Research on

PARAMETRIC PUMPING

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PARAMETRIC PUMPING IS A new separation technique that should rightfully take its place alongside other chemical engineering unit operations. Parametric pumping is a cyclic separation process characterized by flow reversal coupled to a change in a thermodynamic variable. The change in the intensive variable induces separation of the components of a fluid mixture in a two-phase system consisting of one mobile and one immobile phase (gas-solid, liquid-solid, or liquid-liquid). The oscillating direction of fluid flow enhances the separation normally achieved in adsorption-desorption or liquid-liquid extraction processes. Parametric pumping has received considerable attention in recent years.

Parapumping represents a new development in separation science, both because of its novelty and because of its adaptability to techniques commonly used in the separation of fluid mixtures, i.e., adsorption, extraction, affinity chromatography, and ion-exchange chromatography. The adaptation can be made in principle to any system where alteration of an applicable intensive variable, such as temperature, pressure, pH, ionic strength, or electric field, results in a differential shift in the distribution of solutes between the mobile and immobile phases.

The new separation technique has the following features:

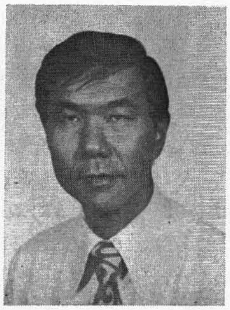
1) **Batch chromatographic separations can be made semi-continuous or continuous; continuous operation minimizes processing time (thereby reducing degradation of sensitive substances like proteins) and maximizes production rate.**
2) **The semi-continuous or continuous process, when optimized, has a high separation capability, and the solutes can be concentrated to certain desired levels by setting the relative volumes of the appropriate product streams.**
3) **No regeneration chemicals are needed to clean the adsorbent, so chemical contamination of the product streams is eliminated.**

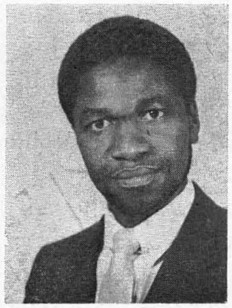
A similar process which utilizes cyclic variation of an intensive variable, but no change in flow direction, called "cycling zone adsorption," was developed by Pigford and co-workers.

The late Wilhelm and co-workers [1] invented the batch parapump and introduced a semi-continuous parapumping process in 1966. Since that time, a pre-existing industrial process, known as "pressure swing adsorption," has been identified as operating on the parametric-pumping principle [2, 3]. A similar process which utilizes cyclic variation of an intensive variable, but no change in flow direction, called "cycling zone adsorption," was developed by Pigford and co-workers in 1969 [4]. A number of review papers are available: Sweed, 1971 and 1972 [5, 6]; Wankat, 1974 and 1978 [7, 8]; Rice, 1976 [9]; and Chen, 1979 [10]. We intend to concentrate this discussion on the parametric pumping research work done in our laboratories.

PARAPUMPING RESEARCH AT N.J.I.T.

AN EXTENSIVE AMOUNT OF work has been done by Chen and co-workers using temperature and pH as the intensive variables for parametric pumping separations. Other intensive variables under investigation are pressure, ionic strength, and electric field. The overall objective of these research projects is to demonstrate that parametric pumping is a feasible process for the separation of fluid mixtures commonly found in life sciences, and in chemical and pharmaceutical industries. The research is oriented towards the development of sound experimental programs and suitable mathematical models for design, scale-up, and optimization of the processes. Following is a brief review of these research projects.





Hung-Tsung Chen was Professor of Chemical Engineering and Assistant Chairman of the Graduate Program. He taught at N.J.I.T. from 1966 until his death in 1981. He received his B.S. degree from National Taiwan University in 1958 and his M.S. and Ph.D. degrees from the Polytechnic Institute of New York in 1962 and 1964. He was the author of a number of publications in the fields of parametric pumping and photopolymerization reactor design, and held grants from the National Science Foundation for fundamental research in these areas. **(L)**

Charles Kerobo has been a Research Associate at N.J.I.T. in the field of parametric pumping since 1975. He received his B.S.Ch.E. and M.S.Ch.E. degrees from N.J.I.T. in 1976 and 1979, respectively. He is currently a Ph.D. candidate, and his parametric pumping research experience includes pressure-, pH-, and temperature-driven parapump systems. **(LC)**

Helen Hollein has been an Adjunct Professor at N.J.I.T. since 1978. She received her B.S.Ch.E. degree from the University of South Carolina in 1965, and worked for Exxon Research and Engineering Company following graduation. She earned her M.S. degree at N.J.I.T. in 1979 and is currently a Ph.D. candidate working on protein separations via parametric pumping. **(RC)**

