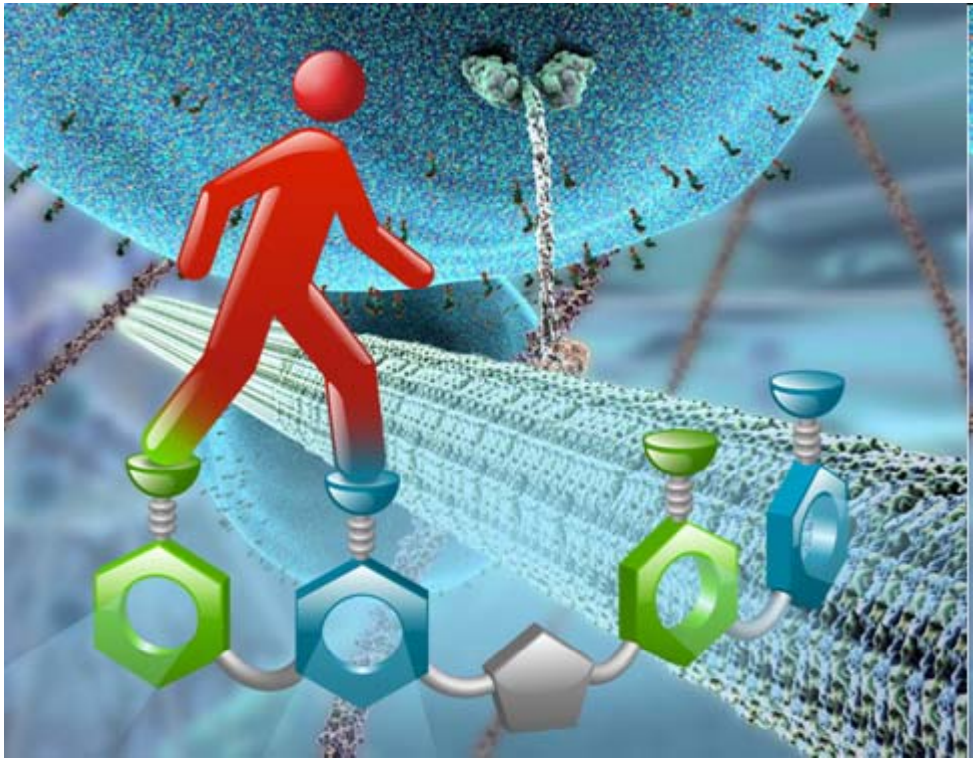
A synthetic small molecule that can walk down a track



Max von Delius, Edzard M Geertsema, David A Leigh,
Nature Chem, **2010**, *2*, 96-101.

