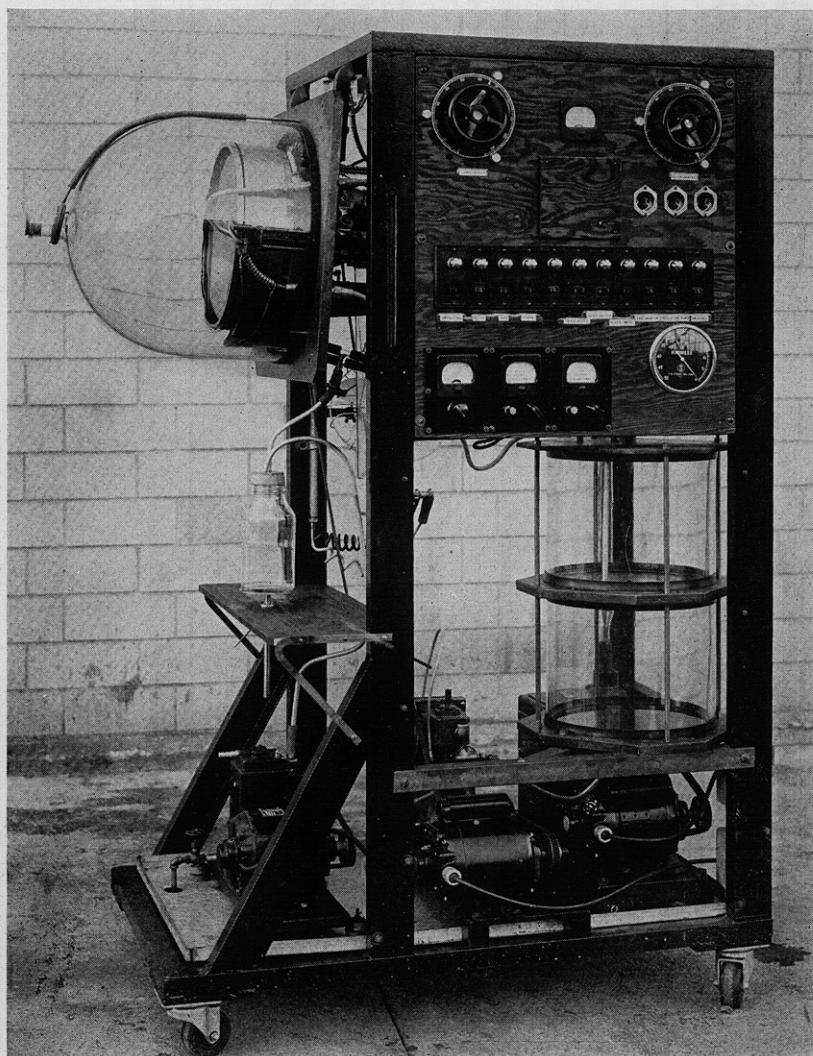


FIG. 27. Cyclic molecular still; large batch type with centrifugal evaporator

ciation,” which cause partial pressures to follow Henry’s law instead of Raoult’s. In the study of natural mixtures of similar origin, for instance, various samples of soybean oil, the association phenomena remain substantially the same from one distillation to another and the elimination curves of the substances under study maintain their accustomed shape and position. But let the solute be transferred to a different substrate, as when a concentrate of soybean non-

saponifiables is dispersed in petroleum oils, then the shape and the maxima of the constituents may be altered and the positions of near neighbors reversed. This effect of the substrate, predicted years ago by E. McDonald (85), is liable

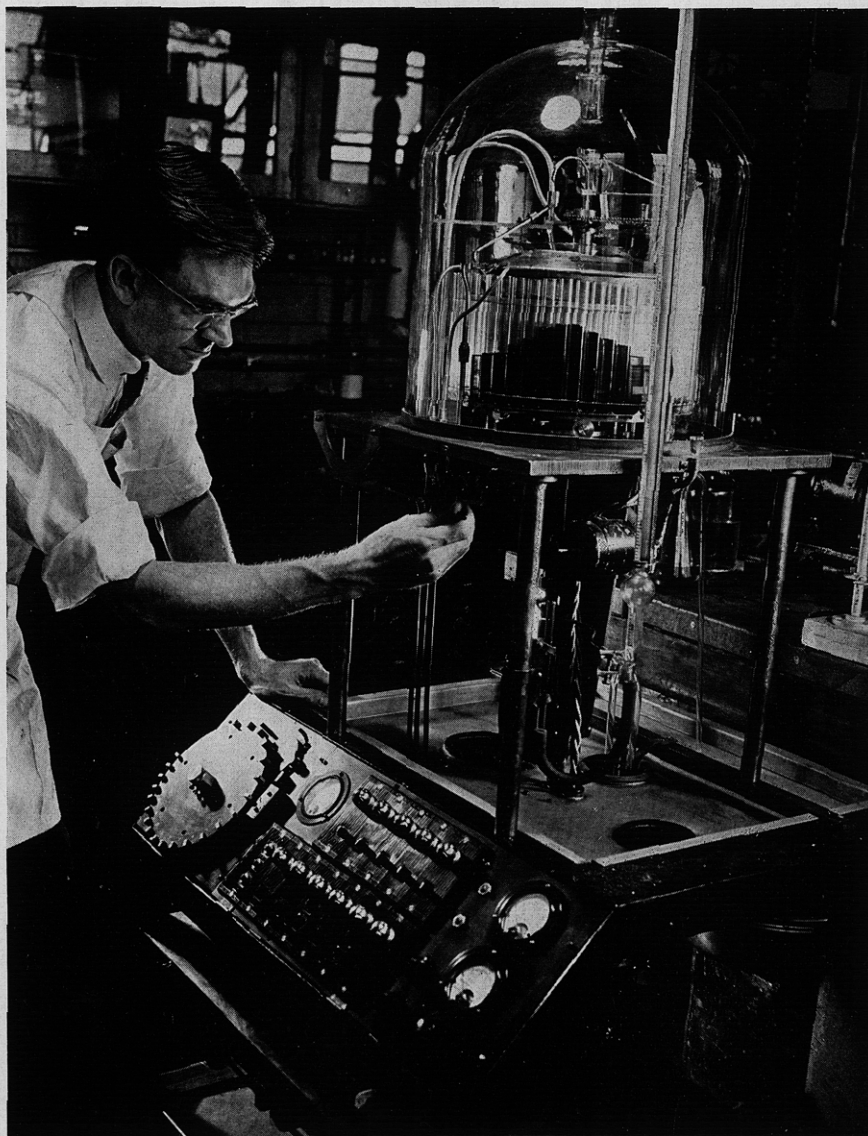


FIG. 28. Automatic, analytical, centrifugal cyclic still. Distillate tubes are seen in the crescent surrounding the evaporator.

