Basic Neuroscience

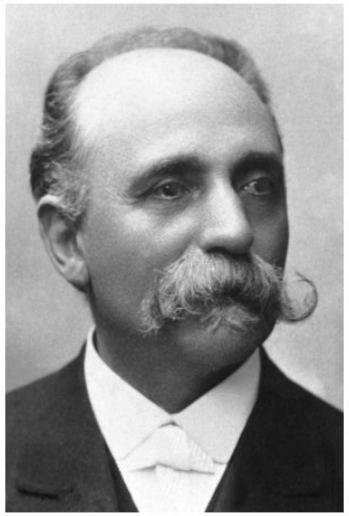
Li Yao
28/9/2021

1. Neuron and Glia

2. Resting potential and Action potential

3. Technologies

1. Neuron and Glia
神经元和胶质细胞

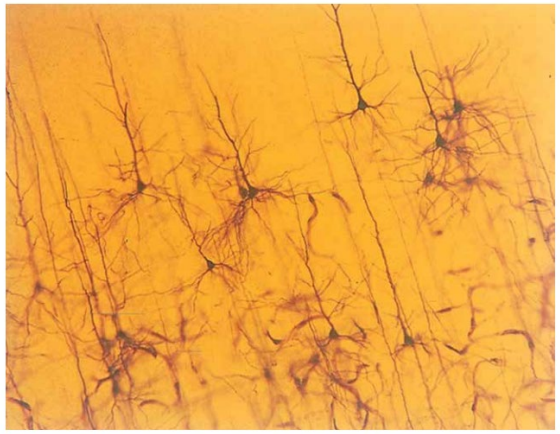


Camillo Golgi Santiago Ramón y Cajal

The Nobel Prize in Physiology or Medicine 1906 was awarded jointly to Camillo Golgi and Santiago Ramón y Cajal "in recognition of their work on the structure of the nervous system."

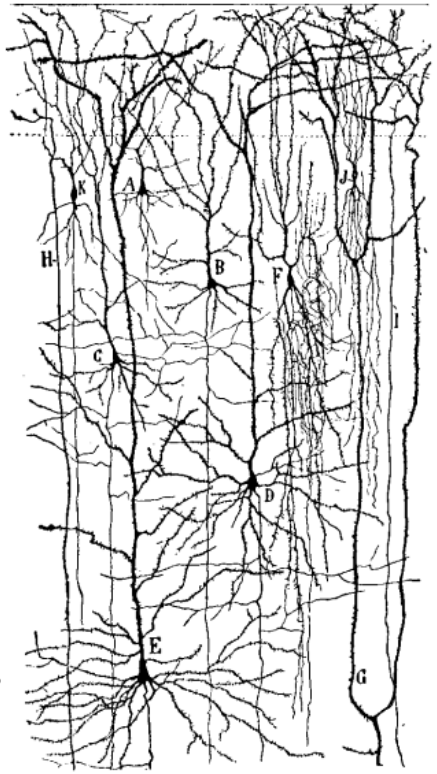
https://www.nobelprize.org/prizes/medicine/1906/summary/

Golgi-stained neurons



One of Cajal's many drawings of brain circuitry

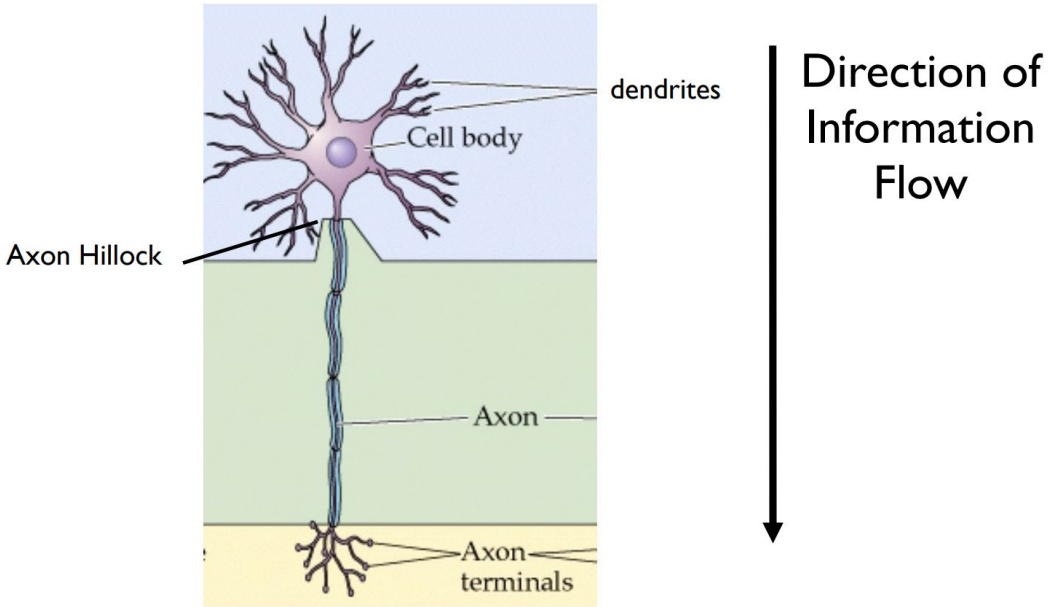
Neuroscience: Exploring the brain (2007)



Neuron Doctrine: The neurites of different neurons are not continuous with each other and communicate by contact, not continuity.

Neuron

Basic Anatomy of a Nerve Cell or Neuron

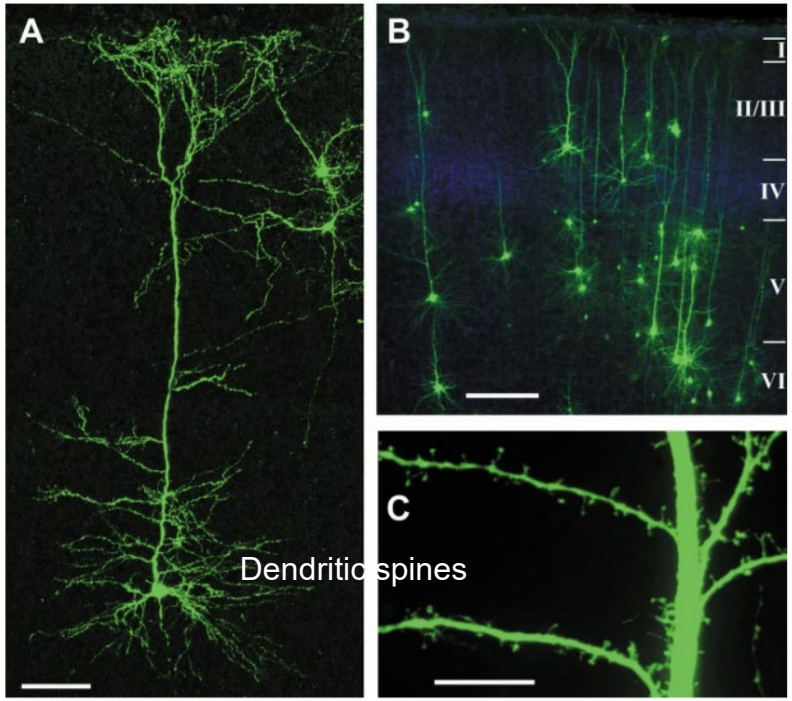


Direction of Information Flow

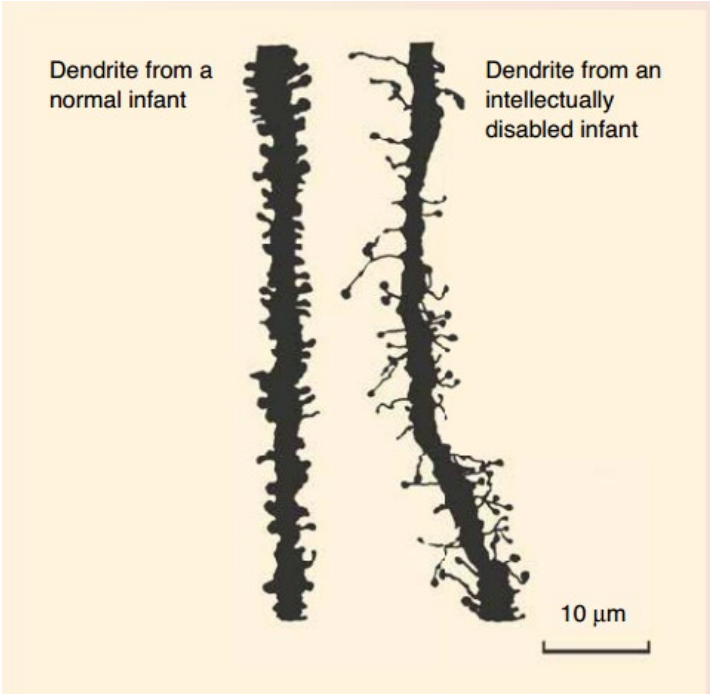
The soma: 20 μm
Cytosol: high K+
Dendrite: 树突
Axon: 轴突

Dendrite: Dendrites receiving synaptic inputs from axon terminals.

树突

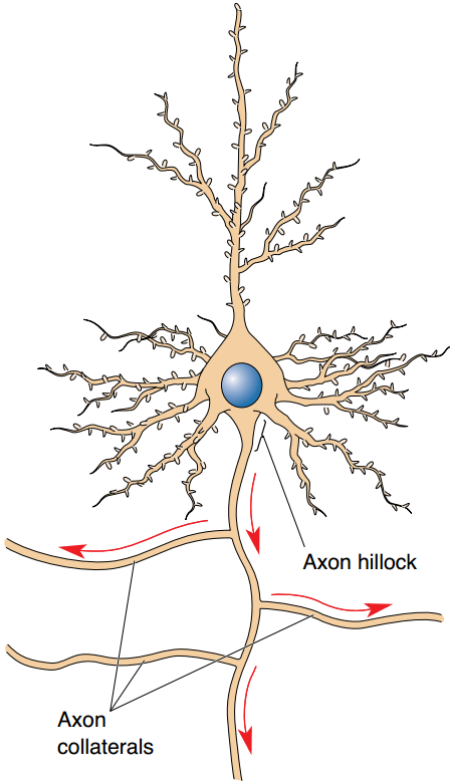


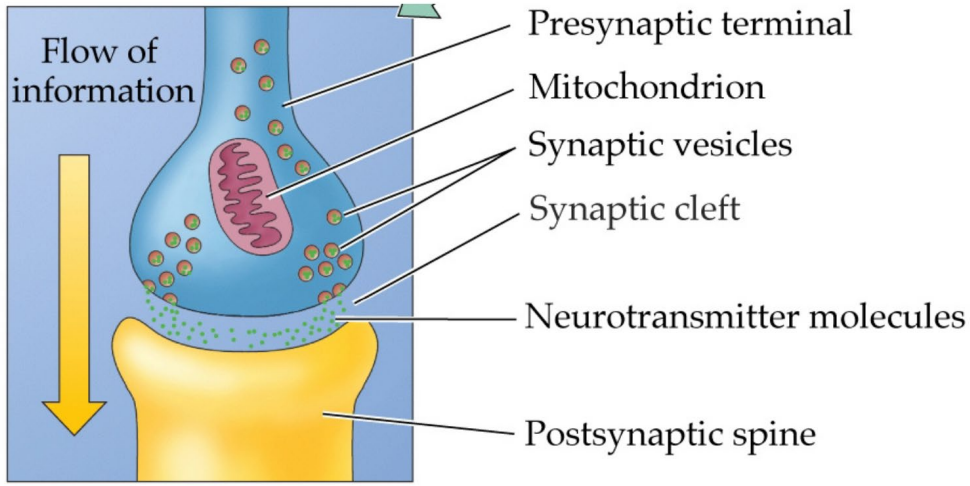
Annual Review in Neuroscience, 2002



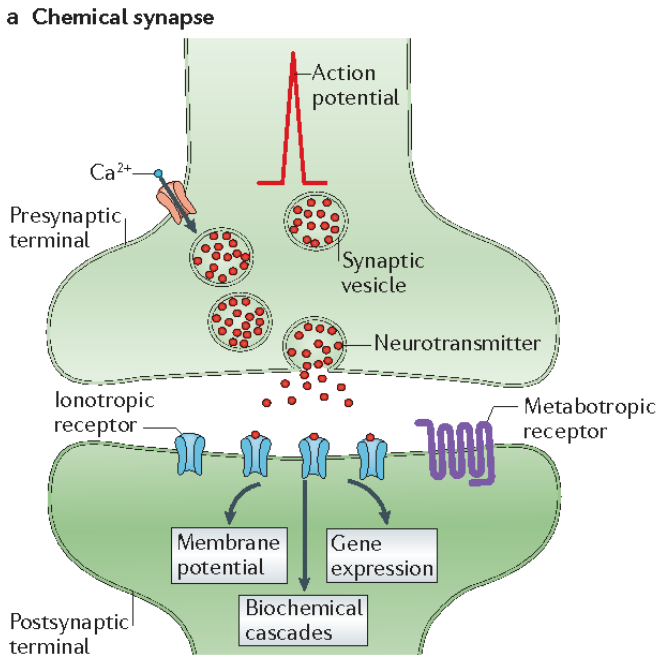
Intellectual Disability and Dendritic Spines

