Applications of Nanotechnology to Medicine

Seventh Science Conclave

IIIT Allahabad

December 2014

Nanotechnology in Biomedical Science

Areas of impact

- Drug delivery and new therapies
- Diagnostic analyses
- Biological research

Drug Delivery

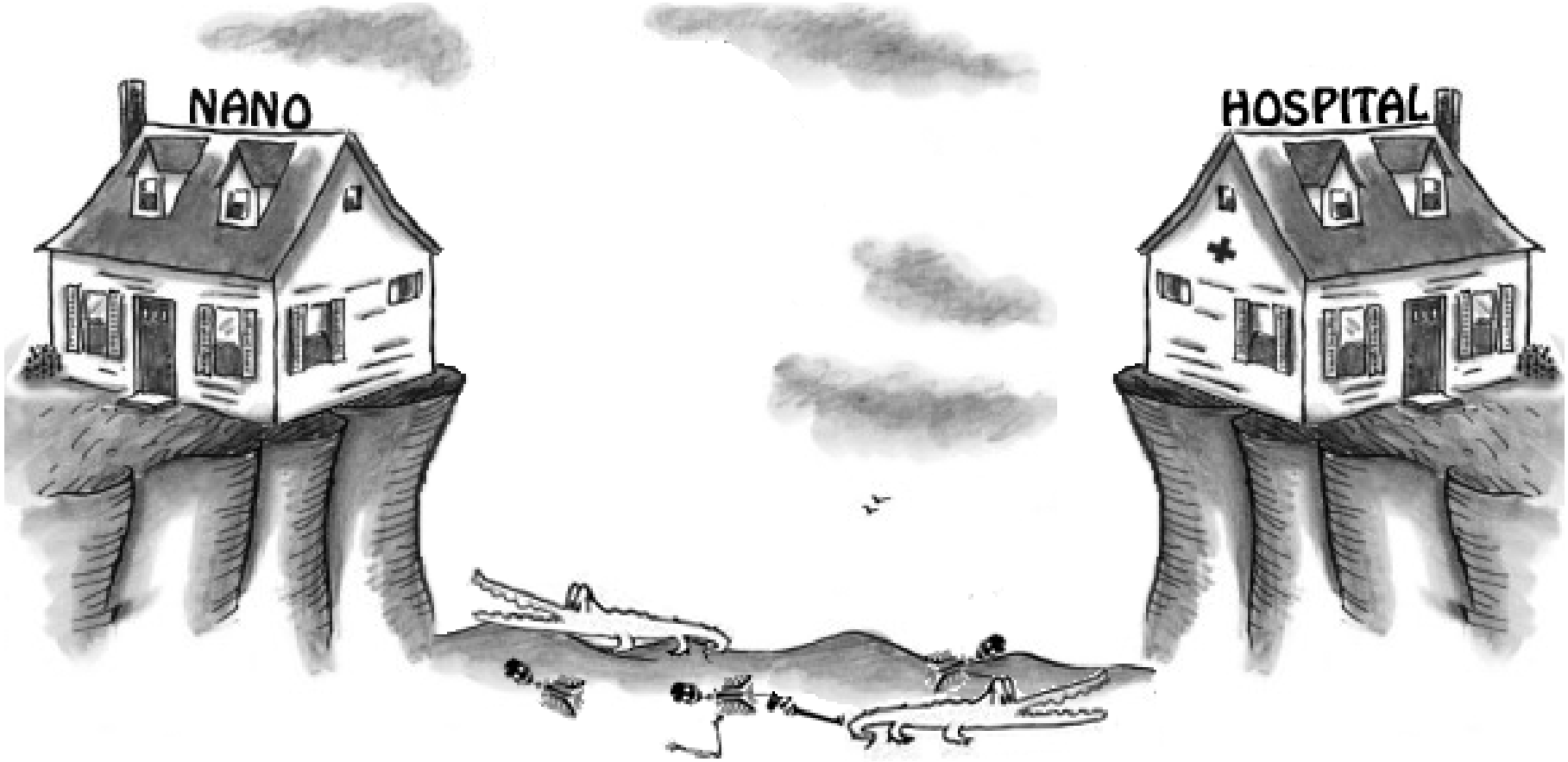
RICE

Nanoscience, translation, clinic

http://lapotko.rice.edu

RICE

Nanoscience, translation, clinic



http://lapotko.rice.edu

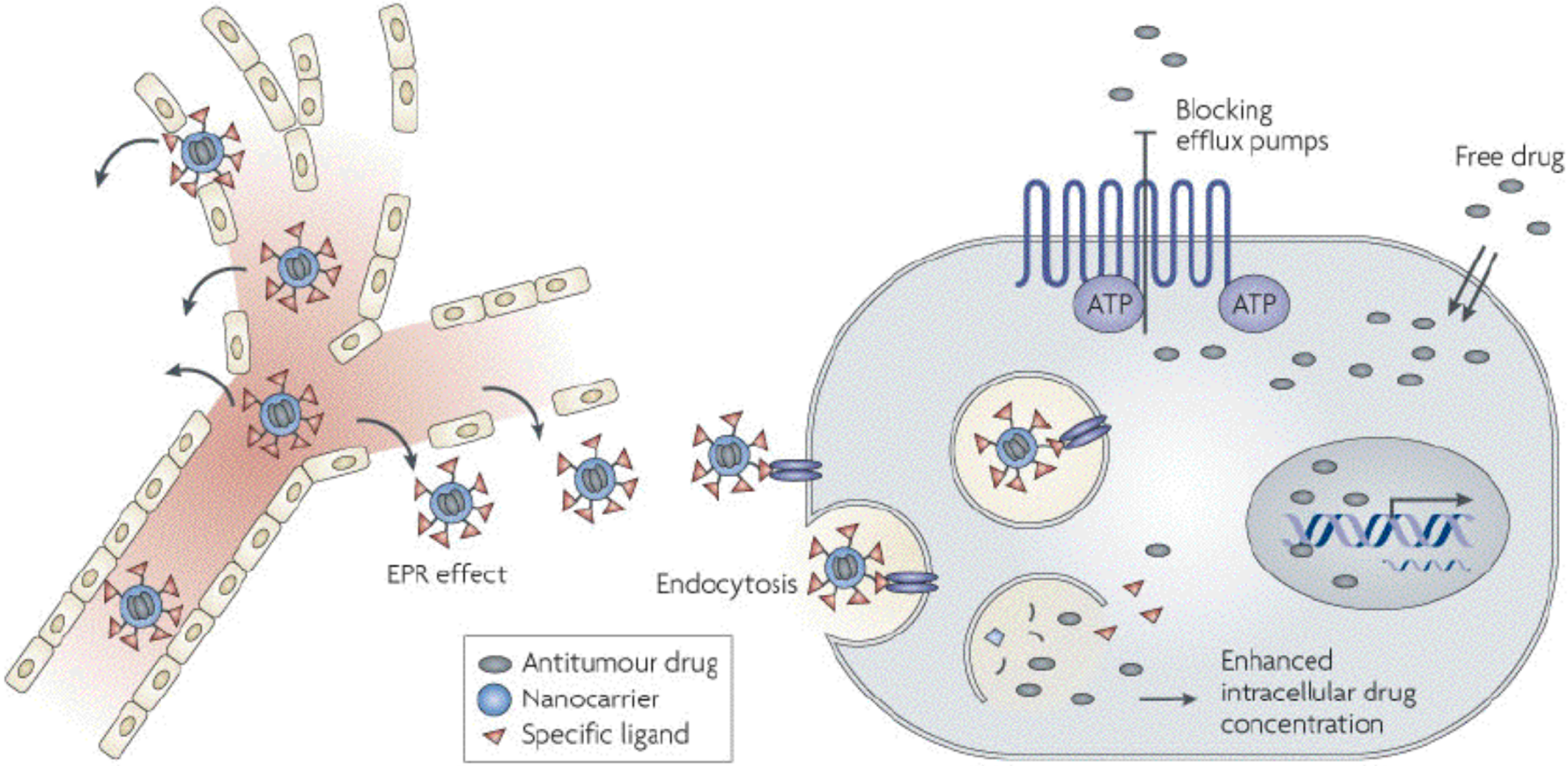
Commercial Nanotherapeutics

Selected nano-based therapeutics and their 2009 sales (*represents 2008 sales)

Product	Particle type	Drug /Application	Technology by /Licensed to	Status	2009 Sales ($M)
TriCor	Nanocrystal	Fenofibrate	Elan/Abbott	Marketed	1,125.0
Rapamune	Nanocrystal	Sirolimus	Elan/Wyeth	Marketed	343.0
Ambisome	Liposomal	Amphotericin B	Gilead Sciences	Marketed	258.6
Abraxane (since 2005)	Nanoparticle	Paclitaxel	American Bioscience	Marketed	350
Doxil *	Liposomal	Doxorubicin	ALZA	Marketed	227.0
Emend	Nanocrystal	Aprepitant	Elan/Merck	Marketed	313.1
Abelcet	Liposomal	Amphotericin B	Elan	Marketed	22.6
Triglide	Nanocrystal	Fenofibrate	SkyePharma Pharmaceuticals	Marketed	28.0
Amphotec *	Liposomal	Amphotericin B	ALZA/Three Rivers Pharmaceuticals	Marketed	3.7
Total					**$2,671M**

Source: Nanotechnology research directions for societal needs in 2020

Action of anticancer nanoparticle



Nanoparticle therapeutics: an emerging treatment modality for cancer, M. E. Davis, Z. Chen and D. M. Shin, *Nature Reviews: Drug discovery* **7**, 771 (2008).

