

# **Mechanism of Facilitated Diffusion during DNA Search in Crowded Environments - Supporting Information**

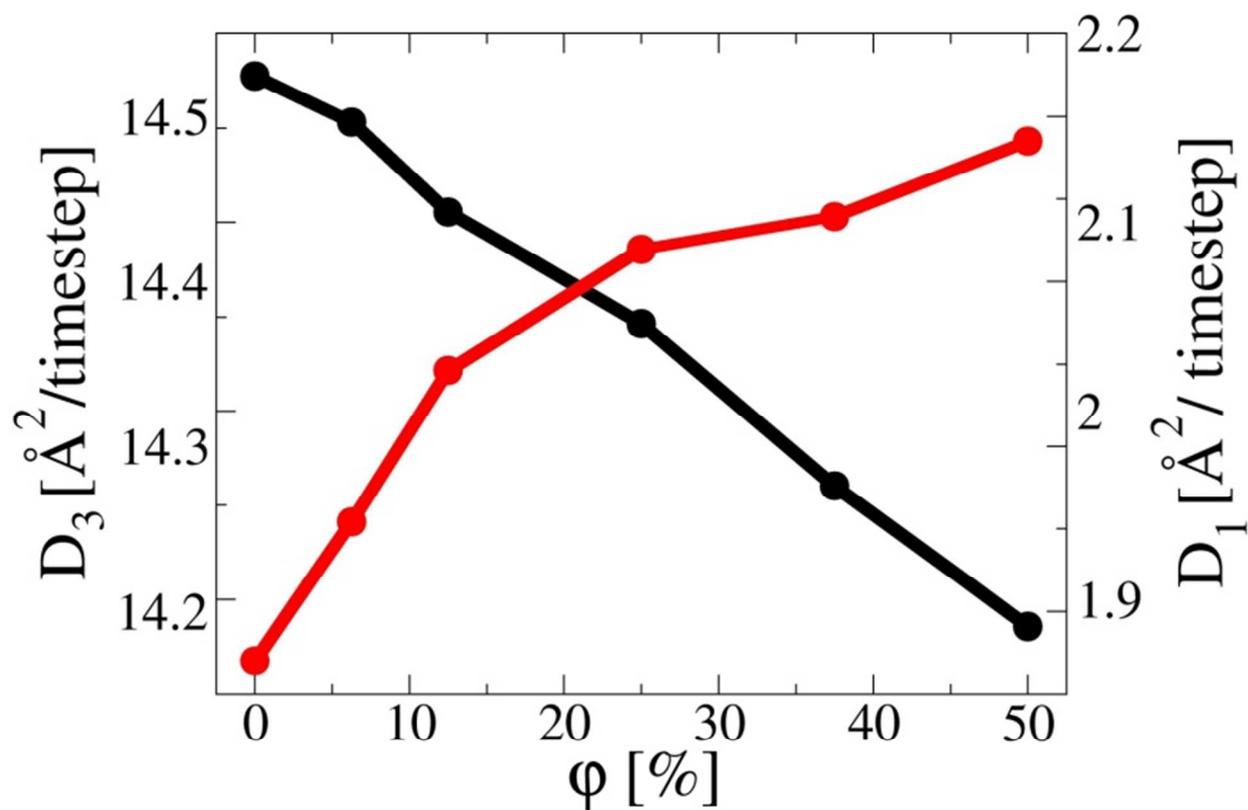
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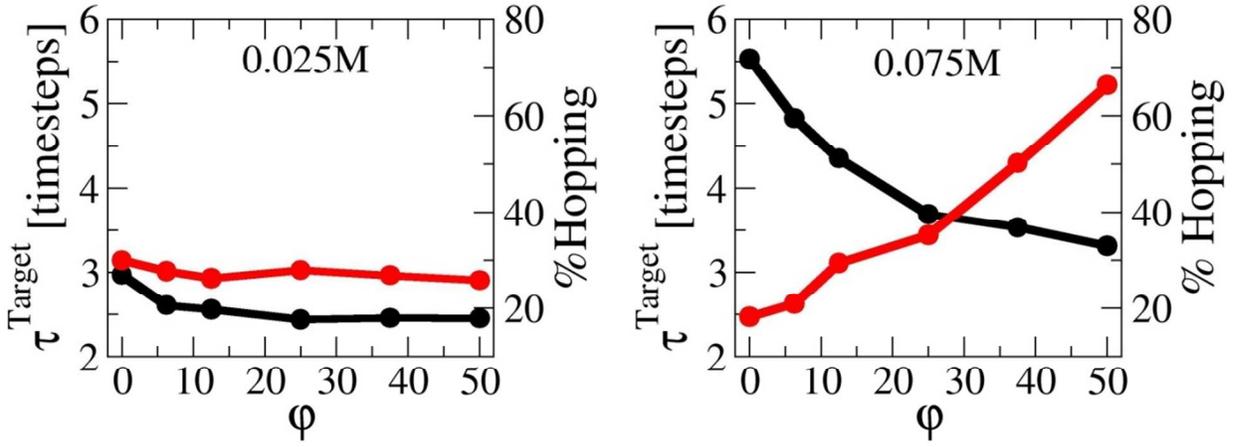
