Workshop on ”Sensor technologies for cleaner water”

2022-04-06

Detection of single biomolecules using fluorophores and quantum dots

Jan Linnros
Department of Applied Physics, KTH

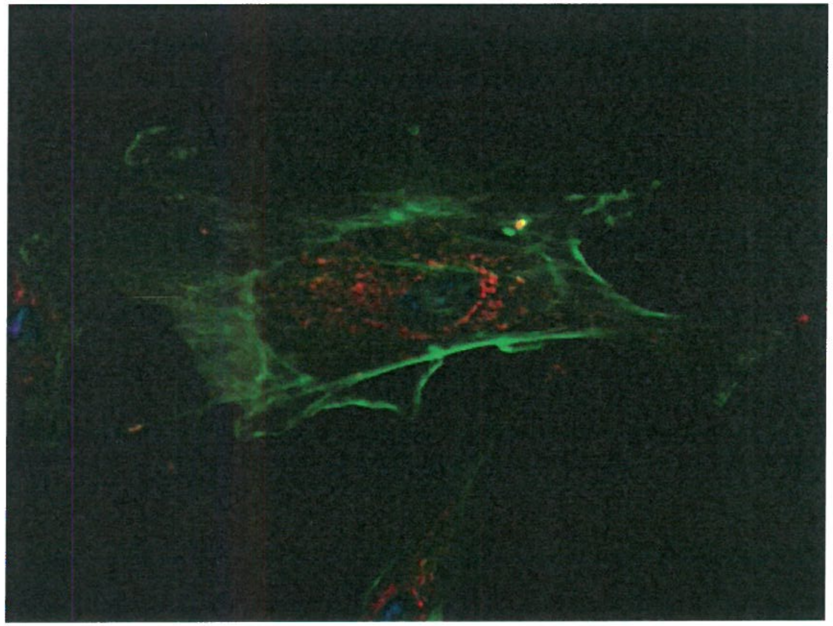
Outline

- fluorescent markers
- quantum dots
- biosensing based on an electrokinetic effect
- towards sensing in water
- conclusions

Fluorophores

(from Wikipedia)

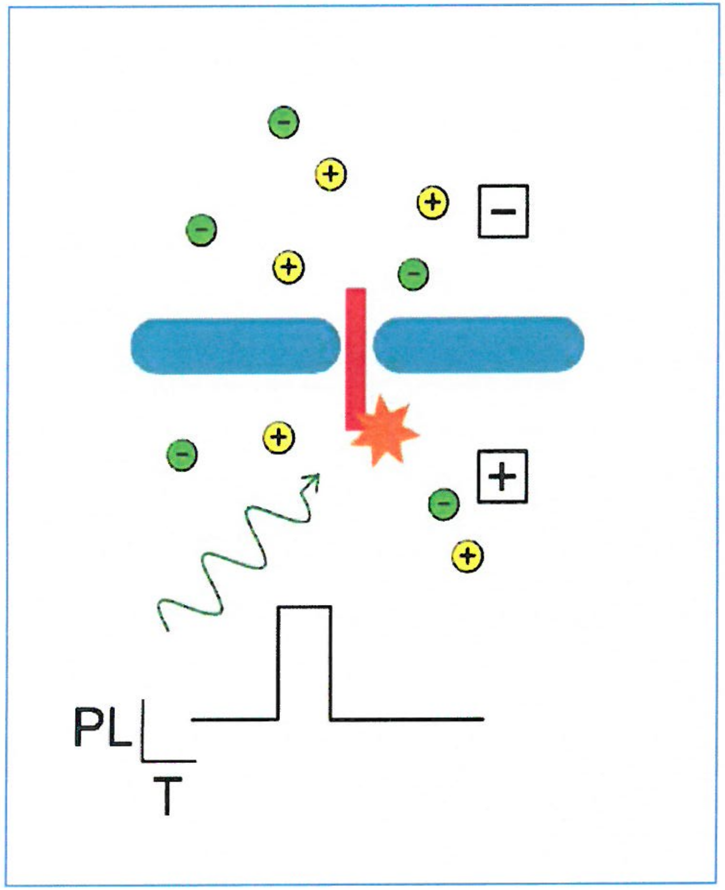
Fluorescence of different substances under UV light. Green is a fluorescein, red is Rhodamine B, yellow is Rhodamine 6G, blue is quinine, purple is a mixture of quinine and rhodamine 6g. Solutions are about 0.001% concentration in water.



Bovine Pulmonary Artery Endothelial cell nuclei stained blue with DAPI, mitochondria stained red with MitoTracker Red CMXRos, and F-actin stained green with Alexa Fluor 488 phalloidin and imaged on a fluorescent microscope.

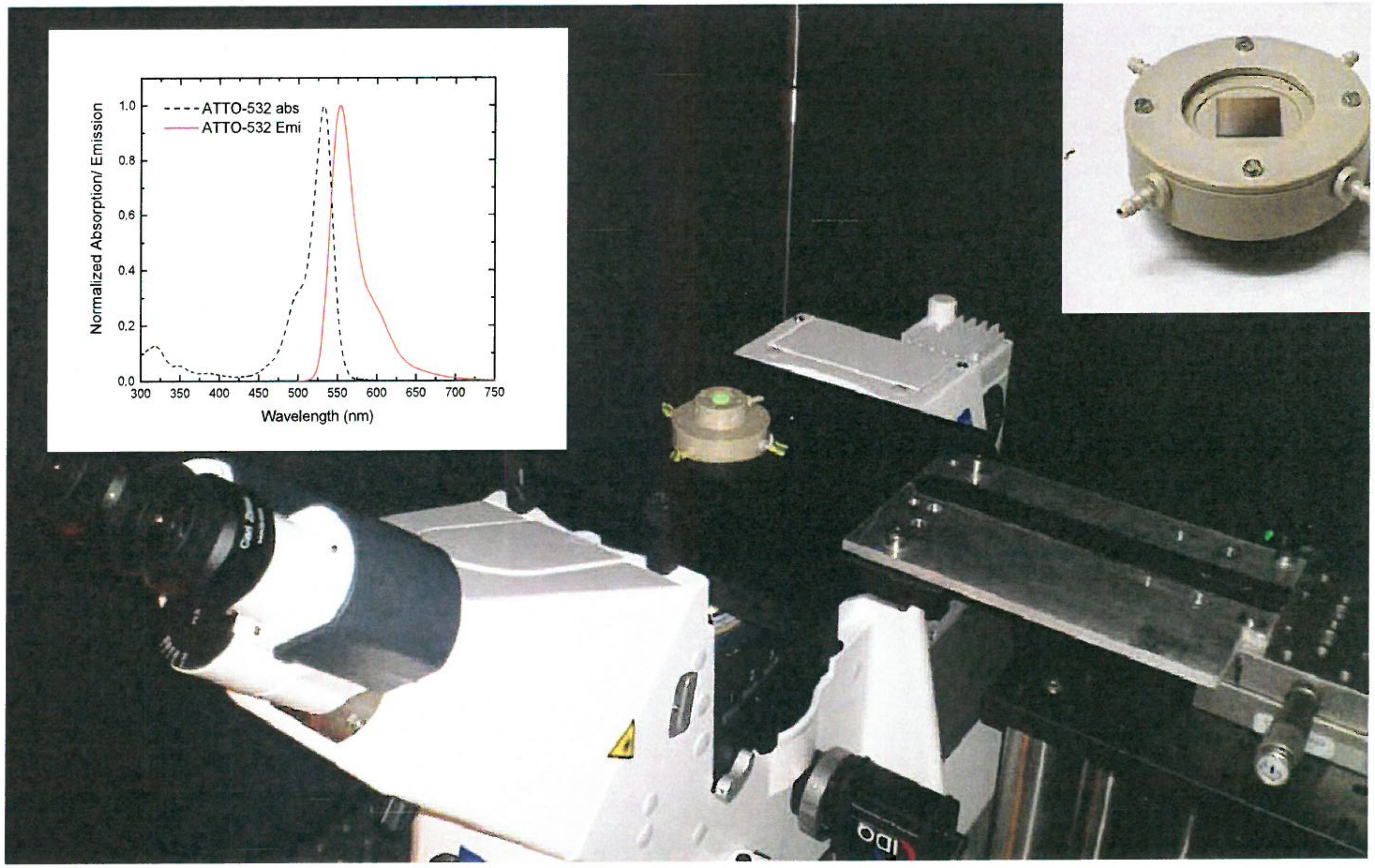
Detection of DNA translocation through nanopore

