Engineering Application of Nanoscale Biology

Lecture 3
Synthetic Nanostructures - II

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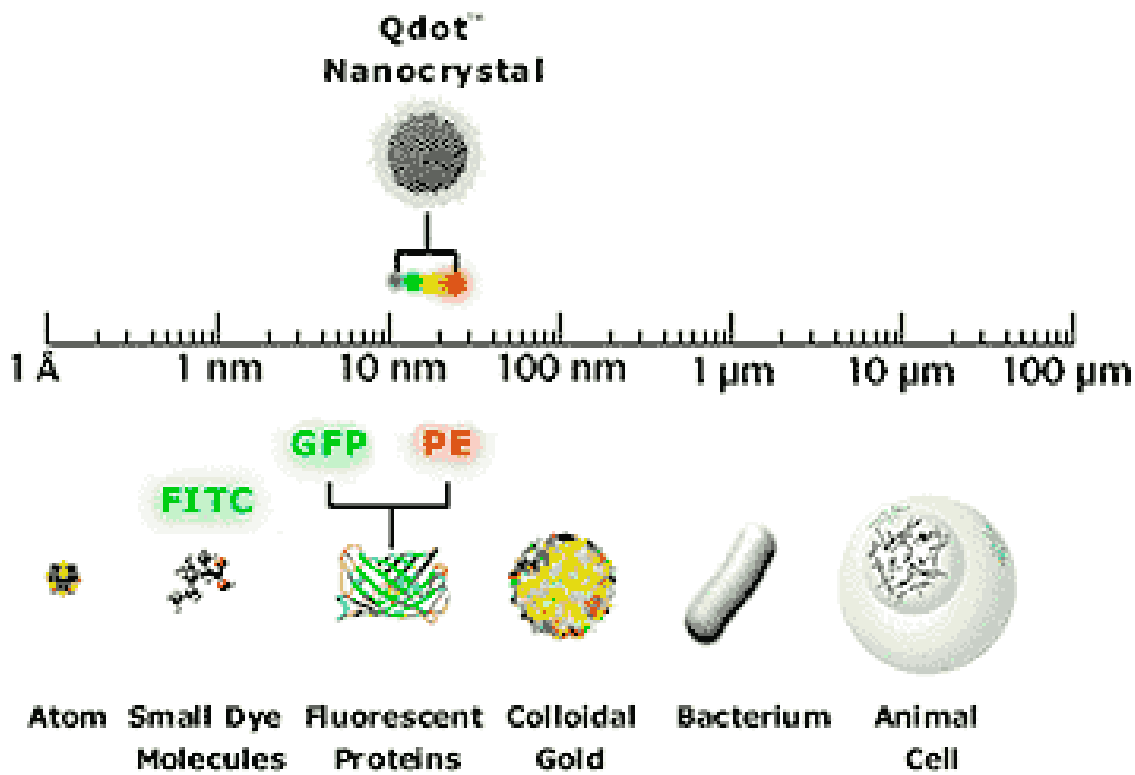
Topics Covered

