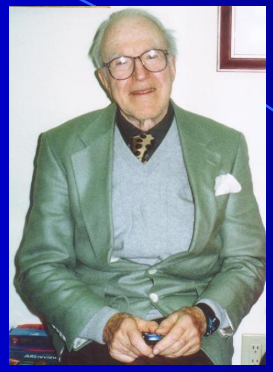
Convergence of Biotechnology & Nanotechnology

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"Convergence of Biotechnology and Nanotechnology",
October 18, 2001,
Workshop to Honor Britton Chance on his 88th Birthday,
The University of Texas Southwestern Medical Center,
Dallas, Texas, USA.

Industrial Age

- **Throughout the Industrial Age, we radically altered our society and environment**
  - **By extracting massive amounts of inanimate materials. Metals, minerals, fossil fuels are mined, filtered, pumped and dug from Earth.**
- **They are burned, forged, soldered, melted, reconstructed and recombined to create machines, structures, and artifacts**

buzzword is manufacturing.

Biotechnology

- In the Biotechnology Age, add living materials to the inanimate matter
- But what is the use or profitability of isolating genetic materials unless they
  - Can be copied
  - Can be reproduced in industrial quantities
- In order to establish an efficient living matter production line process, bioengineers need to invent a process for industrial-scale reproduction of life forms

Buzzword is biofacturing.

Alcehmy to Algeny

Pyrotechnology

- All metals are gold *in potentia*
- Possible to accelerate natural process by procedure
- Fusing metals together
- Fire is indispensable

Biotechnology

- Living world *in potentia*
- Accelerate natural process - new more efficient creations
- Slicing in and out genetic materials
- Recombinant DNA tool indispensable

Nanotechnology

- January 21, 2000, Former President Bill Clinton at Caltech made nanotechnology a top science and technology priority

National Nanotechnology Initiative – Leading to the next industrial revolution, Intragagency Working Group on Nanoscience, Engineering and Technology, National Science and Technology Council, 2000

Table 2. The investments of six U.S. departments and independent agencies in nanotechnology. (Adapted from National Nanotechnology Initiative).

Department/Agency	FY1997	FY1999	FY2001
NSF	65	85	150
DoD	32	70	110
DoE	7	58	93
NIST	4	16	10
NASA	3	5	20
NIH	5	21	39
Total	**116**	**255**	**422**

Now Nanotechnology

- The ability to move matter in molecular or atomic levels
- The ultimate goal is to create functional materials, devices and systems through the control of matters at the nanoscale

nanoscale = ~ 1-100 nm.

Science & Engineering

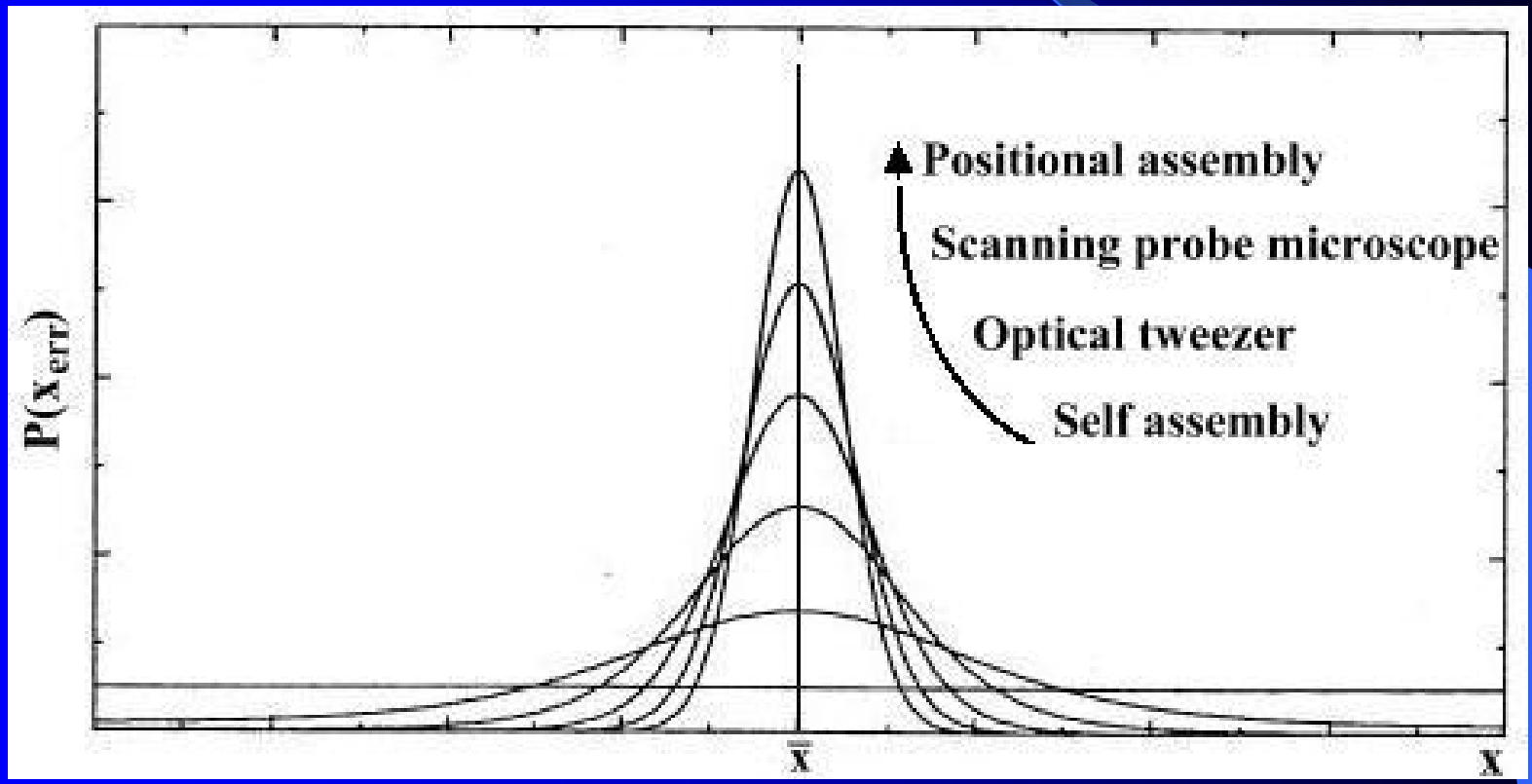
- Similar to other technologies in science and engineering, nanotechnology can be broadly divided into two major fields:
  - nanoscience and nanoengineering
- It is important that nanoscientists first lay the foundations for nanotechnology through new findings
- so that nanoengineers can develop nano-systems and nano-devices.

