

Investigating the rate(kinetics) for an asymmetric potential barrier using molecular dynamics

A Thesis

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by

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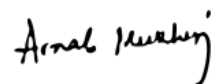
Supervisor: Dr. Arnab Mukherjee

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Certificate

This is to certify that this dissertation entitled Investigating the rate(kinetics) for an asymmetric potential barrier using molecular dynamicstowards the partial fulfilment of the BS-MS dual degree programme at the Indian Institute of Science Education and Research, Pune represents study/work carried out by Swapnil Bhiseat Indian Institute of Science Education and Research under the supervision of Dr. Arnab Mukherjee, Associate Professor, Department of Chemistry , during the academic year 2019-2020.



Dr. Arnab Mukherjee

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This thesis is dedicated to my family and my late grandmother.

Declaration

I hereby declare that the matter embodied in the report entitled Investigating the rate(kinetics) for an asymmetric potential barrier using molecular dynamics are the results of the work carried out by me at the Department of Chemistry, Indian Institute of Science Education and Research, Pune, under the supervision of Dr. Arnab Mukherjee and the same has not been submitted elsewhere for any other degree.



Swapnil Bhise

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Thanks to Dr SS Patil for his all his medical help that I needed throughout the course of this project

Abstract

According to the transition state theory, the rate of forward and backward reaction should be the same as long as the potential energy, ΔG of both the reactant and product is the same. However, Kramer's theory takes into account the curvature of the energy profile. Our experiment tests whether the rates would still be the same if we simulated a particle on an asymmetric potential energy barrier using molecular dynamics simulations.

Contents

Abstract	xi
1 Rate theories	3
1.1 Transition State Theory	3
1.2 Kramers Theory	7
1.3 Grote Hynes theory	10
2 Methods	11
2.1 Asymmetrical energy profile	11
2.2 System generation	16
2.3 Simulation details	16
3 Results and discussions	19
3.1 Results	19
3.2 Discussion	24
4 Conclusions	27

Introduction

Molecular dynamics simulations are computer simulations to study the physical movements of atoms and molecules. The atoms and molecules are allowed to interact for a particular time period, giving us a dynamic view of the evolution of the system. Generally, the trajectories of these atoms and molecules are determined by solving the Newtons equations of motion for a system of interacting particles. The forces between particles are calculated using interatomic potentials and force fields.

The constraints that matter when running a molecular dynamics simulation are simulation time, simulation size, and timestep so that the calculation can finish within a given time period. The time span should match the kinetics of a particular natural process under study in order to make statistically valid conclusions from the simulations.

Nuclei are heavy enough that they behave as classical particles and the dynamics can thus be simulated by solving Newtons second equation, $F = ma$, which can be also written as

$$\frac{-dV}{dr} = \frac{md^2r}{dt^2}$$

We use molecular dynamics simulations to obtain the relationship between the transmission coefficient given by the Kramers theory and the reaction rate.

Chapter 1

Rate theories

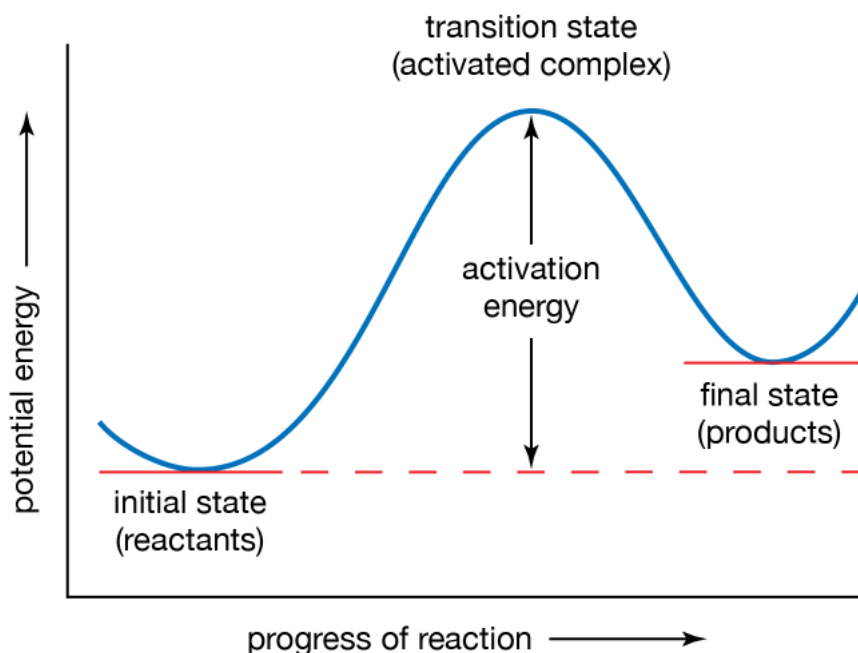
1.1 Transition State Theory

The transition state theory was formulated by Henry Eyring and Michael Polyani in 1935, used to understand how chemical reactions take place quantitatively.

Generally, chemical reactions occur more rapidly at higher temperatures. When thermal energy of molecules rises, there is increased motion and molecules collide with each other more vigorously. This also increases the chance of bonds being broken or rearranged. In this way, chemical reactions are faster at higher temperatures and slower at lower temperatures.

Svante Arrhenius combined the concepts of collisions and Boltzmann distribution law and came up with this equation called the Arrhenius equation:

$$k = Ae^{\frac{-E_a}{RT}}$$



Here, k is the reaction rate constant.