Principle



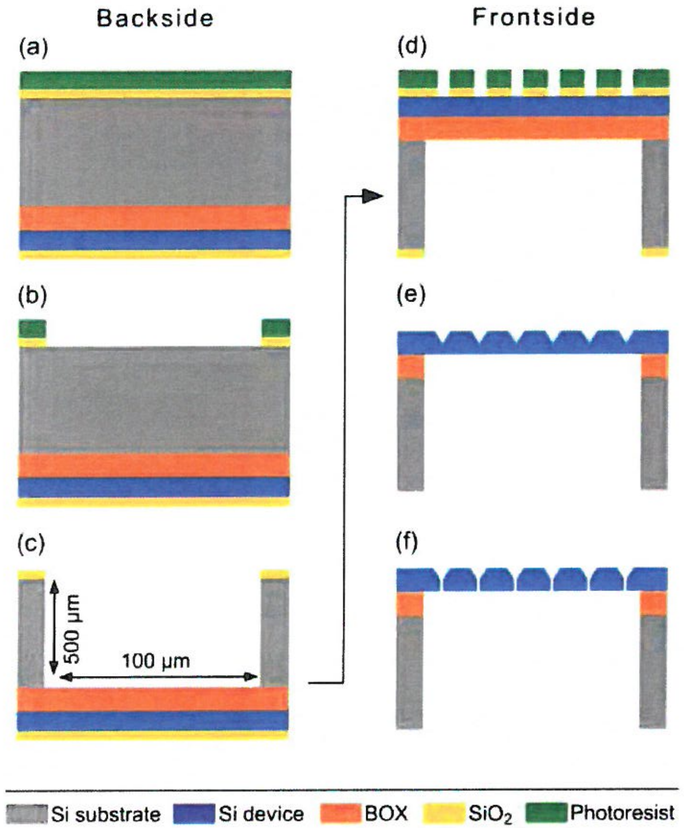
Fluorophore absorption/emission

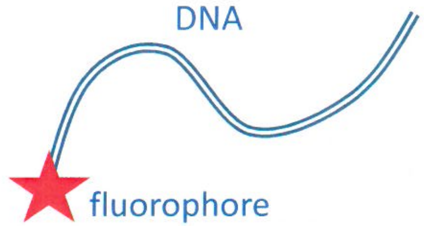
Fluidic cell with c

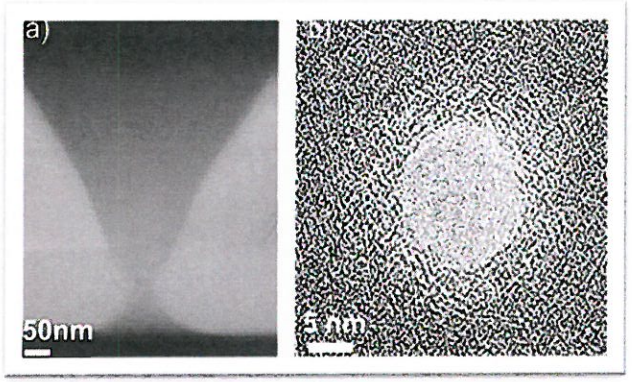


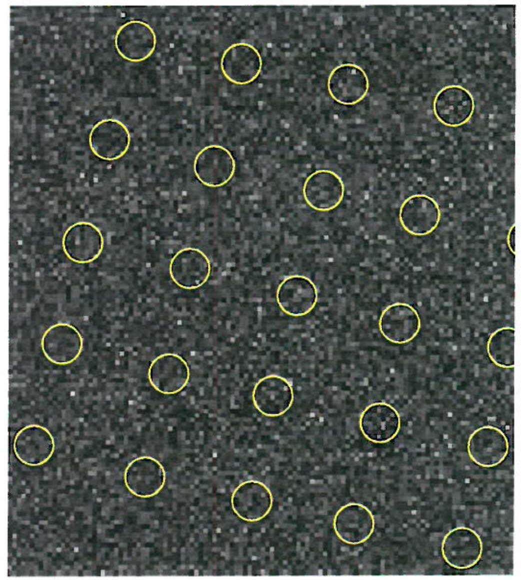
Microscope setup

Nanopores – detection of DNA translocation









Torsten Schmidt (postdoc)

Miao Zhang (PhD student)

Frame rate: 1 KHz
Area: 20 µm × 20 µm
Depth of field:~1 µm
Power density: ~10^4 W/cm^{-2}

Zhang, M et al, Nanotechnology, 25, 355302, (2014)

Torsten Schmidt, et al. Nanotechnology 26, 314001 (2015).

Zhang et al., ACS Nano 2018

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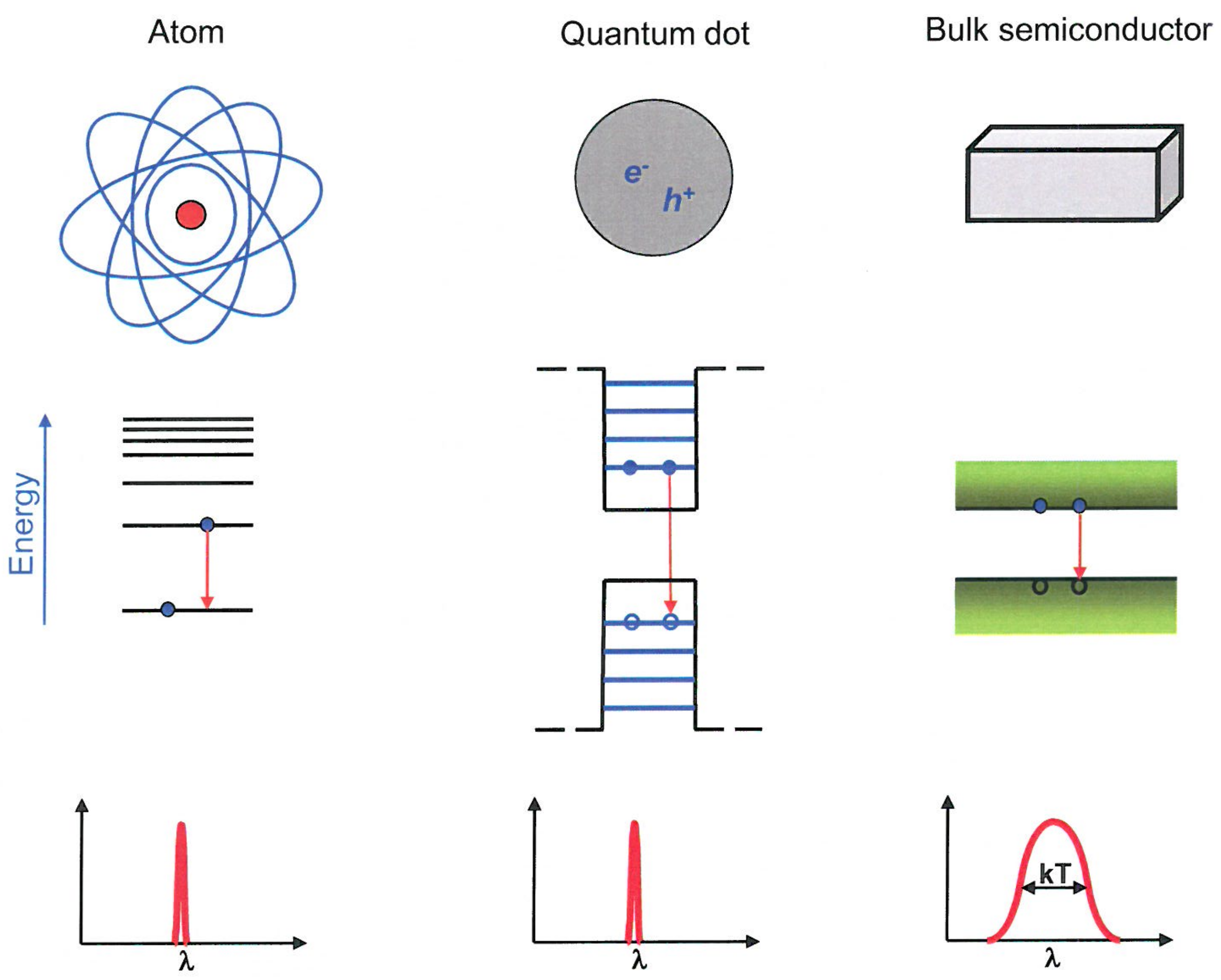
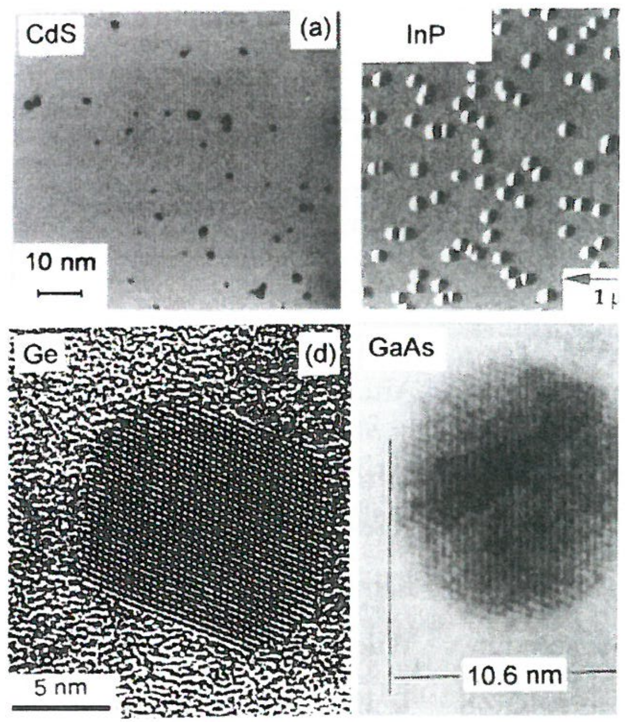
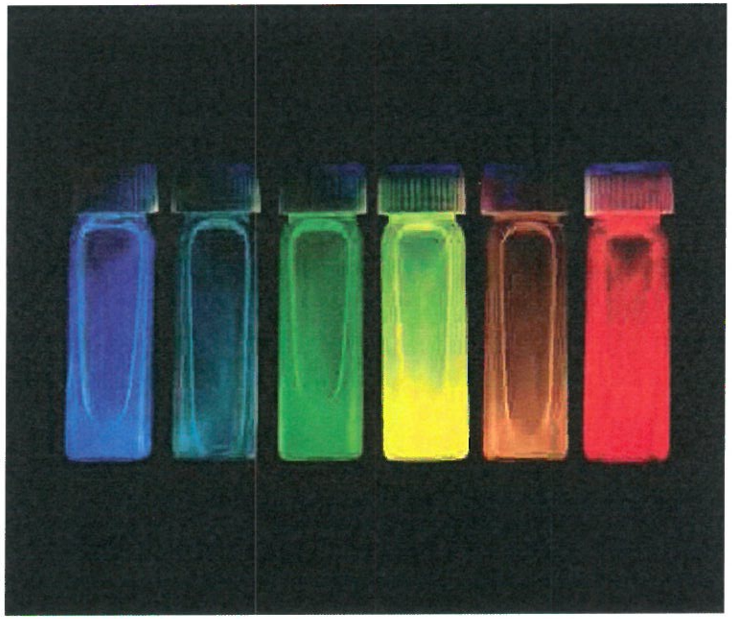
Quantum dot – ‘artificial atom’





