

Stability of Amyloid Structures

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INTRODUCTION

- Amyloid diseases (Alzheimer's, insulin) are made up of long protein fibrils. These structures are extremely stable making them hard to dissolve or treat with medicine(Michael, 2007). The strength in these structures can be quantified by measuring the residue-residue energy.
- To gather this data, MDS can be used to simulate the interactions of these amyloid structures with solutions of water and other solvents (Ma B.,2006). From this, data can be obtained that shows specific points of weakness or strength between amino acids.

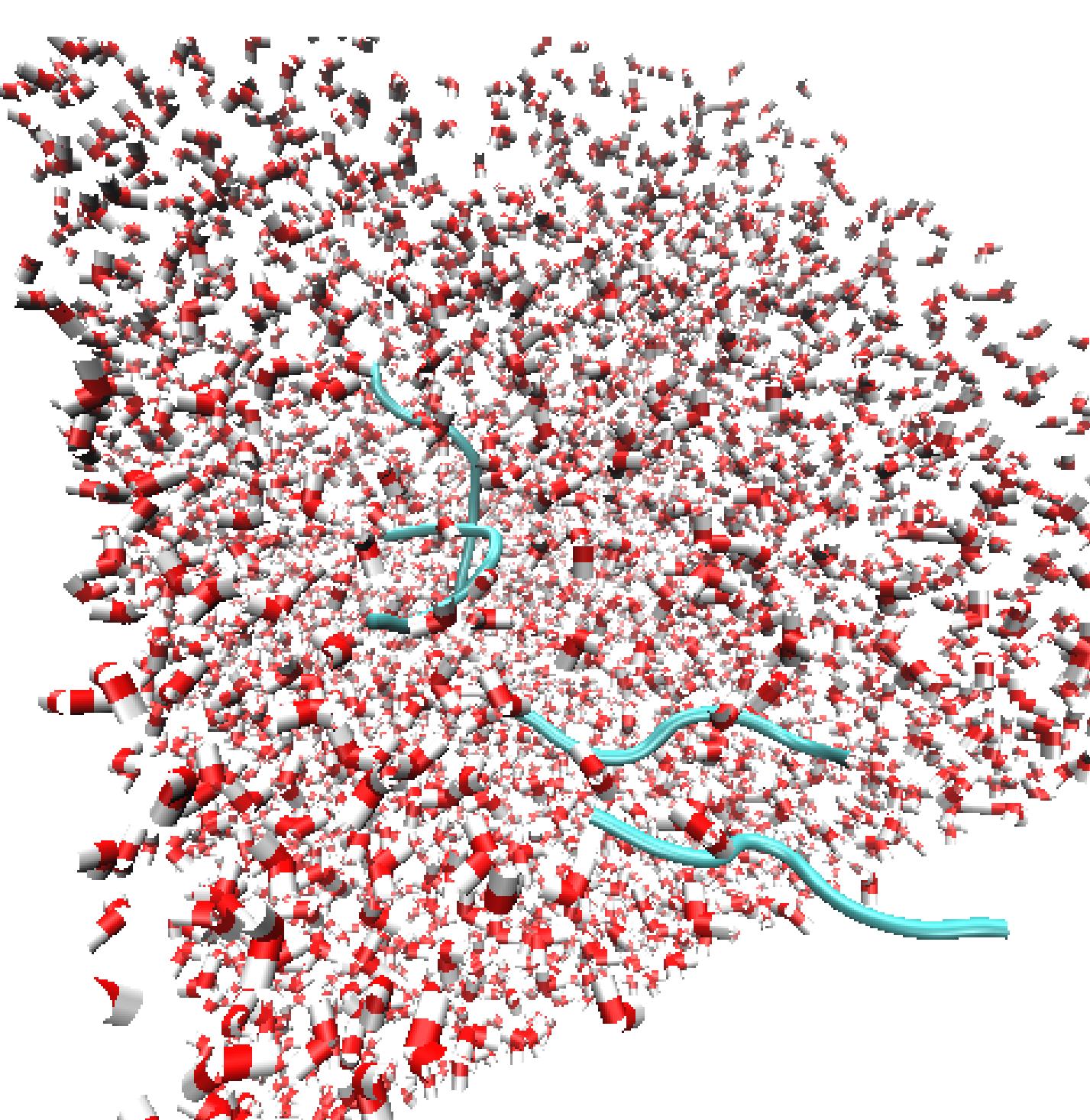
OBJECTIVE

- Characterize points of stability in the amyloid structure in a multitude of solution types using Molecular Dynamics Simulations (MDS)

