Supplementary Information

The Fundamental Role of Flexibility on the Strength of Molecular Binding

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Determination of Binding Status

Binding status was determined every 4000 steps based on the number of inter-chain contacts. An inter-chain contact was defined as the close approach of a pair of beads, one from each chain, with a separation distance less than 1.6 reduced length units. Instantaneous configurations with 10 or more inter-chain contacts were defined as being in the bound state and configurations with less than 10 inter-chain contacts were defined as being in the unbound state. In Figure S1, binding state is shown as a function of simulation time by the vertical position of the solid red line, with the bound state indicated by upper position and the unbound state indicated by the lower position. As only two states are possible, the binding state line conveys only two values related to current state, i.e. bound and unbound, as indicated by labels on the right hand ordinate.

The binding state (red line) is overlapped on the potential energy (black line) as a function of time. It is evident that the potential energy is lower for bound than unbound structures, indicating that use of inter-chain contacts provides a reasonable definition of binding status. Data presented are from a simulation of chain pairs with k_{bend} = 0.42. Only a tiny fraction of the entire simulation run is shown, such that individual binding/unbinding events can be discerned. The data are representative of simulations with other k_{bend} values, although the duration of binding events does vary significantly as a function of k_{bend}.

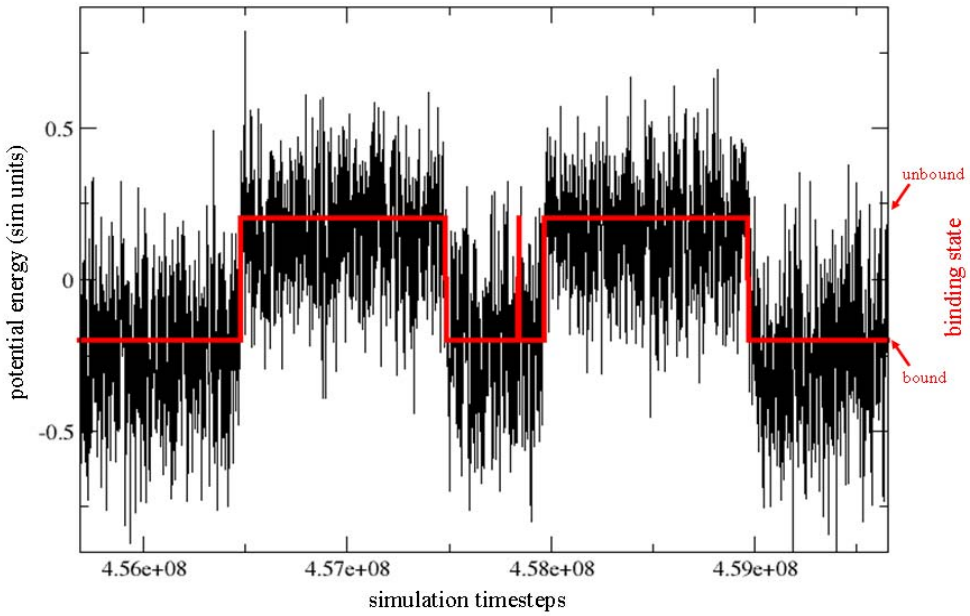

Fig. S1. Binding Status and Potential Energy as a Function of Simulation Time. Binding status is plotted in red and potential energy in black. Data are from a matched-flexibility simulation of an N = 20 and k_{bend} = 0.42. Only a tiny fraction of the total simulation time is represented, such that individual binding/unbinding transitions are apparent.

The number of transitions between the bound and unbound states is shown as a function of k_{bend} in Figure S2. Data are shown for three different chain lengths: N=25 (black), N=30 (red), and N=35 (green). Fewer transitions are observed for high and low k_{bend}, where higher binding affinity leads to binding events of greater duration and therefore fewer transitions between binding states. Similarly, for longer chains, fewer binding transitions are observed, as chains remain in the bound state for longer durations. For the majority of chain lengths and k_{bend} values studied, many thousands of binding transitions occur during the course of the simulation. For the longest chain lengths, for both very high and very low k_{bend} values, the number of binding transitions is considerably lower. Nonetheless, the behavior of k_a, ΔH, and ΔS as a function of k_{bend} (Figure S2) are consistent for all chain lengths studied, suggesting that a sufficient statistics are obtained for all conditions studied.

