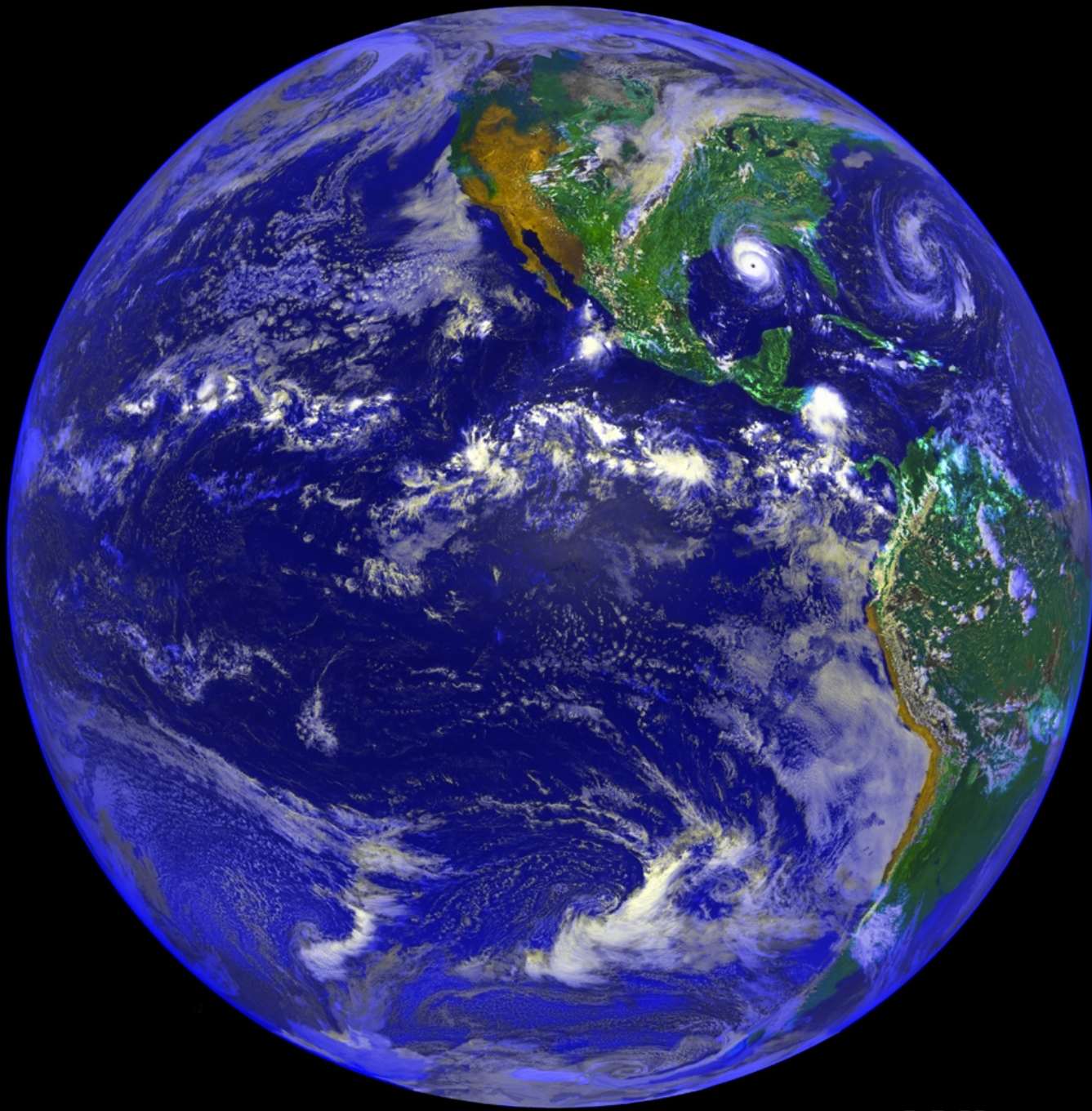


The Origin of Consciousness

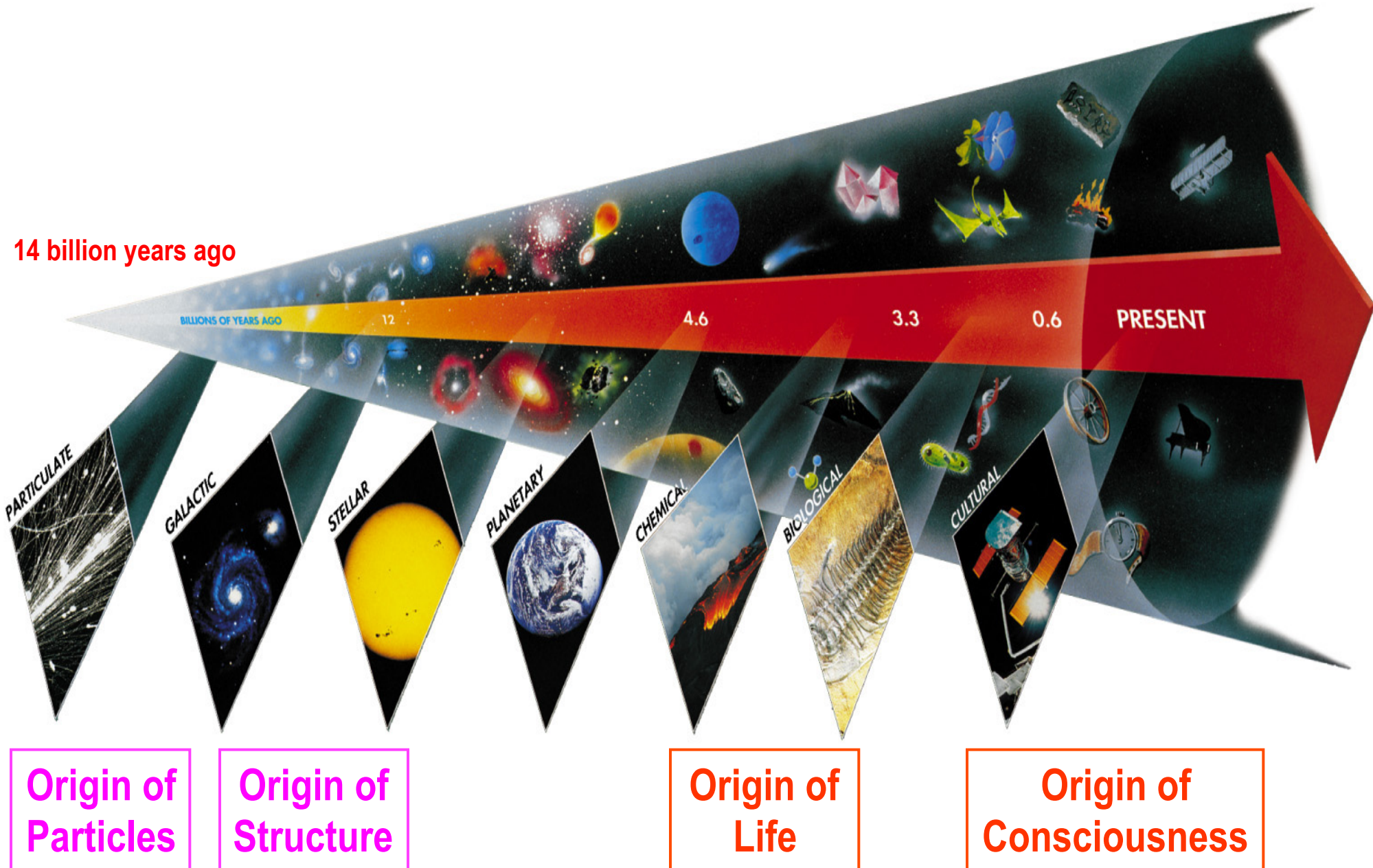
Katsushi Arisaka

***University of California, Los Angeles
Department of Physics and Astronomy***

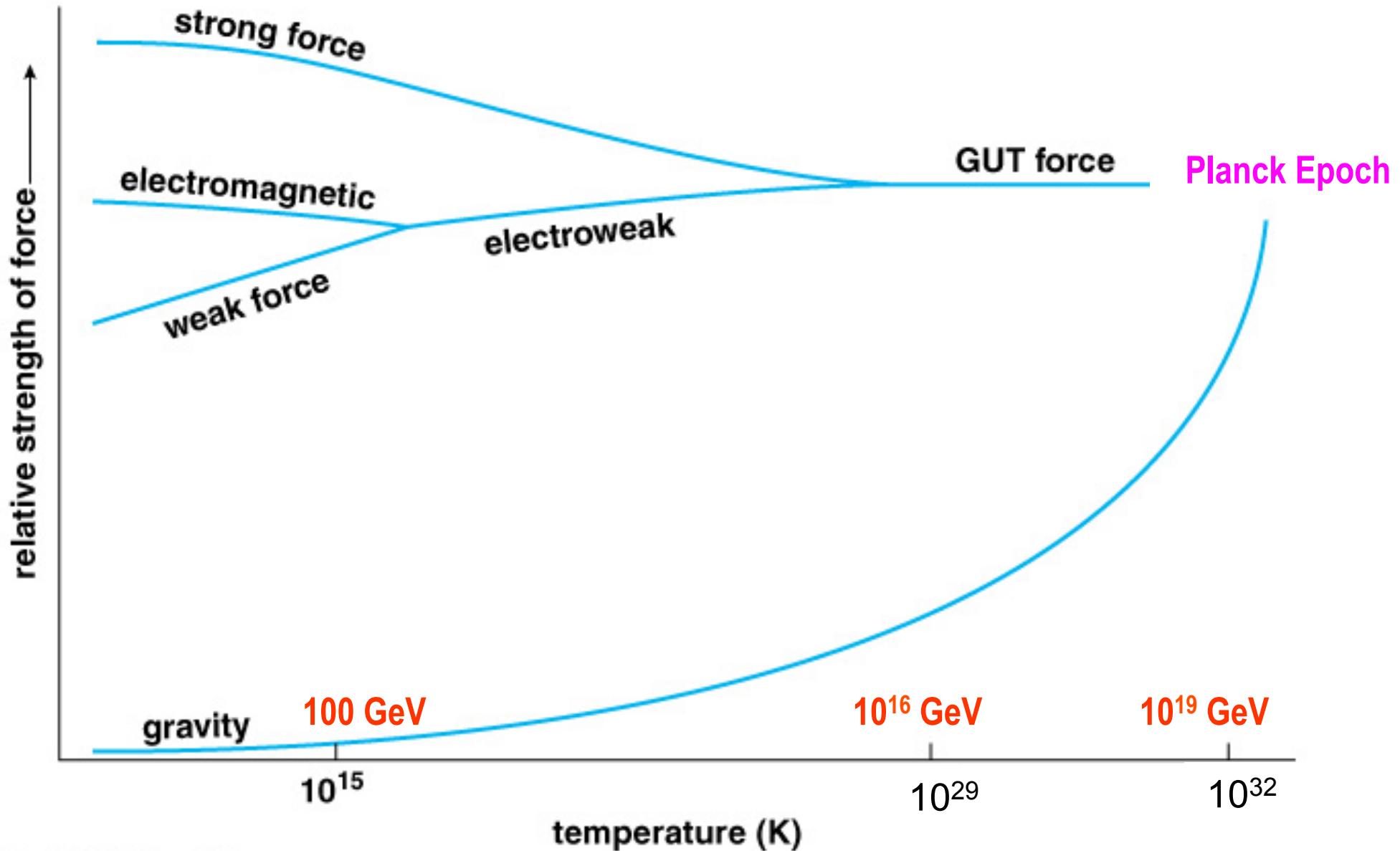


Why are we here?

Seven Phases of Cosmic Evolution

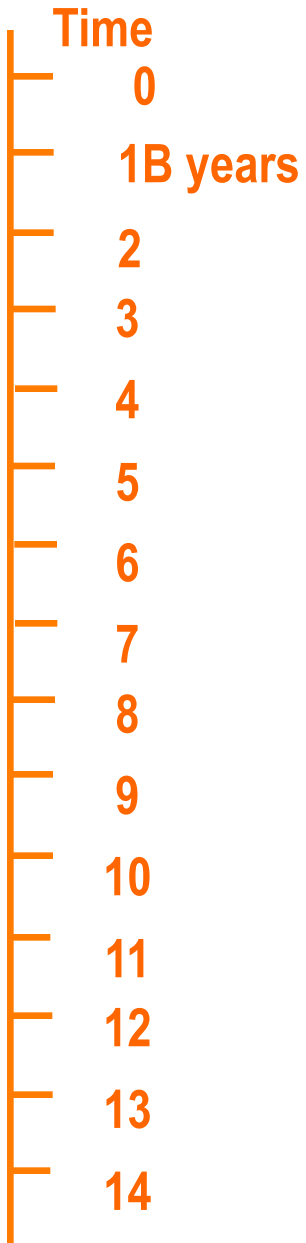


Unification of Forces



Copyright © Addison Wesley.

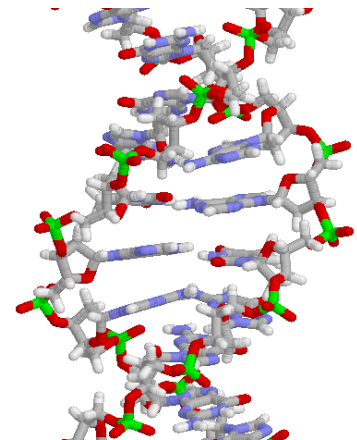
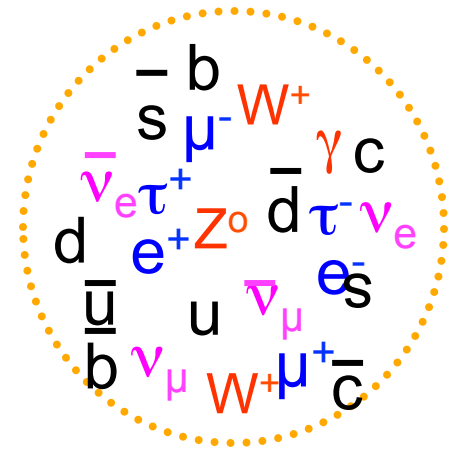
Symmetry Breaking



Simple

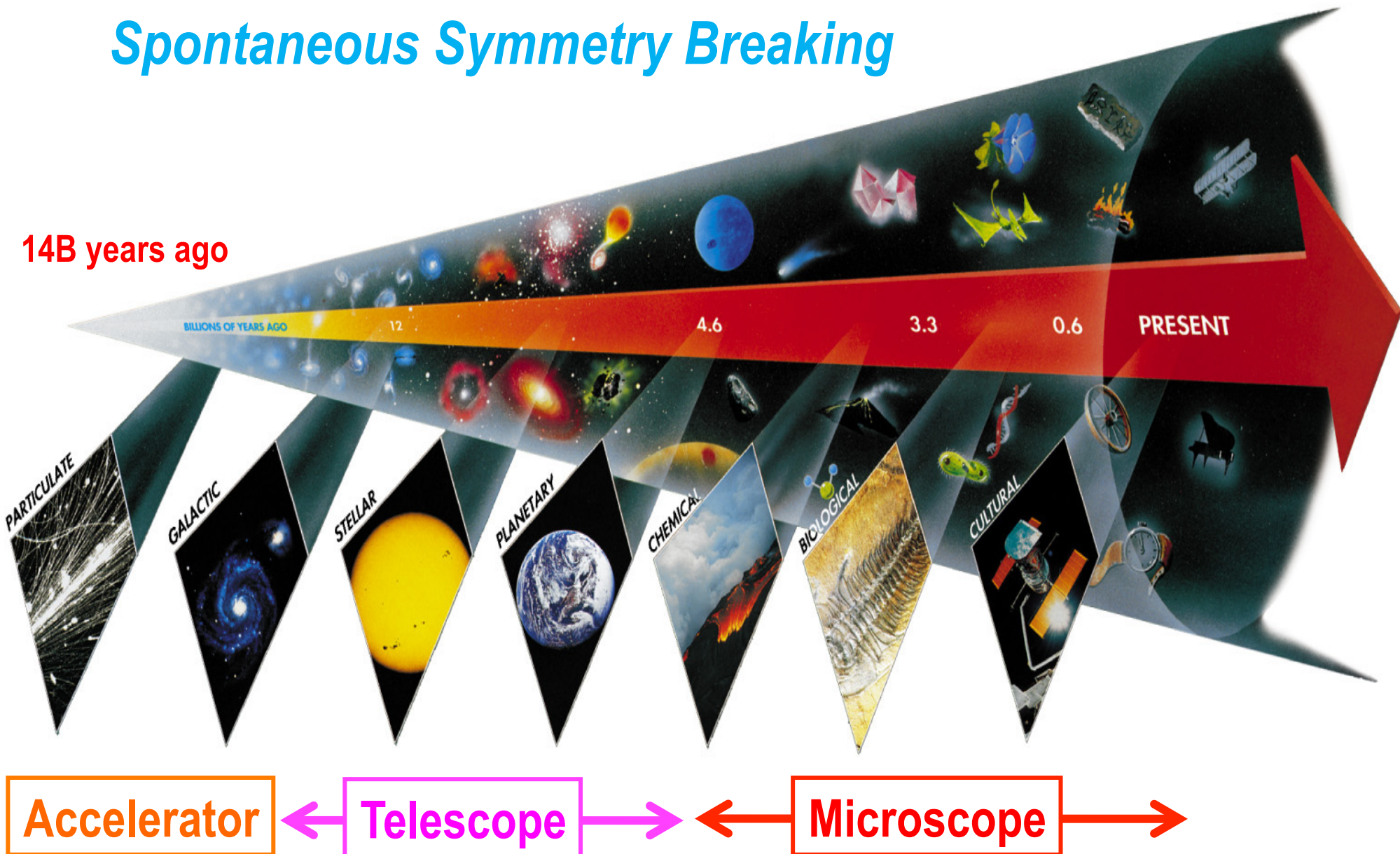
*Symmetry
Break Down*

Complex



Seven steps of cosmic evolution

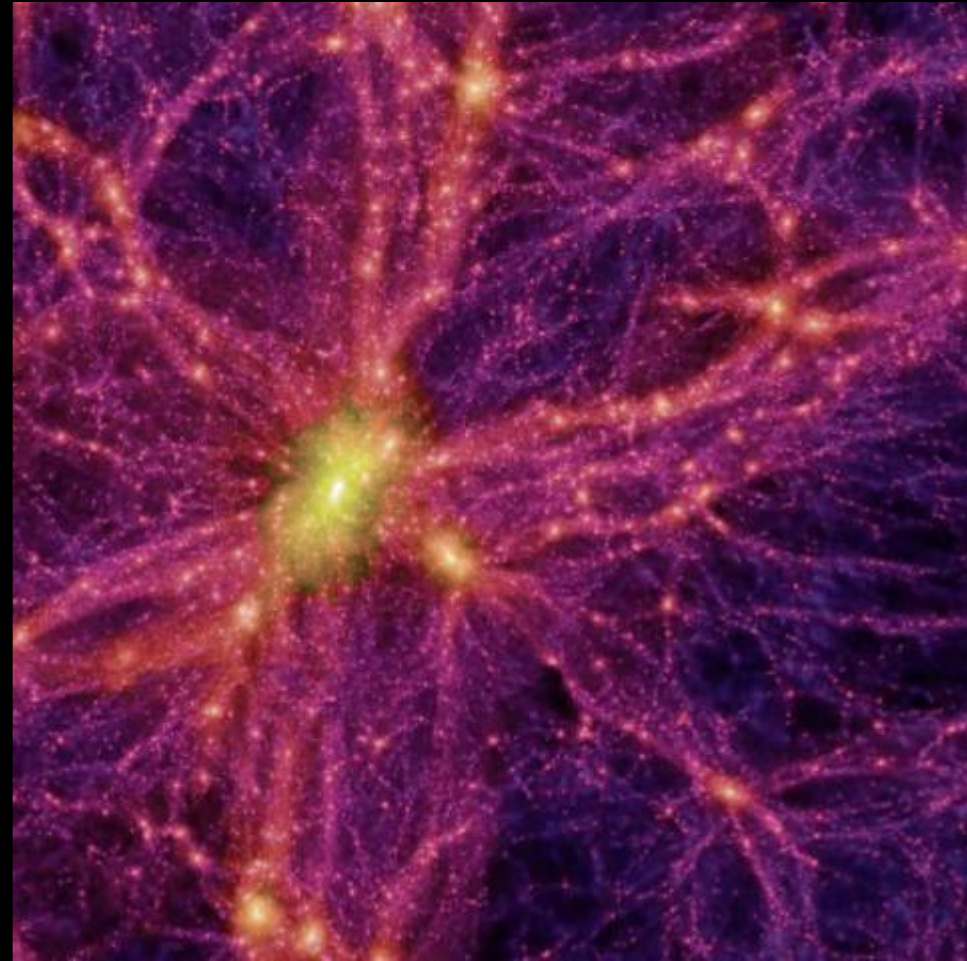
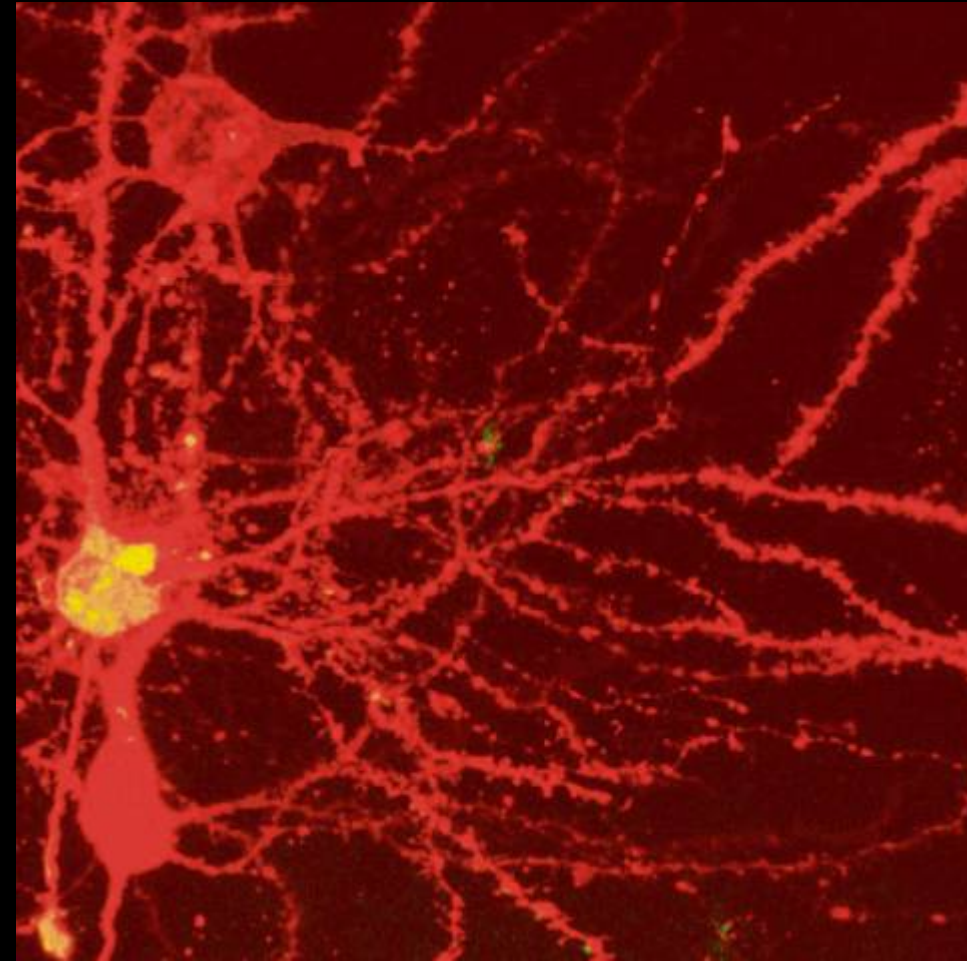
Spontaneous Symmetry Breaking



