Study of Artificial Molecular Engines Action Through COMSOL Multiphysics Program

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Abstract: Rotaxanes are a class of molecules recently developed in laboratory that have been heralded as possible molecular motors. The motor is constituted by a linear molecule (thread) and a ring-shaped molecule (macrocycle), which is free to move along the thread, switching between two, or more, energetically stable interaction points (stations).
Molecular motors start their functioning far from chemical equilibrium and, moving towards equilibrium, turn chemical energy into motion and mechanical power. Their theoretical and computational study is possible through the help of statistical mechanics. Starting from a diffusion equation and including casual, or Brownian, events, the differential equations that describe the motion of particles and/or molecules are well known. Langevin has long ago proposed one of the simpler descriptions, where the associated differential equation can be solved analytically only in a few cases. The Fokker-Planck equation is an alternative stochastic description of the evolution of a chemical system that rarely has an analytic solution and is here investigated with COMSOL Multiphysics program.

Keywords: Molecular motors, Statistical mechanics, Fokker-Planck equation, Rotaxanes.

1. Introduction

The existence in Nature of molecular systems able to undergo unidirectional mechanical movements, such as rotations or translations is well known. They evolved to perform functions necessary for life and have been investigated for decades. Only recently, however, completely artificial molecular systems, capable of generating mechanical work, have been developed. These systems are usually referred to as molecular machines and convert chemical energy into motion, but only in rare occasions useful work has been obtained.

The chemical reaction that "switch on" the machine can be of a various types and include pH variations and light irradiation of a proper energy. The external stimulus drives the molecule in a state away from chemical equilibrium; the system then restores equilibrium by Brownian motion.

The object of this study is a class of molecular machines known as rotaxanes (figure 1). They consist of a ring, or rota (from Latin) that can freely move along a linear thread, or axis, terminated at both ends by two stoppers.
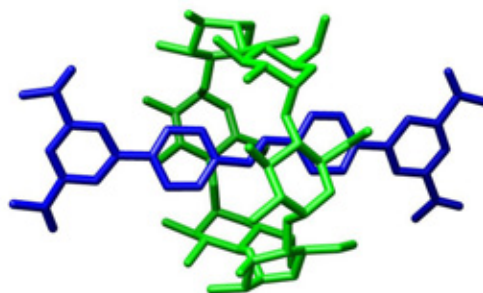

Figure 1. An example of a simple rotaxane.

The linear thread can be a simple linear organic molecule such as an alkyl chain and the stoppers are bulky groups that do not allow falling off of the ring (also called walker).

An energetically stable situation is obtainable by inserting in the chain one or more complexing groups, or stations, that can establish strong interactions with the ring, usually hydrogen bonds or ionic interactions. In the case of a simple alkyl chain, the complexing moiety can be a NH_2^+ group (1).

At the chemical equilibrium, the ring is positioned at the station, which in a potential energy diagram is represented by a well.

If an external impulse changes the depth of the energy well making it less deep (for example one can think of removing a proton from the amino group by the addiction of a base), the ring can have enough thermal energy to overcome the potential barrier and locate itself at any position on the linear thread. Once restored the initial conditions, the ring will return to the more

chemical stable position exerting a force and work on the surrounding environment.

More interesting systems are those where, on the same linear thread, there are two stations, which can generate bistability. In the initial conditions, the probability to find the ring is centred at the deeper well. If the molecule is properly designed, with an external impulse, it is possible to modify the energy gap between the wells, making the initially less deep well stable than the other and causing the ring to move towards the latter. If the initial situation is restored, the ring returns to the initial stable position. This process, with appropriate impulses, can be repeated an unlimited number of times.

The theoretical and computational study of the dynamics of these systems is important to fully understand the mechanisms underlying the motion and to predict and quantify the mechanical work that can be extracted together with the timescales in which the phenomena occur. It is also necessary for the design of systems that are suited for the purpose for which they are intended.

2. The model

In a rotaxane without stations, the position of the ring and its speed are completely random variables, which vary continuously over time subject to the impact of the solvent molecules that move rapidly and randomly due to thermal fluctuations. The motion of the ring in this situation is describable as that of a Brownian particle.

