Curriculum Vitae

Ann Martin Graybiel

Education and Positions:

Harvard University, A.B.	1964
Magna cum Laude, Phi Beta Kappa	
Tufts University, Department of Biology	1965-1966
Woodrow Wilson Fellow	
Massachusetts Institute of Technology, Ph.D.	1971
Department of Psychology and Brain Science	
Research Associate, M.I.T.	1971-1973
Assistant Professor in Psychology, M.I.T.	1973-1976
Associate Professor in Psychology, M.I.T.	1976-1980
Professor of Neuroanatomy, Dept. of Psychology, M.I.T.	1980-1983
Head, Course in Neuroscience and Professor, HST Division, Harvard Medical School	1986-1988
Professor of Neuroscience, Department of Brain and Cognitive Sciences, M.I.T.	1983-
Walter A. Rosenblith Professor of Neuroscience, M.I.T.	1994-2008
Investigator, McGovern Institute for Brain Research, M.I.T.	2001-
Affiliate, Picower Center for Learning and Memory, M.I.T.	2001-2012
Institute Professor, M.I.T.	2008-

Awards and Honors:

Porter Fellowship Award, American Physiological Society	1967
Williams and Wilkins Award, American Association of Anatomists	1970
Associate, Neuroscience Research Program (first woman)	1978
Charles Judson Herrick Award, American Association of Anatomists	1978
McKnight Senior Investigator Award	1985
Member, National Academy of Sciences, USA	1988
Javits Neuroscience Investigator Award, National Institutes of Health	1988, 1995
Honorary Member, Royal Academy of Medicine, Seville, Spain	1989
Member, American Academy of Arts and Sciences	1991
Member, National Academy of Medicine, USA (formerly the Institute of Medicine)	1994
Fellow, American Academy of Neurology	1997
President, International Basal Ganglia Society	1997-1998
Teaching Prize for Excellence in Graduate Education, School of Science, MIT	2000
Outstanding Women in Neuroscience Award, Brown University, Providence, Rhode Island	2001
National Medal of Science, USA	2001
James Rhyne Killian Jr. Faculty Achievement Award, M.I.T.	2002
Robert S. Dow Neuroscience Award	2002
Honorary Doctor of Science, Mount Sinai School of Medicine, New York, New York	2003
2004 Woman Leader of Parkinson's Science, Parkinson's Disease Foundation, New York, New York	2004
MERIT Award of the National Institutes of Health	2004
Radcliffe Alumnae Recognition Award	2004
Prix Plasticité Neuronale from the IPSEN Foundation	2005
Honorary Doctor of Science, Tufts University, Medford, Massachusetts	2005
Harold S. Diamond Honorary Professorship, National Parkinson Foundation	2005
NARSAD Distinguished Investigator Award	2007
Honorary Doctor of Philosophy, The Hebrew University, Jerusalem	2007
Honorary Doctor of Medical Science, Queens University, Belfast	2007
C. David Marsden Lectureship Award, Movement Disorder Society	2008
Vanderbilt Prize in Biomedical Science	2008
M.I.T. Institute Professor	2008

Honorary Member Award – Movement Disorders Society	2010
The Kavli Prize	2012
Diana Helis Henry and Adrienne Helis Malvin Medical Research Foundations Joint Award Lecture Series in Parkinson's Disease Research	2015
Member, American Philosophical Society	2016
The Gruber Neuroscience Prize	2018

Honorary Memberships:

Royal Academy of Medicine, Spain	1989
International Basal Ganglia Society	2007
The Movement Disorder Society	2010
Foreign Member, The Norwegian Academy of Science and Letters	2012

Selected Named Lectures:

