Supplementary Materials

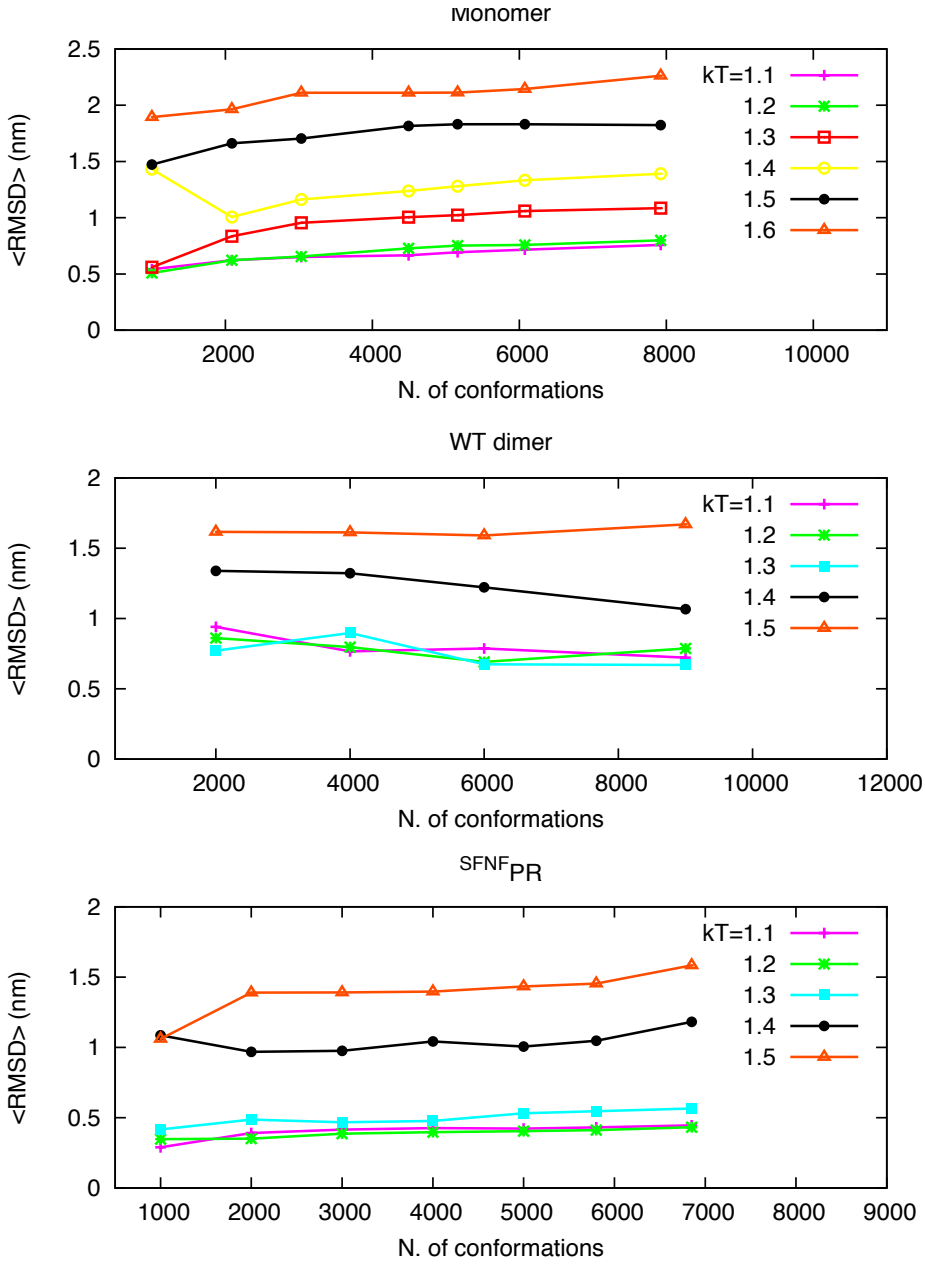
