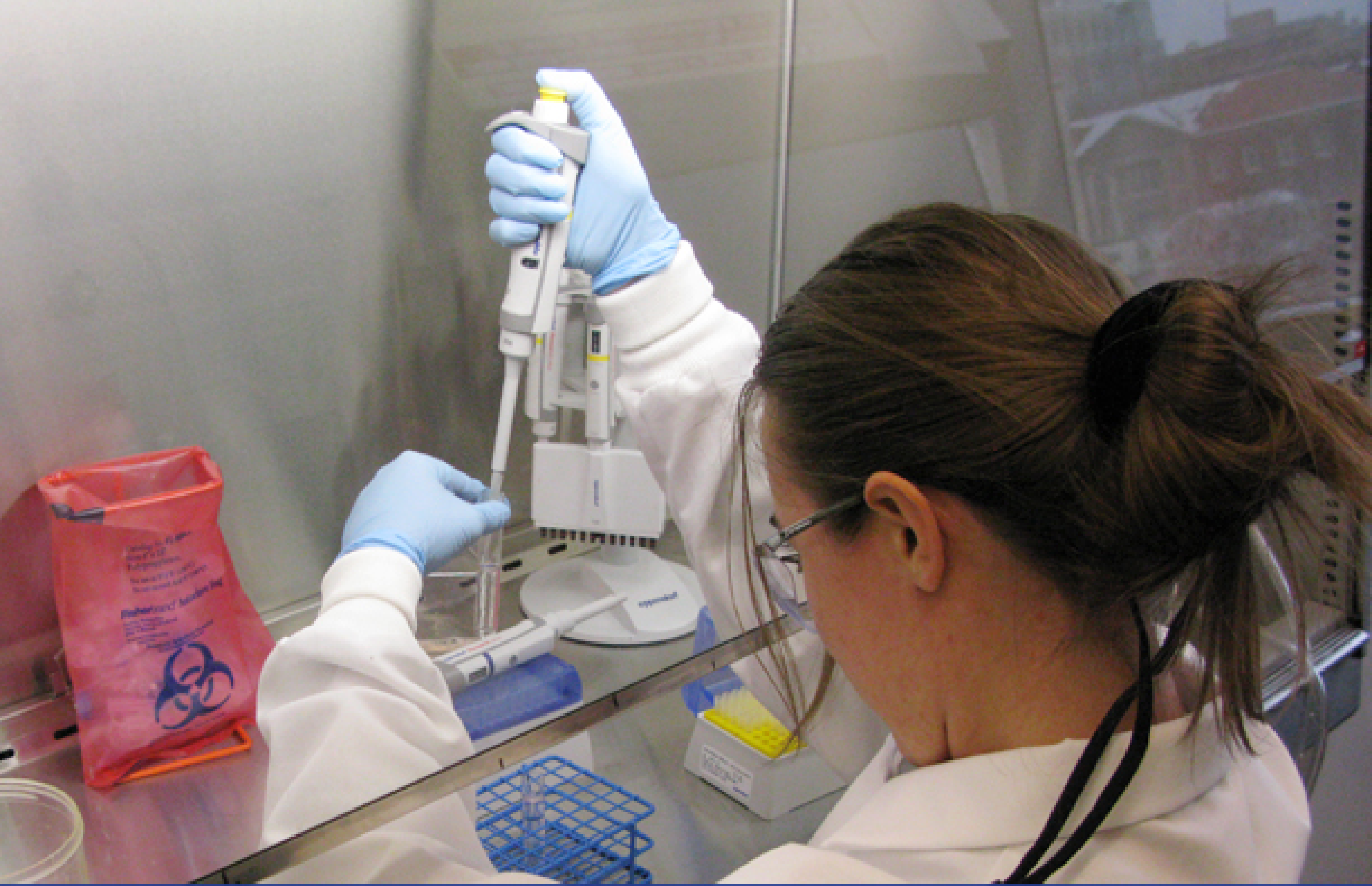

Unit Operations, Technology, Processes and Tools of
Chemical Engineering

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Chapter- 1

Chemical Reaction Engineering and Chemical Synthesis

Chemical Reaction Engineering

Chemical reaction engineering (reaction engineering or reactor engineering) is a specialty in chemical engineering or industrial chemistry dealing with chemical reactors. Frequently the term relates specifically to catalytic reaction systems where either a homogeneous or heterogeneous catalyst is present in the reactor. Sometimes a reactor *per se* is not present by itself, but rather is integrated into a process, for example in reactive separations vessels, retorts, certain fuel cells, and photocatalytic surfaces.

Origin of Chemical Reaction Engineering

Chemical reaction engineering as a discipline started in the early 1950s under the impulse of researchers at the Shell Amsterdam research center and the university of Delft. The term chemical reaction engineering was apparently coined by J.C. Vlugter while preparing the 1st European Symposium on Chemical Reaction Engineering which was held in Amsterdam in 1957.

Discipline

Chemical reaction engineering aims at studying and optimizing chemical reactions in order to define the most optimal reactor design. Hence, the interactions of flow phenomena, mass transfer, heat transfer, and reaction kinetics are of prime importance in order to relate reactor performance to feed composition and operating conditions. Although originally applied to the petroleum and petrochemical industries, its general methodology combining reaction chemistry and chemical engineering concepts allows to optimize a variety of systems where modeling or engineering of reactions is needed. Chemical reaction engineering approaches are indeed tailored for the development of new processes and the improvement of existing technologies.

A few Chemical Reaction Engineering books

- Chemical Reaction Engineering (3rd Edition), Octave Levenspiel, 1999, John Wiley & Sons
- Elements of Chemical Reaction Engineering (4th Edition), H. Scott Fogler, 2005, Prentice Hall
- Chemical Reactor Analysis and Design (2nd Edition), Gilbert F. Froment and Kenneth B. Bischoff, 1990, John Wiley & Sons
- Fundamentals of Chemical Reaction Engineering (1st Edition), Mark E. Davis and Robert J. Davis, 2003, The McGraw-Hili Companies, Inc.

Chemical Reaction Engineering symposia

The most important series of symposia are the International Symposia on Chemical Reaction Engineering or ISCRE conferences. These three-day conferences are held every two years, rotating among sites in North America, Europe, and the Asia-Pacific region, on a six-year cycle.

Chemical synthesis

In chemistry, **chemical synthesis** is purposeful execution of chemical reactions to get a product, or several products. This happens by physical and chemical manipulations usually involving one or more reactions. In modern laboratory usage, this tends to imply that the process is reproducible, reliable, and established to work in multiple laboratories.

A chemical synthesis begins by selection of compounds that are known as reagents or reactants. Various reaction types can be applied to these to synthesize the product, or an intermediate product. This requires mixing the compounds in a reaction vessel such as a chemical reactor or a simple round-bottom flask. Many reactions require some form of work-up procedure before the final product is isolated . The amount of product in a chemical synthesis is the reaction yield. Typically, chemical yields are expressed as a weight in grams or as a percentage of the total theoretical quantity of product that could be produced. A **side reaction** is an unwanted chemical reaction taking place that diminishes the yield of the desired product.

The word *synthesis* in the present day meaning was first used by the chemist Adolph Wilhelm Hermann Kolbe.

Strategies

Many strategies exist in chemical synthesis that go beyond converting reactant A to reaction product B. In cascade reactions multiple chemical transformations take place within a single reactant, in multi-component reactions up to 11 different reactants form a single reaction product and in a telescopic synthesis one reactant goes through multiple transformations without isolation of intermediates.

Organic synthesis

Organic synthesis is a special branch of chemical synthesis dealing with the synthesis of organic compounds. In the total synthesis of a complex product it may take multiple steps to synthesize the product of interest, and inordinate amounts of time. Skill in organic synthesis is prized among chemists and the synthesis of exceptionally valuable or difficult compounds has won chemists such as Robert Burns Woodward the Nobel Prize for Chemistry. If a chemical synthesis starts from basic laboratory compounds and yields something new, it is a purely synthetic process. If it starts from a product isolated from plants or animals and then proceeds to a new compounds, the synthesis is described as a semisynthetic process.

Other meanings

The other meaning of **chemical synthesis** is narrow and restricted to a specific kind of chemical reaction, a *direct combination reaction*, in which two or more reactants combine to form a single product. The general form of a direct combination reaction is:

$A + B \rightarrow AB$

where A and B are elements or compounds, and AB is a compound consisting of A and B. Examples of combination reactions include:

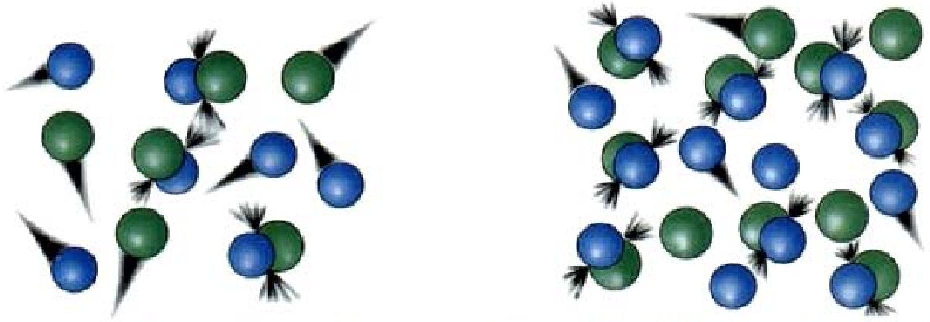
$2Na + Cl_2 \rightarrow 2\,NaCl$ (formation of table salt)
$S + O_2 \rightarrow SO_2$ (formation of sulfur dioxide)
$4\,Fe + 3\,O_2 \rightarrow 2\,Fe_2O_3$ (iron rusting)
$CO_2 + H_2O \rightarrow H_2CO_3$ (carbon dioxide dissolving and reacting with water to form carbonic acid)

4 special synthesis rules:

metal-oxide + $H_2O \rightarrow$ metal(OH)
non-metal-oxide + $H_2O \rightarrow$ oxi-acid
metal-chloride + $O_2 \rightarrow$ metal-chlorate
metal-oxide + $CO_2 \rightarrow$ metal(CO_3)

Chapter- 2

Chemical Kinetics



Low concentration = Few collisions High concentration = More collisions

Reaction rate tends to increase with concentration - a phenomenon explained by collision theory.

Chemical kinetics, also known as **reaction kinetics**, is the study of rates of chemical processes. Chemical kinetics includes investigations of how different experimental conditions can influence the speed of a chemical reaction and yield information about the reaction's mechanism and transition states, as well as the construction of mathematical models that can describe the characteristics of a chemical reaction. In 1864, Peter Waage and Cato Guldberg pioneered the development of chemical kinetics by formulating the law of mass action, which states that the speed of a chemical reaction is proportional to the quantity of the reacting substances.

Chemical kinetics deals with the experimental determination of reaction rates from which rate laws and rate constants are derived. Relatively simple rate laws exist for zero-order reactions (for which reaction rates are independent of concentration), first-order reactions, and second-order reactions, and can be derived for others. In consecutive reactions the rate-determining step often determines the kinetics. In consecutive first-order reactions, a steady state approximation can simplify the rate law. The activation energy for a reaction is experimentally determined through the Arrhenius equation and the Eyring equation. The main factors that influence the reaction rate include: the physical state of the reactants, the concentrations of the reactants, the temperature at which the reaction occurs, and whether or not any catalysts are present in the reaction.

Factors affecting reaction rate

Nature of the reactants

Depending upon what substances are reacting, the reaction rate varies. Acid/base reactions, the formation of salts, and ion exchange are fast reactions. When covalent bond formation takes place between the molecules and when large molecules are formed, the reactions tend to be very slow. Nature and strength of bonds in reactant molecules greatly influences the rate of its transformation into products. The reactions which involve lesser bond rearrangement proceed faster than the reactions which involve larger bond rearrangement.

Physical state

The physical state (solid, liquid, or gas) of a reactant is also an important factor of the rate of change. When reactants are in the same phase, as in aqueous solution, thermal motion brings them into contact. However, when they are in different phases, the reaction is limited to the interface between the reactants. Reaction can only occur at their area of contact, in the case of a liquid and a gas, at the surface of the liquid. Vigorous shaking and stirring may be needed to bring the reaction to completion. This means that the more finely divided a solid or liquid reactant, the greater its surface area per unit volume, and the more contact it makes with the other reactant, thus the faster the reaction. To make an analogy, for example, when one starts a fire, one uses wood chips and small branches—one doesn't start with large logs right away. In organic chemistry, On water reactions are the exception to the rule that homogeneous reactions take place faster than heterogeneous reactions.

Concentration

Concentration plays a very important role in reactions, because according to the collision theory of chemical reactions, molecules must collide in order to react together. As the concentration of the reactants increases, the frequency of the molecules colliding increases, striking each other more frequently by being in closer contact at any given point in time. Think of two reactants being in a closed container. All the molecules contained within are colliding constantly. By increasing the amount of one or more of the reactants it causes these collisions to happen more often, increasing the reaction rate.

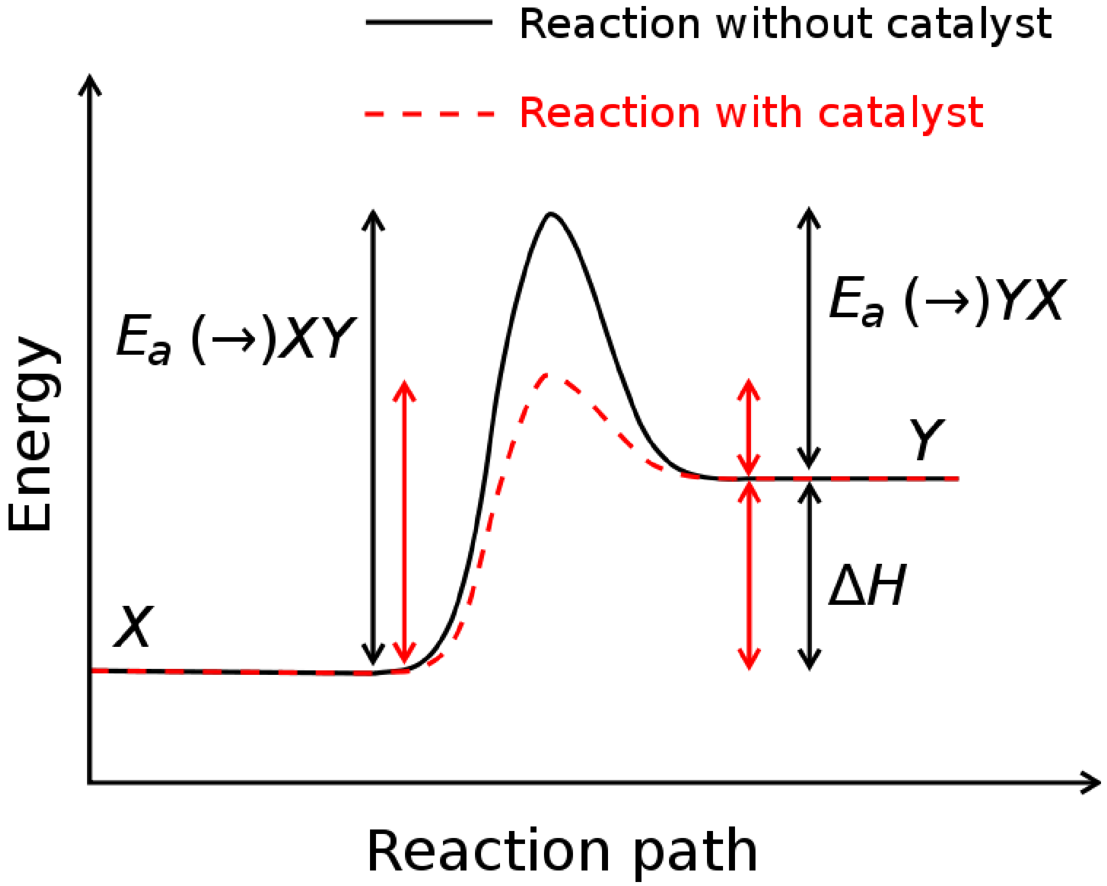
Temperature

Temperature usually has a major effect on the rate of a chemical reaction. Molecules at a higher temperature have more thermal energy. Although collision frequency is greater at higher temperatures, this alone contributes only a very small proportion to the increase in rate of reaction. Much more important is the fact that the proportion of reactant molecules with sufficient energy to react (energy greater than activation energy: $E > E_a$) is significantly higher and is explained in detail by the Maxwell–Boltzmann distribution of molecular energies.

The 'rule of thumb' that the rate of chemical reactions doubles for every 10 °C temperature rise is a common misconception. This may have been generalized from the special case of biological systems, where the Q_{10} (temperature coefficient) is often between 1.5 and 2.5.

A reaction's kinetics can also be studied with a temperature jump approach. This involves using a sharp rise in temperature and observing the relaxation rate of an equilibrium process.

Catalysts



Generic potential energy diagram showing the effect of a catalyst in an hypothetical endothermic chemical reaction. The presence of the catalyst opens a different reaction pathway (shown in red) with a lower activation energy. The final result and the overall thermodynamics are the same.

A catalyst is a substance that accelerates the rate of a chemical reaction but remains chemically unchanged afterwards. The catalyst increases rate reaction by providing a different reaction mechanism to occur with a lower activation energy. In autocatalysis a reaction product is itself a catalyst for that reaction leading to positive feedback. Proteins that act as catalysts in biochemical reactions are called enzymes. Michaelis-Menten kinetics describe the rate of enzyme mediated reactions. A catalyst does not affect the position of the equilibria, as the catalyst speeds up the backward and forward reactions equally.

In certain organic molecules, specific substituents can have an influence on reaction rate in neighbouring group participation.

Agitating or mixing a solution will also accelerate the rate of a chemical reaction, as this gives the particles greater kinetic energy, increasing the number of collisions between reactants and therefore the possibility of successful collisions.

Pressure

Increasing the pressure in a gaseous reaction will increase the number of collisions between reactants, increasing the rate of reaction. This is because the activity of a gas is directly proportional to the partial pressure of the gas. This is similar to the effect of increasing the concentration of a solution.

Equilibrium

While chemical kinetics is concerned with the rate of a chemical reaction, thermodynamics determines the extent to which reactions occur. In a reversible reaction, chemical equilibrium is reached when the rates of the forward and reverse reactions are equal and the concentrations of the reactants and products no longer change. This is demonstrated by, for example, the Haber–Bosch process for combining nitrogen and hydrogen to produce ammonia. Chemical clock reactions such as the Belousov–Zhabotinsky reaction demonstrate that component concentrations can oscillate for a long time before finally attaining the equilibrium.

Free energy

In general terms, the free energy change (ΔG) of a reaction determines whether a chemical change will take place, but kinetics describes how fast the reaction is. A reaction can be very exothermic and have a very positive entropy change but will not happen in practice if the reaction is too slow. If a reactant can produce two different products, the thermodynamically most stable one will generally form except in special circumstances when the reaction is said to be under kinetic reaction control. The Curtin–Hammett principle applies when determining the product ratio for two reactants interconverting rapidly, each going to a different product. It is possible to make predictions about reaction rate constants for a reaction from free-energy relationships.

The kinetic isotope effect is the difference in the rate of a chemical reaction when an atom in one of the reactants is replaced by one of its isotopes.

Chemical kinetics provides information on residence time and heat transfer in a chemical reactor in chemical engineering and the molar mass distribution in polymer chemistry.

Applications

The mathematical models that describe chemical reaction kinetics provide chemists and chemical engineers with tools to better understand and describe chemical processes such as food decomposition, microorganism growth, stratospheric ozone decomposition, and the complex chemistry of biological systems. These models can also be used in the design or modification of chemical reactors to optimize product yield, more efficiently separate products, and eliminate environmentally harmful by-products. When performing catalytic cracking of heavy hydrocarbons into gasoline and light gas, for example, kinetic models can be used to find the temperature and pressure at which the highest yield of heavy hydrocarbons into gasoline will occur.

Chapter- 3

Chemical Engineering

Process engineers design, construct and operate plants

Chemical engineering is the branch of engineering that deals with the application of physical science (e.g., chemistry and physics), and life sciences (e.g., biology, microbiology and biochemistry) with mathematics and economics, to the process of converting raw materials or chemicals into more useful or valuable forms. In addition to producing useful materials, modern chemical engineering is also concerned with pioneering valuable new materials and techniques - such as nanotechnology, fuel cells and biomedical engineering. Chemical engineering largely involves the design, improvement and maintenance of processes involving chemical or biological transformations for large-scale manufacture. Chemical engineers ensure the processes are operated safely, sustainably and economically. Chemical engineers in this branch are usually employed under the title of **process engineer**. A related term with a wider definition is chemical technology. A person employed in this field is called a chemical engineer.

Chemical engineering timeline

In 1824, French physicist Sadi Carnot, in his "On the Motive Power of Fire", was the first to study the thermodynamics of combustion reactions. In the 1850s, German physicist Rudolf Clausius began to apply the principles developed by Carnot to chemical systems at the atomic to molecular scale. During the years 1873 to 1876 at Yale University, American mathematical physicist Josiah Willard Gibbs, the first to be awarded a Ph.D. in engineering in the U.S., in a series of three papers, developed a mathematical-based, graphical methodology, for the study of chemical systems using the thermodynamics of Clausius. In 1882, German physicist Hermann von Helmholtz, published a founding thermodynamics paper, similar to Gibbs, but with more of an electro-chemical basis, in which he showed that measure of chemical affinity, i.e., the "force" of chemical reactions, is determined by the measure of the free energy of the reaction process. The following timeline shows some of the key steps in the development of the science of chemical engineering:

- **1805** – John Dalton published Atomic Weights, allowing chemical equations to be balanced and the basis for chemical engineering mass balances.
- **1882** – a course in "Chemical Technology" is offered at University College London
- **1883** – Osborne Reynolds defines the dimensionless group for fluid flow, leading to practical scale-up and understanding of flow, heat and mass transfer
- **1885** – Henry Edward Armstrong offers a course in "chemical engineering" at Central College (later Imperial College), London.
- **1888** – There is a Department of Chemical Engineering at Glasgow and West of Scotland Technical College offering day and evening classes.
- **1888** – Lewis M. Norton starts a new curriculum at Massachusetts Institute of Technology (MIT): Course X, Chemical Engineering
- **1889** – Rose Polytechnic Institute awards the first bachelor's of science in chemical engineering in the US.
- **1891** – MIT awards a bachelor's of science in chemical engineering to William Page Bryant and six other candidates.
- **1892** – A bachelor's program in chemical engineering is established at the University of Pennsylvania.

- **1898** – Bachelor of science program in chemical engineering is established at the University of Michigan.
- **1901** – George E. Davis produces the *Handbook of Chemical Engineering*
- **1905** – the University of Wisconsin awards the first Ph.D. in chemical engineering to Oliver Patterson Watts.
- **1908** – the American Institute of Chemical Engineers (AIChE) is founded.
- **1922** – the UK Institution of Chemical Engineers (IChemE) is founded.

Applications

Chemical engineering is applied in the manufacture of a wide variety of products. The chemical industry has a large scope, manufacturing inorganic and organic industrial chemicals, ceramics, fuels and petrochemicals, agrochemicals (fertilizers, insecticides, herbicides), plastics and elastomers, oleochemicals, explosives, detergents and detergent products (soap, shampoo, cleaning fluids), fragrances and flavors, additives, dietary supplements and pharmaceuticals. Closely allied or overlapping disciplines include wood processing, food processing, environmental technology, and the engineering of petroleum, glass, paints and other coatings, inks, sealants and adhesives. A variety of substances found in everyday life have been made under the supervision of a chemical engineer.Overview

Chemical engineers operate processes at plants, above is the image of processes at an industry control room

Chemical engineers design processes to ensure the most economical operation. This means that the entire production chain must be planned and controlled for costs. A chemical engineer can both simplify and complicate "showcase" reactions for an economic advantage. Using a lower pressure or temperature makes several reactions easier; ammonia, for example, is simply produced from its component elements in a high-pressure reactor. On the other hand, reactions with a low yield can be recycled continuously, which would be complex, arduous work if done by hand in the laboratory. It is not unusual to build 8-step, or even 10-step evaporators to reuse the vaporization energy for an economic advantage. In contrast, laboratory chemists evaporate samples in a single step.

The individual processes used by chemical engineers (e.g., distillation or filtration) are called unit operations and consist of chemical reactions, mass-, heat- and momentum-transfer operations. Unit operations are grouped together in various configurations for the purpose of chemical synthesis and/or chemical separation. Some processes are a combination of intertwined transport and separation unit operations, (e.g., reactive distillation).

Three primary physical laws underlying chemical engineering design are conservation of mass, conservation of momentum and conservation of energy. The movement of mass and energy around a chemical process are evaluated using mass balances and energy balances, laws that apply to discrete parts of equipment, unit operations, or an entire plant. In doing so, chemical engineers must also use principles of thermodynamics, reaction kinetics, fluid mechanics and transport phenomena. The task of performing these balances is now aided by process simulators, which are complex software models that can solve mass and energy balances and usually have built-in modules to simulate a variety of common unit operations.

Design

Chemical engineers design chemical production equipment and entire chemical plants:

- Piping and pump sizing and specification
- Chemical reactors
    - Continuous stirred-tank reactor
    - Plug flow reactor
    - Catalytic reactor
- Separation equipment
    - Distillation column
    - Extraction column
    - Evaporation
    - Filtering
    - Reverse osmosis
- Process Systems Engineering
    - Process control and instrumentation

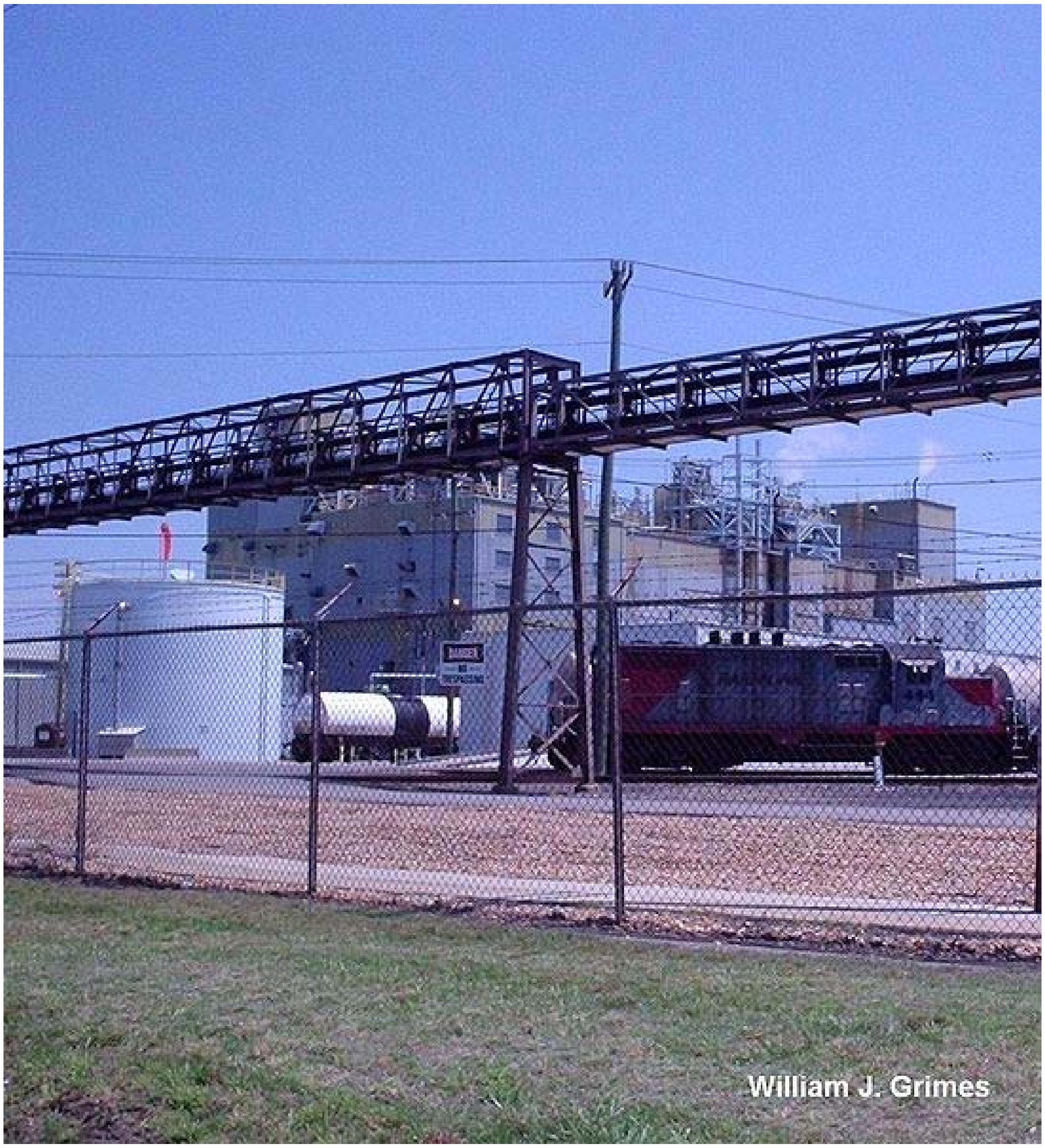
Design is worked through in a number of phases. With the process concept and intended chemical reactions in hand, a flowsheet is designed, which includes all material flows in the process, including not only starting materials and products, but all intermediates, wastes and unit operations. Preliminary design is done to approximate cost, space and environmental requirements to further evaluate the viability of the concept. Later stages require the design and specification of all parts and each piece of equipment in the process, and finally, cost calculation and project planning. Supervision of the work, testing, simulation follow. Running the process and its maintenance continues, with continual improvement, for the life of the process, followed by shutdown and cleanup of the site.

Modern chemical engineering

The modern discipline of chemical engineering encompasses much more than just process engineering. Chemical engineers are now engaged in the development and production of a diverse range of products, as well as in commodity and specialty chemicals. These products include high performance materials needed for aerospace, automotive, biomedical, electronic, environmental, space and military applications. Examples include ultra-strong fibers, fabrics, dye-sensitized solar cells, adhesives and composites for vehicles, bio-compatible materials for implants and prosthetics, gels for medical applications, pharmaceuticals, and films with special dielectric, optical or spectroscopic properties for opto-electronic devices. Additionally, chemical engineering is often intertwined with biology and biomedical engineering. Many chemical engineers work on biological projects such as understanding biopolymers (proteins) and mapping the human genome. The line between chemists and chemical engineers is growing ever more thin as more and more chemical engineers begin to start their own innovation using their knowledge of chemistry, physics and mathematics to create, implement and mass produce their ideas.

Chapter- 4

Chemical Plant



BASF Chemical Plant Portsmouth Site in the West Norfolk area of Portsmouth, Virginia, United States. The plant is served by the Commonwealth Railway.

A **chemical plant** is an industrial process plant that manufactures (or otherwise processes) chemicals, usually on a large scale. The general objective of a chemical plant is to create new material wealth via the chemical or biological transformation and or separation of materials. Chemical plants use special equipment, units, and technology in the processes. Other kinds of plants, such as polymer, pharmaceutical, food, and some beverage production facilities, power plants, oil refineries or other refineries, natural gas processing and biochemical plants, water and wastewater treatment, and pollution control equipment use many technologies which have similarities to chemical plant technology such as fluid systems. Some would consider an oil refinery or a pharmaceutical or polymer manufacturer to be effectively a chemical plant.

Petrochemical plants (plants using petroleum as a raw material) are usually located adjacent to an oil refinery to minimize transportation costs for the feedstocks produced by the refinery. Specialty chemical plants are usually much smaller and not as sensitive to location.

Chemical processes

Chemical plants typically use chemical processes, which are detailed industrial-scale methods, to produce the chemicals. The same chemical process can be used at more than one chemical plant, with possibly differently scaled capacities at each plant. Also, a chemical plant at a site may be constructed to utilize more than one chemical process.

A chemical plant commonly has usually large vessels or sections called **units** that are interconnected by piping or other material-moving equipment which can carry **streams** of material. Such material streams can include fluids (gas or liquid carried in piping) or sometimes solids or mixtures such as slurries. An overall chemical process is commonly made up of steps called unit operations which occur in the individual units. A raw material going into a chemical process or plant as input to be converted into a product is commonly called a **feedstock**, or simply **feed**. In addition to feedstocks for the plant as a whole, an input stream of material to be processed in a particular unit can similarly be considered feed for that unit. Output streams from the plant as a whole are final products and output streams from individual units may be considered intermediate products for their units. However, final products from one plant may be intermediate chemicals used as feedstock in another plant for further processing. For example, some products from an oil refinery may used as feedstock in petrochemical plants.

Either the feedstock(s), the product(s), or both may be individual compounds or mixtures. It is often not worthwhile separating the components in these mixtures completely based on product requirements and economics.

Continuous and batch operation

Chemical processes may be run in continuous or batch operation. In **batch** operation, production occurs in time-sequential steps in batches. A batch of feedstock(s) is fed into a process or unit, then the chemical process takes place, then the product(s) and any other outputs are removed. Such batch production may be repeated over again and again with new batches of feedstock. Batch operation is commonly used in smaller scale plants such as pharmaceutical or specialty chemicals production.