Quantum dots – quantum size effect

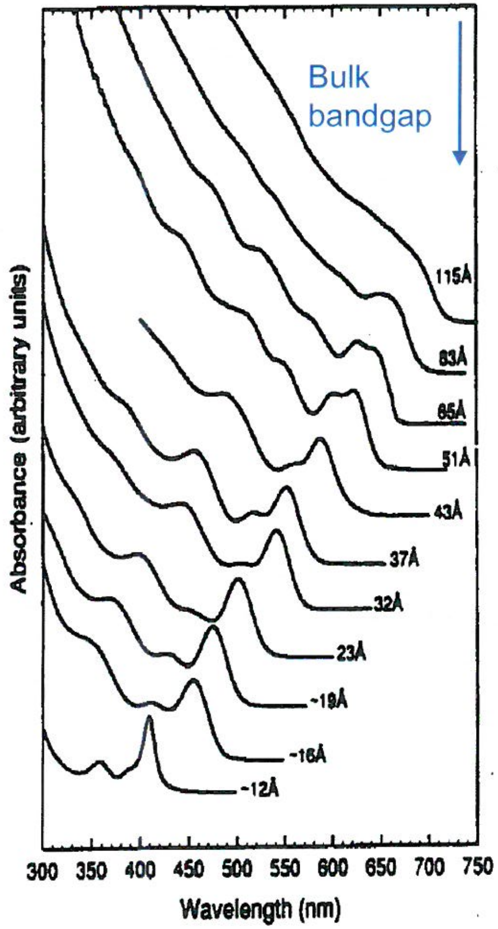
Emission



2.0 nm 2.4 nm 2.8 nm 3.2 nm 4.1 nm 5.0 nm

Diameter

Absorption

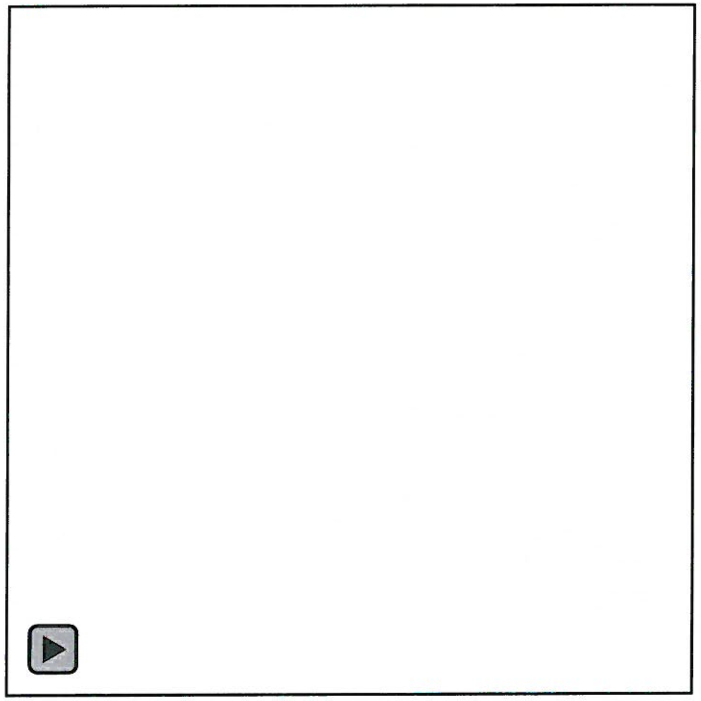


CdSe – cadmium selenide !!

Murray, Norris, Bawendi, MIT

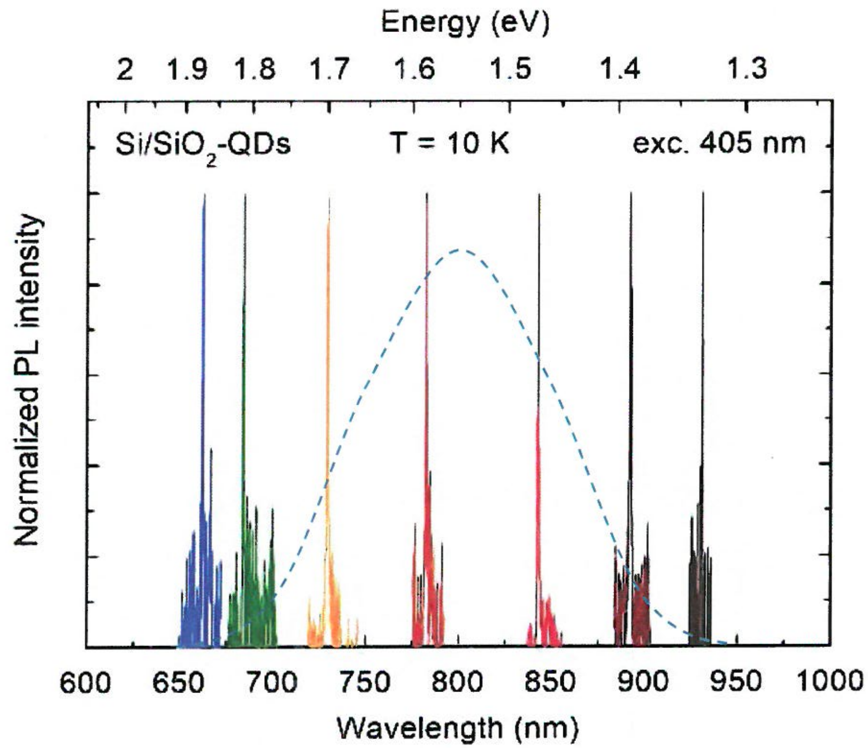
Silicon quantum dots

Individual Si quantum dots – on/off blinking



work by Benjamin Bruhn
And Federico Pevere
Nano Letters 2011, 2012
J. Chem. Phys.