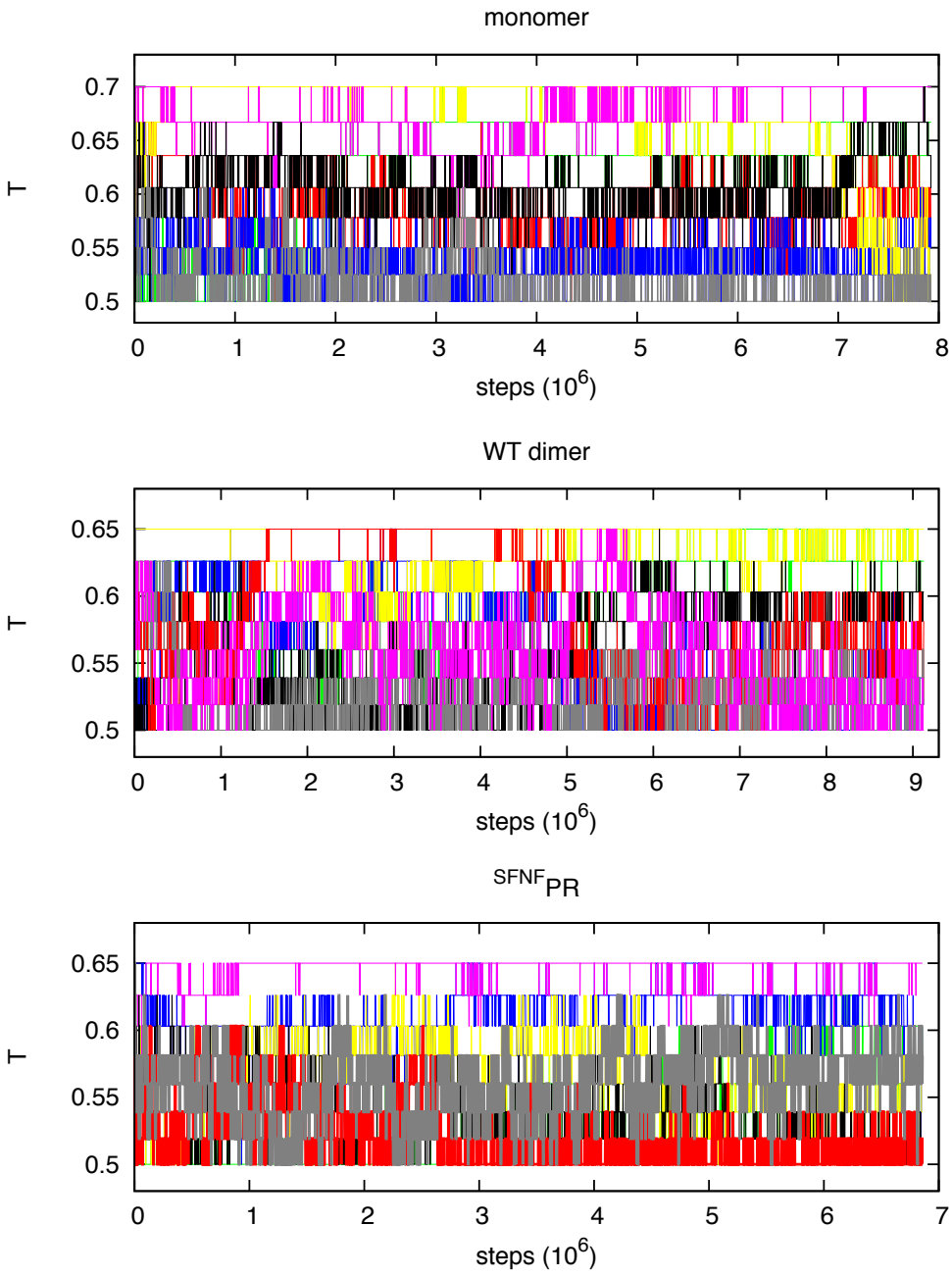