METHODS

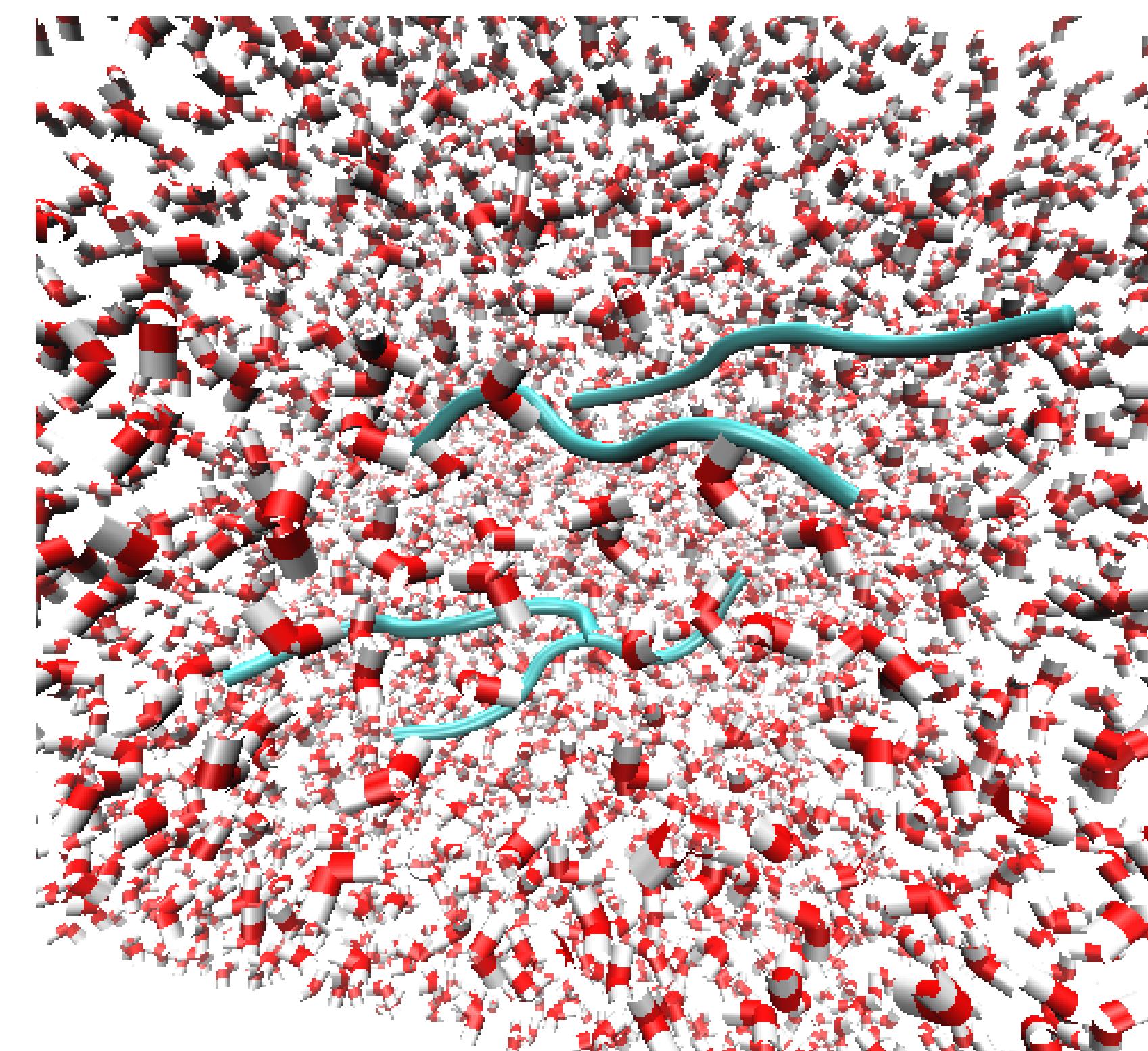
- The Amyloid Peptide is isolated in a box of dimension 5x5x5 and filled with water molecules. Salt molecules (Sodium Chloride, NaCl) of varying concentrations is then added to the box in amounts to neutralize the contents of the box. The simulations are sensitive to the overall charge of the system. Simulations are then run using the GROMACS program to perform energy minimization, equilibrium and obtain the final simulation parameters. The simulation parameters are evaluated to estimate the structural stability of the peptide sequence.

