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Nanotechnology Inspired by Nature

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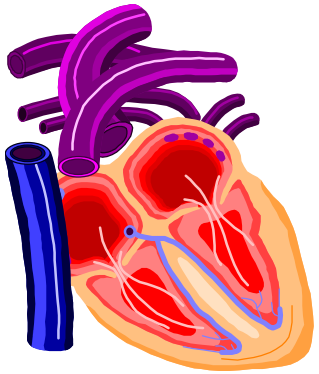
Biology can Lead to New Capabilities in Nanotechnology

- Studies of biological functions, materials, and interfaces can enable new sensors and microsystems
  - Membrane-based sensors
  - Motor-protein driven assembly

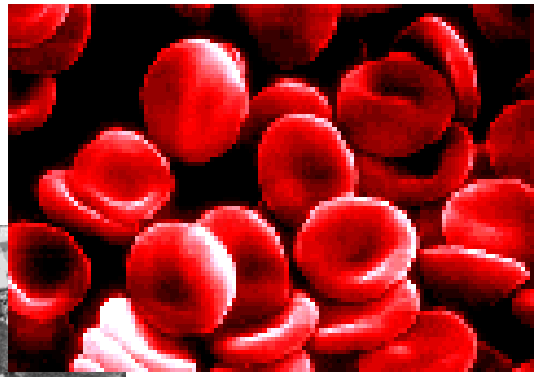
- (Note that nanotechnology tools also enable new methods for probing biological systems)

Living systems use Nanotechnology to achieve micro- and macro- function

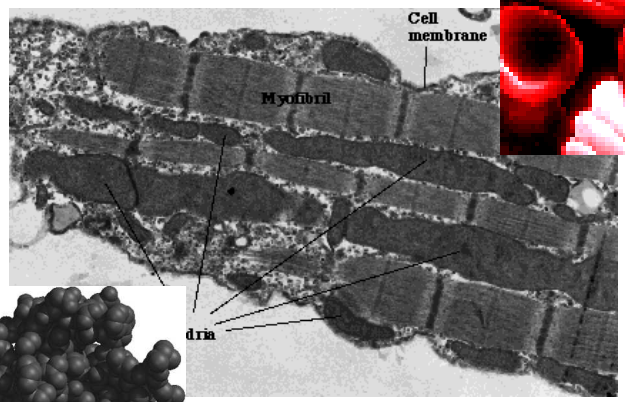
Integrated structures combine multiple length scales and functions.



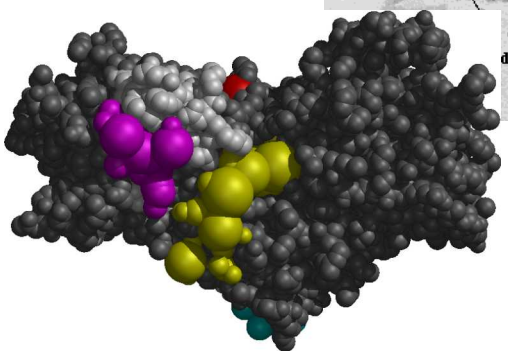
Organs and Tissues



Cells



Sub-cellular mechanical structure



Molecules and Chemical Pathways

Cells have developed highly specific and sensitive detection methods

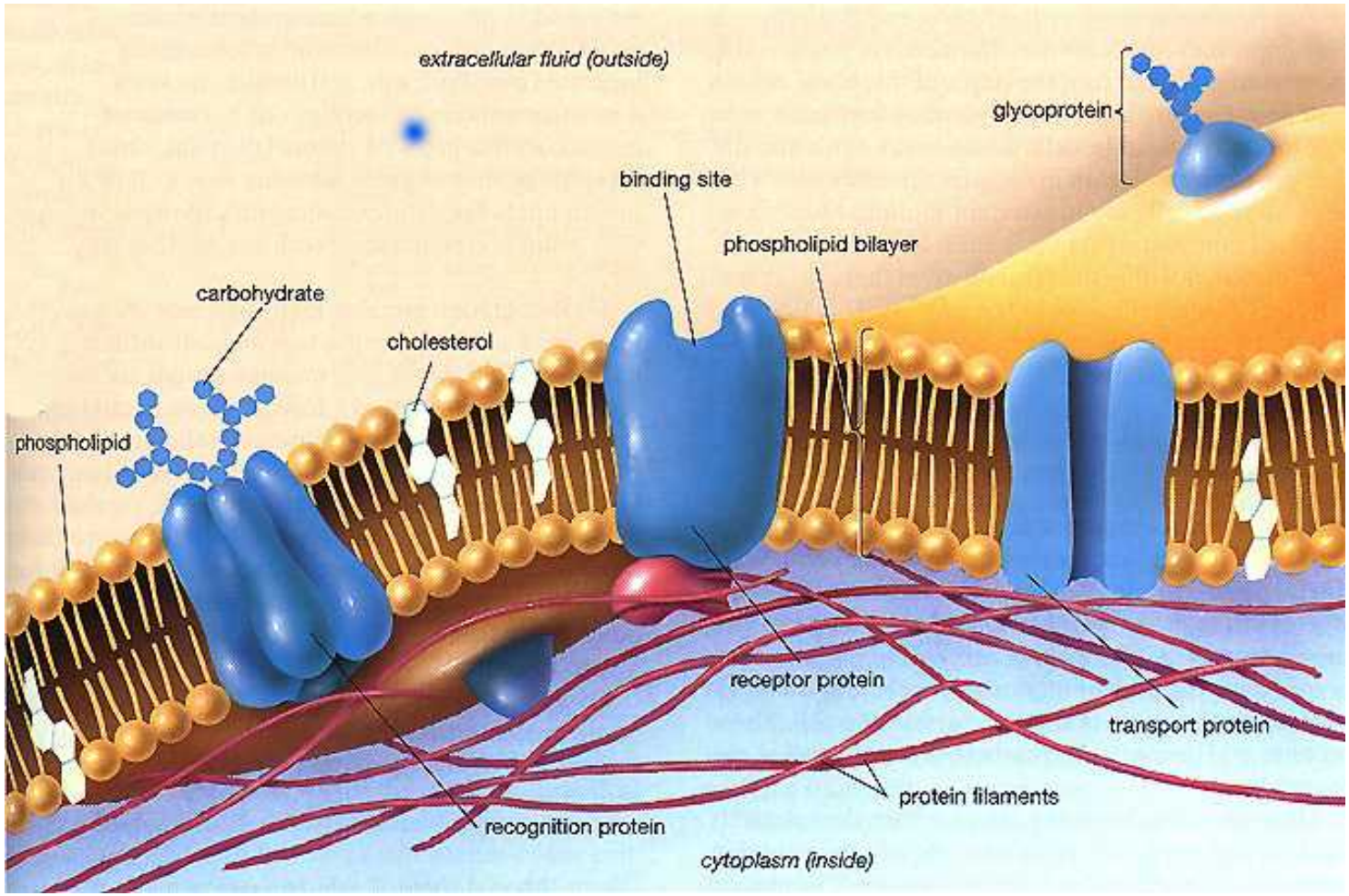
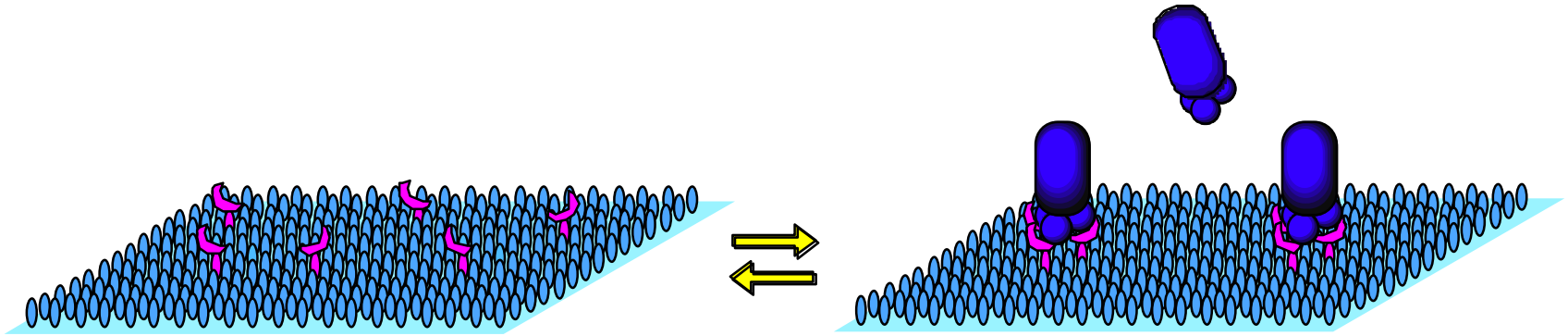


Image from: http://sun.menloschool.org/~cweaver/cells/c/cell_membrane/

Host Guest Interactions at Cell Membranes Induce Molecular Reorganization



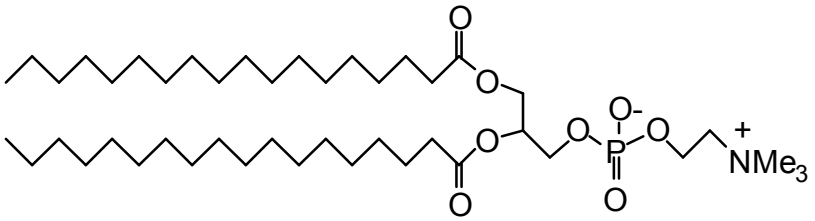
membrane receptors

molecular recognition induced aggregation

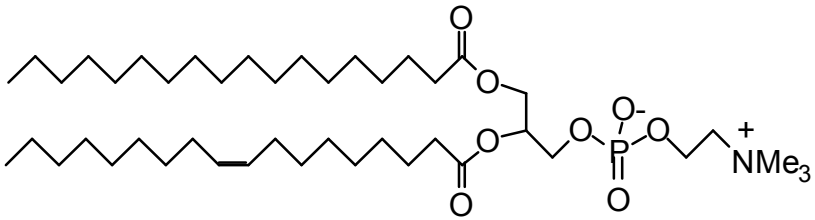
- Substrate recognition by membrane receptor induces formation of receptor aggregates initiating cellular signaling or other activities (examples include receptors for interleukin-2, acetylcholine, T-cells).