Fig. S1: The convergence of RMSD along the replica-exchange simulations for the three systems under study, obtained averaging it over a subset of all sampled conformations. For WT dimer and for precursor, the RMSD are evaluated for two subunits separately.


monomer
T
0.7
0.65
0.6
0.55
0.5
0
1
2
3
4
5
6
7
8
steps (10^6)
WT dimer
T
0.65
0.6
0.55
0.5
0
1
2
3
4
5
6
7
8
9
steps (10^6)
^{SFNF}PR
T
0.65
0.6
0.55
0.5
0
1
2
3
4
5
6
7
steps (10^6)

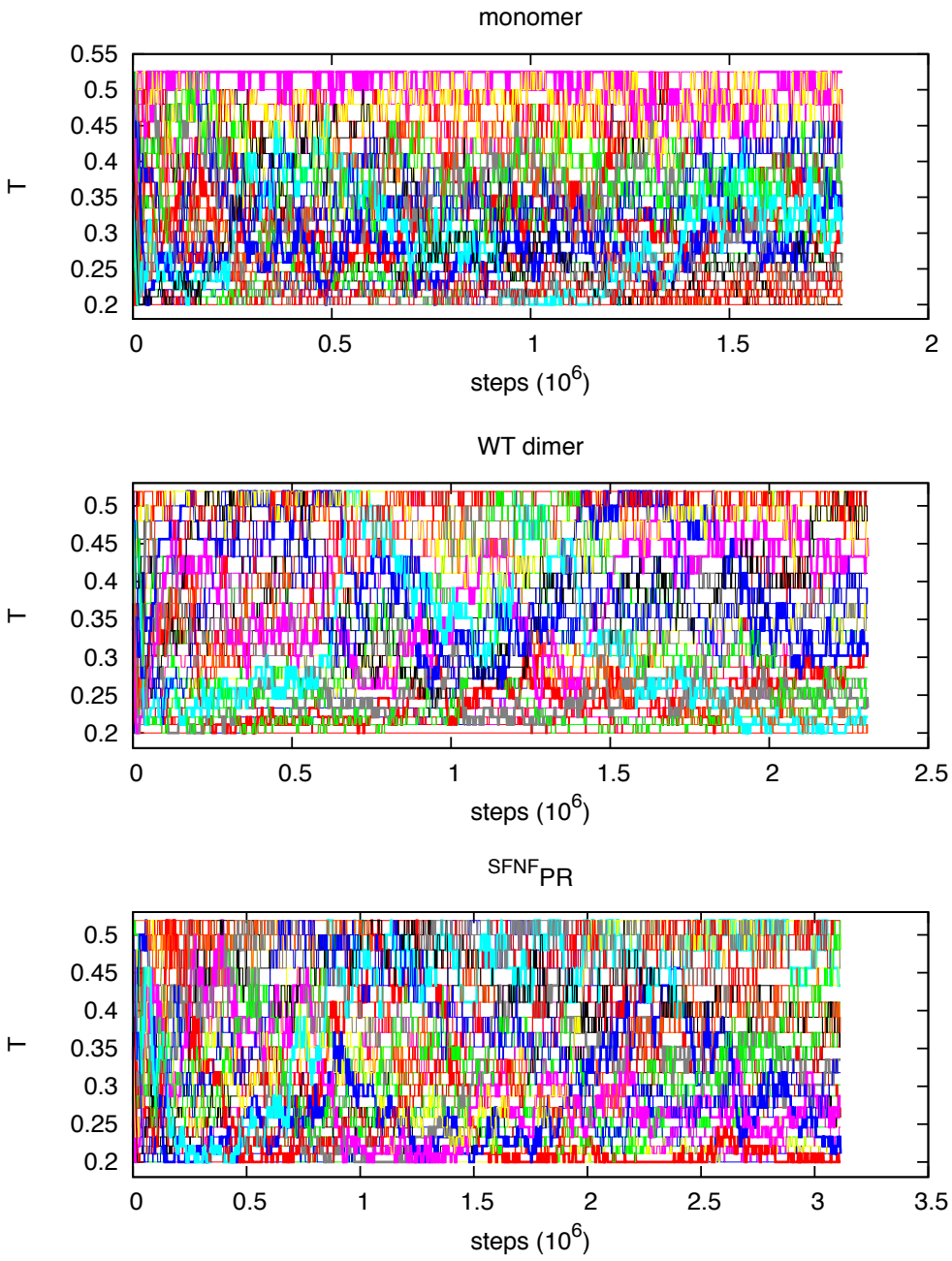


Fig. S2: Examples of temperature exchange of replicas in the simulations for the monomer, the WT dimmer and SFNFPR in the preliminary simulation with 8 temperature, and in the further simulation with 20 temperatures.

