

## Supporting Information for: Spontaneous Dimer States of the A $\beta$ <sub>21-30</sub> Decapeptide

Micholas Dean Smith, J. Srinvasa Rao, and Luis Cruz\*

*Department of Physics, 3141 Chestnut Street, Drexel University, Philadelphia, PA 19104.*

### **Organization and layout of this section.**

This section contains details on the measurement method for determining dimer lifetimes, along with tables and figures that supplement the computational methods and conclusions contained in the main text. Although similar figures are presented in the text, the results are provided in an extended form for better comprehension.

**\*Corresponding Author: Luis Cruz**

Email: [ccruz@drexel.edu](mailto:ccruz@drexel.edu)

## Dimer Lifetime Measurements:

The determination of the lifetimes of the parallel and anti-parallel dimer states described in the text requires four steps: (i) simulation of pre-formed dimers up to a “breaking” time, (ii) generation of binary dimer state time series, (iii) computation of the autocorrelation function for the generated time series, and (iv) fitting of the autocorrelation functions to the exponential function  $e^{-\tau/t}$ . In order to accomplish this, twenty simulations (of length 350 ns each) were generated and split into two groups with starting conformations of parallel and anti-parallel dimers. With the generation of these trajectories, measurements of hydrogen-bonding and chain-chain end-to-end dot products were made. From the hydrogen-bond and dot product measures, two binary time series were created by assigning frames with the corresponding dimer type (parallel/anti-parallel) to 1 and all others to 0. These binary series were then truncated at the “breaking time,” which we define as the first region with a root-mean-square deviation greater than 0.4 nm in the dimer's alpha-carbons from their initial configuration. Autocorrelation functions (with maximum lag times equal to one-fourth the truncated binary series) were then computed and fitted to an exponential function with cutoffs at the points where the autocorrelation function reached a value of 0, or had a correlation value below 0.1 and a positive slope. With the fit, the lifetimes were given as the time-constant ( $\tau$ ) multiplied by the frame saving rate (10 ps).

<b>Simulation Type</b>	<b>Simulation Parameters</b>	<b>Number of trajectories</b>	<b>Trajectory Length</b>	<b>Initial Configurations</b>
Serial: dimer formation	GROMACS 4.0.7: OPLS-AA force-field, TIP3P water, Berendsen baro/thermostats, $\Delta t = 4$ fs, $T = 283\text{K}$ , $P = 1$ atm; $V \sim 151.3$ nm <sup>3</sup>	20	400 ns	Spatially separated parallel random-coils
Serial: dimer lifetimes	GROMACS 4.0.7: OPLS-AA force-field, TIP3P water, Berendsen baro/thermostats, $\Delta t = 4$ fs, $T = 283\text{K}$ , $P = 1$ atm; $V \sim 151.3$ nm <sup>3</sup>	20 (10 per initial configuration)	350 ns	Parallel; Anti-parallel dimer
REMD	GROMACS 4.0.7/4.5.6: OPLS-AA force-field, TIP3P water, Nose-Hoover thermostat, Parrinello-Rahman barostat, $\Delta t = 2$ fs, $T = 276\text{-}405$ K (exponential distribution: 278.0, 280.3, 282.7, 285.0, 287.4, 289.8, 292.2, 294.6, 297.0, 299.5, 301.9, 304.4, 306.9, 309.4, 312.0, 314.5, 317.0, 319.6, 322.2, 324.8, 327.5, 330.1, 332.8, 335.4, 338.1, 340.8, 343.6, 346.3, 349.1, 351.9, 354.7, 357.5, 360.3, 363.2, 366.1, 369.0, 371.9, 374.9, 377.8, 380.8, 383.8, 386.8, 389.8, 392.9, 395.9, 399.0, 402.1, 405.3); $P = 1$ atm; $V \sim 129.5$ nm <sup>3</sup>	2 REMD (1 per initial configuration)	150 ns	Parallel; Anti-parallel dimer

*Table S1.* Simulation Details. The size of the periodic box was constructed such that the edges of the box were 0.8 nm from any atom associated with either peptide chain. GROMACS 4.5.6 was used for the anti-parallel replica simulation due to the need for a convenient method for the restarting and continuation of replica-exchange simulations without having to read the entire trajectory and generate new input files.

