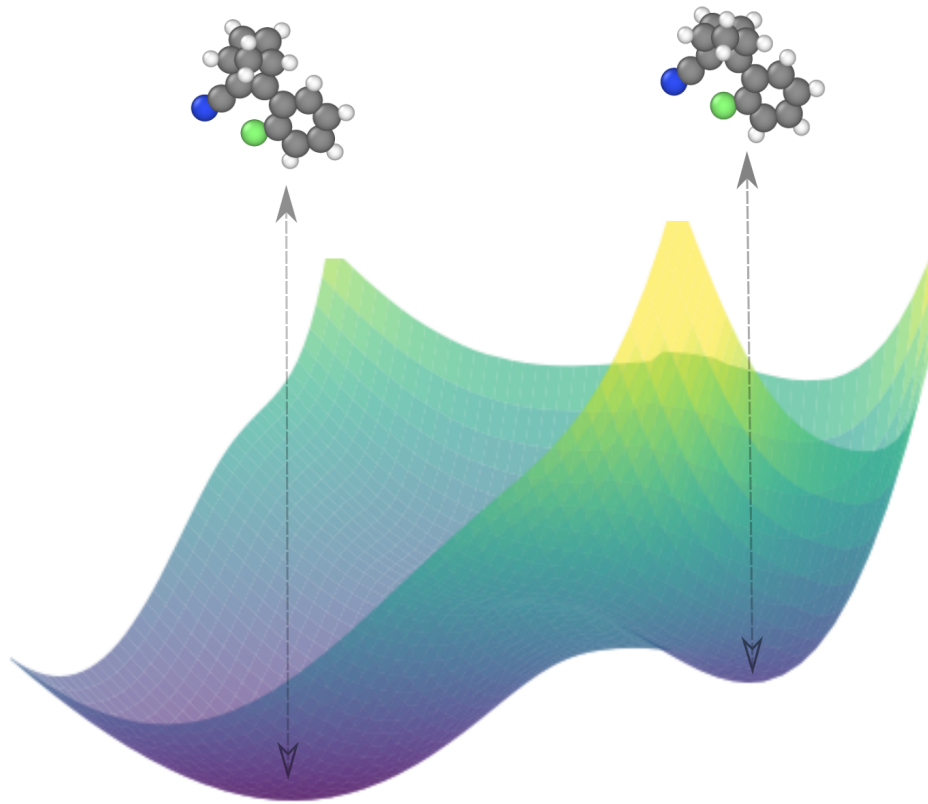




CHALMERS
UNIVERSITY OF TECHNOLOGY



Machine learning models for molecular potential energy surfaces

Symmetric gradient domain machine learning models for norbornadienes

Master's thesis in Physics

VIKTOR MARTVALL

DEPARTMENT OF PHYSICS

CHALMERS UNIVERSITY OF TECHNOLOGY

Gothenburg, Sweden 2022

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Symmetric gradient domain machine learning models for norbornadiene photoswitches
Viktor Martvall

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Cover: Potential energy surface obtained from a machine learning model for a derivative of norbornadiene showing two isomers, corresponding to local minima on the potential energy surface.

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Abstract

Molecular solar thermal storage (MOST) systems is a type of energy storage system which consist of photo switchable molecules that can convert solar energy into chemical energy which can be released on demand. One important property of a MOST system is that it the energy storage time should be long which means that the so-called back-conversion barrier should be large. Recently an experimental study showed that a substitution in the ortho position of the molecular photo switch norbornadiene leads to a significant increase of the back-conversation barrier. However in the same study the back-conversion barrier was also investigated with electronic structure calculations and this behavior was not seen. This thesis aimed to understand this discrepancy by investigating the temperature dependence of the back-conversion for two derivatives of norbornadiene by combining a machine learning (ML) method called symmetric gradient domain machine learning (sGDML) with electronic structure calculations to obtain computationally efficient models describing the dynamical landscape of the molecules studied. It was seen that sGDML models could describe the dynamical landscape of such molecules to a good approximation, however more work is required to obtain models which are accurate enough to to study the temperature dependence of the back-conversion.

Keywords: molecular solar thermal storage, photo switches, machine learning, sGDML, potential energy surfaces.

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Viktor Martvall, Gothenburg, June 2022

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Acronyms

BO Born-Oppenheimer. 7, 8

DFT density functional theory. ix, 7–12, 15, 21–28, 38

F fluorine. ix, 4, 5

GDML gradient domain machine learning. vii, 12, 13

GGA generalized gradient approximation. 11

GP Gaussian process. 12

LDA local density approximation. 10, 11

MD molecular dynamics. ix, 15–19, 21–25, 31–33, 35, 38

MEP minimum energy path. ix, x, 27–33, 37, 38

ML machine learning. iii, 4, 7, 12, 21, 37

MOST molecular solar thermal storage. iii, ix, 1–3

N-Q norbornadiene-quadricyclane. ix, 3, 4

PES potential energy surface. 8, 12, 21, 25, 28

RMSE root-mean-square error. ix, xi, 22–25, 30, 37

sGDML symmetric gradient domain machine learning. iii, vii, 7, 12–15, 21, 25–27, 30, 37–39

WHAM weighted histogram analysis method. 20, 31, 33

1. Introduction

In the last decades the mean surface temperature on earth has increased by approximately 1 °C due to increased usage of non-renewable energy resources such as oil, gas, and coal. In order to avoid further temperature increase several countries aim to reach net zero emissions between the years 2045 and 2060 [1]. However, as the majority of energy is still generated from non-renewable energy sources and the world wide energy consumption continues to increase by about 2% per year there is a need for an increased usage of renewable energy sources.

One of the most prominent renewables is solar energy as the sun is a virtually inexhaustible energy source. Currently one of the limitations with solar energy are the fluctuations in both supply and demand. A solution to this issue is to use existing energy storage technologies such as batteries which, however, rely on rare or depletable materials. One technology that has the possibility to overcome this issue is based on molecular solar thermal storage (MOST) systems which consist of molecular photo-switches [2], which are molecules that can absorb photons and transform them into chemical energy. The chemical energy can then later be released by either a catalytic or thermally induced reaction, which enables storing solar energy. In this thesis the dynamics of two MOST system based on norbornadiene will be studied using computational methods. Specifically, machine learning models for the interatomic interactions in norbornadiene will be developed with the purpose of using these models to study the free energy behavior of different molecular states. The reminder of this chapter will consist of a more extensive description of the background to the subject.

1.1 Background

MOST systems consist of molecular photo-switches which have the ability to both absorb and store solar energy. Figure 1.1 illustrates the main concepts of how a MOST operates. By absorbing a photon, a low energy isomer can get excited from the electronic ground state (S_0) to an excited state (S_n with $n > 0$), where $n = 1$ in Figure 1.1. Secondly, the excited molecule can with a certain probability, the photoisomerization quantum yield, undergo a photoconversion process into a higher energy isomer. This is known as photoisomerization. The time that the molecule will remain in the higher energy isomer state is related to the height of the energy barrier that separates the higher energy isomer from the lower energy isomer. The height of the energy barrier is the difference in enthalpy between the higher energy isomer and the saddle point, the point with the highest energy along the reaction pathway between the higher and lower energy isomer. Thirdly, the higher energy

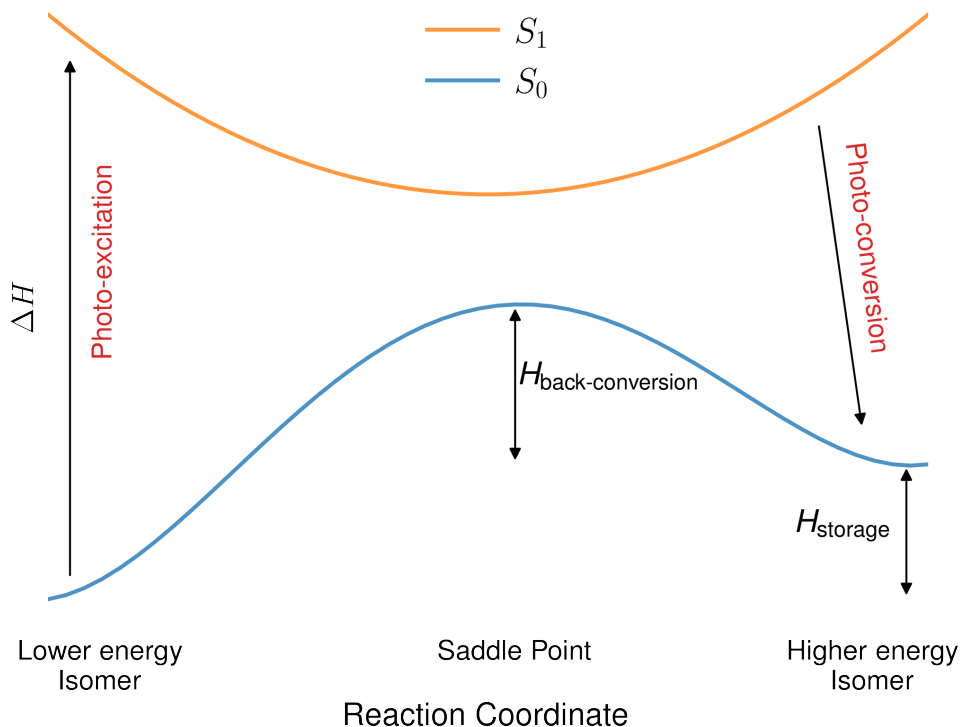


Figure 1.1: Schematic which illustrates the main concepts of how a MOST operates.

isomer can be back-converted to the lower energy isomer by a catalytic (or thermal) reaction releasing an amount of energy equal to the difference between the higher and lower energy isomer [2].

For a molecular system to effectively function as a MOST system there are several qualities that need to be fulfilled: (1) For the lower energy isomer to become excited due to solar irradiation the absorption spectrum of the lower energy isomer needs to overlap with the solar spectrum, in which 50 % of the incoming photons originate from the interval between 300 and 800 nm. (2) The time that the energy can be stored should be high, meaning that the energy barrier between the higher energy isomer and the lower energy isomer should be large. (3) The energy storage density should be high, meaning that both the amount of energy that can be stored as well as the molecular weight need to be considered. (4) The photoisomerization quantum yield should be close to one such that there is a high probability for photo isomerization to occur. (5) There should exist an efficient catalytic reaction such that the stored energy can be released when desired. (6) The absorption spectrum of the higher energy isomer should not overlap with the lower energy isomer to avoid competition of absorption between the states. (7) The system should be able to sustain several cycles of charge and discharge without any performance loss. (8) The MOST system should preferably not contain any toxic compounds [2], [3].

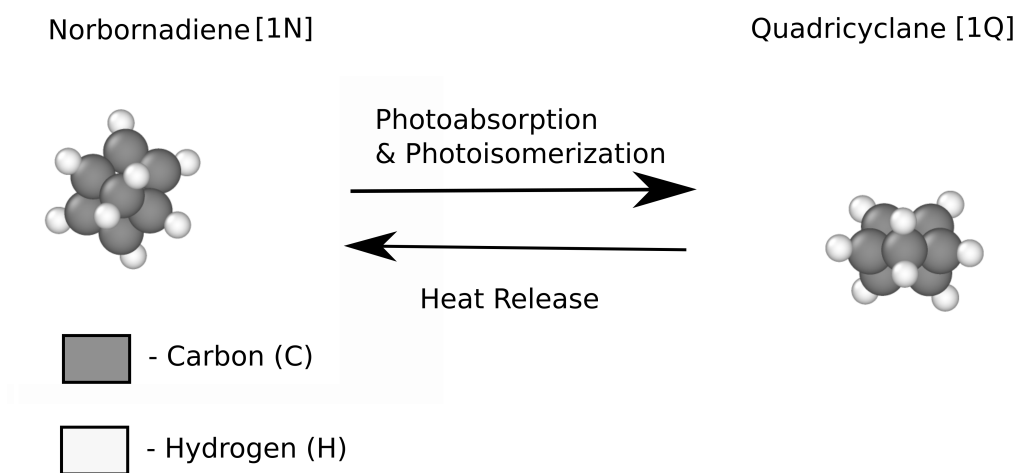


Figure 1.2: Illustration of the unsubstituted norbornadiene-quadricyclane (N-Q) system. Norbornadiene (**1N**) can via photoabsorption and photoisomerization convert to quadricyclane (**1Q**) where energy can be stored. The energy can later be released in the form of heat.

In this thesis MOST systems which are based on the N-Q system, where norbornadiene is the lower energy isomer and quadricyclane is the higher energy isomer, are studied. In Figure 1.2 the unsubstituted N-Q system is illustrated, and throughout this thesis this system will be referred to as **1**, norbornadiene will be referred to as **N**, quadricyclane as **Q** and the saddle point as **S**. Generally, **1** cannot effectively function as a MOST system. Although it has a high energy storage density, the absorption spectrum of **1N** does not overlap sufficiently with the solar spectrum, the system has a relatively short lifetime, and a low photoisomerization quantum yield. It is however possible to functionalize the molecule by adding substituents and it has been observed that certain substituents can increase the photoisomerization yield and red-shift the absorption spectrum such that it better overlaps with the solar spectrum [2].

