

**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Sulzer, David		POSITION TITLE Professor of Neurobiology in Psychiatry, Neurology, and Pharmacology	
eRA COMMONS USER NAME (credential, e.g., agency login) sulzerd			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
Michigan State University	B.S.	6/79	Genetics, Botany
Columbia University	Ph.D.	11/88	Biology
Columbia University	Postdoctoral	5/94	Neuroscience

**A. Personal Statement**

This is to express my support for the School of Neuroscience in Rome, administered by Prof. Nicola Mercuri.

My group investigates the interaction between the synapses of the cortex and the basal ganglia, including the dopamine system, in normal behavior, including habit formation, planning, decision making, and action selection; and the diseases of the system. In the case of this proposal, these specifically include drug dependence and other features of addiction.

I have administered numerous NIH and private grants, all of which have met the aims of projects. We have published over peer reviewed 120 papers, most in high profile journals, I have a demonstrated record of successful and productive research projects in an area of high relevance for this Program. As a mentor, I have trained 4 graduate students and 22 postdocs, of which 9 are current. Eight of my 13 postdocs who finished their training are now professors directing their own laboratories at Institutes including Columbia, Rutgers, Cornell, Yale, Lund, Tufts, and the University of Washington, while two run labs at large pharmaceutical companies, and one runs a large Optical Facility at Columbia University.

I also founded and ran the NIDA funded T32 in Basic Neuroscience at CUMC from 2004-2012. Of the trainees I have mentored in this T32, six of the seventeen who have finished their training are now professors, at SUNY, Technion, Oregon State, University of Texas, Columbia, and New York State Psychiatric Institute. As no trainee received a PhD prior to 2004, I believe that this is an outstanding record. We have also had good success at finding trainees from diverse backgrounds, with 6 of the 23 participants from underrepresented groups. Among the activities I am responsible for in this program are 1) leading a weekly seminar series, 2) critiquing the grant applications written by each trainee (at least one per year per trainee), 3) assisting them in arranging University-wide seminars on this subject.

As a scientist, I have the expertise, leadership and motivation necessary to successfully advise trainees in their proposed work. I have a broad background in neuroscience, particularly in neurotransmission and neurodegenerative disease, with specific training and expertise in key research areas for this application. Several of the techniques used in this field were originally developed in my lab, some in collaboration with other mentors on this proposal. Some of my work related to basal ganglia cell biology and physiology include:

- co-development of the first system for postnatal culture of midbrain dopamine neurons (Rayport et al 1992 *J Neurosci*),
- discovered co-release of glutamate from dopamine neurons (Sulzer et al 1998 *J Neurosci*)
- introduction of the weak base mechanism of amphetamine action (Sulzer & Rayport, 1990, *Neuron*) and the first direct measurement of reverse transport, an important property of amphetamine (Sulzer et al 1995, *J Neurosci*)
- the first recording of quantal neurotransmitter release, using amperometry at dopamine terminals, (Pothos 1998, *J Neurosci*)

- discovery of multiple means to alter quantal size, including the effects of L-DOPA, amphetamine, vesicle transporter expression (with Robert Edwards), rebound hyperacidification, and fusion pore flickering (multiple publications)
- introduction the role of autophagic degradation in methamphetamine toxicity, and later in Parkinson's disease and Huntington's disease (multiple publications), including the first identification of chaperone-mediated autophagy in neurons (Cuervo et al, 2004, *Science*)
- the first optical analysis of corticostriatal transmission, showing the role of activity, dopamine, and acetylcholine in synaptic selection, using FM1-43, and showing the effects with amphetamine and cocaine (Bamford 2004, 2008, *Neuron*),
- introduction of fluorescent false neurotransmitters, which provide the first means to observe neurotransmitter release from CNS terminals (with Dalibor Sames: Gubernator) 2009, *Science*),
- characterization of the roles of alpha-synuclein and cytosolic dopamine in Parkinson's models (multiple publications)
- demonstrating how nicotine effects DA release in a stimulation-dependent manner at synaptic terminals (Zhang 2004, *Nature Neuroscience*)
- introduced role of presynaptic autophagy in regulation of neurotransmission (Hernandez 2012,

## B. Positions and Honors

### Positions and Employment

1988-91	Postdoctoral Research Fellow, Center for Neurobiology & Behavior, Columbia University and New York State Psychiatric Institute, Dr. Stephen Rayport, <i>advisor</i>
1989-	Associate Research Scientist, Columbia University
1994-2002	Assistant Professor, Depts. Psychiatry and Neurology, Columbia University
2002- 2008	Associate Professor, Depts. Psychiatry and Neurology, Columbia University
2008-	Professor of Neurobiology, Depts. Psychiatry, Neurology, Pharmacology, Columbia University

### Other Experience and Professional Memberships

1997-	Peer review committees for NIDA, NINDS, NIH (BDCN-3, MDCN), VA, Parkinson's Disease Foundation, advisor Alfred P. Sloan Foundation, US Army, Hereditary Disease Foundation
-------	--

