Nanotechnology-based Materials and Devices for Biomedicine

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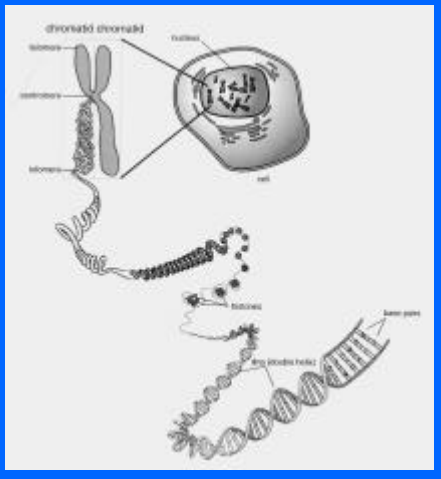
Outline

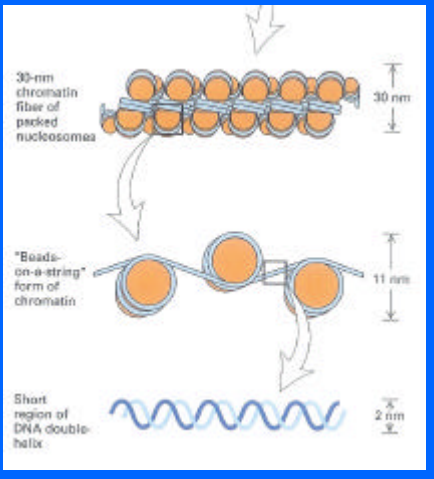
- Single-molecule Studies of Chromatin Fibers
- Bacteriophages: Molecular Nano-machines
- Crystalline Colloidal Arrays: Molecular Sensing Photonic Crystals
- Nanophotonic Chip Technologies for Instrumentation

Nanoscience and Technology

- 1-100 nm length scale: atomic, molecular or macromolecular levels
- Properties not predictable from those at micro or macro scale
- New phenomena associated with surface/interface effects and quantum size effects in confined structures
- New modes of transports, collective phenomena, chemical reactivities, physical properties, etc.
- In living systems:
  - multiple length scales and functions (molecules and chemical pathways, sub-cellular mechanical structure, cells, organs and tissues)

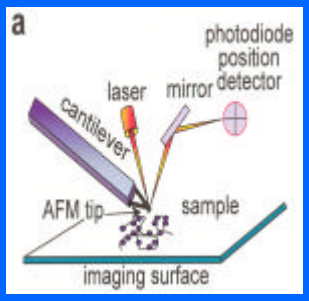
Hierarchical Structure of Chromosome

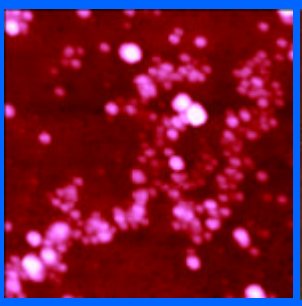




Single-molecule Approach to Chromatin Structure and Dynamics

Visualization of the three dimensional arrangement of nucleosomes in the chromatin fiber



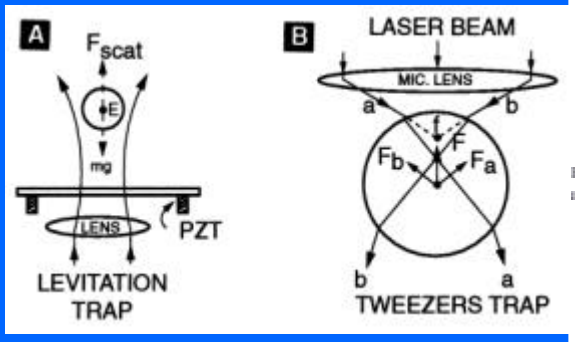


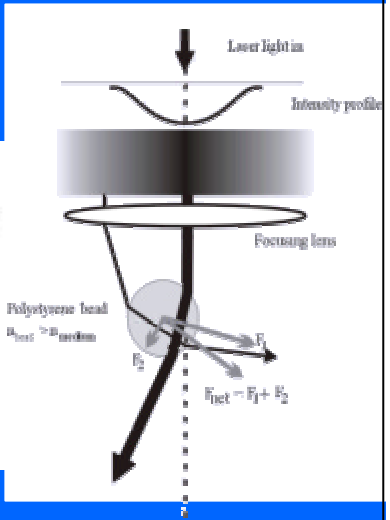
Atomic Force Microscope

After linker histone removal

S.H. Leuba and J. Zlatanova, Eds. (2001) Biology at the single-molecule level, Pergamon