In a previous study it was also experimentally observed that a substitution in the so-called ortho position of an aromatic substituent can have a large effect on the back conversion rate, leading to a larger back conversion barrier and a longer energy storage time [4]. In this study the back-conversion barrier was extracted by measuring the so-called back-conversion rate

$$k = \frac{k_b T}{h} e^{\frac{-\Delta G^\ddagger}{RT}} = \frac{k_b T}{h} e^{\frac{\Delta S^\ddagger}{R}} e^{-\frac{\Delta H^\ddagger}{RT}}. \quad (1.1)$$

Here, k_b is Boltzmann's constant, T is the temperature, h is Planck's constant, R is the gas constant, $\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger$ is the Gibbs energy of activation, $\Delta S^\ddagger$ is the entropy of activation, and $\Delta H^\ddagger$ is the enthalpy of activation (back-conversion barrier). Note that here the entropy (enthalpy) of activation refers to the difference in entropy (enthalpy) between **S** and **Q**. By measuring the rate of back-conversion at a fixed temperature one can extract the value of $\Delta G^\ddagger$ at that temperature. Furthermore

by measuring rate of back-conversion for several temperatures one can obtain the values of $\Delta S^\ddagger$ and $\Delta H^\ddagger$, assuming that they have no temperature dependence. In the same study, the back-conversion barrier ($\Delta H^\ddagger$) was computed using electronic structure calculations, which showed a large discrepancy between these calculations and the experimental value for molecules with substitutions in the ortho position of an aromatic substituent.

To understand this discrepancy, here, the goal is to compute $\Delta G^\ddagger$ at different temperatures. This is, however, difficult as this requires an accurate description of the dynamics of the atoms in each molecule along the reaction path. Methods which are sufficiently accurate for this purpose are all based on electronic structure calculations, which is a set of quantum mechanical methods that allow one to compute energies and forces for a system of atoms. An issue with these method is however that they scale poorly with system size, i.e., the number of electrons in the system. In fact, for the systems considered in this thesis it is practically impossible to compute $\Delta G^\ddagger$ at non-zero temperatures by only using electronic structure calculations. A possible solution to circumvent this issue is the use of machine learning (ML) models. By training a ML model on forces and energies from electronic structure calculations it should be possible to obtain a computationally efficient model with an accuracy comparable to the underlying quantum mechanical method. Thus by the use of ML models it should be possible to compute the Gibbs free energy at finite temperatures.

The purpose of this thesis is therefore to develop ML models to describe the dynamical landscape along the reaction path between **N** and **Q** with the overarching motivation of developing a method to explain why molecules with substitutions in the ortho position of an aromatic substituent have a substantially higher back-conversion barrier. To do so two, derivatives of the N-Q system will be studied, referred to as **2** and **3**. In Figure 1.3 these two derivatives are illustrated in their **N** and **Q** forms. The only difference between these two molecules is that **2** has the fluorine (F) atom in the para position while **3** has the F atom in the ortho position. Thus, the experiment performed in [4] measured a substantially higher back conversion barrier for **3**, while the computational calculations made in the same study predicted **2** and **3** to have approximately the same back-conversion barrier.

When constructing ML models to study these two systems it is important to control that the ML models can in fact describe the relevant properties. Apart from the fact that the ML models should be able to describe the general dynamical landscape of these molecules, they should also be able to describe the reaction path between **N** and **Q** and according to [4] a specifically important property is the rotation of the side group containing the F atom. This rotation is illustrated by the dashed arrows in Figure 1.3 and is of specific interest, since if this rotation is limited it can affect the entropy of the system and thus also the Gibbs free energy.

An important limitation that needs to be discussed is that in this thesis project the difference in electronic energies will be considered instead of the difference in enthalpy. This is motivated by a previous study which has shown that the main contribution

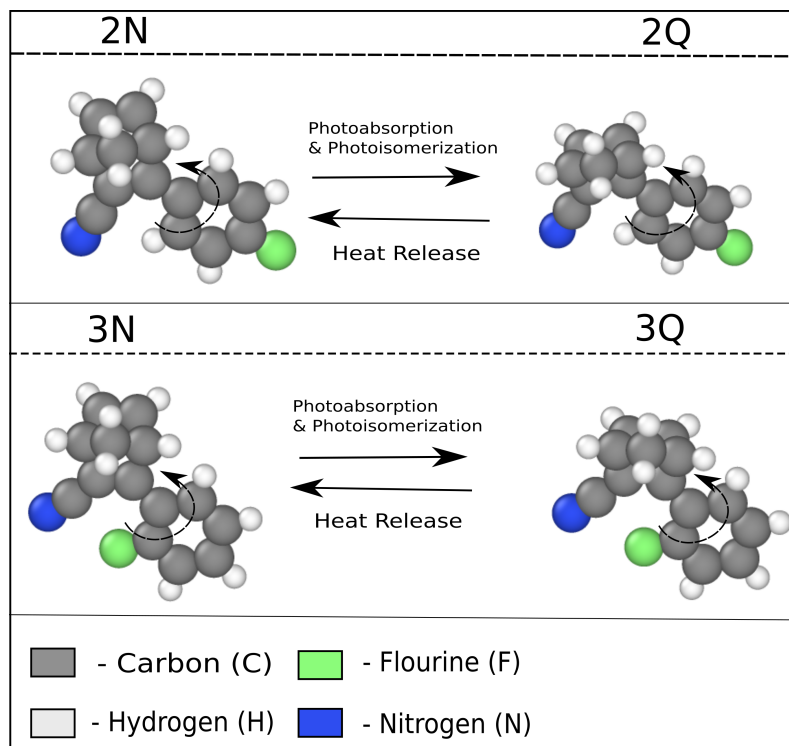


Figure 1.3: Illustration of derivatives of norbornadiene which will be studied in this thesis. The curved arrow illustrates that the side group containing the F atom can rotate.

to the difference in enthalpy is due to the difference in electronic energies [3]. Thus $\Delta E^\ddagger$ is considered instead of $\Delta H^\ddagger$ and the Gibbs free energy is replaced with the Helmholtz free energy, which will be referred to as the free energy, $F = U - TS$ where U is the internal energy, i.e the potential and kinetic energy of the molecule.

2. Methodology

As mentioned in the previous chapter this thesis project combines ML models with quantum mechanical calculations to study a specific type of molecules. In this chapter it will firstly be explained how a molecule is described in the context of quantum mechanics. Secondly, density functional theory (DFT) which is a quantum mechanical method to solve the electronic Schrödinger equation will be explained. Thirdly, a ML model called symmetric gradient domain machine learning (sGDML) will be introduced. Lastly, molecular dynamics simulations and statistical mechanics will be discussed.

2.1 The molecular Hamiltonian

A molecule can be described as a quantum mechanical system that is characterized by its wave function. To obtain the wave function for a molecule consisting of N_e electrons at positions $\mathbf{r} = (\mathbf{r}_1, \mathbf{r}_2, \dots, \mathbf{r}_{N_e})$, N_i ions at positions $\mathbf{R} = (\mathbf{R}_1, \mathbf{R}_2, \dots, \mathbf{R}_{N_i})$, with charges $(Z_1, Z_2, \dots, Z_{N_i})$ and masses $(M_1, M_2, \dots, M_{N_i})$ one in principle needs to solve the Schrödinger equation

$$\hat{H}\Psi(\mathbf{r}, \mathbf{R}) = [\hat{T}_e + \hat{T}_i + \hat{V}_{ee} + \hat{V}_{ei} + \hat{V}_{ii}] \Psi(\mathbf{r}, \mathbf{R}) = E\Psi(\mathbf{r}, \mathbf{R}). \quad (2.1)$$

The Hamiltonian, which specifies the total energy of a system, is for a molecule given by the sum of the kinetic energy of the electrons $\hat{T}_e$, the kinetic energy of the ions $\hat{T}_i$, the potential energy between the electrons $\hat{V}_{ee}$, the potential energy between the electrons and the ions $\hat{V}_{ei}$, and the potential energy between the ions $\hat{V}_{ii}$

$$\begin{aligned} \hat{T}_e &= -\sum_{i=1}^{N_e} \frac{\hbar^2}{2m_e} \nabla_{\mathbf{r}_i}^2 & \hat{T}_i &= -\sum_{i=1}^{N_i} \frac{\hbar^2}{2M_i} \nabla_{\mathbf{R}_i}^2 \\ \hat{V}_{ee} &= \sum_{i=1}^{N_e} \sum_{j=1}^{N_e} \frac{e^2}{4\pi\epsilon_0 |\mathbf{r}_i - \mathbf{r}_j|} & \hat{V}_{ei} &= -\sum_{i=1}^{N_e} \sum_{j=1}^{N_i} \frac{Z_i e^2}{4\pi\epsilon_0 |\mathbf{r}_i - \mathbf{R}_j|} \\ \hat{V}_{ii} &= \sum_{i=1}^{N_i} \sum_{j=1}^{N_i} \frac{Z_i Z_j e^2}{4\pi\epsilon_0 |\mathbf{R}_i - \mathbf{R}_j|}. \end{aligned} \quad (2.2)$$

Unfortunately there is no analytical solution to this equation (except for the hydrogen atom) and due to the pairwise interactions present in the terms $\hat{V}_{ee}$, $\hat{V}_{ei}$ and $\hat{V}_{ii}$ it is very computationally demanding to solve the equation numerically for larger molecules. One approximation which can be used to simplify this problem is the Born-Oppenheimer (BO) approximation.

2.1.1 Born-Oppenheimer approximation

The BO approximation is the assumption that the motion of the electrons and the motion of the ions can be separated [5]. This is possible since the motion of the electrons is much faster than the motion of the ions due to the large mass difference between electrons and protons/neutrons. Under this approximation the Schrödinger equation can be split into two parts. One part that describes the electronic wave function for fixed positions of the ions

$$\hat{H}_e \psi(\mathbf{r}) = [\hat{T}_e + \hat{V}_{ee} + \hat{V}_{ei} + \hat{V}_{ii}] \psi(\mathbf{r}) = E(\mathbf{R}) \psi(\mathbf{r}) \quad (2.3)$$

and one part that describes the motion of the ions

$$i \frac{\partial}{\partial t} \chi(\mathbf{R}, t) = [\hat{T}_n + E(\mathbf{R})] \chi(\mathbf{R}, t). \quad (2.4)$$

By solving Eq. (2.3) for a specific value of the atomic configuration $\mathbf{R}'$, the potential energy of the system $E(\mathbf{R}')$ is obtained. Solving this equation for all possible values of all $\mathbf{R}$ yields the potential energy surface (PES) $E(\mathbf{R})$. As the ions are assumed to be static the PES describes the energy of the system at zero Kelvin. By analyzing the PES it is possible to identify (meta)stable states of a molecule as they correspond to minima of the PES; one can also calculate reaction paths between two stable states by computing the minimum energy pathway between these two states. Furthermore, one can also use the PES in Eq. (2.4) to solve for the wave function $\chi(\mathbf{R}, t)$ which enables one to also account for the dynamics of the ions such that one can compute quantities, such as the back-conversion barrier, at finite temperature. For the purpose of this thesis this is, however, too computationally demanding and instead a classical approximation will be made for the ions. This implies that quantum mechanical properties, such as tunnelling and zero point vibrations, are neglected and Eq. (2.4) is replaced with Newton's equation of motion

$$\mathbf{F}_i = -\frac{\partial E(\mathbf{R})}{\partial \mathbf{R}_i} = M_i \frac{d^2 \mathbf{R}_i}{dt^2} = M_i \mathbf{a}_i. \quad (2.5)$$

2.2 Density functional theory

To evaluate states on the PES Eq. (2.3) needs to be solved. This is a challenging problem as the wave function depends on $3N_e$ spatial coordinates. In DFT this is circumvented by instead working with the ground state density

$$n(\mathbf{r}) = N_e \int d^3 \mathbf{r}_2 \cdots \int d^3 \mathbf{r}_{N_e} |\psi(\mathbf{r}, \mathbf{r}_2, \dots \mathbf{r}_{N_e})|^2. \quad (2.6)$$

The advantage of working with the density is that it only depends on three spatial coordinates and according to the first Hohenberg-Kohn theorem all observables in the ground state can be expressed as functionals of this quantity [6]. Furthermore, according to the second Hohenberg-Kohn theorem the ground state density can be

found by minimizing the total energy with respect to the ground state density. By defining $T[n(\mathbf{r})]$, the kinetic energy functional for interacting electrons, and $U[n(\mathbf{r})]$, the potential energy functional for interacting electrons, the total energy functional (in Hartree units) can be written as

$$E[n(\mathbf{r})] = \int v_{ei}(\mathbf{r})n(\mathbf{r})d\mathbf{r} + T[n(\mathbf{r})] + U[n(\mathbf{r})] + E_{ii}, \quad (2.7)$$

where

$$v_{ei}(\mathbf{r}) = - \sum_{i=1}^{N_i} \frac{Z_i}{|\mathbf{r} - \mathbf{R}_i|} \quad (2.8)$$

is the potential between the electrons and the ions. From this equation it is clear that to write the total energy as a functional of the density one needs to write the kinetic and potential energy as functionals of the density. For interacting electrons this is, however, not trivial and one instead uses the Kohn-Sham approach.