- Quantum dots
- Polymers
  - Micelles
  - Dendrimers
  - PEG

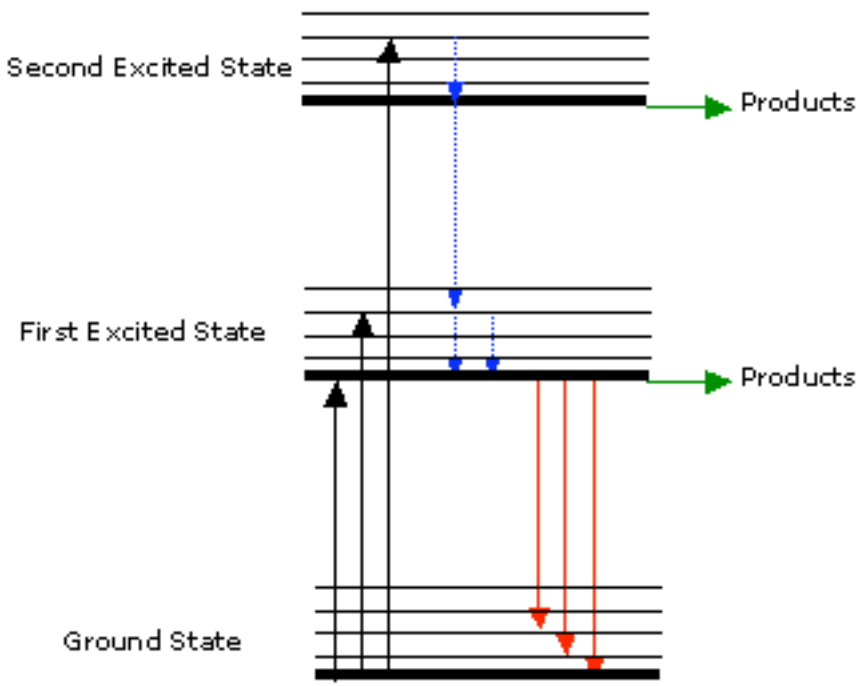
Quantum Dots

- Also known as semiconductor nanocrystals



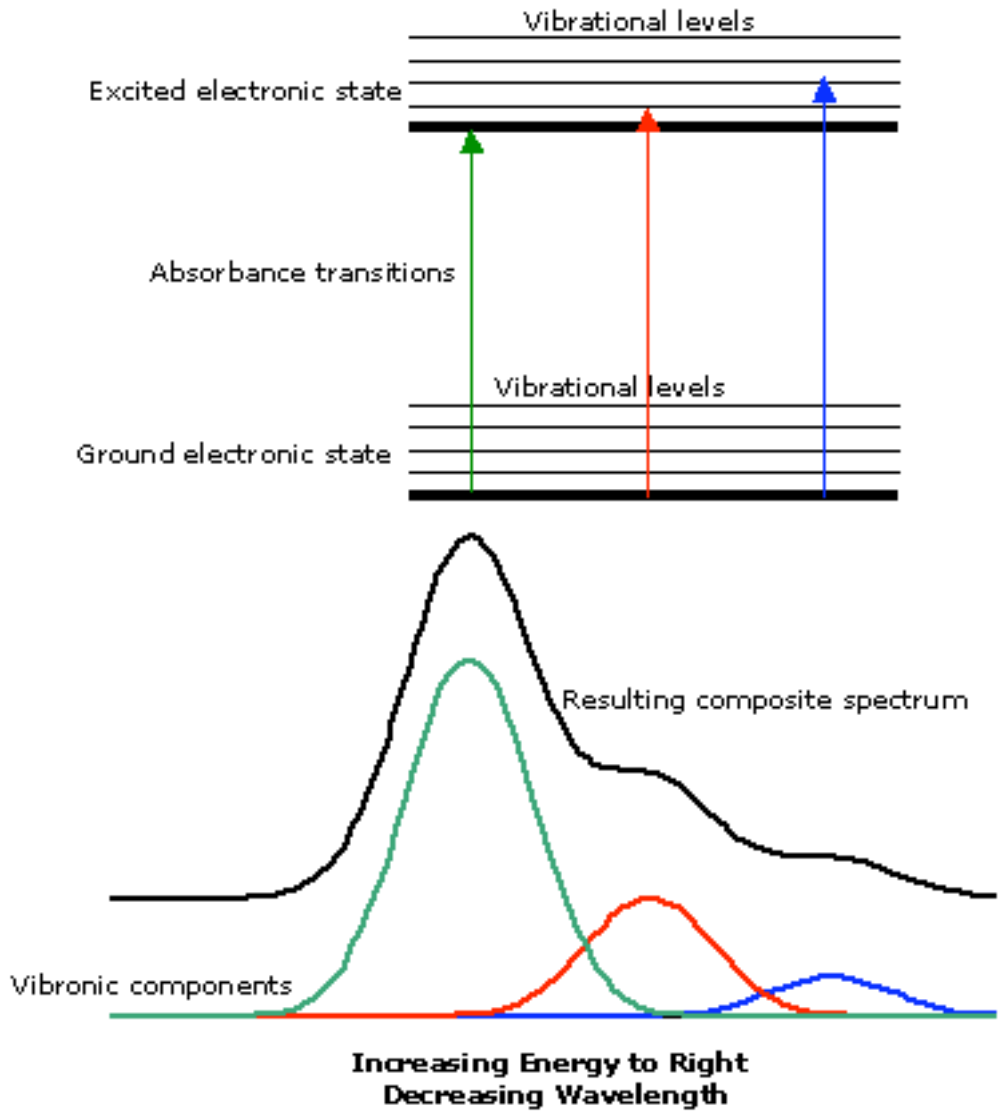
Source: http://www.qdot.com

Photophysics of Qdots



- Different Energy Transitions
- Black: Absorption
- Blue: Internal equilibriation
- Red: Fluorescence
- Green: Photochemical conversion

Absorbance Spectrum



- Different transitions permissible in different atoms
- Resulting in a confounding absorbance spectrum

Quantum Yield

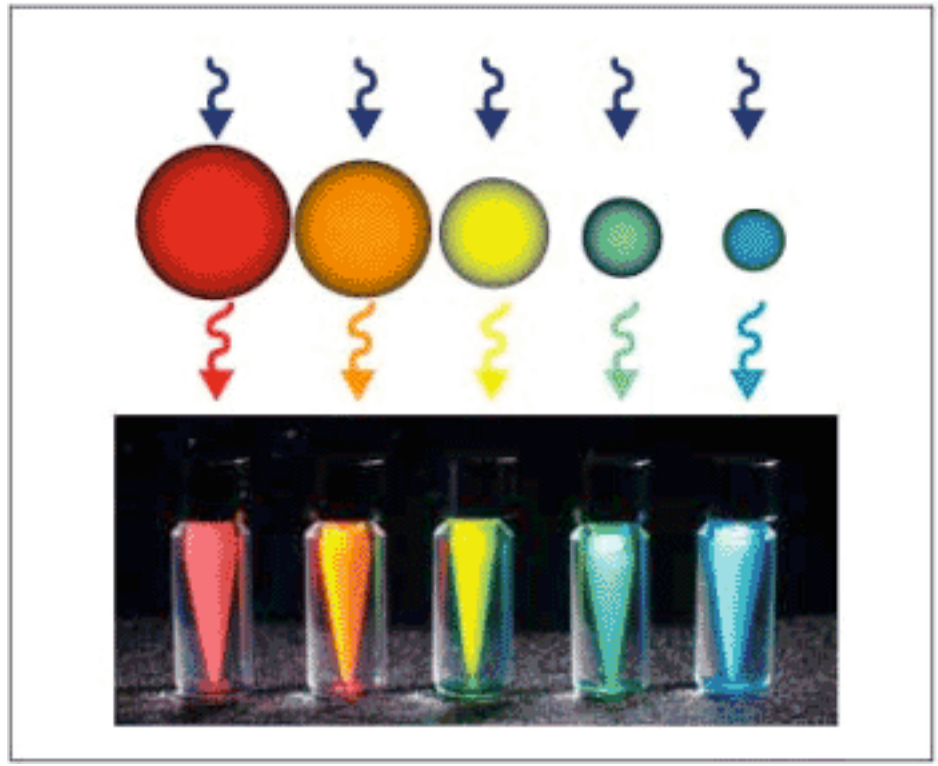
- Light is absorbed: Part of it leads to photochemical processes, part of it is emitted again.
- Ratio of light emitted to light absorbed is quantum yield.
- A QY of 0.7 means that 70% of the light energy absorbed results in emissions
- QY is efficiency - not brightness

Core-Shell-Coating Morphology

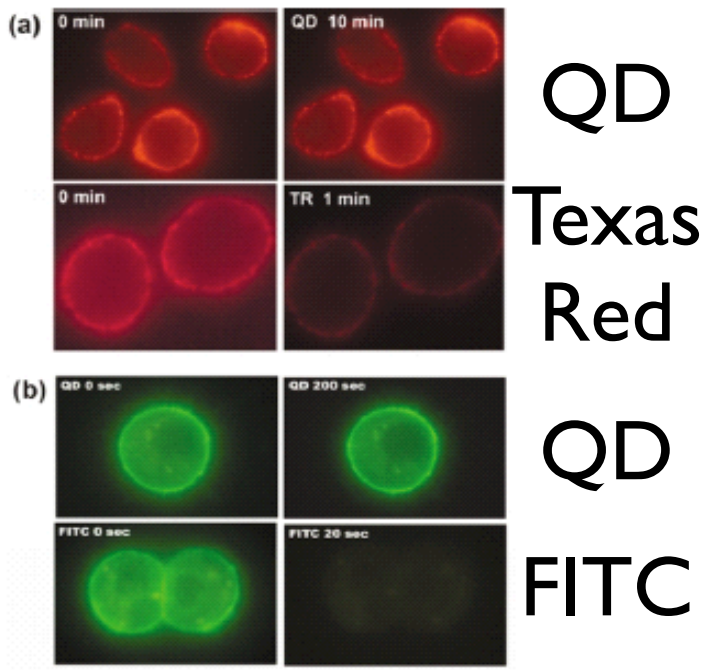
- CdS (UV-Blue), CdSe (Vis), CdTe (Red, NIR, IR) cores
- ZnS shell
- Emission tuning: Coarse control with materials, fine control with size
- Coating provides biological function