Outline

- 1. Introduction of Prof. *D. A Leigh.*
- *2.* Molecular motor.
- 3. Tiny steps

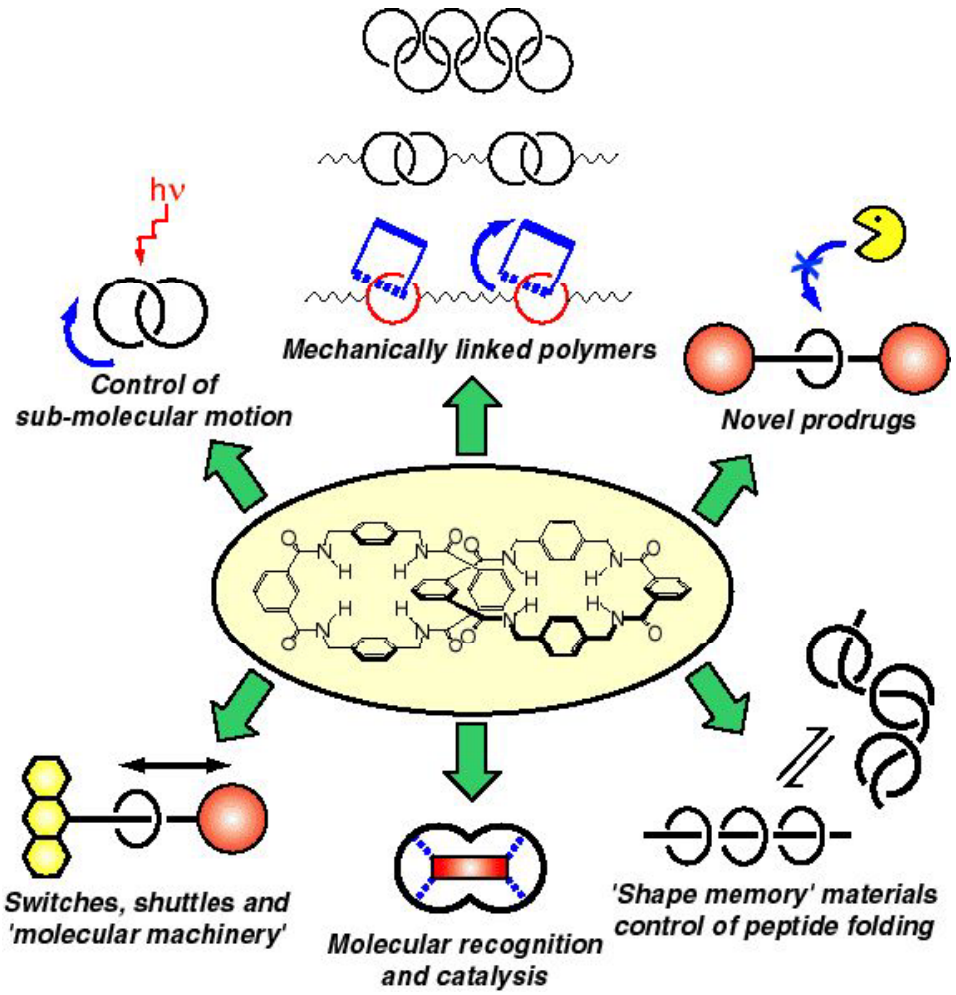
Professor David A. Leigh

- Forbes Professor of Organic Chemistry & EPSRC Senior Research Fellow
  School of Chemistry, University of Edinburgh

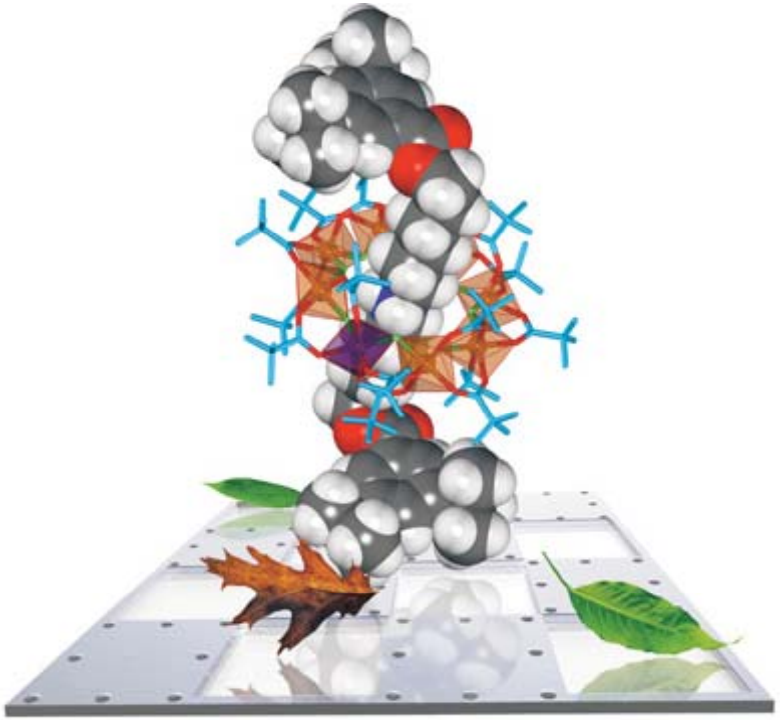
- B.Sc. (1984); Ph. D. (1987) University of Sheffield

- 2007 International Izatt-Christensen Award in Macrocyclic Chemistry
- 2007 Royal Society of Chemistry-Real Sociedad Española de Química (RSC-RSEQ) Prize for Chemistry
- 2007 Chancellor's Award for Research
- 2007 Feynman Prize for Nanotechnology
- 2007 Descartes Prize for Research
- 2008 ERC Advanced Grant (inaugural call)
- 2009 Elected Fellow of the Royal Society (London), the National Academy of Science of the UK and the Commonwealth
- 2009 Royal Society of Chemistry Merck Award

- Member of the American Chemical Society, the American Association for the Advancement of Science and the Edinburgh Magic Circle. Fellow of the Royal Society of Chemistry, the Royal Society of Edinburgh and the Royal Society (London). Associate Editor of Chemical Science.



