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A Classification of Separation Methods

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A general classification of separation methods is attempted. The two criteria were phase transformations and interfacial transfers. All separation methods of homogenous mixtures were divided into five groups: (i) methods that are based on the formation of new phases by substances to be separated; (ii) methods that are based on differences in the interphase distribution processes, chromatographic methods being singled out as a separate group; (iii) membrane methods that are based on induced transfers of substances from one phase into another one across a third phase, which separates the two; (iv) separation methods within a single phase that are based on velocity and direction differences in spatial displacement of particles of substances to be separated within one fluid phase under the action of various fields; and (v) combined methods working combining previously listed methods.

Descriptions of each group of separation methods include their intragroup classification and information on the most important techniques as well as the least known of them. These descriptions are in the form of reviews of fundamental and most important publications, regardless of the time they appeared. For the well-known classical methods of the first group all necessary information can be found in university textbooks.

Keywords: Characteristic properties, classification, separation methods, phase, state of aggregation

INTRODUCTION

There is a constant growth in the number of problems, for which a separation of substances is required. Consequently, there is a growth in the number of separation methods as well. However, until now there has been no generally accepted system of criteria for both combining and differentiating the groups of single-type separation methods (1). Significant evidence of a lack of such classification is shown in modern analytical chemistry textbooks: the popular and often- reprinted textbook by M. Otto (2), as well as the all-European textbook by a group of authors (3), can be taken as examples. In both textbooks, separation methods are mentioned unsystematically, in particular, great attention is given to chromatographic methods. In one of the textbooks (2), chromatography is listed under "instrumental methods of analysis that are based on physical interactions."

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In the second textbook (3), one of the co-authors, M. Otto, who is also the author of reference (2), chromatographic methods are discussed in the "Chemical Methods of Analysis" section. Also, in (3, Ch.5), a "Review of Chromatographic Methods" subsection is included without specifying which methods are meant, wherein, out of any logical relationship, a number of chromatographic methods are mentioned in the form of a Table (5.1.1), where "Classification of Column Chromatography Methods" is given. It is unclear why only column chromatography is considered.

Last, it is hard to agree with (2) that "the most important separation and concentration methods are:

- Distillation of volatile components;
- Precipitation or co-precipitation;
- Extraction and ion exchange;
- Electrolytic isolation;
- Column chromatography and sorption.

To point out serious problems in such a statement two contradictions are that column chromatography and sorption

belong to different categories. Column chromatography is a possible scheme for the implementation of a chromatographic process, whereas sorption is a chemical mechanism of the interphase distribution process, indeed used in some chromatographic separation methods. At last, why is a very seldom applied electrolytic isolation related to the most important methods, whereas membrane methods are not mentioned at all?

The absence of relevant information in textbooks is a logical consequence of a limited number of publications devoted to classifications of separation methods and/or a consequence of insufficiency of earlier suggested classifications. One of these early classifications was made in 1973 by chromatographers (4). Mentions of some other classifications can be found in an article by J. C. Giddings (5), wherein the author suggests a classification of his own and proves convincingly its necessity. The lack of clear classification of separation methods renders the choice of an adequate methodical and technological separation solution complicated. In discussing the number of criteria for a comprehensive classification of separation methods, J.C. Giddings (5) pointed out two important ones: flow condition and continuous or discontinuous forces.

Such approach made it possible for J. C. Giddings to divide separation methods into six main groups: state condition, parallel flow and perpendicular flow condition, and different forces acting on the system.

The first version of this classification was complemented in a monograph published in 1991 (6). With all deepest respect to the author, whose contribution to separation science is immense, there are a number of points in the suggested classification that cannot be agreed upon. In particular, the use of driving forces and occurrence or absence of flow as classification criteria seems to be quite arguable. An additional differentiation of driving forces into continuous and discontinuous ones, as well as into their direction relative to the flow wherein separation occurs, do not clarify the fundamental principles and boundaries among individual separation methods. These criteria are understandable considering individual groups of separation methods, in the first place, membrane- and separation methods within a single phase. Afterwards these criteria will be used in our corresponding intragroup classifications, but we do not consider them as fundamental for a general classification.

As a result of such approach to the general classification, in the same groups of methods there appear, for example, such methods as single extraction and dialysis (by the "static system" and "driving force" criteria), filtration and zone melting (by the "parallel flows" and "discontinuous force" criteria); lastly, distillation, adsorption and crystallization (by the "perpendicular flow" and "discontinuous force" criteria). The methods given above, which are far from each other as regards their physicochemical principles and technologies of implementing separation processes, are difficult to apprehend as the related ones that belong to same groups.

In 1992, Giddings' ideas were supported in a monograph by Macasek and Navratil (7). A section of this article: "Generalization and Classification of Separation Processes" begins with an epigraph from Giddings' paper: "By and large history of separation science has been of diverging pathways. The consequence has been much reducing in the independent design and optimization of system that are based on common theory, and lost opportunities in technological spinoff from the more advanced methods to those at less sophistical stage of development." One cannot but agree with this, but there are no new approaches to classification suggested by the authors (5).

Finally, the most comprehensive of currently available classifications can be found in Volume 4 of a Reference Series edited by Ahuja in 2003 (8). However, even this classification is questionable. It includes several general principles of separation of homogeneous mixtures: interphase distribution in various phase systems, rate processes, diffusion through permeable barriers, field separations and miscellaneous separation methods. Nevertheless, there is practically no internal logic present in the choice of these criteria. The monograph title "chromatography" is considered by the author to be apart from separation science as a whole. An unclear, unexpected and undocumented change is made by the author from his suggested classification to that of J. C. Giddings (5).

All the classifications mentioned above, including those of J. C. Giddings, have become substantially obsolete, and, as judged by the absence of any mention in analytical chemistry textbooks, have not attracted any wide attention from separation specialists. In addition, a number of new separation methods emerged recently, for which there is no place in these classifications. The author of this article takes up the challenge to suggest one more version of such separation classification thinking such that, in many respects, it differs from the previous ones.

HOMOGENEOUS AND HETEROGENEOUS MIXTURES OF SUBSTANCES AND SEPARATION METHODS USED

According to the idea put forward already in (4), one important criteria differentiating separation methods can be the specific properties of mixtures of substances to be separated. For the most general case, mixtures of substances to be separated are homogeneous phases either liquid or gas. When there is a necessity arising of separating solid-phase mixtures, these are to be pre-crushed and dispersed or dissolved in the fluidic phases. As a result, the problem of separation is reduced to the most general case of fluids. Depending on dispersion degree of the substances to be separated in the fluid phases, all separation methods can be tentatively divided into two groups: separation methods for heterogeneous (macroscopically non-uniform) mixtures and methods

for homogenous (macroscopically uniform) mixtures. Such differentiation is as tentative as is the boundary between heterogeneous and homogenous media.

Each group of separation methods of heterogeneous mixtures has its own preferred field of application. It is heterogeneous mixtures and corresponding separation methods that have to be encountered most frequently when resolving industrial problems: examples can be found in the mining industry, in processing various raw materials, in purification of wastewater and air pollutant discharges of industrial enterprises. The relatively small number of methods that are used to separate heterogeneous mixtures include: flotation, filtration, sedimentation, centrifuge and magnetic separation. Each of these methods is well known and does not require any additional comment.

The issue is more complicated with methods that are used for separating homogenous mixtures of substances, which are equally often encountered in practice when resolving both analytical and industrial problems. In doing so, the emergence and development of novel separation methods for homogenous mixtures, as a rule, begins with the solution of analytical problems, whereas the analytical separation methods themselves often serve as prototypes for future industrial technologies. The number of methods in this group is large, and should be classified first.

Methods that are used for separating homogenous mixtures of substances can be classified by the nature of characteristic properties of these substances, which determine the possibility of separating when using the specific method, and by external impacts on the system that are necessary for these properties to be revealed (Table 1). The use of "external impacts on the system" as a classification criterion is analogous to "effective forces" once suggested as a classification criterion by Giddings (5).

Each of the classes of separation methods, which are listed in Table 1, comprises a number of individual methods, their number within each class and their role in various fields of chemistry and chemical technology being far from equivalent. In their turn, these methods need to be classified within each class. The most multivariate and highly demanded methods are those based on differences in interphase distribution that could explain most of the attention to be paid to this class of methods in the present article, as well as to a separate consideration of the group of chromatographic methods included in the class.

SEPARATION METHODS BASED ON THE FORMATION OF NEW PHASES OF COMPOUNDS TO BE ISOLATED

Methods that were used for separating homogenous mixtures began from the methods based on the formation of new phases (Table 2). The first attempt to classify this group was made in the already mentioned monograph (4), but the authors limited themselves only to separating similar methods into an individual group without a discussion of their characteristic properties.

The main criterion used to classify separation methods of this group is the aggregation state of the initial mixture of substances and of the phases to be isolated. Of all the possible combinations of aggregation states in the initial mixture and that of the newly formed phases, some additional possible classification criteria are characteristic properties of substances, which determine the potential for their separation. In accordance with the latter, the methods, which are based on transition from one aggregation stae into another, are divided into separate groups depending on the reason for the change of the aggregation state: either due to chemical transformations or phase transitions at definite temperatures and pressures. The separation methods of the group under consideration were the first ones to be introduced in analytical, preparative and industrial practice. The distinctive feature of the methods is relative simplicity of their instrumentation, but, at the same time, they are time- and labor-consuming and are thus difficult to automate.

TABLE 1
Methods used for separating homogenous mixtures: general classification

№.	*Characteristic properties of substances*	*External actions on the system*	*Classification of separation methods*
1	Transition to other aggregate states as a result of chemical transformations or phase transitions.	Chemical reactions with suitable reagents; uptake and withdrawal of thermal energy	Methods based on the formation of new phases of substances to be separated.
2	Interphase distribution in two-phase systems with a definite distribution constant.	Establishing certain conditions for interphase distribution (to achieve an interphase contact).	Methods based on differences in interphase distribution; chromatographic methods.
3	Induced transition from one phase to another one through the separating third phase.	Gradients of chemical or electrical potentials, pressure and temperature.	Membrane methods
4	Speed and direction of spatial motion within one phase in a scalar field.	Gravitational, electric, magnetic, or thermal fields.	Methods of separation within a single phase
5	Several characteristic properties, which are simultaneously different in their nature.	Several simultaneous actions, corresponding to the nature of characteristic properties.	"Combination" methods

TABLE 2
Separation methods based on the formation of new phases of compounds to be isolated

№.	*State of Aggregation:* *Of the initial mixture*	*State of Aggregation:* *Of a new phase*	*Characteristic Properties of Substances to be Separated*	*Separation Methods*
1	Liquid	Solid	The ability to undergo chemical reactions to form poorly soluble chemical compounds	Precipitation
2	Liquid	Solid	The ability to change to solid state as a result of the action of electricity (electric field-induced phase transitions)	Electro-precipitation
3	Liquid or gaseous	Solid	The ability to corresponding phase transitions at a definite temperature	Freezing
4	Liquid	Gaseous	The ability to form gaseous compounds due to chemical reactions in solution	Distillation with a conversion of the separated substance into (related) gaseous species.
5	Liquid	Gaseous	The ability to a "liquid-gas" phase transition at a definite temperature	Distillation and rectification, fractional distillation, evaporation
6	Solid	Gaseous	Ability to a "solid-gas" phase transition when heated to a definite temperature	Sublimation, vapor distillation
7	Solid	Liquid,Supercritical fluid	Ability to dissolve in a solution of definite composition	Selective dissolution, solvent- and supercritical fluid extraction

Precipitation methods have retained a certain "niche" in preparative chemistry for obtaining preparations of purified substances with a definite stoichiometry of their components. Apart from the solution of preparative problems, precipitation and electro-precipitation methods are the first stages of gravimetric and electrogravimetric methods of analysis, respectively. More detailed information on precipitation methods, reagents used and conditions for precipitates to be formed and separated can be found in practically all analytical chemistry textbooks.

Among methods of this group, the most popular are various types of distillation methods. Distillation as a method of separating mixtures is most frequently resorted to for such simple separation tasks as water desalination or its purification by removing mineral impurities, an analogous technique finding its application for purification of organic solvents as well. However, in the latter case, in order to enhance efficiency of the separation of substances, which is based on "liquid-gas" phase transitions principles, a rectification method is more frequently chosen, in which repetitive evaporation-condensation processes are used. Ultimately, the separation coefficient of the two components can reach the value of the relative volatility factor to the N^{th} power, where N is the number of the repetitive evaporation-condensation steps.

