Exploring the Origin of Life and Consciousness by Ultra high-speed Microscopes

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Department of Physics and Astronomy
Why are we here?
The Origin of Universe

- **Big Bang!**
- **First Galaxy formed**
- 1B years
- **Solar System formed**
- 9
- **First life on the Earth**
- 10
- **Plants, Fish...**
- 13
- **Homo sapiens**
- 14

We were born.
Brief History of Universe and Life

Time

0

Big Bang!

1B years

First Galaxy formed

2

Solar System formed

3

First life on the Earth

4

Plants, Fish...

5

Homo sapiens

6

You were born.

7

8

9

Telescopes

10

11

Fossils

12

13

14
~100 Billions Stars in a Galaxy

ANDROMEDA GALAXY
Hubble Deep Field

~100 Billion Galaxies
Red shift up to ~10
Hubble’s Law: Expansion of the Universe

Big Bang!

Sun/Earth

Horizon of Universe

14 Billion Light Years

Moving Away at Speed of Light
The Origin of Universe and Particles

- **Time**
  - 0: Big Bang!
  - 1B years: First Galaxy formed
  - 2
  - 3
  - 4
  - 5
  - 6
  - 7
  - 8
  - 9: Solar System formed
  - 10
  - 11: First life on the Earth
  - 12
  - 13: Plants, Fish...
  - 14: Homo sapiens
  - We were born.

- **Origin of Universe**
- **Origin of Particles**
- **Telescopes**
- **Accelerators**
- **Fossils**
Fermi Lab near Chicago

6km Circumference
1+1=2 TeV
Unification of Forces

- strong force
- electromagnetic
- electroweak
- gravity

Relative strength of force vs. temperature (K)

- 100 GeV
- $10^{15}$
- $10^{16}$ GeV
- $10^{19}$ GeV
- $10^{29}$
- $10^{32}$

Planck Epoch
Physicists’ View of Early Universe

Fiat lux
Let there be light
Physicists’ View of Early Universe

Lorentz Invariance
Local Gauge Invariance
Structure of DNA
Symmetry Breaking

Simple

Symmetry Break Down

Complex

Time
0
1B years
2
3
4
5
6
7
8
9
10
11
12
13
14

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Everything was the same ↔ Perfect symmetry.
- All the particles are the same as photons.
- All four forces are the same.

The Universe was 10 dimension.
CERN and LHC in Geneva

27km Circumference
7+7=14 TeV
LHC Tunnel with Magnets
The Biggest Experiment Ever
(And It’s European)

The new CERN collider in Geneva
First Event at LHC – Recreation of the Big Bang!  (Nov 7, 2009)
The Four Largest Mysteries in Nature

Time
- 0: Big Bang!
- 1B years: First Galaxy formed
- 2: Solar System formed
- 3: Origin of Life
- 4: Origin of Universe
- 5: Origin of Particles
- 6: Origin of Conscience
- 7: Telescopes
- 8: Microscopes
- 9: Plants, Fish...
- 10: First life on the Earth
- 11: Homo sapiens
- 12: You were born.

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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 ↔ Microscope

- Take advantages of the state of art “Photon Detectors” in particle physics.
Origin of Life
Organic Polymers (4.5B → 4B years)

- Organic monomers from space
- Organic polymers
- Inorganic molecules from Earth
RNA Word  \( (4B \rightarrow 3.5B \text{ years ago}) \)


2. RNA molecules become self-replicating.

3. Membrane-enclosed pre-cells arise.

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

- Cell made by proteins
- Gene made by DNA

- Microfilaments
- Mitochondria
- Lysosome
- Peroxisome
- Centrioles
- Microtubules
- Smooth Endoplasmic Reticulum
- Golgi Apparatus
- Cilia
- Rough Endoplasmic Reticulum
- Ribosomes
- Nucleus
- Nuclear Pores
- Nuclear Envelope
- Plasma Membrane
- Chromatin
- Chromosome
- DNA
- Histone

- Up to ~2 m long
- 2 nm wide
- 10 – 50 µm
What is Life?

- Emergent Property
  - Strongly-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
The H33D detector attaches to a standard fluorescence microscope. It will permit to track multicolor qdot-labeled proteins in live cells virtually background-free.