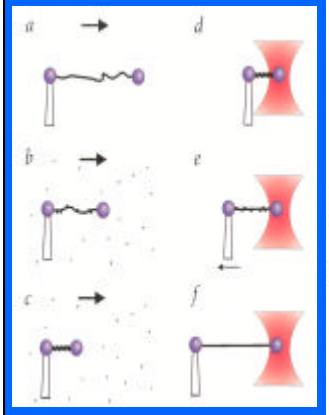
Optical Trapping

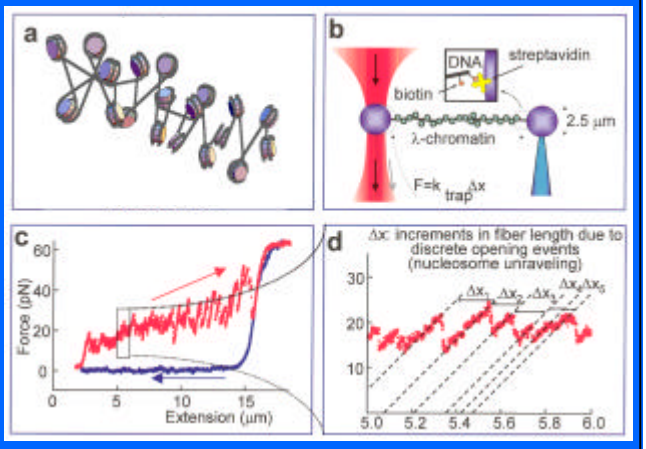




A. Ashkin, PNAS, 94, 4853 (1997)

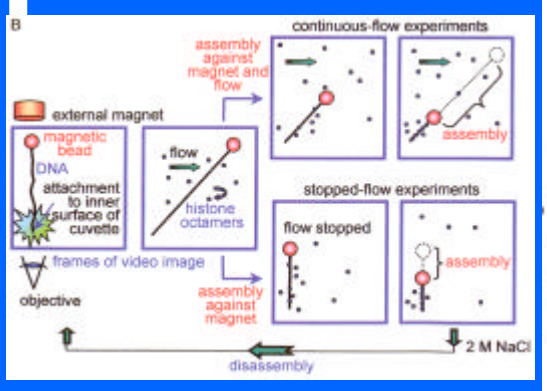
Unfolding Individual Nucleosomes
Optical tweezers study

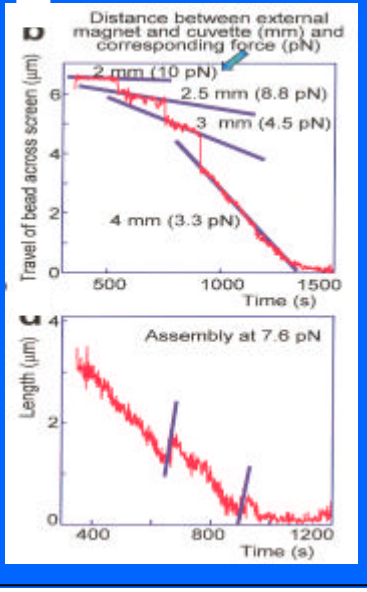




S.H. Leuba et al., Nature Struct. Biol. 8, 606 (2001)

Assembly of Single Chromatin Fibers
Magnetic tweezers study

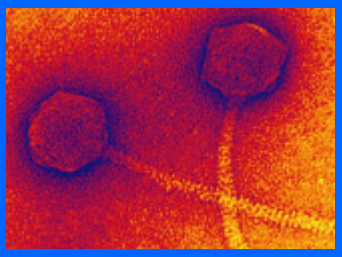




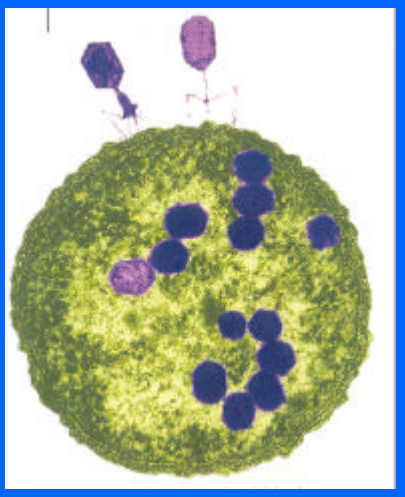
S.H. Leuba et al., PNAS, 100, 495 (2003)

