Supporting Information

Multiple Binding Configurations of Fis Protein Pairs on DNA: Facilitated Dissociation versus Cooperative Dissociation

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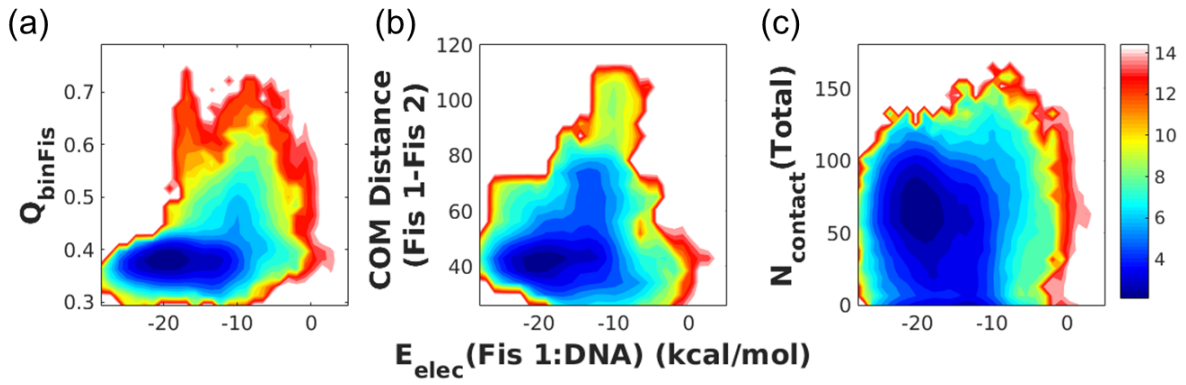

Figure S1. Free energy surfaces as a function of several of trial collective coordinates are shown. (a) Q value of the binary-Fis configuration (Q_{binFis}) (b) Center-of-mass distance between Fis1 and Fis2 on the DNA (c) The total number of protein contacts ($N_{contact}$).

