Autonomous systems and synthetic biology

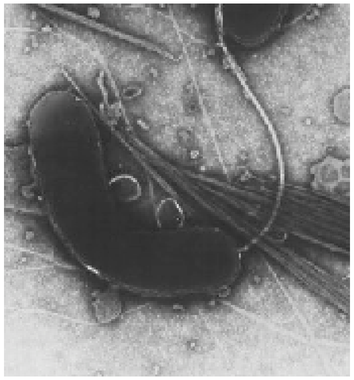
Henry Hess

Department of Biomedical Engineering, Columbia University

NASA's
Mars Exploration Rover

Woods Hole's Autonomous
Benthic Explorer

Nature's
Sperm

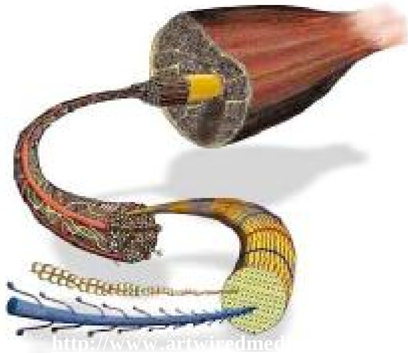


Nature's
Vibrio cholerae

H. Durrant-Whyte's
fish counting robot

KIVA Systems'
distribution center robot

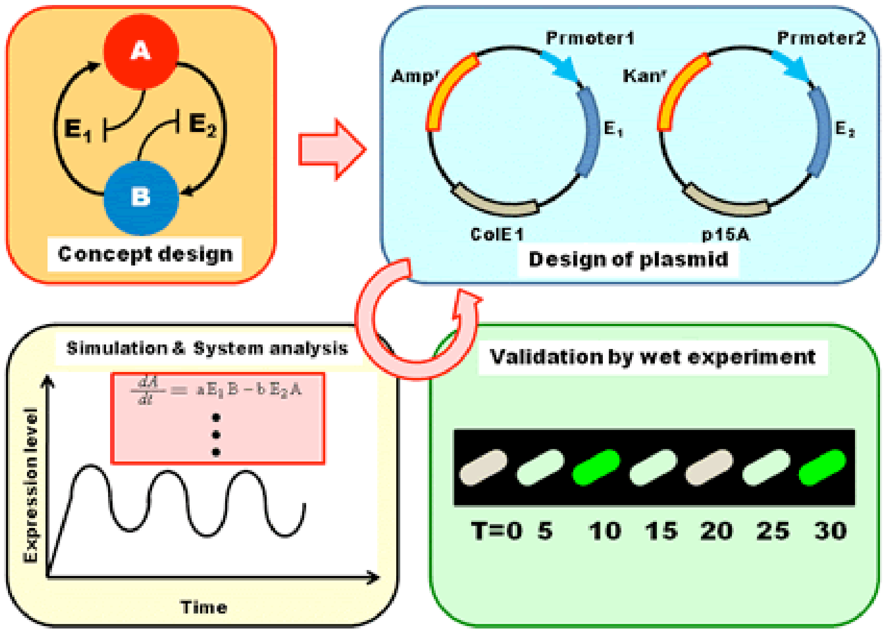
Nature's
leaf



Nature's
muscle

Synthetic biology: Re-programming vs. re-assembling

Design of artificial genetic circuit based on synthetic biology

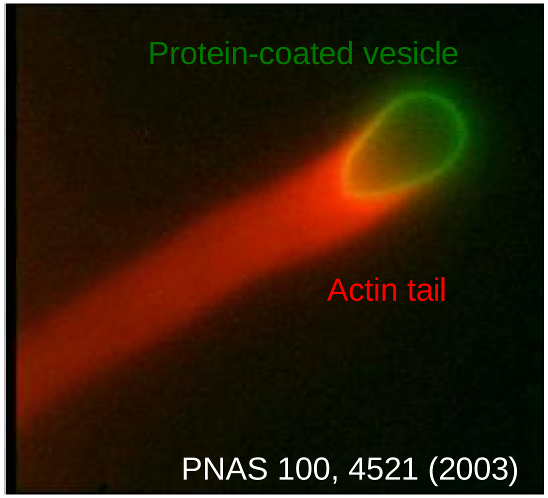


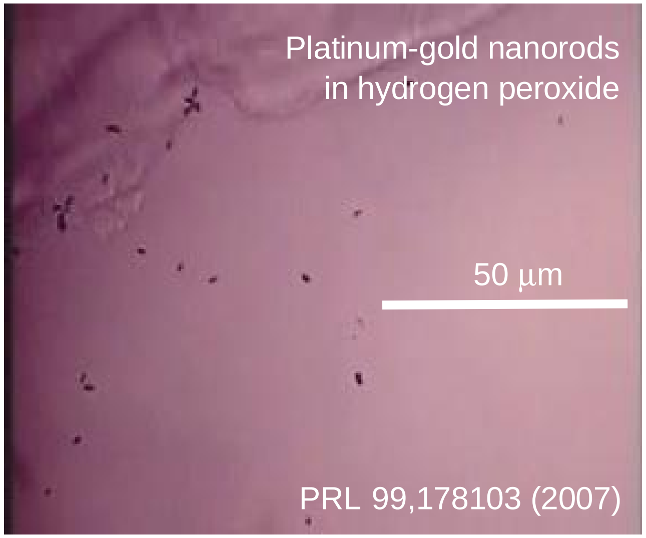
Laboratory for Bioinformatics, Kyushu University

Michael Specter: A life of its own. The New Yorker

Synthetic biology: Re-assembling

R. Feynman: “What I cannot create,
I do not understand.”





Schwille & Diez: “Synthetic biology of minimal systems”
Critical Reviews in Biochemistry and Molecular Biology 44(4), 223 (2009)

Hybrid devices to explore design principles and applications

Information, communication,
and emergence

Surface imaging

Control of activation

Active self-assembly

Mechanical engineering at the molecular scale

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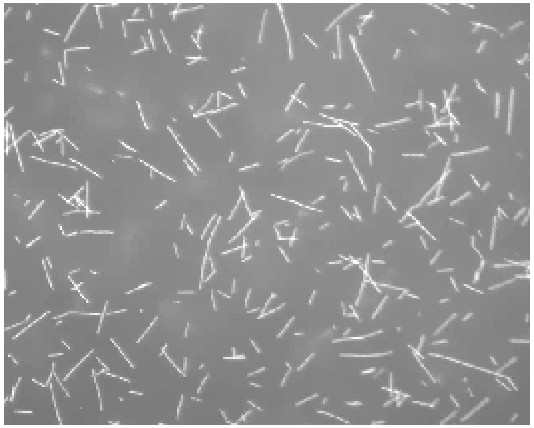
Fascinating building blocks: Kinesin motors and microtubules

Movie extracted from: Alain Viel, Robert A. Lue, and John Liebler/XVIVO “The inner life of a cell”
BioVisions at Harvard University

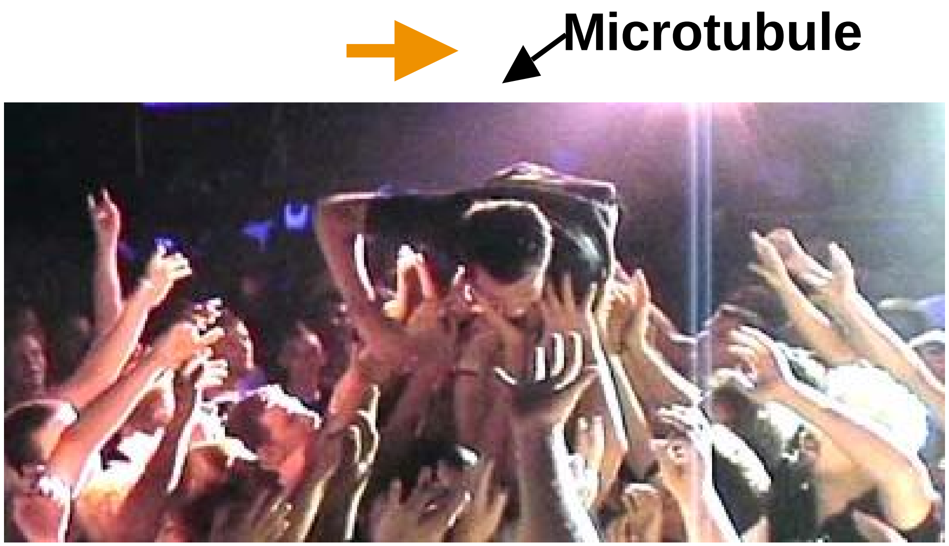
Molecular Shuttles:

Nanoscale transport systems assembled

from kinesins and microtubules

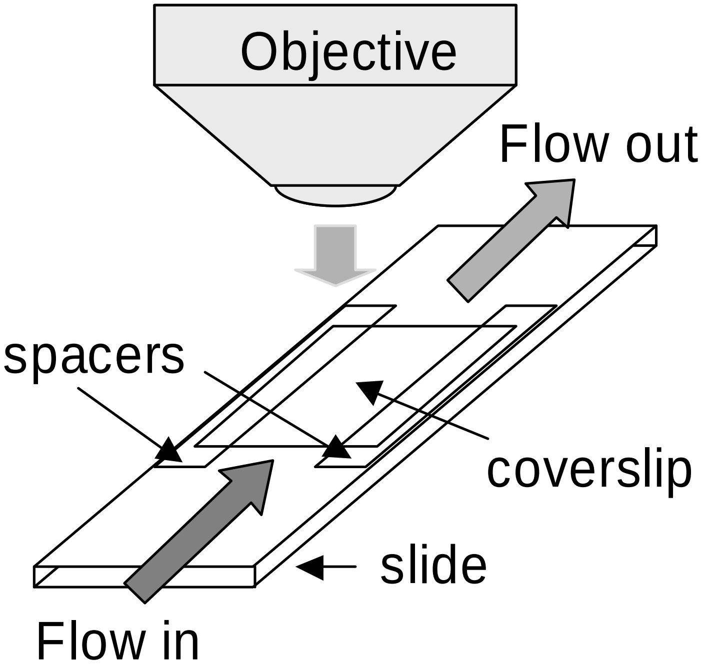


Force: 5 pN per Kinesin

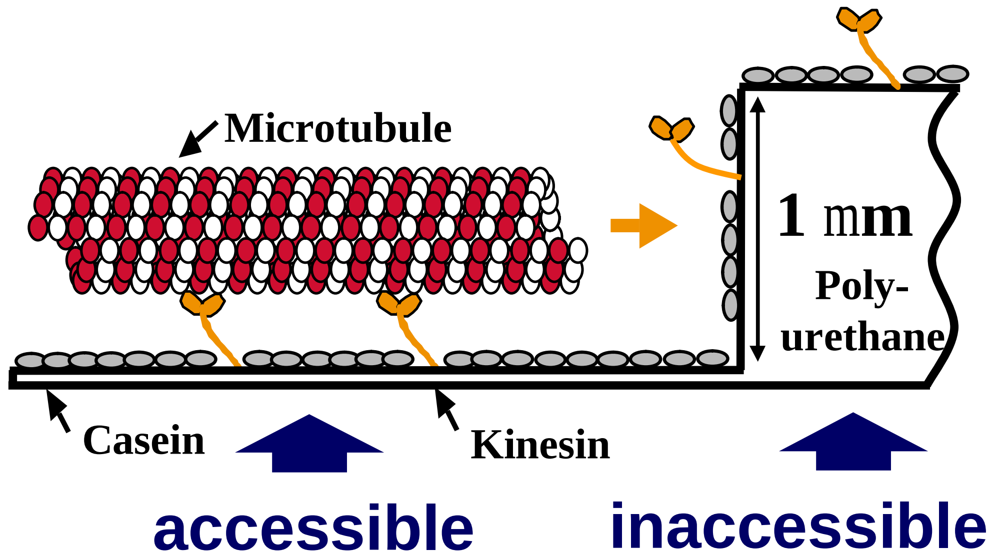


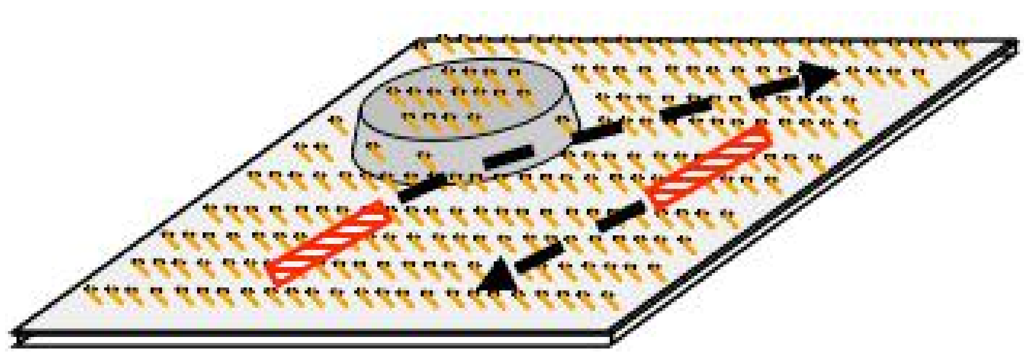
Speed: 800 nm/s at 1 mM ATP

Fluorescence microscope

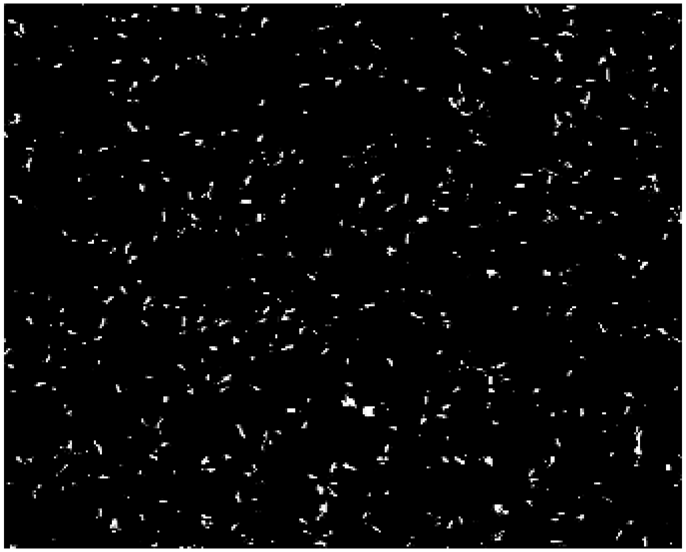


Molecular shuttles image surfaces as self-propelled probes





Molecular shuttles image surfaces as self-propelled probes

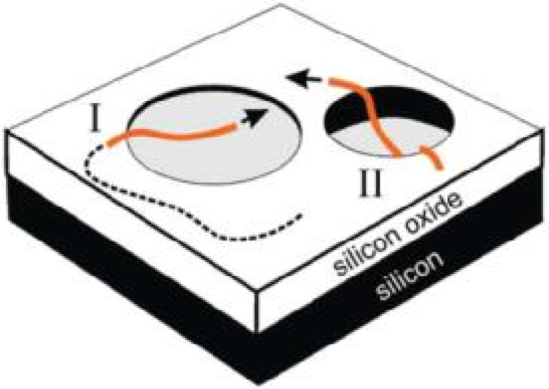


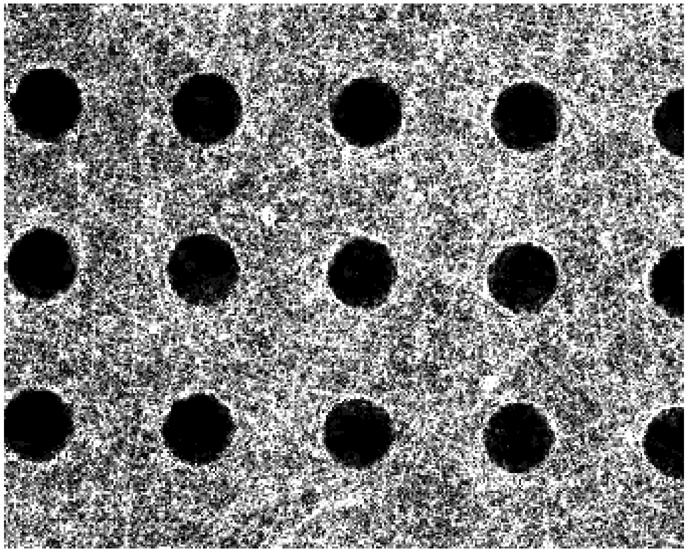
500 frames observed in 2500 s

20 µm

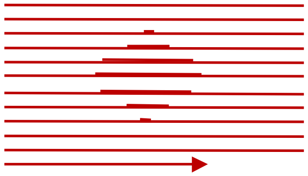
Nano Letters **2**, 113 (2002)

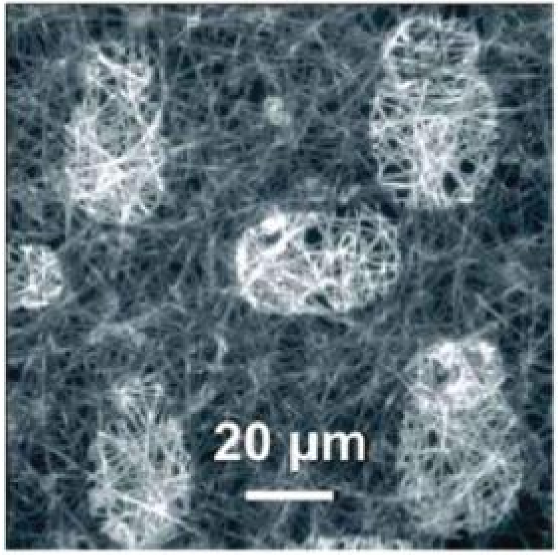
Kerssemakers, Diez et al. Small **5**, 1732 (2009)





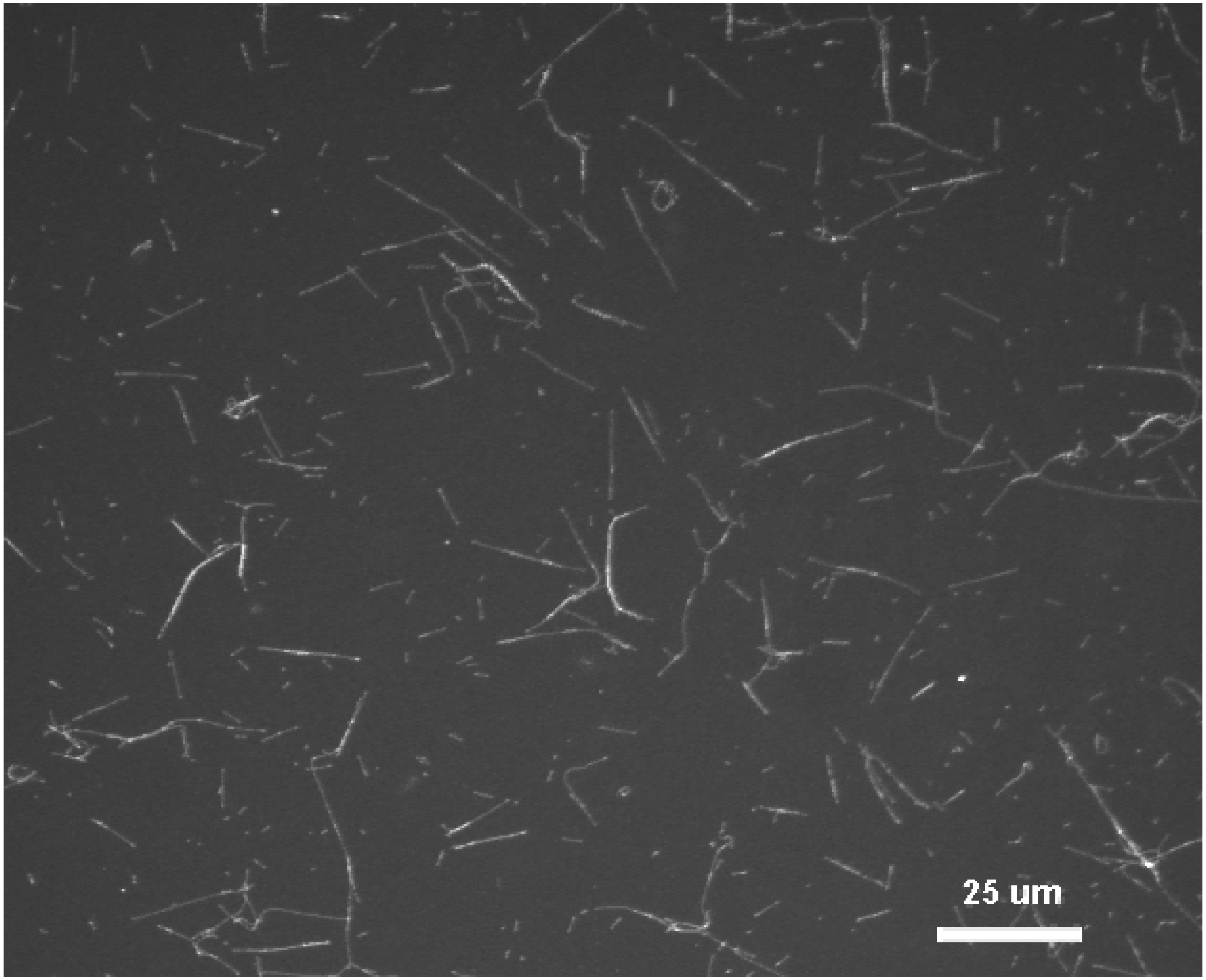
Imaging by scanning:





Emergent behavior: Self-assembly by active transport results in non-equilibrium structures

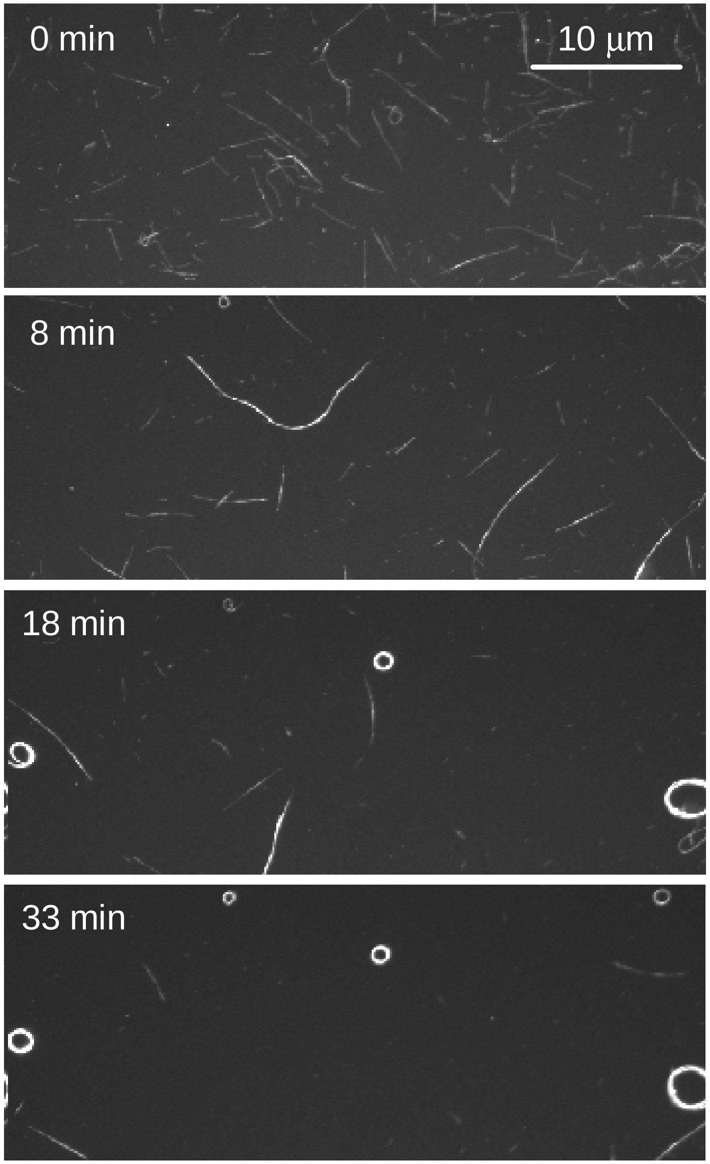
Biotinylated microtubules partially coated with streptavidin
=
"Sticky microtubules"

