Nano-Scale Engineering – 2

Nanoparticles, Nanowires and Graphene

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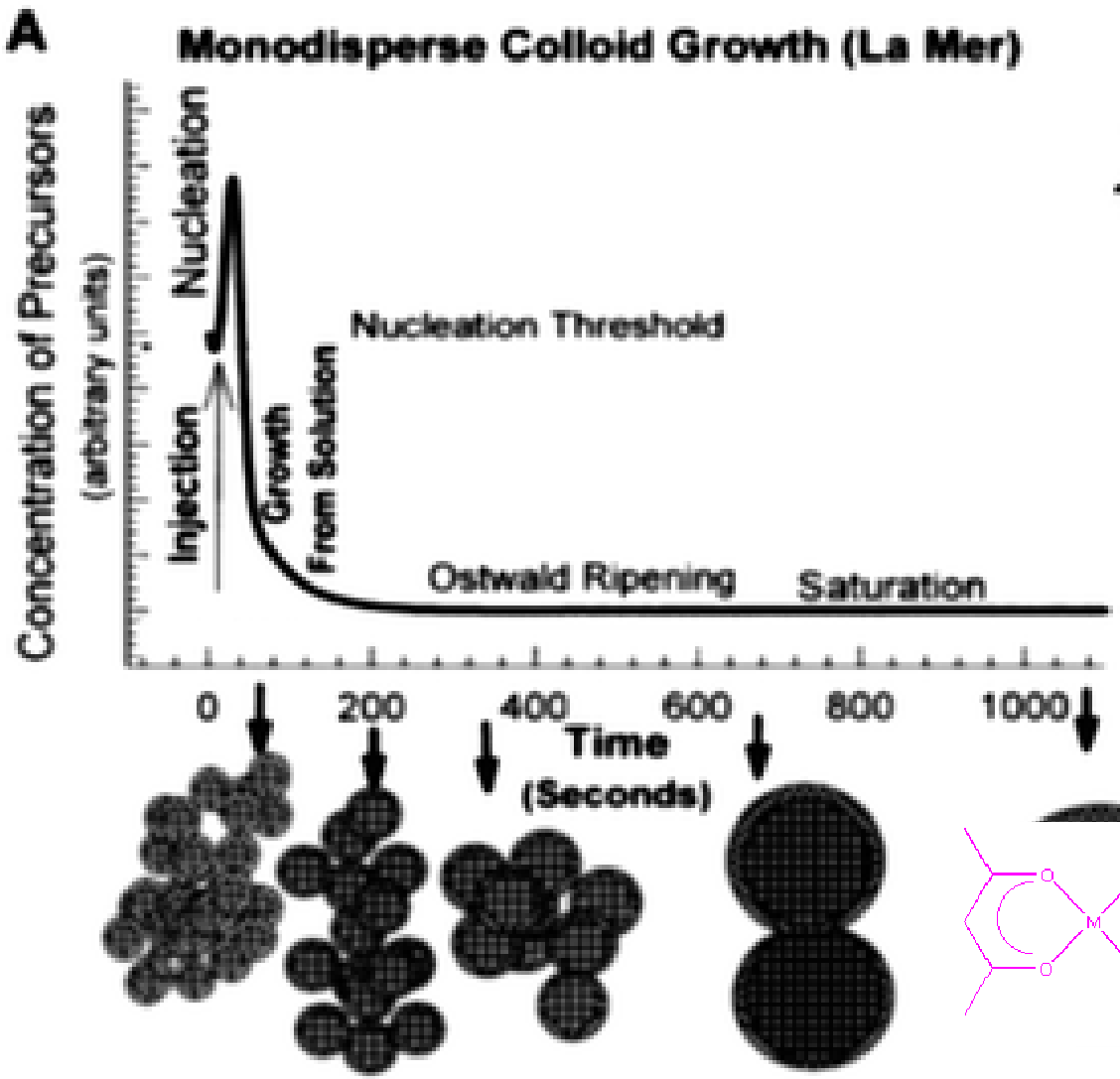
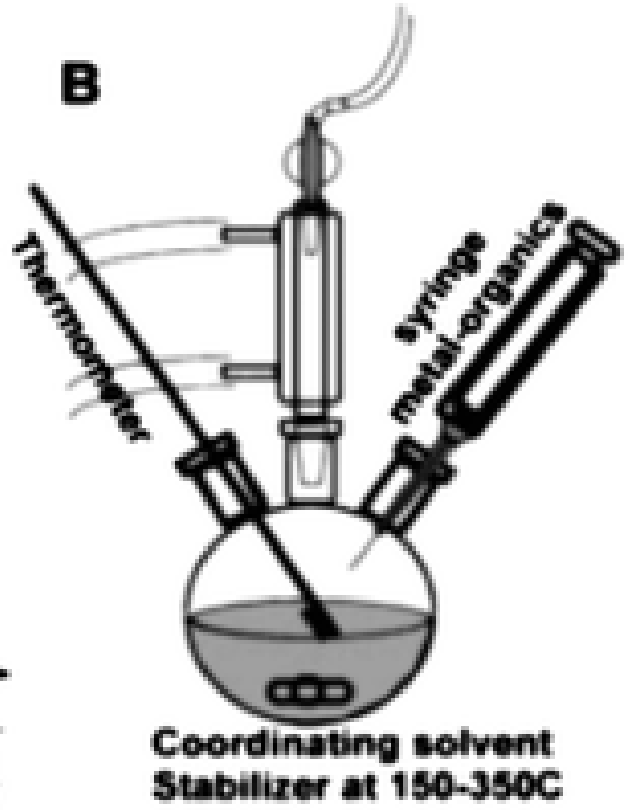
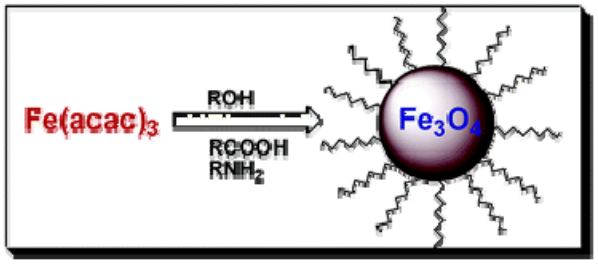
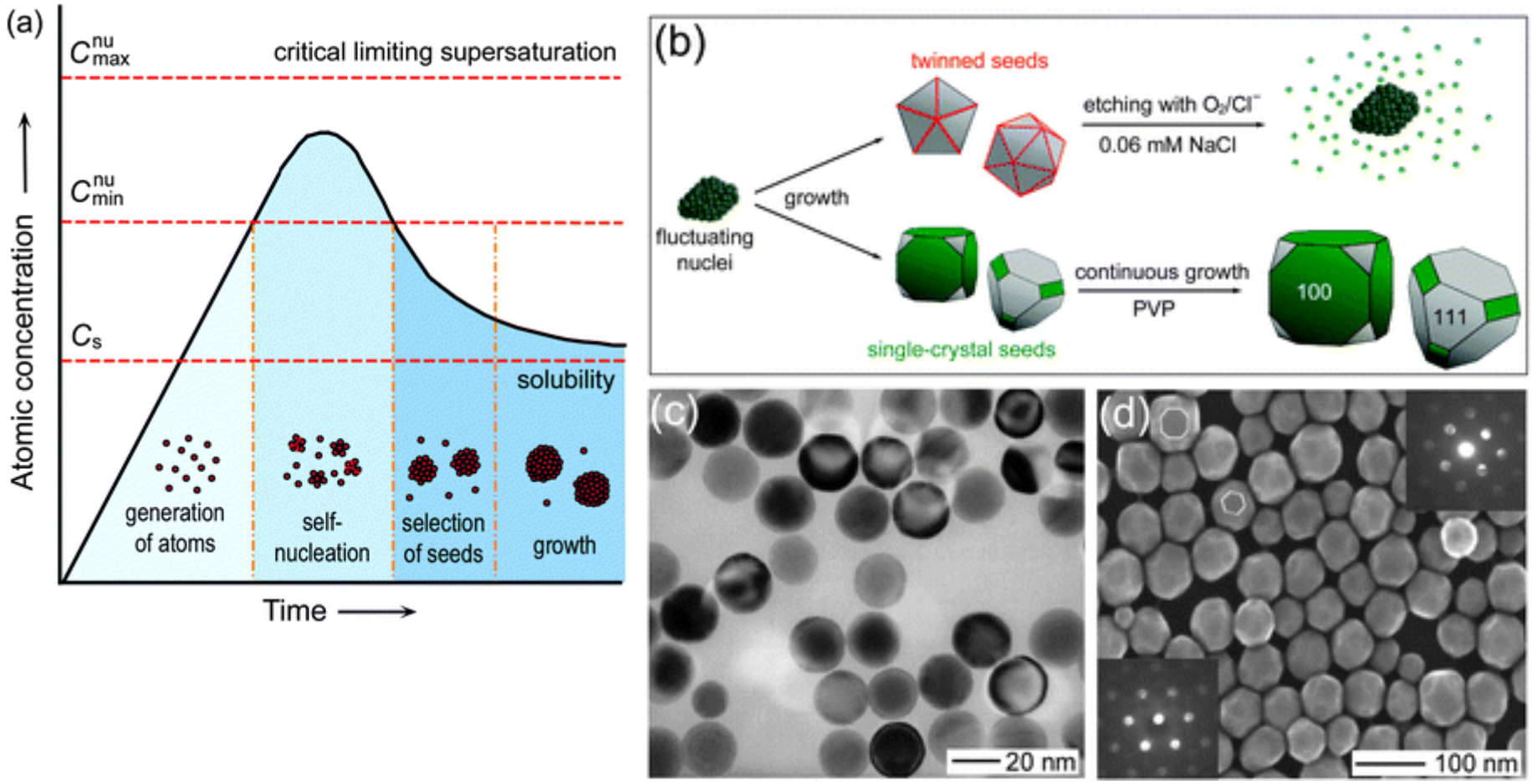
La Mer Model for Nucleation, Growth & Ripening to Form Nanoparticles







Controlled synthesis of colloidal silver nanoparticles in organic solutions: empirical rules for nucleation engineering

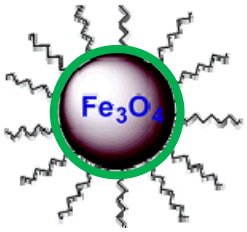


Yugang Sun, Chem. Soc. Rev., 2013, 42, 2497.

Self-Assembled Monolayers

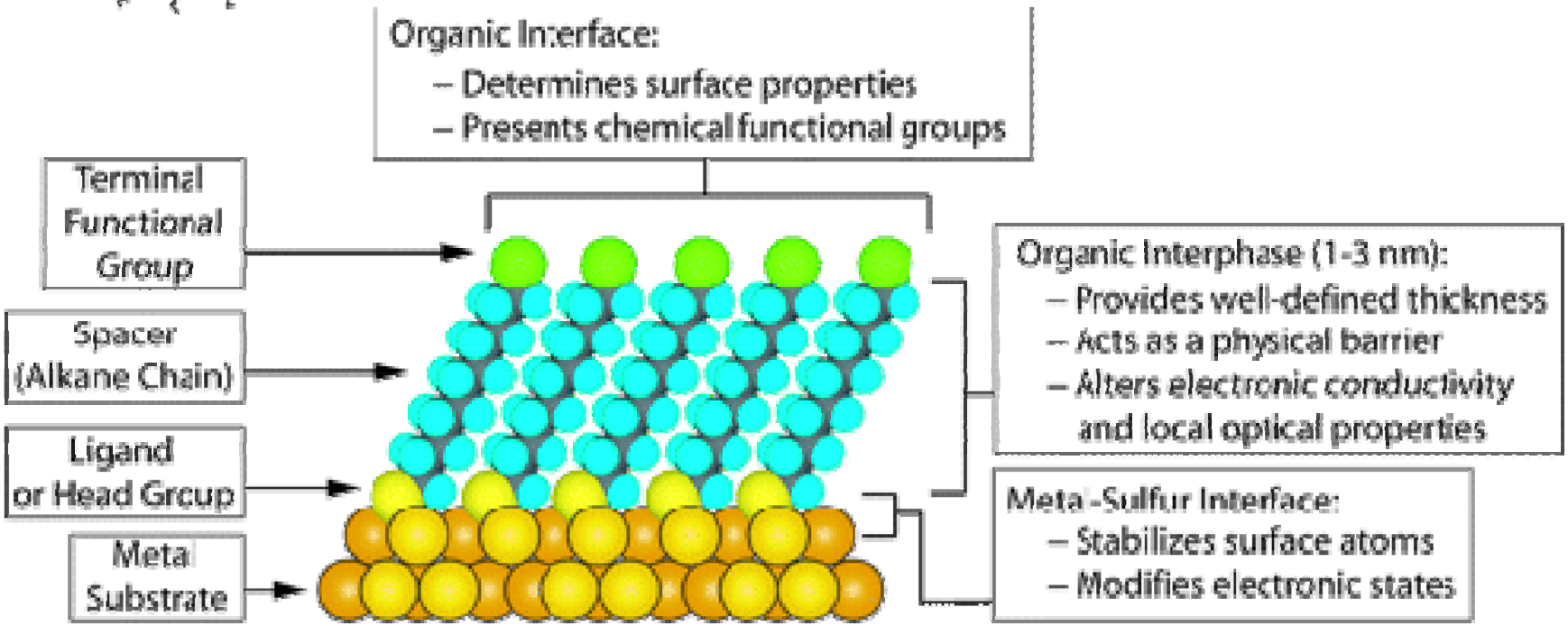
A single, nanoscale layer of ordered molecules adsorbed on a substrate due to bonding between the surface and molecular head groups.

