Supplementary Information: Probing the Modulation in Facilitated Diffusion Guided by DNA-Protein Interactions in Target Search Processes

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SI-A. Impact of Relative Dynamics of Protein and DNA:

The impact of the individual dynamics of the protein and DNA on the target search process is explicitly captured in our computational study where we provide a comparative analysis on the search rate k with ε_{ns}, for the target placed on a rigid DNA, considering i) where we fix the mass to all particles (including the DNA beads and also the protein), $m = 1$, with another situation ii) where we changed the protein particle mass as, $m = 3$, however everything else remains the same as before. This analysis has been depicted in Fig. S1. The k profiles in Fig. S1 suggest that, as the mass of the protein particle increases, it slows down the diffusive motion and hence affects the rate of target search by lowering the value of k vs ε_{ns} in Fig. S1. However, despite the difference in the mass of the searcher protein in these two cases, it is noteworthy that the overall trend remains the same, as expected for the rigid DNA case, indicating a similar underlying target search strategy in both cases. Thus, this comparative analysis depicts the effect of modulation in target search kinetics, specifically due to the change in protein dynamics, without affecting the dynamics of DNA beads.

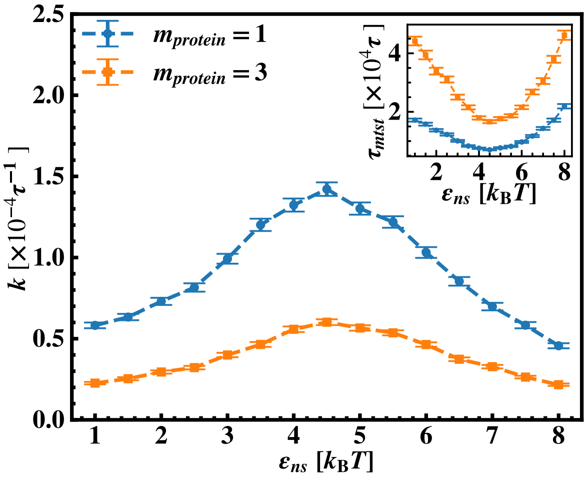

Figure S1: The target search rate, k, is plotted as a function of non-specific interaction strength, ε_{ns}, when the mass of the protein, $m_{protein} = 1$ (blue '–●–' line), and $m_{protein} = 3$ (orange '–■–' line) and for rigid DNA with the target is at the center.

Continuing with the same background in another investigation involving the rigid

DNA chain with the target positioned at the center, the rate profile of target search has been computed and graphically represented in Fig. S2 for DNA with two different contour lengths: $L = 101$ (blue dashed line) and $L = 201$ (orange dashed line). It is evident from the figure that as the length of the DNA strand increases, there is a corresponding decrease in the target search rate, k, highlighting the impact of the system size effect of the DNA protein chain. Despite the change in DNA length, the rate profiles exhibit similar trends, suggesting that the underlying dynamics remain unchanged in both scenarios.

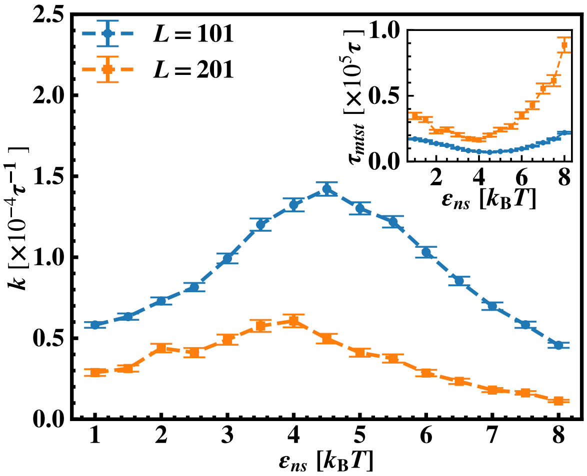

Figure S2: The target search rate, k, is plotted as a function of non-specific interaction strength, ε_{ns}, when the target is at the center and is spatially fixed and DNA is rigid with a contour length of $L = 101$ (blue '$-\bullet-$' line), and $L = 201$ (orange '$-\blacksquare-$' line)