In **continuous** operation, all steps are ongoing continuously in time. During usual continuous operation, the feeding and product removal are ongoing streams of moving material, which together with the process itself, all take place simultaneously and continuously. Chemical plants or units in continuous operation are usually in a steady state or approximate steady state. Steady state means that quantities related to the process do not change as time passes during operation. Such constant quantities include stream flow rates, heating or cooling rates, temperatures, pressures, and chemical compositions at every point (location). Continuous operation is more efficient in many large scale operations like petroleum refineries. It is possible for some units to operate continuously and others be in batch operation in a chemical plant; for example, see Continuous distillation and Batch distillation. The amount of primary feedstock or product per unit of time which a plant or unit can process is referred to as the **capacity** of that plant or unit. For examples: the capacity of an oil refinery may be given in terms of barrels of crude oil refined per day; alternatively chemical plant capacity may be given in tons of product produced per day. In actual daily operation, a plant (or unit) will operate at a percentage of its full capacity.

Units and fluid systems

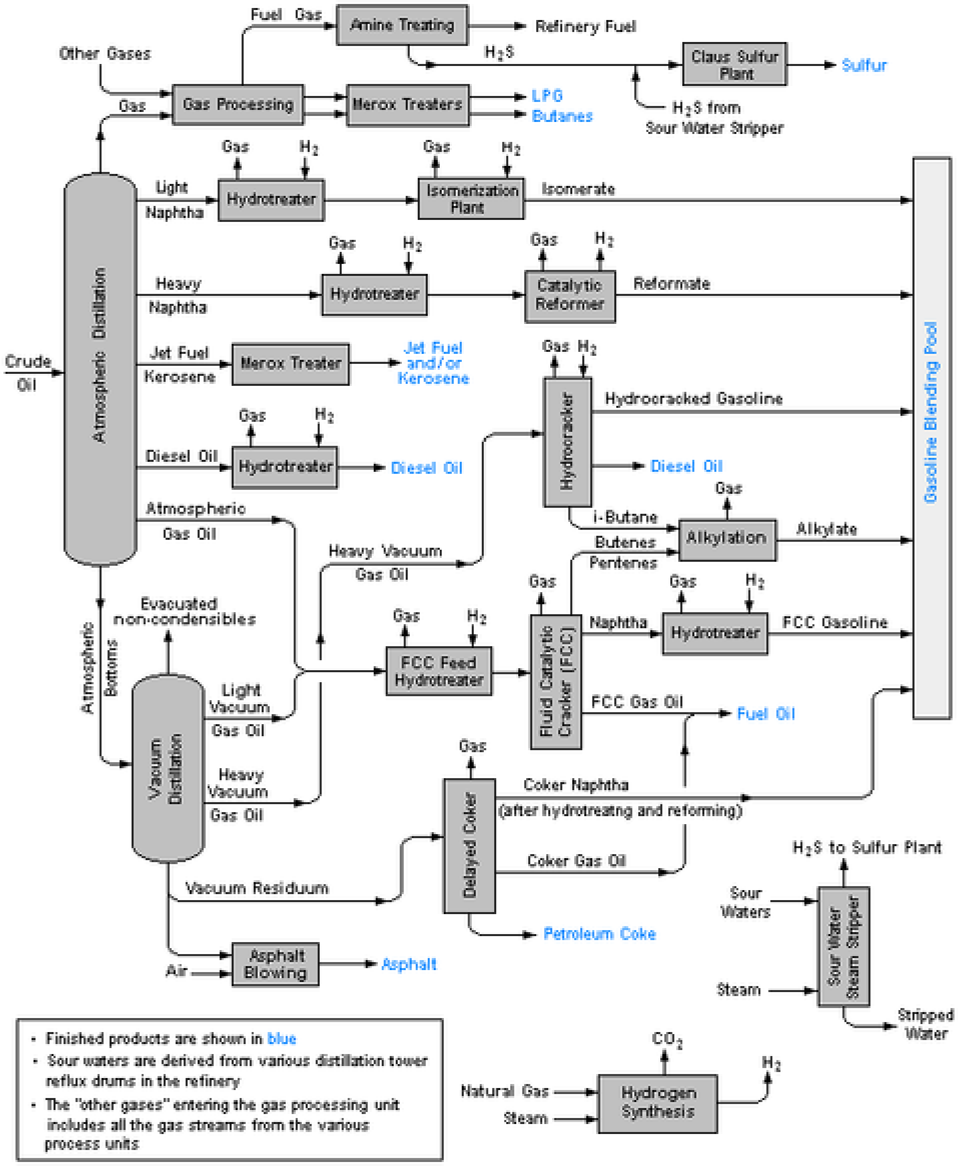
Various kinds of unit operations are conducted in various kinds of units. Although some units may operate at ambient temperature or pressure, many units operate at higher or lower temperatures or pressures. Vessels in chemical plants are often cylindrical with rounded ends, a shape which can be suited to hold either high pressure or vacuum. Chemical reactions can convert certain kinds of compounds into other compounds in chemical reactors. Chemical reactors may be packed beds and may have solid heterogeneous catalysts which stay in the reactors as fluids move through. Since the surface of solid heterogeneous catalysts may sometimes become poisoned from deposits such as coke, regeneration of catalysts may be necessary. Fluidized beds may also be used in some cases. There can also be units (or subunits) for mixing (including dissolving), separation, heating, cooling, or some combination of these. For example, chemical reactors often have stirring for mixing and heating or cooling going on in them. When designing plants on a large scale, heat produced or absorbed by chemical reactions should be considered. Some plants may have units with organism cultures for biochemical processes such as fermentation or enzyme production.

Distillation plant in Italy

Separation processes include filtration, settling (sedimentation), extraction or leaching, distillation, recrystallization or precipitation (followed by filtration or settling), reverse osmosis, drying, and adsorption. Heat exchangers are often used for heating or cooling, including boiling or condensation, often in conjunction with other units such as distillation towers. There may also be storage tanks for storing feedstock, intermediate or final products, or waste. Storage tanks commonly have level indicators to show how full they are. There may be structures holding or supporting sometimes massive units and their associated equipment. There are often stairs, ladders, or other steps for personnel to reach points in the units for sampling, inspection, or maintenance. An area of a plant or facility with numerous storage tanks is sometimes called a *tank farm*, especially at an oil depot.

Fluid systems for carrying liquids and gases include piping and tubing of various diameter sizes, various types of valves for controlling or stopping flow, pumps for moving or pressurizing liquid, and compressors for pressurizing or moving gases. Vessels, piping, tubing, and sometimes other equipment at high or very low temperature are commonly covered with insulation for personnel safety and to maintain temperature inside. Fluid systems and units commonly have instrumentation such as temperature and pressure sensors and flow measuring devices at select locations in a plant. Online analyzers for chemical or physical property analysis have become more common. Solvents can sometimes be used to dissolve reactants or materials such as solids for extraction or leaching, to provide a suitable medium for certain chemical reactions to run, or so they can otherwise be treated as fluids.

Chemical plant design



- Finished products are shown in blue
- Sour waters are derived from various distillation tower reflux drums in the refinery
- The "other gases" entering the gas processing unit includes all the gas streams from the various process units

Flow diagram for a typical oil refinery

The fundamental aspects of designing chemical plants are done by chemical engineers. In plant design, typically less than 1% of ideas for new designs ever become commercialized. During this solution process, typically, cost studies are used as an initial screening to eliminate unprofitable designs. If a process appears profitable, then other factors are considered, such as safety, environmental constraints, controllability, etc. The general goal in plant design, is to construct or synthesize “optimum designs” in the neighborhood of the desired constraints.

Many times chemists research chemical reactions or other chemical principles in a laboratory, commonly on a small scale in a "batch-type" experiment. Chemistry information obtained is then used by chemical engineers, along with expertise of their own, to convert to a chemical process and scale up the batch size or capacity. Commonly, a small chemical plant called a pilot plant is built to provide design and operating information before construction of a large plant. From data and operating experience obtained from the pilot plant, a scaled-up plant can be designed for higher or full capacity. After the fundamental aspects of a plant design are determined, mechanical or electrical engineers may become involved with mechanical or electrical details, respectively. Structural engineers may become involved in the plant design to ensure the structures can support the weight of the units, piping, and other equipment.

The units, streams, and fluid systems of chemical plants or processes can be represented by block flow diagrams which are very simplified diagrams, or process flow diagrams which are somewhat more detailed. The streams and other piping are shown as lines with arrow heads showing usual direction of material flow. In block diagrams, units are often simply shown as blocks. Process flow diagrams may use more detailed symbols and show pumps, compressors, and major valves. Likely values or ranges of material flow rates for the various streams are determined based on desired plant capacity using material balance calculations. Energy balances are also done based on heats of reaction, heat capacities, expected temperatures and pressures at various points to calculate amounts of heating and cooling needed in various places and to size heat exchangers. Chemical plant design can be shown in fuller detail in a piping and instrumentation diagram (P&ID) which shows all piping, tubing, valves, and instrumentation, typically with special symbols. Showing a full plant is often complicated in a P&ID, so often only individual units or specific fluid systems are shown in a single P&ID.

In the plant design, the units are sized for the maximum capacity each may have to handle. Similarly, sizes for pipes, pumps, compressors, and associated equipment are chosen for the flow capacity they have to handle. Utility systems such as electric power and water supply should also be included in the plant design. Additional piping lines for non-routine or alternate operating procedures, such as plant or unit startups and shutdowns, may have to be included. Fluid systems design commonly includes isolation valves around various units or parts of a plant so that a section of a plant could be isolated in case of a problem such as a leak in a unit. If pneumatically or hydraulically actuated valves are used, a system of pressurizing lines to the actuators are needed. Any points where process samples may have to be taken should have sampling lines, valves, and access to them included in the detailed design. If necessary, provisions should be made for reducing high pressure or temperature of a sampling stream, such including a pressure reducing valve or sample cooler.

Units and fluid systems in the plant including all vessels, piping, tubing, valves, pumps, compressors, and other equipment must be rated or designed to be able to withstand the entire range of pressures, temperatures, and other conditions which they could possibly encounter, including any appropriate safety factors. All such units and equipment should also be checked for materials compatibility to ensure they can withstand long-term exposure to the chemicals they will come in contact with. Any closed system in a plant which has a means of pressurizing possibly beyond the rating of its equipment, such as heating, exothermic reactions, or certain pumps or compressors, should have an appropriately sized pressure relief valve included to prevent overpressurization for safety. Frequently all of these parameters (temperatures, pressures, flow, etc.) are exhaustively analyzed in combination through a *Hazop* or *fault tree analysis*, to ensure that the plant has no known risk of serious hazard.

Within any constraints the plant is subject to, design parameters are optimized for good economic performance while ensuring safety and welfare of personnel and the surrounding community. For flexibility, a plant may be designed to operate in a range around some optimal design parameters in case feedstock or economic conditions change and re-optimization is desirable. In more modern times, computer simulations or other computer calculations have been used to help in chemical plant design or optimization.

Plant operation

Process control

In process control, information gathered automatically from various sensors or other devices in the plant is used to control various equipment for running the plant, thereby controlling operation of the plant. Instruments receiving such information signals and sending out control signals to perform this function automatically are process *controllers*. Previously, pneumatic controls were sometimes used. Electrical controls are now common. A plant often has a control room with displays of parameters such as key temperatures, pressures, fluid flow rates and levels, operating positions of key valves, pumps and other equipment, etc. In addition, operators in the control room can control various aspects of the plant operation, often including overriding automatic control. Process control with a computer represents more modern technology. Based on possible changing feedstock composition, changing products requirements or economics, or other changes in constraints, operating conditions may be re-optimized to maximize profit.

Workers

As in any industrial setting, there are a variety of workers working throughout a chemical plant facility, often organized into departments, sections, or other work groups. Such workers typically include engineers, plant operators, and maintenance technicians. Other personnel at the site could include chemists, management/administration and office workers. Types of engineers involved in operations or maintenance may include chemical process engineers, mechanical engineers for maintaining mechanical equipment, and electrical/computer engineers for electrical or computer equipment.

Transport

Large quantities of fluid feedstock or product may enter or leave a plant by pipeline, railroad tank car, or tanker truck. For example, petroleum commonly comes to a refinery by pipeline. Pipelines can also carry petrochemical feedstock from a refinery to a nearby petrochemical plant. Natural gas is a product which comes all the way from a natural gas processing plant to final consumers by pipeline or tubing. Large quantities of liquid feedstock are typically pumped into process units. Smaller quantities of feedstock or product may be shipped to or from a plant in drums. Use of drums about 55 gallons in capacity is common for packaging industrial quantities of chemicals. Smaller batches of feedstock may be added from drums or other containers to process units by workers.

Maintenance

In addition to feeding and operating the plant, and packaging or preparing the product for shipping, plant workers are needed for taking samples for routine and troubleshooting analysis and for performing routine and non-routine maintenance. Routine maintenance can include periodic inspections and replacement of worn catalyst, analyzer reagents, various sensors, or mechanical parts. Non-routine maintenance can include investigating problems and then fixing them, such as leaks, failure to meet feed or product specifications, mechanical failures of valves, pumps, compressors, sensors, etc.

Statutory and regulatory compliance

When working with chemicals, safety is a concern. In the United States, the law requires that employers provide workers working with chemicals with access to a Material Safety Data Sheet (MSDS) for every kind of chemical they work with. An MSDS for a certain chemical is prepared and provided by the supplier to whoever buys the chemical. Other laws covering chemical safety, hazardous waste, and pollution must be observed, including statutes such as the Resource Conservation and Recovery Act (RCRA) and the Toxic Substances Control Act (TSCA), and regulations such as the Chemical Facility Anti-Terrorism Standards in the United States. Hazmat (hazardous materials) teams are trained to deal with chemical leaks or spills. Process Hazard Analysis (PHA) is used to assess potential hazards in chemical plants. In 1998, the U. S. Chemical Safety and Hazard Investigation Board has become operational.

Plant facilities

The actual production or process part of a plant may be indoors, outdoors, or a combination of the two. The actual production section of a facility usually has the appearance of a rather industrial environment. Hard hats and work shoes are commonly worn. Floors and stairs are often made of metal grating, and there is practically no decoration. There may also be pollution control or waste treatment facilities or equipment. Sometimes existing plants may be expanded or modified based on changing economics, feedstock, or product needs. As in other production facilities, there may be shipping and receiving, and storage facilities. In addition, there are usually certain other facilities, typically indoors, to support production at the site.

Although some simple sample analysis may be able to be done by operations technicians in the plant area, a chemical plant typically has a laboratory where chemists analyze samples taken from the plant. Such analysis can include chemical analysis or determination of physical properties. Sample analysis can include routine quality control on feedstock coming into the plant, intermediate and final products to ensure quality specifications are met. Non-routine samples may be taken and analyzed for investigating plant process problems also. A larger chemical company often has a research laboratory for developing and testing products and processes where there may be pilot plants, but such a laboratory may be located at a site separate from the production plants.

A plant may also have a workshop or maintenance facility for repairs or keeping maintenance equipment. There is also typically some office space for engineers, management or administration, and perhaps for receiving visitors. The decorum there is commonly more typical of an office environment.

Corrosion and use of new materials

Corrosion in chemical process plants is a big issue that consumes billions of dollars yearly. Electrochemical corrosion of metals is pronounced in chemical process plants due to the presence of acid fumes and other electrolytic interactions. Recently, FRP (Fibre-reinforced plastic) is used as a material of construction. The British standard specification BS4994 is widely used for design and construction of the vessels, tanks, etc.

Chapter- 5

Chemical Industry

Oil refinery in Louisiana - an example of chemical industry

The **chemical industry** comprises the companies that produce industrial chemicals. Central to the modern world economy, it converts raw materials (oil, natural gas, air, water, metals, and minerals) into more than 70,000 different products.

Products

Polymers and plastics, especially polyethylene, polypropylene, polyvinyl chloride, polyethylene terephthalate, polystyrene and polycarbonate comprise about 80% of the industry's output worldwide. Chemicals are used to make a wide variety of consumer goods, as well as thousands inputs to agriculture, manufacturing, construction, and service industries. The chemical industry itself consumes 26 percent of its own output. Major industrial customers include rubber and plastic products, textiles, apparel, petroleum refining, pulp and paper, and primary metals. Chemicals is nearly a $3 trillion global enterprise, and the EU and U.S. chemical companies are the world's largest producers.

Product Category Breakdown

1928 《Future war and the German chemical industry》

Sales of the chemical business can be divided into a few broad categories, including basic chemicals (about 35 to 37 percent of the dollar output), life sciences (30 percent), specialty chemicals (20 to 25 percent) and consumer products (about 10 percent).

Basic chemicals, or "commodity chemicals" are a broad chemical category including polymers, bulk petrochemicals and intermediates, other derivatives and basic industrials, inorganic chemicals, and fertilizers. Typical growth rates for basic chemicals are about 0.5 to 0.7 times GDP. Product prices are generally less than fifty cents per pound. Polymers, the largest revenue segment at about 33 percent of the basic chemicals dollar value, includes all categories of plastics and man-made fibers. The major markets for plastics are packaging, followed by home construction, containers, appliances, pipe, transportation, toys, and games. The largest-volume polymer product, polyethylene (PE), is used mainly in packaging films and other markets such as milk bottles, containers, and pipe. Polyvinyl chloride (PVC), another large-volume product, is principally used to make pipe for construction markets as well as siding and, to a much smaller extent, transportation and packaging materials. Polypropylene (PP), similar in volume to PVC, is used in markets ranging from packaging, appliances, and containers to clothing and carpeting. Polystyrene (PS), another large-volume plastic, is used principally for appliances and packaging as well as toys and recreation. The leading man-made fibers include polyester, nylon, polypropylene, and acrylics, with applications including apparel, home furnishings, and other industrial and consumer use. The principal raw materials for polymers are bulk petrochemicals.

Chemicals in the bulk petrochemicals and intermediates are primarily made from liquefied petroleum gas (LPG), natural gas, and crude oil. Their sales volume is close to 30 percent of overall basic chemicals. Typical large-volume products include ethylene, propylene, benzene, toluene, xylenes, methanol, vinyl chloride monomer (VCM), styrene, butadiene, and ethylene oxide. These chemicals are the starting points for most polymers and other organic chemicals as well as much of the specialty chemicals category.

Other derivatives and basic industrials include synthetic rubber, surfactants, dyes and pigments, turpentine, resins, carbon black, explosives, and rubber products and contribute about 20 percent of the basic chemicals' external sales. Inorganic chemicals (about 12 percent of the revenue output) make up the oldest of the chemical categories. Products include salt, chlorine, caustic soda, soda ash, acids (such as nitric, phosphoric, and sulfuric), titanium dioxide, and hydrogen peroxide. Fertilizers are the smallest category (about 6 percent) and include phosphates, ammonia, and potash chemicals.

Life sciences (about 30 percent of the dollar output of the chemistry business) include differentiated chemical and biological substances, pharmaceuticals, diagnostics, animal health products, vitamins, and pesticides. While much smaller in volume than other chemical sectors, their products tend to have very high prices—over ten dollars per pound—growth rates of 1.5 to 6 times GDP, and research and development spending at 15 to 25 percent of sales. Life science products are usually produced with very high specifications and are closely scrutinized by government agencies such as the Food and Drug Administration. Pesticides, also called "crop protection chemicals", are about 10 percent of this category and include herbicides, insecticides, and fungicides.

Specialty chemicals are a category of relatively high valued, rapidly growing chemicals with diverse end product markets. Typical growth rates are one to three times GDP with prices over a dollar per pound. They are generally characterized by their innovative aspects. Products are sold for what they can do rather than for what chemicals they contain. Products include electronic chemicals, industrial gases, adhesives and sealants as well as coatings, industrial and institutional cleaning chemicals, and catalysts. Coatings make up about 15 percent of specialty chemicals sales, with other products ranging from 10 to 13 percent.

Specialty Chemicals are sometimes referred to as "fine chemicals"

Consumer products include direct product sale of chemicals such as soaps, detergents, and cosmetics. Typical growth rates are 0.8 to 1.0 times GDP.

Every year, the American Chemistry Council tabulates the U.S. production of the top 100 basic chemicals. In 2000, the aggregate production of the top 100 chemicals totalled 502 million tons, up from 397 million tons in 1990. Inorganic chemicals tend to be the largest volume, though much smaller in dollar revenue terms due to their low prices. The top 11 of the 100 chemicals in 2000 were sulfuric acid (44 million tons), nitrogen (34), ethylene (28), oxygen (27), lime (22), ammonia (17), propylene (16), polyethylene (15), chlorine (13), phosphoric acid (13) and diammonium phosphates (12).

Companies

The largest corporate producers worldwide, with plants in numerous countries, are BASF, Dow, Degussa, Eastman Chemical Company, PPG Industries, Shell, Bayer, INEOS, ExxonMobil, DuPont, SABIC, Braskem and Mitsubishi, along with thousands of smaller firms.

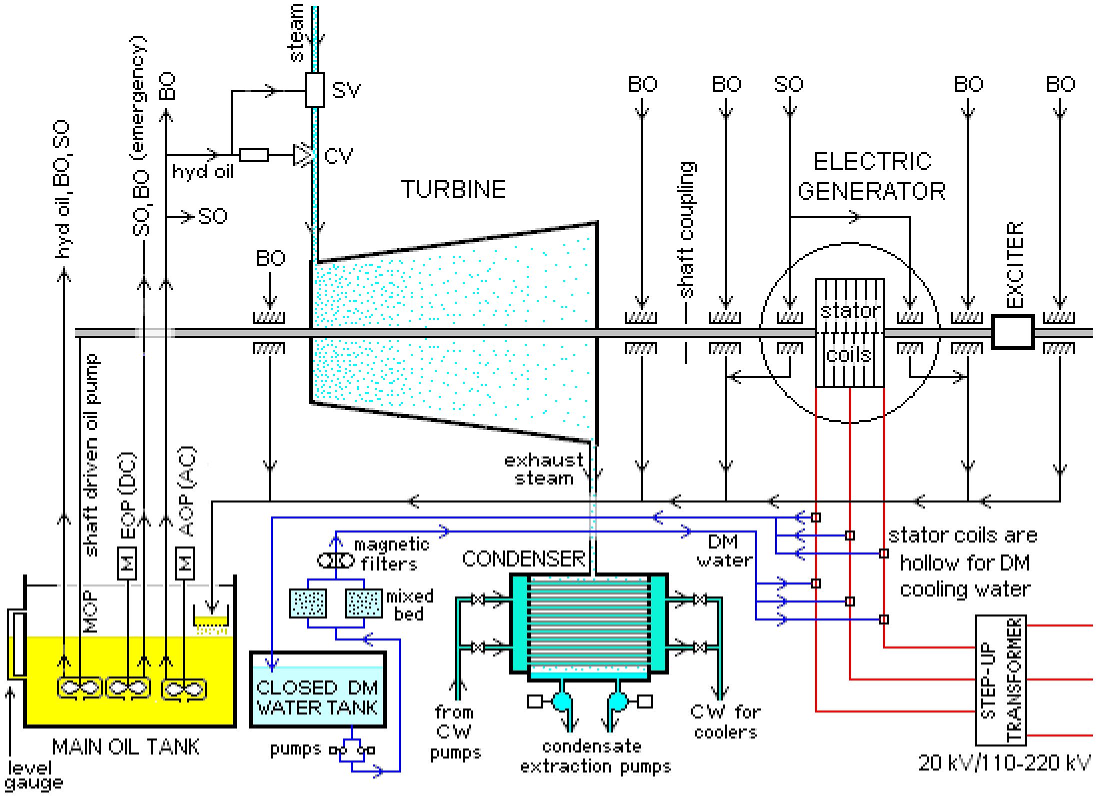
In the U.S. there are 170 major chemical companies. They operate internationally with more than 2,800 facilities outside the U.S. and 1,700 foreign subsidiaries or affiliates operating. The U.S. chemical output is $400 billion a year. The U.S. industry records large trade surpluses and employs more than a million people in the United States alone. The chemical industry is also the second largest consumer of energy in manufacturing and spends over $5 billion annually on pollution abatement.

In Europe, especially Germany, the chemical, plastics and rubber sectors are among the largest industrial sectors. Together they generate about 3.2 million jobs in more than 60,000 companies. Since 2000 the chemical sector alone has represented 2/3 of the entire manufacturing trade surplus of the EU. The chemical sector accounts for 12% of the EU manufacturing industry's added value.

The chemical industry has shown rapid growth for more than fifty years. The fastest growing areas have been in the manufacture of synthetic organic polymers used as plastics, fibres and elastomers. Historically and presently the chemical industry has been concentrated in three areas of the world, Western Europe, North America and Japan (the Triad). The European Community remains the largest producer area followed by the USA and Japan.

The traditional dominance of chemical production by the Triad countries is being challenged by changes in feedstock availability and price, labour cost, energy cost, differential rates of economic growth and environmental pressures. Instrumental in the changing structure of the global chemical industry has been the growth in China, India, Korea, the Middle East, South East Asia, Nigeria, and Brazil.

Turbine generator systems



SO-seal oil; BO-bearing oil; hyd oil-hydraulic oil; SV-stop valve; CV-control valve;
MOP-main oil pump; EOP-emergency oil pump; AOP-auxiliary oil pump; M - motor
CW-circulating water; DM-demineralised (water); DC - direct current; AC - alternating current

This is a process diagram of a turbine generator. Knowing how to design a sustainable process in which the system can withstand or manipulate process halting conditions such as; heat, fiction, pressure, emissions, contaminants, is essential for engineers working to produce a sustainable process for use in the chemical industry.

As accepted by chemical engineers, the chemical industry involves the use of chemical processes such as chemical reactions and refining methods to produce a wide variety of solid, liquid, and gaseous materials. Most of these products are used in manufacture of other items, although a smaller number are used directly by consumers. Solvents, pesticides, lye, washing soda, and portland cement are a few examples of product used by consumers. The industry includes manufacturers of inorganic- and organic-industrial chemicals, ceramic products, petrochemicals, agrochemicals, polymers and rubber (elastomers), oleochemicals (oils, fats, and waxes), explosives, fragrances and flavors. Examples of these products are shown in the Table below.

The novel chemical reactor reduces the amount of solvents used from 1000 litres to just 4 litres.

Product Type	Examples
inorganic industrial	ammonia, nitrogen, sodium hydroxide, sulfuric acid, nitric acid
organic industrial	acrylonitrile, phenol, ethylene oxide, urea
ceramic products	silica brick, frit
petrochemicals	ethylene, propylene, benzene, styrene
agrochemicals	fertilizers, insecticides, herbicides
polymers	polyethylene, Bakelite, polyester
elastomers	polyisoprene, neoprene, polyurethane
oleochemicals	lard, soybean oil, stearic acid
explosives	nitroglycerin, ammonium nitrate, nitrocellulose

fragrances and flavors benzyl benzoate, coumarin, vanillin

Although the pharmaceutical industry is often considered a **chemical industry** , it has many different characteristics that puts it in a separate category. Other closely related industries include petroleum, glass, paint, ink, sealant, adhesive, and food processing manufacturers.

Chemical processes such as chemical reactions are used in chemical plants to form new substances in various types of reaction vessels. In many cases the reactions are conducted in special corrosion resistant equipment at elevated temperatures and pressures with the use of catalysts. The products of these reactions are separated using a variety of techniques including distillation especially fractional distillation, precipitation, crystallization, adsorption, filtration, sublimation, and drying. The processes and product or products are usually tested during and after manufacture by dedicated instruments and on-site quality control laboratories to ensure safe operation and to assure that the product will meet required specifications. The products are packaged and delivered by many methods, including pipelines, tank-cars, and tank-trucks (for both solids and liquids), cylinders, drums, bottles, and boxes. Chemical companies often have a research and development laboratory for developing and testing products and processes. These facilities may include pilot plants, and such research facilities may be located at a site separate from the production plant(s).

History

Chandler (2005) argues the relative success or failure of American and European chemical companies is explained with reference to three themes: "barriers to entry," "strategic boundaries," and "limits to growth." He says successful chemical firms followed definite "paths of learning" whereby first movers and close followers created entry barriers to would-be rivals by building "integrated learning bases" (or organizational capabilities) which enabled them to develop, produce, distribute, and sell in local and then worldwide markets. Also they followed a "virtuous strategy" of reinvestment of retained earnings and growth through diversification, particularly to utilize "dynamic" scale and scope economies relating to new learning in launching "next generation" products.

Companies in the 21st century

The chemical industry includes large, medium, and small companies located worldwide. Companies with sales of chemical products greater than $10 billion dollars in fiscal year 2007 appear listed below. For some of these companies the chemical sales might represent only a portion of their total sales; (for example ExxonMobil's chemical sales covered only 8.7 percent of their total sales in 2005).

COMPANY, HEADQUARTERS	2007 Chemical Sales, billions	Rank	Country
BASF SE, Ludwigshafen, Germany	$65.3	1	🇩🇪
Dow Chemical, Midland, Michigan, USA	$53.5	2	🇺🇸
INEOS, Lyndhurst, UK	$43.6	3	🇬🇧
LyondellBasell, Houston, Texas, USA	$42.8	4	🇺🇸
Formosa Plastics, Taiwan	$31.9	5	🇹🇼
DuPont, Wilmington, Delaware, USA	$28.5	6	🇺🇸
Saudi Basic Industries Corporation, Riyadh, Saudi Arabia	$26.4	7	🇸🇦
Bayer, AG, Leverkusen, Germany	$24.2	8	🇩🇪
Mitsubishi Chemical, Tokyo, Japan	$22.2	9	🇯🇵
Akzo Nobel/Imperial Chemical Industries(ICI), Amsterdam/London	$19.9	10	🇳🇱🇬🇧
Air Liquide, Paris, France	$16.3	11	🇫🇷
Sumitomo Chemical, Tokyo, Japan	$15.2	12	🇯🇵
Evonik Industries, AG, Essen, Germany	$15.0	13	🇩🇪
Mitsui Chemicals, Tokyo, Japan	$14.3	14	🇯🇵
Asahi Kasei, Tokyo, Japan	$13.8	15	🇯🇵
Toray Industries, Tokyo, Japan	$13.1	16	🇯🇵
Chevron Phillips, The Woodlands, Texas, USA	$12.5	17	🇺🇸
DSM NV, Heerlen, Netherlands	$12.1	18	🇳🇱
PPG Industries, Pittsburgh, Pennsylvania, USA	$11.2	19	🇺🇸
Shin-Etsu Chemical Co., Ltd., Tokyo, Japan	$11.1	20	🇯🇵

Just as companies emerge as the main producers of the chemical industry, we can also look on a more global scale to how industrialized countries rank, with regards to the billions of dollars worth of production a country or region could export. Though the business of chemistry is worldwide in scope, the bulk of the world's $3.7 trillion chemical output is accounted for by only a handful of industrialized nations. The United States alone produced $689 billion, 18.6 percent of the total world chemical output in 2008.

Global Chemical Shipments by Country/Region (billions of dollars)	1998	1999	2000	2001	2002	2003	2004	2005	2006	2008	2009
United States of America	416.7	420.3	449.2	438.4	462.5	487.7	540.9	610.9	657.7	664.1	689.3
Canada	21.1	21.8	25.0	24.8	25.8	30.5	36.2	40.2	43.7	45.4	47.4
Mexico	19.1	21.0	23.8	24.4	24.3	23.5	25.6	29.2	32.0	33.4	37.8
North America	**456.9**	**463.1**	**498.0**	**487.6**	**512.6**	**541.7**	**602.7**	**680.3**	**733.4**	**742.8**	**774.6**

Brazil	46.5	40.0	45.7	41.5	39.6	47.4	60.2	71.1	82.8	96.4	126.7
Other	59.2	58.1	60.8	63.4	58.6	62.9	69.9	77.2	84.6	89.5	102.1
Latin America	**105.7**	**98.1**	**106.5**	**104.9**	**98.2**	**110.3**	**130.0**	**148.3**	**167.4**	**185.9**	**228.8**
France	79.1	78.5	76.5	76.8	80.5	99.6	111.1	117.5	121.3	138.4	158.9
Germany	124.9	123.2	118.9	116.1	120.1	148.1	168.6	178.6	192.5	229.5	263.2
Italy	63.9	64.6	59.5	58.6	64.5	75.8	86.6	89.8	95.3	105.9	122.9
United Kingdom	70.3	70.1	66.8	66.4	69.9	77.3	91.3	95.2	107.8	118.2	123.4
Belgium	27.1	27.0	27.5	27.1	28.7	36.1	41.8	43.5	46.9	51.6	62.6
Ireland	16.9	20.1	22.6	22.9	29.1	32.3	33.9	34.9	37.5	46.0	54.8
Netherlands	29.7	29.4	31.3	30.6	32.2	40.1	49.0	52.7	59.2	67.9	81.7
Spain	31.0	30.8	30.8	31.9	33.4	42.0	48.9	52.7	56.7	63.7	74.8
Sweden	11.1	11.4	11.2	11.0	12.5	15.9	18.2	19.3	21.2	21.2	22.6
Switzerland	22.1	22.2	19.4	21.1	25.5	30.3	33.8	35.4	37.8	42.7	53.1
Other	27.1	26.8	25.9	26.4	27.9	33.5	38.6	42.9	46.2	50.3	58.9
Western Europe	**503.1**	**504.0**	**490.4**	**488.8**	**524.4**	**630.9**	**721.9**	**762.7**	**822.4**	**935.4**	**1,076.8**
Russia	23.8	24.6	27.4	29.1	30.3	33.4	37.5	40.9	53.1	63.0	77.6
Other	22.3	20.3	21.9	23.4	25.3	31.4	39.6	46.2	55.0	68.4	87.5
Central/Eastern Europe	**46.1**	**44.9**	**49.3**	**52.5**	**55.6**	**64.8**	**77.1**	**87.1**	**108.0**	**131.3**	**165.1**
Africa & Middle East	**52.7**	**53.2**	**59.2**	**57.4**	**60.4**	**73.0**	**86.4**	**99.3**	**109.6**	**124.2**	**160.4**
Japan	193.8	220.4	239.7	208.3	197.2	218.8	243.6	251.3	248.5	245.4	298.0
Asia-Pacific excluding Japan	215.2	241.9	276.1	271.5	300.5	369.1	463.9	567.5	668.8	795.5	993.2
China	80.9	87.8	103.6	111.0	126.5	159.9	205.0	269.0	331.4	406.4	549.4

India	30.7	35.3	35.3	32.5	33.5	40.8	53.3	63.6	72.5	91.1	98.2
Australia	11.3	12.1	11.2	10.8	11.3	14.9	17.0	18.7	19.1	22.8	27.1
Korea	39.3	45.5	56.3	50.4	54.9	64.4	78.7	91.9	103.4	116.7	133.2
Singapore	6.3	8.5	9.5	9.4	12.5	16.1	20.0	22.0	25.8	28.9	31.6
Taiwan	21.9	23.7	29.2	26.8	28.4	34.3	44.5	49.5	53.8	57.4	62.9
Other Asia/Pacific	24.8	29.1	30.9	30.8	33.3	38.8	45.5	52.9	62.9	72.2	90.8
Asia/Pacific	**409.0**	**462.3**	**515.7**	**479.7**	**497.7**	**587.8**	**707.5**	**818.8**	**917.3**	**1041.0**	**1291.2**
Total world shipments	**1573.5**	**1625.5**	**1719.0**	**1670.9**	**1748.8**	**2008.5**	**2325.6**	**2596.4**	**2858.1**	**3160.7**	**3696.8**

Chapter- 6

FRP Tanks and Vessels

FRP (Fibreglass Reinforced Plastics, also known as GRP, or Glass Reinforced Plastics) is a modern composite material of construction for chemical plant equipment like tanks and vessels. Chemical equipment that range in size from less than a metre to 20 metres are fabricated using FRP as material of construction.