Origin of Consciousness

Brain

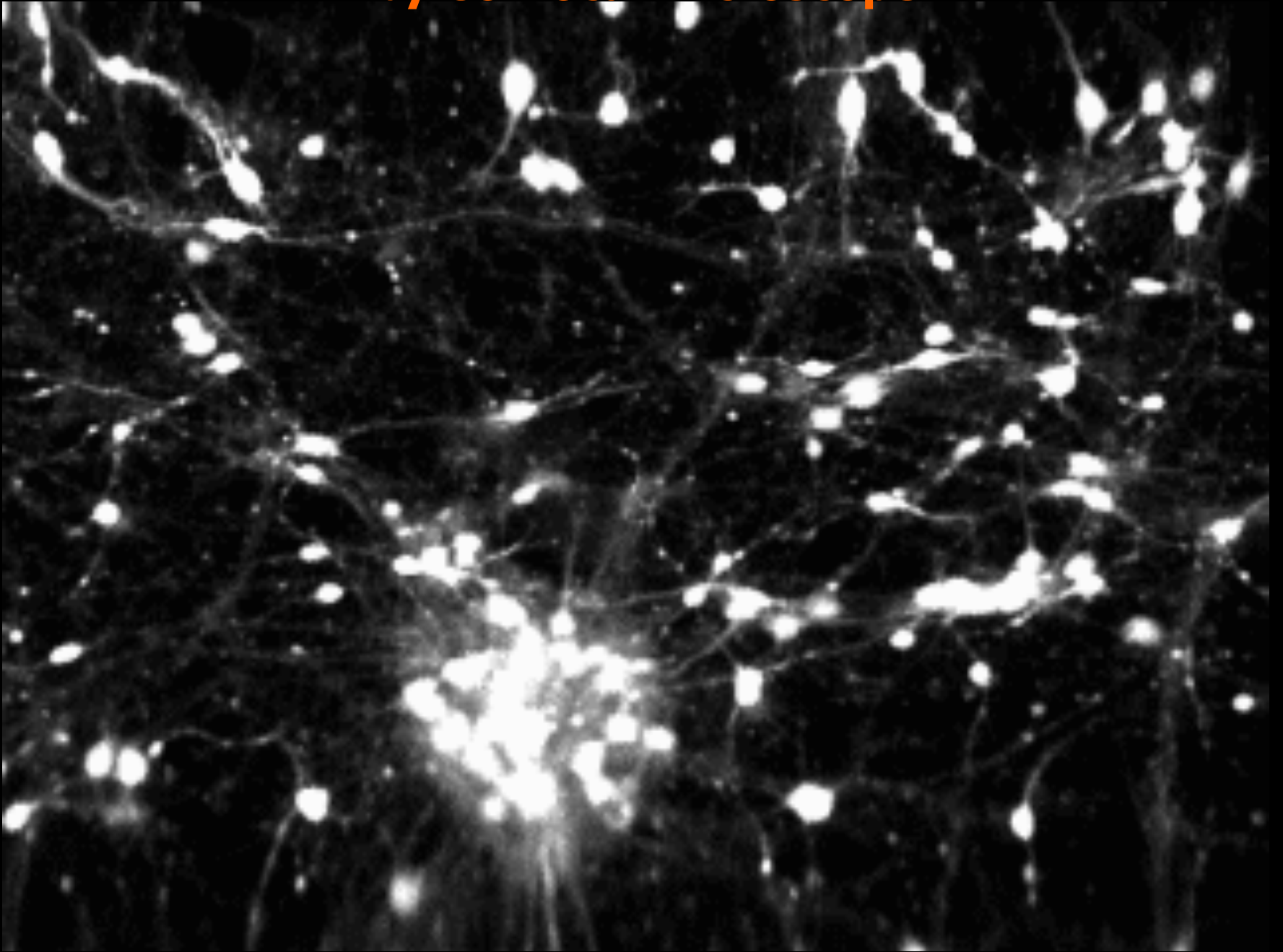
Universe



100 Billions Neurons

100 Billions Galaxies

Ca²⁺ Signal in cultivated Rat's Brain by Confocal Microscope

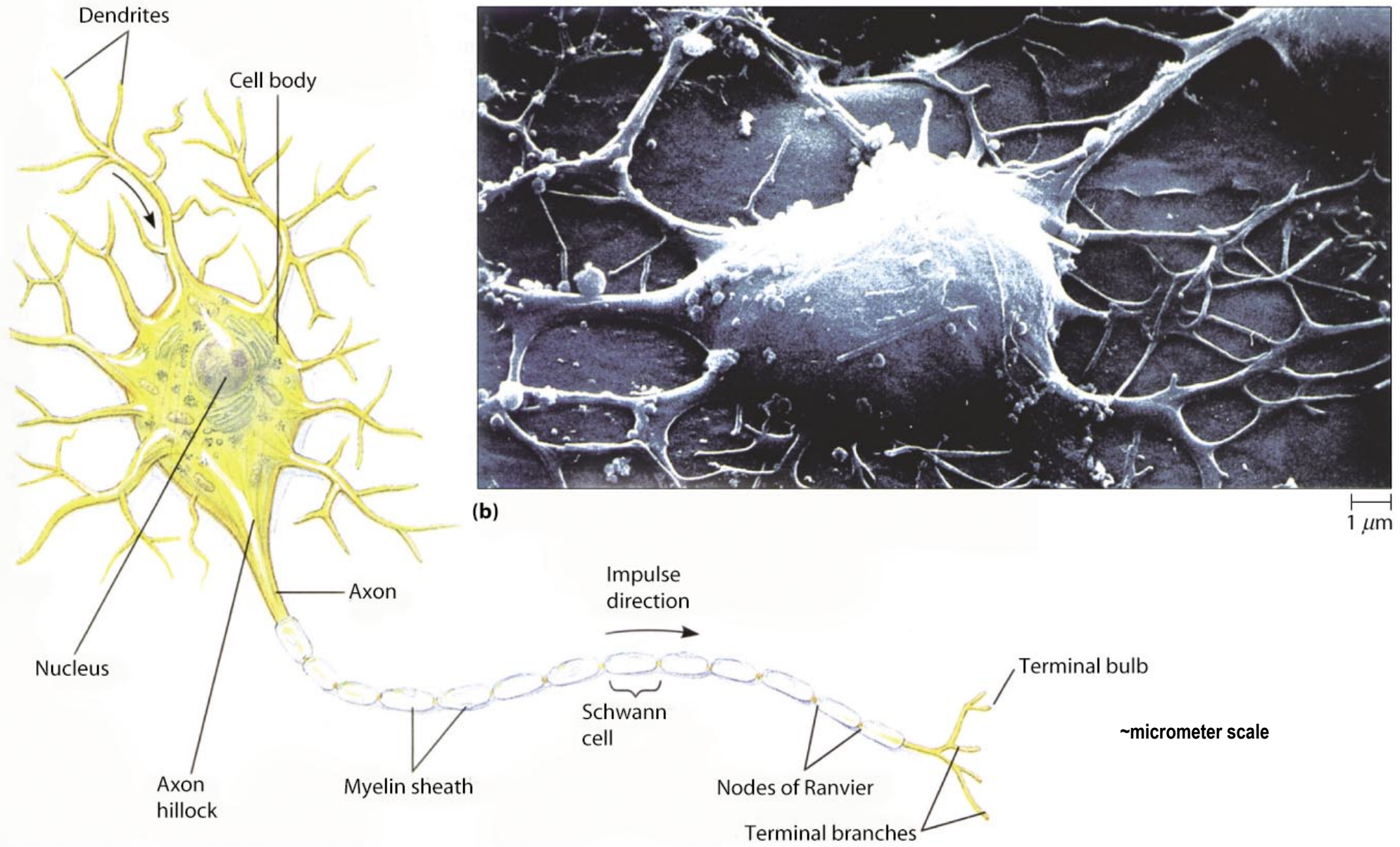


Andrew Charles (Neurobiology)

15 frame/sec




Neurons

Each Neuron has ~1,000 connections ($10^{11} \times 1000 = 10^{14}$)



IBM's Watson on 'Jeopardy!': The machine has won

February 16, 2011 | 9:11 pm

 (42)  (19)  Comments (2)



The machine has won.

Watson defeated the two biggest "Jeopardy" winners of all time: Ken Jennings and Brad Rutter.

The IBM computer finished the final round of competition on Wednesday night with \$77,147 in winnings over Jennings' \$24,000 and Rutter's \$21,600.

Jennings holds the record for number of consecutive Jeopardy matches won, with 74. Rutter has won more money than anyone else on Jeopardy.

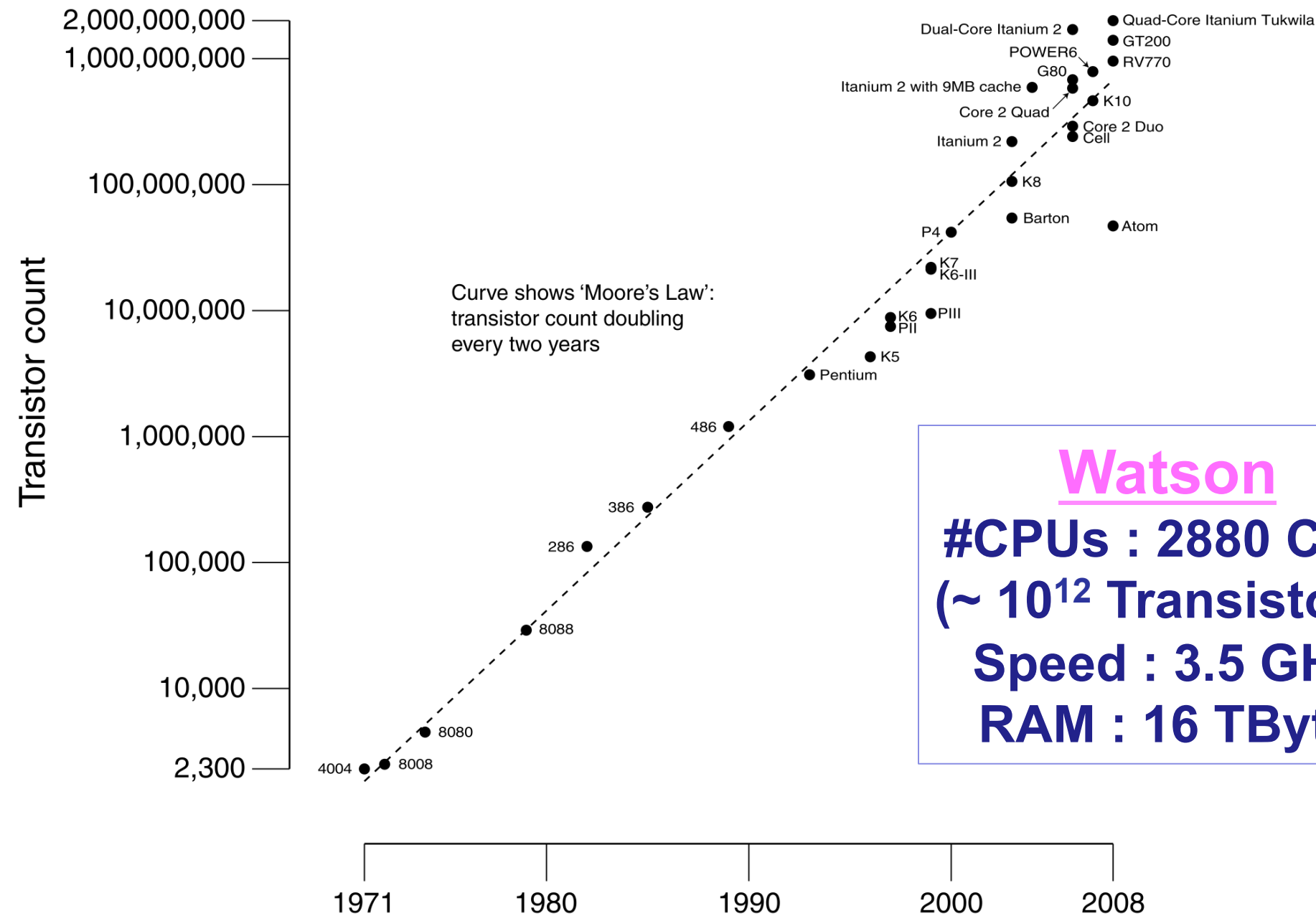
The two men competed against each other in a 2005 tournament that resulted in a Rutter victory.

Since Watson won, IBM is awarded \$1 million -- all of it going to charities [World Vision](#) (an anti-poverty group) and [World Community Grid](#) (which builds computer grids to address social issues such as water shortages).

Katsushi Arisaka, UCLA

“Moore’s Law” Transistors in Computer

Watson



Watson
#CPUs : 2880 CPU
(~ 10¹² Transistors)
Speed : 3.5 GHz
RAM : 16 TByte

From No Brain to Big Brain



Paramecium (Single Cell)



Bullfrog ($\sim 10^7$ neurons)



Lymnaea ($\sim 1,000$ neurons)



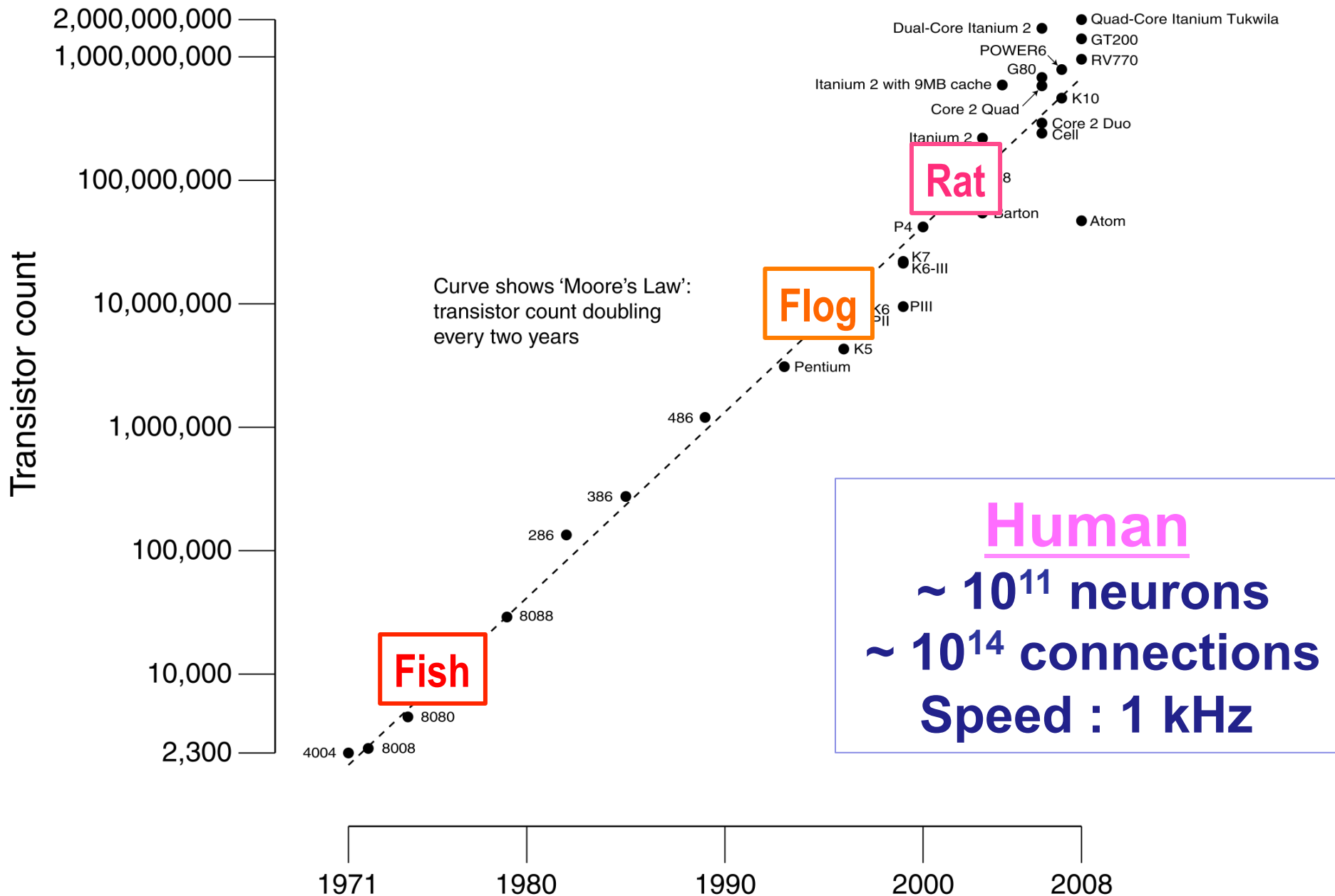
Zebrafish ($\sim 10,000$ neurons)



Rat ($\sim 10^8$ neurons)

Neurons in Brain

Human

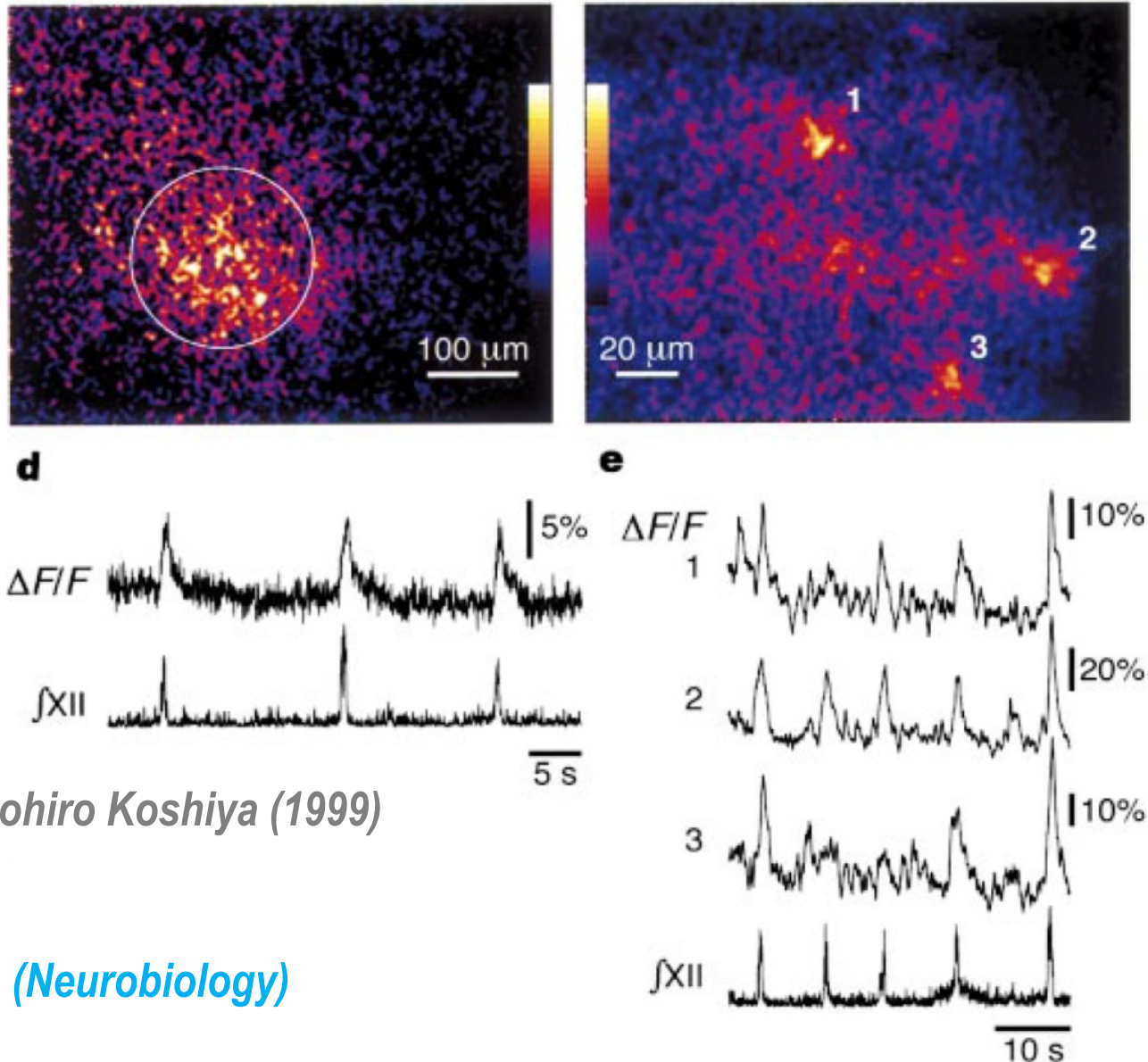


Computer vs. Brain

	Computer (Watson)	Human Brain
<i>Key Unit</i>	Transistor	Neuron
<i>No. of units</i>	$\sim 10^9$ ($\sim 10^{12}$)	$\sim 10^{11}$
<i>Connection</i>	Copper Wire	Axon + Dendrite
<i>No. of Connections</i>	$\sim 10^{10}$ ($\sim 10^{13}$)	$\sim 10^{14}$
<i>Signal Carrier</i>	Electrons	Ions (Na ⁺ , Ca ⁺ , K ⁺)
<i>Clock Speed</i>	~ 1 GHz	~ 1 kHz
<i>Method</i>	Sequential	Parallel Processing

Neural Networks for Breathing

~300 neurons in rat's brain (pre-Botzinger Cells) responsible for breathing



Nature by Naohiro Koshiya (1999)

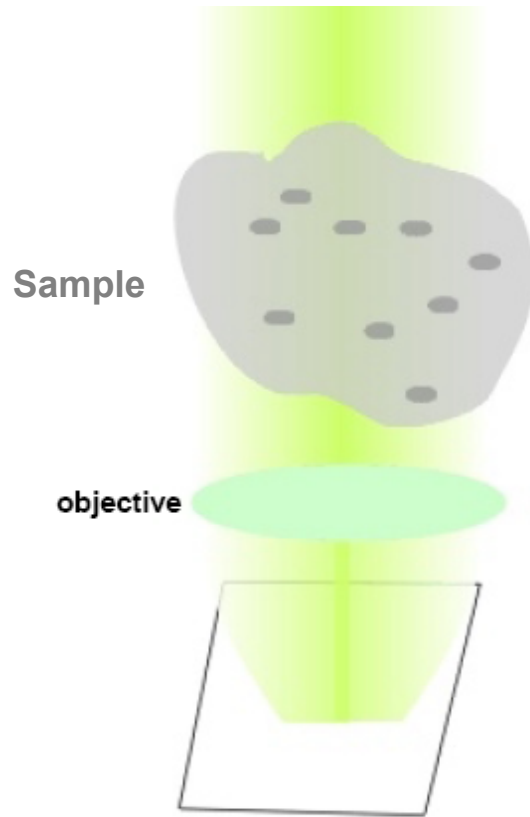
Jack Feldman (Neurobiology)

How to speed up microscopes

- All the existing microscopes are limited by the narrow bandwidth of readout.
 - Just one channel of FADC (Flash Analog to Digital Converter) running at 10 – 50 MHz
 - So-called Video Rate (30 frame/sec)
- The first step is to adopt multiple channels of FADC for massive parallel processing.
 - Like high energy experiments (such as LHC)
- In addition, we need Single Photon Sensitivity with high Quantum Efficiency.