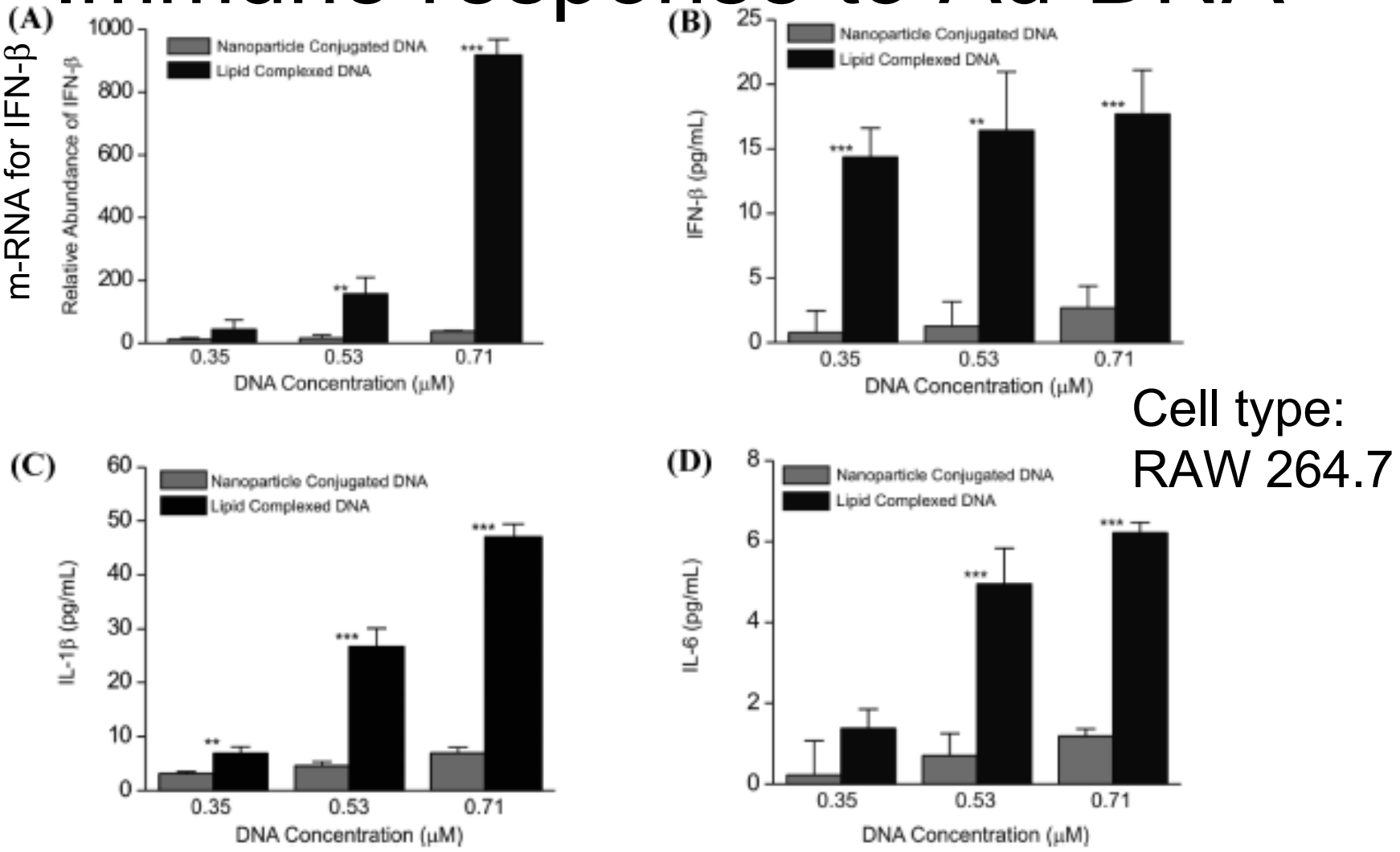
Nanoparticle drug delivery (possible uses)

- Cancer therapy,antifungal,antiemetic, cholesterol control (previous slide)
- MRI contrast agents
- Radioactivity imaging agents
- Osteoporosis drugs
- Antibacterial or antiviral delivery

Drug delivery advantages

- Can excite minimal immune responses.