FRP Chemical Equipments are manufactured mainly by Hand Lay-up and filament winding processes. BS4994 still remains a key standard for this class of items.

Dual Laminate

Due to the corrosion resistant nature of FRP, the tank can be made entirely from the composite, or a second liner can be used. In either case, the inner liner is made using different material properties than the structural portion (Hence the name dual (meaning two) and laminate (a word commonly used for a layer of a composite material))

The liner, if made of FRP is usually resin rich and utilizes a different type of glass, called "C-Glass", while the structural portion uses "E-Glass". The thermoplastic liner is usually 2.3 mm thick (100 mils). This thermoplastic liner is not considered to contribute mechanical strength. The FRP liner is usually cured before winding or lay-up continues, by using either a BPO/DMA system, or using an MEKP catalyst with cobalt in the resin.

If the liner is not made of FRP, there are multiple choices for a thermoplastic liner. The engineer will need to design the tank based on the chemical corrosion requirement of the equipment. PP, PVC, PTFE, ECTFE, ETFE, FEP, CPVC, PVDF are used as common thermoplastic liners.

Due to FRP's weakness to buckling, but immense strength against tensile forces and its resistance to corrosion, a hydrostatic tank is a logical application for the composite. The tank is designed to withstand the hydrostatic forces required by orienting the fibres in the tangential direction. This increases the hoop strength, making the tanks anisotropically stronger than steel (pound per pound).

FRP which is constructed over the liner provides the structural strength requirements to withstand design conditions such as internal pressure or vacuum, hydrostatic loads, seismic loads (including fluid sloshing), wind loads, regeneration hydrostatic loads, and even snow loads.

Applications

FRP tanks and vessels designed as per BS 4994 are widely used in the chemical industry in the following sectors: chlor-alkali manufacturers, fertilizer, wood pulp and paper, metal extraction, refining, electroplating, brine, vinegar, food processing, and in air pollution control equipment, especially at municipal waste water treatment plants and water treatment plants.

Types

FRP Vessels and Tanks are used in multiple applications, requiring a strong, corrosion resistant environment.

Scrubbers

FRP Scrubbers are used for scrubbing fluids. In air pollution control technology, scrubbers come in three varieties, Dry Media, Wet Media, and Biological.

Dry Media

Dry media typically involved a dry, solid media (such as activated carbon) suspended in the middle of the vessel on a system of beam supports and grating. The media controls the concentration of a pollutant in the incoming gas via adsorption and absorption.

These vessels have several design constraints. They must be designed for

- Unloading and Reloading the media
- Corrosive effects of the fluid to be treated
- Internal and External Pressure
- Environmental Loads
- Support Loads for the grating and support system
- Lifting and Installing the Vessel
- Regenerating the media inside the vessel
- Internal Stack supports for a dual bed construction
- Redundancy for preventative maintenance
- Demisting to remove liquids that degrade the dry media
- Condensate removal, to remove any liquid that condenses inside the vessel

Wet media

Wet media scrubbers typically douse the polluted fluid in a scrubbing solution. These vessels must be designed to more stringent criteria. The design constraints for wet media scrubbers typically include:

- The corrosive effects of the polluted fluid and the scrubbing solution.
- The high pressures and loading of a spray system
- Aerodynamics of the internal media to ensure that there is no bypass
- Internal Support systems
- Reservoir of scrubbing fluid for recirculation.
- Internal and External Pressure
- Environmental Loads
- Lifting and Installing the vessel
- Plumbing of the scrubbing fluid to the vessel
- Draining to remove vessel sump fluids

In the case of a *decarbonator*, used in reverse osmosis systems to limit the concentration of gases in the water, the air is the scrubbing fluid and the sprayed liquid is the polluted stream. As the water is sprayed out of the scrubber, the air strips the aqueous gasses out of the water, to be treated in another vessel.

Biological

Biological scrubbers are structurally identical to the wet media scrubbers, but vary in their design. The vessel is designed to be larger, so the air moves slower through the vessel. The media is designed to encourage biological growth, and the water that sprays through the vessel is filled with nutrients to encourage bacteria to grow. In such scrubbers, the bacteria scrub the pollutant. Also, instead of a single, large support system (typically 10 feet depth of media for chemical scrubbers), there are multiple stages of media support, that can change the design requirements of the vessel.

Tanks

A typical storage tank made of FRP has an inlet, an outlet, a vent, an access port, a drain, and an overflow nozzle. However, there are other features that can be included in the tank. Ladders on the outside allow for easy access to the roof for loading. The vessel must be designed to withstand the load of someone standing on these ladders, and even withstand a person standing on the roof. Sloped bottoms allow for easier draining. Level gauges allow someone to accurately read the liquid level in the tank. The vessel must be resistant to the corrosive nature of the fluid it contains. Typically, these vessels have a secondary containment structure, in case the vessel bursts.

Size

The size of FRP Vessels is rarely limited by manufacturing technology, but rather by economics. Tanks smaller than 7,500 liters (2,000 gallons) are easily manufactured out of cheaper materials, such as HDPE or PVC. Tanks larger than four meters are generally limited by shipping constraints, and the economics suggest a concrete or steel tank fabricated at the tank's location.

For chemical storage and air pollution control, the choice is to make multiple tanks of smaller diameters. For example, one of the largest odor control projects in California, the Orange County Sanitation District will utilize 24 vessels total to treat 188,300 cfm (86,200 L/s) of odorous air, with a design of up to 50 ppm of hydrogen sulfide. For an equivalent single vessel to perform as well as the 13 headworks trickling filters, the single vessel would have to be over 36 feet in diameter. This would be impractical due to the high shipping requirements, internal supports, spray nozzles and other internals. Plus this single vessel would not incorporate redundancy for preventive maintenance.

Limitations

Typical FRP temperature limits are almost entirely based on the resin. The thermoplastic resin will suffer from creep at elevated temperatures and ultimately fail. However, new chemistry has produced resins that claim to be able to achieve even higher temperatures, which expand this field immensely. The typical maximum is 110 degrees celsius.

Design standards

GRP Tanks fall under regulation of several groups.

- Bs4994-87 is the British Standards Standard for FRP Tanks and Vessels
- ASME RTP-1 (Reinforced Thermoset Plastic Corrosion Resistant Equipment) is the standard for FRP tanks and vessels held within the United States under 15 psig and located partially or fully above ground. Typical design parameters and specifications will require either compliance with ASME RTP-1 or accreditation from ASME.
- ASTM 3299 which is only a product specification, governs the filament winding process for tanks. It is not a design standard

Bs4994

It is to avoid the uncertainty associated with specifying the thickness alone, that BS4994 introduced the concept of "unit properties". It is property per unit width, per unit mass of reinforcement. For example, UNIT STRENGTH is defined as load in Newton per millimeter (of laminate width) for a layer consisting of 1 kg of glass per square meter. i.e. the unit is N/mm per Kg/m2 glass

ASME RTP-1

In RTP-1 specifications, the primary concerns relate stress and strain, such as hoop stress, axial stress, and breaking stress to the physical properties of the material, such as Young's modulus (which may require an anisotropic analysis due to the filament winding process). These are related to the loads of the design, such as the internal pressure and strain.

BS EN 13121

All are afraid of this new standard emerged as a new version of BS4994. This standard is famous for complications and now all from the industry is trying to get BS4994 restored. This standard was reviewed by industry worldwide and all feel that it is very complicated, unintelligible, incomprehensible, not understandable, giving rise to uncertainties, source of formulae unknown, many errors and inconsistencies. This damaged the credibility of code.

A number of talented engineers have set out to investigate this standard and their conclusion: Errors; no idea where some formulae originated; very complicated. One such analysis produced a list of forty two (42) errors or inconsistencies.

GRP tank making industry lobbied BSI to have EN13121 withdrawn and BS4994 reinstated. BS4994 is now again reinstated to "current" status and is now live.

Chapter- 7

Abrasive Blasting

Sandblasting a stone wall

Diesel powered compressor used as an air supply for sandblasting

A corrosion pit on the outside wall of a pipeline at a coating defect before and after abrasive blasting.

Abrasive blasting is the operation of forcibly propelling a stream of abrasive material against a surface under high pressure to smooth a rough surface, roughen a smooth surface, shape a surface, or remove surface contaminants. The first abrasive blasting process was patented by Benjamin Chew Tilghman on October 18, 1870.

There are several variants of the process, such as bead blasting, sandblasting, and sodablasting.

Operations

Abrasive blasting is a method of propelling abrasive using a pressurized fluid (typically air) or centrifugal wheel. Common nomenclature for abrasive blasting include bead blasting, sandblasting, and sodablasting. Sometimes, people will lump water jetting (pressurized water) with abrasive injection into the category of abrasive blasting.

Bead blasting

Bead blasting is the process of removing surface deposits by applying fine glass beads at a high pressure without damaging the surface.

It is used to clean calcium deposits from pool tiles or any other surfaces, and removes embedded fungus and brightens grout color. This process is notably used as an efficiently popular way to clean tile surfaces in swimming pools. It is also used in auto body work to remove paint.

Wheel blasting

In wheel blasting, a wheel uses centrifugal force to propel the abrasive against the substrate. It is typically categorized as an airless blasting operation because there is no propellant (gas or liquid) used. A wheel machine is a high-power, high-efficiency blasting operation with recyclable abrasive (typically steel or stainless steel shot, cut wire, grit or similar sized pellets). Specialized wheel blast machines propel plastic abrasive in a cryogenic chamber, and is usually used for deflashing plastic and rubber components. The size of the wheel blast machine, and the number and power of the wheels vary considerably depending on the parts to be blasted as well as on the expected result and efficiency. The first blast wheel was patented by Wheelabrator in 1932.

Hydro-blasting

Hydro-blasting, commonly known as water blasting, is popular because it usually requires only one operator. In hydro-blasting, a highly pressured stream of water is used to remove old paint, chemicals, or buildup without damaging the original surface. This method is ideal for cleaning internal and external surfaces because the operator is generally able to send the stream of water into places that are difficult to reach using other methods. Another benefit of hydro-blasting is the ability to recapture and reuse the water, reducing waste and the impact on the environment.

Micro-abrasive blasting

Micronblaster dual pen micron sandblaster.

Micro-abrasive blasting is dry abrasive blasting process that uses small nozzles (typically 0.25 mm to 1.5 mm diameter) to deliver a fine stream of abrasive accurately to a small part or a small area on a larger part. Generally the area to be blasted is from about 1 mm^2 to only a few cm^2 at most. Also known as pencil blasting, the fine jet of abrasive is accurate enough to write directly on glass and delicate enough to cut a pattern in an eggshell. The abrasive media particle sizes range from 10 micrometres up to about 150 micrometres. Higher pressures are often required. The abrasive media is generally not recycled, since the particles tend to shatter on impact or lose their sharp edges.

The most common micro-abrasive blasting systems are commercial bench-mounted units consisting of a power supply and mixer, exhaust hood, nozzle and gas supply. The nozzle can be hand-held or fixture mounted for automatic operation. Either the nozzle or part can be moved in automatic operation.

Automated blasting

A fully automated blasting system usually includes contained surface preparation and coating applications.

Dry ice blasting

In this type of blasting air and dry ice are used and with the help of a huge mass and air pressure the parent material is cleaned without destroying the properties of the parent material. It is also very cost effective.

Equipment

Device used for adding sand to the compressed air (top of which is a sieve for adding the sand)

Portable blast equipment

Mobile dry abrasive blast systems, are typically powered by a diesel air compressor. The air compressor provides a large volumes of high pressure air to a single or multiple "blast pots". Blast pots are pressurized, tank like containers, filled with abrasive material, used to allow an adjustable amount of blasting grit into the main blasting line. The number of blast pots is dictated by the volume of air the compressor can provide. Fully equipped blast systems are often found mounted on semi-tractor trailers, offering high mobility and easy transport from site to site.

In wet blasting, the abrasive is introduced into a pressurized stream of water or other liquid, creating a slurry. Wet blasting is often used in applications where the minimal dust generation is desired. Portable applications may or may not recycle the abrasive.

Blast cabinet

A sand blasting cabinet

A blast cabinet is essentially a closed loop system that allows the operator to blast the part and recycle the abrasive. It usually consists of four components; the containment (cabinet), the abrasive blasting system, the abrasive recycling system and the dust collection. The operator blasts the parts from the outside of the cabinet by placing his arms in gloves attached to glove holes on the cabinet, viewing the part through a view window, turning the blast on and off using a foot pedal or treadle. Automated blast cabinets are also used to process large quantities of the same component and may incorporate multiple blast nozzles and a part conveyance system.

There are three systems typically used in a blast cabinet. Two, siphon and pressure, are dry and one is wet:

1. A siphon blast system (aka suction blast system) uses the compressed air to create vacuum in a chamber (known as the blast gun). The negative pressure pulls abrasive into the blast gun where the compressed air directs the abrasive through a blast nozzle. The abrasive mixture travels through a nozzle that directs the particles toward the surface or workpiece.

Nozzles come in a variety of shapes, sizes, and materials. Tungsten carbide is the liner material most often used for mineral abrasives. Silicon carbide and boron carbide nozzles are more wear resistant and are often used with harder abrasives such as aluminum oxide. Inexpensive abrasive blasting systems and smaller cabinets use ceramic nozzles.

2. In a pressure blast system, the abrasive is stored in the pressure vessel then sealed. The vessel is pressurized to the same pressure as the blast hose attached to the bottom of the pressure vessel. The abrasive is metered into the blast hose and conveyed by the compressed gas through the blast nozzle.

3. Wet blast cabinets use a system that injects the abrasive/liquid slurry into a compressed gas stream. Wet blasting is typically used when the heat produced by friction in dry blasting would damage the part.

Blast room

A blast room is a larger version of a blast cabinet and the blast operator works inside the room. A blast room includes three of the four components of a blast cabinet: the containment structure, the abrasive blasting system and the dust collector. Most blast rooms have recycling systems ranging from manual sweeping and shoveling the abrasive back into the blast pot to full reclaim floors that convey the abrasive pneumatically or mechanically to a device that cleans the abrasive prior to recycling.

Media

In the early 1900s, it was assumed that sharp-edged grains provided the best performance, but this was later demonstrated to not be correct.

Mineral: Silica sand is the most commonly used type of mineral abrasive. It tends to break up quickly, creating large quantities of dust, exposing the operator to the potential development of silicosis, a debilitating lung disease. To counter this hazard, silica sand for blasting is often coated with resins to control the dust. Using silica sand as an abrasive is not allowed in Germany or Portugal for this reason.

Another common mineral abrasive is garnet. Garnet is more expensive than silica sand, but if used correctly, will offer equivalent production rates while producing less dust and no safety hazards from ingesting the dust. Magnesium sulphate (kieserite) is often used as an alternative to baking soda.

Agricultural: Typically, crushed nut shells or fruit kernels. These soft abrasives are used to avoid damaging the underlying material such when cleaning brick or stone, removing graffiti, or the removal of coatings from printed circuit boards being repaired.

Synthetic: This category includes corn/wheat starch, sodium bicarbonate, and dry ice. These "soft" abrasives are also used to avoid damaging the underlying material such when cleaning brick or stone, removing graffiti, or the removal of coatings from printed circuit boards being repaired. Sodablasting uses baking soda (sodium bicarbonate) which is extremely friable, the micro fragmentation on impact exploding away surface materials without damage to the substrate.

Additional synthetic abrasives include process byproducts (e.g., copper slag, nickel slag and coal slag), engineered abrasives (e.g., aluminum oxide, silicon carbide aka carborundum, glass beads, ceramic shot/grit) and recycled products (e.g., plastic abrasive, glass grit).

Metallic: Steel shot, steel grit, stainless steel shot, cut wire, copper shot, aluminum shot, zinc shot.

Many coarser media used in sandblasting often result in energy being given off as sparks or light on impact. The colours and size of the spark or glow varies significantly, with heavy bright orange sparks from steel shot blasting, to a faint blue glow (often invisible in sunlight or brightly lit work areas) from garnet abrasive.

Safety

Cleaning operations using abrasive blasting can present risks for workers' health and safety, specifically in portable air blasting or blast room (booth) applications. Although many abrasives used in blasting rooms are not hazardous in themselves, (steel shot and grit, cast iron, aluminum oxide [aka corundum], garnet, plastic abrasive and glass bead), other abrasives (silica sand, copper slag, nickel slag, and staurolite) have varying degrees of hazard (typically free silica or heavy metals). However, in all cases their use can present serious danger to operators, such as burns due to projections (with skin or eye lesions), falls due to walking on round shots scattered on the ground, exposure to hazardous dusts, heat exhaustion, creation of an explosive atmosphere, and exposure to excessive noise. Blasting rooms and portable blaster's equipment have been adapted to these dangers.

OSHA (Occupational Safety and Health Administration) mandates engineered solutions to potential hazards, however silica sand continues to be allowed even though most commonly used blast helmets are not sufficiently effective at protecting the blast operator if ambient levels of dust exceed allowable limits. (Respiratory protection is approved by NIOSH - National Institute for Occupational Safety and Health).

Typical safety equipment for operators include:

- Positive pressure blast hood or helmet - The hood or helmet includes a head suspension system to allow the device to move with the operator's head, a view window with replaceable lens or lens protection and an air feed hose.

- Grade D air supply (or self contained oil-less air pump) - The air feed hose is typically attached to a grade D pressurized air supply. Grade D air is mandated by OSHA to protect the worker from hazardous gases. It includes a pressure regulator, air filtration and a carbon monoxide monitor/alarm. An alternative method is a self contained oil-less air pump to feed pressurized air to the blast hood/helmet. An oil-less air pump does not require an air filter or carbon monoxide monitor/alarm, because the pressurized air is coming from a source that cannot generate carbon monoxide.

- Ear protection - ear muffs or ear plugs.

- Body protection - Body protection varies by application but usually consists of gloves and overalls or a leather coat and chaps. Professionals would wear a cordura/canvas blast suit (unless blasting with steel abrasives, then they would use a leather suit).

In the past, when sandblasting was performed as an open-air job, the worker was exposed to risk of injury from the flying material and lung damage from inhaling the dust. The silica dust produced in the sandblasting process would cause silicosis after sustained inhalation of the dust. In 1918, the first sandblasting enclosure was built, which protected the worker with a viewing screen, revolved around the workpiece, and used an exhaust fan to draw dust away from the worker's face.

Several countries and territories now regulate sandblasting such that it may only be performed in a controlled environment using ventilation, protective clothing and breathing air supply.

Worn look jeans

Many consumers in Western societies are willing to pay extra for jeans that have the appearance of being used. To give the fabrics the right worn look sandblasting is used. Sandblasting has the risk of causing silicosis to the workers, and in Turkey, more than 5,000 workers in the textile industry have been stricken with this disease, and 46 people are known to have died due to this. Sweden's Fair Trade Center conducted a survey among 17 textile companies that showed very few were aware of the dangers caused by sandblasting jeans manually. Several companies said they would abolish this technique from their own production.

Applications

Specialized applications

The lettering and engraving on most modern cemetery monuments and markers is created by abrasive blasting.

Sandblasting can also be used to produce three dimensional signage. This type of signage is considered to be a higher end product as compared to the flat signs. These signs often incorporate gold leaf overlay and sometimes crushed glass backgrounds which is called smalts.

Sandblasting can be used to refurbish buildings or create works of art (carved or frosted glass). Modern masks and resists facilitate this process, producing accurate results.

Sandblasting techniques are used for cleaning boat hulls, as well as brick, stone and concrete work. Sandblasting is used for cleaning industrial as well as commercial structures, but is rarely used for non-metallic workpieces.

Chapter- 8

Laboratory Centrifuge

Laboratory centrifuge

A tabletop laboratory centrifuge

Uses	Separation
Related items	Gas centrifuge Ultracentrifuge

A **laboratory centrifuge** is a piece of laboratory equipment, driven by a motor, which spins liquid samples at high speed. There are various types of centrifuges, depending on the size and the sample capacity.

Like all other centrifuges, laboratory centrifuges work by the sedimentation principle, where the centripetal acceleration is used to separate substances of greater and lesser density.

Operation

Increasing the effective gravitational force will more rapidly and completely cause the precipitate to gather on the bottom of the tube as a "pellet". The remaining solution is called the "supernate" or "supernatant".

The supernatant liquid is then either quickly decanted from the tube without disturbing the pellet, or withdrawn with a Pasteur pipette. The rate of centrifugation is specified by the acceleration applied to the sample, typically measured in revolutions per minute (RPM) or relative centrifugal force (RCF). The particles' settling velocity in centrifugation is a function of their size and shape, centrifugal acceleration, the volume fraction of solids present, the density difference between the particle and the liquid, and the viscosity.

The use of a centrifuge is known as centrifugation.

Types

Laboratory centrifuge

There are various types of centrifugation:

- Differential centrifugation, often used to separate certain organelles from whole cells for further analysis of specific parts of cells
- Isopycnic centrifugation, often used to isolate nucleic acids such as DNA
- Sucrose gradient centrifugation, often used to purify enveloped viruses and ribosomes, and also to separate cell organelles from crude cellular extracts

There are different types of laboratory centrifuges:

- **Microcentrifuges**

(devices for small tubes from 0.2 ml to 2.0 ml (micro tubes), up to 96 well-plates, compact design, small footprint; up to 30.000 g)

- **Clinical centrifuges**

(devices used for clinical applications like blood collection tubes, low-speed devices)

- **Multipurpose benchtop centrifuges**

(devices for a broad range of tube sizes, high variability, big footprint)

- **Stand alone centrifuges**

(heavy devices like the ultracentrifuge)

Many centrifuges are available with (refrigerated device) or without cooling function. There are different providers of laboratory centrifuges like Eppendorf, Thermo-Heraeus, Thermo-Sorvall, Hettich, Beckmann-Coulter, MSE and Sigma.

History

A 19th century hand cranked laboratory centrifuge.

English military engineer Benjamin Robins (1707-1751) invented a whirling arm apparatus to determine drag. In 1864, Antonin Prandtl invented the first dairy centrifuge in order to separate cream from milk. In 1879, Gustaf de Laval demonstrated the first continuous centrifugal separator, making its commercial application feasible.

Different sizes of centrifuges were developed. The range of applications varied from Liter-scale to Milli-Liter-scale.

Regarding the laboratory microcentrifuge, in 1962 the Hamburg-based company “Netheler & Hinz Medizintechnik” (nowadays known as “eppendorf”) developed the

“Microliter System” for laboratory usage. Besides the first piston stroke pipette, based on the work of Dr. Schnittger (Marburg/ Germany), the plastic-made micro test tube and the first microcentrifuge (model 3200) were introduced for applications in routine analysis labs in microliter scale. This first real microcentrifuge had one control knob for the time and space for up to 12 micro test tubes in a fixed-angle rotor. Common up-to-date features like cooling, programming, automatic imbalance detection, noise reduction, or changeable rotor systems were completely missing.

The “Microliter System” was the starting point for a broad range of tools for the molecular lab, developed by all different kinds of biotech and labware companies.

Design

A large laboratory centrifuge.

Laboratory centrifuges are used in chemistry, biology, and biochemistry for isolating and separating solids from liquids in a suspension. The solids can be insoluble compounds, biomolecules, cell organelles, or whole cells. They vary widely in speed and capacity. They usually comprise a rotor containing two, four, six, or many more numbered wells within which centrifuge tubes may be placed.

When a suspension in a centrifuge tube is centrifuged, the solids settle at the bottom of the centrifuge tube; having a tapered wall helps to concentrate the solids, making it easier to decant the supernatant solution, leaving the solids.

Generally spoken, there are two main types of rotors:

Fixed-angle rotor

The rotor (mainly made of aluminium) is very compact. There are boreholes with a specific angle (like 45°) within the rotor. These boreholes are used for the sample tubes.

Swing-out rotor (= horizontal rotor)

The rotor looks like a cross with gondolas, called buckets. Within these buckets, different tubes can be centrifuged. For a safe centrifugation, a specific adadpter for every tube shape is mandatory.

The rotor is closed by a rotor lid. The rotor is located in a rotor chamber which is covered by a metall centrifuge lid. The open lid prevents the motor from turning the rotor when the rotor chamber is open. During the run, the lid is locked. The lid protects the user from being injured by touching a rapidly spinning rotor. The rotor chamber and the lid of high quality centrifuges are robust enough to survive a rotor failure at full speed. This robustness protects the user and the laboratory from crashing fragments in case the rotor fails catastrophically. After a rotor crash, a centrifuge should not be reused as the enormous forces during a crash may have damaged essential parts of the device.

The rotor must be balanced by placing samples or blanks of equal mass opposite each other. Since most of the mass is derived from the solvent, it is usually sufficient to place blanks or other samples of equal volume. As a safety feature, some centrifuges may stop turning when wobbling is detected.

Centrifuge tubes

Centrifuge tubes or **centrifuge tips** are tapered tubes of various sizes made of glass or plastic. They may vary in capacity from tens of millilitres, to much smaller capacities used in microcentrifuges used extensively in molecular biology laboratories. The most commonly encountered tubes are of about the size and shape of a normal test tube (~ 10 cm long). Microcentrifuges typically accommodate microcentrifuge tubes with capacities from 250 µl to 2.0 ml. These are exclusively made of plastic.

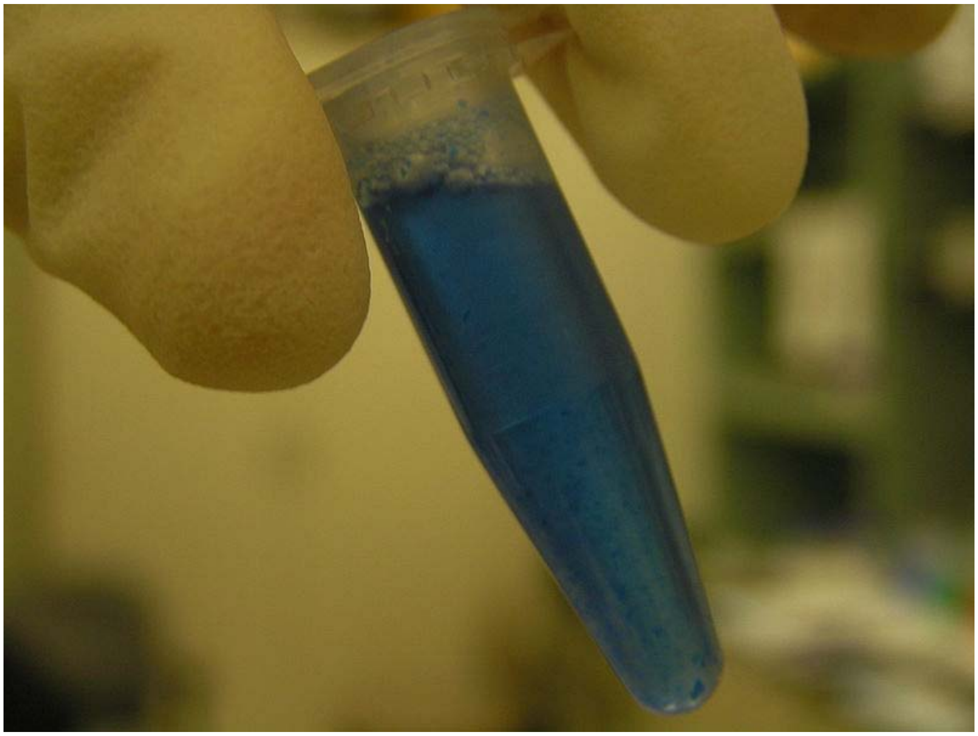
Glass centrifuge tubes can be used with most solvents, but tend to be more expensive. They can be cleaned like other laboratory glassware, and can be sterilized by autoclaving. Plastic centrifuge tubes, especially microcentrifuge tubes tend to be less expensive. Water is preferred when plastic centrifuge tubes are used. They are more difficult to clean thoroughly, and are usually inexpensive enough to be considered disposable.

Microcentrifuge tubes

Microcentrifuge tubes or **microfuge tubes** are small, cylindrical plastic containers with conical bottoms, typically with an integral snap cap. They are used in molecular biology and biochemistry to store and centrifuge small amounts of liquid. As they are inexpensive and considered disposable, they are used by many chemists and biologists as convenient sample vials in lieu of glass vials; this is particularly useful when there is only a small amount of liquid in the tube or when small amounts of other liquids are being added, because microcentrifugation can be used to collect the drops together at the bottom of the tube after pipetting or mixing.

Made of polypropylene, they can be used in very low temperature (-80 °C to liquid nitrogen temperatures) or with organic solvents such as chloroform. They come in many different sizes, generally ranging from 250 μL to 2.0 mL. The most common size is 1.5 mL. Disinfection is possible (1 atm, 120 °C, 20 minutes) and is commonly performed in work related to DNA or microbes, where purity of the sample is of utmost importance. Due to their low cost and the difficulty in cleaning the plastic surface, they are usually discarded after each use.

Eppendorf tube has become a genericized trademark for *microfuge tubes* or *microcentrifuge tubes*. Eppendorf is a major manufacturer of this item, but is not the only one.



Microcentrifuge tube with Coomassie Blue solution.

left|Three microcentrifuge tubes: 2 mL, 1.5 mL and 200 µL (for PCR).

Four screw-top microcentrifuge tubes.

Safety

The load in a laboratory centrifuge must be carefully balanced. Small differences in mass of the load can result in a large force imbalance when the rotor is at high speed. This force imbalance strains the spindle and may result in damage to the centrifuge or personal injury. Some centrifuges have an automatic rotor imbalance detection feature that immediately discontinues the run when an imbalance is detected.

Before starting a centrifuge, an accurate check of the rotor and lid locking mechanisms is mandatory. Centrifuge rotors should never be touched while moving, because a spinning rotor can cause serious injury. Modern centrifuges generally have features that prevent accidental contact with a moving rotor as the main lid is locked during the run.

Centrifuge rotors have tremendous kinetic energy during high speed rotation. Rotor failure, caused by mechanical stress from the high forces imparted by the motor, can occur due to manufacturing defects, routine wear and tear, or improper use and maintenance. Such a failure can be catastrophic failure, especially with larger centrifuges, and generally results in total destruction of the centrifuge. While centrifuges generally have safety shielding to contain these failures, such shielding may be inadequate, especially in older models, or the entire centrifuge unit may be propelled from its position, resulting in damage to nearby personnel and equipment. Uncontained rotor failures have shattered laboratory windows and destroyed refrigerators and cabinetry. To reduce the risk of rotor failures, centrifuge manufactures specify operating and maintenance procedures to ensure that rotors are regularly inspected and removed from service or derated (only operated at lower speeds) when they are past their expected lifetime.

Another potential hazard is the aerosolization of hazardous samples during centrifugation. To prevent contamination of the laboratory, rotor lids with pecial aerosol-tight gaskets are available. The rotor can be loaded with the samples within a hood and the rotor lid fixed on the rotor. Afterwards, the aerosol-tight system of rotor and lid is transferred to the centrifuge. The rotor can then be fixed within the centrifuge without opening the lid. After the run, the entire rotor assembly, including the lid, is removed from the centrifuge to the hood for further steps, maintaining the samples within a closed system.

