Designing Intelligent Nano/Microbots:
Fantastic Voyage

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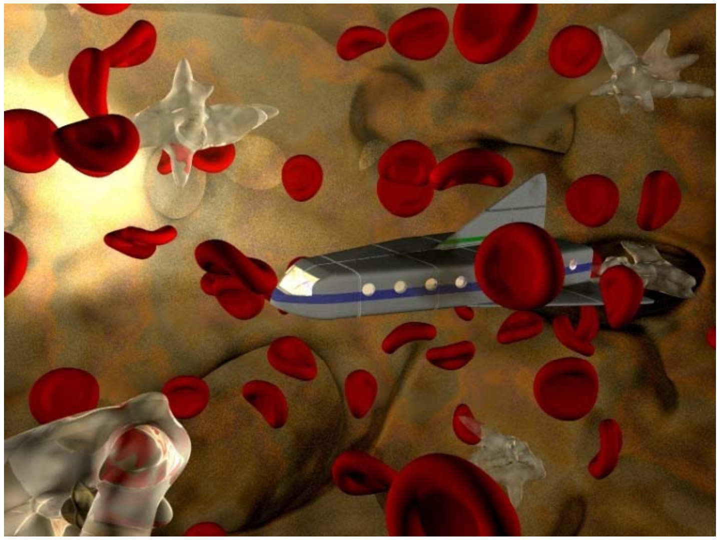


***Nano Today*, 2013**
***Angew. Chem.*, 2012**
***Phys. Chem. Chem. Phys.*, 2010**
***Angew. Chem.*, 2006**
***Scientific American*, May, 2009**

Grand Challenge

Master Energy & Information at the Nano/Micro Scale

Design intelligent systems.

Create technologies that rival those of living organisms.

Use free energy to fabricate organized systems driven far from equilibrium.

Mallouk and Sen, *Scientific American,* May, 2009

ehydroponics.com

Grand Challenge:

Master Energy & Information at the Nano/Micro Scale

- Design intelligent systems
- Use free energy to fabricate organized systems driven far from equilibrium

Code

Information

⇩

Gradient: Chemical, Optical, …

Decode

Ability to process information

⇩

Self-powered object

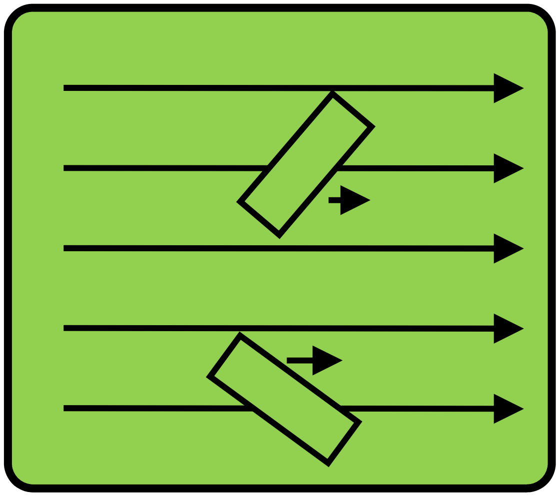
Information + Information Processing

Collective/Emergent behavior

- ❑ Re-configurable Spatial and/or Temporal Assemblies
- ❑ Analyte-Triggered Motion and Cargo Delivery

Sources of Free Energy

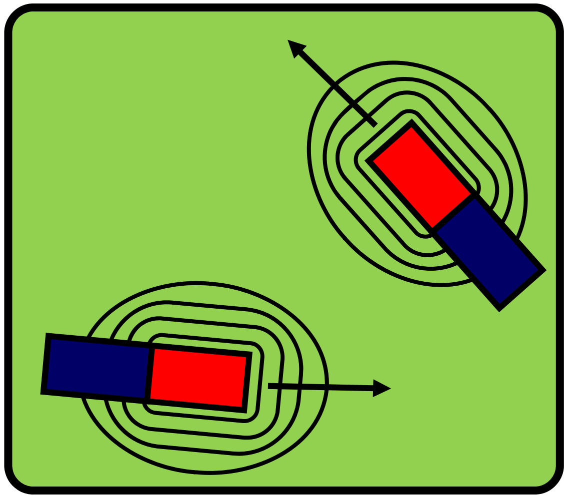
External Vector Field



- Many types of fields:
  (*magnetic, electric, thermal, ..*)
- Energy applied from external source
- Ensemble behavior of all particles
- Motion is defined by the field, not the particle: *not a motor*

Anderson, *Ann. Rev. Fluid. Mech.*, **1989**

Self-Generated Field



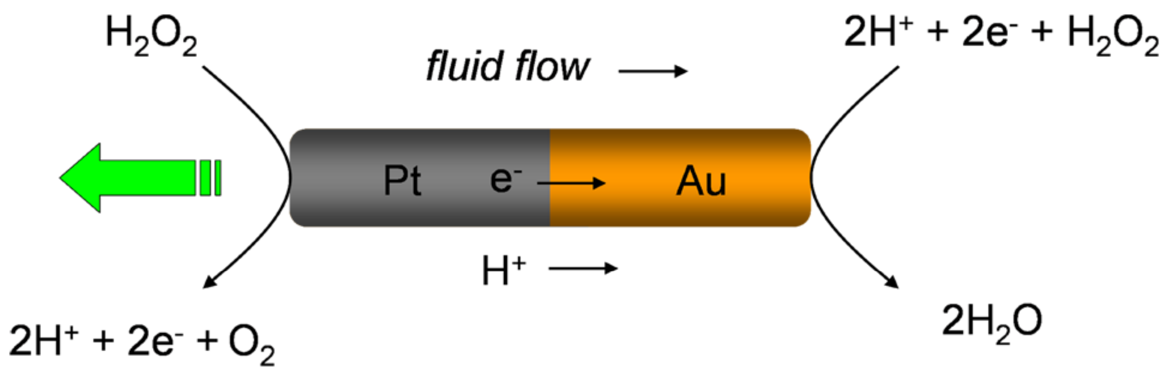
- Catalytically generated fields:
  (*chemical, thermal, electric, ..*)
- Energy harvested locally
- Motors move independently
  Motors store or react to information at the *local* level
- Catalysis and asymmetry

Mallouk, Sen, *Chem. Eur. J.*, **2005**

Design Elements in Intelligent Nano/Microbots

- ❑ Autonomous movement through energy harvesting
- ❑ Control of directionality by chemical or light gradients
- ❑ Inter-bot communication via chemical signals
- ❑ At low Reynolds number regime, asymmetric gradients along surfaces are optimal for powering objects

Electrokinetic Propulsion

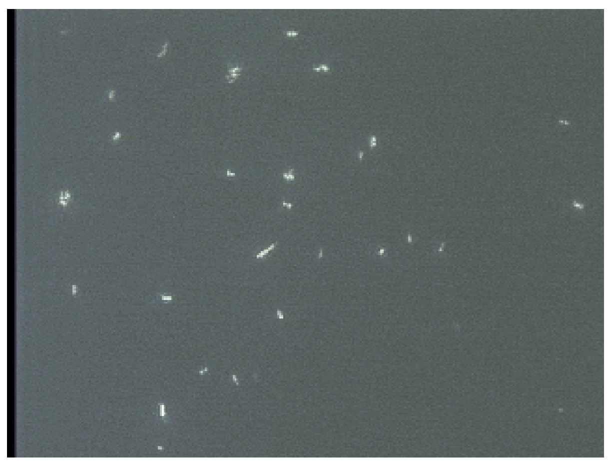


$$i_{e^-} = i_{H^+}$$

$$E = \frac{J_{H^+}}{\sigma}$$

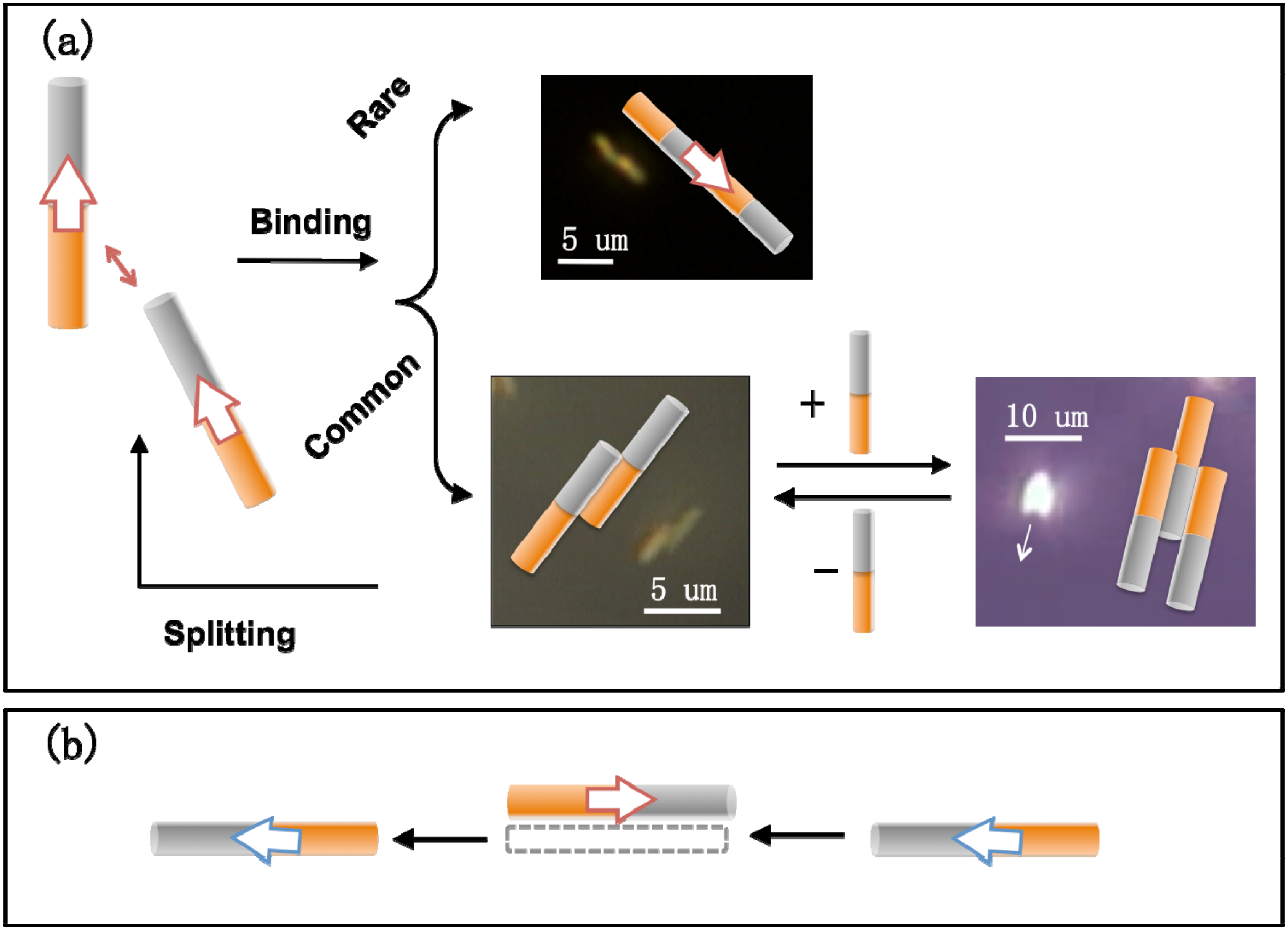
$$v = \frac{\zeta \varepsilon E}{\mu} f$$

J = current density
σ = conductivity
E = electric field



Mallouk, Sen, *J. Am. Chem. Soc.*, 2004, 2006

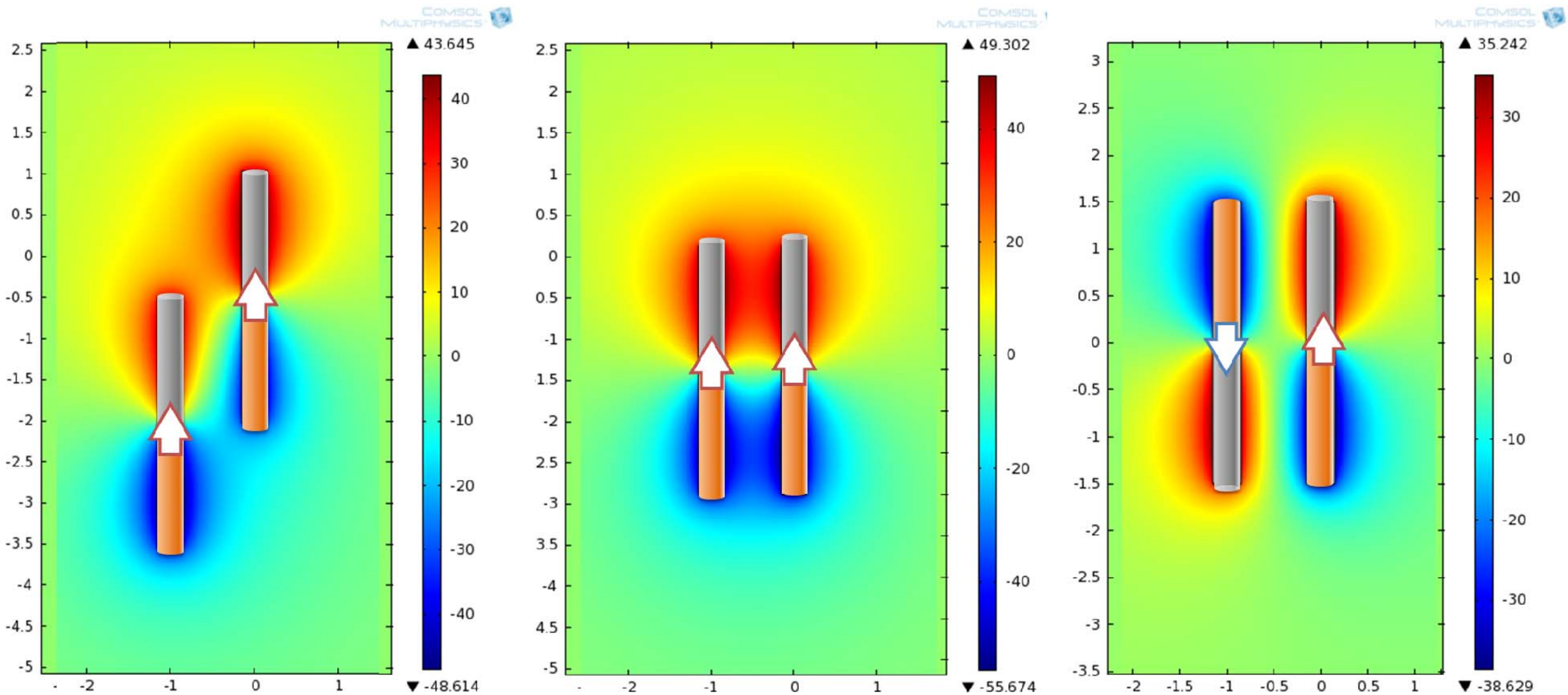
Dynamic Interactions Between Catalytic Nanomotors



Mallouk, Sen, *PNAS*, 2013

Dynamic Interactions Between Catalytic Nanomotors

Origin of the Staggered Shape of Doublets

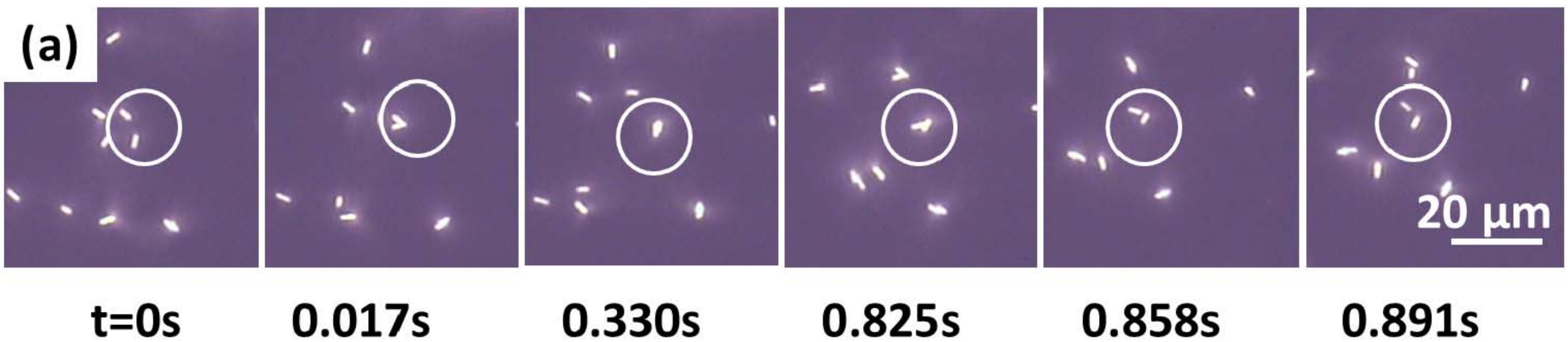


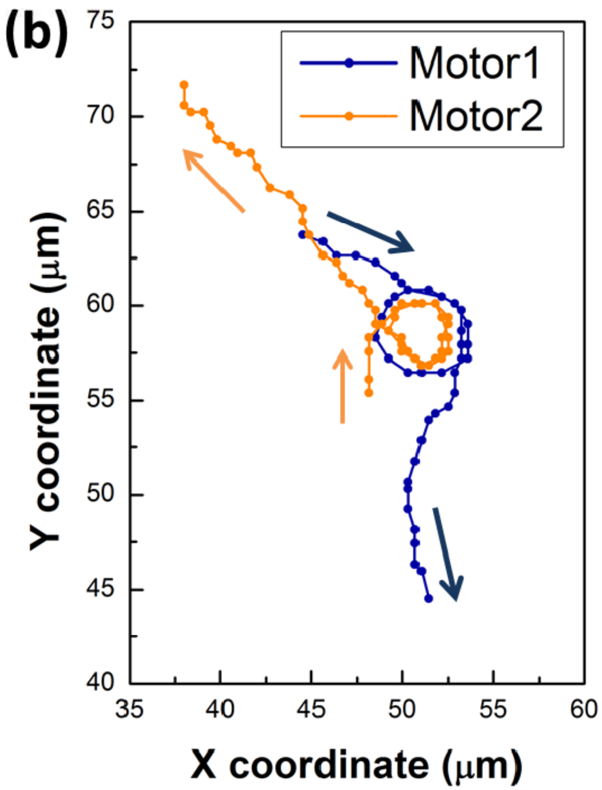
Space Charge Density from Simulation

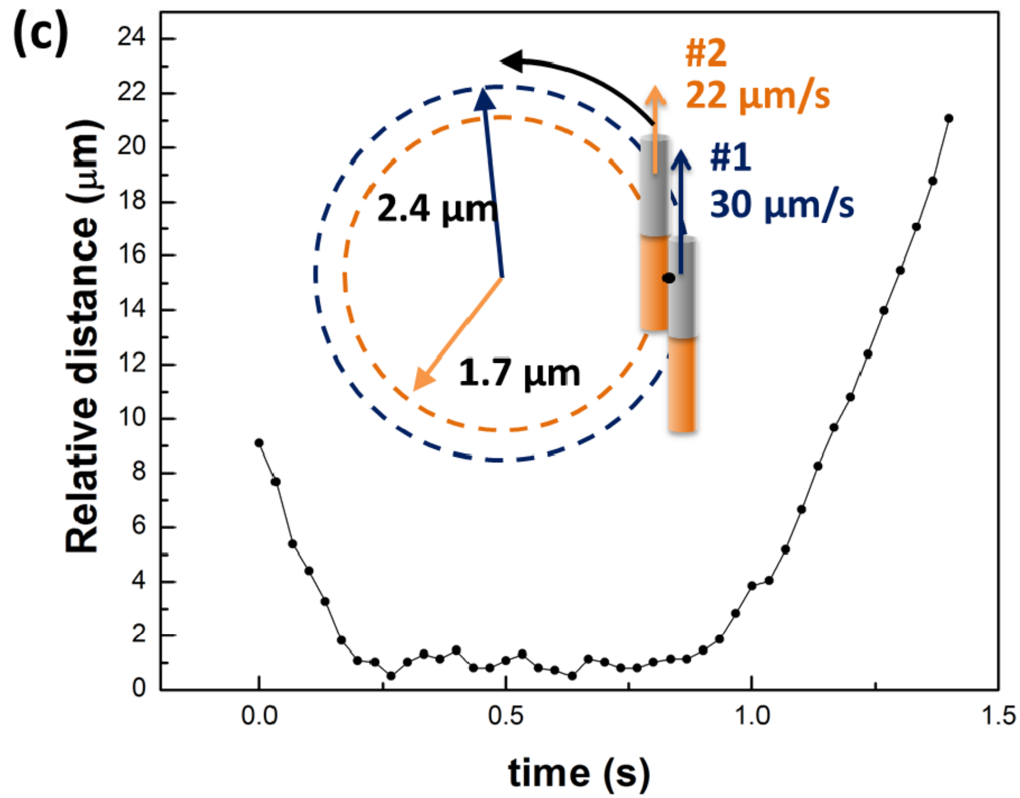
(Moran & Posner, *J. Fluid Mech.* **2011**, *680*, 31)

