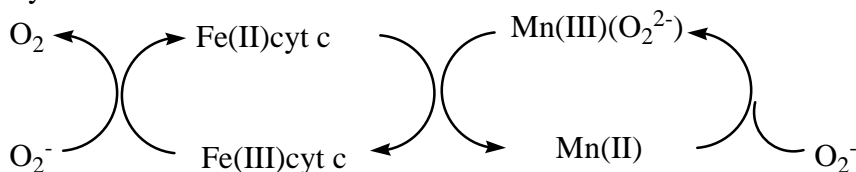


# Ionic $\text{Mn}^{2+}$ is not a Superoxide Dismutase

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Earlier studies have shown that  $\text{Mn}^{2+}$  ions and some simple chelated  $\text{Mn}^{2+}$  compounds possess an apparent superoxide dismutase (SOD)-like activity. These studies used indirect SOD activity assays that follow the rate of reduction of cytochrome c. However, those results are in conflict with results obtained using pulse radiolysis, a direct SOD activity assays which uses a higher concentration of superoxide than indirect methods. The pulse radiolysis studies have demonstrated that  $\text{Mn}^{2+}$  reacts with superoxide in a stoichiometric fashion and does not have significant SOD activity. We have repeated the cytochrome c experiments using superoxide produced enzymatically (with xanthine oxidase + xanthine) or produced through high-energy gamma particles (Co-60/formate) and confirmed the apparent SOD-like activity. In order to resolve the apparent contradiction between the indirect and direct assays, we investigated further the reaction of superoxide with cytochrome c in the presence of  $\text{Mn}^{2+}$ . We find that superoxide oxidizes ferrocytochrome c in the presence of  $\text{Mn}^{2+}$ . This reaction does not occur in the absence of  $\text{Mn}^{2+}$  and is quenched by the addition of metal ion chelators such as DTPA. Since the indirect SOD assay is based upon observation of inhibition of the rate of reduction of ferricytochrome c by superoxide, the manganese-mediated re-oxidation of ferrocytochrome c makes the assay unsuitable for this system:



Our results suggest that  $\text{Mn}^{2+}$  reacts with superoxide to form an intermediate, possibly a Mn(III) peroxo complex, that oxidizes ferrocytochrome c to give ferricytochrome c. This intermediate may play a role in the antioxidant effects of high levels of ionic manganese observed for some prokaryotes.