

# **Exploring the Origin of Life and Consciousness by high-speed Optical Microscopes**

**Katsushi Arisaka**

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

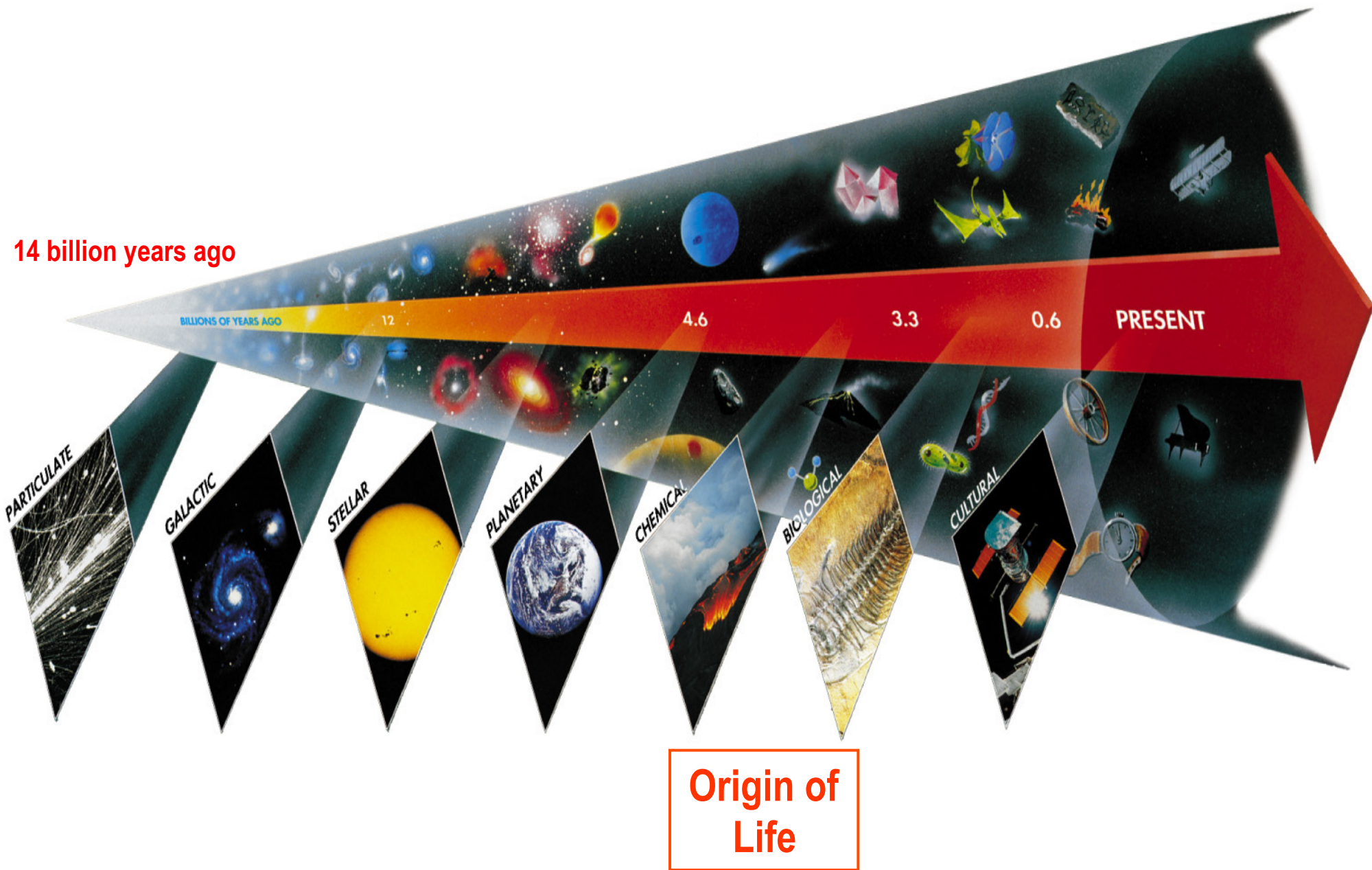
# Talk Outline

- Part I : Particle Physics & Cosmology ~50 min.
  - Introduction to Cosmology: Origin of Universe
  - CMS at CERN: Origin of Particles
  - Detection of Dark Matter: Origin of Structure in Universe
  
- Lab Tour ~15 min.
  
- Part II : Bio-imaging and Neuro-physics ~50 min.
  - Introduction to High-speed Bio-imaging
  - Single Molecule: Origin of Life
  - Neurophysics: Origin of Consciousness

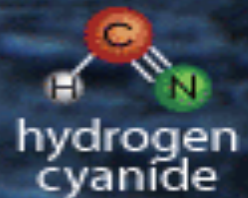
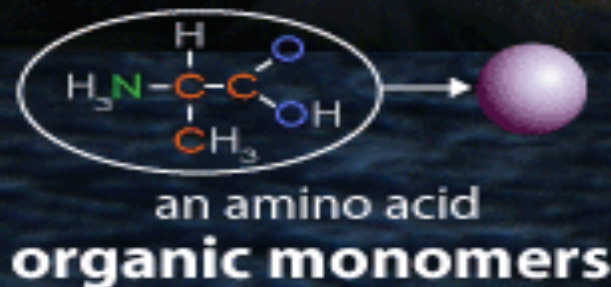
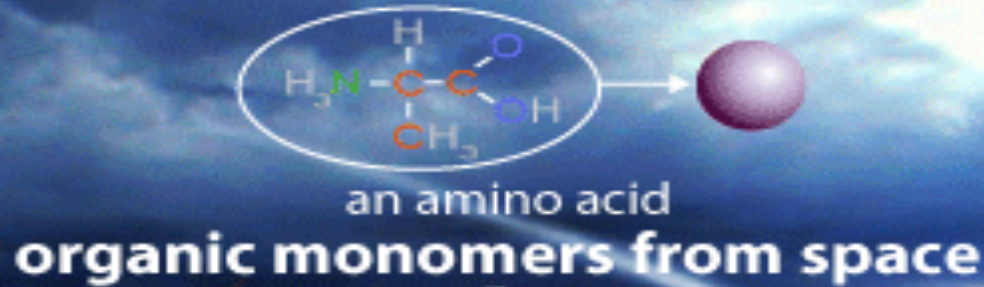
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# Origin of Life

# Seven Phases of Cosmic Evolution

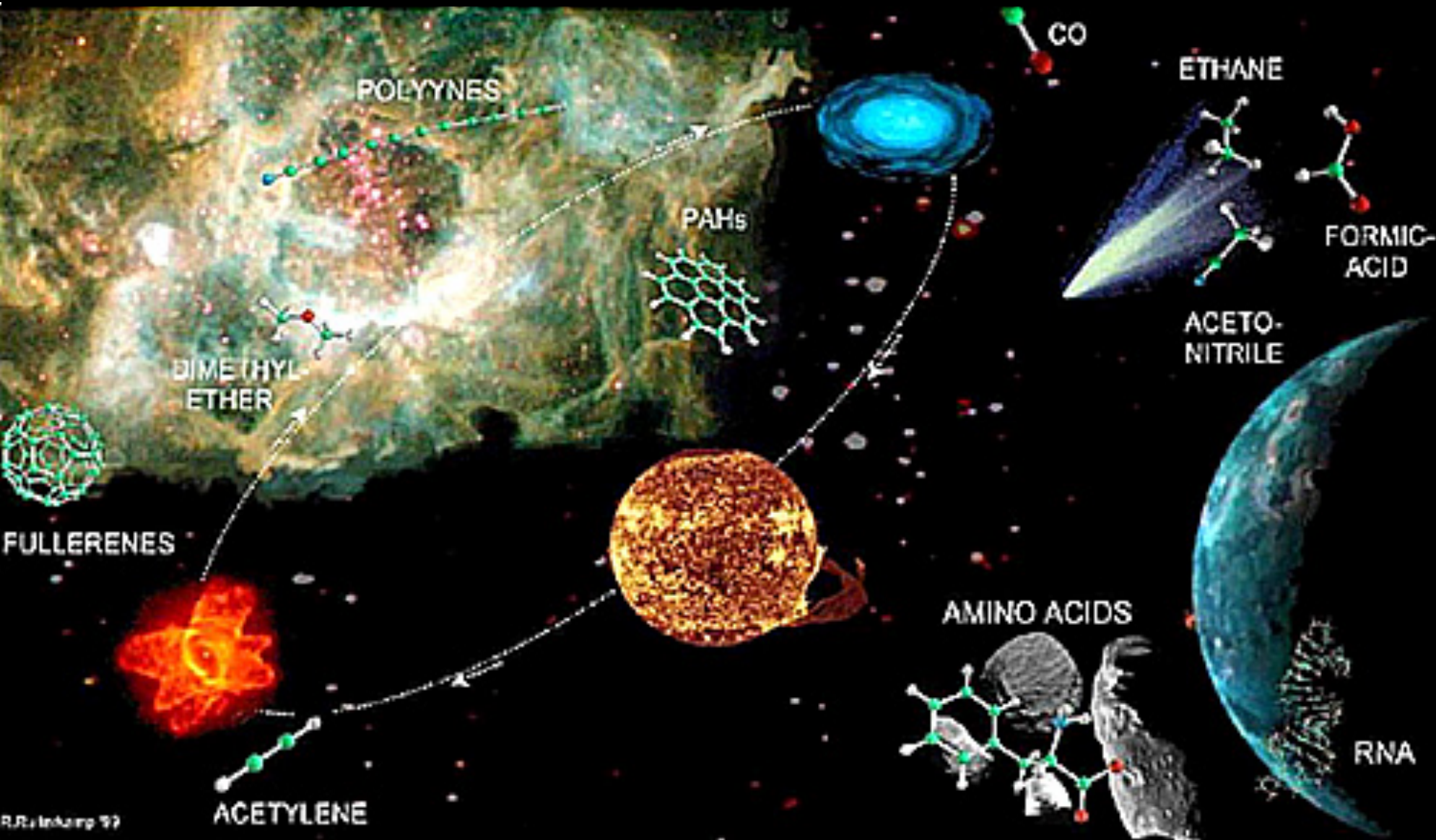


# Organic Polymers (4.5B → 4B years)

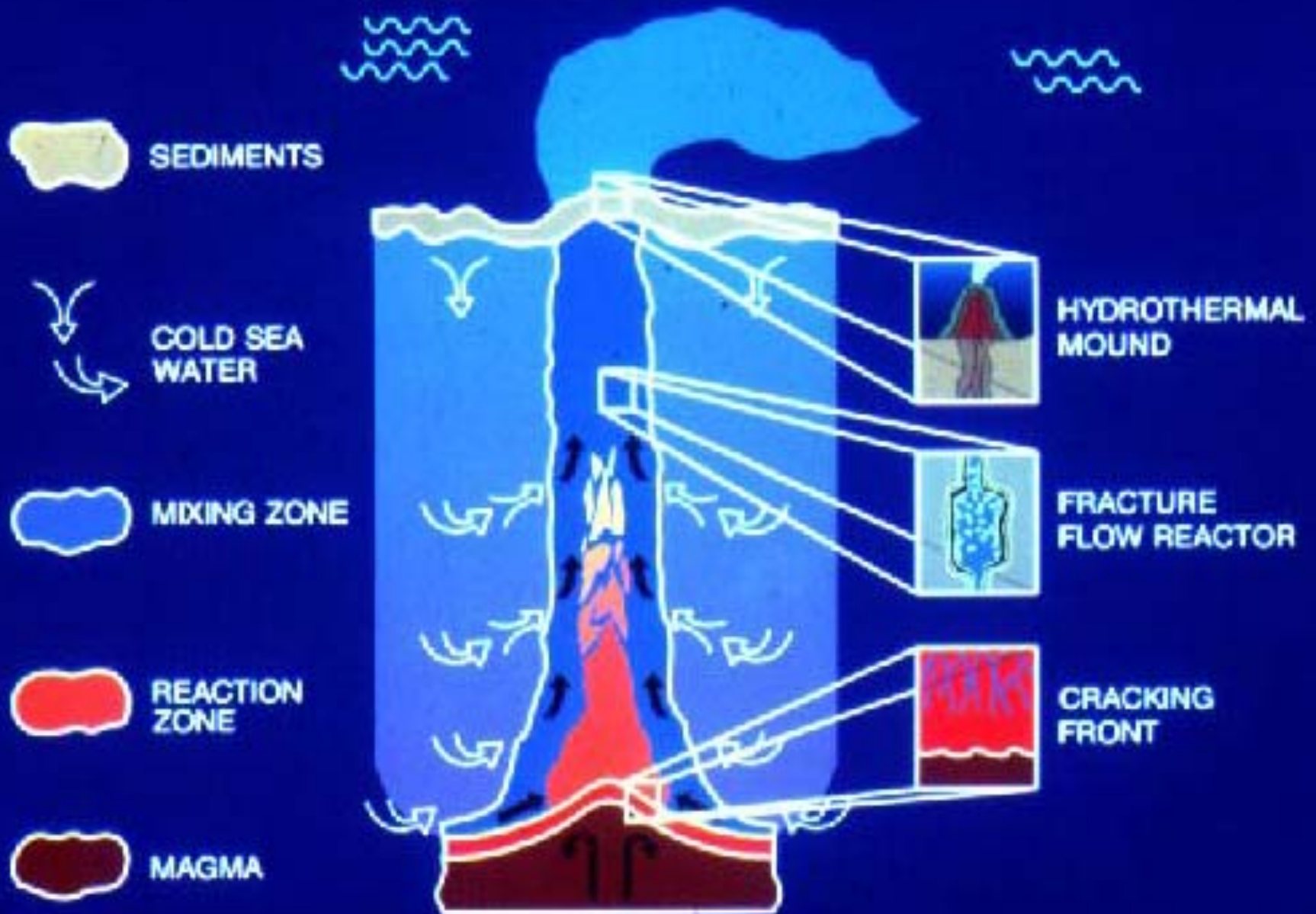


**inorganic molecules from Earth**

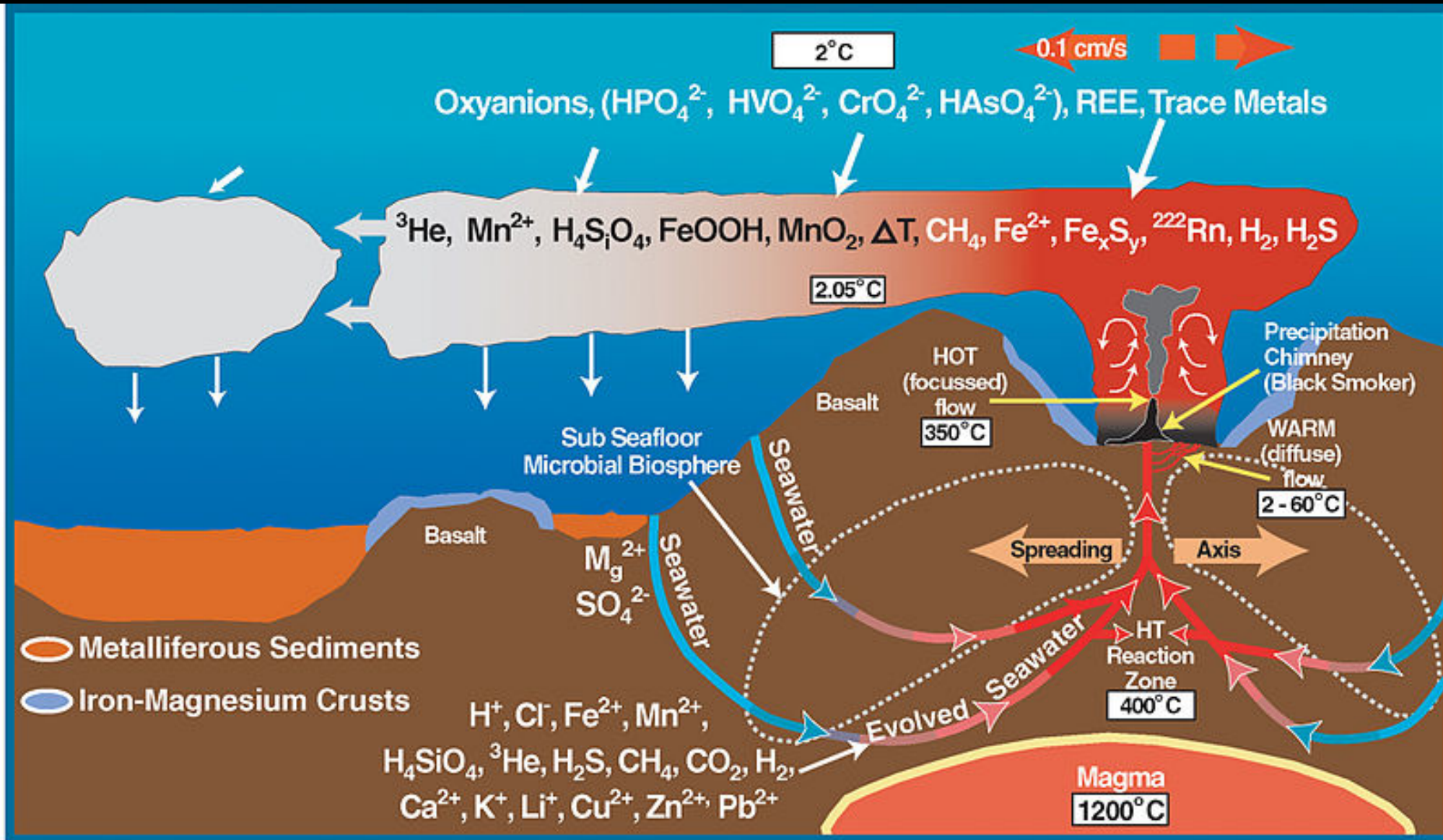
# Organic molecules from outer space



# Volcano under deep ocean



# Volcano under deep ocean

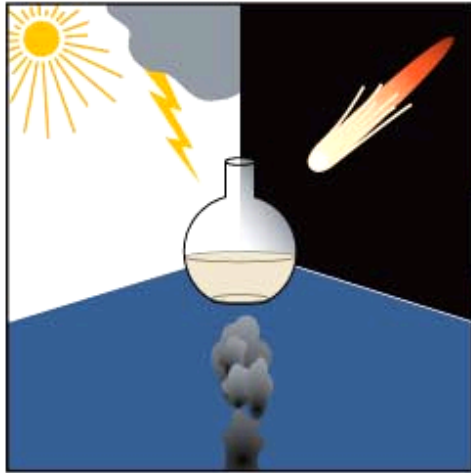


# Deviation from Thermal Equilibrium

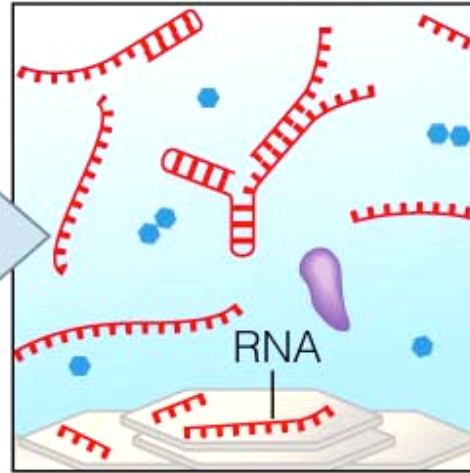
- **Particles** — **Quark, Leptons...**
  - **Spontaneous Symmetry Breaking (Higgs Mechanism)**
- **Atoms** — **Carbon, Oxygen, Iron ...**
  - **Explosion of Supernova**
- **Organic Molecules** — **Ammonia, Amino Acid ...**
  - **Evolution of molecules in outer space by UV**
- **Origin of Life** — **RNA, Protein, DNA**
  - **Volcano under deep ocean**

# RNA World (4B → 3.5B years ago)

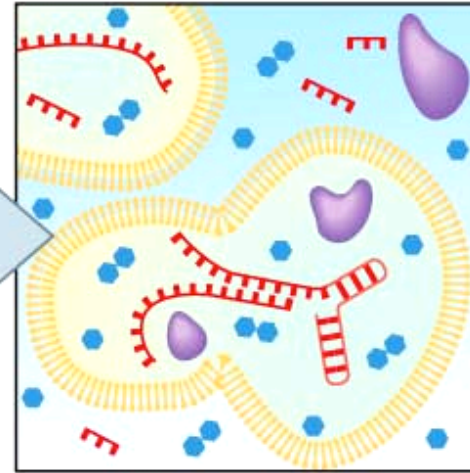
1. Organic precursor molecules appear.



2. RNA molecules become self-replicating.

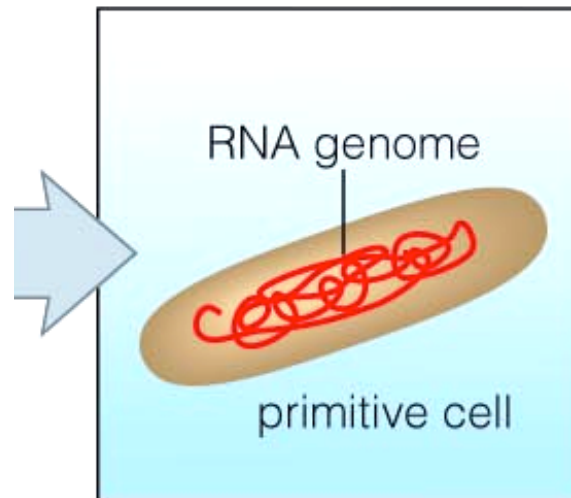


3. Membrane-enclosed pre-cells arise.

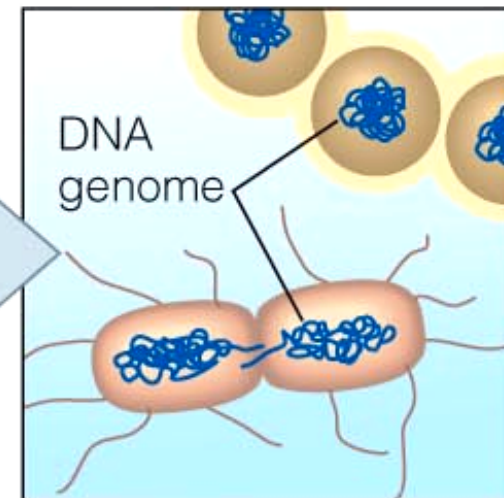


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4. True cells with RNA genome appear.



5. Modern cells with DNA genome evolve.



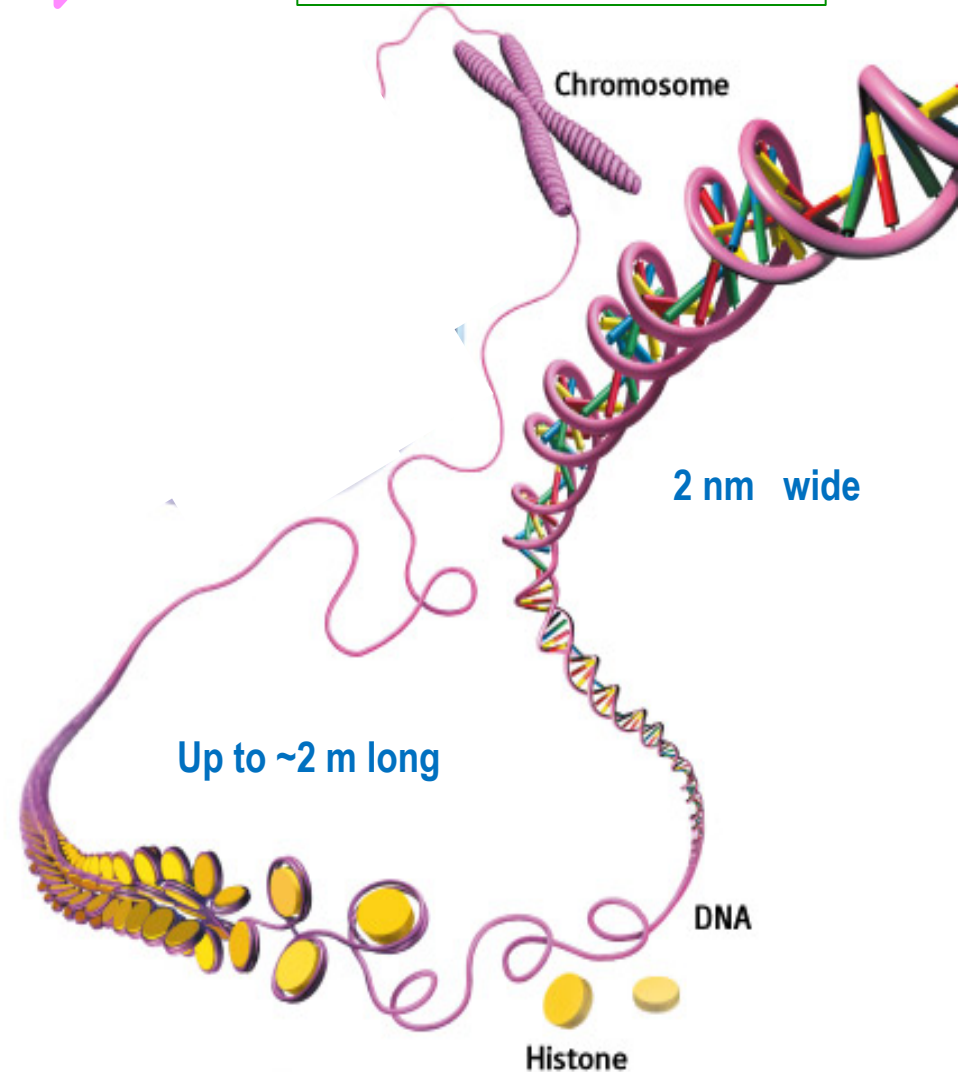
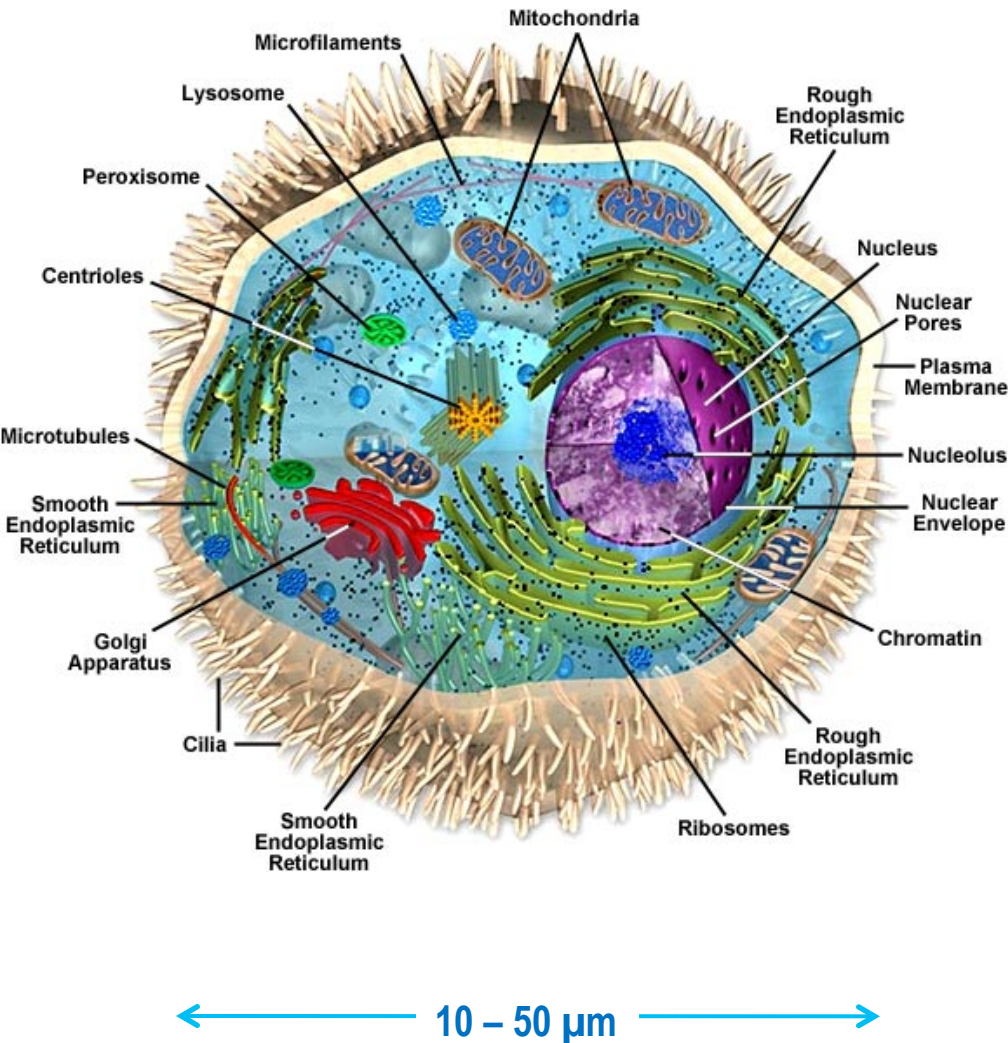
# Eukaryote (~2B years ago)

