The Faculty of Medicine of Harvard University
Curriculum Vitae

Date Prepared:	May 1, 2023
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Education:

05/2011	B.S.	Mechanical & Aerospace Engineering	Cornell University, Ithaca, NY
09/2017	Ph.D.	Biomedical Engineering (Advisor: M. Selim Ünlü)	Boston University, Boston, MA

Postdoctoral Training:

09/17-07/18	Postdoctoral Fellow	Electrical & Computer Engineering (Advisor: M. Selim Ünlü)	Boston University, Boston, MA
07/18-01/23	Postdoctoral Fellow	Center for Engineering in Medicine & Surgery (Advisor: Mehmet Toner)	Massachusetts General Hospital Boston, MA

Faculty Academic Appointments:

01/2023-	Instructor in Surgery	Harvard Medical School, Boston, MA

Appointments at Hospitals:

01/2023-	Research Staff	Massachusetts General Hospital , Boston, MA

Professional Societies:

2017-	Optical Society of America	Member
2017-	SPIE	Member
2019-	Society for Cryobiology	Member

2023-	Biomedical Engineering Society	Member

Editorial Activities:

- **Ad hoc Reviewer**

Lab on a Chip
Chemical Science
Sensors and Actuators B: Chemical

Report of Funded and Unfunded Projects

Current

2022-2026 Intracellular delivery of DNA-editing proteins by viscoelastic cell stretching
NIH NIAID 1K99AI167063-01A1 – Pathway to Independence Award
PI ($550,000 total direct costs)
This project seeks to develop a very fast microfluidic method of permeabilizing the plasma membrane of mammalian cells ex vivo for transfection of DNA-editing proteins.

Report of Local Teaching and Training

Research Supervisory and Training Responsibilities:

2015-2018	Supervision and training of junior graduate students (about 2 per year)	Boston University Daily training & supervision for about 16 weeks.
2016-2018	Supervision of undergraduate Senior Research Project teams and individual undergraduate research projects (2 per year)	Boston University Daily training and supervision, weekly meetings 2 hours per week per team/student
2020-	Training and certification for flow cytometry and high-speed microscopy (About 5 fellows per year)	MGH 5-10 hours per fellow per year
2021-	Training for microfluidics fabrication (About 2 fellows per year)	MGH 10-20 hours per fellow per year
2022-	Mentor, CEMS Summer Academy (1 undergraduate/high school student yearly)	MGH 16 hours per week for about 12 weeks

Other Mentored Trainees and Faculty:

2021- Carlie Rein, laboratory technician, MGH
Mentoring role: Supervisor. *Accomplishments*: First-author manuscript in preparation. Applying to PhD programs in Biomedical Engineering for Fall 2023 start dates.

Local Invited Presentations:

☒ *No presentations below were sponsored by 3rd parties/outside entities*

☐ *Those presentations below sponsored by outside entities are so noted and the sponsor(s) is (are) identified.*

2018 "Single-molecule microarrays with interferometric detection of plasmonic nanorod labels"

Boston University, Boston, MA (BU Postdoctoral Association)

2018 "Digital DNA microarrays: Beating fluorescence with plasmonics"
Boston University, Boston, MA (BU OSA/SPIE Student-organized conference)

Report of Regional, National and International Invited Teaching and Presentations

☒ *No presentations below were sponsored by 3rd parties/outside entities*

☐ *Those presentations below sponsored by outside entities are so noted and the sponsor(s) is (are) identified.*

Regional

2018 "Interferometric biosensing for sensitive molecular diagnostics"
MIT Lincoln Laboratory, Lexington, MA (IEEE Interferometry Workshop)

International

2020 "Programmable uptake and release of cryoprotective agents from semipermeable hydrogel beads.
Society of Cryobiology Annual Meeting, 22 Jul 2020 (Virtual)

Report of Technological and Other Scientific Innovations

Method and system for enhanced single particle reflectance imaging (2015-2018)	As a graduate student in the Ünlü lab, I invented a technology for rapid optical detection of individual nanoparticles on a structured thin film substrate. This strategy enables multiplexed single molecule biosensing as well as single virus detection for ultrasensitive viral diagnostics. US Patent App 2019/0162647 A1
Disposable fluidic cartridge for interferometric reflectance imaging sensor (2015-2018)	As a graduate student in the Ünlü lab, I invented a disposable microfluidic biosensor chip for binding affinity studies, based on semiconductor materials and laminate adhesives. US Patent App 2021/0069706 A1
Systems and methods for imaging microwell plate samples (2016-2018)	As a graduate student in the Ünlü lab, I invented a scheme for imaging semiconductor biosensor chips in a microwell plate format, for high throughput and multiplexed screening of biomolecule affinity. US Patent 10,585,042 B2
Dynamic tracking of captured targets for enhanced digital biosensing (2016-2018)	As a graduate student in the Ünlü lab, I invented a strategy for ultrasensitive single-molecule molecular diagnostics, which improves upon existing single-molecule detection schemes by also dynamically monitoring the duration of individual molecular binding events. US Patent App 2019/0339268 A1

