

Whither Chemical Engineering?

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Abstract

The strong core base in chemical engineering during the latter half of the 20th century enabled chemical engineers to contribute extensively to many areas outside of the traditional. The depth of such involvement has led researchers to confront questions much more engaging to the field of application, thus adopting and cultivating expertise more native to it than to secure chemical engineering as a discipline. The progress of knowledge in science and engineering must leave a strong trail of fundamental understanding through developed methodologies that can assist in continuing progress. If this tenet is acknowledged, this article yields considerable scope for discussion on whether chemical engineering research is continuing to provide for a growing core that has endowed chemical engineers with the ability to formulate and solve important societal problems in which material systems undergo changes in composition and energy. We discuss opportunities for hopefully serving the issues of concern.

Introduction

Contemporary research in any branch of engineering is seen of late to transgress its traditional academic borders to an extent that its relationship to the embryonic beginnings of the field is often unclear. This occurrence is a consequence of the notable strides in fundamental understanding of natural phenomena and its powerfully unifying effect. In this regard, chemical engineering, in view of its empirical roots, has had the most striking advances in the last several decades. The early development of any engineering discipline has been to cater to some selected societal need (or set of needs) served by the formulation of core subjects towards maintaining some territorial integrity. Thus, chemical engineering began naturally by being associated with industrial chemistry, which was the art of producing chemicals for multifarious applications towards meeting diverse societal needs. This beginning is reflected well in the manner in which core chemical engineering progressed from unit processes to unit operations, and further on to the use of chemical kinetics and thermodynamics, the framework of continuum mechanics to study transport processes in fluids, with parallel development of statistical mechanics and molecular theories.

The use of mathematics in chemical engineering climbed precipitously during the fifties, sixties, and seventies in the last century with a healthy influx of analysis particularly in chemical reaction engineering, fluid mechanics, transport phenomena, and the process systems area. Graduate core courses in most chemical engineering departments came to include Transport Phenomena, Thermodynamics, Chemical Reaction Engineering, and Applied Mathematics. Although these core courses have remained about the same over the years, there has occurred some withering of intensity, probably because faculty interests have tended to shift away from areas that benefit directly from such background. Not infrequently, junior faculty in pursuit of greener pastures elsewhere have subconsciously compromised the level at which core courses are taught. These observations cannot be said to be emanating from obscure corners of the profession. They seem largely prevalent viewpoints, often expressed but more often held back. As mentioned earlier, the objective of this article is to provoke discussion, at least to the extent of examining the evolutionary course of the profession. There is the familiar quip of “Chemical Engineering is what chemical engineers do!” Ignoring

the “circularity” of this definition, we may inquire into whether or not chemical engineering is served well by such a stance. Arbitrary activity is no one’s objective. Also, the propitiousness of a researcher’s direction will be tempered by the response of the profession at large.

This article seeks to argue for a rationally infinite domain for the creativity of chemical engineers to flourish by formulating inquiries as to whether or not their activity results in some attributes on which we could expect some degree of consensus. While some attributes may not be contested, others could spark debate:

1. As all research, engineering research must be creative as well as impactful. The focus of most researchers is impact as expressed by citations and, perhaps to a lesser extent, through recognition by a professional arm of the field as awards or keynote invitations to perspective conferences.
2. Contributions by chemical engineers must display some distinctive traits which must contribute to the solution of a significant problem. In the absence of such traits, the researcher’s message is subsumed into the multitude of contributions in the field of application by researchers more directly connected to the subject. The area of biology, which represents perhaps the most exciting opportunity for chemical engineers to contribute creatively, is a particular case in point. Often, the only response to a question on relevance of the research to chemical engineering has been that the scale of observation is a reactor which does not attract the attention of a biologist. While reactor-scale work is certainly of importance, the contribution derives merit not from the scale of the observed system but from how the reactor is coaxed to work with quantitative use of biological principles.
3. A traditional chemical engineering audience often views askance research seminars that are stacked with biological facts or hypotheses without a lateral conduit to a clarifying conceptual source in chemical engineering for interpretation.
4. Another measure that seems important for chemical engineering activity in a different field is its potential to modify or enhance the core. Indeed, this feature is tied to securing core strength towards preserving a more liberal version of “territorial integrity” than before; “more liberal” implying generality rather than insularity. One may inquire into whether or not the contribution of engineers is generating new perspectives by virtue of tools that define the parent discipline, and further if this experience has widened as well as sharpened the tools that were used.
5. As in all other areas of science and engineering, opportunities abound in chemical engineering for the use of data science, machine learning, and artificial intelligence methods in dealing with complex systems.