✓ spontaneous process



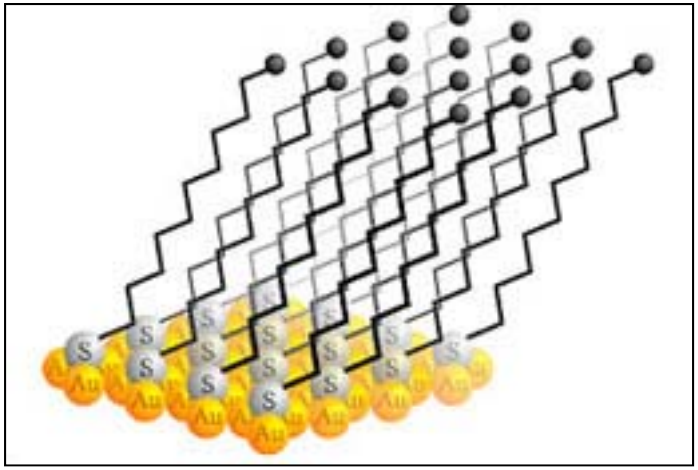
Importance of SAMs:

• modification of adhesion and wetting properties of surfaces; corrosion protection; chemical and biochemical sensors; insulating layers in microelectronic circuits; optoelectronic thin films; and "molecular electronics"

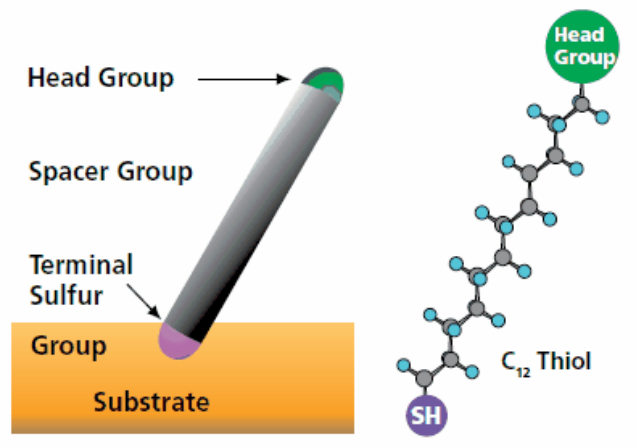


Two main types of SAM

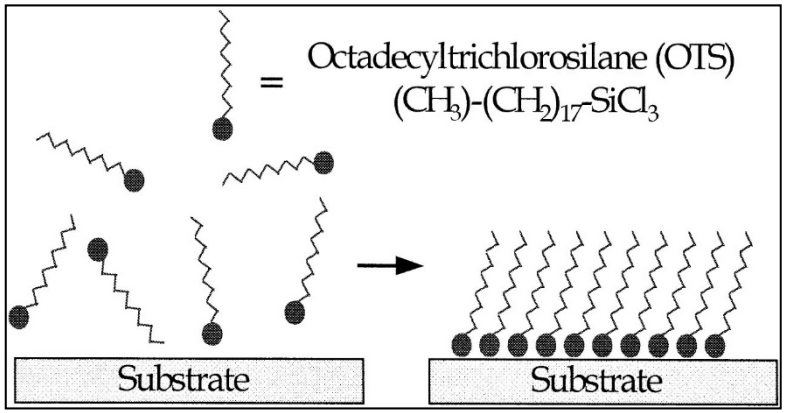
1. Alkylthiol SAMs



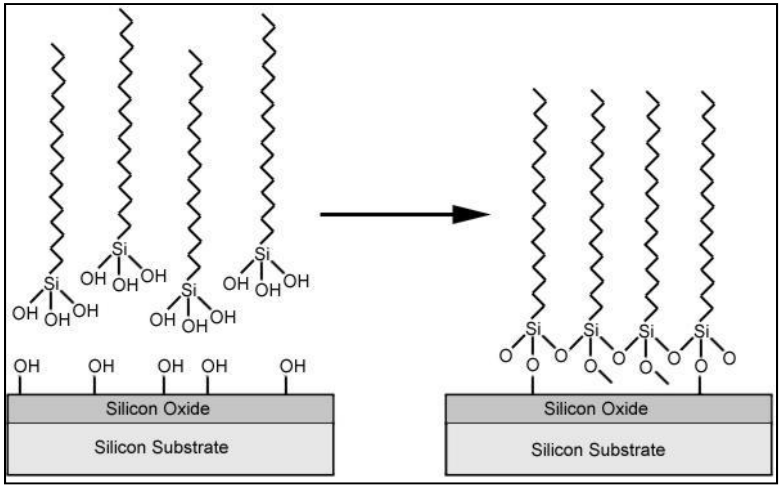
- Adsorption best on gold
- Elimination of H to form bond



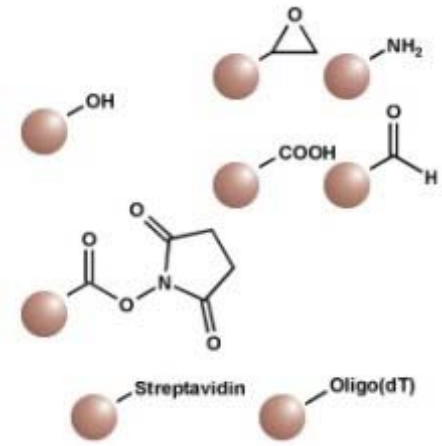
2. Chlorosilane -based SAMs

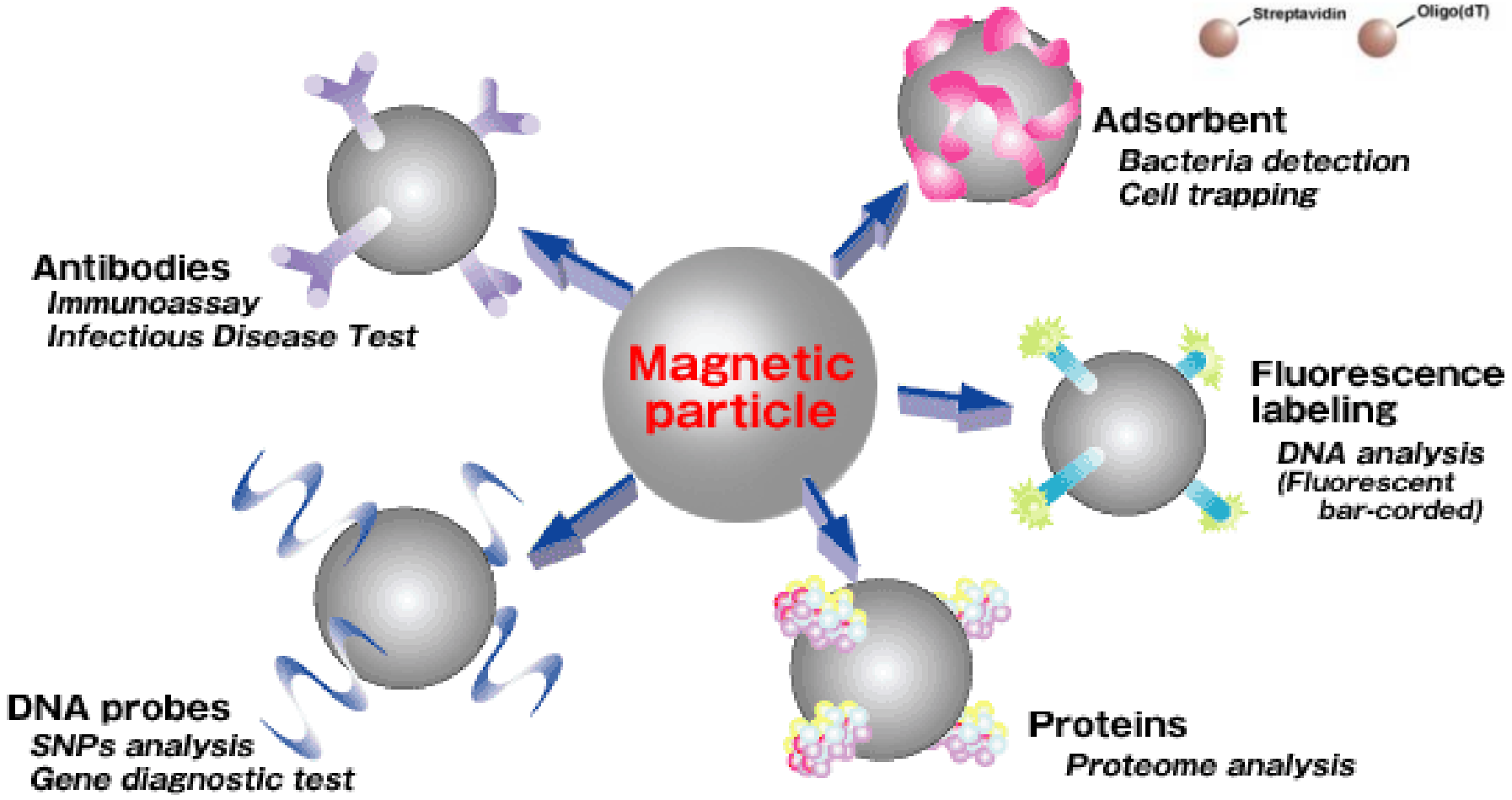


- Adsorption best on an oxide…-OH groups
- SAM is hydrolized
- Elimination of H_2O to form O-Si-O bond



Functionalization of Beads

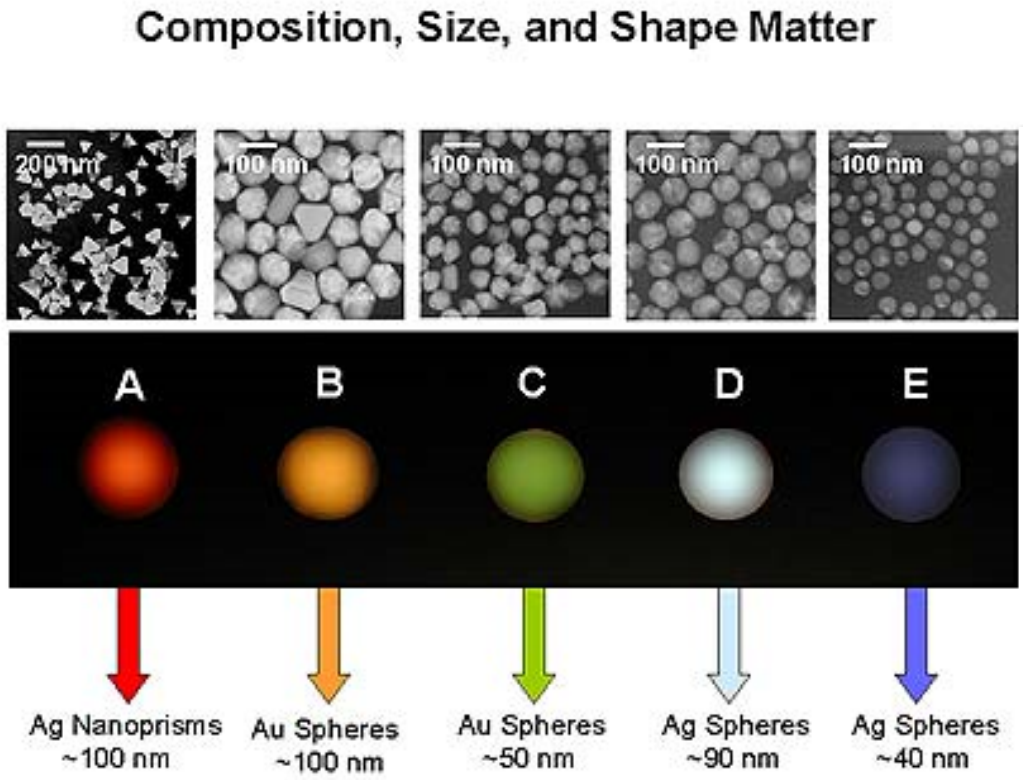


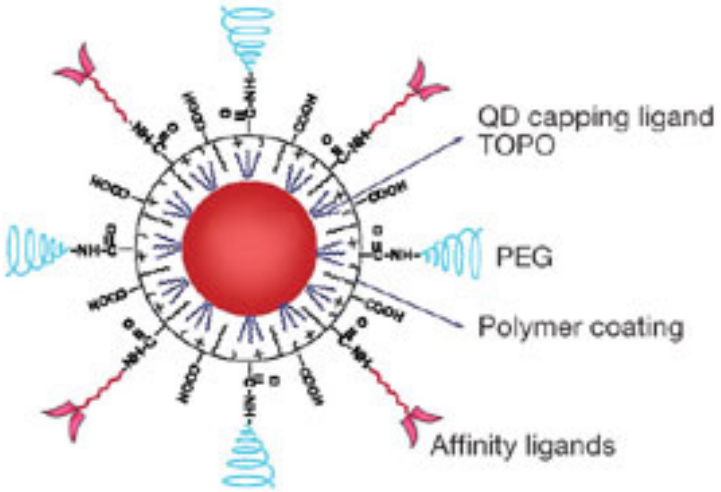


Imaging Using Quantum Dots

Reference: Nature Biotech. 22 (2004) pp. 969.

