# DIAMOND-BASED TECHNOLOGIES FOR CELL SENSING

Federico Picollo

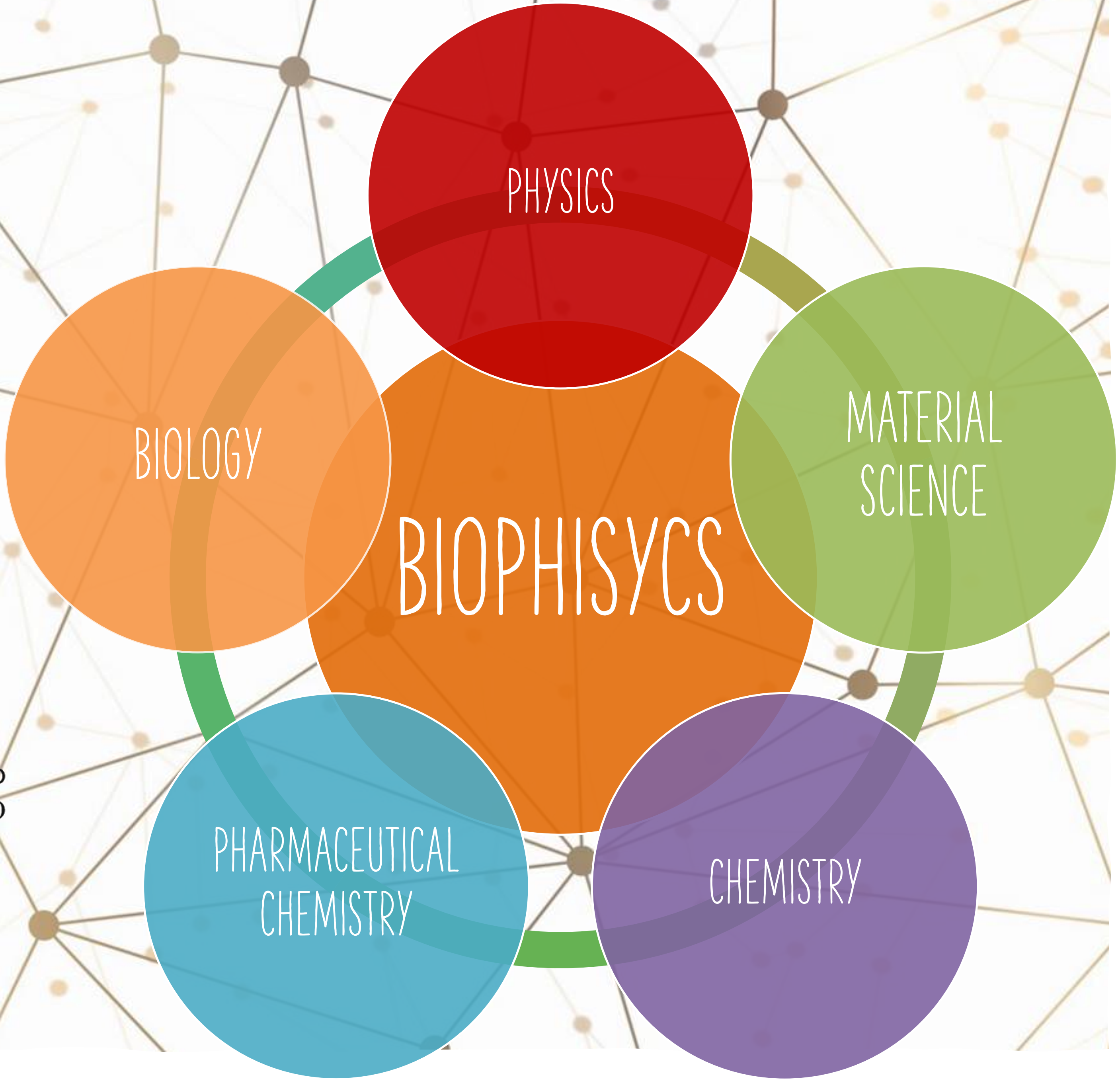
Giornate di Studio sui Rivelatori - Scuola F. Bonaudi e E. Chiavassa 2023, June 26th-30th

# MULTIDISCIPLINARITY


Fisica Torino

DSTF
Dipartimento di Scienza
e Tecnologia del Farmaco
UNIVERSITÀ DI TORINO

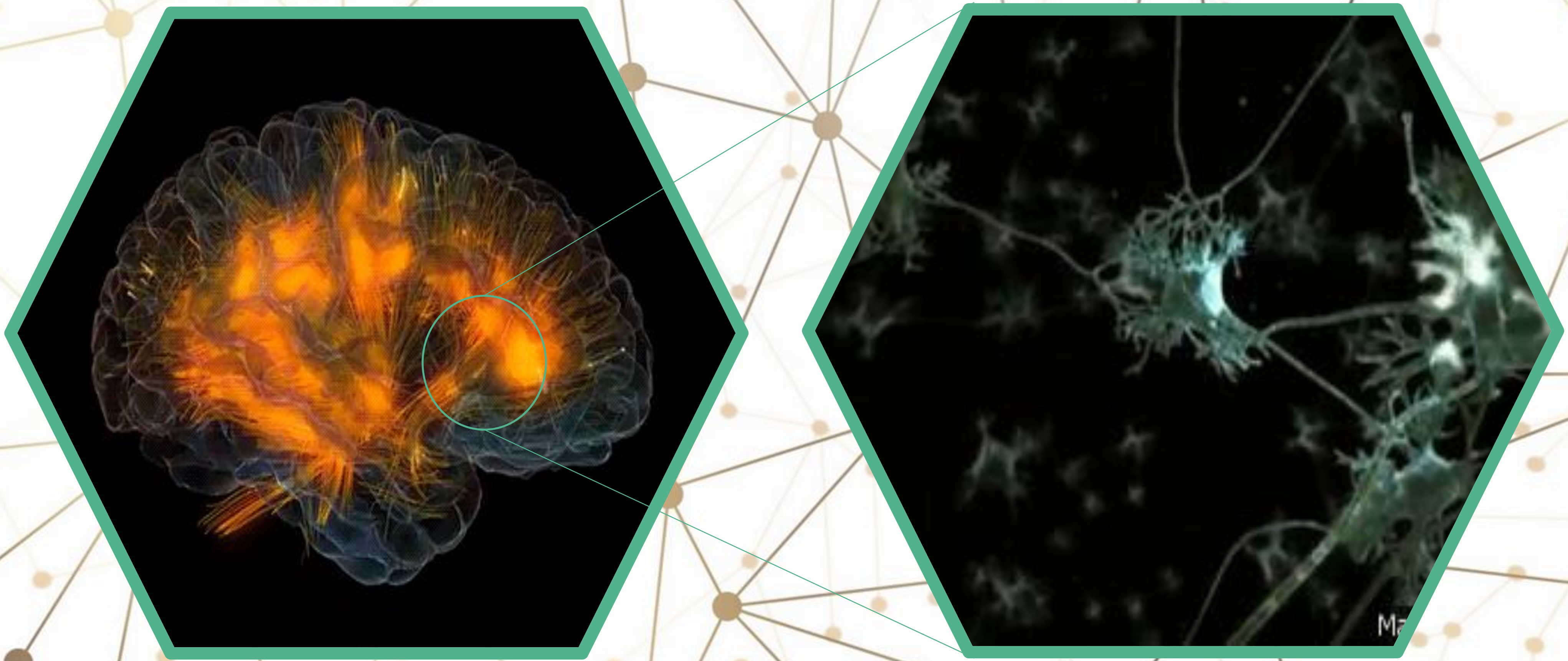
nis



# OUTLINE

- A bit of cell biology… (from a NOT biologist)
- Standard tools for electrophysiology experiments
- Artificial DIAMOND for sensors development
- Some examples of cell signals detection
- Diamond particle detectors
- Radiobiology using diamond-base sensors
- New frontiers: quantum sensing (e.g. intracellular temperature detection)

# BRAIN



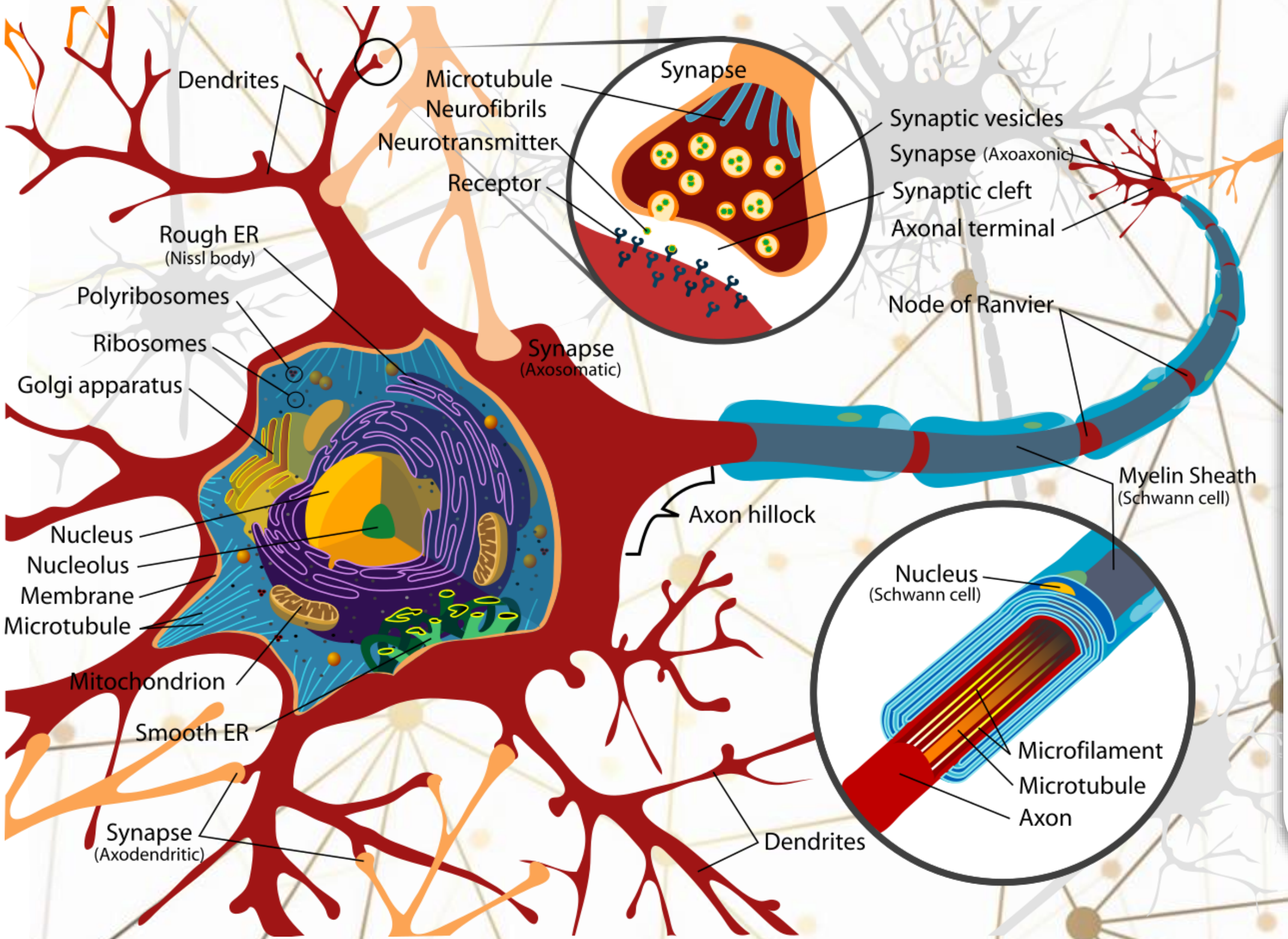
# BRAIN

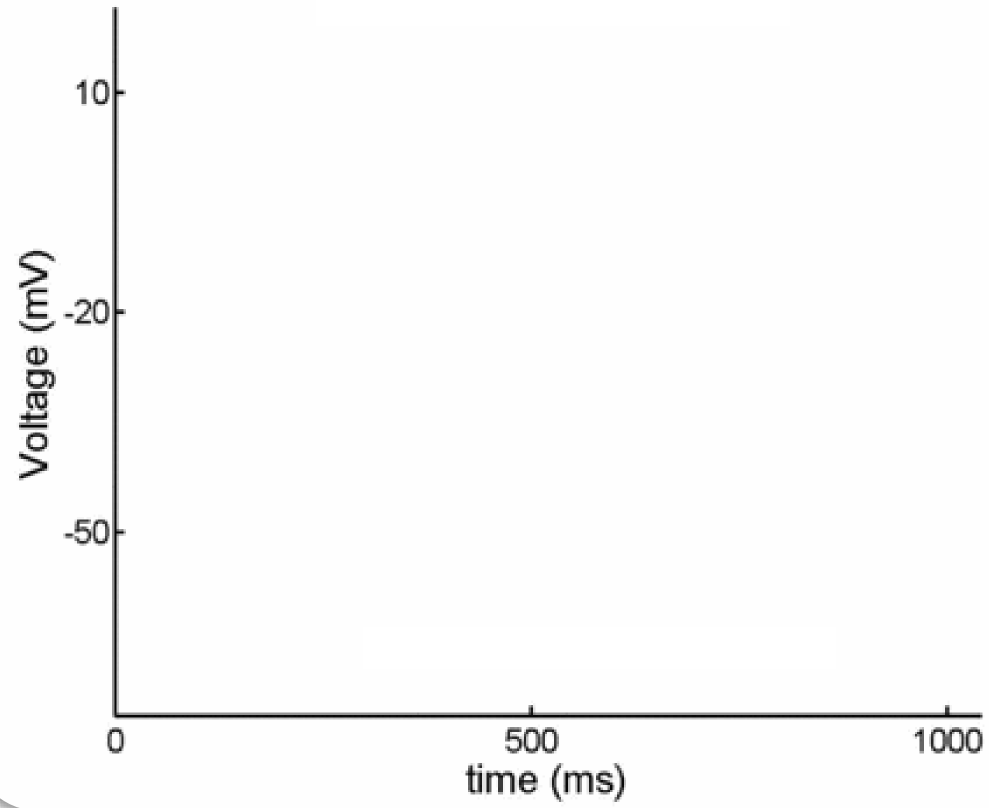
- A synapse can contain on the order of **1000 switches** on a molecular scale
- A typical brain houses between **100/200 billion** (**$10^9$**) nerve cells
- interconnected by between **$10^{13}$ and $10^{15}$ synapses**!

In the Milky Way there are between **100/400 billion ($10^9$)** stars

**There are more synapses than stars in the Milky Way!**

# COMMUNICATION MECHANISM: ACTION POTENTIAL



George Simon Ohm

$V = R \cdot I$

1827

Andrè Marie Ampere

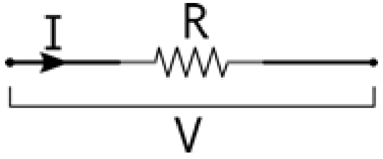
Intensità della corrente elettrica

1820

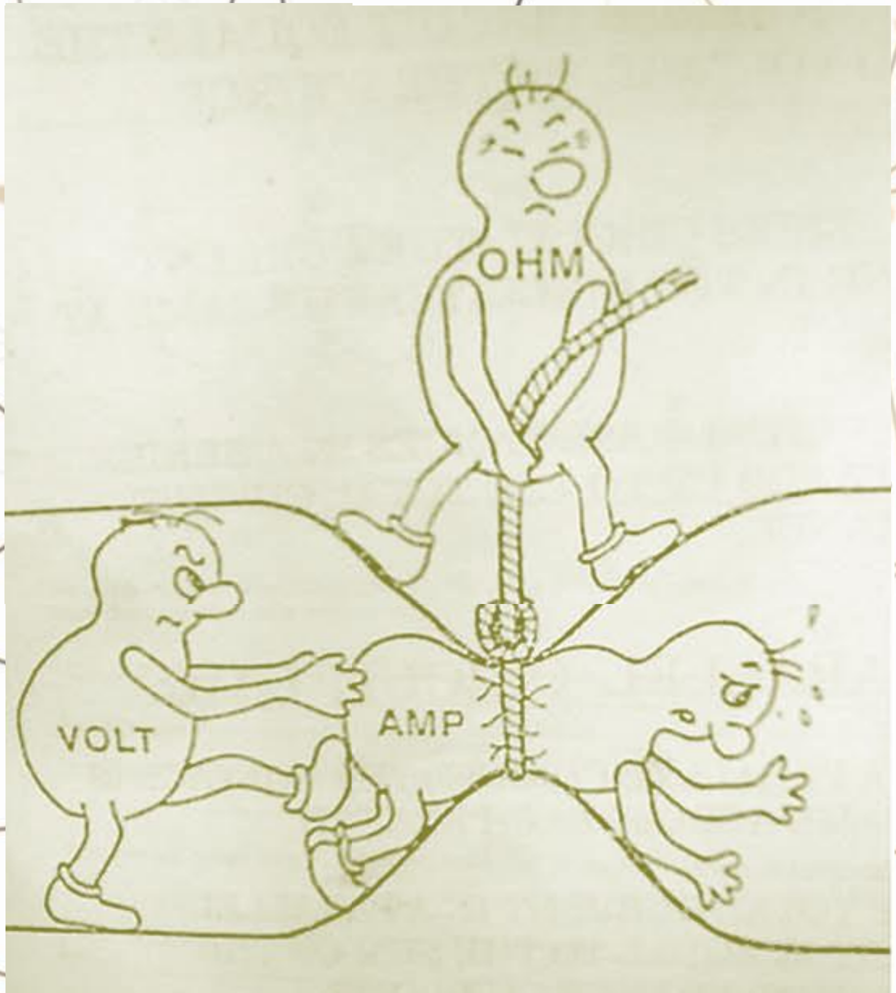
Alessandro Volta

Condensatore

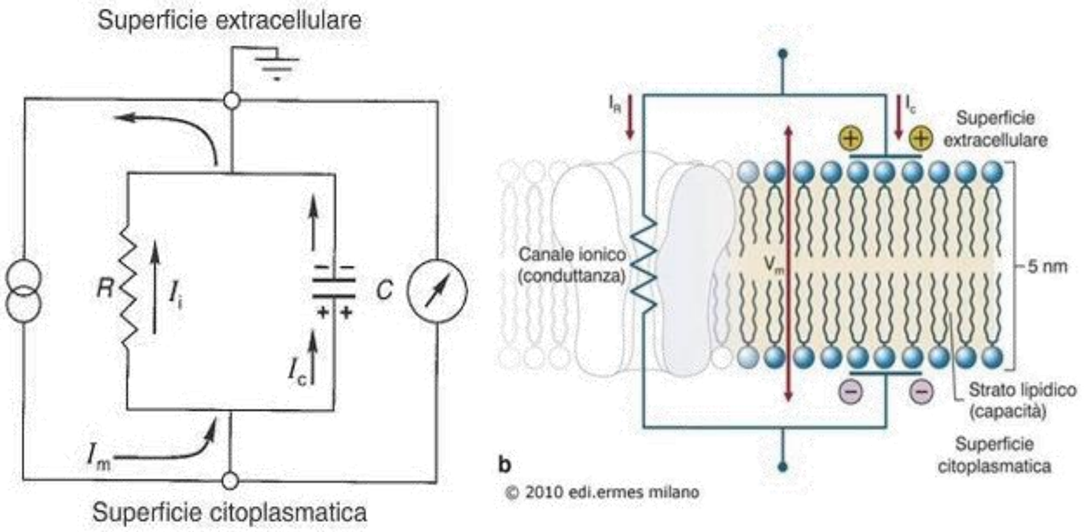
1780

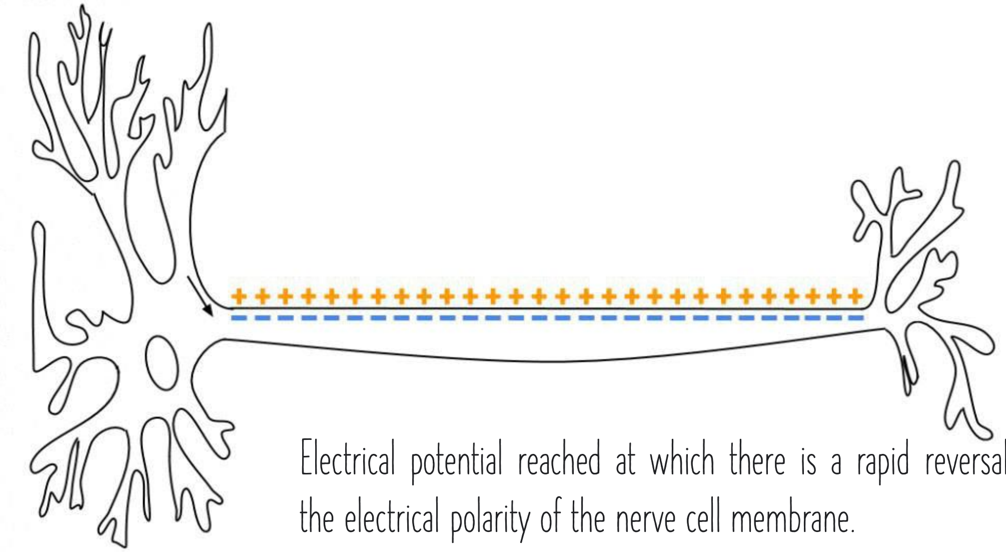



$$R = \frac{V}{I} = \frac{[V]}{[A]} = [\Omega]$$

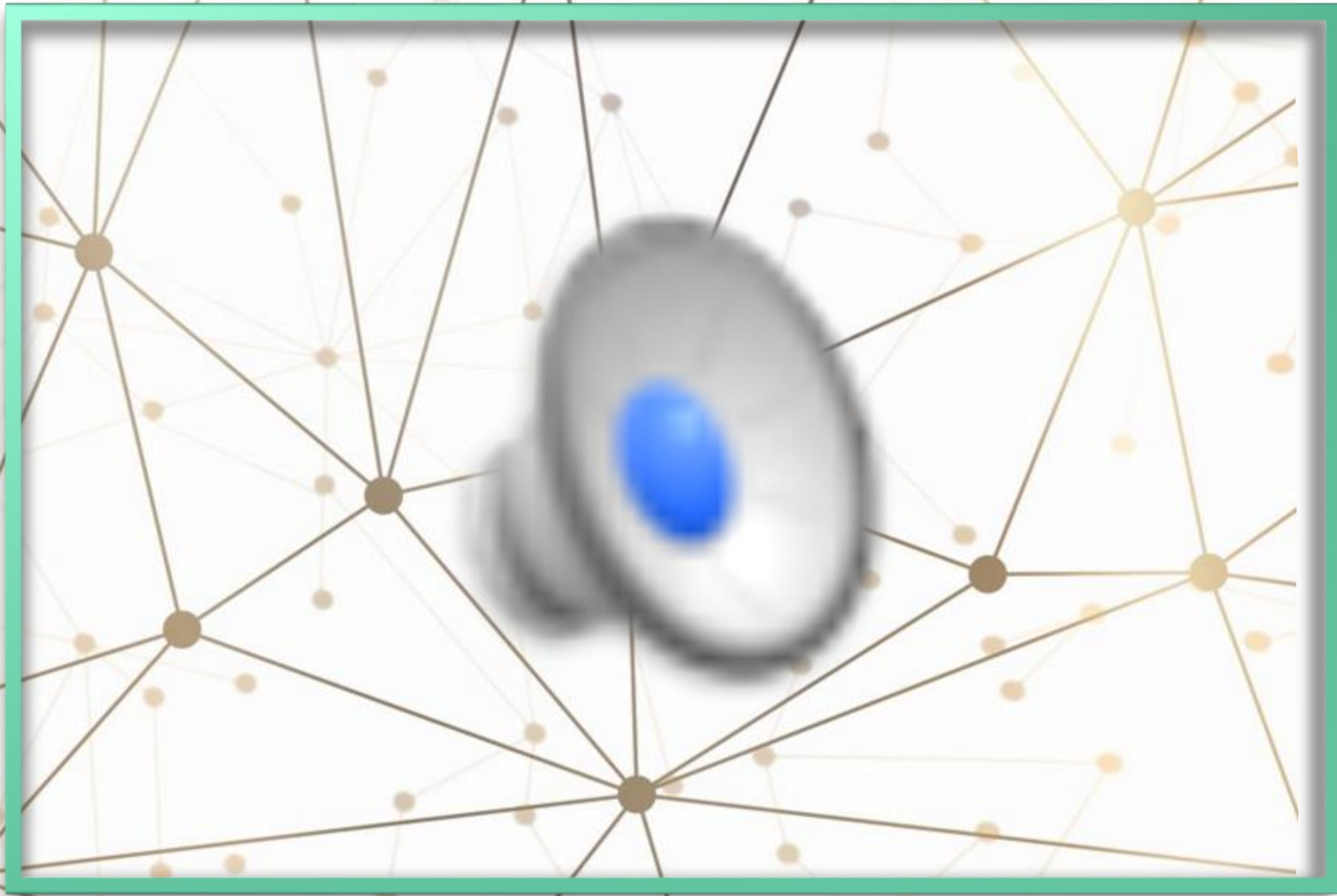


# RC CIRCUIT DESCRIPTION OF CELL MEMBRANE

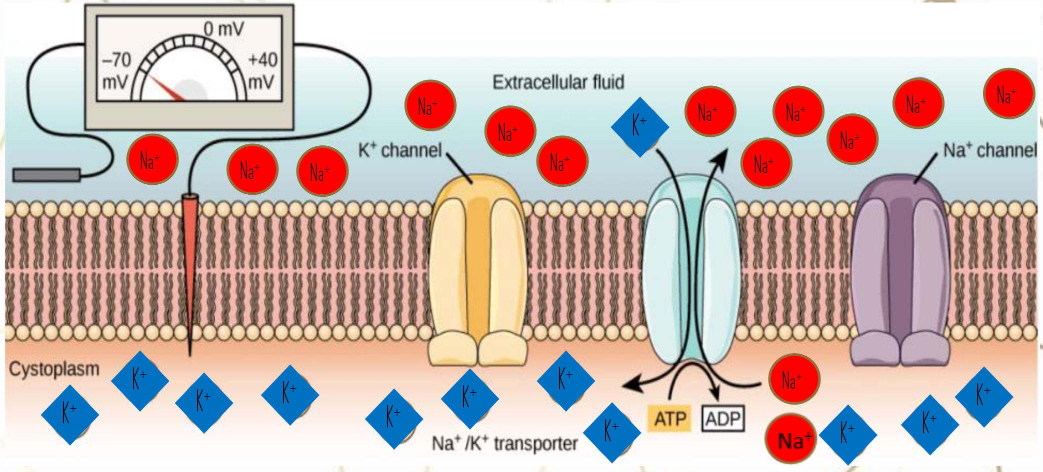


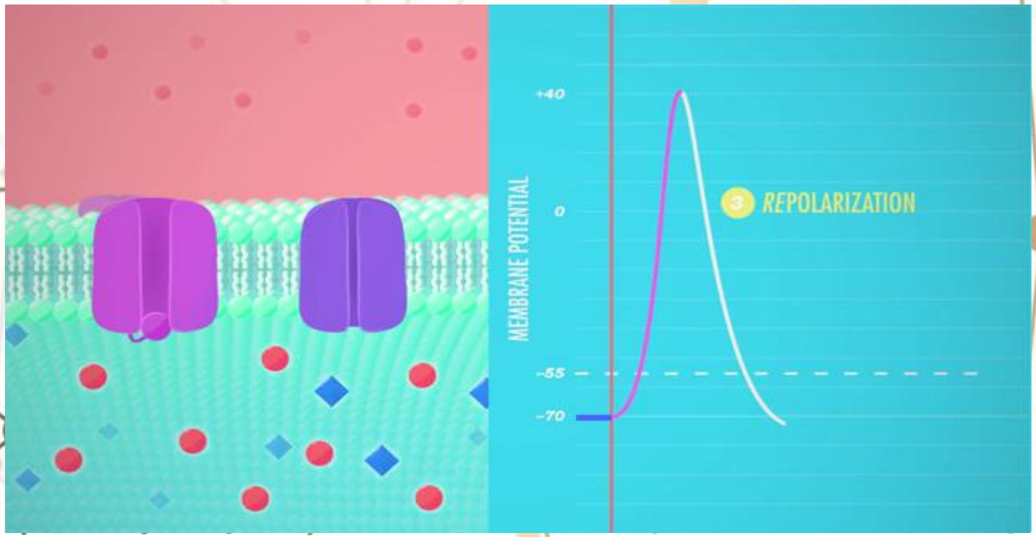



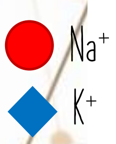
Electrical potential reached at which there is a rapid reversal of the electrical polarity of the nerve cell membrane.

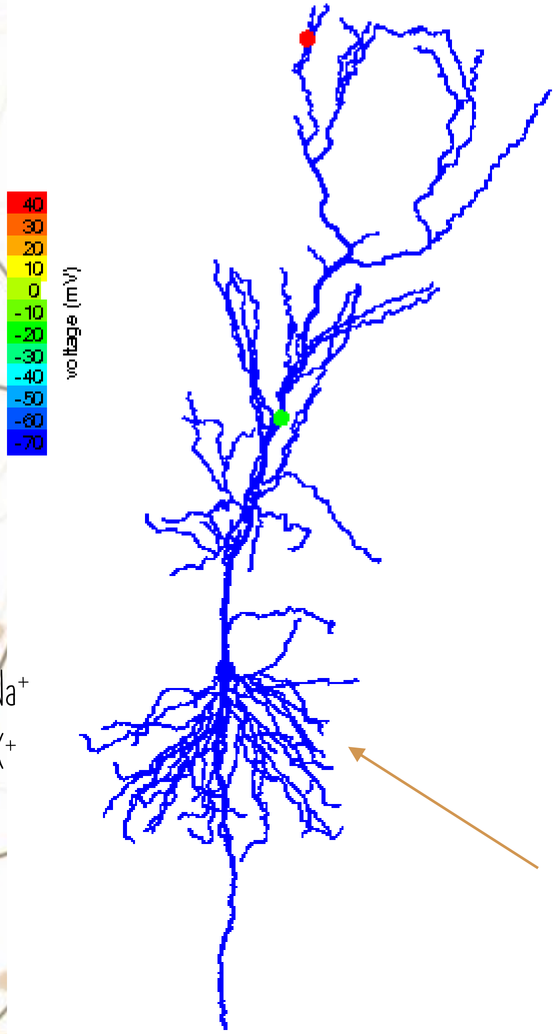


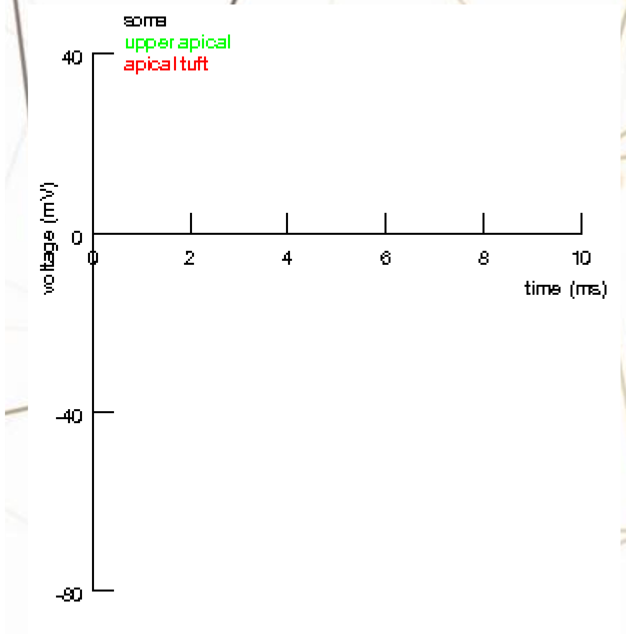
# RC CIRCUIT DESCRIPTION OF CELL MEMBRANE



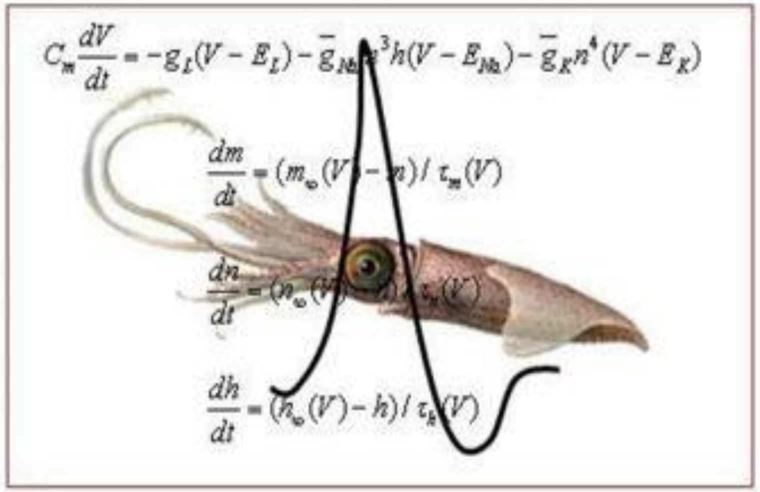




The action potential involves a rapid reversal of ddp, due to the entry of positive ions into the cell through specific proteins that act as channels.

