

P020 Effects of high pressure on morphinone reductase studied by computational methods

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Morphinone reductase (MR) catalyses hydride transfer between the FMN and NAD cofactors by H-tunnelling. Experimental studies using the pressure dependence of kinetic isotope effects as a probe for hydrogen tunnelling suggested that an increase in pressure from 1 bar to 2 kbar would cause a decrease in the tunnelling distance by approximately 0.7 Å. We have performed molecular dynamics simulations to probe the nature of the structural changes in MR as the pressure is increased - simulations were run for 10 ns at five different pressures: 1 bar, 500 bar, 1 kbar, 1.5 kbar and 2 kbar. The simulations show that the protein is stable over this range of pressures. The overall secondary structure does not change as the pressure is increased, except for a slight increase in the helical content. Trajectory analysis shows a decrease in the average distance between the donor and acceptor atoms of 0.24 Å as the pressure is increased from 1 bar to 2 kbar - consistent with the picture emerging from experiment. This work also provides a platform for furthering our understanding of protein dynamics in driving hydrogen tunnelling.