2.2.1 Kohn-Sham DFT

In the Kohn-Sham approach of DFT the system of interacting electrons is replaced by a system of non-interacting electrons and to account for all interaction related effects the so-called exchange-correlation functional $E_{xc}[n(\mathbf{r})]$ is introduced [7]. The exact form of this functional is not known and therefore it has to be approximated. There are many different types of approximations and some of them will be discussed in section 2.2.2. The total energy functional for the system of non-interacting electrons is given by

$$E[n(\mathbf{r})] = \int v_{ei}(\mathbf{r})n(\mathbf{r})d\mathbf{r} + T_s[n(\mathbf{r})] + E_H[n(\mathbf{r})] + E_{xc}[n(\mathbf{r})] + E_{ii}. \quad (2.9)$$

with

$$E_H[n(\mathbf{r})] = \frac{1}{2} \int \frac{n(\mathbf{r})n(\mathbf{r}')}{|\mathbf{r} - \mathbf{r}'|} d\mathbf{r}d\mathbf{r}' \quad (2.10)$$

and $T_s[n(\mathbf{r})]$ being the kinetic energy of non-interacting electrons. From this expression the effective potential of the system can be found as

$$v_s(\mathbf{r}) = v_{ei}(\mathbf{r}) + \int \frac{n(\mathbf{r}')}{|\mathbf{r} - \mathbf{r}'|} d\mathbf{r}' + v_{xc}[n(\mathbf{r})] \quad v_{xc}[n(\mathbf{r})] = \frac{\delta E_{xc}[n(\mathbf{r})]}{\delta n(\mathbf{r})}. \quad (2.11)$$

The Schrödinger equation for this system is

$$\left[-\frac{1}{2}\nabla^2 + v_s(\mathbf{r}) \right] \phi_i(\mathbf{r}) = \epsilon_i \phi_i(\mathbf{r}), \quad (2.12)$$

and as the electrons are non-interacting the density is given by

$$n(\mathbf{r}) = \sum_i^{N_e} |\phi_i(\mathbf{r})|^2, \quad (2.13)$$

where the sum is over the N_e orbitals with the lowest energy. If $v_s(\mathbf{r})$ is known it is in principle possible to directly solve for $n(\mathbf{r})$. This is, however, not possible as $v_s(\mathbf{r})$

is a function of $n(\mathbf{r})$. To deal with this issue one instead solves the above equations iteratively until self consistency is reached as illustrated in Figure 2.1.

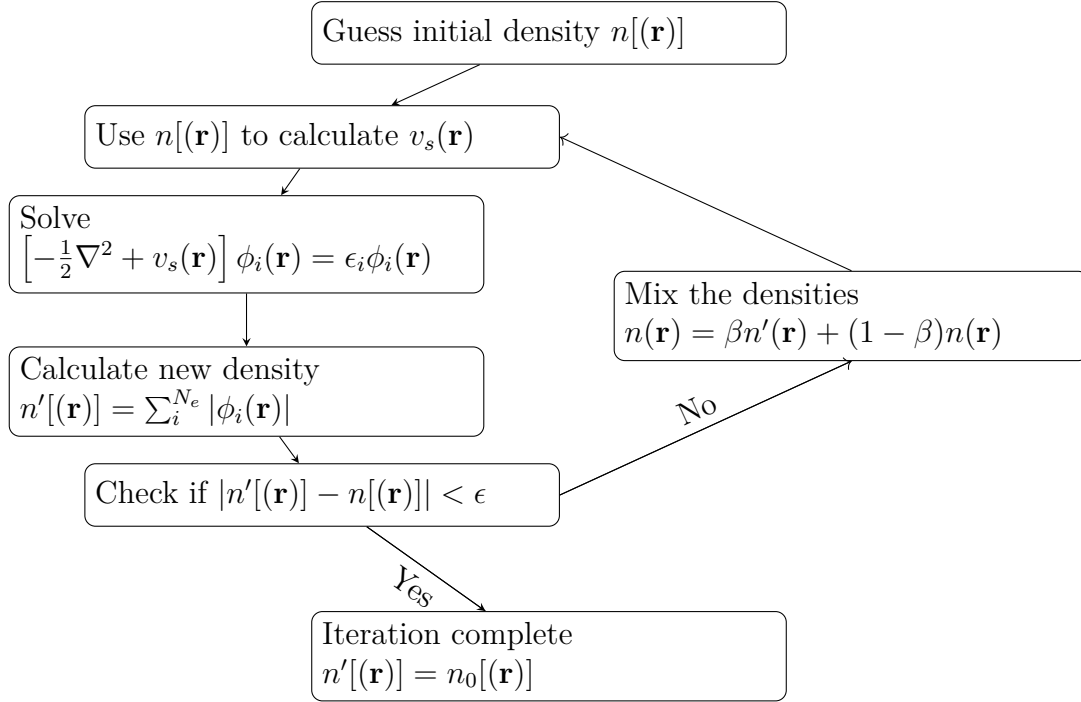


Figure 2.1: Illustration of the self consistent iteration used to find the ground state density in DFT.

An initial density is guessed and Eq. (2.12) is solved to obtain a new density. If the difference between the two densities is smaller than some convergence criterion the iteration is complete otherwise the density is updated using a mixing parameter $\beta \in (0, 1]$.

Once the ground state density is found one can evaluate the energy of the system and the force on each atom as

$$\mathbf{F}_i = -\frac{\partial E}{\partial \mathbf{R}_i} = -\int d\mathbf{r} n(\mathbf{r}) \frac{\partial v_{ei}(\mathbf{r})}{\partial \mathbf{R}_i} - \frac{\partial E_{ii}}{\partial \mathbf{R}_i}. \quad (2.14)$$

2.2.2 Exchange-correlation functionals

Comparing Eq. (2.7) with (2.9) it is clear that the role of the exchange-correlation functional is to account for the fact that $T[n(\mathbf{r})]$ is replaced with $T_s[n(\mathbf{r})]$ and $U[n(\mathbf{r})]$ is replaced by $E_H[n(\mathbf{r})]$. The exchange correlation functional is thus given by

$$E_{xc}[n(\mathbf{r})] = (T[n(\mathbf{r})] - T_s[n(\mathbf{r})]) + (U[n(\mathbf{r})] - E_H[n(\mathbf{r})]). \quad (2.15)$$

As neither $T[n(\mathbf{r})]$ nor $U[n(\mathbf{r})]$ are known this expression has to be approximated. The simplest approximation is the so-called local density approximation (LDA). In

this approximation the exchange correlation functional is approximated as

$$E_{xc}[n(\mathbf{r})] = \int d\mathbf{r} n(\mathbf{r}) \varepsilon_{xc}^{hom}(n(\mathbf{r}), \mathbf{r}), \quad (2.16)$$

with $\varepsilon_{xc}^{hom}(n(\mathbf{r}), \mathbf{r})$ being the exchange-correlation energy per electron of the homogeneous electron gas. This is often a reasonable approximation for solids as their electronic structure resembles that of an uniform electron gas [8]. A more general approximation is a class of exchange-correlation functionals known as generalized gradient approximations (GGAs). In this approximation the exchange correlation functional is approximated as

$$E_{xc}[n(\mathbf{r})] = \int d\mathbf{r} n(\mathbf{r}) \varepsilon_x^{hom}(n(\mathbf{r}), \mathbf{r}) F_{xc}(n(\mathbf{r}), |\nabla n(\mathbf{r})|), \quad (2.17)$$

where F_{xc} is a function which differs between GGAs [8]. In comparison to the LDA, GGAs tend to be better at predicting total energies, structural energy differences, and energy barriers but can sometimes soften bonds [9]. Furthermore there are hybrid functionals, which are obtained by combining (semi-local) density dependent functionals with exact or screened exchange at the level of the Hartree-Fock approximation.

In the context of this thesis the most important observation from this section is that there are several different types of exchange-correlation functionals and that the result of a DFT calculation is sensitive to the choice of exchange-correlation functional. In this thesis the functional was used is the so-called B3LYP functional [10], [11]. This is motivated by the fact that it has been used in previous studies of norbornadienes and shown results in good agreement with experiments [3]. Furthermore, the software that was used for DFT calculations was NWchem [12].

2.2.3 Limitations of DFT

A limitation of DFT is that the underlying electronic wave function essentially is assumed to be a Slater determinant of one kind of atomic orbitals,

$$\Psi(\mathbf{r}_1, \mathbf{r}_2, \dots, \mathbf{r}_{N_e}) = \frac{1}{\sqrt{N_e!}} \begin{vmatrix} \phi_1(\mathbf{r}_1) & \phi_2(\mathbf{r}_1) & \cdots & \phi_{N_e}(\mathbf{r}_1) \\ \phi_1(\mathbf{r}_2) & \phi_2(\mathbf{r}_2) & \cdots & \phi_{N_e}(\mathbf{r}_2) \\ \vdots & \vdots & \ddots & \vdots \\ \phi_1(\mathbf{r}_{N_e}) & \phi_2(\mathbf{r}_{N_e}) & \cdots & \phi_{N_e}(\mathbf{r}_{N_e}) \end{vmatrix} = \det(\phi(\mathbf{r})). \quad (2.18)$$

This is problematic for the system studied in this thesis as this means that only one type of orbitals can be occupied. In **N** only π -orbitals are occupied, in **Q** only σ -orbitals are occupied, whereas in **S** both π and σ orbitals are occupied. Thus regular DFT can describe both **N** and **Q** well but fails to describe **S** [3]. To accurately describe **S** one needs to use so-called multi-reference methods, in which the underlying wave function is allowed to be a linear combination of several Slater determinants such that several kinds of orbitals can be (fractionally) occupied. These method are, however, computationally much more demanding than regular DFT calculations and in this thesis the electronic structure of **S** will be approximated by using unrestricted open-shell DFT. This has been done in previous studies and it was observed to be a viable approximation [4].

2.3 Symmetric gradient domain machine learning

In the previous section it was discussed how DFT can be used to calculate energies and forces for different atomic geometries. As mentioned this is, however, a computationally demanding method. To obtain a more computationally efficient model, ML models can be trained using forces and energies from DFT calculations to obtain an approximation of the PES and the interatomic forces. In this thesis, the ML model that will be used is sGDML. This is a specific type of gradient domain machine learning (GDML), which also exploits the symmetries of the system. To understand how sGDML works it is required to understand the basics of GDML.

2.3.1 Gradient domain machine learning

In GDML energy conserving force fields are explicitly constructed by inferring the known relation between the energy of the molecule and the forces acting on each atom,

$$\hat{f}_F(\vec{x}) = -\nabla \hat{f}_E(\vec{x}). \quad (2.19)$$

Here, $\vec{x} \in \mathbb{R}^{3N}$ corresponds to the positions of the N atoms in the molecule, $\hat{f}_F(\vec{x}) : \mathbb{R}^{3N} \rightarrow \mathbb{R}^{3N}$ is the estimator for the forces and $\hat{f}_E(\vec{x}) : \mathbb{R}^{3N} \rightarrow \mathbb{R}$ is the estimator for the energy of the system.

In GDML the estimator for the energy is modeled as a Gaussian process (GP) with a zero mean function,

$$\hat{f}_E(\vec{x}) \sim \mathcal{GP}[0, k(\vec{x}, \vec{x}')]. \quad (2.20)$$

As $\hat{f}_F(\vec{x}) = -\nabla \hat{f}_E(\vec{x})$ the forces can be expressed as

$$\hat{f}_F(\vec{x}) \sim \mathcal{GP}[0, \nabla_{\vec{x}} k(\vec{x}, \vec{x}') \nabla_{\vec{x}'}^T]. \quad (2.21)$$

Here, $k(\vec{x}, \vec{x}')$ is the covariance function also referred to as the kernel function. It is important to note that the estimator for the energies is a single-output GP whereas the estimator for the forces is a multi-output GP predicting forces on the atoms in all spatial dimensions with the covariance function $\nabla_{\vec{x}} k \nabla_{\vec{x}'}^T = \text{Hess}_{\vec{x}}(k) = k_H(\vec{x}, \vec{x}') \in \mathbb{R}^{3N \times 3N}$.

Assuming one has a set of training geometries the predictor for the forces is firstly constructed as

$$\hat{f}_F(\vec{X}') = \vec{\alpha} K_H(\vec{X}', \vec{X})^T = \sum_i^M \sum_j^{3N} (\alpha_i)_j \frac{\partial}{\partial x_j} \nabla k(\vec{X}', \vec{X}_i) \quad (2.22)$$

with

$$\vec{\alpha} = (K_H(\vec{X}, \vec{X}) + \lambda \mathbf{I})^{-1} \vec{y}_F, \quad (2.23)$$

where $\vec{X} \in \mathbb{R}^{M \times 3N}$ are the training geometries, $\vec{y}_F \in \mathbb{R}^{3NM}$ are the forces corresponding to the training geometries (flattened into a one-dimensional vector), $\vec{X}' \in \mathbb{R}^{L \times 3N}$ are the L geometries we wish to predict the forces for, $k(\vec{X}', \vec{X}_i) \in \mathbb{R}^L$ is a vector of

covariances between $\vec{X}'$ and $\vec{X}_i$ and λ is a regularization parameter. Furthermore the matrix $K_H(\vec{A}, \vec{B})$ with $\vec{A} \in \mathbb{R}^{L \times 3N}$ and $\vec{B} \in \mathbb{R}^{K \times 3N}$ corresponds to a block matrix with block elements $K_H(\vec{A}, \vec{B})_{lk} = k_H(\vec{a}_l, \vec{b}_k)$ with $1 \leq l \leq L$ and $1 \leq k \leq K$ such that $K_H(\vec{A}, \vec{B}) \in \mathbb{R}^{3NL \times 3NK}$.