Immune response to Au-DNA



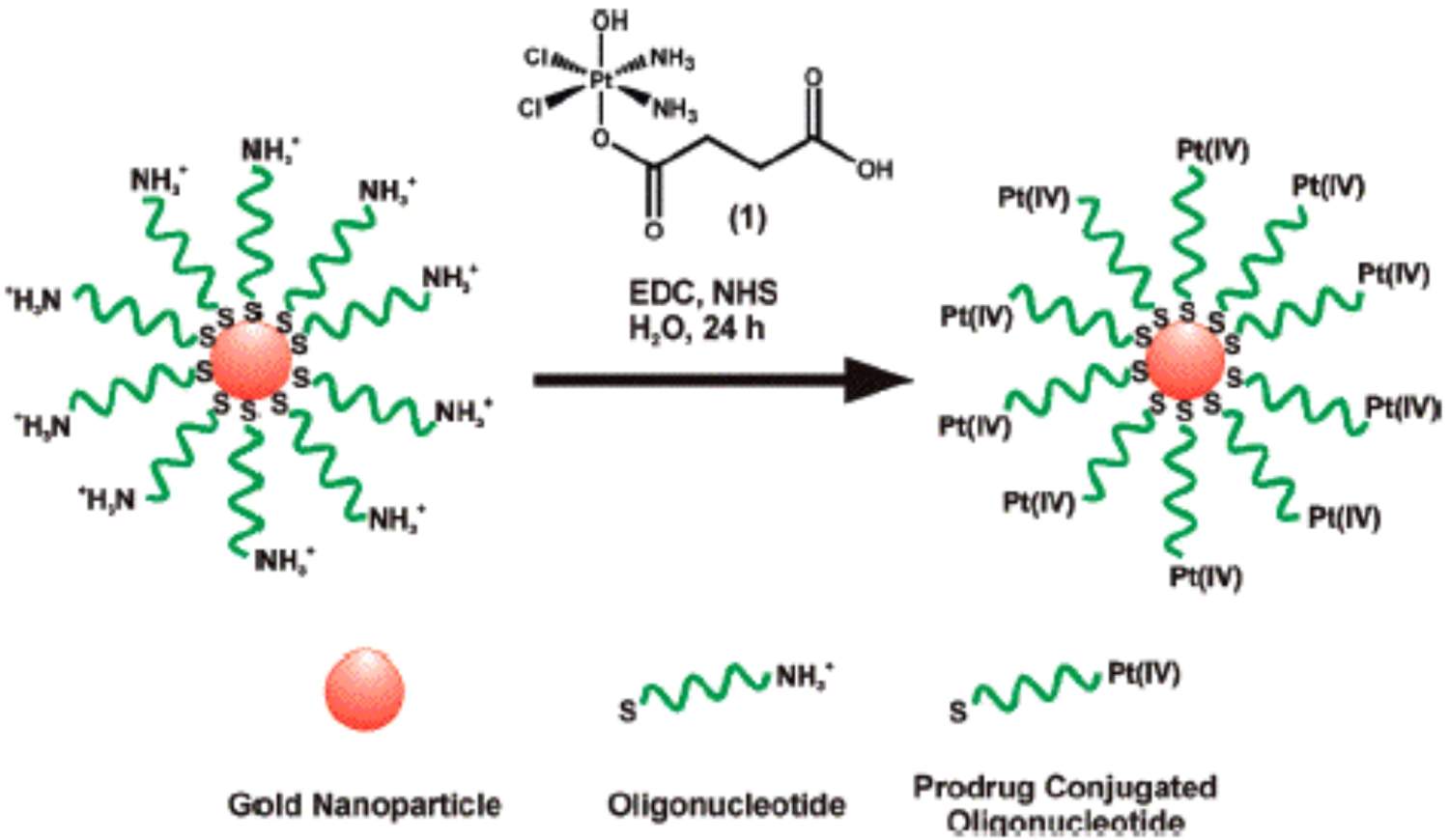
Cell type:
RAW 264.7

M. D. Massich, D. A. Giljohann, D. S. Seferos, L. E. Ludlow, C. M. Horvath, and **C. A. Mirkin**, Regulating Immune Response Using Polyvalent Nucleic Acid-Gold Nanoparticle Conjugates, Molecular Pharmaceutics **6** 1934 (2009).

Drug delivery advantages

- Can excite minimal immune responses.
- Can carry a large payload.

Au delivery of Pt anticancer drug



S. Dhar, W. L. Daniel, D. A. Giljohann, **C. A. Mirkin**, and **S. J. Lippard**, Polyvalent Oligonucleotide Gold Nanoparticle Conjugates as Delivery Vehicles for Platinum(IV) Warheads, J. Am. Chem. Soc. **131**, 14652 (2009).

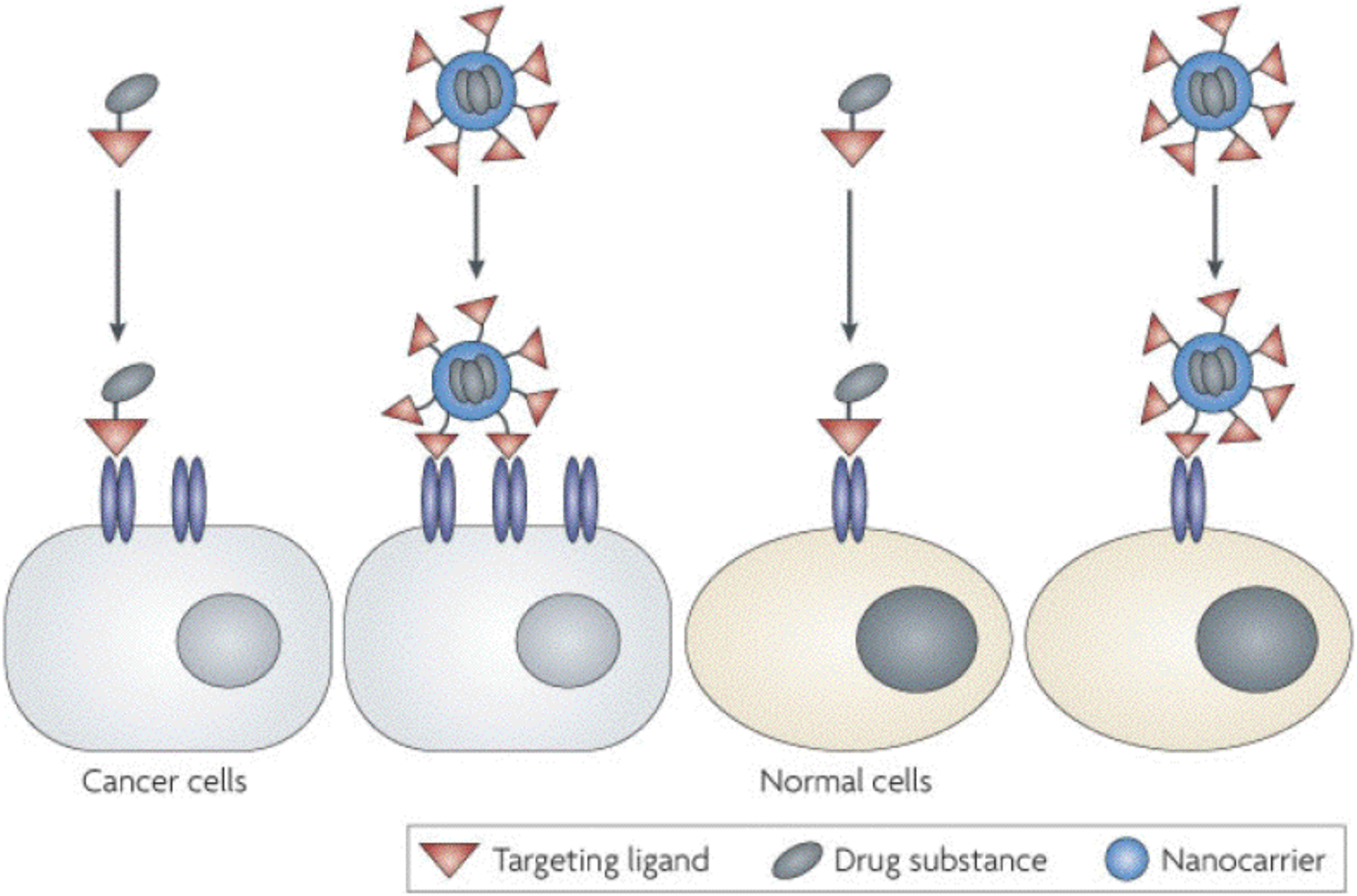
The Pt oxidation state matters

Pt(IV) complexes are reduced in the intracellular milieu to yield the cytotoxic Pt(II) species through reductive elimination of axial ligands.