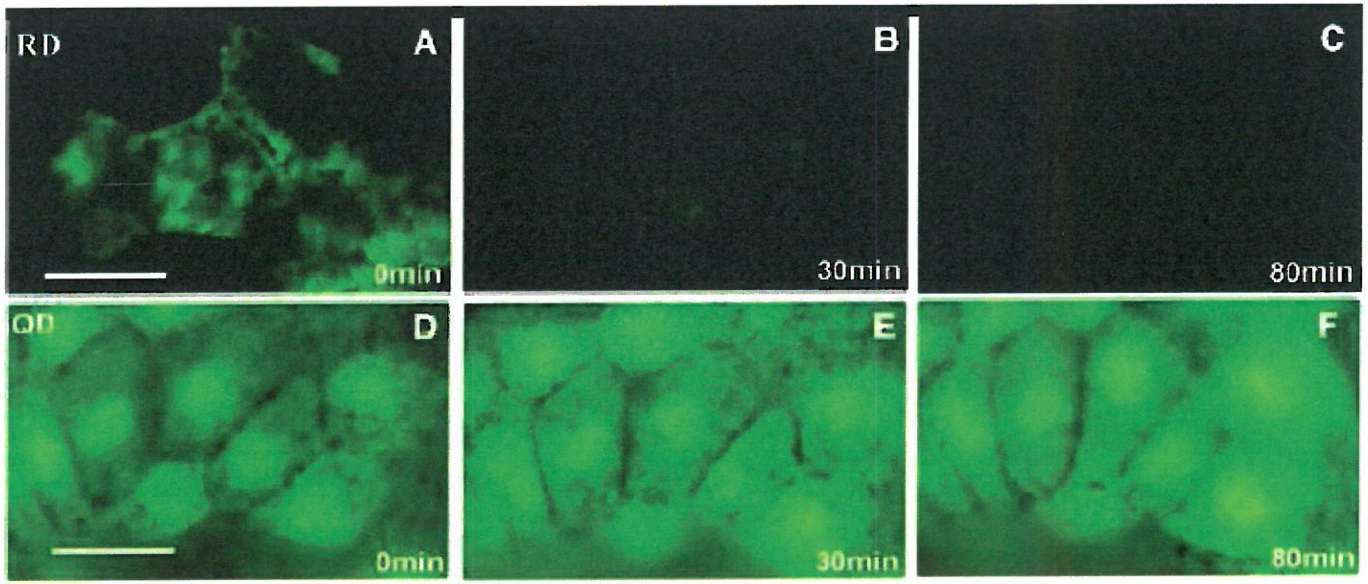
Individual Si quantum dots – spectra



Federico Pevere, Zhou Jingjian et al., Nanotechnology 2020

Bleaching – QD's vs dyes

Rhodamine Green Dextran



CdSe quantum dot

Dubertret et al.
Nature -02

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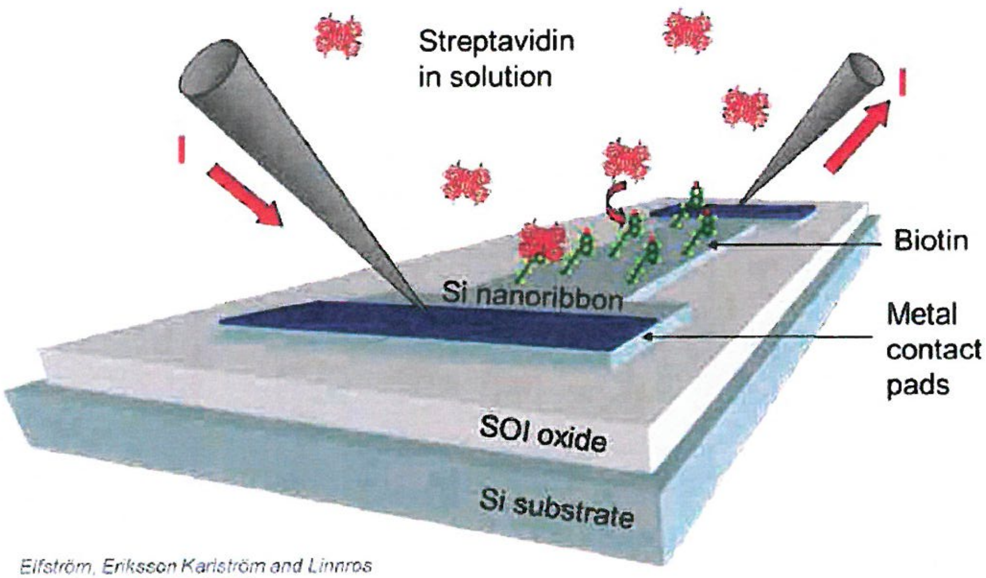
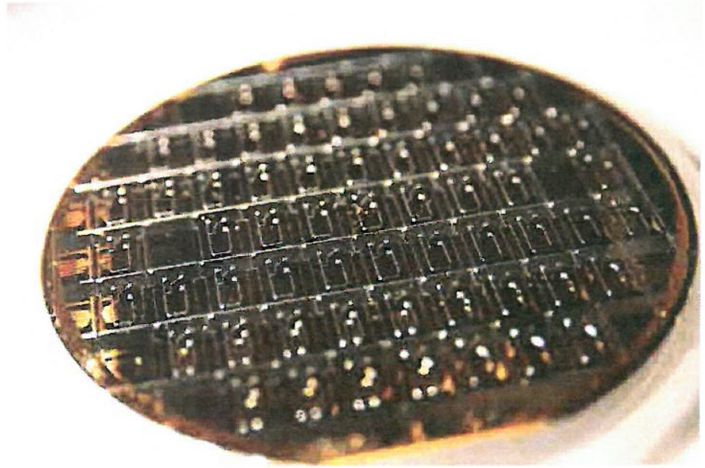
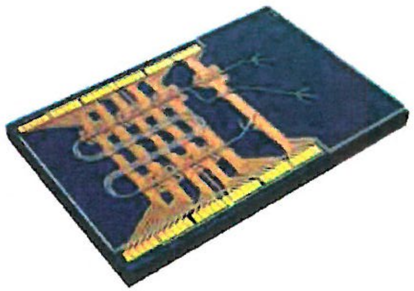
Biomolecule sensing with CMOS ISFET - nanoribbon



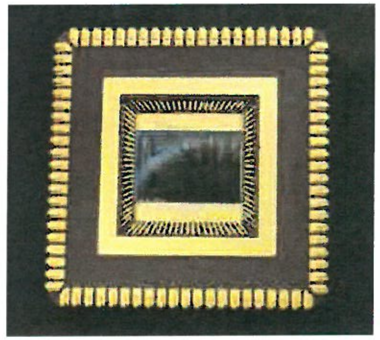
Elfström, Eriksson Karlström and Linnros
Nano Letters 8, 945 (2008)



4" wafer with chips

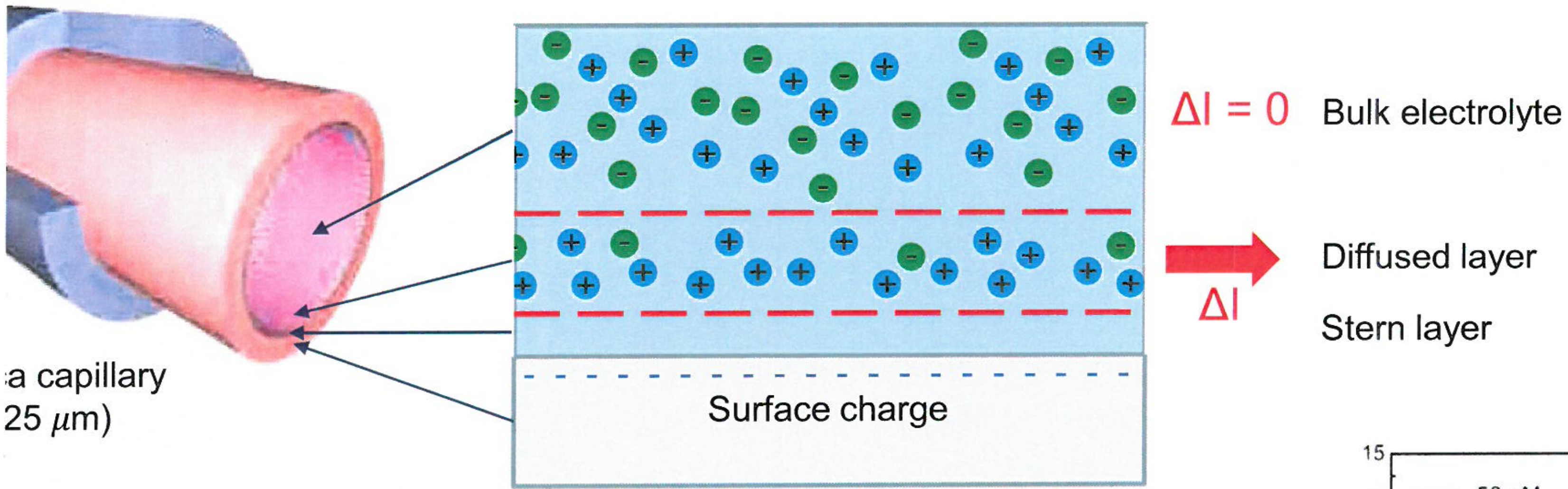


Chip with microfluidics



Wire-bonded chip

Electrokinetic effect – streaming current

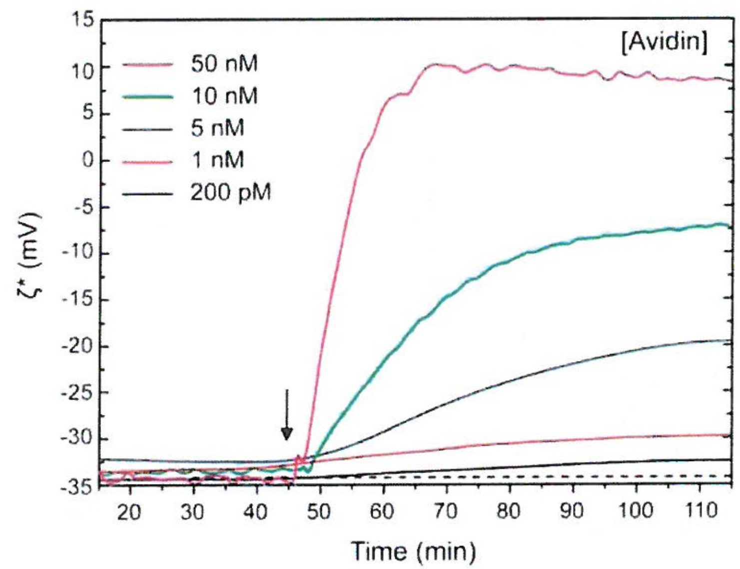


measured current

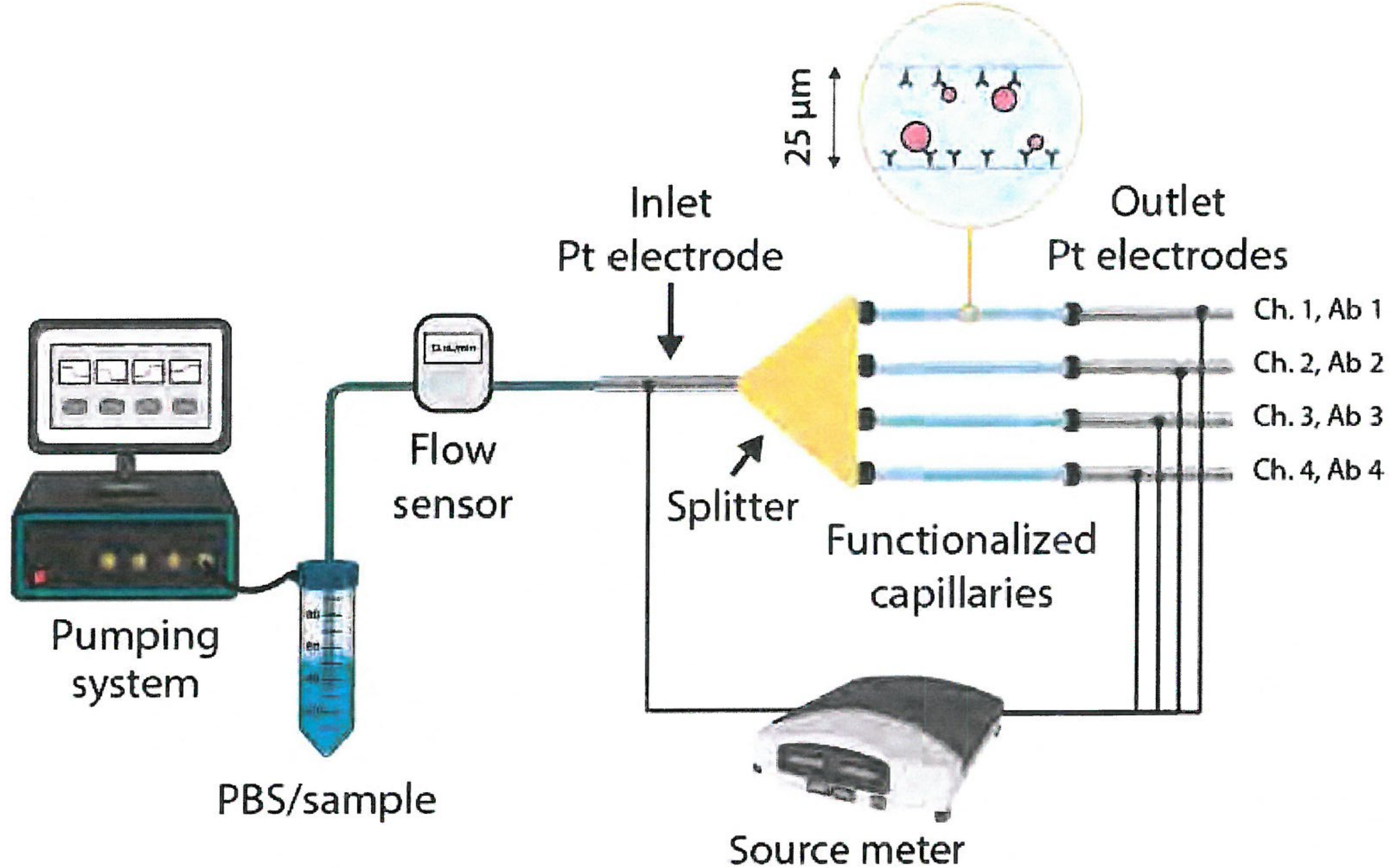
Zeta potential:

$$\zeta^* = \frac{\Delta I}{\Delta P} \frac{\eta}{\varepsilon \varepsilon_0} \frac{L}{A}$$