January 2006

Shimon Weiss (Chemistry)

Nano Technology

Particle Physics Detector

Single Molecule Imaging

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Emission of Quantum Dot

Shimon Weiss (Chemistry)

Wavelength (nm)

2.1nm CdSe 4.6nm InP InAs
Protein Folding by single pair Förster Resonant Energy Transfer (spFRET)

$[\text{GdCl}] = \text{Conformational Coordinate}$

G = Energy

R = Reaction coordinate

Unfolded

Intermediate

Native

Shimon Weiss (Chemistry)
Förster Resonant Energy Transfer (FRET)

nm $\rightarrow$ nsec
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

The graph shows the quantum efficiency of UBA, GaAsP, and GaAs as a function of wavelength (nm). The quantum efficiency is plotted on a logarithmic scale from 1 to 100. For GaAsP, it is highlighted with a box and marked with "50% QE."
True photon counting

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

Output Pulse Height

Frequency

1, 2, 3, 4, 5, 6 Photo-electrons
Decay Time Measurement by HAPD

\[
\text{FWHM}_{\text{IRF}} = 210 \text{ ps} \\
\tau_{\text{FITC}} = 3.94 \text{ ns}
\]

Time Resolution = 80 psec

Pulse Shape

FWHM = 1.5 ns

Decay Time

No after pulse
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

Sample

objective

CCD + FADC (10 – 50 MHz)

CMOS [ FADC (50 MHz) * 100 ]

Confocal

Sample

objective

Pinhole

PMT + FADC (10 – 50 MHz)

[ HAPD + FADC (1 GHz) ] * 64
Block Diagram of Multi-beam Confocal Microscope

- **Fiber Bundle Encoder Box**
- **64 ch Photon Detector**
- **Pre Amp**
- **FADC**
- **FPGA**
- **Memory**
- **10 TB RAID**
- **xyz Beam Scanner**
- **Objective Lens**
- **Sample Scanner**
- **Ti:Sa Laser**
- **Beam Splitter**
- **Dichroic Filter Box**
- **4 ch Digitizer x 16**
- **4 ch DAQ System x 16**
- **CPU**
- **Timing Position Controller**

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Micron 1.3M-Pixel CMOS Sensor

2 μsec/row
2 msec/frame

(10 bits, 66MHz)
### Photron SA-5 CMOS Camera

#### Frame Rate vs. Maximum Resolution

<table>
<thead>
<tr>
<th>Frame Rate (fps)</th>
<th>Maximum Resolution Horizontal</th>
<th>Maximum Resolution Vertical</th>
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<tr>
<td>1,000,000</td>
<td>64</td>
<td>16</td>
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</tbody>
</table>
Gold nano particle (40nm) attached to Transferrin Receptor (TfR) on Cancer Cell

Manuel Penichet (Oncology), John Miao (Physics)
Mean Square Displacement $<r^2>$ of TfR on a Human Multiple Myeloma Cell vs. Time

Type A

Type B

Brownian Motion

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Campus-wide Collaborations on High-Speed Bio-imaging

California Nano Systems Institute (CNSI, Laurent Bentolila)

Dept. of Physics & Astronomy (Dolores Bozovic, John Miao, Mayank Mehta)

Dept. of Electrical Engineering (Bahram Jalali)

Dept. of Chemistry & Biochemistry (Shimon Weiss)

Industrial Partners (Hamamatsu Photonics, Photron, Leica)

Dept. of Surgical Oncology (Manuel Penichet)

Dept. of Neurology & Neurobiology (Carlos Portera-Cailliau, Jack Feldman, Tom Otis, Andrew Charles)

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

4D Nano Biophysics

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Image Intensified CMOS Camera

Photron

MCP (Micro Channel Plate)

CMOS Camera (> 1,000 frame/sec)

GaAsP Photocathode (50% QE)

Multi-channel High-speed Digitization
MCP (Micro Channel Plate)

Gain = 100 - 1000

(5 – 10 μm φ)
**FocusScope SV200-i**

Designed specifically for high speed microscopy, the *FocusScope SV200-i* incorporates the latest Generation III image intensifier technology to offer enhanced image resolution and broad spectral response.

Providing recording rates of up to 2,000 fps at 512x512 pixel image resolution the FocusScope SV200-i utilizes the high resolution performance and broad spectral response of Generation III image intensifier technology to provide an integrated imaging solution for high speed microscopy applications.

To obtain the highest optical efficiency the FocusScope SV200-i camera head incorporates a 512x152 pixel advanced CMOS imaging sensor fiber optically coupled to a 18mm Generation III image intensifier module. The camera head provides a C-mount thread for attachment to standard optical microscopes and objective lenses. Image intensifier controls are conveniently located on the camera head.

A single 6 meter cable connects the SV200-i camera head to a standard PCI format control card. Incorporated on the control card is 2.6GB recording memory allowing a recording time of 8.2 seconds at 1,000 fps with 512x512 pixel image resolution.