First Special Lecture, Society for Neuroscience, Dallas, Texas	1985
Gordon H. Scott Memorial Lectureship, Detroit, Michigan	1986
John D. French Lectureship, UCLA, Los Angeles, California	1994
Olsweski Lectureship, Montreal Neurological Institute, Montreal, Canada	1994
Rushton Lecture, Florida State University, Tallahassee, Florida	1995
Servier Lecture, University of Montreal, Montreal, Canada	1995
Ragnar Granit Lecture, Karolinska Institute, Stockholm, Sweden	1995
Special Lecture, Society for Neuroscience, Washington, D.C.	1996
Grass Lecture, University of Indiana, Bloomington, Indiana	1999
George B. Murray Lecture, Massachusetts General Hospital, Boston, Massachusetts	1999
Melvin D. Yahr Lecture, Mt. Sinai School of Medicine, CUNY, New York, New York	1999
Distinguished Visiting Scientist Lecture, Albany Medical College, Albany, New York	2000
Plenary Lecture, French Movement Disorder and Basal Ganglia Societies, Paris, France	2000
NIH Tri-Institute Seminar, Bethesda, Maryland	2001
Robert S. Dow Neuroscience Award Lecture, Portland, Oregon	2002
NIH Director's Lecture, Bethesda, Maryland	2002
Plenary Lecture, 6th IBRO World Congress of Neuroscience, Prague, Czech Republic	2003
John Flynn Memorial Lecture, Yale University, New Haven, Connecticut	2004
Norman Geschwind Memorial Lecture, Beth Israel-Deaconess Hospital, Boston, Massachusetts	2004
Distinguished Lecture and Rodolfo Rivas Memorial Lecture, University of Maryland, College Park, Maryland	2005
Plenary Lecture, Gordon Conference on Catecholamines, Andover, New Hampshire	2005
Plenary Lecture, Spanish Society on Neuroscience, Madrid, Spain	2005
Heller Lecture in Computational Neuroscience, Hebrew University, Jerusalem, Israel	2006
Millward Memorial Lecture, Brown University, Providence, Rhode Island	2006
Special Lecture, Society for Neuroscience, Atlanta, Georgia	2006
American Academy of Neurology Annual Meeting, Plenary Lecture, Chicago, Illinois	2008
C. David Marsden Lecture, Movement Disorder Society's 12th International Congress, Chicago, Illinois	2008
M.I.N.D. Institute Distinguished Lecture, Davis, California	2008
Lord Adrian Lecture, Cambridge, England	2008
Mildred Trotter Lecture, Washington University, St. Louis, Missouri	2009
David Smith Lecture, Oxford University, Oxford, England	2010
The Mellon Award Lecture, University of Pittsburgh, Pittsburgh, Pennsylvania	2010
Narabayashi Lecture, International Congress of Clinical Neurophysiology, Kobe, Japan	2010
Plenary Lecture, Turkish Neuroscience Meeting, Istanbul, Turkey	2011
Presidential Lecture, Society for Neuroscience, Washington, D.C.	2011
Segerfalk Lecture, Lund University, Lund, Sweden	2012
National Taiwan University Lecture, Taipei, Taiwan	2012
The Kavli Laureate Lecture, Oslo, Norway	2012
The Kavli Public Lecture, Bergen, Norway	2012

Carnegie Foundation Kavli Laureate Lecture, Washington, DC	2012
Druker Memorial Lecture, Beth Israel Deaconess Medical Center, Boston, Massachusetts	2013
Dean for Science Lecture in Neuroeconomics, New York University, New York, New York	2014
Jan and Dan Duncan Neurological Research Institute Distinguished Lecture, Houston, Texas	2014
Diana Helis Henry and Adrienne Helis Malvin Medical Research Foundations Joint Lecture Series in Parkinson's Disease Research	2015
McClintock Lecture, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York	2016
Plenary Lecture, 10th Annual Canadian Association for Neuroscience Meeting, Toronto, Canada	2016
Ruth K. Broad Foundation Seminar Series on Neurobiology and Disease, Duke University, Durham, North Carolina	2017

Advisory Boards and Committees (National and International):