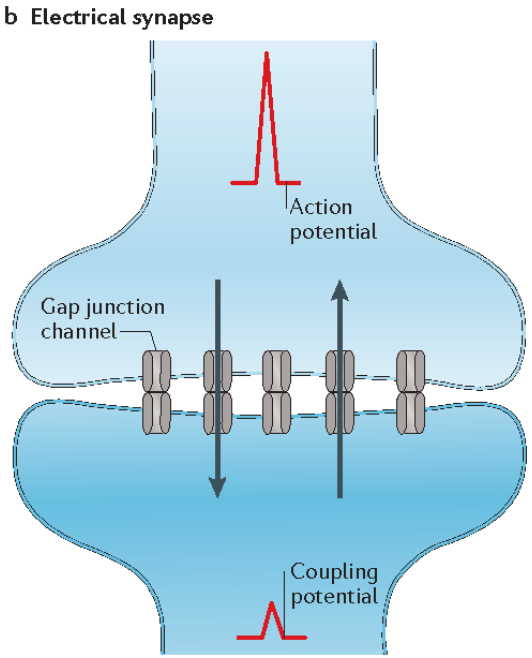
Axon and Synapse
轴突和突触

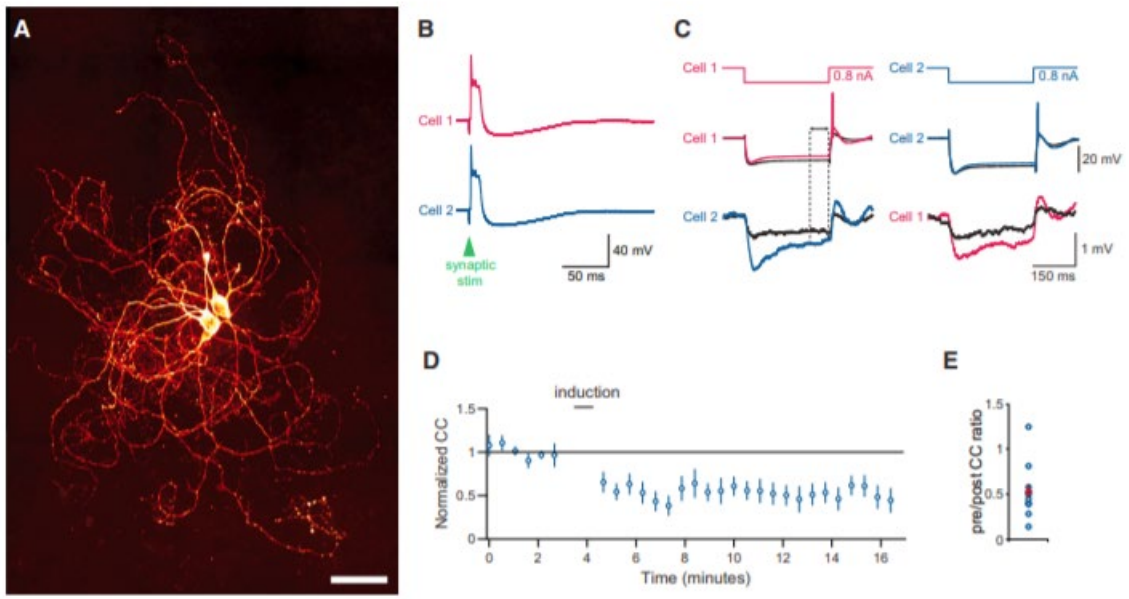




Electrical to chemical to electrical transformation of information



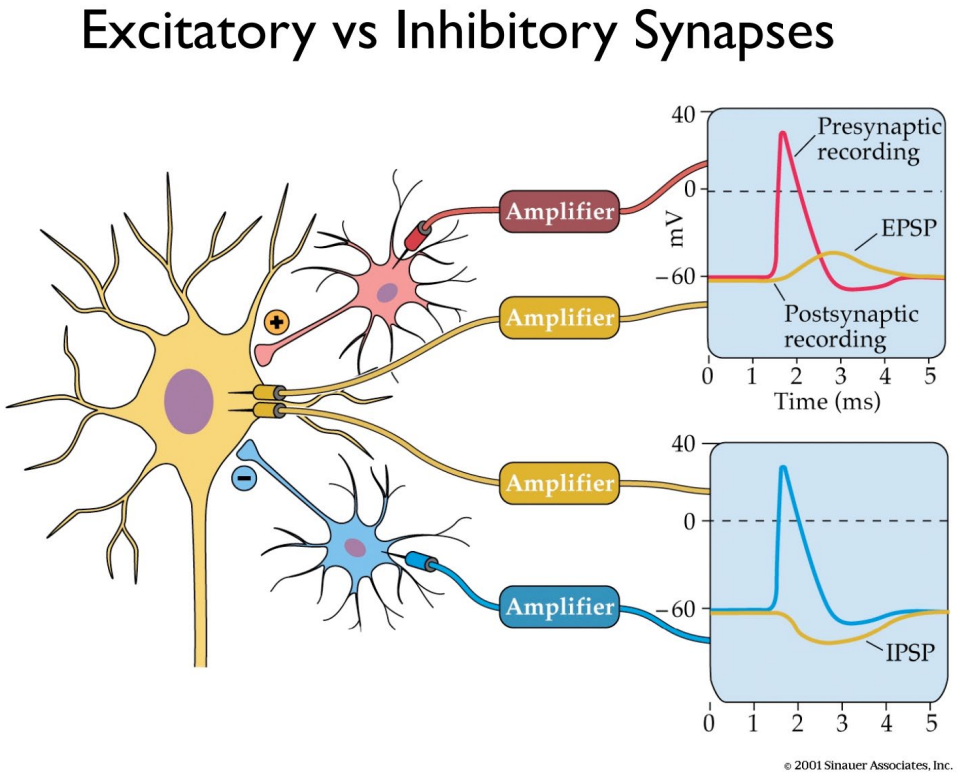


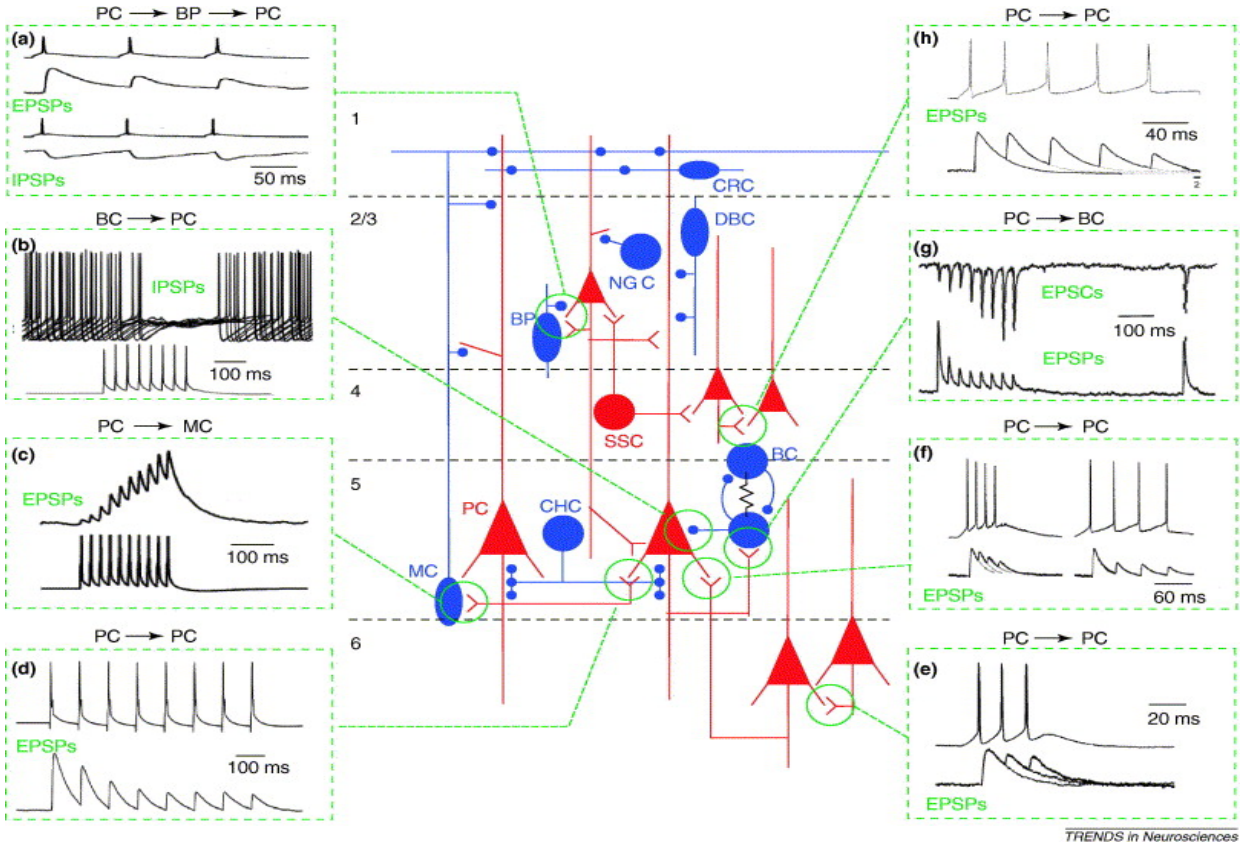


Long-term depression of electrical coupling between inferior olivary neurons

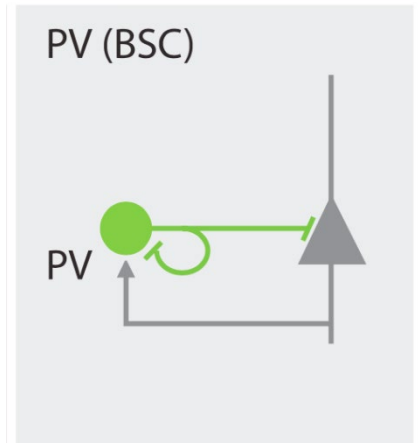
Alexandre Mathy et al, *Neuron*, 2014

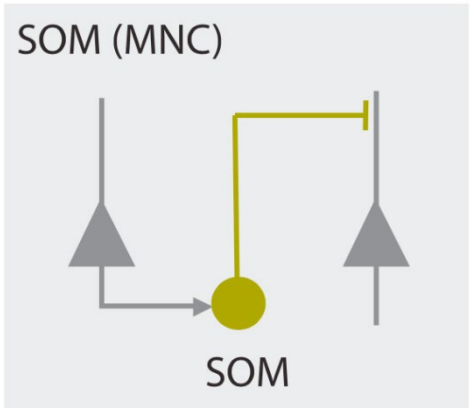
Excitatory and Inhibitory Synapses
兴奋性和抑制性突触

