Information about BB101 Quiz to be conducted on May 31st 2023 (8-9:30 am)

1. Weightage = 10% of the part taught by R Mallik
2. There will be no “Re-Quiz”. No Crib-Sessions or Crib-Emails for Quiz
3. If you miss the Quiz for genuine reasons then :-
   - Your Endsem Marks can be scaled up to compensate for the missed Quiz
   - To do this, you must send an Email from your IITB-ID to Head-TA (cc R Mallik) with the following Information :-
     - Your Name and Roll number
     - Reason for missing the Quiz

Otherwise we cannot re-scale your EndSem marks.

Reason Genuine/Not Genuine will be decided according to IITB Academic rules

SECTION 1 : THE MOLECULES THAT GENERATE MOTION

RECALL FROM PREVIOUS LECTURES

LECTURE 4 : ARTIFICIAL MOTORS

Roop Mallik, BSBE – IIT Bombay

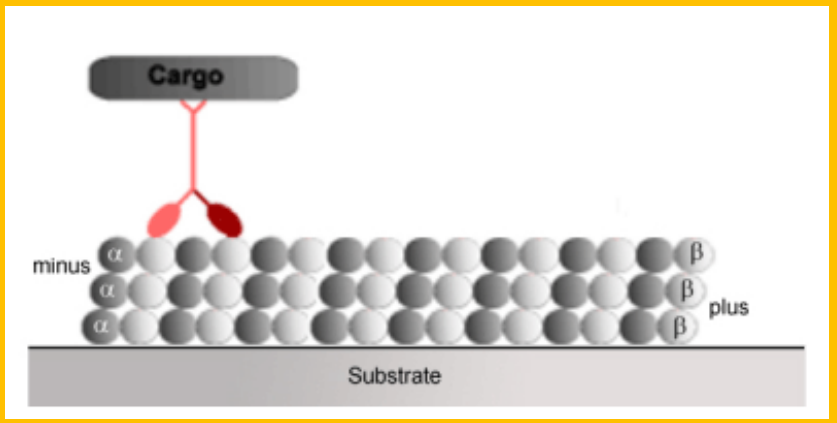
BB101 – Biology. Autumn Semester 2022-2023

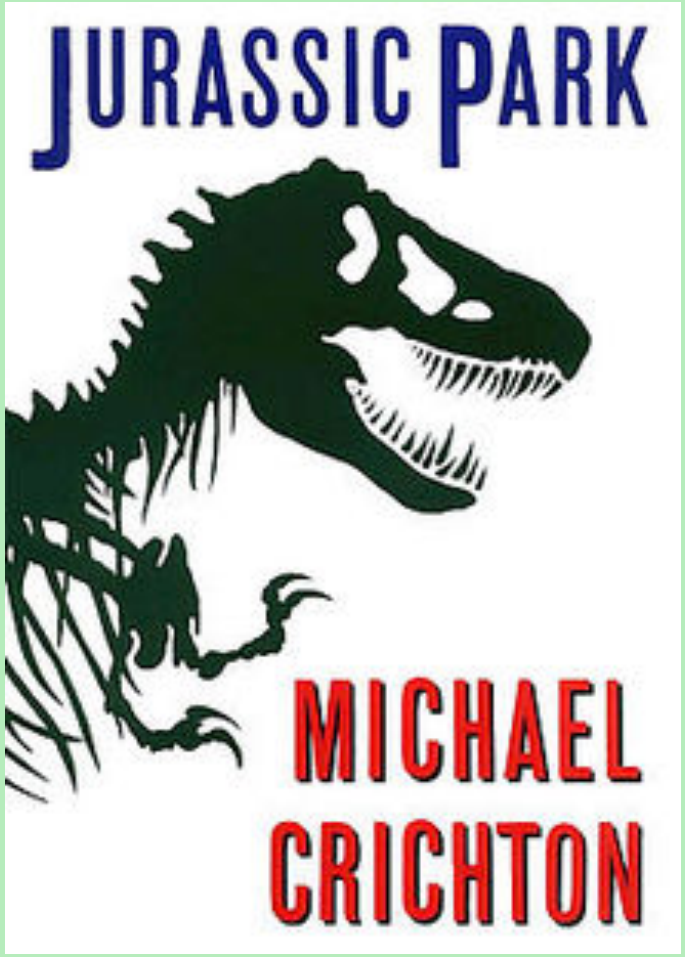
RESOURCES

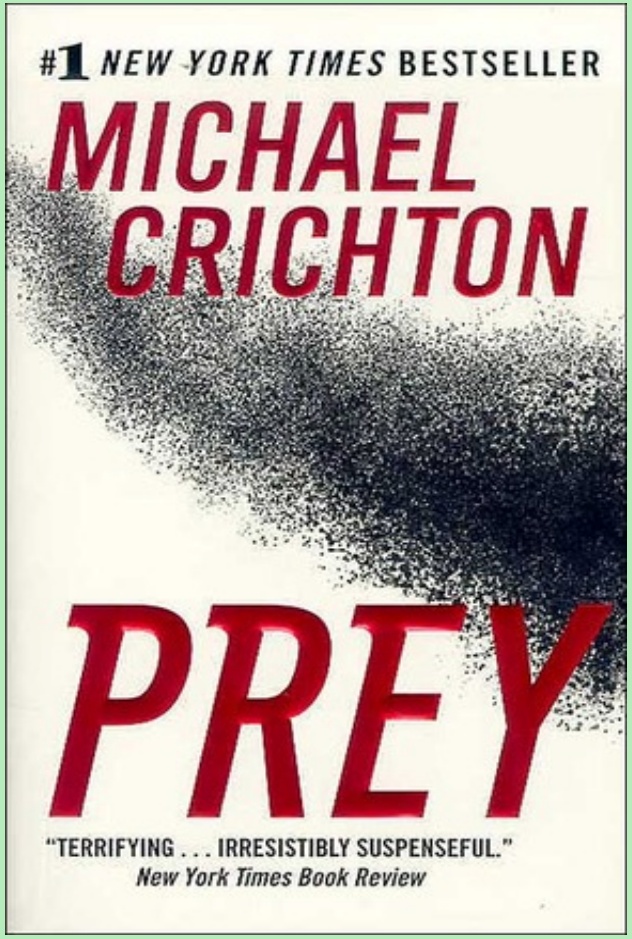
Molecular Machines, Nobel Prize 2016
Artificial Molecular Machines