Secondly, a predictor for the energies can be obtain by integrating Eq. (2.22)

$$\hat{f}_E(\vec{X}') = \vec{\alpha} K_G(\vec{X}', \vec{X})^T = \sum_i^M \sum_j^{3N} (\alpha_i)_j \frac{\partial}{\partial x_j} k(\vec{X}', \vec{X}_i) + c, \quad (2.24)$$

where c is the integration constant

$$c = \frac{1}{M} \sum_i^M [E_i + \hat{f}_E(\vec{X}_i)] \quad (2.25)$$

with E_i being the energy of training geometry i [13].

The reason for firstly constructing a predictor for the forces and then integrating that predictor to obtain the energies is due to error-propagation. In essence, the error for the predictor of the energies will be smaller than the error for the predictor of the forces due to integrating the force predictor to obtain the energy predictor. If one were to construct a predictor for the energies first and then take the derivative to obtain the predictor for the forces the energy would instead be amplified [14].

2.3.2 Descriptors

The Cartesian coordinates are not well suited to describe a specific atomic geometry since they are neither rotationally nor translationally invariant. A more common way to describe a particular atomic geometry is therefore via descriptors that map the Cartesian coordinates of a atomic geometry to another set of coordinates which are invariant to symmetries, i.e.,

$$\vec{x} \rightarrow D(\vec{x}), \quad (2.26)$$

where $D(\vec{x})$ is the descriptor function. When using descriptors in GDML, the kernel functions introduced above become

$$k(\vec{x}, \vec{x}') \rightarrow J_D \nabla_D k_D \quad (2.27)$$

and

$$k_H(\vec{x}, \vec{x}') \rightarrow J_D (\nabla_D k_D \nabla_{D'}^T) J_{D'}^T, \quad (2.28)$$

with $k_D = k(D(\vec{x}), D(\vec{x}'))$ being the covariance in descriptor space and J_D being the jacobian of the descriptor function.

2.3.3 From GDML to sGDML

Although descriptors can be used to account for general symmetries such as rotational and translational symmetries, specific molecules have specific kinds of symmetries.

To estimate the forces and the potential energy surface using fewer training points, leading to better data efficiency, these symmetries need to be taken into account. Normally extracting symmetries of a molecule requires knowledge about the system at hand. However, in sGDML permutation matrices $\vec{P}(\tau)$, corresponding to symmetries in the molecules, are discovered automatically with the use of a method called data-driven multi-partite matching. With this method a set of matrices are obtained $\{\vec{P}_a\}_{a=1}^S$ one for each symmetric transformation. As the permutation matrices transform an atomic geometry into a physically equivalent, yet different, atomic geometry they can be inserted into Eqs. (2.22) and (2.24) to account for symmetries [15],

$$\hat{f}_F(\vec{X}') = \sum_i^M \sum_j^{3N} \sum_q^S (\vec{P}_q \alpha_i)_j \frac{\partial}{\partial x_j} \nabla k(\vec{X}', \vec{P}_q \vec{X}_i) \quad (2.29)$$

and

$$\hat{f}_E(\vec{X}') = \sum_i^M \sum_j^{3N} \sum_q^S (\vec{P}_q \alpha_i)_j \frac{\partial}{\partial x_j} k(\vec{X}', \vec{P}_q \vec{X}_i) + c. \quad (2.30)$$

In this thesis a Python implementation of sGDML is used [16]. The descriptor used in this implementation is a flattened matrix with entries

$$D(\vec{x}_i, \vec{x}_j) = \begin{cases} \|\vec{x}_i - \vec{x}_j\|^{-1} & i > j \\ 0 & i \leq j \end{cases}, \quad (2.31)$$

where $\vec{x}_i$ corresponds to the Cartesian coordinates of the i -th atom in the molecule. The kernel function used in this implementation is the 5/2-Matérn kernel

$$k(\vec{x}, \vec{x}') = \left[1 + \frac{\sqrt{5} \|\vec{x} - \vec{x}'\|}{\sigma} + \frac{5 \|\vec{x} - \vec{x}'\|^2}{3\sigma^2} \right] \exp \left(-\frac{\sqrt{5} \|\vec{x} - \vec{x}'\|}{\sigma} \right), \quad (2.32)$$

with σ being the length scale, a hyperparameter that needs to be determined through training and testing. When deciding what value to use for the length scale it is important to consider that the kernel function essentially describes how correlated two points are. For example, if $\vec{x}$ is known and $\vec{x}'$ is unknown the kernel function $k(\vec{x}, \vec{x}')$ describes how much the value of $\vec{x}$ should affect the prediction of $\vec{x}'$. Thus if two points $\vec{x}$ and $\vec{x}'$ are highly correlated and $\|\vec{x} - \vec{x}'\| = \ell$ then the length scale should be on the order of ℓ such that the kernel function between these points is non-zero. If, however, $\vec{x}$ and $\vec{x}'$ are not correlated at all then the length scale should be much smaller than ℓ such that the kernel function between these points is close to zero.

As mentioned previously, the kernel function is used to construct a matrix $\mathbb{R}^{3NM \times 3NM}$ where N is the number of atoms in the molecule and M is the number of training points. A large limitation when training a sGDML model is the possibility of storing this matrix in memory as the dimensions of this matrix quickly blows up. For example, to store a float in memory one needs 4 bytes; thus to train a model with 26 atoms on 1,000 training geometries requires $(4 \times 78,000)^2$ bytes or ≈ 24 Gb.

2.4 Molecular dynamics & statistical mechanics

Solving the electronic Schrödinger equation allows one to compute the electronic properties of the molecule. To compute thermodynamic properties of a molecule, however, one needs to consider the dynamics of the atoms in the molecule. By generating data using DFT calculations and training a sGDML model a method to compute the forces on all atoms can be obtained. Under the classical approximation discussed in section 2.1.1 the forces can be used in combination with Newton's equations of motion to numerically calculate the positions and momenta of all atoms as a function of time. This is known as performing a molecular dynamics (MD) simulation. Knowing the positions and momenta of all atoms is of course not very interesting as these are not the quantities that can be measured experimentally. In general quantities that are measured in experiments are macroscopic quantities averaged over a large number of particles and averaged over time. To compute such quantities one needs knowledge from statistical mechanics.

2.4.1 The microcanonical ensemble

Statistical mechanics provides a framework that relates the microscopic properties of atoms/molecules to macroscopic quantities. To understand how this works we will consider an isolated system of N identical particles with positions

$$\mathcal{R} = (\mathbf{r}_1, \mathbf{r}_2, \dots, \mathbf{r}_N) \quad (2.33)$$

and momenta

$$\mathcal{P} = (\mathbf{p}_1, \mathbf{p}_2, \dots, \mathbf{p}_N) \quad (2.34)$$

confined to a volume V . The time evolution of the system is governed by the Hamiltonian of the system

$$\mathcal{H} = \frac{\mathcal{P}^2}{2m} + V(\mathcal{R}), \quad (2.35)$$

which depends on the positions and the momenta. For this system the macroscopic variables (N, V, E) are all conserved and (N, V, E) is referred to as a macrostate of the system. In general, there are many combinations of the microscopic variables $(\mathcal{R}, \mathcal{P})$, the combination of which is referred to as a microstate, that yield the same macrostate and the collection of all possible states of this system is known as the microcanonical ensemble. In real physical situations the conditions for the microcanonical ensemble are not particularly common as most physical systems can in some way exchange energy with their environment. It is, however, a good starting point for introducing the main concepts of statistical mechanics.

An important underlying assumption of statistical mechanics is the assumption of equal *a priori* probabilities. This means that all microstates with the same energy are visited for an equal amount of time. This enables us to relate time averages which is what is measured in an experiment

$$\bar{f} = \lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t f(\mathcal{R}(t), \mathcal{P}(t)) dt, \quad (2.36)$$

to ensemble averages

$$\langle f \rangle = \frac{\int f(\mathcal{R}, \mathcal{P}) \rho(\mathcal{R}, \mathcal{P}) d\mathcal{R} d\mathcal{P}}{\int \rho(\mathcal{R}, \mathcal{P}) d\mathcal{R} d\mathcal{P}}, \quad (2.37)$$

which is an average over all microstates of a system. Here, $\rho(\mathcal{R}, \mathcal{P})$ is a density function describing how likely it is to visit the microstate and $f(\mathcal{R}, \mathcal{P})$ is an observable. As the total energy of this system is conserved the density is

$$\rho(\mathcal{R}, \mathcal{P}) = \delta(E - \mathcal{H}(\mathcal{R}, \mathcal{P})) \quad (2.38)$$

and

$$\langle f \rangle = \frac{\int f(\mathcal{R}, \mathcal{P}) d\Omega(E)}{\Omega(E)} \quad (2.39)$$

where $\Omega(E)$ is the number of microstates with energy E and $\int d\Omega(E)$ is the integral over all microstates with energy E . Furthermore, as each microstate with energy E is assumed to be visited for an equal amount of time we have

$$\hat{f} = \langle f \rangle. \quad (2.40)$$

This is known as the ergodicity hypothesis which enables us to relate time-averaged properties, which can be obtained from MD simulations, to thermodynamic properties derived as ensemble averages [17].

2.4.2 The canonical ensemble

As mentioned above, the microcanonical ensemble is not particularly relevant for most physical systems. In the scope of this thesis the most relevant ensemble is rather the canonical ensemble. This ensemble deals with a system of N particles at constant volume V and constant temperature T . In this system the density function is given by $\rho(\mathcal{R}, \mathcal{P}) = e^{-\beta \mathcal{H}(\mathcal{R}, \mathcal{P})}$ where $\beta = 1/k_B T$ with k_B being Boltzmann's constant. Ensemble averages can then be written as [17]

$$\langle f \rangle = \frac{\int f(\mathcal{R}, \mathcal{P}) e^{-\beta \mathcal{H}(\mathcal{R}, \mathcal{P})} d\mathcal{R} d\mathcal{P}}{\mathcal{Z}} \quad \mathcal{Z} = \int e^{-\beta \mathcal{H}(\mathcal{R}, \mathcal{P})} d\mathcal{R} d\mathcal{P}. \quad (2.41)$$

Here, $\mathcal{Z}$ is called the partition function, from which several ensemble averages can be calculated from. In the scope of this thesis the most important quantity is the free energy

$$F = U - TS = -k_B T \ln(\mathcal{Z}). \quad (2.42)$$

The free energy of a system describes the maximum amount of thermodynamic work that a system can perform at a constant temperature. In the above equation, the free energy is a constant, describing the free energy of the entire system. In this thesis, however, we are mainly interested in computing the difference in free energy between different molecular configurations. If we denote the variables that characterize these states as Γ and denote all other degrees of freedom as Ω , the partition function can be computed as a function of Γ via

$$\mathcal{Z}(\Gamma) = \int \rho(\Gamma, \Omega) d\Omega = \int e^{-\beta \mathcal{H}(\Gamma, \Omega)} d\Omega = P(\Gamma). \quad (2.43)$$

In this context the partition function corresponds to a probability distribution of the variables Γ , and under the assumption that the system is ergodic the probability distribution can be computed as

$$P(\Gamma = \Gamma') = \lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t p(\Gamma'(t)) dt, \quad (2.44)$$

where $p(\Gamma')$ is a function which counts the number of times that Γ falls within some interval of Γ' . In the exact case the width of this interval is infinitesimal but in actual calculations it is a finite width that essentially determines the resolution of the probability distribution with respect to Γ [18]. From the probability distribution for Γ the free energy can be computed as a function of Γ

$$F(\Gamma) = -k_b T \ln(\mathcal{Z}(\Gamma)). \quad (2.45)$$

With $\Gamma_{\mathbf{S}}$ being the value of Γ in $\mathbf{S}$ and $\Gamma_{\mathbf{Q}}$ being the value of Γ in $\mathbf{Q}$, the free energy difference between $\mathbf{S}$ and $\mathbf{Q}$, can be computed as $\Delta F^\ddagger = F(\Gamma_{\mathbf{S}}) - F(\Gamma_{\mathbf{Q}})$.