Mechanically-interlocked rings in biological chemistry(peptide and protein rotaxanes, novel prodrug systems), catalysis(hydrogen bonding), macromolecules,smart materials(devices)



- the first discrete rotaxane molecules in which inorganic and organic components are linked together mechanically at the molecular level.

‘*Hybrid Organic-Inorganic Rotaxanes and Molecular Shuttles*’, Chin-Fa Lee, David A Leigh, Robin G Pritchard, David Schultz, Simon J Teat, Grigore A Timco and Richard E P Winpenny, *Nature*, **458**, 314-318 (2009).

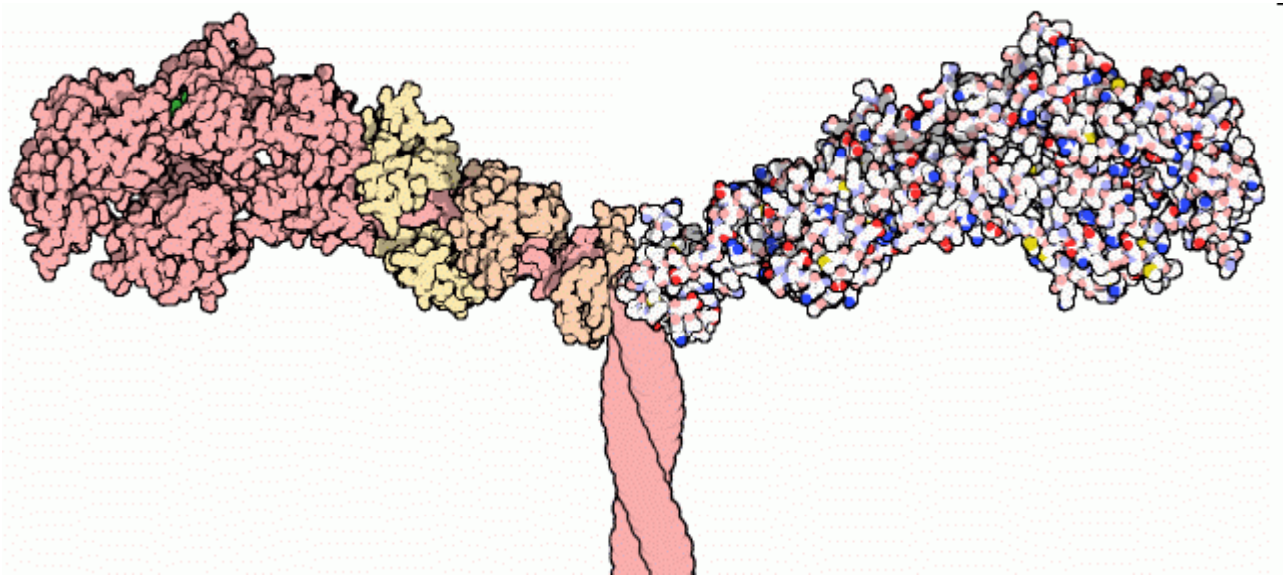
Molecular motor

Examples

- Cytoskeletal motors: Myosin, Kinesin, Dynein
- Polymerisation motors
- Rotary motors:
- Nucleic acid motors: transcribes RNA from a DNA template

- Synthetic molecular motors: created by chemists that yield rotation, possibly generating torque

Myosin

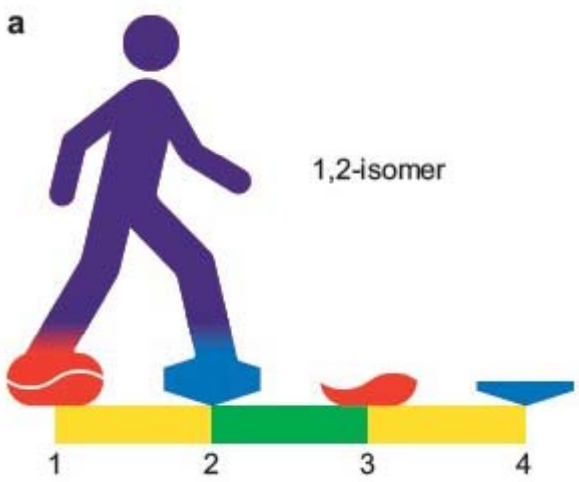


a large family of motor proteins found in eukaryotic tissues.