We Can Engineer Molecules for Specific Affinities

Matrix-Lipids

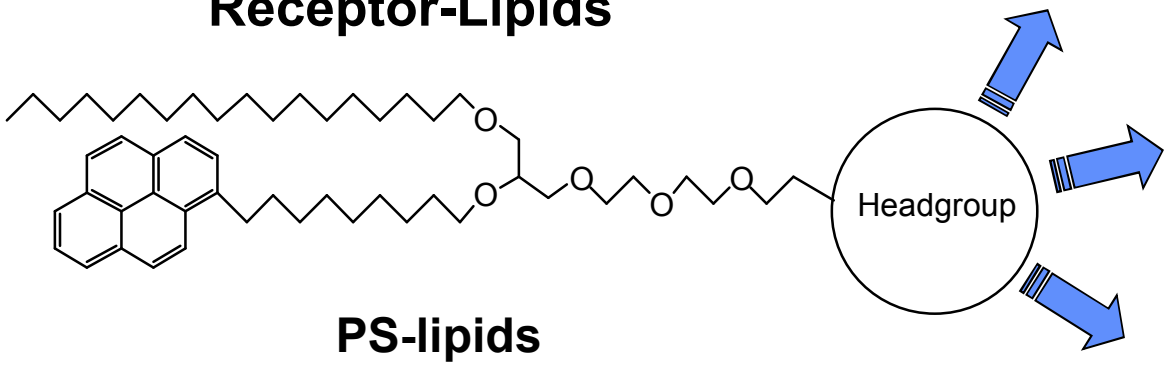


DSPC
(T_g = 55 °C)



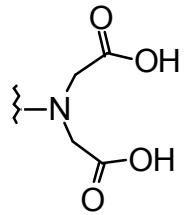
SOPC
(T_g < r.t.)

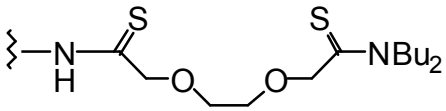
Receptor-Lipids

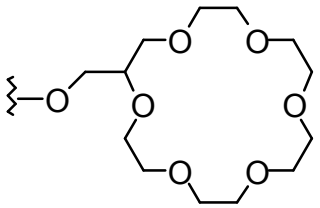


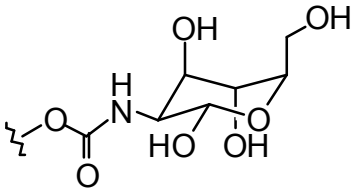
PS-lipids
(T_g < r.t.)

Headgroups

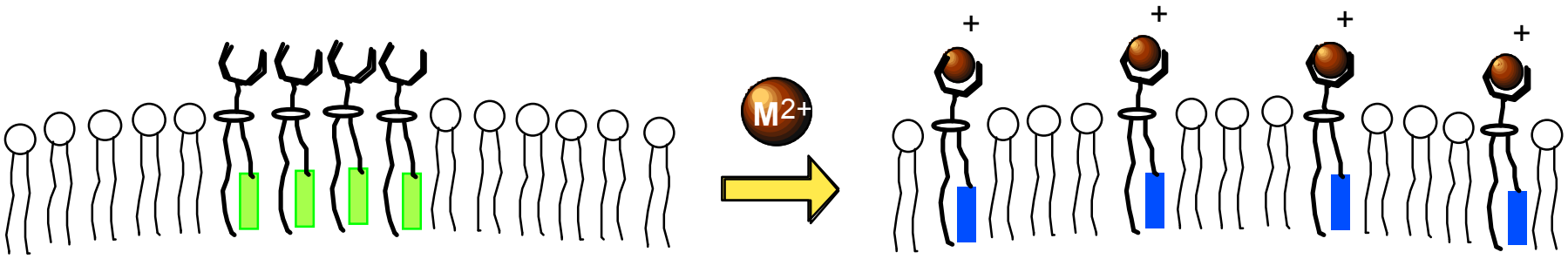


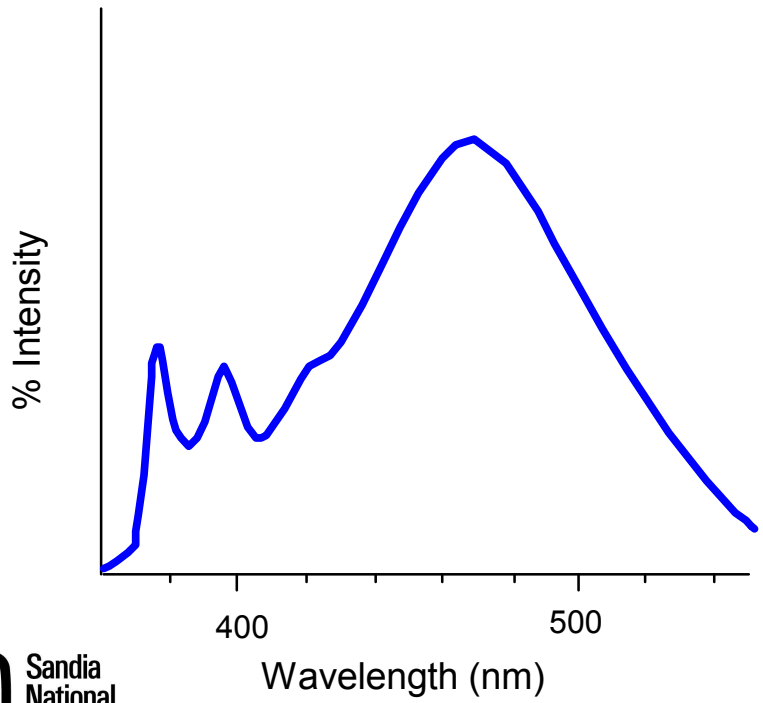


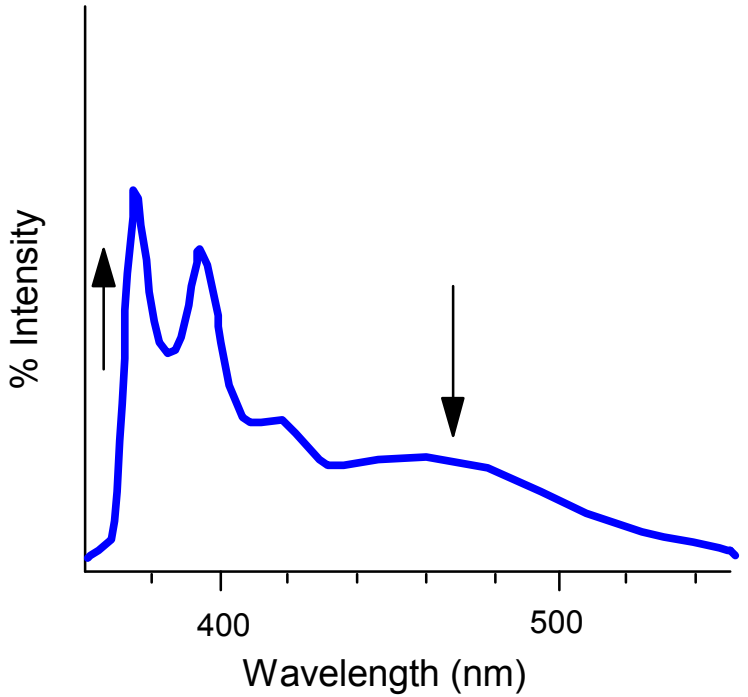




Engineered Molecules Can Create Sensors Using Processes Analogous to Those in Cells







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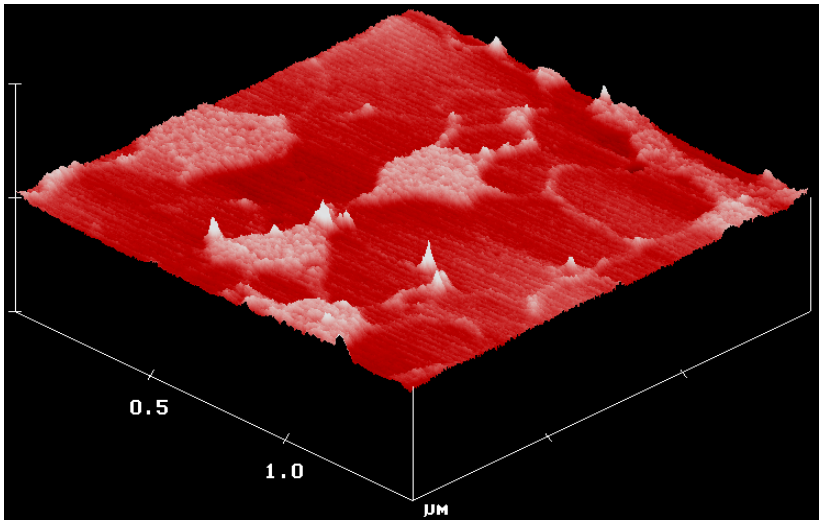
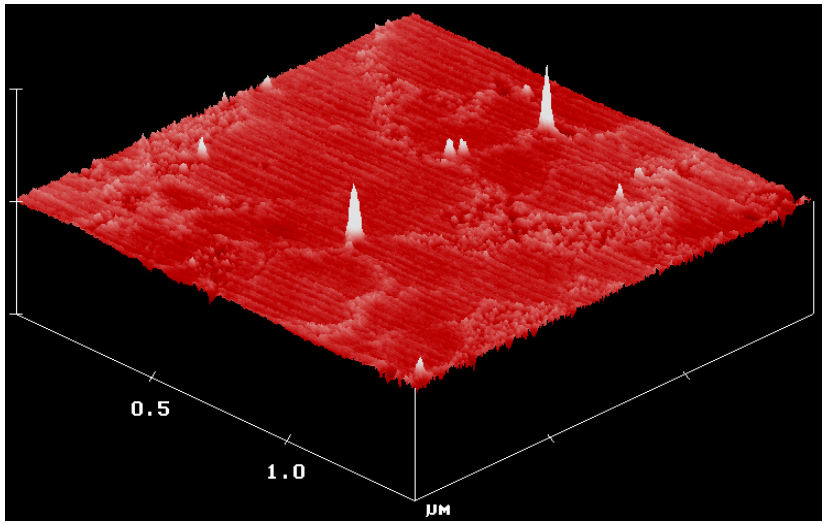
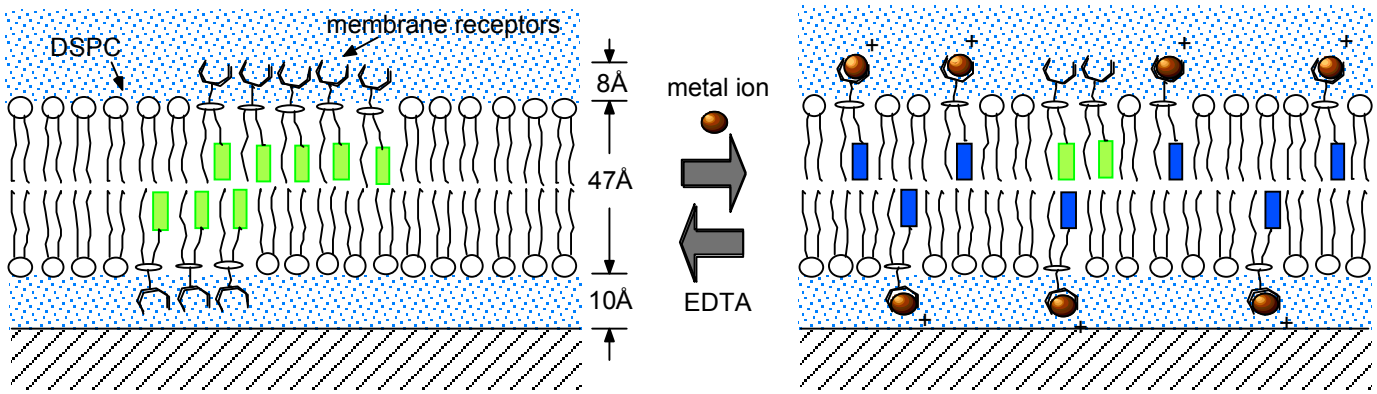
Nanoscale imaging shows details of lipid membrane reorganization