Phages
The small but powerful living dead

Small genomics (~10^4 bp)
Evolution over 3.5 billion years
Global population > 10^{30} phages

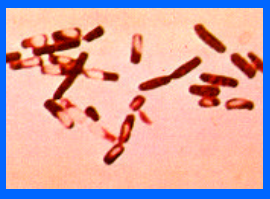


R. Hendrix and G. Hatfull



Fighting back:
Using viruses to attack bacterial pathogens

- Bacterial pathogens: natural killers and potent bioweapons
- Bacteriophages (viruses that infect bacteria) are their natural enemies
- Phages - or phage derivatives - can be employed in many ways to battle pathogens and bioweapons



Anthrax

Tuberculosis and Anthrax:
Common Strategies

- Identify organism
- Determine drug sensitivity
- Immediate & effective treatment

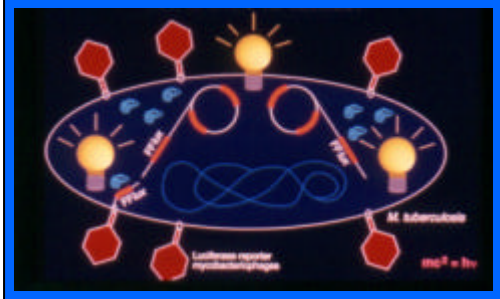
Phage "Corndog"