Rotary Motors

Linear Motors





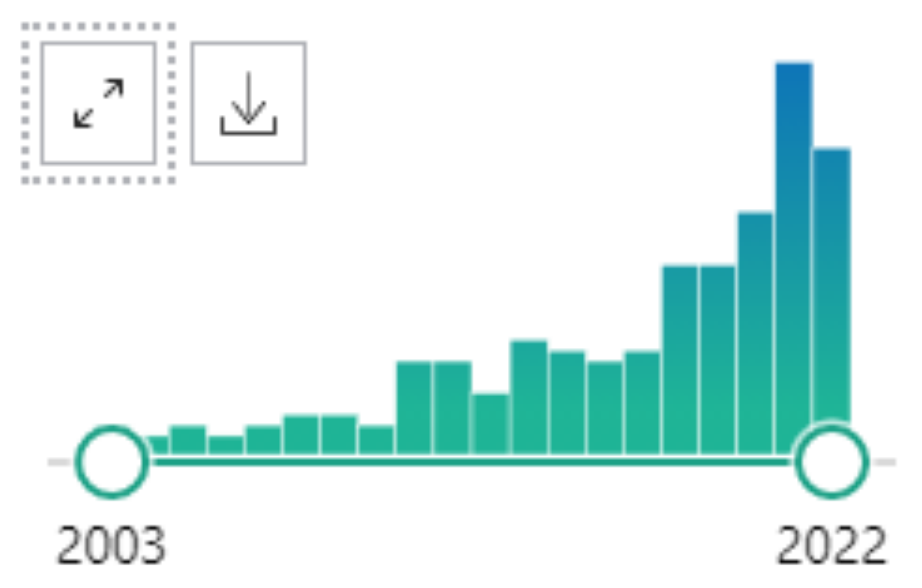


A self-replicating swarm of predatory molecules is rapidly evolving ….

Massed together, the molecules form an intelligent organism that is anything but benign. More powerful by the hour, it has targeted the eight scientists as prey.

www.michaelcrichton.com

NANOMOTORS Search on PUBMED



1 Cite Share
Application of Nanotechnology in Thrombus Therapy.
Zhou S, Zhao W, Hu J, Mao C, Zhou M.
Adv Healthc Mater. 2022 Dec 12:e2202578. doi: 10.1002/adhm.202202578. Online ahead of print.
PMID: 36507827 Review.

2 Cite Share
Nanoengineering of biohybrid micro/nanobots for programmed biomedical applications.
Shivalkar S, Chowdhary P, Afshan T, Chaudhary S, Roy A, Samanta SK, Sahoo AK.
Colloids Surf B Biointerfaces. 2022 Nov 24;222:113054. doi: 10.1016/j.colsurfb.2022.113054. Online ahead of print.
PMID: 36446238 Review.

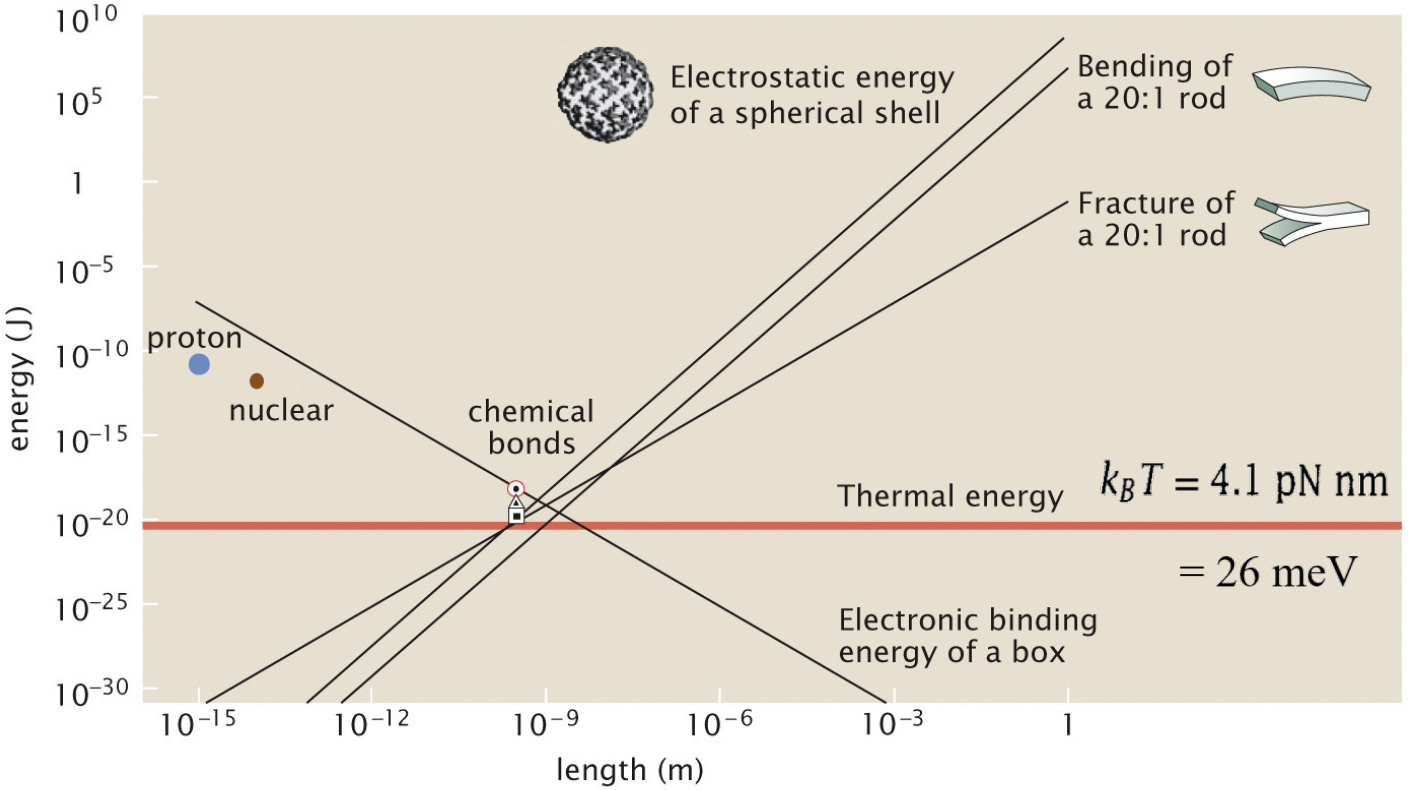
3 Cite Share
Controlled propulsion of micro/nanomotors: operational mechanisms, motion manipulation and potential biomedical applications.
Liu T, Xie L, Price CH, Liu J, He Q, Kong B.
Chem Soc Rev. 2022 Dec 12;51(24):10083-10119. doi: 10.1039/d2cs00432a.
PMID: 36416191 Review.