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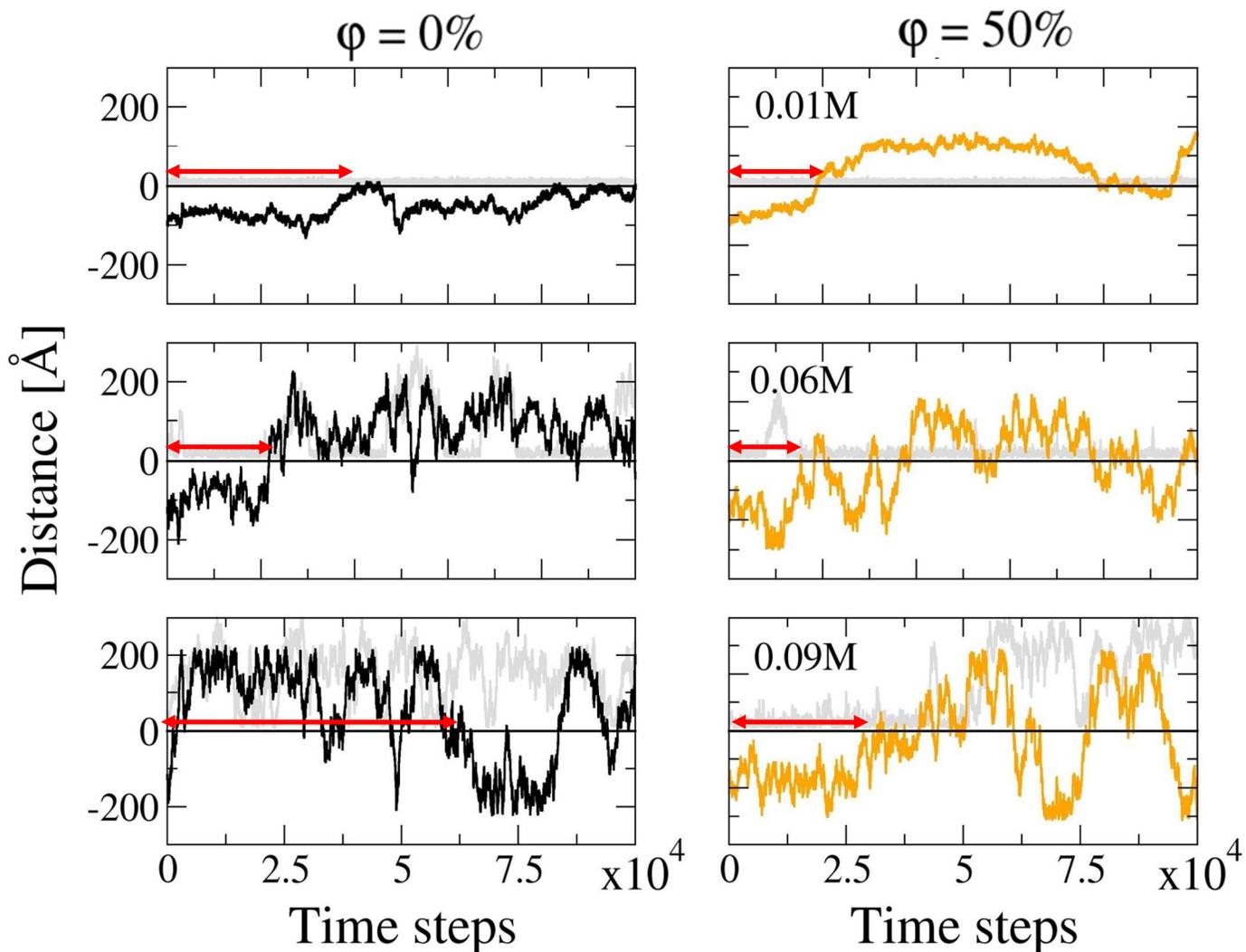
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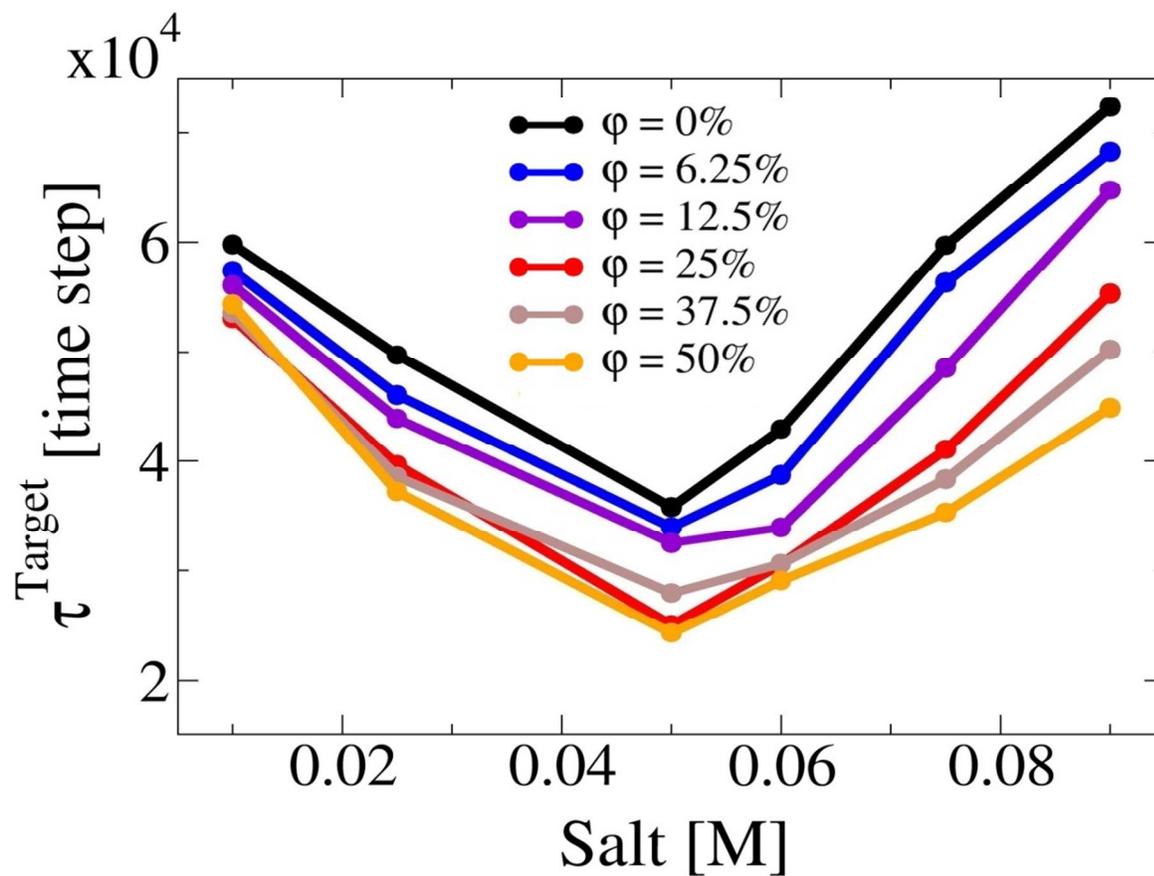
**Figure S1.** The values of the 1D and 3D diffusion coefficient ( $D_1$  in red and  $D_3$  in black) as a function of the fractional volume of the crowding molecules. These values were taken from Figures 2B and 2D.



