The Neal Amundson Era. Rapid Evolution of Chemical Engineering Science

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Neal Amundson (1916–2011) influenced the chemical engineering profession more profoundly than any other single individual, and in this article the author has attempted to capture the man and his era, as well as his lasting legacy. His influence extended well beyond those of other chemical engineers of renown, whether they were known for exploring and establishing new avenues, or for the resolution of outstanding issues, or for other forms of creative endeavors. Amundson reached into the depths of the profession, noted for its expanse, complexity and diversity that had led earlier efforts into a shrine of empiricism, to foster a culture of strongly scientific thinking with a mathematical edifice, which must be the crux of all engineering. The growth of chemical engineering science owes most significantly to Amundson's extraordinary role as an educator, department head and leader, and to the lasting impact of his contributions to chemical engineering research and practice. This article is in salutation of the man who came to be known as the Minnesota Chief, and was responsible for an academic movement that raised the intellectual level of the chemical engineering profession. © 2013 American Institute of Chemical Engineers *AIChE J*, 59: 3147-3157, 2013
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Introduction

Olaf A. Hougen once challenged the author of this article to produce an equation in a book out of which he had taught chemical engineering in the 1920s. His challenge was of course prompted by the book's scrupulous freedom from equations! As an outgrowth of an engineering profession for the production of chemicals, chemical engineering had its beginnings in dissecting chemical processes into unit processes and unit operations. Unit processes were concerned with the nature of chemical transformations while unit operations focused on physical processes of separation, mixing, and so on. The underlying methodology was largely empirical with performance described by correlations linking independent dimensionless groups of the system. The prevailing view of the early chemical engineer was that of a mechanical engineer, who focused on the manufacture of chemicals.

The introduction of material and energy balances by Lewis and Radasch[1] and Hougen and Watson,[2] was a significant development in this growth phase of the chemical engineering profession. It sowed the seeds of rationally thinking about systems and analyzing them with conservation and thermodynamic principles. It was a precursor to the more microscopic view that followed with the institution of transport phenomena by Bird et al.[3] which laid the foundation for unifying the apparent diversity of unit operations and unit processes.

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The arrival of Neal Russell Amundson into the chemical engineering scene must be regarded as heralding his deliberate effort to build the scientific base of chemical engineering. Mathematics was indeed to play a key role in this process but, in his leadership role, it was a quest for the import of basic concepts of all science. This was not simply to be a paradigm shift, but a major cultural change. It deeply involved the creation of model images of systems; penetrate them to their pathological limits with mathematical tools, and eliciting guidance for experimentation in search of more complete understanding. The department he built at Minnesota was a reflection of this philosophy. It is the objective of this article to reflect on the Neal Amundson era and the evolution of chemical engineering science during this period. In so doing, we will deliberate not only on Amundson's contributions and their impact, but also on his overall influence on the chemical engineering profession.

Educational Background and Early Academic Days

Amundson obtained his Bachelor's degree in chemical engineering from the University of Minnesota in 1937, and joined Standard Oil Co. (now ExxonMobil) in Baton Rouge as a Process Control Engineer. Neal did not recall the experience as particularly interesting, because engineers were denied access to the company's R&D facilities where the fluidized catalytic cracker was in its early development. There were too many "nonproductive" activities that consumed his energy of which he had "had enough" by the end of 2 years, and he returned to the University of Minnesota for graduate studies. He enrolled for a Master's degree in chemical engineering there. The Dept. of Chemical Engineering, at that time housed in the chemistry building, was relatively young but "competent" as Neal described it. He observed, however, that the research in the department was "mostly experimental and dull." Interestingly, Amundson received his Master's degree in chemical engineering in 1941 with the first ever nonexperimental thesis!

There had been "very little mathematics" taught during his undergraduate days at Minnesota so that Neal's interest in mathematics was not aroused until after his bachelor's degree. Curiously, while he was at Standard Oil, he and a few of his colleagues attended evening classes at LSU on differential equations taught by a Norman Rutt, whom Amundson fondly recalled as a very "charming fellow"! This seems to have sowed the seeds of his subsequent involvement with mathematics. One wonders whether such excursions are at all a part of students taking courses during graduate work today!

The years that followed were highly consequential for Neal. In light of finding little mathematics in the Chemical Engineering Dept., he switched to a PhD in mathematics under the supervision of Hugh Turrittin at the University of Minnesota. A student of Rudolph Langer of Wisconsin, Turrittin's lineage stretched two generations back to the famous American mathematician, G. D. Birkhoff. The final year of Neal's doctoral thesis was spent at Brown University where his advisor was on sabbatical leave. This could well have been the defining period of Neal's career, for he experienced at Brown an extraordinary atmosphere of mathematics that he felt as if had "pulled him out of the water"! He returned to Minnesota in 1945 with a PhD in mathematics, euphoric about his experience at Brown in the company of eminent mathematicians, and ideas that perhaps molded his own academic contributions the most. His doctoral dissertation bore the title "Solution of a Nonlinear Partial Differential Equation of the Parabolic Type."

Neal began his academic career at the University of Minnesota as an Assistant Professor of Mathematics. Even as a young, junior faculty member, his instinct for leadership had begun to surface, for he had played an active role in changing the face of Minnesota mathematics by initiating the move of an eminent mathematician by the name Stephen Warschawski from Brown University to head the Dept. of Mathematics at Minnesota. With Warschawski's arrival, many new courses were instituted, a full year of partial differential equations to note in particular.

During this time, Dr. Charles Mann, then Head of the Dept. of Chemical Engineering, would often approach Amundson suggesting that he move his department to help with teaching, and educate students and faculty about how mathematics could be applied to chemical engineering. After a few such encounters that had appeared somewhat casual, Amundson asked Mann to desist from such feelers if he was not going to be serious about making him an offer! That indeed made the difference and Amundson transferred to the chemical engineering department as an Associate Professor in 1947.

Of his own admission, this move was most crucial to Amundson's career as a chemical engineering academic, and the leadership he came to exert on the profession. His interest in chemical engineering had a surging revival at this stage. There was a crying need for the application of nonlinear mechanics to chemical reaction systems, and with the timely arrival of Olegh Bilous, an astute French student, the time was ripe for this activity to flourish. Also Neal had noticed that chemical engineers were not familiar with matrices and introduced them in his courses. The application of matrices could not have had a better beginning than through the arrival of Andreas Acrivos as a graduate student on the scene, who subsequently grew to be one of the most distinguished academicians of chemical engineering. With Neal's research contributions to be discussed later in this article, we turn to other aspects of his academic career.

Following Doc Mann's unfortunate death in 1949, Neal became the Acting Head of the department, while an external search was initiated by Dean Spilhaus for a new Head. After some unsuccessful attempts, it was clear that someone within the department should take over as Head. Edgar Piret, a senior colleague of Neal was a potential candidate, but had been rejected by the faculty. Any residual inkling that Dean Spilhaus may have had in offering the Headship to Piret, was eradicated after his encounter with Neal on the issue. Thus, began the stellar academic career of Neal Amundson, a full Professor at age 35, and Head of the Dept. of Chemical Engineering at Minnesota in 1951.