Mallouk, Sen, *PNAS*, 2013

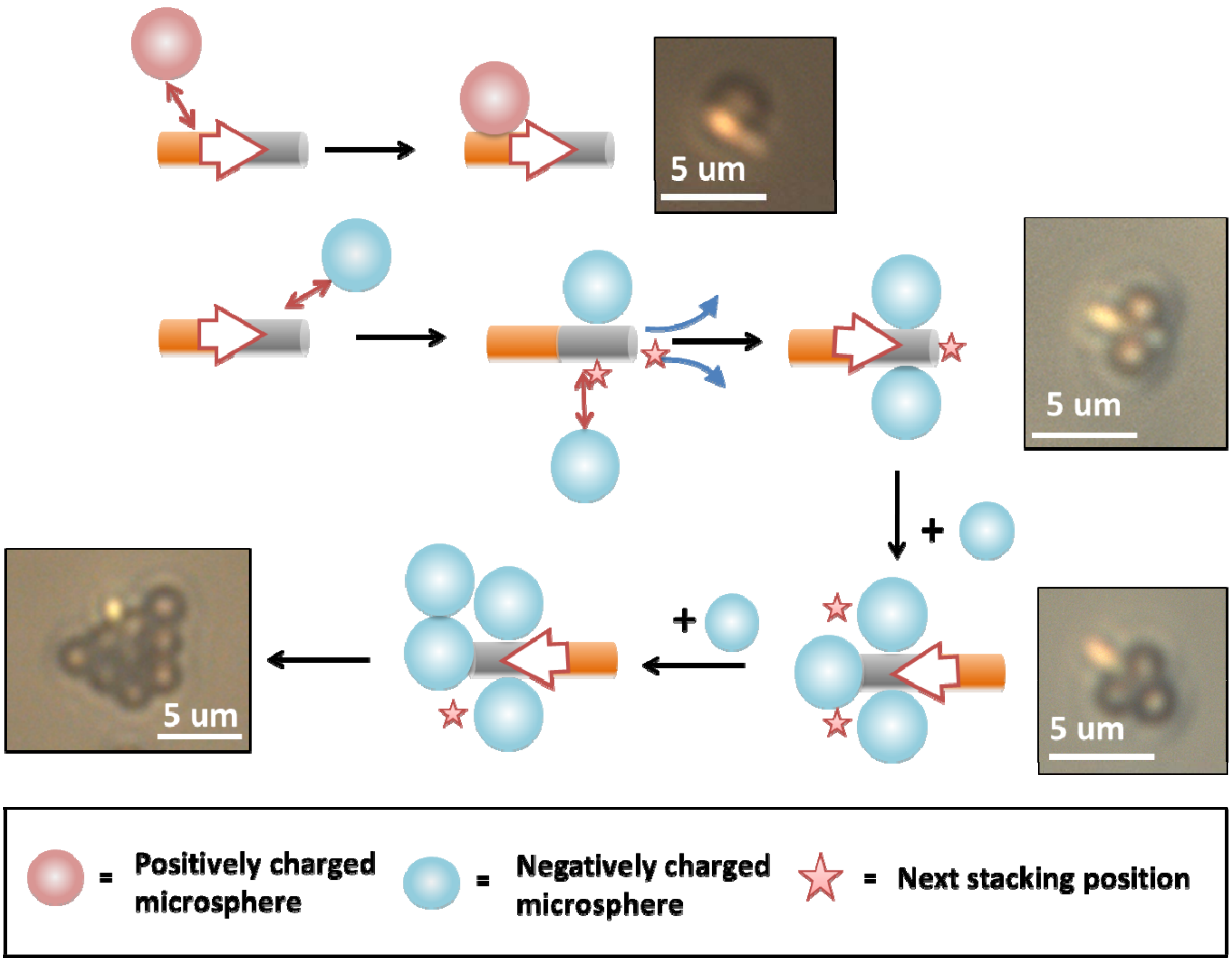
Tracking Analysis





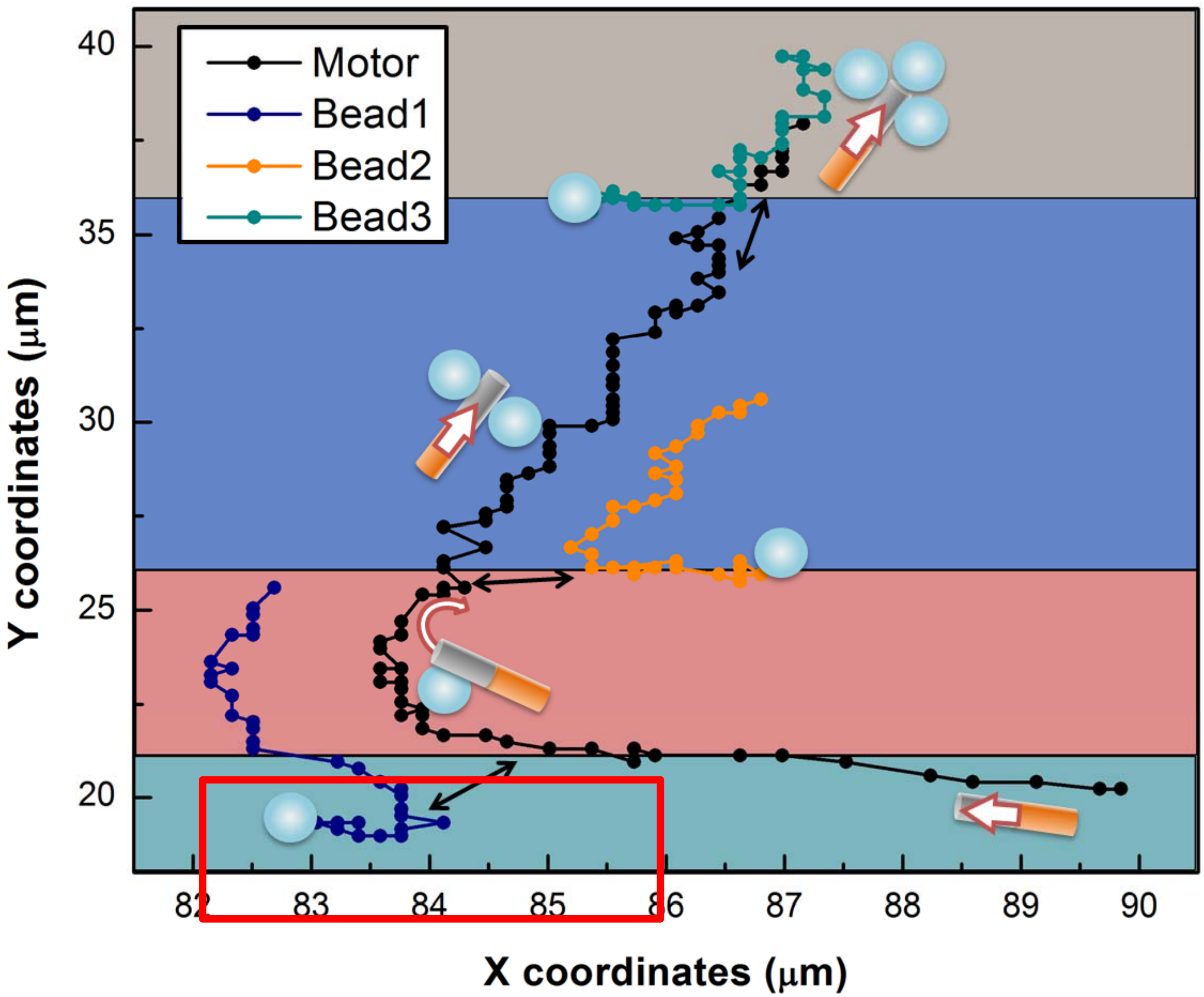


Dynamic Assembly of Charged Tracer Particles



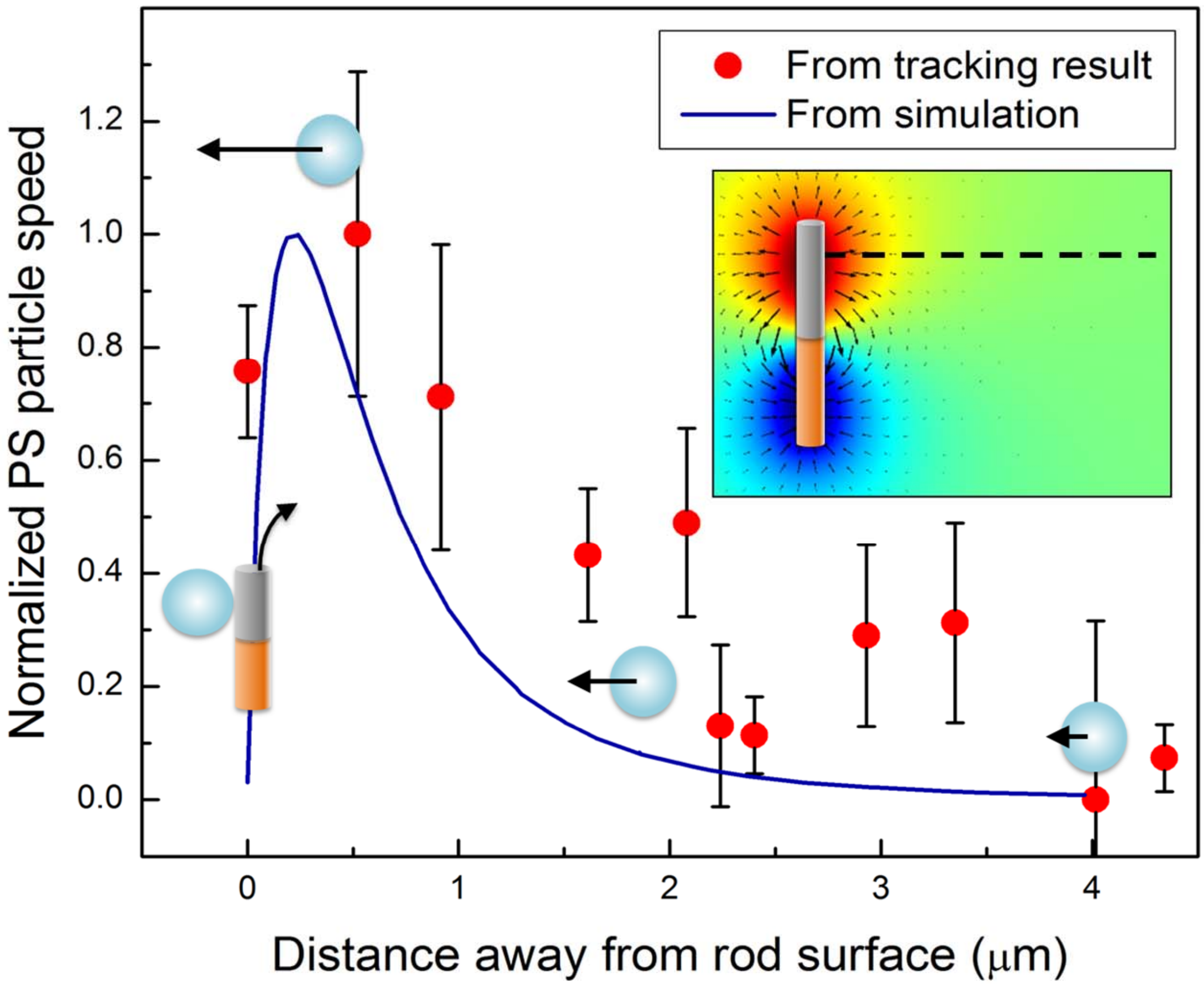
Dynamic Assembly of Charged Tracer Particles

Tracking Analysis



Mallouk, Sen, *PNAS*, 2013

Electrophoretic Migration of Particles



Mallouk, Sen, *PNAS*, 2013

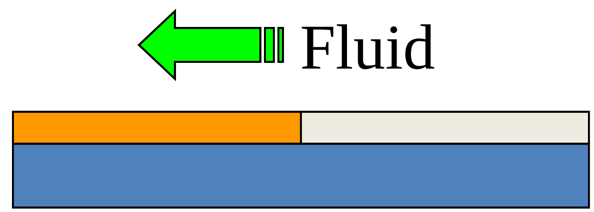
From Motors to Micropumps

Motor

Suspended motor moves itself

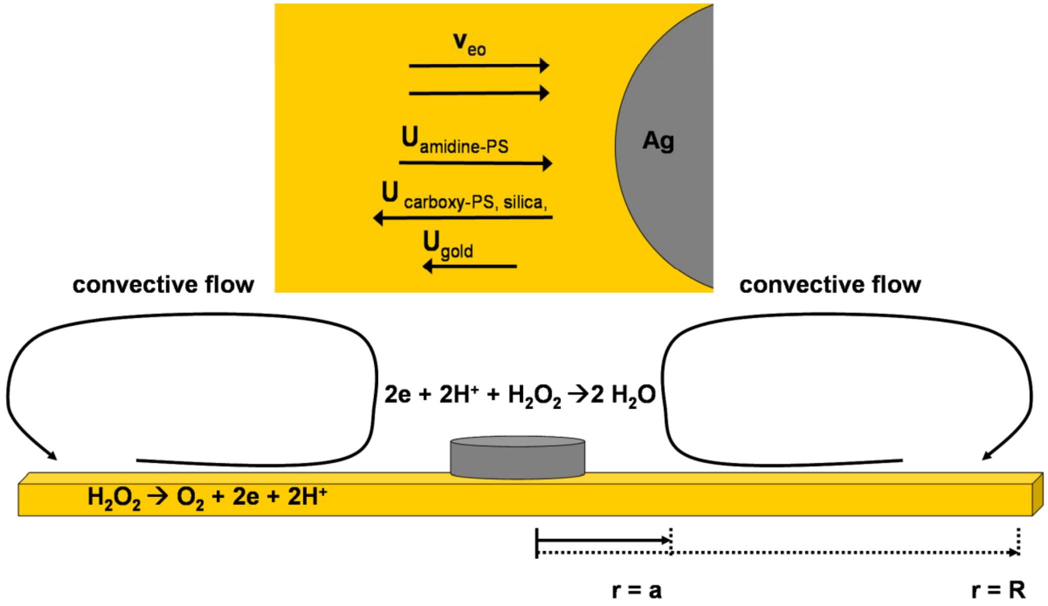
Micropump

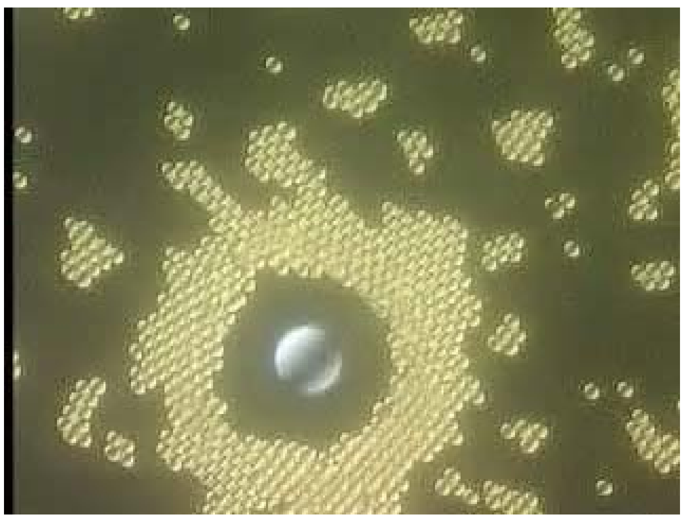
- Immobilized motor moves surrounding fluid
- Channel-free directed fluid flow



***J. Am. Chem. Soc.*, 2005, 2006**

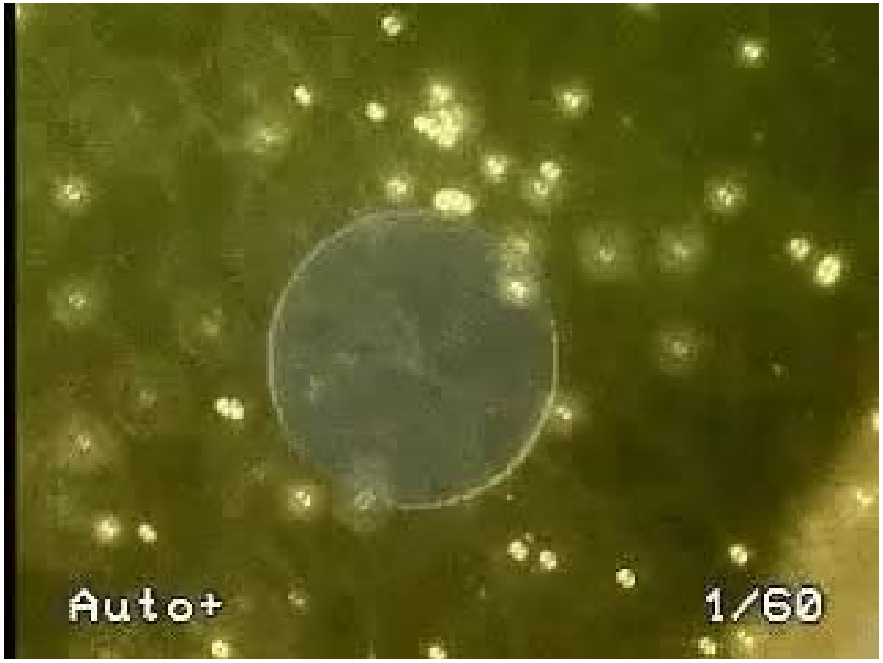
Catalytically Induced Fluidic Pumping





J. Am. Chem. Soc., 2005, 2006; *J. Phys. Chem. B.* 2006

Colloid Behavior as a Function of the Surface Charge



Real-time convective-motion of amidine terminated polystyrene (2 μm) spheres on Ag patterned gold surface at 500x

Real-time pattern formation of 1 μm polystyrene spheres on Ag patterned gold surface at 500x*

Why are polystyrene spheres of the same density behaving differently when only the colloid surface properties differ?

Quorum-Sensing Collective Behavior of Autonomous Nano/Microbots

- Bots secrete ions
- Electric field results from different diffusion rates of the cations vs. anions
- Bots move in response to the electric field
- Bots move cooperatively in response to neighbors’ ion gradients

AgCl System: *Angew. Chem.*, 2009; *ACS Nano*, 2010
TiO_2 System: *Adv. Func. Mat.*, 2010

Diffusiophoretic Motion of Particles

Triggered by a gradient of electrolyte concentration

Electrophoresis tends to dominate over Chemophoresis

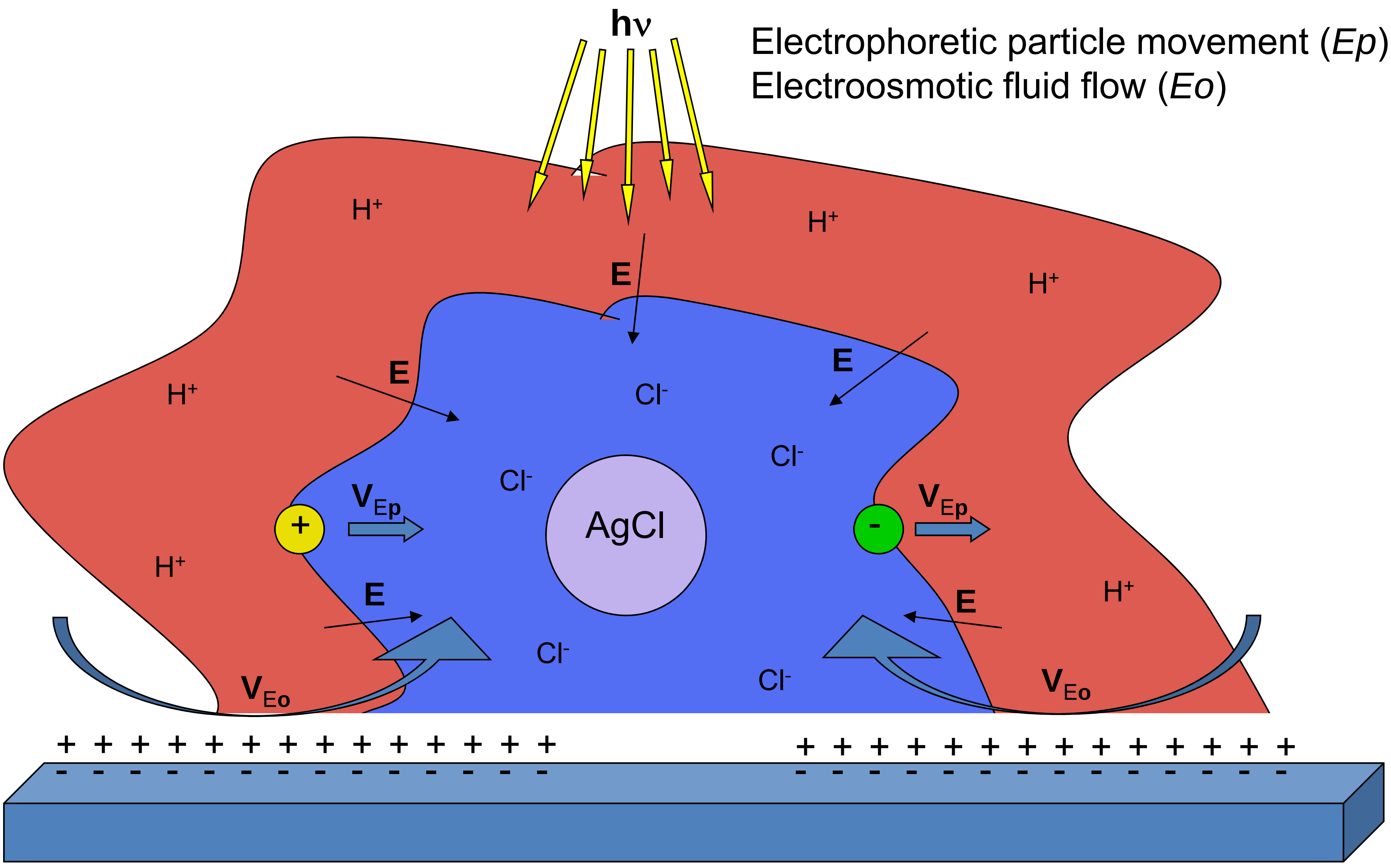
$$U = \underbrace{\left(\frac{dLn(C)}{dx}\right)\left(\frac{D_C - D_A}{D_C + D_A}\right)\left(\frac{k_B T}{e}\right)}_{\text{Electric Field}} \frac{\varepsilon\left(\zeta_p - \zeta_w\right)}{\eta}$$

$$+ \underbrace{\left(\frac{dLn(C)}{dx}\right)\left(\frac{2\varepsilon k_B^2 T^2}{\eta e^2}\right)\left\{Ln\left[1 - \tanh^2\left(\frac{e\zeta_W}{4k_B T}\right)\right] - Ln\left[1 - \tanh^2\left(\frac{e\zeta_P}{4k_B T}\right)\right]\right\}}_{\text{Chemophoretic Term}}$$

Speed proportional to ion gradient and charge on the particle

Under low Reynolds number conditions (*R*~10^{-5}), the mass and radius of the particle are *not* important

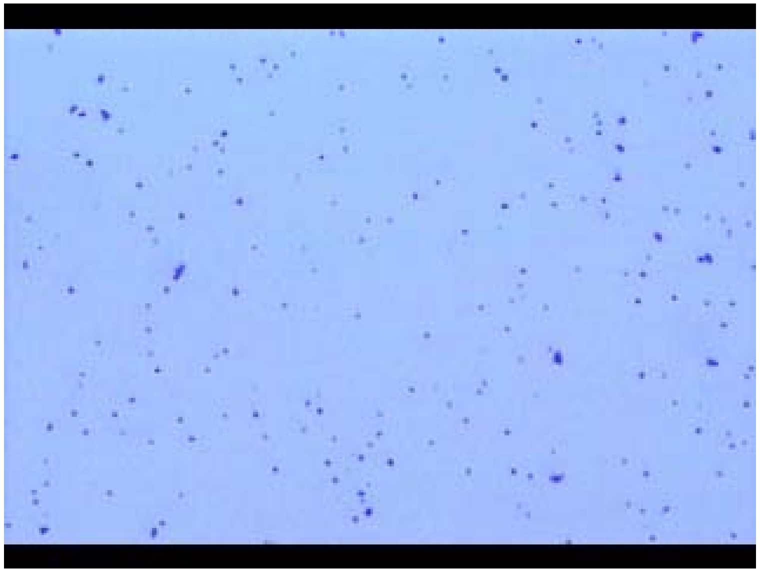
Photochemistry of Silver Chloride



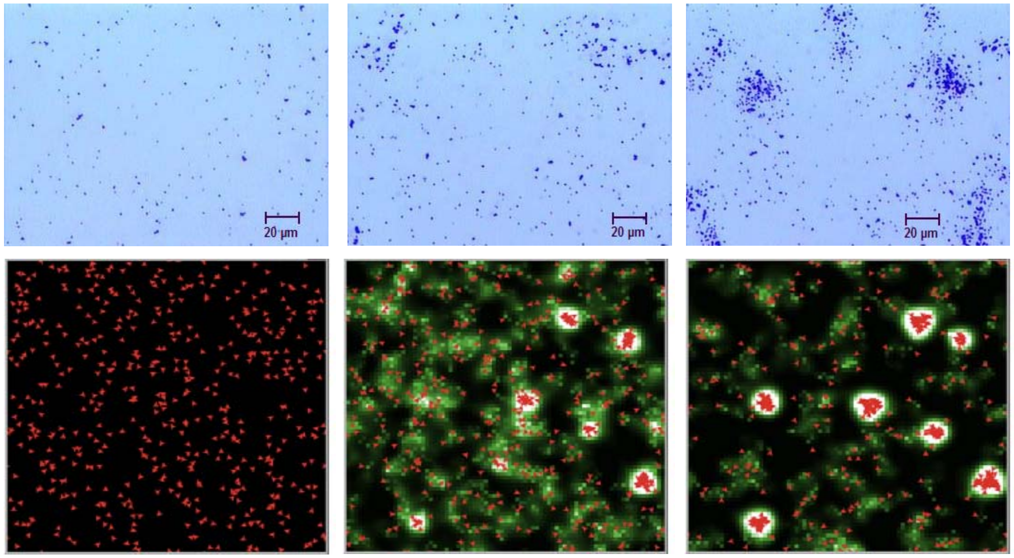
$$4\ AgCl + 2\ H_2O \xrightarrow{h\nu,\ Ag^+} 4\ Ag + 4\ H^+ + 4Cl^- + O_2$$

Emergent Collective Behavior

Through Communication via Chemical Signals



Silver chloride particles move when UV light is switched on. Large particle schools form within mins.



Comparison between schooling of silver chloride particles (top) and NetLogo model of slime mold behavior (bottom).
NetLogo: http://ccl.northwestern.edu/netlogo/models/Slime

***Angew. Chem.*, 2009; *Faraday Discuss*., 2009**

Also, N_2H_4-induced swarming of Au particles in 10% aq. H_2O_2: Wang, 2011

Change in concentration at a given lattice site with time:

$$\underbrace{C_{x,y}(t+\Delta t)}_{New\ Conc.} = \underbrace{(1-b)}_{Bulk\ Loss}\left\{ \underbrace{C_{x,y}(t)}_{Original\ Conc.} + \underbrace{an_{x,y}}_{Chemical\ Production} + \underbrace{D\left[C_{x+1,y}(t)+C_{x-1,y}(t)+C_{x,y+1}(t)+C_{x,y-1}(t)-4C_{x,y}(t)\right]}_{Diffusion} \right\}$$

Chemical gradient across a lattice site in x and y directions

$$\psi_x = C_{x+1,y}(t) - C_{x-1,y}(t)$$

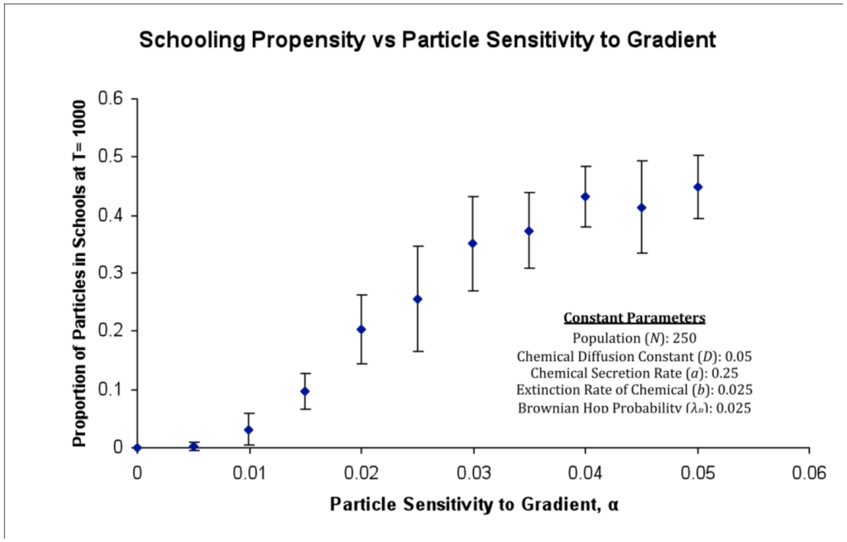
$$\psi_y = C_{x,y+1}(t) - C_{x,y-1}(t)$$

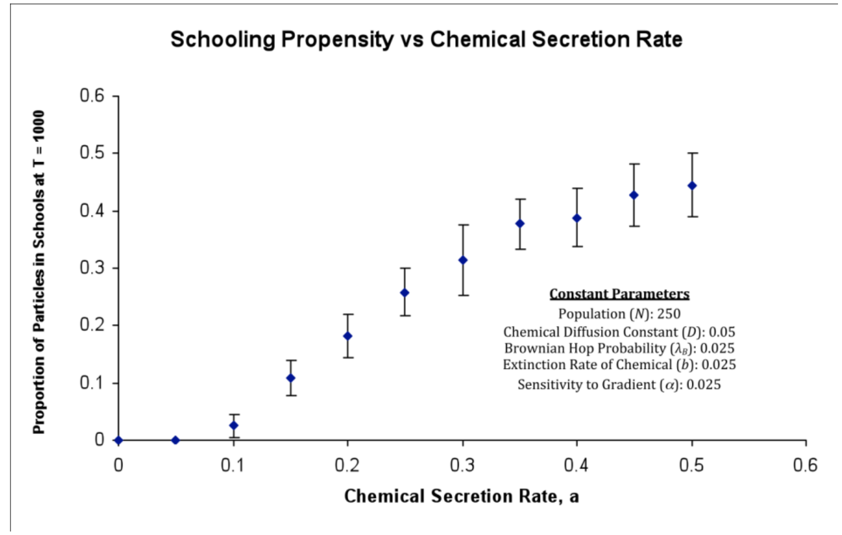
Probability of hopping in a given direction,
***in addition* to user-defined Brownian hop probability, λ_B**

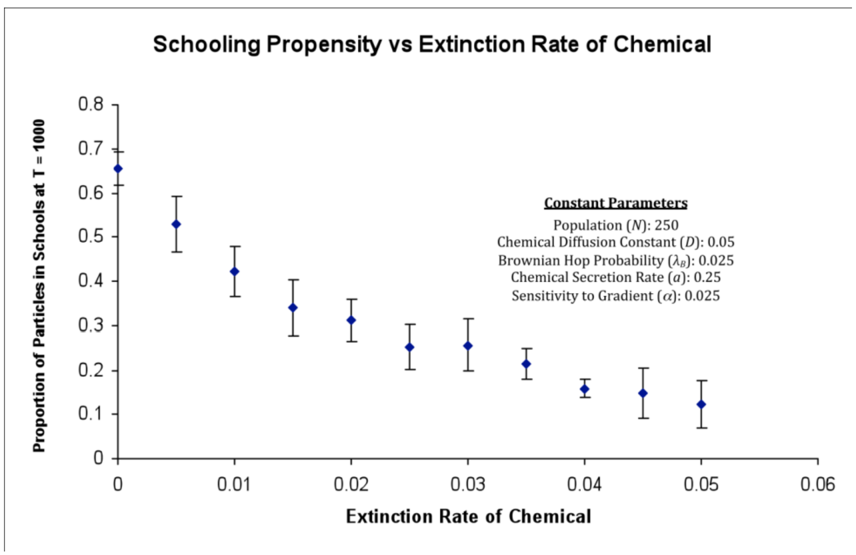
$$\lambda_x(t) = \alpha\left|\psi_x\right|$$

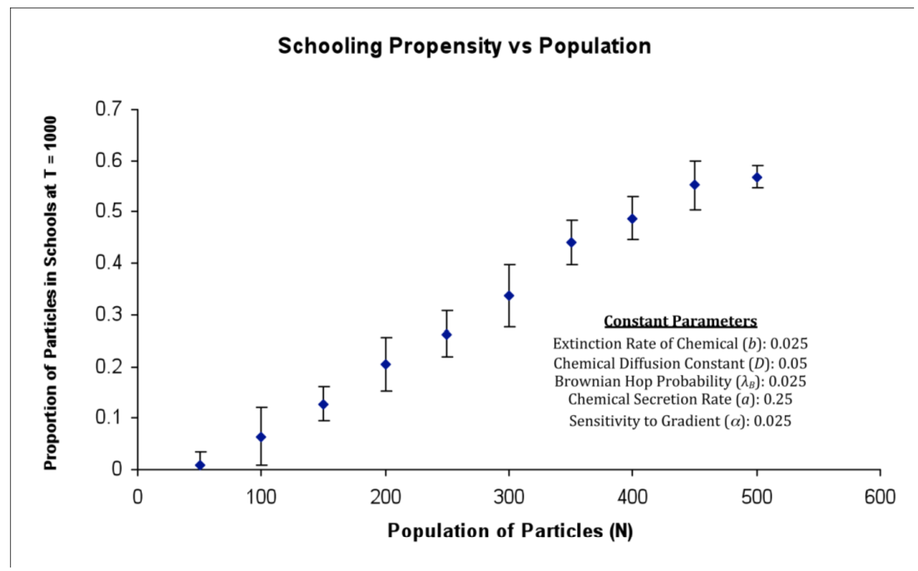
$$\lambda_y(t) = \alpha\left|\psi_y\right|$$

The modified NetLogo program was run for 1000 time steps with schooling defined as 4+ particles occupying a single lattice site