Principle of High-speed Bio Imaging

Wide Field

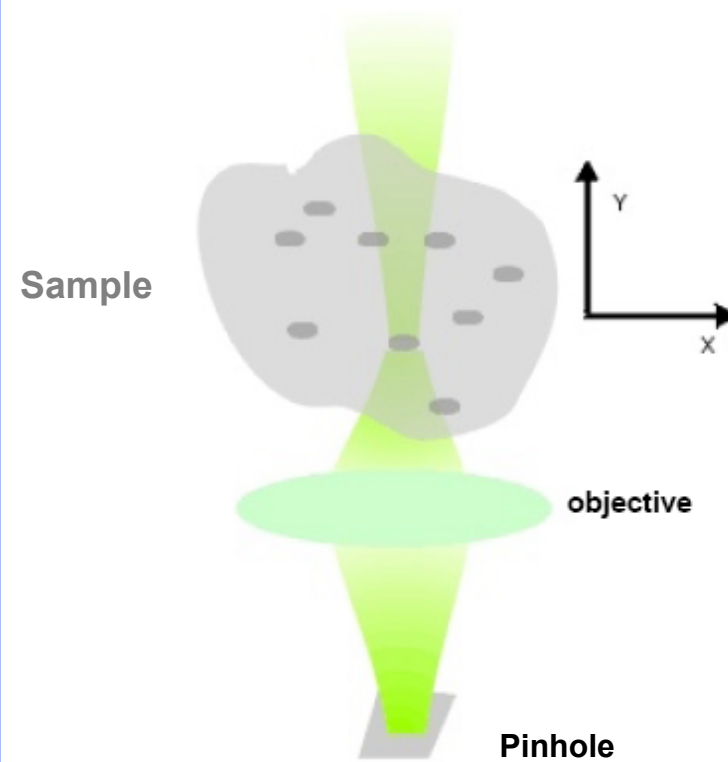


CCD + FADC (10 – 50 MHz)



CMOS [FADC (50 MHz) * 100]

Confocal



PMT + FADC (10 – 50 MHz)

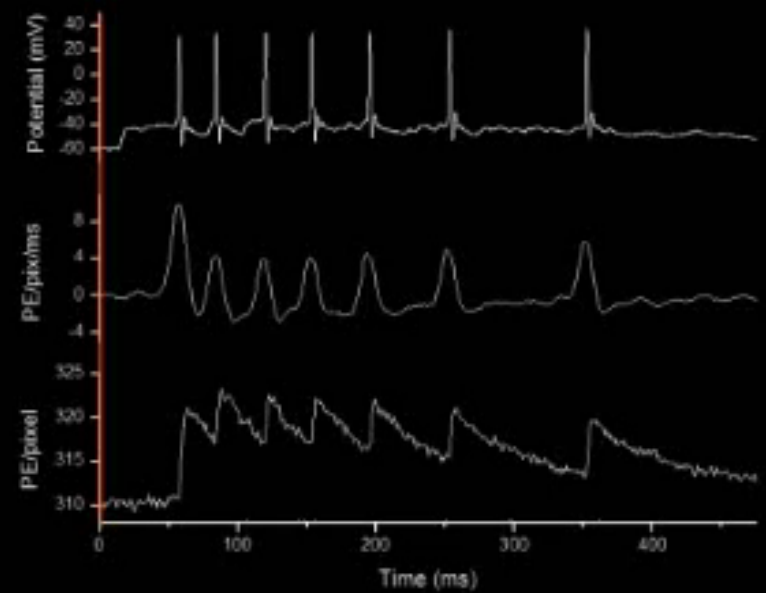
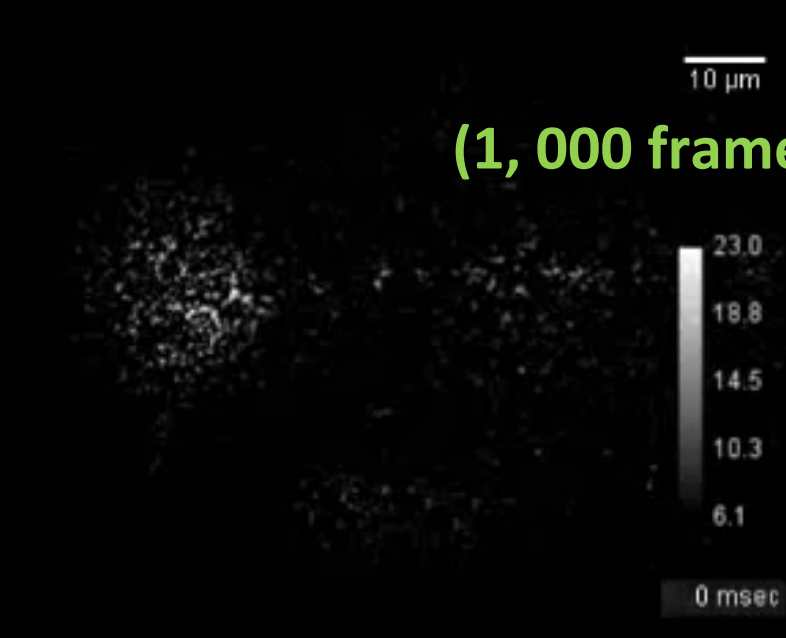
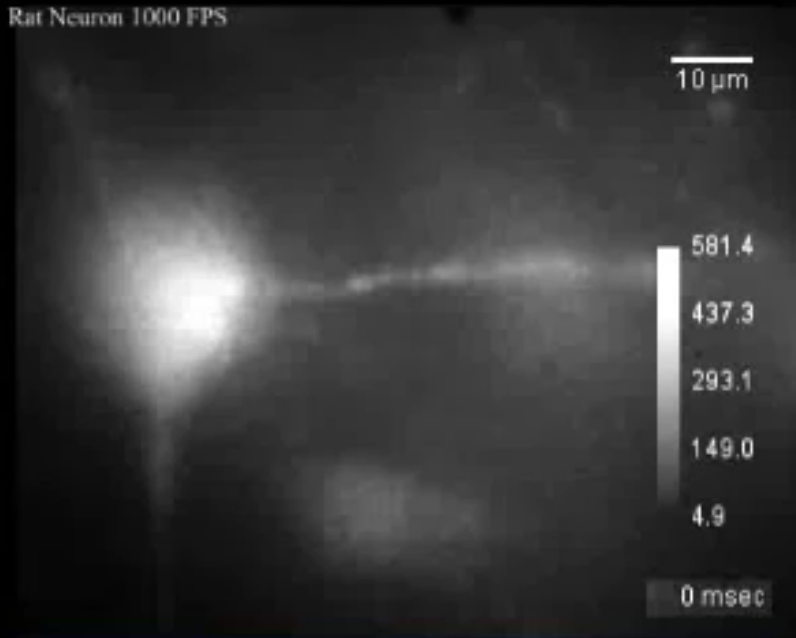


[HAPD + FADC (1 GHz)] * 64

High-speed Ca^{2+} Imaging of pre-Botzinger Cells of Rats

Prof. Jack Feldman (Neurobiology)

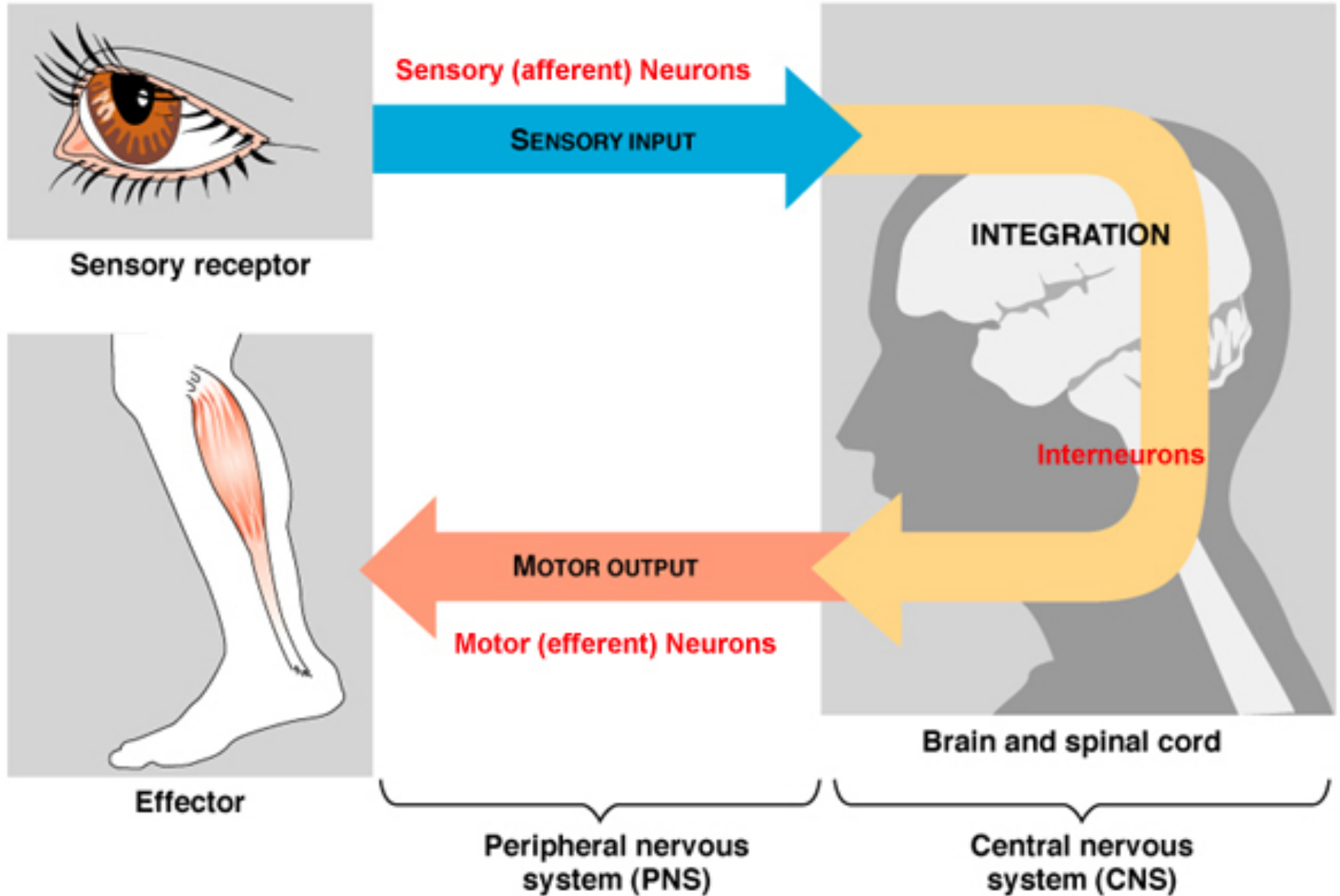
(1,000 frame/sec)



UCLA Ultra-fast Bio-imaging Group

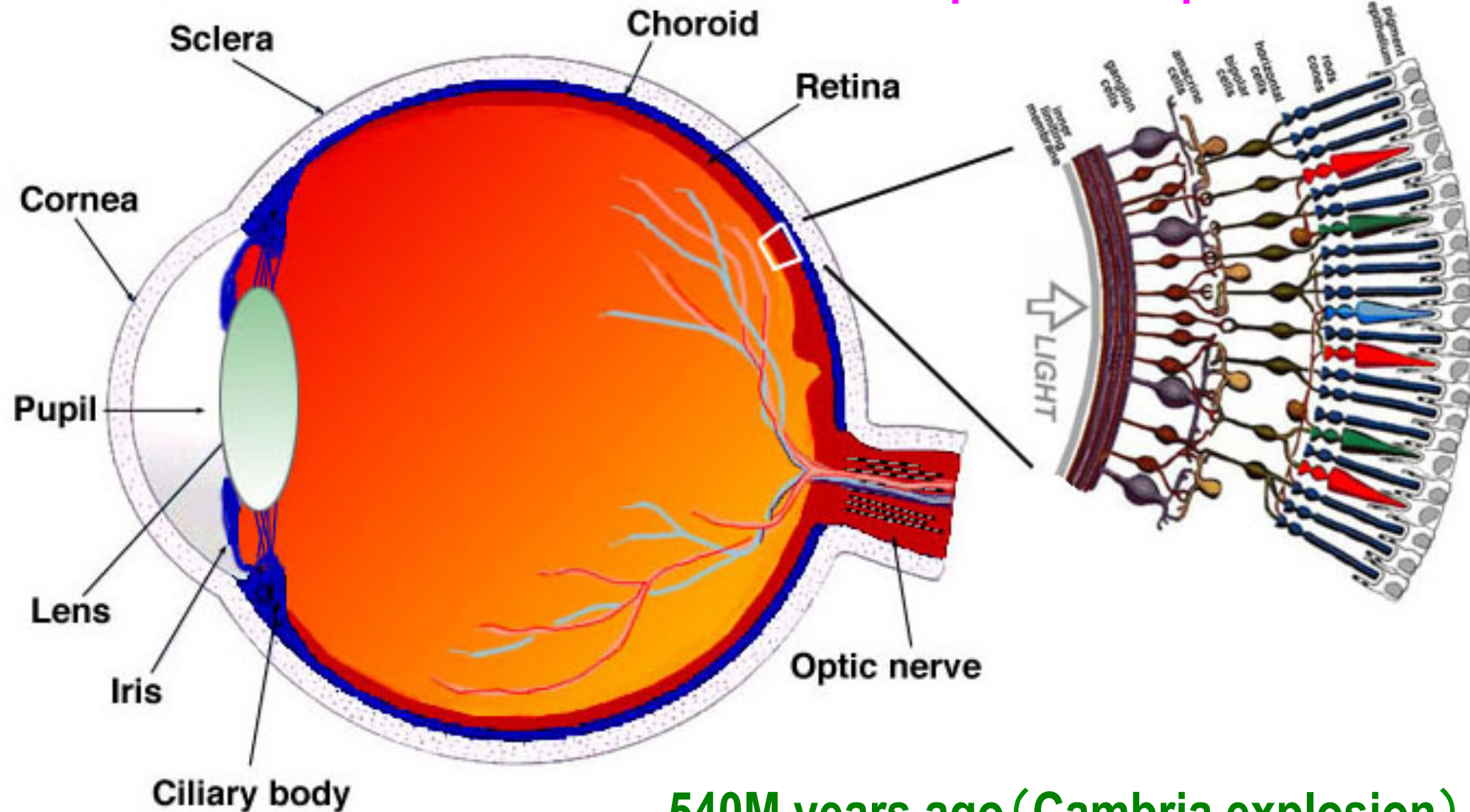
C. Morgado, A. Cheng, L. Frederickson, K. Arisaka, J. Feldman

Sensory Input and Decision Making in Brain



Human Eyes

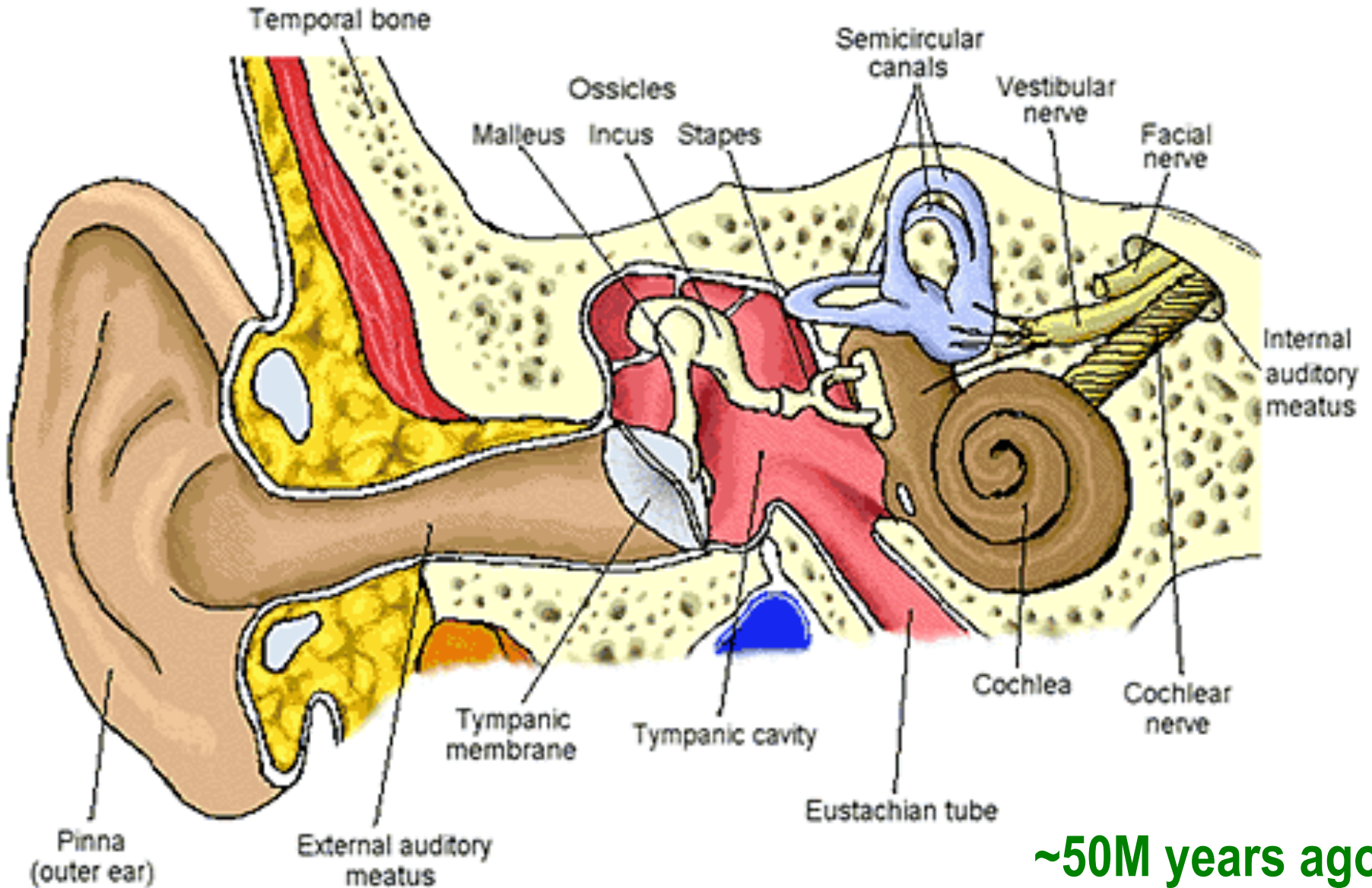
~100M photo receptors



540M years ago (Cambria explosion)

Human Ears

~10,000 Hair Cells



~50M years ago

Anatomy of Inner Ear

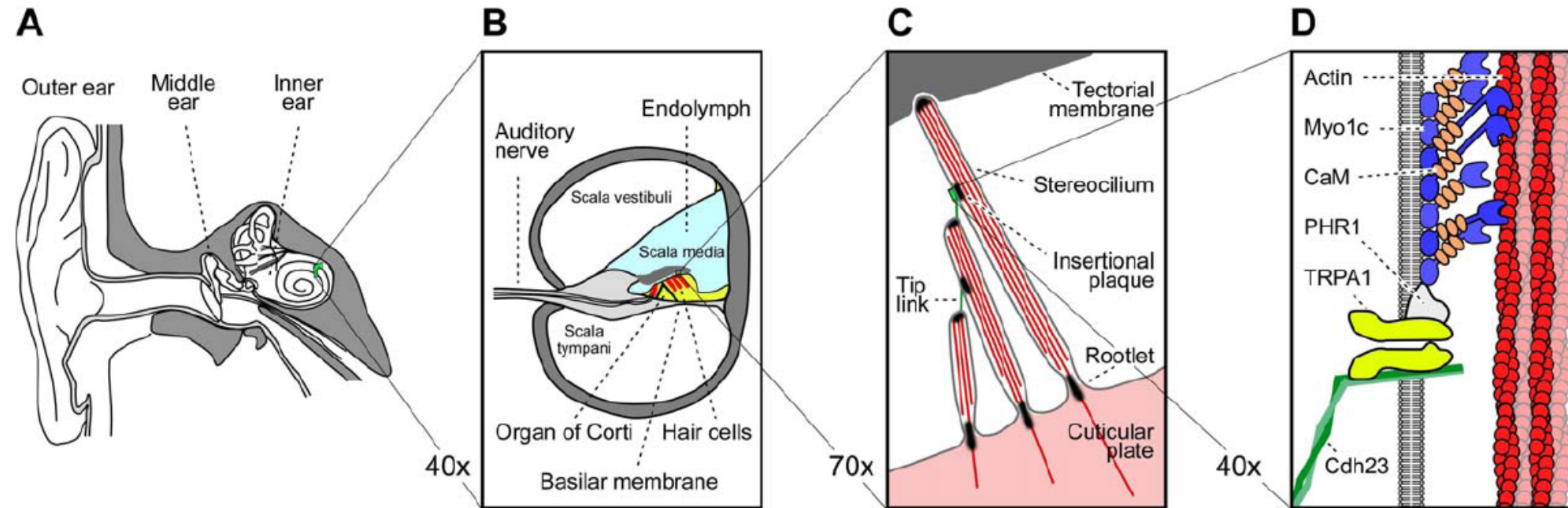
Dolores Bozovic (Physics)