“Artificial Atoms”

- Electronic confinement in “zero” dimensions leads to confined electronic states
- Different QDs held against handheld UV light



Applications and photobleaching



QD

Texas Red

QD

FITC

Fig. 4 Immunofluorescence labeling of human breast tumor cells with antibody-conjugated quantum dots, and comparison of signal brightness and photostability with organic dyes. (a) Cancer cells labeled with antibody-conjugated QD or Texas Red (TR) targeting cell surface antigen uPAR. (b) Cancer cells labeled with antibody-conjugated QD or FITC targeting cell surface antigen Her-2/neu. Excitation from a 100 W mercury lamp caused negligible photobleaching of QDs, compared to the two organic fluorophores. (Courtesy of Dr Xiaohu Gao, Emory University.)

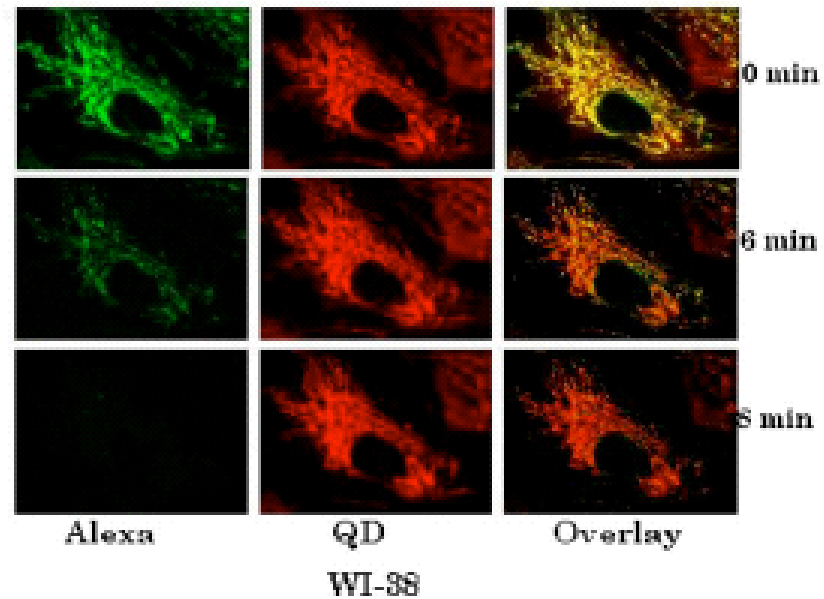
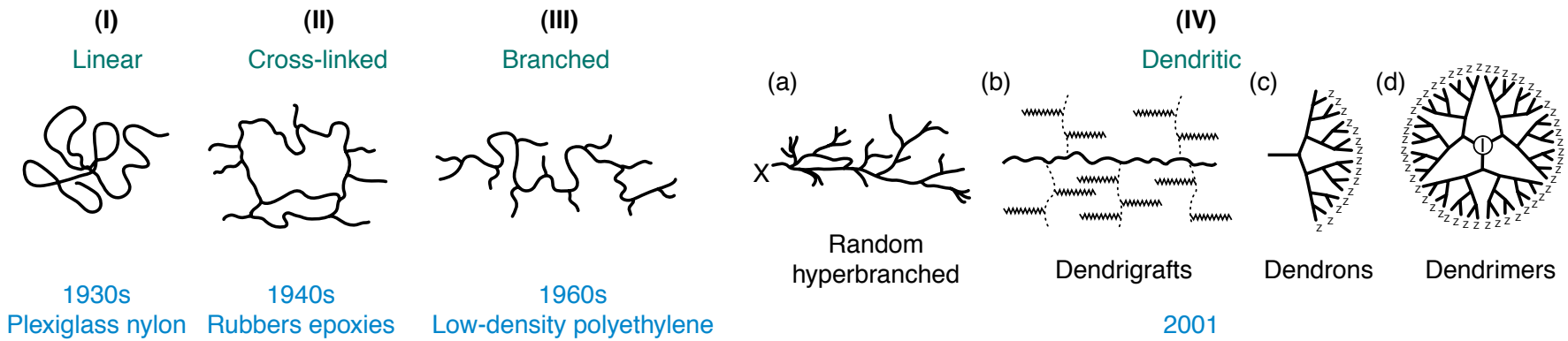


Fig. 3. Immunofluorescence images of mortalin to compare the photostability between Alexa 488 and quantum dots in normal human cells. The specimens were illuminated for 9 min with light from a 100 W mercury lamp under a 100 × 1.30 oil-immersion objective. Images were captured with a cooled CCD camera at 1 min intervals for each color. When labeling signals of Alexa 488 started fading and became undetectable, the signals of QD showed no obvious change for the entire 9 min illumination period [25].

Questions on Quantum Dots?