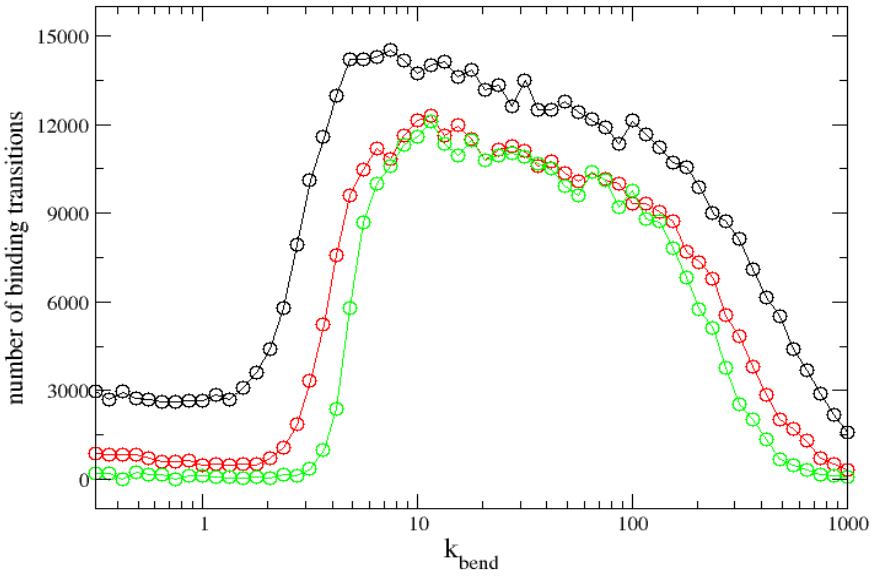

Fig. S2. Number of Binding Transitions as a Function of k_{bend} and Chain Length. As low and high k_{bend} pairs spend more time in the bound state, fewer transitions are observed in the course of the simulation.

Binding of Mixed-flexibility Chain Pairs

For completeness, we have considered the binding of N = 20 chain pairs with un-matched flexibility. We have investigated the full bending energy parameter space by allowing the flexibility of each chain in a pair to vary independently. Such association between chains of mismatched flexibility is more generally relevant than matched-flexibility pairs, for example to ligand/receptor pairs and to polymer blends. For purposes of discussion, it is convenient to arbitrarily designate one of the chains as the 'receptor' and the other chain as the 'ligand'. The equilibrium structure of both chains remains the fully extended state, as was the case for the matched-flexibility study.

In Figure S3, we plot the strength of association, in the form of the order parameter, ϕ, as a function of 'ligand' rigidity. In Figure S3a, we hold the 'receptor' to be flexible (k_{bend} = 1) and in Figure S3b, we hold the 'receptor' to be infinitely rigid (no internal degrees of freedom). As can be seen, when the 'receptor' is flexible (Figure S3a), association strength increases with 'ligand' flexibility. However, when the 'receptor' is rigid (Figure S3b), association strength increases with 'ligand' rigidity. Thus, as was the case with matched flexibility pairs, we find strongest association strength for the highly rigid and highly flexible limits. However, while rigid/rigid and flexible/flexiblepairings strongly associate, flexible/rigid chain pairs display very weak association, suggesting that matched-flexibility pairs represent an upper limit on association strength.

In Figure S4, a contour plot of relative binding affinity is presented, with 'ligand' rigidity increasing along the ordinate and 'receptor' rigidity increasing along the abscissa. Each square in the plot represents the value of k_a determined from a full 7 x 10^8 step simulation. k_{bend} values considered range from 0 to 5623, with incremental positions along each axis representing equal log scale increments in k_{bend} as follows: k_{bend} = 0.00, 1.00, 1.78, 3.16, 5.62, 10.00, 17.78, 31.62, 56.23, 100.00, 177.83, 316.23, 562.34, 1000.00, 1178.00, 3162.00, and 5623.00. Relative binding affinity is indicated by color, with low affinity in blue and high affinity in red. The set of simulations were performed for three different temperatures T = 0.9, T = 1.0, and T = 1.1. Binding is stronger at lower temperatures and weaker at higher

temperatures, as expected. Binding is strongest at the lower left hand and upper right hand corners, reaffirming that highly flexible and highly rigid pairs form the strongest associations.

