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Figures and figure supplements

Encounter complexes and dimensionality reduction in protein–protein association

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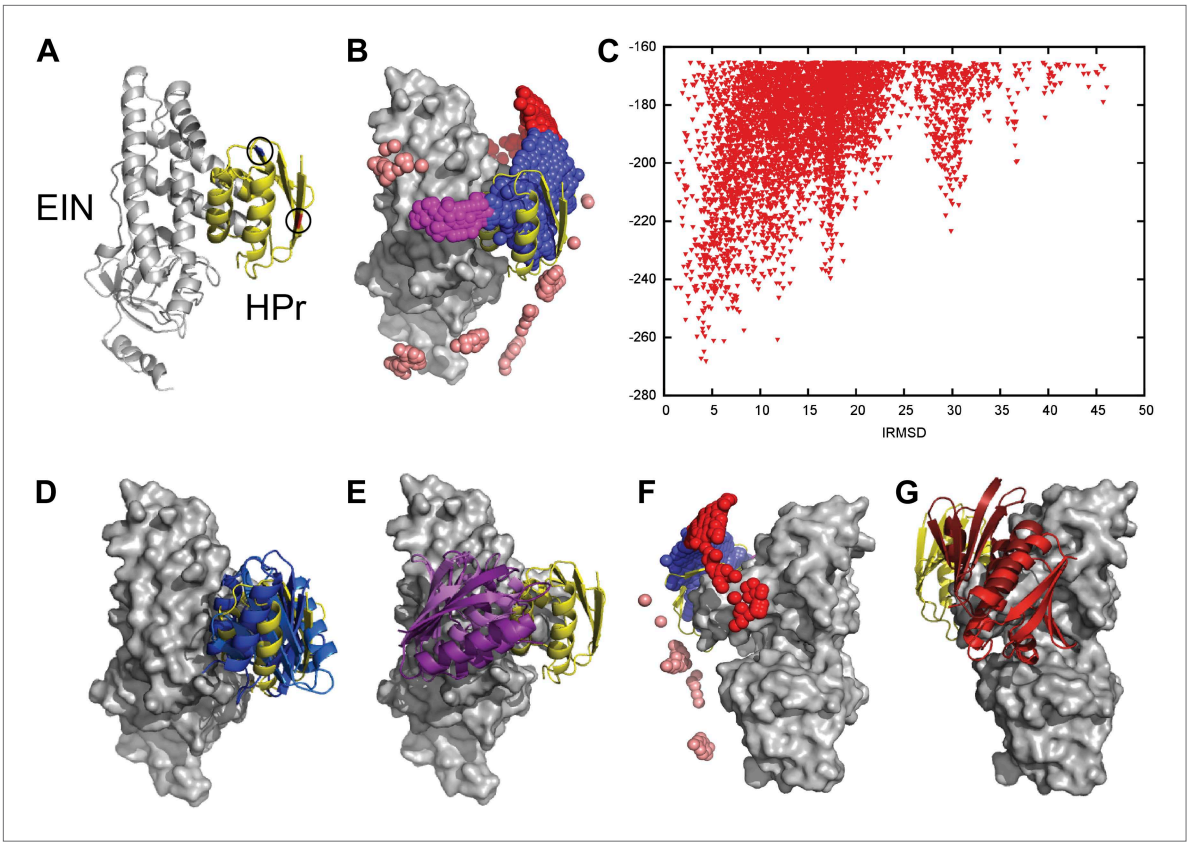