Nanoparticle Biomolecular Tags:





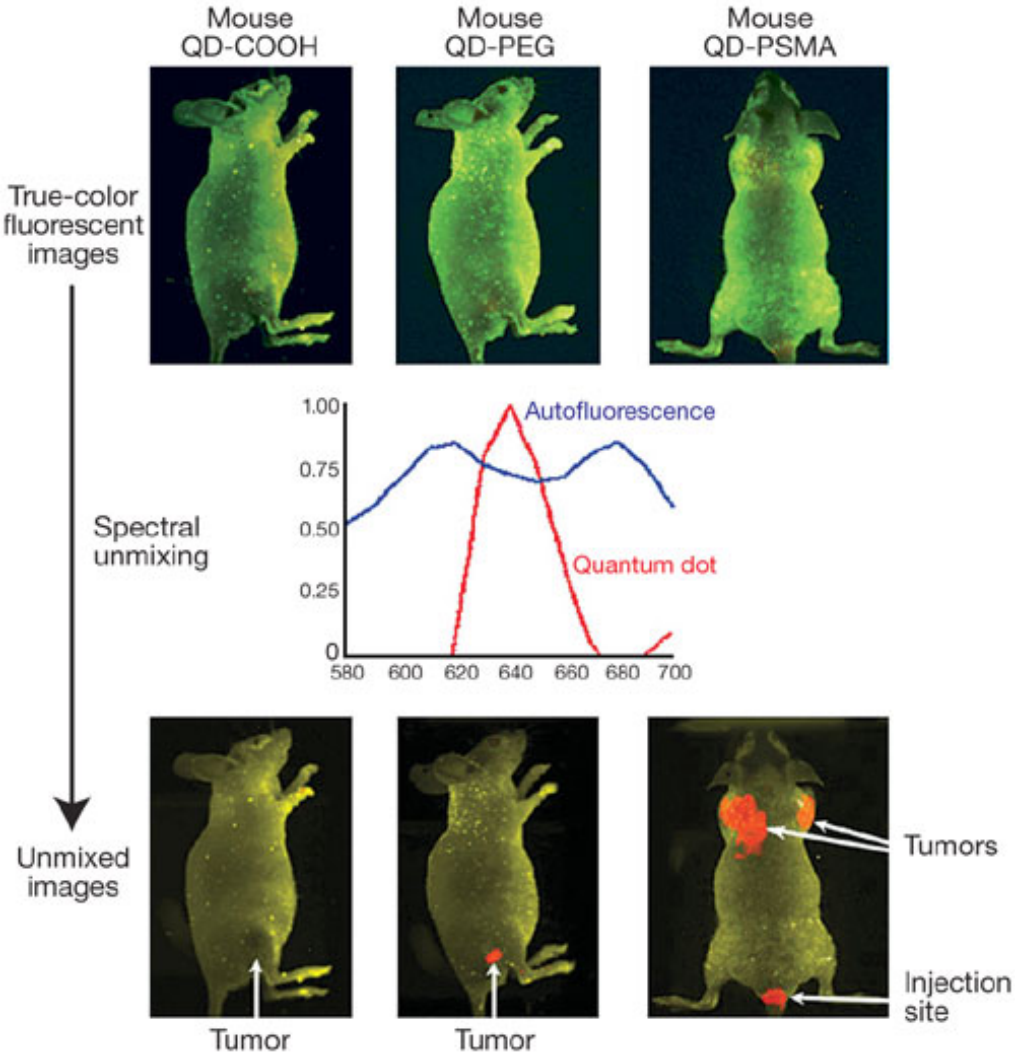
Nanoparticle ground state absorption energy:

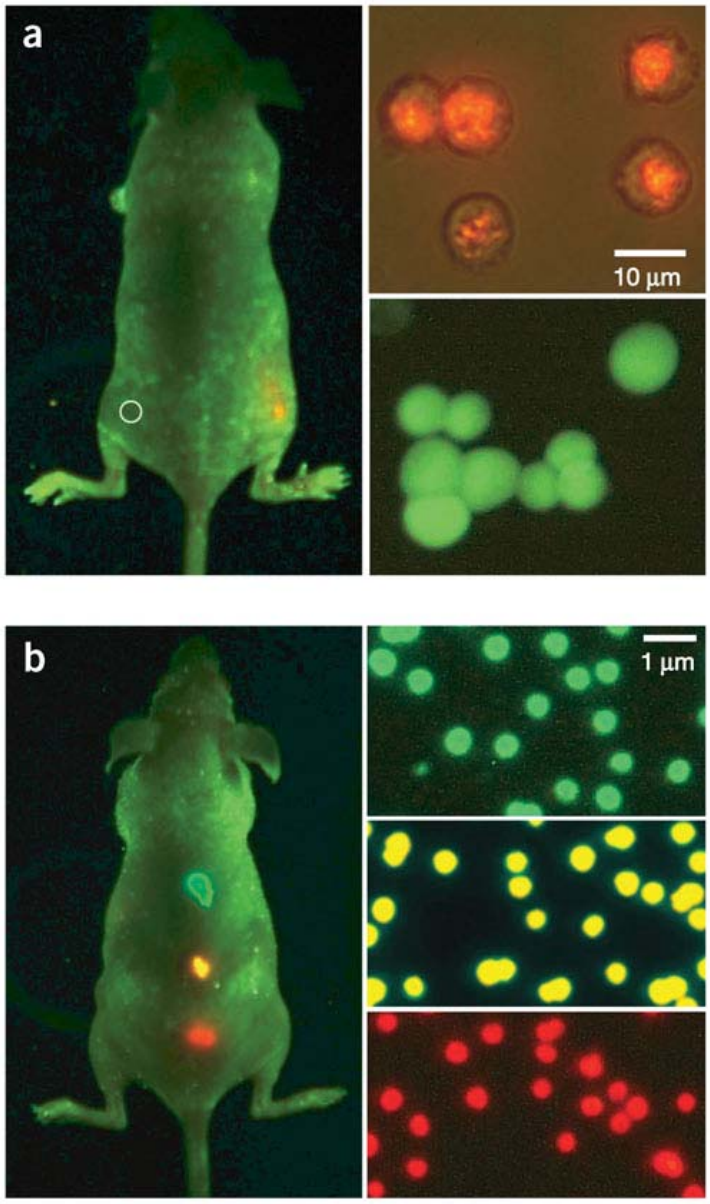
$$\hbar\omega = E_g + \frac{\hbar^2}{2m_e^* r^2}\pi^2$$

E_g = bulk semiconductor bandgap
r = nanoparticle radius

➡ Size dependent!

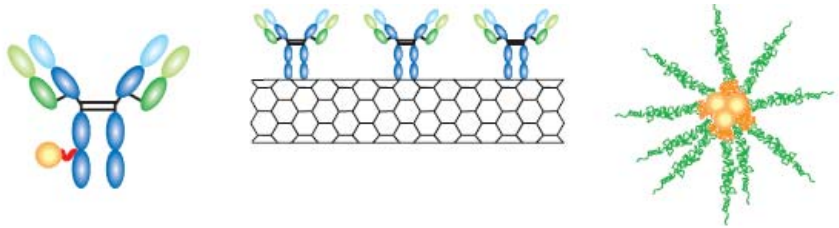
Nanoparticles for Imaging

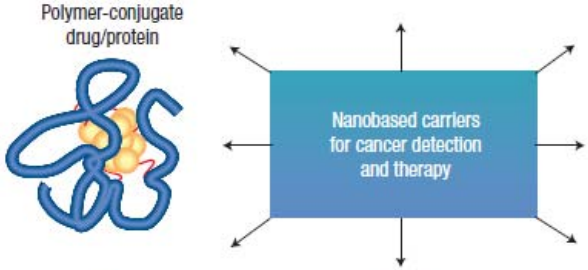


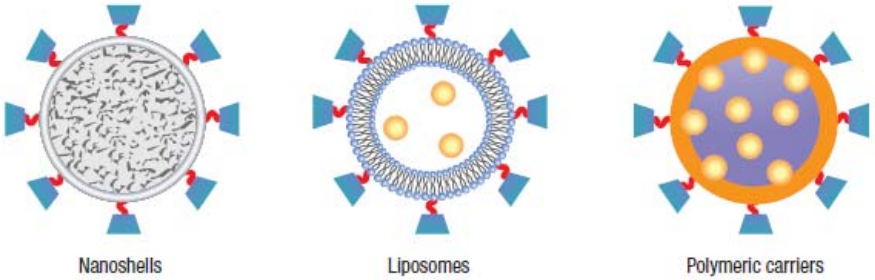


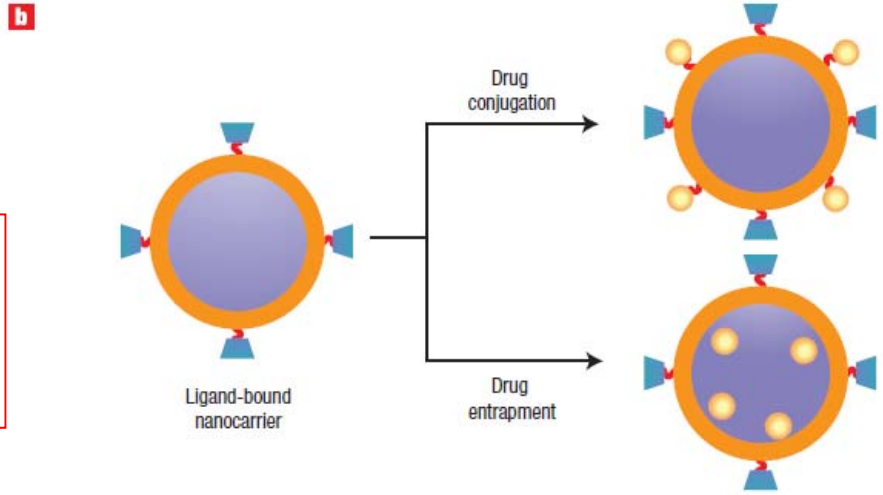
Multi-color experiments

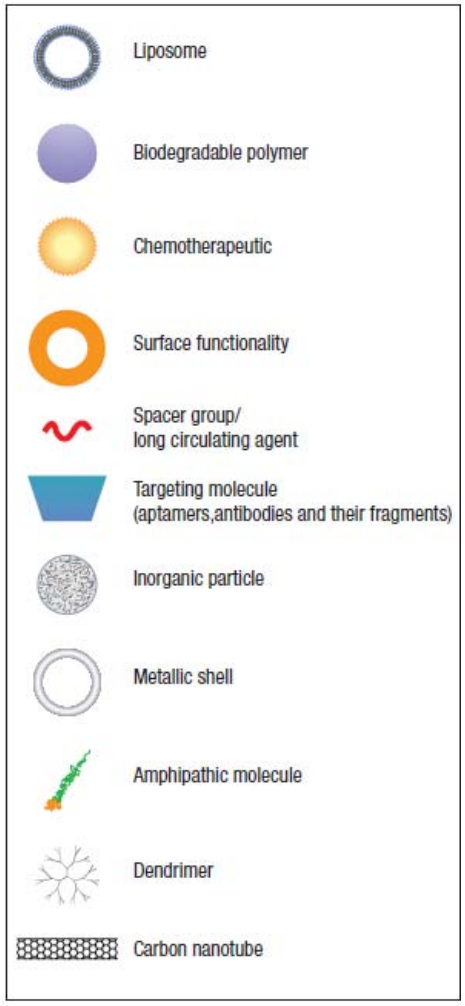
Nanocarriers for targeting cancer cells





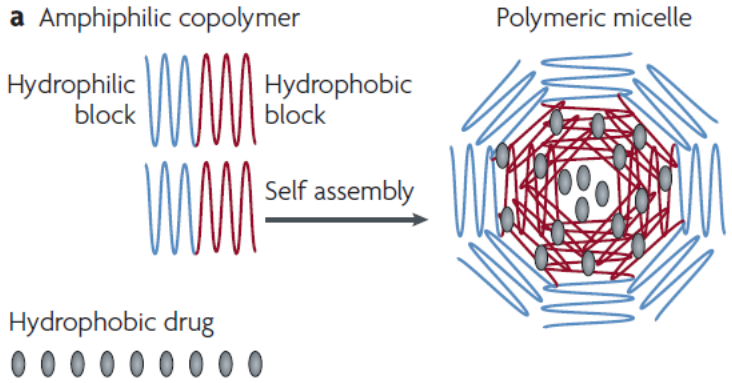


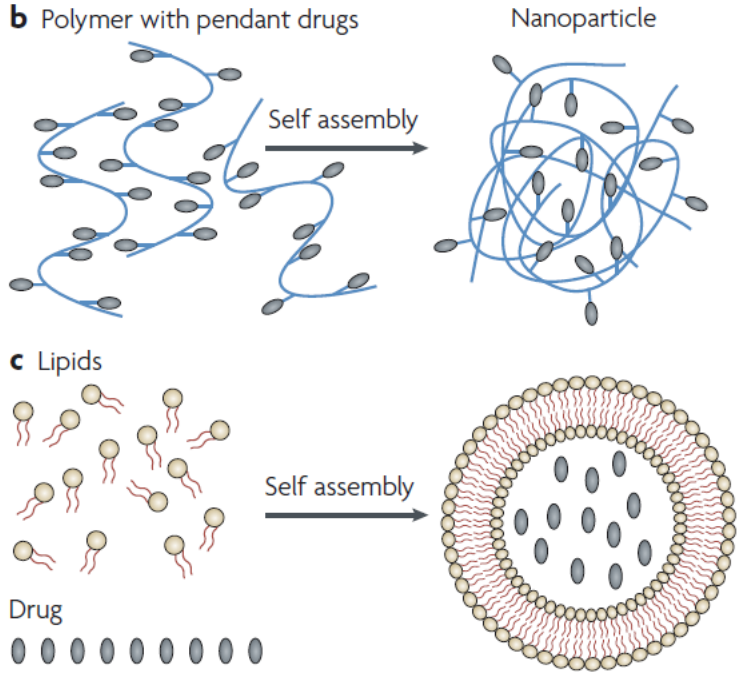


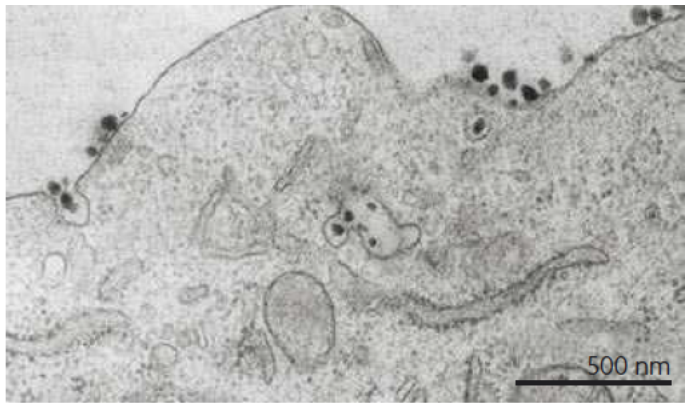


Peer et al., Nanocarriers as an emerging platform for cancer therapy, nature nanotechnology, Vol. 2, Dec. 2007, pp. 751-760.