### Honors and Awards

1988	Howard Hughes Postdoctoral Award	
1989	NARSAD Young Investigator Award	2004 Picower Foundation Award
1995	Aaron Diamond Foundation Award	2005 Coordinator of NIH T32 Basic Neuroscience at Columbia
1996	James T. Shannon Award, N.I.D.A.	
1999-	Organizing Committee, Conference on In Vivo Methods	2007 Columbia Integrated Science & Engineering Award
1999	NARSAD Independent Investigator Award	2007 Plenary Symposia, 50 Years of Dopamine, Gothenburg, Sweden
2000	Leadership Award, Huntington's Disease Society of America	2008 McKnight Award in Neuroscience for Technological Innovation
2002	Frontiers of Neuroscience Lecture, Emory University	2008 Simons Foundation Award
2002	Killam Lecture, McGill University	2008 Spring Symposium Symposia, Univ. Mich.
2003	Full member, BDCN-3, NIH (5 years)	2011 Full member MDCN, NIH (5 years)
2003	Chair (2005), Co-Chair (2003), Gordon Conference on Catecholamines	2011 JPB Foundation Award
2003	Cassy Bachner Award, Huntington's Disease Society of America	2011 Vatican Symposia, Dopamine and Parkinson's disease, Vatican City
2004-	Editorial Boards, <i>Neurotoxicity Research</i> , <i>Autophagy</i> , <i>Basal Ganglia</i>	2012 Keynote Lecture in Cellular Neuroscience Yale University

**2012 Frontiers in Neuroscience C. Selected Peer-reviewed Publications** (Fifteen selected for relevance to this project from 120 peer-reviewed publications)

- 1) **Sulzer D.**, and Rayport, S. (1990). Amphetamine and other psychostimulants reduce pH gradients in midbrain dopaminergic neurons and isolated chromaffin granules: a proposed mechanism of action. *Neuron*, 5:797-808. PMID: 2268433
- 2) **Sulzer D.**, Chen TK, St. Remy C., Lau YY, Kristense H., Rayport S., and Ewing AG. (1995). Amphetamine redistributes dopamine from synaptic vesicles to the cytosol and promotes reverse transport. *Journal of Neuroscience*, 15: 4102-4108. PMID: 7751968
- 3) Pothos E., Davila V., and **Sulzer D.** (1998). Presynaptic recording of quanta from midbrain dopamine neurons and modulation of the quantal size. *Journal of Neuroscience*, 18:4106-4118. PMID: 9592091
- 4) **Sulzer D.**, Joyce MP, Lin L., Geldwert D., Haber SN, Hattori T., and Rayport, S. (1998). Dopamine neurons make glutamatergic synapses *in vitro*. *Journal of Neuroscience*, 18:4588-4602. PMID: 9614234
- 5) Pothos, E.N., Larsen, K.E., Krantz, D.E., Liu, Y.-J., Setlik, W., Gershon, M. D., Edwards, R.H., and **Sulzer, D.** (2000) Synaptic vesicle transporter expression regulates vesicle phenotype and quantal size. *Journal of Neuroscience*, 20:7297-7308. PMID: 11007887
- 6) Schmitz, Y., Lee, C.J., Schmauss, C., Gonon, F., and **Sulzer, D.** (2001) Amphetamine distorts synaptic dopamine overflow: effects on vesicular stores, D2 autoreceptors, and uptake. *Journal of Neuroscience*, 21: 5916-5924. PMID: 11487614
- 7) Larsen K.E., Fon, E., LaVoie, M., Hastings, T.G., Edwards, R.H., **Sulzer, D.** (2002) Methamphetamine-induced degeneration of dopaminergic neurons occurs via autophagy triggered by elevated cytosolic dopamine. *J Journal of Neuroscience*, 22:8951-8960. PMID: 12388602
- 8) Staal, R.G.W., Mosharov, E.V., **Sulzer, D.** (2004). Small synaptic vesicle exocytosis occurs via a rapidly flickering fusion pore. *Nature Neuroscience*, 7:341-346. PMID: 14990933
- 9) Bamford, N.S., Schmitz, Y., Schmauss, C., Zakharenko, S.S., Zablow, L., **Sulzer, D.** (2004) Dopamine selects sets of corticostriatal synapses. *Neuron*, 42:653-663. PMID: 15157425
- 10) Cuervo AM, Stefanis L., Fredenburg R., Lansbury P., **Sulzer D.** (2004). Impaired degradation of mutant alpha-synuclein by chaperone-mediated autophagy. *Science*, 305:1292-5. PMID: 15333840
- 11) Bamford, N.S., Zhang, H., Joyce, J.A., Scarlis, C.A., \*\*Harleton, E., **Sulzer, D.** (2008). Chronic methamphetamine induces reversible long-term depression at corticostriatal terminals. *Neuron*, 58:1-15. PMID: 18400166
- 12) Mosharov EV, Larsen KE, Phillips KA, Wilson K, Kanter E., Schmitz Y., Krantz D.E., Edwards R.H., **Sulzer D.** (2009) Interplay between cytosolic dopamine, calcium and alpha-synuclein causes selective death of substantia nigra neurons. *Neuron*, 30:218-29. PMID: 19409267
- 13) \*\*Gubernator, N.G., Zhang, H., Staal, R.G.W., Mosharov, E.V., Pereira, D., \*\*Yue, M., Balsanek, V., Vadola, P.A., Mukherjee, B., Edwards, R.H., \***Sulzer, D.**, \*Sames, D. (\*corresponding co-author) (2009) "Fluorescent false neurotransmitters visualize dopamine release from individual presynaptic Terminals" *Science*, 324: 1441-1444. PMID: 19423778
- 14) Schmitz, Y., \*\*Luccarelli, J., Kim, M., \*\*Wang, Mi., **Sulzer, D.** (2009) Glutamate controls growth rate and branching of dopaminergic axons. *Journal of Neuroscience*, 29:11973-81. PMID: 19776283
- 15) \* **Daniela Hernandez**, \*\*Ciara A. Torres, Wanda Setlik, Carolina Cebrián, Eugene V. Mosharov, Guomei Tang, Hsiao-Chun Cheng, Nikolai Kholodilov, Olga Yarygina, Robert E. Burke, Michael Gershon, **David Sulzer** (2012). Regulation of presynaptic neurotransmission by macroautophagy. *Neuron*, in press.