to be misleading unless anticipated, but interpreted correctly it affords a useful clue as to the relative polarity, solubility, affinity, and thus *structure* of the solutes. Substances which can be separated no further from a glyceride sub-

strate can be transferred to a petroleum oil and the separation continued. Quantitative experiments on the influence of chemical structure on the behavior of

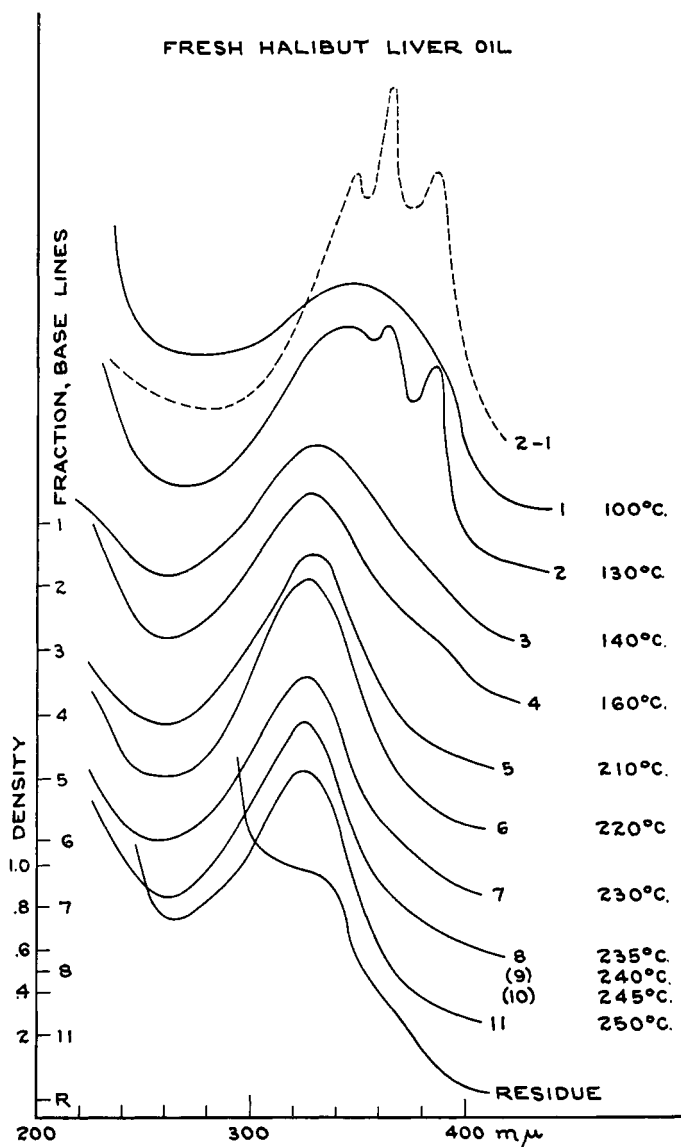


FIG. 29. Superimposed ultraviolet spectra of a succession of fish liver oil distillates

solvent and solute in the molecular still are in their infancy but should offer an approach to the fundamental study of evaporation.

The experimenter who has obtained a curve of the predicted shape remains uninformed as to its degree of nearness to the steepest possible curve corre-

sponding to the maximum separation of one theoretical plate. He must, therefore, assess the merits of the curve by comparing it with others of similar origin. Now it so happens that a good elimination curve coincides nearly with a triangle of similar area: $a = \frac{1}{2}bh$, when b and h are the dimensions of base line and height. Evidently for a *fixed height* the sharpness of separation is inversely proportional to the length of base line, or, in the case of the true elimination curve, of the area under the curve. When the elimination curve is plotted on graph paper, using 10°C . for one unit of base line, we find that the relation

$$\epsilon = \frac{5h}{a}$$

approximates unity in most experimental cases, where ϵ is the *elimination coefficient*, h is the height of the elimination curve, and a is the area under the curve,

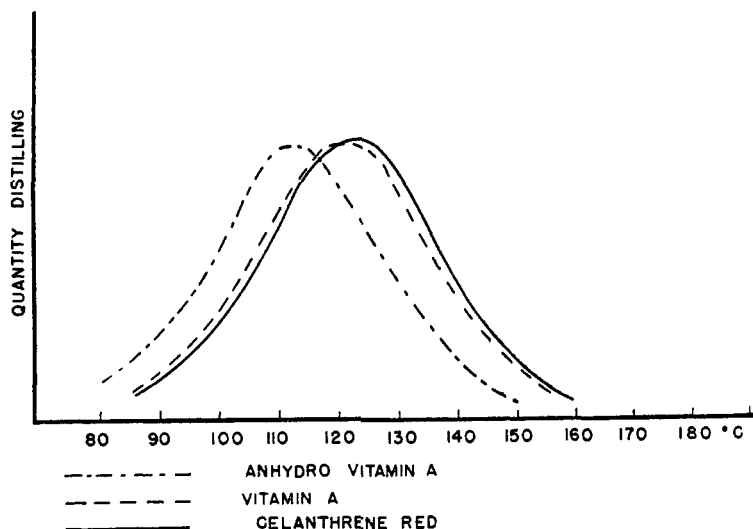


FIG. 30. Comparative elimination curves of vitamin A-like materials

the units of base line corresponding with temperature intervals of 10°C . If other temperature intervals are employed, the equation becomes

$$\epsilon = \frac{h \cdot \Delta t^{\circ}\text{C.}}{2a}$$

The elimination technique has been tested most thoroughly in relation to the fat-soluble vitamins and the diaminoanthraquinone pilot dyes. The earliest analytical distillations provided curves of predicted shape. Thus, a distillation of a non-saponifiable fraction of a fish liver oil, dissolved in glyceride controlled-yield oil, gave series of fractions which when examined in the ultraviolet spectrograph provided a set of spectra of the kind shown in figure 29. Two distinct spectral curves are discernible: the three-pronged curves typical of anhydro-vitamin A (8, 29, 93) and the simpler absorption curves, with maximum at 328

microns, of vitamin A itself. If the part of the extinction coefficient at 328 millimicrons attributable to vitamin A is plotted against fraction number, the curve shown in figure 30 results, where vitamin A alcohol is seen to have an elimination maximum at 126°C. compared with Celanthrene Red at 127°C. If the earlier fractions are combined and redistilled and the extinction coefficient at 363 millimicrons is determined for each subfraction, the elimination curve for anhydrovitamin A with maximum at 108°C. is secured. Thus, in one or two distillations it is possible to determine the relative boiling points of as many substances as there are available separate and independent tests of changes in concentration. Had the distillation of the liver oil non-saponifiable been done from a mineral constant-yield oil and residue mixture, the maxima of the constituents would have occurred in different order (data from Shantz).