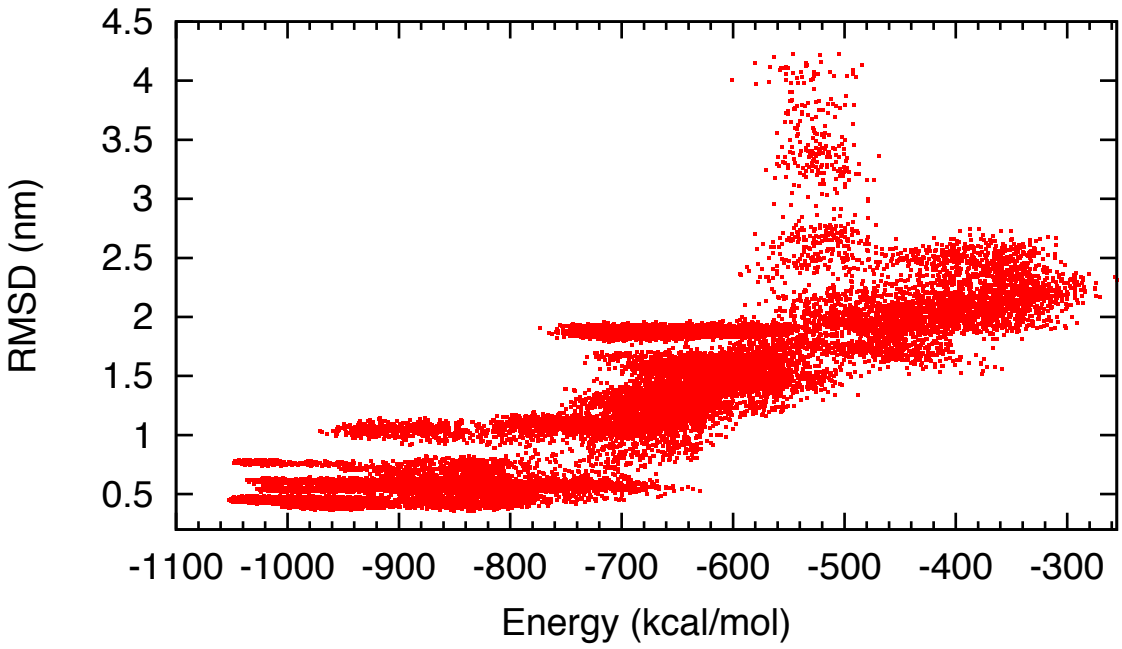


Fig. S3: the RMSD of the low-energy conformations found during the sampling of the conformational space of the WT dimer.

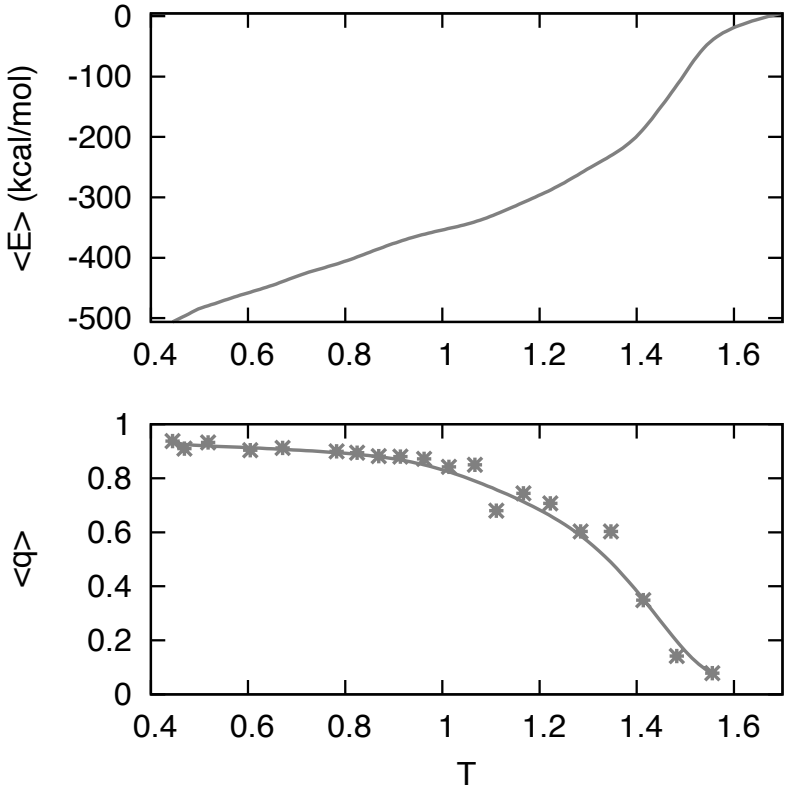


Fig. S4(a) Energy and fraction q of native contacts for the monomer as a function of temperature. A native contact between two heavy atoms is defined if they are closer than 0.35 nm. The average energy is calculated with a weighted-histogram algorithm, while the average q directly from the trajectories at different temperatures. In the latter case, the continuous curve is meant to guide the eye.