Human auditory system

Cross-section of the cochlear

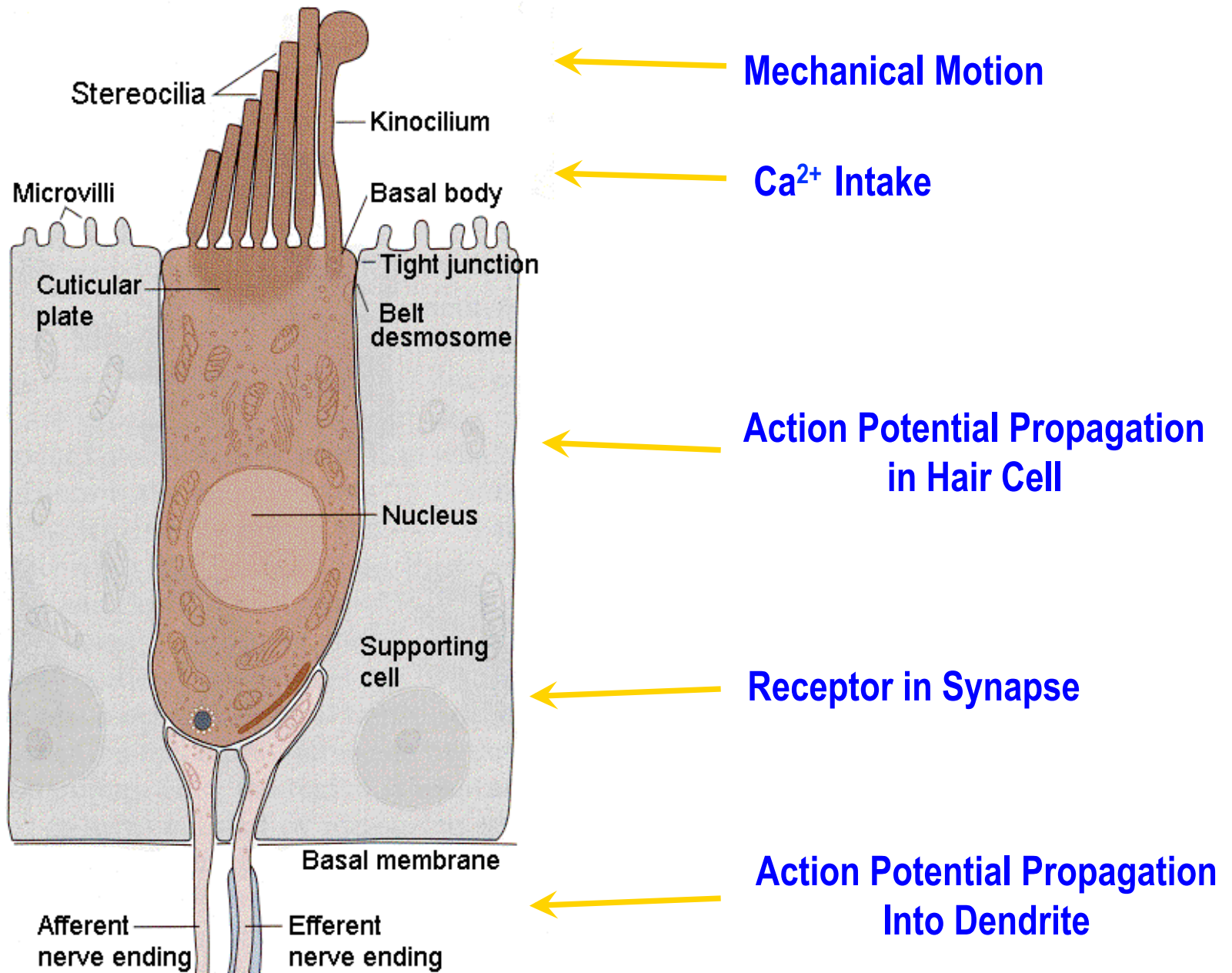
Hair bundle

Molecular mechano-transduction machinery



Meredith LeMasurier and Peter G. Gillespie, *Neuron*, Vol. 48, 2005

Simultaneous observation of entire process



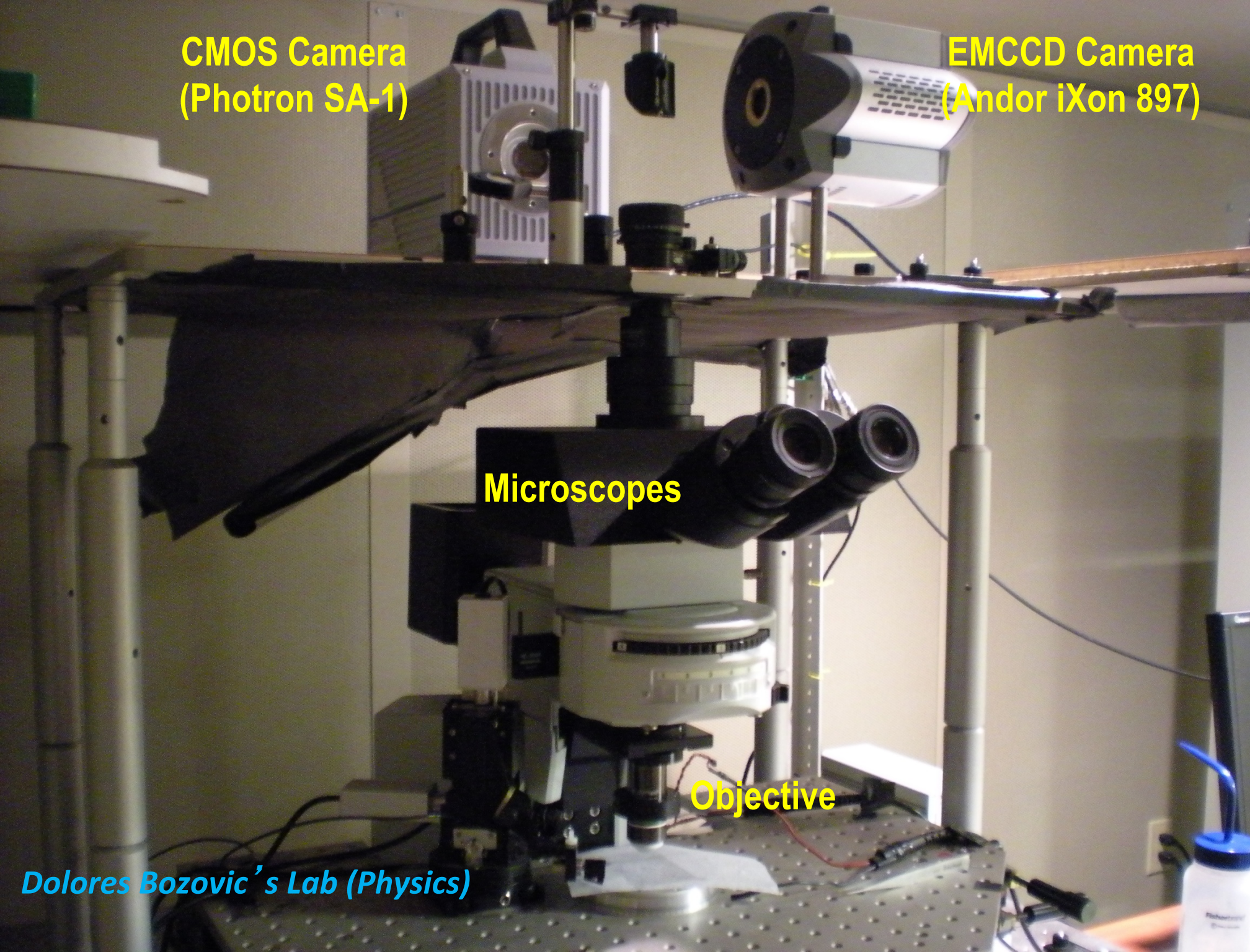
**CMOS Camera
(Photron SA-1)**

**EMCCD Camera
(Andor iXon 897)**

Microscopes

Objective

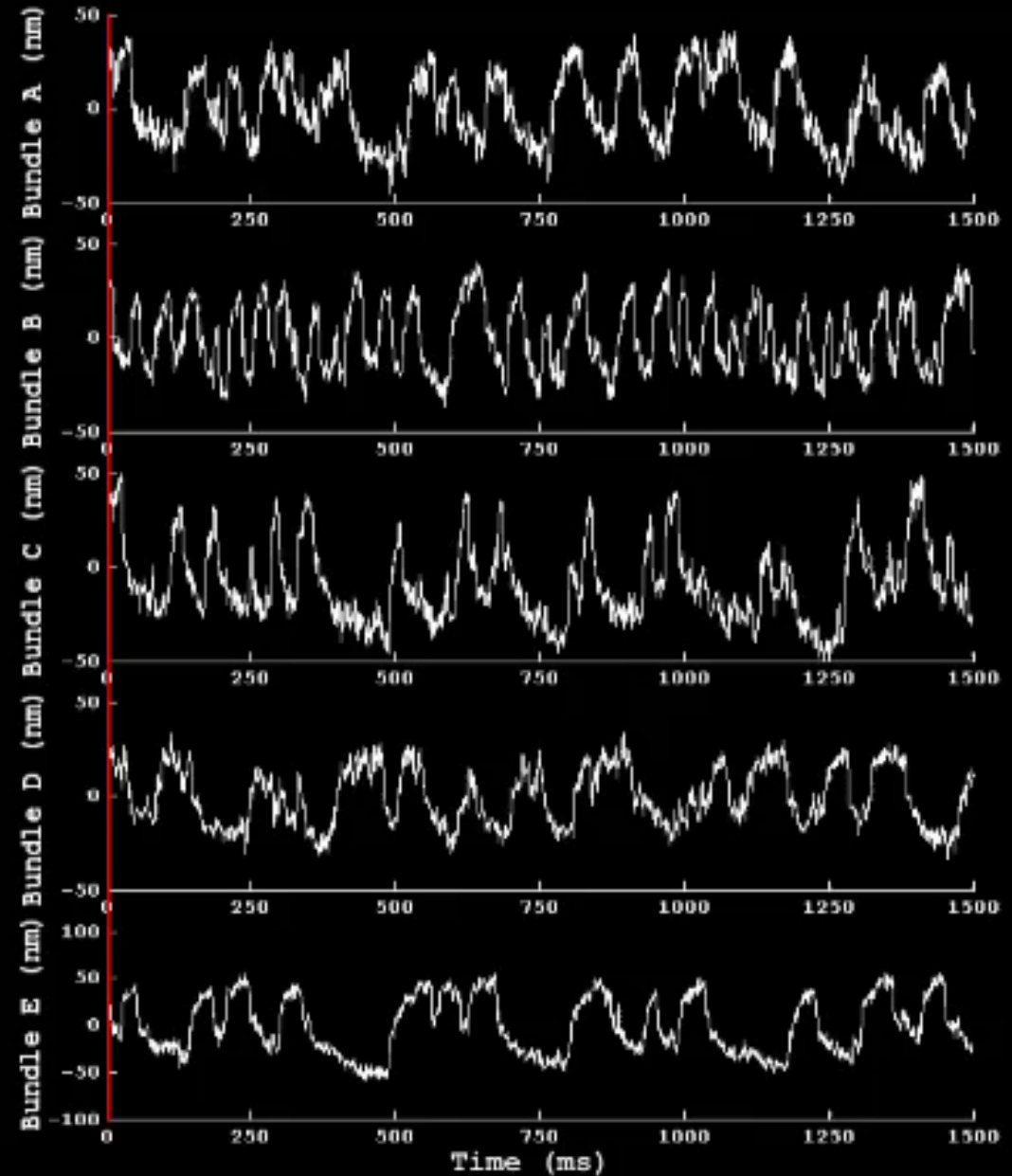
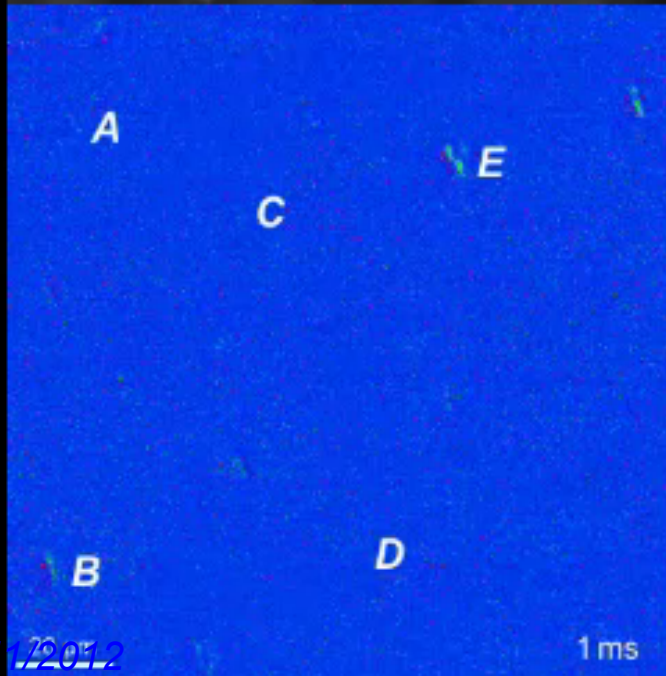
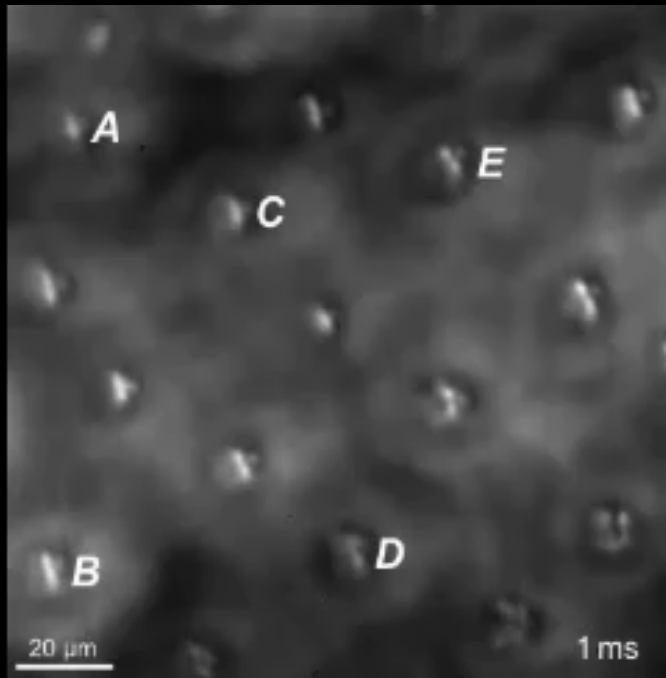
Dolores Bozovic's Lab (Physics)



Mechanical Motion of Hair Cells in Inner Ear

Prof. Dolores Bozovic (Physics)

(1,000 frame/sec)



UCLA Fast Bio-Imaging Group

L. Fredrickson, A. Cheng, J. C. Jewhurst, C. E. Strimbu, D. Bozovic, K. Arisaka

Mystery of Hearing

- **Extremely wide dynamic range in amplitude.**
 - 10^6 compressed to 100
 - Smallest amplitude is 0.3 nm
- **Extremely wide frequency range.**
 - 20 Hz – 20 kHz
 - Dynamic range of 1000
 - Corresponding to 10^6 in k
 - **Selectivity of 0.2%**
 - up to 5 kHz
 - **How can the brain handle up to 20 kHz?**
 - miss match to the speed of action potential of 1 kHz

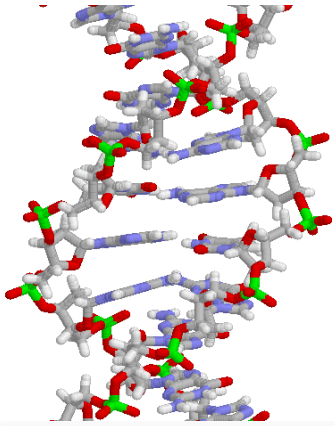
$$\omega = \sqrt{\frac{k}{m}}$$

How can I recognize a woman so far away?

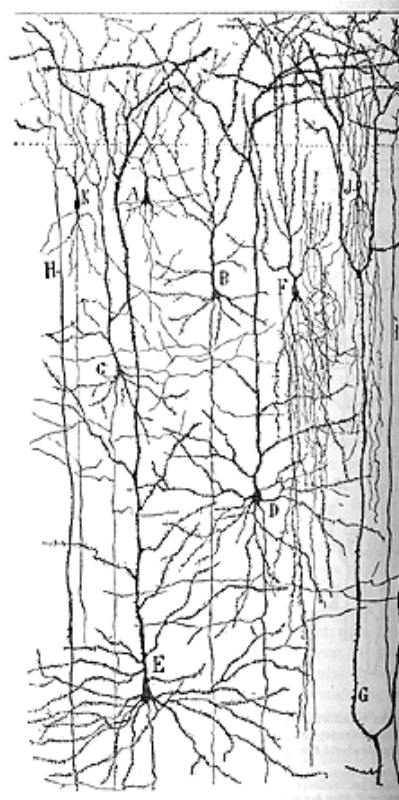


- Genetically encoded?
- Learning and memory?

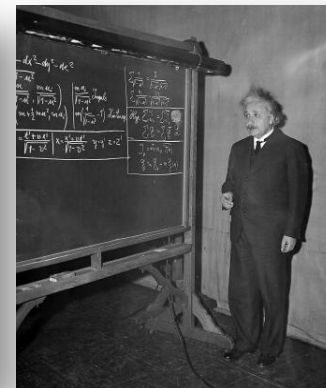
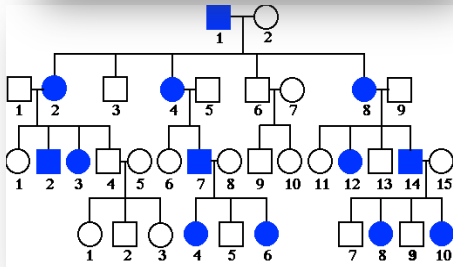
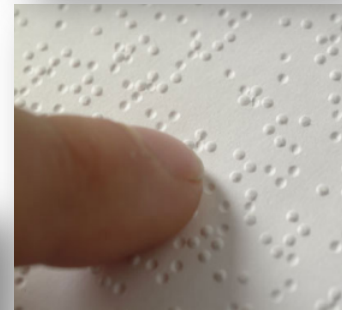
Nature vs. Nurture



Nature

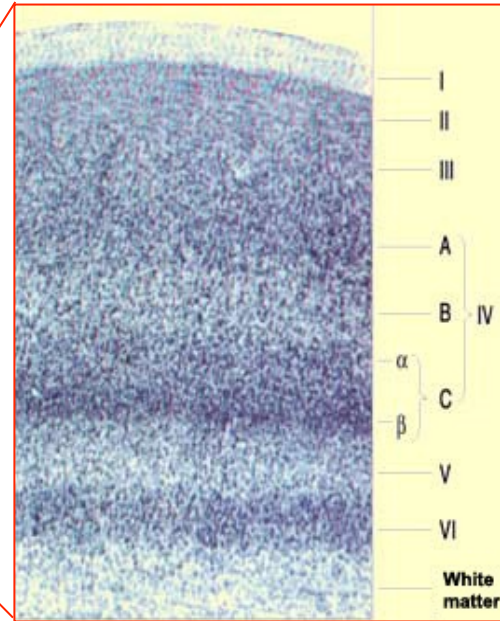
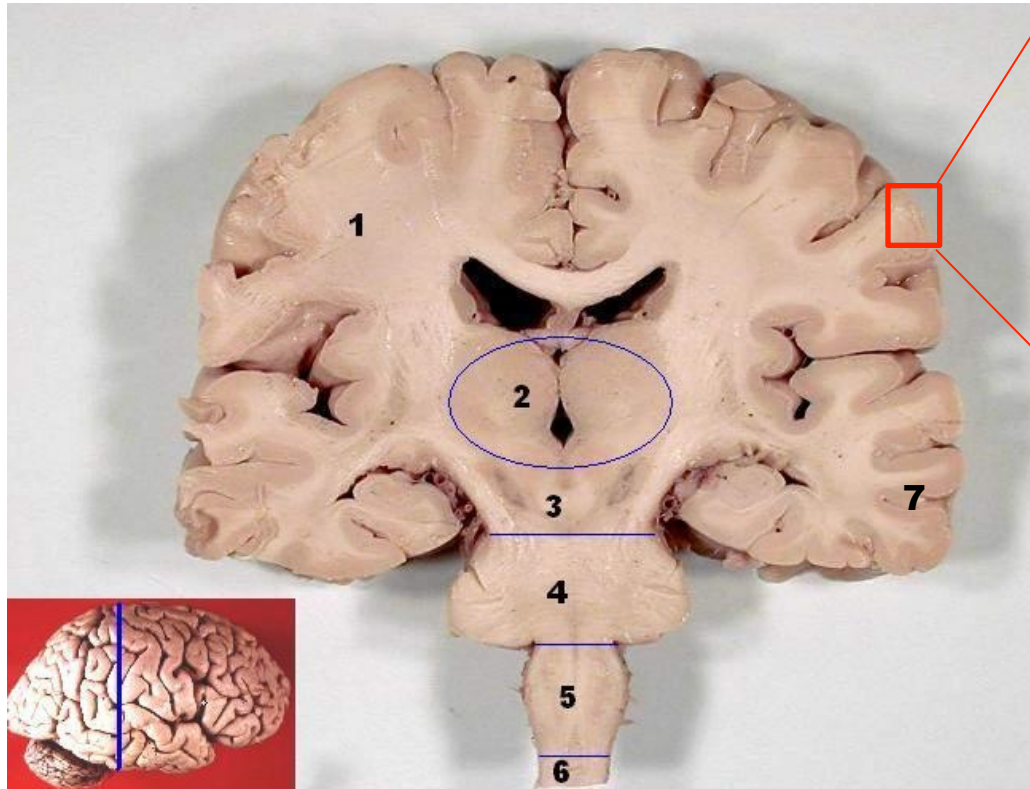