4 Cite Share
Achieving Control in Micro-/Nanomotor Mobility.
Fusi AD, Li Y, Llopis-Lorente A, Patiño T, van Hest JCM, Abdelmohsen LKEA.
Angew Chem Int Ed Engl. 2022 Nov 22:e202214754. doi: 10.1002/anie.202214754. Online ahead of print.
PMID: 36413146 Review.

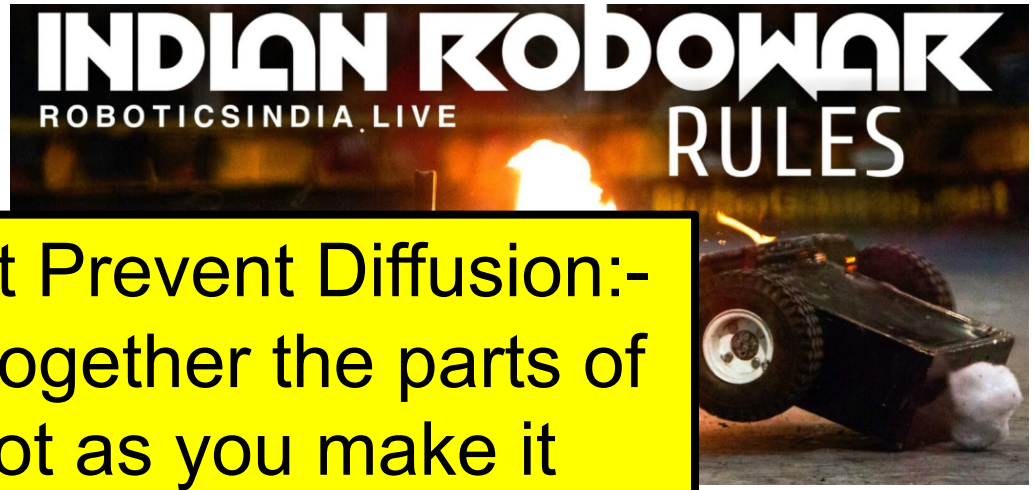
5 Cite Share
"Motile-targeting" drug delivery platforms based on micro/nanorobots for tumor therapy.
Zhang D, Liu S, Guan J, Mou F.
Front Bioeng Biotechnol. 2022 Sep 16;10:1002171. doi: 10.3389/fbioe.2022.1002171. eCollection 2022.
PMID: 36185435 Free PMC article. Review.

TRUTHS OF LIFE AT THE NANOSCALE : **(1) DIFFUSION** **(2) OVERDAMPING**

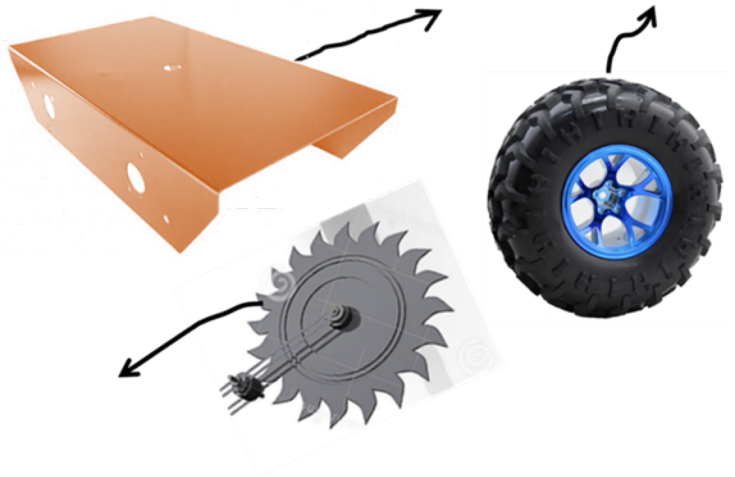
These defy the most basic assumptions of Macroscale Machines



ROBOWARS with **NANOSCALE** Robots (LESSON #1 – DIFFUSION DOMINATES)



Must Prevent Diffusion:-
Tie together the parts of Robot as you make it



CLAIM

Robot Components are GONE within seconds

How fast does something diffuse ?

$$D = \frac{k_B T}{6\pi\eta a}$$

Derived by Einstein in 1905

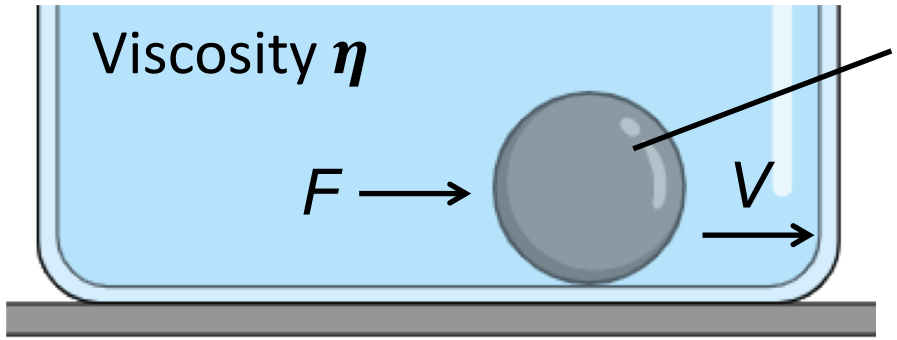
D = diffusion constant
$k_B T$ = Thermal energy at abs. temp. T
η = Visc. of water = 0.001 N-sec/m^2
a = Radius of diffusing object