A is the pre exponential factor, which relates to molecular collision. It also deals with the frequency of molecules colliding with appropriate orientation taking into account the energy to initiate the reaction. This pre exponential factor is determined experimentally since it varies with different reactions. Also, it is temperature dependant because it is directly related to molecular collision.

E_a is the energy of activation. It is the least amount of energy the reactants need to reach the transition state of the energy barrier. Once it reaches the transition state, the reaction can go in forward direction to form products or backward direction to reactants. Reaction barrier having a large activation energy need a much more energy to reach the transition state.

R is the universal gas constant and T is the temperature at which the reaction is being carried out in Kelvin.

The Arrhenius equation shows us that the rate constant of the reaction increases exponentially as the energy of activation decreases, which implies that the rate of the reaction also increases exponentially since rate of the reaction is directly related to the rate constant

of the reaction.

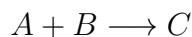
The Arrhenius rate law giving the rate constant of the reaction is used to give determine the energies for the reaction barrier. However, the Arrhenius equation is empirical and overlooks the possibility of the formation of one or more intermediates during the course of the reaction. The transition state theory further explains the reaction dynamics and provides a better alternative to the Arrhenius equation.

The TST, defines the transition state existing between the reactants and products where the reactants are combined in an activated complex. This activated complex is one of the deciding factors on whether the reaction can occur or not. This way, TST is used to understand how chemical reactions take place. Also, the TST assumes that there is a special type of equilibrium (quasi equilibrium) between the reactants and products. It relies mainly on the following assumptions:

1. Reactants are in constant equilibrium with the activated complex.
2. Energies of the particles can be obtained using the Boltzmann distribution.
3. The activated complex does not collapse back to the reactant once the reactants reach the transition state.

Rates of the reaction can be obtained by understanding the activated complexes at the transition state, which as mentioned earlier are in quasi equilibrium with the reactants.

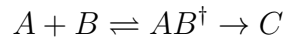
Consider a bimolecular reaction,



the equilibrium constant K for this reaction is given by

$$K = \frac{[C]}{[A][B]}$$

According to the transition state theory, we have an activated complex AB



$$K^\ddagger = \frac{[AB]^\ddagger}{[A][B]}$$

The high energy complex known as the activated state is an unstable intermediate. Product formation follows when the energy of activation is achieved by the reactants.

Here the rate of the reaction can be given by,

$$\begin{aligned} \text{rate} &= v [AB^\ddagger] \\ &= v[A][B]K^\ddagger \end{aligned}$$

Thus, the rate can then be written as

$$\text{rate} = k[A][B]$$

Hence, we have

$$k[A][B] = v[A][B]K^\ddagger$$

and

$$k = vK^\ddagger$$

Here, v is the frequency of vibration, k is the rate constant of the reaction and K^\ddagger is the thermodynamic equilibrium constant.

The frequency of vibration v is also given by

$$v = \frac{k_B T}{h}$$

The equation then transforms to

$$k = \frac{k_B T}{h} K^\ddagger$$

At equilibrium, the Gibbs free energy change is given by

$$\Delta G^\ddagger = -RT \ln K^\ddagger$$

We can get the equilibrium constant from here with

$$[K]^\ddagger = e^{-\frac{\Delta G^\ddagger}{RT}}$$

Taking into account the enthalpy and entropy change for the reaction we have

$$\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger$$

Finally arranging all terms we get,

$$k = \frac{k_B T}{h} e^{\Delta S^\ddagger/R} e^{-\Delta H^\ddagger/RT}$$

This equation which is similar to the Arrhenius equation is called the Eyring equation. However, this equation is based on the transition state theory and shows the dependence of the pre-exponential factor on the temperature. On the other hand, Arrhenius equation gives the relation between the rate constant of the reaction and the temperature of the reaction.

1.2 Kramers Theory

Kramers theory deals with one of the limitations of the transition state theory. The transition state theory assumes that the trajectories originating from the reactants and achieving activation energy will always go on to directly form products with no recrossings at the transition state. However, there might be a case when a strongly interacting solvent hinders

the crossing of the reactants on the barrier at the transition state through collisions. This can thus lead to recrossings and decrease the value of the rate constant below the TST value.

The transition state theory as discussed earlier explains the nature of the reactive barrier passage such that the activated complex in quasi equilibrium with the reactants proceeds to form products. Continual collisions because of the interaction with the solvent can lead to the incorrect estimation of the rate constant. If a certain trajectory recrosses the transition state surface the rate will be over estimated because of the assumption that every crossing towards the product contributes to the overall rate. Kramer's theory suggests a correction to the transition state theory taking into account these solvent effect due to dynamical recrossing.

The recrossing effect is accounted by the transmission coefficient κ .

$$k = \kappa \frac{k_B T}{h} e^{\frac{-\Delta G}{RT}}$$

Taking the transmission coefficient into account the TST equation then transforms to

$$k = \kappa k_{TST}$$

According to Kramers, the reacting system is modeled as an effective particle of mass μ . It is considered that this mass is moving on an imaginary inverted parabolic potential in the transition state region. The frequency of the same is ω_b and the solvent friction is η . The solvent friction is defined as the time correlation function of the random force exerted by the solvent on the reaction coordinate,

$$\eta = \int_0^\infty dt \eta(t)$$

The time correlation function is given by the fluctuation dissipation theorem,

$$\eta(t) = \frac{1}{\mu k_B T} \langle F F(t) \rangle$$

Here, F is the solvent force on the effective particle as earlier described which has a mass μ , and $\langle \rangle$ represents a solvent phase space average.