Figure 1. Docking results for the EIN–HPr complex. Unbound structures were used both for the receptor, EIN (chain A from PDB entry 1ZYM) and for the ligand, HPr (chain P from PDB entry 2JEL). Encounter complexes were generated using Fast Fourier transform (FFT) based sampling. (**A**) Cartoon of the specific complex formed by EIN and HPr, shown in grey and yellow, respectively. The locations of the paramagnetic tags E5C-EDTA-Mn^{+} and E32C-EDTA-Mn^{2+} on HPr are encircled and are shown in red and blue, respectively. (**B**) Centers of HPr structures in the encounter complex ensemble. Colors indicate classification as follows (*8*): blue, Class I (i.e., overlapping with the specific complex); magenta, patch 1 of Class II (i.e., non-overlapping) positions; red, patch 2 of Class II positions; and pink, additional Class II position outside the main patches. (**C**) Ligand IRMSD vs PIPER energy score. (**D**) Two representative HPr poses, colored light blue and dark blue, from Class I. (**E**) Two representative HPr poses (in different shades of magenta) from Patch 1 of Class II. (**F**) View of the EIN–HPr complex and the centers of HPr poses after rotating 180° around the vertical axis (the bound HPr is now on the left side, almost completely hidden by EIN). (**G**) Representative HPr poses (in different shades of red) from Patch 2 of Class II, shown in the rotated view.
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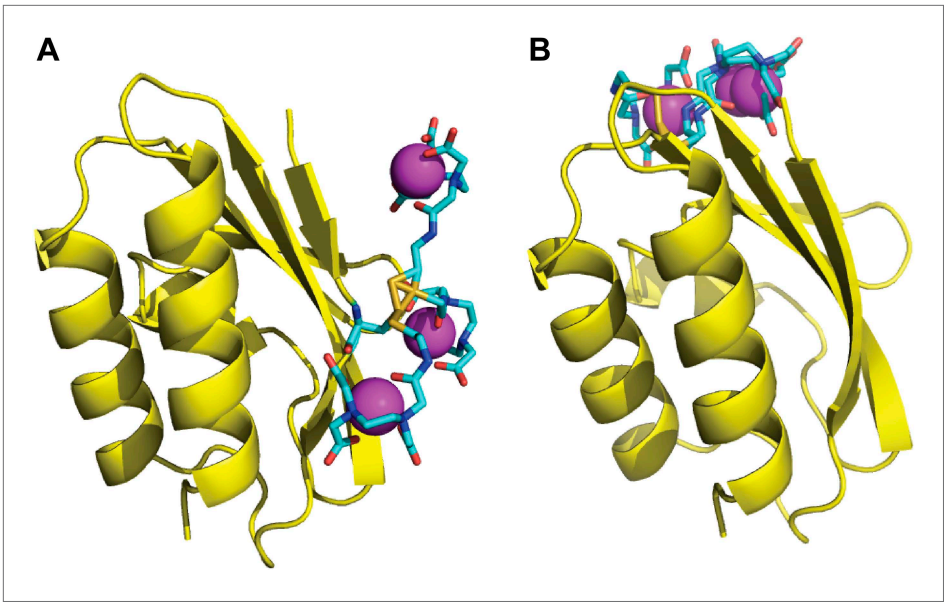

