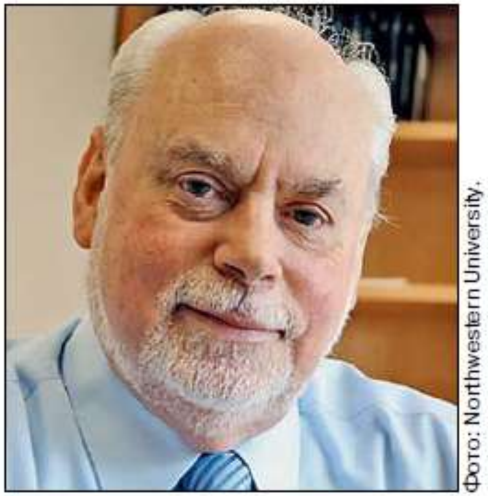
Петербургский институт ядерной физики им Б. П. Константинова, Санкт-Петербург

Нобелевская премия за 2016 год в области химии «Разработка и синтез молекулярных машин»

В. А. Аветисов
Институт химической физики им Н. Н. Семенова, Москва

Нобелевские лауреаты

Жан-Пьер Соваж (Франция)



Джеймс Стоддарт (США)

Бернард Феринга (Нидерланды)

The Royal Swedish Academy of Sciences has decided to award

Jean-Pierre Sauvage*, *Sir James Fraser Stoddart* and *Bernard (Ben) L. Feringa

the Nobel Prize in Chemistry 2016 “for the design and synthesis of molecular machines” .

Although development towards highly complex and useful molecular machines is still in its infancy, the laureates have successfully demonstrated that the rational design and synthesis of molecular machines are indeed possible.

"молекулярная машина" (в понимании Нобелевским комитетом, и лауреатами, конечно)

A molecular-level machine can be defined as “an assembly of a distinct number of molecular components that are designed to perform machinelike movements (output) as a result of an appropriate external stimulation (input)”.

"… машина – это то, что совершает машино-подобные движения … " — замечательное определение!

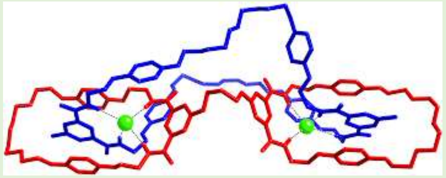
две принципиальные, по мнению Нобелевского комитета, разработки

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.

I. Mechanical bonds

A substantial part of the progress made towards molecular machinery has its roots in the emergence of interlocked molecular assemblies based on mechanical bonds. In such assemblies, the individual parts are not directly connected and held together by covalent bonds, but inseparably entangled through, for example, loops and stoppers.

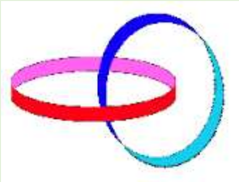
катенаны и ротаксаны

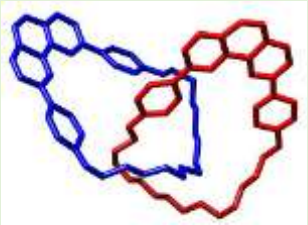


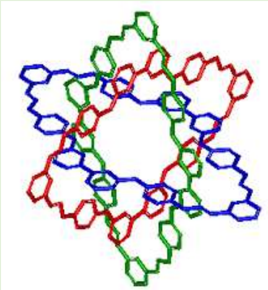
Catenane **–**

two interlocked rings

Латынь : Catena – неразделяемая последовательность, цепь







Первые публикации:

Wasserman, E. The Preparation of Interlocking Rings: A Catenane. *J. Am. Chem. Soc.* 1960, *82* (16), 4433

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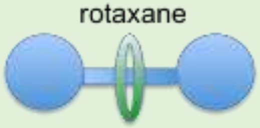
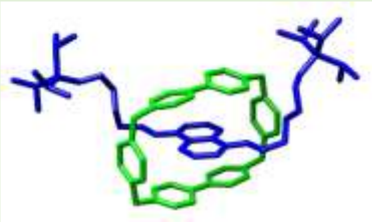
Rotaxane **–**

a ring threaded over an axle with stoppers at each end.





Латынь: Rota + axle – колесо + ось

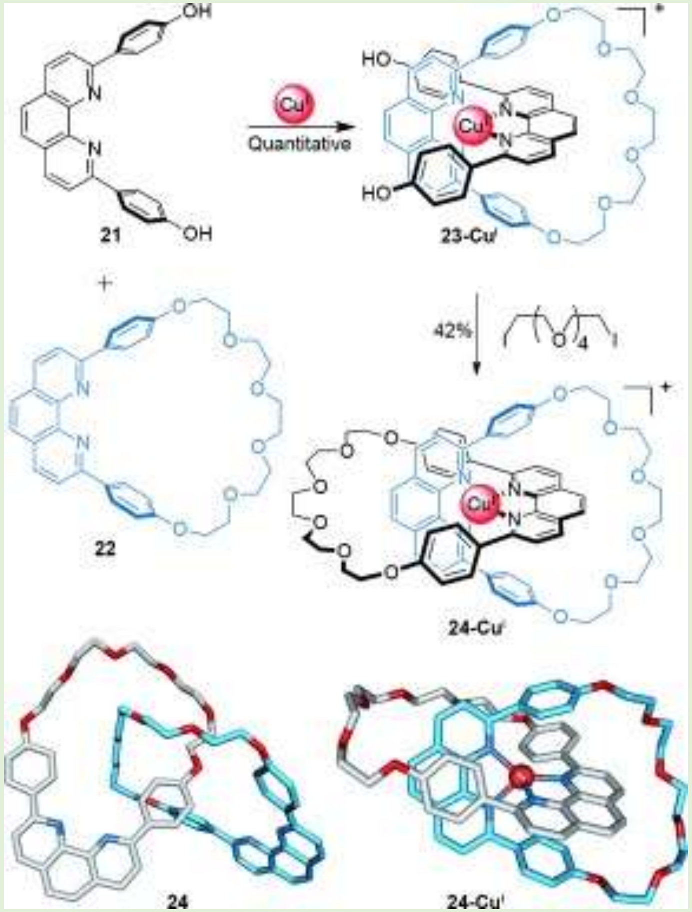
Первые публикации:

T. Harrison and S. Harrison "Synthesis of a stable complex of a macrocycle and a threaded chain". J. Am. Chem. Soc. 1967, 89 (22): 5723–5724.

Ж-П. Соваж придумал как эффективно синтезировать катенаны и ротаксаны

In 1983 the field took a giant leap forward when Jean-Pierre Sauvage and his co-workers introduced template synthesis as a straightforward route to catenanes and rotaxanes. Using metal coordination, the threading of the chains could easily be accomplished, with much higher overall yields as a consequence.

This discovery marked a true breakthrough that dramatically invigorated the field of topological chemistry and subsequently led to molecular machinery. As a consequence, the scientific community gained access to substantial amounts of these complex entities, and the methodology has resulted in a vast range of structures of differing topology.