VEALYL TAKEAWAY

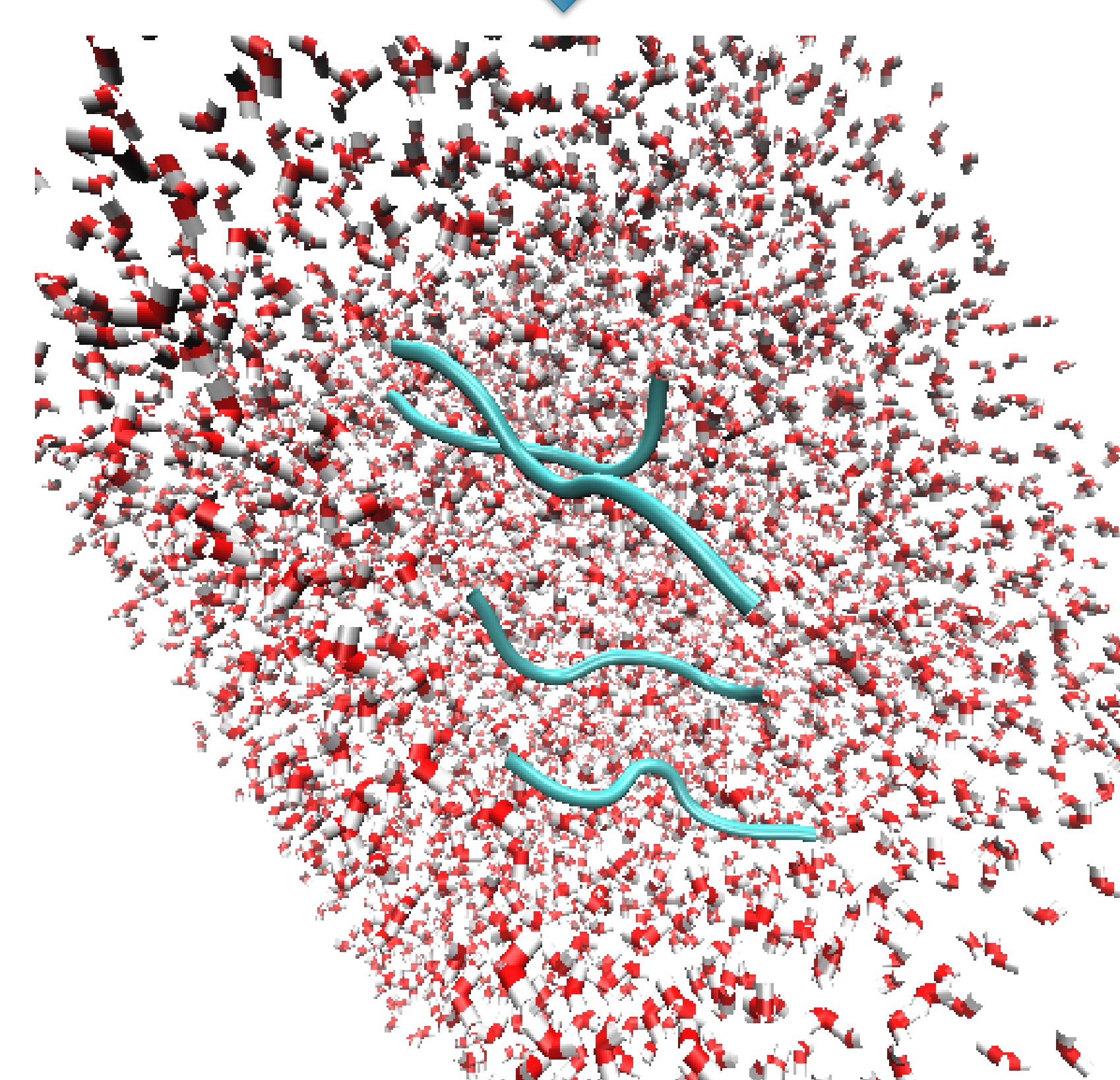


- 81 nanoseconds. This shows the complete dissociation of the amyloid structure.