For a Globular Protein of Radius = 5 Nanometers
$D \approx 50$ micron^2/second in water (Do it yourself)

Distance diffused in time t is $d = \sqrt{2nDt}$
For 3 dimensions (n = 3) :-
$d \approx$16000 Nanometers in 1 second

For a Robot of Radius = 1 Meter
Repeat the above Calculations, you will find :-
$d \approx$ 1 Nanometer in 1 second (Robot is still there)

ROBOWARS with NANOSCALE Robots (LESSON #2 – VISCOSITY DOMINATES)



Mass m
Radius a

Apply Force.
Object Starts Moving

This is Useless at the Nanoscale …

$$m\frac{dV}{dt} + \gamma V = F \qquad (\gamma = 6\pi\eta a)$$

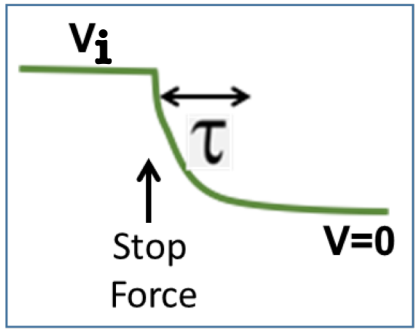
Now, stop the Force (F = 0)

$$v(t) = v_i * \exp(-t/\tau)$$

Relaxation time

$$\tau = \frac{m}{\gamma}$$

Vel. Drops 1/e (37%)



Cricket Ball
Mass = 200 gm
Radius = 3.5 cm
} τ = 300 sec

Protein Machine
Mass = 100 KiloDalton = 10^{-19} gm
Radius = 5 nanometer
} τ = 1 Nanosecond

OVERDAMPING AT NANOSCALE. Inertia negligible. Need constant energy to move predictably

The Nobel Prize in Chemistry 2016

… For the Design and Synthesis of Molecular Machines

Jean-Pierre Sauvage
University of Strasbourg

Sir James Fraser Stoddart
Northwestern University,
Evanston, IL, USA

Bernard Lucas Feringa
University of Groningen,
Netherlands

To make a Molecular Machine, need Mechanically Interlocked molecular assemblies that have significant freedom of movement.

→ Need Loops and Stoppers for confinement

Scientific Background on the Nobel Prize in Chemistry 2016

MOLECULAR MACHINES

MORE INFO :-
LINK

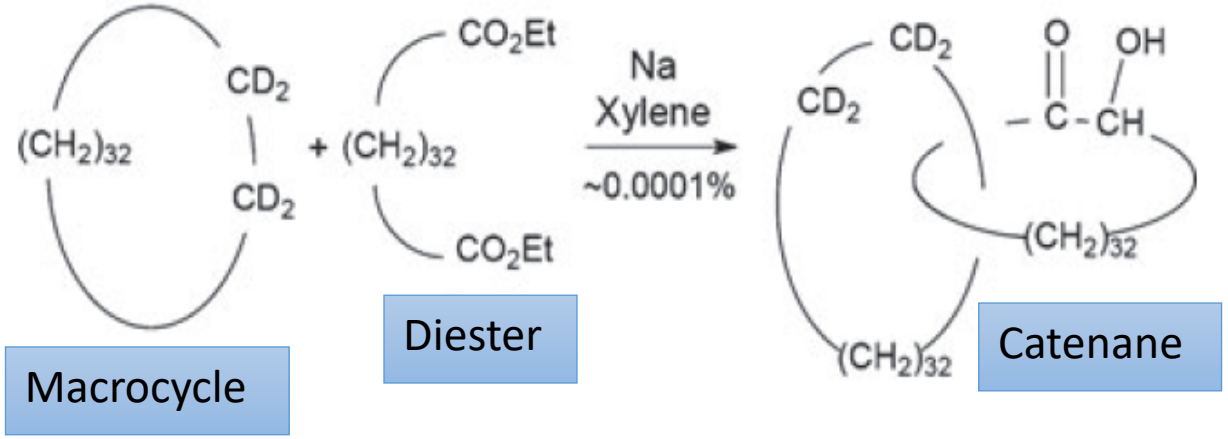
compiled by the Class for Chemistry of the Royal Swedish Academy of Sciences

Two major technology advances have proven particularly useful in addressing the complex challenge of constructing machines at the molecular scale. The first of these involves *topological entanglement* and so-called *mechanical bonds*, while the second is based on *isomerisable (unsaturated) bonds*, and both advances have resulted in large ranges of complex structures with machine-like functions.

Extremely difficult to synthesize Interlinked chemical structures (Very low yields in previous attempts)

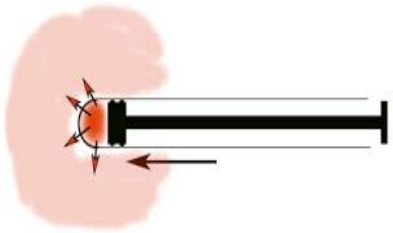
CATENANE

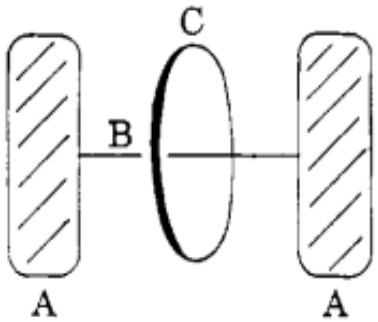
Wasserman, E.
The Preparation of Interlocking Rings: A Catenane.
JACS **1960**