Figure 1—figure supplement 1. Rotamers of the paramagnetic labels E5C-EDTA-Mn^{2+} and E32C-EDTA-Mn^{2+} on HPr.
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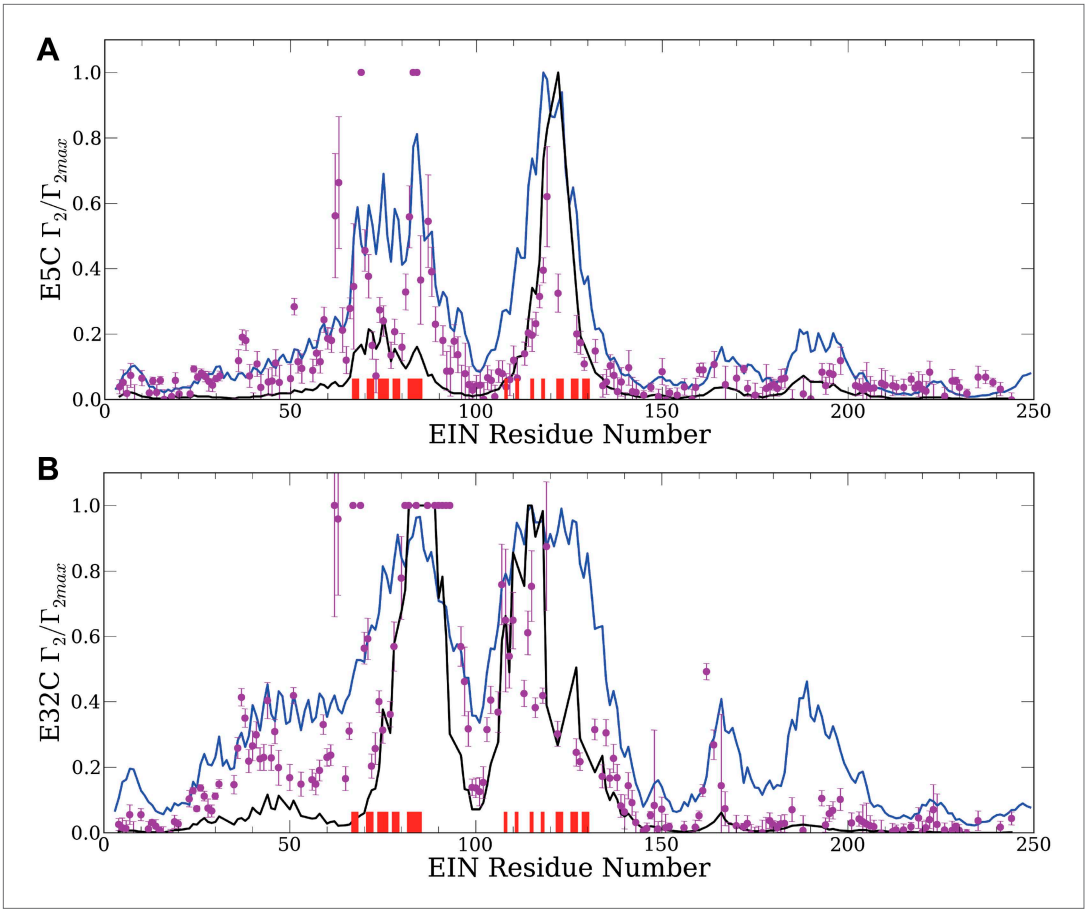

Figure 2. Normalized intermolecular PRE profiles for the EIN–HPr complex. PRE measurements were carried out at 300 μM EIN, 300 μM HPr, and 150 mM NaCl (***Fawzi et al., 2010***). Theoretical intermolecular PREs, calculated only from the coordinates of the specific EIN/HPr complex, are shown as black lines. Calculated PRE values, based on all generated encounter complexes, are shown as blue lines, and reveal substantial contributions by the non-specific structures. The experimental PRE rates (Γ_2) are displayed as filled-in magenta circles. Points representing Γ_2 values that were too large (>60 s^{-1}) to be determined accurately are placed at the saturation level $\Gamma_2/\Gamma_{2max} = 1$. Interface residues are indicated by red ticks on the x-axis. (**A**) Results for EIN/HPr-E5C-EDTA-Mn^{2+} complexes. (**B**) Results for EIN/HPr-E32C-EDTA-Mn^{2+} complexes.