Ching-Rong Huang came to N.J.I.T. in 1966 and is currently Professor of Chemical Engineering and Assistant Chairman for the Graduate Program of the Department. He received his chemical engineering degrees from National Taiwan University (B.S., 1954), Massachusetts Institute of Technology (M.S., 1958), and the University of Michigan (Ph.D., 1966). He also earned an M.S. in mathematics at the University of Michigan in 1965. His research interests are in the areas of rheology, transport phenomena, and mathematical modeling. **(R)**

THERMAL PARAMETRIC PUMPING

Chen and Hill [11] introduced the first completely continuous parametric pumping process in 1971. Five different versions of the thermal parapump (two continuous, two semi-continuous, and the batch pump) were analyzed in terms of the equilibrium theory and the appropriate mass transport equations. The mathematical model indicates that, under certain operating conditions, the batch pump and pumps with feed at the enriched end have the capacity for complete removal of a solute from one product fraction and for arbitrarily large enrichment of that solute in the other fraction. Separation factors and enrichment are modest for pumps with feed at the depleted end. Experimental verifications of these models for the system toluene-n-heptane on silica gel have been subsequently presented [12, 13, 14].

Continuous thermal parametric pumping was extended to the separation of multicomponent mixtures. The model system used was toluene, aniline, and n-heptane on silica gel [15]. A simple method for predicting multicomponent separations was developed. This method invokes the assumption that a multicomponent mixture contains a series of pseudo-binary systems. Each binary system consists of one solute (toluene or aniline) plus the common inert solvent (n-heptane). Experimental data agreed reasonably well with the analytical predictions.

The multicomponent system, glucose-fructose-water on a cation exchanger (Bio-Rad AG50W-X4, calcium form) was also studied [16]. Agreement between experiment and theory was roughly equivalent to that obtained above. Earlier studies on the glucose-fructose-water system used fuller's earth (LVM 16-30 Mesh) and activated carbon as the adsorbent [17, 18].

Mathematical expressions for determining optimal performance of equilibrium pumps were derived, based on the separation of $NaNO_3$ from water via an ion-retardation resin [19]. Emphasis was placed on the operating conditions necessary for achieving high separation factors with maximum yield.

The performance of non-equilibrium continuous pumps for the case of NaCl separation from water via an ion-retardation resin was also studied [20]. The criterion for approach to equilibrium operation was established for the cases where large separations were deemed possible.

A scale-up of the continuous thermal parapumping system was made and the design equations were developed [21]. Proposals were outlined for the construction and operation of the parapump assembly; the auxiliary equipment and the instrumentation were also outlined. The commercial parapump assumes the configuration of

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multiple parallel tubes in a heat exchanger shell; this design facilitates direct thermal mode operation. The energy requirements were shown to be of the same order of magnitude as that for distillation.

All of the thermal processes investigated by Chen and co-workers were operated in the so-called direct mode, i.e., the intensive variable is applied instantaneously over the entire bed. This is the more common method of operation for thermal parametric pumping [7, 8]. Rice and Foo [22] have recently carried out a direct-mode process for the continuous desalination of water, using a dual-column system.

pH PARAMETRIC PUMPING

PARAMETRIC PUMPING PROCESSES which are based on pH variation are usually operated in the so-called recuperative mode, i.e., the intensive variable is set at a different level in the streams entering either end of the bed. In this mode, the pH change moves across the bed as the entering streams penetrate the chromatographic column.

Sabadell and Sweed [23] developed pH parametric pumping in 1970 for the separation of aqueous solutions of K^+ and Na^+ on a cation exchange resin. In 1975, Shaffer and Hamrin [24] reported a pH parapumping process for trypsin removal from an enzyme mixture (α -chymotrypsin plus trypsin) using a Sepharose type ion exchanger. Since then, Chen and co-workers have researched protein separations via pH parametric pumping, with emphasis on maximum separation and continuous operation.

A semi-continuous pH parametric pump was experimentally investigated using the model system of the two arbitrarily mixed proteins, human serum albumin and human hemoglobin in aqueous solution on Sephadex cation exchanger [25, 26]. These two proteins have different isoelectric points, and the processes developed for the model system may be applied to any mixture of proteins having different isoelectric points. Proteins carry a net positive charge and will adsorb on a cation exchanger at pH's below their isoelectric points; proteins carry a net negative charge at pH's above their isoelectric points. The semi-continuous pump, which had a center feed between an enriching column and a stripping column, was operated batchwise during upflow and continuously during downflow. Two pH levels were imposed periodically on the system. Various factors affecting the separation were examined, including pH levels and ionic strength of the protein solutions, reservoir displacement, and product flow rate. Hemoglobin was stripped from the top stream and enriched in the bottom stream; the separation factor for hemoglobin reached a limit of six in the best run. The albumin concentration remains unchanged in this process, but removal of hemoglobin from the top stream leaves the top product relatively richer (by weight fraction) in albumin.