National Science Foundation	
Panel for Neurobiology	1976-1979
Neuroscience Oversight Review Board	1986
Society for Neuroscience	
Council	1976-1980
Program Committee	1976-1978
Gerard Prize Selection Committee	1989,1991
Board of Scientific Counselors of the NINCDS (National Institutes of Health)	1980-1984
American Association of Anatomists	
Cajal Club, Program Committee	1977
President, Cajal Club	1983-1984
C. Judson Herrick Award Committee	1985
Max Planck Institute for Psychiatry, Munich, Germany	1985-1989
Institute of Basic Research Scientific Advisory Board	1989-1998
The McKnight Endowment Fund for Neuroscience	1986-1996
Vice President	1986-1996
Board of Directors	1986-1996
Research Project Awards Committee	1986-1996
Development Awards Committee	1986-1996
Member, Senior Review Committee	1987-1996
Tourette Syndrome Association	1986-1992
Scientific Advisory Board	
Dystonia Medical Research Foundation	
Scientific Advisory Board	1989-1994
United Parkinson's Disease Foundation	
Scientific Advisory Board	1989-
International Brain Research Organization	
Executive Committee	1991-1997
Encyclopedia of Neuroscience	
Scientific Advisory Board	1993-
National Academy of Sciences	
Neuroscience Award Selection Committee, Chair	1993
Class II Membership Committee	1995-1998
Chair, Section of Neurobiology	1995-1998
Class II Secretary	2001-
Beckman Institute	
External Advisory Committee	1993-2007
Institute of Medicine	
Board on Neuroscience and Behavioral Health	1997-2001
Chair, Board on Neuroscience and Behavioral Health	2000-2001
National Parkinson Foundation	
Scientific Advisory Board	1997-2008

National Institute of Mental Health	
National Advisory Mental Health Council	1997-1999
Hereditary Disease Foundation	
Scientific Advisory Board	2000-2006
Alzheimer Research Forum	
Scientific Advisory Board	2000-
Max Planck Institute for Cybernetic Biology, Tübingen, Germany	
Scientific Advisory Board	2000-2006
American Association for the Advancement of Science	
Member-at-Large, Section Committee, Section on Neuroscience	2001-2005
Movement Disorder Society	
International Executive Committee	2001
Member, American College of Neuropsychopharmacology	2003
Society for Neuroscience International Affairs Committee – US National Committee (IAC-USNC)	
to the International Brain Research Organization (IBRO)	2007
Stockholm Brain Institute, Stockholm, Sweden	
Scientific Advisory Board	2007- 2010
Institut du Cerveau et de la moelle épinière (ICM)	
Scientifie Advisory Board	2008-2013
Ernst Strüngmann Forum, Frankfurt, Germany	
Scientific Advisory Board	2008-
Biomedical Science Advisory Board at Vanderbilt University	2010-
Eidgenossische Technische Hochschule Zurich Scientific Advisory Board	2010-
Dopamine International Advisory Board	2011
MIT Presidential Search Committee	2012
Foundation IPSEN	2012-2016
Neuronal Plasticity Prize Jury	
Max Planck Florida Institute	
Scientific Advisory Board	2013-
Beckman Institute, University of Illinois at Urbana-Champaign	
External Advisory Committee	2013-
Bachmann-Strauss Dystonia & Parkinson Foundation, Inc.	
Scientific Advisory Board	2013-
Troland Research Award Selection Committee	2013
The Lurie Center for Autism	2013-
Scientific Advisory Board	
Pradel Research Award Committee (NAS)	2014
NINDS Committee for Research Challenges and Opportunities for Parkinson's Disease	2014
American Philosophical Society, the Karl Spencer Lashley Award	2017
Selection Committee Member	

Editorial Boards:

Neuroscience Letters	1975-1984
Neuroscience	1976-1999
Journal of Comparative Neurology	1980-1984
	2008-2012
Neuroscience Research Communications	1986-
Movement Disorders	1989-1993
Neurodegeneration	1991-1997
Journal of Neurophysiology	1992-
Journal of Neuroscience	1980-1983
	1988-2004
Synapse	1992-2004
Biological Psychiatry	1993-

Anales de Anatomía	1993
Parkinsonism and Related Disorders	1994-1999
Neuroscience Research	2000
Neuropsychopharmacology	2000-
Frontiers in Neuroscience	2008-
Journal of Parkinson's Disease	2010-

Research: Ann Graybiel discovered that the striatum, the largest subcortical structure of the mammalian forebrain, has a modular organization that is now recognized as shaping molecular signaling in the striatum and plasticity related to habit learning, repetitive behavior, motivational control, and human neurologic and neuropsychiatric disorders.