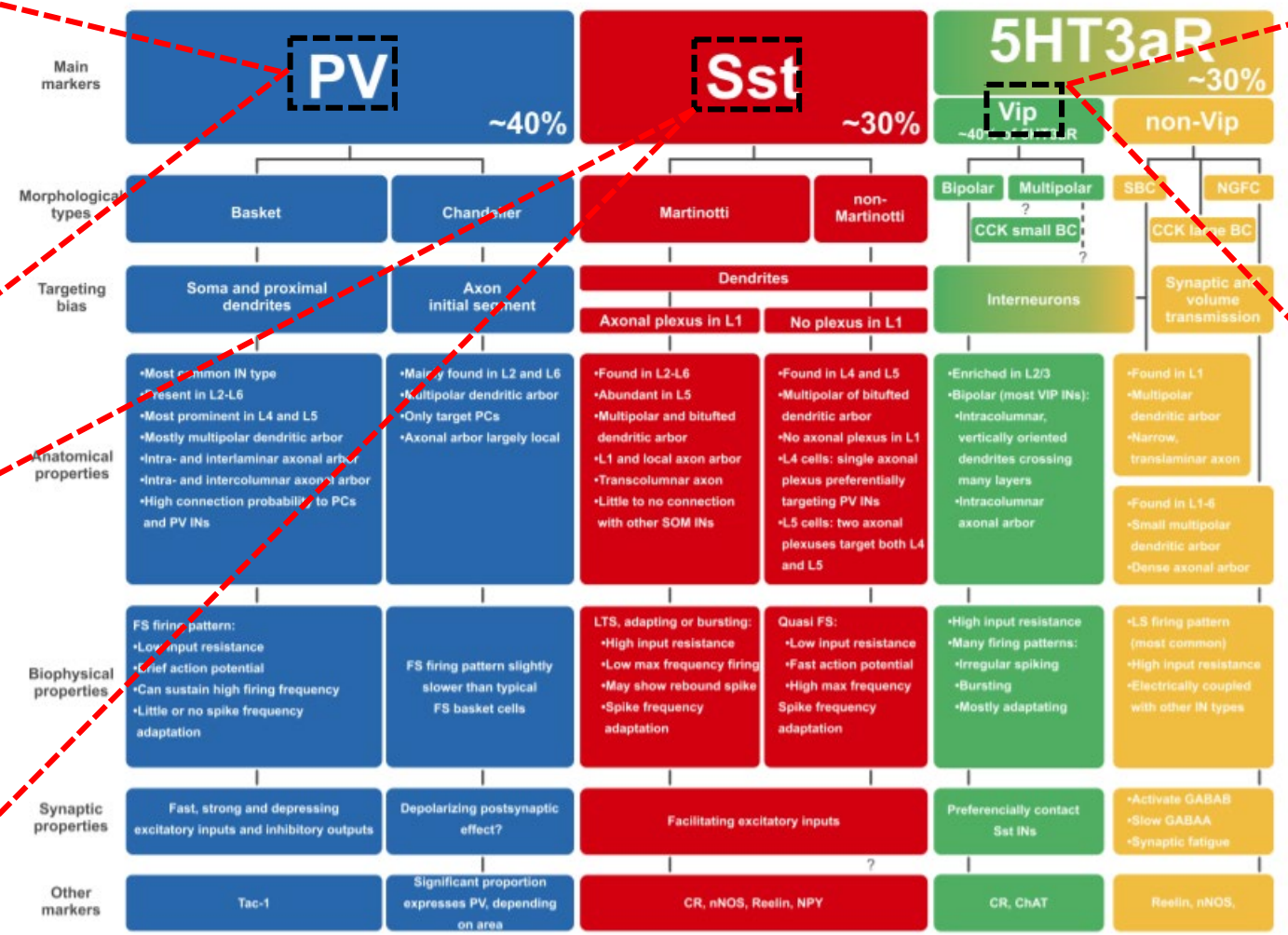


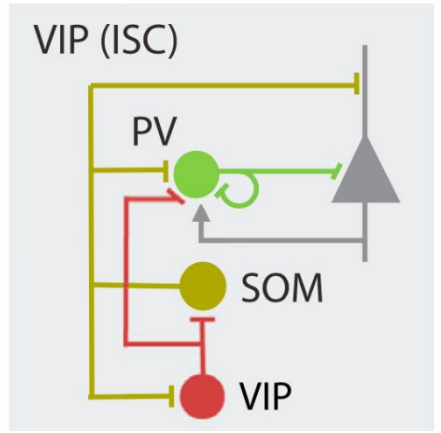


Diversity, classification, and properties of neocortical GABAergic INs





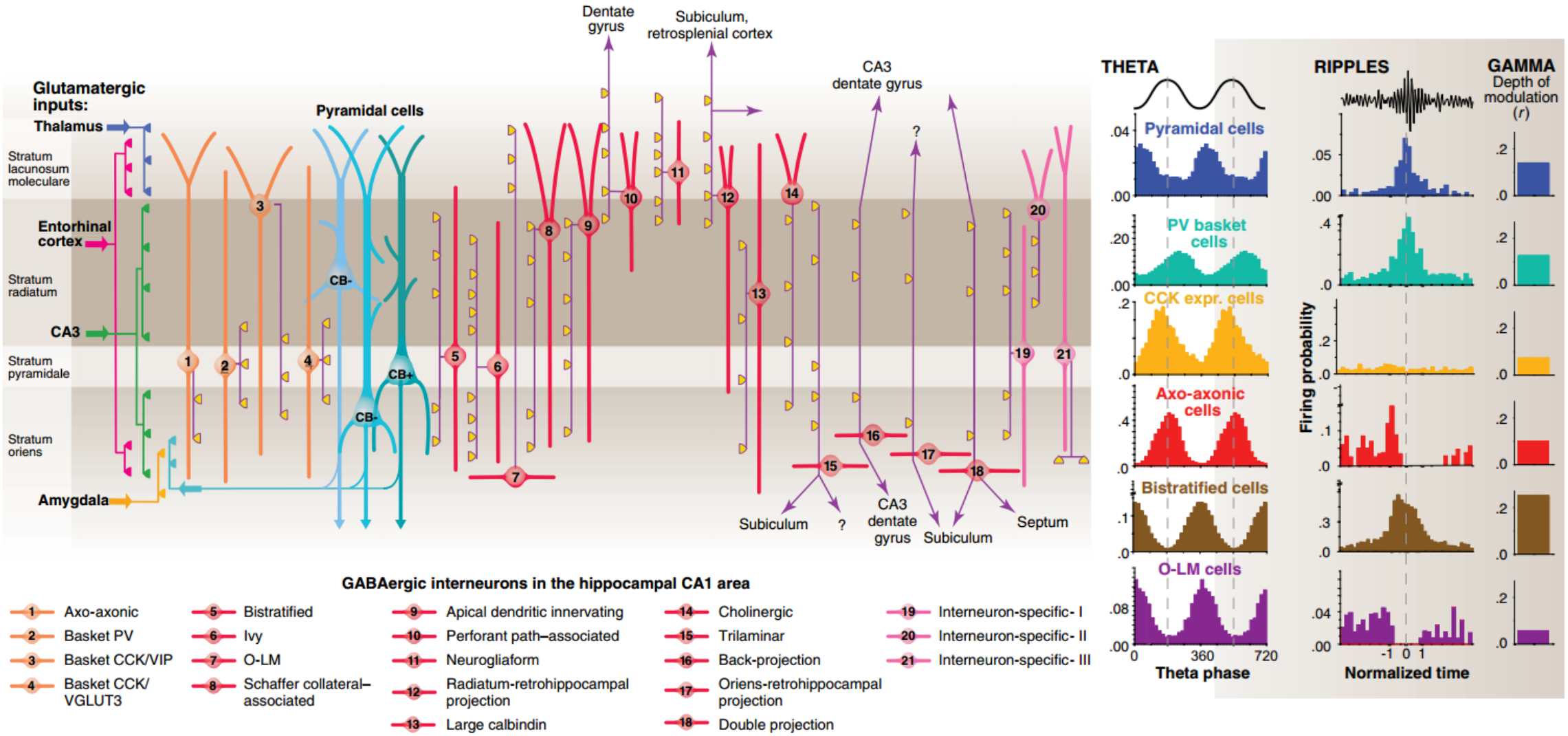




PV: 小清蛋白
SST: 生长抑素
VIP: 血管活性肠肽

Josh Huang et al, *Neuron*, 2014
Bernardo Rudy et al, *Neuron*, 2016

GABAergic interneurons during network oscillations in the hippocampal CA1 area

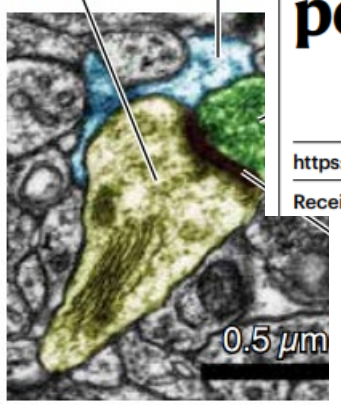


GABAergic interneurons in the hippocampal CA1 area

1. Axo-axonic
2. Basket PV
3. Basket CCK/VIP
4. Basket CCK/VGLUT3
5. Bistratified
6. Ivy
7. O-LM
8. Schaffer collateral–associated
9. Apical dendritic innervating
10. Perforant path–associated
11. Neurogliaform
12. Radiatum-retrohippocampal projection
13. Large calbindin
14. Cholinergic
15. Trilaminar
16. Back-projection
17. Oriens-retrohippocampal projection
18. Double projection
19. Interneuron-specific- I
20. Interneuron-specific- II
21. Interneuron-specific- III

Peter Somogyi et al, *Science*, 2008

Gila : astrocyte, oligodendrocyte, microglia



Astrocytes envelop

chemical content of the
space

d repair

ebris

Article

Astrocytes close a motor circuit critical period

https://doi.org/10.1038/s41586-021-03441-2
Sarah D. Ackerman[1], Nelson A. Perez-Catalan[1,3], Marc R. Freeman[2] & Chris Q. Doe[1]
Received: 21 July 2020

Cell

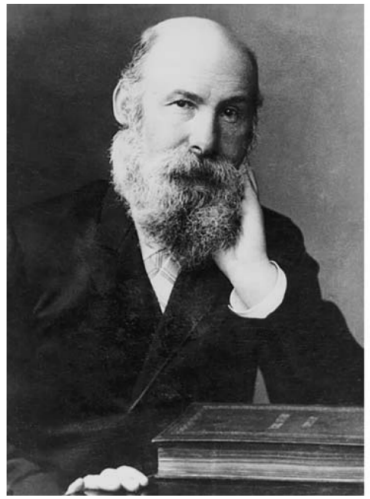
CellPress

Article

GABA-receptive microglia selectively sculpt developing inhibitory circuits

Emilia Favuzzi,[1,2] Shuhan Huang,[1,2,10] Giuseppe A. Saldi,[2,3,10] Loïc Binan,[4] Leena A. Ibrahim,[1,2] Marian Fernández-Otero,[1,2] Yuqing Cao,[1,2] Ayman Zeine,[1] Adwoa Sefah,[1,2] Karen Zheng,[5] Qing Xu,[6] Elizaveta Khlestova,[1] Samouil L. Farhi,[4] Richard Bonneau,[3,7,8] Sandeep Robert Datta,[1] Beth Stevens,[2,9] and Gord Fishell[1,2,11,*]

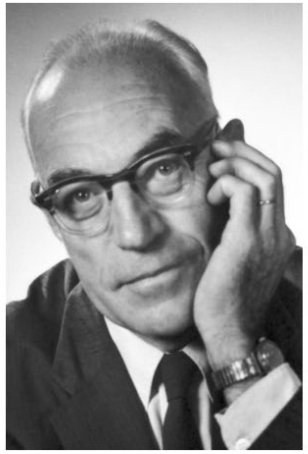
2. Resting potential and Action potential
静息电位和动作电位



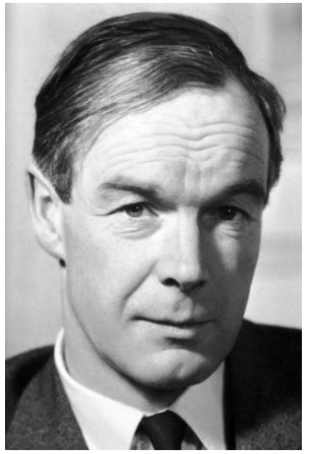
Julius Bernstein

Membrane theory: *"that the electrical potential of the lesioned muscle is caused by the electrolytes, in particular by inorganic salts such as K_2HPO_4, already contained in the undamaged muscle fiber"*

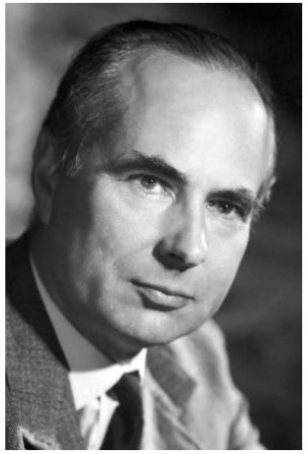
Bernstein, *Pflügers Arch*, 1902



Sir John Eccles



Alan Hodgkin

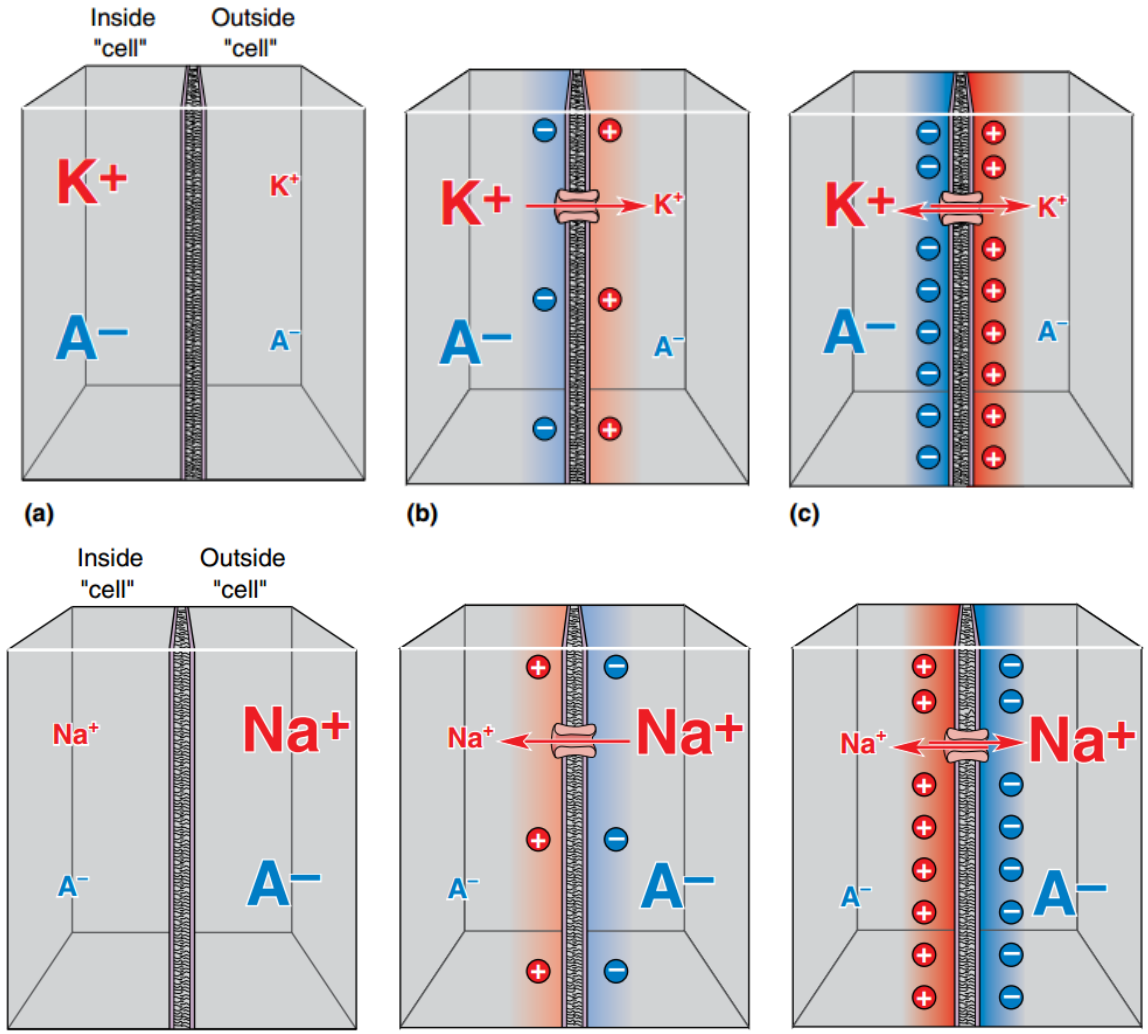


Andrew Huxley

The Nobel Prize in Physiology or Medicine 1963 was awarded jointly to Sir John Carew Eccles, Alan Lloyd Hodgkin and Andrew Fielding Huxley "for their discoveries concerning the ionic mechanisms involved in excitation and inhibition in the peripheral and central portions of the nerve cell membrane."