The dynamics of these systems can be rationalized with the Langevin equations; these are equations of motion that describes the motion of a particle subjected to the action of a random variable that simulates the impacts of the molecules of the fluid against the Brownian particle.

A generic Langevin equation for the description of the mono-dimensional Brownian motion of particle of a mass m is

$$m\frac{d^2 x}{dt^2} = -\ \frac{dx(t)}{dt} + F(t) \qquad (1.1)$$

where $\gamma = \alpha/m$ in which α is the friction coefficient obtainable by the Stoke's law.

Equation (1.1) is nothing but a Newton's motion equation to which a random force, $F(t)$, called Langevin force, is added. The force is useful to describe the impact of the molecules of the solvent against the Brownian particle, and must satisfy some properties.

The first property is that its mean is zero

$$\langle F(t) \rangle = 0 \qquad (1.2)$$

Furthermore, its autocorrelation function, is equal to

$$\langle F(t)F(t') \rangle = q\ \ (t - t') \qquad (1.3)$$

Given equation (1.3), $F(t)$ is called δ-correlated and the parameter q is an indication of the strength of the correlation. Calculation of the spectral density of (1.3) through a harmonic analysis gives a result that is completely independent of the frequency. A function with these properties is called white noise.

Equation (1.1) contains a stochastic variable and was the first example of a stochastic differential equation whose solution is achievable only in the form of average values (2).

The greatest limitation of the model proposed by Langevin is that the equations are difficult to apply to macroscopic systems. For systems of an Avogadro number of particles, $N \approx 10^{23}$, one has to solve the equation (1.1) for all the particles knowing in advance for each of them the initial position and velocity.

Moreover, for systems where there are potential wells they lose all their apparent simplicity.

An approach of this kind is hence not effective for obtaining information on the dynamics of complex and macroscopic systems.

A more efficient approach to describe the dynamics of systems operating far from equilibrium is achieved with the use of statistical mechanics. Starting from the Langevin approach, it is possible to obtain the probability distributions of the stochastic variable $F(t)$ and the variables derived from it, such as speed and position, of the set of Brownian particles (3).

The equation that describes the variation in time of the probability distribution is the Fokker-Planck equation. If the random variable is the

position (in the x coordinate), the general form of the Fokker-Planck equation, FPE, is

$$\frac{\partial W(x,t)}{\partial t} = \left[-\frac{\partial}{\partial x} D^1(x) + \frac{\partial^2}{\partial x^2} D^2(x) \right] W(x,t)$$

(1.4)

where $D^2(x) > 0$ is the diffusion coefficient and $D^1(x)$ is the drift coefficient.

Equation (1.4) is an equation of motion for the probability distribution function $W(x,t)$ and, mathematically, is a linear second order partial derivates differential equation, of a parabolic type. It is also known as forward Kolmogorov equation.

In case the drift coefficient represents a force, due to a potential energy $U(x)$, with an appropriate transformation of variable, the general FPE can always be transformed into an equation where the diffusion coefficient is a space independent constant (3); the general Fokker-Planck equation becomes

$$\frac{\partial W(x,t)}{\partial t} = \left[\frac{\partial}{\partial x} U'(x) + D \frac{\partial^2}{\partial x^2} \right] W(x,t)$$

(1.5)

Where $U'(x)$ is a space derivate of the potential. This equation can be rewritten as

$$\frac{\partial W(x,t)}{\partial t} = L_{FP} W(x,t)$$

(1.6)

Where L_{FP} is the Fokker-Planck operator.

In the past decades, one-dimensional Fokker-Planck equations have received particular attention, especially in the case of a bistable, time-independent potentials because it provides a useful model for investigating the evolution of stochastic systems from an initial unstable state to a final stable state (4,5).