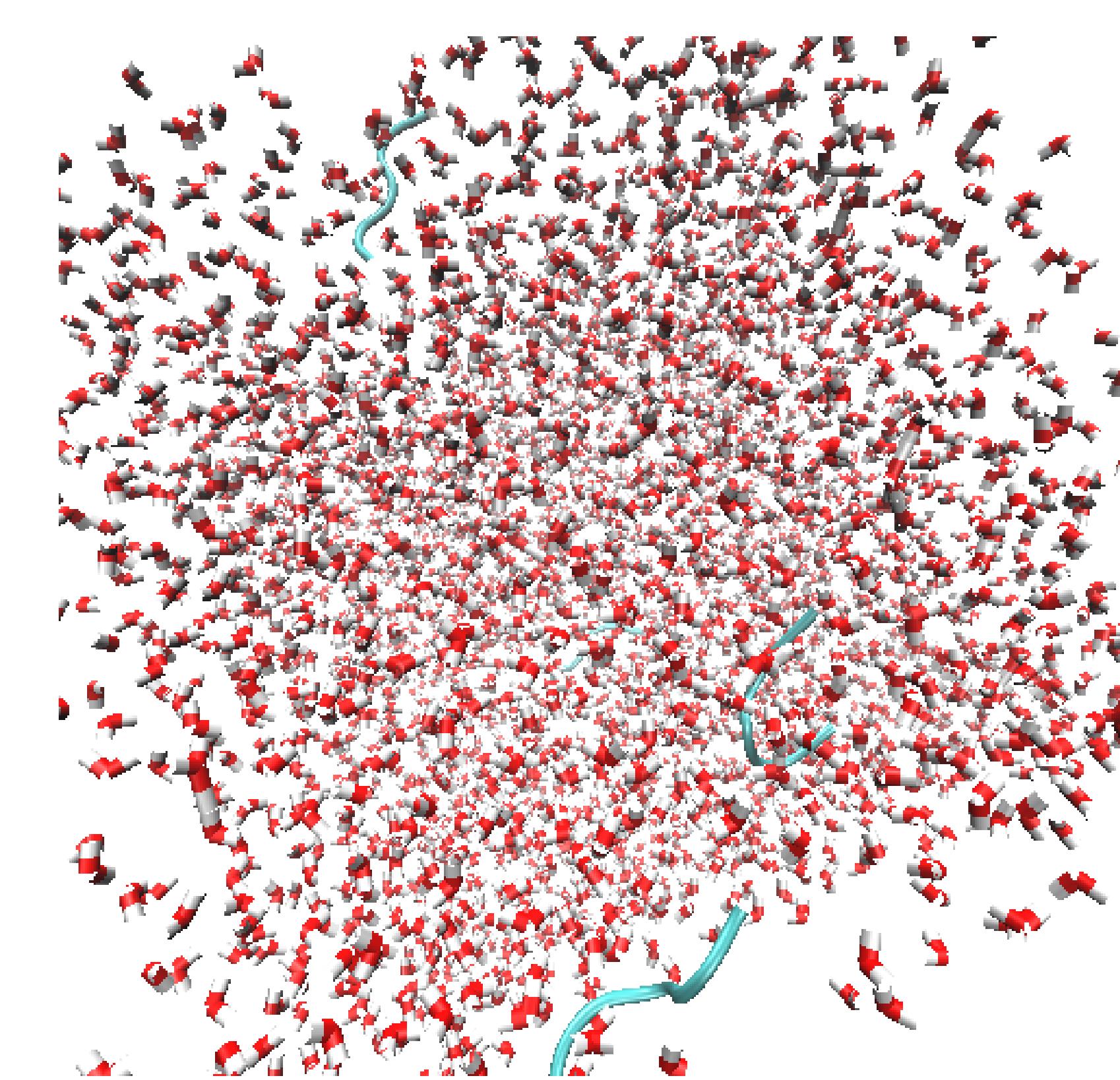
VEALYL RESULT



- Initial configuration