Our deliberations will focus on biology, on which chemical engineering has had a major impact. Not surprisingly, many ChE departments have added “biological” or “biomolecular” engineering to their names. However, we begin with briefly reflecting on the traditional core areas, starting first with applied mathematics and transport phenomena.

Applied Mathematics and Transport

A comprehensive account of mathematics in chemical engineering over the past several decades has appeared in this journal.¹The mathematical culture that prevailed in the latter half of the twentieth century spurred the use of analytical tools in chemical engineering applications. While Amundson and Aris were the chief architects of this movement, there were others such as Horn, Acrivos, Brenner, Churchill, and Stewart, to mention only a few, whose publications reflected a significantly higher level of mathematics. It is interesting to note that scholarship pervaded in the early sixties even among industrial circles such as the Socony Mobil Oil (now a part of ExxonMobil) hosting Truesdell’s lectures in continuum mechanics.² Numerous in-depth mathematical applications emerged from industry such as the determination of rate constants of catalytic reaction systems using spectral information from suitably designed experiments,³ the analysis of lumping reaction systems,⁴ and so on. Such applications thrived from an edifice that espoused analysis as well as computation.

Fluid mechanics thrived through a major pioneering effort by Acrivos and his group. In particular, Acrivos established the use of matched asymptotic expansions for problems in transport with several analytical

results.⁵ Aris' *Vectors, Tensors and the Equations of Fluid Mechanics* provided a rare perspective of the subject more akin to a physicist's view.⁶ Scriven's study of fluid interfaces and Marangoni instability and subsequent involvement with interfacial driven flow set a tone in fluid mechanics distinctly higher than the prevailing level.⁷ *Transport Phenomena* by Bird, Stewart, and Lightfoot most effectively changed the teaching of Transport.⁸ The growth of this development continued with the publication of their (long delayed) second edition. The books of Leal⁹ and Deen¹⁰ deserve special mention in preserving the graduate version of transport phenomena. It is puzzling, however, that undergraduate courses in transport phenomena have suffered some loss of level. There are notable exceptions to this observation but consensus may be said to exist on this impression. The unique expertise of chemical engineers on mass transfer is at risk with dwindling attention to this subject. Often a single semester course in graduate Transport is unable to include mass transfer, in spite of its high importance to chemical and biological systems encountered in research and in industrial practice.

Mathematical software such as Matlab and Comsol have enormously eased the application of mathematical models in engineering. The capabilities of symbolic software such as Maple and Mathematica are prodigious in that computation can be postponed to the very final stage when parameter values are to be inserted for numerical evaluation of a mathematical model. Matlab is routinely used in undergraduate courses. Sometimes their premature use has been at the expense of time that could be better spent on issues of formulation and analysis that harbor the essence of innovation. Notwithstanding the strongly positive role of mathematical software in education, most undergraduate instructors sense a drop in the comfort level of chemical engineering students in mathematics. Under these circumstances, elimination of a first-level core course in Applied Mathematics in ChE graduate programs would appear to be patently unwise. Schools strong in the systems area are, however, an exception in this regard since this field of research has made notable strides over the years.

Generally, computational work can be said to be thriving but often without recognition that it can sometimes be coaxed to gain from a timely input of analytical reasoning. For example, instances can be cited in which parameter estimation can be notably improved by local analysis of nonlinear dynamic behavior with bifurcation methods. It is unclear whether the age-old practice of inaugurating the introductory chemical engineering course with dimensional analysis and the Buckingham Pi Theorem is still in vogue. Clearly, parameter estimation of nonlinear models can be aided by non-dimensionalization, as the number of dimensionless parameters is less than the original set; furthermore, a better rationale is frequently available for their initial estimates for iterative computation.

The argument in favor of analytical reasoning is not made to diminish in any way the importance of computational methods but rather to point to its effectiveness in organizing computation. A culture of analysis has the facility to cultivate creative ideas in the profession, for in its absence, there would not be the likes of Gavalas,¹¹ who introduced topological methods in reactor analysis, Balakotiah and Luss,¹² for their work on singularity theory, Feinberg,¹³ who made intriguing contributions to chemical reaction network theory, and Jackson,¹⁴ who published many interesting papers on particle flows as well as in chemical reaction engineering. Of course, there are many more who deserve mention, but the goal here is to argue for more analysis than provide an exhaustive list of creative analysts.