Stationary solution of equation (1.5) can be easily found with an appropriate transformation finalized to make the diffusion coefficient an arbitrary constant which is completely space independent. For a time independent, confining potential, $U(x)$, such as that of figure 2, and diffusion constant D, with following boundary conditions

$$W(x,t) = 0 \quad \text{for} \quad x = \pm\infty$$

it is

$$W_{ST}(x) = N \exp[-U(x)/D]$$

(1.7)

Where ST stays for stationary and N is the normalization constant which is

$$N = \left\{ \int_{-\infty}^{\infty} \exp[-U(x)/D]dx \right\}^{-1}$$
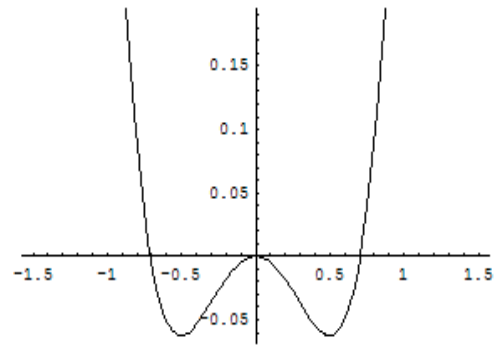
(1.8)

Figure 2. A typical bistable confining potential described by the quartic function $y=0.25x^4-0.5x^2$.

The analytical solution of the FPE, and the equations derived from it, is yet not immediate and is known only for some special systems. In general, it is even more complicated in the case when a nonstationary solution is required.

Since nonstationary solution are more difficult to obtain. A general expression for them can be found only for special drift and diffusion coefficients. The problem can be approximate in two ways. It can be treated as a Wiener process, a process, which is described by equation 1.4 with a vanishing drift coefficient and a constant diffusion coefficient. Alternatively, the process can be treated as a Ornstein-Uhlenbeck process where the drift coefficient is linear and the diffusion coefficient is constant.

If the problem can not be approximated in the latter two models, an efficient way of work is to carry out an Eigen function expansion to obtain a Schrödinger-type diffusion equation, SE, where the diffusion constant is arbitrary and completely space independent (3).

The transformation that leads from the FPE to a SE, transforms the one-dimensional Fokker-Planck operator L_{FP} into an Hermitian operator L

$$L = D \frac{\partial^2}{\partial x^2} - V(x) \qquad (1.9)$$

Where $V(x)$ represents the external potential that is given by

$$V(x) = \frac{1}{4} \left[\frac{dU(x)}{dx} \right]^2 / D - \frac{1}{2} \left[\frac{d^2U(x)}{dx^2} \right] \qquad (1.10)$$

Where to obtain the correct dimensionality, one should notice that x is a space coordinate weighted on the mass of the particle and on the friction coefficient.

With these transformations the one dimensional Fokker-Planck equation becomes

$$L\Psi_n = -\,_n\Psi_n \qquad (1.11)$$

where the integers n=0,1,2,.. label the eigenfunctions with $\lambda_0=0$ and $\lambda_0 < \lambda_1 < \lambda_2 < \ldots$

Equation (1.11) is a time dependent Schrödinger-type diffusion equation where the wave function evolves in imaginary time $-i\hbar t$ for a particle with a mass given by $m=\hbar/(2D)$.

Once the eingenfunctions and the eigenvalues are calculated, it is possible to obtain the corresponding distribution probability.

In this way, a nonstationary solution is obtainable using a state-dependent diagonalization (6) or with others mathematical methods (7,8).

A particular type of Fokker-Planck equation, known as Smoluchowski equation, is very useful for the description of the time evolution of systems in the presence of high friction constants, i.e. condensed phases, where the motions of the Brownian particles satisfy the relation

$$v \gg ma \qquad (1.12)$$

this equation implies that is possible to ignore the inertial effects on the particle.

The Smoluchowski equation is a good description of processes where the particles have negligible masses (9); in this instance the diffusion and drift coefficients reads

$$D^{(1)} = (m\ )^{-1} F(x) = -(m\ )^{-1} \frac{\partial}{\partial x} U(x) \qquad (1.13)$$

$$D^{(2)} = k_B T(m\ )^{-1} \qquad (1.14)$$

where $\gamma=\alpha/m$; α is given by the Stokes law, m is the mass of the particle, k_B is Boltzmann constant and $U(x)$ is the energy potential that describes the shape of the potential energy wells, in the present case constituted by the stations of the rotaxane.