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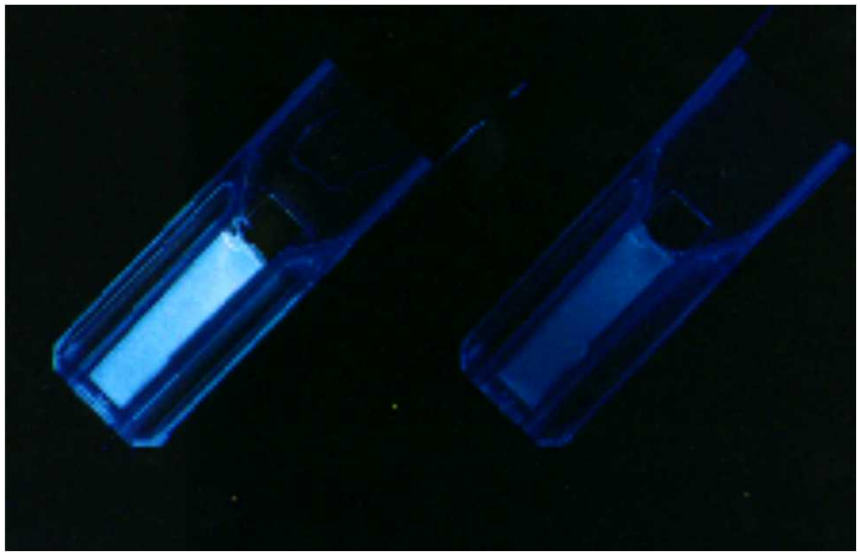
Obvious Changes Can be Seen in Fluorescence Response

Solution

without Cu(II) with Cu(II) 10 μM

Sol-gel Entrapped



without Cu(II) with Cu(II) 10 μM

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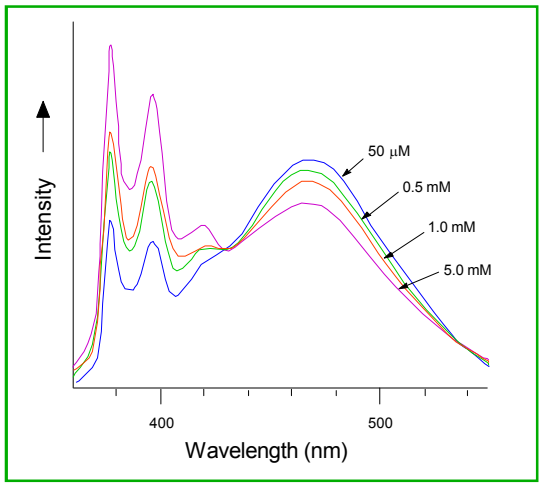
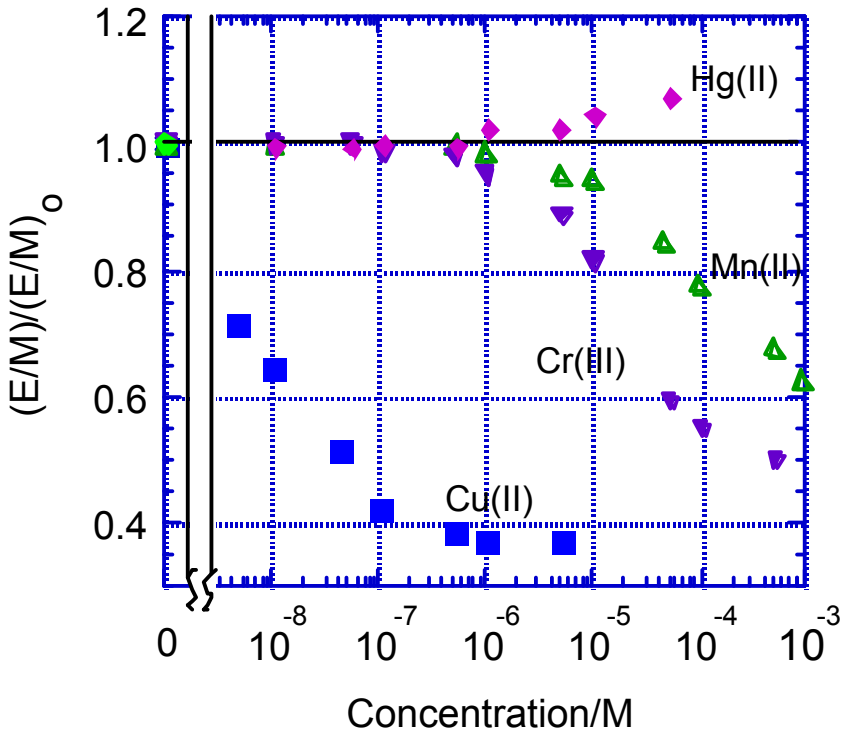
Molecular assemblies offer unique platforms for high substrate selectivity and rapid response





- PSIDA/DSPC lipid bilayers exhibit sub-ppb selective fluorescence response to Cu(II)
- Headgroup controls selectivity
- Response time of seconds

Sasaki, D. Y.; Shnek, D. R.; Pack, D. W.; Arnold, F. H.
Angew. Chem., Int. Ed. Engl. **1995**, *34*, 905.

Fluorescence response results from a change in molecular organization induced by metal ion binding.

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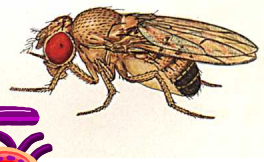
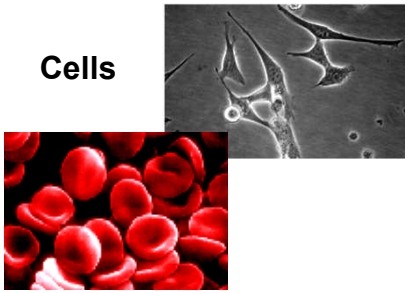
Combining Nano- and Biotechnology Can Lead to Completely New Capabilities

