

# *Ab Initio* Molecular Dynamics Simulations of Phosphate Hydrolysis Using Neural Network Potentials

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# Foreword

# **Contribution statement**

# Summary

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# **Chapter 1**

## **Introduction**

- 1.1 Role of phosphates in biological systems**
- 1.2 Enzymes involved in phosphate hydrolysis**
- 1.3 Reaction mechanism**
- 1.4 Research goals**



# Chapter 2

## Theory

### 2.1 A brief introduction to statistical mechanics

#### 2.1.1 Classical forcefields and molecular dynamics

#### 2.1.2 The canonical ensemble and free energy calculations

#### 2.1.3 Enhanced sampling techniques

Metadynamics and its well-tempered flavour

Kinetics from metadynamics

### 2.2 Density functional theory

#### 2.2.1 The Kohn-Sham approach

#### 2.2.2 Generalised gradient approximation and PBE functional

#### 2.2.3 *Ab initio* molecular dynamics and GPW method

### 2.3 Extended tight binding

### 2.4 Neural network potentials

#### 2.4.1 Deep neural networks

Multilayer perceptron

Graph neural networks

Message passing neural networks

#### 2.4.2 Invariance and equivariance

#### 2.4.3 Robust Perrinello neural network potentials

# **Chapter 3**

## **Computational Details**

### **3.1 Training dataset generation**

#### **3.1.1 System preparation**

#### **3.1.2 Initial equilibration using the classical forcefields**

#### **3.1.3 xTB based exploration of the configuration space**

#### **3.1.4 Data labeling**

#### **3.1.5 Iterative training of the neural network potential**

First round

Second round

Third round

### **3.2 Production runs at different temperatures**

### **3.3 Validation of the transition states**

### **3.4 Data analysis and visualisation**

## **Chapter 4**

### **Results and Discussion**

## **Chapter 5**

## **Conclusions**

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# **Appendix A**

## **Supplementary information**



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