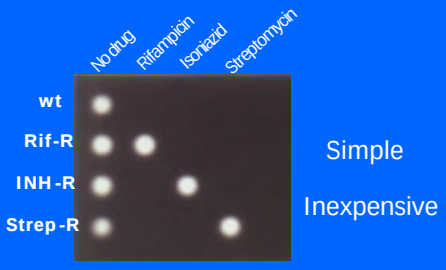
G. Hatfull

Luciferase Reporter Phages

Rapid, sensitive detection of bacterial cells

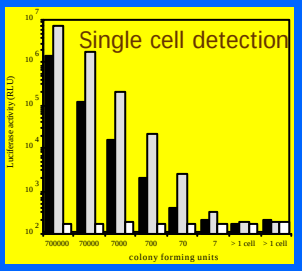
Phage-delivery of a reporter gene





Simple

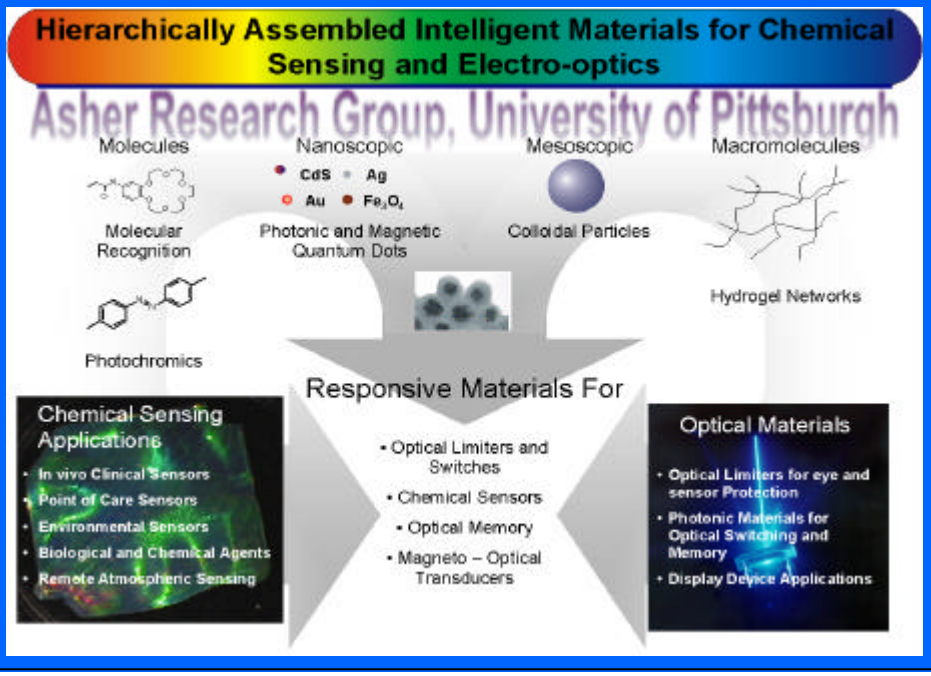
Inexpensive



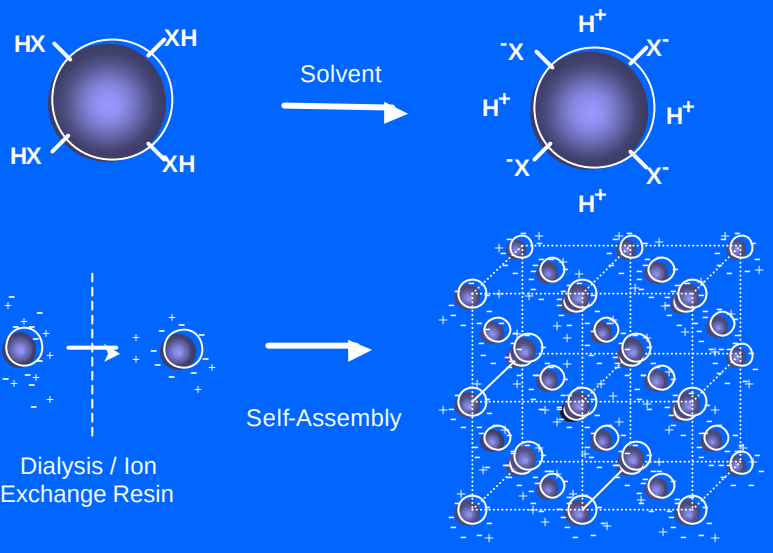
Drug-susceptibility testing

G. Hatfull

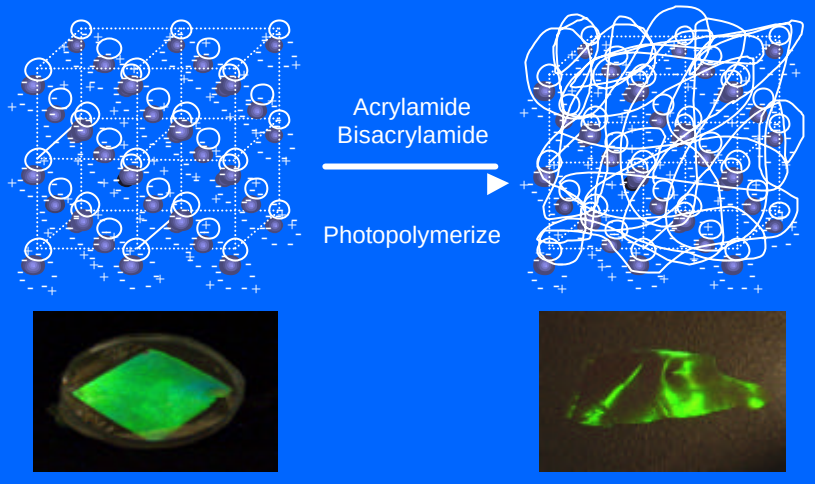
S. Asher, Dept of Chemistry



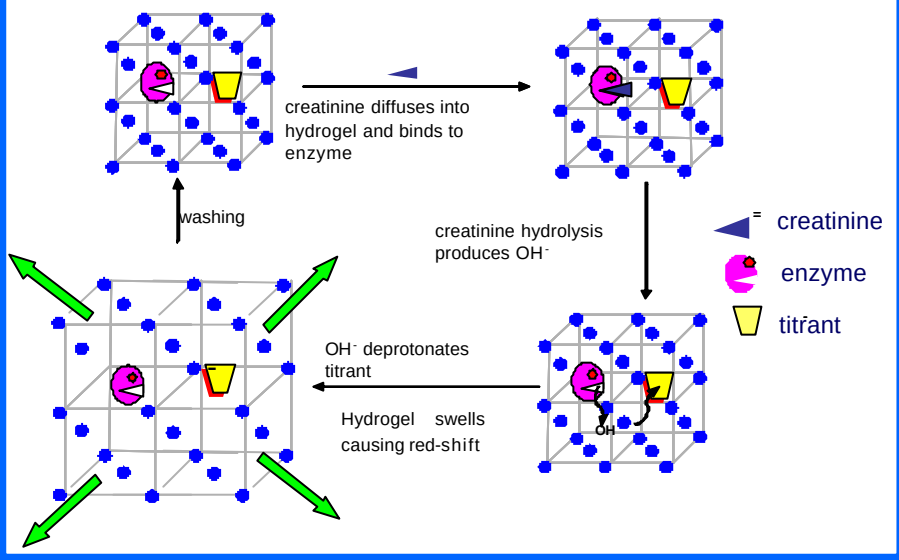
Crystalline Colloidal Array Self-Assembly