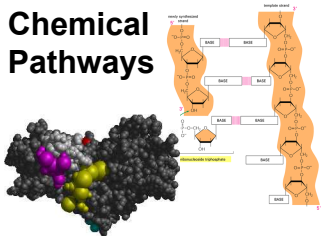
Organs and Entities



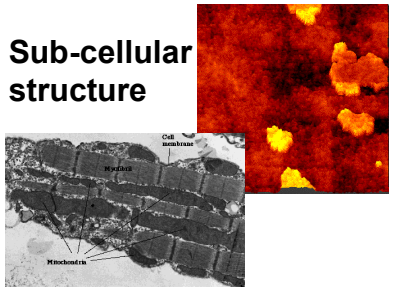
Cells



Molecules and Chemical Pathways



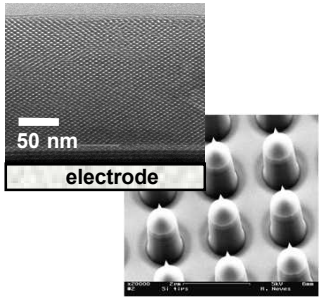
Sub-cellular structure



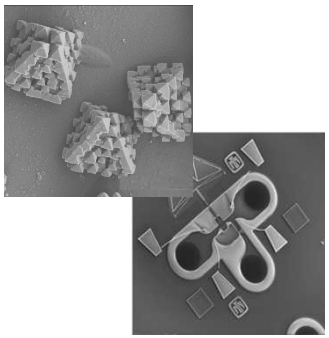
Biological Systems

New Combined Systems

Inanimate Systems

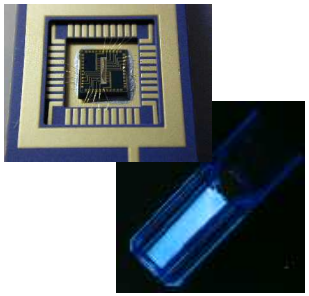


Nanoscale structures

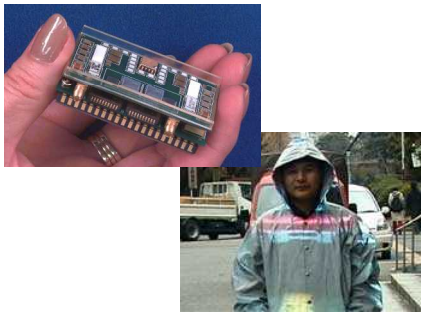


Microscale assemblies

Functional Components



Microsystems and Materials



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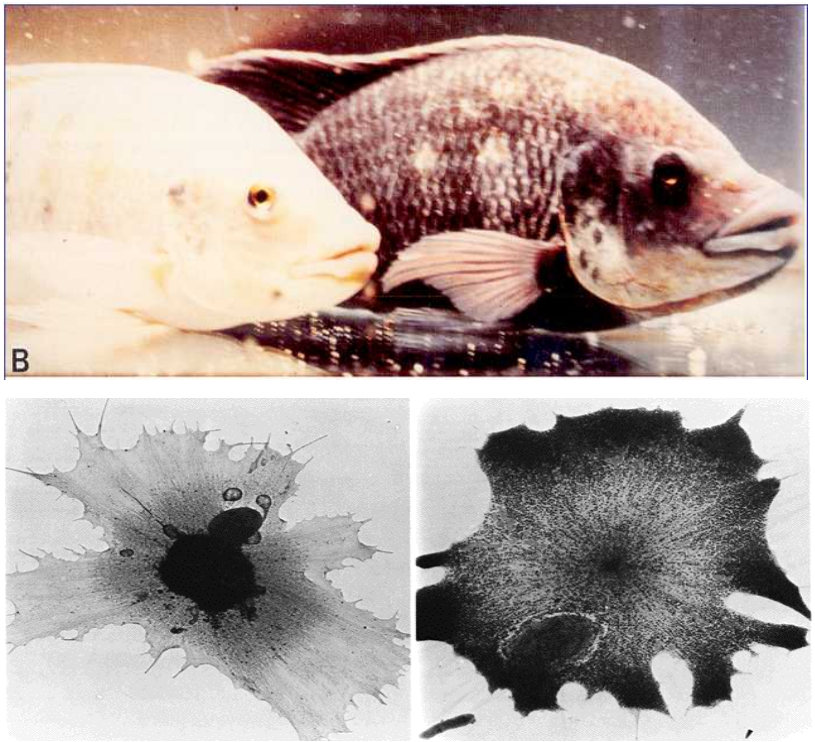
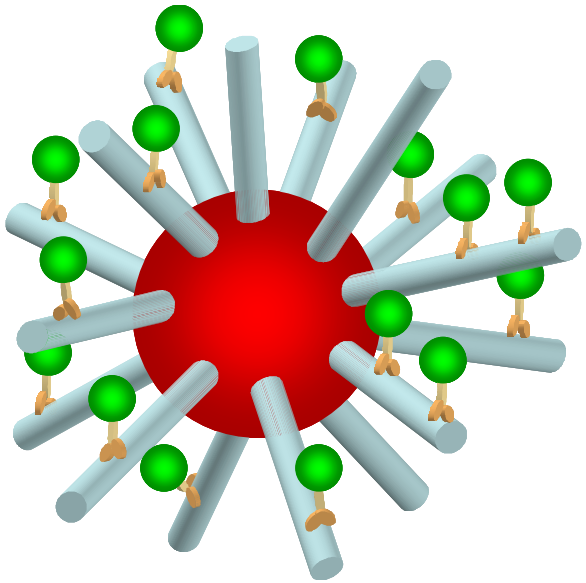
Living Systems Actively Alter Their Characteristics

Living systems utilize energy-driven, non-equilibrium processes to assemble and organize nanoscale materials in a dynamic and adaptive manner.



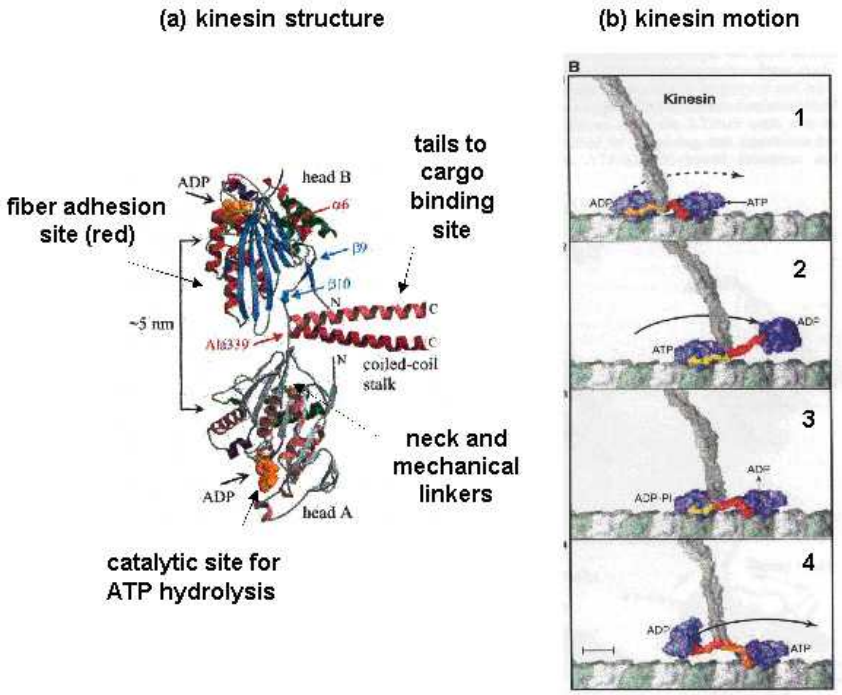
Adapted from: http://wilkes-fs1.wilkes.edu/~terzaghi/BIO-226/lectures/24.html

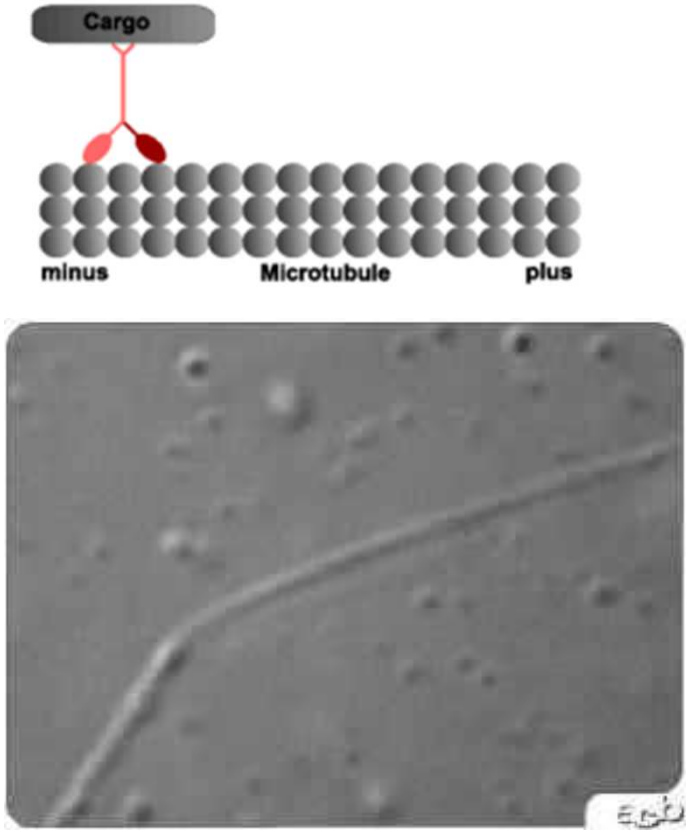
Can such processes be exploited for creating artificial, dynamic, and adaptive nano-materials and devices?



Motor Proteins are Key to Active Transport

Motor Proteins provide directed translation of molecular cargo as a result of energy consumption, and are Nature's way to overcome diffusion problems and concentration gradients.





*From: Alberts et al. (1998) "Essential Cell Biology."

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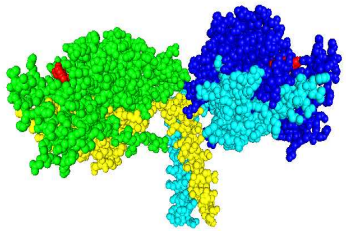
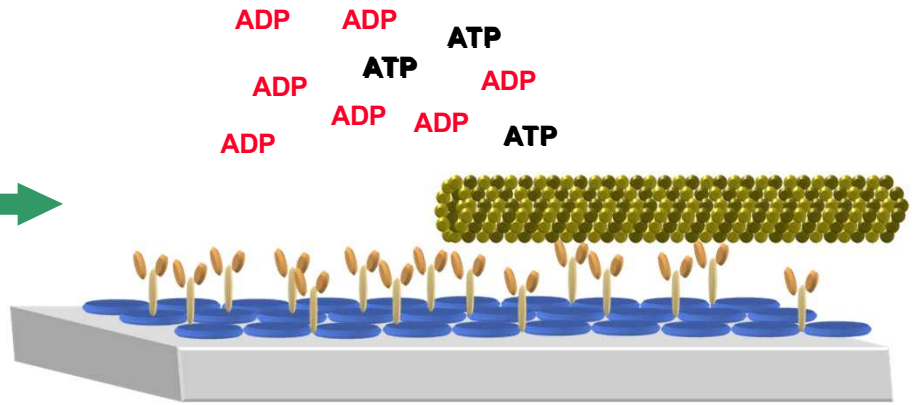
Kinesin and Microtubules can form an *in vitro* Transport System

Kinesin Motor Proteins



Microtubules (MTs)

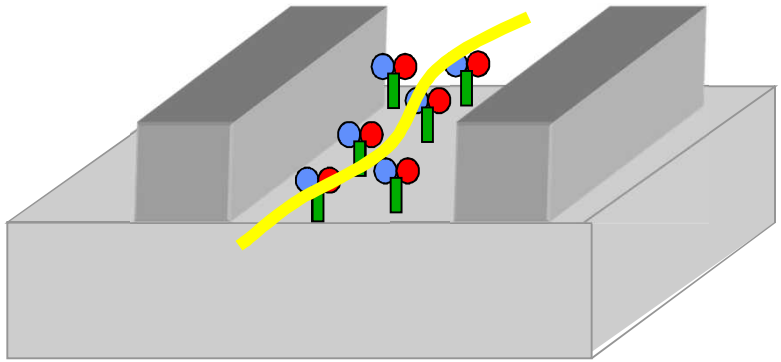


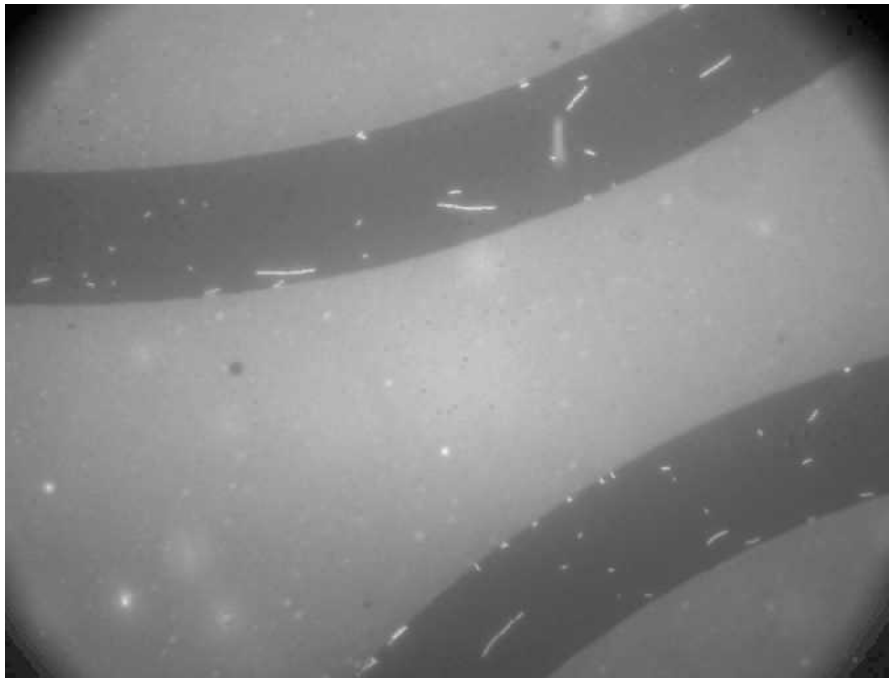
Transport rates 0.1 – 5.5 μm/sec

The gliding motility geometry can be used *in vitro* as a "molecular shuttle" to transport an array of nanoscale cargo over millimeter distances through the conversion of chemical energy into mechanical work (50% efficiency).