With these parameters the corresponding Smoluchowski equation reads

$$\frac{\partial W(x,t)}{\partial t} = \frac{1}{m} \left[-\frac{\partial}{\partial x} F(x) + k_B T \frac{\partial^2}{\partial x^2} \right] W(x,t) \qquad (1.15)$$

where $F(x)$ is the force due to the potential $U(x)$.

Once the normalized distribution probability is obtained, it is possible to find a variety of important physical quantities, such the mean displacement that shows the directionality of the motion. It is also possible to obtain the variation of entropy in time and the work done.

For our purposes, it is necessary to find a nonstationary solution of the equation (1.15) in order to obtain a realistic description of the motion of the ring; we study the motion of rotaxane with two stations and seek a solution of the Smoluchowski equation for a symmetric bistable potential.

3. Use of COMSOL Multiphysics

The initial target with the COMSOL program was to find the solution of the equation (1.5) compatible with the correct analytical solution obtainable from the corresponding Schrödinger type equation (1.11) (6).

We created a model compatible with the theoretical work carried out by other research groups to find a nonstationary solution of the Fokker-Planck equation for a Brownian particle that moves under the action a bistable potential.

With the function plotter of COMSOL it is possible to model the potential shown in figure 3 which is described by the function $y=ax^4-bx^2$.
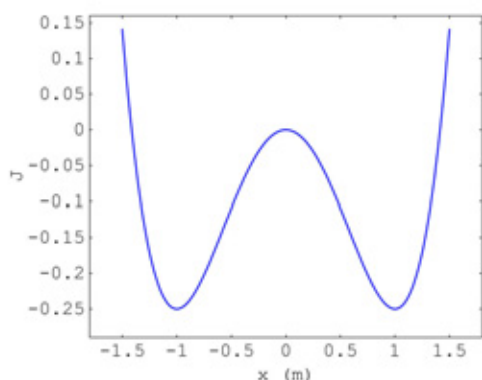
Figure 3. The bistable potential modelled for the preliminary study of the system whtih $a=0.5 J/m^2$ and $b=0.25 J/m^4$.

Notice that this potential is macroscopic. It does not have chemical meaning; it is useful only for making the match between the theoretical work and the COMSOL solution.

After having modelled the potential, we created the mathematical model in COMSOL PDE module. In the 1-D section, we selected the PDE coefficient form for a time-dependent analysis and the coefficients were modified to match equation (1.5); the initial conditions of the probability distribution is a very sharp Gaussian bell centred at the middle of the domain. The boundary conditions, BC, used here are the default Dirichlet BC of the model that impose that the function is zero at the two limits of the domain. They account for the physical nature of the rotaxane where the two stoppers situated at both ends makes the probability to find the ring there equal to zero.

With a simple automatic mesh, it is possible to start the simulation. In order to follow the theoretical works, in this first test, we have used a diffusion constant $D=0.1$ m^2/s; the results for an interval of 6 seconds are plotted in figure 4 and match perfectly the exact solution of (6-8).

Figure 5 shows a typical rotaxane (10) for which the corresponding Smoluchowski equation is solved.

The distance between the two stations, i.e. the potential minima, is 10 Å and their potential energy is set to -14 kcal/mol.
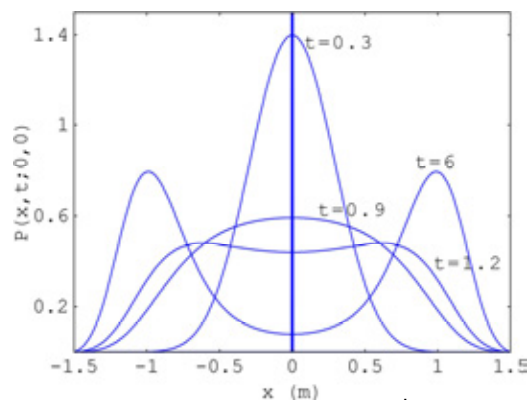

Figure 4. Distribution probability $P(x,t \mid 0,0)$ for the bistable potential of fig. 3 at times $t=0.3$, $t=0.9$, $t=1.2$ and $t=6$.
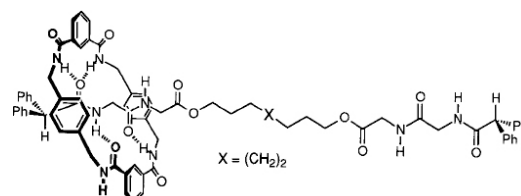

Figure 5. The rotaxane whose dynamics is the subject of this study.

