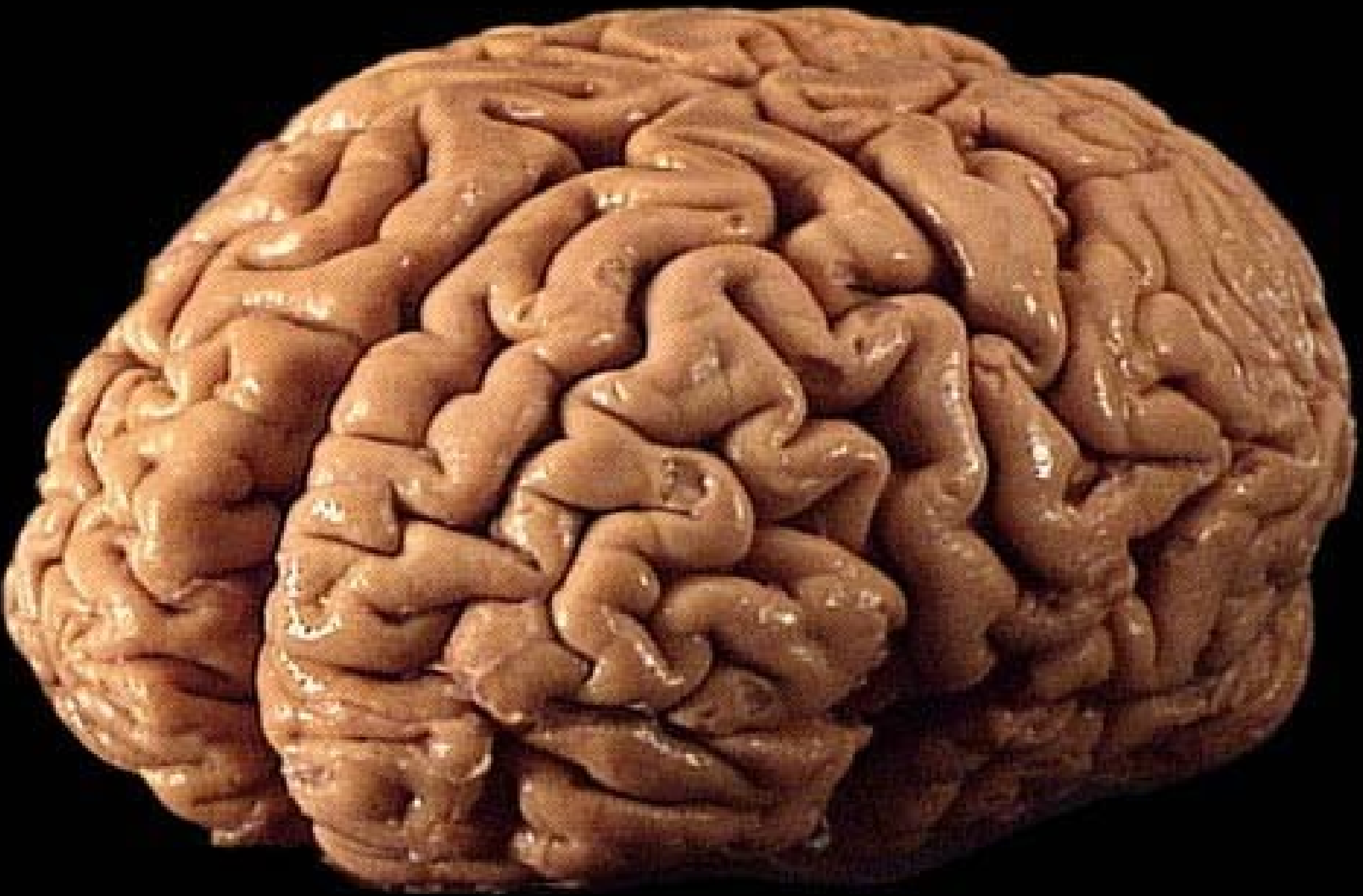


# Neuroscience and Informatics



Donald Doherty, Ph.D.  
Founder and Chief Executive Officer  
Brainstage, Inc.

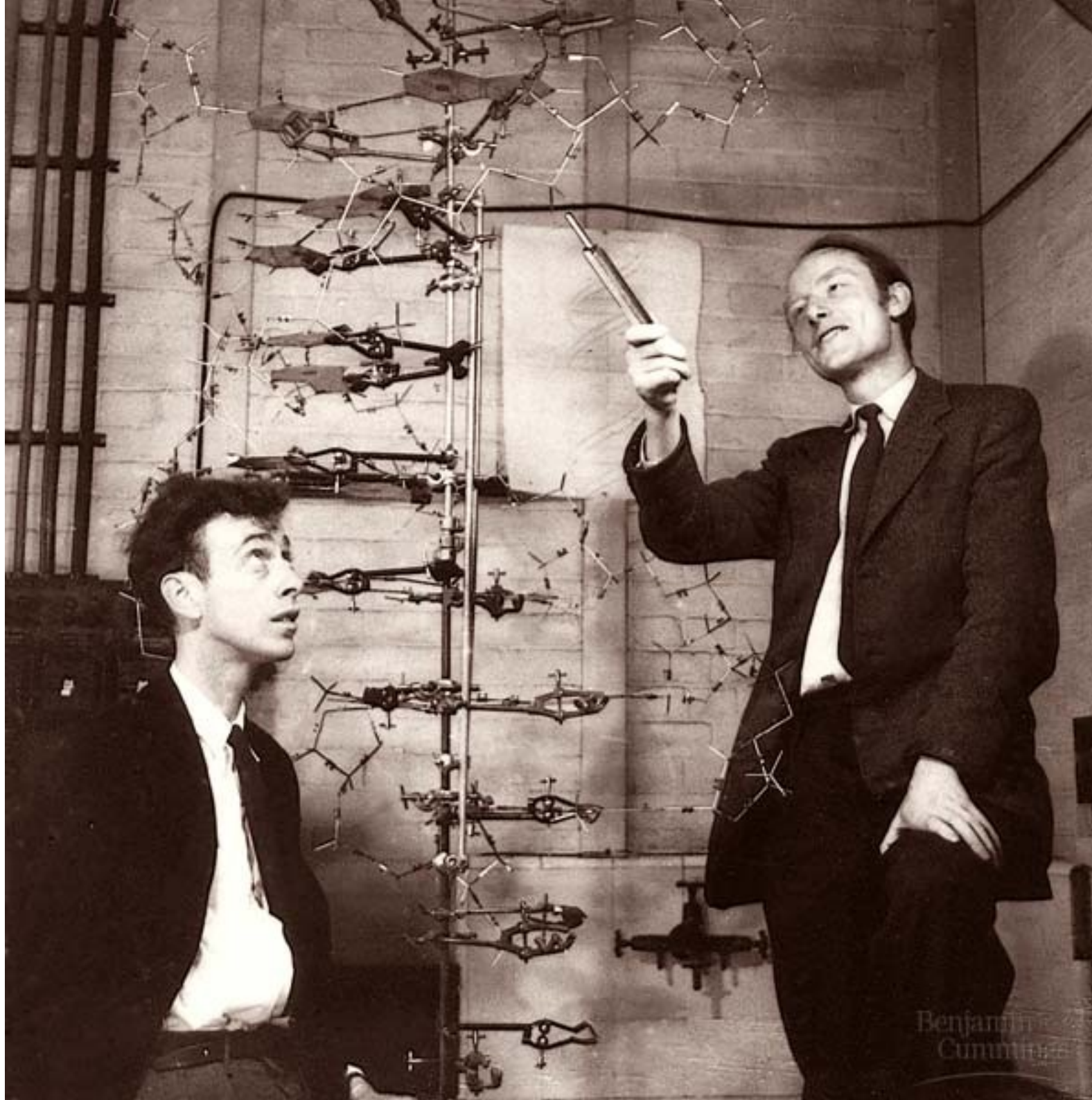


# Nicolaus Steno 1638-1686

“There are two ways only of coming to knowing a machine: one is that the master who made it should show us its artifice; the other is to dismantle it and examine its most minute parts separately and as a combined unit.”

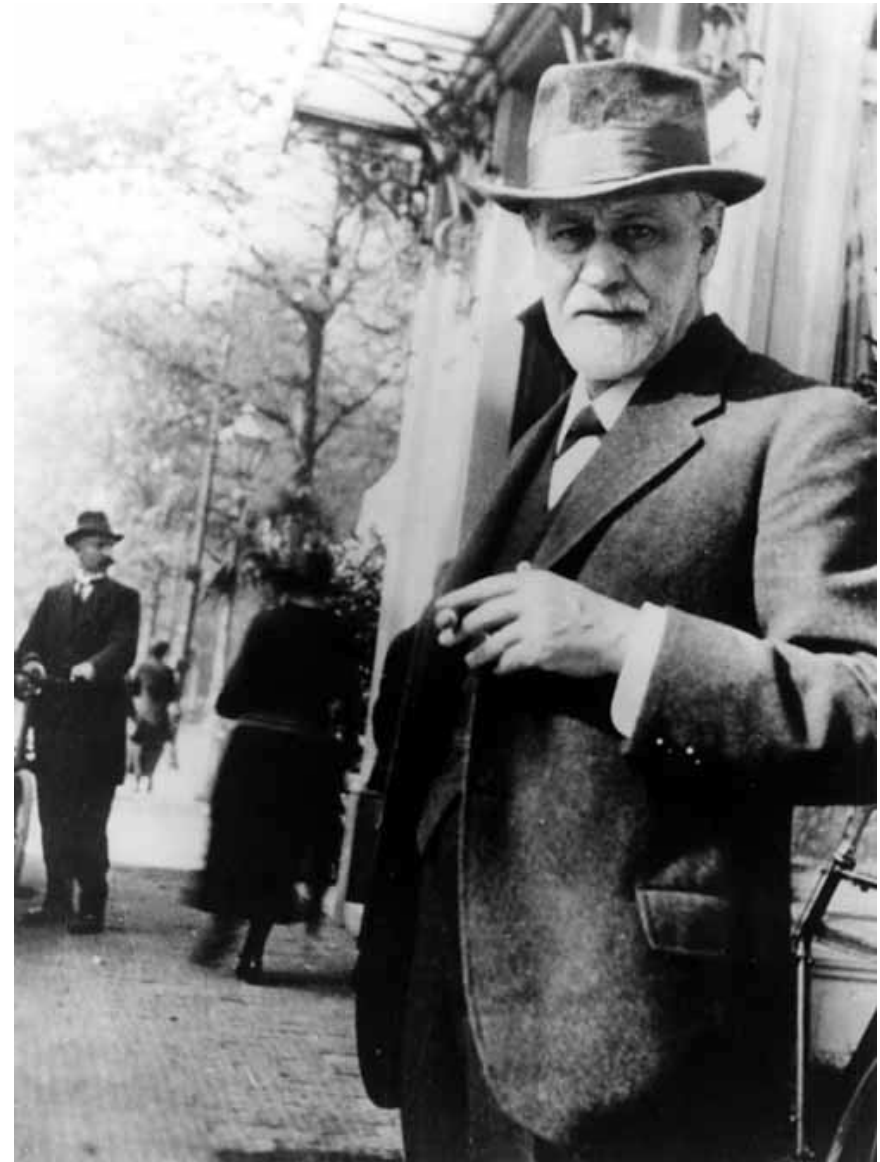
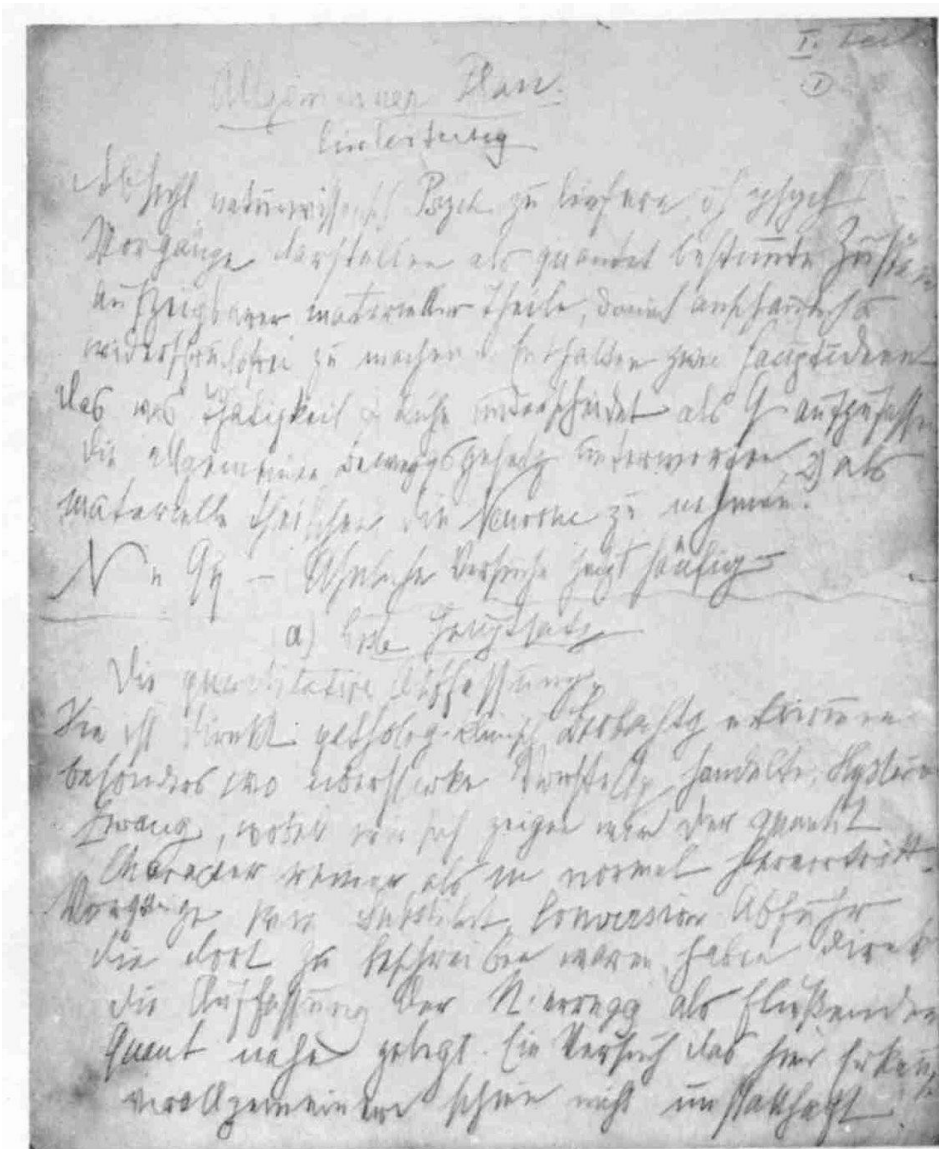
Discours de Monsieur Stenon sur  
L'Anatomie du Cerveau ("M. Steno's lecture  
on the anatomy of the brain", Paris 1669)