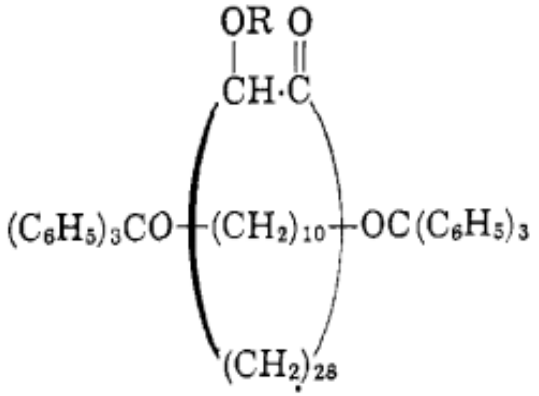


ROTAXANE

Harrison, I. T.; Harrison, S.
Synthesis of a Stable Complex of a Macrocycle and a Threaded Chain.
JACS **1967**

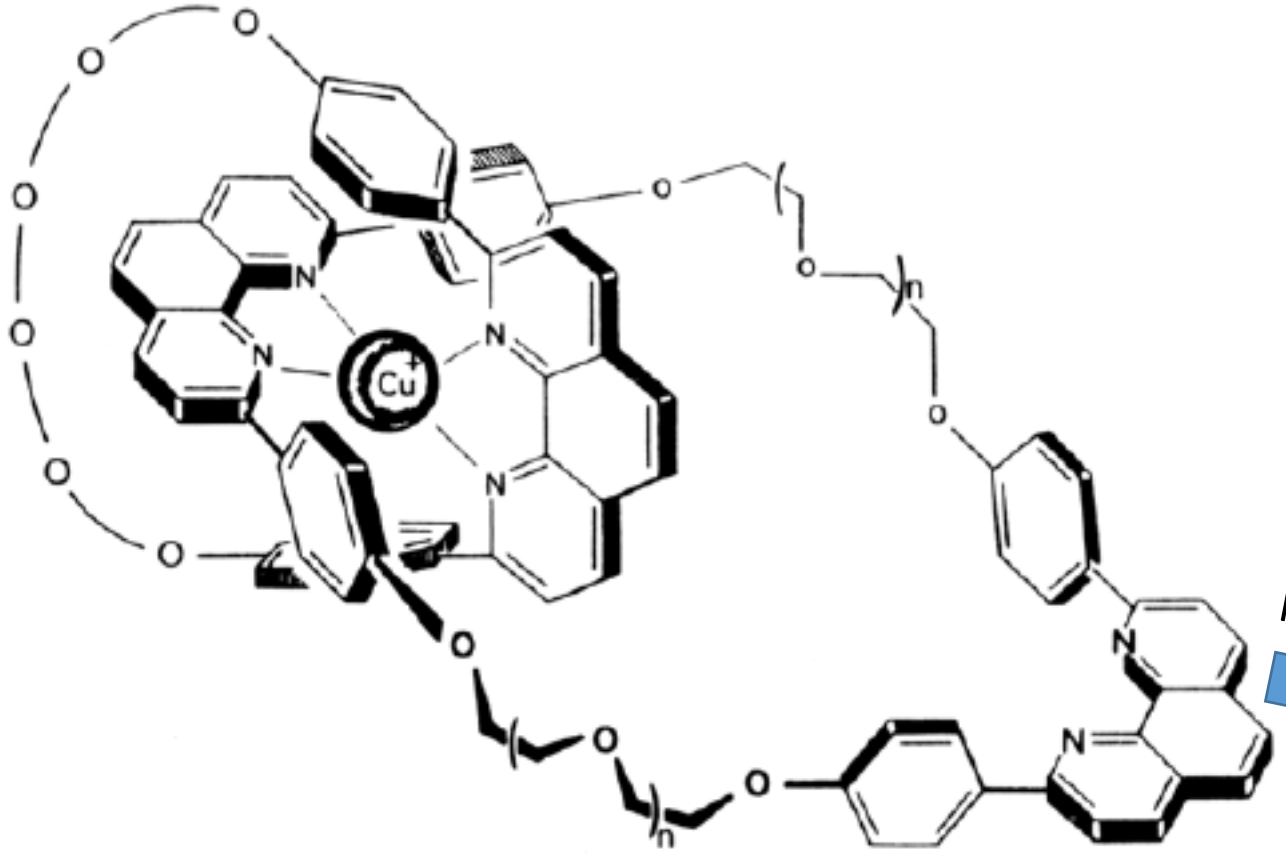


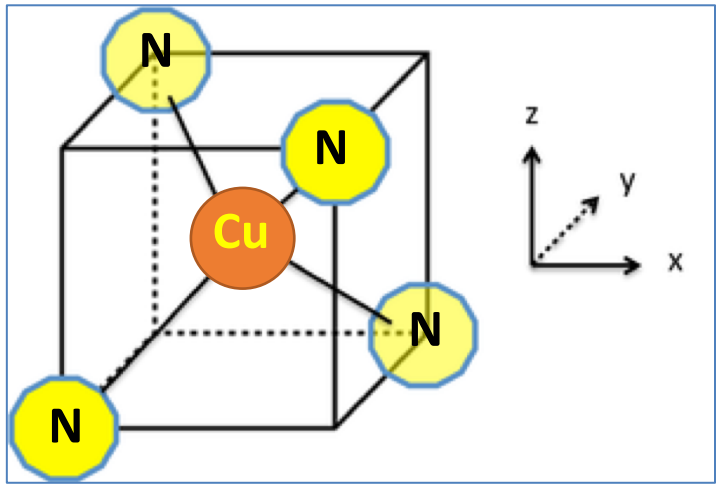




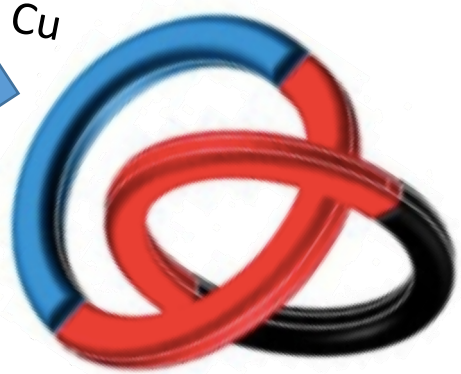
Jean-Pierre Sauvage

Copper(I) template synthesis of an interlocked Catenane





Remove Cu



Only thermal motion (cannot extract useful work)