Substantially greater separation selectivity is obtained when the formation of a gas phase from a liquid one is a result of chemical reactions. Based on the principles of distillation with a conversion of the substances to be separated into gaseous species, there are methods for deep purification, e.g., of important elements such as boron, silicon and germanium. They are selectively separated as BF_3, SiF_4 and $GeCl_4$ gases, respectively. In doing so, the technique of dissolving compounds of these elements in the corresponding hydrohalogen acids with additives of oxidizers has proved equally convenient both for deep purification of these elements in preparative and industrial applications, and for analytical tasks of concentrating their impurities, which, for most of the elements of the Periodic Table, and under the same conditions, do not form gaseous compounds. However, as one of the methods based on phase transitions from the condensed phase into the gaseous one, sometimes a variant of the sublimation method is used in chemical analysis with a conversion of the elements to be separated into gaseous species. Examples are routine analytical tasks such as the determination of carbon and sulfur in steels by separating CO_2 and SO_2, correspondingly, after the samples of steel are oxidized in a flow of oxygen.

The last of the methods mentioned in Table 2 is selective dissolution and solvent extraction. This method implies a selective dissolution of one of the components of the mixture under separation: either the solid matrix or microcomponents, which are present there, with the purpose of concentrating the latter. An example is the dissolution of steels and alloys in some mineral (hydrochloric and/or phosphoric) acids in order to determine nonmetallic inclusions, e.g., carbides and nitrides, which are practically insoluble in these acids.

The method of liquid extraction is analogous, with the only difference in that it is usually applied for the isolation of organic substances such as components of plant raw materials used in pharmacy. In recent years, solvent extraction, as a method of component isolation from biological sources, still finds wide applications, as it is practically the only method of the group under consideration that has not stopped developing. A number of variants of the method appeared there, which have become known under a general ASE abbreviation that may correspond to both "accelerate solvent extraction" (9) and "assisted solvent extraction." The former, in its turn, is often mentioned as "pressurized liquid extraction" (PLE), which has such own varieties as "pressurized hot solvent extraction" (PHSE) and "subcritical water extraction" (SWE). The latter, when the authors wish to stress the mechanism of intensifying the process of extraction, is called "pressurized low polarity water extraction" (PLPW).

Of a great number of possible extractants, it is water that is preferred as the most environmentally safe compound. The main parameters that enable the extraction process to be controlled are pressure and temperature, as reflected in the names of numerous variants of ASE. Data on these variants can be found in greater detail in (10). In turn, solvent extraction methods differ in the dependence of the nature of external actions affecting the extraction process. More often, these are ultrasound (10) and microwave radiation (11).

Supercritical fluid extraction (SFE) is competing with diverse variants of solvent extraction methods, especially when there is a problem of isolating biologically active compounds. SFE is based on the use of compounds in their supercritical state, both as solvents and extractants, either directly or with added modifiers. Most often, it is carbon dioxide with ethanol that is used for the isolation of biologically active compounds, whereas vegetable oils are used to isolate nonpolar organic compounds (12).

SEPARATION METHODS BASED ON DIFFERENCES IN THE INTERPHASE DISTRIBUTION OF SUBSTANCES

Intragroup Classification and General Characteristics of the Methods

Among methods used for separating homogenous mixtures, irrespective of applications, the most important are the methods based on differences in the interphase distribution of substances. One of the phases, the source one, where the target components are separated, is the initial mixture of substances in their liquid or gaseous states, whereas the second one, the receiving phase, is selected so as to provide the maximum of characteristic properties of substances to be separated when in contact with this phase. The characteristic property, on which methods of this group are based, is the ability of substances to be distributed between the phases so as their transition is predominant from the source phase into the receiving one. Specifics of methods of this group, apart from the aggregation state of the source and receiving phases, are in the conditions for implementation of the interphase distribution processes. Consequently, these conditions are chosen as additional criteria for differentiating the methods of this group (Table 3). The very principle of differentiating the methods by aggregation state of phases and phase equilibria have been used in (4), but without the use, as one criteria, of the conditions for implementation of the interphase distribution process, which results in static,

TABLE 3
Intragroup classifications of separation methods based on differences in the interphase distribution of substances and chromatographic methods

	Methods—or groups of separation methods depending on interphase distribution process conditions		
Aggregation state of the source- and receiving phase	*Batch conditions*	*Dynamic conditions*	*Chromatographic way of implementation**
Liquid-Liquid	Batch liquid –liquid extraction, fire assaying	Countercurrent liquid –liquid extraction	Countercurrent chromatography (CCC)
Liquid-Solid	Batch sorption, batch solid-phase solvent extraction, co-precipitation	Dynamic sorption, dynamic solid-phase extraction, zone melting and oriented crystallization	Liquid-solid-phase chromatography (LSPC) **
Liquid – Gas, Gas – Liquid	Batch gas extraction and liquid absorption	Bubbling, dynamic gas extraction and liquid absorption	Gas-liquid chromatography (GLC) Liquid – gas chromatography (LGC)
Gas – solid	Static adsorption	Dynamic adsorption	Gas-solid-phase chromatography (GSPC)
Condensed phase (liquid or solid) - substance in its supercritical state	Supercritical fluid extraction (SFE)	—	Supercritical fluid chromatography (SFC)

*The possibility of viewing chromatography as a specific way of implementing interphase distribution processes is substantiated separately later, in a description devoted to chromatographic separation methods.

**Numerous LSPC variants that differ in the retention mechanism of substances to be separated are dealt with in detail in Table 4.

dynamic and chromatographic methods being in the same groups.

The conditions needed to realize interphase distribution processes, which correspond to different separation methods, are characterized both by the existence or absence of relative spatial motions of phases and the number of (elementary) redistribution steps of the separated substances between the contacting phases. As to the first criterion, all ways of realizing the interphase distribution of substances are divided into two groups: batch and dynamic. By the criteria of specific chromatographic conditions of the dynamic interphase distribution, a separate group of methods is singled out.

All methods of the group under discussion are multivariate ones and need to be classified on their own. This is especially so for chromatographic methods which, apart from diversity and special importance in methodology of separations, have their own theoretical basis. Therefore, chromatographic methods, which are to be singled out in what follows as an independent class of separation methods, will be dealt with separately from other methods that are based on differences in the interphase distribution of substances.

Liquid-Liquid Extraction. Intragroup Classification of Extraction Methods

Liquid-liquid extraction comprises two different methods, regarding their essence: liquid-liquid extraction mentioned in the preceding section and liquid-solid-phase extraction of target components. The most widely used is liquid-liquid extraction, which is a separation method based on the distribution difference of substances between two liquid phases, most often, between aqueous solutions and organic solvents.

Taking account of a wide variety of extraction systems and technologies used for implementing extraction processes in the liquid-liquid extraction variant, this group of methods needs a classification of its own. In (5) only single extraction is mentioned, without any review of variants of extraction methods in the dependence of extraction mechanisms. Depending on the interphase transfer mechanism of substances to be isolated, “liquid-liquid” extraction systems may be divided into two large subgroups: extraction by the mechanism of “physical” distribution, and that of reactive extraction. For the first subgroup, the substance to be separated goes into the receiving (extracting) phase as the same species as it is in the source phase, the driving force of the process being differences in solvation and hydration energies of molecules of substances to be isolated. Here, the extraction process is always reversible.

With this mechanism, large nonpolar or low-polar molecules are readily extracted into organic solvents. Of inorganic compounds, these include $GeCl_4$, I_2, OsO_4 and some others. Taking account of the fact that the number of similar inorganic compounds is extremely small, the physical extraction mechanism has found primary application in the separation, from aqueous solutions, of admixtures of nonpolar and low-polarity organic substances, e.g., petrochemicals. As extractants for isolating substances through the physical distribution extraction mechanism, neutral organic solvents are most often used such as hexane, chloroform and carbon tetrachloride. The physical distribution extraction of nonpolar organic substances is accomplished nonselectively, since for most of them there is no substantial difference in solvation energies, and these are always higher than their hydration energies. Therefore, this extraction mechanism is more frequently used for group separations and concentrating admixtures of nonpolar organic substances from various aqueous media.

For the extraction isolation of inorganic substances the strongest possibilities are opened up by reactive extraction, which is the process similar to a heterogeneous chemical reaction characterized by a constant known as the extraction constant, K_{ex}. However, since the stoichiometric ratio of the substance to be isolated to the extractant in the extracted compound is rarely known and usually kept constant in reactive extraction, this constant is only rarely used to characterize extraction processes. Instead, using the universal distribution constant, D is preferred.

Classifications are based on the type of extractants used: neutral, acid or basic. However, such classification is far too indefinite because many extractants can change their properties depending on the composition of the aqueous phase, e.g., chelate-forming extractants can have both acidic and basic functional groups. Therefore, as a more informative variant, a classification of extractants is suggested, based on two criteria: first, on the nature of donor atoms, which are chemically bonded to the extracted compound, and second, on the structural similarity of molecules of the extractants. On the basis of the first criterion, three main classes of extractants are singled out: oxygen, nitrogen, and sulfur-containing ones. As to the second criterion of structural similarity, there are chelate-forming- (13) and macrocyclic (14, 15) extractants that can be singled out. Then, a new and independent class of extractants, ionic liquids (*ILs*), has also recently drawn much attention (16, 17).

Oxygen-containing extractants are the most widely used for industrial applications such as isolation of uranium when processing raw materials and irradiated nuclear fuels, since they enable reversibility of the extraction process to be achieved. For analytical applications to extract metal ions, the most preferable are chelate-forming extractants: in many cases, they form colored or luminescent compounds with the isolated analytes. It allows combining the extraction isolation of substances with their subsequent determination by one of the suitable optical methods, directly in the extractant phase. So far, the use of macrocyclic compounds for extraction has not yet been completely understood.

As for all separation methods based on differences in the interphase distribution of substances, an additional criterion

used to differentiate extraction methods is the conditions needed to implement the interphase distribution process. In the simplest case this is the already mentioned (5) single extraction. On an industrial scale, countercurrent extraction (18) is used to tackle substance separation issues. Also, there are a number of techniques that are based on the principles of liquid-liquid extraction, which differ in the way of implementing extraction processes adapted for specific analytical methods or chemical technologies. For example the liquid-liquid segmented flow technique (19) is used in flow methods of analysis. Some variations of membrane extraction are described later.

Sorption Methods: Intragroup Classification

The retention mechanism of sorbates on the sorbent may serve as the first sign for differentiating sorption methods. Depending on the mechanism of retention of sorbates on the solid-phase sorbent, the sorption methods may be subdivided into:

- molecular adsorption caused by van der Waals forces acting between sorbate molecules and atoms on the sorbent surface, or hydrogen bonds formed between them;
- ion exchange, which is a heterogeneous chemical reaction of a reversible stoichiometric exchange of ions between the contacting liquid and solid phases;
- sorption with complex-formation, when functional groups of the sorbent act as ligands to be coordinated by the absorbed metal ions;
- stereospecific sorption, which is a consequence of sorbate molecule penetrations into pores of a suitable size in special sorbents with regular pores of specified dimensions;
- sorption by "restricted access materials" (RAM) (20) that are capable of excluding macromolecules, whereas their inner porous surface with hydrophobic or ion-exchange functional groups can retain low molecular weight analytes due to hydrophobic or electrostatic interactions;
- biospecific sorption, which is characterized by a specific affinity for biologically active substances or for affinity ligands or affinants (21).

Regardless of the mechanism of retention of sorbates by sorbents, an additional differentiating sign of sorption methods is the conditions under which the sorption process is accomplished: either batch or dynamic, and chromatographic sorption methods.

Molecular adsorption

Sorption under the mechanism of weak intermolecular interactions finds its primary application for separating admixtures from the gaseous phase and for the separation of gaseous compounds, more often in gas-adsorption chromatography. In the case of liquid media, sorption under this mechanism is commonly used for isolating and concentrating organic compounds. Apart from individual properties of sorbate molecules, the strength of molecular adsorption is determined by the specific surface of the adsorbent and chemical nature of its surface. Depending on the type of functional groups on the sorbent surface, they can be polar and nonpolar. The former include silica gels, zeolites, alumina, oxides of titanium and zirconium and others, as well as polymer sorbents with polar groups implanted onto them. Similar sorbents are used for separating and concentrating polar compounds.

Intermolecular interactions of sorbate molecules with the sorbent surface are caused by universal dispersion, induction and orientation forces. The use of such sorbents for the concentration of substances from a wet gas and/or aqueous solutions is limited due to their high affinity to water molecules, which are adsorbed more strongly than many other, even relatively higher molecular weight compounds. Therefore, these sorbents are used for concentrating polar compounds from nonpolar organic and gaseous media, also being, as a rule, highly efficient desiccants for the latter.

Properties of nonpolar adsorbents are manifested by carbonic- and nonpolar polymeric adsorbents, as well by silica gels modified by first grafting nonpolar, alkyl groups to it. Among carbonic adsorbents, the use of which had started from active charcoal, most attention has been attracted in recent years to fullerenes and nanotubes (22). Nonpolar adsorbents are used for the isolation and concentration of polar and nonpolar compounds from gaseous- and polar liquid phases, as well as for separating these compounds. Intermolecular interactions of sorbates with the surface of nonpolar absorbents are caused by hydrophobic interactions.