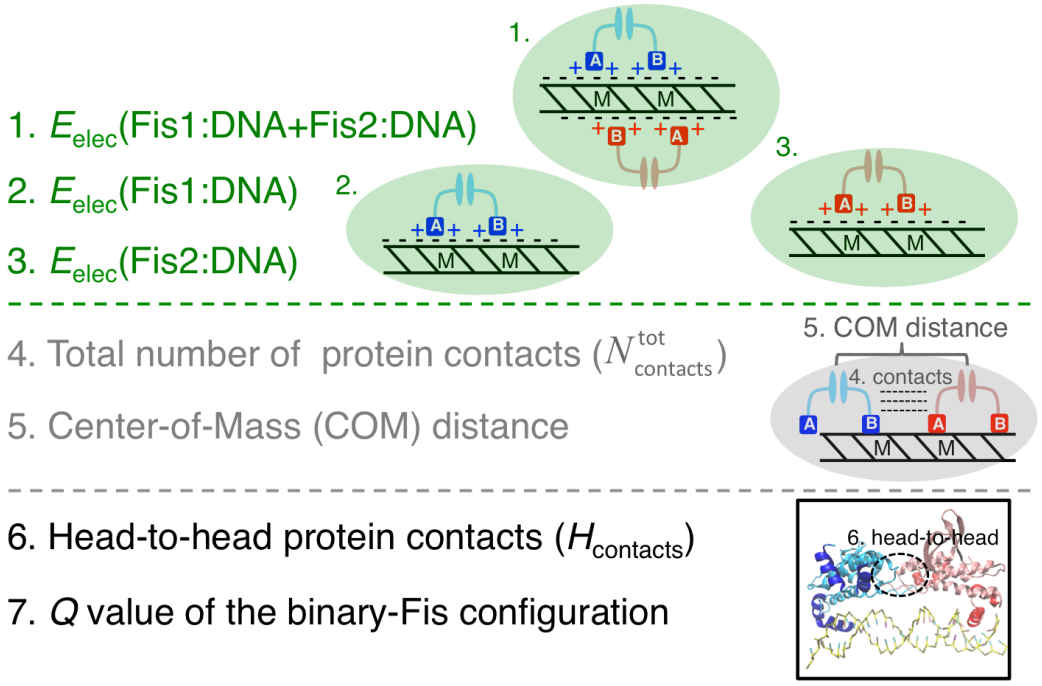

Figure S2. The trial collective basis variables that are used in the principal component analysis. These collective variables are grouped. (*Top*) Items 1-3 (in green) describe the electrostatic interactions between the protein and DNA. (*Middle*) Items 4-5 (in gray) describe physical protein contacts and geometric position between proteins on DNA. (*Bottom*) Items 6-7 describe structural specificity that distinguishes several of the particular protein quaternary structures from each other.

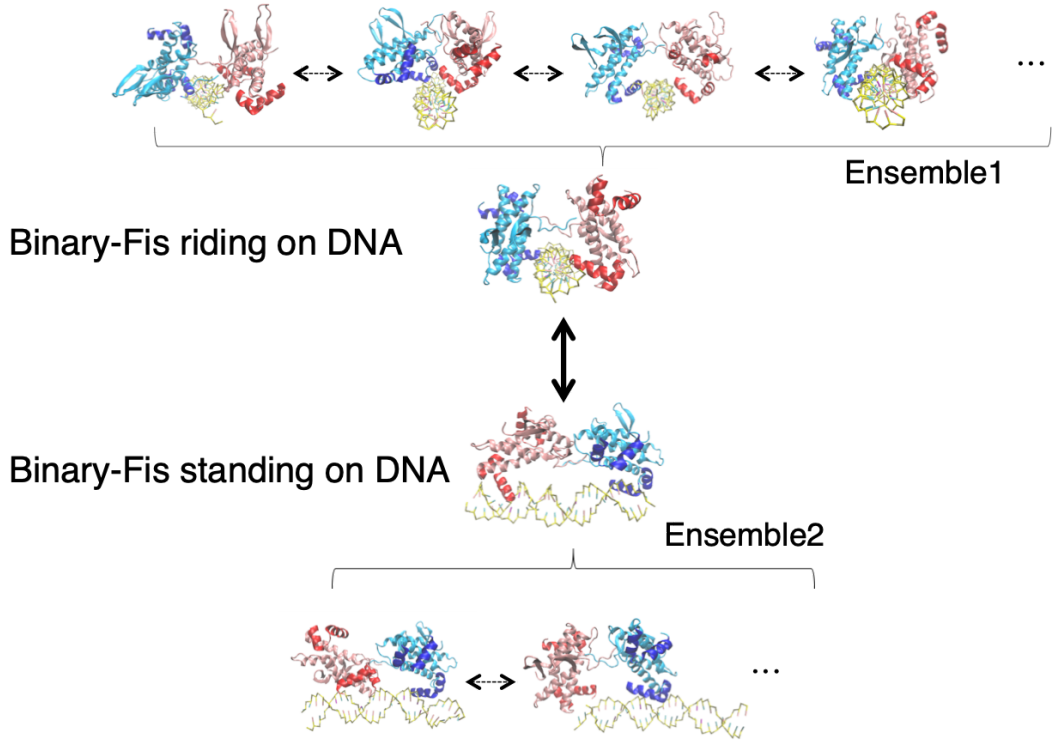

Figure S3. The structural ensemble of the binary-Fis configuration and their mutual dynamic switching are schematically shown.

The structural ensemble of the binary-Fis configuration on DNA contains two major categories of orientation: riding and standing. The binary-Fis structure can dynamically switch between the two distinct orientations by sliding along the DNA, denoted by a *black-thick* line with double arrows. In each of the categories, the structure of the protein-DNA ternary assemblies also shows multiple configurations. The *dashed-thin* lines with double arrows within individual ensemble 1 and 2 describe dynamic switching between each other. Note that only some example structures are shown.