## Symmetry breaking

Cell made by proteins



Gene made by DNA



# Photosynthesis and Breathing

## Spontaneous Symmetry Breaking

**Plants**  
Chloroplast



**Animals**  
Mitochondria

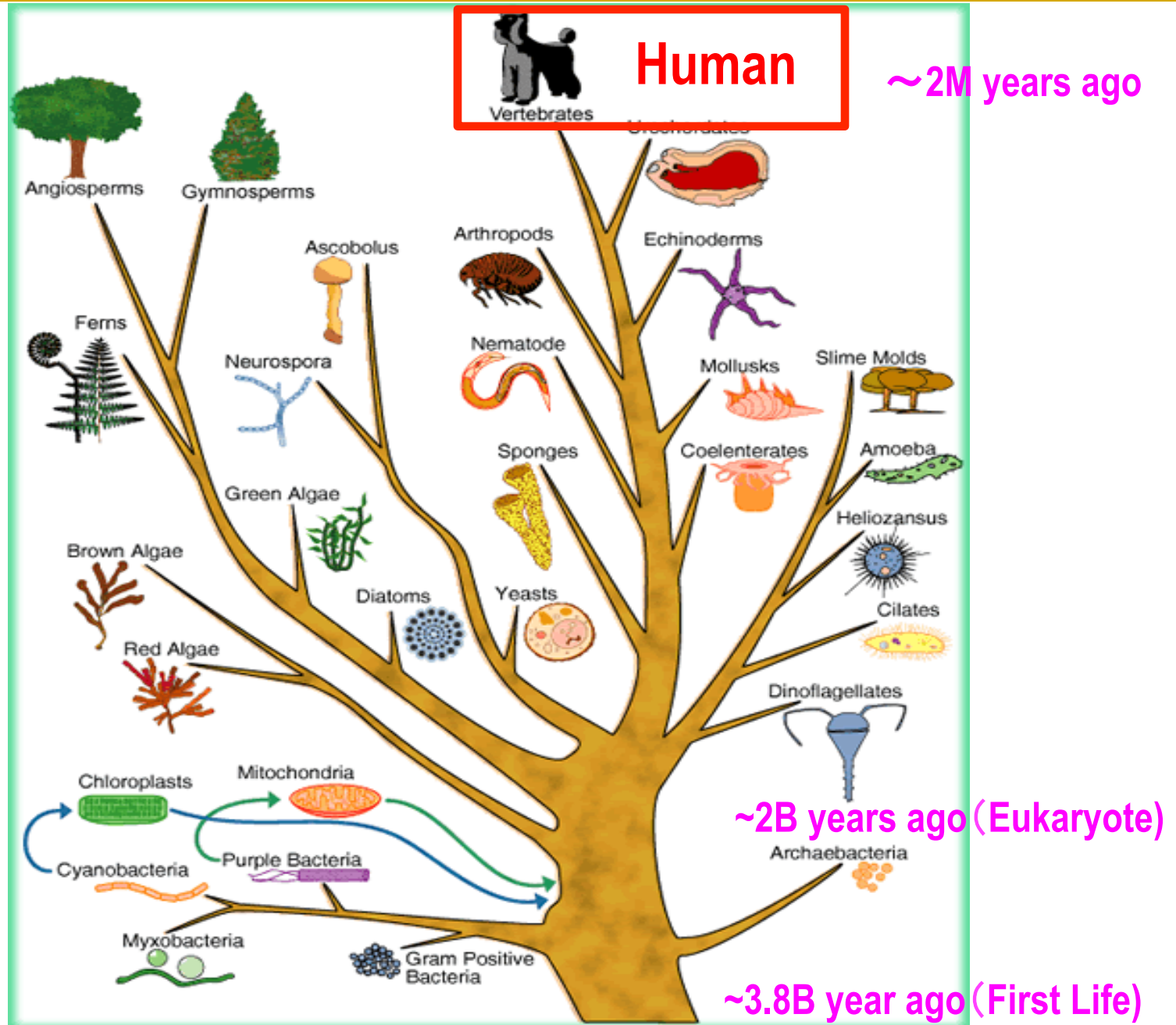
**Photosynthesis**



**Breathing**



# Tree diagrams of evolution



# What is Life?

## ➤ Emergent Property

- Strong-interacting, complex system
- $\sim 10^4$  of different proteins in one cell
- $\sim 10^{14}$  cells in one life

## ➤ Continuous, countless “symmetry breaking” towards coherent states

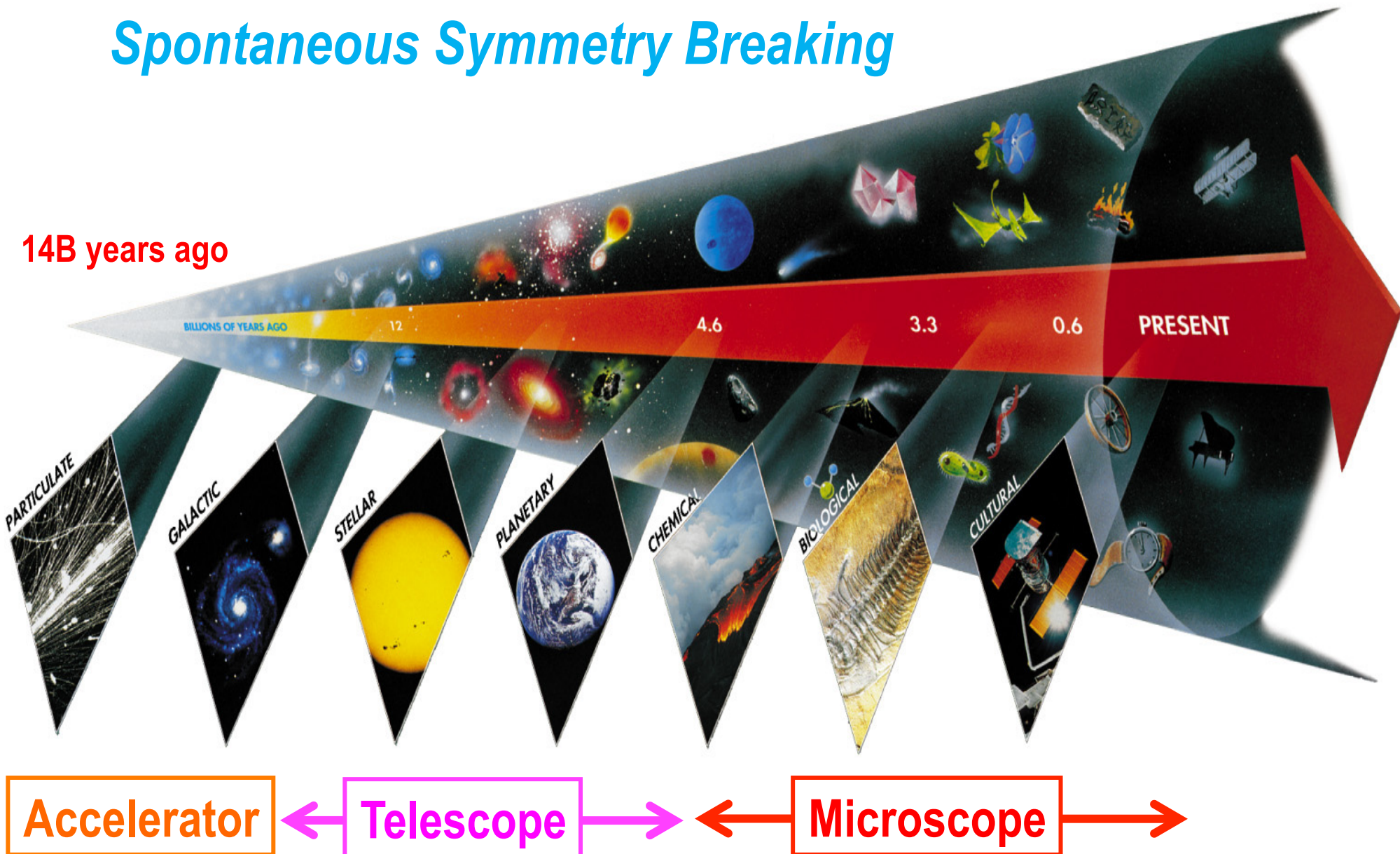
- Origin of life
- Evolution of life
- Growth from a single cell to a multi-cell body
- Learning and memory

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# High-speed Bio-imaging

# Seven steps of cosmic evolution

## Spontaneous Symmetry Breaking



# How to observe the Life and Consciousness ?

- We must look for “**Live Life**”
- Exactly the same way as we look for the “**Origin of Universe**”

**Telescope** vs. **Microscope**

- Take advantages of the state of art “**Photon Detectors**” in particle physics.

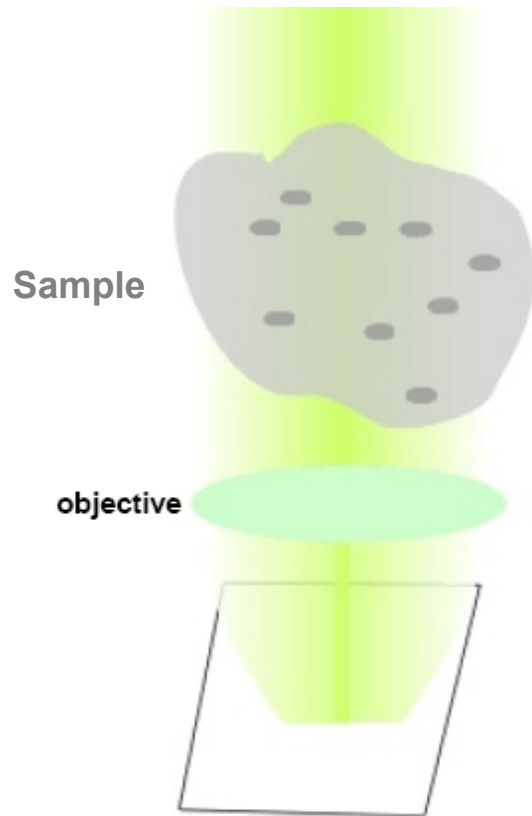


# How to speed up microscopes

- 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

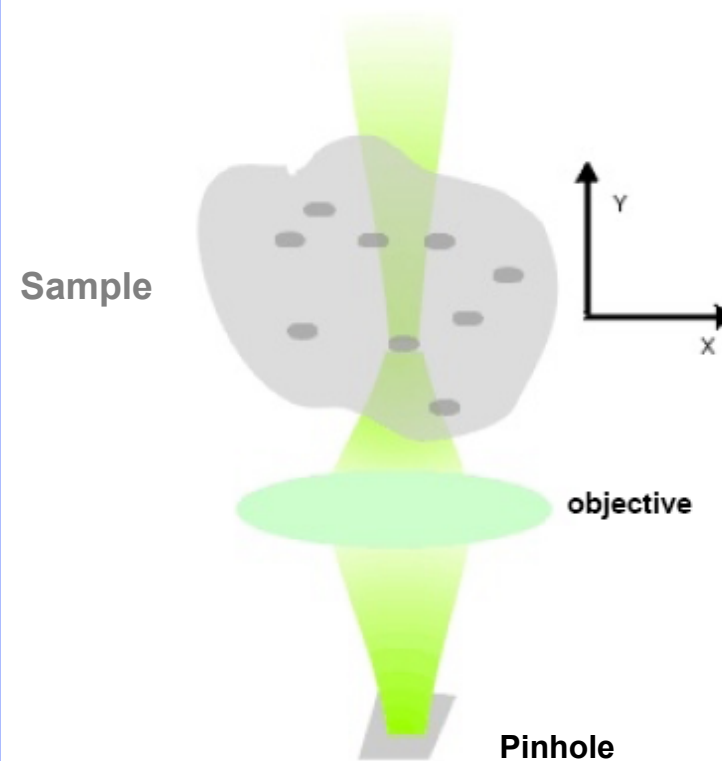


CCD + FADC (10 – 50 MHz)



CMOS [ FADC (50 MHz) \* 100 ]

## Confocal



PMT + FADC (10 – 50 MHz)



[ HAPD + FADC (1 GHz) ] \* 64

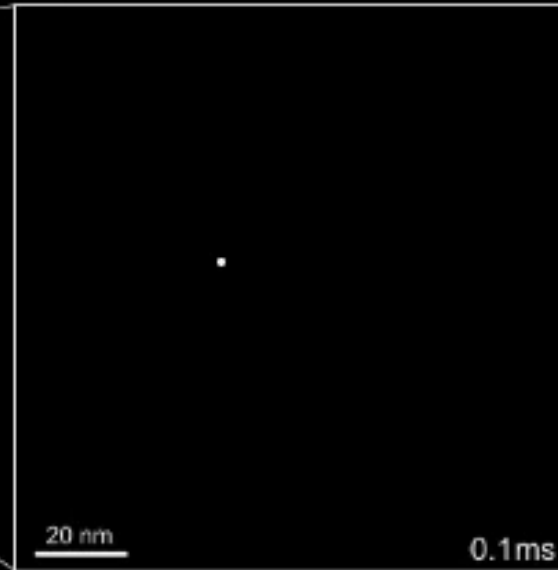
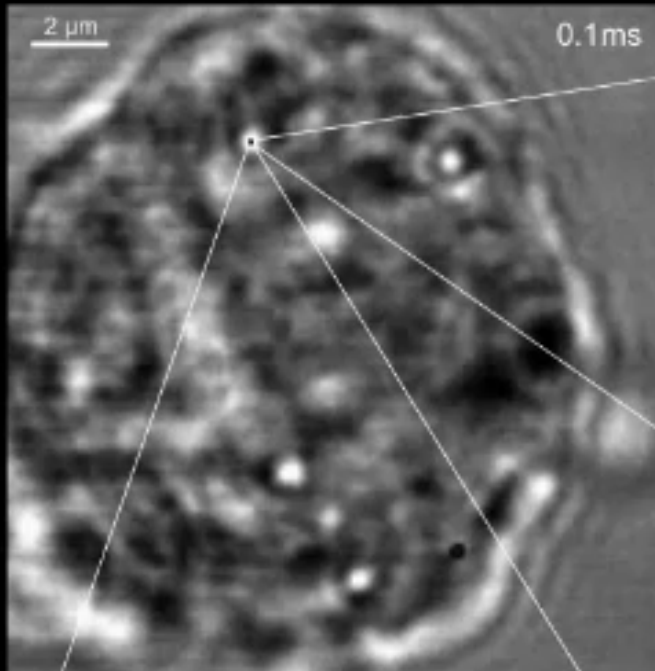
# Photron SA-5 CMOS Camera



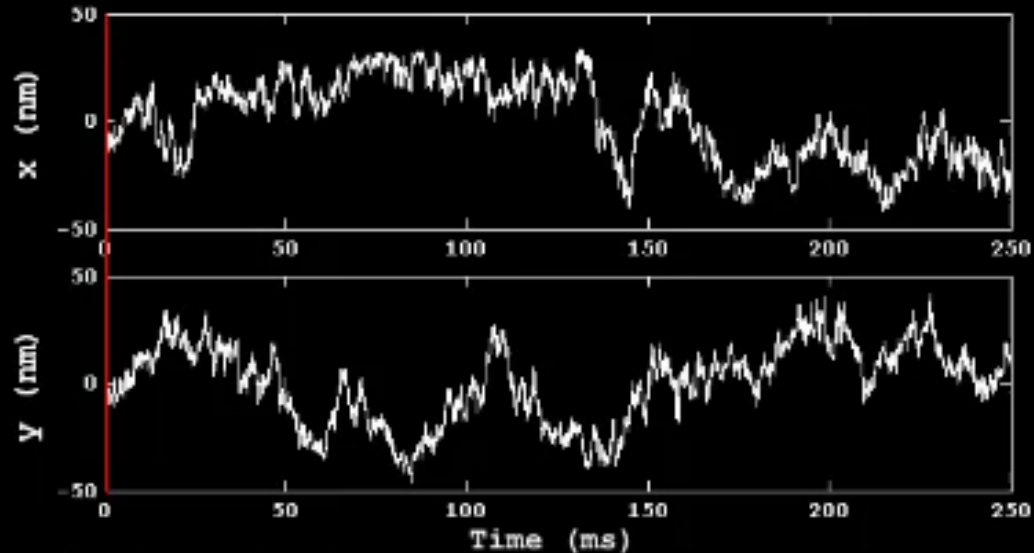
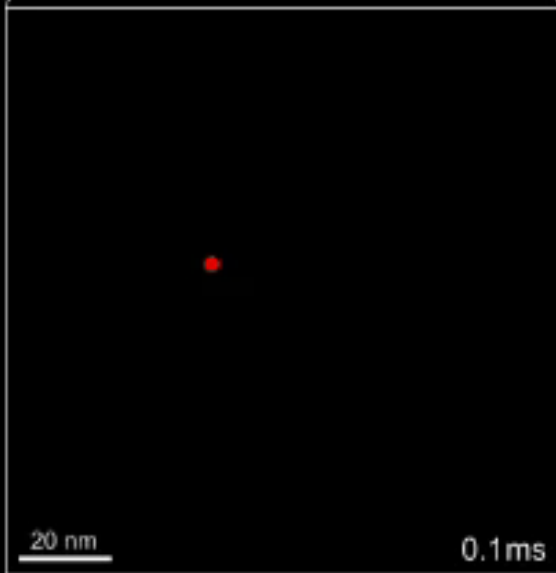
FRAME RATE (fps)	MAXIMUM RESOLUTION	
	Horizontal	Vertical
1,000	1,024	1,024
2,000	1,024	1,024
4,000	1,024	1,024
5,000	1,024	1,024
7,000	1,024	1,024
7,500	1,024	1,000
9,300	1,024	800
10,000	1,024	744
15,000	960	528
20,000	832	448
30,000	768	320
50,000	512	272
75,000	320	264
100,000	320	192
150,000	256	144
300,000	256	64
420,000	128	64
525,000	128	48
775,000	128	24
930,000	128	16
1,000,000	64	16

# Gold nano particle (40nm) attached to Transferrin Receptor (TfR) on Cancer Cell

Prof. Manuel Penichet (Oncology)



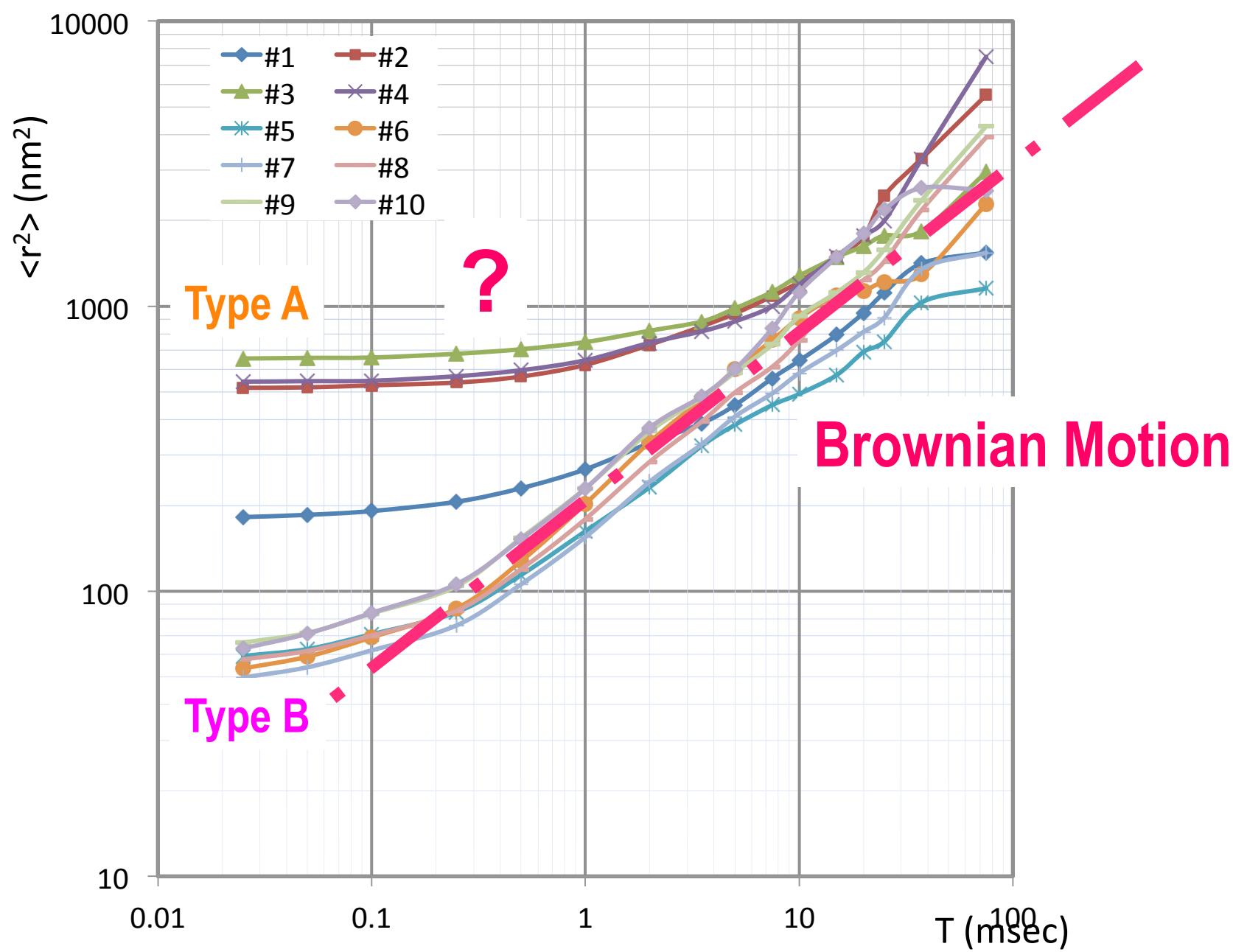
(10,000 frame/sec)