2.4.3 Molecular dynamics in the canonical ensemble

As mentioned previously MD simulations is a numerical method for solving Newton's equations of motion to obtain positions and momenta for a system of N atoms a function of time. If the forces on all atoms, $\mathbf{F} = (\mathbf{F}_1, \mathbf{F}_2, \dots, \mathbf{F}_N)$, are known for all possible positions of the atoms a straightforward approach is to use, e.g., the so-called velocity-Verlet algorithm [19]. This algorithm numerically solves Newton's equation for the positions, $\mathbf{R} = (\mathbf{R}_1, \mathbf{R}_2, \dots, \mathbf{R}_N)$ and the velocities, $\mathbf{v} = (\mathbf{v}_1, \mathbf{v}_2, \dots, \mathbf{v}_N)$, of all atoms using a finite time step Δt . At each time step the positions and velocities are updated according to

$$\begin{aligned} \mathbf{v}(t + \Delta t/2) &= \mathbf{v}(t) + \frac{\mathbf{F}(t)\Delta t}{2\mathbf{M}} \\ \mathbf{R}(t + \Delta t) &= \mathbf{R}(t) + \mathbf{v}(t + \Delta t/2) \\ \mathbf{v}(t + \Delta t) &= \mathbf{v}(t + \Delta t/2) + \frac{\mathbf{F}(t + \Delta t)\Delta t}{2\mathbf{M}}, \end{aligned} \quad (2.46)$$

where $\mathbf{M} = (M_1, M_2, \dots, M_N)$. As this algorithm solves Newton's equations and $\mathbf{F}$ is a conservative force field the total energy is conserved, i.e., this algorithm leads to a MD simulation in the microcanonical ensemble. To instead perform a MD simulation in the canonical ensemble, the system should rather have constant temperature. There are several ways to achieve this but in this thesis an implementation of Langevin dynamics in the Python package Atomic Simulation Environment is used [20]. In this approach the force is altered by adding a small friction term and a fluctuating force for each atom. The force on all atoms then becomes

$$\mathbf{F}' = \mathbf{F} + \begin{bmatrix} -\gamma M_1 \mathbf{v}_1 + \mathbf{f}_1 \\ -\gamma M_2 \mathbf{v}_2 + \mathbf{f}_2 \\ \vdots \\ -\gamma M_{N_i} \mathbf{v}_{N_i} + \mathbf{f}_{N_i} \end{bmatrix}, \quad (2.47)$$

where $\mathbf{f}_j = [f_j^x, f_j^y, f_j^z]$ is a vector of random numbers drawn from the normal distribution with zero mean, $\mu = 0$, and variance $\sigma_j^2 = 2M_j\gamma k_B T / \Delta t$ where T is the desired temperature of the MD simulation.

By combining the above expression for the force with the velocity-Verlet algorithm, it is possible to run a MD simulation at constant temperature. This procedure is illustrated in Figure 2.2. Firstly one needs to choose an initial configuration for the atoms. In general the initial configuration of the atoms should be compatible with the type of structures one aims to simulate. It is also important to select a reasonable value of the time step. If it is too small one will not be able to run sufficiently long MD simulations, and if it is too large the algorithm can be unstable and the dynamics of the atoms might not be accurately resolved. In general the time step should be at least one to two orders of magnitude lower than the fastest occurring process in the system. For the molecule studied in this thesis, the fastest occurring process are the carbon-hydrogen bond vibrations, which have a vibrational frequency of about 3000cm^{-1} . This process thus occurs on a timescale of about 10 fs and a reasonable time step is 0.5 fs. With a chosen time step, an initial configuration and a function which computes the forces on all atoms it is straightforward to run Langevin dynamics by combining Eqs. (2.46) and (2.47) and running the iteration for a sufficiently long time.

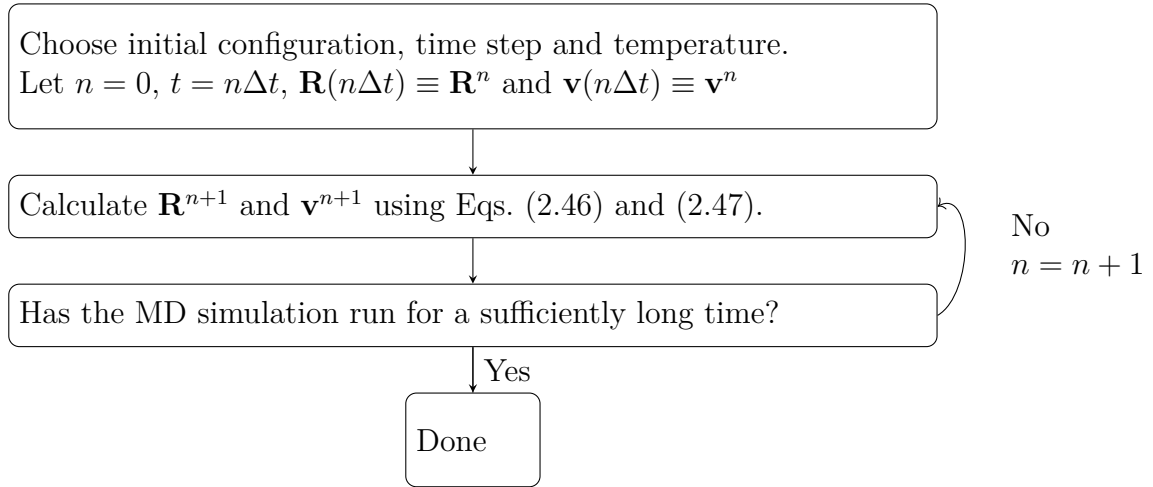


Figure 2.2: Illustration an MD simulation.

After having run a MD simulation one will have obtained a discrete set of positions and velocities as a function of time

$$\mathbf{R}_{\text{MD}} = (\mathbf{R}^0, \mathbf{R}^1, \dots, \mathbf{R}^N), \quad (2.48)$$

and

$$\mathbf{v}_{\text{MD}} = (\mathbf{v}^0, \mathbf{v}^1, \dots, \mathbf{v}^N), \quad (2.49)$$

where N is the number of time steps that the MD simulation was run. By the ergodicity hypothesis discussed in section 2.4.1, it is possible to use these sets to

estimate ensemble-averaged quantities and probability distributions such as the one in Eq. (2.44), which allows the computation of free energy differences. One should however note that the microscopic temperature of the simulation which is a function of the temperature,

$$T(t) = \sum_{i=1}^{N_i} \frac{M_i[\mathbf{v}^i(t)]^2}{k_b(3N_i - 3)}, \quad (2.50)$$

might not stabilize around the desired value for the first few steps as here we use an initial velocity of zero. It is therefore important to analyze the temperature (and other quantities of interest) as a function of time before computing averages and probabilities. If the temperature has not stabilized around the desired value for the first few iteration these should be discarded.

2.4.4 Umbrella sampling

To be able to accurately estimate the free energy as a function of some variables Γ from a MD simulation it is important that all relevant values of Γ are sufficiently sampled in the MD simulation. In general a MD simulation samples regions around local minima well, but struggles to accurately sample regions with higher energies and therefore it is difficult to compute $F(\Gamma)$ by only using standard MD simulations. There are several techniques that can be used to sample regions with higher energy such that $F(\Gamma)$ can be computed but in this project a method called umbrella sampling will be used.

The general idea of umbrella sampling is to add a bias potential, $V(\Gamma)$, to a MD simulation with the intent of balancing out the energy differences such that values of Γ that correspond to high-energy regions are sampled accurately. The addition of an external potential will alter the probability distribution of Γ but can be normalized to the unbiased probability distribution via

$$P_u(\Gamma) = P_b(\Gamma) \exp(\beta V(\Gamma)) \langle \exp(-\beta V(\Gamma)) \rangle \quad \beta = \frac{1}{k_b T}, \quad (2.51)$$

where the subscripts u and b indicate biased and unbiased probability distributions, respectively. Choosing a bias potential is not an easy task and the outcome of the sampling is heavily dependent on choosing a bias potential such that all relevant values of Γ are well sampled. A common approach is to sample Γ in windows where each window m consists of a MD simulation with a harmonic bias potential with strength k centered around the value Γ_m

$$w_m(\Gamma) = \frac{k}{2}(\Gamma - \Gamma_i)^2. \quad (2.52)$$

By adding sufficiently many windows, it is possible to assure that all relevant values of Γ are sampled [18].

When using this approach the biased probabilities cannot be converted into unbiased probabilities with the help of Eq. (2.51). The equation holds for each window, i.e.,

$$P_u^m(\Gamma) = P_b^m(\Gamma) \exp(\beta w_m(\Gamma)) \langle \exp(-\beta w_m(\Gamma)) \rangle, \quad (2.53)$$

but each window will only sample Γ around Γ_m . To compute the probability distribution for all values of Γ the windows need to be combined which can be achieved using a method called weighted histogram analysis method (WHAM). In this method the total unbiased probability is written as a weighted sum over the unbiased probabilities from each window

$$P_u(\Gamma) = \sum_m^N p_m P_b^i(\Gamma), \quad (2.54)$$

where p_m are the weights that minimize the variance of $P_u(\Gamma)$

$$\frac{\partial \sigma^2(P_u(\Gamma))}{\partial p_m} = 0, \quad (2.55)$$

with the constraint that $\sum_m^N p_m = 1$. It is possible to show that

$$p_m = \frac{a_m}{\sum_j a_j} \quad \text{with} \quad a_i(\Gamma) = N_m \exp(-\beta w_i(\Gamma) + \beta F_i), \quad (2.56)$$

where N_m is the number of sampled point in each window and

$$\exp(-\beta F_m) = \int P_u(\Gamma) \exp(-\beta w_m(\Gamma)) d\Gamma. \quad (2.57)$$

As F_m is a function of the unknown probability distribution $P_u(\Gamma)$, the above equation has to be solved iteratively until $P_u(\Gamma)$ has converged. This means that an initial guess for $P_u(\Gamma)$ has to be made, secondly p_i can be computed for all windows, and thirdly $P_u(\Gamma)$ can be recomputed. This procedure is continued until $P_u(\Gamma)$ changes less than some small tolerance [18].

3. Model Construction

The purpose of this thesis is to create ML models that can describe the energy landscape along the reaction path between **N** and **Q** for **2** and **3**, i.e., models that can accurately describe the PES and the forces on all atoms. In this chapter, the process of constructing these models will be described. Firstly, **1** will be considered to describe how training data for the models were generated, how the models were validated, and the importance of choosing a suitable value of the kernel length scale will be discussed. Secondly, the models for **2** and **3** will be considered and it will be shown how well they can predict PES and forces, especially for the side group rotation and the reaction path.

3.1 Models for **1**

As both the time of an DFT calculation and the time of training of an sGDML model scale with system size it is convenient to test the process of data generation and training on a small system. Thus before considering **2** and **3** which consist of it 26 atoms is reasonable to first consider **1** which only consist of 15 atoms.

3.1.1 Models for **1N** and **1Q**

Before creating models that incorporate data from **1N**, **1S**, and **1Q**, two separate models were created. One with the aim of describing **1N**, and one with the aim of describing **1Q**. The reason for doing so is because **N** and **Q** are local minima, thus these regions are stable and should be easier to describe. Furthermore, according to the discussion in section 2.2.3, regular DFT calculations can be used to calculate energies and forces for atomic geometries in these neighborhoods. To this end, two ML models were trained on energies and forces from 230 atomic geometries, one model for **1N** and **1Q** each and as the data is noiseless the regularization term was chosen to be a small value, $\lambda = 10^{-12}$. As the performance of a ML model generally is heavily dependent on the quality of the training data it is important to address how these geometries were generated.

Mainly two different types of approaches were used to generate data for these models: randomly displacing all atoms starting from an initial configuration of the molecule, and generating atomic geometries by running a MD simulation with a ML model trained on such geometries. Initially, only the atomic geometries for **N** and **Q** were known and to generate more training data all atoms of these two geometries were randomly displaced to generate 50 additional geometries. The random displacement was done by adding $\epsilon = [\epsilon_x, \epsilon_y, \epsilon_z]$ to each atom’s position, where $\epsilon_x, \epsilon_y, \epsilon_z$ are random numbers generated from a normal distribution with zero mean and $\sigma = 0.03 \text{ \AA}$.

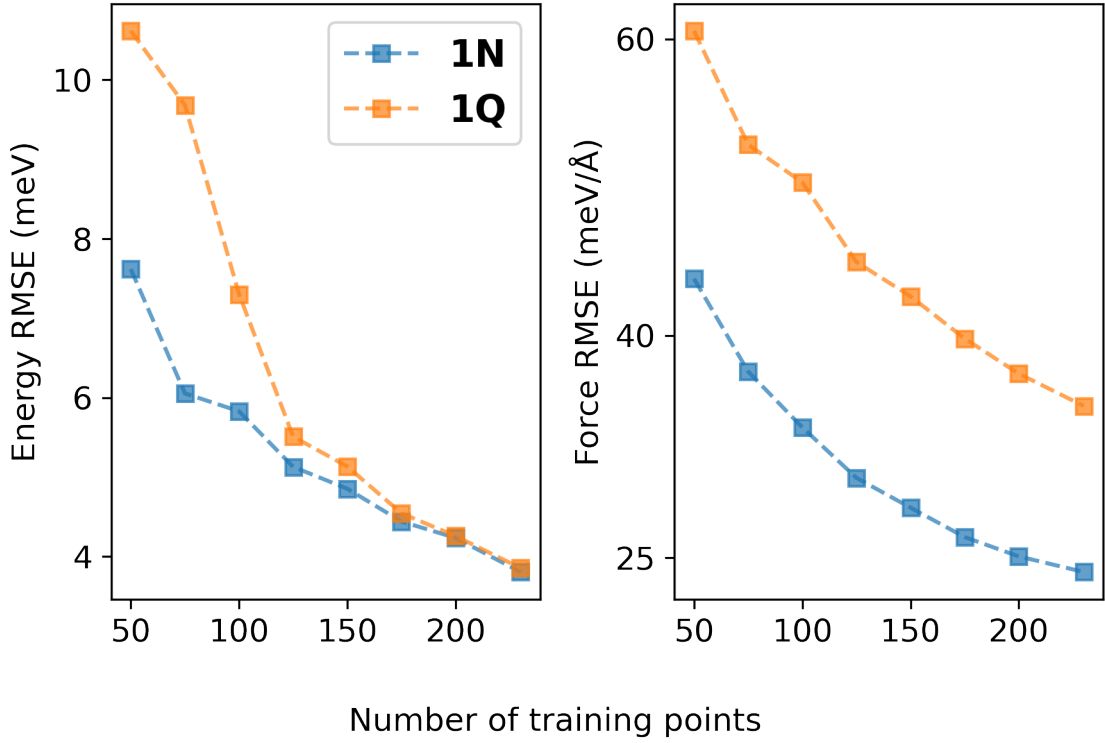


Figure 3.1: Illustrating how the energy/force root-mean-square errors (RMSEs) decrease when adding more data to the models for **1N** and **1Q**.