Benjamin  
Cummings

# Freud's Project for a Scientific Psychology (1895)





Review

## The Project for a Scientific Psychology (1895): a Freudian anticipation of LTP-memory connection theory

Diego Centonze<sup>a,b,\*</sup>, Alberto Siracusano<sup>c</sup>, Paolo Calabresi<sup>a,b</sup>, Giorgio Bernardi<sup>a,b</sup>

<sup>a</sup>*Clinica Neurologica, Dipartimento di Neuroscienze, Università Tor Vergata, Rome, Italy*

<sup>b</sup>*IRCCS Fondazione Santa Lucia, Rome, Italy*

<sup>c</sup>*Clinica Psichiatrica, Dipartimento di Neuroscienze, Università Tor Vergata, Rome, Italy*

Accepted 6 July 2004

Available online 18 August 2004

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### Abstract

Long-term potentiation (LTP) of synaptic transmission is considered a reliable cellular model of several forms of learning and memory. Described for the first time in 1973, this synaptic phenomenon consists in the enduring facilitation of the communication between two neurons in response to the sustained activation of the synapses by which they are interconnected. In a book of 1895 entitled *Project for a Scientific Psychology*, Sigmund Freud theorized about the possibility of representing memory at the synaptic level as “a permanent alteration following an event”, and anticipated several crucial physiological properties of LTP.

In the present article we aim at presenting Freudian theory on the functional organization of the nervous system developed in the *Project*, with particular respect to his ideas of the cellular bases of memory.

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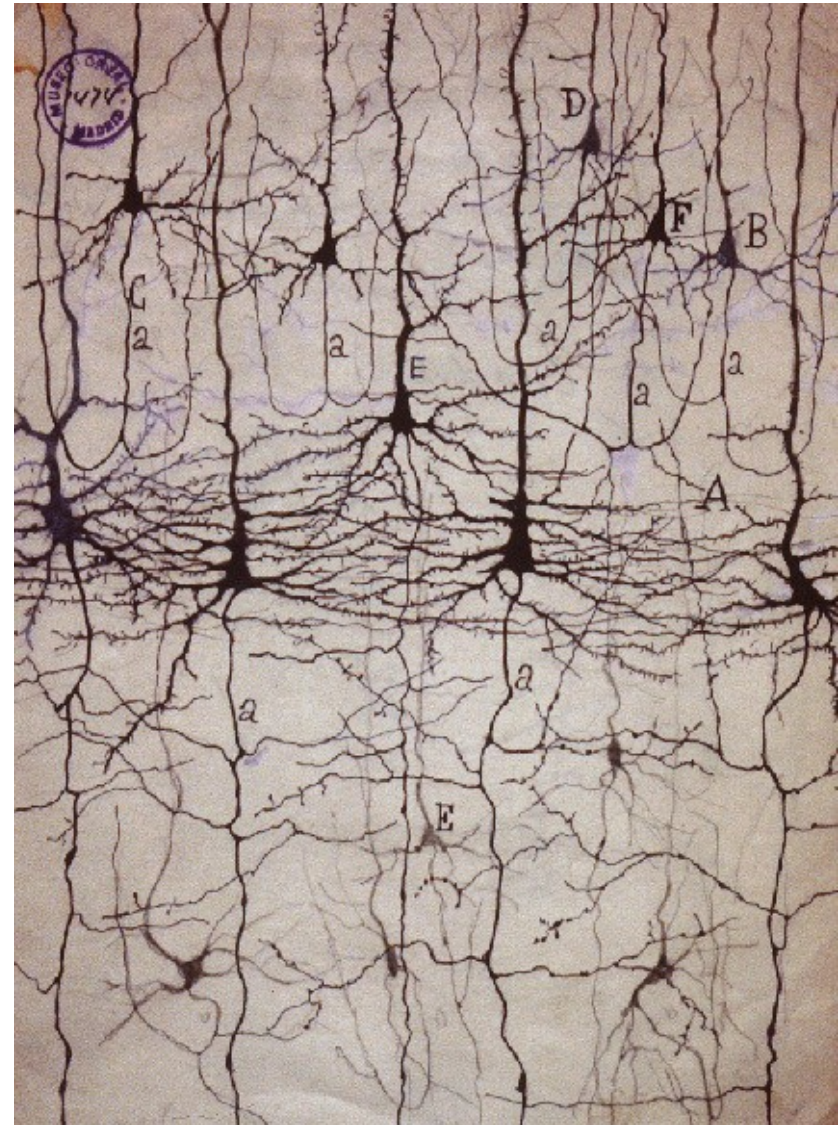
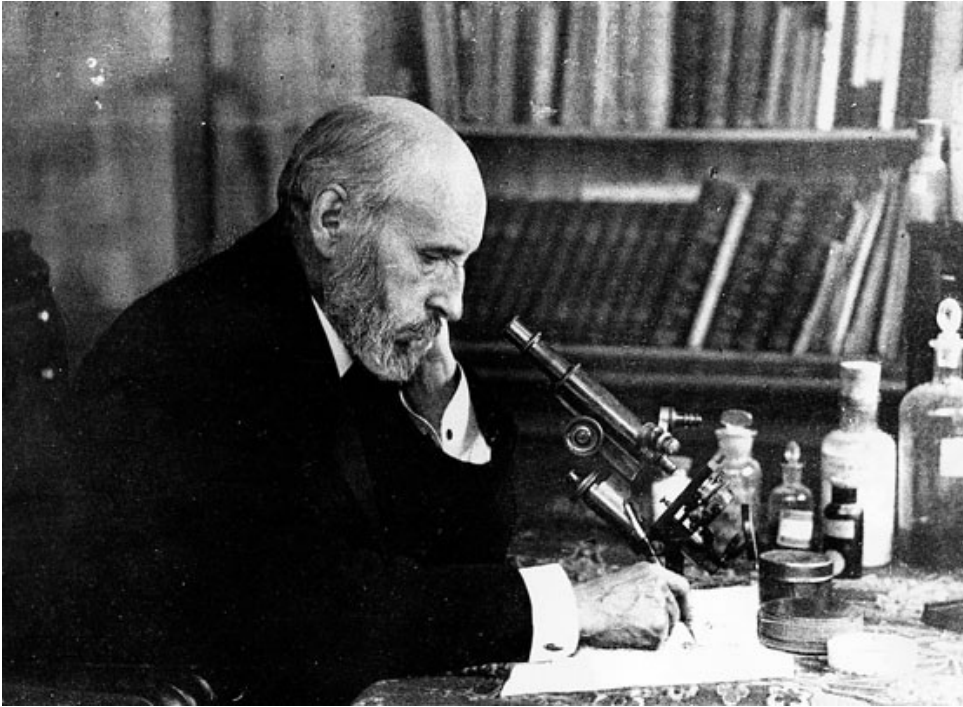
*Theme:* Neural basis of behavior

*Topic:* Learning and memory: physiology

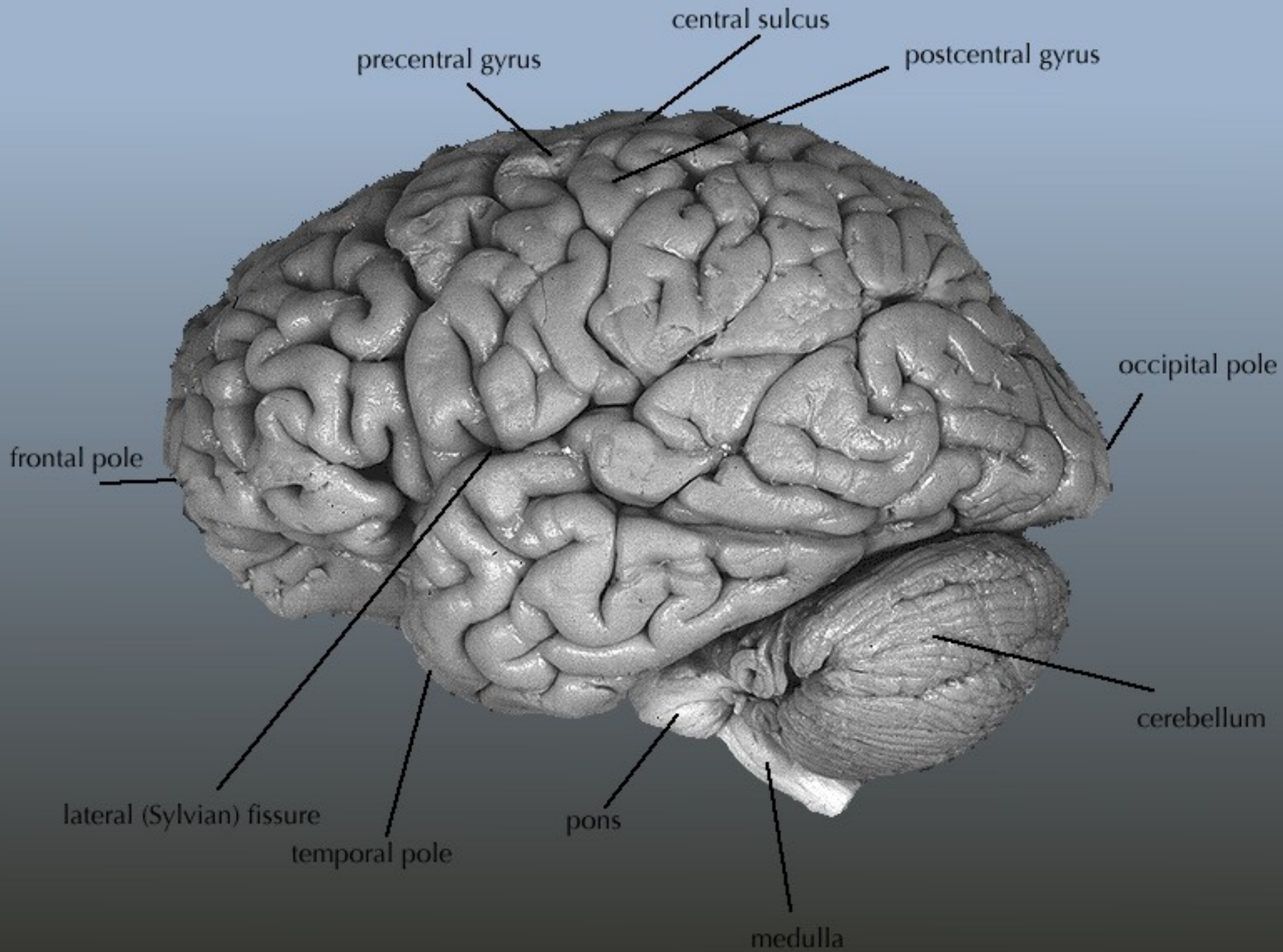
*Keywords:* Sigmund Freud; Donald Hebb; Synaptic plasticity; Learning; Memory; Psychoanalysis