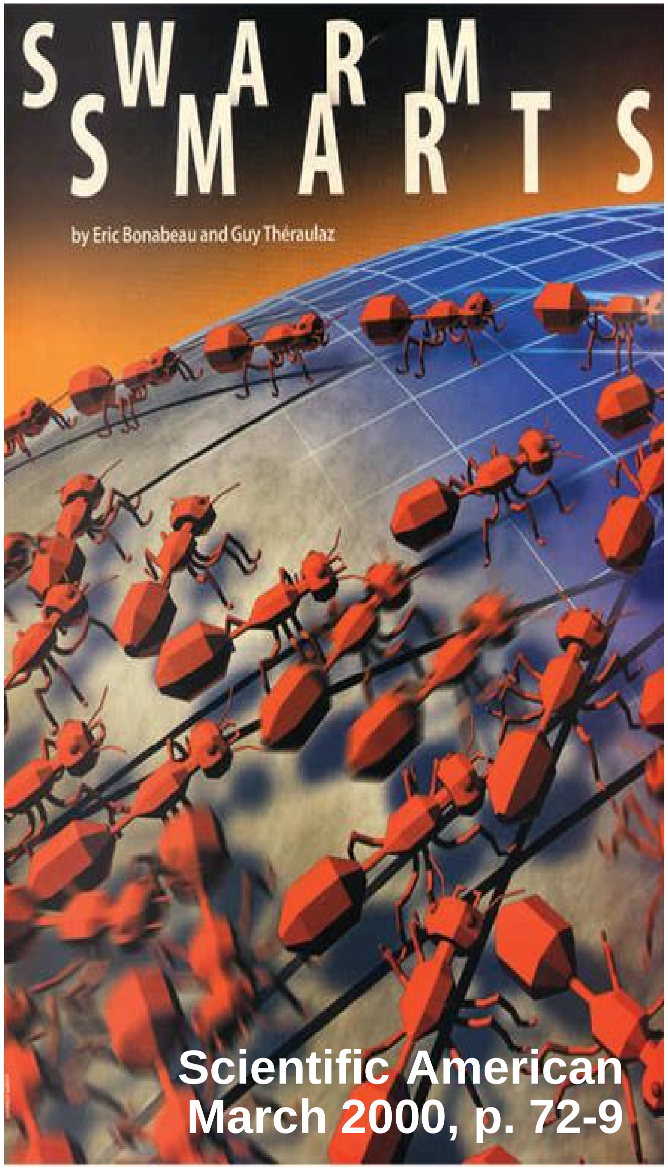


1 s movie
= 100 s
real time

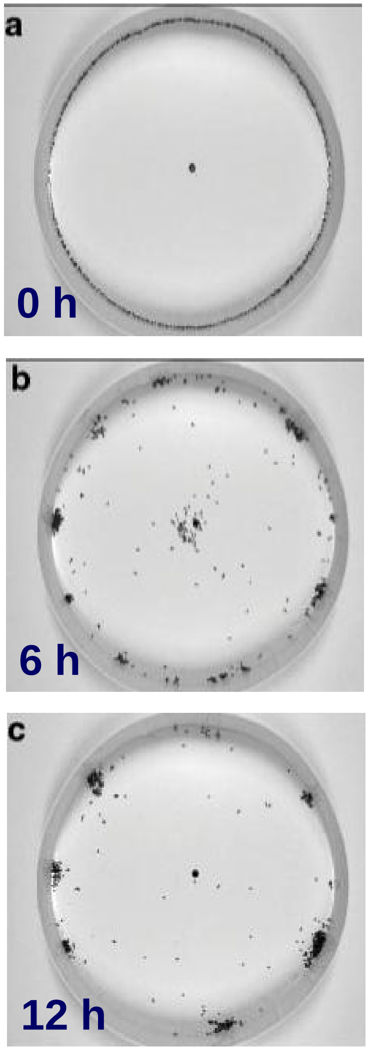
50 µm

Emergent behavior





Scientific American
March 2000, p. 72-9



Theraulaz et al. **Spatial patterns in ant colonies**. *PNAS* 2002, **99**:9645

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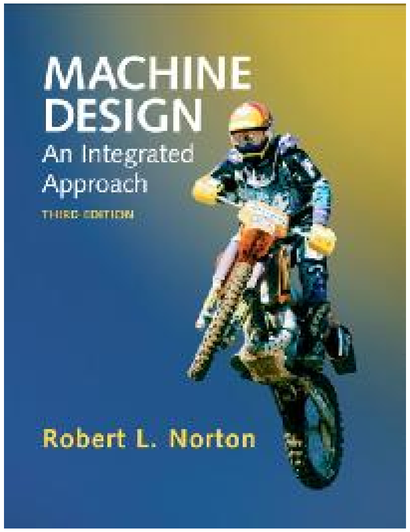
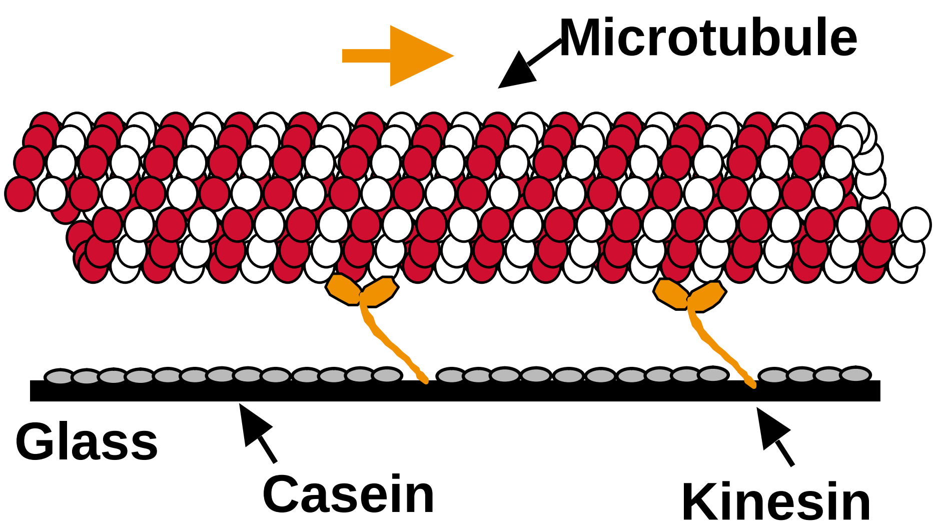
Design of Molecular Machines



1. Introduction to Design
2. Materials and Processes
3. Load Determination
4. Stress, Strain, and Deflection
5. Static Failure Theories
6. Fatigue Failure Theories
7. Surface Failure (Wear)
8. Design Case Studies
9. … 16. Bearings, Gears, etc.

"Fatigue failures always begin at a crack."

"There are three ways to fail: obsolescence, breakage, or wearing out"



Energy flow:

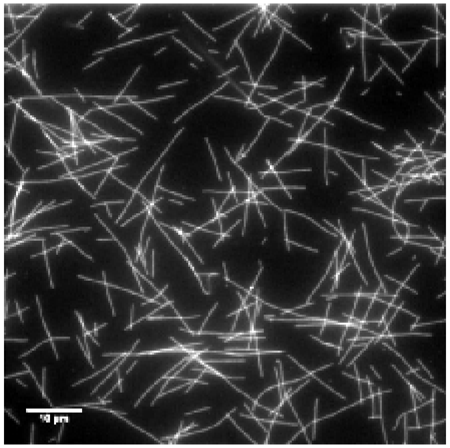
Chemical energy (ATP)

enters the system

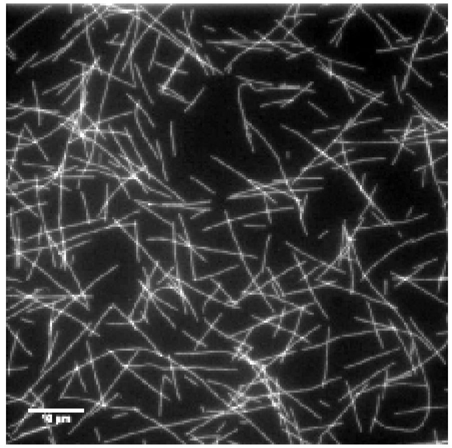
and is converted to

mechanical work and heat.

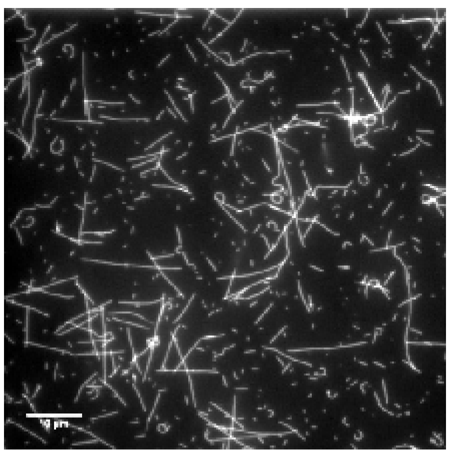
Wear of Molecular Shuttles



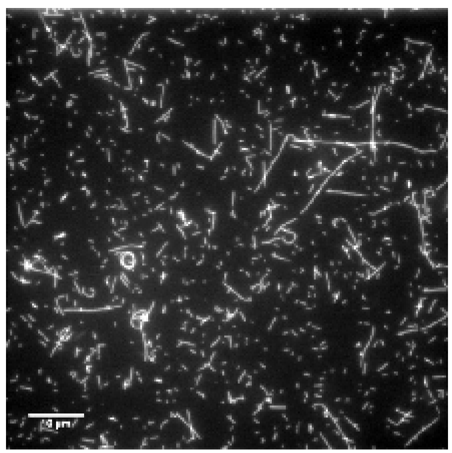
Inactive motors; t = 1 h



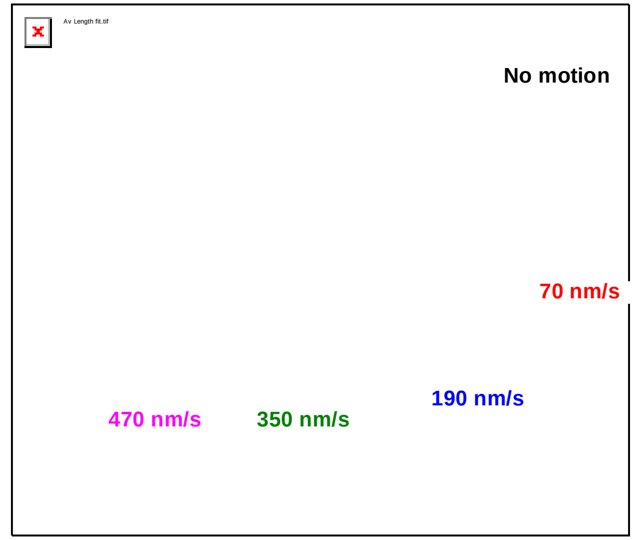
Inactive motors; t = 4 h

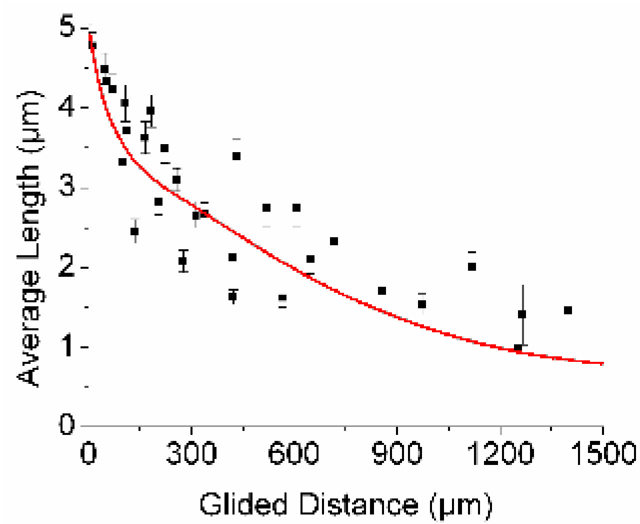


Active motors; t = 1 h



Active motors; t = 4 h





Degradation (shrinking, breaking) is proportional to traveled distance.

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Self-pumping membranes

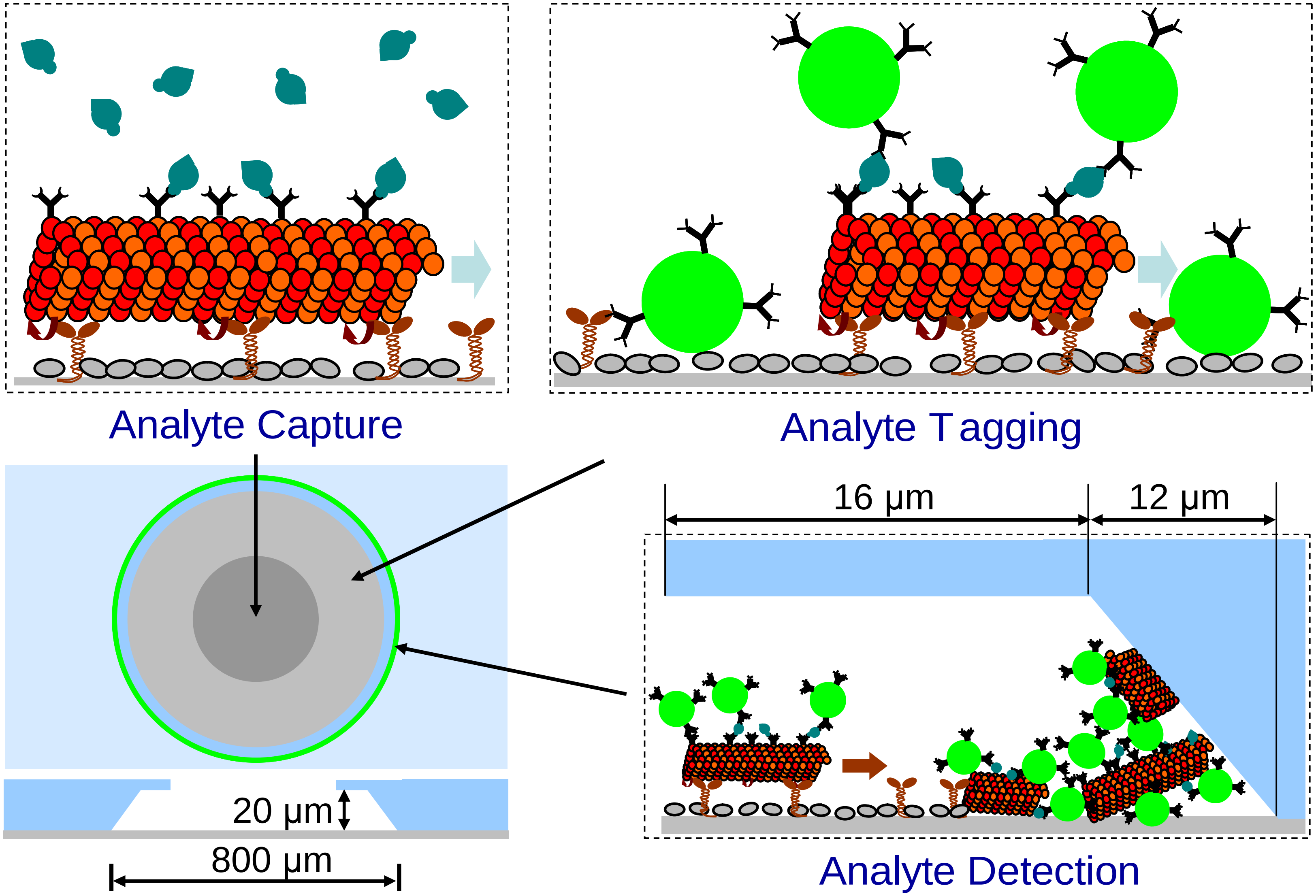
Smart dust sensor for remote detection of chem/bio agents