II. Translational isomerism:

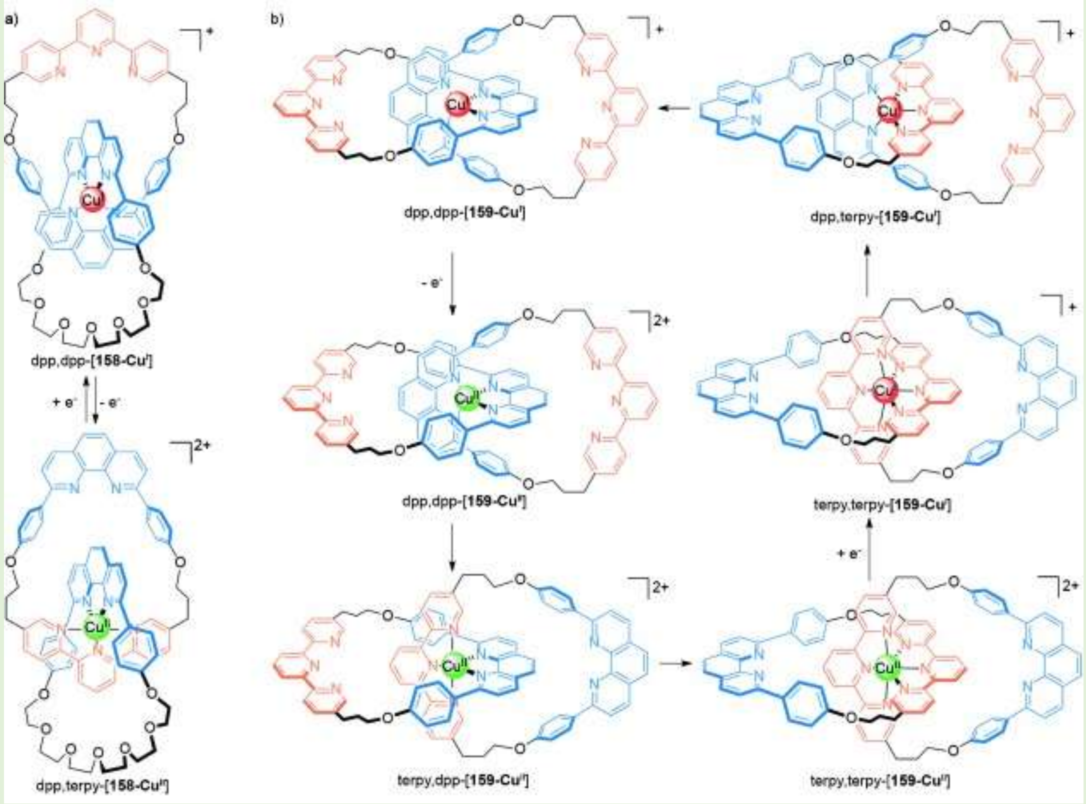
“machine-like movements” of catenanes and rotaxanes designed by J-P. Sauvage and D. Stoddart

Unidirectional rotation in a catenane

Cesario, M.; Dietrich-Buchecker, C.; Guilhem, J.; Pascard, C.; Sauvage, J.-P. Molecular Structure of a Catenand and Its Copper(I) Catenate: Complete Rearrangement of the Interlocked Macrocyclic Ligands by Complexation. *J. Chem. Soc. Chem. Commun.* 1985, 244–247.

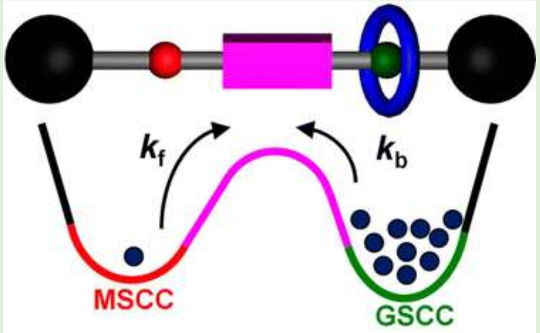
Based on the catenanes developed, Sauvage and co-workers were subsequently able to demonstrate the potential of the structures for *translational isomerism*.

Dramatic, reversible changes in the catenanes' molecular shape were thus observed upon decomplexation and recomplexation of the metal coordination entities with Cu(I).



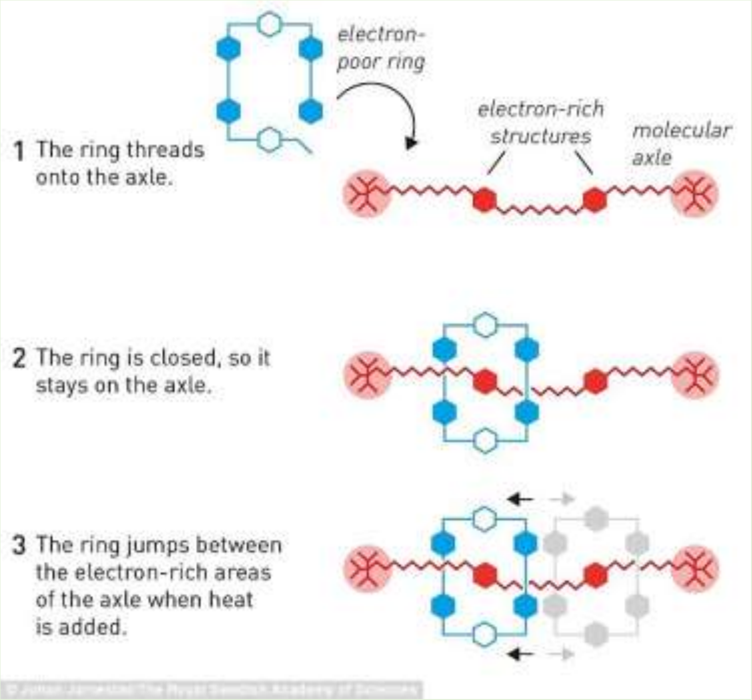
molecular shuttle

Anelli, P. L.; Spencer, N.; Stoddart, J. F. A Molecular Shuttle. *J. Am. Chem. Soc.* 1991, *113* (13), 5131–5133.



The field took another big leap forward in 1991, when a clear demonstration of translational isomerism was reported by the group of Sir James Fraser Stoddart …

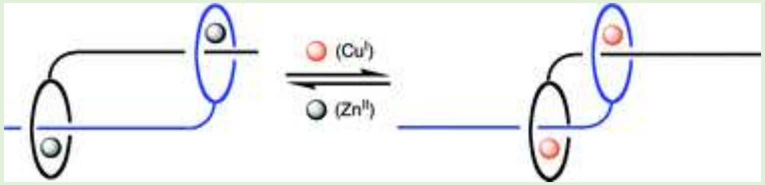
Stoddart and co-workers had been working in the 1980s <…> in the development of a <rotaxane ring>, which could be “clipped” around an axle containing two hydroquinol units separated by a linker. The resulting rotaxane ring could be shown to act as a molecular shuttle, able to move between the two hydroquinol stations on the axle.



