KUNGL. VETENSKAPS-AKADEMIEN
THE ROYAL SWEDISH ACADEMY OF SCIENCES

Royal Swedish Academy of Sciences
Nobel Committee for Chemistry

Fraser Stoddart Nobel Lecture

Thursday 8 December 2016

Design and Synthesis of Molecular Machines based on The Mechanical Bond

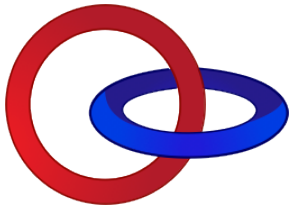
The University of Edinburgh · Queen's University · The University Of Sheffield. · ICI · University of Birmingham · UCLA · Northwestern University 1851

WHAT IS A MECHANICAL BOND?

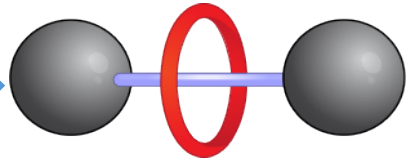
Since there is no Covalent Bond

between the Components

in a



Catenane or **Rotaxane**



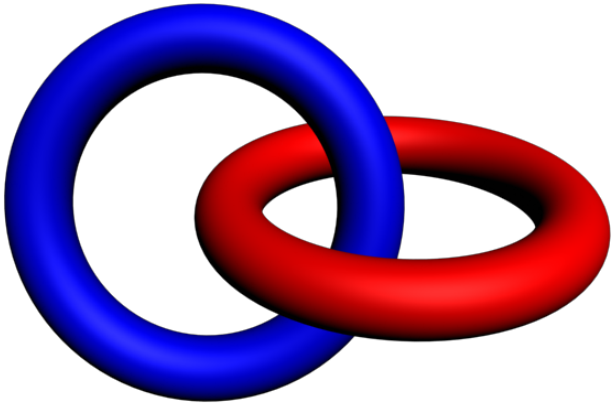
the Linkage

has been called a

Mechanical Bond

H. Frisch *Monatsh. Chem.* **1953**, *84*, 250

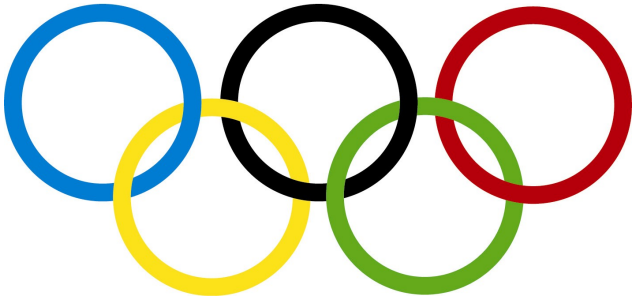
CATENANES AND ROTAXANES

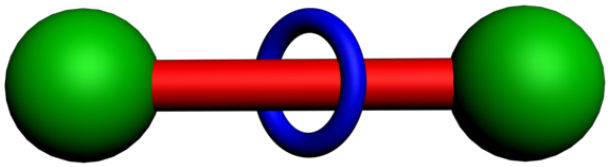


A **Catenane** is a mechanically-interlocked molecular architecture consisting of two or more interlocked macrocycles.

Wikipedia

Lt – *Catena*
Chain

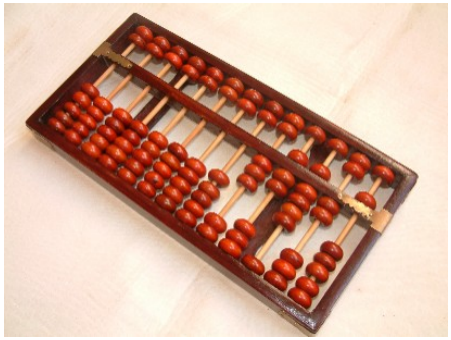




A **Rotaxane** is a mechanically-interlocked molecular architecture consisting of a dumbbell-shaped component threaded through one or more macrocycles.

Wikipedia

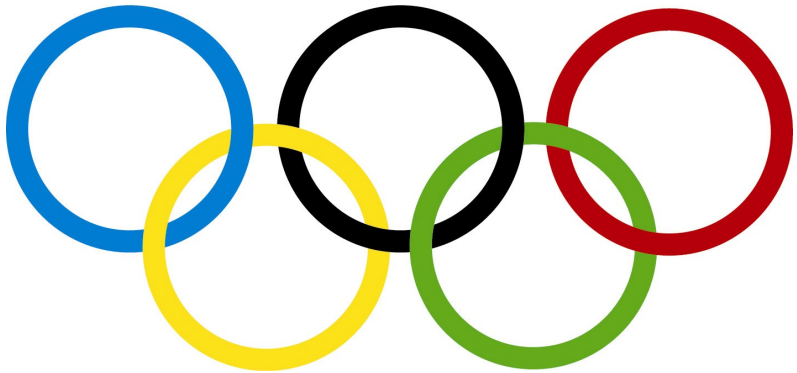
Lt – *Rota / Axis*
Wheel / Axle

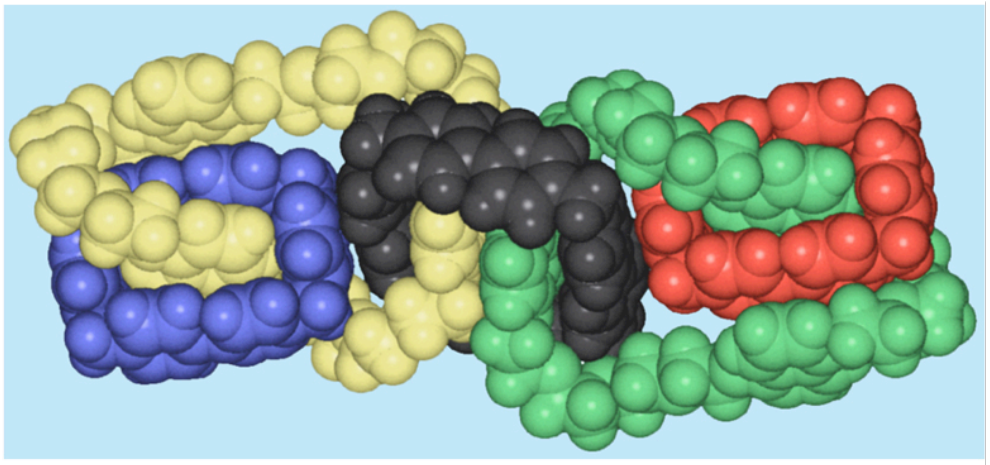


MECHANICALLY **I**NTERLOCKED **M**OLECULEs **MIM**s

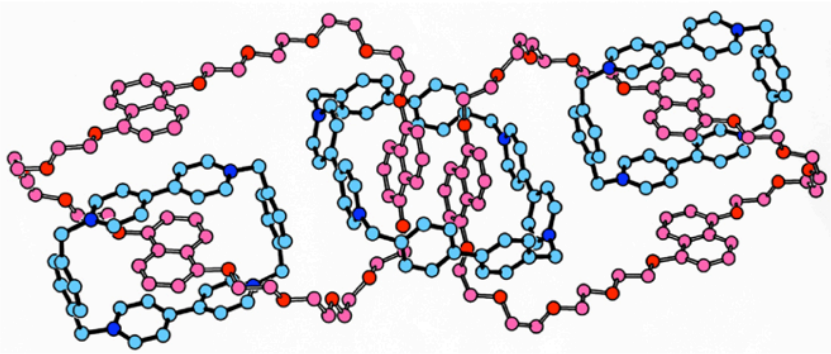
Chem. Soc. Rev. **2009**, *38*, 1802

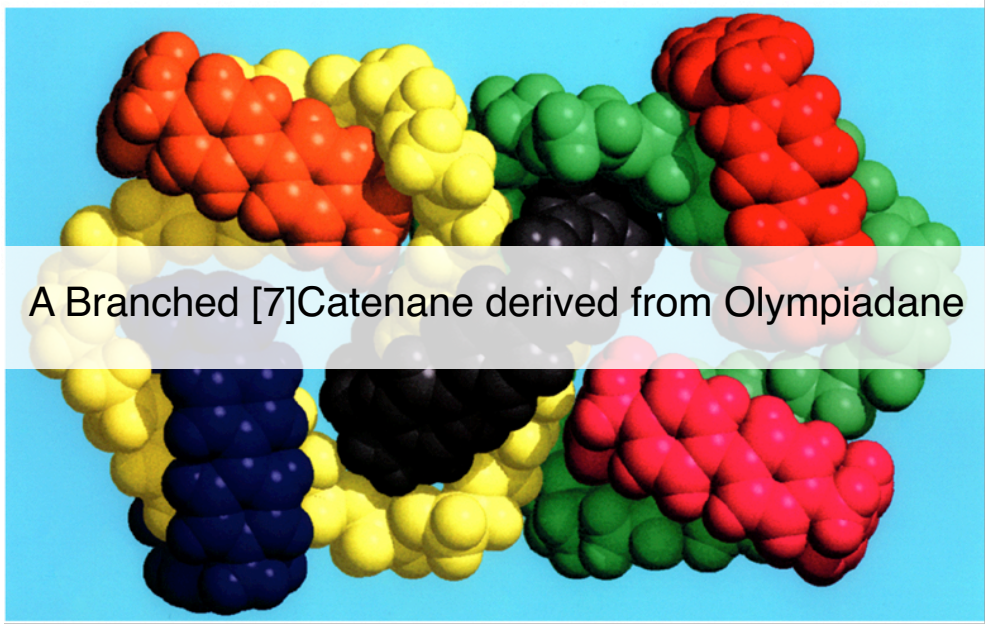
1994 OLYMPIADANE 1997



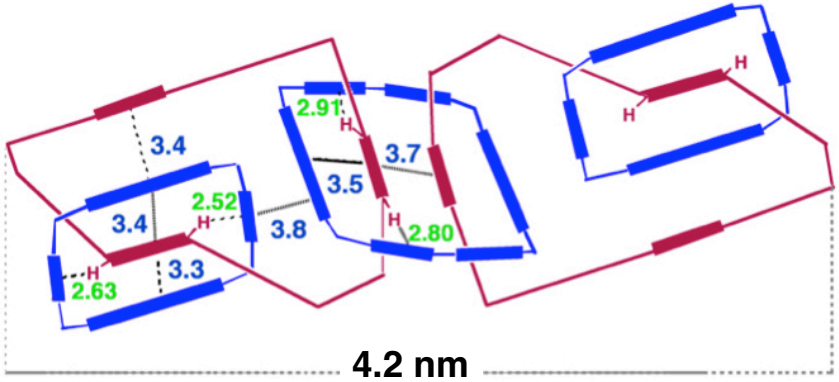


Angew. Chem. Int. Ed. Engl. **1994**, *33*, 1286





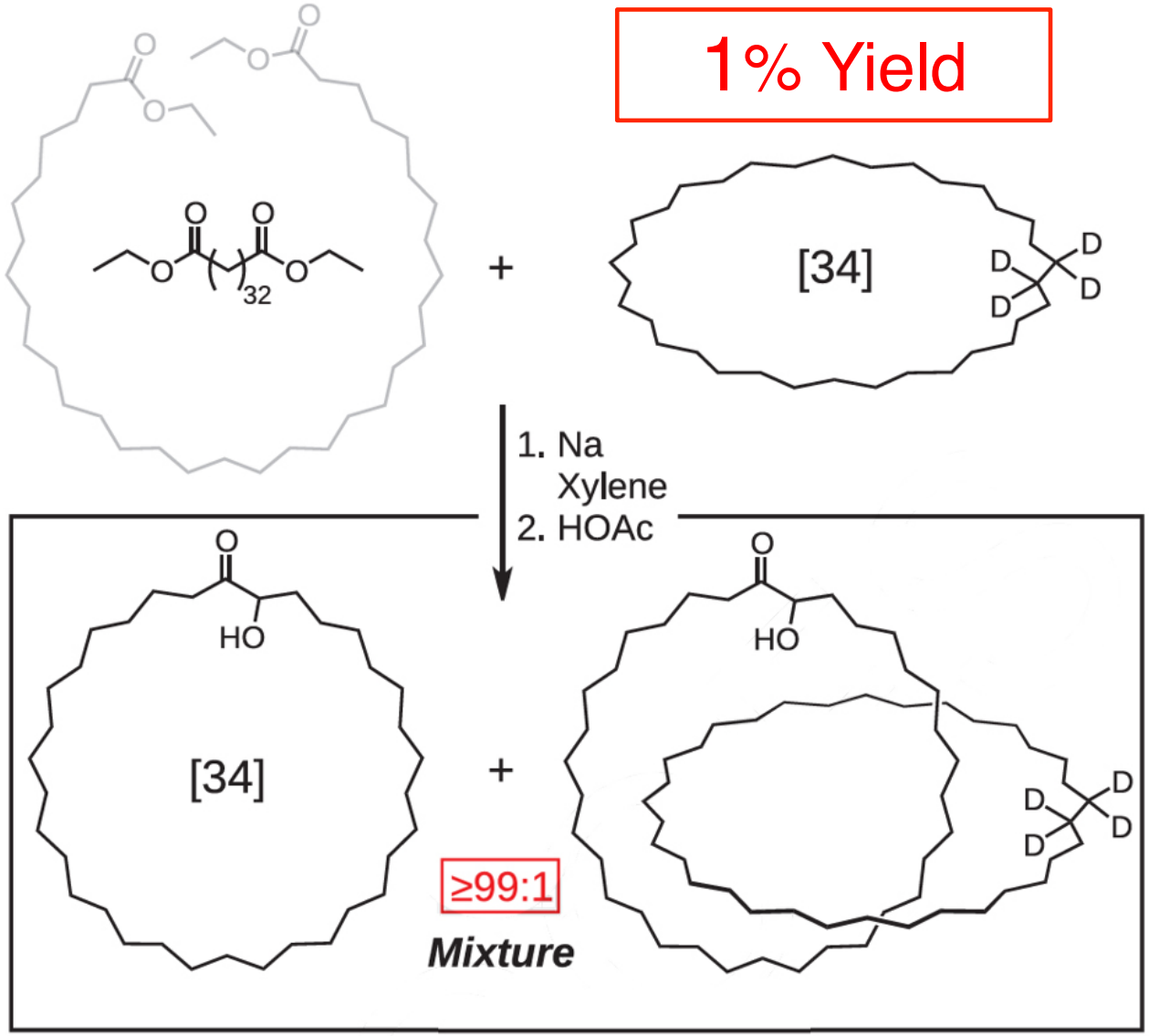
A Branched [7]Catenane derived from Olympiadane