Clemmens et al., *Lab Chip* **4**, 83 (2004), Hess et al. *Nano Lett.* **3**, 1651 (2003); Clemmens et al., *Langmuir* **19**, 10967 (2003); Hess et al. *Appl. Phys. A-Mater. Sci. Process.* **75:**309 (2002) .

Topography Guided Microtubule Transport Has Been Demonstrated





Kinesin motor proteins shuttle microtubule fibers through microfabricated channels

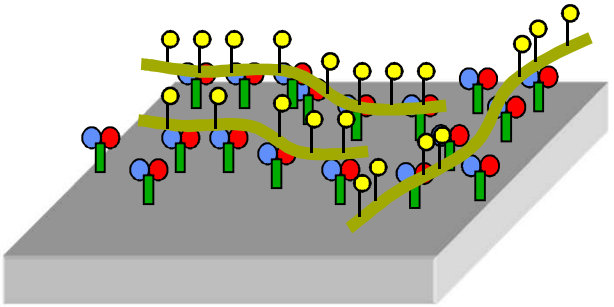
Physical confinement by the channel walls, combined with selective coatings to control the location of the motor proteins, guide the translocation of the fibers across a surface

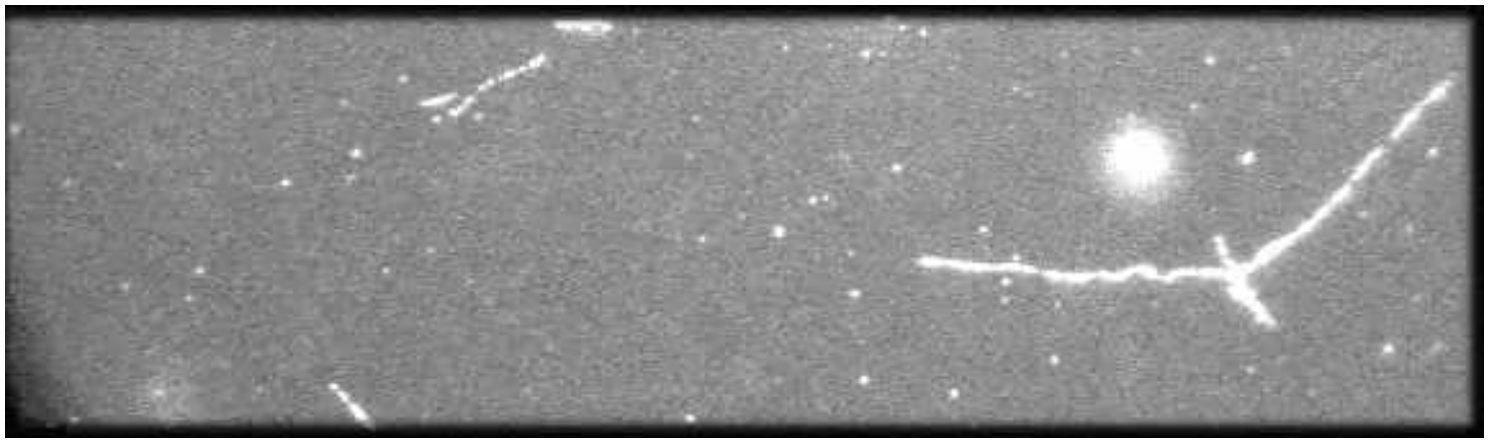
This demonstrates an approach to transport materials across a surface in a programmed manner

Clemmens et al., *Lab Chip* **4**, 83 (2004), Hess et al. *Nano Lett.* **3**, 1651 (2003); Clemmens et al., *Langmuir* **19**, 10967 (2003); Hess et al. *Appl. Phys. A-Mater. Sci. Process.* **75:**309 (2002) .

Transport of Gold-Coated Microtubules

- Gold-conjugated microtubules
  Au streptavidin: biotinylated tubulin
- Kinesin motors on glass



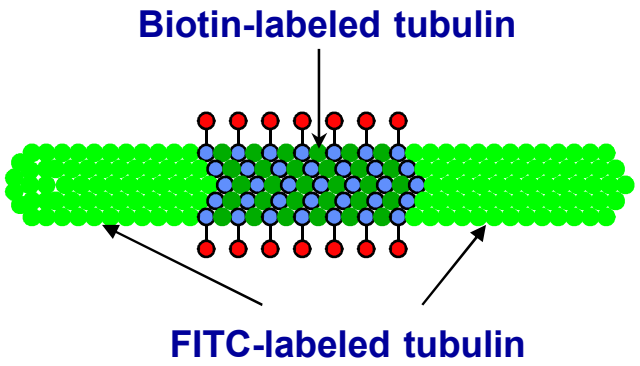


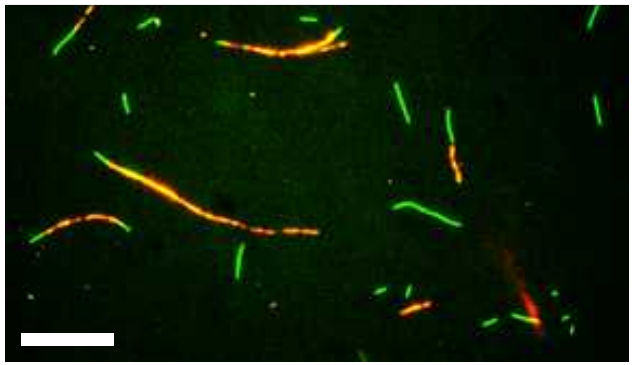
1 sec video = 16 sec real-time

Specific Regions for Cargo Transport can be Defined

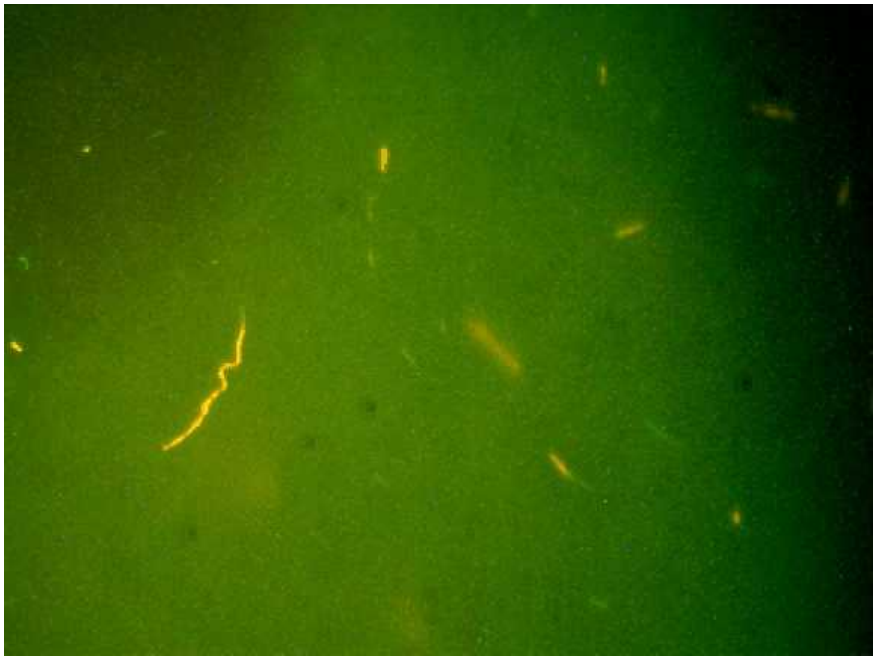
Cargo-binding regions

- Polymerize 100% biotinylated tubulin
- Add taxol & centrifuge "cargo regions"
- "Cargo regions" + FITC-labeled tubulin





Scale = 5 μm



Nanoparticle transport is dependent on particle type/composition

- Localization of nQDs in a central cargo-binding regions permits unabated adhesion and transport of functionalized shuttles

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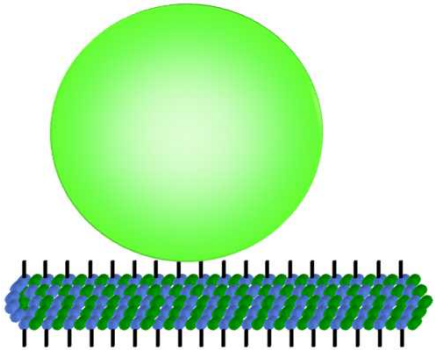
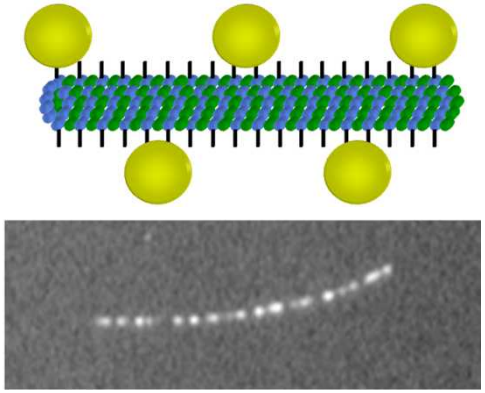
Different Nanoparticles can be Transported

- Nanoparticles can be assembled on microtubule scaffolds using biotin-streptavidin linkage.
- Transport can be achieved, but is critically dependent on maintaining kinesin – microtubule interactions.