Theory

Protocols for centrifugation typically specify the amount of acceleration to be applied to the sample, rather than specifying a rotational speed such as revolutions per minute. The acceleration is often quoted in multiples of g, the acceleration due to gravity at the Earth's surface. This distinction is important because two rotors with different diameters running at the same rotational speed will subject samples to different accelerations.

The acceleration can be calculated as the product of the radius and the square of the angular velocity.

Relative centrifugal force (RCF) is the measurement of the force applied to a sample within a centrifuge. This can be calculated from the speed (RPM) and the rotational radius (cm) using the following calculation.

$$\mathrm{g} = \mathrm{RCF} = 0.00001118 \times r \times N^2$$

where:

g = Relative centrifuge force
r = rotational radius (centimetre, cm)
N = rotating speed (revolutions per minute, r/min)

To avoid having to perform a mathematical calculation every time, one can find nomograms for converting RCF to rpm for a rotor of a given radius. A ruler or other straight edge lined up with the radius on one scale, and the desired RCF on another scale, will point at the correct rpm on the third scale. Example Based on automatic rotor recognition, up to date centrifuges have a button for automatic conversion from RCF to rpm and vice versa.

Chapter- 9

Cross-Flow Filtration

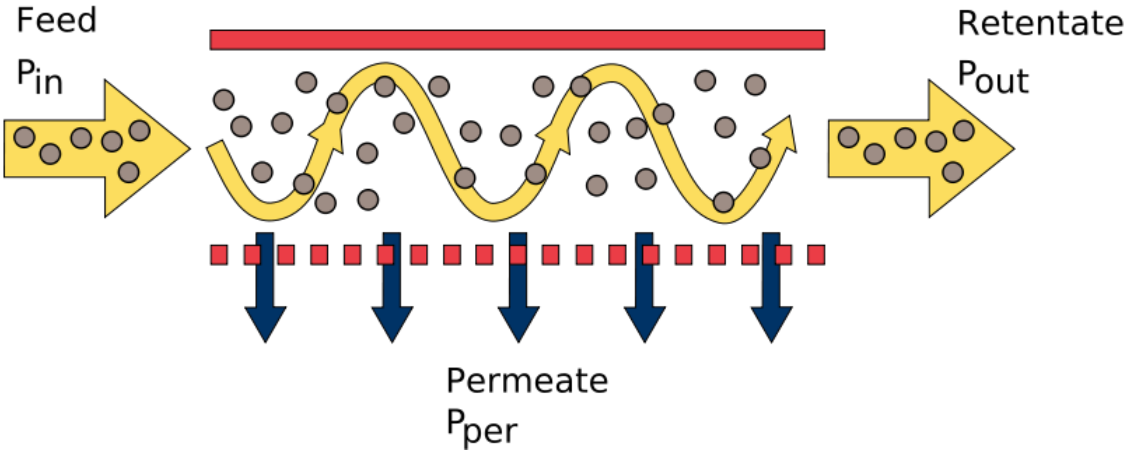


Diagram of cross-flow filtration

In chemical engineering, biochemical engineering and protein purification, **crossflow filtration** (also known as **tangential flow filtration**) is a type of filtration (a particular unit operation). Crossflow filtration is different from dead-end filtration in which the feed is passed through a membrane or bed, the solids being trapped in the filter and the filtrate being released at the other end. Cross-flow filtration gets its name because the majority of the feed flow travels tangentially *across* the surface of the filter, rather than into the filter. The principal advantage of this is that the filter cake (which can blind the filter) is substantially washed away during the filtration process, increasing the length of time that a filter unit can be operational. It can be a continuous process, unlike batch-wise dead-end filtration.

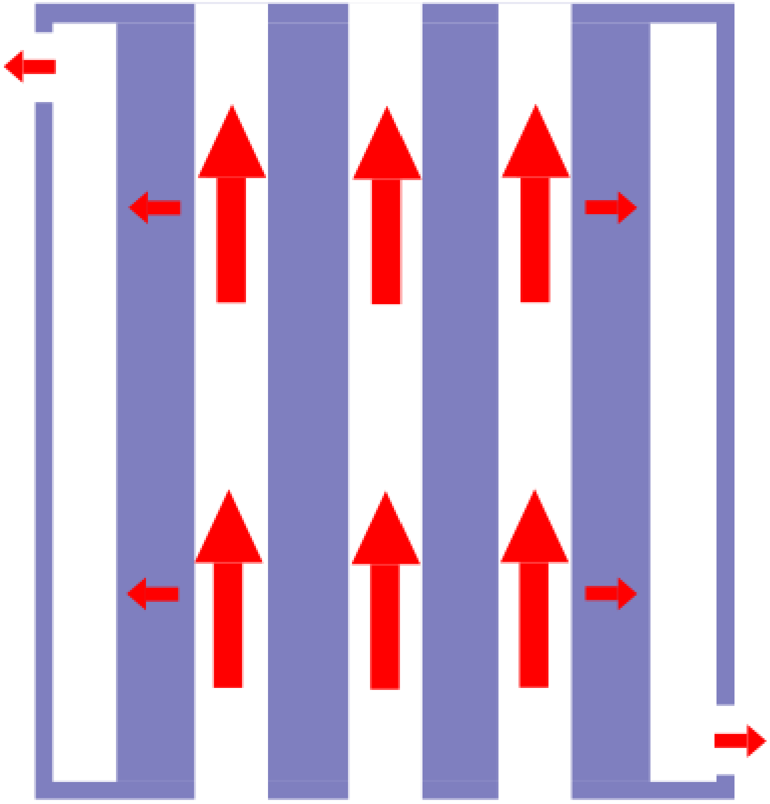


Diagram of cross-flow filtration

This type of filtration is typically selected for feeds containing a high proportion of small particle size solids (where the permeate is of most value) because solid material can quickly block (blind) the filter surface with dead-end filtration. Industrial examples of this include the extraction of soluble antibiotics from fermentation liquors.

Operation

Ceramic membrane for industrial cross-flow filtration

In crossflow filtration, the feed is passed across the filter membrane (tangentially) at positive pressure relative to the permeate side. A proportion of the material which is smaller than the membrane pore size passes through the membrane as permeate or filtrate; everything else is retained on the feed side of the membrane as retentate.

With crossflow filtration the tangential motion of the bulk of the fluid across the membrane causes trapped particles on the filter surface to be rubbed off. This means that a crossflow filter can operate continuously at relatively high solids loads without blinding.

Benefits over conventional filtration

- A higher overall liquid removal rate is achieved by the prevention of filter cake formation
- Process feed remains in the form of a mobile slurry, suitable for further processing
- Solids content of the product slurry may be varied over a wide range
- It is possible to fractionate particles by size

Industrial applications

Filtration unit for industrial cross-flow filtration

Cross flow membrane filtration technology has been used widely in industry globally. Filtration membranes can be polymeric or ceramic, depending upon the application. The principles of cross-flow filtration are used in reverse osmosis, nanofiltration, ultrafiltration and microfiltration. When purifying water, it can be very cost effective in comparison to the traditional evaporation methods.

In protein purification, the term Tangential Flow Filtration (TFF) is used to describe cross-flow filtration with membranes. The process can be used at different stages during purification, depending on the type of membrane selected.

In the photograph of an industrial filtration unit (right), it is possible to see that the recycle pipework is considerably larger than either the feed pipework (vertical pipe on the right hand side) or the permeate pipework (small manifolds near to the rows of white clamps). These pipe sizes are directly related to the proportion of liquid flows through the unit. A dedicated pump is used to recycle the feed several times around the unit before the solids-rich retentate is transferred to the next part of the process.

Techniques to improve performance of cross flow filtration

Backwashing

In backwashing, the transmembrane pressure is periodically inverted by the use of a secondary pump, so that permeate flows back into the feed, lifting the fouling layer from the surface of the membrane.

Clean-in-place

Clean-in-place systems are typically used to remove fouling from membranes after extensive use. The CIP process may use detergents, reactive agents such as sodium hypochlorite and acids and alkalis such as citric acid and sodium hydroxide.

Concentration

The volume of the fluid is reduced by allowing permeate flow to occur. Solvent, solutes, and particles smaller than the membrane pore size pass through the membrane, while particles larger than the pore size are retained, and thereby concentrated. In bioprocessing applications, concentration may be followed by diafiltration.

Diafiltration

In order to effectively remove permeate components from the slurry, fresh solvent may be added to the feed to replace the permeate volume, at the same rate as the permeate flow rate, such that the volume in the system remains constant. This is analogous to the washing of filter cake to remove soluble components.. Dilution and re-concentration is sometimes also referred to as "diafiltration."

Process Flow Disruption (PFD)

A technically simpler approach than backwashing is to set the transmembrane pressure to zero by temporarily closing off the permeate outlet, which increases the attrition of the fouling layer without the need for a second pump. PFD is not as effective as backwashing in removing fouling, but can be advantageous.

Flow rate calculation

The flux or flow rate in cross-flow filtration systems is given by the equation:

$$J = \frac{\Delta p}{(R_m + R_c)\mu}$$

in which:

- J: liquid flux
- ΔP: transmembrane pressure (should also include effects of osmotic pressure for reverse osmosis membranes)
- R_m: Resistance of the membrane (related to overall porosity)
- R_c: Resistance of the cake (variable; related to membrane fouling)
- μ: liquid viscosity

Note: R_m and R_c include the inverse of the membrane surface area in their derivation; thus, flux increases with increasing membrane area.

Chapter- 10

Vacuum Distillation

Under atmospheric pressure, Dimethyl sulfoxide boils at 189°C. Under a vacuum, it distills off into the connected receiver at only 70°C.

Vacuum distillation is a method of distillation whereby the pressure above the liquid mixture to be distilled is reduced to less than its vapor pressure (usually less than atmospheric pressure) causing evaporation of the most volatile liquid(s) (those with the lowest boiling points). This distillation method works on the principle that boiling occurs when the vapor pressure of a liquid exceeds the ambient pressure. Vacuum distillation is used with or without heating the solution.

Laboratory-scale applications

Laboratory-scale vacuum distillation is used when liquids to be distilled have high atmospheric boiling points or chemically change at temperatures near their atmospheric boiling points. Temperature sensitive materials (such as beta carotene) also require vacuum distillation to remove solvents from the mixture without damaging the product. Another reason vacuum distillation is used is that compared to steam distillation there is a lower level of residue build up. This is important in commercial applications where temperature transfer is produced using heat exchangers.

Vacuum distillation is sometimes referred to as low temperature distillation.

There many laboratory applications for vacuum distillation as well as many types of distillation set-ups and apparatuses.

Safety is an important consideration when using glassware as part of the set-up. All of the glass components should be carefully examined for scratches and cracks which could result in implosions when the vacuum is applied. Wrapping as much of the glassware with tape as is practical helps to prevent dangerous scattering of glass shards in the event of an implosion.

Rotary evaporation

Rotary evaporation is a type of vacuum distillation apparatus used to remove bulk solvents from the liquid being distilled. It is also used by environmental regulatory agencies for determining the amount of solvents in paint, coatings and inks.

Rotary evaporation set-ups include an apparatus referred to as a *Rotovap* which rotates the distillation flask (sometimes called the *still pot*) to enhance the distillation. Rotating the flask throws up liquid on the walls of the flask and thus increases the surface area for evaporation.

Heat is often applied to the rotating distillation flask by partially immersing it in a heated bath of water or oil. Typically, the vacuum in such systems is generated by a water aspirator or a vacuum pump of some type.

Distillation of high-boiling and/or air sensitive materials

Some compounds have high boiling point temperatures as well as being air sensitive. A simple laboratory vacuum distillation glassware set-up can be used, in which the vacuum can be replaced with an inert gas after the distillation is complete.

However, this is not a completely satisfactory system if it is desired to collect fractions under a reduced pressure.

For better results or for very air sensitive compounds, either a Perkin triangle distillation set-up or a short-path distillation set-up can be used.

Perkin triangle distillation set-up

The Perkin triangle set-up (Image 5) uses a series of Teflon valves to allow the distilled fractions to be isolated from the distillation flask without the main body of the distillation set-up being removed from either the vacuum or the heat source, and thus can remain in a state of reflux.

To do this, the distillate receiver vessel is first isolated from the vacuum by means of the Teflon valves.

The vacuum over the sample is then replaced with an inert gas (such as nitrogen or argon) and the distillate receiver can then be stoppered and removed from the system.

Vacuum distillation set-up using a short-path head

Vacuum distillation of moderately air/water-sensitive liquid can be done using standard Schlenk-line techniques (Image 6).

When assembling the set-up apparatus, all of the connecting lines are clamped so that they cannot pop off.

Once the apparatus is assembled, and the liquid to be distilled is in the still pot, the desired vacuum is established in the system by using the vacuum connection on the short-path distillation head. Care is taken to prevent potential "bumping" as the liquid in the still pot degases.

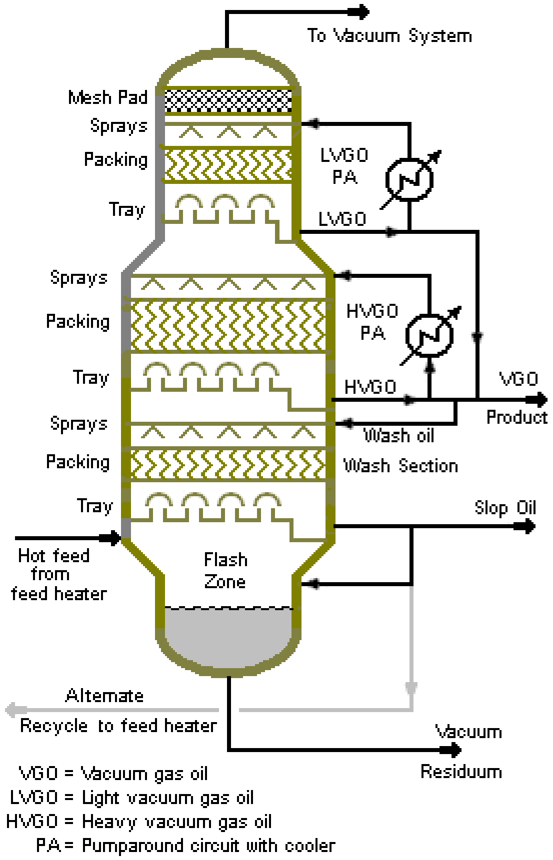
While establishing the vacuum, the flow of coolant is started through the short-path distillation head. Once the desired vacuum is established, heat is applied to the still pot.

If needed, the first portion of distillate can be discarded by purging with inert gas and changing out the distillate receiver.

When the distillation is complete: the heat is removed, the vacuum connection is closed, and inert gas is purged through the distillation head and the distillate receiver. While under the inert gas purge, remove the distillate receiver and cap it with an air-tight cap.

The distillate receiver can be stored under vacuum or under inert gas by using the side-arm on the distillation flask.

Industrial-scale applications



Simplified drawing of a typical dry vacuum distillation column as used in oil refineries

Large-scale vacuum distillation tower at Fawley oil refinery

Typical industrial applications utilize the heat pump cycle to maximize efficiency. This type of distillation is in use in the oil industry where common ASTM standards are D1160, D2892, D5236. These standards describe typical applications of vacuum distillation at pressures of about 1-100 mbar. Pilot plants up to 60 L can be built in accordance with these standards.

Industrial-scale vacuum distillation has several advantages. Close boiling mixtures may require many equilibrium stages to separate the key components. One tool to reduce the number of stages needed is to utilize vacuum distillation. Vacuum distillation columns (as depicted in the drawing to the right) typically used in oil refineries have diameters ranging up to about 14 metres (46 feet), heights ranging up to about 50 metres (164 feet), and feed rates ranging up to about 25,400 cubic metres per day (160,000 barrels per day).

Vacuum distillation increases the relative volatility of the key components in many applications. The higher the relative volatility, the more separable are the two components; this connotes fewer stages in a distillation column in order to effect the same separation between the overhead and bottoms products. Lower pressures increase relative volatilities in most systems.

A second advantage of vacuum distillation is the reduced temperature requirement at lower pressures. For many systems, the products degrade or polymerize at elevated temperatures.

Vacuum distillation can improve a separation by:

- Prevention of product degradation or polymer formation because of reduced pressure leading to lower tower bottoms temperatures,

- Reduction of product degradation or polymer formation because of reduced mean residence time especially in columns using packing rather than trays.

- Increasing capacity, yield, and purity.

Another advantage of vacuum distillation is the reduced capital cost, at the expense of slightly more operating cost. Utilizing vacuum distillation can reduce the height and diameter, and thus the capital cost of a distillation column.

Vacuum distillation in petroleum refining

Petroleum crude oil is a complex mixture of hundreds of different hydrocarbon compounds generally having from 3 to 60 carbon atoms per molecule, although there may be small amounts of hydrocarbons outside that range. The refining of crude oil begins with distilling the incoming crude oil in a so-called *atmospheric distillation column* operating at pressures slightly above atmospheric pressure.

In distilling the crude oil, it is important not to subject the crude oil to temperatures above 370 to 380 °C because the high molecular weight components in the crude oil will undergo thermal cracking and form petroleum coke at temperatures above that. Formation of coke would result in plugging the tubes in the furnace that heats the feed stream to the crude oil distillation column. Plugging would also occur in the piping from the furnace to the distillation column as well as in the column itself.

The constraint imposed by limiting the column inlet crude oil to a temperature of more than 370 to 380 °C yields a residual oil from the bottom of the atmospheric distillation column consisting entirely of hydrocarbons that boil above 370 to 380 °C.

To further distill the residual oil from the atmospheric distillation column, the distillation must be performed at absolute pressures as low as 10 to 40 mmHg (also referred to as Torr) so as to limit the operating temperature to less than 370 to 380 °C.

Image 1 is a photograph of a large vacuum distillation column in a petroleum refinery and Image 2 is a process diagram of a petroleum refinery vacuum distillation column that depicts the internals of the column.

The 10 to 40 mmHg absolute pressure in a vacuum distillation column increases the volume of vapor formed per volume of liquid distilled. The result is that such columns have very large diameters.

Distillation columns such those in Images 1 and 2, may have diameters of 15 meters or more, heights ranging up to about 50 meters, and feed rates ranging up to about 25,400 cubic meters per day (160,000 barrels per day).

The vacuum distillation column internals must provide good vapor-liquid contacting while, at the same time, maintaining a very low pressure increase from the top of the column top to the bottom. Therefore, the vacuum column uses distillation trays only where withdrawing products from the side of the column (referred to as *side draws*).

Most of the column uses packing material for the vapor-liquid contacting because such packing has a lower pressure drop than distillation trays. This packing material can be either structured sheet metal or randomly dumped packing such as Raschig rings.

The absolute pressure of 10 to 40 mmHg in the vacuum column is most often achieved by using multiple stages of steam jet ejectors.

Many industries, other than the petroleum refining industry, use vacuum distillation on a much a smaller scale.

Chapter- 11

Centrifugation

Centrifugation is a process that involves the use of the centrifugal force for the separation of mixtures with a centrifuge, used in industry and in laboratory settings. More-dense components of the mixture migrate away from the axis of the centrifuge, while less-dense components of the mixture migrate towards the axis. Chemists and biologists may increase the effective gravitational force on a test tube so as to more rapidly and completely cause the precipitate ("pellet") to gather on the bottom of the tube. The remaining solution is properly called the "supernate" or "supernatant liquid". The supernatant liquid is then either quickly decanted from the tube without disturbing the precipitate, or withdrawn with a Pasteur pipette.

The rate of centrifugation is specified by the acceleration applied to the sample, typically measured in revolutions per minute (RPM) or *g*. The particles' settling velocity in centrifugation is a function of their size and shape, centrifugal acceleration, the volume fraction of solids present, the density difference between the particle and the liquid, and the viscosity.

In the chemical and food industries, special centrifuges can process a continuous stream of particle-laden liquid.

Centrifugation is the most common method used for uranium enrichment, relying on the slight mass difference between atoms of U238 and U235 in uranium hexafluoride gas.

Centrifugation in biotechnology

Microcentrifuges and superspeed centrifuges

In microcentrifugation, centrifuges are run in batch to isolate small volumes of biological molecules or cells (prokaryotic and eukaryotic). Nuclei is also often purified via microcentrifugation. Microcentrifuge tubes generally hold 1.5-2 mL of liquid, and are spun at maximum angular speeds of 12000-13000 rpm. Microcentrifuges are small and have rotors that can quickly change speeds. Superspeed centrifuges work similarly to microcentrifuges, but are conducted via larger scale processes. Superspeed centrifuges are also used for purifying cells and nuclei, but in larger quantities. These centrifuges are used to purify 25-30 mL of solution within a tube. Additionally, larger centrifuges also reach higher angular velocities (around 30000 rpm) and also use a larger rotor.

Ultracentrifugation

Ultracentrifugation makes use of high centrifugal force for studying properties of biological particles. While microcentrifugation and superspeed centrifugation are used strictly to purify cells and nuclei, ultracentrifugation can isolate much smaller particles, including ribosomes, proteins, and viruses. Ultracentrifuges can also be used in the study of membrane fractionation. This occurs because ultracentrifuges can reach maximum angular velocities in excess of 70000 rpm. Additionally, while microcentrifuges and supercentrifuges separate particles in batch, ultracentrifuges can separate molecules in batch and continuous flow systems.

In addition to purification, analytical ultracentrifugation (AUC) can be used for determination of macromolecular properties, including the amino acid composition of a protein, the protein's current conformation, or properties of that conformation. In analytical ultracentrifuges, concentration of solute is measured using optical calibrations. For low concentrations, the Beer-Lambert law can be used to measure the concentration. Analytical ultracentrifuges can be used to simulate physiological conditions (correct pH and temperature).

In analytical ultracentrifuges, molecular properties can be modeled through sedimentation velocity analysis or sedimentation equilibrium analysis. In sedimentation velocity analysis, concentrations and solute properties are modeled continuously over time. Sedimentation velocity analysis can be used to determine the macromolecule's shape, mass, composition, and conformational properties. During sedimentation equilibrium analysis, centrifugation has stopped and particle movement is based on diffusion. This allows for modeling of the mass of the particle as well as the chemical equilibrium properties of interacting solutes.

Centrifugation analysis

Lamm equation

Particle dispersion and sedimentation can be analyzed using the Lamm equation. The calculation of the sedimentation coefficient and diffusion coefficient is useful for determining the physical properties of the molecule, including shape and conformational changes. However, the Lamm Equation is most ideal for modeling concentrations of ideal, non-interacting solutes. Chemical reactions are unaccounted for by this equation. Additionally, for large molecular weight particles, sedimentation is not always smooth. This may lead to the overestimation of the diffusion coefficient, or oscillation effects at the bottom of a solution cell.

Sigma analysis

Sigma analysis is a useful tool determining centrifuge properties. It is similar to the continuity equation that relates volumetric flow rate Q, fluid velocity u, and flow path cross-sectional Area A:

$Q = uA$

In the case of sigma analysis, u is replaced by v_g,the settling velocity at centripetal acceleration of g (9.81 m/s^2), Σ replaces area, and is a property of the type of centrifuge, and Q is the input fluid flow rate. Σ has the same units as area.

$Q = 2v_g\Sigma$

Other applications

- Separating textile.
- Removing water from lettuce after washing it in a salad spinner
- Separating particles from an air-flow using cyclonic separation.
- The clarification and stabilization of wine

Clarification and stabilization of wine

The clarification process can bring out the clarity and brightness of a wine.

The **clarification and stabilization of wine** in winemaking involves removing insoluble and suspended materials that may cause a wine to become cloudy, gassy, form unwanted sediment deposit or tartaric crystals, deteriorate quicker or develop assorted wine faults due to physical, chemical or microbiological instability. These processes may include fining, filtration, centrifugation, flotation, refrigeration, barrel maturation, pasteurization and racking. Most of these processes will occur after the primary fermentation and before the wine is bottled. The exception is for white wine production which will usually have the must separated from some of the grape skins and particles prior to fermentation so as to avoid any unwanted maceration. The timing and exact methods used will vary by producer, depending on the desired finish product -- such as a completely bright and clear wine or a wine that still retains some of the flavor and color phenols. Some of the materials that are removed from the must during this stage of winemaking include dead yeast cells (lees), bacteria, tartrates, proteins, pectins, various tannins and other phenolic compounds, and pieces of grape skins, pulp, stems and gums.

Clarifying wine

A method of natural clarification takes place as wine ages in the barrel with suspended particles gradually precipitating and collecting at the bottom.

In wine tasting, a wine is considered "clear" when there are no visible particles suspended in the liquid and (mostly in regards to white wines) there is some degree of transparency. This is demonstrated by holding the glass up to a piece of paper with writing and seeing if one could read through the wine. Some red wine grape varieties have a naturally high concentration of coloring phenols that make the wine more translucent or opaque. For these wines, the brightness or "vividness" of the wines color is considered. A wine with a lot of suspended particles will appear less clear and more dull in brightness. While lack of clarity and brightness may not negatively affect the taste of wine, it may make the wine less visually appealing to the consumer. In the modern wine industry there has been a premium placed on wines being both clear and bright. To achieve this, wines are usually clarified through some means in order to remove suspended particles.

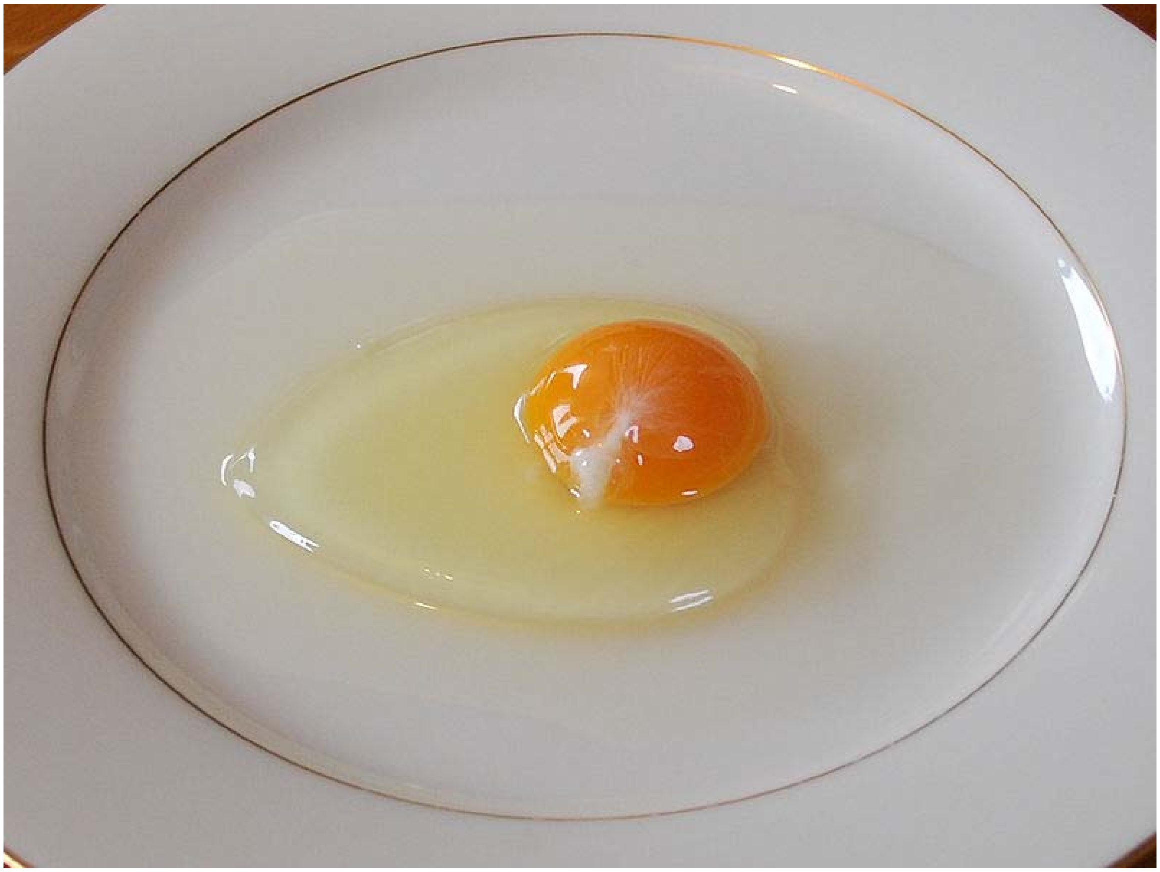
These suspended particles are normally insoluble solids such as lees, fragments of grape skins, pulp and seeds as well as colloids that are not visible to the unaided eye like gums, pectins, proteins, tartrates, active yeast and bacteria. The forces of gravity can achieve natural clarification through the process of settling (French *débourbage*) where the larger suspended particles gradually settle to the bottom of the storage vessel. The wine is then siphoned or "racked" off the compact solids into a new container. This natural process can be very lengthy, sometimes requiring many months or even a couple years as well as several rackings in order to produce a perfectly clear wine. Producers can accelerate the process by using fining agents, filtration or flotation.

The timing of these methods vary depending on producer and type of wine being made. White wine, particularly aromatic varieties such as Riesling and Sauvignon blanc, is often settled and racked soon after the grapes are crushed and pressed. This is to minimize maceration and exposure to the phenolic compounds present in the grapes' skin, seeds and stems that can leach out into the must and cause the wine to prematurely brown in color as well as diminish the fruit flavors of the wine. Other varieties, such as Chardonnay, may spend some time in contact with the skins and particulate matter in order to gain complexity before being settled and racked. To aid in this clarification of white wine, pectin-splitting enzymes, sulfur dioxide and fining agents such as bentonite are added to the must to encourage the agglomeration and settling of the colloids while the holding tank is brought to low temperatures and held for 24 hours prior to rack. While most red wines are clarified after fermentation, the pectin-splitting enzymes may be added prior to fermentation to make post-fermentation clarification easier.

Fining

Bentonite

In winemaking, fining is the process where a substance (fining agent) is added to the wine to create an adsorbent, enzymatic or ionic bond with the suspended particles, making them a larger molecule that can precipitate out of the wine easier and quicker. Unlike filtration, which can only remove particulates (such as dead yeast cells and grape fragments), fining is effective in removing soluble substances such as polymerized tannins, coloring phenols and proteins. Given enough time in a stable environment, many of these suspended particles would gradually precipitate out on their own. The use of fining agents speeds up the process at lower cost. White wines are fined to remove particles that may cause the wine to brown or lose color as well as removing heat-unstable proteins that could cause the wine to appear hazy or cloudy should it be exposed to high temperatures after bottling. Red wines are fined for the same reason but also for the added benefit of reducing the amount of bitter, astringent tannins which makes these wines smoother and more approachable sooner after bottling and release. Throughout history a wide range of substances have been used as fining agents, such as dried blood powder, but today there are two general types of fining agents — organic compounds and solid/mineral materials.



Winemakers can use the whites of eggs (discarding the yolk) as a fining agent

Organic compounds used as fining agents are generally animal based, which may bring concerns for a vegan diet. The most common organic compounds used include egg whites, casein derived from milk, gelatin and isinglass obtained from the bladders of fish. Pulverized minerals and solid materials can also be used as fining agents with bentonite clay being one of the most common fining agent used due to its effectiveness in absorbing proteins and some bacteria. Activated carbon derived from charcoal is used to remove some phenols that contribute to browning colors as well as some particles that produce "off-odors" in the wine. In a process known as **blue fining**, potassium ferrocyanide is used to remove copper and iron particles that may have entered the wine through the use of metal winery and vineyard equipment, vineyard sprays such as the bordeaux mixture, and the use of bentonite as a fining agent . Due to the potential of potassium ferrocyanide forming hydrogen cyanide, its use is highly regulated and is illegal in many wine producing countries. Other inorganic materials use include silica and kaolin.

Some countries, such as Australia and New Zealand, have wine labeling laws that require the use of fining agents that may be an allergenic substance to appear on the wine label, as there may be trace amounts of the substance still in the wine. However a study conducted by the University of California, Davis Department of Viticulture and Enology found that no detectable amount of inorganic fining agents such as bentonite are present in wine that has been fined and only negligible trace amount of proteinaceous agents such as egg whites can be detected.

As with filtration, there is the risk of some loss of flavor with fining due to desirable flavor molecules being precipitated out along with the more undesirable particles. Some producers of premium wine will do less fining or do it much later in the production process in order to leach as much flavor and aromatics from the phenols before they are removed. Still, fining is considered a less harsh process than filtration, with its advocates believing that it better mimics the natural clarification and stabilization process.

Filtration

Depth filters are often made from diatomaceous earth *(sample pictured)*

While fining clarifies wine by binding to suspended particles and precipitating out as larger particles, filtration works by passing the wine through a filter medium that captures particles that are larger than the hole size of the medium. Complete filtration may require a series of filtering through progressively finer filters which can be expensive but will be considerably quicker than letting gravity naturally settle the wine and using racking to siphon the clear wine out. Most filtration in a winery can be classified as either depth filtration or surface filtration.