As Department Head

Amundson went about building his department with admirable support from Dean Spilhaus, who discovered early that Amundson thrived when he was otherwise left alone. Resources were scant at the University for building a strong research program. The focus had to be on hiring theoreticians but perhaps also partially out of conviction that the profession needed theory at its stage of development. Chemical engineering theoreticians were an undefined community so that they had to be sought from other disciplines. Amundson was not interested in hiring chemical engineers who professed interest in conventional areas like heat and mass transfer. They had to be involved in arresting new directions in depth. Bill Ranz, whom he hired with a PhD from the University of Wisconsin, came as close to traditional ChE as possible, but he certainly was an unusual thinker. His highly cited work on packed beds with Bob Marshall of Wisconsin had won him the AIChE Colburn award in 1955.

The story of Amundson's discovery of Rutherford Aris, has often been told but bears repetition because it is an extraordinary one. While a Fulbright Scholar at Cambridge University in 1954/55, Amundson had the opportunity to visit ICI (Imperial Chemical Industries). There in their research department he met young Rutherford Aris who had had no formal degree education. He had obtained an external Master's degree from the University of Edinburgh which did not require him to attend the university. They went to lunch together and Aris asked Amundson about spending some time at Minnesota. Amundson had clearly been impressed in the short time they had been together and agreed to have him visit for a year which was to be spent collaborating on some articles. Before the work was completed, Aris had an offer from the University of Edinburgh. He promised to return the next summer to finish up the articles, which he did. During the summer, however, he met his future wife Claire. They returned to Scotland but Claire was keen to return to Minnesota and so Aris asked Amundson if he could come back. Amundson secured Aris an appointment as an Assistant Professor without a formal PhD degree with Dean Spilhaus' approval! Such a scenario was unimaginable even in those days anywhere else in the United States! Aris had about 12 publications then which obtained him an external Doctor of Science from the University of London, U.K., but one with which he was not satisfied. Amundson suggested the topic of dynamic programming for a fresh dissertation that subsequently provided Aris with a regular PhD degree from the University of London. This culminated in the book entitled *The Optimal Design of Chemical Reactors* published by Academic Press, which has since become a classic.[4]

The foregoing story best captures the pioneer spirit with which Amundson built the faculty at Minnesota. Amundson had one simple strategy on hiring: "If I thought I was smarter than the fellow I was interviewing, I wouldn't hire him!" That sums up his philosophy rather well. So there was an array of truly outstanding individuals that joined the Minnesota faculty. Skip Scriven, who had obtained his BS in chemical engineering from the University of California at Berkeley and PhD from the University of Delaware under the supervision of Bob Pigford, was a significant addition. He was an astounding theoretical fluid mechanician, who had then published a very fundamental article in Chemical Engineering Science on the formulation of surface equations, and had won the Colburn Award with his colleague in Shell Development, C. V. Sternling for their epochal contribution on Marangoni instability.

Neal had a special eye for talent and saw it early. He recognized it in Arnie Fredrickson, who got his BS and MS degrees in chemical engineering at Minnesota, and persuaded him to go to Wisconsin for his doctoral work. Arnie got his PhD under Bob Bird's supervision and returned to Minnesota as an Assistant Professor. John Dahler arrived with a PhD in molecular theory from Joe Hirschfelder's group at Wisconsin. This had occurred in response to a plea from Neal to Joe some years earlier for an exceptional student from the latter's group. Shortly thereafter, Ted Davis joined the faculty from the University of Chicago with a doctoral degree in Theoretical Chemistry under the supervision of Stuart Rice. They were followed by Lanny Schmidt, a surface scientist from the University of Chicago, Ken Keller, a chemical engineer with a Biomedical engineering background from Johns Hopkins (who subsequently became President of the University of Minnesota: 1985–1988), and Bob Carr, a Harvard Kineticist. Also worthy of note is the hiring of Henry Tsuchiya, an experimental bacteriologist with whom Arnie Fredrickson teamed up to start one of the earliest bioengineering programs in the country.

Neal's grand idea was clearly to facilitate the import of basic science into chemical engineering by hiring scientists and then encouraging the cross fertilization of different fields. He realized that this idea could succeed only if there was a way to introduce non-ChE's to the field of chemical engineering. This requirement was brilliantly met by a system of team teaching of undergraduate core courses, whose success has been awe-inspiring! Bill Ranz is known to have crafted this system, in which junior faculty began with being recitation instructors under the guidance of a course instructor in charge of the main lectures. While the main lectures had a sizeable number of students (well over 60 in the early days), the recitation classes had about a score or more of students. Recitation instructors were required to attend the main lectures, thus, providing experience toward being instructors-in-charge at a later stage. The instructor in charge made up recitation sheets that laid down the agenda for each class. Especially when Skip or Arnie made them up, the recitation

Figure 1. Front row: Lanny Schmidt, Ken Keller, Neal Amundson, Ted Davis, Gus Aris, Bob Carr, Skip Scriven, Wei-Shou Hu; second row: Arnie Fredrickson, John Weaver, Alfonso Franciosi, Christie Geankopolis, Klavs Jensen, Richard Oriani, Ed Cussler; third row: Bill Smyrl, Bill Gerberich, Henry White, Martha Mecartney, Fennell Evans, David Shores, Friedrich Srienc.

sheets generally featured items that involved grueling preparations reaching into late hours of the night. It is amusing to recall occasional instances of one recitation instructor calling another (instead of the instructor-in-charge!) for answers to questions only to discover that neither was any closer to the solution!

The underlying message in the foregoing account is that there was no way to emerge from the recitation experience without a healthy understanding of chemical engineering! It would be a stretch to expect that a surface scientist such as Lanny Schmidt would teach a process control course anywhere else! This rigorous introduction to chemical engineering and interaction with ChE colleagues helped develop strong collaborative research programs. The highly successful Davis-Scriven collaboration in the areas of transport in porous media and interfacial processes is an outstanding example (Figure 1). It is gratifying to know that even today Minnesota continues to vigorously maintain this system under Frank Bates' leadership.

The Minnesota faculty seemed much attuned to the system just as the author was during his 1965/67 stay there as a temporary Assistant Professor. Amundson's leadership has had much to do with it, for it is not clear that such a system would have been acceptable to faculty elsewhere.

The department's reputation was surging in the early 1960s and was attracting the best graduate students from the US and abroad. Many talented postdocs and distinguished professors came visiting the department from all over the world. Gordon Beveridge (Scotland), Richard Mah (Singapore), Horst Brodowsky (Germany), Howard Brenner (Brooklyn) and Bill Schowalter (Princeton) are some examples.