Angew. Chem. Int. Ed. Engl. **1997**, *36*, 2070

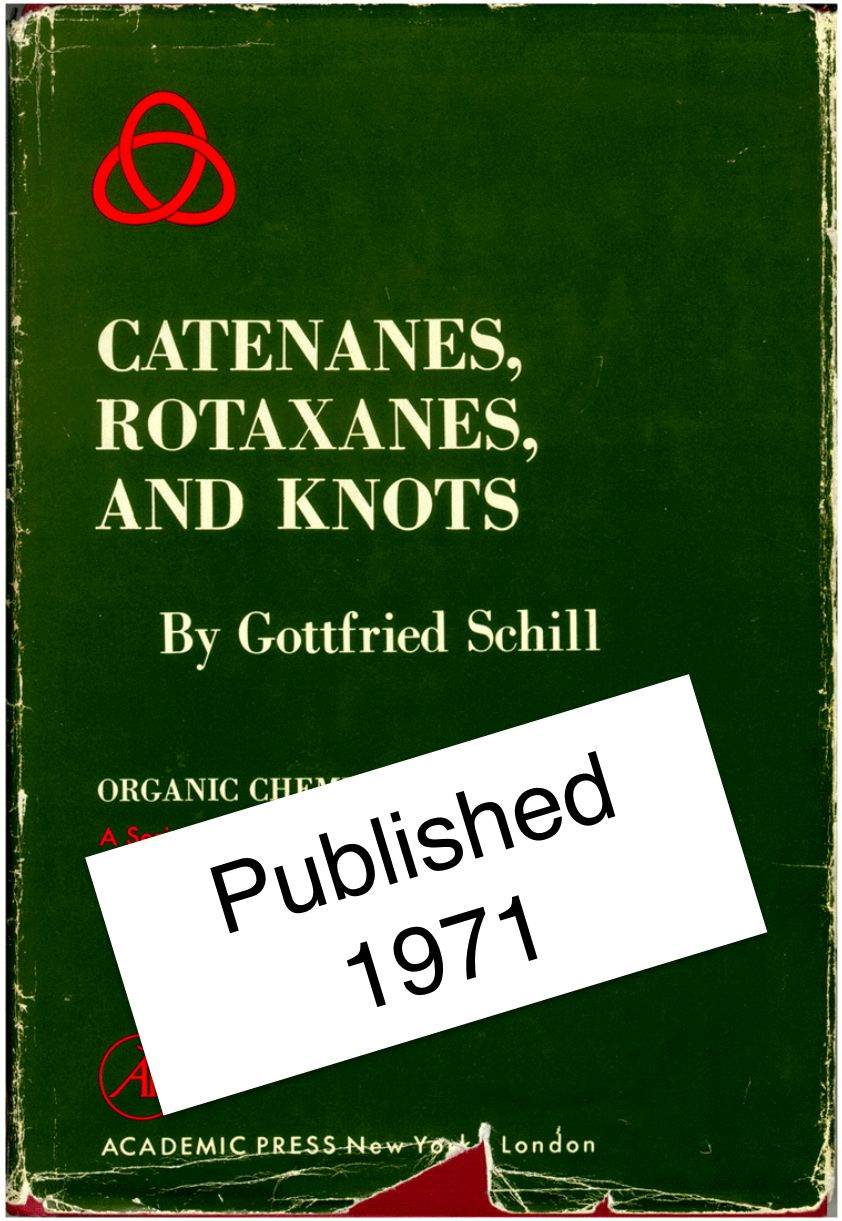
1960 STATISTICAL SYNTHESIS 1960

Ed Wasserman

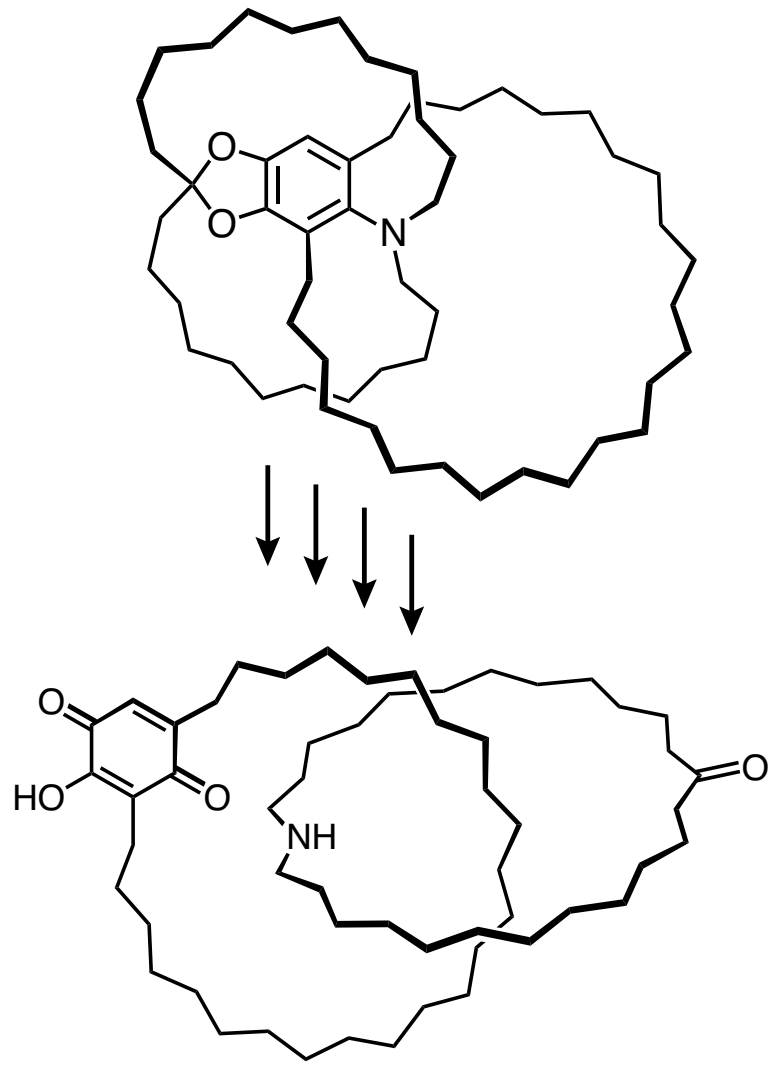


J. Am. Chem. Soc. **1960**, *82*, 4433

1964 DIRECTED COVALENT SYNTHESIS 1964

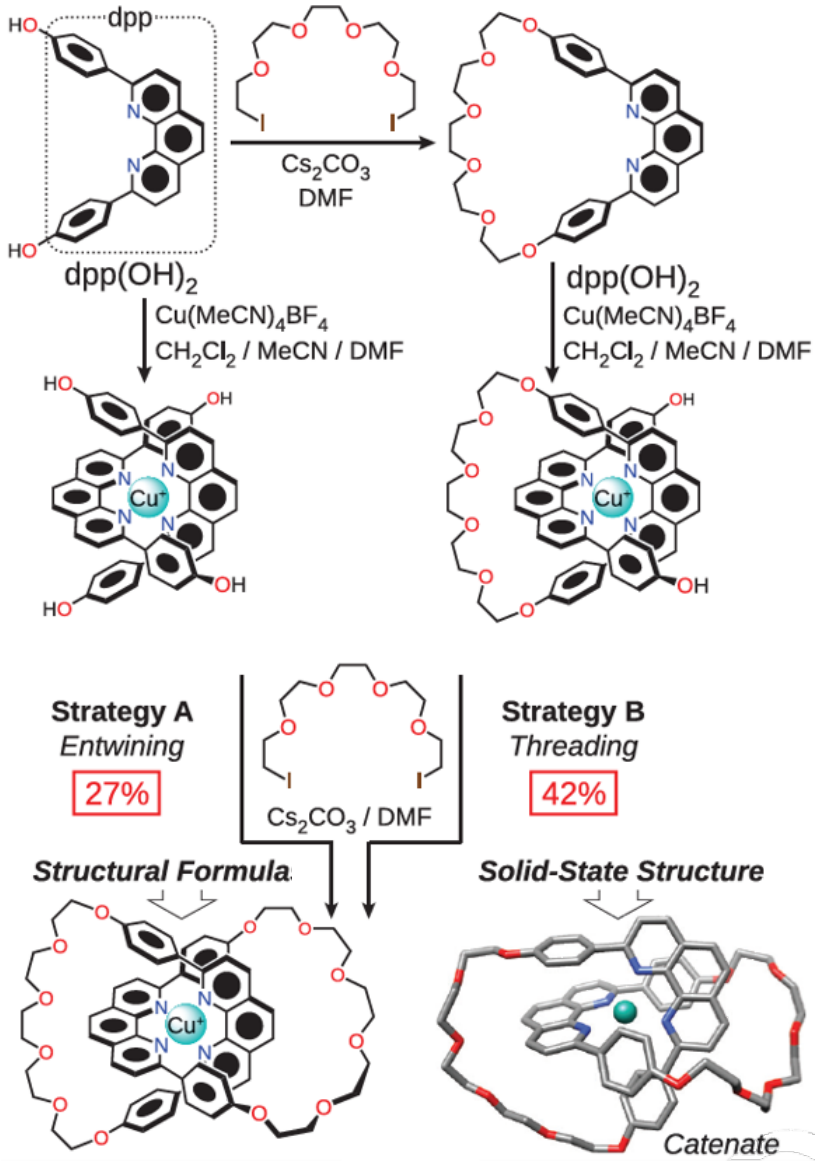


Gottfried Schill



Angew. Chem. Int. Ed. Engl. **1964**, *3*, 546

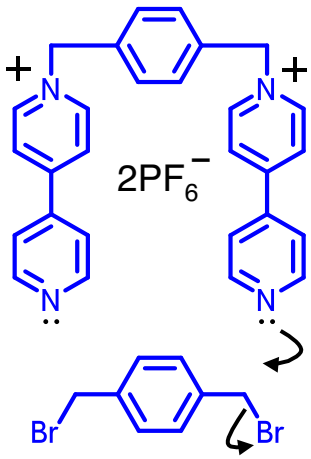
1983 TRANSITION METAL TEMPLATION 1983



Tetrahedron Lett. **1983**, *24,* 5095

Jean-Pierre Sauvage

1989 DONOR-ACCEPTOR TEMPLATION 1989

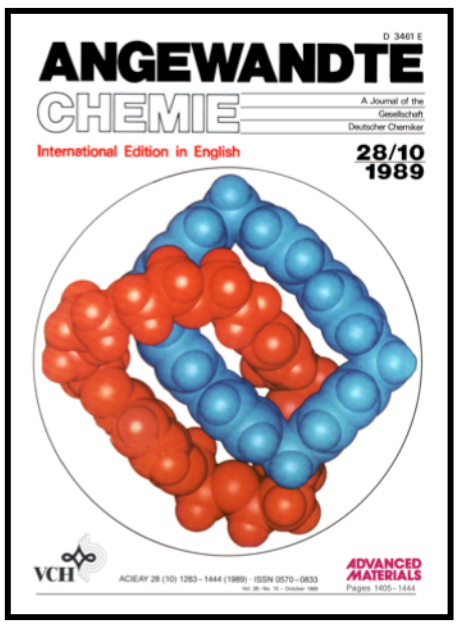


MeCN

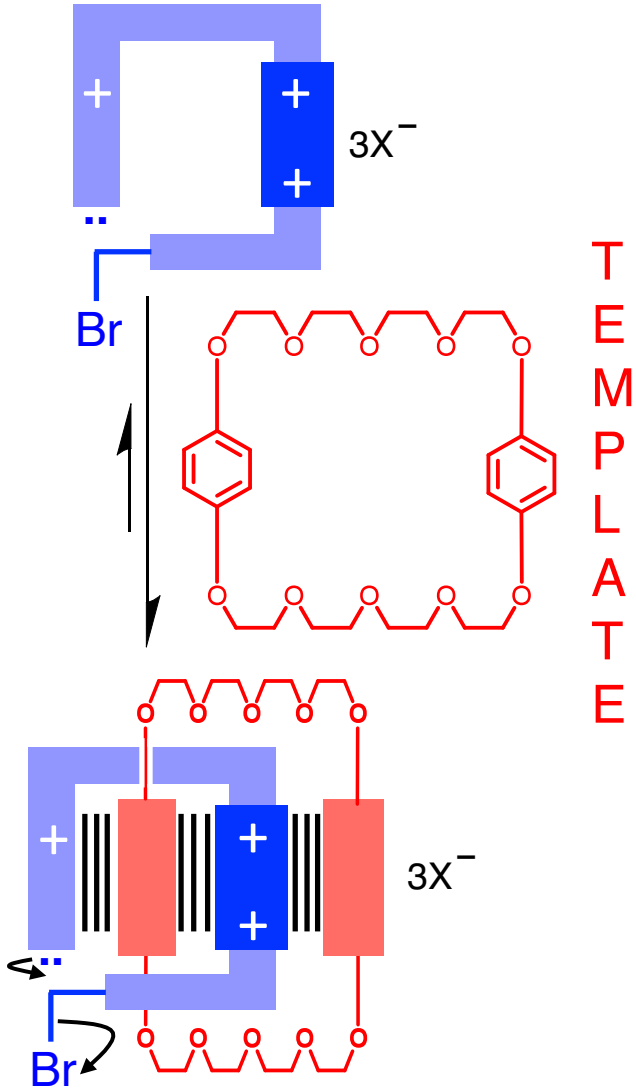
Room Temperature

70%

NH_4PF_6 / H_2O

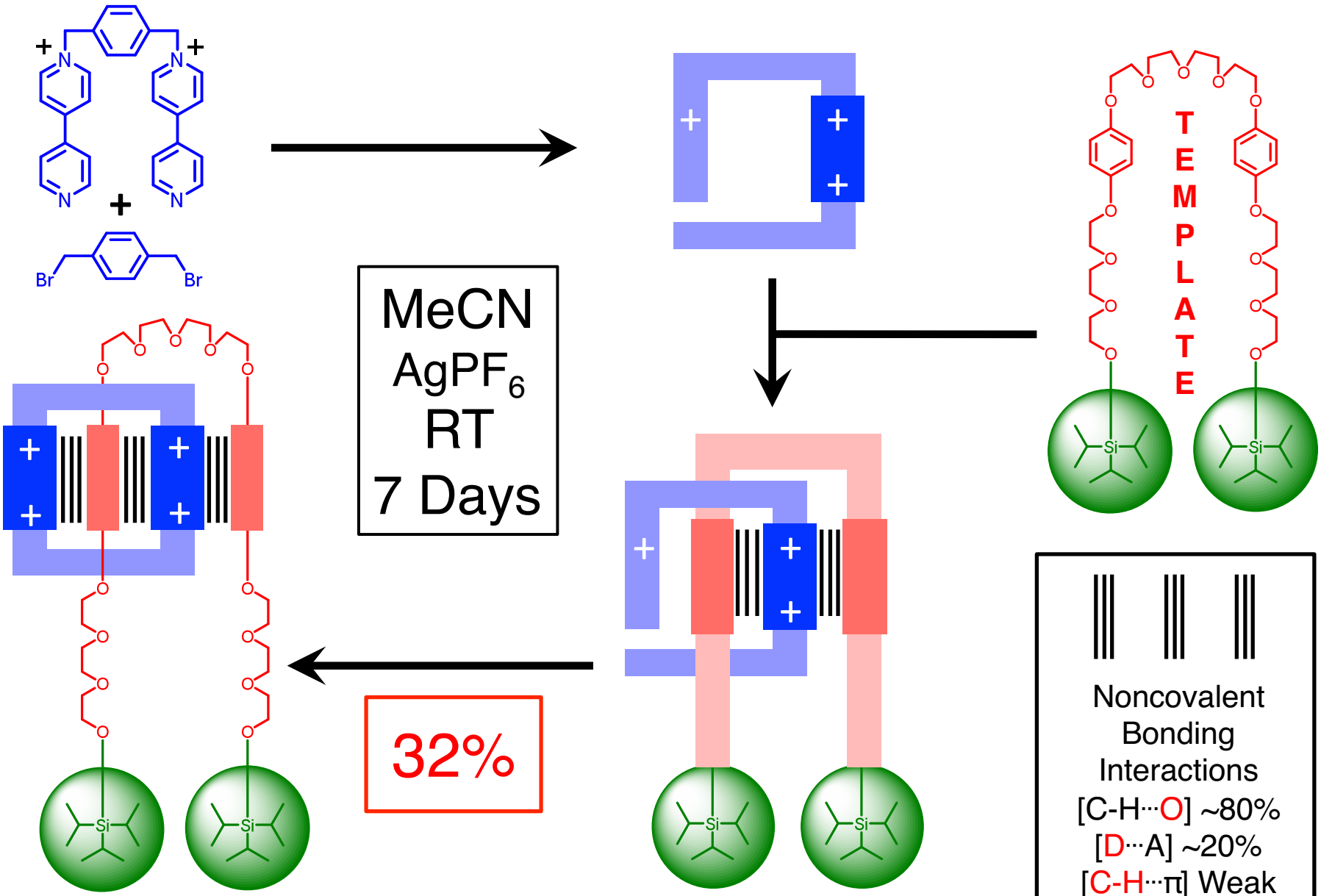


Noncovalent Bonding Interactions
[C–H···O] ~80%
[D···A] ~20%
[C–H···π] Weak



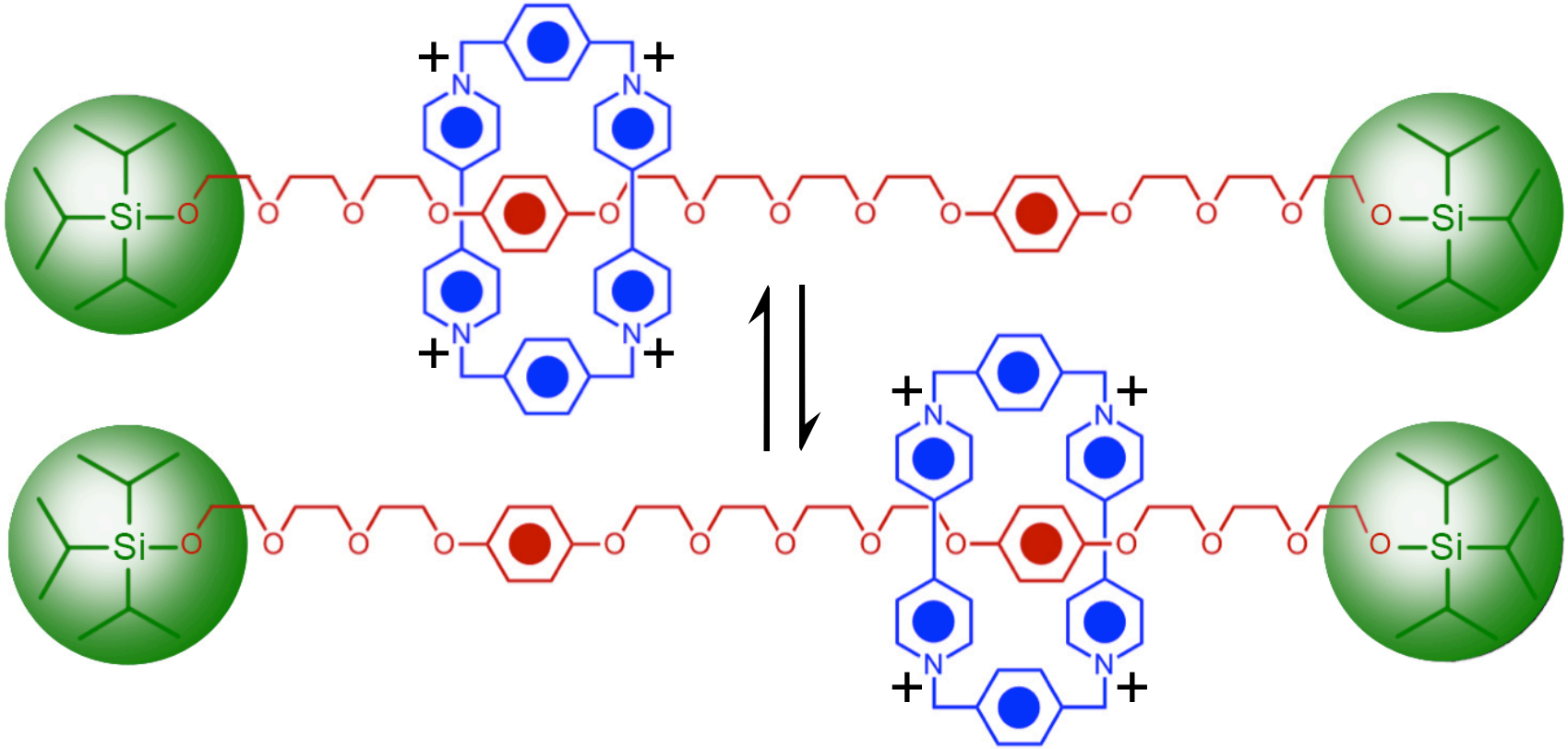
Angew. Chem. Int. Ed. Engl. **1989**, *28*, 1396