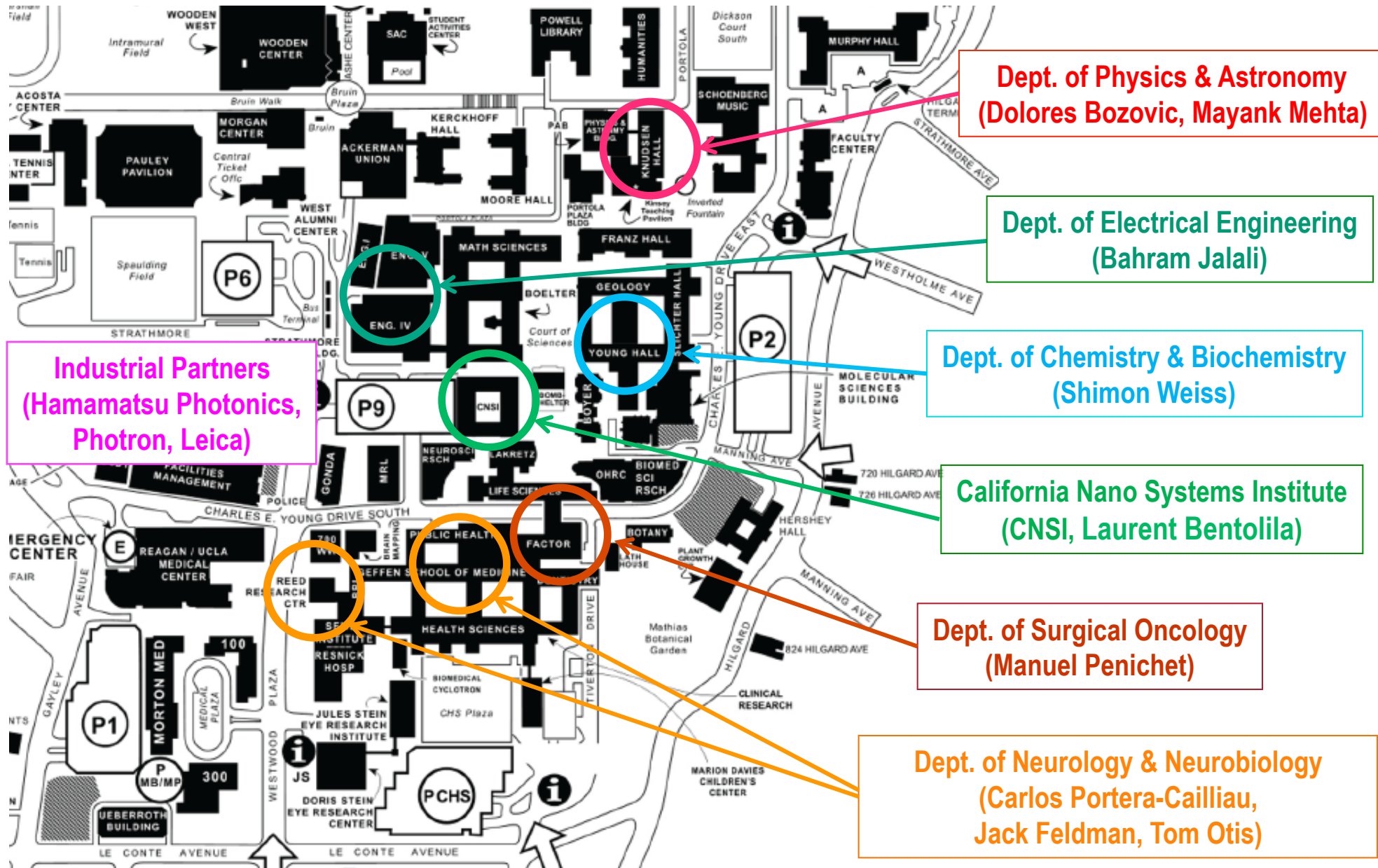
UCLA Fast Bio-Imaging Group

L. Fredrickson, J. Rodriguez, A. Cheng, K. Jewhurst, J. Miao, K. Arisaka

# Mean Squire Displacement $\langle r^2 \rangle$ of TfR on a Human Multiple Myeloma Cell vs. Time



# Arisaka's Campus-wide Collaborations on High-Speed Bio-imaging



# User-shared Core Facility of High-speed Microscopes at CNSI

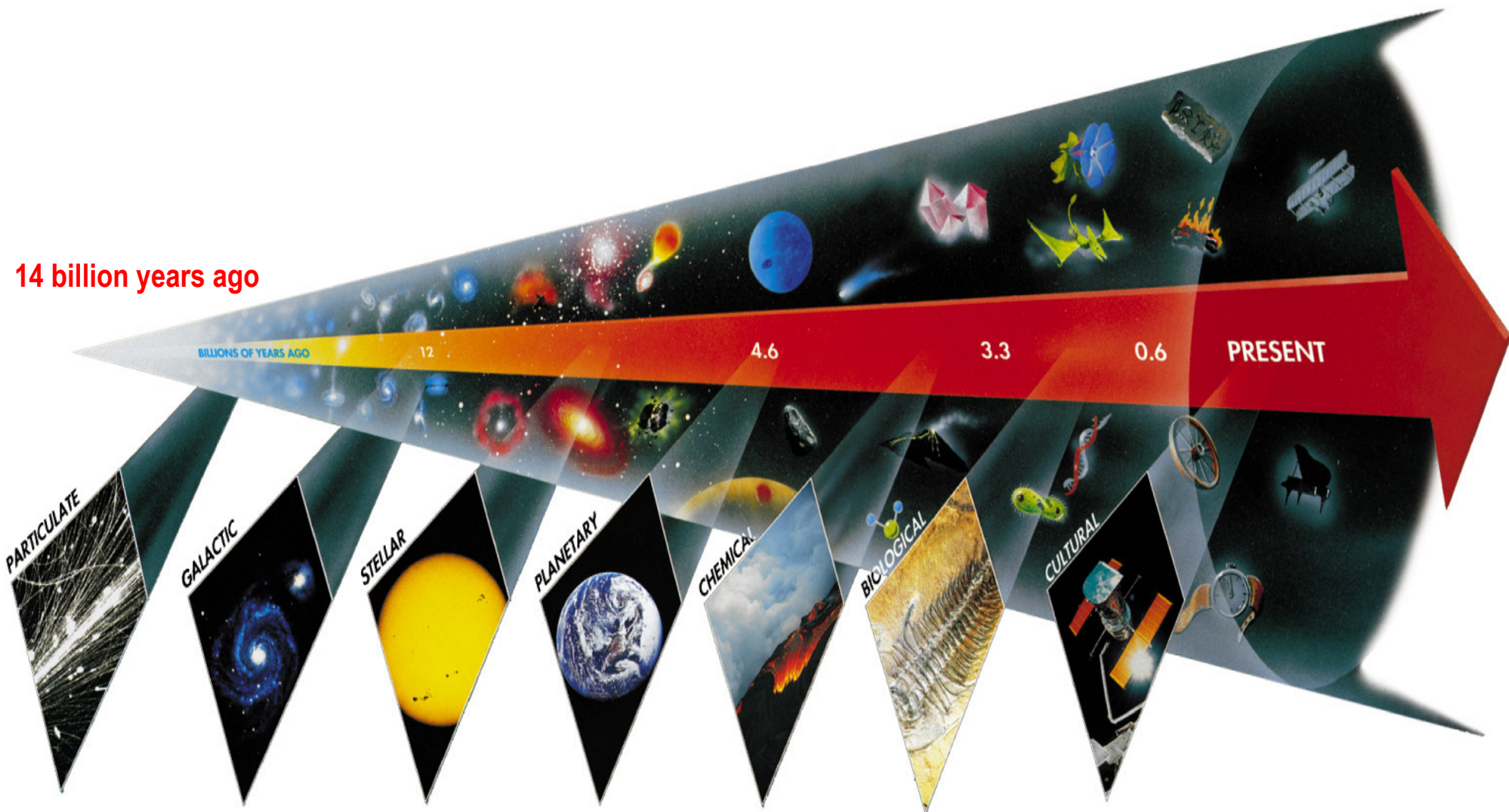


**4D Nano Biophysics**

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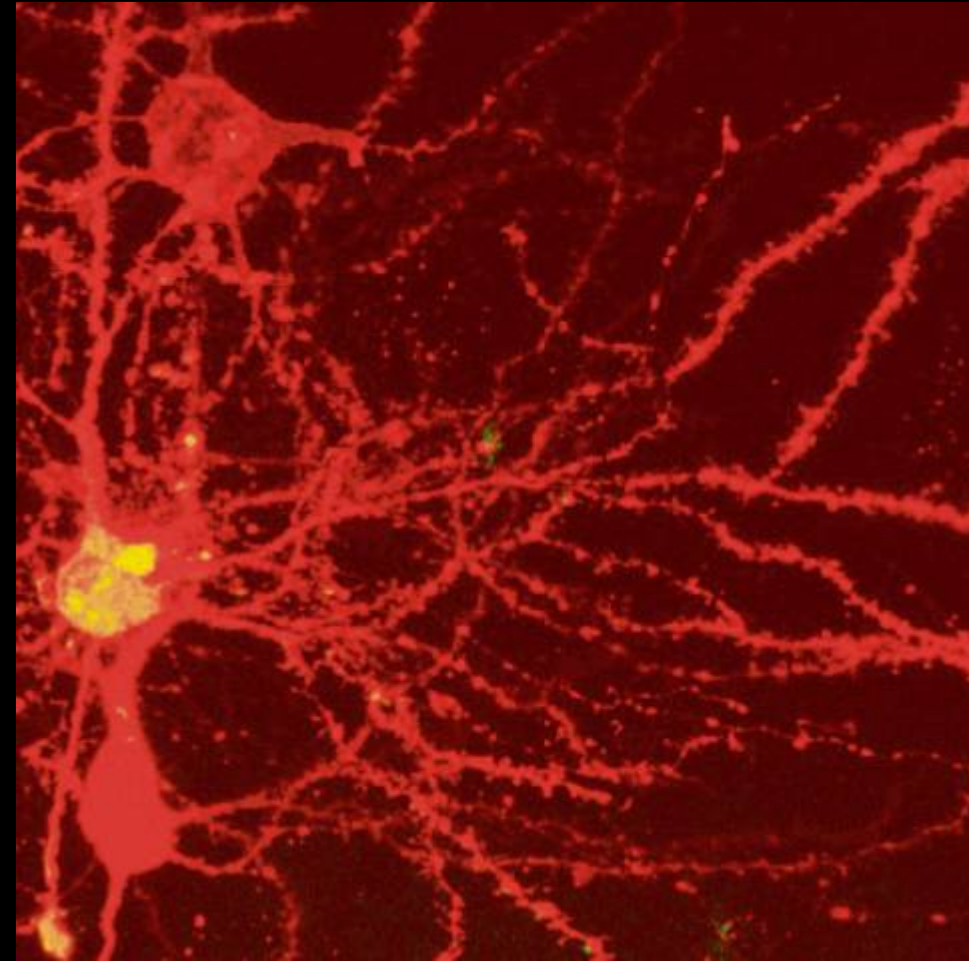
# Origin of Consciousness

# Seven Phases of Cosmic Evolution



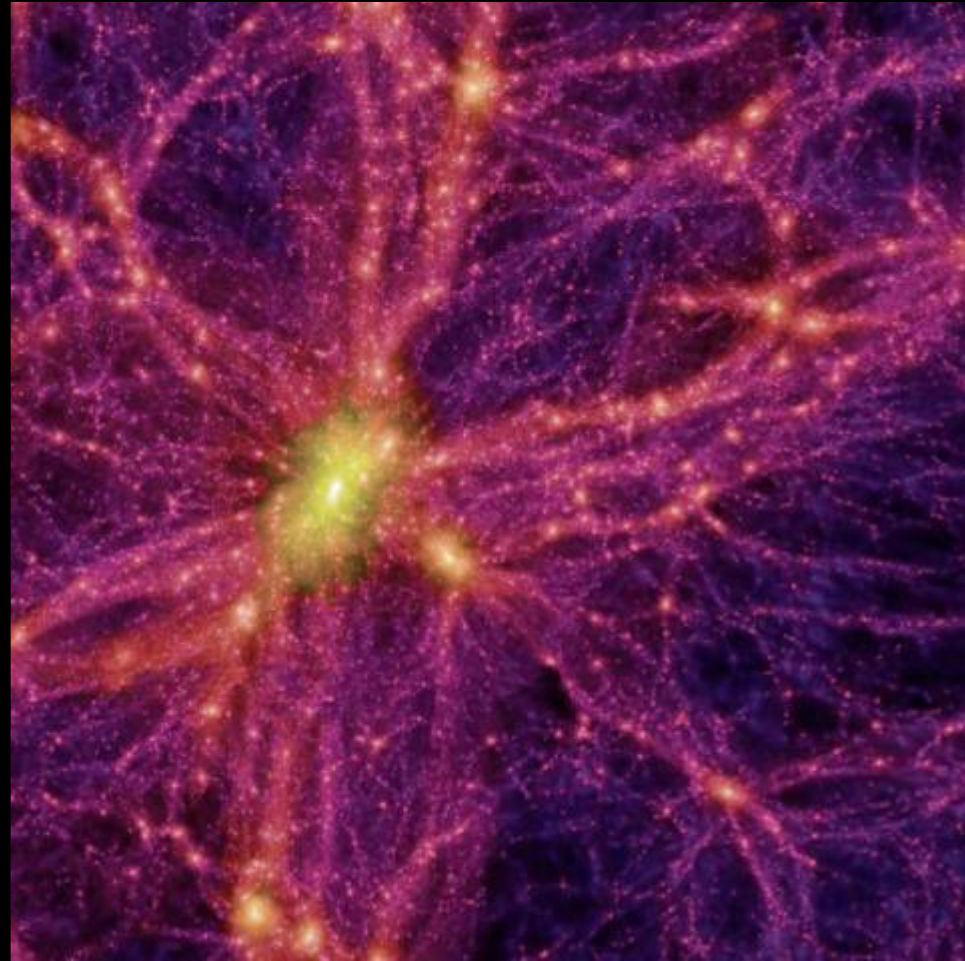
Origin of  
Consciousness

# Brain



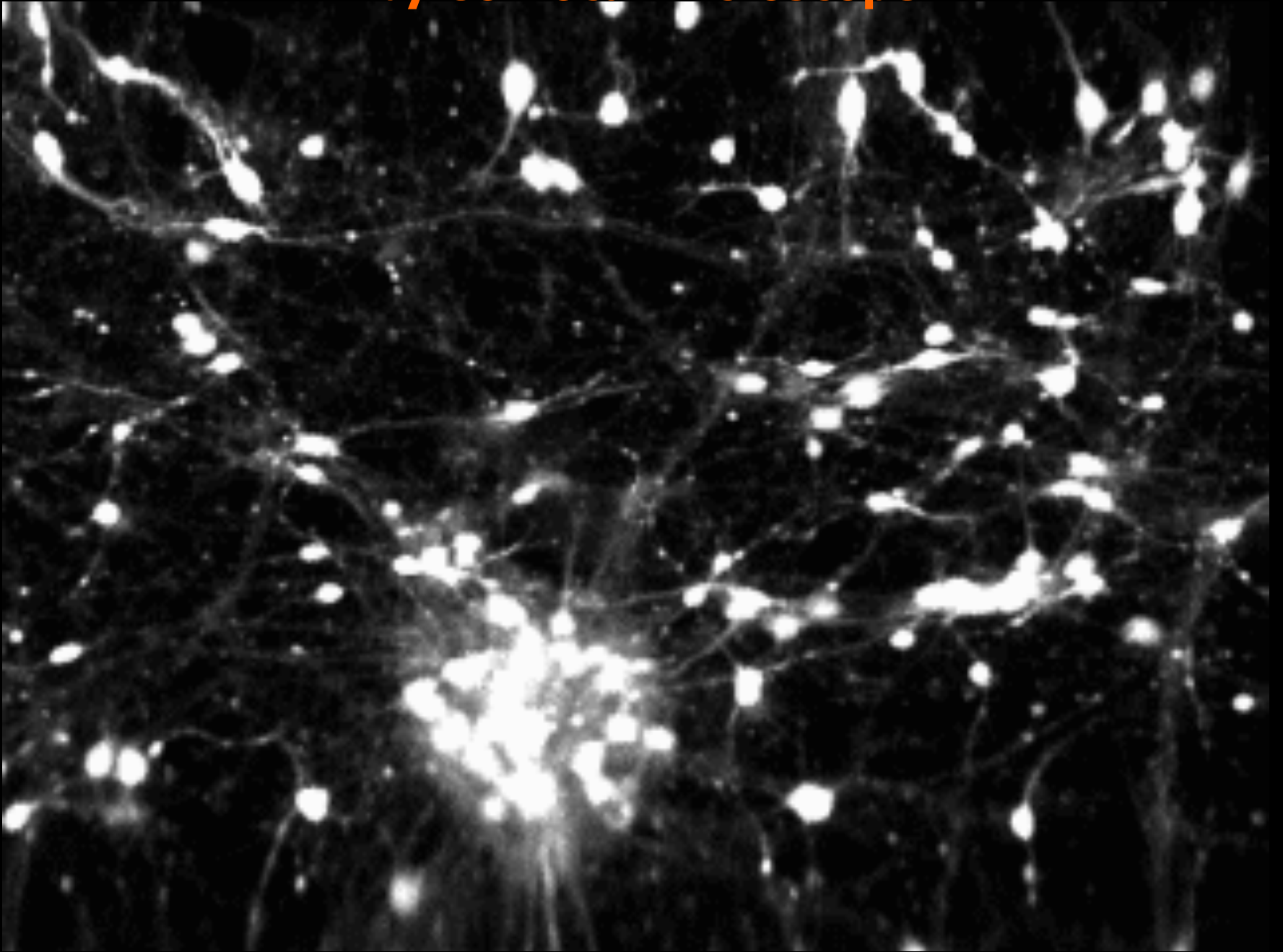
**100 Billions Neurons**

# Universe



**100 Billions Galaxies**

# Ca<sup>2+</sup> Signal in cultivated Rat's Brain by Confocal Microscope

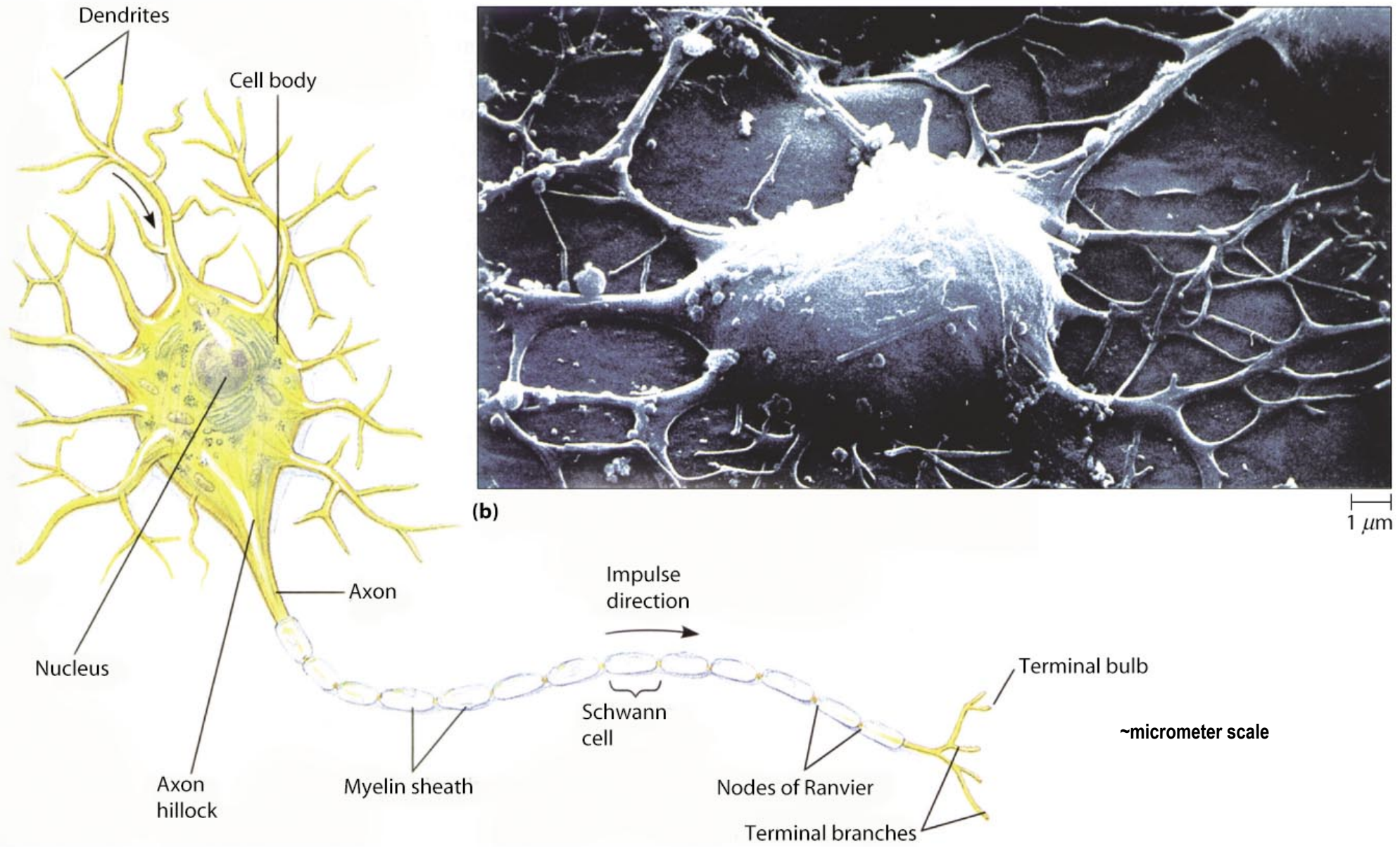


*Andrew Charles (Neurobiology)*

**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.

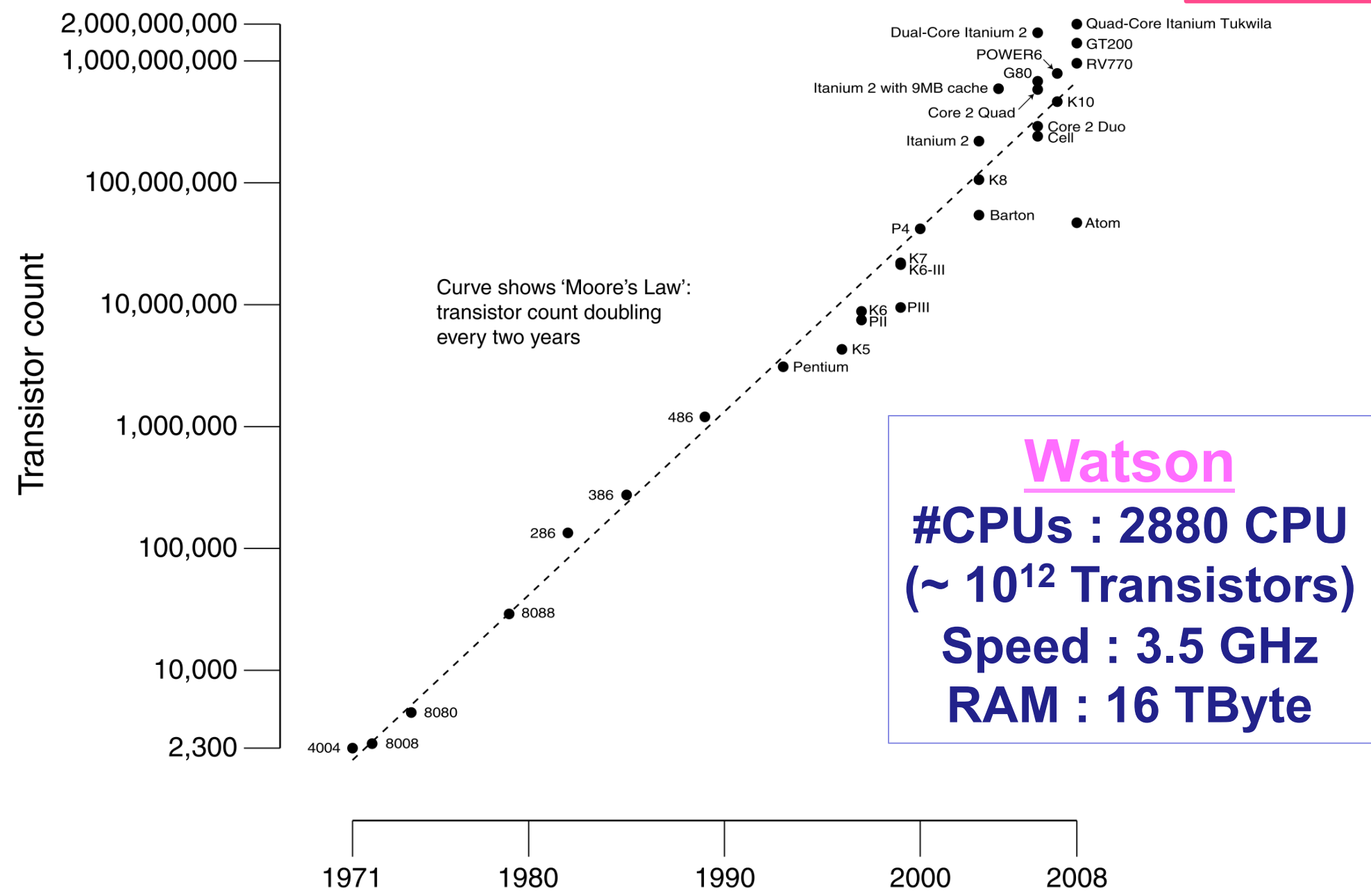
Jennings holds the record for number of consecutive Jeopardy matches won, with 74. Rutter has won more money than anyone else on Jeopardy.

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).