A "continuous" pH parametric pump was used to separate the model system hemoglobin-albumin on CM Sepharose cation exchanger [27]. This pump configuration had protein feed solutions at low pH and at high pH (relative to the isoelectric point of hemoglobin) introduced respectively to the bottom and top of a chromatographic column. It was shown that increasing the volume of the top product to some optimum level relative to the volume of the bottom product gave the pump the capacity for large enrichment of hemoglobin in the bottom product stream. Note that this system is currently considered to be "semi-continuous," because each cycle contains two stages where product is not withdrawn. A completely continuous parapumping process for protein separations is being developed.

A mathematical model with finite mass transfer was developed for the model system hemoglobin-albumin on CM Sepharose [28]. This model agrees quite well with the experimental data. Various factors affecting the separation were examined, including the addition of recycle stages to the one-column process.

An equilibrium theory was used in a theoretical analysis of the batch single-column and multi-column pH parametric pump [29]. Simple graphical procedures for predicting separation showed that a parapump consisting of a series of columns packed alternately with cation and anion exchangers is capable of yielding very high separation factors. Experimental results, based on a comparison of albumin enrichment in one-column and two-column systems packed with CM and DEAE Sepharose, were shown to support the theory.

Fractionation of multicomponent protein mixtures by multi-column pH parametric pumping was investigated theoretically and experimentally [30]. The parapump consists of a series of chromatographic columns packed alternately with cation and anion exchangers. Separation of a mixture of n proteins requires a parametric pumping system consisting of n columns and n+2 reservoirs. Various methods of operation of the parapump were discussed. Preliminary experimental data was shown in this paper for the two-column batch separation of the model system hemoglobin-albumin on CM and DEAE Sepharose, and this data was in qualitative agreement with the calculated results. Optimization of the batch two-column system has been recently completed and separation factors as large as twenty-five were obtained for the mixture [31]. The semicontinuous multicolumn data is being currently obtained.

PRESSURE PARAMETRIC PUMPING

PRELIMINARY WORK HAS BEEN done on the separation of gas mixtures. An equilibrium plug-flow model for the batch isothermal system (propane-argon on activated carbon) was studied using presure swing adsorption [32]. Effects of temperature, pressure, and concentration were investigated. A continuous pressure parapump was studied for the model system carbon dioxide-helium on silica gel [33]. The experimental results were analyzed by means of an equilibrium theory, and the various operating parameters necessary for the complete removal of the solute (CO_2) were investigated.

The continuous process was extended to the separation of a ternary mixture, propylene-carbon dioxide-helium on silica gel [34]. Various performance characteristics were examined. Using the same model system, an experimental and theoretical study was done based on a non-equilibrium theory and linear adsorption isotherms [35]. A comparison was made for the binary and ternary gas mixtures, and the conditions necessary for the separation of the multi-component mixtures were established.

SCOPE OF CURRENT RESEARCH

EXPERIMENTAL STUDIES ARE currently in progress on two pressure swing systems: one for the removal of organics from hydrogen streams and one for the separation of hydrogen isotopes. Although pressure swing adsorption is a common industrial process, fundamental studies are limited in the open literature [36]. The separation of hydrogen isotopes on vanadium hydride was recently reported by Wong, Hill and Chan [37].

The purification of the enzyme (alkaline phosphatese) by parametric pumping with pH and ionic strength has been investigated using a semi-continuous process [38]. Alkaline phosphatese, extracted from the human placenta, contains some undesired proteins which have isoelectric points approximately equal to that of the enzyme; hence, the additional intensive variable (ionic strength) is required. This new process is the first one reported which uses ionic strength as the intensive variable for parametric pumping. Comparison of enzyme purification by parametric pumping and cycling zone adsorption shows that the former

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process has a higher purification factor and larger % enzyme activity recovered, while the latter process has a higher rate of production. Optimization studies on the enzyme system indicate that a parapump operation with the proper combination of the two intensive variables, pH and ionic strength, is superior to a parapump system based on only pH or ionic strength [39]. A comparison of the purification of alkaline phosphatese via parametric pumping to the purification which can be obtained via a conventional process, such as polyacrylamide gel electrophoresis, is nearly completed.

