

BIOGRAPHICAL SKETCH

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NAME: Ashleigh B. Theberge

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

POSITION TITLE: Assistant Professor

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Williams College, Williamstown, MA	B.A.	06/2006	Chemistry
University of Cambridge, Cambridge, UK	Ph.D.	05/2012	Chemistry
University of Wisconsin-Madison, Madison, WI	Postdoctoral	02/2014	Biomedical Engineering, Urology, and Toxicology
University of Wisconsin-Madison, Madison, WI	NIH K Awardee	12/2015	Biomedical Engineering & Urology

A. Personal Statement

My research centers on understanding how chemical signaling underlies fundamental cellular processes such as inflammation as well as diseases such as asthma, kidney disease, prostate disease, and testis dysfunction. I develop methods for the analysis of biomolecular signals in normal and disease states using microfabricated culture platforms to model systems-level complexity (particularly cell-cell, cell-extracellular matrix, and host-microbe interactions); I study the metabolomics of these systems using novel particle-based methods and mass spectrometry. My group also studies the fundamental physics of fluid flow and interfacial chemistry in open biphasic microfluidics and develops methods to advance microfluidic device fabrication (e.g., injection molding for scalable production). To achieve these goals, I draw on my didactic background in chemistry, doctoral training in microfluidics, postdoctoral training in biomedical engineering, and NIH K Award training in translational research. Overall, this approach has been well received: I have built close collaborations with clinicians and biological researchers across numerous universities; I was elected to co-Chair the Gordon Research Conference on Microfluidics in 2021; and my work has received over 1400 citations to date.

Extended Biosketch Components (as indicated in FOA):

Willingness to embrace new approaches and cross fields: After a PhD in chemistry, I sought postdoctoral training in two new areas: biology and engineering. I attended group meetings with biologists and clinicians (Drs. Will Ricke and Wade Bushman, MD, PhD) and attended biological Gordon Conferences and the Society for Basic Urologic Research (SBUR) annual meeting. I worked hard to choose clinically relevant biological problems and to understand the biological mechanisms underlying them. These efforts were recognized by an NIH K Career Development Award, and in my independent career at Washington by an invited plenary presentation at the SBUR (2016, in which I spoke to an audience of clinicians and basic biologists and was likely the only chemist/engineer in the room), a multidisciplinary Kavli Microbiome Ideas Challenge Award (2017, one of three funded proposals worldwide), and a Beckman Young Investigator Award (2018, one of ten funded nationwide).

Track-record of mentoring and independent research: At the end of my postdoctoral fellowship I received an NIH K12 Career Development Award at the University of Wisconsin-Madison. The NIH K12 program is different from the more common K99 program in that K12 grants are typically given to independent faculty, whereas the K99 is awarded to postdocs still engaged in mentored research. During my K Award phase I led and funded a group of five undergraduate students and professional staff, independent of my postdoctoral advisor. The K12 provided

sufficient funds for personnel, equipment, and reagents to conduct independent research, which I have since built upon in my lab in Washington.

I started as an Assistant Professor at the University of Washington in 2016. I currently lead a group of seven PhD students, five undergraduates, and a professional staff member. Undergraduate students regularly co-author papers, and I mentor all students individually and in project teams. I also mentor a Urology resident (Tristan Nicholson, MD, PhD), who joined my group for her Research Year during residency. In addition to Dr. Nicholson, our group collaborates with medical doctors at the University of Washington Kidney Research Institute, UW/Fred Hutchinson Cancer Research Center prostate cancer researchers, the University of Wisconsin-Madison Pulmonary & Critical Care Division, and the University of Chicago North Shore Health System Urology group. We also collaborate with basic science researchers in microbiology and the physics of interfaces and fluid flow. Regular discussions with clinicians and basic scientists in other fields are an important part of our interdisciplinary approach and training for my group's graduate and undergraduate students.