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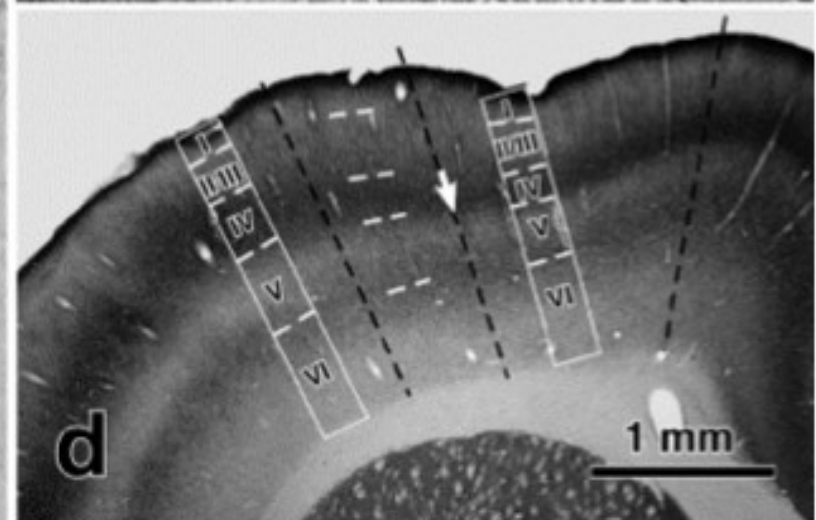
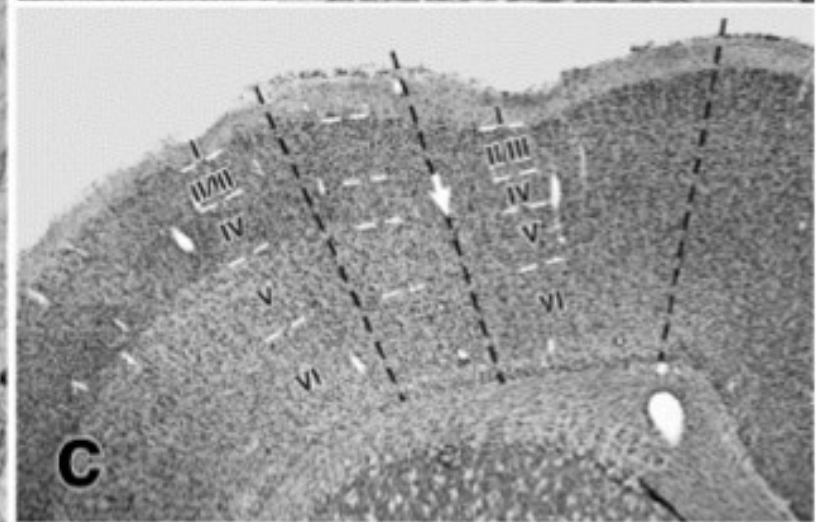
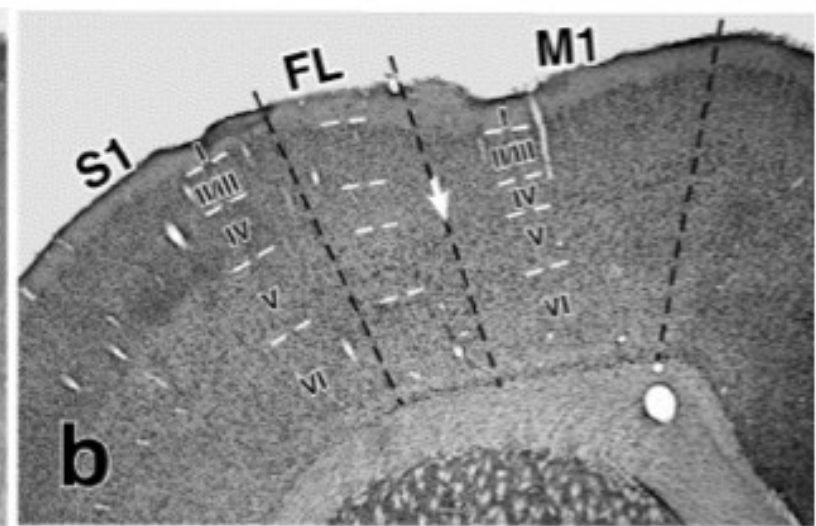
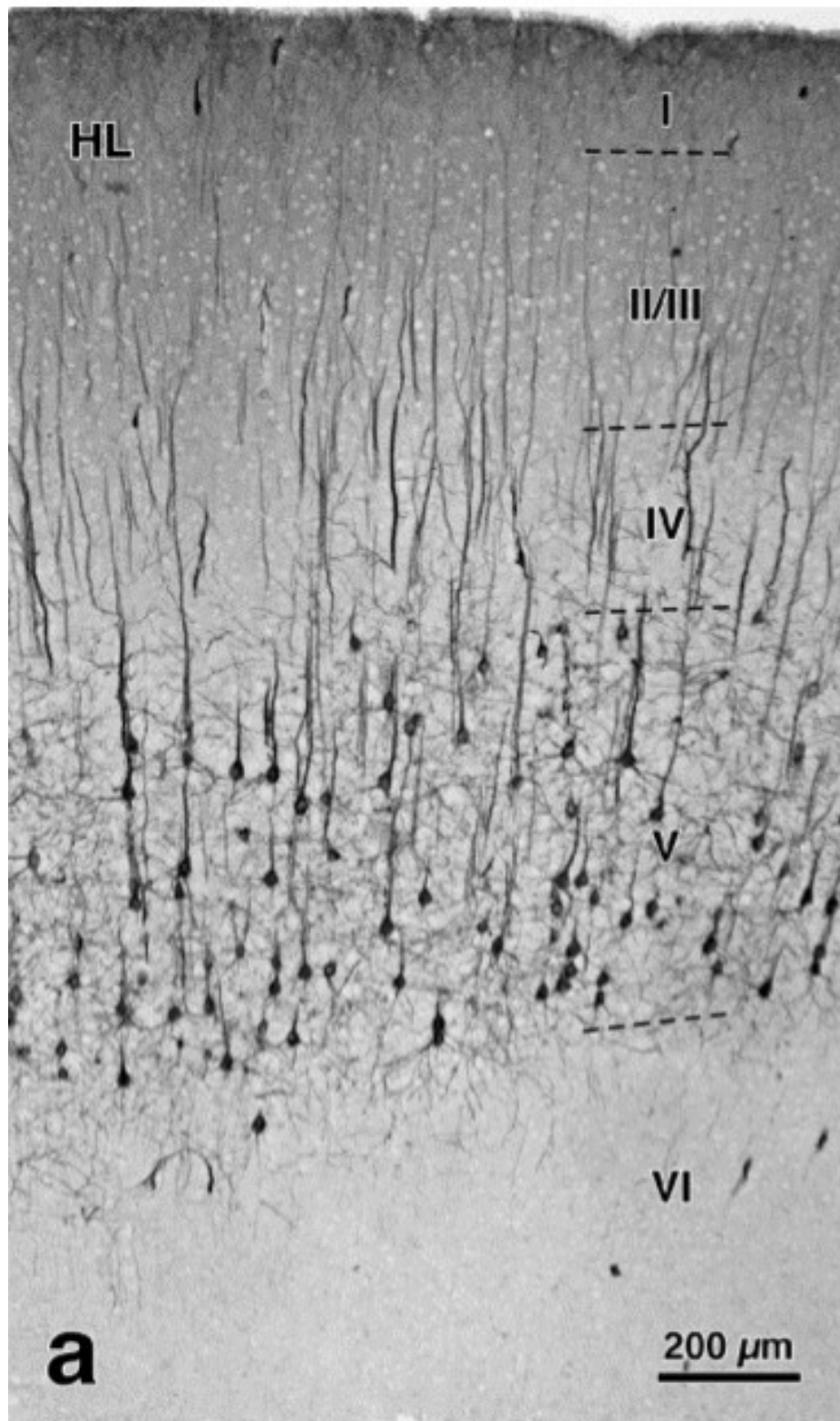
# Santiago Ramon y Cajal (1852-1934)

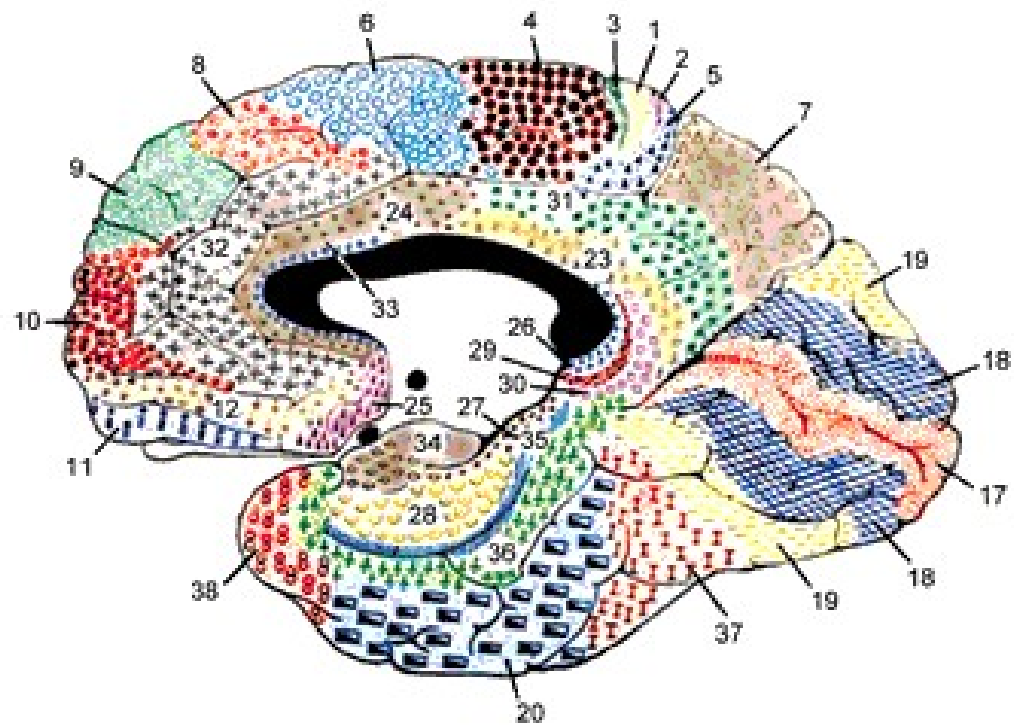
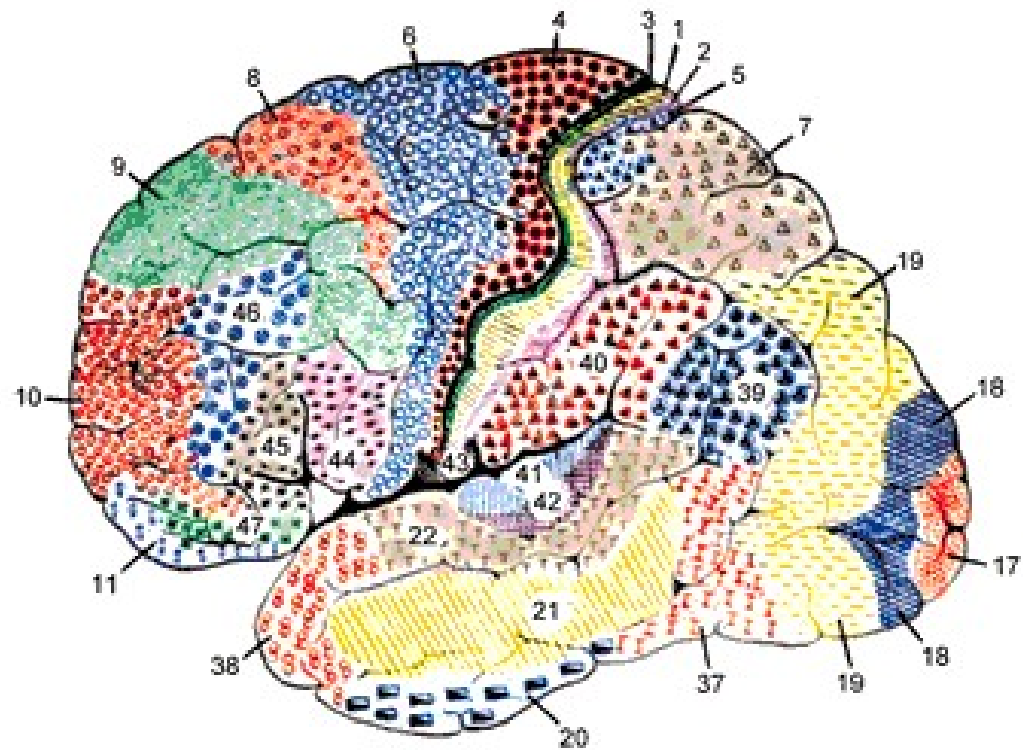


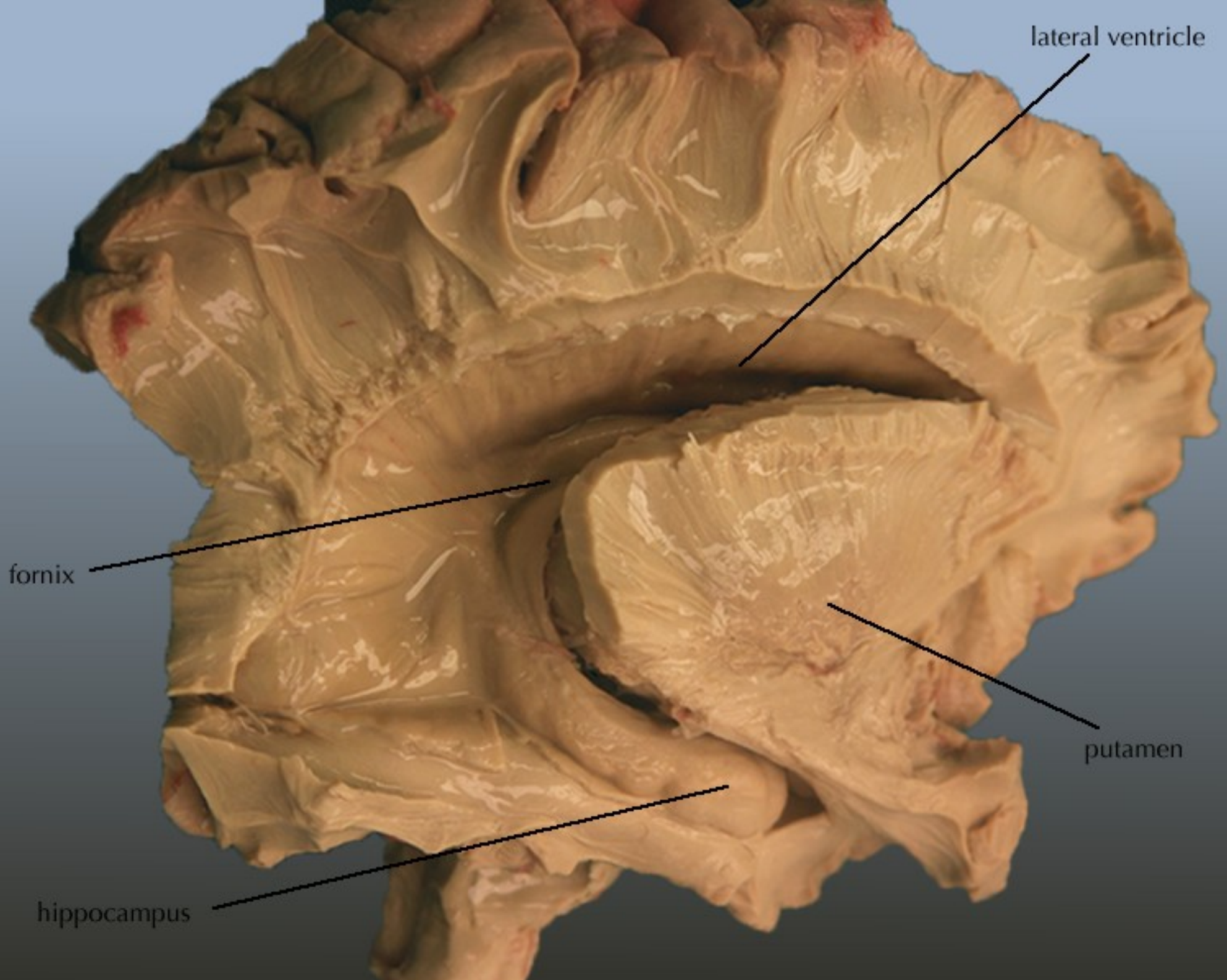
- the neuron doctrine
- the law of dynamic polarization