A new semi-continuous parapumping process based on cyclic variation of pH and electric field has been shown to be capable of splitting two proteins in a mixture from each other, using a single-column set-up [40]. The same model system was used as in previous protein separation studies, i.e., hemoglobin and albumin in aqueous solution on CM Sepharose cation exchanger. The separation obtained in the single-column, semi-continuous pH parametric pumping process is enhanced by inducing an electric field across the chromatographic column during certain stages of the process. Separation factors as high as 120 are reported for the mixture. Mathematical analysis of this system is currently underway. Separation, recovery and production rate for this system will be compared to the multicolumn pH system, when the semi-continuous multicolumn data is available. Other researchers have shown electrochemical parapumping to be potentially useful for desalination of water [41, 42].

Separation of protein mixtures by multi-affinity chromatography combined with cyclic operation is being investigated [43]. The system consists of a series of columns packed alternately with anion and cation exchangers (Sephadex (G150) and Sepharose (4B)). Two cyclic methods are being considered: semi-continuous parametric pumping and continuous simulated moving bed operation. This process is being adapted for the separation of lectine mixtures, such as Convalin A and Ricinus Communis Agglutinin I.

A staged sequence multicolumn cyclic process is being developed for the separation of liquid mixtures. This continuous process eliminates the mixed reservoirs normally used in parametric pumping. (Note that reservoir mixing tends to reduce separation [22].) Separation of a mixture of n solutes by the direct-mode of operation requires a set-up with n+1 columns and n driving forces. The feed and product ports are fixed in the staged sequence process, but different components can be directed to exit from specified ports by synchronizing the feed and product positions with the appropriate intensive variable. Preliminary experimental results for semi-continuous operation in a one-column system are being extended to the continuous multicolumn system. A mathematical model which fits the one-column data is being modified to predict the continuous separation.

From the discussion of active research areas, it is evident that parametric pumping is a very useful and versatile process in separation technology. It is our belief that commercialization of some of these parapumping systems would be economically feasible.

ACKNOWLEDGEMENT

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POSTSCRIPT

This article was initiated by Dr. Chen at the request of CEE, prior to the tragic automobile accident which ended his life on April 21, 1981, and completed by his co-workers in his memory.

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In Memoriam

HUNG TSUNG CHEN

Hung Tsung Chen was killed in an auto accident on April 21, 1981. His numerous students, faculty colleagues, and members of the New Jersey Institute of Technology community will miss him a great deal. The work he did in the area of parametric pumping and polymer engineering was exemplary and he is irreplaceable. We all extend our sympathies to his wife Vera, his son, Andrew, and his daughter, Carol.

Dr. Chen was born in Taiwan, Republic of China, on August 23, 1935. He attended the National Taiwan University and obtained his BS degree in chemical engineering in 1958. He came to the United States and received both the MS (1962) and PhD (1964) in chemical engineering from Brooklyn Polytechnic Institute. He worked under the supervision of Dr. Othmer.

Following his graduate studies he worked for FMC Corporation. In 1966, he joined the faculty of the Department of Chemical Engineering and Chemistry at New Jersey Institute of Technology where he worked until his untimely death. Dr. Chen was a Full Professor and Assistant Chairman of the Graduate Program. He has served as a consultant for numerous companies including Bookhaven National Laboratory. He was an excellent undergraduate and graduate teacher and was highly admired by his students. He worked in the area of parametric pumping and had developed into one of the leading international authorities on the subject. He had more than 20 graduate students working with him in this area and polymerization reactor technology. Dr. Chen, a prolific publisher, had more than 40 publications. He also contributed to Handbook of Separation Techniques for Chemical Engineers. One publication in the AIChE Journal was accepted without any revision needed. The Editor called this a "first."

He served the department and Institute on many committees. He was an active member of AIChE, Sigma Xi, Omega Chi Epsilon and was a registered professional engineer.

Dr. Chen was an invited speaker at the Gordon Conference (1980), had numerous NSF grants, was named "Outstanding Educator of America," was listed in Who's Who in the East, American Men of Science, Community Leaders and Noteworthy Americans, Directory of International Biography, and Men of Achievement.

On May 28, 1981, at our Institute's Centennial Year Commencement exercise, Dr. Chen received (posthumously) the first Harlan J. Perlis Award for Excellence in Research given by our Institute. The award was received by his wife, Vera, with a standing ovation.

Dr. Chen can never be forgotten. He is irreplaceable and future generations of chemical engineering students have been deprived of his attention by our great loss. Dr. Chen will always be with us, and will represent a standard of high achievement and excellence. He will be missed very much by our chemical engineering profession.

Deran Hanesian
Angelo Perna