Professional service: My professional service experience includes organizing an invited session focused on analytical methods to study chemical signaling across kingdoms (human, fungal, bacterial, plant) at Pittcon 2017, a national analytical chemistry meeting. I am co-Chair of the Poster Award Committee for microTAS 2017 and 2018, an international microfluidics and microtechnology meeting; this involves inviting and coordinating 39 faculty from around the world as poster judges. I was elected co-Vice Chair (2019) and co-Chair (2021) for the Gordon Research Conference on the Physics and Chemistry of Microfluidics, which I have attended and contributed to regularly since I was a PhD student. At the University of Washington, I serve on advisory boards for a microfabrication and characterization facility (with Mechanical, Chemical, and Bio Engineering faculty) and the UW Medicine Men's Health Steering Committee (with Urology and Medicine faculty). Additionally, I review for numerous journals (Analytical Chemistry, Lab on a Chip, Nature Biotechnology, Nature Communications, etc.) and have served as an *ad hoc* reviewer for several grant agencies.

Relevant recent publications: The following four papers highlight work from my independent career at the University of Washington, which advance the field of open microfluidics for cell signaling studies [a], biphasic droplet systems [c], and metabolomics [d]. Reference [b] characterizes and validates a fabrication method, 'rapid' injection molding, that my group uses to make our microscale platforms readily available to biological and clinical collaborators (creating batches of 500-10,000 devices).

(§ Denotes corresponding author)

- a. S. B. Berry*, T. Zhang*, J. H. Day, X. Su, I. Z. Wilson, E. Berthier, A. B. Theberge§, "Upgrading well plates using open microfluidic patterning." *Lab Chip*, 2017. 17, 4253-4264. No NIH funding; PMCID not applicable.
- b. U. N. Lee, X. Su, D.J. Guckenberger, A. M. Dostie, T. Zhang, E. Berthier, A. B. Theberge§, "Fundamentals of rapid injection molding for microfluidic cell-based assays." *Lab Chip*, 2018. 18, 496-504. PMCID: PMC5790604. (Also available on bioRxiv: <https://doi.org/10.1101/194605>)
- c. J. J. Lee*, J. Berthier*, K. A. Brakke, A. M. Dostie, A. B. Theberge, E. Berthier§, "Droplet behavior in open biphasic microfluidics." *Langmuir*. 2018. 18, 5358-5366. No NIH funding; PMCID not applicable.
- d. U. N. Lee, J. Berthier, J. Yu, E. Berthier, A. B. Theberge§, "Stable biphasic interfaces for open microfluidic platforms." In review at *Anal. Chem.* (bioRxiv preprint DOI: <https://doi.org/10.1101/392258>)

B. Positions and Honors

Positions and Employment

2002, 2003	Medicinal Chemistry Intern, Merck Research Laboratories, Rahway, NY
2002-2004	Microbiology Undergraduate Research Associate, Williams College, Williamstown, MA
2004-2006	Organic Chemistry Undergraduate Research Associate, Williams College, Williamstown, MA
2004	Materials Chemistry Intern, Argonne National Laboratory, Argonne, IL
2005	Summer Researcher, Single Molecule Spectroscopy, Williams College, MA
2006	Analytical Chemistry Intern, Merck Research Laboratories, Westpoint, PA
2006-2011	Ph.D. Candidate, Department of Chemistry, University of Cambridge, Cambridge, UK
2009-2010	Visiting Scientist, Université de Strasbourg, Strasbourg, France

2011-2014 Postdoctoral Fellow, Departments of Biomedical Engineering and Urology, University of Wisconsin-Madison
2014-2015 NIH K Career Development Award Scholar, Departments of Urology and Biomedical Engineering, University of Wisconsin-Madison
2016 Assistant Professor, Department of Chemistry, University of Washington, Seattle, WA
2016 Adjunct Professor, Department of Urology, University of Washington, School of Medicine, Seattle, WA