Drug delivery advantages

- Can excite minimal immune responses.
- Can carry a large payload.
- Can carry multiple binding ligands.

Nanoparticles hold multiple ligands



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Drug delivery advantages

- Can excite minimal immune responses.
- Can carry a large payload.
- Can carry multiple binding ligands.
- Can carry multiple different drugs.

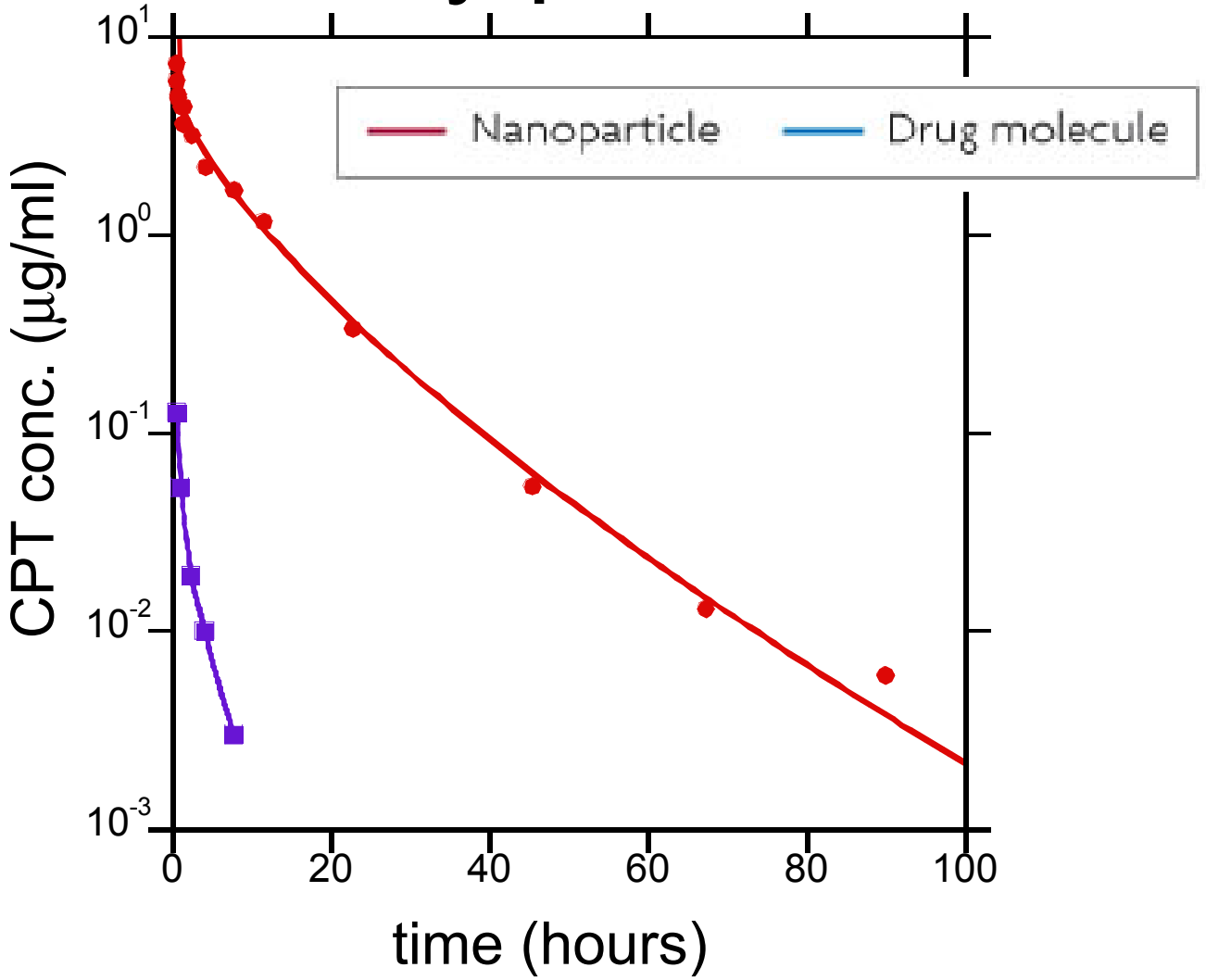
Overcoming evolution

Both bacteria and cancer cells evolve defenses against therapeutic agents. These defenses can be attacked by same nanoparticle that carrys the cell killer.

Drug delivery advantages

- Can excite minimal immune responses.
- Can carry a large payload.
- Can carry multiple binding ligands.
- Can carry multiple different drugs.
- Can maintain drug concentrations longer.