Chemical Reaction Engineering

Graduate courses in Chemical Reaction Engineering have tended to become more oriented to catalytic science because of significant developments in this field. Discussion of transport effects in reaction systems appears to have lost some of its prevalence. Dispersed phase reactors receive no more than a modicum of mention due to limited familiarity with the use of population balance equations. It is heartening, however, that an industrial reaction engineering course organized by Hickman¹⁵ under the auspices of Purdue CISTAR provided an excellent picture of reaction engineering practice.

Process Systems Engineering

Process systems engineering (PSE) is the application of systems engineering to biophysicochemical processes,

where *systems engineering* is the methodical approach for the design of systems via mathematical modelling, data analytics, optimization, and control, and a *system* is a set of units that interact. Numerous journal papers have been published in the last decade in which authors provide various perspectives on process systems engineering.¹⁶ Some papers argue that the discipline of process systems engineering was founded in the 1950s, whereas others argue for the 1960s or even later. The process systems engineering field actually can be traced back to the 1930s to early 1940s, when the use of mathematical modeling to design controlled process systems was already practiced in the chemical industry.^{17 18 1920 21} Process systems engineering was an active research area by the 1950s, with pioneering work by Rutherford Aris, Neal Amundson, and Roger Sargent in various types of chemical reactors and separations.^{2223 24 2526 27} The use of numerical computing in process systems engineering, which had already been applied in industry in the 1950s, became widely studied by the 1960s, with additional research teams including that of Ernst Gilles, Lowell Koppel, Leon Lapidus, Dale Rudd, W. Harmon Ray, Larry Evans, Reuel Shinnar, and Art Westerberg.^{28 2930 31 3233 34 3536 37 3839 40 4142}

The 1970s saw the development of many research groups in process systems engineering, including by G.V. Reklaitis, George Stephanopoulos, Iori Hashimoto, John Perkins, Thomas Edgar, Ignacio Grossmann, Dale Seborg, Michael Doherty, Manfred Morari, Charles Cutler (at Shell), and Jeffrey Sirola (at Eastman Chemical).^{43 44 4546 47 4849 50} Much of the research was in developing PSE solutions for specific classes of processes. Other research considered processes more generally, and precise mathematical formulations were derived for much of the PSE technologies used in today's industry, including for model predictive control, data reconciliation, and process scheduling. Methods were developed for better handling of practical considerations such as uncertainties and mixed continuous-discrete operations. At the same time, several research groups were making an impact outside of the field of chemical engineering, alongside their contributions within the field. As in earlier years, many individuals within the PSE community were widely known outside of PSE, including in reaction engineering and separations.

The 1980s to mid-1990s saw the founding of a large number of PSE research groups worldwide, with a large proportion focusing their attention only within the PSE community, with very little interaction outside of PSE, either within or outside of chemical engineering. A small proportion became highly engaged outside of PSE, in some cases becoming very well known outside of PSE, including in the areas of optimization and control theory and in applications such as to energy systems, pharmaceutical manufacturing, and biomedical devices. Individuals at such interfaces included James Rawlings, Lorenz Biegler, Nikolaos Sahinidis, Babatunde Ogunnaike, and Frank Doyle.

Data analytics, which was an active area of research within a subset of the PSE community and applied in industry for decades, has become of increased activity with the meteoric rise (and some rebranding) of machine learning. Recent years have seen PSE faculty increasingly collaborating with non-PSE faculty to apply PSE methodologies to their research problems, which has resulted in an increase in the number of publications by PSE faculty in highly scientific venues including *Nature*, *Science*, *Cell*, and *PNAS*. These collaborations include applications of machine learning, systems analysis, and process design, operations, and control. The "PSE community" is largely two distinct groups today, with one group being very inward-looking and focused on publishing papers in traditional PSE publication venues, and another group whose primary goal is to make an impact in other communities. The interactions between the two groups are rather limited, although some individuals have received some level of acceptance by both groups. The outward-looking community is likely to continue to grow, as automation, high-throughput experimentation, sensor technologies, and computing continue to favor methods that make best use of these trends.

