

# American Chemical Society

## National Awards Nomination Packet

### ACS Award in Chromatography:2018 for: David Hage

Received: 10/06/2016

Cycle Year: 3

*"For his pioneering work and contributions in the development of novel methods for high-performance affinity chromatography, chromatographic immunoassays, and chromatographic-based studies of biological interactions"*

#### **NOMINATOR:**

Xiao Zeng  
Univ of Nebraska  
PO Box 880304  
Lincoln, NE 68588-0304  
UNITED STATES

Email: xzeng1@unl.eduXXX

- Have you discussed this award nomination with the nominee? Yes

#### **NOMINEE:**

David Hage  
Univ of Nebraska  
704 Hamilton Hall  
Lincoln, NE 68588-0304  
UNITED STATES

Tel: (402)472-2744  
Email: dhage1@unl.eduXXX

ACS Current Member: Yes  
Years of Service: 34  
Date of birth: 01/01/1961  
Present Position: Hewett University Professor  
Industry: Academia

#### **SAFETY PROTOCOLS:**

- Does the nominee employ and require good safety protocols and practices in his/her laboratory? Yes

#### **CODE OF CONDUCT:**

- To the best of my knowledge, including past and present circumstances, the nominee:
  1. Employs and requires good safety protocols and practices in his/her laboratory and/or work environment;
  2. Upholds the highest ethical standards in his/her laboratory and/or work environment; and
  3. Otherwise engages in conduct that is consistent with both the objects of the American Chemical Society as stated in Article II Section 1 of its Constitution and the Chemical Professional Code of Conduct.

Code of Conduct Answer: Yes

#### **SUPPORTER 1**

Frantisek Svec  
1 Dow Ct  
Alameda, CA 94501-6407  
UNITED STATES

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Fax: (510)486-7413  
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#### **SUPPORTER 2**

Irving Wainer  
National Institute on Aging/NIH  
251 Bayview Blvd  
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October 4, 2016

Dear ACS Awards Committee:

I am pleased to nominate Dr. David S. Hage, James Hewett University Professor in the Department of Chemistry at the University of Nebraska-Lincoln, for the 2018 ACS Award in Chromatography. Professor Hage is an international leader in high-performance affinity chromatography (HPAC) and in the creation of novel affinity-based separation methods. These methods have advanced the field by making use of biological agents such as antibodies, transport proteins or nucleic acids as the stationary phase, which can be combined with various supports and formats to produce a wide range of selective and novel chromatographic approaches for chemical analysis. For these reasons, Professor Hage is an excellent candidate for the ACS Award in Chromatography.

One important and unique focus of Professor Hage's work has been the creation of new antibody-based HPLC methods, or "chromatographic immunoassays" (e.g., see Ref. [8] in his publication list). For instance, he was one of the first to use on-line immunoextraction in multi-dimensional LC [4], and he pioneered the use of chromatographic theory to describe the behavior and response of HPLC-based immunoassays [1]. He also has developed ultrafast affinity extraction, which can be used to isolate biological targets in the sub-second time domain and to directly measure the biologically-active fractions of drugs and hormones in clinical or pharmaceutical samples [7,14].

Professor Hage also has been a leader in using HPAC for examining biomolecular interactions [9]. For example, he described a new method in *Nature Biotechnology* (2004), which used HPAC for the bi-directional characterization of drug-protein systems involving allosteric interactions [11]. In addition, he recently demonstrated how drug-protein binding studies can be conducted by HPAC on small samples from individuals (e.g., for personalized medicine) and used with mass spectrometry to study both disease-related structural and functional changes in proteins [18]. Furthermore, he has been active in the field of protein-based chiral separations [2,5], and he has been at the forefront in using novel affinity chromatographic methods for high-throughput drug screening and to provide data on both the kinetics and equilibrium constants for drug-protein interactions in solution and at therapeutic/physiological concentrations [6,17,19].

