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EDITORIAL

Biophysical Reviews 'Meet the Editors Series' — a profile of Sabrina Leslie

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Abstract
It is my pleasure to introduce myself to the readers of *Biophysical Reviews* as part of the 'Meet the Editors Series'.

Undergraduate studies: choosing physics (1998–2002, UBC)

I began my undergraduate studies in the Science One Program at the University of British Columbia (UBC) in 1998, in Vancouver, BC, Canada (Fig. 1). This honours programme integrated first-year undergraduate courses in mathematics, physics, chemistry, and biology in a unique way. Four professors and instructors, together with sixty or so keen students, gathered daily in one large room to engage in lectures and tutorials. This inspired a culture of curiosity and questioning assumptions, appreciation of cross-disciplinary approaches and perspectives, and flow of conversations, projects, and friendships.

Following this positive experience and my appreciation of the interactions enabled by smaller honours programmes, I pursued my B.Sc. in Honours Physics and Mathematics. Not only did this programme offer challenging courses with stimulating peer groups, but also it provided the quantitative tools and rigorous foundation necessary to explore a wide array of research. I enjoyed thinking and problem solving, was encouraged by my professors to follow my intuition and talent for physics, and this settled my decision to continue in scientific research rather than music as a profession — although I have continued to play the oboe in amateur orchestras over the years.

Complementing the intense theoretical coursework during my academic year, I used my summers to travel and gain practical experience in research labs. In the Summer of 1999, I travelled to Halifax to work with Dr. Mary Anne White in the Dept. Chemistry and Physics at Dalhousie University, supported by an Undergraduate Summer Research Award (USRA) from the National Science and Engineering of Canada (NSERC). In the Summers of 2000 and 2001, I travelled to Ottawa to work with Drs. David Rayner and Paul Corkum at the Steacie Institute for Molecular Sciences in Ottawa, supported by a Women in Engineering and Science (WES) Award from the National Research Council of Canada (NRC). I made a number of lifelong friendships with fellow scientists. Reflecting back on this time, one of the nice things about becoming a faculty member today has been the pleasure of supporting young researchers — cumulating in over 40 undergraduate projects today, over the past 10 years in my lab.

Graduate studies: choosing imaging (2002–2008, U.C. Berkeley)

I travelled to U.C. Berkeley to pursue my Ph.D. in Physics in 2002. I was not confident about my field of specialization when I arrived because I had interests ranging from the cosmology of our universe to physical chemistry of new nanomaterials and had been advised that the most important decision would be my selection of mentors.

By the end of my first year, I selected to focus my graduate studies on atomic molecular and optical (AMO) physics with Drs. Dan Stamper-Kurn and Birgitta Whaley who were developing high-resolution imaging and theoretical tools to study the spin dynamics of quantum gases at ultra-high vacuum and zero kelvin. I was attracted by investigating what had never been seen before, the precision and control of these experiments — but was aware that what I was working

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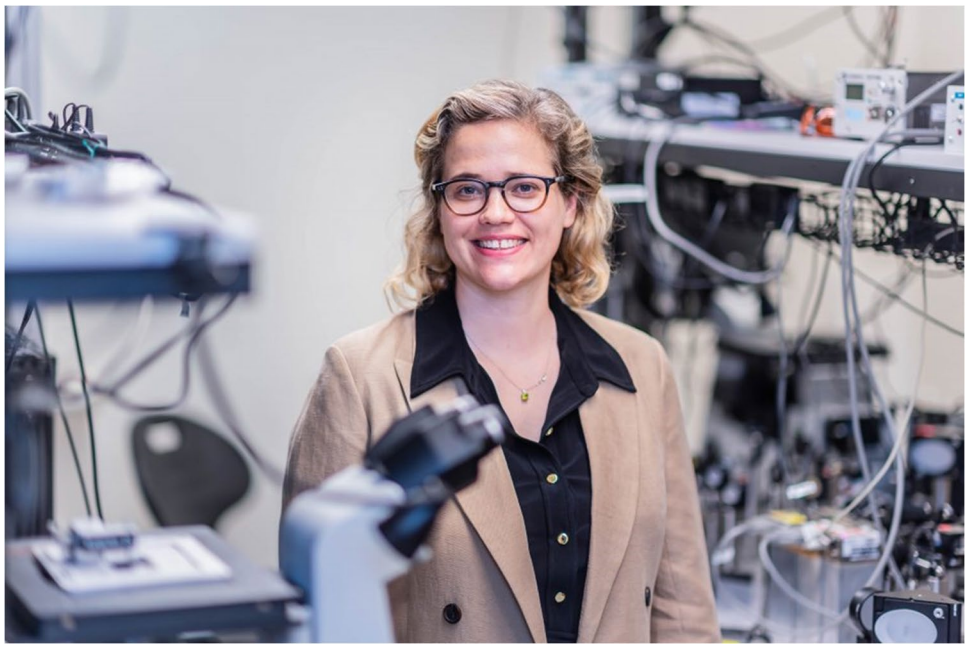