## PHYSIOLOGY NOBEL PRICE
## 1963

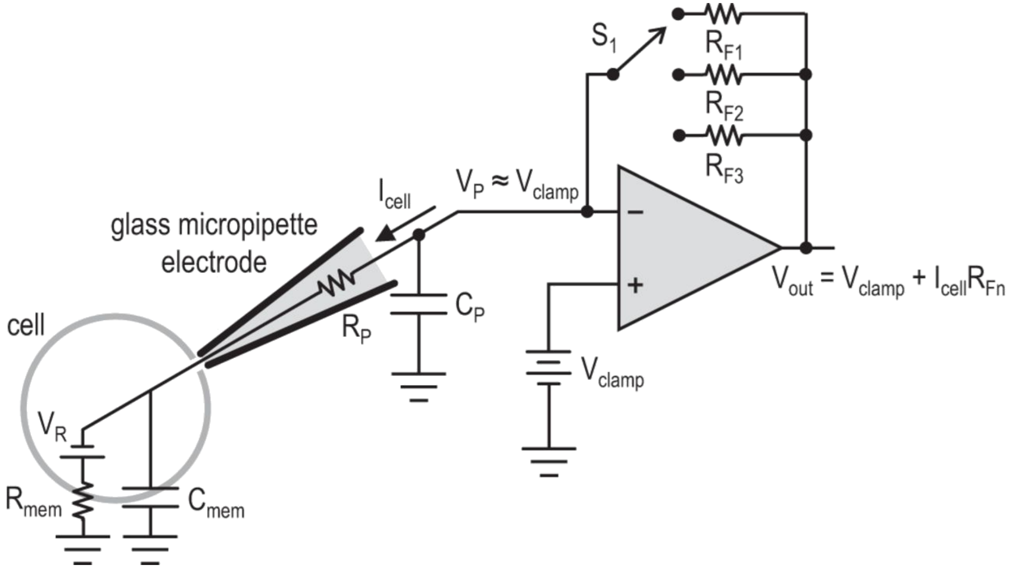
A. Hodgkin



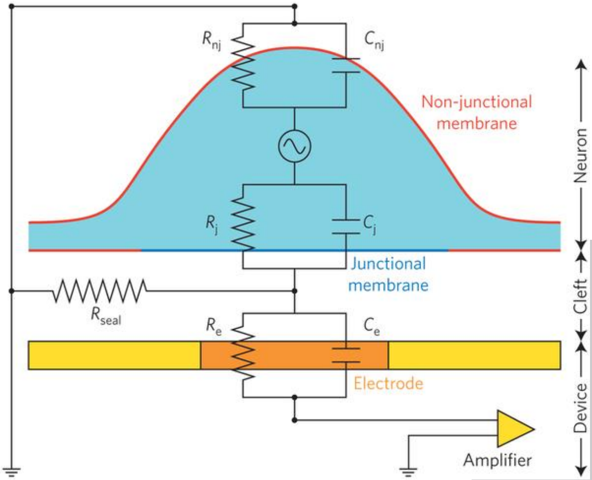

A. Huxley

## PHYSIOLOGY NOBEL PRICE
## 1991

E. Neher

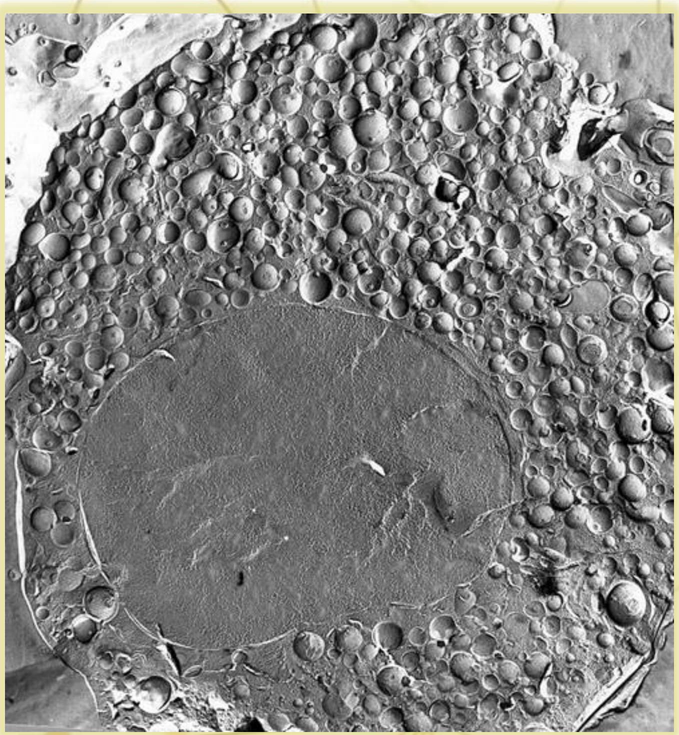



B. Sakmann



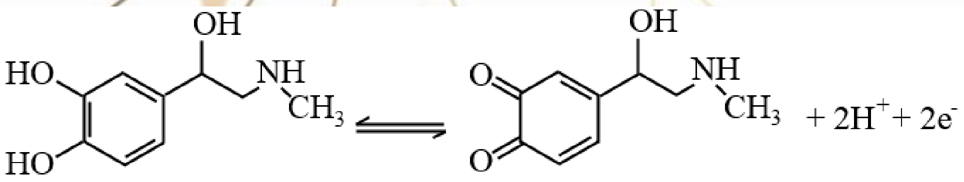

*M.E. Spira & A Hai,*
**Nature Nanotechnology,**
8, 83 (2013)

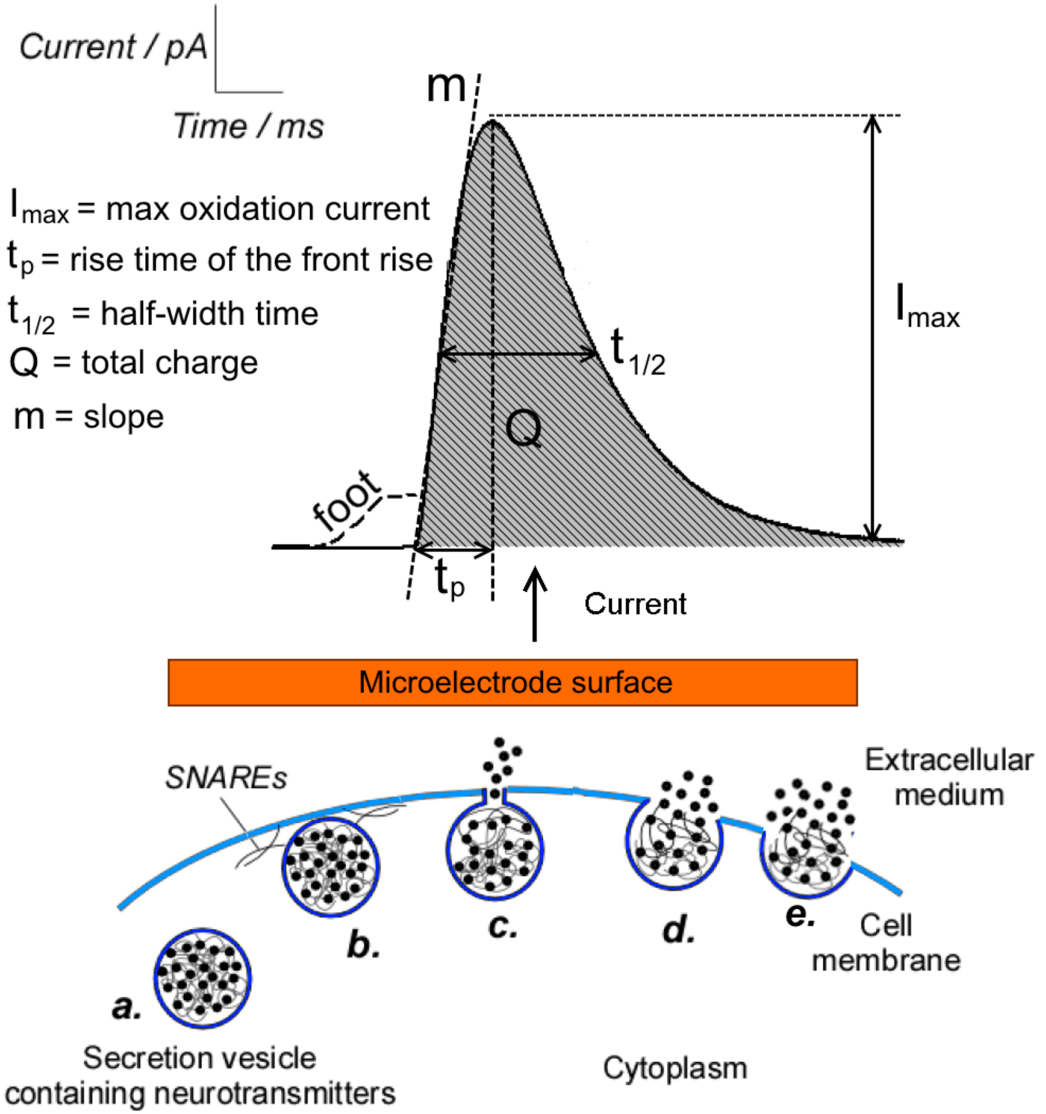
# BIO-SIGNALS DETECTION: EXOCYTOSIS



- **secretion of catecholamines** (adrenaline, noradrenaline, etc.)
- catecholamines are **secreted from vesicles** in which they are highly concentrated → **strong signal**
- secretion from 1 vesicle: 50-100 ms
- **detection of the oxidized species** in correspondence of a biased electrode
- **electrically or chemically stimulated**

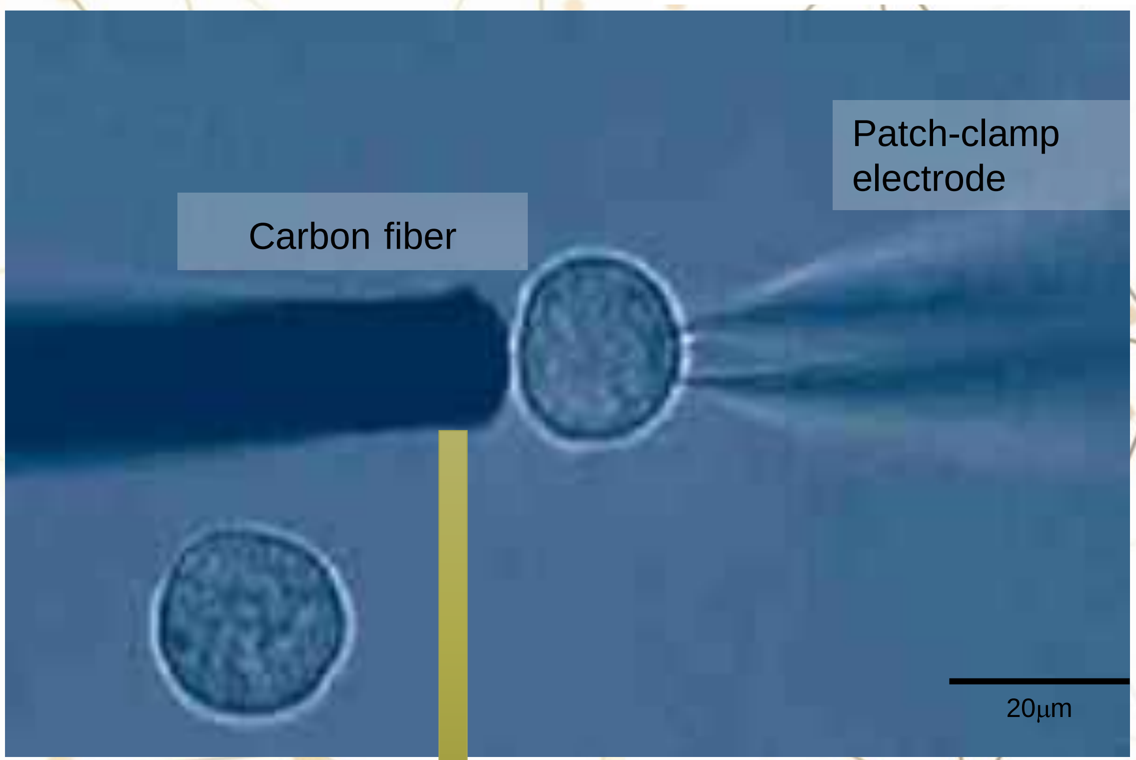
**Adrenaline oxidation**




F. Lema^tre et al., **ElectrochimicaActa**140,457(2014)

# BIO-SIGNALS DETECTION: EXOCYTOSIS

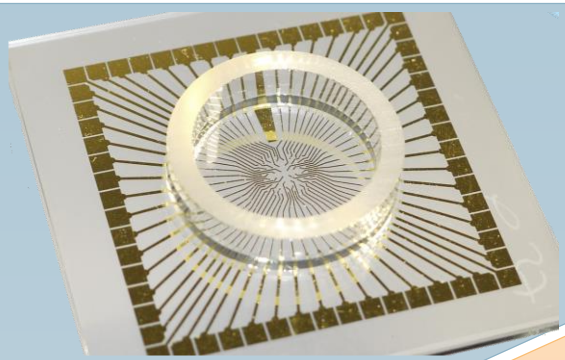



Amperometry (direct measurement)

Capacitance measurement
(indirect measurement)

$$C \propto S$$

# Biosensing on excitable cells



**Standard commercial detector**

→ Multi electrode arrays (MEA) ←

**Detection technique**

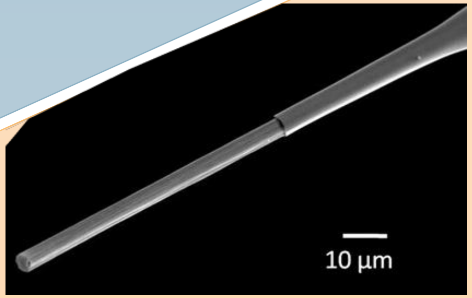
- Potentiometry

**Drawback**

- Only potentiometric measurement

ACTION POTENTIAL

EXOCYTOSIS




**Standard commercial detector**

→ Carbon fiber electrodes (CFE) ←

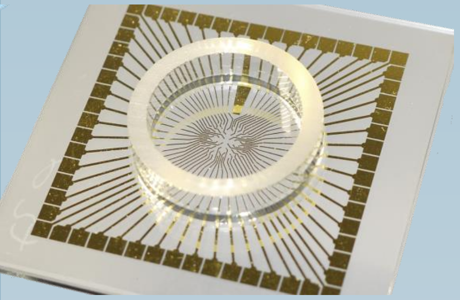
**Detection technique**

- Amperometry

**Drawback**

- One cell measure + only amperometric measurement

# Biosensing on excitable cells



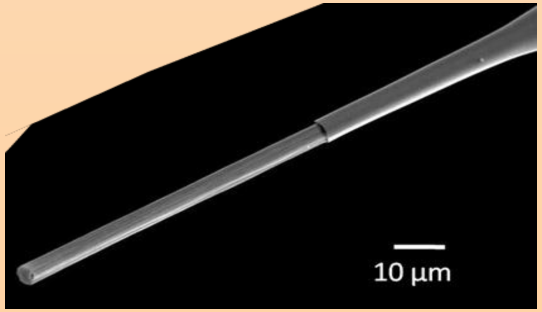
ACTION POTENTIAL

potentiometry

Multi technique
diamond biosensor

amperometry

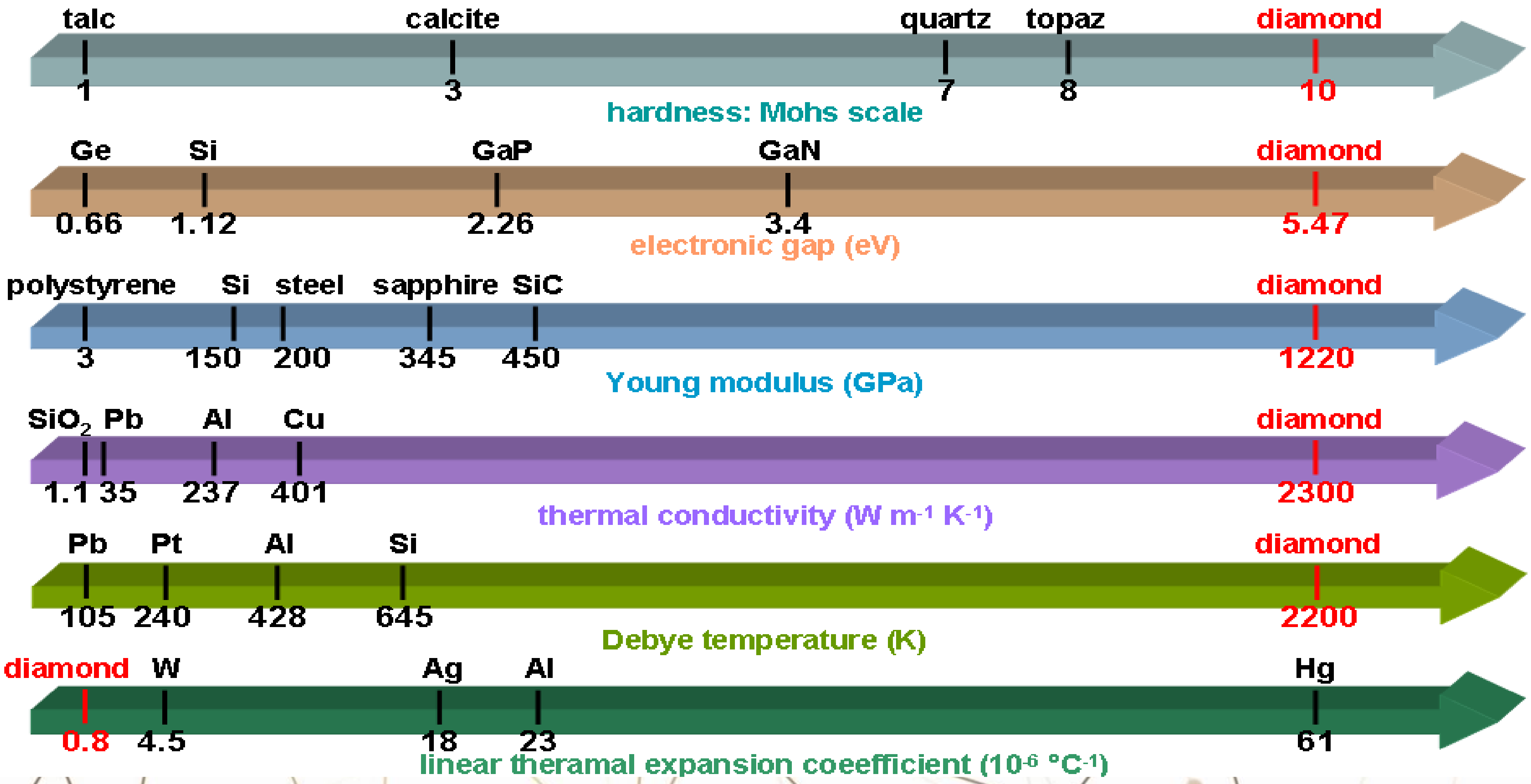
EXOCYTOSIS



# OUTLINE

- ✓ A bit of cell biology… (from a NOT biologist)
- ✓ Standard tools for electrophysiology experiments
- Artificial DIAMOND for sensors development
- Some examples of cell signals detection
- Diamond particle detectors
- Radiobiology using diamond-base sensors
- New frontiers: quantum sensing (e.g. intracellular temperature detection)

# DIAMOND PROPERTIES



# DIAMOND PROPERTIES

*Cellular bio-sensor*

- **bio-compatibility**
- **chemical inertness**
- **optical transparency**

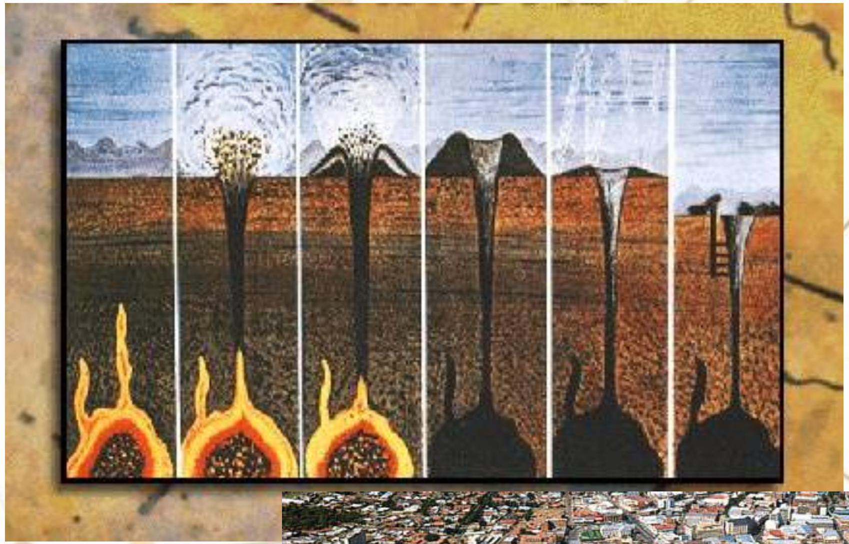
- **diamond synthesis: a mature technology: availability of synthetic monocrystalline samples of high quality (electronic grade)**

- **diamond fabrication: Ion Beam Lithography**

# NATURAL DIAMOND

**In the depths of the earth (lithosphere: 140-190 km below the surface, below relatively stable continental plates):**

- ✓ **pressure: 4.5 – 6 GPa**
- ✓ **temperature: 900 – 1300 °C**



Kimberley Mine, il più grande buco nella terra

The transport of diamonds to the earth's surface occurs through volcanic eruptions that originate particularly deep underground.

Magma does not transport diamonds directly, but the rocks within which they have formed at depth (xenoliths).

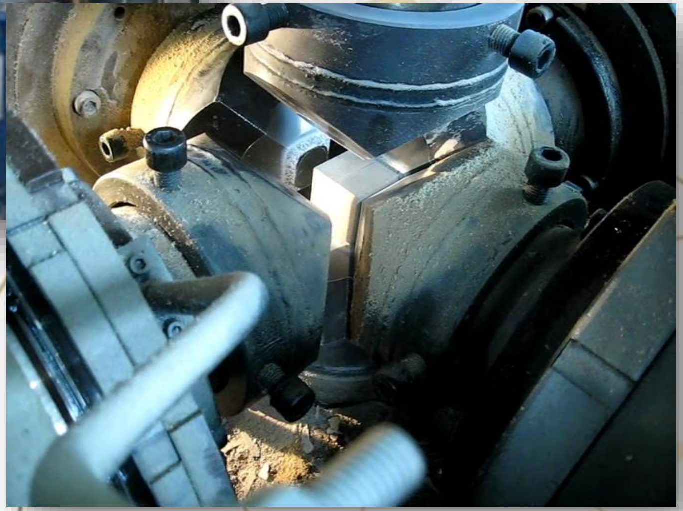
**Primary sources**: volcanoes
**Secondary sources**: sites where diamonds are eroded out of the rocks that contain them (kimberlite, lampronite)

# ARTIFICIAL DIAMOND : "HPHT"


**Pressa per la sintesi del diamante artificiale**

**© Kobelco, anni '80**

**Temperatura 3000 °C**
**Pressione 3.5 GPa**



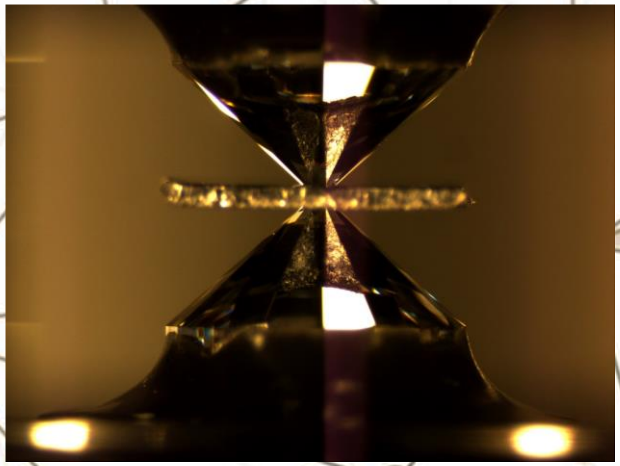
In 1941, the US companies General Electric, Norton and Carborundum entered into an agreement to develop the artificial synthesis of diamond.

In the following years, World War II interrupted the experiments.

The experiments resumed in 1951 at General Electric.

The first systematic and commercially viable synthesis of artificial diamond is achieved on 15 December 1954 and announced on 14 February 1955.

The presses used were an improvement on the first machines developed by Percy Bridgman, winner of the 1946 **Nobel Prize** for his studies of the physics of high pressures.

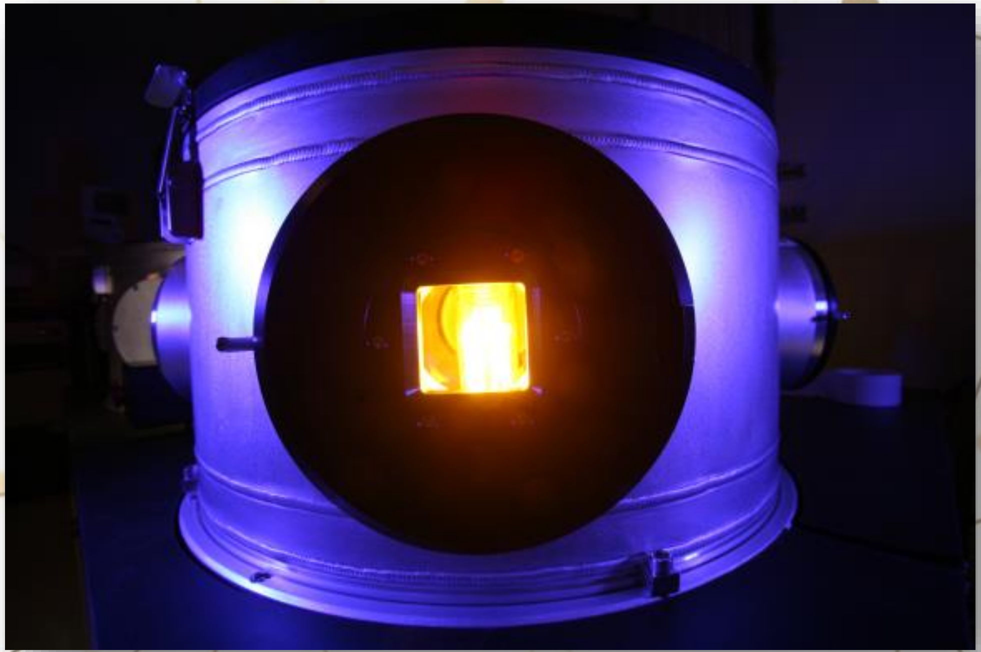


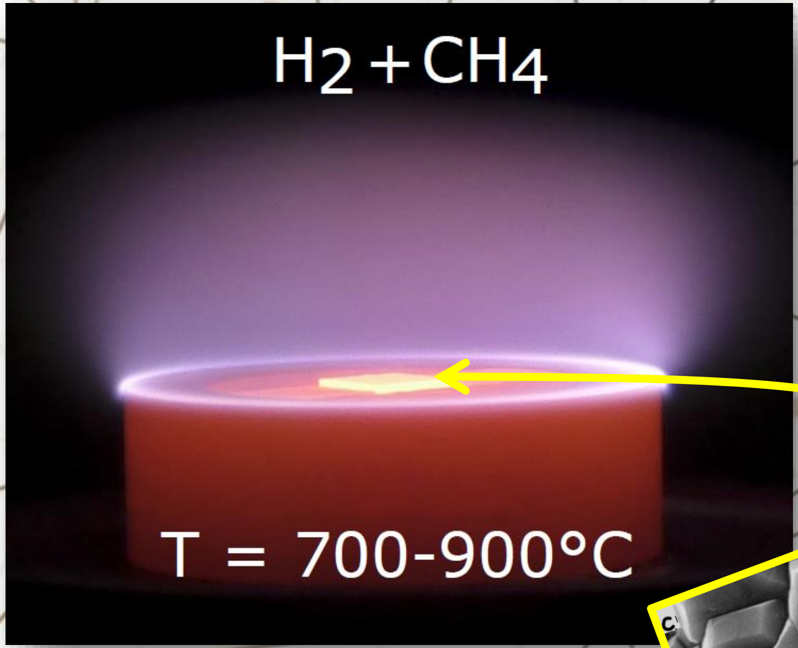
***P. Bridgman, 1882-1961***

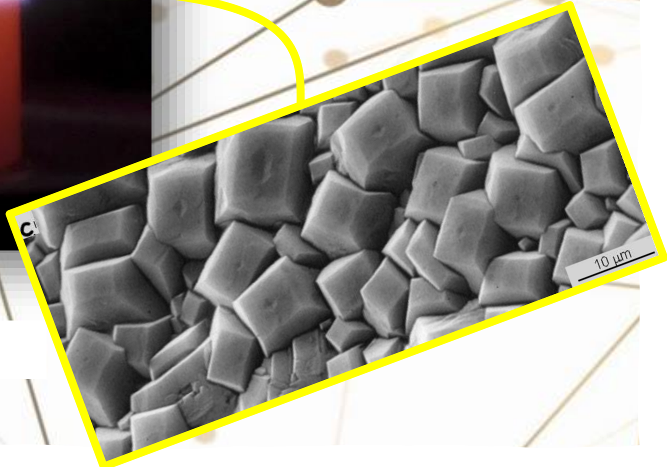
# ARTIFICIAL DIAMOND : "CVD"

A (surprising) alternative to high pressure and temperature production:very low pressure and (relatively) low temperature

**Vapour phase deposition (CVD)**






**CVD: 'condensation' of carbon in diamond form from a 'hot' plasma to a 'cold' substrate**

# ARTIFICIAL DIAMOND : "CVD" SHOPPING

elementsix™
DE BEERS GROUP

Diamond Materials
Advanced Diamond Technologies

**SC Plate CVD 4.5x4.5mm, 0.50mm thick, P2**

General
Single Crystal

145-500-0055

**$265.00**

ADD TO CART | VIEW

**Large Area SC Plate CVD 6.0x6.0mm, 1.2mm thick, P2**

General
Single Crystal

145-500-0218

**$2,155.00**

ADD TO CART | VIEW

ELSC™ Series

**EL SC Plate 2.0x2.0mm, 0.50mm thick**

Quantum / Radiation Detectors
Single Crystal

145-500-0385

**$865.00**

CONTACT TO PURCHASE

VIEW

ELSC™ Series

**EL SC Plate 4.5x4.5mm, 0.50mm thick**

Quantum / Radiation Detectors
Single Crystal

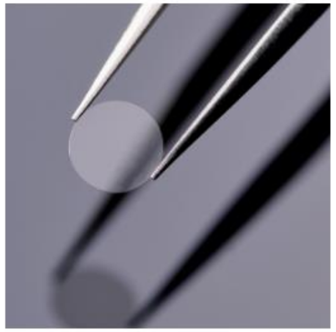
145-500-0390

**$2,825.00**

CONTACT TO PURCHASE

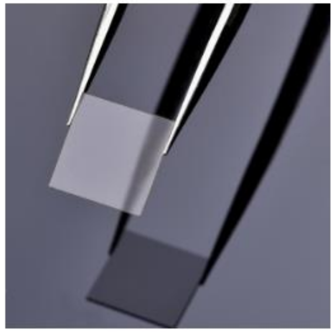
VIEW

CVD diamond plate, polycrystalline, polished, 4x4 mm
**€80.00**



CVD diamond disk, polycrystalline, polished, Ø = 5.0 mm
**€95.00**

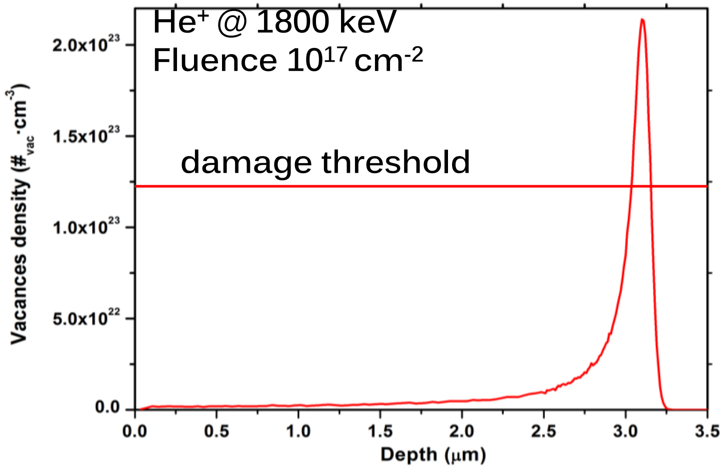
CVD diamond disk, polycrystalline, polished, Ø = 10.0 mm
**€480.00**

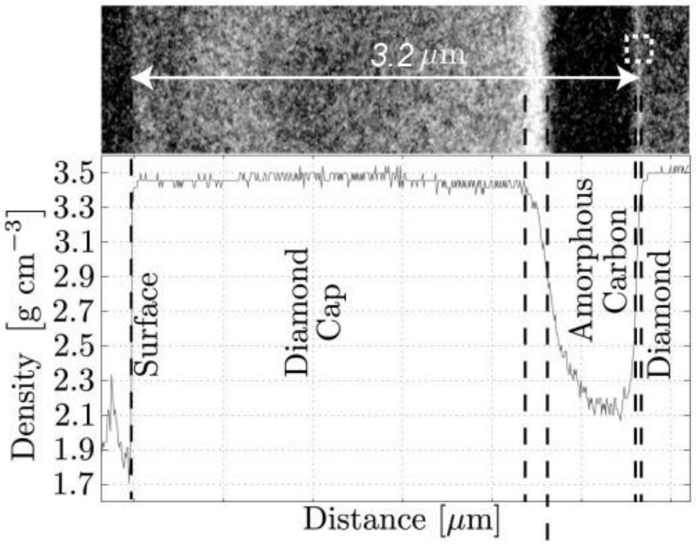


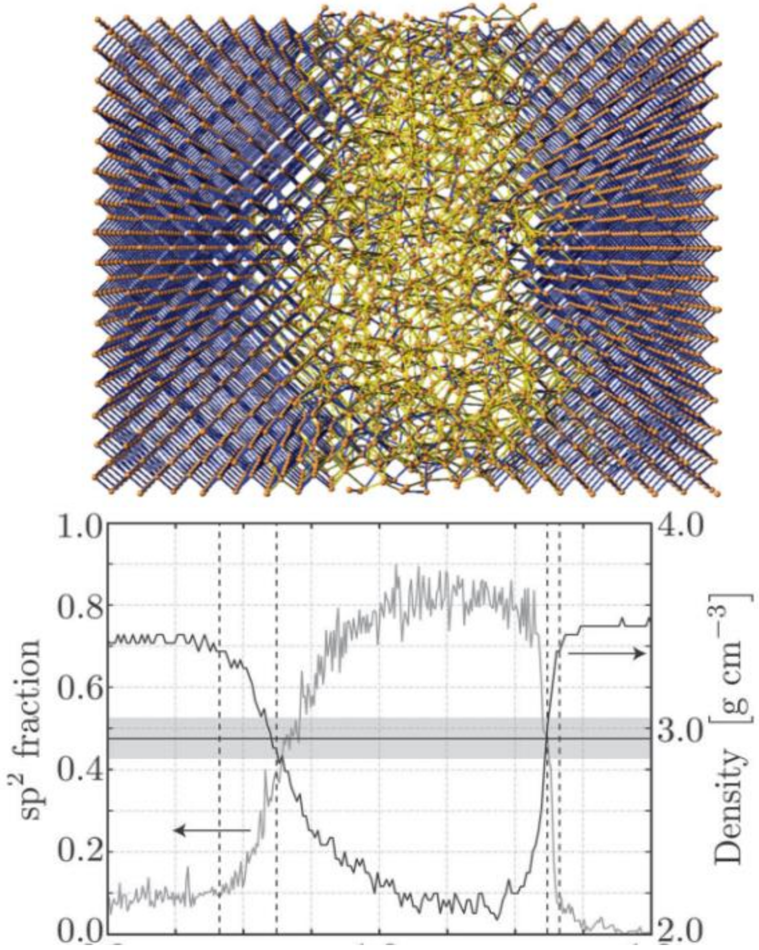
CVD diamond plate, polycrystalline, polished, 10x10 mm
**€490.00**

# MEV ION INDUCED DAMAGE IN DIAMOND

**High fluence implantation** → formation of an amorphous carbon layer where the damage density exceeds a threshold



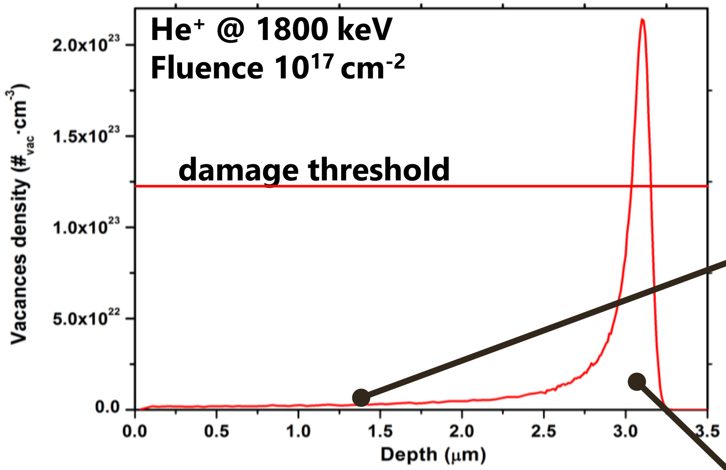



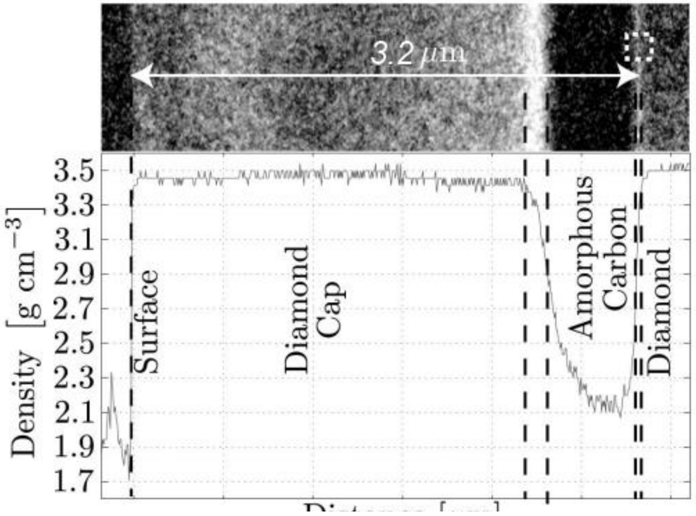




A. Silverman et al., **Physical Review B** 83, 224206 (2011)

B. A. Fairchild et al., **Advanced Materials** 24, 2024 (2012)

# MEV ION INDUCED DAMAGE IN DIAMOND





Below threshold: diamond with Frenkel defects → **diamond**

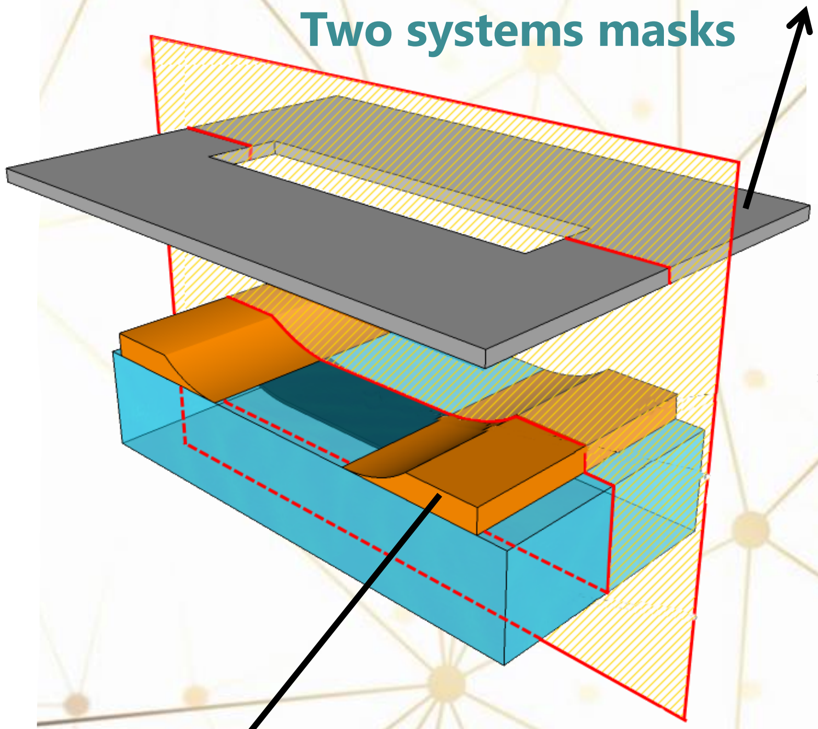
**High fluence implantation** → formation of an amorphous carbon layer where the damage density exceeds a threshold


Above threshold: amorphous carbon → **nanocrystalline graphite**

A. Silverman et al., **Physical Review B** 83, 224206 (2011)
B. A. Fairchild et al., **Advanced Materials** 24, 2024 (2012)

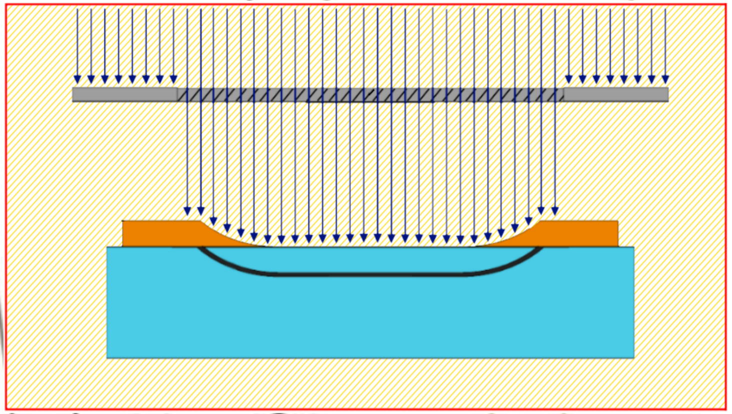

SRIM Main Menu
Calculation
2
Logo
?
SRIM
The Stopping and Range of Ions in Matter
?
Stopping / Range Tables
?
TRIM Calculation
?
Experimental Stopping Powers
J. F. Ziegler
U.S.N.A.
Annapolis, MD, USA
J. P. Biersack
Hahn-Meitner Inst.
Berlin, Germany
SRIM Version
SRIM-2012.03
SRIM Tutorials
SRIM Textbook
Legal Notice
Quit
Significant contributions by Helmut Paul (Linz), Roger Webb (Surrey), Xiao Yu (Beijing)
(c) 1984,1989,1998, 2008, 2012 by J. F. Ziegler, M.D. Ziegler, J. P. Biersack (SRIM.com)