Professor Hage also has been highly active in the creation of new immobilization schemes, supports, and column formats for affinity-related separations. For example, he developed new methods for creating restricted-access affinity supports, preparing affinity microcolumns, and entrapping proteins in HPAC supports [7,13,14]. He has created and optimized various immobilization schemes for agents such as antibodies and transport proteins [3,13], and he has explored the use of isotopic labeling and mass spectrometry to characterize protein immobilization sites on chromatographic supports [15]. In addition, he was one of the first to use HPAC with monolithic supports, which he has utilized in ultrafast immunoextraction,

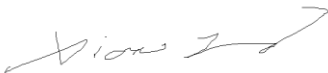
chiral separations, chromatographic immunoassays, and various unique approaches for studying biointeractions [10,12].

The impact of Professor Hage's research is reflected by his authorship of ~275 peer-reviewed papers, book chapters, books and patents, with an *h*-index of 51 (Google Scholar; 41, Web of Science). As demonstrated in his CV, he has earned many awards for his work, including the 2015 EAS Award for Outstanding Achievements in Separation Science. To enable his research program, Professor Hage has secured competitive extramural funding from a variety of sponsors, including over 25 years of continuous support from the NIH as well as support from the NSF, DOD, EPA, and other sources.

Professor Hage has further advanced chromatography by writing and editing the *Handbook of Affinity Chromatography* (2006) [16], which is a leading reference in the field of affinity-based separations. In addition, he is an editor for the *Journal of Chromatography B* and the lead author for an undergraduate textbook on the topic of chemical analysis, including chromatographic methods [20]. Professor Hage also is committed to preparing the next generation of separation chemists, as evidenced through his mentoring and training of numerous graduate and undergraduate students and postdoctoral fellows.

In summary, Professor Hage's contributions in chromatography and affinity-based separations are outstanding and highly novel. His research has made a major impact in chromatography and holds great potential to benefit society, as demonstrated by its use in areas such as clinical chemistry, pharmaceutical chemistry and biomedical research. I believe these contributions make Professor Hage an ideal recipient for the 2018 ACS Award in Chromatography, and I give my strongest support to him for this award.

Sincerely,



Xiao Cheng Zeng

Chancellor's University Professor  
& Chair of Chemistry Awards Committee

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Chemistry Department  
University of Nebraska  
Lincoln, NE 68388-0304 (USA)

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# CURRICULUM VITA

-David S. Hage-

**TITLE:** *Hewett University Professor, Analytical & Bioanalytical Chemistry*

**BIRTHDATE:** April 13, 1961

**CITIZENSHIP:** USA

**CONTACT INFORMATION:** Chemistry Department, 704 Hamilton Hall, University of Nebraska, Lincoln, NE 68588-0304 (USA); Tel: (402) 472-2744; FAX: (402) 472-9402; Email: dhage1@unl.edu; Website: <http://www.chem.unl.edu/faculty/hage.shtml>

## EDUCATIONAL BACKGROUND:

B.S.	Biology & Chemistry	Univ. Wisc., La Crosse, WI	1983
Ph.D.	Analytical Chemistry	Iowa State Univ., Ames, IA	1987
Postdoctoral	Clinical Chemistry	Mayo Clinic, Rochester, MN	1989

## PROFESSIONAL EXPERIENCE:

James Hewett University Professor	Chemistry Dept., Univ. Nebraska	2012-Present
Editor	<i>Journal of Chromatography B</i>	2009-Present
Editorial Board	<i>Bioanalysis</i>	2008-Present
Charles Bessey Professor	Chemistry Dept., Univ. Nebraska	2006-2012
Editorial Board	<i>Journal of Pharmaceut. Biomed. Analysis</i>	2003-2007
Full Professor	Chemistry Dept., Univ. Nebraska	2000-Present
Editorial Board	<i>Journal of Chromatography B</i>	1999-2007
Associate Professor	Chemistry Dept., Univ. Nebraska	1995-2000
Assistant Professor	Chemistry Dept., Univ. Nebraska	1989-1995
Postdoctoral Fellow	Dept. Laboratory Medicine, Mayo Clinic	1987-1989
Temporary Instructor	Chemistry Dept., Iowa State University	1987
Graduate Assistant	Chemistry Dept., Iowa State University	1983-1987

