DIFFERENT INTERACTIONS ON NANOSCALE

RECOGNITION, ACTIVE TRANSPORT

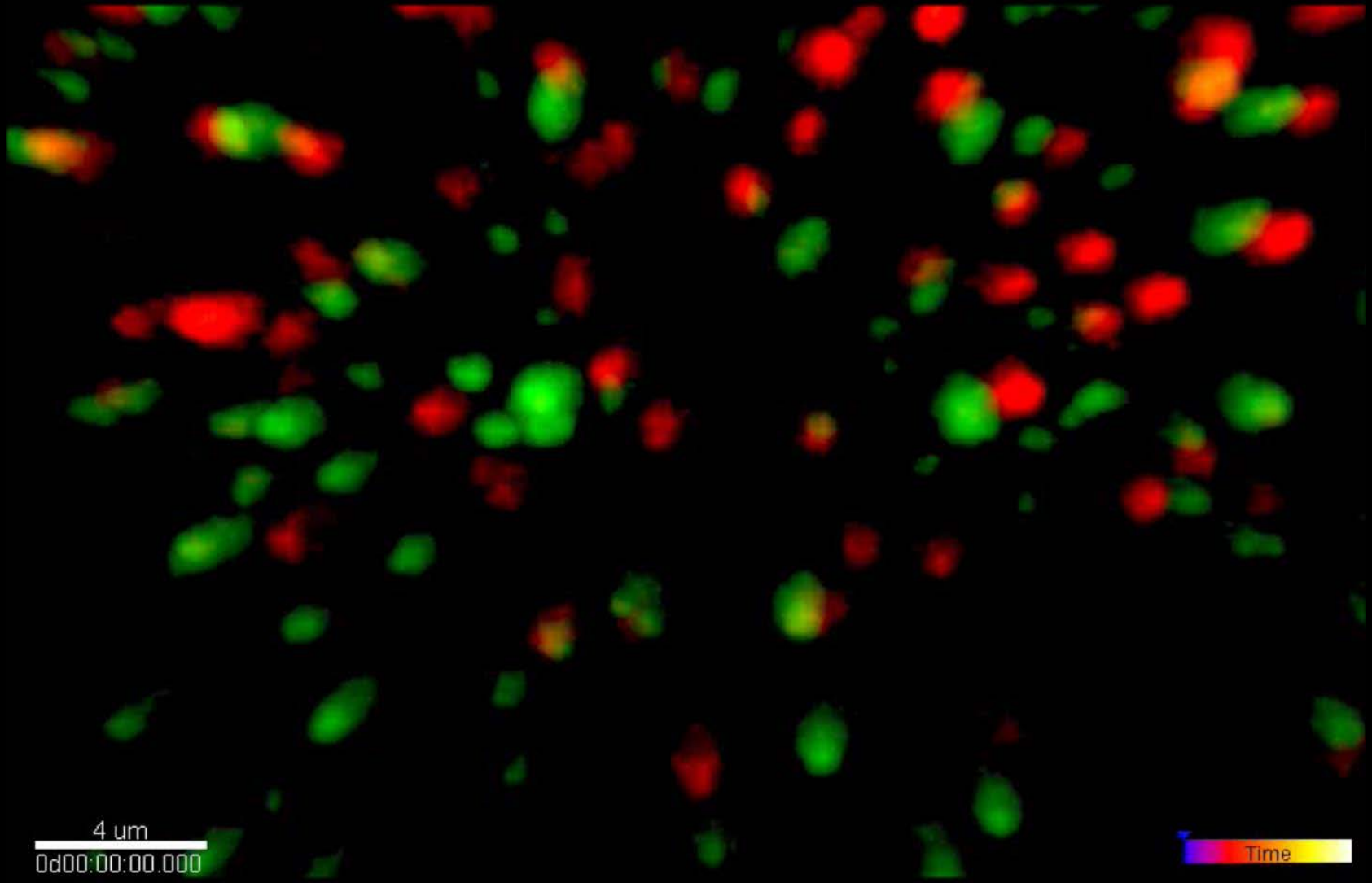
ACCUMULATION AND FATE

ENABLING AND REGULATING THE FUTURE

GLOBAL CONVERSATION AND COR

NANOPARTICLES ACT DIFFERENTLY FROM CHEMICALS

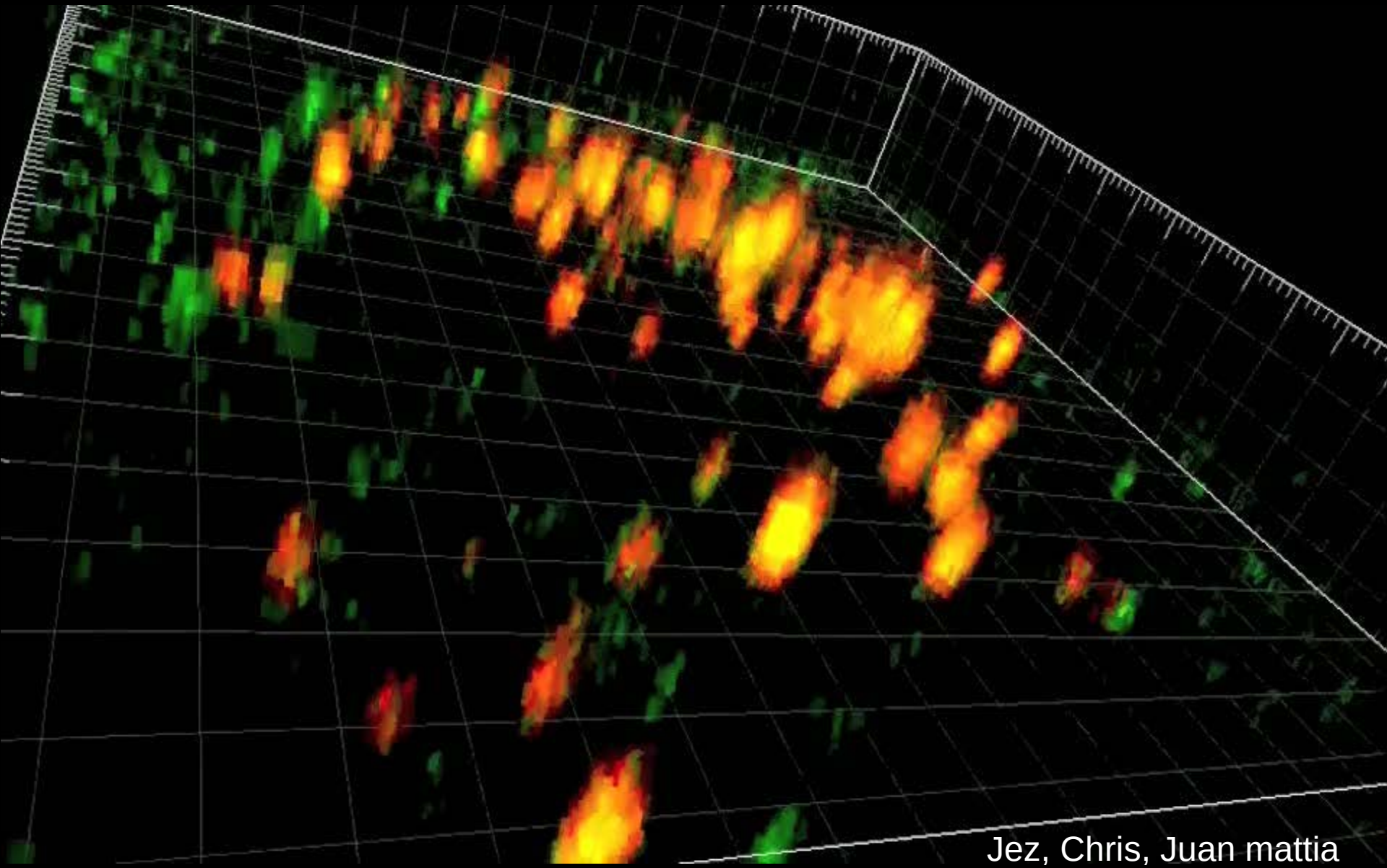
green 40nm PS particles red lysosomes