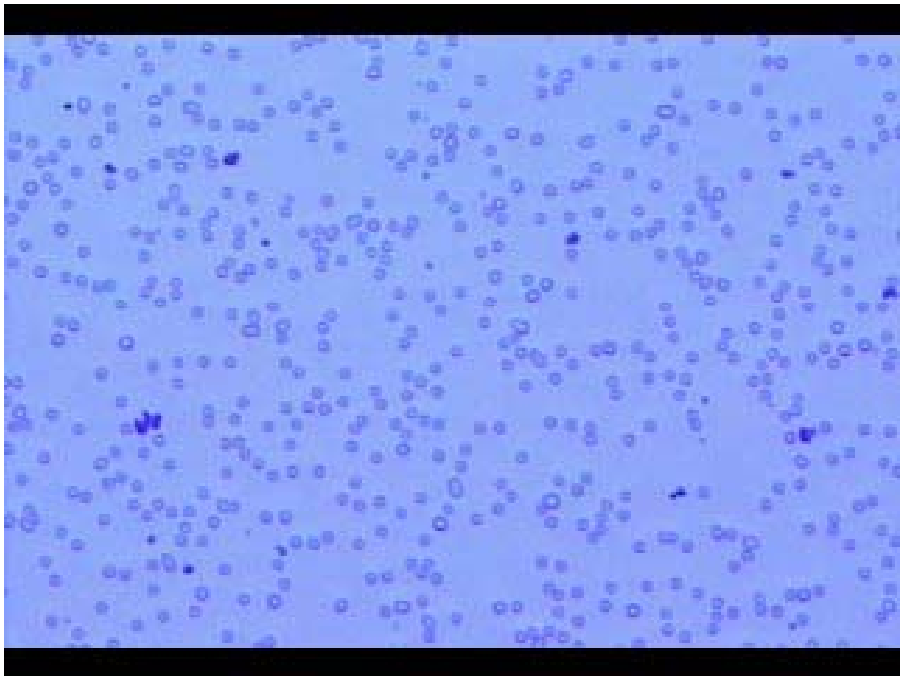






Faraday Discuss., 2009

Predator-Prey Behavior



Silver chloride particles (dark objects) with silica particles

***Angew. Chem.*, 2009**

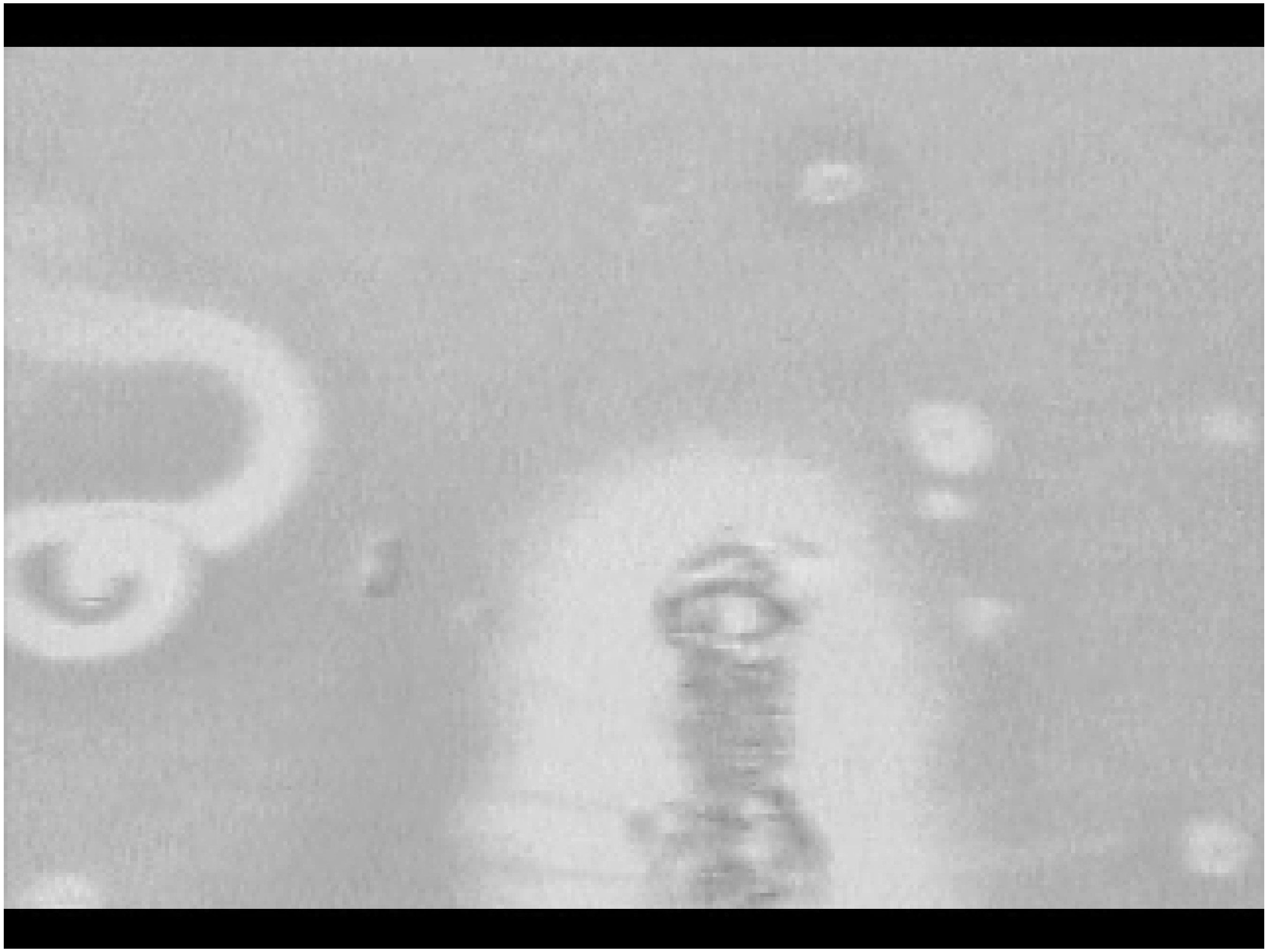
New Design Principles

❑ Two or more different particle types can move autonomously to organize themselves spatially

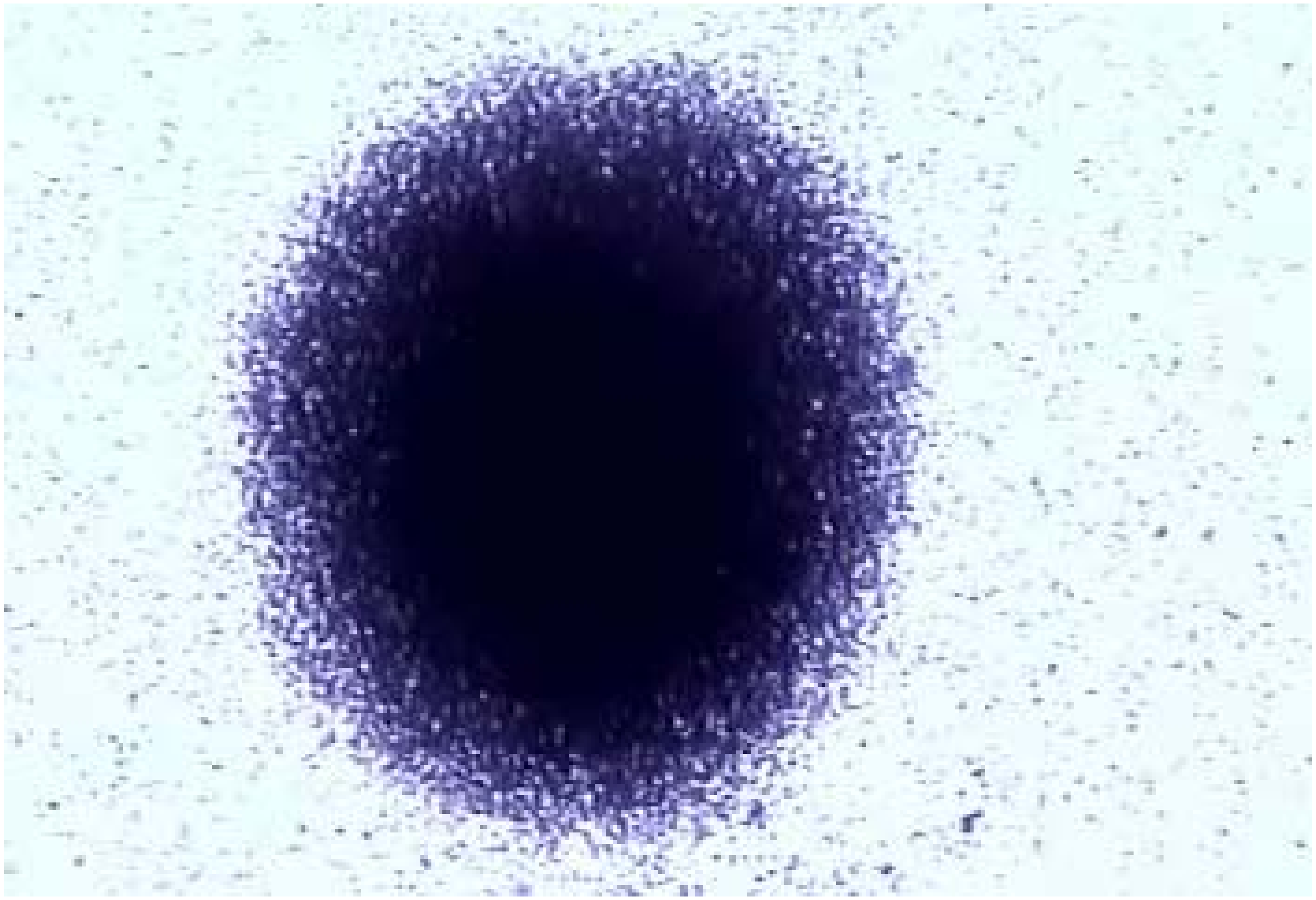
❑ Allows coordinated movement of dissimilar particles that are *not* attached to each other making it easier to transport and deliver cargo at designated area

❑ Particles with different functions can act collectively, simplifying design of intelligent assemblies

Shark Chasing a School of Fish



Reversible Spatio/Temporal Assemblies

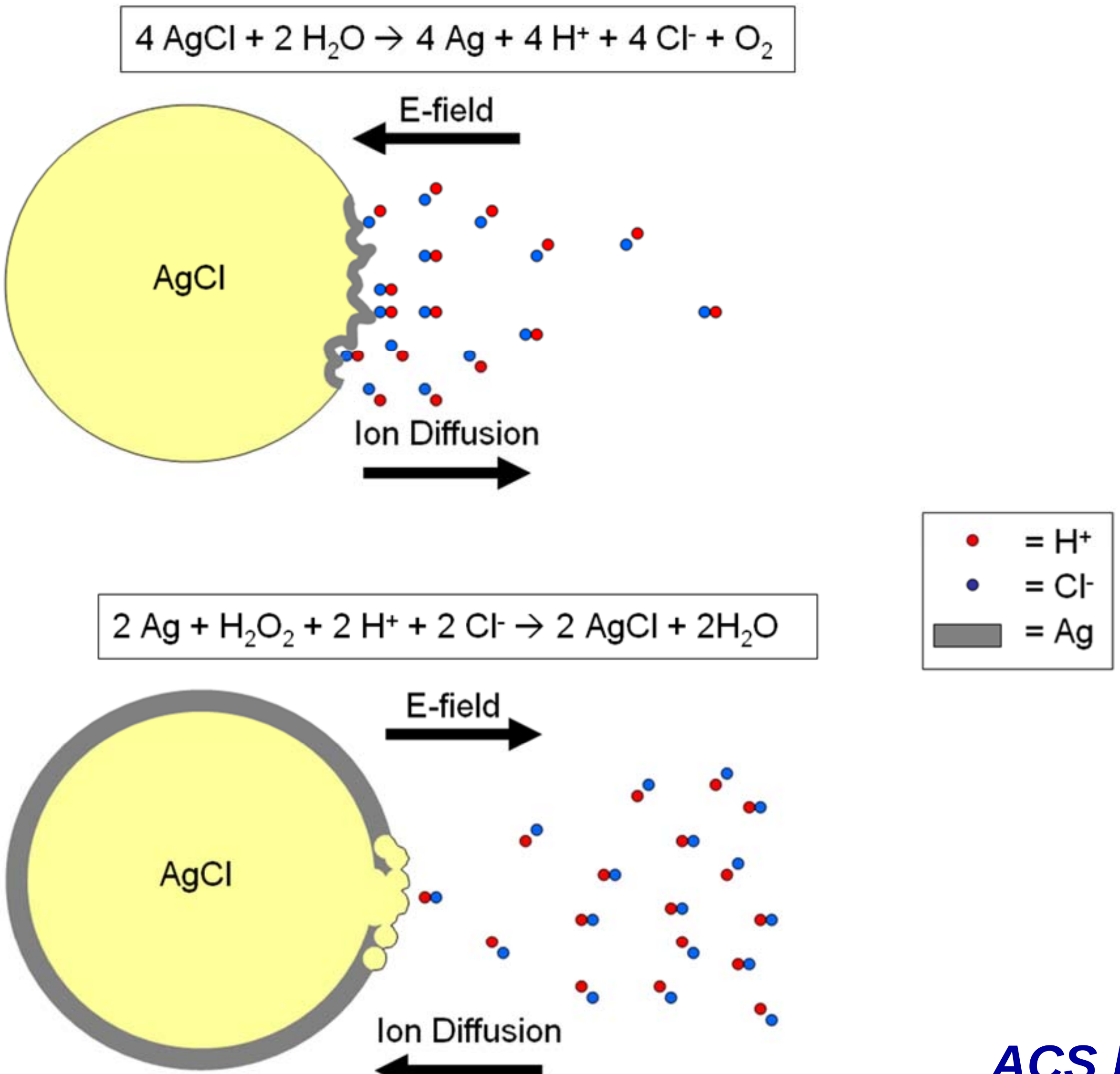


The UV light is alternately turned ON and OFF

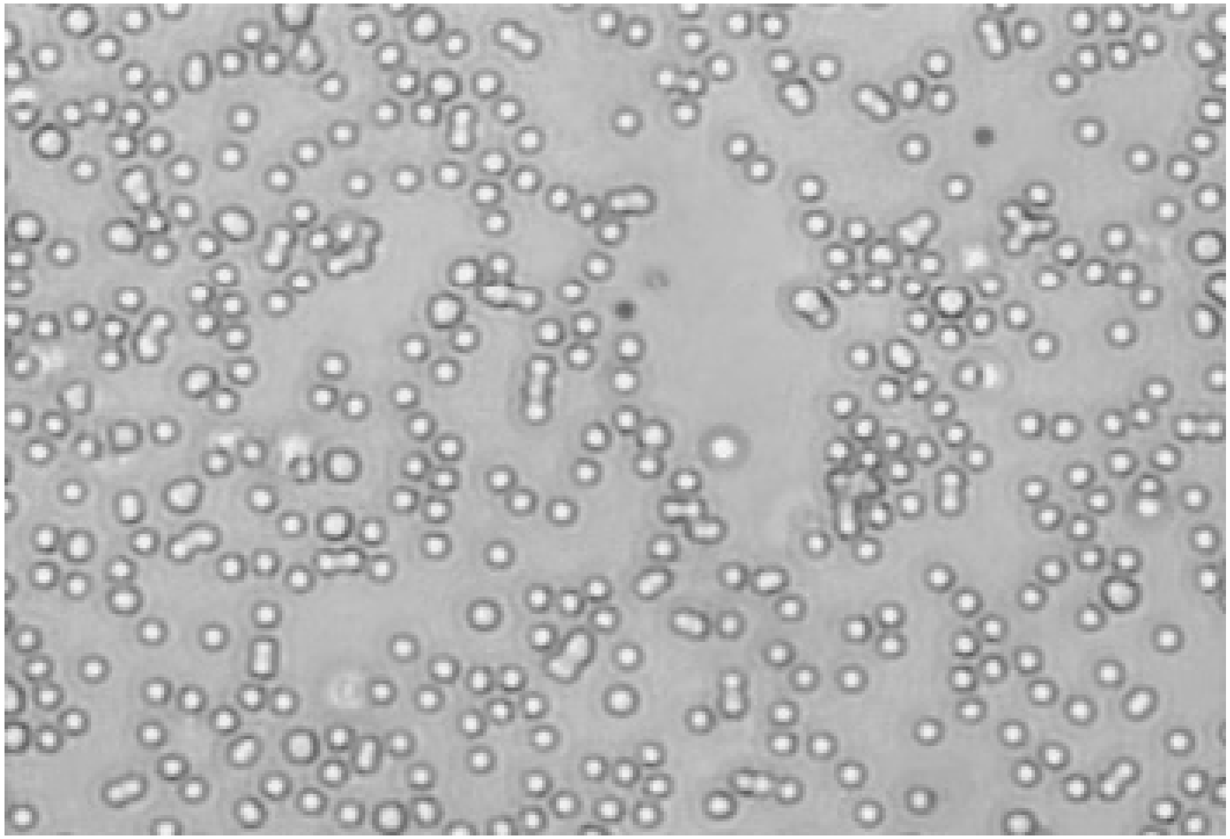
Real time video

***Angew. Chem.*, 2009**

Oscillatory Behavior and Emergent Synchronization of Particles Under Redox Conditions



***ACS Nano*, 2010**



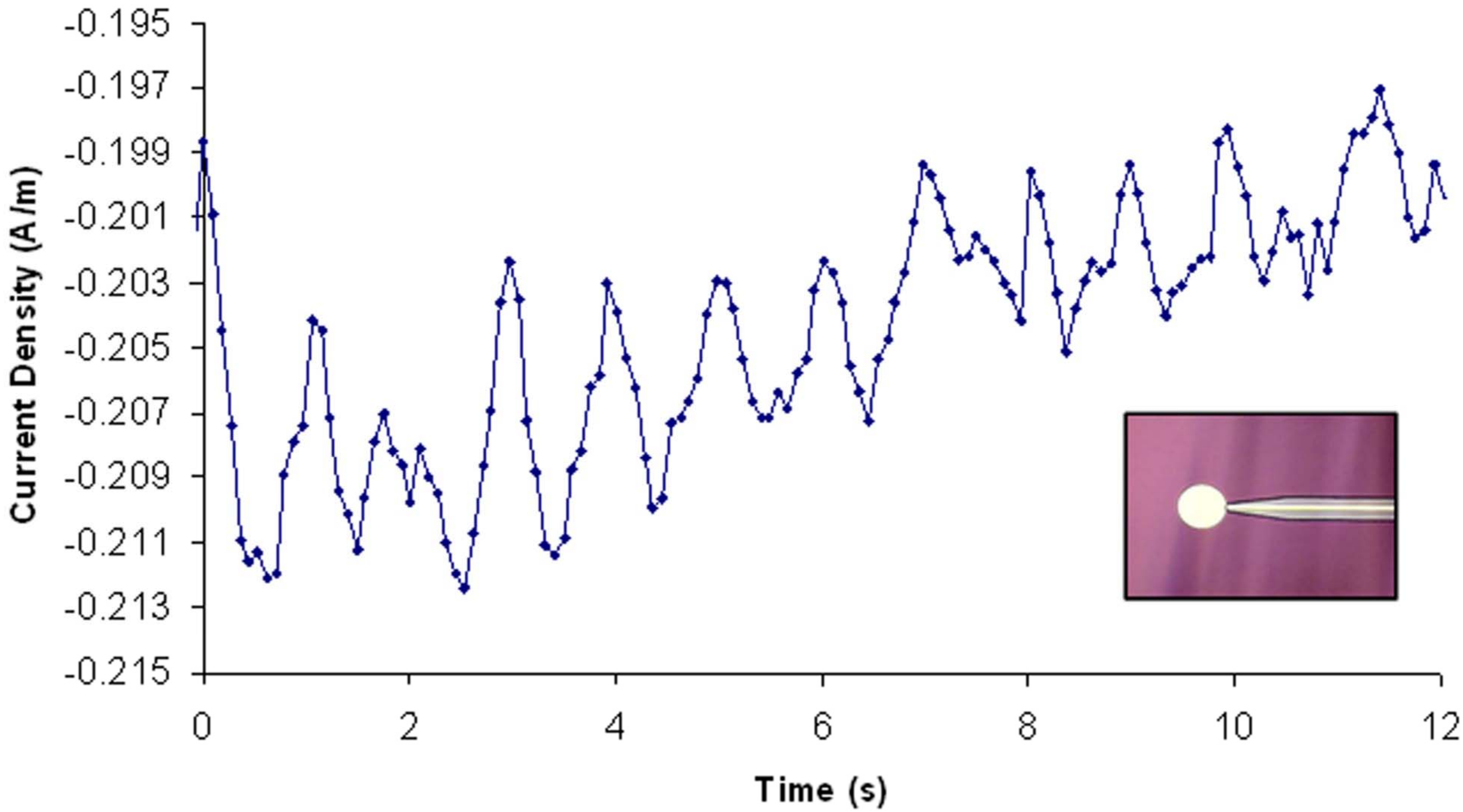
A solution containing AgCl particles (darker objects), silica tracer spheres (lighter objects), and 1% (v/V) H_2O_2 in water. The particles are illumined with UV light over a microscope slide. The AgCl particles are seen to move through solution, and alternately bind and release the silica tracer particles. The video is 194 μm in width. Movie plays in real-time.

***ACS Nano*, 2010**

Real-time video
(30 fps)

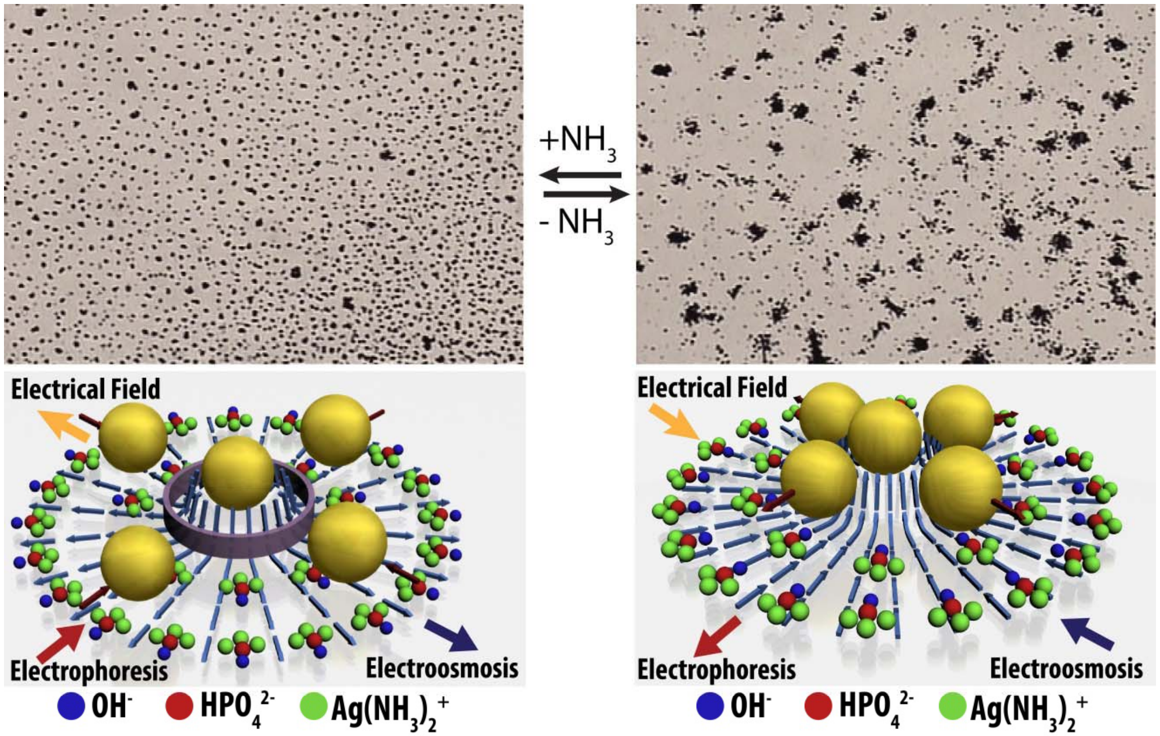
A UV-illuminated aqueous solution containing 2.3 μm silica tracer particles, 0.33 mM HCl, and 0.17% (v/V) H_2O_2 is imaged above an array of 9 μm diameter silver disks with 11 μm spacings.

As a traveling wave of tracer particle motion passes the array, the disks appear to flash on and off as their color alternates between reflective silver and darkened AgCl.



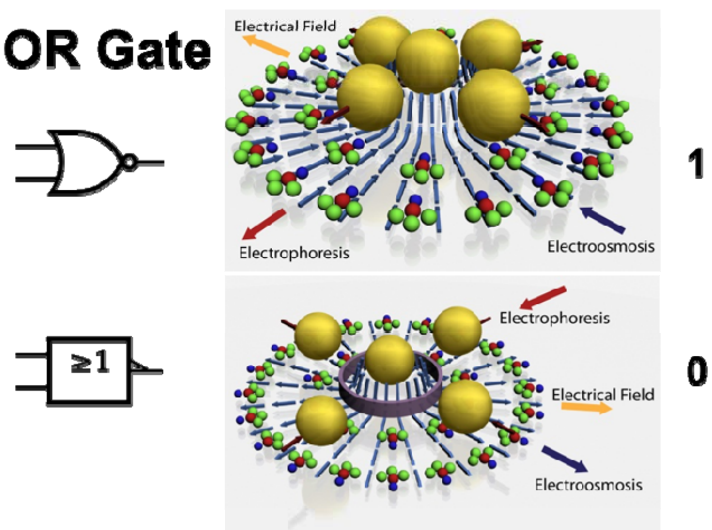
Current from a 90 µm silver disk patterned on a SiO_2 wafer in the presence of 0.17% (v/V) H_2O_2, 0.17 mM HCl and silica tracer spheres, under UV illumination. After a few seconds of illumination, current oscillations are recorded which match the oscillations of tracer particles. Negative currents are oxidative with respect to the silver surface. **Inset**, the 90 µm diameter silver disk connected to an insulated silver wire that monitored the reaction current on the disk surface.

