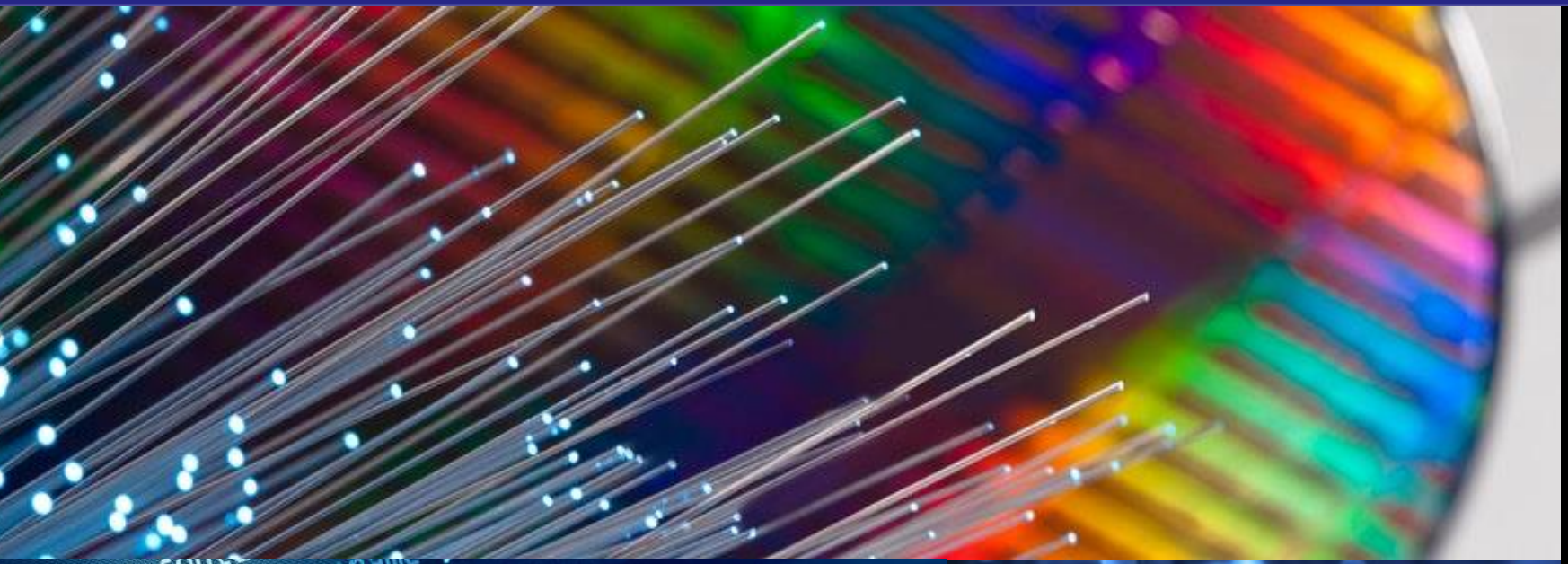
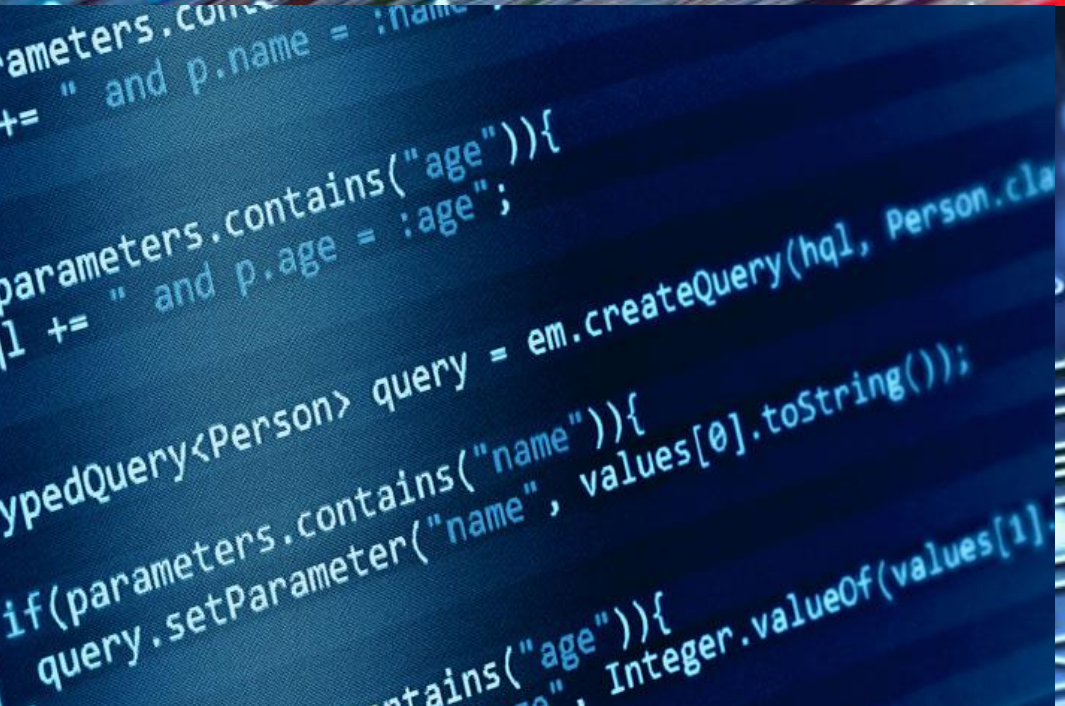
Australian Government
Australian Research Council

Centre for Nanoscale BioPhotonics
ARC CENTRE OF EXCELLENCE

Professor Ewa Goldys,
Deputy Director, ARC Centre of Excellence
for Nanoscale Biophotonics, UNSW

Using light, high energy radiation and theranostic nanomaterials to engineer interactions with biological systems

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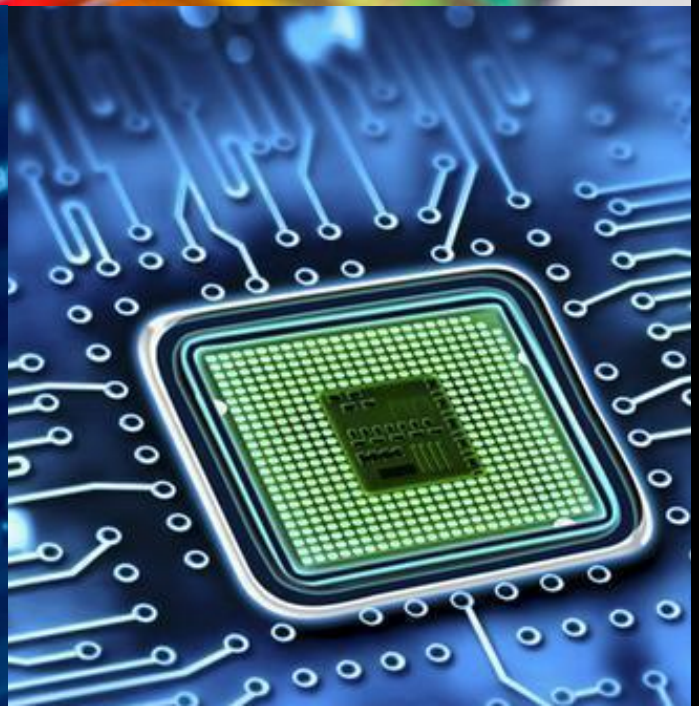

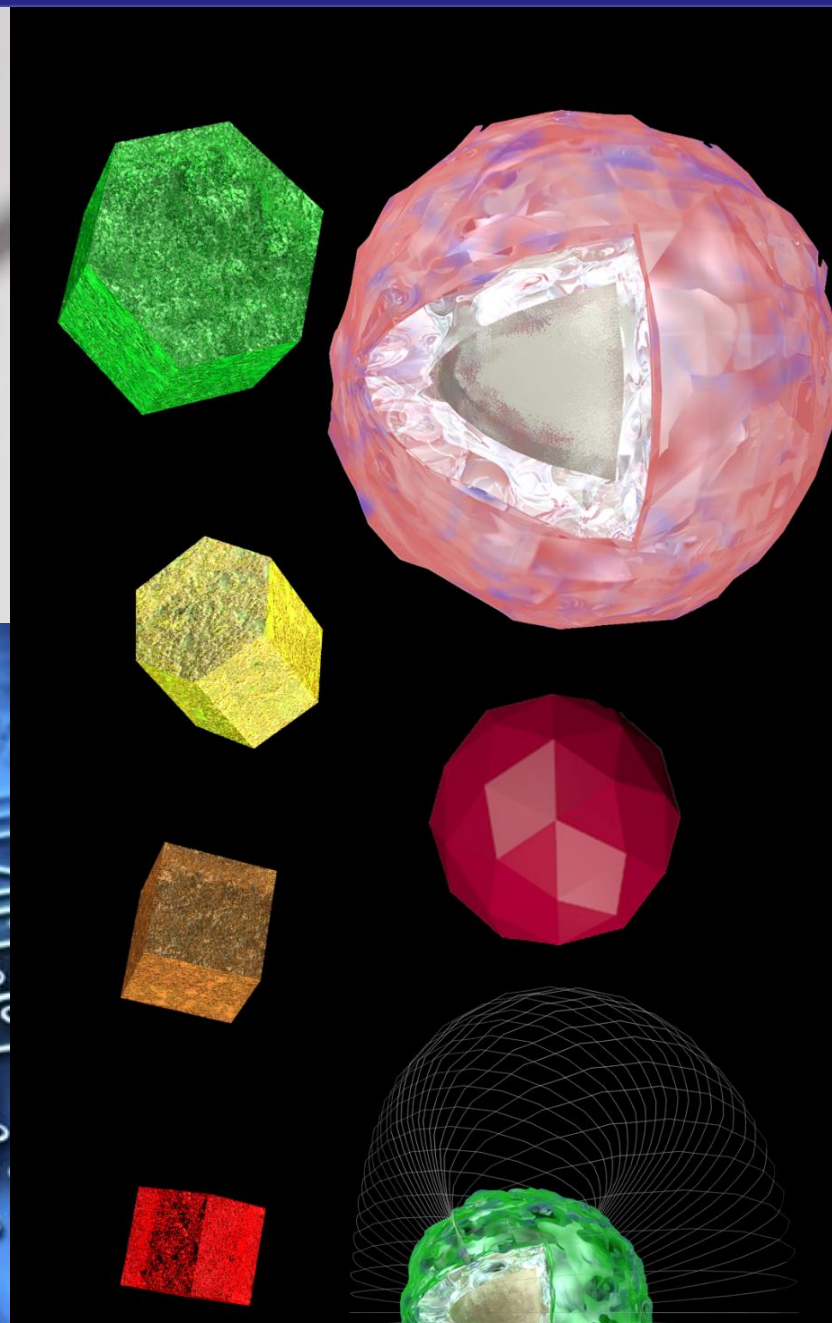


+= " and p.name = :name
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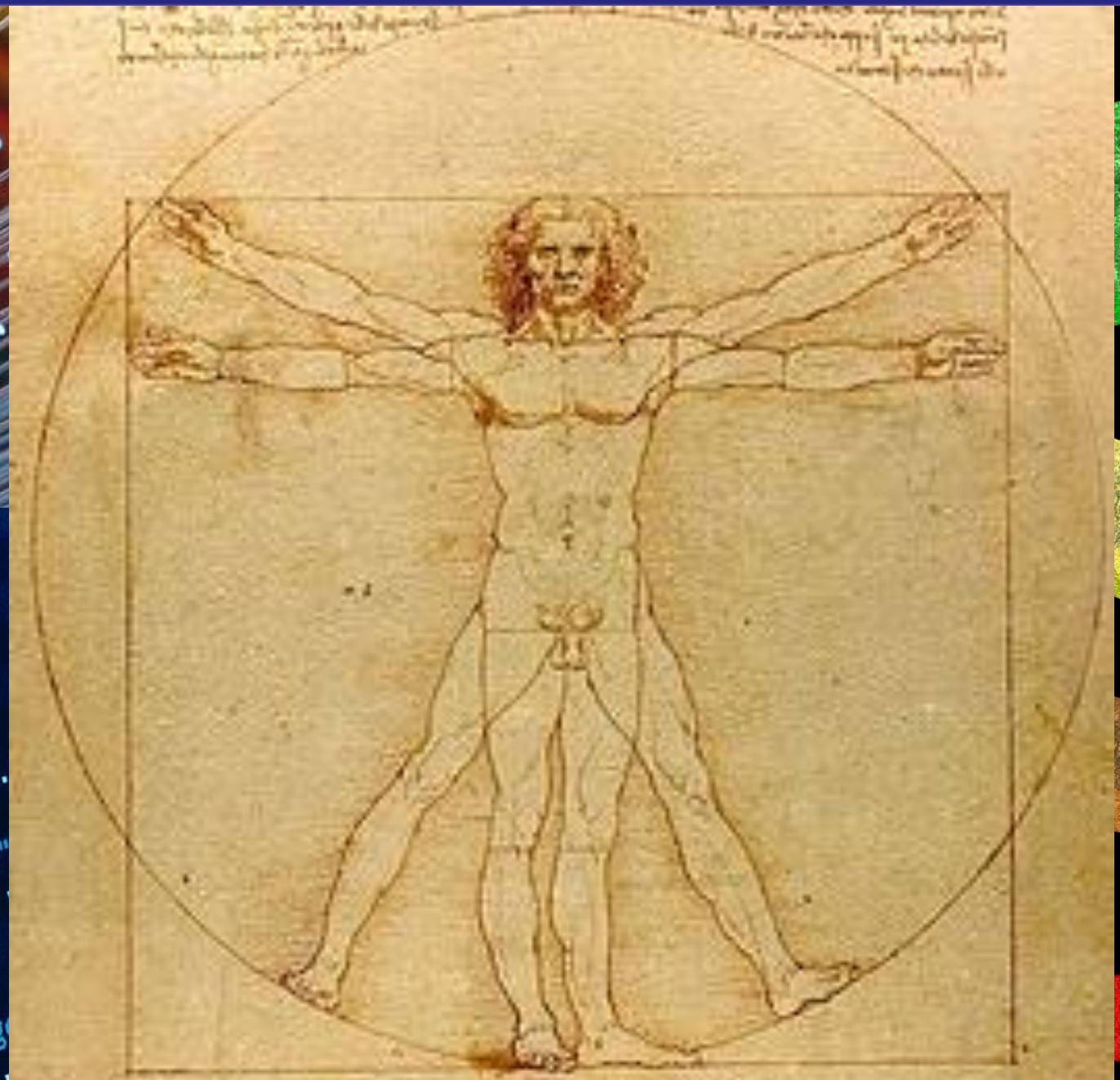
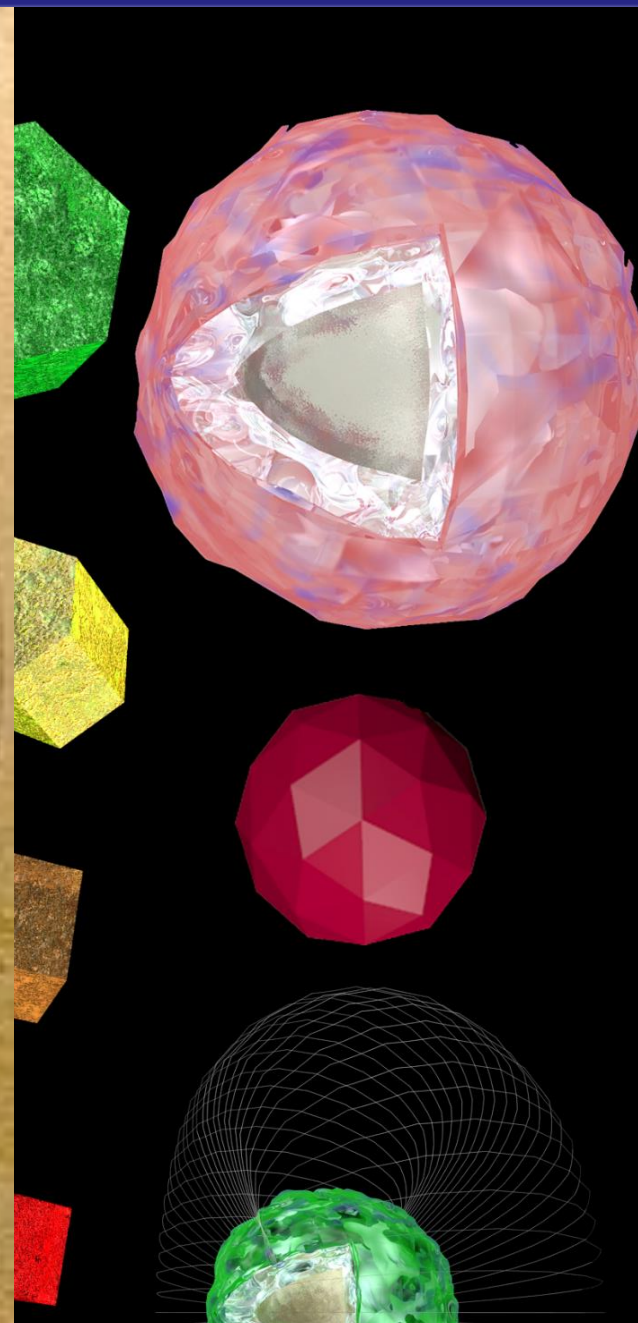
query.setParameter("name",

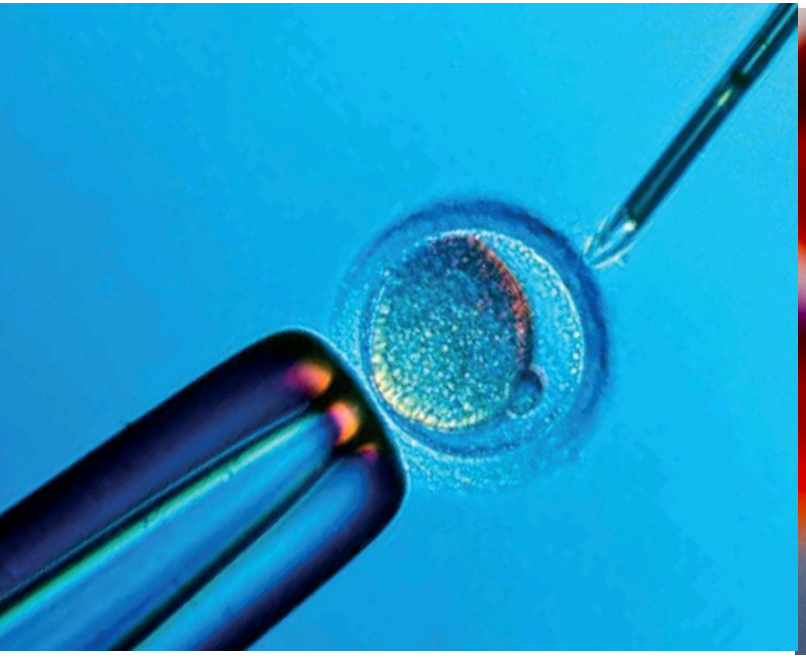


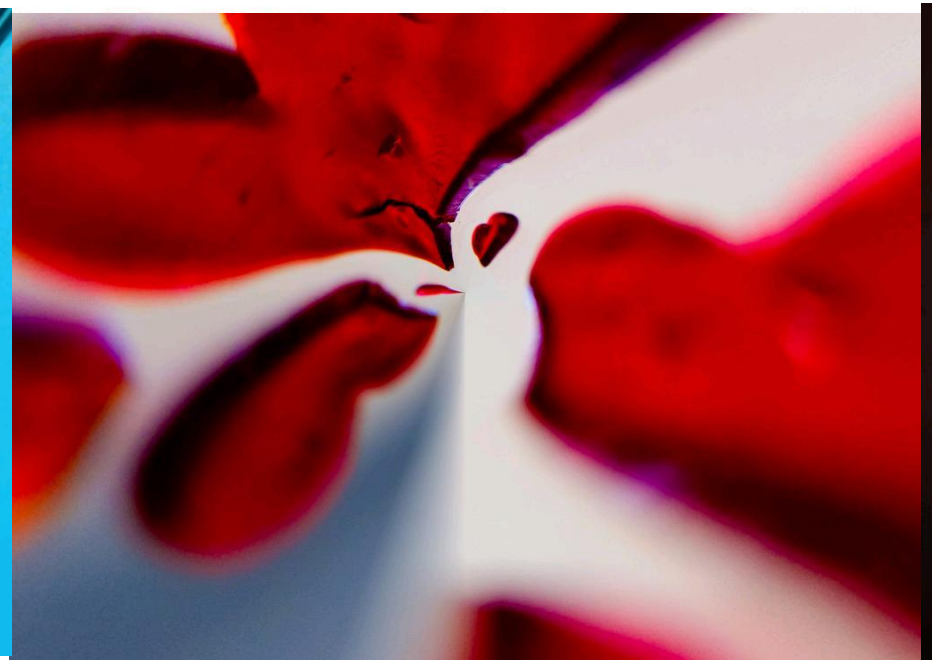


Core aim of ARC Centre for Nanoscale Biophotonics

New approaches to measuring nano-scale dynamic phenomena

in living systems





in-vivo real-time portable? point-of-care?

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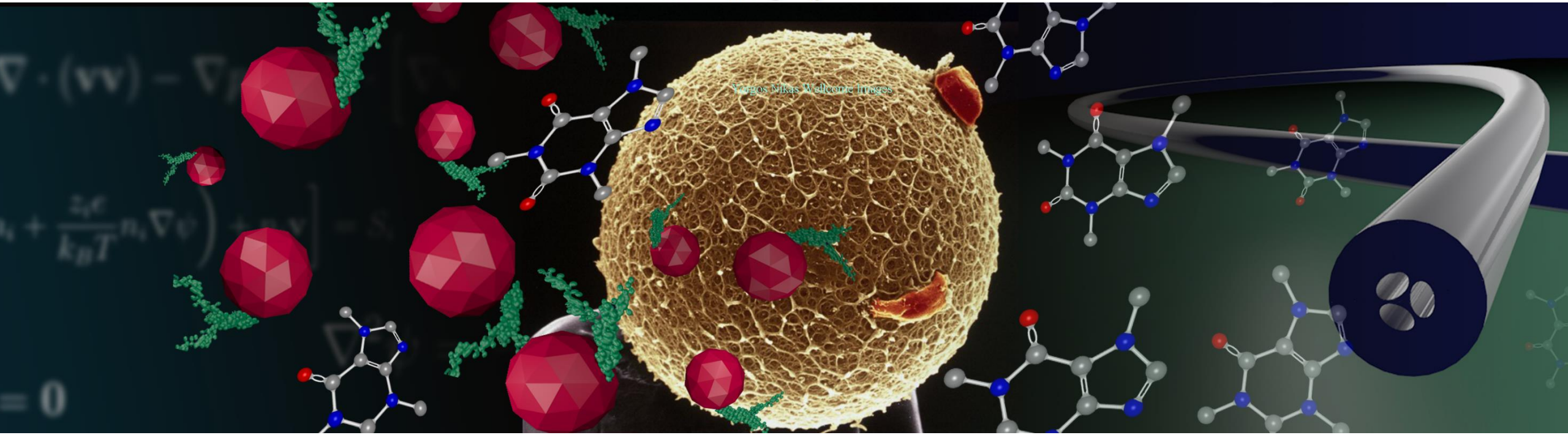

in-vivo real-time portable? point-of-care?

Challenges

- **Ultrasensitive detection of specific molecules in real environments**: trace or single molecule detection, background problem "needle in a haystack problem"
- **Molecular complexity**: need to detect many diverse molecular species
- **Minimally-invasive probing of real systems** *in - vivo* - requirement of crossing of length scales
- **Control of therapeutical interventions**

Approaches

1. Amplification
2. High contrast imaging
3. Multiplexing
4. Devices for chemical sensing in deep tissue
5. Triggering of molecular interventions in the body

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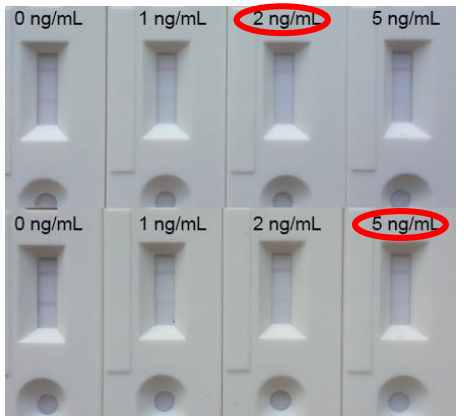
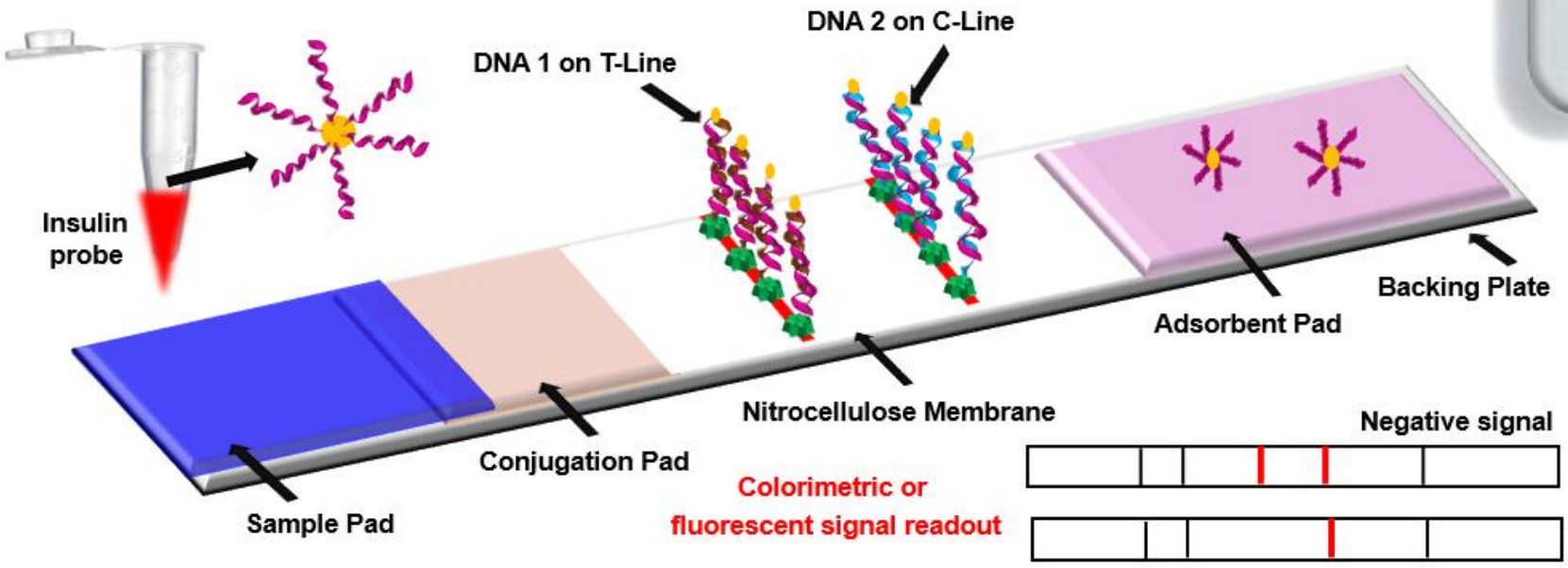
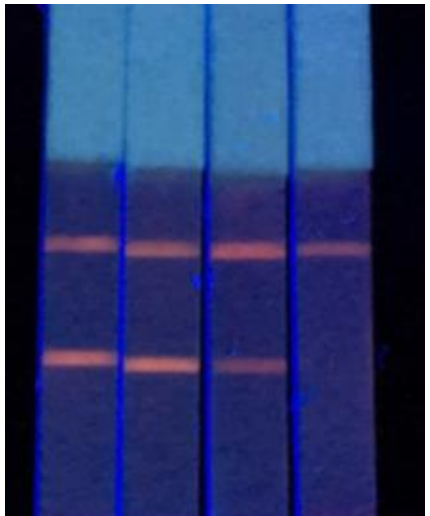
Amplified assay technologies provide effective molecular diagnostic tools for medicine

- Personalised genetic analysis for individuals
- Therapies targeted to disease type and individual drug response
- Improved infectious disease diagnostics
- Targeted therapies against antibiotic resistant pathogens
- Rapid pathogen detection in health and industry

- Complex body fluids
- Simple rapid detection at low concentration (single 1 µm microbe in 100 µl of blood

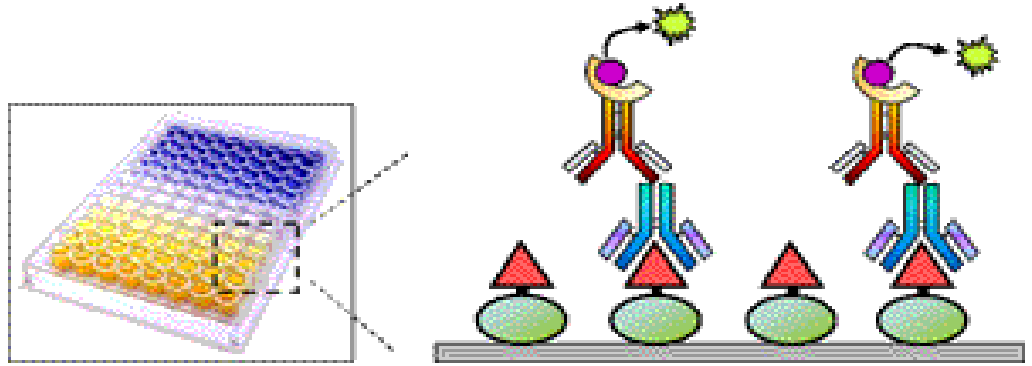




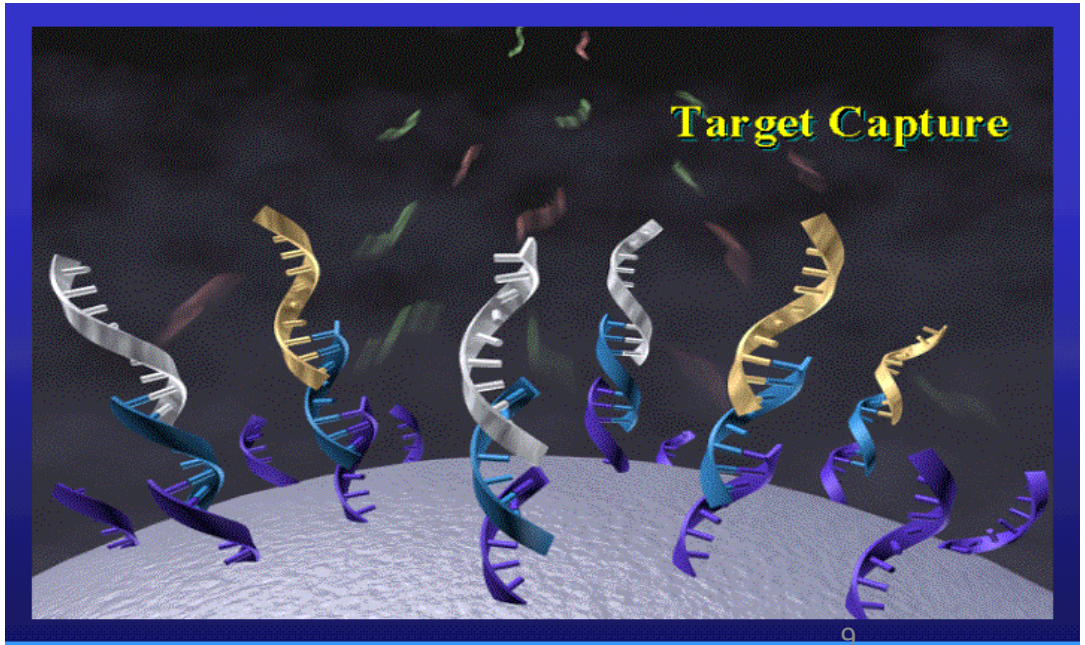


Molecular recognition enables molecularly specific assays

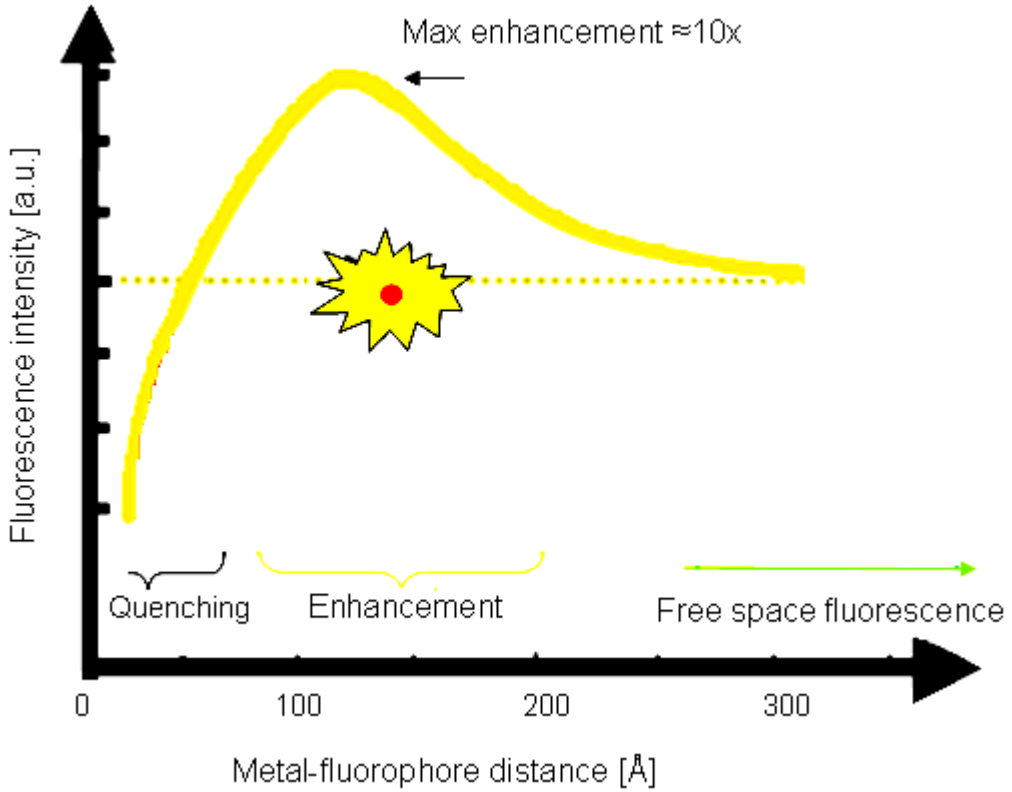
- Immunoassays –
  extremely specific bio-chemical reactions between antibody and antigen proteins



- Complementary nucleic acid sequences –
  strong binding between corresponding base pairs



Plasmonics - enhanced biosensing



Effect of metal on fluorescence signal as a function of fluorophore-metal distance

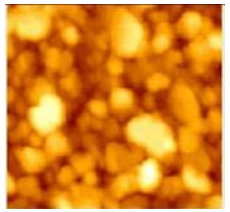
The effect of distance between metal surface and the fluorophore on MIFE:

(a) 0 – 5 nm, quenching;

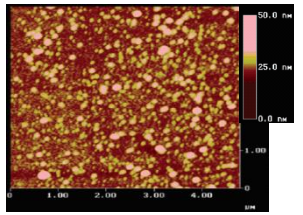
(b) 5-20 nm, enhancement;

(c) > 20 nm, free space fluorescence.

