



USING THE MARKOV MODEL TO STUDY THE CHEMICAL KINETICS OF MAGNESIUM ION IN AQUEOUS SOLUTION



Jaynista Sujai^{1,2} and Dr. Wasut Pornpatcharapong^{1,2,*}

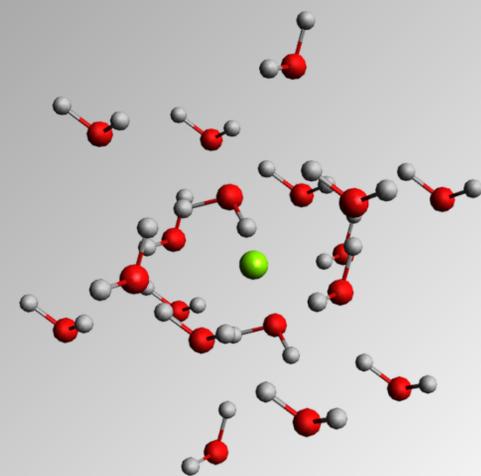
¹ Division of Chemistry, Department of Chemistry, Faculty of Science, Chiangmai University, Chiang Mai, Thailand

² Department of Chemistry, Faculty of Science, Chiang Mai University, Chiang Mai 50200, Thailand

* Wasut.p@cmu.ac.th

ABSTRACT

The kinetics of water exchange around Mg^{2+} ions in aqueous solutions can be elucidated using molecular dynamics (MD) simulations, time-independent component analysis (tICA), and Markov State Modeling (MSM) to explore the underlying mechanisms. Well-Tempered Metadynamics (WT-MTD) simulations were used to sample different states of the system, including Contact Ion Pair (CIP), Transition State (TS), and Solvent-Separated Ion Pair (SSIP). From these, 30 representative structures were selected for tICA, which reduces the complexity of the data and identifies the slowest-changing features. The results show that the slowest motion is mainly determined by the distance between Mg^{2+} and oxygen in water molecules (dMgO), while the second slowest motion is linked to the distance between Mg^{2+} and a randomly chosen water molecule (dMgO,2). MSM provides a more accurate estimate of the timescales for water exchange, showing that these processes take much longer than suggested by tICA alone, as expected for rare and slow events. The Chapman-Kolmogorov (CK) test confirms that the MSM correctly describes the system's behavior over time. This study highlights the effectiveness of combining tICA and MSM to analyze slow molecular processes and identify key factors in ion exchange dynamics. The approach provides a strong foundation for future research on ion solvation, ligand exchange reactions, and other rare events in chemical and biological systems.



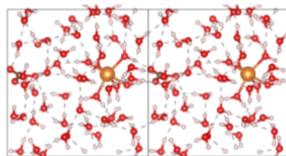
First and Second solvation shells

HIGHLIGHTS

- Identification of the slowest water exchange motions using tICA.
- Markov State Model provides accurate timescales for ion-water exchange.
- CK test confirms MSM validity in modeling rare events.

INTRODUCTION

Magnesium ions (Mg^{2+}) play a fundamental role in various chemical and biological processes, particularly in aqueous environments where they exhibit strong solvation interactions. Understanding the mechanisms of Mg^{2+} hydration and ligand exchange dynamics is crucial for applications in biochemistry, environmental chemistry, and materials science. In aqueous solutions, Mg^{2+} forms a stable octahedral coordination complex, $[Mg(H_2O)_6]^{2+}$, due to its high charge density and strong electrostatic interactions with water molecules. Experimental techniques such as terahertz spectroscopy and X-ray analysis provide insights into exchange kinetics but are limited by cost and complexity. Computational methods, including ab initio and classical MD simulations, offer alternative approaches. MSM, in combination with tICA, allows for the identification of key reaction coordinates and improved kinetic modeling.



PROJECT OBJECTIVE

The goal of this study is to employ MSM and tICA to investigate the slowest molecular processes governing Mg^{2+} -water exchange dynamics and determine the relevant kinetic parameters.