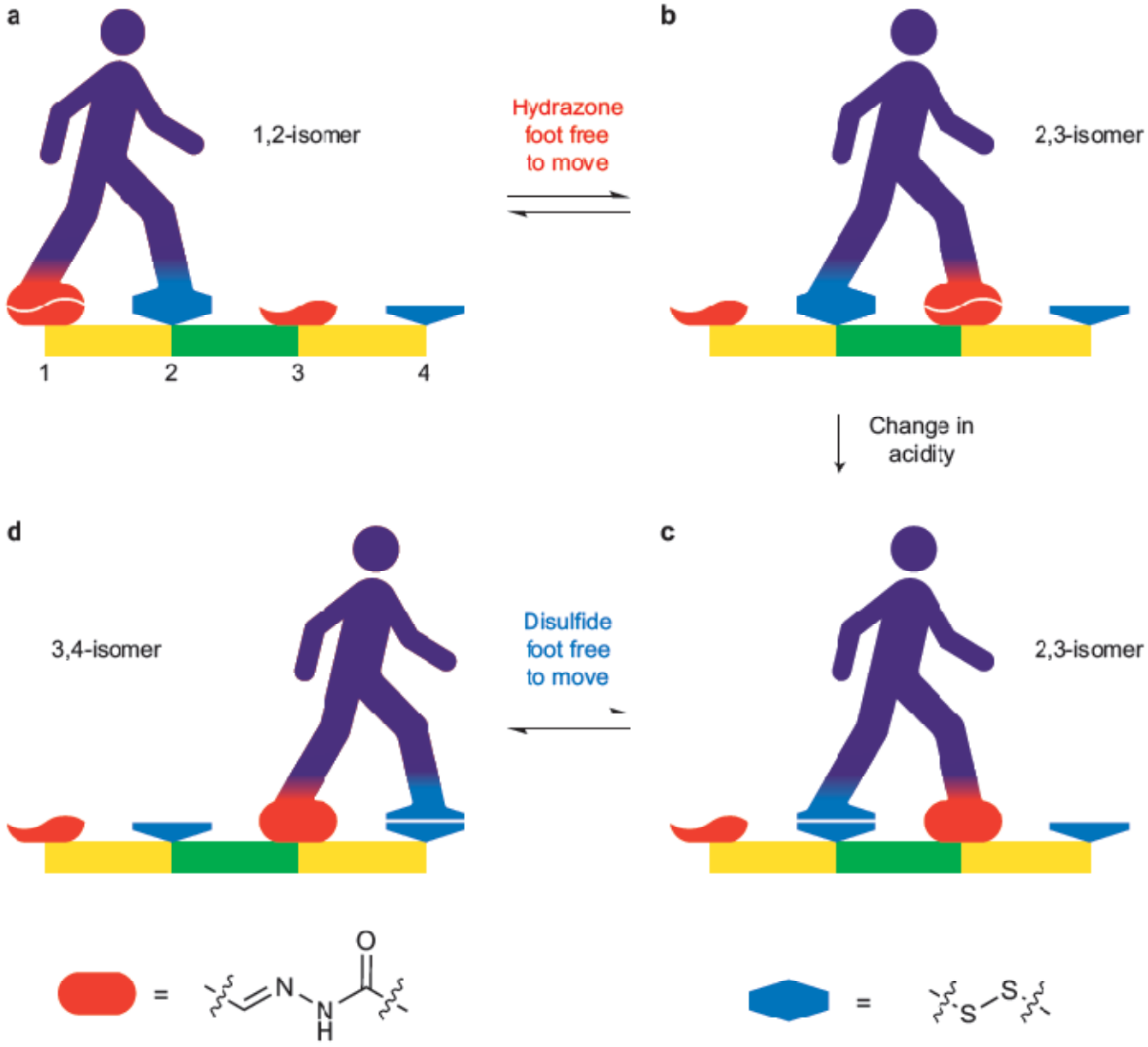
responsible for actin-based motility.