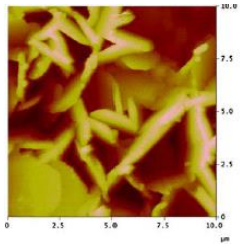
Metal structure design can optimise radiative scattering of fluorescence



Ag Island Films:
Malicka J. et al, Anal. Biochem. 315 (2003)



Ag Colloids:
Geddes C. et al, J. Phys. Chem. A **2003,** *107*



Ag Nanorods:
Kadir A. et al, *J. Phys. Chem. B* **2005,** *109*

Lakowicz et al. Analytical Biochemistry **301,** 261–277 (2002)

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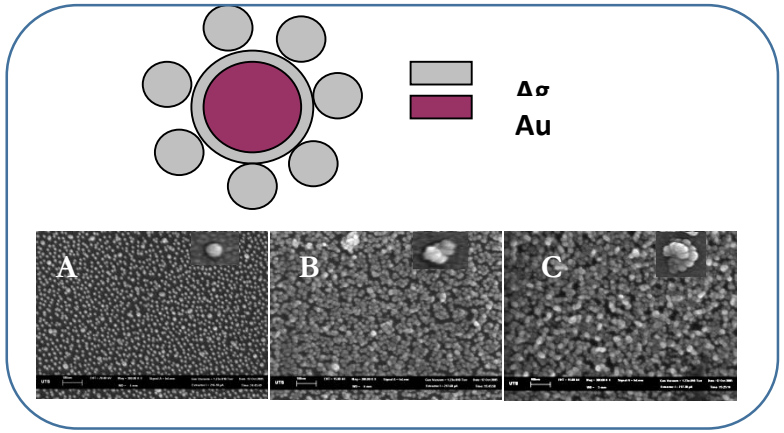
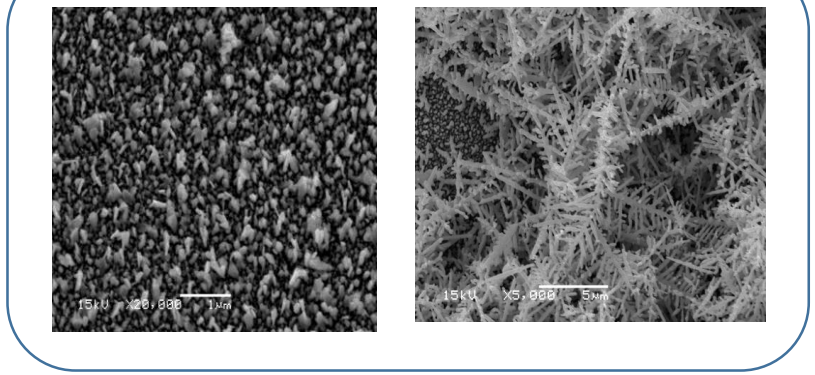
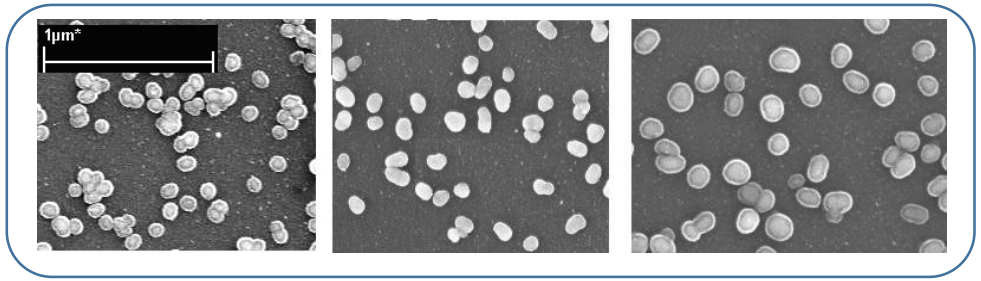
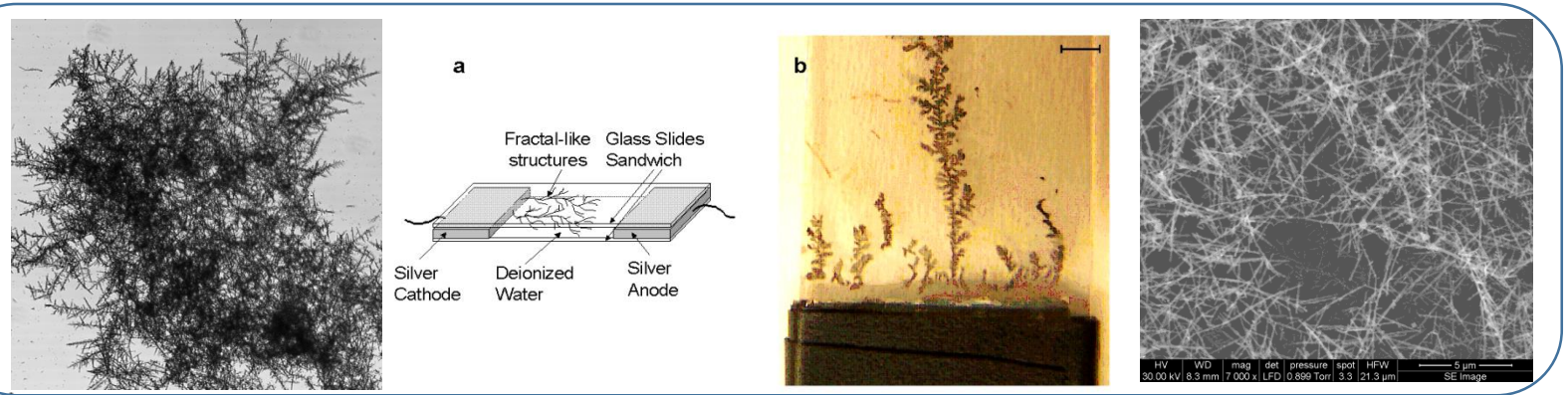
Fluorescence Amplifying Substrates



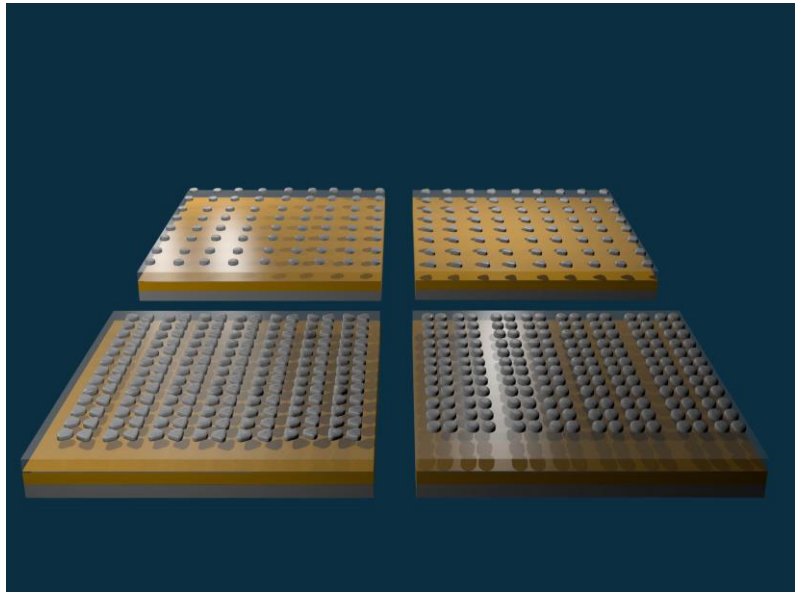




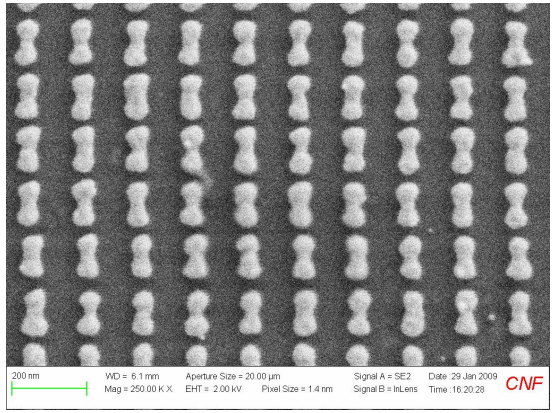
Metals: silver, gold, or both; Wet chemistry
Achieved amplification factor x70
Journal of the American Chemical Society (2007), 129(40), 12117-12122.



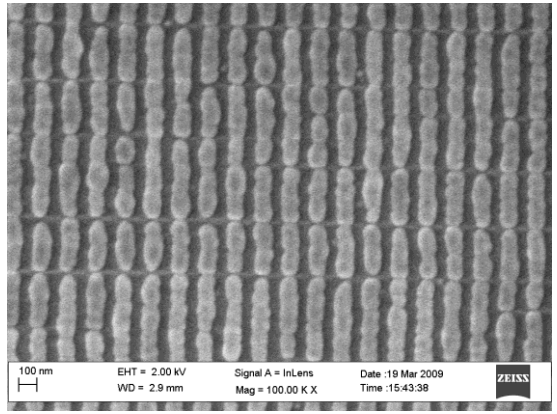
Fluorescence amplifying substrates

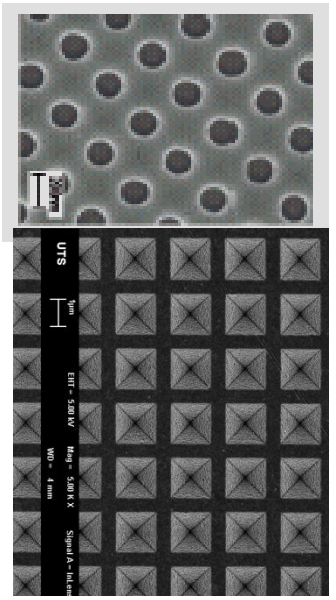


E-beam nanostructures: rational design of plasmonic properties, optimise enhancement

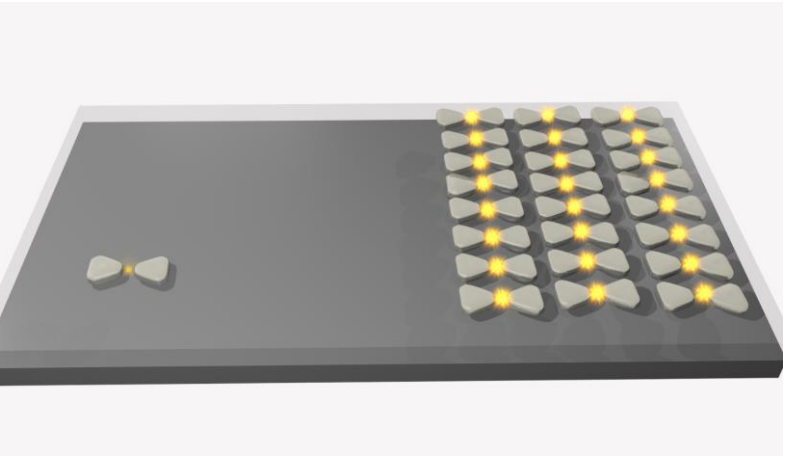


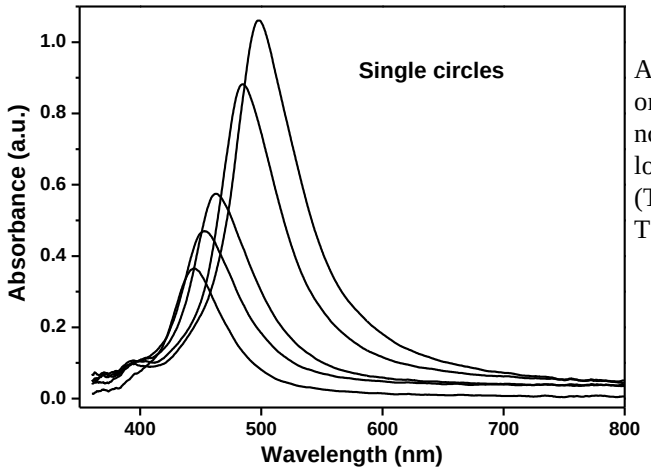
Ag on quartz

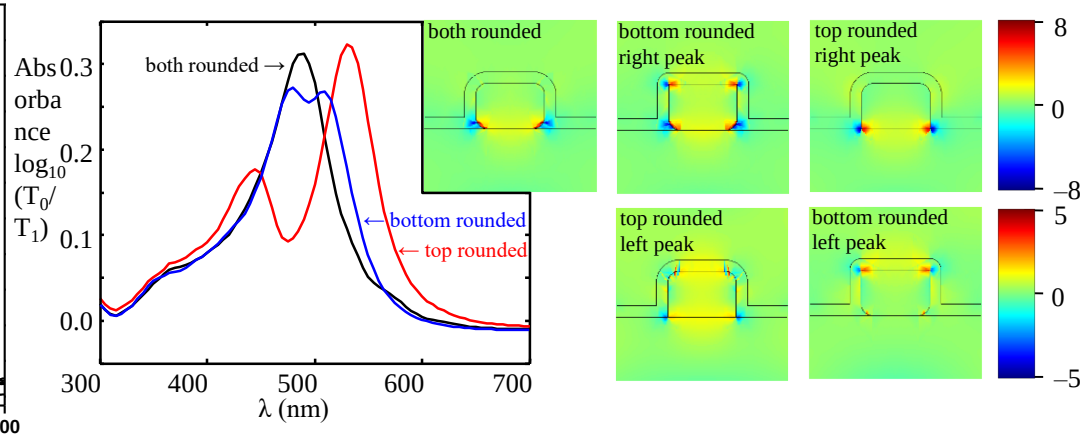




Klarite

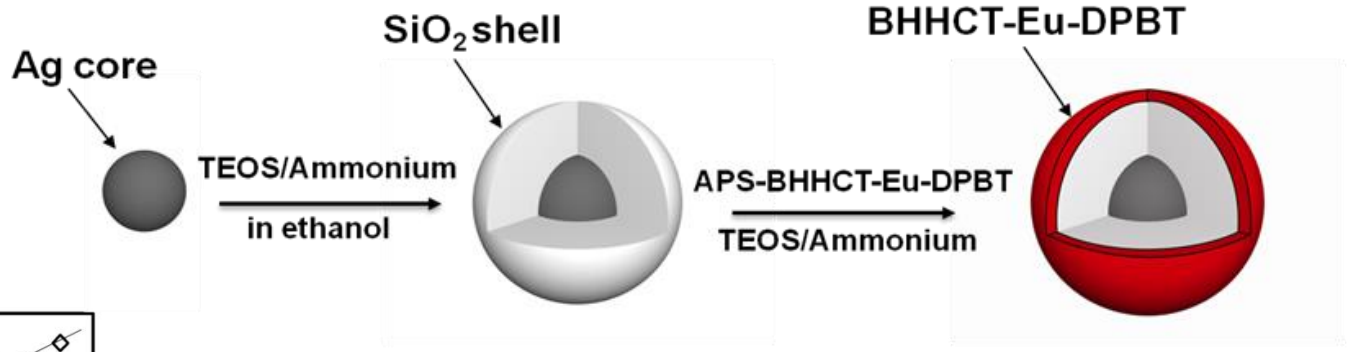


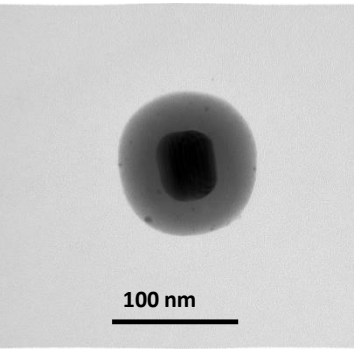


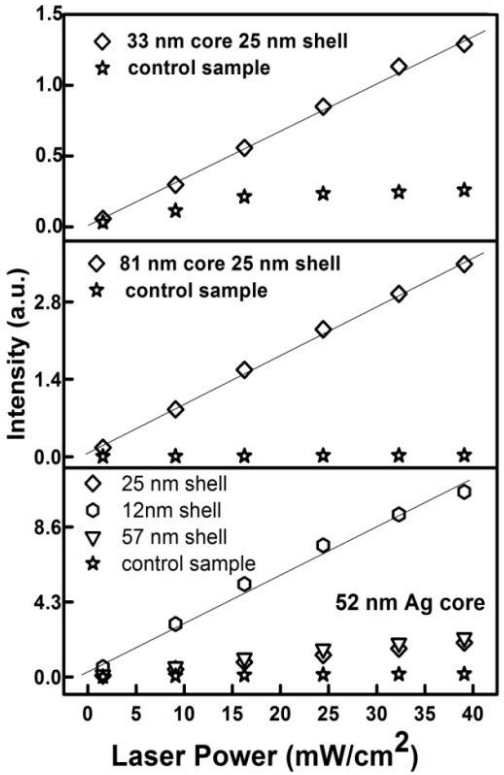


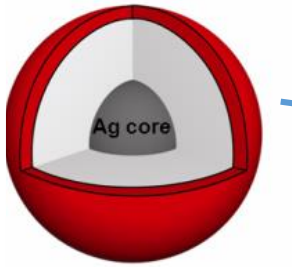
Langmuir 28 (24), 9071-9081 (2012)

Ultrabright Eu-doped plasmonic labels

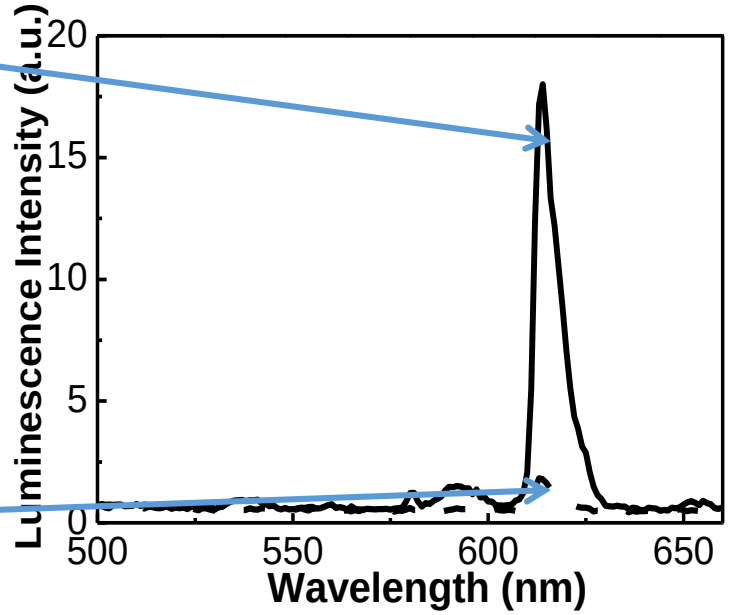




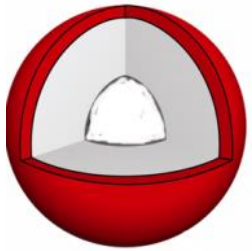




X 10.7 plasmonic fluorescence enhancement

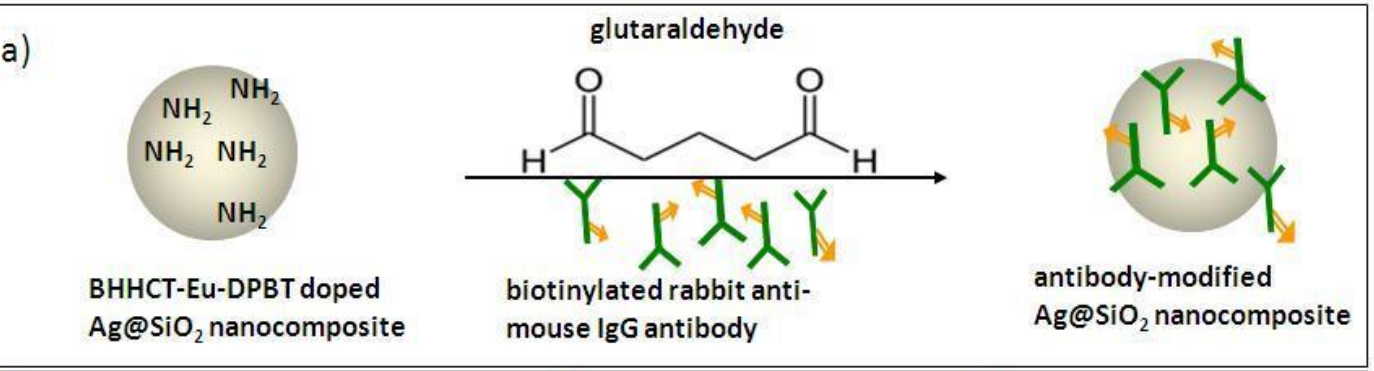


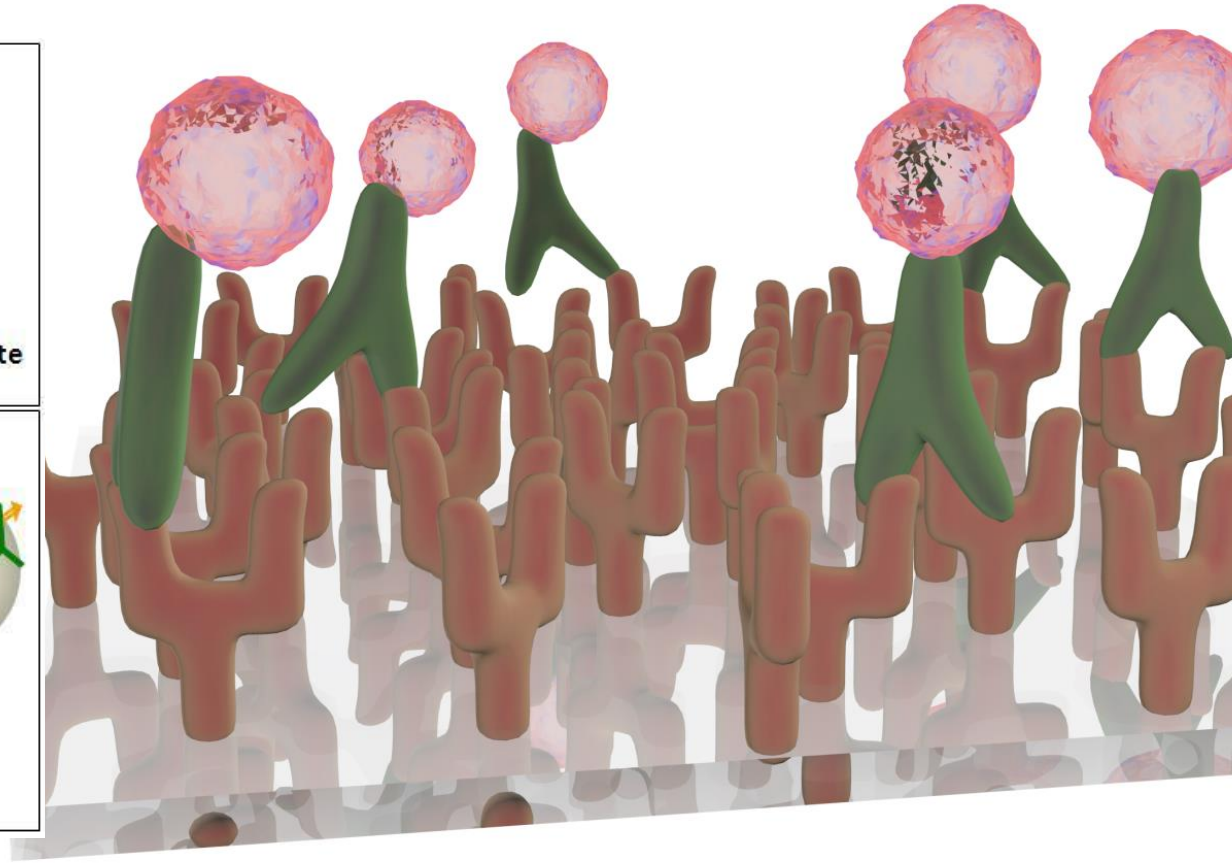
Controls



Advanced Materials 23 (40), 469-4654 (2011)

Amplified model assay



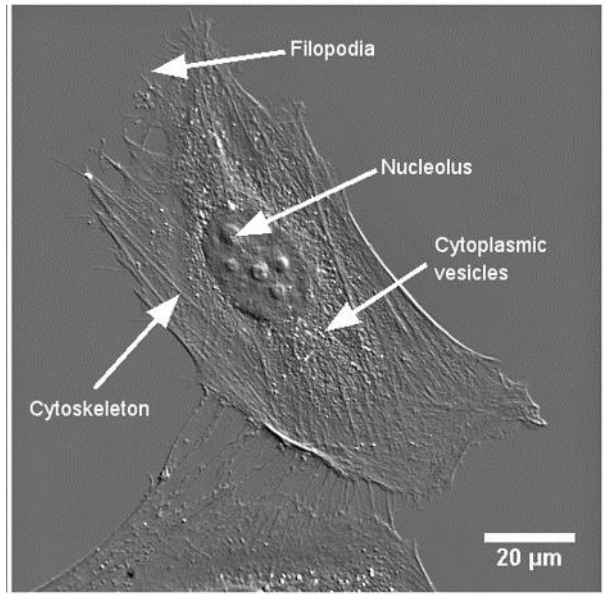


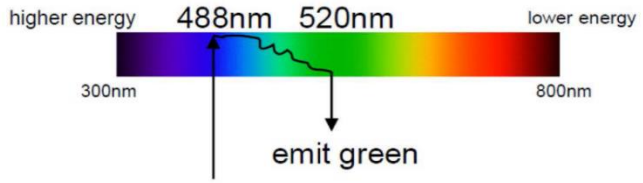
X 120 enhancement

Advanced Materials 23 (40), 469-4654 (2011)

Fluorescent labeling

Motivation: visualise molecular events





excite blue

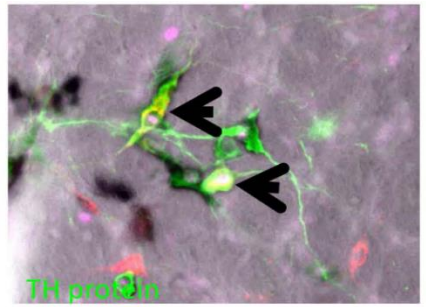
Spectral Properties of DyLight Fluorescent Dyes

Emission	Fluor	Ex/Em†	See Spectra	ε††	Spectrally Similar Dyes
Blue	DyLight 350	353/432		15K	Alexa Fluor® 350, AMCA
Blue	DyLight 405	400/420		30K	Alexa Fluor 405, Cascade Blue®
Green	DyLight 488	493/518		70K	Alexa Fluor 488, fluorescein, FITC
Yellow	DyLight 550	562/576		150K	Alexa Fluor 546, Alexa Fluor 555, Cy3®, TRITC
Red	DyLight 594	593/618		80K	Alexa Fluor 594, Texas Red®
Red	DyLight 633	638/658		170K	Alexa Fluor 633
Red	DyLight 650	652/672		250K	Alexa Fluor 647, Cy5®
Near IR	DyLight 680	692/712		140K	Alexa Fluor 680, Cy5.5®
Near IR	DyLight 750	752/778		210K	Alexa Fluor 750
Infrared	DyLight 800	777/794		270K	IRDye® 800

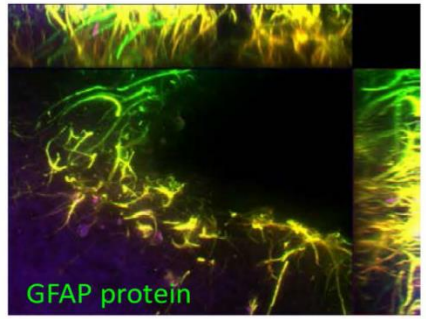
†Excitation and emission maxima in nanometers (+/- 4nm) in phosphate-buffered saline (PBS)
††Molar extinction coefficient (M^{-1} cm^{-1}) at the absorption maximum

Antibody molecules enable very specific attachment of fluorescent labels to their target

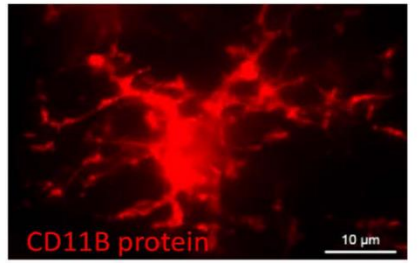
neurons



astrocytes

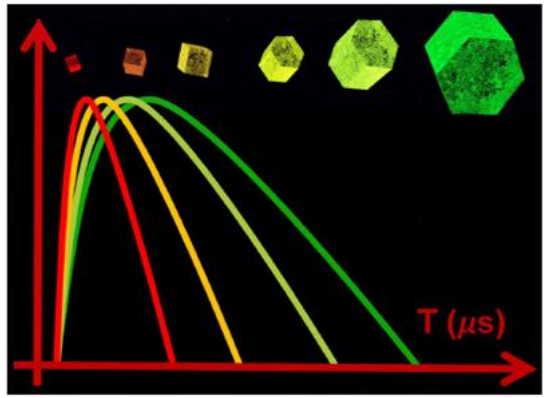


microglia

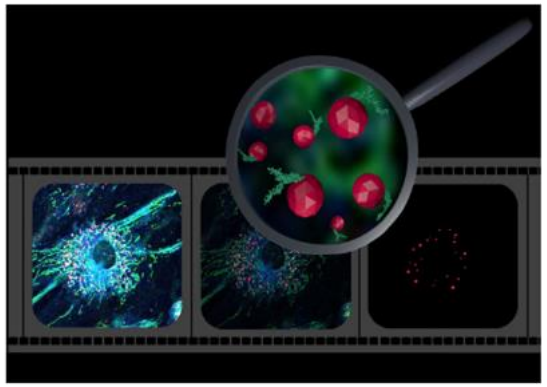


Lindsay Parker, Macquarie

Nanoparticles



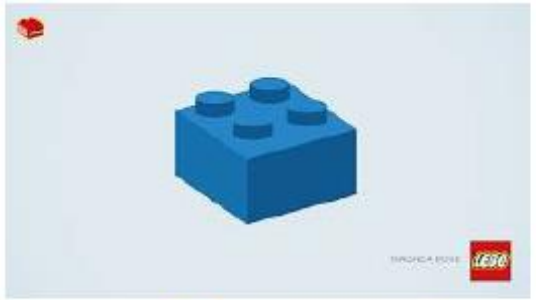
UCNP: J. Zhao et al. Nanoscale, 5, 944, (2013)
"Super-Dots": J. Zhao et al. Nature Nanotechnology 8, 729, (2013)



Nanoruby: A. Kelf et al., Particle and P. Char. 30, 6, 483, (2013)