A549 cell and LysoTracker Red 30 min after 10 min pulse of 100 μg/mL 40 nm green ps particles

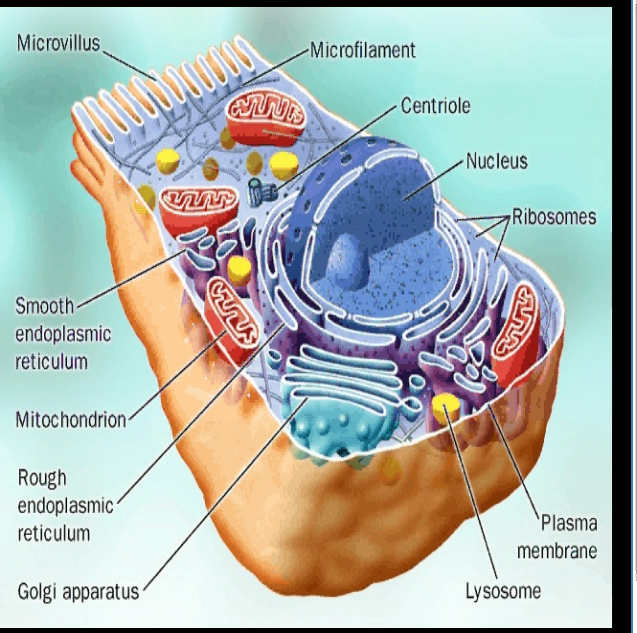
They Travel on Highways, using the transport Process of Cell

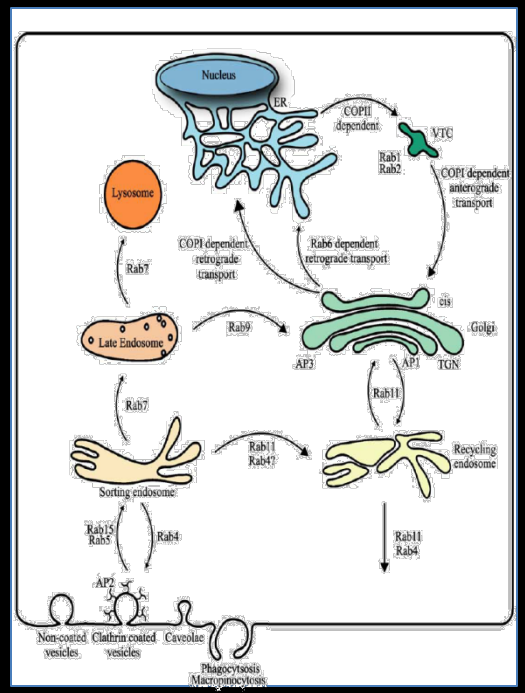
Same system-4 hours later-many particles have reached lysosomes