Nurture

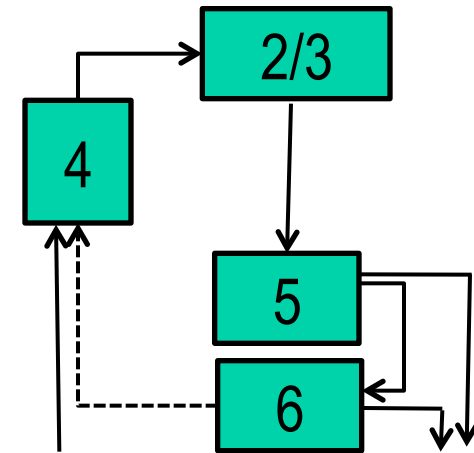


The Cerebral Cortex

Conscious
↑



↓
Unconscious

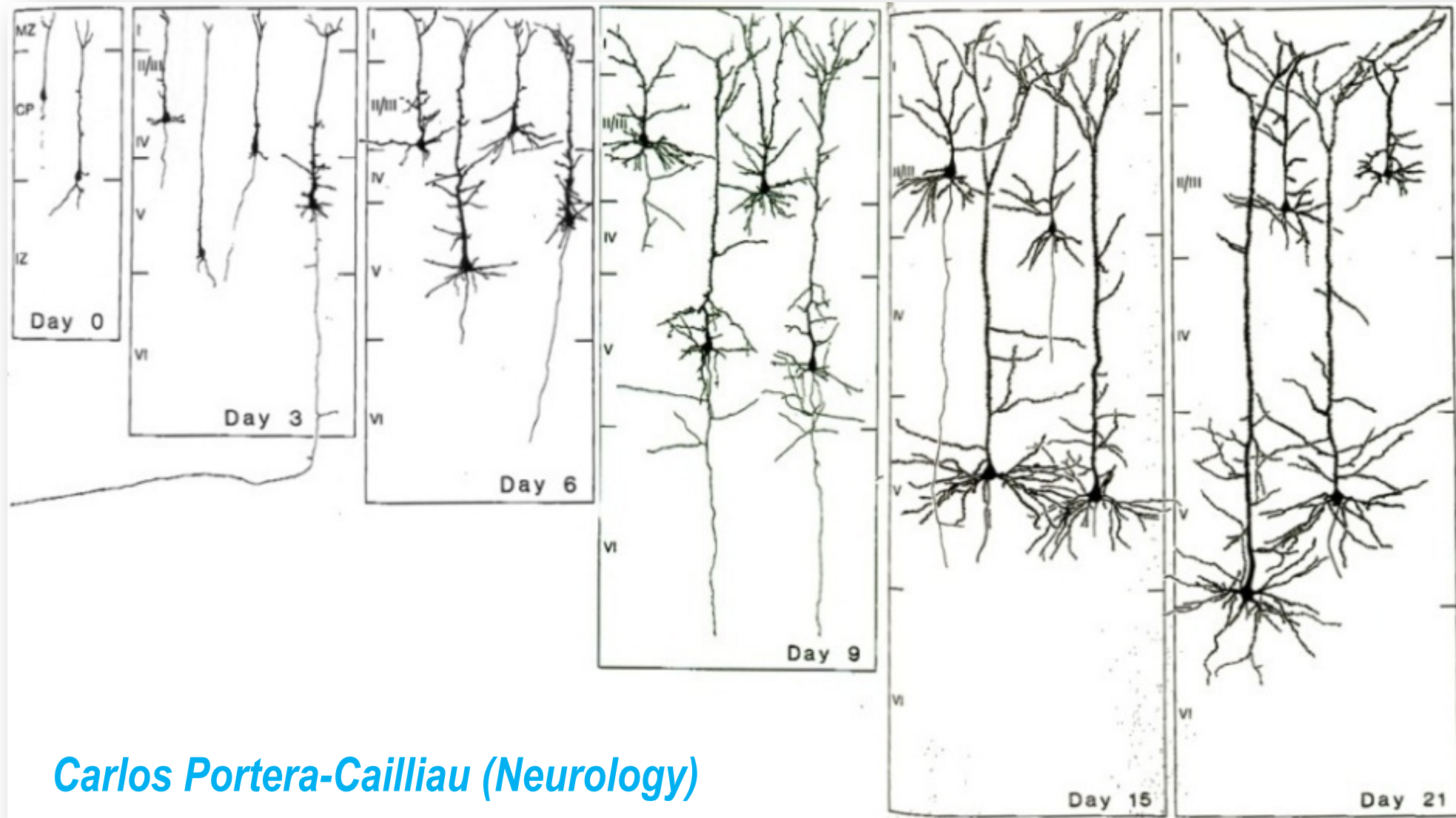


Thalamus

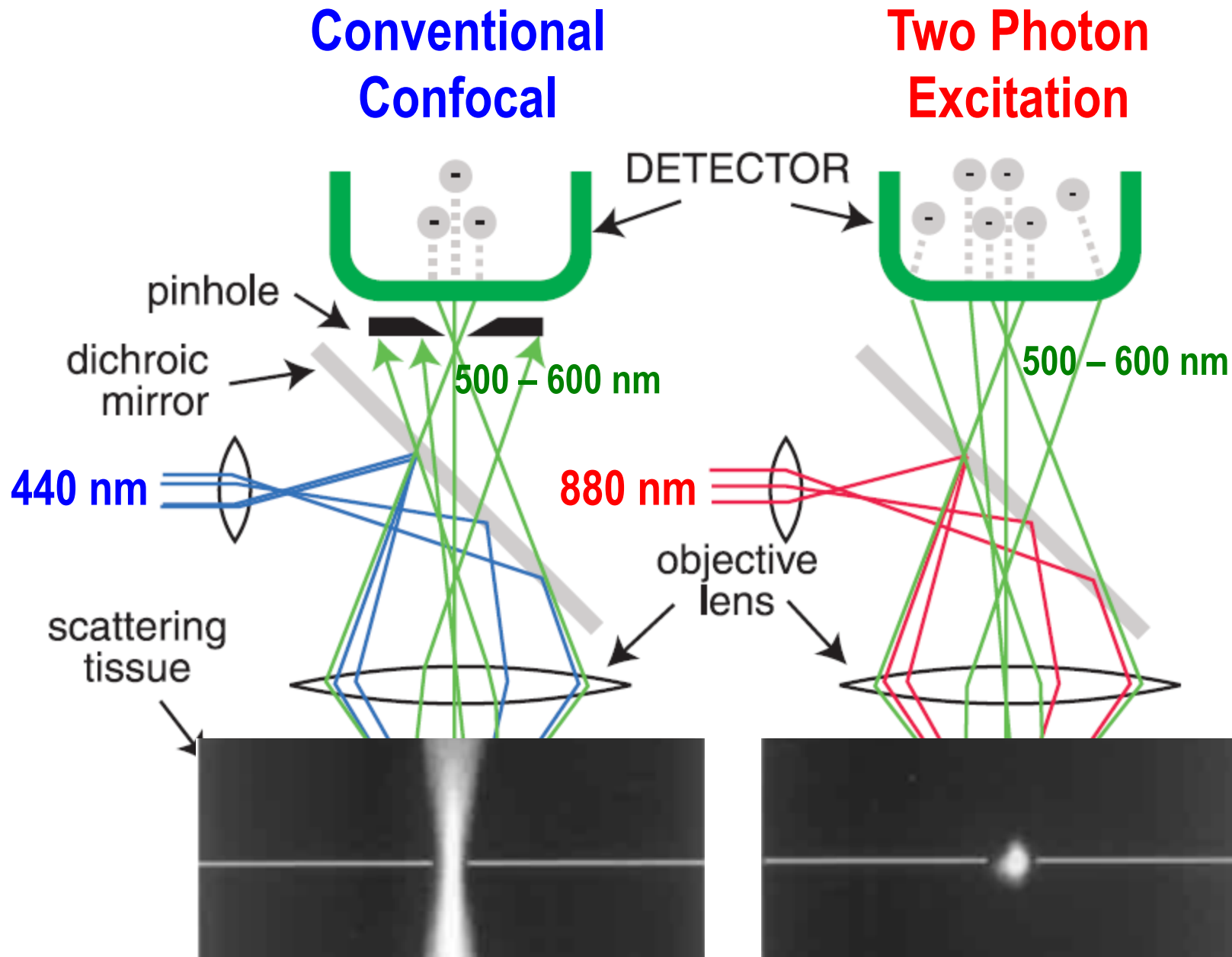
Subcortical areas

Assembly of rat's cortical circuits during development

How/when do neurons establish networks? → *Symmetry Breaking*

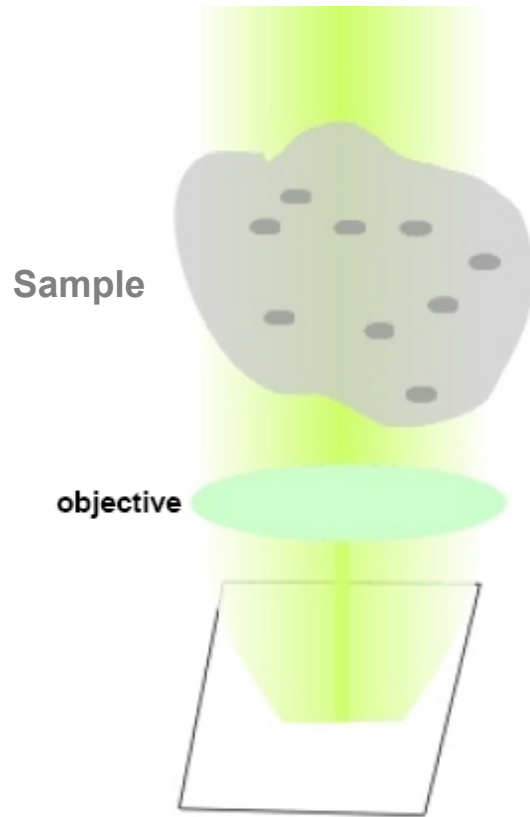


Multiphoton Microscope



Principle of High-speed Bio Imaging

Wide Field

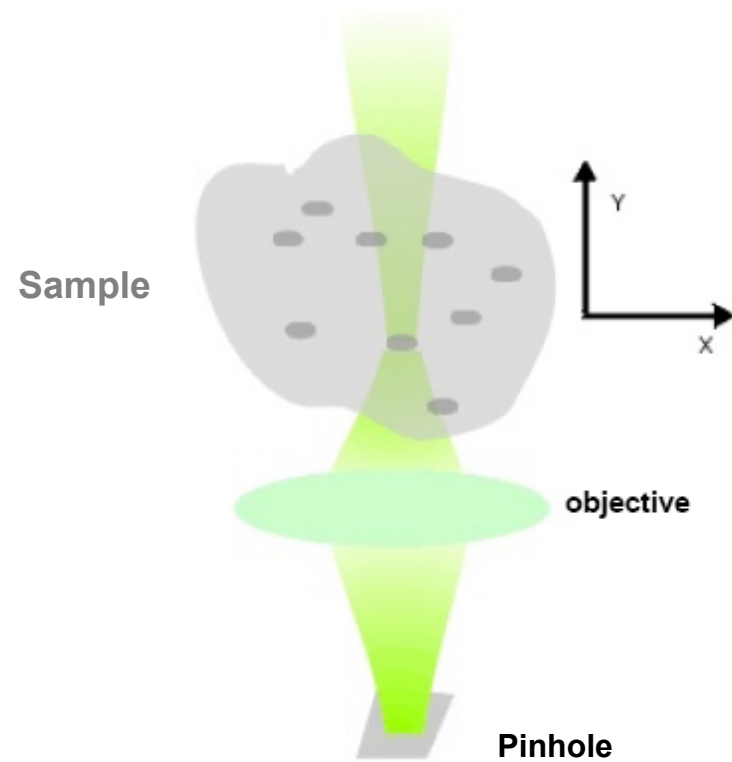


CCD + FADC (10 – 50 MHz)



CMOS [FADC (50 MHz) * 100]

Confocal

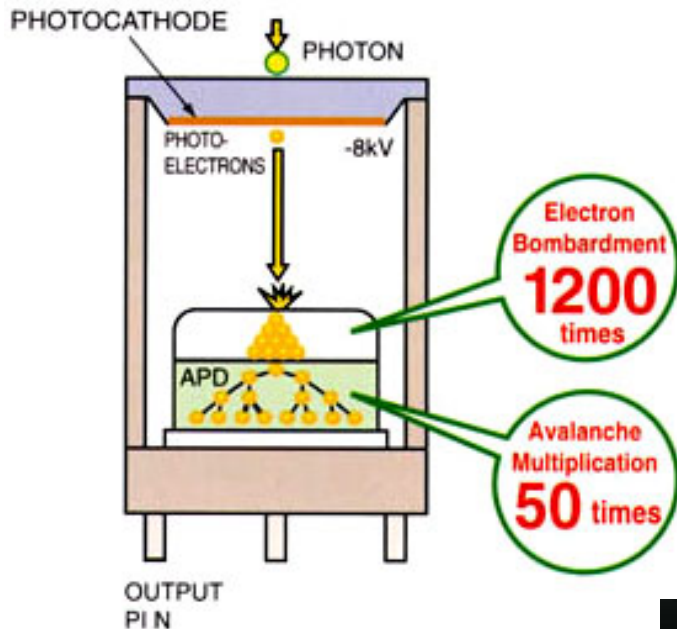


PMT + FADC (10 – 50 MHz)



[HAPD + FADC (1 GHz)] * 64

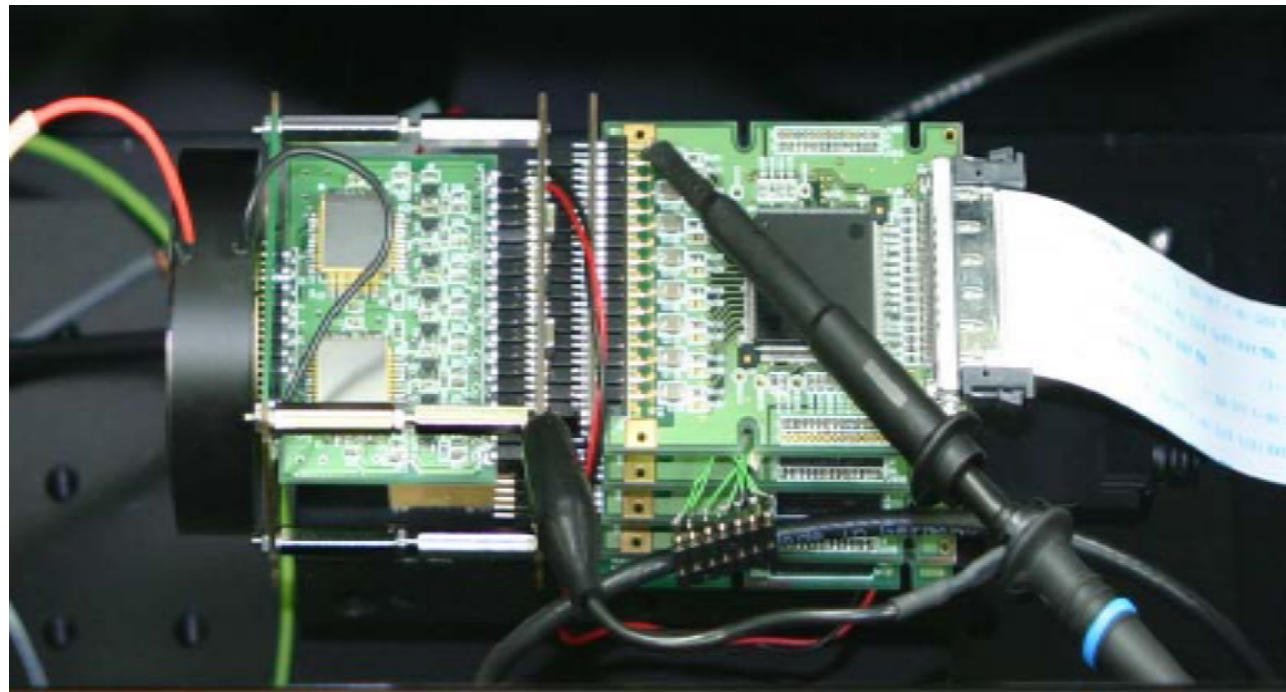
Hamamatsu Hybrid APD



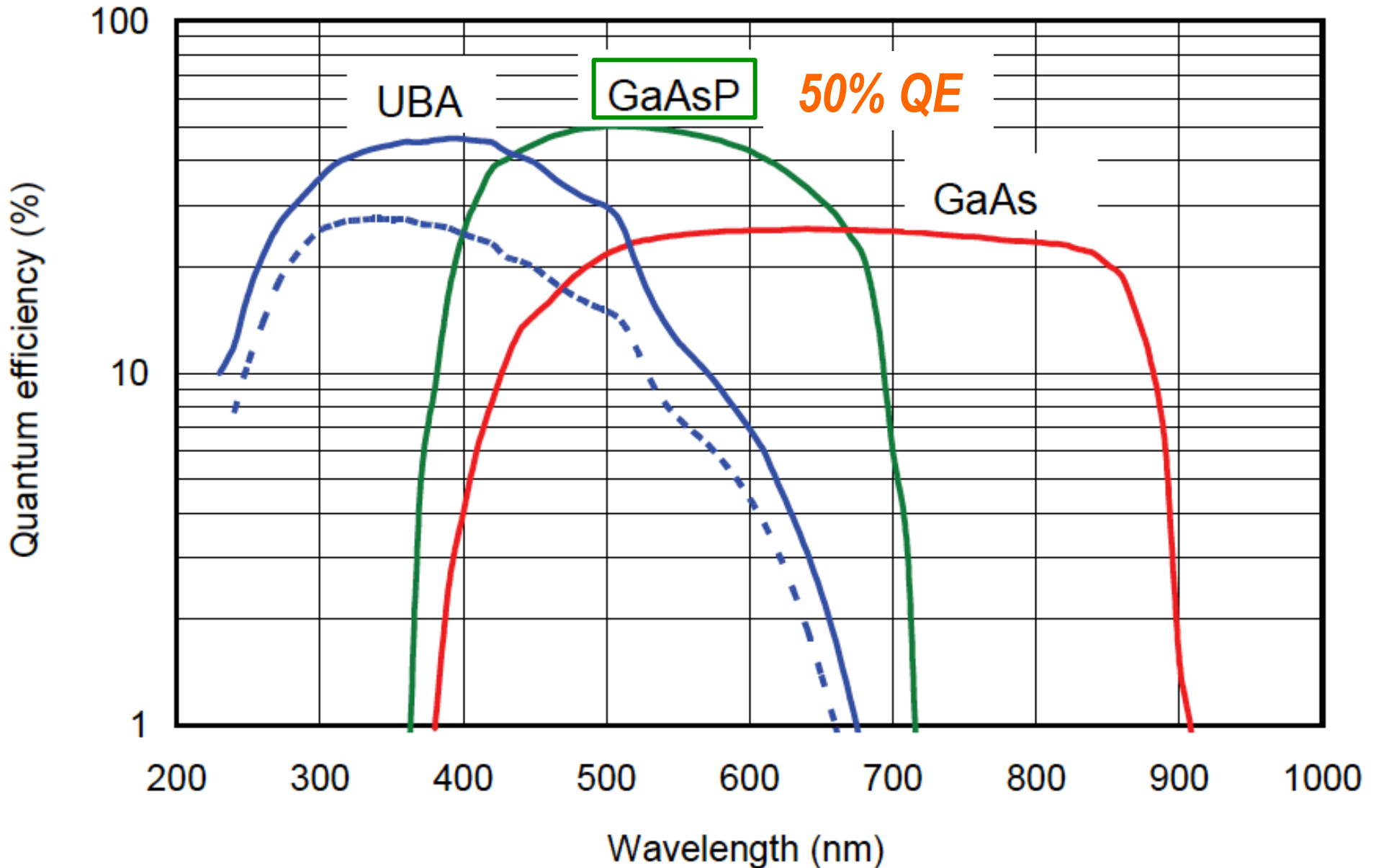
Single Channel
HAPD

64 Channel HAPD
+ Readout

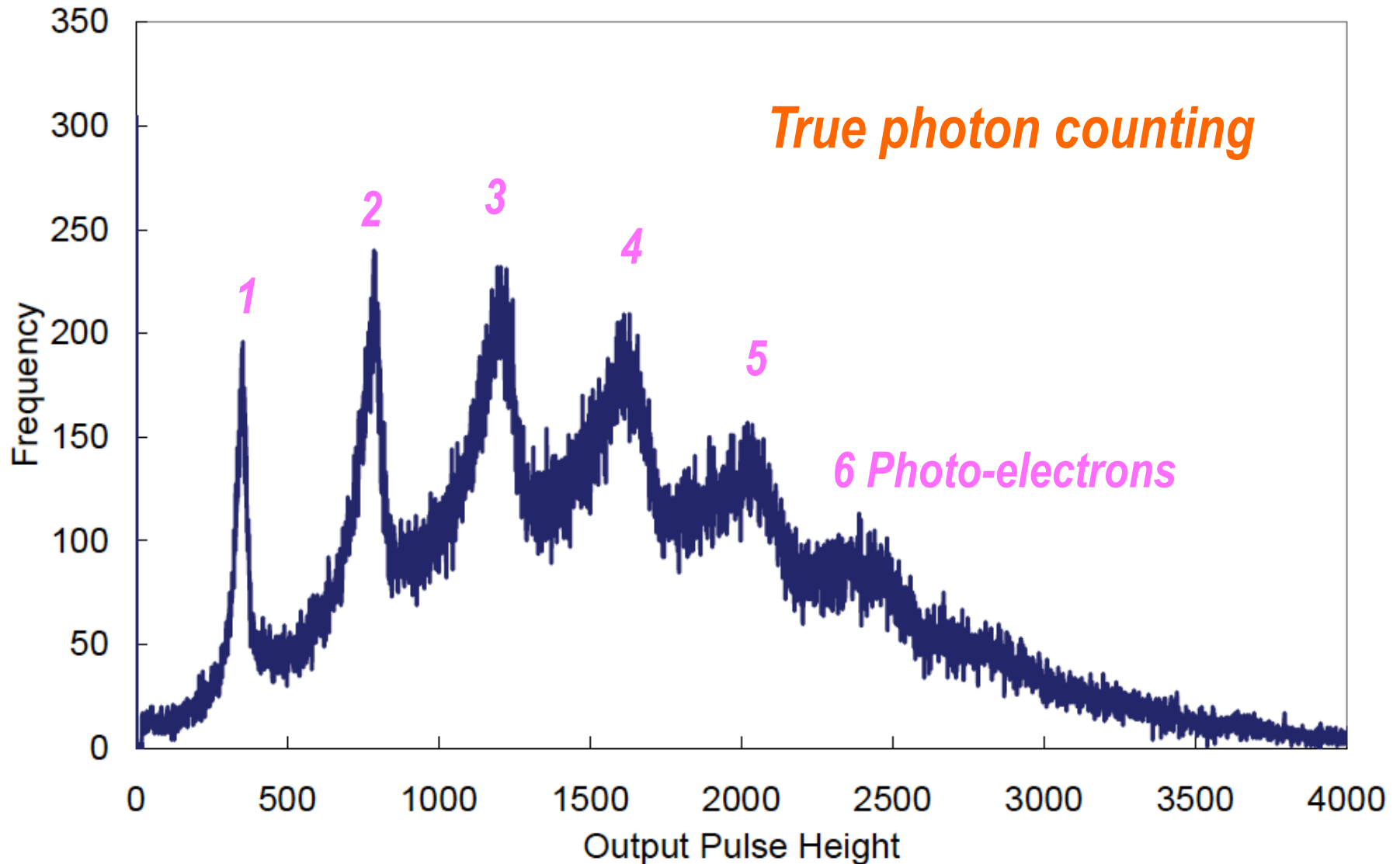
Motohiro Suyama
(Hamamatsu)
Xavier Michalet
Shimon Weiss
(Chemistry)



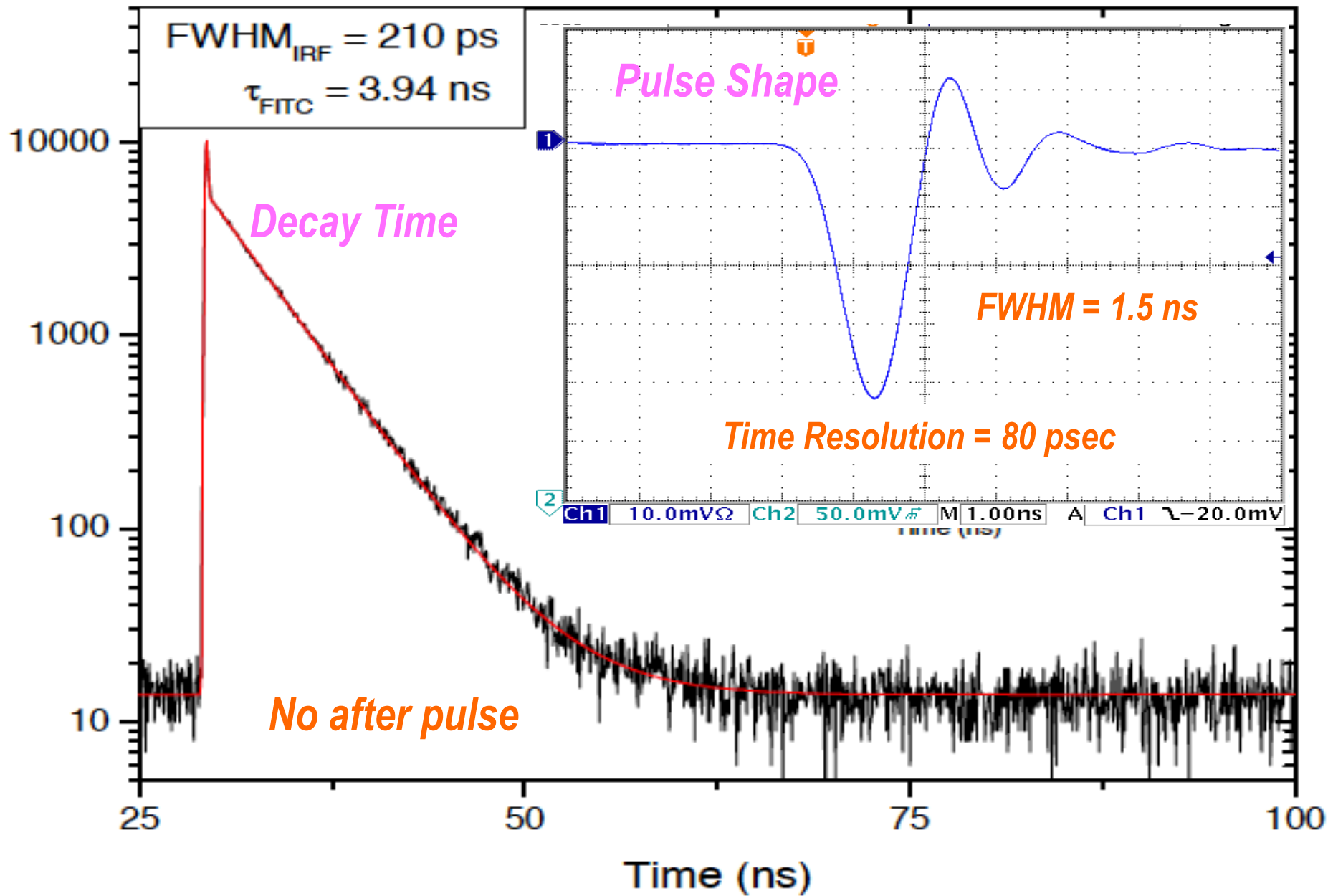
Quantum Efficiency of UBA, GaAsP and GaAs



1, 2, 3 ... Photo-electron Distribution



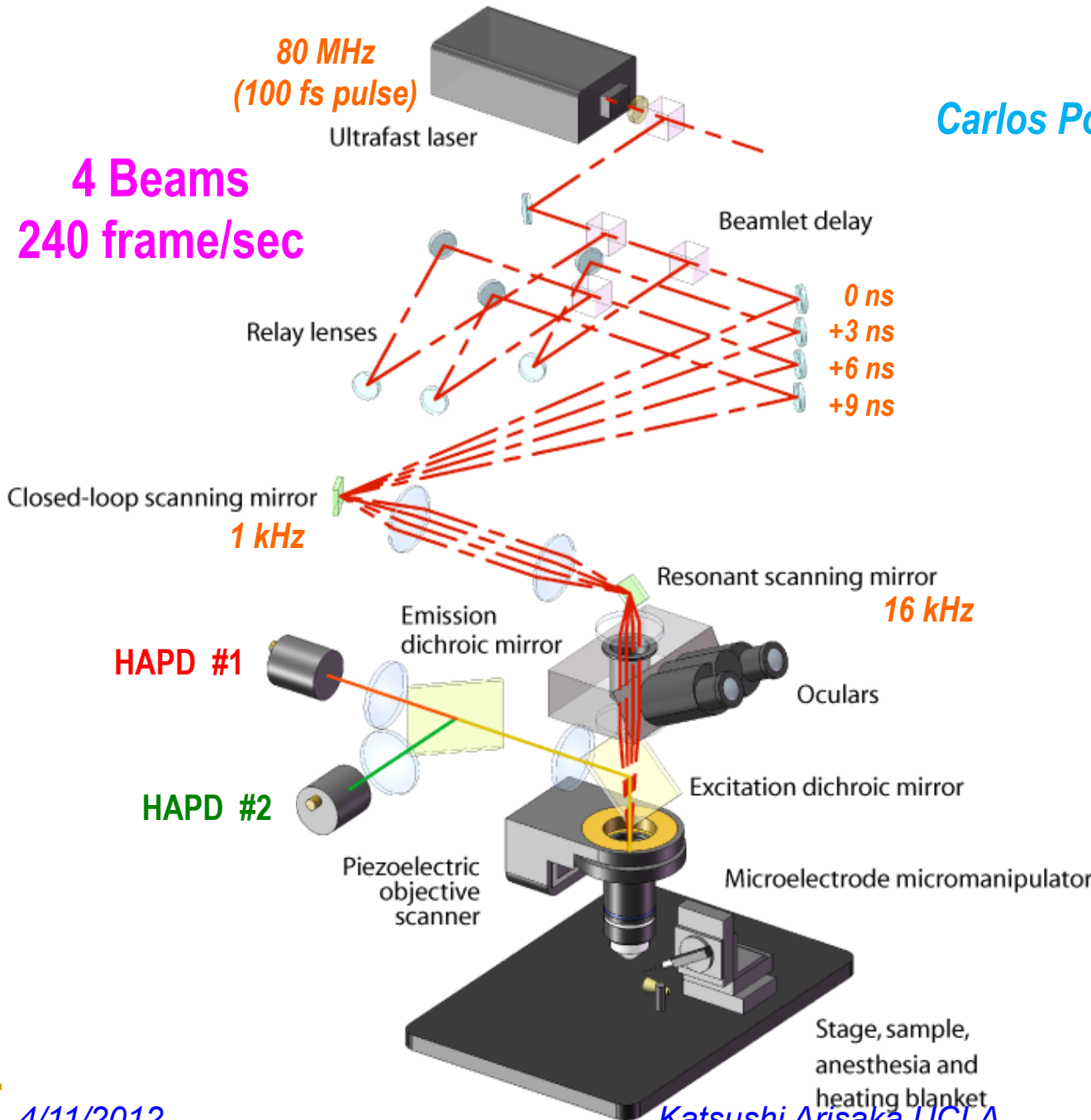
Decay Time Measurement by HAPD



Spatio-Temporal Excitation-Emission Multiplexing (STEM) Microscope

Adrian Cheng (Physics)