**Table 1***Nature Neuroscience* **6**, 795 - 799 (2003)

Published online: 28 July 2003; | doi:10.1038/nn1096

**From gene networks to brain networks**

Mihall Bota, Hong-Wei Dong &amp; Larry W Swanson

**Table 1 Limbic system connections (cell group to cell group)**

Era	Major techniques	Total	Valid today	% Valid
<b>Hypothalamus</b>				
1940	Normal silver/myelin degeneration <sup>31,32</sup>	55	10	18%
1969	Axon degeneration (Nauta method) <sup>33,34</sup>	75	38	51%
1987	Axonal transport (autoradiography/HRP) <sup>35</sup>	450	400	90%
2002	PHAL/dyes/histochemistry <sup>a</sup>	3,000	2,850	95%
<b>Hippocampus-amygdala-septum</b>				
1969	Axon degeneration <sup>36-38</sup>	57	40	70%
2002	PHAL/dyes/histochemistry <sup>a</sup>	2,000	1,900	95%
<b>Hypothalamus + Hippocampus-amygdala-septum</b>				
1969	Axon degeneration	116 <sup>b</sup>	70	60%
2002	PHAL/dyes/histochemistry	4,000 <sup>b</sup>	3,800	95%

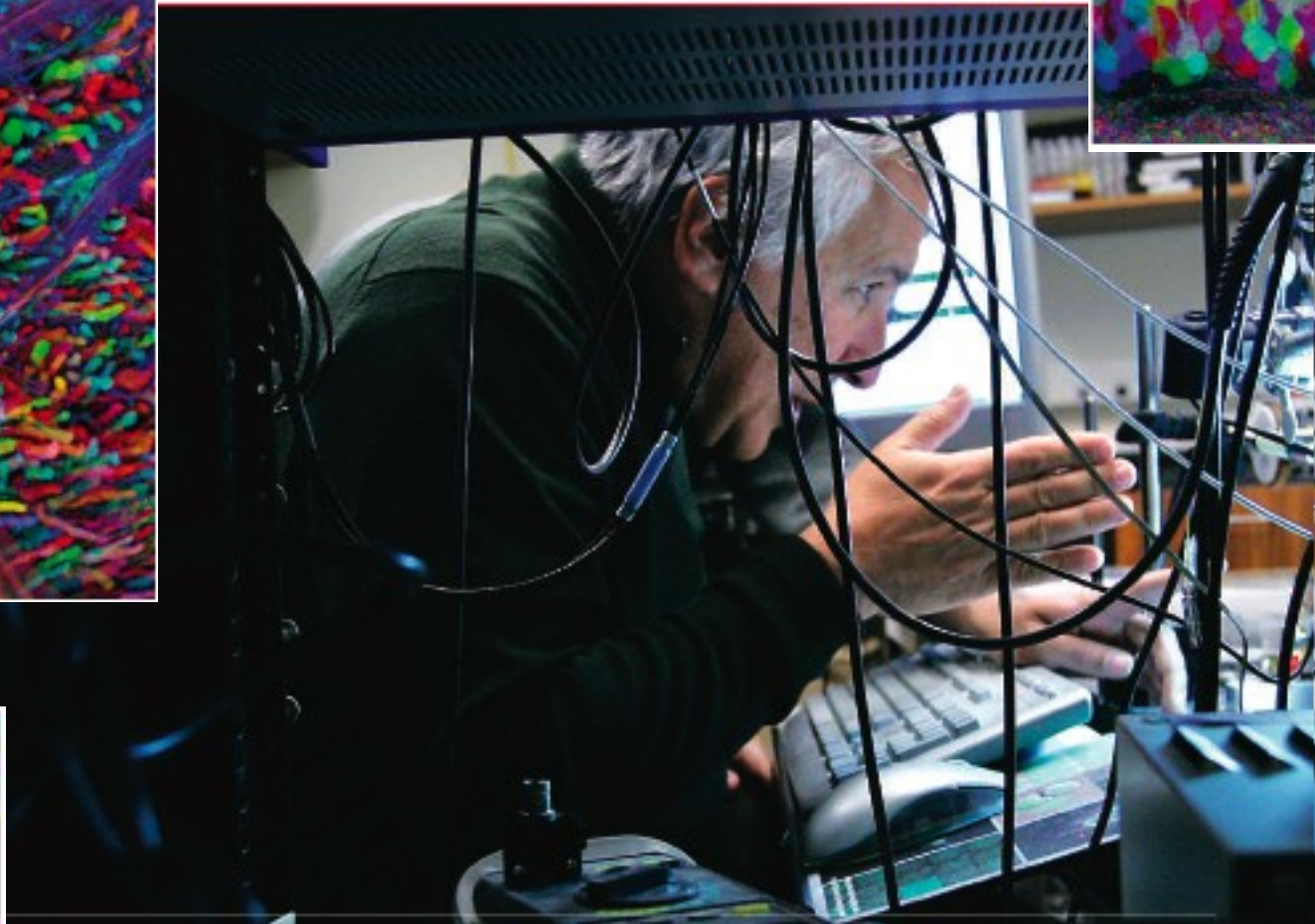
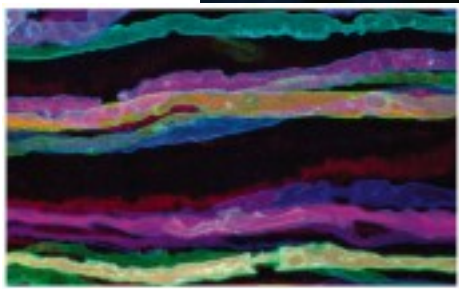
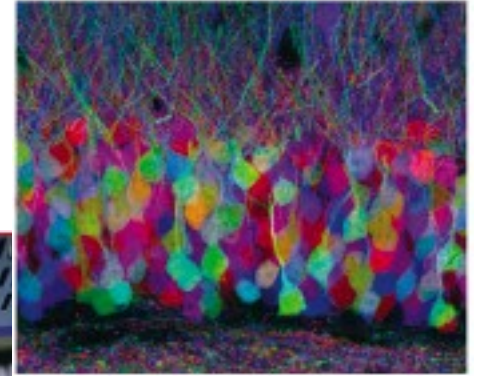
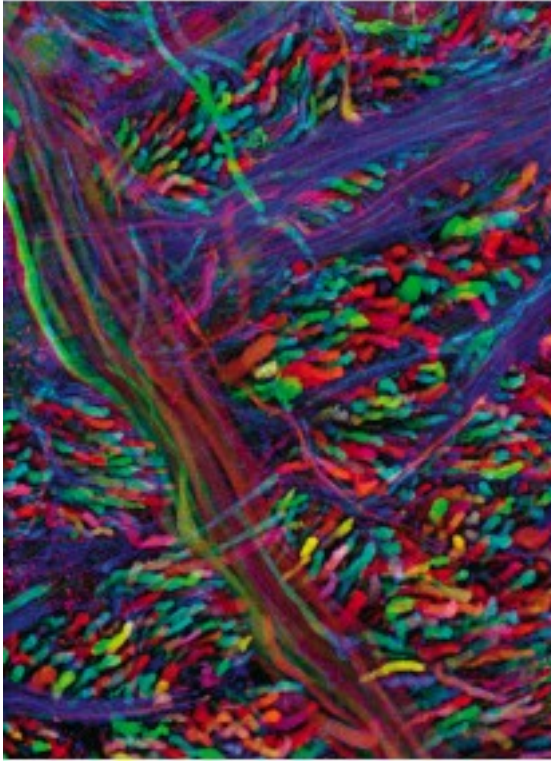
<sup>a</sup>Estimate based on informal survey of the literature. <sup>b</sup>Some connections of the hypothalamus are with the hippocampus-amygdala-septum.

Close window

**Table 1.** Databases and datasets containing information about neuroanatomical connections.

Database	Available Connectivity Information	URL
Brain Architecture Management System (BAMS) [2,26]	Projections in rodent brain, curated manually from existing literature	<a href="http://brancusi.usc.edu/bkms/">http://brancusi.usc.edu/bkms/</a>
Collations of Connectivity Data on the Macaque Brain (CoCoMac) [23,24]	Projections in macaque brain, curated manually from existing literature	<a href="http://www.cocomac.org">http://www.cocomac.org</a>
Functional Anatomy of the Cerebro-Cerebellar System (FACCS) [29]	3D atlas of axonal tracing data in rat cerebro-cerebellar system	<a href="http://ocelot.uio.no/nesys/">http://ocelot.uio.no/nesys/</a>
BrainMaps.org [59]	Tables of connections from literature and primary data for some tracer injections	<a href="http://brainmaps.org">http://brainmaps.org</a>
BrainPathways.org	Multiscale visualization of connectivity data from collated literature reports	<a href="http://brainpathways.org">http://brainpathways.org</a>
Human Brain Connectivity Database	Curated reports of connectivity studies in postmortem human brain tissue	<a href="http://brainarchitecture.org">http://brainarchitecture.org</a>
Internet Brain Connectivity Database	Estimated connectional data between human cortical gyral areas	<a href="http://www.cma.mgh.harvard.edu/ibcd/">http://www.cma.mgh.harvard.edu/ibcd/</a>
Surface Management System DataBase (SumsDB) [64]	Connection densities from macaque retrograde tracer injections mapped to surface-based atlas	<a href="http://sumsdb.wustl.edu/sums/">http://sumsdb.wustl.edu/sums/</a>
SynapseWeb	Reconstructed volumes and structures from serial section electron microscopy	<a href="http://synapses.clm.utexas.edu/">http://synapses.clm.utexas.edu/</a>
Neocortical Microcircuit Database [71]	Connection data between single cells in mammalian cortex	<a href="http://microcircuit.epfl.ch/">http://microcircuit.epfl.ch/</a>
ICBM DTI-81 Atlas [72]	Probabilistic atlas of human white matter tracts based on diffusion tensor imaging	<a href="http://www.loni.ucla.edu/Atlases/Atlas_Detail.jsp?atlas_id=15">http://www.loni.ucla.edu/Atlases/Atlas_Detail.jsp?atlas_id=15</a>
Anatomy Toolbox Fiber Tracts [32]	Probabilistic atlas of human white matter tracts based on postmortem studies	<a href="http://www.fz-juelich.de/ime/spm_anatomy_toolbox">http://www.fz-juelich.de/ime/spm_anatomy_toolbox</a>
WormAtlas [30]	Full neuronal wiring data for <i>C. elegans</i>	<a href="http://www.wormatlas.org">http://www.wormatlas.org</a>

# New Techniques to See Wiring



Jeff Lictman from Nature (2009) vol. 457:524-527.

# Connectome

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PLoS COMPUTATIONAL BIOLOGY

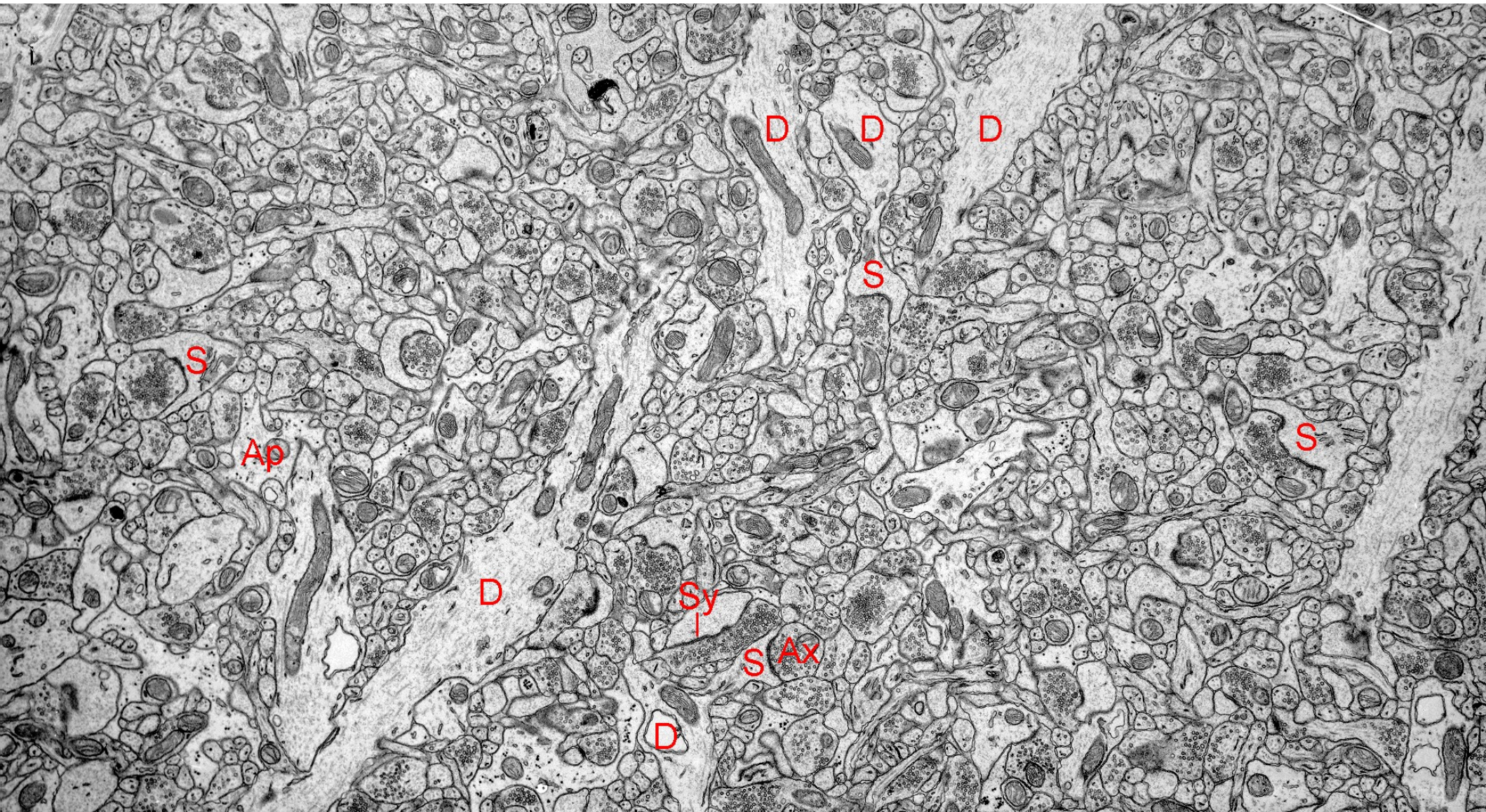
## Review

### A Proposal for a Coordinated Effort for the Determination of Brainwide Neuroanatomical Connectivity in Model Organisms at a Mesoscopic Scale