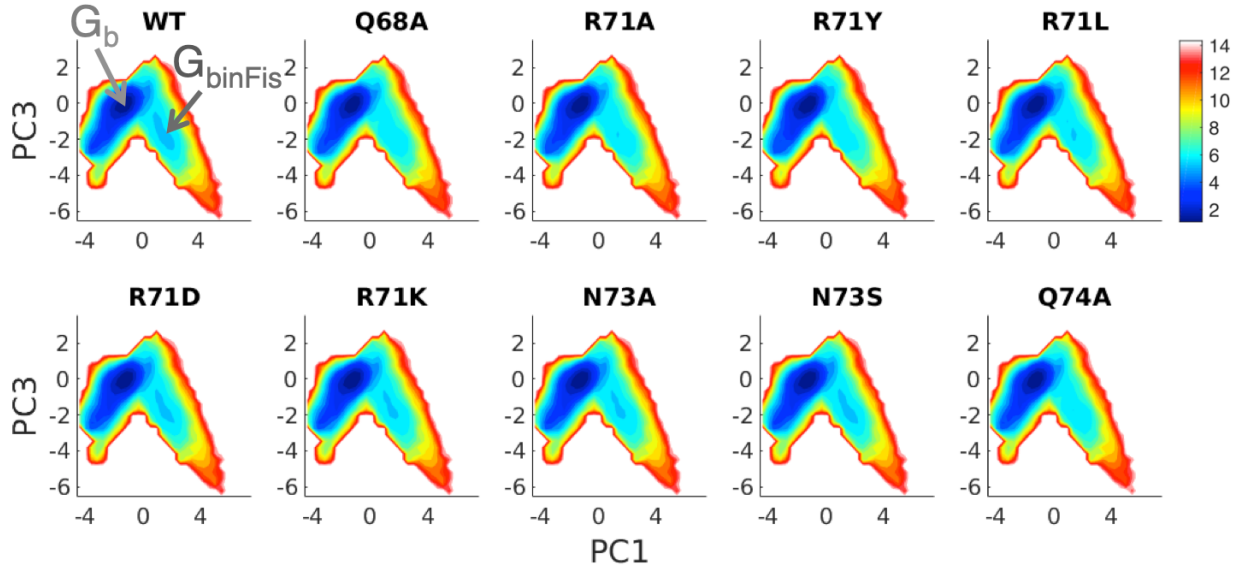

Figure S4. A free energy surface survey (free energy projected onto PC3-PC1) over a range of Fis mutants for the stability change of the binary-Fis molecular dyad is shown.

The free energy of the binary-Fis molecular dyad (G_{binFis}, shown in *dark gray*) is calculated with respect to the bound state (G_b, shown in *light gray*). One can thus calculate the free energy change $\Delta G_{WT} = G_{binFis} - G_b$; Similarly for all of the mutants $\Delta G_{binFis}(mut) = G_{binFis}(mut) - G_b$. The $\Delta\Delta G_{binFis}(mut)$ is then calculated according to $\Delta\Delta G_{binFis}(mut) = \Delta G_{binFis}(mut) - \Delta G_{WT}$.

