Conformational ensemble of human α-synuclein physiological form predicted by molecular simulations

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SUPPLEMENTARY INFORMATION

Additional Computational Details

Each replica was equilibrated to the relative effective temperature by performing 200 ps of gradual annealing and by applying positional constraints on the protein atoms ions (force constant of 1000 J mol^{-1} $Å^{-2}$). The temperature of the solvent was kept at 300 K. Then, 400 ps of MD simulation were run at the replica effective temperature with softer harmonic potentials (force constant of 500 J mol^{-1} $Å^{-2}$). Finally, in the following 400 ps of MD simulation, each replica was left free to move at the replica effective temperature. The MD computational setup is described in the main text.

We ran 32 replicas for each of the six conformation at different effective temperatures of the solute, from 300 to 500 K, (300, 304, 308, 313, 317, 322, 327, 332, 337, 342, 348, 353, 359, 365, 371, 378, 384, 391, 398, 404, 412, 419, 426, 433, 441, 449, 457, 465, 474, 482, 491, and 500 K) following the REST2 technique.[1, 2] The set of effective temperatures was estimated on the basis of the predictions done following the procedure proposed in ref. [3]. At given time intervals (2 ps), the simulation algorithm provides adjacent replicas with the chance to swap their coordinates, allowing low temperature replicas to explore higher temperatures and vice versa. In this study we took advantage of λ-dynamics implementation in the GROMACS 4.5.5 program package[4] to run REST2 simulations.[1, 2] The average exchange probability between adjacent replicas was 30%. The MD computational setup is described in the main text.

Convergence of the calculations

In order to address the convergence of our REST2 calculations we have followed the approach of Wise-Scira and co-workers, [5, 6] namely we have plotted the cumulative averages of calculated properties as a function of the number of geometries obtained from REST2 calculations. In particular we have considered the convergence of both local properties (NMR chemical shifts) and global properties (secondary structure content). The cumulative averages of NMR Cα chemical shifts of the first 6 residues are shown in figure S1, while the secondary structure content is shown in figure S2. Comparison with experiments (figure 1 and 4 in the main text) ensures that these properties have converged to the experimental value, therefore validating our simulations.

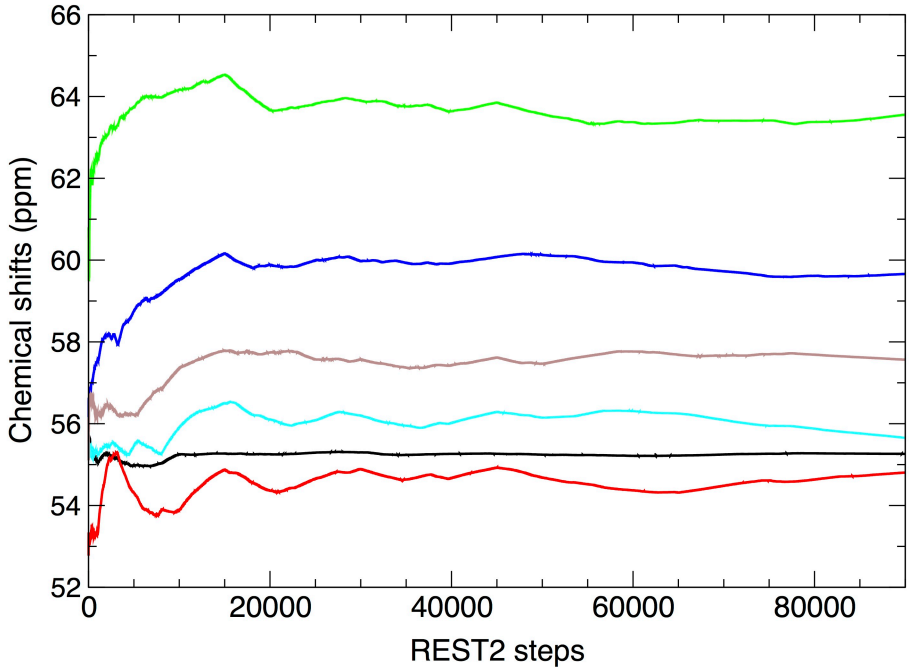

Figure S1. Cα chemical shifts of M1 (black), D2 (red), V3 (green), F4 (blue), M5 (cyan) and K6 (brown) as a function of the number of REST2 steps.

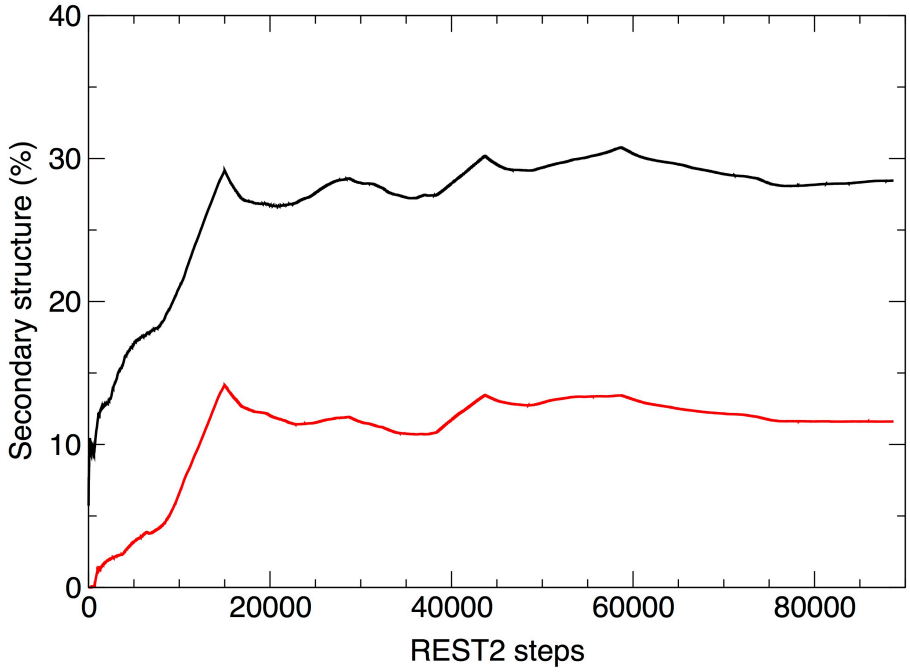

Figure S2. Total secondary structure (black) and α-helix content (red) as a function of the number of REST2 steps.

Supplementary References

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