Decay profiles

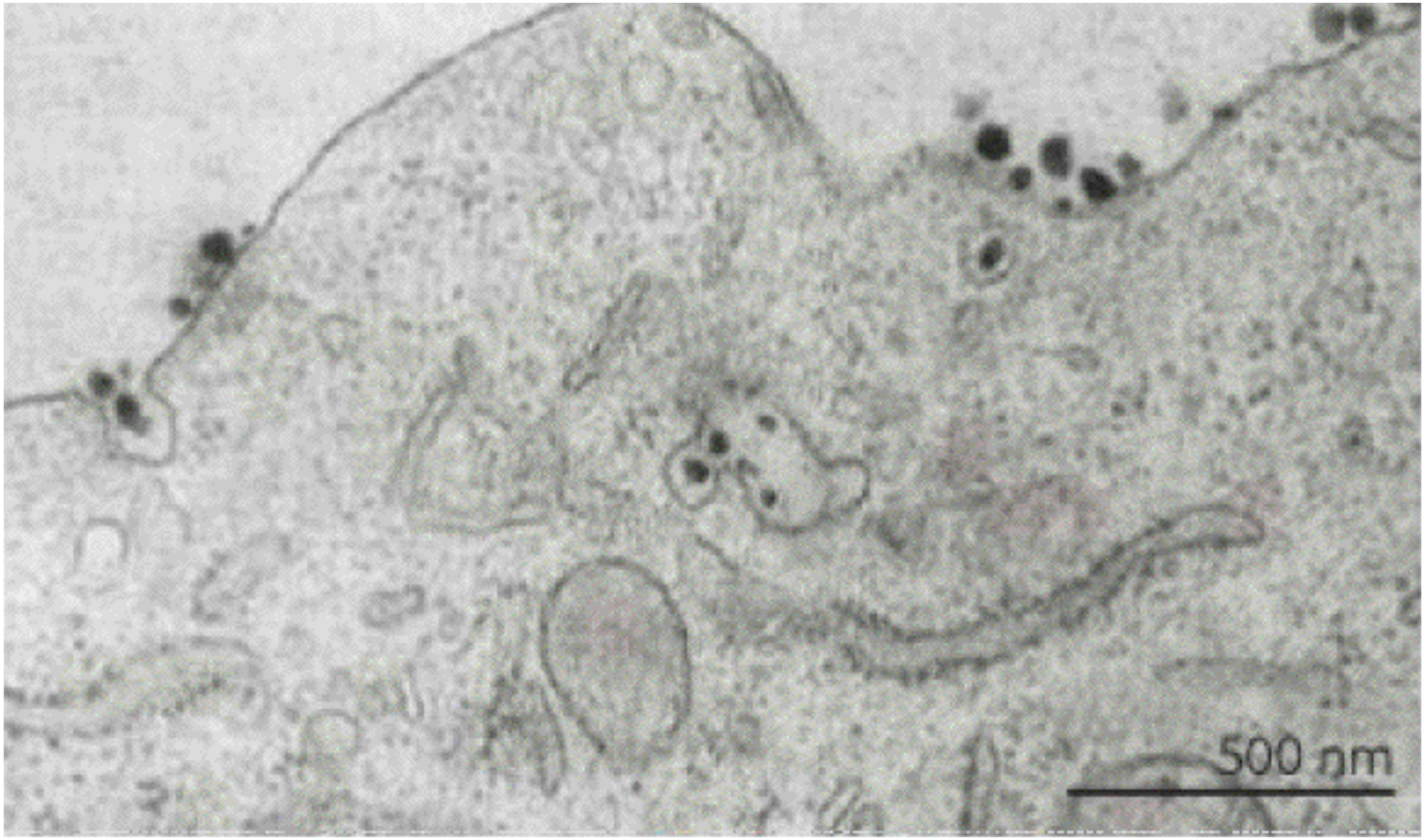


T. Schluep, J, Cheng, K. T. Khin, M. E. Davis, *Cancer Chemother Pharmacol* (2006) 57: 654. (redrawn)

Drug delivery advantages

- Can excite minimal immune responses.
- Can carry a large payload.
- Can carry multiple binding ligands.
- Can carry multiple different drugs.
- Can maintain drug concentrations longer.
- Typically they enter by endocytosis, which can bypass some resistance mechanisms.

TEM of nanoparticles entering cell through endocytosis



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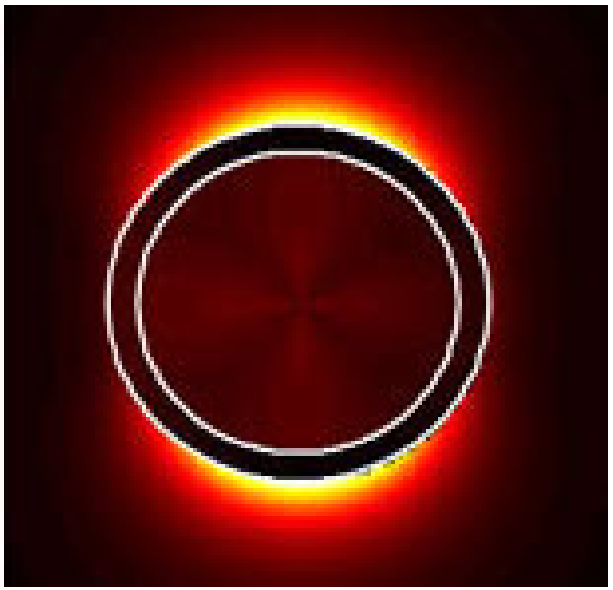
Au nanoshells tune absorption λ

