



Introduction: Special Issue in Honor of Eva Syková

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Eva Syková has had an illustrious academic career. It is clear that she was identified as an effective leader early on, and rapidly promoted through the ranks. Many scientists with this degree of responsibility would have given up research as they gained seniority, but Eva has not done this. Instead, she built up an excellent group of co-workers and collaborators, allowing her to continue to be active in research and to incorporate a wide range of topics and experimental studies in her scientific life. Eva's publications show an interest in a variety of topics: sequential, recurring and overlapping. She has more than 350 publications. Eva's most cited papers include an approximately 50:50 split between topics in diffusion/extracellular ion regulation, along with glia, reflecting her earlier studies, and the later work on CNS pathology and

the possible use of stem cells and advanced biomaterials in CNS repair. In this brief essay, only a few selected publications can be mentioned.

Before starting her formal training, Eva benefited from early research experience in the laboratory of the distinguished Czech neuroscientist, Jan Bureš. Between 1970 and 1983 Eva completed her doctoral and postdoctoral training mostly at the Czechoslovak Academy of Sciences, Prague with an excursion to the University of Goteborg, Sweden, in 1977. From 1983 to 1990 she was Head of the Laboratory of Neurohumoral Regulations, Institute of Physiological Regulations, at the Academy of Sciences. During this period, she managed to be a visiting professor at the University of Heidelberg, Germany (1984) and a visiting Senior Research Fellow at the University of Western Australia, Perth (1985–1986).

Until the Velvet Revolution in 1989, Czechoslovakia was under a Communist regime and quality research was difficult, so the fact that Eva's early papers immediately gained international recognition is a tribute to her drive and ability. In 1993 Czechoslovakia split into the Czech Republic and Slovakia. Meanwhile Eva became Head of the Department

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of Neuroscience, Institute of Experimental Medicine, Academy of Sciences of the Czech Republic (ASCR), Prague in 1991 and from 2001 she rose to the position of Director, Institute of Experimental Medicine ASCR and Principal coordinator for an EU Center for Excellence. Between 1996 and 2012, Eva also was Chair of the Department of Neuroscience, 2nd Medical School, Charles University, Prague. In 2012, Eva's illustrious career took a new direction when she became a Senator in the Parliament of the Czech Republic, a position that she held until 2018. In 2016 Eva retired from the Institute of Experimental Medicine. Characteristically, she continues her academic work on the spinal cord, stem cells and Alzheimer's disease with a position as Senior Researcher at the Institute of Immunology, Slovak Academy of Sciences and as a Scientific Director of a biotechnology company near Prague.

Eva Sykova's early work on the CNS, beginning in 1972 involved cell–cell interaction, including synaptic transmission and changes in extracellular K^+ , much of it in the spinal cord. Along with her Czech colleagues Vyklický, Kříž and Ujec [1], Eva was a pioneer in the use of ion-selective microelectrodes and co-authored many papers using this technology. By 1980 Eva had begun collaboration on K^+ measurements with Dick Orkand [2], already well known in the blood–brain barrier community. Eva's 1983 review [3] on extracellular K^+ accumulation during neural activity was an important landmark and was expanded into a book in 1992 [4]. In 1980, from July 8–11, she co-organized a conference in Prague on the use of ISMs that also resulted in a co-edited book [5].

About 1980, Charles Nicholson visited Eva's lab in Prague and discovered that Alexandr (Saša) Chvátal was writing a program to analyze diffusion in the extracellular space (ECS). The Nicholson lab in New York already had written such a program called VOLTORO that measured the volume fraction and tortuosity of the extracellular space using the probe ion tetramethylammonium (TMA) and it was decided to use that in Eva's lab. This method became known as the Real-Time Iontophoretic (RTI) method and VOLTORO, and its updates, subsequently played a role in more than 25 of the studies from the Prague laboratory on the diffusion properties in the ECS. This began a scientific interaction and friendship spanning more than 40 years that produced two highly-cited reviews [6, 7]. The RTI work continues today in the laboratory of Lýdia Vargová who heads the Department of Neuroscience at Charles University, Prague.