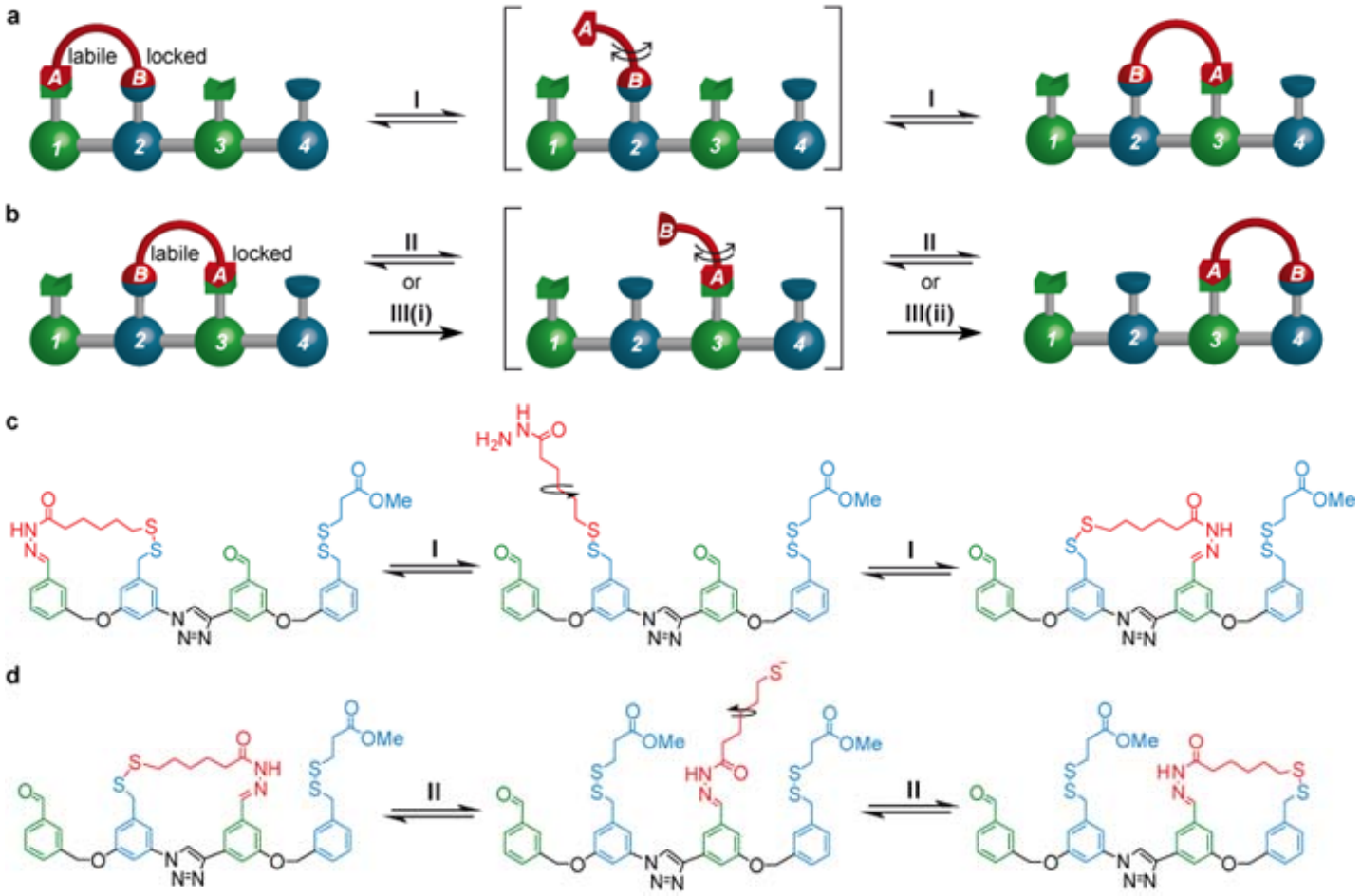
Tiny steps

1. A molecular ‘walker’ can be made to move up and down a molecular ‘track’ by alternately locking and unlocking the two different types of covalent bonds that join the two components together.



2. By changing the conditions under which one of the bond forming / bond-breaking processes occurs, a directional bias for walking can be achieved.


a
1,2-isomer
1
2
3
4
Hydrazone
foot free
to move
b
2,3-isomer
Change in
acidity
d
3,4-isomer
Disulfide
foot free
to move
c
2,3-isomer
=
N
N
H
O
=
S
S



I. treatment with TFA leads to about half of the walker units to step onto the middle of the track. (this hydrazone exchange is fully reversible).