Directed by: George Bachand   Produced by: Sandia National Lab

In collaboration with:
Viola Vogel, ETH Zurich
Banahalli Ratna, Naval Research Lab
Peter Satir, Albert Einstein College of Medicine
Henry Hess, University of Florida

With support from the DARPA Biomolecular Motors program

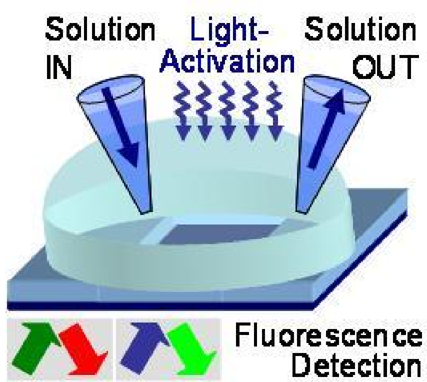
Smart dust sensor for remote detection of chem/bio agents

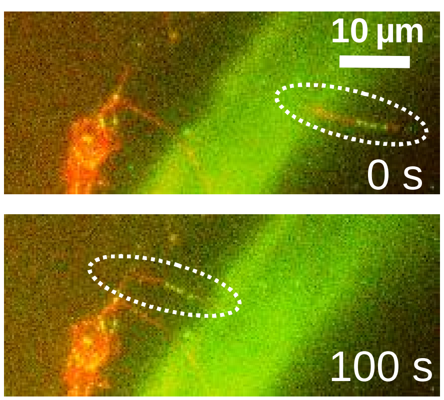


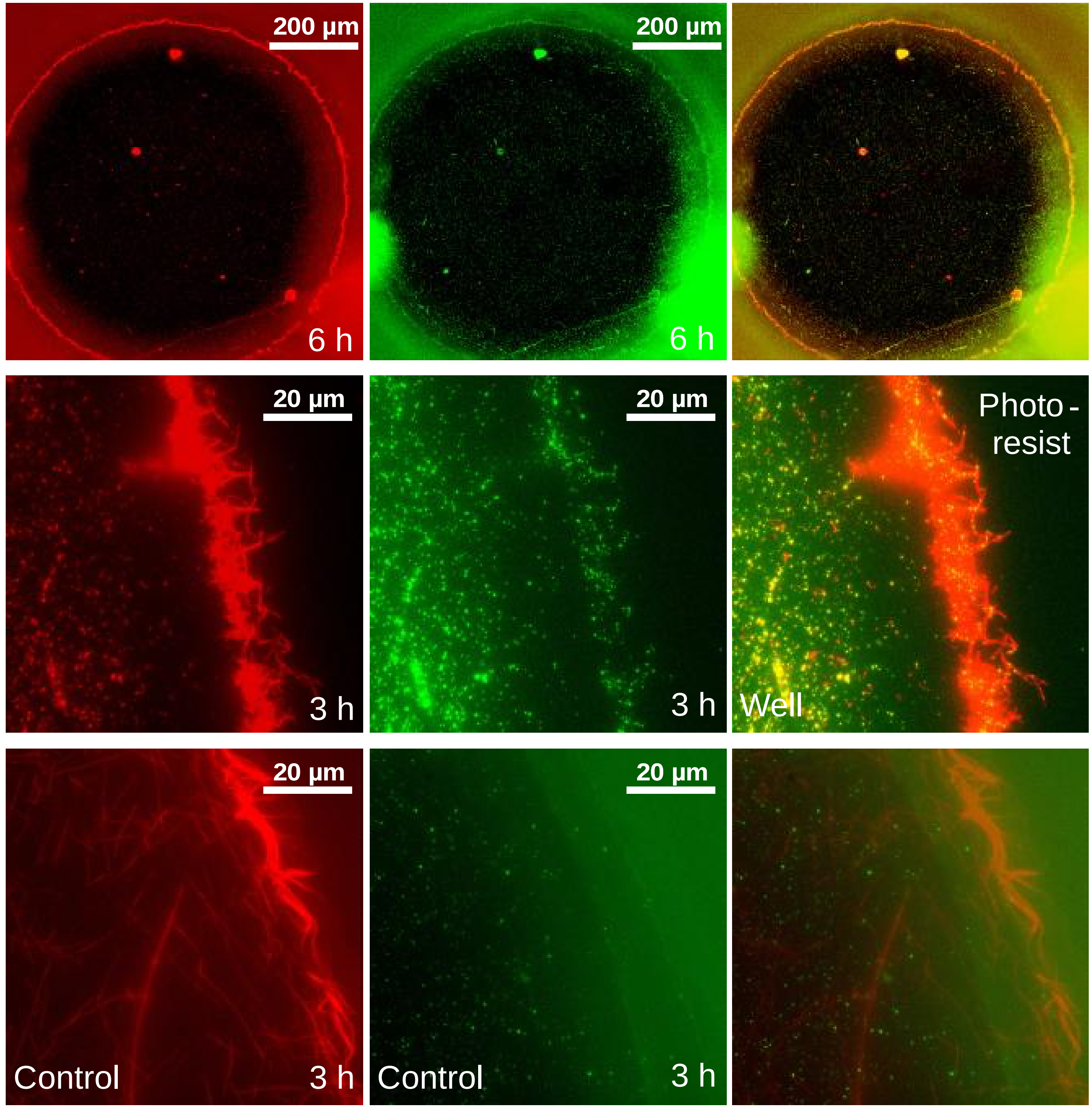
Fischer, Agarwal & Hess, Nature Nano **4**, 162 (2009)

Smart dust sensor:

1 nM streptavidin







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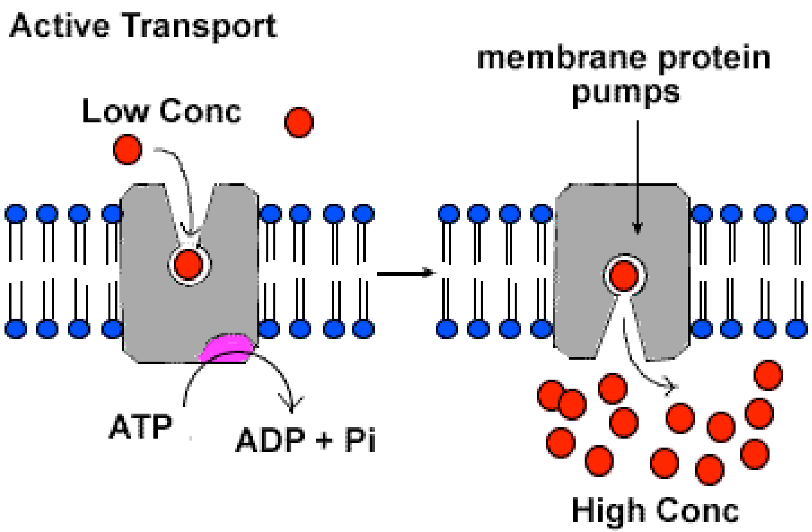
A biomimetic, self-pumping membrane



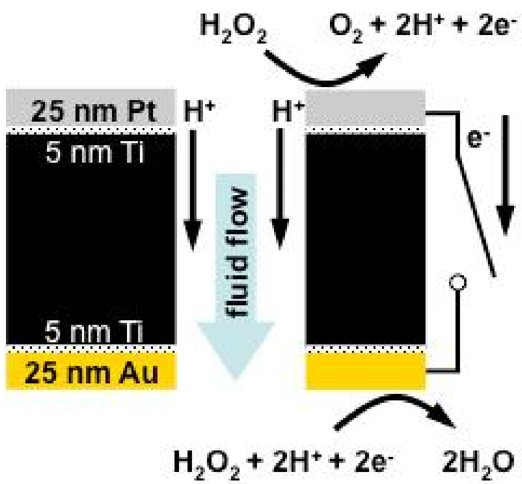
Harvesting of chemical energy, close coupling of energy conversion with transport

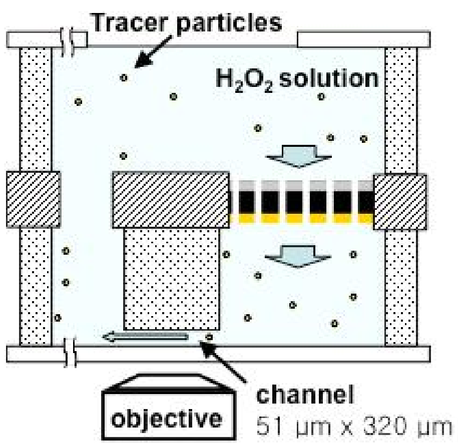
Microscale integration of chemical to mechanical energy conversion

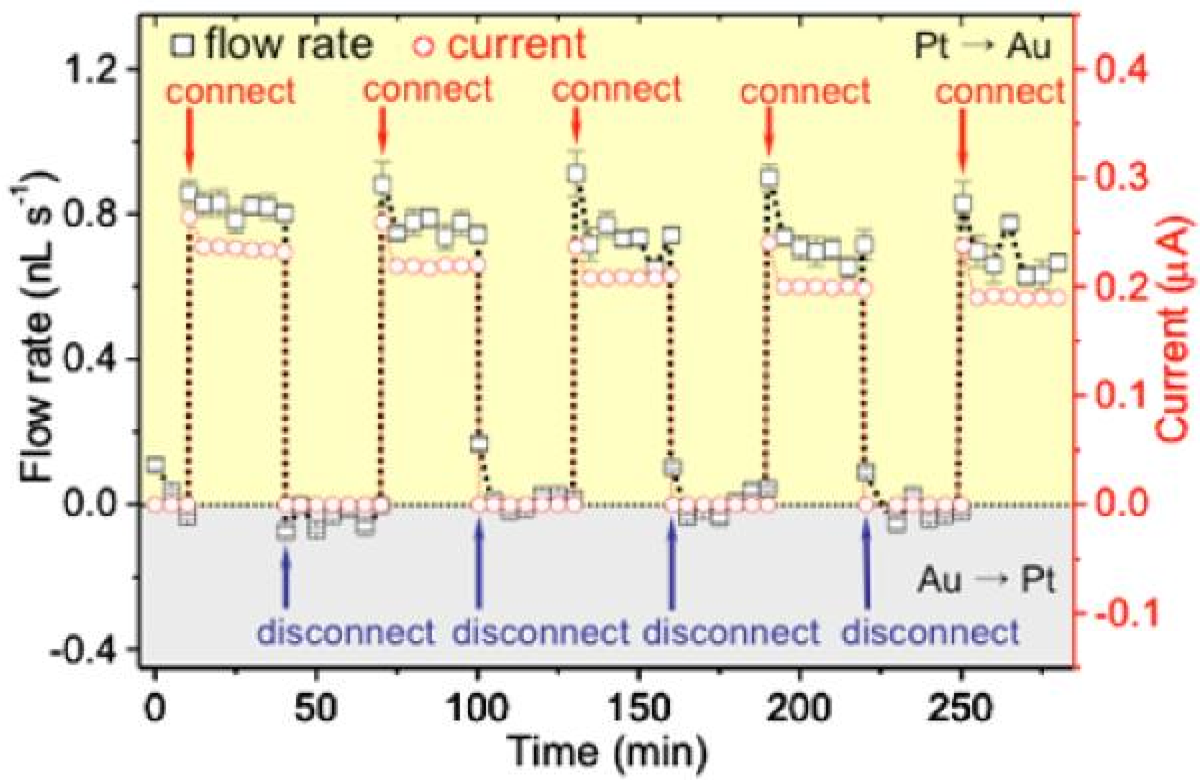
in an active composite material made of metals and plastic