When Graybiel began her work, the striatum was known by physicians as being important for extrapyramidal motor disorders, but the striatum was largely ignored by basic scientists, as it was thought to be a primitive, homogeneous structure. Graybiel nevertheless focused on the striatum, and in 1978, with student Ragsdale, discovered the neurochemical compartments of the human striatum, which she named as striosomes and the surrounding matrix. It is now known that this striosome-matrix architecture is altered in some human neurological and neuropsychiatric disorders and in animal models of these conditions, and that this architecture is critical to the cholinergic-dopaminergic balance required for normal motor and motivational function.

Graybiel and her students discovered that nearly all striatal neurotransmitter systems, including the critical dopaminergic-cholinergic systems, are differentially expressed according to this striosome-matrix architecture. She and her group discovered that this molecular modularity is observed by the distributions of the input-output circuits of the striatum, by the lineage programs giving rise to striatal neurons, and by the development of their dopaminergic innervation in species ranging from rodents to humans. Critically, Graybiel showed that striosomes correspond to the sites at which the dopamine-containing nigrostriatal tract first terminates during development. She and her students went on to suggest that striosomes are critical components of striato-nigro-striatal loops affected in Parkinson's disease. In successive studies, she and her group found selective striosome-matrix neuronal vulnerability patterns in non-human primate and rodent models of Parkinson's disease, in models of dopa-responsive dystonia and L-dopa induced dyskinesias, and with colleagues discovered that striosomes are selectively vulnerable in Huntington's patients exhibiting pronounced mood problems. She and her students then found that striosomes have differential sensitivity to many dopaminergic drugs, further pointing to dopamine-related functions. Reinforcing these findings, Graybiel and group discovered novel CalDAG-GEF genes that link Ca^{2+} and DAG signaling to Ras superfamily (Ras, Rap) signaling that have complementary expression in striosome and matrix compartments. They showed that these genes are dysregulated in human Parkinson's and Huntington's brain samples and in corresponding mouse models. In her latest work, she and her group have, using mice that they have engineered, discovered that striosomes specifically target subsets of nigral dopamine-containing neurons and their bundled dendrites in highly elaborated arbors forming 'striosome-dendron bouquets'.

In parallel, Graybiel with her students discovered that the large matrix compartment surrounding striosomes is itself modular, with 'matrisomes' organizing information flow from neocortex to basal ganglia output nuclei. Graybiel likened this physical architecture to learning architectures in computational models and suggested that this organization could underlie habit learning. She put this hypothesis to the test: her group made the first chronic recording from ensembles of neurons in the striatum and neocortex of awake, behaving animals as they learned new tasks and developed habits. They discovered wholesale plasticity in response properties of the striatal neurons as habits were formed, with activity eventually marking the beginning and end of the habitual behaviors as though chunking together positively reinforced behavioral repertoires. The task-bracketing patterns that they found in rodents, and now in non-human primates, suggest a potential biomarker of habitual behavior.

Capitalizing on newly available optogenetic methods, Graybiel and her group then manipulated the corticostriatal circuits they had identified electrophysiologically. They discovered that they could block the formation of habits, block the expression of already formed habits and even toggle habits on and off, and that they could selectively block compulsive behavior in a mouse model of compulsive behavior. This work, still on-going, suggests a stunning level of on-line control of even apparently semi-automatic behaviors. Graybiel and group linked these neural patterns to oscillatory field potential patterns important in Parkinson's and related disorders. In long-term, chronic fast-scan cyclic voltammetric recordings in behaving animals, they discovered a ramping dopamine release related to proximity to reward during learning, suggesting a novel form of dopamine signaling paralleling classical phasic dopamine signaling.