Carlos Portera-Cailliau (Neurology)



Single beam



Oscilloscope



Histogram

Spatio-temporally multiplexed MMM



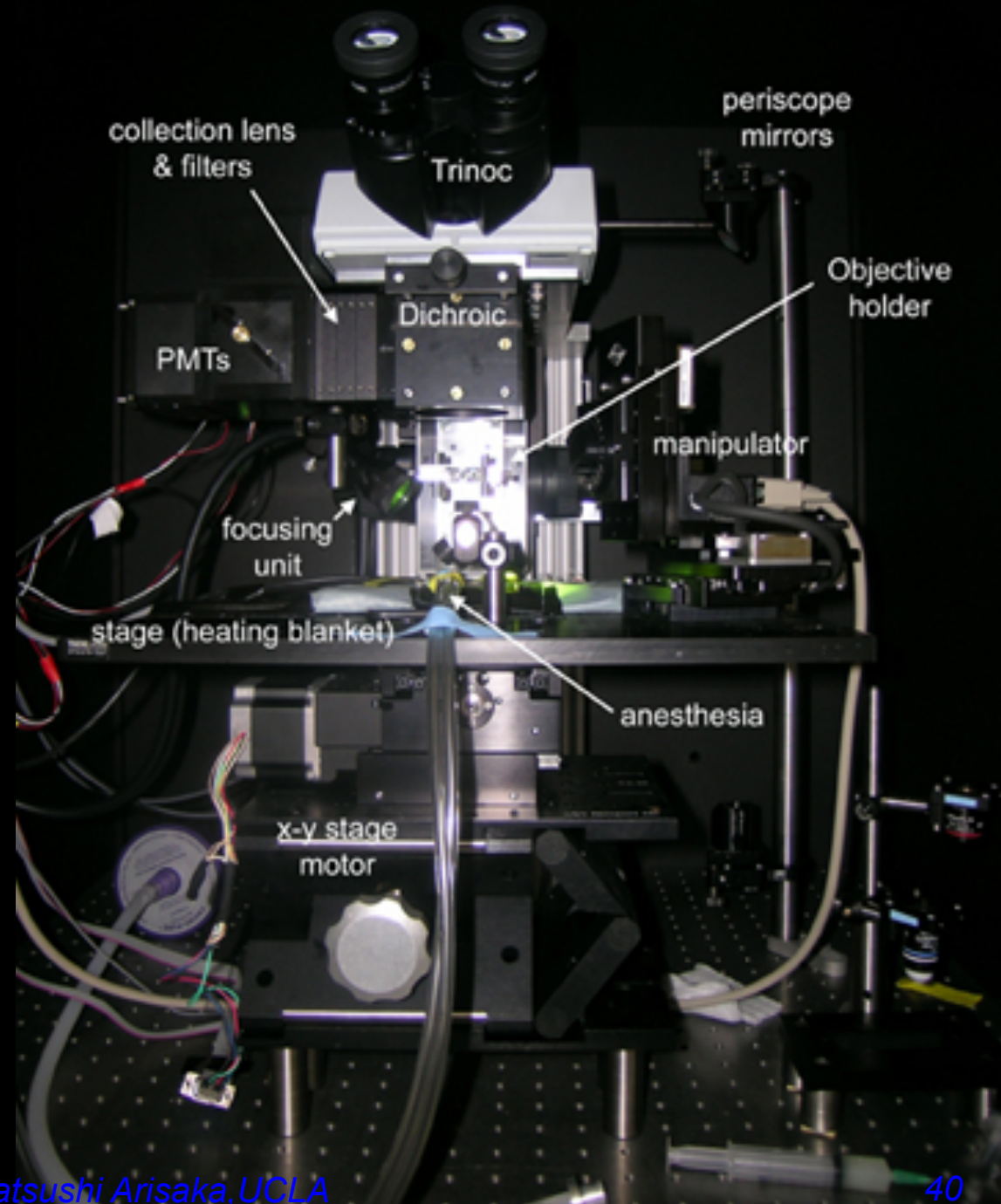
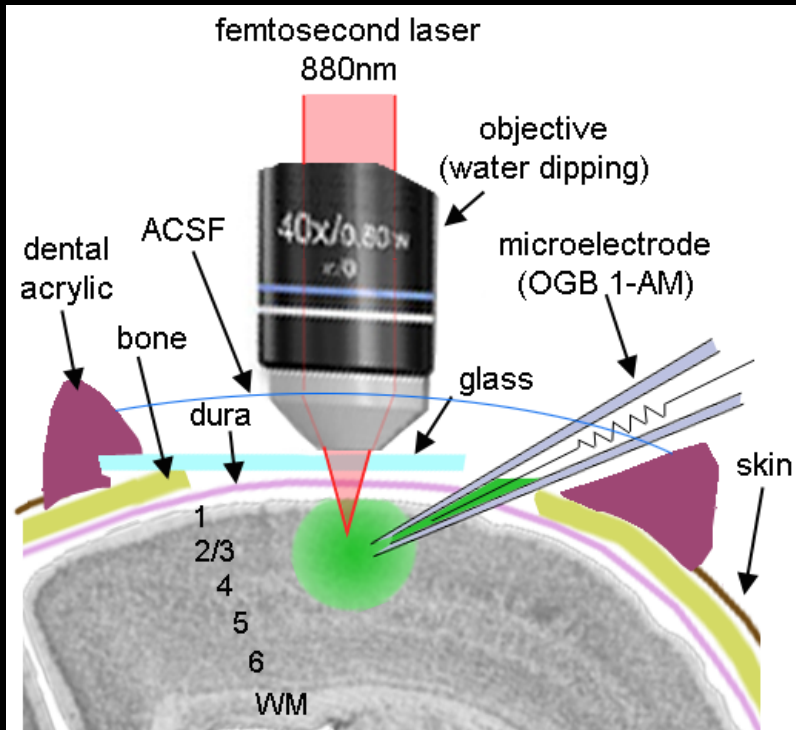
Oscilloscope



Histogram

12 ns

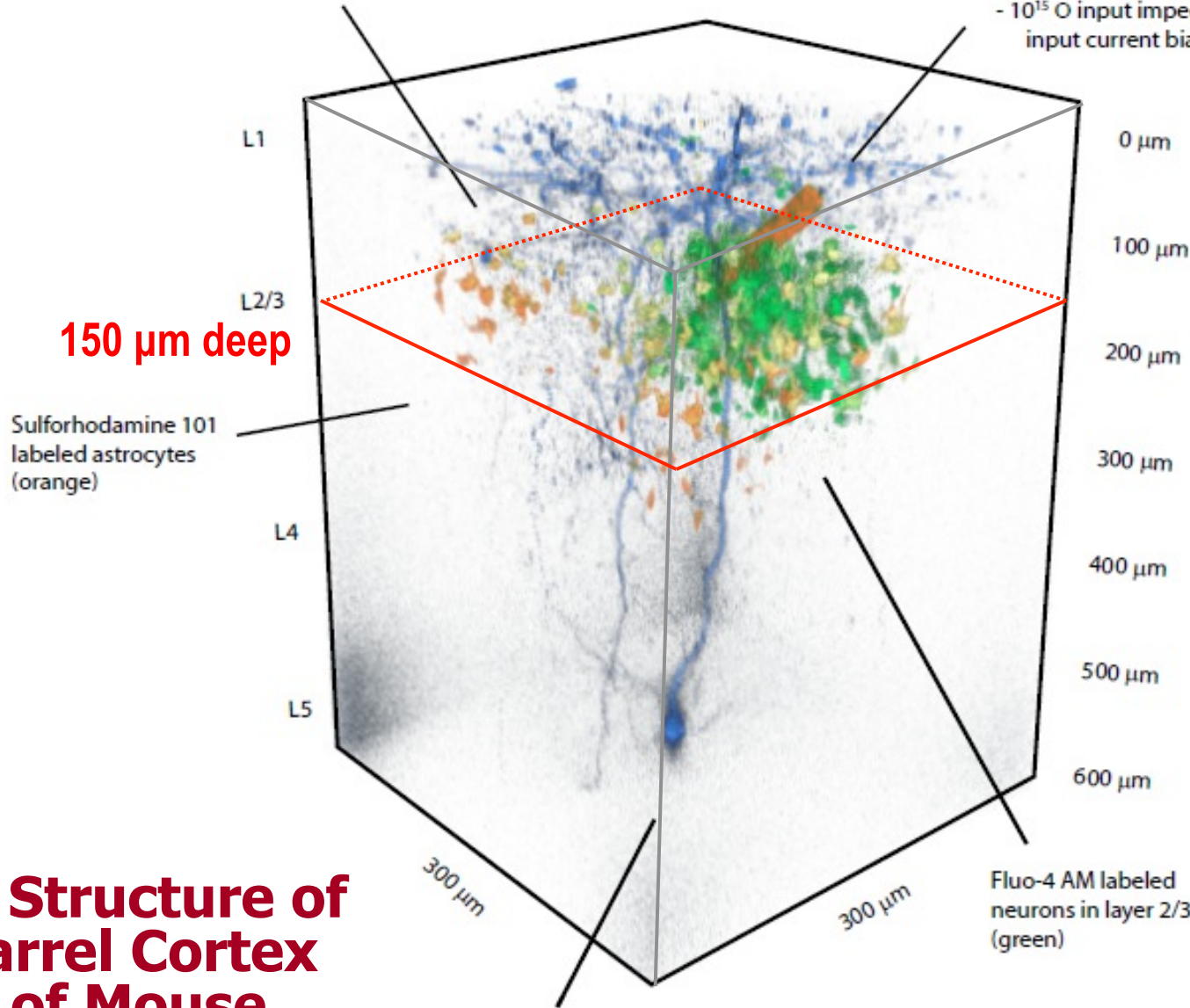
In vivo calcium imaging of neuronal activity



Fluo-4 AM labeled astrocytes are colabeled with sulforhodamine 101 to eliminate background (yellow)

Glass microelectrode for dye injection and electrophysiology

- cell-attached voltage follower
- whole-cell voltage/current clamp
- $10^{15} \Omega$ input impedance, $< 150 \text{ fA}$ input current bias



150 μm deep

Sulforhodamine 101 labeled astrocytes (orange)

Fluo-4 AM labeled neurons in layer 2/3 (green)

Layer 5 pyramidal neuron soma and apical dendrite from a transgenic animal demonstrates imaging depth (blue)

Adrian Cheng
(Physics)

Tiago Goncalves,
Peyman Golshani,
Carlos Portera-Cailliau
(Neurology)

3D Structure of Barrel Cortex of Mouse

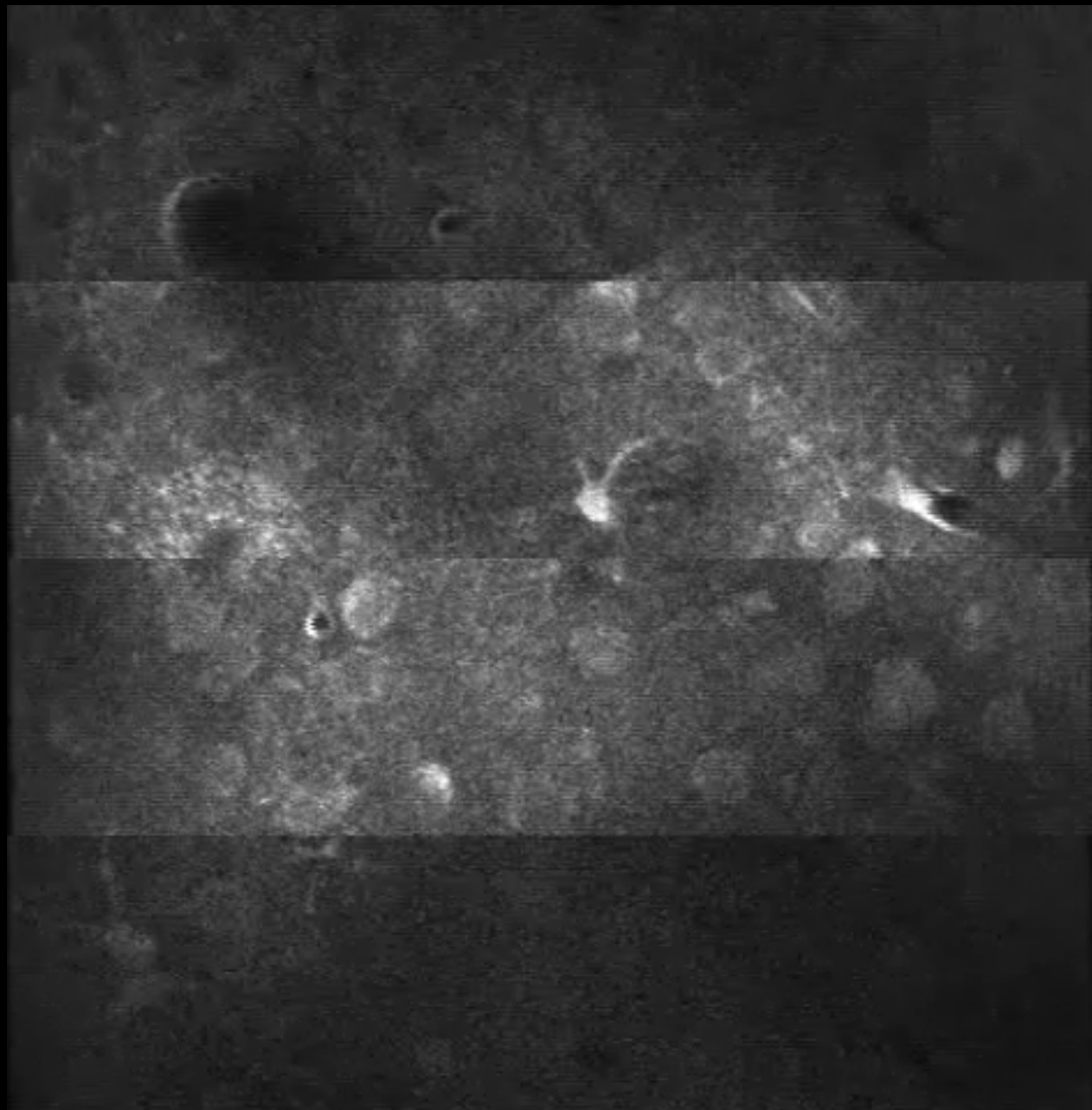
In vivo calcium imaging of Barrel Cortex of Mouse

**Barrel Cortex
Layer 2/3**

150 μm deep

**240 fps
Raw Data**

**(x3 faster
than real)**



**Beam 1
(0 ns)**

**Beam 2
(+3 ns)**

**Beam 3
(+6 ns)**

**Beam 4
(+9 ns)**

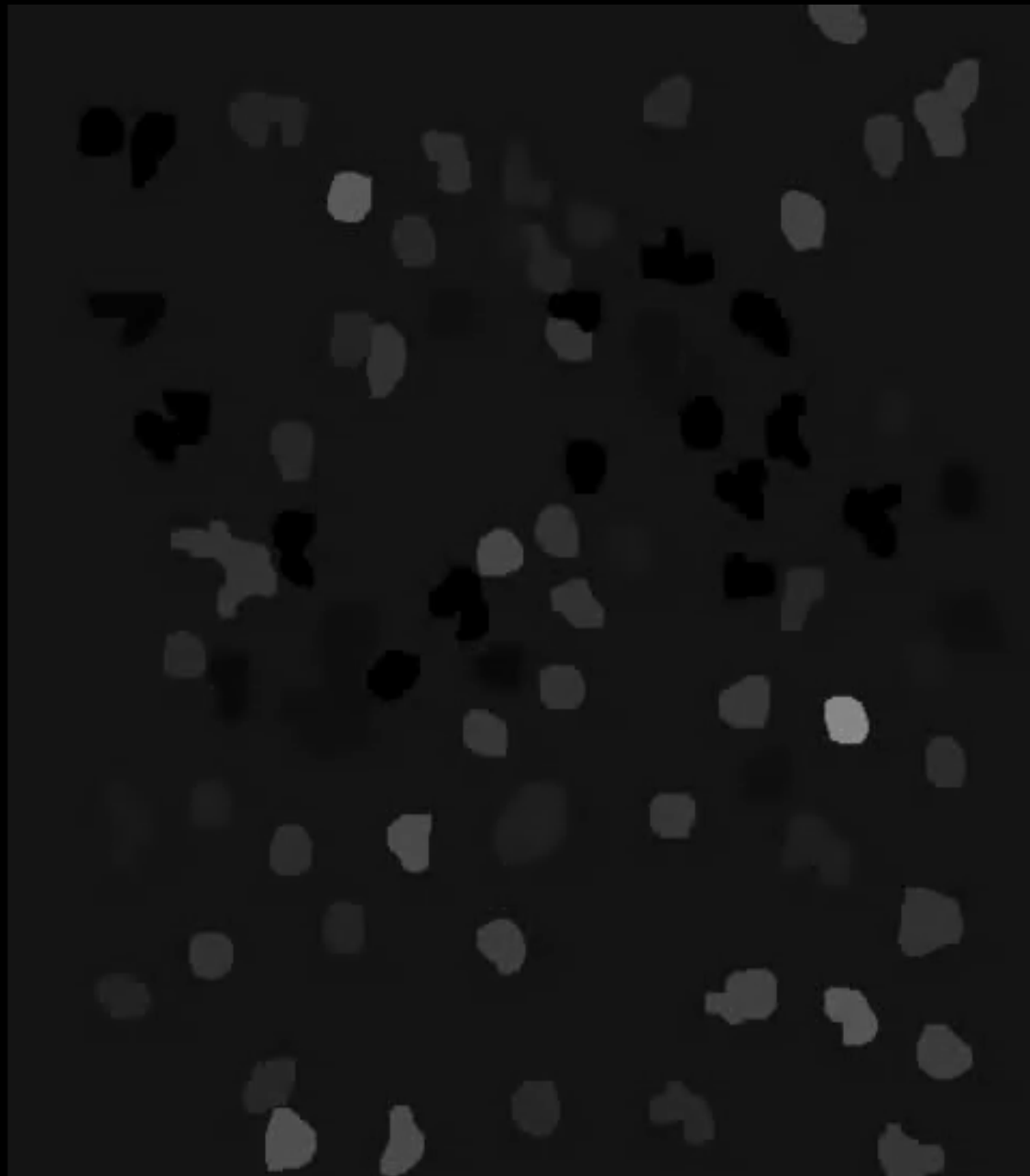
In vivo calcium imaging of Barrel Cortex of Mouse

Barrel Cortex
Layer 2/3

150 μm deep

After
averaging

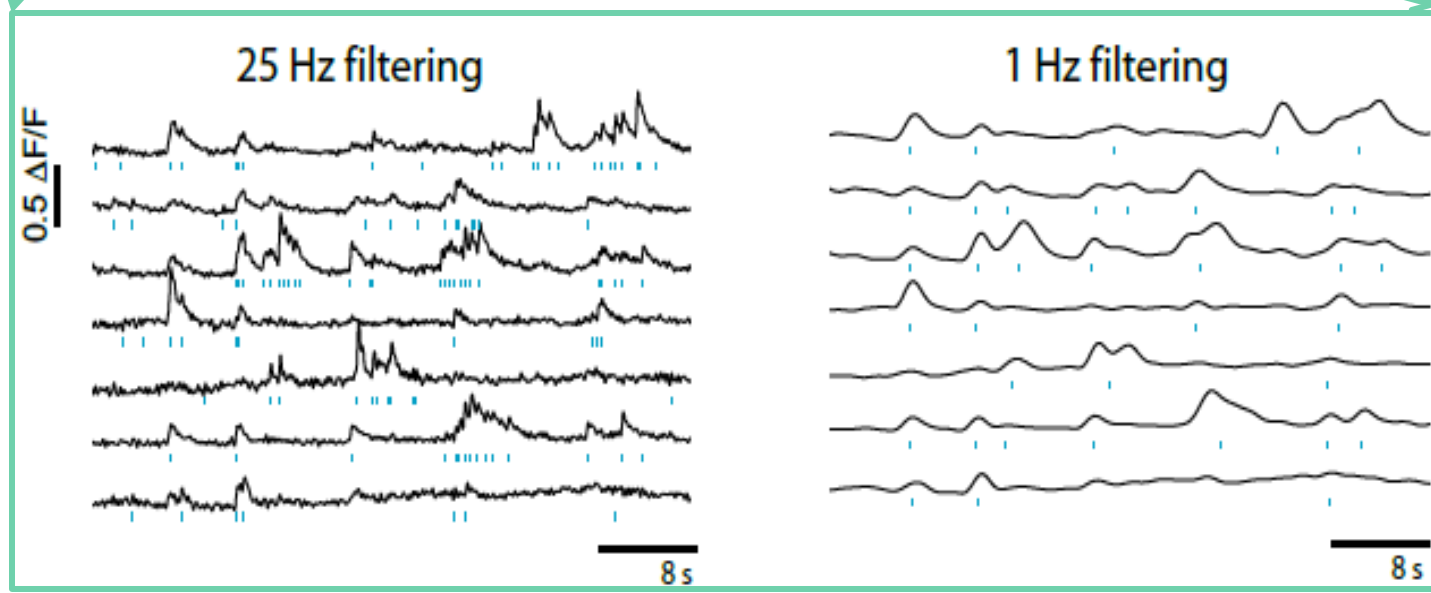
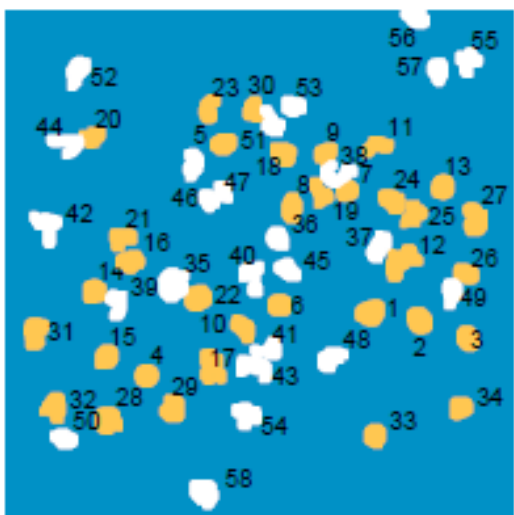
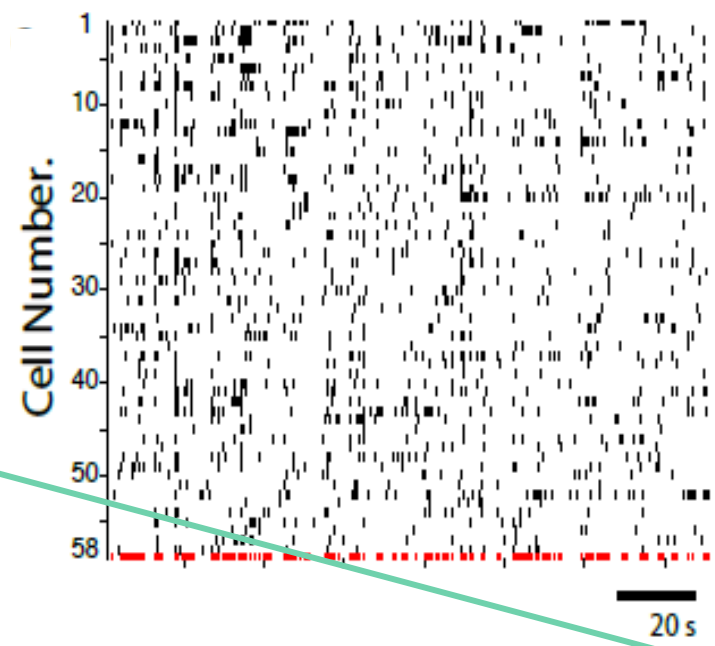
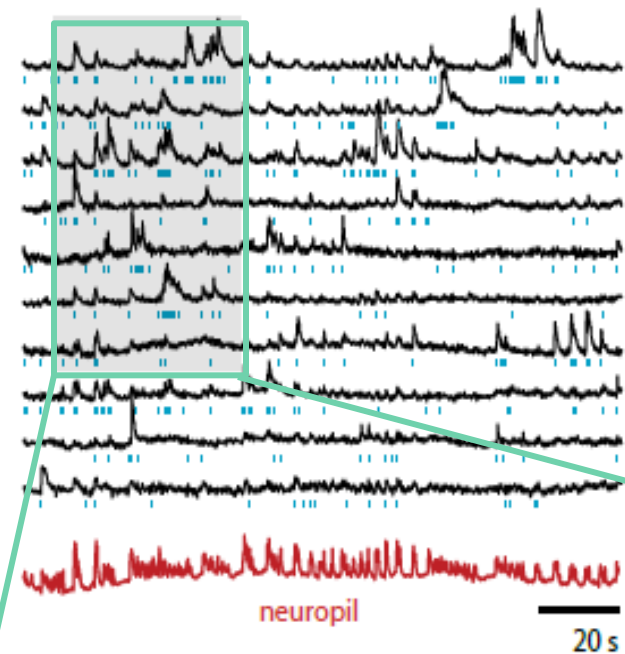
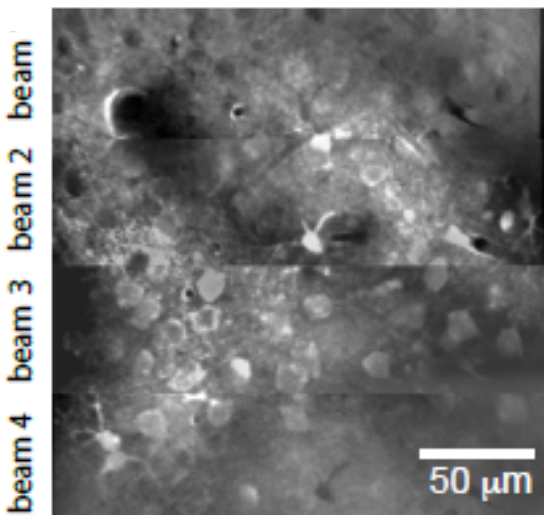
(x3 faster
than real)