In-kook Jun & H. Hess, Advanced Materials (DOI: 10.1002/adma.201001694)

A biomimetic, self-pumping membrane



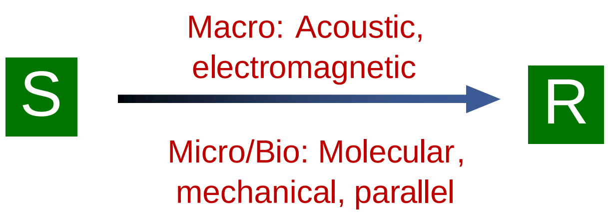




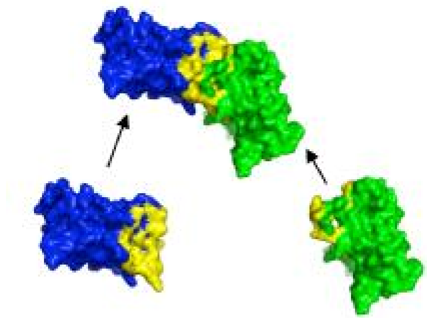
In-kook Jun & H. Hess, Advanced Materials (DOI: 10.1002/adma.201001694)

Hybrid devices to explore design principles and applications

Communication, information processing and emergence



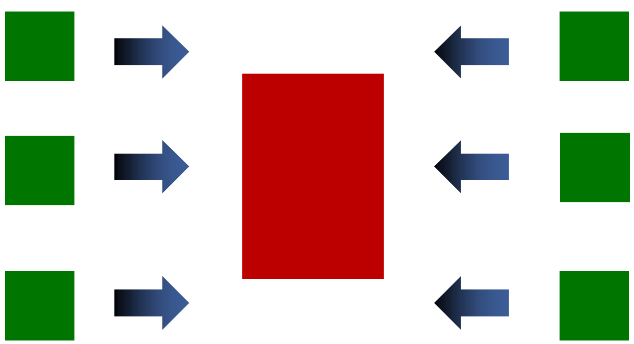
Mechanical engineering at the molecular scale



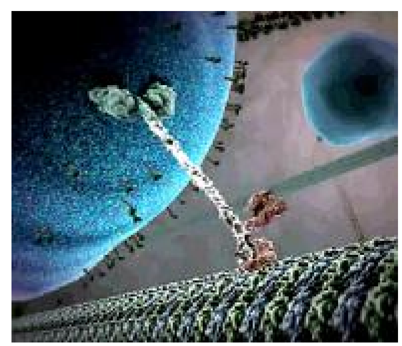
Macro: Well-defined, static, predictable, intuitive

Micro&Bio: Complex, dynamic, unpredictable?

Integration (physical and functional)



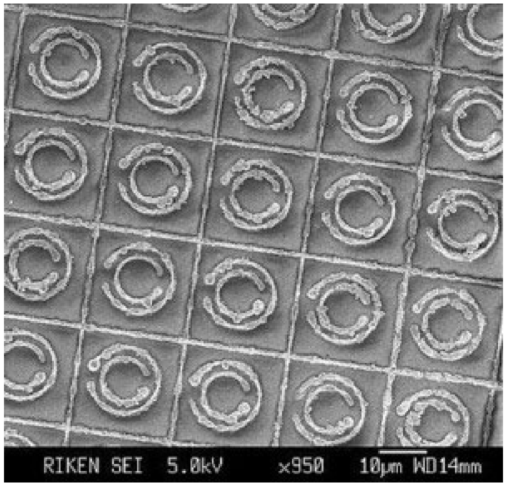
Transitioning to microscopic synthetic devices

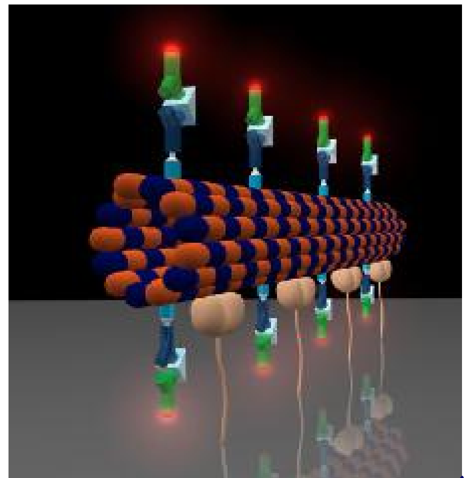


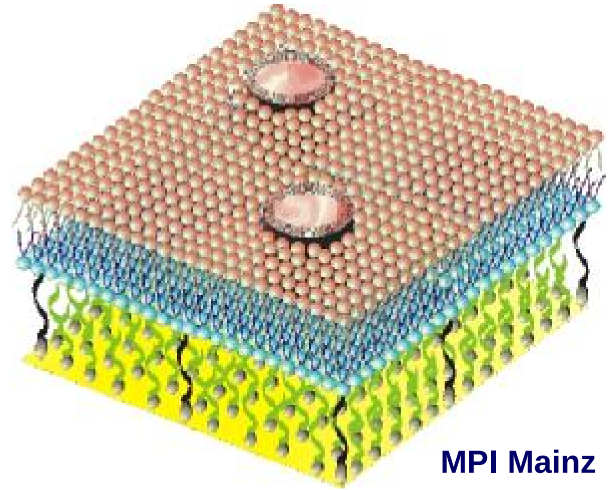
Acknowledgements:

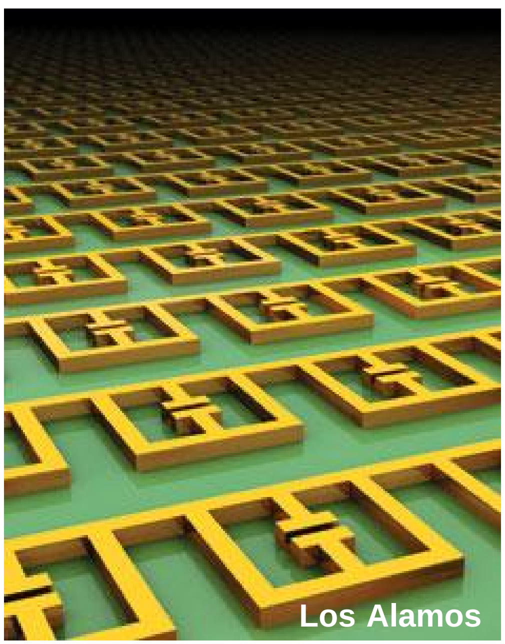
The Columbia team:	Emmanuel Dumont, Ofer Idan, Rodney Agayan
The UF nanomotor team:	Robert Tucker, Isaac Luria, Parag Katira, Ashutosh Agarwal, Thorsten Fischer, Yolie Jeune Krishna Nittala, Shruti Banavara-Seshadri Jasmine Davenport
The UW molecular shuttle team:	**Viola Vogel (ETH Zurich since ‘04)** **Jonathon Howard (MPI-CBG Dresden since ‘02)** John Clemmens, Robert Doot, Christian Brunner, Karl-Heinz Ernst, Robert Tucker, Sheila Luna, Di Wu, Sujatha Ramachandran, Scott Phillips
The SNL motor team:	**Bruce C. Bunker, George D. Bachand**
Gifu University:	**Takahiro Nitta,** A. Tanahashi, M. Hirano
The MPI-CBG bionano group:	**Stefan Diez,** J. Howard, Jacob Kerssemakers
The U. of Michigan team:	**Joerg Lahann**, Hsien-Yeh Chen, Xuwei Jiang
Funding:	DOE-BES Biomolecular Materials Program DARPA Biomolecular Motors Program NSF CAREER Award UF Center for Sensor Materials and Technologies Volkswagen Foundation

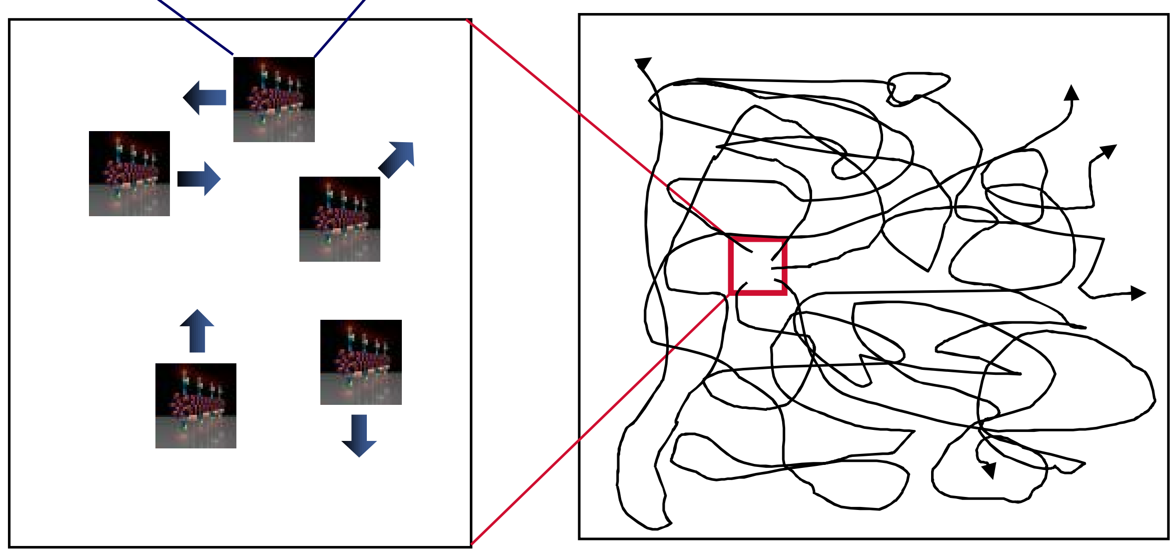
Molecular shuttle coatings: An active and soft "metamaterial"











The future is more and smaller motors!

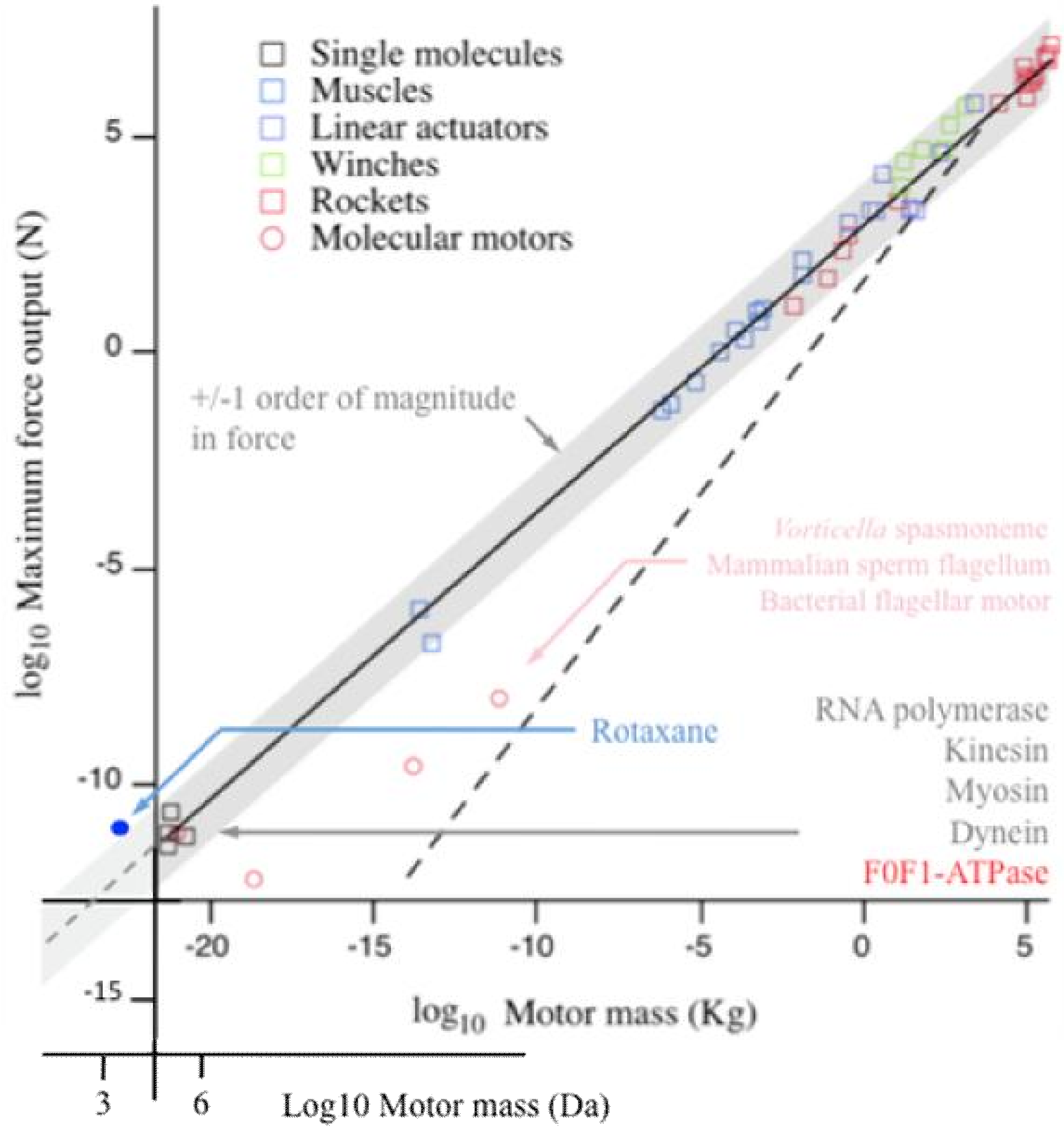
Example:

Car (1925) – 1 motor
1 m in size

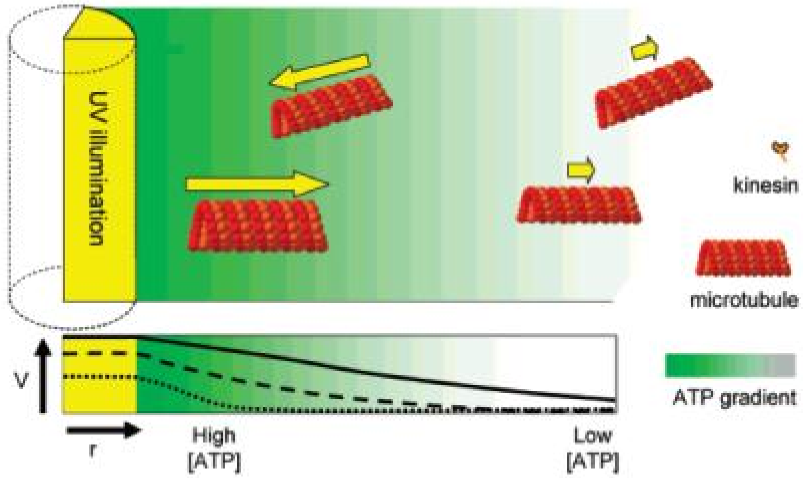
Car (2010) – 1 gasoline engine,
~100 electric motors to adjust various components
1 cm – 1 m in size

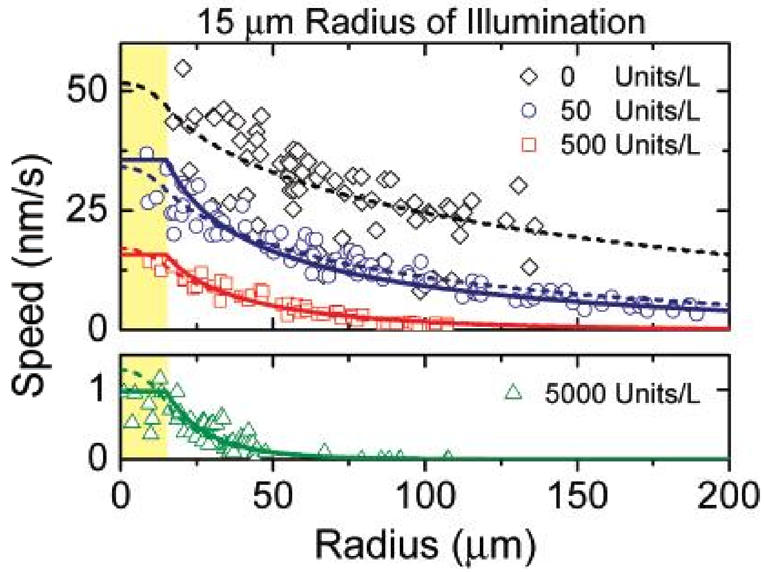
Car (2095) – 10,000 motors
100 mm – 1 m in size

)



Communicating with **individual** molecular shuttles?





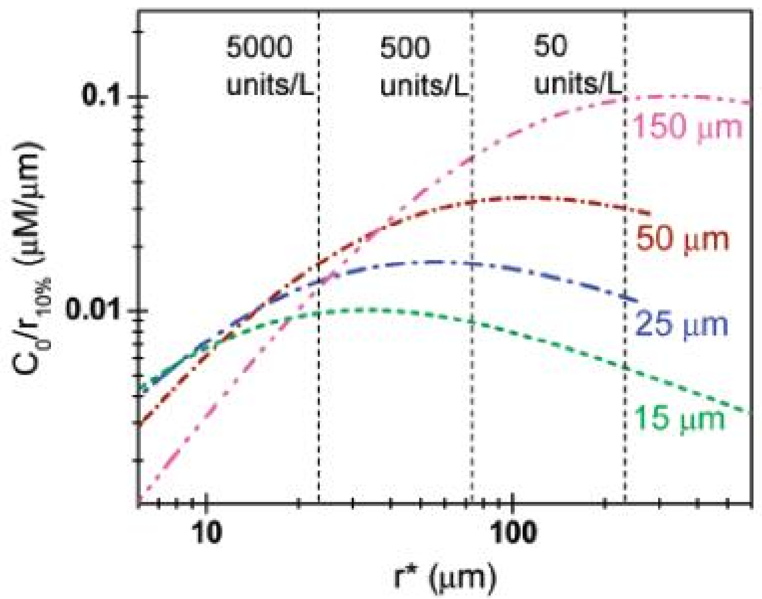
$$C = C_0\sqrt{\frac{r_i}{r}}\cdot\exp\left[\frac{(r_i - r)}{r^*}\right] \qquad C_0 = \frac{C_{cATP}kI_{h\nu}}{D\left(\frac{1}{r^*} + \frac{1}{r_i}\right)^2}$$

$r^{*2} = K_m D/A$

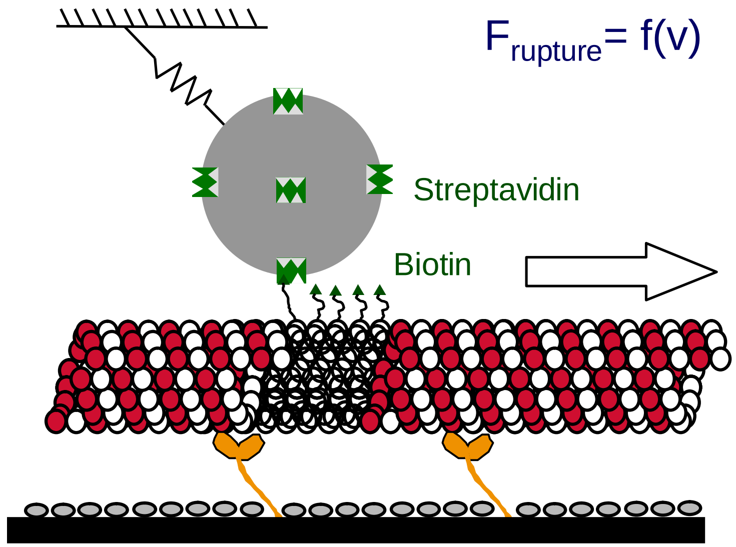
Increasing localization ➡ Decreasing activation

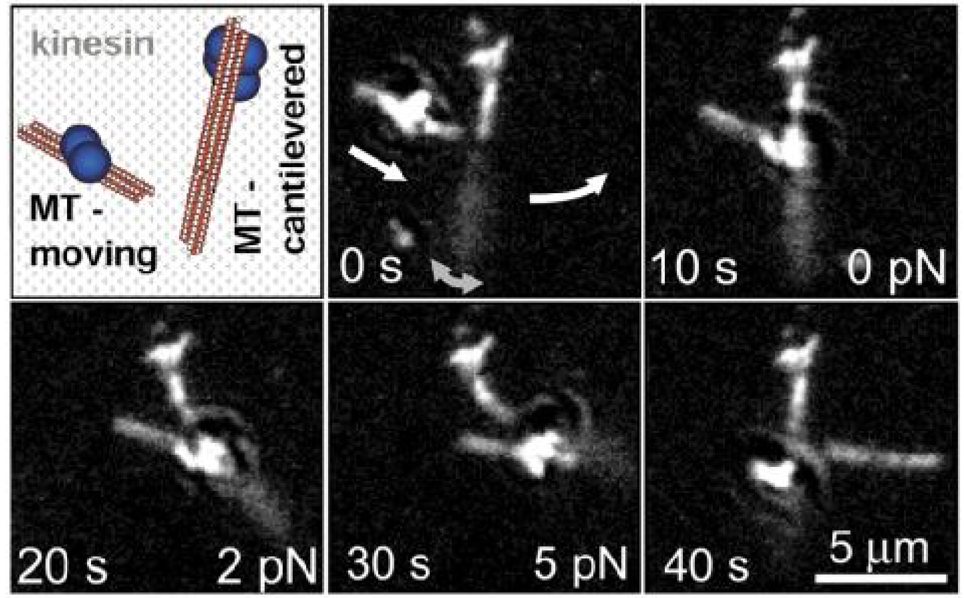
Diffusing molecules as messengers require
either diffusion barriers to address specific recipients
or a swarm-based approach.

Nano Letters 8, 221 (2008)