Later work:- Electrochemically induced predictable motion

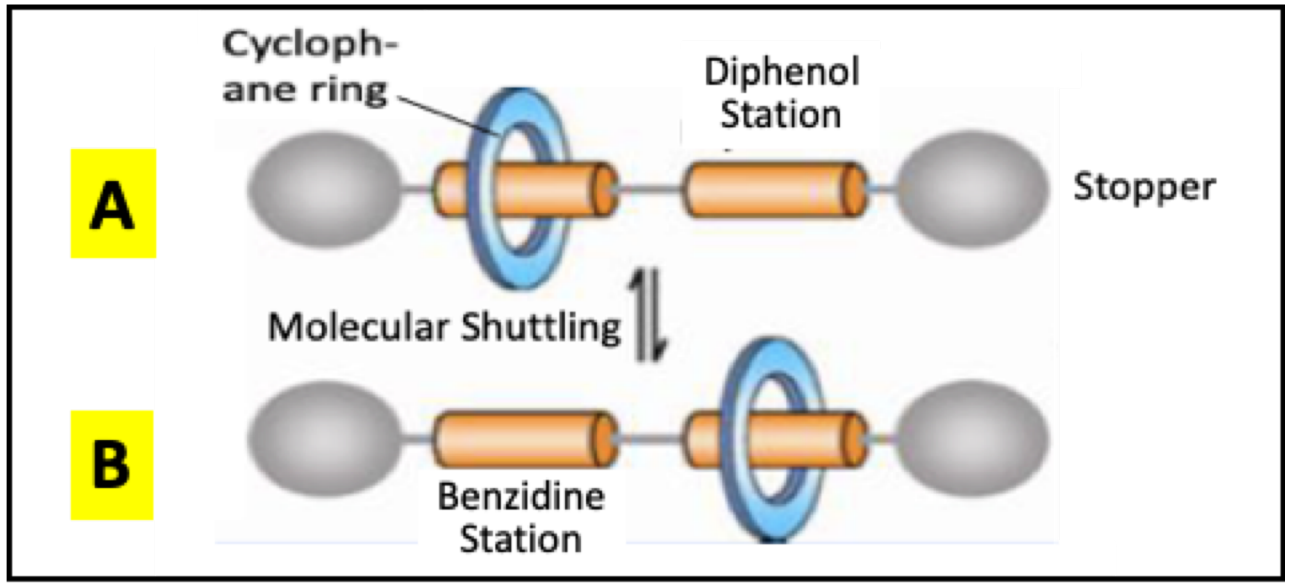
LINK (Fig 1)

MORE INFORMATION : LINK

James Fraser Stoddart

Synthesized mechanically interlocked molecules **(Rotaxanes)** with interactions between electron-rich and electron-poor aromatic groups