Critically, in early work, Graybiel, with fellow Eblen, discovered that striosomes in macaques receive preferential input from cortical regions implicated, in humans, in anxiety, depression and emotional tone. With the chronic multi-electrode methods that her group developed for non-human primates, Graybiel and Amemori then found that they could modulate emotion-related decision-making by electrical microstimulation of these striosome-projecting cortical regions, inducing pessimistic or optimistic choices, and have shown that these effects are reversible by anxiolytic treatment. In rodents, she with her fellows has now provided causal evidence that cortico-striosomal circuits are critical for decision-making requiring cost-benefit integration. Graybiel with her group has thus discovered functionally critical neural circuits leading from affect-related cortical regions through striosomes to the dopamine system. This work has uncovered a pivotal role for striosomal circuits in the modulation of motivational signaling affected in a range of human disorders. Graybiel's work has ever-increasing importance for understanding circuits disrupted in neurological and neuropsychiatric disorders, their cellular and genetic basis, and the therapeutic strategies needed to relieve them.

Synopsis of Scientific Contributions of Graybiel and coworkers (please see list of publications for manuscripts):

Visuomotor Systems

- Identified multiple-channel cortical connectivity of the pulvinar system of the thalamus. 1970-1983
- Delineated brainstem connections of oculomotor and visuomotor systems and discovered nearly every extrageniculate visual and visuo-oculomotor pathway in the brainstem. 1974-1980
- Identified mosaic organization of systems afferent to the superior colliculus. 1975-1978
- Delineated chemical compartments and mosaic organization of the superior colliculus. 1978-1984
- Identified sensory maps in the claustrum. 1980
- Identified chemical compartments of the visual thalamus and related these to the afferent-efferent subdivisions of these thalamic regions. 1980-1983

Basal Ganglia

Striosomes and Matrisomes

- Identified histochemical compartments of the human striatum (striosomes and matrix). 1978
- Demonstrated that striatal inputs and outputs are organized in relation to striosomes. 1979-present
- Identified chemical compartments of embryonic and neonatal striatum and showed that these correspond to dopamine islands. 1980-1984
- Demonstrated that neuropeptides in striatum follow striosomal architecture and, subsequently, that most other neurotransmitter-related substances do so as well. 1981
- Demonstrated that striosomes are ontogenetic units of the striatum with defined developmental birthdates of striatal neurons. 1982
- Identified mosaic organization of the striatal matrix (matrisomes) using combined electrophysiology and anatomy. 1986
- Demonstrated that psychomotor stimulants induce immediate-early genes in striosome/matrix-specific patterns in the striatum. 1990-1993
- Identified convergent-divergent architecture of functionally-defined corticostriatal and striatopallidal circuits and likened this architecture to expert-systems learning architectures. 1991-1995
- Demonstrated that chronic psychomotor stimulant exposure induces network-level changes in gene expression in the striatum leading to striosome-enhanced induction patterns in rodents. 1996
- Demonstrated high correlation between striosome-predominant striatal gene expression patterns and stereotypic behavior induced by chronic exposure to psychomotor stimulants. 1999-2000
- Demonstrated that natural movement and sensorimotor inputs activate striatal matrix. 2002
- Demonstrated that after chronic psychomotor exposure, the stimulant induces striosome-predominant early-gene expression in the primate striatum. 2004
- Demonstrated that mood dysfunction in Huntington's disease patients is correlated with differential degeneration in striosomes of the striatum. 2006
- Demonstrated that differential degeneration of striosomes occurs in a mouse model of DOPA-responsive dystonia. 2008
- Demonstrated that DYT-3 dystonia-related protein N-TAF1 is enriched in the striosomal compartment of the striatum. 2011
- Demonstrated that microstimulation in striosome-projecting region of macaque anterior cingulate cortex induces negative value-based decision-making in non-human primates. 2012
- Identified a specific striosome-targeting corticostriatal circuit that selectively mediates decision-making under cost-benefit conflict conditions. 2015
- Demonstrated highly patterned prenatal development patterns of birth-dated striosomal and matrix neurons. 2015
- Demonstrated striosome-matrix developmental patterning of an autism spectrum disorder gene and its regulation. 2016
- Discovered 'striosome-dendron bouquets', elaborate input arbors of striosomal fibers intertwined with the bundled dendrites of dopamine-containing neurons of the substantia nigra. 2016
- Discovered that cholinergic interneurons in the striatum innervate differentially striosomes and matrix and can affect spike timing of their neurons by mechanisms blocked by 2017

stereotypy-inducing levels of amphetamine.