# “Moore’s Law” Transistors in Computer

Watson



# From No Brain to Big Brain



**Paramecium (Single Cell)**



**Bullfrog ( $\sim 10^7$  neurons)**



**Lymnaea ( $\sim 1,000$  neurons)**



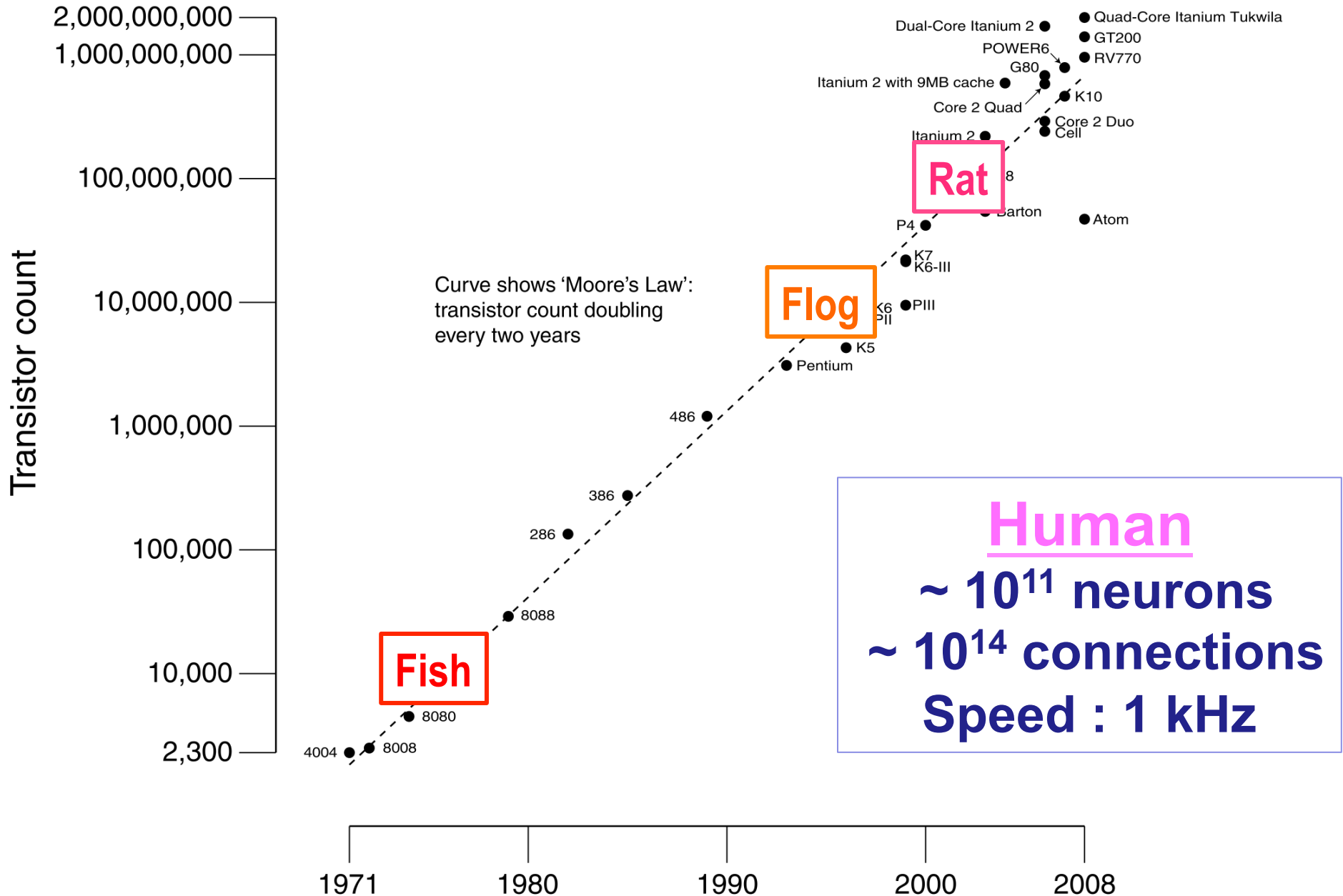
**Zebrafish ( $\sim 10,000$  neurons)**



**Rat ( $\sim 10^8$  neurons)**

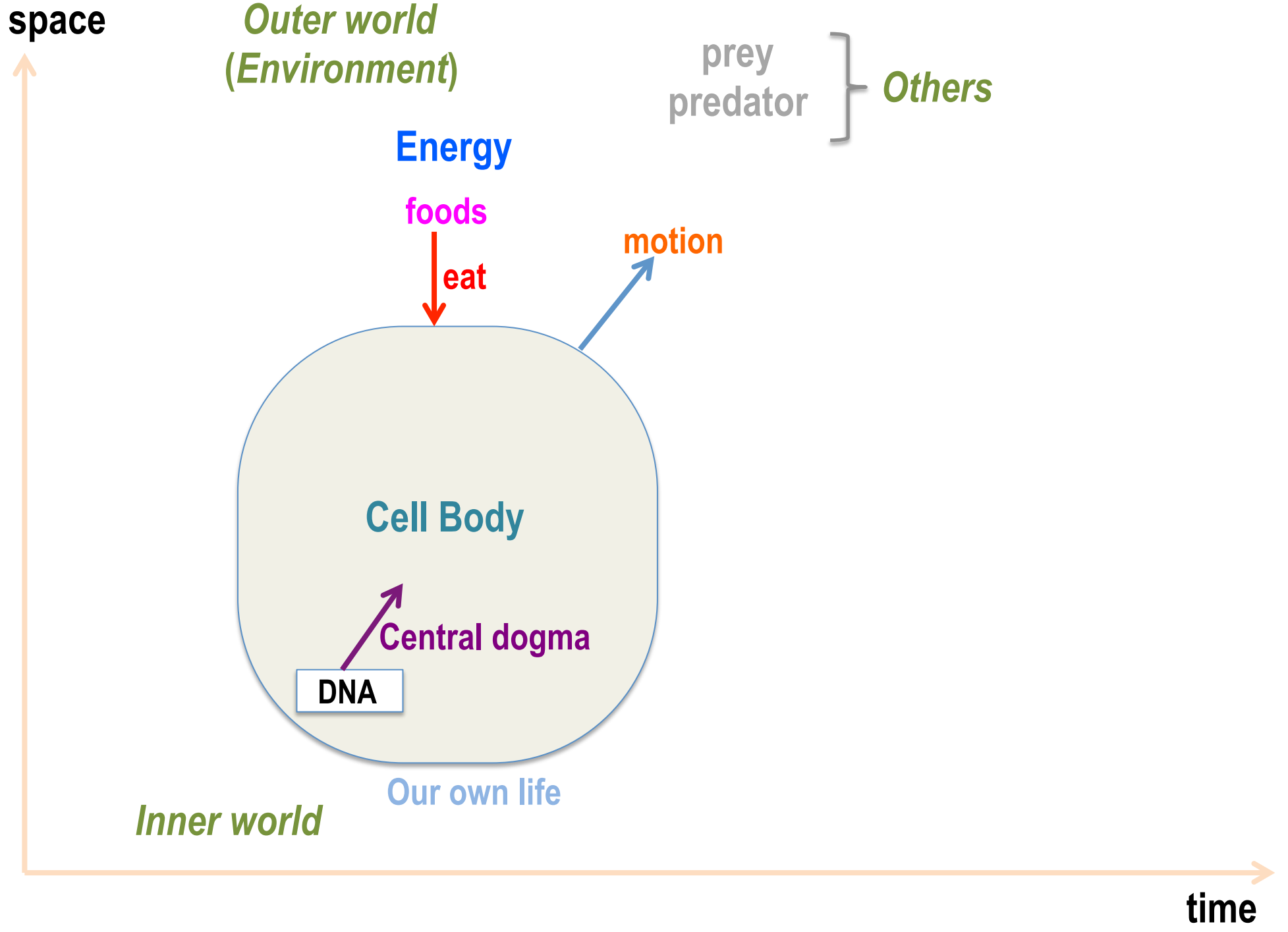
# Neurons in Brain

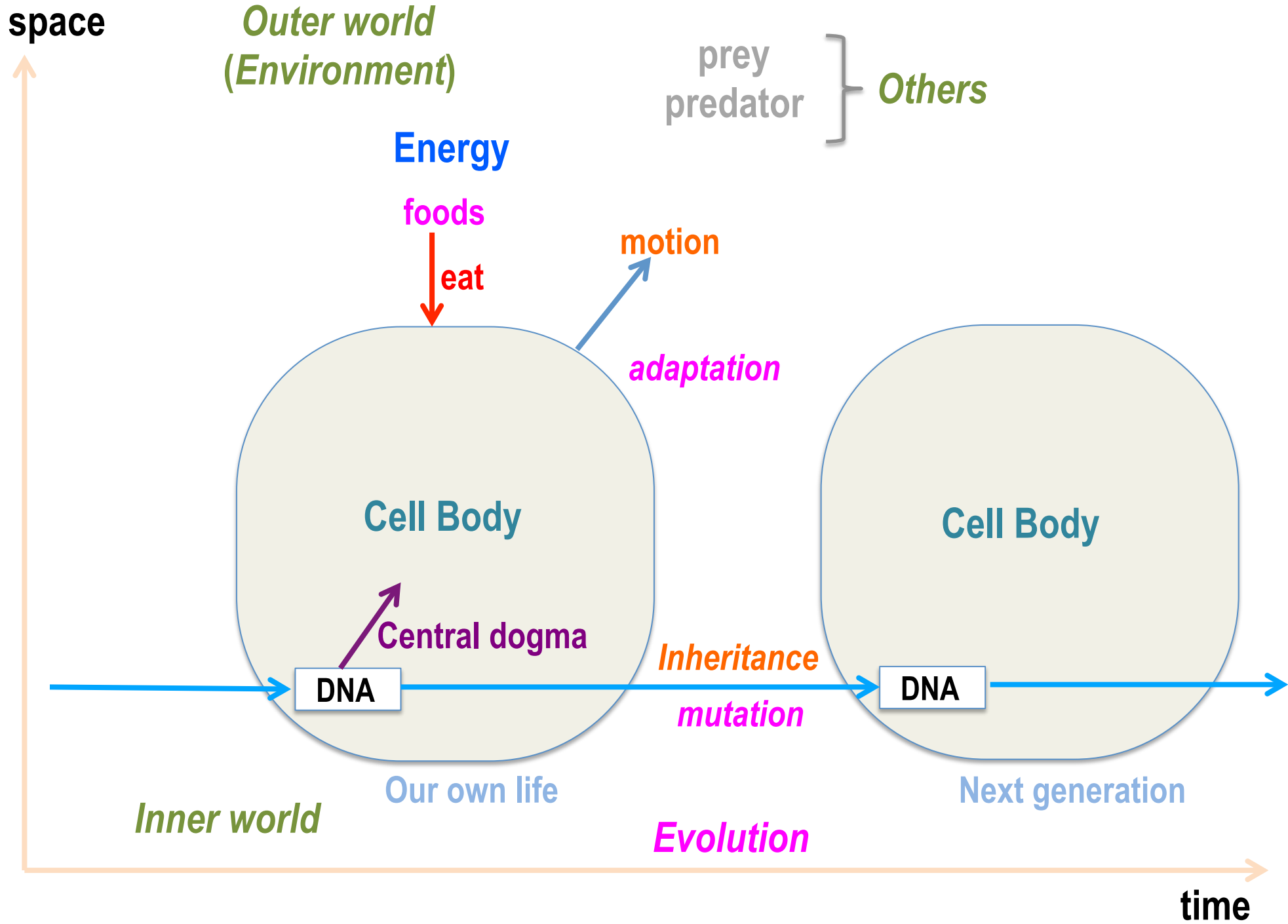
Human

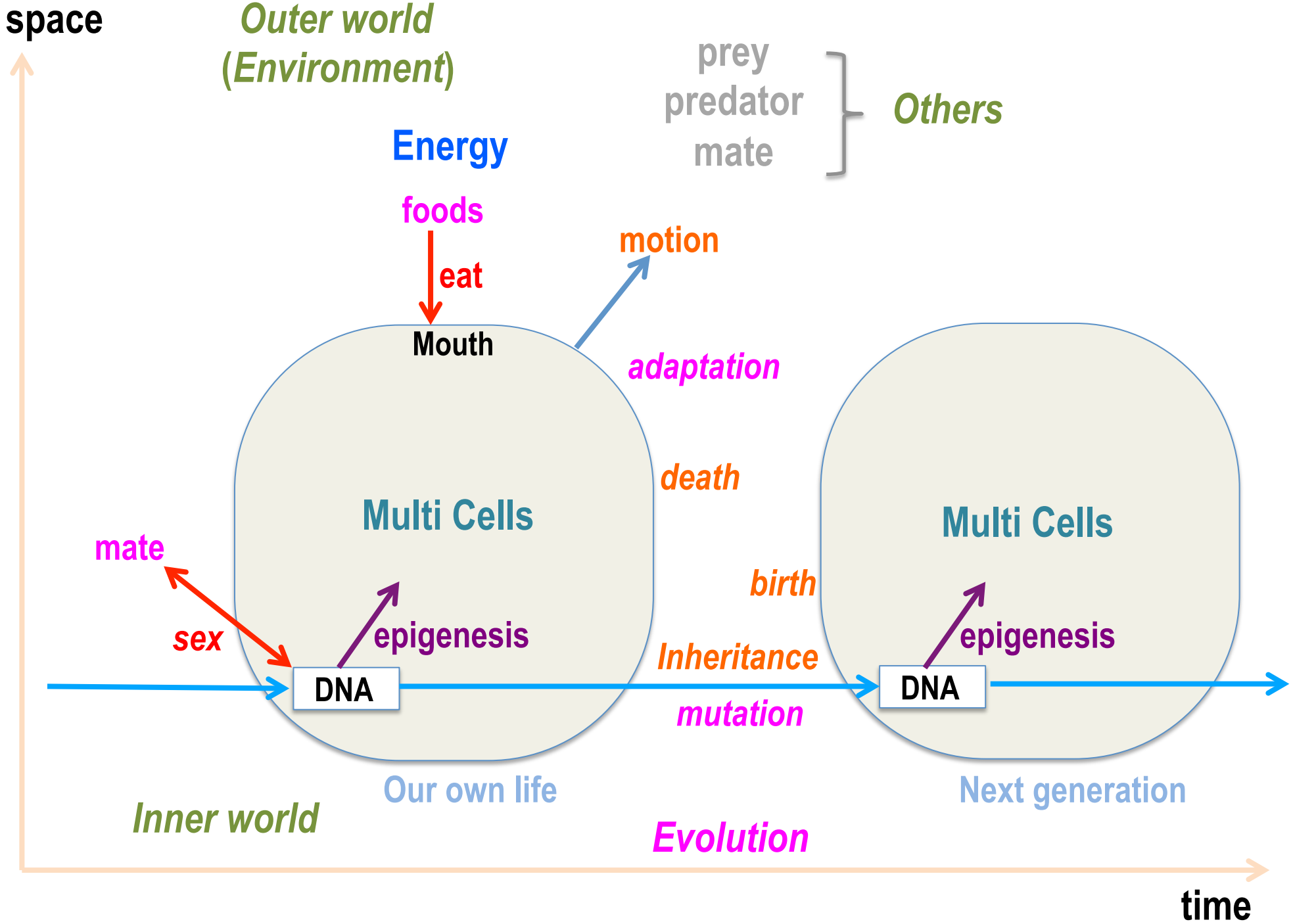


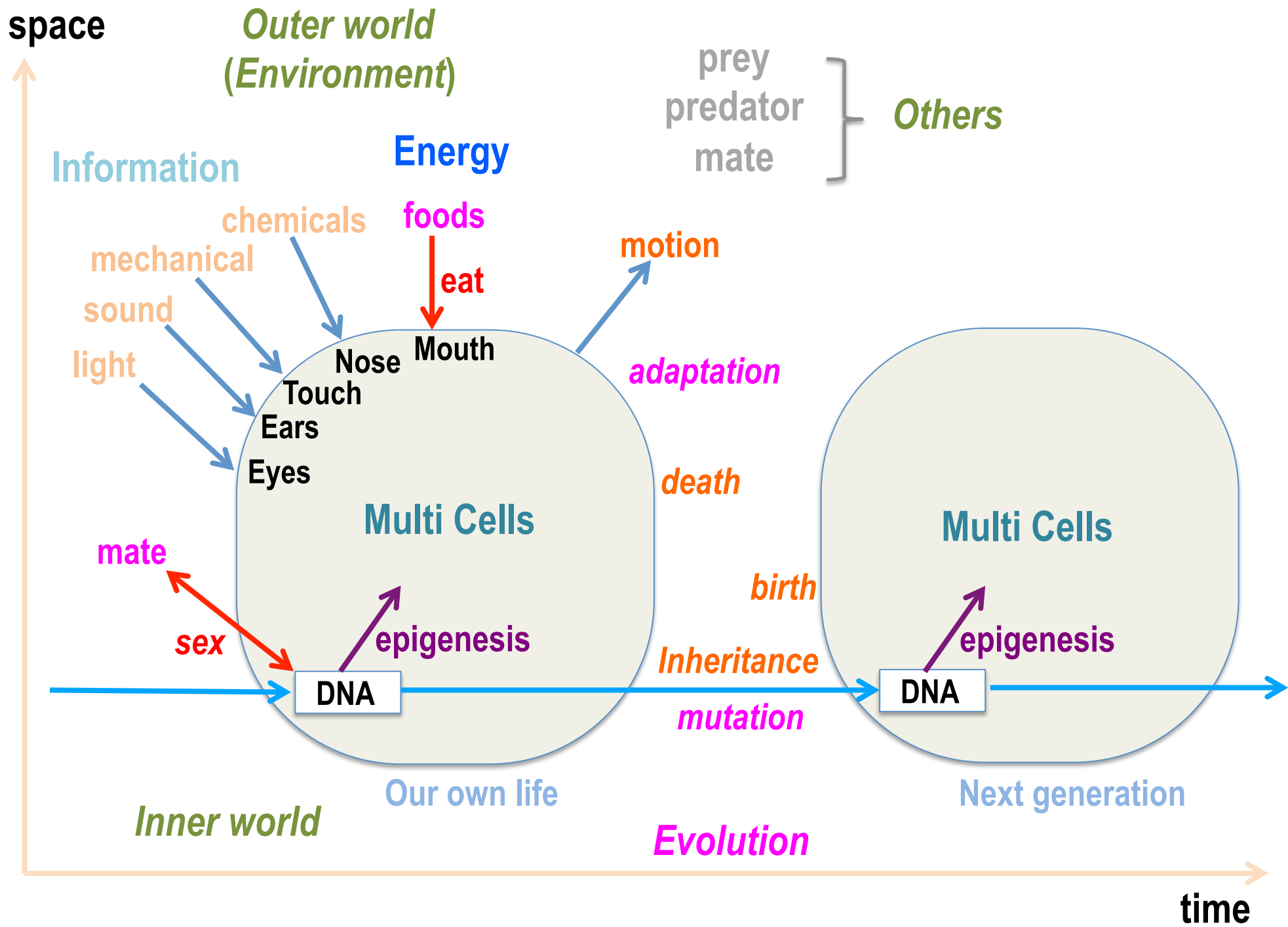
# Computer vs. Brain

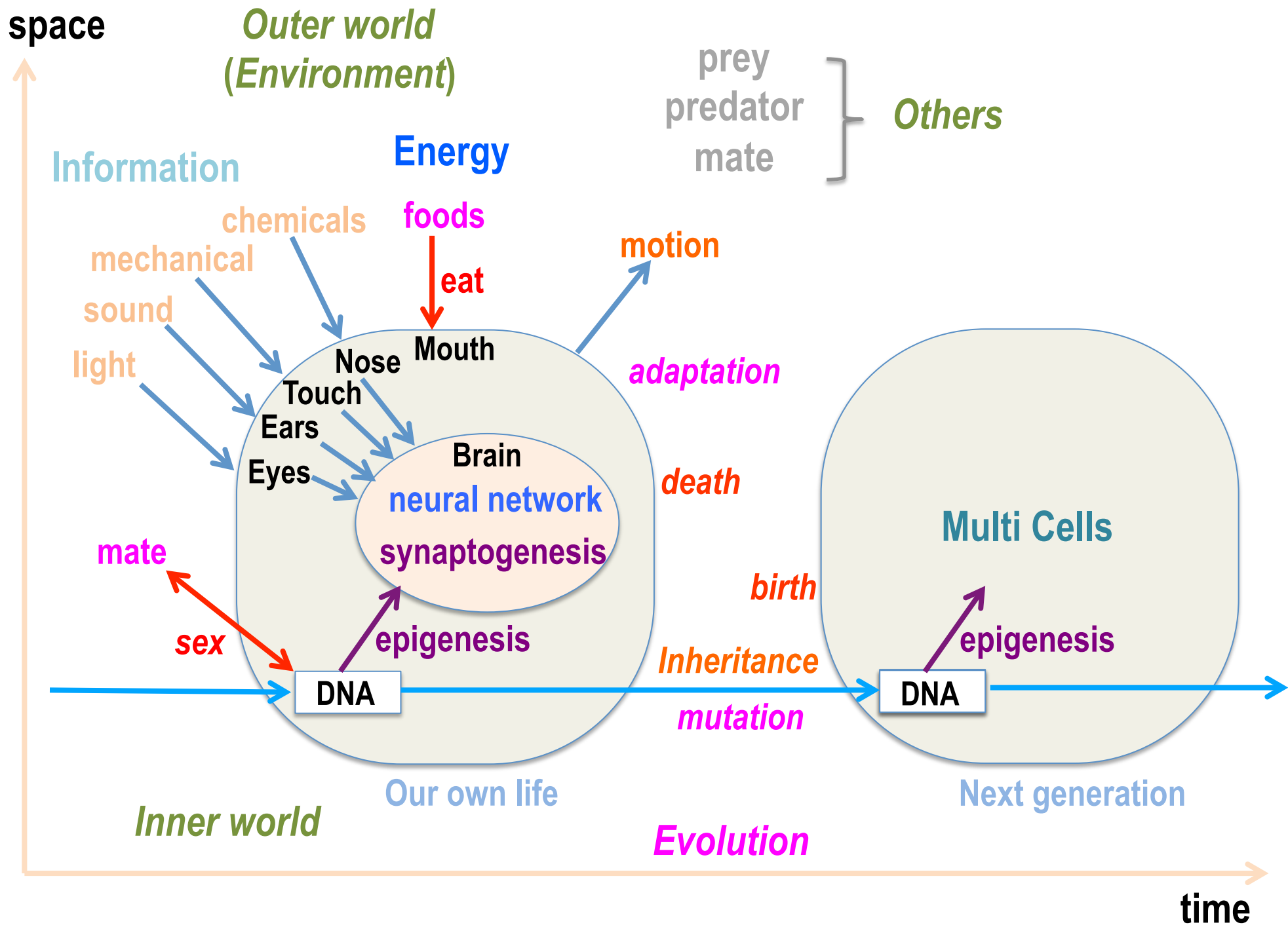
	Computer (Watson)	Human Brain
<b>Key Unit</b>	Transistor	Neuron
<b>No. of units</b>	$\sim 10^9$ ( $\sim 10^{12}$ )	$\sim 10^{11}$
<b>Connection</b>	Copper Wire	Axon + Dendrite
<b>No. of Connections</b>	$\sim 10^{10}$ ( $\sim 10^{13}$ )	$\sim 10^{14}$
<b>Signal Carrier</b>	Electrons	Ions (Na <sup>+</sup>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

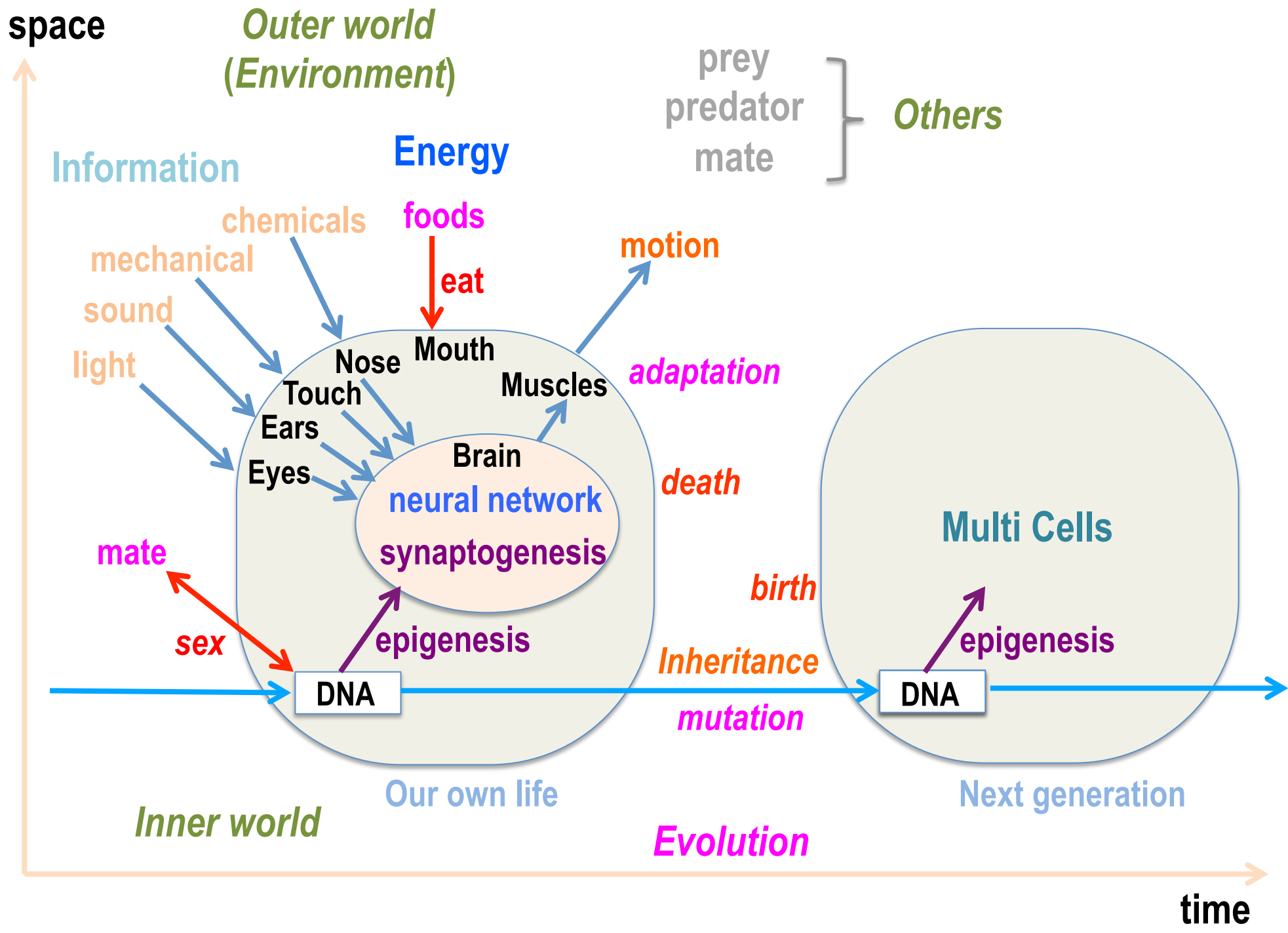






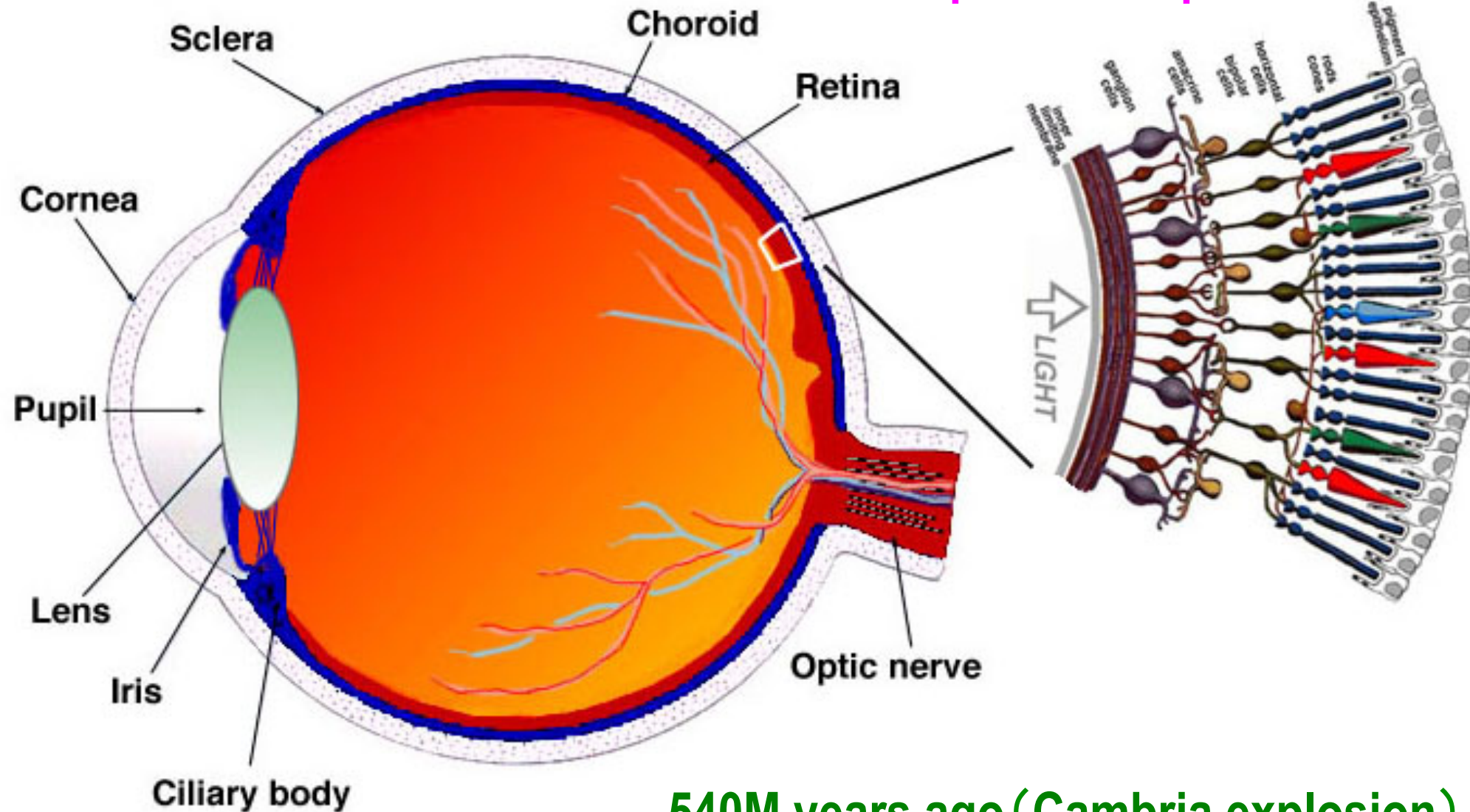






# Human Eyes

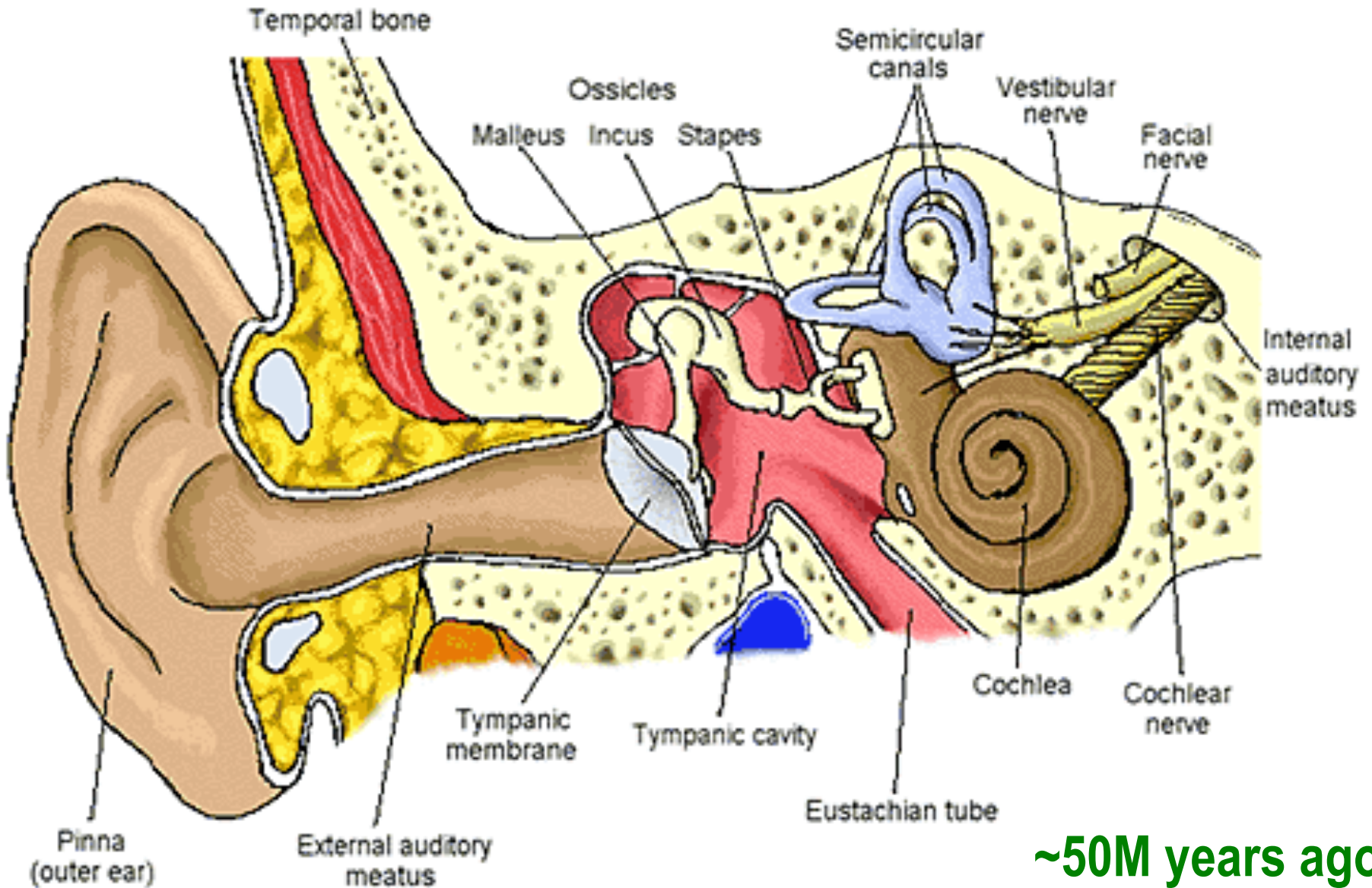
~100M photo receptors



540M years ago (Cambria explosion)