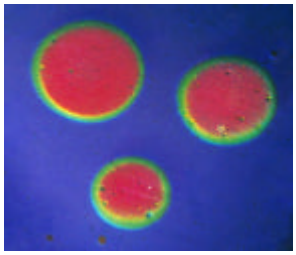
Polymerized CCA Fabrication

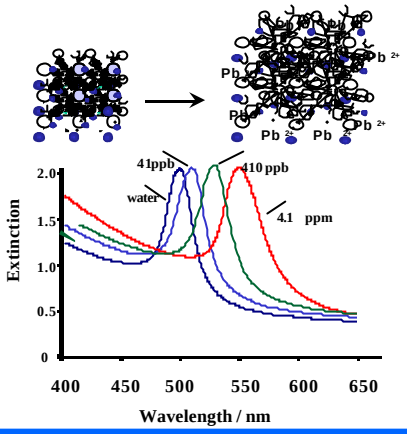


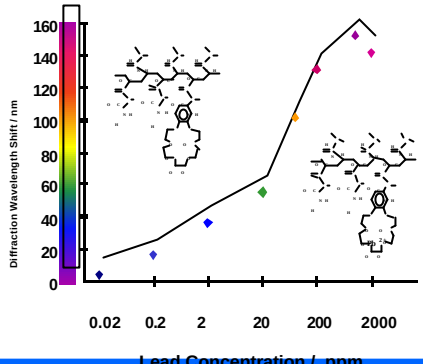
General Clinical Sensing Motif



Chelation of Pb^{2+} ion results in immobilization of the counter ion. Osmotic pressure swells the gel, which results in the red shift of diffraction.