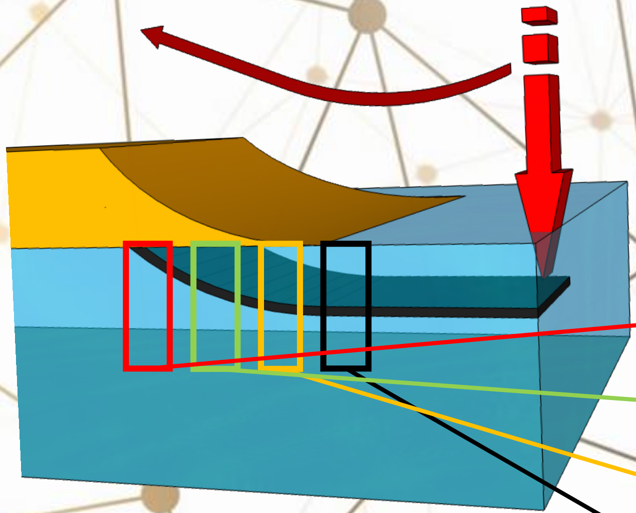
# MEV COLLIMATED ION BEAM LITHOGRAPHY

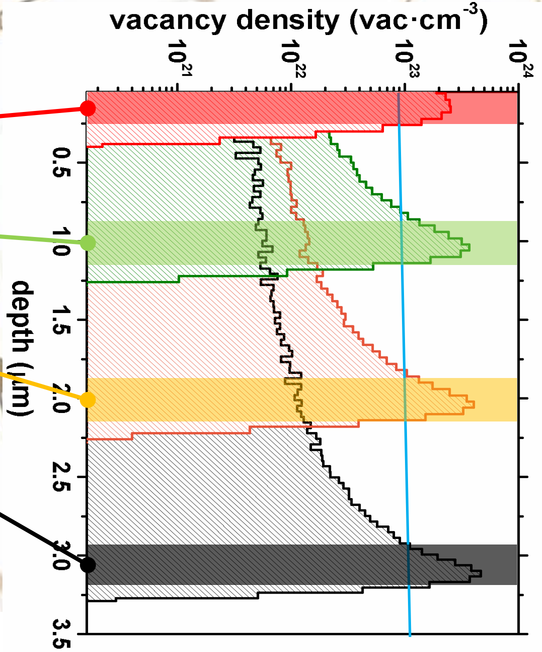



**Freestanding mask - collimation**

- laser microfabricated thin metal film (>5µm)
- definition of lateral geometry of electrodes





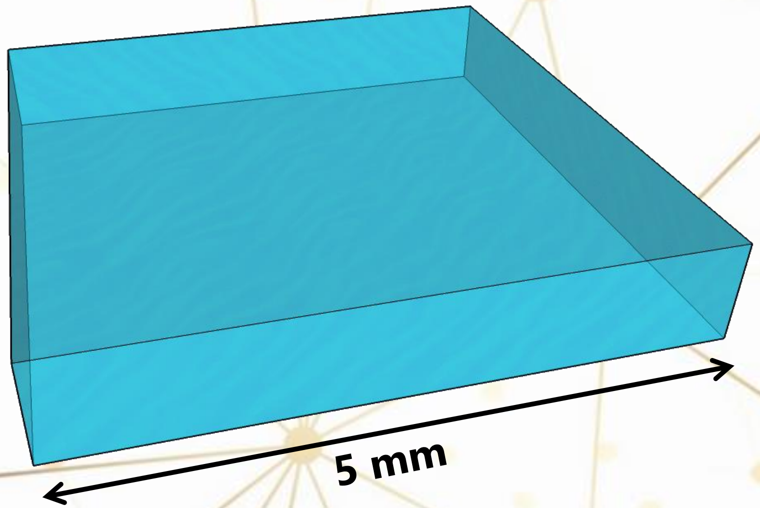



**Variable thickness mask – depth modulation**

- Deposition of metal over diamond surface (>5µm)
- Control of ion penetration = depth of electrode

# MEV COLLIMATED ION BEAM LITHOGRAPHY

Direct fabrication of graphitic electrodes into diamond crystal




Parallel fabrication

| | |
|---|---|
| Sensor dimensions: | up to 20 $mm^2$ |
| Electrodes resolution: | 100 – 300 nm |

High power laser or Focused Ion Beam **micro/nano machined mask** for broad MeV ion beam implantation

- Variable thickness mask -

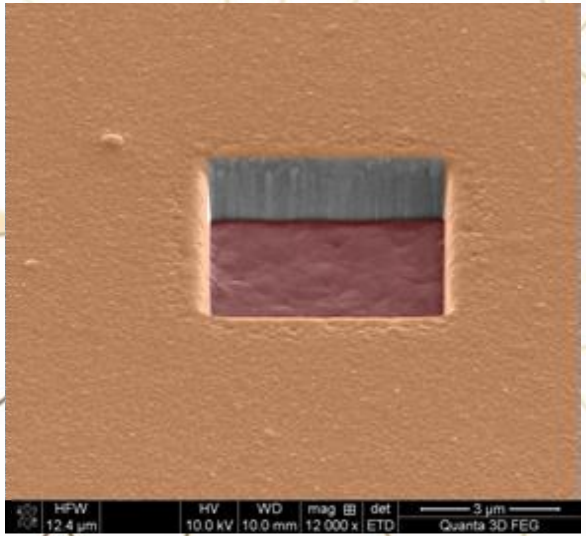
F. Picollo, et al., **New Journal of Physics 14 (2012) 053011**

F. Picollo, et al., **Scientific Reports 6, (2016) 20682**

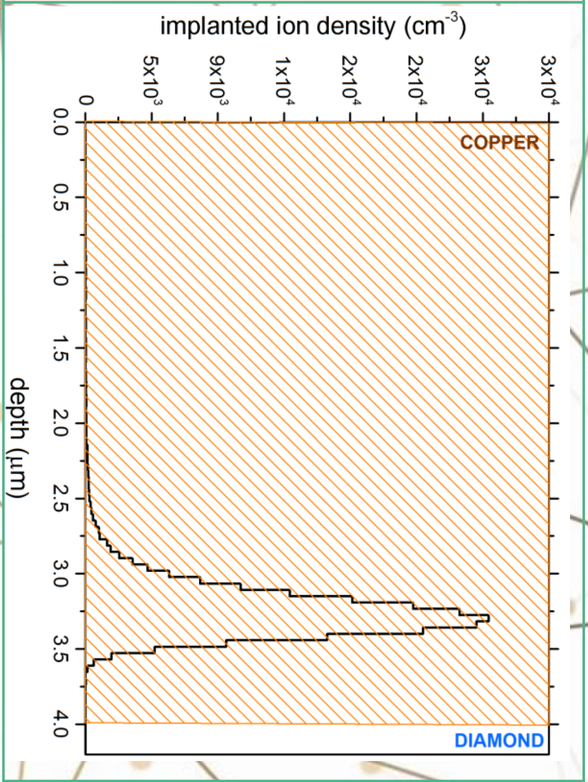
# What is the best resolution achievable?

- low thickness metal deposition on diamond (<5µm)
- FIB milling of metal
- protective layer leaved to avoid diamond superficial damaging

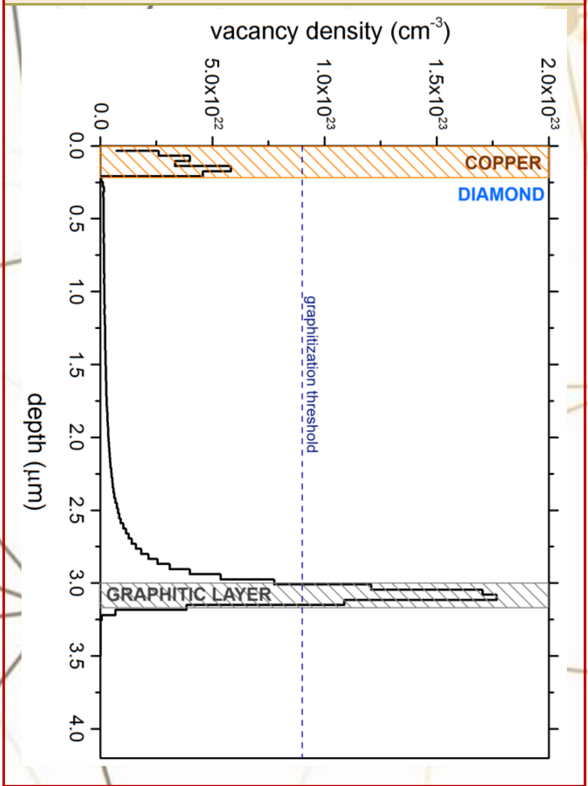
*Quanta 3D FEG DualBeam*




NOT milled metal layer

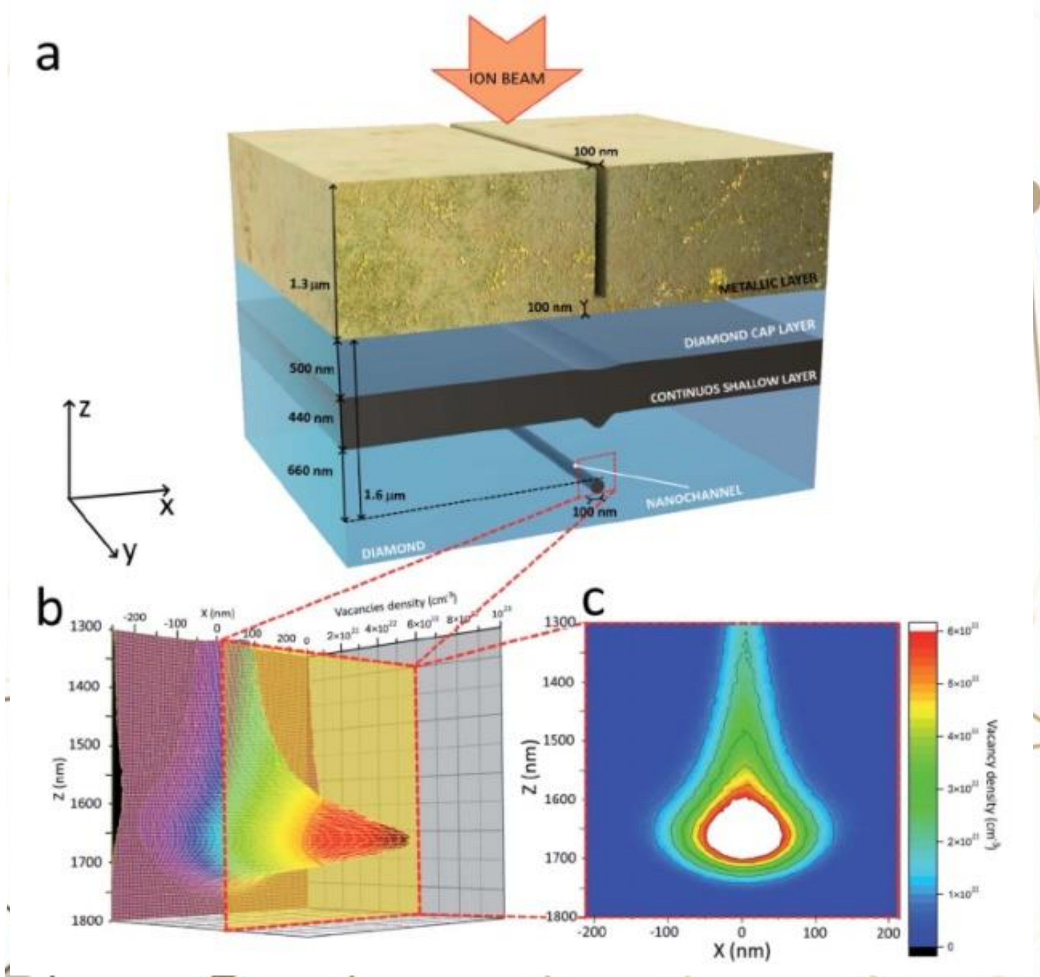


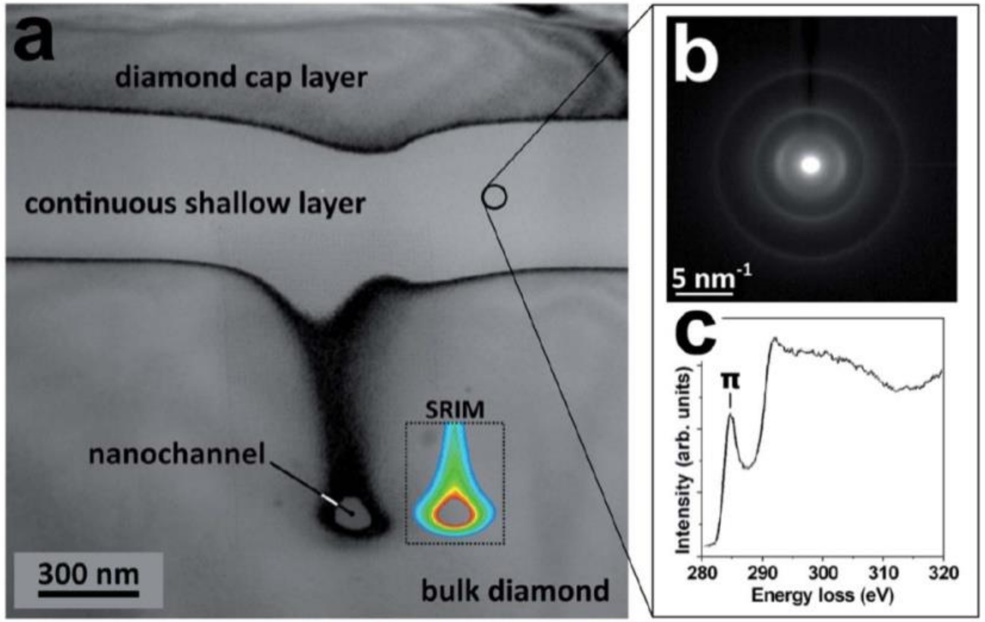

FIB milled metal layer

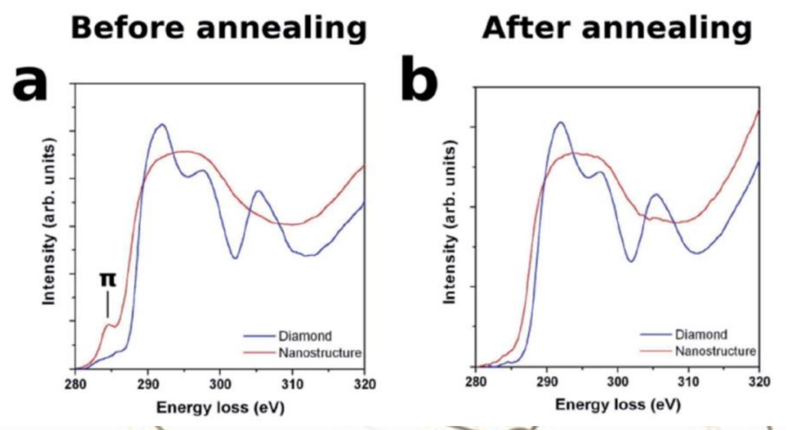


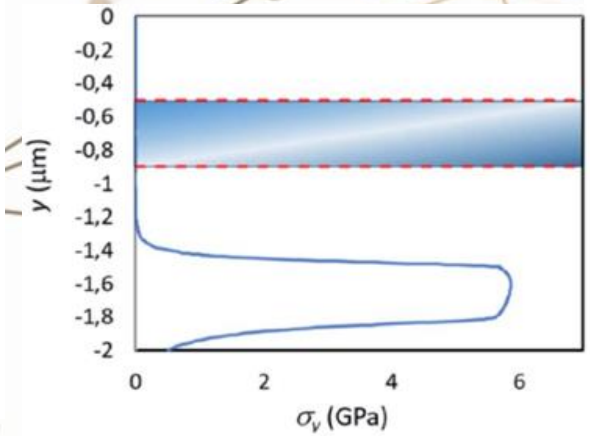

"**Realization of a diamond based high density multi electrode array by means of deep ion beam lithography**",
F. Picollo, et al., **Nuclear Instruments and Method: B 348**, (2015) 199-202

# What is the best resolution achievable?



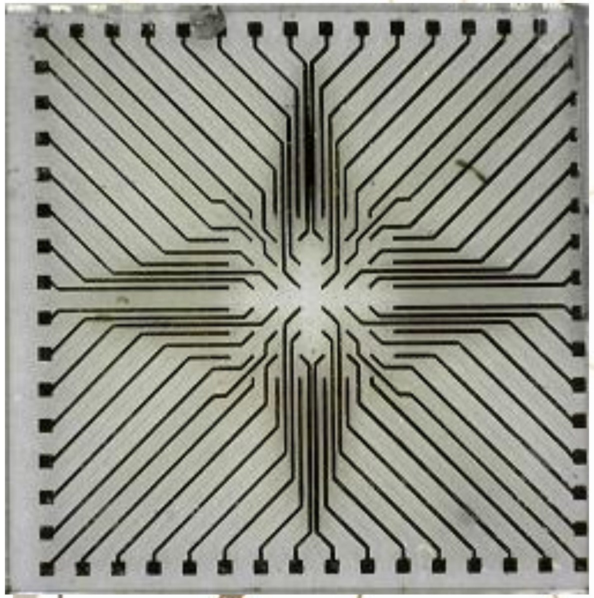



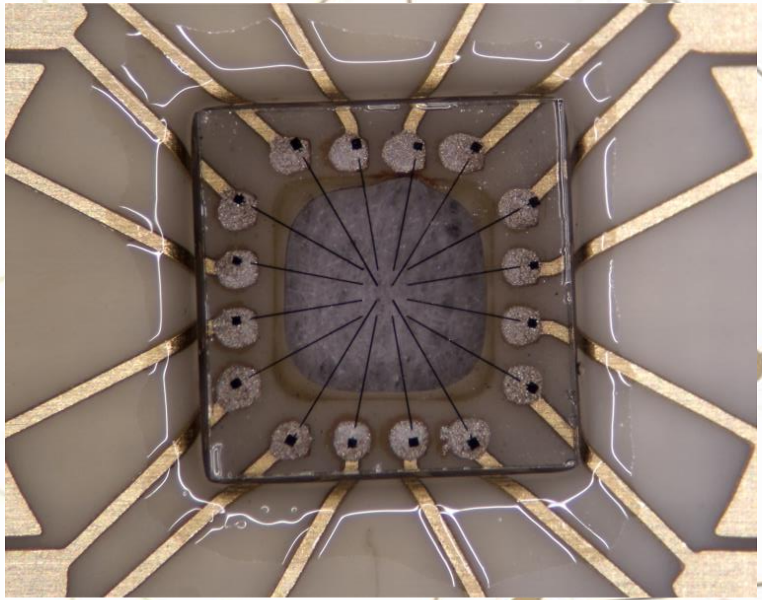
# DIAMOND BIOSENSORS

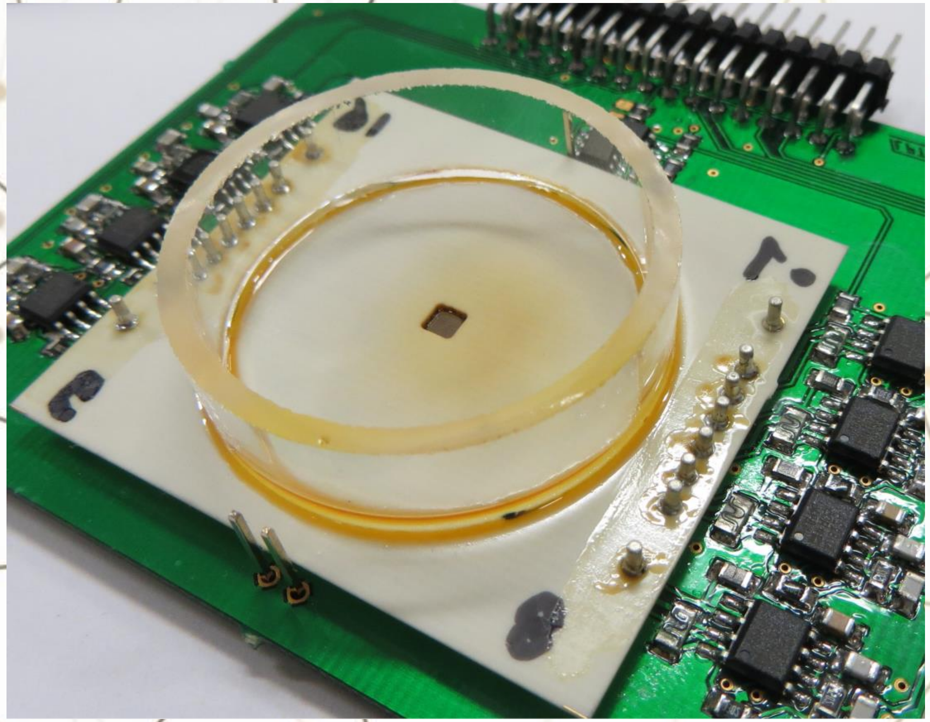
diamonds:
- Chemical Vapour Deposition
- single crystal
- type IIa
- 4.5×4.5×0.5 $mm^3$

implantation:
- $He^+$ @ 1.2 MeV
- fluence $1.2 \cdot 10^{17}$ $cm^{-2}$
- penetration depth ~2 μm

thermal treatment:
- 950 °C for 2 hours
- ~$10^{-6}$ mbar





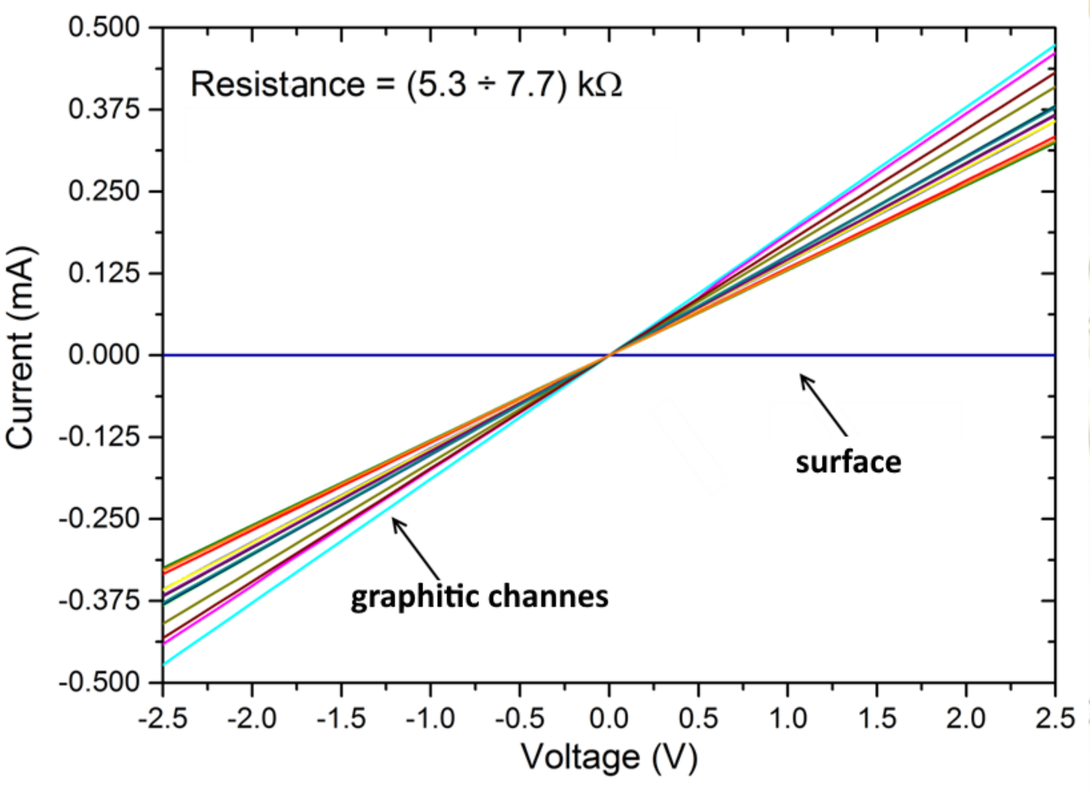


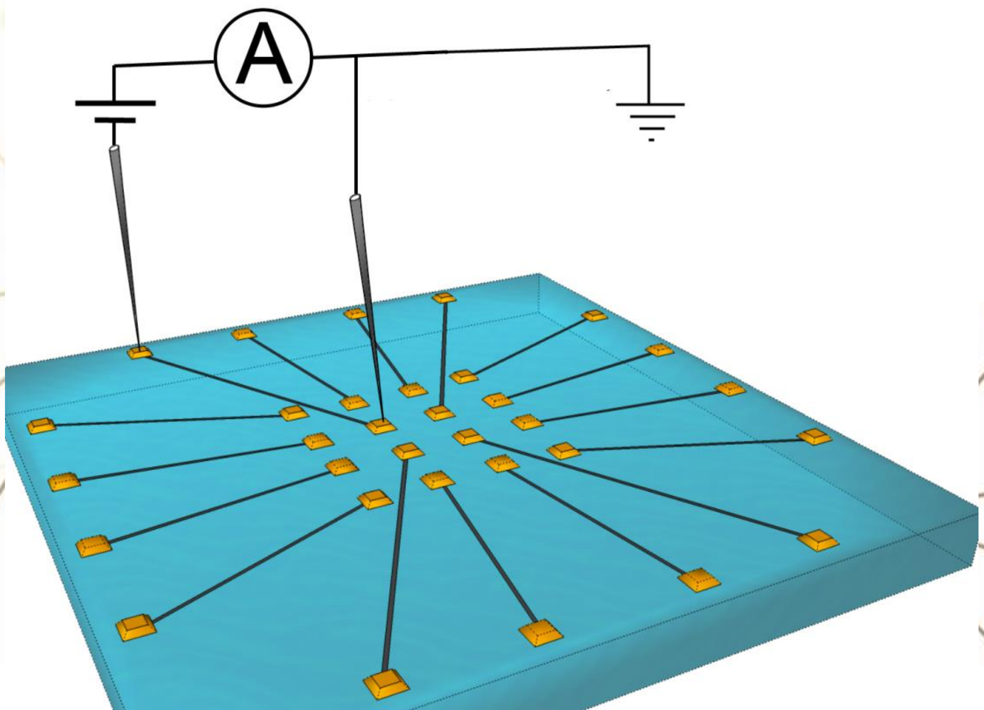
F. Picollo, et al., **Analitycal Chemistry 88 (2016) 7493**

# Electrical characterization

## Current – Voltage characteristic

- Ohmic conduction
- Channels resistivity comparable with graphite one




R ~ 6.5 kΩ

w= 22 μm
l = 1400 μm
t= 0.20 μm

$$\rho = R\frac{w \cdot t}{l} \cong (2.1 \pm 0.3)\ \text{m}\Omega\cdot\text{cm}$$

polycrystalline graphite **ρ = 1.3 mΩ·cm**

# Preliminary characterization

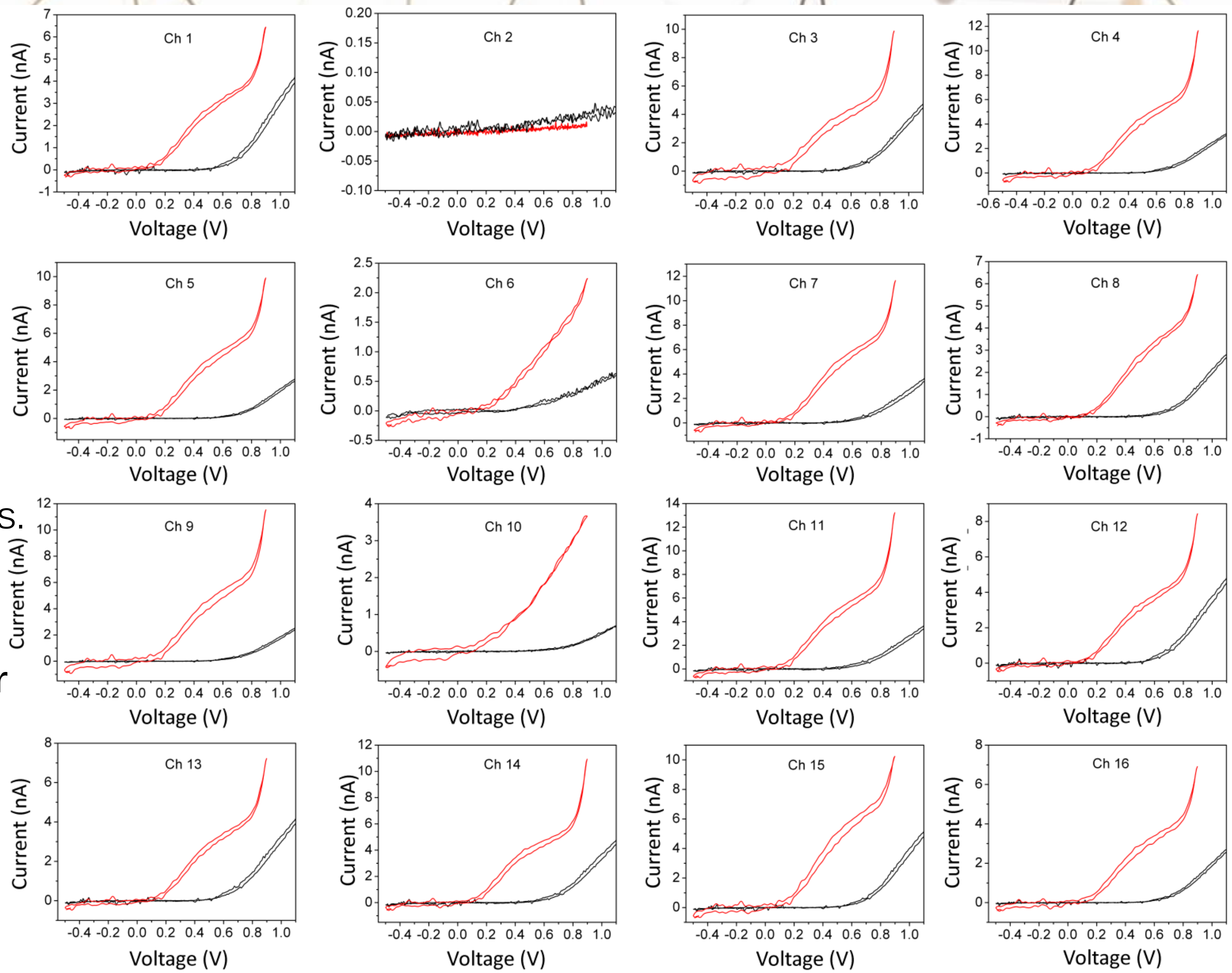
## Cyclic voltammetry characterization

scans rate = **20 mV s$^{-1}$**

voltage = **-0.5 ÷ 1.2 V**
(applied to all electrodes vs. Ag/AgCl electrode)

Solution #1= **Tyrode buffer**

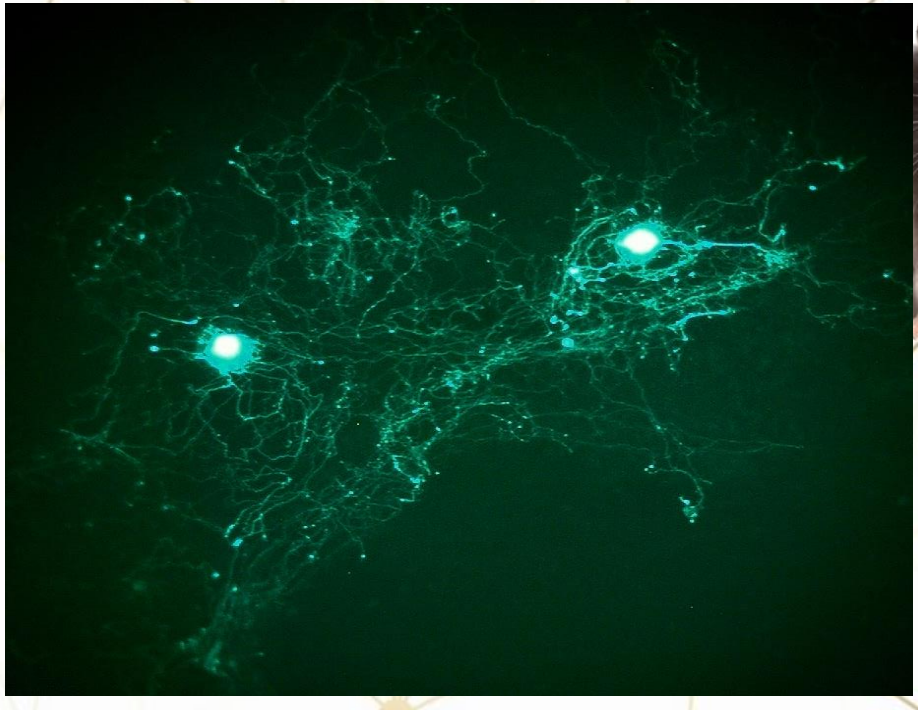
Solution #2= **Adrealine [100 mM]**

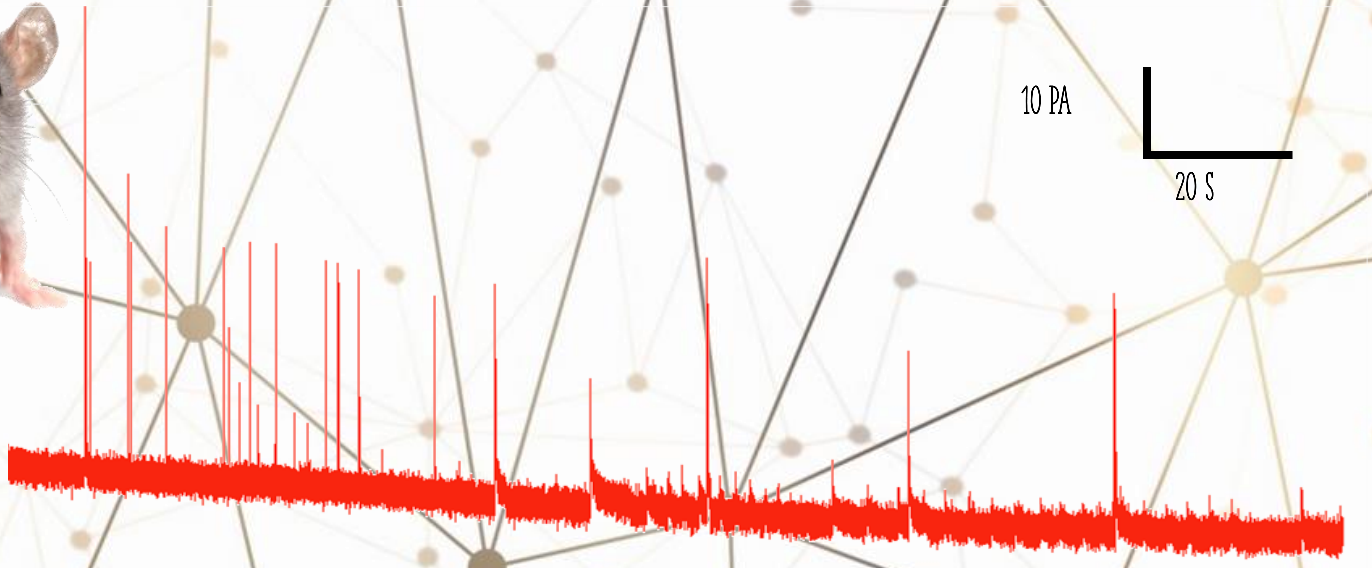


# OUTLINE

- ✅ A bit of cell biology... (from a NOT biologist)
- ✅ Standard tools for electrophysiology experiments
- ✅ Artificial DIAMOND for sensors development
- Some examples of cell signals detection
- Diamond particle detectors
- Radiobiology using diamond-base sensors
- New frontiers: quantum sensing (e.g. intracellular temperature detection)

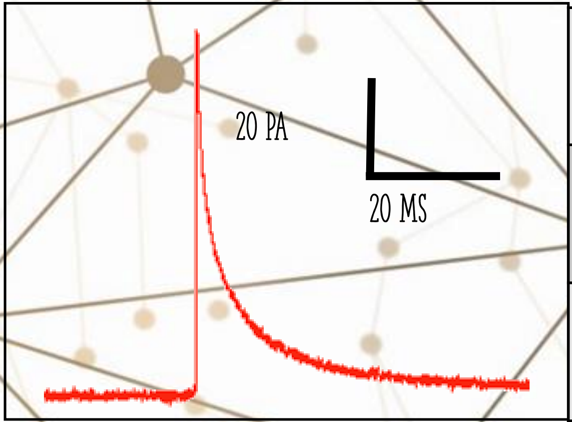
# Exocytosis detection from *substantia nigra* neurons





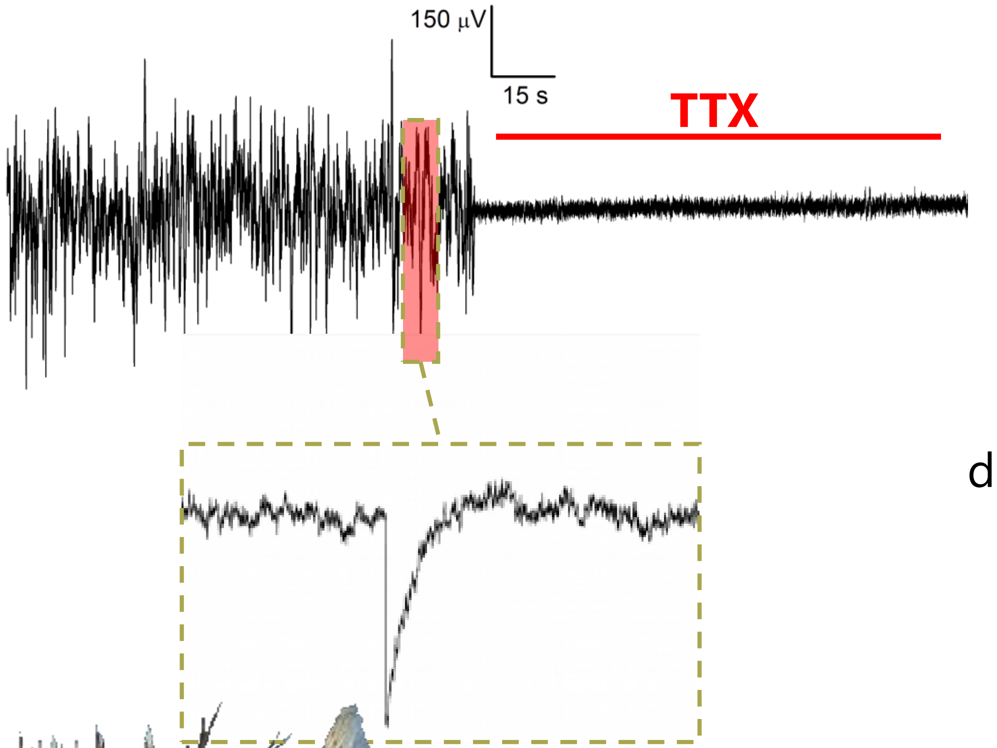

**Network of *substantia nigra* neurons**

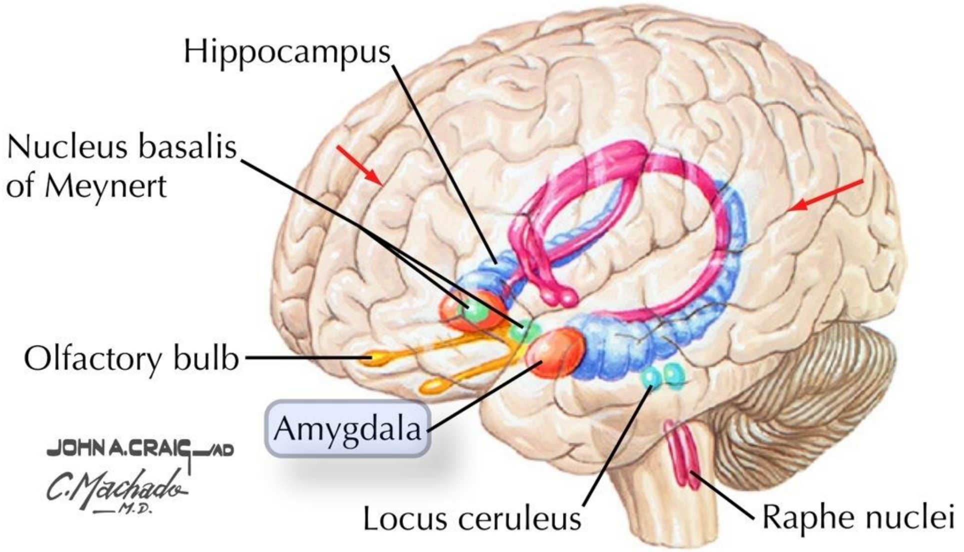
- Experiment performed after 21 DIV
- Cell network threated with L-Dopa for 1 h
  → increasing of vesicles dimension
- Stimulation with KCl solution