With the growth of computing and data, process systems engineering continued to grow in methods, software, and applications to the point of becoming indispensable in the design and operation of modern chemical and biotechnological processes. Today software for computer-aided process systems engineering such as Aspen Plus, gPROMS, DMCplus, and DeltaV is ubiquitous in the process industries. While systematic methods for addressing such characteristics as time delays, nonlinearities, disturbances, and uncertainties have been developed since the early days of the process systems engineering discipline,⁵¹ algorithms and

software have become increasingly powerful since then, enabling increasingly complex systems and types of design problems to be addressed. The engineering designs are only as good as the mathematical formulation of the process systems engineering problem to be solved, and chemical engineers need to continue to be trained in the language of mathematics and in chemical and process systems engineering fundamentals to be able to address the increasingly complex chemical and biological systems that arise in today's and tomorrow's technological problems.

Biological Engineering

The traditional core background of chemical engineers constituted an ideal fit for the study of biological systems in which enzyme-catalyzed reactions and physical transport occurred aplenty albeit in a very complex setting. The early entrants to the bio area such as Lightfoot, Fredrickson, and Tsuchiya, and many other trend-setters were able to show that chemical engineers can make unique contributions to this area. Not surprisingly, the models were gross abstractions of the system with a few ordinary differential equations and lumped chemical species. Fredrickson et al.^{52,53,54} demonstrated the applicability of kinetic models of microbial systems with structured biomass from the perspective of an “average” cell. In an early development of the population balance framework, Fredrickson et al.⁵⁵ developed models that could accommodate population heterogeneity. In the course of time, however, the models grew in sophistication including metabolic networks of increasing complexity. Bailey,⁵⁶ Stephanopoulos,⁵⁷ Palsson,⁵⁸ Lauffenburger,⁵⁹ and many others developed models with detailed metabolic perspectives. In particular, metabolic engineering in which the genetic background of cells is altered to change their metabolic potential was founded by Bailey. Further, the flow cytometer had its early beginnings in Bailey's laboratory under the name microfluorometer. The foregoing accomplishments were impressive as they notably changed the quantitative approach to modeling biological systems. The development of flow cytometry also led to assessing the heterogeneity of microbial populations and identification through population balance models.^{60,61}

Metabolic modeling brims with many interesting perspectives that reaction engineers will find attractive. However, its popularity in ISCRE (International Symposia on Chemical Reaction Engineering Conferences) has been surprisingly limited. A detailed metabolic network may appear at first to be of daunting complexity. The recognition that external nutrients enter the cells at rates much slower than those at which intracellular reactions occur, however, offers the comfort of a pseudo-steady state for intracellular components thus effecting linear coupling of the various intracellular fluxes. Metabolic flux analysis (MFA) is built on this edifice with matrices of stoichiometric coefficients accounting for connectivity of metabolites in the network. An excellent treatment of MFA with numerous examples of applications is contained in Stephanopoulos et al.⁵⁷ Clearly, the fluxes obtained by such computation are *regulated* versions. Thus, if the regulatory scenario is different for one reason or another, the fluxes would be altered and must again be obtained experimentally.

In a complex network, many “reaction paths” are conceivable as cellular alternatives. A truly creative concept associated with these alternatives is that of an *elementary* mode. Crudely, it may be viewed as comprising the uptake of an external nutrient into the cell to be engaged in a sequence of intracellular reactions culminating in the excretion of an ultimate product into the environment. Obviously, there would be a countless number of such reaction paths and it would be unrealistic to expect that *all* of them will be commissioned by the cell. (One could imagine, with some comfort, the potential reality of a single path as arising from the absence of catalytic enzymes that could divert metabolic species away from the specific reaction path).