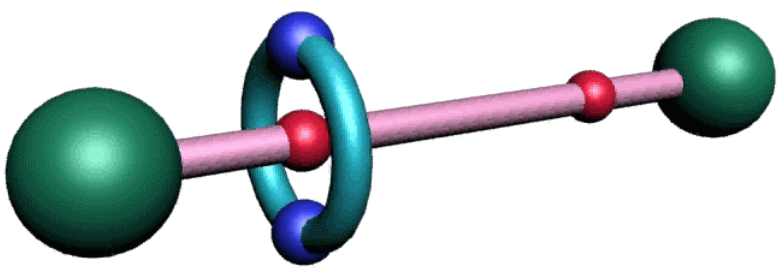
1991 A DEGENERATE [2]ROTAXANE 1991



J. Am. Chem. Soc., **1991**, *113*, 5131

A MOLECULAR SHUTTLE

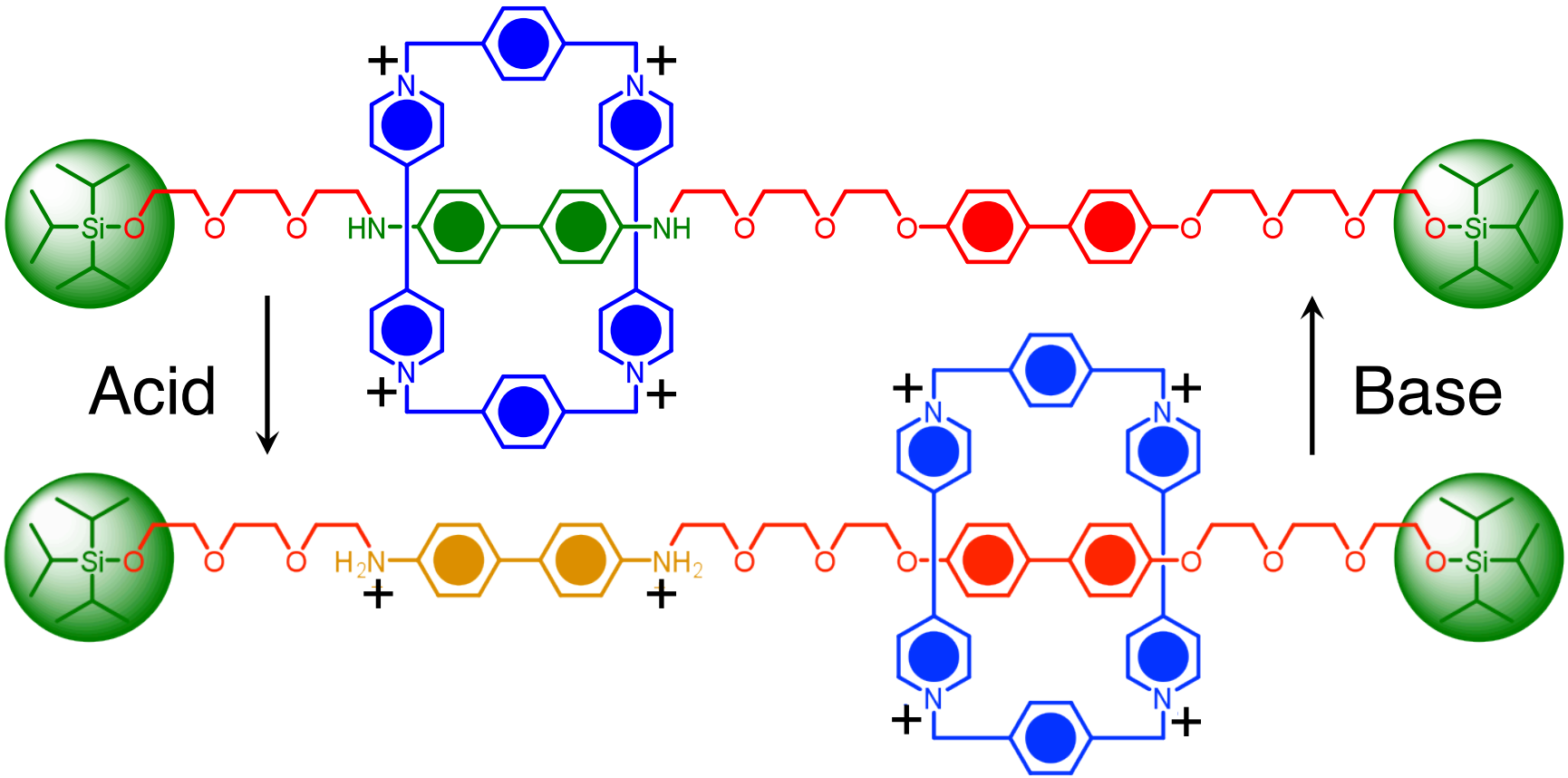


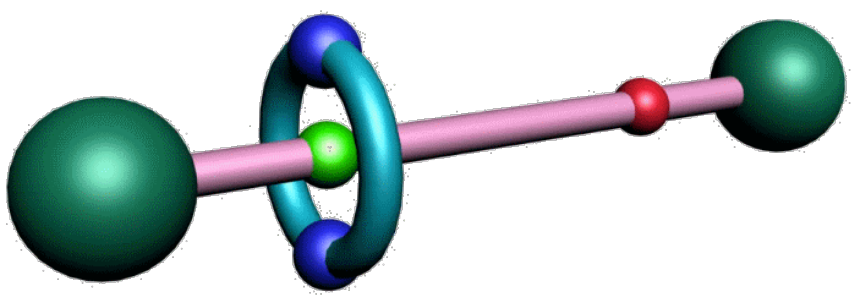


~ 2000 times / sec
@ RT in CD_3COCD_3

J. Am. Chem. Soc. **1991**, *113*, 5131

1994 A MOLECULAR SWITCH 1994



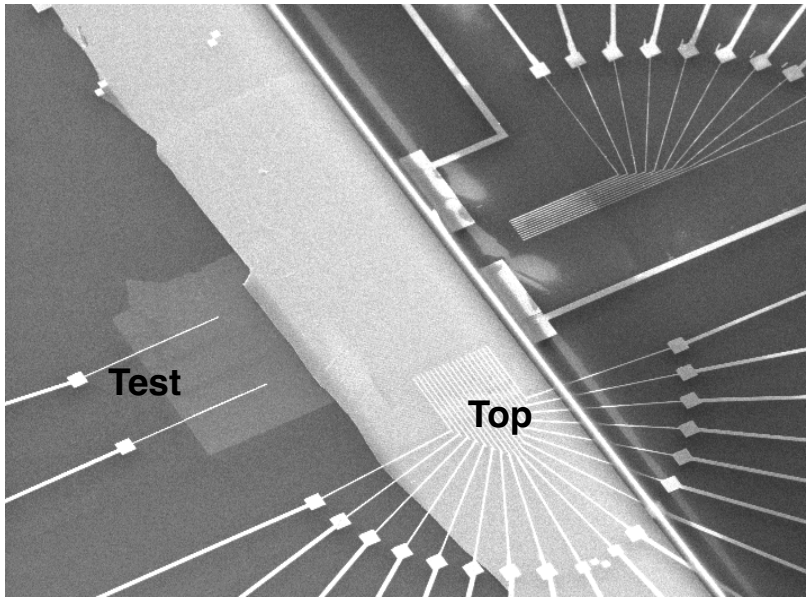


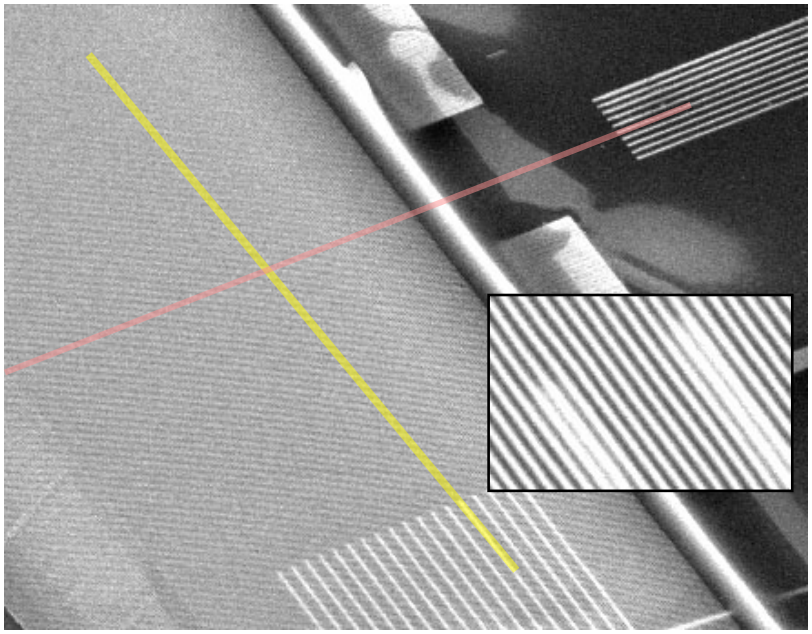
Under pH Control in CD_3CN

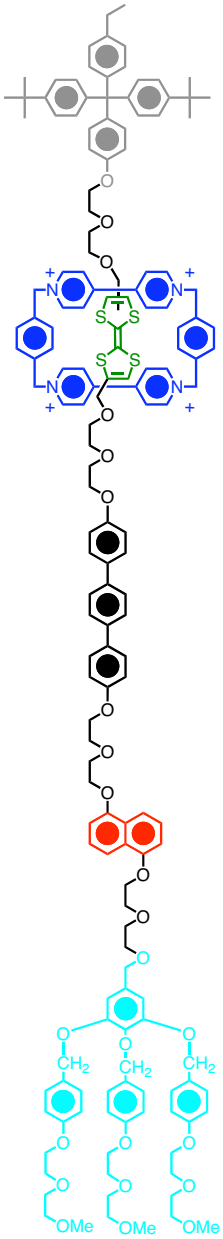
Nature **1994**, *369*, 133

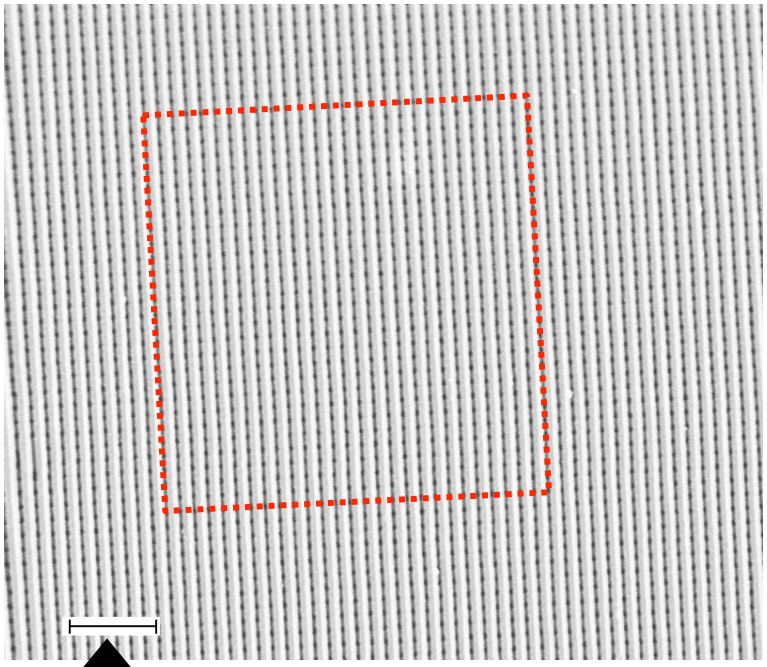
FABRICATING CROSSBAR DEVICE

160-KBit MOLECULAR RAM









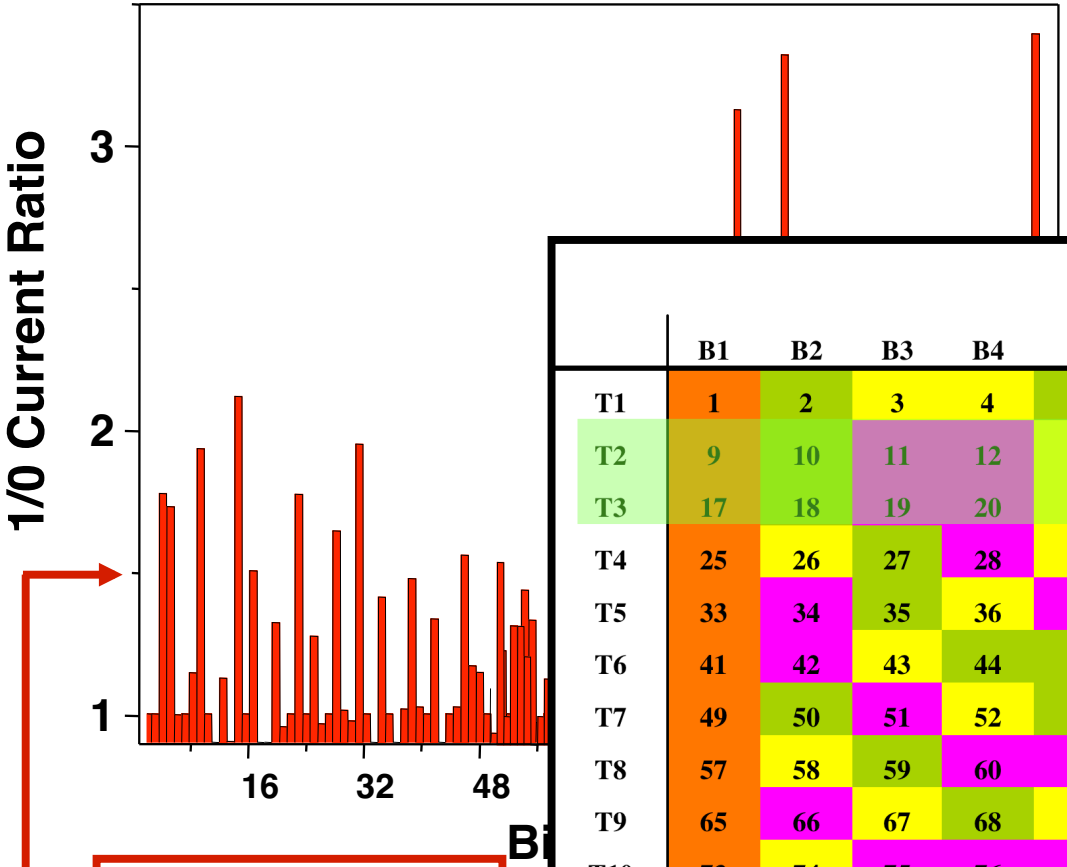
200 nm Scale Bar

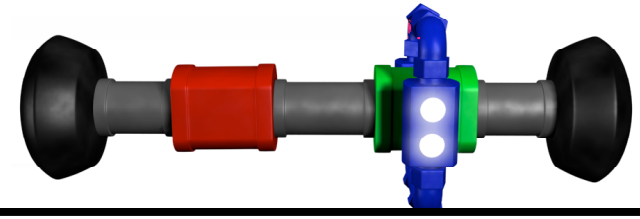
Wires 16 nm Wide
~100 Bistable Rotaxanes
@ each Junction
2500 Junctions
out of
160000 Probed
0.08% Circuit Capacity
Tested