Following Amundson's strategy for hiring faculty is unimaginable in today's circumstances, for he is reported to have kept close tabs on the impression left by the candidate on his faculty, as the interview was in progress, in order to be able to make an offer often by the end of the day!

Amundson rarely had faculty meetings. In Arnie Fredrickson's words, "He led the department and ran it by consensus. He had ways to find out what each of his faculty members were thinking on issues and to inform them not only collectively but also individually of what he was thinking about the issues and if there was consensus on doing something we had a department meeting and took a voice vote (ayes 12, nays none). If there was no consensus on a proposed action there was no meeting and the thing was not done. No doubt all of the things that he wanted the department to do did not get done, but most of them did get done, because everyone could see the rightness of what he wanted to do." The faculty had little sense of the bureaucracy that prevailed, probably, because Amundson protected them from it.

The faculty met virtually every day at the Campus Club for lunch where important departmental issues were frequently discussed. The chemical engineering table was well-known and often savored by colleagues from other departments usually chemistry or mathematics. Not surprisingly, the department had an unusual measure of collegiality! This was academic leadership at its best! One must concede, however, that Amundson's methods could have had unacceptable consequences if they were in the wrong hands. Indeed academia has evolved to ensure against such odds, but, sadly insulated from the boons of such inspired leadership!

George Stephanopoulos was Amundson's last hire which Neal is reported to have celebrated with "having hired Jesus Christ", a quip that would have been clear to anyone then familiar with the looks of George! Indeed this was a significant hire that led to an outstanding academic family of researchers in Process Systems Engineering.

Neal was a colorful personality with a great sense of humor; for a particularly entertaining account of this, the reader is referred to an unpublished article by Arnie Fredrickson who can be contacted for a copy of the same by email at fredr001@umn.edu. An article by Acrivos and Luss for the National Academy of Sciences provides another exciting account of Neal Amundson's life.[5]

As An Academic Researcher and Leader

Although Amundson's main research area was, what came to be known as, Chemical Reaction Engineering, many of his earlier articles were designed to show the utility of mathematical tools that had not been adequately explored in the past. Broadly, he was driven by a desire to squeeze every bit of understanding out of a system, by imposing all the mathematical tools at his disposal on its model. Deeply ad-mixed with this was a curiosity for interesting pathologies that frequently led him to quip: "I like to work on interesting problems!" The essence of this remark could be understood only by one who had experienced the discovery of an unexpected system behavior and the unusual insight that derives from it!

Neal seized the ripe opportunity for mathematical analysis of adsorption columns toward application to chromatography. In light of the application of chromatography to a diverse variety of separation processes, the Lapidus-Amundson articles continue to be highly cited; the one published in 1952[6] has currently 723 citations. Relating the nonlinearity of adsorption equilibria to the appearance of shocks and discontinuous solutions of hyperbolic systems, required serious exposition. Thus, the three volumes of *First Order Partial Differential Equations*, published by PrenticeHall,[7] with Hyun-Ku Rhee and Rutherford Aris, followed in subsequent years.

Chemical engineering, with numerous stage-wise operations, created a natural need for familiarity with linear algebra. Blending of petroleum stocks for specific products with defined properties provided a perfect scenario for the application of linear programming. (The introduction of linear programming to chemical engineers had occurred in an article by Fenech and Acrivos[8]). As a graduate student in 1960, the author recalls, a special set of notes compiled by Amundson on *Linear Programming* as part of his applied math course sequence that all entering graduate students had to take. There is much to be said about this course sequence, which was the most popular in the Minnesota graduate program.

First, because of its focus on chemical engineering examples, it greatly motivated students. All too often, engineering students have come away unable to see the relevance of mathematics to engineering, when math instruction is left entirely to mathematicians.

Second, far from being a mindless prescription of algorithmic procedures for solving equations, it dealt with theory in sufficient pith to create notable returns from its use. For example, Acrivos and Amundson[9] showed how the use of matrix theory could lead to calculation of downstream compositions in a multicomponent rectification column without involving any of the intermediate plate compositions. Using a similar approach to the stripping section, a mass balance at the feed plate becomes feasible simply from specification of the tops and bottoms product of a distillation column of arbitrary height! Such insight will not accrue from routine use of algorithms.

Third, the course delved into mathematical concepts and promoted mathematical thinking, thus, arousing the curiosity of engineering students to take more advanced courses in mathematics. Amundson's book on *Mathematical Methods in Chemical Engineering*; *Matrices and their Application*, was published by Prentice Hall in 1966.[10]

Amundson maintained close contact with the Mathematics department at Minnesota. At one time he even had to take the mantle of Headship of the math department for an interim period. Chemical engineering students were encouraged to take high-level courses in applied mathematics. James Serrin, Hans Weinberger, Don Aronson, Larry Markus, George Sell, Willard Miller and many others of the Dept. of Mathematics were close allies of Amundson and Aris. Graduate students enjoyed this atmosphere with many developing new applications of mathematical methods. It was definitely a period of change in which chemical engineers raised questions about how to think quantitatively about systems. Neal's belief in communication with mathematicians was infectious. The author, in particular, was greatly influenced by this. To efficiently communicate with mathematicians called for being mathematically literate, which involves some territorial transgression into mathematics. Neal used to refer to a need for familiarity with "poor man's functional analysis" that led us to collaborate for several years on a book published by Prentice Hall in 1985,[11] that exposed chemical engineers to linear operator methods in solving problems with chemical reaction and transport. This collaborative effort, often at our homes (Figure 2), had numerous scholarly discussions interspersed with scotch and lively conversation during happy hour that presented a picture of Neal in a domestic environment. Neal had an earthy integrity about him, and a sense of modesty that matched his intolerance for nonsense. The author often has nostalgic reminiscences of his wife Shirley's extraordinary hospitality during these visits.

Neal was among the first in ChE to introduce the use of computers, which started with Univac 1103, followed by

Figure 2. The author and Neal Amundson discussing applied mathematics at Ramkrishna's home.

[Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Control Data 1604. The graduate students in the department were well into regularly using them on their thesis projects. The analog computer had special attraction in the 1950s and 60s because they were easy to patch up for examining solution trends quickly with variation of system parameters. It is believed that the first analog plot was published in ChE by Acrivos and Amundson,[12] who investigated the solution of transient stage-wise operations. This influenced similar plots by other students (e.g., Ramkrishna et al.[13] who analyzed bioreactors). Liu and Amundson[14] solved on a digital computer approximately 200 simultaneous ordinary differential equations for a polymerization system. Indeed the use of a computer emerged as a natural complement to the formulation of mathematical models that resulted from the perspective that Amundson generated. Hence, these foregoing firsts must be viewed as having heralded the computational approach to chemical engineering problems in the years to come.