Nanotech Age

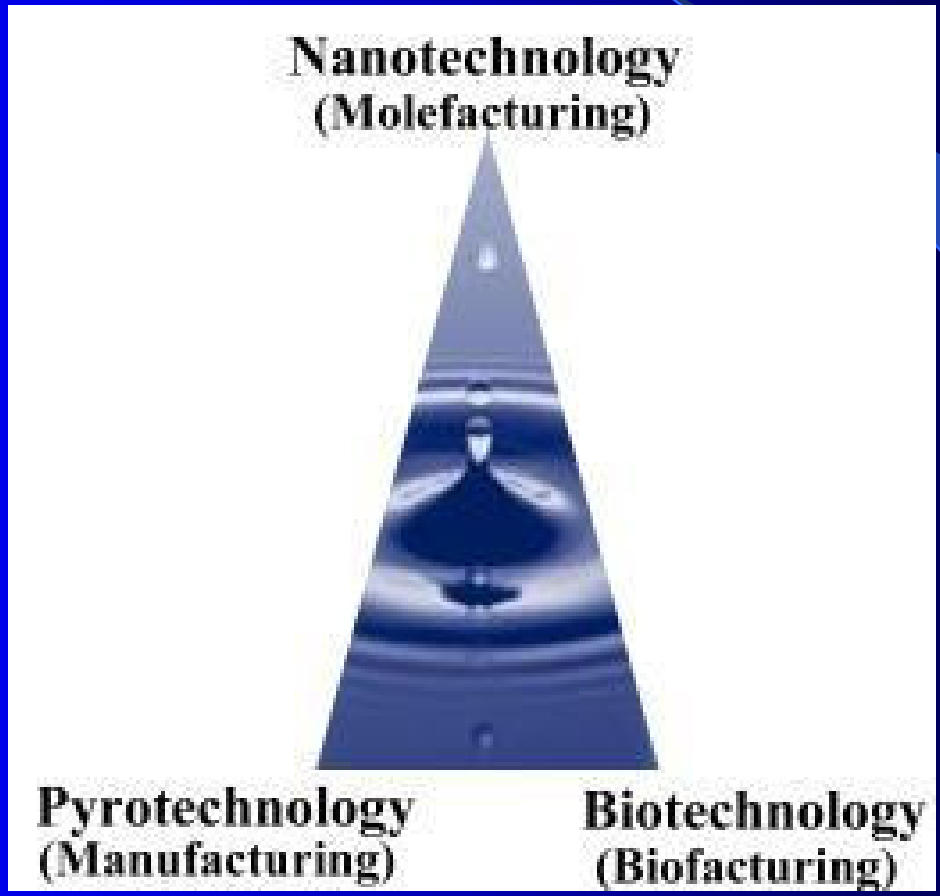
- In the Nanotechnology Age, get essentially every atom in the right place, and make almost any structure consistent with basic laws of physics and chemistry
- The process will be futile unless we can
  - Have manufacturing costs not greatly exceeding the cost of required raw materials and energy
  - Positional assembly, which means we need molecular robotics for assembling
  - Self-replication or be able to make copies of self and produce useful products

Buzzword – Molefacture.

Self Assembly Vs Positional Assembly



Pyro-Bio-Nano



Mimicking Nature

- Aspired by nature, but not blindly mimick
  - Flight, airplanes are different form birds

Biomimetics.