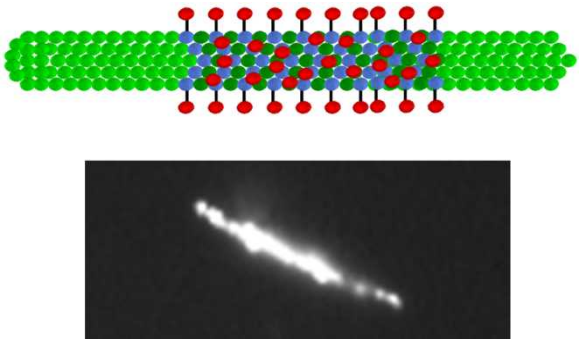
Polystyrene spheres

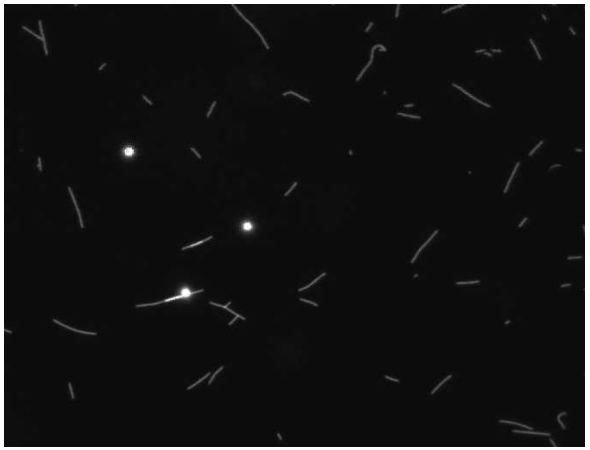


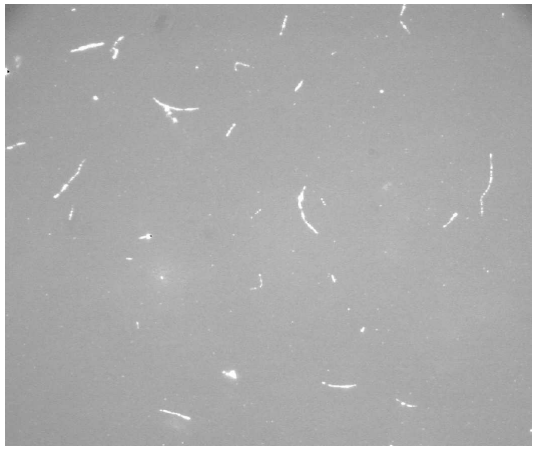
Gold nanoparticles

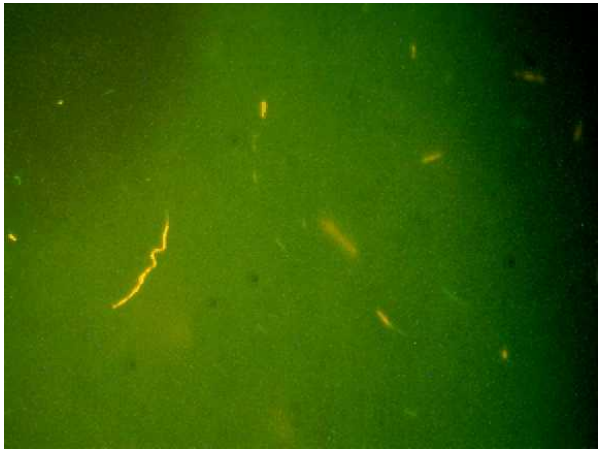


Nanocrystal quantum dots









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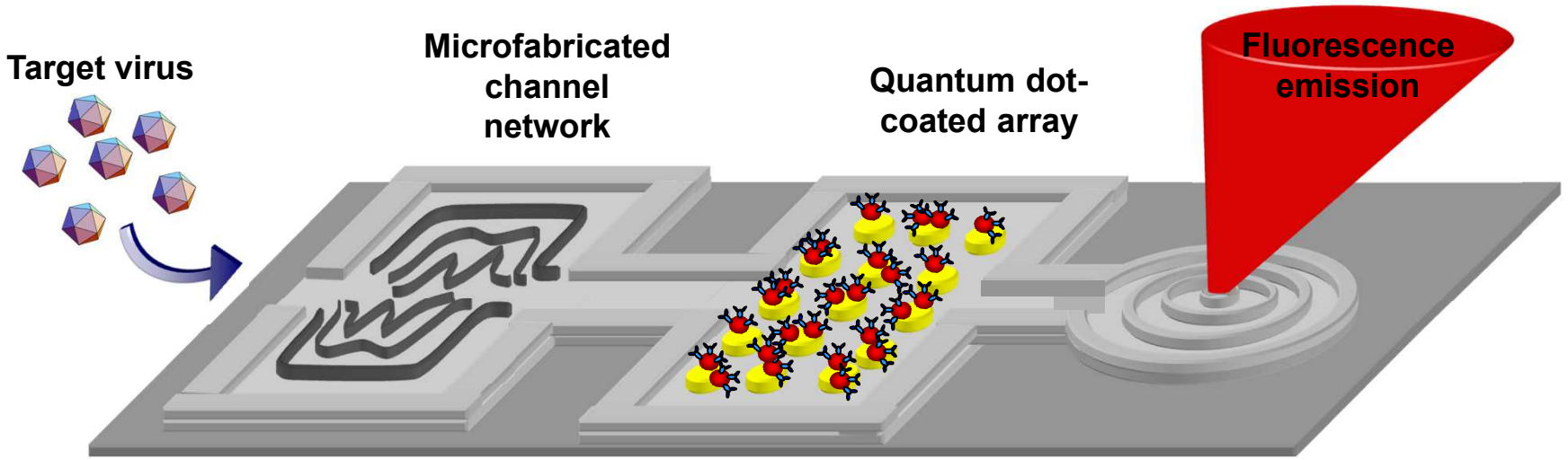
Bachand et al., *Nano Lett.*, **4**, 817 (2004); Bachand et al., *Proc. MRS Symp. A* **782**, A1.1.1 (2004), Bachand et al., *J. Nanosci. Nanotechol.* **5**, 718 (2005); Boal et al., Nanotechnology 17, 349 (2006).

These Demonstrations Lead to a New Biosensor Concept

Goal: To develop a biosensor device for remote detection scenarios, and is powered exclusively by biomolecular motors.