Neal Amundson, along with Rutherford Aris (Figure 3), arguably founded the subject of chemical reaction engineering with its full complement of reactor dynamics, optimization and control. The articles by Bilous and Amundson,[5] and Aris and Amundson,[15] raised the issue of steady-state multiplicity with the mathematical arsenal of Liapunov stability, which spurred a splurge of articles on the subject. Despite this, skepticism raged among practitioners on the reality of such nonlinear effects until the articles of Schmitz (a distinguished former student of Amundson) and coworkers[16] laid it to rest by vivid, experimental demonstration of steady-state multiplicity, hysteresis and other aspects of nonlinear behavior. The author also recalls a successful consulting experience[17] with Conoco-Phillips in which a continuous Fischer-Tropsch reactor switched, under the same conditions, from a steady state with liquid hydrocarbon product to one with a gaseous product, containing largely methane, apparently due to some "unknown" perturbation! Nonlinear analysis of chemical reactors has since grown in powerful ways with the use of bifurcation theory (Uppal et al[18,19], Balakotaiah and Luss[20]).

Figure 3. Neal Amundson and Rutherford Aris.

[Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

While computation was the hallmark of much of the foregoing work, the mathematician in Amundson sought to find ways in which *a priori* analytical criteria for steady-state multiplicity could be derived, using mathematical analysis without involving much computation. He published some of these articles by himself,[21] numerous others with Dan Luss[22], and with Arvind Varma.[23] The growth of mathematics in the chemical engineering profession, which must be viewed as largely due to the Amundson-Aris School, is traced in an article by Ramkrishna and Amundson.[24]

Neal constantly strove for insights that could simplify mathematical models. An early example is that of polymerization in which Zeman and Amundson[25] sought to convert a discrete polymer distribution, described by a large number of ordinary differential equations, into a continuous distribution of polymers satisfying a single-partial differential equation. This concept spread to other areas such as the analysis of reaction mixtures (Gavalas and Aris[26]) and to distillation models.[4] He was also the earliest, along with Valentas and Bilous,[27] to model dispersed phase systems using population balances.

As the first American editor of Chemical Engineering Science from 1956 to 1972, Amundson actively promoted articles that dealt with theory. (For a time, Danckwerts, the editor from England had felt an overdose of mathematics in the journal although he was himself a trailblazer in its use!). Chemical Engineering Science grew to be a premier chemical engineering journal with several outstanding publications in those formative years. Subsequent American editors, Arnie Fredrickson, Rutherford Aris, Matt Tirrell, and Bob Brown all had Minnesota roots of one kind or another. This is also true of the AIChE Journal which has had editors Morton Denn, Matt Tirrell, Stan Sandler, the present editor Mike Harold and Associate Editor, George Stephanopoulos with similar roots.

Amundson's accolades grew steadily over the years both in the US and abroad. Not surprisingly, he won the top AIChE honors, was elected to the US National Academies of Engineering, Science and of Arts and Sciences, and bestowed with Honorary doctorate degrees from many universities. After 25 years of his Headship at Minnesota, Amundson perhaps felt the urge to make way for new leadership. He may have sensed a completion to his mission, but cultural changes in the university may also have added to his desire to step down. May be it was an opportune time for relocation to warmer weather!

The Houston Years

Amundson's move to the University of Houston in 1977 was spearheaded by Dan Luss, one of his highly distinguished students, who headed the Dept. of Chemical

Figure 4. Amundson at one of his birthday parties at Houston with Andy Acrivos, Gus Aris, Dan Luss, Skip Scriven.

Engineering there. Clearly, Dan had inherited not only Neal's creative instincts in research but also some of the latter's astuteness for leadership (Figure 4). His maneuver of Neal's move to the University of Houston was a masterly accomplishment that soon sent the ranking of his department soaring to a spot in the top 10 in the country!

At Houston, Amundson continued his activity in reaction engineering with fervor, graduating many outstanding students. Deserving special mention are Sankaran Sundaresan, Stratis Sotirchos and Srinivas Bette. For a while, he was absorbed in many fundamental issues with the Stefan Maxwell equations for multicomponent mass transfer that seemed to have not received prior attention. He held a joint appointment with the mathematics department at Houston, which led him to teach an undergraduate calculus course for a while. In 1987, he became the Dean of Faculty and served in that capacity for 2 years. In course of time, his involvement with the Dept. of Mathematics grew progressively with collaborating colleagues there. He published numerous articles with a young junior colleague, Jiwan He for whom he had often expressed special appreciation. It is the author's view that Neal was moving more toward computation than analysis during this period of time. Yet he retained a special place in his heart for creative analysts like Marty Feinberg, now at Ohio State University.

Neal collaborated for several years with John Seinfeld of Caltech on atmospheric modeling publishing several landmark articles[28–30] on thermodynamic phase equilibria in aerosol systems. John is a distinguished member of Amundson's academic tree as a former student of Leon Lapidus, one of Amundson's early graduate students.

Academic Descendants

Amundson's inspiring guidance of graduate students produced many outstanding leaders in academia and industry. Lapidus joined the chemical engineering department at Princeton and pioneered the computational area of chemical engineering, publishing numerous articles on process synthesis and control. He soon rose to be the department head but his life ended prematurely at the age of 52. In the short span of his life, he had published numerous books on applied mathematics and risen to stardom by winning several awards. Lapidus' academic tree got off to an impressive start with a spurt of outstanding academics such as John Seinfeld, Tom Edgar and others who distinguished themselves in unique ways.

Andreas Acrivos, another of Amundson's early graduate students (PhD, 1954) is one of the most distinguished academicians in chemical engineering. After a doctoral dissertation on the use of matrix theory in distillation, he established his own School of fluid mechanics that has led to a rich genealogy replete with a flourishing family of outstanding academics with a first generation comprising Gary Leal, Bill Russell, John Brady, and many others.

A stream of exceptional academics from Amundson followed of whom, Dale Rudd, Roger Schmitz, Hyun-Ku Rhee, Dan Luss, Arvind Varma and Sankaran Sundaresan are but a sample! Omission of mention of many other academics of high quality is indeed regrettable. A somewhat more detailed yet very incomplete account of the many outstanding academic graduates can be had from a publication of his collected works.[31]

Many of Amundson's students subsequently rose to be Department Heads, Deans, Provosts or Presidents, of which Lapidus, Acrivos, Schmitz, Luss, Varma, Rhee, Zygourakis represent outstanding examples. Numerous others joined industry to become corporate leaders. Perhaps the most distinguished of them is Lee Raymond who rose to be the President of ExxonMobil (Figure 5). Ron Zeman (Dow Corning), Ken Valentas (General Mills, Pillsbury), and Dick Schmeal (Shell Development) and many more rose to high positions in their respective organizations.

Amundson's strategy was to allow graduate students considerable freedom for developing their work. He did not breathe down their necks, but the author does recall some of Amundson's students feeling stretched further just when they had the image of being done with their theses!