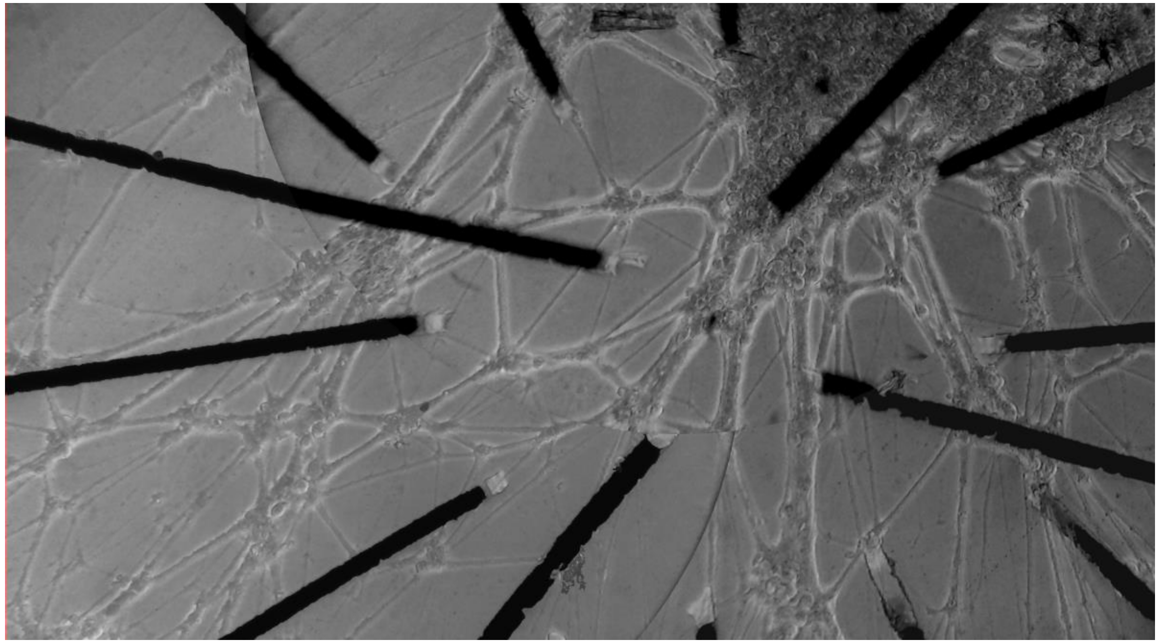

| | |
|---|---|
| **$t_{1/2}$ (ms)** | 2.89 ± 0.15 |
| **$I_{max}$ (pA)** | 37.4 ± 1.5 |
| **Q (pC)** | 1.1 ± 0.4 |

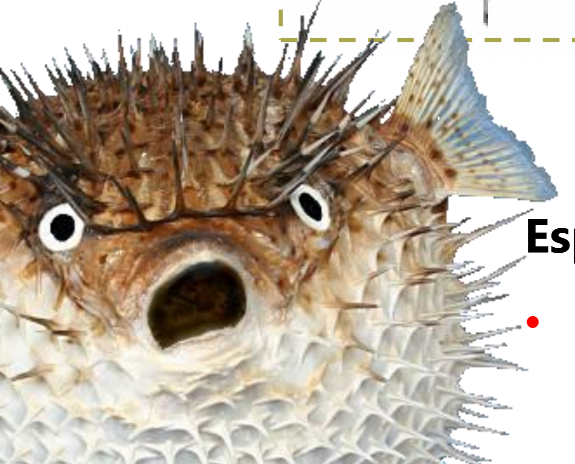
# POTENZIALE D'AZIONE DI NEURONI DELL'IPPOCAMPO




Cellule piastrate sul dispositivo per 18 giorni

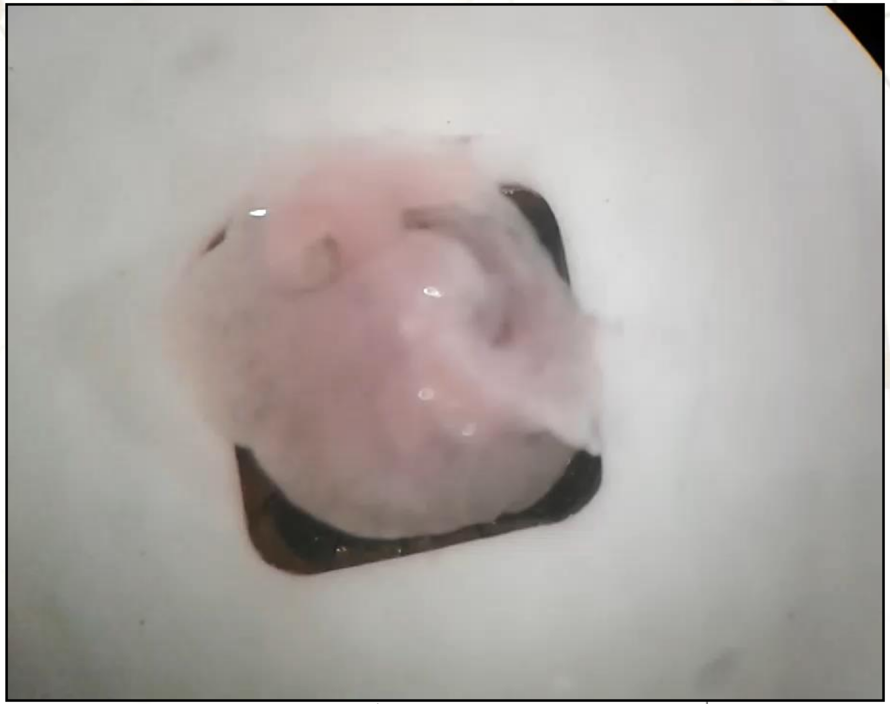




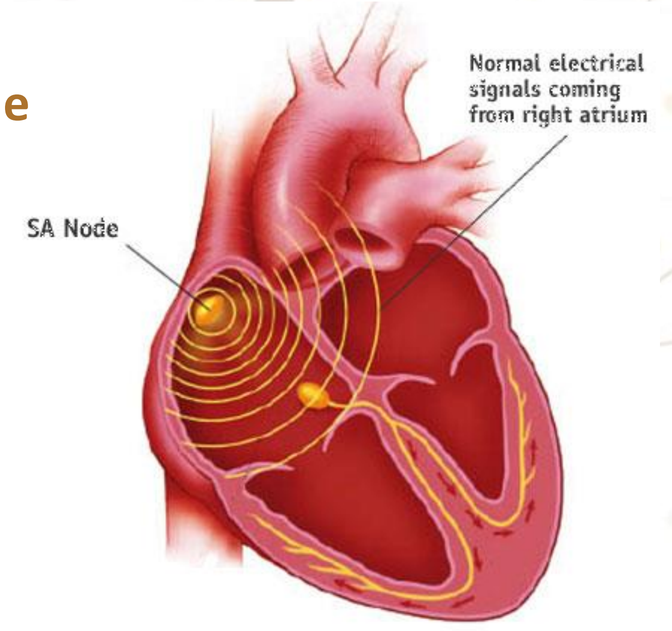
**Esperimento farmacologico**

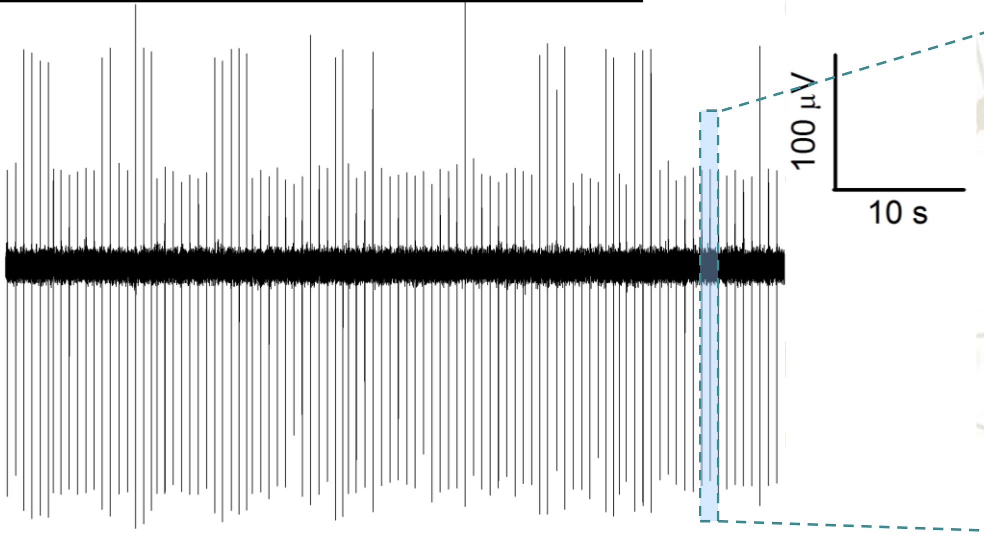
- **Somministrata TTX (Tetrodotoxin)**

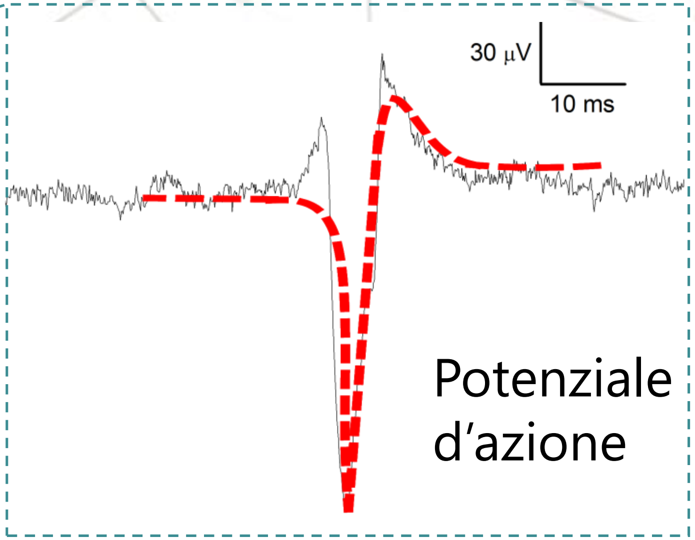
# POTENZIALE D'AZIONE DA FETTINA DEL NODO SENOATRIALE



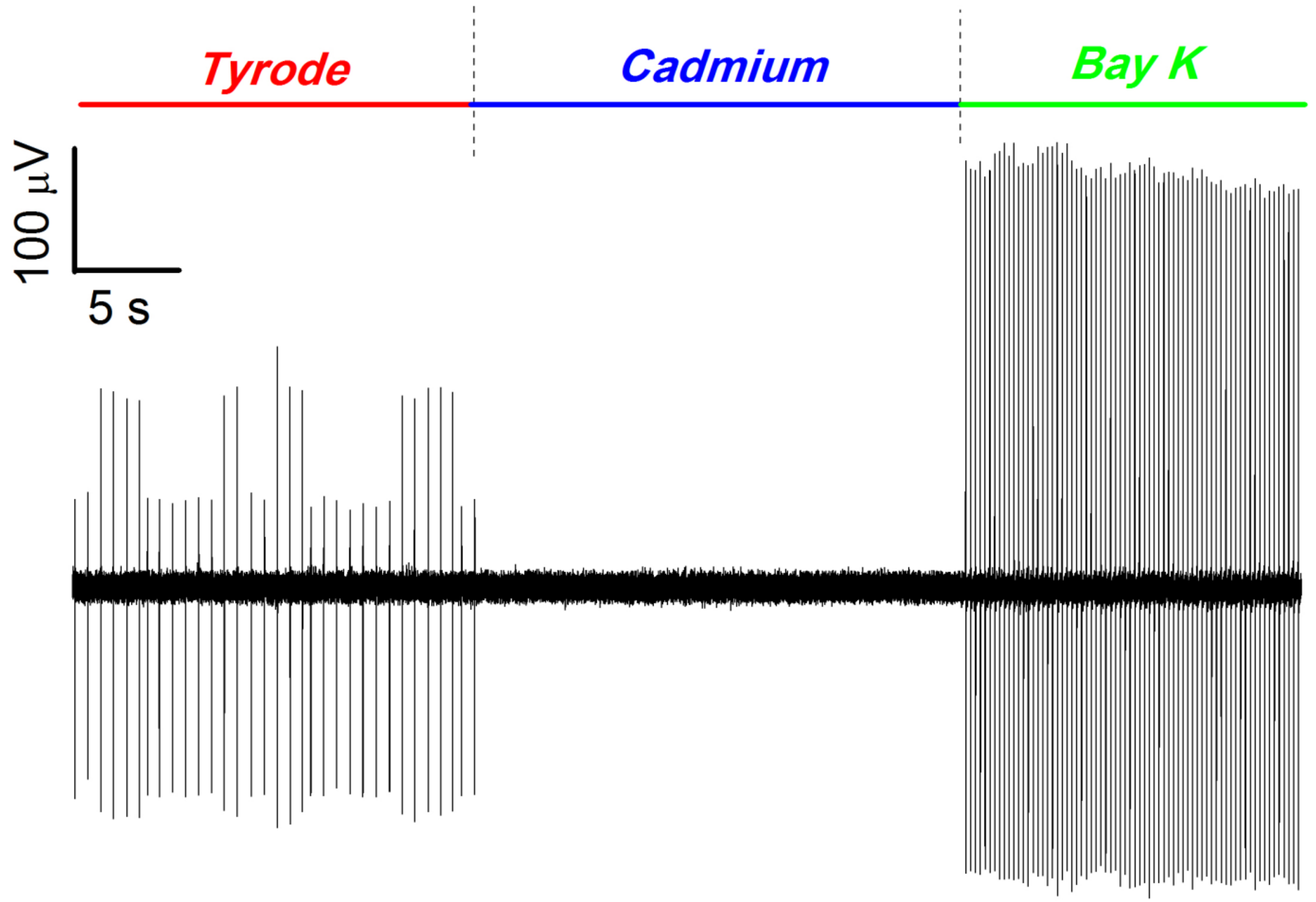
**Fettina del nodo senoatriale**
con tessuto muscolare residuo



# POTENZIALE D'AZIONE DA FETTINA DEL NODO SENOATRIALE




**Soluzione salina**
***(Tyrode)***

*f ~ 2 Hz*
*I ~ 300 µV*

**Soluzione di cadmio**
***500 µM***

Bloccante dei canali del calcio

***Soluzione Bay K***
***10 µM***

*f ~ 5 Hz*
*I ~ 600 µV*

Migliora la cinetica dei canali del calcio

# OUTLINE

- ✅ A bit of cell biology... (from a NOT biologist)
- ✅ Standard tools for electrophysiology experiments
- ✅ Artificial DIAMOND for sensors development
- ✅ Some examples of cell signals detection
- Diamond particle detectors
- Radiobiology using diamond-base sensors
- New frontiers: quantum sensing (e.g. intracellular temperature detection)

# DIAMOND IONIZING RADIATION DETECTOR

*Ionizing radiation detector*

- **Radiation hardness**
- **Tissue equivalence**
- **High carrier mobility**
- **High breakdown field**

| Properties | Diamond | Silicon | GaAs |
|---|---|---|---|
| Density (g/cm$^3$) | 3.5 | 2.33 | 5.32 |
| Band gap (eV) | 5.5 | 1.12 | 1.43 |
| Atomic charge | 6 | 14 | 31.33 |
| Resistivity (Ωcm) | $> 10^{11}$ | $2.3 * 10^5$ | $1 * 10^8$ |
| Energy to form e-h pair (eV) | 13 | 3.6 | 4.2 |
| Electron mobility (cm$^2$V$^{-1}$s$^{-1}$) | 1800 | 1350 | 8500 |
| Hole mobility (cm$^2$V$^{-1}$s$^{-1}$) | 1200 | 480 | 400 |
| Saturation velocity (mm/ns) | 220 | 82 | 80 |
| Dielectric constant | 5.7 | 11.9 | 13.1 |
| Breakdown voltage (V/cm) | $10^7$ | $3 * 10^5$ | $4 * 10^5$ |
| Average minimum ionizing particle signal in 100 mm (electrons) | 3600 | 9200 | 13000 |

solid-state ionization chamber

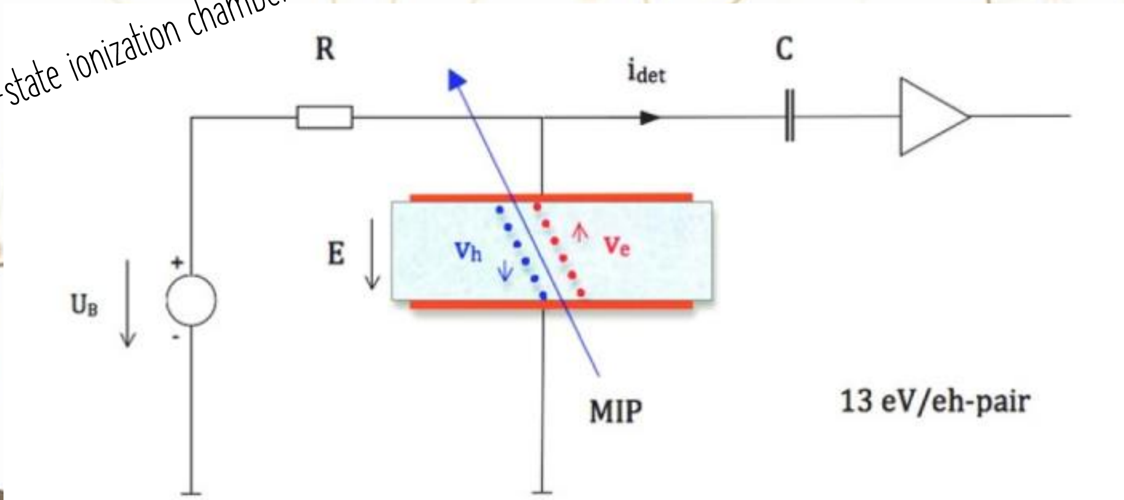
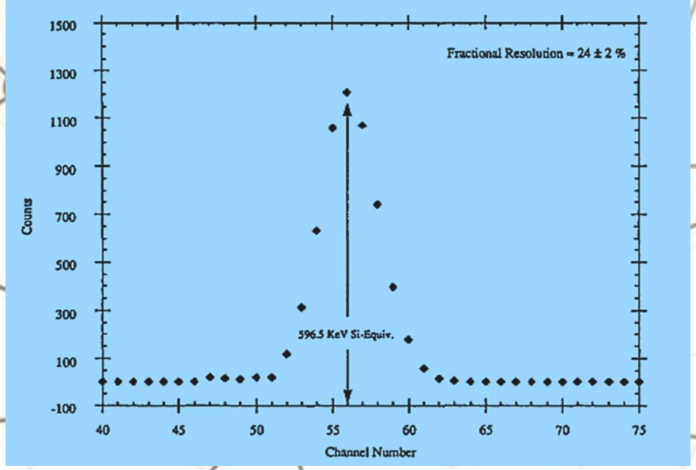


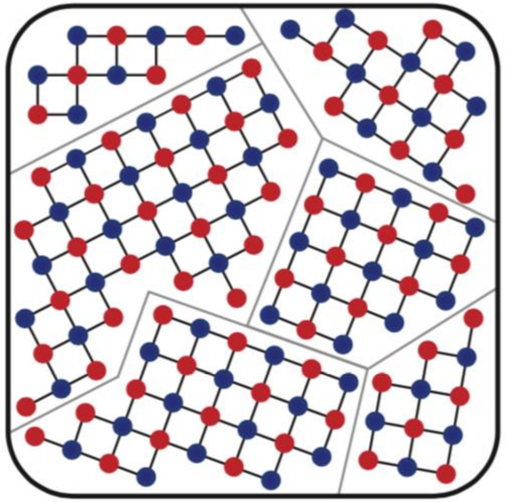

**Fig. 2.** Schematic diagram of the diamond radiation detector. The detection of incident radiation is done by measuring the induced current (charge).




Spectrum of α particle (source: 241Am emitting at 5.5 MeV) from a **type IIa natural diamond**, 14.5 μm thickness, biased at 10 V.

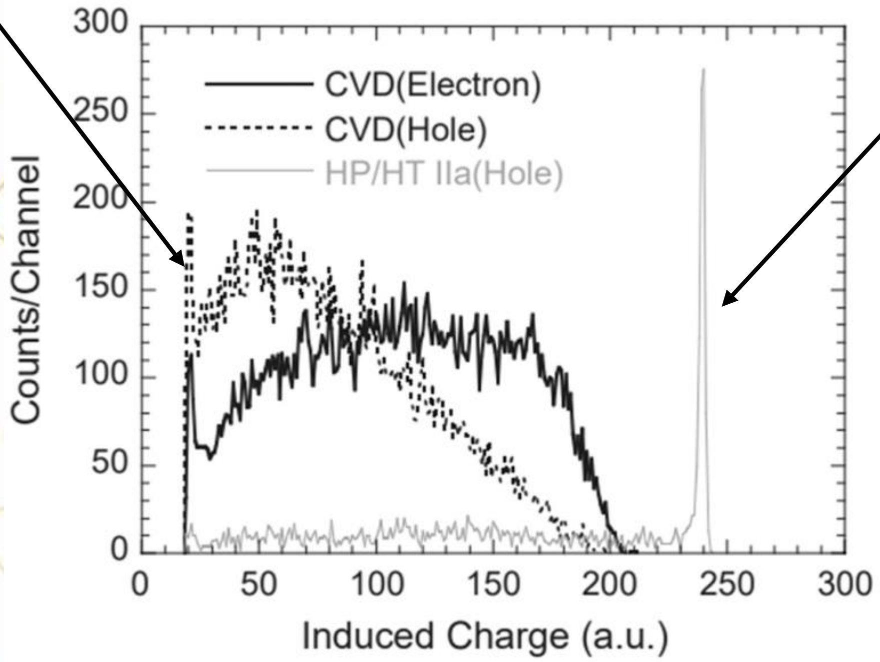
F.C. Champion, S.B. Wright, Proc. Phys. Soc. 73 (1959) 385

# DIAMOND IONIZING RADIATION DETECTOR

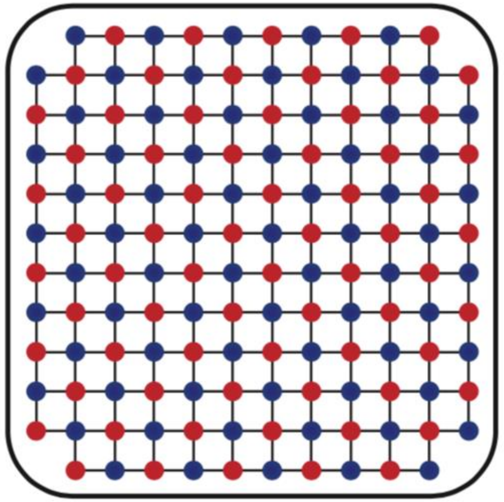


Polycrystalline

Energy resolution

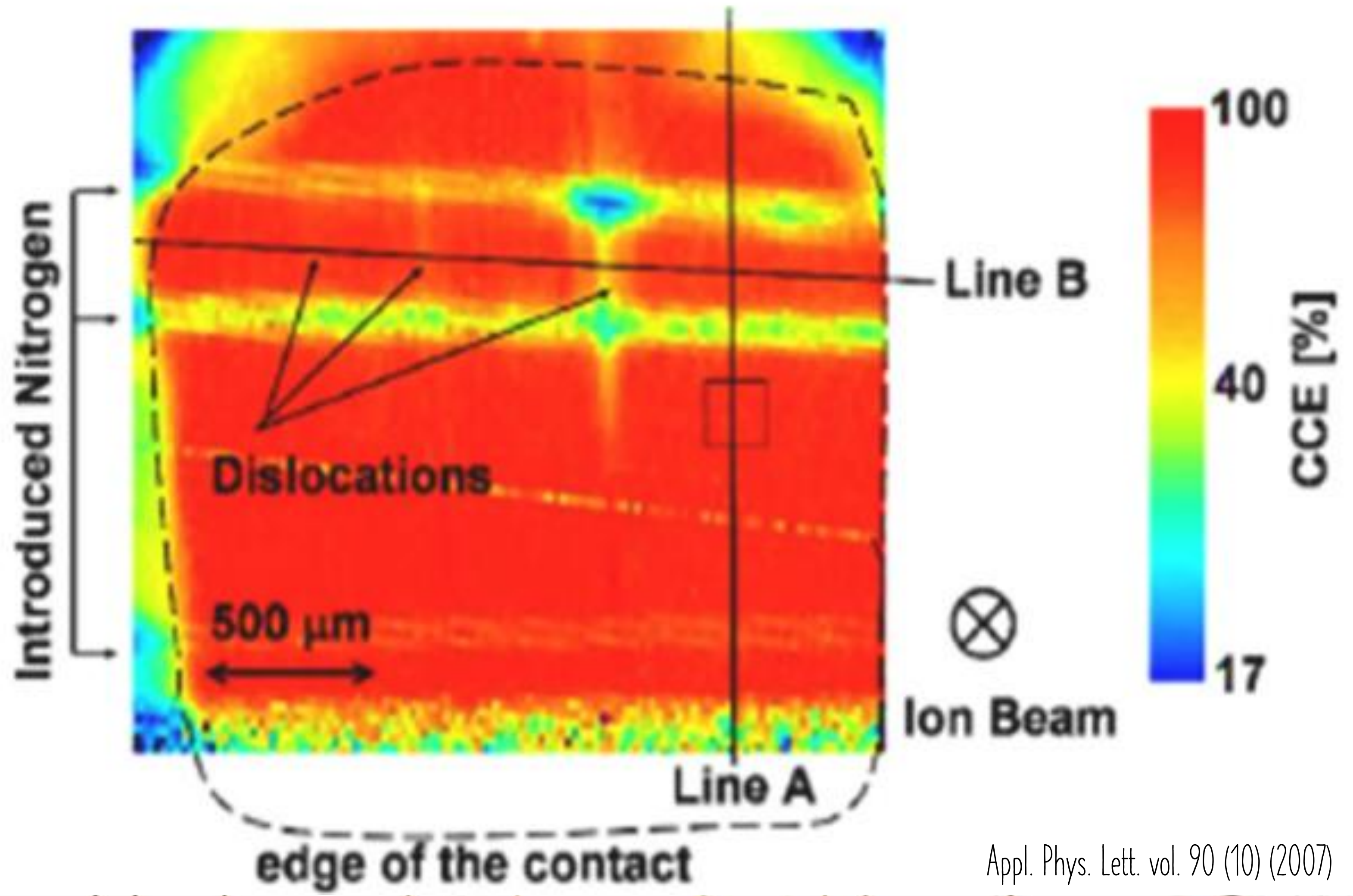



Diamond and Related Materials, 14(11 - 12), 2027 - 2030

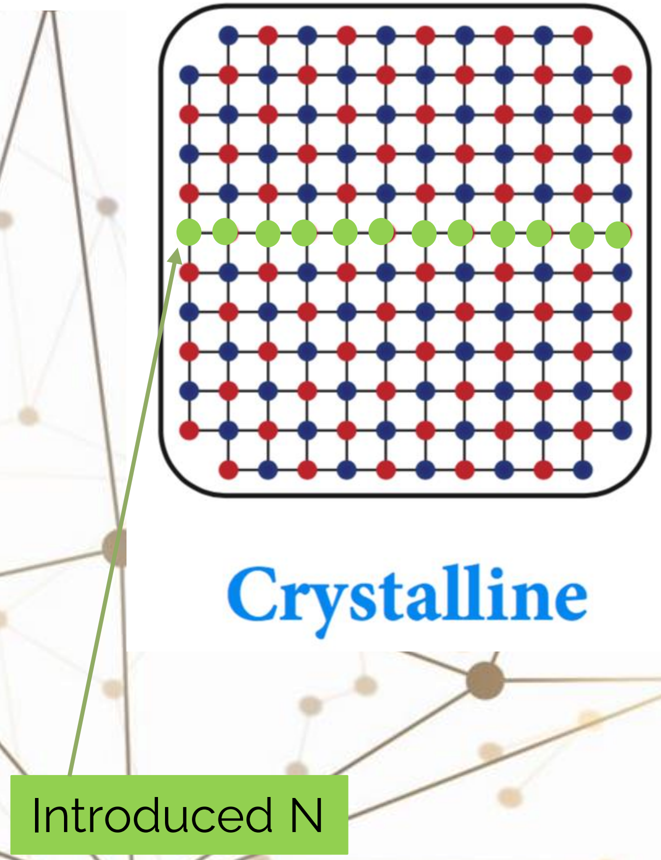


Crystalline

# DIAMOND IONIZING RADIATION DETECTOR



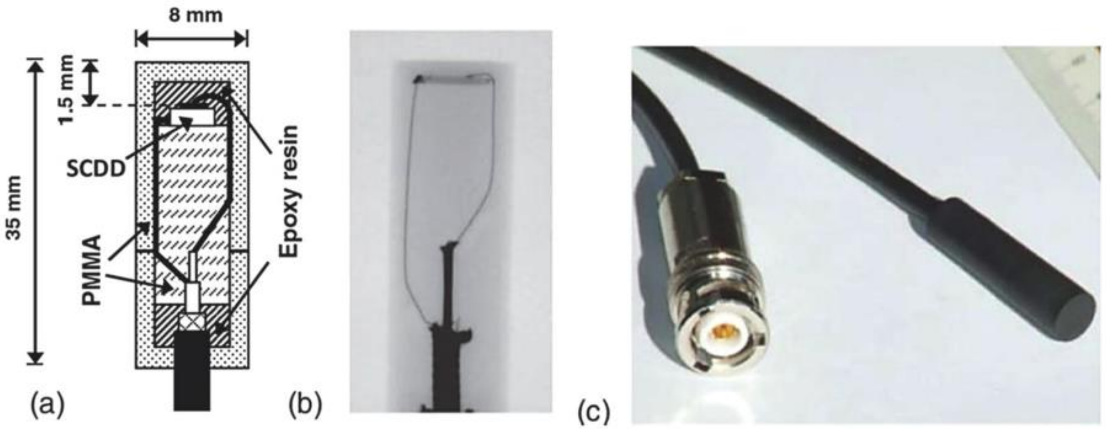

Appl. Phys. Lett. vol. 90 (10) (2007)



# DIAMOND IONIZING RADIATION DETECTOR

| S/ NO | Company | Product | Technology | Comments on Features | Website/Link |
|---|---|---|---|---|---|
| 1 | Gemtrue | Handheld Diamond Selector | Thermal Conductivity | | https://www.gemtrue.com/ |
| 2 | Presidium Gem Instruments | Diamond Mate Tester | Thermal Conductivity | Examines loose and mounted diamonds | https://www.presidium.com.sg/ |
| 3 | GemOro | Ultratester 3 + | Thermal Conductivity | Dual testing modes, Compact and portable design | https://www.gemoroproducts.com |
| 4 | Yehuda Diamond | Yehuda Diamond Tester | Proprietary Technology | Effective differentiation between natural and lab-grown diamonds | https://www.yehuda.com/ |
| 5 | MIZAR | Diamond Tester | Electrical Conductivity | | https://www.ourweigh.co.uk/diamond-testers/rs-mizar-prestige-series-ii-diamond-tester.html |
| 6 | Gemlogis | Diamond Tester | Thermal Conductivity | | https://www.gemlogisusa.com/ |
| 7 | Gemlogis | Master Set Diamond Tester | Thermal Conductivity, Electrical Conductivity | Comprehensive diamond testing set | https://www.gemlogisusa.com/ |
| 8 | Cividec Instrumentation | NMR Diamond Analyzer | Nuclear Magnetic Resonance (NMR) | Highly sensitive and non-destructive diamond analysis | https://cividec.at/ |
| 9 | HDE | Portable Diamond Tester | Electrical Conductivity | One-button operation for on-the-go use | |
| 10 | DigiWeigh | Diamond Scale | Weight Measurement | Precise weighing of diamond | https://www.digiweigh-usa.com |
| 11 | PTW Dosimetry | Diamond Detector | Ionization Chamber | | https://www.ptwdosimetry.com/en/ |

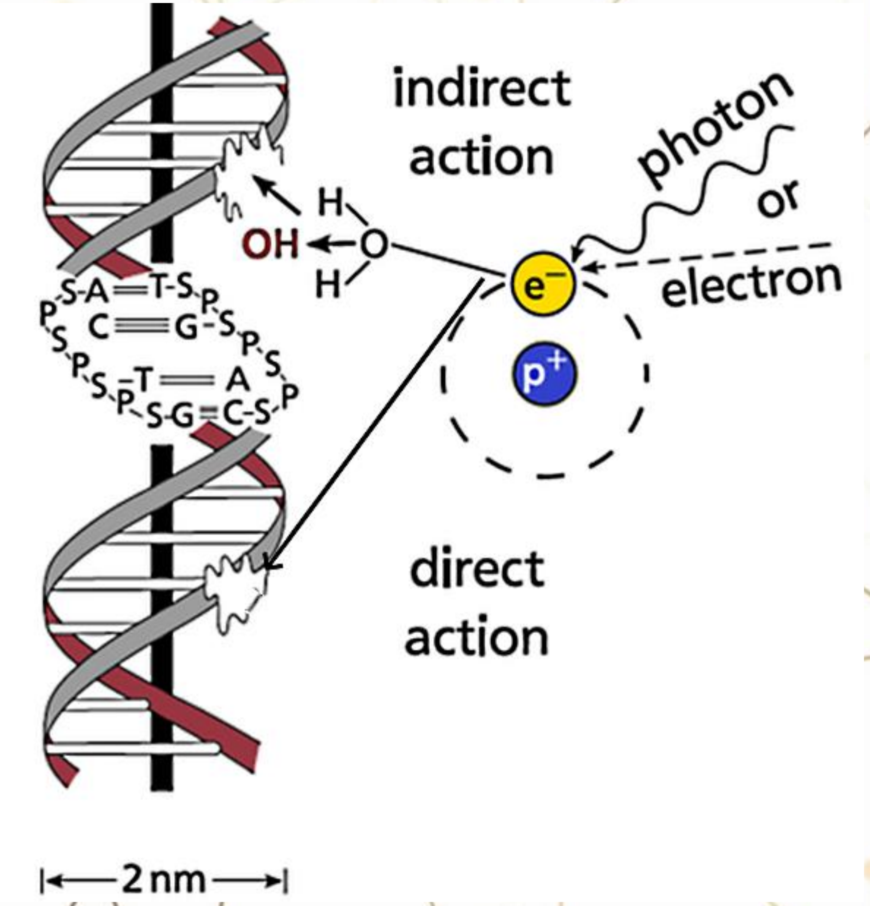
Med Phys. vol. 39 (7Part1) (2012) 4493 - 4501

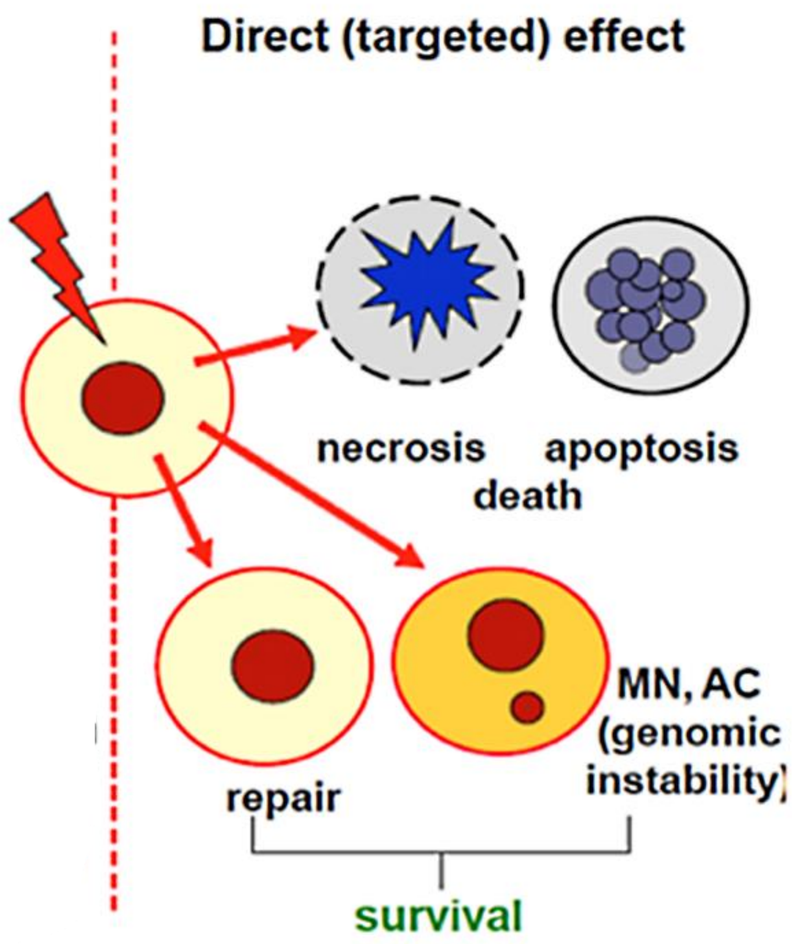


# OUTLINE

- ✓ A bit of cell biology… (from a NOT biologist)
- ✓ Standard tools for electrophysiology experiments
- ✓ Artificial DIAMOND for sensors development
- ✓ Some examples of cell signals detection
- ✓ Diamond particle detectors
- Radiobiology using diamond-base sensors
- New frontiers: quantum sensing (e.g. intracellular temperature detection)