Fig. 1 Dr. Sabrina Leslie at Michael Smith Labs July 2021, credit UBC

on was actually colder than deep space. The experience of designing and building instrumentation which ranged from lasers, to magnetic and optical traps, to high-voltage electronics, balanced with theoretical modelling and quantitative understanding of our imaging results, gave me the strong training as an experimental physicist that I sought. Over time, though, cold atomic physics felt increasingly remote and while I enjoyed the challenge, my curiosities shifted closer to life.

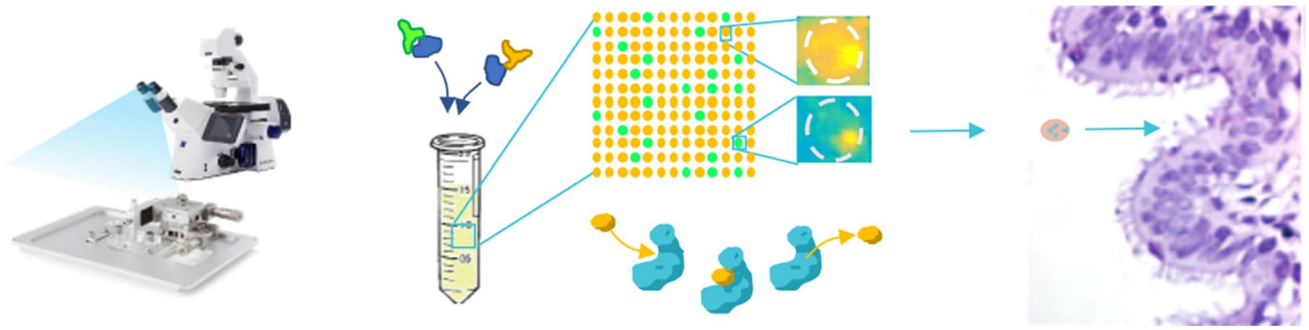
I'd always been fascinated by biology, particularly at the small scale — molecular and cellular biology. *How do life-preserving processes work? How our cells divide and replicate? How does our DNA get repaired? And how does all this happen in such a robust way?* Towards the end of my PhD, I began to explore Biophysics sessions of the American Physics Society (APS) Annual March meeting rather than the AMO sessions, for example. In 2008, I made the decision to accept a Mary Fieser Postdoctoral Fellowship in the Department of Chemistry and Chemical Biology at Harvard University with Adam Cohen and to switch fields. It was there that I got into biophysics, and in everything I did I just kept wanting to take a closer look. That inspiration is the origin of the next steps of my career in biophysics and biotechnology development.

Postdoctoral studies: inspired by biophysics and biotechnology (2009–2011, Harvard)

My postdoctoral work at Harvard University aimed to address widely recognized shortcomings of existing single-molecule techniques due to their requirement for complex surface-tethering chemistry or applied electromagnetic fields that introduced variability and altered the behaviour of the molecules. To overcome these limitations, I developed a novel confinement technique that was able to produce the first high-quality images of individual, freely diffusing and interacting molecules in out-of-equilibrium, cell-like conditions (Leslie et al. 2010; Shaheen et al. 2022). I presented this *Convex Lens-induced Confinement* (CLiC) imaging work at the 2010 Gordon Research Conference on *Single-molecule Approaches to Biology* and was recognized with the top poster prize by Dr. W.E. Moerner and Dr. Julio Fernandez (Leslie et al. 2010). I was very grateful for this appreciation of my work and for my supervisor's encouragement to apply for an Assistant Professor position which popped up at McGill University shortly after this meeting. I am grateful for his advice and support to take my preliminary data and innovations and to build a lab of my own. Without this confidence and push, and the opportunity to attend this GRC meeting in Italy, I may have been hesitant to take that important step and at the right time.