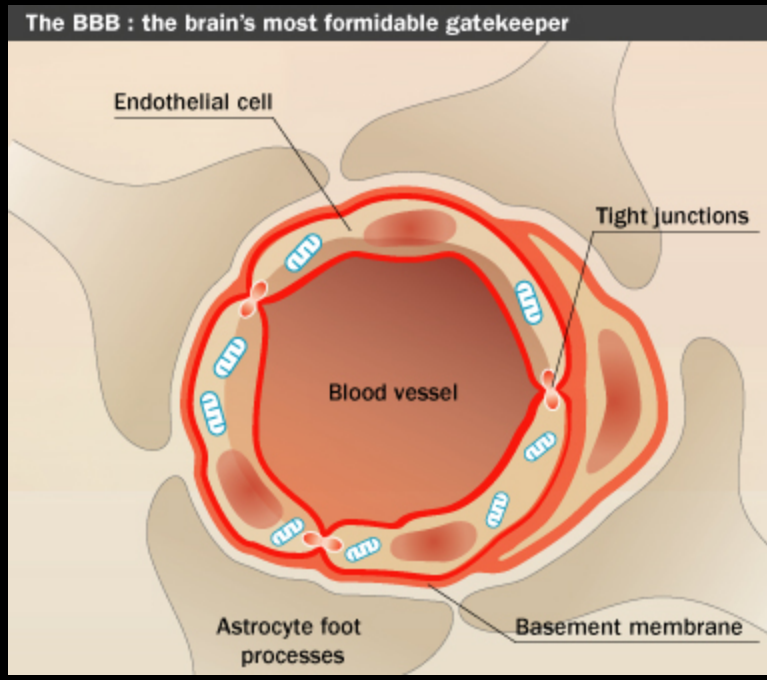


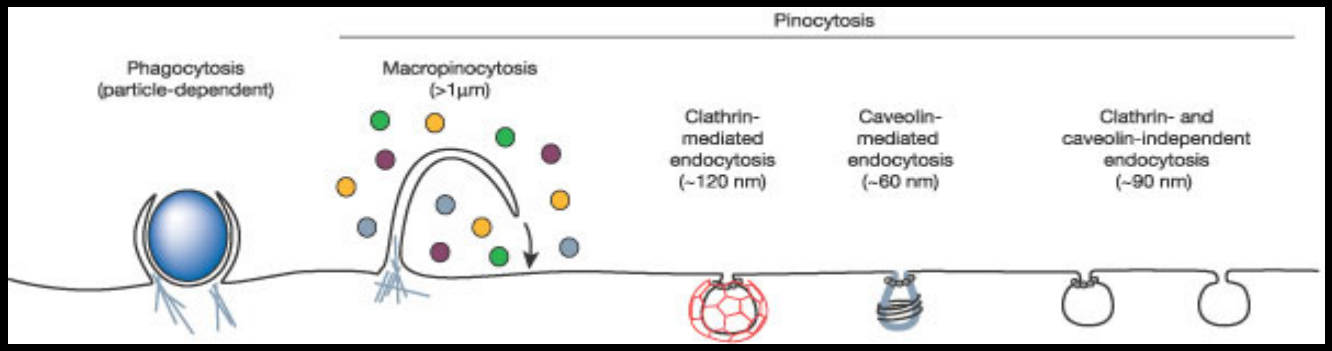
Jez, Chris, Juan mattia

NEW SCIENCE





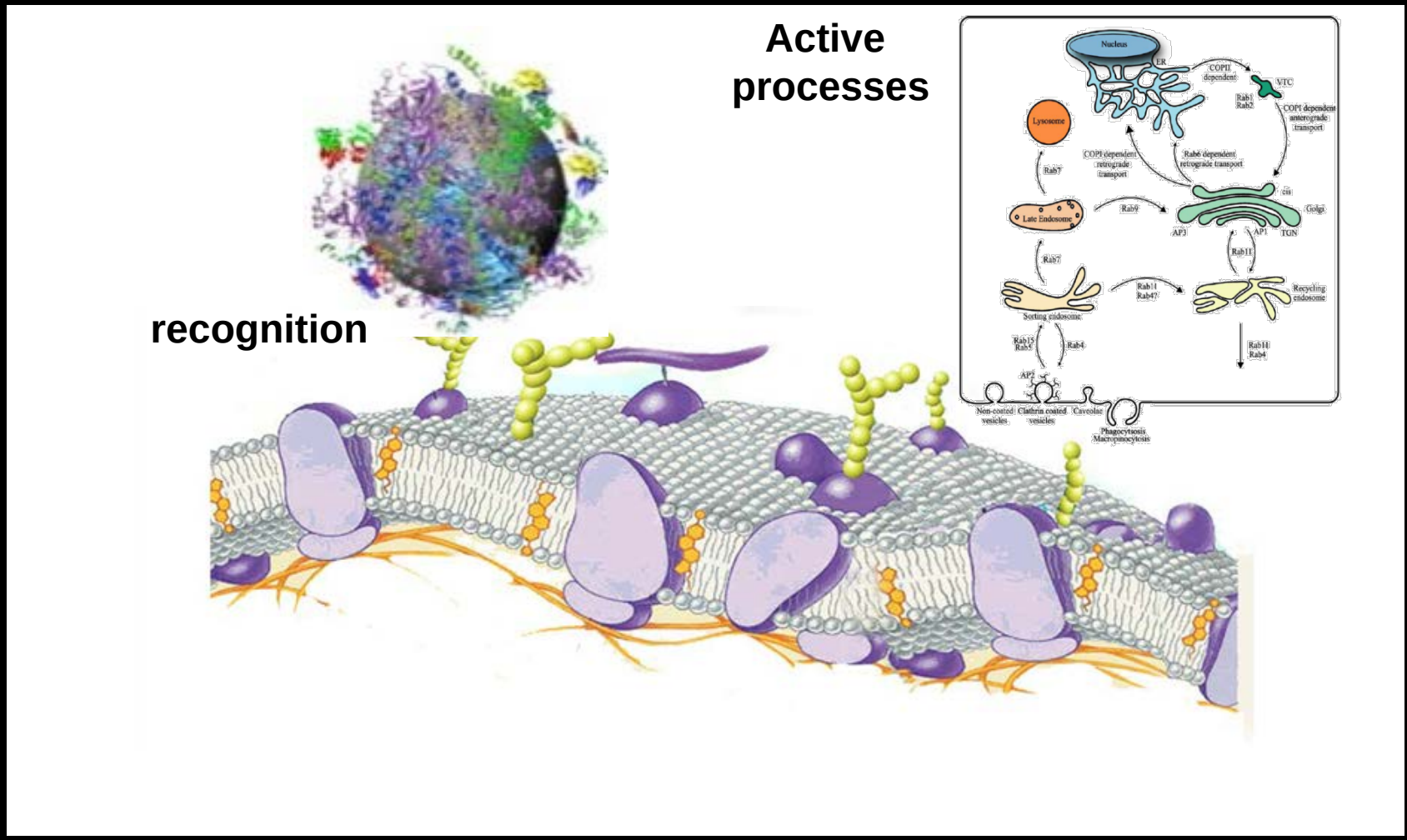




Chemicals Partition but Nanoparticles processed-energy of cell used

RECOGNITION

Nanoscale engages with intrinsic (endogenous) active cellular processes ; Such interactions invariably involve recognition especially of the in situ interface