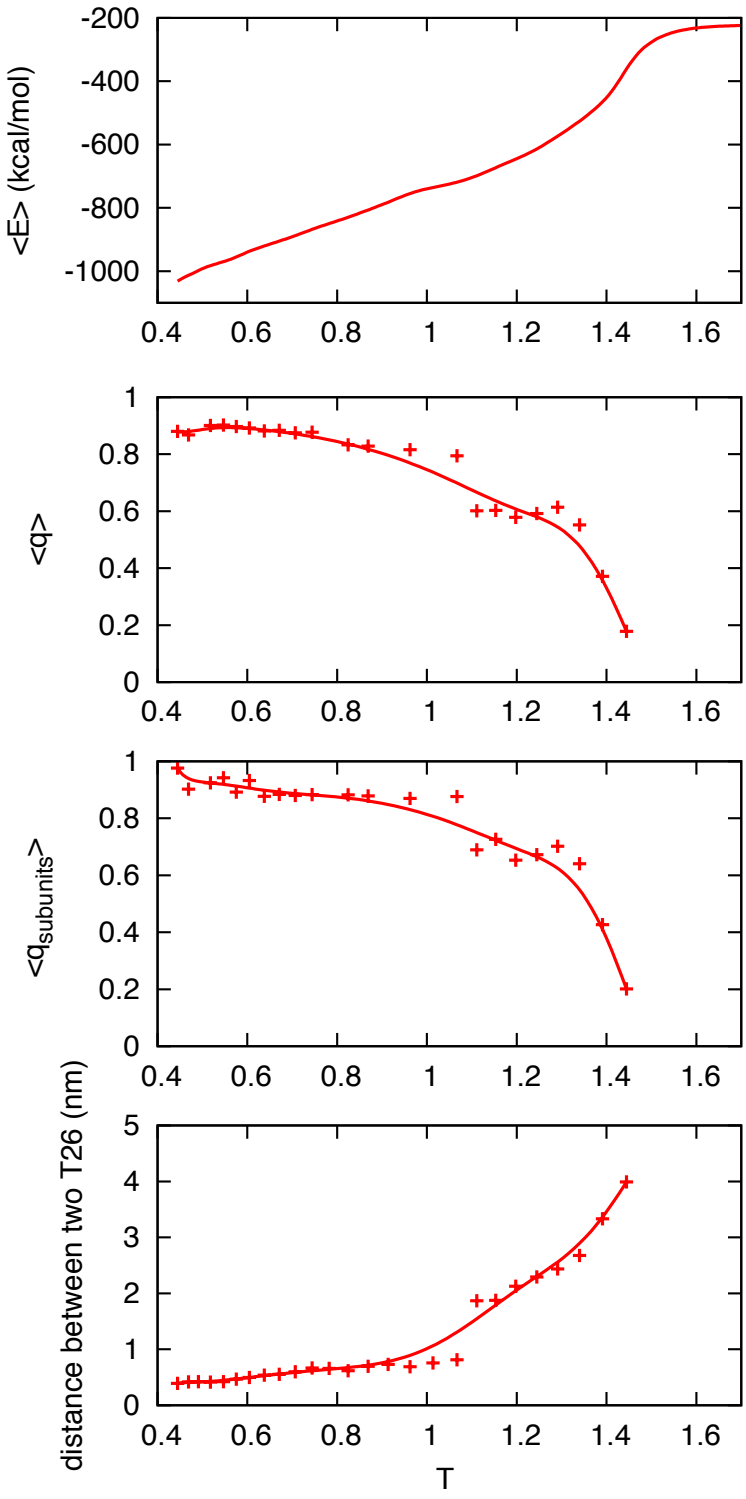


Fig. S4(b) The energy, the fraction q of native contacts in both intra- and inter-subunits, the fraction of native contacts in subunits and distance between the two T26 which participate to the active site for the WT dimer, as a function of temperature.