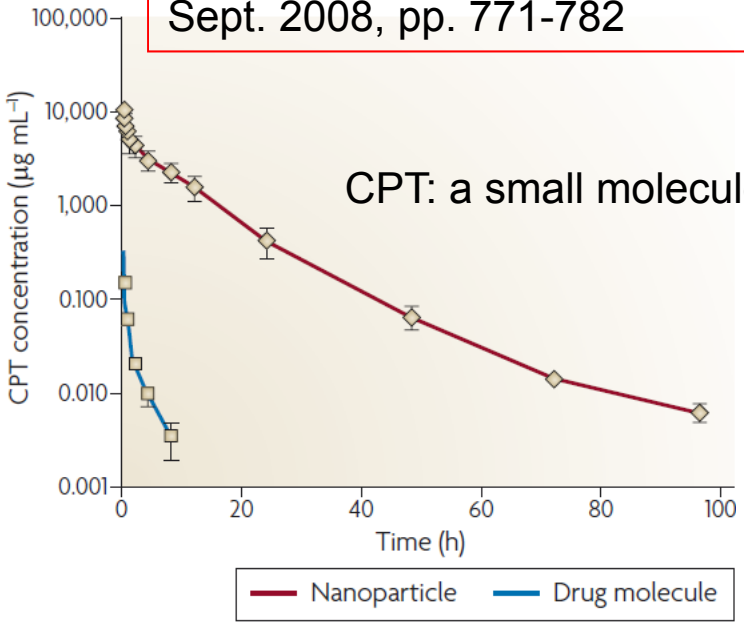
Nanoparticle therapeutics: an emerging treatment modality for cancer







Davis et al., Nature Reviews, Vol. 7, Sept. 2008, pp. 771-782



CPT: a small molecule drug

Hydrophobic and Hydrophilic Surfaces

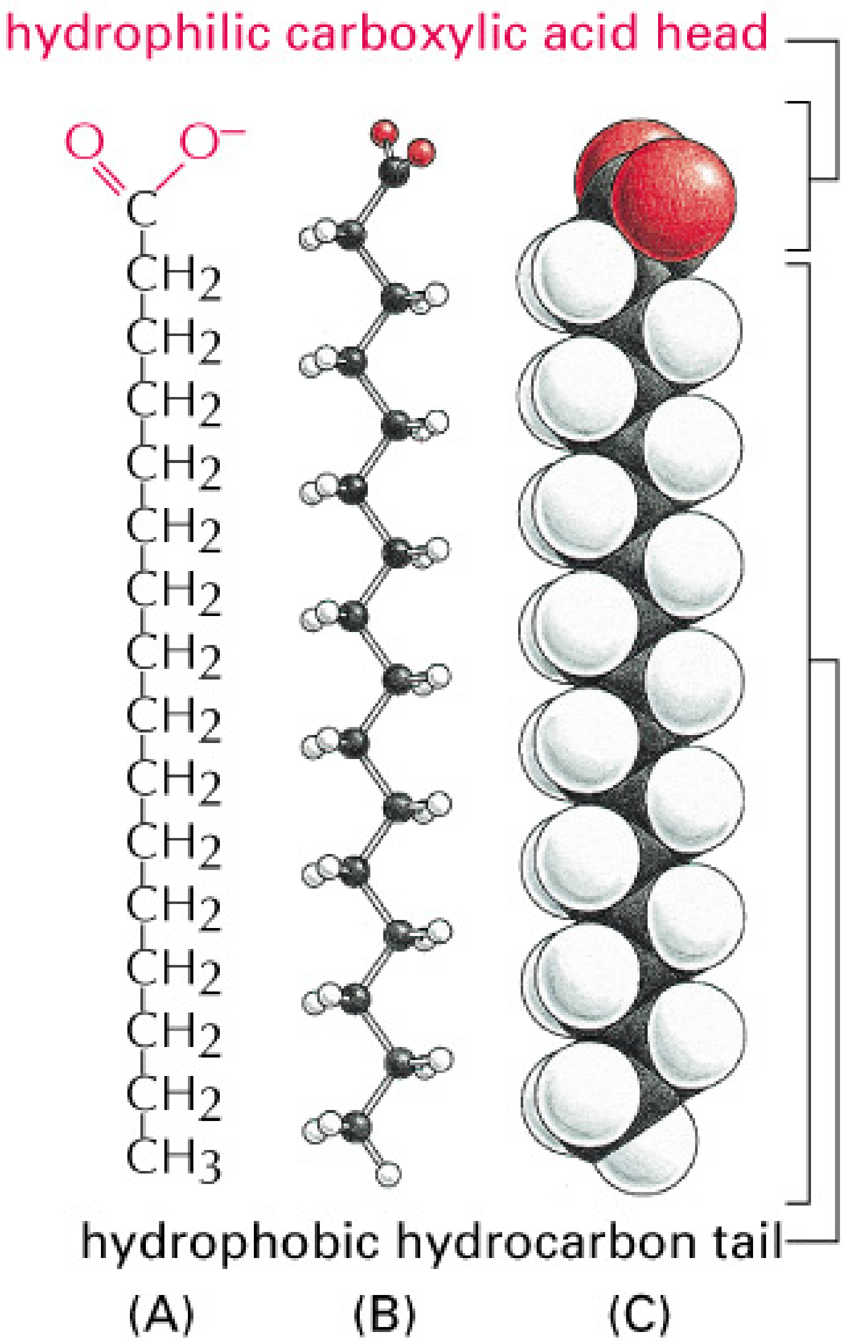
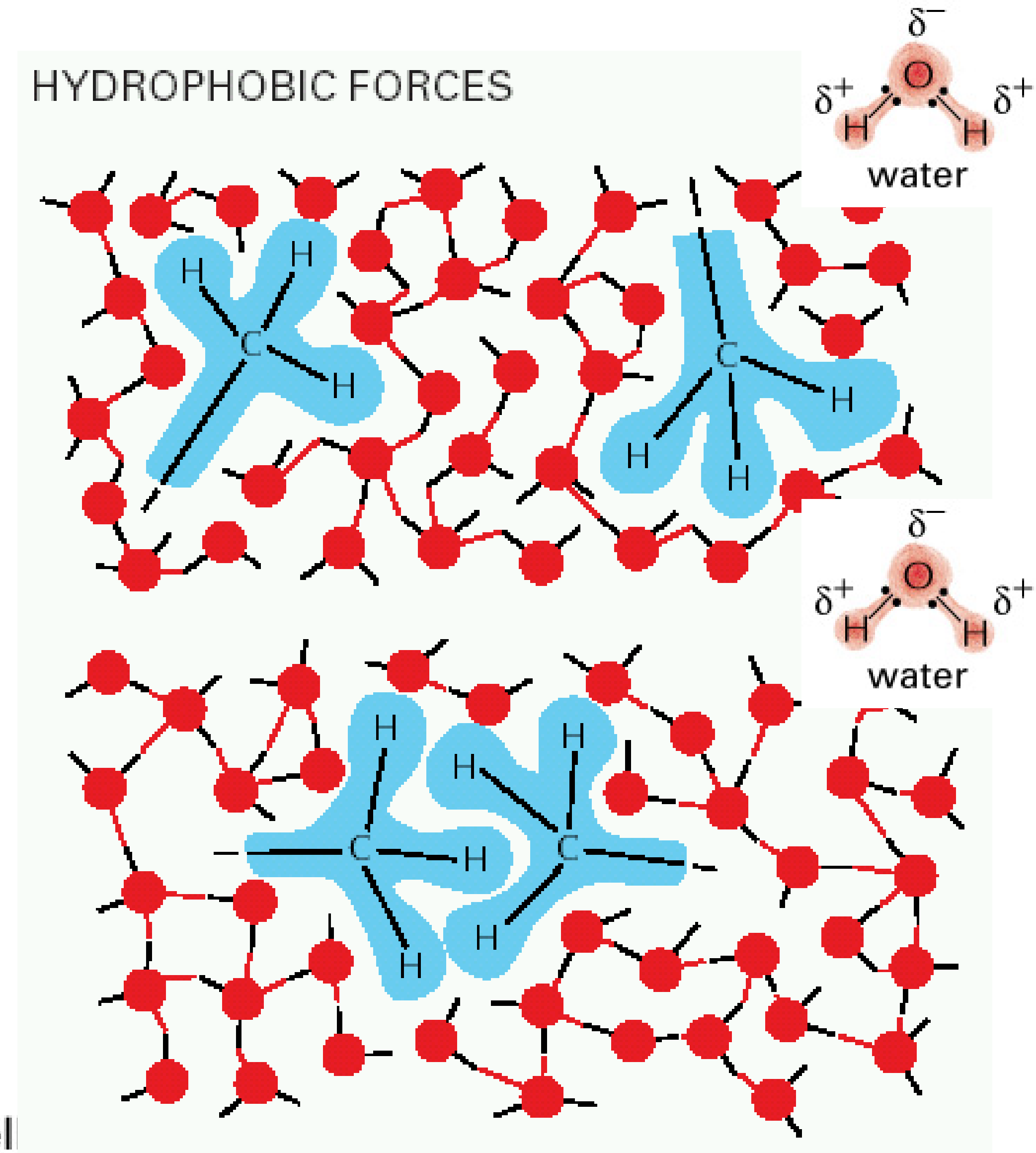
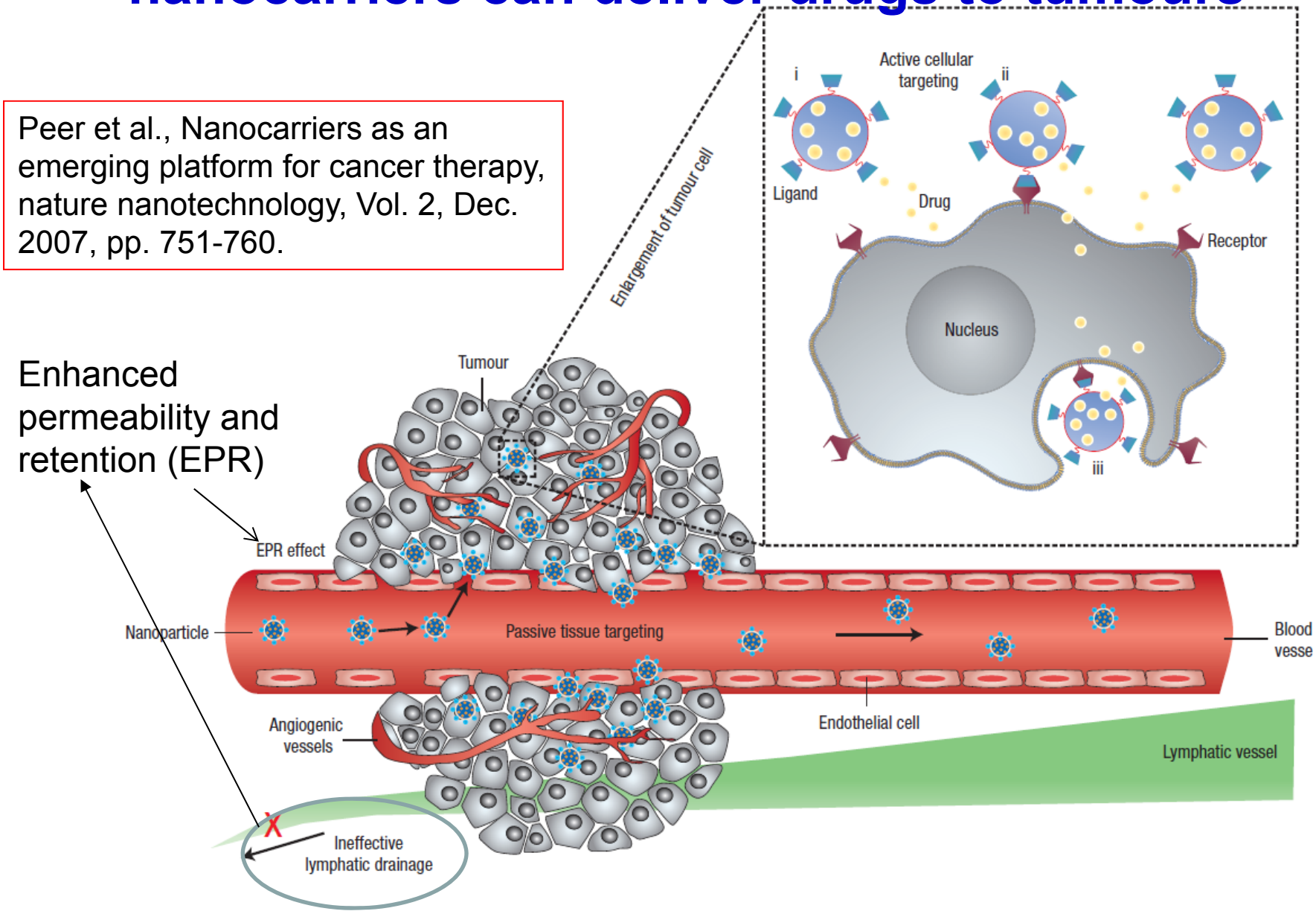


Figure 2–21. Molecular Biology of the Cel

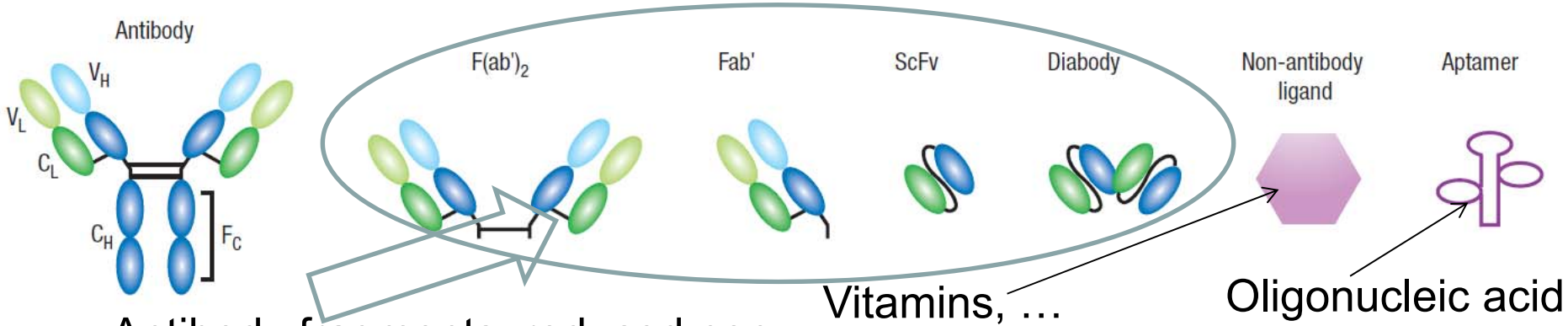


Different mechanisms by which nanocarriers can deliver drugs to tumours

Peer et al., Nanocarriers as an emerging platform for cancer therapy, nature nanotechnology, Vol. 2, Dec. 2007, pp. 751-760.



