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Review

Evolution of ion-exchange: from Moses to the Manhattan Project to Modern Times

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Abstract

This article explores the history of ion-exchange from records of desalination in the Old Testament and the writings of Aristotle, to the identification of the phenomenon of ion-exchange by two English agricultural chemists, to the invention of suppressed conductivity by Small et al. [Anal. Chem. 54 (1975) 462]. It then focuses on the characteristics of the gradual and continuous evolution of ion chromatography with suppressed conductivity to its current state, with an emphasis on those discoveries that punctuated or revolutionized this evolution.
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Keywords: Reviews; Ion chromatography; Ion exchange

Contents

1. Introduction 712
   1.1. From Moses 712
   1.2. . . . to the Manhattan Project 713
   1.3. . . . to Modern Times 714
2. Ion chromatography 714
   2.1. The idea 714
   2.2. The competition 716
3. The evolution 717
   3.1. Hardware 717
   3.2. The suppressor 717
   3.3. The column 718
   3.4. The eluent 719
   3.5. Gradient elution 720
   3.6. A complete system 722
   3.7. An evolutionary dead end? 722
4. Recapitulation and conclusion 723
Acknowledgements 724
References 724

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1. Introduction

This issue celebrates the 100th anniversary of Mikhail Semenovich Tswett's first report on chromatography, presented at the meeting of the Biological Section of the Warsaw Society of Natural Scientists [1,2]. However if one were not aware of the ''fossil'' record (i.e. the preceding 999 issues of *Journal of Chromatography*), one would find it hard to believe that the work described in this volume evolved from Tswett's original work. This year also marks the 151st anniversary of J. Thomas Way's lecture to the Royal Agricultural Society where the principles of ion-exchange were first enunciated [3]. Again, one would find it incredulous that Way's study ''*On the Power of Soils to Absorb Manure*'' was the forerunner of modern ion chromatography.

Evolution is traditionally viewed to occur in a continuous manner, with the organism gradually acquiring new traits. However, the geological fossil record of evolution is characterized by long periods of virtual standstill (''equilibrium''), ''punctuated'' by episodes of very fast development of new forms. This led Niles Eldridge and Stephen Jay Gould to propose their ''punctuated equilibrium'' theory in 1972, as an explanation of the gaps in the fossil record.[1] The evolution of liquid chromatography was characterized in such a manner by Ettre [4] who identified five *Sternstunden* or key moments that laid the foundation for modern HPLC. This article will follow the punctuated evolution of ion chromatography from ancient times to its modern form, focusing on the key moments within its development.

1.1. From Moses . . .

The first recorded use of ion-exchange is from the Old Testament of the Holy Bible in the book of Exodus, Chapter 15, verses 22–25, which describes Moses leading the children of Israel from bondage into the wilderness.

> 22: *So Moses brought Israel from the Red sea, and they went out into the wilderness of Shur*; *and they went three days in the wilderness, and found no water*.
>
> 23: *And when they came to Marah, they could not drink of the waters of Marah, for they were bitter*: *therefore the name of it was called Marah*.
>
> 24: *And the people murmured against Moses, saying, What shall we drink*?
>
> 25: *And he cried unto the LORD*; *and the LORD shewed him a tree, which when he had cast into the waters, the waters were made sweet*.

Thus Moses rendered the water potable by using ion-exchange to remove salt-bearing minerals containing sodium, calcium, and magnesium. For those that find it inappropriate to quote the Old Testament in a discussion of evolution, ancient secular records also indicate an early knowledge of such desalination techniques. For instance, Aristotle's *Problematica* indicates that sand filters were used for the purification of sea and impure drinking waters, and in *Sylva Sylvarum: A Naturall Historie in Ten Centuries* Sir Francis Bacon wrote of this method of obtaining fresh water as it was practiced on the coast of Barbary:

> *Digge a hole of the sea-shore somewhat above high-water mark and as deep as low-water mark, which when the tide cometh will be filled with fresh water and potable*.

Bacon also remembers ''to have read that trial hath been made of salt water passed through earth through ten vessels, one within another, and yet it hath not lost its saltness as to become potable'' but when ''drayned through twenty vessels hath become fresh''. A century later, Dr Stephen Hales read a paper before the Royal Society in 1739 entitled ''Some attempts to make sea-water wholesome''. Within this he quotes the authority of Mr. Boyle Godfrey that ''sea water being filtered through stone cisterns, the first pint that runs through will be pure water, having no taste of salt, but the next pint will be as salt as usual''.

Thus, practical applications of ion-exchange were widely recognized well before the Tswett era. How-

[1]The popular science books such as *Ever Since Darwin* by the late Stephen Jay Gould are highly recommended as a primer on modern evolutionary theory.

ever, an understanding of the underlying process was lacking. In *Problematica* (Book 23 Part 20), Aristotle suggested that desalination resulted from density effects:

> *. . . water which flows readily can percolate through the earth; and if water can percolate, the thickest and heaviest part of it is always carried to the bottom, while the light and clean element becomes separated. For salt water is heavy and fresh water is light. And so flowing water is fresh. It is for the same reason that salt water, when it is set in motion and undergoes change, becomes fresher; for it becomes lighter and weaker owing to motion.*

Even Jöns Berzelius, who developed the concepts of the ion and ionic compounds did not recognize the mechanism underlying ion-exchange. He had observed that upon filtering solutions of common salt through sand, the first portions that passed through were quite free from saline impregnation. These observations were extended by Professor Matteucci to other salts, but then were erroneously attributed to capillary action (Sur les phénomènes physiques des corps vivants, p. 29, Paris, 1847.) Credit for recognition of the phenomenon of ion-exchange is generally attributed to two agriculture chemists, H.S. Thompson and J. Thomas Way. In 1848, Thompson reported to Way that after ''filtration of liquid manure . . . through a bed of an ordinary loamy soil . . . the urine was deprived of colour and smell—in fact, that it went in manure and came out water.'' [5]. Way then proceeded to perform an exhaustive set of 96 experiments, from the absorption of ammonia by a $16'' \times \frac{3}{4}''$ tube filled with ''Mr. Pusey's red soil'' to filtration of putrid urine with 18″ of ''Mr. Huxtable's light soil'' [6].[2] Using these results J. Thomas Way then formulated a remarkably accurate description of the ion-exchange process [3]. Amongst Way's conclusions were: the exchange of ions in soil involved the exchange of equivalent quantities; certain ions were more readily exchanged than others; and exchange of ions differed from true physical adsorption. Eichorn [7] later proved that the adsorption of ions by clay constitutes a reversible reaction.