The walker can be positioned everywhere along the thread and, for our work, its starting point is in the middle of the molecule. The first problem is how to describe the potential energy that acts on the walker. In many papers, it is modelled as a quartic potential as shown in figure 3 with two parameters a and b. It is, however, difficult to model accurately the position and the depth of the potential wells. In this study, using the function modeller of COMSOL, we have created a curve that is the combination of two Gaussian bells, where the variables are their position, depth and width.

In the real molecule the two potential energy wells are equal to -14 kcal/mol, or $1.38945 \cdot 10^{-19}$ J, and the distance between them is 10Å, the resulting function is plotted in figure 6.

The distance over which a typical Hydrogen bond exerts its action is about 2Å, and is the value used for the bell width. The starting function is a very sharp bell curve centred in the middle of the domain.
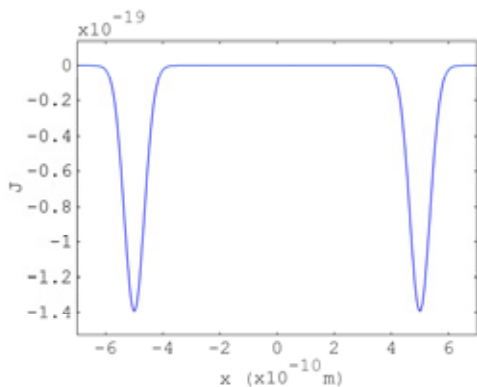
Figure 6. The potential wells modeled with COMSOL

The other variable that needs to be set is the diffusion coefficient that depends strongly on the temperature and on the viscosity of the medium; the rotaxane studied here has shown its fastest dynamics in solvents like DMF or MeOH (11) which have viscosity coefficients of 0.00092 $pa·s$ and 0.0006 $pa·s$. The ring of the rotaxane is 533 g/mol and in the modelling is assumed to be a sphere with a radius of 1 nm. With these values and equation (1.14), a diffusion coefficient $D=3.64·10^{-10}m^2/s$ for methanol at 298K is obtained. Since the ring is not free to move in the

medium because of the linear thread of the rotaxane, the diffusion coefficient can, to a first approximation, be halved with the result of an effective diffusion coefficient $D=1.82·10^{-10}m^2/s$ at 298K in MeOH.

As in the first model created, it is possible to modify the coefficients of the PDE to match perfectly of equation (1.15); with a mesh of about 30000 equally spaced elements, it is possible to obtain the solution plotted in figure 6.

The system evolves from an initial unstable situation to a stationary stable state in about 1 ns that corresponds to a velocity of about 0.5 mm/s. It is interesting to note that ~90% of the distribution probability is at the equilibrium position after only half of the total evolution time.

If the same problem is solved for higher temperatures, with a higher diffusion coefficient, the system is faster to reach equilibrium.