Depth filtration is often the first type of filtration a wine sees after fermentation when the wine is pushed through a thick layer of pads made from cellulose fibers, diatomaceous earth or perlite which traps the particles and can be removed from the wine. If the producers wish to further filter the wine, they may go to surface filtration. Surface filtration involves running the wine along a thin film of polymer material filled with holes tinier than the particles that are being filtered out. Running the wine parallel to filter surface (known as "Cross-flow" surface filtration) will minimizing the amount of potential clogging of the filter. Most membranes are made from plastic or ceramic. Another step in surface filtration, usually taking place right before bottling, is microfiltration where the fine is passed through a membrane with holes small enough to trap yeast and bacteria cells. An alternative to filtration is centrifugation where wine is put through a centrifuge decanter and gravity separates the particles from the wine.

The use of filtration is a controversial subject in winemaking with some producers feeling that the technique strips the wine of too much of its natural flavors and characteristics.

Some producers will add the phrase "unfiltered" to their wine label as a marketing tool. Wine can go through a natural clarification and stabilization process by aging in a wood barrel where the subtle oxidative effects can aid in the precipitation of larger particles (particularly proteins, tartrates and malates). This process takes time, however, and producers who bottle their wine too early, and without the assurance of sterile bottling equipment, can risk microbial contamination and instability. Wines that have not been filtered are much more likely to develop sediment as the wine ages.

Flotation

The winemaking technique of flotation was adapted from the froth flotation process used in the mining industry for ore refining. In this process, small bubbles of air (or compressed nitrogen) are injected into the bottom of a tank. As the bubbles rise through the must, grape solids have a natural tendency to cling to the bubbles creating a froth that can be removed from the wine. This technique has to take place prior to fermentation since the biological activity of yeast cells serves as an inhibitor to the flocculation needed for the froth to form. Since phenolic compounds that are prone to oxidation and browning are highly reactive to the air bubbles, wines that have gone through the flotation process are often more resistant to oxidative browning if exposed to air later.

Stabilization

The process of cold stabilization causes tartrates to crystallize and precipitate out of the wine. These crystals, while harmless, can look like shards of broken glass if they develop in the wine bottle.

As a chemical substance dependent on the activity of microorganisms and complex chemical reaction, wine can be very unstable and reactive to changes in its environment. After bottling, a wine can be exposed to extremes in temperatures and humidity as well as violent movement during transportation and storage that can encourage the wine to go through additional chemical changes that may produce faults or undesirable traits to emerge in the wine. These can include carbonic gas, formation of sediment deposits or tartaric crystals, hazy or cloudy appearance, rapid deterioration of flavor and spoilage. Eliminating suspended particles in a wine can increase the stability of a wine and prevent some of these undesirable characteristic to emerge. The process of clarification does, in itself, increase the stability of the wine by removing some of these particles. Conversely, the process of stabilization can also increase the clarity and brightness of a wine.

Temperature instability

Tartaric acid is the most prominent acid in wine with the majority of the concentration present as potassium acid salt. During fermentation, these tartrates bind with the lees, pulp debris and precipitated tannins and pigments. While there is some variance among grape varieties and wine regions, generally about half of the deposits are soluble in the alcoholic mixture of wine. The crystallization of these tartrates can happen at unpredictable times if the wine is exposed to low temperature. These crystals can appear in a wine bottle looking like broken glass (though they are in fact harmless) and their presence may be undesirable to consumers. To prevent this from happening after the wine has been bottled, winemakers stabilize the wine by putting it through a **cold stabilization** process where it is exposed to temperatures below freezing to encourage the tartrates to crystallize and precipitate out of the wine. Some white grape varieties (such as Muscat) have significant quantities of proteins that are "heat-unstable" and will coagulate if the wine is exposed to excessive amount of heat fluctuations, making the wine appear hazy and cloudy. Winemakers will use fining agents, such as bentonite, to remove these proteins and increase the heat stability of the wine.

Microbiological instability

Dead yeast cells (lees-*pictured*), still present in a wine can make wine look hazy and cloudy. Active yeast cells can trigger a secondary fermentation.

Both active yeast cells and bacteria may be present in a wine after it has gone through the fermentation process and is bottled. If the wine still contains some residual sugar, the active yeast cells will initiate a secondary fermentation process inside the bottle that will create dissolved carbonic gas as a by-product. When the wine is opened, it will be gassy or "sparkling". While this may be a desirable trait for some wines (such as Champagne where a deliberate initiation of a secondary fermentation is part of production), it is not desirable for wines intended to be still or non-sparkling--such as Burgundy Pinot noir or a Washington Merlot. The easiest way to stabilize the wine is to ensure that there is no fermentable sugars left in the wine but in cases where some residual sugar in desirable (such as to balance the acidity of the wine) other methods can be taken to stabilize the wine. One method is sterile filtration and bottling which ensures that no active yeast are present in the wine. Another method is the addition of sulfur dioxide and sorbic acid which can inhibit the growth of yeast cells.

Modern advances in hygiene has eliminated many of the bacterial concerns that contribute to wine stability. Historically the presence of bacteria played a larger role in the developing of various wine faults. The primary concern in modern wineries is the presence of acetobacter which can turn wine into vinegar and lactic acid bacteria that can initiate malolactic fermentation which may not be desirable for certain wines. Acetobacter is active in the presence of oxygen so taking preventative measures, such as the use of sulfur dioxide, can suppress the growth of acetobacter. Eliminating the presence of fermentable sugars and malic acid can inhibit the growth of lactic acid bacteria and stabilize the wine.

Other methods of stabilization

The clarification methods of fining and filtration also act to stabilize wine by removing some of the same particles that can promote instability. The subtle oxidation that occurs with oak barrel aging has a naturally stabilizing effect on the wine.

Pasteurization

A wine can be stabilized by a method of heat sterilization, commonly known as pasteurization. The purpose of this technique is to bring the wine up to high enough temperatures that all micro-organisms in the wine (namely yeast and bacteria) are killed. For kosher wines, the production of *mevushal* wines (literally "cooked" or "boiled") heat sterilizes the wine to where non-Jews and non-observant Jews can handle the wine and still maintain its kosher status. In the process of pasteurization, wines are brought up to temperatures of 185°F (85°C) for a minute and then quickly cooled to a temperature of 122°F (50°C) where it is kept for up to 3 days. The wine may then be allowed to cool down to room temperature or be bottled "hot" and cooled by water sprays. This process can be rough on a wine and could diminish flavors and aging potential. A more gentle procedure known as flash pasteurization has been developed which heats the wine to 205°F (95°C) for a few seconds, followed by rapid cooling.

Premium wine production

Not all producers decide to thoroughly clarify and stabilize their wines, believing that some of a wine's flavor, aging potential and complexity come from some of the suspended particles. Wine experts, such as Tom Stevenson, notes that techniques like filtration can improve wine quality in moderation but can also diminish quality if used excessively. The consumers of some premium wines (such as Bordeaux and Port) may expect to see tartrates and sediment from a wine that has been aging and not thoroughly filtered.

Chapter- 12

Crystallization

Crystallization is the (natural or artificial) process of formation of solid crystals precipitating from a solution, melt or more rarely deposited directly from a gas. Crystallization is also a chemical solid-liquid separation technique, in which mass transfer of a solute from the liquid solution to a pure solid crystalline phase occurs.

Frost crystallization on a shrub.

Process

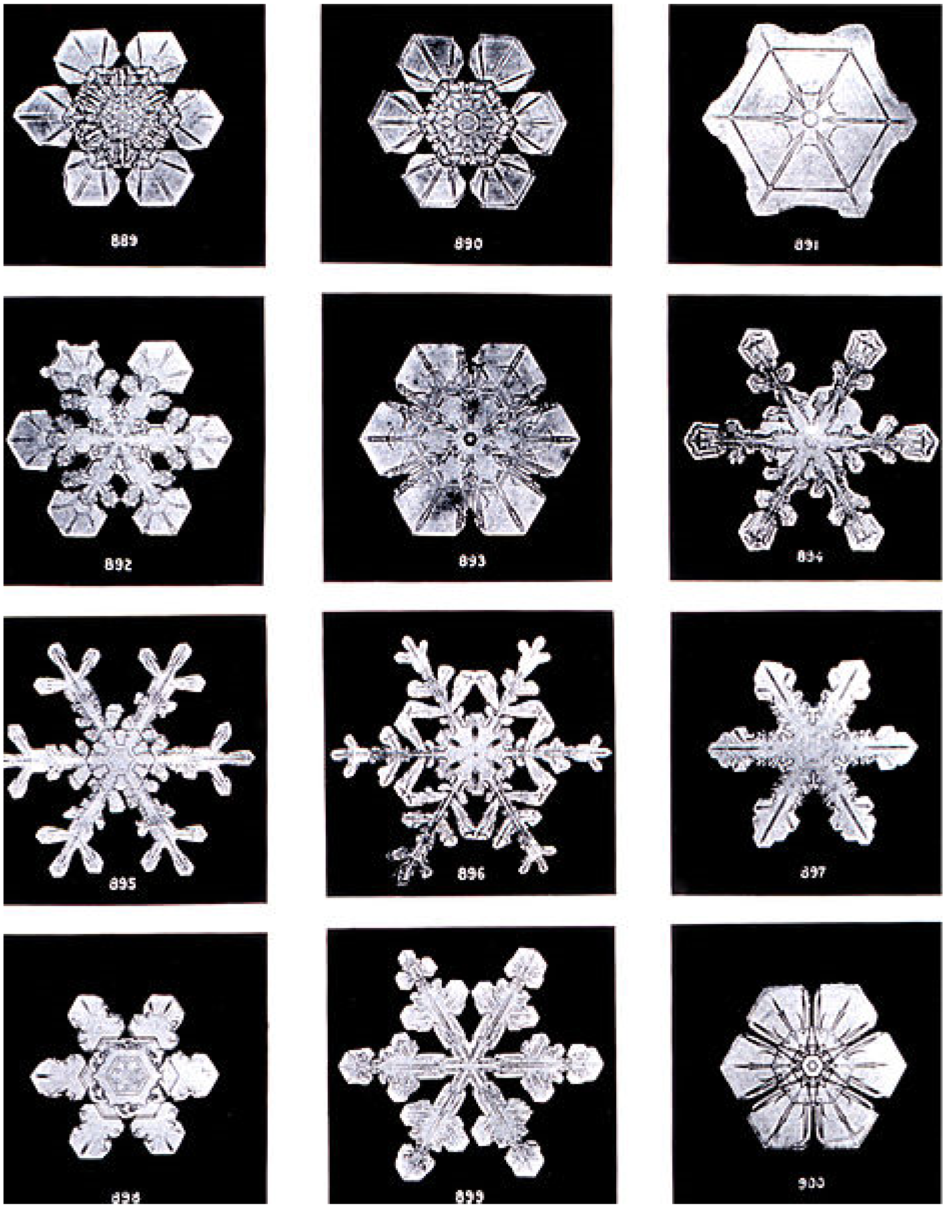
Time-lapse of growth of a citric acid crystal. The video covers an area of 2.0 by 1.5 mm and was captured over 7.2 min.

The crystallization process consists of two major events, *nucleation* and *crystal growth*. *Nucleation* is the step where the solute molecules dispersed in the solvent start to gather into clusters, on the nanometer scale (elevating solute concentration in a small region), that becomes stable under the current operating conditions. These stable clusters constitute the nuclei. However when the clusters are not stable, they redissolve. Therefore, the clusters need to reach a critical size in order to become stable nuclei. Such critical size is dictated by the operating conditions (temperature, supersaturation, etc.). It is at the stage of nucleation that the atoms arrange in a defined and periodic manner that defines the crystal structure — note that "crystal structure" is a special term that refers to the relative arrangement of the atoms, not the macroscopic properties of the crystal (size and shape), although those are a result of the internal crystal structure.

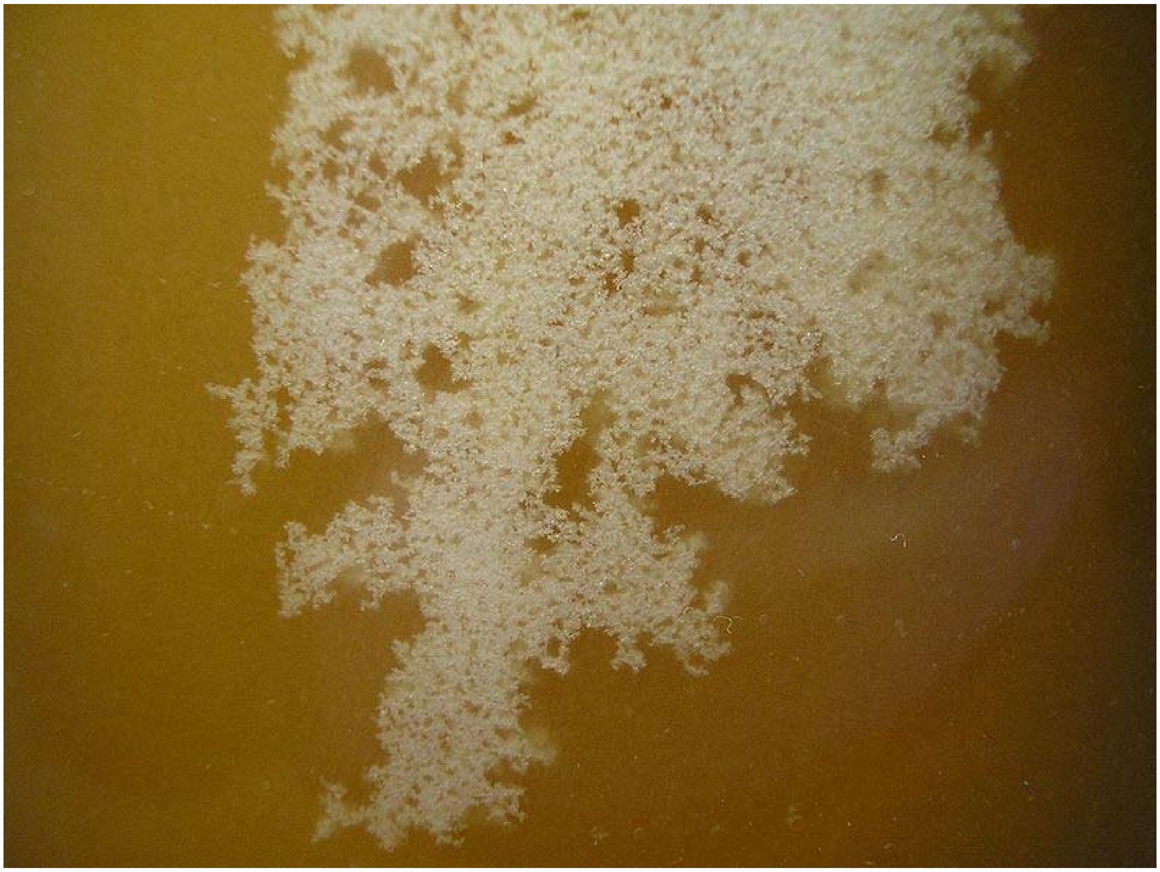
The *crystal growth* is the subsequent growth of the nuclei that succeed in achieving the critical cluster size. Nucleation and growth continue to occur simultaneously while the supersaturation exists. Supersaturation is the driving force of the crystallization, hence the rate of nucleation and growth is driven by the existing supersaturation in the solution. Depending upon the conditions, either nucleation or growth may be predominant over the other, and as a result, crystals with different sizes and shapes are obtained (control of crystal size and shape constitutes one of the main challenges in industrial manufacturing, such as for pharmaceuticals). Once the supersaturation is exhausted, the solid-liquid system reaches equilibrium and the crystallization is complete, unless the operating conditions are modified from equilibrium so as to supersaturate the solution again.

Many compounds have the ability to crystallize with different crystal structures, a phenomenon called polymorphism. Each polymorph is in fact a different thermodynamic solid state and crystal polymorphs of the same compound exhibit different physical properties, such as dissolution rate, shape (angles between facets and facet growth rates), melting point, etc. For this reason, polymorphism is of major importance in industrial manufacture of crystalline products.

Crystallization in nature



Snowflakes are a very well known example, where subtle differences in *crystal growth* conditions result in different geometries.



Crystallized honey

There are many examples of natural process that involve crystallization.

Geological time scale process examples include:

- Natural (mineral) crystal formation;
- Stalactite/stalagmite, rings formation.

Usual time scale process examples include:

- Snow flakes formation;
- Honey crystallization (nearly all types of honey crystallize).

Artificial methods

For crystallization to occur from a solution it must be supersaturated. This means that the solution has to contain more solute entities (molecules or ions) dissolved than it would contain under the equilibrium (saturated solution). This can be achieved by various methods, with (1) solution cooling, (2) addition of a second solvent to reduce the solubility of the solute (technique known as antisolvent or drown-out), (3) chemical reaction and (4) change in pH being the most common methods used in industrial practice. Other methods, such as solvent evaporation, can also be used. The spherical crystallization has some advantages (flowability and bioavailability) for the formulation of pharmaceutical drugs

Applications

There are two major groups of applications for the *artificial crystallization* process: *crystal production* and purification.

Crystal production

From a material industry perspective:

- *Macroscopic crystal* production: for supply the demand of natural-like crystals with methods that "accelerate time-scale" for massive production and/or perfection.
    - *Ionic crystal* production;
    - *Covalent crystal* production.
- *Tiny size crystal*s:
    - *Powder, sand and smaller sizes*: using methods for powder and controlled (nanotechnology fruits) forms.
        - *Mass-production*: on chemical industry, like salt-powder production.
        - *Sample production*: small production of tiny crystals for material characterization. Controlled recrystallization is an important method to supply unusual crystals, that are needed to reveal the molecular structure and nuclear forces inside a typical molecule of a crystal. Many techniques, like X-ray crystallography and NMR spectroscopy, are widely used in chemistry and biochemistry to determine the structures of an immense variety of molecules, including inorganic compounds and bio-macromolecules.
    - Thin film production.

Massive production examples:

- "Powder salt for food" industry;
- Silicon crystal wafer production.
- Production of sucrose from sugar beet, where the sucrose is crystallized out from an aqueous solution.

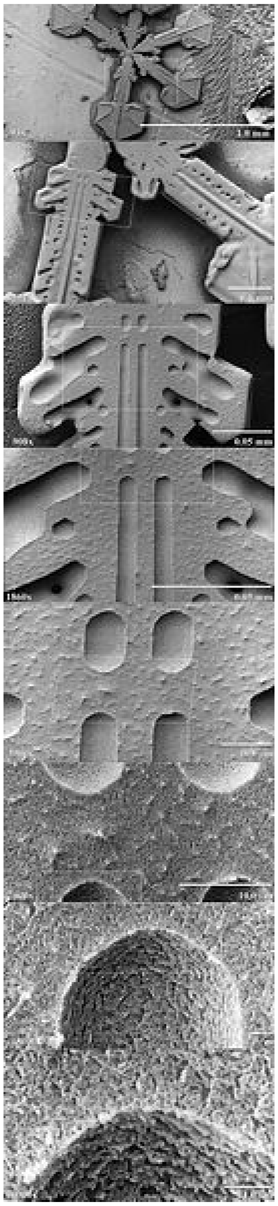
Purification

Used to improve (obtaining very pure substance) and/or verify their purity.

Crystallization separates a product from a liquid feedstream, often in extremely pure form, by cooling the feedstream or adding precipitants which lower the solubility of the desired product so that it forms crystals.

Well formed crystals are expected to be pure because each molecule or ion must fit perfectly into the lattice as it leaves the solution. Impurities would normally not fit as well in the lattice, and thus remain in solution preferentially. Hence, molecular recognition is the principle of purification in crystallization. However, there are instances when impurities incorporate into the lattice, hence, decreasing the level of purity of the final crystal product. Also, in some cases, the solvent may incorporate into the lattice forming a *solvate*. In addition, the solvent may be 'trapped' (in liquid state) within the crystal formed, and this phenomenon is known as *inclusion*.

Thermodynamic view



Low-temperature SEM magnification series for a snow crystal. The crystals are captured, stored, and sputter coated with platinum at cryo-temperatures for imaging.

The nature of a crystallization process is governed by both thermodynamic and kinetic factors, which can make it highly variable and difficult to control. Factors such as impurity level, mixing regime, vessel design, and cooling profile can have a major impact on the size, number, and shape of crystals produced.

Now put yourself in the place of a molecule within a pure and *perfect crystal*, being heated by an external source. At some sharply defined temperature, a bell rings, you must leave your neighbours, and the complicated architecture of the crystal collapses to that of a liquid. Textbook thermodynamics says that melting occurs because the entropy, S, gain in your system by spatial randomization of the molecules has overcome the enthalpy, H, loss due to breaking the crystal packing forces:

$$T(S_{liquid} - S_{solid}) > H_{liquid} - H_{solid}$$

$$G_{liquid} < G_{solid}$$

This rule suffers no exceptions when the temperature is rising. By the same token, on cooling the melt, at the very same temperature the bell should ring again, and molecules should click back into the very same crystalline form. The entropy decrease due to the ordering of molecules within the system is overcompensated by the thermal randomization of the surroundings, due to the release of the heat of fusion; the entropy of the universe increases.

But liquids that behave in this way on cooling are the exception rather than the rule; in spite of the second principle of thermodynamics, crystallization usually occurs at lower temperatures (supercooling). This can only mean that a crystal is more easily destroyed than it is formed. Similarly, it is usually much easier to dissolve a perfect crystal in a solvent than to grow again a good crystal from the resulting solution. The nucleation and growth of a crystal are under kinetic, rather than thermodynamic, control.

Equipment for crystallization

1. *Tank crystallizers*. Tank crystallization is an old method still used in some specialized cases. Saturated solutions, in tank crystallization, are allowed to cool in open tanks. After a period of time the mother liquid is drained and the crystals removed. Nucleation and size of crystals are difficult to control. Typically, labor costs are very high.
2. *Scraped surface crystallizers*. One type of scraped surface crystallizer is the Swenson-Walker crystallizer, which consists of an open trough 0.6 m wide with a semicircular bottom having a cooling jacket outside. A slow-speed spiral agitator rotates and suspends the growing crystals on turning. The blades pass close to the wall and break off any deposits of crystals on the cooled wall. The product generally has a somewhat wide crystal-size distribution.
3. *Double-pipe scraped surface crystallizer*. Also called a *votator*, this type of crystallizer is used in crystallizing ice cream and plasticizing margarine. Cooling water passes in the annular space. An internal agitator is fitted with spring-loaded scrapers that wipe the wall and provide good heat-transfer coefficients.

4. *Circulating-liquid evaporator-crystallizer*. Also called *Oslo crystallizer*. Here supersaturation is reached by evaporation. The circulating liquid is drawn by the screw pump down inside the tube side of the condensing stream heater. The heated liquid then flows into the vapor space, where flash evaporation occurs, giving some supersaturation.The vapor leaving is condensed. The supersaturated liquid flows down the downflow tube and then up through the bed of fluidized and agitated crystals, which are growing in size. The leaving saturated liquid then goes back as a recycle stream to the heater, where it is joined by the entering fluid. The larger crystals settle out and slurry of crystals and mother liquid is withdrawn as a product.
5. *Circulating-magma vacuum crystallizer*. The magma or suspension of crystals is circulated out of the main body through a circulating pipe by a screw pump. The magma flows though a heater, where its temperature is raised 2-6 K. The heated liquor then mixes with body slurry and boiling occurs at the liquid surface. This causes supersaturation in the swirling liquid near the surface, which deposits in the swirling suspended crystals until they leave again via the circulating pipe. The vapors leave through the top. A steam-jet ejector provides vacuum.
6. *Continuous oscillatory baffled crystallizer* (*COBC*). The COBC is a tubular baffled crystallizer that offers plug flow under laminar flow conditions (low flow rates) with superior heat transfer coefficient, allowing controlled cooling profiles, e.g. linear, parabolic, discontinued, step-wise or any type, to be achieved. This gives much better control over crystal size, morphology and consistent crystal products.

Chapter- 13

Crystallization (engineering aspects)

In chemical engineering **crystallization** occurs in a **crystallizer**. Crystallization is a unit operation through which a chemical compound, dissolved in a given solvent, precipitates under certain conditions to allow successive separation between the phases.

Crystallization is therefore an aspect of precipitation, obtained through a variation of the solubility conditions of the solute in the solvent, as compared to precipitation due to chemical reaction.

History

Crystallization is one of the pristine unit processes. It may be assumed that our ancestors used sodium chloride found in crevices of the surface rocks after drying caused by the sun: this process is still in use in modern solar ponds.

Other crystallization processes, for example sucrose production (this is the crystalline product with the largest world production, followed by sodium chloride), or in pigment manufacturing, were used in ancient times. These substances were sometimes produced by crystallizing the solutes of some more or less natural brine.

In more recent times, the fast expansion of the chemical industry has required a thorough study of the dynamics of crystallization, and this unit operation is now used in many industrial manufacturing areas: table salt, sugar, sodium sulfate, urea, just to name a few, are produced by crystallization from solutions.

Crystallizer technology has progressed alongside with the new processes. Once simple tanks in which, through cooling, evaporation or maybe through pH variation a crystal was obtained, nowadays continuous machines ensure a remarkable consistency in the product characteristics. Among the first models of modern crystallizers were probably the *calandria* type, being today the standard crystallizer for sucrose, and the *Oslo*, named after the Norwegian capital, since it was developed to produce salt in a climate not particularly fit for solar ponds, salt being widely used in Norway in stockfish production. The Oslo type was probably the first crystallizer designed specifically for the control of crystal growth.

Crystallization dynamics

As mentioned above, a crystal is formed following a well-defined pattern, or structure, dictated by forces acting at the molecular level. As a consequence, during its formation process the crystal is in an environment where the solute concentration reaches a certain critical value, before changing status. Solid formation, impossible below the solubility threshold at the given temperature and pressure conditions, may then take place at a concentration higher than the theoretical solubility level. The difference between the actual value of the solute concentration at the crystallization limit and the theoretical (static) solubility threshold is called supersaturation and is a fundamental factor in crystallization dynamics. Supersaturation is the driving force for both the initial nucleation step and the following crystal growth, both of which could not occur in saturated or undersaturated conditions.

Nucleation

Nucleation is the initiation of a phase change in a small region, such as the formation of a solid crystal from a liquid solution. It is a consequence of rapid local fluctuations on a molecular scale in a homogeneous phase that is in a state of metastable equilibrium. Total nucleation is the sum effect of two categories of nucleation - primary and secondary.

Primary nucleation

Primary nucleation is the initial formation of a crystal where there are no other crystals present or where, if there are crystals present in the system, they do not have any influence on the process. This can occur in two conditions. The first is homogeneous nucleation, which is nucleation that is not influenced in any way by solids. These solids include the walls of the crystallizer vessel and particles of any foreign substance. The second category, then, is heterogeneous nucleation. This occurs when solid particles of foreign substances cause an increase in the rate of nucleation that would otherwise not be seen without the existence of these foreign particles. Homogeneous nucleation rarely occurs in practice due to the high energy necessary to begin nucleation without a solid surface to catalyse the nucleation.

Primary nucleation (both homogeneous and heterogeneous) has been modelled with the following:

$$B = \frac{dN}{dt} = k_n(c - c^*)^n$$

- B is the number of nuclei formed per unit volume per unit time.
- N is the number of nuclei per unit volume.
- k_{np} is a rate constant.
- c is the instantaneous solute concentration.
- c^* is the solute concentration at saturation.
- $(c-c^*)$ is also known as supersaturation.

- n is an empirical exponent that can be as large as 10, but generally ranges between 3 and 4.

Secondary nucleation

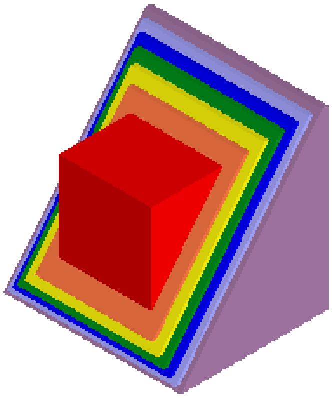
Secondary nucleation is the formation of nuclei attributable to the influence of the existing microscopic crystals in the magma. The first type of known secondary crystallization is attributable to fluid shear, the other due to collisions between already existing crystals with either a solid surface of the crystallizer or with other crystals themselves. Fluid shear nucleation occurs when liquid travels across a Crystal at a high speed, sweeping away nuclei that would otherwise be incorporated into a Crystal, causing the swept-away nuclei to become new crystals. Contact nucleation has been found to be the most effective and common method for nucleation. The benefits include the following

- Low kinetic order and rate-proportional to supersaturation, allowing easy control without unstable operation.
- Occurs at low supersaturation, where growth rate is optimum for good quality.
- Low necessary energy at which crystals strike avoids the breaking of existing crystals into new crystals.
- The quantitative fundamentals have already been isolated and are being incorporated into practice.

The following model, although somewhat simplified, is often used to model secondary nucleation:

$$B = \frac{dN}{dt} = k_1 M_T^j (c - c^*)^b$$

- k_1 is a rate constant.
- M_T is the suspension density.
- j is an empirical exponent that can range up to 1.5, but is generally 1.
- b is an empirical exponent that can range up to 5, but is generally 2.



Crystal growth

Crystal growth

Once the first small crystal, the nucleus, forms it acts as a convergence point (if unstable due to supersaturation) for molecules of solute touching - or adjacent to - the crystal so that it increases its own dimension in successive layers. The pattern of growth resembles the rings of an onion, as shown in the picture, where each colour indicates the same mass of solute; this mass creates increasingly thin layers due to the increasing surface area of the growing crystal. The supersaturated solute mass the original nucleus may *capture* in a time unit is called the *growth rate* expressed in kg/(m^2*h), and is a constant specific to the process. Growth rate is influenced by several physical factors, such as surface tension of solution, pressure, temperature, relative crystal velocity in the solution, Reynolds number, and so forth.

The main values to control are therefore:

- Supersaturation value, as an index of the quantity of solute available for the growth of the crystal;
- Total crystal surface in unit fluid mass, as an index of the capability of the solute to fix onto the crystal;
- Retention time, as an index of the probability of a molecule of solute to come into contact with an existing crystal;
- Flow pattern, again as an index of the probability of a molecule of solute to come into contact with an existing crystal (higher in laminar flow, lower in turbulent flow, but the reverse applies to the probability of contact).

The first value is a consequence of the physical characteristics of the solution, while the others define a difference between a well- and poorly designed crystallizer.

Crystal size distribution

The appearance and size range of a crystalline product is extremely important in crystallization. If further processing of the crystals is desired, large crystals with uniform size are important for washing, filtering, transportation, and storage. The importance lies in the fact that large crystals are easier to filter out of a solution than small crystals. Also, larger crystals have a smaller surface area to volume ratio, leading to a higher purity. This higher purity is due to less retention of mother liquor which contains impurities, and a smaller loss of yield when the crystals are washed to remove the mother liquor. The theoretical crystal size distribution can be estimated as a function of operating conditions with a fairly complicated mathematical process called population balance theory (using population balance equations).

Main crystallization processes

The main factors influencing solubility are, as we saw above:

- Concentration
- Temperature

So we may identify two main families of crystallization processes:

- Cooling crystallization
- Evaporative crystallization

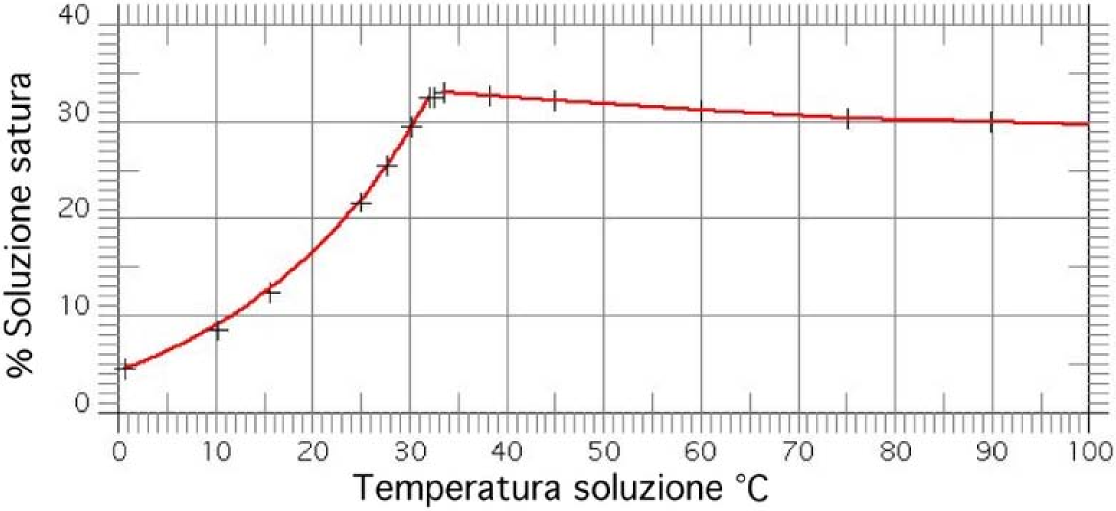
This division is not really clear-cut, since hybrid systems exist, where cooling is performed through evaporation, thus obtaining at the same time a concentration of the solution.

A crystallization process often referred to in chemical engineering is the Fractional crystallization. This is not a different process, rather a special application of one (or both) of the above.

Cooling crystallization

Application

Most chemical compounds, dissolved in most solvents, show the so-called *direct* solubility that is, the solubility threshold increases with temperature.



