**Alexander Friedman, PhD**

Research Scientist

McGovern Institute for Brain Research

Massachusetts Institute of Technology

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**Research Interest:**

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 neuropychiatric 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.

**Education:**

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

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

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

**Academic Positions and Teaching Experience:**

2014-Present: Research Scientist, McGovern Institute for Brain Research, MIT, USA.

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

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

Courses: Systems Physiology, Zoology, Bio-statistics.

2003-2004: Teaching Assistant, Department of Bioinformatics and Biotechnology, JCT, Israel. Courses: General Chemistry, Organic Chemistry.

**Selected Publications:**

1. **Friedman, A.,** Homma, D., Bloem, B., Gibb, L.G., Amemori, K., Hu, D., Delcasso, S., Truong, T.F., Yang, J., Hood, A.S., Yang, J. Hood, A. S., Mikofalvy, K. A., Beck, D. W., Nguyen, N., Nelson, E. D., Toro Arana, S. E., Vorder Bruegge, R. H., Goosens, K. A., Graybiel A. M. (2017). Chronic Stress Alters Striosome-Circuit Dynamics Leading to Aberrant Decision-Making. **Cell** 171, 1191–1205.

*Featured by the editor with preview written by: Amy F.T. Arnsten, Daeyeol Lee, and Christopher Pittenger*

2. **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. & Graybiel, A.M. (2016). Analysis of complex neural circuits with nonlinear multidimensional hidden state models. **PNAS** 113(23):6538-43.

3. **Friedman, A.,** Keselman, M.D., Gibb LG & Graybiel, A.M. (2015) A multistage mathematical approach to automated clustering of high-dimensional noisy data. **PNAS** 112(14):4477-4482.

4. **Friedman, A.**, Homma, D., Gibb, L.G., Amemori, K., Rubin, S.J., Hood, A.S., Riad, M.H., & Graybiel A.M. (2015). A Corticostriatal Path Targeting Striosomes Controls Decision-Making under Conflict. **Cell** 161, 1320-1333.

*Featured by the editor with preview written by Matthew Rushworth*

5. **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.

6. **Friedman, A.**, Frankel, M., Flaumenhaft, Y., Merenlender, A., Pinhasov, A., Feder, Y., Taler, M., Gil-Ad, I., Abeles, M., and Yadid, G. (2009). Programmed acute electrical stimulation of ventral tegmental area alleviates depressive-like behavior. Neuropsychopharmacology 34, 1057-1066.

**Additional publications:**

7. Lax\*, E., **Friedman**\***,** **A**., Massart, R., Barnea, R., Abraham, L., Cheishvili, D., Zada, M. Ahdoot, H., Bareli, T., Warhaftig, G., Visochek, L., Suderman, M., Cohen-Armon, M. Szyf, M., Yadid, G. (2016). 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, 570-579.8.

8. 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.

9. 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.

10. 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.

11. 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.

12. **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.

13. **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.

14. **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.

15. 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.

16. **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.

17. 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.

18. 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.

19. **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.

20. **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.

21. **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.

**\***Asterisk indicates co-first author

**Mentoring Experience:**

*Supervision of Graduate projects:*

* Tulmakov D. and Slocum J. (2013-2016, MIT), published in publication No. 2
* Frankel M. and Flaumenhaft Y. (2006-2010, Bar-Ilan), published in publication No. 6.
* Lax E., Abraham L., and Flaumenhat Y. (2006-2010, Bar-Ilan), published in publications Nos. 5, 12-15.

*Undergraduate projects supervision:*

* Truong, T.F., Yang, J., Hood, A.S., Yang, J. Hood, A. S., Mikofalvy, K. A., Beck, D. W., Nguyen, N., Nelson, E. D., Toro Arana, S. E., (2010-2017, MIT), published in publication No. 1.
* Keselman M., Fryman A. (2011-2016, MIT). Published in Publication No. 3.
* 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. 4.
* Rosenstein M, Lubin N (2006, Bar-Ilan), published in publication No. 16.
* Goutkin S., Kravchinsky E. (2005, Bar-Ilan), published in publication No. 20.

**Patents:**

1. **Friedman A**, Keselman MD, Gibb LG, & Graybiel AM (2015) Fully Unsupervised Clustering Algorithm Optimized for Spike Sorting.