If the problem is solved for another solvent, such as DMF, with a higher viscosity coefficient, the system reaches equilibrium in a longer time (Figure 7).
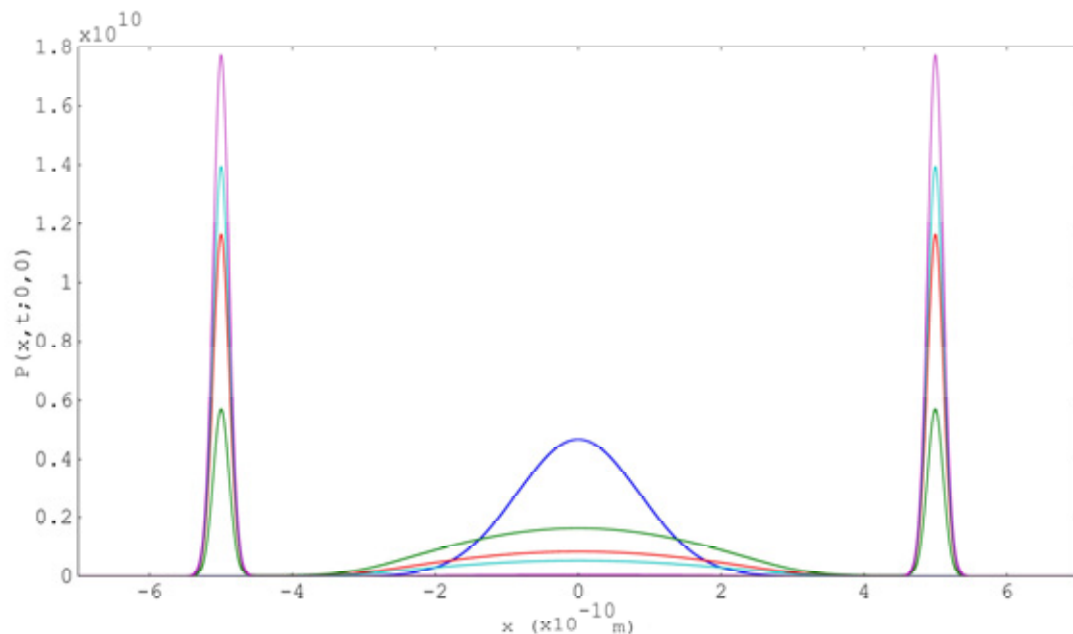

Figure 6. Distribution probability as a solution of the Smoluchowski equation (1.16) for times 0.02ns, 0.15ns, 0.3ns, 0,4ns and 1ns
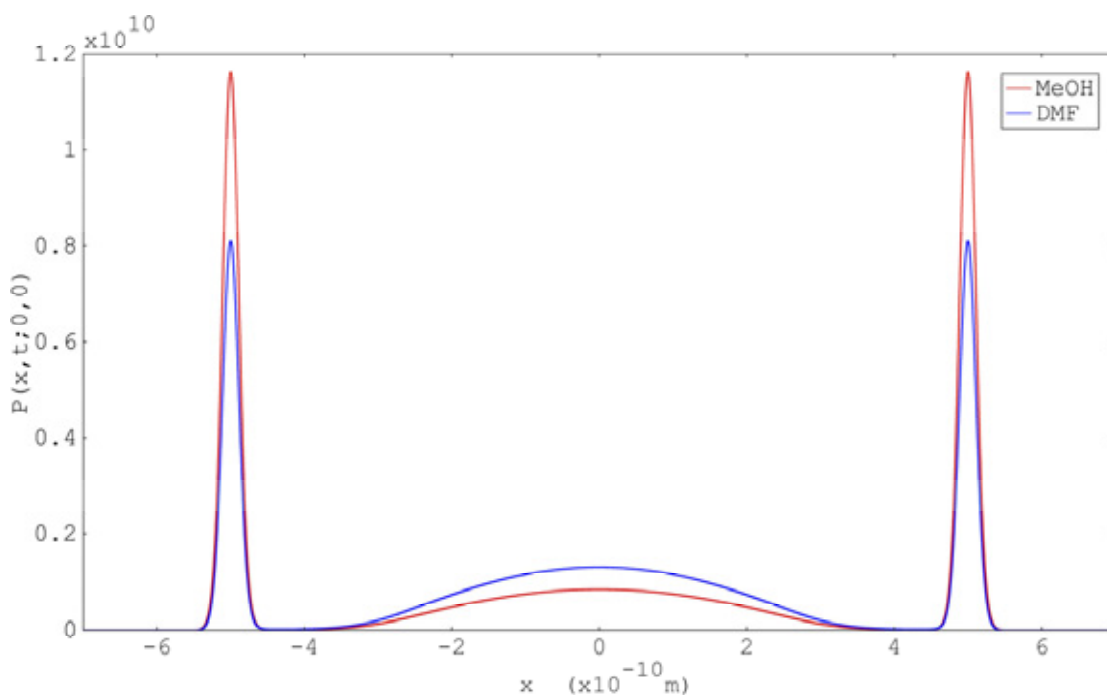
Figure 7. Distribution probability for two different solvents at t=0,3ns.