Jim Heath

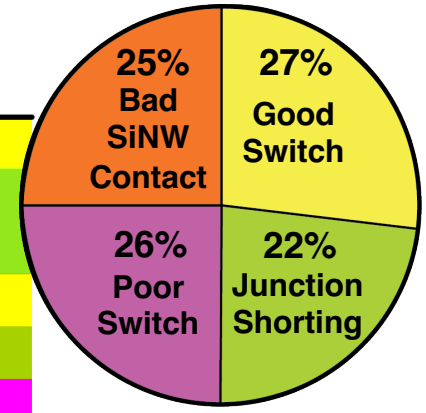
Nature **2007**, *445*, 414

TESTING 128 BITS





	B1	B2	B3	B4	B5	B6	B7	B8
T1	1	2	3	4	5	6	7	8
T2	9	10	11	12	13	14	15	16
T3	17	18	19	20	21	22	23	24
T4	25	26	27	28	29	30	31	32
T5	33	34	35	36	37	38	39	40
T6	41	42	43	44	45	46	47	48
T7	49	50	51	52	53	54	55	56
T8	57	58	59	60	61	62	63	64
T9	65	66	67	68	69	70	71	72
T10	73	74	75	76	77	78	79	80
T11	81	82	83	84	85	86	87	88
T12	89	90	91	92	93	94	95	96
T13	97	98	99	100	101	102	103	104
T14	105	106	107	108	109	110	111	112
T15	113	114	115	116	117	118	119	120
T16	121	122	123	124	125	126	127	128



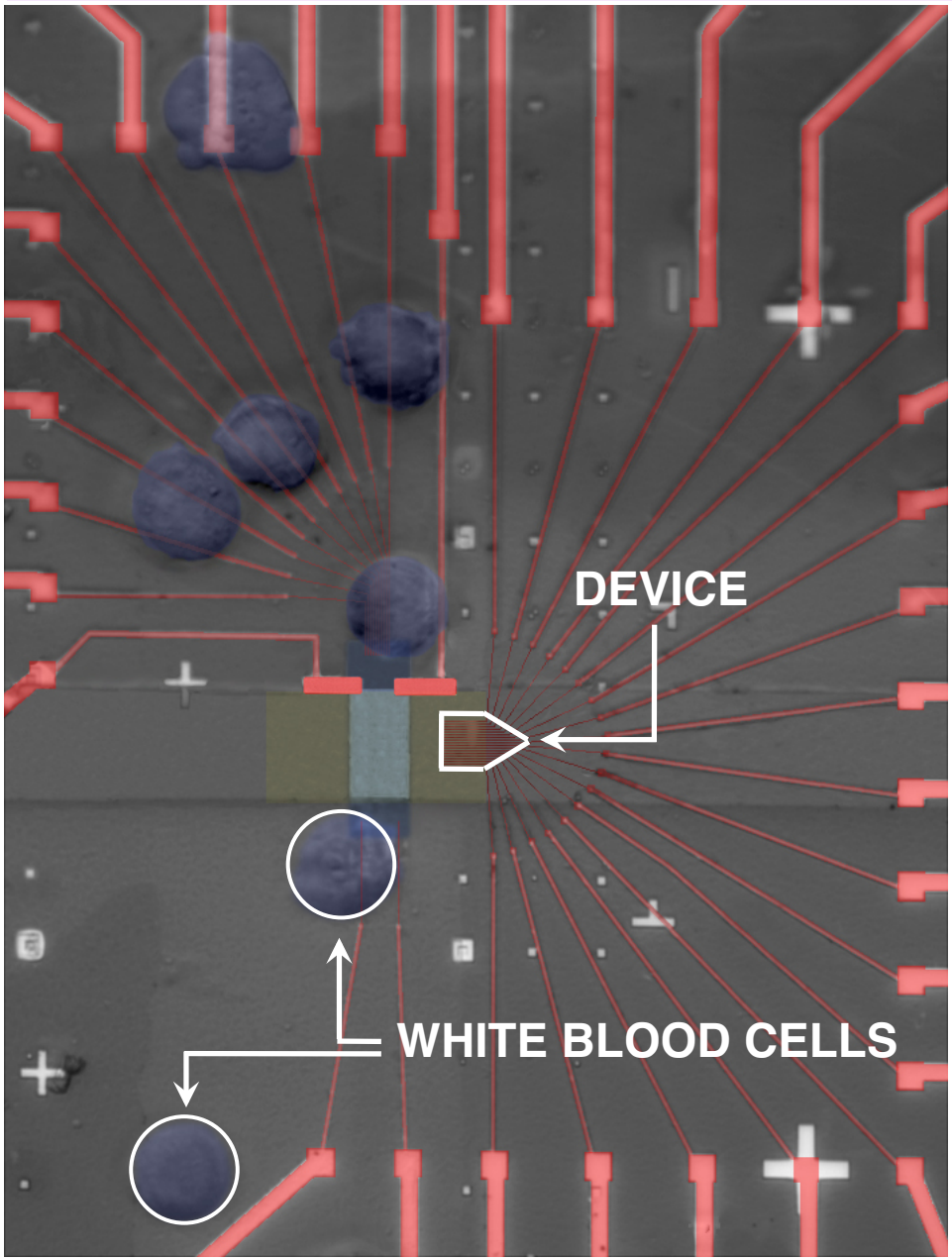
Adjacent Nanowires Shorted

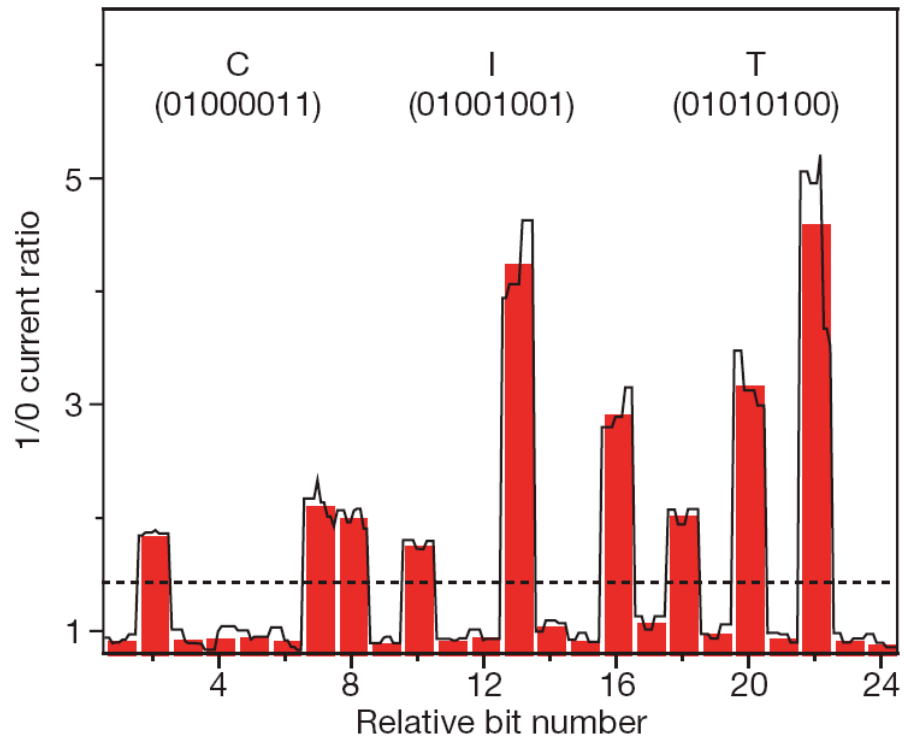
12.5%

Non fatal

Threshold for a Good Bit ~1.5

MOLECULAR RAM AT 10^{11} BITS / cm^2



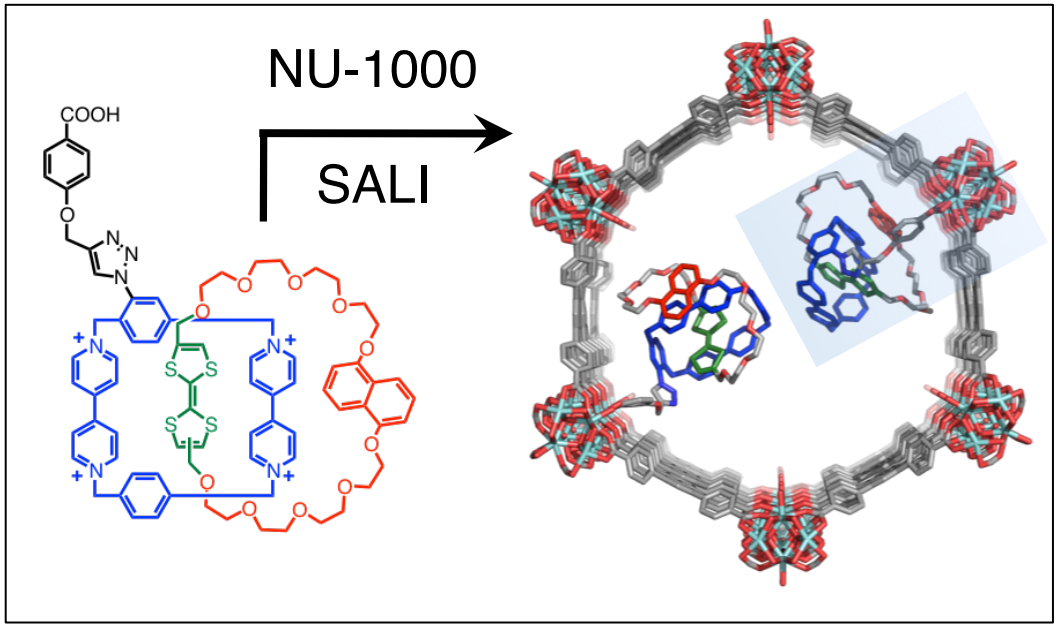


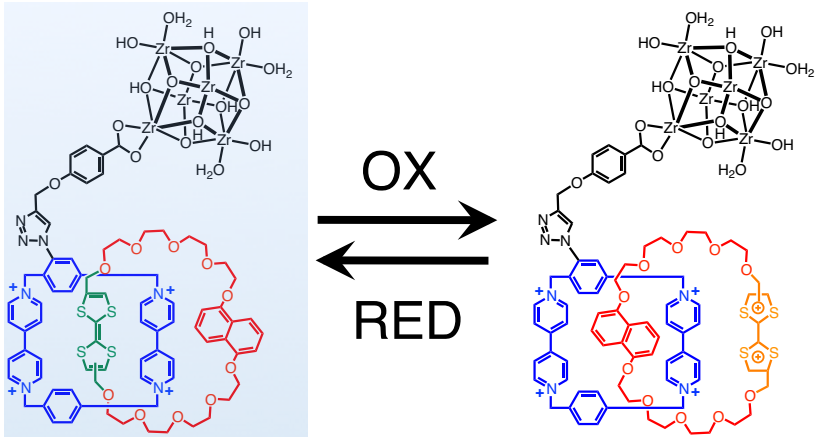
Roughly analogous to the dimensions of a DRAM circuit projected to be available by

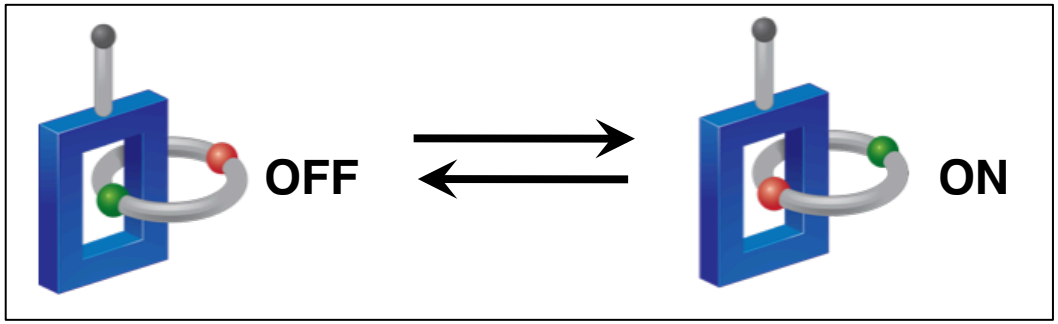
2020

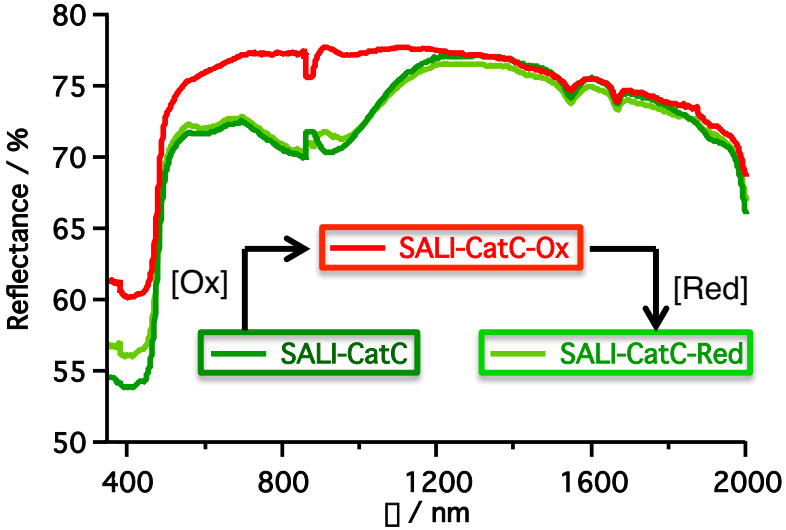
2005 International Technology Roadmap for Semiconductors

BISTABLE [2]CATENANE SWITCHING INSIDE A MOF









Joe Hupp

Omar Farha

MOF ≡ Metal-Organic Framework

SALI ≡ Solvent-Assisted Ligand Incorporation

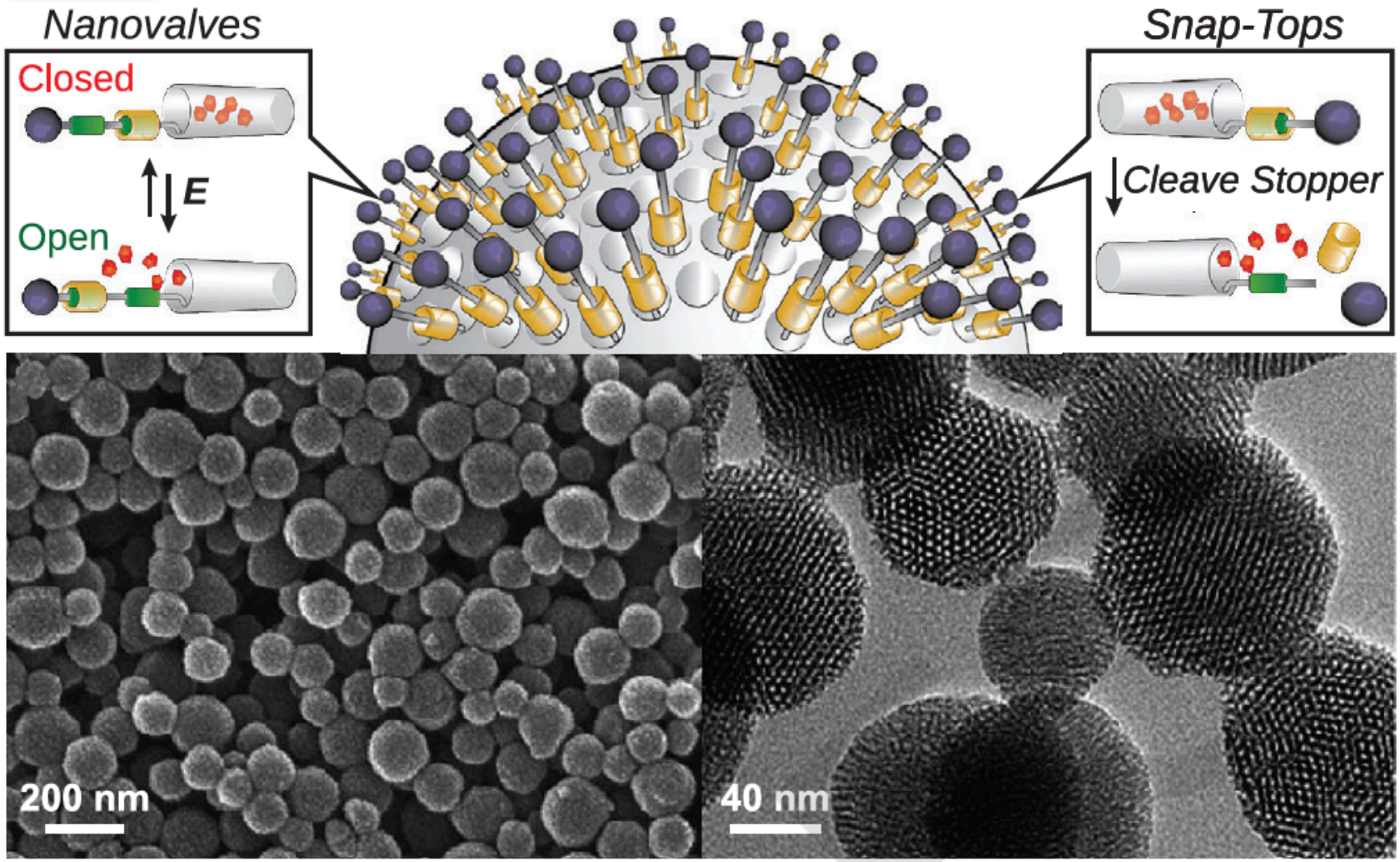
J. Am. Chem. Soc. **2016**, *138*, 14242