By computing energies and forces via DFT for these 50 atomic geometries an initial model could be trained. Although the initial models were not very accurate they could be used to perform a MD simulation to generate more atomic geometries. By calculating the forces and energies on these atomic configurations via DFT the training set could be extended to include more points and the model could be retrained. This procedure was repeated until an accurate enough model had been obtained. It should be noted that MD simulations performed using a model trained on ≤ 150 atomic configurations were not stable, i.e., after some time the energy diverged and unrealistic geometries were obtained, such configurations were however not included in the training set.

To see how the model improves over several generations, one can look at how the model predicts the forces and energies for atomic geometries that are not in the training set. Here, this is achieved by monitoring the energy RMSE

$$E_{\text{RMSE}} = \sqrt{\sum_{i=1}^N \frac{(E_{\text{predicted}} - E_{\text{target}})^2}{N}} \quad (3.1)$$

and the force RMSE

$$F_{\text{RMSE}} = \sqrt{\sum_{i=1}^N \frac{(\mathbf{F}_{\text{predicted}} - \mathbf{F}_{\text{target}})^2}{3N}}. \quad (3.2)$$

Here, $E_{\text{predicted}}$ and $\mathbf{F}_{\text{predicted}}$ are the energies and forces that the model predicts and E_{target} and $\mathbf{F}_{\text{target}}$ are the respective target values, i.e., in the present thesis values from DFT calculations. The sum is taken over a validation set, consisting of N atomic geometries. In Figure 3.1 the energy and force RMSEs are illustrated for the **1N** and **1Q** models. The validation set which was used to compute the RMSEs in Figure 3.1 was constructed by using the models trained on 230 training geometries to run an MD simulation and extracting 50 atomic geometries, and then using DFT to calculate the target energies and forces. It is seen that the RMSE decreases as more training data is added. This indicates that the method for generating data described above is an acceptable method for generating training data of decent quality.

3.1.2 Model for **1NSQ**

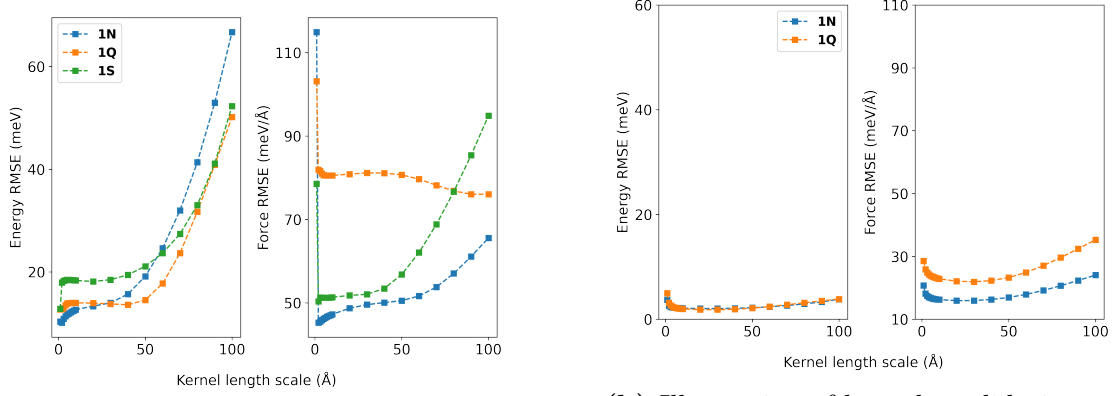
To be able to compute the reaction path between **1N** and **1Q**, a model which can simultaneously describe **1N**, **1Q**, **1S**, and points in between these regions was trained. For brevity this type of model will be referred to as **1NSQ**. To train such a model additional training geometries had to be generated. The training geometries used to train the models for **1N** and **1Q** can be reused but new data around **1S** and in between **1N** and **1Q** needs to be generated. These regions are not local minima and therefore standard MD simulations cannot be used to generate data for these regions as MD only samples regions of low energy well. However, as the atomic geometry of **1S** is known from previous studies, [3], training data could be generated by randomly displacing the atoms of this geometry. Furthermore, to generate atomic geometries between **1N**, **1Q**, and **1S** linear paths between these atomic geometries were computed.

As discussed in section 2.2.3, regular DFT calculations cannot be used to describe atomic geometries close to the saddle points and therefore unrestricted open shell DFT calculations were used as an approximation to compute forces and energies for the training geometries. In total 446 training geometries were used to train the model for **1NSQ** and in Figure 3.2a the energy and force RMSEs are illustrated as a function of the kernel length scale σ , which is a hyper parameter that needs to be optimized. The model was validated on validation data from **1N**, **1S**, and **1Q**. The validation errors for the energies are lower for smaller values of σ while validation errors for the forces are large for $\sigma = 1\text{\AA}$, then exhibit a sharp drop and for the data from **1N** and **1S** the error increases with σ while the opposite is seen for data from **1Q**.

This kind of behavior is not seen for the models only trained on either **1N** and **1Q** (and also only validated on either **1N** and **1Q**). In Figure 3.2b the validation errors for both of these models are illustrated as a function of σ and it is seen that the validation errors are quite small for all values of σ and that both the force and energy RMSEs have a minimum at around $\sigma = 25\text{\AA}$. From these results it is clear that when creating a model for **NSQ** the choice of σ is much more relevant for the performance of the model. From Figure 3.2a choosing $\sigma = 2\text{\AA}$ yields both relatively low energy and force RMSEs. From the discussion of the kernel length scale in section 2.3.3 it

3. Model Construction

is reasonable that one should choose a shorter length scale when training a model which contains data from **N**, **S**, and **Q** since atomic geometries from **N** should not have a large influence on the prediction of atomic geometries close to **S** or **Q**.



(a) Illustration of how the validation errors for the **1NSQ** model varies with the kernel length scale. The model is validated on data from **N**, **S**, and **Q**.

(b) Illustration of how the validation errors for the **1N** and **1Q** models varies with the kernel length scale. The model for **1N** (**1Q**) is validated on data from **N** (**Q**).

Figure 3.2: Illustration of how the validation errors varies with the kernel lengthscale.

3.2 Models for 2 and 3

After testing the process of data generation and model validation on **1** models for **2** were created by following a similar approach.

3.2.1 Models for 2N, 2Q, 3N and 3Q

Following the approach in section 3.1.1 models for describing **2N**, **2Q**, **3N** and **3Q** were also created. The models were validated by running an MD simulation at 300 K for 10^{-2} ns, selecting 50 atomic geometries from the obtained trajectory, calculating the energy and forces for each atomic configuration with DFT, and then comparing with the predicted energies and forces. In Table 3.1 the RMSEs for the validation data is provided. The RMSEs for all models are relatively low and that all models have comparable RMSEs for the energy and the forces.

	2N	2Q	3N	3Q
RMSE Energy (meV)	7.42	10.12	11.39	10.76
RMSE Force (meV/Å)	36.73	49.81	48.80	58.05

Table 3.1: The energy and force RMSEs for the models **2N**, **2Q**, **3N** and **3Q**.

As mentioned in section 1.1 an important property of **2** and **3** is the rotation of the side groups. To analyze how well the models can predict this property the so-called rotational energy landscape was calculated. The rotational energy landscape is essentially the minimal potential energy for each molecule under the constraint that the side group is rotated by a specific angle. To calculate this quantity constrained energy minimization was performed, i.e., for each model the energy was minimized while fixing the angle, θ , for the side group to a specific value. By performing the minimization for several $\theta \in [0, 360]$ the rotational energy landscape was obtained. To validate the performance of the models DFT calculations were carried out for the atomic geometries obtained through constrained energy minimization. In Figure 3.3 the predicted rotational energy landscape for all models is shown along with the corresponding DFT data. It is seen that the sGDML models predict the rotational energy landscape with high accuracy.

From the results shown in this section it can be concluded that sGDML can successfully interpolate the knowledge in the training data to predict with high accuracy the PES for other atomic geometries sufficiently similar to the training data. This is apparent from the fact that the RMSEs for the validation data along the MD trajectories are relatively low for all models and the predictions of the rotational energy landscapes agree with DFT data.

3.2.2 Models for **2** and **3**

After validating that sGDML can with a high accuracy be used to describe **2N**, **2Q**, **3N**, and **3Q**, models for **2NSQ** and **3NSQ** were trained following the approach in section 3.1.2 with $\sigma = 2\text{\AA}$ and $\lambda = 10^{-12}$. Both training sets consisted of approximately 900 atomic geometries and in Table 3.2 and Table 3.3 the RMSEs for validation data in **N**, **S**, and, **Q** is shown for the two models. It is seen that the RMSEs are larger than for the models trained only on either **N** or **Q**. This is, however, expected as the models are trained on much more diverse atomic geometries, which influence the predictions.

	2N	2S	2Q
RMSE Energy (meV)	30.90	66.29	17.59
RMSE Force (meV/ $\text{\AA}$)	91.63	103.81	77.91

Table 3.2: The energy and force RMSEs for model **2NSQ** validated on data from **2N**, **2S** and **2Q**.

	3N	3S	3Q
RMSE Energy (meV)	35.39	54.10	26.77
RMSE Force (meV/ $\text{\AA}$)	78.50	108.35	84.16

Table 3.3: The energy and force RMSEs for model **3NSQ** validated on data from **3N**, **3S** and **3Q**.

Following the approach in the previous section the rotational energy landscapes were also calculated for **N**, **Q**, and **S** using the **2NSQ** and **3NSQ** models. Figure 3.3 shows the rotational energy landscape predicted by these models for **N** and **Q** along with DFT data and the rotational energy landscape for the models only trained on either **N** or **Q**. It is seen that the models for **2NSQ** and **3NSQ** can predict the rotational energy landscape to the same accuracy as the previous models, in fact for **3N** and **3Q** it appears even to be more accurate than the previous models. This can be explained by the fact that points along the rotational energy landscapes were inserted into the training set when training these models. The reason for doing so is that according to the discussion in section 1.1 it is important that the models can predict the side group rotation with good accuracy when computing the free energy difference along the reaction path. In Figure 3.4 the predicted rotational energy landscape at **S** is seen for the two models along with DFT calculations on atomic geometries from the predicted rotational energy landscapes. In general the sGDML models predict the rotational energy landscapes well but there are some small errors, around 90° and 270° for **2S**, and between 150° and 230° for **3S**.

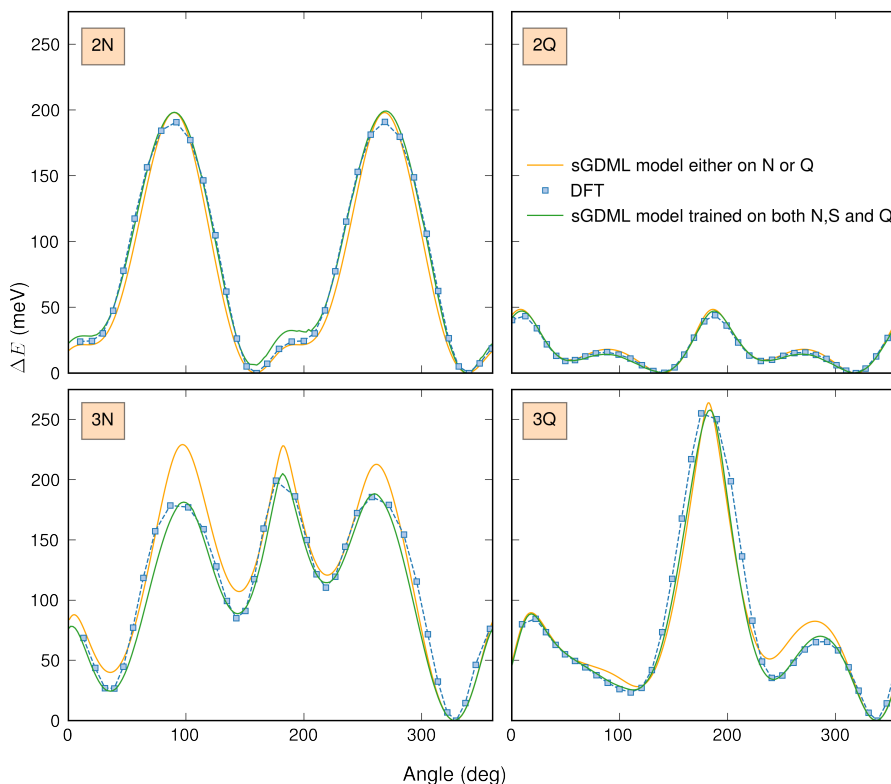


Figure 3.3: Illustration of the predicted rotational energy landscapes for **2N**, **2Q**, **3N** and **3Q** along with DFT calculations on atomic geometries from the predicted rotational energy landscapes. The yellow lines corresponds to the models for **2N**, **2Q**, **3N** or **3Q** and the green lines correspond to the **2NSQ** and **3NSQ** models.