https://www.nobelprize.org/prizes/medicine/1963/summary/

Equilibrium Potentials 平衡电位



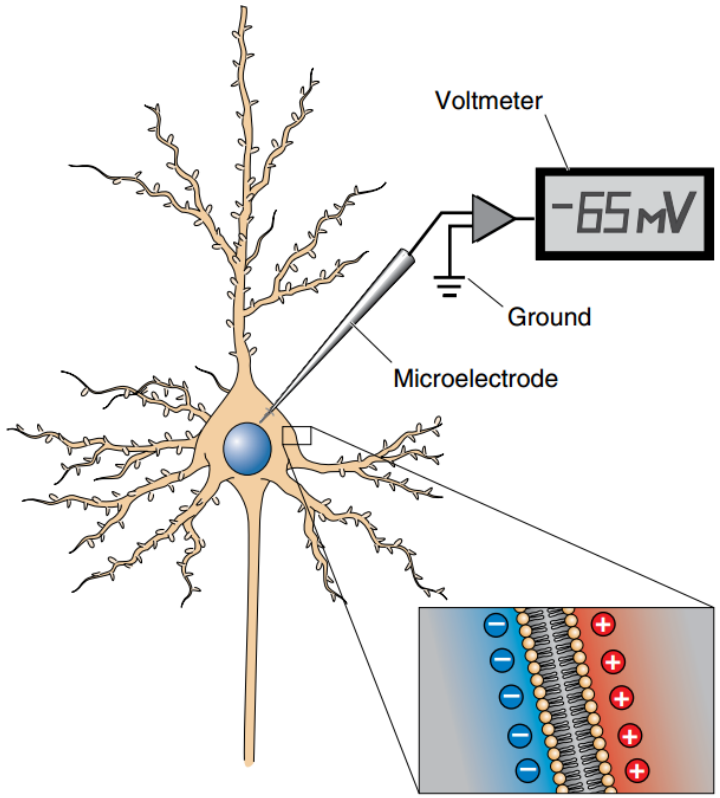
The Nernst Equation

$$E_{ion} = 2.303 \frac{RT}{zF} \log \frac{[ion]_o}{[ion]_i}$$

E_{ion} = ionic equilibrium potential
R = gas constant
T = absolute temperature
z = charge of the ion
F = Faraday's constant
log = base 10 logarithm
$[ion]_o$ = ionic concentration outside the cell
$[ion]_i$ = ionic concentration inside the cell

Ion	Concentration outside (in mM)	Concentration inside (in mM)	Ratio Out : In	E_{ion} (at 37∞C)
K^+	5	100	1 : 20	−80 mV
Na^+	150	15	10 : 1	62 mV
Ca^{2+}	2	0.0002	10,000 : 1	123 mV
Cl^-	150	13	11.5 : 1	−65 mV

Resting potential



The Goldman Equation

$$V_m = 61.54 \text{ mV} \log \frac{P_K [K^+]_o + P_{Na} [Na^+]_o}{P_K [K^+]_i + P_{Na} [Na^+]_i}$$

$$V_m = 61.54 \text{ mV} \log \frac{40\ (5) + 1\ (150)}{40\ (100) + 1\ (15)}$$

$$= 61.54 \text{ mV} \log \frac{350}{4015}$$

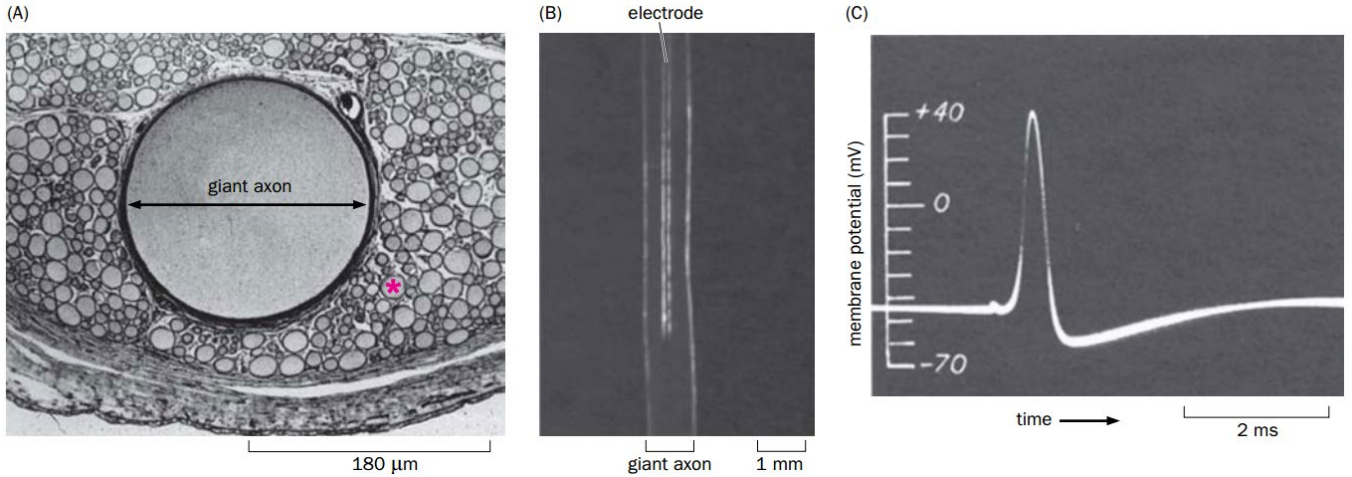
$$= -65 \text{ mV}$$

The Resting Potential is determined by more than one type of ions.

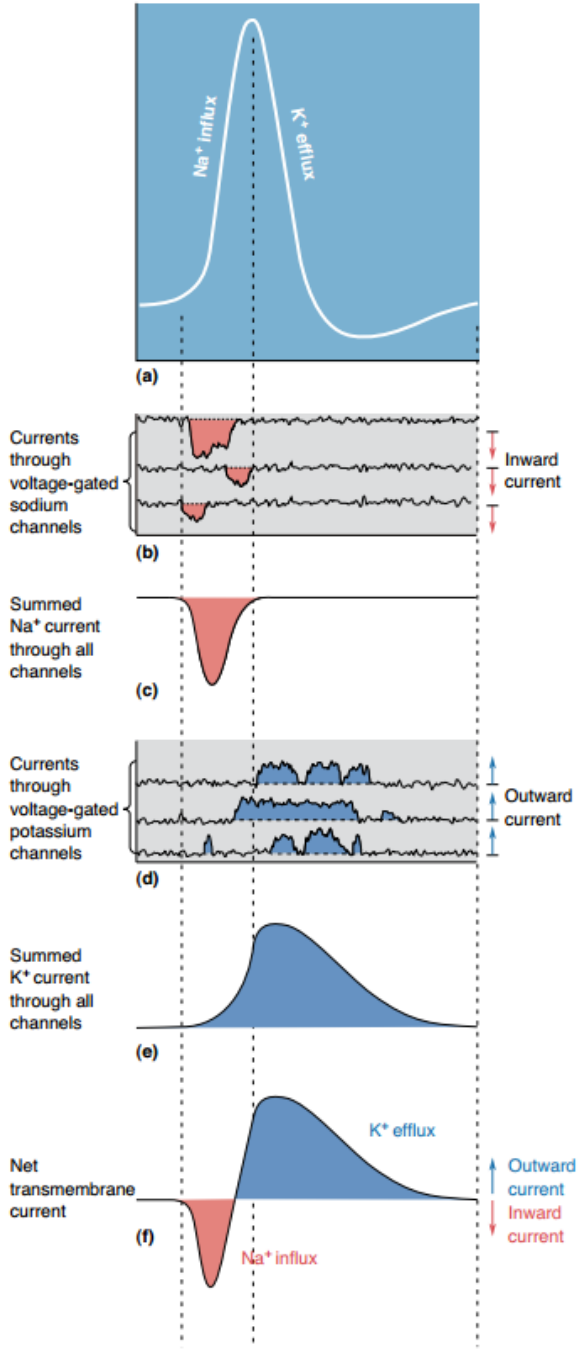
Action potential

Principles of neurobiology (2016)

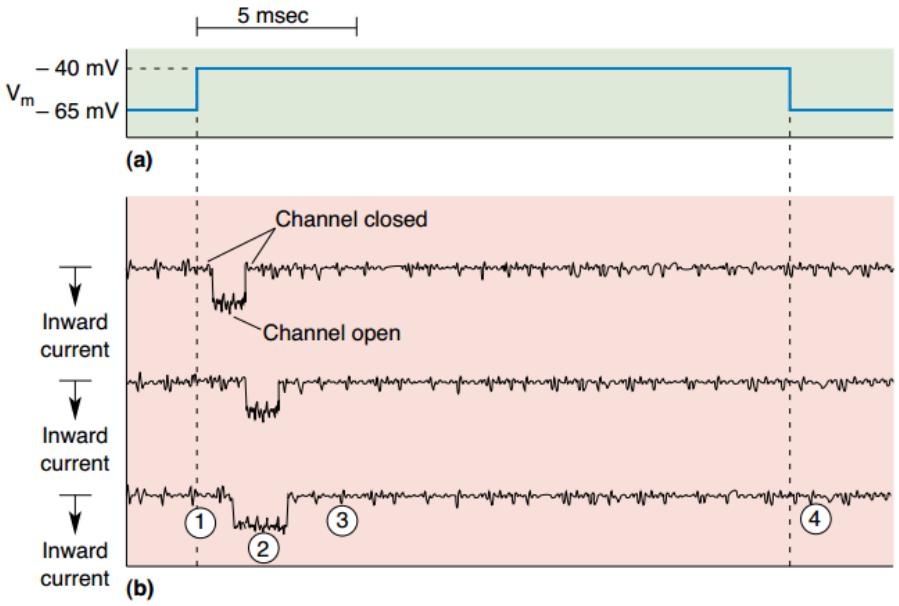
Rapid escape response of a zebrafish larva

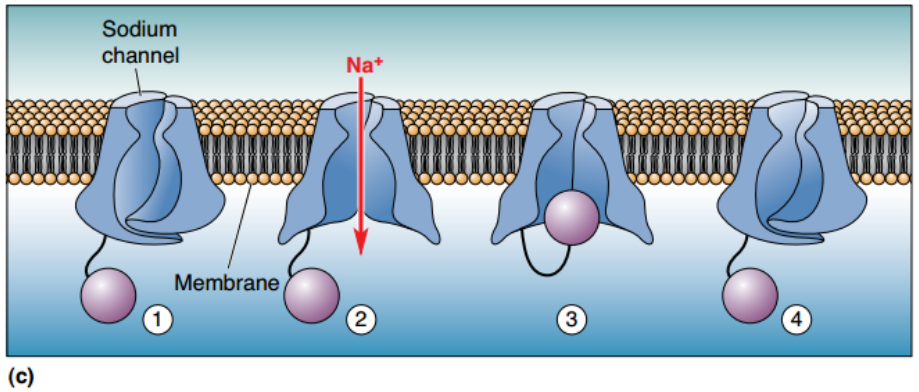


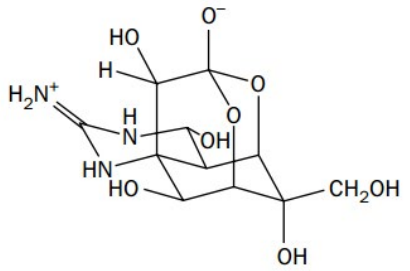
Studying action potentials in the squid giant axon



The molecular basis of the action potential





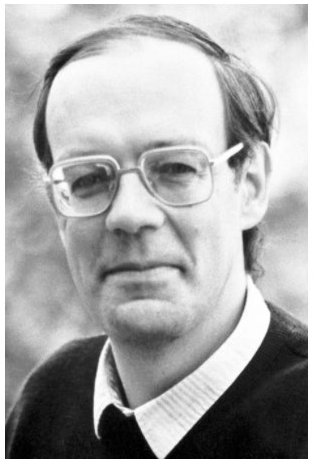


The puffer fish, source of TTX

The effects of Tetrodotoxin (TTX) on the voltage-gated sodium channel

3. Technologies： Electrophysiology 电生理
The Patch-Clamp 膜片钳

Erwin Neher

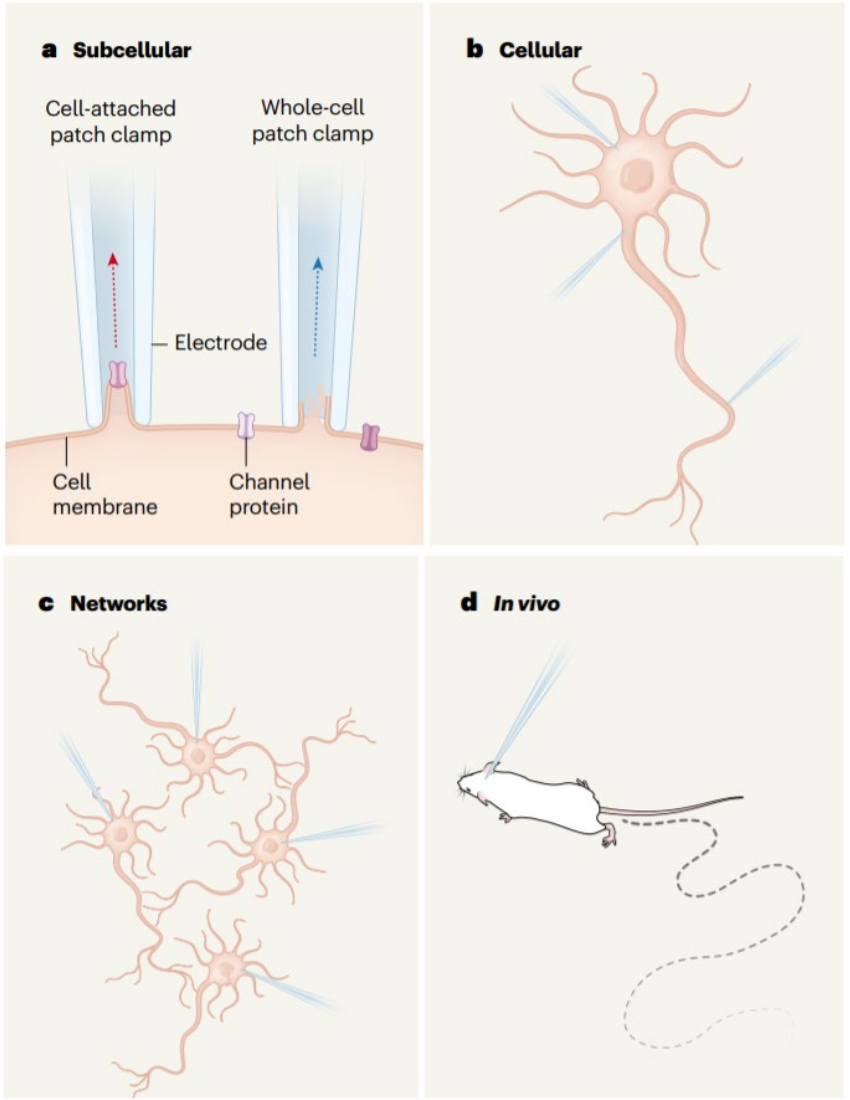


Bert Sakmann

The Nobel Prize in Physiology or Medicine 1991 was awarded jointly to Erwin Neher and Bert Sakmann "for their discoveries concerning the function of single ion channels in cells."

https://www.nobelprize.org/prizes/medicine/1991/summary/

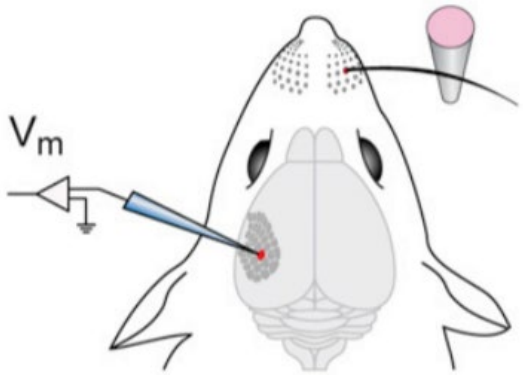
"Patch-clamp recording is arguably still the most effective way of studying electrical signals in the brain."