DRUG DELIVERY SYSTEMS

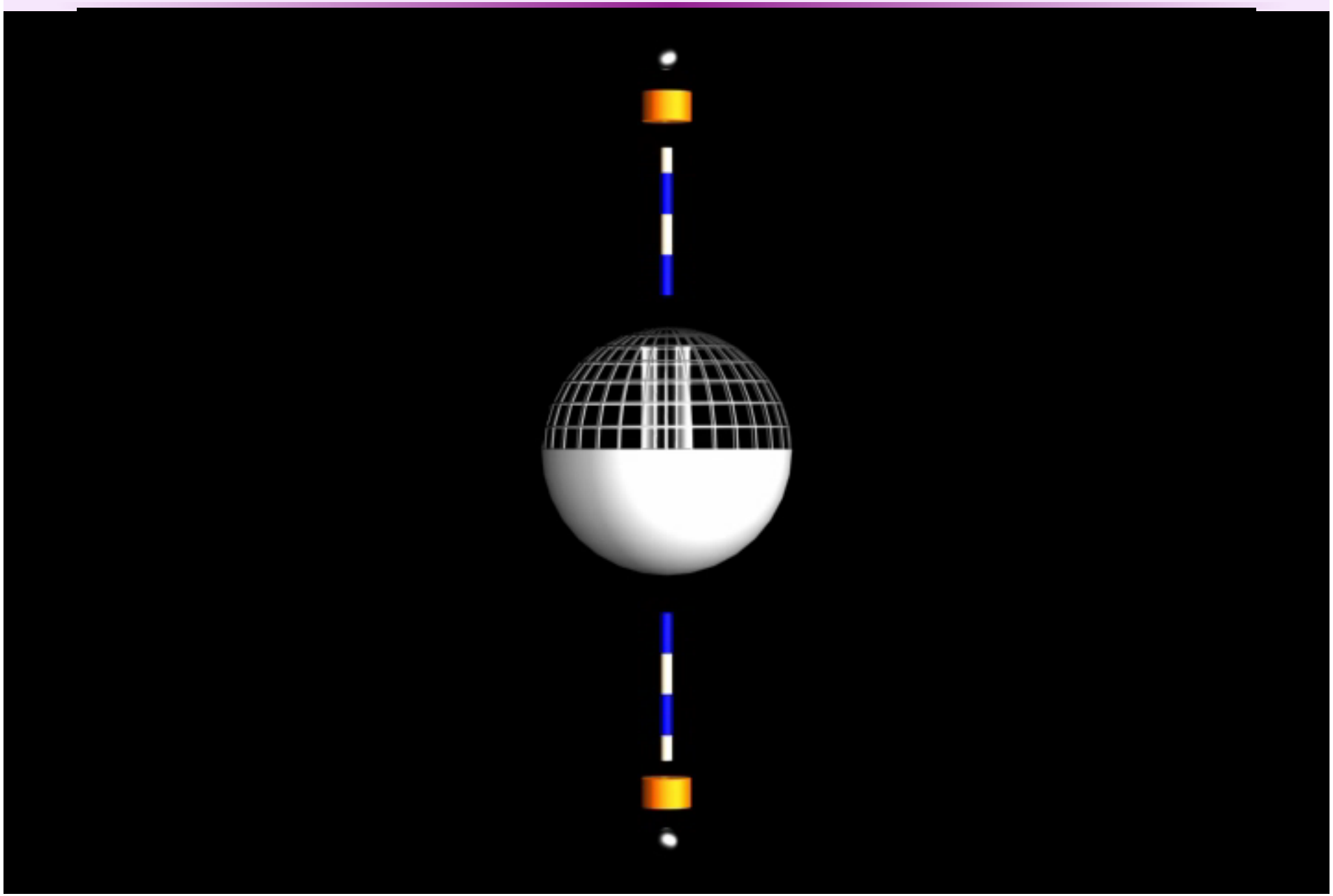
Jeff Zink

Chem. Soc Rev. **2012**, *41*, 2590

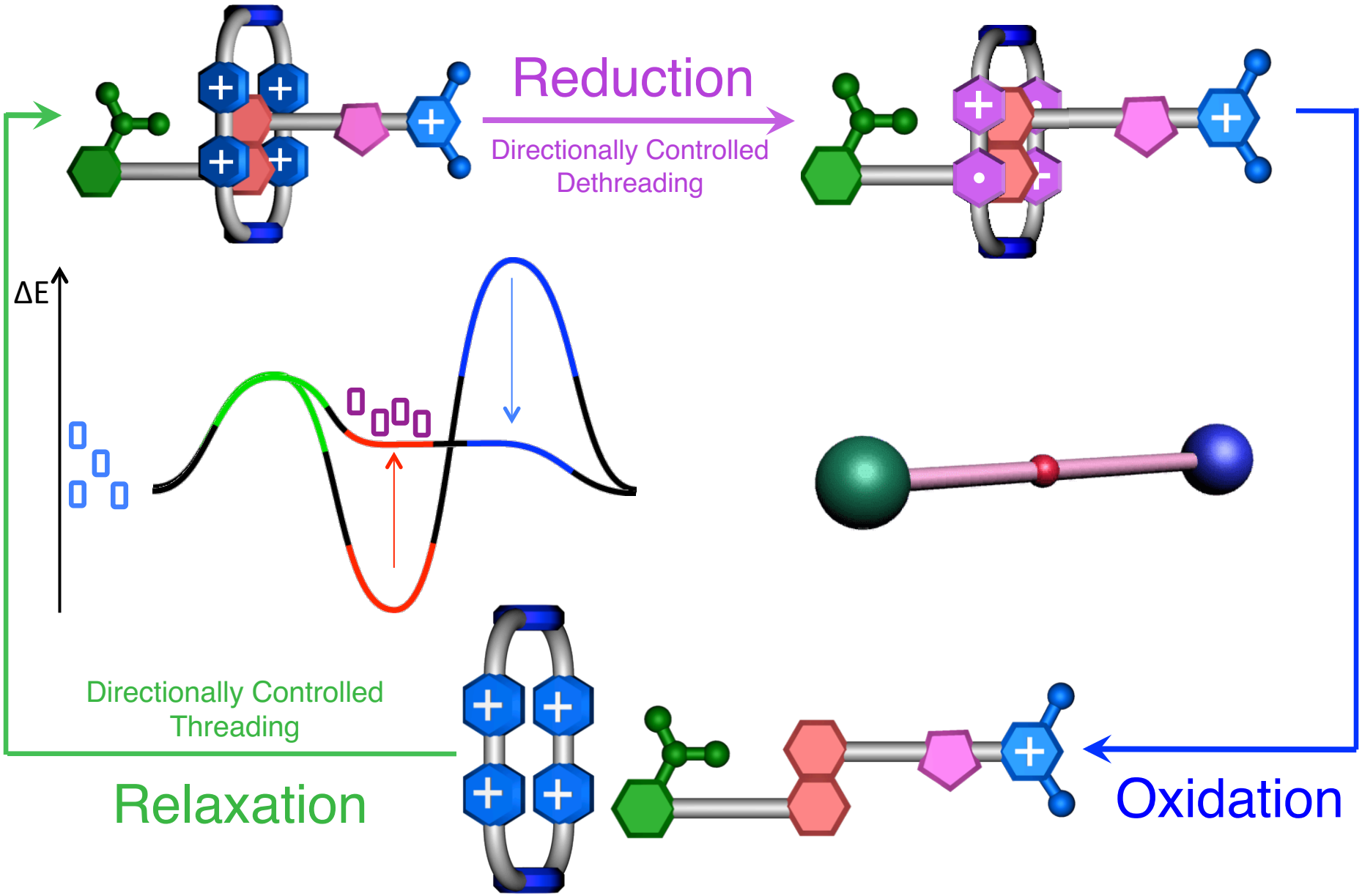
Mesoporous Silica Nanoparticles / MSNPs



DRUG DELIVERY WITH MECHANIZED MSNPs



FLASHING ENERGY RATCHET

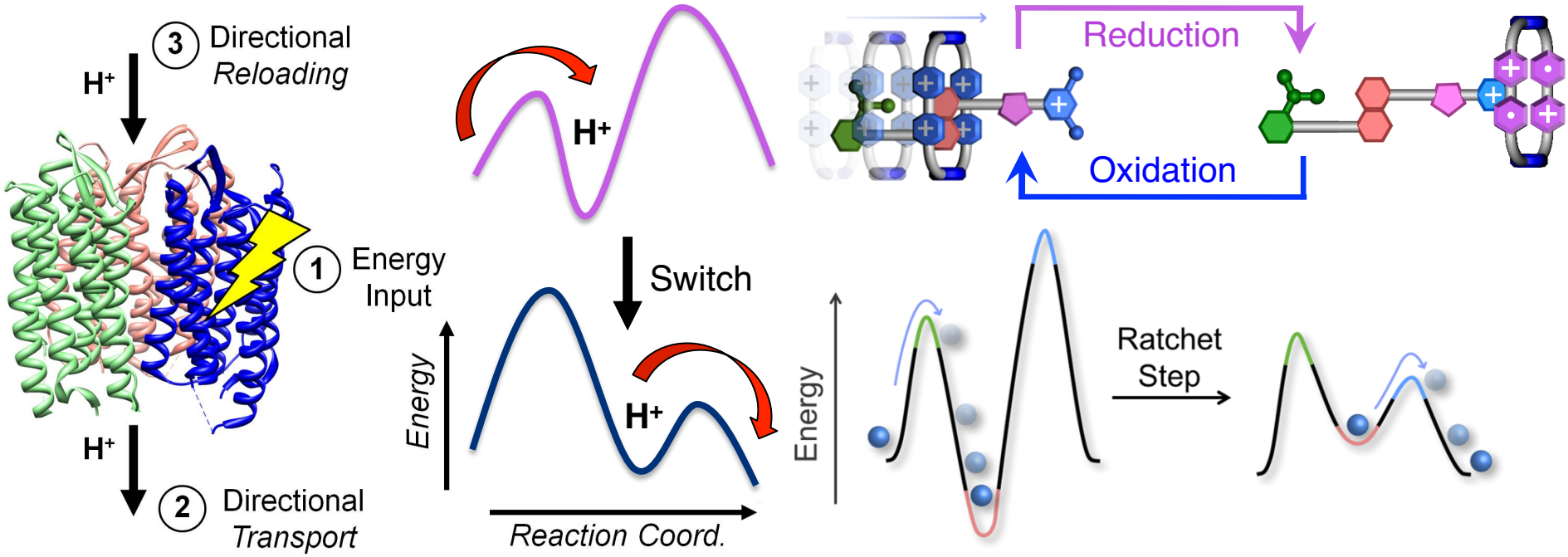


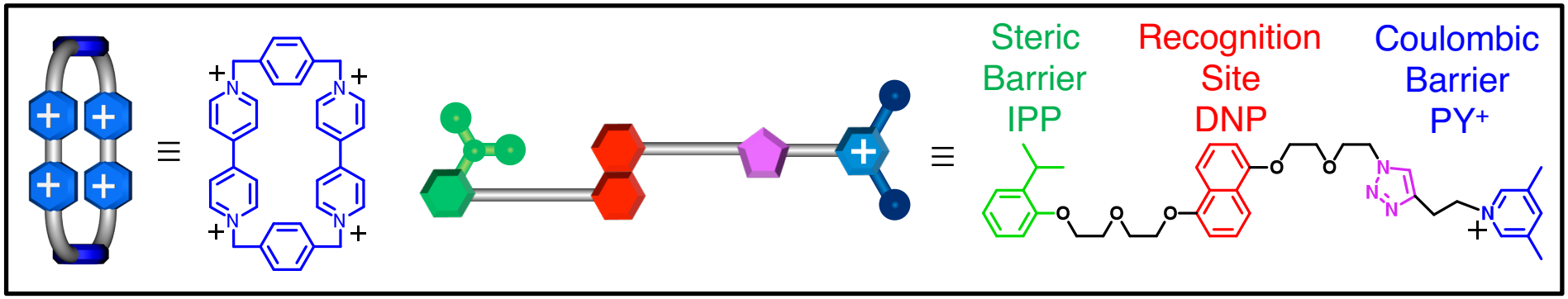
J. Am. Chem. Soc. **2013,** *135*, 18609

