THE TRANSFORMATION OF FREE AMINO ACIDS TO PROTEIN RESIDUES A STUDY ON DISSOLVENCE

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INTRODUCTION

The formation of complex systems is accompanied by the emergence of properties that are non-existent in the components. At the same time the properties and behavior of integrated components undergo substantial changes (constraints) when compared to their free (unbound) state. This phenomenon, termed downward causation or dissolvence, has recently gained increasing interest, since it may be considered as a process generating information which drives the self-organization of complex systems [1].

Due to their fundamental importance in living systems, proteins and their monomers appear as particularly promising objects in the study of dissolvence. Our recent study was focused on the conformational behavior of the side chain of residues in a model protein (profilin Ib), compared to the free amino acids (in zwitterionic form) [2]. MD simulations (2 ns) revealed strong conformational constraints in the “chi space” of residues. These constraints were quantified using the Shannon entropy (SE) of the χ dihedral angles, showing a clear gain in information content.

Here we present the results of 10 ns MD simulations repeated for the previously investigated objects and presented for new systems with a different level of complexity. First, end-capped amino acids were used to avoid possible interactions of polar side chains with ionized (COO^- and NH_3^+) groups. Second, amino acids were located at the center of nonapeptide (AAAAXAAAA) maintained in an alpha-helical structure to limit the influence of changes in backbone angles on side chains behavior. Also, trypsin was studied as a second protein for the comparison of results and in order to draw more general conclusions. The longer time of MD runs was applied to better explore the “chi space” of the side chains of protein residues.

RESULTS AND DISCUSSION

As can be clearly seen from Figure 1, the global average SE values calculated from all the dihedral angles χ_1 and χ_2 are essentially stable after 10 ns. Generally, the close vicinity of backbone atoms made χ_1 be more restricted than χ_2 which is visible in their significantly lower SE values (SE_{χ_2}-SE_{χ_1} = 0.49-0.78). Apart from a small increase in SE found for all the systems, their relative order remained similar throughout the simulation. Strong conformational constraints (i.e. the lowest SE values) were experienced by the residue side chains in both the proteins studied compared to amino acids in their zwitterionic and end-capped forms. In the case of α-helical peptide, only the χ_1 dihedral angle was affected, revealing constraints of intermediate intensity, whereas an average SE value for χ_2 was close to that of capped amino acids.

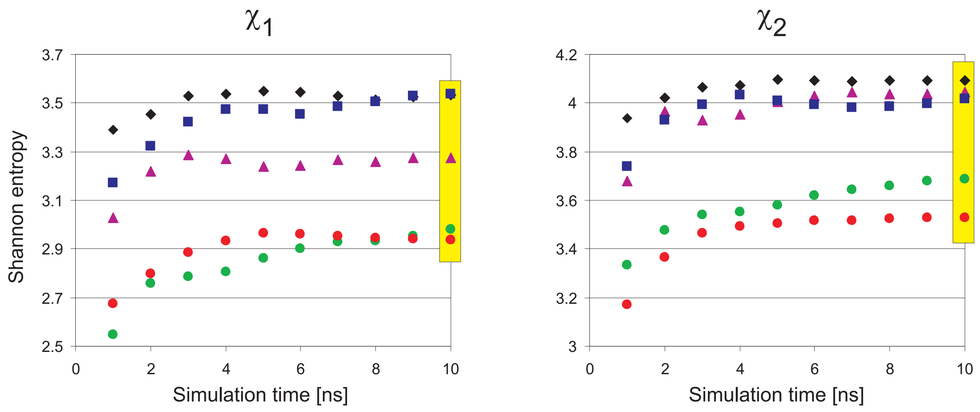

Figure 1. Changes in the global average SE for dihedral angles χ_1 and χ_2 during the 10 ns MD simulation calculated for all the five model systems: ◆ free aa, ■ capped aa, ▲ central residue in α-helix, ● residues in profilin and ● residues in trypsin. The results after 10 ns (highlighted in yellow) are further analyzed in Figure 2.

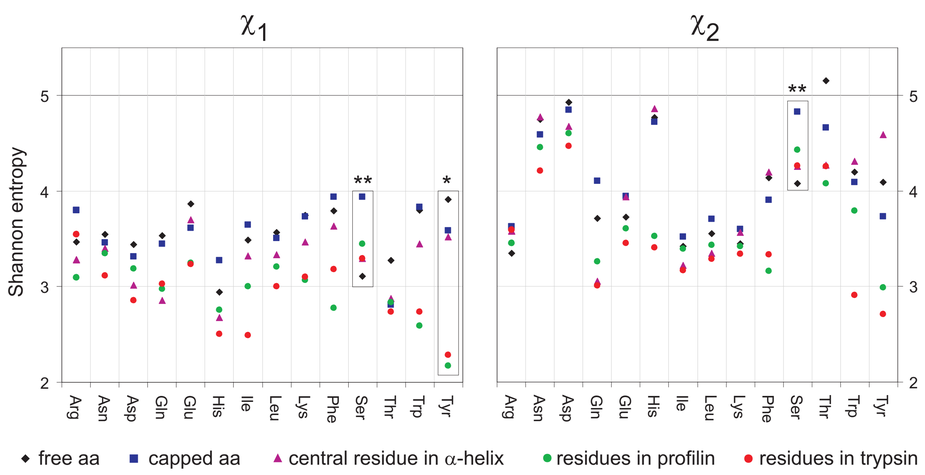

Figure 2. A plot of SE values for χ_1 and χ_2 for different amino acids calculated from the10 ns MD simulation. In the case of both proteins, an average SE for particular types of the residue side chain is shown. * For details see Figure 3. ** For details see Figure4.