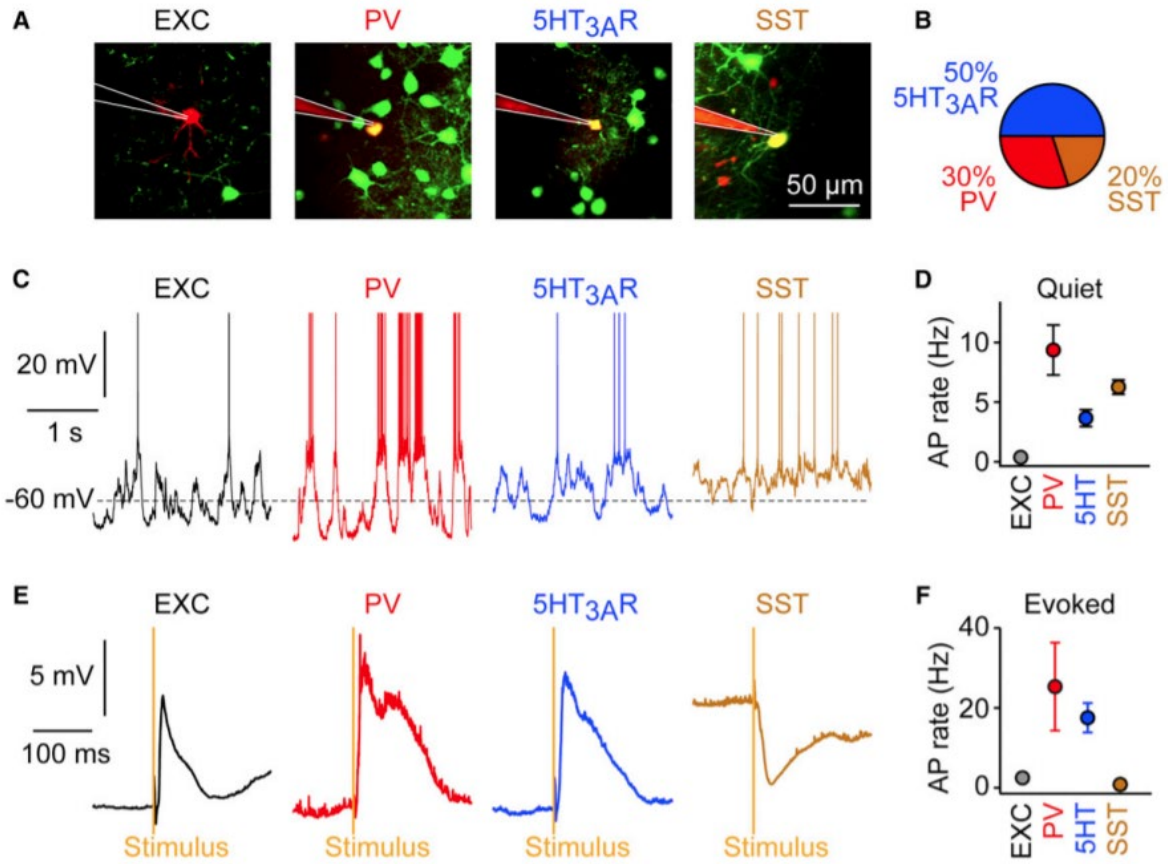


Alexander et al, *Nature*, 2019

Cell type-specific activity of GABAergic neurons in L2/3 barrel cortex of awake mice

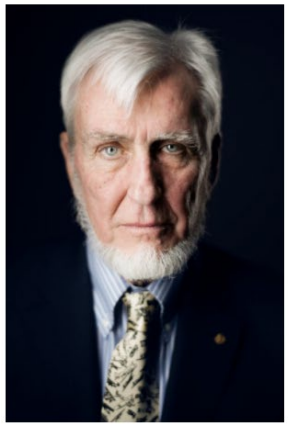
Carl C.H. Petersen
EPFL





Carl C.H. Petersen et al, *Neuron*, 2013

Tetrode, Multi-unit recording

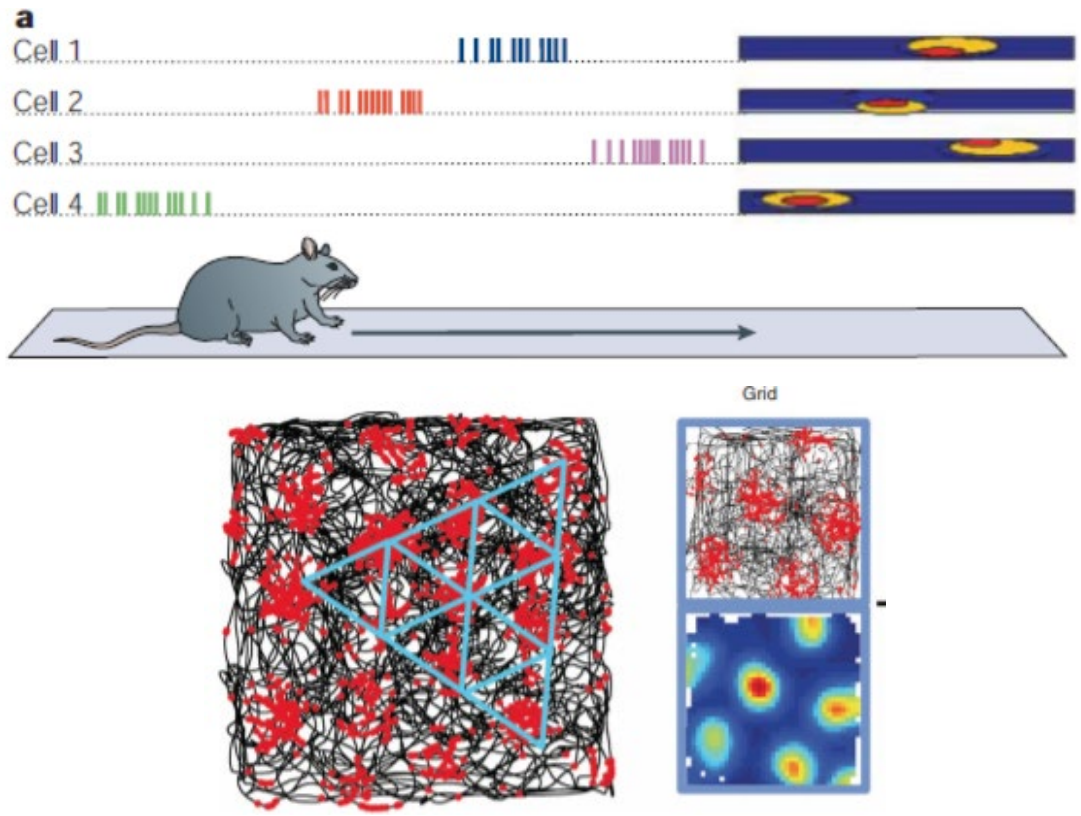

John O'Keefe


May-Britt Moser


Edward Moser

The Nobel Prize in Physiology or Medicine 2014 was divided, one half awarded to John O'Keefe, the other half jointly to May-Britt Moser and Edvard I. Moser "for their discoveries of cells that constitute a positioning system in the brain."

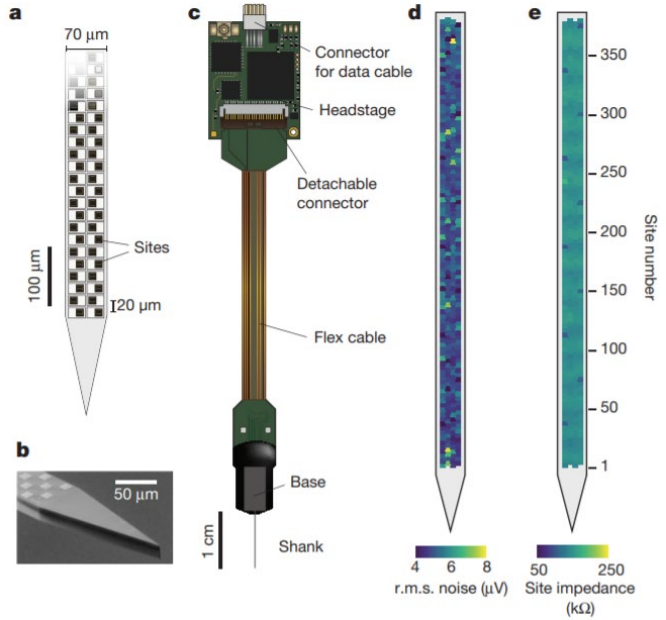
https://www.nobelprize.org/prizes/medicine/2014/summary/

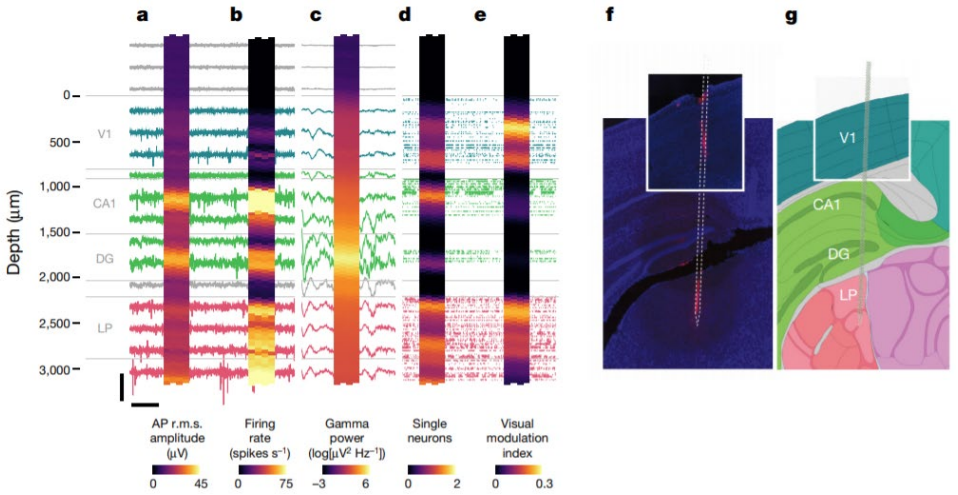


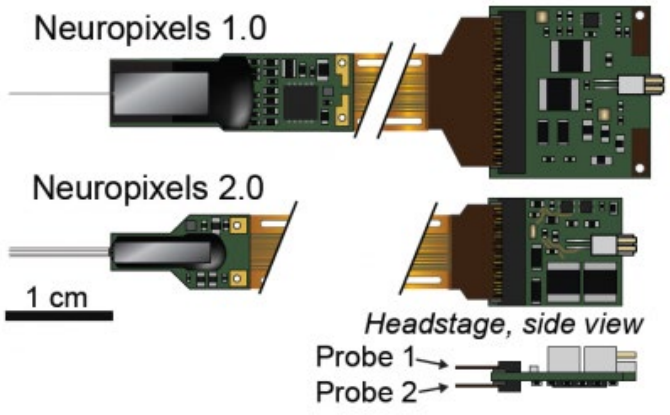
Moser. *Cold Spring Harb Perspect Biol*. 2015

Neuropixels

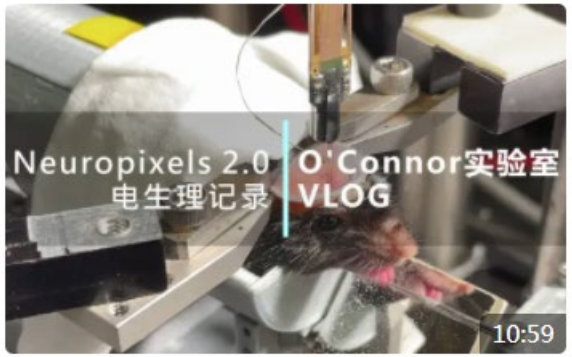
Timothy Harris
Janelia Research Campus







https://www.ucl.ac.uk/neuropixels/
Janelia Research Campus
Allen Institute for Brain Science