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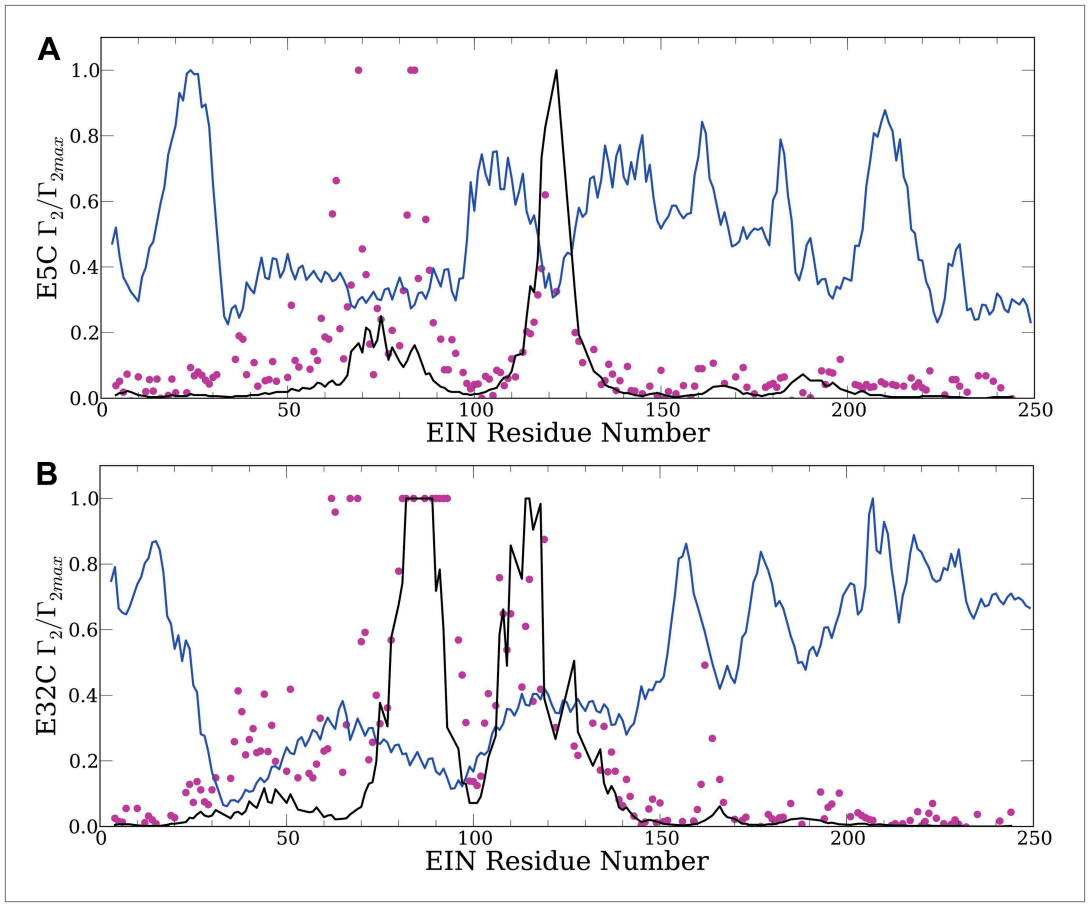

Figure 2—figure supplement 1. Controls emphasizing the need for accurate energy function in docking: theoretical PRE profiles for the EIN/HPr complex, based on complexes generated by using only the van der Waals energy (blue line).

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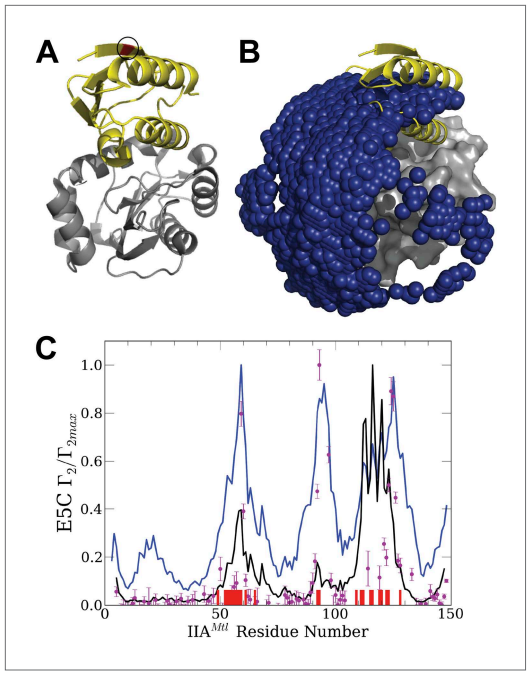

Figure 2—figure supplement 2. Normalized intermolecular PRE profiles and encounter compexes for the IIA^{Mannitol}/HPr interactions.