SUBSTANCE	ELIMINATION MAXIMA*	
	Glyceride substrate	Petroleum substrate
	°C.	°C.
Vitamin A.....	109	102
Vitamin A ₂	110	102
Anhydrovitamin A.....	90	90
Anhydrovitamin A ₂	109	108
Celanthrene Red.....	110	95

* These distillations were carried out at 5° intervals, using two cycles per temperature. Maxima obtained using one cycle at 10° intervals are about 16° higher.

A secondary effect which may distort the elimination curves is reactivity of the substance under examination at high temperature. Pilot dyes, for instance, can become chemically altered during distillation. This is particularly true with glyceride oils containing a high proportion of fatty acid. The dialkylanthraquinones are observed to exchange radicals with the fat or fatty acids, giving rise to distorted curves; the distortion, since the exchange occurs more markedly at high temperatures and long exposure, is generally observed in the high-temperature limb of the elimination curve. When this has happened it may generally be recognized, except when the exchange merely broadens the peak of the curve and thus shifts the apparent maximum upwards. Ester exchange seldom occurs in entirely neutral fats when handled quickly, and it appears to be absent when the pilot dyes are distilled from mineral oils.

During the distillation of vitamins, sterols, and other substances which can exist as esters, a sharp upturn to the distillation curve is occasionally noted at higher temperatures. Also, it is generally the higher temperature limb which shows any distortions or irregularities. When these are observed it always denotes the presence of more than one molecular species obeying the identifying test, but a careful survey should be made to find whether the extra substances were present originally or have been formed during distillation. We were unaware of this effect when examining the complexity of vitamin D (68) in cod liver

oil and our conclusions that there were extra D-vitamins of a very high boiling point and hence high molecular weight are open to suspicion. Our finding that there were low-boiling D-vitamins (8) would appear not to require revision, since interaction between a sterol and glyceride at the lower temperature has not yet been detected. A rare phenomenon, but one which would seem to be established, is a great increase in volatility due to momentary conversion to free radical. Thus, a blue condensate has been found on the fore-vacuum side of the condensation pump when using the pilot dye dipropylaminoanthraquinone which evaporates in the molecular still at about 150°C. It is unlikely that the dye would have passed through the condensation pump in any quantity unless it were momentarily disassociated.

II. APPLICATIONS OF THE ELIMINATION-CURVE TECHNIQUE

The earliest applications of the method substantiated Bacharach's (3) observation that vitamin A exists in marine oils as an ester. Two widely separated maxima were found, and it was demonstrated that the high-boiling material could be distilled entirely at the lower temperature if saponified first. Vitamin D proved to exist as a mixture of free sterol and sterol esters, though there was from 30 to 40 per cent of free material in contrast to the 0 to 5 per cent free vitamin A found in the oils. A study of the keeping qualities of various fractions of fish liver oil, coupled with measurements made by the Emmerie and Engel test (33), showed that preservative substances, later recognized by Robeson (92a) as tocopherols, distill at temperatures intermediate between the vitamin A alcohol and esters. Distillation curves of the odor, the free fatty acids, and anhydrovitamin A have been compiled, so that it is possible to present a distillation map of a typical fish liver oil showing the interrelation (52) of constituents important to the user. This is given in figure 31.

The map shown in figure 31 is more than an academic compilation. It is the foundation of an industry which has considerably augmented the supplies of vitamin A in a time of world-wide shortage. It shows that passage through the molecular still with carefully controlled rates of distillation will concentrate the natural vitamin A esters and natural preservative into a single distillate, rejecting the undesirable acids and odors in a lighter fraction and leaving the bulk of the esters of the other unsaponifiables and the parent oil undistilled and substantially unchanged. This oil, with trifling mechanical loss, is left available for food or industrial use. The process, which dates from 1930 (59), should be clearly distinguished from the distillation of vitamin A alcohol produced by saponification. In the latter case the whole of the fish liver oil must first be changed into soap, while the free vitamin A is later purified by small-scale distillation. Some of the properties of free and esterified preparations of vitamin A are listed in table 6.

When Lederer and Rosanova (83) discovered another factor in the unsaponifiable fraction of fresh water fish oils, this was soon identified as a new vitamin A (100) which resembled the old in many (43) respects, the chief difference in

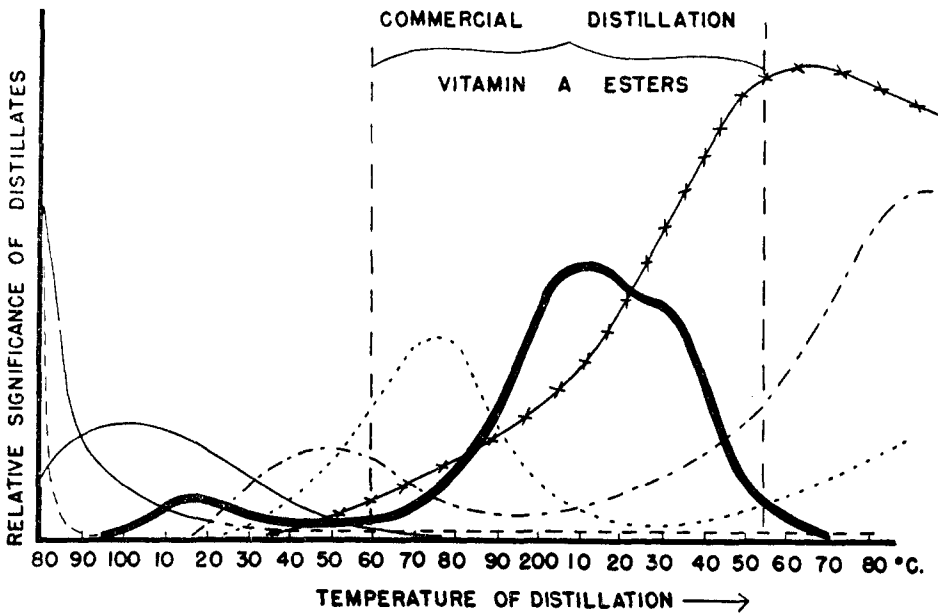


FIG. 31. Distillation map of a fish liver oil. ----, residual protein odor;-----, rancidity and reversion odor; ———, free fatty acids; -----, sterols, vitamin D, glyceride ethers, and their esters; -----, preservatives, tocopherols, and their esters; ———, vitamin A and esters; -x-x-, glyceride fat.