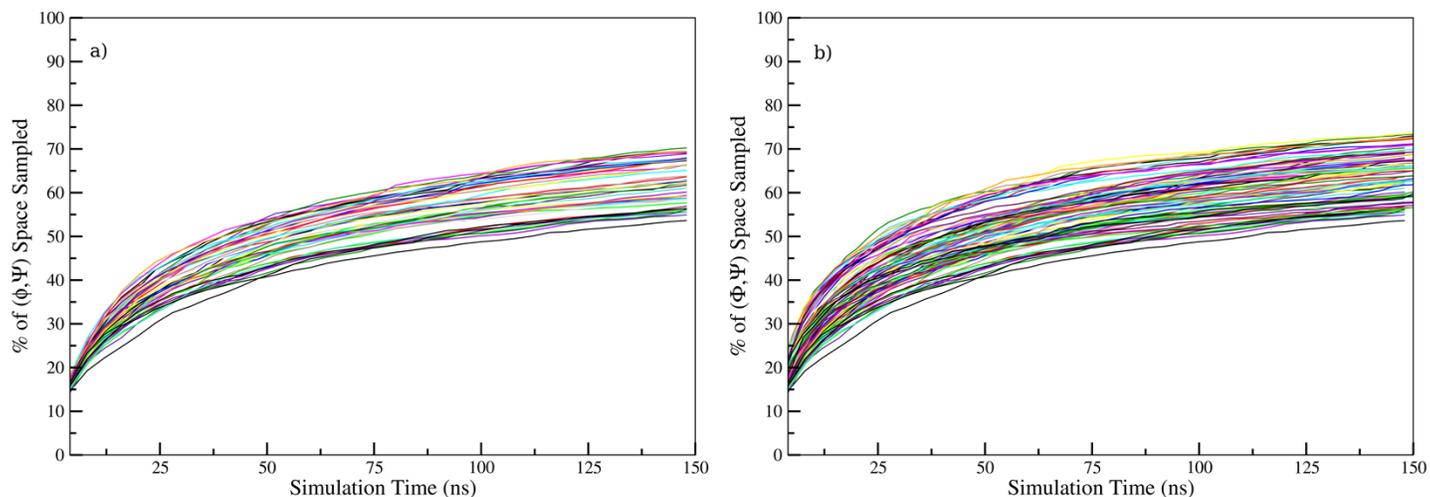


Figure S1. Measure of convergence for REMD trajectories. (a) anti-parallel and (b) parallel dimers. Each line represents a trajectory at a different temperature.

### Measures of Convergence:

Convergence of simulations is measured by measuring the amount of backbone  $\phi/\psi$  space sampled as a function of simulation time. As a simulation converges, the rate at which the sampling of new phi-psi space decreases indicating that the system has sufficiently sampled the conformational space. This method was adopted from Scott, K. A.; Alonso, D. O. V.; Sato, S.; Fersht, A. R.; Daggett, V. *Proc. Natl. Acad. Sci. U.S.A.* 2007, **104**, 2661–2666.

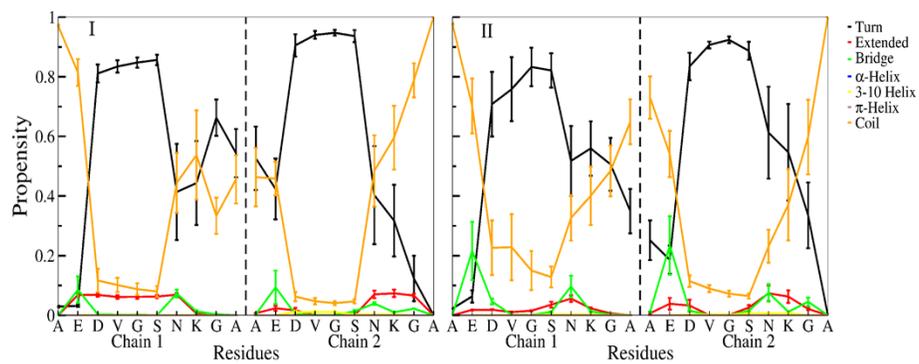


Figure S2. Secondary structure propensities, shown per residue per chain. Due to degeneracy issues, this measure is not generally correct, but is included as it does highlight differences at the termini.

