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EDITORIAL

Mikhail S. Tsvet—pioneer of chromatography—150 years from his birth

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> "Progress in science depends on new techniques, new discoveries and new ideas, probably in that order."
> *Sydney Brenner, 1980*

Mikhail Semenovich Tsvet (also, Tswett, especially in botanical literature, 1872–1919, Fig. 1) was born in Italy, grew up in Switzerland, received his education at the University of Geneva, and moved to his father's Russian homeland. His Swiss PhD degree was not recognized, and he had to augment his training; finally, earning a Master's degree. He was a botanist who invented chromatography, which developed into one of the major tools of chemical and biochemical research in the twentieth century, alas, leaving Tsvet in relative obscurity. We remember him on the occasion of the 150th anniversary of his birth.

Mikhail Semenovich Tsvet invented chromatography in 1906, and it took decades before it, and its derivatives became widely used. Methodological and instrumentational advances are always the motors of progress in scientific research. For twentieth-century chemistry, two such methodological advances can be singled out as having extraordinary impact on research. One is X-ray crystallography and the other is chromatography. For X-ray crystallography, its pioneers were recognized for their milestone discoveries from the very beginning, virtually from the moment of their discoveries. Suffice it to mention the Nobel Prizes to Max von Laue in 1914 and the two Braggs, William Henry Bragg and William Lawrence Bragg, in 1915. There were then a number of recognitions throughout the century for seminal discoveries or contributions utilizing X-ray crystallography. Tsvet's discovery remained unrecognized even though he lived for more than a decade after his discovery [1]. Only later were Nobel Prizes awarded for the discovery of derivatives of chromatography and for discoveries by employing chromatography.

Tsvet was a botanist, and the invention of chromatography happened while he was working in Warsaw, Poland, which was at the time part of the Russian Empire. He prepared an extract of leaves and he filtered this extract through a narrow glass tube, which he packed with powdered chalk. We don't know what he expected from this experiment, but it has been recorded that he was startled by what he observed. There were distinct bands of the different chlorophyll greens and carotenoid yellows, reds, and oranges, as the liquid was percolating through the column. It was "like the light rays in a spectrum" [2]. The less strongly adsorbed pigments migrated more rapidly through the column and emerged from it, consecutively, as relatively pure substances. Tsvet called it a chromatogram. These first observations were made on chlorophyll pigments, but Tsvet realized that the adsorption phenomena he observed were not at all restricted to them. All kinds of colored as well as colorless chemical compounds could be subjected to the same process.

Chromatography has become a most common technique in the laboratory, so common that Tsvet is hardly ever being referred to in its applications. The great scholar of citation habits, Eugene Garfield, referred to such a phenomenon when a well-known discovery or invention is no longer cited, "obliteration by incorporation" [1]. Tsvet's invention has had far-reaching applications in vastly different areas of science and technology. We mention one example. The Manhattan Project employed ion-exchange chromatography with charged adsorbents to purify elements for fission fuel for the atomic bombs. This development was preceded by constructing the first chromatography column based on ion exchange in a zeolite phase in the experiments of the Nobel laureate Harold C. Urey and T. I. Taylor.

Other techniques of chromatography were invented over the ensuing decades. Archer J.P. Martin and R.L.M. Synge invented partition chromatography and received the 1952 Nobel Prize in Chemistry for it. Frederick Sanger used this

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Fig. 1 Mikhail S. Tsvet, about 1900, by unknown photographer (Wikimedia, public domain)

new and very powerful fractionation technique in his work on creating the methodology of sequencing proteins. Actually, Sanger used a new development of partition chromatography—paper chromatography. Sanger greatly benefited from personal interactions with Martin, through A.C. Chibnall, Professor of Biochemistry at Cambridge, the man in charge when Sanger started his career at Cambridge. This was as if being present at the creation of the new technique, Sanger could take advantage of it even before it became an accepted new tool in chemical research [3]. Sanger received the Nobel Prize in Chemistry in 1958 for sequencing proteins. This was his first Nobel Prize, and it was unshared. He went on to work out a methodology for sequencing nucleic acids for which he received a share of the 1980 Nobel Prize in Chemistry. He spoke with great admiration and appreciation about partition chromatography and especially about Archer Martin's genius behind it [3]. Stanford Moore and William H. Stein received the Nobel Prize in 1972 in Chemistry for their uncovering the connection between chemical structure and catalytic activity in their research on the active center of the ribonuclease molecule. In their Nobel lecture, they emphasized the importance of the "renaissance of chromatography" [4].