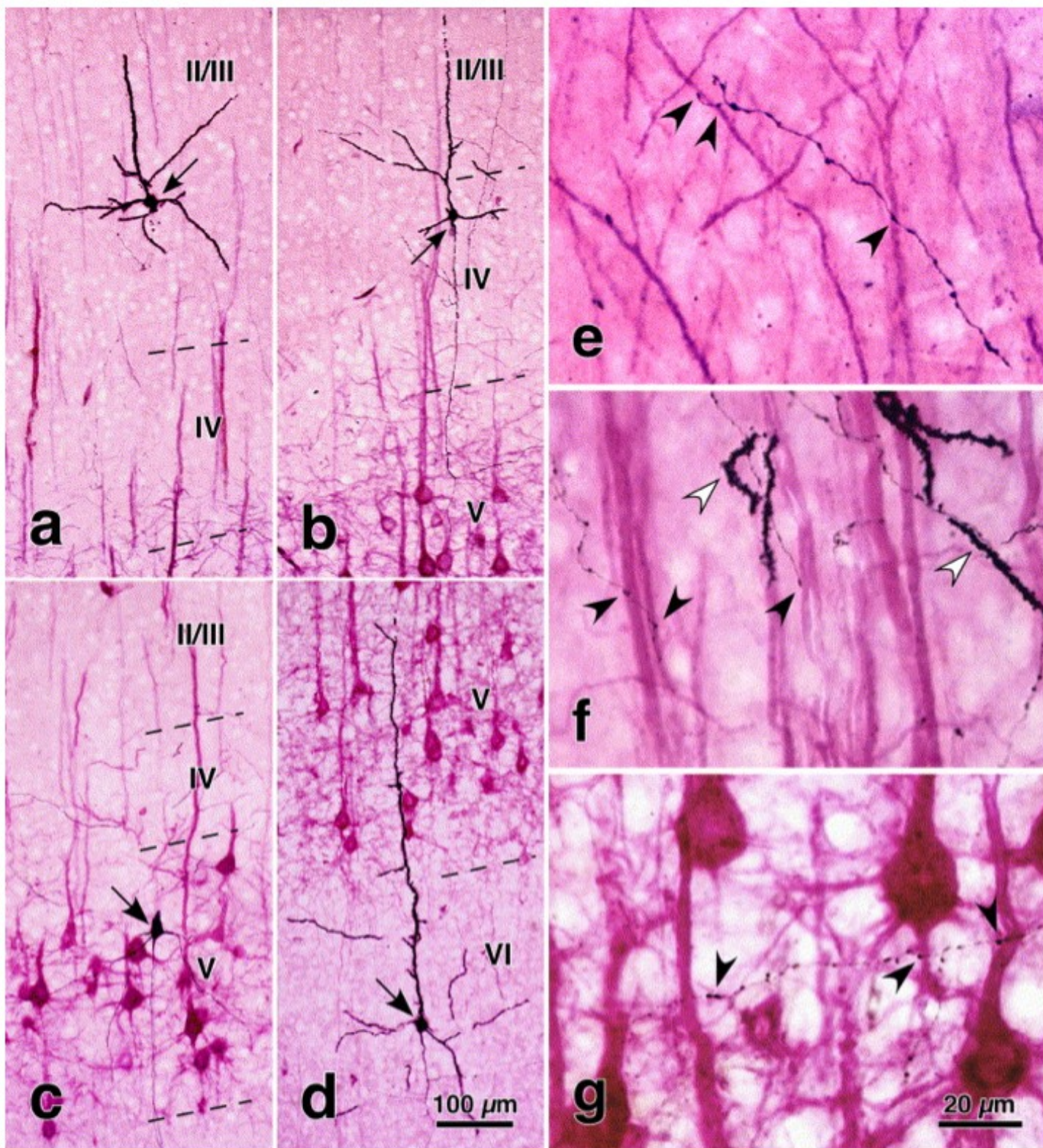
**Jason W. Bohland<sup>1\*</sup>, Caizhi Wu<sup>1</sup>, Helen Barbas<sup>2</sup>, Hemant Bokil<sup>1</sup>, Mihail Bota<sup>3</sup>, Hans C. Breiter<sup>4</sup>, Hollis T. Cline<sup>1</sup>, John C. Doyle<sup>5</sup>, Peter J. Freed<sup>6</sup>, Ralph J. Greenspan<sup>7</sup>, Suzanne N. Haber<sup>8</sup>, Michael Hawrylycz<sup>9</sup>, Daniel G. Herrera<sup>10</sup>, Claus C. Hilgetag<sup>11</sup>, Z. Josh Huang<sup>1</sup>, Allan Jones<sup>9</sup>, Edward G. Jones<sup>12</sup>, Harvey J. Karten<sup>13</sup>, David Kleinfeld<sup>14</sup>, Rolf Kötter<sup>15</sup>, Henry A. Lester<sup>16</sup>, John M. Lin<sup>1</sup>, Brett D. Mensh<sup>17</sup>, Shawn Mikula<sup>12</sup>, Jaak Panksepp<sup>18</sup>, Joseph L. Price<sup>19</sup>, Joseph Saffdieh<sup>20</sup>, Clifford B. Saper<sup>21</sup>, Nicholas D. Schiff<sup>20</sup>, Jeremy D. Schmahmann<sup>22</sup>, Bruce W. Stillman<sup>1</sup>, Karel Svoboda<sup>23</sup>, Larry W. Swanson<sup>3</sup>, Arthur W. Toga<sup>24</sup>, David C. Van Essen<sup>19</sup>, James D. Watson<sup>1</sup>, Partha P. Mitra<sup>1</sup>**

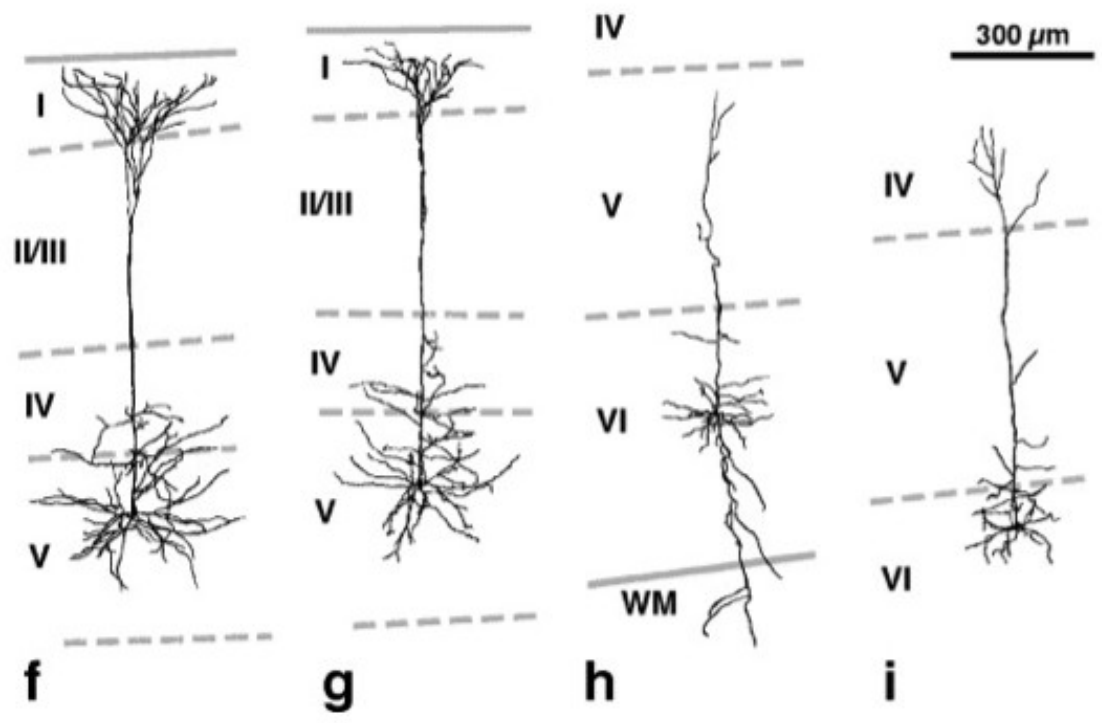
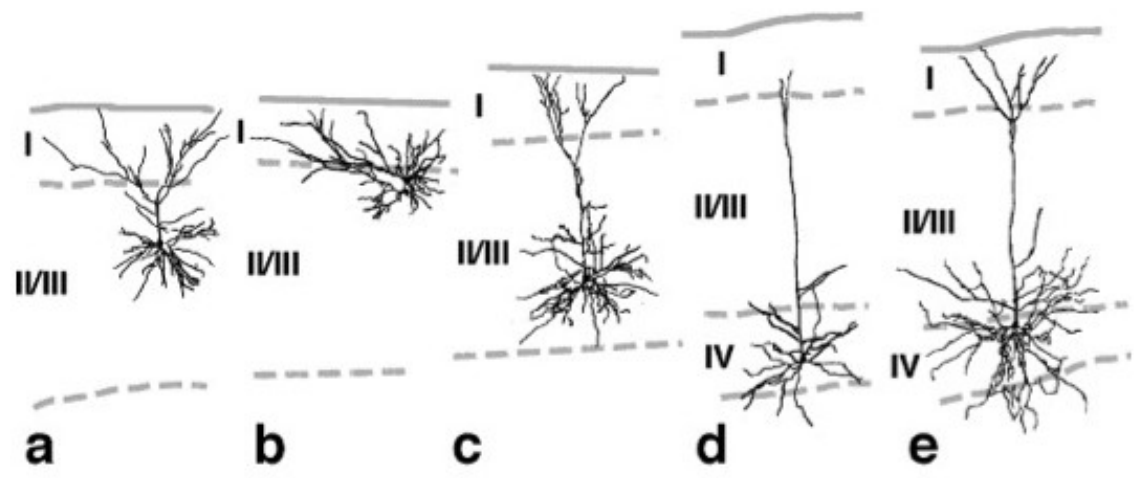
**1** Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, United States of America, **2** Department of Health Sciences, Boston University, Boston, Massachusetts, United States of America, **3** Department of Biological Sciences, University of Southern California, Los Angeles, California, United States of America, **4** Department of Radiology, Massachusetts General Hospital, Charlestown, Massachusetts, United States of America, **5** Department of Electrical Engineering, California Institute of Technology, Pasadena, California, United States of America, **6** New York State Psychiatric Institute, Columbia University Medical Center, New York, New York, United States of America, **7** The Neurosciences Institute, San Diego, California, United States of America, **8** Department of Pharmacology & Physiology, University of Rochester Medical Center, Rochester, New York, United States of America, **9** Allen Institute for Brain Science, Seattle, Washington, United States of America, **10** Department of Psychiatry, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, United States of America, **11** School of Engineering and Science, Jacobs University Bremen, Bremen, Germany, **12** Center for Neuroscience, University of California Davis, Davis, California, United States of America, **13** Department of Neurosciences, University of California San Diego School of Medicine, La Jolla, California, United States of America, **14** Department of Physics, University of California San Diego, La Jolla, California, United States of America, **15** Donders Institute for Brain, Cognition, and Behaviour, Department of Cognitive Neuroscience, NeuroPI, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands, **16** Department of Biology, California Institute of Technology, Pasadena, California, United States of America, **17** Department of Psychiatry, Columbia University Medical Center, New York, New York, United States of America, **18** College of Veterinary Medicine, Washington State University, Pullman, Washington, United States of America, **19** Department of Anatomy & Neurobiology, Washington University School of Medicine, St. Louis, Missouri, United States of America, **20** Department of Neurology, Weill Cornell Medical College, New York, New York, United States of America, **21** Department of Neurology, Beth Israel Deaconess Medical Center, Boston, Massachusetts, United States of America, **22** Department of Neurology, Massachusetts General Hospital, Boston, Massachusetts, United States of America, **23** Janella Farm Research Campus, Howard Hughes Medical Institute, Ashburn, Virginia, United States of America, **24** Laboratory of Neuroimaging, Department of Neurology, University of California Los Angeles School of Medicine, Los Angeles, California, United States of America