Building my first research lab (2012–2020, McGill Physics)

At McGill, I had the opportunity to found and lead my first independent research team and lab, replete with many lessons and growth experiences (Fig. 2). Over the next ten years, we developed CLiC imaging into a platform and used it for new single-molecule studies of nucleic acids and their interactions (Henkin et al. 2016) and how these interactions are mediated by DNA structure (Scott et al. 2018, 2019);



a) Enabling single-molecule visibility b) Capturing drug-target interactions c) Understanding delivery in cells

Fig. 2 Conceptual schematic of research programme

proteins (Elting et al. 2013); protein droplets and polymer models (Shayegan et al. 2019); DNA polymers and the effects of confinement (Leith et al. 2016) as well as applications to genomics (Berard et al. 2014); as well as cells (Jia et al. 2016) and their response to therapeutics (Thiombane et al. 2019). After promotion to Associate Professor with tenure in 2017, I used my sabbatical to co-found a start-up company *ScopeSys* — which I envision as a vehicle for practical translation of our work and an output of my research which simultaneously enables new career opportunities for Canadian biophysicists.

My group's research focuses on understanding the biophysical mechanisms underlying the function of biomolecules such as DNA, RNA, and proteins, exploiting new tools based on single-molecule microscopy (Ahamed et al. 2016; Arsenault et al. 2015; Berard et al. 2013; Berard and Leslie 2018; Mahshid et al. 2015). I am especially interested in collaborative projects directed towards the development and optimization of genetic medicines and RNA vaccines, and their delivery systems using these insights. Over the past ten years, I have enjoyed publishing 32 peer-reviewed papers and travelling to give 70 invited presentations in different corners of the world. Since 2009, I have also been the lead inventor on 4 patents (2 awarded, 2 pending), which are now exclusively licensed by Harvard and McGill Universities to our biotech start-up, *ScopeSys*, who are supportive partners in our vision for the translation of our work to practice.

Building it back better: towards precision measurements of genetic medicines and vaccines using our single-molecule imaging platform (2021–, UBC Physics and Astronomy, Michael Smith Biotechnology Labs, and School of Biomedical Engineering).

In the midst of the pandemic, I moved my lab to the interdisciplinary *Michael Smith Laboratory* (MSL) at UBC to take up a joint position bridging this biotechnology hub, the Physics and Astronomy Department, and the School of Biomedical Engineering. I am now working at the leading edge of my field, pioneering high-resolution imaging techniques that are supporting drug and vaccine discovery and development. This work is in close touch with collaborators and partners who are concentrated in Vancouver and California. I am excited to have established active collaborations with academic and private sector partners who helped to pioneer the lipid nanoparticle (LNP) delivery systems that were used in the Pfizer and Moderna mRNA vaccines approved during the COVID-19 pandemic such as Dr. Pieter Cullis (UBC Biochemistry). This collaboration led to our recent publication in *ACS Nano* of a novel method for simultaneous measurement of LNP size and RNA loading (Kamanzi et al. 2021). Single-particle imaging of mRNA-LNPs is especially important because the per-particle mRNA-loading can be on the order of unity for standard vaccine formulations, and their structural and dynamic properties are functional but not yet optimized. Through these collaborations and others, my team and I are excited to work at the interface of single-molecule biophysics and therapeutics.

Our vision is to apply our 'bottom-up' microscopy measurements of the biophysics of interactions of biomolecules, in combination with multi-level measurements (in cells and tissues, and the results of clinical trials), to accelerate and advance genetic medicines and vaccines.

Mentorship

Outreach is an energizing dimension of my work. I am passionate about science and sharing my curiosity and dedication to discovery. Public advocacy for science and supporting the next generation of scientists is also important to me. I especially enjoy speaking to and interacting with diverse audiences, for example as the keynote speaker at the 2020 *ScienceFest* event at Dawson College, and as interviewee for Future Tech Podcast's 2018 piece 'I see Molecules' (2018). Looking forward, I'm excited to connect with schools through MSL's well-established outreach platform and UBC PHAS's *Physics Circle*, and to develop a new workshop at