58 neurons

(~100 billions
neurons
in our brain)

In vivo calcium imaging of layer 2/3 neurons in barrel cortex with STEM

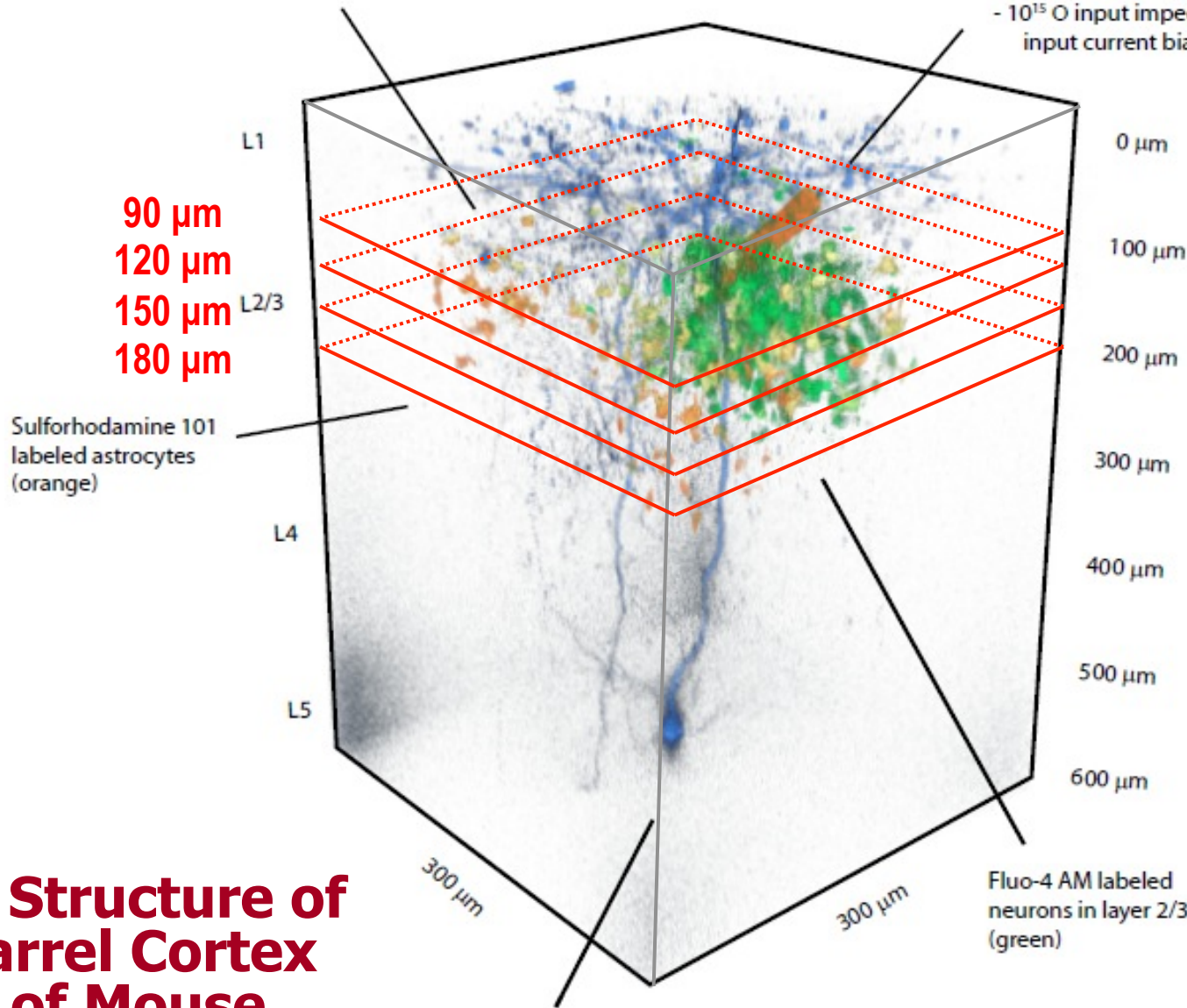


Adrian Cheng (Physics)

Fluo-4 AM labeled astrocytes are colabeled with sulforhodamine 101 to eliminate background (yellow)

Glass microelectrode for dye injection and electrophysiology

- cell-attached voltage follower
- whole-cell voltage/current clamp
- $10^{15} \Omega$ input impedance, $< 150 \text{ fA}$ input current bias



3D Structure of Barrel Cortex of Mouse

*Adrian Cheng
(Physics)*

*Tiago Goncalves,
Peyman Golshani,
Carlos Portera-Cailliau
(Neurology)*

Layer 5 pyramidal neuron soma and apical dendrite from a transgenic animal demonstrates imaging depth (blue)

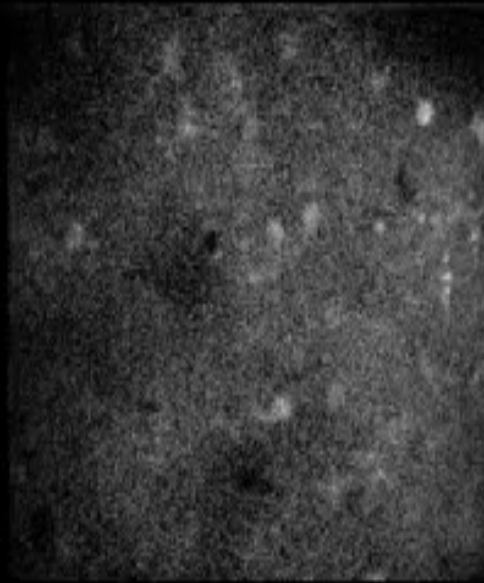
Fluo-4 AM labeled neurons in layer 2/3 (green)

Simultaneous in vivo calcium imaging in 4 axial planes

Barrel
Cortex
Layer 2/3

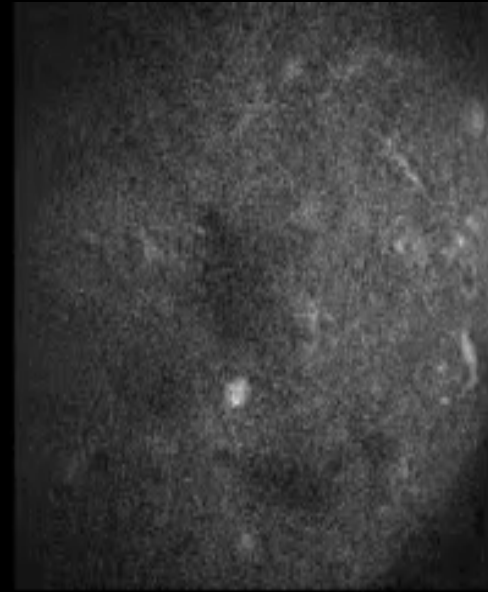
60 fps

(x3 faster
than real)

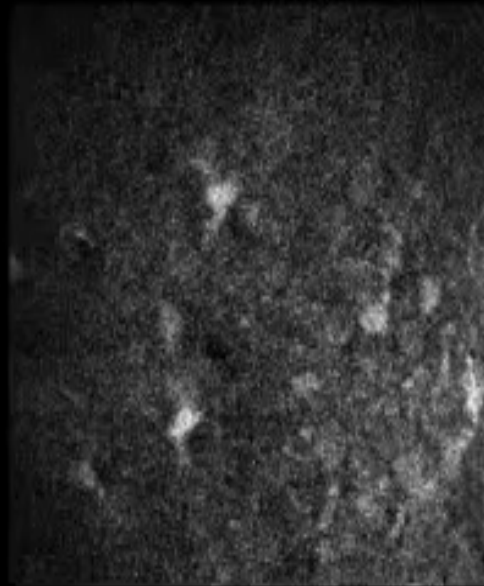


Beam 1

90 μm

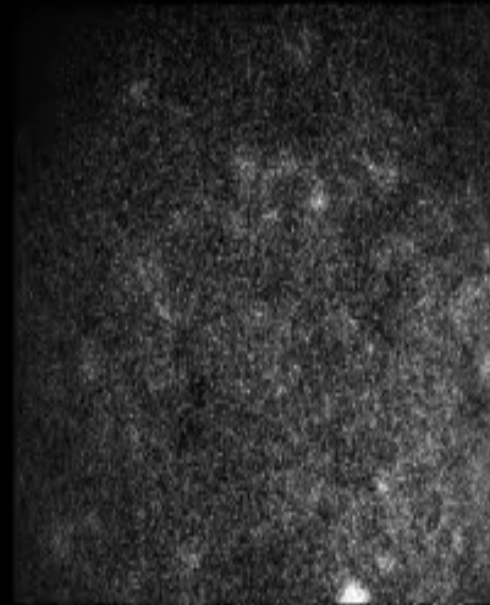


Beam 2 120 μm



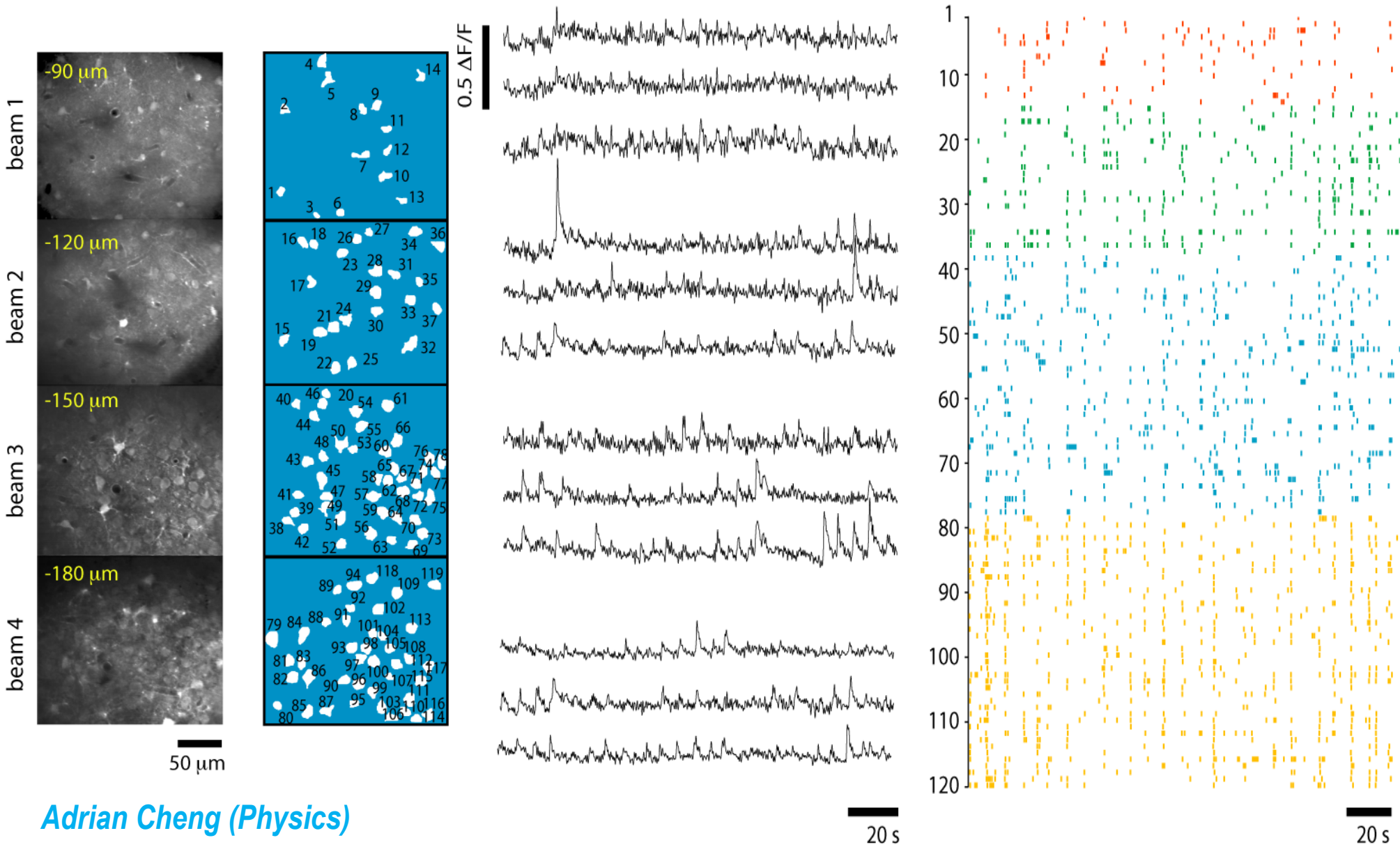
Beam 3

150 μm



Beam 4 180 μm

Simultaneous in vivo calcium imaging of neuronal activity in 4 axial planes with STEM



Adrian Cheng (Physics)

UCLA Newsroom on January 11, 2011

January 11, 2011

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New UCLA-designed microscope records firing of thousands of individual neurons in 3-D

Imaging system could help reveal 'miscommunications' in autism, schizophrenia

By **Mark Wheeler** | January 11, 2011



Some disorders of the brain are obvious — the massive death of brain cells after a stroke, the explosion in the growth of cells that marks a tumor. Other disorders, such as autism, schizophrenia and mental retardation show no physical signs of damage and are believed to be caused by problems in how brain cells communicate with one another.

To understand the root of the problem of these latter diseases, visualizing brain activity is key. But even the best imaging devices available — fMRIs and PET scans — can only give a "coarse" picture of brain activity.

UCLA neuroscientists have now collaborated with physicists to develop a non-invasive, ultra-high-speed microscope that can record in real time the firing of thousands of individual neurons in the brain as they communicate, or miscommunicate, with each other.

"In our view, this is the world's fastest two-photon excitation microscope for three-dimensional imaging *in vivo*," said UCLA physics professor Katsushi Arisaka, who designed the new optical imaging system with UCLA assistant professor of neurology and neurobiology Dr. Carlos Portera-Cailliau and colleagues.

Their research appears in the Jan. 9 edition of the journal *Nature Methods*.

Because neuropsychiatric diseases like autism and mental retardation often display no physical brain damage, it's thought they are caused by conductivity problems — neurons not firing properly. Normal cells have patterns of electrical activity, said Portera-Cailliau, but abnormal cell activity as a whole doesn't generate relevant information for the brain circuit.



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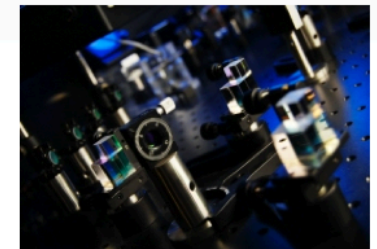


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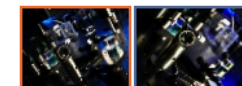
Media Contacts

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Related Images

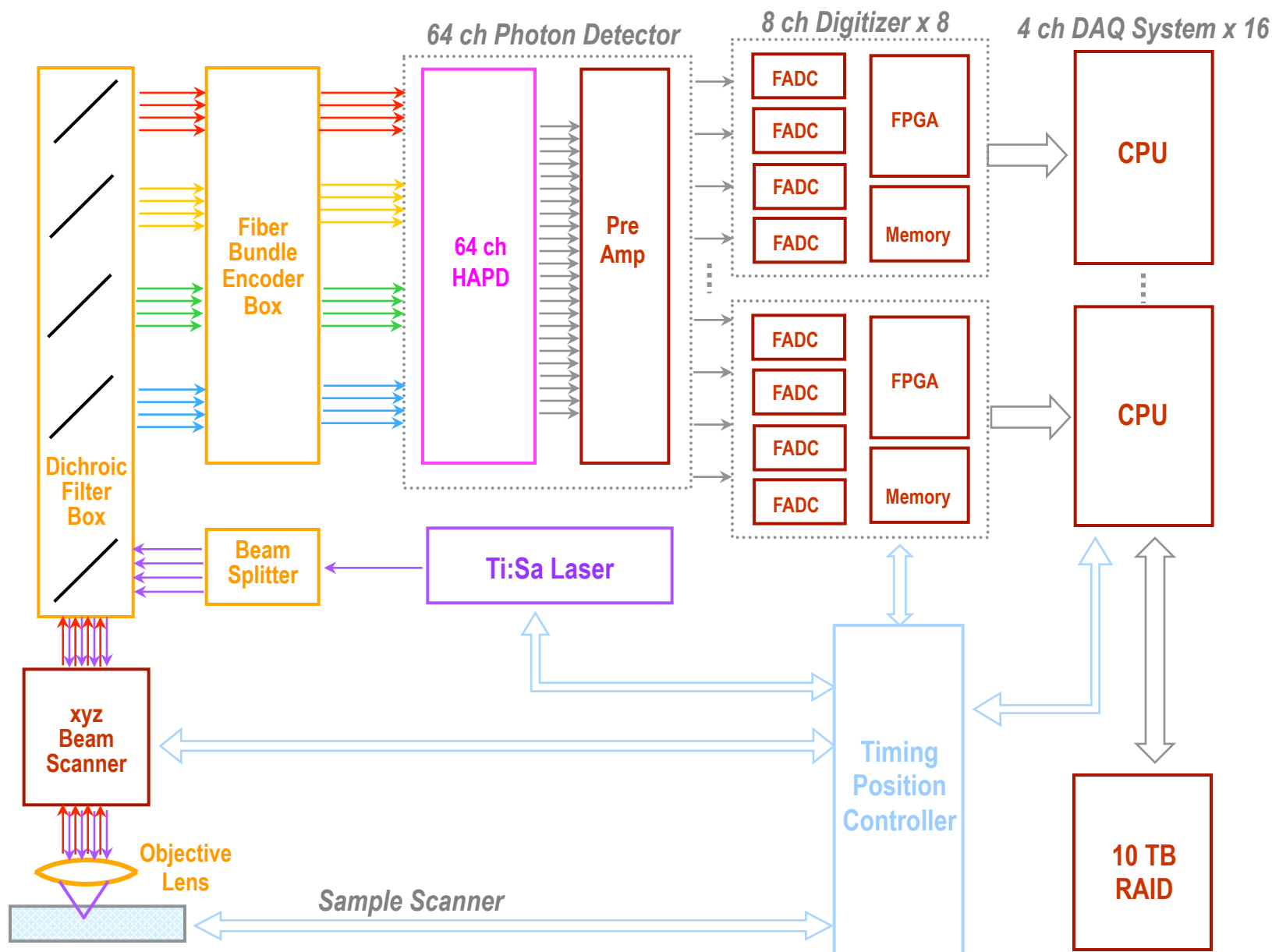


STEM microscope designed at UCLA



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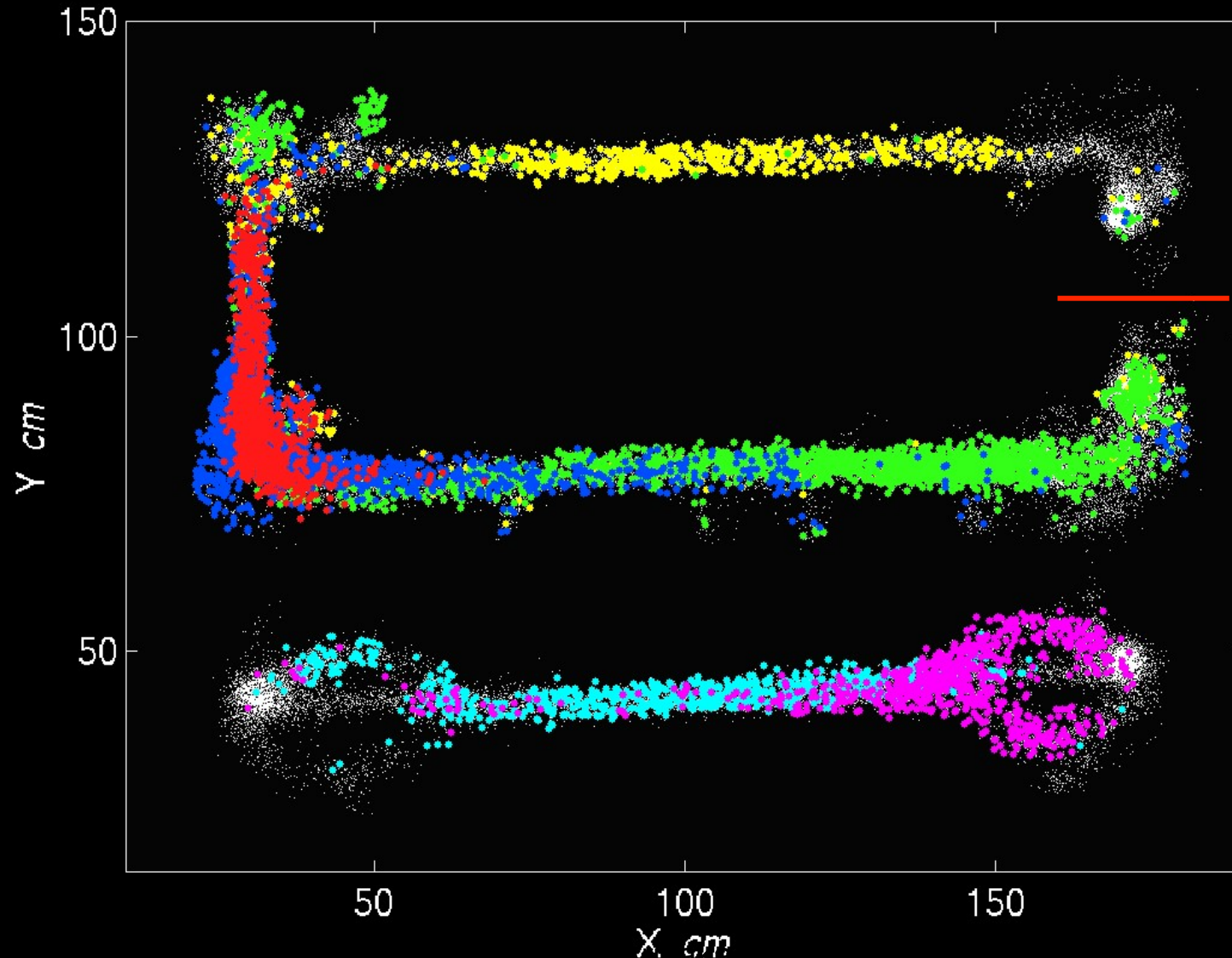
Block Diagram of Multi-beam Confocal Microscope