The work of Thompson and Way was followed up by many soil chemists and geochemists. However, it was not until the early twentieth century that practical applications of ion-exchange started to emerge. Contemporary with Tswett's work, Gans [8] used natural and synthetic aluminum silicates for industrial water softening. The first analytical application of ion-exchange was in 1917 by Folin and Bell [9]. They used a synthetic zeolite for the collection and separation of ammonium from urine. The sample was shaken together with the zeolite, which absorbed the ammonium ions thus separating it from the interfering amino acids. The ammonium was eluted with sodium hydroxide and determined colorimetrically using Nessler's reagent. The first use of ion-exchange in column chromatography was the separation of amines from biological solutions by Whitehorn in 1923 [10]. Finally, the first use of an ion-exchange column for anion analysis was the determination of sulfate in natural waters by Bahrdt in 1927 [11].

1.2. . . . to the Manhattan Project

The field of ion-exchange underwent a revolution in the 1930s as a result of Adams and Holmes' observation that crushed phonograph records exhibited ion-exchange properties. This observation ultimately led them to the synthesis of the first organic ion-exchangers in 1935 by condensation of phenol or its derivatives with formaldehyde [12]. These stable high capacity resins were superior to any prior ion-exchangers.

The versatility of these resins was soon recognized by many academic and industrial chemists, leading to the rapid development of a wide variety of new and unique applications of ion-exchange. However, it was within the Manhattan Project that these synthetic ion-exchangers made their greatest impact [13]. In particular, the analysis of reactor fission products was essential to plutonium production. Among the products were radioactive isotopes of the lanthanides which needed to be analyzed for a multitude of reasons. These included estimation of the yield of nuclear weapons and assessment of the radiotox-

[2] This is a delightful paper in the true tradition of the gentleman scientist. Most of the historical accounts of water purification discussed above came from this paper.

icological hazards of the fission products. The lanthanides posed a particularly challenging separation problem because of their closely related properties. In theory, the lanthanides might be separated by precipitation and fraction crystallization (attempted by Otto Hahn and other German scientists) or by ion-exchange (used in the Manhattan Project). In 1942–1943, Boyd and co-workers at the Metallurgical Laboratories at the University of Chicago and Oak Ridge demonstrated the applicability of ion-exchange for adsorption of fission products in trace amounts [14]. This led to the development of ion-exchange methods for the separation of individual lanthanides using cation-exchange resins and elution with complexing agents such as citric acid–ammonium citrate [15]. The discovery of promethium (element 61), an element not found in nature, is attributed to ion-exchange [16].

Due to the confidential nature of the Manhattan Project, none of this work was published until after the war. The first report of the impressive capabilities of ion-exchange was at a special symposium held during the fall 1947 American Chemical Society (ACS) meeting in New York City. This symposium was followed by the publication of 13 articles on ion-exchange in a single issue of the *Journal of the American Chemical Society*. This pioneering work was soon followed by the development of extremely stable and versatile ion-exchange resins derived from styrene and the acrylics [17,18]. So rapid was the development of the field that by April 1953, Osborn [19] classified over a thousand papers on the analytical uses of ion-exchange, and by the following year had revised this estimate up by another thousand [20]. However, while application of ion-exchange in analytical chemistry was undergoing explosive growth, the speed and efficiency of such separations was limited. For instance, Fritz and Pietrzyk's 1961 [21] anion-exchange separation of chloride complexes of Ni^{2+}, Co^{2+}, Cu^{2+} and Zn^{2+} required more than 9 h.[3]

1.3. . . . to Modern Times

By Volume 100 of *Journal of Chromatography* in 1974, high-performance liquid chromatography (HPLC) had demonstrated tremendous potential as an analytical technique. For instance, Verpoorte and Svendsen [22] effused that ''high-speed liquid chromatography promises to be the most effective technique ever devised for the separation of complex mixtures.'' The hallmarks of HPLC relative to classical LC were of course its high efficiency and high speed. However an equally important characteristic of HPLC was the ability to perform continuous on-line monitoring of the effluent. As is the case today, UV absorbance was the predominant mode of detection. For ions that could be monitored using UV, HPLC method development was straightforward, and many high speed ion-exchange separation were available. Unfortunately, only a few ions (e.g. NO_3^-, Br^-, I^-) are amenable to such detection. As a consequence, the evolution of ion-exchange as a mode of HPLC was thwarted by the absence of a suitable detector.

2. Ion chromatography

2.1. The idea

Conductivity had been proposed and occasionally tried as a detector for ion-exchange chromatography. However it achieved very limited success because the analyte conductivity was overwhelmed by the conductance of the much more abundant eluting electrolyte. Modern ion-exchange chromatography had its beginnings with the work of Hamish Small and co-workers at Dow Chemicals in Midland, Michigan, starting in the early 1970s and culminating in their seminal paper in 1975 [23]. A schematic diagram of their instrument configured for anion separations is shown in Fig. 1. In this instrument anions are resolved by standard elution chromatography on an anion-exchange separation column. For monovalent ions the fundamental equilibrium is:

$$\text{Resin} - E^- + A^- \rightleftharpoons \text{Resin} - A^- + E^- \quad (1)$$

where the eluent ion (E^-) on the resin is displaced by an analyte anion (A^-) initially in the mobile phase. In the original IC instrument (Fig. 1) the effluent from the anion-exchange column then flowed through a *stripper column* (now generally

[3] With respect to my own personal evolution, this paper by my academic great grandfather and grandfather, respectively, was accepted a month prior to my birth.