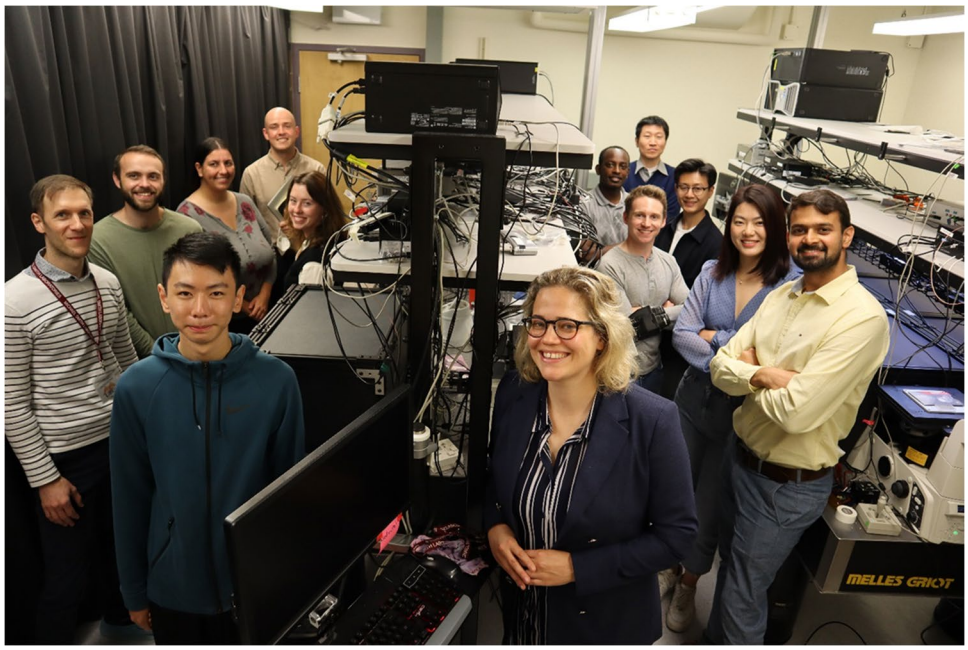


Fig. 3 Photo of the team in one of our new microscope rooms at the Michael Smith Labs in 2021

MSL-UBC based on CLiC imaging to share my passion for single-molecule biophysics and biotechnology. My experience in hosting my pilot CLiC imaging workshop and training more than 50 attendees was exciting (2017) and as travel restrictions drop, I'd love to host another.

I believe in active mentoring and consciously building a positive culture. I value listening, forming teams, and emphasizing communication with an adaptive style. My research requires training in optics, molecular and cell biology, instrumentation, micro/nanodesign and fabrication, and computational, theoretical, and data analysis and I enjoy mentoring all of these (Fig. 3).

Community

Leadership is a growing dimension of my career. In particular, I appreciate the chance to listen and support young women entering as well as considering STEM careers. For example, when I joined the McGill Physics Department, I identified a need for a *Women in Physics* Committee, to engage with and support diversity in science, founded this committee, and energized its growth. At a more junior level, I visited my former high school to accept their *Junior Alumni Achievement Award*, which was an honour but what I valued even more was the opportunity to meet with women students there to offer my encouragement for pursuing careers in science, technology, and entrepreneurship. Curriculum is another vehicle through which I lead change. I lead the design of the *Biophysics Streams—Majors and Honours* for McGill Physics, which is now established and guiding students. Recently I hosted *Biophysics Day* for the four biophysics groups within UBC Physics and Astronomy to share our science and meet one another in person.

I am excited to be working at the interface between biophysics and therapeutics communities, at a time when our single-molecule and single-cell imaging tools may help us guard against future pandemics, and to be doing this work in my home in BC.

Conclusion

In closing, I am grateful to the readers of *Biophysical Review* to share this story of my career. I look forward to, in my role as an Editorial Board Member, inviting, reviewing, and handling articles on your research.

Declarations

Conflict of interest The author declares no competing interests.

References

Ahamed MJ, Mahshid S, Berard D, Michaud F, Sladek R, Reisner W, Leslie S (2016) Continuous confinement fluidics: getting lots of molecules into small spaces with high fidelity. Macromolecules 49(7):2853–2859. https://doi.org/10.1021/acs.macromol.5b02617

Arsenault A, Leith J, Henkin G, McFaul C, Tarling M, Talbot R, Berard D, Michaud F, Scott S, Leslie S (2015) Open-frame system for single-molecule microscopy. Rev Sci Instrum 86:033701. https://doi.org/10.1063/1.4913271

Berard D, Leslie S (2018) Miniaturized flow cell with pneumatically-actuated vertical nanoconfinement for single-molecule imaging

and manipulation. Biomicrofluidics 12(5):054107. https://doi.org/10.1063/1.5052005