The distribution of SE values for the investigated types of the amino acids located in different model systems is shown in Figure 2. Except for Ser and Arg, average SE values for all the other types of protein residues were lower than for the respective free and capped amino acids. The most significant constraints were observed for tyrosine residues of both proteins. A detailed description including all the trajectories of χ_1 is shown in Figure 3. Of all the 14 Tyr residues, only trypsin Tyr94 exhibited a few “jumps” in the dihedral angle χ_1 and its SE value was higher by at least one unit, reaching the level of the capped amino acid and of that located in the peptide. Such an “unusual behavior” of Tyr94 is fully understandable - since unlike other Tyr residues - it is located at a flexible loop with a side chain pointing at the outside of the protein.

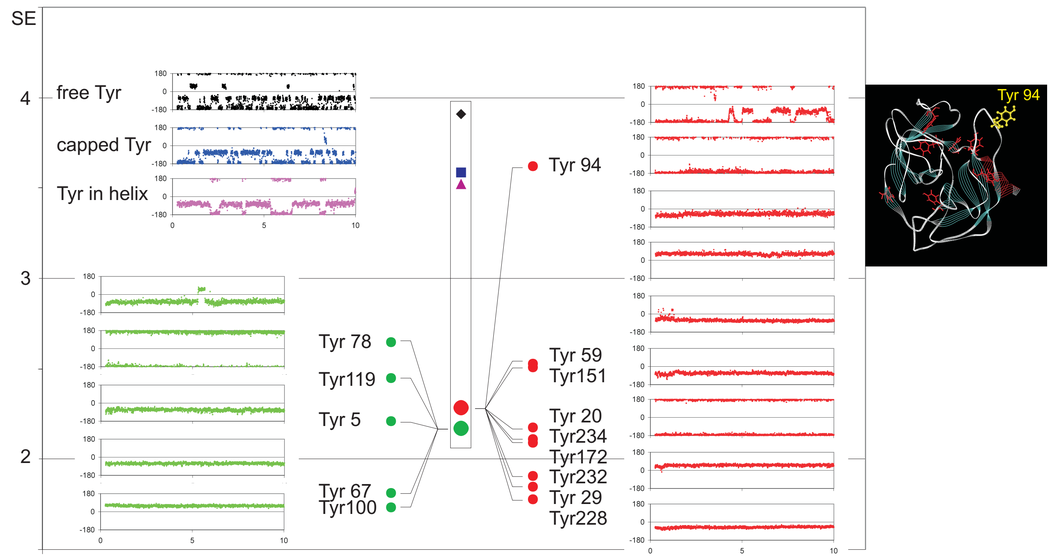

Figure 3. Trajectories of χ_1 in the side chain of tyrosine located in different model systems show different levels of rotational constraints. The position of Tyr94 (characterized by the highest SE) in tyrosine is highlighted.

The unexpected restriction of both dihedral angles, observed for free serine, was caused by the H-bond between the hydroxy group and the protonated amine (Figure 4.). That conformational constraint was removed in the end-capped amino acid as well as in the peptide.

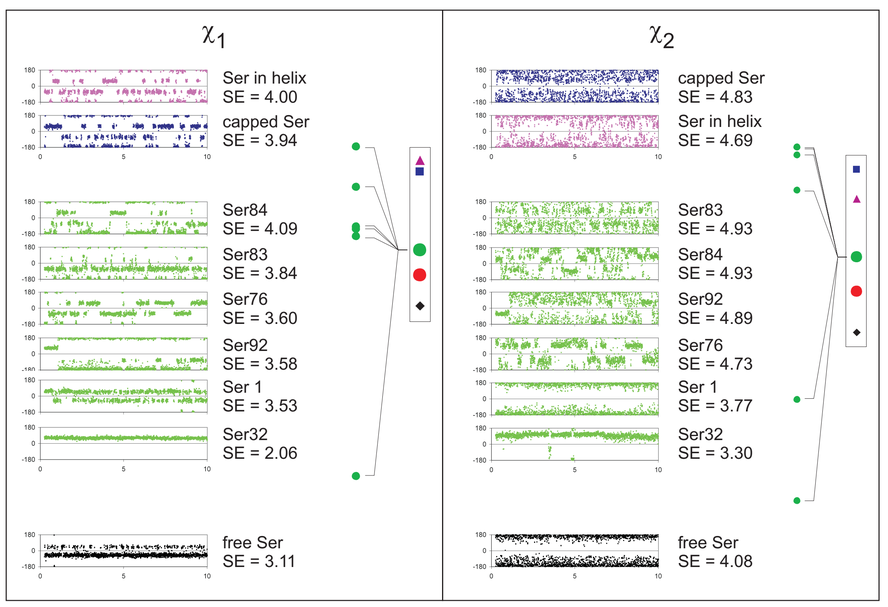

Figure 4. Trajectories of χ_1 and χ_2 in the side chain of serine, studied in different model systems.

In summary, the dissolvence - which is an inherent feature of complexity - was investigated in the present study at a quantitative level. That phenomenon was analyzed as conformational constraints experienced by the side chains of protein residues compared to free or end-capped amino acids. The Shannon entropy of the χ_1 and χ_2 dihedral angles showed a substantial reduction after increasing the level of complexity (amino acid to protein residue transformation). Since SE is a measure of the relative information content of a dataset, the described conformational constraints contribute to the increased information content of the protein, which could have further implications for protein recognition properties.

REFERENCES

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