Future Directions - Virtual Reality -

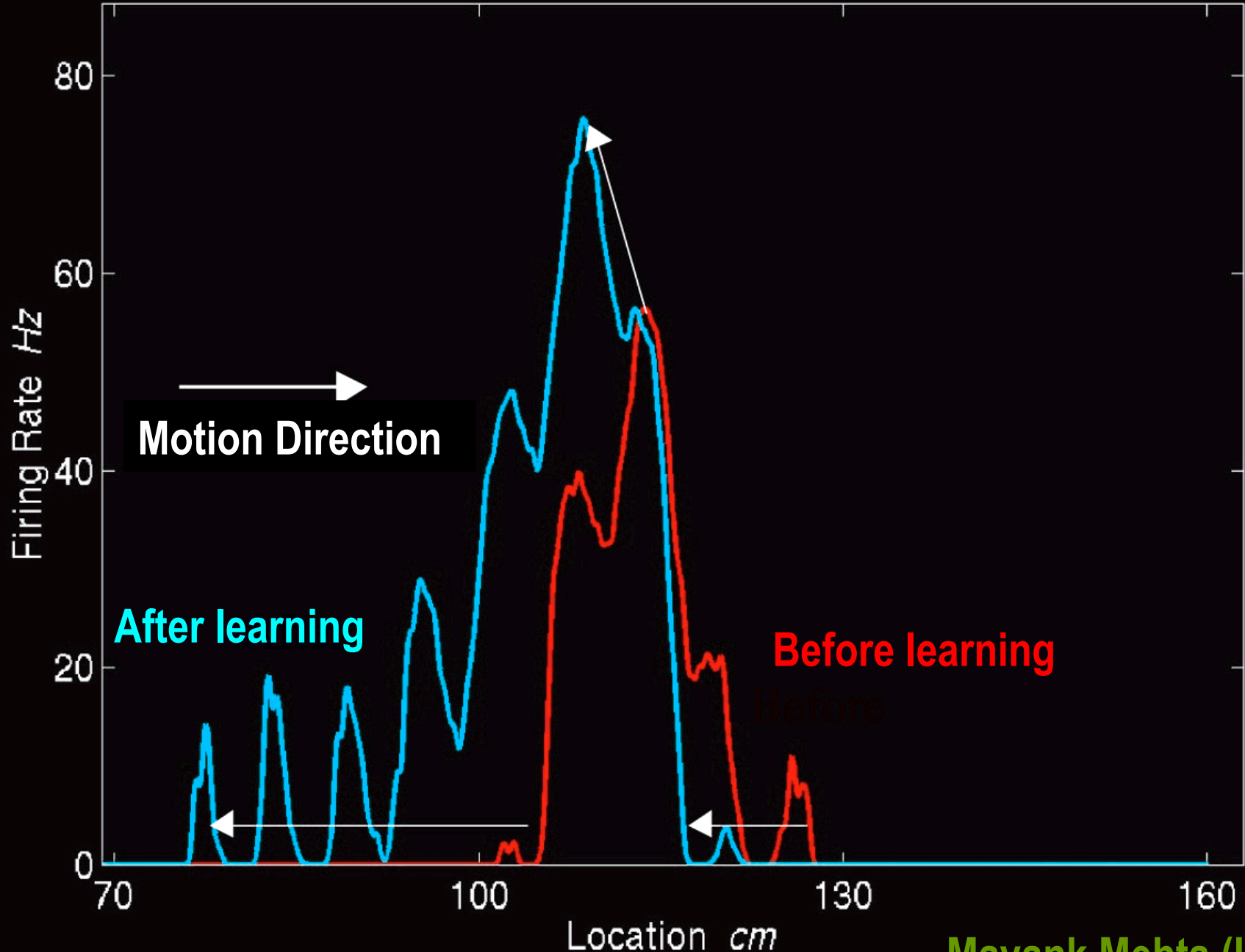
Activity of (excitatory) pyramidal neurons in CA depends on rat's position: place cells

Mayank Mehta (Physics, Neurology)



Hippocampus has a cognitive map of space

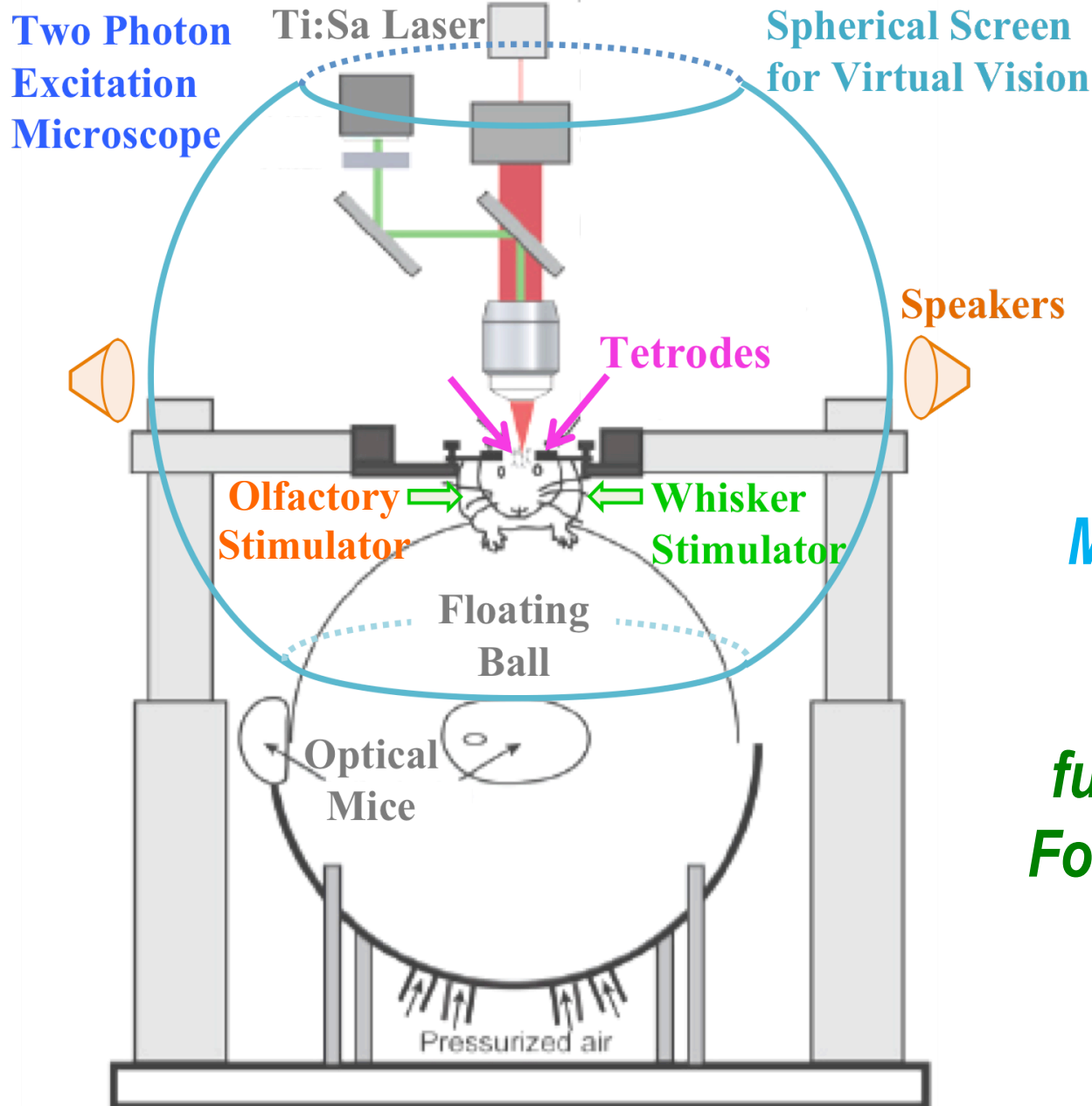
Learning and Memory by Hippocampus



Origin of the Brain

- **Brains were evolved for animals to predict necessary motions for survival.**
 - **Find preys**
 - **Escape away from predators**
 - **Find mates for sex**
- **A brain “consciously” makes the best decision at a given time.**
- **Complex activities of brains are the results of evolution of life.**

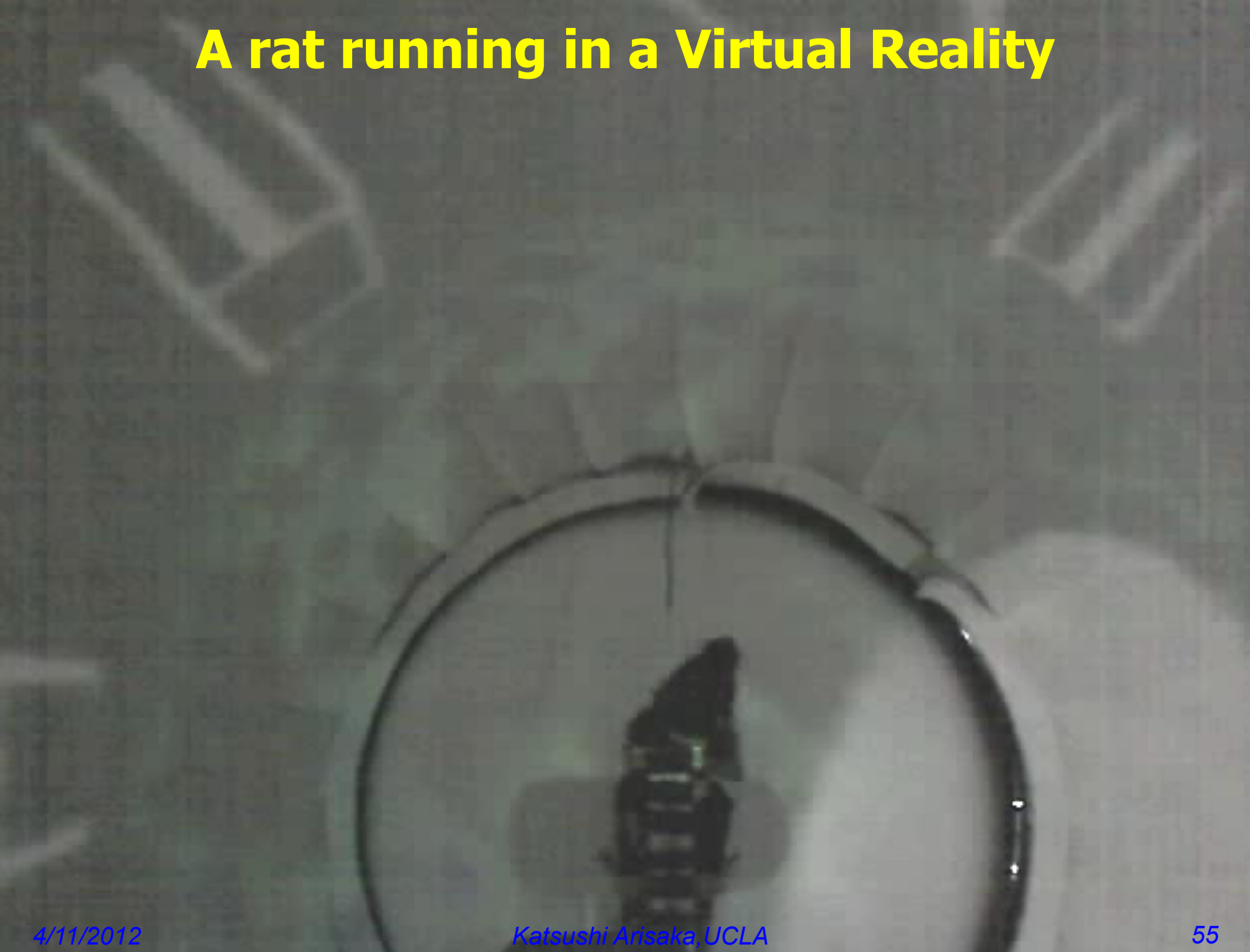
Virtual Reality Experiment on Awake Rats



Mayank Mehta
(Physics)

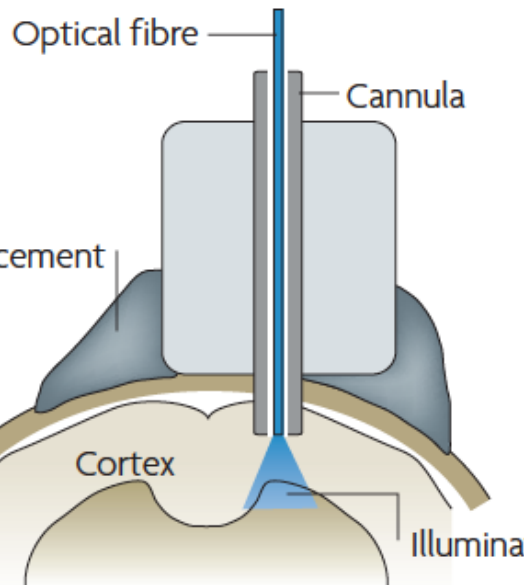
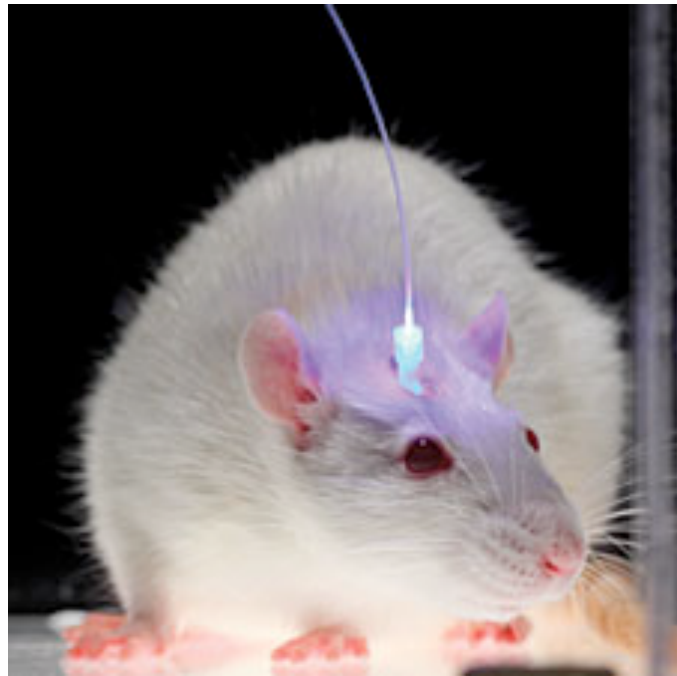
*funded by Keck
Foundation (\$1M)*

A rat running in a Virtual Reality

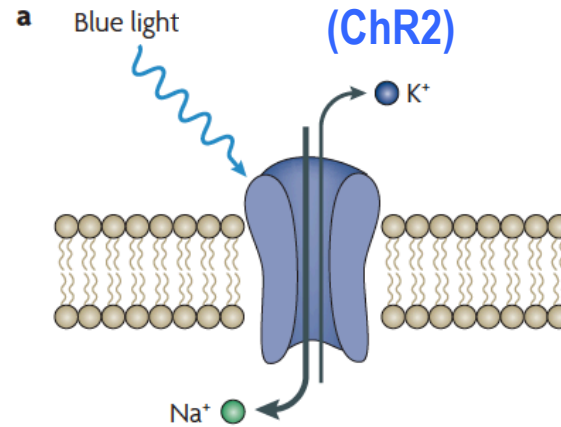


Optogenetic Excitation of Neurons

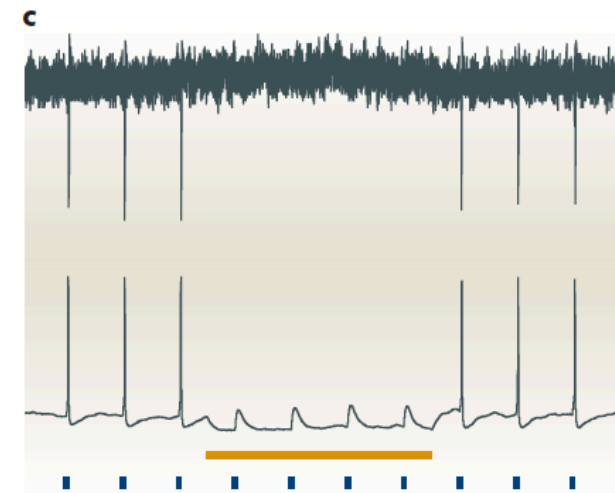
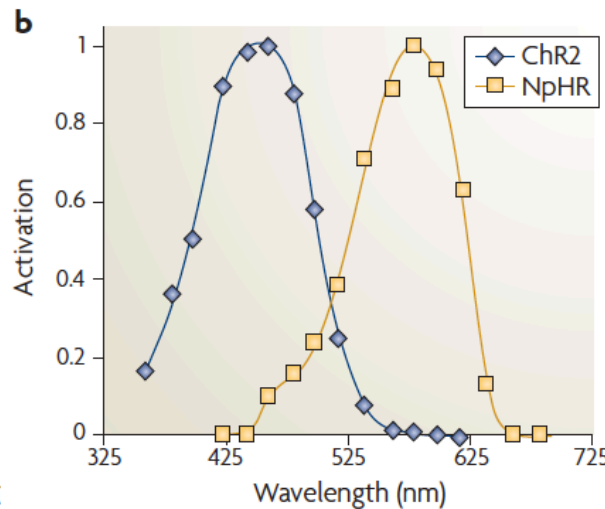
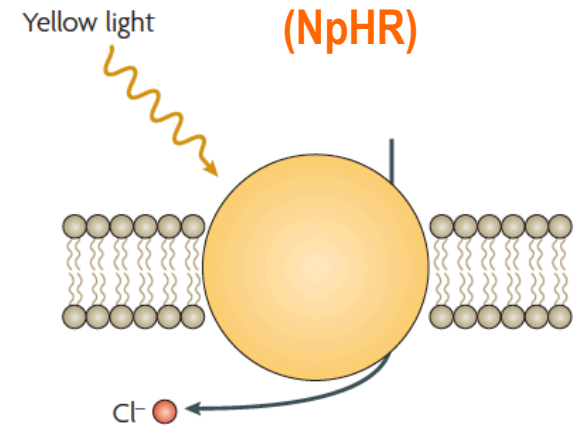
Karl Deisseroth (Stanford)



Excitation by
Channelrhodopsin-2
(ChR2)



Inhibition by
Halorhodopsin
(NpHR)



Outer world vs. Inner world

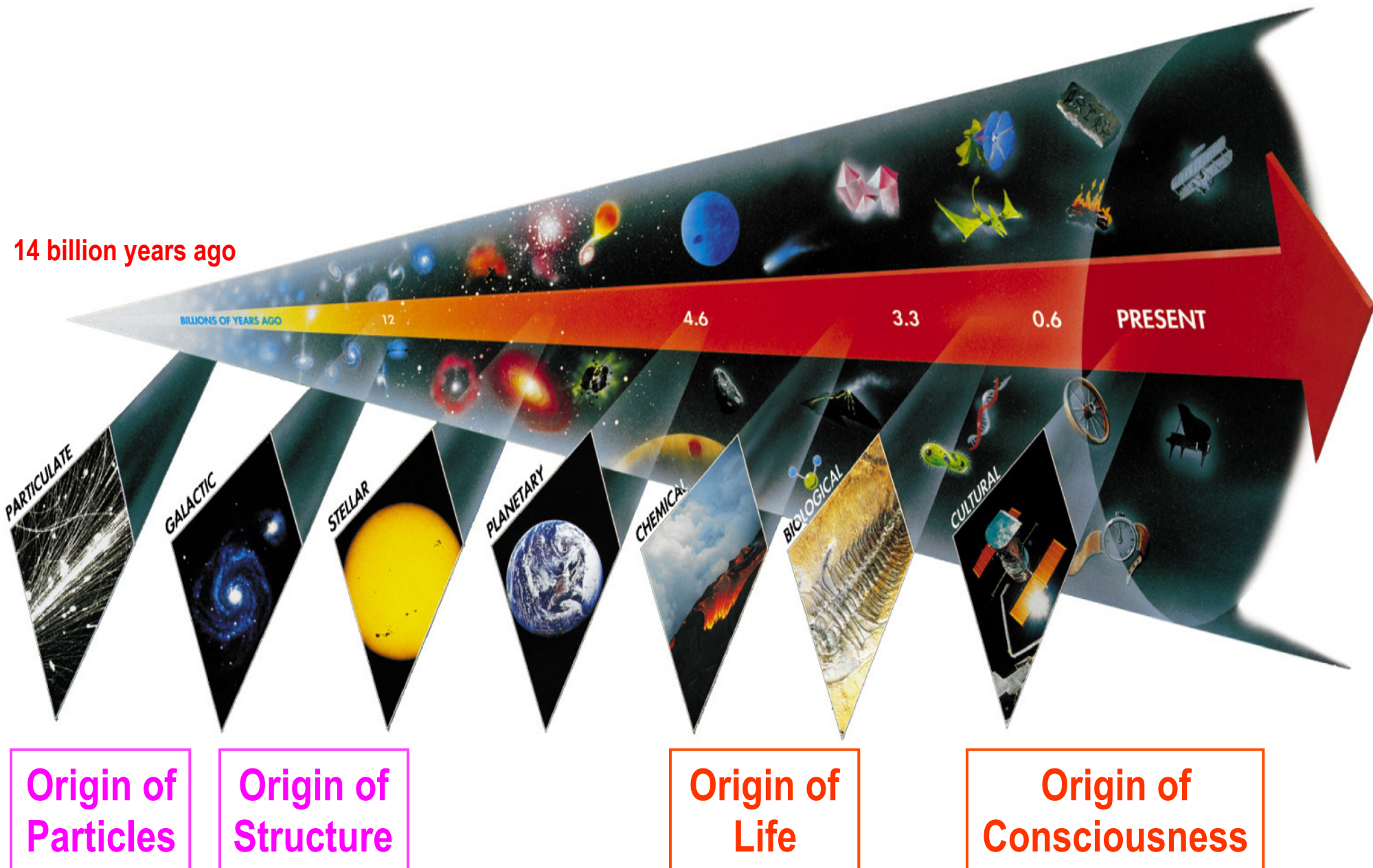
- Outer world : Five senses → Manipulate by Virtual Reality
 - Vision
 - Sound
 - Touch
 - Smell
 - Taste
- Inner world → Manipulate by Photo Excitation of single neurons
 - Neural network in brain
- Establish direct link between Inner world & Outer world
 - Control outer world – Virtual reality
 - Control inner world – Neural reality

The Origin of Consciousness

- Our brains are making enormous parallel processing “unconsciously” all the time.
 - Image processing
 - Language
 - Recognition of space-time
- “Consciousness” is merely the outcome of the decision making processes which have been performed unconsciously.
 - Language and logics are just left-over from the past.
 - We realize what we said only after we spoke.

Summary

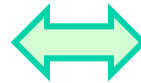
Seven Phases of Cosmic Evolution



Four Major Science

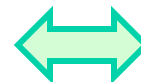
Origin of Particles
Particle Physics

Origin of Universe
Cosmology



Origin of Life
Molecular Biology

Origin of Consciousness
Neurophysics



Future of Ultra High-speed Bio Imaging

➤ Origin of Life:

- Networks of molecules in/on a cell
- Competition against Brownian : 10 – 100 nm / 1 msec

➤ Origin of Consciousness:


- Neural networks
- Action potentials: 1 msec



➤ > 1,000 frame/sec with nano second time stamp.

- Gated Image Intensified CMOS
- Super-PIAS (GHz Photon-counting Imager)
- 6D Imaging by Streak-CMOS Camera

Concluding Remarks

- **“Life” is a complex system in 4 dimensional space-time.**
 - Emergent property
 - Strongly interacting
 - **Countless “spontaneous symmetry breakings” during the evolutionary and developing process of life**
 - **Fully controlled experiments by “Virtual Reality” under way.**
 - Outer world (environment) vs. Inner world (brain)
- 
- **“Ultra high-speed optical imaging” may reveal the fundamental principle of the brain function such as consciousness.**