TAKING INSPIRATION FROM NATURE

Bacteriorhodopsin

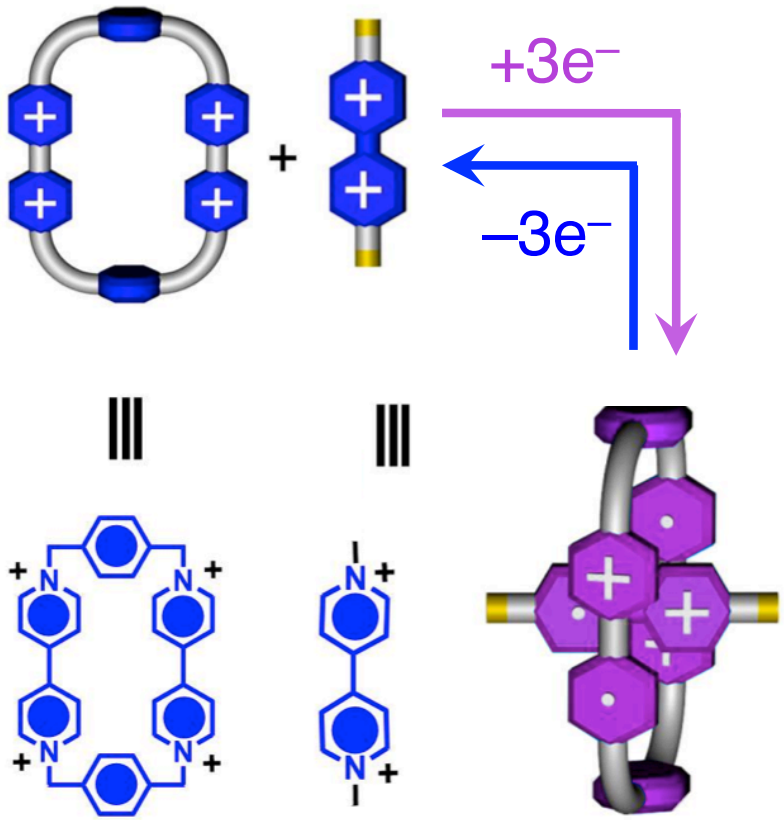
Molecular Pump Prototype





J. Am. Chem. Soc. **2013**, *135*, 18609.

INTRODUCING RADICALS



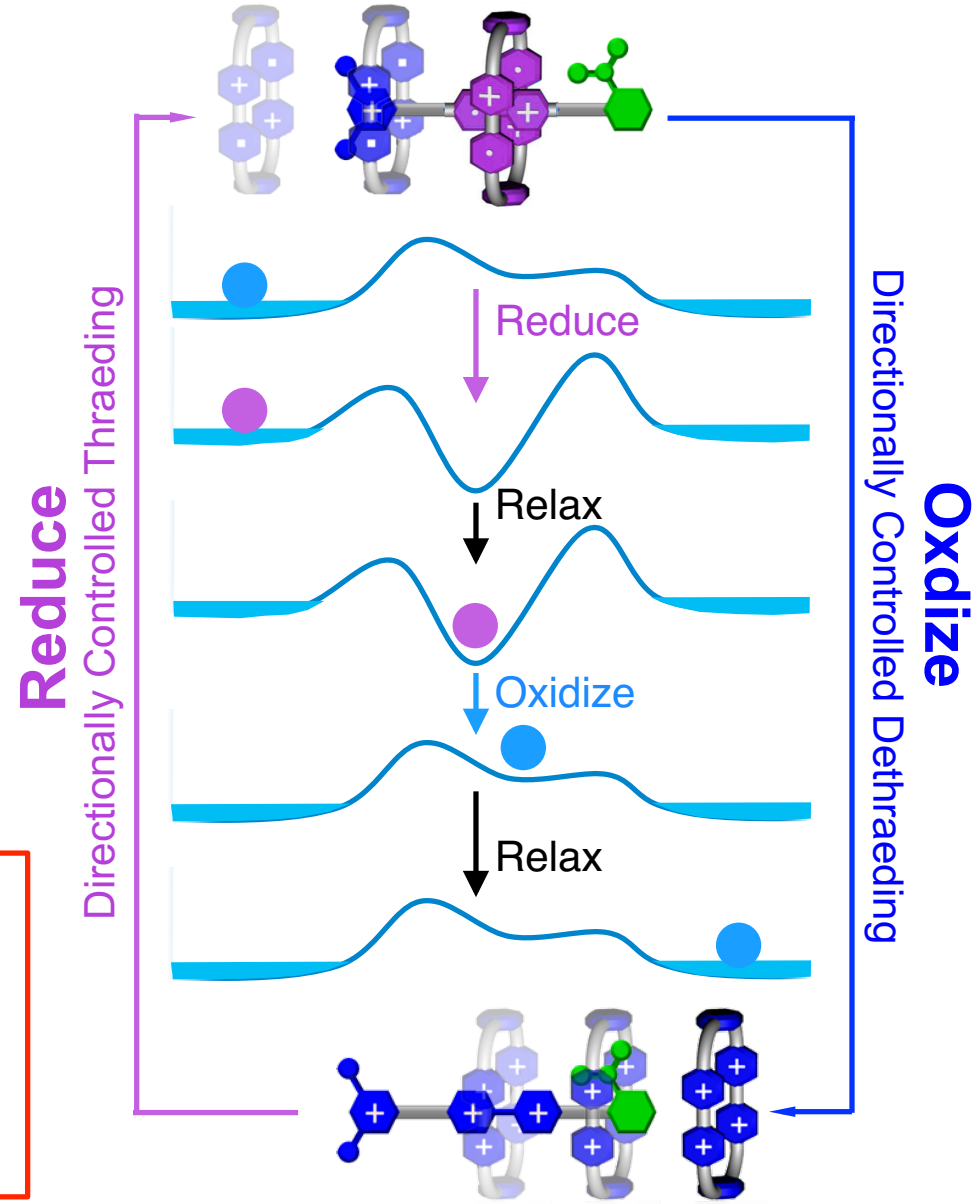
K_α = 50400 M^{-1}

ΔG = – 6.4 kcal mol^{-1}

Attraction under reduced conditions

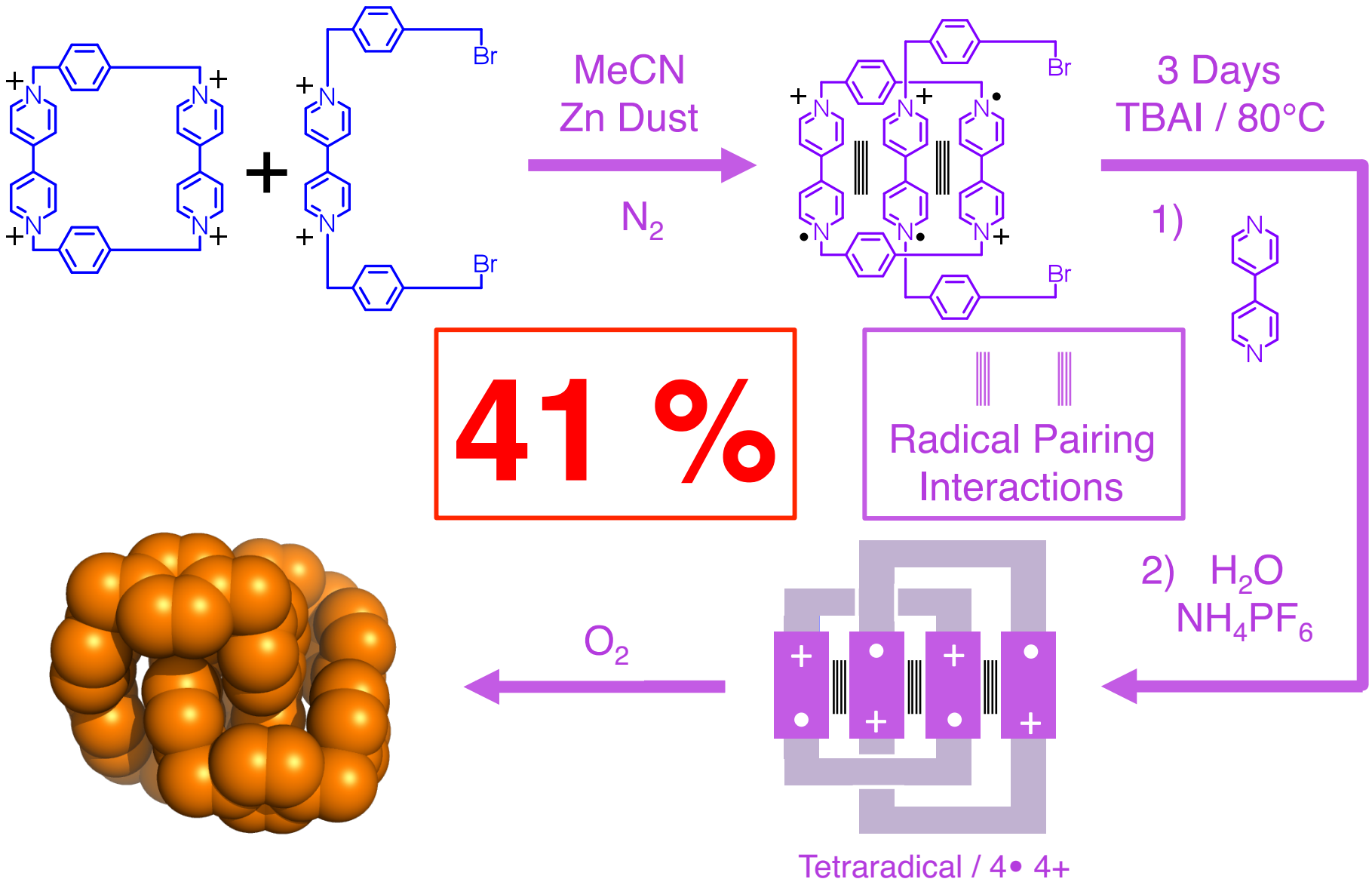
Repulsion under oxidized conditions

Nature Chem. **2010**, *2*, 42



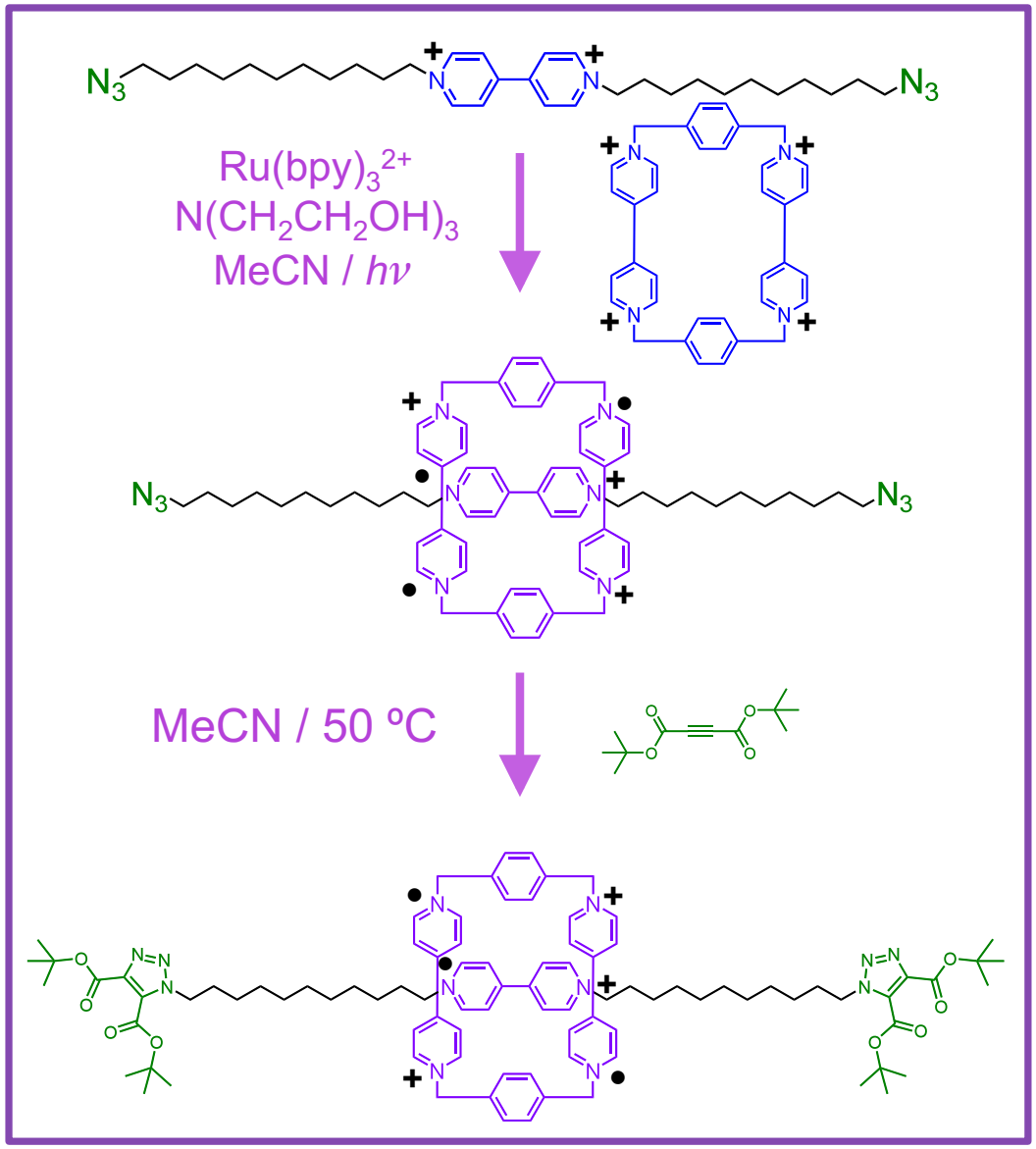
J. Am. Chem. Soc. **2014**, *136*, 14702