Figure 5. Neal Amundson with former student Lee Raymond former CEO of ExxonMobil.

[Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Amundson's Impact on Chemical Engineering

Amundson's impact on the chemical engineering profession must be measured not just from his own research contributions or from those of the impressive array of leaders on his academic tree. The influence that his presence has had on the evolution of chemical engineering science in general profoundly contributes to his impact. In this regard, it is of interest to do some retrospective evaluation of Amundson's adventurous pursuit of hiring scientists that invoked criticism from conservative sources. Our focus below is on how the scientists that Amundson hired collaborated with chemical engineers in the faculty to establish new directions and produce new leaders in their respective fields.

The impact that Aris has had on the use of mathematics in reaction engineering, and chemical engineering in general has no parallel. Aris' academic tree has an imposing collection of high-powered academics such as Morton Denn, George Gavalas, Harmon Ray and many more. Furthermore, the collaboration of Lanny Schmidt with Gus Aris also produced outstanding chemical engineers like Yannis Kevrekedis, Dion Vlachos and several others. Besides being responsible for the growth of surface science, Lanny established himself a premier reputation as a chemical reaction engineer. Of Rutherford Aris, an intellectual giant in his own right, not enough could ever be said that will do justice either to his rare scholarship or to his exemplary collegiality!

Amundson's hiring of Henry Tsuchiya, a bacteriologist, in the late fifties must be regarded as an exceptional stroke of insight. Henry teamed up with Arnie Fredrickson to produce a long pioneering program of Biological Engineering with which the author had the distinct pleasure of being associated early. Fredrickson, Tsuchiya and Aris produced many of today's leaders in Bioengineering such as Greg Stephanopoulos, Mike Shuler and others. Doug Lauffenburger, another outstanding bioengineering leader in the same light, came from Ken Keller's group.

Ted Davis' rise to stardom was phenomenal. His collaborative activity was exceptional over the years as it included not only Skip Scriven but also many others on the faculty both old and new (Figure 6). The Davis-Scriven collaboration that lasted many years produced outstanding academics such as Ron Larson, Eric Kaler (the current President of the University of Minnesota), and many others. This group of students made pioneering contributions to the understanding of nanoparticles, micellar solutions and transitions, behavior of fluid interfaces, flow and transport through porous media, and so on. Ted's energy knew no bounds as, in the midst of all his activity, he served 12 years as Department Head and 10 years as Dean.

Figure 6. Matt Tirrell, Rutherford Aris, Ken Keller, Neal Amundson, and Ted Davis.

[Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

It should be evident that what was viewed as a gamble by some, when Amundson sought to overhaul chemical engineering culture, has clearly led to a profession rich in its scientific content, able to contribute in many more ways to societal issues than ever before. This is an extraordinary accomplishment by an individual with so many different facets that, to evaluate Amundson's accomplishments, the pundits must discard the metrics that academics have come to love these days and find something quite different!

Finally, it will be interesting to reflect on the many ways in which Amundson has contributed to the engineer's thought process in quantitative understanding of things in engineering and science. In this regard, the field of biological sciences, a significant area of current chemical engineering research, seemed ideally suited for discussion. Although Amundson had actively organized the development of biological research at Minnesota from as early as the 1950s, his own activity had not encompassed even in a minor way any issues of biological interest. Yet many developments in biological modeling have gained from his insight on chemical reaction systems. Toward establishing this, we will focus on the very important area of mathematically modeling living cells. It derives its importance from the diversity with which cellular activity impacts society through implications to environment, energy and health, and to products of varied interests such as food, cosmetics, pharmaceuticals and drugs.

Modeling cells has been of interest to researchers of diverse backgrounds, biophysicists, biochemists, biologists, computer scientists, and engineers of almost all kinds. Consequently, there have been different approaches, ranging from ultrasimplified models to very complex models that do virtually everything occurring in the cell. Naturally, there are different goals associated with such varied models. Thus, an ultrasimplified model (of which the Monod model is an example) can only be expected to describe some gross features such as how much biomass can be produced from a certain amount of carbon substrate in a batch reactor, or for estimating the dilution rate in a continuous reactor to prevent washout, and so on. An example of the most complex model may be found in a recent article by Karr et al.[32] Evaluation of different models would of course require rational consideration of the returns on investment, which can be fairly sophisticated. However, for our present purposes, we will examine how compromises can be made on complexity through ideas that have often moved Amundson to find simpler descriptions of systems.

Metabolism involves a very large number of chemical reactions involving external nutrients, and thousands of intra and extracellular metabolites. The cell is an (expanding) open system with transport of nutrients into it and products transported out. The steady state description involves a very large number of homogeneous algebraic equations with many more unknowns than equations. Cellular metabolism is, thus, to be described by a large number of reaction rates contained in a *metabolic flux vector* of stupendous dimension. Targeting the calculation of intracellular reaction rates based on measurements of relatively accessible exchange rates with the environment is tantamount to wrestling with a set of equations far outnumbered by the number of

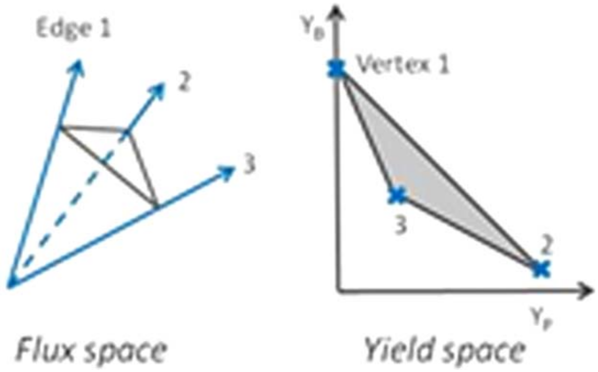

Figure 7. Convex solution space of a metabolic system.

[Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

unknowns. Of early concern to Amundson[4] was the solution of linear algebraic equations precisely under the circumstances just outlined earlier? The strategy in biochemical systems theory[33] of using least squares to estimate either fluxes (or rate constants in a dynamic framework) is a consequence of defining the generalized inverse of nonsquare matrices.

A very astute approach to metabolic modeling due to Palsson and coworkers[34,35] is the postulate that cellular metabolism is guided by the objective of maximizing the yield of cell mass. The formulation does away with many possible pathway options out of a large network and, with a mere single measurement of the rate of substrate uptake from the environment, positions itself to predict the entire metabolic flux vector (Figure 7). This exceptional leverage of a meager measurement is enabled by the power of linear programming in awesome confluence with the stoichiometric edifice that is the hallmark of all chemical reactions. This is the very scenario in the petrochemical setting, which offered several alternative paths to manufacturing a product that led Amundson to introduce linear programming several years earlier in a graduate course. Students became familiar with the algebraic formulation of chemical reactions in terms of intrinsic reaction rates. Exposure to linear programming further led to familiarity with convex sets, convex analysis, and the simplex strategy of switching from one extreme point to another in quest of the optima of linear functionals, and so on. These have come to be essential concepts of metabolic analysis!

