

## CURRICULUM VITAE

### Alexander Friedman, PhD

#### *Research Interest:*

My goal is to find principles of brain computation that can mechanistically relate neuronal circuit dynamics to cognitive function. By iterating between computation and experimentation, I can guide experiments with computational modeling and analyze experimental results in new ways. I have built novel computational approaches to parse multidimensional big data obtained from cutting-edge circuit recording techniques in order to facilitate understanding of the mechanisms behind neuropsychiatric and neurological disorders. My current work combines three directions: first, I have created mathematical and computational approaches to analyze complex biological data sets; second, I have designed and implemented rodent models of psychiatric disorders; and third, I have recorded and manipulated neural circuits using methods including high-density electrophysiology, multicolor photometry, cell calcium imaging using miniaturized scopes, optogenetic targeting, and chemogenetic manipulation. In my future work, I plan to use my combined data science and biological approaches to develop a set of principles that outline neuronal behavior. Combining these principles with biologically-informed manipulations, I will design treatments for various psychiatric disorders that coincide with dysfunction of neuronal circuits.

#### *Personal Information:*

Date of Birth: July 5, 1983

Place of Birth: Minsk, Belarus

Citizenship: USA, Israel

#### *Education/Training:*

**2000-2004:** B.A. in Computer Science (Magna Cum Laude), Department of Computer Science, Jerusalem College of Technology, Israel. Thesis Advisors: Yzi Sandler and Yaakov Friedman.

**2005-2010:** Ph.D. in Brain Physiology (Summa Cum Laude). Brain Research Center, Bar-Ilan University, Israel. Advisors: Gal Yadid and Moshe Abeles.

**2010-2015:** Post-doctoral training. Department of Brain and Cognitive Sciences and McGovern Institute for Brain Research, MIT, USA. Advisor: Ann M Graybiel.

#### *Positions:*

**2005-2010:** Teaching Assistant, Department of Life Science, Bar-Ilan University, Israel.

**2009-2010:** Lecturer, Dept. of Bioinformatics and Biotechnology, JCT, Israel. Courses: General Chemistry.

**2015-2020:** Research Scientist, McGovern Institute for Brain Research, MIT, USA.

**2020-Present** Assistant Professor, University of Texas at El Paso, Department of Biological Sciences.

#### *Honors:*

2003-2004: JCT Rector's stipend for outstanding research students.

2006-2010: BIU President's stipend for outstanding Ph.D. students.

2009: NIDA mini-conference, poster prize

2009: The Institute for Advanced Studies at The Hebrew University of Jerusalem, poster prize

2018: Best publication of MIT in 2017.

#### *Peer-Reviewed Primary Publications:*

1) **Friedman, A.**, Dremencov, E., Crown, H., Levy, D., Mintz, M., Overstreet, D.H., and Yadid, G. (2005). Variability of the mesolimbic neuronal activity in a rat model of depression. *Neuroreport* 16, 513-516.

