BIOGRAPHICAL SKETCH

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NAME: Fleischmann, Alexander

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

POSITION TITLE: Associate Professor of Neuroscience

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Vienna, Vienna, Austria	MS	03/1997	Biochemistry
University of Vienna, Vienna, Austria	PhD	12/2000	Genetics
Research Institute for Molecular Pathology (IMP), Vienna, Austria	(Postdoctoral)	09/2001	Molecular Genetics
Columbia University, New York	(Postdoctoral)	09/2006	Neuroscience
Columbia University, New York	(Research Associate)	12/2010	Neuroscience

A. Personal Statement

At my laboratory at Brown University, I study the formation and function of neural circuits underlying sensory processing and behavior. Understanding the role of neuronal diversity in neural circuit function has been the main driving force of my research.

My lab has extensive expertise in molecular biology approaches to characterizing neural cell types and their connections, including single cell RNA sequencing, RNA FISH and immunohistochemistry, and viral-genetic tracing. My lab has made major contributions to understanding the diversity of olfactory sensory neurons in the nose, and of principal neurons in the olfactory bulb and olfactory cortex of mice. Our expertise in exploring the molecular identities of neurons is central to this proposal.

My laboratory has also developed in vivo imaging approaches combined with behavioral analyses to reveal circuit mechanisms for representing odor information in the olfactory bulb and cortex. We have developed advanced data science pipelines to analyze, visualize and share the large data sets generated through state-of-the-art molecular biology, imaging and behavioral experiments. Thus, my lab is ideally positioned to lead this collaboration aimed at integrating functional, structural and molecular approaches to understand the role of neural diversity in olfactory circuits. I have established extensive interdisciplinary national and international collaborations, supported by grants from the BRAIN Initiative (U19), NSF (CRCNS), and Carney Institute for Brain Science (Innovation Award).

As the director of the neuroscience graduate program at Brown University, I support graduate student teaching and diversity, inclusion and equity in recruitment and mentoring. I teach a hands-on lab course entitled 'Big Data Neuroscience Ideas Lab', in which students explore large open-source data sets to develop their independent research projects. I have successfully trained undergraduate and graduate students and postdocs; I promote an inclusive research environment and support my students to develop a wide set of experimental, analytical and personal skills to succeed in their future careers.

Ongoing and recently completed projects that I would like to highlight include:

1 R01 DC020478-01A1
NIH/NIDCD
PI: Alexander Fleischmann
3/1/2023 – 2/28/2028
Gene regulatory network control of olfactory cortex cell type specification

U19NS112953-01
NIH/NINDS
PI: Dima Rinberg
Role: Co-PI
Cracking the olfactory code
9/1/2019 – 5/31/2024

1-R01-DC017437-01
NIH/NIDCD
PI: Alexander Fleischmann
12/1/2018 – 11/30/2023
Odor Memory Traces in the Mouse Olfactory Cortex

Carney Innovation Award
Carney Institute for Brain Science
PI: Alexander Fleischmann
12/1/2019 – 5/30/2023 (completed)
New biomarkers for neurodegenerative disease

OVPR Seed Award
Brown University
PI: Alexander Fleischmann
7/1/2021 – 12/30/2021 (completed)
New biomarkers for neurodegenerative disease

CRCNS – ANR Computational Neuroscience, ANR-17-NEUC-0002-01
PI: Kevin Franks
Role: Co-PI
2017-2021 (Completed)
Odor processing by cortical neural circuits

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2018- Present	Associate Professor of Neuroscience, Department of Neuroscience, Brown University, Providence, RI
2013-2018	Tenured Scientist, INSERM CR1
2011-2018	Group leader, CIRB, College de France, Paris
2006-2010	Associate Research Scientist, Department of Neuroscience, Laboratory of Dr. R. Axel, Columbia University, New York
2001-2006	Postdoctoral Fellow, Department of Neuroscience, Laboratory of Dr. R. Axel, Columbia University, New York
2001	Postdoctoral Fellow, Laboratory of Dr. E. Wagner, IMP Vienna

Honors

C. Contributions to Science

1. Odor processing

My lab has made major contributions to understanding how olfactory bulb input is transformed into cortical odor representations and behavior. We recently identified molecularly distinct olfactory bulb principal cells that preferentially project to different cortical target regions. Earlier, I generated transgenic mice with a "monoclonal nose", in which I eliminated the large repertoire of odorant receptors expressed in olfactory sensory neurons. Using electrophysiological recordings, two-photon imaging and behavioral experiments, my lab revealed the remarkable capacity of olfactory circuits to normalize sensory inputs.