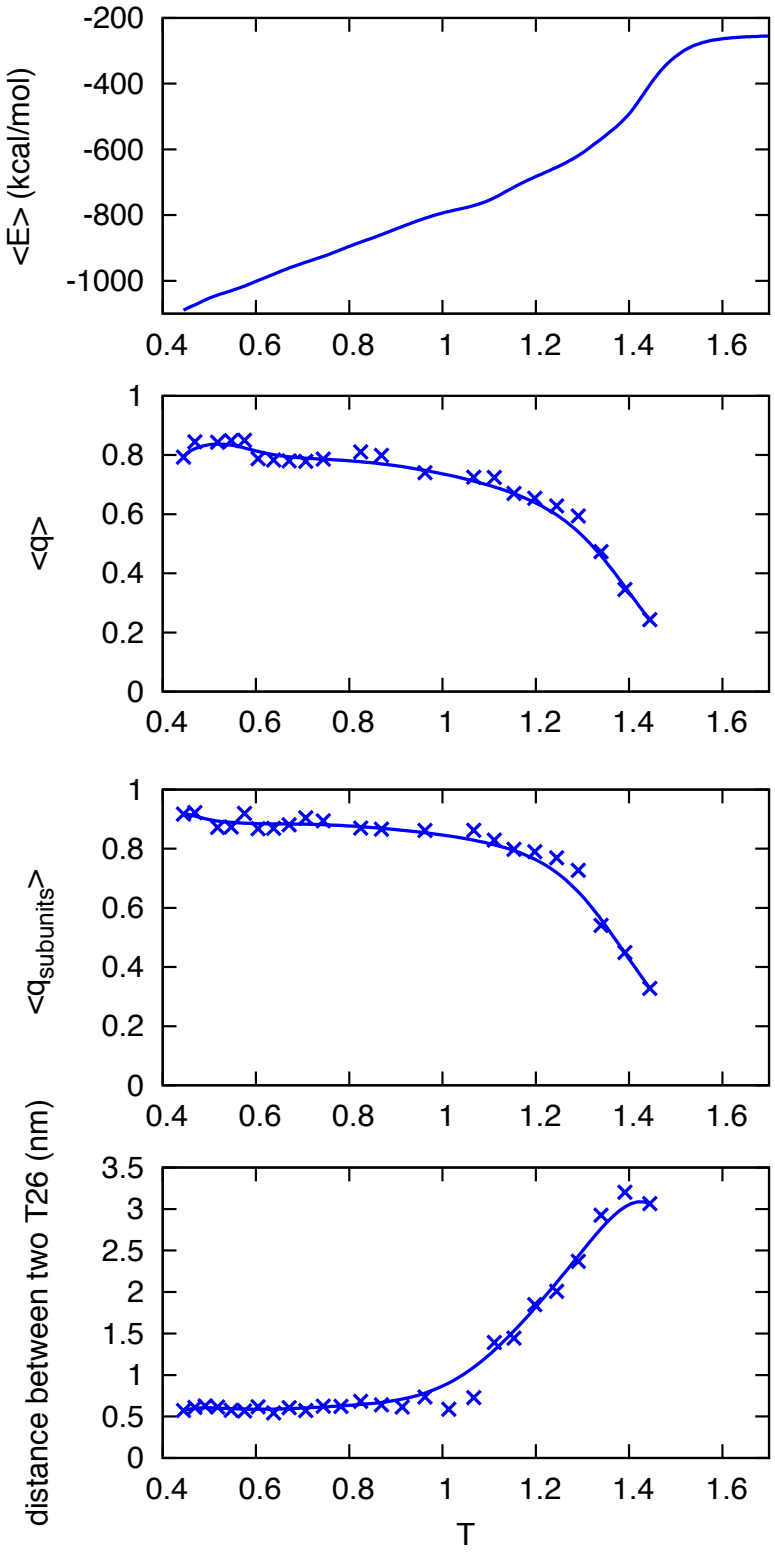


Fig. S4(c) The average energy, the fraction q of native contacts, the fraction of native contacts in subunits and the distance between two T26 for ^{SFNF}PR, as a function of temperature.

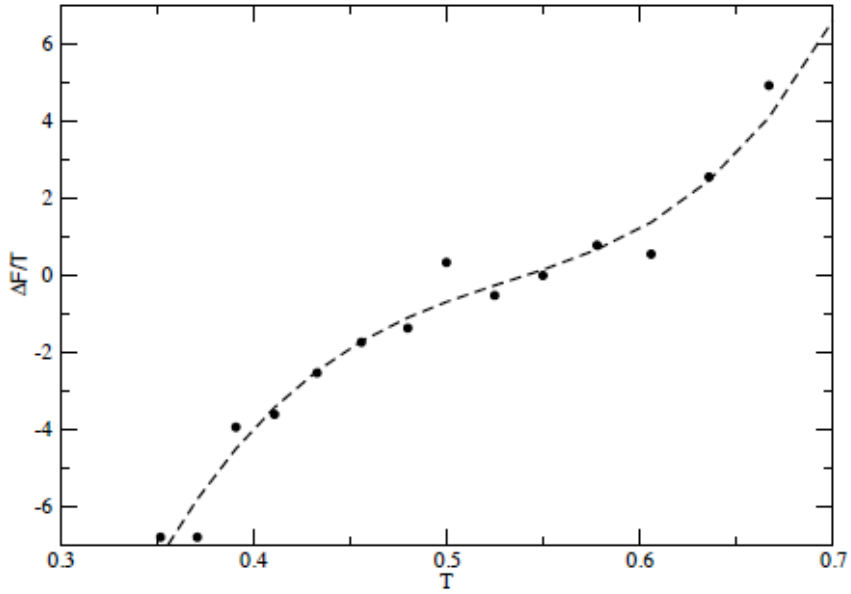


Fig. S5 Folding free energy (ΔF) divided by temperature as a function of temperature calculated from the simulation of the monomer. Temperature is given here in the units of the Medusa force field employed in the simulations. The value of $\Delta F/T$ is calculated as $-log[p_N/(1-p_N)]$, where p_N is defined as the probability of CA contacts (both native and non-native) in the monomer, that is if the two CA atoms are closer than 0.5 nm. Room temperature is defined as the one at which $\Delta F/T$ is equal to the experimental value of -2.25, obtained for the Δ96-99 variant of the protease (see ref. {Noel:2009be} in the text).