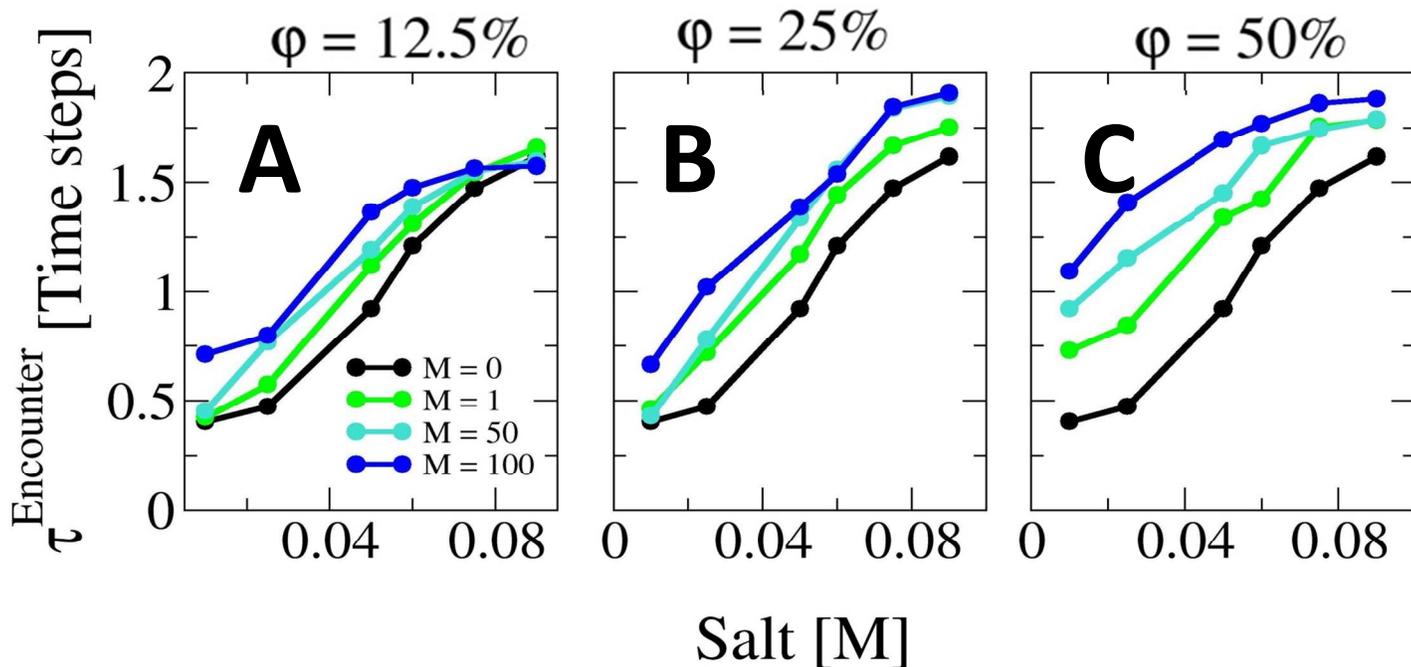
**Figure S2.**  $\tau^{\text{Target}}$  (black) and hopping (red) at different fractional volume. The values correspond to plot 2A and 3A.



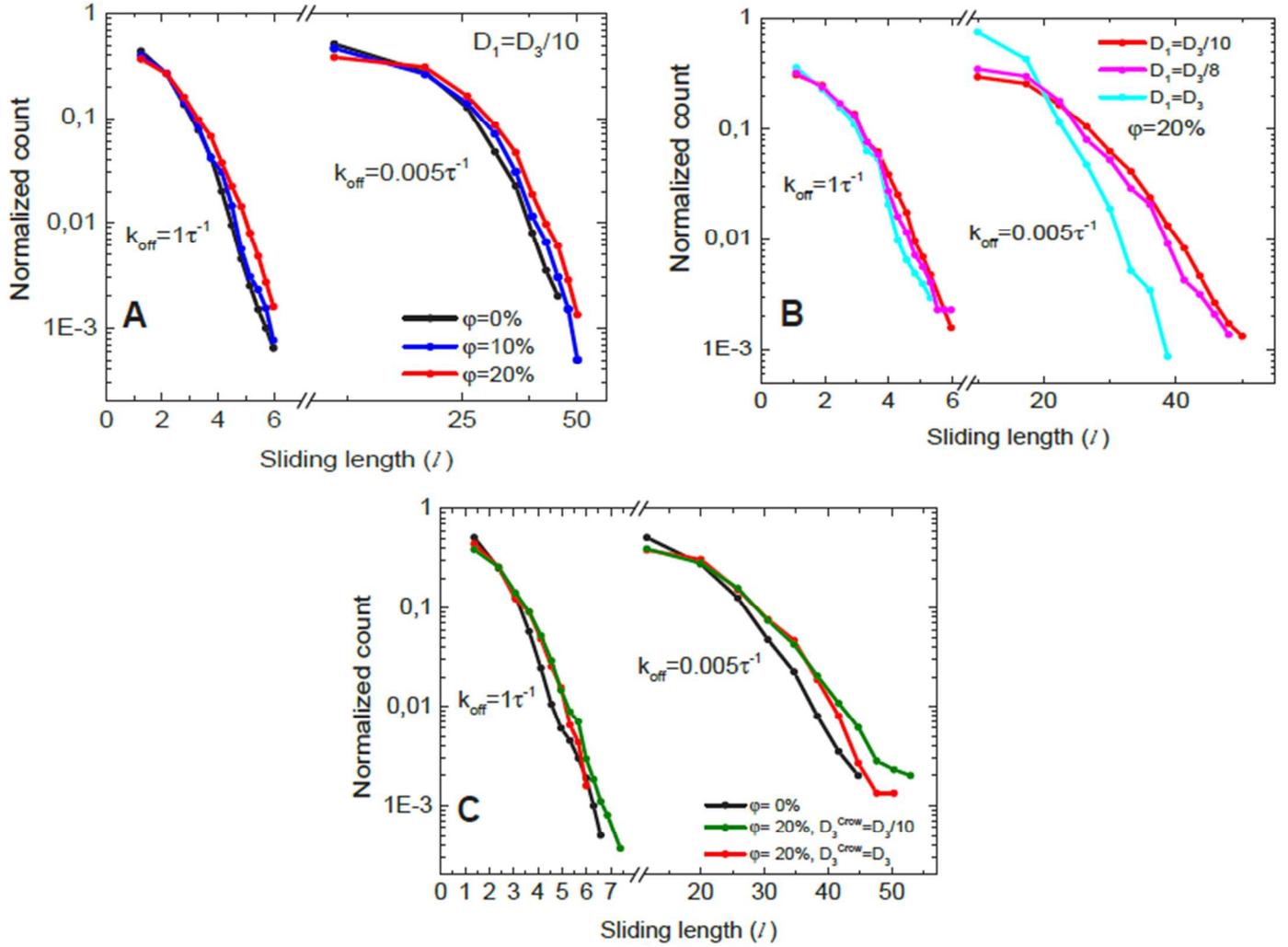
**Figure S3.** Raw trajectories data of the displacement of the protein during  $10^5$  time steps along the DNA axis under salt concentrations of 0.01M (upper panels), 0.06M (middle panels) and 0.09M (lower panels) at  $\phi=0\%$  (left panels, black lines) and  $\phi=50\%$  (right panels, orange lines). At each trajectory, Protein displacement from DNA axis is shown as grey lines. At each trajectory red arrow represents the value of  $\tau^{\text{Target}}$ . Corresponding to Fig. 3A in the main text,  $\tau^{\text{Target}}$  decreases with increasing fractional volume,  $\phi$ , for all three salt concentrations.



**Figure S4.** The effect of molecular crowding (modeled as  $\phi$ , the fractional volume) on  $\tau^{\text{Target}}$ , when placing the protein far from the DNA, at different salt concentrations. Although this results in higher values of  $\tau^{\text{Target}}$ , the overall shape resembles that of Fig. 3A in main text, with  $\tau^{\text{Target}}$  decreasing with increasing fractional volume,  $\phi$ , for all salt concentrations.



**Figure S5.** The effect of molecular crowding mass on  $\tau^{\text{Encounter}}$  when placing the protein far from the DNA at fractional volumes of  $\phi=12.5\%$  (left panel),  $\phi=25\%$  (middle panel) and  $\phi=50\%$  (right panel), as a function of salt concentrations. Corresponding to Fig. 4A in main text, the slow movement of crowders induces the effect of confinement, resulting in the increase of  $\tau^{\text{Encounter}}$  with increasing fractional volume,  $\phi$ , for all salt concentrations.



**Figure S6.** Sliding length distributions of the DBP along the DNA for various values of  $k_{\text{off}}$ ,  $D_1$  and  $\phi$ . A) As molecular crowding increases, DBP-DNA binding is enhanced and the sliding length distributions shift towards larger values. B) As the 1D diffusion constant increases, the distributions get narrow around a smaller value of sliding length, because scanning of lattice sites become faster. C) In addition to the enhancement of DBP-DNA binding by crowding, heavy crowdors increase the effect. Sliding length distributions shift towards higher values. We note that despite the enhancement in DBP-DNA binding, the strong effects that heavy crowdors have on 3D diffusion make that the average finding time drastically increases (Fig. 5B main text). All data shown here correspond to  $\phi = 20\%$ .