Horse vs Car

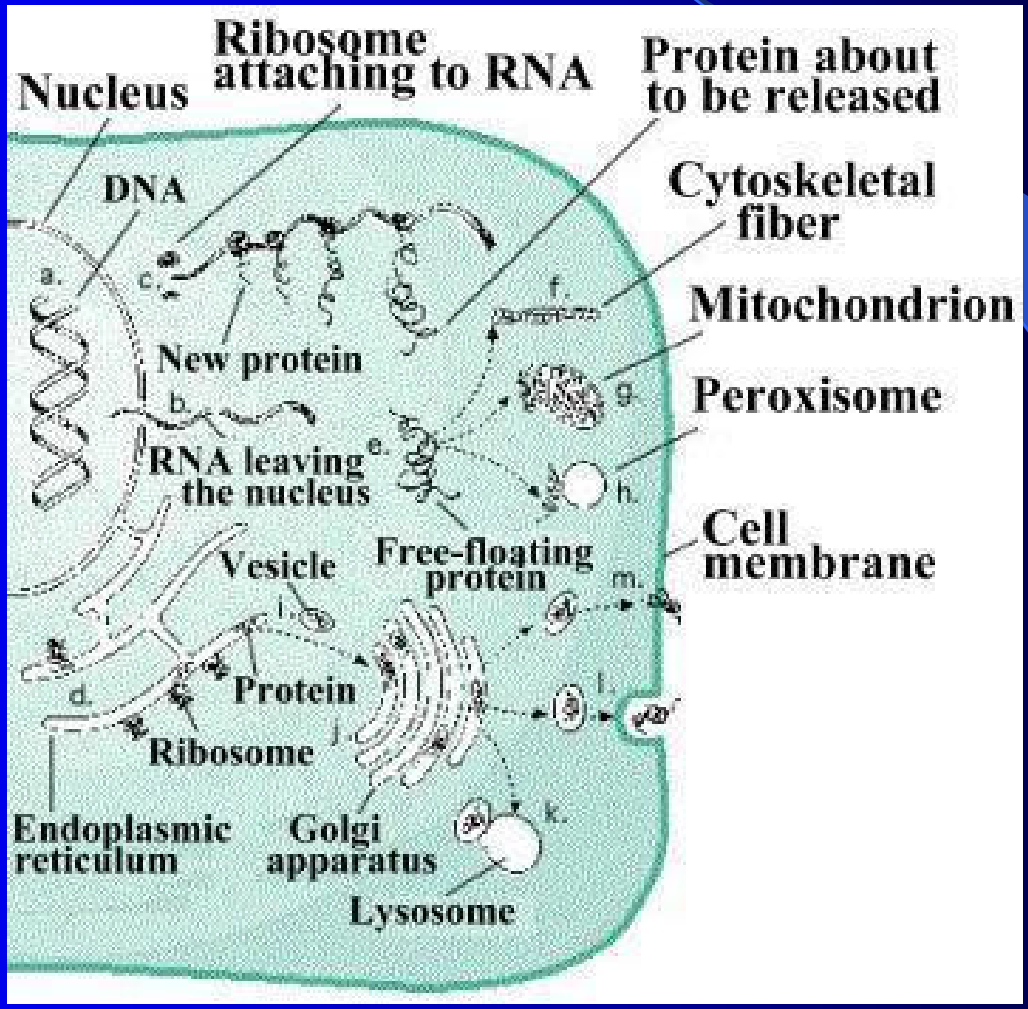
Horse

- Can eat corn, hay…
- Adapt to changes
- Self repair
- More complex at the expense of efficiency

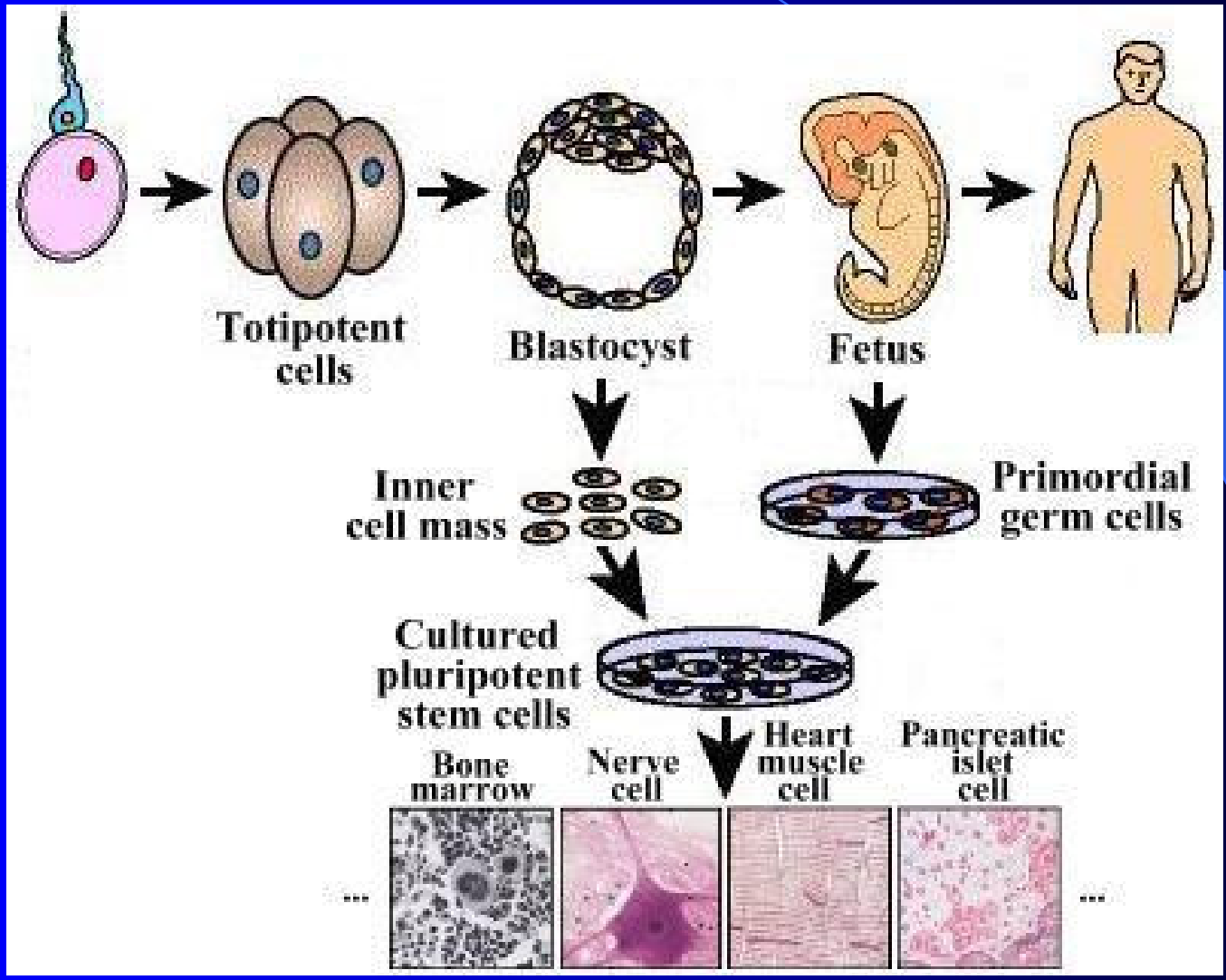
Car

- Consume only gas
- Inflexible, need road
- Have parts, not self repair
- Work because design to work inexpensively