Honors

Intel Science Talent Search Finalist, 2002
Academy of Applied Science, Junior Science and Humanities Symposium Scholarship, 2002-2005
CRC Press Annual Freshman Chemistry Achievement Award, Williams College, 2003
ACS Polymer Chemistry Award for Achievement in Organic Chemistry, Williams College, 2004
ACS Analytical Division Award, Williams College, 2005
Phi Beta Kappa Inductee (awarded to top 5% of class), 2005
Sigma Xi Inductee, 2006
James F. Skinner Prize in Chemistry, 2006
Graduated *magna cum laude* with honors in Chemistry, 2006
Dr. Herchel Smith Fellowship for graduate study at Cambridge, 2006-2009
MicroTAS Student Travel Grant, 2009
Emmanuel College Travel Grant, 2009 and 2010
University of Cambridge, Department of Chemistry Travel Grant, 2010
Cambridge Philosophical Society Research Studentship, 2010
Cambridge Philosophical Society Travel Grant, 2011
Gordon Research Conference on Physics and Chemistry of Microfluidics Poster Award, 2011
National Research Service Award NIEHS Postdoctoral Traineeship, 2011
MB Research Award for Distinction in Practical *In Vitro* and Alternative Toxicology, 2013
Society of Toxicology *In Vitro* and Alternative Methods Specialty Section Postdoctoral Scholar Award, 2013
Fluigent Travel Fellowship, 2013
Society for Basic Urologic Research Travel Award, 2013
Mayo Clinic Angiogenesis Symposium Travel Award, 2014
NIH K Career Development Award (NIDDK), 2014
Kavli Microbiome Ideas Challenge Grant (one of three awarded worldwide), 2017
Beckman Young Investigator Award (one of ten awarded nationwide), 2018
Elected as co-Vice Chair (2019) and co-Chair (2021) for the Microfluidics Gordon Research Conference (GRC)

Memberships: American Chemical Society (ACS), Society for Basic Urologic Research (SBUR), Society of Toxicology (SOT)

C. Contribution to Science

1. Development of microfluidic cell culture systems

I developed a suite of microfluidic devices to enable cell culture in environments that capture salient features of the *in vivo* microenvironment, such as communication across multiple cell types and interactions with the extracellular matrix (ECM). Utilizing these devices, I have studied complex networks of multicellular communication, such as signaling between endothelial cells, fibroblasts, and microenvironment-conditioned macrophages. Importantly, I study the downstream effects of these multicellular signaling events using functional readouts for blood vessel formation [a], steroid hormone synthesis [b], metabolism [c], and nuclear translocation [d].

- a. A. B. Theberge*, J. Yu*, E. W. K. Young, W. A. Ricke, W. Bushman, D. J. Beebe, "Microfluidic multiculture assay to analyze biomolecular signaling in angiogenesis." *Anal. Chem.* 2015. 87, 3239-3246. PMID: PMC4405103.
- b. C. M. Carney, J. L. Muszynski, L. N. Strotman, S. R. Lewis, R. L. O'Connell, D. J. Beebe, A. B. Theberge§, J. S. Jorgensen§, "Cellular microenvironment dictates androgen production by murine fetal Leydig cells in primary culture." *Biol. Reprod.* 2014. 91, Article 85. PMID: PMC4435030.
(§Co-corresponding authors)

- c. X. Su*, A. B. Theberge*, C. T. January, D. J. Beebe, "Effect of microculture on cell metabolism and biochemistry: Do cells get stressed in microchannels?" *Anal. Chem.* 2013. 85, 1562-1570. PMID: PMC3565071.
- d. T. E. de Groot, K. S. Veserat, E. Berthier, D. J. Beebe§, A. B. Theberge§, "Surface-tension driven open microfluidic platform for hanging droplet culture." *Lab Chip.* 2016. 16, 334-344. PMID: PMC4712910. (§Co-corresponding authors)