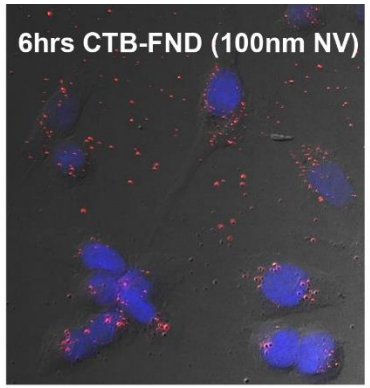
Types of nanoparticles

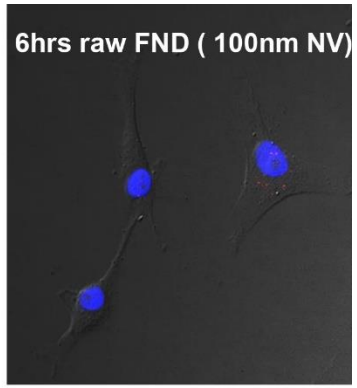
- Gold and silver nanoparticles
- Silica nanoparticles (mesoporous)
- Quantum dots
- Carbon dots, nanotubes and graphene
- Nanodiamonds, upconverting and other luminescent nanoparticles
- Dendrimers and other polymer nanoparticles
- Liposomes and micelles

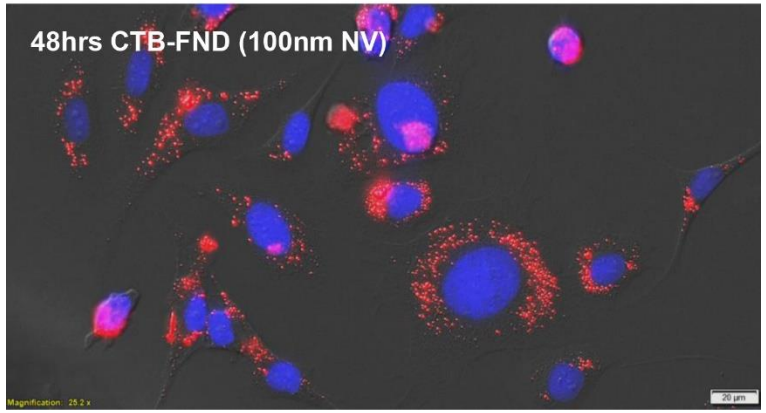


- Most do not photobleach
- Nanoparticles can target molecules

Photostability of nanodiamonds

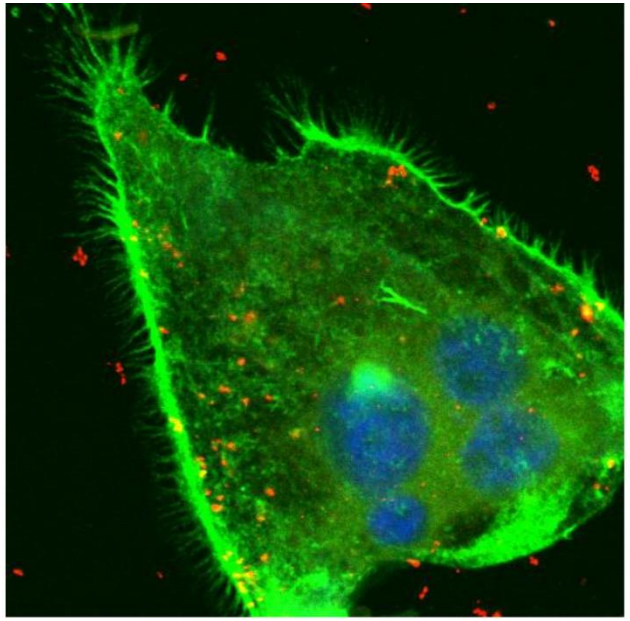




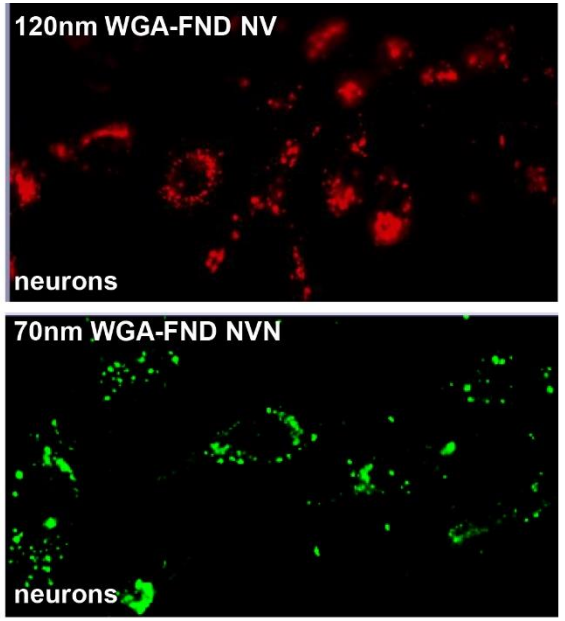


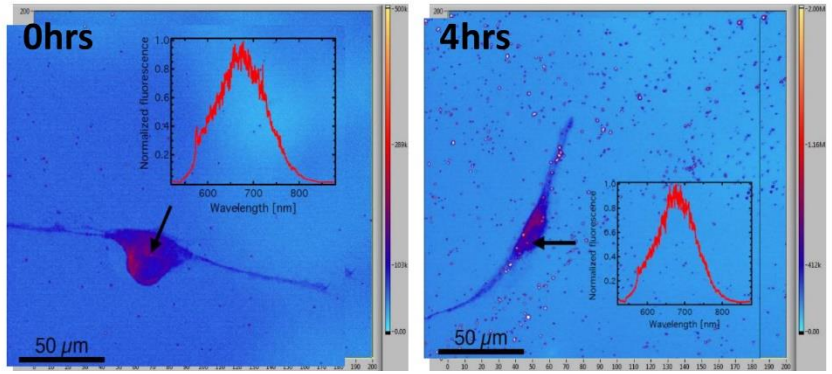
Lindsay Parker, Macquarie

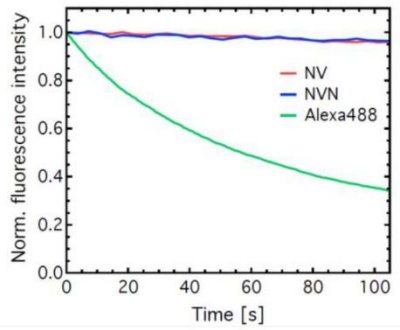
CTB-FND
DAPI
f-actin
(phalloidin Alexafluor 488)



U87 MG astrocytes (isolated from human glioblastoma tumor)







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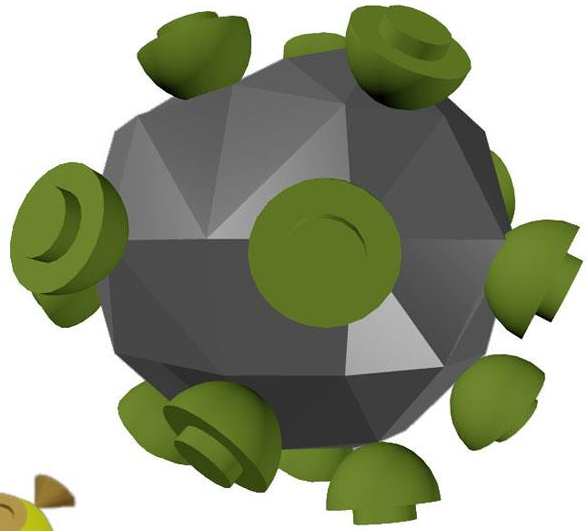
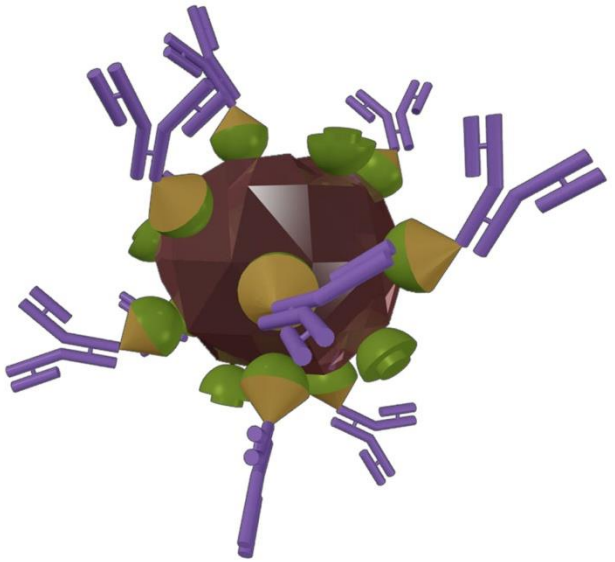
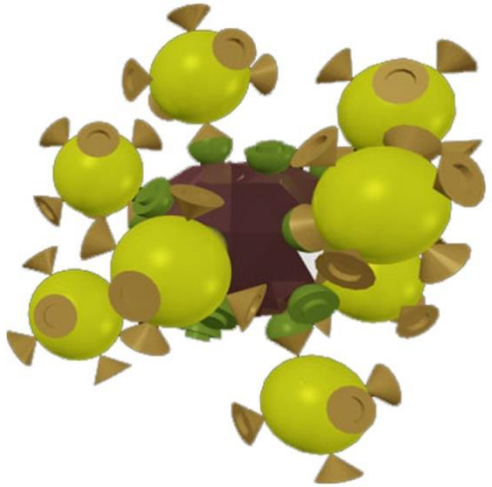
Nanoprobes can be targeted to molecules of interest

Biotin-streptavidin pairs

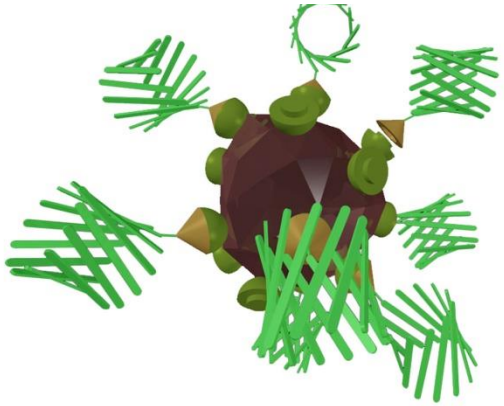


Antibody-antigen pairs



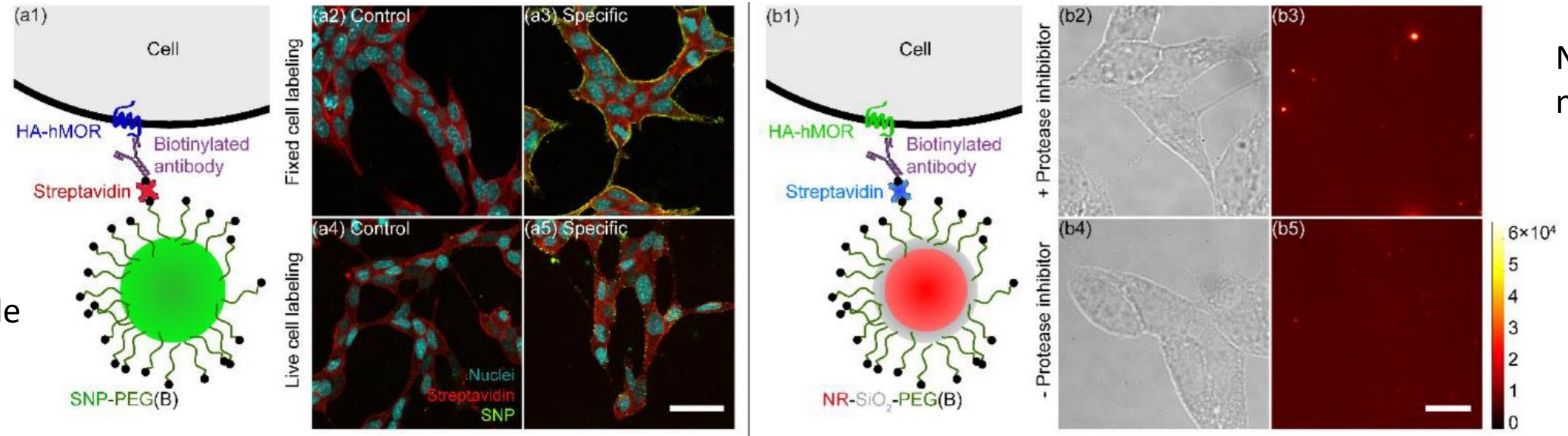


Various nanoparticle-molecule conjugates (e.g. with specific peptides, nucleic acids etc)



Specific labeling of opioid receptors with nanoparticles

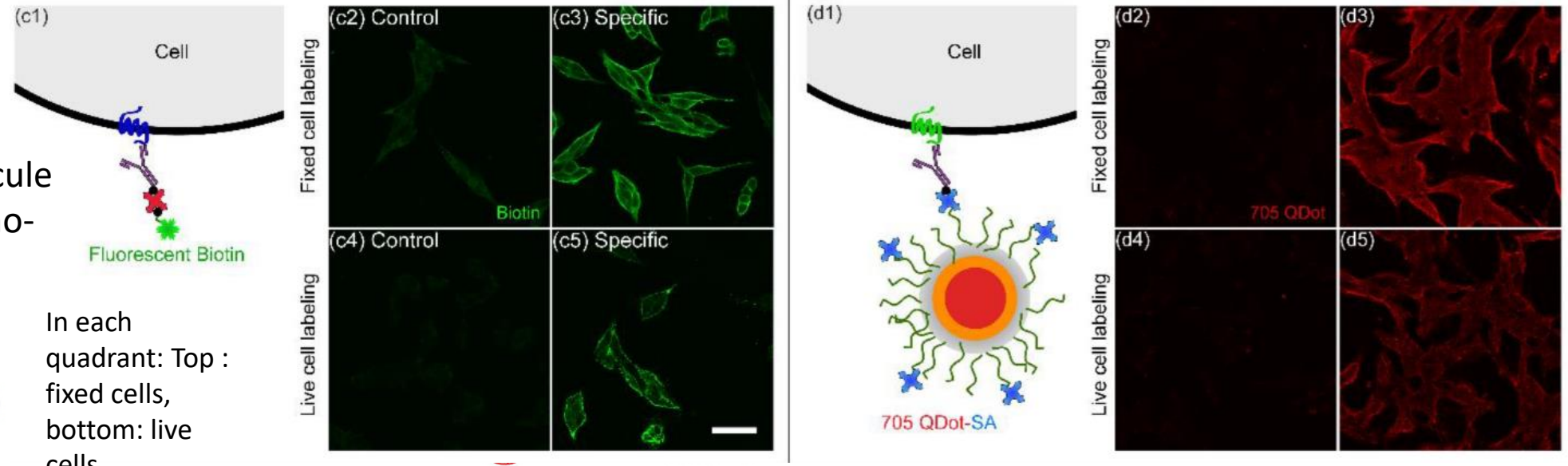
SNP: Silica nano particle



NR: nanoruby

ACS Appl. Mater Interfaces, 2017, 9(45) 39197-39208.

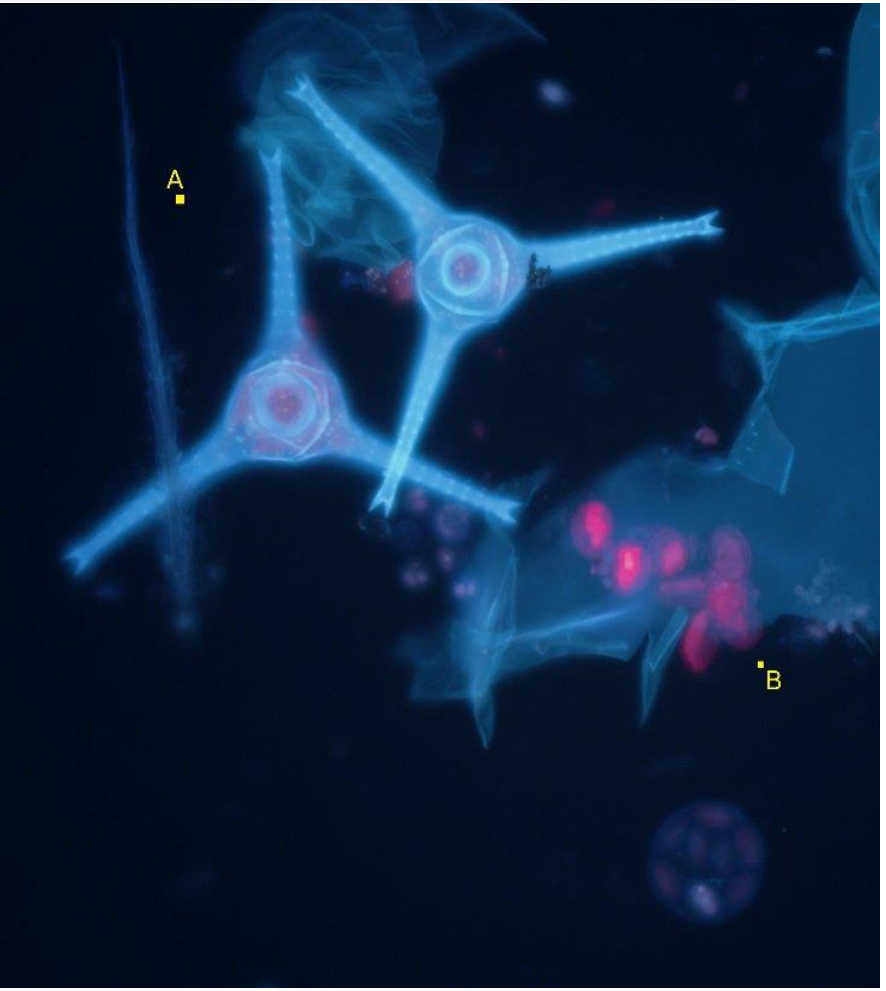
Biotin = molecule not nano-particle

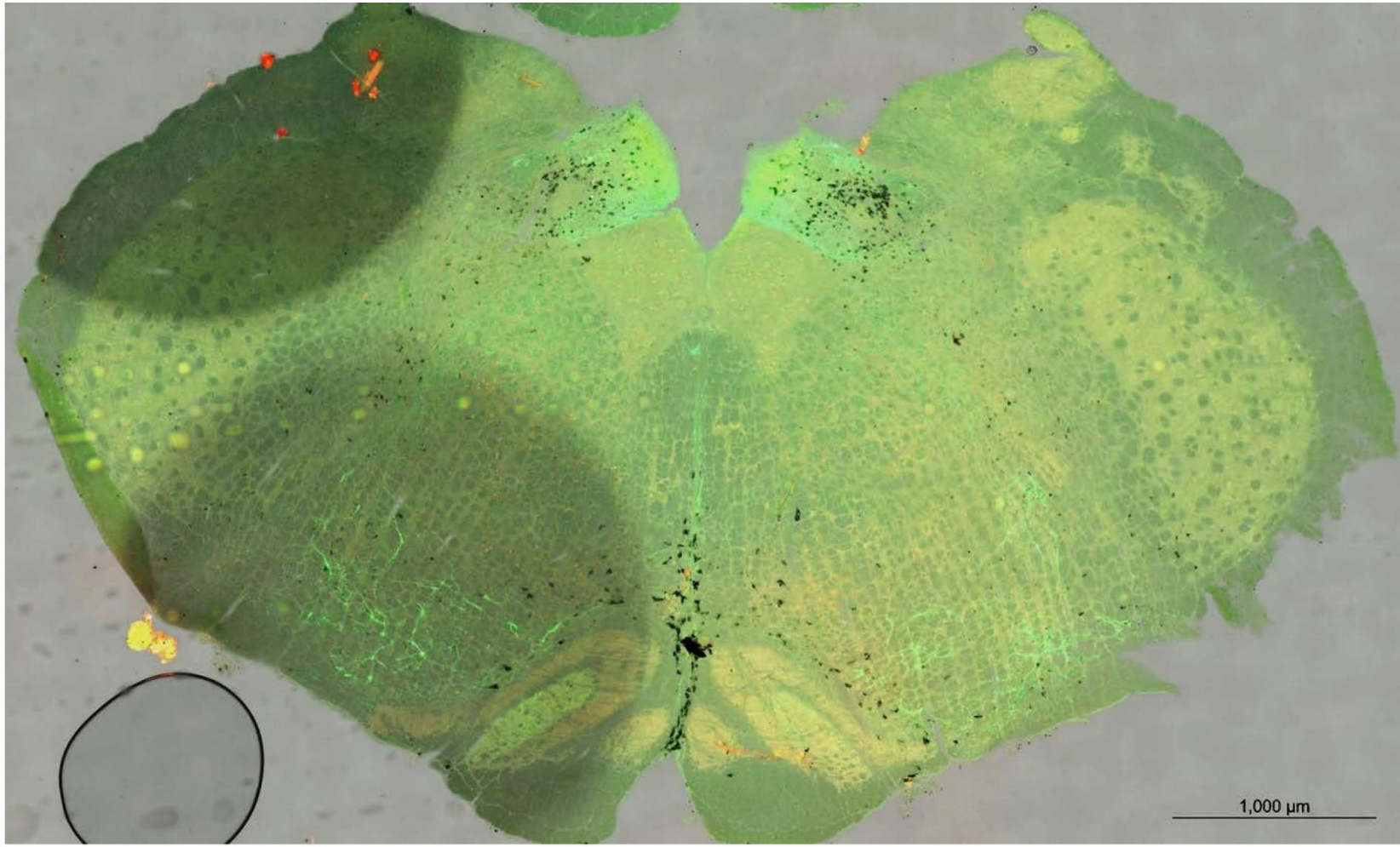


Qdot= Quantum Dot (inorganic nanoparticle ZnSe, CdSe etc)

In each quadrant: Top : fixed cells, bottom: live cells

Autofluorescence





CNS autofluorescence is high especially for blue light excitation due to flavins

Jongen JLM, et al., *PLoS ONE*, **2014**. 9(10): p. e109029.
Jongen JLM, et al., *The Journal of Neuroscience*, **2010**. 30(11): p. 4081-4087.
Spitzer N, et al., *Journal of Neuroscience Methods*, **2011**. 197(1): p. 48-55.

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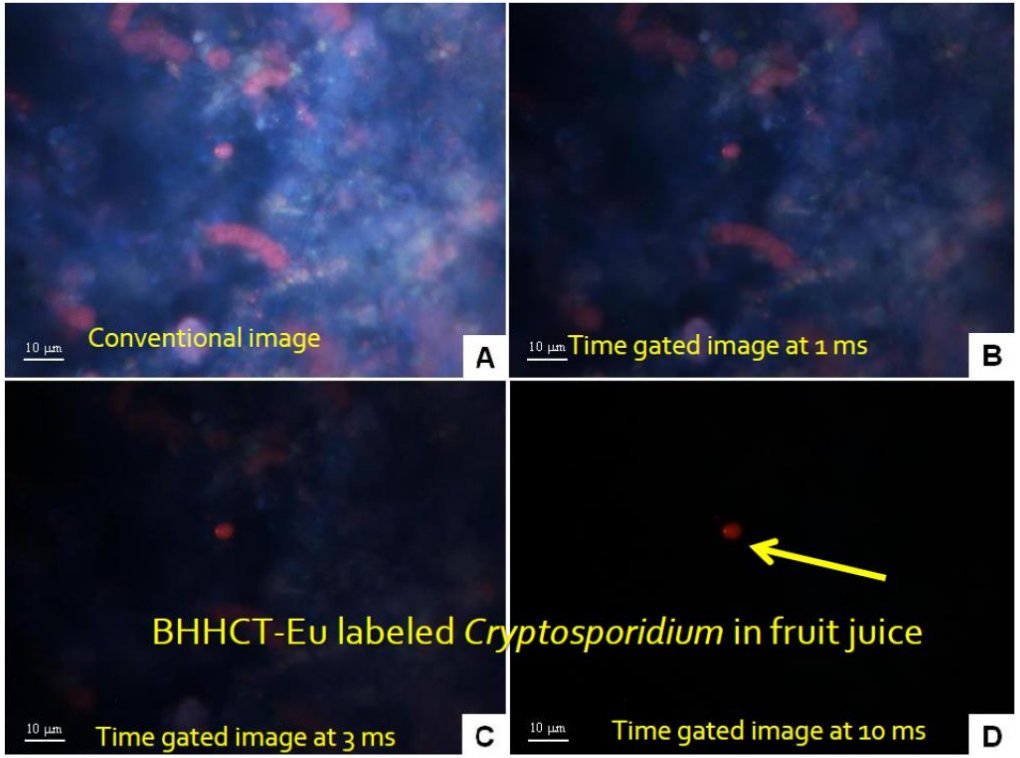
Time-gated imaging

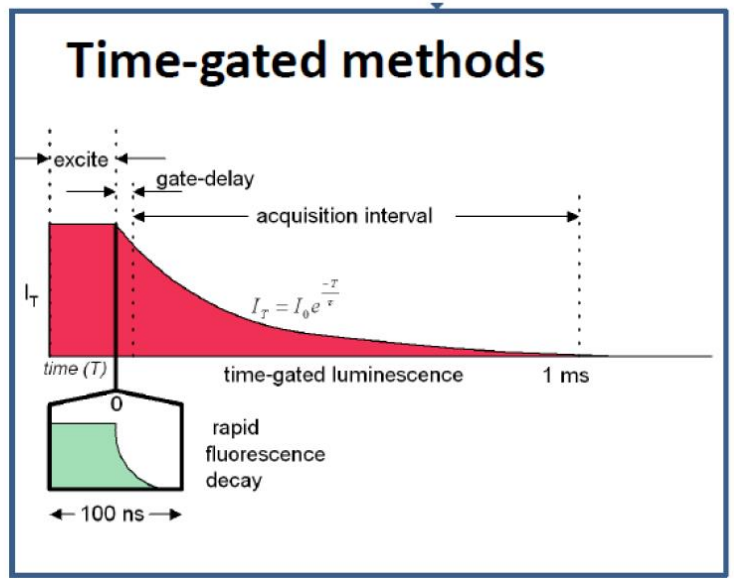
1. Label targets with long-lived label (here:Eu)
2. Excite sample with a light pulse
3. Wait until short-lived autofluorecence decays
4. Collect signal from the label
5. Keep repeating steps 2-4

Data: Russell Connally



Excellent isolation of targets from background

Applicable to microscopy imaging, environmental and medical sensing, pathogen detection, etc



S/N ratio of up to 10^5

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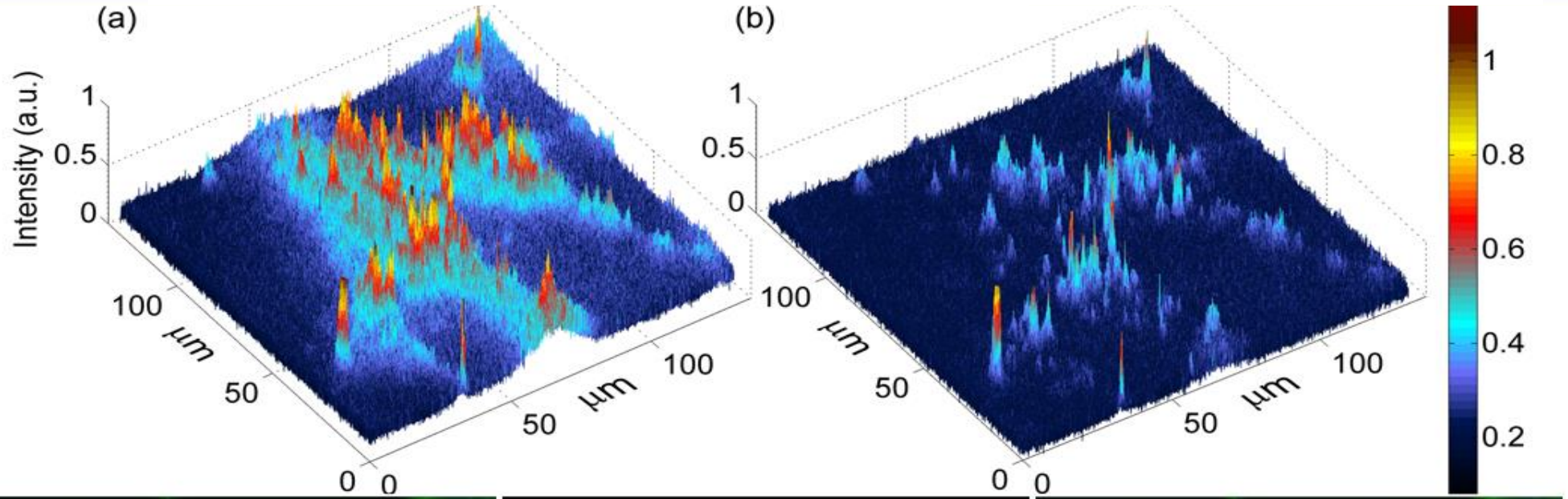
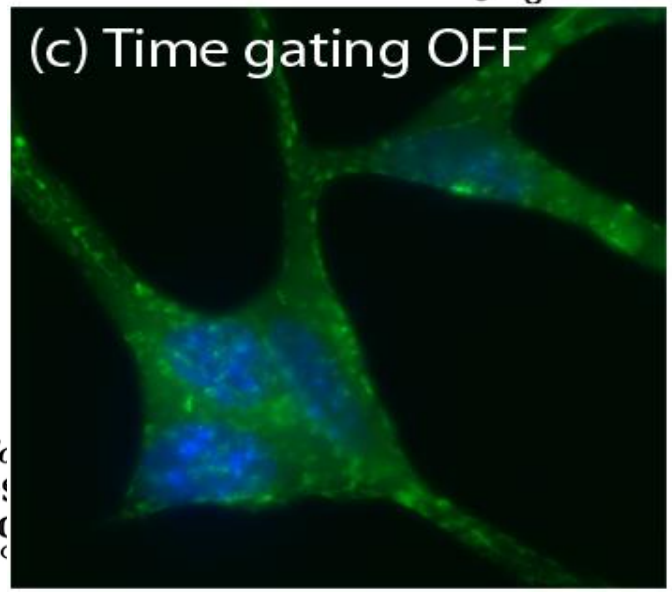
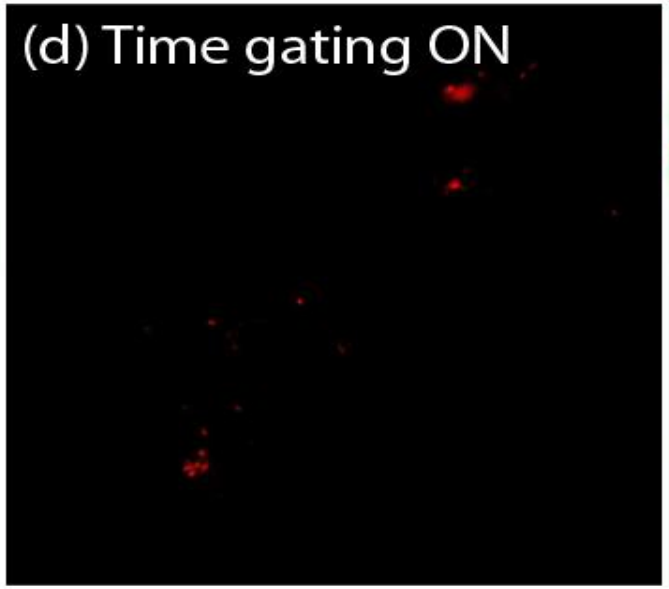
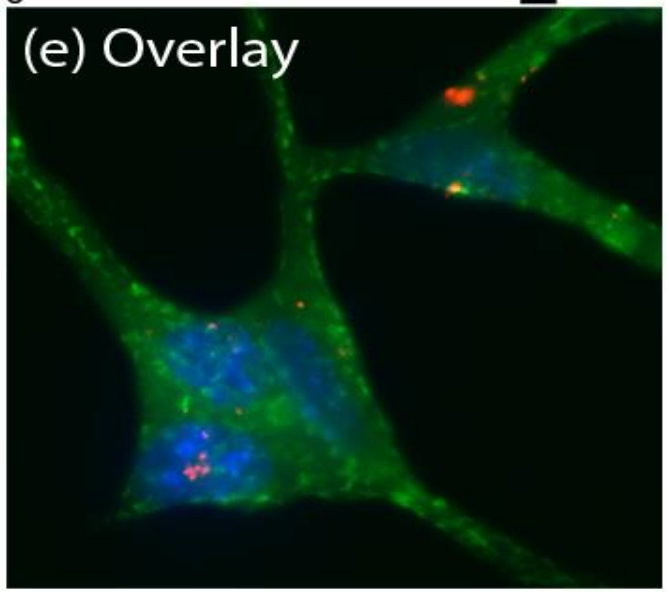
Time-gated imaging with nanorubies