Transition between Collective Behaviors of Micromotors in Response to Different Stimuli



***J. Am. Chem. Soc.*, 2013**

NOR Gate

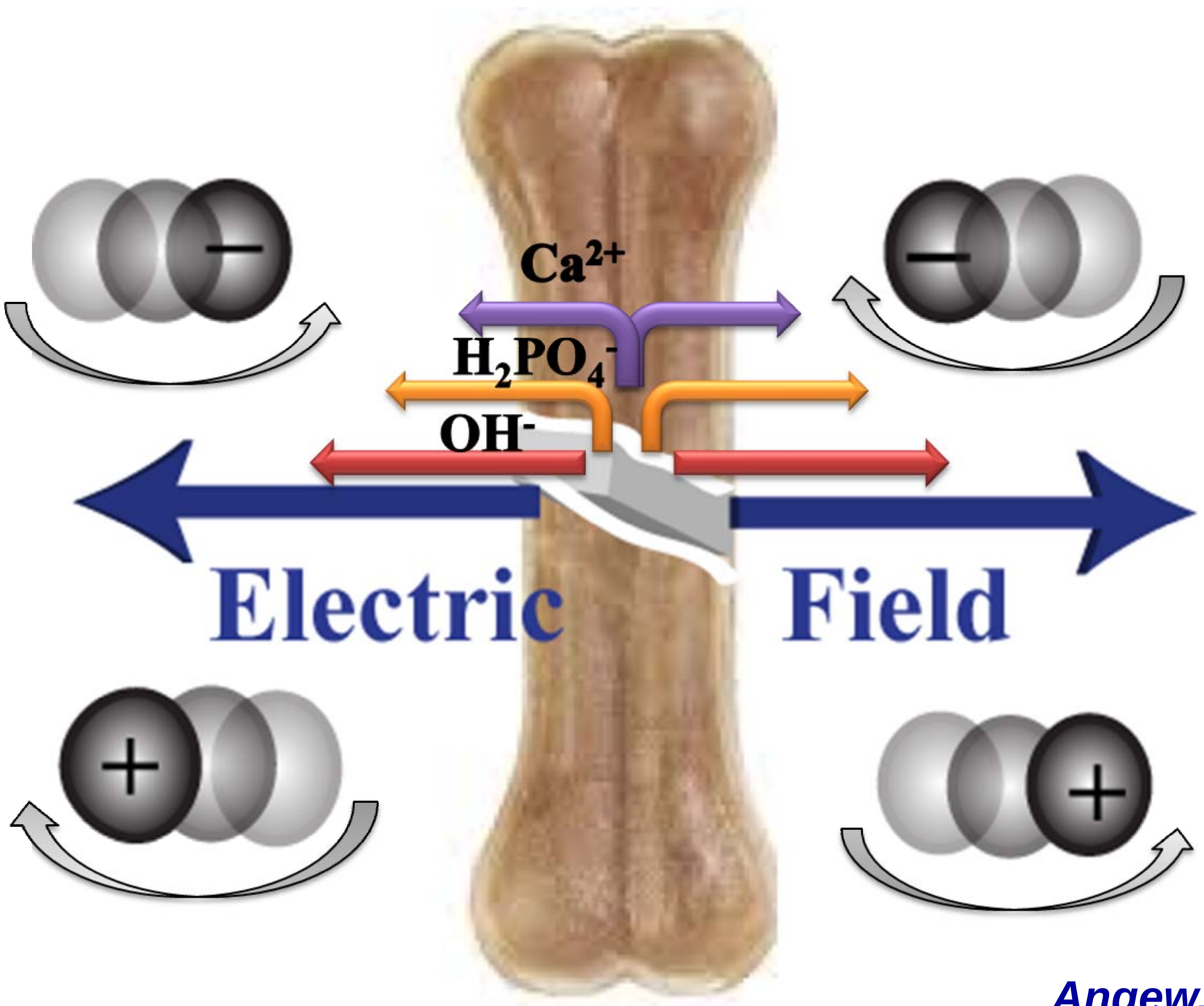


A=UV B=NH_3

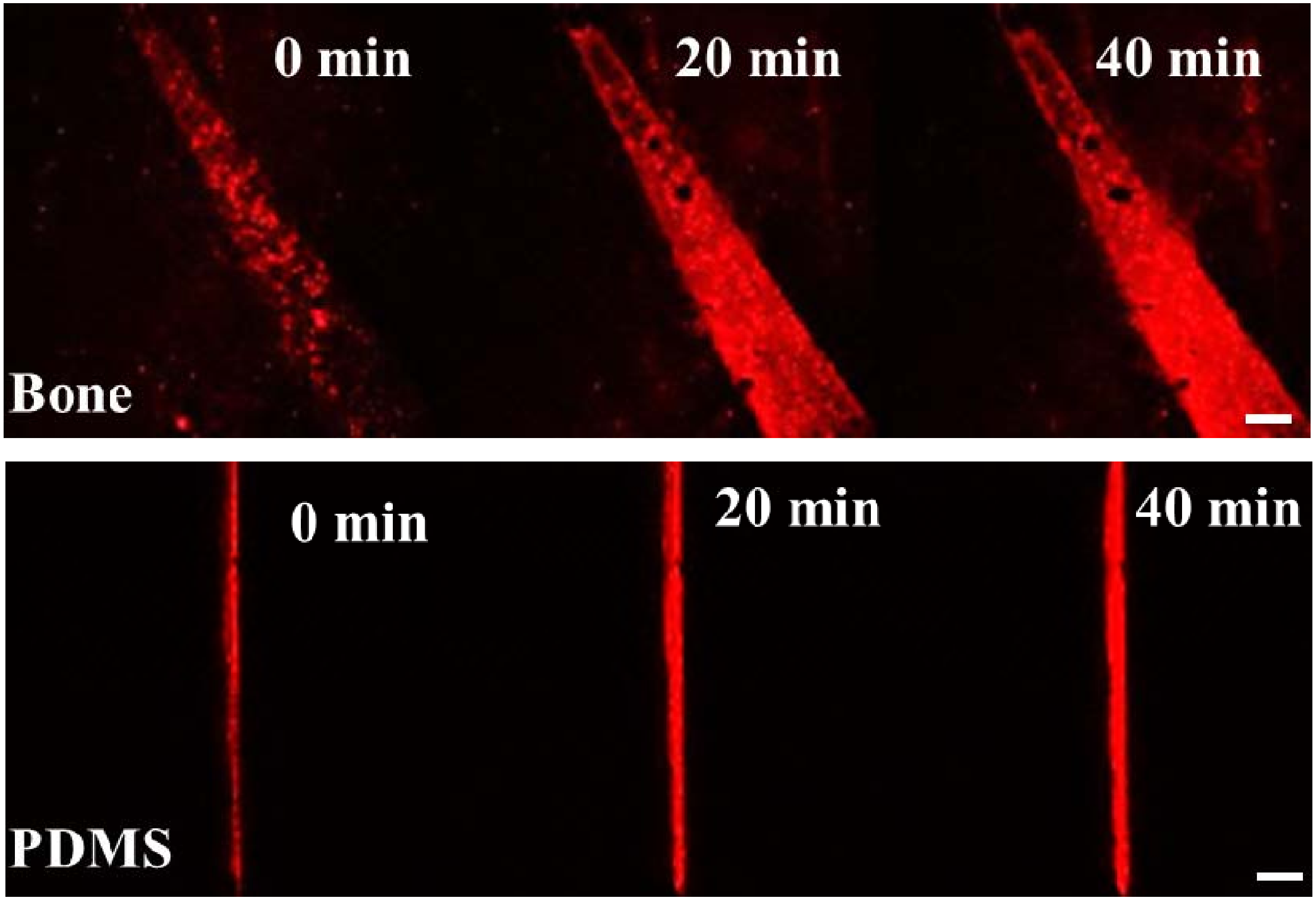
INPUT		OUTPUT
A	B	A NOR B
0	0	1
0	1	0
1	0	0
1	1	0

NOR Gate with UV and ammonia as inputs, collective behaviors as outputs: “schooling” and “exclusion” behaviors as 1 and 0, respectively.

Bone-Crack Detection, Targeting and Repair Using Ion Gradients



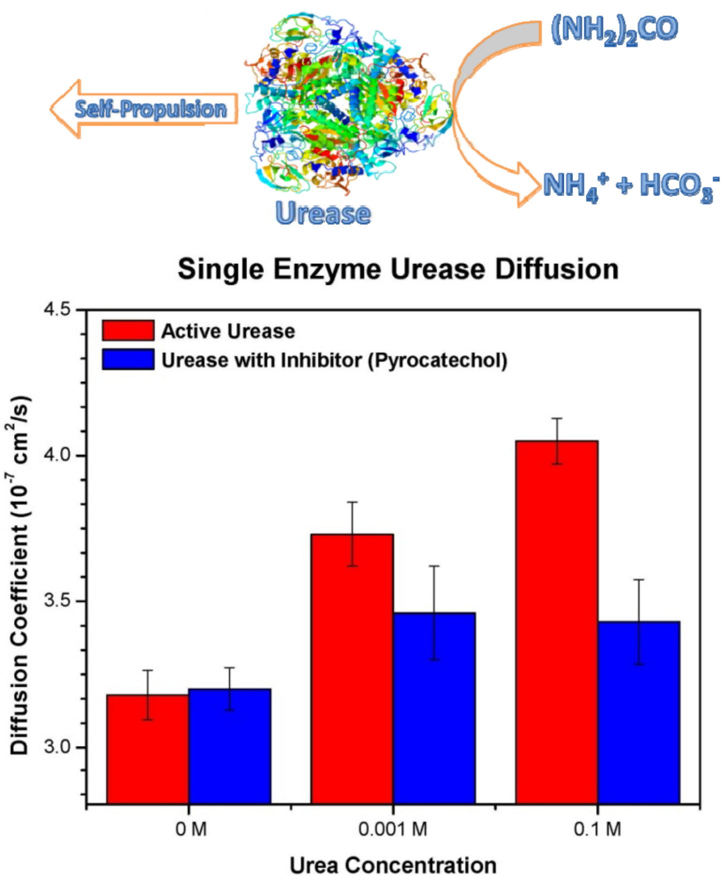
Angew. Chem., 2013

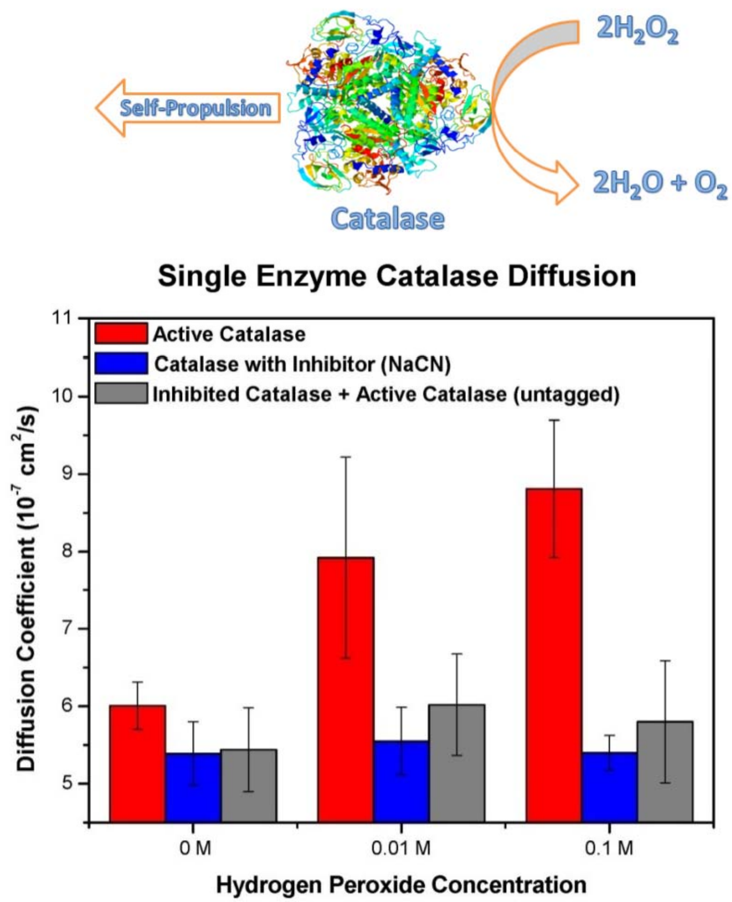


Increasing quantum dot intensity within the crack on bone surface (top) and PDMS surface (bottom) demonstrating an effective damage detection scheme. Scale bar is 60 µm.

Scaling Down to Single Molecules

Substrate Catalysis Enhances *Single* Enzyme Diffusion



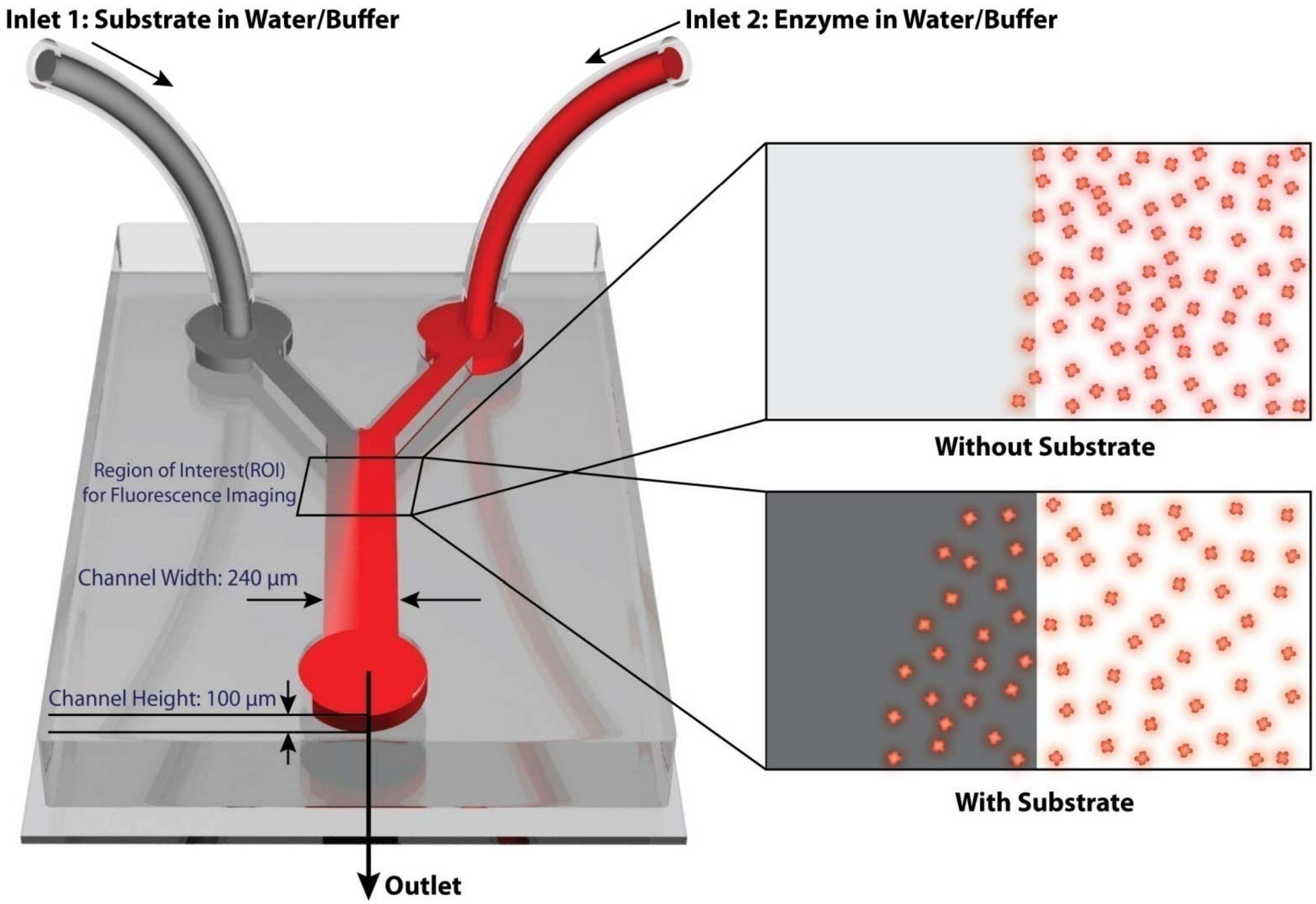


Diffusion of urease increases with increasing substrate concentration

Diffusion of catalase increases with increasing substrate concentration

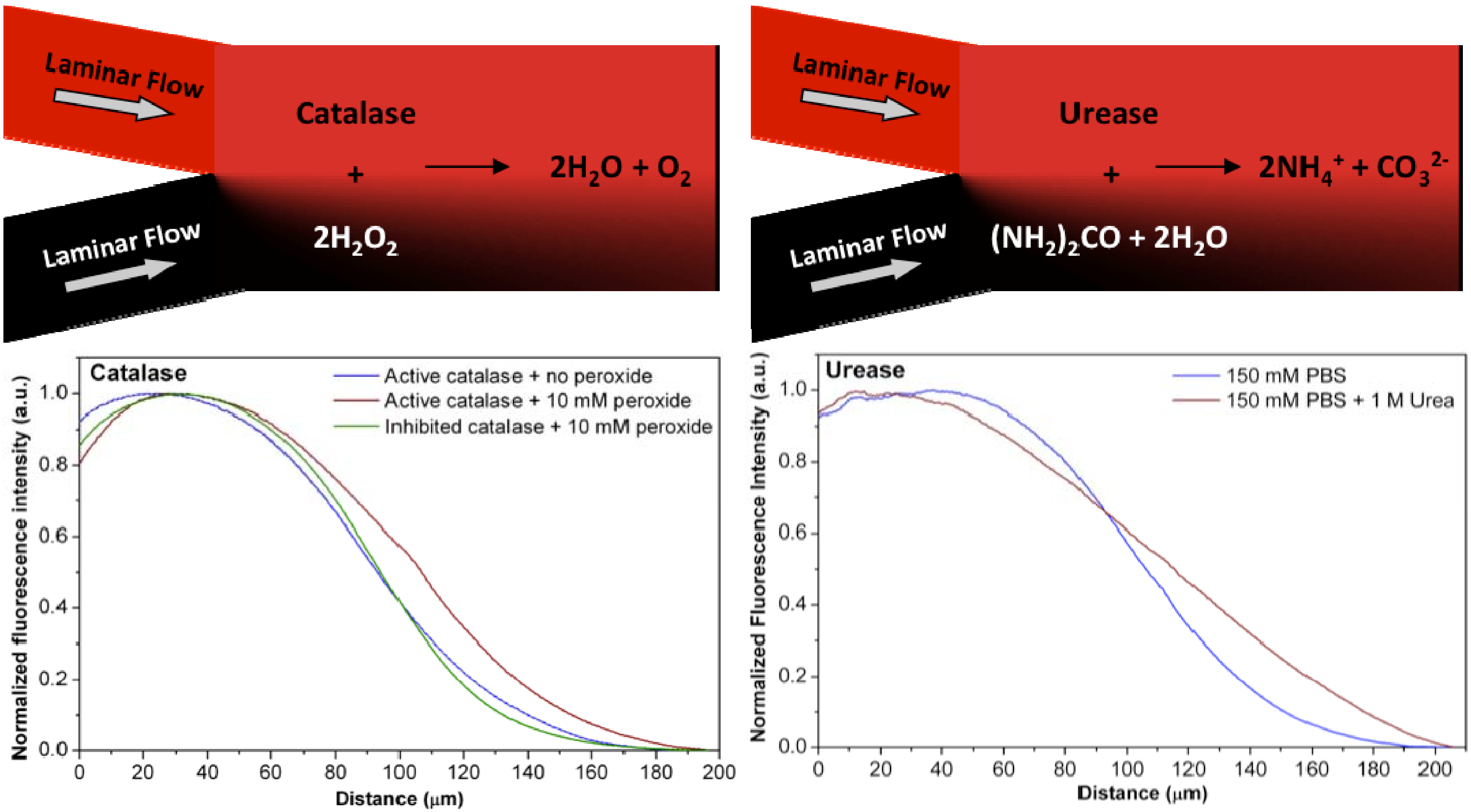
Butler and Sen, *J. Am. Chem. Soc.*, 2010, 2013
Also: Schwartz et al., 2009

“Chemotaxis” of Enzyme Molecules



A Y-shaped microfluidic device generates a gradient in the concentration of substrate, the fuel for an enzyme

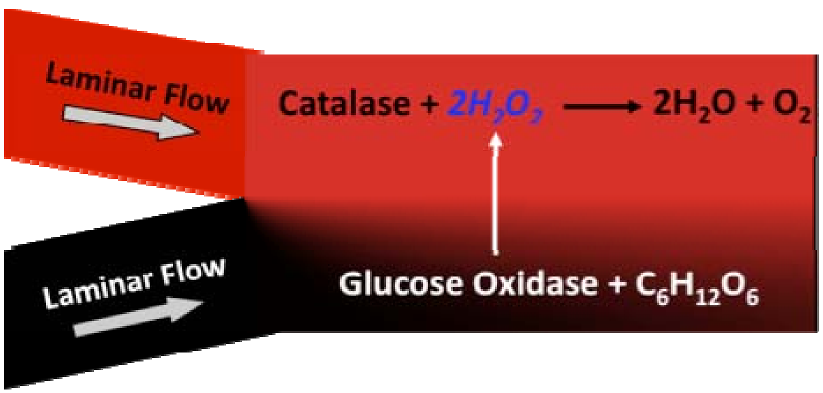
Chemotaxis of Single Enzyme Molecules

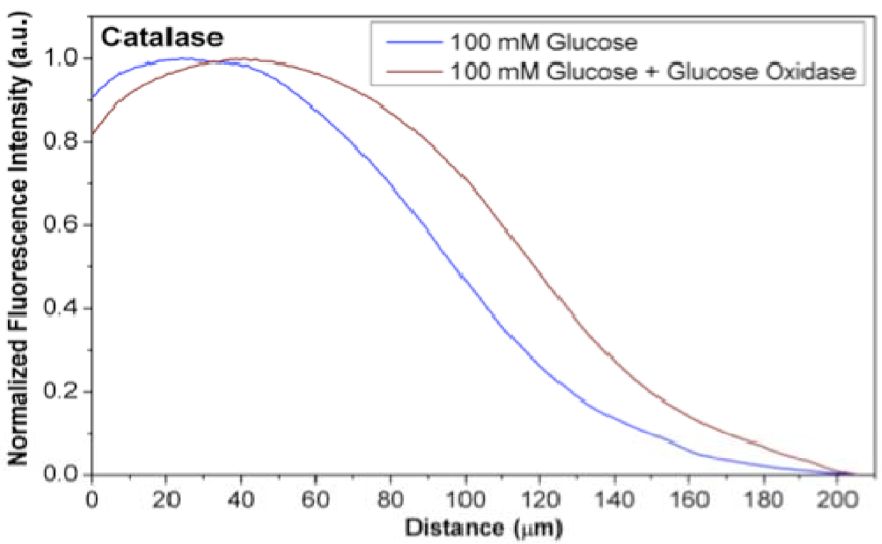


***J. Am. Chem. Soc.*, 2013**

Directed Movement of Catalase towards Glucose Oxidase

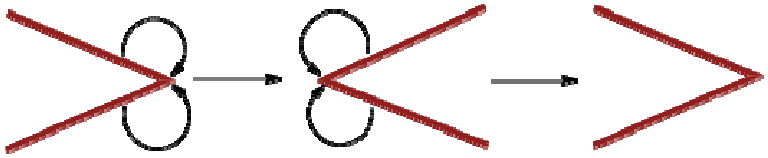
Engineering Cooperativity at the Single Molecule Level



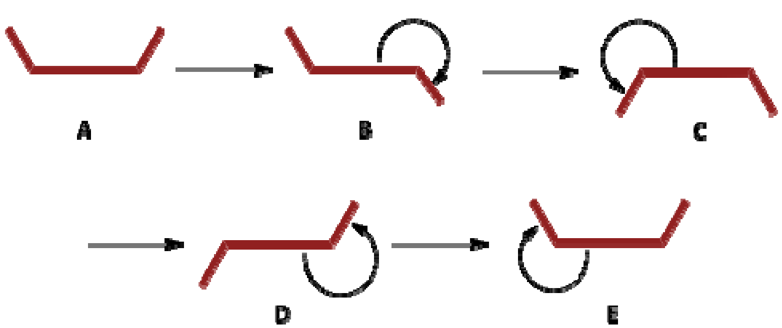


***J. Am. Chem. Soc.*, 2013**

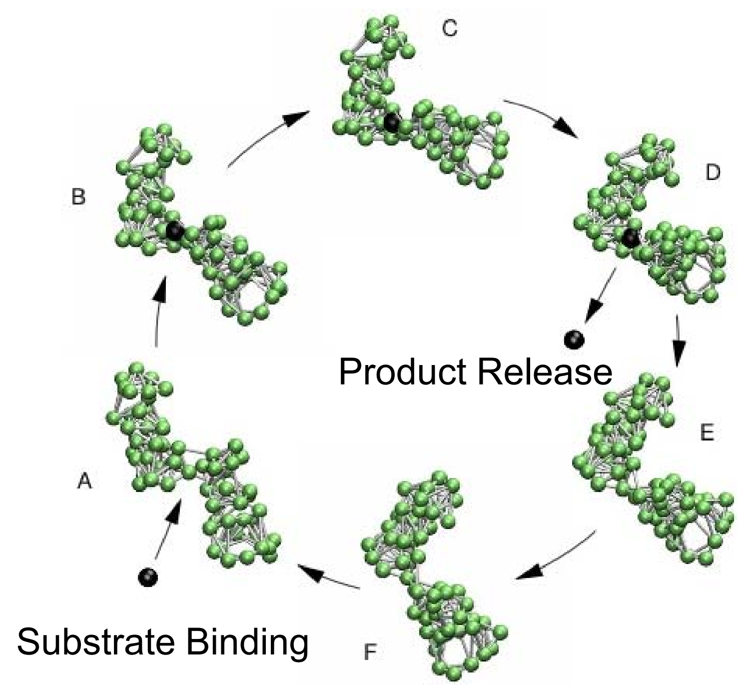
Applicability of the Scallop Theorem



At low Reynolds number propulsion by time-reversible reciprocal motion not possible? (Scallop Theorem)

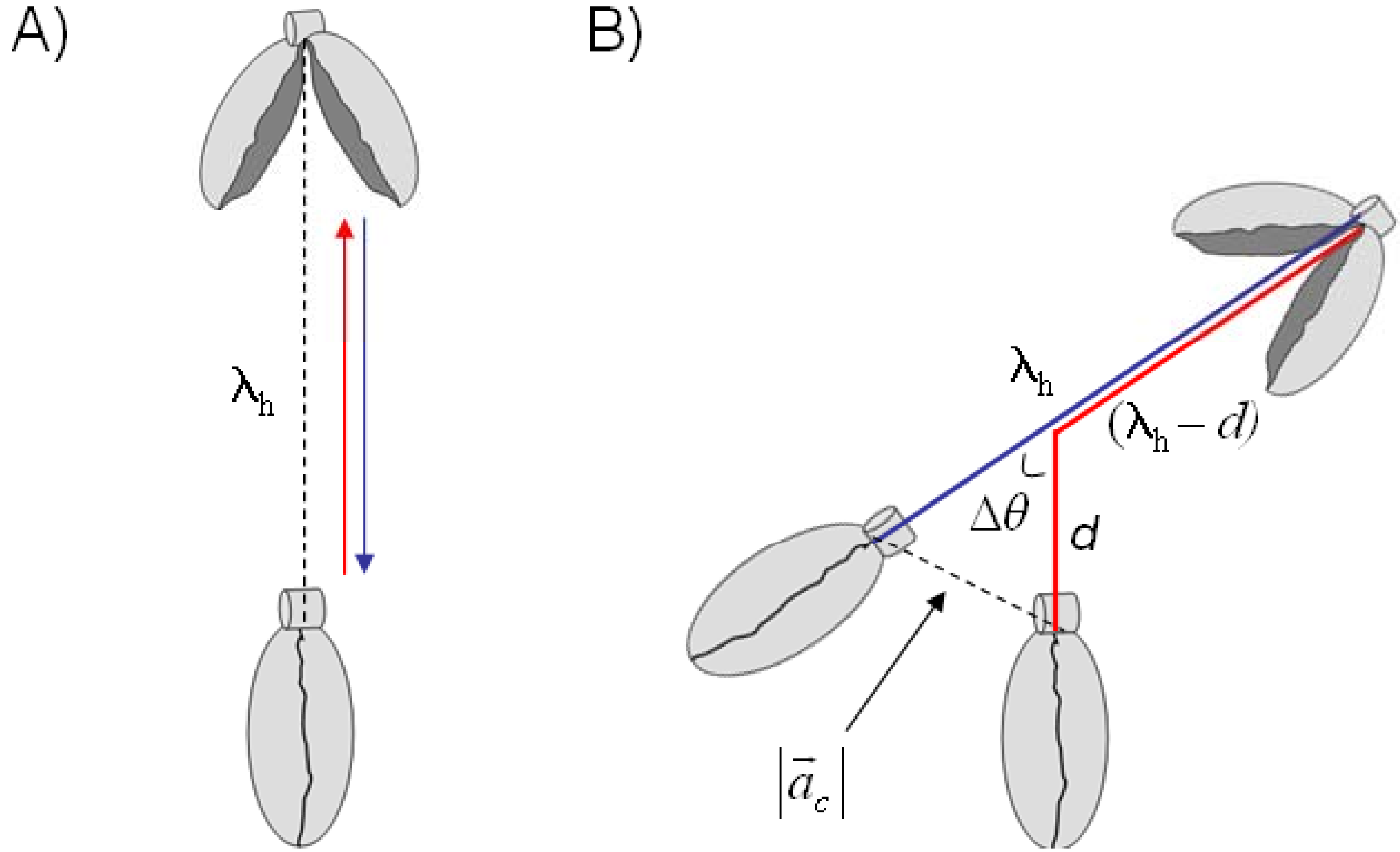


At low Reynolds number propulsion by non-reciprocal motion can be achieved.