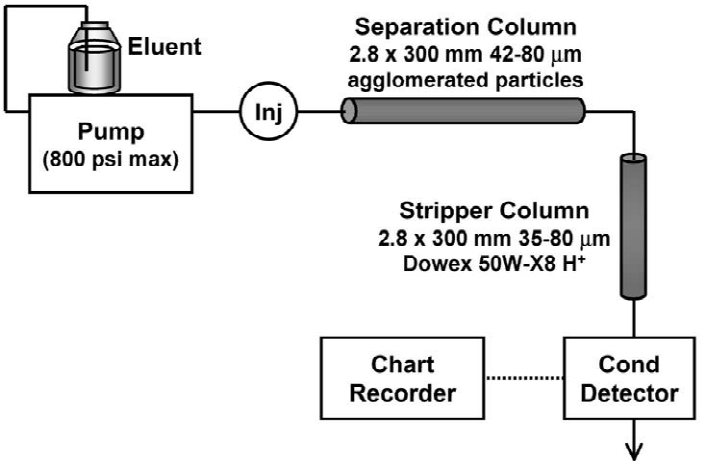

Fig. 1. Schematic diagram of the original suppressed conductivity ion chromatograph of Small et al. [23]. Adapted from Fig. 1 of Ref. [23].

referred to as a *suppressor*). The function of the stripper was to neutralize the eluent ion (E^-) in the effluent. For anion-exchange separations the stripper was a cation-exchange column in the H^+ form. The eluent ion was the anionic form of a weak acid, ideally OH^-. The stripper reaction was then:

$$\text{Resin} - H^+ + Na^+OH^- \rightarrow \text{Resin} - Na^+ + H_2O \quad (2)$$

Thus, the OH^- was neutralized and the background conductivity was reduced to essentially zero. Simultaneous with the neutralization of the eluent, the counter-ion (e.g. Na^+) associated with the analyte anion (A^-) was also exchanged for H^+:

$$\text{Resin} - H^+ + Na^+A^- \rightarrow \text{Resin} - Na^+ + HA \quad (3)$$

If HA was a strong acid, as it is for the seven common anions (F^-, Cl^-, NO_2^-, Br^-, NO_3^-, HPO_4^{2-} and SO_4^{2-}), HA fully dissociates to yield A^- and H^+. Since the conductivity of H^+ (350 S/cm^2/equiv.) is much higher than that of Na^+ (50 S/cm^2/equiv.) and all other cations, there is an overall enhancement in the conductivity signal associated with A^-. Thus, subsequent on-line monitoring of the effluent using conductivity was performed under conditions where the effluent contributed little background and the analyte signal had been enhanced.

Dow Chemicals patented suppressed conductivity and subsequently licensed it to Durrum Instruments, which later became Dionex for commercialization of IC. Dionex exhibited its first IC instrument at the fall 1975 ACS meeting in Chicago, coinciding with the first paper published on this new technique [23]. Fig. 2 shows the state-of-the-art in suppressed ion chromatography at that time. Bear in mind that the measurement of small inorganic ions, such as Cl^- and SO_4^{2-}, at the low-ppm level was a major challenge in the 1970s. Thus the commercial availability of IC instantly revolutionized the determination of inorganic analytes, especially anions, in terms of speed, sensitivity, and convenience. The significance of this development to analytical chemistry is illus-

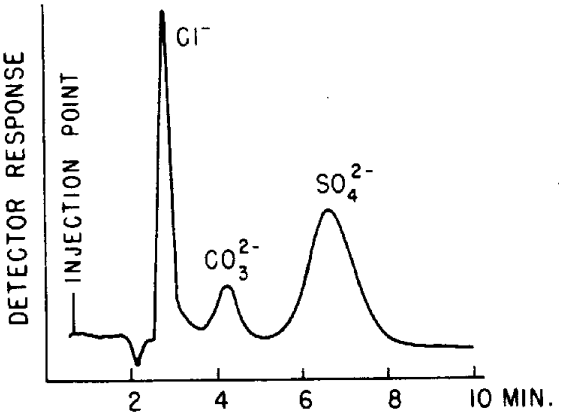

Fig. 2. Anion separation of Lake Huron water, circa 1975. Experimental conditions: column, 2.8×300 mm column of 200–400 Mesh SA Dowex 2 resin; eluent, 0.015 F sodium phenate; injection, 100 μl; suppressed conductivity; flow-rate, 1.0 ml/min. Reprinted from Ref. [23] with permission from the American Chemical Society.

trated by Dionex receiving the 1977 Pittsburgh Applied Analytical Chemistry Award and the Vaaler Award.

Thus from an analyst's perspective the invention and commercialization of IC was a remarkable breakthrough. However, from a chromatographer's perspective suppressed conductivity IC was underwhelming. The peak efficiency in Fig. 2 is only a few hundred plates and the generation of separation efficiency was slow (0.5–2 plates/s). In contrast, contemporary bonded phases on porous silica microspheres were achieving 25 plates/s [24].

The poor chromatographic efficiency of IC relative to other forms of HPLC was largely due to the unique demands implicit in the use of suppression. Firstly, the eluent had to be a base (e.g. OH^-, phenolate, CO_3^{2-}) for anion separations and an acid (e.g. H_2SO_4, methanesulfonic acid (MSA)) for cation separations. Such eluents are obviously incompatible with the silica-based packings which are predominantly used in HPLC. Similarly such eluents would corrode the typical stainless steel components used in HPLC systems. Thus, polymeric materials or glass had to be used instead. These low pressure fittings limited early IC systems to below 800 p.s.i., necessitating the use of packings that were much larger in diameter (25 μm) than the microparticulate (5 μm) silica phases used in 1970s HPLC.

A second restriction imposed by suppressed conductivity detection was that a stripper column was needed. This increased the complexity of the instrument, generated additional band broadening and necessitated periodically taking the instrument offline to regenerate the suppressor.

Small et al. [23] circumvented these problems by physically confining the active ion-exchange sites to the outer surface of the stationary phase particles, much in the manner of pellicular HPLC phases such as Zipax®. They thoroughly ground a strong base anion-exchanger (e.g. Dowex 1) to produce 0.5–2 μm particles. A very dilute suspension of these fine particles was then equilibrated with larger (180–325 Mesh) surface sulfonated polystyrene–divinylbenzene particles. The fine anion-exchange particles agglomerated onto the surface of the larger particle due to electrostatic attraction. The resultant agglomerated ion-exchange particle had low capacity and favorable mass transfer due to its pellicular nature. The ion-exchange capacity could be adjusted by altering the size of the fine particles. Upon, commercialization Dionex used agglomerated packings, but refined the process using smaller core particles (25 μm) and monodispersed latex particles in the 20–100 nm range. Dionex also switched from OH^- to CO_3^{2-}/HCO_3^- as the latter is a stronger eluent system, and so more dilute eluents could be used. This extended the life of the stripper column. However, it also resulted in a large residual background current after suppression. It would take 20 years for IC to return to its ideal OH^- eluent. Regardless, suppressed conductivity IC was the pre-eminent methodology of its day for anion determination. It filled a niche within the analytical laboratory environment wonderfully. One can only imagine that IC would have entered a long period of virtual standstill in evolution, if it had not been for . . .