Polymeric Heirarchy



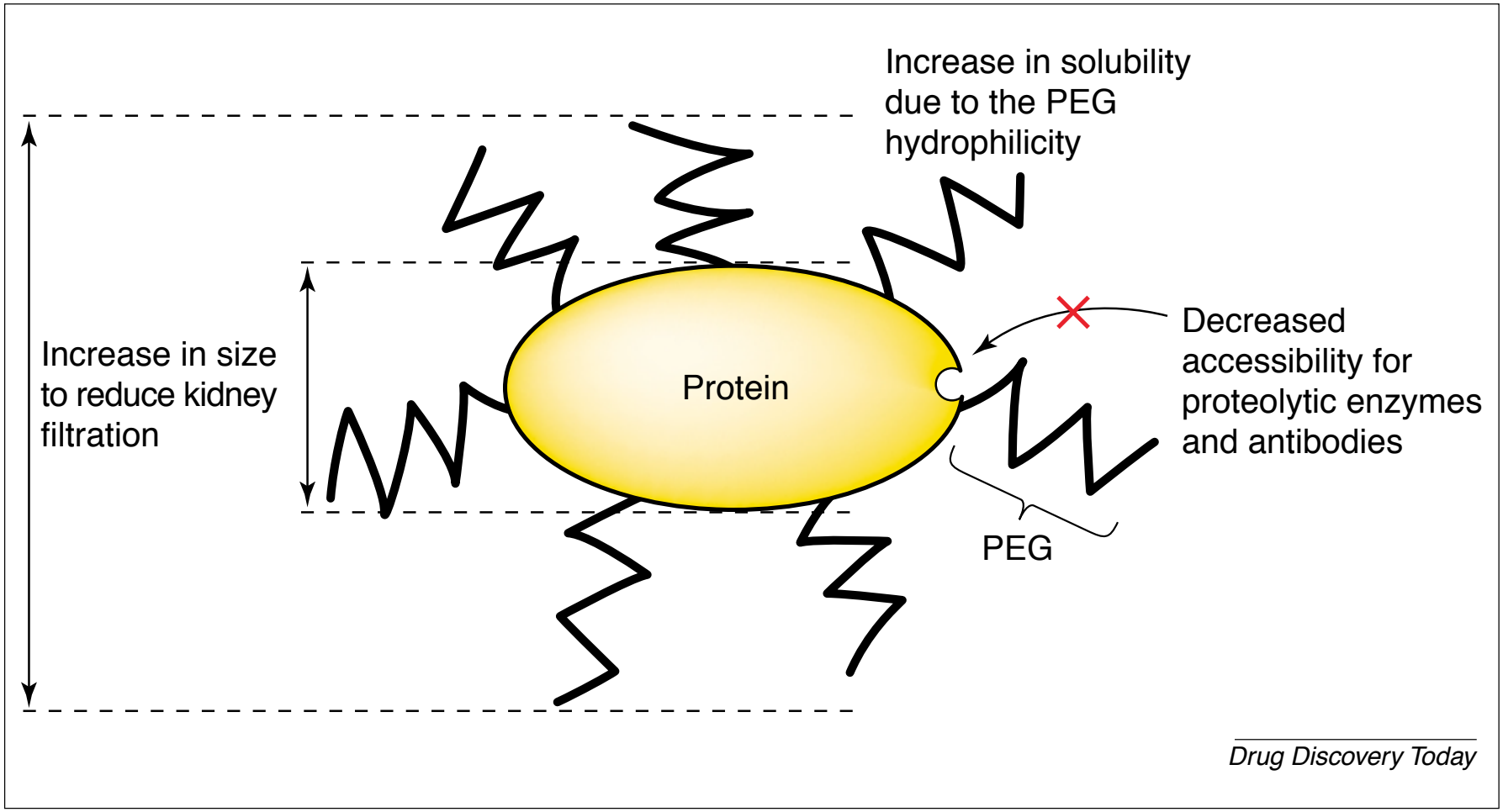
- Started in 1916, after Staudinger's *macromolecular hypothesis*
- Higher levels of complexity allow for better control of topology

Polymeric structures

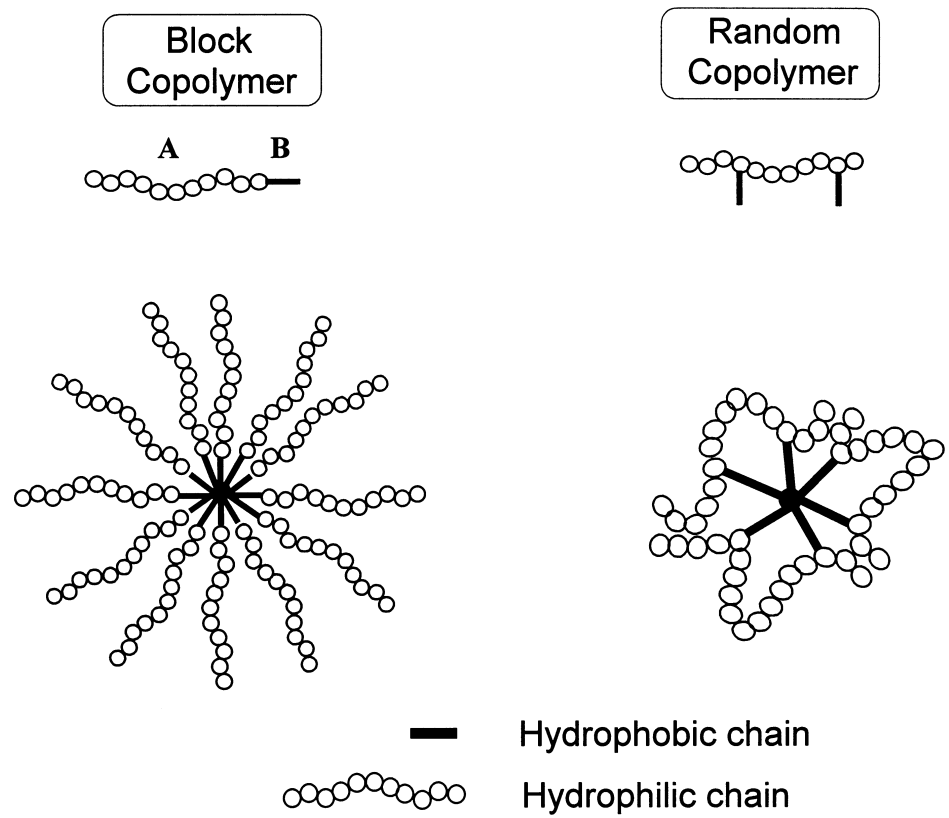
$$HO-(CH_2-CH_2-O)_n-H$$

- Polyethylene Glycol (PEG)
- Pegylation - Adding PEG to another molecule (like a protein) - changes pharmacological properties
- Widely used in cosmetics and laxatives
- Liquid armor (PEG+nanocrystals = Shear Thickening Fluid)