Non-reciprocal conformational changes in a model enzyme

Kapral, Mikhailov, *Eur. Phys. J. B*, 2010
Golestanian, *Phys. Rev. Lett.*, 2010



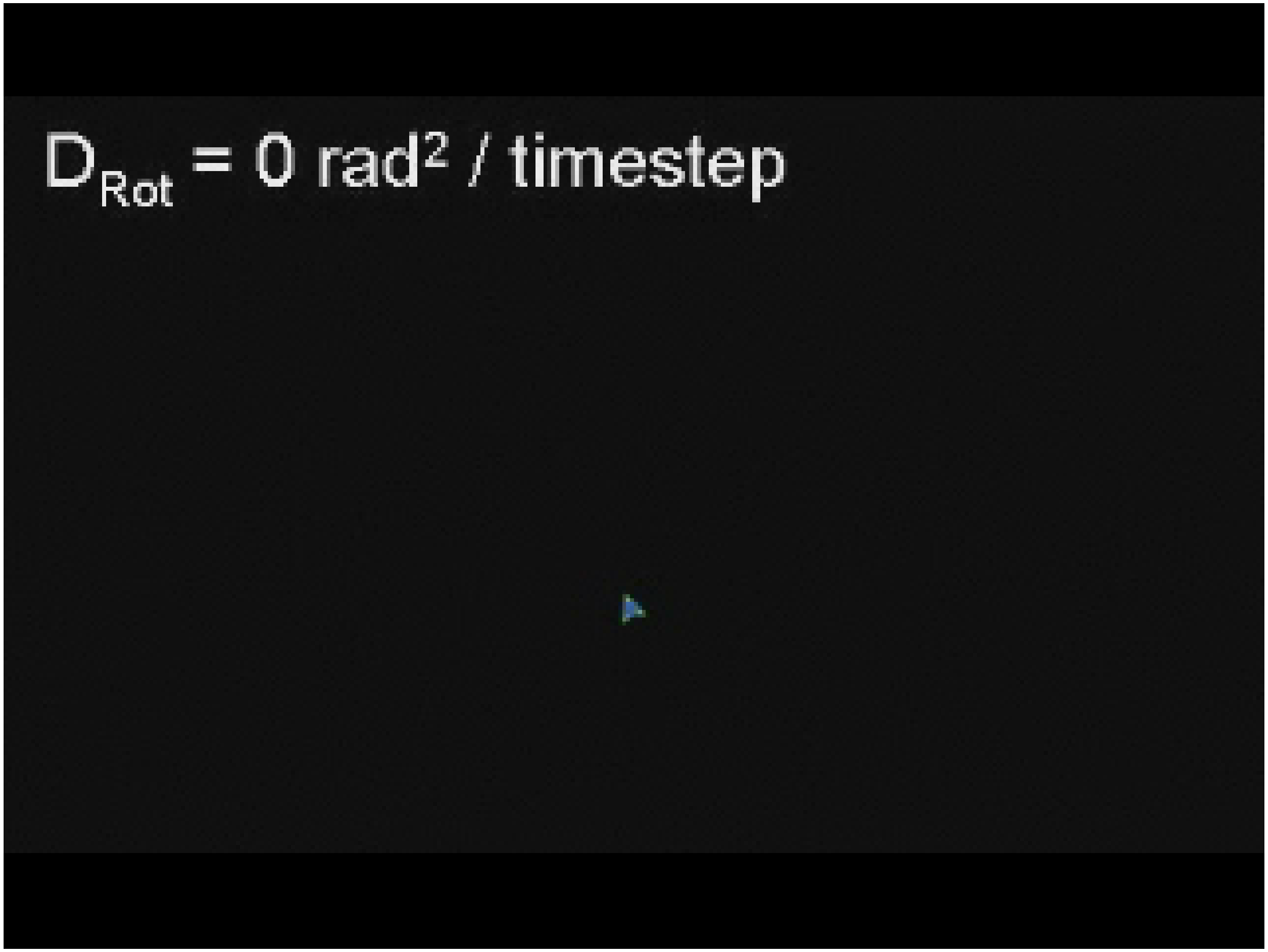
A) The reciprocal swim cycle of an unperturbed scallop opening and closing its shell.

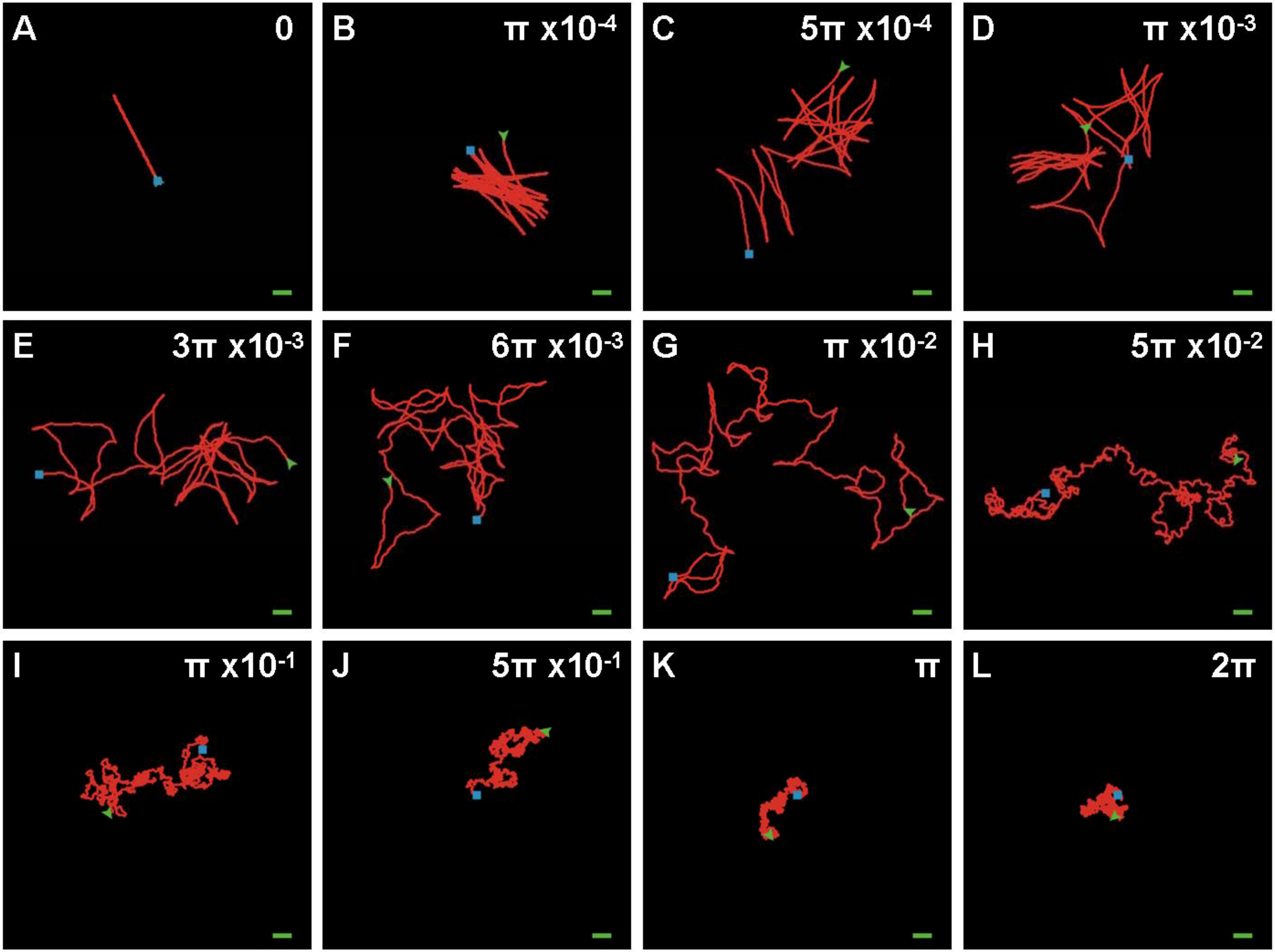
B) The motion path of a similar swimmer which undergoes a single rotation *after* it has traveled a distance (*d*) into its cycle.

The *forward* paths are shown in red,
the *return* paths are shown in blue.

Also, Lauga, *PRL*, 2011

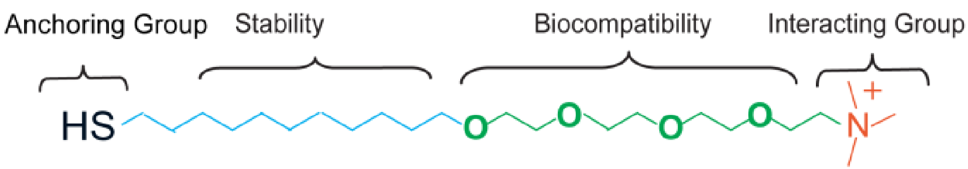
Video showing the reciprocal motion of twelve simulated reciprocal swimmers, each with different ***D_{Rot}* values. Swimmers are shown sequentially with increasing *D_{Rot}* values, which are listed for each motor in the video.***



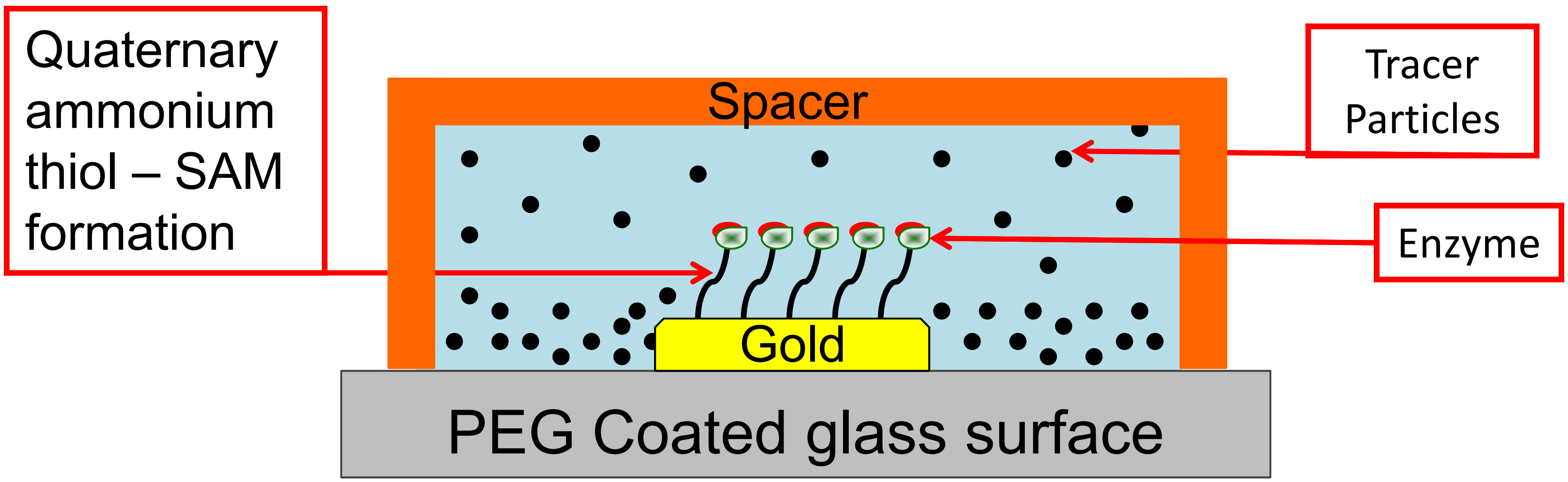


A
0
B
π x10-4
C
5π x10-4
D
π x10-3
E
3π x10-3
F
6π x10-3
G
π x10-2
H
5π x10-2
I
π x10-1
J
5π x10-1
K
π
L
2π

Enzyme-Powered Pumps



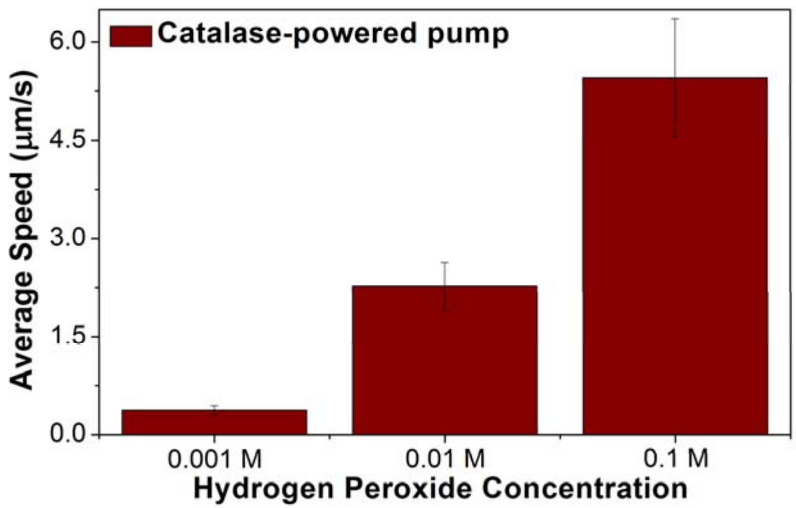
Quaternary ammonium thiol linker



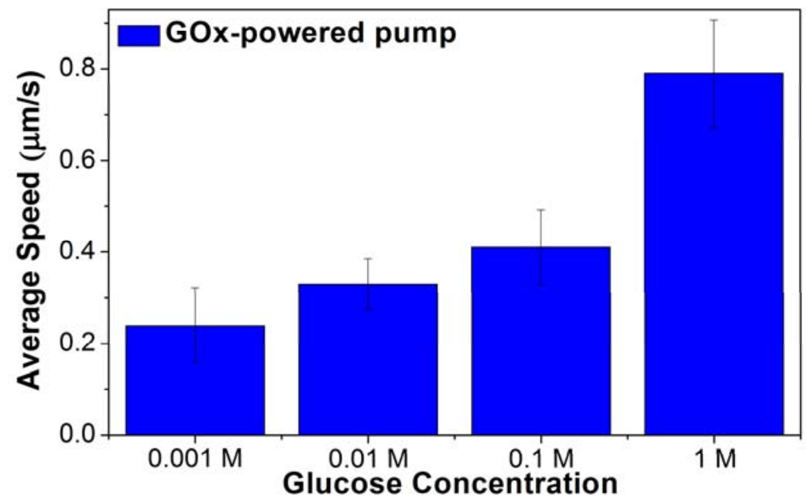
***Nature Chem.*, 2014**

Enzyme-powered Pumps: Catalase and GOx

Catalase Pump



Glucose Oxidase Pump



Gold

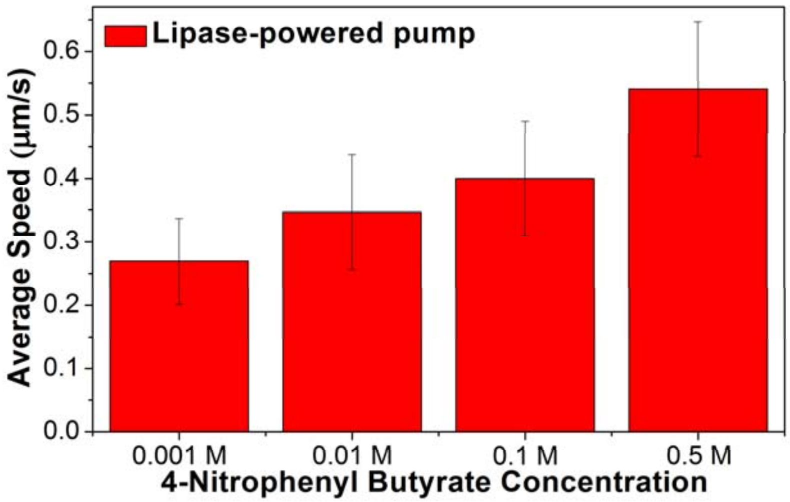
Catalase in 10 mM H_2O_2

Glucose Oxidase in 1 M Glucose

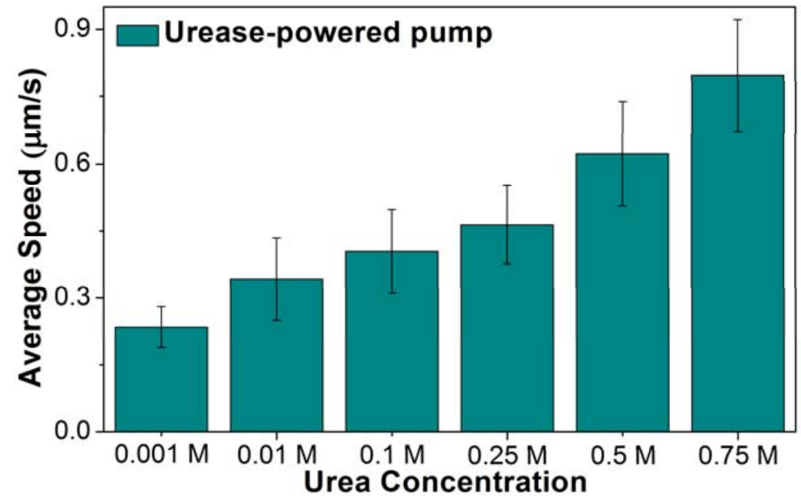
Videos are 5 times faster

Enzyme-powered Pumps: Lipase and Urease

Lipase Pump



Urease Pump



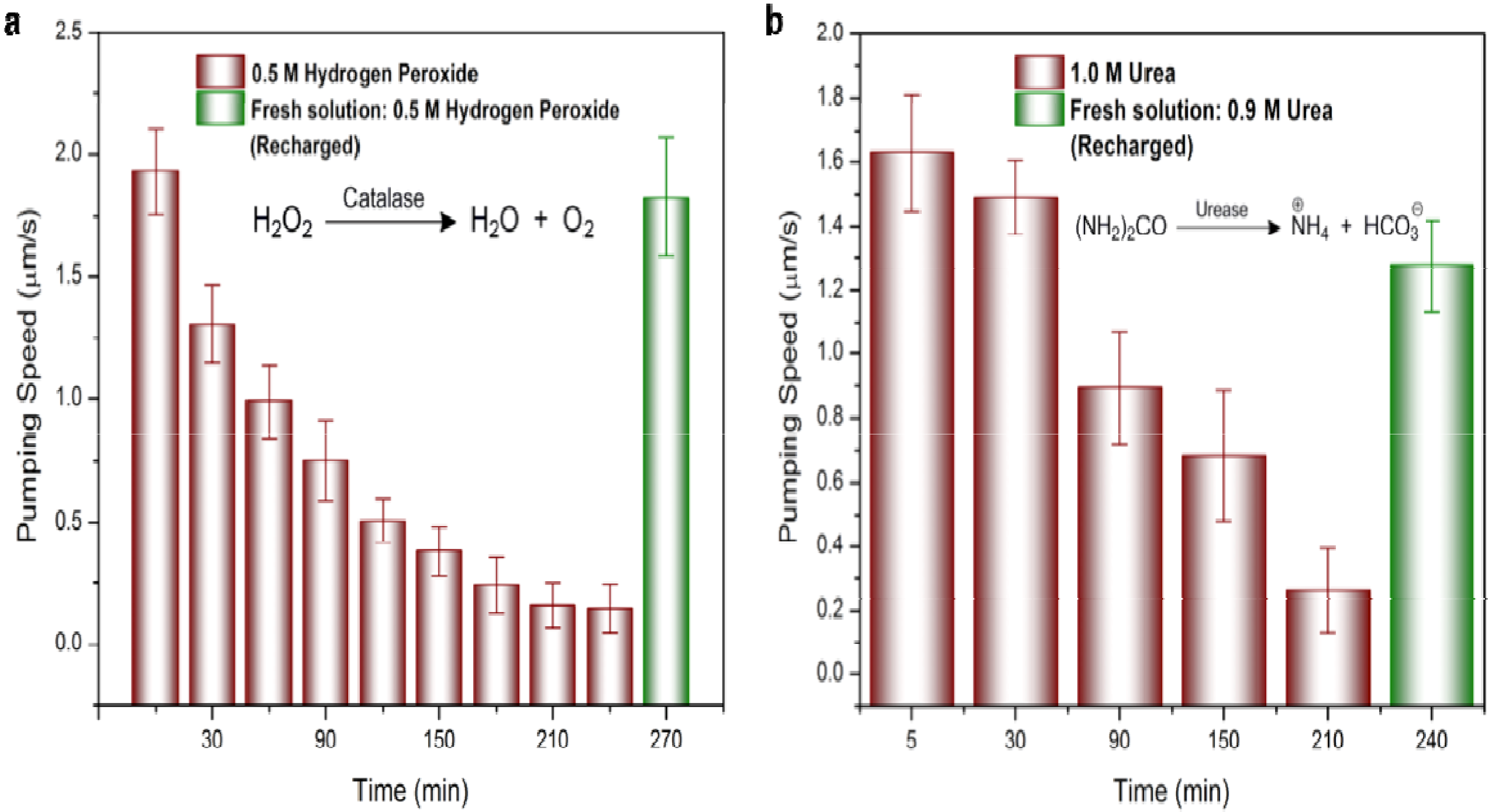
Gold

Lipase in 0.5 M PNB

Urease in 1 M Urea

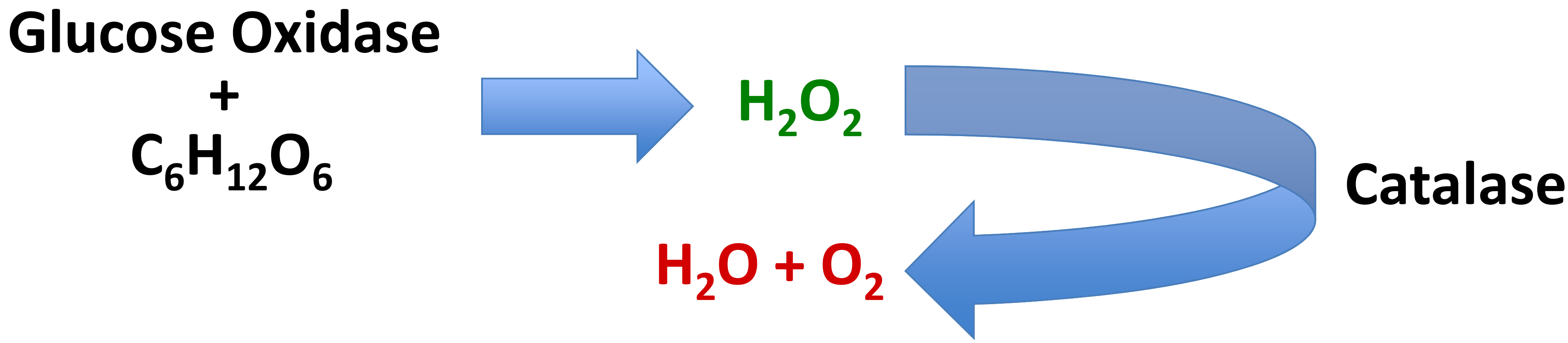
Videos are 5 times faster

Recharging of Enzyme-Powered Micropumps



Nature Chem., **2014**

Triggered Pumping



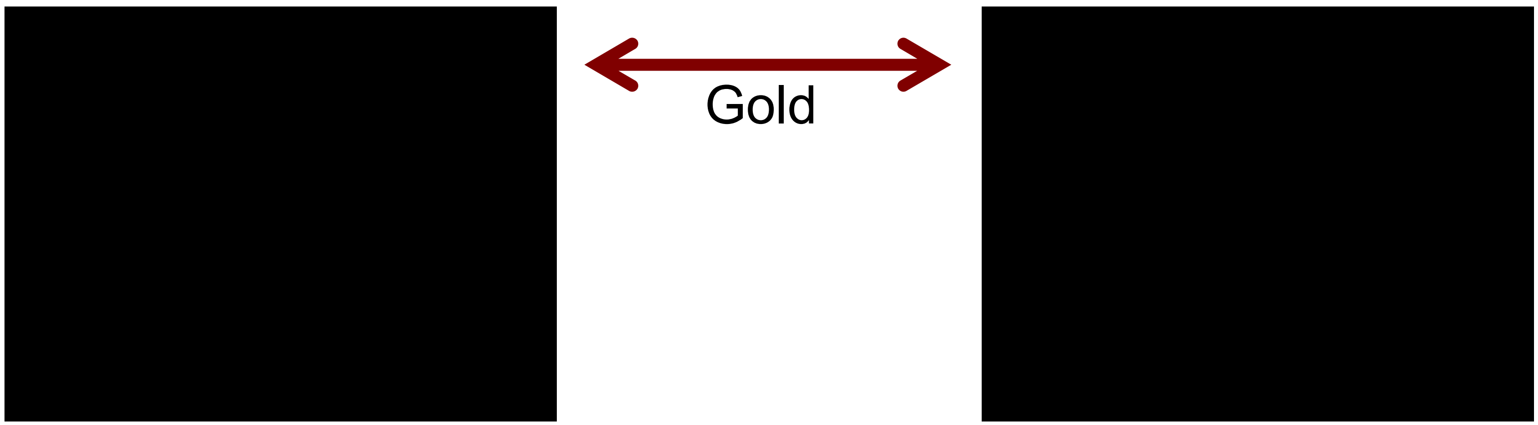
Gold

Catalase in 10 mM Glucose and Glucose Oxidase

Video 5 times faster

Density-Driven Fluid Pumping

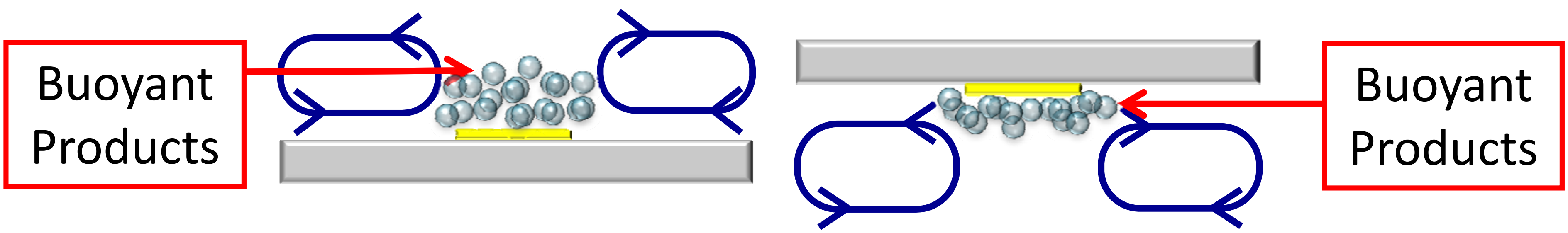
Catalase in 10 mM H_2O_2



Inverted close to the surface

Inverted away to the surface

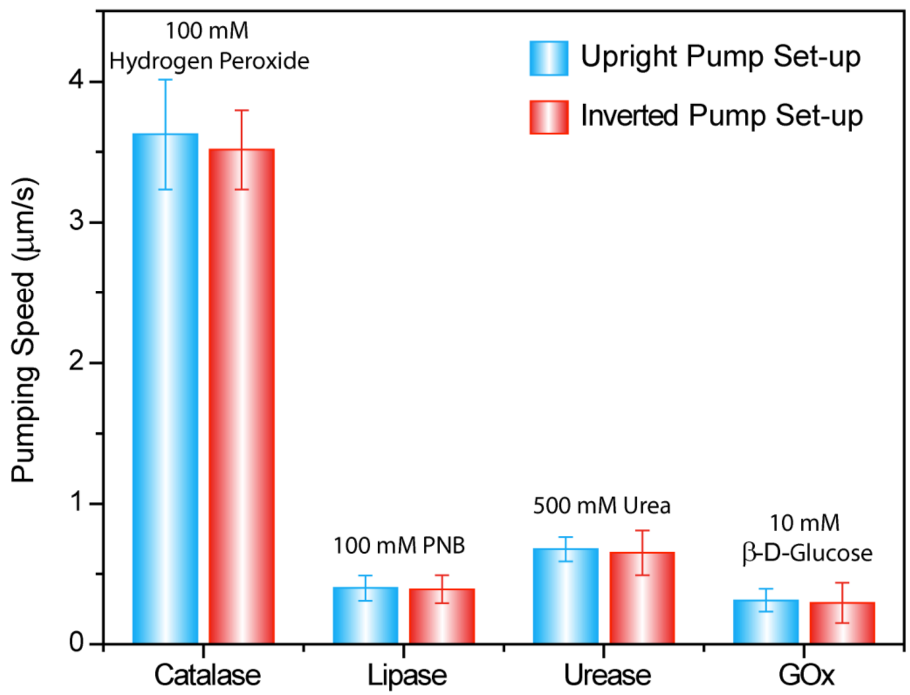
$$2H_2O_2 \longrightarrow 2H_2O + O_2$$



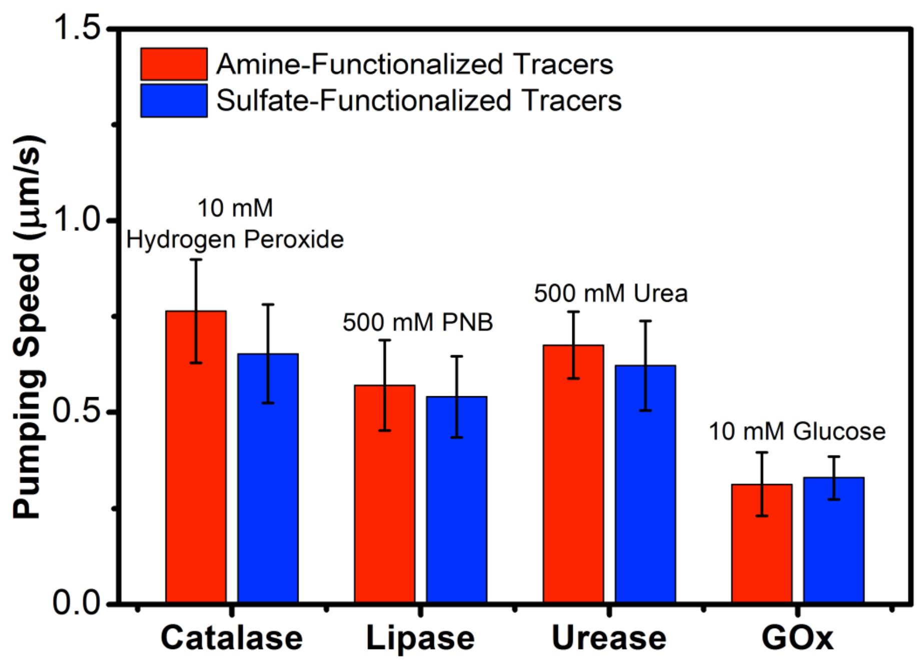
Videos are 5 times faster

Density-Driven Mechanism

Upright *vs.* Inverted Setup



Positive *vs.* Negative Tracers



- ➢ *Fluid pumping speed remains same in upright and inverted cavity*
- ➢ *Fluid pumping speed and direction remains same with positive and negative tracers*