II. strong base DBU, DTT and (MeO2CCH2CH2S)2, resulting in a second reversible step through disulfide exchange.

Unbiased walking – a steady-state minimum energy distribution of walkers on tracks

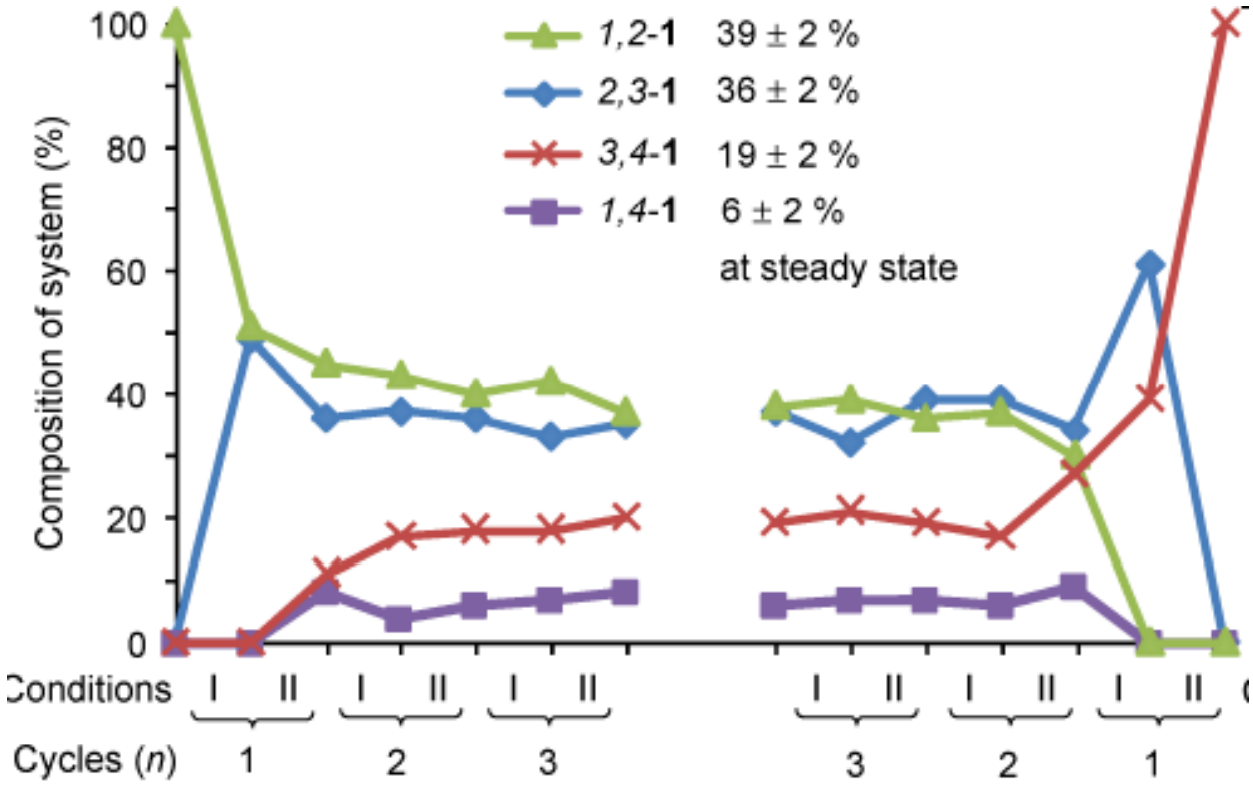
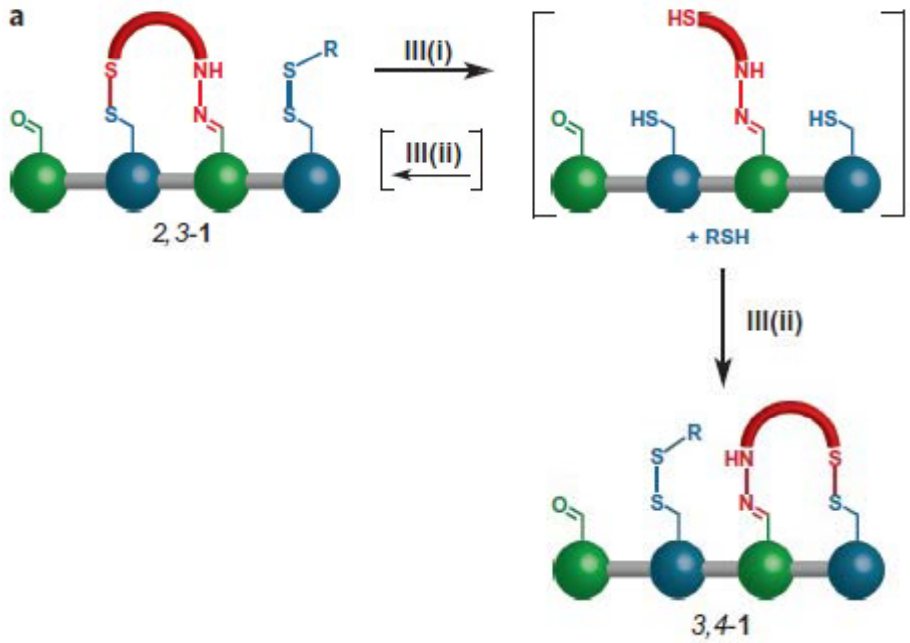