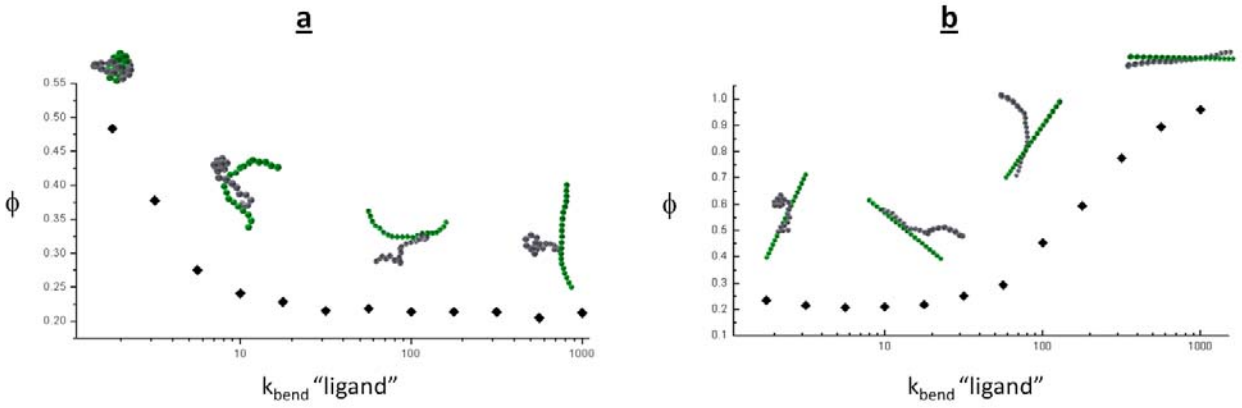

Fig. S3. Binding of Mixed Flexibility Chain Pairs. One member of a chain pair is held at constant kbend value and is arbitrarily denoted "receptor". a) "Receptor" held flexibile, "ligand" flexibility varies; b) "Receptor" held rigid, "ligand" flexibility varies.

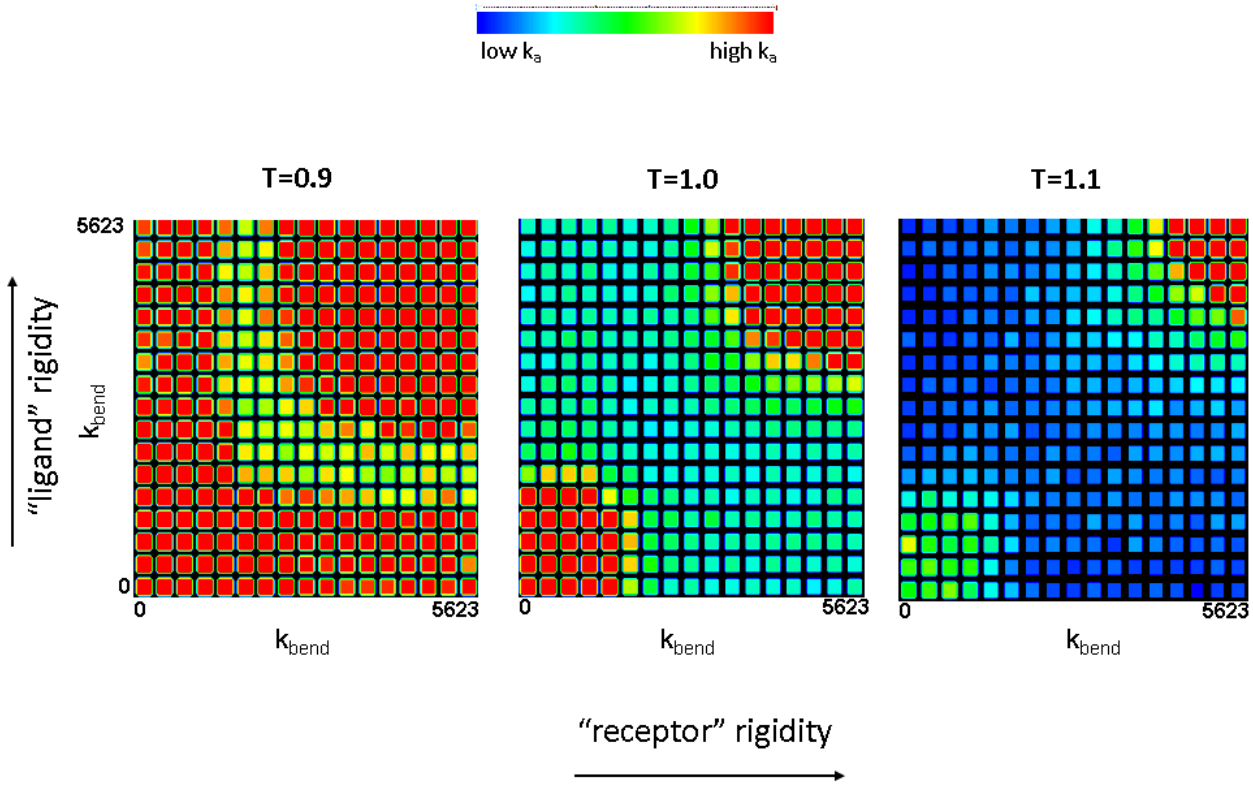

Fig. S4. Binding Affinity as a Function of Full Parameter Space of "Receptor" and "Ligand" Rigidity for Three Different Temperatures. Ligand and Receptor k_{bend} values are varied independently to explore full flexibility parameter space. Grid points along each axis corresponds to equal log-scale increments in k_{bend}.