Self Assembly and Self Repair

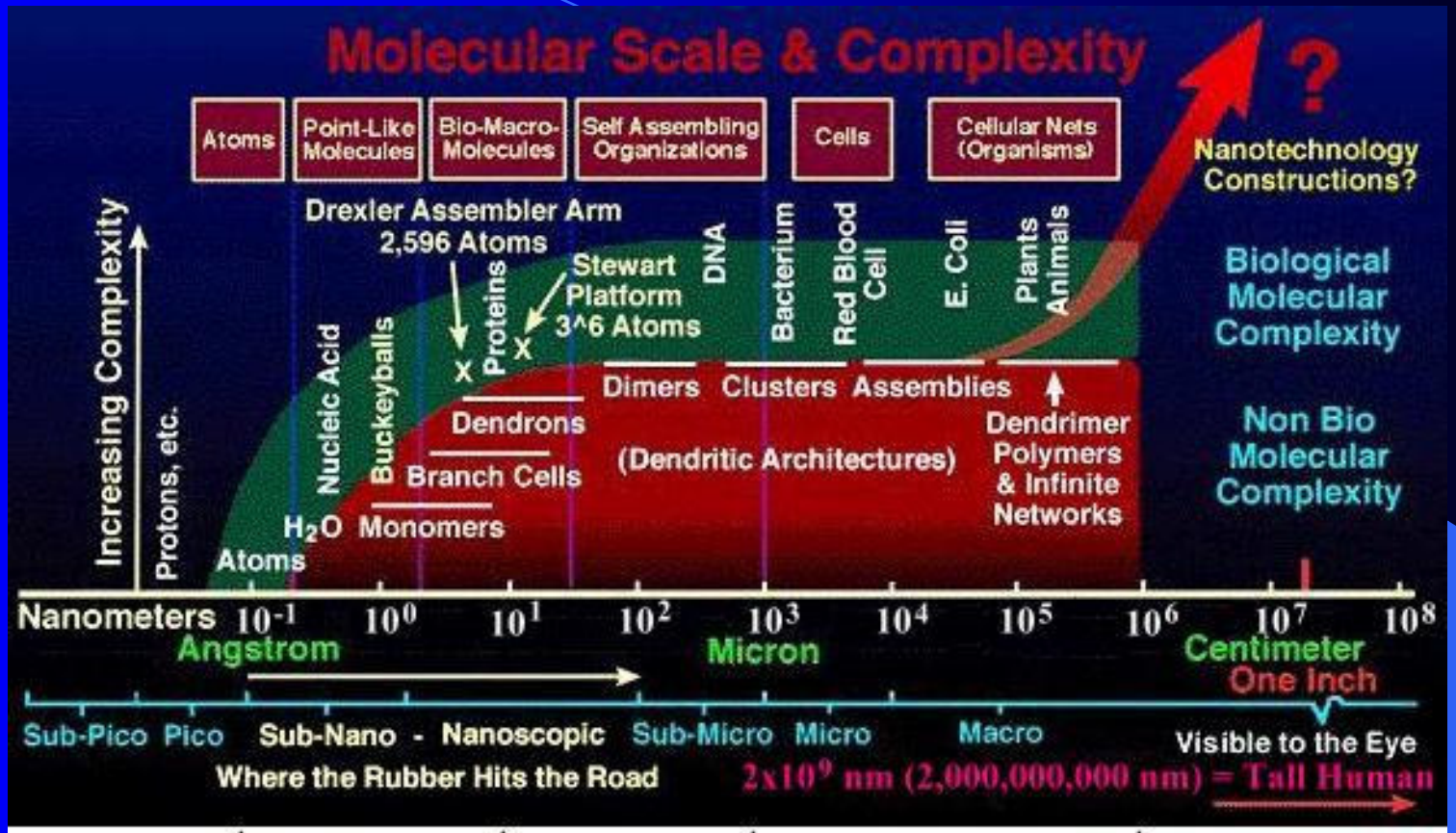


Stem Cell Research



Nano Factory

- Thus, the mechanical designs proposed for nanotechnology are more like a factory than a living system
- Molecular scale robotic arms capable of moving and positioning molecular parts
  - To assemble rigid molecular products
  - using methods more familiar to machine shops
  - than the complex brew of chemicals found within a cell.