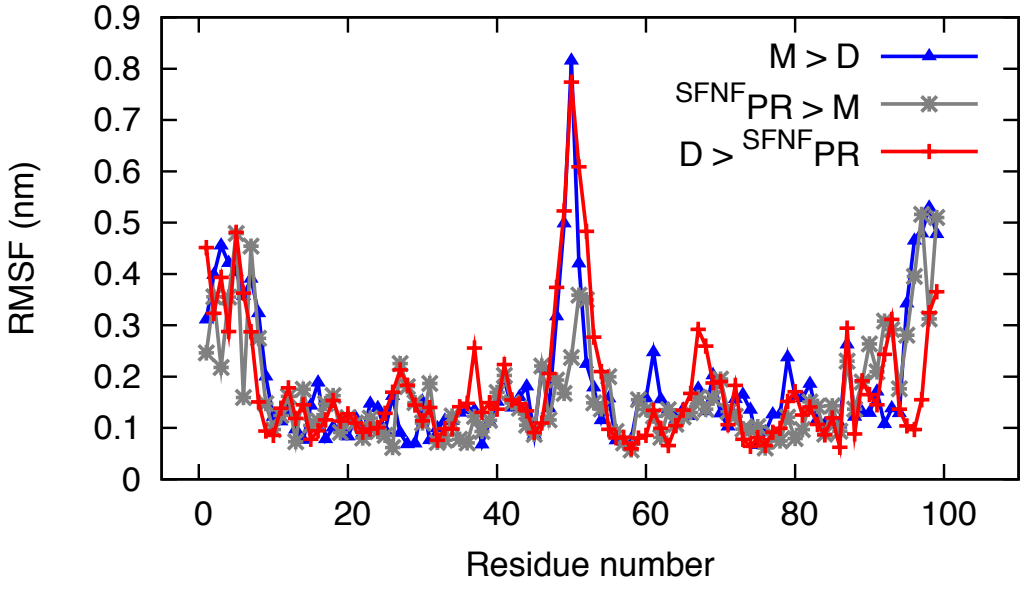


Figure S6: the structural differences, quantified as standard deviation in the atomic positions, between the average structure at biological temperature of monomer and dimer (blue curve), of dimeric precursor and monomer (gray curve), of dimer and dimeric precursor (red curve).

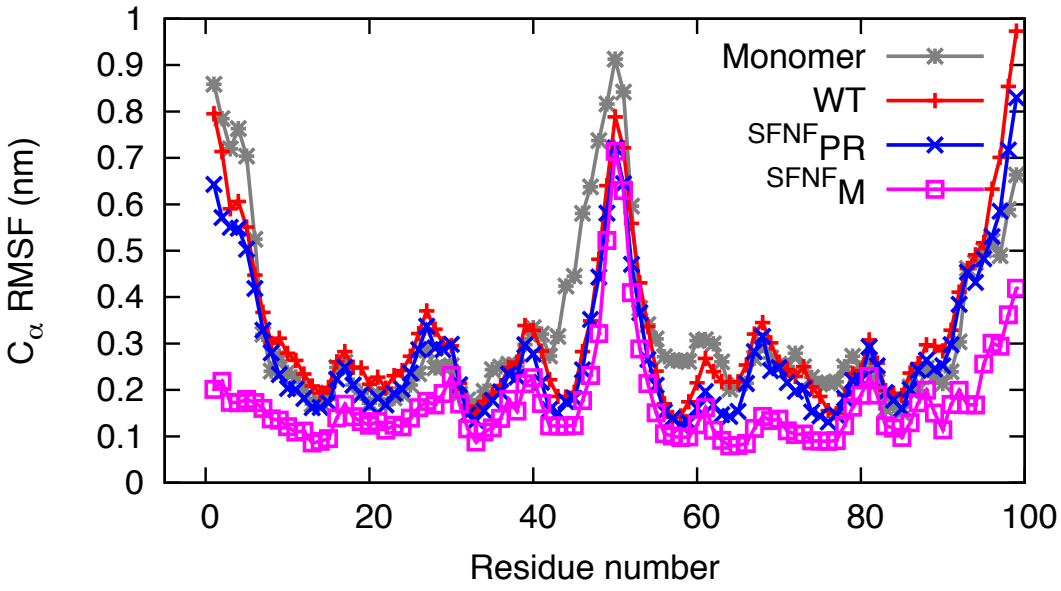


Figure S7: the fluctuations of residues around the average structure.