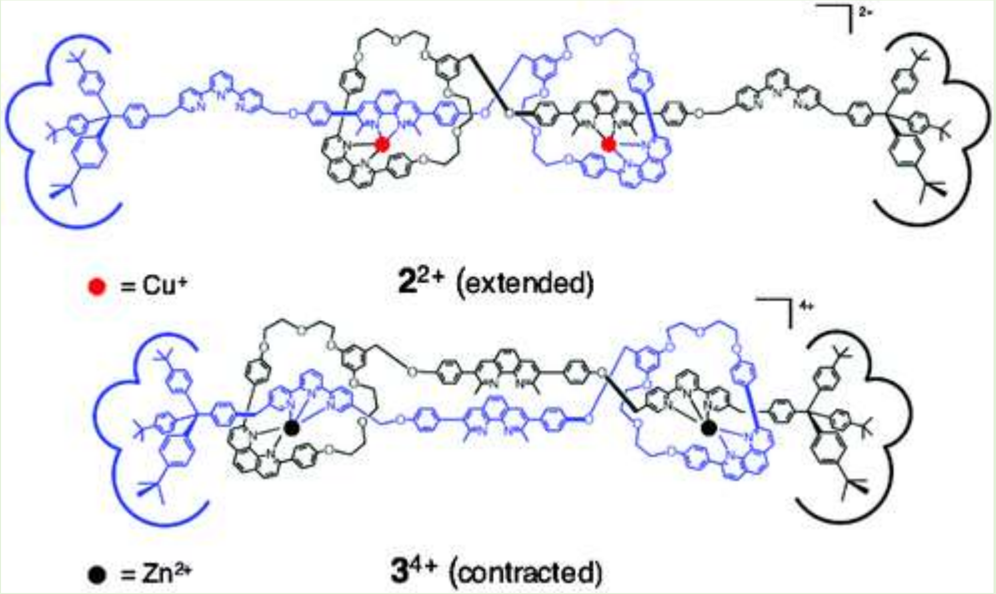
Together with Sauvage’s demonstration of reversible catenane shape-shifting, this work marked the start of applying topological entanglement in the development of molecular machinery.

contraxiton/extention ("muscle-like") molecular machine (J-P Sauvage, since the late of 1990s…)

For review, see Jean-Pierre Sauvage
Chem. Commun., 2005, 1507-1510

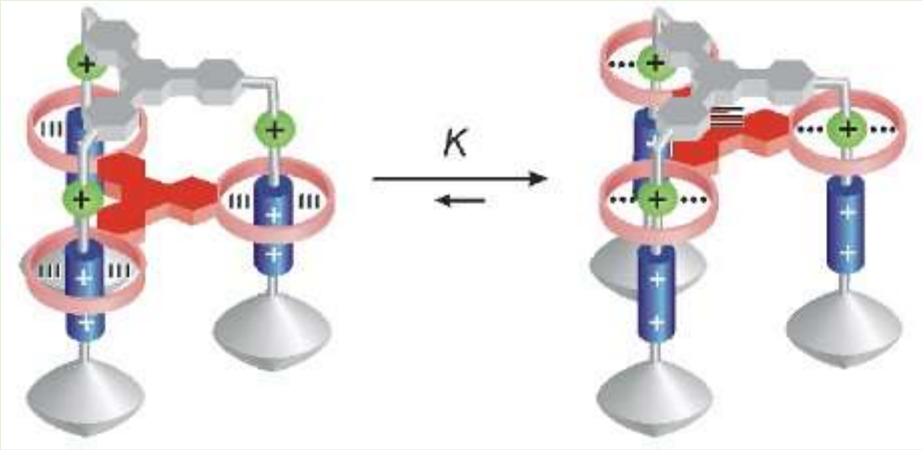


Since the late 1990s, the application part of the field has increasingly been addressed by the groups, and also pursued by many other researchers. Chemical control of molecular contraction/extension, resembling the action of muscles in living systems, was for example demonstrated in a topologically challenging daisy-chain structure by the Sauvage group in 2000 . By integrating two mutually entangled rotaxane functionalities, they were able to achieve high control of translational contraction and extension of ca. 2 nm under chemical stimulus.

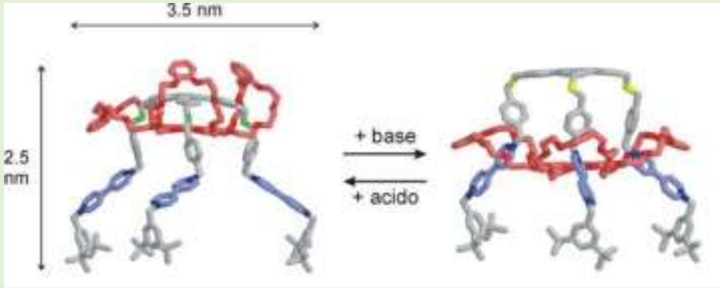


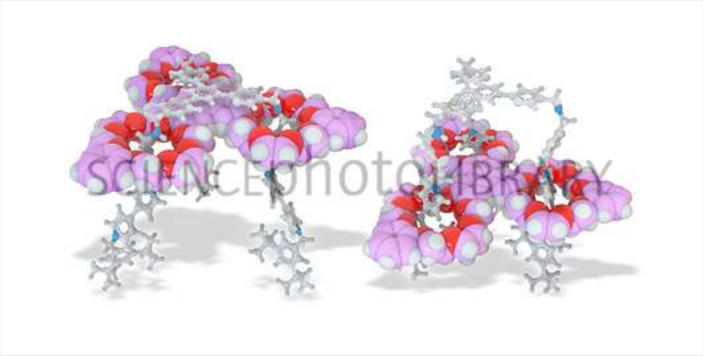
Stoddart's molecular elevator

Badjić, J. D.; Balzani, V.; Credi, A.; Silvi, S.; Stoddart, J. F. A Molecular Elevator. Science 2004, 303 (5665), 1845–1849.



Similarly, the Stoddart group developed a complex rotaxane device called a "molecular elevator" in 2004, where high control of the motion of a moving plane between two "floors" separated by a distance of 0.7 nm could be achieved

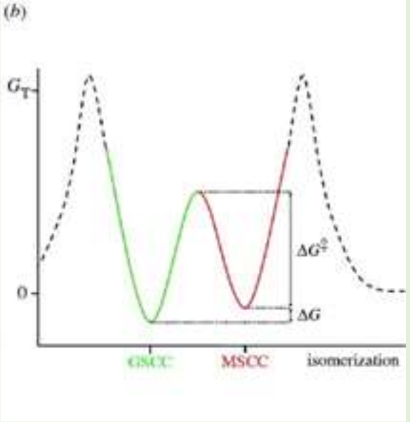




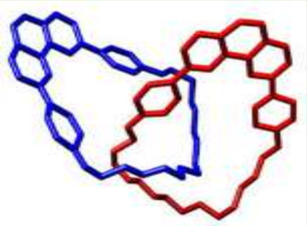
Logic gates and electronic devices based on two-state (Boolean) translational isomerism

Collier, C. P.; Wong, E. W.; Belohradský, M.; Raymo, F. M.; Stoddart, J. F.; Kuekes, P. J.; Williams, R. S.; Heath, J. R. Electronically Configurable Molecular-Based Logic Gates. *Science* 1999, *285* (5426), 391–394

Together with colleagues, the Stoddart group has in addition pursued the development of molecular-scale electronic devices based on rotaxanes and catenanes, with the intention of fabricating molecular logic gates and memories.