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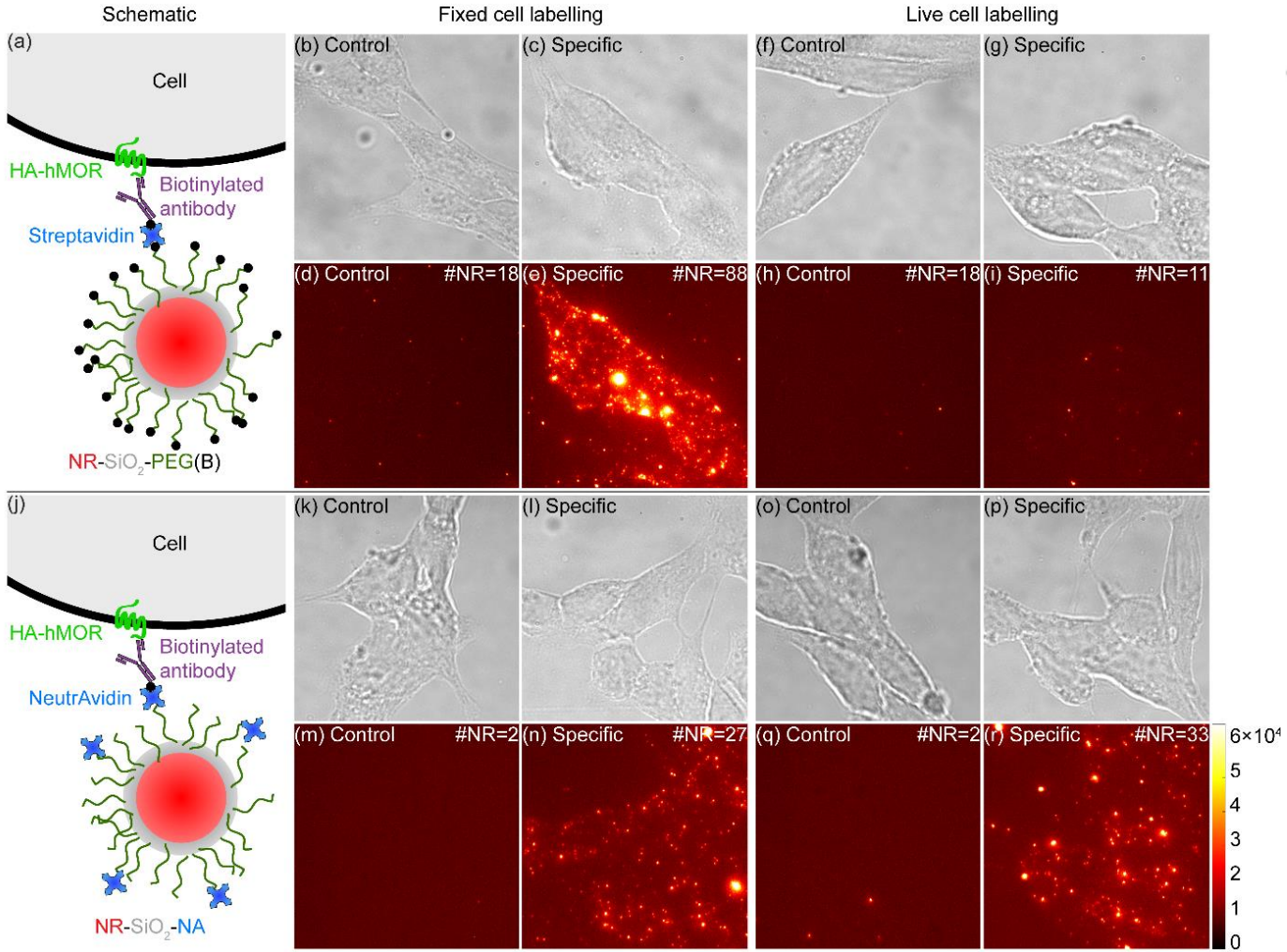
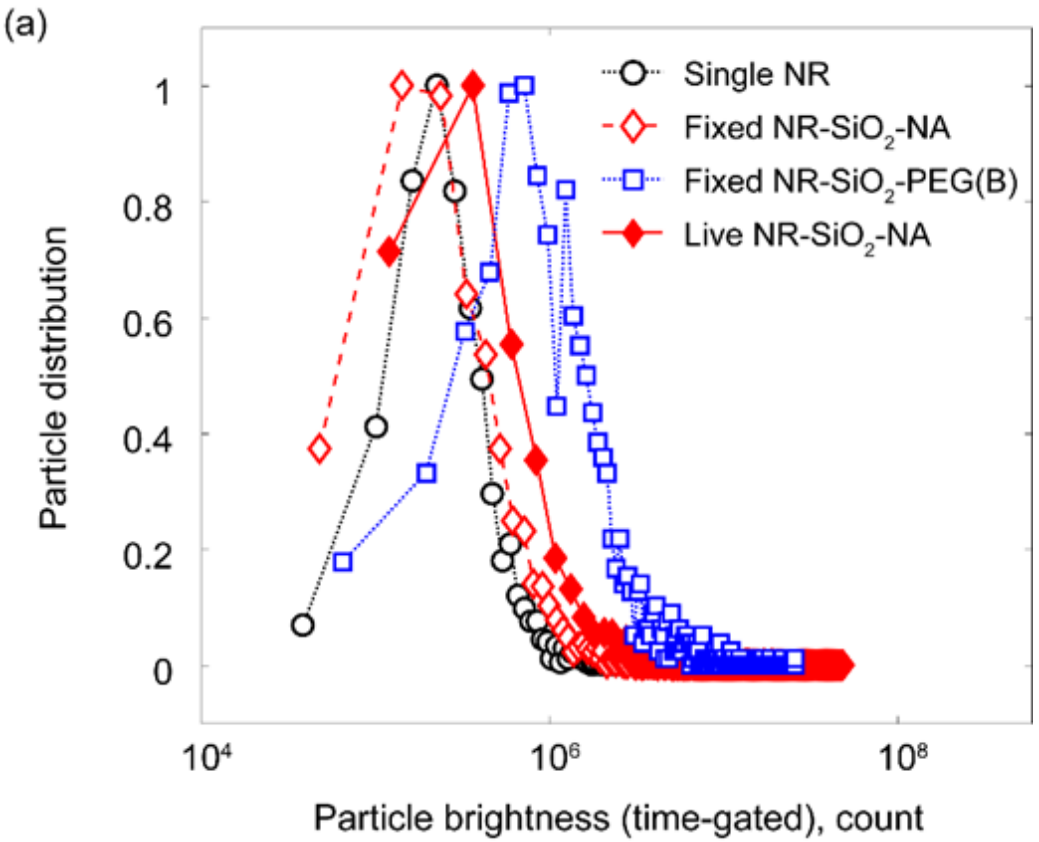
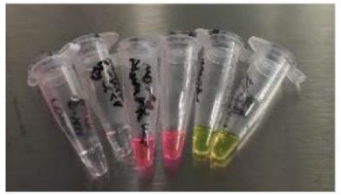
Imaging of single opioid receptors with targeted nanorubies

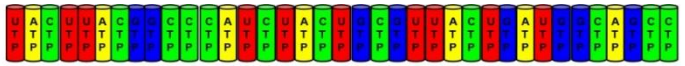




Sreenivasan et al. ACS Appl. Mater Interfaces, 2017, 9(45):39197-39208. doi: 10.1021/acsami.7b12665.

Background-free imaging of mRNA expression

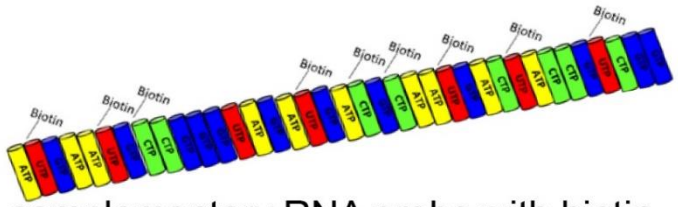




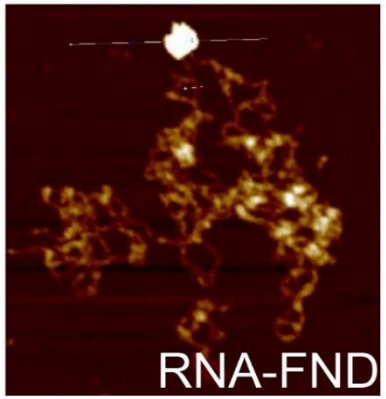
Gene of interest (mRNA sequence)

LISH (lanthanide based)
DISH (nanodiamond based)
SuperFISH (UCNP based)

Lindsay Parker, Macquarie



complementary RNA probe with biotin incorporated



AFM: Dr. Denitza Denkova

streptavidin-nanoparticle

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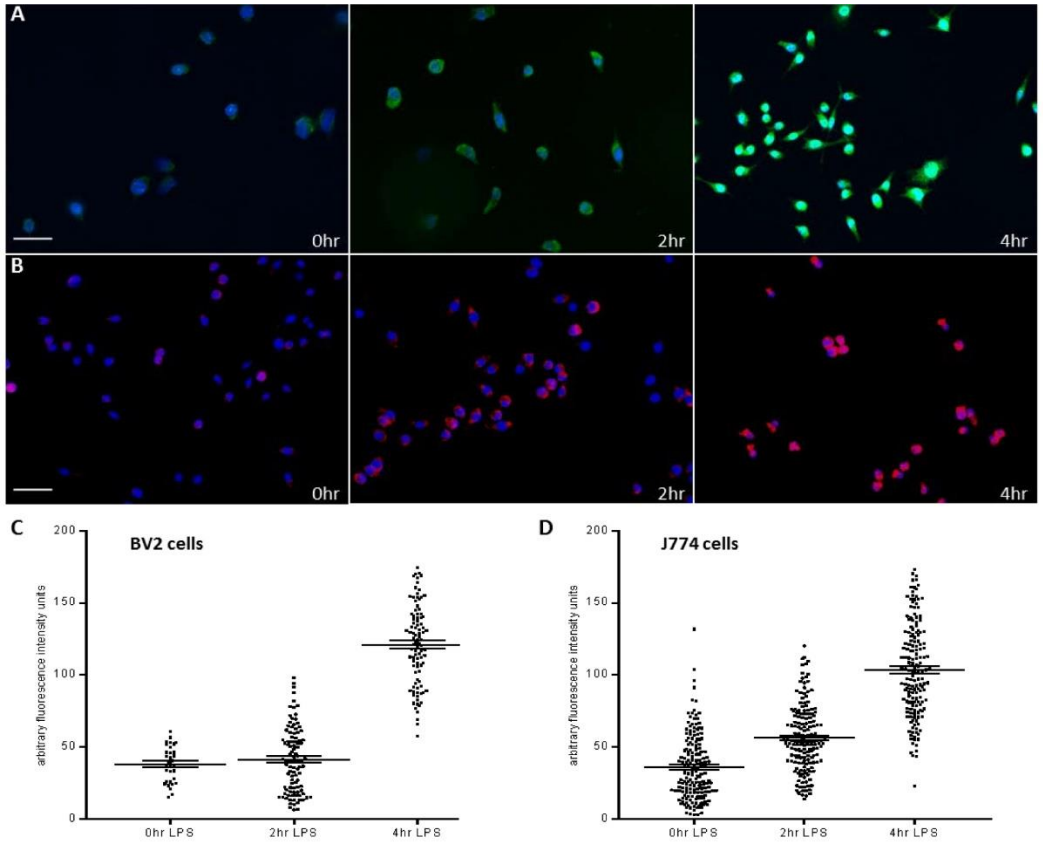
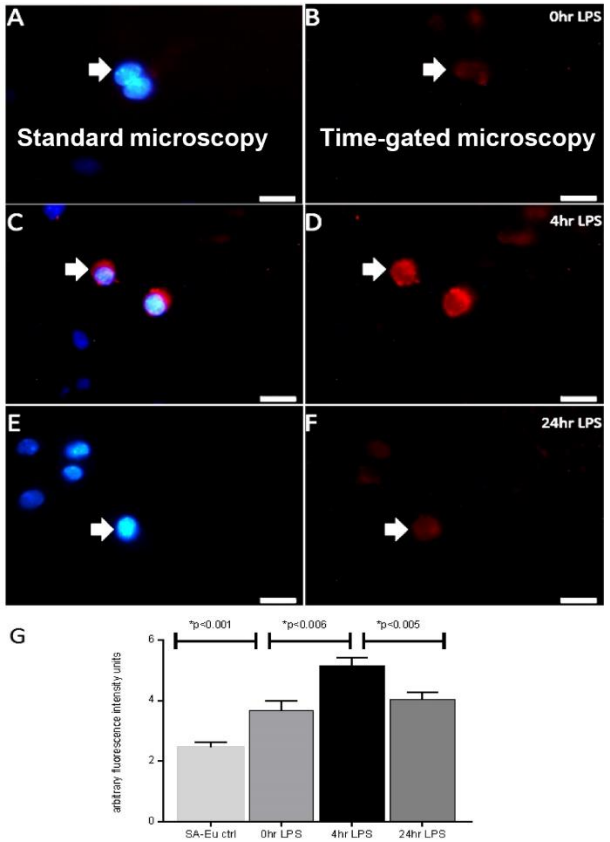
Measuring inflammation in microglia and macrophage cells





Lindsay Parker, Macquarie

FISH- fluorescent *in situ* hybridisation (mRNA detection TLR4)

LISH- luminescent lanthanide *in situ* hybridisation (mRNA detection TLR4)

Upconverting nanoparticles are excited in the IR

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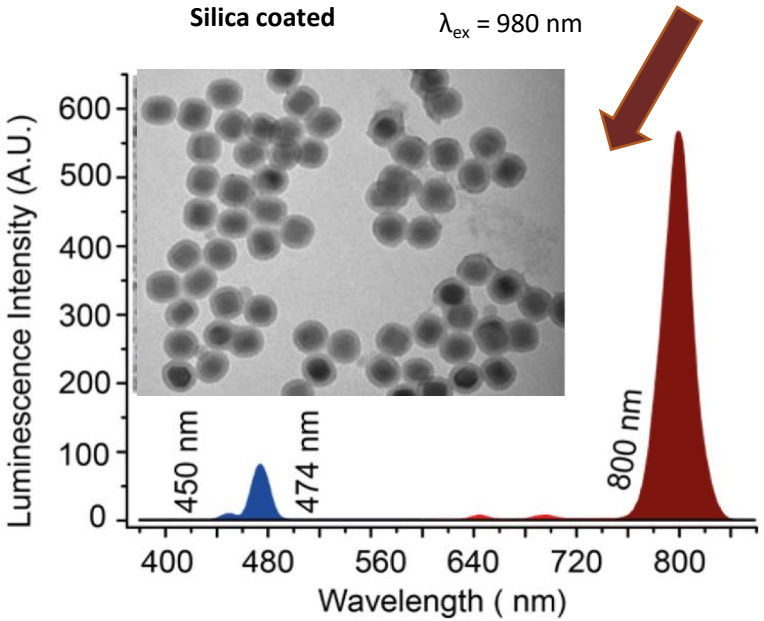
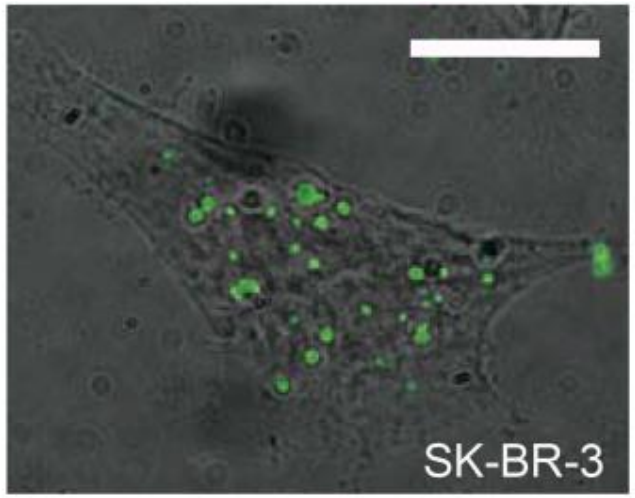
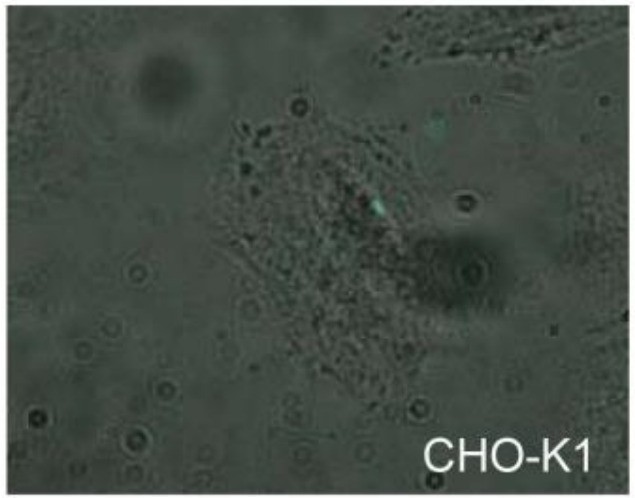
Background-free imaging with IR-excitable nanomaterials

$NaYF_4$,Yb,Tm
Size ~30 nm
Silica coated

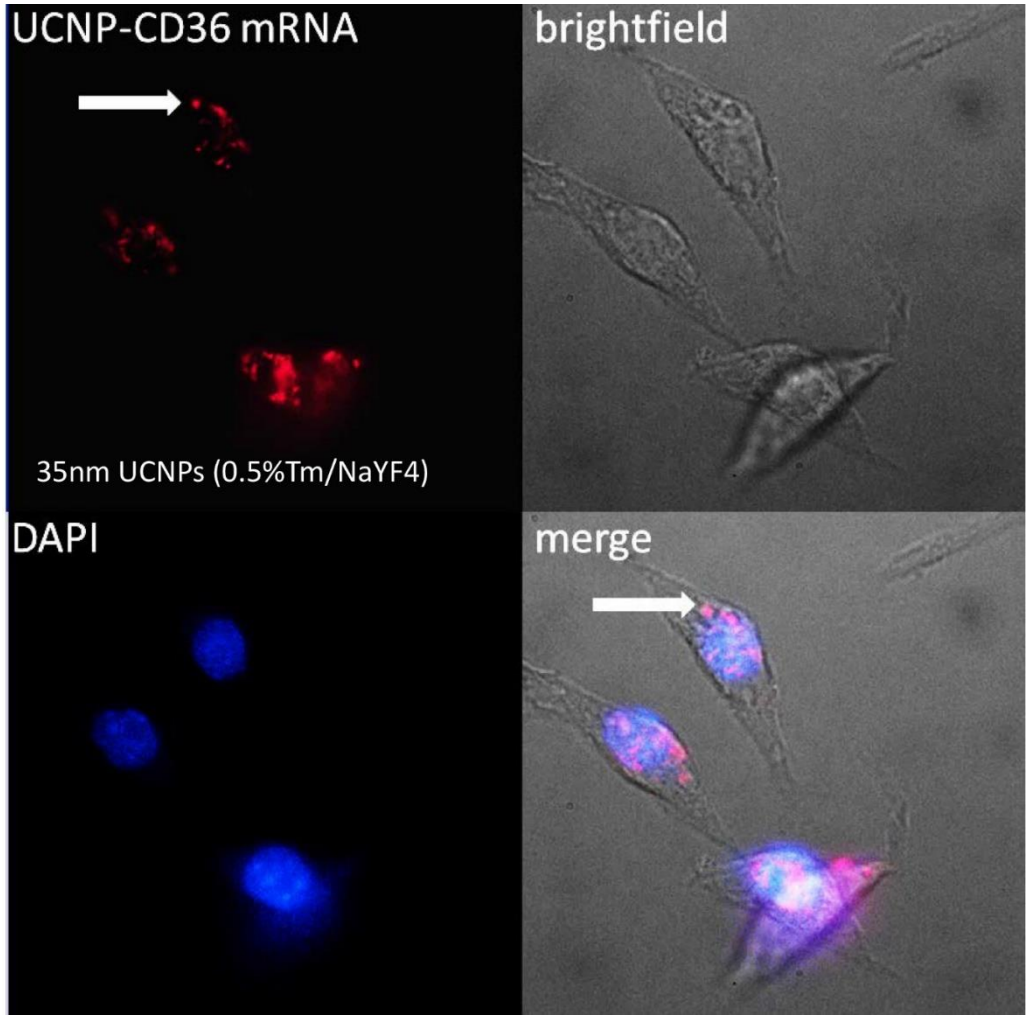
λ_{ex} = 980 nm







UCNPs + antibody against Her2neu receptor over-expressed on SK-BR-3 cells show higher labelling vs control CHO-K1 cells *(Grebenik , Nadort et al. JBO 2013)*

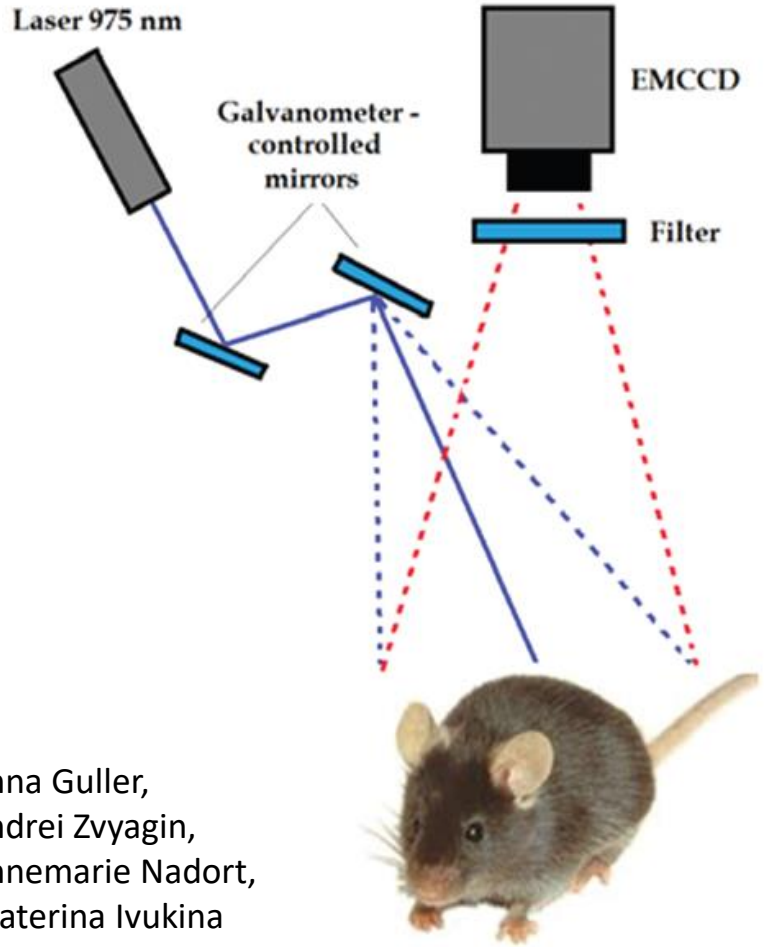


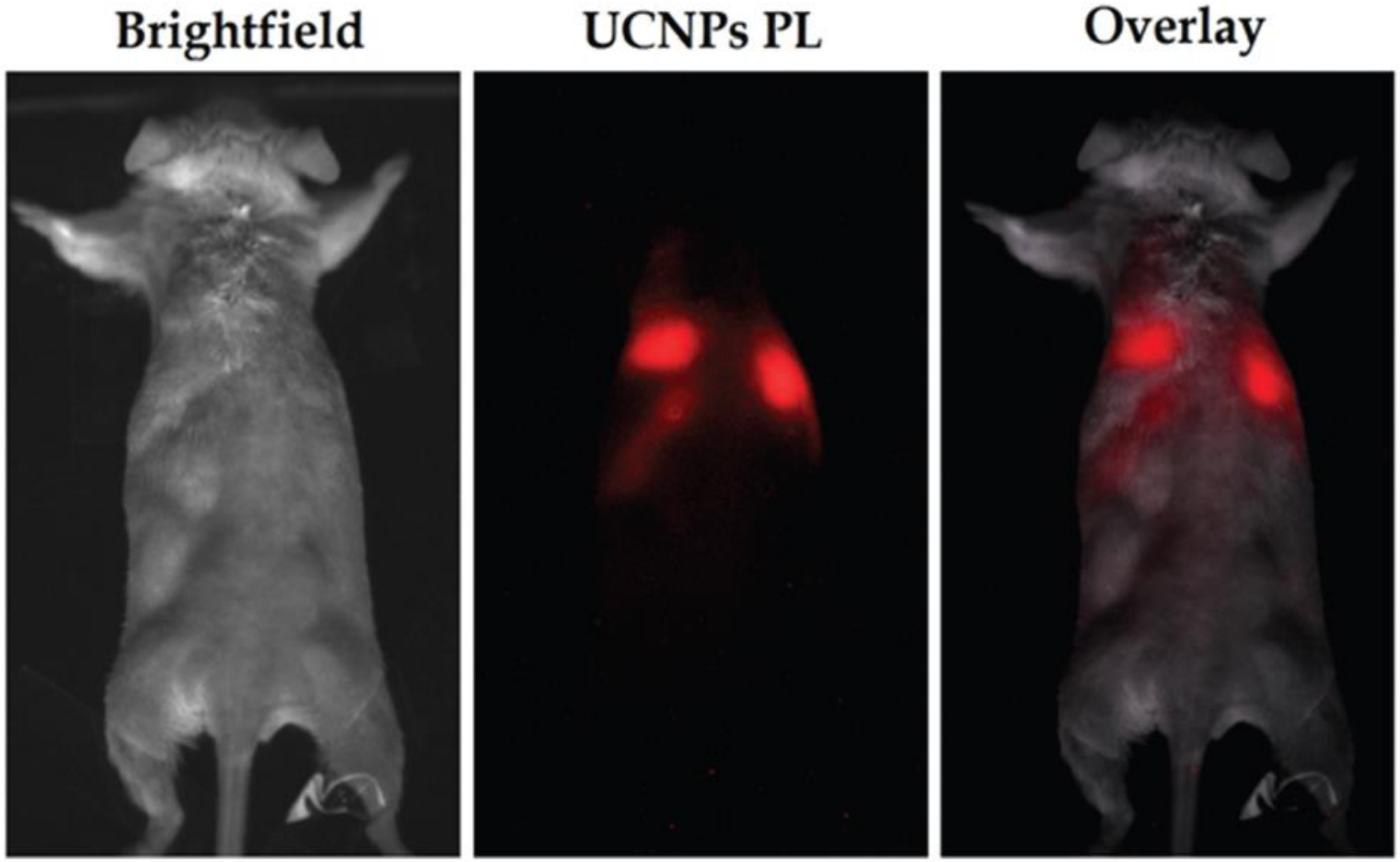
UCNPs labelling of mRNA – Lindsay Parker, unpublished

Tissue imaging with upconverting nanoparticles




Anna Guller,
Andrei Zvyagin,
Annemarie Nadort,
Ekaterina Ivukina



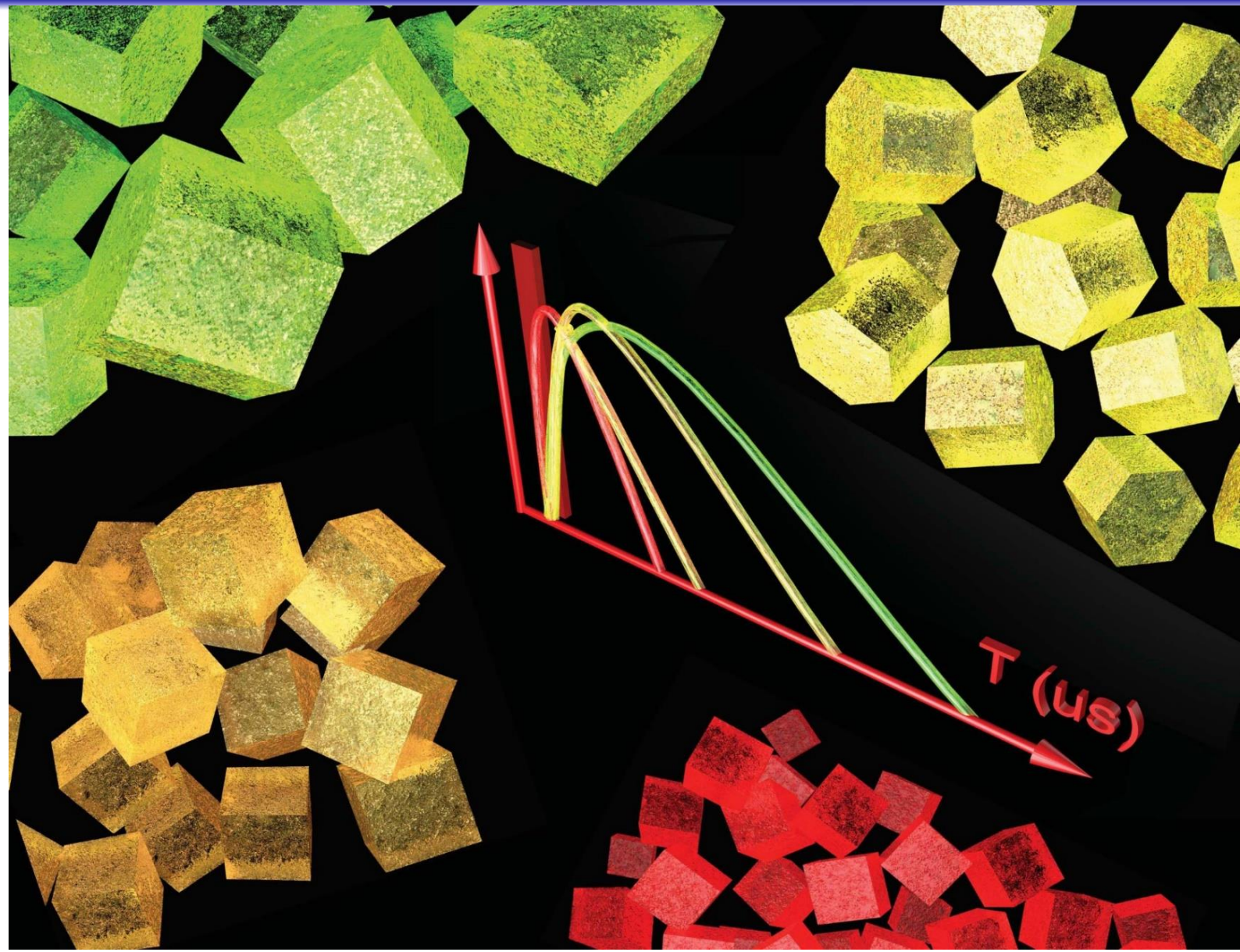


Live mouse, post 1-hour intravenous injection of PA -UNCPs (polyacrolein microbeads with UNCPs inside). Beads accumulate in cancer regions due to enhanced permeability and retention effect (EPR).