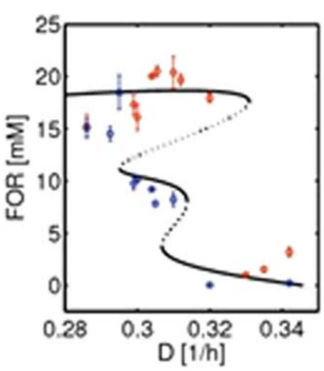

Figure 8. Multiple steady states in a continuous biological reactor.

[Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Palsson's original strategy is one of seeking the edge of a "flux cone" that contains all feasible solutions of the steady-state problem along which the rate of biomass synthesis is maximized. The corresponding scenario in "yield space" is represented by a convex hull with one (or more) of its vertices purporting to be the solution. It is possible to view each vertex as a pathway option of the organism so that the preference for one that maximizes biomass yield may be viewed as a consequence of metabolic regulation.

A singular aspect of metabolism is the presence of regulatory processes, which selectively control syntheses and activities of enzymes that catalyze the numerous cellular reactions. The complexity and diversity of this regulation leave much understanding to be had toward a suitably dynamic description of this reaction system such as Amundson would have preferred. However, dynamic models of metabolism have graced the literature in varying degrees to which regulation has been included or ignored. A dynamic approach to account for regulatory processes in a comprehensive way lies in the author's cybernetic idea[36] that attributes regulation to a survival effort of the organism by optimally investing its constrained resources toward preferential synthesis of enzymes in conjunction with judicious control of their activities. This approach implicates in metabolism many other pathway options with potentially sizeable contributions to the organism's survival goal. The required mathematical framework was that of optimal control theory espoused by Rutherford Aris[37] and Neal Amundson[38] for numerous other chemical engineering applications.

When viewed in the flux cone, the dynamic approach envisages many other edges of the cone that could contribute to metabolic transients. In yield space, the metabolic state becomes a convex combination of many vertices and so could move within the *interior* of the convex hull as, for example, the reactor trajectory in the phase plane plots of Bilous and Amundson.[5] Dynamic optimization in the cybernetic approach leads to a temporally varying convex combination of vertices of the convex hull.

The chemostat or a steady state well-stirred continuous biological reactor fed with a constant concentration of nutrients with simultaneous withdrawal of the culture has been a great tool in the study of metabolic phenomena. Although numerous publications exist in the application of nonlinear analysis to bioreactors featuring mostly extracellular variables, studies of the phenomenon of steady-state multiplicity and investigation of pathological transient behavior have been few in regard to studying metabolism. Consequently, many potential profoundly variable aspects of metabolic behavior remain obscurely buried. For example, bacteria pregrown on glucose, when presented with a mixture of glucose and pyruvate, tend to preferentially consume glucose. However, on prior growth with pyruvate, the bacteria use both pyruvate and glucose right from the beginning. This aspect of regulatory behavior has strange consequences to steady states in a chemostat. Figure 7 shows the steady-state behavior of fermentation product formate in a bacterial chemostat fed with a mixture of glucose and pyruvate.[39] The multiple hysteresis behavior shown in the figure is of course reminiscent of the many articles published by Amundson, Aris and numerous other reaction engineers.

While the foregoing steady state multiplicity is a manifestation of nonlinearity, two interesting issues that stand out are (1) the source of nonlinearity is associated primarily with the optimal choice behavior, and (2) the metabolism may involve not only quantitative differences in specific intracellular reactions but also in the choice of reactions for metabolism. This introduces an element of mechanistic causality in metabolic behavior well beyond the statistical causality that bioinformaticists currently seek from high-throughput data. In other words, an explanation may be available of variability of metabolic behavior by relating to the cybernetic survival goal of the organism.

An area of profound practical significance initiated by Bailey[40] is the area of metabolic engineering in which genetic variations are introduced into a microorganism toward increasing the productivity of some metabolite of interest to a specific application. (Bailey had begun his academic career at the University of Houston in dynamic systems theory and was indeed influenced by Amundson). The nature of network changes that would accomplish the desired increase in productivity becomes a crucial associated question. More precisely, the identity of gene "knock-in" and/or "knock-out" strategies would depend on the *sensitivity* of the governing flux to such changes. The problem of determining sensitivity of reacting systems to various operating parameters was first introduced by Amundson[5] although it was in connection with chemical reactor behavior. The pertinence of this methodology (subsequently further developed by Varma and Morbidelli[41]) to metabolic engineering is further accentuated by the role of "metabolic burden" in assessing the capabilities of an engineered organism.

Amundson's concern for simplified perspectives of complex systems has general import. The characterization, as pointed out earlier, of polymeric reaction systems, in which a single-partial differential equation in polymer length, viewed as a continuous variable, replaces a large number of differential equation for polymers of discrete lengths. A discretized approach to solving such a partial differential equation could entail a scale of polymer length considerably coarser than purely integral values, thus, effectively implying a form of "lumping" polymeric species.[19]

Lumping reaction systems has been of interest to numerous other researchers. In particular reference to metabolic systems, the concept of lumping fluxes of pathway options offers prospects of containing pathway diversity. While the flux balance approach of Palsson and coworkers has been amenable to genome scale metabolic networks, dynamic models for the same must grapple with their identification because of an overabundance of parameters. In this connection, the concept of lumping has considerably enhanced the prospects of applying cybernetic models by drastic reduction in the number of parameters for identification.[42]

It has been the author's objective in this section to show how Amundson's disposition to mathematical modeling and basic thinking has had notable impact even on an area that was not part of his activity. Relating developments in metabolic modeling to Amundson's endeavors has consequently come about by the abstract implications of the latter. This is as it must be, for the power of mathematics lies in its unifying abstraction, notwithstanding the viewpoint of some that abstraction is a deterrent to realistic thinking.

Frontiers in Chemical Engineering: The Amundson Report

Although this section must be regarded as part of Amundson's impact, it deserves to be treated separately. In 1986, the National Research Council appointed Neal Amundson as Chair of a Committee charged with finding the research needs and opportunities for chemical engineering. The committee's task was to identify new high-impact areas, and to find leading experts in them who could define new directions for research. Neal picked James Wei, then at MIT, as the Vice Chair, and a number of other leading chemical engineers in the US. In 1988, the NRC committee submitted its report, entitled "Frontiers in Chemical Engineering," that set new directions to the profession (see Figures 9 and 10).