Mikhail S. Tsvet lived a short life but it was rich in events. His mother was Italian, and his father was a Ukrainian in the foreign service for the Russian Empire. Tsvet was born in Asti, Italy, in the Piedmont region of northwestern Italy. His mother died soon after his birth, and his father brought him to Geneva, Switzerland, and left him there in care of a lady. So, Tsvet grew up in Switzerland, and his father visited him annually, sometimes even twice a year. Tsvet studied in Geneva and in Lausanne and graduated in 1893 with a bachelor's degree from the Department of Physics and Mathematics of the University of Geneva. Notwithstanding the name of the department, the focus of his studies was on chemistry and biology. He stayed on at the University of Geneva for doctoral work. He became a botanist and wrote his dissertation on cell physiology. He was granted his PhD degree in 1896. The excellence of his research was recognized by a Humphry Davy Prize (not to mistake it for the Humphry Davy Medal of the Royal Society, London).

By fortunate coincidence, by the time his father was recalled from foreign service and returned to Saint Petersburg, Tsvet had also completed his education in Geneva, and he also moved to Saint Petersburg. His first work place in 1896 was at the Biological Laboratory of the Russian Academy of Sciences. He had to continue his studies as well, because his Swiss degree was not recognized in Russia. In 1897, he received his appointment to be a teacher of botany for women. His stay in Saint Petersburg is commemorated by a memorial plaque (Fig. 2). The building on whose façade this plaque is erected housed Petr Lesgaft's biological laboratory. It was Tsvet's great luck that he met Petr Francevich Lesgaft (1837–1909) who was an anatomist, anthropologist, psychologist, and pedagogue. He introduced a number of innovations in Russia. He created the system of physical education and a modern biological laboratory. Thanks to Tsvet's interactions

Fig. 2 Memorial plaque on the façade of 25 Soyuz Pechatnikov Street, Saint Petersburg (Михаил Цвет: биография, творчество, карьера, личная жизнь Культура и общество Другое (kakprosto.ru))

with Lesgaft, Tsvet prepared for and passed successfully the requirements for his Master's degree in Russia.

Their interactions lasted until 1902 when Tsvet moved to the Institute of Plant Physiology of the University of Warsaw in Warsaw, Poland (at the time, it was part of the Russian Empire). Tsvet made his milestone discovery while he was in Warsaw. He published his works in Russian, and this greatly slowed their dissemination. His position at the University of Warsaw was assistant professor. He taught at other institutions of higher education in Warsaw. At the beginning of World War I, when the Warsaw Technical University was evacuated to Moscow, Tsvet moved with it. Next, this school and Tsvet moved to Nizhny Novgorod. In 1917, Tsvet, finally, was accorded a professorial appointment. He became professor of botany and director of the botanical gardens at the University of Tartu. Tartu is in Estonia, but Estonia also had a turbulent history, and Tartu had been called Dorpat in German and Yuryev in Russian, and accordingly, its most prestigious university used to have different names. In 1918, German troops occupied Tartu, and the university, or at least a portion of it, was evacuated to Voronezh, a large Russian city in the south of the central region of Russia. It was there that Tsvet contracted a chronic inflammation of the throat and he succumbed to it in 1919.

He has a tomb stone (Fig. 3) in the cemetery of the Alekseevo-Akatov Monastery in downtown Voronezh, but opinions differ whether he is actually buried under this tomb stone. According to one, he was buried in the Chugunovskoe cemetery, which is close to the No. 2 Metropolitan Clinical Hospital where he died. The area was reclaimed after the heavy fights of World War II, and on the territory of the former cemetery, new buildings were erected, including a television center and a sports arena. Accordingly, the tomb stone shown at the Alekseevo-Akatov cemetery is a memorial rather than an actual grave mark. It was unveiled in 1992 to honor Mikhail S. Tsvet's memory, and it has served this purpose well. The professors and students of Voronezh State University visit the grave memorial and keep the memory of this great contributor to chemical science alive.

There was a confluence of reasons why Tsvet, and his invention remained in obscurity for a long time. If comparing this with Mendeleev's fame and the international recognition of his periodic table of the elements, the fact that Tsvet was a Russian scientist could not be the reason. That he published about chromatography only in Russian, however, may have contributed to the obscurity. In Mendeleev's case, Mendeleev did everything to popularize his discovery in the German-language community of chemistry, which was the most important chemistry community at the time. As a result, Mendeleev and his priority were internationally recognized even though there were also British and German chemists who made similar discoveries [5]. Another factor was when in 1912, Richard Willstätter tried to reproduce Tsvet's experiments, he failed, which was not

Fig. 3 Tomb stone of Mikhail S. Tsvet in the cemetery of the Alekseevo-Akatov Monastery (photograph by Ekaterina P. Altova). The text on the memorial reads: "Ему дано открыть хроматографию – разделяющую молекулы и объединяющую людей," that is, "He invented chromatography, separating molecules and uniting people"

Tsvet's fault. Rather, Willstätter used a too strong adsorbent in the column, which destroyed the chlorophyll. Willstätter was an outstanding chemist, much respected, who soon received the Nobel Prize for related discoveries on plant pigments and, in particular, on chlorophyll. So his negative experience was a setback for the recognition of Tsvet and his invention. Fortunately, Tsvet and his pioneering contribution did not vanish completely, and the current anniversary is yet another opportunity to pay tribute to this early contributor to the great successes of twentieth-century chemistry.

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