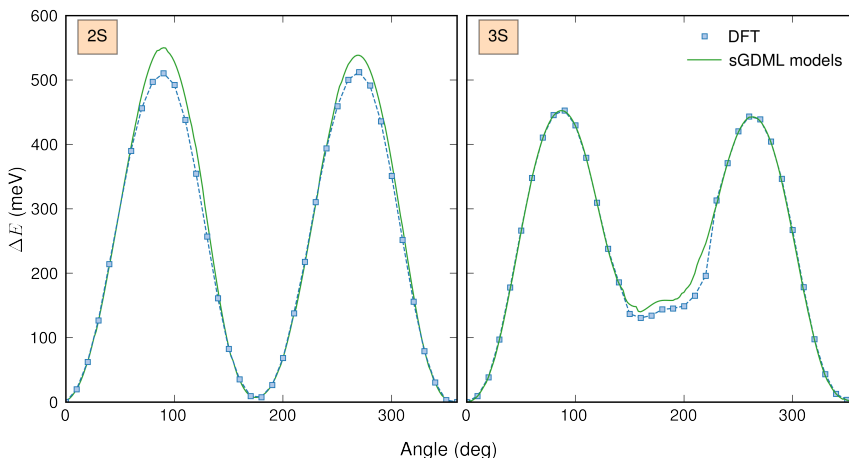


Figure 3.4: Illustration of the predicted rotational energy landscapes for **2S** and **3S** along with DFT calculations on atomic geometries from the predicted rotational energy landscapes.

As mentioned in section 1.1, the reason for investigating the rotation is that it can affect the entropy of the system and in turn the free energy. The entropy of the system corresponds to the number of accessible states and by analyzing the rotational energy landscape it is possible to investigate how the entropy should differ between the molecules based on how the rotation of the side group is limited. From Figure 3.4 one can see that the rotation in **S** should be limited for both **2** and **3** as the energy differences between the different angles are large. For **2** the rotational angle should be confined to around 0° or 180° and for **3** the rotational angle should be confined to around 0° . From Figure 3.3 one can see that the rotation in **Q** should not be too limited for **2** as the energy is fairly low for all angles and that the rotation should be considerably more limited for **3** as the energies are larger. Based on the above discussion it is reasonable that the entropy differences between **S** and **Q**, $\Delta S^\ddagger$, differ between **2** and **3**. Therefore the difference in free energy between **S** and **Q** should have a different temperature dependence according to $\Delta F^\ddagger = \Delta U^\ddagger - T\Delta S^\ddagger$ which could be the reason for **3** having a substantially lower back-conversion rate than **2**.

To be able to compute $\Delta F^\ddagger$ it is important that the models can accurately describe the reaction from **N** to **Q**. Therefore the minimum energy path (MEP) between **N** and **Q** was computed using the trained models. The MEP is the path between **N** and **Q** which requires the least amount of energy to cross. The point with the highest energy on this path is the transition state which is a saddle point, i.e., **S** [21]. The physical significance of this path is that it is the most probable path for the reaction between **N** and **Q** and from this path one can determine the smallest amount of energy that needs to be supplied for the reaction to occur. To obtain this path the nudged elastic band method was used [22].

In Figure 3.5 the MEPs obtained by using the nudged elastic band method with the trained sGDML models is shown along with DFT calculations on the atomic

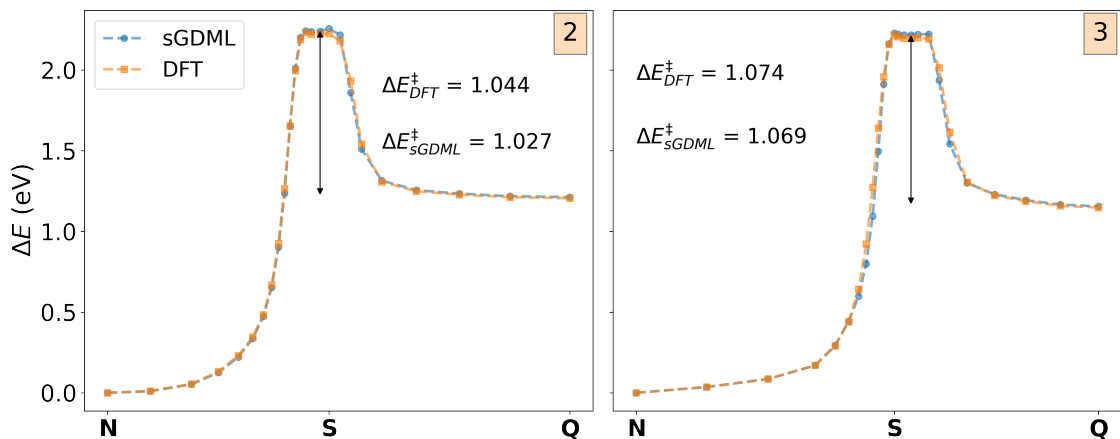


Figure 3.5: Illustration of the predicted MEPs along with DFT calculations on the atomic geometries obtained along the path. The left figure is the MEP for **2** and the right figure is the MEP for **3**.

geometries obtained along the path. It is seen that the predicted energies along the MEP agree well with the DFT calculations close to **N**, **Q**, and **S** but that there are some points which the models fail to predict accurately. These points lie on the part of the MEP where the slope is the largest making them harder to predict. Furthermore, the majority of the training data were atomic geometries close to either **N**, **Q**, and **S** and therefore it is expected that these models are worse at predicting energies in between these points. The most crucial property that both models succeed in predicting is the back-conversion barrier. From Figure 3.5 it is apparent that the back-conversion barrier for **2** and **3** are similar but that **3** is slightly larger. This agrees with the previous computational study [4] but does not agree with the experimental findings in the same study. This is, however, expected as evaluating the MEP directly from the PES corresponds to the MEP at 0 K and thus the entropic contribution to the free energy is zero.

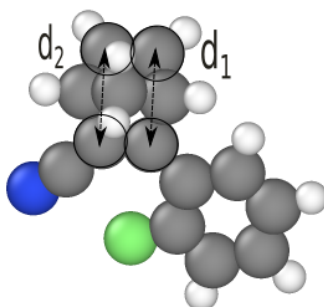


Figure 3.6: Illustration of the two interatomic distances which can be used to describe the transition between **N** and **Q**.

From the obtained MEPs it is possible to investigate the reaction mechanism, i.e., how the reaction from **N** to **Q** occurs. The transition between **N** and **Q** can be conveniently described using the two interatomic distances d_1 and d_2 illustrated in Figure 3.6 for **3N**. For **N** both of these distances are approximately $2.5 \text{ \AA}$ and for **Q** both of these distances are approximately $1.5 \text{ \AA}$. In Figure 3.7 the MEPs and the energy landscape is illustrated as a function of these two distances along with the locations of **N**, **Q**, and **S**. It is seen that at **Q** both d_1 and d_2 are approximately $1.5 \text{ \AA}$, at **S** d_1 has increased to approximately $2.4 \text{ \AA}$ and d_2 has only increased to about $1.6 \text{ \AA}$ and at **N** d_1 and d_2 has increased to approximately $2.5 \text{ \AA}$.

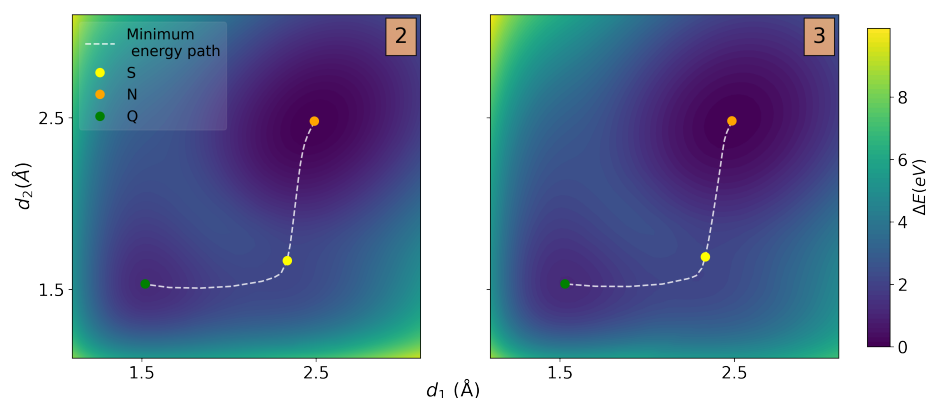


Figure 3.7: Illustration of the MEPs as a function of d_1 and d_2 along with the energy landscape as a function of d_1 and d_2 . The left figure is the MEP and energy landscape for **2** and the right figure is the MEP and energy landscape for **3**.

From the results illustrated in this section it can be concluded that the sGDML models can be generalized, such that one model can be used to describe **N**, **S**, and **Q**. Although the RMSEs on the validation data are larger for these models than for the models for only **N** or **Q**, they can still accurately describe the rotational energy landscapes and the MEPs. Thus by using the models constructed in this section it should be possible to investigate the temperature dependence of $\Delta F^\ddagger$ and thereby explain the difference in back-conversion barriers for **2** and **3**.

4. Free energy calculations

From the analysis of the constructed models in the last chapter it was seen that the combined models, trained on data from **N**, **S**, and **Q**, for **2** and **3** could, to a good approximation, describe both the side group rotations and the reaction path at 0 K. Here the models will firstly be used in combination with umbrella sampling, which was discussed in section 2.4.4, to calculate the free energy along the MEPs to investigate the temperature dependence of $\Delta F^\ddagger$. Secondly, the models will be used to calculate the rotational free energy landscapes.

4.1 Free energy along the MEPs

In section 3.2.2 it was shown that the two main differences between **N**, **S**, and **Q** are the two distances d_1 and d_2 illustrated in Figure 3.6 and it was also discussed that these two distances comprise the main reaction mechanism along the MEPs. Therefore, to investigate the temperature dependence of $\Delta F^\ddagger$, the free energy was computed as a function of these two distances, for $T \in [200, 250, 300, 350, 400]$ K, along the MEPs using umbrella sampling. It should be noted that when computing the free energy as a function of d_1 and d_2 it is not possible to assure that the rotational angle of the side group of the system is fully sampled which will affect the computed value of $\Delta F^\ddagger$. The reason for not including the rotational angle as a parameter in the umbrella sampling routine, which would solve this issue, was due to the time limitations of this thesis project. Furthermore, it was also thought that the sampling of the rotational angle would be sufficiently good to still see a qualitative difference for the temperature dependence of $\Delta F^\ddagger$ for **2** and **3**, assuming that the models can still describe all the relevant properties at finite temperatures.

For both **2** and **3** the umbrella sampling was performed using 40 windows with spring constants $k_{d_1}, k_{d_2} = 50$ eV and in Figure 4.1 the location of the 40 different potentials are seen. For each temperature, window and molecular system a MD simulation was run for 2 ns with a time step of 0.5 fs and the first 0.25 ns of these trajectories were discarded as the temperature had not yet reached the required value. By using the WHAM the free energy was obtained as a function of d_1 and d_2 along the MEPs.

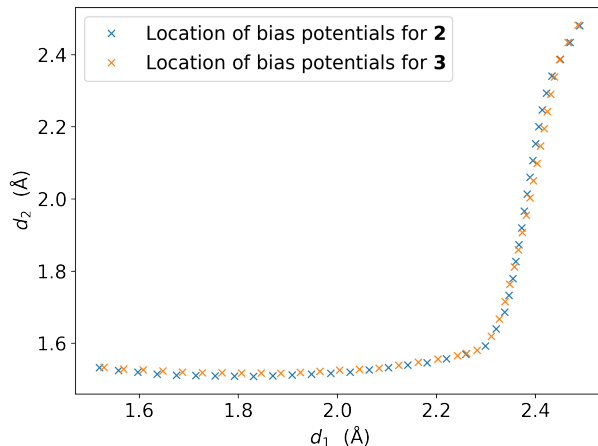


Figure 4.1: Illustration of the location of the bias potentials used when performing umbrella sampling to compute the free energy as a function of d_1 and d_2 along the MEPs.

In Figure 4.2 the free energy is seen for four different temperatures along the MEPs where the 0 K curves correspond to the difference in potential energy, ΔE , and are the MEPs from section 3.2.2. It is seen that the curves for $T \in [200, 300, 400]$ K all have a similar shape to the 0 K curve which indicates that the models can, to a good approximation, be used to sample the MEP at finite temperatures. Generally the curves for ΔF should have a similar shape as the curves for ΔE as ΔE should be the largest contribution to ΔF while the difference kinetic energy due to a finite temperature as well as the entropy should, for these temperatures, be a smaller and mainly alter the amplitude of the free energy. For **2** the free energy at **S** is relatively unchanged for $T \in [200, 300, 400]$ K and the largest changes occur at **Q** where the free energy increases much between 200 K and 300 K but is relatively unchanged between 300 K and 400 K. For **3** the free energy decreases with temperature at **S** and decreases slightly with temperature at **Q**. Furthermore, in Figure 4.3 the difference in free energy between **S** and **Q** is seen as a function of temperature and it is seen that both **2** and **3** share the same approximately linear temperature dependence. From the discussion in section 3.2.2 it was expected that the temperature dependence of the free energy should differ between **2** and **3** due to the difference of the rotational energy landscapes between the two molecular systems. A reason for not seeing a different temperature dependence can be that the rotational angle is not fully sampled in the MD simulation, but it can also be that the models cannot describe the rotational energy landscapes correctly at finite temperatures. To further analyze the temperature dependence of $\Delta F^\ddagger$ it is therefore relevant to investigate the temperature dependence of the rotational energy landscape, i.e compute rotational free energy landscapes.