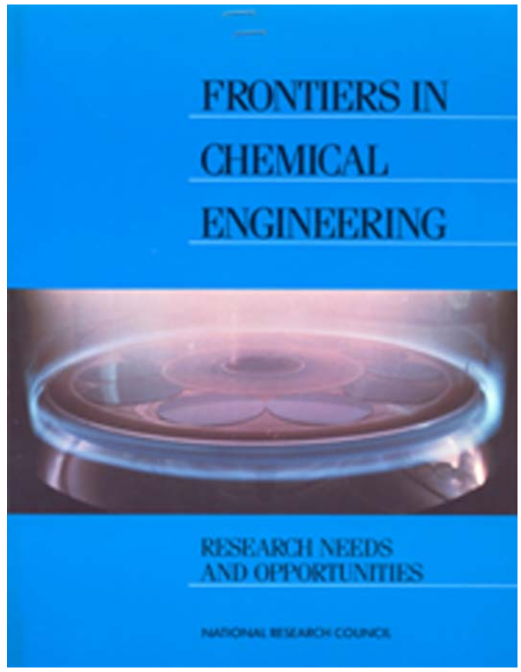

Figure 9. The Amundson Report

[Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

NEWS FOCUS

Report on Chemical Engineering Reflects a Profession in Flux

In surveying research needs and opportunities at the frontiers of chemical engineering, a National Research Council committee finds challenges with major implications for the nature of the profession

Figure 10. On the Amundson Report

Significant aspects of this change are its closer association with the sciences, the very direction in which Amundson had sought to develop chemical engineering at Minnesota and a shift toward product engineering from its almost exclusive past involvement with process engineering. The report stressed focusing on identified new frontier areas, but with a simultaneous need to preserve core competence. That these changes have taken root is clearly evident from the current orientation of most chemical engineering departments in the United States.

An article by Carranza[43] reflects on the Amundson report with reactions from various sources. Particularly noteworthy is the strong criticism by Astarita[44] who foresaw a weakening of core strength in chemical engineering. This perception obviously arose out of concern that exclusive funding of frontier fields would result in progressive neglect of the core areas. Perhaps there will be agreement among most academicians that this is already occurring. The funding focus on interdisciplinary research has virtually eliminated the single investigator! Amundson was himself a victim of this phenomenon that led him to disacknowledge any "alphabetical agency" that provided him support beside the University of Houston.[45] True to the call for interdisciplinary research by the Amundson report, he did of course participate in interdisciplinary research in atmospheric modeling with substantial federal and state funding.

Concluding Remarks and Perspectives

Amundson influenced the course of evolution of the entire profession of chemical engineering in multifarious ways. He recognized the need for replacing empiricism by enforcing a stronger scientific base and orienting chemical engineers to think quantitatively. This he accomplished through (1) his own research in chemical reaction engineering, (2) his leadership as department head by recruiting faculty from the sciences, providing for their training in chemical engineering fundamentals through a unique process of undergraduate teaching, (3) his encouragement of collaborative programs of scientists with chemical engineers in the faculty generating leaders in new areas, (4) his editorship of the journal Chemical Engineering Science, and (5) his national leadership under the auspices of the National Research Council, which helped to define new directions in a changing world, thus, expanding greatly the potential of chemical engineers to contribute to the solution of societal problems. Most impressive examples of this are in academics such as Bob Langer of MIT, and Nicholas Peppas at UT-Austin. Nicholas, in particular, has been vocal in his acknowledgment of the Amundson School even without a formal connection to it!

Indeed, in the years following the Amundson report, the *modus operandi* of engineering research has evolved to performing in groups with complementary expertise, but with a healthy understanding by each of what each research partner brings to the table. This has been a wholesome attribute of engineering research, as it is able to address larger problems with higher impact and relevance to society. While some argue that the multidisciplinary investigatory approach has marginalized the contribution of the single investigator the contribution of chemical engineers to a multitude of far-ranging problems is undeniable.

It is desirable to do some soul searching in regard to chemical engineering education and research in light of the philosophy that drove Amundson's approach. Funding focus on the frontier areas has unfortunately created serious neglect of the core areas of chemical engineering.[46] Faculty are anxious for their students to get started on research with minimal course work. Consequently, most departments have students select their advisors well before their first semester is over in contrast with the earlier practice of almost a year. This is perhaps uncorrectable in current circumstances. Some departments have labored to provide support for graduate students during their first semester or year through endowments. However, the pressure to get an early start on research is not alleviated. The result is graduate students entering frontier areas with a much weaker background of core concepts that brought ChEs to these fields in the first place! Perhaps this issue is more applicable to some areas than others. However, it is definitely a matter of concern that core strength has suffered depletion and would continue in this trend without a concerted effort to reverse it. In this regard, chemical engineering departments must strive to retain a strong program of core chemical engineering courses, viz., Transport Phenomena, Chemical Reaction Engineering, Thermodynamics and Applied Mathematics and Systems Engineering. A further complicating issue in this regard is that entering students seem less prepared with core background from their undergraduate studies. In particular, students seem less prepared with mathematical concepts than before. There is a higher demand for computation in math courses, by faculty colleagues, than for analysis. Often students can solve linear algebraic equations, using standard software, with no clue about the necessary and sufficient conditions for the existence of solutions! Granted that available software such as MATLAB and MATHEMATICA are amazing in their capabilities and it would be wasteful to labor through calculations, by not using them, but the question arises. Should students be using such software, for instance, before learning elementary concepts of vector algebra or to solve linear differential equations? A strong applied math course should focus on concepts, while use of software could be encouraged in application oriented courses.

In order for core areas to grow, interdisciplinary projects must play greater emphasis on participation of core faculty. Although not a sizeable fraction, from the author's experience, there still exist entering graduate students with a strong professed interest in core areas. What opportunities can such students have for academic development with a bright future? If they wanted to pursue an academic career, could they successfully compete with other academic aspirants in the frontier areas? While faculty must wrestle with these issues on their own to some extent, academia on the whole should be concerned about it so that the strong core background that has made chemical engineering such a vibrant profession will continue to thrive. These questions would very much be in accord with Amundson's concerns!

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Literature Cited

1. Lewis WK, Radasch AH. Industrial Stoichiometry Chemical Calculations of Manufacturing Processes. New York: McGraw-Hill; 1926.