SI-B. Target Search Dynamics with Semiflexible DNA:

To investigate the impact of flexibility on k vs ε_{ns}, we conduct additional computations including an extra potential energy term that accounts for the bending rigidity between the individual bond vectors in the DNA that considers a semiflexible chain of DNA. Thus, we have incorporated the following additional expression for the bending potential energy[1,2], in which all the monomeric beads in the DNA interact, with $U^{int} = U^{\text{WCA}} + U^{\text{FENE}} + U^b$ where, $U^b = K[1 + \cos(\theta)]$, and K is the bending energy. Considering $K = 20$, θ is the angle between two adjacent bonds (denoting persistence length as $l_p = 20\sigma$ in the DNA chain inducing semiflexible property) along with the usual potential energy as indicated. Thus, Fig. S3, summarizes the k vs ε_{ns} considering a semi-flexible DNA chain along with the comparative analysis with a rigid and a fully flexible chain of DNA, as obtained before. The primary computational data obtained following this additional inclusion of the potential indicates that the rate profile of the search process with the target placed at the center of a DNA as a semi-flexible chain, falls in between the profiles of the target placed at the center of a DNA for the flexible DNA and rigid DNA cases. Thus, the k vs. ε_{ns} profile obtained for a semiflexible DNA case shows simultaneous similarity with the profiles of the rigid and the flexible cases, such as, indicating an initial increase in the k profile at the lower values of ε_{ns} and consequently decreasing at the higher values of ε_{ns} similar to a rigid DNA case, while also revealing a flat saturated maximum of k after the initial increase with ε_{ns} (Fig. S3), as it is observed for the flexible DNA case. Thus, this

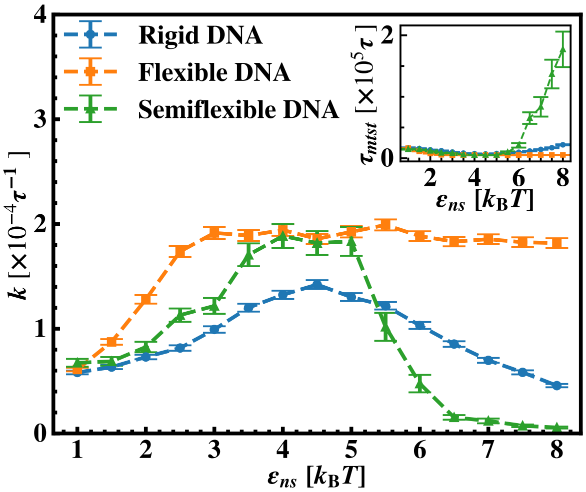

Figure S3: The target search rate, k, is plotted as a function of non-specific interaction strength, ε_{ns}, when the target is at center and is spatially fixed and DNA is rigid (blue '$-\bullet-$' line), fully flexible (orange '$-\blacksquare-$' line) and semiflexible (green '$-\blacktriangle-$' line).

interesting feature illustrates that, as the flexibility of the DNA backbone is gradually increased by tuning the bending energy K in the above expression, the trend in k can be made to transform from a rigid to a flexible chain k profile. Thus, on lowering the rigidity of the backbone, the inverted 'v' shape of k vs ε_{ns} profile obtained for the rigid DNA case gradually starts to show a flatter and flatter k profile at intermediate values of ε_{ns} indicating characteristic features of a semiflexible chain. Finally, on further reduction on the rigidity of the DNA backbone, the k profile merges to a saturated maxima for intermediate to large values of ε_{ns} followed by an initial increase at the early values of ε_{ns}, resembling the characteristics of a fully flexible chain. Thus, this observation once again signifies the importance of chain dynamics in modulating the mechanistic details of the target search event.

References

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[2] O. Kratky and G. Porod, *Recueil des Travaux Chimiques des Pays-Bas*, 1949, **68**, 1106–1122.