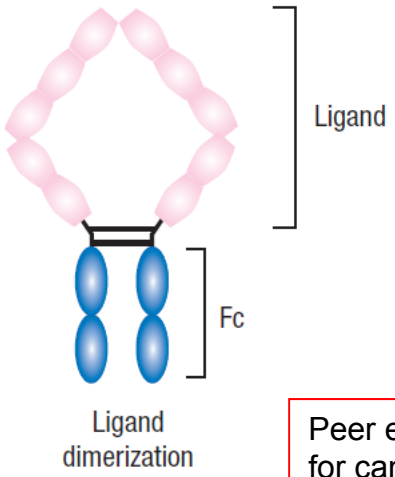
Common targeting agents and ways to improve their affinity and selectivity

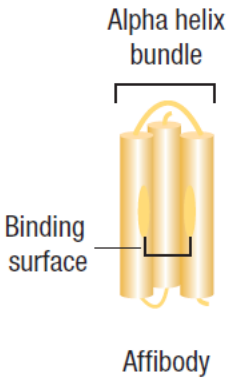


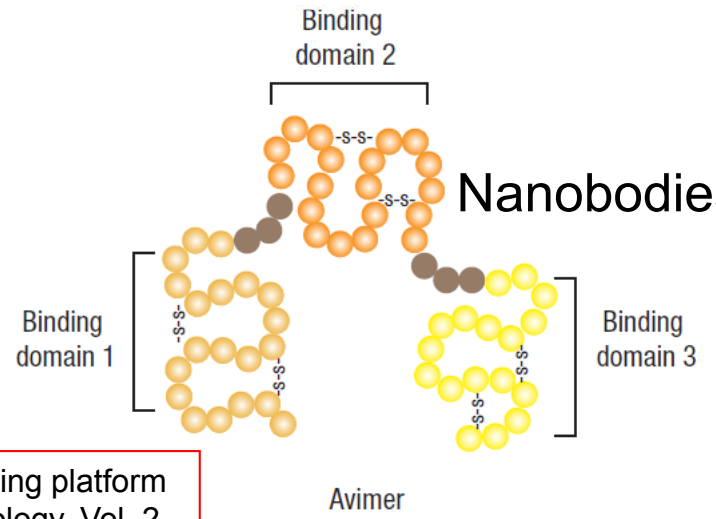
Antibody fragments: reduced non-specific F_c-to-F_c binding→ safer?

Vitamins, …
→ overexpressed receptors for nutrition

Oligonucleic acid (RNA or DNA)



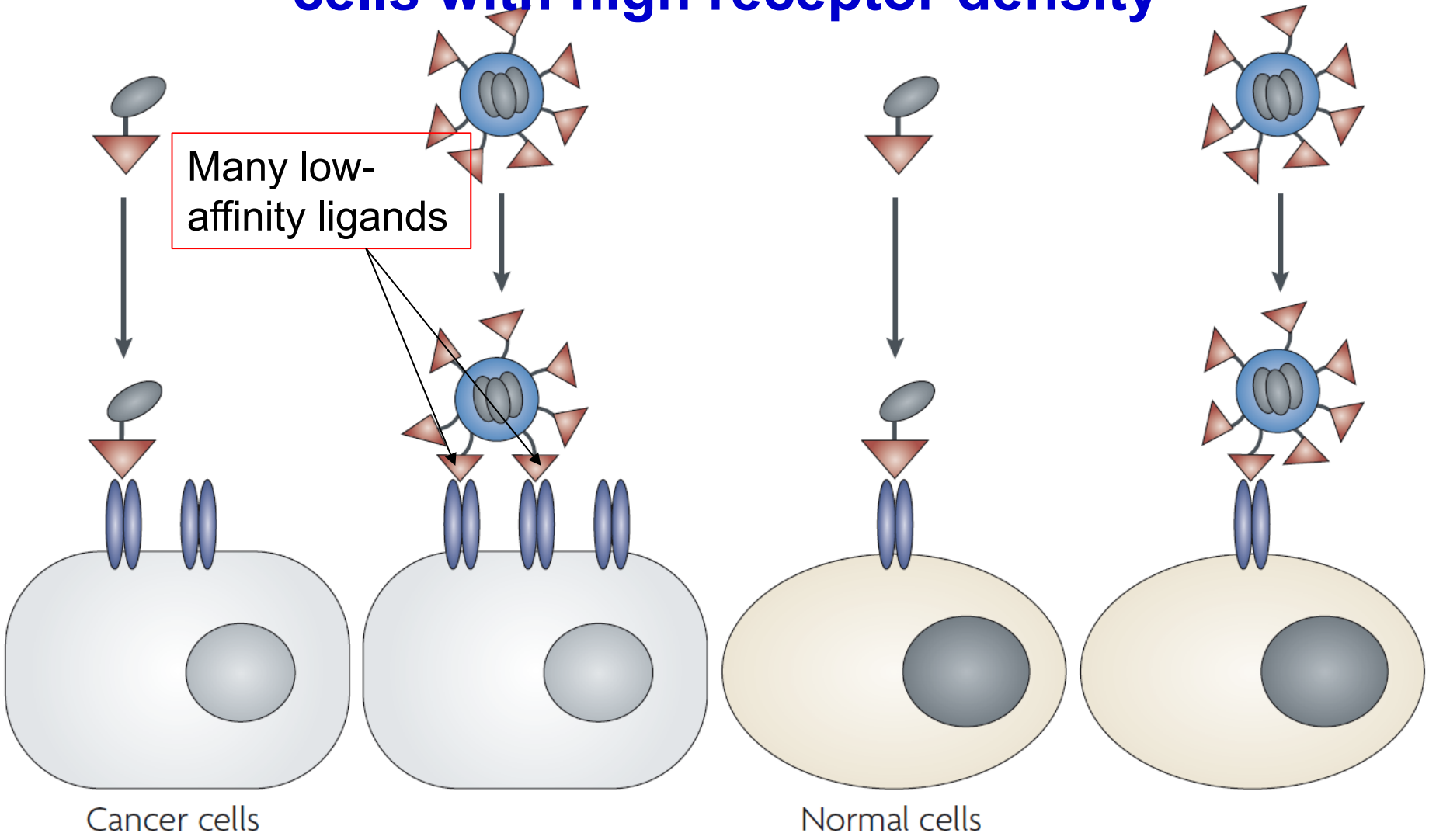




Nanobodies

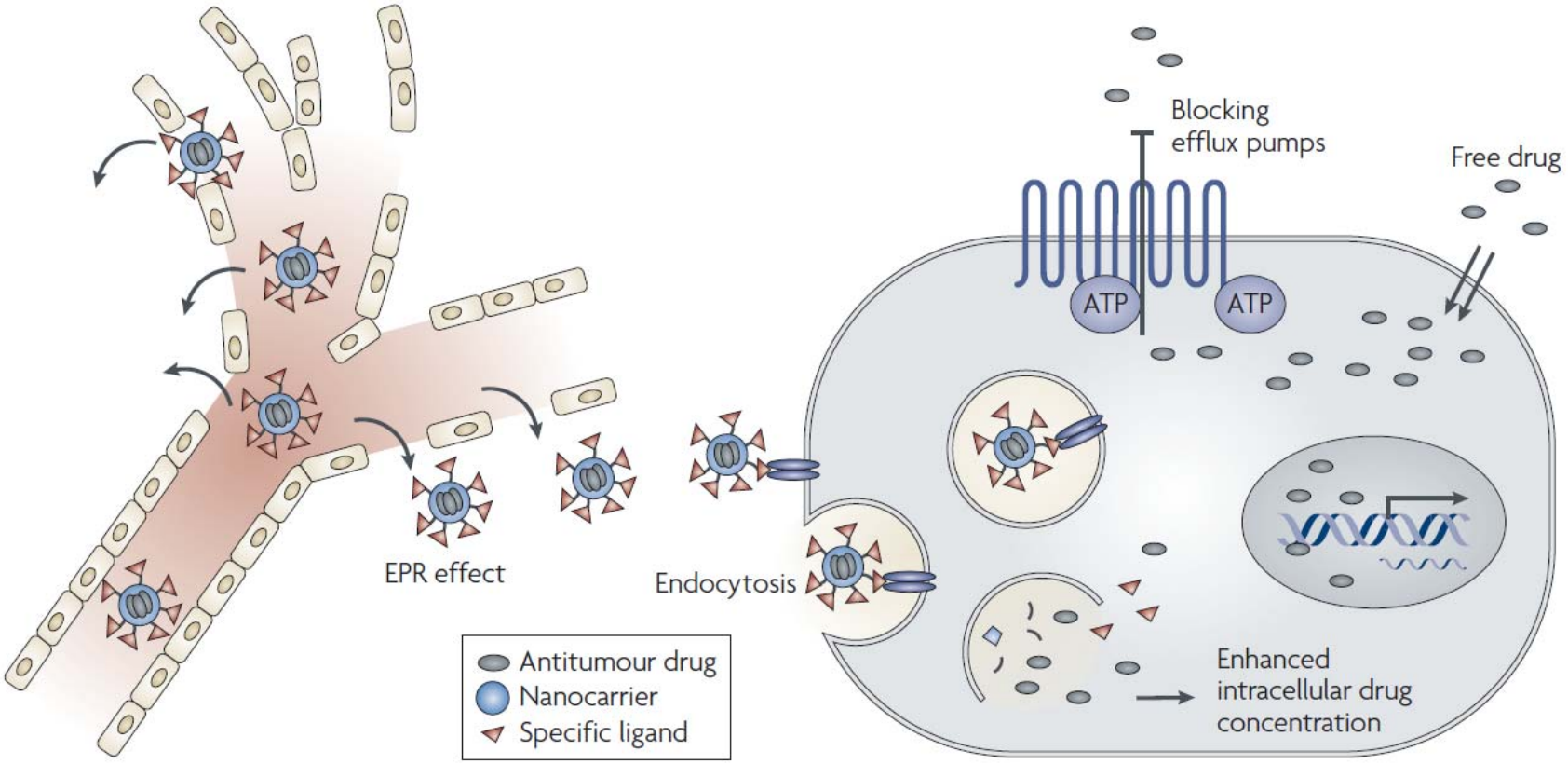
Peer et al., Nanocarriers as an emerging platform for cancer therapy, nature nanotechnology, Vol. 2, Dec. 2007, pp. 751-760.

Multivalent binding to the surface of cells with high receptor density



Davis et al., Nature Reviews, Vol. 7, Sept. 2008, pp. 771-782

Nanoparticles can overcome surface efflux pump mediated drug resistance

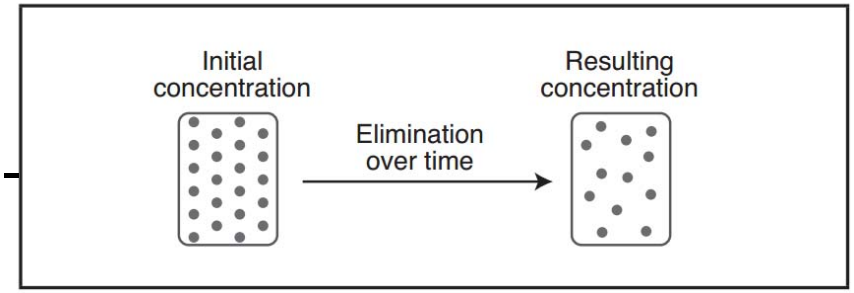


Davis et al., Nature Reviews, Vol. 7, Sept. 2008, pp. 771-782

Basic Pharmacokinetics

- Clearance: Another way of viewing the decrease of concentrations would be to calculate the volume that would be drug-free if the concentration were held constant. Lower clearances are indicative of higher circulation times. The longer circulation times of the nanoparticles compared with the free drug alone can improve tumour uptake.

- Circulation half-life: the time required to eliminate 50 per cent of a known quantity of nanoparticles.



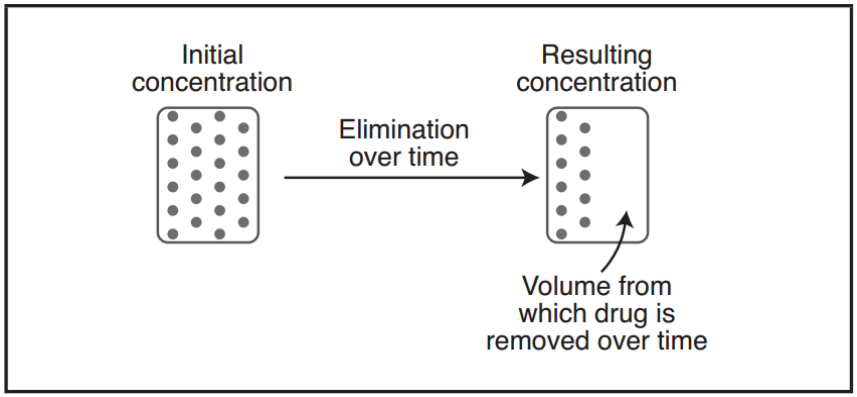


Table 2 | **Comparison of pharmacokinetics (human) of small-molecule drugs with nanoparticle thera**

Name	Formulation	Diameter (nm)	$t_{1/2}$ (h)	Clearance (ml/min•kg)	Comments
Doxorubicin (DOX)	0.9% NaCl	NA	0.8	14.4	Small-molecule drug
SP1049C	Pluronic micelle + DOX	22–27	2.4	12.6	Micelle nanoparticle
NK911	PEG–Asp micelle + DOX	40	2.8	6.7	Micelle nanoparticle
Doxil	PEG–liposome + DOX	80–90	84.0	0.02	PEGylated liposome nanoparticle with long circulation
Taxol (paclitaxel)	Cremophor EL	NA	21.8 (20.5)	3.9 (9.2)	Small-molecule drug
Genexol-PM	PEG–PLA micelle + paclitaxel	20–50	11.0	4.8	Micelle nanoparticle
Abraxane	Albumin + paclitaxel	120*	21.6	6.5	Albumin nanoparticle before injection; status *in vivo* unknown
XYOTAX	PG + paclitaxel	Unknown	70–120	0.07–0.12	Polymer nanoparticle
Camptosar (prodrug of SN-38)	0.9% NaCl	NA	11.7	5.8	Small-molecule prodrug
LE-SN-38	Liposome + SN-38	Unknown	7–58	3.5–13.6	Liposome nanoparticle
Topotecan (camptothecin analogue)	0.9% NaCl	NA	3.0	13.5	Small-molecule drug
CT-2106	PG + camptothecin	Unknown	65–99	0.44	Polymer nanoparticle
IT-101	Cyclodextrin-containing polymer + camptothecin	30–40	38	0.03	Polymer nanoparticle with extended circulation times

No quantitative comparison; however, …

Controlled release using enzyme or hydrolysis

Davis et al., Nature Reviews, Vol. 7, Sept. 2008, pp. 771-782

Nanoparticle therapeutics: an emerging treatment modality for cancer

Size range: 10-100 nm

- A large payload of drug entity and protect it from degradation. 70 nm → 2,000 molecules >> 10's.
- Multiple targeting ligands for multivalent binding.
- Multiple types of drug molecules.
- Controlled release of drug molecules.
- Potential to bypass multidrug resistance mechanisms that involve cell-surface protein pumps (for example, glycoprotein P), as they enter cells via endocytosis.