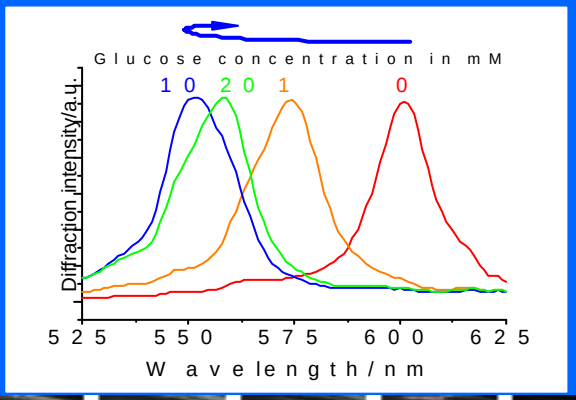




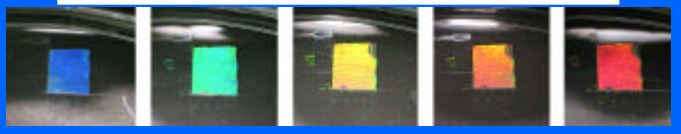


S. Asher et al., Anal Bioanal Chem, 373, 632 (2002)

Photonic Crystal Glucose Sensing
Response to glucose in artificial tear fluid



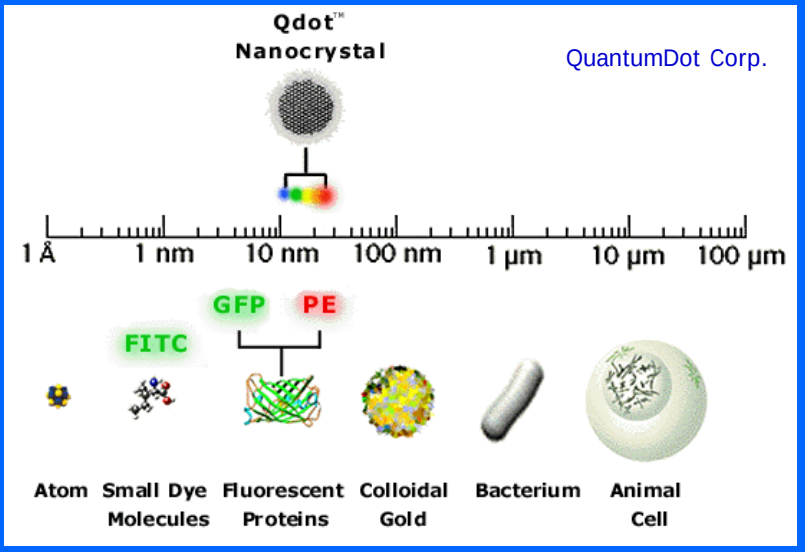
2 mM tris-HCl, pH 8.5;150 mM NaCl



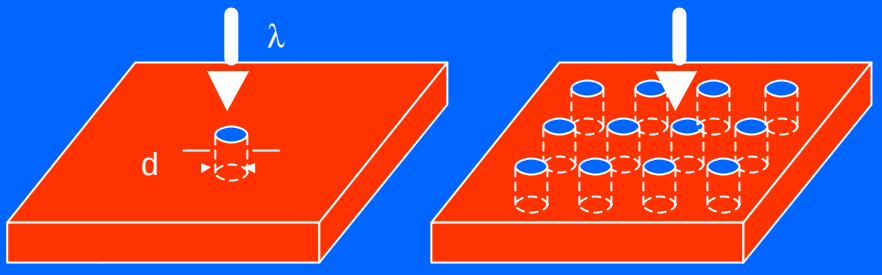
S. Asher et al., Anal. Chem. 75, 2316 (2003)

Point-of-Care Clinical Sensors

Quantum Dot Fluorophores



Transmission of Light through Sub-wavelength Apertures in Metal Films

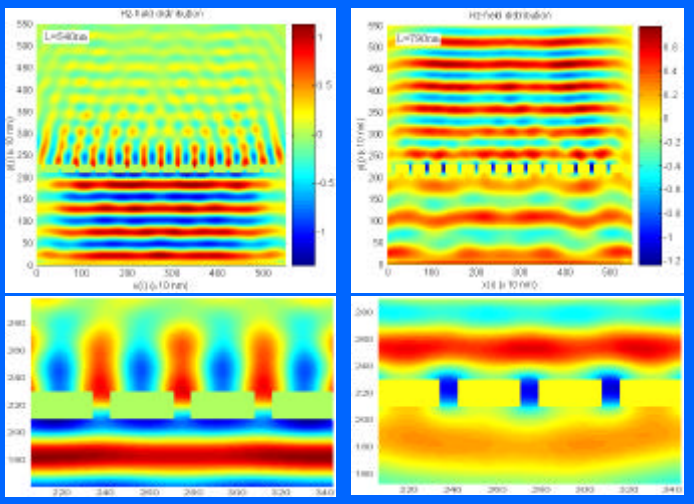


$T/f \sim (d/l)^4$

T ?

Optical Interactions in Metallic Nanoaperture Arrays
Slit width: 80 nm

FDTD simulation

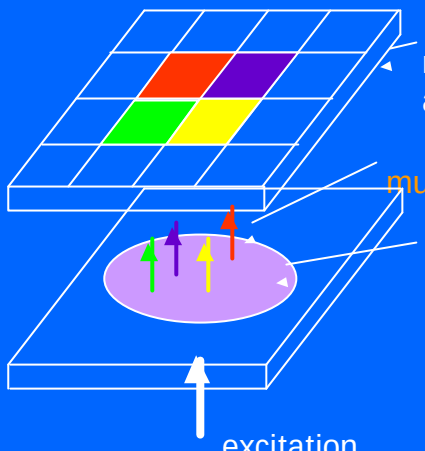


Applications:

Nano-optic filters, beam shaping and concentrating devices beyond diffractive optics