The ratio $\frac{\eta}{\omega_b}$ is important in the determination of κ . When the frictional forces are weak compared to the intrinsic reaction forces, then

$$\frac{\eta}{\omega_b} < 1,$$

$$\kappa \rightarrow 1$$

and

$$k \rightarrow k_{TST}$$

In the other case when the ratio $\frac{\eta}{\omega_b}$ is greater than 1, the solvent plays an important

role in recrossings and the passage from reactants to products over the barrier is essentially diffusion controlled.

1.3 Grote Hynes theory

One of the limitations of the Kramers theory is that it cannot predict the rate constant when the reaction barrier is large and of high frequency. In that case, the diffusion over the barrier decouples the viscosity of the medium. The reaction rate is thus underestimated when the barrier is large and the frequency is also high.

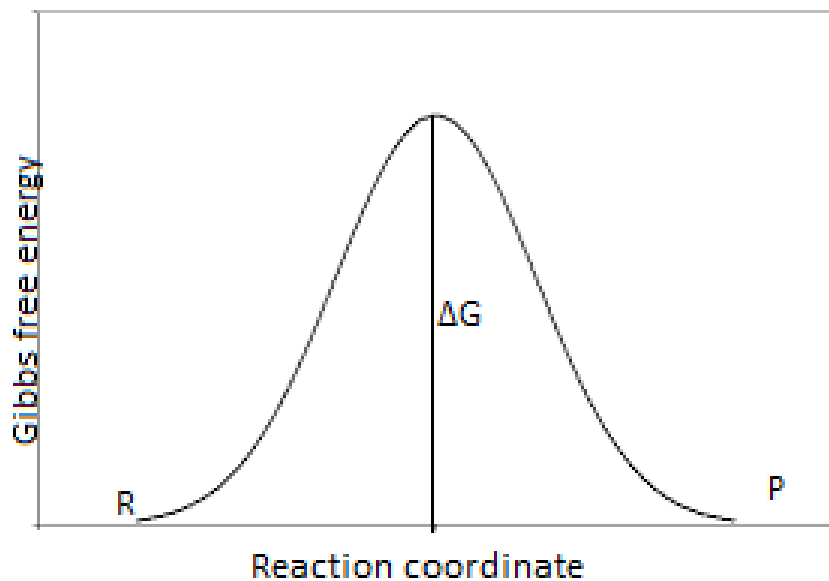
Grote Hynes theory based on the generalized Langevin equations suggests friction which depends on the frequency for chemical reactions in solution phase. Taking frequency dependent friction into account over constant friction allows us to successfully determine the rate constant in all cases especially when the reaction barrier is large and of high frequency.

Chapter 2

Methods

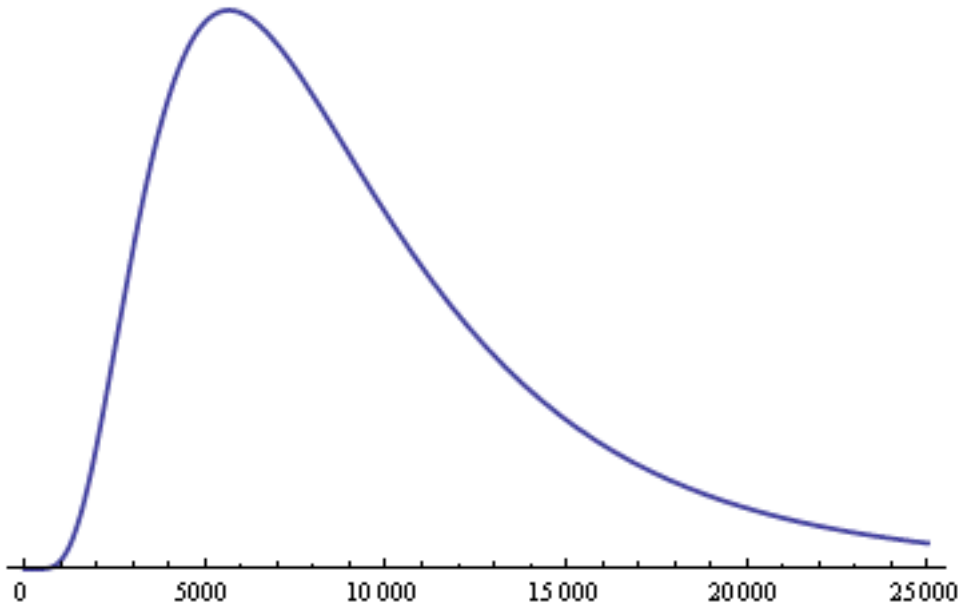
2.1 Asymmetrical energy profile

An asymmetrical energy profile was required for carrying out the simulations. We had to come up with a form of the Gaussian function such that the bell shaped curve would look asymmetric.