It is now known that, even for a network of reasonable size, the number of elementary modes can run into millions. Palsson's choice of reaction paths that *maximize* the biomass yield is a stroke of brilliance because of its capacity for predicting yields of metabolic products with ease even for relatively large networks.⁶² Specification of the substrate uptake rate (readily obtainable experimentally) leads to productivity calculations of all cellular products. Extension of the flux balance analysis (FBA) has been made for dynamic predictions (DFBA) by kinetically modeling uptake rates free of regulatory effects.⁶³

The steady state approach, however, is not suited to accounting for the phenomenon of *metabolic regulation*,

due to which cells preferentially navigate through their metabolic network by controlling the syntheses and activities of enzymes. The development of cybernetic models,^{64,65,66} has led to dynamic modeling of metabolism comprehensively inclusive of regulatory effects. While cybernetic models have been successfully used to demonstrate numerous, dynamic consequences of regulatory phenomena such as different uptake patterns of mixed substrates, and dynamic effects of specific gene knock-outs and gene insertion,⁶⁷ their full exploitation for metabolic engineering is still pending. Song's work on lumped hybrid cybernetic models based on lumping of elementary modes towards reducing model parameters deserves commendation as an example of chemical engineering prowess.⁶⁸

Regulatory processes include transcriptional, transcriptomic, and post-translational regulation. The foregoing cybernetic approach is based on the postulate that the details of the foregoing mechanisms do not need to be included explicitly as they represent the implementing mechanism of the optimal strategies ensuring cellular survival goals. Thus, consistency of regulatory patterns predicted by cybernetic models with temporal gene expression profiles shows their capability to include regulatory effects in metabolism.

Regulatory processes evidently control directly or indirectly the distribution of all components that participate in life processes in various ways. Consequently, modeling of biological processes and the quantitative understanding to be had from it is clearly contingent on consideration of regulation. The success with modeling regulatory effects in bacterial metabolism provides considerable incentive to extend the approach to eukaryotic systems in spite of the latter's greatly added complexity.

Some beginnings have been made by Aboulmouna et al.⁶⁹ with cybernetic modeling of regulation in macrophage cells which are concerned with the organism's immune response. This system is riddled with uncertainties from various sources. First, choices for cellular goals are not as suggestive for eukaryotic cells as they are for bacterial cells. Second, multiple goals may be involved at different stages of the cells' development. Third, metabolic interconnections are not known in their entirety for a rational cause-and-effect representation of all cellular events. Aboulmouna's model was predicated on the goal of maximizing production of the cytokine by cybernetic control of arachidonic metabolism. While the details are best left to the cited reference, multiple goals were included in dealing with different network components. The issue of unknown links between the production rate and those of different metabolites was accomplished by a linear fit of their respective time series data. This model successfully predicted the regulatory consequences of certain perturbations. The terse view just presented is more to provide a broad perspective of the model assemblage than for suggesting any generality of its specific features.

Regulatory processes are studied experimentally in considerably more detail by measuring the concentrations of messenger RNA's (*m*-RNA), constituting crucial data for cybernetic modeling of eukaryotic systems. The regulatory dynamics is represented by the *m*-RNA profiles so that the cybernetic model features *m*-RNA concentrations as variables among other components of metabolism.⁷⁰ The incentive for such modeling is the possibility of laying a foundation for improved quantitative understanding of eukaryotic systems with potential applications to fighting disease and developing drugs.

Population Balances

Although population balances date back to the days of Boltzmann, this is an area in which chemical engineering leadership has been notable since the 1960s.^{71,72,55} The contribution of chemical engineers has been especially creative since the coinage of the term "internal" coordinates by Hulburt and Katz⁷¹ for variables other than spatial location of an entity which opened the flood gates to a plethora of applications. Numerous reviews provide perspectives of population balances.^{73,74,75,76} An application of consequence to biology is the formulation of signal transduction problems in a population setting. The signaling variables become internal coordinates of the cell and the stochastic process characterizing the dynamics of intracellular reactions translating into the convective and diffusive transport of cells in the abstract space of internal coordinates. This transport can also occur in conjunction with spatial transport if the cells were in motion through physical space.^{77,78} The transfer of drug resistance between bacterial species, which has been of major concern in combating bacterial infection, is a significant area of application.^{79,80} This transfer occurs by exchange

of resistance bearing plasmid DNA from the “donor” cell to the “recipient” following signaling reactions in the donor as shown in Figure 1. A single cell stochastic model, oblivious to the presence of other cells in the neighborhood, would show a steady state population distribution in which individual cells exhibit stochastic dynamics, whereas the more relevant population balance model would paint a different picture of the same scenario as shown in Figure 2.