The rotaxanes were mounted between electrodes in a microelectronic device and could be shown to respond to writing potentials, resulting in closed and opened states that could be read at a non-perturbing potential.



160 kbit memories, composed of a few hundred rotaxanes/bit and a density of ca. 100 Gbit/cm2, could be fabricated using this methodology.

III. Isomerisable unsaturated bonds:

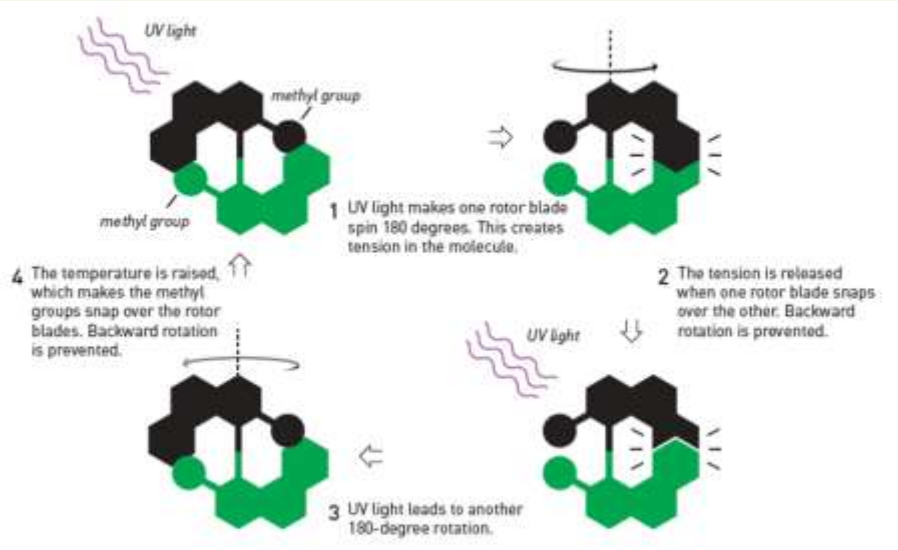
Feringa's molecular rotor

The first example of controlled unidirectional rotation <…> was reported by Bernard L. Feringa.

Koumura, N.; Zijlstra, R. W. J.; Delden, R. A. van; Harada, N.; Feringa, B. L. Light-Driven Monodirectional Molecular Rotor. *Nature* 1999, *401* (6749), 152–155.

In parallel with the advances based on mechanically interlocked structures, isomerisable unsaturated bonds have also been at the core of progress on molecular machines.

This pathway has witnessed a number of important contributions, in which different entities have been designed, synthesised and applied to rotation. The major challenge of achieving controlled unidirectional rotation, however, marks the most fundamental breakthrough in this development.



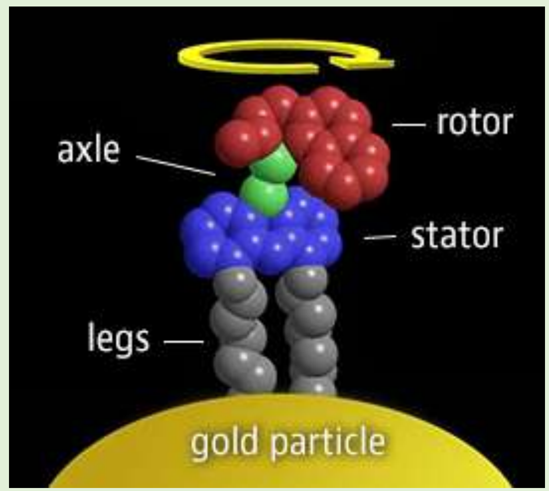
Using so-called overcrowded alkenes, and engineering asymmetries in the molecules, it was possible to obtain unidirectional rotation through cycles of light irradiation and thermal relaxation.

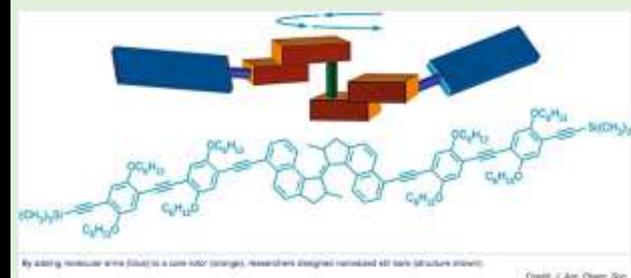
Feringa's molecular motor

Delden, R. A. van; Wiel, M. K. J. ter; Pollard, M. M.; Vicario, J.; Koumura, N.; Feringa, B. L. Unidirectional Molecular Motor on a Gold Surface. *Nature* 2005, *437* (7063), 1337–1340.
Eelkema, R.; Pollard, M. M.; Vicario, J.; Katsonis, N.; Ramon, B. S.; Bastiaansen, C. W. M.; Broer, D. J.; Feringa, B. L. Molecular Machines: Nanomotor Rotates Microscale Objects. *Nature* 2006, *440* (7081), 163–163.
Vachon, J.; Carroll, G. T.; Pollard, M. M.; Mes, E. M.; Brouwer, A. M.; Feringa, B. L. An Ultrafast Surface-Bound Photo-Active Molecular Motor. *Photochem. Photobiol. Sci* 2014, *13*, 241–246.

Following the original breakthrough, several major advances were made. For example, the motor construct was mounted on a gold surface, anchoring the stator part of the device, leading to a surface-mounted, light-driven propeller-type function.

In 2005, another motor system was developed, in this case driven by selective protection/deprotection of phenolic groups < …>, thus allowing for chemical fuelling of the rotational molecular motion. It could also be shown that motor components can be made to controllably rotate in either direction upon addition of a base.