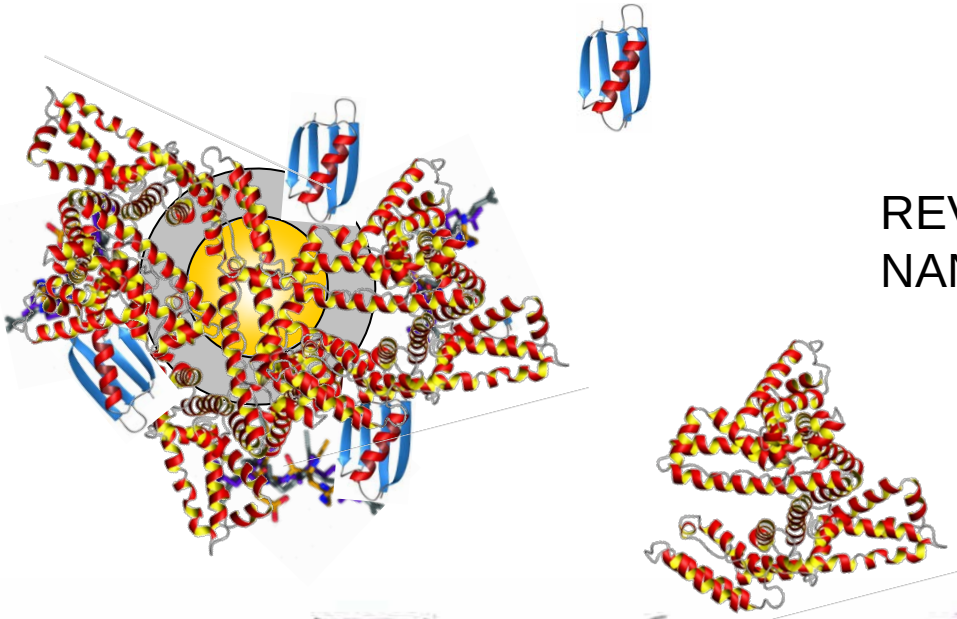


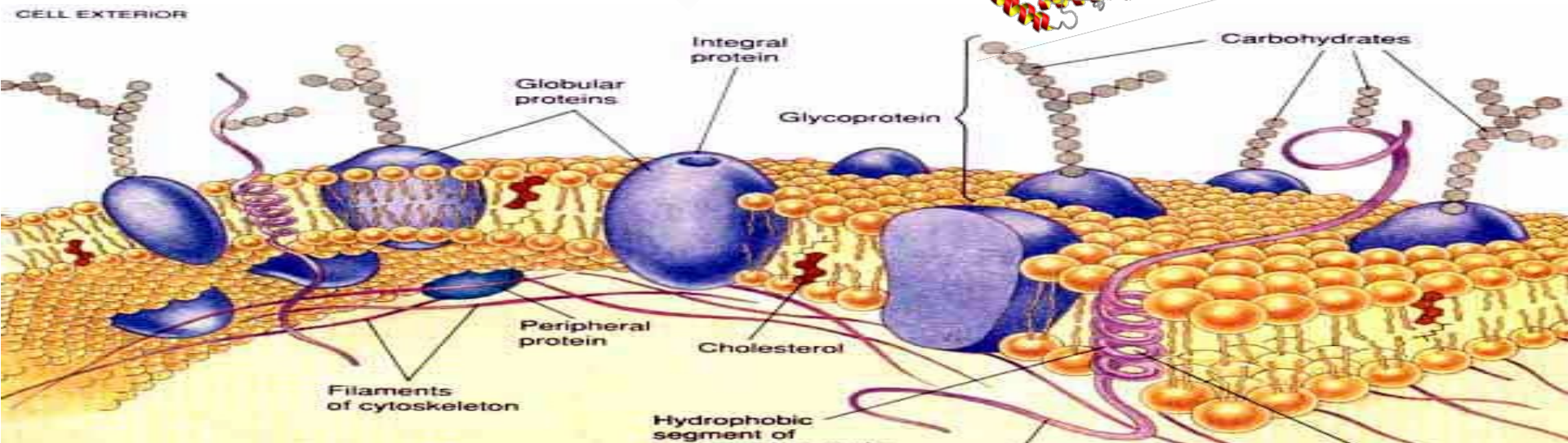
Biological and Environmental Identity *(Contextual)*