This was the basic form of asymmetric normal distribution but it had to be neglected because it did not have minima on either side required for the simulations.

$$y = e^{\frac{-(x^2+x)}{0.1}}$$



The Gaussian distribution also known as the Normal distribution is of the form of

$$f(x) = \frac{1}{\sigma\sqrt{2\pi}} e^{-\frac{1}{2}\left(\frac{x-\mu}{\sigma}\right)^2}$$

which can be parameterised in terms of sine and cosine like

$$a = \frac{\cos^2 \theta}{2\sigma_X^2} + \frac{\sin^2 \theta}{2\sigma_Y^2}$$

$$b = -\frac{\sin 2\theta}{4\sigma_X^2} + \frac{\sin 2\theta}{4\sigma_Y^2}$$

$$c = \frac{\sin^2 \theta}{2\sigma_X^2} + \frac{\cos^2 \theta}{2\sigma_Y^2}$$

Finally, after taking into account all the factors that were resulting into the asymmetric nature of the curve, we came up with something of the form of this

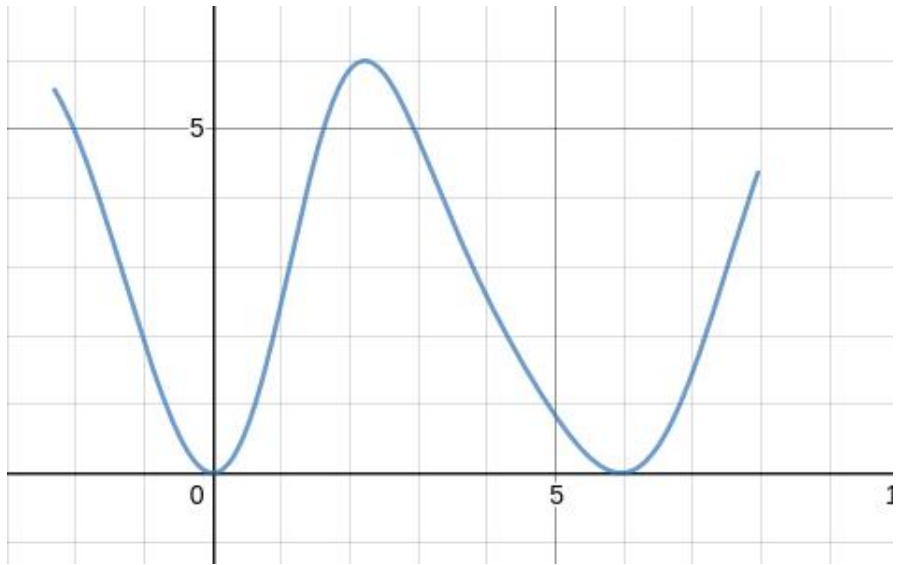
$$y = \cos \left(2.175(0.54x + 1.131) + \left(\sin \left(\frac{(0.59x + 1.131)}{1.6} \right) \right)^{2.5} \right) + 1$$



The problem with this function was that the boundary conditions were not satisfied if the box size was chosen to be the distance between the two minimas since the function was not continuous beyond the minimas.

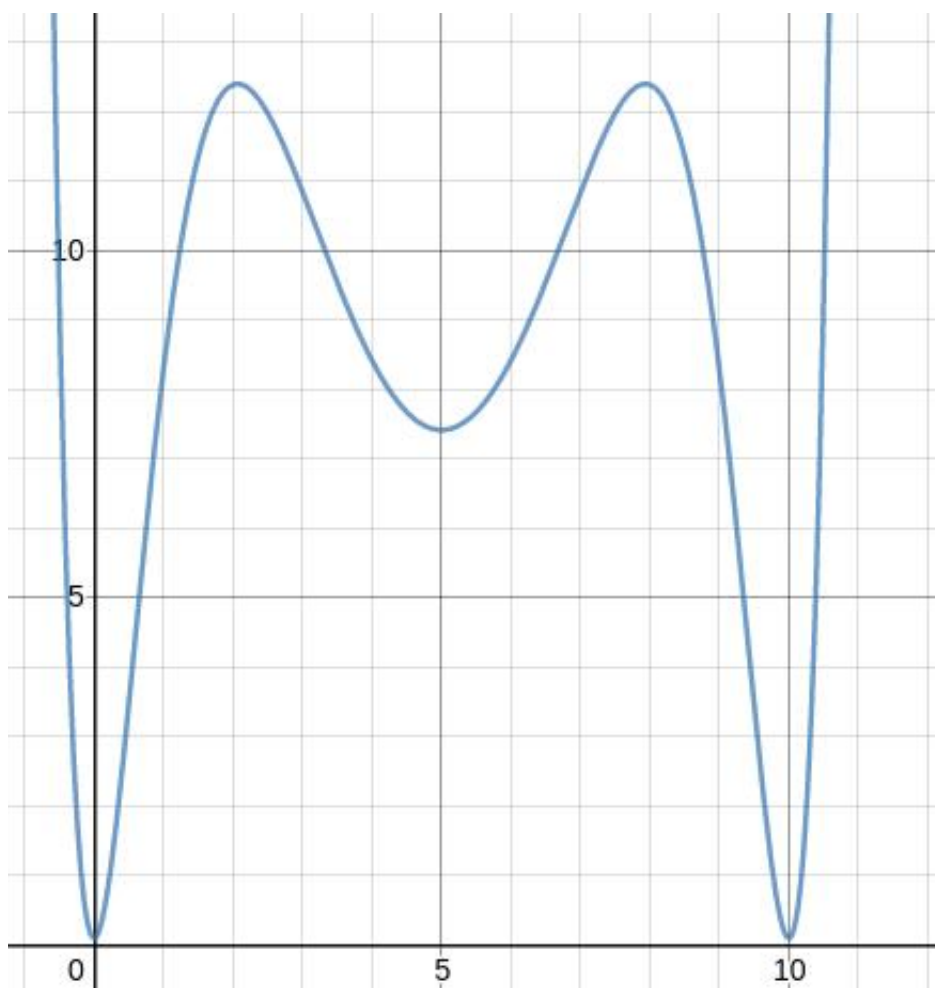
Another function of similar kind was also thought of, but here, along with the boundary conditions problem, the derivative of this part needed to calculate the forces could not be computed due to the infinitesimally small value of the part of the function where the sine term is raised to the power of 4.5.