## RESEARCH INTERESTS:

Bioanalytical/Clinical/Environmental Applications of HPLC (especially Affinity & Immunoaffinity Methods)  
Development of Novel Supports and Immobilization Methods for Affinity HPLC & Solid-Phase Assays (e.g., Affinity Monoliths, Affinity Microcolumns, and Entrapment-Based Immobilization Methods)  
Theory and Development of Chromatographic-Based Immunoassays & Flow-Based Sensors  
Theory, Behavior and Applications of Microscale Affinity-Based Chromatographic Systems  
Theory and Characterization of Biological Interactions by Affinity Chromatography (e.g., Drug-Protein Binding)  
Theory and Mechanisms of Affinity Chromatography & Chiral Separations  
Use of Affinity Separations & Mass Spectrometry in Functional Proteomics and Personalized Medicine

## TEACHING EXPERIENCE:

**Undergraduate courses:** Quantitative Analysis (CHEM 116), Instrumental Analysis (CHEM 421/821), Instrumental Analysis Lab (CHEM 423/823)

**Graduate courses:** Graduate Survey of Analytical Chem. (CHEM 824); Advanced Chemical Equilibria (CHEM 825A); Data Handling and Statistics (CHEM 825E); Chromatographic Separations (CHEM 825G); Advanced Separations (CHEM 921/992A); Introduction to Graduate Research (CHEM 898A); Research Update Interview (CHEM 898-002/898B); Original Proposal Oral (CHEM 898-003/898E)

## INVITED SEMINARS, PRESENTATIONS & WORKSHOPS:

*Presentations/Posters at Scientific Meetings, 486; Invited Talks at Academic Institutions or Industry, 76; Workshops, 11*

## HONORS AND AWARDS:

<u>Honor or Award</u>	<u>Granting Institution</u>	<u>Date(s)</u>
Outstanding Achievements in Separation Science	Eastern Analytical Symposium	2015
James Hewett University Professor	Univ. Nebraska-Lincoln	2012-Present
SAS Poster Award	FACSS/SCIX 2012 Meeting	2012
Faculty Fellow, Environmental Science	Univ. of Nebraska, Environ. Sci. Program	2010-Present
Outstanding Res./Creative Achievement Award	Univ. of Nebraska, College Arts & Sciences	2009
Fellow	National Academy of Clinical Biochemistry	2008-Present
Top Cited Article Award (2002-2007)	Journal of Chromatography	2007
Faculty Development Fellowship	University of Nebraska	2007
Charles Bessey Professorship	University of Nebraska	2006-2012
Top Cited Article Award (2001-2006)	Journal of Chromatography	2006
Excellence in Graduate Education Award	University of Nebraska	2005
Faculty Development Fellowship	University of Nebraska	1999
Young Investigator of the Year	Amer. Assoc. Clin. Chem.	1995
Young Investigator Poster Award	Society of Molecular Recognition	1995
George Holmes Summer Fellowship	Univ. Nebraska-Lincoln	1990
ACS Analytical Fellowship	American Chemical Society	1985-1986
Graduate Research Excellence Award	Iowa State University	1987
Alpha Chi Sigma Research Award	Iowa State University	1986
Noble-Hines Fellowship	Iowa State University	1983-1984

## PROFESSIONAL MEMBERSHIPS:

American Chemical Society, American Association for the Advancement of Science, American Association for Clinical Chemistry, Phi Lambda Upsilon, Univ. Nebraska Center for Environmental Toxicology, Univ. Nebraska Center for Biotechnology, Univ. Nebraska Center for Functional Nanohybrid Materials