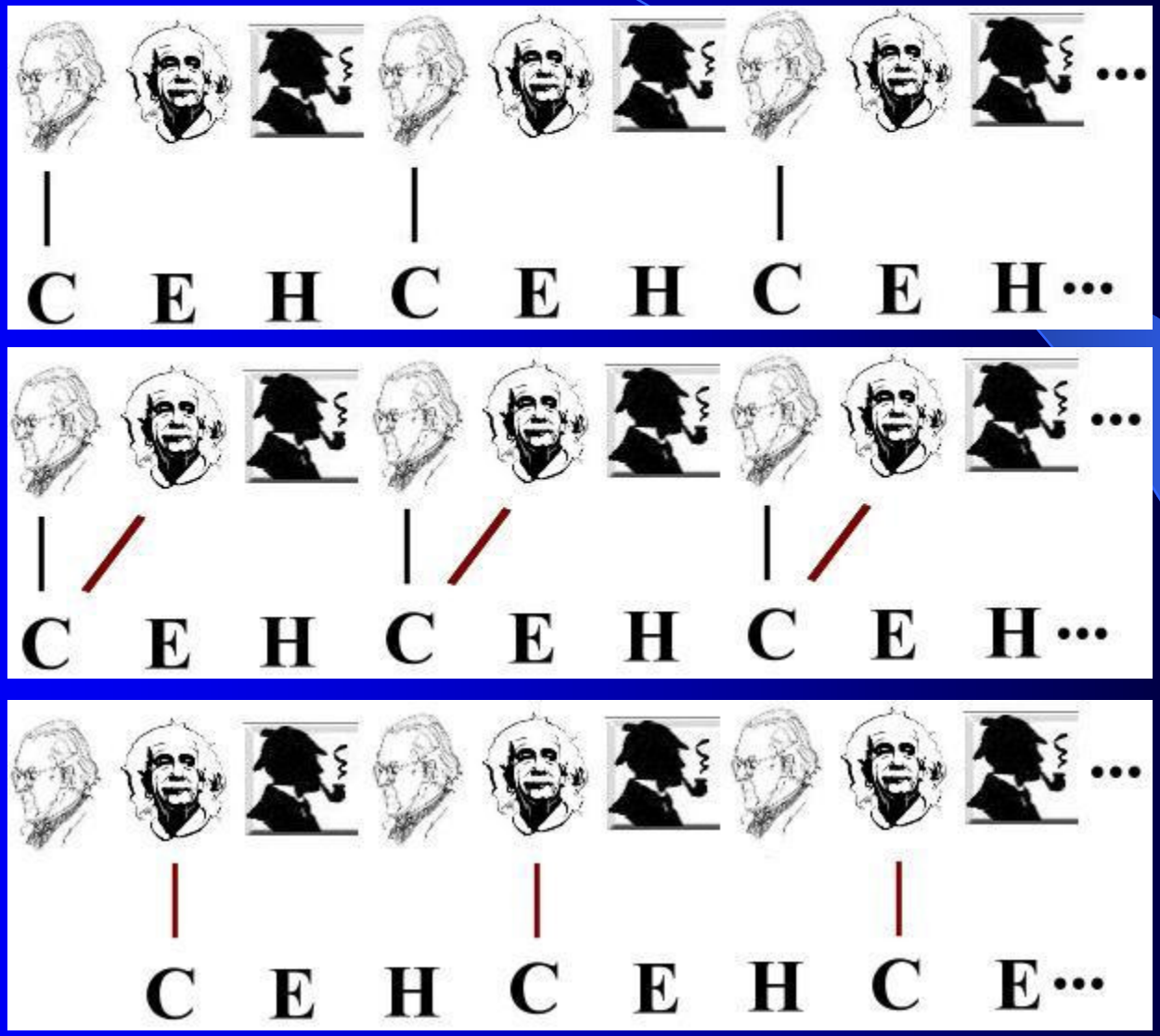


Angstrom	Viruses (10~100 nm)	Red Blood Cells (10 nm)	Fly (10 mm)
Atoms (0.1~0.5 nm)	Antibodies (10 nm)	Bacteria (100 nm~ 10 μm)	Insect (1 mm~1 cm)
Molecules (0.3~23 nm)	Proteins (1~10 nm)	Hair (50 μm)	Human Egg (100 μm)
X-rays (0.1~10 nm)	UV (100 nm)	Visible light (1 μm)	Microwave (1 cm)
		Infrared (10 μm)	

Table 3. Complexity of self-replicating systems. Estimate of the Internet worm is an approximation of the number of bits in the C source code. For biological systems, the complexity is twice the number of base pairs. The complexity of NASA proposal was taken from Advanced Automation for Space Missions. Note that viruses do not qualify as a self-replicating system as they require a living system to infect. Viruses need additional molecular machinery provided by the host environment.[1]

Complexity of self replicating systems	Kilo Bits
Von Neumann's universal constructor	~500,000
Internet worm	~500,000
Mycoplasma genitalium	~1,160,140
E. coli	~9,278,442
Drexler's assembler	~100,000,000
Human	~6,400,000,000
NASA Lunar Manufacturing Facility	>100,000,000,000

Nano Manipulations



Biotech Vs Nanotech

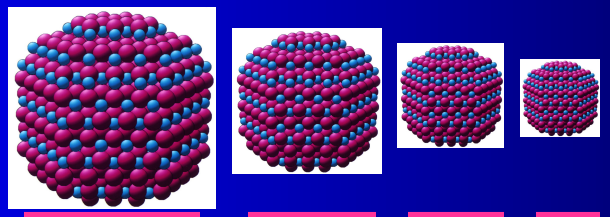
Biotech

- Living world in potentia
- Accelerate natural process by new creations
- Slicing in and out genetic materials
- Recombinant DNA

Nanotech

- Animate & inanimate material in potentia
- To improve and enhance material to perfect performance
- Moving atoms
- Molecular manufacturing