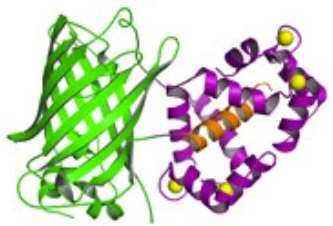
Neuropixels2.0探针上手VLOG 同时记录600+神经

https://space.bilibili.com/

Timothy Harris et al,. *Nature*. 2017

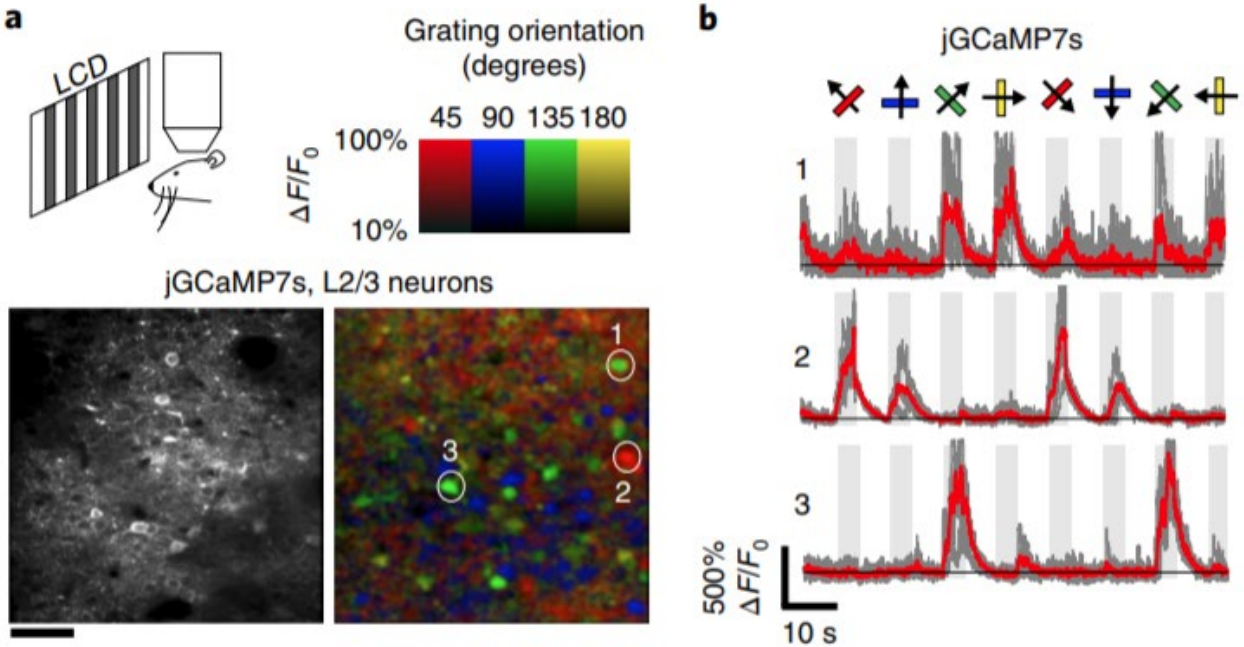
Calcium imaging 钙成像

Neural activity causes rapid changes in intracellular free calcium. **Calcium imaging experiments** have relied on this principle to track the activity of neuronal populations and to probe excitation of small neurons and neuronal microcompartments.



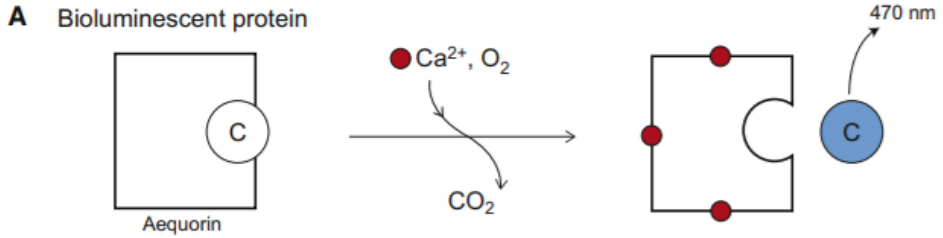
GCaMP6

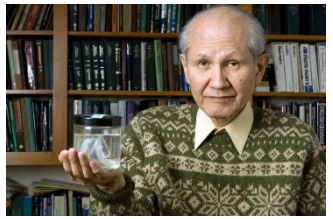
Circularly permuted green flurescent protein (cpGFP)
Calcium-binding protein calmodulin (CaM)
CaM-interacting M13 peptide



Hod Dana et al. *Nature Methods.* 2015

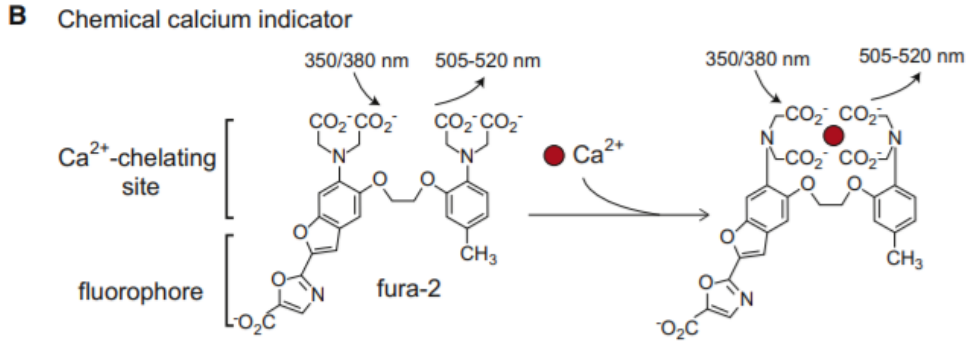
Calcium indicators

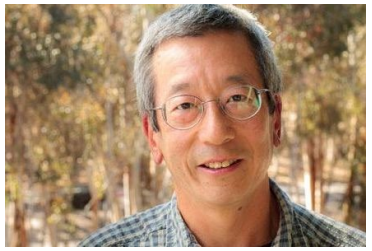




Osamu Shimomura

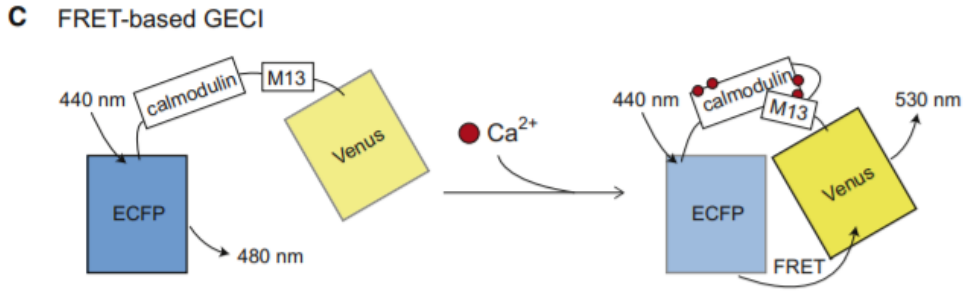
Aequorin
J Cell Comp Physiol 1962 Citation: 2844





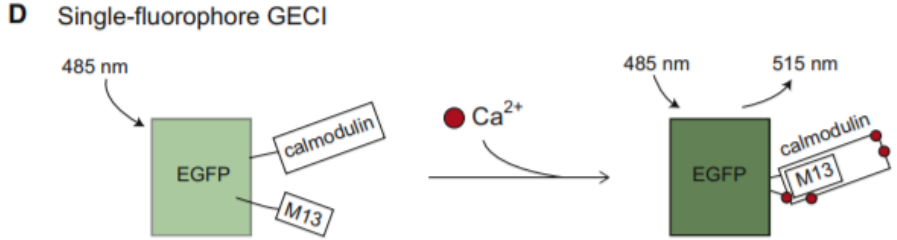
Roger Tsien

Fura-2
JBC 1985 Citation: 25003



Atsushi Miyawaki

YC 3.60
PNAS 2004 Citation: 1115



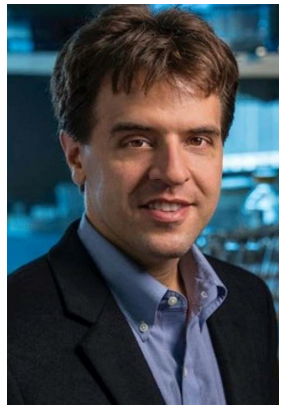
Loren L Looger

GCaMP3
Nature Methods 2009 Citation: 1888

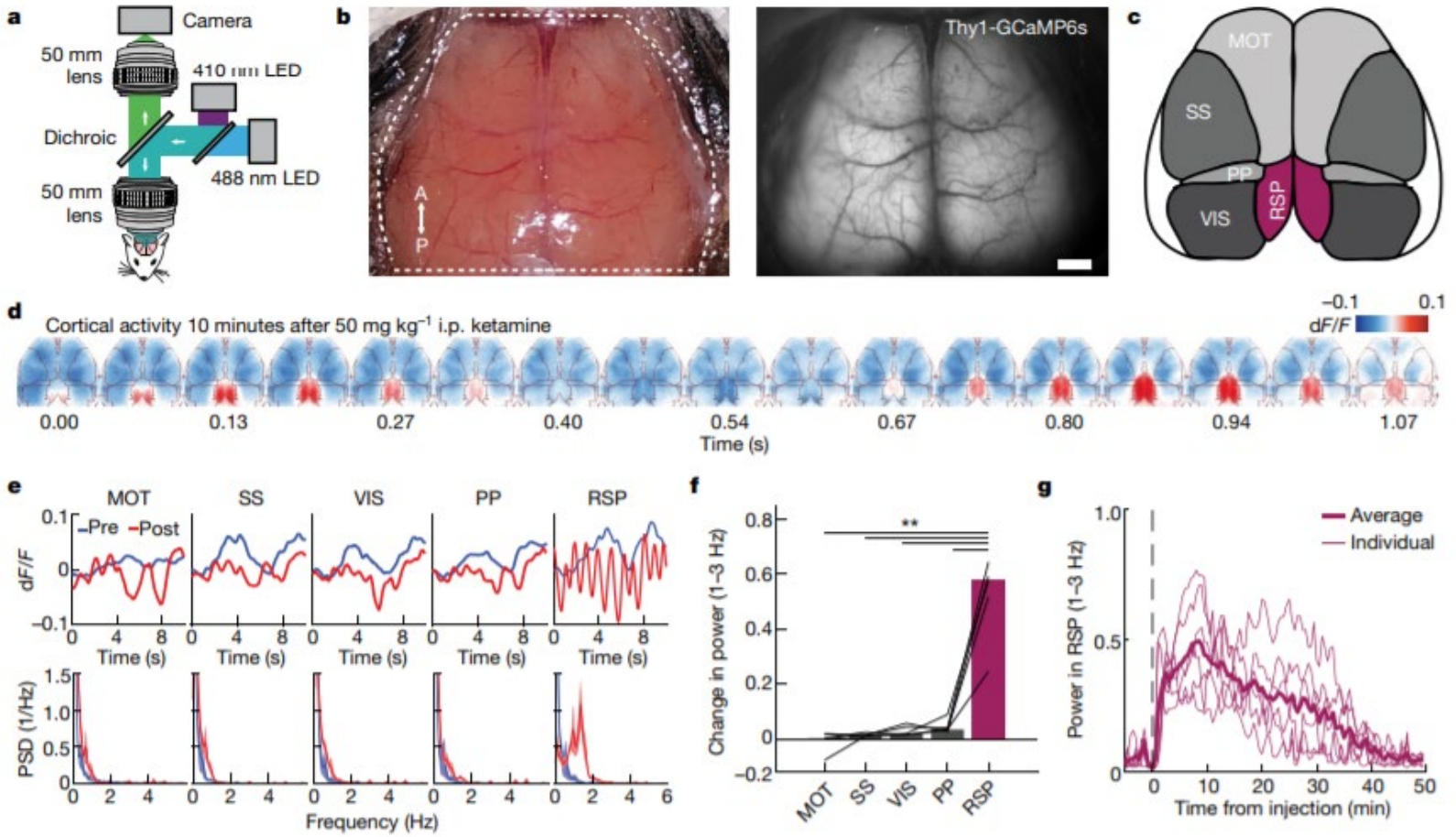
GCaMP6
Nature 2013 Citation: 4155

Konnerth et al, *Neuron*, 2012

Multiregional widefield imaging of cortical activity reveals ketamine-induced retrosplenial rhythm

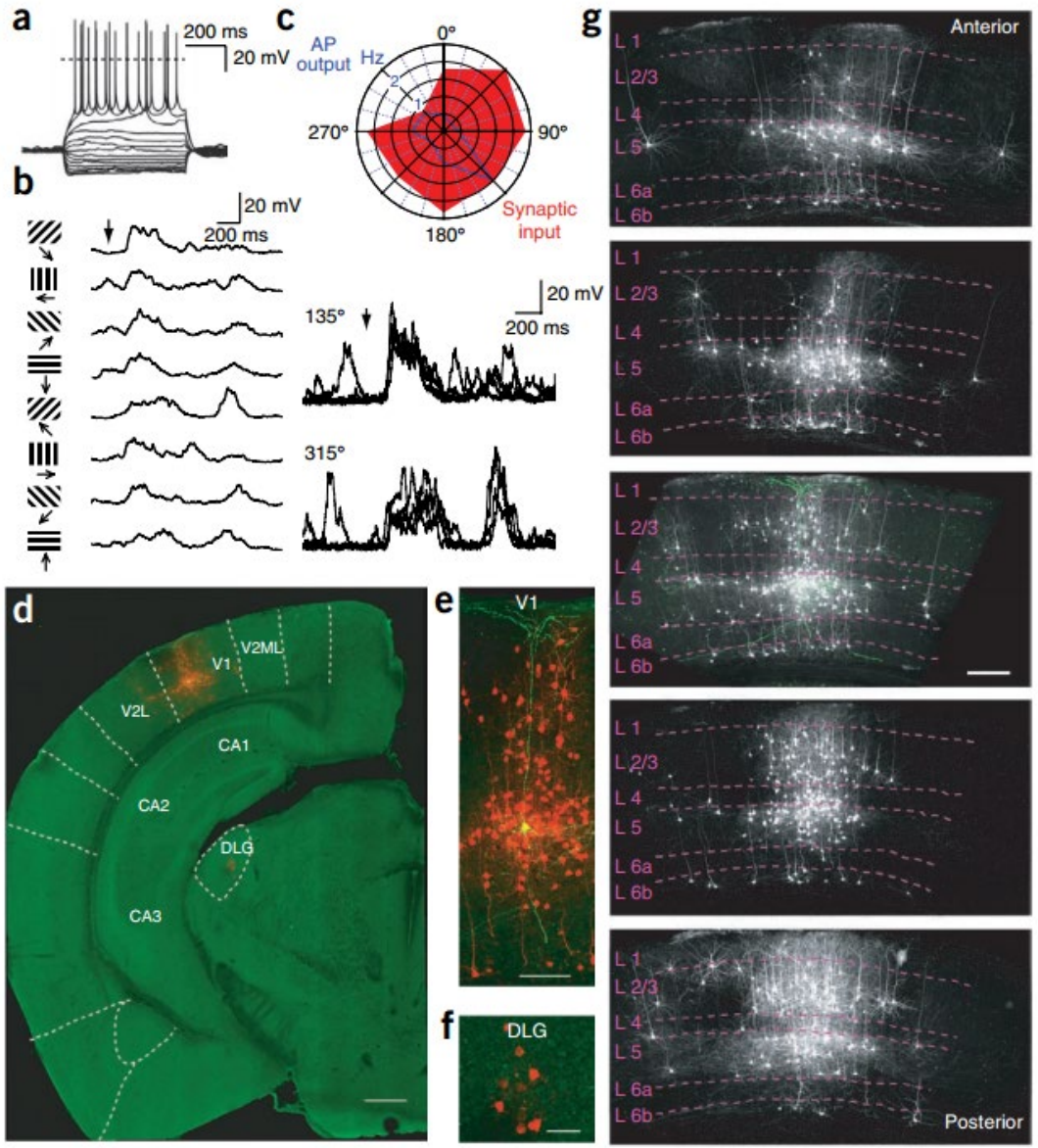


Karl Deisseroth
Standford Univ.