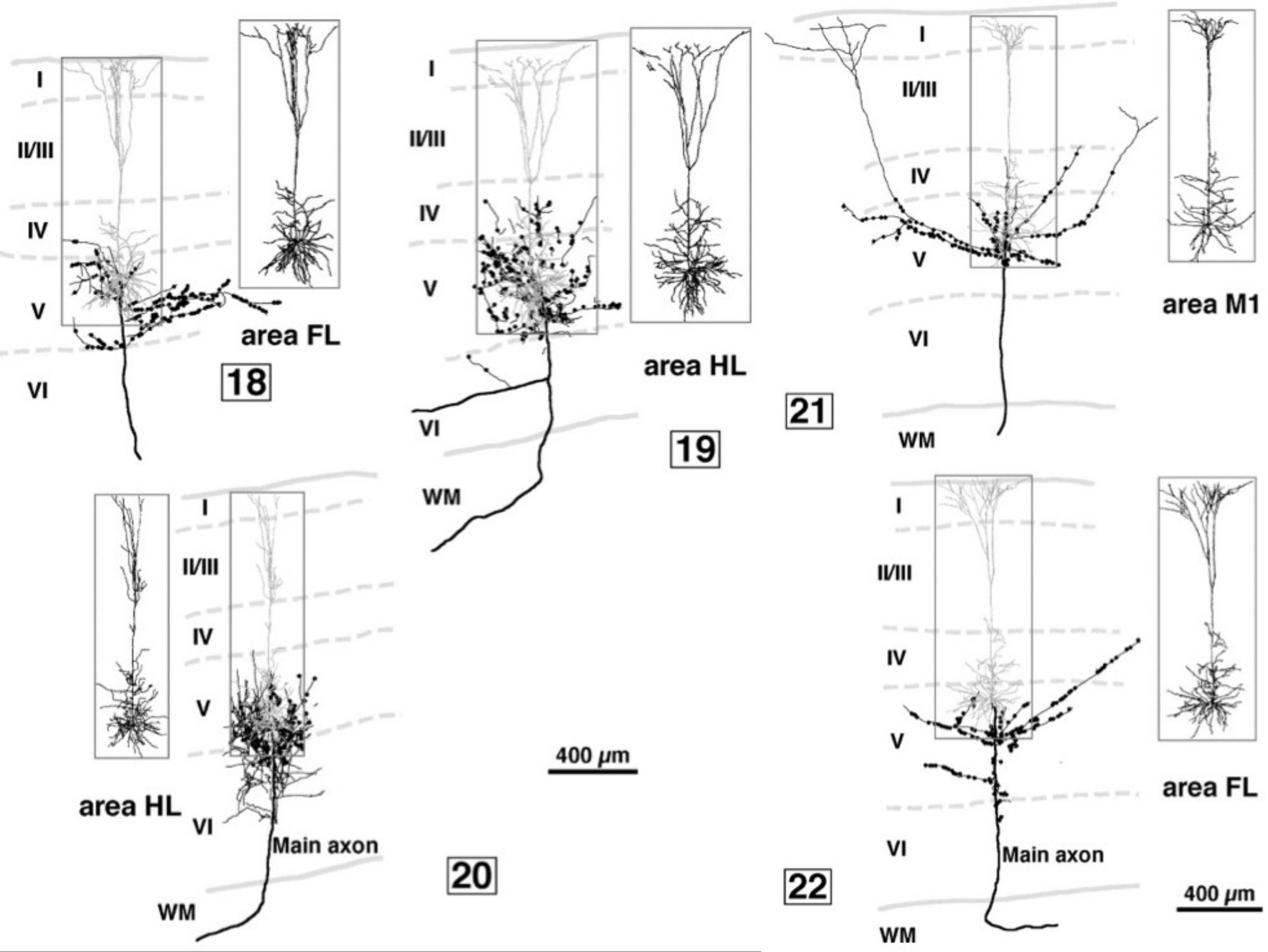
# Neuropil

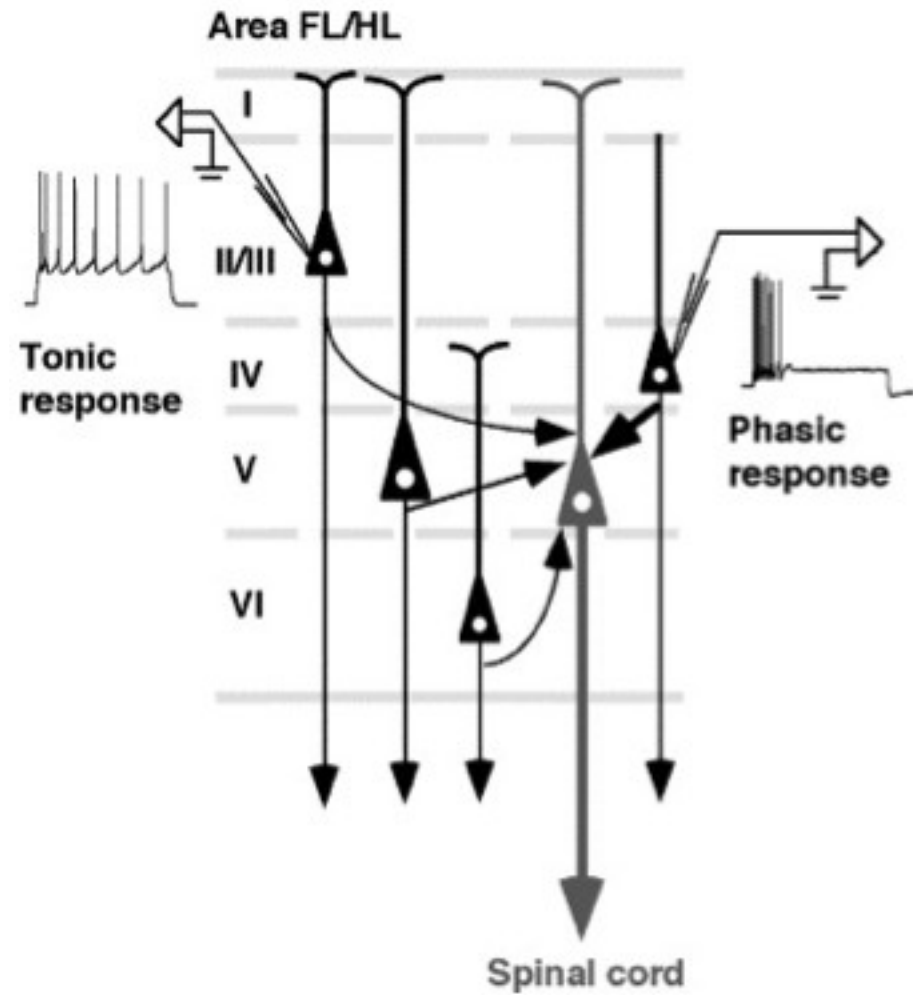
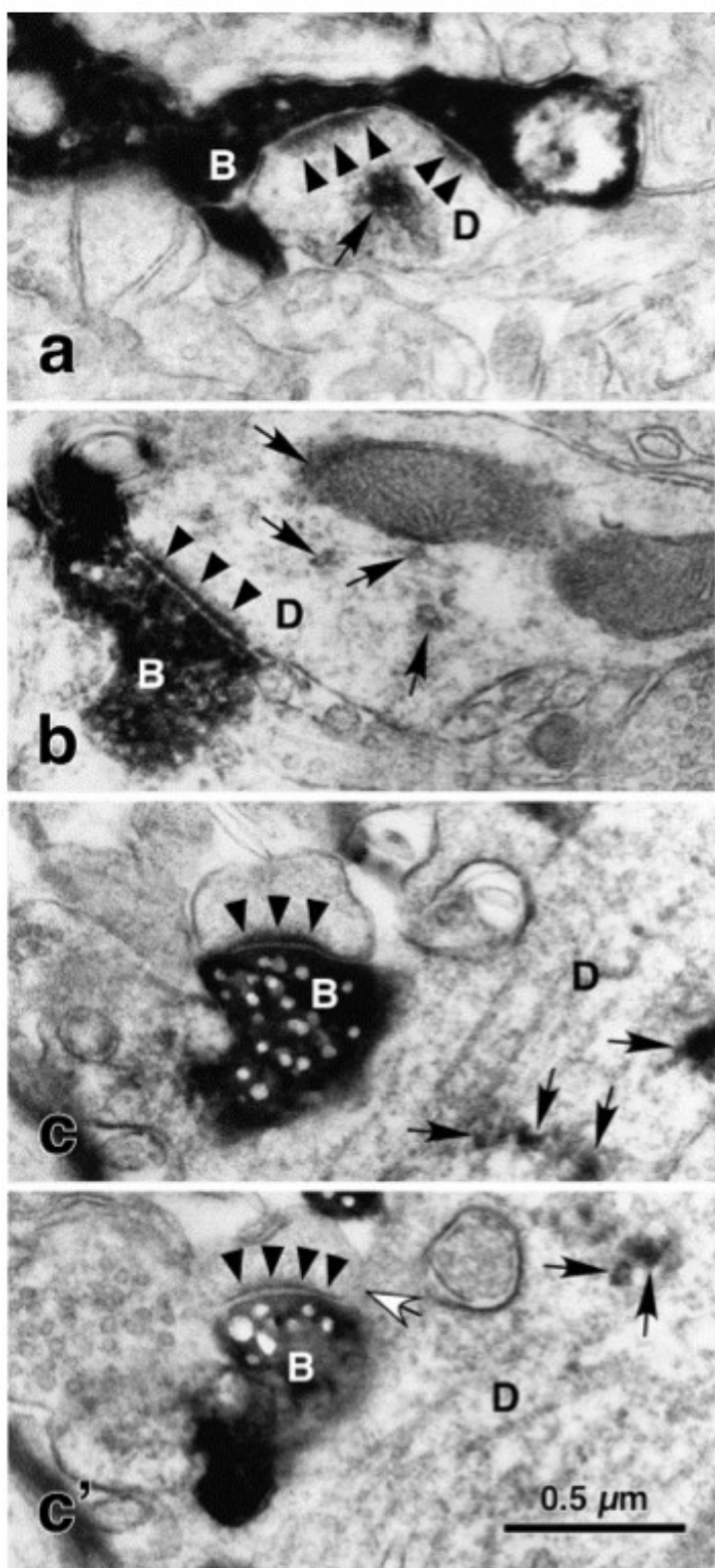












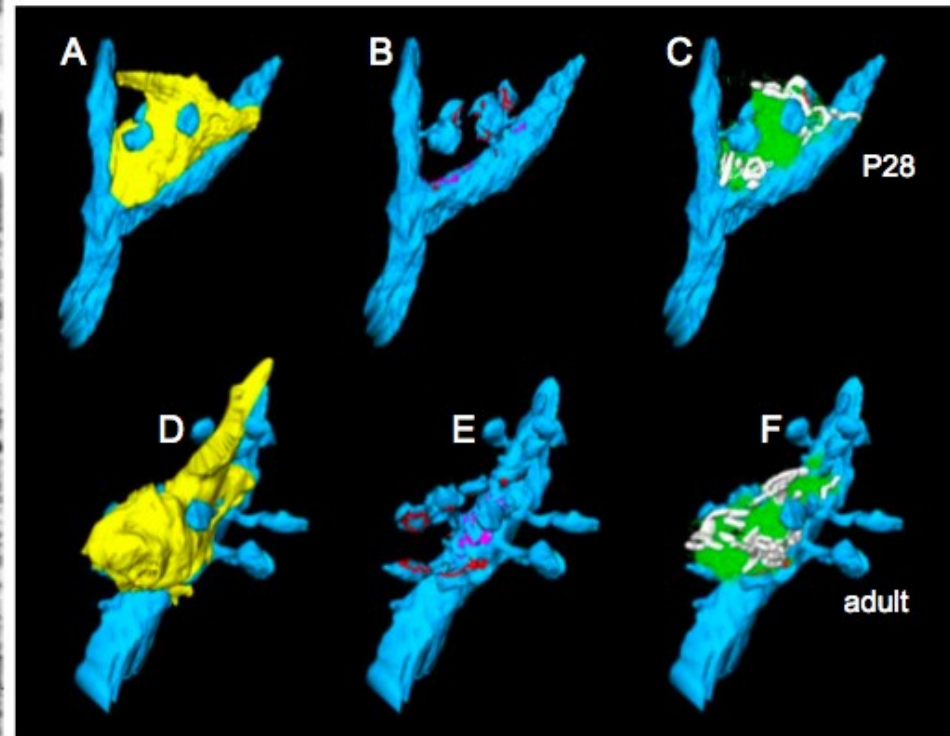
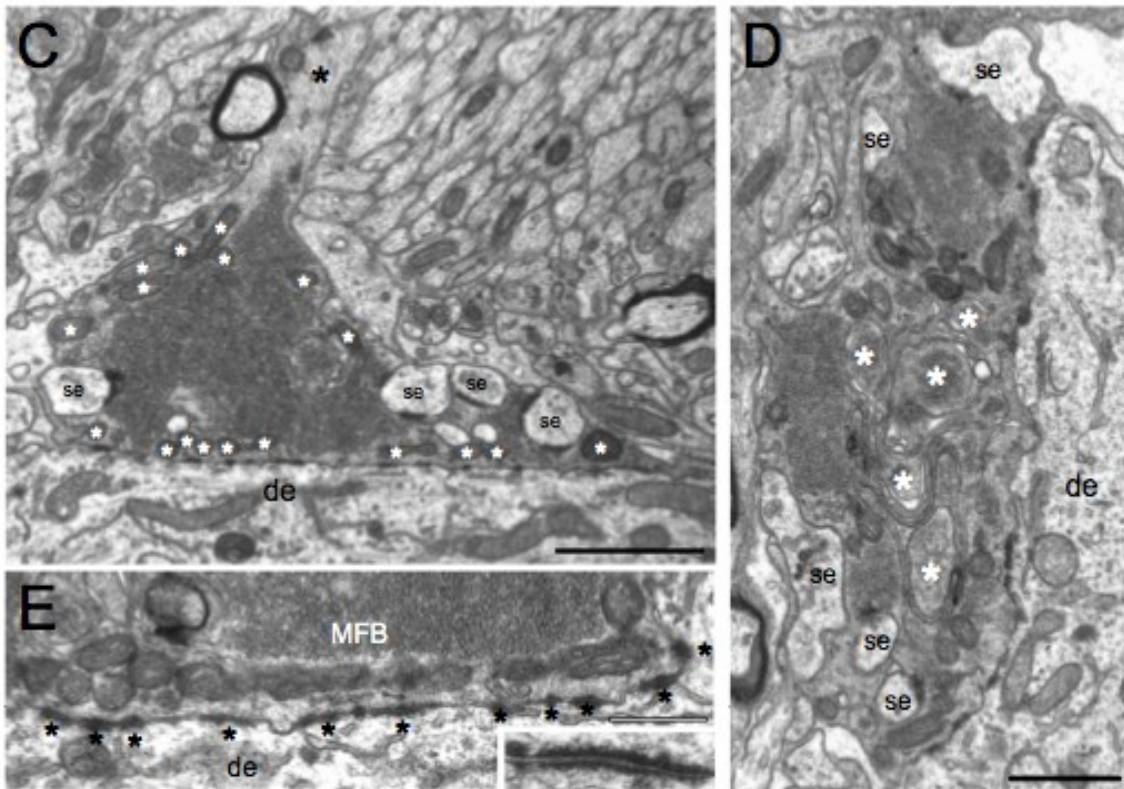
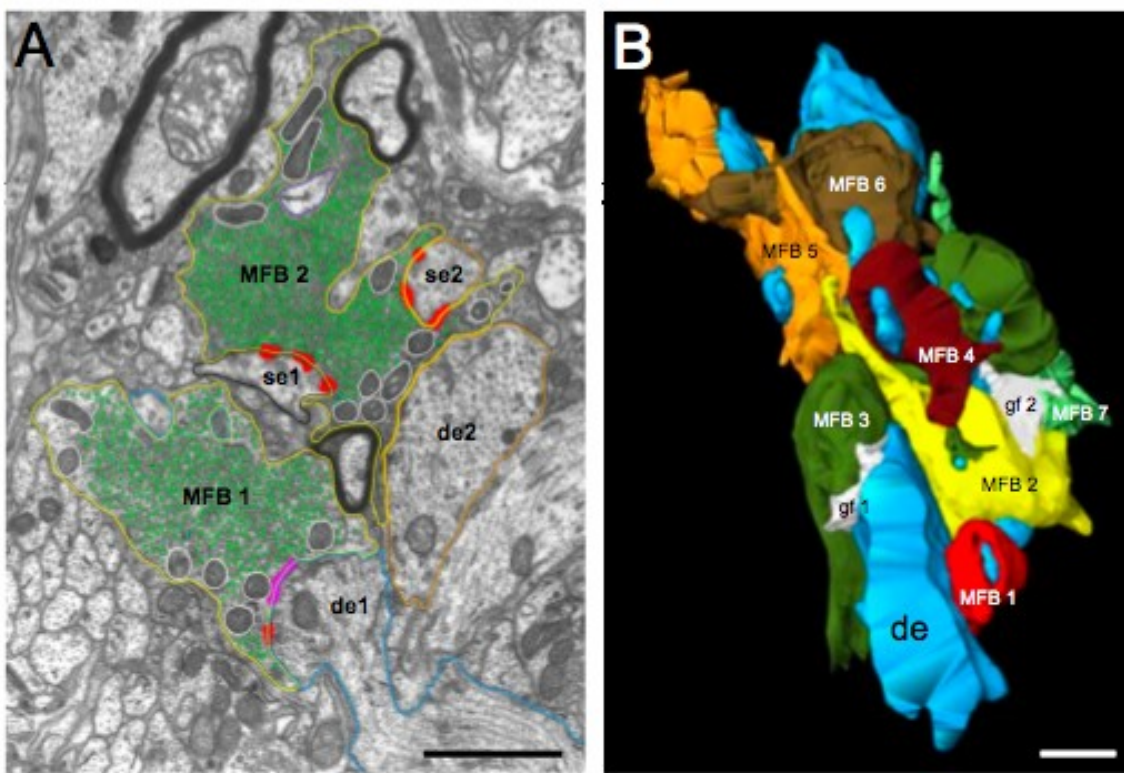
## Structural Determinants of Transmission at Large Hippocampal Mossy Fiber Synapses