The extracellular space has been an abiding theme for Eva; in addition to her studies of extracellular K^+ , she looked at changes in extracellular pH [8], the development of the ECS [9] and extracellular volume transmission [10]. Volume transmission signifies a process by which an agent released by a neuron or glial cell can travel via the ECS

to act at a distance and influence a wider neural territory and was illustrated in detail in the book that Agnati, Fuxe, Nicholson and Syková edited in 2000 [11].

Early on in her career, Eva recognized the importance of glial cells in shaping and modulating the extracellular microenvironment and she has collaborated in experimental studies with several glial experts, including Helmut Kettenmann, beginning in 1987 [12] and in a continuing collaboration with Kettenmann that included Orkand and Chvátal [13] and others [14].

Although Eva has made important contributions to the basic sciences, her abiding focus has been on pathological conditions, both to inform studies on basic research and to extend the reach and relevance to clinical medicine. Eva's papers have included studies relevant to pain [15], neural injury [16], hypoxia and ischemia [17], experimental autoimmune encephalomyelitis (EAE) [18], X-irradiation [19], aging [20], astrogliosis [21], spreading depression [22], hydrocephalus [23], gliomas [24], Alzheimer's Disease [25], epilepsy [26] and extracellular matrix proteins [27].

More recently, Eva has been exploring methods for repairing CNS damage and degeneration. One of Eva's earliest papers on induced neural repair in 1998 [28] involved use of PHPMA hydrogels, followed in 1999 by use of brain grafts [29]. An early stem cell paper [30] used bone-marrow-derived stromal cells; later work benefitted from developments in a number of stem cell lines [31]. From this period until the present, Eva has published many papers featuring the use of stem cells in CNS repair, especially in the spinal cord [32], the majority in collaboration with her long-time colleague Pavla Jendelová. Other studies employed artificial biomaterials, often featuring work with Šarka Kubinová [33]. The role of Ca^{2+} was also investigated in stem-cell treated tissue in collaboration with Alexei Verkhratsky [34].

In this Special Issue, the papers roughly span the evolution of Eva's main areas of interest and include many of her collaborators. *Extracellular Space and Volume Transmission* are represented by the contributions of Borroto-Escuela and Fuxe [35], Lakatos et al. [36], Lehemenkühler and Richter [37], Nicholson and Kamali-Zare [38], Sherpa et al. [39], and Sucha et al. [40]. *Glial Cells* are covered by Shulyatnikova and Verkhratsky [41], Smith et al. [42], Stenovec et al. [43], and Verkhratsky and Chvátal [44]. Finally, *Injury and Repair* feature in the papers of Cizkova et al. [45], Fawcett [46], Jiráková et al. [47], Kubinová [48], Murgoci et al. [49], Roitbak [50], Vymetalova et al. [51], and Wilhelmsson et al. [52].

Eva has also been very active in organizing international symposia in Prague, an excellent way to introduce her teams to the wider community, to develop collaborations, and to show-case novel aspects of the work in Prague. In addition to the first symposium in 1980, mentioned above, they included a workshop from October 23–25, 2001 and another from August 18–31, 2002. The latter was sponsored by IBRO and taught people to use the RTI method for diffusion studies

on the ECS, as well as other techniques. From July 10–15, 2003, the main IBRO meeting was held in Prague and Eva played a prominent role. This was followed by a symposium in Prague from July 16–17, 2003, which focused on the ECS. Eva's Institute also acted as host for a joint meeting between the Czech and UK Physiological Societies in Prague in 1998.

Joan Abbott recalls that she has a vivid memory of one Prague symposium, in which the 'opening remarks' session started with a curtain around the stage, which swept back to reveal a grand piano—and a pianist then played some beautiful Czech music—a very welcome alternative to the usual introduction at such international meetings by a local dignitary or civil servant. Joan also remembers a gala evening reception where many of the international participants simply turned up in the clothes they had been wearing during the day, including jeans and T-shirts for the younger participants. In contrast, Eva appeared in a long evening dress with a magnificent fur stole!

Eva has been a terrific role model for young women scientists, showing how it is possible to build up and sustain an extremely active research group, gain a well-deserved international reputation for outstanding research, and maintain an excellent reputation as a senior figure and leader in national and international neuroscience studies. And to do all this while maintaining an admirable family life. In the latter she has always been ably supported by her husband, Josef Syka, himself an internationally distinguished neuroscientist in the field of audition. We wish her all the best and hope to continue to meet her at international gatherings.

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Guest Editors

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