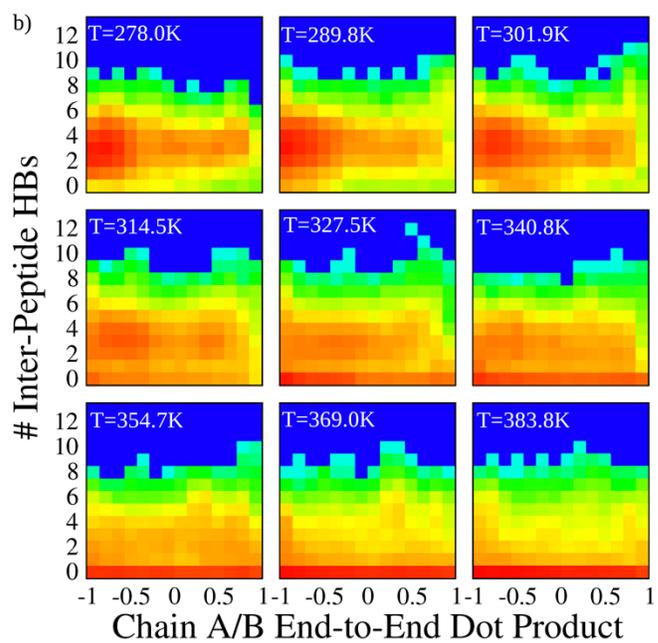
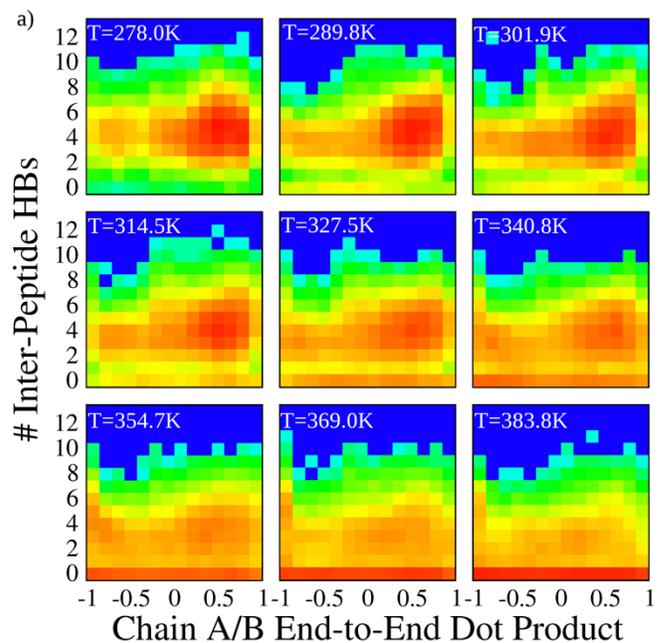
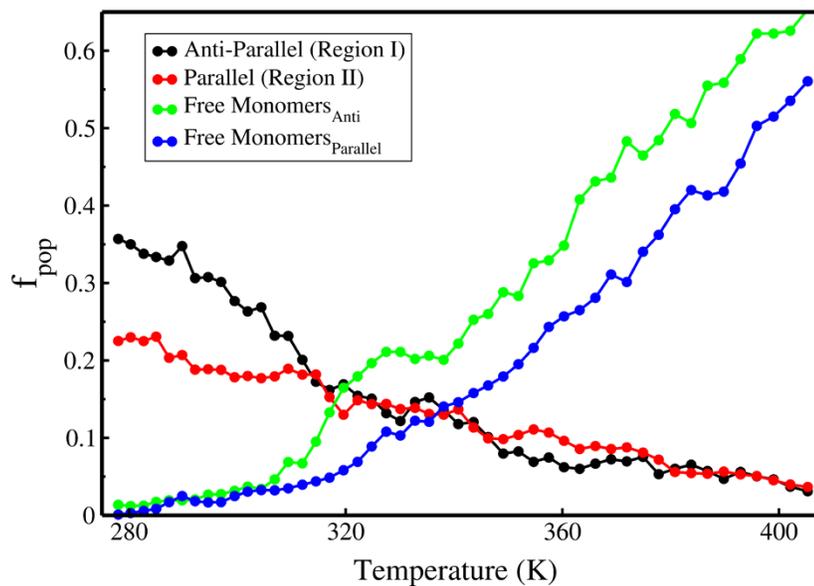


Figure S3. Free-energy landscapes for the dimers starting from: (a) parallel and (b) anti-parallel dimers. Measurements were taken from the last 100ns of their respective REMD simulations.



*Figure S4.* Population fractions of the I and II region dimer conformations along with the free-monomer populations for each replica-trajectory as a function of temperature. Anti- and Parallel subscripts indicate which of the two initial conditions for the REMD trajectories was used for the measure of free monomers. The fractions presented are from the last 100 ns of each REMD trajectory.