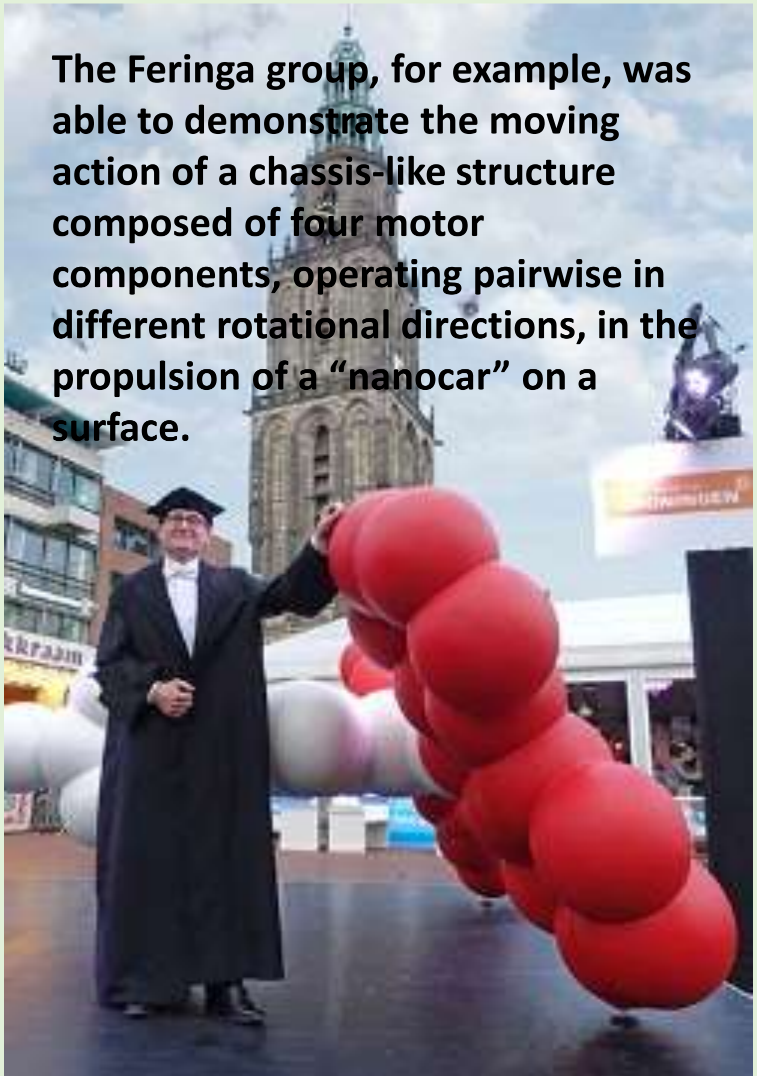




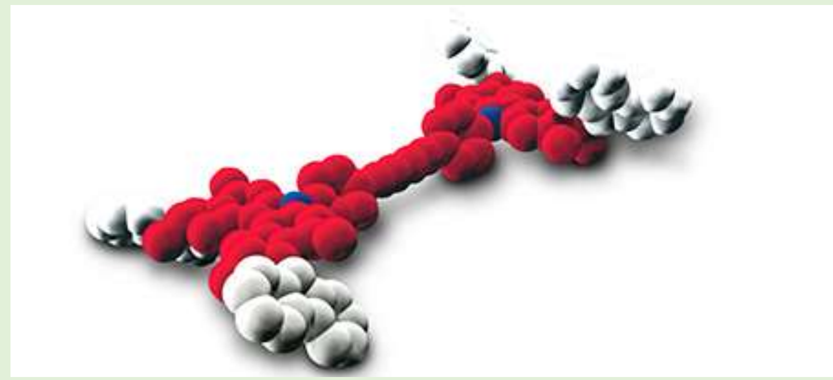
In 2014, for example, an optimised motor structure was demonstrated to rotate with a frequency of over 12 MHz.

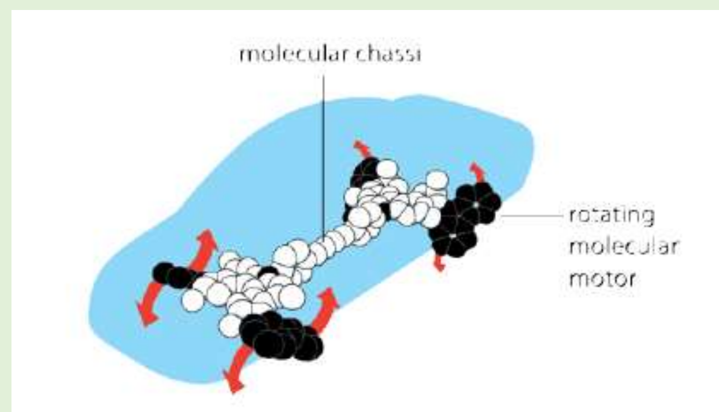
Feringa proposed nanocar

Kudernac, T.; Ruangsupapichat, N.; Parschau, M.; Maci. Electrically Driven Directional Motion of a Four-Wheeled Molecule on a Metal Surface. *Nature* 2011, *479* (7372), 208–211.



The Feringa group, for example, was able to demonstrate the moving action of a chassis-like structure composed of four motor components, operating pairwise in different rotational directions, in the propulsion of a "nanocar" on a surface.





Обзоры:

Richard Feynman.
http://calteches.library.caltech.edu/47/2/1960Bottom.pdf

S. Erbas-Cakmak, D. A. Leigh, C.T. McTernan, and A. L. Nussbaumer . Artificial Molecular Machines. Chem. Rev. 2015, 115, 10081−10206

There's Plenty of Room at the Bottom

An invitation to enter a new field of physics.

by Richard P. Feynman

CHEMICAL REVIEWS
Review
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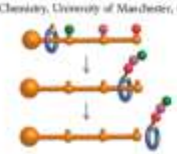
Artificial Molecular Machines

Sundus Erbas-Cakmak, David A. Leigh,* Charlie T. McTernan, and Alina L. Nussbaumer
School of Chemistry, University of Manchester, Oxford Road, Manchester M13 9PL, United Kingdom