Solubility of the system Na_2SO_4 - H_2O

So, whenever the conditions are favourable, crystal formation results from simply cooling the solution. Here *cooling* is a relative term: austenite crystals in a steel form well above 1000 °C. An example of this crystallization process is the production of Glauber's salt, a crystalline form of sodium sulphate. In the picture, where equilibrium temperature is on the x-axis and equilibrium concentration (as mass percent of solute in saturated solution) in y-axis, it is clear that sulphate solubility quickly decreases below 32.5 °C. Assuming a saturated solution at 30 °C, by cooling it to 0 °C (note that this is possible thanks to the freezing-point depression), the precipitation of a mass of sulphate occurs corresponding to the change in solubility from 29% (equilibrium value at 30°C) to approximately 4.5%

(at 0°C) - actually a larger crystal mass is precipitated, since sulphate entrains hydration water, and this has the side effect of increasing the final concentration.

There are of course limitation in the use of cooling crystallization:

- Many solutes precipitate in hydrate form at low temperatures: in the previous example this is acceptable, and even useful, but it may be detrimental when, for example, the mass of water of hydration to reach a stable hydrate crystallization form is more than the available water: a single block of hydrate solute will be formed - this occurs in the case of calcium chloride);
- Maximum supersaturation will take place in the coldest points. These may be the heat exchanger tubes which are sensitive to scaling, and heat exchange may be greatly reduced or discontinued;
- A decrease in temperature usually implies an increase of the viscosity of a solution. Too high a viscosity may give hydraulic problems, and the laminar flow thus created may affect the crystallization dynamics.
- It is of course not applicable to compounds having *reverse* solubility, a term to indicate that solubility increases with temperature decrease (an example occurs with sodium sulphate where solubility is reversed above 32.5 °C).

Cooling crystallizers

The simplest cooling crystallizers are tanks provided with a mixer for internal circulation, where temperature decrease is obtained by heat exchange with an intermediate fluid circulating in a jacket. These simple machines are used in batch processes, as in processing of pharmaceuticals and are prone to scaling. Batch processes normally provide a relatively variable quality of product along the batch.

The *Swenson-Walker* crystallizer is a model, specifically conceived by Swenson Co. around 1920, having a semicylindric horizontal hollow trough in which a hollow screw conveyor or some hollow discs, in which a refrigerating fluid is circulated, plunge during rotation on a longitudinal axis. The refrigerating fluid is sometimes also circulated in a jacket around the trough. Crystals precipitate on the cold surfaces of the screw/discs, from which they are removed by scrapers and settle on the bottom of the trough. The screw, if provided, pushes the slurry towards a discharge port.

A common practice is to cool the solutions by flash evaporation: when a liquid at a given T_0 temperature is transferred in a chamber at a pressure P_1 such that the liquid saturation temperature T_1 at P_1 is lower than T_0, the liquid will release heat according to the temperature difference and a quantity of solvent, whose total latent heat of vaporization equals the difference in enthalpy. In simple words, the liquid is cooled by evaporating a part of it.

Evaporative crystallization

Another option is to obtain, at an approximately constant temperature, the precipitation of the crystals by increasing the solute concentration above the solubility threshold. To obtain this, the solute/solvent mass ratio is increased using the technique of evaporation. This process is of course insensitive to change in temperature (as long as hydration state remains unchanged).

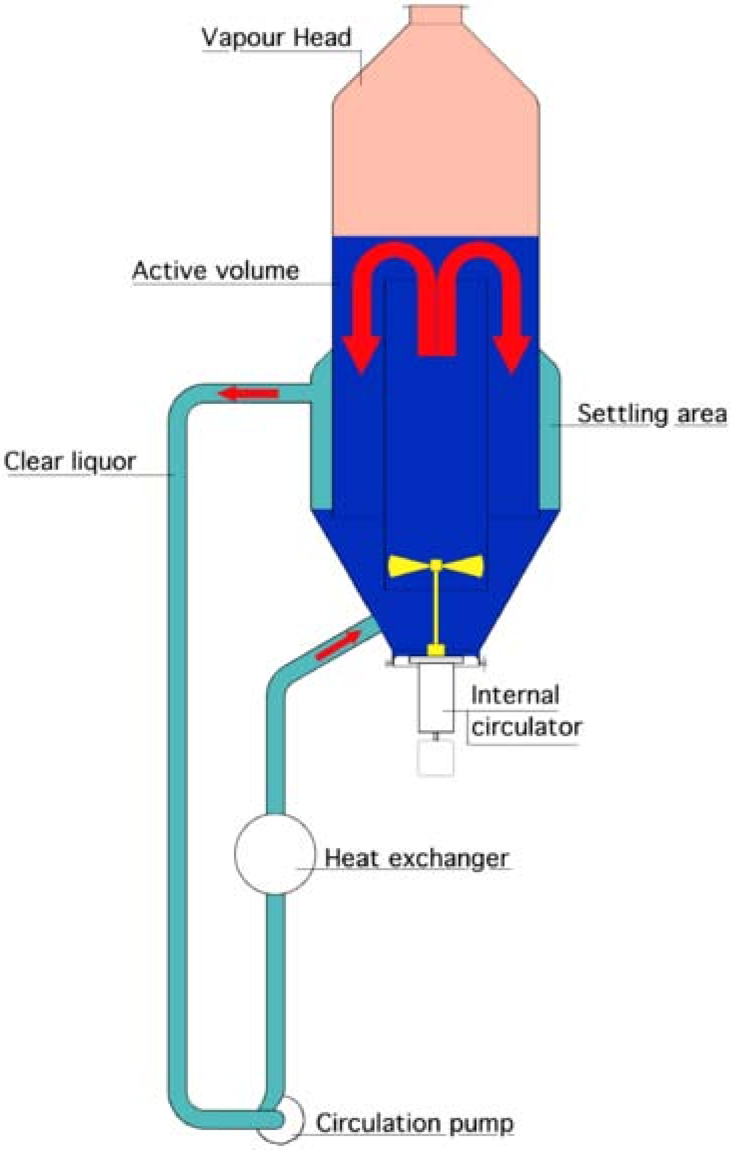
All considerations on control of crystallization parameters are the same as for the cooling models.

Evaporative crystallizers

Most industrial crystallizers are of the evaporative type, such as the very large sodium chloride and sucrose units, whose production accounts for more than 50% of the total world production of crystals. The most common type is the *forced circulation* (FC) model. A pumping device (a pump or an axial flow mixer) keeps the crystal slurry in homogeneous suspension throughout the tank, including the exchange surfaces; by controlling pump flow, control of the contact time of the crystal mass with the supersaturated solution is achieved, together with reasonable velocities at the exchange surfaces. The Oslo, mentioned above, is a refining of the evaporative forced circulation crystallizer, now equipped with a large crystals settling zone to increase the retention time (usually low in the FC) and to roughly separate heavy slurry zones from clear liquid.

The DTB crystallizer

DTB Crystallizer

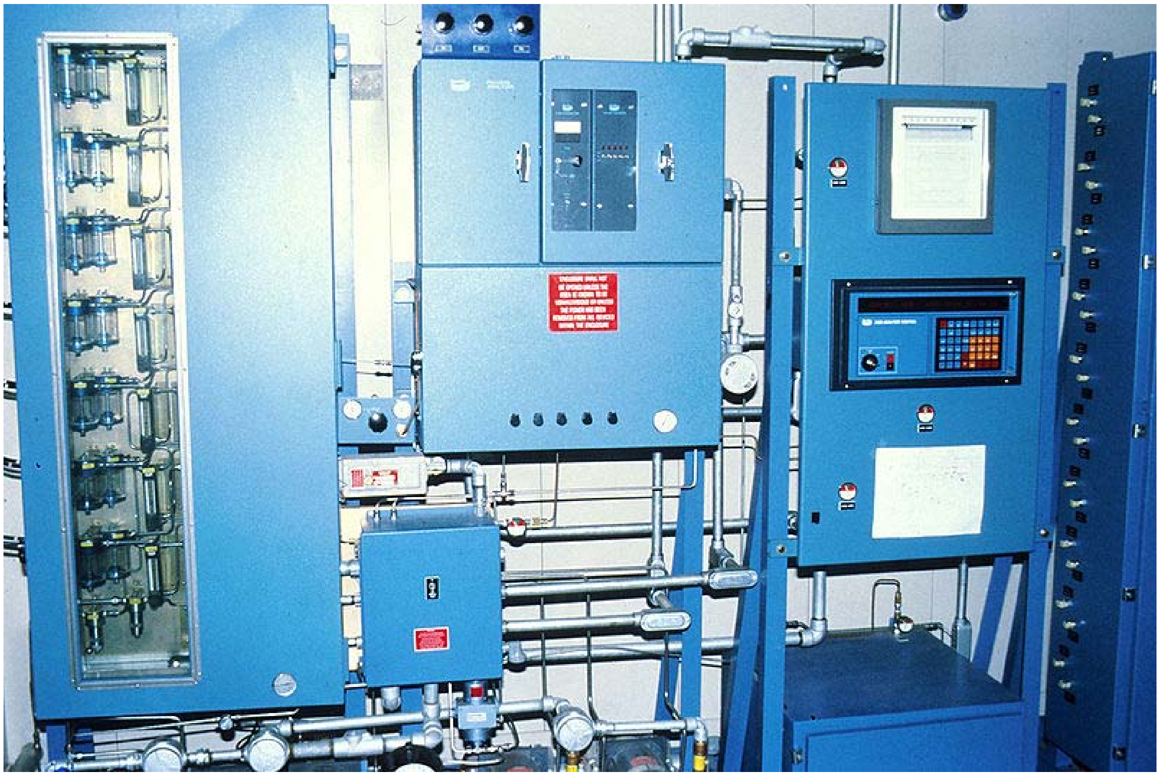


Schematic of DTB

Whichever the form of the crystallizer, to achieve an effective process control it is important to control the retention time and the crystal mass, to obtain the optimum conditions in terms of crystal specific surface and the fastest possible growth. This is achieved by a separation - to put it simply - of the crystals from the liquid mass, in order to manage the two flows in a different way. The practical way is to perform a gravity settling to be able to extract (and possibly recycle separately) the (almost) clear liquid, while managing the mass flow around the crystallizer to obtain a precise slurry density elsewhere. A typical example is the DTB (*Draft Tube and Baffle*) crystallizer, an idea of Richard Chisum Bennett (a Swenson engineer and later President of Swenson) at the end of the 1950s. The DTB crystallizer has an internal circulator, typically an axial flow mixer - yellow - pushing upwards in a draft tube while outside the crystallizer there is a settling area in an annulus; in it the exhaust solution moves upwards at a very low velocity, so that large crystals settle - and return to the main circulation - while only the fines, below a given grain size are extracted and eventually destroyed by increasing or decreasing temperature, thus creating additional supersaturation. A quasi-perfect control of all parameters is achieved. This crystallizer, and the derivative models (Krystal, CSC, etc.) could be the ultimate solution if not for a major limitation in the evaporative capacity, due to the limited diameter of the vapour head and the relatively low external circulation not allowing large amounts of energy to be supplied to the system.

Chapter- 14

Chromatography



Pictured is a sophisticated gas chromatography system. This instrument records concentrations of acrylonitrile in the air at various points throughout the chemical laboratory.

Chromatography (from Greek χρῶμα *chroma* "color" and γράφειν *graphein* "to write") is the collective term for a set of laboratory techniques for the separation of mixtures. It involves passing a mixture dissolved in a "mobile phase" through a *stationary phase*, which separates the analyte to be measured from other molecules in the mixture based on differential partitioning between the mobile and stationary phases. Subtle differences in a compound's partition coefficient result in differential retention on the stationary phase and thus **changing** the separation.

Chromatography may be preparative or analytical. The purpose of preparative chromatography is to separate the components of a mixture for further use (and is thus a form of purification). Analytical chromatography is done normally with smaller amounts of material and is for measuring the relative proportions of analytes in a mixture. The two are not mutually exclusive.

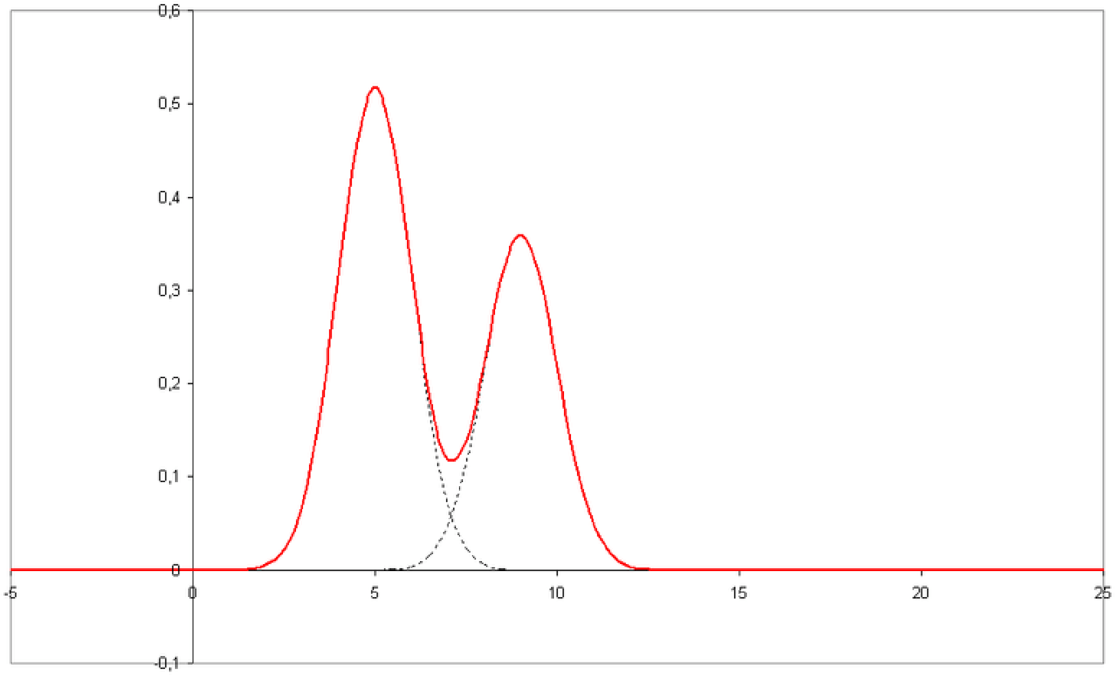
History

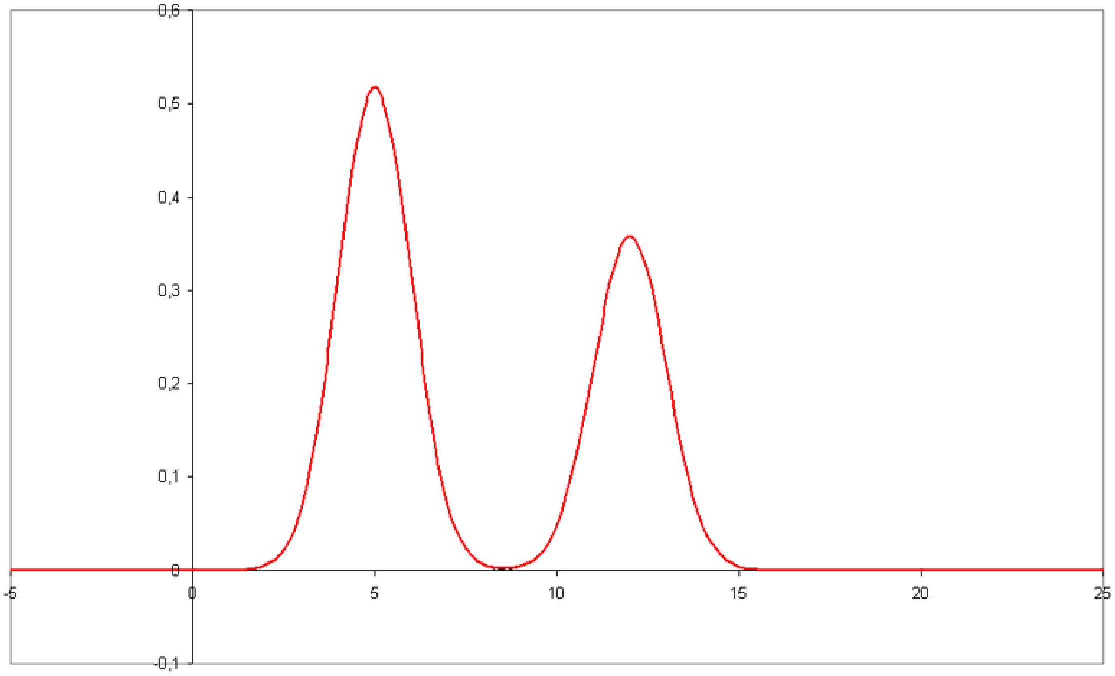
The **history of chromatography** begins during the mid-19th century. Chromatography, literally "color writing", was used—and named— in the first decade of the 20th century, primarily for the separation of plant pigments such as chlorophyll. New types of chromatography developed during the 1930s and 1940s made the technique useful for many types of separation process.

Chromatography became developed substantially as a result of the work of Archer John Porter Martin and Richard Laurence Millington Synge during the 1940s and 1950s. They established the principles and basic techniques of partition chromatography, and their work encouraged the rapid development of several types of chromatography method: paper chromatography, gas chromatography, and what would become known as high performance liquid chromatography. Since then, the technology has advanced rapidly. Researchers found that the main principles of Tsvet's chromatography could be applied in many different ways, resulting in the different varieties of chromatography described below. Simultaneously, advances continually improved the technical performance of chromatography, allowing the separation of increasingly similar molecules.

Chromatography terms

- The **analyte** is the substance to be separated during chromatography.
- **Analytical chromatography** is used to determine the existence and possibly also the concentration of analyte(s) in a sample.
- A **bonded phase** is a stationary phase that is covalently bonded to the support particles or to the inside wall of the column tubing.
- A **chromatogram** is the visual output of the chromatograph. In the case of an optimal separation, different peaks or patterns on the chromatogram correspond to different components of the separated mixture.





Plotted on the x-axis is the retention time and plotted on the y-axis a signal (for example obtained by a spectrophotometer, mass spectrometer or a variety of other detectors) corresponding to the response created by the analytes exiting the system. In the case of an optimal system the signal is proportional to the concentration of the specific analyte separated.

- A **chromatograph** is equipment that enables a sophisticated separation e.g. gas chromatographic or liquid chromatographic separation.

- **Chromatography** is a physical method of separation in which the components to be separated are distributed between two phases, one of which is stationary (stationary phase) while the other (the mobile phase) moves in a definite direction.
- The **eluate** is the mobile phase leaving the column.
- The **eluent** is the solvent that will carry the analyte.
- An **eluotropic series** is a list of solvents ranked according to their eluting power.
- An **immobilized phase** is a stationary phase which is immobilized on the support particles, or on the inner wall of the column tubing.
- The **mobile phase** is the phase which moves in a definite direction. It may be a liquid (LC and CEC), a gas (GC), or a supercritical fluid (supercritical-fluid chromatography, SFC). The mobile phase consists of the sample being separated/analyzed and the solvent that moves the sample through the column. In the case of HPLC the mobile phase consists of a non-polar solvent(s) such as hexane in normal phase or polar solvents in reverse phase chromotagraphy and the sample being separated. The mobile phase moves through the chromatography column (the stationary phase) where the sample interacts with the stationary phase and is separated.
- **Preparative chromatography** is used to purify sufficient quantities of a substance for further use, rather than analysis.
- The **retention time** is the characteristic time it takes for a particular analyte to pass through the system (from the column inlet to the detector) under set conditions.
- The **sample** is the matter analyzed in chromatography. It may consist of a single component or it may be a mixture of components. When the sample is treated in the course of an analysis, the phase or the phases containing the analytes of interest is/are referred to as the sample whereas everything out of interest separated from the sample before or in the course of the analysis is referred to as waste.
- The **solute** refers to the sample components in partition chromatography.
- The **solvent** refers to any substance capable of solubilizing other substance, and especially the liquid mobile phase in LC.
- The **stationary phase** is the substance which is fixed in place for the chromatography procedure. Examples include the silica layer in thin layer chromatography

Chromatography is based on the concept of partition coffecient. Any solute will partition between two immissible solvents. When we make one solvent immobile (by adsorption on a solid support matrix) and another mobile it results in most common applications of chromatography. If matrix support is polar (e.g. paper, sillica etc.) it is forward phase chromatography, and if it is non polar (C-18) it is reverse phase.

Techniques by chromatographic bed shape

Column chromatography

Column chromatography is a separation technique in which the stationary bed is within a tube. The particles of the solid stationary phase or the support coated with a liquid stationary phase may fill the whole inside volume of the tube (packed column) or be concentrated on or along the inside tube wall leaving an open, unrestricted path for the mobile phase in the middle part of the tube (open tubular column). Differences in rates of movement through the medium are calculated to different retention times of the sample.

In 1978, W. C. Still introduced a modified version of column chromatography called **flash column chromatography** (flash). The technique is very similar to the traditional column chromatography, except for that the solvent is driven through the column by applying positive pressure. This allowed most separations to be performed in less than 20 minutes, with improved separations compared to the old method. Modern flash chromatography systems are sold as pre-packed plastic cartridges, and the solvent is pumped through the cartridge. Systems may also be linked with detectors and fraction collectors providing automation. The introduction of gradient pumps resulted in quicker separations and less solvent usage.

In expanded bed adsorption, a fluidized bed is used, rather than a solid phase made by a packed bed. This allows omission of initial clearing steps such as centrifugation and filtration, for culture broths or slurries of broken cells.

Planar chromatography

Thin layer chromatography is used to separate components of chlorophyll

Planar chromatography is a separation technique in which the stationary phase is present as or on a plane. The plane can be a paper, serving as such or impregnated by a substance as the stationary bed (paper chromatography) or a layer of solid particles spread on a support such as a glass plate (thin layer chromatography). Different compounds in the sample mixture travel different distances according to how strongly they interact with the stationary phase as compared to the mobile phase. The specific Retention factor (R_f) of each chemical can be used to aid in the identification of an unknown substance.

Paper chromatography

Paper chromatography is a technique that involves placing a small dot or line of sample solution onto a strip of *chromatography paper*. The paper is placed in a jar containing a shallow layer of solvent and sealed. As the solvent rises through the paper, it meets the sample mixture which starts to travel up the paper with the solvent. This paper is made of cellulose, a polar substance, and the compounds within the mixture travel farther if they are non-polar. More polar substances bond with the cellulose paper more quickly, and therefore do not travel as far.

Thin layer chromatography

Thin layer chromatography (TLC) is a widely employed laboratory technique and is similar to paper chromatography. However, instead of using a stationary phase of paper, it involves a stationary phase of a thin layer of adsorbent like silica gel, alumina, or cellulose on a flat, inert substrate. Compared to paper, it has the advantage of faster runs, better separations, and the choice between different adsorbents. For even better resolution and to allow for quantification, high-performance TLC can be used.

Displacement chromatography

The basic principle of displacement chromatography is: A molecule with a high affinity for the chromatography matrix (the displacer) will compete effectively for binding sites, and thus displace all molecules with lesser affinities. There are distinct differences between displacement and elution chromatography. In elution mode, substances typically emerge from a column in narrow, Gaussian peaks. Wide separation of peaks, preferably to baseline, is desired in order to achieve maximum purification. The speed at which any component of a mixture travels down the column in elution mode depends on many factors. But for two substances to travel at different speeds, and thereby be resolved, there must be substantial differences in some interaction between the biomolecules and the chromatography matrix. Operating parameters are adjusted to maximize the effect of this difference. In many cases, baseline separation of the peaks can be achieved only with gradient elution and low column loadings. Thus, two drawbacks to elution mode chromatography, especially at the preparative scale, are operational complexity, due to gradient solvent pumping, and low throughput, due to low column loadings. Displacement chromatography has advantages over elution chromatography in that components are resolved into consecutive zones of pure substances rather than “peaks”. Because the process takes advantage of the nonlinearity of the isotherms, a larger column feed can be separated on a given column with the purified components recovered at significantly higher concentrations.

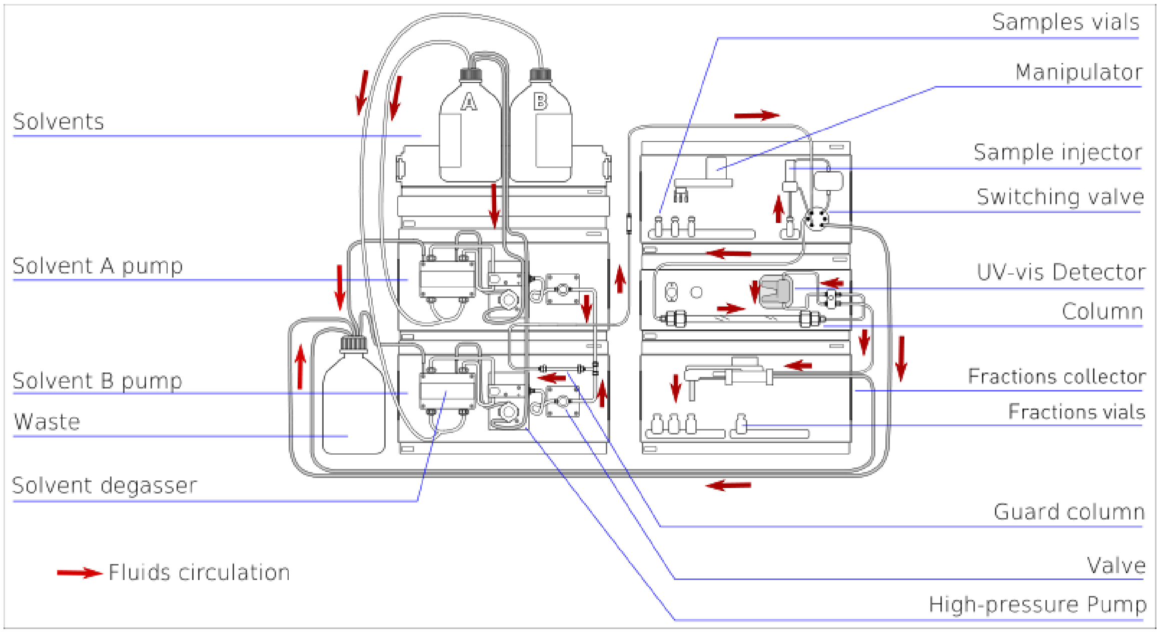
Techniques by physical state of mobile phase

Gas chromatography

Gas chromatography (GC), also sometimes known as Gas-Liquid chromatography, (GLC), is a separation technique in which the mobile phase is a gas. Gas chromatography is always carried out in a column, which is typically "packed" or "capillary" (see below) .

Gas chromatography (GC) is based on a partition equilibrium of analyte between a solid stationary phase (often a liquid silicone-based material) and a mobile gas (most often Helium). The stationary phase is adhered to the inside of a small-diameter glass tube (a capillary column) or a solid matrix inside a larger metal tube (a packed column). It is widely used in analytical chemistry; though the high temperatures used in GC make it unsuitable for high molecular weight biopolymers or proteins (heat will denature them), frequently encountered in biochemistry, it is well suited for use in the petrochemical, environmental monitoring and remediation, and industrial chemical fields. It is also used extensively in chemistry research.

Liquid chromatography



Preparative HPLC apparatus

Liquid chromatography (LC) is a separation technique in which the mobile phase is a liquid. Liquid chromatography can be carried out either in a column or a plane. Present day liquid chromatography that generally utilizes very small packing particles and a relatively high pressure is referred to as high performance liquid chromatography (HPLC).

In the HPLC technique, the sample is forced through a column that is packed with irregularly or spherically shaped particles, a porous monolithic layer (stationary phase) or a porous membrane by a liquid (mobile phase) at high pressure. HPLC is historically divided into two different sub-classes based on the polarity of the mobile and stationary phases. Methods in which the stationary phase is more polar than the mobile phase (e.g. toluene as the mobile phase, silica as the stationary phase) are termed normal phase liquid chromatography (NPLC) and the opposite (e.g. water-methanol mixture as the mobile phase and C18 = octadecylsilyl as the stationary phase) is termed reversed phase liquid chromatography (RPLC). Ironically the "normal phase" has fewer applications and RPLC is therefore used considerably more.

Specific techniques which come under this broad heading are listed below. It should also be noted that the following techniques can also be considered fast protein liquid chromatography if no pressure is used to drive the mobile phase through the stationary phase.

Affinity chromatography

Affinity chromatography is based on selective non-covalent interaction between an analyte and specific molecules. It is very specific, but not very robust. It is often used in biochemistry in the purification of proteins bound to tags. These fusion proteins are labeled with compounds such as His-tags, biotin or antigens, which bind to the stationary phase specifically. After purification, some of these tags are usually removed and the pure protein is obtained.

Affinity chromatography often utilizes a biomolecule's affinity for a metal (Zn, Cu, Fe, etc.). Columns are often manually prepared. Traditional affinity columns are used as a preparative step to flush out unwanted biomolecules.

However, HPLC techniques exist that do utilize affinity chromatogaphy properties. Immobilized Metal Affinity Chromatography (IMAC) is useful to separate aforementioned molecules based on the relative affinity for the metal (I.e. Dionex IMAC) . Often these columns can be loaded with different metals to create a column with a targeted affinity.

Supercritical fluid chromatography

Supercritical fluid chromatography is a separation technique in which the mobile phase is a fluid above and relatively close to its critical temperature and pressure.

Techniques by separation mechanism

Ion exchange chromatography

Ion exchange chromatography uses ion exchange mechanism to separate analytes. It is usually performed in columns but can also be useful in planar mode. Ion exchange chromatography uses a charged stationary phase to separate charged compounds including amino acids, peptides, and proteins. In conventional methods the stationary phase is an ion exchange resin that carries charged functional groups which interact with oppositely charged groups of the compound to be retained. Ion exchange chromatography is commonly used to purify proteins using FPLC.

Size-exclusion chromatography

Size-exclusion chromatography (SEC) is also known as **gel permeation chromatography** (GPC) or **gel filtration chromatography** and separates molecules according to their size (or more accurately according to their hydrodynamic diameter or hydrodynamic volume). Smaller molecules are able to enter the pores of the media and, therefore, molecules are trapped and removed from the flow of the mobile phase. The average residence time in the pores depends upon the effective size of the analyte molecules. However, molecules that are larger than the average pore size of the packing are excluded and thus suffer essentially no retention; such species are the first to be eluted. It is generally a low-resolution chromatography technique and thus it is often reserved for the final, "polishing" step of a purification. It is also useful for determining the tertiary structure and quaternary structure of purified proteins, especially since it can be carried out under native solution conditions.

Special techniques

Reversed-phase chromatography

Reversed-phase chromatography is an elution procedure used in liquid chromatography in which the mobile phase is significantly more polar than the stationary phase.

Two-dimensional chromatography

In some cases, the chemistry within a given column can be insufficient to separate some analytes. It is possible to direct a series of unresolved peaks onto a second column with different physico-chemical (Chemical classification) properties. Since the mechanism of retention on this new solid support is different from the first dimensional separation, it can be possible to separate compounds that are indistinguishable by one-dimensional chromatography. The sample is spotted at one corner of a square plate,developed, air-dried, then rotated by 90° and usually redeveloped in a second solvent system.

Simulated moving-bed chromatography

Pyrolysis gas chromatography

Fast protein liquid chromatography

Fast protein liquid chromatography (FPLC) is a term applied to several chromatography techniques which are used to purify proteins. Many of these techniques are identical to those carried out under high performance liquid chromatography, however use of FPLC techniques are typically for preparing large scale batches of a purified product.

Countercurrent chromatography

Countercurrent chromatography (CCC) is a type of liquid-liquid chromatography, where both the stationary and mobile phases are liquids. It involves mixing a solution of liquids, allowing them to settle into layers and then separating the layers.

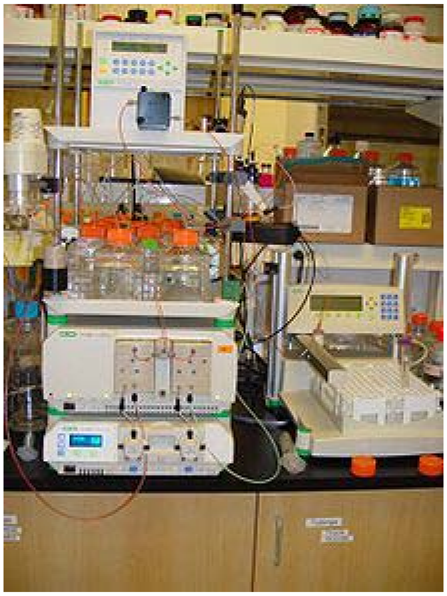
Chiral chromatography

Chiral chromatography involves the separation of stereoisomers. In the case of enantiomers, these have no chemical or physical differences apart from being three-dimensional mirror images. Conventional chromatography or other separation processes are incapable of separating them. To enable chiral separations to take place, either the mobile phase or the stationary phase must themselves be made chiral, giving differing affinities between the analytes. Chiral chromatography HPLC columns (with a chiral stationary phase) in both normal and reversed phase are commercially available.