2.2. The competition

> *Hence, as more individuals are produced than can possibly survive, there must in every case be a struggle for existence, either one individual with another of the same species, or with the individuals of distinct species, or with the physical conditions of life.*
>
> Charles Darwin
> Origin of the Species, Chapter 3.

Just four years after the original description of suppressed IC, Fritz et al. [25] reported an alternative approach for ion analysis which they termed ''nonsuppressed IC''. Like Small et al. [23] they used ion-exchange columns of very low capacity (0.007–0.07 mequiv./g) with the functional groups confined to the surface of the particles. With this low exchange capacity very dilute solutions (ca. 10^{-4} *M*) of aromatic organic acid salts such as benzoate and phthalate could be used as the eluent. Furthermore, these eluent ions had low ionic conductivity (<35 S/cm^2/equiv.), such that the eluent conductance was sufficiently low to allow the analyte conductivity to be monitored directly—without the complexity of a suppressor! Detection limits were comparable or better than suppressed conductivity IC [25,26]. Furthermore, the mild pH of nonsuppressed IC eluents allowed conventional HPLC equipment to be used.

This became all the more true in 1982 when Small and Miller [27] demonstrated that a conventional UV-absorbance detector could be used to monitor inorganic ions indirectly with detection limits superior to those achieved with direct conductivity. Soon, nonsuppressed IC systems were marketed by a number of companies including Waters, Wescan, Metrohm, Vydac and Hamilton.

3. The evolution

> *A large amount of inheritable and diversified variability is favourable . . . by giving a better chance for the appearance within any given period of profitable variations, will compensate for a lesser amount of variability in each individual, and is, I believe, an extremely important element of success.*
>
> Charles Darwin
> Origin of the Species, Chapter 4

Thus, began a period of intense competition within the IC market, with vocal proponents for both suppressed and nonsuppressed conductivity detection. This competition led to fast development of new forms and thus the rapid evolution of IC and a hybrid vigor [28]. The discussion which follows will tend to gloss over the gradual and continuous refinements which occurred over the past three decades so as to focus on the concepts and inventions that have revolutionized the manner in which IC is performed. This discussion will be compartmentalized based on different aspects of the instrumentation, although no characteristic of an organism or instrument evolves independent of the whole. For sake of clarity, only anion separations by ion-exchange is discussed, although equally dramatic developments have occurred in IC determinations of cations, amines, carbohydrates and carboxylates.

3.1. Hardware

The characteristics of punctuated evolution are most clearly evident in the general construct of IC pumps, valves and connecting tubing. The corrosive nature of the IC eluents necessitated that suppressed conductivity IC instruments be metal free. Unfortunately, the plastic and glass low pressure components available in the 1970s and early 1980s dictated that the backpressure of the column had to be less than 800 p.s.i. Furthermore, little attention was initially given to ensuring pulseless pumping since conductivity detection is quite insensitive to small variations in pressure. As instrumentation progressed through the Dionex Models 10, 12, 14 and 16 instruments, performance gradually improved but the separations were still restricted to large (25 μm) particle packings (AS1-3) by the pressure limits of the instrument.

The key ‘‘punctuated’’ step in the evolution in IC hardware was introduction of polyetheretherketone (PEEK) in the mid-1980s. PEEK is chemically inert and compatible with acidic, basic and most organic HPLC solvents. Its high tensile strength and resistance to slip and wear allow it to be machined into complex shapes such as piston heads and valve components. Thus, it is an ideal material for IC. The first PEEK-based IC instrument was the Dionex 2000, which can be considered the first ‘‘high-performance IC’’. Smaller particle packings (AS4, 15 μm) could now be used to yield higher efficiency (1200 plates) and faster (8 min) separations. Then, as the manufacture of fine bore PEEK tubing was refined, the weaker Tefzel tubing was gradually phased out, and the pressure capabilities of IC systems gradually improved. Today the performance characteristics of IC hardware closely match those of stainless steel HPLC systems.

3.2. The suppressor

The conceptualization of suppressed conductivity by Small et al. [23] was *the* seminal idea in the field. However, there were a number of limitations associated with the original column suppressors. These included: the column’s limited suppression capacity which necessitated frequent off-line regeneration; and a large extra-column volume, which became increasingly important as the efficiency of IC columns improved. These problems were largely eliminated in 1981 by the introduction of membrane based suppressors by Stevens et al. [29]. A detailed discussion of the development of suppressor technology is provided by Haddad et al. in this volume [30], and so will not be repeated herein. Developments in mem-

brane suppressor technology have: enabled suppression to be conducted in a continuous and unattended manner; enhanced separation and detection by reducing the system band broadening; and have increased the concentration of eluent that can be suppressed (and thus can be used for separations). The ideal instrument would then couple these capabilities with OH^- eluents (whose conductivity after suppression is only 0.06 μS/cm). However, for OH^- to effectively used improvements in column selectivity and eluent preparation were needed. Fortunately, these improvements have been achieved, as will be discussed below.

Prior to closing discussion on the evolution of suppression, the emergence of a viable sub-species must be noted [31]. A new generation of column-based suppressors are commercially available from Metrohm and Alltech. These are much smaller in volume than their predecessors, thereby minimizing extra column bandbroadening and retention time shifts caused by ion exclusion effects. Also, these column-based suppressors are able to withstand higher flow-rates and pressures than membrane-based suppressors. This new-generation of column suppressors are also reviewed by Haddad et al. [30].

3.3. The column

As indicated above, there were and are a multitude of companies making a wide variety of columns for IC. Given the proprietary nature of such columns, the ‘‘fossil’’ record of column technology is somewhat sketchy and incomplete. Nonetheless, some general trends regarding the desirable characteristics that have been breed into the columns can be noted.