Cozzarelli Prize NAS 2008

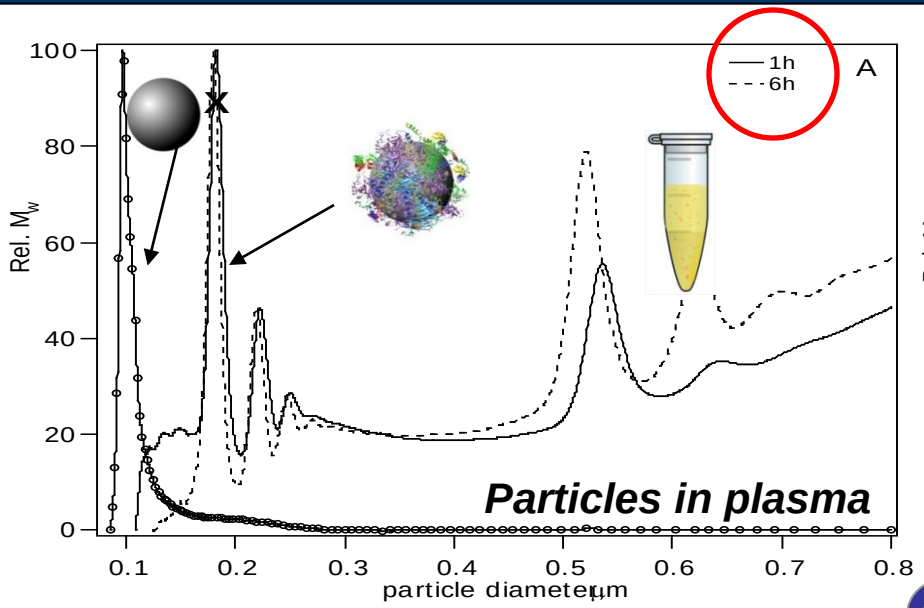
NATURE NANO, 2009, 4, 546
NATURE NANO, 2011, 2012
JACS, 2010, 2011,
ACS Nano 2011

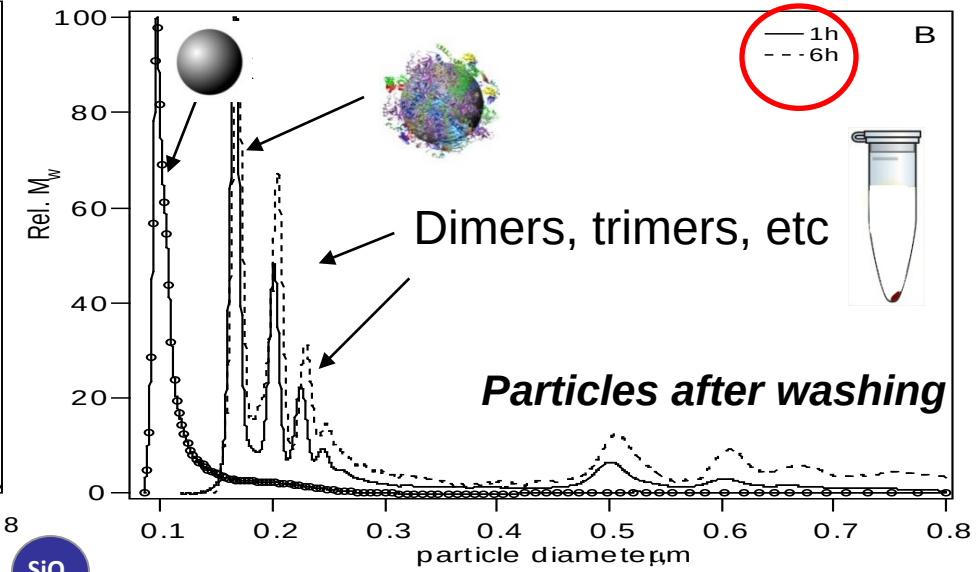
REVIEW NATURE NANO DECEMBER



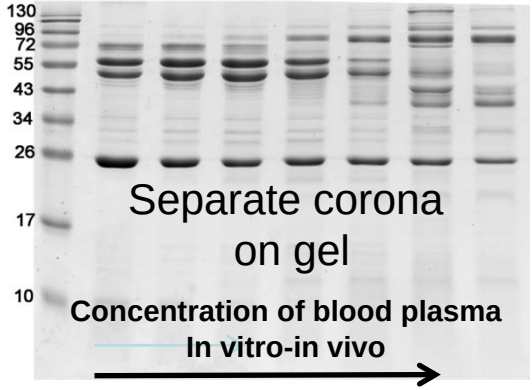


‘Hard Corona’ Common Nanoparticles surface covered by proteins from surrounding





SiO_2



Map out protein composition
Quantitatively mass spec.

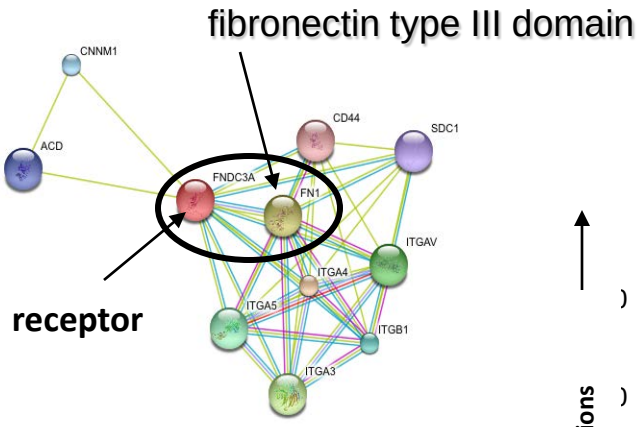
Gel band Mw	Acc number	Protein Identity Spectral Counts	NSpC [10% plasma]	NSpC [55% plasma]
500kDa	P04114	Apolipoprotein B 100	0.96	0.91
120kDa	P07996	Thrombospondin-1	0.01	1.37
90 kDa	P04196	Histidine-rich glycoprotein	4.02	13.93
90 kDa	P00747	Plasminogen	0.87	3.27
90 kDa	P02787	Transferrin	0.02	0.52
72 kDa	P06396	Gelsolin	-	0.63
90 kDa	P02671	Fibrinogen alpha chain	15.43	4.88
72 kDa	P02768	Serum albumin	1.80	9.67
72 kDa	P01042	Kininogen-1	1.54	2.22
60 kDa	P02675	Fibrinogen beta chain	23.92	7.99
50 kDa	P02679	Fibrinogen gamma chain	18.40	6.52
50 kDa	P00748	Coagulation factor XII	1.05	4.15
43 kDa	P49908	Selenoprotein P	0.16	0.87
40 kDa	P02765	Alpha-2-HS-glycoprotein	-	0.16
28 kDa	P02749	Beta-2-glycoprotein	-	0.74
30 kDa	P02649	Apolipoprotein E	3.13	3.87
30 kDa	P02746	Complement C1q subcomponent Beta	2.28	0.58
26 kDa	P02647	Apolipoprotein A-I	9.45	14.83
12 kDa	P01834	Ig kappa chain C region	3.26	5.13