Davis et al., Nature Reviews, Vol. 7, Sept. 2008, pp. 771-782

Challenges

- At present, it remains unknown how nanoparticles move through tumour tissue once they have localized into the tumour area.
- There are valid concerns about nanoparticle toxicity, as little is known about how nanoscale entities behave in humans. Note: some have been approved for humans.
- Third, there are important commercial and regulatory challenges to be tackled with the emerging generation of more complex nanoparticles, in part owing to their multicomponent nature.
- Liposome → Polymer → Ligands → Multivalent binding and multiple components → Manufacturing, Cost & …?

Davis et al., Nature Reviews, Vol. 7, Sept. 2008, pp. 771-782

Workshop

Growth of Ge Nanowires: an Example
(vapor-liquid-solid, VLS method)

gas phase

precursor adsorption

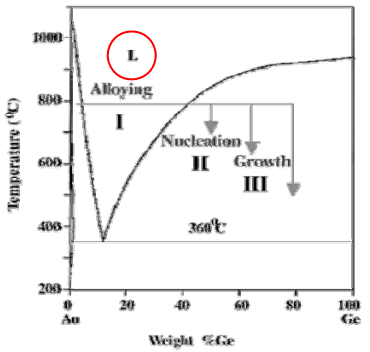
Substrate

Substrate

Remember: high temperature

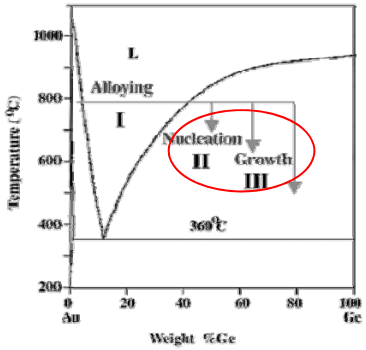
formation of liquid alloy phase (I)

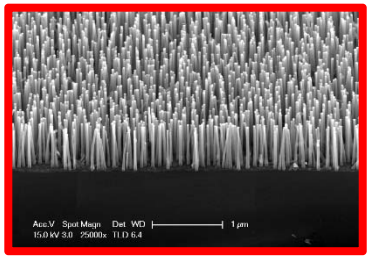
Substrate



saturation of catalyst (II) and
precipitation of solid phase (III)

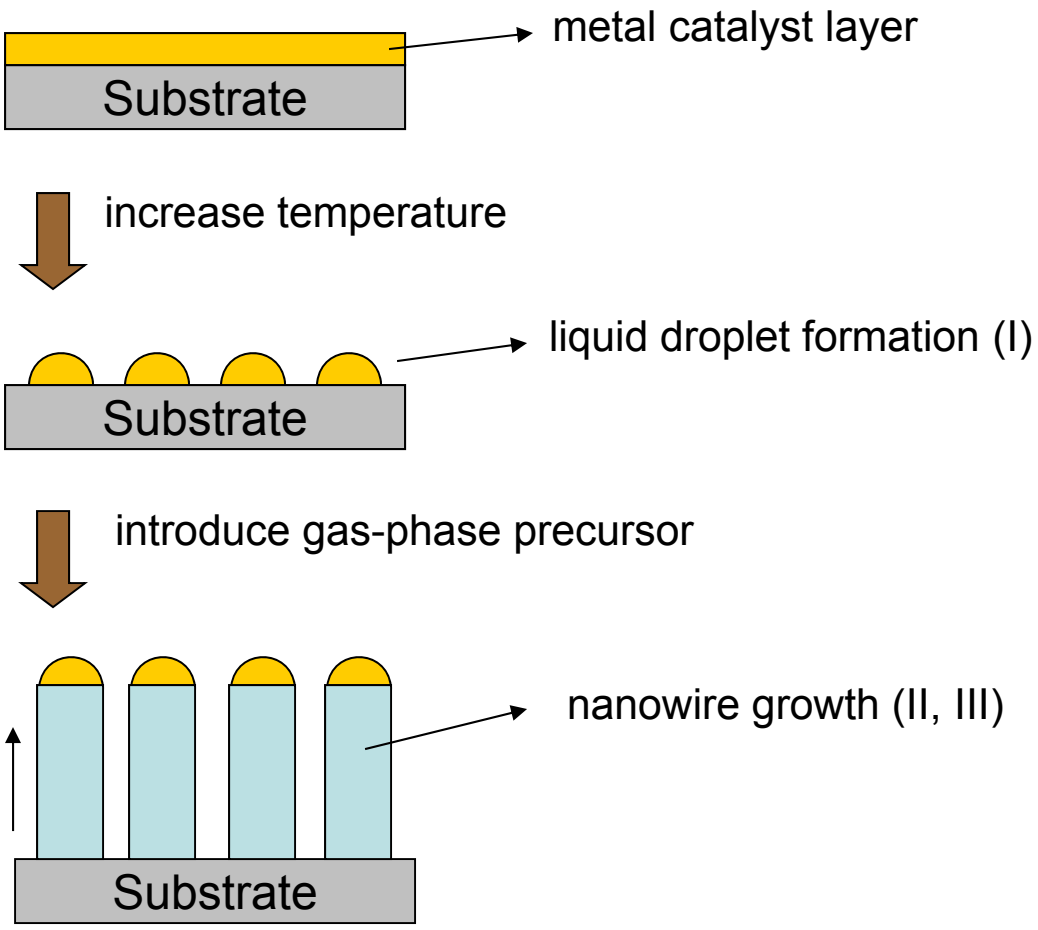
Substrate

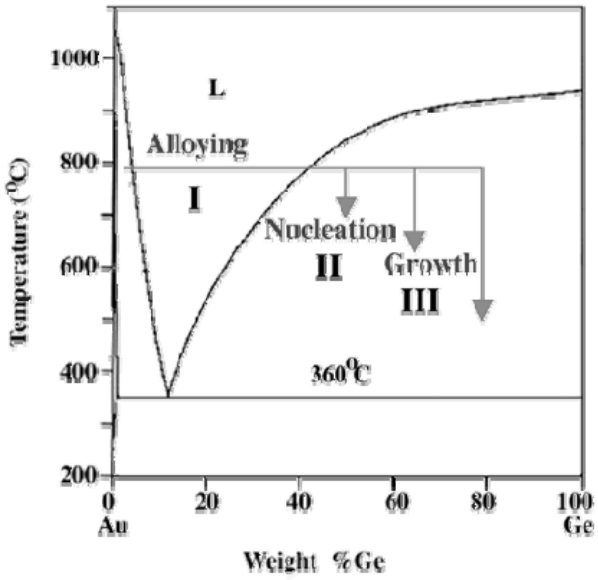




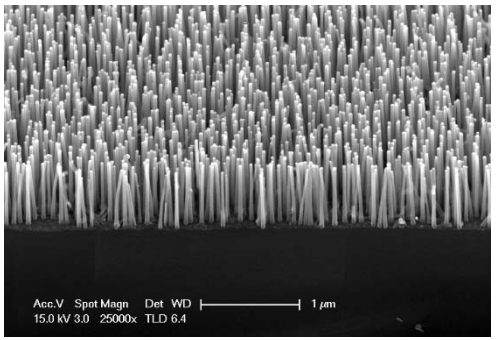
Substrate

Growth of Nanowires
(Use for Si, Ge and other NWs)





Au-Ge Phase Diagram



DARPA *i*MINT Center

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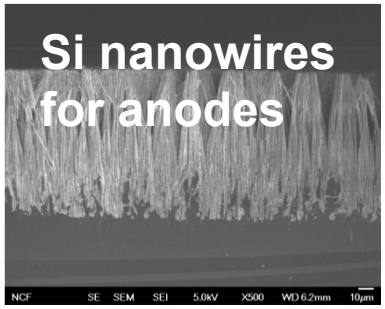
N/MEMS II Final Review , Irvine, CA

August 14, 2012

Fundamental Research Studies and Potential Importance toward Enhancing U.S. Defense Capabilities



Cracking?
10X increase in battery's anode storage.

High Q?
Dissipation mechanisms?
Mass/chem/bio sensors and manufacturing control

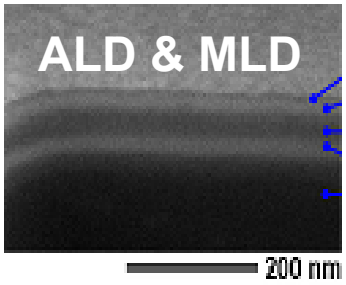
GaN NW Resonator

Repeatable, Predictable & Reliable NW/NT/Graphene-Enabled *i*MINT Microsystem

Embedded Battery

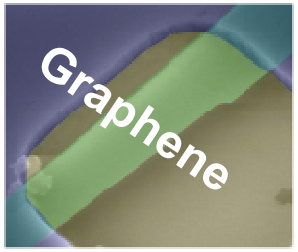
Graphene Switch

All Silicon?



Properties of different ALD/MLD combinations?
Enabling technologies for novel N/MEMS.

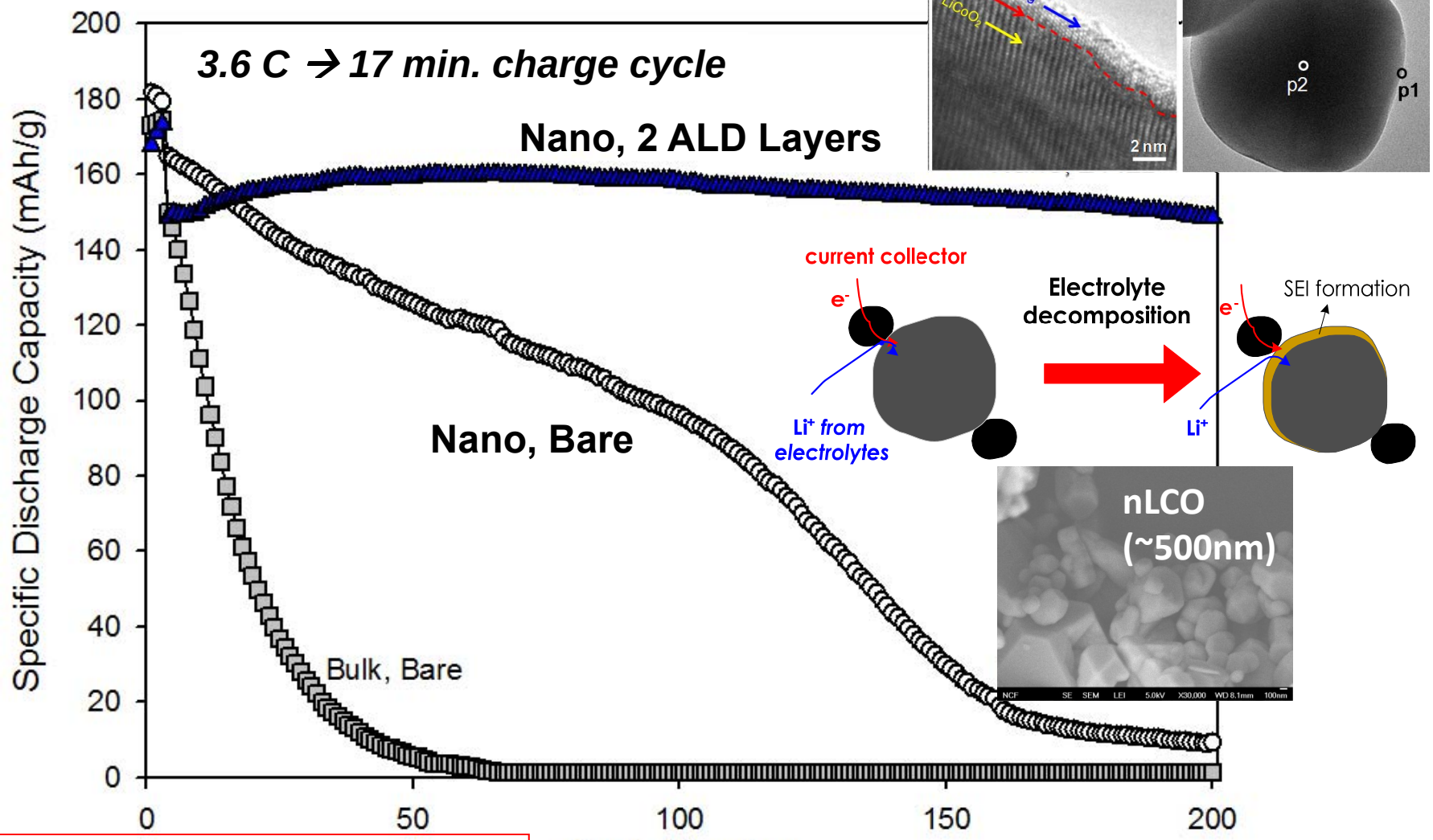
ALD/MLD



Wafer-level processing?
Adhesion? Mechanical computing in harsh environment.