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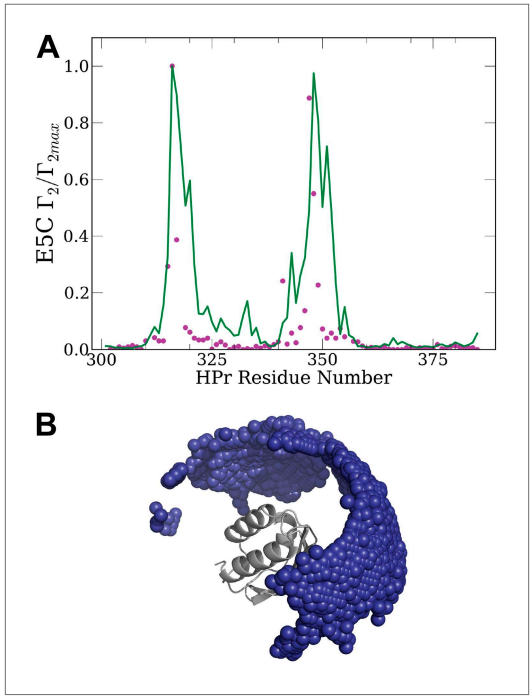

Figure 2—figure supplement 3. Normalized intermolecular PRE profiles and encounter compexes for the HPr/HPr interactions.

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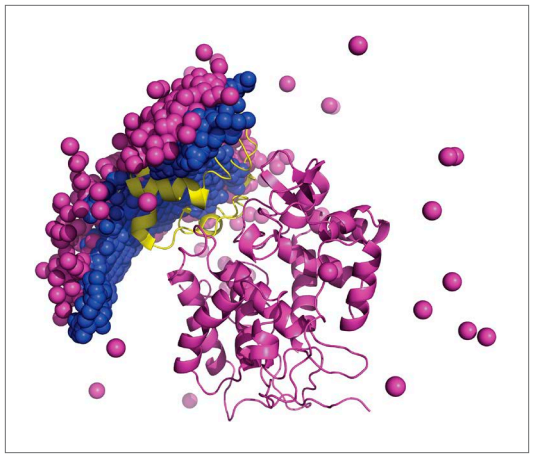