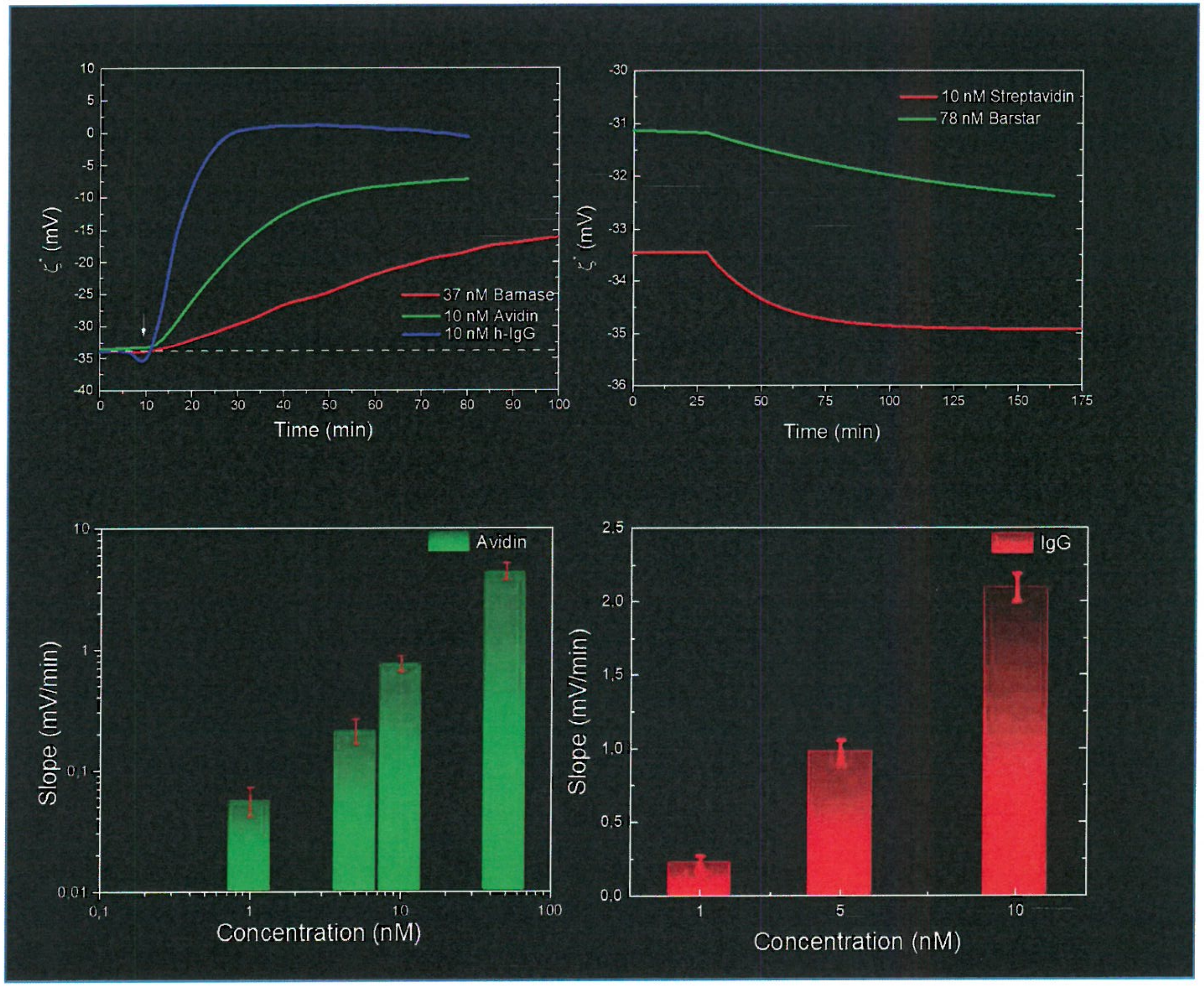
pressure drop



Experimental setup

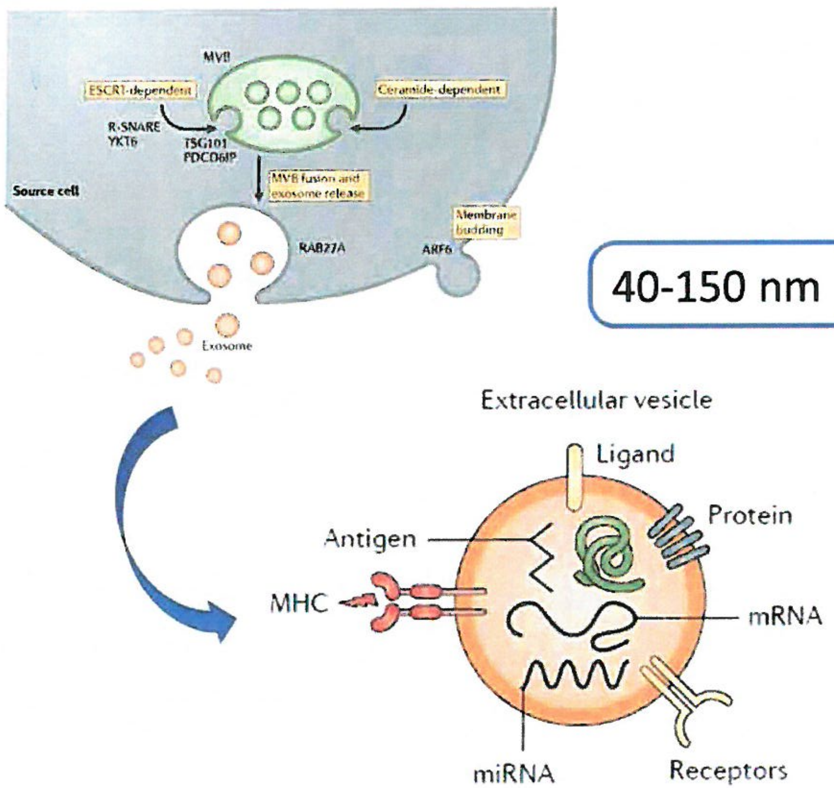


Protein detection using antibody-functionalized capillary

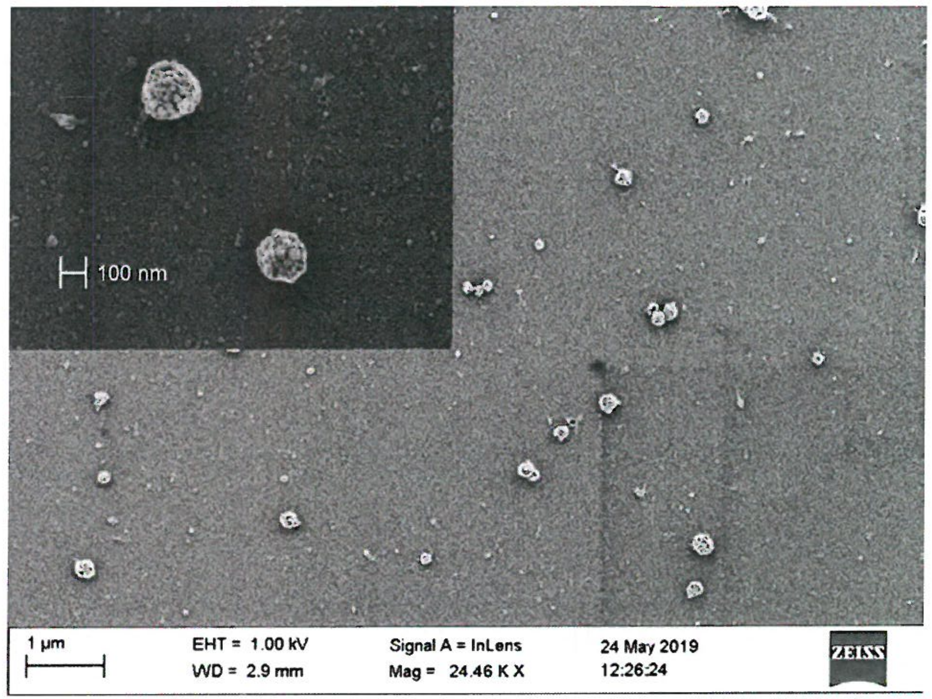


Dev et al *Biosensors & Bioelectronics* 82 (2016) 55

Exosomes – cancer biomarkers?