## CURRENT RESEARCH FUNDING:

- 1.) National Institutes of Health, R01 Research Grant; "Chromatographic Studies of Functional Proteomics"; **D.S. Hage**, P.I.; 7/14-6/18; \$1,075,264 total costs (Years 5-8)
- 2.) National Science Foundation, CMI Research Grant; "Instrumentation Development for Label-free and Rapid 3D-nanostructure Ultrathin Layer Birefringence Imaging Chromatography"; **D.S. Hage**, P.I. (T. Hoffman, Co-P.I.); \$402,483 total costs; 9/13-8/17.
- 3.) United States Department of Agriculture, USDA/NIFA Grant (2016-67017-24431); "Bioactivity of Curcumin and Gut Inflammation", R. Moreau, P.I. (**D.S. Hage**, Co-Investigator); \$480,214 total costs; 10/15-10/19.
- 4.) National Science Foundation, Major Research Instrumentation Program; "MRI – Development of an Ion-Beam-assisted Glancing Angle Deposition Tool for 3D Nanostructure Thin Film Preparation"; E. Schubert, P.I. (**D.S. Hage**, one of five Co-P.I.s); \$441,501 total costs; 10/13-9/17.

## PAST RESEARCH FUNDING:

Total Past Research Funding: ~\$5.41 M, plus \$224 K in equipment donations and \$209 K in student fellowships

**PUBLICATIONS:** ~275 total (more than 260 papers and book chapters; 8 books; 6 patents)

*h*-Index = 51 on Google Scholar, including peer-reviewed papers, books and book chapters; *h*-Index = 41 on Web of Science, focusing on peer-reviewed scientific papers (as of 10/5/2016)

## GRADUATE STUDENTS, UNDERGRADUATE STUDENTS & POSTDOCTORALS:

*Current group:* 10 graduate students, 2 undergraduate students, 2 postdoctoral fellows

*Past graduate students:* 57 total receiving advanced degrees (34 Ph.D.; 23 M.S.)

*Past postdoctoral fellows/visiting scientists advised:* 12      *Past undergraduate students supervised:* 59

## TWENTY REPRESENTATIVE PUBLICATIONS

**-David S. Hage-**

(Out of ~260 papers, 8 books and 7 patents; \*=Author for correspondence; 7,888 citations - 10/04/2016)

(*h*-Index = 51 on Google Scholar, including peer-reviewed papers, books and book chapters;

*h*-Index = 41 on Web of Science, focusing on peer-reviewed scientific papers - 10/05/2016)

- 1) **D.S. Hage\***, D.H. Thomas, M.S. Beck, "Theory of a Sequential Addition Competitive Binding Immunoassay Based on High-Performance Immunoaffinity Chromatography", *Anal. Chem.*, 65 (1993) 1622-1630. (66 citations – Goggle Scholar)

*This research article is an example of how chromatographic theory has been used by D.S. Hage to develop and describe the response of HPLC-based immunoassays.*

- 2) B. Loun, **D.S. Hage\***, "Chiral Separation Mechanisms in Protein-Based HPLC Columns. I. Thermodynamic Studies of *R*- and *S*-Warfarin Binding to Immobilized Human Serum Albumin", *Anal. Chem.*, 66 (1994) 3814-3822. (229 citations)

*This research article illustrates the development of high-performance affinity chromatography as a tool for providing detailed information on drug-protein binding and in examining the retention mechanisms of protein-based chiral separations.*

- 3) P.F. Ruhn, S. Garver, **D.S. Hage\***, "Development of Dihydrazide-Activated Silica Supports for High-Performance Affinity Chromatography", *J. Chromatogr. A*, 669 (1994) 9-19. (103 citations)

*This research article illustrates work in the creation and evaluation of new immobilization schemes for high-performance affinity chromatography, such as applied in this example to antibodies.*

- 4) D.H. Thomas, M. Beck-Westermeyer and **D.S. Hage\***, "Determination of Atrazine in Water using High-Performance Immunoaffinity Chromatography and Reversed-Phase Liquid Chromatography", *Anal. Chem.*, 66 (1994) 3823-3829. (84 citations)

*This research article illustrates work in the development and use of on-line immunoextraction with multi-dimensional LC, as applied here to the measurement of herbicides in environmental samples. A similar scheme has been used to combine on-line immunoextraction with liquid chromatography/mass spectrometry.*

- 5) J. Yang, **D.S. Hage\***, "Role of Binding Capacity versus Binding Strength in the Separation of Chiral Compounds by Protein-Based HPLC Columns", *J. Chromatogr. A*, 725 (1996) 273-285. (94 citations)

*This research article illustrates the use of high-performance affinity chromatography to examine the fundamental factors that affect chiral separations on protein stationary phases.*

