# BIOGRAPHICAL SKETCH

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NAME: WEBER, STEPHEN G

eRA COMMONS USER NAME (credential, e.g., agency login): sweber

POSITION TITLE: Professor of Chemistry

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

| INSTITUTION AND LOCATION | DEGREE (if applicable) | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Case Western Reserve University, Cleveland, OH | BA | 06/1970 | Biology and Chemistry |
| McGill University, Montreal, Quebec | PHD | 05/1979 | Chemistry |

## A. Personal Statement

We want to understand chemical events related to normal and pathological brain. Our laboratory develops, refines, and applies new and quantitative methods to learn more about biological systems. The primary goals are (1) the determination of neurotransmitters by microdialysis with fast, capillary, online liquid chromatography (2) the investigation of neuropeptide processing in the extracellular space and (3) to empower others to make better measurements using our methods. We are experienced in capillary chromatography, electrochemical detection, chromatographic theory, mass transport phenomena, electroosmostic flow in brain, small sample handling, peptide chemistry, and live animal experiments. We also have experience in microscopy, organotypic culturing as well as chemical synthesis and purification, statistical methods, and standard biochemical techniques. Our emphasis is on critical assessment of what information can be obtained from a measurement, and how to obtain more accurate information. We have collaborated with the Michael group for several years in the pursuit of better understanding of the limitations of microdialysis. We use that information to develop ideas of how to avoid the limitations. The best of those ideas become new methodological improvements providing more and better information about the brain.


1. Gu H, Varner EL, Groskreutz SR, Michael AC, Weber SG. In Vivo Monitoring of Dopamine by Microdialysis with 1 min Temporal Resolution Using Online Capillary Liquid Chromatography with Electrochemical Detection. Anal Chem. 2015 Jun 16;87(12):6088-94. PubMed PMID: 25970591; PubMed Central PMCID: PMC4835028.
2. Zhang J, Jaquins-Gerstl A, Nesbitt KM, Rutan SC, Michael AC, Weber SG. In vivo monitoring of serotonin in the striatum of freely moving rats with one minute temporal resolution by online microdialysis-capillary high-performance liquid chromatography at elevated temperature and pressure. Anal Chem. 2013 Oct 15;85(20):9889-97. PubMed PMID: 24020786; PubMed Central PMCID: PMC3899587.
3. Zhang J, Liu Y, Jaquins-Gerstl A, Shu Z, Michael AC, Weber SG. Optimization for speed and sensitivity in capillary high performance liquid chromatography. The importance of column diameter in online monitoring of serotonin by microdialysis. J Chromatogr A. 2012 Aug 17;1251:54-62. PubMed PMID: 22771067; PubMed Central PMCID: PMC3419010.
4. Liu Y, Zhang J, Xu X, Zhao MK, Andrews AM, Weber SG. Capillary ultrahigh performance liquid chromatography with elevated temperature for sub-one minute separations of basal serotonin in submicroliter brain microdialysate samples. Anal Chem. 2010 Dec 1;82(23):9611-6. PubMed PMID: 21062014; PubMed Central PMCID: PMC3008768.


## B. Positions and Honors

## Positions and Employment

| | |
|---|---|
| 1970 - 1974 | Hospital Corpsman (E5), United States Navy, Great Lakes, IL |
| 1979 - 1985 | Assistant Professor, University of Pittsburgh, Pittsburgh, PA |
| 1985 - 1994 | Associate Professor, University of Pittsburgh, Pittsburgh, PA |
| 1991 - 1992 | Visiting Scientist Fellow, Swedish Medical Research Foundation, Goteborg |
| 1994 - | Professor of Chemistry, University of Pittsburgh, Pittsburgh, PA |
| 1999 - 2001 | Associate Chair, University of Pittsburgh, Pittsburgh, PA |
| 2001 - | Director of Graduate Studies, University of Pittsburgh, Pittsburgh, PA |
| 2009 - | Professor, Clinical and Translational Science, University of Pittsburgh, Pittsburgh, PA |

## Other Experience and Professional Memberships

| | |
|---|---|
| 1989 - | Contributing Editor, Trends in Analytical Chemistry |
| 1989 - 2004 | Editorial Board, Journal of Pharmaceutical and Biomedical Analysis |
| 1991 - 1997 | Editor, Comprehensive Analytical Chemistry |
| 2001 - 2004 | Editorial Advisory Board, Analytical Chemistry |
| 2001 - 2004 | Editorial Board, Talanta |
| 2010 - | Editorial Board, Journal of Chromatography A |
| 2011 - | Editorial Board, Chemical Analysis |
| 2016 - 2019 | Editorial Advisory Board, Analytical Chemistry |

