Molecular Insights into NMR Relaxation of Gd(III)-based Contrast Agents for MRI Applications

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In Magnetic Resonance Imaging (MRI), the Nuclear Magnetic Resonance (NMR) relaxation of protons in water is used to probe the state of bodily tissues. These images are enhanced by Gadolinium-based contrast agents (GBCAs) that act by reducing the water proton relaxation time. However, despite the long history of NMR, the molecular-scale processes in MRI remain poorly understood; the modeling and interpretation of the physics of relaxation still rely on severe assumptions. MRI is successful because different tissues present different relaxation times due to variation in the physical and chemical environment; however, there is little understanding of the effects of nano-confinement, temperature, presence of osmolytes, electrolytes, and dissolved oxygen. In this work, we employ quantum and molecular simulations to investigate the effect of temperature and osmolytes concentration on the NMR relaxation of gadolinium(III)-aqua complex and other complexes of such paramagnetic ions. Our simulation results are corroborated and validated by NMR relaxation dispersion measurements. Our investigations show that both temperature and osmolytes concentration can greatly influence the NMR relaxation of gadolinium(III) complexes. Further, we will discuss how the NMR relaxation signal can be decomposed into contributions from "molecular modes," a technique that can prove powerful in providing a physical interpretation of the phenomena and building a library of signals to interpret NMR and MRI signals in otherwise hard to analyze environments.