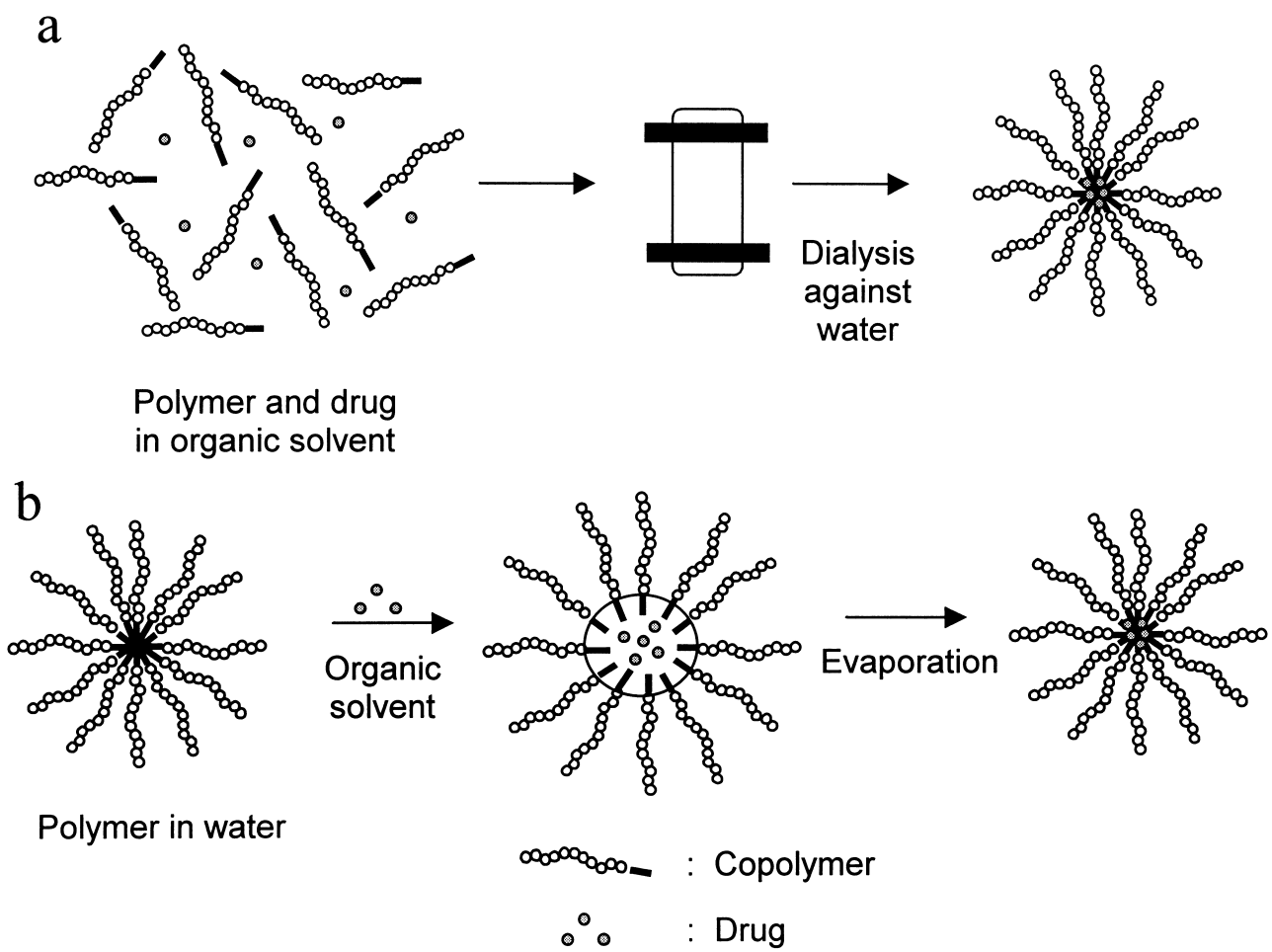
Why PEGylate?



Micelle structures



Micelle loading methods



Micellar organization

- Thermodynamically driven due to hydrophobic-hydrophilic effects or charge repulsion
- Micelles are formed at Critical Micelle Concentration (CMC), usually at 0.0005-10% w/v.
- High CMC structures unstable at low concentrations

Dendrimers

- Dendritic ("tree-like") structures are everywhere: trees, roots, circulatory system, nervous system etc...
- Why? Possibly optimum interface for energy transactions