TABLE 6
Properties of free and of esterified preparations of vitamin A

PREPARATIONS OF VITAMIN A	ELIMINATION MAXIMUM*	AVERAGE POTENCY, U.S.P. UNITS PER GRAM (ORIGINAL)	AVERAGE POTENCY, U.S.P. UNITS PER GRAM (DILUTED FOR KEEPING TEST)†	AVERAGE CONVERSION FACTOR‡	COMPARATIVE STABILITY, HOURS AT 45°C.
	°C.				
U.S.P. Reference Oil II.....	214	1,700	1,700	2000	13
Halibut liver oil.....	212	120,000	120,000	2000	20-30
Distilled vitamin A ester, commercial concentrates.....	214	200,000	2,000	2000	200
Saponified fish liver oil, commercial concentrates.....	123	1,000,000	2,000	1500-1800	50
Crystalline vitamin A alcohol....	123	4,300,000	2,000	2460	50
Crystalline vitamin A acetate....	132	3,520,000	2,000	2350	170
Crystalline vitamin A palmitate...	208	2,310,000	2,000	2520	170

* Celanthrene Red = 126°; diamylaminoanthraquinone = 186°.

† Diluted with refined cottonseed oil.

‡ The protocols for these assays are being published in part and all are available for inspection.

constitution being the number of conjugated double bonds. Two formulae were proposed, as follows, with preference given to the second.

Gray (44) compared the elimination curves of both vitamins and found that the maxima differed by about 3°C. This seemed to disprove the theory that the vitamin chain had been lengthened by two carbon atoms. A recheck of Gray's

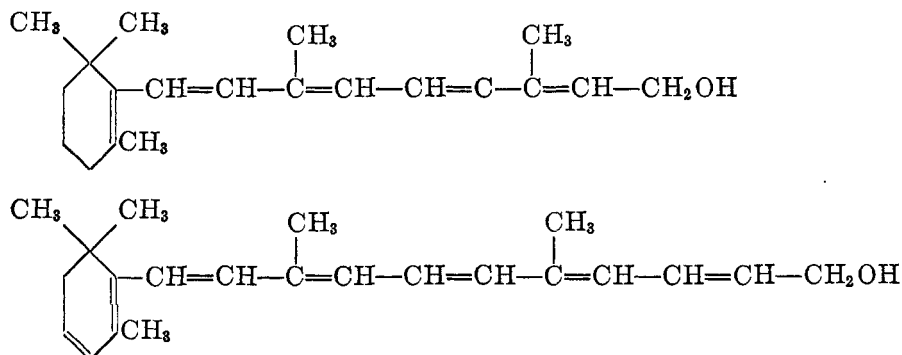


TABLE 7

Maxima of a number of saturated and unsaturated fatty acids

NAME OF ACID	ELIMINATION MAXIMUM FROM GLYCERIDE CONSTANT- YIELD OIL AT 10° INTERVALS
	°C.
Lauric	88.5
Myristic	98.0
Palmitic	108.0
Linoleic	114.0
Oleic	116.0
Stearic	118.0
9,11-Linoleic	123.5
α-Eleostearic	127.0

paper by Embree (32) showed that the difference may be much less, while Shantz and Cawley have shown the maxima to differ at most by 1°C. Gray and Cawley (45) determined the relative maxima of a number of saturated and unsaturated fatty acids (table 7) and demonstrated that the substitution of a double for a single bond shifts the maximum 1° to 3°C. The present evidence from distillation is that vitamins A and A₂ contain the same number of carbon atoms.

Analytical distillation has found an interesting application as yet only partly explored,—investigating the metabolism of those vitamins and sterols which can exist in more than one state of combination. Thus, cholesterol taken from the animal body is found to be a mixture of free and esterified sterol, the shape of the complex elimination curve allowing both the proportions and kinds of the esters to be deduced. Vitamin A is another case in point which has been investigated by Gray and others (47). The vitamin occurs naturally as the carotenoids, as

various esters in butter and marine oils, and as free vitamin A. The questions arose: Do all these substances become one substance or a similar mixture of substances after ingestion? Or is each stored and utilized in the form swallowed? Or is the state of the metabolized vitamin dependent on the species of animal? To investigate the matter six different forms of vitamin A were fed to six groups of young rats. The animals were killed, the livers extracted, the extracts blended with glyceride controlled-yield and residue oil, and distilled. The fractions were tested with antimony trichloride and the extinctions of the blue colors were

ELIMINATION MAXIMA
OF THE SUBSTANCES FED

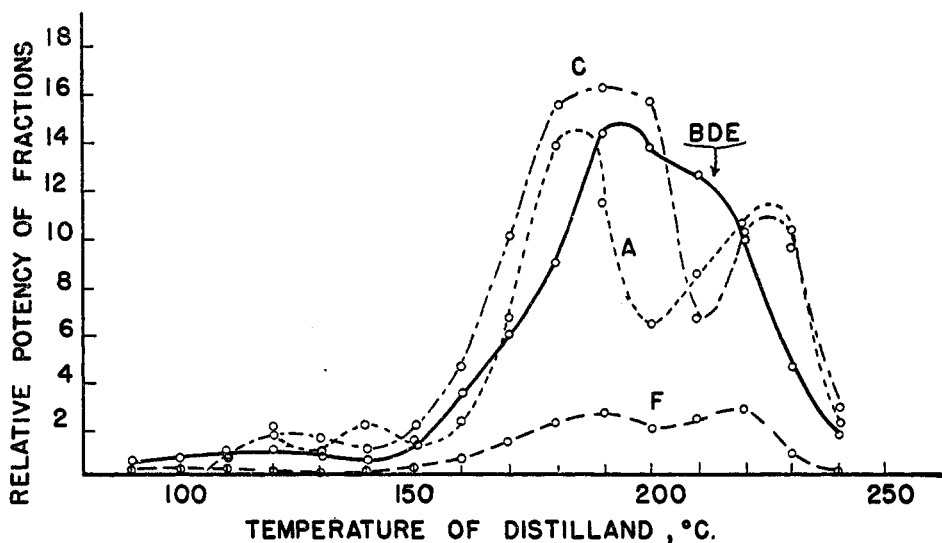
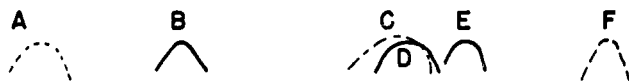


FIG. 32. Distillation map showing condition of various vitamin A compounds after ingestion by rat and extraction from liver. A (---), vitamin A-alcohol, 39 per cent recovery; BDE (—), vitamin A stearate, vitamin A caproate, and distilled ester concentrate, 44.2-50.7 per cent recovery; C(---), U.S.P. Reference Oil I, 55.7 per cent recovery; F(—), β -carotene, 2.7 per cent recovery.

plotted against temperature, as in figure 32. The antimony trichloride measured impartially the free vitamin A, the vitamin esters, anhydrovitamin A, and other vitamin A products. It was established that no matter what form of vitamin was fed there appeared in the rat's liver a few hours later a preponderance of vitamin A ester with an elimination maximum corresponding to palmitate (185°C.), a smaller quantity of higher molecular weight ester (230°C.), a still smaller quantity of free vitamin A (125°C.) with occasional traces of anhydrovitamin A (105°C.), and another vitamin A derivative

(115°C.), both probably produced during the alcohol extraction of the livers (Cawley, 1942). Gray has since found (46) that when the rats are kept alive for some weeks after administration, the heavy ester is absent from the liver, most of the vitamin having been converted to palmitate. We quote these experiments to show that considerable information can be extracted from the relatively poor separating power of the molecular still.