a. Zeppilli S, Ackels T, Attey R, Klimpert N, Ritola KD, Boeing S, Crombach A, Schaefer AT, **Fleischmann A**. Molecular characterization of projection neuron subtypes in the mouse olfactory bulb. eLife, 2021 July 22;10. PMCID: PMC8352594

b. Roland B, Jordan R, Sosulski DL, Diodato A, Fukunaga I, Wickersham I, Franks KM, Schaefer AT, **Fleischmann A** (2016). Massive normalization of odor-evoked activity in the olfactory bulb of mice with a "monoclonal nose". eLife, 2016 May 13;5. pii: e16335. PMCID: PMC4919110

c. Angelo K, Pimentel D, Pichler B, **Fleischmann A**, Rancz E, Margrie T. (2012). A biophysical signature of network affiliation and sensory processing in mitral cells. Nature, Aug16;488(7411):375-8. PMCID: PMC3442227

d. Glinka ME, Samuels BA, Teillon J, Mei DF, Shykind BM, Hen R, **Fleischmann A**. (2012). Olfactory deficits cause anxiety-like behaviors in mice. *J.* Neurosci.*, 32(19):6718-6725. PMCID: PMC3367161

2. Organization and function of the olfactory cortex

My lab established new experimental approaches to investigate the functional organization of the mouse olfactory cortex. We identified genes selectively expressed in distinct subtypes of olfactory cortex projection neurons, and we characterized, using *in vivo* two-photon microscopy, fundamental principles of odor information coding. These findings have allowed us to explore how different neural cell types contribute to odor information coding, how odor information is transmitted to downstream brain areas involved in sensory integration, cognition, and motor control, and how learning and experience alters olfactory neural network functions.

a. Meissner-Bernard C, Dembitskaya Y, Venance L, **Fleischmann A**. Encoding of Odor Fear Memories in the Mouse Olfactory Cortex. Curr Biol. 2018 Dec 24. PMID:30612908

b. Roland B, Deneux T, Franks KM, Bathellier B, **Fleischmann A**. Odor identity coding by distributed ensembles of neurons in the mouse olfactory cortex. eLife, 2017 May 10;6. pii: e26337. PMCID: PMC5438249

c. Diodato A, Ruinart de Brimont M, Yim YS, Derian N, Perrin S, Pouch J, Klatzmann D, Garel S, Choi G, **Fleischmann A** (2016). Molecular signatures of neural connectivity in the olfactory cortex. Nature Commun., 18;7:12238. PMCID: PMC4960301

d. Choi GB, Stettler DD, Kallman BR, Bhaskar ST, **Fleischmann A**, Axel R (2011). Driving opposing behaviors with ensembles of piriform neurons. *Cell,* 146:1004-1015. PMCID: PMC3230930

3. Neuronal diversity of olfactory sensory neurons

I studied the molecular mechanisms underlying the differentiation of olfactory sensory neurons, a paradigmatic example of neural diversification. Using a transgenic approach in mice we have found that the forced expression of an OR suppresses OR gene choice, revealing that OR gene choice is mediated by negative feedback signaling. Subsequent experiments in my own lab revealed that this signaling pathway involves the competition of active OR alleles, and modifies the chromatin structure of OR gene loci to alter the accessibility of OR promoters.

a. Bashkirova EV, Klimpert N, Pourmorady A, Monahan K, Campbell CE, Osinski JM, Tan L, Schieren I, Stecky B, Barnea G, Xie XS, Abdus-Saboor I, Shykind B, Marlin BJ, Gronostajski RM, **Fleischmann A**,

Lomvardas S. Opposing, spatially-determined epigenetic forces impose restrictions on stochastic olfactory receptor choice. bioRxiv (2023) Mar 15: PMCID: PMC10055043.

b. Abdus-Saboor I, Al Nufal MJ, Agha MV, Ruinart de Brimont M, **Fleischmann A**, Shykind B (2016). Expression refinement ensures singular odorant receptor gene choice. Curr. Biol., 25;26(8):1083-90. PMID: 27040780

c. **Fleischmann A,** Abdus-Saboor I., Sayed A., Shykind B (2013). Functional Interrogation of an Odorant Receptor Locus Reveals Multiple Axes of Transcriptional Regulation. PLoS Biol., 11(5): e1001568. PMCID: PMC3660300

d. **Fleischmann A**, Shykind BM, Sosulski DL, Franks KM, Glinka ME, Mei DF, Yonghua S, Kirkland J, Mendelsohn M, Albers MW, Axel R. (2008). Mice with a "monoclonal" nose: perturbations in an olfactory map impair odor discrimination. Neuron, 60:1-14. PMCID: PMC2732586