- 2) **Friedman, A., Deri, I., Friedman, Y., Dremencov, E., Goutkin, S., Kravchinsky, E., Mintz, M., Levi, D., Overstreet, D.H., and Yadid, G. (2007).** Decoding of dopaminergic mesolimbic activity and depressive behavior. *J Mol Neurosci* 32, 72-79.
- 3) **Friedman, A., Friedman, Y., Dremencov, E., and Yadid, G. (2008).** VTA dopamine neuron bursting is altered in an animal model of depression and corrected by desipramine. *J Mol Neurosci* 34, 201-209.
- 4) Maayan, R., Touati-Werner, D., Shamir, D., Yadid, G., **Friedman, A., Eisner, D., Weizman, A., and Herman, I. (2008).** The effect of DHEA complementary treatment on heroin addicts participating in a rehabilitation program: a preliminary study. *Eur Neuropsychopharmacol* 18, 406-413.
- 5) **Friedman, A., Frankel, M., Flaumenhaft, Y., Merenlender, A., Pinhasov, A., Feder, Y., Taler, M., Gil-Ad, I., Abeles, M., and Yadid, G. (2009a).** Programmed acute electrical stimulation of ventral tegmental area alleviates depressive-like behavior. *Neuropsychopharmacology* 34, 1057-1066.
- 6) **Friedman, A., Merenlender, A., Lax, E., Rosenstein, M., Lubin, N., and Yadid, G. (2009b).** Early prediction of the effectiveness of antidepressants: inputs from an animal model. *J Mol Neurosci* 39, 256-261.
- 7) Roth-Deri\*, I., **Friedman\***, A., Abraham, L., Lax, E., Flaumenhaft, Y., Dikshtein, Y., and Yadid, G. (2009). Antidepressant treatment facilitates dopamine release and drug seeking behavior in a genetic animal model of depression. *Eur J Neurosci* 30, 485-492.
- 8) **Friedman, A., Lax, E., Dikshtein, Y., Abraham, L., Flaumenhaft, Y., Sudai, E., Ben-Tzion, M., Ami-Ad, L., Yaka, R., and Yadid, G. (2010).** Electrical stimulation of the lateral habenula produces enduring inhibitory effect on cocaine seeking behavior. *Neuropharmacology* 59, 452-459.
- 9) **Friedman, A., Lax, E., Dikshtein, Y., Abraham, L., Flaumenhaft, Y., Sudai, E., Ben-Tzion, M., and Yadid, G. (2011a).** Electrical stimulation of the lateral habenula produces an inhibitory effect on sucrose self-administration. *Neuropharmacology* 60, 381-387.
- 10) **Friedman, A., Shaldubina, A., Flaumenhaft, Y., Weizman, A., and Yadid, G. (2011b).** Monitoring of circadian rhythms of heart rate, locomotor activity, and temperature for diagnosis and evaluation of response to treatment in an animal model of depression. *J Mol Neurosci* 43, 303-308.
- 11) **Friedman, A., Lax, E., Abraham, L., Tischler, H., and Yadid, G. (2012).** Abnormality of VTA local field potential in an animal model of depression was restored by patterned DBS treatment. *Eur Neuropsychopharmacol* 22, 64-71.
- 12) Dikshtein, Y., Barnea, R., Kronfeld, N., Lax, E., Roth-Deri, I., **Friedman, A., Gispan, I., Elharrar, E., Levy, S., Ben-Tzion, M., et al. (2013).** beta-endorphin via the delta opioid receptor is a major factor in the incubation of cocaine craving. *Neuropsychopharmacology* 38, 2508-2514.
- 13) Lax, E., **Friedman, A., Croitoru, O., Sudai, E., Ben-Moshe, H., Redlus, L., Sasson, E., Blumenfeld-Katzir, T., Assaf, Y., and Yadid, G. (2013).** Neurodegeneration of lateral habenula efferent fibers after intermittent cocaine administration: implications for deep brain stimulation. *Neuropharmacology* 75, 246-254.
- 14) **Friedman, A., Homma, D., Gibb, L.G., Amemori, K., Rubin, S.J., Hood, A.S., Riad, M.H., and Graybiel, A.M. (2015a).** A Corticostriatal Path Targeting Striosomes Controls Decision-Making under Conflict. *Cell* 161, 1320-1333.  
*Featured by the editor with preview written by Matthew Rushworth*
- 15) **Friedman, A., Keselman, M.D., Gibb, L.G., and Graybiel, A.M. (2015b).** A multistage mathematical approach to automated clustering of high-dimensional noisy data. *Proc Natl Acad Sci U S A* 112, 4477-4482.
- 16) Gazit, T., **Friedman, A., Lax, E., Samuel, M., Zahut, R., Katz, M., Abraham, L., Tischler, H., Teicher, M., and Yadid, G. (2015).** Programmed deep brain stimulation synchronizes VTA gamma band field potential and alleviates depressive-like behavior in rats. *Neuropharmacology* 91, 135-141.
- 17) Bruchim-Samuel, M., Lax, E., Gazit, T., **Friedman, A., Ahdoot, H., Bairachnaya, M., Pinhasov, A., and Yadid, G. (2016).** Electrical stimulation of the vmPFC serves as a remote control to affect VTA activity and improve depressive-like behavior. *Exp Neurol* 283, 255-263.
- 18) **Friedman, A., Slocum, J.F., Tyulmankov, D., Gibb, L.G., Altshuler, A., Ruangwises, S., Shi, Q., Toro Arana, S.E., Beck, D.W., Sholes, J.E., et al. (2016).** Analysis of complex neural circuits with nonlinear multidimensional hidden state models. *Proc Natl Acad Sci U S A* 113, 6538-6543.

- 19) **Friedman, A., Homma, D., Bloem, B., Gibb, L.G., Amemori, K.I., Hu, D., Delcasso, S., Truong, T.F., Yang, J., Hood, A.S., et al. (2017). Chronic Stress Alters Striosome-Circuit Dynamics, Leading to Aberrant Decision-Making. *Cell* 171, 1191-1205 e1128. *Featured by the editor with preview written by: Amy F.T. Arnsten, Daeyeol Lee, and Christopher Pittenger.***
- 20) Lax\*, E., **Friedman\***, A., Massart, R., Barnea, R., Abraham, L., Cheishvili, D., Zada, M., Ahdoot, H., Bareli, T., Warhaftig, G., et al. (2017). PARP-1 is required for retrieval of cocaine-associated memory by binding to the promoter of a novel gene encoding a putative transposase inhibitor. *Mol Psychiatry* 22, 570-579.
- 21) Schechter, M., Grigoletto, J., Abd-Elhadi S., Glickstein, H., **Friedman, A.**, Serrano, G.E., Beach, T.G., Sharon, R. (2020). A role for  $\alpha$ -Synuclein in axon growth and its implications in corticostriatal glutamatergic plasticity in Parkinson's disease. *Mol Neurodegener.* 30;15(1):24
- 22) **Friedman, A., Hueske, E., Drammis, S.M., Toro Arana, S.E., Nelson, E.D., Carter, C.W., Delcasso, S., Rodriguez, R.X., Lutwak, H., DiMarco, K.S., et al. (2020). Striosomes Mediate Value-Based Learning Vulnerable in Age and Huntington's Model. *Cell In press.***