Ion exchange

Sorbents that can adsorb substances under the mechanism of ion exchange, are called ionites; they're polymeric substances containing functional groups that, being in contact with electrolyte solutions, are capable of ion exchange. Depending on the chemical nature of the polymeric matrix, ionites are divided into two main classes: inorganic and organic. The former, in their turn, are divided into natural- and synthetic inorganic ionites. Numerous monographs and reviews devoted to ion exchange and ion exchange materials were published primarily in the 1950s–1960s. There are two publications (23, 24), wherein references to the preceding ones can be found. Today inorganic ion exchange materials, both natural and synthetic, have been practically abandoned. Cyanoferrate sorbents may be mentioned because they are exceptionally selective to cesium ions, which enable radionuclides of cesium to be isolated even from seawater.

Organic ionites are the main class of ion exchange sorbents, which are organic polymeric materials with functional groups that are grafted onto a matrix to impart cation or anion exchange properties to the material. In the absence of complex formation in solution, selectivity of ion-exchange resins with acidic and basic functional groups is practically limited by the possibility of separating ions of different charge signs and, to a lesser extent, of the same sign, if they have substantially different ionic radii. To increase the selectivity of ion-exchange separations, a change of chemical species of substances to be separated is used, with complex-formation reactions in solutions being brought into contact with ion-exchangers.

Sorption with complex-formation

In view of the limited selectivity of ion-exchange resins, from the mid-1950s through the 20th century, an extensive search has begun for sorbents that could provide a selective isolation of certain metal ions from aqueous solution regardless of other salts also present. The main direction in the creation of such sorbents is to graft chelate-forming functional groups onto polymeric matrices. The first attempt was to graft the most popular chelate-forming reagent, 8–hydroxyquinoline. As a result, a sorbent has been obtained for a group isolation of heavy metals in the presence of alkali and alkali-earth metals. At present, there are practically no chelate-forming reagents left that have not found analytical applications in their monomeric state, and that have not been used to synthesize the polymer analogues named chelate-forming or complex-forming sorbents (PCSs) (25).

The main mechanism of retention of substances by sorbents of this class is donor-acceptor interactions of sorbates with functional groups of the sorbent, the latter acting as a polymeric ligand. As polymeric matrices for PCSs, the same reticulated copolymers as in ion-exchange resins are preferred. Most often, these are copolymers of styrene and divinylbenzene, methyl methacrylate and acrylonitrile, as well as cellulose. As opposed to ion-exchange resins, which are made in granular form only, some PCSs variants are fibrous sorbents with a polymeric matrix in the form of wool, fabric, threads and strands that have better kinetic characteristics as compared to the granular analogues.

The effect of polymeric matrices on properties of PCSs is more substantial than it is in ion exchange resins. Because the adsorbed metal ions coordinate, as a rule, several functional groups of the sorbent, the possibility of such a coordination depends substantially on matrix flexibility and on its ability to form a certain spatial configuration (conformation) of functional groups. Sorption of ions, which coordinate these groups, is accompanied by a conformational transition. The energy needed for the transition is compensated for by the bond energy of the coordination compound formed. Therefore, the more stable the compound formed, the more rigidly knitted can be the sorbent matrix, and *vice versa*.

Stereospecific sorption

Enhancement in selectivity of isolation of organic compounds is achieved under conditions of stereospecific sorption. Based on principles of the latter are both chromatography and sorption concentration of organic compounds by polymeric sorbents, molecular-imprinted polymers (MIPs) (26, 27).

Selectivity of MIPS is reached using special synthesis technologies. At the synthesis stage of the polymer, a reaction mixture (prepolymerization complex) is prepared of monomers and a template, to form an imprinted matrix. When template molecules are removed, highly specific binding centers, or cavities, are left in the polymer structure, which are complementary in size, form and structure to definite organic molecules. Similar stereospecific sorbents have already found wide applications in chemical analysis: as a means of selective isolation of organic admixtures from various aqueous media (28), for the separation of structurally similar organic compounds, including enantiomers (29), and so on.

Before the appearance of MIPs, the effect of stereospecific sorption has been used in gel chromatography, wherein the retention time of molecules of separated substances that are retained by the stationary phase is determined by the so-called “sieve effect.” It is exhibited in the retention of sorbate molecules in pores of solid materials with a porous structure, the pore size being close to that of molecules of the substances to be isolated. Such materials are called gels and can only conventionally be classified as sorbents, since they are capable of isolating some substances from liquid phases. The conventionality here is that the separated substances are retained in the solution that fills up the porous spaces in gels. Adsorption in gel chromatography separations of substances is just an undesirable accompanying factor. Detailed information on gels used for gel-chromatography can be found in virtually any monograph devoted to liquid chromatography.

Sorption by RAM

Among new sorption methods that are used at the sample preparation stage, a special place is held by sorption of restricted access materials (RAM), which have appeared relatively not long ago (20). In sorbents of this type the inner porous surface with functional groups, which determine its sorption capacity, is accessible only for small molecules, whereas macromolecules are size-excluded and interact only with the outer surface of the sorbent covered with hydrophilic groups, thereby minimizing adsorption of protein molecules. RAM differs in the dependence of the mechanism of protein exclusion. The exclusion of macromolecules can be affected by a physical barrier of pores of a certain size, or by a chemical membrane barrier of a protein- or polymeric mesh-like layer that covers the outer surface of particles.

RAM sorbents can differ in their inner porous surface accessible for small molecules, this surface possibly being the inner surface reverse phase (ISRP). Alternatively, it is carboxylic groups that can be on the inner surface, giving it properties of a weakly acidic cationite. These sorbents enabled analysis of biologic media to be substantially simplified. A typical pore size in sorbents with physical barriers is about 8 nm, which enables proteins with molecular weight in excess of 20,000 Da to be excluded. As a result it is possible to directly introduce a sample of blood into an LC chromatographic column. In doing so, such protein as albumin of molecular weight 65,000 Da will be directly eluted from the column, whereas low molecular weight analytes are retained in the pores of the ISPR phase or via an ion-exchange mechanism.

Until recently, batch, or single-stage, sorption could not find wide applicability, either for technological or analytical purposes. The first exception to this has become the analytical method of solid-phase micro extraction (SPME) (30), suggested at the end of the 1980s. In SPME, the isolation of analytes is done from the analyzed gaseous- or liquid phase into a thin (several μm) layer of a sorbent phase coating on the surface of a fused-silica optical fiber, which can be retracted from the protective metal needle of the microsyringe, and then returned to it again. SPME is used for group concentration of nonpolar and weakly polar organic analytes from aqueous solutions and analytes of various polarity from air for their subsequent determination by gas chromatography. In SPME, when it is carried out from the aqueous phase, as a rule, various nonpolar polymer materials are used as adsorbing phase coatings, for example, polydimethylsiloxane (PDMS), or polyacrylate, and, rarely, carbonic adsorbents, e.g., graphitized carbon. On completion of sorption, the syringe needle with the retracted silica fiber is inserted into the hot injector of the gas chromatograph and the fiber is pushed outside the protective metal needle for thermal desorption and subsequent determination of the adsorbed analytes.

The dynamic variant of sorption is implemented under a scheme wherein a flow of the initial liquid or gaseous feed phase is passed through a sorbent-packed column. It finds practical applications for concentrating microcomponents for analytical or preparative purposes, the former being used to lower the analyte detection limit, whereas the latter are more often used for wastewater treatment and purification of air and process gas emissions. For the subsequent determination of concentrated substances, the sorbate, as a rule, is desorbed, that is, transferred from the sorbent phase into the liquid or gaseous phase. For the case of molecular sorption of analytes from the gaseous phase, it is thermal desorption that is usually applied, which is performed by heating the sorbent-packed concentrating column. When using complex-forming, ion-exchange- and specific variants of sorption, desorption is performed by passing, through the sorption column, aqueous solutions of salts with ions or molecules that are capable of substituting sorbates, or of complex-forming reagents that are capable of converting the sorbate into nonabsorbing species.

A general requirement for desorbants is no interference with the subsequent determination of concentrated analytes or their use in preparative or process applications of the method. By virtue of its versatility and wide variety of mechanisms of sorption processes, dynamic sorption at present is a widely spread concentration method in chemical analysis of gaseous and liquid media for the determination of both organic and inorganic compounds. Not less widely used are dynamic sorption processes in preparative and industrial-scale applications as well. The most widely used application field of sorption under all the above-mentioned mechanisms is chromatographic separation methods in their LSC variant that is discussed in greater detail later.

Separation Methods Based on Partitioning/Distribution of Substances in the "Liquid-Gas" System

Gas extraction

By analogy to the "liquid-liquid" system, in the "liquid-gas" system, the main method is extraction, in this case, gas extraction. Gas extraction is a separation method that is based on partitioning of substances between the condensed (solid or liquid) source phase and the extracting (or receiving) gas phase. It parallels with liquid-liquid extraction in that the basic extraction mechanism is physical distribution. At the same time, a variant is possible of "reactive" gas extraction when the evolved volatile compounds are reaction products of the target component of the initial mixture with reagents introduced into the sample to convert these products into the gaseous state.

The main application field of gas extraction is analytical chemistry: it is on its principles that an analytical method of headspace analysis is based (31). Headspace GC is a method for acquiring information on a composition of liquid and solid media on the basis of analysis of the gas phase that is in contact with the two condensed phases. In doing so, the analysis of the gas phase is conducted, as a rule, by gas chromatographic methods. Isolating analytes from solid media by gas extraction has gained great interest for the determination of monomers accumulated in polymeric materials and for analysis of residual solvents in pharmaceutical or food compounds. One more example of analytical application of gas extraction from solid-phase samples is evolution of gases from metals, which is known as vacuum extraction (32). Regardless of the examples given above, if there is no more precise definition, then the notion of gas extraction covers only the case of extraction into the gaseous phase of volatile compounds from the liquid phase.

The most important characteristic of gas extraction processes is the distribution (partition) coefficient K_{LG}. As opposed to liquid-liquid extraction, the distribution

coefficient here is the ratio of equilibrium component concentration in the source liquid phase to its concentration in the extracting (receiving) gaseous phase, i.e., as to its physical meaning, the coefficient is a reciprocal value of the distribution coefficient in liquid-liquid extraction. Therefore, the smaller the K_{LG} coefficient, the greater component concentration in the extracting gaseous phase, and the more expedient is the use of gas extraction. This process pays homage to traditions in the development of the gas extraction method that emerged and was developed independently of other separation methods based on differences in the interphase distribution of substances.

The factors of most importance, on which K_{LG} depends, are the nature of the liquid phase of the component to be extracted and the process temperature. As for the gaseous phase, it has practically no effect on K_{LG}, since intermolecular interaction forces in the gaseous phase are considerably weaker than in condensed phases. Hence, the choice of the extracting gas is usually practically determined only by its compatibility with the conditions of the subsequent gas chromatographic analysis of the extract and by economic considerations. As in other methods, which are based on differences in the interphase distribution, efficiency of isolating substances by gas extraction depends, alongside with the distribution coefficients, on the conditions under which the process of gas extraction is carried out, i.e., batch, dynamic and continuous flow extraction.

Compared to the batch variant, the dynamic gas extraction method allows for a more complete extraction of the separated substances from the same volume of the liquid sample into a smaller volume of the extracting gas. On carrying out dynamic gas extraction, a flow of the extracting gas leaving the extractor is analyzed either directly or is passed through a sorption column for an additional concentration of analytes. A combination of the dynamic gas extraction method with gas adsorption concentration of analytes is known as the "purge-and-trap" method (or P&T technique) (33). After the adsorbent trap is heated for thermal desorption of the adsorbed analytes, such a scheme of analysis enables levels of analyte detection to be lowered by 2 to 4 orders of magnitude compared to the batch gas extraction variant.

Gas extraction in all its variants given here is widely used as a sample preparation method for gas chromatographic determinations of volatile organic compounds in various aqueous media (natural and sewage waters, tap water), in biological media (whole blood, blood serum/plasma, urea, saliva, etc.), in food (alcoholic beverages and soft drinks, dairy, produce, meat and fish, etc.). Flow variants of gas extraction are applied, in particular, for the continuous determination of halogen-containing hydrocarbon micro-impurities, first of all, chloroform and carbon tetrachloride in chlorinated tap water.

Liquid absorption

The second variant of separation methods, which are based on substance partitioning in the "liquid-gas" system, is liquid absorption. It is a process that is opposite that of gas extraction. When performing liquid absorption, the absorbed components (absorbates) are transferred from the gaseous phase into the liquid phase (absorbent). As a characteristic of liquid absorption processes, the distribution constant, K_{LG}, can be used, which is the same as for gas extraction. In this case, the greater the K_{LG} value, the greater are the concentration factors that can be achieved for the analytes, and, accordingly, the lower are the detection limits.