Density-Driven Mechanism

$$V : \frac{g\beta h^3 r\Delta H}{\nu\kappa\pi R^2} f\left(\frac{R}{h}\right)$$

g = gravitational acceleration

β = coefficient of thermal expansion

h = thickness of the fluid layer

r = rate of reaction

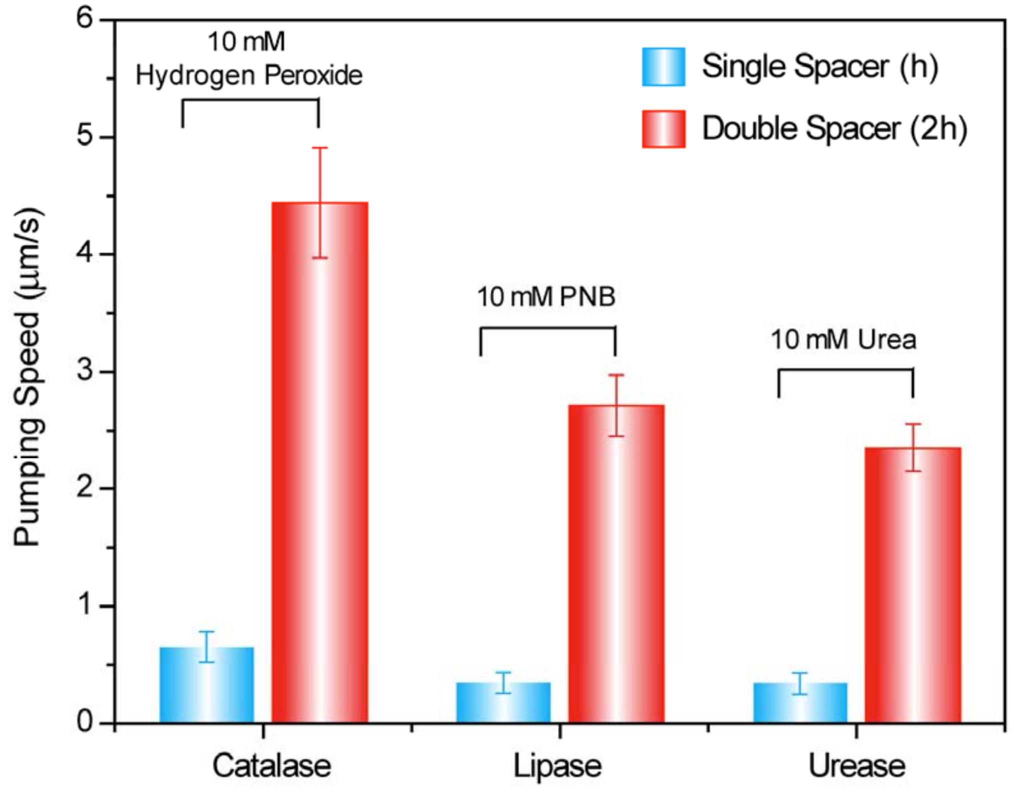
ΔH = enthalpy of reaction

ν = kinematic viscosity

κ = thermal conductivity of fluid

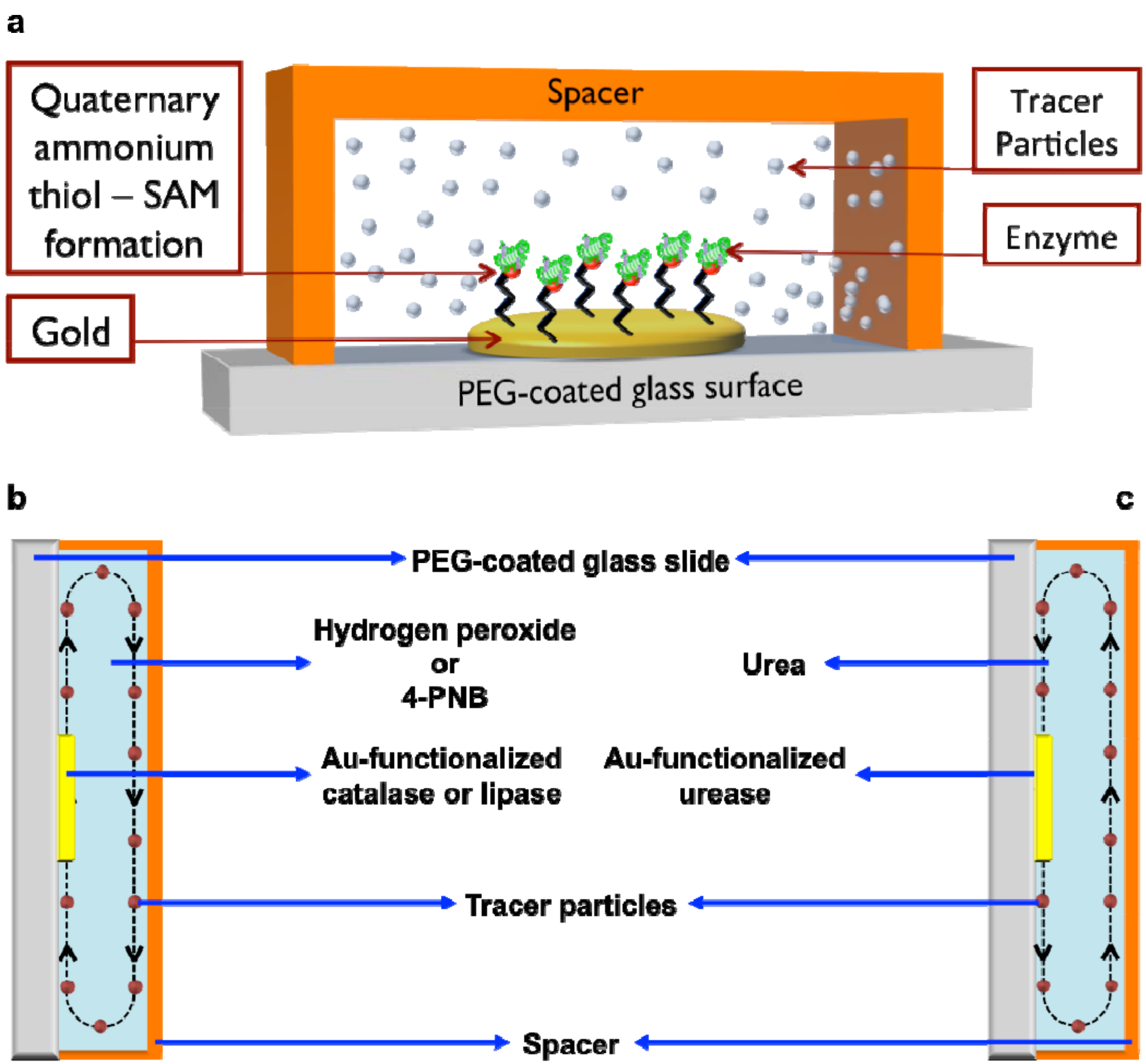
R = Radius of the pump surface

Single (h) *vs.* Double (2h) Spacer

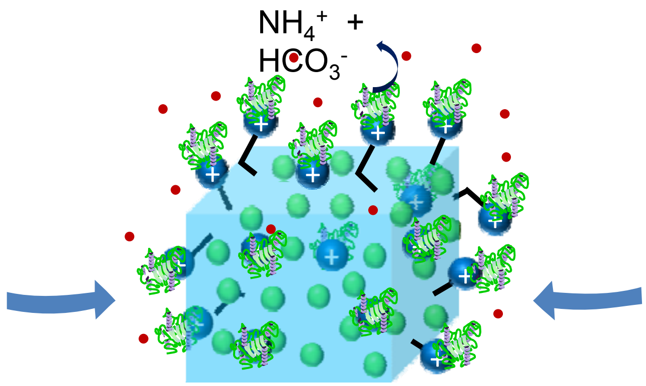


- *Fluid pumping speed increases by ~7 times on doubling the cavity height*

Fluctuations in Local Fluid Density in Enzyme-powered Micropumps



Stimuli-Responsive Release

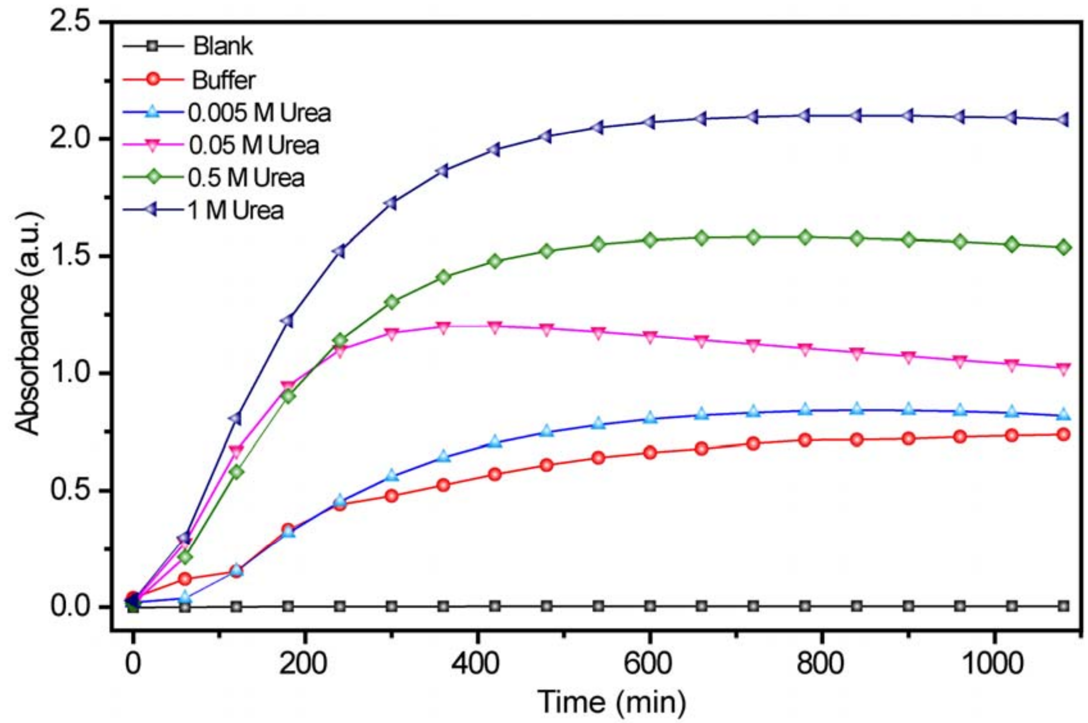


$^+NR_3$

Fluorescein dye (488 nm)

Substrate (Urea)

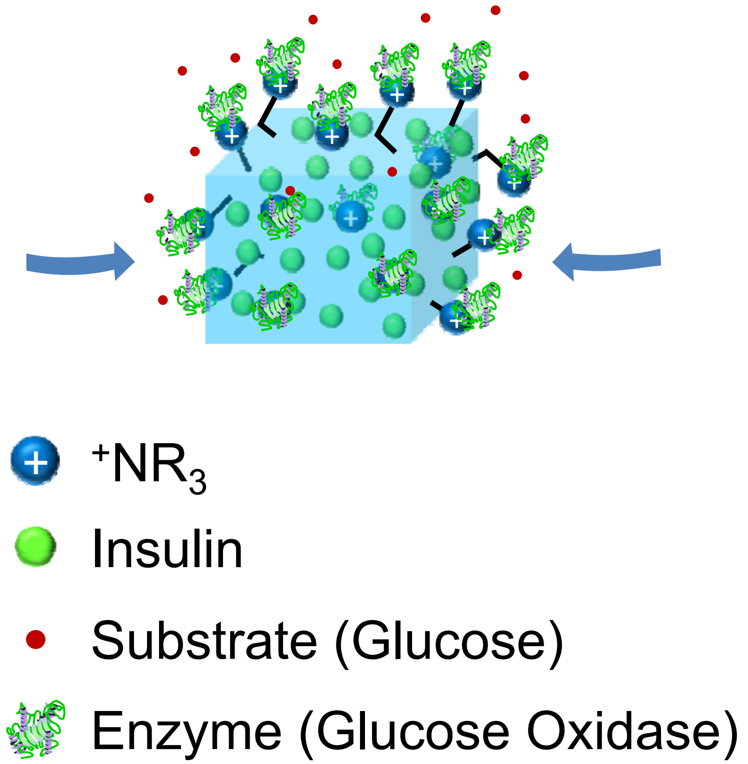
Enzyme (Urease)

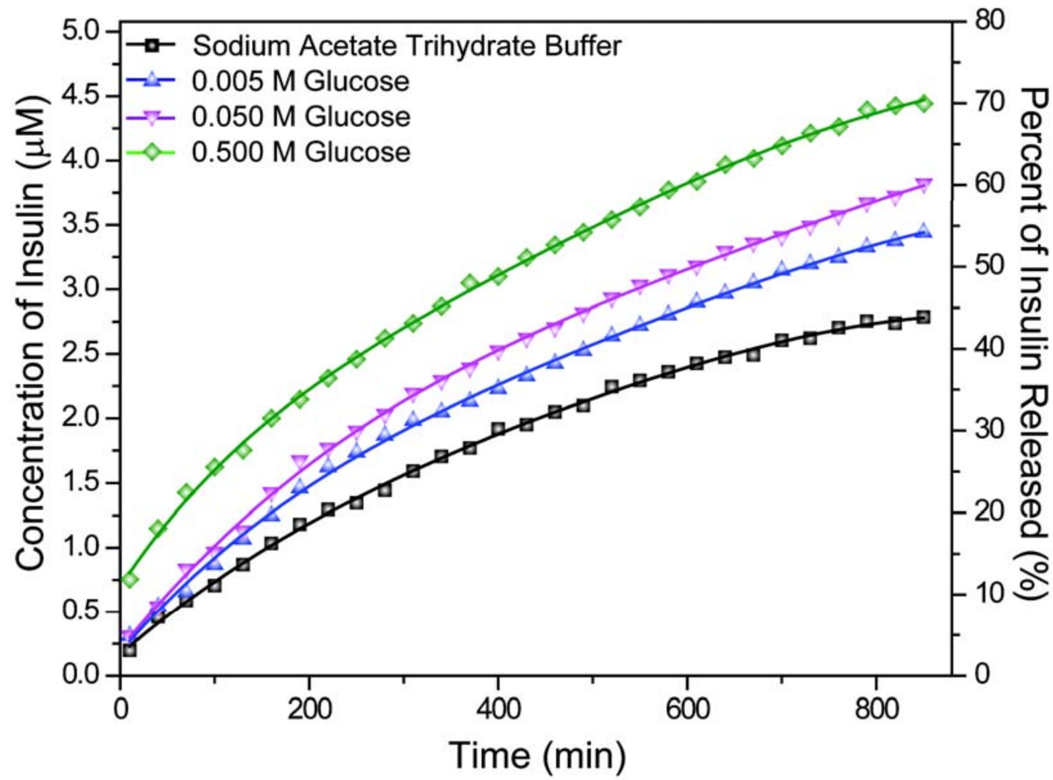


- *Stimuli release autonomous release of small molecules like markers and drugs as a function of substrate concentration*

Animation Courtesy: Isamar Ortiz Rivera

Stimuli-Responsive Release

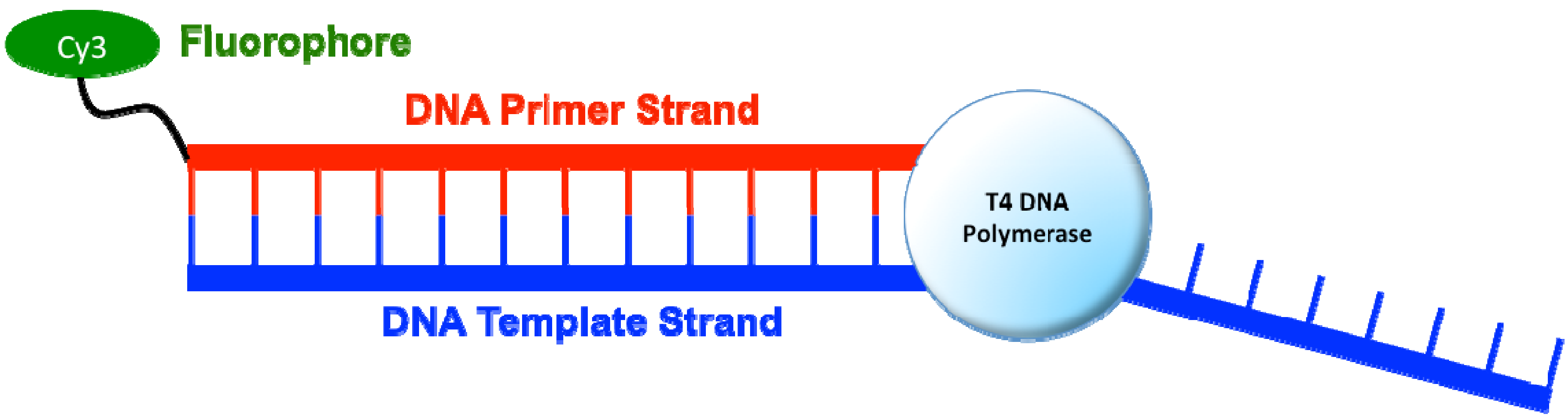




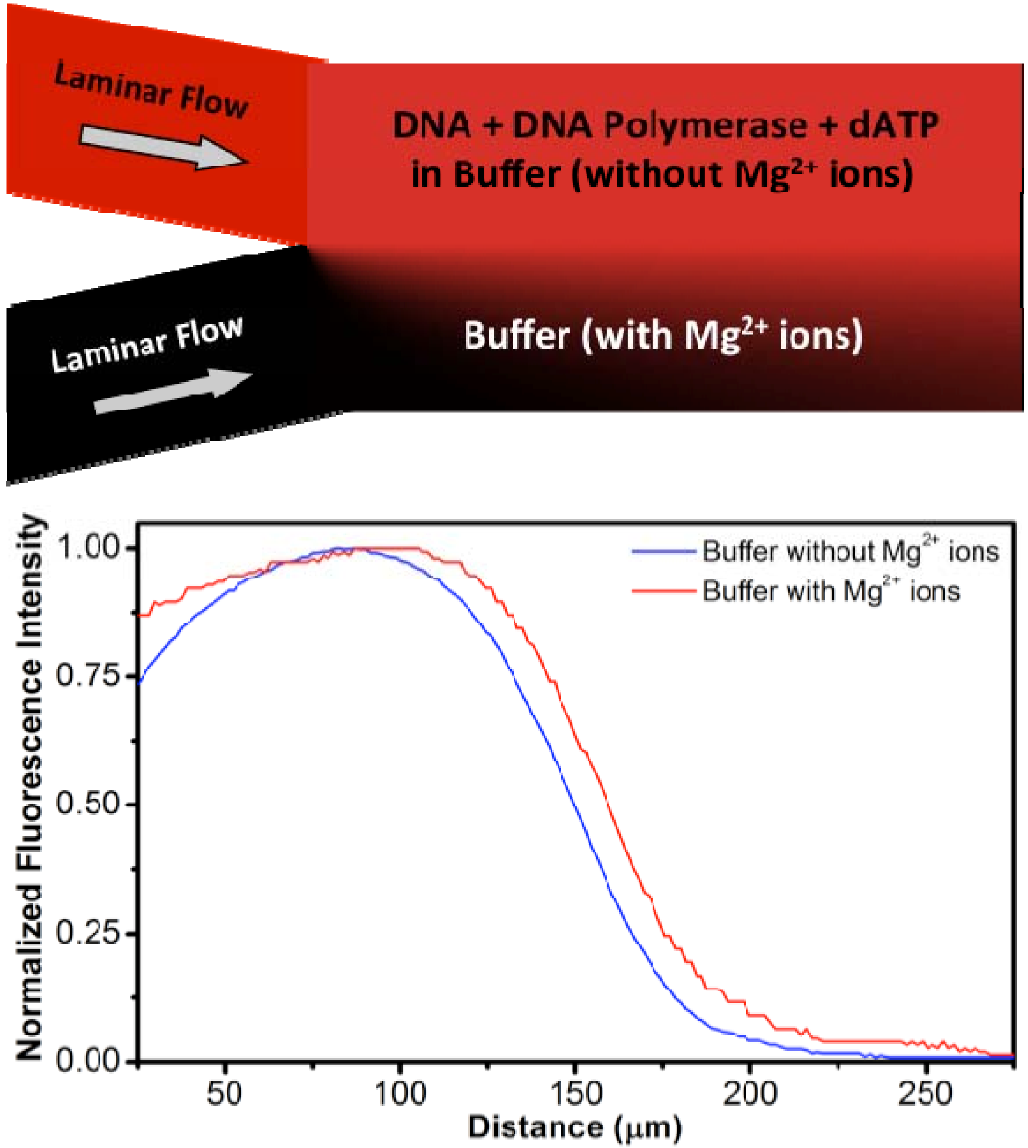
- *Stimuli release autonomous release of small molecules like markers and drugs as a function of substrate concentration*

***Nature Chem.*, 2014**

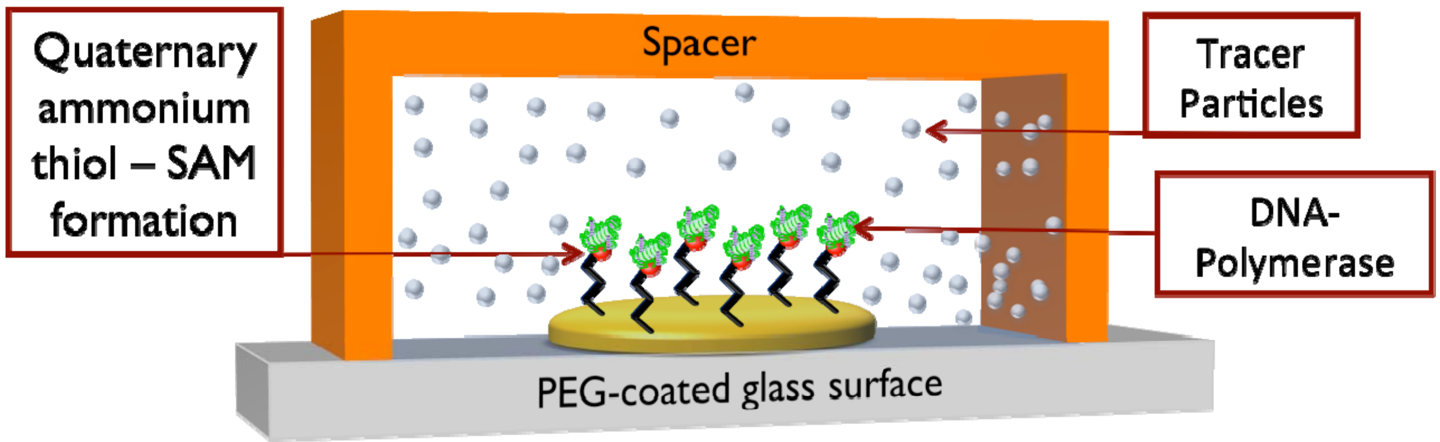
DNA Polymerase as a Molecular Motor



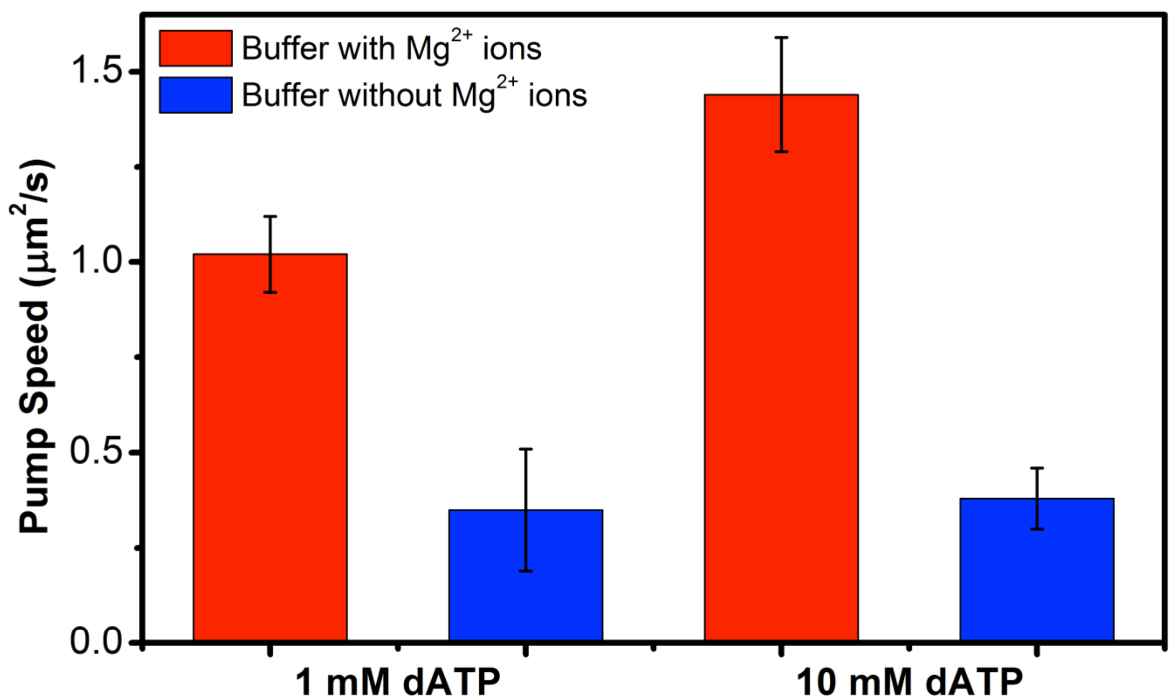
***ACS Nano*, 2014**



Collective migration of an ensemble of DNA-polymerase complex molecules in response to a concentration gradient of cofactor (Mg^{2+})