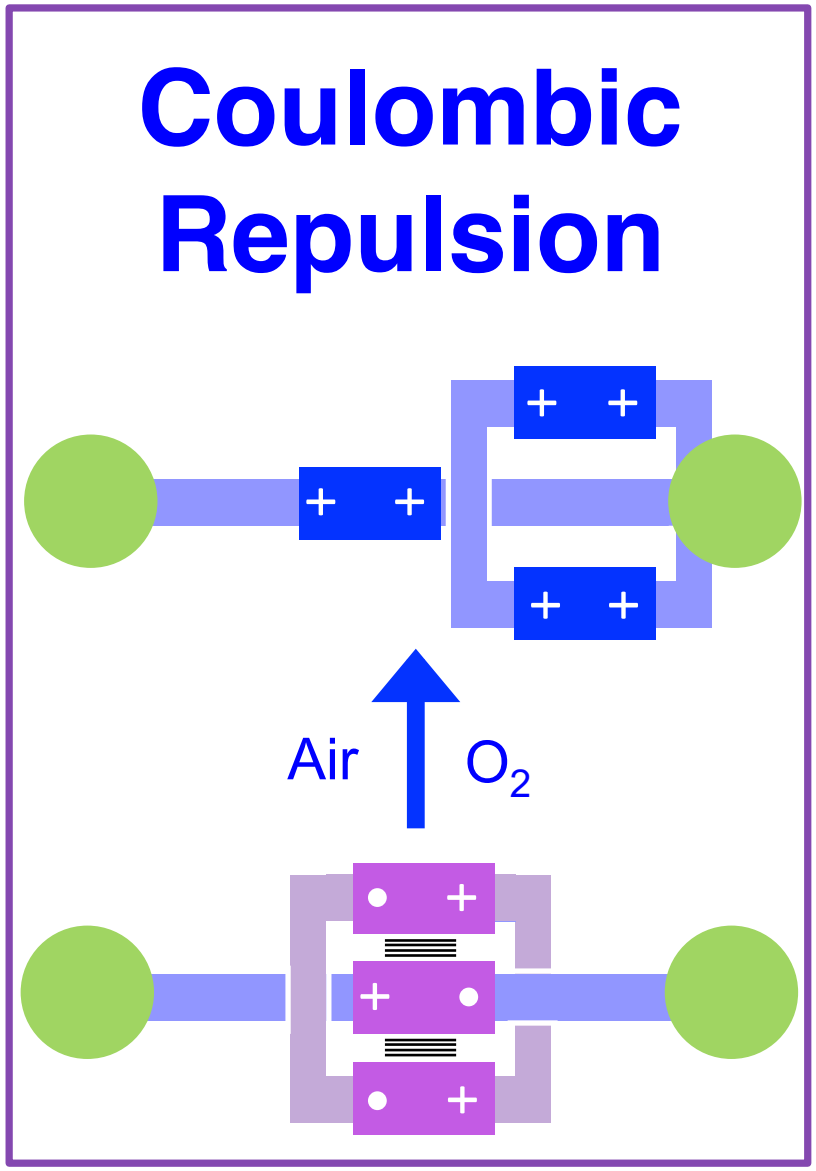
2013 RADICAL TEMPLATION 2013



Science **2013**, *339*, 429

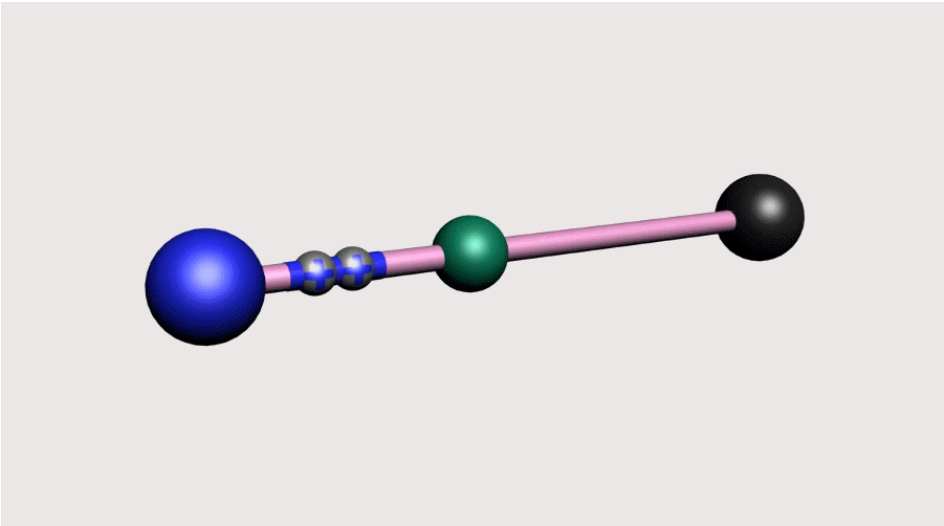
RADICAL TEMPLATION

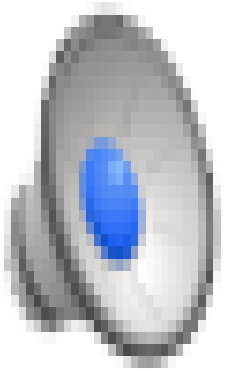


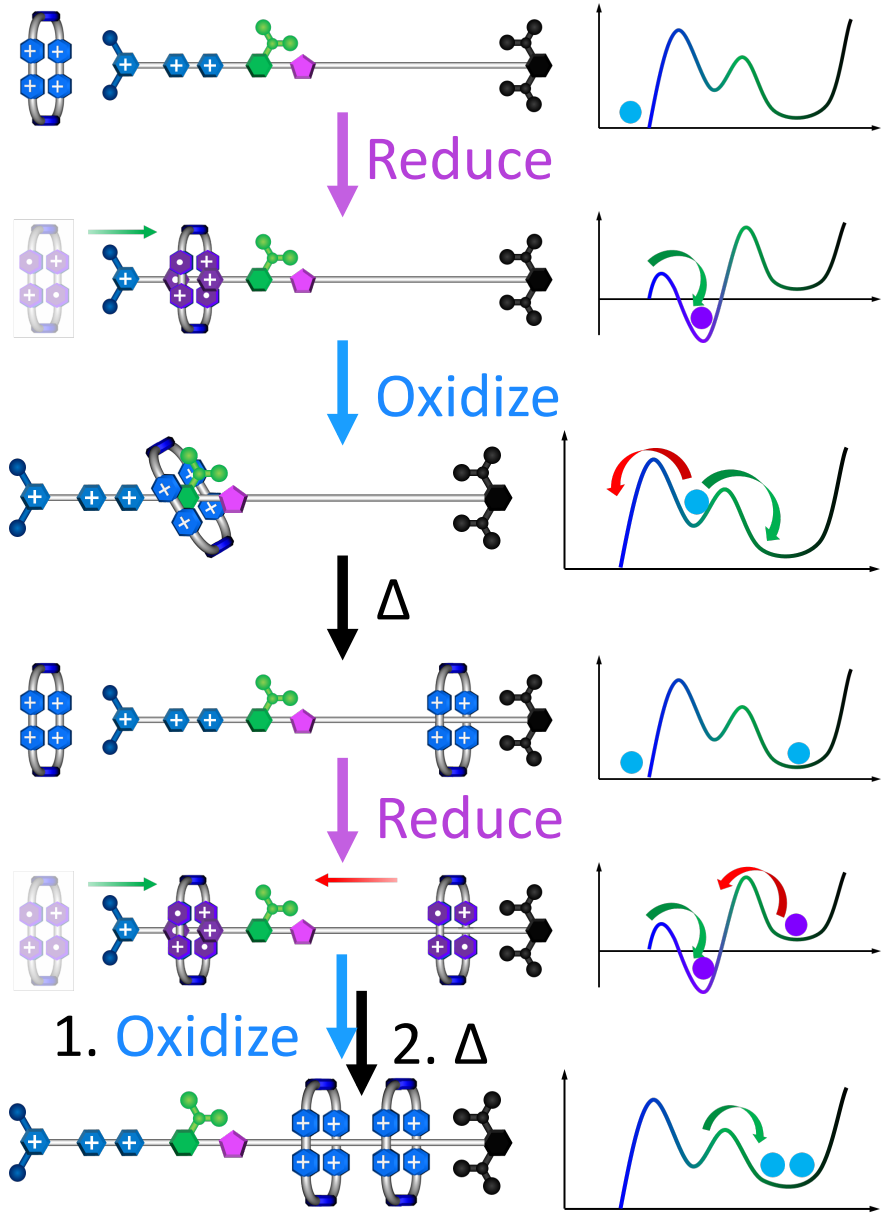


Angew. Chem. Int. Ed. **2010**, *49*, 8260

MOLECULAR PUMP DESIGN BLUEPRINT

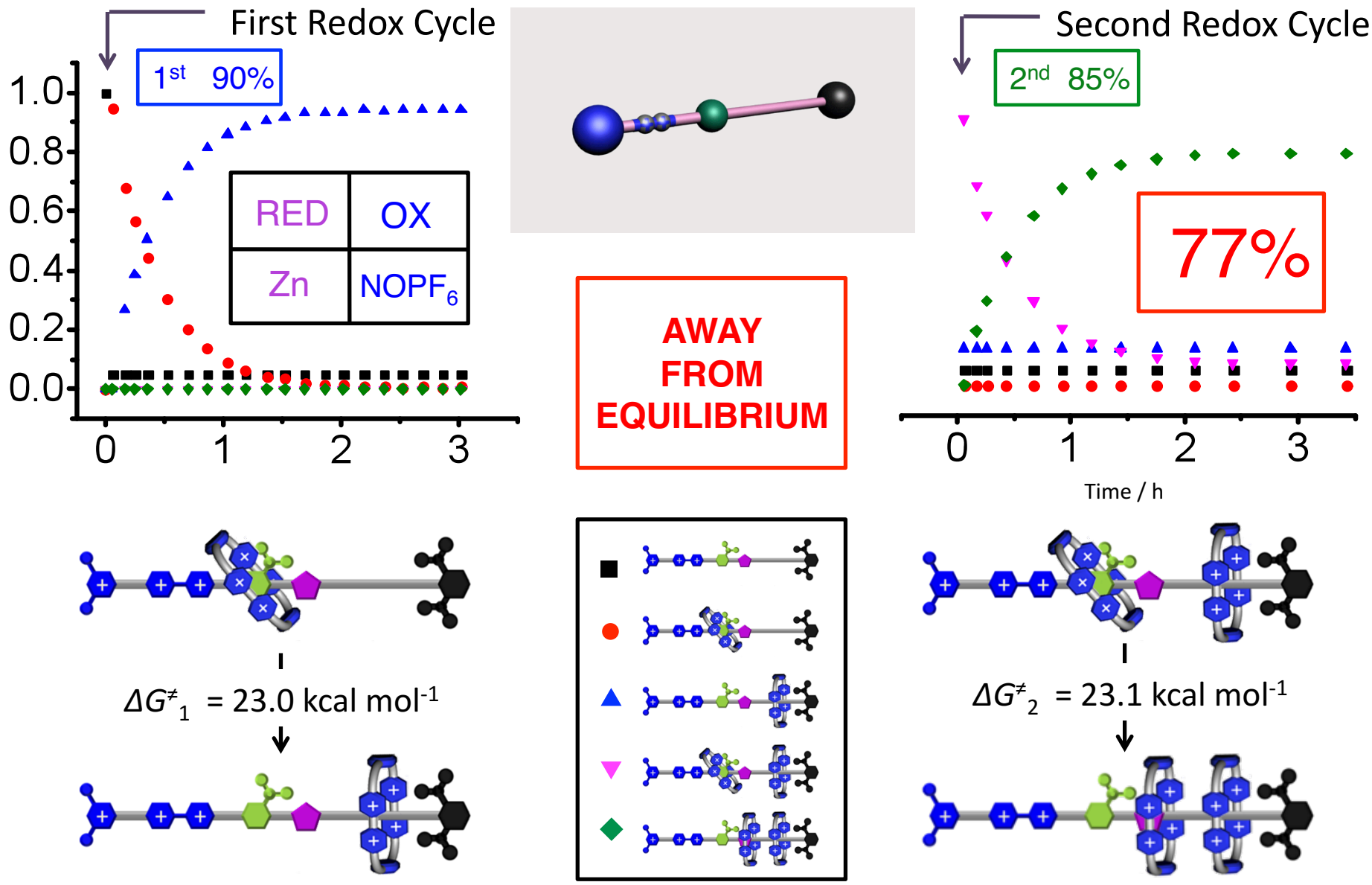






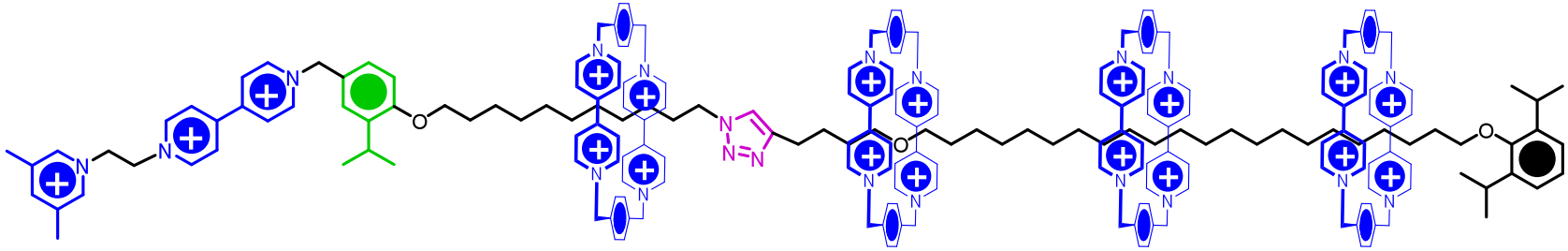
Nature Nanotechnology **2015**, *10*, 547

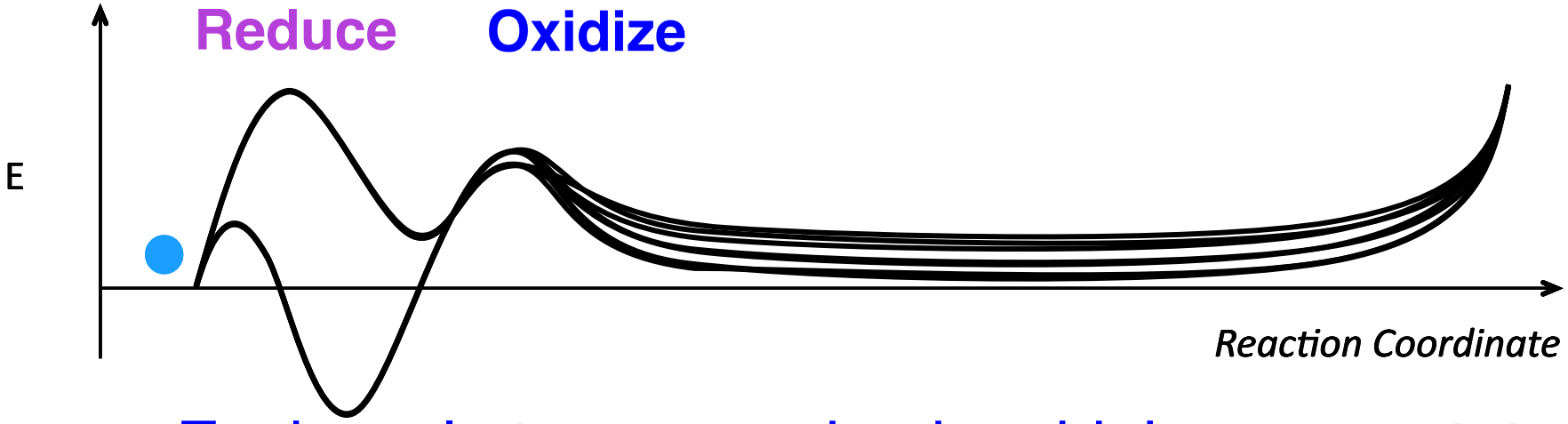
PUMPING ONE FOLLOWED BY TWO RINGS



Nature Nanotechnology **2015**, *10*, 547

A MULTISTROKE MOLECULAR PUMP IN THE MAKING



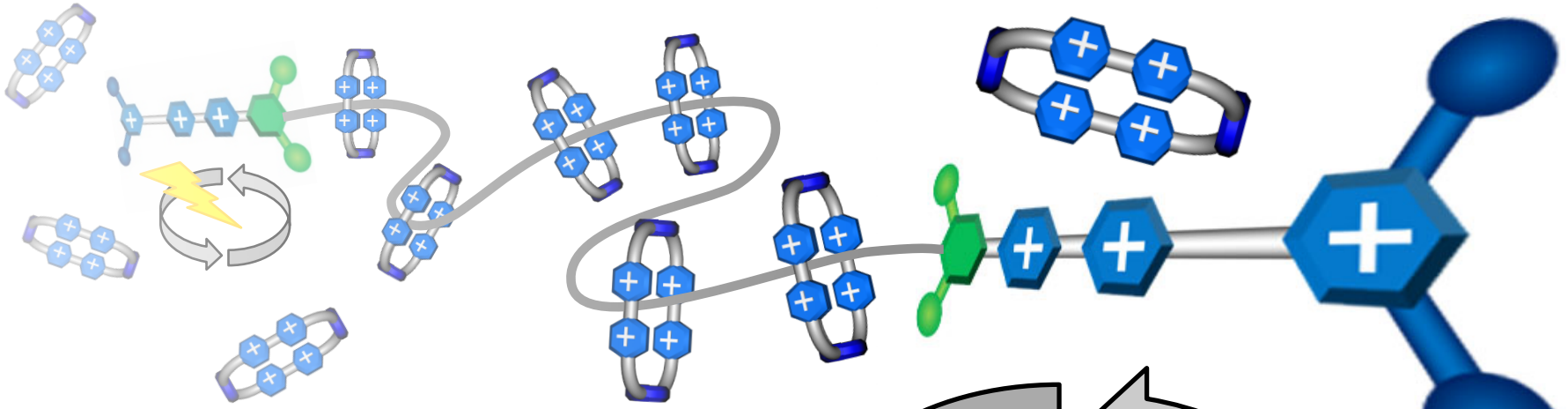


- Each cycle traps one ring in a high energy state
- Some of the energy input is trapped
- Work is done!

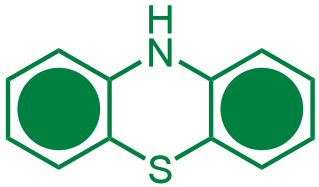
ENTROPICALLY DOMINATED POLYROTAXANES

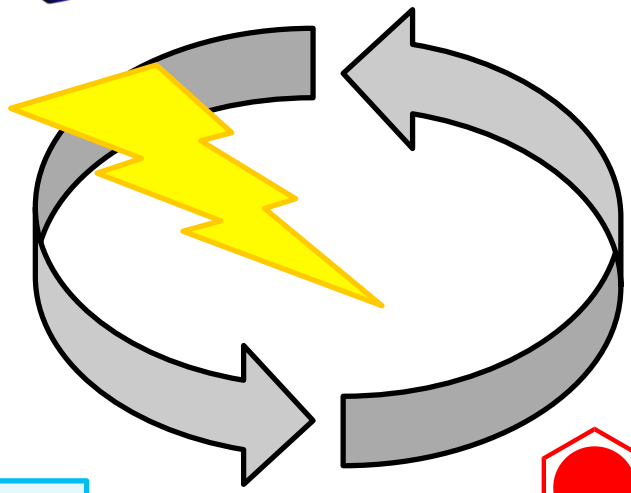
Nature Nanotechnology **2015**, *10, 547*