Figure 2—figure supplement 4. Encounter complexes in the Cytochrome c–Cytochrome c peroxidase interactions as reported on the basis of PRE experiments (***Bashir et al., 2010***), shown as pink spheres, and the ones generated by the PIPER docking program, shown as blue spheres.
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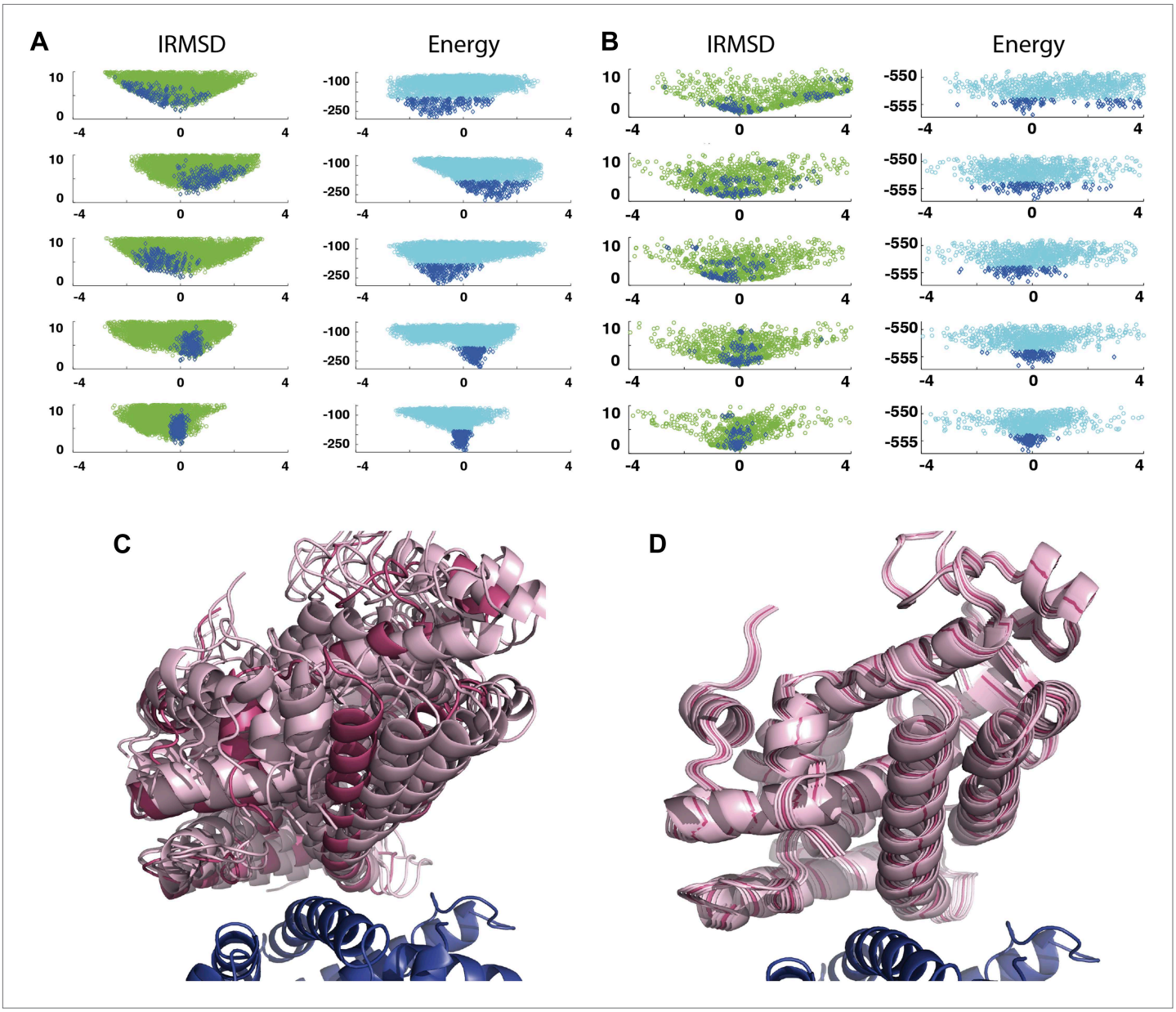

Figure 3. Shape of the energy landscape along the five PCA eigenvectors for the complex of PPAR-γ and RXR-α (PDB code 1K74). (**A**) Distributions of IRMSD (green) and energy (cyan) values based on structures generated by PIPER as functions of the 'balanced' coordinates shown on the x-axis. Dark blue diamonds indicate low energy data points used for the PCA. The IRMSD (y-axis in the left column) is given in Å. The energy values (on the y-axis in the right column) are given by the PIPER scoring function. (**B**) Same as ***Figure 3A***, but based on structures generated by RosettaDock. The energy values (on the y-axis in the right column) are given by the RosettaDock scoring function. (**C**) Encounter complexes along the most permissive direction $\boldsymbol{v}_1$. The ensemble includes mostly translations from the native state. (**D**) Encounter complexes along the most restrictive direction $\boldsymbol{v}_5$.