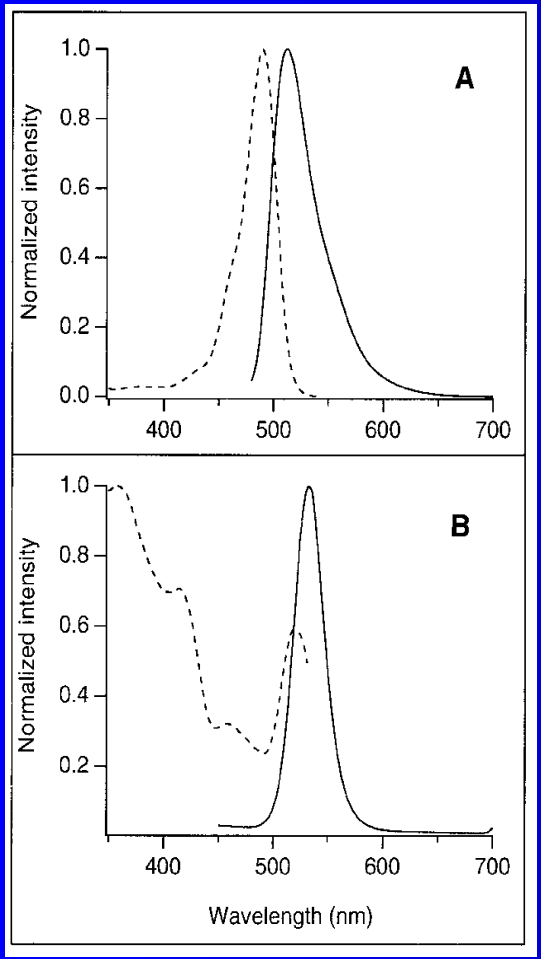
Nanocrystals



Advantages of Nanocrystals

- λ can be tuned to any chosen λ by changing size or material composition
- Remarkable photostability
- Absorb any λ bluer than emission λ
- Sharp color (FWHM < 35 nm)
- High quantum yield (~80%)
- Brightness and simple excitation
- Symmetric emission: ~~red tail~~, ~~cross-talk~~

Comparison of Organic Dye and SCN



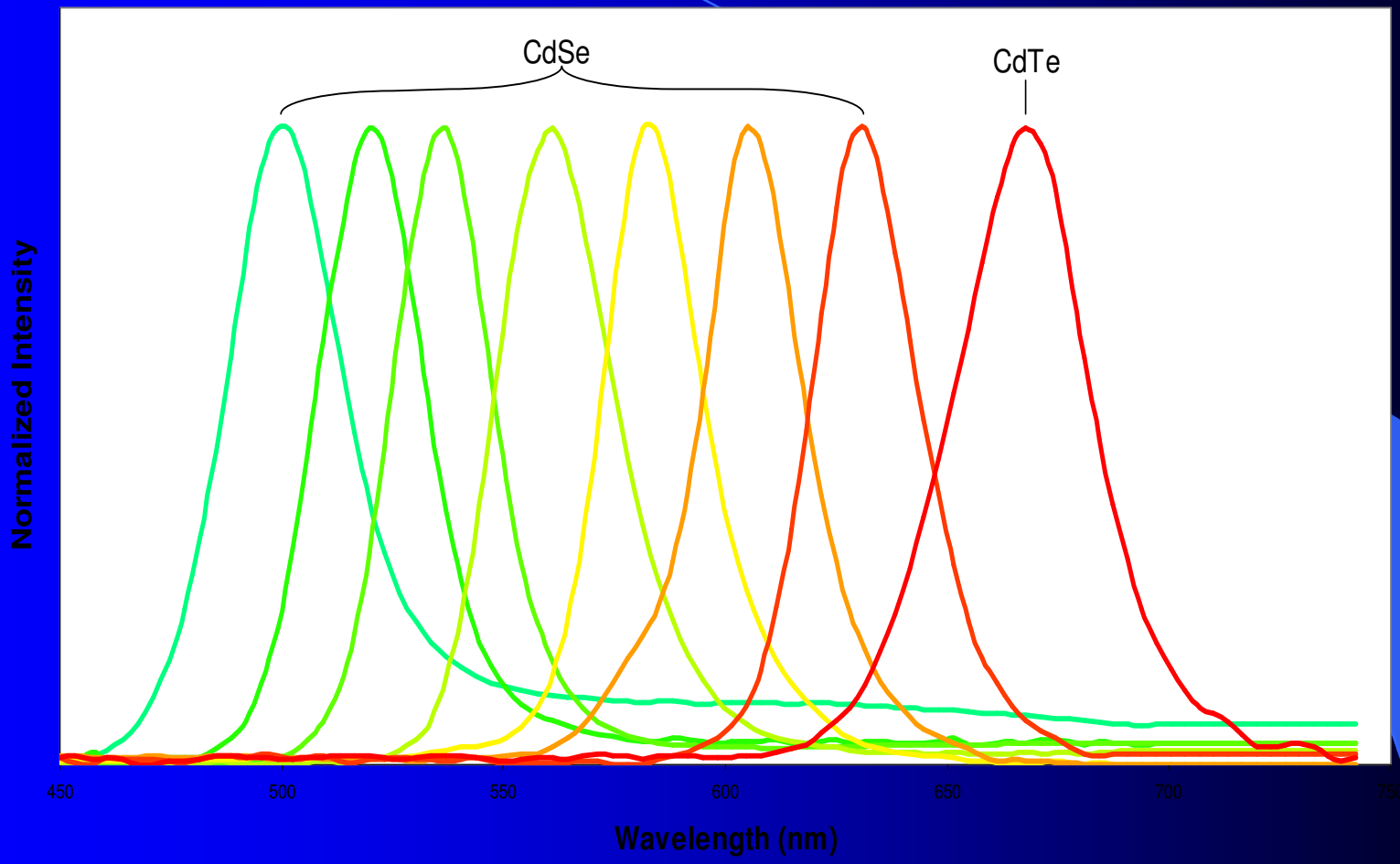
Organic Dyes

- Narrow excitation
- Broad, asymmetric emission, red tail
- Photobleaching
- Small Stokes shift