Poly AMido AMine (PAMAM) dendrimer

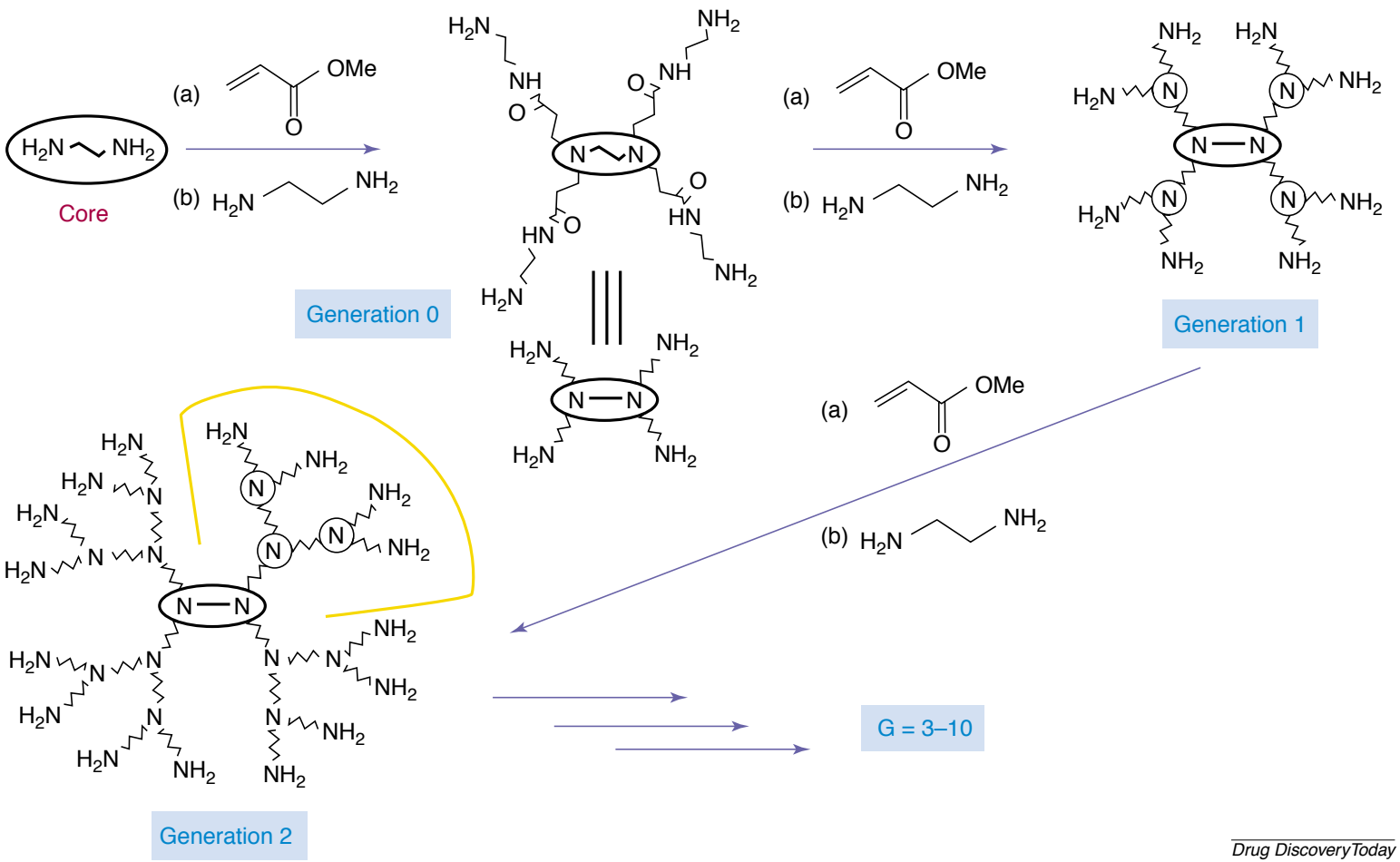


Figure 3. Synthesis of tetra-functional poly(amidoamine) (PAMAM) dendrimers: exhaustive Michael addition of amino groups with methyl acrylate, followed by amidation of the resulting esters with ethylenediamine.

PAMAM synthesis

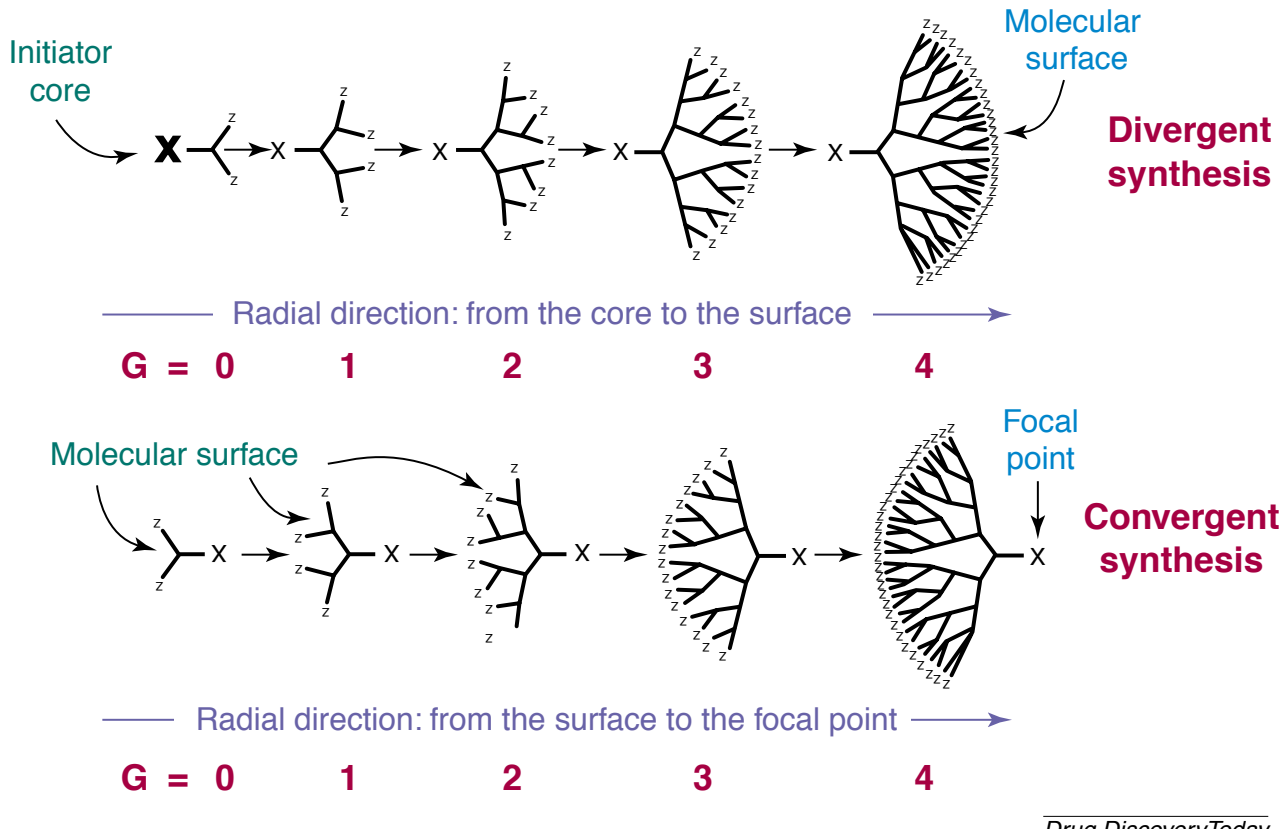


Figure 2. Two principle synthetic methods for constructing dendritic macromolecules (dendrons): **(a)** the divergent method, in which the synthesis begins from a polyfunctional core and continues radially outwards by successive stepwise activation and condensation, **(b)** the convergent method in which the synthesis begins at what will be the periphery of the final macromolecule and proceeds inwards.