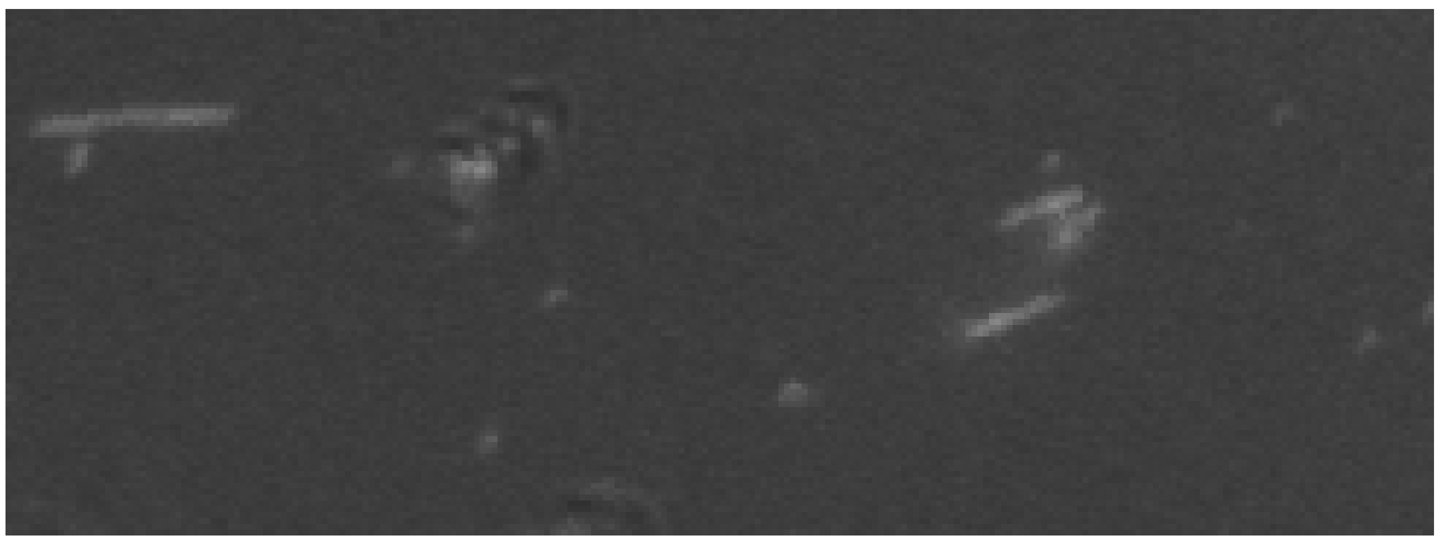
Nanoscale force measurements



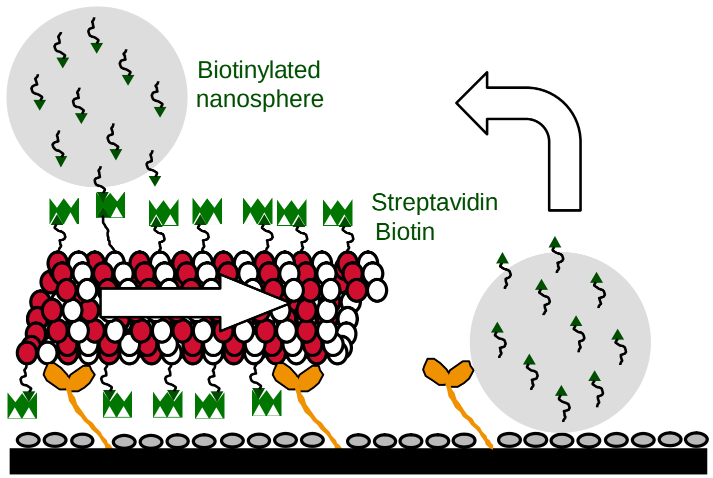


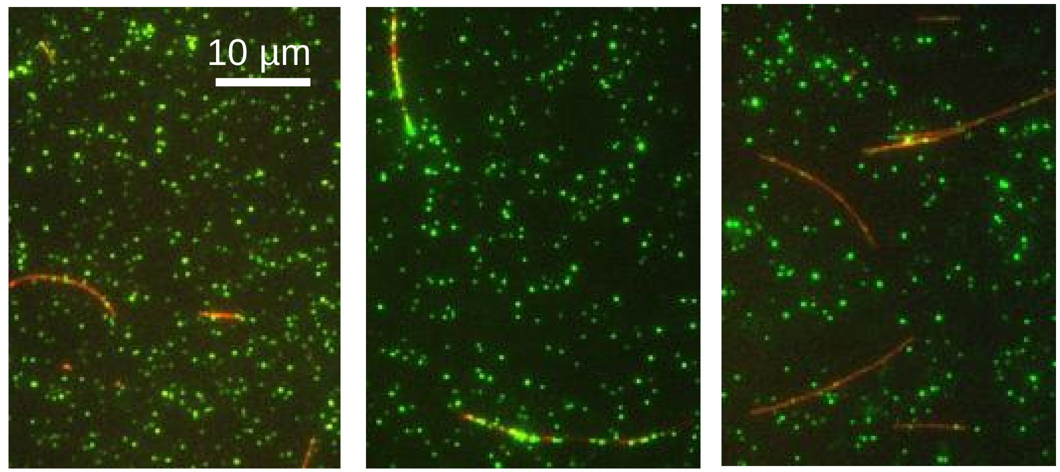
1 s movie = 50 s real time

5 µm

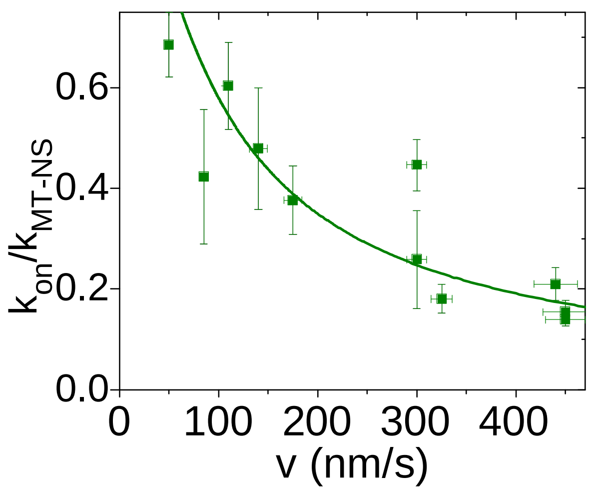


Cargo loading by molecular shuttles

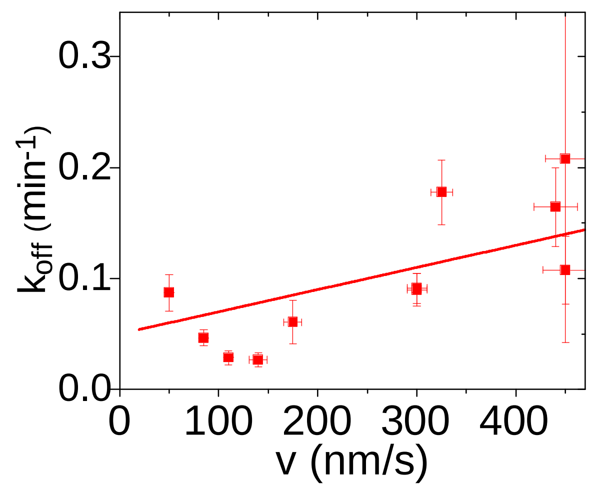




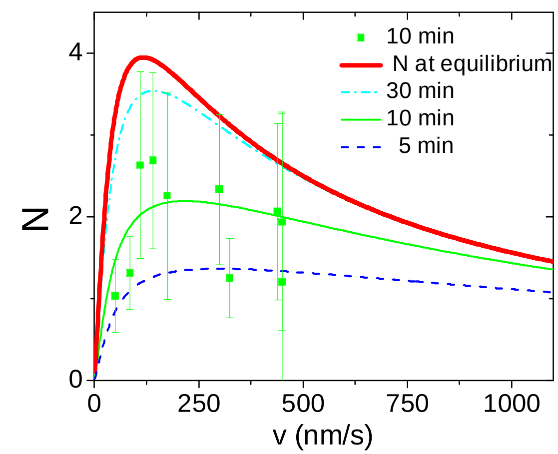
50 nm/s 175 nm/s 450 nm/s



Binding



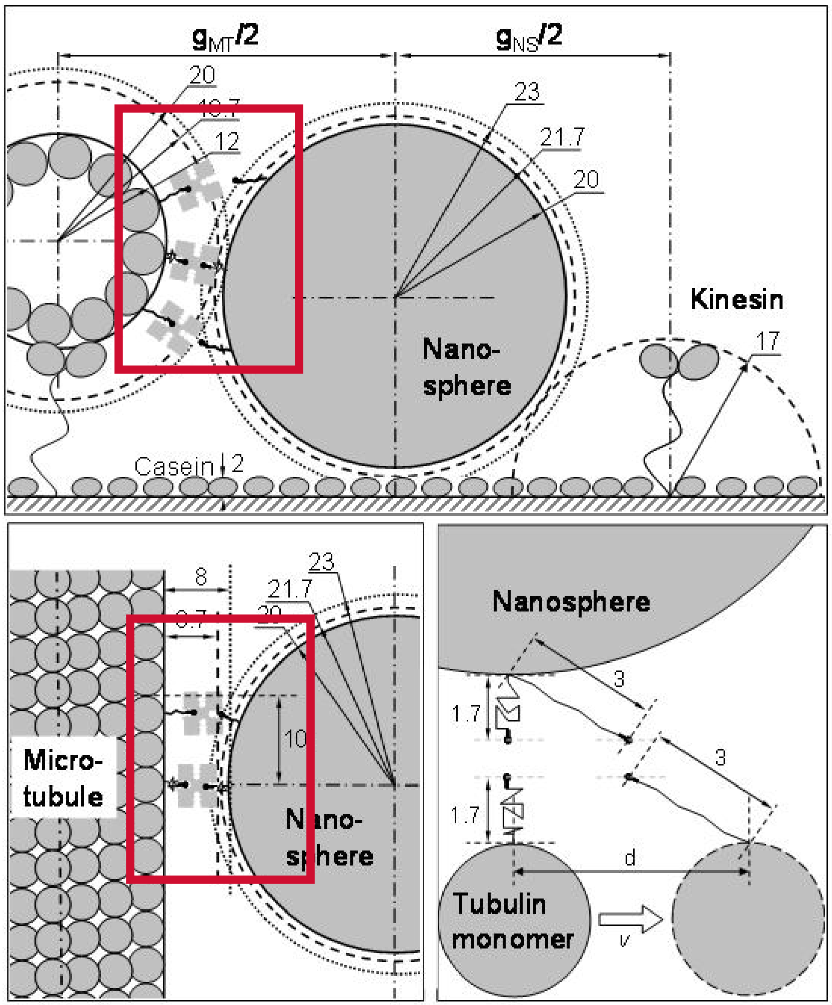
Unbinding



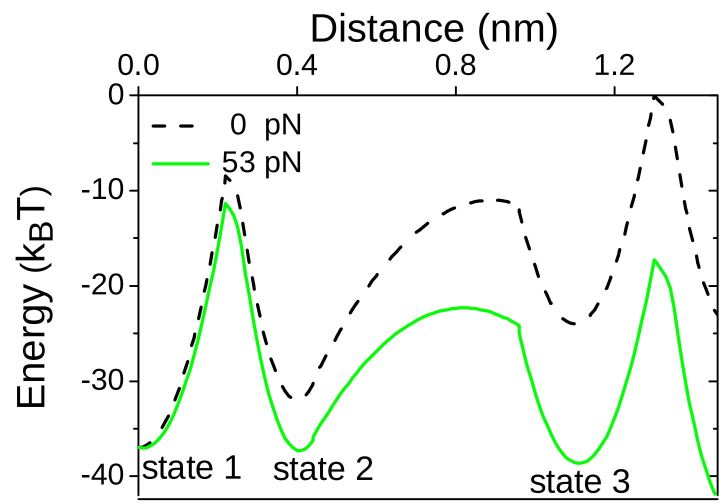
Optimum velocity: 120 nm/s (25% of top speed)

Modeling of process requires engineering AND chemistry; Optimum velocity results from “glue-like” bond

Number of Biotin–Streptavidin Interactions:



Sticking Probability:



Biology exploits

complex molecular interactions

to achieve

complex nanoscale functionalities.

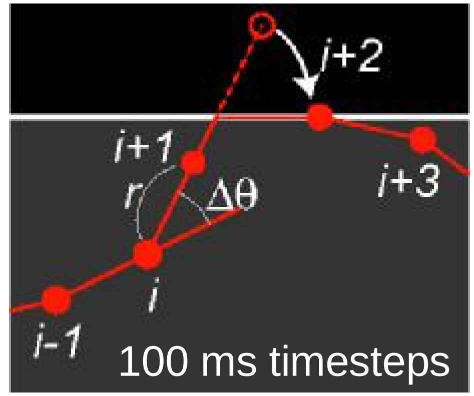
Nano Letters 9, 1170 (2009)

Computer-Aided Design of guiding structures

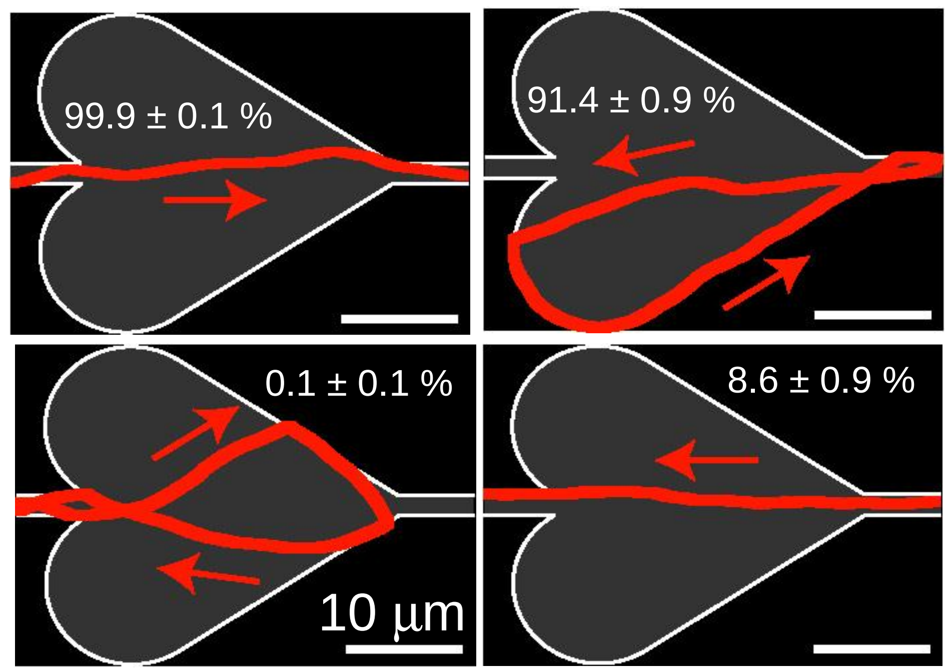
Trajectory persistence length L_p:

$$\left\langle \cos[\Delta q(\Delta t)]\right\rangle = \exp\left(-\frac{v_{avg}\Delta t}{2L_p}\right)$$

