Molecular Dynamics Investigation of the Role of Mg^{2+} in Nonenzymatic RNA Self-Replication

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The nonenzymatic self-replication of RNA is a key concept in origin-of-life research, yet the molecular details of how this process occurs are still not fully understood [1]. In particular, divalent metal ions such as Mg^{2+} play an essential catalytic role in promoting phosphodiester bond formation [2]. In this study, we present a computational investigation of RNA primer extension with imidazole-activated nucleotides, with special attention to how Mg^{2+} ions affect the structural dynamics of different dinucleotide intermediates. By combining molecular dynamics (MD) simulations with quantum mechanics/molecular mechanics (QM/MM) approaches, we examine how Mg^{2+} coordinates with RNA to stabilize reactive conformations and facilitate bond formation. Our simulations are designed to clarify how Mg^{2+} helps maintain conformations that favor bond formation under enzyme-free conditions. Overall, these findings offer new molecular-level insights into the role of metal ions in RNA chemistry and deepen our understanding of RNA's potential for self-replication in prebiotic environments.

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[2]Mittal, S.; Nisler C., and Szostak, J.W. Biophysical Journal, **2024**, 123.12, 1579 – 1591. https://doi.org/10.1016/j.bpj.2024.04.032