Tuneability of lifetimes in upconverting nanoparticles

Upconversion luminescence with tunable lifetime in NaYF4:Yb,Er nanocrystals: role of nanocrystal size, J. Zhao et al. Nanoscale, 5, 3, 944-952, (2013)

Amplified stimulated emission in upconversion nanoparticles for super-resolution nanoscopy, Y. Liu et al. Nature 543, 229–233 (2017)



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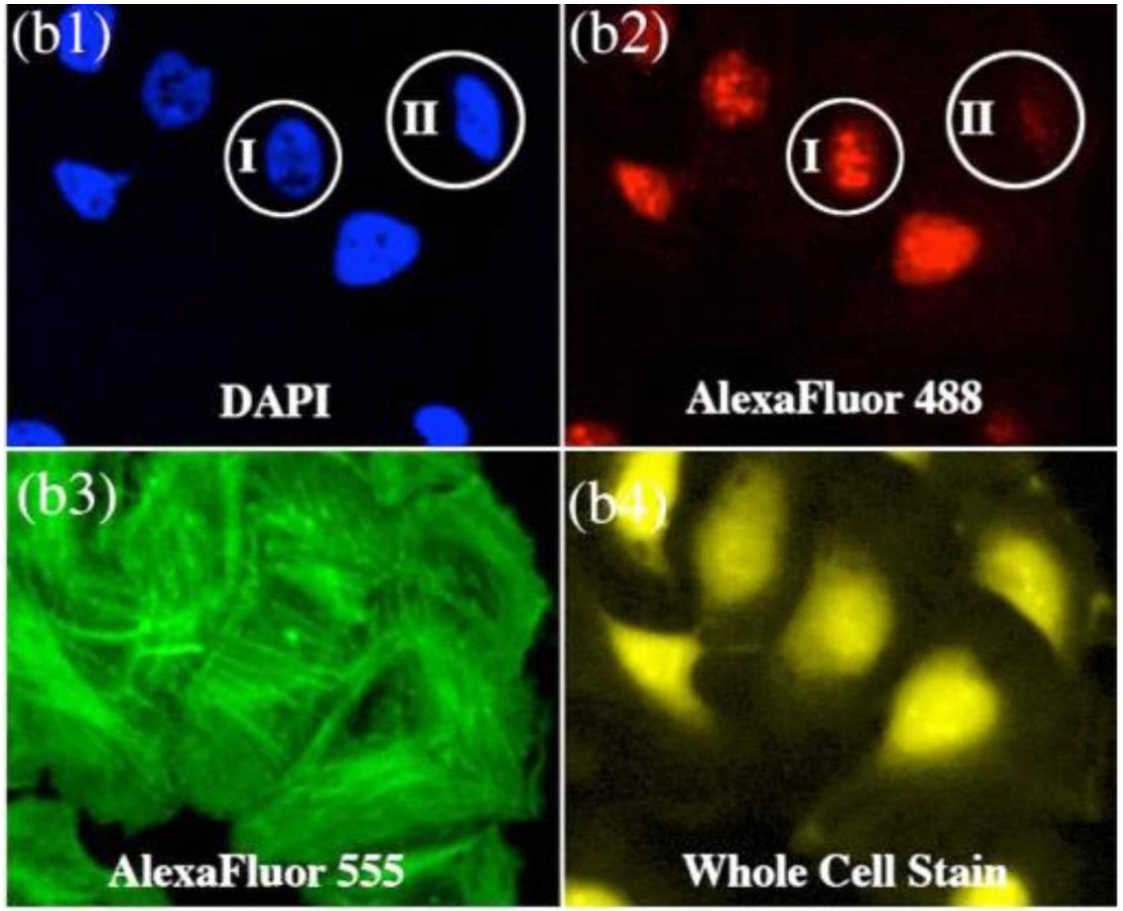
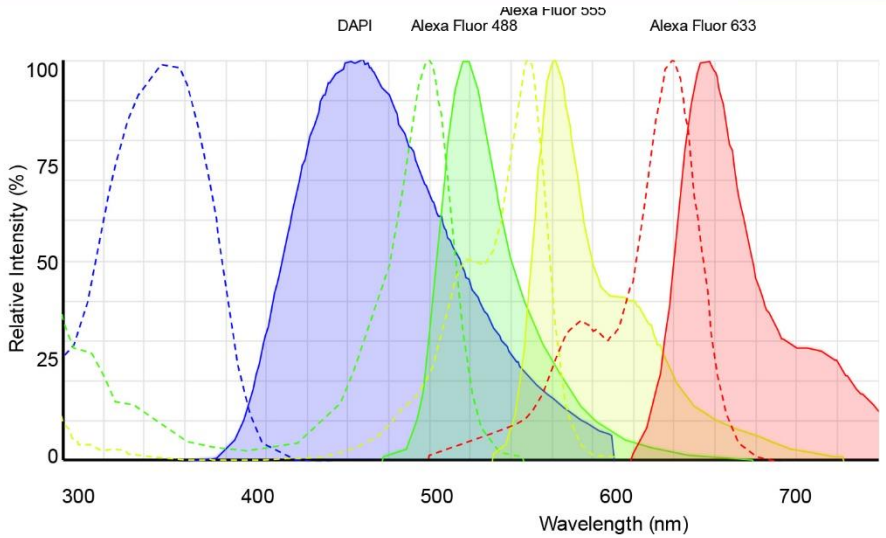
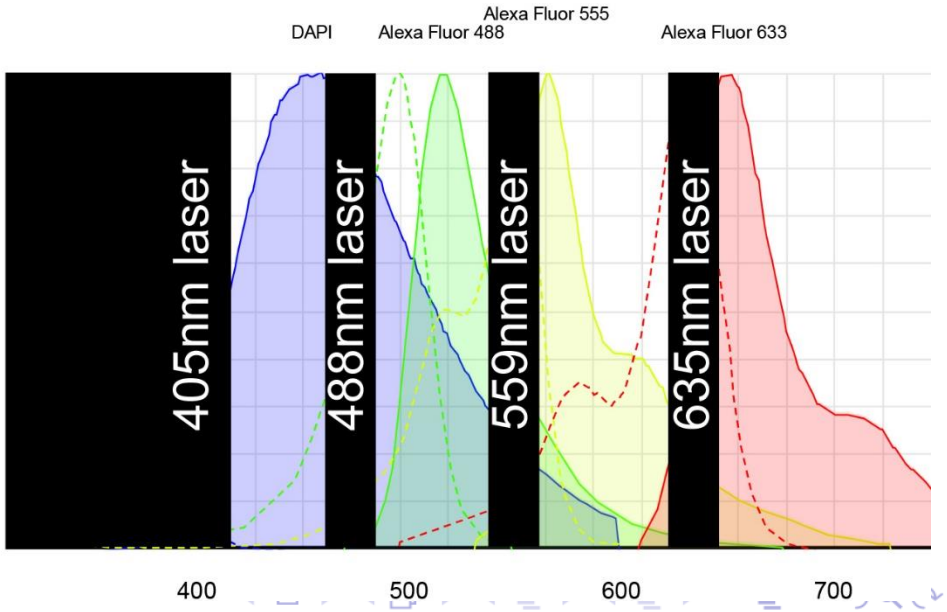
THE UNIVERSITY of ADELAIDE

Limitations of spectral multiplexing



Orth et al., Optica 2 (7) 2015]





Multiplexing: distinguishable labeling for multiple types of molecules

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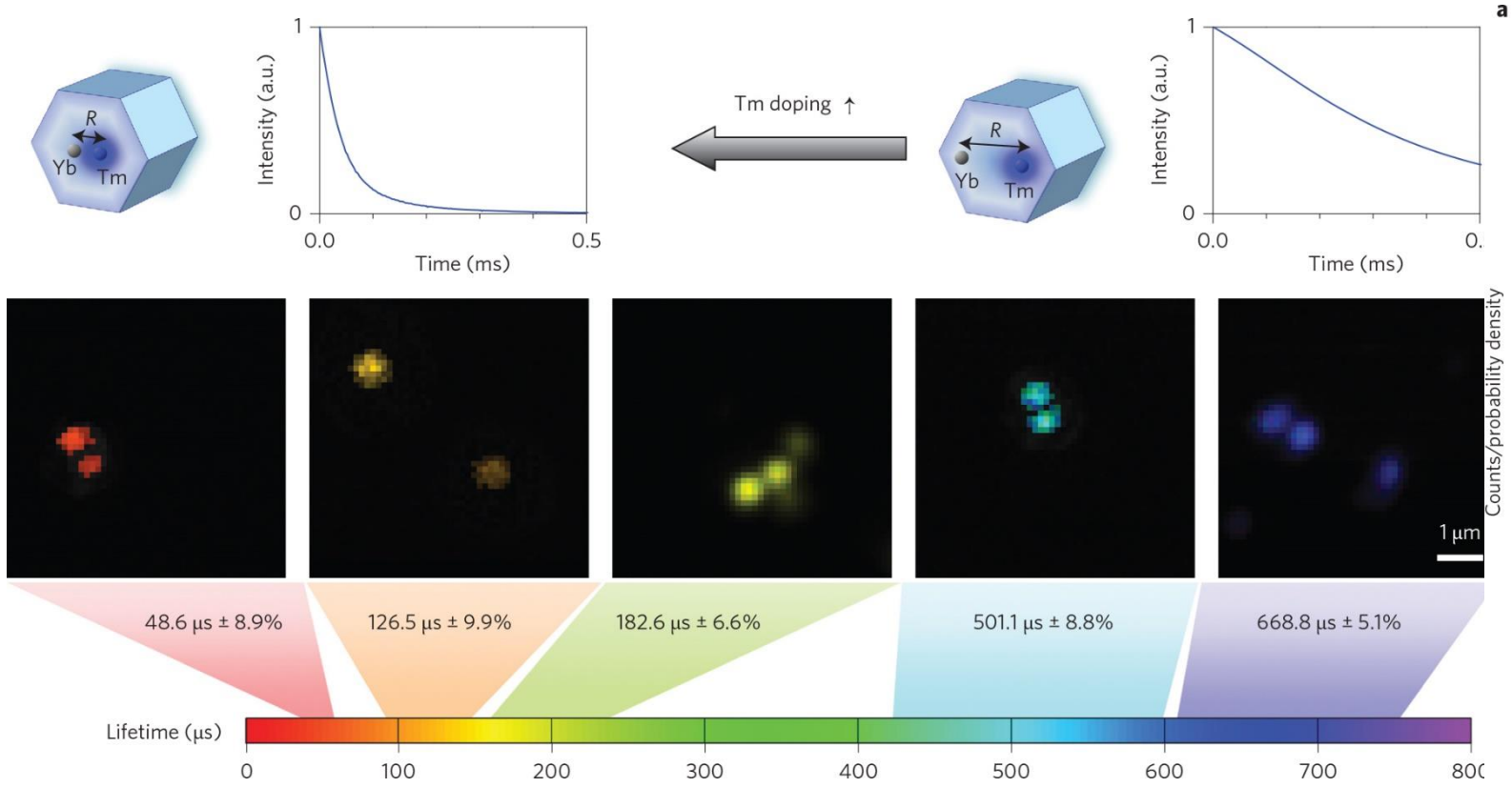
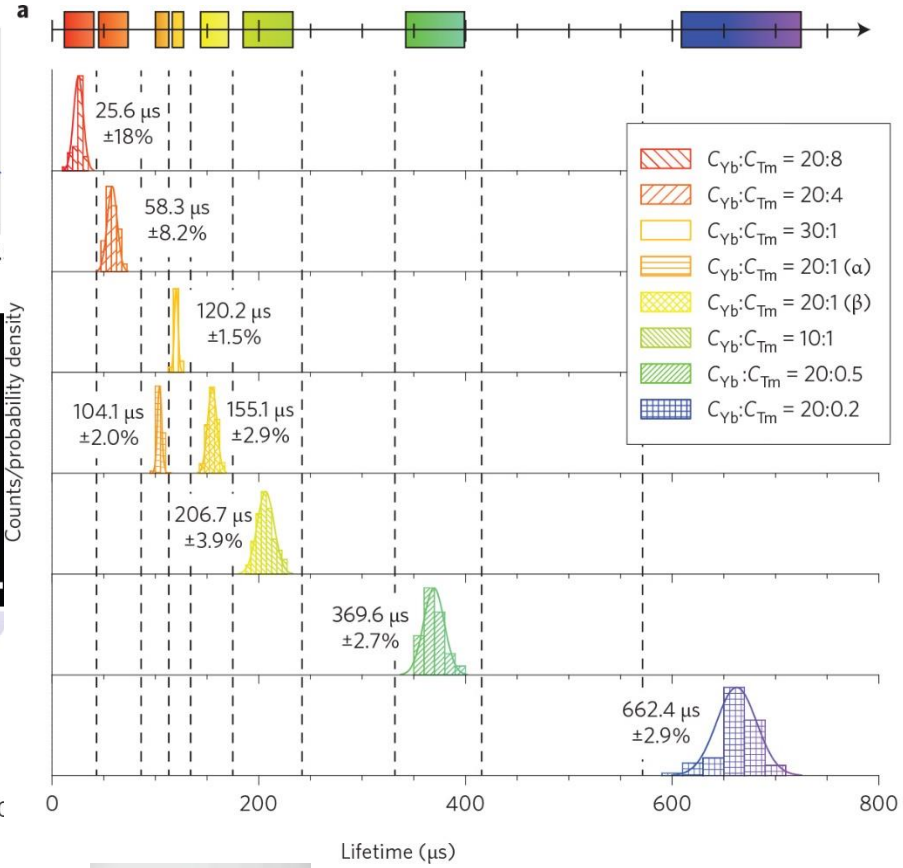
Lifetime control in UCNPs with Yb-Tm distance





Lifetime variations are independent of spectral properties

Yiqing Lu,
Macquarie

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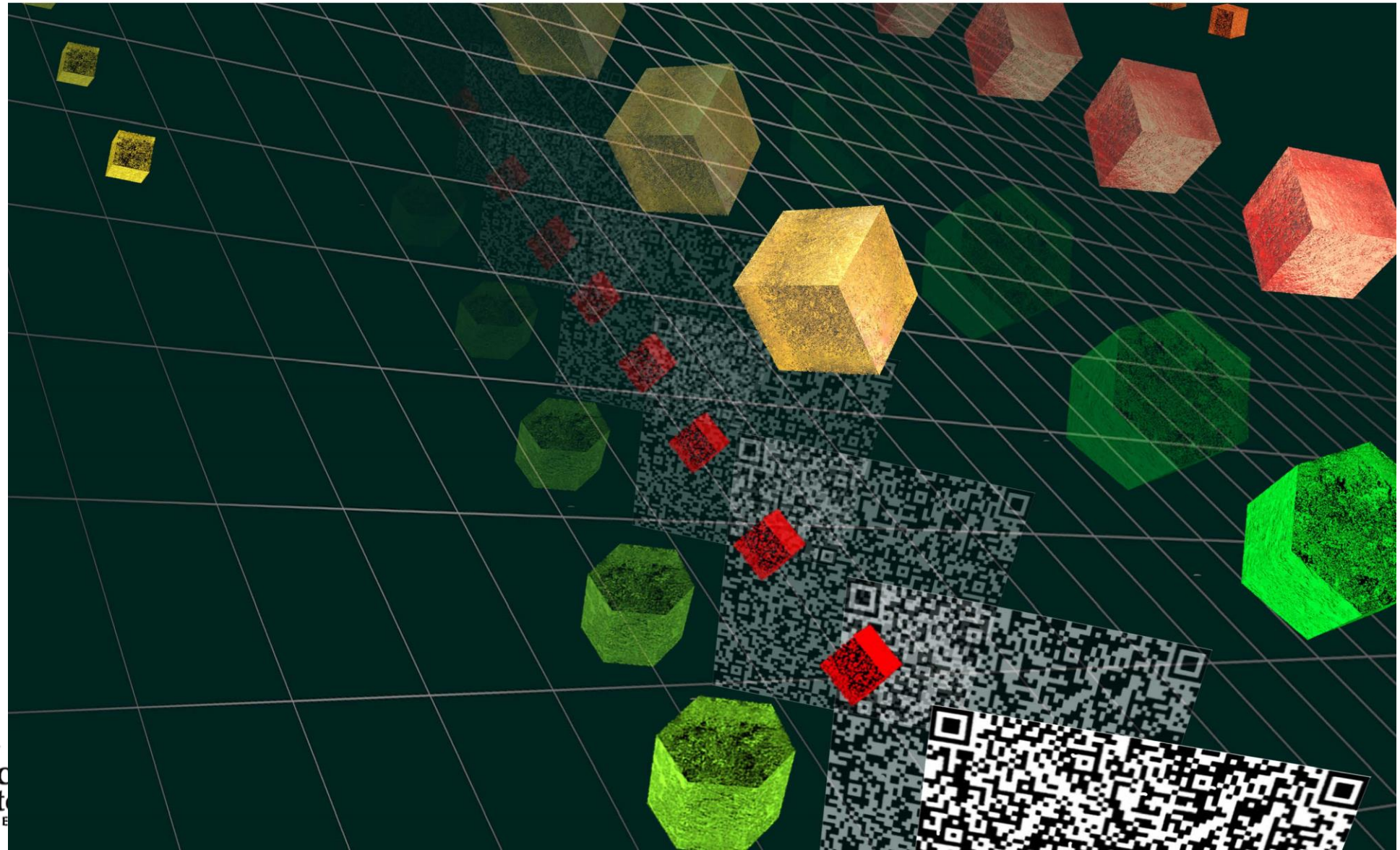
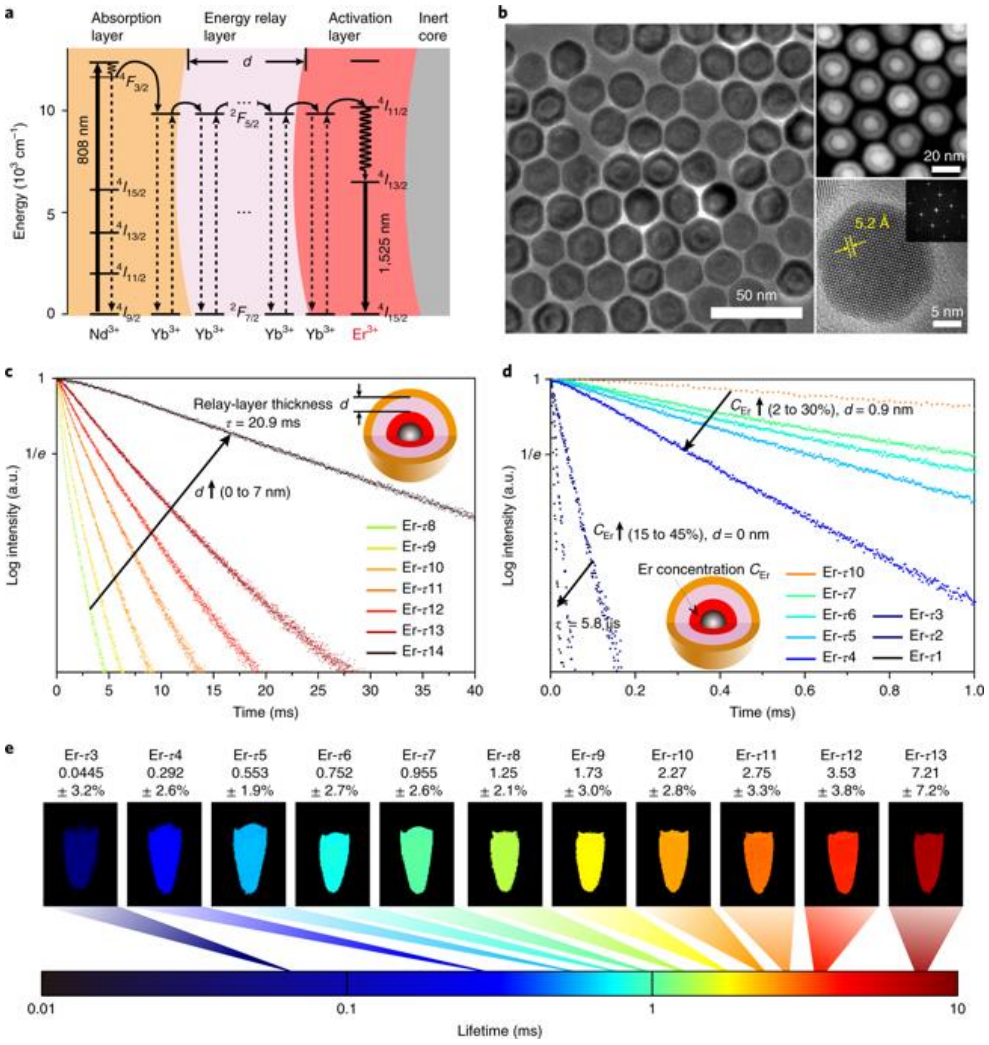
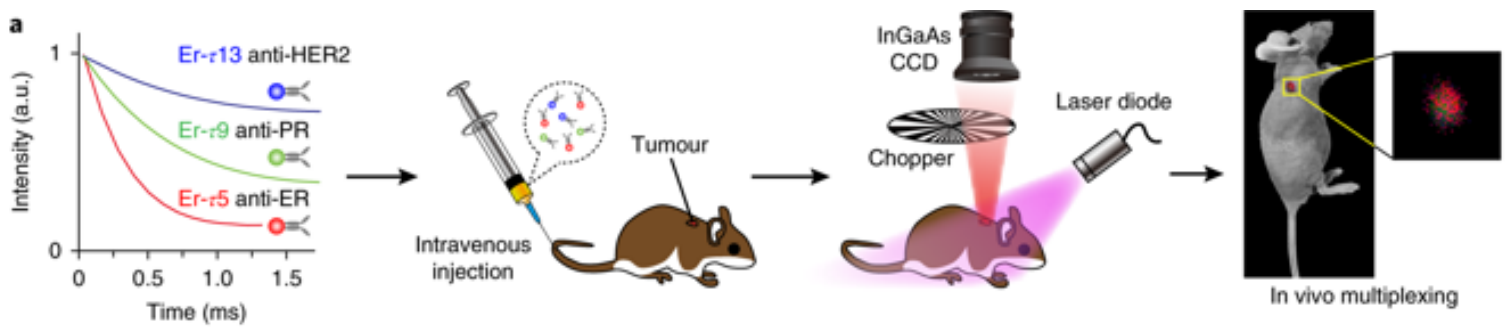
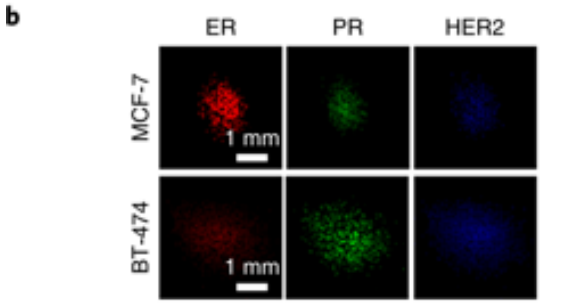
Time - new dimension for optical barcoding

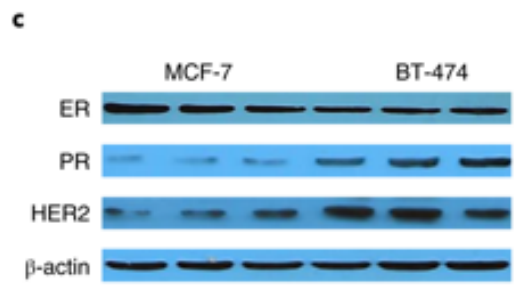


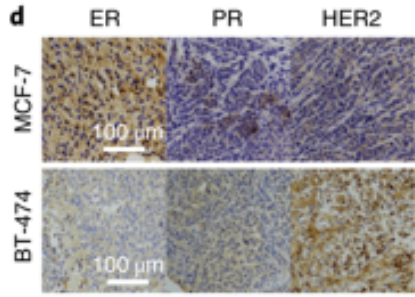
Time-multiplexed in vivo imaging

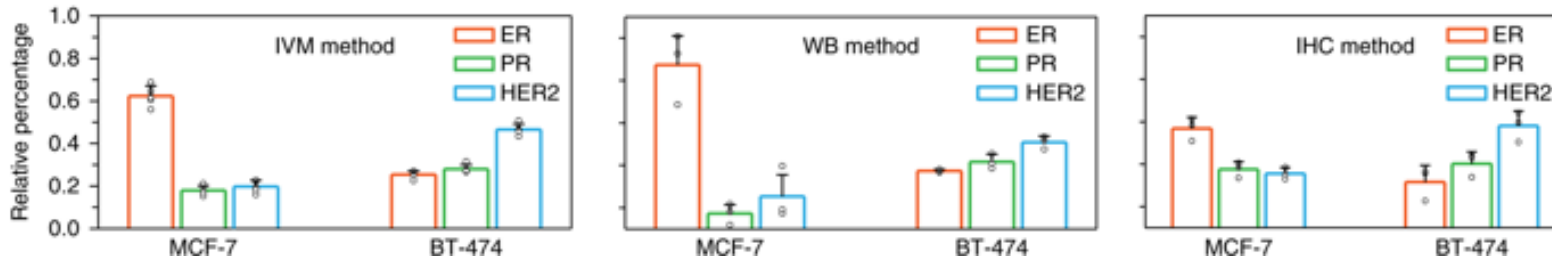






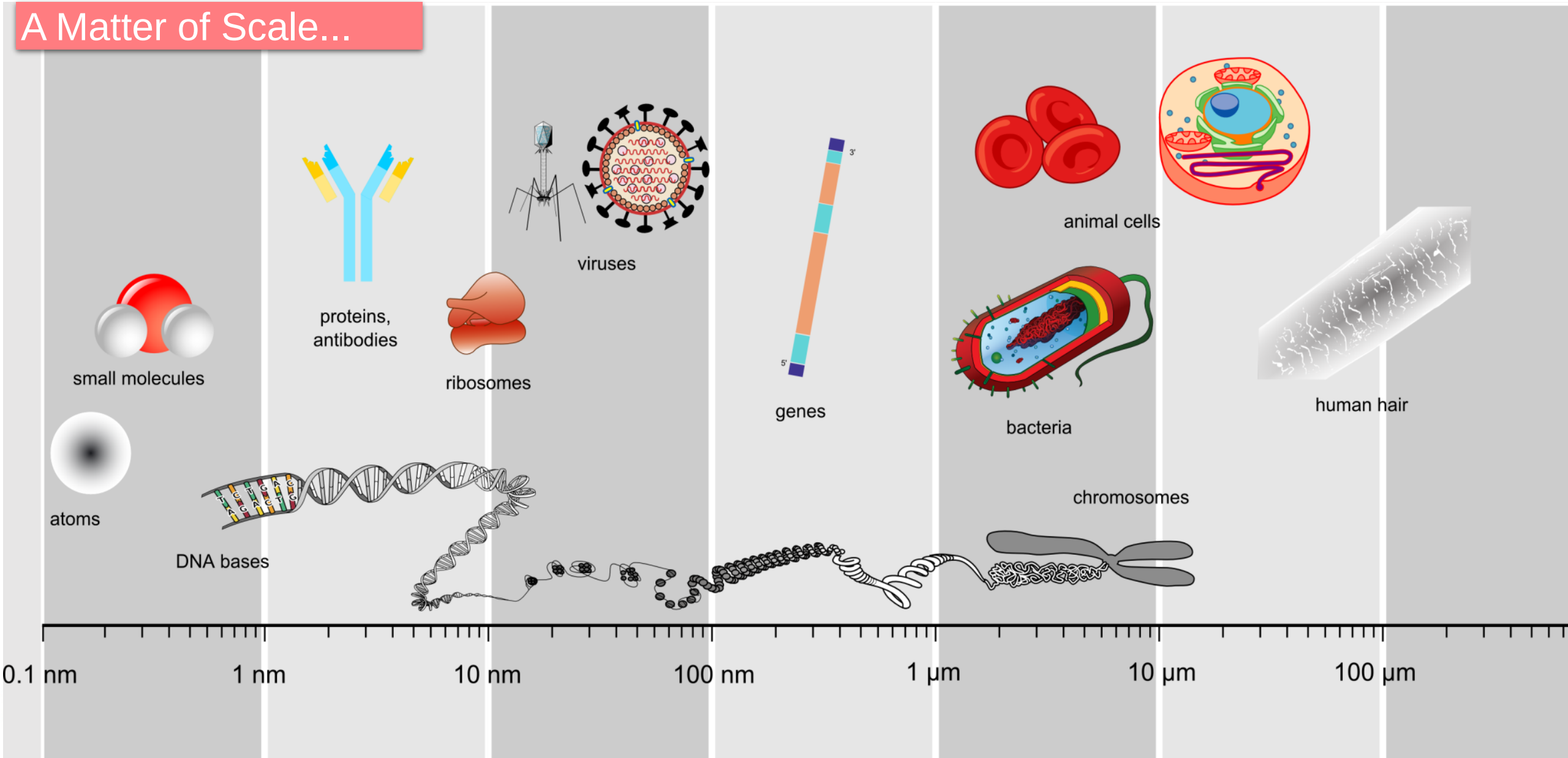




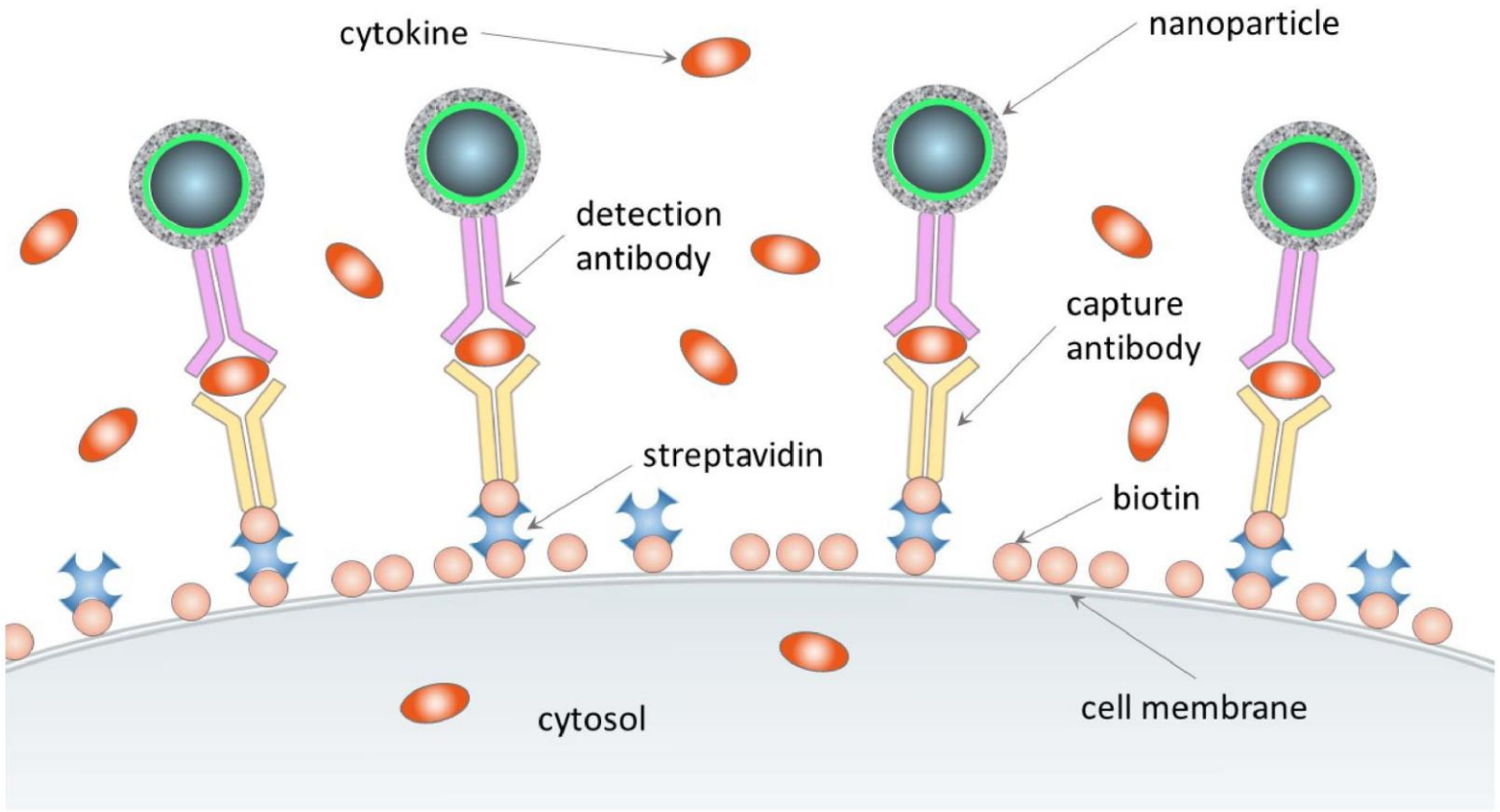


Nature Nanotechnology (2018)
doi: 10.1038/s41565-018-0221-0

A Matter of Scale...