# Human Ears

~10,000 Hair Cells



~50M years ago

# Anatomy of Inner Ear

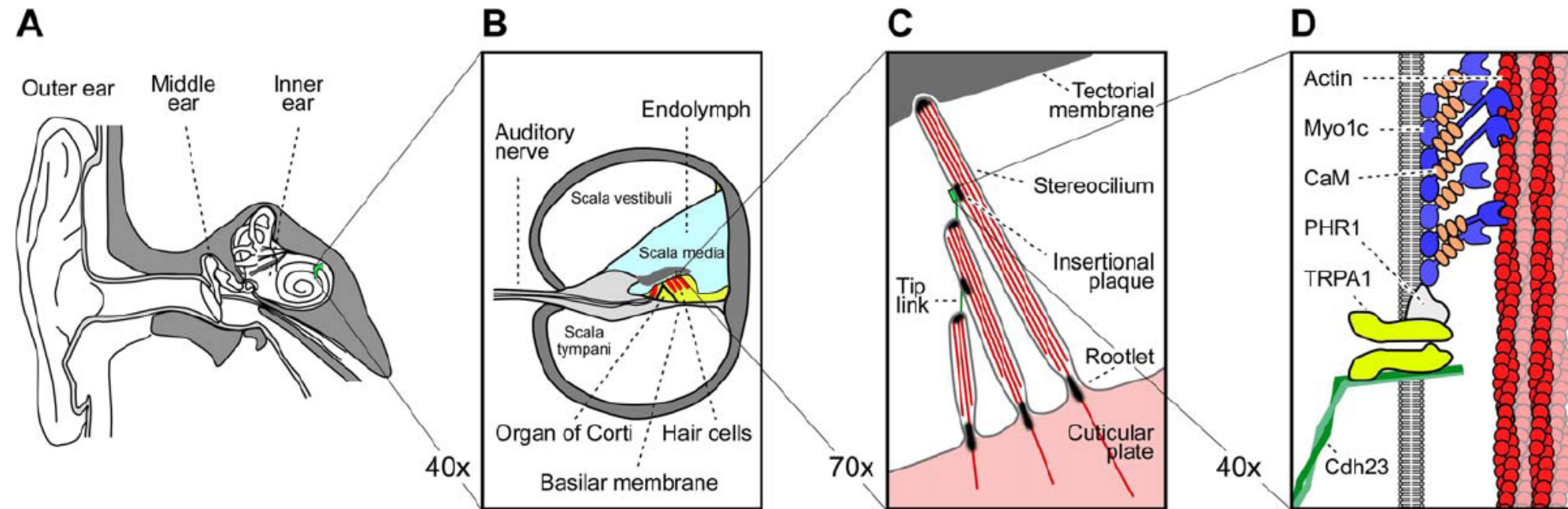
*Dolores Bozovic (Physics)*

Human auditory system

Cross-section of the cochlear

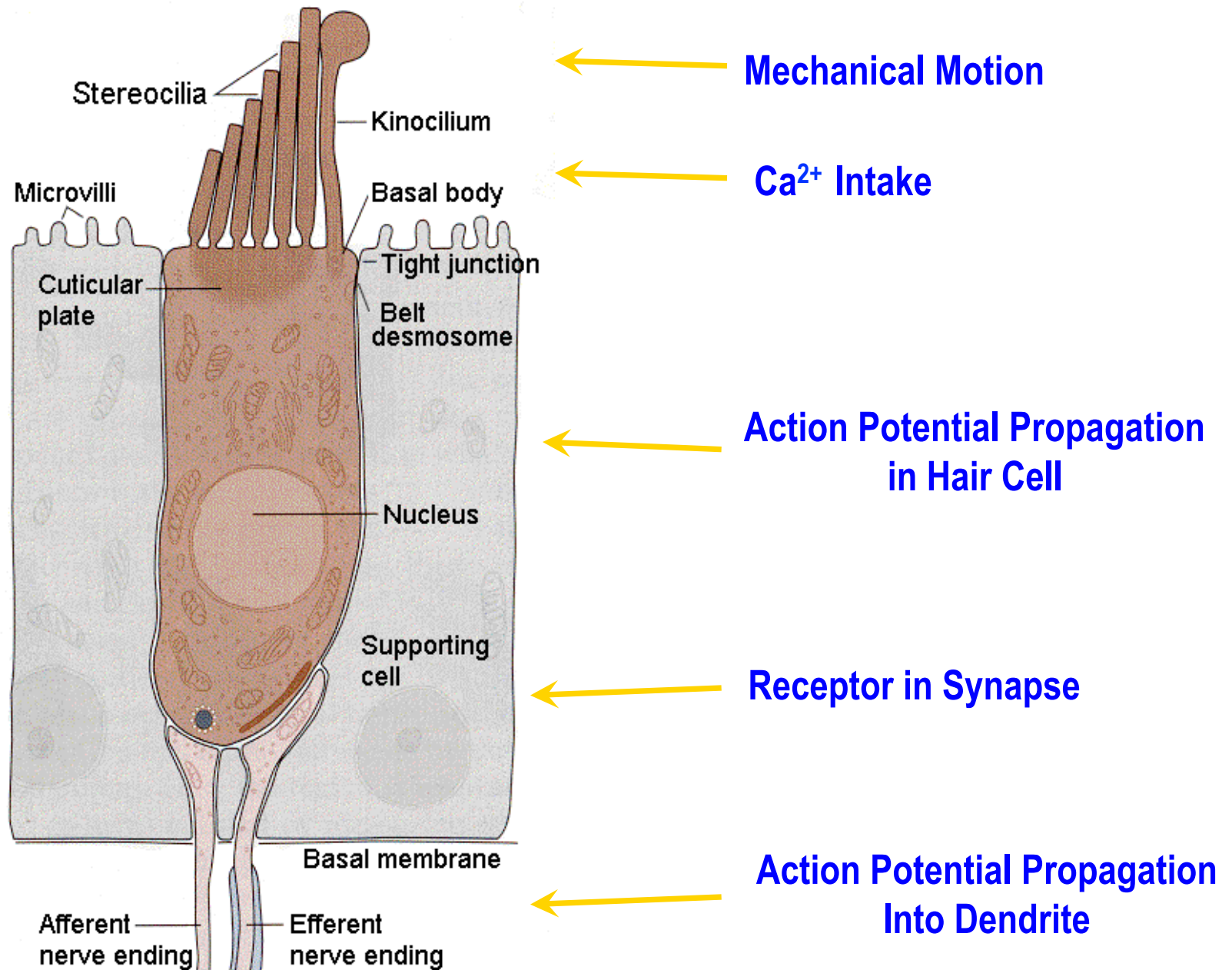
Hair bundle

Molecular mechano-transduction machinery



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

# Simultaneous observation of entire process



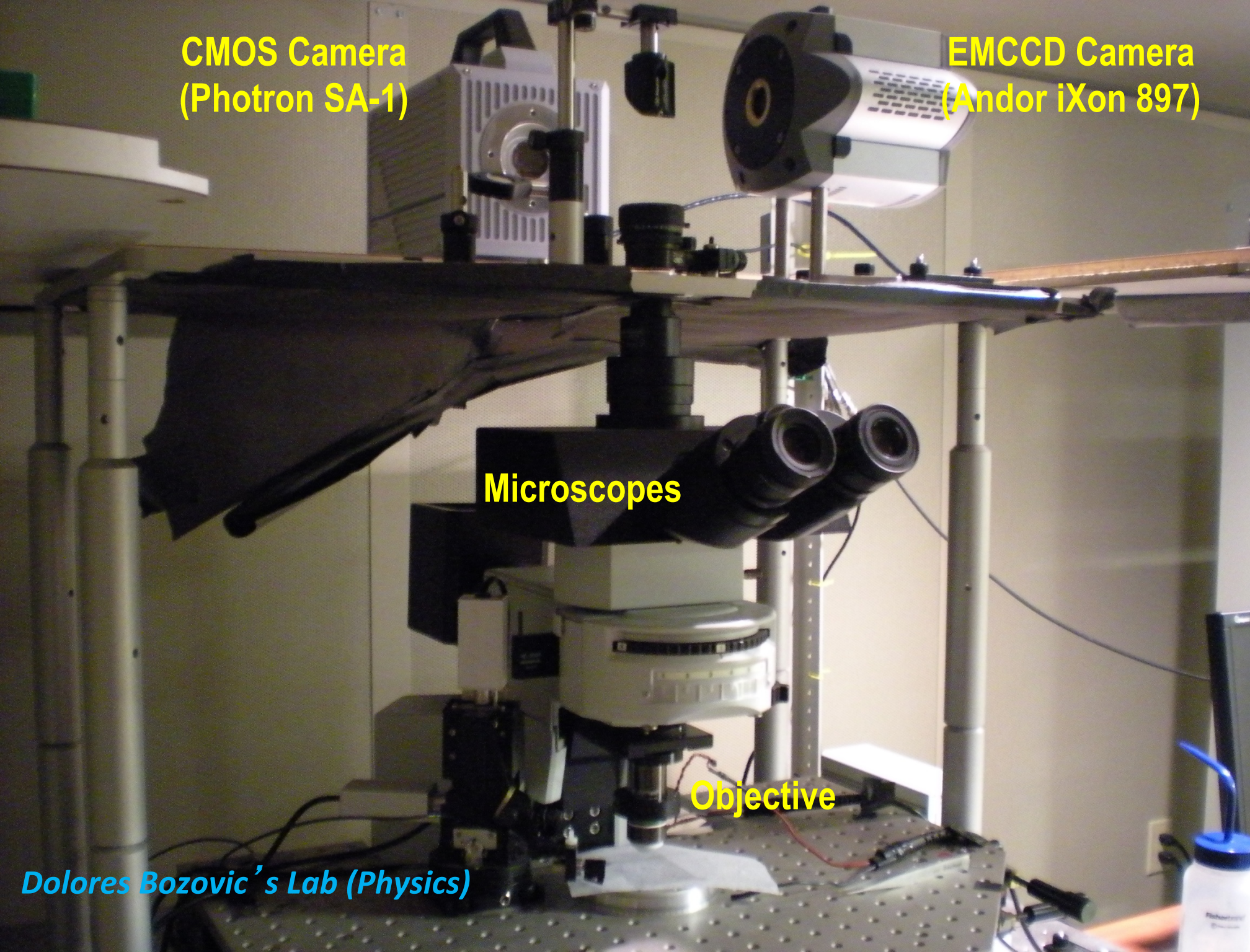
**CMOS Camera  
(Photron SA-1)**

**EMCCD Camera  
(Andor iXon 897)**

**Microscopes**

**Objective**

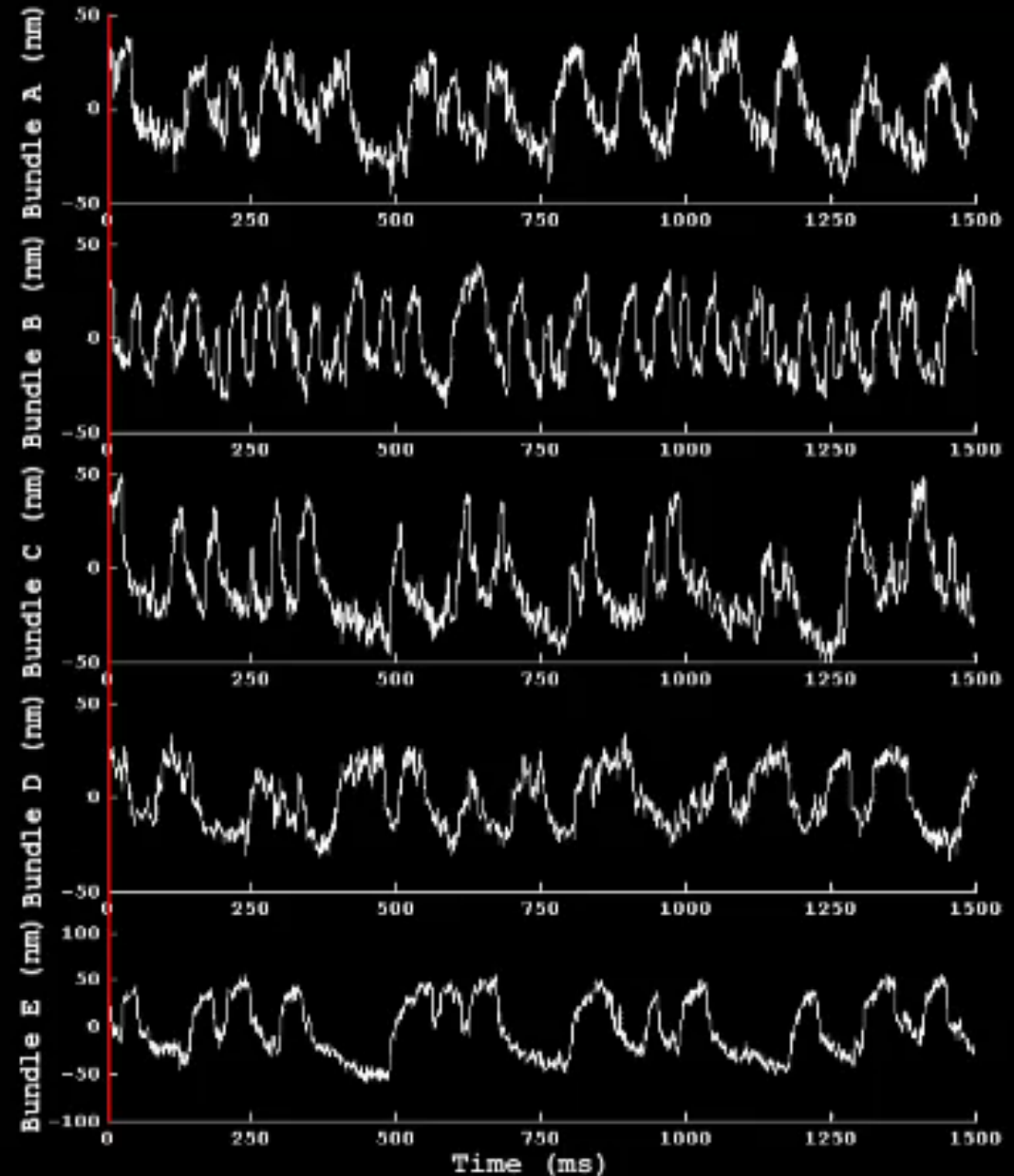
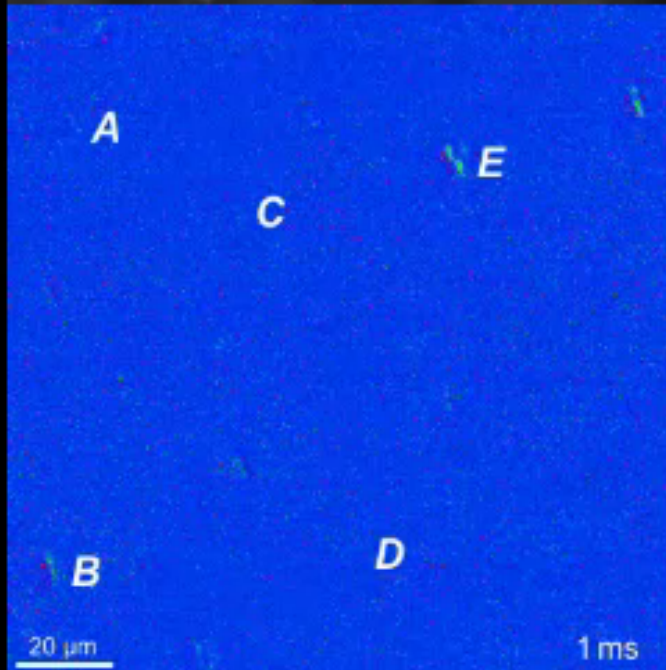
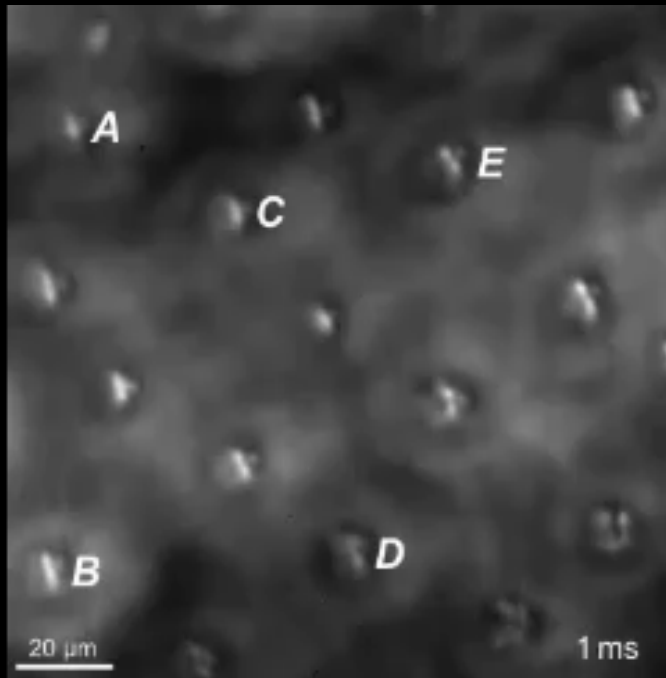
***Dolores Bozovic's Lab (Physics)***



# 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, K. 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

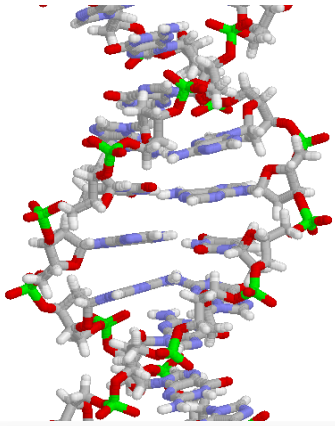
$$\omega = \sqrt{\frac{k}{m}}$$

# How can I recognize a woman so far away?

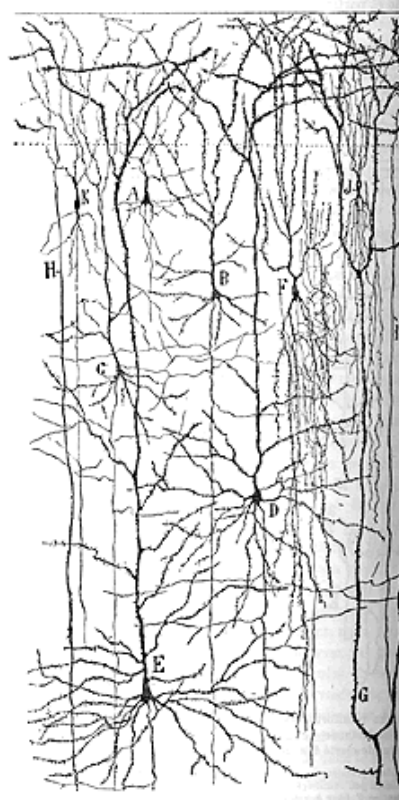


- Genetically encoded?
- Learning and memory?

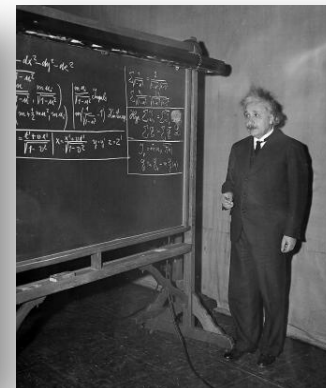
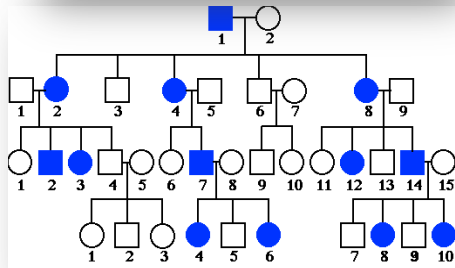
# Nature vs. Nurture



Nature

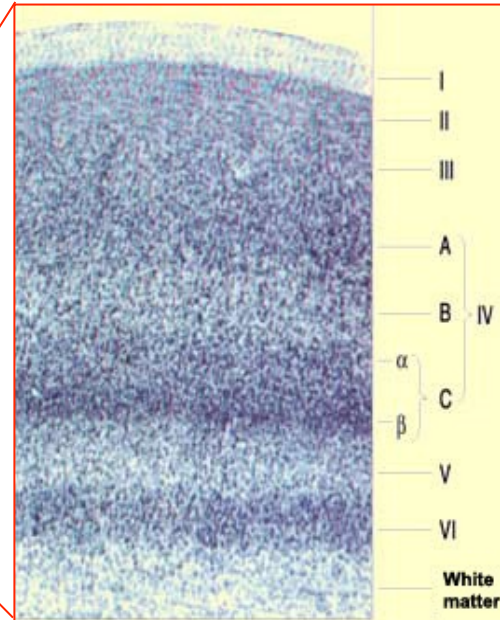
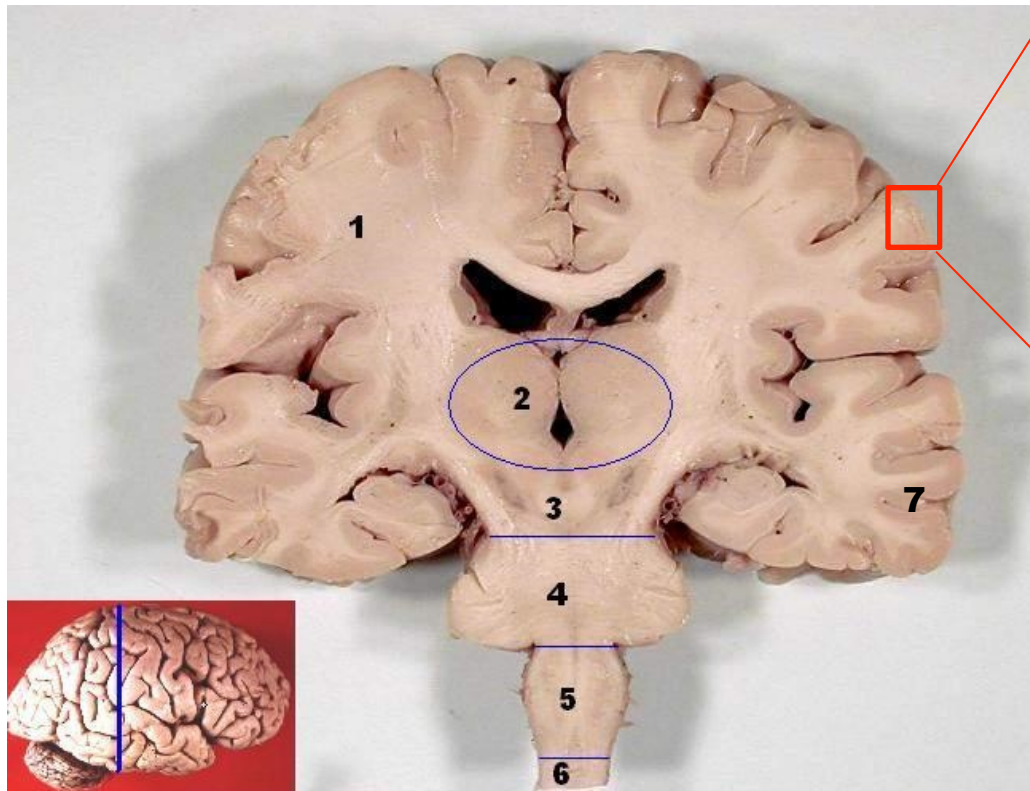