*Other Publications (Review):*

- 23) Yadid, G., and **Friedman, A.** (2008). Dynamics of the dopaminergic system as a key component to the understanding of depression. *Prog Brain Res* 172, 265-286.

\*Asterisk indicates co-first author, **color indicate selected publications**

***Presentations:***

*Special seminars:*

- 1) The Cortico-Striosomal Circuit: a regulator of conflict decision-making with a link to stress-related disorders. Psychological and Brain Sciences department, *Johns Hopkins University*, January 2016.
- 2) The Cortico-Striosomal Circuit: a regulator of conflict decision-making with a link to stress-related disorders. *National Institute on Drug Abuse (NIH)*, April 2016.
- 3) The Cortico-Striosomal Circuit: a regulator of conflict decision-making. School of Psychological Sciences, *Tel Aviv University*, December 2016.
- 4) The Cortico-Striosomal Circuit: a regulator of conflict decision-making. Department of Biological Science, *Carnegie Mellon University*, February 2016.
- 5) The Cortico-Striosomal Circuit: a regulator of conflict decision-making. Edmond and Lily Safra Center for Brain Sciences, *Hebrew University*, October 2017.
- 6) Cortico-Striosomal Circuit is Critical for Regulation of Normal and Aberrant Decision-Making. Department of Neuroscience, *Yale*, January 2018.
- 7) The Role of the Cortico-Striosomal Circuit in Regulation of Conflict Decision-Making and the Critical Link Between its Abnormality and Stress-Related Disorder, *Columbia Theory Center*, August 2018.
- 8) The Role of the Cortico-Striosomal Circuit in Regulation of Conflict Decision-Making and the Critical Link Between its Abnormality and Stress-Related Disorder, *Icahn School of Medicine at Mount Sinai*, October 2018.
- 9) Discover Computational Principles of Multi-Circuit Cortico-Striatal Network Underlying Decision-Making via Development of High Density Behavioral, Computational, and Recording/Manipulation Tools, *USC Viterbi School of Biomedical Engineering*, March 2019.
- 10) Striosomal Compartment of Striatum Encode Expected Cost-Benefit Value and Selectively Effected by Stress, Aging and Huntington Disorder, *Mayo Clinic*, Department of Neuroscience, Jacksonville, September 2019.
- 11) Striosomal Compartment of Striatum Encode Expected Cost-Benefit Value and Selectively Effected by Stress, Aging and Huntington Disorder, *UPEN*, Department of Neuroscience, Philadelphia, January 2020.
- 12) Striosomal Compartment of Striatum Encode Expected Cost-Benefit Value and Selectively Effected by Stress, Aging and Huntington Disorder, *UTEP*, Department of Biological Sciences, El Paso, February 2020.

13) Striosomal Compartment of Striatum Encode Expected Cost-Benefit Value and Selectively Effected by Stress, Aging and Huntington Disorder, *Medical College of Georgia at Augusta University*, Department of Neuroscience, Augustata, February 2020.

Conference presentations:

- 1) Variability of the mesolimbic neuronal activity in a rat model of depression *ISFN*, Eilat, 2004.
- 2) VTA Acute-Electrical-Stimulation: New Treatment for Depression, *Israel Psychiatric Society*, Goshrim, 2007.
- 3) Programmed Acute-Electrical-Stimulation of ventral tegmental area Alleviates Depressive-Like Behavior and normalize local field potentials; *Bar-Ilan University retreat*, 2010.
- 4) Programmed Acute-Electrical-Stimulation of ventral tegmental area Alleviates Depressive-Like Behavior and normalize local field potentials; *Israel Psychiatric Society*, Goshrim, 2010.
- 5) A Corticostriatal Path Targeting Striosomes Controls Decision-Making under Conflict. *Annual McGovern Institute Retreat*, MIT, May 2015.
- 6) A Corticostriatal Path Targeting Striosomes Controls Decision-Making under Conflict. *McGovern Institute Board Meeting*, MIT, Oct 2015.
- 7) Chronic Stress Alters Striosome-Circuit Dynamics, Leading to Aberrant Decision-Making.. *McGovern Institute Board Meeting*, MIT, Oct 2018.
- 7) Chronic Stress Alters Striosome-Circuit Dynamics, Leading to Aberrant Decision-Making. *Safra Center for Brain Sciences Board Meeting*, Washington DC., Nov 2018.
- 8) Novel computational approaches for signal extraction from striatal multi-color photometry recordings and evaluating high-throughput approach avoidance learning applied to Huntington's disease mouse model, *HD2018*, Cambridge, August 2018.

