

Chapter 2

Zechmeister's Influence on the Development of Chromatography

Nowadays, chromatographic analysis is employed in practically every laboratory. It has developed to a technique which provides detailed information about a substance in quite a small amount of time. Leslie S. Ettre mentions that “[a]ll of us who are active in this field should therefore appreciate the genius of the pioneers of this technique” [1]. When flipping through books on the history of chromatography, one will certainly take notice that László Zechmeister is always mentioned among the pioneers in this field of chemistry and among these geniuses. McCollum suggests in his review that “Zechmeister was among the earliest to recognize the high resolving power, great versatility, and analytical usefulness of the technics of selective adsorption” [2]. Unfortunately, it is often not ventilated in how far his work contributed to the development in this field. It takes a more detailed look at his merits, as nowadays other scientists who had also been working with this investigative method are better known than Zechmeister, such as Martin and Synge¹ or Tiselius.²

It is uncontested today that Mikhail Tsvett³ is to be named as the inventor of chromatography.⁴ In fact, by labeling Tsvett the true inventor of chromatography, Zechmeister even initiated a written debate argued out in the journal *Nature*. H. Weil and T. I. Williams responded to this certain claim by accusing Zechmeister of refusing to acknowledge D.T. Day's⁵ pioneering role. László politely countered in a further letter to the journal that he had indeed mentioned Day's contributions [6]. Weil and Williams, on the other hand, expressed their opinion that Zechmeister had ignored really important papers written by Day [7].

¹ A. J. P. Martin (1910–2002) and R. L. M. Synge (1904–1994) received the Nobel Prize in Chemistry in 1952 for their pioneering work in partition chromatography [3].

² A. W. K. Tiselius (1902–1971) received the Nobel Prize in Chemistry in 1948 for his research in electrophoresis and adsorption analysis [4].

³ 1872–1919.

⁴ “Such a preparation I term a chromatogram and the corresponding method, a chromatographic method” (Tsvett cited in [5]).

⁵ 1859–1925.

In the end, László did not give in to any further argument.⁶ In a paper about the historical development of chromatography, however, he stated that “[t]hese experiments [...] might well, under favorable conditions, have developed into systematic chromatography” [9]. That shows that he paid attention to the potential that lay in Day's experiments and theories,⁷ but did not see a fundamental milestone in the invention of chromatography. He also argued that, as opposed to Day, Tsvett “recognized and correctly interpreted chromatographic processes” and that he “devised a useful laboratory method” [10]. Today, it is universally acknowledged that Tsvett was the inventor of the method, even though there had been forerunners in adsorption analysis in the 19th century, such as D. T. Day in the US, or Schönbein and Göppelsröder [11] in Germany, to name but a few.

The “invention” of chromatography, however, is dated to 1906 (the publication of Tsvett's papers [12, 13]), and it took nearly 30 years until chemical laboratories started using it on a larger scale. Zechmeister referred to the time until the method was rediscovered as the “Latenzzeit”⁸ (engl. dormant period) [13]. It is important to note that, in fact, three graduates of the ETH Zurich are among the pioneers: Richard Kuhn, Paul Karrer and László Zechmeister. They all worked together with Richard Willstätter, but not at the same time.⁹ It is reported [15] that the latter was in possession of a German translation of Tsvett's book [16], which had been translated into German especially for him. Willstätter himself did not acknowledge the value of chromatography, but his disciples did. Edgar Lederer¹⁰ assumed that Willstätter had rejected chromatography because he could not obtain any valuable results for chlorophyll due to the inadequate adsorbent used for the packaging of his columns [15].

2.1 Literary Contributions to the History of Chromatography

As already mentioned before, it is difficult to pin down the exact time when Zechmeister started using the technique, but he certainly played a major role in the expansion of its use from the 1930s onwards [18]. Leslie S. Ettre claims that his

⁶ Interestingly enough, the polemics continued between Russian scientists and Weil and Williams, as the latter two challenged Tsvett's priority, which was of course not accepted by the Russians. The communist East would not approve of the bourgeois West “stealing” a Russian invention—even though, Tsvett being born in Italy, being educated in Switzerland, and having worked in Poland, was more of a cosmopolite than Russian [8].