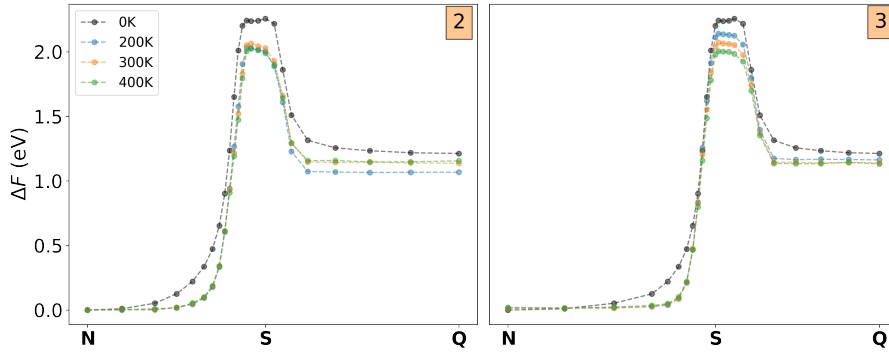


Figure 4.2: Illustration of the predicted free energy along the MEPs for $T \in [0, 200, 300, 400]$ K. The left figure is the MEP for **2** and the right figure is the MEP for **3**.

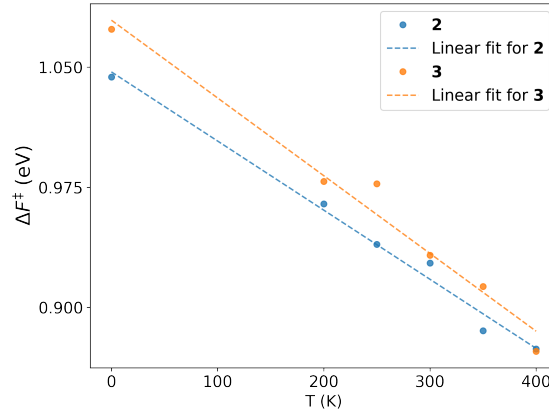


Figure 4.3: Illustration of predicted temperature dependence of $\Delta F^\ddagger$ and a linear fit of $\Delta F^\ddagger$.

4.2 Rotational free energy landscapes

To compute rotational free energy landscapes the free energy was calculated, with umbrella sampling, as a function of the angle describing the side group rotation. This was done for **N**, **S** and **Q**, for both **2** and **3**, and for $T \in [200, 300, 400]$ K. For each temperature and state, 36 windows were used which were centered at $\theta_i = 10i^\circ$ for $i \in [0, 35]$. For **N** and **Q** the value of the spring constant was chosen to be $k = 1.5$ eV and for **S** the value of the spring constant was chosen as $k = 3$ eV. In each window a MD simulation was run for 1 ns and the first 0.25 ns of these trajectories were discarded as the temperature had not yet reached the required value. By using WHAM the free energy was obtained as function of θ for both **2** and **3** in **N**, **S** and **Q**.

In Figure 4.4 the predicted rotational free energy landscape is seen for **2N**, **2Q**, **3N**, and **3Q** for $T \in [0, 200, 300, 400]$ K, where the 0 K curves correspond to the rotational

energy landscape in Figure 3.3. It is seen that the curves for $T \in [200, 300, 400]$ K all have a similar shape to the 0 K curve which according to the discussion in section 4.1 indicates that the models can, to a good approximation, describe the rotational energy landscape at finite temperatures. For **2N**, **3N** and **3Q** it is predicted that free energy decreases with temperature and the most pronounced decrease is seen in **3Q** at the angles $\approx 110^\circ$ and $\approx 250^\circ$ where the free energy drops to zero at 400 K. For **2Q** it is predicted that the free energy increases with temperature and the most pronounced increase is at the two local minima at $\approx 50^\circ$ and $\approx 230^\circ$. Based only on these results one would still expect a different temperature dependence of $\Delta F^\ddagger$ for **2** and **3** as the number of accessible state should become increasingly limited for **2Q** and increasingly more accessible for **3Q** as the temperature increases. To further investigate the temperature of $\Delta F^\ddagger$ the rotational free energy landscape for **S** must also be considered.

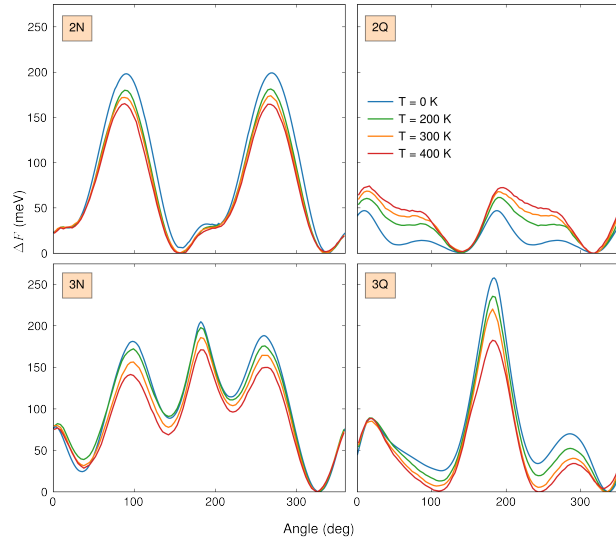


Figure 4.4: Illustration of the predicted rotational free energy landscapes at **N** and **Q** for $T \in [0, 200, 300, 400]$ K.

In Figure 4.5 the predicted rotational free energy landscape is seen for **2S** and **3S** for $T \in [0, 200, 300, 400]$ K where the 0 K curves correspond to the rotational energy landscape in Figure 3.4. It is seen that the shape of the curves for $T \in [200, 300, 400]$ K differs a lot from the rotational energy landscape at 0 K and that in general the free energy is predicted to be much smaller than at 0 K. For **2S** the two peaks at around $\approx 90^\circ$ and $\approx 270^\circ$ are still somewhat present at 200 K but are unrealistically low and for 300 K and 400 K they are further decreased. For **3S** the peak at $\approx 280^\circ$ is present for $T \in [200, 300, 400]$ although it seems to be a bit low and slightly shifted to the right where as the other parts of the rotational free energy landscape does not share a resemblance with the rotational energy landscape at 0 K. These results illustrates that the models cannot accurately describe the rotation of the side group in **S** at finite temperatures. Furthermore, as the models predict rotational energy

landscapes of much smaller energies than expected they in turn predict that the side group is relatively free to rotate and therefore the hypothesis that the temperature dependence of the $\Delta F^\ddagger$ should differ between **2** and **3**, due to the difference in rotational energy landscapes, cannot be investigated with the current state of the models.

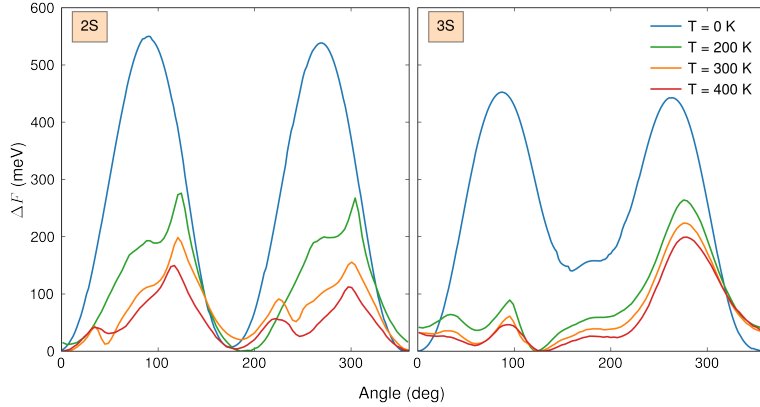


Figure 4.5: Illustration of the predicted rotational free energy landscapes at **S** for $T \in [0, 200, 300, 400]$ K.

To explain why the model fails to describe the side group rotation at **S** it is important to consider how the training data was generated. For both **N** and **Q** it was possible to run MD simulations to iteratively add training geometries in **N** and **Q** as explained in section 3.1.1, however for **S** this was not possible as MD simulations does not sample **S** well and instead geometries were mainly added through random displacements and adding geometries along the rotational energy landscape. It is thus reasonable that the models fail to accurately describe the rotational energy landscape in **S** at finite temperatures as the model has not seen enough data in **S** at finite temperatures. However as the models can successfully describe the rotation of the side groups at **N** and **Q** it should be possible for the models to also describe the side group rotation in **S** by adding more data in this state. This can for example be done by extracting atomic geometries from the MD simulations performed with umbrella sampling in **S** and add them to the training set. This would likely improve the accuracy of the models at **S** and should yield a different temperature dependence of $\Delta F^\ddagger$ than the one seen in Figure 4.3 which could explain the difference in back-conversion barriers for **2** and **3**.

5. Conclusion & outlook

In this chapter the results of this thesis project will firstly be summarized to conclude the main outcome of this study. Secondly, possible improvements to the results and the training of the models will be discussed. Lastly, future opportunities will be discussed.

5.1 Summary & conclusion

In this thesis project ML models for describing the dynamical landscape of **2** and **3** has been developed with the motivation of developing a method to explain why molecules with substitutions in the ortho position of an aromatic substituent have a substantially higher back-conversion barrier. In section 3.1.1 and section 3.1.2 the main process of data generation and model validation was shown for **1** and in section 3.2.1 it was shown that it is possible to train accurate sGDML models which describes either **2N**, **2Q**, **3N** or **3Q**. In section 3.2.2 this result was generalized to create models which can describe **N**, **S**, **Q** and points in between these regions. It was seen that these models had relatively low RMSEs on validation data and that they could, to a good approximation, describe rotational energy landscapes in **N**, **S** and, **Q**, and the MEPs from **N** to **Q**. In section 4.1 it was seen that the models could be used to compute the free energy along the MEPs to investigate the temperature dependence of $\Delta F^\ddagger$ and in section 4.2 it was seen that the models could be used to also compute the free energy rotational energy landscape in **N**, **S**, and **Q**. The prediction of the rotational free energy landscapes at **N** and **Q** seems reasonable however at **S** the models predicted free energies of much smaller amplitude than reasonable. As the models failed to predict the rotational free energy landscape at **S** it was not possible to properly investigate the temperature dependence of $\Delta F^\ddagger$ from the free energy along the MEPs. However, as the models could, to a good approximation, describe the rotational free energy landscape at **N** and **Q** it should be possible to also acquire an accurate description of the rotational free energy landscape at **S** by adding more training data in this state. Furthermore, with an accurate description of the rotational free energy landscape at **S** it should be possible to use the models to properly investigate the temperature dependence of $\Delta F^\ddagger$ for **2** and **3** and explain why **3** has a substantially larger back-conversion barrier. From the discussion above it can be concluded that sGDML can be used to create models which can, to a good approximation, describe the dynamical landscape of **2** and **3**, and that with a sufficient amount of training data it should be possible to use these models to investigate why molecules with substitutions in the ortho position of an aromatic substituent have a substantially higher back-conversion barrier.

5.2 Improvements

An important approximation that was made in this study was the treatment of atomic geometries close to **S** where unrestricted open-shell DFT was used instead of using multi-reference methods as they are much more computationally demanding. Although unrestricted open-shell DFT has been shown to be a viable approximation for **S** it is hard to quantify how viable this approximation is for points which are somewhere between **N**, **S**, and, **Q**. As such points were included in the training set there might exist points in the training set for which this approximation is not viable. Therefore, when performing a more conclusive study one should instead use multi-reference methods to compute the forces and energies. However, if following the same approach regarding data generation as in this thesis project, i.e iteratively adding more data points in regions where the model performs badly, it is reasonable to use unrestricted open-shell DFT while building up the training set and then use the multi-reference calculations on the final training set as they are much more computationally demanding.

A second improvement which can be done is to develop a better method for generating atomic geometries for the training set. The method which was used in this thesis required retraining the model several times, and at each step MD simulations, evaluations of the rotational energy landscapes and/or the MEP had to be made to generate more atomic geometries. This was the most time-consuming process of this thesis project and therefore it would be a drastic improvement if one had an effective method for generating atomic geometries. An example of how such a method could theoretically work is that one could generate a large set of atomic geometries by random displacements of all atoms and then select the most varied subset of N geometries. To quantify the most varied subset one must have a measure which can describe how different the atomic geometries are, i.e some kind of measure which can describe the entropy of the selected dataset. If such a method were available it would be much more straight forward to train the models as one could essentially generate all training data at once, compute energies and forces with electronic structure calculations, and then train the models.

5.3 Future opportunities

In this thesis project two derivatives of norbornadiene were studied and only the electronic ground state was considered. It is however possible to use sGDML for many other purpose by, e.g., training sGDML models to study other kinds of molecules and consider excited states. When training sGDML for other kinds of molecules it is important to consider the size of the molecule, i.e the number of atoms in the molecule. As shown in section 2.3.3 the kernel function is used to construct a square matrix with dimensions $3NM$ with N being the atoms in the molecule and M being the number of training points, thus if the molecule is too large the training of the sGDML models can become infeasible. To train sGDML models for excited states the DFT calculations should be replaced with time dependent density functional

theory calculations which is a method of computing forces and energies for excited states. If one has a cheap method for computing dipole matrix elements it should be possible to compute optical spectra with sGDML by training sGDML models for the electronic ground state and the excited states.

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