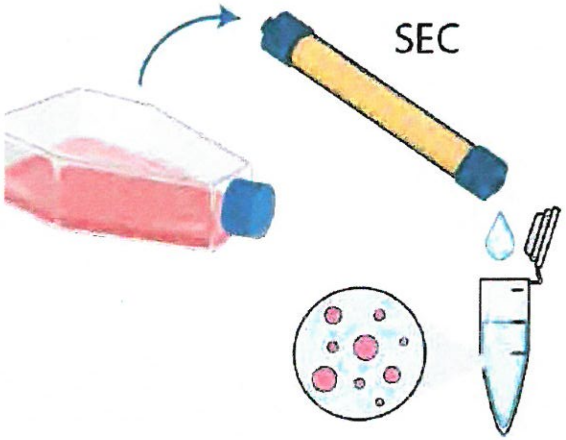


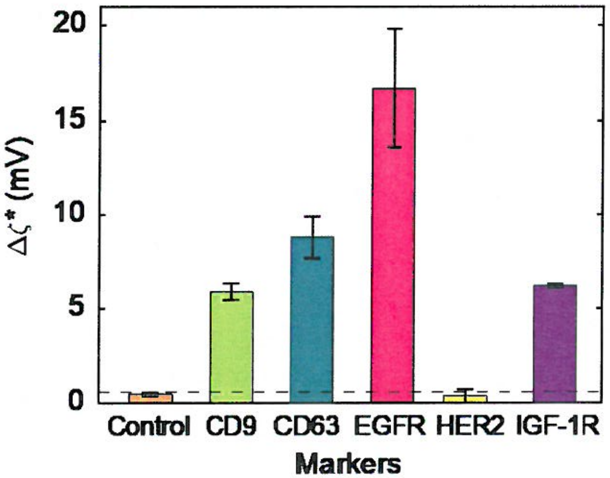
40-150 nm

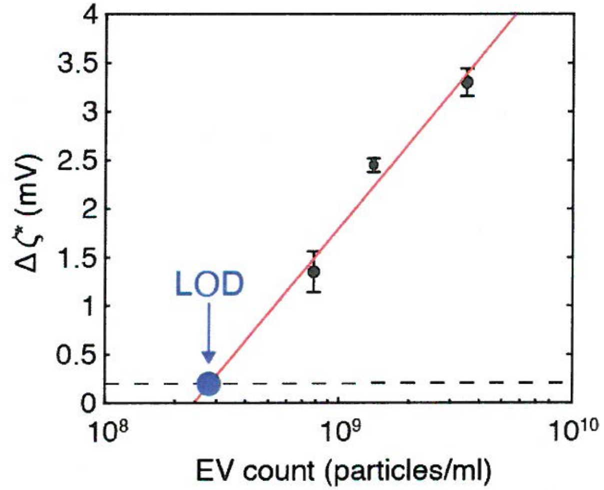


Andaloussi, Nature reviews Drug discovery 12.5 (2013): 347.

Sensor characterization with sEVs from cell lines







Specific detection of EVs

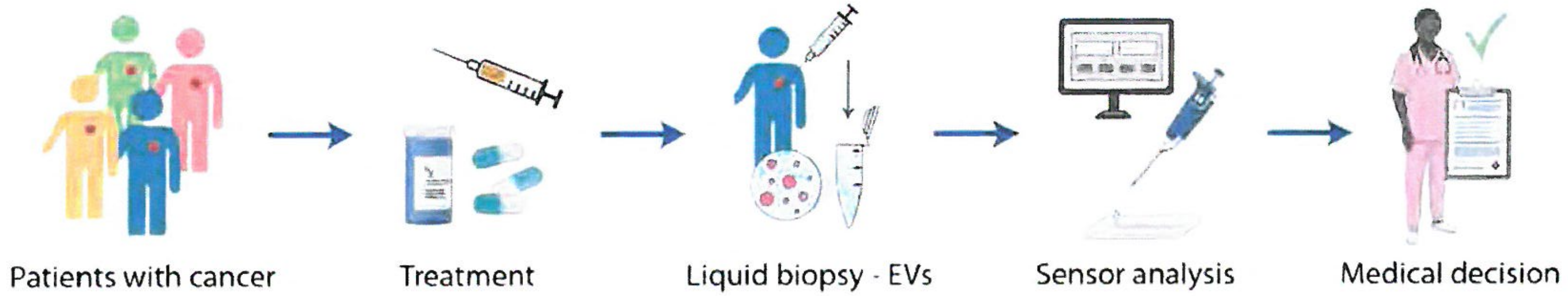
Limit of detection (LOD): 2.8 x 10^8 particles/mL (~0.5 pM)

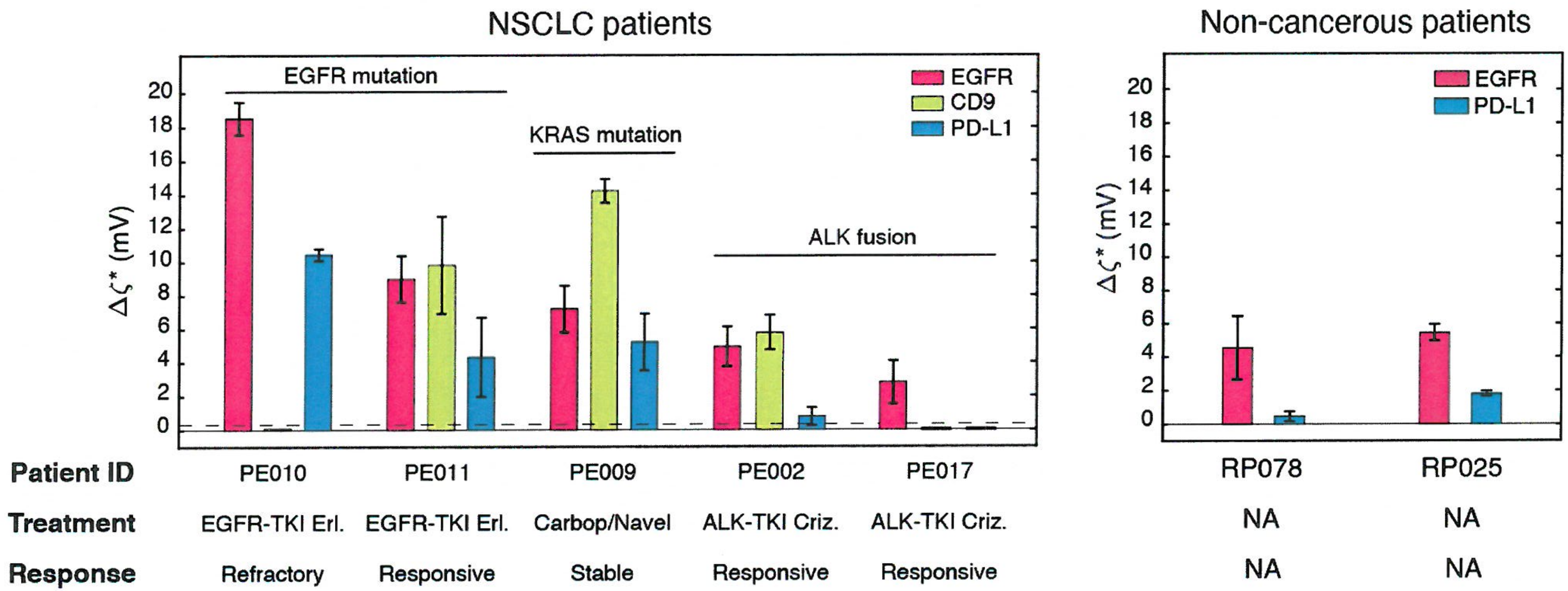
Sensitivity of 10% for EGFR expression levels

Cavallaro, Sara, et al., *ACS sensors* 4, (2019): 1399-1408.
Cavallaro, Sara, et al., *Biosensors and Bioelectronics 193,* (2021), 113568.

From Sara Cavallaro thesi:

Disease monitoring by EV liquid biopsies

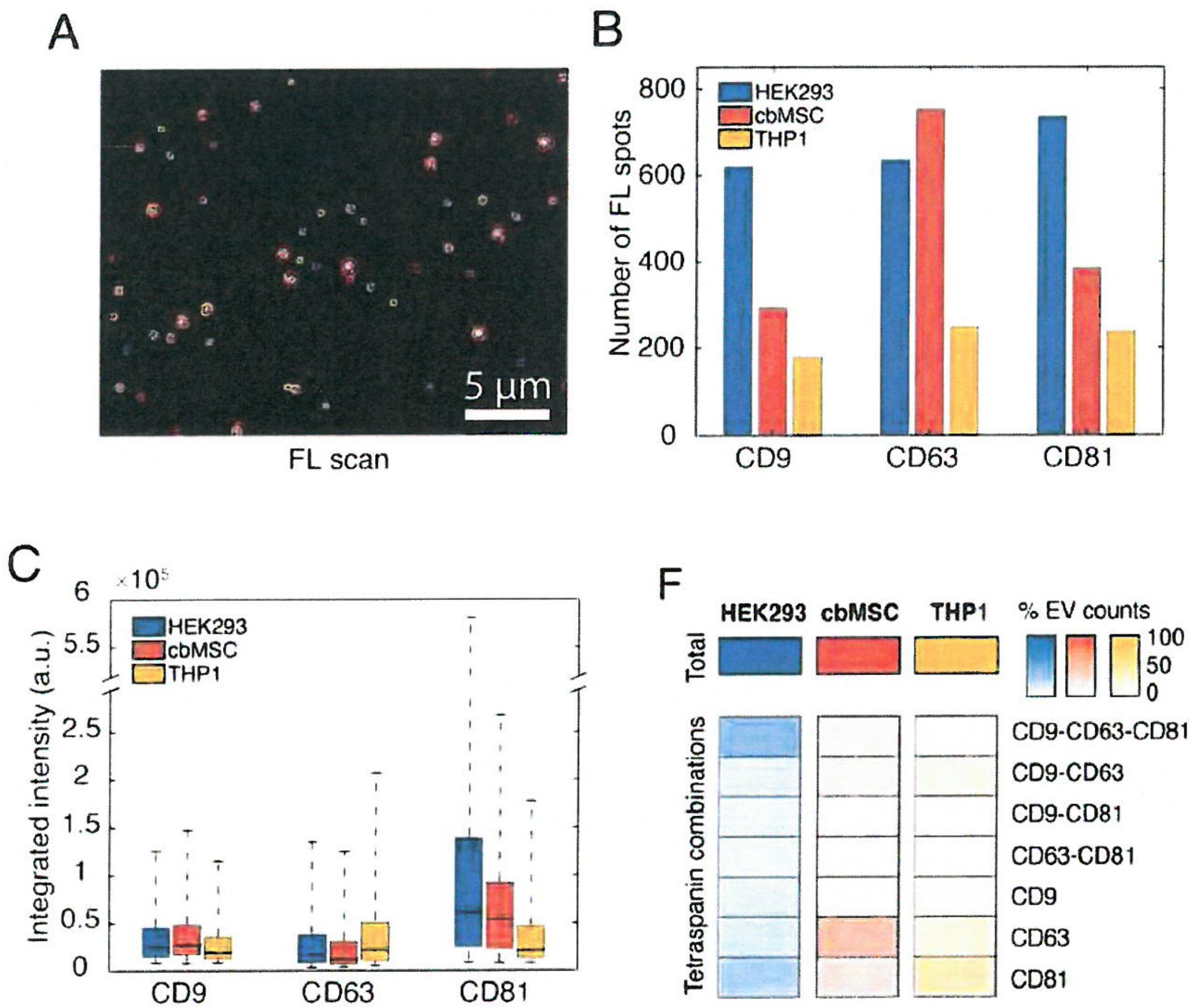




Cavallaro, Sara, et al., *Biosensors and Bioelectronics 193,* (2021), 113568.
BioRender.com.

From Sara Cavallaro thesi:

Fluorescence analysis – surface proteins



From Sara Cavallaro thesi:

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Cu^{2+} sensing

sensors MDPI

Article

Detection of Cu^{2+} Ions with GGH Peptide Realized with Si-Nanoribbon ISFET

Olena Synhaivska [1,2,*], Yves Mermoud [1,2], Masoud Baghernejad [1,†], Israel Alshanski [3], Mattan Hurevich [3], Shlomo Yitzchaik [3], Mathias Wipf [1] and Michel Calame [1,2,*]

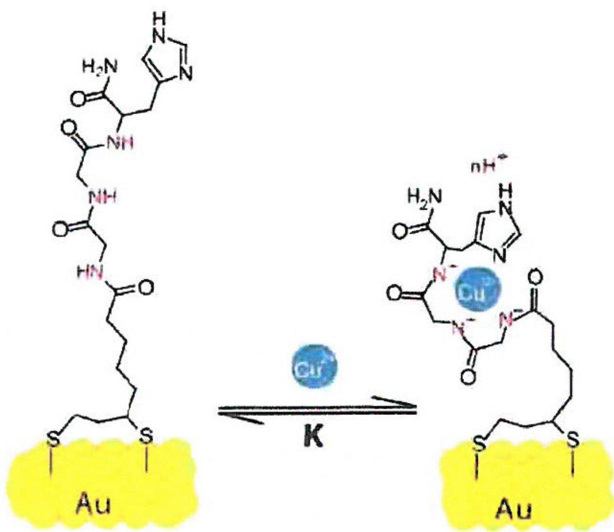
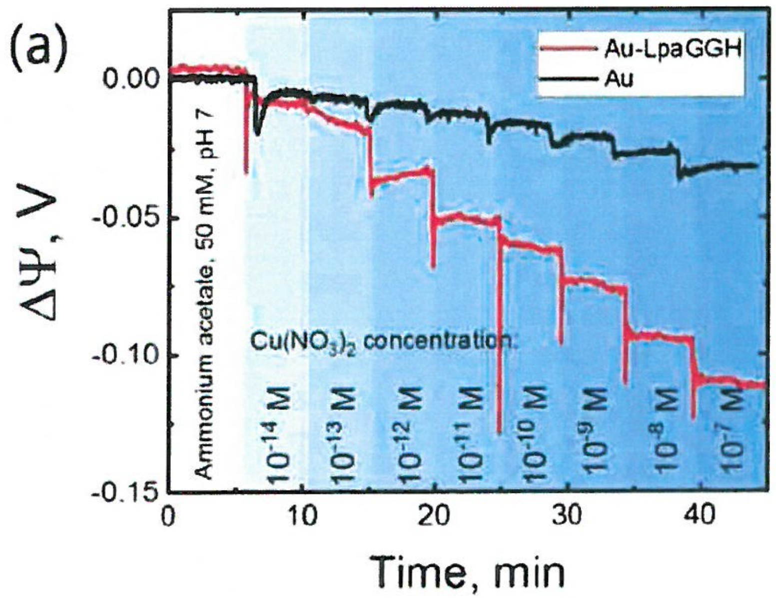


Figure 1. Glycine–glycine–histidine (Gly–Gly–His, GGH) monolayer on a gold surface and the complexation of Cu^{2+} ions. Secondary amines, carrying different charges depending on the electrolyte's pH, are indicated in red.



Fluorescence spectroscopy

Environmental
Science
Water Research & Technology

ROYAL SOCIETY OF CHEMISTRY

PAPER

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Cite this: Environ. Sci.: Water Res. Technol., 2019, 5, 370

Assessing the potential of fluorescence spectroscopy to monitor contaminants in source waters and water reuse systems†

Joseph Wasswa ‡*[a] Natalie Mladenov [a] and William Pearce[b]

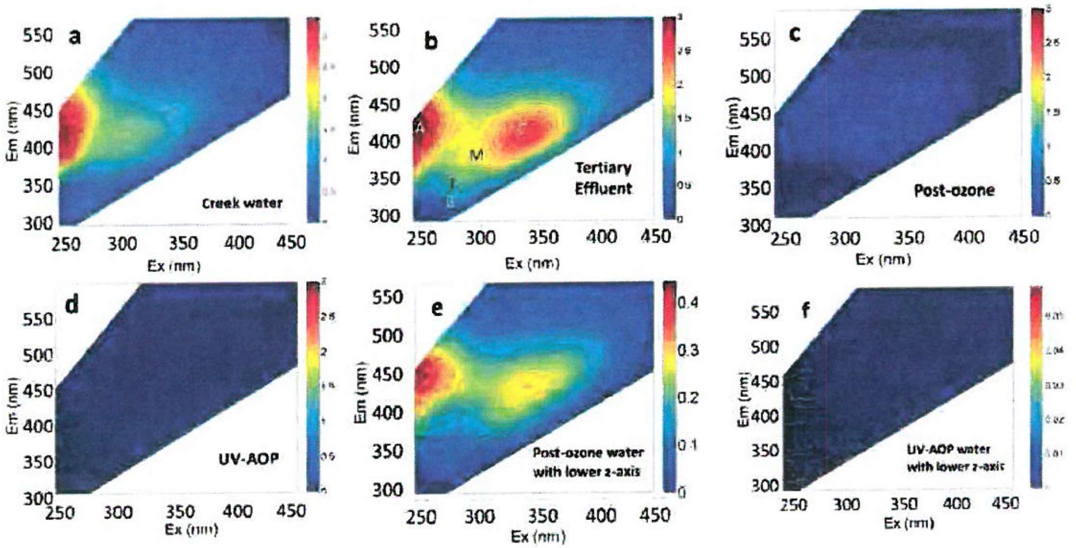
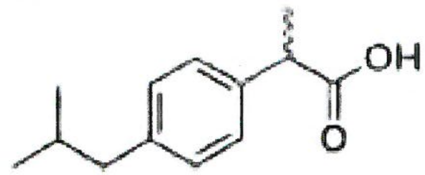
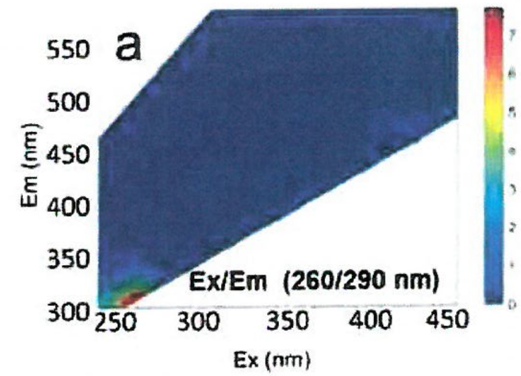


Fig. 1 Typical fluorescence EEM spectra acquired with an Aqualog benchtop fluorometer of the different water types, a) creek water, b) tertiary effluent, c) post-ozone and BAC treated water and d) reverse osmosis and UV-AOP final product water, before the spiking experiments. The same EEMs of post-ozone treated water (e) and UV-AOP product water (f) are shown with lower intensities in the colorbar. The locations of typical peaks B, T, A, C, and M are shown in 1b.

Example:

Ibuprofen



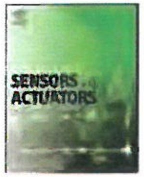


Analysis of metals in water

Contents lists available at ScienceDirect

Sensors and Actuators A: Physical

journal homepage: www.elsevier.com/locate/sna



Development of semiconductor based heavy metal ion sensors for water analysis: A review

Adarsh Nigam[a], Nipun Sharma[a,b], Sudhiranjan Tripathy[c], Mahesh Kumar[a,*]

[a] Department of Electrical Engineering, Indian Institute of Technology Jodhpur, Jodhpur, 342037, India
[b] Department of Mechanical Engineering, Indian Institute of Technology Jodhpur, Jodhpur, 342037, India
[c] Institute of Materials Research and Engineering, A*STAR (Agency for Science, Technology, and Research), Innovis, 2 Fusionopolis Way, 138634, Singapore

Table 1
Standard guideline values for the maximum permissible limit of heavy metals in drinking water recommended by the WHO, EPA, and BIS [5,25,26].