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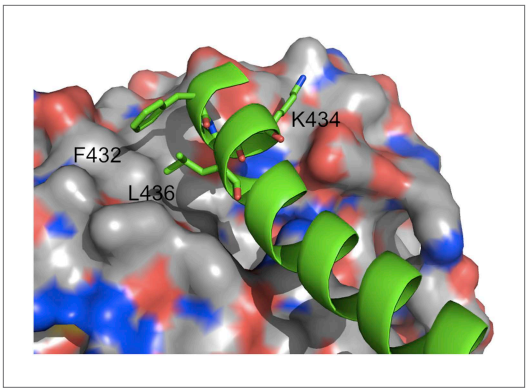

Figure 3—figure supplement 1. Helix H12 of PPARγ with residues of the hydrophobic patch indicated.

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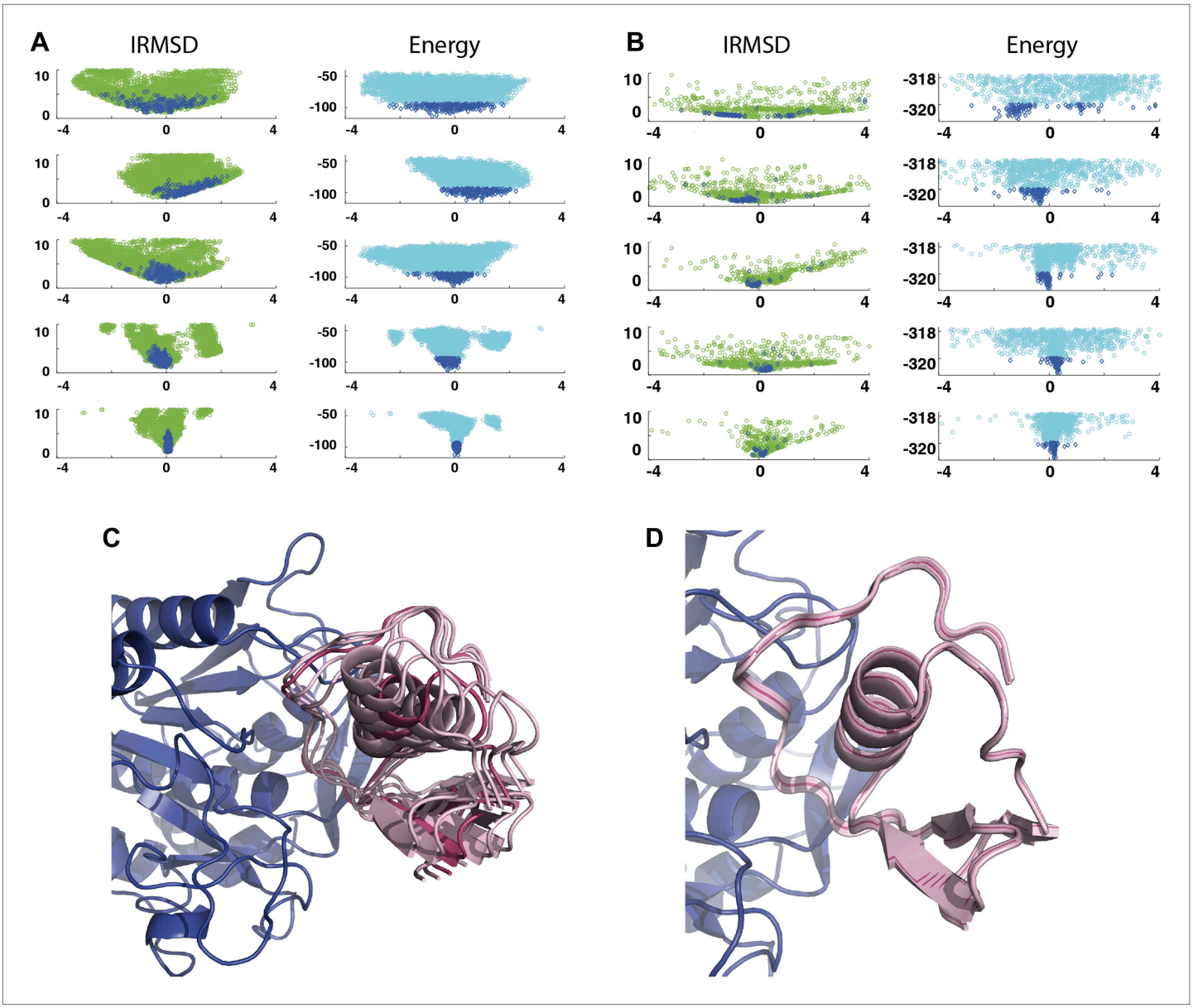