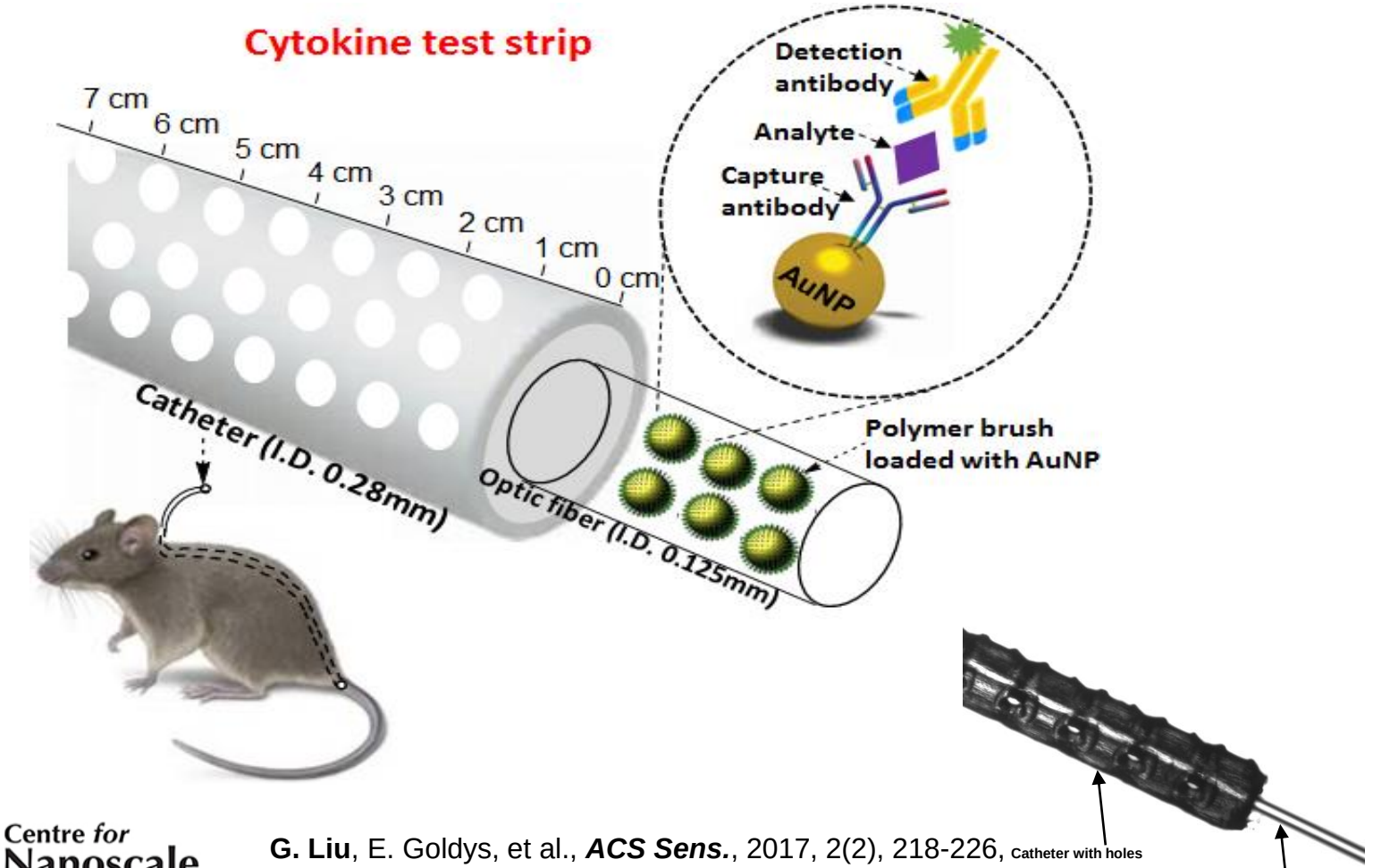
How to detect molecules secreted by cells

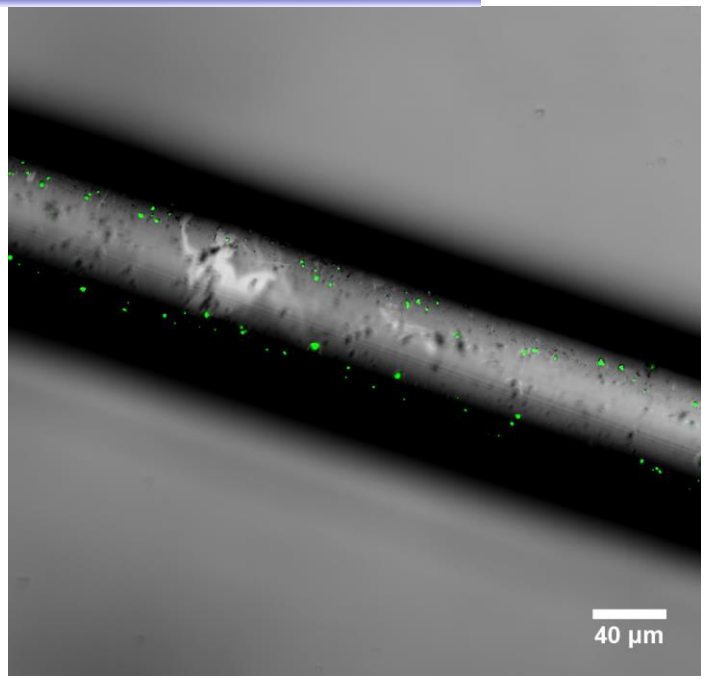


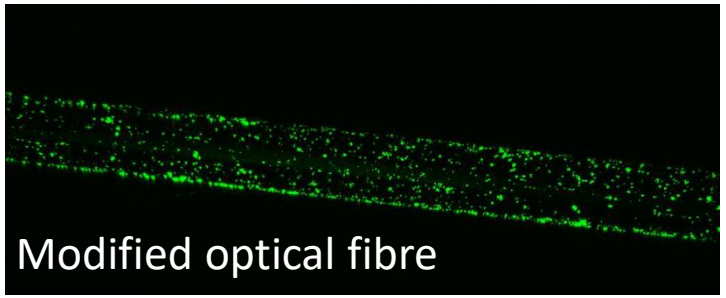
G.Z. Liu, E. Goldys, A. Anwer, Australia Provisional Patent (2015904826), R. Manz, et al, Proc. Natl. Acad. Sci.1995, 92, 1921-1925; P. Holmes, M. Al-Rubeai, J. Immunolog. Methods, 1999, 230, 141-147

Cytokine detection devices

Spatial ELISA sensor



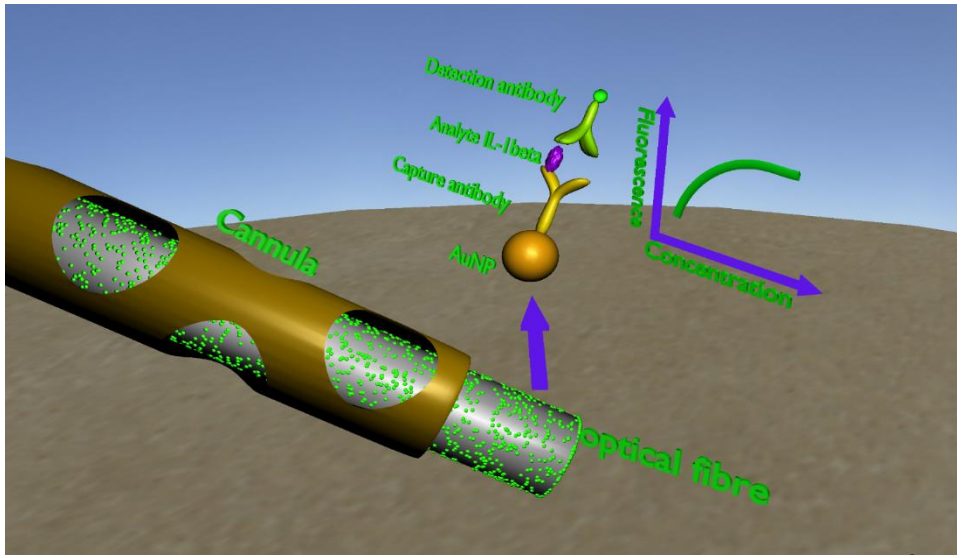


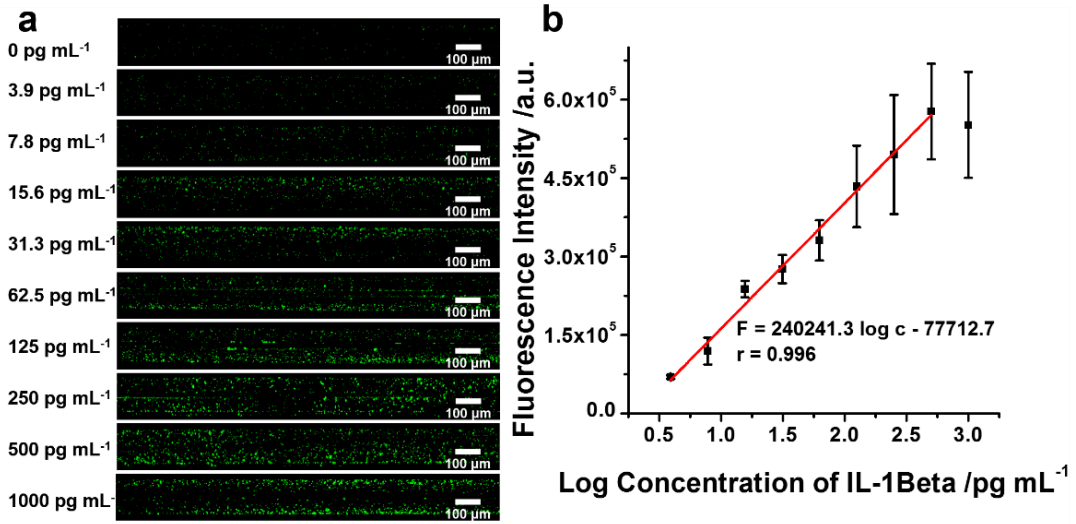


Zoom 1x (FOV 1500 x 1500 micrometer), 10 stacks

G. Liu, E. Goldys, et al., ***ACS Sens.***, 2017, 2(2), 218-226,

How to detect cytokines in specific locations



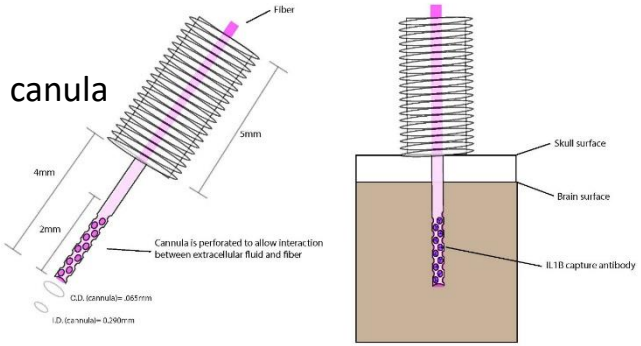


"sandwich immunoassay",

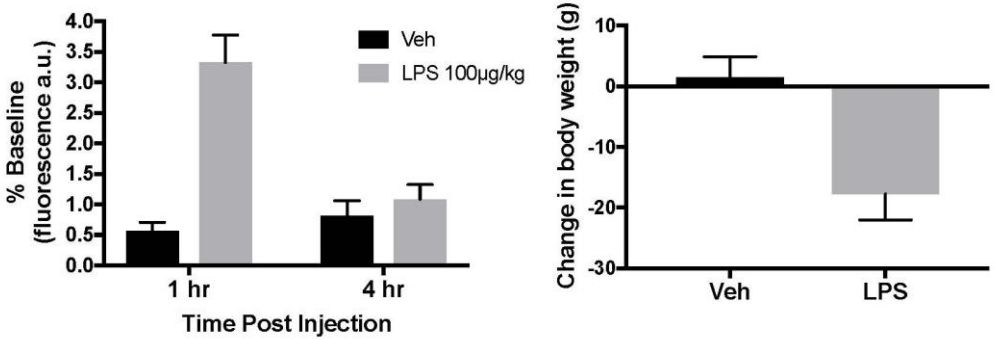
K. Zhang, Macquarie U

Guozhen Liu

Mike Baratta, U Colorado



Living brain (hippocampus)



Brain Behav Immun. 2018 Jul;71:18-22.
doi: 10.1016/j.bbi.2018.04.011

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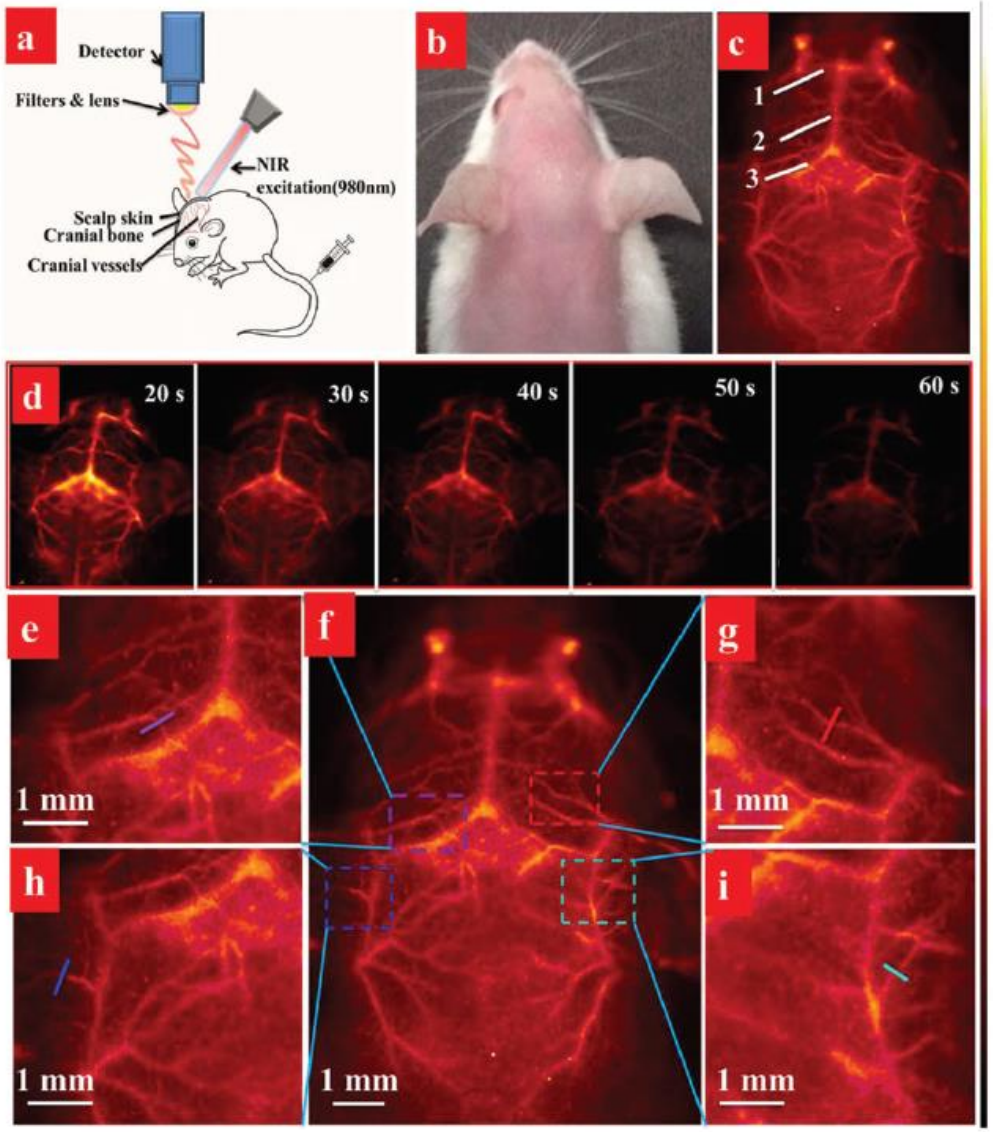
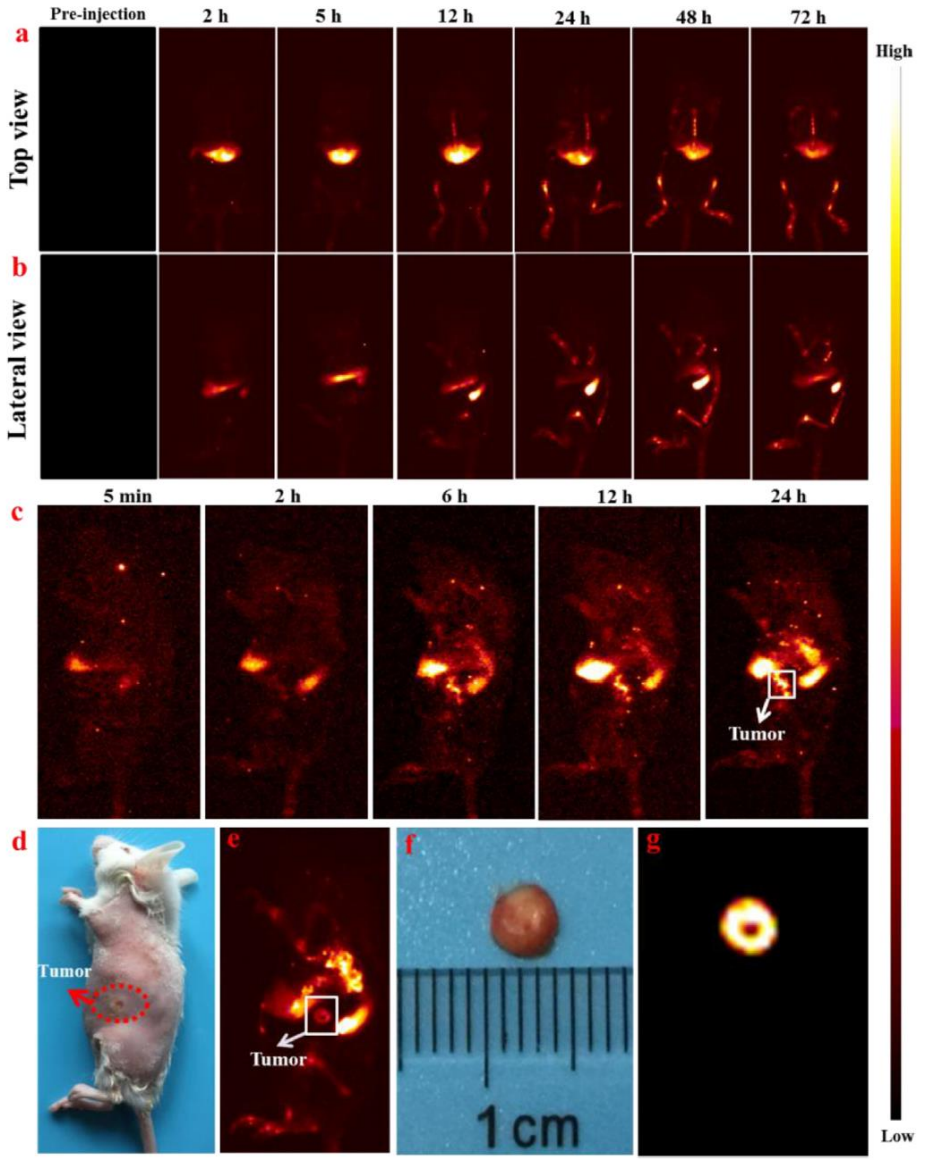
Australian Government Australian Research Council · The University of Adelaide · Macquarie University · RMIT University



NIR II

1550 nm

1700 nm



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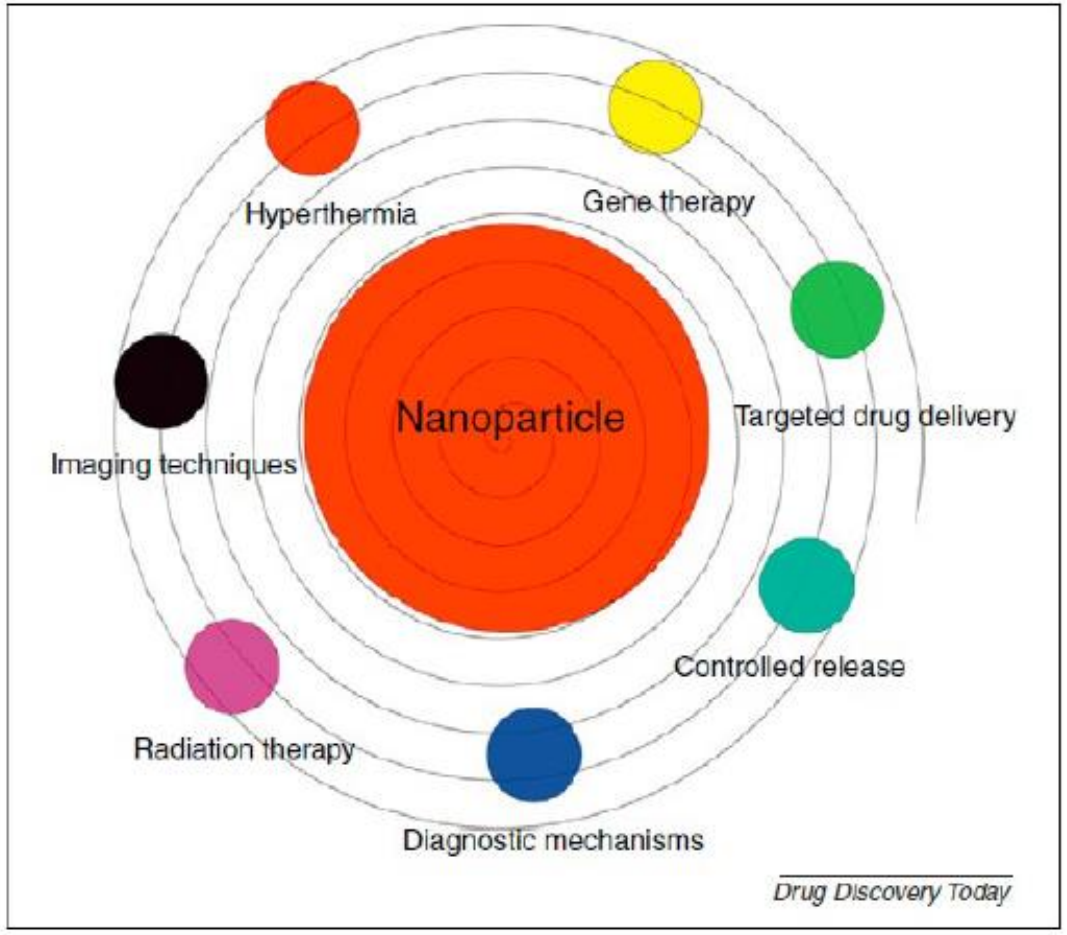
Deng ZM et al **NANOSCALE (2018),** 10,19, 9393-9400

Xue, ZL et al **BIOMATERIALS (2018) ,**171,153-163

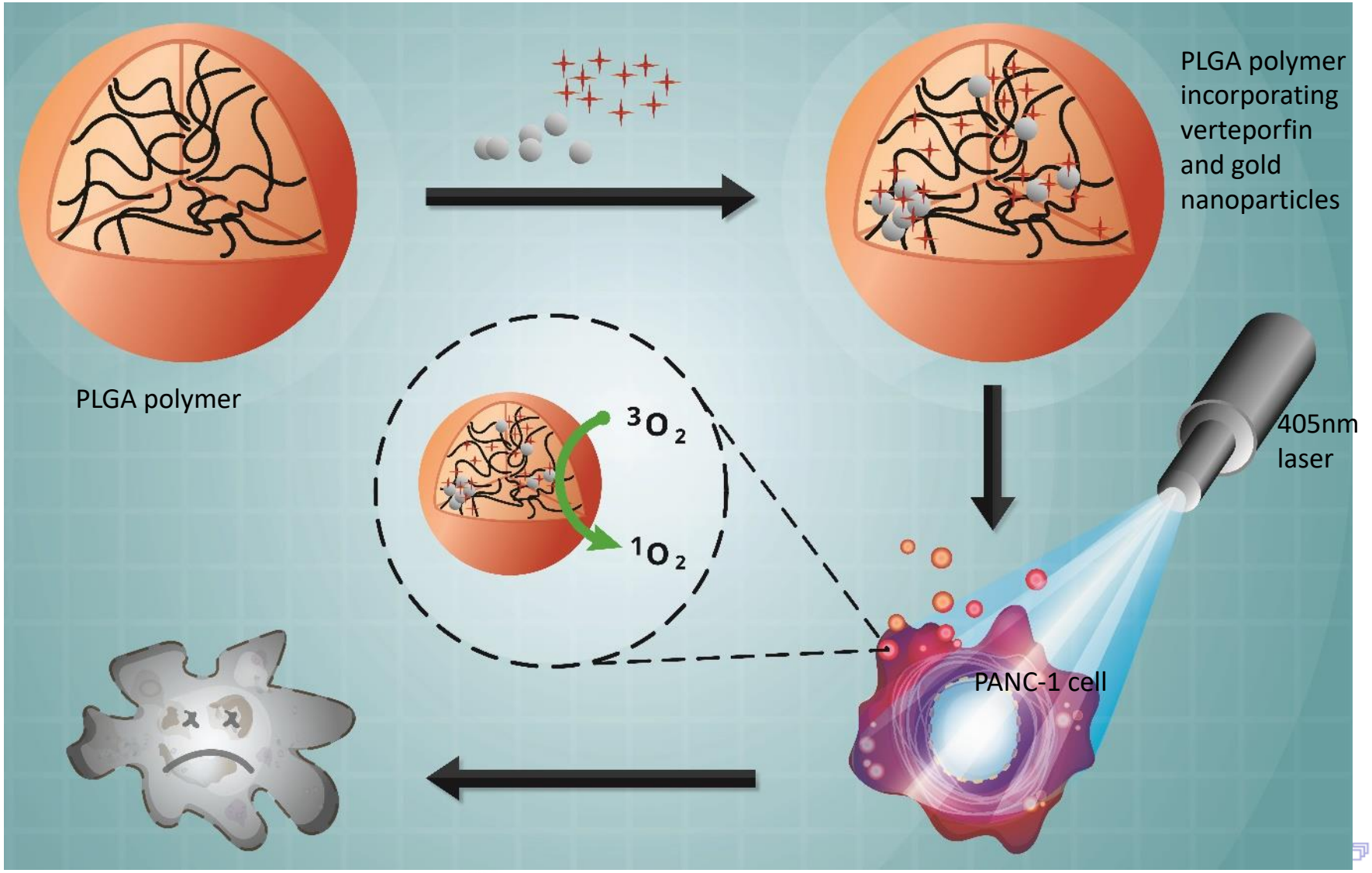
Multifunctional nanoparticles

Drawing on theranostics (= therapy + diagnostics)



N. Ahmed et al. Drug Discovery Today B, 17 - 18 B, 928-934, (2012)

Photodynamic therapy with light and PLGA polymers incorporating verterporfin and gold nanoparticles

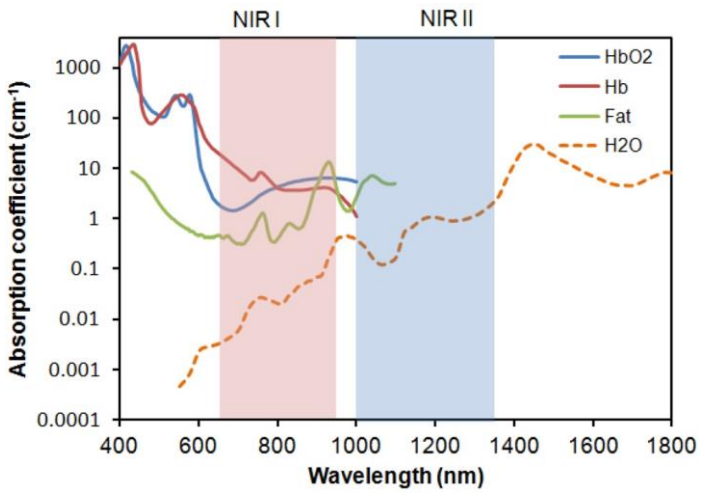


Wei Deng

Zofia Kautzka

RSC Advances 6, 112393-112402, (2016).

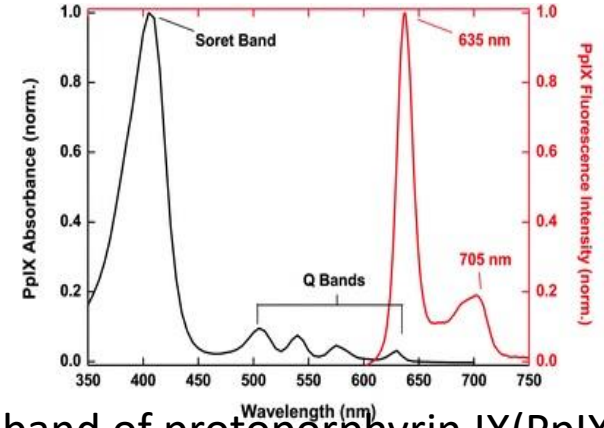
X-ray activated PDT with Nanoparticle-Photosensitizer combinations



Tissue transparency window[1]

Why use X-rays in Photodynamic Therapy ?

Limited penetration depth of UV and visible light



Absorption band of protoporphyrin IX(PpIX)[2]

Sandhya Clement

Why use Nanoparticles in X-ray Photodynamic Therapy ?

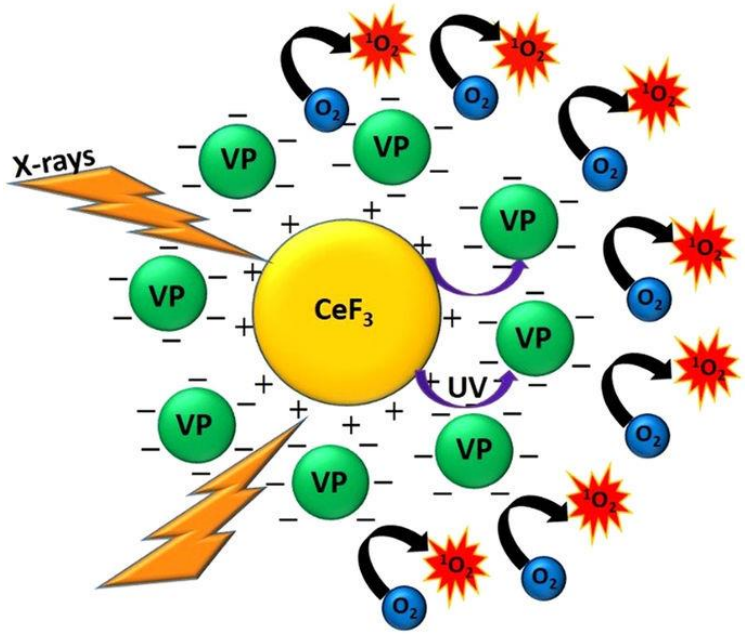
Disadvantages of photosensitiser drugs: poor selectivity, hydrophobic nature, aggregation property in physiological environment and limited therapeutic effect.