- Discovered that the functional dynamics of cortico-striosomal circuits are disrupted by exposure to chronic stress, through stress-induced dysregulation of an intrastriatal local circuit mechanism. 2017
- Demonstrated that the major components of striatal architecture are set up by sharply contrasting neural progenitor programs at the inception of striatal development (in review). 2017
- Developed the first *in vivo* 2-photon imaging of striosomes by combining birthdate-labeling with imaging in mice performing reinforcement learning tasks. 2017

Physiology of Habit Learning and Cortico-Striatal Circuits, Neuroplasticity

- Demonstrated learning-related plasticity in spike activity of striatal tonically active neurons (TANs) during behavioral conditioning in primates, and showed that dopamine modulates expression of this neuroplasticity. 1994-1995
- Demonstrated that the activity of neurons in the striatum undergoes major reorganization as rats learn procedural tasks and form habits. 1999
- Demonstrated that thalamic inputs regulate expression of learning-related plasticity of striatal TANs. 2001
- Demonstrated that striatal TAN activity in macaque monkeys predicts behavioral response probability. 2002
- Identified neural activity in macaque monkeys prefrontal cortex representing boundaries of action sequences. 2003
- Demonstrated that striatal projection neurons exhibit multiple spiking changes during acquisition, extinction and reacquisition of a procedural "habit" task. 2005
- Demonstrated existence of highly contrasting learning-related neural dynamics in associative and sensorimotor striatum. 2010
- Demonstrated that optimal habits emerge without training in non-human primates. 2010
- Demonstrated that already acquired habits can be broken and reinstated in rats by on-line optogenetic inhibition of medial prefrontal cortex. 2012
- Demonstrated that dopamine depletion and L-DOPA treatment have selective effects on plasticity of learning-related ensemble spike activity in the sensorimotor striatum. 2013
- Demonstrated that dorsolateral striatum and medial prefrontal cortical habit-related regions exhibit strikingly different dynamics of neuroplasticity during habit learning, habit loss, and habit reinstatement. 2013
- Demonstrated that habit formation can be blocked by on-line optogenetic inhibition of medial prefrontal cortex. 2013
- Demonstrated that acquired compulsive behavior can be selectively blocked by on-line optogenetic excitation of orbitofrontal cortex and by excitation of orbitofrontal terminals within the striatum. 2013
- Discovered a novel, extended form of dopamine release signaling that occurs during approach to valued goals by use of fast-scan cyclic voltammetry in rats. 2013
- Demonstrated bivalent reinforcement signaling by cholinergic interneurons in ventral striatum during habit learning. 2014
- Demonstrated heightened stereotypy in mice genetically engineered to express exaggerated acetylcholine release. 2014
- Demonstrated that motivation and affective judgments elicit differential responses in cohorts of neurons in prefrontal cortex and cingulate cortex of macaque monkeys. 2015
- Demonstrated that natural habit learning in non-human primates leads to development of a caudate signal representing the integrated cost and benefit of the acquired behavior. 2015
- Demonstrated that acquisition of sequences of movements leads to bracketing of the first and last members of the sequence by spike activity of striatal neurons but not primary motor cortical neurons (in review). 2017

Theoretical

- Proposed that the basal ganglia can act to affect cortical cognitive pattern generators, in addition to brainstem/spinal motor pattern generators. 1997

- Proposed that the basal ganglia act to enable chunking of action repertoires. 1998
- Proposed attractor state model of striatal processing. 2001
- Proposed the concept of 'neural exploration' and 'neural exploitation' to parallel behavioral exploration and exploitation in procedural learning. 2005
- Proposed hierarchical learning model suggesting that striosome-matrisome architecture of the striatum provides template for context-specific learning whereby striosomes and associated cholinergic interneurons generate responsibility signals. 2011
- Proposed a model of the cortico-striosomal circuit in which the circuit performs cost-benefit integration that is elicited under conditions of motivational conflict. 2015
- Developed a non-linear multi-dimensional hidden state (NMHS) approach to complex neural circuit analysis. 2016