Astrid Rollenhagen,<sup>1,4\*</sup> Kurt Sätzler,<sup>2\*</sup> E. Patricia Rodríguez,<sup>2</sup> Peter Jonas,<sup>3</sup> Michael Frotscher,<sup>4</sup> and Joachim H. R. Lübke<sup>1,4</sup>

<sup>1</sup>Institute of Neuroscience and Biophysics INB-3, Research Centre Jülich, D-52425 Jülich, Germany, <sup>2</sup>School of Biomedical Sciences, University of Ulster, Coleraine, County Londonderry BT52 1SA, United Kingdom, and Institutes of <sup>3</sup>Physiology and <sup>4</sup>Anatomy and Cell Biology, Albert Ludwigs University of Freiburg, D-79104 Freiburg, Germany

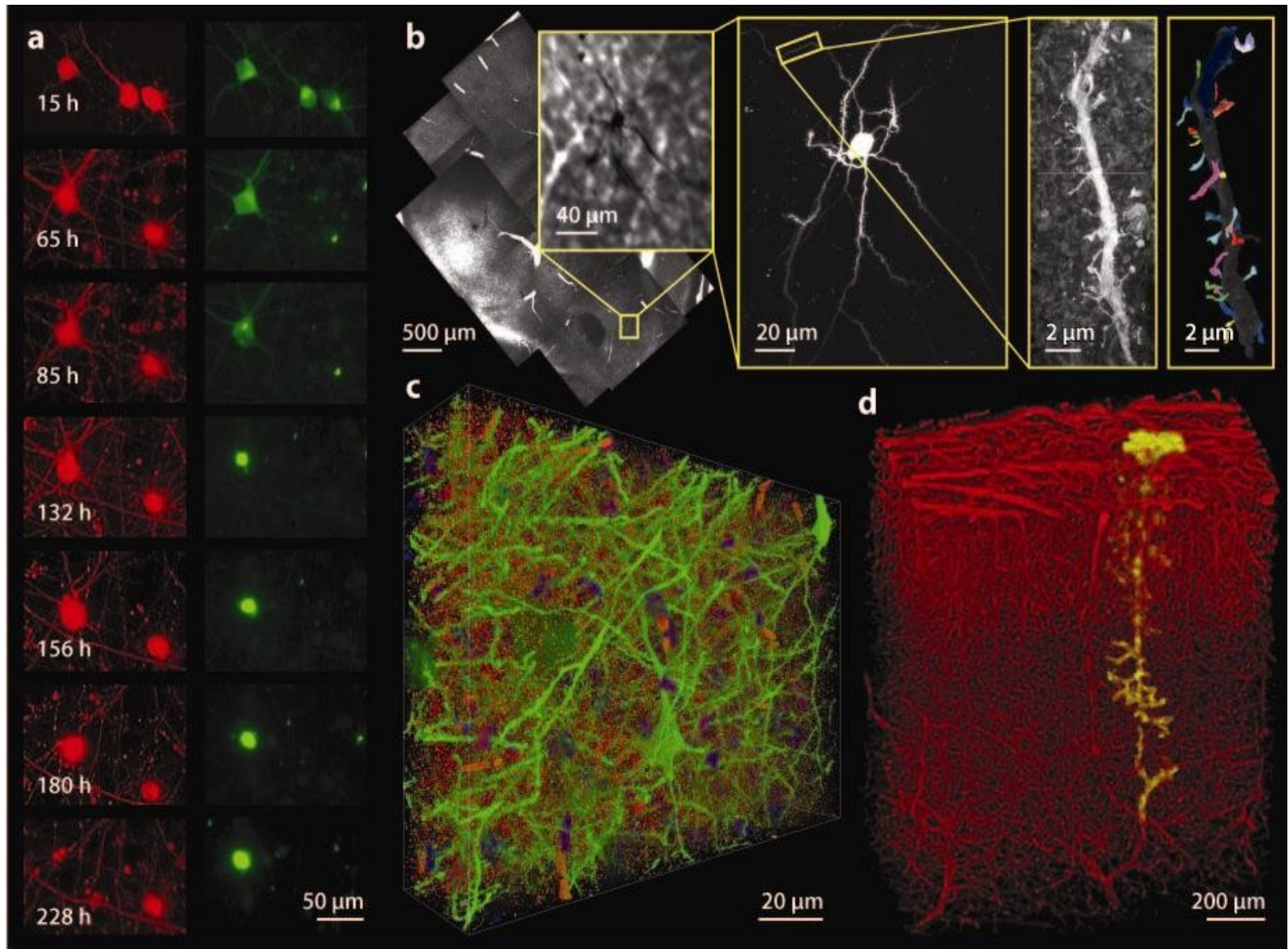
Synapses are the key elements for signal processing and plasticity in the brain. To determine the structural factors underlying the unique functional properties of the hippocampal mossy fiber synapse, the complete quantitative geometry was investigated, using electron microscopy of serial ultrathin sections followed by computer-assisted three-dimensional reconstruction. In particular, parameters relevant for transmitter release and synaptic plasticity were examined. Two membrane specializations were found: active zones (AZs), transmitter release sites, and puncta adherentia. Individual boutons had, on average, 25 AZs (range, 7–45) that varied in shape and size (mean,  $0.1 \mu\text{m}^2$ ; range,  $0.07$ – $0.17 \mu\text{m}^2$ ). The mean distance between individual AZs was  $0.45 \mu\text{m}$ . Mossy fiber boutons and their target structures were mostly ensheathed by astrocytes, but fine glial processes never reached the active zones. Two structural factors are likely to promote synaptic cross talk: the short distance between AZs and the absence of fine glial processes at AZs. Thus, synaptic cross talk may contribute to the efficacy of hippocampal mossy fiber synapses. On average, a bouton contained 20,400 synaptic vesicles;  $\sim 900$  vesicles were located within 60 nm from the active zone,  $\sim 4400$  between 60 and 200 nm, and the remaining beyond 200 nm, suggesting large readily releasable, recycling, and reserve pools. The organization of the different pools may be a key structural correlate of presynaptic plasticity at this synapse. Thus, the mossy fiber bouton differs fundamentally in structure and function from the calyx of Held and other central synapses.

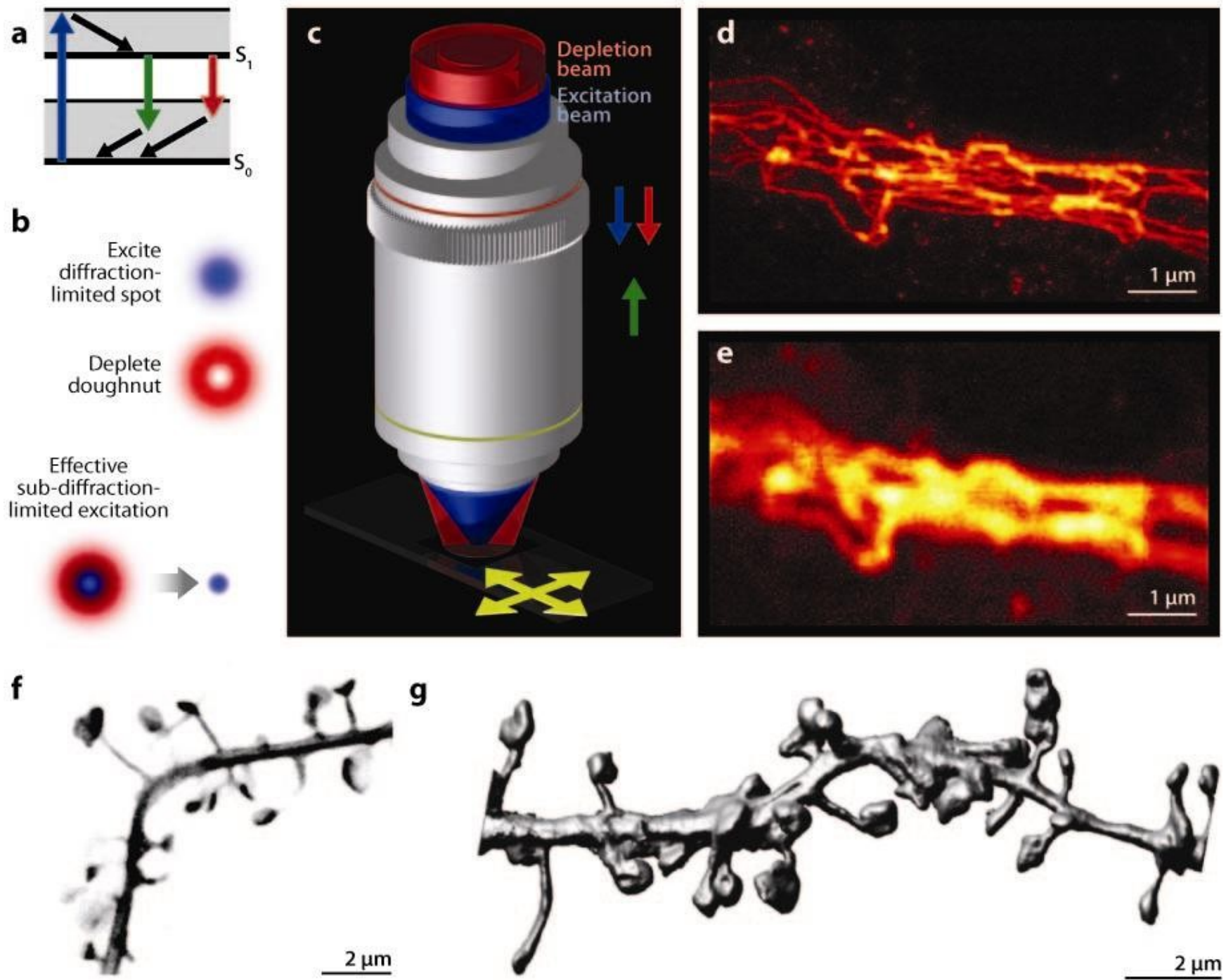
**Key words:** mossy fiber; neuromodulation; synapse; synaptic transmission; synaptic plasticity; synaptic vesicle release