The elimination technique matured at a time when the multiple nature of vitamin D occupied particular attention. Calciferol had been differentiated from fish liver oil vitamin D by the rat-chicken ratio test of Bills and Massengale (87); Bills (7) had listed at least eight substances of vitamin D activity, while Windaus (110) and Brockmann (9) were arguing to the contrary that irradiated 7-dehydrocholesterol was the only important antirachitic substance in tuna and other fish liver oils. It seemed worthwhile to examine the homogeneity of marine vitamin D by molecular distillation. In doing this, Hickman and Gray (68) were confronted with the difficulty that no sensitive chemical test existed for the vitamin, forcing them to use the inexact method of rat assay. Each point on the elimination curve was thus the tombstone of a score of rats, the complete curve marking a cemetery of no mean proportions. The conclusion of some years of work,—namely, that there are at least four and possibly six D vitamins in Norwegian cod liver oil (*Gadus morrhua*),—is still equivocal but the method of approach deserves mention.

The cod liver oil was saponified to destroy vitamin esters and then blended with constant-yield oil and distilled. The highest potency fraction was sought by pilot assay, and assay levels were festooned from this point to cover the probable potencies of the other fractions. There resulted a complex curve which could lie within the ambit of a single curve and might, therefore, be considered merely a measure of the imperfection of the assay were it not that repeated distillations gave substantially the same complex curve. An average of three curves is recorded in figure 33, where the dark central line shows the probable potencies of the fractions and the faint lines show the outside credible limits of potency. The question at issue became: Are the multiple peaks and inversions real or are they—to beg the question—artifacts?

A master distillation was performed to provide in any fraction enough vitamin D to form the starting material for a subdistillation after reblending with constant-yield oil. Fractions coming over between 100° and 130°C. were combined and redistilled as were fractions between 160° and 200°C. If one vitamin only were involved, the secondary distillation curves should each resemble the primary, but if the primary low- and high-boiling fractions contained separate antirachitic substances, second distillations should furnish widely different curves. Figure 34, where the second distillations are superimposed, shows that the difference indeed exists, each curve substantiating the existence of real antirachitic maxima in its own temperature region. The lesson from this experiment is that when the shape of a distillation curve is in doubt after repeated experiment, the contours can be proved or disproved by redistillation of the high and low fractions.

Since the beginning of interest in marine liver oils the spectrograph has revealed many anomalies in the ultraviolet and antimony trichloride absorption curves

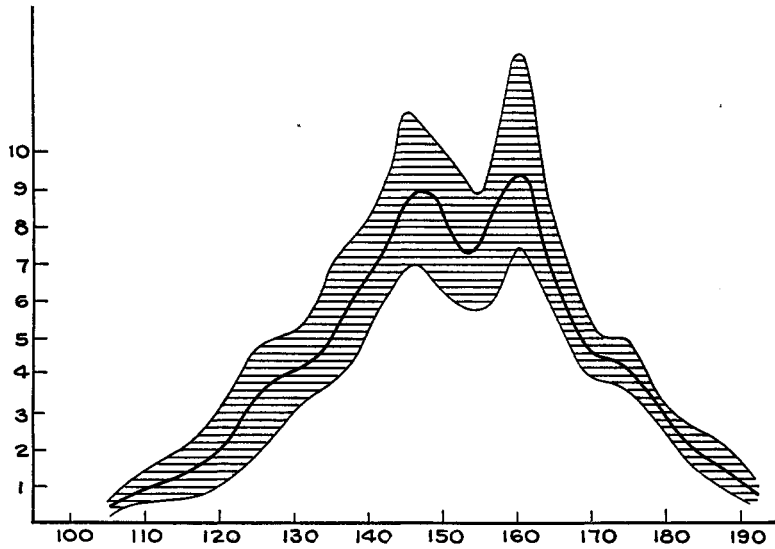


FIG. 33. Averaged elimination curve of the saponified vitamin D from whole cod liver oil

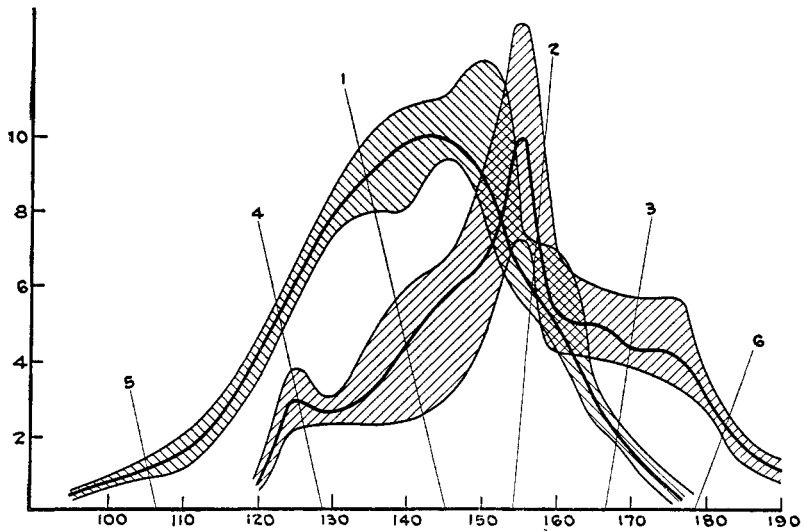


FIG. 34. Superimposed elimination curves of "low-boiling" and "high-boiling" vitamin D distillates. Note that in spite of irregularities of assay the curves fail to overlap except in their central portions, thus demonstrating separation of two varieties of natural vitamin D.

attributed to vitamin A. The abnormalities are gradually being identified with other substances present in the oils. Anhydrovitamin A has been concentrated