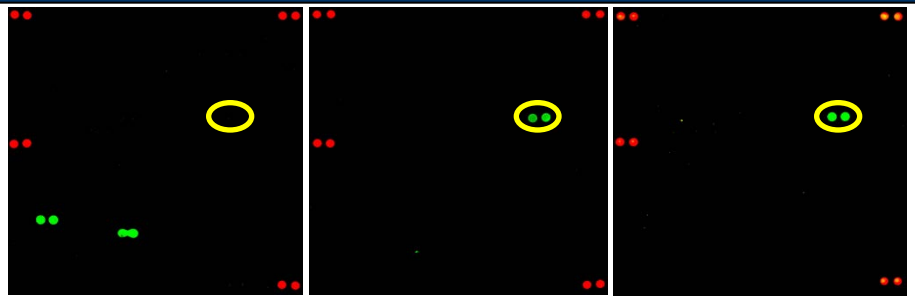
$$\left[\left(\rho_c - \rho_f\right)D^2\right]\cdot t = \frac{18\eta}{\omega^2}\ln\left(\frac{R_f}{R_0}\right)$$

Monopoli, M..Relevance to in Vitro and in Vivo Biological Impacts of Nanoparticles. J Am Chem Soc. February 2, 2011

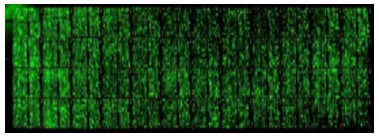
Walczyk, D. *J Am Chem Soc*,(2010) *132*, 5761-5768; Pitek *et al.* JACS 2011