2. Integration of microfluidics with chemical analysis

I developed new methods to integrate microfluidic devices with chemical analysis techniques such as liquid chromatography mass-spectrometry (LC-MS) and quantitative reverse transcription polymerase chain reaction (RT-qPCR). I collaborated with Dr. Erwin Berthier to develop a new class of microfluidic devices for metabolomics at the microscale [a, b]. The devices integrate cell culture and small molecule isolation via liquid-liquid extraction for downstream LC-MS analysis of steroid hormones [b], microbial secondary metabolites [a], and global profiling [a]. The system capitalizes on interfacial tension forces and fluidic behavior specific to the microscale to produce stable aqueous-organic interfaces in microchannels. Additionally, I utilized droplet-based microfluidics, a platform in which femto- to nanoliter droplets are generated and manipulated within an immiscible carrier fluid, to interface with analytical chemistry techniques [c,d]. I compartmentalized chemical mixtures into droplet libraries of pure compounds at a range of concentrations by integrating nano-flow ultra performance liquid chromatography (UPLC) with droplet-based microfluidics [c]. Finally, I utilized spontaneous biphasic flow to execute nucleic acid sample preparation on small volumes [d].

- a. L. Barkal,* A. B. Theberge,* C.-J. Guo,* J. Spraker, L. Rappert, J. Berthier, K. A. Brakke, C. C. C. Wang, D. J. Beebe, N. P. Keller, E. Berthier, "Microbial metabolomics in open microscale platforms." *Nature Comm.* 2016, 7, 10610, PMID: PMC4742997.
- b. B. P. Casavant,* E. Berthier,* A. B. Theberge, J. Berthier, S. I., Montanez-Sauri, L. L. Bischel, K. Brakke, C. J. Hedman, W. Bushman, N. P. Keller, D. J. Beebe, "Suspended microfluidics." *Proc. Natl. Acad. Sci. U.S.A.* 2013. 110, 10111-6. PMID: PMC3690848.
- c. A. B. Theberge,* G. Whyte,* W. T. S. Huck, "Generation of picoliter droplets with defined contents and concentration gradients from the separation of chemical mixtures." *Anal. Chem.* 2010, 82, 3449-3453. No NIH funding; PMID not applicable.
- d. P. C. Thomas, L. N. Strotman, A. B. Theberge, E. Berthier, R. O'Connell, J. M. Loeb, S. M. Berry, D. J. Beebe, "Nucleic acid sample preparation using spontaneous biphasic plug flow." *Anal. Chem.* 2013. 85, 8641-8646. PMID: PMC3858960.

3. Synthesis and manipulation of small molecules in microscale platforms

I established new methods for chemical synthesis and manipulation of small molecules using droplet-based microfluidics [a-d]. I utilized droplet-based microfluidics to advance (1) combinatorial chemistry and (2) controlled interfacial reactions. (1) I developed methods to miniaturize and expedite combinatorial chemistry using Ugi-type multicomponent reactions. I integrated a number of droplet-based microfluidic modules to synthesize drug candidates in picoliter droplets, producing millions of droplets of each reaction (>2000 droplets/second) [a]. (2) I made a new type of droplet-nanoreactor in which the interfaces are catalytically active. I synthesized a novel fluorinated ligand for Suzuki cross-coupling reactions and used this to synthesize biphenyl compounds within microfluidic channels [c]. I also studied the mechanisms underlying 'on water' reactions using controlled organic-aqueous interfaces in microfluidic channels [b].

- a. A. B. Theberge, E. Mayot, A. E. Harrak, F. Kleinschmidt, W. T. S. Huck, A. D. Griffiths, "Microfluidic platform for combinatorial synthesis in picolitre droplets." *Lab Chip.* 2012, 12, 1320-1326. No NIH funding; PMID not applicable.
- b. S. Mellouli, L. Bousekkine, A. B. Theberge, W. T. S. Huck, "Investigation of 'on water' conditions using a biphasic fluidic platform." *Angew. Chem., Int. Ed.* 2012. 51, 7981-7984. No NIH funding; PMID not applicable.
- c. A. B. Theberge, G. Whyte, M. Frenzel, L. M. Fidalgo, R. C. R. Wootton, W. T. S. Huck, "Suzuki-Miyaura coupling reactions in aqueous microdroplets with catalytically active fluorinated interfaces." *Chem. Commun.* 2009, 6225-6227. No NIH funding; PMID not applicable.