Semiconductor Nanocrystals

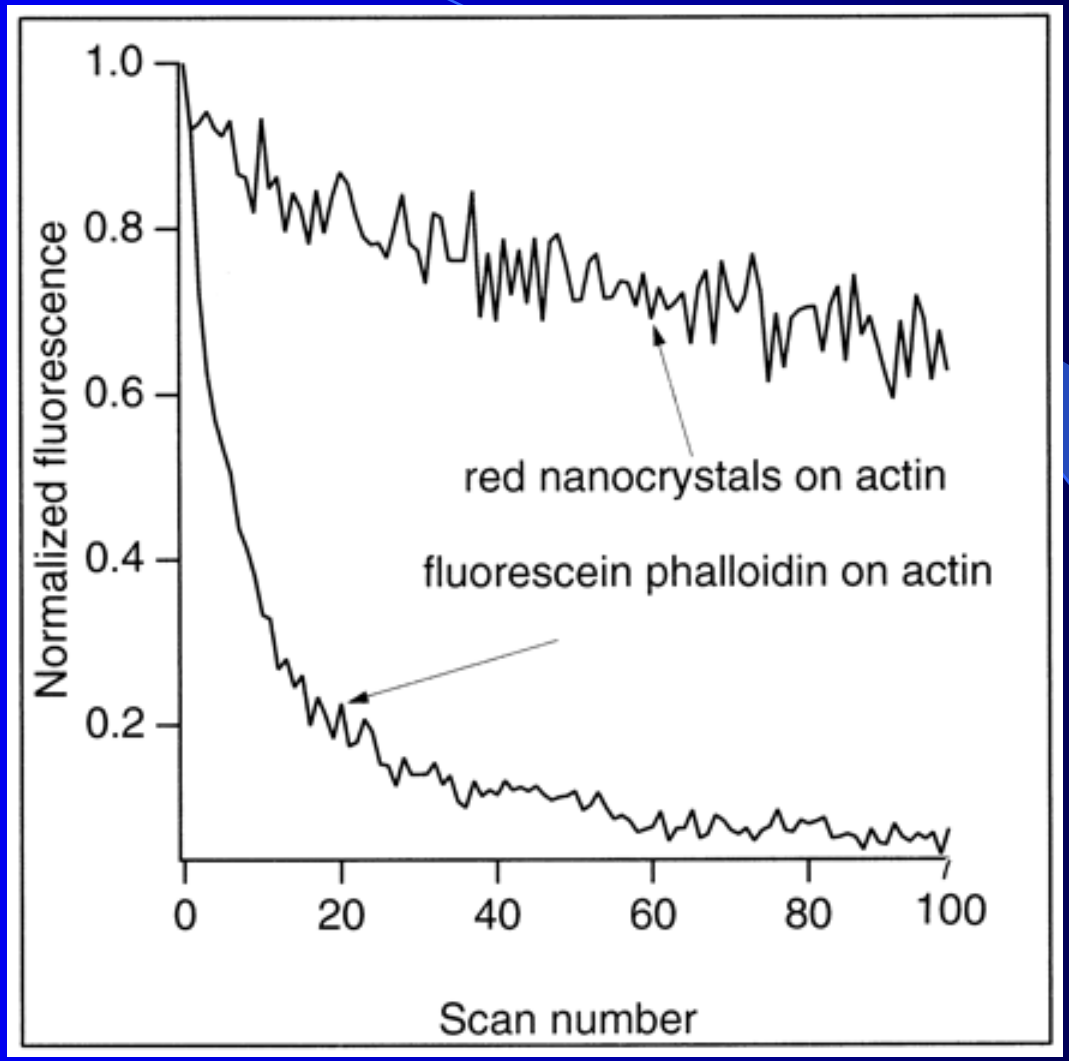
- Broad excitation
- Narrow, symmetric emission
- Photostable
- Size-tunable
- Large Stokes shift

Material and Size Dependance of SCNs



λ can be tuned to any chosen λ by changing size or material composition

Photostability of Semiconductor Nanocrystals

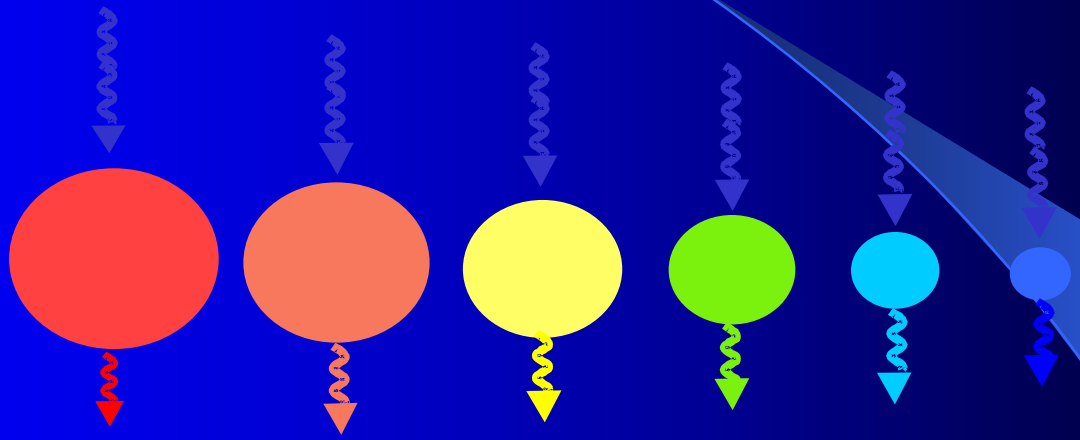


Remarkable photostability

Photophysical Properties of Semiconductor Nanocrystals (SCNs)

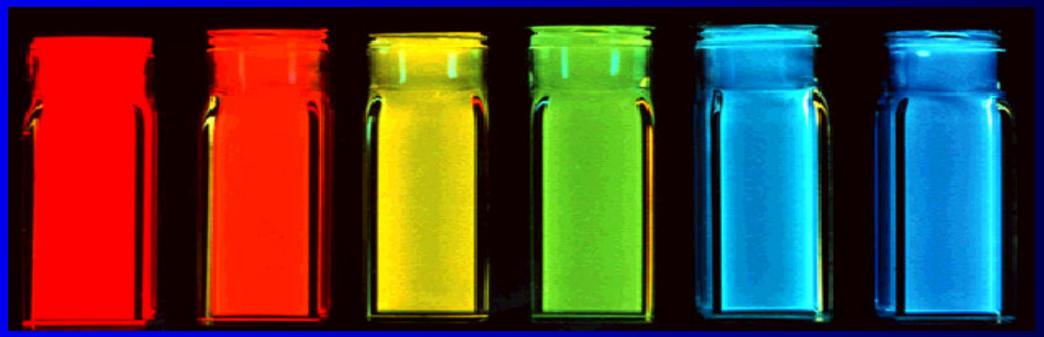
Any light source "bluer" than the emission excites the semiconductor nanocrystals (SCNs) of interest

A.