$$y = 3 \cos \left(2.175(0.49(x + 0.505) + 1.131) + \left(\sin \left(\frac{(0.49x + 1.131)}{1.6} \right) \right)^{4.5} \right) + 3$$



Another form of asymmetric function was made up using part of the function that describes the black body radiation and combined it with an exponential growth function on one side. This function was finally chosen over others since it was continuous as far as the box size mattered and it was also asymmetric. The local minima at $x = 5$ could be considered as the reactant for the simulations and either global minimas were treated as products.

$$y = 0.001 (x^2 e^{-(x-10)} + (x-10)^2 e^x)$$



The box size was then chosen to be 10.002 angstrom according to this potential.

2.2 System generation

A system containing a single carbon atom was generated. It does not have any charge and it was under the influence of a one dimensional potential discussed above. A pdb(protein database) file was generated by stripping out all the other atoms except carbon and it was used to generate coordinates and topologies.

The coordinates and topologies were converted to GROMACS format using *pdb2gmx* program.

For obtaining topologies and coordinates in the GROMACS format, choice of a 'force-field' had to be made.

2.2.1 Force-field

In molecular dynamics, as discussed earlier, a molecule is described as a series of charged points(atoms) linked by springs(bonds).

In order to describe the evolution of parameters like bond lengths and bond angles, along with van der Waals and electrostatic interactions between atoms, a force field is required.

2.3 Simulation details

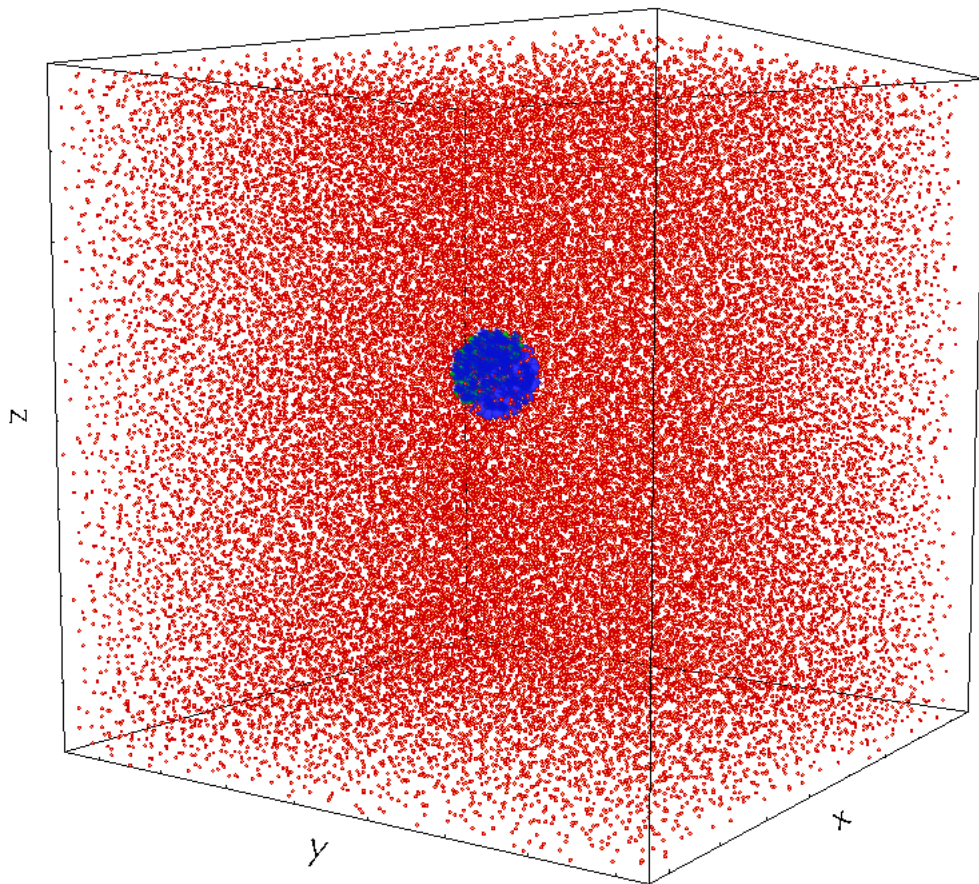
The box dimensions were defined using the *gmx editconf* command in GROMACS and then the box was filled with water to solvate the system.

A cubical box was created around the carbon atom with such that half the box length was equal to the distance between two minimas of the potential. Here, the box length was taken to be 10.002 nm. This cubical box is treated to be a unit cell.

The system is first centred in the box so that periodic boundary conditions are satisfied and force calculations are not spurious.

Once the box was defined, the system was solvated using *gmx solvate* using TIP3P water

molecules with 32772 of them.



This solvated, electroneutral system was then assembled for energy minimization process. Energy minimization is the process of finding an arrangement in the space of a collection of atoms where, according to some computational model, the net interatomic force on each atom is acceptably close to zero. Steepest descent method was used for energy minimization in this case.

Energy minimization ensured that the system had no steric clashes or inappropriate geometry. Now the system needed to be equilibrated to make sure the system does not collapse. The solvent is usually optimized within itself. Equilibration ensures that the system is brought to the temperature at which it is desired and establish proper orientation about the single carbon atom we have here.