TABLE 8
Substances investigated quantitatively by means of the molecular still†*

VITAMIN A CLASS	VITAMIN D CLASS	STEROL CLASS	HORMONE CLASS	DYE CLASS
Vitamin A alcohol* (52) Vitamin A acetate* (47) Vitamin A palmitate* (47) Vitamin A naphthoate Vitamin A acid succinate* (95) Vitamin A succinate* (95) Vitamin A fish liver esters* (52) Vitamin A rat liver esters* (47) Vitamin A ₂ * (44) Anhydrovitamin A* (93) Sub-vitamin A* (99) β-Carotene* (95) α-Carotene (95) Xanthophyll (95) Kitol* (114)	D ₂ calciferol* (68) D ₃ * (68; Windaus) Cod liver oil D* (68) Tuna liver oil D* (68) Swordfish D* (68)	Cholesterol* (54) Sitosterols* (54) Stigmasterol* (54) α-Tocopherol* (54) γ-Tocopherol Tocoquinones Vitamin K	Progesterone (1) Bone marrow anemia factor (74)	Substituted diaminoanthraquinones* (52) Indigo and derivatives* (52) Butter coloring matters (95)

* Only substances marked with asterisks have been examined quantitatively. The elimination maxima are not given because the figures do not yet give a concordant series.

† This list does not include the many investigations of the natural glycerides and heavy petroleum residues.

by distillation to the point where Robeson and Baxter have obtained it in crystals, m.p. 74–75°C., and Embree and Shantz have been able to determine its probable

TABLE 9*
Crystalline vitamin A

VITAMIN A PREPARATIONS	MELTING POINT	BIOLOGICAL POTENCY†	CONVERSION FACTOR BIOLOGICAL POTENCY		
			$E_{1\text{ cm.}}^{12}$ (328 m μ)	$E_{1\text{ cm.}}^{12}$ (528 m μ)	$E_{1\text{ cm.}}^{12}$ (620 m μ)
			°C.	U.S.P. units per gram $\times 10^{-6}$	
Vitamin A alcohol.....	63–64	4.3	1750	2460	4800
Vitamin A acetate.....	57–58	3.52	1510	2350	4580
Vitamin A palmitate.....	27–28	2.31	940	2520	2535
Vitamin A succinate (di).....	76–77	3.14	1240	2630	4450
Vitamin A β -naphthoate.....	74–75	3.44	1090	3160	2940
Anhydrovitamin A.....	76–77	0.015	3650†	4.1	5500
Vitamin A β -naphthoate§.....	78	2.22	1190	1870	
Vitamin A anthraquinone-2-carboxylate (yellow form)§.....	126	1.75	938	1870	
Vitamin A anthraquinone-2-carboxylate (red form)§.....	118–120		1090		

Vitamin E

	MELTING POINT	WAVE LENGTH	$E_{1\text{ cm.}}^{12}$	POTENCY¶ RELATIVE DOSE REQUIRED
	°C.			
Natural α -tocopherol.....		292	73.7	0.8
Natural β -tocopherol.....		297	87.6	1.5
Natural γ -tocopherol.....		298	92.8	8.0
Merck synthetic α -tocopherol.....		292	75	1.0
α -Tocopherol succinate.....	76 – 77	286	37	0.68
α -Tocopherol palmitate.....	42 – 43	286	26.8	
α -Tocopherol acetate.....	26.5– 27.5	285	41.2	
α -Tocopherol allophanate.....	158 –160	286	36	
γ -Tocopherol palmitate.....	44 – 45	286	40.7	8.0
γ -Tocopherol allophanate.....	137 –139	286	46.3	
β -Tocopherol azobenzenecarboxylate.....	69.5– 70.5	328	483	6.0
β -Tocopherol allophanate.....	135 –137	283	44.5	

* Data assembled and checked by Dr. J. G. Baxter.

† Assays by Dr. P. L. Harris using U.S.P. Reference Oil II.

‡ Value at 371 m μ .

§ Values obtained by Mead, Underhill, and Coward. β -Carotene used as standard for biological assay.

¶ By Dr. P. L. Harris using Mason-Bacharach rat test. Values represent median fertility dose as milligram of free tocopherols.

constitution. These workers have also studied “sub-vitamin A” (32) by a combination of distillation and chromatography. Perhaps the most interesting

marine material examined by Embree and Shantz (32a) is a substance, previously recognized by its ultraviolet absorption but otherwise uninvestigated, which occurs in whale liver oil. The substance, tentatively named "kitol", has an absorption band at 285 millimicrons and the antimony trichloride product has a band at 428 millimicrons. When heated to 250°C. kitol disappears, giving rise to vitamin A. The total quantity of vitamin A in whale liver oil is thus *increased* by distillation. Kitol must take its place as a new kind of provitamin A and as the only vitamin A precursor which has been converted to the vitamin *in vitro*. It differs from other known precursors by having no vitamin A activity until heated. Embree and Shantz recently report finding the equivalent precursor of vitamin A₂ in pike liver oil. Both provitamins were discovered by means of *quantitative* molecular distillation.

Some of the substances which have been investigated in the analytical still are listed in table 8. The properties of various vitamin and related substances which have been crystallized by Baxter and Robeson are given, by their kind permission, in table 9. Further applications of the molecular still and the elucidation of the structure of marine glyceride oils are described by Farmer and van den Heuvel (35). A general summary by Embree (30) has appeared in this journal.

III. QUALITATIVE LABORATORY DISTILLATIONS

The elimination technique supplies information rather than actual separation. When the boiling range of the wanted constituent has been learned, larger scale distillation can be done with or without pilot dye, collecting few distillates at the preferred temperatures. Distillation seldom yields a pure product from a crude mixture, only an increase in concentration. This increase, however, may be sufficient to allow the material to be separated by means which were previously ineffective. Materials which could not be crystallized from the crude may crystallize readily from the richer fractions.

IV. FUTURE OF THE METHOD

The simple laboratory still is reaching a stage of development where further great increase in efficiency is unlikely. But even when finality of design is neared, there will remain unexplored the larger and more important field of high-vacuum fractionation. A still with greater fractionating power than one theoretical plate—two would be a signal advance—will extend the method appreciably. We are only just consolidating our knowledge of how to make the molecule take a single leap into empty space from a very thin film of distilland. It remains to train the same molecule to dance precisely through a succession of evaporators and condensers until it loses all competitors and emerges only in the company of its fellows.

The sources of the historical material used have been quoted in the introduction. It remains to pay grateful tribute to the owners of Distillation Products and members of the staff whose support and efforts have made possible the in-

tegrated development of the high-vacuum distillation process and its organized application to research. Mr. George Surridge has been responsible for the machine drawings and much of the design; Mr. F. M. Jenner has superintended the construction of large apparatus; Dr. J. Hecker has brought the apparatus into operation and over a period of years greatly influenced the design. Dr. N. Embree has led in the application of the stills in pure research; his colleagues have been mentioned in the text.