The two types of absorptions can be distinguished as physical and chemical (chemosorption). In chemosorption, a chemical reaction takes place between the absorbate (which is extracted from the gaseous phase) and components of the absorbate to form a nonvolatile (dissolved) product. As a result, the process of isolation is fairly often irreversible, thereby allowing practically unlimited concentration factors to be achieved for the isolated substances.

As opposed to gas extraction, in liquid absorption it is the dynamic variant of the process that is used exclusively, more often by bubbling through an absorber vessel. Dynamic liquid absorption is a versatile method of isolating and concentrating organic and inorganic substances in the analysis of air; it can be readily combined with any method of absorbate analysis. The method is especially efficient for the determination of admixtures of chemically active inorganic compounds in air, such as oxides of nitrogen and sulfur, ammonia and vapors of organic acids. However, for the gas chromatographic determination of relatively inert volatile organic compounds, e.g., hydrocarbons, more preferable is the isolation of analytes by gas absorption with a subsequent thermal desorption of the analyte, which allows substantially lower limits of detection to be achieved due to higher concentration factors.

Supercritical Fluid Extraction

The last of the theoretically possible methods, which are based on differences in the interphase distribution of substances and are classified by the aggregation state criterion of the phases, is supercritical fluid extraction (SFE). The name of the method is identical with extraction by supercritical fluids from solid-phase objects, i.e., there is a complete analogy with liquid extraction. However, as to the physical sense, there are methods to be separated out that implement differences in substance distribution in "Liquid-SF" and "Solid-SF" systems.

SFE advantages are revealed in that substances in the supercritical fluid state have properties that are intermediate between those of gases and liquids. Supercritical fluids, as regards their viscosity and solvation ability are a preferred choice for separating and isolating certain classes of

compounds, mainly high molecular weight ones of a natural origin with moderate polarity. Accordingly, the main applications area for SFE is solving preparative and industrial-scale problems in chemistry of high molecular weight compounds and, particularly, in biochemistry. Also, in recent years SFE has drawn attention in radiochemistry, where fluid CO_2 has found its applications as a convenient solvent for the extraction of actinides (34).

In any case, one of the main advantages of the method is the ease of purification of isolated substances from the supercritical extractant, for which it is sufficient to change pressure and temperature to evacuate it. This advantage is especially substantial for preparative chemistry and industrial-scale applications. So far, the method has not found wide usage for separating and concentrating substances in analytical chemistry. For these, supercritical fluid chromatography is of substantially more interest, which is dealt with in more detail later.

CHROMATOGRAPHIC METHODS

What is Chromatography?

On the basis that the number of chromatographic methods is constantly growing and the newly emerged methods are often dealt with in isolation from the earlier known ones, these chromatographic methods are more in need of a classification than other separation methods. Any attempt at a classification of chromatographic methods results in the emergence of major problems in relation to an ambiguous understanding of the term chromatography itself. This ambiguity appears first when one tries to answer such questions as: "What are chromatographic methods?" and "Are they separation methods or methods of analysis?" The ambiguity has appeared already in the first works of Tswett, the "father of chromatography," published in 1906. Tswett wrote in these publications about chromatography as both "a new physical method of isolating substances," and "adsorption analysis."

The dual understanding of chromatography, from the one hand, as a separation method, and, from the other hand, as a method of analysis, can be traced through all the stages of its development. After Martin and Synge, 1952 Nobel Prize winners, developed and used a chromatographic process in a system of two liquid phases and a "liquid-gas" system, the situation became even more complicated. Martin and Synge discovered variants of chromatographic methods, unfortunately called "partition chromatography," that should be considered, even though this term has become generally recognized.

Initially, Tswett's chromatography also used partitioning, although in another phase system; in principle, nonpartition chromatography is impossible. In Tswett's experiments, the separation of individual chlorophyll components occurred due to differences in distribution coefficients between petroleum-ether and the adsorbent. The fundamental contribution of Martin and Synge to the development of chromatography is in the fact that the stationary phase, relative to which the separated substances are transferred in a flow of another phase, can be not only a solid sorbent but a liquid as well. At last, in the second half of the 20th century it was finally proven that the chromatographic process is realized for any theoretically possible combinations of aggregation states of a stationary and a mobile phase. It is liquid-gas chromatography (LGC) that became the last proof of that the chromatographic process is versatile: here, the gaseous phase is the stationary one, and the mobile phase is a liquid (35, 36). Practically simultaneously, this chromatographic method was predicted by Giddings on the basis of theoretical considerations (37).

After the appearance of such wide variety of chromatographic separation methods, it has become clear that the term "chromatography" is a polysemantic one. On one hand, it is a complex multivariant separation method or, equivalently, there are a large number of chromatographic separation methods corresponding to various combinations of phases as regards their state of aggregation. On the other hand, it means that chromatography can be simultaneously viewed as a universal technique or way of realizing the interphase distribution process and creating conditions for substance separations. The chromatographic way, in its turn, has a number of variants, each one of them, as a rule, being considered as an individual separation method.

Chromatographic Separation Methods

The aggregation state of phases is the main criterion for differentiating various chromatographic separation methods as well as other methods, which are based on differences in the interphase distribution of substances. In so doing, the mechanism of retention of the separated substances by the stationary phase, or the relative polarity of the stationary and mobile phases, and their role in the chromatographic process (either the stationary or mobile phase), may serve as an additional classification criterion for one and the same system of phases (Table 4).

For any of the possible combinations of phases in two- or three-phase systems there are corresponding specific chromatographic methods as listed in Table 4. Apart from it, in the "liquid-solid-phase" system, various mechanisms are capable of retaining the separated substances in the solid stationary phase, the mechanisms being an additional classification criterion for different variants of liquid-solid-phase chromatography: liquid-adsorption, affinity, ion-exchange, ligand-exchange, and size-exclusion chromatography.

The history of chromatographic methods began with normal-phase variant of liquid-adsorption chromatography (NPLAC) wherein polar adsorbents are used as the stationary phase whereas nonpolar or mixed solvents are as the mobile

TABLE 4
Classification of chromatographic separation methods based on the aggregation state of phases, mechanism of retention of separated substances by the stationary phase, and/or their relative polarity and role in the chromatographic process

Aggregation state of phases, participating in the chromatographic process and their role		*Chromatographic methods and their variants on the dependence of the mechanism of retention of separated substances by the stationary phase*
Stationary (immobile) phase	*Mobile phase (the carrier phase)*	
Solid	Liquid	Liquid adsorption chromatography: normal-phase (NPLAC), variant HILIC and reversed-phase (RPLAC), variant HIC Ion exchange Affinity Ligand exchange size-exclusion (SEC)
Polar liquid*	Nonpolar liquid	Normal-phase liquid-liquid chromatography
Nonpolar liquid*	Polar liquid	Reversed-phase liquid-liquid chromatography (RPLLC), Extraction chromatography, Ion-pair chromatography
Solid	Gas	Gas adsorption chromatography (GAC)
Liquid*	Gas	Gas-liquid chromatography (GLC)
Gas*	Liquid	Liquid-gas chromatography (LGC)
Solid and liquid	Gas	gas-liquid solid-phase chromatography (GLSPC)
Solid and gas	Liquid	Liquid-gas-solid-phase chromatography (LGSPC).
Solid or liquid	Supercritical fluid	Supercritical fluid chromatography (SFC)

*Liquid or gas stationary phases are associated with a solid support (porous particles or column wall).

phase. When mixtures of an aprotic polar solvent (e.g., acetonitrile) with trace amounts of water were used as the mobile phase, an effect was discovered of enrichment with water of the mobile phase layer that is in contact with the hydrophilic stationary phase sorbent and, correspondingly, of a depletion of the solution that is not in a direct contact with this sorbent. Then, in addition to the effect of adsorption on the sorbent, there is an effect of partitioning the separated substances between mixed water-organic solutions with various water contents on their retention parameters. Such mixed mechanism was the base of hydrophylic interaction liquid chromatography (HILIC) (38), which is one of NPLAC variants.

Conversely, a reversed-phase variant of liquid-adsorption chromatography (RPLAC) as applied to the separation of biomolecules is (at present) often referred to as hydrophobic interaction chromatography (HIC) (39). HIC is widely used for purification of proteins by separating them due to differences in hydrophobicity of their molecules. There are numerous and easily accessible monographs and reviews devoted to the remaining methods of the "S-L" system, the mechanism of retention of separated substances in each of the methods of Table 4 being clear of the method's name.

In the case of two liquid phases, the variants of chromatographic methods differ depending on the role played by the polar and nonpolar phases. As well as for liquid adsorption chromatography (LAC), there is a normal-phase variant of LLC, where a nonpolar phase is the immobilized one, and a reverse phase variant with the stationary nonpolar phase. Here, in the frames of the general RPLLC–method, there are separate methodical directions: extraction and ion-pair chromatography. The former has emerged as a separation method of inorganic substances and is based on the data acquired in the course of development of liquid-liquid extraction. Its main application fields are preparative isolation of radionuclides in radiochemistry and some problems of inorganic analysis (40). As to organic analysis, it is another RPLLC-variant that has found wide application there: ion-pair chromatography (41). The latter is singled out by the mechanism of retention of substances to be separated, which are ion-pair interactions of dissociating organic substances that lead to the formation of hydrophobic associates being retained by the nonpolar phase.

The methods of gas-solid phase chromatography (GSC) and gas-liquid chromatography (GLC) by retention mechanisms of substances to be separated have remain monovariant until now, the differences within each of them being revealed only in the conditions under which the chromatographic process is realized: it is either in packed or capillary columns.

Capabilities of liquid-gas chromatography (LGC) that were predicted by Giddings as those of the most efficient method of liquid chromatography (37), have not yet been ultimately ascertained and the method finds its applications only for the determination of gases dissolved in water (36). Super-critical fluid chromatography (SFC) has found wide applications in chemistry of high molecular weight compounds and, in the first turn, in biochemistry. A lower viscosity of supercritical fluids as compared to liquid mobile phases allows for working at higher elution speeds than in HPLC, thereby reducing the time for analysis and preparative separations. In SFC, a special place is occupied by studies on the use of water as a fluid in sub- and supercritical states (42).

When a liquid or a gas is used as the stationary phase a solid support is necessary. It is not always possible to find

solid supports, which are completely inert to the separated substances. It means that the retention of substances to be separated is dependent on their adsorption from the fluid stationary phase on the support, which results in the appearance of such chromatographic methods that it is required that all three phases, which participate in the interphase distribution process, should be mentioned in the method names: for example, gas-liquid-solid-phase chromatography. Here, the stationary (retaining) phases are both the liquid and the solid-phase support, simultaneously with an "additive" contribution of each phase into retention of substances in the chromatographic column, their additional contribution into the retention and adsorption on the solid phase support is most strongly revealed for stationary gaseous phases. Taking into account the fact that when using polar mobile phases there is a film of the stationary phase practically always present on porous hydrophobic supports, the effect of adsorption on the support from the stationary phase is revealed in reversed-phase liquid-liquid chromatography as well (43).

Chromatographic Methods That Correspond to Different Variants of the Chromatographic Way of Realizing the Interphase Distribution Process

The chromatographic way of realizing the interphase distribution process is in a relative spatial motion of one phase relative to the other. The space wherein the chromatographic process is realized can have the shape of a cylindrical channel or a flat layer. The first corresponds to column chromatography, the second, to planar chromatography, which, in its turn, can be paper- and thin-layer chromatography. The obligatory condition for the realization of the chromatographic process is the maximum possible area of the interphase contact, which is achieved in two ways: by dispersion of the stationary phase down to the minimal size possible or by fixing the phase as a thin film on the surface of the walls that are boundaries of the possibly narrowest channel for the stationary phase to pass through. Such a channel is usually a capillary tube and the chromatographic process, which can be realized therein, is called capillary chromatography, which is the opposite of packed-column chromatography, in which the space where the chromatographic process takes place is filled with a dispersed stationary phase, which is called the column packing.

In addition to conventional variants of packed column and capillary chromatography, in recent years a new type of setup for chromatographic separation of substances has appeared. Monolithic capillary columns (44) contain a solid monolithic porous medium, which is synthesized directly in the column's volume. Monolithic stationary phases enabled efficiency of the chromatographic process to be sharply enhanced. The final effect of chromatographic separation, irrespective of the shape of the space for the separation to be performed, is achieved by multiple repetitive interphase distribution steps under conditions of relative spatial motion of phases that are in mutual contact.

There are three different variants of the chromatographic way of realizing the interphase distribution process. Elution, although it is logical its name would be "zone chromatography," proceeds with successive injections of the initial mixture of substances into eluents introduced in the space filled with the stationary phase (a column or a flat layer of the stationary phase). In the process of elution, the initial common zone of a mixture of substances moves with the flow of eluent through the separation space. Then the injected mixture is divided into zones of individual components according to their distribution coefficients in the phase system used.