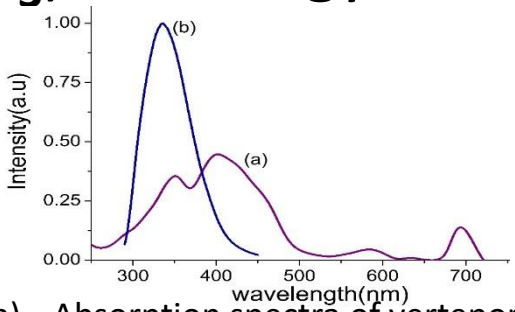
- Scintillating Nanoparticles (**CeF_3**) as energy transducers
- Metal nanoparticles (**Au**) as singlet oxygen ($^1O_2$) amplifiers
- Polymer nanoparticles (**PLGA**) as Drug carrier for X-ray PDT

1. C.H. Quek and K. W. Leong. *Near-infrared fluorescent nanoprobes for in vivo optical imaging. Nanomaterials* ***2(2), 92 (2012)***
2. R. M. Valentine, S. H. Ibbotson, K. Wood, C. T. A. Brown, and H. Moseley. *Modelling fluorescence in clinical photodynamic therapy. Photochemical&Photobiological* Sciences **12(1), 203 (2013).**

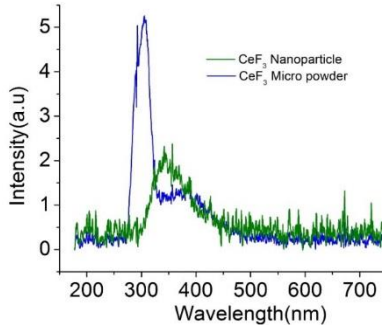
Scintillating Nanoparticles (CeF_3) as energy transducers

PDT Mechanism in CeF3 nanoparticles



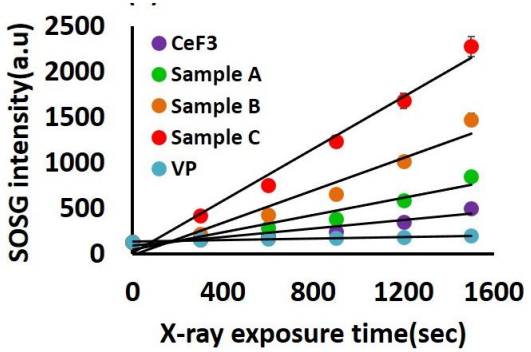


(a) Absorption spectra of verteporfin
(b) Emission of CeF_3 nanoparticles



X-ray luminescence

Singlet oxygen generation

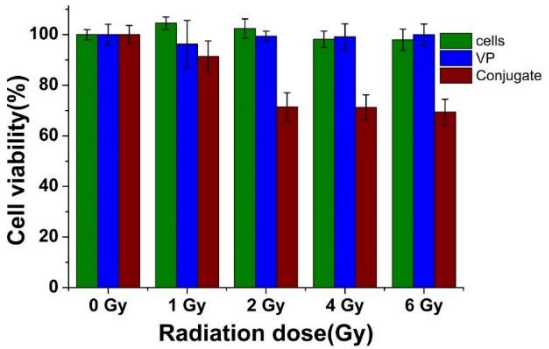


	CeF3	Conjugate sample A	Conjugate sample B	Conjugate sample C
$^1O_2$ molecules per absorbed 8 keV X-ray	1000 ± 170	2100 ± 280	3900 ± 470	6300 ± 380
X-ray singlet oxygen quantum yield (η)	0.13±.02	0.26 ± 0.04	0.49 ± 0.06	0.79 ± 0.05

Dose partition

Energy	30 keV	6 MeV
CeF_3	89%	28%
Tissue	11%	72%

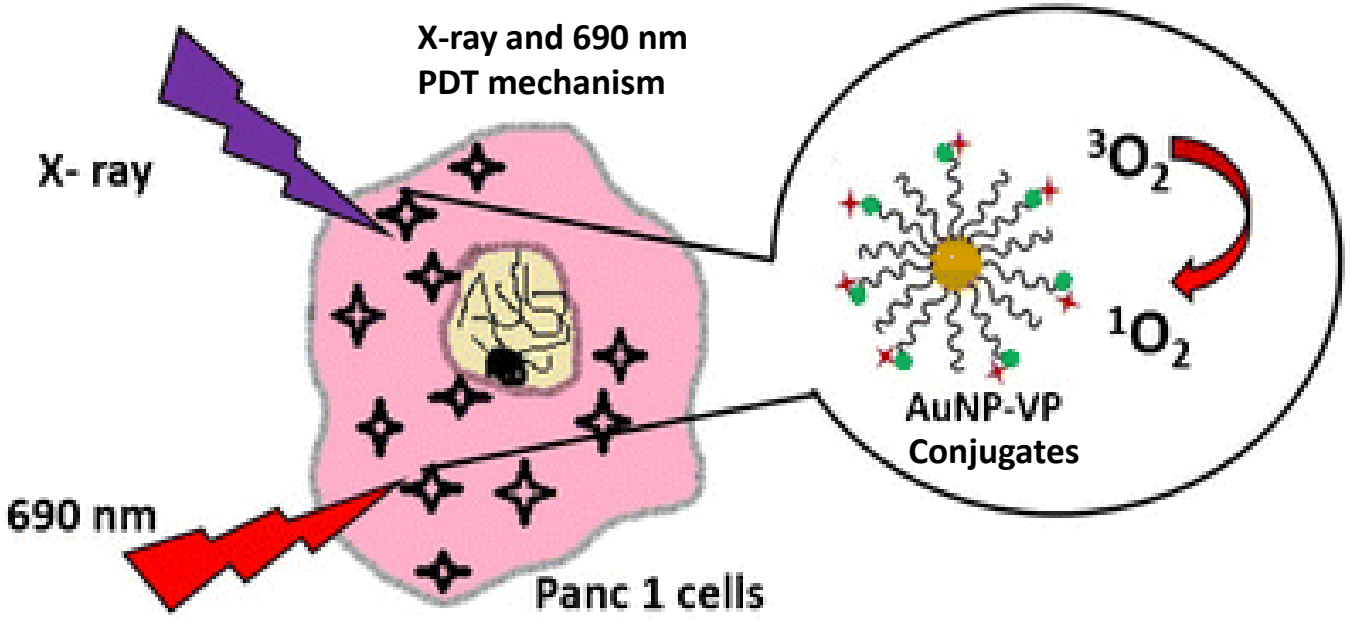
Based on experimental and theoretical calculations, the number of singlet oxygen generated per cell for 6MeV X-ray energy is $(2\pm0.7)\times10^8$. This is comparable with Neidre dose $(5)\times10^7$



Cell level PDT Demonstration:
Cancer cell: Panc 1
Radiation source: Elekta XiO planning system (Elekta AB, Sweden) (6 MV photons)
Cell viability: MTS assay

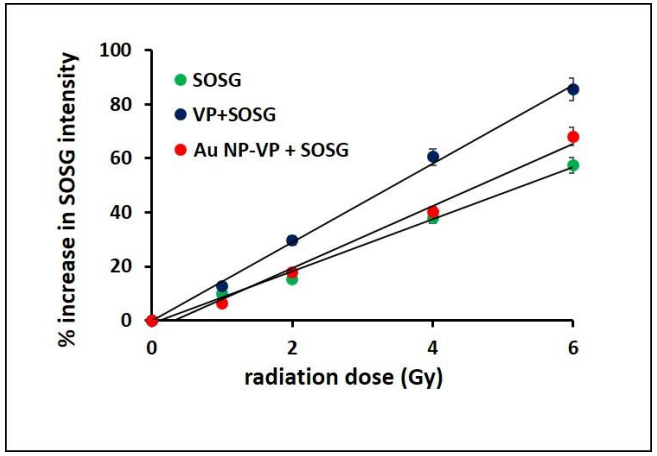
- *Clement, S.; Deng, W.; Drozdowicz-Tomsia, K.; Liu, D.; Zachreson, C.; Goldys, E. M. Bright, water-soluble CeF3 photo-, cathodo-, and X-ray luminescent nanoparticles. J Nanopart Res 2015, 17, 1-9*
- *Clement, S. et al. X-ray induced singlet oxygen generation by nanoparticle-photosensitizer conjugates for photodynamic therapy: determination of singlet oxygen quantum yield. Sci. Rep. 6, 19954; doi: 10.1038/srep19954 (2016).*

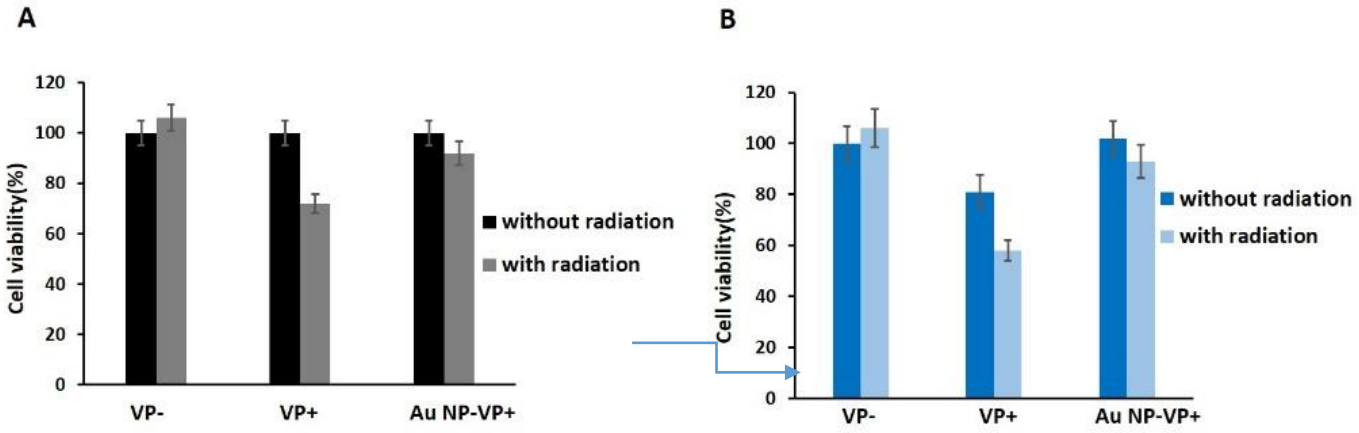
Metal nanoparticles (**Gold-Au**) as singlet oxygen ($^1O_2$) amplifiers



Clement, S., Chen, W., Anwer, A. G., & Goldys, E. M. (2017). Verteprofin conjugated to gold nanoparticles for fluorescent cellular bioimaging and X-ray mediated photodynamic therapy. Microchimica Acta, 1-7.

Singlet oxygen generation

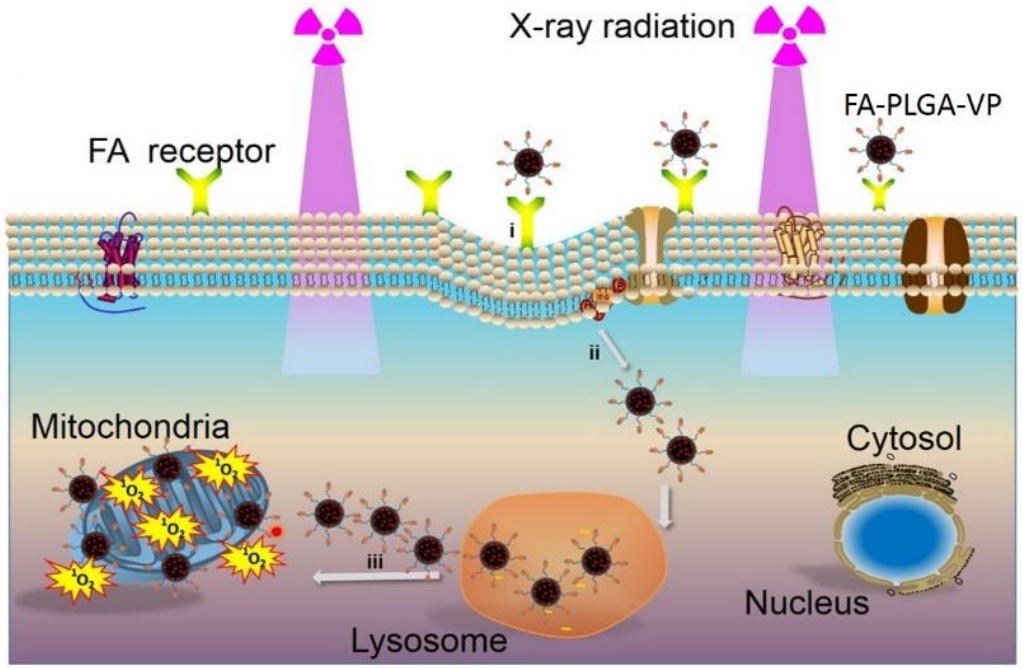


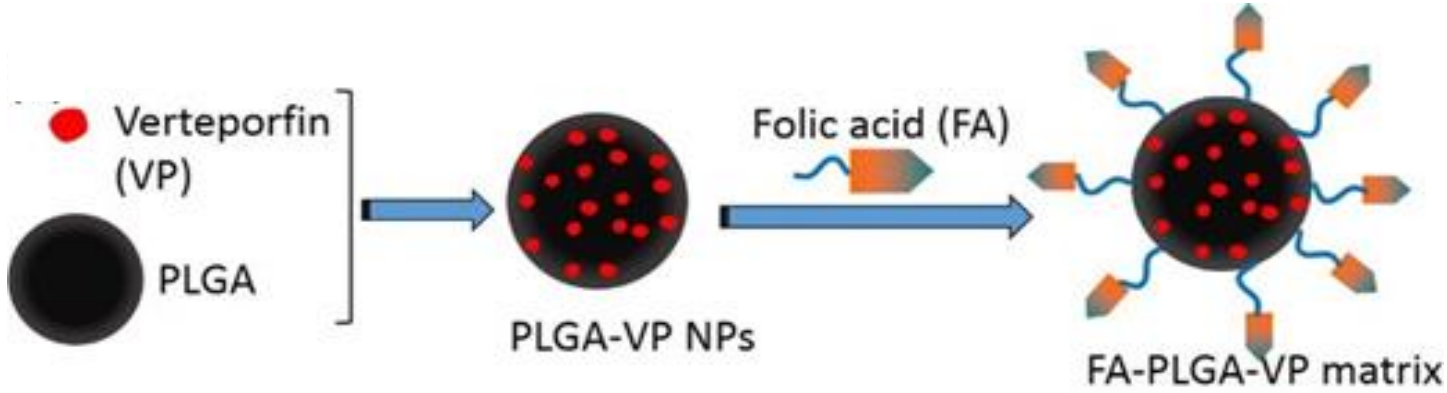


PDT effect in Panc 1 cancer cell line

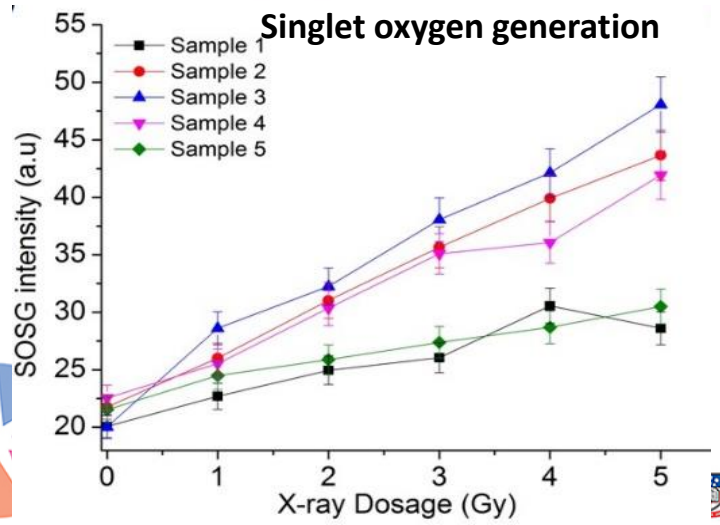
We show a proof-of-principle that PDT can be carried out with therapeutic X-rays both with molecular photosensitizer VP and with AuNP-VP conjugates. The conjugates synthesized in this work were less effective than the VP alone but they were also less cytotoxic in the absence of sensitizing radiation.

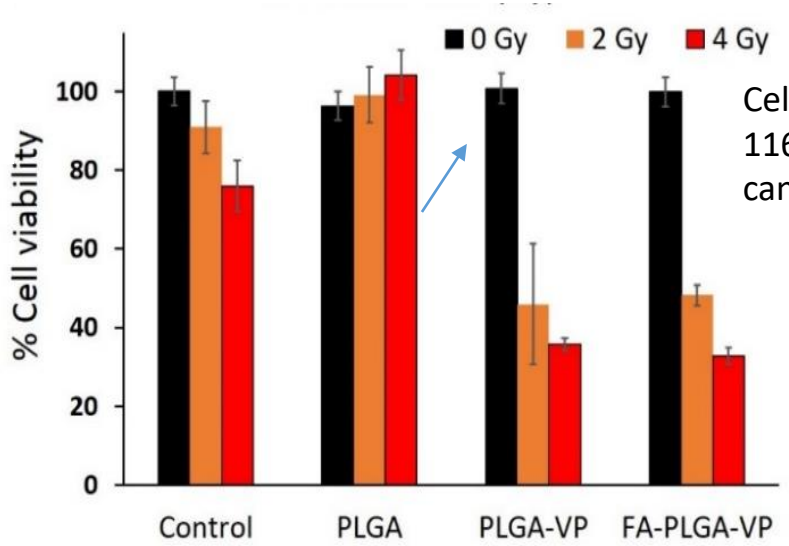
Polymer nanoparticles (**PLGA**) as a drug carrier for X-ray PDT





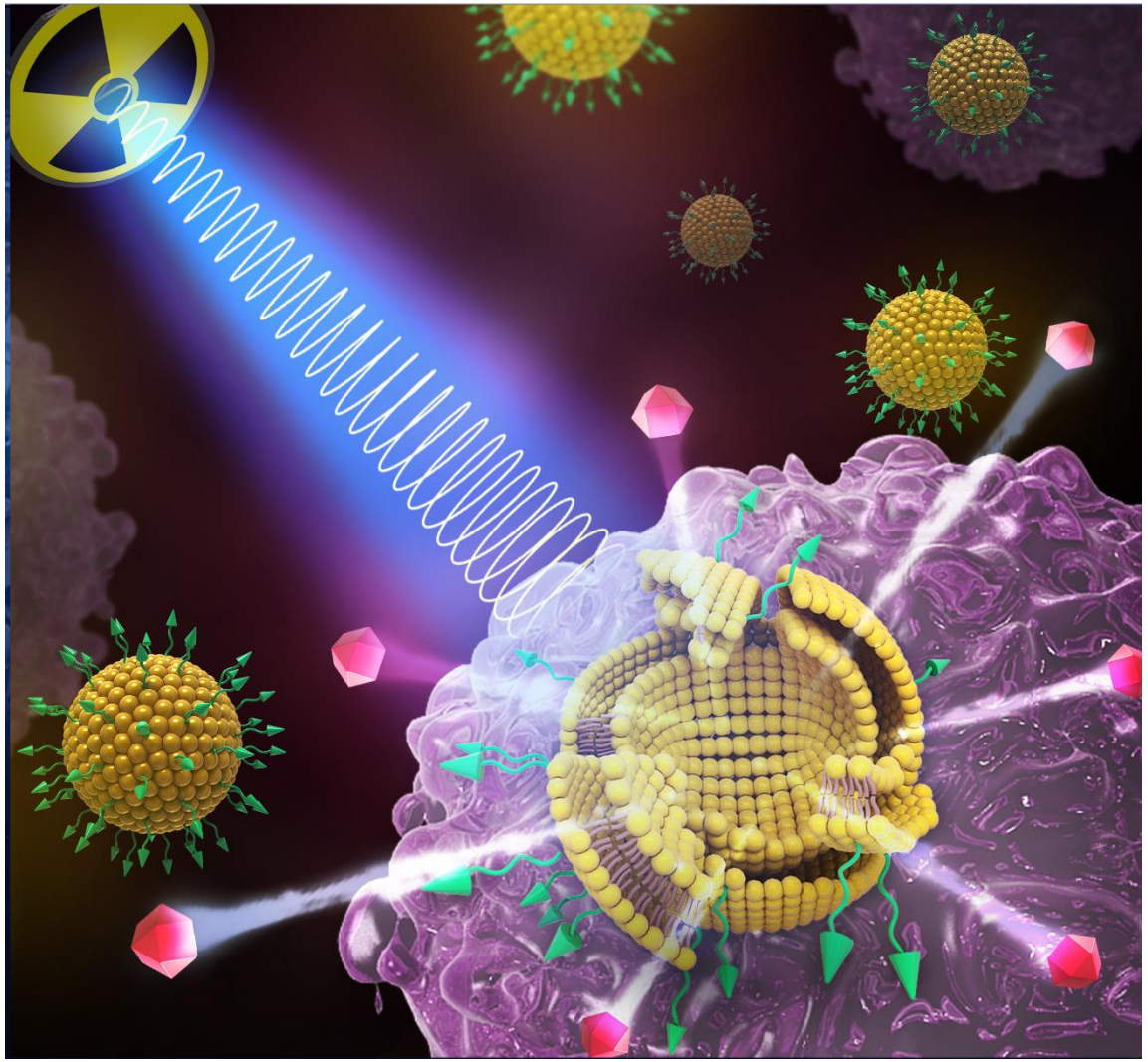
Singlet oxygen generation



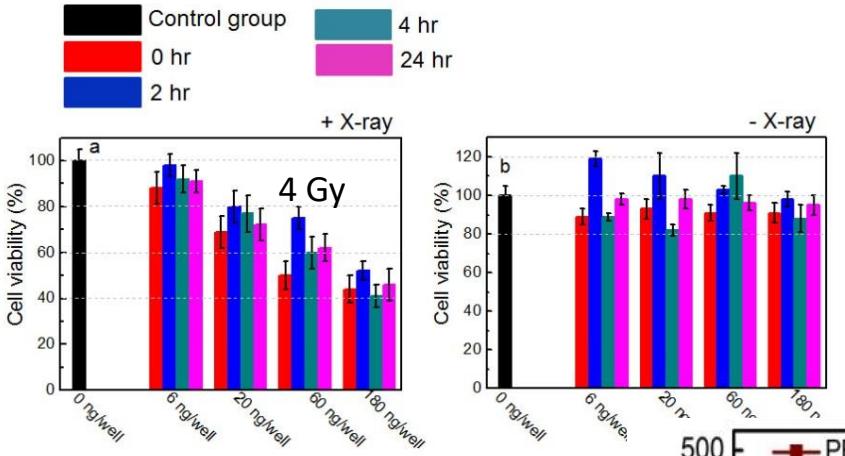


Cell line : HCT 116 , colorectal cancer cell line

In vitro PDT assays suggest that the conjugates effectively kill HCT116 cells in the presence 6 MeV radiation. In X-ray radiation, the 6 MeV radiation from linear accelerator produces energetic secondary electrons and Cerenkov radiation in the samples, which, in turn excite the VP molecules.

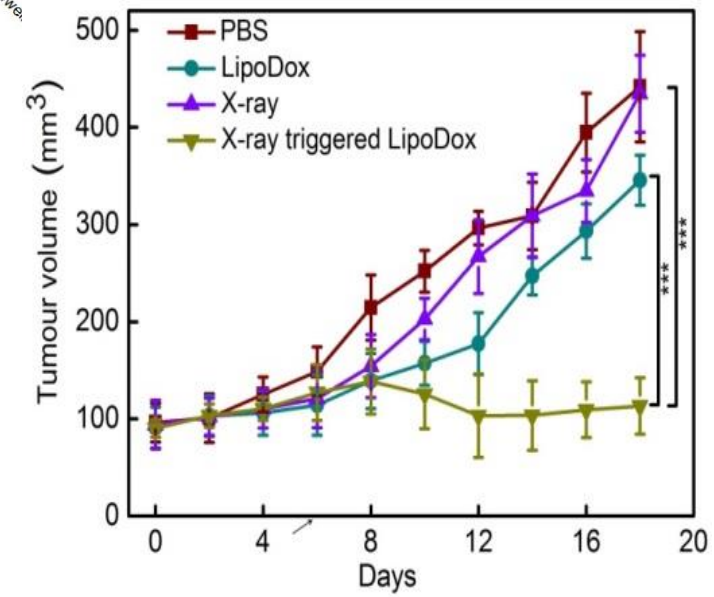


Beyond PDT: drug/gene release from X-ray triggered liposomes incorporating verteporfin (VP) and gold nanoparticles



Wei Deng

In vivo therapeutic effect in a mouse model with colorectal cancer



Nature Communications **volume 9**, Article number: 2713 (2018)

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Challenges

- **Ultrasensitive detection of specific molecules in real environments**: trace or single molecule detection, background problem "needle in a haystack problem"
- **Molecular complexity**: need to detect many diverse molecular species
- **Minimally-invasive probing of real systems** *in - vivo* - requirement of crossing of length scales
- **Control of therapeutical interventions**

Approaches

1. Amplified assays
2. Bright nanoparticle labels
3. High contrast imaging (time-gated and IR excitation)
4. Multiplexing
5. Sensing devices,
6. Light and X-ray triggered release (ROS, drug and gene)

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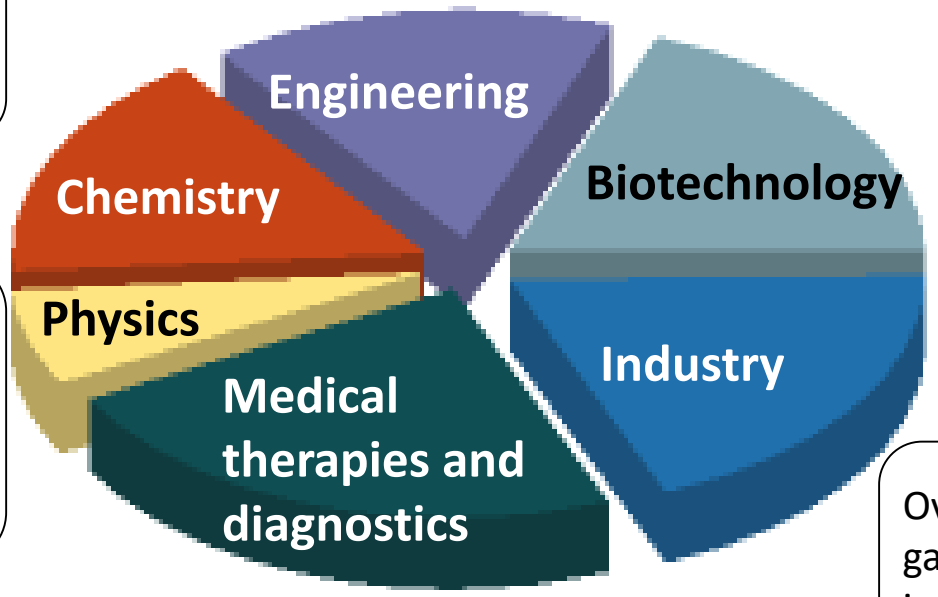
Increase sensitivity of end-user assays
by several orders of magnitude
(5 orders – single molecules sensitivity)
Molecularly sensitive imaging in vivo

Develop simple and low cost methods of nanostructure synthesis



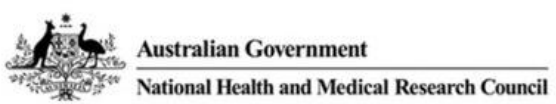
Develop simple and low costs assays and devices

Design and demonstrate plasmonic and dielectric structures for optimised enhancement (fluorescence, SERS, absorption)

Overcome the R&D gap and take the inventions to the market

Clinical adoption of technologies

Acknowledgements



Acknowledgements

Collaborators - presented work:
Sutton-McDowall ML, Gosnell M, Anwer AG, White M, Purdey M, Abell AD, Thompson JM, Nadort A, Hutchinson MR, Y.Q. Lu, J.B. Zhao, R.C. Leif, J.A. Piper, J.P. Robinson, D.Y. Jin, Zhang, K., Ma, K., Care, A. Mahbub, S. B, Cassano, J. C. Sue, C. M., Perinchery, S. M., Inglis, D. W., Adhikary, P. P. Jazayeri, J. A., Cahill, M. A., Saad, S., Pollock C.A., Chandra Bala, D. Rowe, G. Vesey, Razali, W. A. W., Sreenivasan, V. K. A., Bradac, C., Connor, M., Zvyagin, A. V, Dawes, J. M, Purdey, M, RB Gilchrist, DK Gardner, A. Habbibalahi, V. Staikopoulos, M. Baratta, S.Mustafa, B.Gibson and others.


THANK YOU

Spare slides

Publications on fluorescence amplification, substrates

• "Extreme sensitivity of optical properties of metal nanostructures to minor variations in geometry is due to highly localised electromagnetic field modes", Ewa M. Goldys , Nils Calander, and Krystyna Drozdowicz-Tomsia, accepted Journal of Physical Chemistry C (2010).

•"Deposition of Silver Dentritic Nanostructures on Silicon for Enhanced Fluorescence", Drozdowicz-Tomsia, Krystyna; Xie, Fang; Goldys, Ewa M., Journal of Physical Chemistry C (2010), 114(3), 1562-1569.

•"Metalllic nanomaterrials for sensitivity enhancement of fluorescence detection", Fang Xie, EM. Goldys , Sensors (2008), 8, 886-896,

•

• "Enhanced Fluorescence Detection on Homogeneous Gold Colloid Self-Assembled Monolayer Substrates", Xie, Fang; Baker, Mark S.; Goldys, Ewa M. Chemistry of Materials (2008), 20(5), 1788-1797.

• "Fluorescence Amplification by Electrochemically Deposited Silver Nanowires with Fractal Architecture", Goldys, Ewa M.; Drozdowicz-Tomsia, Krystyna; Xie, Fang; Shtoyko, Tanya; Matveeva, Eva; Gryczynski, Ignacy; Gryczynski, Zygmunt", Journal of the American Chemical Society (2007), 129(40), 12117-12122.

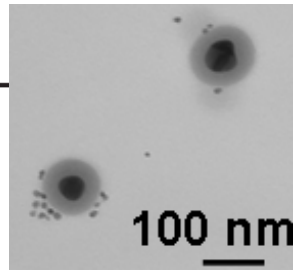
• "Preparation of Homogeneous Silver-Coated Nanoparticles and their Application for Fluorescence Enhancement", Fang Xie, Mark Baker, Ewa Goldys, *J. Phys. Chem. B.* 110 (46), 23085-23091, (2006)

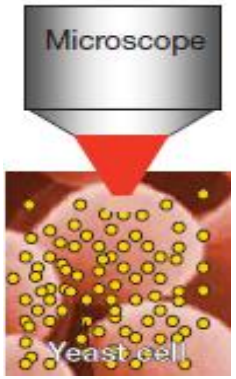
•

•SPR enhancement

•" Modeling of the SPR resolution enhancement for a nanoparticle inclusive sensor by using statistical hypothesis testing" Anne Barnett, Ewa M Goldys; Optics Express (2010), Volume 18, Issue 9, Pages: 9384-9397

Smart particles … *Our own Ag/ SiO_2 SHINs*





Shell-isolated nanoparticle-enhanced Raman spectroscopy … SHINERS

- **Novel SERS enhancement, by 'dusting-on' a powder of plasmonic nanoparticles …**

Jian Feng Li[1], Yi Fan Huang[1], Yong Ding[1,2], Zhi Lin Yang[1], Song Bo Li[1], Xiao Shun Zhou[1], Feng Ru Fan[1,2], Wei Zhang[1], Zhi You Zhou[1], Bo Yin Ren[1], Min Hao Ren[1], Zhong Lin Wang[1] & Zhong Qun Tian[1]