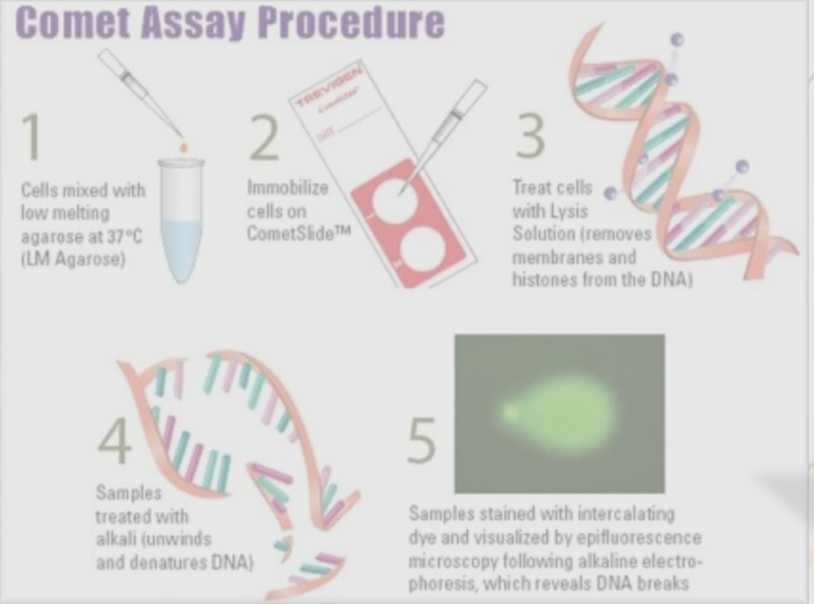
# RADIOBIOLOGY



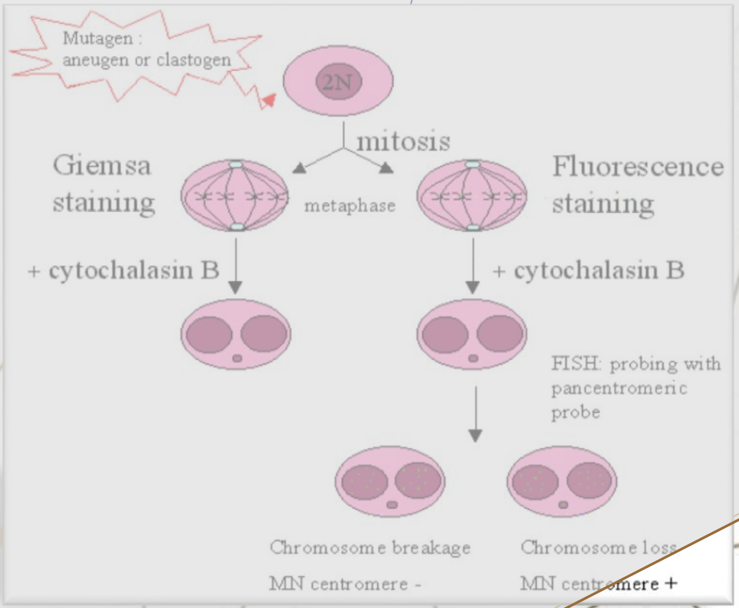




Branch of biophysics concerned with the effects of ionizing radiation on organisms

# STANDARD RADIOBIOLOGY TESTS




Micronucleus assay scheme

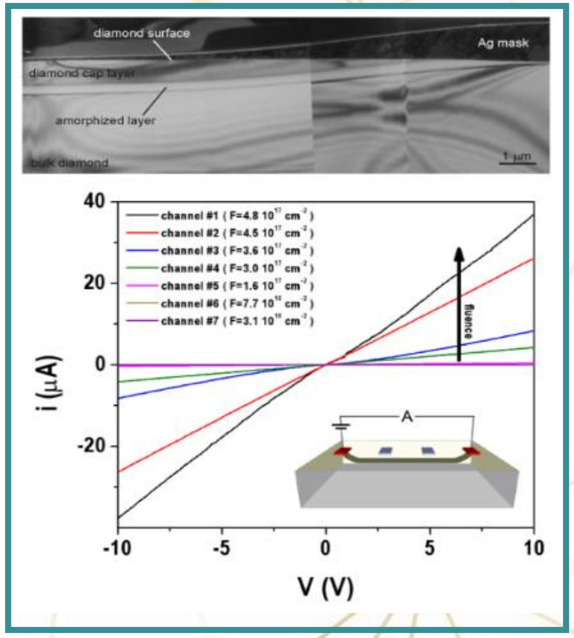



Standard radiobiological expermeint need to evaluate irradiation effects only **off-line**

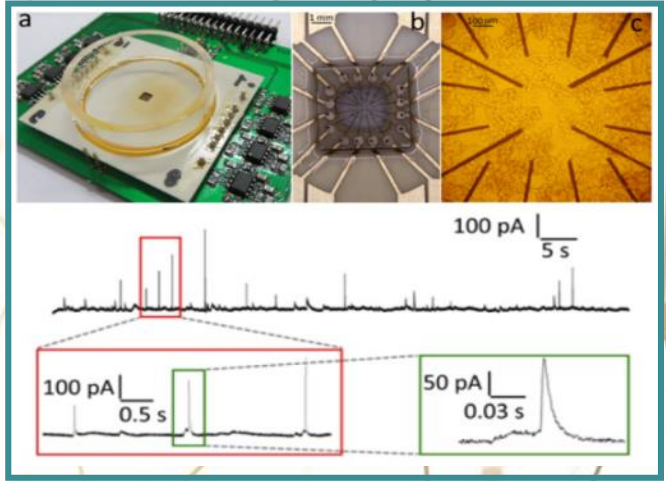
**Diamond-based biosensor:**
**simoultaneous detection of cellular signals and ionizing radiation dose**

- ✓ study of cell-cell communication phenomena
- ✓ real-time monitoring of cellular activity

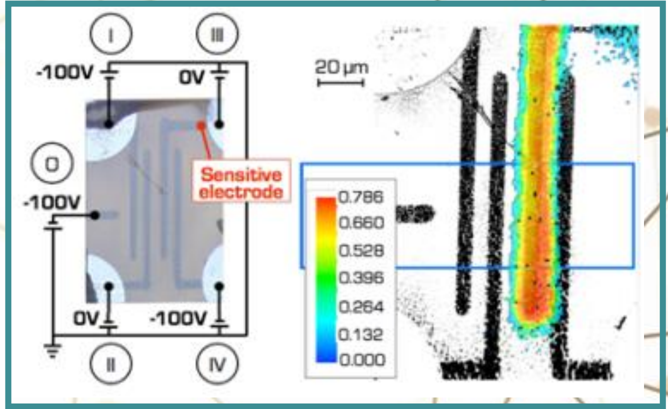
# DIACELL SENSOR



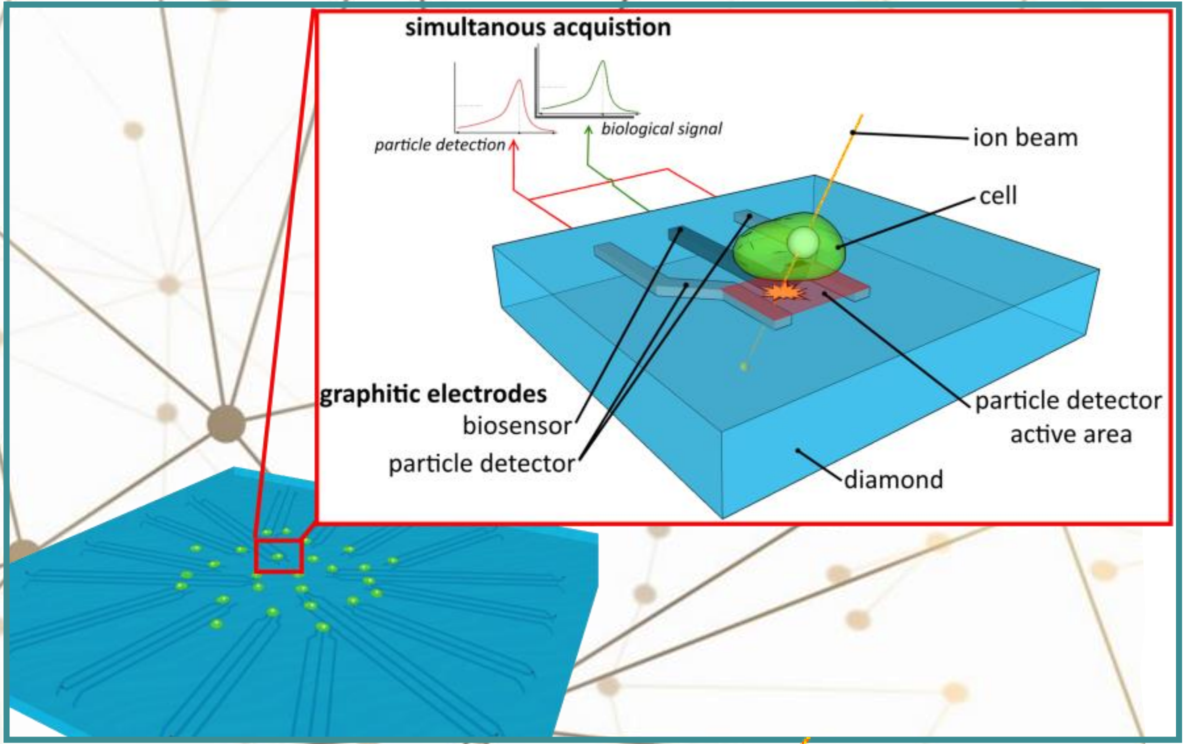

Deep ion beam lithography




Cellular bio-sensors




Radiation detectors

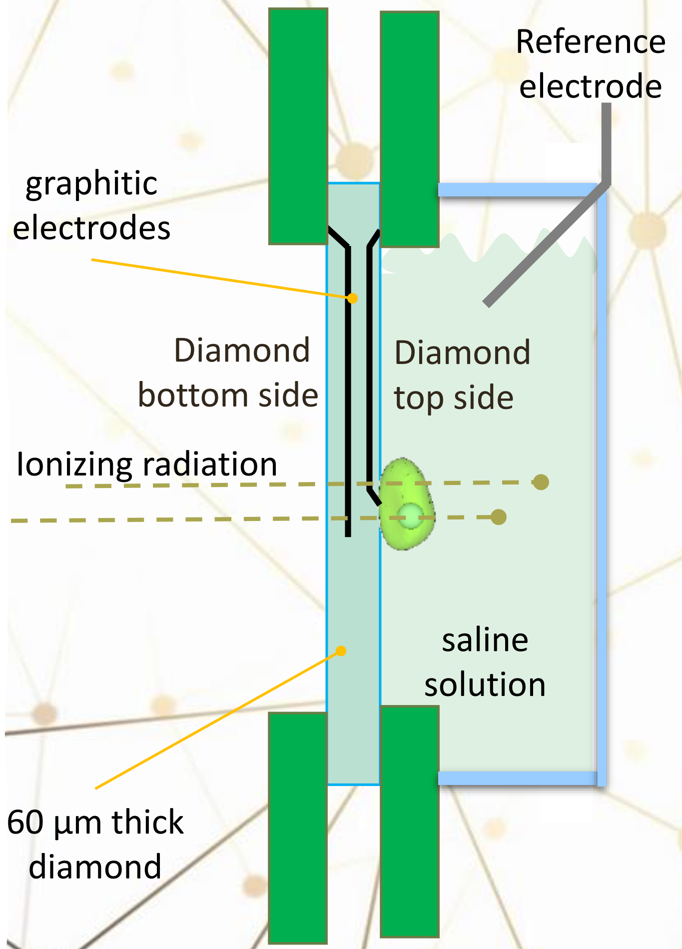


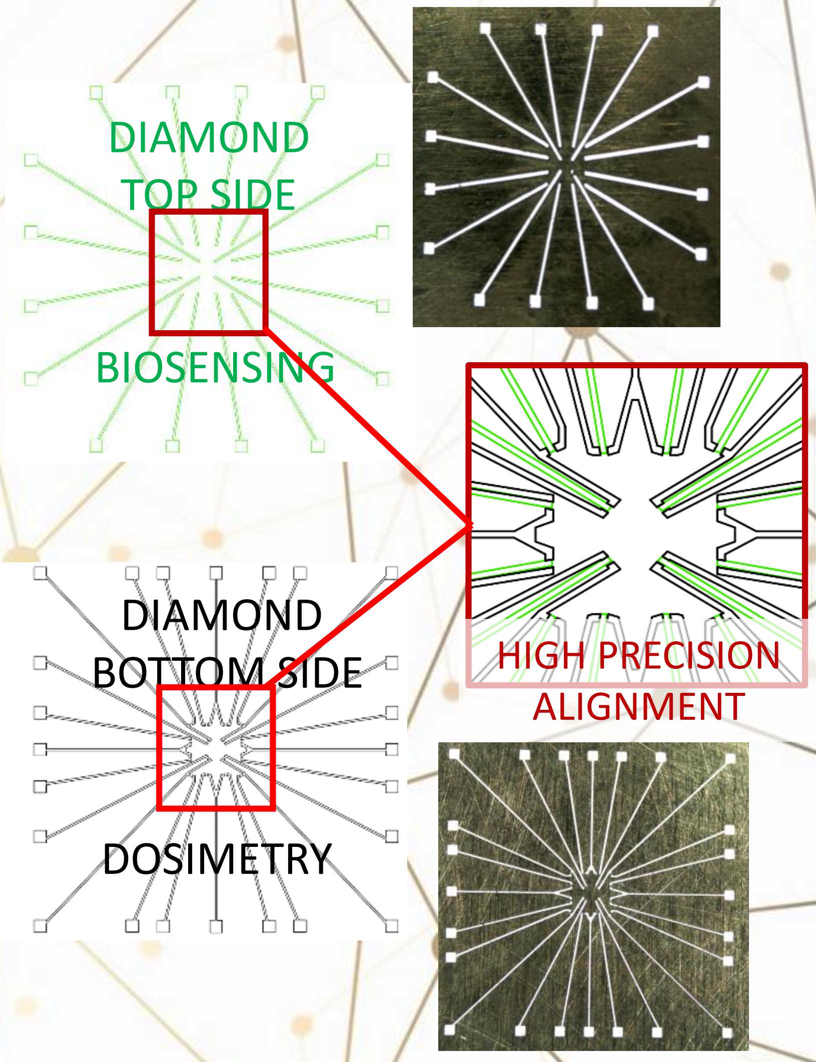

Integrated device

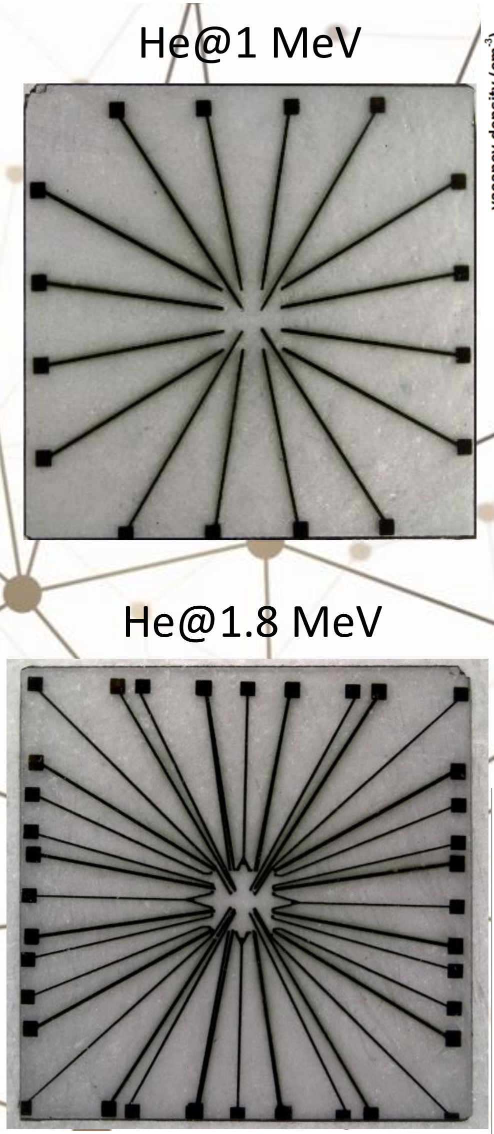
DiA CELL SENSOR

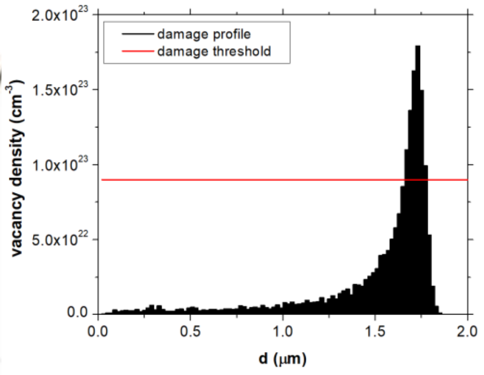
P. Olivero, et al., **NIMB 269 (2011) 2340–2344**
J. Forneris, et al., **EPL, 108 (2014) 18001**

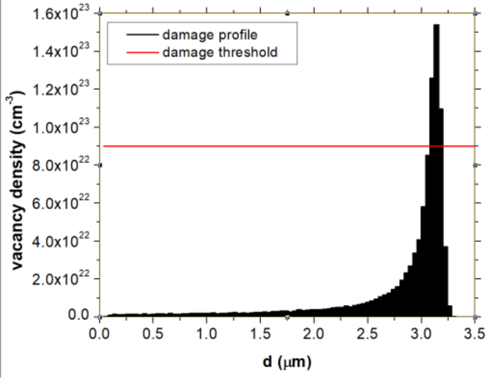
# DIACELL sensor fabrication: IBL



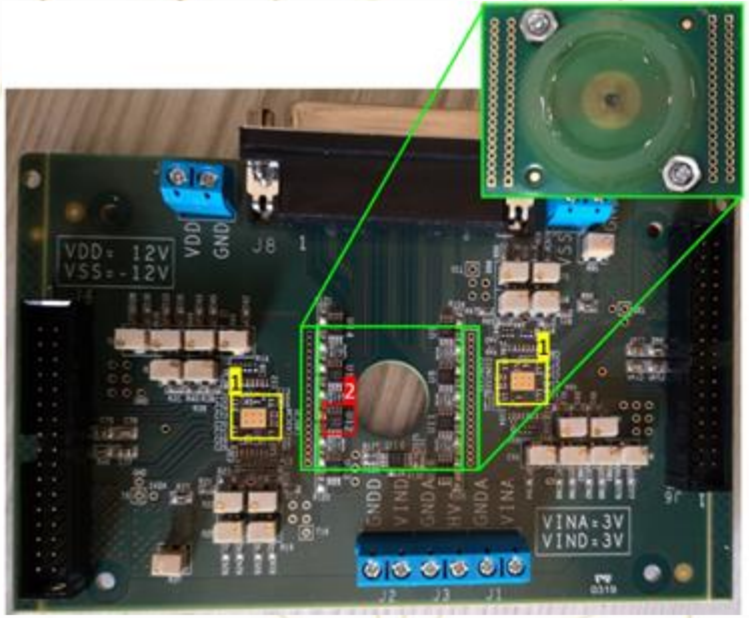



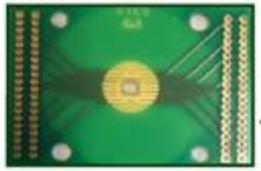




- ✓ Vertical irradiation
- ✓ Thin detector grade diamond

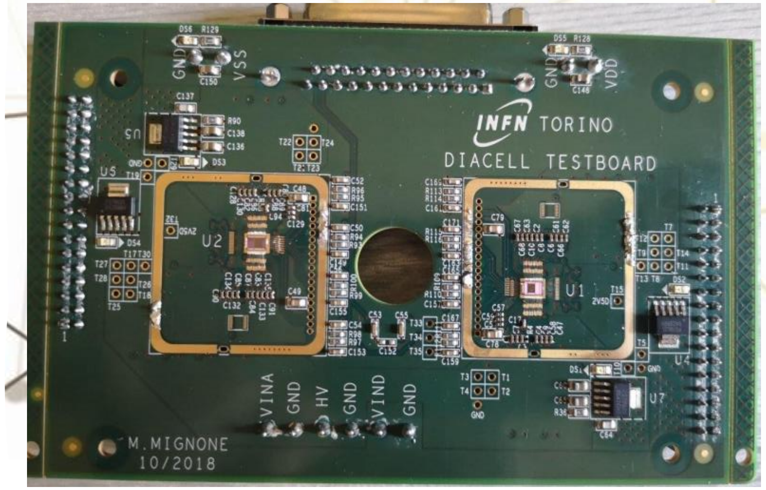
# Front-end electronics




Biosensing chip carrier



Dosimetric chip carrier




## Biophysical signals detection

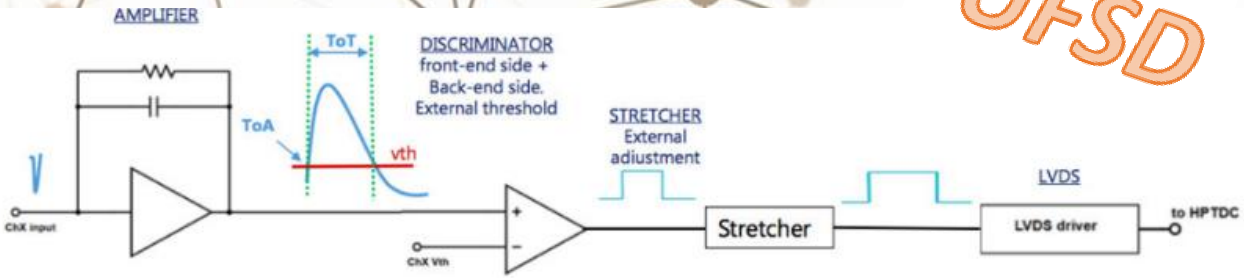
16 low noise transimpedance amplifiers + National Instrument ADC

*Amperometric detection*

*Current noise < 5pA*

*25 kHz sampling rate*

## Ionizing radiation detection



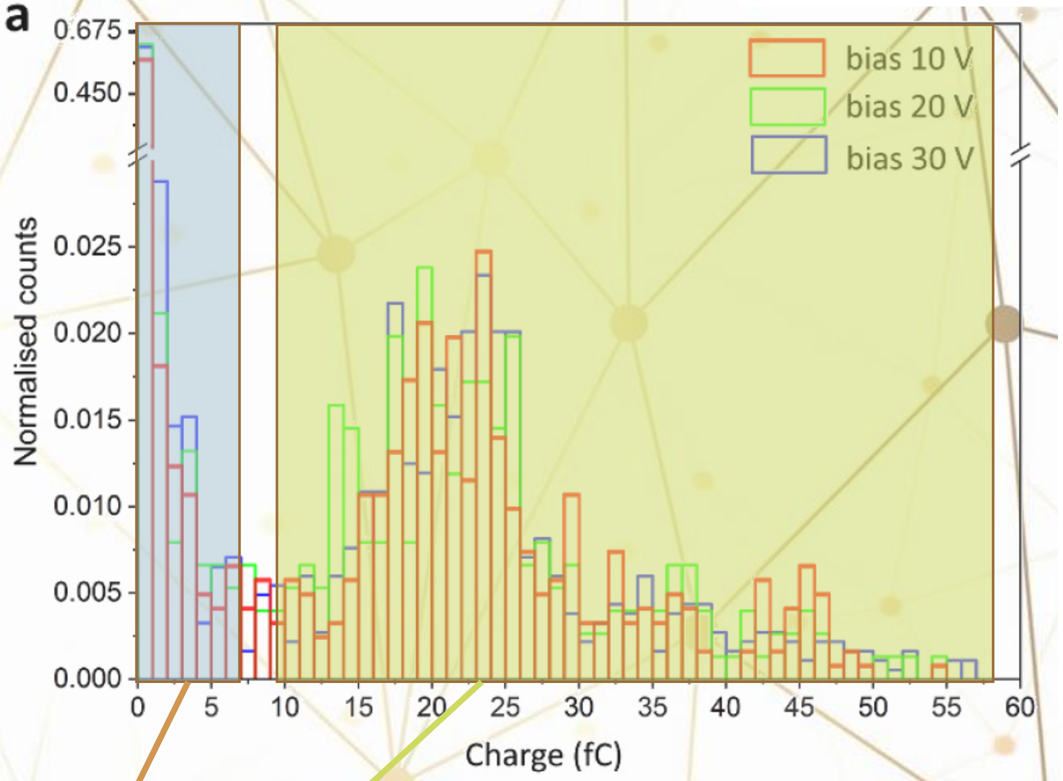

*TOFFEE - Time of Flight Front End Electronics*

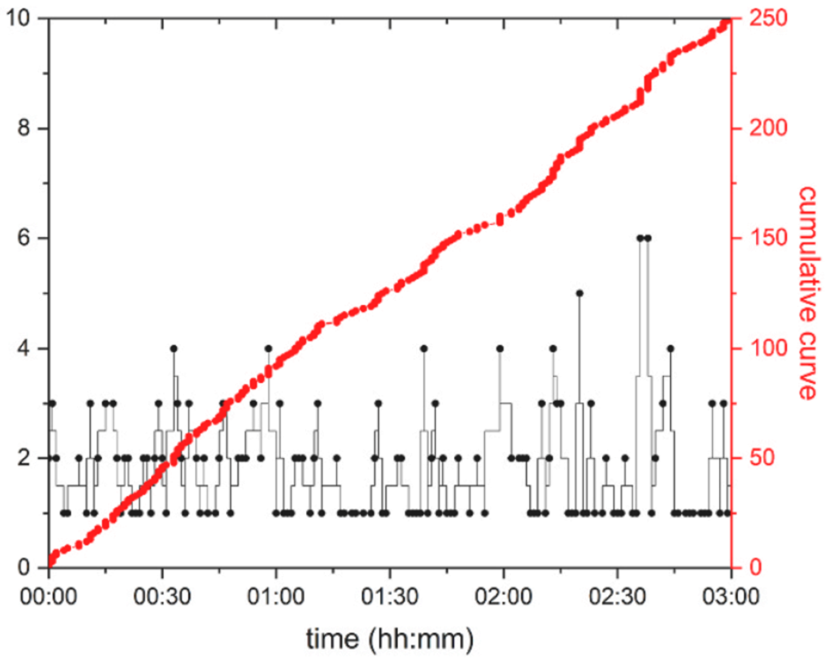
- ✓ Amplification stage
- ✓ Variable threshold discriminator
- ✓ LVDS output

F. Cenna et al., **Journal of Instrumentazion** 12, C03031 (2017)

# α-particle detection

Calibration source (**$Am^{241}$**)
**α-particle @ 5.5 MeV**





Activity = **9.775 kBq**

Expected emitted particles impinging electrode ~ 270

**Counting efficiency**~ 95%

Particle detected into the active area

Particle imping «far» from the active area

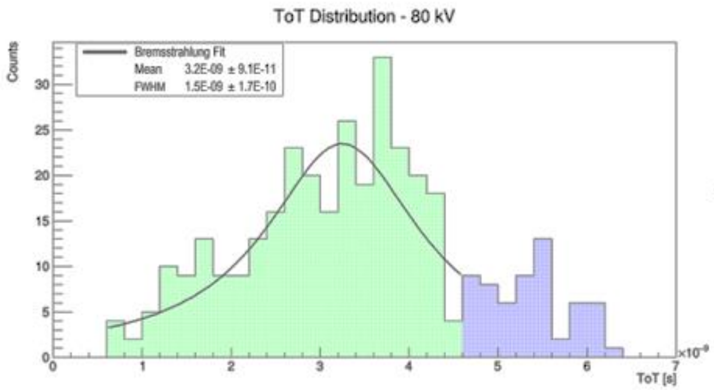
~13 eV per electron-hole pairs

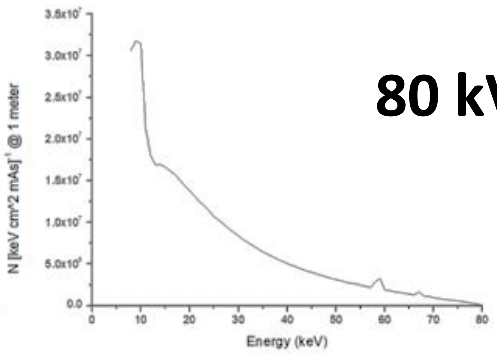
~ 70 fC charge induced by a single **α-particle**

Charge Collection Efficiency ~ 30 %

# X-rays detection

**Microfocus X-Ray Source (Hamamatsu L8121-03)**

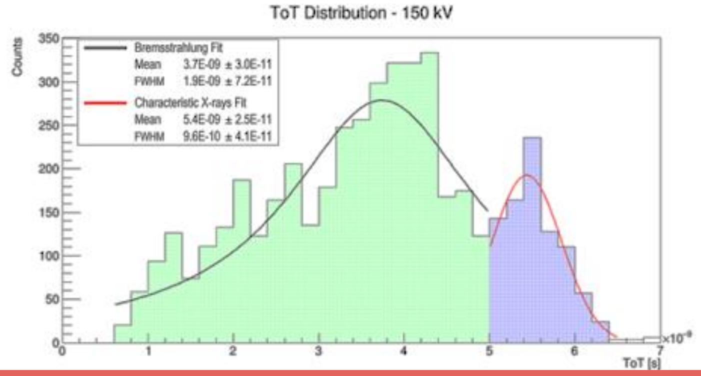


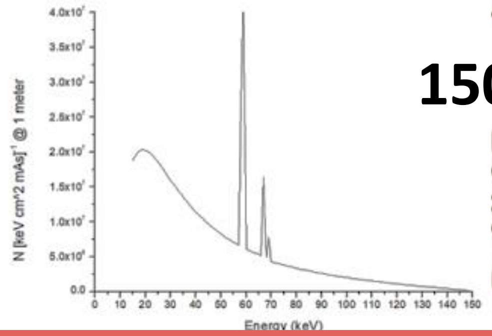




**80 kV**

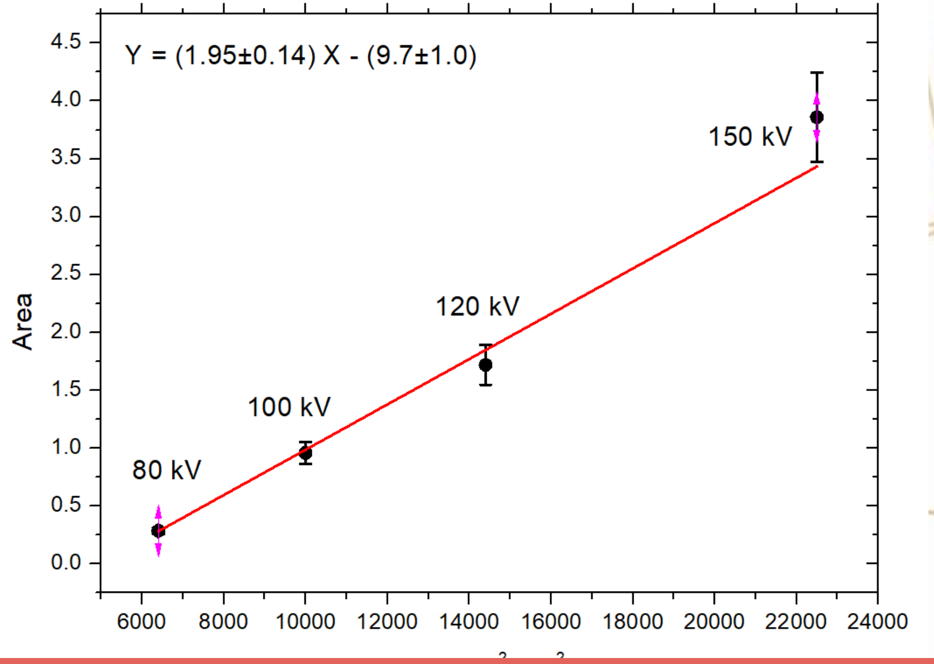
Bremsstrahlung

Characterstic X-Ray



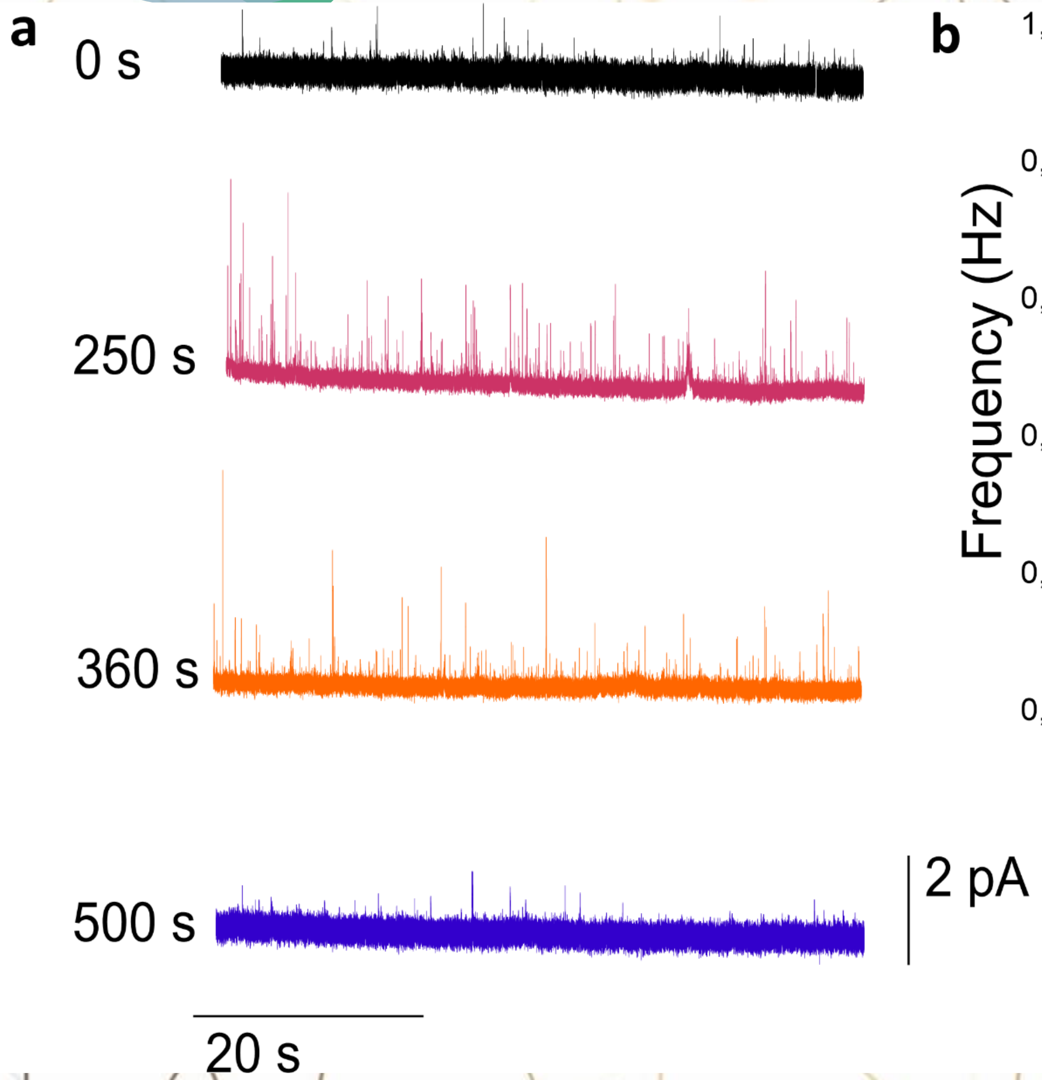



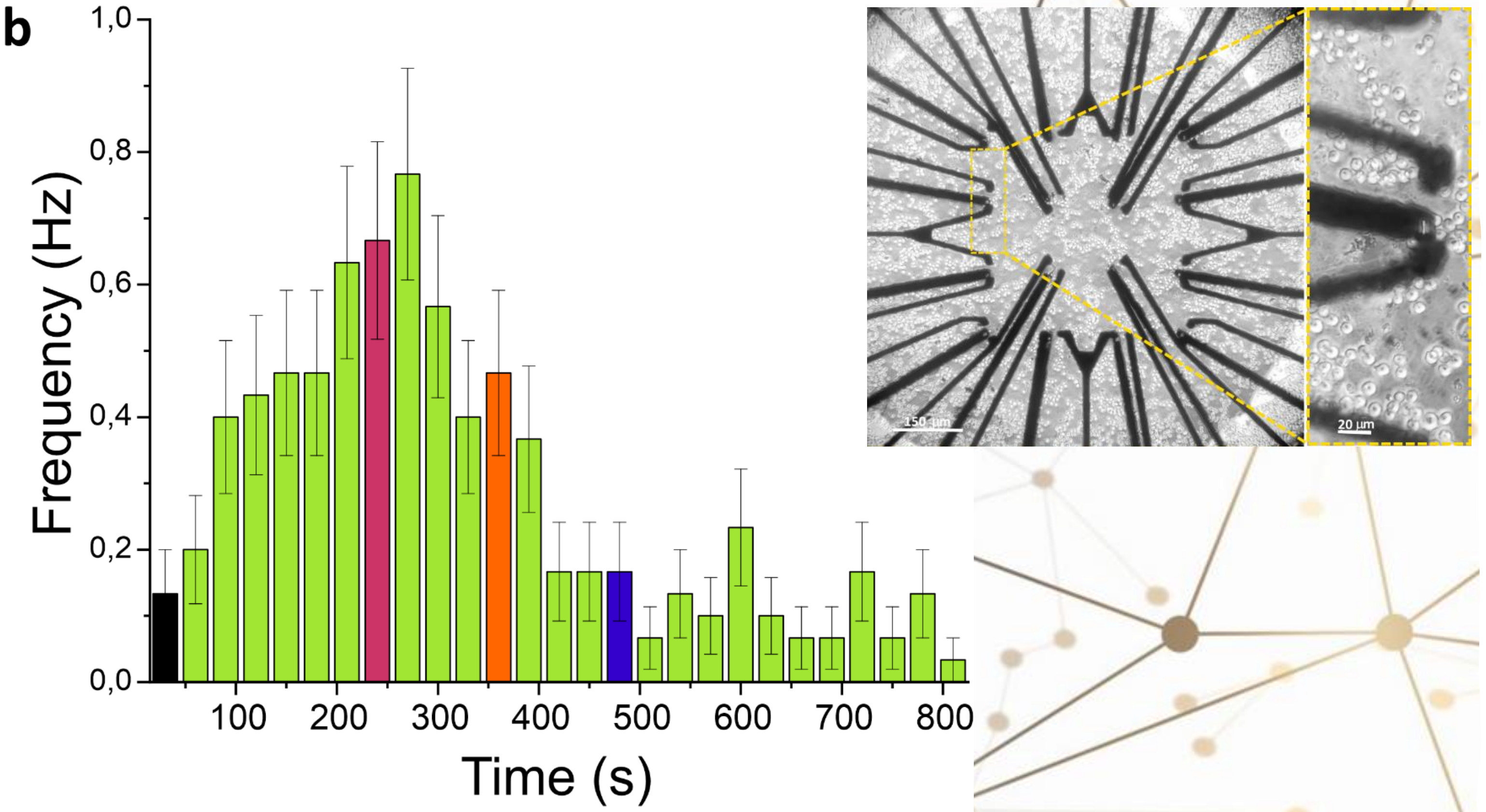

**150 kV**




G. Tomagra, et al., **Biosensors and Bioelectronics 220 (2023) 114876**

# CONTROL MEASUREMENT: EXOCYTOSIS VS TIME

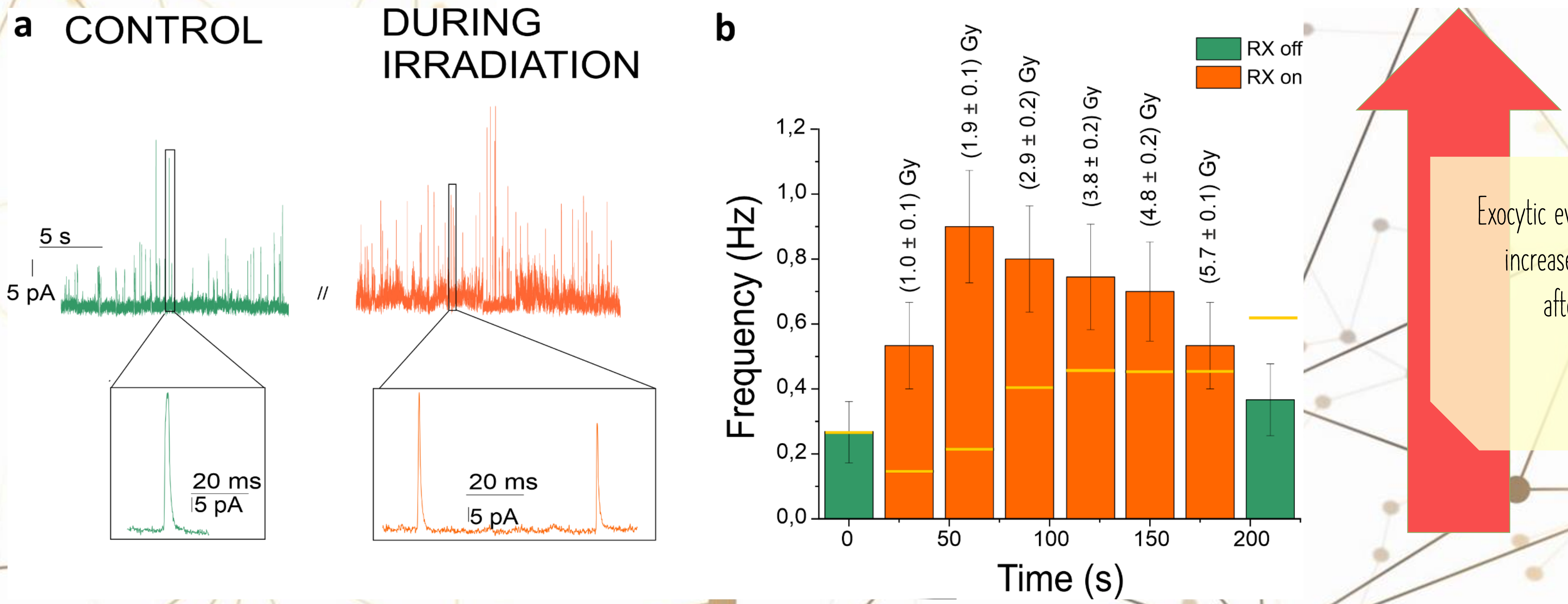



| $I_{max}$ (pA) | Q (fC) | $t_{1/2}$(ms) |
|---|---|---|
| 10.3 ± 1.0 | 147 ± 1 | 5.5 ± 1.0 |