Posters:

- 1) *Correlation* of the bursting mesolimbic neuronal activity and dopamine release: a role in antidepressant effect, *ISFN*, Eilat, 2005.
- 2) Cluster-Like Form of Dopaminergic Mesolimbic neuronal activity is altered in an animal model of depression and corrected by desipramine; *Israel Psychiatric Society*, Goshrim, 2006.
- 3) Programmed Acute-Electrical Electrical-Stimulation to the VTA: a New Treatment for Depression, *Israel Psychiatric Society*, Goshrim, 2008.
- 4) Deep brain stimulation of the lateral habenula impairs natural and psychostimulant reinforcement; *SFN, Annual Meeting* Washington DC, 2008.
- 5) Deep brain stimulation of the lateral habenula impairs natural and psychostimulant reinforcement; *Society of Biological Psychiatry, Annual Meeting* Washington DC, 2008.
- 6) Single-trial electrical stimulation of the lateral habenula produces enduring inhibitive effects on sucrose and cocaine seeking behavior; *Invited poster, National Institute on Drug Abuse (NIDA) mini conference*, Chicago, 2009.
- 7) Programmed Acute-Electrical-Stimulation of ventral tegmental area Alleviates Depressive-Like Behavior and normalize local field potentials; *SFN, Annual Meeting* Chicago, 2009.
- 8) Novel mathematical approach to fully unsupervised spike-sorting validated for striatal and cortical neurons. Part I: enhancing signal-to-noise ratio and evaluating separability, *SFN, Annual Meeting San Diego*, 2013.
- 9) Striatal high-firing interneurons mediate inhibitory prefrontal-striosomal signaling during cost-benefit conflict decision-making, *SFN Annual Meeting*, Chicago, 2015.
- 10) Non-linear multi-dimensional hidden state models for the analysis of neural circuits, *SFN, Annual Meeting*, San Diego, 2016.
- 11) A shift in the excitation-inhibition balance of a cortico-striosomal circuit underlies, *SFN Annual Meeting*, Washington D.C., 2017.

12) Novel computational approaches for signal extraction from striatal multi-color photometry recordings and evaluating high-throughput approach-avoidance learning applied to Huntington's disease mouse model, *SFN Annual Meeting*, San Diego, 2018.

### *Patents:*

1. **Friedman** A, Keselman MD, Gibb LG, & Graybiel AM (2015) Fully Unsupervised Clustering Algorithm Optimized for Spike Sorting. - *Licensed to Neuralynx*
2. Yadid G, **Friedman** A & Abeles M (2008) A Device and Method for Deep Brain Stimulation as a New Form of Treating Chronic Depression.

### *Mentoring Experience:*

#### *Graduate projects supervision:*

1. Frankel M., Lax E., Abraham L., and Flaumenhaft Y. (2006-2010, Bar-Ilan), published in publication Nos. 5-9, 11,13
2. Homma D. (2010-2011, MIT), published in publications Nos. 14 and 19.
3. Tulmakov D. and Slocum J. (2013-2016, MIT), published in publication No. 18.
4. Drammis S. M. (2018-present, MIT), manuscript in preparation.

#### *Undergraduate projects supervision:*

1. Goutkin S., Kravchinsky E., Rosenstein M, Lubin N (2005-2006, Bar-Ilan), published in publication Nos. 2 and 6.
2. Rubin S., Crayton R., Rajan L., Quisenberry L.C. , Felhofer A.D., Choi J., Xu H., Maeda M. J., Song. H., Wall T., Gavrin M., Michael M., Yang L., Jackson K., Hood A., Shi Q., Ruangwises S., Kim M., Yang J., Hu V., Toro Arana S., Jaitly K., Mikofalvy K., Vijaykumar B. (2010-2016, MIT), published in publication No. 14.
3. Keselman M., Fryman A. (2011-2016, MIT). Published in Publication No. 15.
4. Truong, T.F., Yang, J., Hood, A.S., Yang, J. Hood, A. S., Mikofalvy, K. A., Beck, D. W., Nguyen, N., Toro Arana, S. E., (2010-2017, MIT), published in publication No. 19.
5. Lutwak, H., Toro Arana, S. E., Rakocevic, L. I., Rodriguez, R. X., Fajardo J. D., Xiong, J. K., (2017-2019, MIT), manuscript in preparation.