LINK :- Switchable Molecular Shuttle. *Nature* **1994**

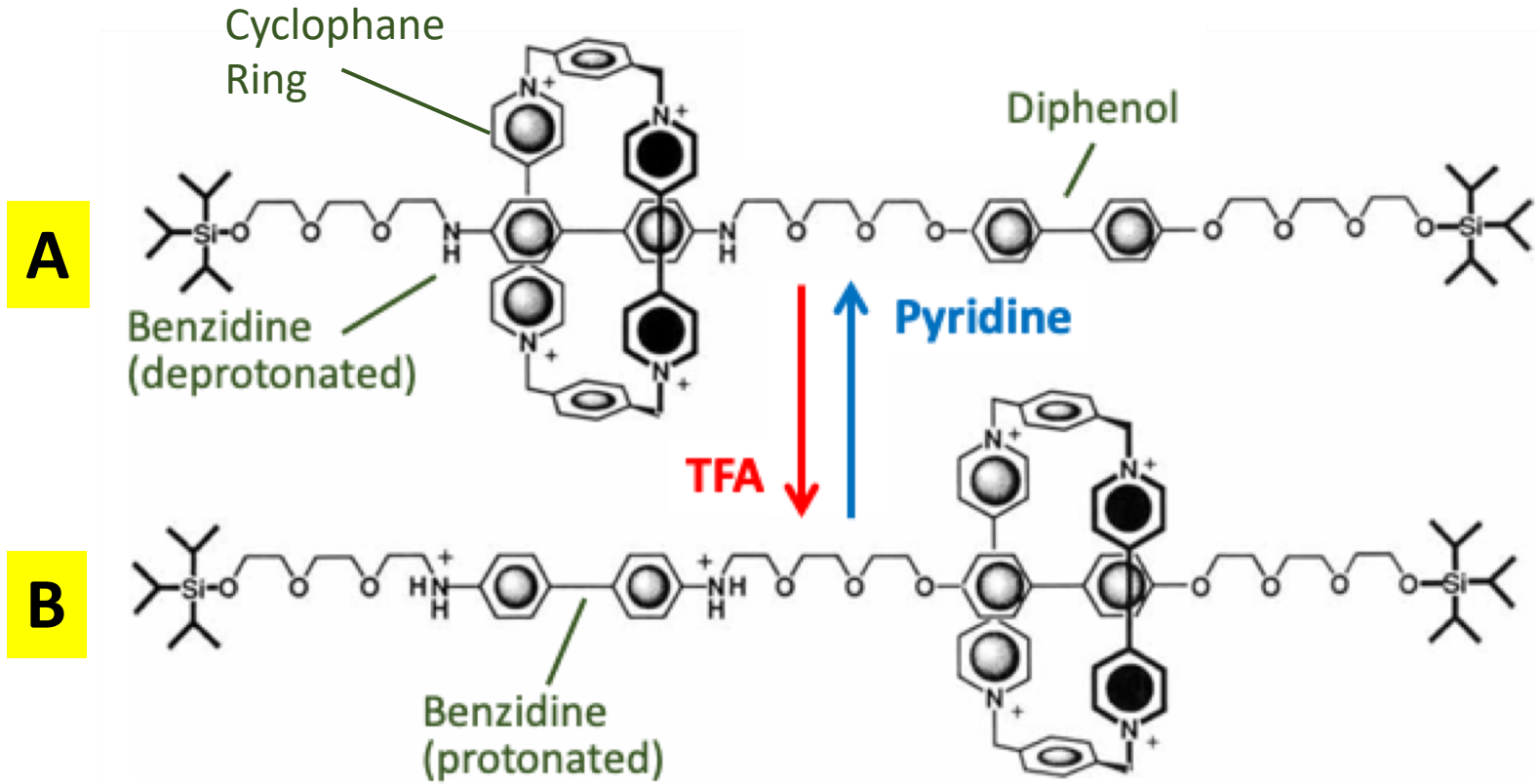


Add TFA (an acid)

→ Benzidine group is protonated
→ Protonated Benzidine repels the cationic Cyclophane Ring
→ Ring moves to Diphenol group

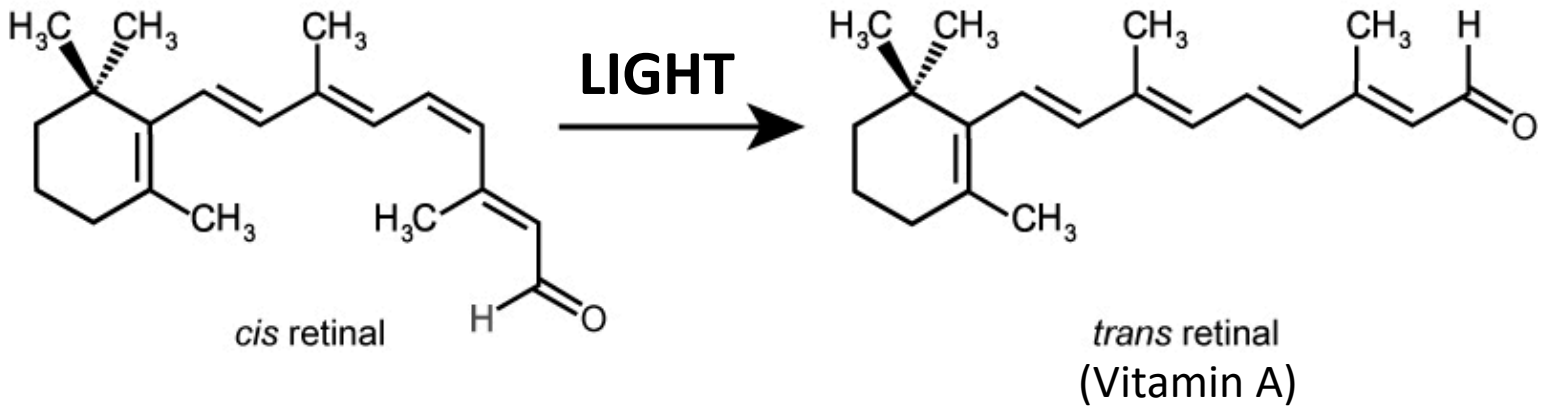
Add Pyridine (a weak base)

→ Benzidine is deprotonated
→ Deprotonated Benzidine binds stronger to Cyclophane Ring than Diphenol



Bernard L. Feringa

Light-Driven Monodirectional Molecular Rotor.
Nature **1999**



Feringa was inspired by the mechanism of VISION to make Rotary motors

Rod cells (photoreceptor cells) in the eye have a trans-membrane protein called Rhodopsin.

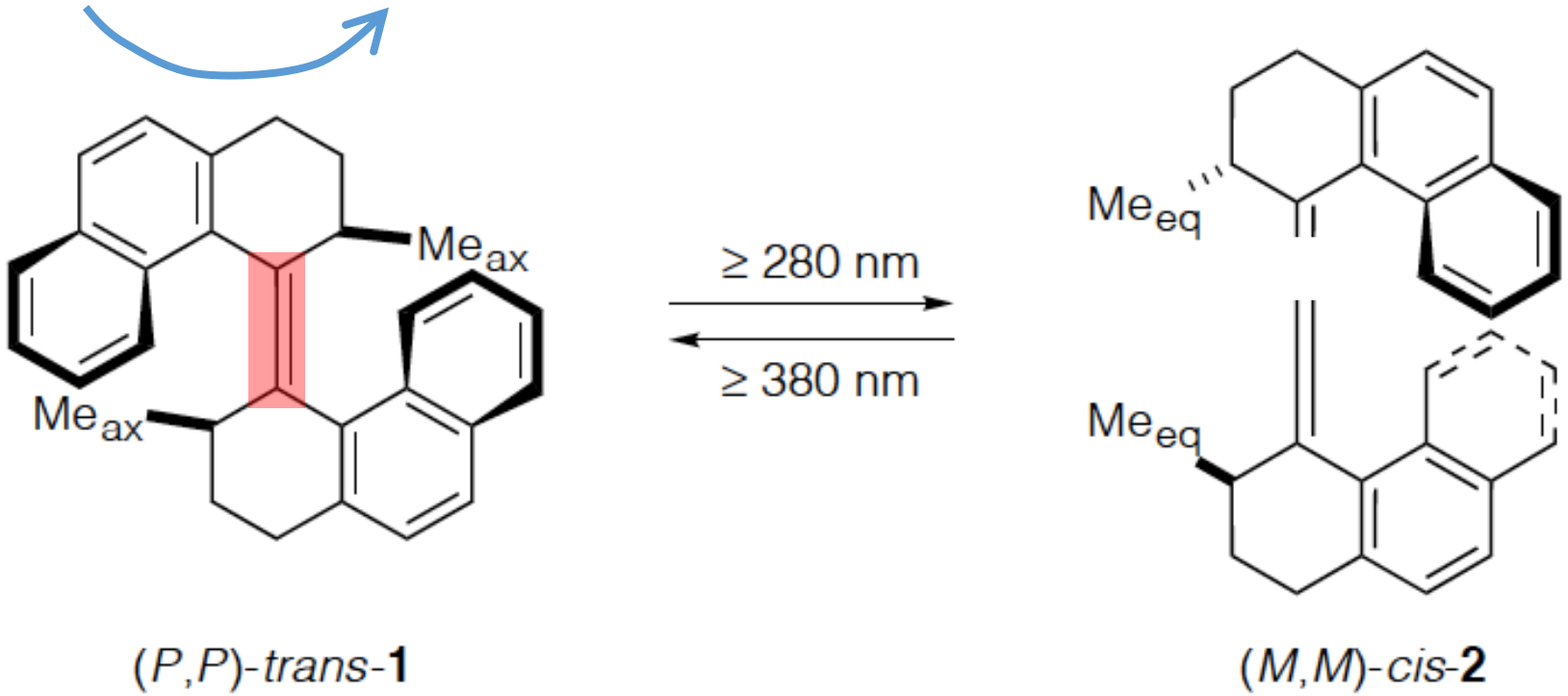
The Retinal molecule fits into Rhodopsin.
Retinal undergoes cis-trans isomerization in response to light