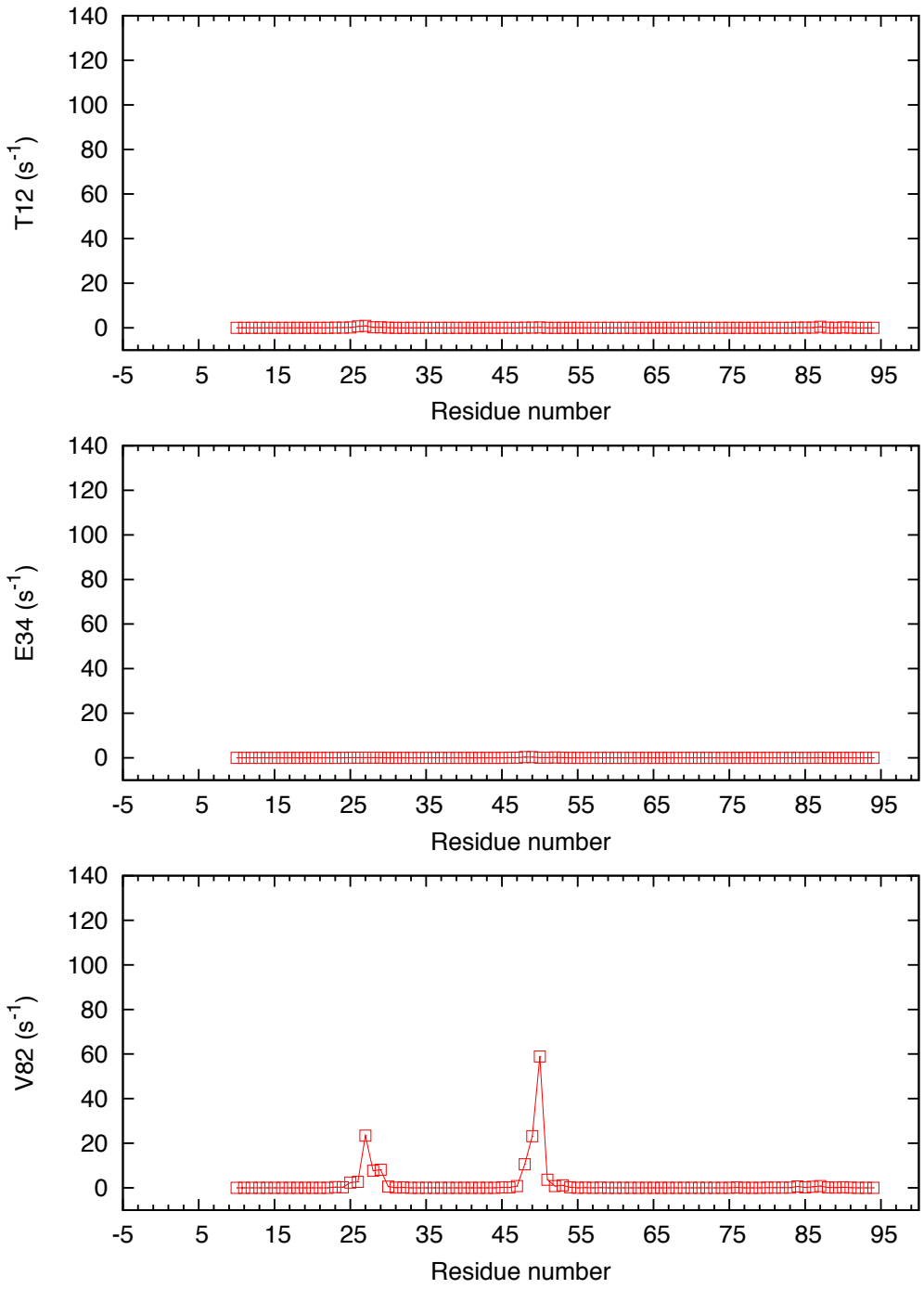


Fig. S8: the values of $\langle r^{-6} \rangle$ calculated between T12, E34, V82 residues of a subunit and the core residues (10 to 94) of the other subunit in the WT dimer.

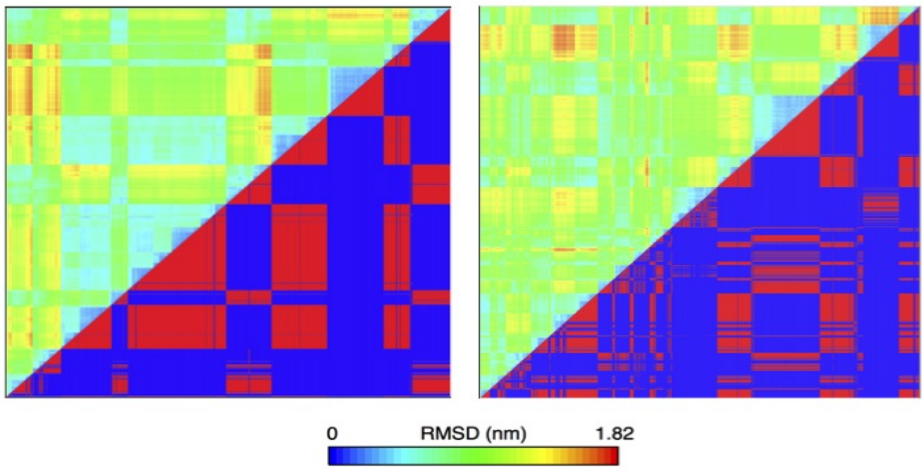


Figure S9: above the diagonal, the RMSD associated to the clustering of the mature dimer (left) and of the precursor (right). The red dots in the lower diagonal group snapshots which belong to the same cluster.