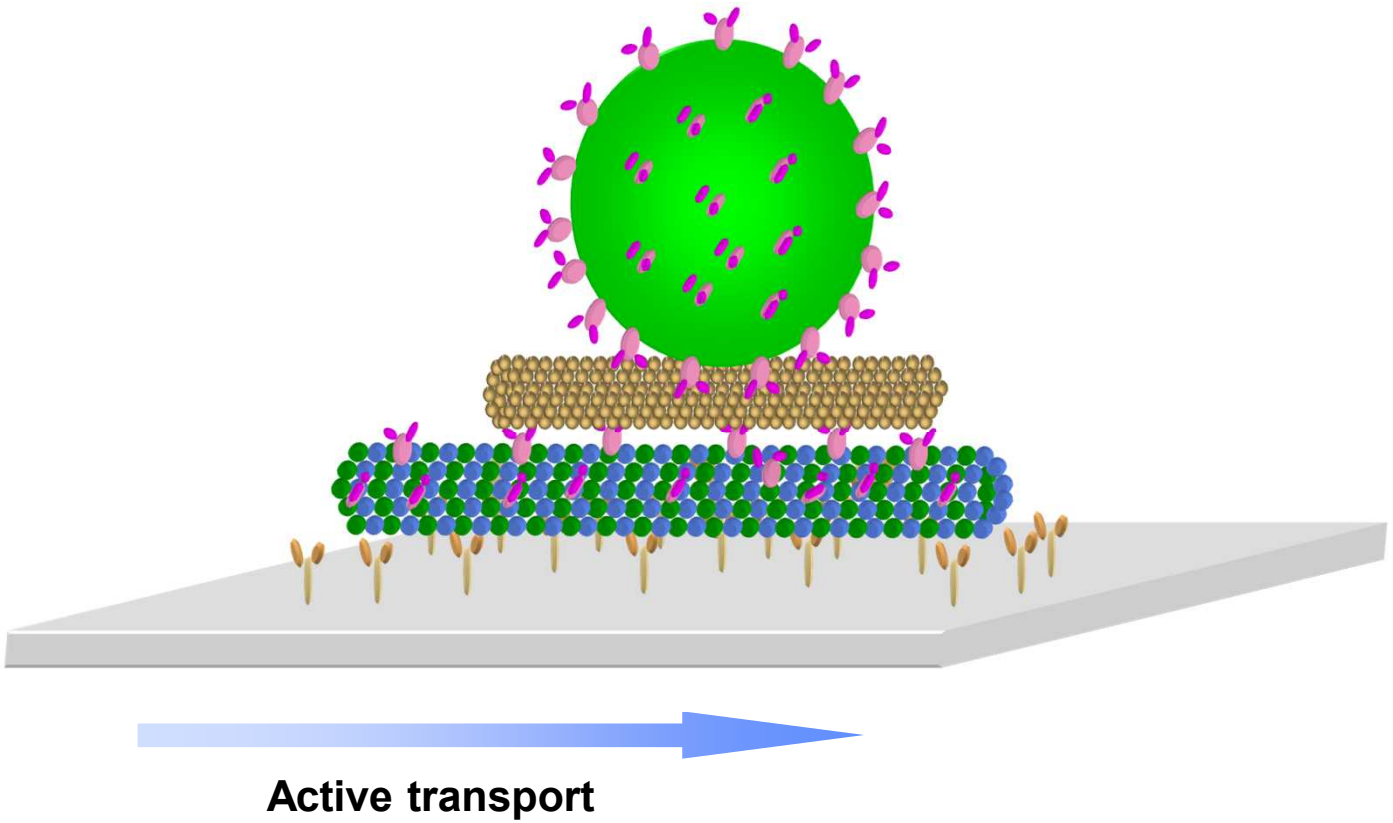


Molecular shuttles actively harvest target virus from sample solution

Target virus tagged with quantum dots via molecular shuttle transport

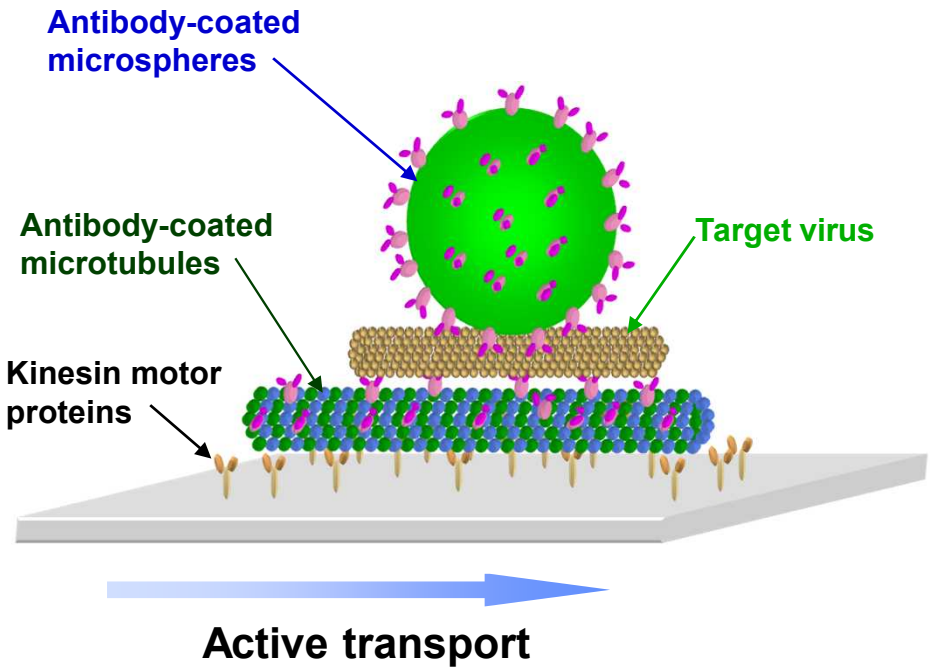
Aggregated quantum dots emit characteristic emission spectra

Concept for Capture and Transport of Viruses

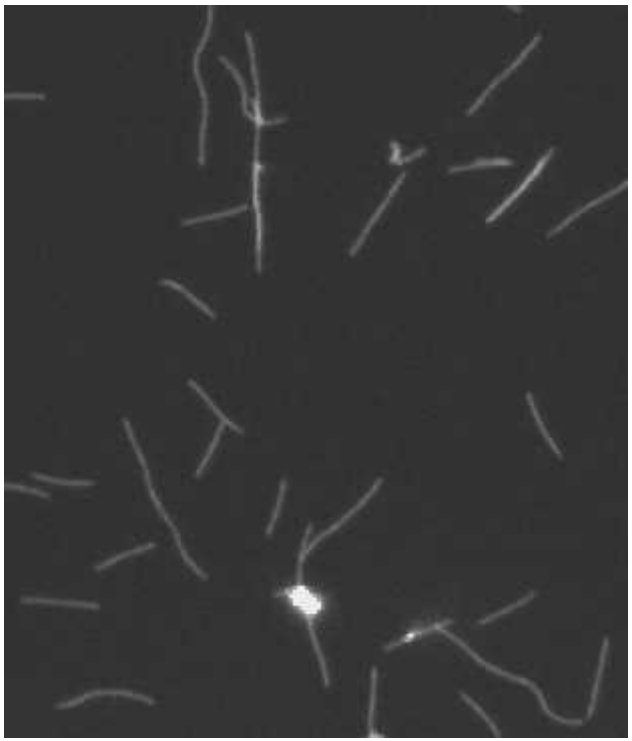


Demonstration of Virus Transport by Molecular Shuttles

Kinesin biomolecular motors can transport antibody-coated microtubules, which in turn may be used to capture, transport, and optically tag target viruses particles.



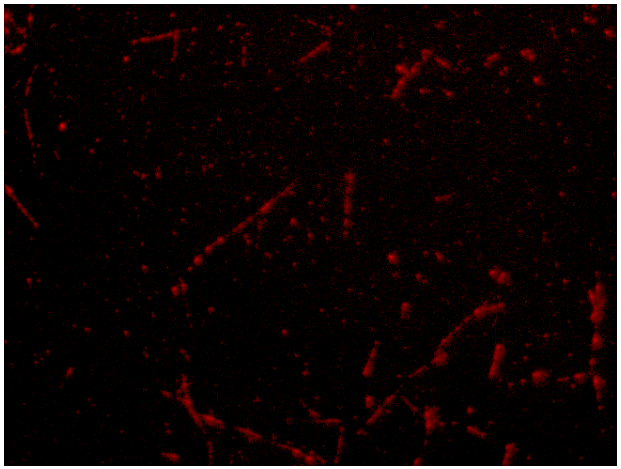
Transport of target virus



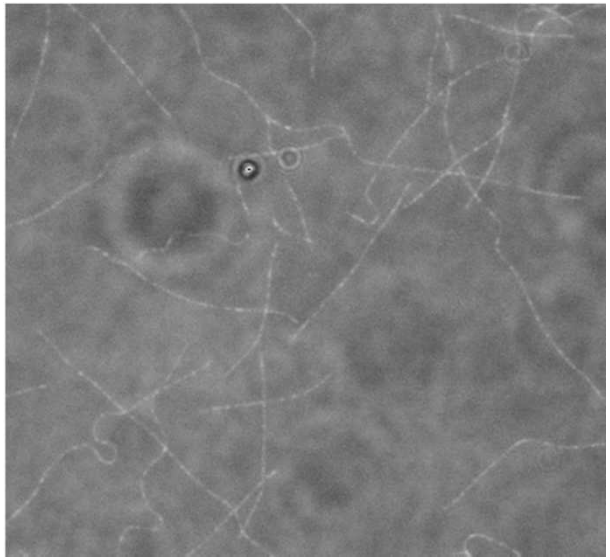
A Variety of Target Analytes can be Captured and Transported

Ab-MTs can efficiently capture and transport a range of target analytes at nanohybrid interfaces.

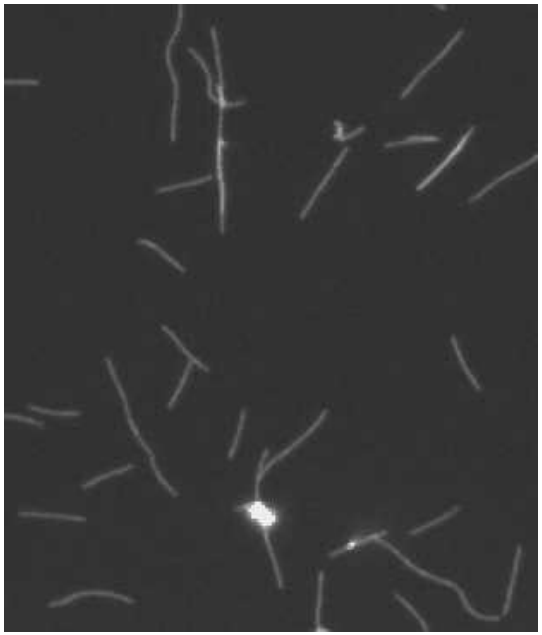
Protein



Bacterium



Virus



Enabling technology for the development of nanofluidic sensors that can be applied without the electrical power requirements.

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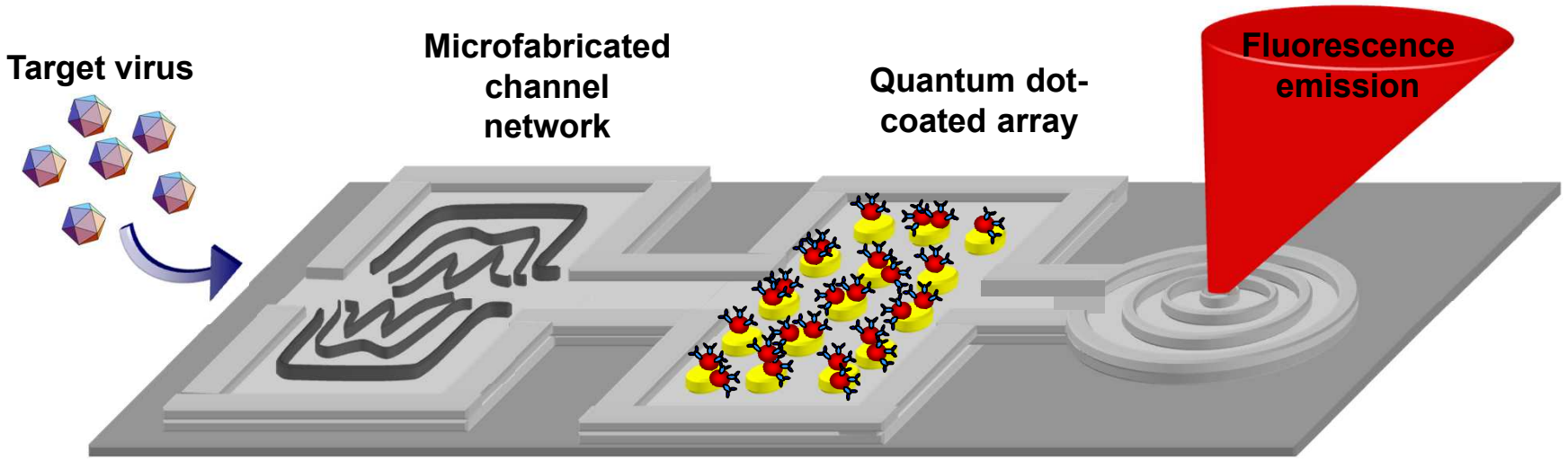
Bachand et al., (2006) *Small* **2**: 381, Boal et al. (2006), *Small* **2**: (in press)
Ramachandran et al. (2006) *Small* 2: 330. (Cover).

These Demonstrations Lead to a New Biosensor Concept

Goal: To develop a biosensor device for remote detection scenarios, and is powered exclusively by biomolecular motors.