In the first phase of equilibration, the system was subjected to an NVT ensemble (constant number of particles, volume and temperature). This NVT equilibration was carried

out for 500000 steps every step longing for 1 femtosecond, at constant temperature of 300 K.

This was followed by NPT(constant number of particles, pressure and temperature) equilibration, which stabilizes the pressure and thus the density also of the system. NPT equilibration was also carried out for the same number of steps as that of NVT and same temperature.

Upon completion of the two equilibration phases, the system was well-equilibrated at the desired temperature and pressure. The system was then placed at the transition state using position restraint and corresponding MD simulation was run for 500 ps using the md integrator maintaining the temperature and pressure of the system.

After position restraining the system at the transition state, the system was then used for production MD using the PLUMED package for position restraint.

Followed by that, 1000 simulations of 100ps each were run in both forward and backward directions starting from the transition state with the same velocities but it was found out that the system did not end up on either sides of the barrier in most of the cases. The recrossing was seen to be more than the reaction in this case.

So, we increased the time of simulations and 1000 simulations of 200 ps each were run in both forward and backward directions starting from the transition state.

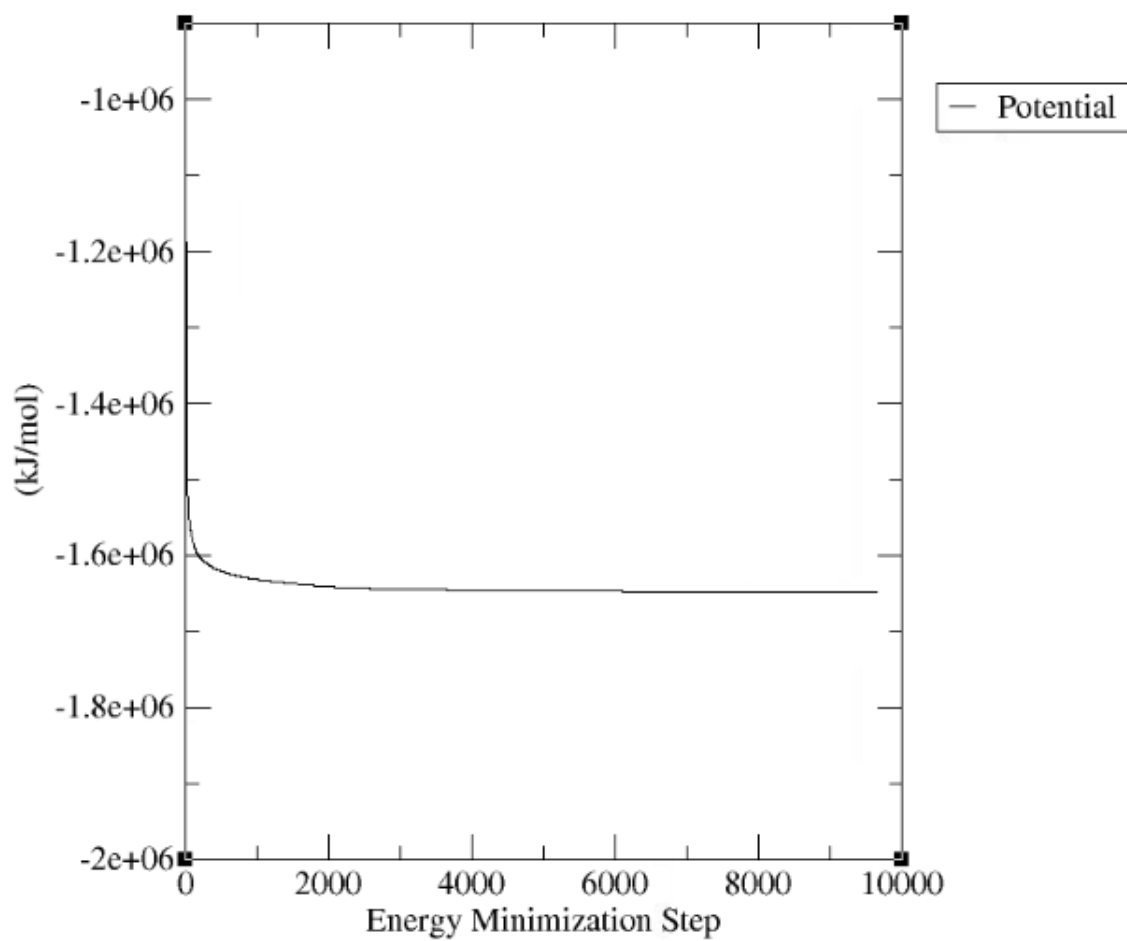
Chapter 3

Results and discussions

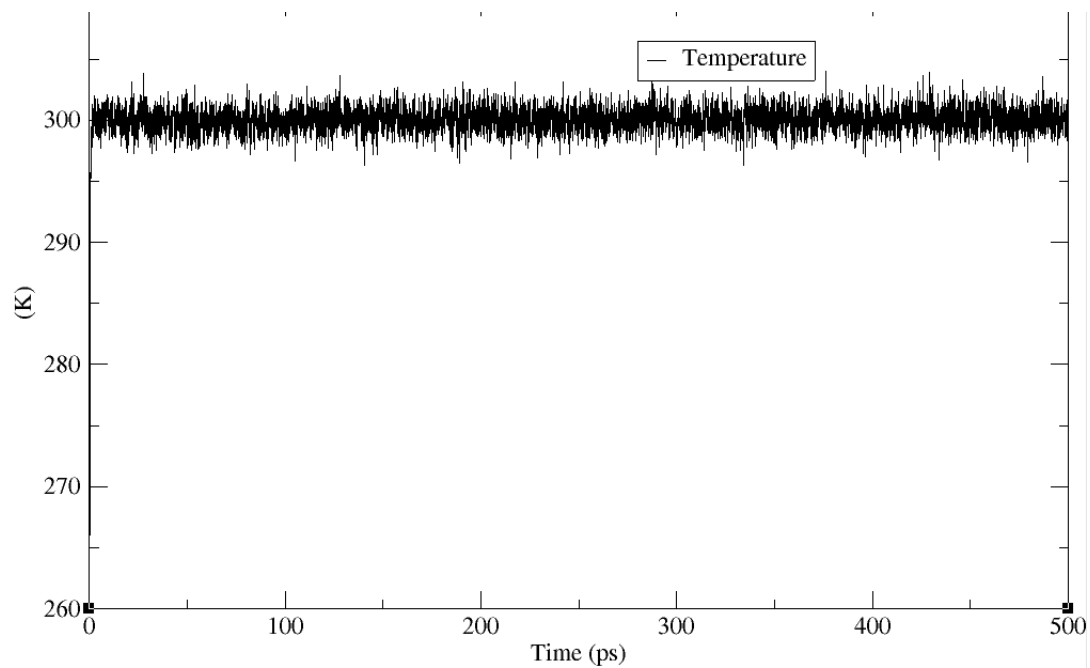
3.1 Results

After energy minimization, we get a curve like this which shows the steady convergence of E_{pot}

Gromacs Energies

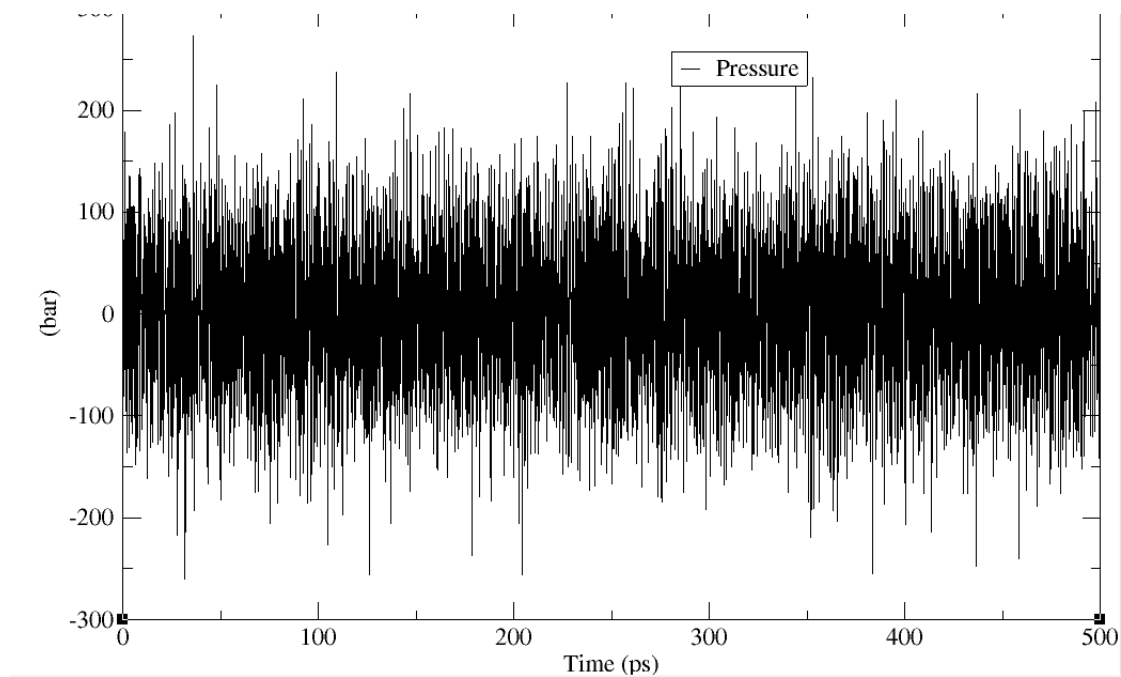


The NVT equilibration stabilised the temperature of the system and the average temperature was found out to be 300 K as desired.