Chapter- 15

Size-Exclusion Chromatography

Size-exclusion chromatography



Equipment for running size-exclusion chromatography. The buffer is pumped through the column (right) by a computer-controlled device

Acronym	SEC
Classification	Chromatography
Analytes	macromolecules synthetic polymers biomolecules
	Other techniques
Related	High performance liquid

chromatography

Aqueous Normal Phase

Chromatography

Ion exchange chromatography

Micellar liquid chromatography

Size-exclusion chromatography (SEC) is a chromatographic method in which molecules in solution are separated by their size, not by molecular weight. It is usually applied to large molecules or macromolecular complexes such as proteins and industrial polymers. Typically, when an aqueous solution is used to transport the sample through the column, the technique is known as **gel-filtration chromatography**, versus the name **Gel permeation chromatography**, which is used when an organic solvent is used as a mobile phase. SEC is a widely used polymer characterization method because of its ability to provide good Mw results for polymers.

Applications

The main application of gel-filtration chromatography is the fractionation of proteins and other water-soluble polymers, while gel permeation chromatography is used to analyze the molecular weight distribution of organic-soluble polymers. Either technique should not be confused with gel electrophoresis, where an electric field is used to "pull" or "push" molecules through the gel depending on their electrical charges.

SEC is a widely used technique for the purification and analysis of synthetic and biological polymers, such as proteins, polysaccharides and nucleic acids. Biologists and biochemists typically use a gel medium — usually polyacrylamide, dextran or agarose — and filter under low pressure. Polymer chemists typically use either a silica or crosslinked polystyrene medium under a higher pressure. These media are known as the **stationary phase**.

Advantages

The advantages of this method include good separation of large molecules from the small molecules with a minimal volume of eluate, and that various solutions can be applied without interfering with the filtration process, all while preserving the biological activity of the particles to be separated. The technique is generally combined with others that further separate molecules by other characteristics, such as acidity, basicity, charge, and affinity for certain compounds. With size exclusion chromatography, there are short and well-defined separation times and narrow bands, which lead to good sensitivity. There is also no sample loss because solutes do not interact with the stationary phase. Disadvantages are, for example, that only a limited number of bands can be accommodated because the time scale of the chromatogram is short, and, in general, there has to be a 10% difference in molecular mass to have a good resolution

Discovery

The technique was invented by Grant Henry Lathe and Colin R Ruthven, working at Queen Charlotte's Hospital, London. They later received the John Scott Award for this invention. While Lathe and Ruthven used starch gels as the matrix, Jerker Porath and Per Flodin later introduced dextran gels; other gels with size fractionation properties include agarose and polyacrylamide. A short review of these developments has appeared.

There were also attempts to fractionate synthetic high polymers; however, it was not until 1964, when J. C. Moore of the Dow Chemical Company published his work on the preparation of Gel Permeation Chromatography (GPC) columns based on cross-linked polystyrene with controlled pore size, that a rapid increase of research activity in this field began. It was recognized almost immediately that with proper calibration, GPC was capable to provide molar mass and molar mass distribution information for synthetic polymers. Because the latter information was difficult to obtain by other methods, GPC came rapidly into extensive use.

Theory and method

One requirement for SEC is that the analyte does not interact with the surface of the stationary phases. Differences in elution time are based solely on the volume the analyte "sees". Thus, a small molecule that can penetrate every corner of the pore system of the stationary phase "sees" the entire pore volume and the interparticle volume, and will elute late (when the pore- and interparticle volume has passed through the column ~80% of the column volume). On the other extreme, a very large molecule that cannot penetrate the pore system "sees" only the interparticle volume (~35% of the column volume) and will elute earlier when this volume of mobile phase has passed through the column. The underlying principle of SEC is that particles of different sizes will elute (filter) through a stationary phase at different rates. This results in the separation of a solution of particles based on size. Provided that all the particles are loaded simultaneously or near-simultaneously, particles of the same size should elute together.

However, as there are various measure of the size of a macromolecule (for instance, the radius of gyration and the hydrodynamic radius), a fundamental problem in the theory of SEC has been the choice of a proper molecular size parameter by which molecules of different kinds are separated. Experimentally, Benoit and co-workers found an excellent correlation between elution volume and a dynamically based molecular size, the hydrodynamic volume, for several different chain architecture and chemical compositions. The observed correlation based on the hydrodynamic volume became accepted as the basis of universal SEC calibration.

Still, the use of the hydrodynamic volume, a size based on dynamical properties, in the interpretation of SEC data is not fully understood. This is because SEC is typically run under low flow rate conditions where hydrodynamic factor should have little effect on the separation. In fact, both theory and computer simulations assume a thermodynamic separation principle: the separation process is determined by the equilibrium distribution (partitioning) of solute macromolecules between two phases --- a dilute bulk solution phase located at the interstitial space and confined solution phases within the pores of column packing material. Based on this theory, it has been shown that the relevant size parameter to the partitioning of polymers in pores is the mean span dimension (mean maximal projection onto a line). Although this issue has not been fully resolved, it is likely that the mean span dimension and the hydrodynamic volume are strongly correlated.

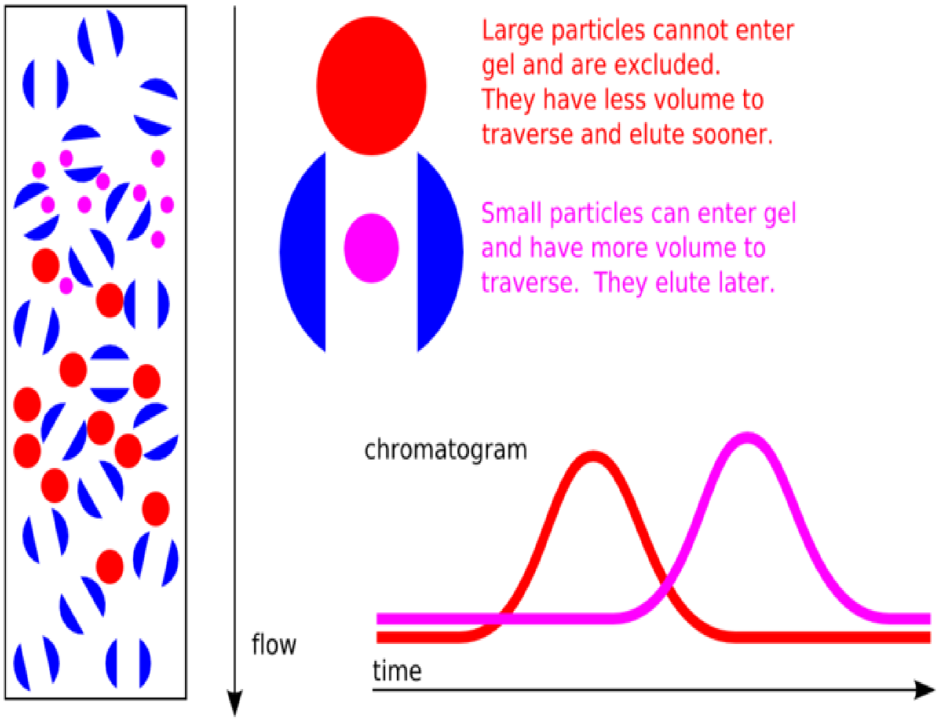
Each size exclusion column has a range of molecular weights that can be separated. The exclusion limit defines the molecular weight at the upper end of this range and is where molecules are too large to be trapped in the stationary phase. The permeation limit defines the molecular weight at the lower end of the range of separation and is where molecules of a small enough size can penetrate into the pores of the stationary phase completely and all molecules below this molecular mass are so small that they elute as a single band

A size exclusion column.

This is usually achieved with an apparatus called a column, which consists of a hollow tube tightly packed with extremely small porous polymer beads designed to have pores of different sizes. These pores may be depressions on the surface or channels through the bead. As the solution travels down the column some particles enter into the pores. Larger particles cannot enter into as many pores. The larger the particles, the faster the elution.

The filtered solution that is collected at the end is known as the **eluate**. The **void volume** includes any particles too large to enter the medium, and the solvent volume is known as the **column volume**.

Factors affecting filtration



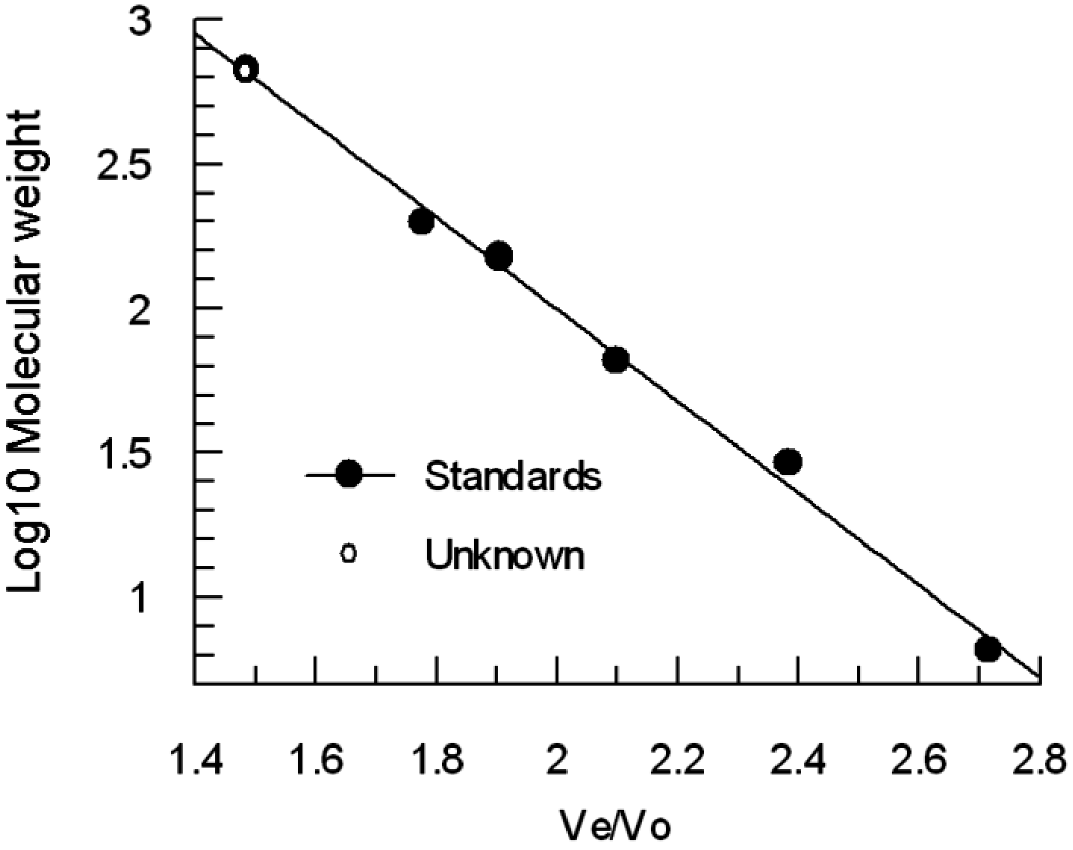
A cartoon illustrating the theory behind **size exclusion chromatography**

In real-life situations, particles in solution do not have a fixed size, resulting in the probability that a particle that would otherwise be hampered by a pore passing right by it. Also, the stationary-phase particles are not ideally defined; both particles and pores may vary in size. Elution curves, therefore, resemble Gaussian distributions. The stationary phase may also interact in undesirable ways with a particle and influence retention times, though great care is taken by column manufacturers to use stationary phases that are inert and minimize this issue.

Like other forms of chromatography, increasing the column length will enhance the resolution, and increasing the column diameter increases the capacity of the column. Proper column packing is important to maximize resolution: An overpacked column can collapse the pores in the beads, resulting in a loss of resolution. An underpacked column can reduce the relative surface area of the stationary phase accessible to smaller species, resulting in those species spending less time trapped in pores. Unlike affinity chromatography techniques, a solvent head at the top of the column can drastically diminish resolution as the sample diffuses prior to loading, broadening the downstream elution.

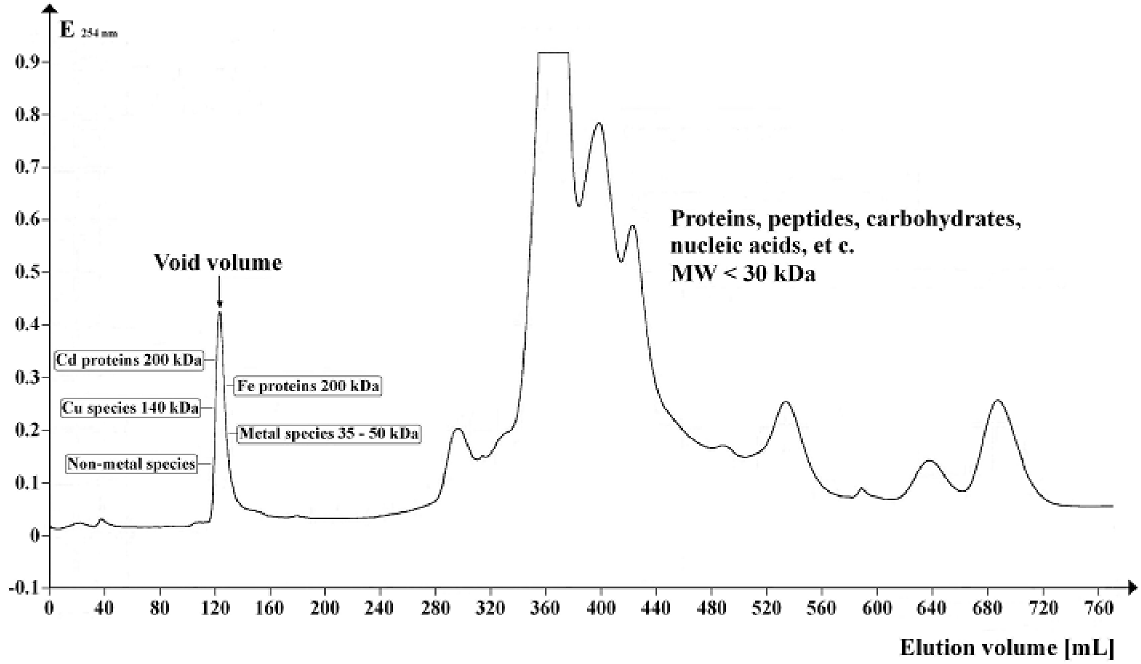
Analysis

In simple manual columns, the eluent is collected in constant volumes, known as fractions. The more similar the particles are in size the more likely they will be in the same fraction and not detected separately. More advanced columns overcome this problem by constantly monitoring the eluent.



Standardization of a size exclusion column.

The collected fractions are often examined by spectroscopic techniques to determine the concentration of the particles eluted. Common spectroscopy detection techniques are refractive index (RI)and ultraviolet (UV). When eluting spectroscopically similar species (such as during biological purification), other techniques may be necessary to identify the contents of each fraction. It is also possible to analyse the eluent flow continuously with RI, LALLS, Multi-Angle Laser Light Scattering MALS, UV, and/or viscosity measurements.



SEC Chromatogram of a biological sample.

The elution volume (Ve) decreases roughly linearly with the logarithm of the molecular hydrodynamic volume. Columns are often calibrated using 4-5 standard samples (e.g., folded proteins of known molecular weight), and a sample containing a very large molecule such as thyroglobulin to determine the void volume. (Blue dextran is not recommended for Vo determination because it is heterogeneous and may give variable results) The elution volumes of the standards are divided by the elution volume of the thyroglobulin (Ve/Vo) and plotted against the log of the standards' molecular weights.

Applications

Biochemical applications

In general, SEC is considered a low resolution chromatography as it does not discern similar species very well, and is therefore often reserved for the final "polishing" step of a purification. The technique can determine the quaternary structure of purified proteins that have slow exchange times, since it can be carried out under native solution conditions, preserving macromolecular interactions. SEC can also assay protein tertiary structure, as it measures the hydrodynamic volume (not molecular weight), allowing folded and unfolded versions of the same protein to be distinguished. For example, the apparent hydrodynamic radius of a typical protein domain might be 14 Å and 36 Å for the folded and unfolded forms, respectively. SEC allows the separation of these two forms, as the folded form will elute much later due to its smaller size.

Polymer synthesis

SEC can be used as a measure of both the size and the polydispersity of a synthesised polymer, that is, the ability to be able to find the distribution of the sizes of polymer molecules. If standards of a known size are run previously, then a calibration curve can be created to determine the sizes of polymer molecules of interest in the solvent chosen for analysis (often THF). In alternative fashion, techniques such as light scattering and/or viscometry can be used online with SEC to yield absolute molecular weights that do not rely on calibration with standards of known molecular weight. Due to the difference in size of two polymers with identical molecular weights, the absolute determination methods are, in general, more desirable. A typical SEC system can quickly (in about half an hour) give polymer chemists information on the size and polydispersity of the sample. The preparative SEC can be used for polymer fractionation on an analytical scale. .

Drawback

In SEC, mass is not measured so much as the hydrodynamic volume of the polymer molecules, that is, how much space a particular polymer molecule takes up when it is in solution. However, the approximate molecular weight can be calculated from SEC data because the exact relationship between molecular weight and hydrodynamic volume for polystyrene can be found. For this, polystyrene is used as a standard. But the relationship between hydrodynamic volume and molecular weight is not the same for all polymers, so only an approximate measurement can be arrived at. Another drawback is the possibility of interaction between the stationary phase and the analyte. Any interaction leads to a later elution time and thus mimics a smaller analyte size.

Absolute size-exclusion chromatography

Absolute size-exclusion chromatography (ASEC) is a technique that couples a dynamic light scattering (DLS) instrument to a size exclusion chromatography system for absolute size measurements of proteins and macromolecules as they elute from the chromatography system.

The definition of absolute used here is that it does not require calibration to obtain hydrodynamic size, often referred to as hydrodynamic diameter (D_H in units of nm). The sizes of the macromolecules are measured as they elute into the flow cell of the DLS instrument from the size exclusion column set. It should be noted that the hydrodynamic size of the molecules or particles are measured and not their molecular weights. For proteins a Mark-Houwink type of calculation can be used to estimate the molecular weight from the hydrodynamic size.

A big advantage of DLS coupled with SEC is the ability to obtain enhanced DLS resolution. Batch DLS is quick and simple and provides a direct measure of the average size but the baseline resolution of DLS is 3 to 1 in diameter. Using SEC, the proteins and protein oligomers are separated, allowing oligomeric resolution. Aggregation studies can also be done using ASEC although the aggregate concentration may not be calculated, the size of the aggregate will be measured only to be limited by the maximum size eluting from the SEC columns.

Limitations of ASEC include flow-rate, concentration, and precision. Because a correlation function requires anywhere from 3–7 seconds to properly build, a limited number of data points can be collected across the peak.

Chapter- 16

Ion and Affinity Chromatography

Ion chromatography

Ion exchange chromatography

Acronym	IC, IEC
Classification	Chromatography
	Other techniques
Related	High performance liquid chromatography Aqueous Normal Phase Chromatography Size exclusion chromatography Micellar liquid chromatography

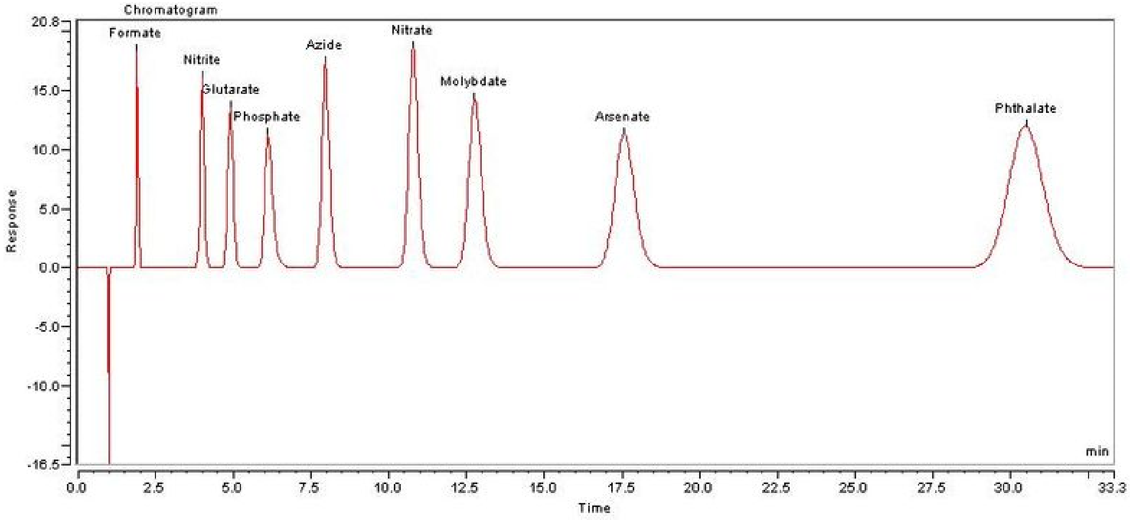
Ion-exchange chromatography (or *ion chromatography*) is a process that allows the separation of ions and polar molecules based on their charge. It can be used for almost any kind of charged molecule including large proteins, small nucleotides and amino acids. The solution to be injected is usually called a *sample*, and the individually separated components are called *analytes*. It is often used in protein purification, water analysis, and quality control.

History

Ion methods have been in use since 1850, when H. Thompson and J. T. Way, researchers in England, treated various clays with ammonium sulfate or carbonate in solution to extract the ammonia and release calcium. In 1927, the first zeolite mineral column was used to remove interfering calcium and magnesium ions from solution to determine the sulfate content of water. The modern version of IEC was developed during the wartime Manhattan Project. A technique was required to separate and concentrate the radioactive elements needed to make the atom bomb. Researchers chose adsorbents that would latch onto charged transuranium elements, which could then be differentially eluted.

Ultimately, once declassified, these techniques would use new IE resins to develop the systems that are often used today for specific purification of biologicals and inorganics. In the early 1970s, ion chromatography was developed by Hamish Small and co-workers at Dow Chemical Company as a novel method of IEC usable in automated analysis. This later led to the formation of Dionex Corp (Dow -Ion Exchange). IC uses weaker ionic resins for its stationary phase and an additional neutralizing stripper, or suppressor, column to remove background eluent ions. It is a powerful technique for determining low concentrations of ions and is especially useful in environmental and water quality studies, among other applications.

Principle



Ion Chromatogram

Ion exchange chromatography retains analyte molecules on the column based on coulombic (ionic) interactions. The stationary phase surface displays ionic functional groups (R-X) that interact with analyte ions of opposite charge. This type of chromatography is further subdivided into cation exchange chromatography and anion exchange chromatography. The ionic compound consisting of the cationic species M+ and the anionic species B- can be retained by the stationary phase.

Cation exchange chromatography retains positively charged cations because the stationary phase displays a negatively charged functional group:

$$\text{R-X}^-\text{C}^+ + \text{M}^+\text{B}^- \rightleftarrows \text{R-X}^-\text{M}^+ + \text{C}^+ + \text{B}^-$$

Anion exchange chromatography retains anions using positively charged functional group:

$$\text{R-X}^+\text{A}^- + \text{M}^+\text{B}^- \rightleftarrows \text{R-X}^+\text{B}^- + \text{M}^+ + \text{A}^-$$

Note that the ion strength of either C+ or A- in the mobile phase can be adjusted to shift the equilibrium position and thus retention time.

The ion chromatogram shows a typical chromatogram obtained with an anion exchange column.

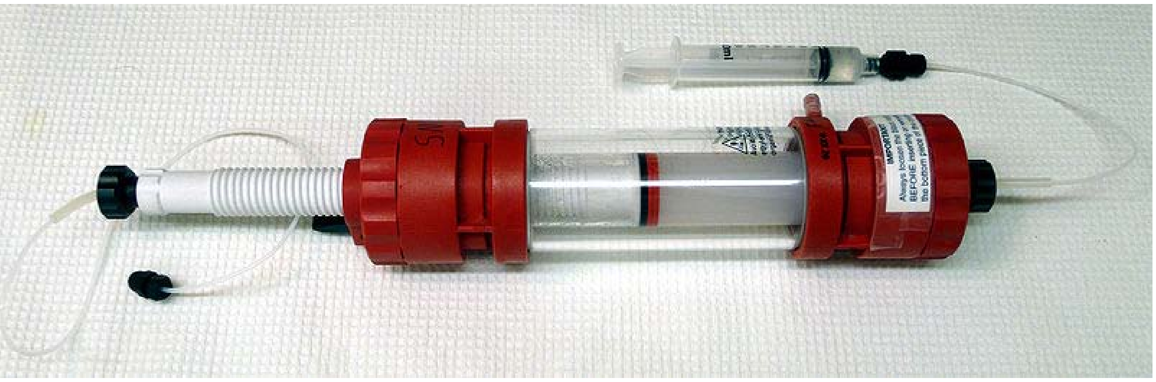
Typical technique

Metrohm 850 Ion chromatography system

A sample is introduced, either manually or with an autosampler, into a sample loop of known volume. A buffered aqueous solution known as the mobile phase carries the sample from the loop onto a column that contains some form of stationary phase material. This is typically a resin or gel matrix consisting of agarose or cellulose beads with covalently bonded charged functional groups. The target analytes (anions or cations) are retained on the stationary phase but can be eluted by increasing the concentration of a similarly charged species that will displace the analyte ions from the stationary phase. For example, in cation exchange chromatography, the positively charged analyte could be displaced by the addition of positively charged sodium ions. The analytes of interest must then be detected by some means, typically by conductivity or UV/Visible light absorbance.

In order to control an IC system, a chromatography data system (CDS) is usually needed. In addition to IC systems, some of these CDSs can also control gas chromatography (GC) and HPLC

Separating proteins



Preparative-scale ion exchange column used for protein purification.

Proteins have numerous functional groups that can have both positive and negative charges. Ion exchange chromatography separates proteins according to their net charge, which is dependent on the composition of the mobile phase. By adjusting the pH or the ionic concentration of the mobile phase, various protein molecules can be separated. For example, if a protein has a net positive charge at pH 7, then it will bind to a column of negatively-charged beads, whereas a negatively charged protein would not. By changing the pH so that the net charge on the protein is negative, it too will be eluted.

Elution by changing the ionic strength of the mobile phase is a more subtle effect - it works as ions from the mobile phase will interact with the immobilized ions in preference over those on the stationary phase. This "shields" the stationary phase from the protein, (and vice versa) and allows the protein to elute.

Affinity chromatography

Affinity chromatography is a method of separating biochemical mixtures and based on a highly specific biological interaction such as that between antigen and antibody, enzyme and substrate, or receptor and ligand. Affinity chromatography combines the size fractionation capability of gel permeation chromatography with the ability to design a chromatography that reversibly binds to a known subset of molecules. The method was discovered and developed by Cuatrecasas P, Wilchek M,and Meir Wilchek for which the Wolf Prize in Medicine was awarded in 1987. Due to its interdisciplinary nature, affinity chromatography has been the means by which many scientists from different disciplines have been introduced into the fields of modern biology.

Uses

Affinity chromatography can be used to:

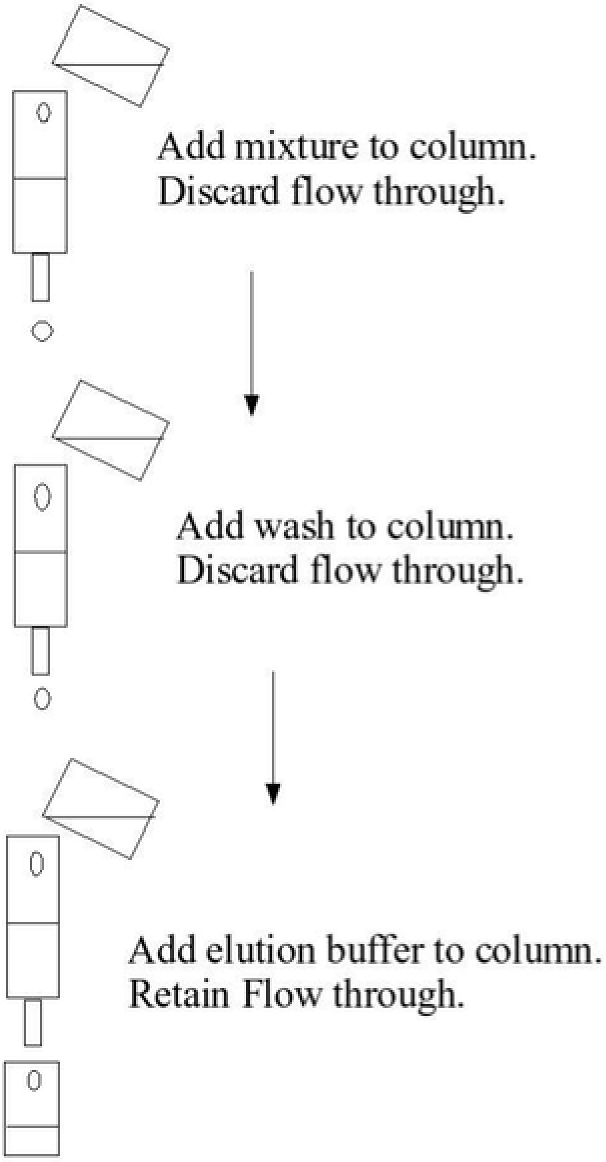
- Purify and concentrate a substance from a mixture into a buffering solution
- Reduce the amount of a substance in a mixture

- Discern what biological compounds bind to a particular substance, such as drugs
- Purify and concentrate an enzyme solution.

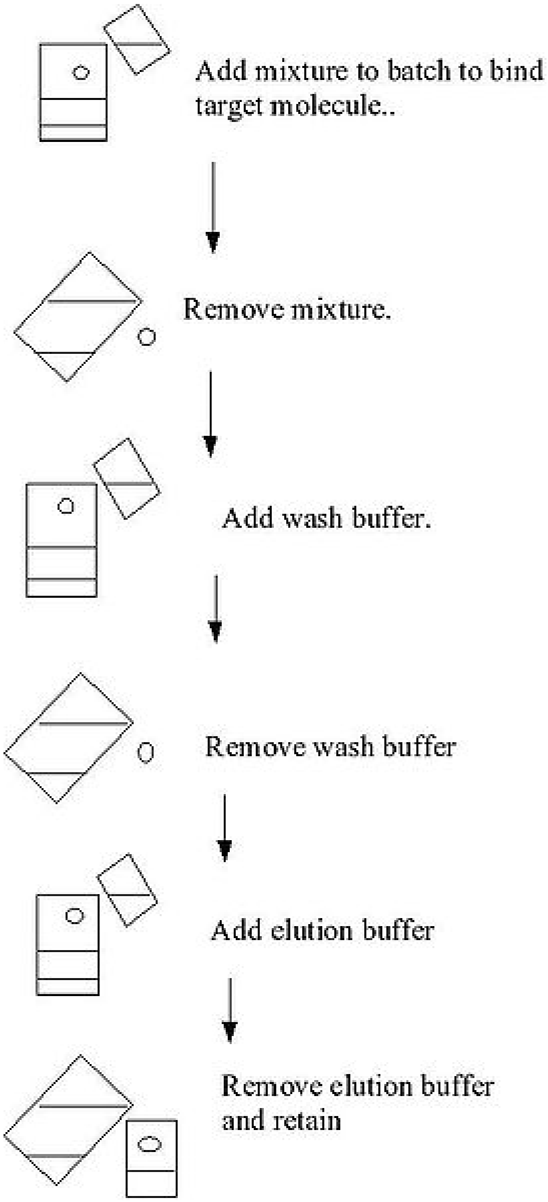
Principle

The immobile phase is typically a gel matrix, often of agarose; a linear sugar molecule derived from algae. Usually the starting point is an undefined heterogeneous group of molecules in solution, such as a cell lysate, growth medium or blood serum. The molecule of interest will have a well known and defined property which can be exploited during the affinity purification process. The process itself can be thought of as an entrapment, with the target molecule becoming trapped on a solid or stationary phase or medium. The other molecules in solution will not become trapped as they do not possess this property. The solid medium can then be removed from the mixture, washed and the target molecule released from the entrapment in a process known as elution. Possibly the most common use of affinity chromotography is for the purification of recombinant proteins.

Batch and column setup



Column chromatography



Batch chromatography

Binding to the solid phase may be achieved by column chromatography whereby the solid medium is packed onto a column, the initial mixture run through the column to allow setting, a wash buffer run through the column and the elution buffer subsequently applied to the column and collected. These steps are usually done at ambient pressure. Alternatively binding may be achieved using a batch treatment, by adding the initial mixture to the solid phase in a vessel, mixing, separating the solid phase (for example), removing the liquid phase, washing, re-centrifuging, adding the elution buffer, re-centrifuging and removing the eluate.

Sometimes a hybrid method is employed, the binding is done by the batch method, then the solid phase with the target molecule bound is packed onto a column and washing and elution are done on the column.

A third method,expanded bed adsorption, which combines the advantages of the two methods mentioned above, has also been developed. The solid phase particles are placed in a column where liquid phase is pumped in from the bottom and exits at the top. The gravity of the particles ensure that the solid phase does not exit the column with the liquid phase.

Specific uses

Affinity chromatography can be used in a number of applications, including nucleic acid purification, protein purification from cell free extracts, and purification from blood.