This causes a change in the rhodopsin molecule and transmits a signal
(so that we can see)

Rotary Motors

Light induced Rotational Isomerism

Cis-Trans



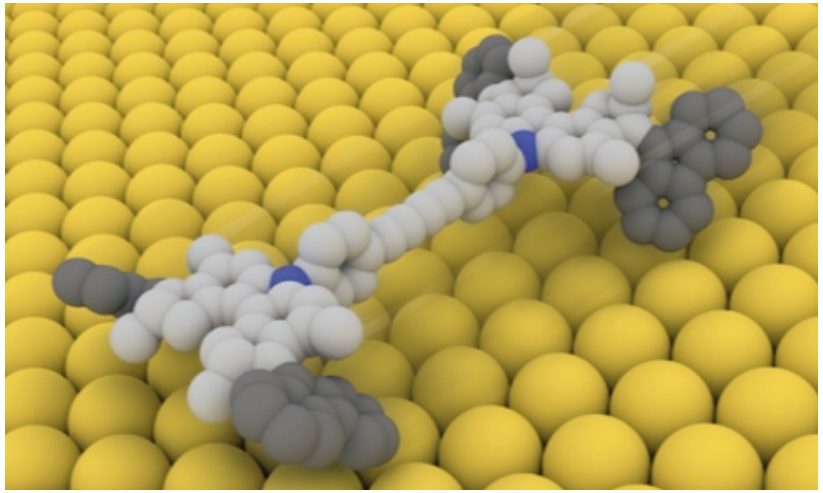
(*P*,*P*)-*trans*-**1** (*M*,*M*)-*cis*-**2**

Light-Driven Monodirectional Molecular Rotor. *Nature* **1999**

Only Light-driven part of the cycle shown

For more details, go to the Link shown

Human Made	Natural
We have to make it	Self-replicating (From DNA)
Non-autonomous*	Autonomous
→ Can we make an ATP driven motor ?	
Single part that moves	**Multiple integrated parts**
Single Machines:- Cooperativity ?	Large arrays of Machines can function
How to connect to the Macroscopic world?	**Already connected**
Synthesis is massively parallel	**Rate Limited by many biological factors**
**Nature, June 2016 : An autonomous chemically fuelled small-molecule motor, D. Leigh group*	

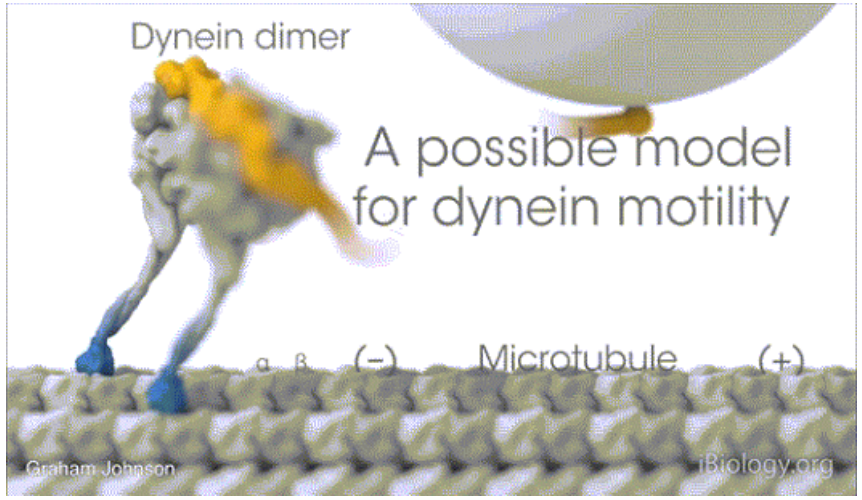


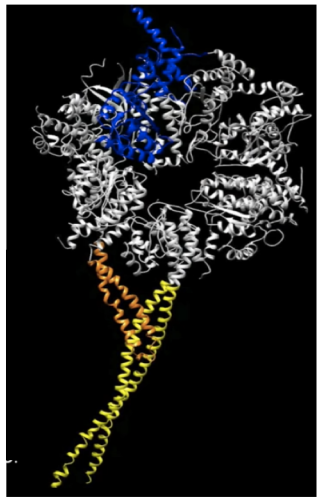
Kudernac, et al
Nature **2011**

Why is all this useful ?

... a little bit like asking stone age man/woman, when he/she's built the wheel, to predict motorways -- David Leigh

Dynein (Biological motor)





iBiology.org, Ron Vale

Nanocar (Human made)
Kudernac, et al, *Nature* **2011**

FOR YOU TO THINK ABOUT

- Read about the Reynolds number. Calculate Reynolds number for following in Water :-

(1) Protein of 100 KDa (2) E. Coli bacteria (3) Human being

How is this relevant to design of Nano/Micro scale machines ?

- What is the potential energy landscape of the Rotaxane complex (Feringa experiment)?

How does this landscape change when TFA or Pyridine are added?