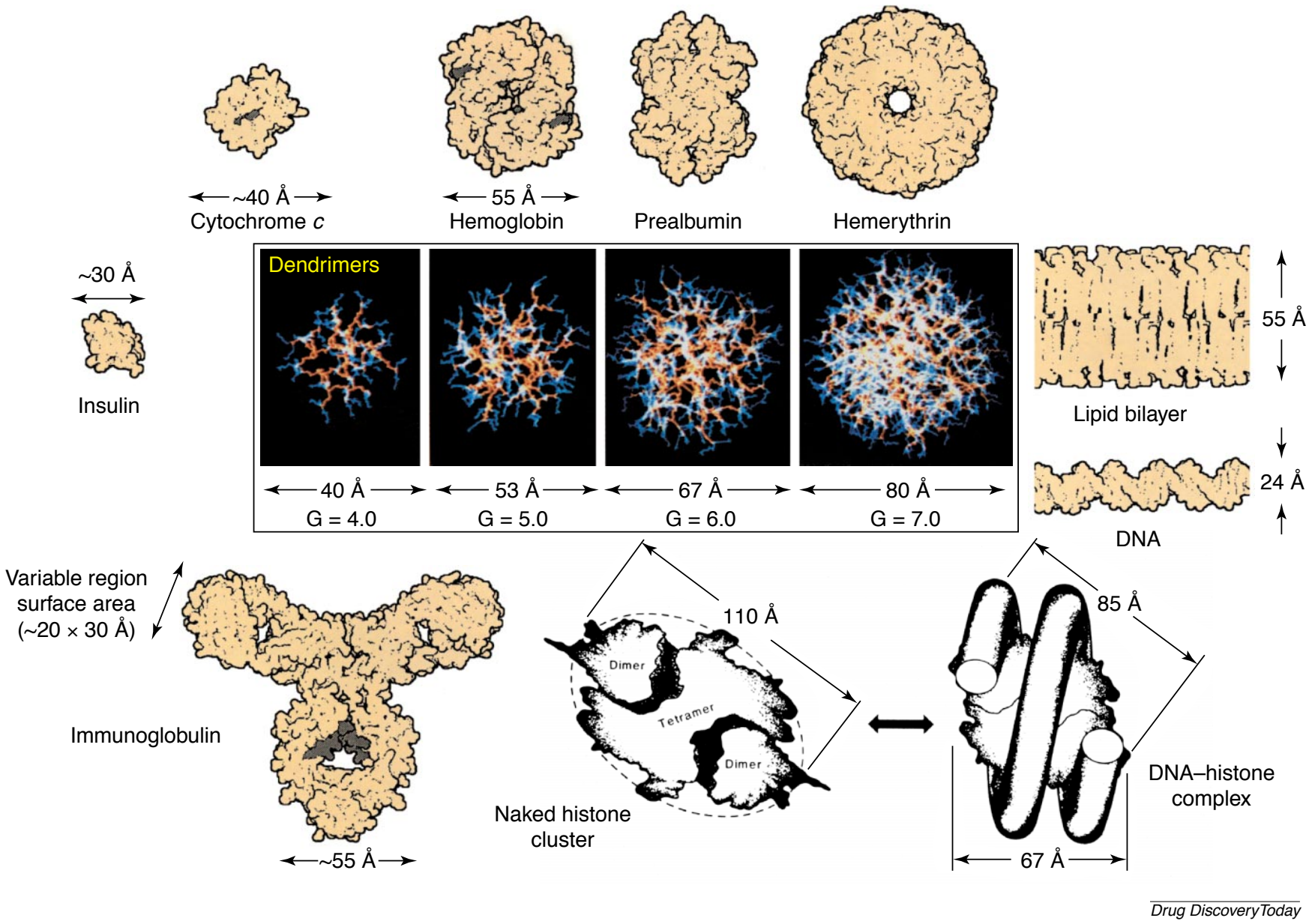
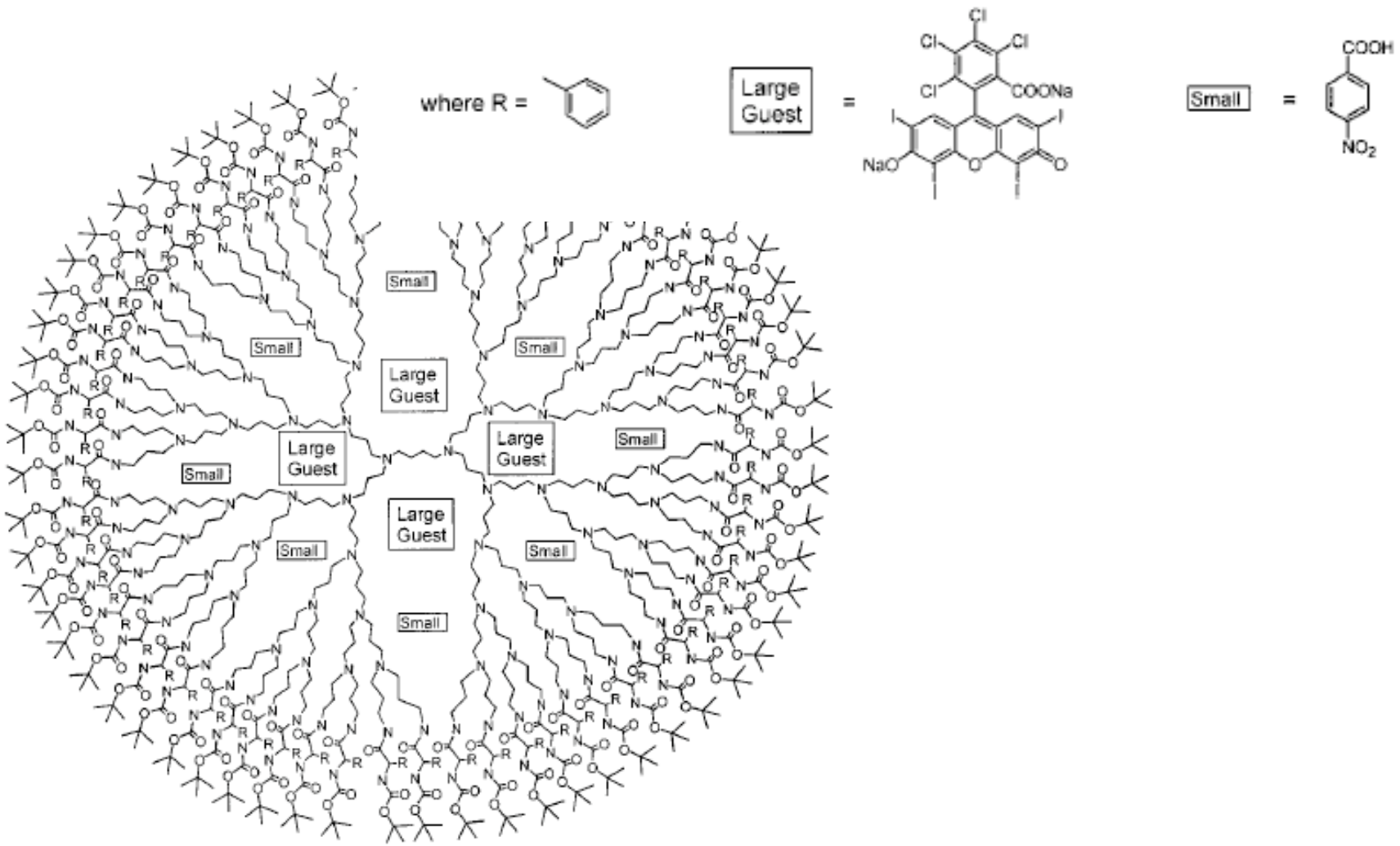


Figure 4. A dimensionally scaled comparison of a series of poly(amidoamine) (PAMAM) dendrimers (NH_3 core; G = 4–7) with a variety of proteins, a typical lipid-bilayer membrane and DNA, indicating the closely matched size and contours of important proteins and bioassemblies.