Firstly, the efficiency of IC columns has steadily improved. This is largely evident in the decreasing particle sizes used. The early columns by Small et al. [23] and Fritz et al. [25] utilized particles in excess of 40 μm and generated only about 120 and 300 plates, respectively. With the first commercial IC column, the Dionex AS-1, the particle size was reduced to 25 μm and efficiencies increased to 700 plates. Further improvements in efficiency were tightly coupled to the improvements in hardware which allowed ever increasing backpressure and ever decreasing dead volume of the suppressors. By the mid-1980s 15 μm particles were being used in columns which yielded 1200 plates. Current columns such as the Dionex AS-14A and Metrohm Sep. 5 are packed with 5-μm particles and generate high efficiency separations, on the order of 5000–7000 plates, as shown in Fig. 3.

Secondly, early suppressed and nonsuppressed IC required low column capacities. These columns were easily overloaded by high sample concentrations. Increasing suppression capacity has enabled ever-increasing eluent concentrations and in turn increasing column capacities. The use of macroporous particles is one means of increasing the surface area of the packing, and thus its capacity. For instance, columns packed with nonporous Dionex AS11 particles have a capacity of 45 μequiv., whereas columns packed with the macroporous (2000 Å) AS11-HC have a capacity of 290 μequiv. The capacity of agglomerated stationary phases can also be controlled through the size of the latex particle attached to the surface of the solid core. A larger latex particle diameter means a larger capacity. However, the efficiency suffers if the latex particles become too large. Thus, high capacity polymeric particles are

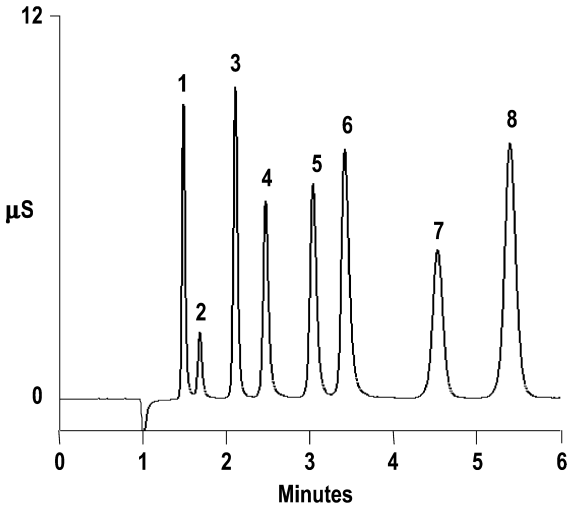

Fig. 3. Example of the state-of-the-art isocratic ion chromatography separation, ca. 2001. Experimental conditions: column: Dionex AS14A-5 μm (3×150 mm); eluent, 8.0 m*M* Na_2CO_3/1.0 m*M* $NaHCO_3$; injection, 5 μl; detection, suppressed conductivity; flow-rate, 0.8 ml/min; temperature, 30 °C. Peaks: 1=fluoride (5 mg/l); 2=acetate (20); 3=chloride (10); 4=nitrite (15); 5=bromide (25); 6=nitrate (25); 7=phosphate (40); 8=sulfate (30). Courtesy of Dionex Corporation.

prepared by chemically grafting the functionality directly onto the particles. A grafted film is typically very thin (1–5 nm) and produces high efficiency and high capacity stationary phases. The Dionex Ion Pac AS14-A and Ion Pac CS12A employ this technology. However, in general agglomerated stationary phases produce higher efficiencies and better peak shapes than grafted stationary phases.

Typical column capacities are now 30–120 μequiv. (quoted for 4×250 mm column dimensions), with the higher capacity columns typically being used for more complex matrices. This is illustrated in the extreme by the Dionex CS16 column which has a capacity of 8400 μequiv., and can be used to determine NH_4^+ in the presence of a 10 000-fold excess of Na^+ [32].

Thirdly, the columns have become increasingly robust. Early IC columns were not solvent compatible. The polymer beads that made up the core of the agglomerated phases were lightly crosslinked (<5%) polystyrene–divinylbenzene. These polymer beads would swell dramatically in the presence of even a small amount of solvent, causing increased backpressure and voids. Advances in polymer chemistry enabled much greater crosslinking of the core particle. Today the core particles are more than 50% crosslinked, and fully compatible with common HPLC solvents [33].

Fourthly, the columns have become more hydrophilic. Intuitively, selectivity in ion-exchange is based on electrostatics. That is, the more highly charged an ion, the more strongly it is retained by an ion-exchange resin. However, a secondary factor in ion-exchange is the role of the solvent. Ions in solution are accompanied by waters of hydration. When an ion leaves the mobile phase to enter the ion-exchanger, it must rearrange and eventually partially shed its solvation sphere. The more effectively an ion sheds its solvation sphere, the more closely it associates with the ion-exchange site (i.e. is retained). Generally speaking, an ion-exchanger most strongly retains ions with the smallest hydration spheres. Thus, the typical retention order is F^-, Cl^-, Br^- for anions and Li^+, Na^+, K^+ for cations. Early IC columns were based on polystyrene–divinylbenzene with strong base functionalities such as $-N(CH_3)_3^+$, and so were strongly hydrophobic. As a consequence, highly hydrated ions such as F^- were weakly retained, and so would elute near the water dip. Refinements in the polymeric support material and the addition of polar functionalities to the ion-exchange site increased the hydrophilicity of IC stationary phases. For instance, addition of alkanols to the ion-exchange site increases the column hydrophilicity such that the highly hydrated OH^- becomes a much more effective eluent. Thus, columns can be tailored for OH^- or carbonate eluents by using $-N(CH_3)_2(CH_2OH)^+$ or $-N(CH_3)_3^+$, respectively, as the ion-exchange site. Also, increasing the hydrophilicity of the column increases F^- retention so as to free it from the water dip at the dead volume and separate it from other weakly retained anions such as acetate, as evident in Fig. 3. Finally, increasing the hydrophilic character of the column reduces the retention of polarizable (or more correctly chaotropic) anions such as SCN^- and ClO_4^-, such that they can be eluted in reasonable time with reasonable eluent concentrations.