Striatal Oscillations

- Demonstrated that beta-band (10-25 Hz) oscillations are a prominent feature of striatal activity in normal, awake behaving macaques. 2003
- Demonstrated temporally coordinated LFP activity in simultaneous recordings from neocortex and striatum of awake, behaving macaques. 2005
- Demonstrated that theta rhythms in the striatum and hippocampus become coordinated during procedural learning. 2007-2008
- Demonstrated network-level shifts in frequencies of oscillatory rhythms and synchronized spike firing in ventromedial striatum during habit learning. 2011
  Discovered that multiple oscillatory frequency bands in local field potentials are selectively altered by dopamine depletion and L-DOPA treatment. 2012
- Demonstrated different co-occurring learning-related theta sub-band oscillation activity in sensorimotor and associative striatal regions during habit learning. 2014
- Demonstrated that brief bursts of beta oscillation mark the end of successfully completed task performance in non-human primates. 2015

Other work on basal ganglia

- Demonstrated that mouse weaver mutation depletes dopamine in patterns resembling those of Parkinson's disease. 1984
- Identified chemical compartments in substantia nigra pars compacta. 1989
- Demonstrated that intrastriatal grafts of fetal striatal cells develop striatal phenotype. 1989-1994
- Documented brain and behavioral consequences of dopamine D1 and D3 dopamine receptor deletion in transgenic mice. 1994-1996
- Introduced striatal organotypic slice cultures for studying regulation of gene expression in developing striatum. 1994
- Demonstrated that spatially selective phosphatase gates control cAMP-and Ca^{2+}-mediated CREB phosphorylation in developing striatum using organotypic slice cultures. 1996
- Identified chemospecific compartments ("nigrosomes") in human substantia nigra pars compacta and demonstrated that they are markers for neurodegeneration patterns in Parkinson's disease. 1999
- Demonstrated existence of time-stamp encodings of time in cortico-basal ganglia circuits. 2009
- Demonstrated sharp increases in thyrotropin releasing hormone in striatum correlate with L-DOPA-induced dyskinesias. 2010
- Developed a chronic recording system for non-human primates with >100 independently movable electrodes. 2011
- Discovered that humanized Foxp2, engineered into mice, enhances learning to shift from place to habit strategies of performance. 2014
- Demonstrated, with colleagues, that Foxp2 is a critical controller of corticostriatal synapse formation during development. 2016

Methodological Development

- Developed microiontophoretic method for *in vivo* tracer experimentation. 1974
- Developed a silver intensification method for immunohistochemistry. 1996
- Developed a multi-electrode recording technique and devise with independently movable 2012

electrodes for long-term, chronic neural recording in non-human primate.

- Developed a non-invasive head-holding devise for chronic non-human primate neural recording to avoid use of invasive head immobilization. 2015
- Developed novel multi-stage algorithm for automated spike-sorting of high-dimensional neuronal data with high background noise. 2015
- Developed novel multi-channel recording probes for fast-scan cyclic voltammetry and recording. 2017

Novel Gene Families

- Cloned and characterized the cAMP-GEF family of brain-enriched genes. 1998
- Cloned and characterized the CalDAG-GEF family of brain-enriched genes and demonstrated that they are striatum-enriched and have differential striosome-enriched (CalDAG-GEFII) and matrix-enriched (CalDAG-GEFI) distributions in the striatum. 1998
- Demonstrated that CalDAG-GEFI is essential for platelet aggregation and thrombus formation. 2004
- Demonstrated that CalDAG-GEFI is essential to neutrophil adhesion and trafficking. 2006
- Demonstrated that CalDAG-GEFI is essential for specific forms of neuroplasticity in the striatum including the development of drug-induced sensitization of stereotypic behavior and long-term potentiation (abstract only, in progress). 2005-present
- Demonstrated, with collaborators, that that the human LAD-III syndrome is associated with defective expression of CalDAG-GEFI in the hematopoietic system. 2007
- Demonstrated that the striatum-enriched genes CalDAG-GEFI and CalDAG-GEFII are strongly and inversely dysregulated in relation to severity of L-DOPA-induced dyskinesias (AIMs) in rat model of Parkinson's disease. 2009
- Demonstrated that CalDAG-GEFI down-regulation is protective in a model of Huntington's disease neurodegeneration and related to lowered expression of Htt nuclear aggregates. 2010
- Demonstrated that CalDAG-GEFI constitutive and conditional deletion in mice promotes behavioral repetitiveness and affects selectively a muscarinic cholinergic receptor-driven signaling pathway in the mouse striatum (in preparation and on-going). 2014-present
- Discovery with collaborators of patients with CalDAG-GEFI mutations (in preparation) 2017