The two other schemes of chromatographic separation are frontal chromatography and displacement chromatography. They are seldom used compared to elution. The frontal scheme allows for the individual isolation (although only partially) of only one component, which is the least retained by the stationary phase. The displacement scheme is of interest in the particular case of preparative chromatographic separations where the partial zone overlap is compensated for by the maximum loading of the column with the substances to be separated.

An idea of continuous chromatography, called continuous two-dimensional chromatography (CTDC), was first suggested by Martin (45). According to the idea, for a continuous separation of a mixture of substances, it is required that an infinitely long bed of sorbent be continuously moving, from one hand, relatively to stationary feed systems of substances to be separated and eluents and, from the other hand, relative to the eluate collection system. To simulate the infinite long bed, Martin suggested it be made in the shape of a hollow rotating cylinder.

As an alternative solution, a gas-liquid variant of CTDC was suggested where the chromatographic process is realized in a narrow gap between two flat, highly polished discs that held layers of a liquid stationary phase on the contacting surfaces (46). A system of these two discs is constantly rotating, whereas a carrier gas flow is fed into the narrow gap between discs, through a fixed cap, connected to the rotating discs by a mercury seal. Simultaneously, a mixture to be separated is fed through a capillary to one of the points of the inner circumference, fractions of the separated components being collected in the carrier gas flow from the outside circumference of the disc (46).

Between 1955 and 1975, numerous attempts were taken to construct continuous two-chamber chromatographs based on the principle of most chromatographic separation methods, beginning with paper chromatography (47) and including diverse variants of gas chromatography (48,49), extraction chromatography (50), reversed-phase liquid-liquid chromatography (51) and ion-exchange chromatography (52).

Among the above-mentioned variants of realizing the CTDC scheme with a dense bed of the sorbent of a cylindrical or of a ring shape, a special place is held for the works of Taramasso, who was the first to suggest an CTDC variant where a movement of the dense sorbent bed is simulated by periodic switching of inlets and outlets of identical chromatographic columns, their system being placed along an element of a cylinder (53).

In parallel with attempts at realizing the chromatographic process in a two-dimensional moving-bed variant as suggested by Martin, there were numerous attempt made at implementing a scheme of continuous countercurrent chromatography (CCC) (54). Contrary to CTDC, the latter makes it possible to continuously separate a mixture of substances into only two fractions. At the same time, CCC is interesting in its ability to simulate separations of mixtures of closely similar substances on an infinitely long chromatographic column with an infinite number of theoretical plates. Two technical solutions have appeared there to implement continuous CCC: a method of countercurrent centrifugal chromatography was suggested (55) in a system of two liquid phases.

In this method, as compared with other LLC methods, there is no need for a support of one of the phases. Dispersion of one of these phases in a flow of another one and its movement opposite to this flow is provided by the action of centrifugal forces in spirally-shaped columns upon their rotation around the external axis of the centrifuge or simultaneously around the two axes, its own and that of the centrifuge. If the two phases that take part in a chromatographic process are introduced at opposite ends into such rotating spirally-shaped column, the phases are mutually dispersed and be moving countercurrently relative to each other, whereas substances in the system be partitioned between the phases under the laws of CCC.

In parallel with continuous CCC, a simulated moving bed chromatography (SMB) (56) was suggested to solve analogous problems in a countercurrent variant of LSC, and the problem of creating a countercurrent stream of the sorbent is solved in CCC similarly to Taramasso's in CCTDC (53): the movement of a dense bed of the sorbent is simulated by a system of serially connected chromatographic columns, and the mobile phase is simulated by outlet and inlet streams of feed, eluent, product and raffinate solutions, the outlet of one column being connected with the inlet of the next column and all columns being in a closed loop.

The ideas of continuous CCC and SMB have been successfully applied at large-scale industrial level and gained practical applications for the separation of biologically active compounds. In particular, SMB, which provides the possibility of simulating a chromatographic column of any length, makes it possible to solve one of the most important problems of substance separation: enantiomer separations (57).

Each of the chromatographic separation methods given earlier can be implemented as a variant of the way to realize the chromatographic processes discussed here. In turn, any combination of some of the possible chromatographic separation methods being combined with different systems for the detection of separated substances can lead to the emergence of a number of chromatographic methods of analysis.

Chromatographic Methods of Analysis

The first general criterion that can be used for a classification of chromatographic methods of analysis is the aggregation state of the mobile phase: accordingly, there are gas, liquid, and supercritical fluid chromatography states. A particular case of liquid chromatography, which is singled out according to the (analyte) chemical species, is ion chromatography. The second general criterion for a chromatographic method of analysis is the system of detection of the analytical signal, which is different depending on whether analytes are determined in the mobile phase at the exit from the separation space, or in the mobile phase, which is directly within that space. It is the eluent scheme of chromatographic analysis that corresponds to the first case, whereas the development scheme corresponds to the second one.

The development of the eluent scheme of chromatography, which at present has become the most used one, started when the gas chromatograph was invented. Despite widespread use of gas (and now liquid and supercritical fluid) chromatographs, it should be noted that a variant of the chromatographic scheme of analysis, in which the detection of separated substances is performed in the effluent, has one general disadvantage. The concentration of substances in the eluate is by K_{Di} times less than in the stationary phase (K_{Di} is the distribution/partition coefficient of the i^{th} substance under elution conditions). Here, the forced dilution will lead to a loss in sensitivity for the eluent scheme of chromatographic analysis as compared to the sensitivity that can be reached when detecting analytes directly in the stationary phase.

Therefore, the scheme of chromatographic analysis where substances are detected in the stationary phase, directly in the chromatographic column, or in a thin layer, looks more preferable as regards the limits of detection that can be reached for the analyte. Unfortunately, technical constraints impede intracolumn detection directly in the stationary phase, so this detection scheme is used only in thin layer chromatography (58). Detection in a stationary phase is most easily performed using radiochemical analysis, when analytes, which are radionuclides there, can be determined by their characteristic γ- radiation (59). Recently, a tendency has been seen there for a wider range of applications of this scheme in a capillary variant of column chromatography,

using primarily luminescent detection methods. At this new stage of the development of chromatography, there is actually a return to Tswett's visual monitoring of chromatograms directly on the column.

However, instead of a visual control on a qualitative level, plates or columns are scanned along the length or height, respectively, the simultaneous determination of the content of substances being made and quantitative results obtained. As a flow of the eluent passes through layers of the stationary phase, zones of individual components of the analyzed mixture are developed there, which is similar to the appearance of a visible image, instead of the latent and invisible one, in photography after processing a photographic plate or a film with a developing reagent (59).

A Generalized Scheme: Classification of Chromatographic Methods

The variants discussed here for a classification of chromatographic methods, which is based on a meaning assigned to the term "chromatography" can be generalized in the form of a General Classification Scheme given in Table 5.

The meaning of Table 5 terms such as "classical" and "high-performance," which are also used to characterize chromatographic separation methods, follows from fundamentals of the chromatographic theory. Efficiency of chromatographic methods is determined, first, by resolution of the peaks of separated substances, which depends on the width of their zones at the outlet of the separation space and, second, on the time needed to obtain the final result. An enhanced resolution and reduced time consumed are reached by using stationary phases with minimum particle size or with a minimum thickness of their films in a capillary tubing and, finally, by the use of special sorbents of the "core shell" design, enabling the length of diffusion path of separated particles to be decreased in the sorbent phase, as well as by the use of the already-mentioned monolithic sorbents. It often happens that high-performance chromatography is confused with high-pressure chromatography (HPC), the latter being far from adequate to the essence of the chromatographic process. If the first term reflects the final result, i.e., a good peak resolution, the second one stresses the necessity of using finely dispersed sorbents and, correspondingly, higher pressure needed for the eluent to be passed through layers of such sorbent.

Nevertheless, seeking to enhance efficiency of the chromatographic process and the necessity of using columns with finely dispersed packing call for high pressure capacity of pumps that could work at up to 40 KPa/400 atmospheres. At a new stage of development, there appeared a variant known in the literature as Ultra High Pressure Liquid Chromatography (UHPLC) (60) for pressures of up to 100 KPa/1000 atmospheres.

The Table 5 classification scheme covers practically all chromatographic methods with rare exceptions of their "nonsystemic" variants, such as centrifugal countercurrent chromatography (CCC) (55), where a support-free liquid stationary phase is formed by the action of centrifugal forces used with a liquid mobile phase.

TABLE 5
Classification of chromatographic methods based on the meaning assigned to the term "chromatography"

№.	*Meaning of the term "chromatography"*	*Criteria for differentiating the methods*	*Corresponding chromatographic methods*
1	Multivariant separation method	Aggregation state of the phases and their role in the chromatographic process Mechanism of interaction of the separated substances with the stationary phase Purpose/applications Elution conditions when using a zonal scheme of separation	Liquid-solid-phase, Liquid-liquid, Gas-liquid, etc. Liquid-adsorption, Ion (ion-exchange), Gas-adsorption, etc. Analytical, Preparative Isothermal, temperature programming, gradient, isocratic, etc.
2	A way of realizing the interphase distribution process	Separation scheme Geometry of the space for the chromatographic process to be accomplished in. Ways of dispersing and fixing the stationary phase relative to the mobile phase flow Dispersion degree or film thickness of the stationary phase Conditions and direction of relative movements	Zone/zonal, Frontal, Displacement Column, Planar Packed column, Capillary Classical, High-Performance Conventional, CTDC
3	Multivariant method of analysis	Aggregation state of the mobile phase or chemical species of analytes A scheme to determine the separated substances.	Gas, liquid, supercritical fluid, ionic chromatography Elution, development

MEMBRANE SEPARATION METHODS

Intragroup Classification of Membrane Separation Methods

According to the general classification of separation methods, which is based on principles of phase transformations and interphase transfers, the third group of methods includes those methods where separations are because of specific properties exhibited by the substances when a mass transfer is induced, under the action of some forces, from one phase to another, through the third phase, which separates the two. The intermediate phase, which is a partition between the two other phases, is named exactly in accordance with the Latin word "membrane," meaning a diaphragm. Hence, the corresponding separation methods are known as "membrane."

As well as for the two previous cases, it is the aggregation state of the phases, which take part in the separation process, that can be used as a general criterion for an intragroup classification. An additional specific classification criterion for this group of methods is the driving force of the interphase mass transfer process, which causes the transferred substances to reveal their inherent characteristic properties such as the size, charge and mass of their particles or the whole complex of properties. These will determine the substance ability of penetrating membranes under the action of forces of various nature: gradients of chemical and electrochemical potentials, or pressure (Table 6), specifics of a separation method being determined by the nature of these forces rather than whether they are continuous or discontinuous as was earlier suggested from the classification given in (5).

The Table 6 classification where the aggregation state of the phases is taken into account in the system that permits separation of substances enables membrane methods to be considered in a logical sequence with other separation methods. At the same time, membrane methods differ substantially from other separation methods, discussed earlier, both in their capabilities and applications. The change from methods, which are based on a "one-step" equilibrium partitioning of substances between the phases, to chromatographic separation methods, is justified primarily in view of significantly higher separation factors. As a rule, membrane separation methods do not provide substantial advantages over the methods based on a "one-step" interphase partitioning of substances. These advantages are usually that they allow achieving higher throughput and continuous separation. That is why numerous studies in the field of membrane separation methods are predominantly conducted with the prospects for developing new technologies on an industrial large scale.

The ability of substances to be separated and reveal their individual characteristic properties in the membrane separation process is primarily determined by the material and structure of the membranes used (61). It means that in order to subdivide the methods of this group, in addition to their own classification, another is needed based on the existing types of membranes. All known membranes may be conventionally divided into several groups by a number of classification criteria (Figure 1).

Following the classification suggested in Table 5, the first such criterion is the aggregation state of the membrane phase. By this criterion, membranes are divided into solid-phase and liquid membranes. The former, in turn, are subdivided by the mechanism of mass-transfer of the separated substances, into inert and reactive membranes, whereas, if it is done by their structure, into solid and porous ones, a wide variety of the latter, depending on the pore size: macro- and microporous membranes, with regular and nonregular pores. Additionally, depending on their configuration, solid-phase membranes are subdivided into diaphragm-type and hollow fiber membranes.