Immunoaffinity

Another use for the procedure is the affinity purification of antibodies from blood serum. If serum is known to contain antibodies against a specific antigen (for example if the serum comes from an organism immunized against the antigen concerned) then it can be used for the affinity purification of that antigen. This is also known as Immunoaffinity Chromatography. For example if an organism is immunised against a GST-fusion protein it will produce antibodies against the fusion-protein, and possibly antibodies against the GST tag as well. The protein can then be covalently coupled to a solid support such as agarose and used as an affinity ligand in purifications of antibody from immune serum.

For thoroughness the GST protein and the GST-fusion protein can each be coupled separately. The serum is initially allowed to bind to the GST affinity matrix. This will remove antibodies against the GST part of the fusion protein. The serum is then separated from the solid support and allowed to bind to the GST-fusion protein matrix. This allows any antibodies that recognize the antigen to be captured on the solid support. Elution of the antibodies of interest is most often achieved using a low pH buffer such as glycine pH 2.8. The eluate is collected into a neutral tris or phosphate buffer, to neutralize the low pH elution buffer and halt any degradation of the antibody's activity. This is a nice example as affinity purification is used to purify the initial GST-fusion protein, to remove the undesirable anti-GST antibodies from the serum and to purify the target antibody.

A simplified strategy is often employed to purify antibodies generated against peptide antigens. When the peptide antigens are produced synthetically, a terminal cysteine residue is added at either the N- or C-terminus of the peptide. This cysteine residue contains a sulfhydryl functional group which allows the peptide to be easily conjugated to a carrier protein (e.g.Keyhole Limpet Hemocyanin (KLH)). The same cysteine-containing peptide is also immobilized onto an agarose resin through the cysteine residue and is then used to purify the antibody.

Immobilized metal ion affinity chromatography

Immobilized metal ion affinity chromatography (IMAC) is based on the specific coordinate covalent bond of amino acids, particularly histidine, to metals. This technique works by allowing proteins with an affinity for metal ions to be retained in a column containing immobilized metal ions, such as cobalt, nickel, copper for the purification of histidine containing proteins or peptides, iron,zinc or gallium for the purification of phosphorylated proteins or peptides. Many naturally occurring proteins do not have an affinity for metal ions, therefore recombinant DNA technology can be used to introduce such a protein tag into the relevant gene. Methods used to elute the protein of interest include changing the pH, or adding a competitive molecule, such as imidazole.

Recombinant proteins

Possibly the most common use of affinity chromatography is for the purification of recombinant proteins. Proteins with a known affinity are protein tagged in order to aid their purification. The protein may have been genetically modified so as to allow it to be selected for affinity binding, this is known as a fusion protein. Tags include glutathione-S-transferase, hexahistidine (his), and maltose binding protein (MBP). His tags have an affinity for nickel or cobalt ions which are coordinate covalent bond with a chelator for the purposes of solid medium entrapment. For elution, an excess amount of a compound able to act as a metal ion ligand, such as imidazole, is used. GST has an affinity for glutathione which is commercially available immobilized as glutathione agarose. During elution, excess glutathione is used to displace the tagged protein.

Lectins

Lectin affinity chromatography is a form of affinity chromatography where lectins are used to separate components within the sample. Lectins, such as Concanavalin A are proteins which can bind specific carbohydrate (sugar) molecules. The most common application is to separate proteins based on their Glycosylation groups.

Chapter- 17

Liquid-Liquid Extraction

Liquid-liquid extraction, also known as **solvent extraction** and **partitioning**, is a method to separate compounds based on their relative solubilities in two different immiscible liquids, usually water and an organic solvent. It is an extraction of a substance from one liquid phase into another liquid phase. Liquid-liquid extraction is a basic technique in chemical laboratories, where it is performed using a separatory funnel. This type of process is commonly performed after a chemical reaction as part of the work-up.

The term *partitioning* is commonly used to refer to the underlying chemical and physical processes involved in *liquid-liquid extraction* but may be fully synonymous. The term *solvent extraction* can also refer to the separation of a substance from a mixture by preferentially dissolving that substance in a suitable solvent. In that case, a soluble compound is separated from an insoluble compound or a complex matrix.

Solvent extraction is used in nuclear reprocessing, ore processing, the production of fine organic compounds, the processing of perfumes, the production of vegetable oils and biodiesel, and other industries.

Liquid-liquid extraction is possible in non-aqueous systems: In a system consisting of a molten metal in contact with molten salt, metals can be extracted from one phase to the other. This is related to a mercury electrode where a metal can be reduced, the metal will often then dissolve in the mercury to form an amalgam that modifies its electrochemistry greatly. For example, it is possible for sodium cations to be reduced at a mercury cathode to form sodium amalgam, while at an inert electrode (such as platinum) the sodium cations are not reduced. Instead, water is reduced to hydrogen. A detergent or fine solid can be used to stabilize an emulsion, or third phase.

Measures of effectiveness

Distribution ratio

In solvent extraction, a distribution ratio is often quoted as a measure of how well-extracted a species is. The distribution ratio (*D*) is equal to the concentration of a solute in the organic phase divided by its concentration in the aqueous phase. Depending on the system, the distribution ratio can be a function of temperature, the concentration of chemical species in the system, and a large number of other parameters.

Note that D is related to the ΔG of the extraction process.

Sometimes, the distribution ratio is referred to as the partition coefficient, which is often expressed as the logarithm. Note that a distribution ratio for uranium and neptunium between two inorganic solids (zirconolite and perovskite) has been reported. In solvent extraction, two immiscible liquids are shaken together. The more polar solutes dissolve preferentially in the more polar solvent, and the less polar solutes in the less polar solvent. In this experiment, the nonpolar halogens preferentially dissolve in the nonpolar mineral oil.

Separation factors

The separation factor is one distribution ratio divided by another; it is a measure of the ability of the system to separate two solutes. For instance, if the distribution ratio for nickel (D_{Ni}) is 10 and the distribution ratio for silver (D_{Ag}) is 100, then the silver/nickel separation factor ($SF_{Ag/Ni}$) is equal to $D_{Ag}/D_{Ni} = SF_{Ag/Ni} = 10$.

Decontamination factor

This is used to express the ability of a process to remove a contaminant from a product. For instance, if a process is fed with a mixture of 1:9 cadmium to indium, and the product is a 1:99 mixture of cadmium and indium, then the decontamination factor (for the removal of cadmium) of the process is 0.1 / 0.01 = 10.

Slopes of graphs

The easy way to work out the extraction mechanism is to draw graphs and measure the slopes. If for an extraction system the D value is proportional to the square of the concentration of a reagent (Z) then the slope of the graph of $\log_{10}(D)$ against $\log_{10}([[Z]])$ will be two.

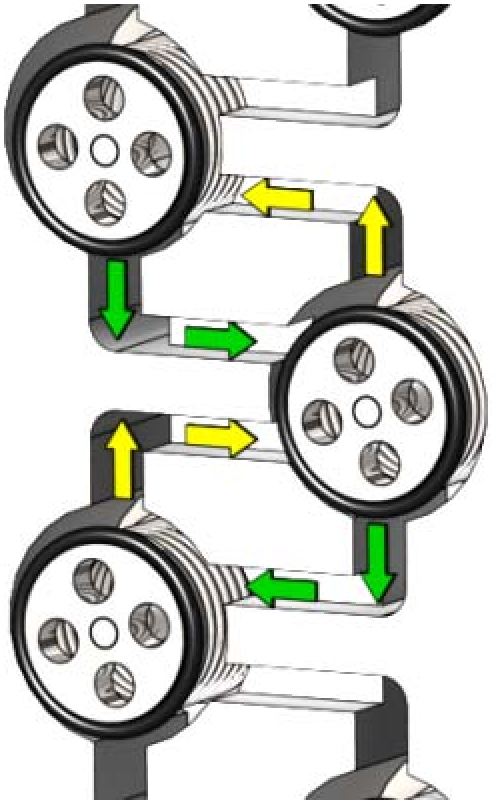
Techniques

Batchwise single stage extractions

This is commonly used on the small scale in chemical labs. It is normal to use a separating funnel. For instance, if a chemist were to extract anisole from a mixture of water and 5% acetic acid using ether, then the anisole will enter the organic phase. The two phases would then be separated.

The acetic acid can then be scrubbed (removed) from the organic phase by shaking the organic extract with sodium bicarbonate. The acetic acid reacts with the sodium bicarbonate to form sodium acetate, carbon dioxide, and water.

Multistage countercurrent continuous processes



Coflore Continuous Counter Current Extractor

These are commonly used in industry for the processing of metals such as the lanthanides; because the separation factors between the lanthanides are so small many extraction stages are needed. In the multistage processes, the aqueous raffinate from one extraction unit is fed to the next unit as the aqueous feed, while the organic phase is moved in the opposite direction. Hence, in this way, even if the separation between two metals in each stage is small, the overall system can have a higher decontamination factor.

Multistage countercurrent arrays have been used for the separation of lanthanides. For the design of a good process, the distribution ratio should be not too high (>100) or too low (<0.1) in the extraction portion of the process. It is often the case that the process will have a section for scrubbing unwanted metals from the organic phase, and finally a stripping section to obtain the metal back from the organic phase.

Multistage Podbielniak contactor centrifuges produce three to five stages of theoretical extraction in a single countercurrent pass, and are used in fermentation-based pharmaceutical and food additive production facilities.

Extraction without chemical change

Some solutes such as noble gases can be extracted from one phase to another without the need for a chemical reaction. This is the simplest type of solvent extraction. When a solvent is extracted, two immiscible liquids are shaken together. The more polar solutes dissolve preferentially in the more polar solvent, and the less polar solutes in the less polar solvent. Some solutes that do not at first sight appear to undergo a reaction during the extraction process do not have distribution ratio that is independent of concentration. A classic example is the extraction of carboxylic acids (**HA**) into nonpolar media such as benzene. Here, it is often the case that the carboxylic acid will form a dimer in the organic layer so the distribution ratio will change as a function of the acid concentration (measured in either phase).

For this case, the extraction constant k is described by $k = [[\mathbf{HA}_{\text{organic}}]]^2/[[\mathbf{HA}_{\text{aqueous}}]]$

Solvation mechanism

Using solvent extraction it is possible to extract uranium, plutonium, or thorium from acid solutions. One solvent used for this purpose is the organophosphate tri-n-butyl phosphate. The PUREX process that is commonly used in nuclear reprocessing uses a mixture of tri-n-butyl phosphate and an inert hydrocarbon (kerosene), the uranium(VI) are extracted from strong nitric acid and are back-extracted (stripped) using weak nitric acid. An organic soluble uranium complex $[UO_2(TBP)_2(NO_3)_2]$ is formed, then the organic layer bearing the uranium is brought into contact with a dilute nitric acid solution; the equilibrium is shifted away from the organic soluble uranium complex and towards the free TBP and uranyl nitrate in dilute nitric acid. The plutonium(IV) forms a similar complex to the uranium(VI), but it is possible to strip the plutonium in more than one way; a reducing agent that converts the plutonium to the trivalent oxidation state can be added. This oxidation state does not form a stable complex with TBP and nitrate unless the nitrate concentration is very high (circa 10 mol/L nitrate is required in the aqueous phase). Another method is to simply use dilute nitric acid as a stripping agent for the plutonium. This PUREX chemistry is a classic example of a solvation extraction.

Here in this case $D_U = k\ TBP^2[[NO_3]]^2$

Ion exchange mechanism

Another extraction mechanism is known as the ion exchange mechanism. Here, when an ion is transferred from the aqueous phase to the organic phase, another ion is transferred in the other direction to maintain the charge balance. This additional ion is often a hydrogen ion; for ion exchange mechanisms, the distribution ratio is often a function of pH. An example of an ion exchange extraction would be the extraction of americium by a combination of terpyridine and a carboxylic acid in *tert*-butyl benzene. In this case

$D_{\text{Am}} = k\ \text{terpyridine}^1 \text{carboxylic acid}^3 \text{H+}^{-3}$

Another example is the extraction of zinc, cadmium, or lead by a dialkyl phosphinic acid (R_2PO_2H) into a nonpolar diluent such as an alkane. A non-polar diluent favours the formation of uncharged non-polar metal complexes.

Some extraction systems are able to extract metals by both the solvation and ion exchange mechanisms; an example of such a system is the americium (and lanthanide) extraction from nitric acid by a combination of 6,6'-*bis*-(5,6-dipentyl-1,2,4-triazin-3-yl)-2,2'-bipyridine and 2-bromohexanoic acid in *tert*-butyl benzene. At both high- and low-nitric acid concentrations, the metal distribution ratio is higher than it is for an intermidate nitric acid concentration.

Ion pair extraction

It is possible by careful choice of counterion to extract a metal. For instance, if the nitrate concentration is high, it is possible to extract americium as an anionic nitrate complex if the mixture contains a lipophilic quaternary ammonium salt.

An example that is more likely to be encountered by the *'average'* chemist is the use of a phase transfer catalyst. This is a charged species that transfers another ion to the organic phase. The ion reacts and then forms another ion, which is then transferred back to the aqueous phase.

For instance, the 31.1 kJ mol^{-1} is required to transfer an acetate anion into nitrobenzene, while the energy required to transfer a chloride anion from an aqueous phase to nitrobenzene is 43.8 kJ mol^{-1}. Hence, if the aqueous phase in a reaction is a solution of sodium acetate while the organic phase is a nitrobenzene solution of benzyl chloride, then, when a phase transfer catalyst, the acetate anions can be transferred from the aqueous layer where they react with the benzyl chloride to form benzyl acetate and a chloride anion. The chloride anion is then transferred to the aqueous phase. The transfer energies of the anions contribute to that given out by the reaction.

A 43.8 to 31.1 kJ mol^{-1} = 12.7 kJ mol^{-1} of additional energy is given out by the reaction when compared with energy if the reaction had been done in nitrobenzene using one equivalent weight of a tetraalkylammonium acetate.

Aqueous two-phase extraction

Using an aqueous two-phase system, it is possible to generate two immiscible water phases. This can then be used to extract proteins, which would denature if exposed to organic solvents.

Kinetics of extraction

It is important to investigate the rate at which the solute is transferred between the two phases, in some cases by an alteration of the contact time it is possible to alter the selectivity of the extraction. For instance, the extraction of palladium or nickel can be very slow because the rate of ligand exchange at these metal centers is much lower than the rates for iron or silver complexes.

Aqueous complexing agents

If a complexing agent is present in the aqueous phase then it can lower the distribution ratio. For instance, in the case of iodine being distributed between water and an inert organic solvent such as carbon tetrachloride then the presence of iodide in the aqueous phase can alter the extraction chemistry.

Instead of $D_{\mathrm{I+2}}$ being a constant it becomes $D_{\mathrm{I+2}} = k[[\mathrm{I}_{2\cdot\mathrm{Organic}}]]/[\mathrm{I}_{2\cdot\mathrm{Aqueous}}]\ [[\mathrm{I}^{-}{}_{\cdot\mathrm{Aqueous}}]]$

This is because the iodine reacts with the iodide to form I_3^-. The I_3^- anion is an example of a polyhalide anion that is quite common.

Industrial process design

In a typical scenario, an industrial process will use an extraction step in which solutes are transferred from the aqueous phase to the organic phase; this is often followed by a scrubbing stage in which unwanted solutes are removed from the organic phase, then a stripping stage in which the wanted solutes are removed from the organic phase. The organic phase may then be treated to make it ready for use again.

After use, the organic phase may be subjected to a cleaning step to remove any degradation products; for instance, in PUREX plants, the used organic phase is washed with sodium carbonate solution to remove any dibutyl hydrogen phosphate or butyl dihydrogen phosphate that might be present.

Equipment

Two layers separating during a liquid-liquid extraction.

An organic MTBE solution is extracted with aqueous sodium bicarbonate solution. This base removes benzoic acid as benzoate but leaves non-acidic benzil (yellow) behind in the upper organic phase.

While solvent extraction is often done on a small scale by synthetic lab chemists using a separatory funnel or Craig apparatus, it is normally done on the industrial scale using machines that bring the two liquid phases into contact with each other. Such machines include centrifugal contactors, thin layer extractors, spray columns, pulsed columns, and mixer-settlers.

Extraction of metals

The extraction methods for a range of metals include:

- Cobalt - The extraction of cobalt from hydrochloric acid using alamine 336 in *meta*-xylene. Cobalt can be extracted also using Cyanex 272 {*bis*-(2,4,4-trimethylpentyl) phosphinic acid}.

- Copper - Copper can be extracted using hydroxyoximes as extractants, a recent paper describes an extractant that has a good selectivity for copper over cobalt and nickel.

- Neodymium - This rare earth is extracted by di(2-ethyl-hexyl)phosphoric acid into hexane by an ion exchange mechanism.

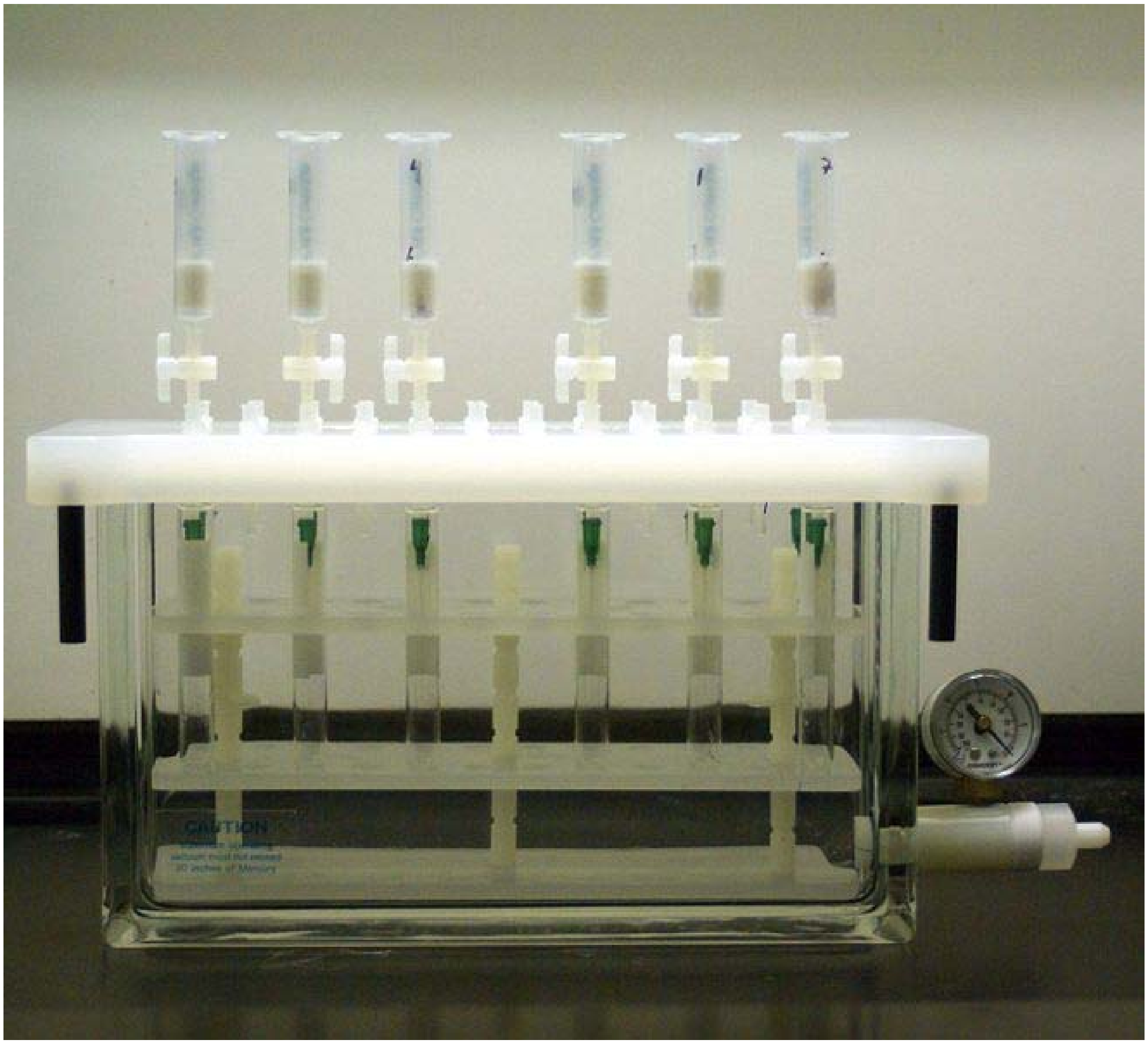
- Nickel - Nickel can be extracted using di(2-ethyl-hexyl)phosphoric acid and tributyl phosphate in a hydrocarbon diluent (Shellsol).

- Palladium and platinum - Dialkyl sulfides, tributyl phosphate and alkyl amines have been used for extracting these metals.

- Zinc and cadmium - The zinc and cadmium are both extracted by an ion exchange process, the *N,N,N′,N′*-tetrakis(2-pyridylmethyl)ethylenediamine (TPEN) acts as a masking agent for the zinc and an extractant for the cadmium. In the modified Zincex process, zinc is separated from most divalent ions by solvent extraction. D2EHPA (Di (2) ethyl hexyl phosphoric acid) is used for this. A zinc ion replaces the proton from two D2EHPA molecules. To strip the zinc from the D2EHPA, sulfuric acid is used, at a concentration of above 170g/l (typically 240-265g/l).

Chapter- 18

Solid Phase Extraction



A typical solid phase extraction manifold. The cartridges drip into the chamber below, where tubes collect the effluent. A vacuum port with gauge is used to control the vacuum applied to the chamber.

Solid-phase extraction (**SPE**) is a separation process by which compounds that are dissolved or suspended in a liquid mixture are separated from other compounds in the mixture according to their physical and chemical properties. Analytical laboratories use solid phase extraction to concentrate and purify samples for analysis. Solid phase extraction can be used to isolate analytes of interest from a wide variety of matrices, including urine, blood, water, beverages, soil, and animal tissue.

SPE uses the affinity of solutes dissolved or suspended in a liquid (known as the mobile phase) for a solid through which the sample is passed (known as the stationary phase) to separate a mixture into desired and undesired components. The result is that either the desired analytes of interest or undesired impurities in the sample are retained on the stationary phase. The portion that passes through the stationary phase is collected or discarded, depending on whether it contains the desired analytes or undesired impurities. If the portion retained on the stationary phase includes the desired analytes, they can then be removed from the stationary phase for collection in an additional step, in which the stationary phase is rinsed with an appropriate eluent.

The stationary phase comes in the form of a packed syringe-shaped cartridge, a 96 well plate or a 47- or 90-mm flat disk, each of which can be mounted on its specific type of extraction manifold. The manifold allows multiple samples to be processed by holding several SPE media in place and allowing for an equal number of samples to pass through them simultaneously. A typical cartridge SPE manifold can accommodate up to 24 cartridges, while a typical disk SPE manifold can accommodate 6 disks. Most SPE manifolds are equipped with a vacuum port. Application of vacuum speeds up the extraction process by pulling the liquid sample through the stationary phase. The analytes are collected in sample tubes inside or below the manifold after they pass through the stationary phase.

Solid phase extraction cartridges and disks are available with a variety of stationary phases, each of which can separate analytes according to different chemical properties. Most stationary phases are based on silica that has been bonded to a specific functional group. Some of these functional groups include hydrocarbon chains of variable length (for reversed phase SPE), quaternary ammonium or amino groups (for anion exchange), and sulfonic acid or carboxyl groups (for cation exchange).

Normal Phase SPE procedure

A selection of solid phase extraction cartridges, available in many sizes, shapes, and types of stationary phase.

A typical solid phase extraction involves four basic steps. First, the cartridge is equilibrated with a non-polar solvent or slightly polar, which wets the surface and penetrates the bonded phase. Then water, or buffer of the same composition as the sample, is typically washed through the column to wet the silica surface. The sample is then added to the cartridge. As the sample passes through the stationary phase, the analytes in the sample will interact and retain on the sorbent while the solvent, salts, and other impurities pass through the cartridge. After the sample is loaded, the cartridge is washed with buffer or solvent to remove further impurities. Then, the analyte is eluted with a non-polar solvent or a buffer of the appropriate pH.

A stationary phase of polar functionally bonded silicas with short carbons chains frequently makes up the solid phase. This stationary phase will adsorb polar molecules which can be collected with a more polar solvent.

Reversed phase SPE

Reversed phase SPE separates analytes based on their polarity. The stationary phase of a reversed phase SPE cartridge is derivatized with hydrocarbon chains, which retain compounds of mid to low polarity due to the hydrophobic effect. The analyte can be eluted by washing the cartridge with a non-polar solvent, which disrupts the interaction of the analyte and the stationary phase.

A stationary phase of silicon with carbon chains is commonly used. Relying on mainly non-polar, hydrophobic interactions, only non-polar or very weakly polar compounds will adsorb to the surface.

Ion exchange SPE

Ion exchange sorbents separate analytes based on electrostatic interactions between the analyte of interest and the positively charged groups on the stationary phase. For ion exchange to occur, both the stationary phase and sample must be at a pH where both are charged.

Anion exchange

Anion exchange sorbents are derivatized with positively charged functional groups that interact and retain negatively charged anions, such as acids. Strong anion exchange sorbents contain quaternary ammonium groups that have a permanent positive charge in aqueous solutions, and weak anion exchange sorbents use amine groups which are charged when the pH is below about 9. Strong anion exchange sorbents are useful because any strongly acidic impurities in the sample will bind to the sorbent and usually will not be eluted with the analyte of interest; to recover a strong acid a weak anion exchange cartridge should be used. To elute the analyte from either the strong or weak sorbent, the stationary phase is washed with a solvent that neutralizes the charge of either the analyte, the stationary phase, or both. Once the charge is neutralized, the electrostatic interaction between the analyte and the stationary phase no longer exists and the analyte will elute from the cartridge.

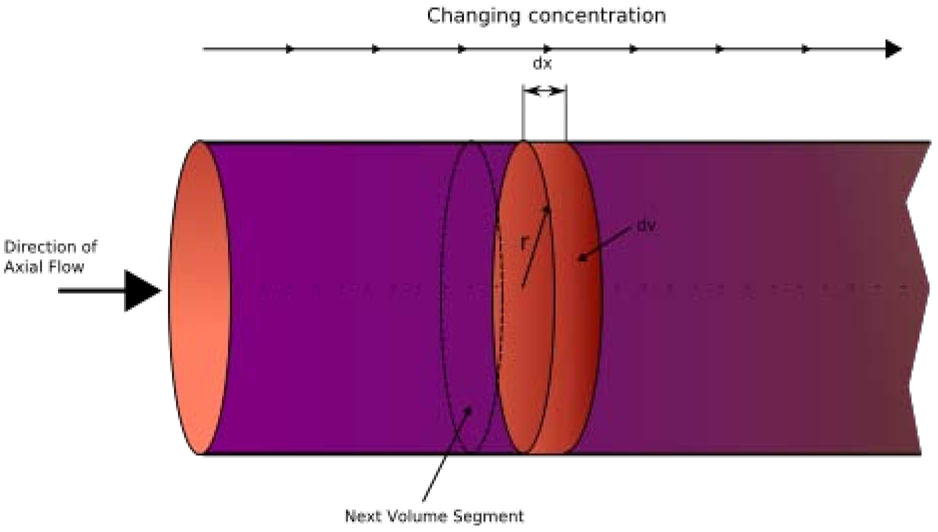
Cation Exchange

Cation exchange sorbents are derivatized with functional groups that interact and retain positively charged cations, such as bases. Strong cation exchange sorbents contain aliphatic sulfonic acid groups that are always negatively charged in aqueous solution, and weak cation exchange sorbents contain aliphatic carboxylic acids, which are charged when the pH is above about 5. Strong cation exchange sorbents are useful because any strongly basic impurities in the sample will bind to the sorbent and usually will not be eluted with the analyte of interest; to recover a strong base a weak cation exchange cartridge should be used. To elute the analyte from either the strong or weak sorbent, the stationary phase is washed with a solvent that neutralizes ionic interaction between the analyte and the stationary phase.

Chapter- 19

Plug Flow Reactor Model

The **plug flow reactor** (**PFR**) model is used to describe chemical reactions in continuous, flowing systems. The PFR model is used to predict the behaviour of chemical reactors, so that key reactor variables, such as the dimensions of the reactor, can be estimated. PFR's are also sometimes called Continuous Tubular Reactors (CTR's).



Schematic diagram of a Plug Flow Reactor (PFR)

Fluid going through a PFR may be modeled as flowing through the reactor as a series of infinitely thin coherent "plugs", each with a uniform composition, traveling in the axial direction of the reactor, with each plug having a different composition from the ones before and after it. The key assumption is that as a plug flows through a PFR, the fluid is perfectly mixed in the radial direction but not in the axial direction (forwards or backwards). Each plug of differential volume is considered as a separate entity, effectively an infinitesimally small batch reactor, limiting to zero volume. As it flows down the tubular PFR, the residence time (τ) of the plug is a function of its position in the reactor. In the ideal PFR, the residence time distribution is therefore a Dirac delta function with a value equal to τ.

PFR modeling

PFRs are frequently referred to as piston flow reactors, or sometimes as continuous tubular reactors. They are governed by ordinary differential equations, the solution for which can be calculated providing that appropriate boundary conditions are known.

The PFR model works well for many fluids: liquids, gases, and slurries. Although turbulent flow and axial diffusion cause a degree of mixing in the axial direction in real reactors, the PFR model is appropriate when these effects are sufficiently small that they can be ignored.

In the simplest case of a PFR model, several key assumptions must be made in order to simplify the problem, some of which are outlined below. Note that not all of these assumptions are necessary, however the removal of these assumptions does increase the complexity of the problem. The PFR model can be used to model multiple reactions as well as reactions involving changing temperatures, pressures and densities of the flow. Although these complications are ignored in what follows, they are often relevant to industrial processes.

Assumptions:

- plug flow
- steady state
- constant density (reasonable for some liquids but a 20% error for polymerizations; valid for gases only if there is no pressure drop, no net change in the number of moles, nor any large temperature change)
- constant tube diameter
- single reaction

A material balance on the differential volume of a fluid element, or plug, on species *i* of axial length *dx* between *x* and *x* + *dx* gives

[accumulation] = [in] - [out] + [generation] - [consumption]

1. $F_i(x) - F_i(x + dx) + A_t dx \nu_i r = 0$.

When linear velocity, *u*, and molar flow rate relationships, F_i, $u = \frac{\dot{v}}{A_t} = \frac{4\dot{v}}{\pi D^2}$ and $F_i = A_t u C_i$, are applied to Equation 1 the mass balance on *i* becomes

2. $A_t u[C_i(x) - C_i(x + dx)] + A_t dx \nu_i r = 0$.

When like terms are canceled and the limit $dx \rightarrow 0$ is applied to Equation 2 the mass balance on species *i* becomes

3. $$u\frac{dC_i}{dx} = \nu_i r,$$

where $C_i(x)$ is the molar concentration of species i at position x, A_t the cross-sectional area of the tubular reactor, dx the differential thickness of fluid plug, and ν_i stoichiometric coefficient. The reaction rate, r, can be figured by using the Arrhenius temperature dependence. Generally, as the temperature increases so does the rate at which the reaction occurs. Residence time, τ, is the average amount of time a discrete quantity of reagent spends inside the tank.

Assume:

- isothermal conditions, or constant temperature (k is constant)
- single, irreversible reaction ($\nu_A = -1$)
- first-order reaction ($r = kC_A$)

After integration of Equation 3 using the above assumptions, solving for $C_A(L)$ we get an explicit equation for the output concentration of species A,

4. $$C_A(V) = C_{Ao}e^{-k\tau},$$

where C_{Ao} is the inlet concentration of species A.

Operation and uses

PFRs are used to model the chemical transformation of compounds as they are transported in systems resembling "pipes". The "pipe" can represent a variety of engineered or natural conduits through which liquids or gases flow. (e.g. rivers, pipelines, regions between two mountains, etc.)

An ideal plug flow reactor has a fixed residence time: Any fluid (plug) that enters the reactor at time *t* will exit the reactor at time *t* + τ, where τ is the residence time of the reactor. The residence time distribution function is therefore a dirac delta function at τ. A real plug flow reactor has a residence time distribution that is a narrow pulse around the mean residence time distribution.

A typical plug flow reactor could be a tube packed with some solid material (frequently a catalyst). Typically these types of reactors are called packed bed reactors or PBR's. Sometimes the tube will be a tube in a shell and tube heat exchanger.

Advantages and disadvantages

CSTRs (Continuous Stirred Tank Reactor) and PFRs have fundamentally different equations, so the kinetics of the reaction being undertaken will to some extent determine which system should be used. However there are a few general comments that can be made with regards to PFRs compared to other reactor types.

Plug flow reactors have a high volumetric unit conversion, run for long periods of time without maintenance, and the heat transfer rate can be optimized by using more, thinner tubes or fewer, thicker tubes in parallel. Disadvantages of plug flow reactors are that temperatures are hard to control and can result in undesirable temperature gradients. PFR maintenance is also more expensive than CSTR maintenance.

Through a recycle loop a PFR is able to approximate a CSTR in operation. This occurs due to a decrease in the concentration change due to the smaller fraction of the flow determined by the feed; in the limiting case of total recycling, infinite recycle ratio, the PFR perfectly mimics a CSTR.

Applications

Plug flow reactors are used for some of the following applications:

- Large-scale reactions
- Fast reactions
- Homogeneous or heterogeneous reactions
- Continuous production
- High-temperature reactions