REFERENCES

- (1) ALLEN, W. M.: *J. Biol. Chem.* **98**, 591 (1932).
- (2) ALMQUIST, H. J.: *J. Biol. Chem.* **115**, 589 (1936); **120**, 635 (1937).
BREUSCH, F.: *Z. physiol. Chem.* **227**, 242 (1934).
- (3) BACHARACH, A. L., AND SMITH, E. L.: *Quart. J. Pharm.* **1**, 539 (1928).
- (4) BANCROFT, F. E.: British patent 428,719 (May 15, 1935).
- (5) BAXTER, J., AND HICKMAN, K.: *J. Franklin Inst.* **221**, 383 (1936).
- (6) BAXTER, J., AND TISCHER, A.: *Ind. Eng. Chem.* **29**, 1112 (1937).
- (7) BILLS, C. E.: *J. Am. Med. Assoc.* **108**, 13 (1937).
- (8) BILLS, C. E., MASSENGALE, O. N., HICKMAN, K., AND GRAY, E. LEB.: *J. Biol. Chem.* **126**, 241 (1938).
- (9) BROCKMANN, H.: *Z. physiol. Chem.* **241**, 104 (1936); **245**, 96 (1937).
- (10) BRÖNSTED, J. N., AND HEVESY, G. VON: *Phil. Mag.* **43**, 31 (1922).
- (11) BURCH, C. R.: *Nature* **122**, 729 (1928).
- (12) BURCH, C. R.: *Proc. Roy. Soc. (London)* **A123**, 271 (1929).
- (13) BURCH, C. R., AND VAN DIJCK, W. J. D.: *J. Soc. Chem. Ind.* **58**, 39 (1939).
- (14) BURCH, C. R., *et al.*: British patent 303,078 (December 21, 1928); reissued as U.S. patent 1,955,321 (April 17, 1934).
- (15) BURCH, C. R., *et al.*: U.S. patent 1,955,321 (April 17, 1934); reissued from British patent 303,078 (December 21, 1928).
- (16) BURROWS, G.: *J. Soc. Chem. Ind.* **58**, 50 (1939).
- (17) BURROWS, G.: British patent 475,062 (November 12, 1937).
- (18) CALDWELL, K. S., AND HURTLEY, W. H.: *J. Chem. Soc.* **95**, 853 (1909).
- (19) CAROTHERS, W. H., AND HILL, J. W.: *J. Am. Chem. Soc.* **54**, 1557 (1932).
- (20) CARR, F. H., AND JEWELL, W.: *Nature* **131**, 92 (1933).
- (21) CHEVREUL: *Les corps gras*, pp. 23, 77, 178, 186.
- (22) DAM, H., AND LEWIS, L.: *Biochem. J.* **31**, 17 (1937).
DAM, H., AND SCHÖNHEYDER, F.: *Nord. med. Tid.* **12**, 1097 (1936).
- (23) DETWILER, S. B., JR.: *Oil & Soap* **16**, 2 (1939); **17**, 241 (1940).
- (24) DETWILER, S. B., JR.: "Abstracts of Articles and Patents on Molecular or Short-Path Distillation." U. S. Regional Soybean Industrial Products Laboratory, Urbana, Illinois (1941).
- (25) DETWILER, S. B., JR., AND MARKLEY, K. S.: *Ind. Eng. Chem., Anal. Ed.* **12**, 348 (1940).
- (26) DUNOYER, L.: *Vacuum Practice*. D. Van Nostrand and Company, New York (1926).
- (27) DUSHMAN, S.: *High Vacuum*. General Electric Review Press, Schenectady, New York (1922).
- (28) EMBREE, N. D.: *Ind. Eng. Chem.* **29**, 975 (1937).
- (29) EMBREE, N. D.: *J. Biol. Chem.* **128**, 187 (1939).
- (30) EMBREE, N. D.: *Chem. Rev.* **29**, 317 (1941).
- (31) EMBREE, N. D., AND SHANTZ, E. M.: *J. Biol. Chem.* **132**, 619 (1940).
- (32) EMBREE, N. D., AND SHANTZ, E. M.: *J. Am. Chem. Soc.* **65**, 906 (1943).
- (32a) EMBREE, N. D., AND SHANTZ, E. M.: *J. Am. Chem. Soc.* **65**, 910 (1943).
- (33) EMMERIE, A., AND ENGEL, C.: *Rec. trav. chim.* **57**, 1351 (1938).