Finally, the most diverse contribution to the possible types of solid-state membranes is made by a classification based on the nature of material used in the manufacturing process: e.g., glass, ceramic, metal, polymeric membranes. The main criterion by which liquid membranes can be classified is the way to fix the membrane phase between the source (feed) and the receiving (product) phases. By this criterion, liquid membranes can be subdivided into free-phase, plasticized, impregnated and emulsion membranes. As to the nature of the membrane

TABLE 6
Intragroup classification of membrane separation methods

Driving force of the process	*Method in the dependence of the aggregation state of the phase system*				*Subgroup of the methods*
	Liquid-solid-liquid	*Liquid-liquid-liquid*	*Liquid-solid- gas*	*Gas-solid -gas*	
Gradient of chemical potential	Dialysis, Donnan dialysis	Dialysis through liquid membranes	Evaporation through membranes	Gas diffusion separation	Diffusion
Gradient of electric potential	Electrodialysis, electro-osmosis	Electro-dialysis through liquid membranes	—	—	Electromembrane
Pressure gradient	Ultrafiltration, Reverse osmosis, Piezodialysis	—	—	Micro- and ultrafiltration	Baromembrane methods

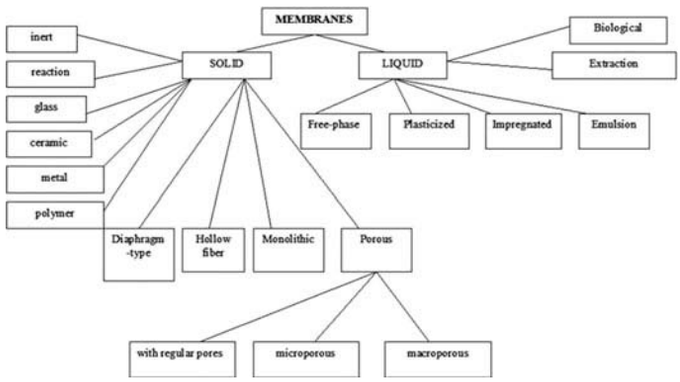

FIGURE 1 The types of membranes used in membrane separation methods.

transport process, liquid membranes can be subdivided into biological liquid membranes and extraction liquid membranes.

Of the membranes given in Figure 1, the most often used are solid-phase membranes with regular pores, i.e., close in size. These are primarily polymer membranes of the Millipore type and nuclear filters of the Nuclepore type. Both have rectilinear pores that are perpendicular to the membrane surface, but are substantially different considering properties such as area percent porosity. The percent ratio of the total cross-sectional area of all pores to the total surface area of the membrane is the area percent porosity. For Millipore membranes it can reach 80%, whereas for Nuclepore membranes the maximum area percent porosity is less than 10%. The limited percent porosity of Nuclepore membranes is related to their hydro and aerodynamic permeability. This low porosity is partially compensated by a smaller thickness (10 μm) associated with a preserved mechanical strength.

The usual thickness of Millipore membranes lies in the range 100 μm to 150 μm level. These differences are due to the nature of materials used in manufacturing membranes. Millipore membranes are manufactured from cellulose and, therefore, are wettable with water and aqueous solutions, and have minimum pore size distribution in the range of several hundredths μm, whereas Nucleopore membranes are manufactured from hydrophobic polymers (Lavsan/Mylar, polypropylene, etc.), which have been subjected to irradiation with charged nuclear particles. Etching the tracks left by these particles makes it possible to produce porous membranes with parallel rectilinear pores, close in size. Given their pore size uniformity, Millipore membranes are preferable when filtering aqueous solutions, whereas Nuclepore membranes are for gaseous media due to the lower gas viscosity.

The use of a specific type of membrane in membrane separation methods is primarily determined by the driving force of the membrane transport process that can be diffusion, electrical field, or pressure.

Diffusion Membrane Methods

The driving force of the membrane transport process here is the gradient of chemical potential at interphase boundaries, which is a function of the concentration difference of the transferred substance in the source (feed) and receiving (product) phases and, accordingly, in the membrane phase (61).

For the selective isolation of substances by diffusion membrane methods, such membranes are needed that are capable of ensuring a preferential transfer of substances to be isolated from the source phase into the membrane phase, as well as sufficiently high diffusion coefficients, thickness of membranes themselves being minimal. To the maximum extent, these requirements are met by cell membranes of living organisms possessing unique selectivity. Living cells are separated from one another by a lipid membrane layer. This lipid layer is selectively permeable for water molecules and some ions. The transport of these substances through cell membranes is accomplished through channels that are specific for each type of substances. The channel here is not a classical cylindrical pore; it is more a substance, a carrier (transporter) for specific molecules and ions through the membrane lipid layer. Thus, the water "channel,"i.e., the substance, which is responsible for carrying/transporting water molecules, is a specific protein that is given the name of Aquaporin 1 (AQP1).

Based on the biochemical model of the selective transport of substances across cell membranes, their artificial analogues should have a layer of nonpolar organic solvent that is analogous to the lipid layer of cell membranes, containing the molecules in its composition, which are capable of binding selectively and transporting the isolated substances across the layer of the solvent, i.e., of functioning as "channels" in biological membranes. There have been numerous attempts at creating artificial analogues of cell membranes, with, so far, limited success. Various schemes of membrane extraction have been practically implemented, wherein the lipid layer of the cell membrane is substituted for liquid extractants.

There have been several ways suggested for fixing the extractant between the source (feed) and receiving (product) phases. In a variant using a free-phase liquid membrane, the extractant layer moves between the two nonselective solid-phase hydrophilic membranes. In another variant, analogous to extraction chromatography, the extractant is fixed in the pores of a polymer wetted by the extractant. The first so-called impregnated membranes were used with porous PTFE plates (62). In these two schemes, the membrane phase preserves all physical and chemical properties of the free extractant. In a third scheme, called plasticized membranes (63), the extractant is held in the volume of the polymer by solvation interactions, losing some of its properties. A fourth scheme is membrane extraction in "multiple" emulsions (64). Here, an emulsifying agent is added to the extractant, which is used as a membrane, enabling stable emulsions to be formed wherein droplets of the receiving phase are surrounded with a thin film of the liquid membrane.

Based on the obvious analogy between biological and extraction membranes, further searches for selectively permeable membranes to be used for isolating substances from aqueous solutions, have been focused on the field of liquid membranes. In doing so, all the known schemes of their technical realization are employed: free liquid, supported liquid, and liquid emulsion membranes. Polymeric hollow fiber porous supports were successfully impregnated by liquid extractants giving efficient microextractors for concentrating analytes (65). Unfortunately, liquid extraction membranes have not yet found wide practical applications because of unreliability of the two first schemes of their fixation as partitions between the source and receiving phases and technical difficulties in the implementation of the third scheme.

Among diffusion methods wherein solid-phase membranes are employed, of the most practical interests are gas-diffusion methods where the substances to be isolated are gaseous compounds. Gas-diffusion separations are effected from one fluid phase into the other through a solid-phase membrane, which is a partition between these phases. Under this scheme, the most often-solved problem is that of controlled dispensing of gaseous components into gaseous media, e.g., of in-flow generation of standard gas mixtures to calibrate gas analyzers. To generate the standard gas mixtures, the most convenient scheme is based on the use of ampules made of a gas-impermeable polymer (usually PTFE), the ampules being filled with a solution with the substance to be dispensed.

To solve many membrane diffusion problems, the most preferable material is chemically inert solid- or porous polymeric membranes. For a continuous sampling, it is microporous PTFE or polypropylene membranes that are mostly often used. To adjust the acidity of solutions by diffusion of acetic acid or ammonia through membranes, the more reliable material is silicone rubber.

In gas-diffusion methods, membranes are used to isolate gaseous and easily volatile substances without their separation from other gaseous components. Practically, one exception among gas-permeable membranes, regarding their capability of separating only one target component from a mixture of gases, are metal membranes based on palladium and its alloys (61). The permeability of such membranes toward hydrogen is several orders of magnitude higher than toward any other gases. This allows to produce pure hydrogen with a productivity higher than that of all electrolytic methods. Using palladium membranes, the most attractive is a combined method wherein hydrogen is isolated on the hollow palladium cathode, its walls simultaneously serving as gas-diffusion membranes. In the inner volume of such a cathode, hydrogen of maximum purity is evolved. Based on this, similar electrolyzers are used in laboratory hydrogen generators for preparative purposes.

Among diffusion membrane methods of separation, pervaporation (evaporation through a membrane) occupies a special place (66). The method is based on selective permeability of some natural and synthetic materials to different components of liquid mixtures. The driving force of the process, as in other diffusion membrane methods, is the difference of chemical potentials of the substance to be separated on both sides of the membrane. The method of pervaporation finds practical applications predominantly on an industrial-scale. In particular, one of these is the separation of water-alcohol liquid mixtures (dehydration of alcohols), when the use of standard distillation methods is limited due to the formation of azeotropes. A possibility being considered is pervaporation through membranes for water desalination. So far, economically the method is inferior for this task compared to the method of reverse osmosis, but it is not ruled out that the economic limitations could be overcome.

Electromembrane Methods

As the most widely used variety of reactive membranes, ion-exchange membranes have a polymeric structure, which is, to the accuracy of the polymeric matrix composition, analogous to the structure of ion-exchange resins, cationites and anionites. Consequently, similar membranes make it possible to separate cationic and anionic species of elements by electrodialysis.

Generally, selectivity of ion-exchange membranes is limited by the selective transport of cations and anions. The transport numbers for ions of the same sign in the best ion-exchange membranes exceed 95%. At some point, the interest in the method was connected with the industrial-scale problem of water desalination, but it faded significantly after the advent of the reverse osmosis method, which is dealt with later. There are single examples known of the use of electrodialysis through ion-exchange membranes for

analytical and preparative applications in biochemistry, for desalination of protein solutions and for the separation of amino acids.

Electro-osmotic filtration also uses membranes. Traditionally electro-osmosis has been viewed as an electrokinetic phenomenon accompanying electrodialysis, presenting no independent practical interest. The discovery of the effect of retention of electrically charged polluting admixtures by porous PTFE membranes in electro-osmotic filtration of water through them allowed electro-osmosis to be considered as a promising membrane method of separation (67, 68). In analytical applications of the method, advantages of electro-osmotic filtration are best exhibited in analysis of high-purity water, which is produced and used at an industrial scale in thermal and nuclear power engineering, biochemical technologies, microelectronics, etc.

In these fields, among reagent-free concentration methods of electrolytic solutions, electro-osmotic filtration has proved to be the most attractive alternative to evaporation as it is substantially superior, both as an express method and due to the completeness of admixture separations. The presence of undissociated or weakly dissociated compounds in solution has practically no effect on parameters of electro-osmotic concentration. Consequently, electro-osmosis can be used for concentrating and isolating charged species from aqueous solutions of polar organic and weakly dissociated inorganic compounds (such as ethylene glycol, glucose, hydrogen peroxide, boric acid, etc.) and also organic mixtures.

Electro-osmosis through inert porous membranes, apart from solving analytical problems, provides the possibility of producing high-purity water. The process of electro-osmotic water deionization is realized via successive operations of electro-osmotic filtration of water through two membranes with different charges of their surfaces. An advantage of the electro-osmotic deionization process over the ion-exchange one lies in the absence of degradation products of ion-exchange resins in the purified water. At the same time, capabilities of the method are (objectively) limited by the total content of ionic admixtures in the starting water to be purified at the level of 1×10^{-3} M, since the volumetric rate of electro-osmotic flow (EOF) falls sharply with the increase of total salt content, which allows electro-osmotic filtration to be seen only as a method of final purification of water after distillation or reverse osmosis.

Baromembrane Methods

The third group of membrane methods is based on the transport of substances through porous membranes under the action of pressure gradients. Depending on the membrane pore sizes, the following processes and corresponding methods are to be distinguished: reversed osmosis (membrane pore sizes of 1–10 nm), ultrafiltration (pores 10–100 nm), and microfiltration (0.1–10 μm). Reversed osmosis is sometimes called hyperfiltration and is used only for aqueous solutions. The other two methods are equally efficient for isolating admixtures, both from liquid and gaseous media. For each of the pore size ranges, in the corresponding baromembrane separation methods, a narrow distribution of the pore size is required.

In any baromembrane method, the mechanism of isolating particles from the filtered fluid medium can be considered as particle size exclusion. A substantial contribution into particle retention, especially from the gaseous phase, is made by electrostatic interactions. Consequently the membrane retains particles of significantly smaller size than pore diameter. Therefore, in the case of micro- and ultrafiltrations, a strict correspondence of particle size to be separated to the membrane pore size cannot be guaranteed. Accordingly, membrane filtration methods allow both to effect primarily an overall isolation of particles that exceed a certain size and to make only a certain approximation as to particle size-fractionation. The boundaries of the size range of particles, which have been isolated in such a way, prove to be substantially diffused.

Among barometric methods, a special place is taken by reverse osmosis. Reverse osmosis is realized under conditions of filtration when a hydrostatic pressure is applied that is greater than the osmotic pressure (70). Despite a number of technological problems, which emerge on a practical realization of similar processes, reverse osmosis finds wide applications. Originally, it was developed for desalination of seawater, and is still most frequently used in water treatment technologies instead of distillation to produce low mineral content water. At present, it is widely used to lower salt concentrations in moderately and weakly salted waters in a number of industries (71). The most important of the problems being solved is the treatment of industrial and municipal wastewaters. A list of industries that use reverse osmosis for wastewater and sewage treatment is constantly growing. One of the main advantages of reverse osmosis is in its significant energy savings; it requires a mere 25% of the energy needed for distillation.