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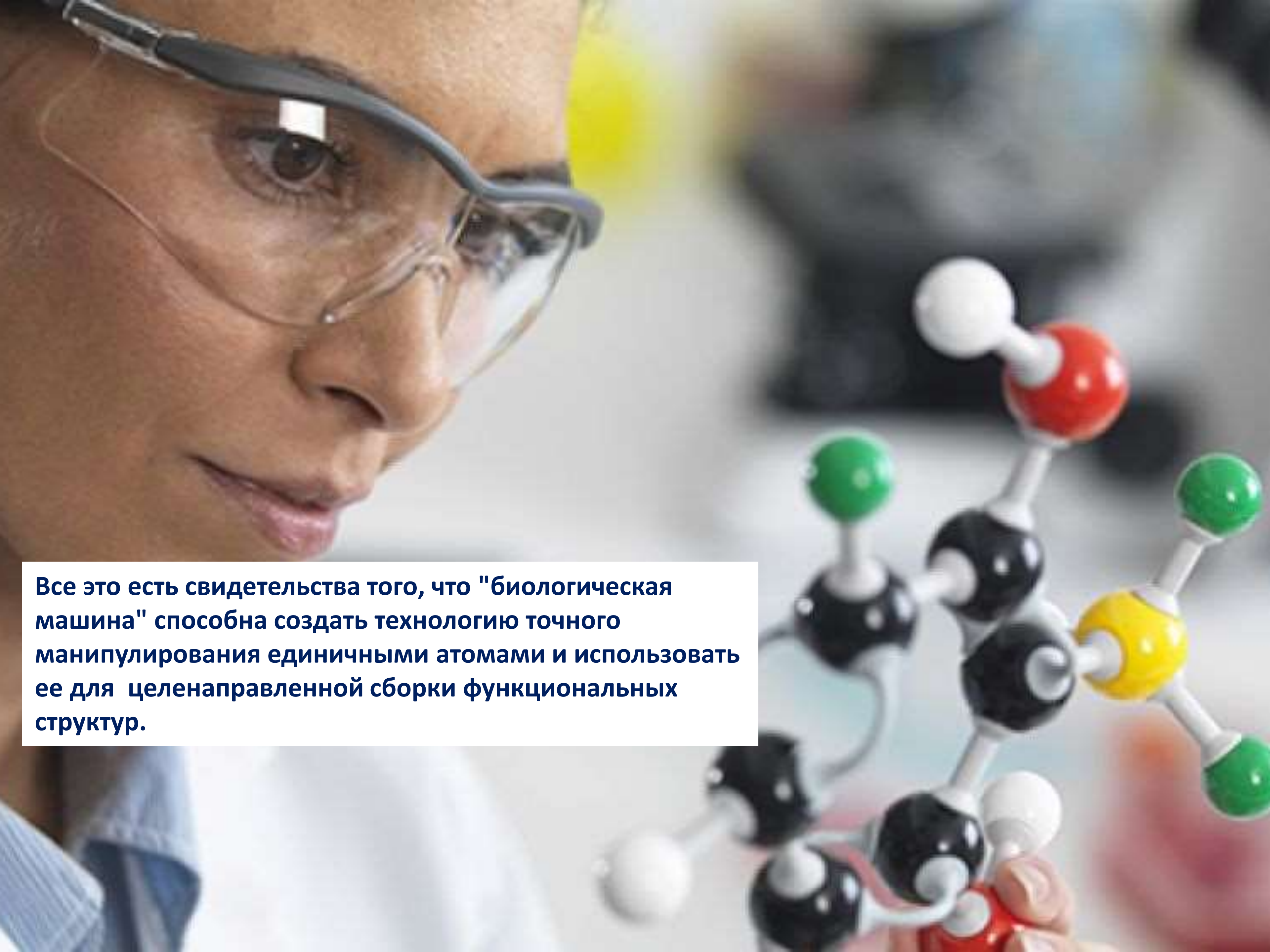
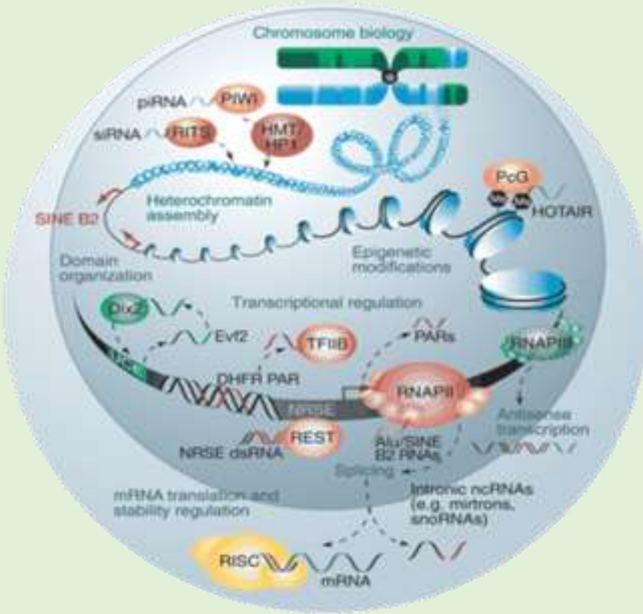
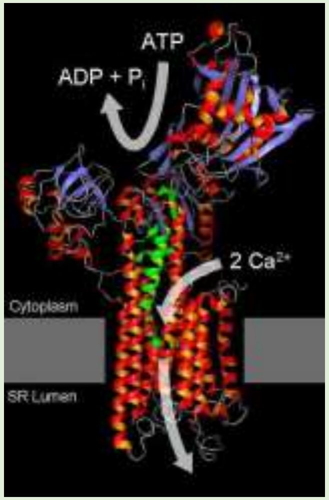


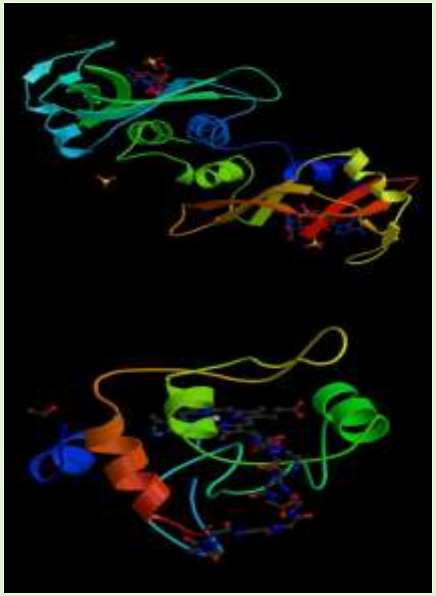
Все это есть свидетельства того, что "биологическая машина" способна создать технологию точного манипулирования единичными атомами и использовать ее для целенаправленной сборки функциональных структур.

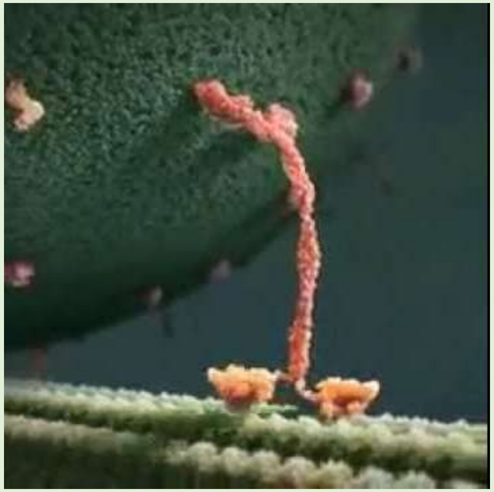
Аналогичная технология есть и в природе, и возникла она "самопроизвольно", без всякого участия человека.

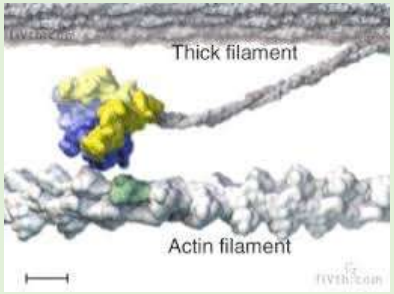
Цель у Природы была та же – точная сборка сложных молекулярных структур с помощью молекулярных машин, но машины она сделала принципиально другие, основанные не на трансляционном или поворотном изомеризме, а на конформационной динамике полимеров.

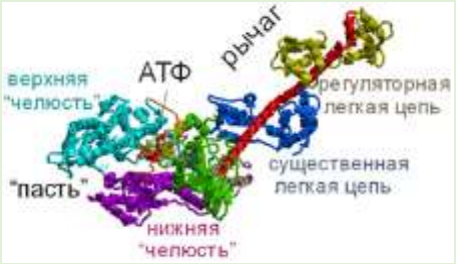










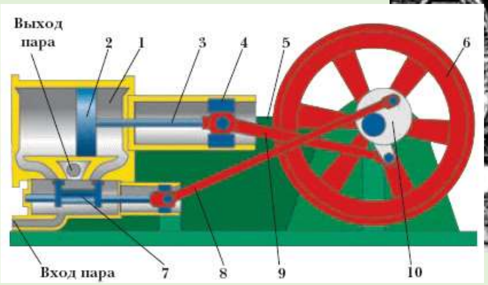


Природные (биологические) молекулярные машины — это динамические системы, и создавая такие системы следует, в первую очередь, смотреть на их физические свойства.

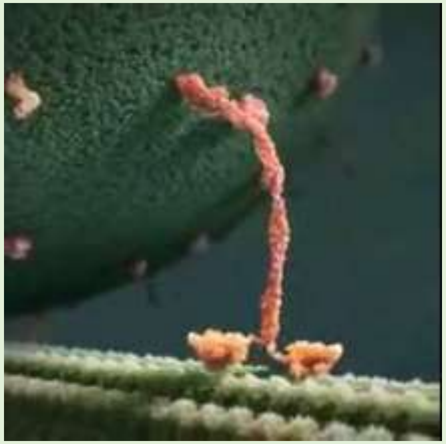
Какие?