G. Tomagra, et al., **Biosensors and Bioelectronics 220 (2023) 114876**

# DURING IRRADIATION: EXOCYTOSIS VS TIME




Exocytic event frequency increased of 220% after 1 Gy

*CONTROL*

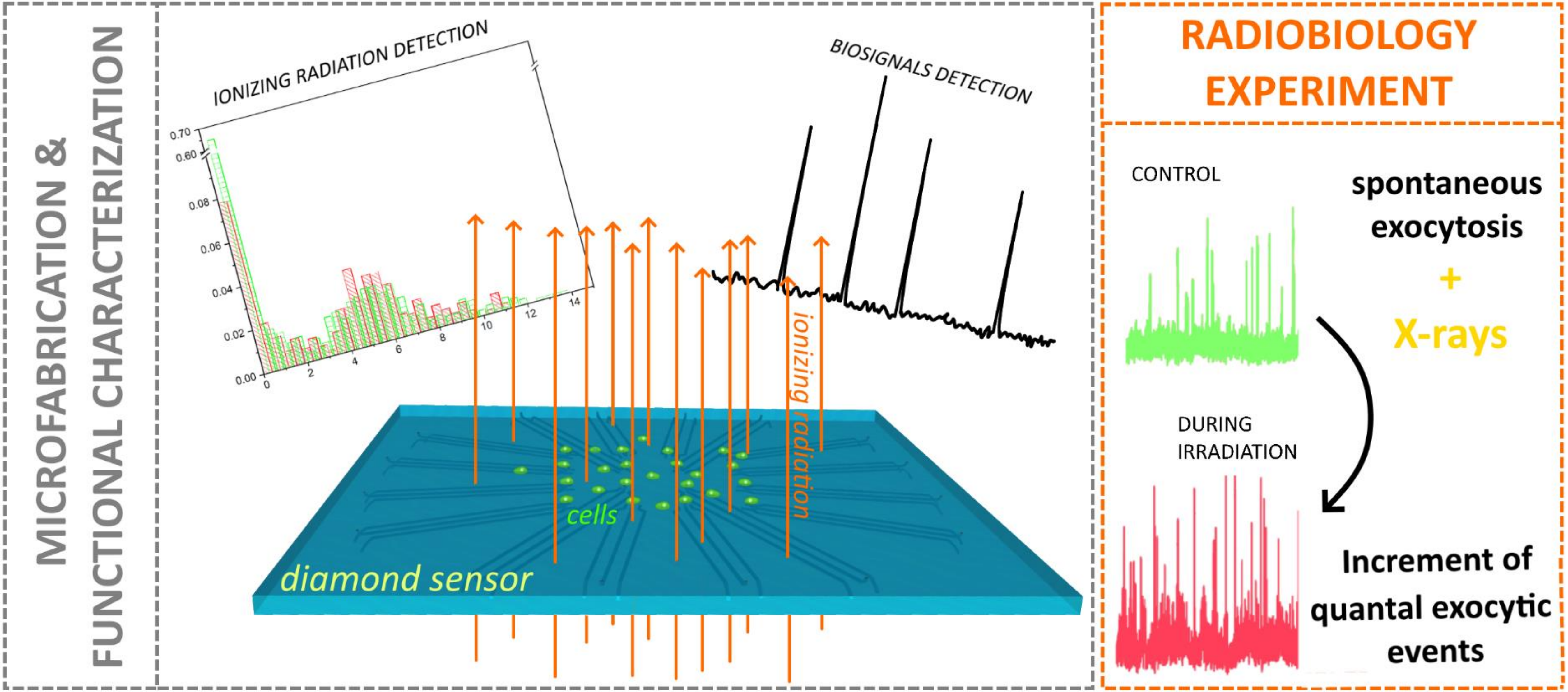
| $I_{max}$ (pA) | Q (fC) | $t_{1/2}$(ms) |
|---|---|---|
| 10.3 ± 1.0 | 147 ± 1 | 5.5 ± 1.0 |

=

*DURING IRRADIATION*

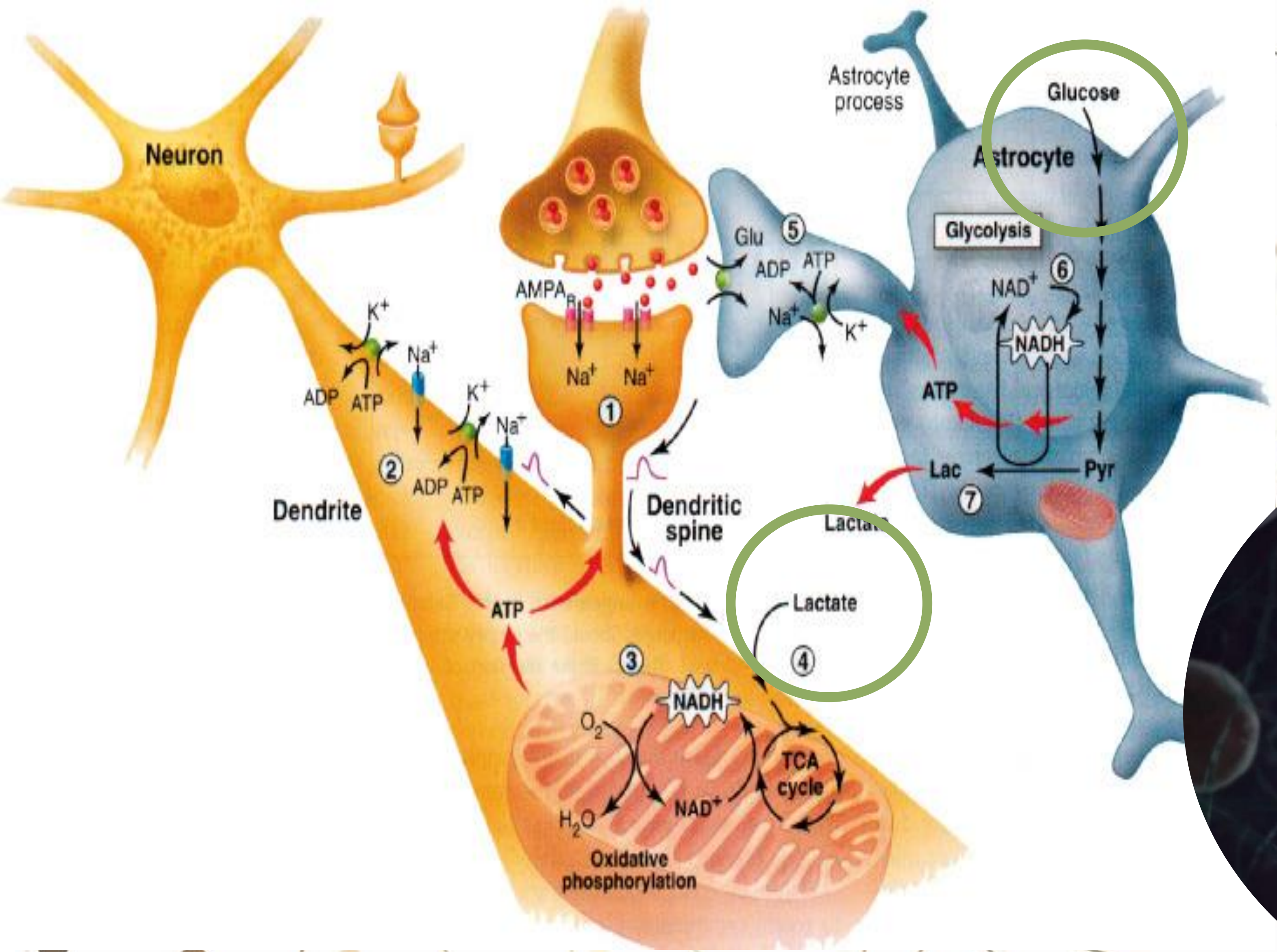
| $I_{max}$ (pA) | Q (fC) | $t_{1/2}$(ms) |
|---|---|---|
| 10.4 ± 1.4 | 120 ± 20 | 6.3 ± 0.6 |

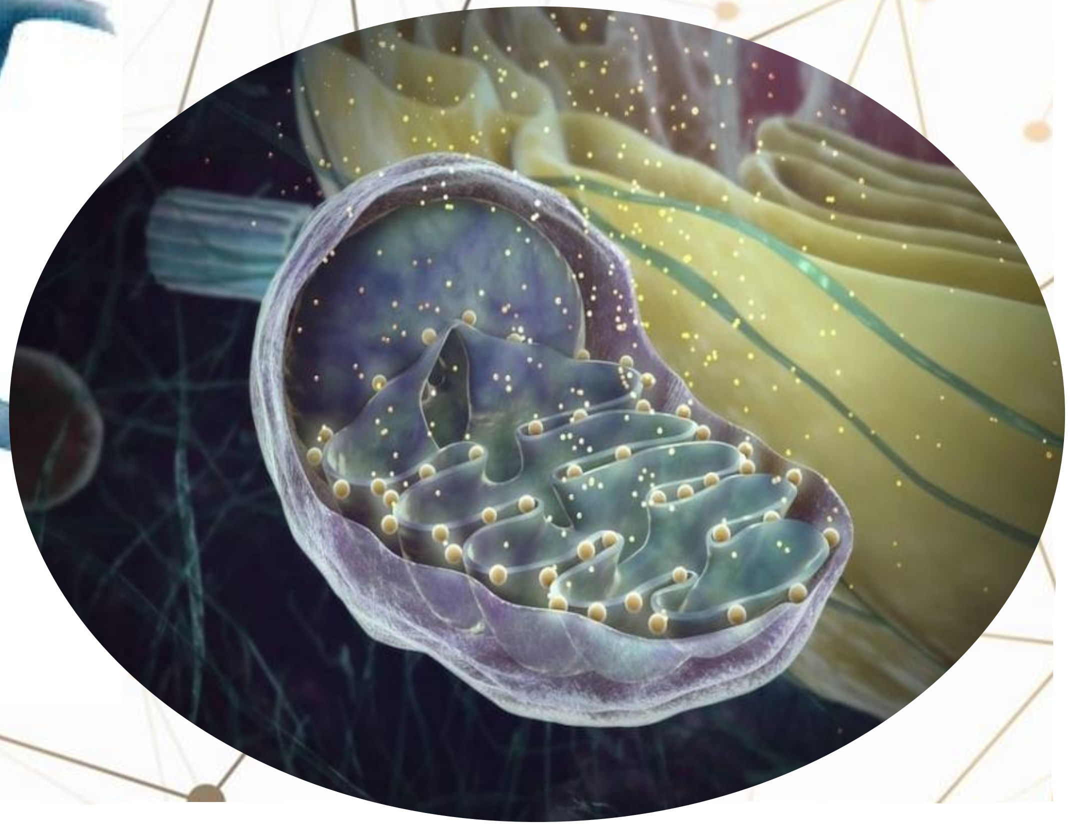
G. Tomagra, et al., **Biosensors and Bioelectronics 220 (2023) 114876**

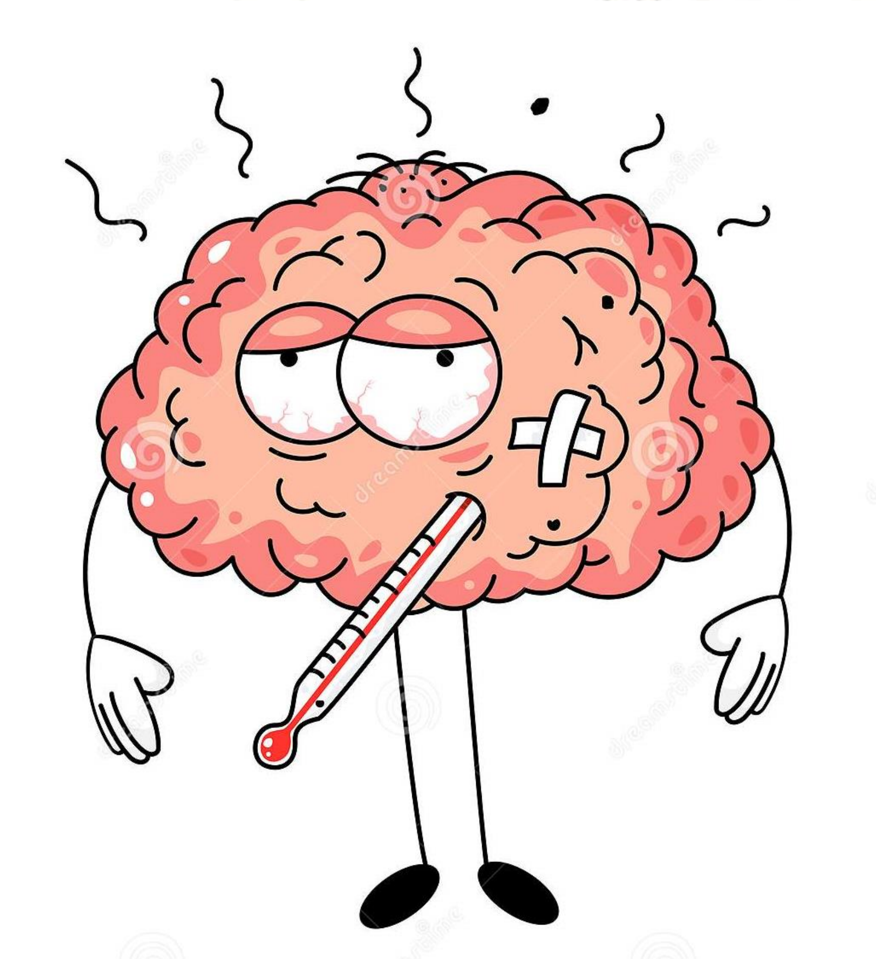

MICROFABRICATION &
FUNCTIONAL CHARACTERIZATION
IONIZING RADIATION DETECTION
BIOSIGNALS DETECTION
ionizing radiation
cells
diamond sensor
RADIOBIOLOGY EXPERIMENT
CONTROL
spontaneous exocytosis
+
X-rays
DURING IRRADIATION
Increment of quantal exocytic events

# OUTLINE

- ✓ A bit of cell biology… (from a NOT biologist)
- ✓ Standard tools for electrophysiology experiments
- ✓ Artificial DIAMOND for sensors development
- ✓ Some examples of cell signals detection
- ✓ Diamond particle detectors
- ✓ Radiobiology using diamond-base sensors
- New frontiers: quantum sensing (e.g. intracellular temperature detection)


Neuron
Astrocyte
process
Glucose
Astrocyte
Glycolysis
Glu
5
ADP
ATP
$Na^+$
$K^+$
AMPA
$Na^+$
$Na^+$
1
$K^+$
$Na^+$
ADP
ATP
2
Dendrite
ADP
ATP
NAD⁺
6
NADH
ATP
Lac
Pyr
7
Lactate
Dendritic
spine
ATP
Lactate
4
3
NADH
$O_2$
$H_2O$
NAD⁺
TCA
cycle
Oxidative
phosphorylation



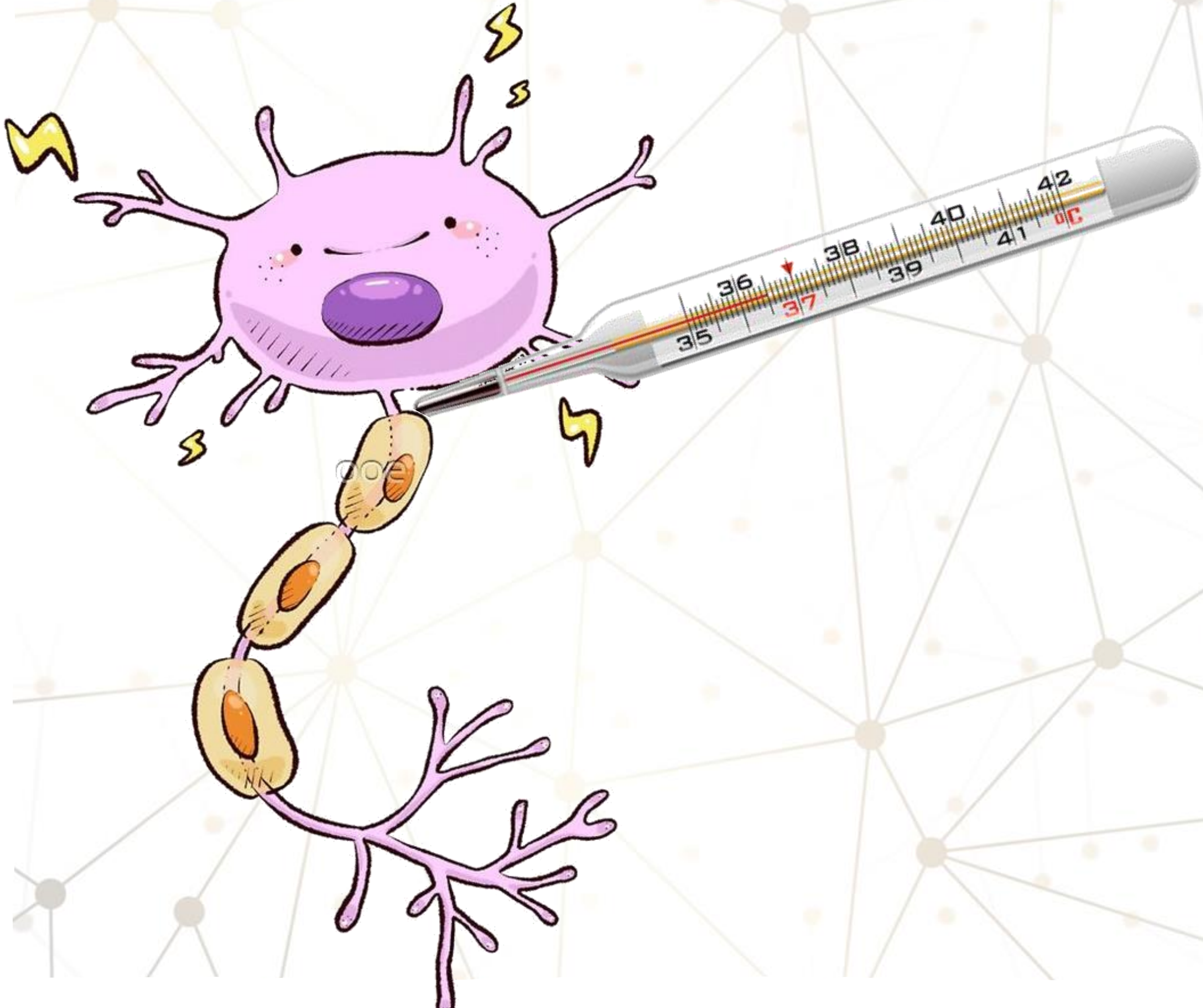



LAVORO E...

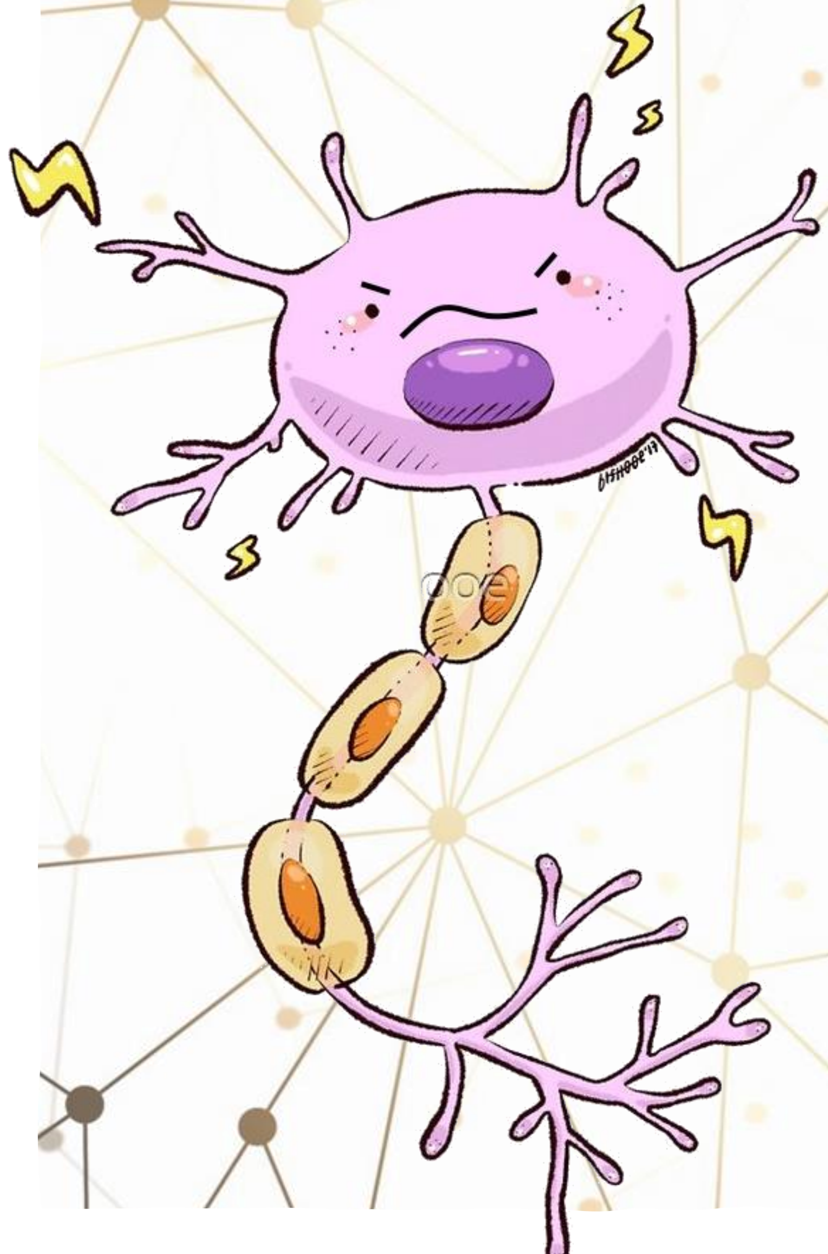
ENERGIA
METABOLISMO CELLULARE

TEMPERATURA

# MA COME SI MISURA LA TEMPERATURE AD UN NEURONE???



# COME SI MISURA LA TEMPERATURE AD UN NEURONE???



5 - 100 µm

Termometro è almeno
1000 volte
più grande di un neurone

# BIOMEDICAL APPLICATIONS OF NANODIAMONDS

**BIO-IMAGING**

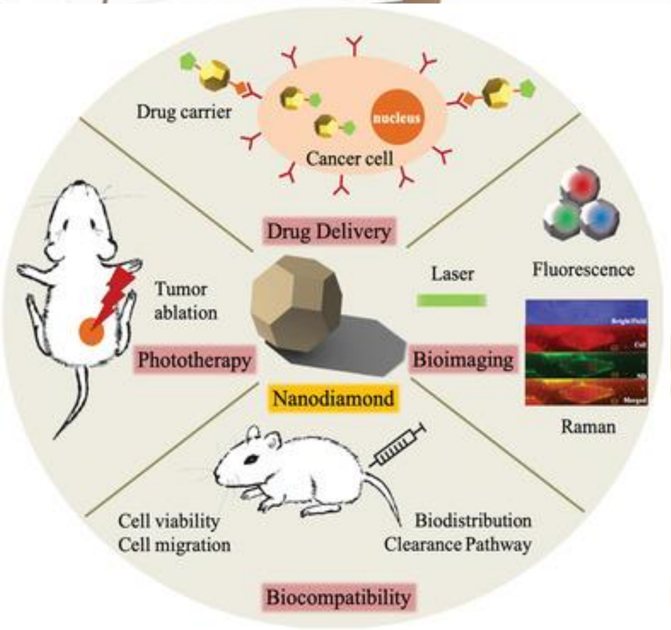
- DYE LABELLING
- PARTICLE TRACKING
- PHOTOACOUSTIC IMAGING
- MRI

**QUANTUM SENSING**

- NV MAGNETOMETRY
- NV THERMOMETRY

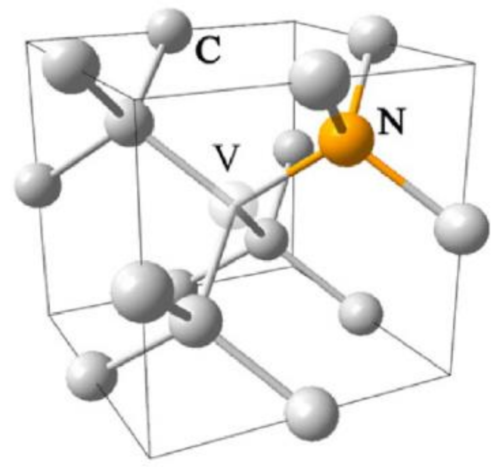
**DRUG DELIVERY**

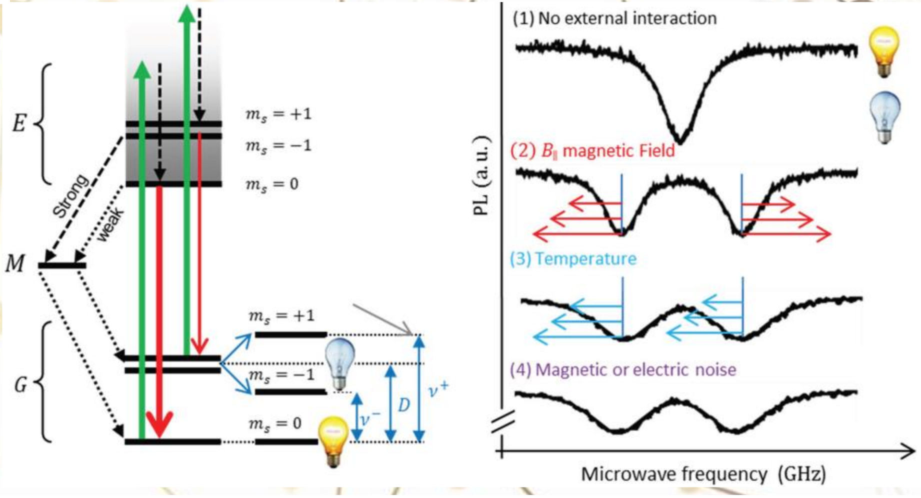
- ANTI-CANCER DRUGS
- DNA, MICRO RNA
- ANTIBIOTICS




Gao, G. Y. Et al., *Small* 2019, 15, 1902238

NV CENTER (NITROGEN-VACANCY):

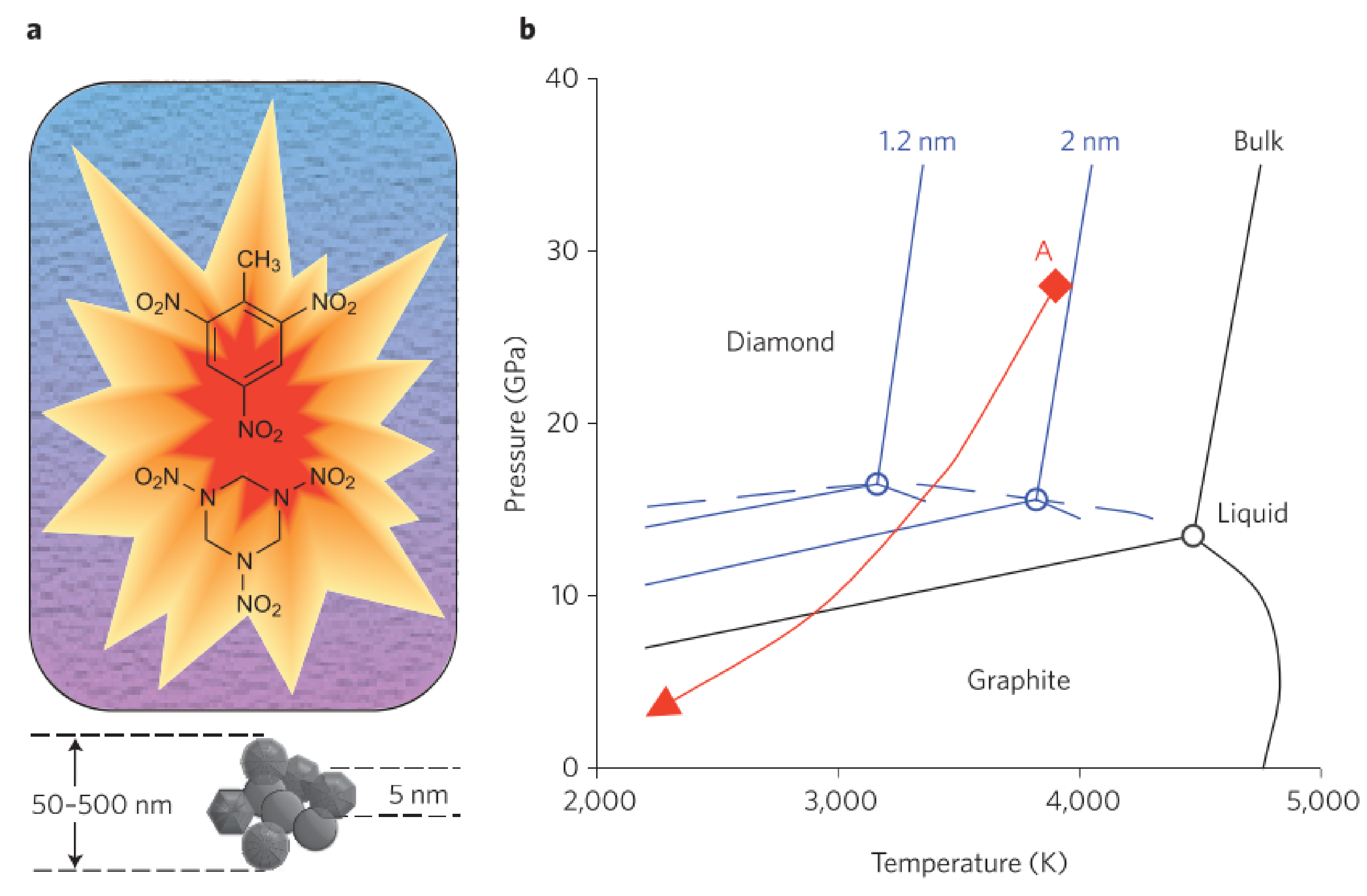


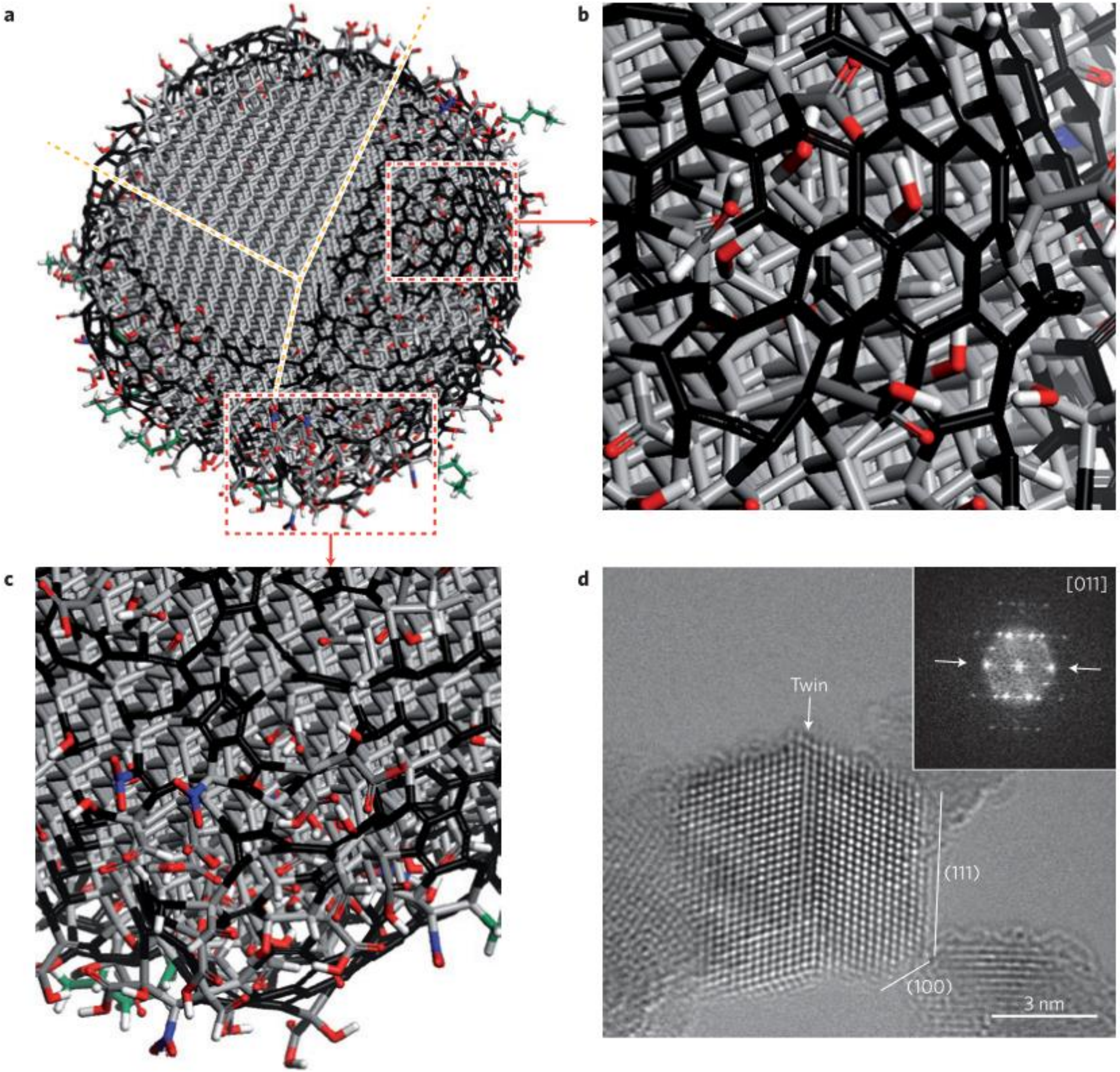

van der Laan, K. J., Hasani, M., Zheng, T., Schirhagl, R., *Small* 2018, 14, 1703838

$NV^-$ CENTER ELECTRONIC STRUCTURE CAN BE PERTURBATED BY A MAGNETIC FIELD AND BY TEMPERATURE VARIATIONS

# DND: DETONATION NANODIAMOND




detonazione di composti altamente esplosivi contenenti carbonio, tra cui miscele di trinitrotoluene (TNT) e ciclotrimetilentrinitroammina (RDX)


a
b
c
d
[011]
Twin
(111)
(100)
3 nm

# PROPRIETÀ DEI NANODIAMANTI #3

- Prodotti per frammentazione di diamante monocristallino o per detonazione di composti esplosivi contenenti carbonio