COMPUTATIONAL METHODOLOGY

System Setup:

- a single Mg^{2+} ion in 629 TIP3P water molecules, simulated in a cubic box of dimensions $2.7 \times 2.7 \times 2.7 \text{ nm}^3$ using OpenMM.
- Simulation Parameters: NVT ensemble, 300 K temperature, Langevin dynamics, and a timestep of 2 fs

Main Tools:



Enhanced Sampling via Well-Tempered Metadynamics (WT-MTD):

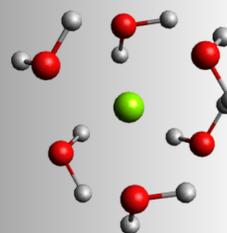
- WT-MTD simulations were run for 40 ns with Gaussian biases deposited every 1,000 steps. The collective variable was defined as the Mg^{2+} -oxygen distance (dMgO).
- The Gaussian width was set to 0.01 nm, and the initial bias height was 1.6 kJ/mol with a bias factor of 20.

specific Tools:



30 Frame Selection Process for tICA & MSM Construction :

Contact Ion Pair (CIP), Transition State (TS), and Solvent-Separated Ion Pair (SSIP).



First solvation shell



Data Analysis:

Time-Independent Component Analysis (tICA)

- Trajectory Processing: Handled using mdTraj package.
- tICA Analysis Performed Using: PyEMMA software.

Clustering & MSM Construction

- KMeans clustering was applied to group the MD simulation frames into 100 microstates based on the tICA projection.
- Chapman-Kolmogorov (CK) test was performed to check the Markovian property.

specific Tools:



RESULTS AND DISCUSSION

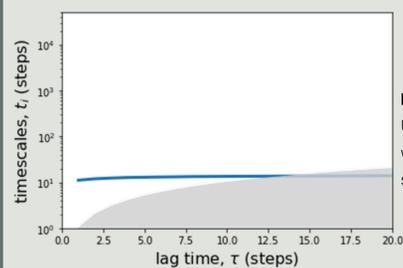


Figure 1: Underlying motions of the water exchange process separated using tICA.

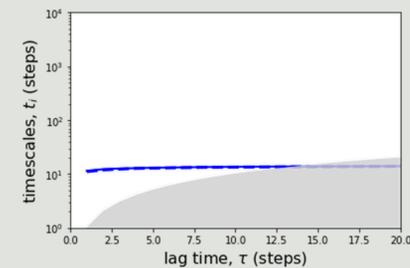


Figure 3: Implied timescale from performing MSM on the system, where the slowest motion has several orders of magnitude higher implied timescale than obtained from tICA.

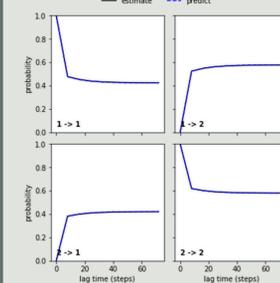


Figure 2: Chapman - Kolmogorov (CK) test to test the Markovianity of the dynamics for a two-state process. The agreement between predicted and estimate probabilities enables constructing MSM for the process. Nevertheless, the probability suggests inadequate rare event sampling.

CONCLUSIONS

This study successfully applied tICA and MSM to investigate water exchange dynamics around Mg^{2+} ions. The analysis revealed that MSM provides a more accurate estimate of slow timescales than tICA alone. The CK test confirmed the Markovian nature of the constructed model. These results highlight the effectiveness of combining tICA and MSM for studying rare molecular events and provide a strong computational framework for analyzing slow dynamical processes in aqueous systems. Future work should focus on improving transition state sampling to enhance kinetic modeling accuracy.

ACKNOWLEDGEMENTS

This research was supported by the Faculty of Science, Chiang Mai University. The authors thank their research colleagues for valuable contributions.

REFERENCES

- Boyn, J-N. and Carter, E. A. Characterizing the Mechanisms of Ca and Mg Carbonate Ion-Pair Formation with Multi-Level Molecular Dynamics/Quantum Mechanics Simulations. *J. Phys. Chem. B*, 2023, 127, 10824-10832.
- Ghorbani, B.; Brooks B. R. and Klaua J. B. Conformational Fluctuations in β 2-Microglobulin Using Markov State Modeling and Molecular Dynamics. *J. Phys. Chem. B* 2023, 127, 6887-6895.