A LIGHT-POWERED POLYROTAXANE SYNTHESIZER



Light-powered autonomous molecular machine

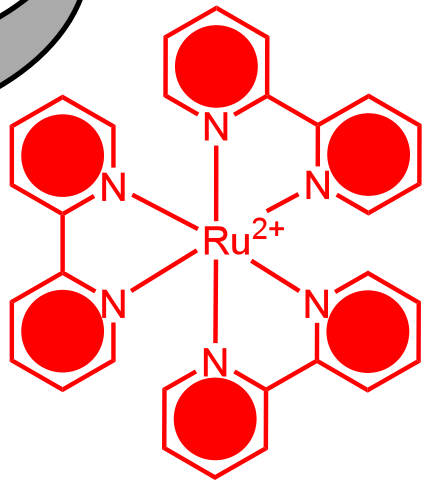




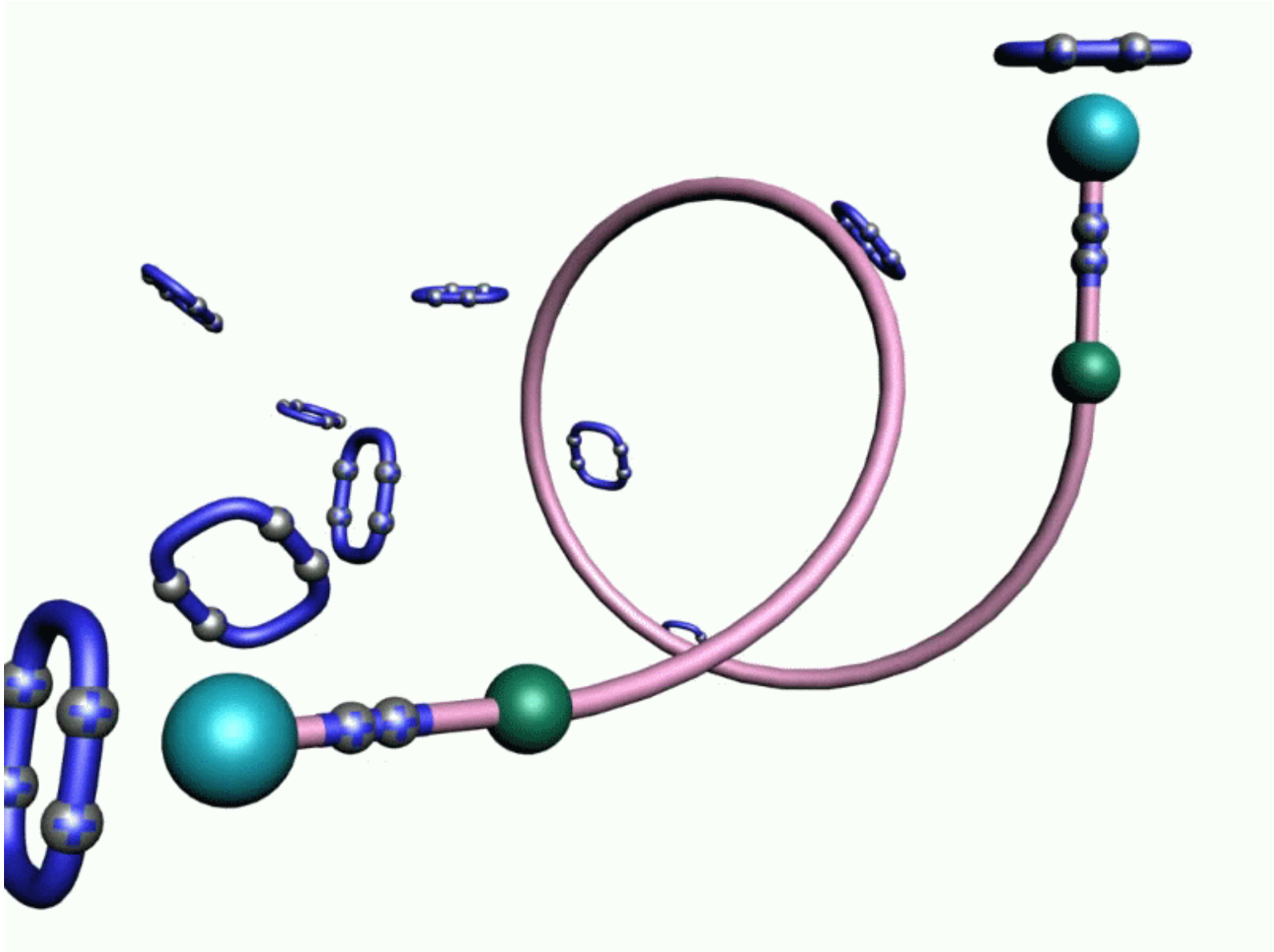
Work progressively and repetitively

Entropically dominated polyrotaxane formation

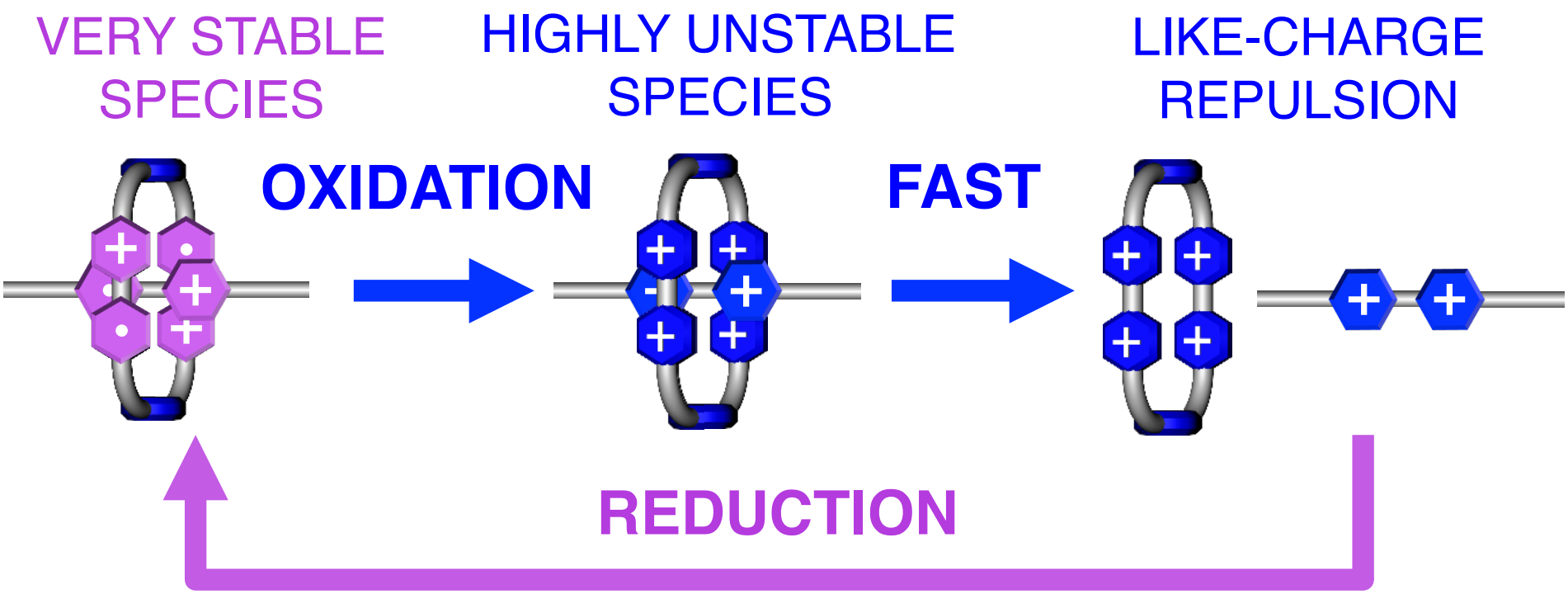
Ongoing Research



PUMPING RINGS ON TO POLYMERS WITH DUAL PUMPS



KEY FACTORS IN DESIGNING NON-EQUILIBRIUM SYSTEMS



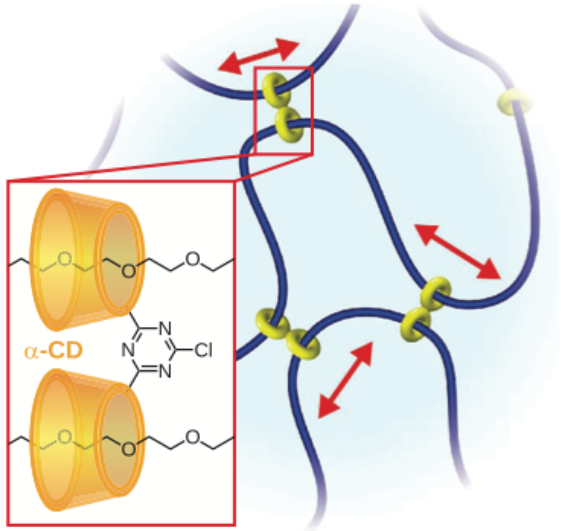
Kinetics of Association and Dissociation Can be modulated

ACS Nano **2015**, *9*, 8872

CHEMISTRY AWAY-FROM-EQUILIBRIUM

Slide-Ring Gels

Kohzo Ito and Kazuaki Kato

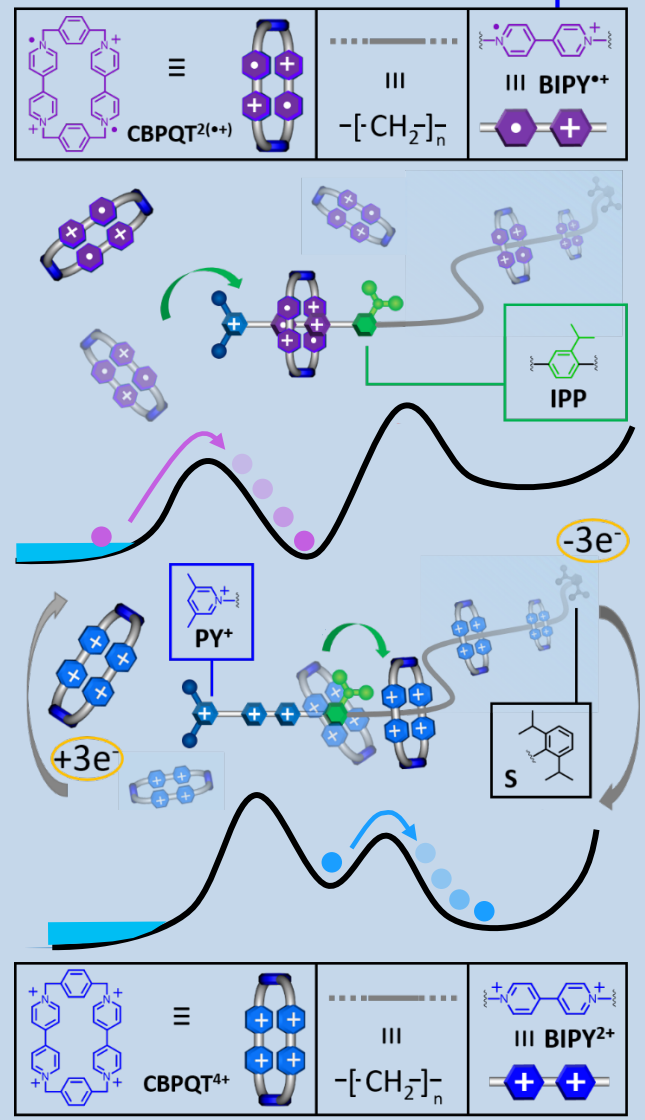


How do we design systems that operate repetitively and progressively away-from-equilibrium?

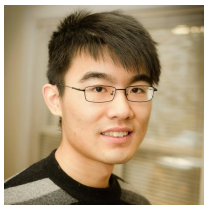
WHAT ARE SOME OF THE BIG QUESTIONS?

What are the consequences of dissipation on materials properties?

Artificial Molecular Pump



Nature Nanotechnology
2015, *10*, 547–553



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Cristian Pezzato
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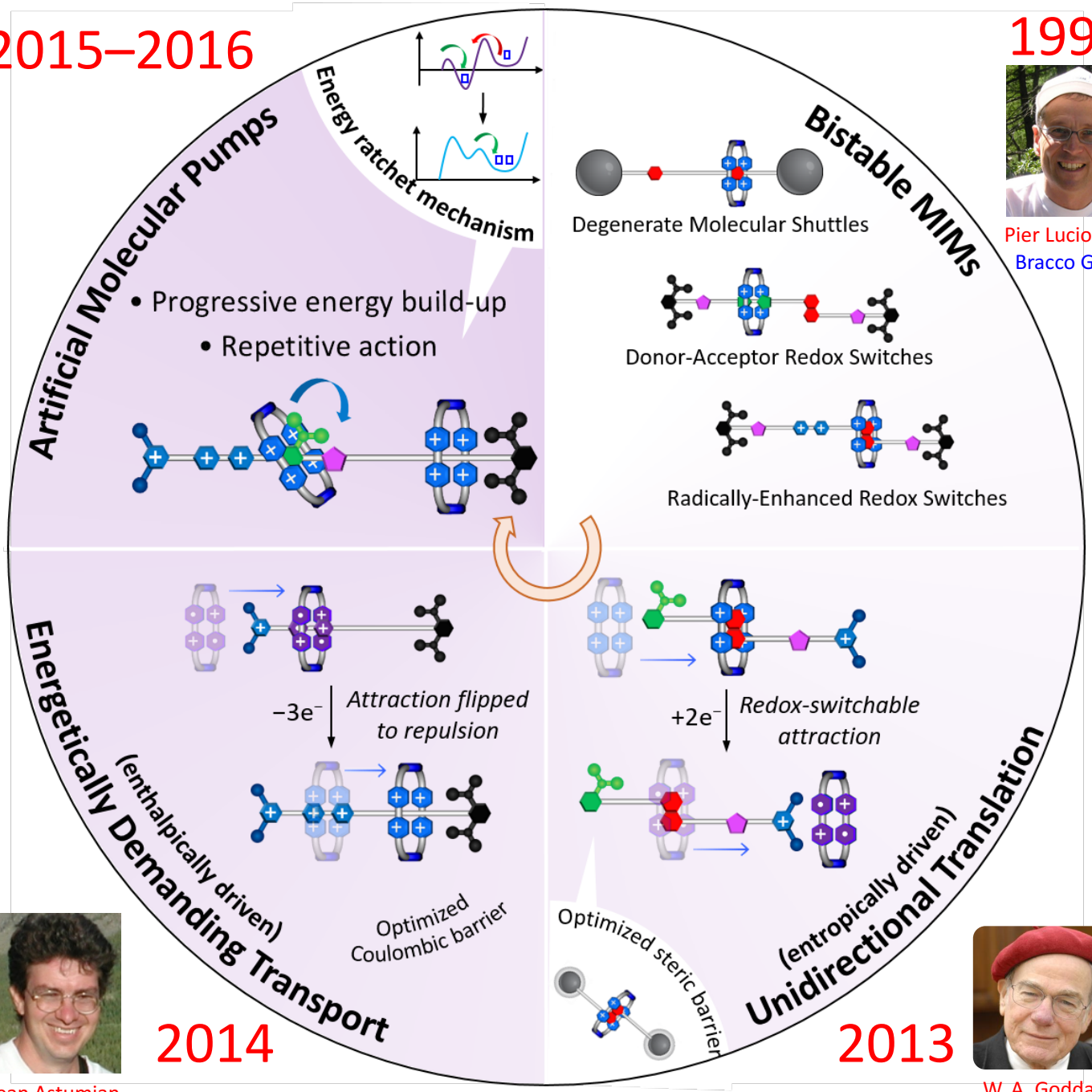
N. A. Vermeulen
Northwestern

Jonathan Barnes
Washington U

Dean Astumian
U of Maine



ACS Nano, **2015**, *9*, 8672

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Bracco Group

Neil Spencer
Birmingham

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Peakdale

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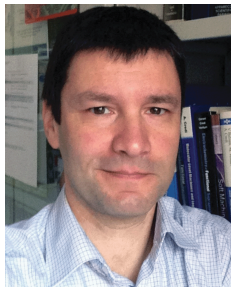
W. A. Goddard
CALTECH

M. Frasconi
U Padova

LEADING MOLECULAR MACHINISTS



Alberto Credi

Vincenzo Balzani

Nicolas Giuseppone

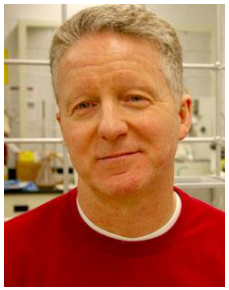
Ivan Aprahamian

David Leigh

Dean Astumian

Rafal Klajn

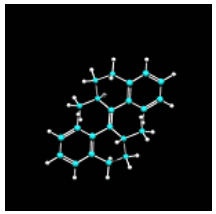
Amar Flood

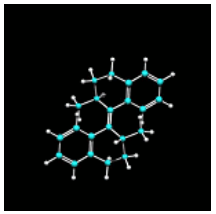


Steve Loeb

Josef Michl

Ben Feringa





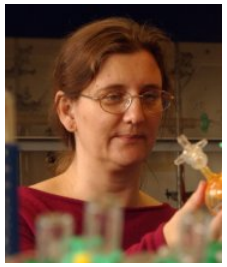
Miguel Garcia-Garibay

Edie Sevick

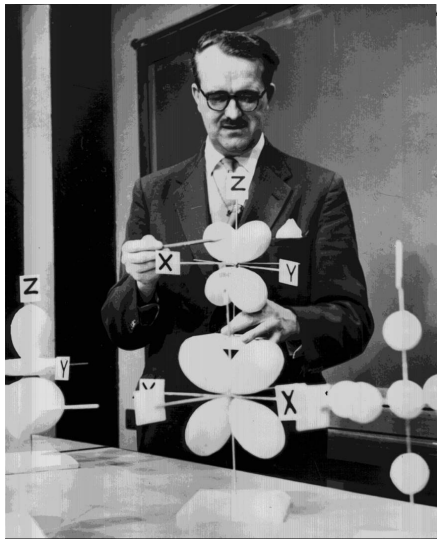
COORDINATION WITH Alfred Werner

David Williams
Imperial College

Howard Colquhoun
University of Reading



Alexandra Slawin
St Andrews University



Joseph Chatt
1914–1994

Alfred Werner
1866–1919

Second-Sphere Coordination

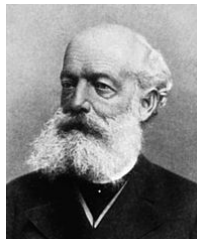
"Scientific discovery is not yet predictable. If you have an exciting road to follow do not be put off by those who say there is nothing at the end of it; they do not know. Persevere, and enjoy the excitement of exploring the unknown."

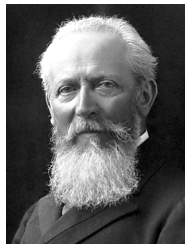
Chatt, J. *Platinum Met. Rev.* **1985**, *29*, 126

HUMAN AND FINANCIAL RESOURCE MATRIX

Friedrich Wöhler

Jons Jacob Berzelius


August Kekulé


Otto Wallach

Walter Norman Haworth

Edmund Langley Hirst

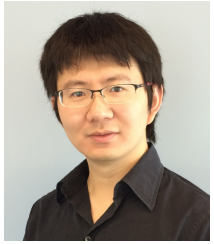
J Ken N Jones

Ron Smalldone

Jeremiah Gassensmith

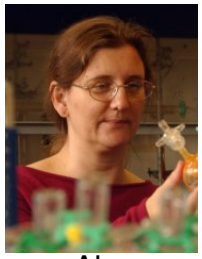
Ross Forgan

Zhichang Liu


Chenfeng Ke

Xisen Hou

Avik Samanta


Alex Slawin
ST ANDREWS

Sam Stupp
NORTHWESTERN

Chad Mirkin
NORTHWESTERN

Mike Wasielewski
NORTHWESTERN

Omar Yaghi
BERKELEY

Youssry Botros
PANACEANANO

Roger Pettman
CYCLODEX

RESEARCH LIFELINES

Biotechnology and Biological Science Research Council

Engineering and Physical Sciences Research Council

University of Sheffield

University of Birmingham

Imperial Chemical Industries

University of California Los Angeles

American Chemical Society

National Science Foundation

National Institutes of Health

Department of Energy

Northwestern University

International Institute for Nanotechnology

CCNE Center of Cancer Nanotechnology Excellence

MURI Multidisciplinary University Research Initiative

Microelectronics Advanced Research Corporation

MRSEC Materials Research Science and Engineering Center

King Abdulaziz City for Science and Technology