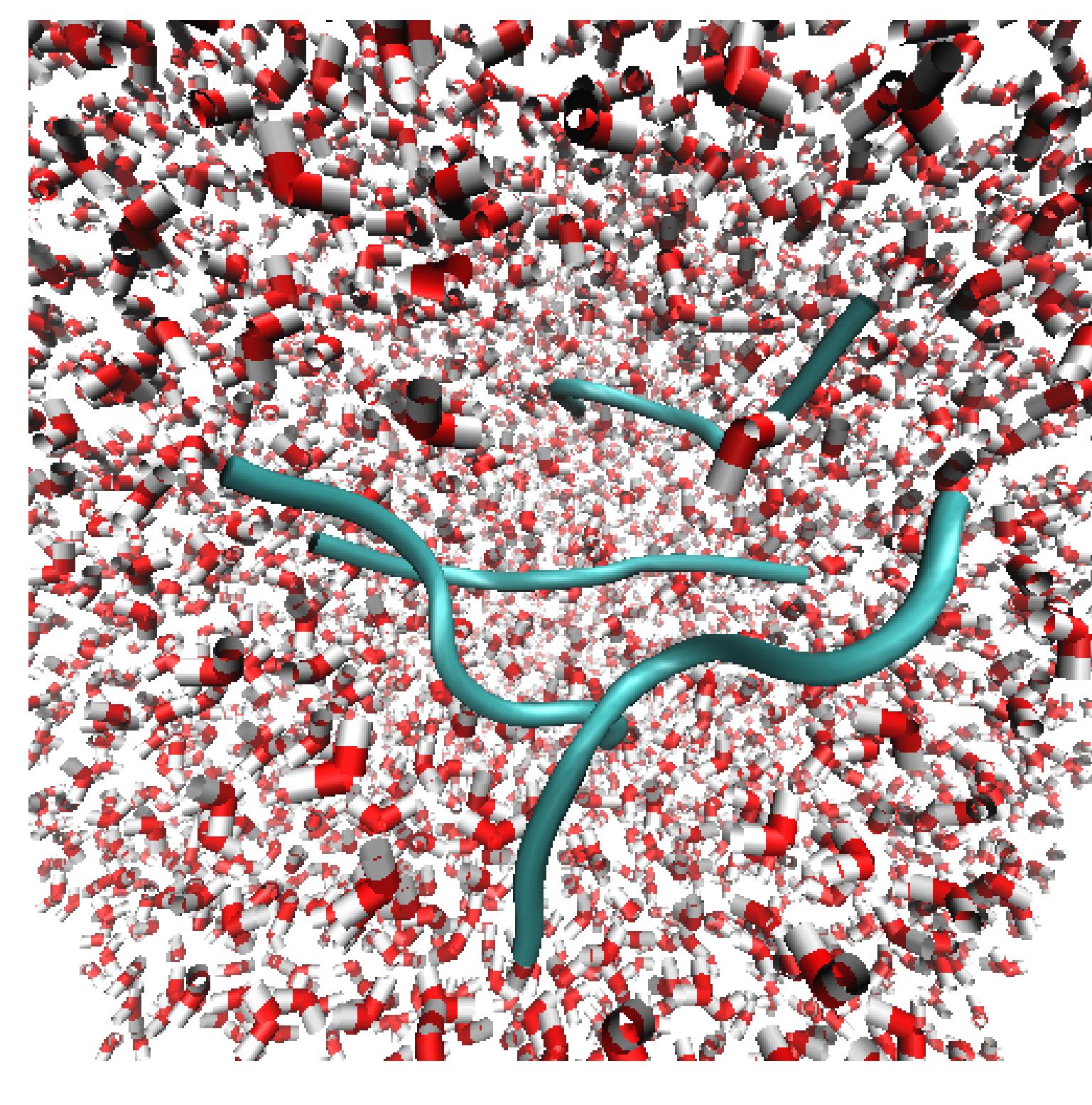
- At 55 nanoseconds