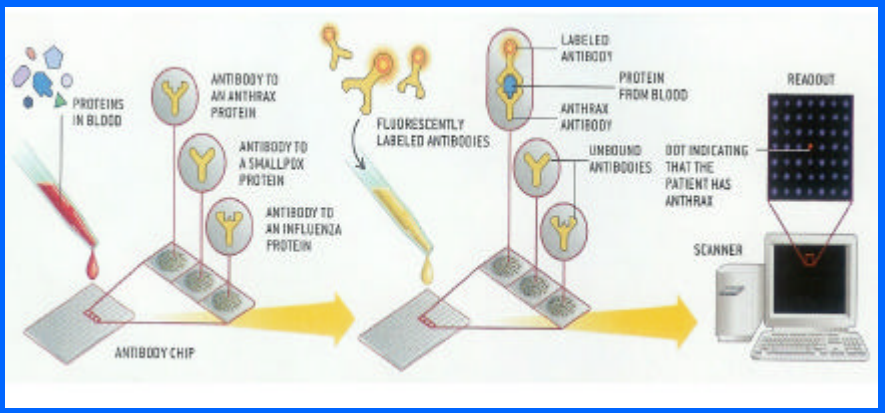
H.K. Kim et al., Appl. Phys. Lett. 83, 3021 (2003)

Nano-optic Multispectral Fluorescence Detection



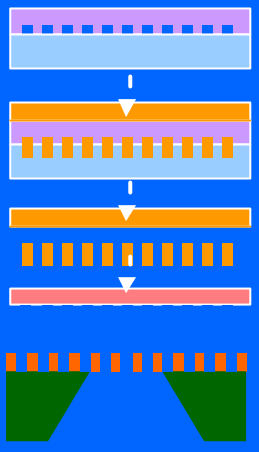
H.K. Kim

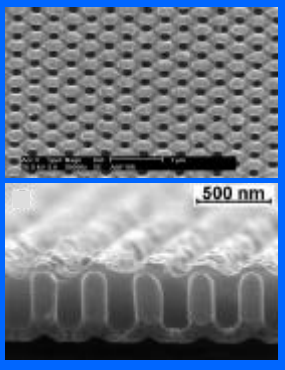
Protein Arrays

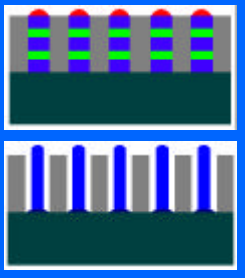


Functional nanoelement arrays on a chip

Template / Molding / Replication





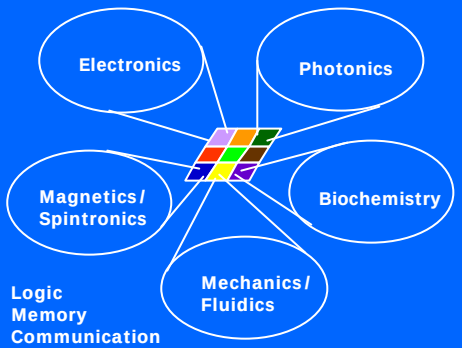


Separation (such as antibody-based nanomembranes for drug separation) and absorbent media, catalytic surface and supports

High-density sensor arrays and electrochemical electrodes (nanoprobe arrays)

H.K. Kim et al., Appl. Phys. Lett. 81, 3458 (2002)

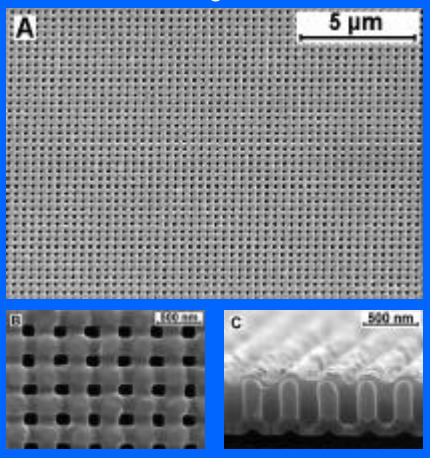
Nanosystems-on-a-chip based on self-organized nanochannel arrays



Logic
Memory
Communication
Control
Sensing
Separation
Absorbent
Actuation

Pore diameter: > 5 nm
Inter-pore distance: > 50 nm
(pore density ~10^{11} cm^{-2})

Nanopore arrays formed on silica with a directed self-organization method



Single-domain, square-lattice array of holes over entire chip area (~cm^2)