Berard D, McFaul C, Leith J, Arsenault A, Michaud F, Leslie S (2013) Precision platform for convex lens-induced confinement microscopy (2013) Precision platform for convex lens-induced confinement microscopy. Rev Sci Instrum 84:103704. https://doi.org/10.1063/1.4822276

Berard D, Michaud F, Mahshid S, Ahamed MJ, McFaul CMJ, Leith JS, Bérubé P, Sladek R, Reisner W, Leslie S (2014) Convex lens-induced nanoscale templating. Biophysics and Computational Biology 111(37):13295–13300. https://doi.org/10.1073/pnas.1321089111

Elting MW, Leslie S, Churchman LS, Korlach J, McFaul C, Leith JS, Levene MJ, Cohen AE, Spudich JA (2013) Single-molecule fluorescence imaging of processive myosin with enhanced background suppression using linear zero-mode waveguides (ZMWs) and convex lens induced confinement (CLIC). Opt Express 21(1):1189–1202. https://doi.org/10.1364/OE.21.001189

Henkin G, Berard D, Stable F, Shayegan M, Leith JS, Leslie S (2016) Manipulating and visualizing molecular interactions in customized nanoscale spaces. Anal Chem 88(22):11100–11107. https://doi.org/10.1021/acs.analchem.6b03149

Jia B, Wee T, Boudreau CG, Berard D, Malik A, Juncker D, Brown CM, Leslie S (2016) Parallelized cytoindentation using convex micropatterned surfaces. Biotechniques 61(2):73–82. https://doi.org/10.2144/000114436

Kamanzi A, Gu Y, Tahvildari R, Friedenberger Z, Zhu X, Berti R, Kurylowicz M, Witzigmann D, Kulkarni J, Leung J, Andersson J, Dahlin A, Hook F, Sutton M, Cullis P, Leslie S (2021) Simultaneous, single-particle measurements of size and loading give insights into the structure of drug-delivery nanoparticles. ACS Nano 15(12):19244–19255. https://doi.org/10.1021/acsnano.1c04862

Leith JS, Kamanzi A, Sean D, Berard D, Guthrie AC, McFaul C, Slater GW, de Haan HW, Leslie S (2016) Free energy of a polymer in slit-like confinement from the Odijk regime to the bulk. Macromolecules 49(23):9266–9271. https://doi.org/10.1021/acs.macromol.6b01805

Leslie S, Fields AP, Cohen AE (2010) Convex lens-induced confinement for imaging single molecules. Anal Chem 82(14):6224–6229. https://doi.org/10.1021/ac101041s

Mahshid S, Ahamed MJ, Berard D, Amin S, Sladek R, Leslie S, Reisner W (2015) Development of a platform for single cell genomics using convex lens-induced confinement. Lab Chip 15:3013–3020. https://doi.org/10.1039/C5LC00492F

Scott S, Xu ZM, Kouzine F, Berard DJ, Shaheen C, Saunders L, Gravel B, Hofkirchner A, Leroux C, Laurin J, Levens D, Benham C, Leslie S (2018) Visualizing structure-mediated interactions in supercoiled DNA molecules. Nucleic Acid Res 46(9):4622–4631. https://doi.org/10.1093/nar/gky266

Scott S, Shaheen C, McGuinness B, Metera K, Kouzine F, Levens D, Benham CJ, Leslie S (2019) Single-molecule visualization of the effects of ionic strength and crowding on structure-mediated interactions in supercoiled DNA molecules. Nucleic Acid Res 47(12):6360–6368. https://doi.org/10.1093/nar/gkz408

Shaheen C, Hastie C, Metera K, Scott S, Zhang Z, Chen S, Gu G, Weber L, Munsky B, Kouzine F, Levens D, Benham C, Leslie S (2022) Non-equilibrium structural dynamics of supercoiled DNA plasmids exhibits asymmetrical relaxation. Nucleic Acids Res 50(5):2754–2764. https://doi.org/10.1093/nar/gkac101

Shayegan M, Tahvildari R, Metera K, Kisley L, Michnick SW, Leslie S (2019) Probing inhomogeneous diffusion in the microenvironments of phase-separated polymers under confinement. J American Chemical Society 141(19):7751–7757. https://doi.org/10.1021/jacs.8b13349

Thiombane NK, Coutin N, Berard D, Tahvildari R, Leslie S, Nislow C (2019) Single-cell analysis for drug development using convex lens-induced confinement imaging. Biotechniques 67(5):210–217. https://doi.org/10.2144/btn-2019-0067