2. Yadid G, **Friedman A** & Abeles M (2008) A Device and Method for Deep Brain Stimulation as a New Form of Treating Chronic Depression.

**Invited Presentations:**

Cortico-Striosomal Circuit is Critical for Regulation of Normal and Aberrant Decision-Making.

 *Department of Neuroscience Symposium, Yale*, January 2018.

A shift in the excitation-inhibition balance of a cortico-striosomal circuit underlies, *SFN Annual Meeting,* Washington D.C., November 2017.

The Cortico-Striosomal Circuit: a regulator of conflict decision-making.

 *Special seminar at Edmond and Lily Safra Center for Brain Sciences, Hebrew University*, October 2017.

The Cortico-Striosomal Circuit: a regulator of conflict decision-making.

 *Special seminar at Department of Biological Science, Carnegie Melon University*, February 2016.

The Cortico-Striosomal Circuit: a regulator of conflict decision-making.

*Special seminar at School of Psychological Sciences, Tel Aviv University*, December 2016.

Non-linear multi-dimensional hidden state models for the analysis of neural circuits, *SFN, Annual Meeting,* San Diego, November 2016.

The Cortico-Striosomal Circuit: a regulator of conflict decision-making with a link to stress-related disorders.

*Special seminar at National Institute on Drug Abuse (NIH) / National Institute on Drug Abuse (NIDA)*, April 2016.

The Cortico-Striosomal Circuit: a regulator of conflict decision-making with a link to stress-related disorders.

*Special seminar at Psychological and Brain Sciences, Johns Hopkins University*, January 2016.

Striatal high-firing interneurons mediate inhibitory prefrontal-striosomal signaling during cost-benefit conflict decision-making, *SFN Annual Meeting,* Chicago, November 2015.

A Corticostriatal Path Targeting Striosomes Controls Decision-Making under Conflict. *Annual McGovern Institute Retreat, MIT,* May 2015.

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*, November 2013.

Programmed Acute-Electrical-Stimulation of ventral tegmental area Alleviates Depressive-Like Behavior and normalize local field potentials; Israel *Psychiatric Society, Goshrim*, 2010.

Programmed Acute-Electrical-Stimulation of ventral tegmental area Alleviates Depressive-Like Behavior and normalize local field potentials; *Bar-Ilan University retreat*, 2010.

Programmed Acute-Electrical-Stimulation of ventral tegmental area Alleviates Depressive-Like Behavior and normalize local field potentials; *SFN, Annual Meeting Chicago*, 2009.

Single-trial electrical stimulation of the lateral habenula produces enduring inhibitive effects on sucrose and cocaine seeking behavior; *Invited presentation at National Institute on Drug Abuse (NIDA) mini conference,* Chicago, 2009.

Deep brain stimulation of the lateral habenula impairs natural and psychostimulant reinforcement; *Society of Biological Psychiatry, Annual Meeting* Washington DC, 2008.

Deep brain stimulation of the lateral habenula impairs natural and psychostimulant reinforcement; *SFN, Annual Meeting* Washington DC, 2008.

Programmed Acute-Electrical Electrical-Stimulation to the VTA: a New Treatment for Depression, *Israel Psychiatric Society*, Goshrim, 2008.

VTA Acute-Electrical-Stimulation: New Treatment for Depression*, Israel Psychiatric Society*, Goshrim, 2007.

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.

Correlation of the bursting mesolimbic neuronal activity and dopamine release: a role in antidepressant effect, *ISFN*, Eilat, 2005.

Variability of the mesolimbic neuronal activity in a rat model of depression *ISFN*, Eilat, 2004.

**Prizes and Awards:**

2018: Best publication of MIT in 2017.

2009: NIDA mini-conference, poster prize

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

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

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

**Personal:**

Born: July 5, 1983

Marital status: married.

Languages: English, Hebrew, Russian, Belarusian.

Citizenship: Israeli with permanent residency in the USA

**References:**

Ann M. Graybiel - Institute Professor at MIT (Post-Doctoral advisor)

Moshe Abeles- Distinguished Professor, Bar-Ilan University (PhD advisor)

Gal Yadid- Professor, Bar-Ilan University (PhD advisor)

Edward Boyden, Associate Professor at MIT (Collaborator)

Yaakov Friedman, Distinguished Professor, JCT (Collaborator; no relation)

Ki Ann Goosens, Assistant Professor at MIT (Collaborator)