## Honors

| | |
|---|---|
| 1991 | Visiting Scientist Fellowship, Swedish Medical Research Council |
| 1998 | Fisher Lectureship, Bucknell University |
| 2005 | Gold Medal of Assiut University, Assiut University |
| 2008 | Frontiers Lectureship, Wayne State University |
| 2008 | Pittsburgh Award of the American Chemical Society, American Chemical Society |
| 2012 | Excellence in Mentoring, University of Pittsburgh |
| 2015 | Palmer Award, Minnesota Chromatography Forum |
| 2016 | Dal Nogare Award, Chromatography Forum of the Delaware Valley |

## C. Contribution to Science

1. Recent work has focused on the development and application of techniques to understand neurochemical function in vitro (organotypic hippocampal slice cultures, OHSCs) and in vivo. We have developed the idea that electroosmotic flow is a better and more controllable method for tissue perfusion than pressure flow. We are applying that to the determination of ectopeptidase activity and thiol metabolism in OHSCs.

    a. Guy Y, Muha RJ, Sandberg M, Weber SG. Determination of zeta-potential and tortuosity in rat organotypic hippocampal cultures from electroosmotic velocity measurements under feedback control. Anal Chem. 2009 Apr 15;81(8):3001-7. PubMed PMID: 19298057; PubMed Central PMCID: PMC2736137.

    b. Xu H, Guy Y, Hamsher A, Shi G, Sandberg M, Weber SG. Electroosmotic sampling. Application to determination of ectopeptidase activity in organotypic hippocampal slice cultures. Anal Chem. 2010 Aug 1;82(15):6377-83. PubMed PMID: 20669992; PubMed Central PMCID: PMC2920223.

    c. Wu J, Sandberg M, Weber SG. Integrated electroosmotic perfusion of tissue with online microfluidic analysis to track the metabolism of cystamine, pantethine, and coenzyme A. Anal Chem. 2013 Dec 17;85(24):12020-7. PubMed PMID: 24215585; PubMed Central PMCID: PMC3899583.

    d. Ou Y, Wu J, Sandberg M, Weber SG. Electroosmotic perfusion of tissue: sampling the

extracellular space and quantitative assessment of membrane-bound enzyme activity in organotypic hippocampal slice cultures. Anal Bioanal Chem. 2014 Oct;406(26):6455-68. PubMed PMID: 25168111; PubMed Central PMCID: PMC4184924.

2. Capillary liquid chromatography, cLC, is ideally suited to the small, complex samples obtained from tissue culture perfusion or microdialysis in vivo. However, improvements can make it operate faster, with higher sensitivity and greater flexibility.

   a. Groskreutz SR, Horner AR, Weber SG. Temperature-based on-column solute focusing in capillary liquid chromatography reduces peak broadening from pre-column dispersion and volume overload when used alone or with solvent-based focusing. J Chromatogr A. 2015 Jul 31;1405:133-9. PubMed PMID: 26091787; PubMed Central PMCID: PMC4488902.
   b. Liu Y, Zhang J, Xu X, Zhao MK, Andrews AM, Weber SG. Capillary ultrahigh performance liquid chromatography with elevated temperature for sub-one minute separations of basal serotonin in submicroliter brain microdialysate samples. Anal Chem. 2010 Dec 1;82(23):9611-6. PubMed PMID: 21062014; PubMed Central PMCID: PMC3008768.
   c. Zhang J, Liu Y, Jaquins-Gerstl A, Shu Z, Michael AC, Weber SG. Optimization for speed and sensitivity in capillary high performance liquid chromatography. The importance of column diameter in online monitoring of serotonin by microdialysis. J Chromatogr A. 2012 Aug 17;1251:54-62. PubMed PMID: 22771067; PubMed Central PMCID: PMC3419010.
   d. Groskreutz SR, Weber SG. Temperature-assisted on-column solute focusing: a general method to reduce pre-column dispersion in capillary high performance liquid chromatography. J Chromatogr A. 2014 Aug 8;1354:65-74. PubMed PMID: 24973805; PubMed Central PMCID: PMC4100596.