Nurture

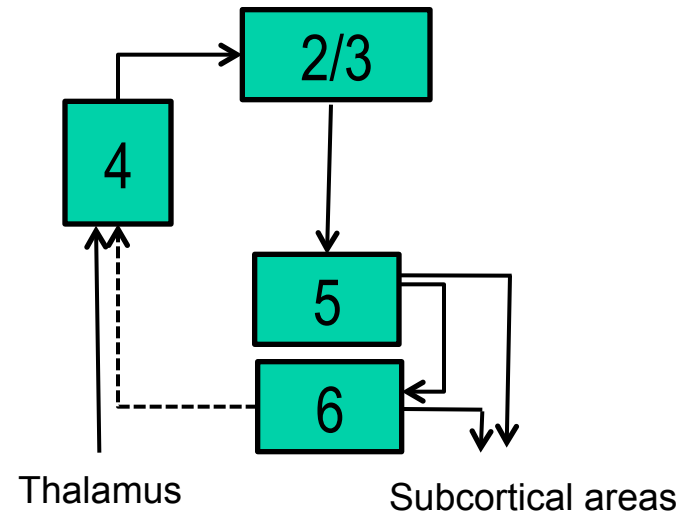


# The Cerebral Cortex

**Conscious**  
↑

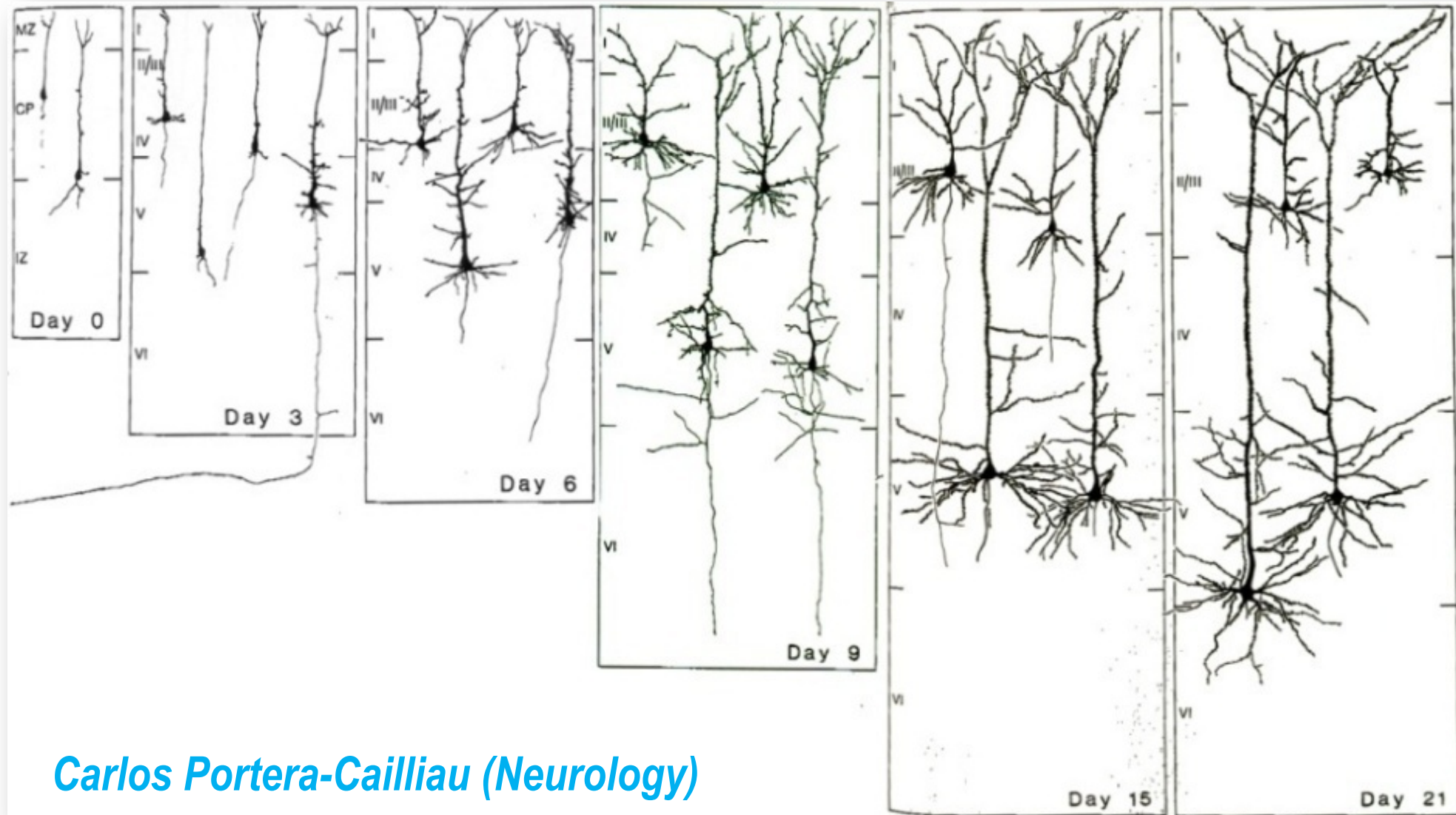


↓  
**Unconscious**



# Assembly of rat's cortical circuits during development

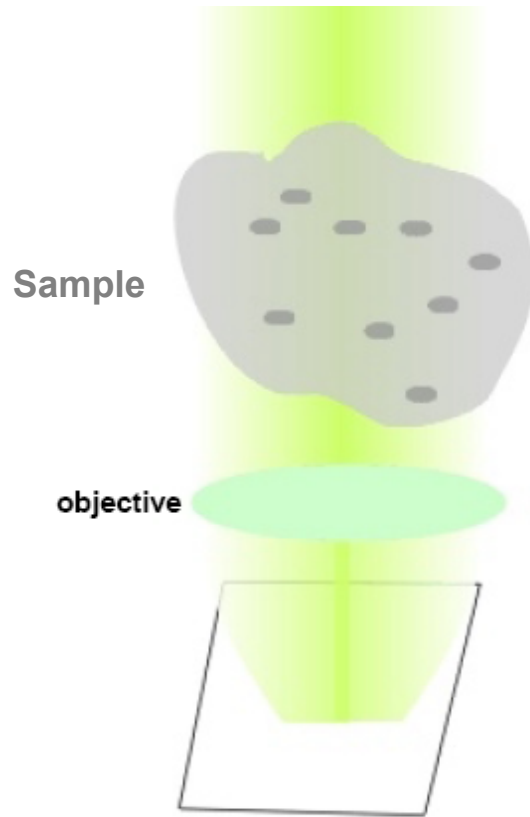
How/when do neurons establish networks? → *Symmetry Breaking*



*Carlos Portera-Cailliau (Neurology)*

# Principle of High-speed Bio Imaging

## Wide Field

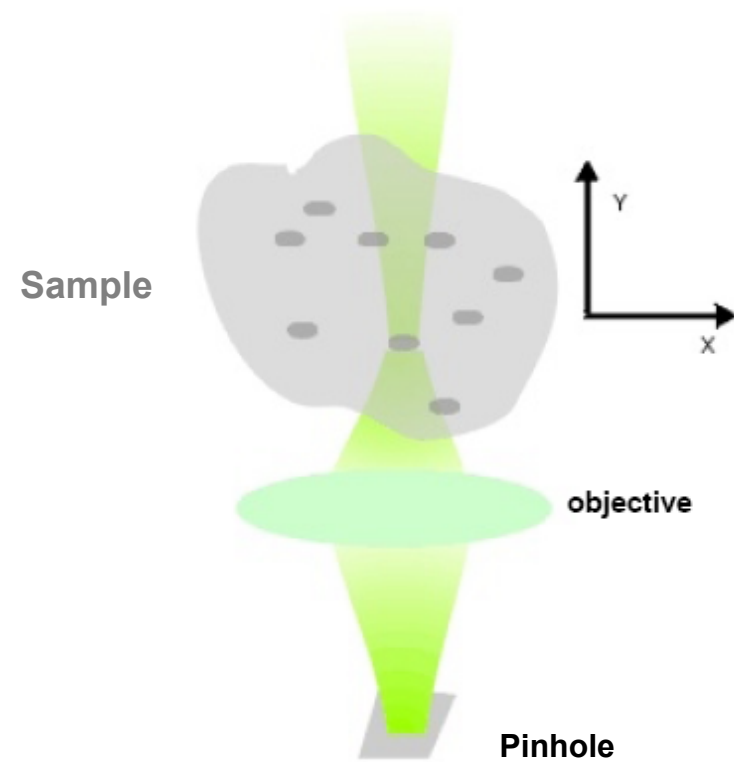


CCD + FADC (10 – 50 MHz)



CMOS [ FADC (50 MHz) \* 100 ]

## Confocal

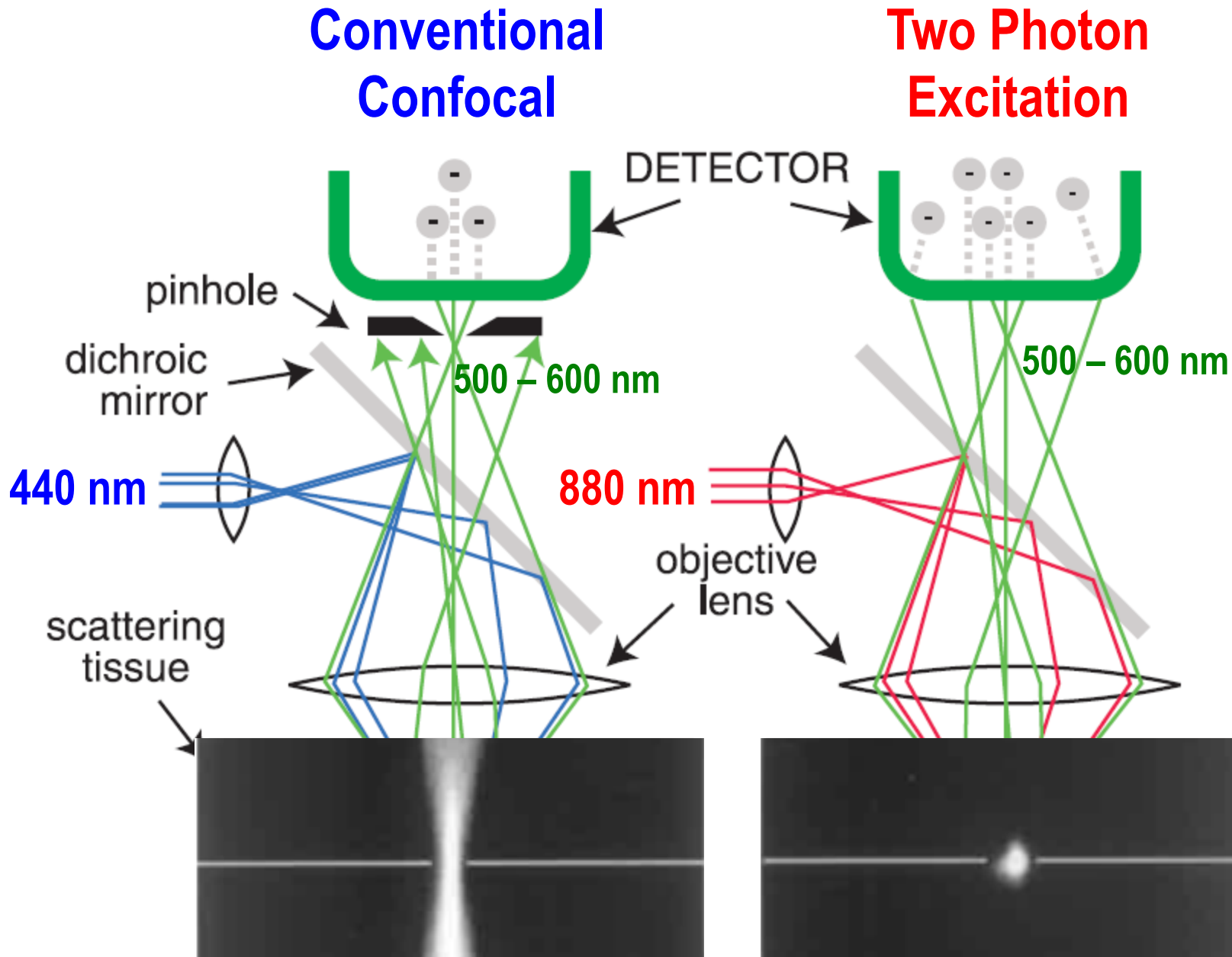


PMT + FADC (10 – 50 MHz)



[ HAPD + FADC (1 GHz) ] \* 64

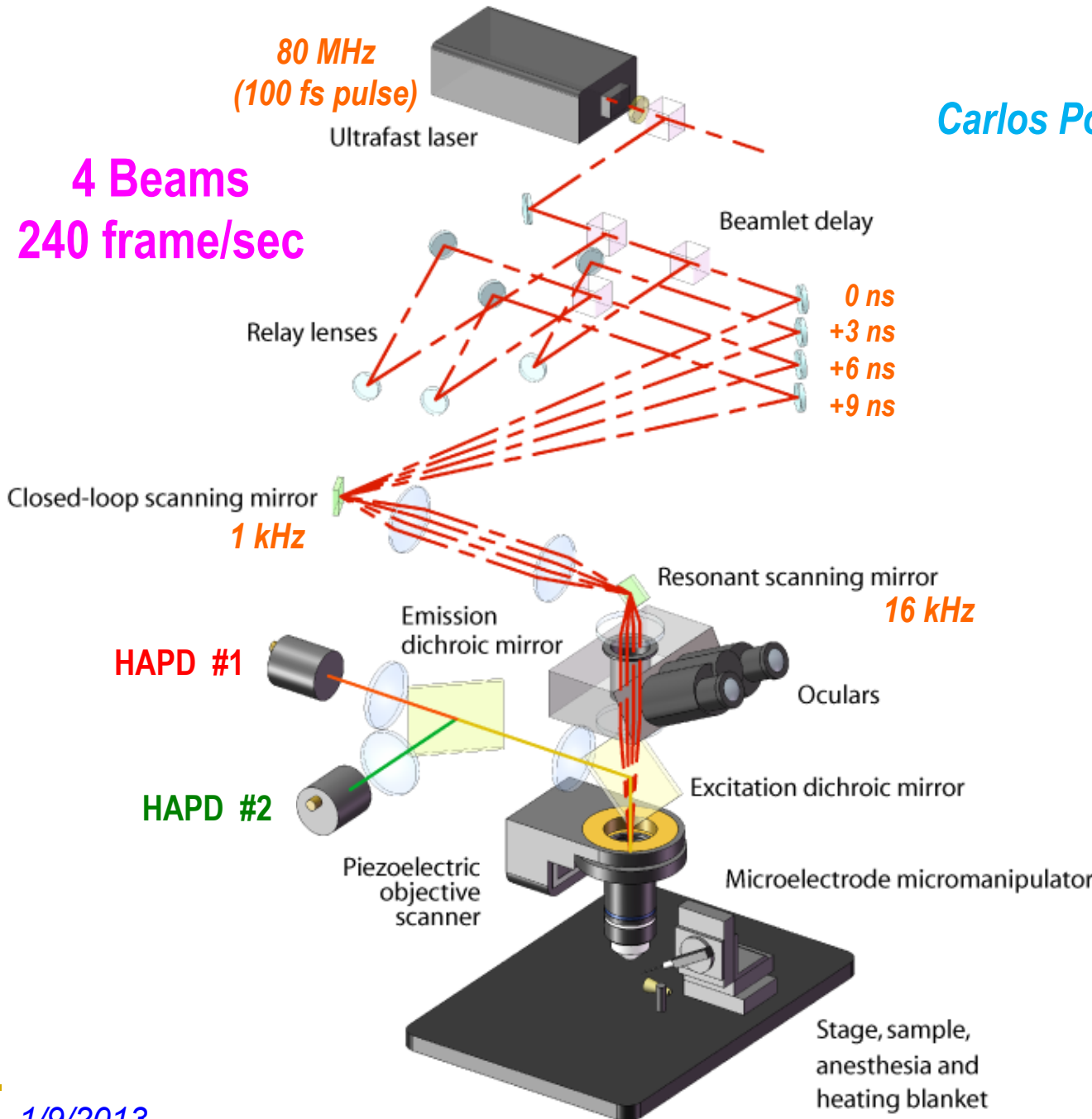
# Multiphoton Microscope



# Spatio-Temporal Excitation-Emission Multiplexing (STEM) Microscope

Adrian Cheng (Physics)

Carlos Portera-Cailliau (Neurology)



Single beam



Oscilloscope



Histogram

Spatio-temporally multiplexed MMM



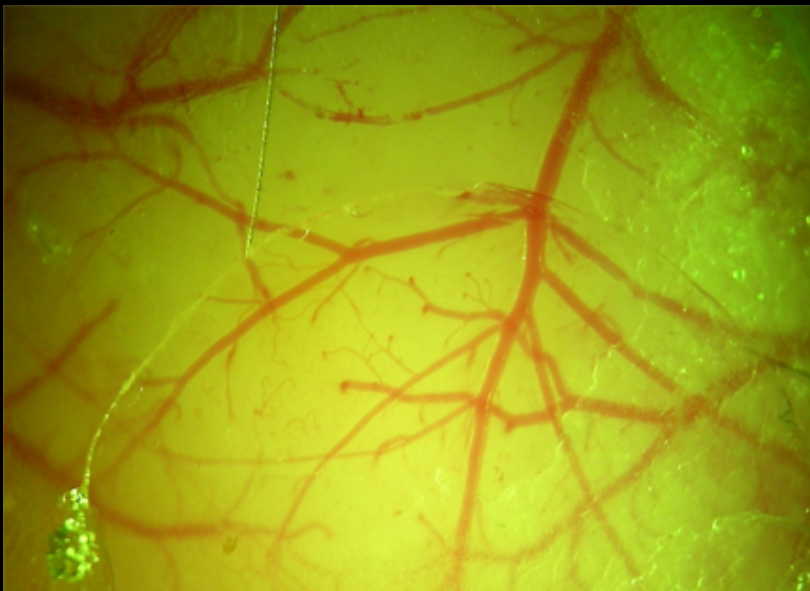
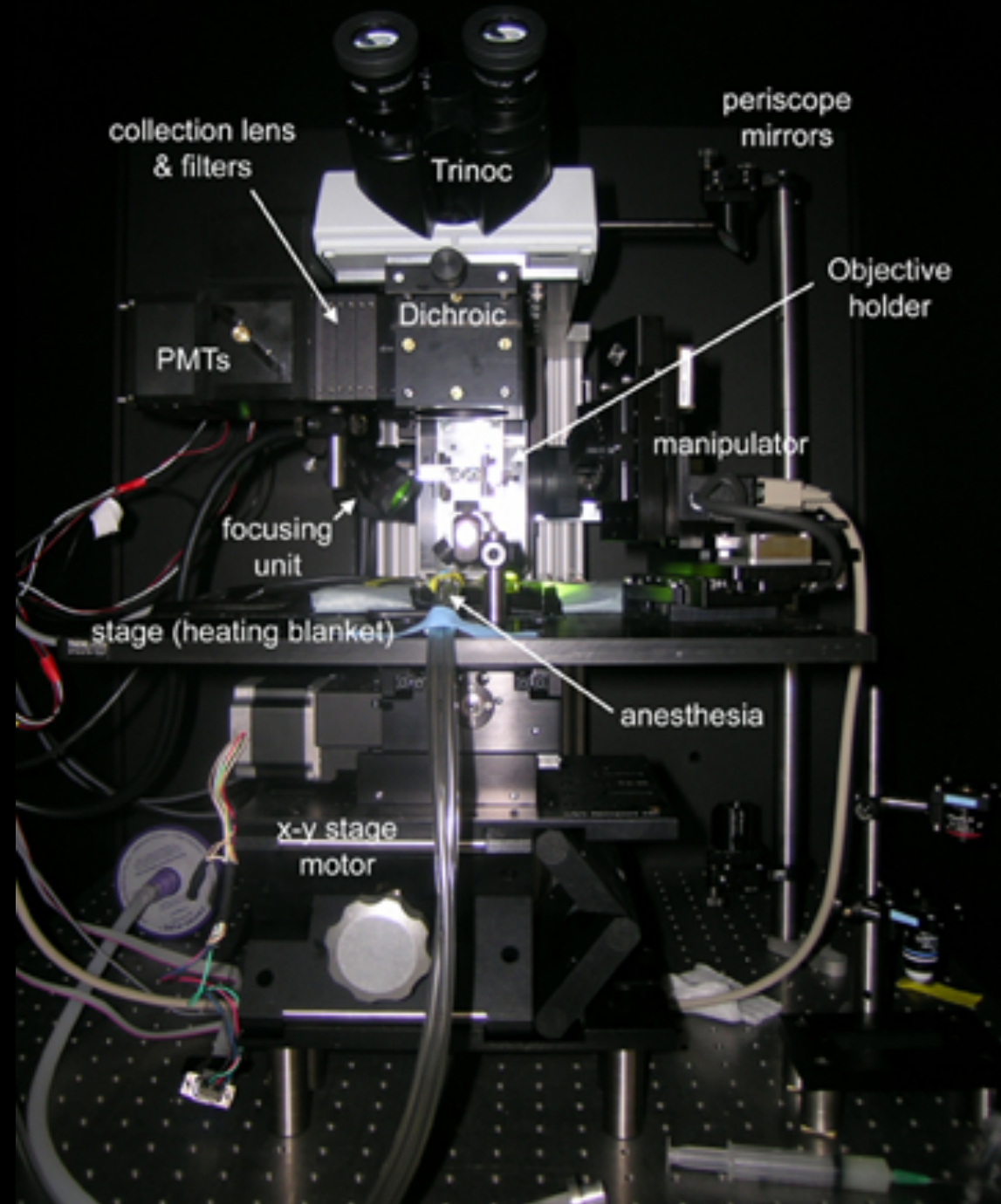
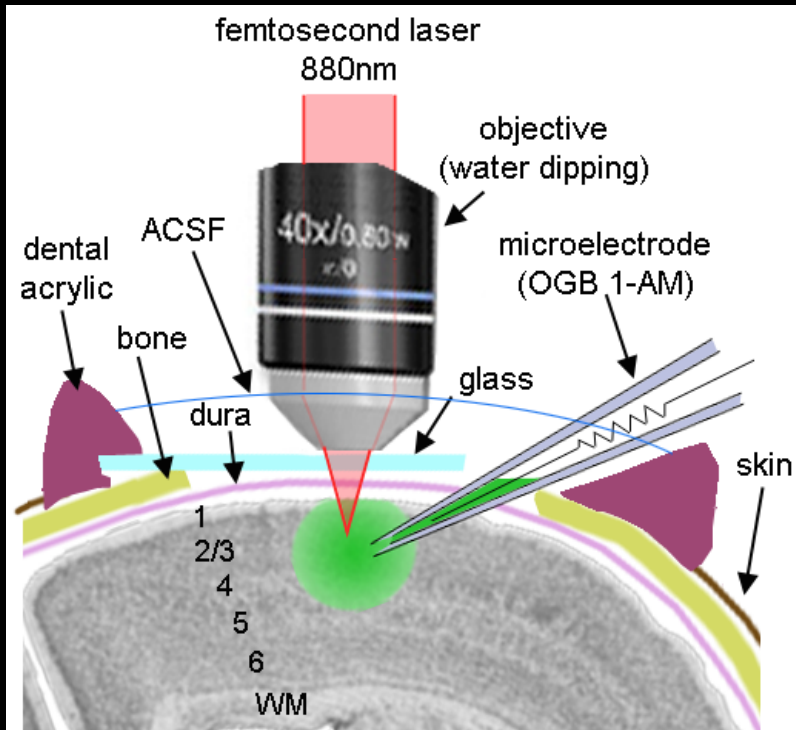
Oscilloscope



Histogram

12 ns

# In vivo calcium imaging of neuronal activity



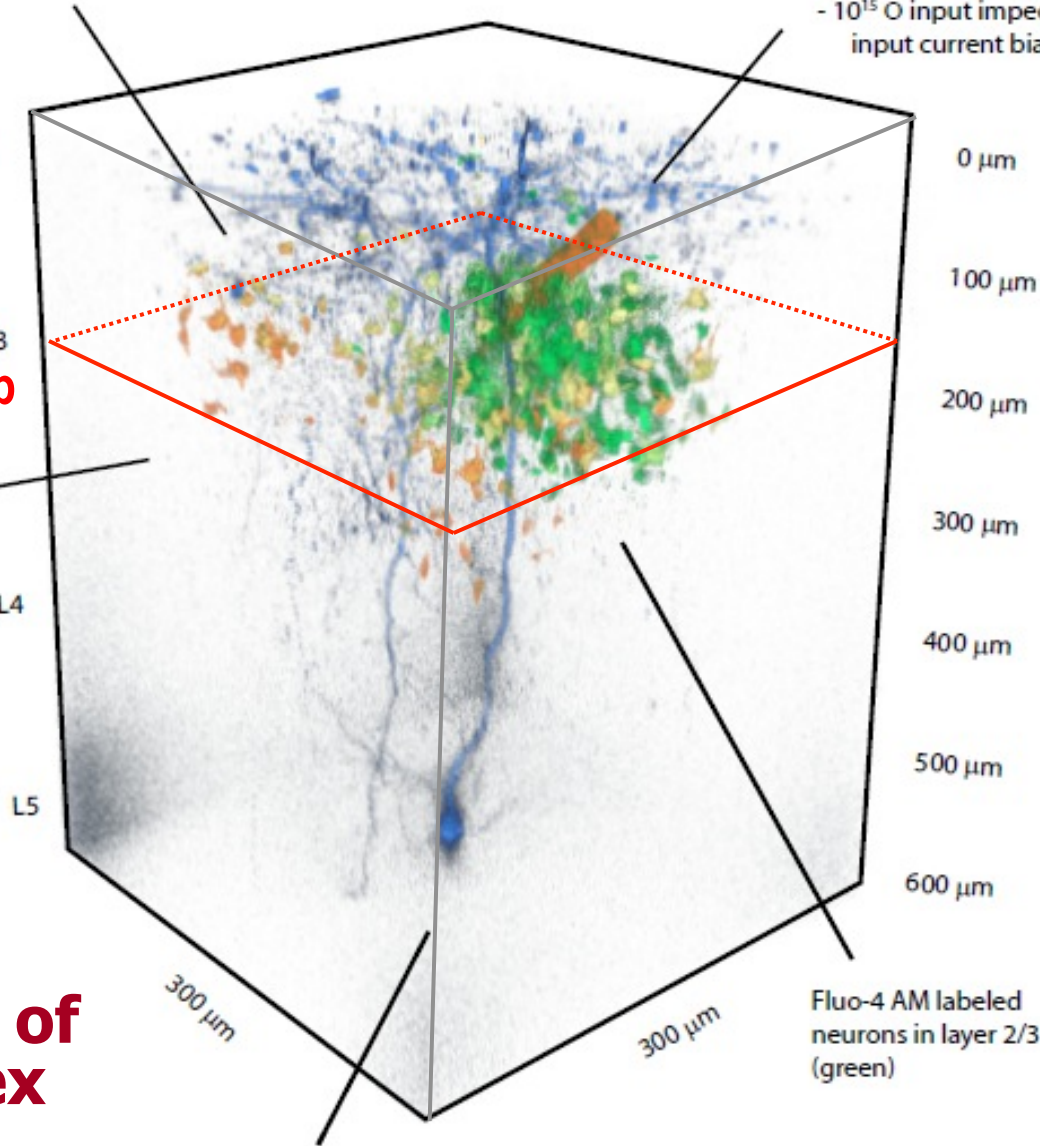
Fluo-4 AM labeled astrocytes are colabeled with sulforhodamine 101 to eliminate background (yellow)