The two last baromembrane methods, micro- and ultrafiltration, do predominantly find applications in analytical and preparative microbiological practice. In microbiological analysis, microfiltration, for example, is used for the determination of the content of bacteria of the colon bacillus group (CBG) in water. In doing so, the use of the membrane filtration method has contributed to the substantial progress in the analysis as compared to the previously applied methods, which were based on indirect evidence for the presence of CBG. For the group isolation of viruses, ultrafiltration through membranes is used with the pore size of 25 nm.

For ultrafiltration, the main application area is the group concentration of macromolecules, e.g., proteins. Only rarely is it used for the fractionation of molecules according to their size, thereby complementing the method of size-exclusion chromatography. Major applications of ultrafiltration are for process technologies in pharmacology, microelectronics, in

the food/milk industry, i.e., where there is a need for the isolation of high-molecular weight admixtures from aqueous media or purification of the media from similar samples.

The methods of micro- and ultrafiltration were originally developed for isolating admixtures from aqueous media, but very soon found their applications for isolating aerosols as well. In the analysis of aerosols and atmospheric particulate matter, membrane filters possess objective advantages over the ones made from fibrous materials. The particulate matter, which is retained on a membrane filter, is left on its surface, wherein it can be analyzed microscopically or by chemical methods. Prior to the development of membrane filters, the size distribution analysis by microscope of aerosol particles present in the atmospheric air was more laborious.

An independent line of developing membrane filtration of air is the method of filtration through reactive impregnated membranes, that is, membranes that have been impregnated with an absorbing solution. Cellulose filters are generally used as a support for the absorbing solution. Membranes, which are impregnated with a solution of specific reagents, are usually highly selective towards the substances to be separated. For example, membranes that are impregnated with sulfanilamide are selective towards NO_2.

INTRAPHASE SEPARATION METHODS

Principles of Intraphase Separations and an Intragroup Classification of the Methods

This group comprises the methods based on characteristic properties of ions, atoms and molecules, which are exhibited within one fluid phase upon the action of electric, magnetic, gravitational and thermal fields or centrifugal forces. The separation effect is achieved due to a difference in the rate and/or direction of the spatial motion of particles within the phase wherein the separation occurs. The most evident case is electrophoretic separation of ions in solution due to a difference in their migration rates in an electric field. Differences in mass and charge are mostly revealed upon the action on the particles of an accelerating electric field and deflecting magnetic or other electric field in vacuum. This action on the system is the basis of mass-separation methods. In the separation under the action of centrifugal forces, ultracentrifugation, the mass of molecules proves to be the determining factor.

Apart from these intraphase separation methods, which have already become traditional, wherein differences are used in the rates and directions of spatial motion of substances, in the late 1960s, the whole group of methods appeared that was named Field-Flow Fractionation (FFF) (72). To name a particular FFF method, one or two letters are added to characterize the acting force nature: EFFF (electrical field-flow fractionation), SFFF (sedimentation) or GrFFF (gravitational), and TFFF (thermal field).

Any of the known intraphase separation methods can be characterized by the aggregation state of the phase, within which the separation occurs, and by the nature of forces that drive the spatial motion of ions, atoms or molecules within this phase (Table 7).

A characteristic feature of most methods of this group is the absence of a distinguished boundary in applications for the separation of homogenous and heterogeneous mixtures of substances. For example, electrophoresis has emerged, and sometimes is seen until now, only as a method for separating colloidal particles. Moreover, in its essence it is a method for the separation of any charged particles under the action of electric field due to their different mobility within fluidic phases. In a general case, the particle size is not specified and the application field of the method covers both simple ions and macro-ions of amine acids, as well as charged colloidal particles and suspensions. The same is true for ultracentrifugation and FFF-methods.

Even in the cases when the method has fairly distinguished application boundaries as to the size and mass of particles to be separated, their position on a conventional scale of particle dispersion is not related to the accepted boundary of homogeneity. FFF-methods that have attracted great attention of chemists/analysts are now under successful development owing to the substantially extended capabilities of separating substances by the size and configurations of molecules, both for preparative and analytical purposes (72). For the latter, some related "hybride" FFF-based methods of analysis began to appear under analytical schemes that are analogous to chromatographic ones. In these methods, with FFF-separation devices, fractionators, flow-through detectors were combined, which are analogous to detectors used in liquid chromatography.

In the majority of cases, for separation techniques within a single phase it is sophisticated instrumentation that is characteristic for these methods, and their applications in analytical

TABLE 7
Intraphase separation methods: An intragroup classification

	The nature of forces, which drive the spatial motion of ions, atoms and molecules, and the related separation methods			
Aggregation state of the phase, where the separation occurs	*Electric field*	*Electric and magnetic field*	*Centrifugal force or gravitational field*	*Thermal field*
Liquid	Electrophoresis, EFFF	—	Ultracentrifugation, SFFF	TFFF
Gas (vacuum)	Electrophoresis	Mass-separation	Ultracentrifugation	—

chemistry is justified if the possibilities are opened up that cannot be provided by simpler methods. Among methods of this group, the most simple, as to its technical realization, is the method of electrophoretic (electromigrational) ion separation in solution, which has found widespread use in analytical chemistry. The main applications of electrophoresis in the gaseous phase are for trapping aerosol particles from gaseous streams and, primarily, for isolating mineral components or unburned fuel particles from effluents of thermal power stations, and boiler-rooms.

Mass separation as a separation method is interesting initially as it is the basis for one of the most efficient "hyphenated" methods of chemical analysis, mass spectrometry. In this method, it is even closer integration of the separation method and the method of final determination that has taken place than in the case of chromatographic methods of analysis, which makes it unjustified to separately examine the method of mass separation and mass-spectral methods of analysis. Information on mass separation is mainly in inaccessible literature on isotope enrichment. Principles of mass separation can be easily understood from the voluminous literature on mass-spectral analysis (73). The traditional rating of mass spectrometry as a spectral method of analysis is explained by the formal analogy of mass separation with spectral decomposition of electromagnetic radiation, and that is where the very name of the method, mass spectrometry, originates.

Electrophoresis and its Variants

The history of this separation method, which is based on differences in the rates of spatial motion of electrically charged particles in solutions, is more than a century long. After all this time, a great number of names have been suggested for actually the same method: electrophoresis, ionophoresis, ionography, electrochromatophoresis, electrophoregraphy, electromigration is far from a complete list of synonyms that have appeared for this period. Along with subjective factors, in the desire of authors of any new name for discovering a new method, there are objective reasons as well. Electrophoresis has emerged in the field of colloid chemistry as one of electrokinetic phenomena, which is opposite to electro-osmosis: the motion of electrically charged particles of the solid phase relative to the solution. Its application for separating ions explains the appearance of such separation methods as ionophoresis and ionography. Electromigration methods, as a generalizing term, has been in use long enough, but in the recent years it is again electrophoresis that has become the most frequently used term, i.e., it is a comeback of the original name.

Electrophoresis is formally similar to chromatographic methods. Here, separations are conducted in a cylindrical column or on a plane. In doing so, in order to minimize the effect of a convective mixing of the solution on the separation results, the inner volume of the column and a flat gap between the walls of the separation space are filled with a fine-dispersed granulated material, which, to a maximum extent, is inert towards the ions to be separated and towards the medium wherein they are. Another way of preventing a convective mixing of the solution is to conduct electrophoretic separation in a capillary. In this case, there is a formal analogy to capillary chromatography. If electrophoretic separation is conducted on a layer of specially treated paper, which retains an electrolyte solution within its pores, then it is completely similar in appearance to paper chromatography (74).

There are other similarities as well. For example, a moving boundary technique that appeared at the forefront of electrophoresis development, is analogous to frontal analysis in chromatography. In this technique, the separation of ions in an electric field occurs directly in the solution of their mixture. In the most widespread method of zone electrophoresis there is a general similarity with the zone separation mode in chromatography, the separation efficiency being analogously characterized by the height equivalent to a theoretical plate and by the number of plates. At the same time, there are some specific variants of the method, such as isotachophoresis, in which conditions are created for ion migration with the same electromigration rate despite differences in their mobility. To enhance the separation of ampholites, a technique of isoelectric focusing is applied.

Paper, cellulose acetate, quartz sand, starch-based gels, gelatin, agar, polyacrylamide and some others are used as packing materials for electrophoretic separations, but the most preferable scheme for such separations is a stabilization of the electrolyte layer in a capillary. The capillary variant of electrophoretic separation was known relatively long ago, but recently it has been gaining increased interest with the development of microdetection techniques. A combination of electrophoretic separation in a capillary with flow-through detectors has led to the emergence of a new "hybrid" method of analysis, capillary electrophoresis (74). At present, this method has gone beyond the scope of inorganic analysis and finds wide applications for the analysis of biologic media.

FFF Methods

Separations by FFF methods occur in a flat ribbon-like channel formed by two flat parallel blocks with maximally smooth surfaces that form the channel. The channel thickness (W) is chosen to ensure the maximally steep parabolic flow profile of the carrier solution to be developed along the channel cross-section. In the industrially manufactured apparatus for polymer separation and analysis, fractionators, thickness W is usually not more than 250 μm. Substance particles introduced into the channel with the carrier flow are subjected to the action of a field applied perpendicular to the flow direction. As a result, molecules or larger particles are deflected towards one of the channel walls, which is called the accumulation (or analytical) wall, and are driven into lower velocity flow layers.

The amount of deflection depends on the particle size and the force of the acting external field. Individual zones of particles of certain size, which are formed about the accumulation wall, are driven back to the channel center by counteracting diffusion force, these zones being particle size dependent (l_A or l_B, where A and B are indices of the substances to be separated). The total flow rate for these zones along the channel will depend on the flow velocity area in which the zones are. If the component B goes to the higher velocity area than the component A, it will be the first one to leave the channel, whereas the component A, the second (75).

Field-flow fractionation was described by the method's inventor, Giddings, as "one-phase chromatography" (72). In the frames of physicochemical principles of this group of methods, one can hardly agree with such analogy, since any chromatographic method, by definition, is based on the interphase distribution and cannot be a one-phase. An analogy can be seen here in another aspect: similarly to chromatography, field-flow fractionation is not a specific method, but a general methodology or a general principle of separation for the whole group of methods: for their individual classification, the most important criterion is the nature of the force of the field, which is applied perpendicular to the flow to drive the particles to be separated across the flow, that was considered by the author of the method to be the general classification criterion for all separation methods (75).

By measuring the concentration of separated substances at the channel outlet, a fractogram can be obtained, which is a curve on the "migration time (eluted volume) vs. detector response" plot, which is analogous to a chromatogram, wherein there are peaks corresponding to each component with their own retention parameters.

Theoretically, any field can be applied to act on macromolecules or colloidal particles. The more the zone *1* smears out by diffusion, the higher is its velocity in the flow along the channel, since the flow velocity will increase as the flow goes further away from the confining channel walls. The most important methods of this group, which have already been tried and put into practice, are given in Table 8.

One of the first and most thoroughly studied FFF methods is SFFF, wherein perpendicular to the flow direction of the feed/carrier solution there is acting gravitational field or centrifugal force generated by a centrifuge. The molecular mass of substances to be separated is determined by the acting field force. In a flat channel and under the action of gravitational field only, large particles are easily separated in the size range of 1 to 2 μm. For the separation of smaller particles, the separating membrane needs to be placed into a centrifugal force field. To reach the lower limit of molecular mass of $\sim 5 \times 10^5$ Da, the centrifugal acceleration should be $\sim 10^5$ G. The method has found applications for the determination of particle size distribution of suspensions of both inorganic and organic origin. Most interest in the method is its capacity to separate biopolymers and particulates of biological origin, e.g., viruses (75).

Thermal field-flow fractionation is also an earlier FFF method. In this case, the TFFF separation system is the simplest. The size- and mass-range of molecules in TFFF are substantially wider than in SFFF. With TFFF, molecules can be separated in the molecular mass range of $\sim 10^3$ Da, the best results were achieved for SFFF in the molecular mass range of 10^7–10^9 Da.

The most uniform (and easily controlled by its force) field across the channel can be obtained in EFFF. To do this, the channel walls are made using electroconducting membranes that are nonpermeable to electrically charged particles to be separated. Due to its relative simplicity, one of the most actively implemented FFF methods is FlFFF. The "field" in this FFF method is an auxiliary flow of carrier (the cross-flow), which is in the direction perpendicular to the main longitudinal flow in the channel. To obtain the cross-flow in the channel, one of its walls is made permeable to the carrier solution. The wall is of a porous material, which is permeable to the carrier solution, but not to the substances to be separated. The lower fractionation limit for molecular masses and, hence, molecular size, is dependent on the pore size of the porous material, whereas the upper limit can reach 1 μm.