Biological Identity derived from *in situ* Interface

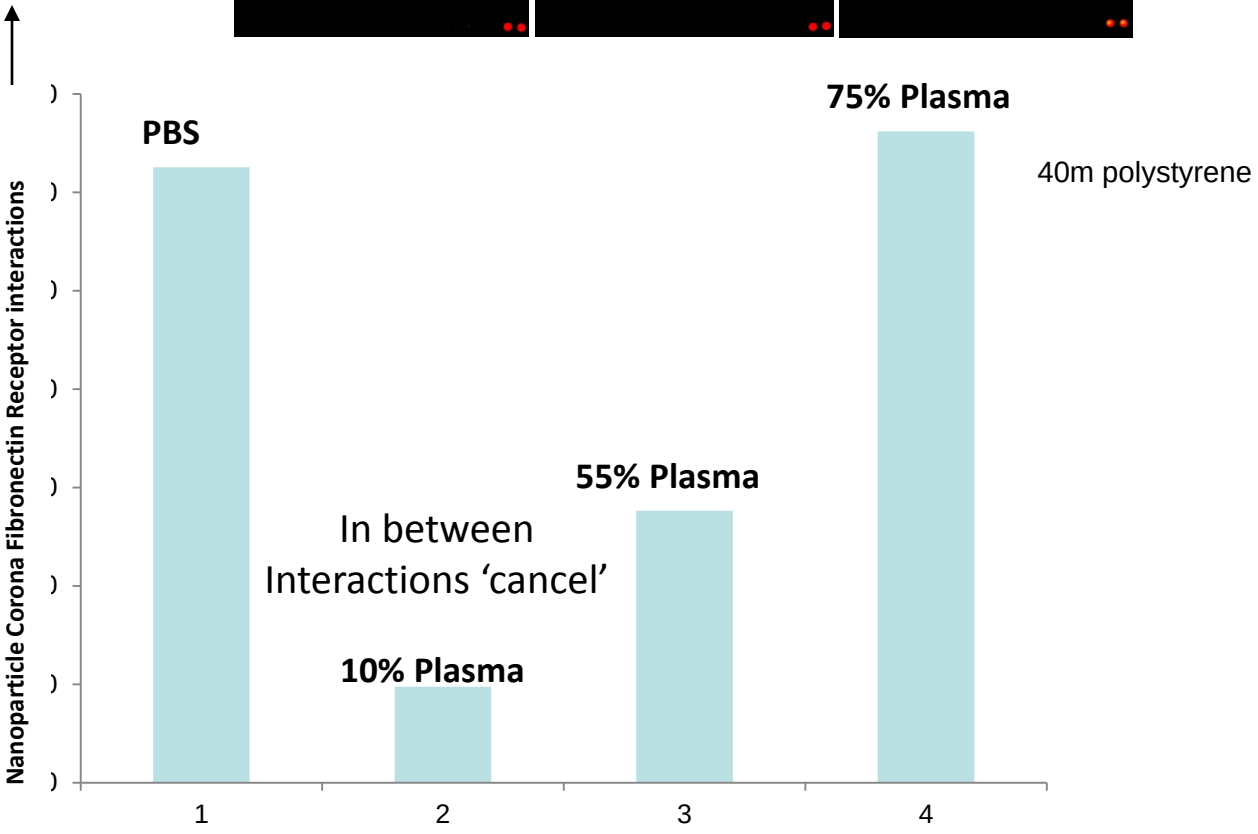




In PBS Non-Specific nanoparticle surface Interactions general

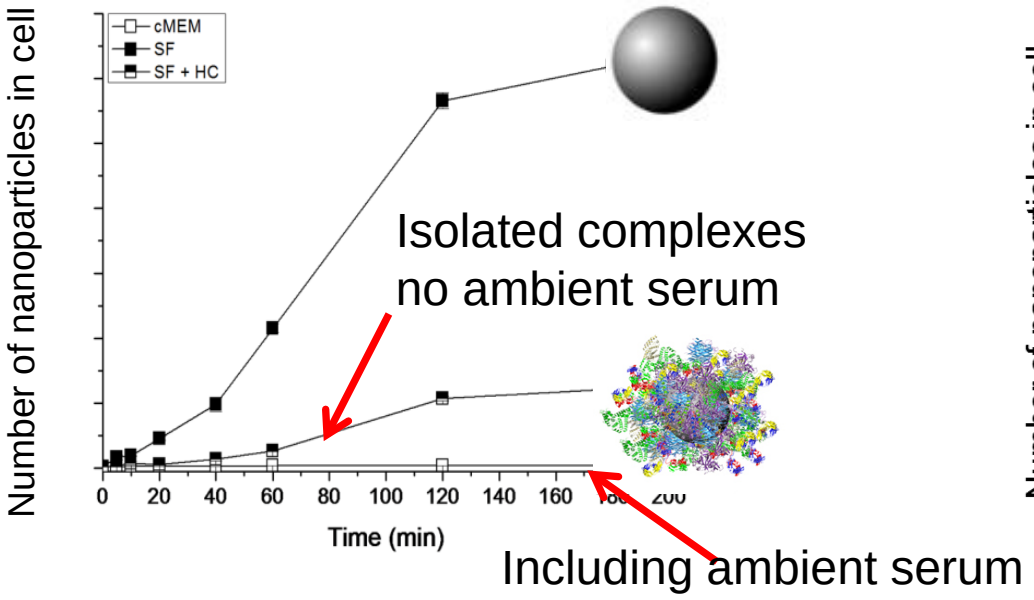


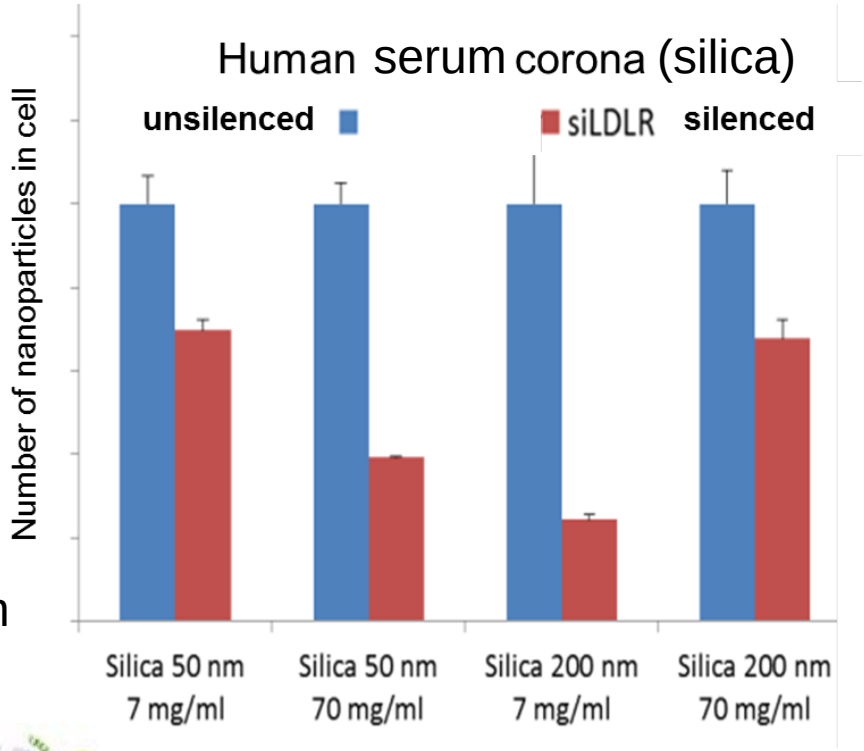
In presence of High Protein, Specific interactions

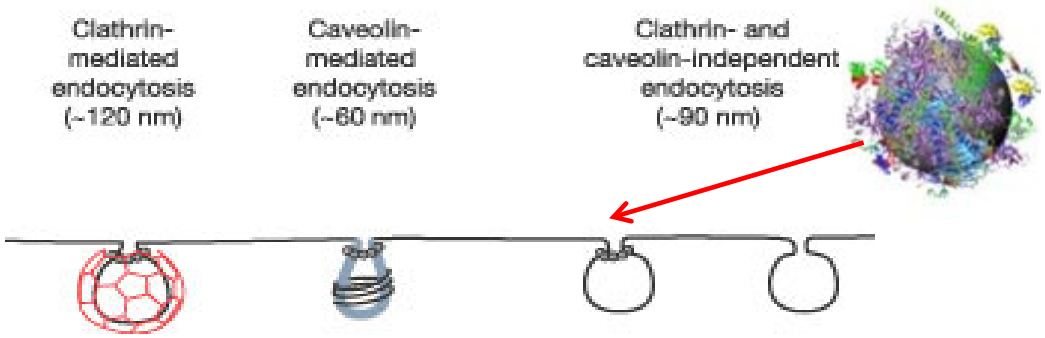


D.C. David OC, Marco

Recognition; the amount *and pathway* of cellular uptake determined corona (*in situ* interface)