Publications of Ann Martin Graybiel:

Books:

1. Kimura, M. and Graybiel, A. M., eds. (1995) *Functions of the Cortico-Basal Ganglia Loop.* Springer-Verlag: New York.
2. Graybiel, A.M., Delong, M.R., and Kitai, S.T., Eds. (2003) *The Basal Ganglia VI*. New York: Kluwer Academic/Plenum.
3. Grillner, S. and Graybiel, A.M., Eds. (2006) *Microcircuits: The Interface between Neurons and Global Brain Function*. Cambridge, MA: MIT Press.

Papers:

1. Graybiel, A.M. and Held, R. (1970) Prismatic adaptation under scotopic and photopic conditions. *J. Exp. Psychol.*, 85:16-22.
2. Graybiel, A.M. (1970) Some thalamocortical projections of the pulvinar-posterior system of the thalamus in the cat. *Brain Res.*, 22:131-136.
3. Graybiel, A.M. (1971) Some fiber connections of the posterior thalamus in the cat. Doctoral dissertation, Massachusetts Institute of Technology.
4. Graybiel, A.M. (1972) Some extrageniculate visual pathways in the cat. *Invest. Ophthalmol.*, 11:322-332.
5. Graybiel, A.M. (1972) Some fiber pathways related to the posterior thalamic region in the cat. *Brain Behav. Evol.*, 6:363-393.
6. Graybiel, A.M. (1972) Some ascending connections of the pulvinar and nucleus lateralis posterior of the thalamus of the cat. *Brain Res.*, 44:99-125.
7. Graybiel, A.M. (1973) The thalamo-cortical projection of the so-called posterior nuclear group: a study with anterograde degeneration methods in the cat. *Brain Res.*, 49:229-244.
8. Graybiel, A.M., Nauta, H.J.W., Lasek, R.J., and Nauta, W.J.H. (1973) A cerebello-olivary pathway in the cat: an experimental study using autoradiographic tracing techniques. *Brain Res.*, 58:205-211.
9. Graybiel, A.M. (1974) Studies on the anatomical organization of posterior association cortex. In: *The Neurosciences: Third Study Program*, F.O. Schmitt and F.G. Worden, Eds. Cambridge: MIT, pp. 205-214.
10. Graybiel, A.M. and Devor, M. (1974) A microelectrophoretic delivery technique for use with horseradish peroxidase. *Brain Res.*, 68:167-173.
11. Graybiel, A.M. (1974) Visuo-cerebellar and cerebello-visual connections involving the ventral lateral geniculate nucleus. *Exp. Brain Res.*, 20:303-306.
12. Graybiel, A.M. and Hartwieg, E.A. (1974) Some afferent connections of the oculomotor complex in the cat: an experimental study with tracer techniques. *Brain Res.*, 81:543-551.
13. Graybiel, A.M. (1975) Wallerian degeneration and anterograde tracer methods. In: *The Use of Axonal Transport for Studies of Neuronal Connectivity,* W.M. Cowan and M. Cuénod, Eds. Amsterdam: Elsevier, pp. 174-216.
14. Graybiel, A.M. (1975) Anatomical pathways in the brain stem oculomotor system. In: *Eye Movements and Movement Perception*, J. Lott Brown, Ed. Rochester, NY: Center for Visual Science, pp. 37-38.
15. Graybiel, A.M. (1975) Anatomical organization of retinotectal afferents in the cat: an autoradiographic study. *Brain Res.*, 96:1-23.
16. Gould, B.B. and Graybiel, A.M. (1976) Afferents to the cerebellar cortex in the cat: evidence for an intrinsic pathway leading from the deep nuclei to the cortex. *Brain Res.*, 110:601-611.
17. Graybiel, A.M. (1976) Evidence for banding of the cat's ipsilateral retinotectal connection. *Brain Res.*, 114:318-327.
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