Schematic of a DNA/polymerase-powered micropump



Fluid pumping in a DNA-polymerase complex-powered micropump

Calculation of Input Power

Number of moles of enzymes over the gold patch $= \dfrac{7.7\times10^{11}}{6.023\times10^{23}} = 1.28\times10^{-12}$ mols

Turnover frequency of DNA polymerase in 'idling mode' = 0.2 s^{-1}

Free energy of ATP hydrolysis = 30.66 kJ mol^{-1}

Therefore, input power $P_i = 1.28\times10^{-12}\times0.2\times30.66\times10^{3}\ \text{Js}^{-1} = 7.85\times10^{-9}$ W

Calculation of Output Power

Viscosity of the solution, $\eta = 0.001$ Pa.s

Area of the bottom surface, $A = 3\times10^{-4}\ \text{m}^2$

Height of the experimental chamber, $h = 1.3\ \text{mm} = 1.3\times10^{-3}$ m

Pumping speed, $v = 1\times10^{-6}\,\text{ms}^{-1}$

Therefore, output power $P_{out} = \eta A\dfrac{v}{h}.v = \dfrac{\eta A v^2}{h} = 2.31\times10^{-16}$ W

To establish a convective flow of the order of 1 µm/s through a *purely thermal gradient*, the system needs to have a power input of approximately 10^{-4} W

Enzymes as Motors and Pumps

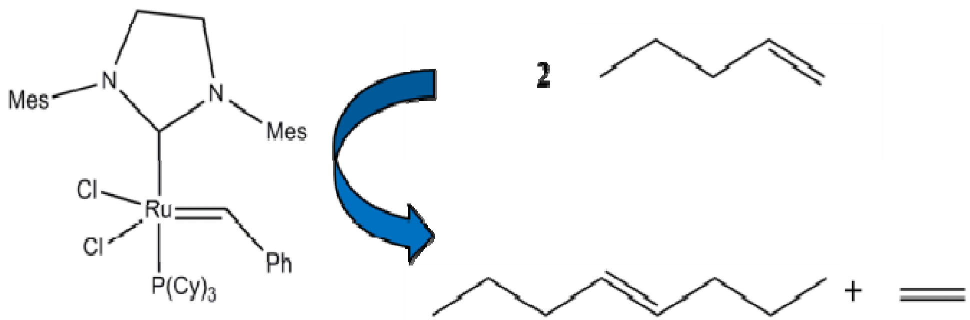
- Single enzyme molecules generate sufficient mechanical force through substrate turnover to cause their own movement.
- Movement becomes directional through the imposition of a gradient in substrate concentration.
- All enzymes, and not just ATP-dependent enzymes, may act as pumps.
- Enzyme Pump: Precisely controlled flow rate and turns on in response to specific analyte. Cargo (e.g., drug) delivery on demand.

Results open up a new area of mechanobiology:
Intrinsic force generation by non ATP-dependent enzymes and their role in biochemical regulation of cell function

Even Smaller Organometallic Molecular Motor

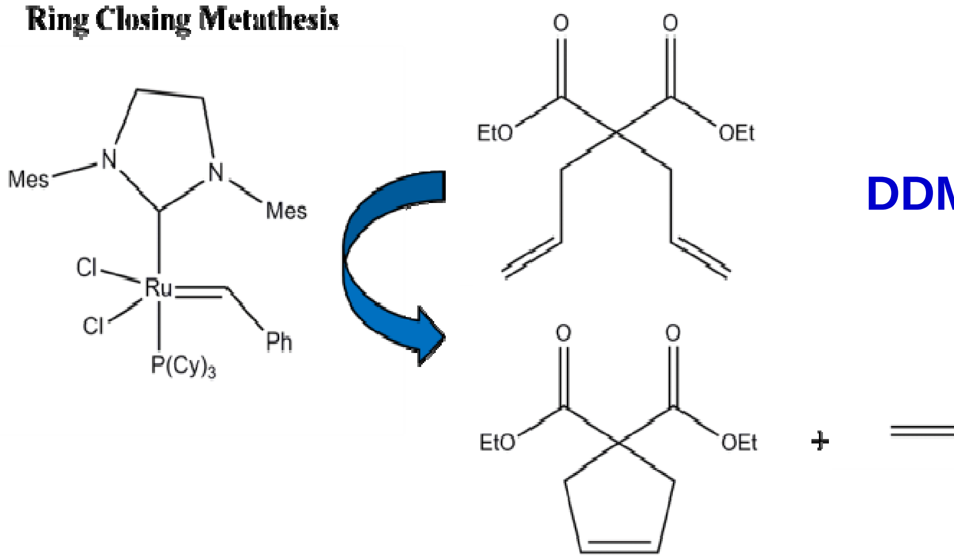
Cross Metathesis

Grubbs catalyst



Ring Closing Metathesis

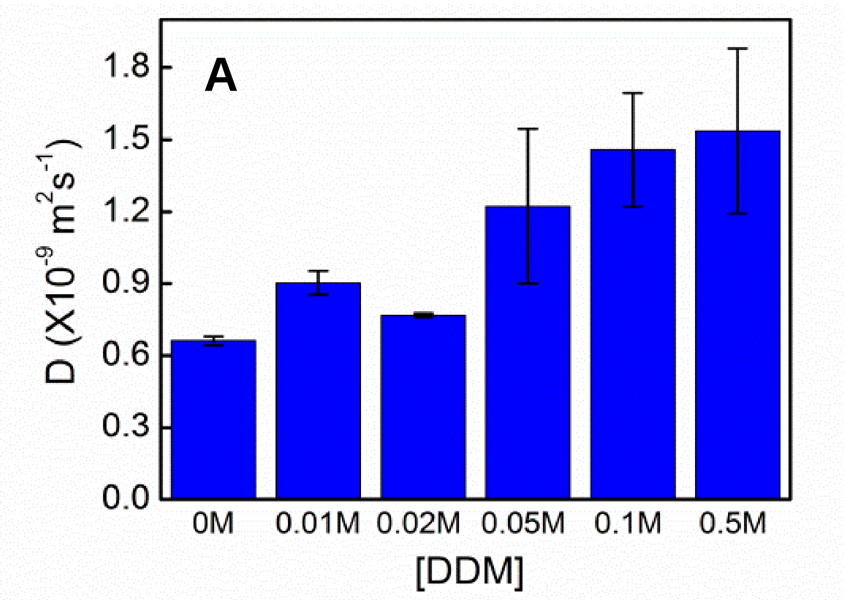
Grubbs catalyst

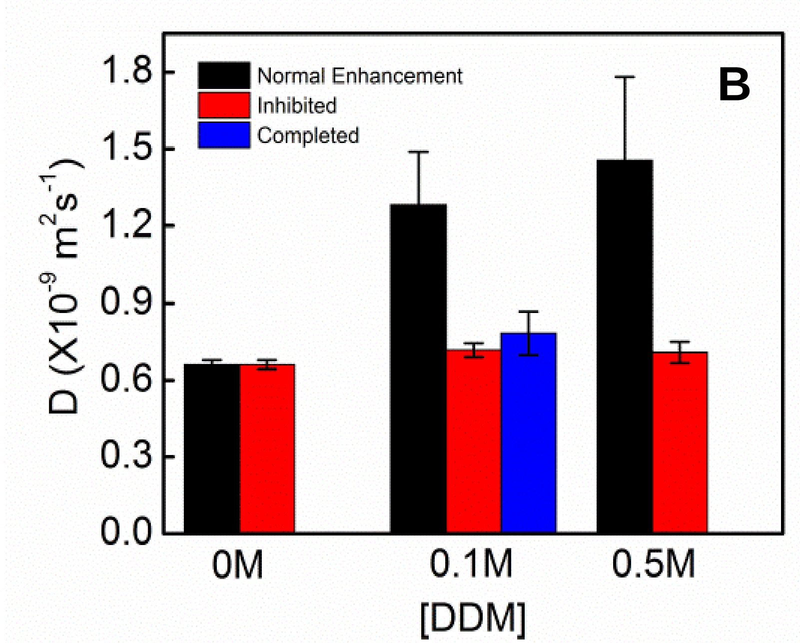


DDM

***Nanoscale*, 2014**

Diffusion Coefficient by NMR Spectroscopy





(A) Diffusion coefficients of catalyst over a range of concentrations of DDM.

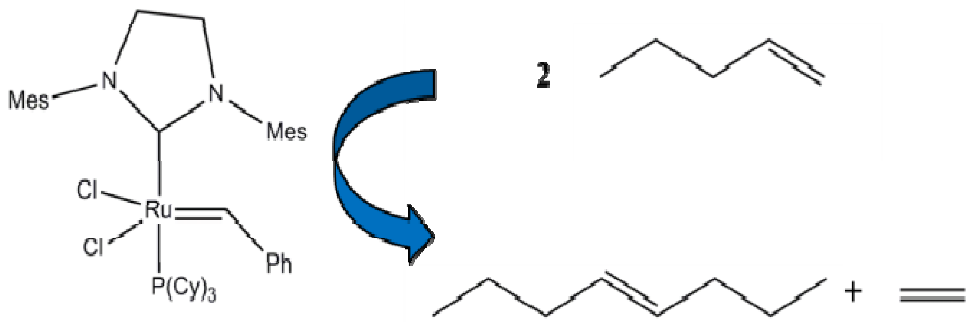
(B) The diffusion coefficient is reduced to the base value in presence of the inhibitor and when the reaction reaches equilibrium.

***Nanoscale*, 2014**

Even Smaller Organometallic Molecular Motor

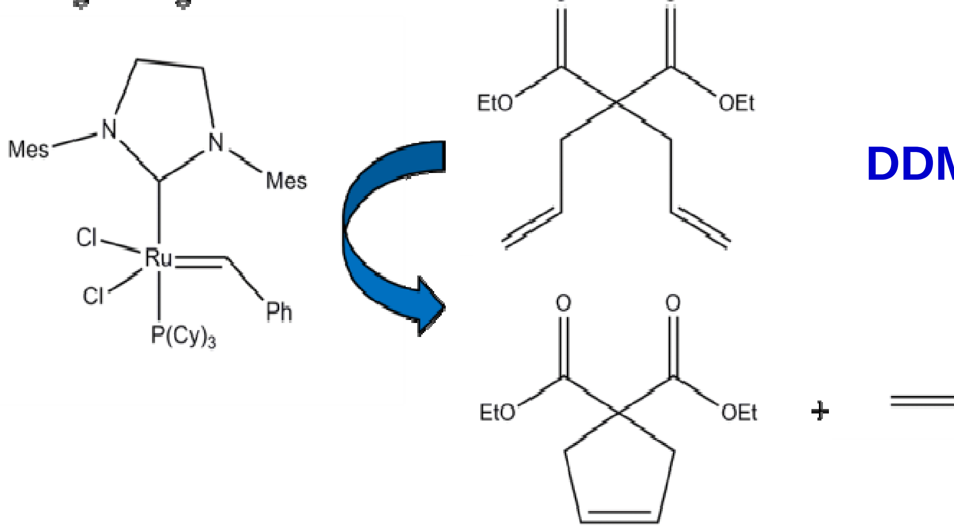
Cross Metathesis

Grubbs catalyst



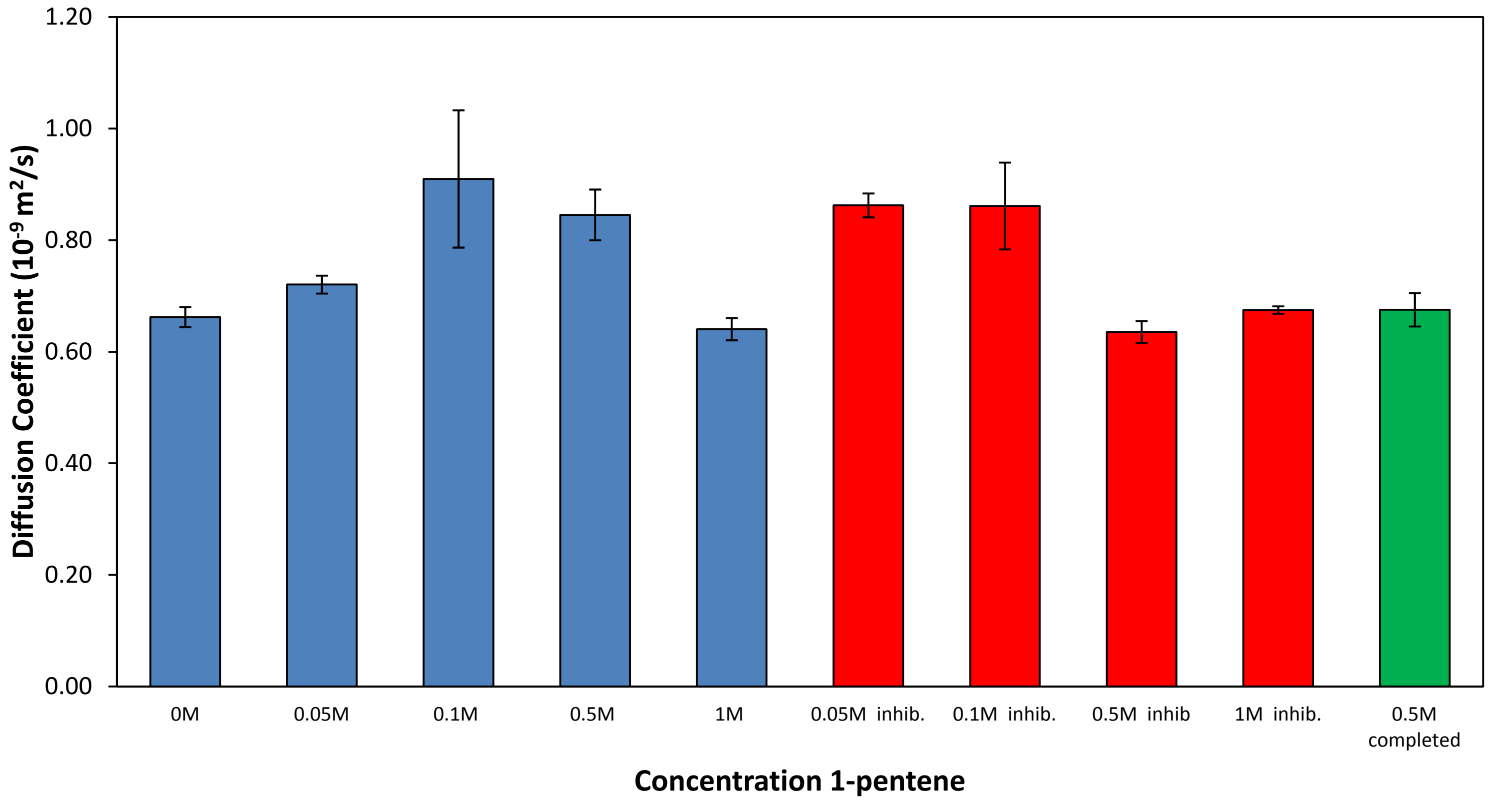
Ring Closing Metathesis

Grubbs catalyst



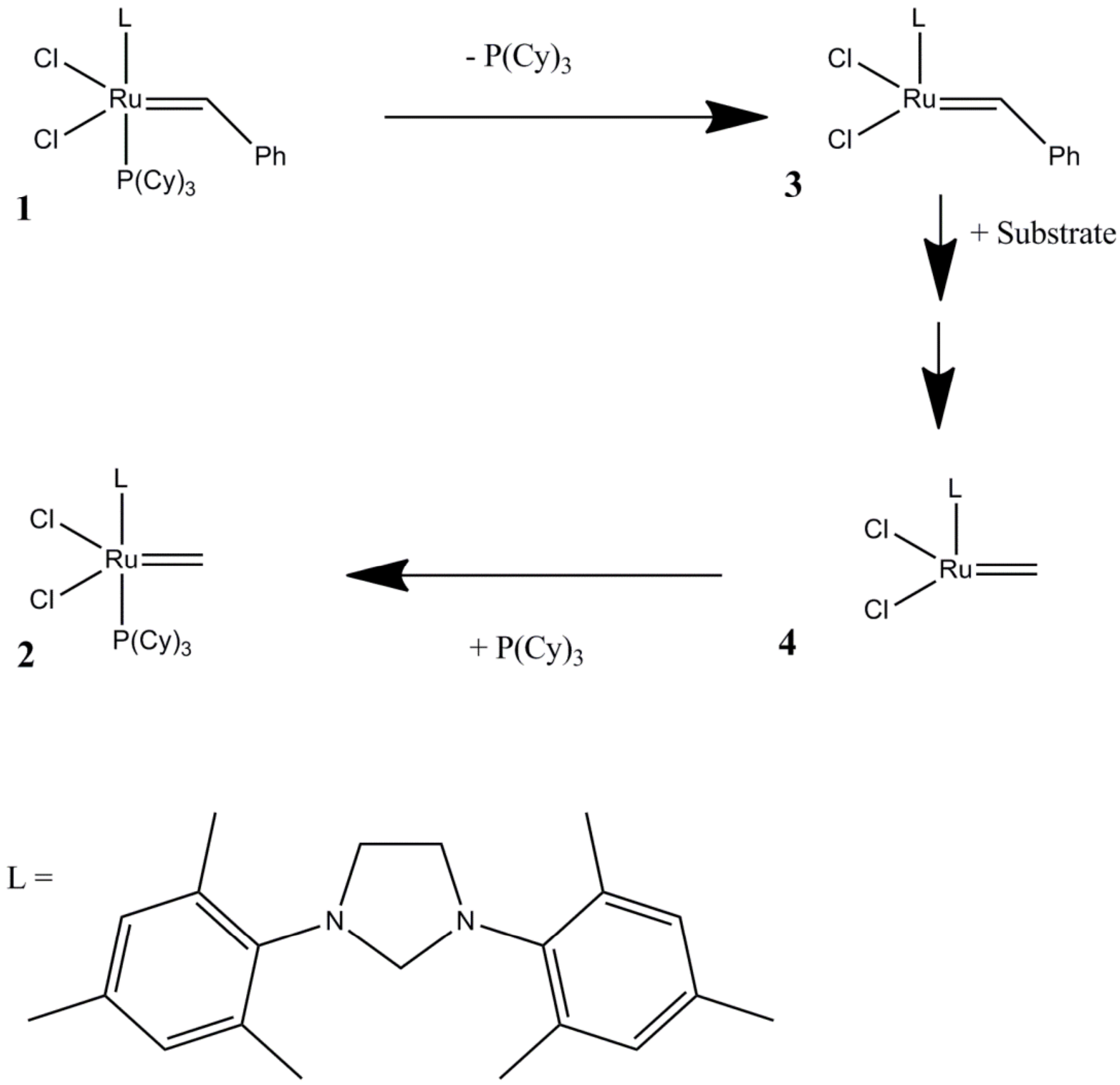
DDM

Diffusion Coefficient by NMR Spectroscopy



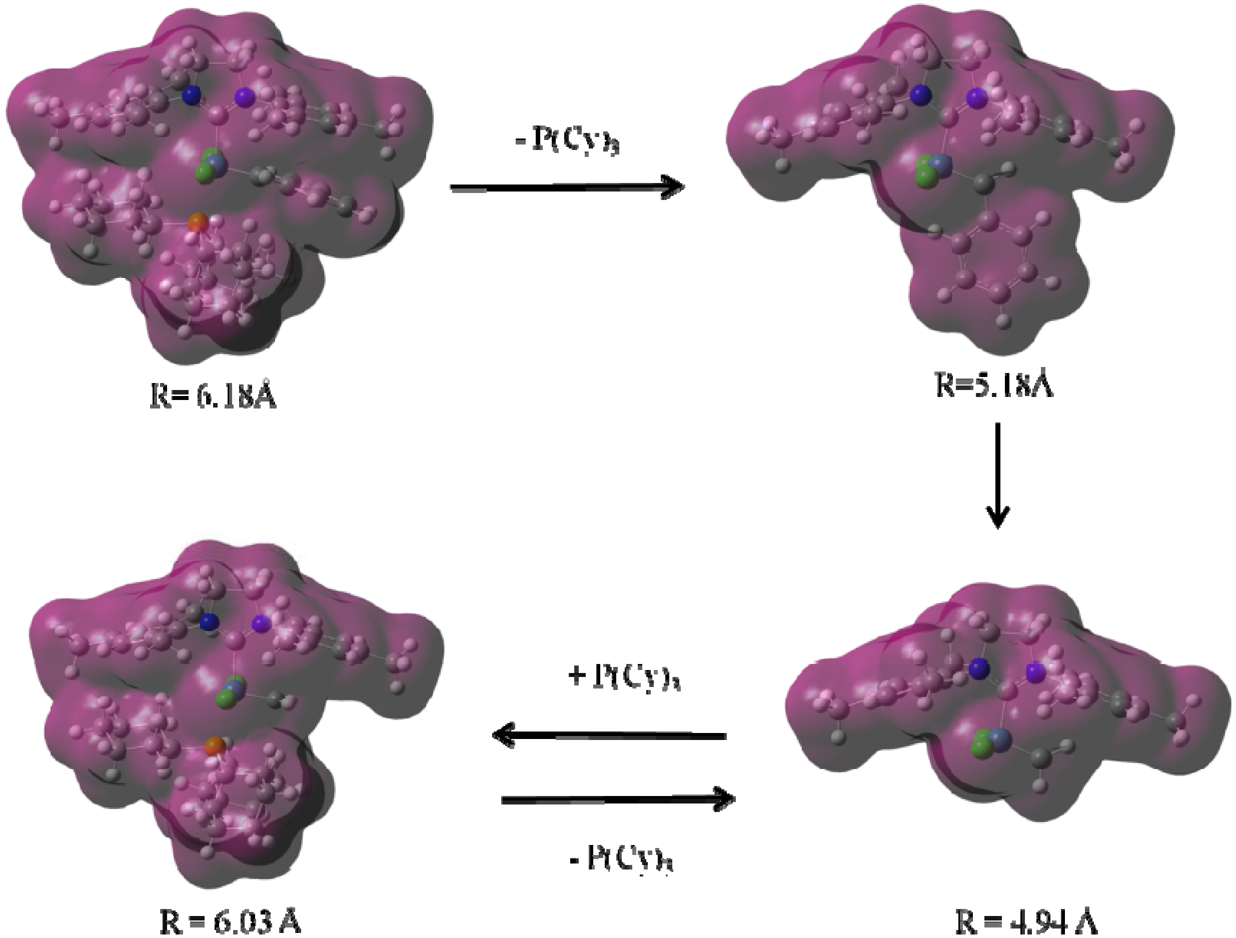
Diffusion coefficient at various concentrations of 1-pentene.
No significant change in diffusion was observed.

Structural Changes to the Catalyst During Catalytic Cycle



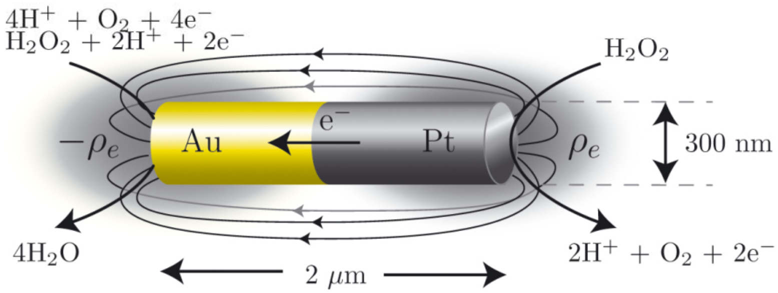
DFT Calculated Structures

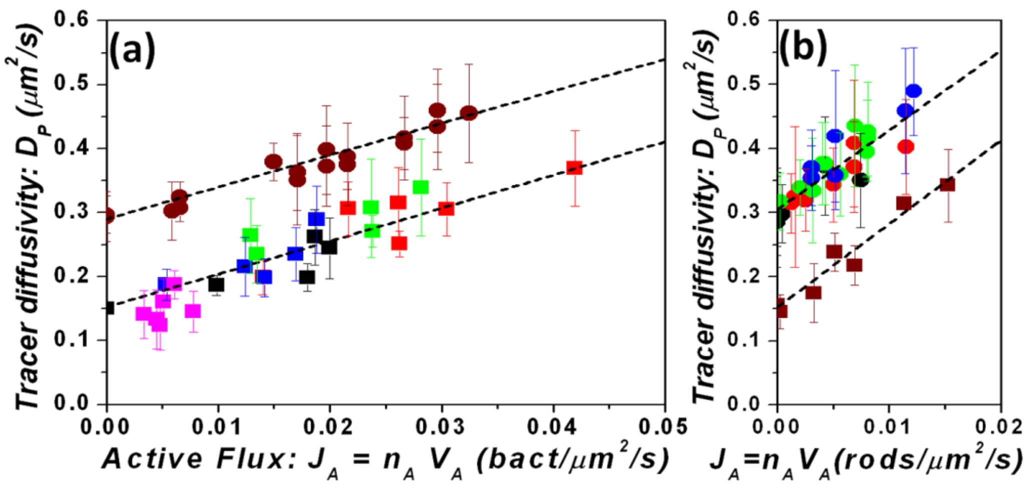
$(H_2Ies)(PCy_3)Cl_2Ru{=}CHPh$ $(H_2IMes)(PCy_3)Cl_2Ru{=}CH_2$



$(H_2IMes)(PCy_3)Cl_2Ru{=}CH_2$ $(H_2IMes)Cl_2Ru{=}CH_2$

Living Bacteria vs. Inanimate Micromotors: Similar Interaction Physics!





Bacteria and nanorod motors have similar sizes, speeds, and fractions of active swimmers.