Measurement: L_p = 0.1 mm



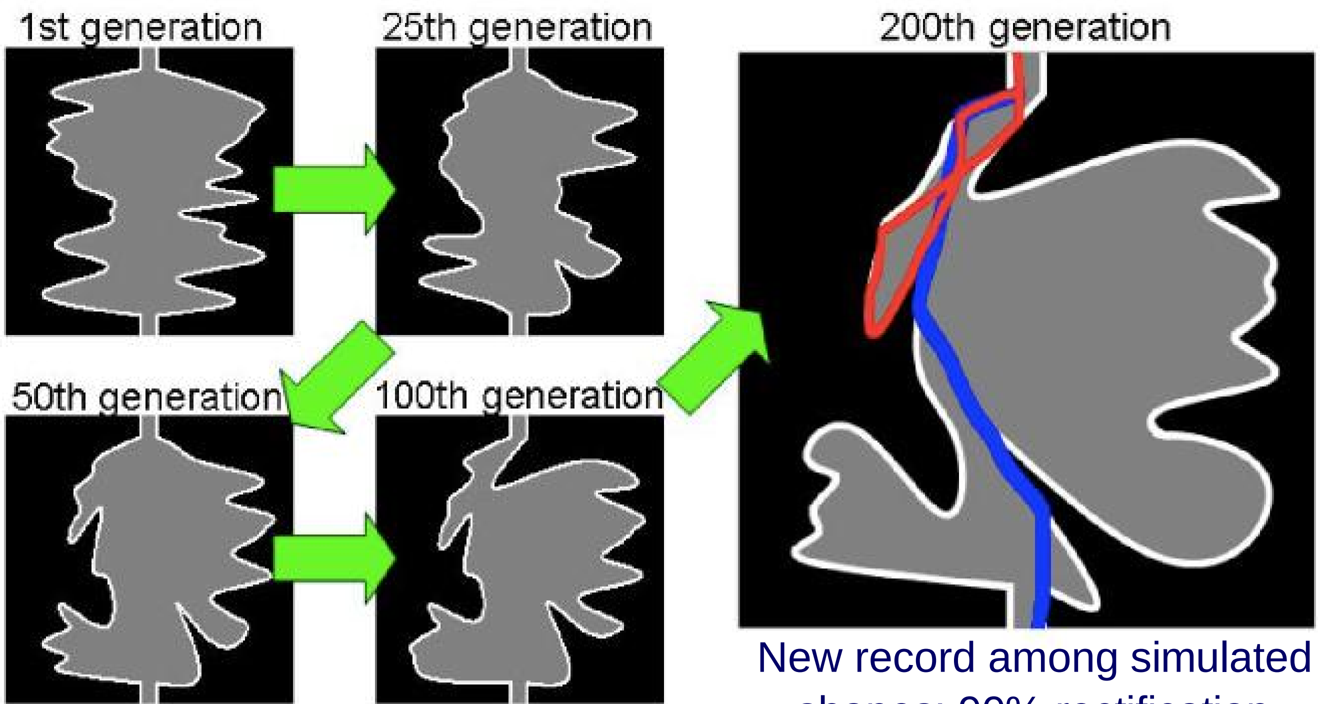
Takahiro Nitta, et al.: "Simulating molecular shuttle movements", Lab on a Chip 6, 881 (2006)



M.G.L. van den Heuvel et al., Nano Letters **5**, 1117 (2005)

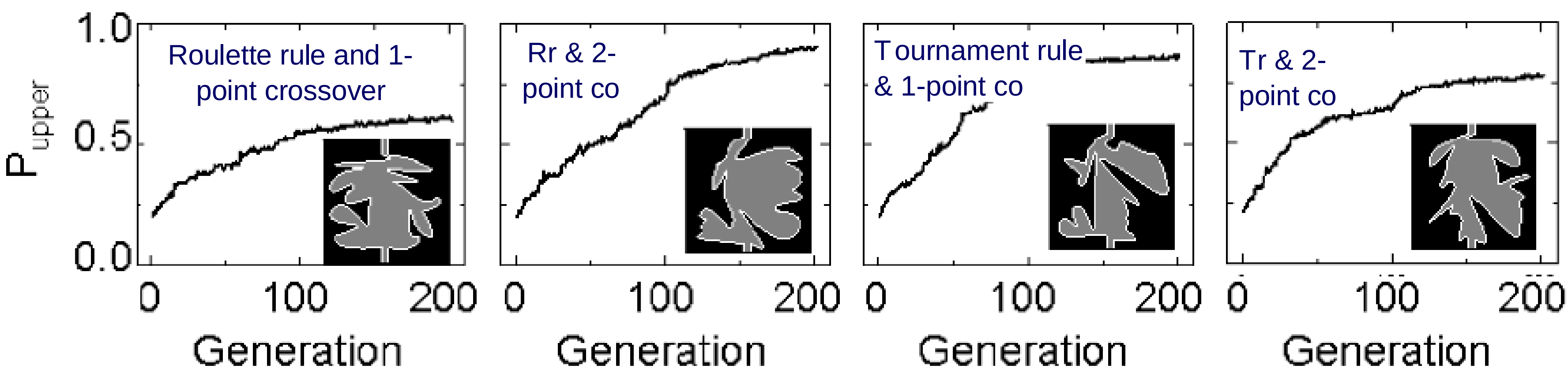
Experiment:	98%	88%
	1%	12%

Removing the need for molecular intuition: Design by ES

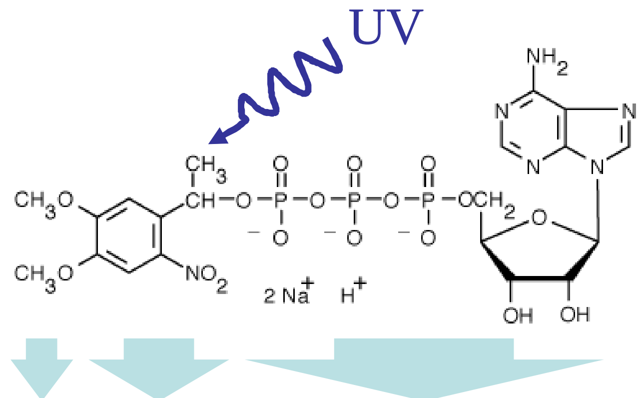


New record among simulated shapes: 90% rectification

Takahiro Nitta, et al. “Evolutionary optimization of guiding track designs …”, Proceedings of µTAS 2009



Communicating with molecular shuttles

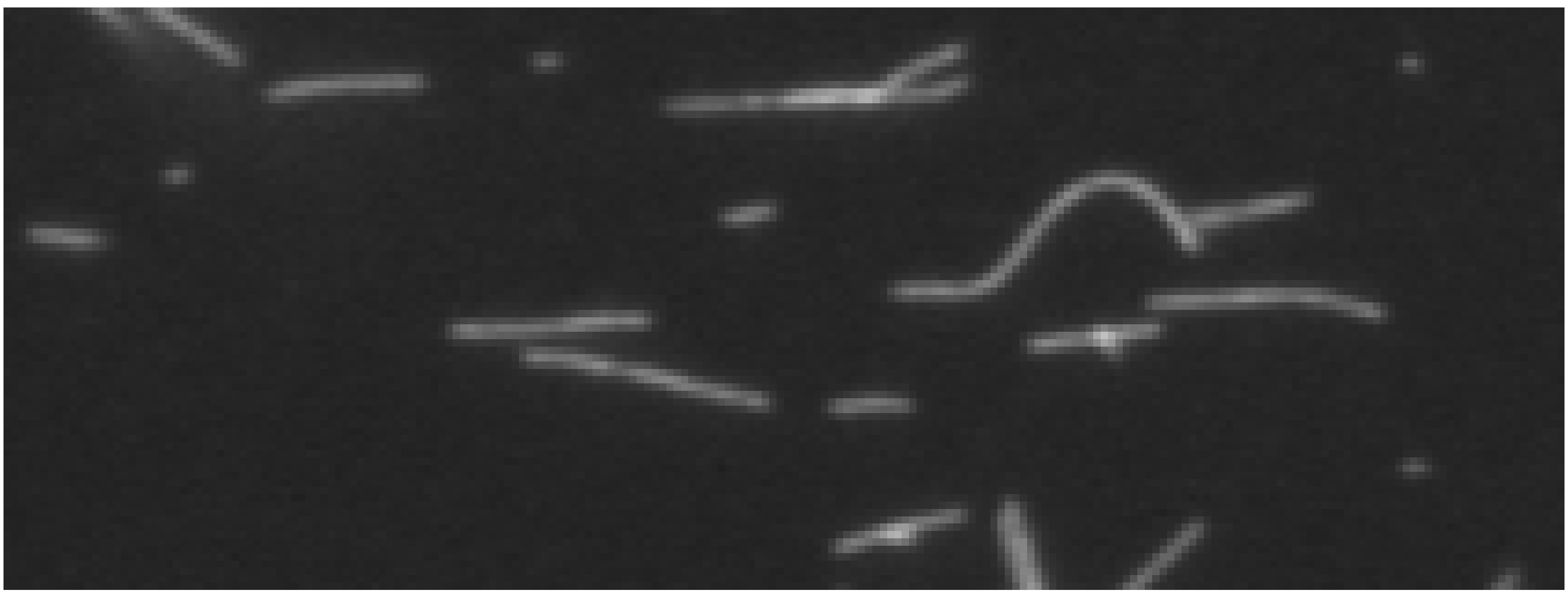


DM – NPE – ATP

UV-light releases, Hexokinase sequesters ATP

5 µm

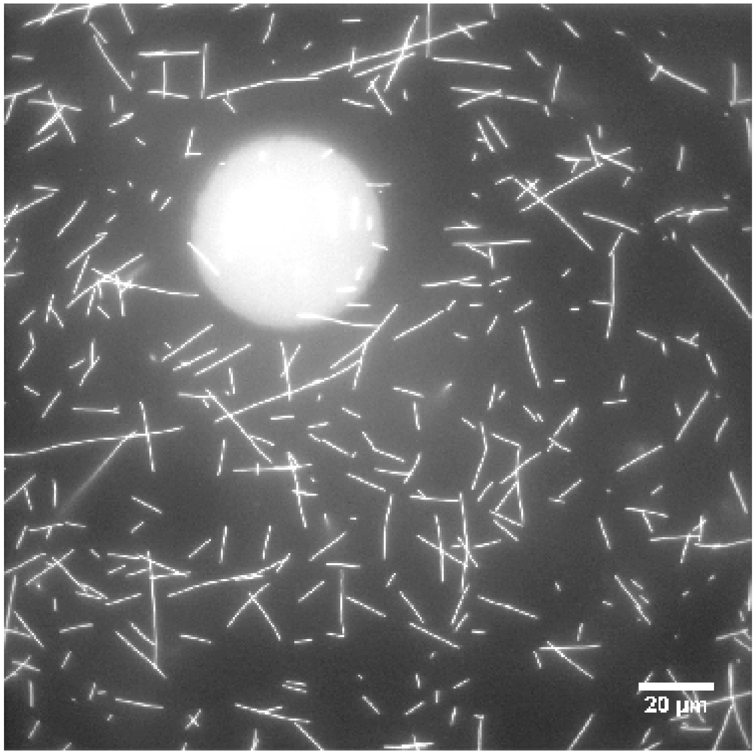
1 s movie = 300 s real time



Communicating with **individual** molecular shuttles?

patterned exposure to UV light
rapid diffusion of ATP
delocalized movement of shuttles

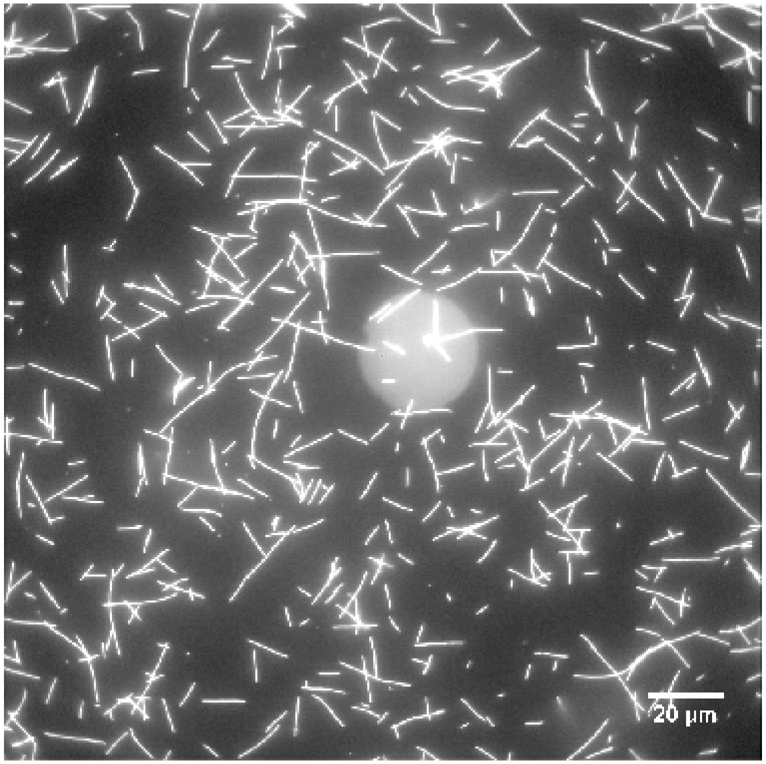
patterned exposure to UV light
diffusion + sequestration of ATP
localized movement



no HK, time 360x

D(ATP) =
400 µm²/s

50 µm



5000 units HK, time 3600x