System control is achieved through Photron FASTCAM Viewer software providing an intuitive operation environment. FASTCAM SDK software provided with the system allows user specific control commands to be integrated within other environments.

**FEATURES**

- System designed for extreme low light fluorescence and microscope recording at high frame rates.
- Advanced CMOS imaging sensor offering 512 x 512 pixel image resolution at frame rates up to 2,000 frames per second.
- 10 bit sensor dynamic range.
- Global electronic shutter providing exposure durations from 1/frame rate to 4μs independent of frame rate.
- Extreme light sensitivity provided through a fiber optically coupled Generation III high resolution image intensifier. [luminous gain 2.2 x 10^4 (lm/m^2)/lx]
- GaAsP photocathode providing broad spectral response over the range 280 – 720nm (peak sensitivity 530nm).
- Intensifier over brightness protection through phosphor surface current detection.
- Small and lightweight camera head suitable for integration with standard optical microscopes.
- User selectable Start, Centre, End and Manual trigger modes.
- Integrated system operation through FASTCAM Viewer control software and FASTCAM SDK.
Yokogawa CSU-X1

2,000 fps

Confocal Dual Spinning Disk

ICMOS Camera
High-speed Confocal Microscope with ICMOS at CNSI (1,000 frame/s)

ICMOS Camera (Photron SV200i)

EMCCD Camera (Ando iXon 897)

Leica Microscope

Confocal Spinner (Yokogawa CSU-X1)

Laurent Bentolila (CNSI)
Imaging Flow Cytometer by Planar Illumination

Speeding up evolution of life by accelerating mutations.
Origin of Consciousness
Brain

100 Billions Neurons

Universe

100 Billions Galaxies

Ca^{2+} Signal in cultivated Rat’s Brain by Confocal Microscope

Andrew Charles (Neurobiology)
Neural Networks for Breathing

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

Nature by Naohiro Koshiya (1999)

Jack Feldman (Neurobiology)
High-speed Ca$^{2+}$ Imaging of pre-Botzinger Cells of Rats

Jack Feldman (Neurobiology)

1,000 frame/sec
Sensory Input and Decision Making in Brain

Sensory (afferent) Neurons → Sensory Input → Integration → Motor Output

Peripheral nervous system (PNS) → Central nervous system (CNS)

Sensory receptor → Motor (efferent) Neurons → Effector

Brain and spinal cord

Interneurons

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Anatomy of Inner Ear

Human auditory system

Cross-section of the cochlear

Hair bundle

Molecular mechano-transduction machinery

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

Dolores Bozovic, Lea Fredrickson (Physics)

1,000 frame/sec

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UCLA Fast Bio-Imaging Group

How can I recognize a woman so far away?

- Genetically encoded?
- Learning and memory?
Nature vs. nurture

Nature

Nurture

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The Cerebral Cortex

Conscious

Unconscious

Thalamus

Subcortical areas
Assembly of rat’s cortical circuits during development

How/when do neurons establish networks? ➔ Symmetry Breaking

Carlos Portera-Cailliau (Neurology)
Spatio-Temporal Excitation-Emission Multiplexing (STEM) Microscope

4 Beams
240 frame/sec

Ultrafast laser

80 MHz
(100 fs pulse)

Beamlet delay

Relay lenses

Closed-loop scanning mirror
1 kHz

Resonant scanning mirror
16 kHz

Emission dichroic mirror

Oculars

Excitation dichroic mirror

Piezoelectric objective scanner

Microelectrode micromanipulator

HAPD #1

HAPD #2

Stage, sample, anesthesia and heating blanket

Adrian Cheng (Physics)

Single beam

Histogram

Oscilloscope

Spatio-temporally multiplexed MMM

12 ns

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In vivo calcium imaging of neuronal activity
3D Structure of Barrel Cortex of Mouse

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

Sulforhodamine 101 labeled astrocytes (orange)

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

Glass microelectrode for dye injection and electrophysiology
- cell-attached voltage follower
- whole-cell voltage/current clamp
- $10^{15}$ Ohm input impedance, < 150 fA input current bias

150 µm deep

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

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In vivo calcium imaging with STEM

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)

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In vivo calcium imaging with STEM

Barrel Cortex Layer 2/3
150 µm deep

After averaging (x3 faster than real)

58 neurons (~100 billons neurons in our brain)
In vivo calcium imaging of layer 2/3 neurons in barrel cortex with STEM

Arisaka, UCLA
Adrian Cheng (Physics)
3D Structure of Barrel Cortex of Mouse

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
- $10^{15}$ Ohm input impedance, < 150 fA input current bias

90 µm
120 µm
150 µm
180 µm

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)

7/1/2010
Katsushi Arisaka, UCLA
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)

Katsushi Arisaka, UCLA
Future Directions
How can we recognize and memorize the space?