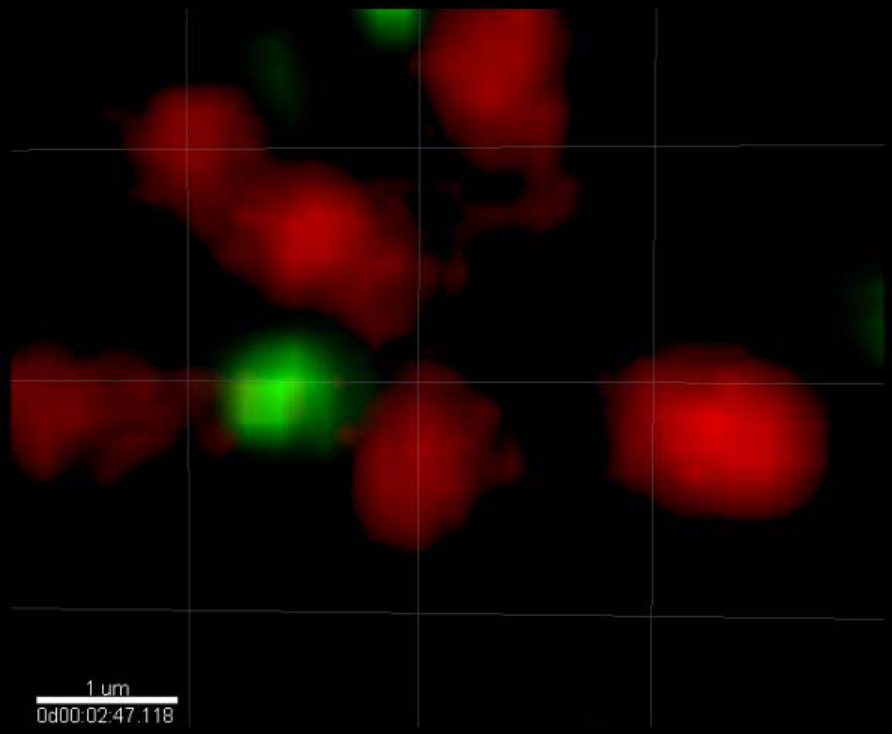




LDL is on surface
When LDL Receptor is silenced
Particle uptake greatly reduced

Lesniak et al ACS Nano 2012
Salvati et al Nature Nano 2012

FATE



Bio-accumulation
Long Term, Repeated Dose
'Low Acute Toxicity'

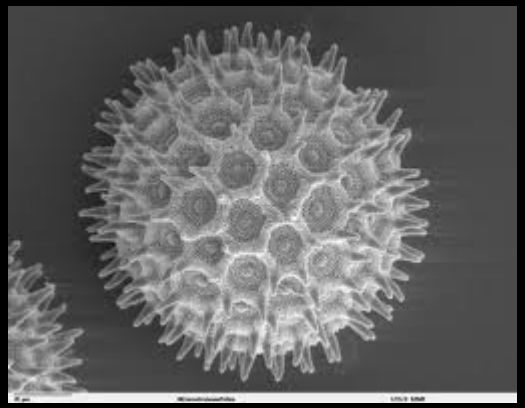
•Biological processing at Nanoscale, recognition and accumulation

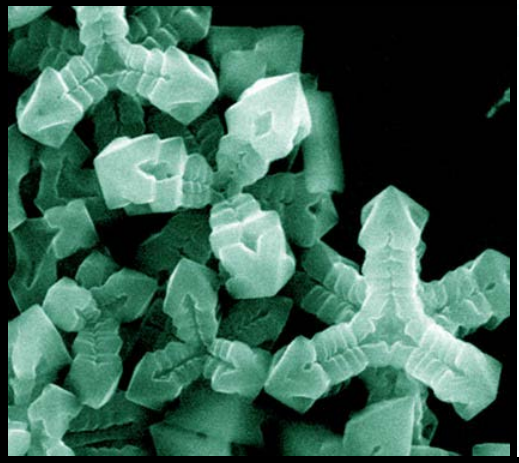
•Non-degradable or slowly degradable materials for long periods in new places in organisms and environment

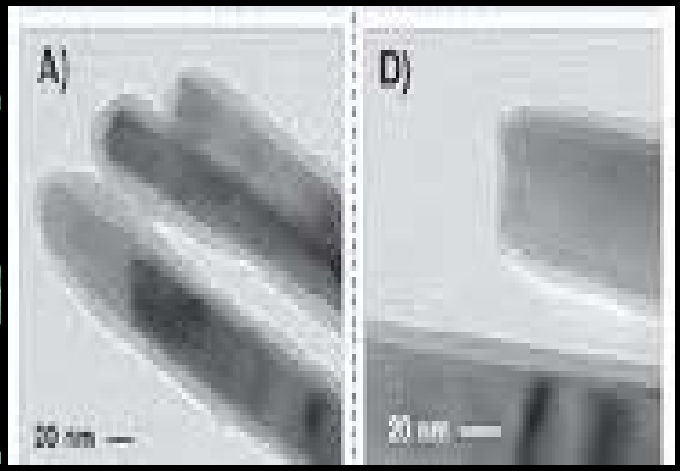
IN ORGANISMS AND ENVIRONMENT

THE FUTURE-IS HERE

TIME TO MOVE ON, AND DEAL WITH ENORMOUS RANGE OF NEW MATERIALS?

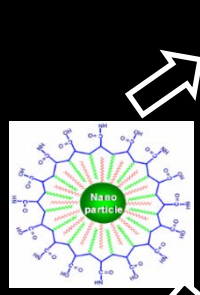






Name These, Classify these

REGULATION FOR FUTURE
A PRACTICAL WAY FORWARD?



Application 2 – *in vitro* sensor

Application 1 – composite

Application 3 - cosmetic

Application 4 – solar cell

Material manufacturing

Concerns:
Occupational exposure
Production waste

Product formulation

Concerns:
Occupational exposure
Production waste

Product in use

Concerns:
Consumer exposure
Domestic waste

End of life / disposal

Concerns:
Environmental exposure
Recycling costs
Food chain effects

VALUE CHAIN REGULATION-WITHOUT PREJUDICE?

GLOBAL CONVERSATIONS

- EXPOSED TO WHAT (EXACTLY) DURING LIFE CYCLE (COR1)
  - Characterization modifications from environment, formulation,
- FUTURE MATERIALS, NAME THEM, CLASSIFY PREDICTION
  - Predictors of biodistribution, fate (COR2,3)
  - Parameters of biodistribution, ***useful*** classification and organization of data, safety by design (COR5)
- ENABLING AND REGULATING THE FUTURE (COR6)
  - Risk Management, Risk Control to *enable* (safely)
  - Priviliged pathways of lowered risk