- 6) A. Sengupta, **D.S. Hage\***, "Characterization of Minor Site Probes for Human Serum Albumin by High-Performance Affinity Chromatography", *Anal. Chem.*, 71 (1999) 3821-3827. (72 citations)

*This research article illustrates work in the creation of new theoretical and experimental methods for solute- or drug-protein binding studies based on high-performance affinity chromatography.*

- 7) W. Clarke, A.R. Choudhuri, **D.S. Hage\***, "Analysis of Free Drug Fractions by Ultra-fast Immunoaffinity Chromatography", *Anal. Chem.*, 73 (2001) 2157-2164. (50 citations)

*This research article demonstrates the development of an immunoaffinity chromatographic method that can be carried out in the sub-second time domain, as used for analysis of the free (or non-bound) fraction of a drug in a drug/protein mixture.*

- 8) **D.S. Hage\***, M.A. Nelson, "Chromatographic Immunoassays", *Anal. Chem.*, 73 (2001) 198A-205A. (58 citations)  
*This review was the cover article for this issue and describes the various assay formats and applications that have been developed by Prof. Hage and others in the area of chromatographic immunoassays.*
- 9) **D.S. Hage\***, "High-Performance Affinity Chromatography: A Powerful Tool for Studying Serum Protein Binding", *J. Chromatogr. B*, 768 (2002) 3-30. (201 citations)  
*This review discusses the theory and experimental methods based on high-performance affinity chromatography that have been developed by D.S. Hage and others to study drug interactions with proteins in blood. This paper resulted in two top-cited article awards from the Journal of Chromatography A/B for the five year periods spanning from 2001-2006 and 2002-2007.*
- 10) R. Mallik, T. Jiang, **D.S. Hage\***, "High-Performance Affinity Monolith Chromatography: Development & Evaluation of Human Serum Albumin Columns", *Anal. Chem.*, 76 (2004) 7013-7022. (106 citations)  
*This research article illustrates D.S. Hage's work in the development and use of affinity monolith chromatography, as applied here to chiral separations and the analysis of drug-protein binding.*
- 11) J. Chen, **D.S. Hage**, "Quantitative Analysis of Allosteric Drug-Protein Binding by Biointeraction Chromatography", *Nature Biotechnol.* 22 (2004) 1445-1448. (72 citations)  
*This research article describes a new chromatographic approach that was developed for characterizing either competitive or allosteric interactions in biological systems, as applied here to the study of drug-protein interactions. Nature Biotechnology published a special feature article (I.W. Wainer, Nature Biotechnol., 22, 2004, 1376-1377) to highlight this paper by D.S. Hage.*
- 12) T. Jiang, R. Mallik, **D.S. Hage**, "Affinity Monoliths for Ultrafast Immunoextraction", *Anal. Chem.* 77 (2005) 2362-2372. (80 citations)  
*This research article illustrates Prof. Hage's work in affinity monolith chromatography, as used in this example to create small columns containing antibodies for use in ultrafast immunoextraction.*
- 13) **David S. Hage**, Chunling Wa, Hai Xuan, Abby Jackson, "Restricted Access Media and Methods for Making Restricted Access Media", U.S. Patent Application 8,268,570 (Awarded 9/18/12).  
*This patent describes a new approach for the entrapment of soluble proteins within chromatographic supports and the production of restricted access affinity media.*
- 14) William Clarke, John E. Schiel, Annette Moser and **David S. Hage\***, "Analysis of Free Hormone Fractions by an Ultrafast Immunoextraction/Displacement Immunoassay: Studies Using Free Thyroxine as a Model System", *Anal. Chem.*, 77 (2005) 1859-1866. (41 citations)  
*This research article illustrates work by D.S. Hage in the development of novel chromatographic immunoassays, as applied here to a new format for measuring the biologically-active form of a hormone in clinical samples.*
- 15) C. Wa, R.L. Cerny, **D.S. Hage**, "Identification and Quantitative Studies of Protein Immobilization Sites by Stable Isotope Labeling and Mass Spectrometry" *Anal. Chem.* 78 (2006) 7967-7977. (29 citations)  
*This research article illustrates work by D.S. Hage in the use of mass spectrometry to characterize affinity supports or modified proteins (e.g., for comparison with functional data obtained through affinity chromatographic-based binding studies). In this specific example, protein digestion and isotopic labeling (i.e., the  $^{16}\text{O}/^{18}\text{O}$ -labeling method) were used to provide quantitative data on the immobilization sites for a protein that was covalently coupled to a chromatographic support.*