The emission of SCNs can be tuned by changes in their sizes

B.



Absorb any λ bluer than emission λ

Applications in Biotechnology

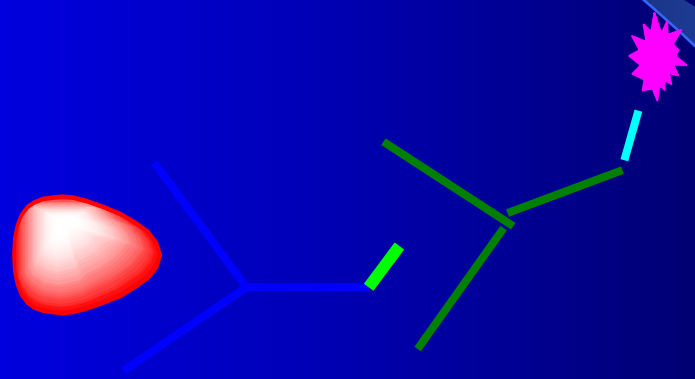
- A New Platform of Arrays
  Possible application -
  a. Protein detection arrays
  b. 2D electrophoresis and SCN bioconjugates
  c. Ultrasensitive biological detection and labeling

Biotin-Straptavidin based Detection

- Tumor analysis
  - Primary antibody against surface antigen
  - Biotinylated secondary antibody recognizing primary antibody is applied
  - Strong biotin-straptavidin interaction → bioconjugate of SCN-straptavidin
  - Extremely sensitive detection.

Immunohistochemical Detection

- Antibody-SCN bioconjugate provides a remarkable immunohistochemical staining
  - Simple SCN-antibody can recognize common epitope on primary antibody
  - Primary antibody can be raised to recognize any target: antigens, proteins, nucleic acids, saccharides, cells and tissues



A universal immunohistochemical staining technology for ultrasensitive detection and dignostics. A primary antibody (in blue) recognizing its target (in red) bears **a universal epitope** (in green) that is recognized by a secondary antibody (in dark green) that is conjugated to a fluorescent nanoparticle (in pink). It is worth to stress that the primary antibody can be any member of a library while the epitope and the bioconjugate are universal. This will provide an exceedingly efficient pathway for us to quickly develop our platform technology.

Diagnostics of Tumor, FACs

- Conjugates of antibodies recognizing markers of tumors offer sensitive diagnostic tools.

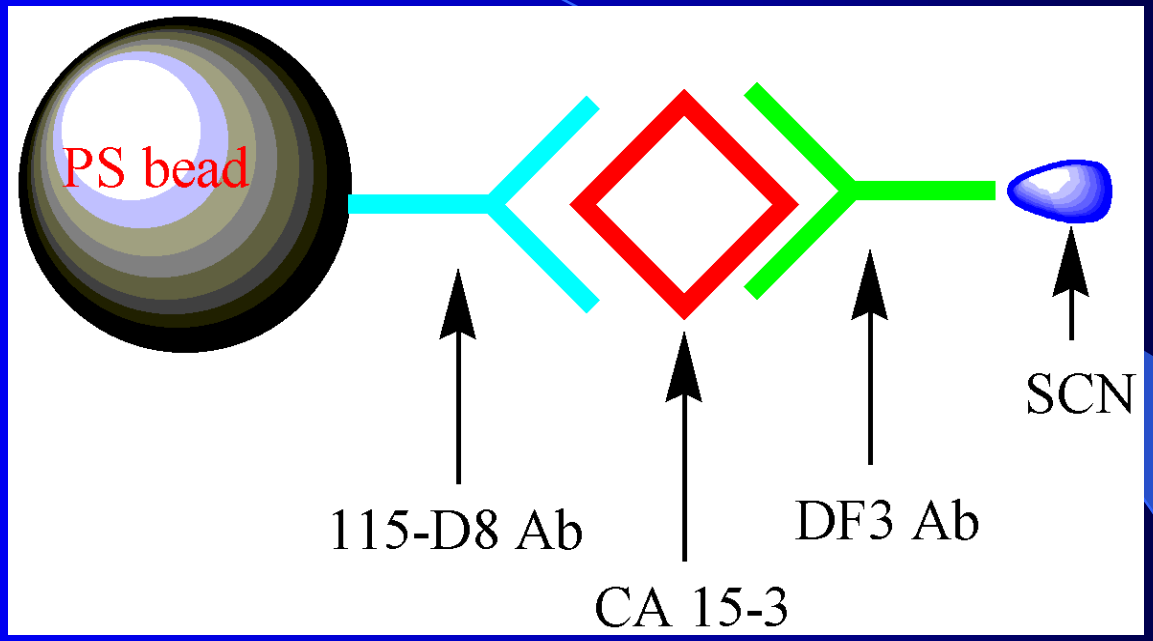


Figure 2. Cancer diagnostics using the tumor marker of CA 15-3 in a double-determinant or sandwich fluoroimmunoassay. The monoclonal antibody 115-D8 (in light blue), attached to a polystyrene bead, binds to the mucin-like membrane glycoprotein CA 15-3 (in red), pulling it out of solution. The SCN (in blue)-labeled monoclonal antibody DF3 (in green) binds the CA 15-3 and the polystyrene beads are then subjected to FACS analysis.

Thank you