Enzymatic assay to measure long-term adherence to pre exposure prophylaxis and antiretroviral therapy (2018-2021)	As a postdoc in the Toner lab and together with collaborators at the University of Washington, I invented a biochemical assay for antiretroviral drug activity based on targeted inhibition of viral reverse transcriptase. This assay is being developed further for near-patient testing of antiretroviral medication adherence to improve HIV treatment and prevention. US Patent App 2022/0307066 A1
Viscoelastic mechanoporation systems and methods of use thereof (2020-)	As a postdoc in the Toner lab, I invented a transfection technology which enables the temporary mechanical disruption of the plasma membrane (so-called mechanoporation) of individual cells *ex vivo* by using microfluidic control of viscoelastic flow forces on the cell membrane. US Patent App 2022/012098

Report of Scholarship

Peer-Reviewed Scholarship in print or other media:

Research Investigations

Google Scholar profile: https://scholar.google.com/citations?user=2QAce2gAAAAJ&hl=en
ORCID: 0000-0002-0327-5638
(1–17)

1. Sevenler D, Buckley MR, Kim G, van der Meulen MCH, Cohen I, Bonassar LJ. Spatial periodicity in growth plate shear mechanical properties is disrupted by vitamin D deficiency. J Biomech. 2013 Jun 21;46(10):1597–603.

2. Sevenler D, Ünlü MS. Numerical techniques for high-throughput reflectance interference biosensing. J Mod Opt. 2015 Dec 17;0(0):1–6.

3. Scherr SM, Daaboul GG, Trueb J, Sevenler D, Fawcett H, Goldberg B, et al. Real-Time Capture and Visualization of Individual Viruses in Complex Media. ACS Nano. 2016 Feb 23;10(2):2827–33.

4. Ekiz-Kanik F, Sevenler DD, Ünlü NL, Chiari M, Ünlü MS. Surface chemistry and morphology in single particle optical imaging. Nanophotonics. 2017;6(4):713–30.

5. Sevenler D, Avci O, Ünlü MS. Quantitative interferometric reflectance imaging for the detection and measurement of biological nanoparticles. Biomed Opt Express. 2017 Jun 1;8(6):2976–89.

6. Trueb J, Avci O, Sevenler D, Connor JH, Ünlü MS. Robust Visualization and Discrimination of Nanoparticles by Interferometric Imaging. IEEE J Sel Top Quantum Electron. 2017 Mar;23(2):1–10.

7. Sevenler D, Daaboul GG, Ekiz Kanik F, Ünlü NL, Ünlü MS. Digital Microarrays: Single-Molecule Readout with Interferometric Detection of Plasmonic Nanorod Labels. ACS Nano. 2018 Jun 26;12(6):5880–7.

8. Sevenler D, Trueb J, Ünlü MS. Beating the reaction limits of biosensor sensitivity with dynamic tracking of single binding events. Proc Natl Acad Sci. 2019 Feb 18;201815329.

9. Drain P, Bardon A, Simoni J, Cressey T, Anderson P, Sevenler D, et al. Point-of-care and Near Real-time Testing for Antiretroviral Adherence Monitoring to HIV Treatment and Prevention. Curr HIV/AIDS Rep. 2020 Oct 1;17(5):487–98.

10. Jaskiewicz JJ, Sevenler D, Swei AA, Widmer G, Toner M, Tzipori S, et al. Cryopreservation of infectious Cryptosporidium parvum oocysts achieved through vitrification using high aspect ratio specimen containers. Sci Rep. 2020 Jul 16;10(1):11711.

11. Olanrewaju AO, Sullivan BP, Zhang J, Bender AT, Sevenler D, Lo TJ, et al. An enzymatic assay for rapid measurement of antiretroviral drug levels. ACS Sens [Internet]. 2020 Apr 6 [cited 2020 Apr 9]; Available from: https://doi.org/10.1021/acssensors.9b02198

12. Sevenler D, Bardon A, Fernandez Suarez M, Marshall L, Toner M, Drain P, et al. Immunoassay for HIV Drug Metabolites Tenofovir and Tenofovir Diphosphate. ACS Infect Dis. 2020 Jul 10;6(7):1635–42.