Mayank Mehta (Physics, Neurology)
Activity of (excitatory) pyramidal neurons in CA depends on rat’s position: place cells

Hippocampus has a cognitive map of space

Mayank Mehta (Physics, Neurology)
A mouse running in a Maze of Virtual Reality

David Tank (Princeton)
Virtual Reality Experiment on Awake Rats

Daniel Aharoni
Bernard Willers
Mayank Mehta
(Physics)
Optogenetic Excitation of Neurons

Karl Deisseroth (Stanford)

Excitation by Channelrhodopsin-2 (ChR2)

Inhibition by Halorhodopsin (NpHR)

- Blue light activates ChR2, increasing Na+ and decreasing K+.
- Yellow light activates NpHR, increasing Cl-

Diagram showing the interaction of light with neuronal membranes and the resulting changes in ion concentrations.
Outer world vs. Inner word

- **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
Ca^{2+} Signal in cultivated Rat’s Brain by Confocal Microscope
LCOS (Liquid Crystal on Silicon) for SLM (Spatial Light Modulator)

Hamamatsu

X10468 Head and Controller

LCOS chip inside the Head

Optical Tweezers
Voltage Sensing Dye by FRET

DPA

DiO

Tom Otis (Neurobiology)

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Voltage Sensing Dye

Tom Otis (Neurobiology)
Ca^{2+} Signal in cultivated Rat’s Brain by Confocal Microscope

Photo Excitation

SLM + Voltage Sensing
Summary
The Four Largest Mysteries in Nature

- **Big Bang!**
  - 0 years
  - First Galaxy formed
  - 1B years

- **Origin of Universe**
  - Time: 11 years
  - Origin of Particles
  - Accelerators

- **Origin of Life**
  - Time: 10 years
  - Solar System formed
  - First life on the Earth

- **Origin of Consciousness**
  - Time: 14 years
  - Plants, Fish...
  - Homo sapiens
  - You were born.

- **Microscopes**
  - 12 years

- **Telescopes**
  - 9 years

- **7/1/2010 Katsushi Arisaka, UCLA**
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
“Life” is a complex system in 4 dimensional space-time.
- Emergent property
- Strongly interacting

Countless “spontaneous symmetry breakings” during the evolutinal and developing process of life

Fully controlled experiments by “Virtual Reality” under way.
- Outer world (environment) vs. Inner world (brain)

“Ultra high-speed imaging” may reveal the fundamental principle of the complex life like ours.
- How can life overcome thermal fluctuation?
- Networks in a cell and between cells (neurons)
and thanks to wonderful collaborators!

<table>
<thead>
<tr>
<th>Scientific Objectives</th>
<th>Department</th>
<th>Prime PI</th>
<th>Other Senior Person</th>
<th>Grad Students</th>
<th>Sample</th>
<th>High-speed Microscopes</th>
<th>Funding</th>
<th>Activities</th>
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<tbody>
<tr>
<td>Hair cell motion</td>
<td>Physics &amp; Astronomy</td>
<td>Dolores Bozovic</td>
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<td>Lea Fredrickson</td>
<td>Frog</td>
<td>CMOS</td>
<td>NSF MRI</td>
<td>2007 - Now</td>
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<td>Single Molecule</td>
<td>Chemistry</td>
<td>Shimon Weiss</td>
<td>Xavier Michalet, Ryan Colyer</td>
<td>Daniel Aharoni</td>
<td>Cells</td>
<td>64ch FCS, ALEX</td>
<td>NIH R01</td>
<td>2006 - Now</td>
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<td>TtR tracking on Cancer cells</td>
<td>Oncology, Physics &amp; Astronomy</td>
<td>Manuel Penichet, John Miao</td>
<td>Gustavo Helguera, Jose Rodriguez</td>
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<td>Cells</td>
<td>CMOS, ICMOS</td>
<td>(NSF MRI shared)</td>
<td>2007 - Now</td>
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<td>Neural networks for breathing</td>
<td>Neurobiology</td>
<td>Jack Feldman</td>
<td>Consuelo Morgado</td>
<td>Adrian Cheng</td>
<td>Rat</td>
<td>ICMOS, Confocal</td>
<td>(NSF MRI shared)</td>
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<td>Bernard Willers</td>
<td>Sliced Brain</td>
<td>ICMOS, 2PE</td>
<td>NIH Rec. Act</td>
<td>2009 - Now</td>
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<td>High-speed Imaging Flow Cytometer</td>
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<td>Core facility of High-speed Bio-imaging</td>
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<td>Laurent Bentolila</td>
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<td>CMOS, ICMOS</td>
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<td>2007 - Now</td>
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<td>High-speed Microscope</td>
<td>Leica</td>
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<td>CMOS, ICMOS, 2PE</td>
<td>Microscope discounted</td>
<td>2008 - Now</td>
</tr>
</tbody>
</table>