3.4. The eluent

In their seminal paper Small et al. [23] recognized that hydroxide was the ideal eluent for IC. Its conductivity after suppression is far lower than that of any other eluent. However, a number of impediments stood in the way of using OH^- as an eluent. Firstly, OH^- was a weak eluent. Thus, high concentrations of OH^- were needed to elute analytes in a reasonable time. This quickly exhausted the early column suppressors and exceeded the suppression capacity of the early membrane suppressors. Gradually the capacity of these membrane suppressors increased, as detailed above. Furthermore, improvements in column chemistry increased the hydrophilic character of the ion-exchange sites which increased the effective eluent strength of OH^-.

Secondly, there was the difficulty of preparing OH^- eluents. Carbonate contamination due to dissolution of CO_2 from the atmosphere strongly altered the eluent strength of OH^- solutions. Indeed, the realization that HCO_3^-/CO_3^{2-} could be an effective eluent in suppressed IC resulted from Small et al. [34] being bewildered by an old 0.01 *M* OH^- solution which was just as effective an eluent as a fresh 0.05 *M* OH^-. Ultimately, this ‘‘happy acci-

dent'' led to the adoption of HCO_3^-/CO_3^{2-} as the eluent of choice upon commercialization of IC.

The continuous improvements in column chemistry and suppressor technology gradually moved IC towards the day when its ideal eluent, hydroxide, could be used. However, the Achille's heal remained the ability to produce OH^- eluents reproducibly and conveniently. In the early 1990s Dasgupta and co-workers [35,36] pioneered the generation of OH^- eluents on-line using electrodialysis. This device evolved from their earlier development of electrolytic suppressors [37]. A commercial automated Eluent Generation Module (EG40) for on-line generation of KOH or MSA eluent was introduced by Dionex in 1997 [38]. A schematic diagram of the Eluent Generation Model configured for KOH production is shown in Fig. 4. The eluent generator consists of a KOH generation chamber and a K^+ ion electrolyte reservoir. These are separated by a cation-exchange connector. To generate a KOH eluent, distilled water is pumped through the KOH generation chamber and a d.c. current is applied between the anode and cathode of the cartridge. Under the applied field, electrolysis of water occurs generating H^+ and OH^-. The H^+ ions generated at the anode are displaced by K^+ within the cation-exchange connector in essentially a reverse-suppression process. The K^+ from the electrolyte reservoir combines with the OH^- generated at the cathode to produce KOH. The eluent then passes through an on-line degas tubing to eliminate the electrolysis gases. The concentration of the resultant KOH eluent is directly related to the electrical current and inversely proportional to the eluent flow-rate. At 1.0 ml/min, the EG40 can generate up to 100 m*M* KOH. More importantly, this eluent is free of carbonate and other impurity ions, and thus has a reduced background conductivity. Manually prepared NaOH exhibits a conductivity of 2–5 μS/cm after suppression. With on-line KOH generation, the background conductivity is about 0.3 μS/cm after suppression [35,38]. For comparison, pure water has a conductivity of 0.06 μS/cm.

3.5. Gradient elution

Probably the feature that has most distinguished HPLC from IC is gradient elution. For most of its existence IC has been an isocratic method. In part this is because excellent separations of the common

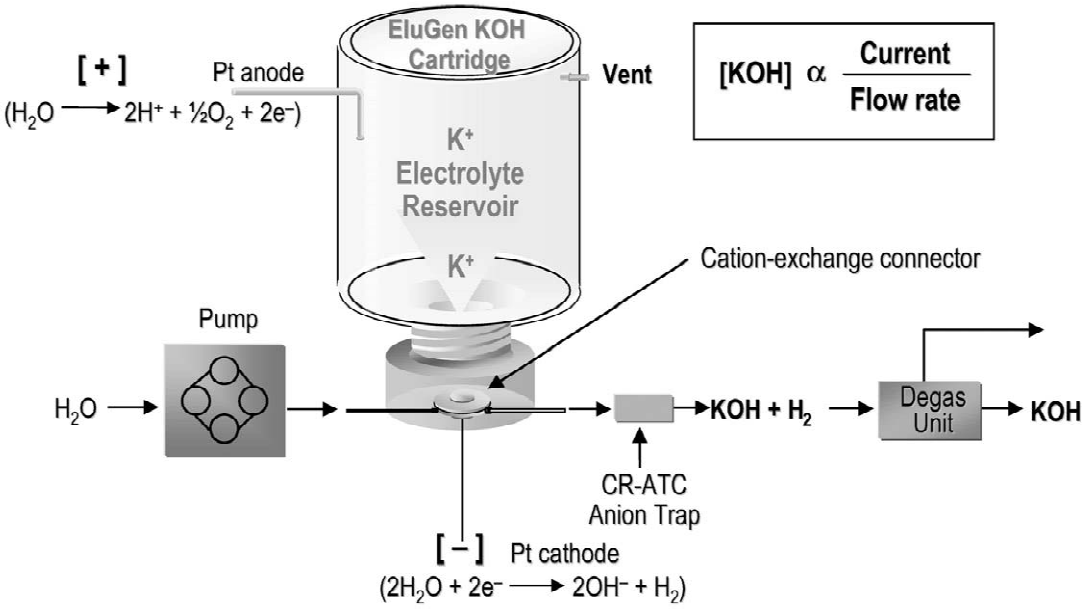

Fig. 4. Schematic diagram of an electrodialytic on-line KOH eluent generator. Based on the Dionex Eluent Generation Model EG40. Courtesy of Dionex Corporation.

anions can be achieved in this manner, as can be seen in Fig. 3. Nonetheless, to elute ions with widely differing retention, such as mono-, di-, tri- and tetravalent ions, it is necessary to vary the composition of the eluent during the run. The impediment to performing such gradients in IC was the large change in the background conductance that accompanied changes in eluent strength, particularly HCO_3^-/CO_3^{2-}. Even with care to minimize carbonate contamination, OH^- gradients such as shown in Fig. 5 exhibit baseline shifts of several μS [39]. This is comparable in magnitude to the response for the 10 ppm analytes in Fig. 5. Thus, trace analysis was impossible under gradient elution conditions. Furthermore, trace contaminants such as Cl^-, SO_4^{2-} and CO_3^{2-}, which are ubiquitous in even high grade NaOH, concentrate at the head of the column, and thus interfere with the determination of these anions.