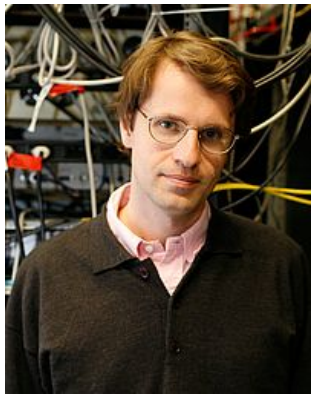


Sam Vesuna et al, *Nature*, 2020

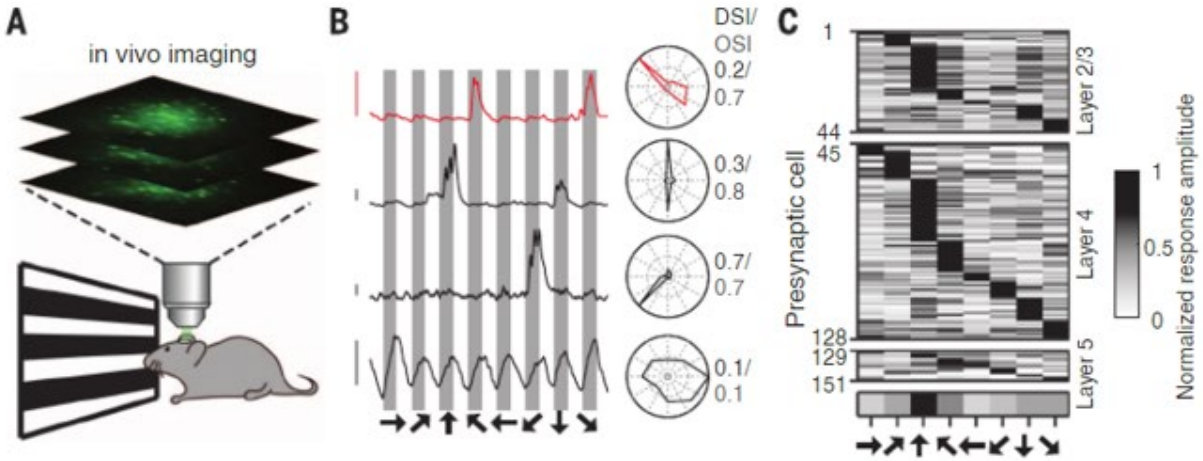
Ephys and Imaging



Troy Margrie
UCL



Botond Roska
Univ. of Basel



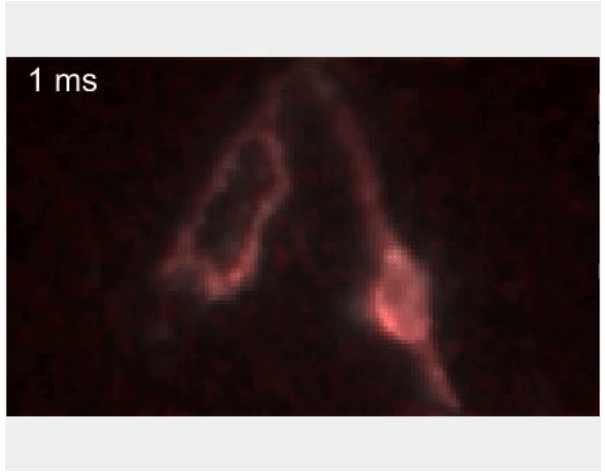
Single-cell–initiated monosynaptic tracing reveals layer-specific cortical network modules

Ede Rancz et al, *Nature Neuroscience*, 2011

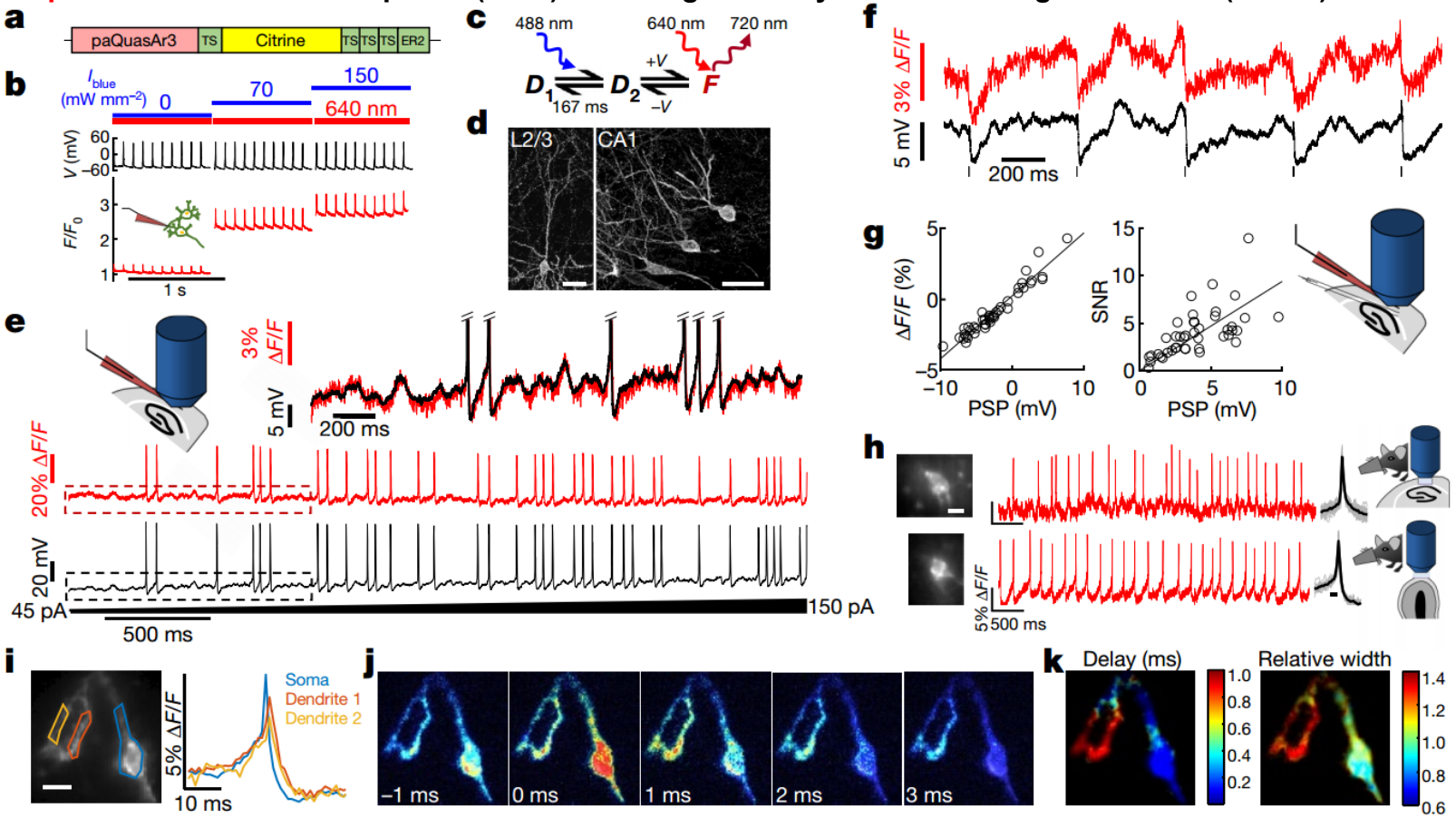
Adrian Wertz et al, *Science*, 2015

Voltage imaging 电压成像

Adam Cohen
Harvard Univ.

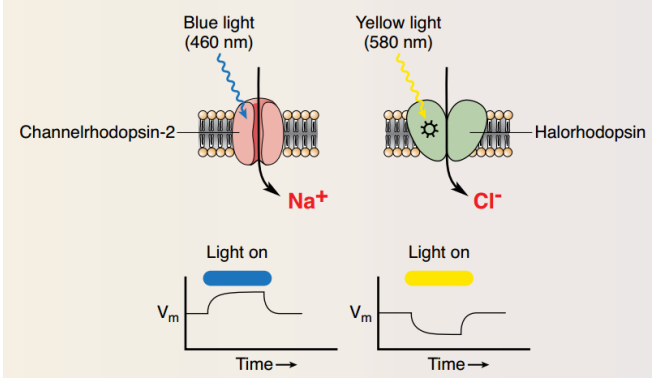


paQuaAr3: Archaerhodopsin 3 (Arch)-derived genetically encoded voltage indicators (GEVIs)



Opotogenetic 光遗传

Combination of optics and genetics in technologies that are designed to control (by eliciting or inhibiting) well-defined events in cells of living animal tissue



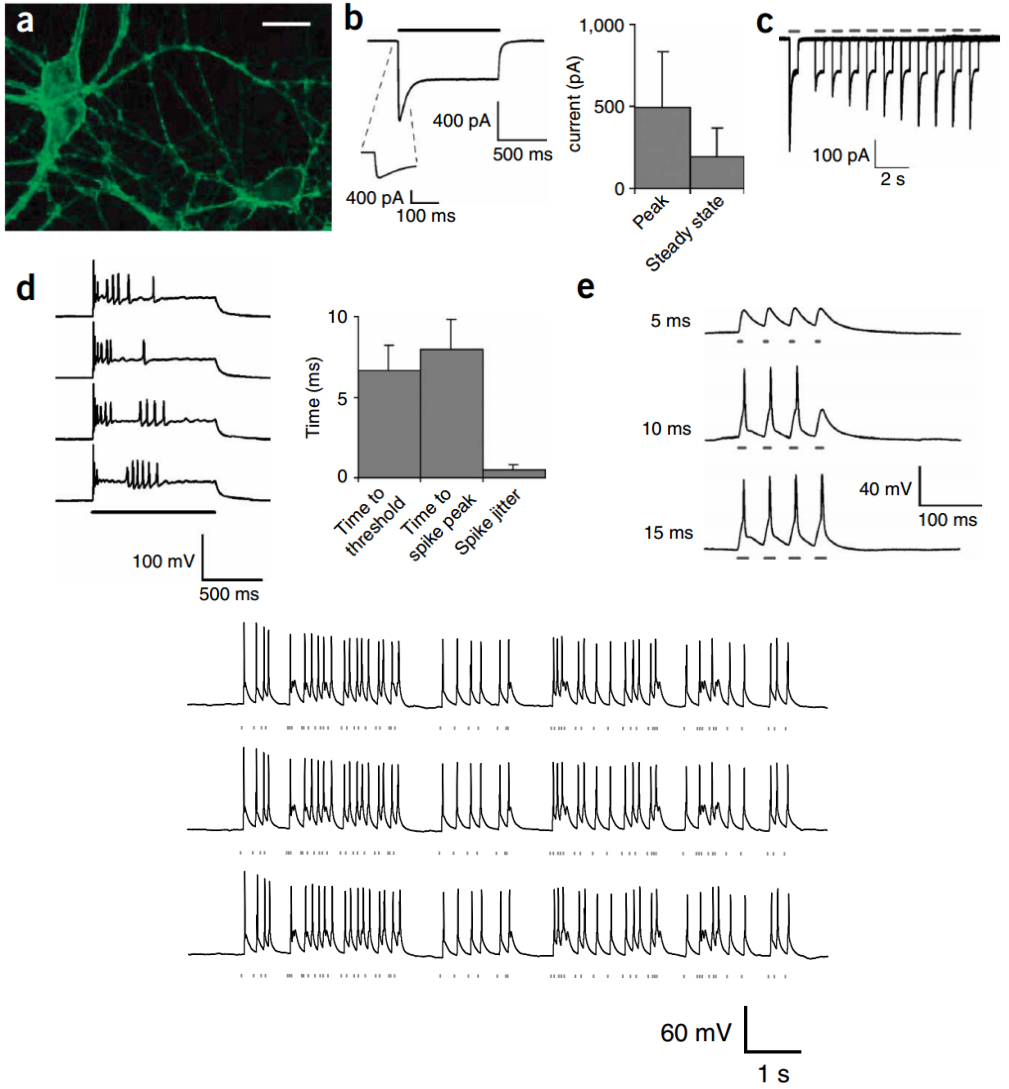
Peter Hegemann
Humboldt Univ.