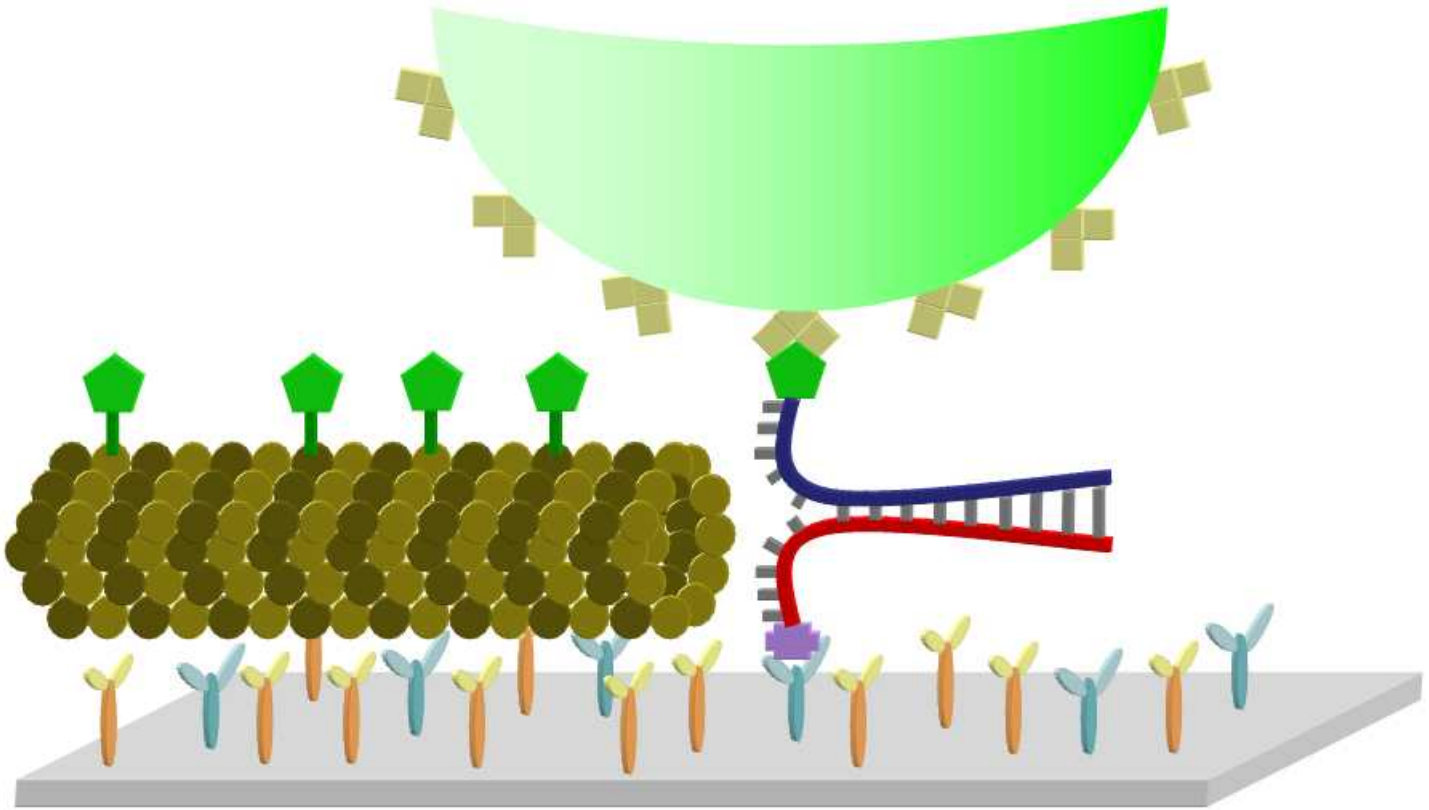


Molecular shuttles actively harvest target virus from sample solution

Target virus tagged with quantum dots via molecular shuttle transport

Aggregated quantum dots emit characteristic emission spectra

Concept for Tagging with Quantum Dots

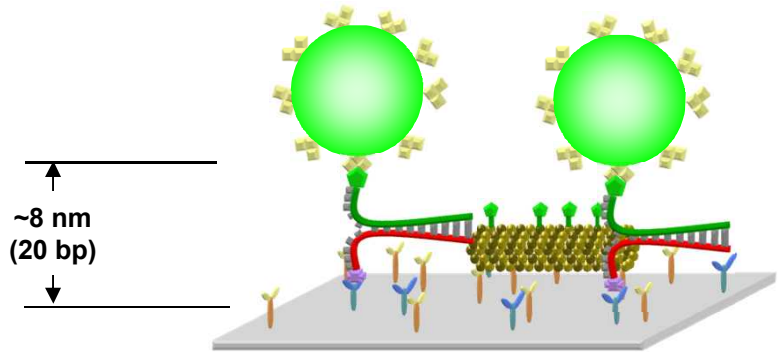


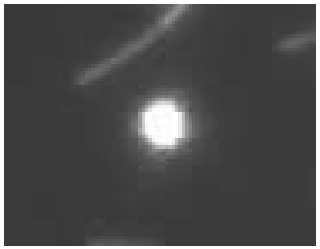
Unzipping forces = 10 pN for polyA-T bond & 20 pN for polyG-C bond

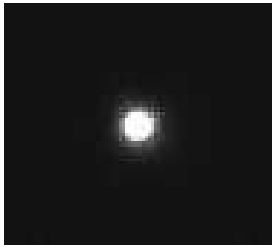
Each bond is independently broken, thus DNA length may be adjusted w/o changing unzipping force.

Demonstration of DNA Tethers

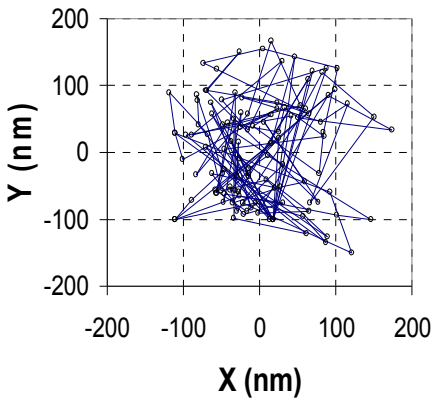
- DNA tether:
  - 45-bp partially double-stranded, forked DNA tether
- Surface attached via DIG/α-DIG Ab
- Attached to microsphere via biotin/streptavidin

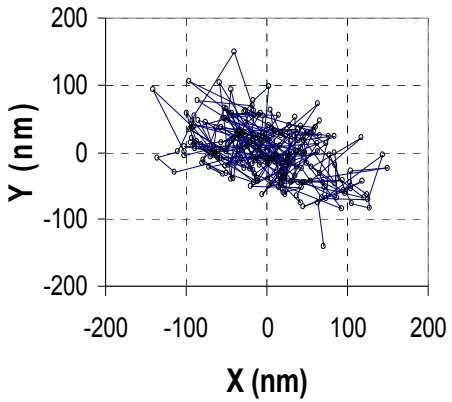






Tethering by single DNA molecules may be confirmed by tracking the motion of the microsphere.





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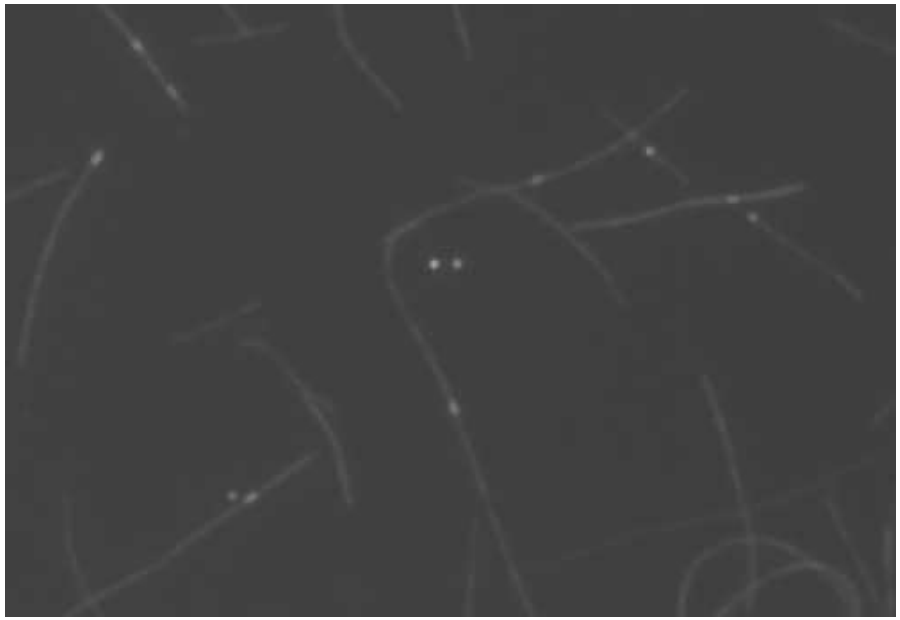
Quantum Dots can be Picked up by Unzipping DNA

Pick-up of surface-tethered QDs was successfully achieved through unzipping DNA.

Longer transport distances than with fluorospheres, and less frequent transfer was observed

Remaining Questions:

1) What is the overall pick-up efficiency?
2) Does velocity affected pick-up efficiency?
3) Does size affect pick-up?



We are Close to Demonstrating this New Biosensor Concept

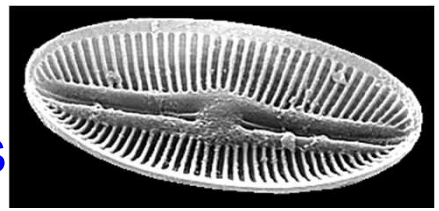
Objective: To develop integrated sensor devices for chem/bio agents that are:

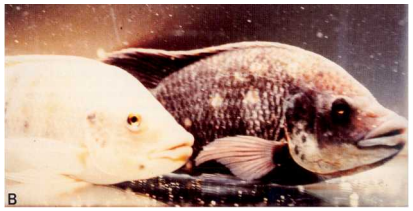
- powered exclusively by biomolecular motors (kinesin & microtubules) and chemical energy (i.e., ATP)
- capable of remote detection by UAVs or other technologies
- deployed as "smart dust" on target battlefields
- multiplexed for multiple target analytes, each with an individual signature

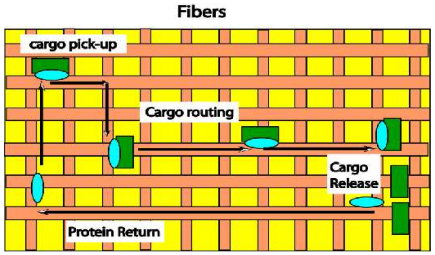
Animation by Jerry Gorman, SNL Creative Arts

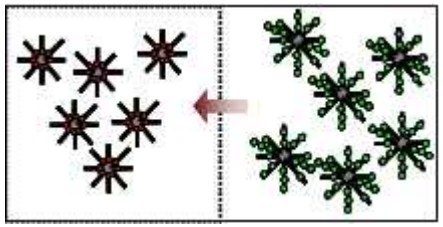
A Variety of Other Possible Applications Exist

- Rapid assessments of building contamination
- Highly sensitive (comparable to ELISA) biological or chemical assays
- Early detection of infection
- Reconfigurable microsystems
- Adaptive materials
- Active camouflage
- ……









Biology can Lead to New Capabilities in Nanotechnology

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