- 16) **D.S. Hage** (Editor), *Handbook of Affinity Chromatography*, 2<sup>nd</sup> Ed., CRC Press, Boca Raton, 2006. (294 citations for overall book and sections by D.S. Hage)
- D.S. Hage edited and led in the creation of this ~1000 page and 30 chapter reference book, which involved efforts by both his group and 20 other research groups from around the world. This text covers both fundamental and practical aspects of affinity chromatography, its various forms and applications, and related affinity-based methods of analysis (e.g., affinity mass spectrometry and affinity CE).*
- 17) J.E. Schiel, C.M. Ohnmacht, **D.S. Hage\***, "Measurement of Drug-Protein Dissociation Rates by High-Performance Affinity Chromatography and Peak Profiling", *Anal. Chem.*, 81 (2009) 4320-4333. (33 citations)
- This research article describes a new approach based on band-broadening measurements to determine the rate constants for a drug- or solute-protein interaction by using high-performance affinity chromatography.*
- 18) J. Anguizola, K.S. Joseph, O.S. Barnaby, R. Matsuda, G. Alvarado, W. Clark, R.L. Cerny, **D.S. Hage\***, "Development of Affinity Microcolumns for Drug-Protein Binding Studies in Personalized Medicine: Interactions of Sulfonylurea Drugs with *in vivo* Glycated Human Serum Albumin", *Anal. Chem.*, 85 (2013) 4453-4460. (23 citations)
- This research article illustrates recent work by Prof. Hage in combining immunoextraction, high-performance affinity chromatography and affinity microcolumns as tools for drug-binding studies and personalized medicine, as used here for the analysis of drug interactions with serum protein samples obtained from individual patients with diabetes.*
- 19) X. Zheng, Z. Li, M. Podariu, **D.S. Hage\***, "Determination of Rate Constants and Equilibrium Constants for Solution-Phase Drug-Protein Interactions by Ultrafast Affinity Extraction", *Anal. Chem.*, 86 (2014) 6454-6460. (15 citations)
- This research article describes a new approach, based on ultrafast affinity chromatography and affinity microcolumns, for determining both the rate constants and equilibrium constants for drug interactions with soluble proteins.*
- 20) **D.S. Hage**, J.D. Carr, *Analytical Chemistry and Quantitative Analysis*, Pearson/Prentice Hall, Upper Saddle River, NJ, 2011.
- D.S. Hage is the lead author for this college textbook, which is designed for use in a sophomore/junior level-course at the undergraduate level in analytical chemistry. This text has already been translated into several languages and discusses many techniques, including the various forms of chromatography, through the use of real world applications.*



October 19, 2014

To whom it may concern:

It is my great privilege to support nomination of Professor David Hage for the 2016 ACS Award in Chromatography. This support is based on my strong belief that his outstanding research significantly advances the affinity chromatography techniques as demonstrated with his numerous publications and addresses an extremely important area of chromatographic separations. Although Dr. Hage worked in a variety of chromatography related areas, I want to focus my support on the field I am quite familiar with, it is the design, preparation, and application of monolithic separation media. Dr. Hage's "signature" achievements in this area relate to novel monolithic stationary phases accommodating affinity and bioaffinity ligands that he pioneered. His deep studies of the immobilization of ligands using supports based on poly(glycidyl methacrylate-co-ethylene dimethacrylate) monoliths enabled "tailoring" the chemistry of the stationary phases to match the needs of specific separations. His early works concerned preparation of monolithic scaffolds in a typical column format followed by immobilization of high molecular weight ligands such as bovine serum albumin. This monolith turned out to be an excellent medium for the enantioseparations of racemic drugs. Here, he also clearly demonstrated the wide variability of chemistries that can be achieved starting from the glycidyl methacrylate-based material. Even more interesting and groundbreaking was Hage's reduction in length of the column from 5 cm long rod to a mere 0.95 mm thin disc that was used in a specially designed holder. He then immobilized different antibodies onto the disc and used the product for affinity immunoextractions. Thanks to the rapid mass transport typical of monoliths, he achieved extraction of an antigen in less than 100 ms! This ultrafast separation had no precedent in the literature and until now has not been reached by other groups. He also tested monolithic silica-based monoliths for immobilization of affinity ligands and for the first time demonstrated their wide applicability in rapid affinity chromatography again using devices differing in length. For example, a 1 mm thin disc was used for the determination of the dissociation rate of drugs from human serum albumin. This approach facilitates pharmacological research and has an enormous impact on development and testing of new drugs. Dr. Hage's influence on affinity chromatography is felt throughout the field as demonstrated by numerous review articles and book chapters citing his pioneering work. Therefore, I strongly support his nomination.

Sincerely,



Frantisek Svec

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Dr. Frantisek Svec  
The Molecular Foundry  
E.O. Lawrence Berkeley National Laboratory  
1 Cyclotron Rd  
Mailstop 67R6110.  
Berkeley, CA 94720-8139, USA

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Biomedical Research Center  
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October 17, 2014

Awards Office  
American Chemical Society  
1155 16<sup>th</sup> Street, NW  
Washington, DC 20036-4801

RE: Professor David S. Hage  
ACS Award in Chromatography

It is my pleasure to support the nomination of Professor David S. Hage for the ACS Award in Chromatography. While David has made many important and seminal contributions to chromatographic science, his key work in the area of high performance affinity chromatography (HPAC). He helped define this field through the reviews and overviews that he has written and by the publication of his book *Handbook of Affinity Chromatography* (2006).

Using the HPAC approach, David demonstrated the application of immobilized protein-based stationary phases to the study of protein binding interactions including the site and stereoselectivity of these interactions. This technique was expanded to include antibodies and other proteins of pharmacological and biochemical interest, such as  $\alpha$ -glycoprotein and high-density lipoproteins. His development of flow-based ultrafast immunoextraction and immunoassay technology (*Analytical Chemistry*, 2011) is a revolutionary advance in bioanalysis and high throughput drug screening. His recent work in this area demonstrates that a combination of immunoextraction and HPAC using affinity microcolumns can be used as tools for personalized medicine (2013) and for the rapid determination of both the rate constants and equilibrium constants for drug interactions with soluble proteins (2014). David also demonstrated the application of HPAC to the determination and characterization of allosteric binding interactions between proteins and ligands, and his 2004 paper in *Nature Biotechnology* was ground breaking in this area as it provided a direct method to determine and measure complex protein binding interactions.

David has also applied HPAC to pharmacological and biological studies, as illustrated by his recent publications on the effect of protein modifications, such as glycosylation, on binding to human serum albumin. This is a vital approach to determination of the effect of subtle changes on the pharmacological activities of a broad array of carried and receptor proteins. David's work provides a relatively simple approach to a complex experimental problem, which sets the stage for other scientists to explore the effects of post-translational modifications.

There is no question that David's work in HPAC has resulted in a paradigm shift in the application of chromatographic techniques in pharmacological and biomedical research. This technology is no longer just used to measure concentrations, but also to probe basic biochemical interactions.

David is a productive and recognized scientist and human being and an excellent candidate for the ACS Award in Chromatography. I support his nomination without reservation.

With best regards,

A handwritten signature in black ink, appearing to read 'I. W. Wainer', with a long horizontal flourish extending to the right.