13. Olanrewaju AO, Sullivan B, Gim A, Sevenler D, Bender A, Drain P, et al. REverSe TRanscrIptase Chain Termination (RESTRICT) for Selective Measurement of Nucleotide Analogs Used in HIV Care and Prevention. 2021 Sep 20 [cited 2021 Oct 20]; Available from: https://chemrxiv.org/engage/chemrxiv/article-details/614789914853d27d08aa7647

14. Sevenler D, Bean H, Toner M, Sandlin RD. Slow-delivery and distributed exchange of cryoprotective agents with hydrogel beads. Cryobiology [Internet]. 2021 Sep 22 [cited 2021 Oct 4]; Available from: https://www.sciencedirect.com/science/article/pii/S0011224021001528

15. Sevenler D, Niu X, Dossantos S, Toner M, Cressey TR, Sandlin RD, et al. Point-of-care semi-quantitative test for adherence to tenofovir alafenamide or tenofovir disoproxil fumarate. J Antimicrob Chemother. 2022 Apr 1;77(4):996–9.

16. Ekiz Kanik F, Celebi I, Sevenler D, Tanriverdi K, Lortlar Ünlü N, Freedman JE, et al. Attomolar sensitivity microRNA detection using real-time digital microarrays. Sci Rep. 2022 Sep 28;12(1):16220.

17. Rein C, Toner M, Sevenler D. Rapid prototyping for high-pressure microfluidics. Sci Rep. 2023 Jan 22;13(1):1–9.

Non-peer reviewed scholarship in print or other media:

Reviews, chapters, and editorials

1. **Sevenler D**, Ünlü NL, Ünlü MS. Nanoparticle Biosensing with Interferometric Reflectance Imaging. In: Nanobiosensors and Nanobioanalyses. Springer, Tokyo; 2015. p. 81–95.

Other non-peer reviewed scholarship

1. Ahn S, **Sevenler D**, Monroe M, editors. Biosensors: Innovations in nanobiosensing and biophotonics at Boston University. Boston University, Boston MA; 2013.

Thesis:

Sevenler D. Development of a Digital Microarray with Interferometric Reflectance Imaging [Ph.D.]. Boston University.

Abstracts, Poster Presentations, and Exhibits Presented at Professional Meetings:

1. **Sevenler D**, Daaboul GG, Ekiz Kanik F, Trueb J, Ünlü MS. Digital DNA microarrays: high-throughput genomic & transcriptomic analysis with single-molecule readout. Gordon Research Conference on Liquid Biopsy, 2018 Aug 5.
    - Outstanding Presentation Award

Narrative Report

My PhD studies in biomedical engineering were focused on ultrasensitive molecular diagnostics and biosensing—technologies to 'read' the biological information in a sample at the molecular scale. As a postdoc in the laboratory of Mehmet Toner, I developed technologies to more precisely deliver or 'write' new molecular information into human cells for therapeutic applications. My research program in biomedical engineering is focused on developing nanoscale devices, microfluidics, biomaterials, photonics, and automation systems to address emerging translational biomedical problems in molecular diagnostics, therapeutics, and disease prevention. My vision is to continue to leverage emerging tools and technologies from the physical sciences and engineering to accelerate our ability to both read and write the molecular information of life, to better understand and prevent disease.

My graduate research at Boston University was focused on using nanophotonic biosensors to push the limits of ultrasensitive molecular diagnostics and single molecule detection. The most significant contribution of my graduate work was the invention of the first so-called 'Dynamic' single molecule detection scheme, which showed that the final remaining performance bottleneck for existing 'endpoint' single molecule detection schemes, such as digital droplet PCR or single-molecule immunoassays, could be surpassed. In brief, the Dynamic detection scheme involves measuring the duration of every molecular binding event between individual analyte molecules and molecular probes (e.g. antibodies). This work was a valuable and lasting contribution because it showed how endpoint molecule assay technologies remain fundamentally limited by the affinity and specificity of the nonideal molecular probes that exist in practice and showed that this 'reaction limit' for nonideal probes could be surpassed, both in theory and in practice. This was a technically demanding measurement that was enabled by my prior work developing a record-breaking imaging system which could detect individual 60 nm plasmonic gold nanorods across the entire field of view of a 10x objective. For the sake of comparison, this is like detecting and tracking individual 2 meter-tall people within a single photograph of a region 21 km by 29 km (e.g. an area about five times the size of Boston, or about half the size of Los Angeles).

During the start of my postdoctoral studies with Professor Mehmet Toner at MGH, I worked with a multidisciplinary team including bioengineers, clinicians, and global health experts to develop a rapid point-of-care test for a biomarker of HIV medication adherence. Over the course of two years, I led the assay development program from the antibody screening stage to immunoassay development in microwell plates, transferring the assay to a lateral flow strip format, and validating the assay with hundreds of patient samples. Along the way, I also invented a new synthetic biology approach to assaying the active form of antiretroviral medications in blood samples based on *in vitro* inhibition of reverse transcriptase.

My current long-term research goal is to accelerate the development, manufacturing, and safety of cell and gene therapies. Towards this goal, I am currently developing a very fast microfluidic transfection method for precision gene editing of mammalian cells *ex vivo*. A major thrust of my current research is to investigate new microfluidic devices and materials to improve the safety, accuracy, and efficiency of methods for delivering genetic material and gene editing systems into mammalian cells.