Heavy metal ions	Standard guideline values (in ppm)		
	WHO	EPA	BIS
As^{3-}	0.01	0.01	0.0[illegible]
Cd^{2+}	0.003	0.005	0.0[illegible]
Cr^{3+}	0.05	0.1	0.0[illegible]
Cu^{2+}	2	1.3	0.0[illegible]
Pb^{2+}	0.01	0.015	0.0[illegible]
Hg^{2+}	0.001	0.002	0.0[illegible]

Table 3
Brief summary of the Semiconducting materials for heavy metal ion detection.

Semiconducting Material	Method Used	Target Heavy Metal Ion	Limit of Detection (LoD)	References
MoS_2/Au	AlGaN/GaN HEMT	Hg^{2+}	0.01152 ppb	[91]
AuNP/GCE	Electrochemical	Hg^{2+}	0.15×10^{-3}	[111]
Magnesium oxide (MgO) nanoflowers	Stripping Voltammetry	Pb^{2+} and Cd^{2+}	2.1 pM and 81 pM	[75]
Zr/ZrO_2	Electrochemical	Cd^{2+}, Pb^{2+}, Hg^{2+} and Cu^{2+}	–	[76]
ZnO quantum dot	Fluorescence	Cu^{2+}	16 pM	[79]
1 T-WS_2 micro flowers	Electrochemical	Hg^{2+}	79.8 pM	[99]
SnO_2/RGO nanocomposite	Electrochemical	Cd^{2+}, Pb^{2+}, Cu^{2+}	–	[107]
Si-NWs	ISFET	Cu^{2+}	1×10^{-9} M	[112]
AuNP decorated rGO	FET	Hg^{2+}	2.5×10^{-8} M	[113]

Analysis of metals in water

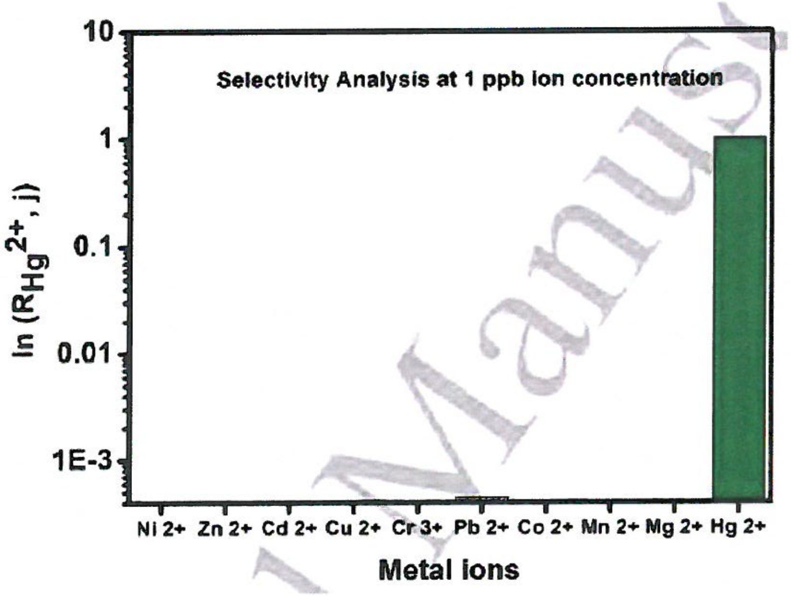
1T and 2H Heterophase MoS_2 for Enhanced Sensitivity of GaN transistor-based Mercury ions Sensor

Nipun Sharma[1,2], Adarsh Nigam[1], Surani Bin Dolmanan,[3] Ankur Gupta[2], Sudhiranjan Tripathy[3, a)], and Mahesh Kumar[1,b)*]

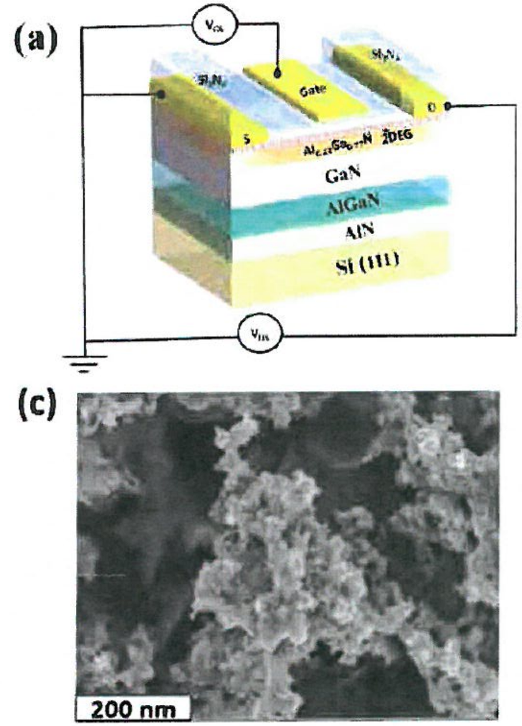
[1]*Department of Electrical Engineering, Indian Institute of Technology Jodhpur, Jodhpur-342037 India*

[2]*Department of Mechanical Engineering, Indian Institute of Technology Jodhpur, Jodhpur-342037 India*

[3]*Institute of Materials Research and Engineering, A*STAR (Agency for Science, Technology and Research), Innovis, 2 Fusionopolisway, Singapore 138634*



Just published in Nanotechnology



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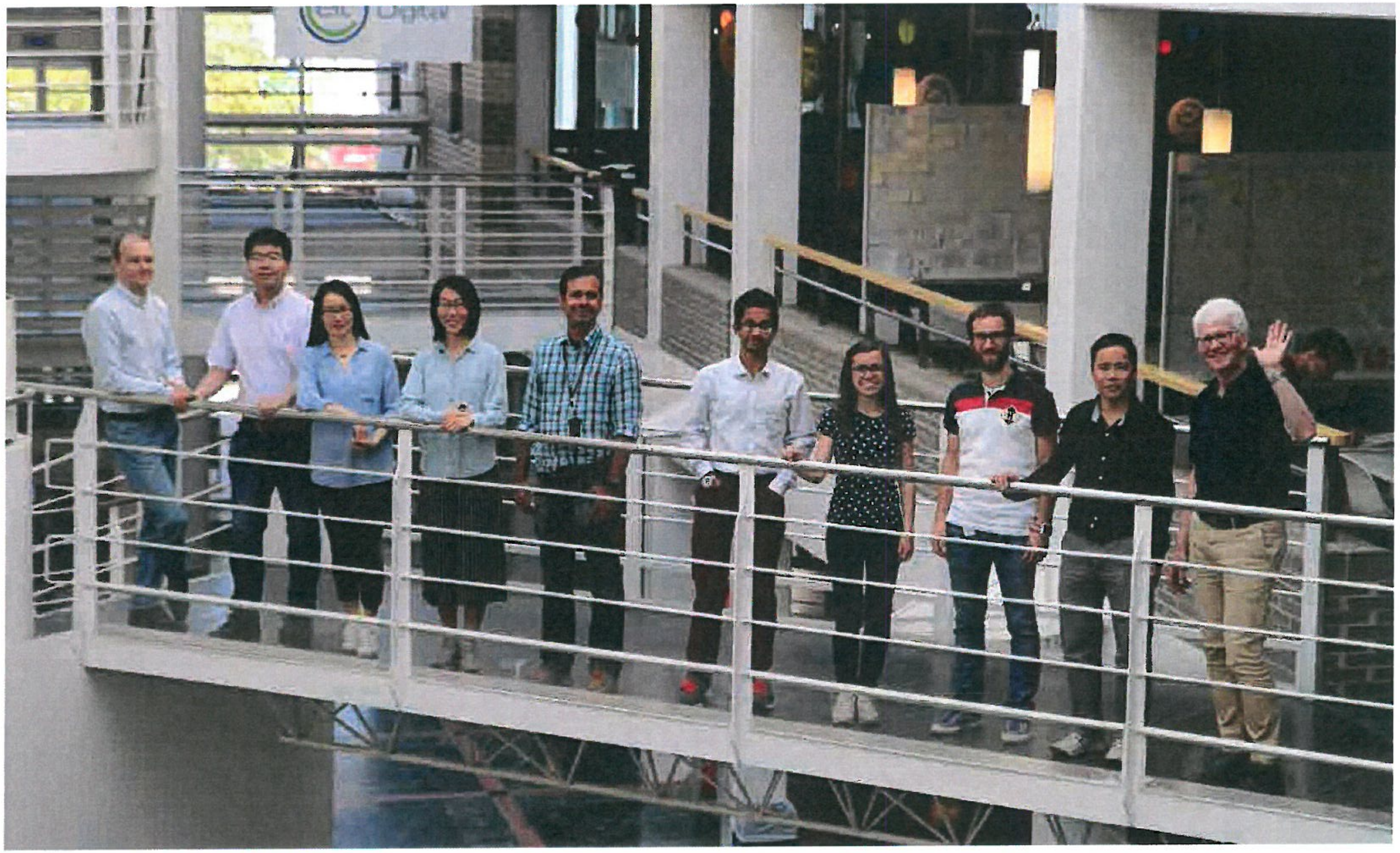
Conclusions

- fluorescent markers
  - used for detection of biomolecules – proteins, DNA
  - normally conjugated to a specific antibody
- quantum dots
  - inorganic, needs functionalization + antibodies
  - less bleaching
  - common QDs like CdSe toxic
  - Si QDs non-toxic but relatively weak luminescence
- biosensing based on an electrokinetic effect
  - CMOS compatible processing
  - many channels on a chip => detection with different antibodie
  - portable device possible
- towards sensing in water
  - heavy metals – needs special sensing concept like "Metal-organic framework"

Nanosilicon group (former)



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Familjen Erling Perssons Siftelse
Previous funding: Vinnova, SSF, Carl Trygger Foundation, Göran Gustafsson Foundation