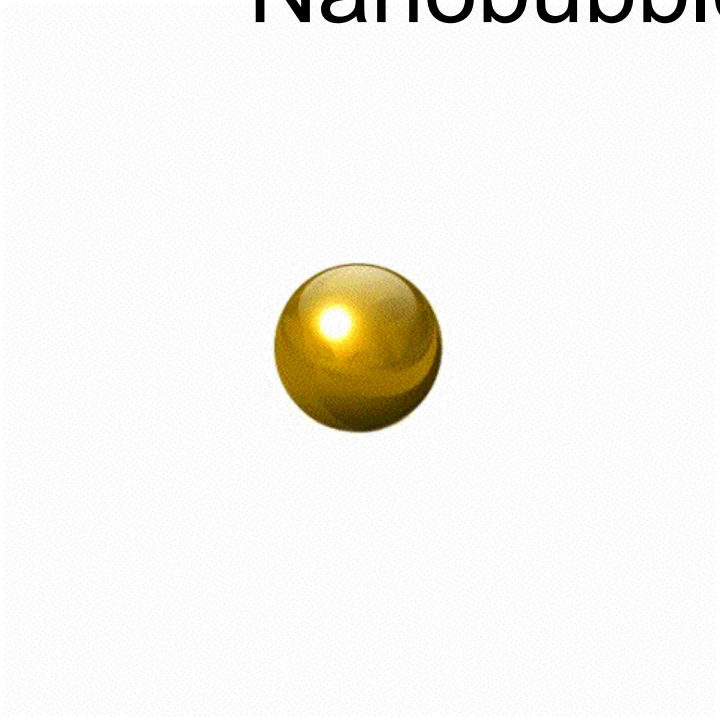


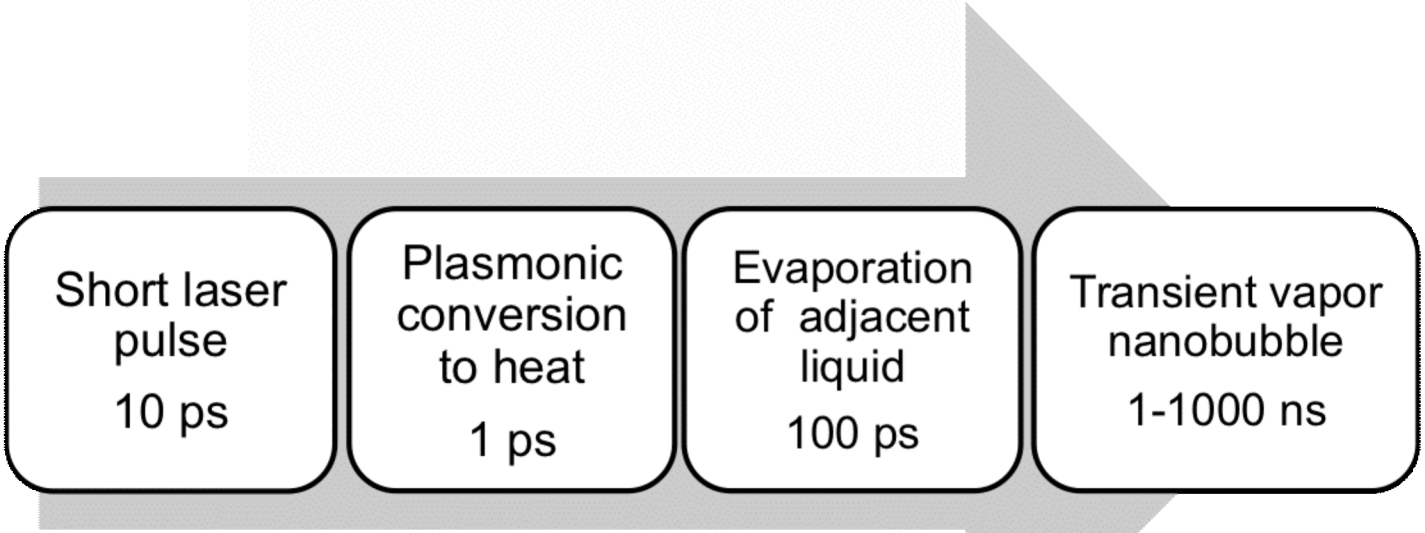
N. Halas, Rice University website

Cancer phototherapy

- Use a near-IR laser to heat gold nanoshells and destroy the cancer cell (N. J. Halas, J. L. West).
- Use a pulsed near-IR laser to explode a cluster of gold nanoshells and destroy the cancer cell (D. O. Lapotko).