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Energy Resolution
Energy Resolution ($\sigma/E$)

- **In ideal case:**
  \[
  \frac{\sigma}{E} = \frac{\sqrt{N_\gamma}}{N_\gamma} = \sqrt{\frac{1}{N_\gamma}}
  \]

- **In reality:**
  \[
  \frac{\sigma}{E} = \sqrt{\frac{ENF}{N_\gamma \cdot QE \cdot CE}} + \left(\frac{ENC}{N_\gamma \cdot QE \cdot CE \cdot G}\right)^2
  \]

- $N_\gamma$: Number of incident photons
- $QE$: Quantum Efficiency
- $CE$: Collection Efficiency
- $ENF$: Excess Noise Factor (from Dynodes)
- $ENC$: Equivalent Noise Charge (Readout Noise)
- $G$: Gain
Excess Noise Factor (ENF)

**Definition:**

\[ ENF \equiv \frac{\sigma_{\text{Output}}^2}{\sigma_{\text{Input}}^2} \]

**In case of PMT:**

\[ ENF = 1 + \frac{1}{\delta_1} + \frac{1}{\delta_1 \cdot \delta_2} + \cdots + \frac{1}{\delta_1 \cdot \delta_2 \cdots \delta_n} \]
Energy Resolution of HPD

- HPD can count 1, 2, 3... PE separately.
  - ENF=1.0

- But it is still suffering from poor QE.
  - We can never beat the Poisson statistics!

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<table>
<thead>
<tr>
<th></th>
<th>QE</th>
<th>CE</th>
<th>$\delta_i$</th>
<th>ENF</th>
<th>G</th>
<th>ENC</th>
<th>$\sigma/E$</th>
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<tbody>
<tr>
<td><strong>Ideal</strong></td>
<td>1.0</td>
<td>1.0</td>
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<td>1.0</td>
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<td>$\sqrt{1/N}$</td>
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<tr>
<td><strong>PMT</strong></td>
<td>0.5</td>
<td>0.8</td>
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<td><strong>PD</strong></td>
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<td>-</td>
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<td>200</td>
<td>$\sqrt{1.3/N+(300/N)^2}$</td>
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<tr>
<td><strong>APD</strong></td>
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<td>2</td>
<td>2.0</td>
<td>50</td>
<td>200</td>
<td>$\sqrt{2.5/N+(5/N)^2}$</td>
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<tr>
<td><strong>HPD</strong></td>
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<td>0.9</td>
<td>1000</td>
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<td>$10^3$</td>
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<td>$\sqrt{2.2/N+(1.1/N)^2}$</td>
</tr>
<tr>
<td><strong>HAPD</strong></td>
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<td>0.9</td>
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<td>1.0</td>
<td>$10^5$</td>
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<td>$\sqrt{2.2/N}$</td>
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<tr>
<td><strong>CCD</strong></td>
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<td>-</td>
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<td>1</td>
<td>50</td>
<td>$\sqrt{1.3/N+(60/N)^2}$</td>
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<tr>
<td><strong>ICCD / ICMOS</strong></td>
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<td>0.7</td>
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<tr>
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<td><strong>EBCCD / EBCMOS</strong></td>
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Energy Resolution

![Graph depicting energy resolution for different photodetectors. The x-axis represents the number of photons, and the y-axis represents the resolution as a fraction of Poisson noise. The graph shows curves for PMT, PD, APD, HPD, HAPD, ICCD, CCD, ICCD/ICMOS, EMCCD, and EBCCD/EBCMOS. Each photodetector type is represented by a different line color. The graph illustrates the relative performance of each photodetector across various photon levels.]
sCMOS
Scientific CMOS Technology
A High-Performance Imaging Breakthrough

5.5 Megapixel sCMOS
100 frames/sec

1.3 Megapixel interline
11 frames/sec

sCMOS – 1.5 e^ noise
Interline CCD – 5 e^ noise
ORCA®-Flash 2.8
DIGITAL CAMERA

- Low noise: 3 electrons (r.m.s.)
- High resolution: 2.8 megapixel
- High-speed readout: 45 frames/second (1920 × 1440)
  Up to 1273 frames/second
- High dynamic range: 4500:1