Fig 4. Dynamic behaviour of molecular walker–track conjugates1,2-1 and 3,4-1, each under cycling of the conditions (acid–base) for reversible covalent bonding of each foot with pairs of footholds on the track.



III. To drive the walker distribution away from the minimum energy distribution(kinetic control):

1. foot ‘B’ is completely detached from the track (reduction (III(**i**))), giving the intermediate compound.

2. this compound can then be reoxidised (III(**ii**))., leads to a different outcome compared to the reversible process under conditions **II.**

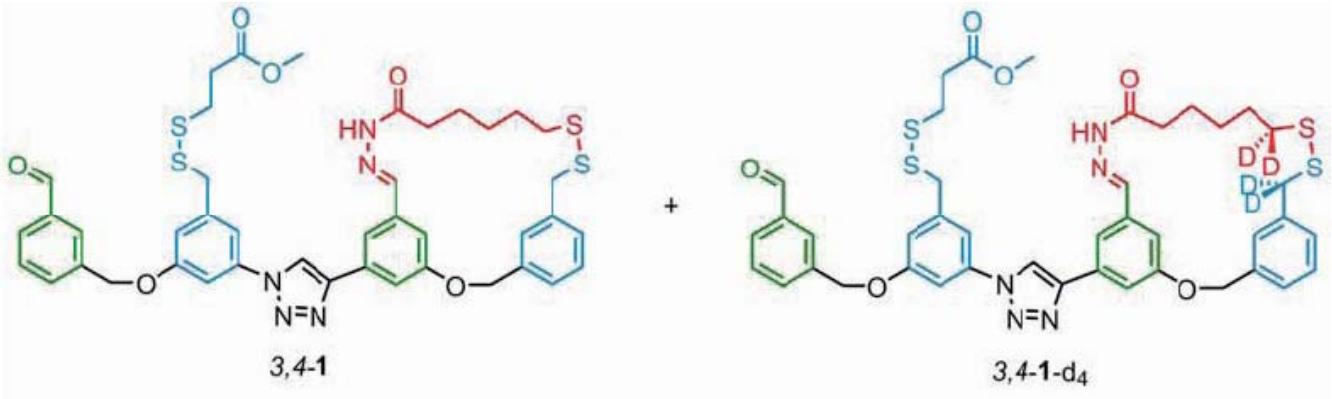
Biased walking – walkers that are transported with intrinsic directionality along a track

Cycles	0	0.5	1	1.5	Steady state from Fig. 4b, *n* = 3
Conditions		I	III	I	
1,2-**1**	100	52	28	24	39
2,3-**1**	0	48	20	24	36
3,4-**1**	0	0	28	**43**	**19**
1,4-**1**	0	0	24	9	6

Fig 5. Evolution of the mixture of positional isomers over three acid–redox operations compared to the acid–base sequence.

After three operational steps, **43%** of the walker units are connected to footholds 3 and 4, while the corresponding number for the steady state obtained using conditions I and II is only **19%.**

Processivity Study - Double-labelling crossover experiment under successive acid-base (non-biased) operation



II (DBU, DTT)

3,4-**1** + *2,3*-**1** + oligomers + *3,4*-**1**-d_4 + *2,3*-**1**-d_4 + oligomers

I (TFA)

II (DBU, DTT)

I (TFA)

3,4-**1** + *2,3*-**1** + *1,2*-**1** + *1,4*-**1** + oligomers + *3,4*-**1**-d_4 + *2,3*-**1**-d_4 + *1,2*-**1**-d_4 + *1,4*-**1**-d_4 + oligomers

Any scrambling,
i.e. d_2 species ?

- the small-molecule walker is highly processive under the operating conditions, with a mean step number of 37 before losing its processivity,

- which corresponds to an average run length of 26 nm on a hypothetical infinite track.