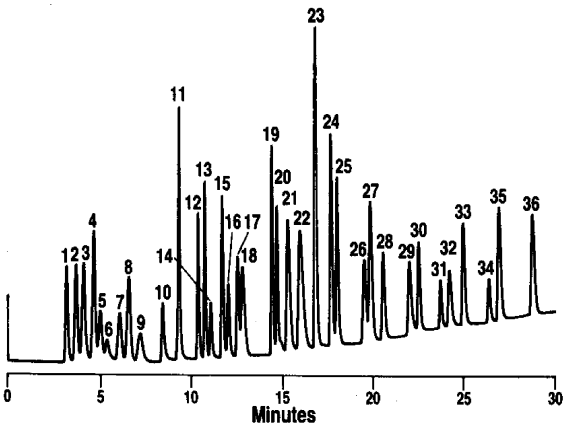

Fig. 5. Anion separation using hydroxide gradient. Experimental conditions: gradient, 0.75 m*M* KOH for 0–5 min, 0.75–30 m*M* from 5 to 15 min, 30–86 m*M* from 15 to 30 min; eluent source, manually prepared NaOH; flow-rate, 1.0 ml/min; column, Dionex AS5; injection, 10 μl; detection, suppressed conductivity; sensitivity, 30 μS full scale. All anions are 10 ppm unless otherwise noted. Peaks: 1=fluoride (1.5 ppm); 2=α-hydroxybutyrate; 3=acetate; 4=glycolate; 5=butyrate; 6=gluconate; 7=α-hydroxyvalerate; 8=formate (5.0); 9=valerate; 10=pyruvate; 11=monochloroacetate; 12=bromate; 13=chloride (3.0); 14=galacturonate; 15=nitrite (5.0); 16=glucuronate; 17=dichloroacetate; 18=trifluoroacetate; 19=phosphite; 20=selenite; 21=bromide; 22=nitrate; 23=sulfate; 24=oxalate; 25=selenate; 26=α-ketoglutarate; 27=fumarate; 28=phthalate; 29=oxalacetate; 30=phosphate; 31=arsenate; 32=chromate; 33=citrate; 34=isocitrate; 35=*cis*-aconitate; 36=*trans*-aconitate. From Ref. [39]; courtesy of Dionex Corporation.

Nonetheless, the separation in Fig. 5 is truly impressive—36 anions ranging in charge from −1 to −3 in a single run [39]! This illustrates the tremendous potential of gradient elution in IC.

On-line generation of OH^- eluents using electrodialysis [35,36,38] makes it possible to fully exploit this potential. Fig. 6 shows the gradient elution of 15 anions using on-line generation of 1–35 m*M* KOH. The background conductivity change is barely perceptible across the gradient. Note that this ‘‘gradient’’ is also generated using a simple isocratic pump (Fig. 7). Furthermore, as the eluent source is pure water, contamination from species such as Cl^-, SO_4^{2-} and CO_3^{2-} are no longer an issue. In a similar manner, on-line generated KOH can be used to modify the pH of other isocratic eluent such as carbonate [40]. Finally, HCO_3^-/CO_3^{2-} gradients can be performed as the background conductivity is suppressed by on-line degas removal of the residual carbonic acid after suppression [31]. Using such a suppression device the baseline shifts only 0.4 μS/

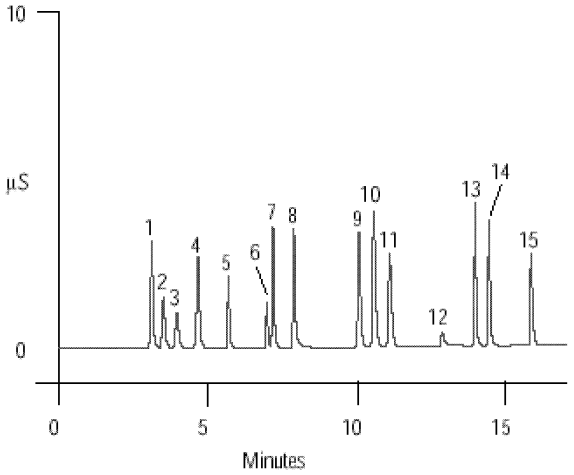

Fig. 6. Anion separation using a potassium hydroxide gradient delivered by an on-line eluent generator. Experimental conditions: gradient, 1 m*M* KOH for 0–3 min, 1–12 m*M* from 3 to 10 min, 12–35 m*M* from 10 to 14 min; eluent source, EG40; flow-rate, 1.5 ml/min; column, Dionex IonPac AG17, AS17, 4 mm; temperature, 30 °C; injection, 10 μl; detection, suppressed conductivity. Analytes are at 5 mg/l unless otherwise noted. Peaks: 1=fluoride (2.0 mg/l); 2=acetate; 3=propionate; 4=formate; 5=chlorite; 6=bromate; 7=chloride (3.0); 8=nitrite; 9=bromide (10.0); 10=nitrate (10.0); 11=chlorate (10.0); 12=carbonate (20.0); 13=sulfate; 14=oxalate; 15=phosphate (10.0). Courtesy of Dionex Corporation.

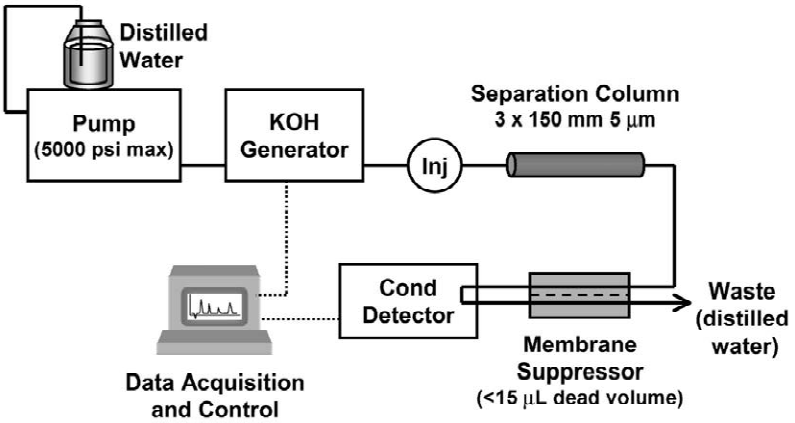

Fig. 7. Schematic of an ion chromatography system for suppressed conductivity determination of anions, ca. 2001. The system depicted is essentially that used for the gradient elution separation shown in Fig. 6.

cm upon switching from distilled water to 5 m*M* HCO_3^-/CO_3^{2-}.