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  $\mu\text{m}$  deep

Sulforhodamine 101 labeled astrocytes (orange)



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

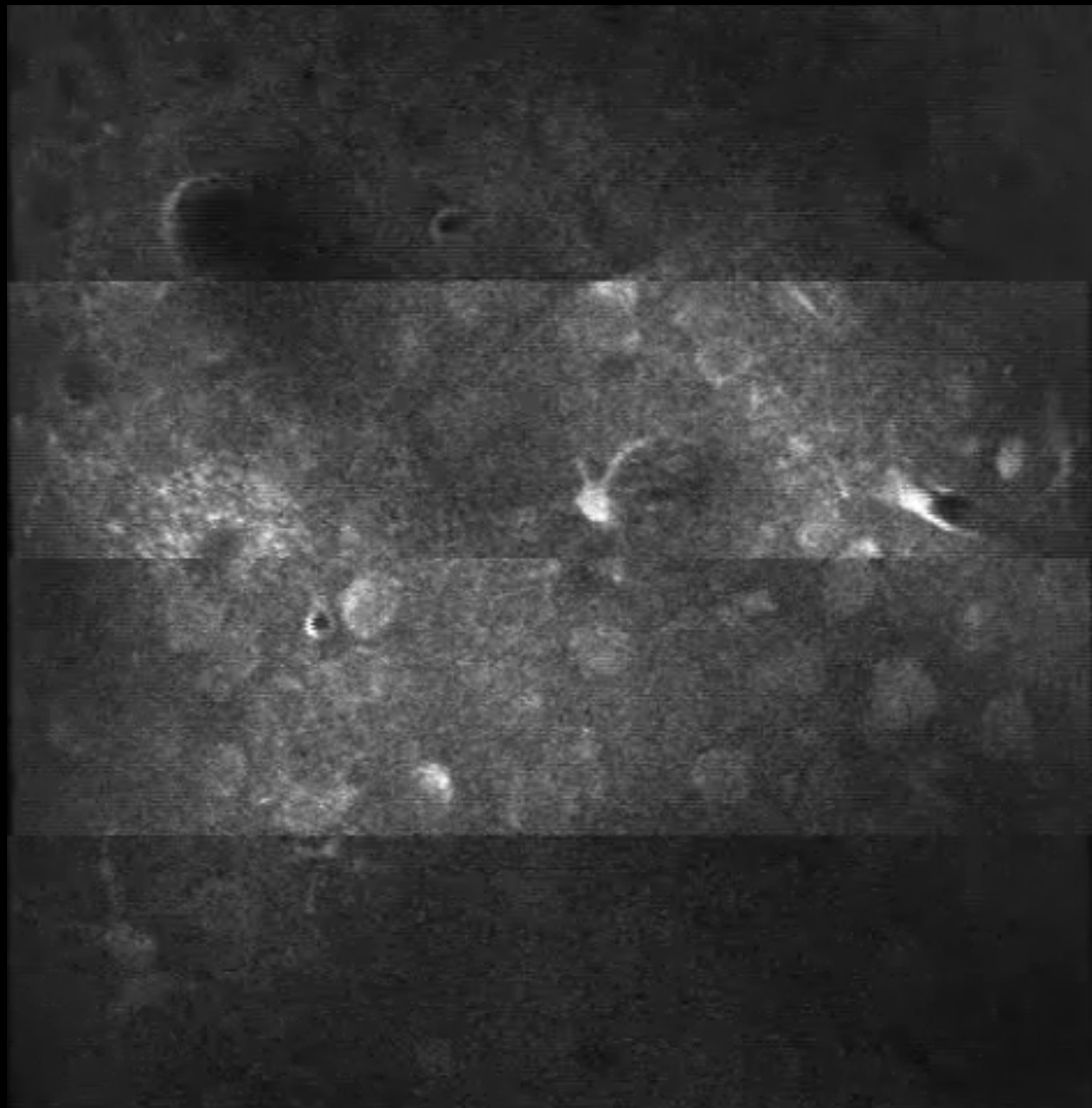
# In vivo calcium imaging of Barrel Cortex of Mouse

**Barrel Cortex  
Layer 2/3**

**150  $\mu\text{m}$  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)**

**← 300  $\mu\text{m}$  →**

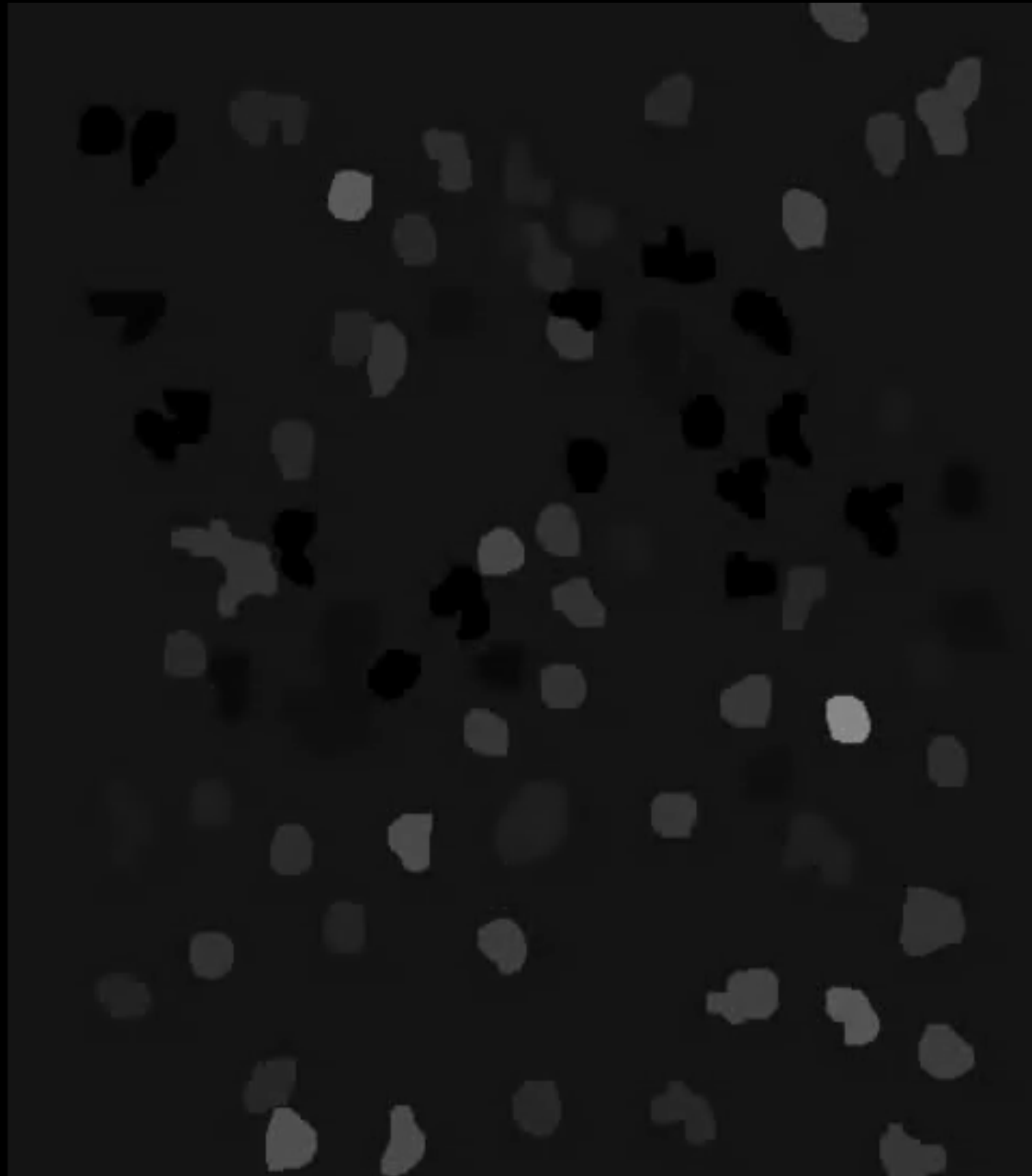
# In vivo calcium imaging of Barrel Cortex of Mouse

**Barrel Cortex  
Layer 2/3**

**150  $\mu\text{m}$  deep**

**After  
averaging**

**(x3 faster  
than real)**



*58 neurons*

*(~100 billions  
neurons  
in our brain)*

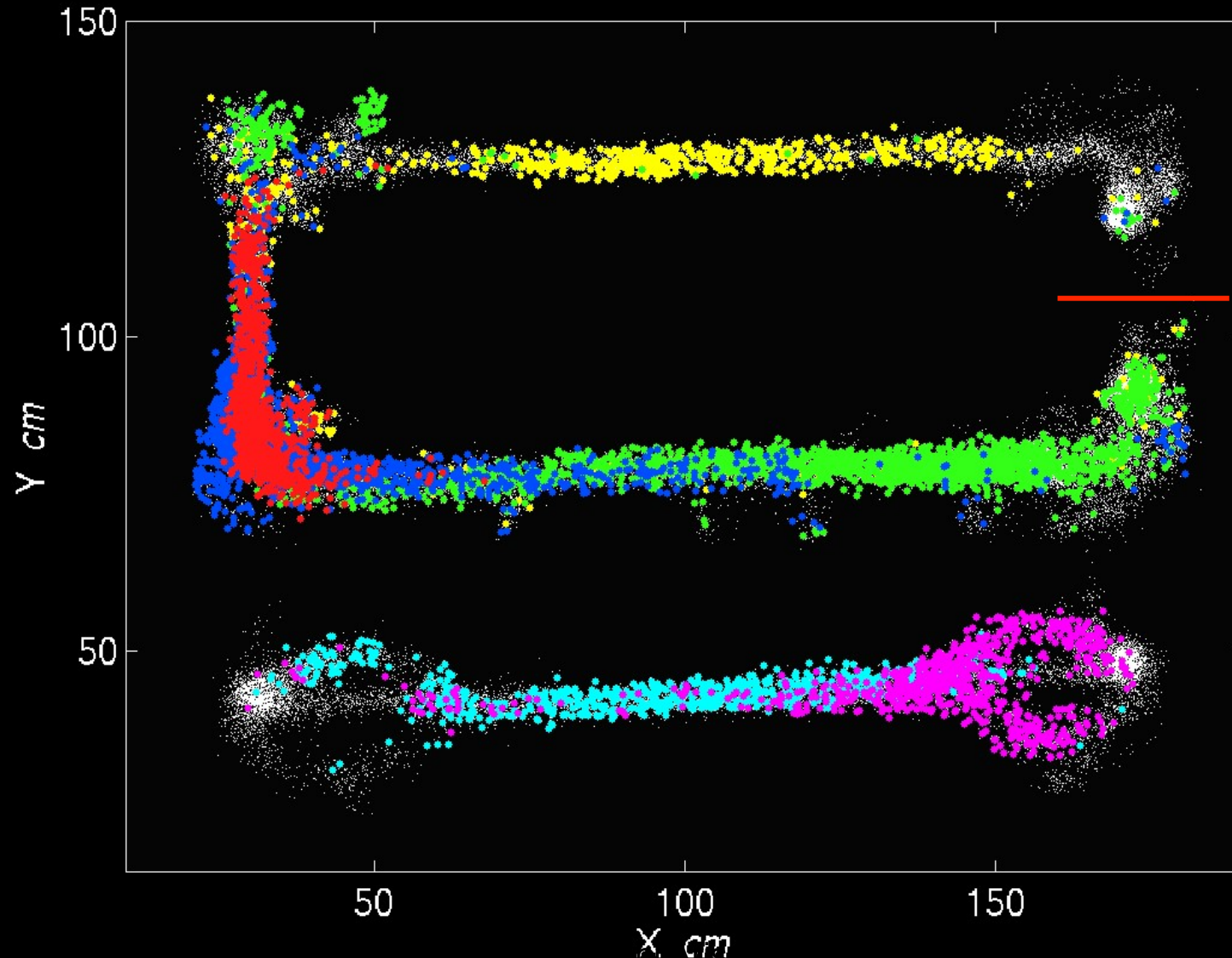
**← 300  $\mu\text{m}$  →**

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# **Future Directions - Virtual Reality -**

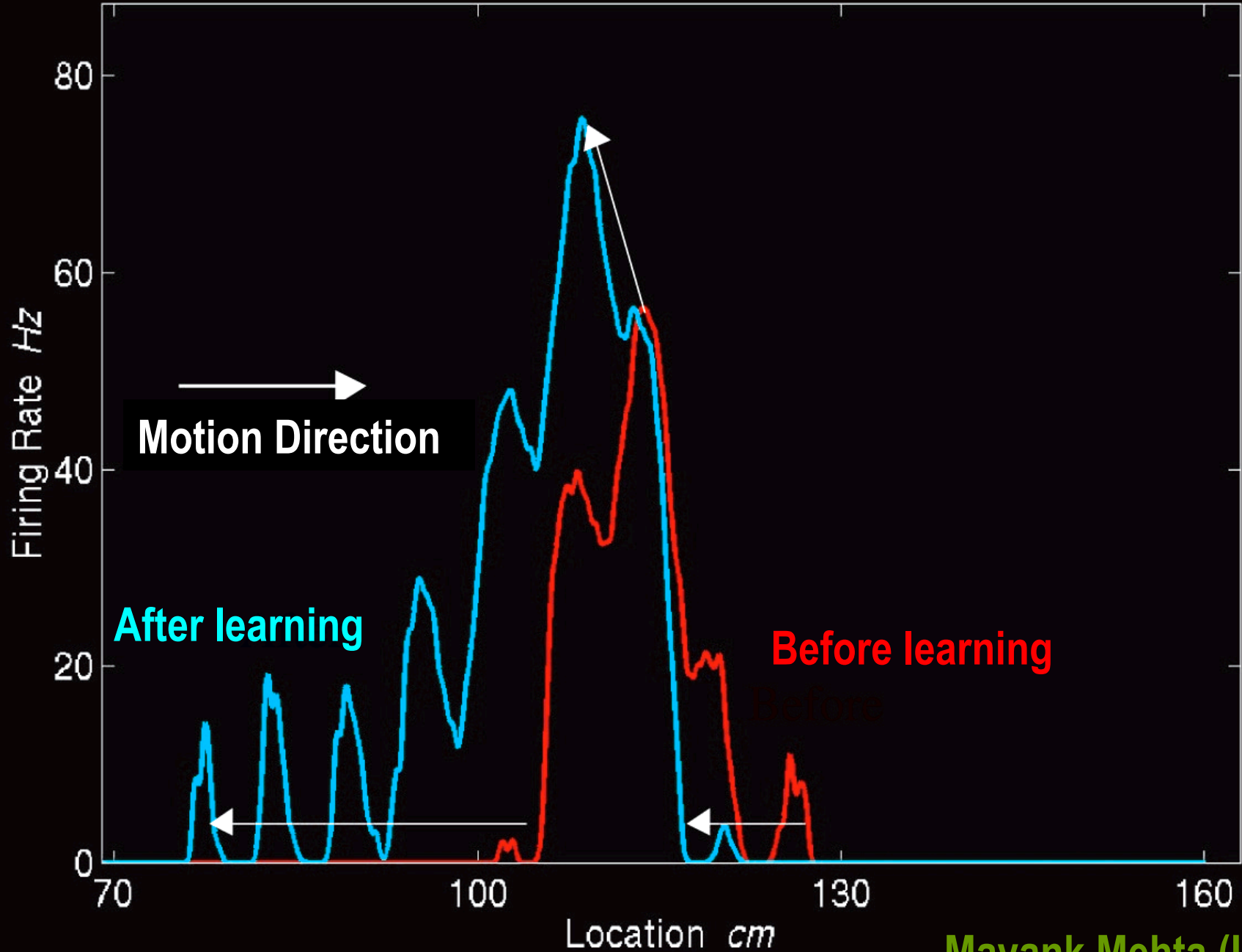
# Activity of (excitatory) pyramidal neurons in CA depends on rat's position: place cells

*Mayank Mehta (Physics, Neurology)*



**Hippocampus has a cognitive map of space**

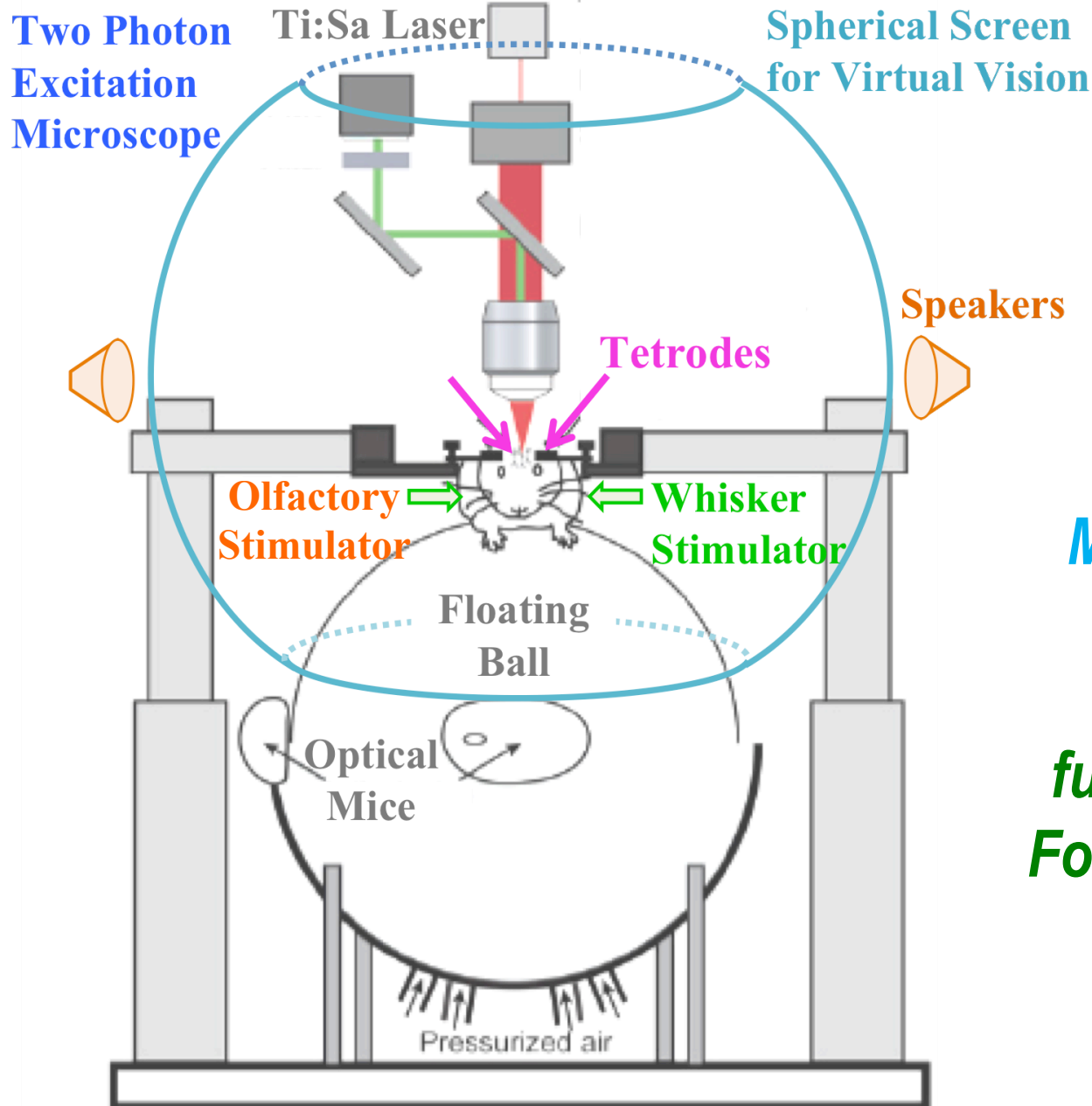
# Learning and Memory by Hippocampus



# 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.**

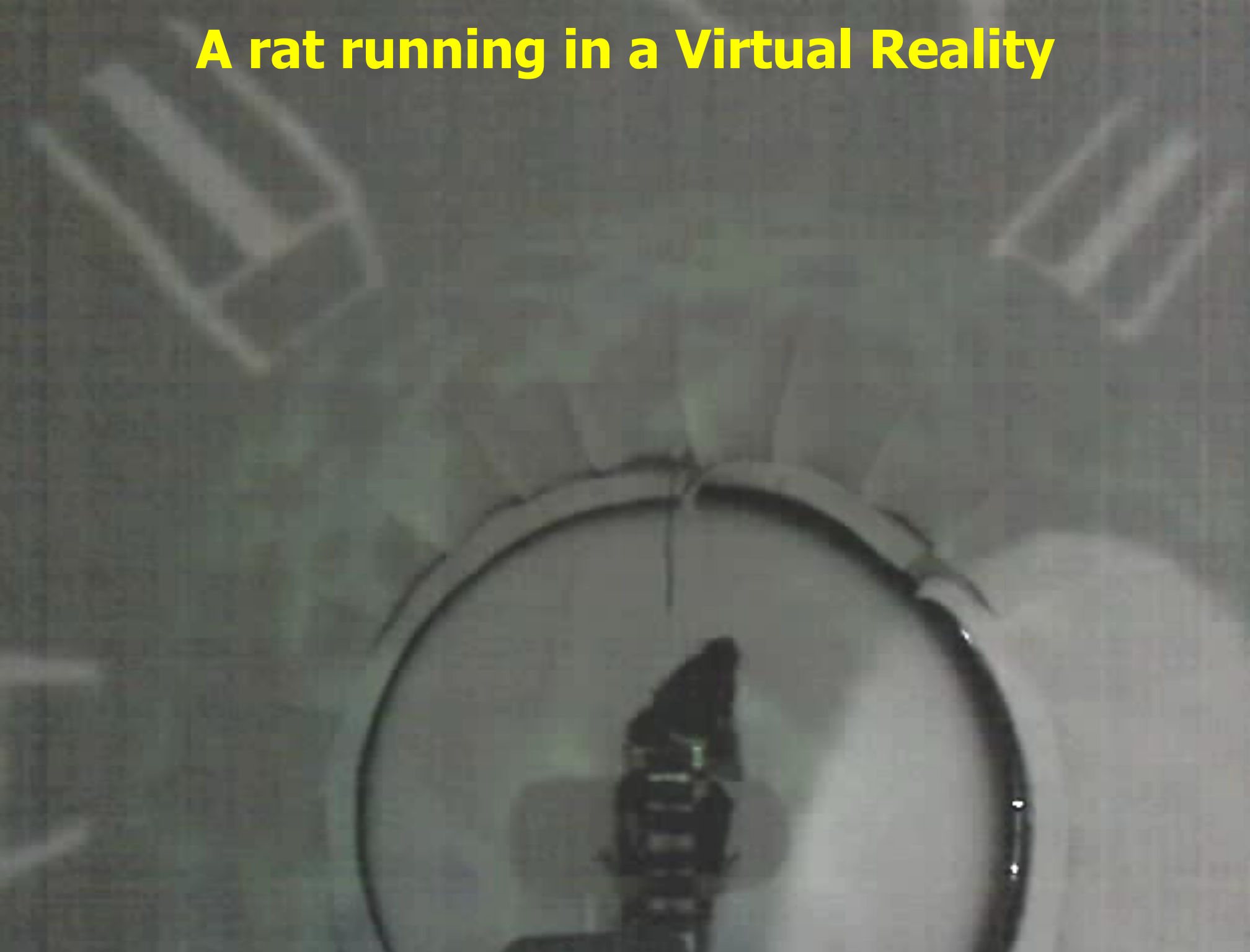
# Virtual Reality Experiment on Awake Rats



*Mayank Mehta  
(Physics)*

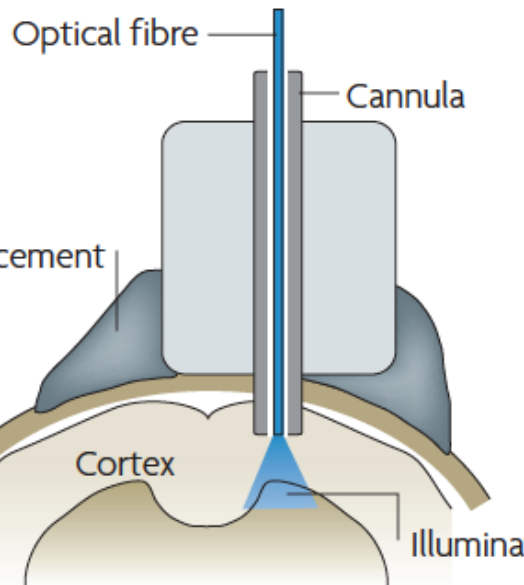
*funded by Keck  
Foundation (\$1M)*

# A rat running in a Virtual Reality

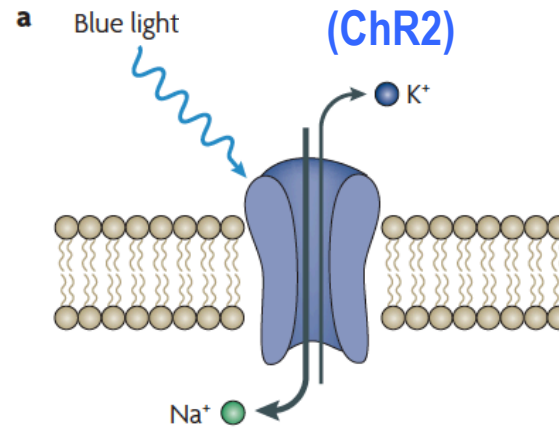


# Optogenetic Excitation of Neurons

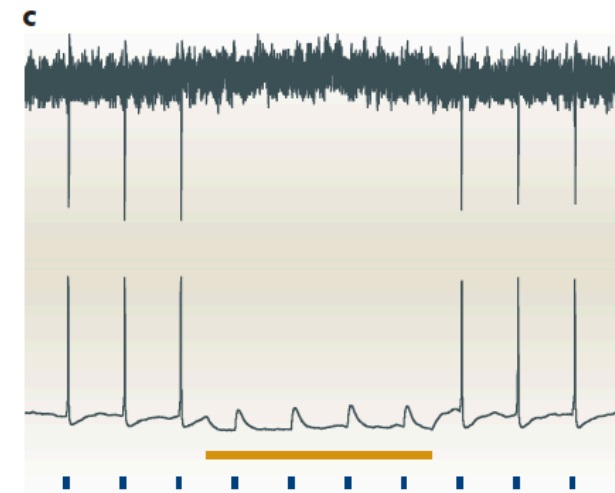
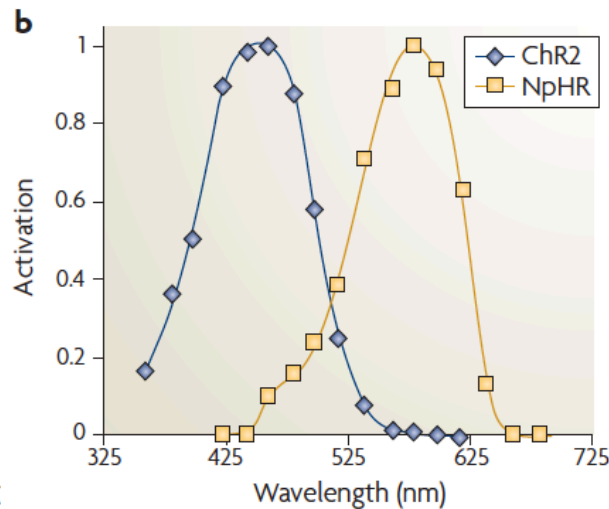
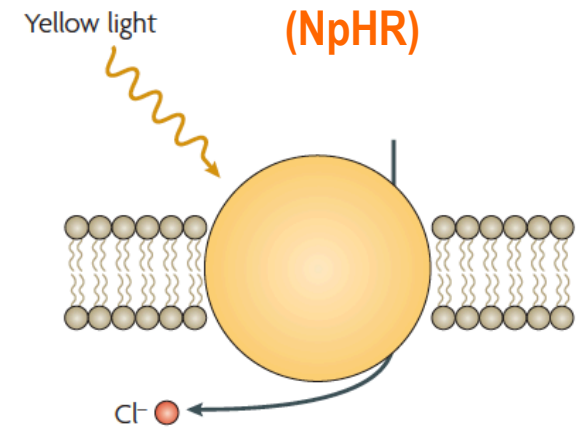
Karl Deisseroth (Stanford)