⁷ In 1897, Day formulated a paper explaining selective adsorption when Pennsylvania earth oil is pressed through limestone [9].

⁸ “*Man kann das von 1906 bis 1931 reichende Vierteljahr-hundert als die Latenzzeit in der Geschichte der Chromatographie bezeichnen*” [14].

⁹ Willstätter occupied the chair of chemistry at the ETH Zurich from 1905 until 1912 [15].

¹⁰ 1908–1988; in 1931, Lederer made chromatography well-known through his demonstration of separating xanthophylls in egg yolk in 1931; during that time he was working with Kuhn [17].

most important contribution was the book *Die Chromatographische Adsorptionsmethode* published in 1937 together with his collaborator and later successor at the University of Pécs László Chohnoky¹¹ [19]. The text was composed in German, the language of science at that time. In a letter from 1939, the German publisher Julius Springer reports to Zechmeister that sales for the book were very satisfying and that a substantial amount of volumes were sold to foreign countries [20]. It was so popular that it had to be reprinted in a second edition one year later. This second edition was translated into English by A. L. Bacharach and F. A. Robinson [2] and made available for purchase in 1941 under the title *Principles and Practice of Chromatography*. Ettre also states that “[t]his was the right book, published at the right time...” [19]. What made this monograph such a bestseller was the fact that it contained methodology and detailed instructions on the analyses of various substances. In addition, Ettre mentions that Zechmeister is to be accredited for making classical column chromatography a simple tool [21]. F.P. Zscheile, for instance, recommends this book especially to biological chemists as the technique was very useful for the separation and purification of compounds found in plants [22].

Letters between the publishing house *John Wiley & Sons, Inc.* and Zechmeister illustrate the many decisions that had to be taken concerning further editions of the *Principles and Practice of Chromatography*. The author wanted to add a more extended bibliography and changes, as at that point of time the book was already seven years old and a bit out-of-date [23]. Wiley refused to that considering the high manufacturing costs and argued “that the sale is not large enough to warrant extensive changes in this reprinting” [24]. One year later, Zechmeister approved of the reprint of the monograph as it stood, since he wished “to keep it absolutely on the American market” as to his perception “the interest for it is rather increasing than decreasing” [25]. As a reprint of the book including changes had been refused before, László intended to publish a second volume under the title *Principles and Practice in Chromatography, Volume II. Progress in Chromatography 1938–1947* in 1949 [26]. This volume was compiled in order to review the literature on this scientific field in the mentioned years. Indeed, the book entered the market in 1950 under the shortened title *Progress in Chromatography 1938–1947*. This time, he had learnt from his mistakes from the past and conducted negotiations regarding the royalties for his book more wisely. In a letter to Mr. Parr of the publishing house, he wrote:

I absolutely protest against providing Wiley's with sheets of the new book unless the royalty question is settled beforehand to my satisfaction. [...] According to my estimate, the “Principles and Practice of Chromatography” represented a turnover of about \$20,000 of which, as you know, I did not get out practically anything. This is now a matter of the past, but you will understand that I am not willing and cannot afford even a partial repetition of this situation [27].

¹¹ 1899–1967.

According to Ettre [28], “[t]his book received excellent reviews, calling him ‘a master in the application of chromatography’ who can make ‘chromatography interesting and easy to use for every biochemist.’”

László Zechmeister wrote many articles about the history of chromatography. There is one introductory chapter to the first edition of the book *Chromatography* by Erich Heftmann¹² that I would like to go in detail with. The *Caltech archives* store letters of the conversation between Zechmeister and Heftmann about this contribution. The latter stated that László’s “historical introduction is a very stimulating and attractive account of the beginnings of chromatographic methods and will be a great asset to our book” [30]. Most of the content of the letters relates to editing and corrections. What catches the eye is a postscript [31], where Zechmeister wrote: “Please do not print my first name anywhere; it is unpronounceable and being invariably misspelled”. Indeed, he always signed letters and articles by using the abbreviation ‘L.’ for his first name. Heftmann reacted to that the following way: “I don’t think it’s unpronounceable—I once had a very dear friend by that name. But that was long ago and far away...” [32]. Erich Heftmann was born in Vienna [33], and his familiarity with this name or the Hungarian language might be explicable considering the proximity of this town to Hungary.