- d. A. B. Theberge, F. Courtois, Y. Schaerli, M. Fischlechner, C. Abell, F. Hollfelder, W. T. S. Huck, "Microdroplets in microfluidics: An evolving platform for discoveries in chemistry and biology." *Angew. Chem., Int. Ed.* 2010, 49, 5846-5868. No NIH funding; PMCID not applicable.

Complete List of Published Work on PubMed:

<http://www.ncbi.nlm.nih.gov/pubmed/?term=theberge+ab>

- 23 total peer-reviewed publications; 12 publications as first, co-first, or co-senior author
- >1400 citations, h-index=13, determined using Google Scholar on July 1, 2018

D. Research Support

Ongoing research support (overlap: none)

Beckman Young Investigator Award, Arnold and Mabel Beckman Foundation 09/1/2018-08/31/2020
Theberge (PI)

Uncovering chemical signals in complex cellular environments with open microfluidic methods

The major goals of this technology-driven project are to develop a novel 3D printing method to make biomimetic organs and to develop a stackable multiculture platform to integrate biomimetic blood vessels and airway epithelial cells.

Kavli Microbiome Ideas Challenge 04/14/2017-10/14/2018
Theberge (PI), Keller (Co-PI), Berthier (Co-I)

Deciphering multikingdom communication molecules using engineered cellular traps

The major goals are to develop methods for isolating chemical signals exchanged in multikingdom systems (such as fungal-bacterial or fungal-bacterial-human cultures). Funding source: Kavli Foundation in partnership with the American Society for Microbiology, the American Chemical Society, and the American Physical Society.

NIH (NICHD), 1R01HD090660-01A1 08/16/2017-04/30/2022
Jorgensen and Jefcoate (Co-PIs), Theberge (Co-I)

Mediators for dynamic regulation of star transcription: comparing fetal and adult Leydig cells

The goal is to study the role of Star, the known gatekeeper in controlling access of cholesterol to enzymatic activity of the series of steroidogenic enzymes required for conversion to testosterone, in fetal and adult testis cells.

NIH (NCATS), 1UG3TR002158-01 07/25/2017-06/30/2019
Himmelfarb (PI), Theberge (Co-I)

A microphysiological system for kidney disease modeling and drug efficacy testing

The goal is to develop numerous biomimetic platform technologies to study kidney physiology. This is a large scale collaborative grant, and the Theberge group is contributing one of the many technologies proposed.

UW Technology Transfer Office, STEP Grant 04/03/2018-10/03/2018
Theberge (PI), Berthier (co-PI)

Pilot funding to develop CellRail Insert MVP

Pilot funding to develop a manufacturable, commercially viable well plate multiculture device.

Selected completed research support

NIH Multidisciplinary K12 Urologic Research Career Development Program

03/01/2014-12/31/2015

Theberge (NIH K Award Scholar)

The role of stromal paracrine signals in angiogenesis in benign prostatic hyperplasia

The goal was to identify how stromal signals regulate angiogenesis in benign prostatic hyperplasia utilizing a novel microfluidic cell culture platform and a mouse model of benign prostatic hyperplasia/lower urinary tract symptoms (BPH/LUTS).

NIH West Coast Metabolomics Center (WCMC) Pilot Project Grant

06/01/2014-05/30/2015

Berthier (PI), Keller (Co-PI), Theberge (Co-I)

Aspergillus fumigatus oxylipins disrupt host immune eicosanoid signaling

The goal was to study eicosanoid signaling between host and fungus. We developed new microfluidic platforms to enable multikingdom culture and integrated eicosanoid extraction prior to lipidomic analysis via LC-MS.