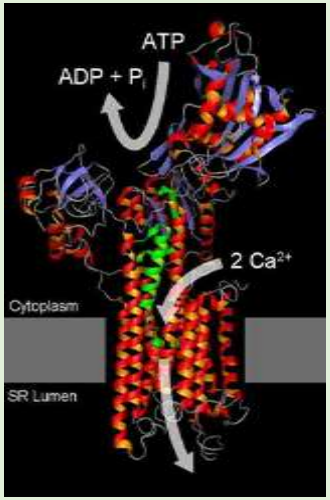
Машины и молекулярные машины.

Машина (тепловая) есть устройство, преобразующее тепловую энергию в механическое движение, …



молекулярная машина – это такое же устройство, только нанометрового масштаба.



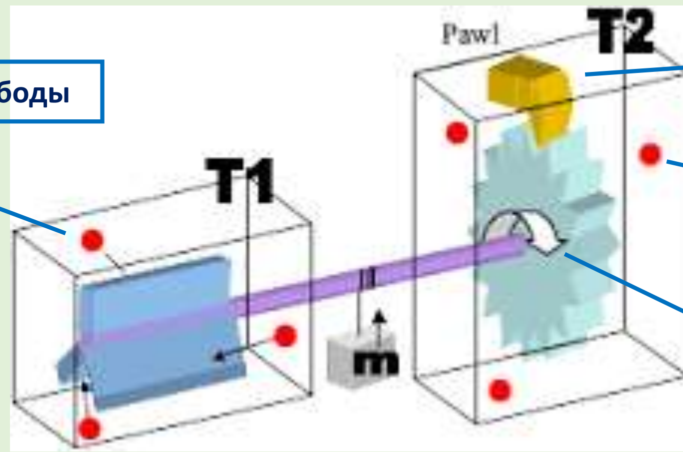


физика:

Молекулярная машина - система наноразмерного масштаба, преобразующая возмущение большого числа быстрых степеней свободы в направленное движение вдоль одной-двух медленных (квазимеханических) степеней свободы.

быстрые степени свободы

выделенное направление



тепловые флуктуации

медленная (механическая) степень свободы

Если не забывать про то, на наномасштабах все "трясется и прыгает", и про то, что механика – это когда масштаб флуктуаций конструкции существенно меньше масштаба движения конструкции, то "броуновская машина" Фейнмана является замечательной моделью молекулярной машины. Ее (машину Фейнмана) цитируют все, и Нобелевский комитет тоже.

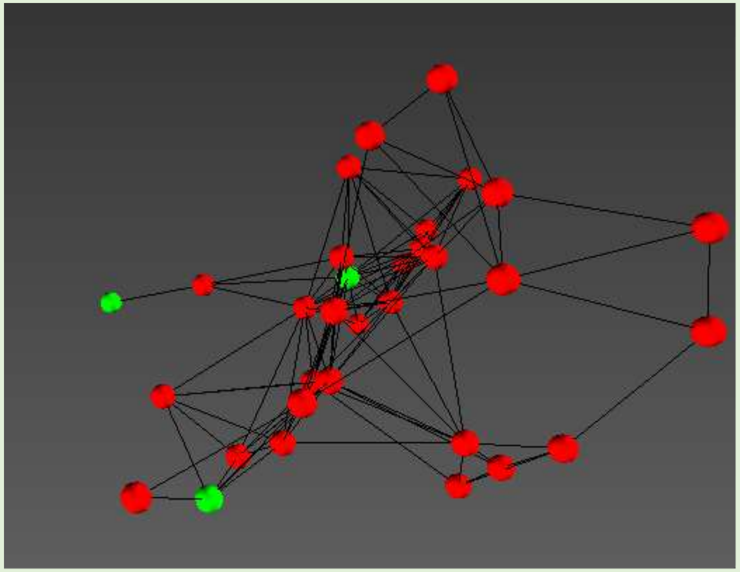
физическая модель

молекулярная структура как эластичная (динамическая) сеть

Уравнения для движения узлов под действием упругих сил (в сильно демпфированном приближении):

$$\frac{d\mathbf{R}_i}{dt} = \sum_{j=1}^{N} a_{ij} \frac{\mathbf{R}_j - \mathbf{R}_i}{|\mathbf{R}_j - \mathbf{R}_i|} (|\mathbf{R}_j - \mathbf{R}_i| - |\mathbf{R}_i^{(0)} - \mathbf{R}_j^{(0)}|)$$

$\mathbf{R}_i$ - положение i-ого узла сети, $\mathbf{R}_i^{(0)}$ -его равновесное положение, a_{ij} -элемент матрицы смежности (связей) сети.



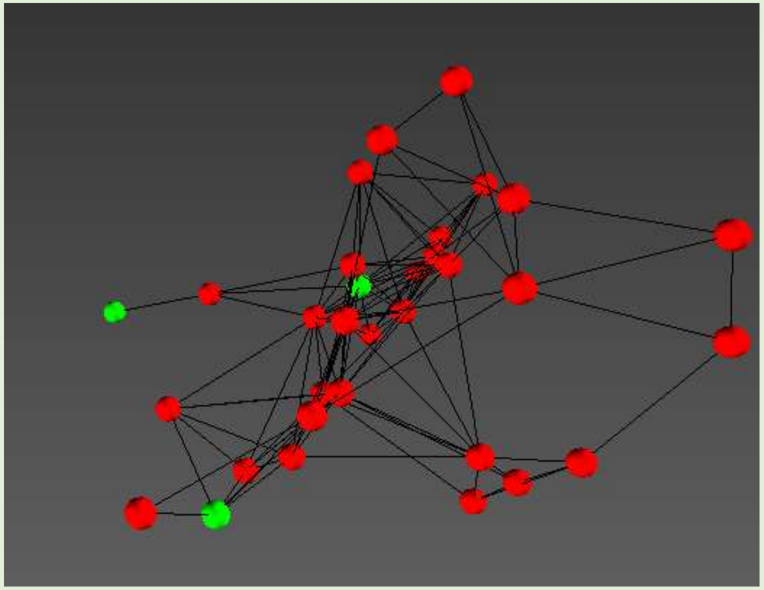
Для малых отклонений $\mathbf{r}_i = |\mathbf{R}_i - \mathbf{R}_i^{(0)}|$, $(|\mathbf{R}_i - \mathbf{R}_i^{(0)}| / \max\{|\mathbf{R}_i^{(0)} - \mathbf{R}_j^{(0)}|\} \ll 1)$:

$$\frac{d\mathbf{r}_i}{dt} = -\sum_{i}^{N} \mathbf{\Lambda}_{ij} \mathbf{r}_j \quad ;$$

Спектр собственных значений матрицы линеаризации $\mathbf{\Lambda}$ есть спектр нормальных релаксационных мод структуры.