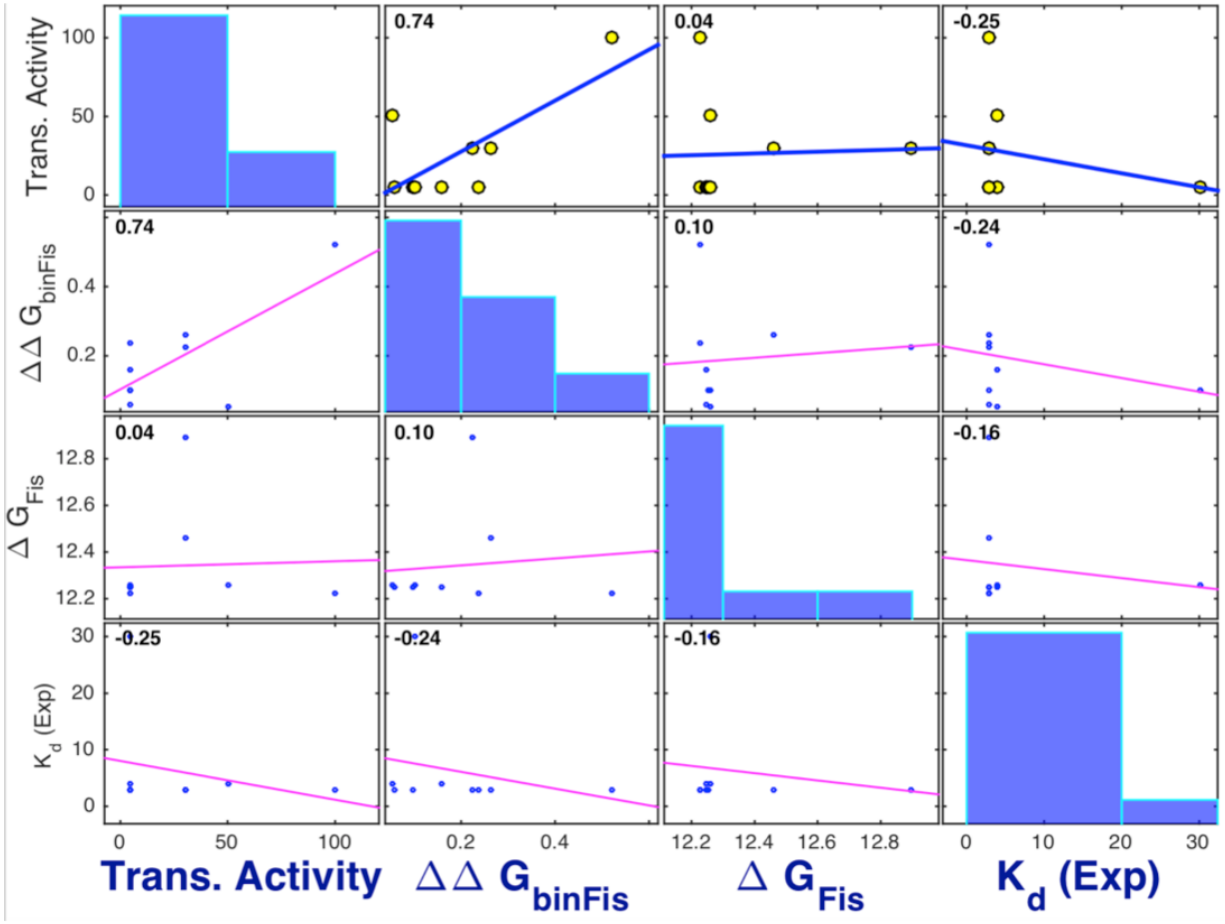

Figure S5. The correlation plot of the Fis transcription activity in relation to different thermodynamic properties due to mutation effects is shown.

Several of the thermodynamic properties such as ΔG_{Fis}(mut), $\Delta\Delta G_{binFis}$(mut), and experimental K_d (dissociation constant[1]) of the mutants are cross-correlated along with their corresponding transcription activity and are compared on the correlation matrix plot (using *corrplot* function in Matlab). The diagonal panels describe the distribution of individual datasets while the off-diagonal panels show the correlation plots of each pair of the variables. Note that $\Delta\Delta G_{binFis}$(mut) = ΔG_{binFis}(mut) - ΔG_{WT} and that ΔG_{Fis} denotes the simulated free energy of dissociation of Fis from DNA. The number shown on the *top-left* of each panel represents the correlation coefficient ($\rho_{X,Y}$). The Fis transcription activity shows a moderate correlation with $\Delta\Delta G_{binFis}$ (with $\rho_{X,Y}$=0.74).

References

(1) Cheng, Y. S.; Yang, W. Z.; Johnson, R. C.; Yuan, H. S. Structural Analysis of the Transcriptional Activation Region on Fis: Crystal Structures of Six Fis Mutants with Different Activation Properties. *J. Mol. Biol.* **2000**, *302* (5), 1139–1151.