3. Collaboration with Prof. Adrian Michael, who is working on minimizing the impact of microdialysis-induced probe damage on microdialysis determinations of neurotransmitter concentrations in vivo in combination with our development of fast and sensitive capillary liquid chromatography will lead to better, more informative neurochemical investigations.

   a. Jung MC, Shi G, Borland L, Michael AC, Weber SG. Simultaneous determination of biogenic monoamines in rat brain dialysates using capillary high-performance liquid chromatography with photoluminescence following electron transfer. Anal Chem. 2006 Mar 15;78(6):1755-60. PubMed PMID: 16536408; PubMed Central PMCID: PMC1488825.
   b. Jaquins-Gerstl A, Shu Z, Zhang J, Liu Y, Weber SG, Michael AC. Effect of dexamethasone on gliosis, ischemia, and dopamine extraction during microdialysis sampling in brain tissue. Anal Chem. 2011 Oct 15;83(20):7662-7. PubMed PMID: 21859125; PubMed Central PMCID: PMC3193568.
   c. Zhang J, Jaquins-Gerstl A, Nesbitt KM, Rutan SC, Michael AC, Weber SG. In vivo monitoring of serotonin in the striatum of freely moving rats with one minute temporal resolution by online microdialysis-capillary high-performance liquid chromatography at elevated temperature and pressure. Anal Chem. 2013 Oct 15;85(20):9889-97. PubMed PMID: 24020786; PubMed Central PMCID: PMC3899587.
   d. Gu H, Varner EL, Groskreutz SR, Michael AC, Weber SG. In Vivo Monitoring of Dopamine by Microdialysis with 1 min Temporal Resolution Using Online Capillary Liquid Chromatography with Electrochemical Detection. Anal Chem. 2015 Jun 16;87(12):6088-94. PubMed PMID: 25970591; PubMed Central PMCID: PMC4835028.

## D. Additional Information: Research Support and/or Scholastic Performance

### Ongoing Research Support

R01 GM044842-25 WEBER, STEPHEN G. (PI) 05/01/91-04/30/19
Sensitive and Selective Detection of Peptides

Role: PI

R01 MH104386-02 WEBER, STEPHEN G. (PI) 08/15/14-05/31/18
Fast Online Microdialysis/Liquid Chromatography for Monoamine Neurotransmitters
Role: PI

1608757, National Science Foundation WEBER, STEPHEN G (PI) 08/01/16-07/31/19
Expanding the Use of Liquid Chromatography Through Active Temperature Control
This project is funded by the Chemical Measurement and Imaging Program of the Division of Chemistry at the National Science Foundation. Professor Stephen Weber and colleagues at the University of Pittsburgh address limitations of liquid chromatography. The team is improving the ability of liquid chromatography techniques to distinguish one substance from another, as well as improving the ability to measure trace concentrations in a variety of samples. Chromatography is based on the principle of partitioning, the tendency of a substance to prefer an oily substance to water-based solution. The outcomes of this project include obtaining more and better information from samples with lower cost and lower environmental burden than has been previously realized. Collaborations with scientists in the fields of proteomics (for example, health, pharmaceuticals, and biochemistry research) and two-dimensional liquid chromatography (for example, pharmaceuticals, chemical industry, agriculture, and the environment) demonstrate the effectiveness of the project goals. The broader impacts are evidenced in that improvements in chromatographic processes that are useful across many fields and applications. Liquid chromatography is used in virtually every industry, for example, environmental, pharmaceutical, nutritional, forensic, toxicology, polymers, chemicals, and cosmetics. A Girl Scout merit badge project is also being developed by Dr. Weber to explore chromatography methods and its uses. The project uses temperature control of the column to achieve greater solute focusing and to control retention in a predictable way. Retention enthalpies, which control the sensitivity of a particular compound to changes in temperature, are determined for a number of related organic compounds. These data are used to determine molecular fragment enthalpies. The temperature dependence of the retention of novel compounds are then predicted. Software to predict chromatographic behavior in the face of changing column temperature aids in chromatographic method development. The temperature control, when used to aid solute focusing, significantly improves concentration detection limits.
Role: PI

## Completed Research Support

R01 GM066018-12 WEBER, STEPHEN G. (PI) 07/01/03-07/31/16
Single Cell Electroporation
Role: PI

R21 MH083134-02 WEBER, STEPHEN G. (PI) 04/01/08-02/28/11
Serotonin Transporter Kinetics In Vivo by Microdialysis/Capillary UPLC
Role: PI

R41 GM067325-01 WEBER, STEPHEN G. (PI) 02/03/03-02/02/06
Supported Fluorous Lipids for Triphasic Reactions
Role: PI