- (34) ERDMAN, E.: Ber. **36**, 3456 (1903).
- (35) FARMER, E. H., AND HEUVEL, F. A. VAN DEN: J. Soc. Chem. Ind. **57**, 24 (1938).
- (36) FAWCETT, E. W.: U. S. patent 2,047,196 (July 14, 1936).
- (37) FAWCETT, E. W.: J. Soc. Chem. Ind. **58**, 43 (1939).
- (38) FAWCETT, E. W.: Private communication.
- (39) FAWCETT, E. W., AND BURROWS, G.: British patent 480,265 (February 21, 1938).
- (40) FAWCETT, E. W., AND McCOWEN, J. L.: British patent 434,726 (March 7, 1934).
- (41) FAWCETT, E. W., *et al.*: U. S. patent 2,128,354 (August 30, 1938).
- (42) FRASER, R. G. J.: British patent 467,028 (December 9, 1935).
- (43) GILLAM, A. E., HEILBRON, I. M., JONES, W. E., AND LEDERER, E.: Biochem. J. **32**, 405 (1938).
- (44) GRAY, E. LEB.: J. Biol. Chem. **131**, 317 (1939).
- (45) GRAY, E. LEB., AND CAWLEY, J. D.: J. Biol. Chem. **134**, 397 (1940).
- (46) GRAY, E. LEB., AND CAWLEY, J. D.: J. Nutrition **23**, 301 (1942).
- (47) GRAY, E. LEB., HICKMAN, K., AND BROWN, E.: J. Nutrition **19**, 39 (1940).
- (48) HICKMAN, K.: Rev. Sci. Instruments **18**, 69 (1929).
- (49) HICKMAN, K.: J. Franklin Inst. **213**, 119 (1932).
- (50) HICKMAN, K.: J. Franklin Inst. **221**, 216 (1936).
- (51) HICKMAN, K.: Ind. Eng. Chem. **29**, 968 (1937).
- (52) HICKMAN, K.: J. Applied Phys. **2**, 302 (1940).
- (53) HICKMAN, K.: Ind. Eng. Chem. **32**, 1451 (1940).
- (54) HICKMAN, K.: Ind. Eng. Chem., Anal. Ed. **14**, 250 (1940).
- (55) HICKMAN, K.: U. S. patent 1,942,858 (January 9, 1934).
- (56) HICKMAN, K.: U. S. patent 2,150,685 (March 14, 1935).
- (57) HICKMAN, K.: U. S. patents 2,080,421 (May 18, 1937); 2,153,189 (April 4, 1939); 2,206,093 (July 2, 1940).
- (58) HICKMAN, K.: U. S. patent Re 20,705 (April 26, 1938); reissued from 1,925,559 (September 5, 1933).
- (59) HICKMAN, K.: U. S. patent 2,180,051 (January 14, 1939).
- (60) HICKMAN, K.: U. S. patent 2,180,053 (November 14, 1939).
- (61) HICKMAN, K.: U. S. patent 2,199,994 (May 7, 1940).
- (62) HICKMAN, K.: U. S. patent 2,210,928 (August 13, 1940).
- (63) HICKMAN, K.: U. S. patent 2,218,240 (October 15, 1940).
- (64) HICKMAN, K.: British patent 540,603 (October 23, 1941).
- (65) HICKMAN, K.: U. S. patent 2,249,526 (July 15, 1941).
- (66) HICKMAN, K., AND GRAY, E. LEB.: Ind. Eng. Chem. **30**, 796 (1938).
- (67) HICKMAN, K., AND SANFORD, C. R.: J. Phys. Chem. **34**, 637 (1930).
- (68) HICKMAN, K., AND WEYERTS, W.: J. Am. Chem. Soc. **52**, 4714 (1930).
- (69) HICKMAN, K., *et al.*: U. S. patent 2,180,052 (November 14, 1939).
- (70) HOUSEKEEPER, W. G.: U. S. patent 1,471,662 (October 23, 1923).
- (71) HURD, C.: J. Am. Chem. Soc. **63**, 2656 (1941).
- (72) In conjunction with Dr. J. D. Porsche of Armour & Company (1940).
- (73) JEANS, J.: *An Introduction to the Kinetic Theory of Gases*, pp. 131-55. The MacMillan Company, New York (1940).
- (74) KNUDSEN, M.: *The Kinetic Theory of Gases*, pp. 21-26. Methuen's Monographs on Physical Subjects. Messrs. Methuen and Company, London (1934).
- (75) KNUDSEN, M.: Ann. Physik **29**, 179 (1909).
- (76) KNUDSEN, M.: Ann. Physik **28**, 75 (1909); **28**, 999 (1909); **32**, 809 (1910); **35**, 389 (1911); **48**, 1113 (1915); **83**, 797 (1927).
- (77) LOEB, L. B.: *The Kinetic Theory of Gases*, pp. 290 et seq. McGraw-Hill Book Company, Inc., New York (1934).
- (78) KRAFFT, F., *et al.*: Ber. **29**, 1316, 2240 (1896); **42**, 202, 210 (1909).
- (79) LANGMUIR, I.: Phys. Rev. **8**, 149 (1916).
- (80) LANGMUIR, I.: J. Franklin Inst. **182**, 719 (1916).
- (81)

- (82) LANGMUIR, I.: U. S. patent 1,393,550 (October 11, 1921).
- (83) LEDERER, E., AND ROSANOVA, V.: *Biokhimiya* **2**, 293 (1937).
- (84) LOEB, L. B.: *The Kinetic Theory of Gases*, p. 281. McGraw-Hill Book Company, Inc., New York (1934).
- (85) McDONALD, E.: *J. Franklin Inst.* **221**, 137 (1936).
- (86) MALTER, L.: U. S. patent 2,112,037 (March 22, 1938).
- (87) MASSENGALE, O. N., AND BILLS, C. E.: *J. Nutrition* **12**, 429 (1936).
- (88) MORSE, R. S.: *Ind. Eng. Chem.* **33**, 1039 (1941).
- (89) OOSTERHOF, D., VLODROP, C. VAN, AND WATERMAN, H. I.: U. S. patent 2,065,728 (December 29, 1936); similar to Dutch patent 35,201 (April 15, 1935).
- (90) PAYNE, E. H.: U. S. patent 1,899,916 (February 28, 1933).
- (91) QUACKENBUSH, F. W., AND STEENBOCK, H.: *Ind. Eng. Chem., Anal. Ed.* **15**, 468 (1943).
- (92) RIEGEL, B., BEISWANGER, J., AND LANZL, G.: *Ind. Eng. Chem., Anal. Ed.* **15**, 417 (1943).
- (92a) ROBESON, C. D., AND BAXTER, J. G.: *J. Am. Chem. Soc.* **65**, 910 (1943).
- (93) SHANTZ, E. M., CAWLEY, J. D., AND EMBREE, N. D.: *J. Am. Chem. Soc.* **65**, 901 (1943).
- (94) STRONG, JOHN: *Procedures in Experimental Physics*. Prentice-Hall Inc., New York (1938).
- (95) Unpublished work, Distillation Products, Inc. Laboratory.
- (96) VAN DIJCK, W. J. D.: U. S. patent 1,950,830 (March 13, 1934).
- (97) VIGERS, B., AND McCOWEN, J.: British patent 458,117 (December 14, 1936); similar to U. S. patent 2,137,553 (November 22, 1938).
- (98) VIGERS, B., AND McCOWEN, J.: British patent 458,118 (December 14, 1936).
- (99) VOLMER, M.: *Z. angew. Chem.* **34**, 149 (1921).
- (100) WALD, G.: *Nature* **139**, 1017 (1937).
- (101) WASHBURN, E. W., *et al.*: *J. Research Natl. Bur. Standards* **2**, 467 (1929).
- (102) WATERMAN, H. I., AND ELSBACH E.: *Chem. Weekblad* **26**, 469 (1929).
- (103) WATERMAN, H. I., AND NIJHOLT, J. A.: *Chem. Weekblad* **24**, 268 (1927).
- (104) WATERMAN, H. I., AND OOSTERHOF, D.: *Rec. trav. chim.* **52**, 895 (1933).
- (105) WATERMAN, H. I., AND RIJKS, H.: *Z. deut. Öl-u. Fett-Ind.* **46**, 177 (1926).
- (106) WATERMAN, H. I., AND VLODROP, C. VAN: *Chimie & industrie* **34**, 1036 (1935).
- (107) WATERMAN, H. I., AND VLODROP, C. VAN: *Rev. chim. ind.* **48**, 314 (1939).
- (108) WATERMAN, H. I. AND VLODROP, C. VAN: *Rev. chim. ind.* **48**, 319 (1939), figure 7.
- (109) WILSON, R. E.: U. S. patent 1,905,201 (April 25, 1933).
- (110) WINDAUS, A., LETTRÉ, H., AND SCHENCK, F.: *Ann.* **520**, 98 (1935).