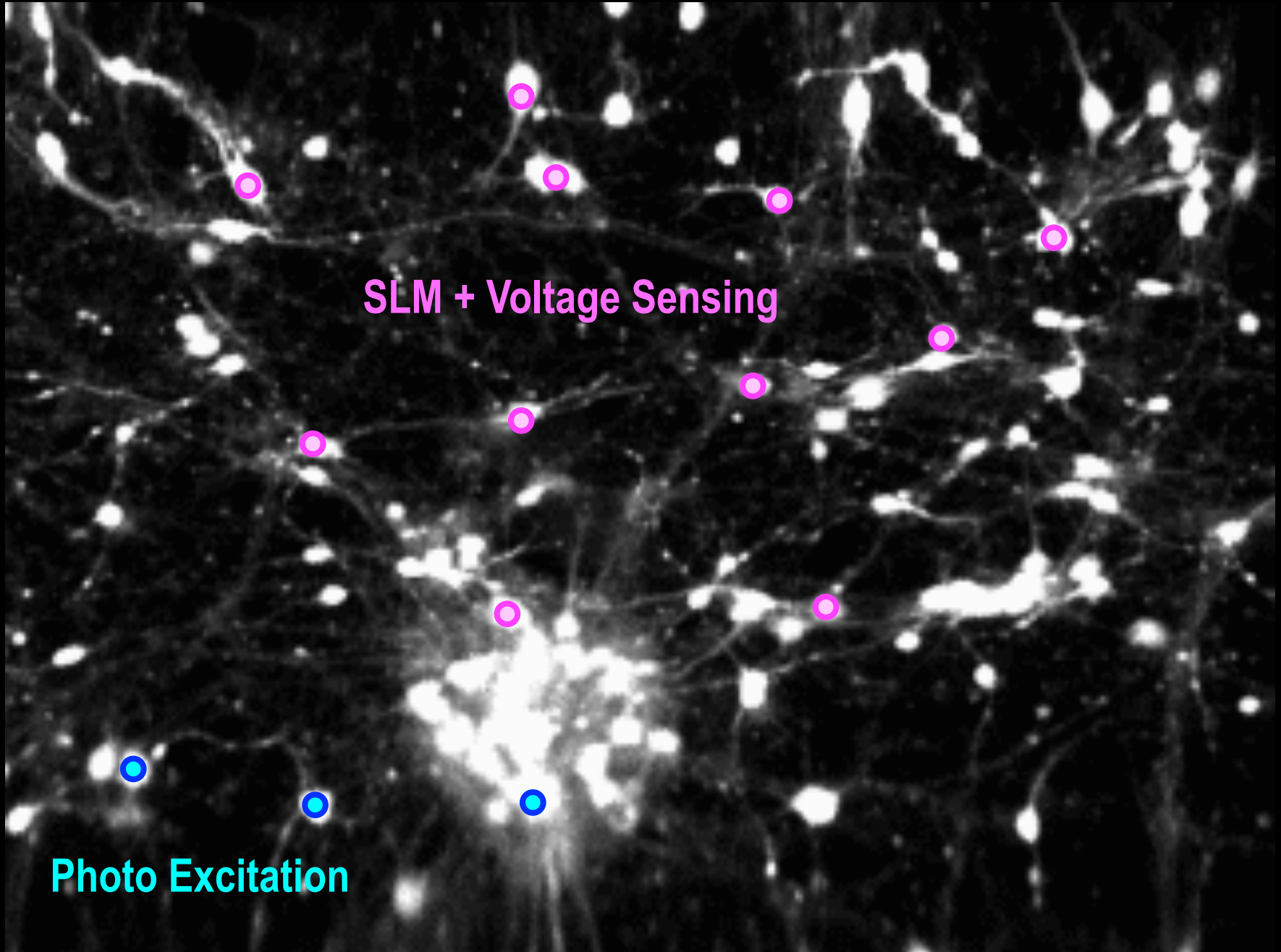
Excitation by  
Channelrhodopsin-2  
(ChR2)



Inhibition by  
Halorhodopsin  
(NpHR)



# Ca<sup>2+</sup> Signal in cultivated Rat's Brain by Confocal Microscope



# 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.

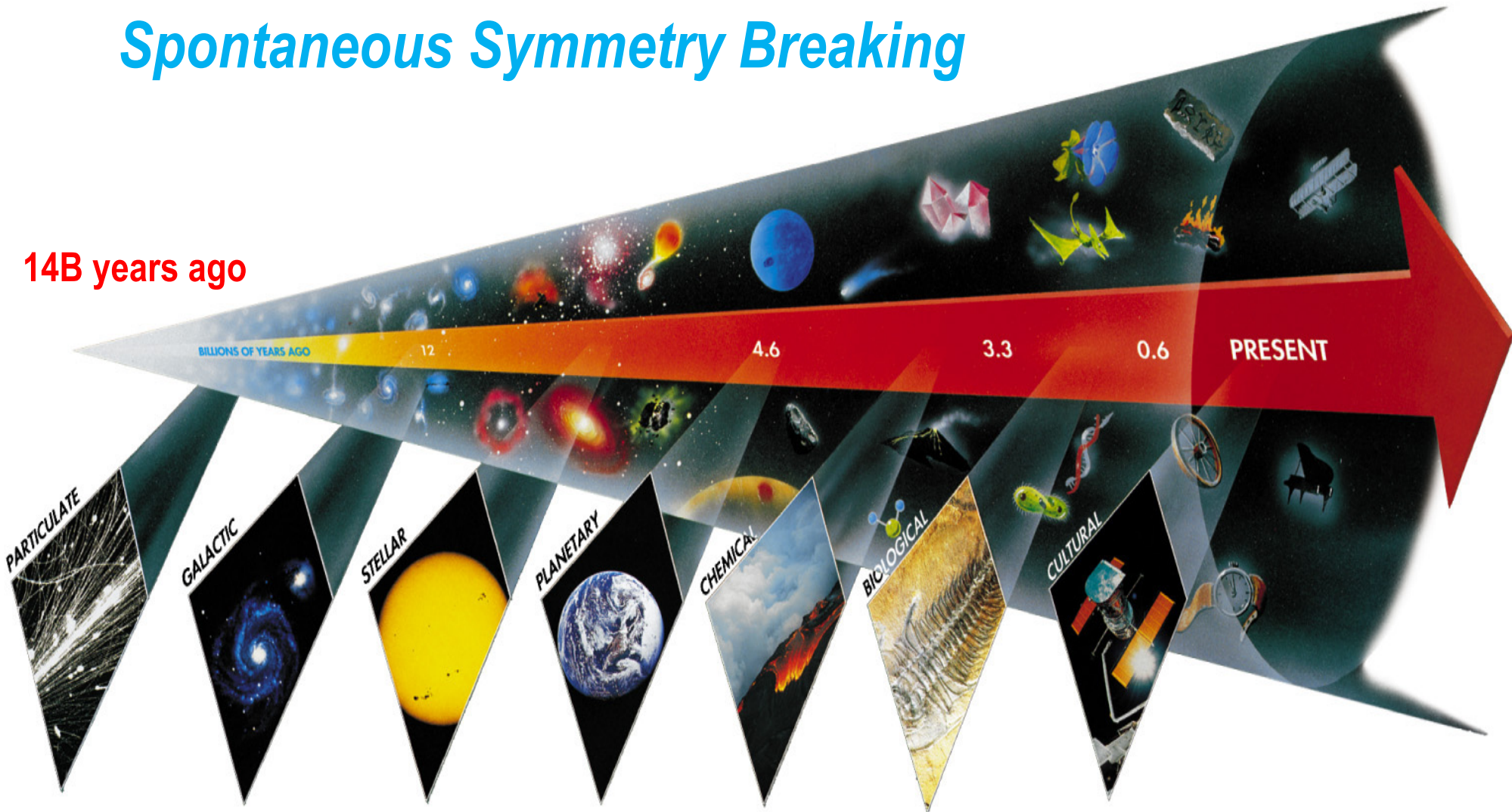
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# Summary

# Seven Phases of Cosmic Evolution

## Spontaneous Symmetry Breaking

14B years ago



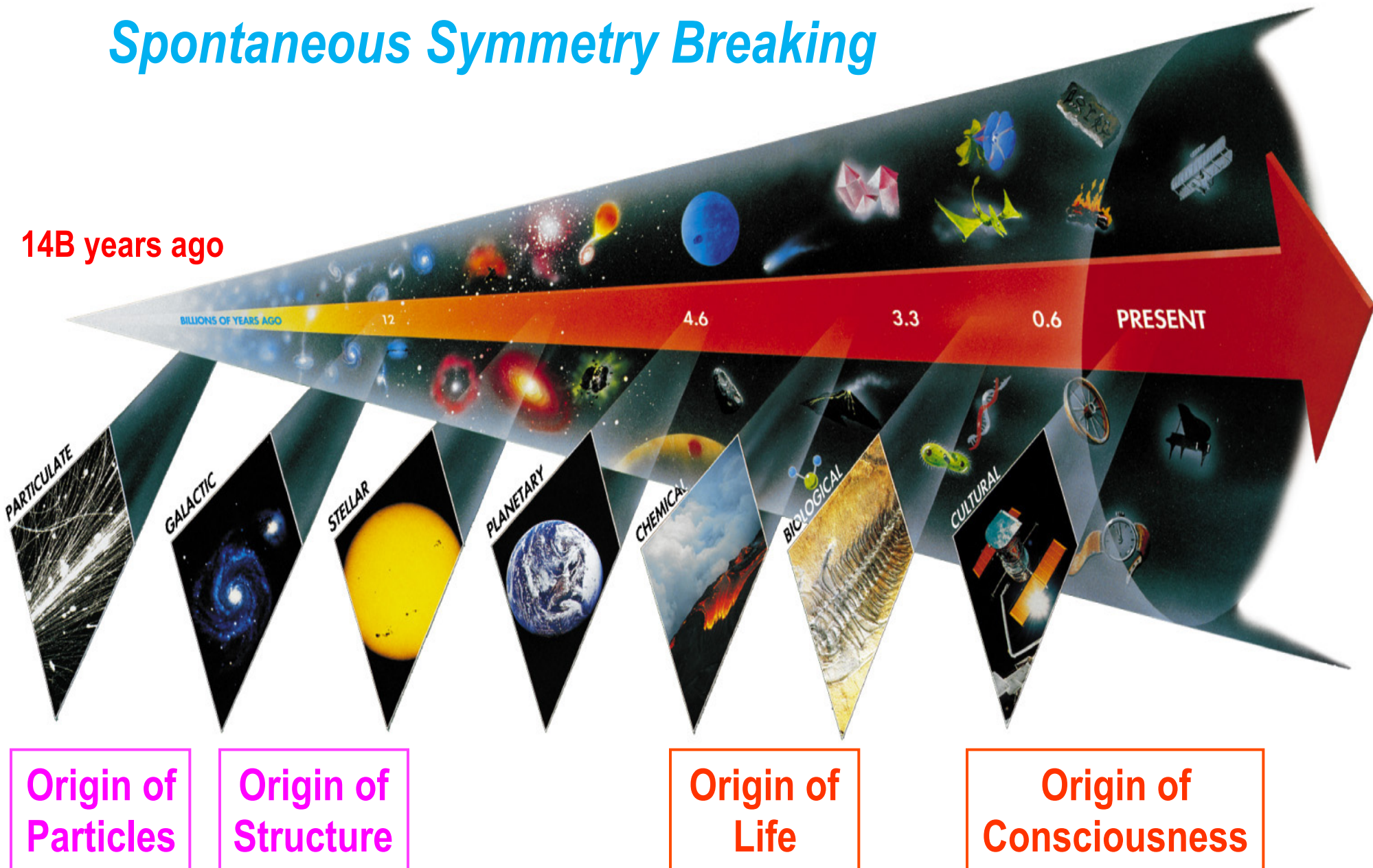
Simple



Coherent Complex System

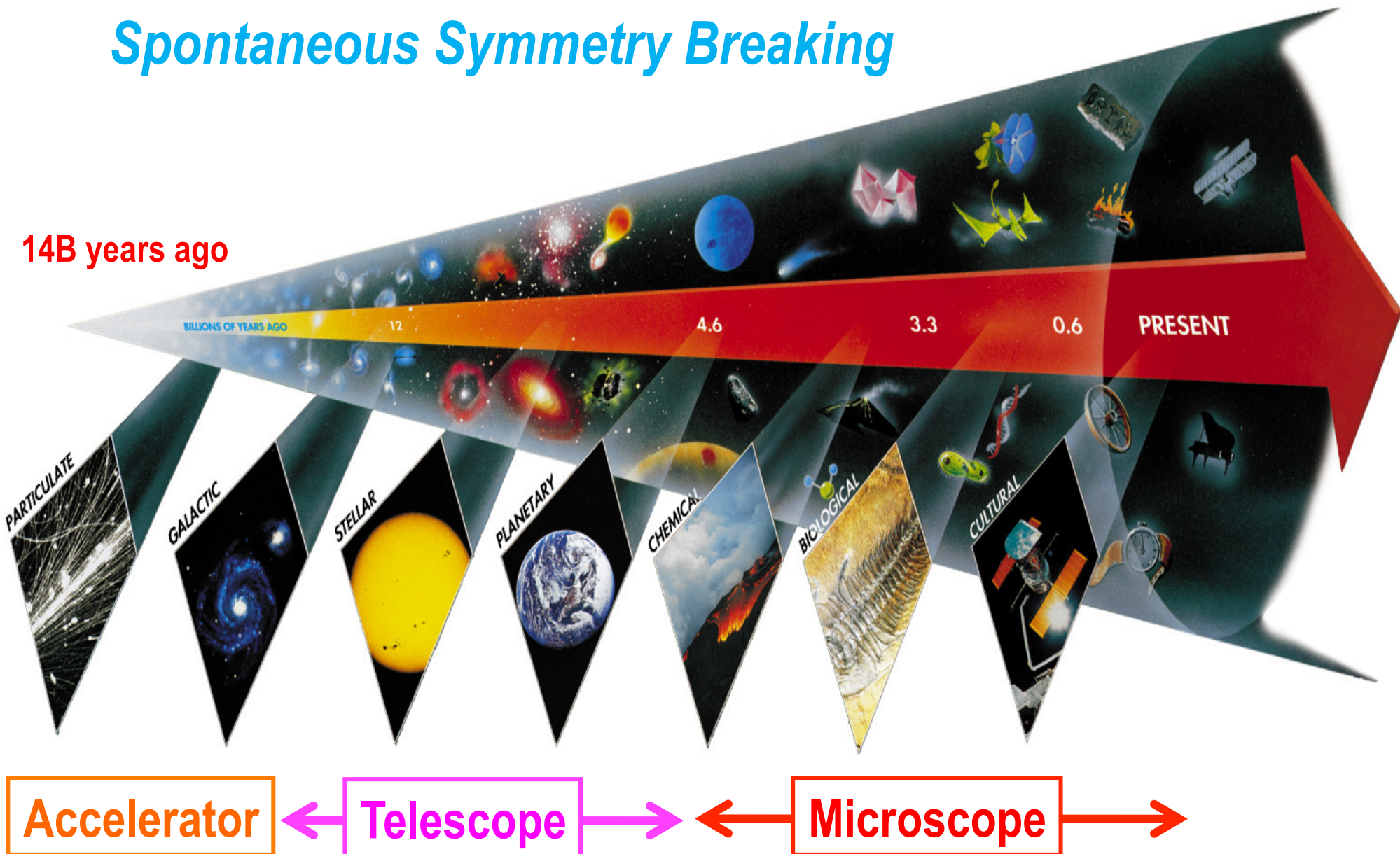
# Seven Phases of Cosmic Evolution

## Spontaneous Symmetry Breaking



# Seven steps of cosmic evolution

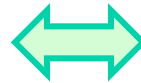
## Spontaneous Symmetry Breaking



# Four Major Science

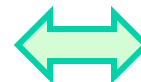
**Origin of Particles**  
**Particle Physics**

**Origin of Universe**  
**Cosmology**



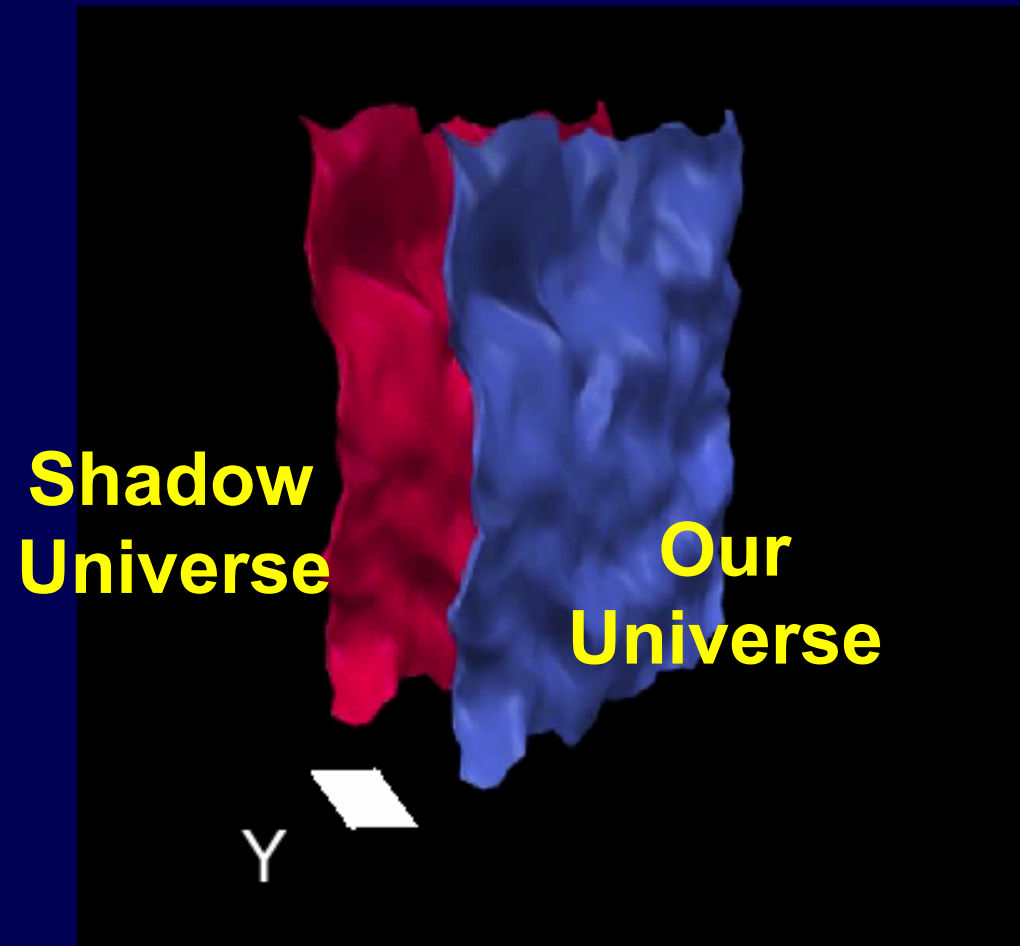
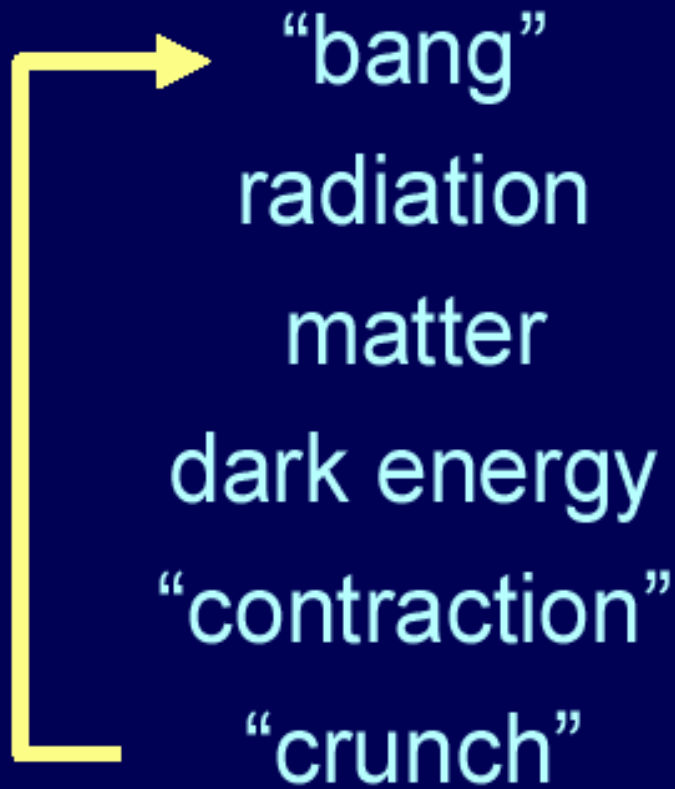
**Origin of Life**  
**Molecular Biology**

**Origin of Consciousness**  
**Neurophysics**



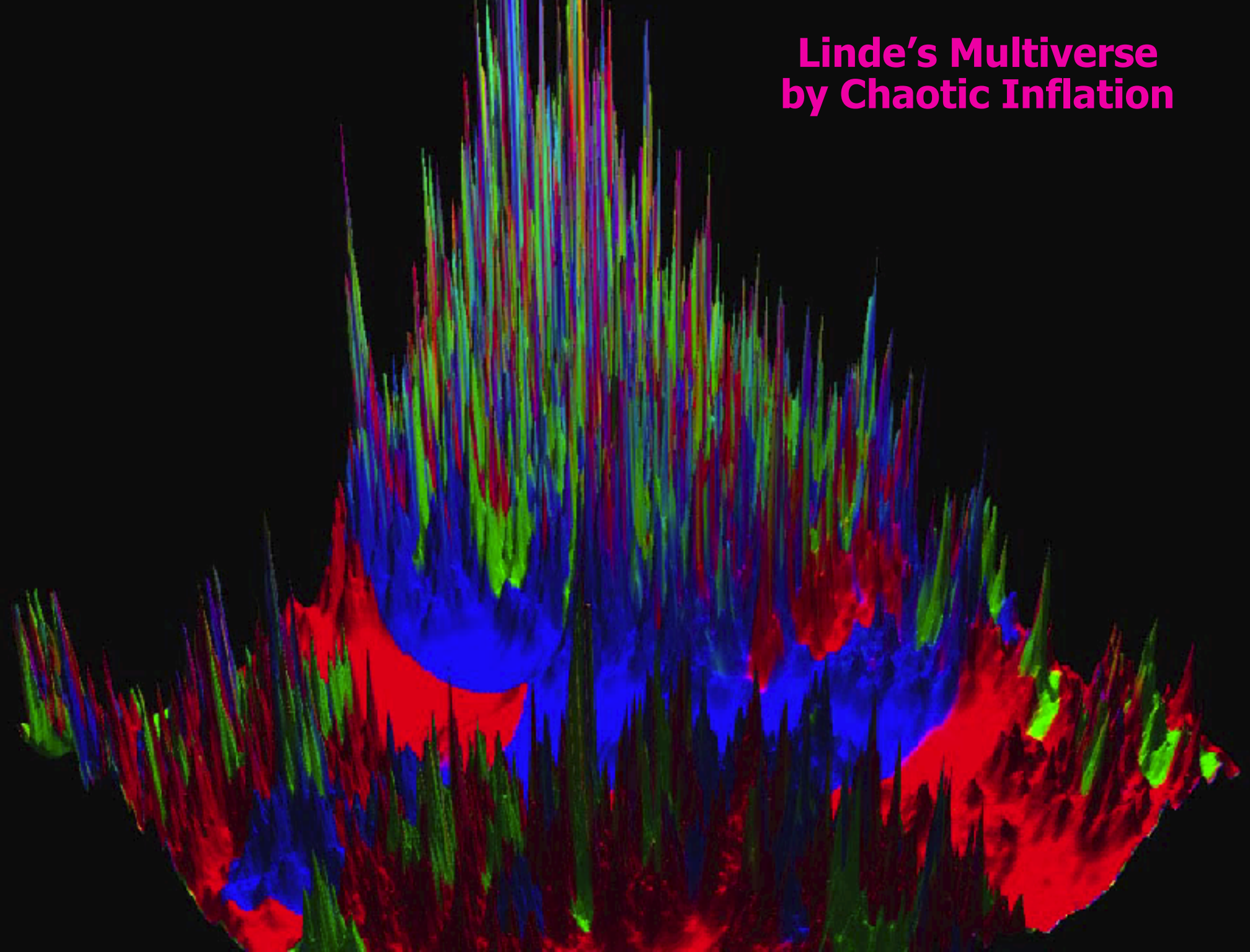
# Cyclic Model

M theory



**Are there more than  
one Universe?**

# Linde's Multiverse by Chaotic Inflation





**There may be ~100 Billion Universes.**

# Summary

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## ➤ Why are we here?

- Endless symmetry breaking → Cosmic evolution
- Extreme fine tuning required.

## ➤ We are so fortunate to be here today.

- Shadow universe?
- Multiverse?

# Welcome to Physics World at UCLA

- Looking for PhD students!
- Feel free to stop by my office any time.
  - Katsushi Arisaka
  - Knudsen 4-145
  - (310) 825-4925
  - [arisaka@physics.ucla.edu](mailto:arisaka@physics.ucla.edu)
- This talk is available at my home page
  - <http://home.physics.ucla.edu/~arisaka/home/>
  - Under “Presentations”