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Characterizing nitric oxide diffusion in a nitrite reductase:nitric oxide reductase complex

Nitrite reductase (NiR) and Nitric oxide reductase (NOR) are two important enzymes in the microbial denitrification. This process sequentially reduces nitrogen-containing compounds: $\text{NO}_3^- \rightarrow \text{NO}_2^- \rightarrow \text{NO} \rightarrow \text{N}_2\text{O} \rightarrow \text{N}_2$ [1]. In this process, NiR produces nitric oxide (NO) from nitrite while NOR catalyzes the reaction using NO as a substrate. While NO is regarded as an important integral signaling molecule in eukaryotes and bacteria[2,3], it is also highly cytotoxic and reactive. How NO molecules can diffuse from periplasmic NiR into water and membrane, and from membrane to membrane-bound NOR remains a question. This is intriguing that almost no NO is detected in the membrane, suggesting an effective NO decomposition system in denitrification[4]. In this study, we characterize NO diffusion in this complex system using molecular dynamics (MD) simulations. We carried out multiple 100-ns independent simulations with a system consisting of NiR, NOR, NO, membrane, water, and counterions. We have found that the NO molecules released from the active site of NiR are able to diffuse out of NiR and enter into the membrane via water. Some NO molecules even reached the active site of NOR within 100 ns simulation timescale. Such rapid NO migration inside and between proteins provides a novel insight into how NiR and NOR functionally regulate and direct NO into the designated region inside protein.

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