BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Alon, Shahar

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

POSITION TITLE: Assistant professor / Senior lecturer Faculty of Engineering, the Gonda Brain Research Center, the Institute for Nanotechnology and Advanced Materials, Bar-Ilan University

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
Bar-Ilan University, Israel	B.Sc.	10/00	Physics
Tel-Aviv University, Israel	M.Sc.	10/08	Neurobiology, Bioinformatics
Tel-Aviv University, Israel	Ph.D.	10/14	Neuroscience, Genomics
Massachusetts Institute of Technology	Postdoc	10/19	Bioengineering, Neuroengineering

A. Personal Statement

I am a senior lecturer (equivalent to assistant professor) and lead the spatial genomics lab at the faculty of engineering, the brain research center, and the nanotechnology institute at Bar-Ilan University. I am a new PI, with a lab established 2 years ago after completing a post-doctoral training at MIT. I am a physicist and neuroscientist in training, and skilled at several domains of engineering, ranging from data science to genomics to bioengineering to optics. I am passionate about the importance of RNA in tissues, in health and disease. Over the last 10 years I have created new technologies and analysis methods to measure RNA. In my lab at Bar-Ilan university I study the 3D location of RNA molecules inside cells and tissues. This aspect is known to be important for the function of cells and tissues but was impossible to investigate due to lack of appropriate technology. Therefore, I co-led the development of a new technology to sequence RNA inside intact cells and tissues, while preserving the exact 3D location of the RNA molecules. I lead a multidisciplinary team with background in engineering, physics, computer science and neuroscience. My team generates experimental data and deciphers the resulting data using statistical and machine learning tools. I collaborate with many labs around the world to bring new technologies and analysis tools to bear upon the study of complex tissues, in health and disease. Currently my lab mainly studies neurodegenerative diseases (Alzheimer's and retinal diseases) and immune-tumor interactions using cancer biopsies from patients.

Ongoing projects that I would like to highlight include:

THE ISRAEL SCIENCE FOUNDATION (ISF) 2958/21 & 3363/21 role: PI 10/1/2021-10/1/2026 Mapping subcellular localization of RNA molecules within neuronal tissues

ISRAEL CANCER ASSOCIATION (ICA) 20220069 role: PI 01/01/2022 - 31/12/2022 Characterizing immune-tumor interactions using expansion sequencing

ISRAEL MINISTRY OF SCIENCE 2180 role: co-PI 01/12/2021 - 30/11/2022 Implantable bridges for neuronal recovery by integrating artificial elements and living cells

BRIGHTFOCUS FOUNDATION 929965 role: co-PI 1/7/2022 - 1/7/2025 Towards nanoscale blueprints of early molecular, synaptic and physiological changes in Alzheimer's Disease

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2019 (Oct)- Senior Lecturer (eq. to Assistant Professor), Faculty of Engineering, the Gonda Brain Research Center, and the Institute for Nanotechnology, Bar-Ilan University, Israel

2019-20 Research Affiliated, MIT Media Lab, Cambridge, MA

2016-19 Howard Hughes Medical Institute Fellow, McGovern Institute, MIT, Cambridge, MA

2014-2016 Rothschild Fellow, Media Lab and McGovern Institute for Brain Research, MIT, Cambridge, MA 2012 Visiting Scientist, Harvard Medical School, Department of Genetics, Boston, MA

2009-2014 The Interdisciplinary Doctoral Program in Neuroscience for Outstanding Students at Tel Aviv

University, Israel

2000-2005 Computational Physicist, Nuclear Research Center - Negev, Department of Physics, Israel

Honors (selected)

2016-2019 Life Science Research Foundation Fellowship (~25 Ph.D. from all the Life Sciences fields receive this scholarship in U.S. each year from more than 1000 applicants)

2014-2016 Rothschild Postdoctoral Fellowship (*12 Ph.D. receive this scholarship in Israel each year*) 2011-2014 Clore Foundation Fellowship for Outstanding Scholars (*10 Ph.D. students from all STEM fields receive this scholarship in Israel each year*)

C. Contributions to Science

1. I created technologies and data analysis tools to allow super-resolution in situ sequencing. The 3D location of RNA molecules inside cells and tissues is known to be important, especially in the nervous system, but was impossible to investigate due to lack of appropriate technology. I therefore built a new technology and data analysis pipeline to sequence RNA inside intact cells and tissues, while preserving the exact 3D location of the RNA molecules. The technology I co-led is currently the only bona fide super-resolution method in the emerging field of spatially resolved transcriptomics.

- a. Alon S*, Goodwin DR*, Sinha A*, Wassie AT*, Chen F*, Daugharthy ER, Bando Y, Kajita A, Xue AG, Marrett K, Prior R, Cui Y, Payne AC, Yao C-C, Suk H-J, Wang R, Yu C-C, Tillberg P, Reginato P, Pak N, Liu S, Punthambaker S, Iyer EPR, Kohman RE, Miller JA, Lein ES, Lako A, Cullen N, Rodig S, Helvie K, Abravanel DL, Wagle N, Johnson BE, Klughammer J, Slyper M, Waldman J, Jané-Valbuena J, Rosen RO, Regev A, IMAXT Consortium, Church GM, Marblestone AH, Boyden ES. Expansion Sequencing: Spatially Precise In Situ Transcriptomics in Intact Biological Systems. Science 371: eaax2656. (2021) *Equal contribution. Covered by: Nature Methods, NIH Director's Blog, GenomeWeb, BusinessWire, GEN, The Jerusalem Post, Phys.org, MIT news, RNA-Seq and more.
- b. Wassie A, Chen F, Boyden ES, Alon S. Nanoscale Imaging of Proteins and Nucleic Acids via Expansion Microscopy. **US Patent** No. 10364457 (2019).
- c. Alon S, Boyden ES, Chen F, Church GM, Daugharthy E, Marblestone A, Tillberg PW. *In situ* nucleic acid sequencing of expanded biological samples. **US patent** No. 10059990 (2018).