In figure 7 are plotted the distribution functions for the time $t=0.3ns$ for the two solvents, MeOH and DMF. Notice that in the latter the system goes to equilibrium more slowly. The same result can be obtained if the rotaxane walker is heavier.

The model is also solvable for a rotaxane with two different stations. If in the molecule of figure 4 one of the stations is destabilized, for instance photochemically and has its binding energy set to -10 kcal/mol, it is possible to model the potential energy profile with the result shown in figure 8.

After the creation of the potential is possible to solve the model. In the same way as before is obtained the probability distribution function shown in figure 9.

All those results demonstrate the power of COMSOL to create physical-chemistry models and to solve them. The present challenge is to use the COMSOL results to provide quantitative estimates of experimentally available parameters such as entropy and experimentally difficult to obtain data such as the force generated by the molecular motor.

It is expected that the results will drive the design of new and highly efficient molecular machines
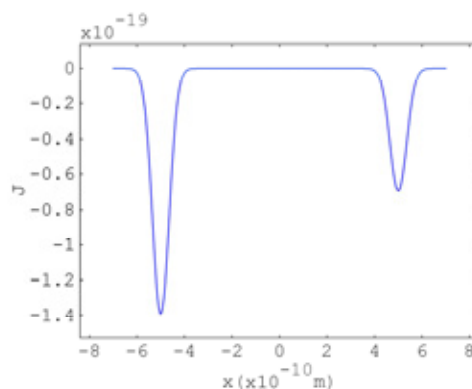

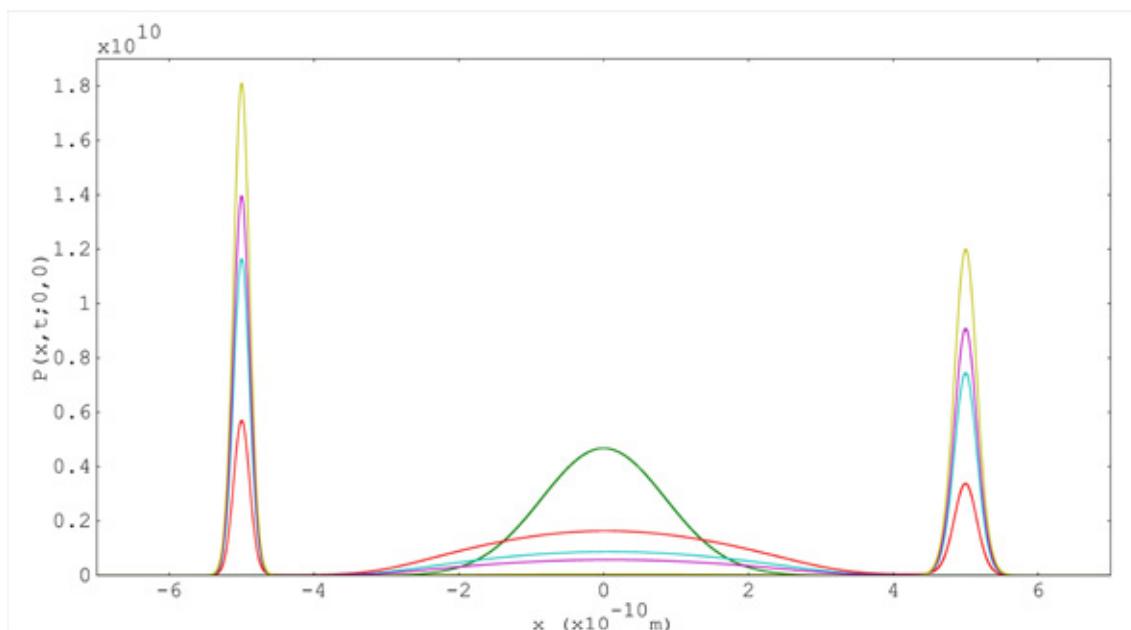**Figure 8. .** Potential energy profile for the "activated" rotaxane.

Figure 9. Distribution probability for the motion of the ring in the "activate" rotaxane like the one in fig. 8

8. References

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