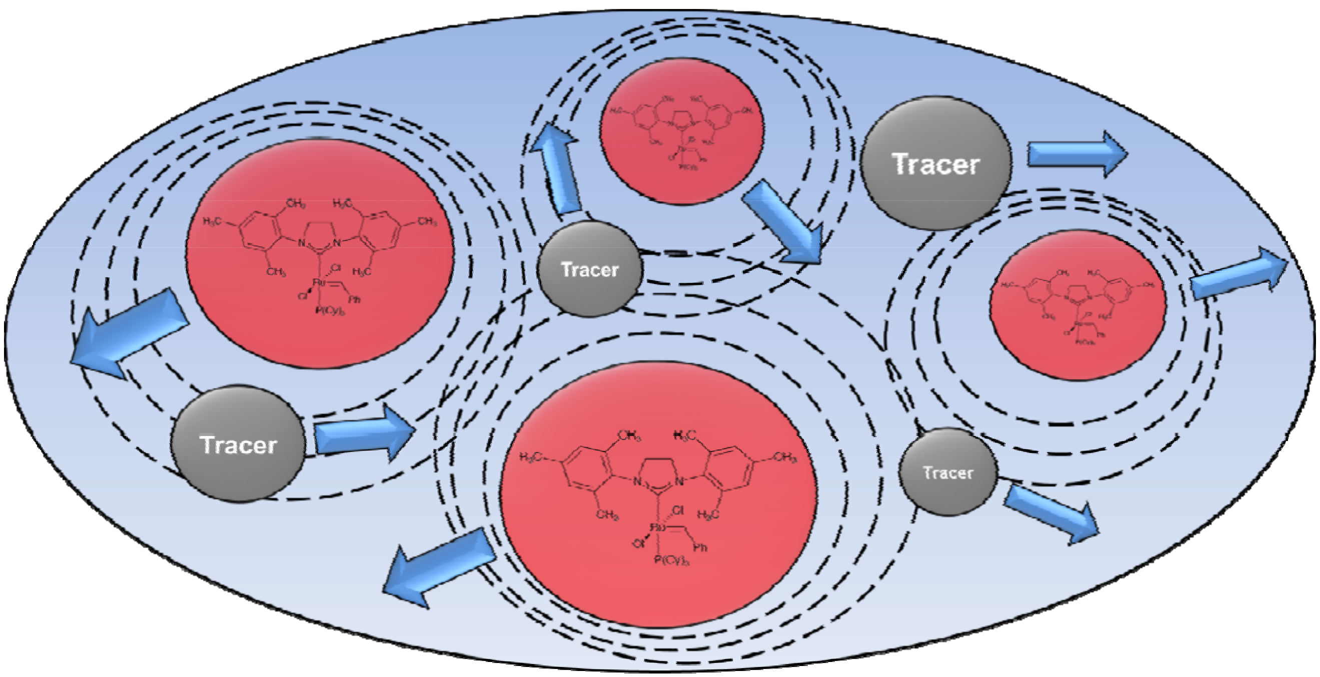
Momentum transfer from active swimmers to tracer particles shows identical scaling for bacteria and nanorods, meaning that the physics of motor-particle interactions is relatively insensitive to propulsion mechanism.

Mallouk and Hoyos, *Phys. Rev. Lett.*, 2011

futurity.org

Coupling of Motion in Solution

- Can individual catalyst molecules influence the motion of the surrounding molecules?
- Phenomenon been observed for micron-scale bacteria, algae, and catalytic rods but *not* Å-scale molecular systems

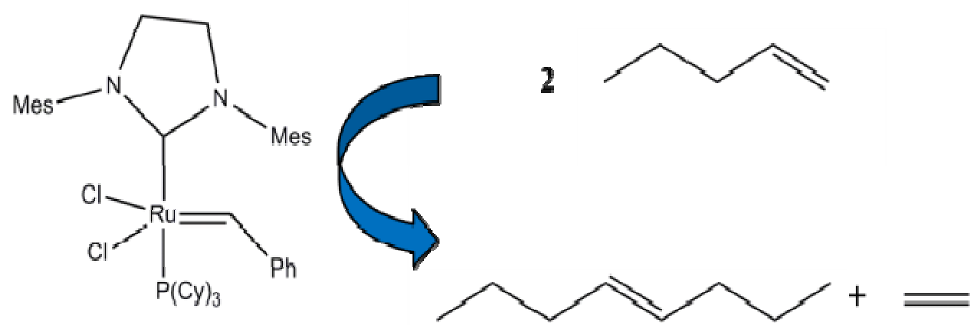


Hoyos and Mallouk *et al.*, *Phys. Rev. Lett.* 2011, *106*, 048102., Gollub, *et al., Proc. Nat. Acad. Sci.* 2011, *108*, 10391.

Even Smaller Organometallic Molecular Motor

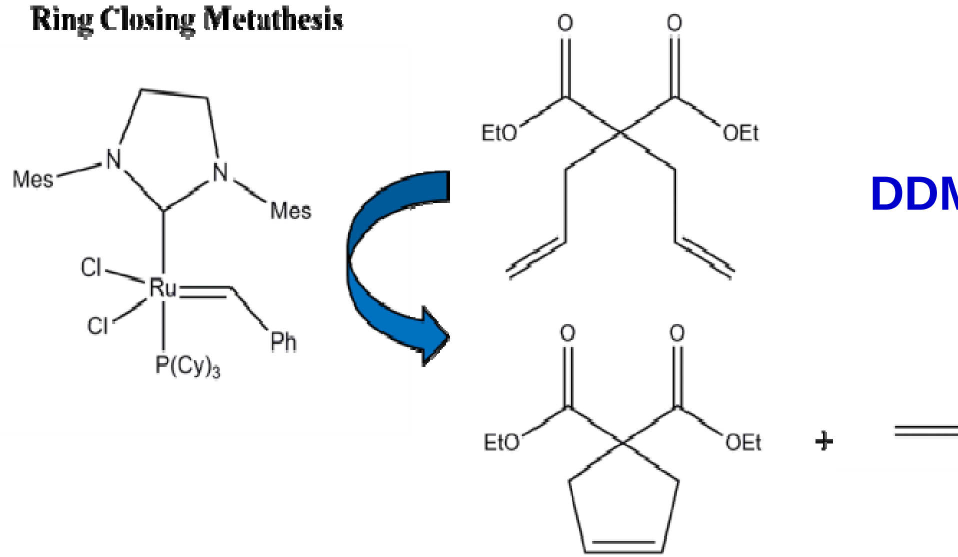
Cross Metathesis

Grubbs catalyst



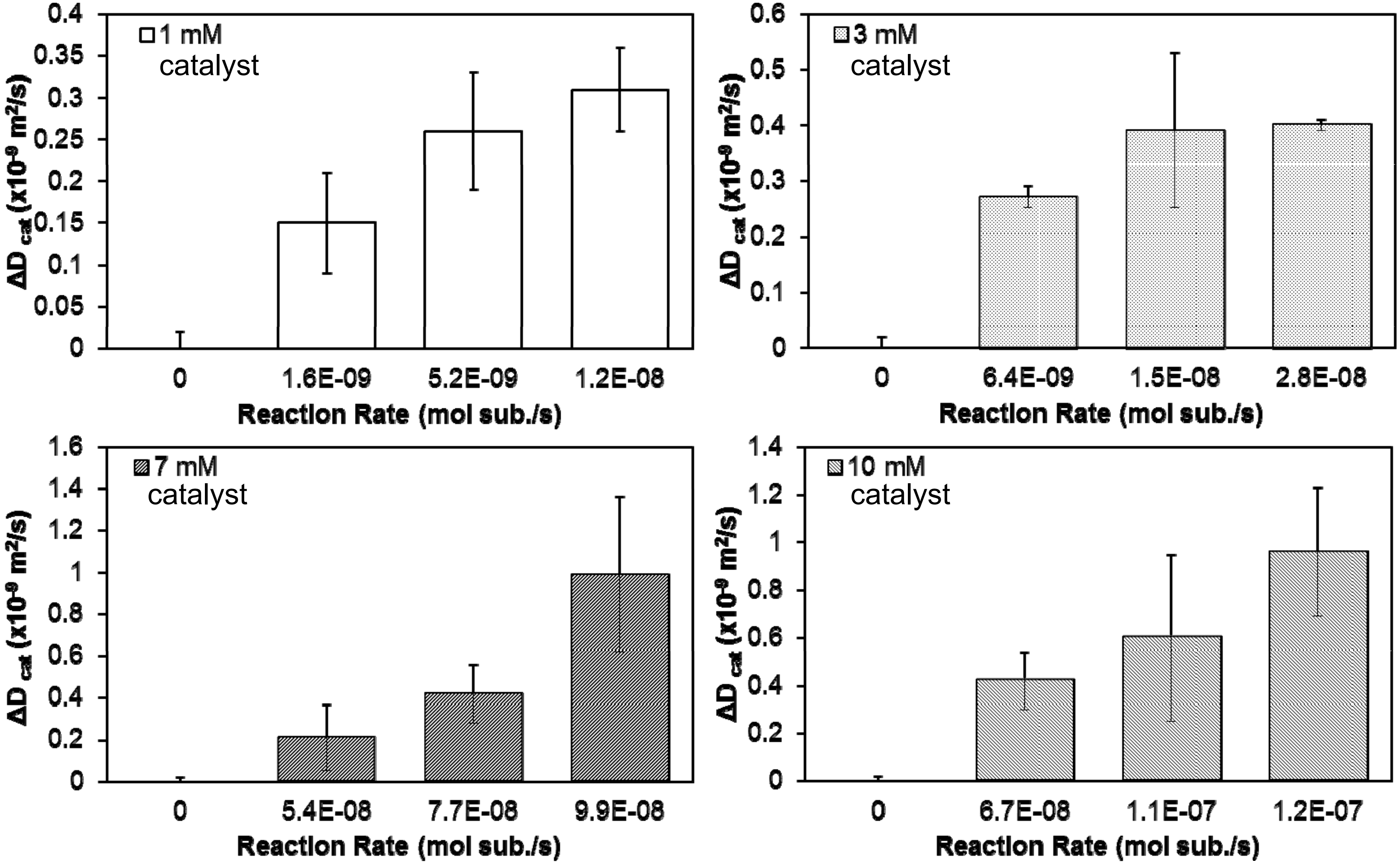
Ring Closing Metathesis

Grubbs catalyst



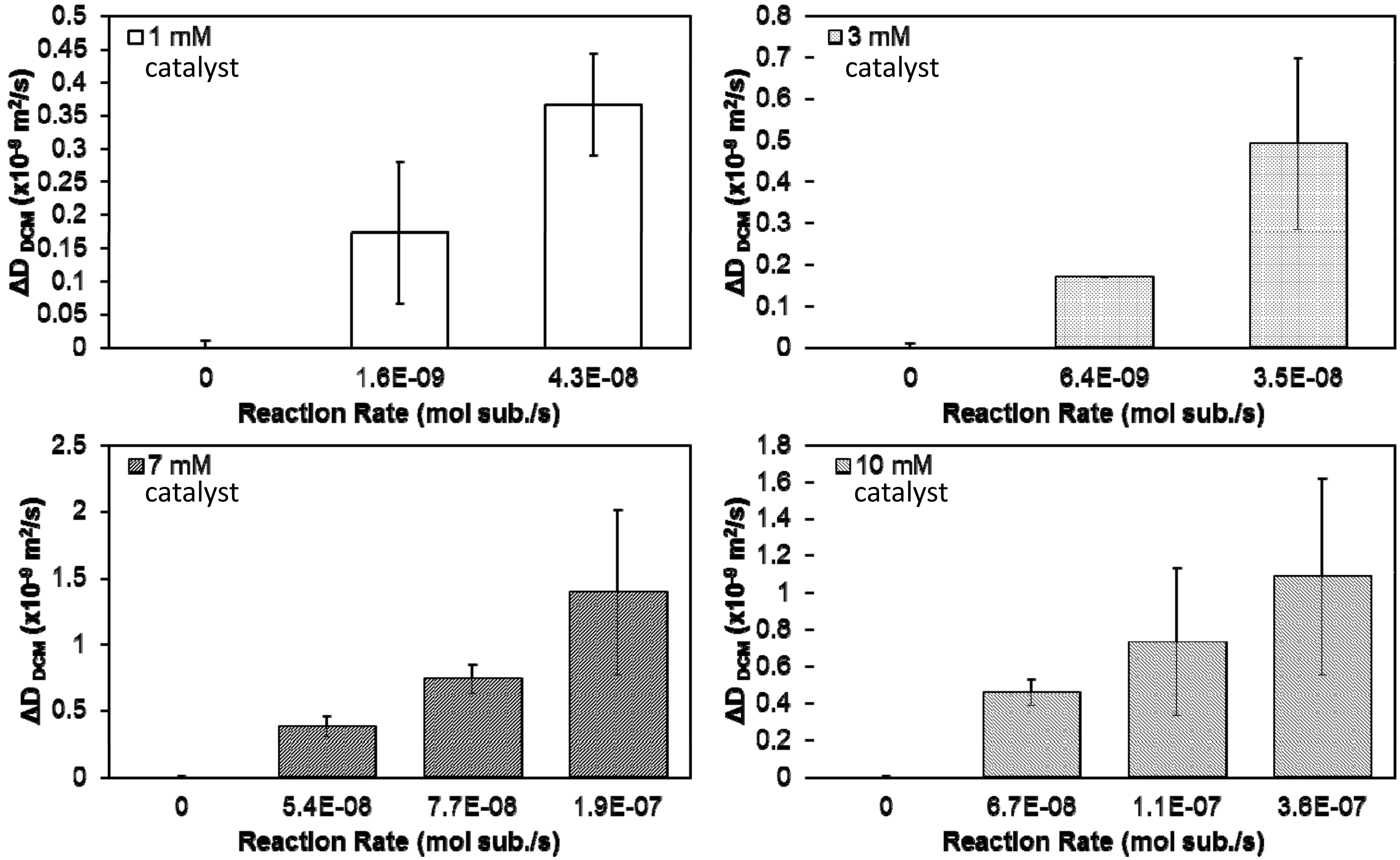
DDM

Catalyst: Dynamic Coupling



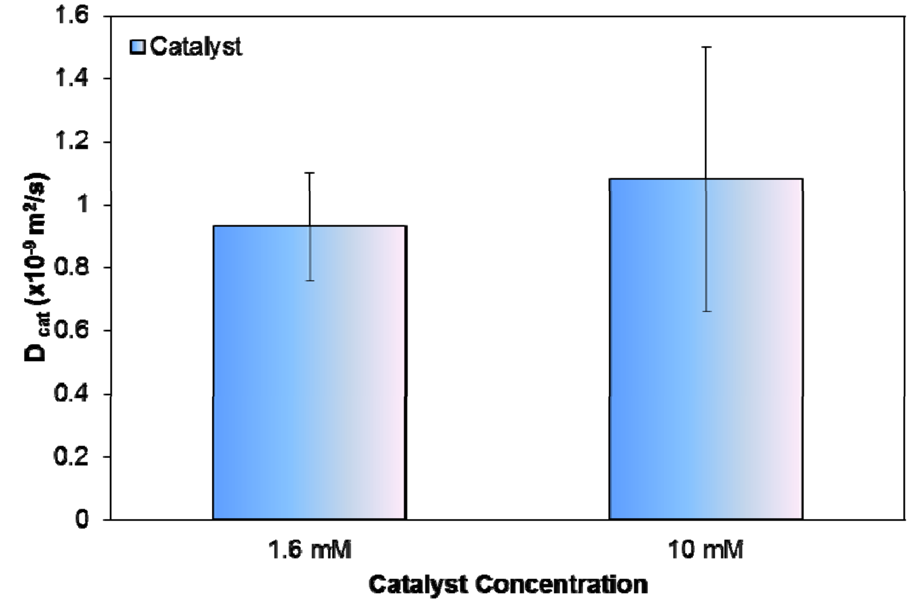
Dynamic Coupling with Spectator Molecules

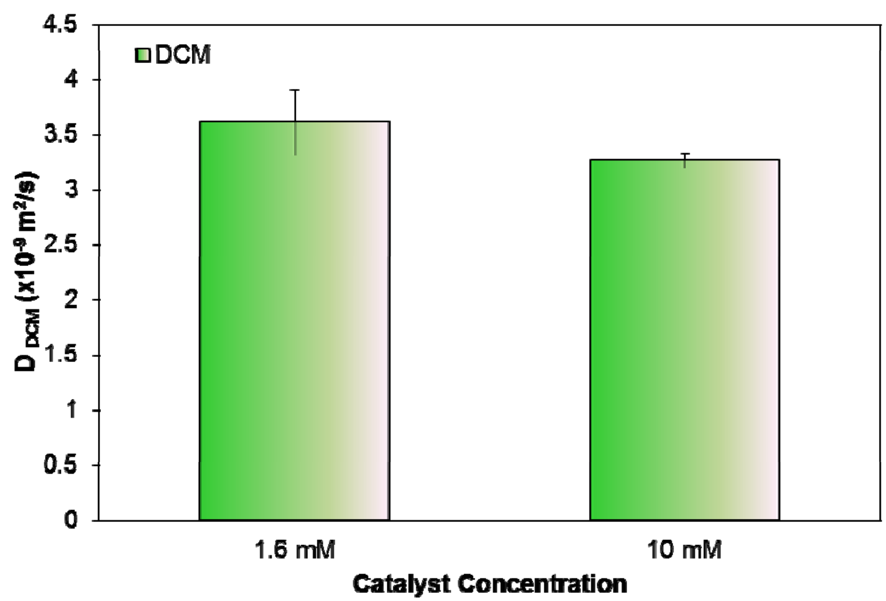
Using a Spectator (DCM, CH_2Cl_2) to Probe the Environment



Distance vs. Rate Dependence

- Easy to control the rate of perturbations (reactions)
- Look at importance of distance by controlling the rate and concentration
- This is not easily done in previously explored systems

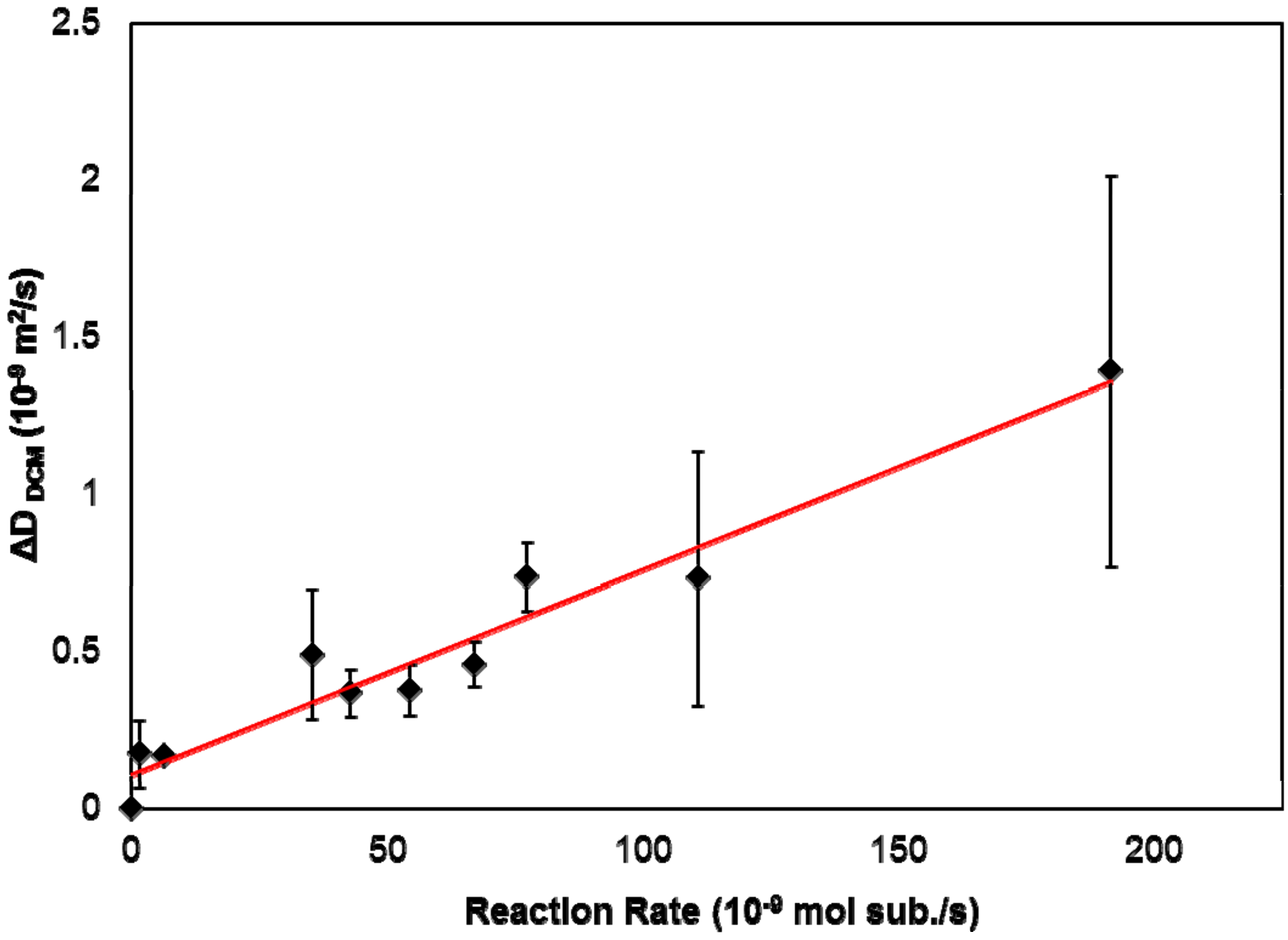




- Both the catalyst (**top**) and spectator (**left**) show no significant difference in diffusion at a constant *total* reaction rate and different catalyst concentration
- Since the distance between catalyst molecules is proportional to the concentration, there is *no* dependence on distance, only on *total* reaction rate

Dependence on Reaction Rate

Similar linear dependence of the diffusion of the spectator on the rate of perturbations (reactions) as in the systems of Mallouk/Hoyos and Gollub!



Where We Are and Where We Are Going:

- Abiotic nano/micro-objects can move autonomously by transducing chemical and photochemical energy into mechanical motion.

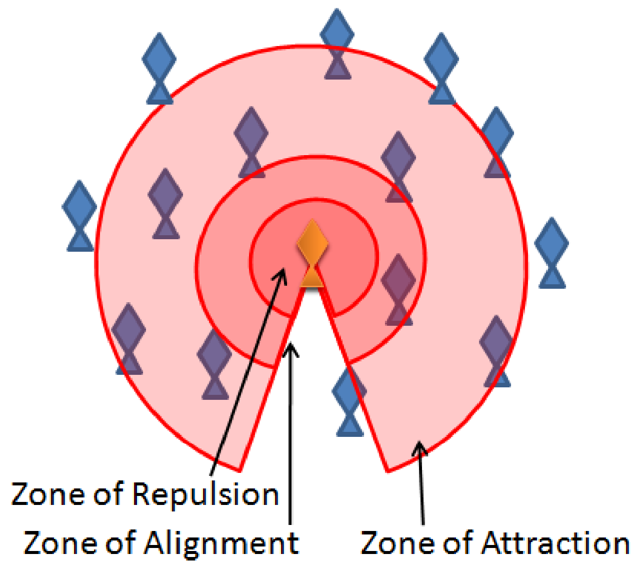
- With minimal information input in the form of chemical, or optical fields, these objects begin to display rich, emergent collective behavior.

- The Galilean inverse, analyte-triggered pumping, was also demonstrated using surface-anchored motors.

- Freed of the usual biological constraints, we now have the opportunity to probe the limits of self-organization in dynamic systems that operate far from equilibrium.

Organized Behavior

- Directional Motion: Sensing, Taxis, Levy walk
- Communication: Emergent collective behavior
- Memory: Individual (internal), Group (external)



Learning from the Birds and the Bees!

Schooling Algorithm in Animals

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Wentao Duan

Wei Wang

Vinita Yadav

Ran Liu (Post-doc)

Krishna dey (Post-doc)

Paul Lammert (Post-doc)

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Vincent H. Crespi (Phys.)

Jeffrey Catchmark (Nanofab. Lab)

Darrell Velegol (Chem. Eng.)

Peter Butler (Bio-eng.)

Scott Phillips (Chem.)

$$

National Science Foundation

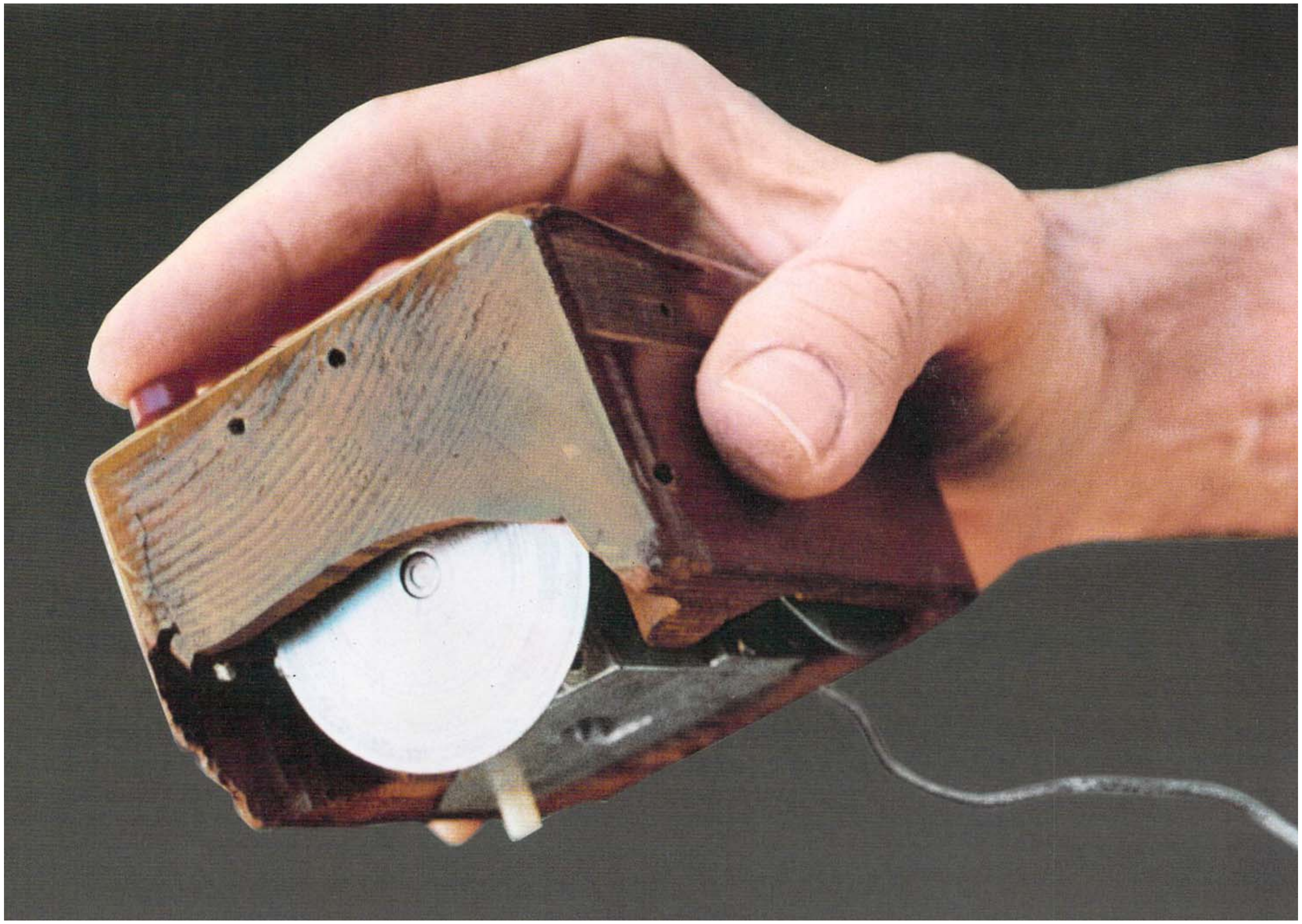
Air Force Office of Scientific Research

Advanced Energy Consortium

Artists drawing of a nanoscale submarine moving through a human capillary

- taken from Audi Magazine, 10/03

First Mouse



X-Y Position Indicator

Engelbart (1968)