Supporting Text

Replica Exchange Method. Replica exchange technique more efficiently samples complex configuration spaces than constant temperature molecular dynamics (MD) simulations by periodically exchanging configurations that are running at a sequence of temperatures (1-4). We followed the two-step algorithm for the replica exchange MD (1). Step 1: A series of independent MD simulations are carried out simultaneously and independently for a certain number of MD steps with an optimal temperature distribution. Step 2: The pairs of configurations corresponding to neighboring temperatures are simultaneously exchanged with the probability determined by a Metropolis criterion that preserves detailed balance. We used the scheme suggested by Okamoto and coworkers (2): The pairing of neighboring temperatures is alternatively exchanged between two possible choices, ($T1$,$T2$), ($T3$,$T4$), ··· and ($T2$,$T3$), ($T4$,$T5$), ··· ($T1<T2<T3<\cdots$). The replica exchange MD simulations with the interchain center-of-mass constraint were carried out in parallel with a modified AMBER package (5).

Simulated Annealing. To sample more thoroughly the conformational space of the symmetrized Gō-type potential, we also performed sets of 50 runs of simulated annealing. These runs were performed with various values of dihedral force constants $K_{\phi}^{(n)}$. The parameters were optimized to approximately account for the flexibility of the dihedral angles without using any *a priori* information regarding domain-swapped structures. In these simulated annealing simulations, we applied a constraint of the form $k\left[\left|(r_{Val43}-r'_{Val43})\right|-R_0\right]^2$ to hold the two monomers close to each other. We set k=0.04ε/r_0^2. r_{Val43} and r'_{Val43} are the positions of residues Val43 in two chains. R_0=5.26r_0 was chosen as a distance between residues Val43 in the crystal domain-swapped structure. We note that although the value of R_0 was determined from the domain-swapped structure, because the value of k is so small, a wide range of values of R_0 yield similar results.

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