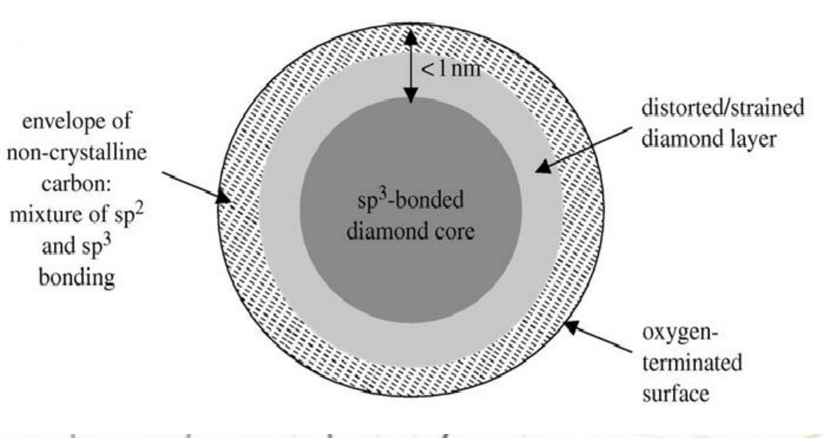
- Dimensione particella primaria:

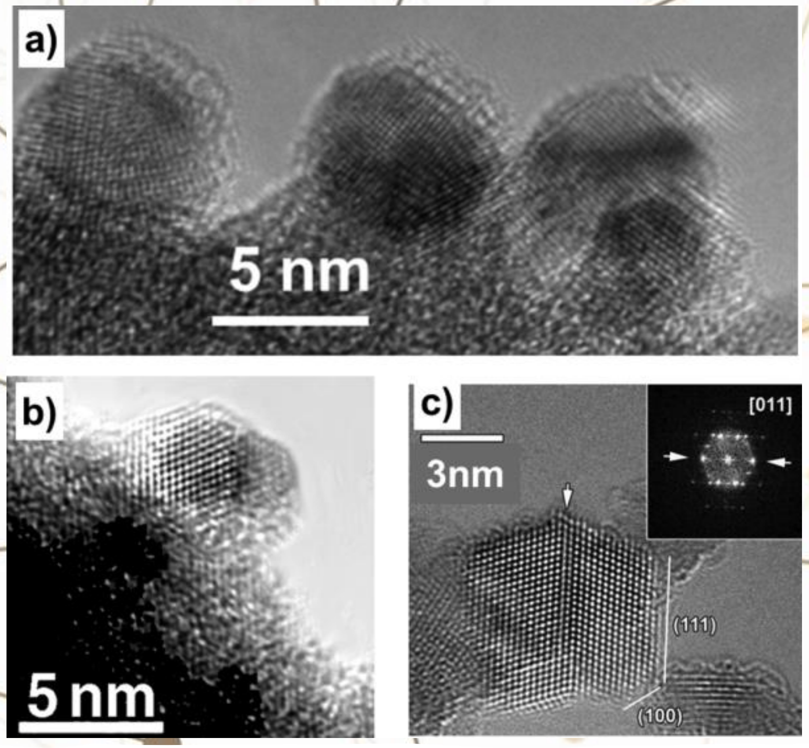
  da 5 nm a 1 µm

- Impurità di N presenti naturalmente:

  10 – 100 ppm

- Contaminazioni superficiali grafitiche e carbonio amorfo



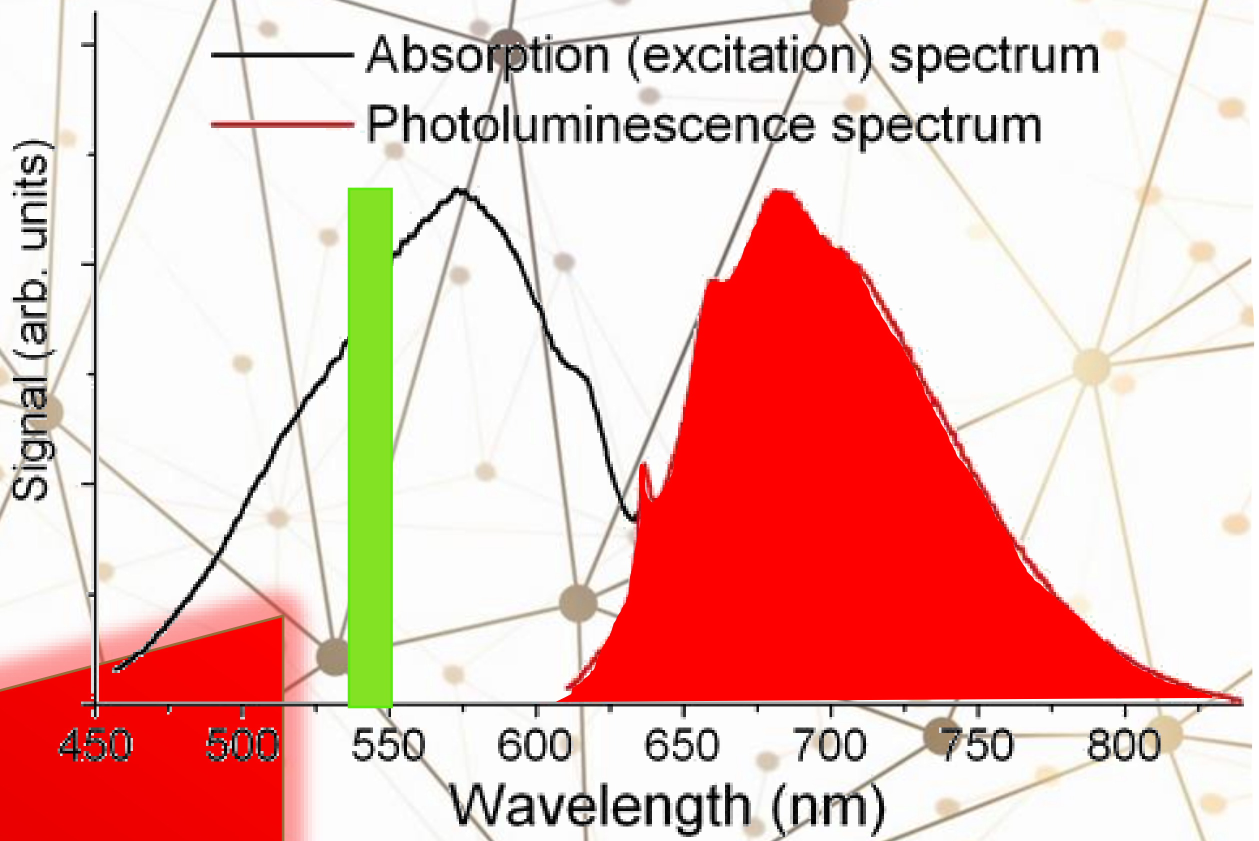
# CENTRI LUMINESCENTI NEL DIAMANTE

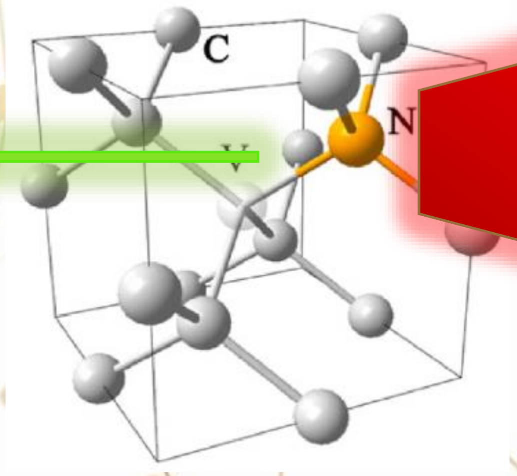
- Difetti nel reticolo cristallino

(vacanze, atomi sostituzionali e/o interstiziali)

Livelli intermedi nella gap proibita

Se eccitati, possibile transizione radiativa



# CHARACTERISTICS OF THE INVESTIGATED ND

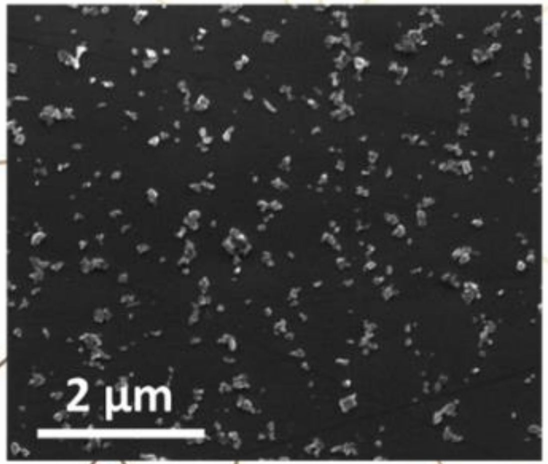
Produced by fragmentation of HPHT diamond

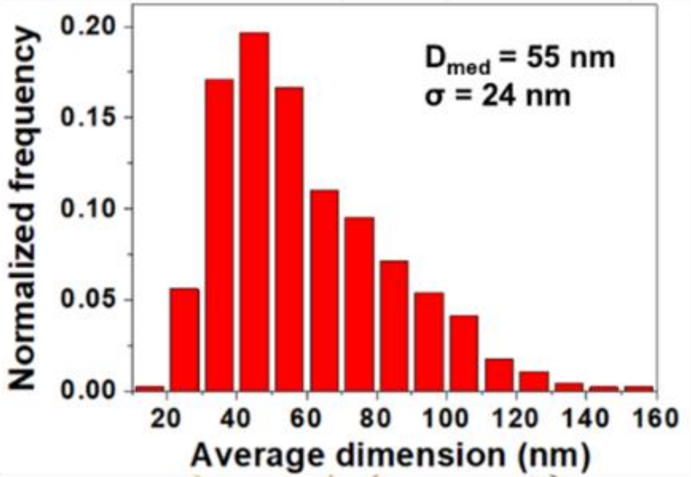
Nitrogen impurities: 100 ppm

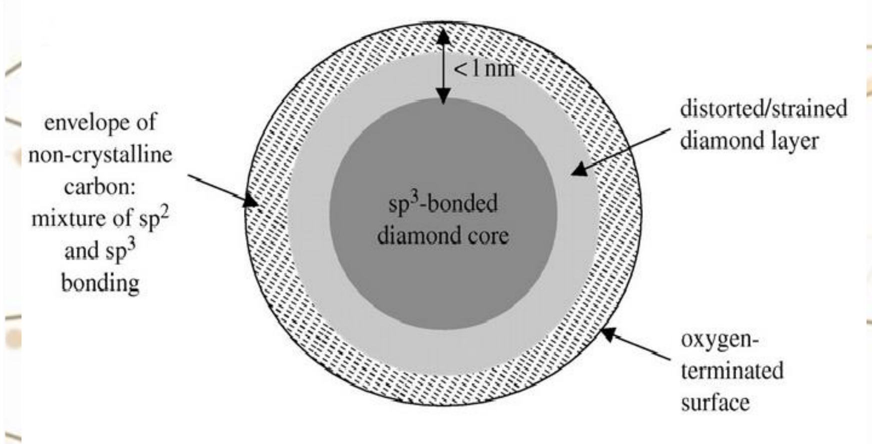
Surface contamination with amorphous and graphitic phases

microdiamant

Morphological and dimensional analysis of the investigated NDs



# THERMAL TREATMENTS ON NDS

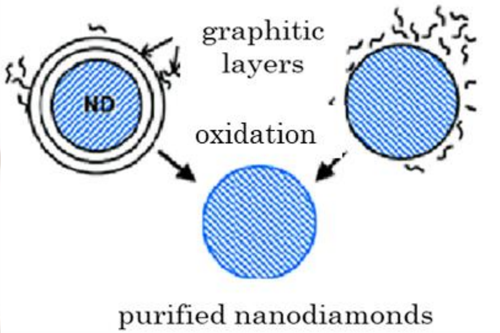
Untreated ND → $N_2$ flow 2 h 800 °C → air exposure 8 h 450 °C

ANNEALING

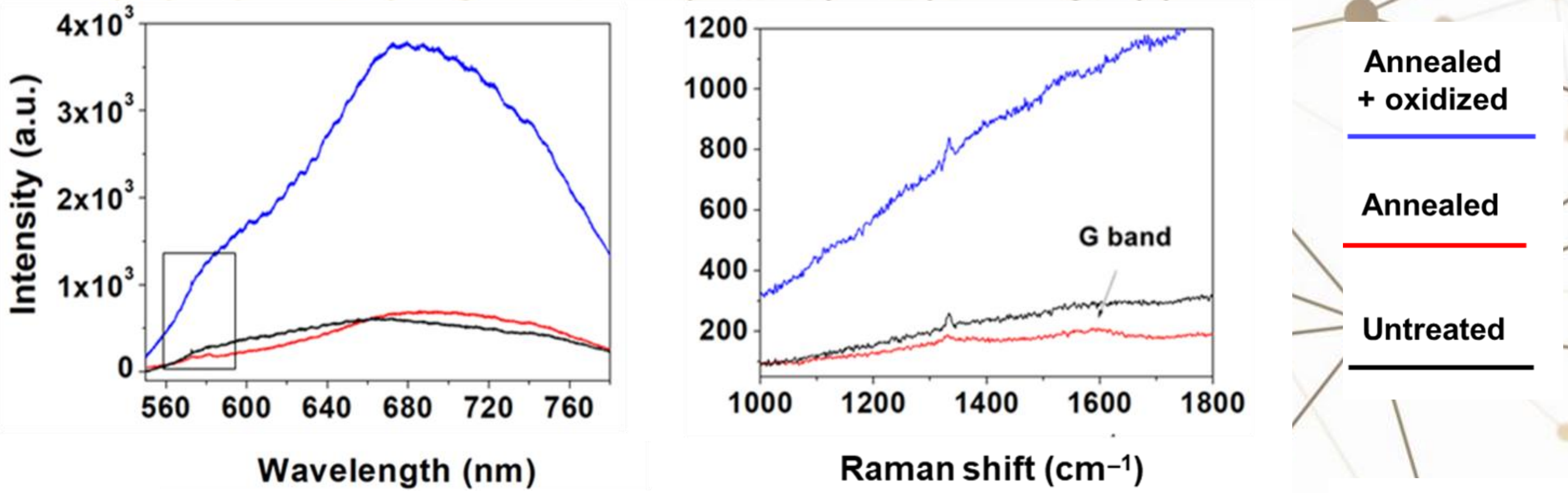
Graphitization of amorphous carbon phases, preserving diamond

OXIDATION

Etching of defective and graphitic layers




## RAMAN/PHOTOLUMINESCENCE SPECTROSCOPY



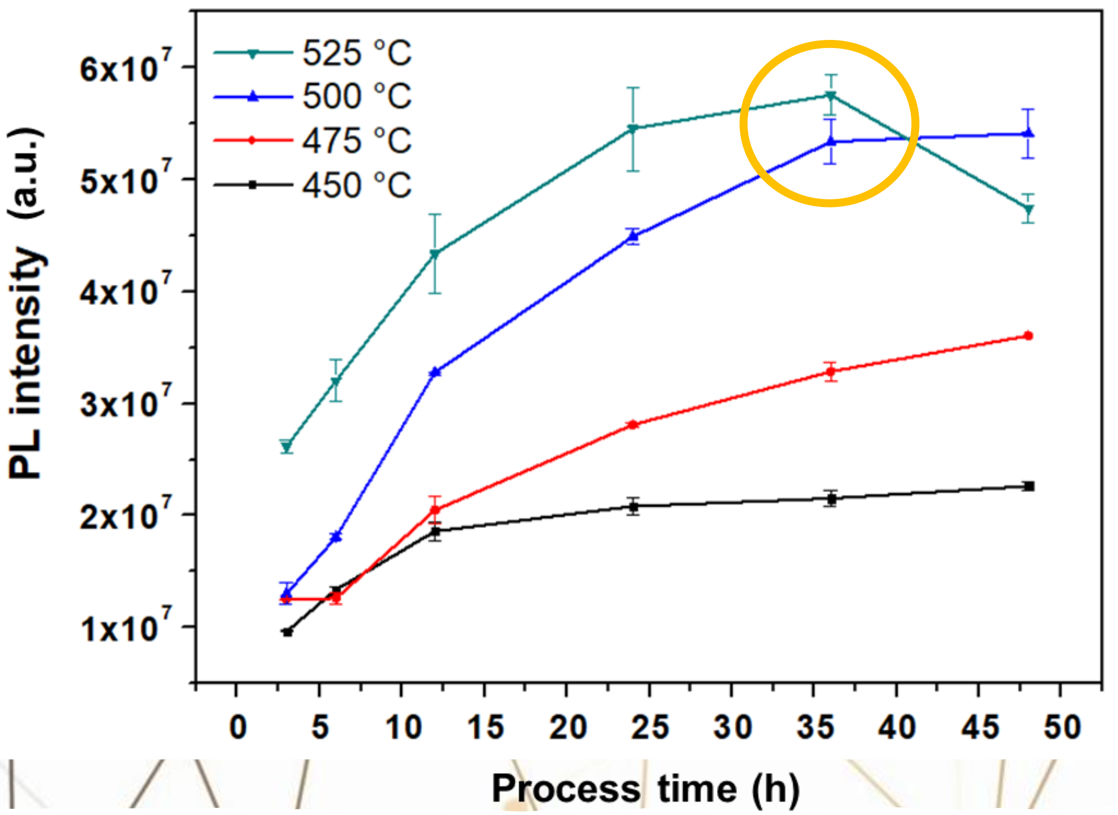

Aprà, P. et al., *Nanomaterials* **2021**, *11*, 2740

# SYSTEMATIC OXIDATIONS

## PL SPECTROSCOPY → FLUORESCENCE

PL intensity (integrated between 565 nm and 780 nm) increase as the oxidation level is higher

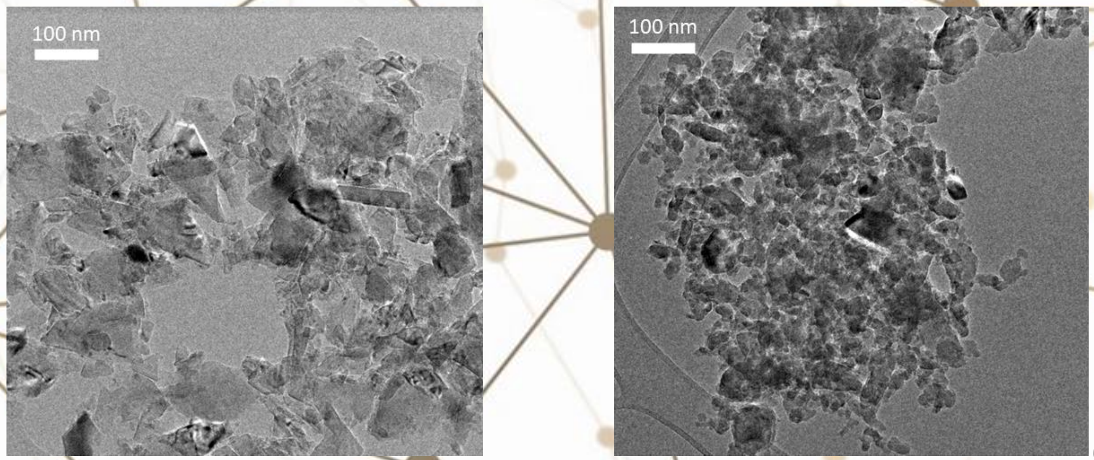
Excessive oxidation (> 36 h at 525 °C ) resulted detrimental, probably due to size reduction




Optimization → air oxidation 36 h 500 °C

**MSY-MND Annealed 2h at 800 °C +**

(a) **Oxidized at 450 °C for 12h** (b) **Oxidized at 525 °C for 48h**



# ION IRRADIATION

NV centers creation

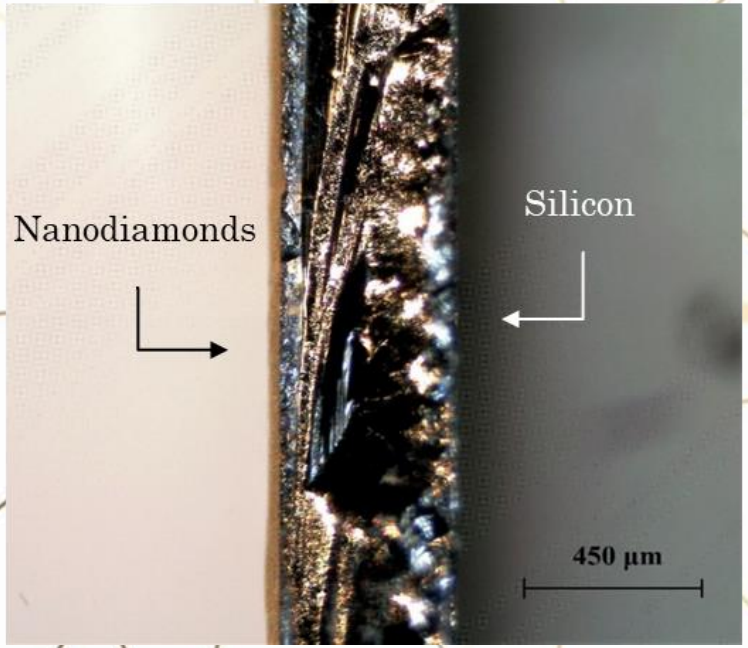
Nitrogen impurities already present (about 100 ppm)

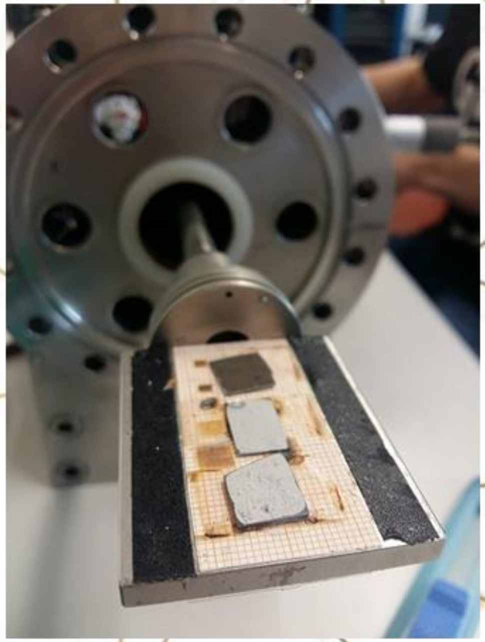
Proton beam irradiation (~ 2 MeV) ⟶ vacancies creation

Fluence range $10^{14}$ - $10^{17}$ $cm^{-2}$

Istituto Nazionale di Fisica Nucleare

"Dia.Fab." beam time

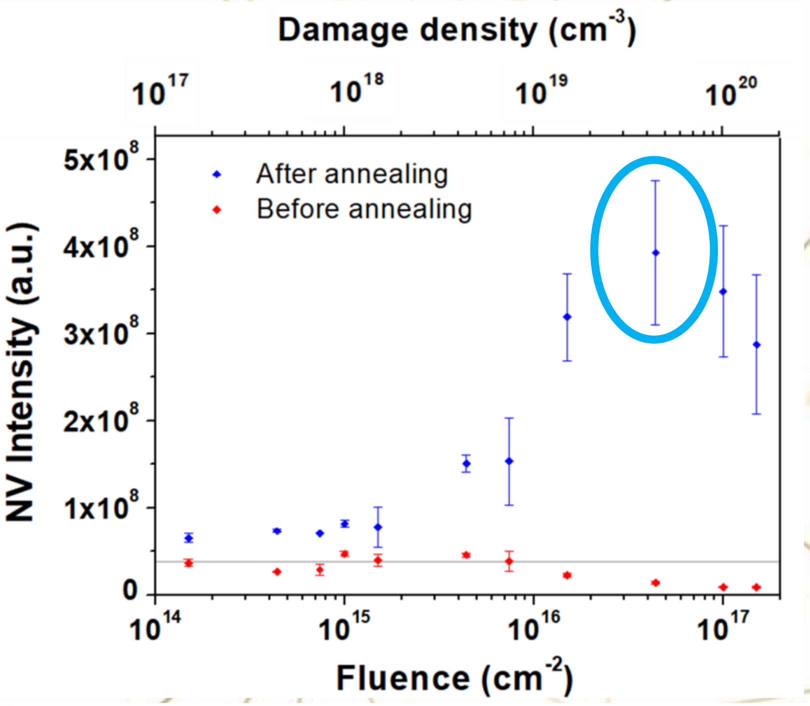


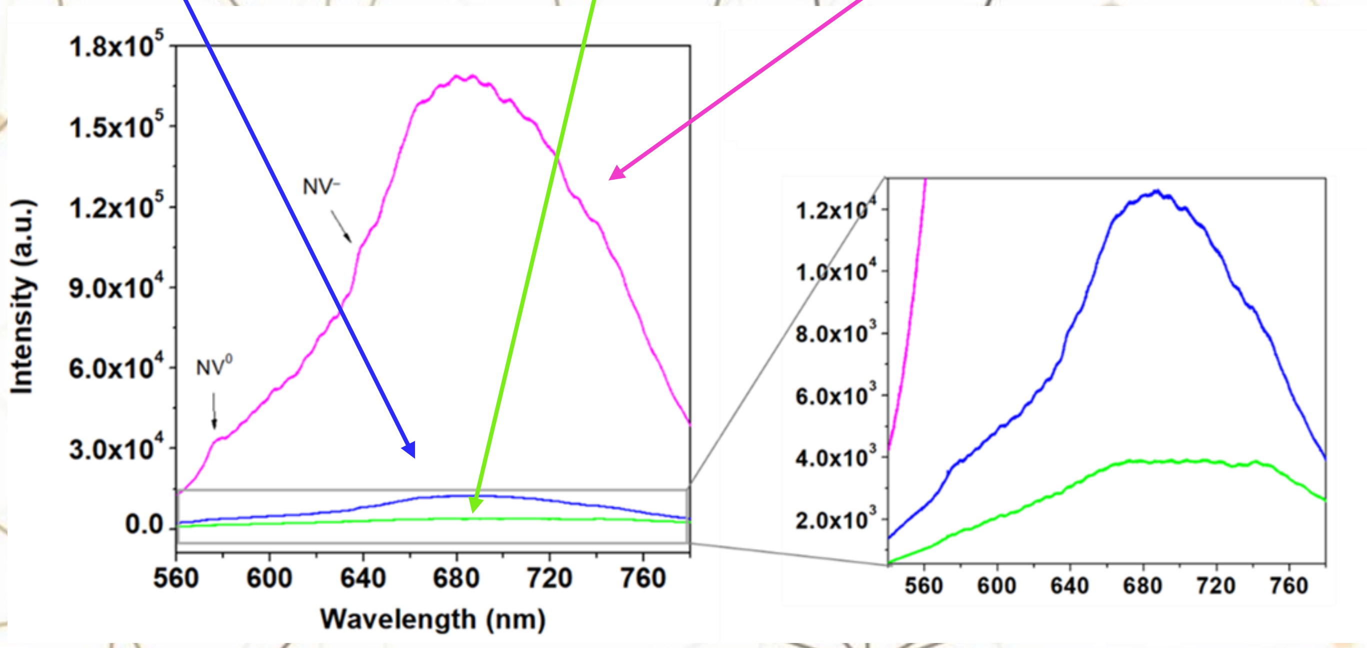
AN2000 INFN-LNL

# CHARACTERIZATION OF IRRADIATED ND

Untreated ND → $N_2$ 2 h 800 °C → air oxidation 8 h 450 °C → $H^+$ 2 MeV $F = 1{\times}10^{14}\ cm^{-2} - 2 \times 10^{17}\ cm^{-2}$ → $N_2$ 4 h 800 °C




Fluorescence following ion irradiation as a function of the fluence

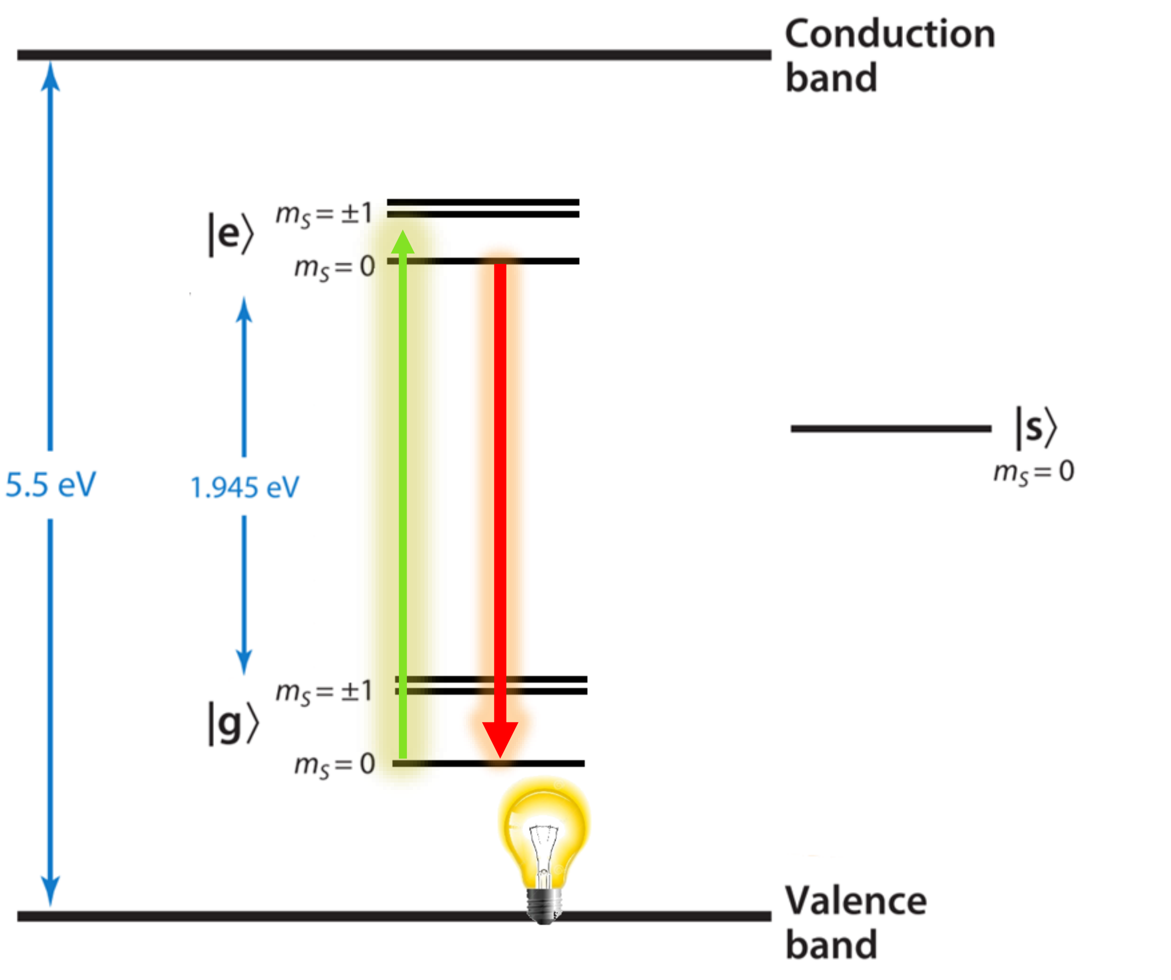


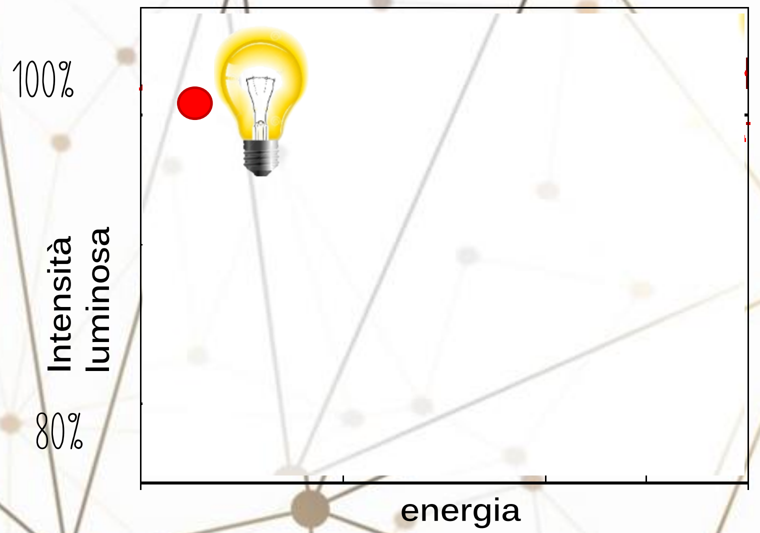

Thermal annealing ⟶ coupling the newly created vacancies with the nitrogen impurities

Max. fluorescence ⇨ $H^+$ 2 MeV $F = 4{\times}10^{16}\ cm^{-2}$

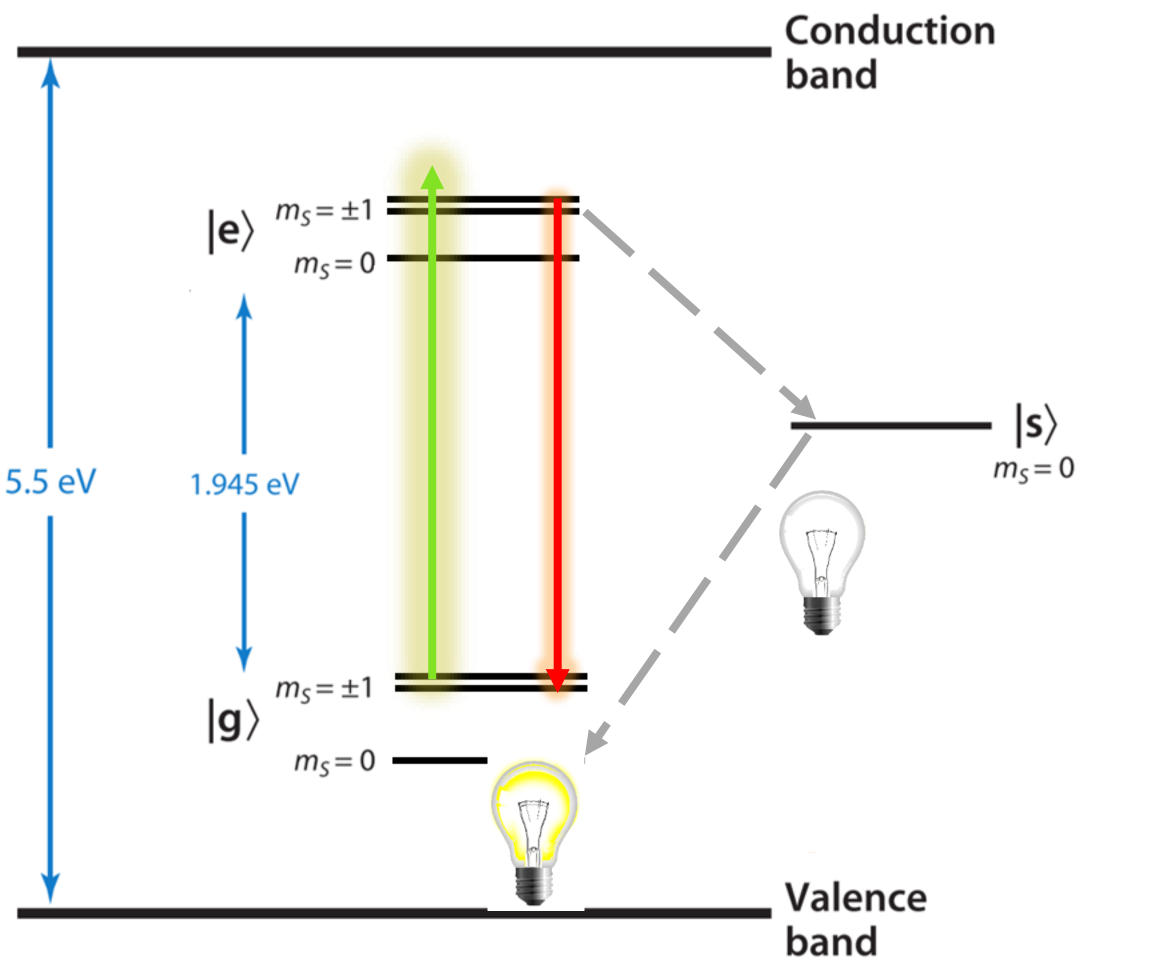
Increase of ~ 1 order of magnitude in fluorescence

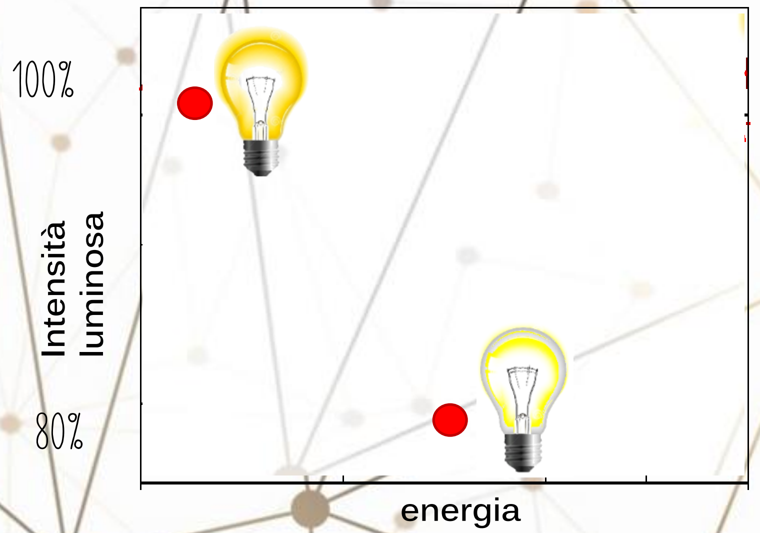
# ODMR - OPTICALLY DETECTED MAGNETIC RESONANCE