3.6. A complete system

The continuous and punctuated refinements of IC have lead to: improved chromatographic efficiencies; the ability to use OH^- as an eluent; the ability to generate this eluent on-line; and the ability to suppress the effluent to essentially distilled water. Thus, IC systems such as that depicted in Fig. 7 have achieved the pinnacle of evolution in which one need ‘‘just add water.’’ That is, the eluent is distilled water, and the only waste produced is distilled water.

The evolution of IC has been so successful that it has surpassed RPLC in the realm of on-line process monitoring. The cost of purchase and disposal of RPLC solvents, and the hazards of these flammable solvents has impeded acceptance of on-line RPLC to such a degree that most on-line HPLC products have been discontinued. In contrast, eluents in IC are non-flammable aqueous solutions and the waste (after suppression) is essentially distilled water. On-line IC has been used for a variety of process applications [41] including monitoring, ultrapure water in nuclear power plants, and various process and wastewater streams. Currently both Dionex and Metrohm market IC systems specifically designed for the production environment.

3.7. An evolutionary dead end?

While IC has achieved a pinnacle of development, it would be naïve to assume that the evolution process has ceased. Numerous refinements and developments continue to appear. For instance, the use of monolithic columns for IC have yielded anion separations in 15 s [42]. There is also a trend towards miniaturization. Microbore (2 mm) columns are becoming increasingly common in IC, and capillary IC systems that fit in a briefcase have been developed for field analyses [43].

Furthermore, this article has focused solely on developments in the determination of the common anions using ion-exchange with suppressed conductivity detection. Cation analysis has seen similar evolution, with the development of new stationary phases, on-line eluent generation and electrolytic suppression [38]. A prime example of this evolution is the gradual trend away from sulfonated cation-exchangers. These stationary phases produce poor separations of cations due to their strong retention of alkaline earth cations relative to alkali metals [44]. This difference meant that the two groups of cations had to be determined sequentially using two different eluent systems, or alternatively using column switching. In 1987, Kolla et al. [45] demonstrated that cation-exchangers containing carboxylate functionalities could perform simultaneous and rapid (20 min) separation of both groups of cations using

dilute mineral acids. This work established the merits of carboxylated stationary phases, such as the Dionex IonPac CS14 and the Alltech Universal Cation Column [46] shown in Fig. 8. Further refinements in cation selectivity have been achieved by incorporating mixtures of carboxylate, phosphonate and crown ether sites into the cation-exchanger, e.g. Dionex IonPac CS15 and CS12A [44].

The determination of transition metals and lanthanides, although not as prevalent as alkali metal, alkaline earth metal and amine determinations, is also seeing diversification. Currently, separations are almost always achieved using sulfonated cation-exchange resins and variants thereof. Novel selectivity can be obtained through the use of a metal-chelating ion-exchange. Selectivity within such chelate phases is governed by the thermodynamics and kinetics of metal complex formation and dissociation, as well as electrostatic attraction [47].

Similarly, the evolutionary tree of ion-exchange has branched out into a variety of other application areas. Pulsed amperometric detection in conjunction with high pH anion-exchange allows picomole to femtomole detection of carbohydrates [48] and more recently amino acids [49]. Combining IC with ICP–MS offers tremendous opportunities in speciation, as discussed by Joe Caruso in this volume [54]. Similarly the dramatic improvements offered by the advancements in sample preparation discussed by Roger Smith in this volume are also apparent in IC [55]. On-line sample preconcentration yields a simple and convenient IC method for routine analysis of ions at the μg/l (ppb) to ng/l (ppt), while solid-phase extraction, on-line dialysis and two-dimensional chromatography allow trace ion determination in ever more complex matrices [50,51]. Even the fundamental phenomenon of ion retention is seeing new developments. Electrostatic ion chromatography uses a zwitterionic stationary phase to retain ions based on their polarizable or chaotropic nature, rather than ion–ion attraction [52,53].

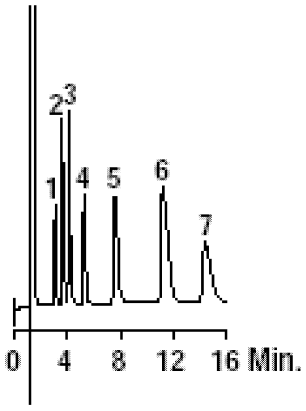

Fig. 8. Separation of alkali and alkaline earth metals on a cation-exchanger possessing carboxylate ion-exchange sites. Experimental conditions: eluent, 3 m*M* methanesulfonic acid; flow-rate, 1.0 ml/min; column, Alltech Universal Cation Column (7-μm silica-coated with polybutadiene/maleic acid copolymer); detection, conductivity. Peaks: 1=lithium (0.16 mg/l); 2=sodium (1.2); 3=ammonium (1.2); 4=potassium (2); 5=morpholine (2); 6=magnesium (1.6); 7=calcium (1.6). Courtesy of Alltech Associates Inc.

4. Recapitulation and conclusion

The 151 years since J. Thomas Way investigated the ability of soil to turn urine into water has seen remarkable growth in ion-exchange. Mikhail Tswett's seminal work laid the foundations for the development of chromatography as an analytical tool. Hamish Small and co-workers then conceptualized ion chromatography in the manner in which it is still performed today. Currently, IC accounts for over $165 million of the $3 billion worldwide liquid chromatography market, with over 2500 IC units sold in 2002. Approximately 4000 applications of IC have been published over the past 25 years [28].

However, current instrumentation little resembles that constructed by Small et al. [23]. Refinements such as on-line eluent generation and electrolytic suppressors inspired by the work of Sandy Dasgupta and many other developments and individuals have brought the technique to its current state. Many of these developments first appeared in the Symposium Volumes of *Journal of Chromatography A* associated with the *International Ion Chromatography Symposium*. To all those that have participated in this evolution, my deepest respect and appreciation—it has been a remarkable journey, one of gradual and continuous refinements, punctuated with exciting and unexpected developments.

There is grandeur in this view of life, with its

several powers, having been originally breathed into a few forms or into one; and that, whilst this planet has gone cycling on according to the fixed law of gravity, from so simple a beginning endless forms most beautiful and most wonderful have been, and are being, evolved.

Charles Darwin
Origin of the Species, Chapter 14.

Acknowledgements

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