For the third edition of *Chromatography*, several changes were made. In 1975, the year of its publication, Zechmeister had been dead for some years. Therefore, the historical introduction was rewritten by Heftmann himself, probably modeled on the former version.¹³

2.2 National Award in Chromatography of the ACS

In 1962, Zechmeister received the National Award in Chromatography of the American Chemical Society for his outstanding contributions in this field and for the development of new methods. He was the second person to win this award, and his address dealt with “Column Chromatography and Geometrical Isomerism”, combining the two subjects in which he had gained quite some reputation, chromatography and the separation of cis/trans- isomers [35]. The prize was originally titled the *American Chemical Society Award in Chromatography and Electrophoresis*, but was reduced to *chromatography* in 1971. This certain accolade is normally assigned to one scientist every year, regardless of their nationality. However, the majority of recipients were Americans [36].

¹² Heftmann was born in Vienna in 1918 and studied medicine from 1936 to 1938. In 1939, Heftmann had to emigrate due to the political situation in Austria. From 1959 to 1969, he was research fellow at the Caltech [29].

¹³ “Death has taken two of our coauthors—L. Zechmeister and [...] Therefore, I have had to substitute as the author of the history of chromatography” [34].

2.3 Working with Chromatography

The post-war period was the time when the superiority of the method had well been accepted [37]. As the technique became more and more popular, so did the term “chromatographer”, about which Zechmeister was not pleased. He addressed this unfortunate expression in a lecture he gave in 1950 at a meeting of the local Southern California section of the *American Chemical Society*:

Recently chromatography became so popular that the English language has been enriched by a new noun “the chromatographer”. I would protest against such a label. In research chromatography should be considered first of all a tool like e.g. fractional distillation; and those of our colleagues who have achieved success by using distillation methods should certainly not be named “distillers” [35].

The term “chromatogram” actually referred to the column with the separated rings of the sample components [37]. Ettre also delivers an explanation about how the adsorption analysis with the classical column—as used by Tsvett and Zechmeister—was conducted:

[T]he adsorbent had to be prepared and packed into a small tube, the sample solution added to the top of the column and then developed using various solvents. The process was stopped before the first sample component emerged from the column. Next, the contents of the tube, with the separated colored rings, were carefully pushed out and the individual rings separated with a sharp knife. Finally, the compounds present in these separate adsorbent fractions were extracted, the solutions were characterized by spectroscopy or by other means, and the pure compounds were obtained by evaporating the solvent [37].

Although Zechmeister is credited with making column chromatography easy and accessible to everyone, Ettre added to his description that this method actually required considerable skill, and that, hence, an easier method, the flow-through chromatogram was developed in the late 1930s. The implementation differs from what is today known as liquid chromatography in that no pressure was applied in order to make the eluent (the mobile phase) pass through the column.

As regards the technique of packing a chromatography column, Zechmeister described that they were using columns of the size 10×15 to 60×260 mm in his laboratories. A perforated porcelain disk was inserted to the lower end of the tube to prevent the packaging from dropping out, and a small portion of cotton wool was piled up on the disk. Then the dried and sieved adsorbent could be funneled. Normally, calcium carbonate or calcium hydroxide was used, but also powdered sugar or fuller’s earth was applied [38].

In the last years of his life, Zechmeister worked on using the chromatographic technique for the separation of stereoisomers. His last monograph, in fact, was about *cis*- and *trans*- isomers of carotenoids. I would like to conclude by quoting Leslie S. Ettre [39] once again:

It is true that Zechmeister was an internationally-accepted authority in the fields of carotenoids, enzymes and other complex organic sub-stances, for example geometric isomers.

László Zechmeister himself stated once that the direction and rate of progress in organic chemistry depended on the availability and effectiveness of physical methods [11], and I would also like to add that without the technique of chromatography many of his research results and scientific achievements in organic chemistry would probably not have been possible.

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Wirth, M.

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