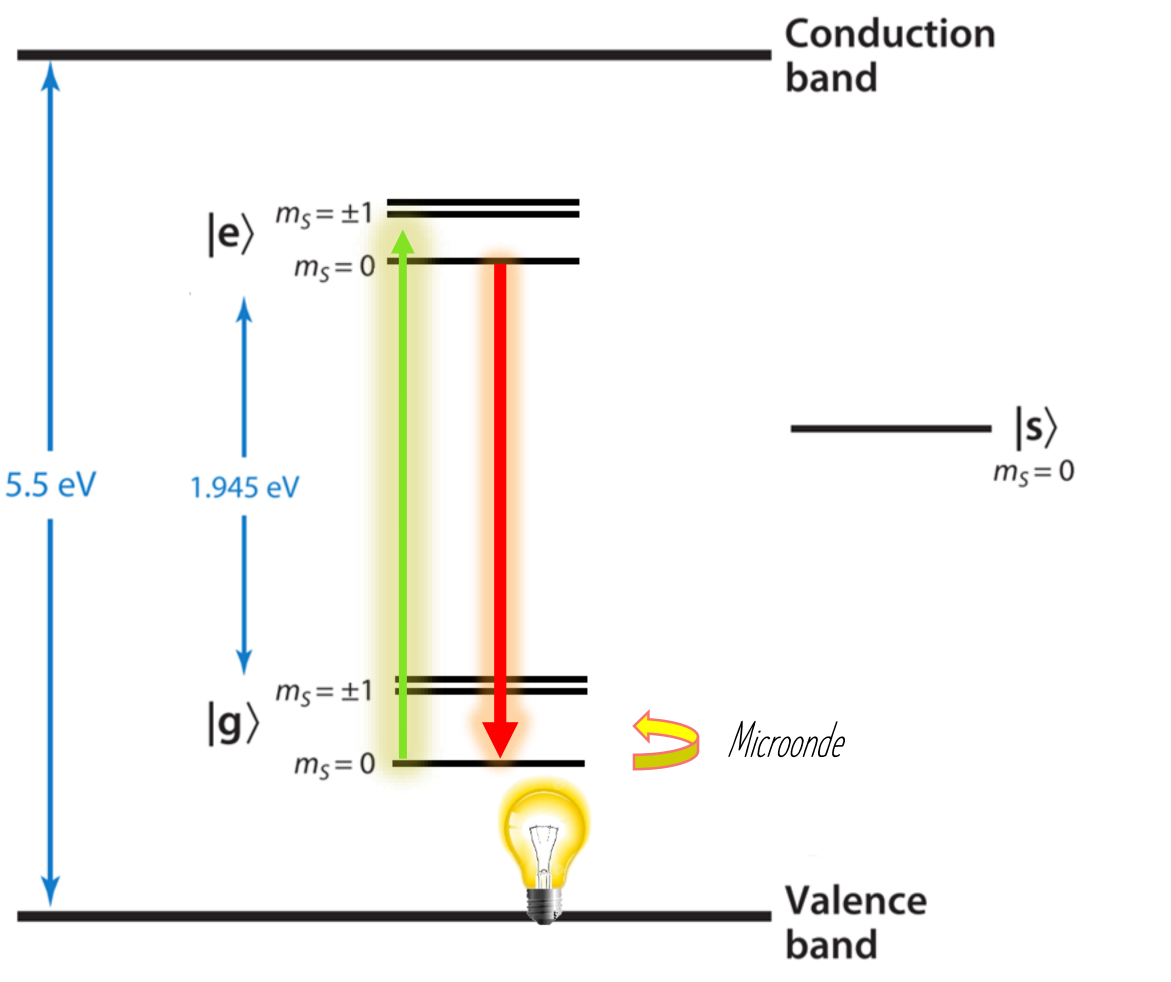



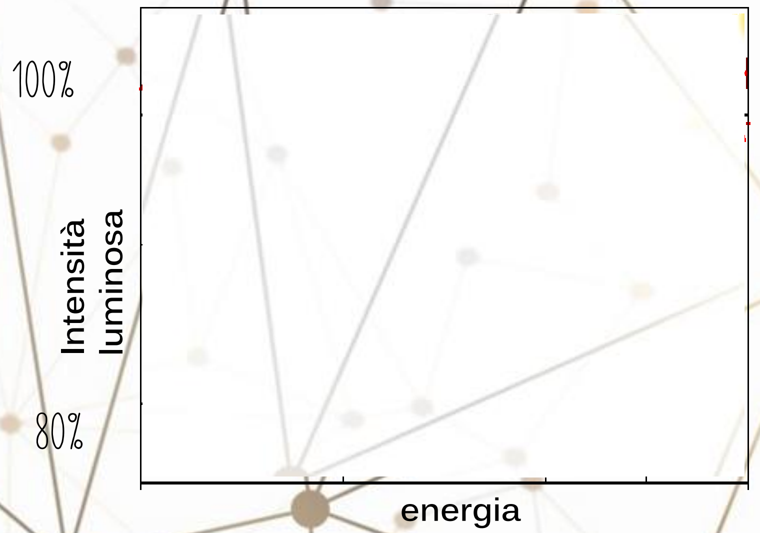
# ODMR - OPTICALLY DETECTED MAGNETIC RESONANCE



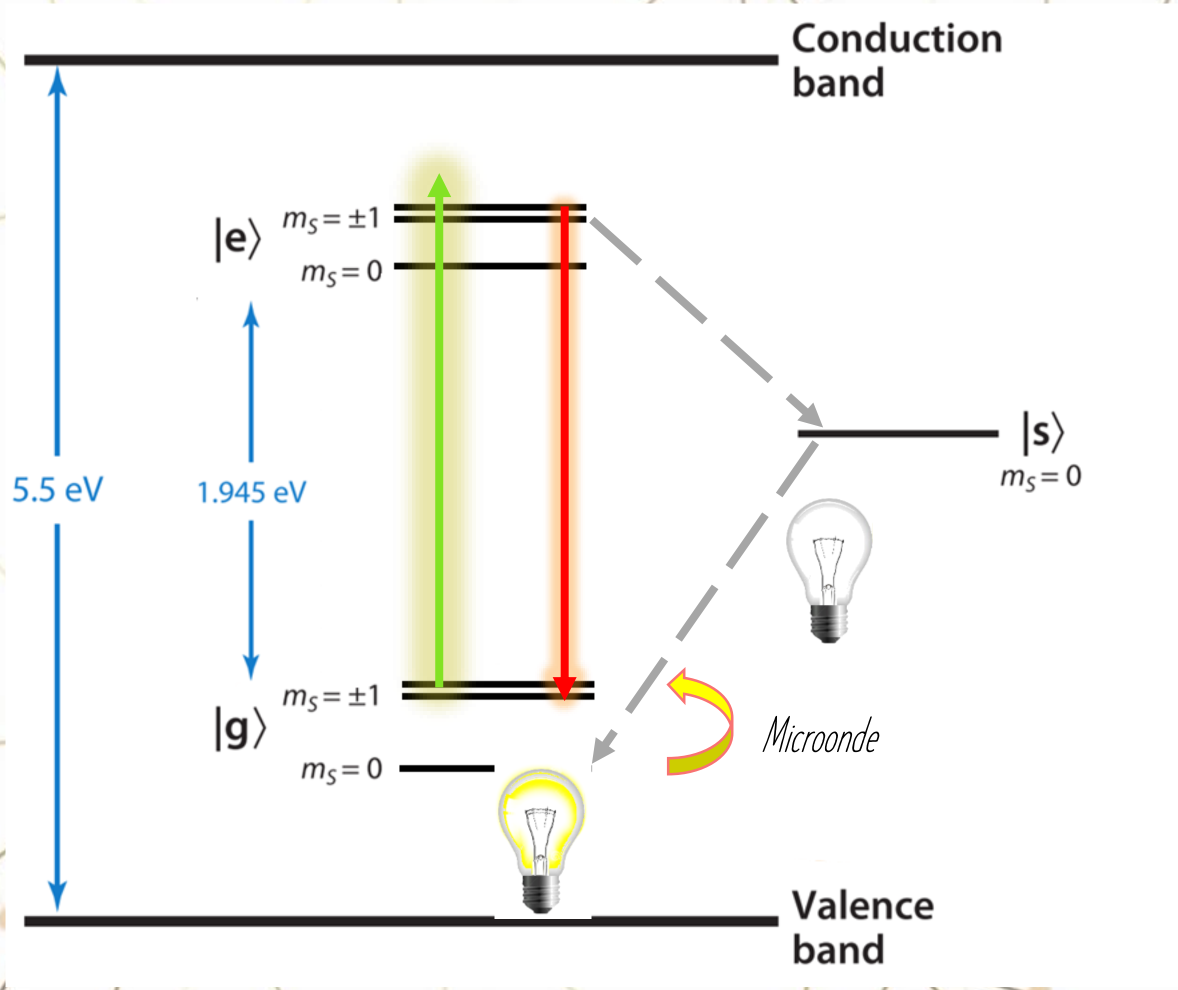



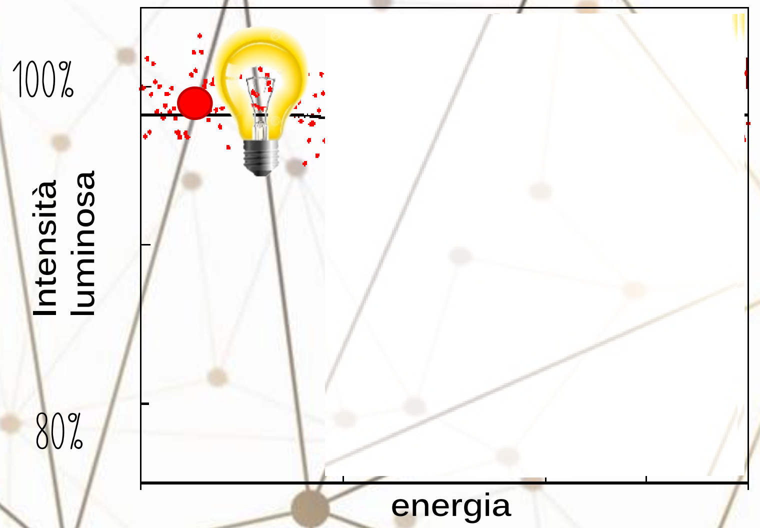
# ODMR - OPTICALLY DETECTED MAGNETIC RESONANCE

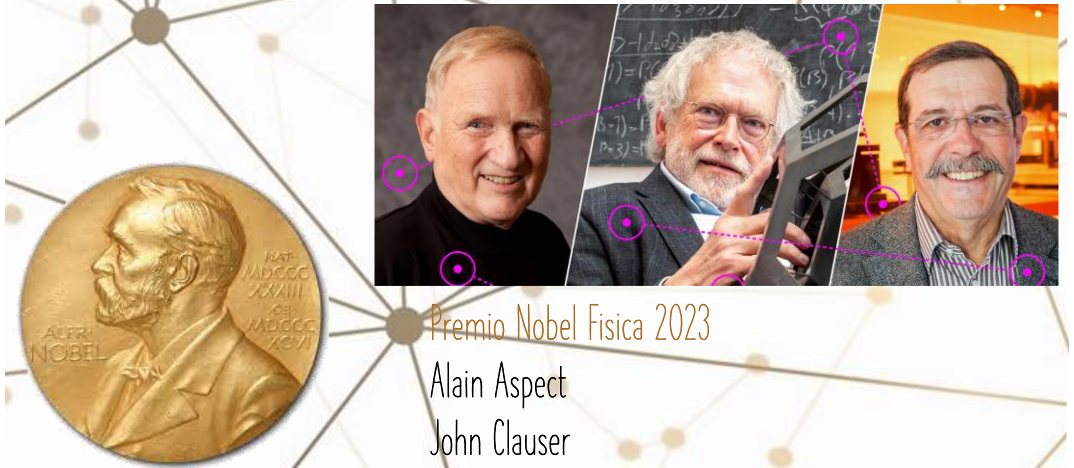


# ODMR - OPTICALLY DETECTED MAGNETIC RESONANCE



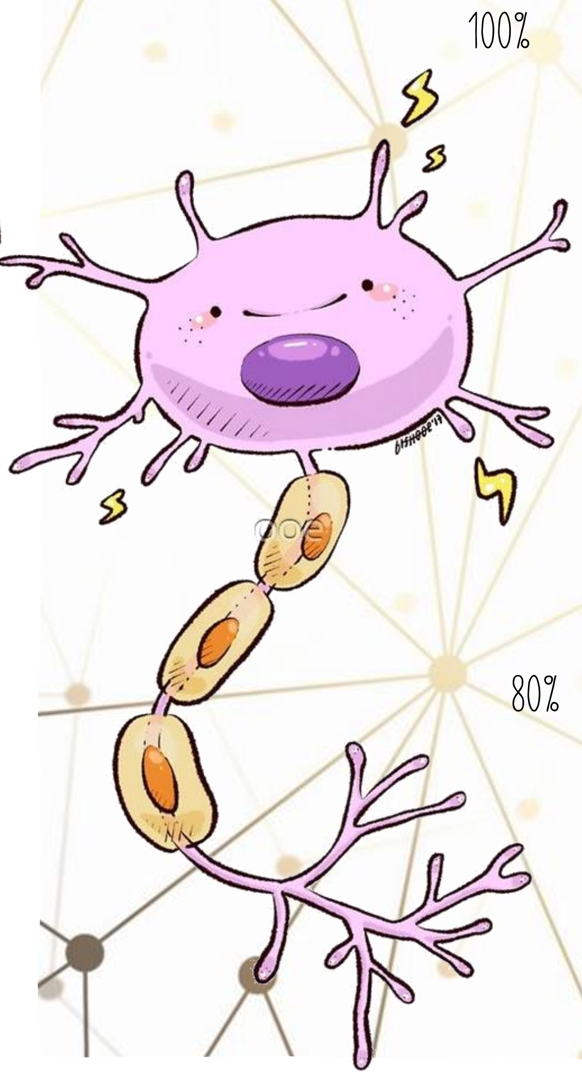
Premio Nobel Fisica 2023

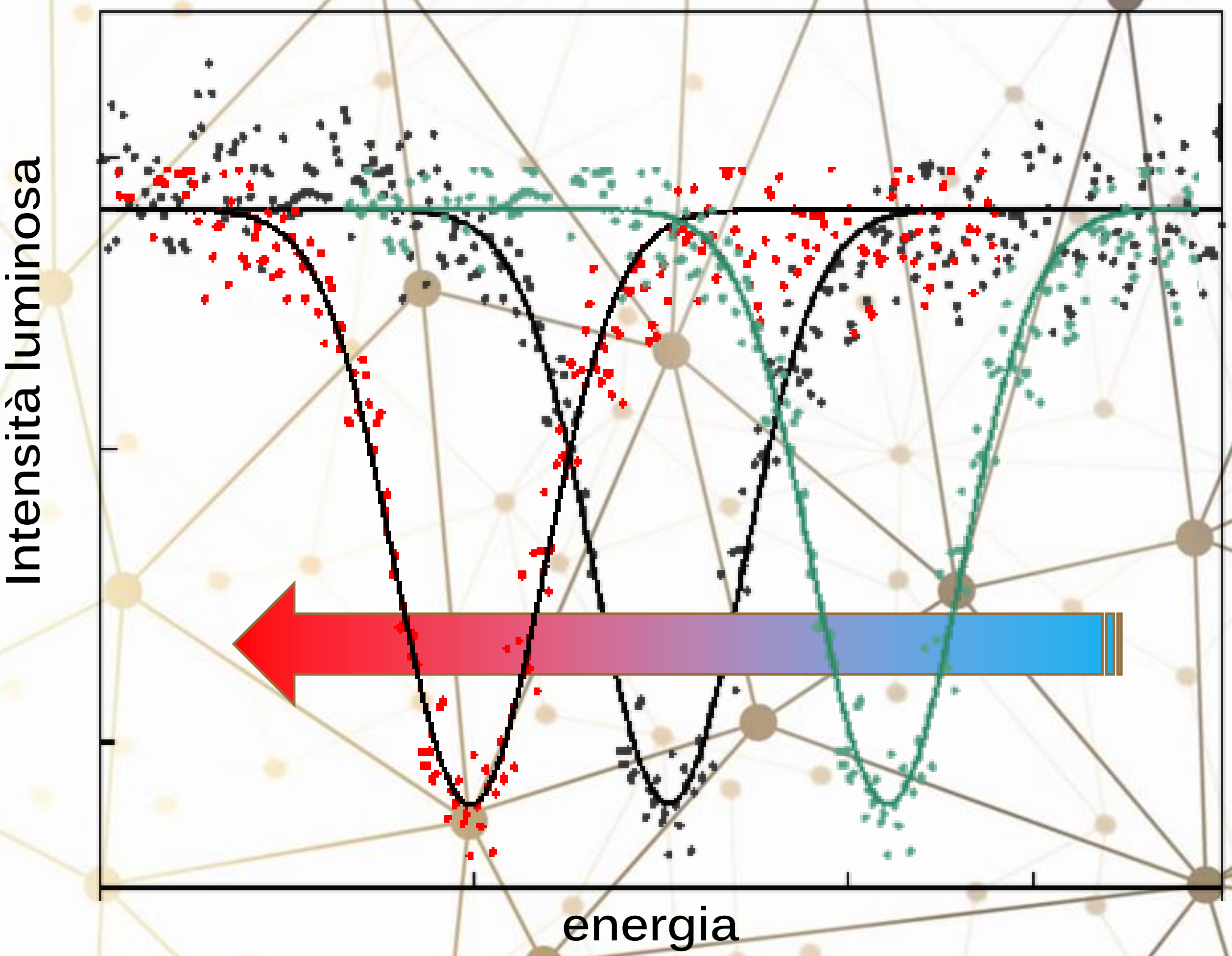
Alain Aspect

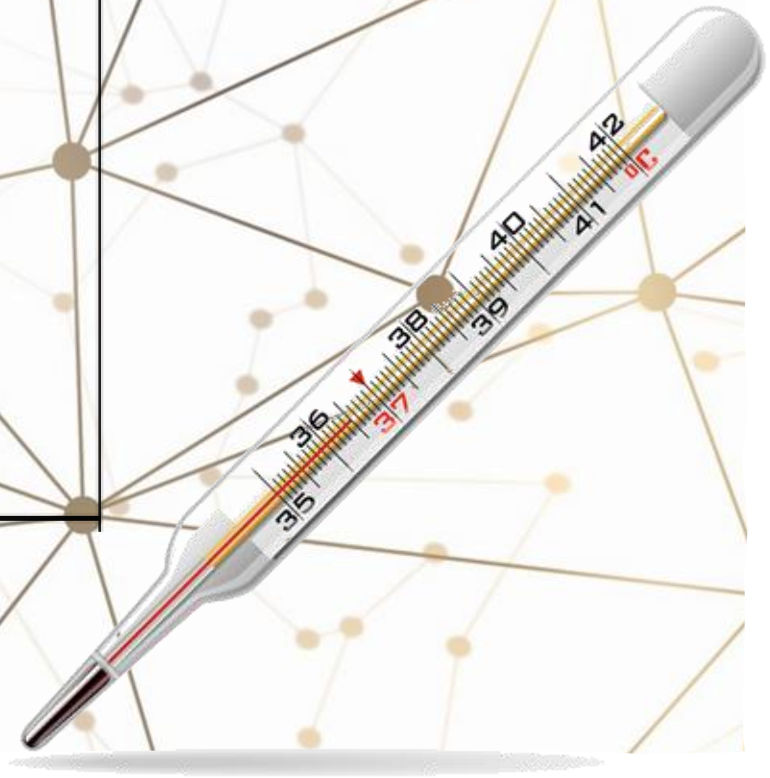
John Clauser

Anton Zeilinger

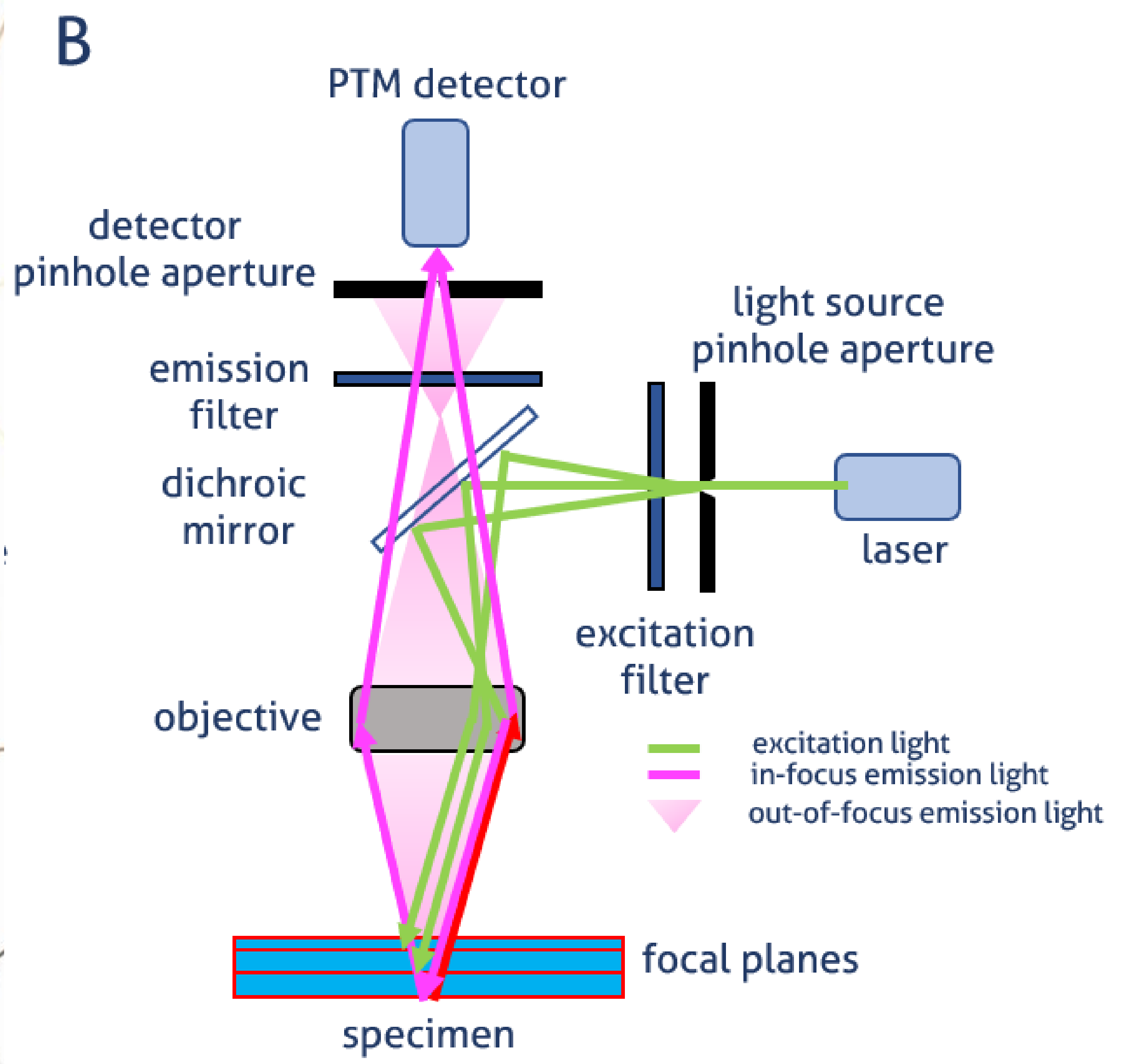
# NANO THERMOMETER!

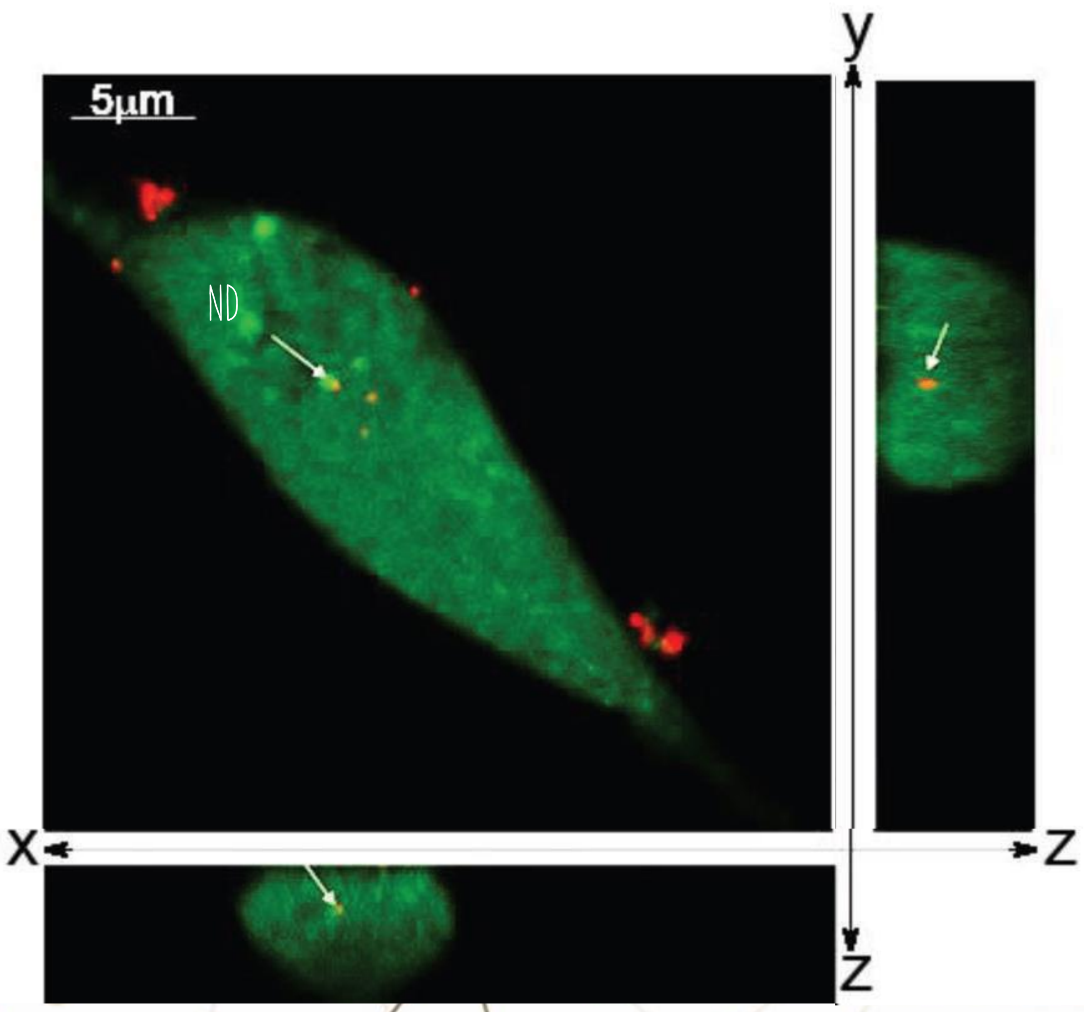


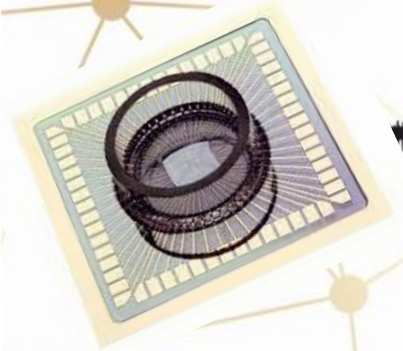



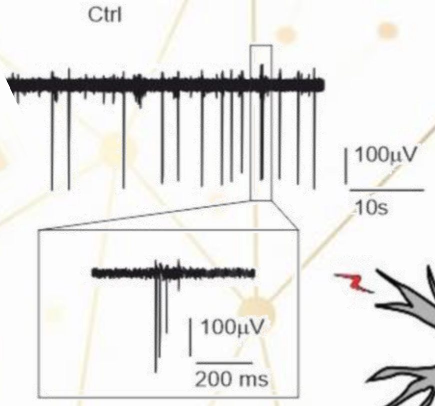
# EXPERIMENTAL SET UP

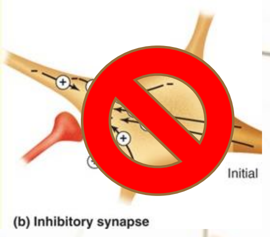


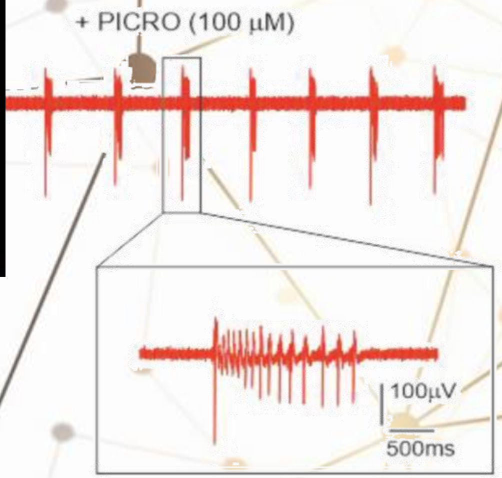



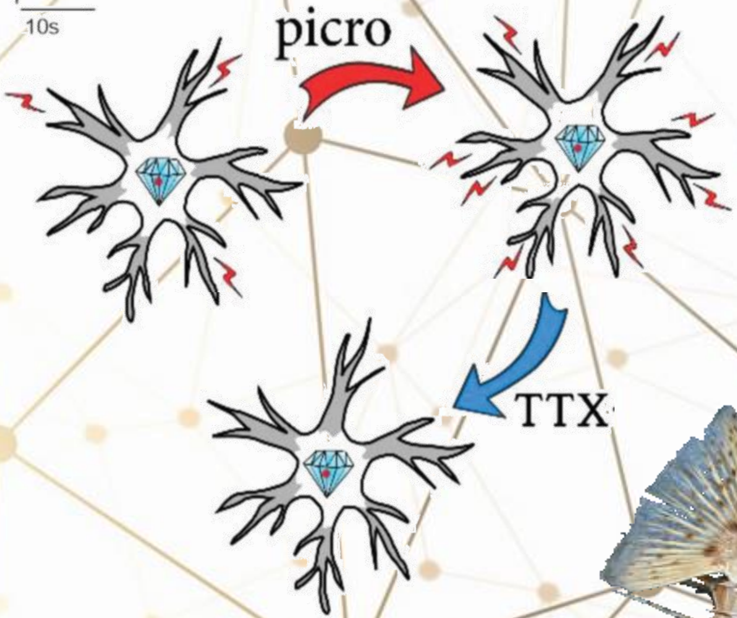
# AP MODULATION

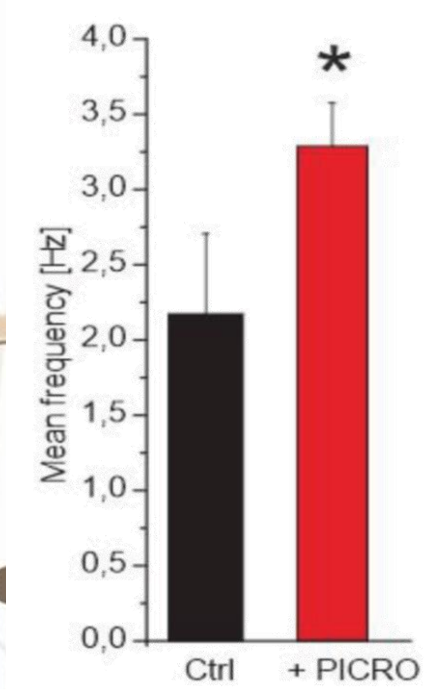


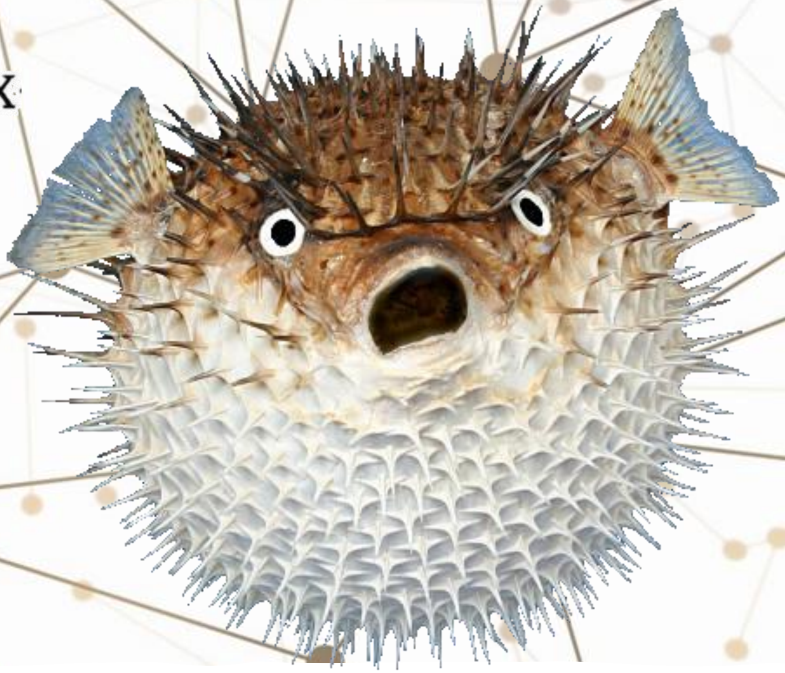


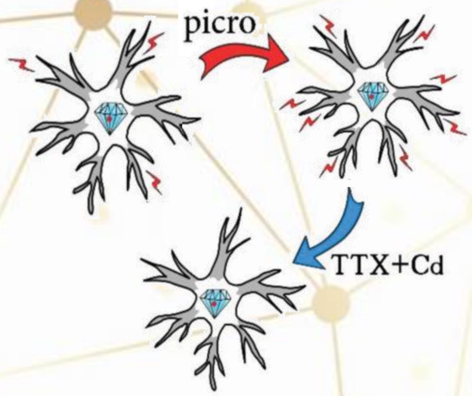



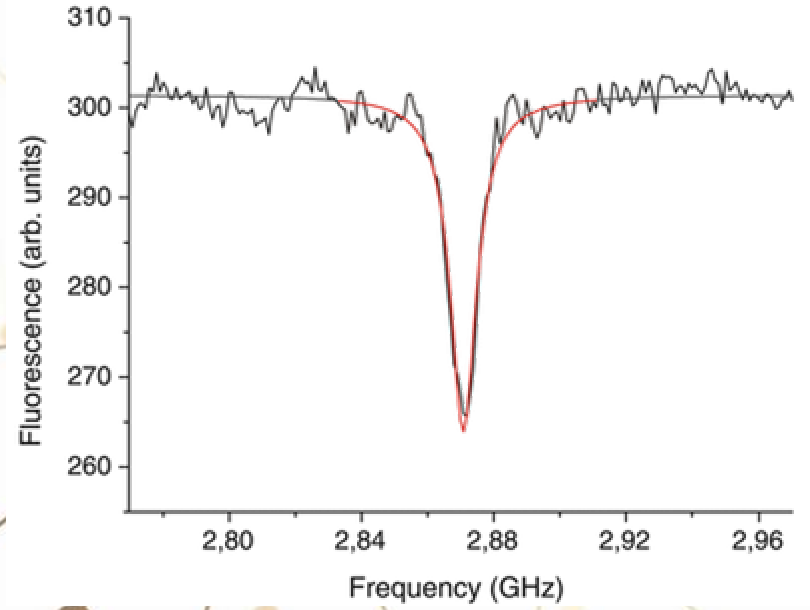



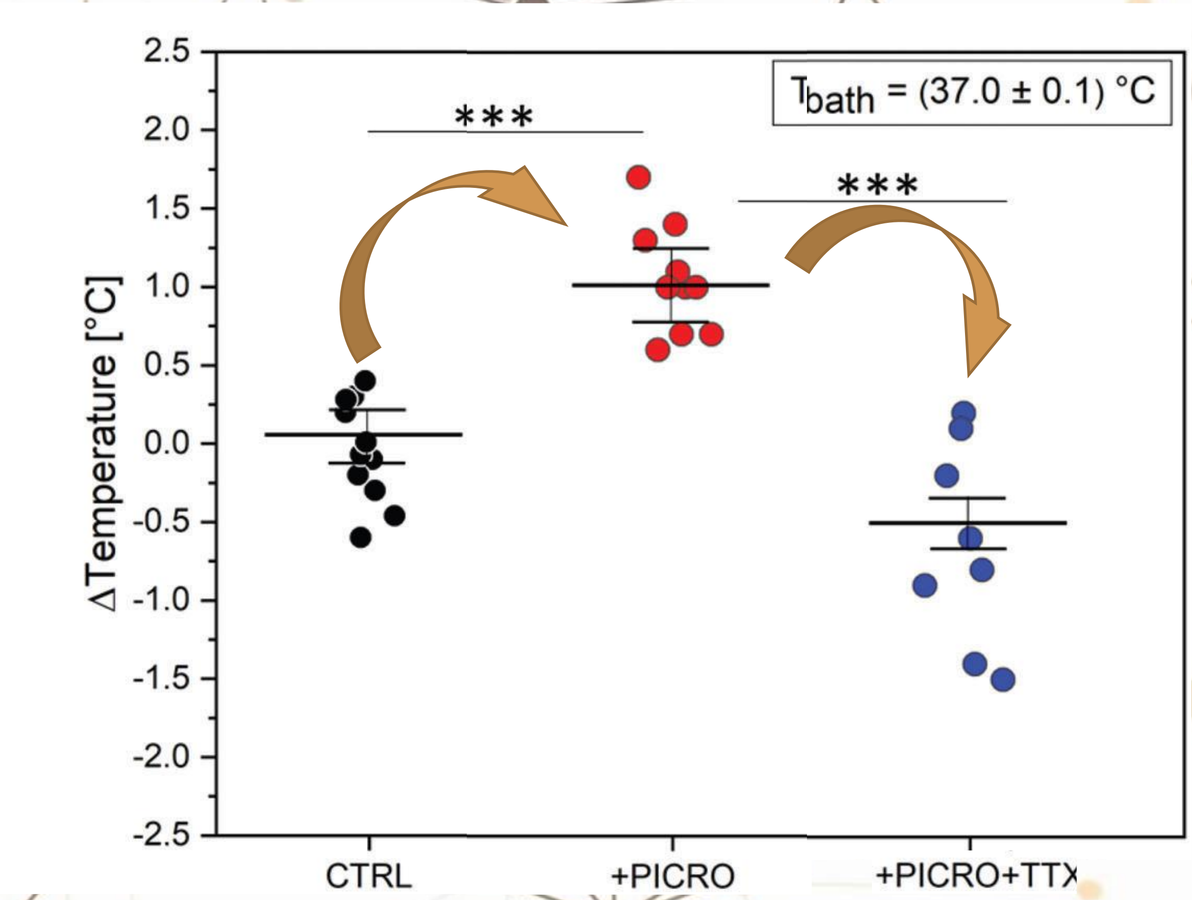



# TEMPERATURE VARIATION




Misura ODMR




Adv. Sci. 2022, 9, 2202014

# CONCLUSIONS

- A bit of cell biology... (from a NOT biologist)
- Standard tools for electrophysiology experiments
- Artificial DIAMOND for sensors development
- Some examples of cell signals detection
- Diamond particle detectors
- Radiobiology using diamond-base sensors
- New frontiers: quantum sensing (e.g. intracellular temperature detection)