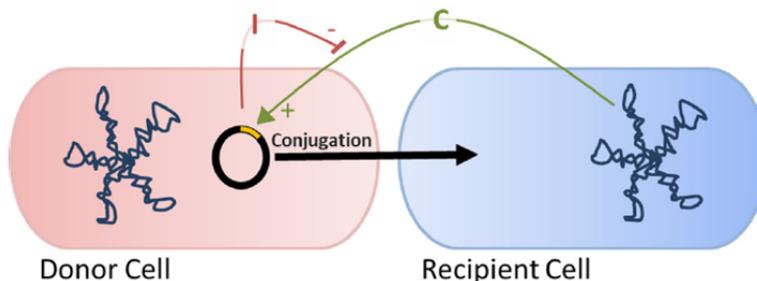
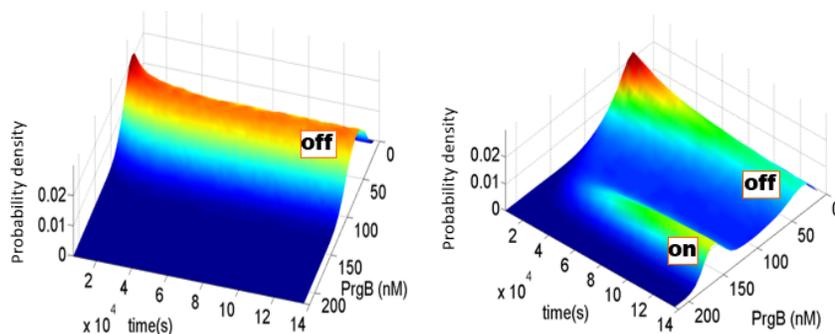


Figure 1. Transfer of antibiotic resistance from donor to recipient through transfer of plasmid.



(a) (b) Figure 2. Temporal evolution of donor population towards steady state. PrgB is a protein made by the donor cell in response to the signal dispatched by the recipient which facilitates transfer of plasmid. The “on” cells are ready to transfer plasmid while the “off” cells are not. Note the substantial difference in the steady states predicted by the population balance model and the single cell model. (a) Population balance model. (b) Single cell model

Data Science and Machine Learning

Data ridden systems are a frequent occurrence in all fields of human endeavor as computers have the means to store an incredible amount of data. Biological engineering, of particular interest to us, is no exception in this regard as advances in measurement techniques have helped collect massive amounts of data in numerous areas in which chemical engineers are active. Venkatasubramanian provides an interesting perspective of artificial intelligence in chemical engineering.⁸¹ He is cautiously optimistic, and observes that data science and machine learning with suitable infusion of first principles could be an attractive combination for chemical engineering applications. Diagnostic issues in health science are indeed a promising area of application. Verma, in quest of the source of peripheral neuropathy from the use of Vincristine in the treatment of leukemic cancer, used machine learning to identify a handful of pain associated metabolites.⁸² Early detection of such metabolites from blood samples could lead to drug dosage adjustments for improving the quality of life.

Lumping of chemical species in systems with a very large number of species has been of interest to chemical reaction engineers. When nonlinear reaction kinetics is involved, lumping strategies could be of interest using

data science and machine learning. Similarly, order parameters or collective variables have been of interest in molecular systems towards reducing their dimension as a means to study rare events such as nucleation. Data science and machine learning could be a potential source to elucidate a small number of collective variables in terms of which the free energy of the system can be determined. While such applications abound, the likelihood of pedestrian usage of the methodology cannot be ignored.

Concluding Remarks

Our objective has been to present a perspective of current educational and research trends in chemical engineering with an eye on maintaining a strong core. It is our position that a conscious effort to nurture core areas of chemical engineering through both education and research would be essential to perpetuate the success of chemical engineers in contributing to society. Chemical engineering embraces analysis of transport and chemical reaction on systems encompassing a wide spectrum of spatio-temporal scales that offer unlimited opportunities for synthesis, optimal design control, and scope for local and global perspectives. The 2018 Nobel Prize of Arnold for deploying directed evolution techniques to engineer new enzymes is a striking example of what chemical engineering expertise can accomplish. Seinfeld's contributions to aerosol science and atmospheric chemistry have paved the way for quality control regulations in the United States. Enormous contributions have come about in the drug delivery area from Langer,⁸³ and Peppas.⁸⁴

Preservation and growth of chemical engineering core areas cannot occur without allocation of resources for teaching and research. Graduate programs, regardless of their research thrusts, must invest in high quality core teaching. The present situation does not appear conducive in this regard as researchers dedicated to core areas have to find sagacious means of survival.

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