Laser pulse + gold = Plasmonic Nanobubble





On-demand non-stationary transient event, not a particle

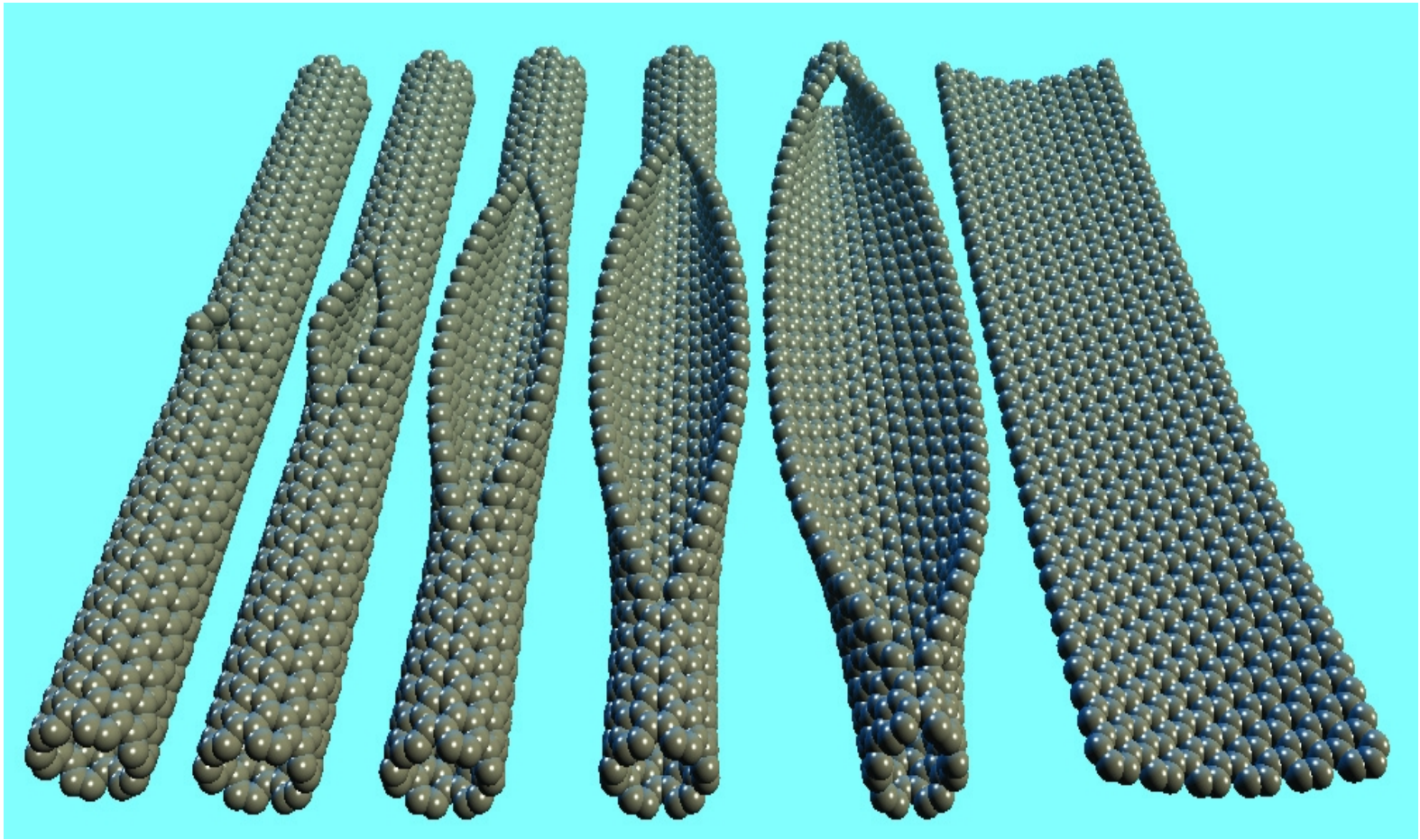
Mitigating Oxygen Radical Damage

When blood flow has been temporarily stopped by a clot as in stroke, affected cells retreat into a new state.

When blood flow is restored, the flood of O_2 creates harmful cell killing radicals.

A group headed by James Tour has developed an oxygen radical destroying drug therapy.

Longitudinal Unzipping of CNTs to Form Graphene Nanoribbons (GNRs)

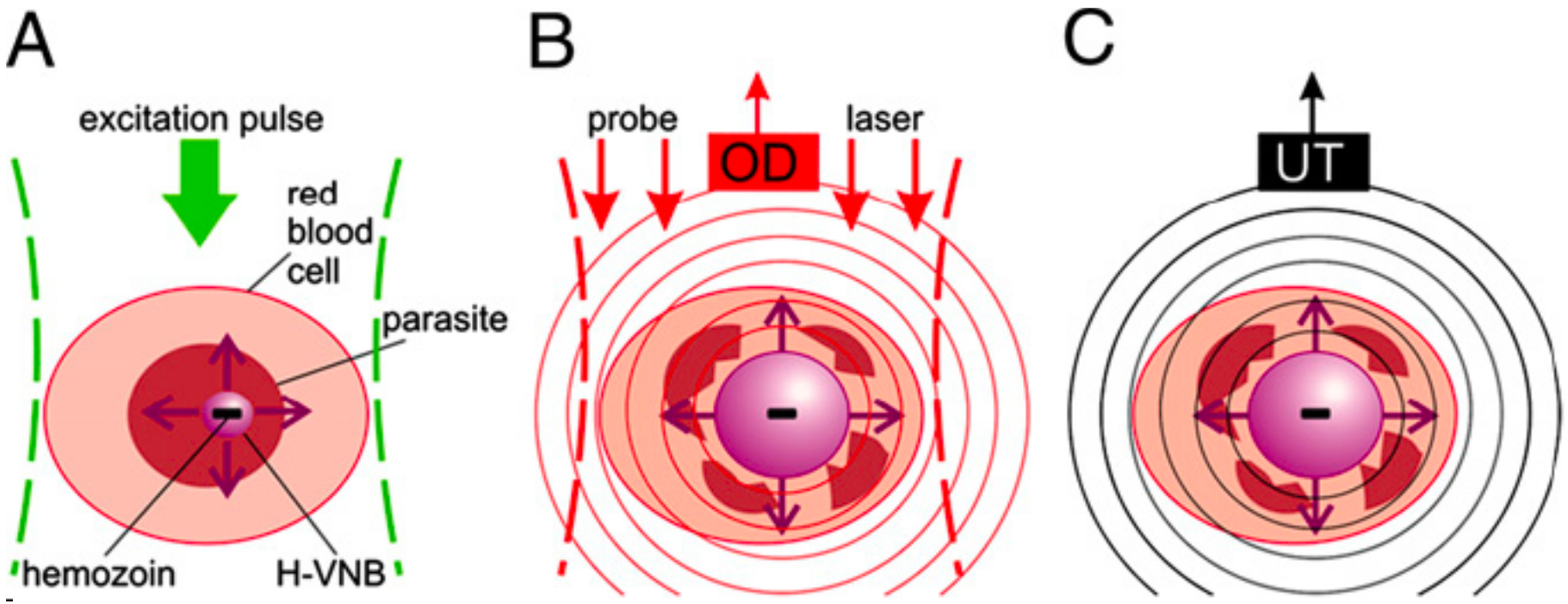


These carbon ribbons are chemically linked to polyethylene glycol (PEG) making them water (and blood) soluble. The result is called PEG-CNP, where CNP stands for carbon nanoparticle.

Injected into the blood along with clot busting drugs, the PEG-CNP greatly reduces oxygen radical damage to cells cut off by the clot.

Diagnostic Analyses

Non-invasive rapid malaria diagnosis



E. Y. Lukianova-Hleb,….,Dmitri Lapotka, Proceedings of the National Academy of Sciences, **111** 900-905 (2014)