2. Hougen OA, Watson KM. Industrial Chemical Calculations. New York: John Wiley; 1936.
3. Bird RB, Stewart BWE, Lightfoot EN. Transport Phenomena. New York: John Wiley & Sons; 1960.
4. Aris R. The Optimal Design of Chemical Reactors. Academic Press; 1960.
5. Acrivos A, Luss D. Neal Russell Amundson. Biographical Memoirs of the US National Academy of Sciences; 2013.
6. Lapidus L, Amundson NR. Mathematics of adsorption in beds. VI. The effect of longitudinal diffusion in ion exchange and chromatographic columns. *J Phys Chem.* 1952;56(8):984–988.
7. Rhee HK, Aris R, Amundson NR. First-Order Partial Differential Equations. Mineola, NY: Dover Publications; 2001:vol. 2.
8. Fenech E J, Acrivos A. The application of linear programming to design problems. *Chem Eng Sci.* 1956;5:93–98.
9. Acrivos A, Amundson NR. On the steady state fractionation of multicomponent and complex mixtures in an ideal cascade: Part 1-Analytic solution of the equations for general mixtures. *Chem Eng Sci.* 1955;4(1):29–38.
10. Amundson N. Mathematical Methods in Chemical Engineering. Englewood Cliffs, NJ: Prentice-Hall; 1966.
11. Ramkrishna D, Amundson NR. Linear Operator Methods in Chemical Engineering with Applications to Transport and Chemical Reaction Systems. Englewood Cliffs NJ: Prentice-Hall; 1985.
12. Acrivos, A.; Amundson, N. R., Solution of transient stagewise operations on an analog computer. *Ind Eng Chem.* 1953;45 (2):467–471.
13. Ramkrishna D, Fredrickson A,Tsuchiya H. Dynamics of microbial propagation: models considering inhibitors and variable cell composition. *Biotechnol Bioeng.* 2004;9(2):129–170.
14. Liu S, Amundson NR. Analysis of polymerization kinetics and the use of a digital computer. *Rubber Chem Technol.* 1961:34(4);995–1133.
15. Aris R, Amundson NR. An analysis of chemical reactor stability and control-I: The possibility of local control, with perfect or imperfect control mechanisms. *Chem Eng Sci.* 1958;7(3):121–131.
16. Vejtasa S A, Schmitz R. An experimental study of steady state multiplicity and stability in an adiabatic stirred reactor. *AIChE J.* 1970; 16(3):410–419.
17. Song HS, Ramkrishna D, Trinh S, Wright H. Operating strategies for Fischer-Tropsch reactors: A model-directed study. *Korean J Chem Eng.* 2004;21(2):308–317.
18. Uppal A, Ray W. Poore A. On the dynamic behavior of continuous stirred tank reactors. *Chem Eng Sci.* 1974;29(4):967–985.
19. Uppal A, Ray W, Poore A. The classification of the dynamic behavior of continuous stirred tank reactors-influence of reactor residence time. *Chem Eng Sci.* 1976;31(3):205–214.
20. Balakotaiah V, Luss D. Analysis of the multiplicity patterns of a CSTR. *Chem Eng Commun.* 1982;19(1-3):185–189.
21. Amundson NR. Some further observations on tubular reactor stability. *Can J Chem Eng.* 2009. doi:10.1002/cjce.5450430201.
22. Luss D, Amundson NR. Some general observations on tubular reactor stability. *Can J Chem Eng.* 1967;45(6):341–346.
23. Varma A, Amundson NR. Some observations on uniqueness and multiplicity of steady states in non-adiabatic chemically reacting systems. *Can J Chem Eng.* 1973;51(2):206–226.
24. Ramkrishna D, Amundson NR. Mathematics in chemical engineering: A 50 year introspection. *AIChE J.* 2004;50(1):7–23.
25. Zeman R, Amundson N. Continuous polymerization models-I: Polymerization in continuous stirred tank reactors. *Chem Eng Sci.* 1965; 20(4):331–361.
26. Aris R, Gavalas GR. On the theory of reactions in continuous mixtures. *Phil Trans Royal Soc Lond Series A Math Phys Sci.* 1966; 260(1112):351–393.
27. Valentas KJ, Bilous O, Amundson NR. Analysis of breakage in dispersed phase systems. *Ind Eng Chem Fund.* 1966;5(2):271–279.
28. Amundson N, Caboussat A, He J, Martynenko A, Seinfeld J. A phase equilibrium model for atmospheric aerosols containing inorganic electrolytes and organic compounds (UHAERO), with application to dicarboxylic acids. *J Geophys Res.* 2007;112: (D24),D24S13.
29. Amundson N, Caboussat A, He J, Seinfeld J. Primal-dual interior-point method for an optimization problem related to the modeling of atmospheric organic aerosols. *J Optimiz Theory Appl.* 2006;130(3): 377–409.
30. Amundson NR, Caboussat A, He J, Landry C, Seinfeld JH. A dynamic optimization problem related to organic aerosols. *Comptes Rendus Math.* 2007;344:(8);519–522.
31. Amundson NR. The Mathematical Understanding of Chemical Engineering Systems: Selected Papers of Neal R. Amundson. New York: Pergamon; 1980.
32. Karr JR, Sanghvi JC, Macklin DN, Gutschow MV, Jacobs JM, Bolival B, Assad-Garcia N, Glass JI, Covert MW. A whole-cell computational model predicts phenotype from genotype. *Cell.* 2012; 150:389–401.
33. Savageau MA. Biochemical systems analysis: I. Some mathematical properties of the rate law for the component enzymatic reactions. *J Theoret Biol.* 1969:25(3);365–369.
34. Orth JD,Thiele I, Palsson BØ., What is flux balance analysis? *Nature Biotechnol.* 2010;28(3):245–248.
35. Reed JL, Palsson BØ. Thirteen years of building constraint-based in silico models of Escherichia coli. *J Bacteriology.* 2003;185 (9): 2692–2699.
36. Ramkrishna D, Song HS. Dynamic models of metabolism: Review of the cybernetic approach. *AIChE J.* 2012.In Press.
37. Swanson C, Aris R, Fredrickson A, Tsuchiya H. Bacterial growth as an optimal process. *J Theoretical Biol.* 1966;12(2):228–250.
38. Bilous O, Amundson NR. Optimum temperature gradients in tubular reactors-I: General theory and methods. *Chem Eng Sci.* 1956;5(2): 81–92.
39. Kim JI, Song HS, Sunkara SR, Lali A, Ramkrishna D. Exacting predictions by cybernetic model confirmed experimentally: Steady state multiplicity in the chemostat. *Biotechnol Progress.* 2012; in press.
40. Bailey JE. Toward a science of metabolic engineering. *Science.* 1991;252(5013):1668.
41. Varma A, Morbidelli M, Wu H. Parametric Sensitivity in Chemical Systems. Cambridge, U.K: Cambridge University Press; 2005.
42. Song H-S, Ramkrishna D, Pinchuk G, Beliaev AS, Konopka AE, Fredrickson JK. Dynamic modeling of aerobic growth of Shewanella oneidensis. Predicting energy requirement for growth, triauxic growth, and flux distributions. *Metab Eng.* 2013;15:25–33.
43. Carranza RG. A Look Back at the Amundson Report. *Chem Eng Prog.* 1990;.
44. Astarita G. Frontiers in chemical engineering and 1992. *Chem Eng Prog.* 1990;86(3):55–59.
45. Amundson NR, Pan TW, Paulsen VI. Diffusing with stefan and maxwell. *AIChE J.* 2003;49(4):813–830.
46. Stephanopoulos G. International Benchmarking of U.S. Chemical Engineering Research Competitiveness. National Research Council, National Academies Press; 2007.

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