Figure 4. Shape of the energy landscape along the five PCA eigenvectors for the complex of subtilisin Carlsberg and its protein inhibitor, OMTKY3. All notations are as in ***Figure 3***. (**A**) Distributions of interface IRMSD and energy values based on the structures generated by PIPER. (**B**) Same as ***Figure 4A***, but based on the RosettaDock dataset. (**C**) Encounter complexes along the most permissive direction $\boldsymbol{v}_1$. The ensemble consists of small rotations that leave the inhibitory loop position largely invariant. (**D**) Encounter complexes along the most restrictive direction $\boldsymbol{v}_5$.

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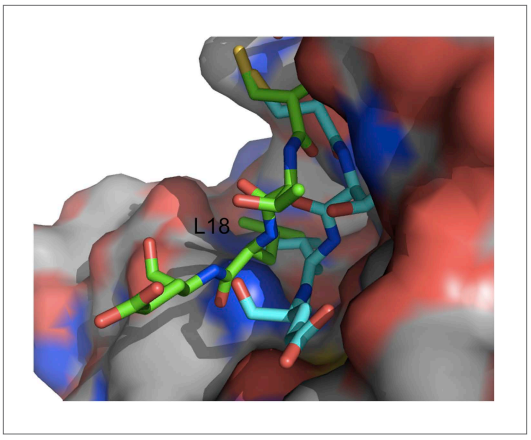

Figure 4—figure supplement 1. Movement of the OMTKY3 inhibitory loop into the active site of subtilisin Carlsberg.

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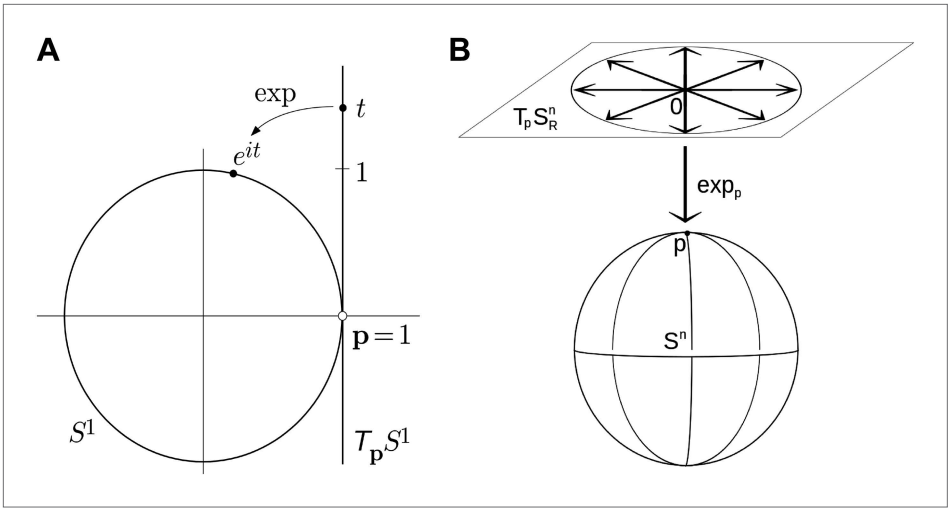

Figure 5. Examples of simple exponential maps. (**A**) Parameterization of the unit circle using an exponential map. The function e^{it} is a local one-to-one mapping of the tangent line around p = 1 onto the unit circle. (**B**) Prameterization of the 3D unit sphere using exponential parameters.

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