Karl Deisseroth
Standford Univ.

Ed Boyden
MIT

Gero Miesenböck
Oxford Univ.

ChR2 enables precisely light-driven neuron spiking in cultured hippocampal neurons



Ed Boyden et al, *Nature Neuroscience*, 2005

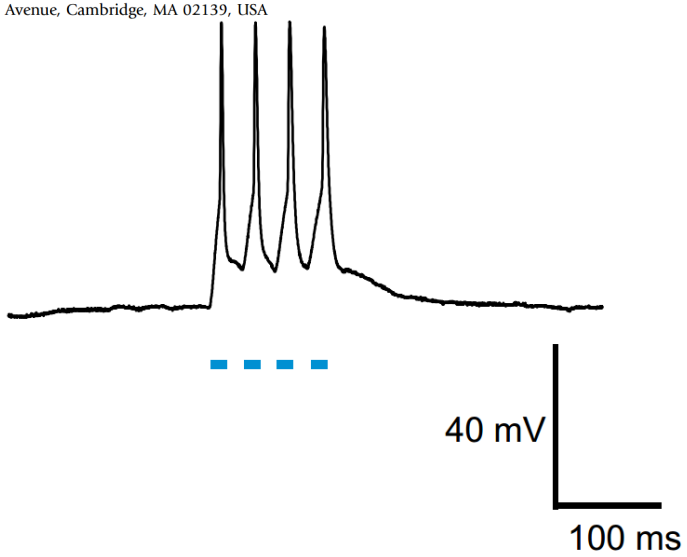
F1000Reports BIOLOGY

Published: 03 May 2011

A history of optogenetics: the development of tools for controlling brain circuits with light

Edward S. Boyden

Address: Media Lab, McGovern Institute, Department of Brain and Cognitive Sciences and Department of Biological Engineering, MIT, 77 Massachusetts Avenue, Cambridge, MA 02139, USA



REC LIVE on YouTube

Antoine Adamantidis	*→ McGill → Bern*	*Matt Lovett-Barron*	*→ UCSD*	*Recent collaborators:*
Raag Airan	*→ Stanford*	*Talia Lerner*	*→ Northwestern*	P. Hegemann; H. Kandori;
Avishek Adhikari	*→ UCLA*	*Conor Liston*	*→ Cornell*	Z. Bao; H. Kato; R. Dror;
Will Allen	*→ Harvard*	*Tim Machado*		B. Kobilka; O. Nureki;
Polina Anikeeva	*→ MIT*	*Jim Marshel*		K. Rajan, S. Ganguli
Claire Bedbrook		*Sean Quirin*		
Andre Berndt	*→ U. Wash.*	*Priya Rajasethupathy*	*→ Rockefeller*	*Staff:* Charu Ramakrishnan,
Ed Boyden	*→ MIT*	*Ethan Richman*		Cynthia Delacruz,
Kwanghun Chung	*→ MIT*	*Vikaas Sohal*	*→ UCSF*	Maisie Lo, Sally Pak
Lief Fenno		*Emily Sylwestrak*	*→ Oregon*	Funding: HHMI, NIMH, NIDA,
Inbal Goshen	*→ Hebrew U.*	*Raju Tomer*	*→ Columbia*	NSF, Simons, DARPA, Gatsby,
Viviana Gradinaru	*→ Caltech*	*Kay Tye*	*→ MIT → Salk*	NARSAD/BBRF
Lisa Gunaydin	*→ UCSF*	*Xiao Wang*	*→ MIT/Broad*	
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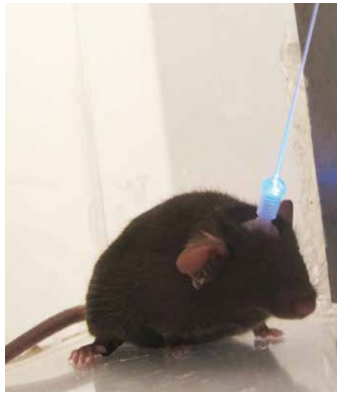
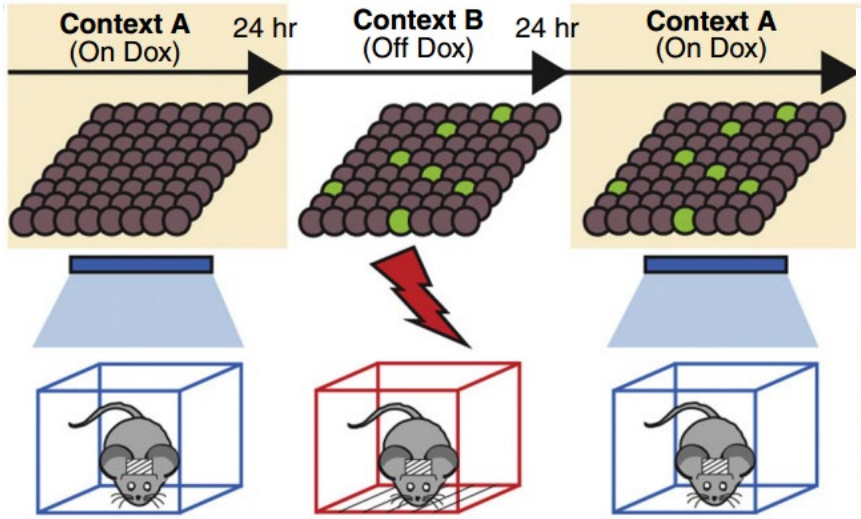
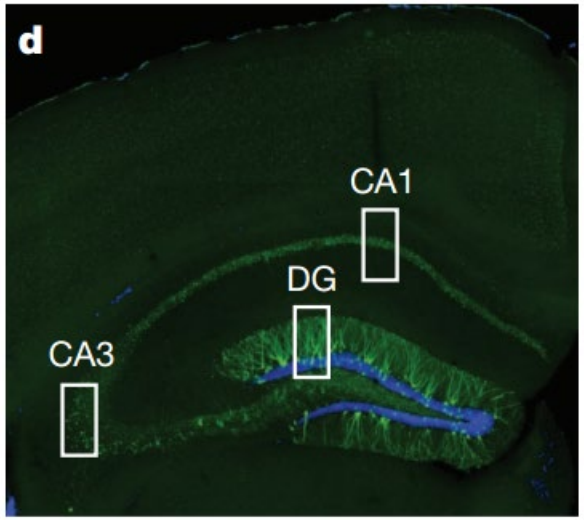
Christina Kim		*Melissa Warden*	*→ Cornell*	optogenetics.org
Sung-Yon Kim	*→ Seoul NU*	*Matt Wright*	*→ Cornell*	clarityresourcecenter.org
Yoon Kim		*Li Ye*	*→ Scripps*	
Jin Hyung Lee	*→ Stanford*	*Ofer Yizhar*	*→ Weizmann*	
Jia Liu	*→ Harvard*	*Feng Zhang*	*→ MIT/Broad*	

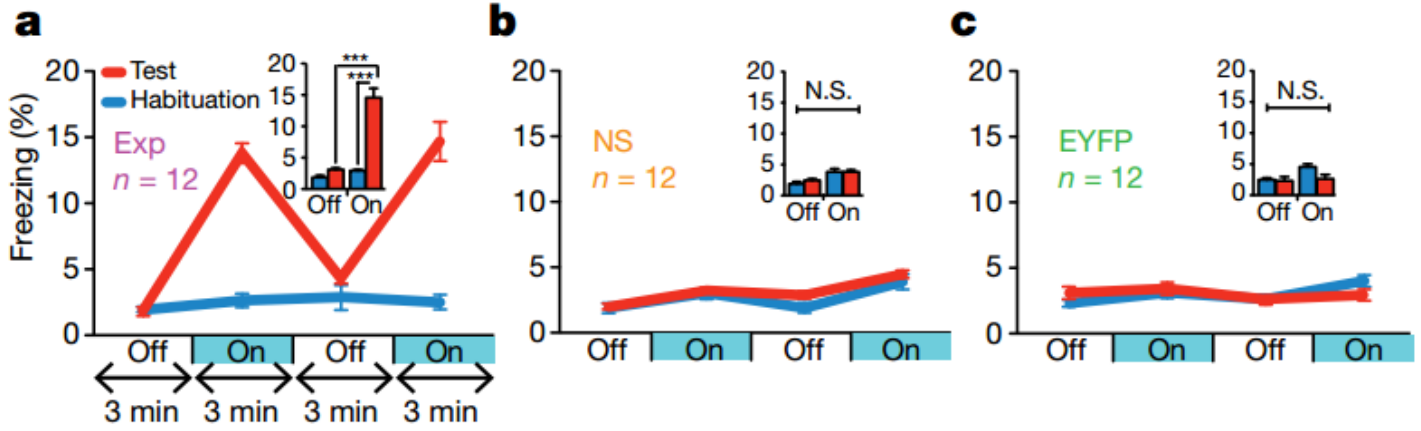
Optogenetic stimulation of a hippocampal neurons activates fear memory recall

Susumu Tonegawa
MIT





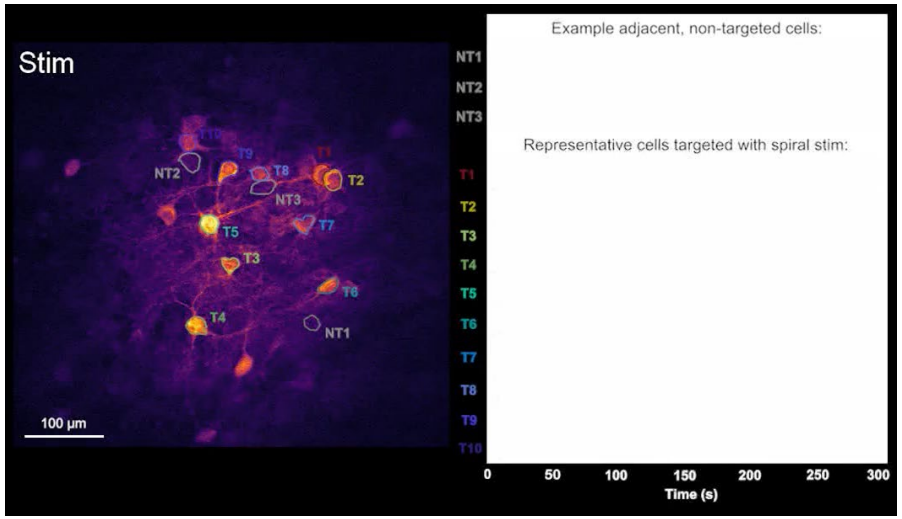




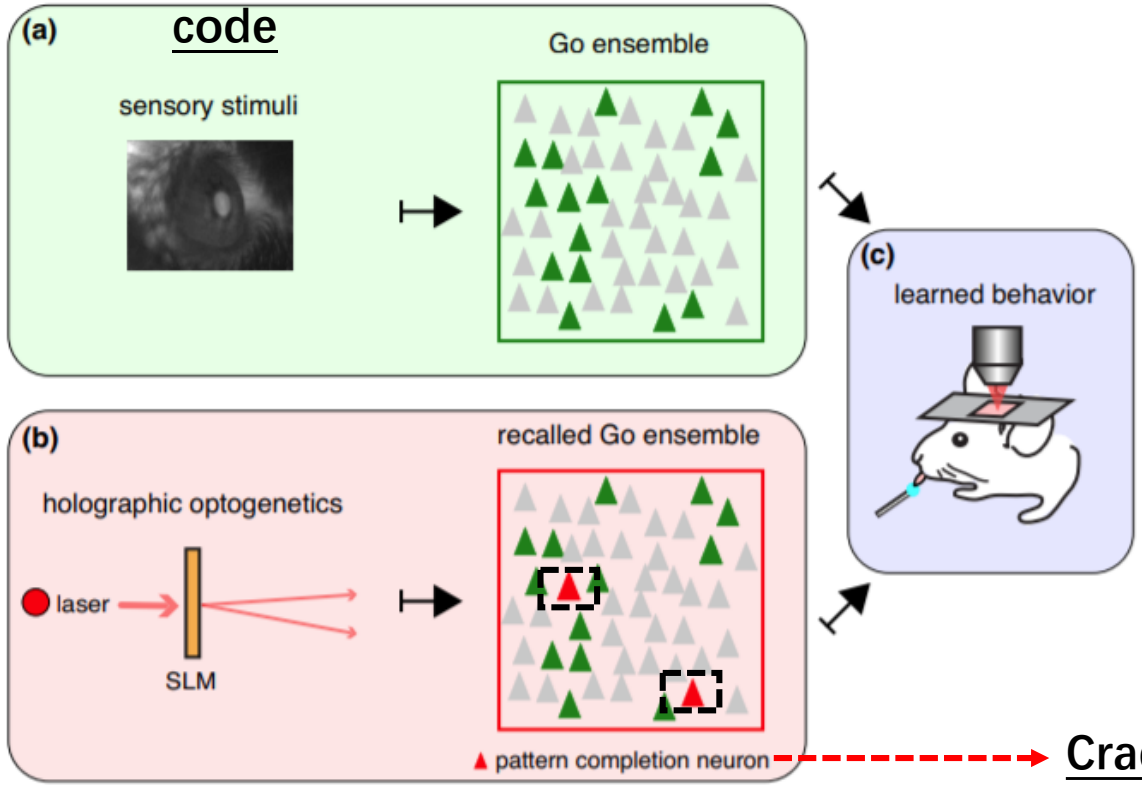
Xu Liu et al, *Nature*, 2012

All-Optical： Imaging and Opotogenetic

Rafael Yuste
Columbia Univ.



Joshua H. Jennings et al, *Nature*, 2019



Probabilistic graphical model

Cracking the neural code

Rafael Yuste et al, *Curr Opin Neurobiol*., 2020

Thank you!