Overall, FFF methods proved to be an essential complement to size-exclusion chromatography. The methods enable mixtures of high molecular weight organic compounds to be separated quickly and efficiently: latexes, polymer materials, proteins, DNAs, polymers, as well as colloid solutions and suspensions of inorganic substances. A comparison of analytical capabilities of size exclusion chromatography and FFF methods shows that the molecular mass range of separated substances for the former method is limited to 10^6 Da, whereas for the latter it is up to 10^{18} Da (72).

TABLE 8
Some widely used FFF methods

No.	*Driving forces*	*Method*
1	Gravitational field or centrifugal forces	Sedimentation FFF (SFFF)
2	Temperature gradient/thermal field	Thermal FFF (TFFF)
3	Electrical field	Electrical FFF (EFFF)
4	Cross flow	Cross-flow FFF (FlFFF)

"COMBINED" SEPARATION METHODS

Basic Principles of Combined Methods

The general and intragroup classifications of separation methods given earlier include the vast majority of well-known methods. However, as with each general rule, there are several exclusions to the six groups of the general classification scheme of separation methods by the aggregation state of the phases that participate in the separation

process: these exclusions do not belong to any of the groups discussed earlier. Those exclusions are methods wherein different separation principles are used simultaneously: the principles that are realized in the group methods discussed earlier.

In doing so, several principles are combined, as a rule, to obtain a synergy effect, i.e., a substantial separation improvement as compared to the individual effect of any of the methods being combined. The term "combined" in relation to separation is not identical to "hybride" or hyphenated methods mentioned earlier and classed as analytical methods based on a combination of separation- and determination methods in one analytical procedure. Among combined separation methods, the most interesting are the three groups: optical, electrochromatographic and chromatomembrane methods.

Optical Separation Methods

The most widely known group of optical separation methods (OSM) are laser methods (76), where a combination of methods is used that is opposite to the combination in hyphenated methods of analysis. In the latter, a preliminary separation of substances is combined with their subsequent determination. In laser separation methods (LSM), the principles of optical analysis methods are combined: selective excitation of atoms or molecules by photons of monochromatic electromagnetic radiation and subsequent separation of the excited particles from the ones that are left in the basic state. In the most widely known and practically claimed variant, LSM have emerged and have developed primarily for preparative and industrial isotope separations, uranium isotope being the main reason.

Relative complexity and high energy consumption in laser isotope separation methods (LISM) are compensated for by the unique selectivity of the method due to the monochromaticity of laser radiation. For an efficient separation, the laser photon energy should maximally coincide with the energy of transition of one of the isotopes in the mixture to be separated, from its ground state to an excited state. An additional mandatory prerequisite is an irreversible transformation of the initial chemical species of the isotope into new chemical species resulting from an induced photochemical reaction, or the sufficiently long lifetime of the ionic state of the isotope, which emerges as a result of photo-excitation, to enable the process of subsequent separation of the isotope to be carried out under the action of an electric field.

One more well-known application of optical separation methods is based on the use of photochemical reactions for the solution of another specific problem: the separation of platinum metals from solutions at the expense of their photochemical reduction (77). In this case, the monochromaticity of electromagnetic radiation is not a mandatory prerequisite. A beam of light of a wide wavelength band is directed into the solution, wherein particles of a photochemical catalyst are dispersed, e.g., those of titanium dioxide. As a result of photoexcitation occurring in the surface layer of such catalysts, electron–hole pairs are created. The electrons formed take part in the reaction of reduction of the metal ions, which is followed by their separation on particles of the catalyst. Both subgroups of optical separation methods are industry-oriented. The last two groups of combined methods—electrochromatographic and chromatomembrane—are primarily of analytical interest.

Electrochromatography

In electrochromatography (EC), the principles of chromatographic and electrophoretic, or electro-osmotic, separation methods are combined. Accordingly, the factor that affects the rate of migration of zones of separated substances in the electrophoretic process, apart from the composition of the stationary and mobile phases, which determine the velocities of chromatographic zones of separated substances, is the electrophoretic mobility of electrically charged species in the mobile phase, or velocity of electro-osmotic flow (EOF). Here, there are two modes possible for the electrophoretic process. In the first, the occurring EOF is superimposed onto hydrodynamic movement of the mobile phase. In the second mode, it is electro-osmosis that is an alternative to the hydrodynamic flow movement.

Among the possible combined effects of various forces on the substances to be separated, it is the second mode above that has found practical applications in electrochromatography, where electro-osmosis causes the mobile phase to move. The electric field applied to produce EOF is actually a substitution for a pump in such an electrochromatograph. In this case, advantages are revealed not only in the opportunity to get rid of mechanical pumps, but in an enhancement of separation efficiency. Because EOF is generated by a collective movement of ions, which form a diffused part of the double electric layer at the boundary with the capillary walls or with the surface of particles of the sorbent, decreasing the capillary radii or particle size of the sorbent will not only cause the liquid flow to stagnate, but, on the contrary, will cause the EOF velocity to increase, and, hence, the velocity of zones of the substances to be separated to increase as well.

As a result, it is made possible to work with very long, thin capillary columns and packed microcolumns, providing the efficiency unattainable with an analogous, as to the phase composition, HPLC variant, wherein the limiting factor, which appears upon decreasing capillary radii and particle size of the packing, is the hydrodynamic resistance of the column. Apart from the opportunity of overcoming the limitations caused by the hydrodynamic resistance, electro-osmosis provides a laminary flow of the practically rectangular profile, which enhances the separation efficiency

even further. A set of advantages mentioned above is realized in a special electrochromatographic method of capillary chromatography (CEC) (78).

In the name of the method, CEC, the term "capillary" has a special meaning, which is different from the one that is conventional for usual chromatography. It characterizes not only geometrical dimensions and configuration of the column, but the very principle of movement of the mobile phase along capillaries due to EOF generated in there upon the application of a sufficient potential difference. As these capillaries, both capillary columns themselves and gaps between particles of the granulated stationary phase can be used, and even the porous space of the monolithic phase as well (79).

EOF is determined by the ξ-potential of the surface. In CEC there are additional requirements to be met for column materials and stationary phases. As a material for columns, fused silica is generally used, which, alongside with its chemical stability and mechanical strength, is characterized by a high electric resistance and sufficiently high value of the ξ-potential. Due to a high efficiency of CEC and the possibility of using monolithic chiral stationary phases in the column, a fairly good separation of enantiomers was successfully achieved (79). On the whole, CEC enables higher efficiency of chromatographic separations to be achieved than it is possible with UHPLC.

CEC, as well as capillary electrophoresis, are objectively limited by their ability of separating only electrically charged compounds. This limitation has been overcome in the method of micellar electrokinetic chromatography (MEKC) (80, 81). The separation of neutral species has been made possible by the introduction of micelle-forming surfactants into the buffer electrolyte solution. The micelles in the mobile phase bear charges and therefore possess electrophoretic mobility and play the role of the pseudostationary phase, the adsorbent, taking part in the interphase distribution of neutral molecules of substances to be separated.

As a complement to the MEKC method, there appeared a method of affine electrokinetic chromatography (82), which is realized by the addition of proteins into the running buffer electrolyte solution. In a particular case, proteins can be immobilized on the walls of a fused silica/quartz capillary (capillary affine gel-electrophoresis). As they are based on the principles of different protein binding of enantiomers, these methods have found applications in the separation of chiral drugs.

Chromatomembrane Mass-Transfer Process and Separation Methods

The chromatomembrane mass-transfer process (CMMP) (83) is a general methodology for the separation of substances in "liquid-liquid" and "liquid-gas" systems, which is based on a combination of principles of chromatographic and membrane separation methods. The principles of the former are revealed in the chromatographic way of realizing the interphase distribution of substances to be separated in these methods. A similarity with membrane methods is evident in two aspects. On one hand, membranes in CMMP are needed for the nonpolar liquid or gaseous phase to be introduced into, and removed from, the separation space wherein the chromatographic process is carried out. From the other hand, a similarity with membrane methods manifests itself in the possibility of a continuous separation of substances.

In order to provide the possibility of a simultaneously independent movement of the flow of two phases through the matrix, it should have two types of pores, which are homogeneous as to their size, the pores of each type being substantially different. The size of macropores should be such as the capillary pressure in them should be negligibly low relative to the polar phase and would not prevent the passage of the phase through the pores. Pores of the second type are conventionally called "micropores." The conventionality here is in that the term "micro" does not comply with the IUPAC size classification: it means only that the pore size is relatively smaller than that of macropores.

The lung functionment will be used to illustrate how chromatomembrane works. In chromatomembrane cells (CMCs), the polar liquid (blood) moves along micropores, and the gas phase does so along macropores, as alveoli are filled with air in the lungs, and micropores (which are microcapillaries here) are filled with blood. In both cases, CMCs and lungs, the mass-transfer process occurs along intersecting boundaries of pores of the two types.

For methods based on mass-transfer in "liquid-liquid" systems, a porous structure of the inner volume of the CMC is analogous to the structure of the packing of a chromatographic column in RPLLC. Micropores in the biporous matrix, as well as the pores in the packing particles, are filled with the nonpolar phase, macropores being the spaces between particles of the packing, through which a flow of the polar phase passes. In accordance with this analogy, the movement of zones of substances to be separated in the CMC with a flow of the polar phase is governed by the same laws as the zone movement in a chromatographic column in RPLLC. Differences are revealed in the conditions for a continuous chromatomembrane process, when a zone moves in flows of the two phases simultaneously. Here, there is a complete analogy to the zone movement in continuous two-dimensional or countercurrent chromatography.

The CMM process can be realized with any combination of fluidic phases, one of which does not wet the surface of the biporous matrix, which is needed to implement the process, whereas the second phase wets the matrix, a number of chromatomembrane separation methods are possible (84), depending on which phase is the source (feed) one and which is the receiving (absorbing) phase. The most important chromatomembrane methods are: chromatomembrane liquid-extraction (CMLE),

chromatomembrane gas extraction (CMGE) and, the reverse method, chromatomembrane liquid absorption (CMLA). Despite the generality of their principles, each of the methods above has its own specificities and applications (85–87).

CONCLUSION

The suggested classification of separation methods does not lay a claim to be alternative to the earlier existing ones. It is rather a further development of Giddings' ideas (6) but with a wider coverage of existing separation methods. Of some widely known methods, in the suggested classification there are none (that have been omitted intentionally), which could have been divided by the criterion of scale, such as the method of microextraction, since this criterion would not impart any significant specificities to the corresponding method and a difference could be revealed only in some practical consequences. In the author's opinion, at present there are no other exceptions left that neither could enter the suggested classification nor find a place to do so, unless they are mentioned in this article. However, the author will be much obliged to the colleagues if they find such exceptions and supplement this classification with other groups of methods.

ABBREVIATIONS

AQP1– Aquaporin 1
ASE– assisted solvent extraction
CBG– colon bacillus group
CCC– countercurrent chromatography
CE– capillary electrophoresis
CEC– capillary electrochromatography
CMC– chromatomembrane cells
CMGE– chromatomembrane gas extraction
CMLA– chromatomembrane liquid absorption
CMLE– chromatomembrane liquid-extraction
CMMP– chromatomembrane mass-transfer process
EC– electrochromatography
ElFFF– electrical field-flow fractionation
EOF– electro-osmotic flow
FFF– Field-Flow Fractionation
FFFF– cross-flow FFF
GC– gas chromatography
GLC– gas-liquid chromatography
HIC– hydrophobic interaction chromatography
HILIC– hydrophylic interaction liquid chromatography
HPLC– high-performance liquid chromatography
LC– liquid chromatography
LAC– liquid adsorption chromatography
LGC– liquid-gas chromatography
LISM– laser isotope separation methods
LLC– liquid-liquid chromatography
LSPC– liquid-solid-phase chromatography
LSM– laser separation methods
MEKC– micellar electrokinetic chromatography
MIP– molecular-imprinted polymer
NPLAC– normal-phase liquid-adsorption chromatography
OSM– optical separation methods
PDMS– polydimethylsiloxane
PTFE– polytetrafluoroethylene
RAM– restricted access materials
RPLAC– reversed-phase liquid-adsorption chromatography
RPLLC– reversed-phase liquid-liquid chromatography
SdFFF– sedimentation field-flow fractionation
SEC– Size exclusion chromatography
SFC– supercritical fluid chromatography
SFE– supercritical fluid extraction
SMB– simulated moving bed
SPE– solid phase extraction
SPME– solid-phase micro extraction
ThFFF– thermal Field-Flow Fractionation.
UHPLC– Ultra high pressure liquid chromatography

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