nature Vol 464|18 March 2010|doi:10.1038/nature08907

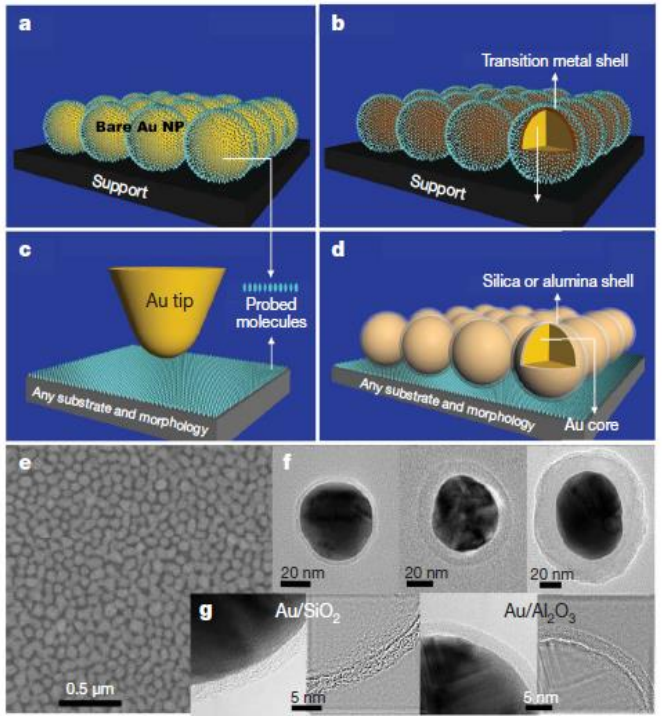
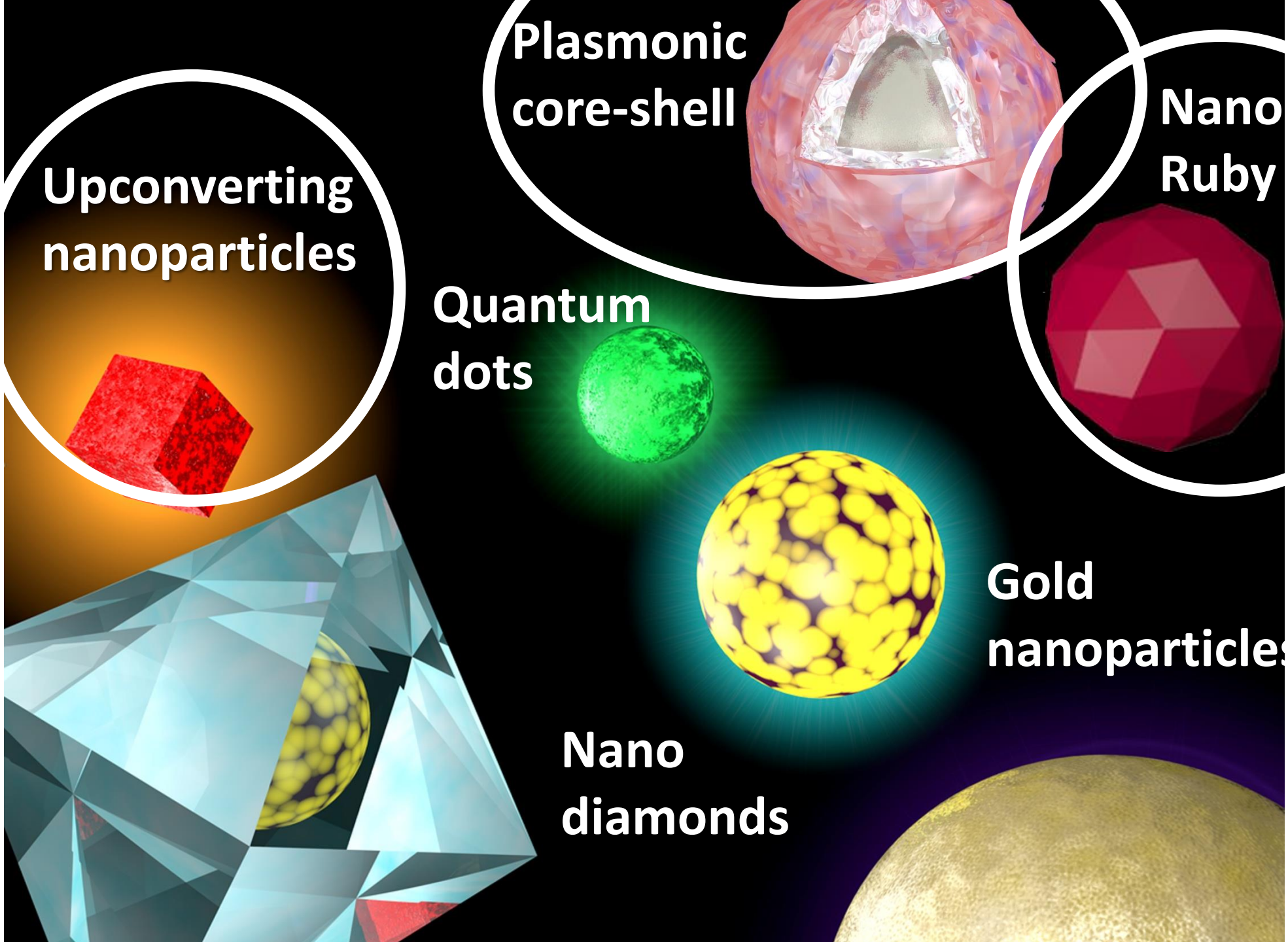
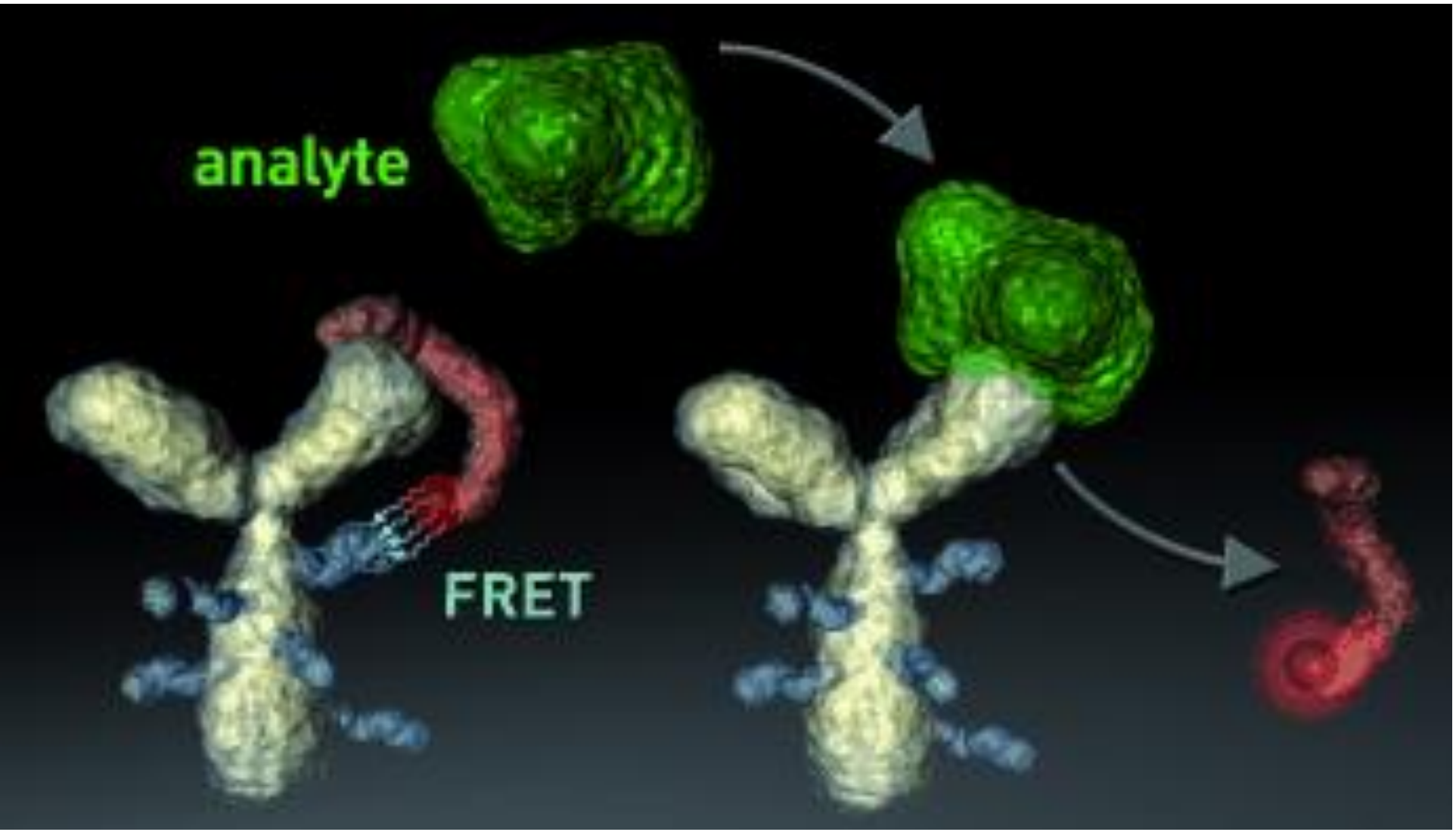
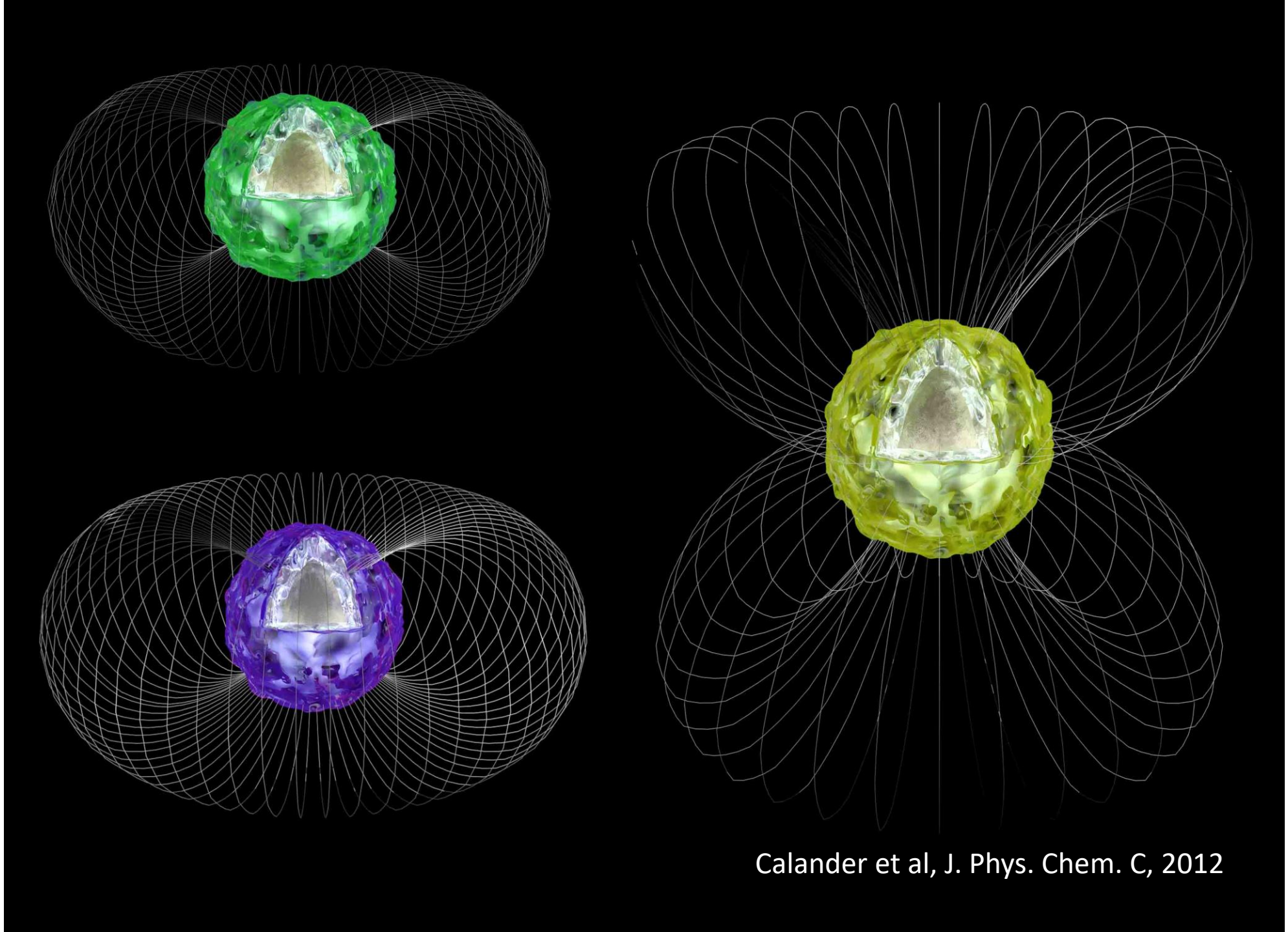


Figure 1 | The working principles of SHINERS compared to other modes. Schematic of the contact mode. **a**, Bare Au nanoparticles: contact mode. **b**, Au core–transition metal shell nanoparticles adsorbed by probed molecules: contact mode. **c**, Tip-enhanced Raman spectroscopy: non-contact mode. **d**, SHINERS: shell-isolated mode. **e**, Scanning electron microscope image of a monolayer of Au/SiO_2 nanoparticles on a smooth Au surface. **f**, HRTEM images of Au/SiO_2 core–shell nanoparticles with different shell thicknesses. **g**, HRTEM images of Au/SiO_2 nanoparticle and Au/Al_2O_3 nanoparticle with a continuous and completely packed shell about 2 nm thick.


Plasmonic
core-shell
Nano
Ruby
Upconverting
nanoparticles
Quantum
dots
Gold
nanoparticles
Nano
diamonds


analyte
FRET



Calander et al, J. Phys. Chem. C, 2012

Photonic and Laser Technologies and Applications

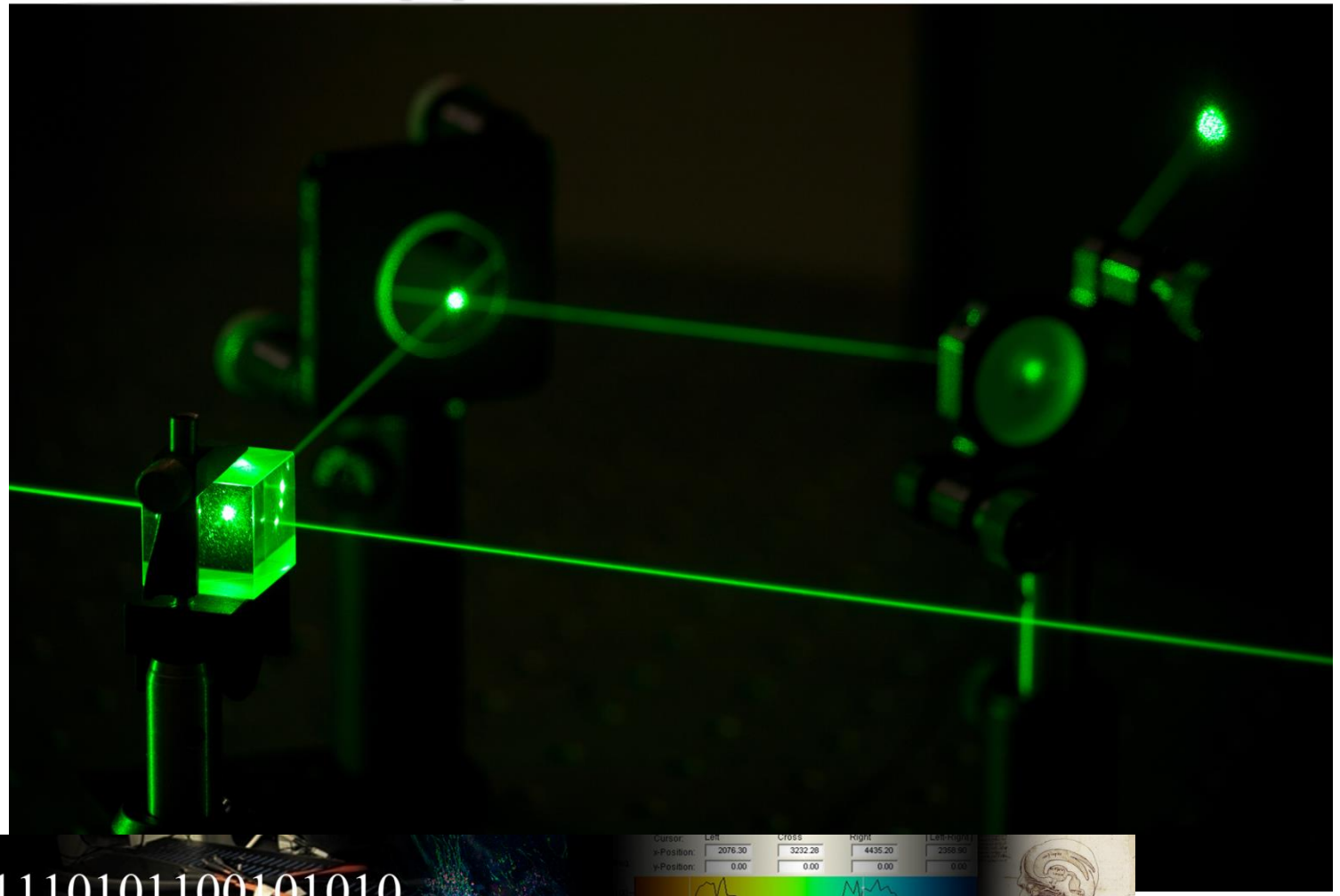
David Spence

Helen Pask

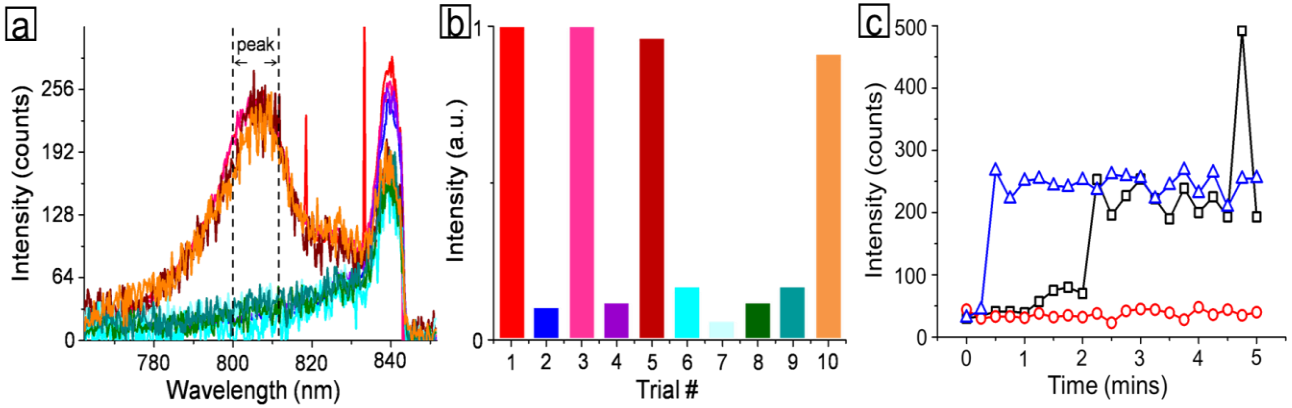
Richard Mildren

Judith Dawes

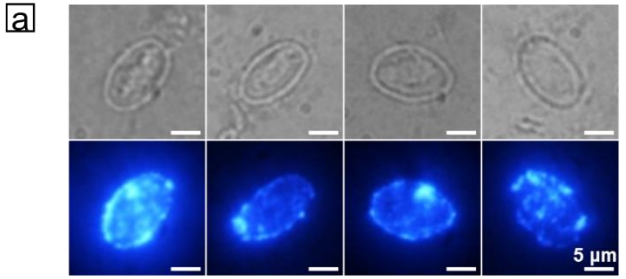
Brian Orr

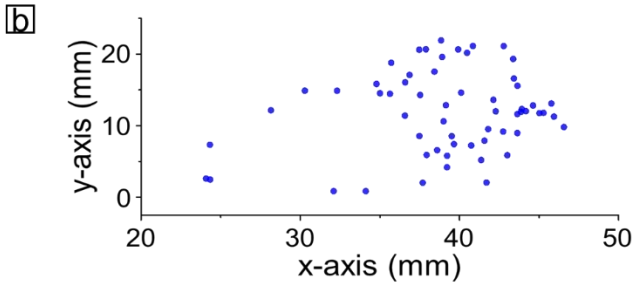


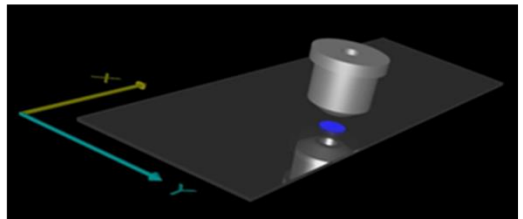
Applications

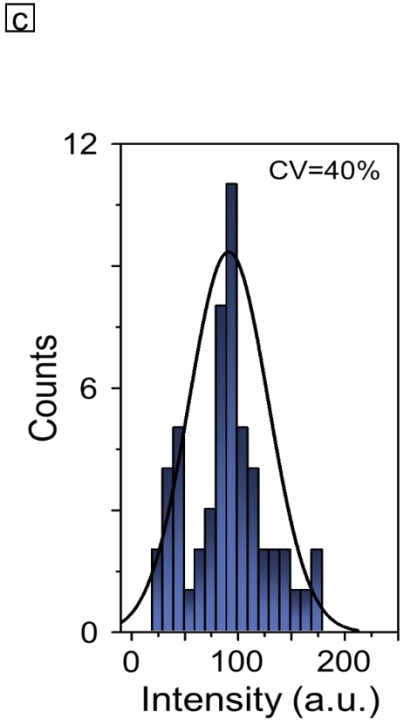


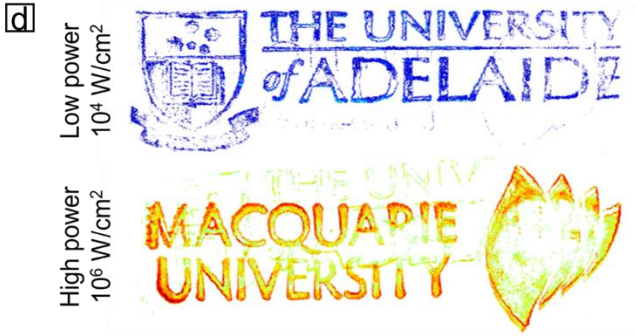
Fibre sensing: single particles
Biolabelling
Rare cell detection
Document security

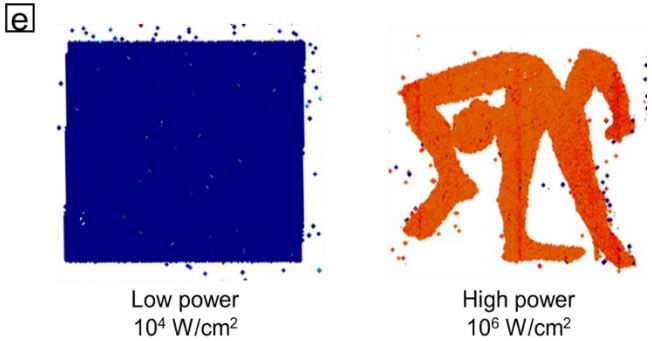












1. Fluorescent nanoprobes

Motivation: Visualise molecular events

Bright labels

(high signal)

Reduced autofluorescence

(low background)

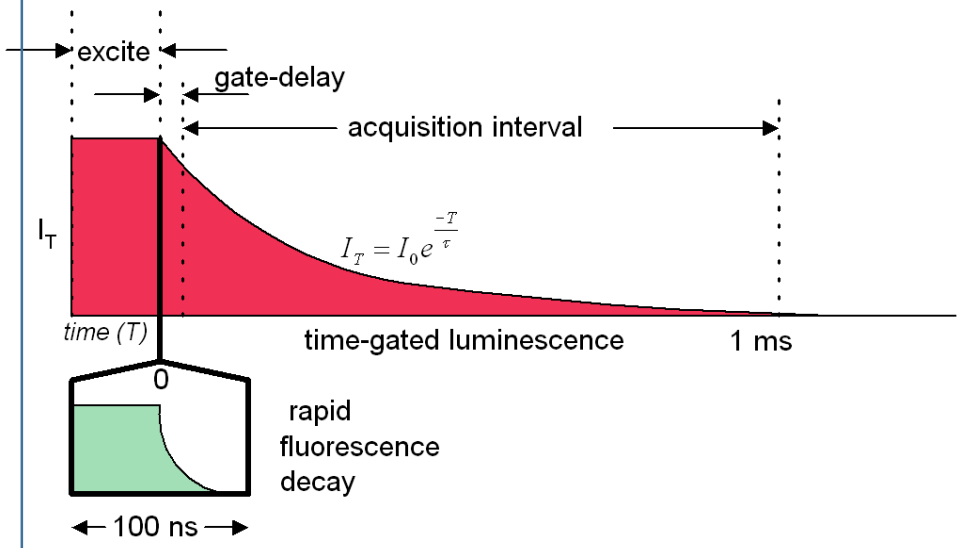
Lanthanides or transition metals

ms lifetimes

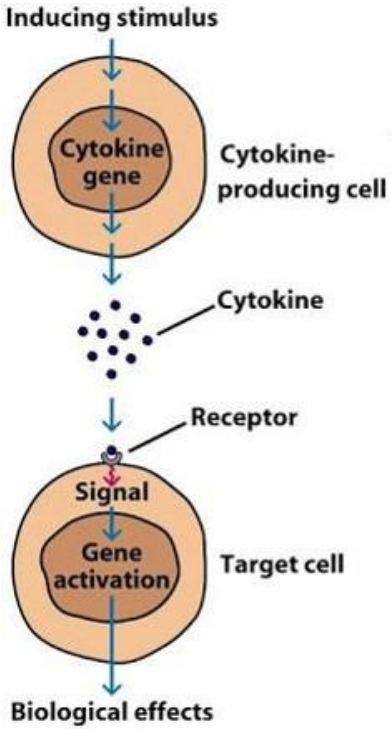
Low photon cycling rates

Not bright enough

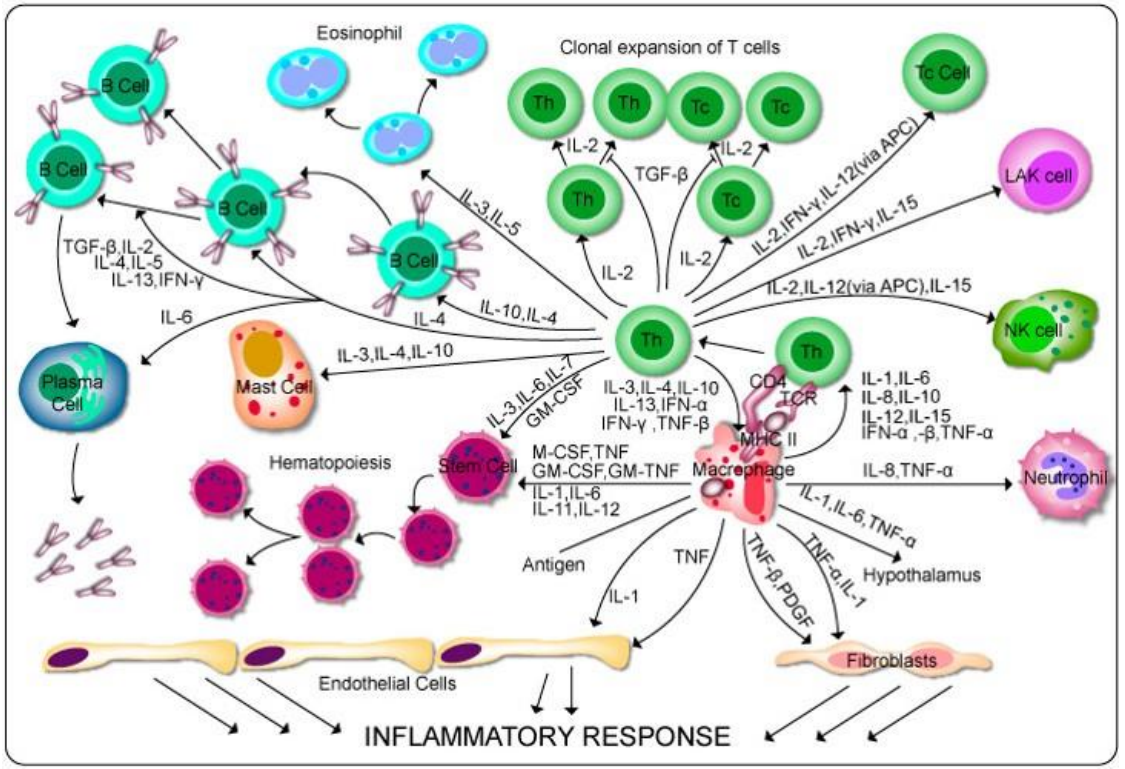
Time-gated methods



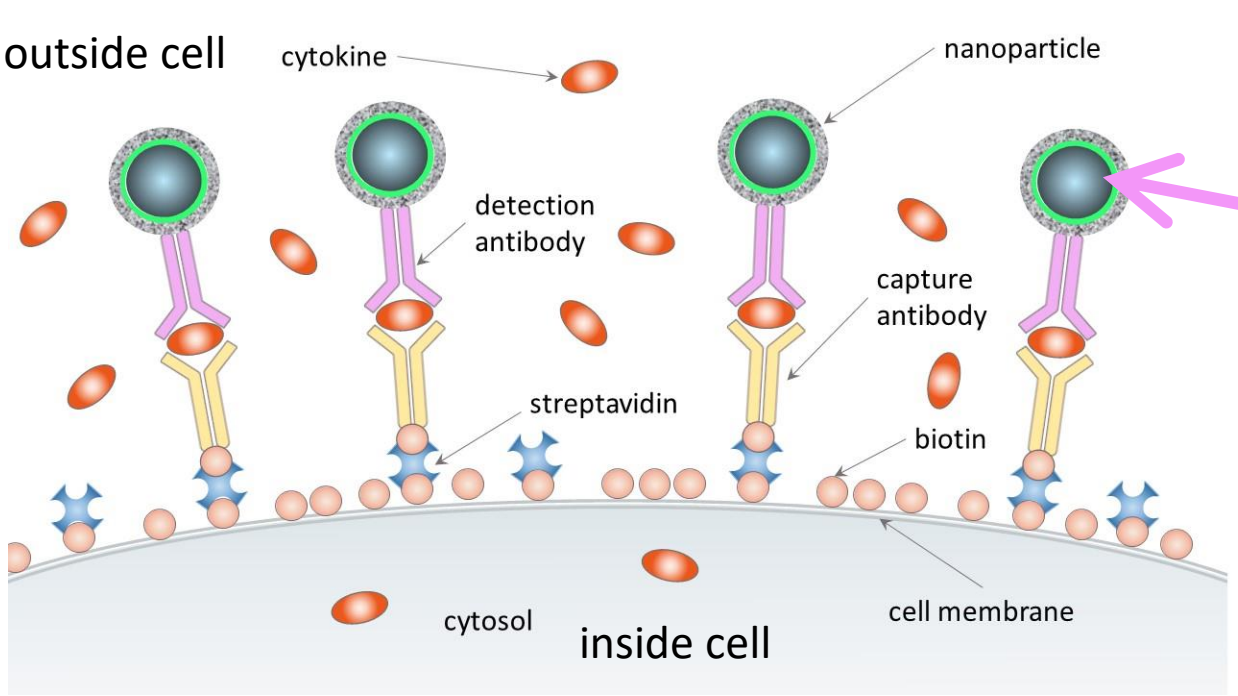
Cytokine analysis

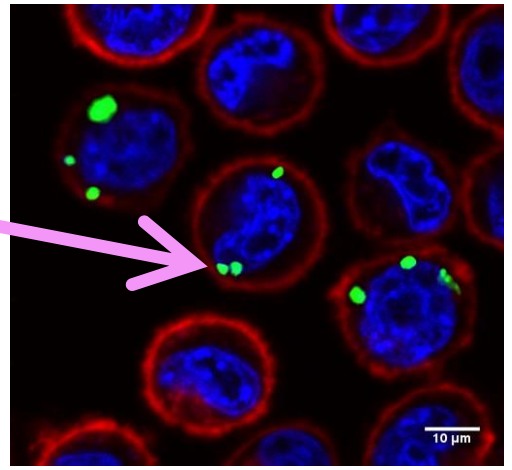


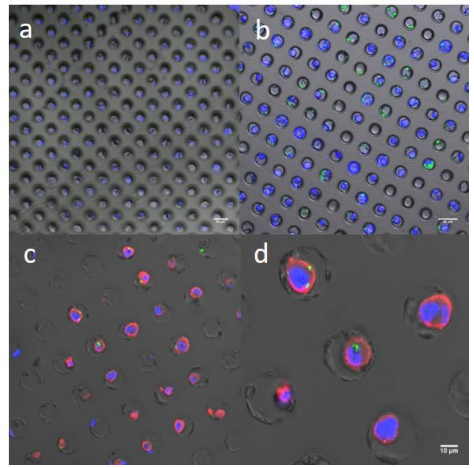
cytokines	Molecular weight (kDa)	Physiological concentration (pg/mL)
Interleukin 1 belta (IL-1β)	17.4	10~45
Interleukin 10 (IL-10)	18	10~50
Interleukin 6 (IL-6)	21	10~75
Tumor necrosis factor alpha (TNF-α)	17.5	5~100
Interferon gamma (IFN-γ)	16.9	10~50
Growth differentiating factor 9 (GDF-9)	20	10~50
Bone morphogenic protein 15 (BMP-15)	34	10~50
Granulocyte macrophage colony-stimulating factor (GM-CSF)	21	10~50
High-mobility group protein B1(HMGB1)	29	10~50
Macrophage migration inhibitory factor (MIF or MMIF)	12.5	10~50
Vascular endothelial growth factor (VEGF)	42	10~50
MD2	17	5~50
Transforming growth factor beta (TGF- β)	20	5~50
Small cell derived factor 1 (SDF-1)	15	5~50
Macrophage colony-stimulating factor (MCSF or CSF1)	14	5~50
Monocyte chemoattractant protein-1 (MCP1)	4	5~50
Fractalkin (a human adipochemokine)	10	5~50

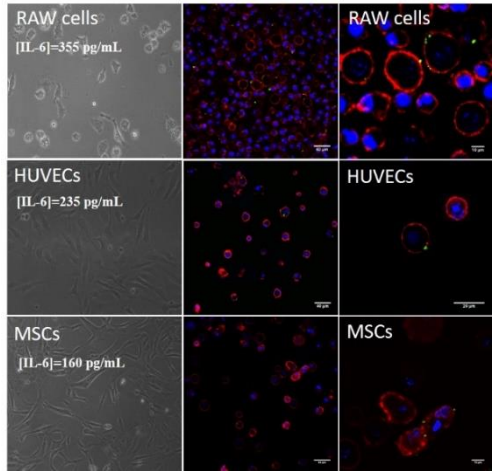


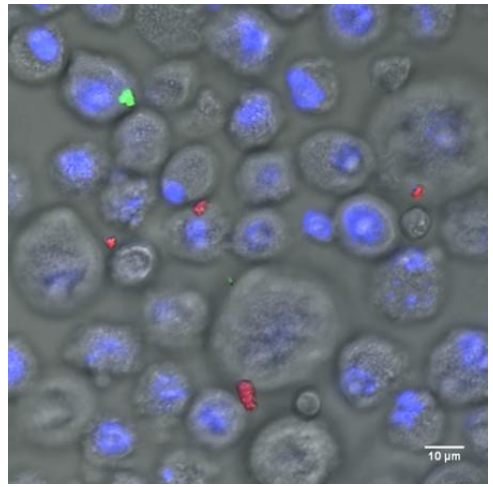
How to detect secreted cytokines





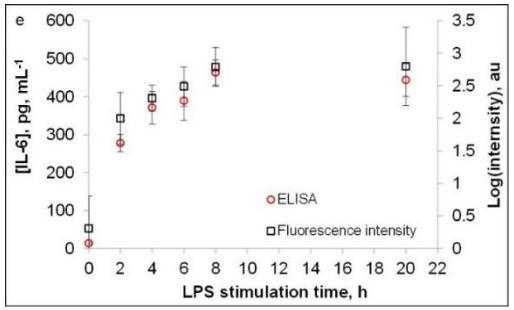






"sandwich immunoassay", Y shapes = antibodies

Guozhen Liu, Macquarie



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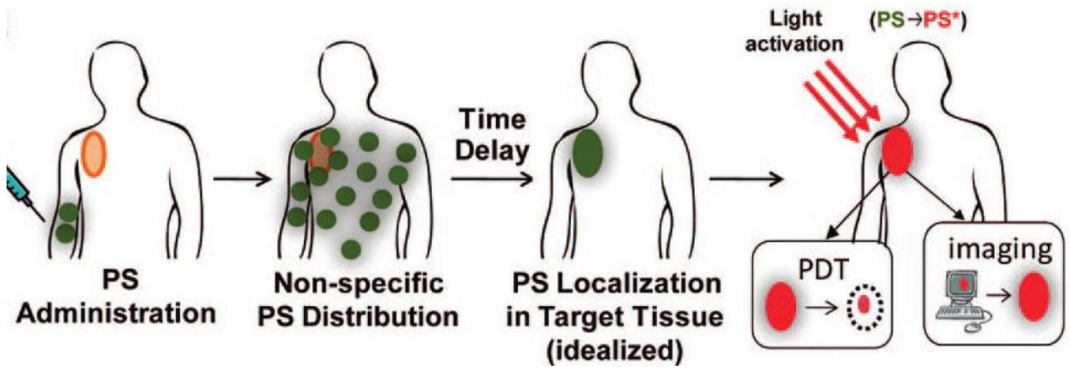
Photodynamic therapy

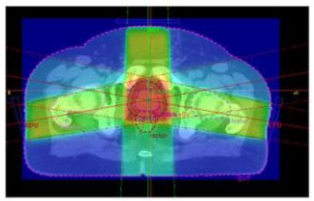


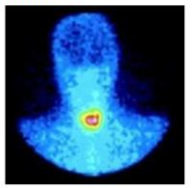
Advantages of PDT (in cancer treatment)

- Can be very effective in destroying tumor tissue
- Minimally-invasive
- Low systemic toxicity, nerve sparing
- Excellent normal tissue healing (does not destroy collagen)
- Repeatable without resistance or intolerance
- Triggers anti-tumor immune response

➢ **PDT via Ionizing Radiation**

Deep tissue penetration
Homogenous tumor irradiation





Existing clinical infrastructure

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