Dendrimers as carriers



But, cargo size depends on geometry

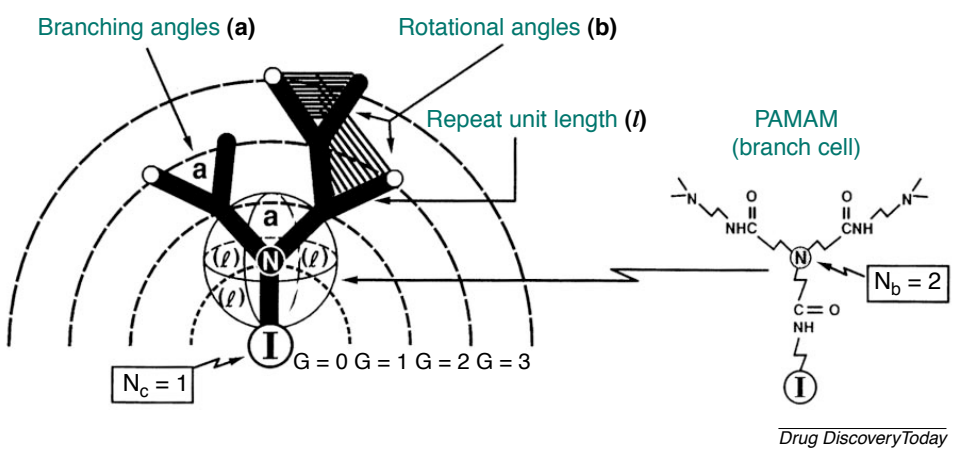


Figure 6. Branch cell parameters: branching angles **(a)**, rotational angles **(b)**, repeat unit length (***l***) and branch cell multiplicity (N_b) are the crucial parameters that determine cargo-space properties within the interior lattice of a dendrimer.

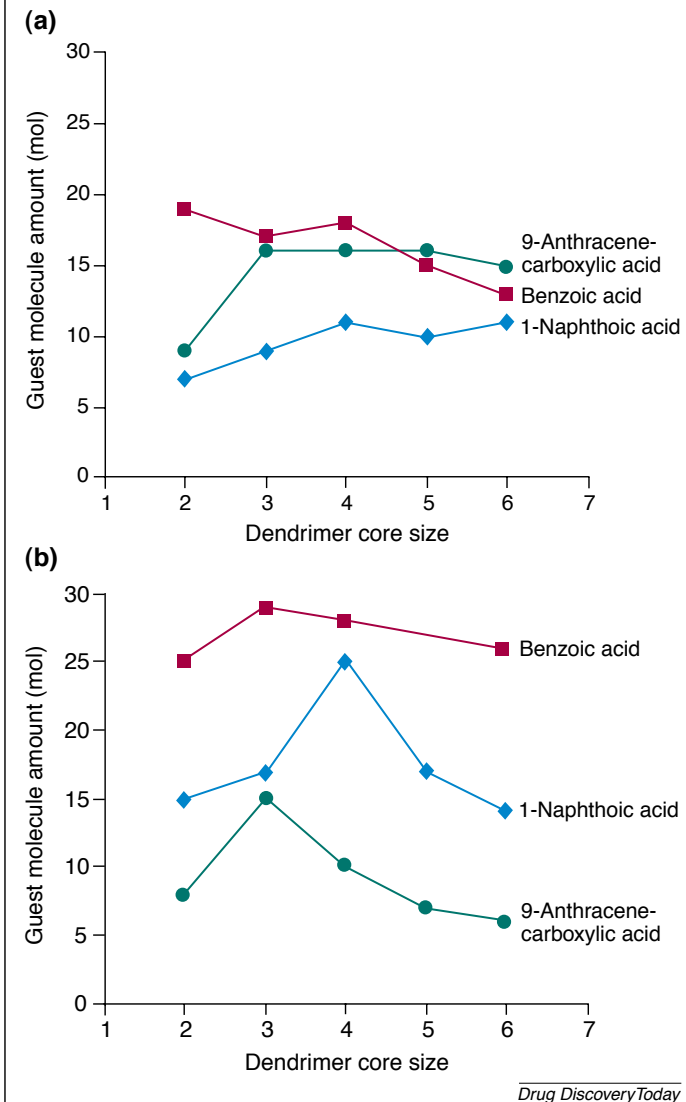


Figure 8. Host–guest interactions between dendrimers and hydrophobic guests, which are sparingly soluble in water. As a result of different internal cavity diameters, each class of dendrimeric host offers a different degree of inclusion complex formation. **(a)** Comparison of molar uptake between benzoic, 1-naphthoic and 9-anthracenecarboxylic acid by G = 2* (24-OH). **(b)** Comparison of molar uptake of between benzoic, 1-naphthoic and 9-anthracenecarboxylic acid by G=3* (48-OH).

Applications For Polymers

- Drug Delivery
  - Cargo capacity, immune response and pharmacokinetics modulation
- Other potential uses....??

Reading List

- PEG:
  - Veronese F.M., and Pasut G. 2005, PEGylation, successful approach to drug delivery. *Drug discovery today*. Vol. 10, No. 21. pp. 1451-1458.
- Micelles:
  - Gaucher et al., 2005, Block copolymer micelles: preparation, characterization and application in drug delivery. *J. Controlled Release* Vol. 109, pp. 169-188.
- Dendrimers:
  - Dykes, G., 2001 Dendrimers: a review of their appeal and applications. *J. Chem. Tech. Biotech.* 76:903-918
  - Esfand R. and Tomalia D.A., 2001 Poly(amidoamine) (PAMAM) dendrimers: from biomimicry to drug delivery and biomedical applications. *Drug delivery today*, Vol. 6 No. 8, pp. 427-436

Questions and Feedback