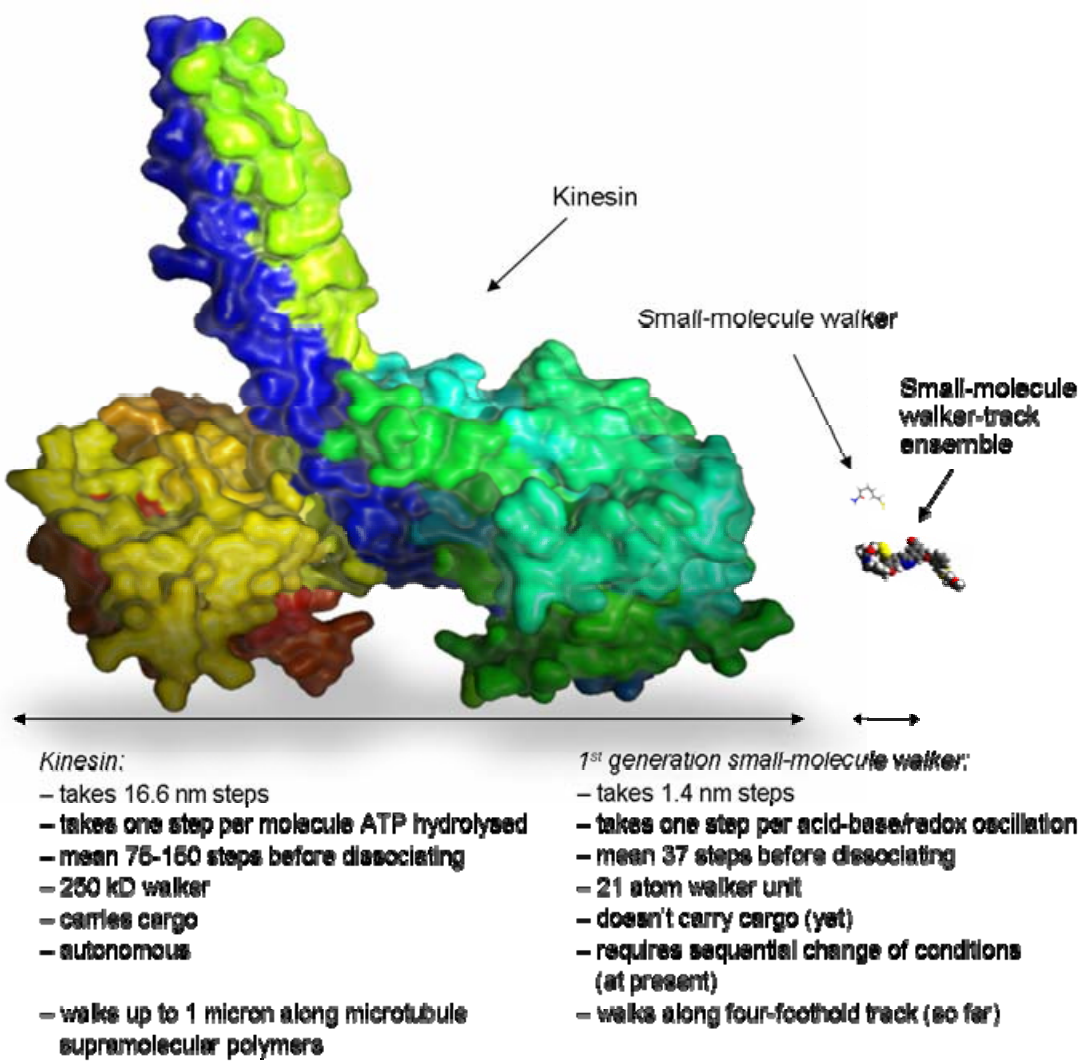


Fig 6. **Size comparison** of wild type kinesin (left) with the synthetic small-molecule walker (right)

Conclusion

1. a system in which a 21-atom molecular walker moves up and down a four-foothold track primarily through a passing-leg gait mechanism, each step induced by an acid–base oscillation.

2. The feet–track interactions feature covalent bonds that are dynamic under mutually exclusive sets of conditions and ensure a level of processivity (mean step number 37) that is 20–50% that of wild-type kinesins.

3. Replacing one of the reactions with a kinetically controlled redox operation biases the directionality of one of the steps.

4. The ultimate goal of such studies is to produce artificial, linear molecular motors that move directionally along polymeric tracks to transport cargoes and perform complex tasks at the nanoscale.

Thank you !!