методика исследования

малые возмущения – вычисляем нормальные релаксационные моды, т.е. собственные значения и собственные векторы матрицы линеаризации полной системы динамических уравнений эластичной сети



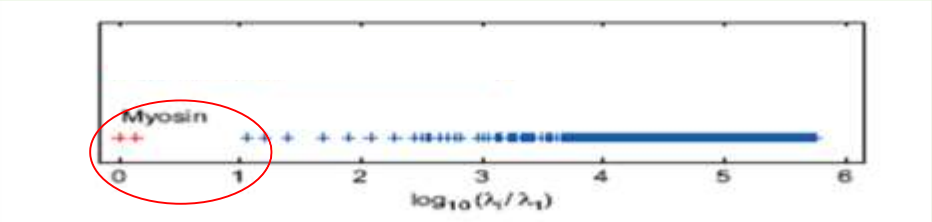
большие возмущения – изучаем динамические траектории и аттракторы в (многомерном) фазовом пространстве системы.

Динамика сети существенно зависит от ее топологических свойств.

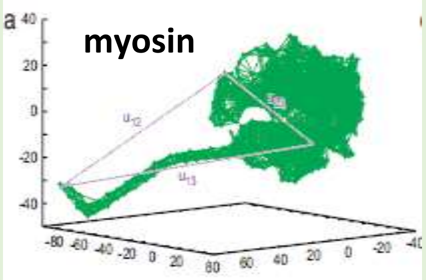
Эластичные сети белков

Yuichi Togashi, and Alexander S. Mikhailov
PNAS 2007;104;8697-8702; originally published online May 16, 2007;

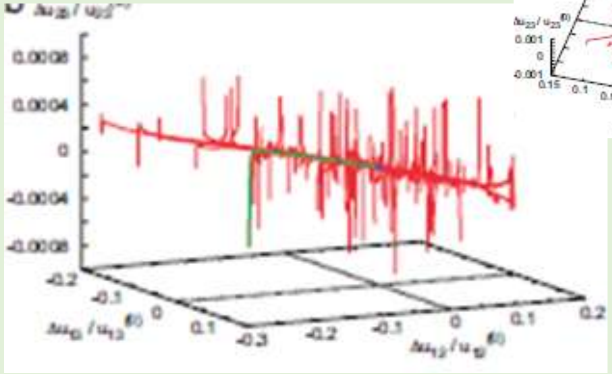
1. Имеется большая спектральная щель, отделяющая две самые медленные релаксационные моды от остальных.

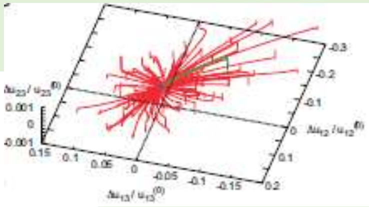


эластичная сеть миозина



2. Имеется низкоразмерное многообразие с большим бассейном притяжения: - траектории вначале быстро притягиваются к двухмерному подпространству двух самых медленных степеней свободы и затем, оставаясь в нем, медленно стягиваются к точке равновесия .



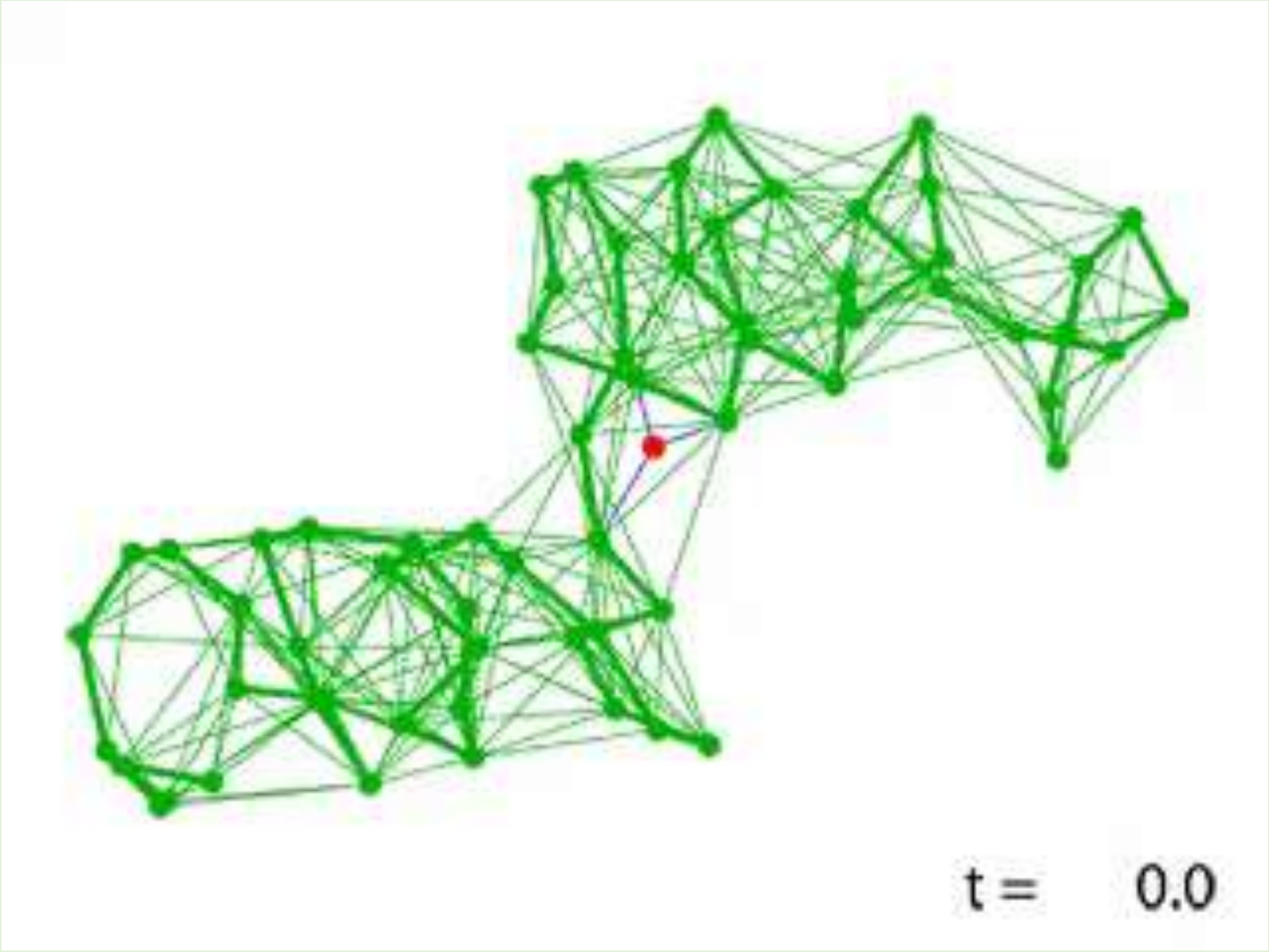


Белки – это действительно молекулярные машины.

Белки преобразуют возмущение быстрых степеней свободы, инициированное химической реакцией в активном центре белка, или поглощением излучения, в движение "механических" субъединиц вдоль одной-двух медленных степеней системы.

Это не совсем то, что сделали Нобелевские лауреаты.

Дизайн молекулярных машин



все только в начале …

…

… а какой путь выбрать – решайте сами.

Успехов вам!