# Large-Scale Neural Circuit Reconstruction

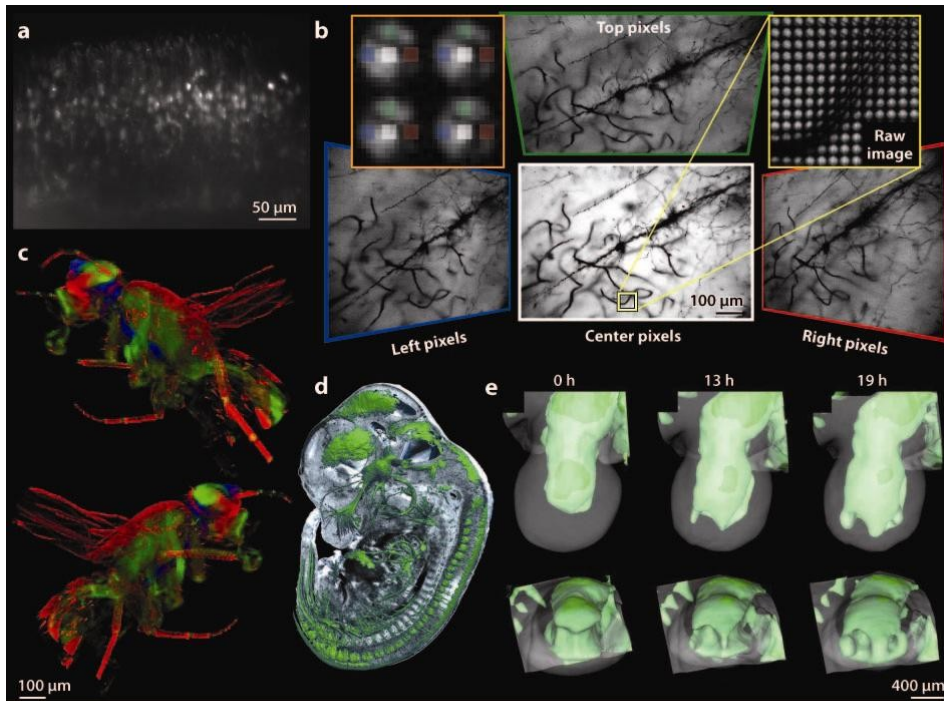
- Complete (dense) mapping of neural network structure is needed
- Manual tracing of most networks of interest would require hundreds to tens of thousands of years in human labor





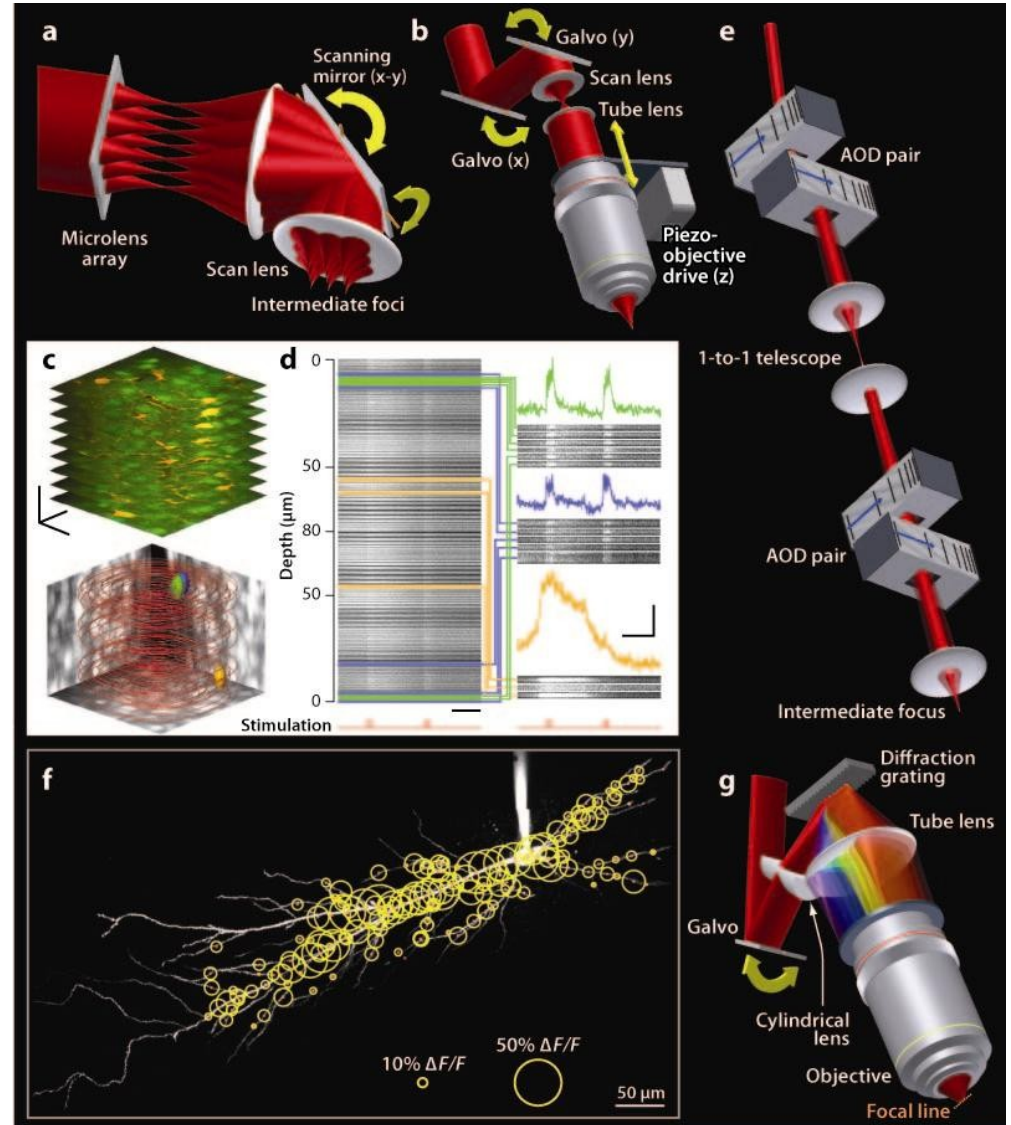


# Signals in the Neuropil



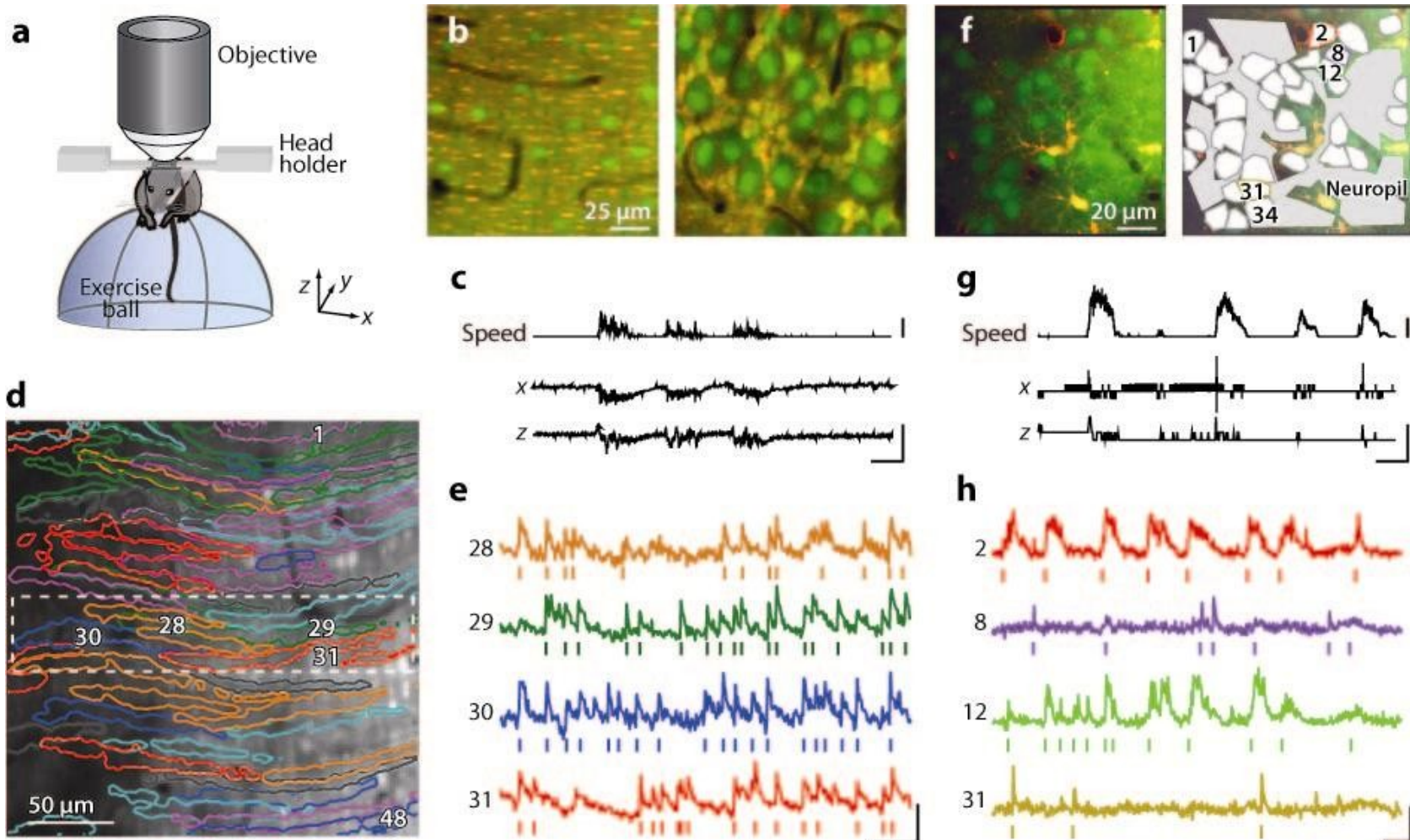
Wilt BA, et al. 2009.  
Annu. Rev. Neurosci. 32:435–506


Electrical conduction characteristics of axons and dendrites



Wilt BA, et al. 2009.  
Annu. Rev. Neurosci. 32:435–506

# Activity in Awake Behaving Animals



 Wilt BA, et al. 2009.  
Annu. Rev. Neurosci. 32:435–506

# Neuroinformatics Challenge

Devise methods for representing, accessing, and integrating vast amounts of diverse and complex data

# Some Exciting Technologies/Projects

- NeuroText
- Human Brain Project (HBP)
- Bioinformatics Research Network (BIRN)
- Neuroinformatics Information Network (NIF)
- SenseLab
  - NeuronDB
  - CellPropDB
- Entity-Attribute-Value/Classes and Relationships (EAV/CR)
- BrainML
- NeuroML
  - NeuroML Development Kit
- MorphML
- Catacomb
- GENESIS
  - EXODUS
- Web Interfacing Repository Manager (WIRM)
- Synapse Web
- NeuroSys
- Common Data Model for Neurosciences (CDM)
- Protege
- Cell Centered Database (CCDB)
- VisANT
- Extensible Markup Language (XML)
- Systems Biology Markup Language (SBML)
- MathML
- Virtual RatBrain Project
- MorphML Viewer
- NEURON
  - ModelView
- NeuroConstruct

# More Exciting Technologies/Projects

- Brain Information Management System (BIMS)
- Digital Anatomist
- Atlas of the Human Brain
- Medical Neuroscience
- Whole Brain Atlas
- BrainMaps.org
- Mouse Brain Library
- LONI
- Allen Brain Atlas
- CoCoMac
- The Brain Architecture Management System (BAMS)
- Neuroscience Information Framework (NIF)
- Unified Medical Language System (UMLS)
- BrainInfo
- Simulator for Neural Networks and Action Potentials (SNNAP)
- International Neuroinformatics Coordinating Facility (INCF)



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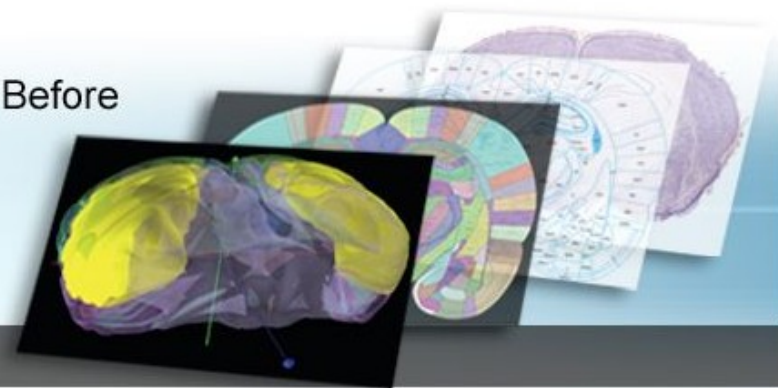
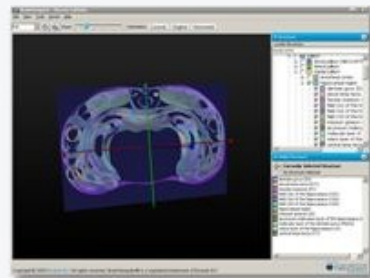
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To all of you attending this year's Neuroscience 2009 meeting in Chicago, we welcome you to visit us at Booth #153 in Publisher's Row. We have a raffle (win \$300 of free Springer books), and are giving away toy "squishy brains" in petri dishes. Come by and say hello!

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2 hours ago




2 more...



**Mike Pascoe** added 3 blog posts  
**Tendon Tap Responses in Stroke Patients.**  
 No Title  
**Becoming Batman and Backyard Brains**

15 hours ago



**V. Alexander STEFAN** added a group  
 **Laser-Neurophysics**  
 Laser-Neuron Interaction

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**V. Alexander STEFAN** posted the link **V. Alexander STEFAN**

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**Mitchell Maltenfort** joined **Nasir Raza Awan's** group

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# Summary

- Help neuroscientists do more effectively, affordably, and conveniently a job they have long been trying to do.
- Drive accessibility and broader practical use.
- Informatics innovation related to large-scale automated data collection.