d. Chen F, Wassie AT, Cote AJ, Sinha A, Alon S, Asano S, Daugharthy ER, Chang JB, Marblestone A, Church GM, Raj A, Boyden ES. Nanoscale Imaging of RNA with Expansion Microscopy. Nature Methods, 13:679-684 (2016).

2. I built computational tools to detect sequence variations in RNA without a reference genome, which enabled the detection of RNA editing events that dramatically change the proteome in cephalopods nervous system. This is considered the best-known example of how RNA editing can create complexity in the nervous system and might explain the sophisticated behavior of squid and octopus.

- a. Liscovitch-Brauer N, Alon S, Porath HT, Elstein B, Unger R, Ziv T, Admon A, Levanon EY, Rosenthal JJC, Eisenberg E. Trade-off between Transcriptome Plasticity and Genome Evolution in Cephalopods.
 Cell, 169:191–202. (2017) <u>Covered by: Cell Journal Cover, Nature, Nature Reviews Genetics, New York Times, Washington Post, Daily Mail, Scientific American, WIRED, The Atlantic and more.</u>
- b. Alon S, Garrett SC, Levanon EY, Olson S, Graveley BR, Rosenthal JJC, Eisenberg E. The majority of transcripts in the squid nervous system are extensively recoded by A-to-I RNA editing. eLife, 4, e05198. (2015) <u>Covered by: Science Magazine Editor's Choice, NHGRI, NSF, Phys.org and more</u>.

3. Using statistical methods, I constructed approaches to detect functionally important sequence variations in microRNA in the human brain, as well as approaches for accurate and multiplexed measurement of microRNA in general. The detected microRNA variations in the human brain are considered the gold standard in the field, and were shown to be important in glioblastoma. The multiplexed measurement protocols that we established were adopted by the community, as well as by commercial companies.

- a. Tomaselli S, Galeano F, Alon S, Raho S, Galardi S, Polito VA, Presutti C, Vincenti S, Eisenberg E, Locatelli F, Gallo A. Modulation of microRNA editing, expression and processing through ADAR2 deaminase in glioblastoma. Genome Biology, 16:5 (2015).
- b. Alon S, Erew M, Eisenberg E. DREAM: a webserver for the identification of editing sites in mature miRNAs using deep sequencing data. **Bioinformatics**, 31:2568-2570 (2015).
- c. Alon S*, Mor E*, Vigneault F*, Gallo A, Locatelli F, Church GM, Shomron N, Eisenberg E. Systematic identification of edited microRNAs in the human brain. **Genome Research**, 22:1533-1540 (2012). *Equal contribution.
- d. Alon S*, Vigneault F*, Eminaga S, Christodoulou D, Seidman J, Church GM, Eisenberg E. Bar-coding bias in high-throughput multiplex sequencing of miRNA. Genome Research, 21:1506–1511 (2011). *Equal contribution.

4. I established computational tools that enable accurate identification of genome-wide rhythms in RNA expression. This allowed detection of daily rhythms of expression in the fish brain, as well as in one of the most ancient animal forms - the coral. The findings point to the evolutionary conserved physiological importance of daily rhythms in gene expression.

- a. Kaniewska P*, **Alon S***, Karako-Lampert S, Hoegh-Guldberg O, Levy O. Signaling cascades and the importance of moonlight in coral broadcast mass spawning. **eLife**, 10.7554/eLife.09991 (2015). <u>Covered by eLife Insight: 'Sex under the moon'</u>. *Equal contribution.
- b. Ben-Moshe Z*, Alon S*, Mracek P, Faigenbloom L, Tovin A, Vatine G, Eisenberg E, Foulkes SN, Gothilf Y (2014). The light-induced transcriptome of the zebrafish pineal gland reveals complex regulation of the circadian clockwork by light. Nucleic Acids Research, doi: 10.1093/nar/gkt1359 (2014). *Equal contribution.
- c. Tovin A*, **Alon S***, Ben-Moshe Z, Mracek P, Vatine G, Foulkes N, Jacob-Hirsch J, Rechavi G, Coon SL, Klein DC, Eisenberg E, Gothilf Y. Systematic identification of rhythmic genes reveals camk1gb as a new element in the circadian clockwork. **PLOS Genetics**, 8(12):e1003116 (2012). *Equal contribution.
- d. Levy O*, Kaniewska P*, Alon S, Eisenberg E, Karako-Lampert S, Bay LK, Reef R, Rodriguez-Lanetty M, Miller DJ, Hoegh-Guldberg O. Complex diel cycles of gene expression in the coral-algal symbiosis. Science, 331:175 (2011). *Equal contribution.

Complete List of Published Work in my Google Scholar page: https://scholar.google.com/citations?user=BJ02tcMAAAJ&hl=en