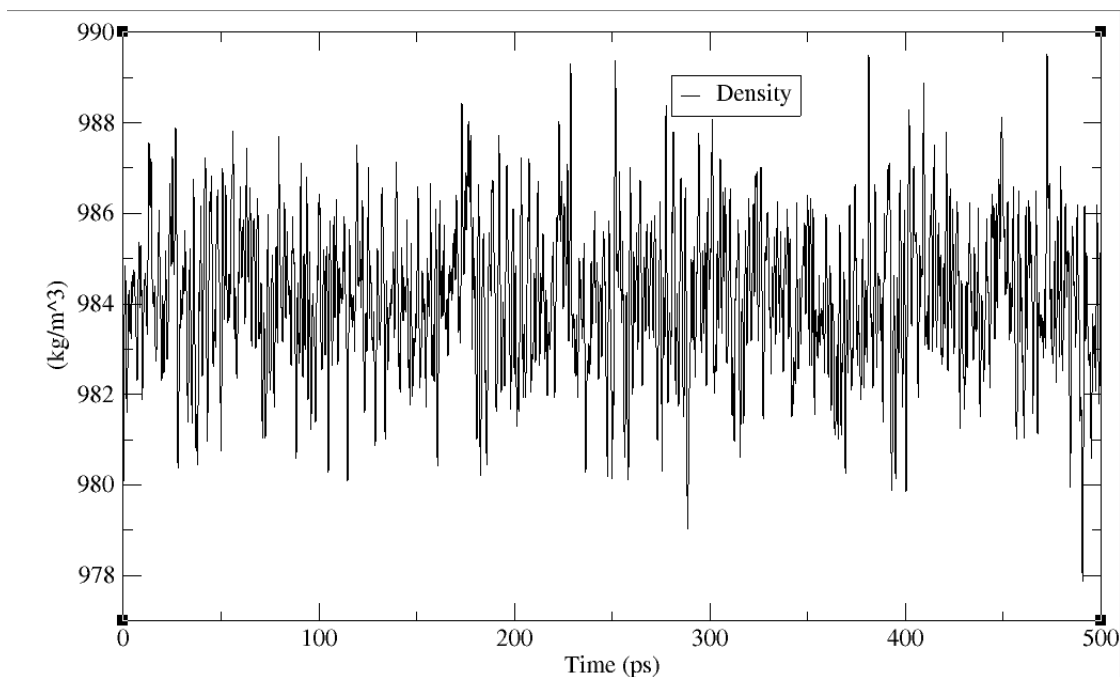
The graph shows a lot of fluctuations which are a result of the small step size used in NVT equilibration without which the system was collapsing. Also, it can be seen that the system attains the desired temperature quickly and then remains stable throughout the process.

The pressure value fluctuates widely over the course of the 500 ps simulation and the average value of pressure was found out to be 0.999 ± 68.615 bar which is close to 1 bar.



The graph shows a lot of fluctuations here as well because of the small step size used in the NPT equilibration.

The average value of density over 500ps was found out to be $984.13 \pm 1.58 \text{ kg/m}^3$



which is close to the experimental value of 1000 kg/m^3 .

3.1.1 Analysing trajectories

The trajectories starting from the Transition state were classified as RP (reactant \rightarrow product) if the forward part of a trajectory (positive time) resulted in the product and the reverse part of the trajectory (negative time) ended up in the reactant basin (see SI section II). If both forward and backward parts of a trajectory led to the reactant basin, it was categorized as RR (reactant \rightarrow reactant). Similarly, if both parts led to the product, it was labeled as PP (product \rightarrow product) trajectory. The last possibility for a trajectory is to end in the product in backward propagation and reactant basin in forward propagation. These were labeled as PR (product \rightarrow reactant) trajectories. The RR and the PP trajectories correspond to the recrossed trajectories. Once these statistics were obtained the transmission coefficient was calculated by reactive flux formalism which defines as the ratio of the actual rate to the rate predicted by TST as

$$\kappa = \frac{\sum_{i,+}^N p_i \|v_i\| Q_i}{\sum_{i,+}^N p_i \|v_i\|}$$

where + represents trajectories with an initial positive flux, p_i is the probability to have the i th initial configuration, and v is the velocity of the reaction coordinate X

The factor Q is given by

$Q_i = 1$ if RP, 0 if RR/PP and -1 if PR.

Out of the 375 trajectories that were used to calculate the transmission coefficient, 331 trajectories were used actually and 44 trajectories had to be discarded because the system did not reach either of the reactant or product in any of them.

Using the above equations and the data from the trajectories, we get

RR	RP	PR	PP
56	98	91	86

The value of kappa that we get from here using reactive flux formalism = 0.04.

The value of the transmission coefficient for positive and negative fluxes was found out to be 0.299 and -0.259 respectively.

3.2 Discussion

As discussed earlier, the rate constant according to the Kramer's theory which takes into account the friction and barrier curvature, is given by

$$k = \kappa \frac{k_B T}{h} e^{-\frac{\Delta G}{RT}}$$

For a perfectly symmetrical barrier, the value of the rate of the reaction both forwards and backwards would be the same, which essentially requires the value of the transmission coefficient to be equal to one.

Also, Hridya et al., (2019) suggests a similar study for proflavine intercalation in which the Grote Hynes and Kramers theories predict the transmission coefficient values close to unity. In this case, the transmission coefficient calculated from the Kramers theory was equal to 0.97 and 0.98 using the Grote Hynes theory, with very little recrossing. However, the reaction barrier was not asymmetric. When the transmission coefficient is close to unity, it suggests that there is very little recrossing at the transition state reaction barrier. This further indicates that the Transition State Theory is essentially perfect for such a reaction.

However, in our case, where an asymmetrical barrier is taken into account, the kappa value is found out to be 0.04. Kramers theory takes into account the curvature of the barrier as well. This shows that the asymmetric nature of the profile causes recrossing to occur. This effect of recrossing makes the Transition State Theory an overestimate of the rate constant and the correction to the Transition State Theory rate constant is given by $\kappa < 1$.

Calculating the rate for such a barrier using the transition state theory would also be an overestimate since rate is directly related to the rate constant which we have studied here. Kramers theory gives an appropriate estimate for the relation between shape of the potential energy barrier and the rate of the reaction.

Chapter 4

Conclusions

We were able to create an asymmetric potential energy barrier using various mathematical alterations to the already existing forms of functions.

We have investigated the presence of recrossing of the simple system containing a carbon atom on an asymmetric energy profile using extensive molecular dynamics simulations.

The value obtained for the transmission coefficient is very small which suggests significant recrossing at the transition state. This could also imply that the TST overestimates the rate of the reaction as suggested by Kramers theory.

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