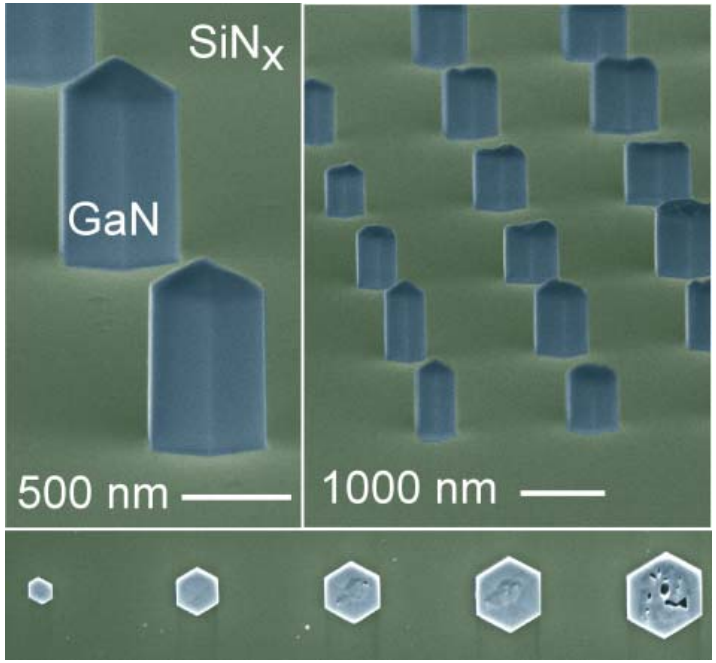
ALD-Protected Cathodes for Li-ion Battery

(Se-Hee Lee, CU-ME and S. M. George, CU-Chemistry)

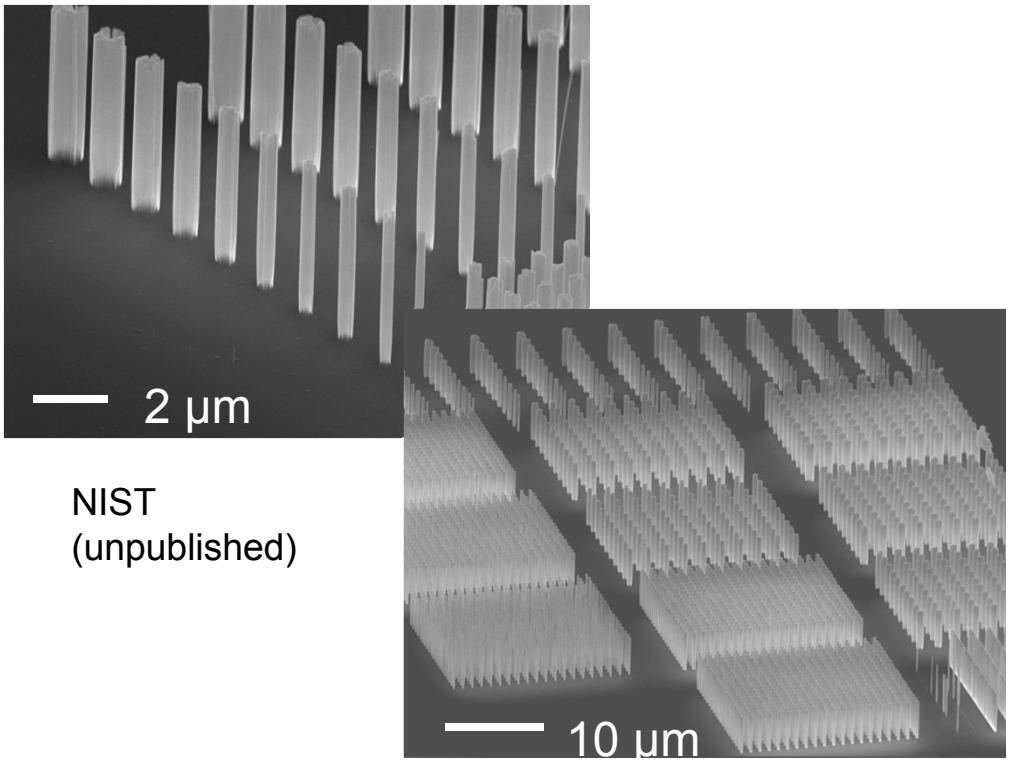


Five papers on the studies on different anodes and cathodes.

Defect-Free GaN NWs: Selective Epitaxy
(Kris Bertness, NIST)



K. A. Bertness, et al., Adv. Func. Mat. *20* (2010) 2911-2915.



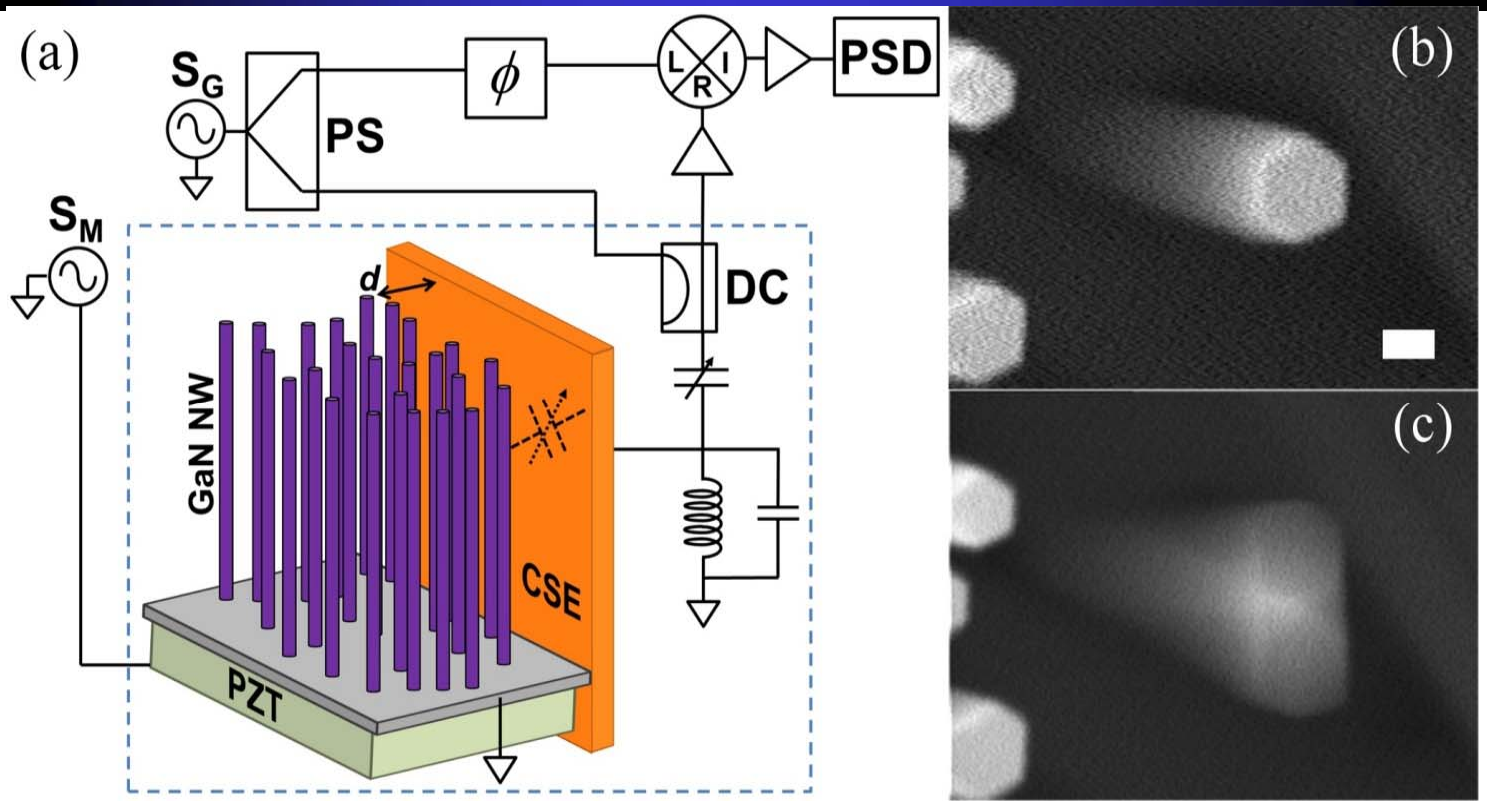
NIST
(unpublished)

- GaN nanowires nucleate in openings in SiN_x mask
- Nucleation condition optimization improved yield and aspect ratio (right)
- Placement and uniformity of diameter is important for integration into MEMS and resonant sensor devices

NIST National Institute of Standards and Technology

GaN NW Microwave Homodyne Detection

(J. Montague, J. Gray and C. Rogers, CU-Boulder; K. Bertness, N. Sanford, NIST)



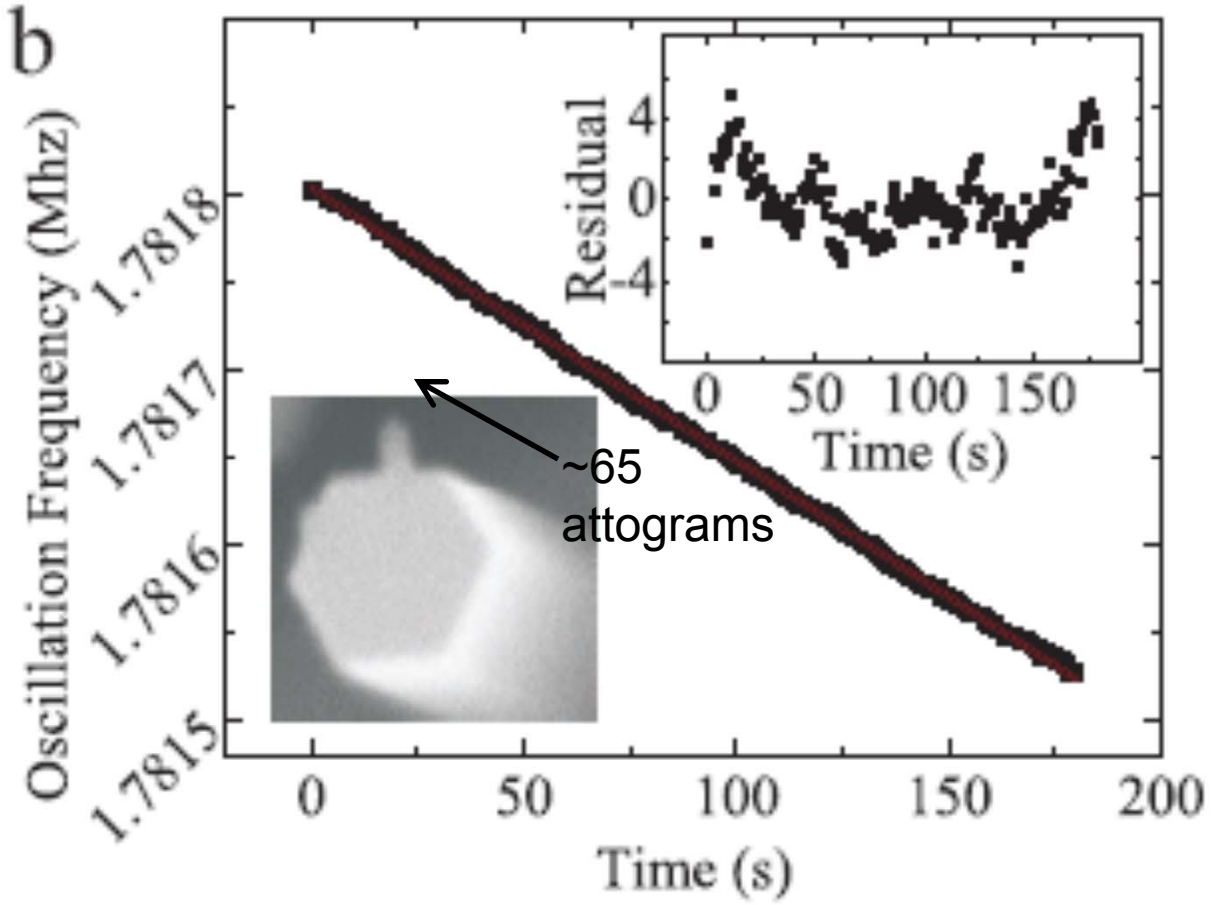
- Multiplexed readout of single and multiple NW resonances.
- Enables the study of large ensembles of sensor NWs
- Sensitive enough to detect thermal NW motion.

An example of university-government lab collaborations

Potential Impact: Sensors

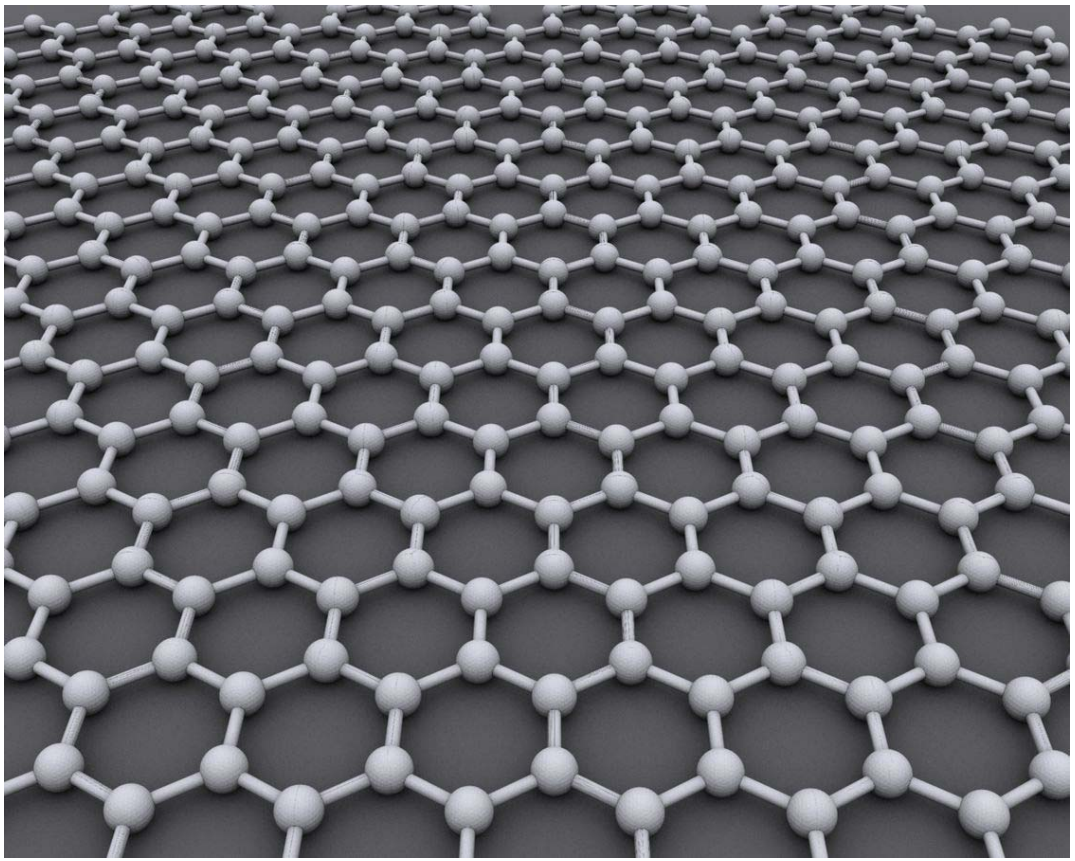
Resonators for:

- Strain/Force
- Pressure
- Temperature
- Biosensing
- Mass sensing

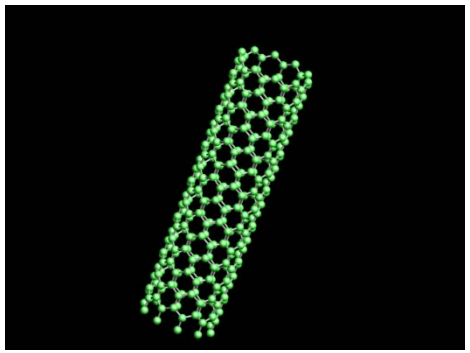


Single nanowire mass sensor. Experimental sensitivity of **~0.2 attograms** (2×10^{-19} grams) in 1 second measurement time. Possible because of high Q (~100,000)

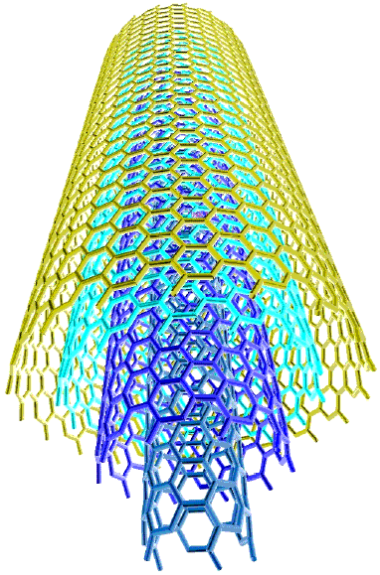
Carbon Nanotubes (1-D) and Graphene (2-D)



Graphene



Single-walled



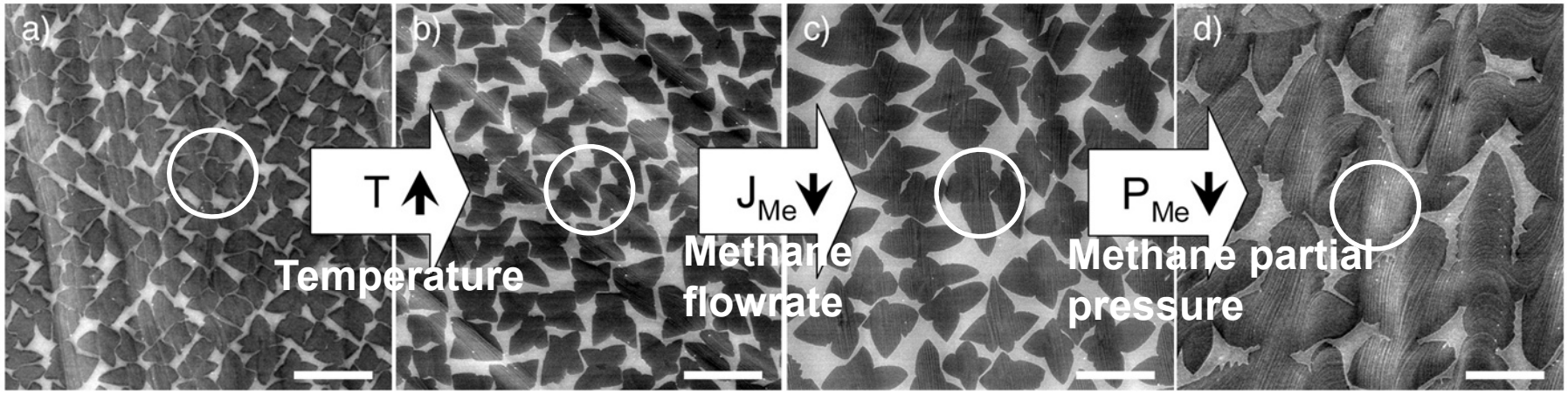
Multi-walled

Growth of Large Domain Graphene and Its Transfer

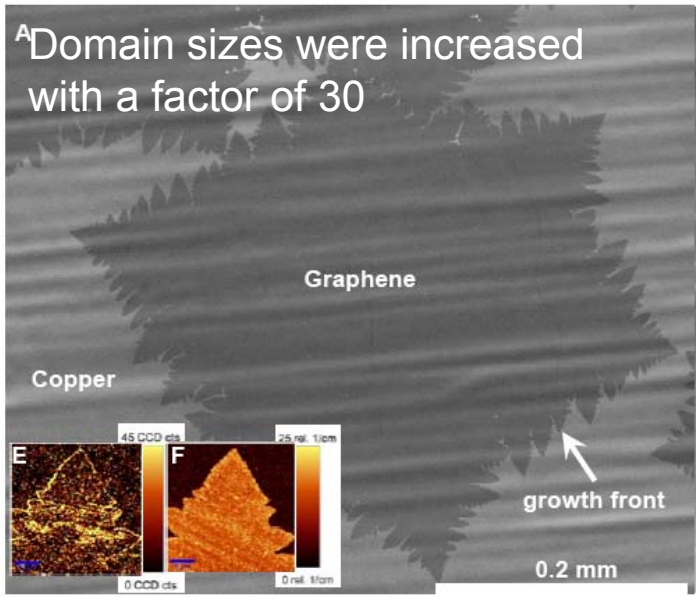
Xuesong Li, Ji Won Suk, and Rodney S. Ruoff, UT-Austin

Non-iMINT Project

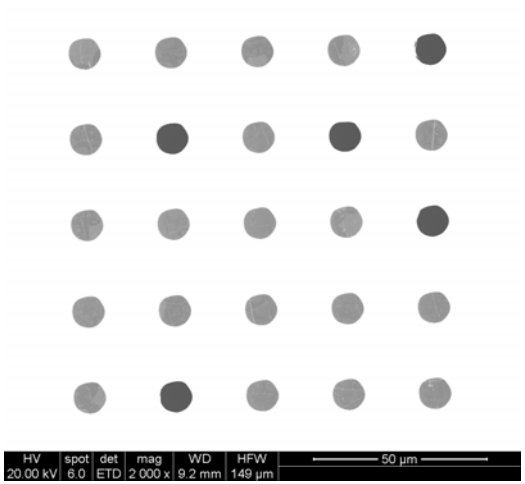
Two-step growth: Investigation of growth parameter effects on domain sizes



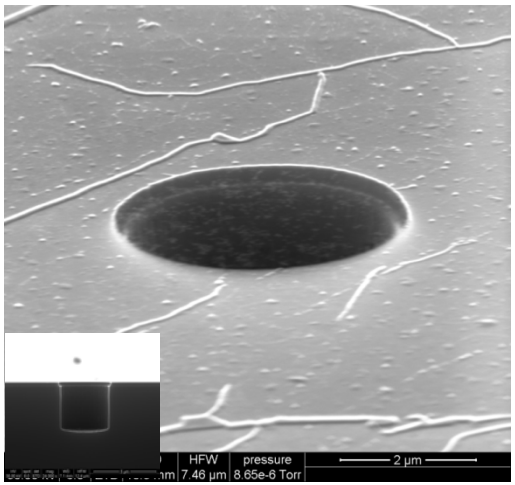
Very low pressure CVD



Graphene suspended over through holes and wells

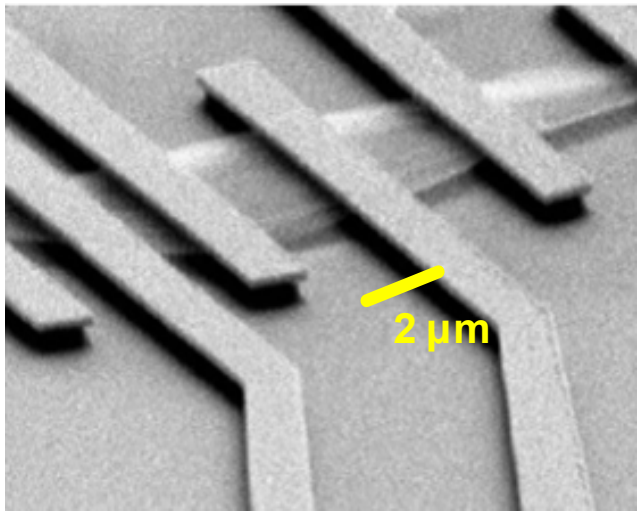


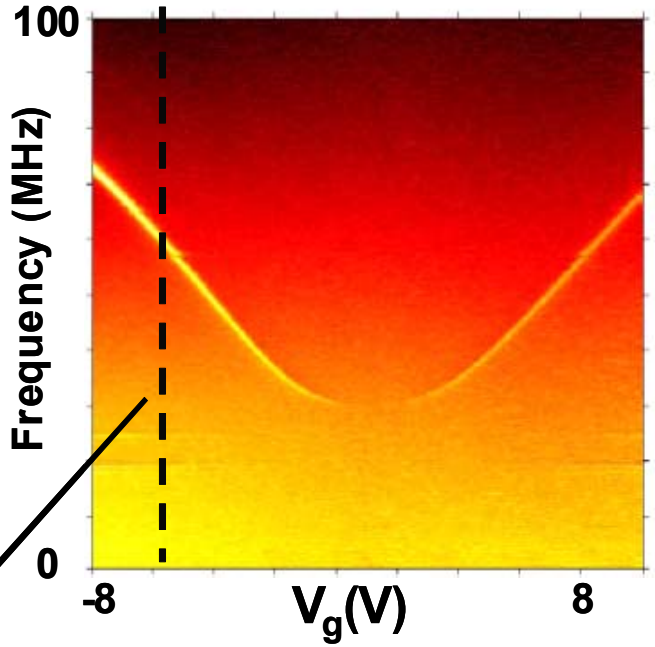
9.6µm diameter through holes

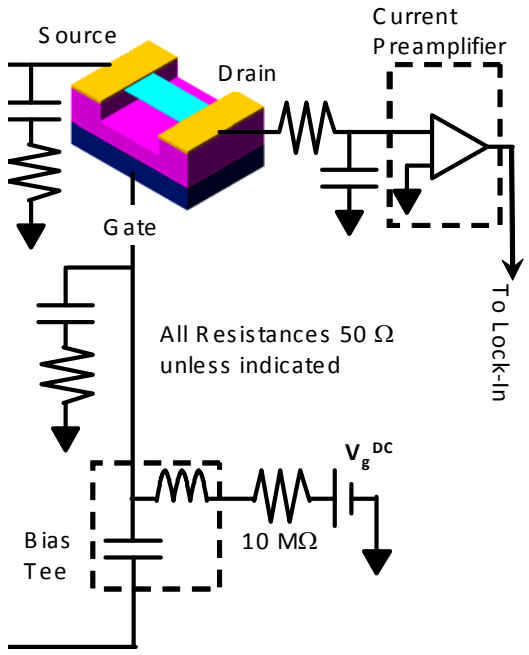


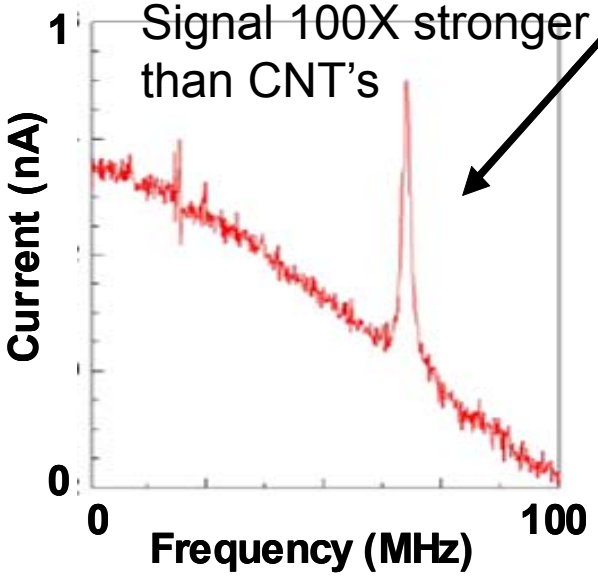
4.5µm diameter well

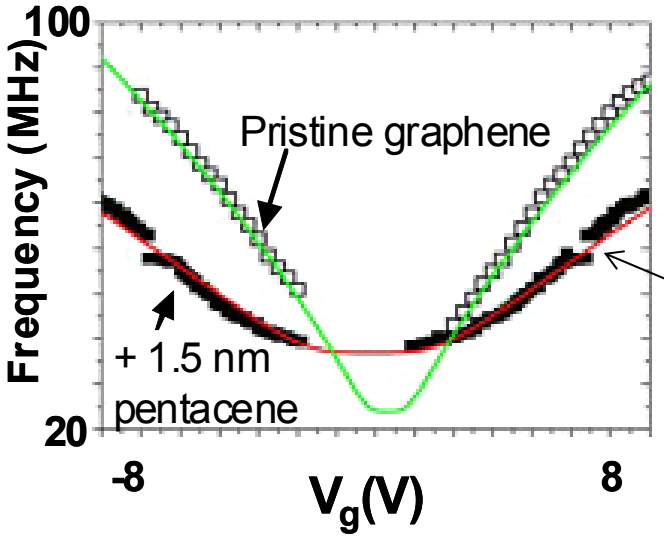
Graphene Resonator: Tunable and Mass Sensing (Jim Hone, Columbia University)











Attogram detection at room temp.

Summary

- Many fabrication processes for various nanoparticles with or without ligands have been developed with different drug molecules encapsulated for nanoparticle therapeutics.
- Clinical trials (phase I, II & III) for nanoparticle therapeutics are ongoing with improving technologies.
- A tremendous science and technology base has been established for nanoparticles, nanowires/nanotubes and graphene → more exciting applications to be explored.