Irving W. Wainer, PhD, DHC  
Senior Investigator  
Intramural Research Program  
National Institute on Aging/NIH

October 19, 2014

To whom it may concern:

It is my great privilege to support nomination of Professor David Hage for the 2016 ACS Award in Chromatography. This support is based on my strong belief that his outstanding research significantly advances the affinity chromatography techniques as demonstrated with his numerous publications and addresses an extremely important area of chromatographic separations. Although Dr. Hage worked in a variety of chromatography related areas, I want to focus my support on the field I am quite familiar with, it is the design, preparation, and application of monolithic separation media. Dr. Hage's "signature" achievements in this area relate to novel monolithic stationary phases accommodating affinity and bioaffinity ligands that he pioneered. His deep studies of the immobilization of ligands using supports based on poly(glycidyl methacrylate-co-ethylene dimethacrylate) monoliths enabled "tailoring" the chemistry of the stationary phases to match the needs of specific separations. His early works concerned preparation of monolithic scaffolds in a typical column format followed by immobilization of high molecular weight ligands such as bovine serum albumin. This monolith turned out to be an excellent medium for the enantioseparations of racemic drugs. Here, he also clearly demonstrated the wide variability of chemistries that can be achieved starting from the glycidyl methacrylate-based material. Even more interesting and groundbreaking was Hage's reduction in length of the column from 5 cm long rod to a mere 0.95 mm thin disc that was used in a specially designed holder. He then immobilized different antibodies onto the disc and used the product for affinity immunoextractions. Thanks to the rapid mass transport typical of monoliths, he achieved extraction of an antigen in less than 100 ms! This ultrafast separation had no precedent in the literature and until now has not been reached by other groups. He also tested monolithic silica-based monoliths for immobilization of affinity ligands and for the first time demonstrated their wide applicability in rapid affinity chromatography again using devices differing in length. For example, a 1 mm thin disc was used for the determination of the dissociation rate of drugs from human serum albumin. This approach facilitates pharmacological research and has an enormous impact on development and testing of new drugs. Dr. Hage's influence on affinity chromatography is felt throughout the field as demonstrated by numerous review articles and book chapters citing his pioneering work. Therefore, I strongly support his nomination.

Sincerely,



Frantisek Svec

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Dr. Frantisek Svec  
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October 17, 2014

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RE: Professor David S. Hage  
ACS Award in Chromatography

It is my pleasure to support the nomination of Professor David S. Hage for the ACS Award in Chromatography. While David has made many important and seminal contributions to chromatographic science, his key work in the area of high performance affinity chromatography (HPAC). He helped define this field through the reviews and overviews that he has written and by the publication of his book *Handbook of Affinity Chromatography* (2006).

Using the HPAC approach, David demonstrated the application of immobilized protein-based stationary phases to the study of protein binding interactions including the site and stereoselectivity of these interactions. This technique was expanded to include antibodies and other proteins of pharmacological and biochemical interest, such as  $\alpha$ -glycoprotein and high-density lipoproteins. His development of flow-based ultrafast immunoextraction and immunoassay technology (*Analytical Chemistry*, 2011) is a revolutionary advance in bioanalysis and high throughput drug screening. His recent work in this area demonstrates that a combination of immunoextraction and HPAC using affinity microcolumns can be used as tools for personalized medicine (2013) and for the rapid determination of both the rate constants and equilibrium constants for drug interactions with soluble proteins (2014). David also demonstrated the application of HPAC to the determination and characterization of allosteric binding interactions between proteins and ligands, and his 2004 paper in *Nature Biotechnology* was ground breaking in this area as it provided a direct method to determine and measure complex protein binding interactions.

David has also applied HPAC to pharmacological and biological studies, as illustrated by his recent publications on the effect of protein modifications, such as glycosylation, on binding to human serum albumin. This is a vital approach to determination of the effect of subtle changes on the pharmacological activities of a broad array of carried and receptor proteins. David's work provides a relatively simple approach to a complex experimental problem, which sets the stage for other scientists to explore the effects of post-translational modifications.

There is no question that David's work in HPAC has resulted in a paradigm shift in the application of chromatographic techniques in pharmacological and biomedical research. This technology is no longer just used to measure concentrations, but also to probe basic biochemical interactions.

David is a productive and recognized scientist and human being and an excellent candidate for the ACS Award in Chromatography. I support his nomination without reservation.

With best regards,

A handwritten signature in black ink, appearing to read 'I. Wainer', with a long horizontal flourish extending to the right.

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