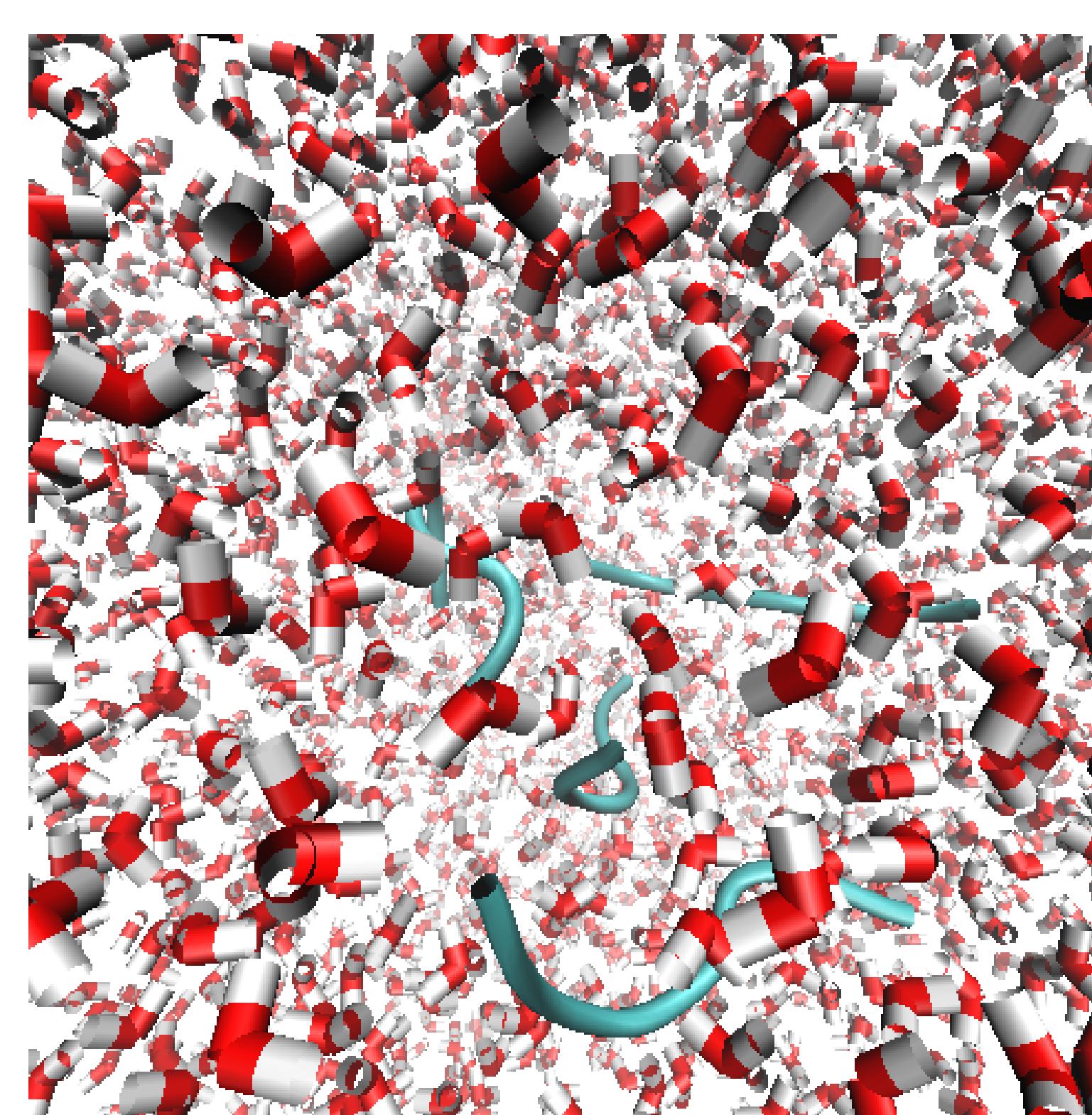
- This is the final configuration

Figure 1: VEALYL Simulation

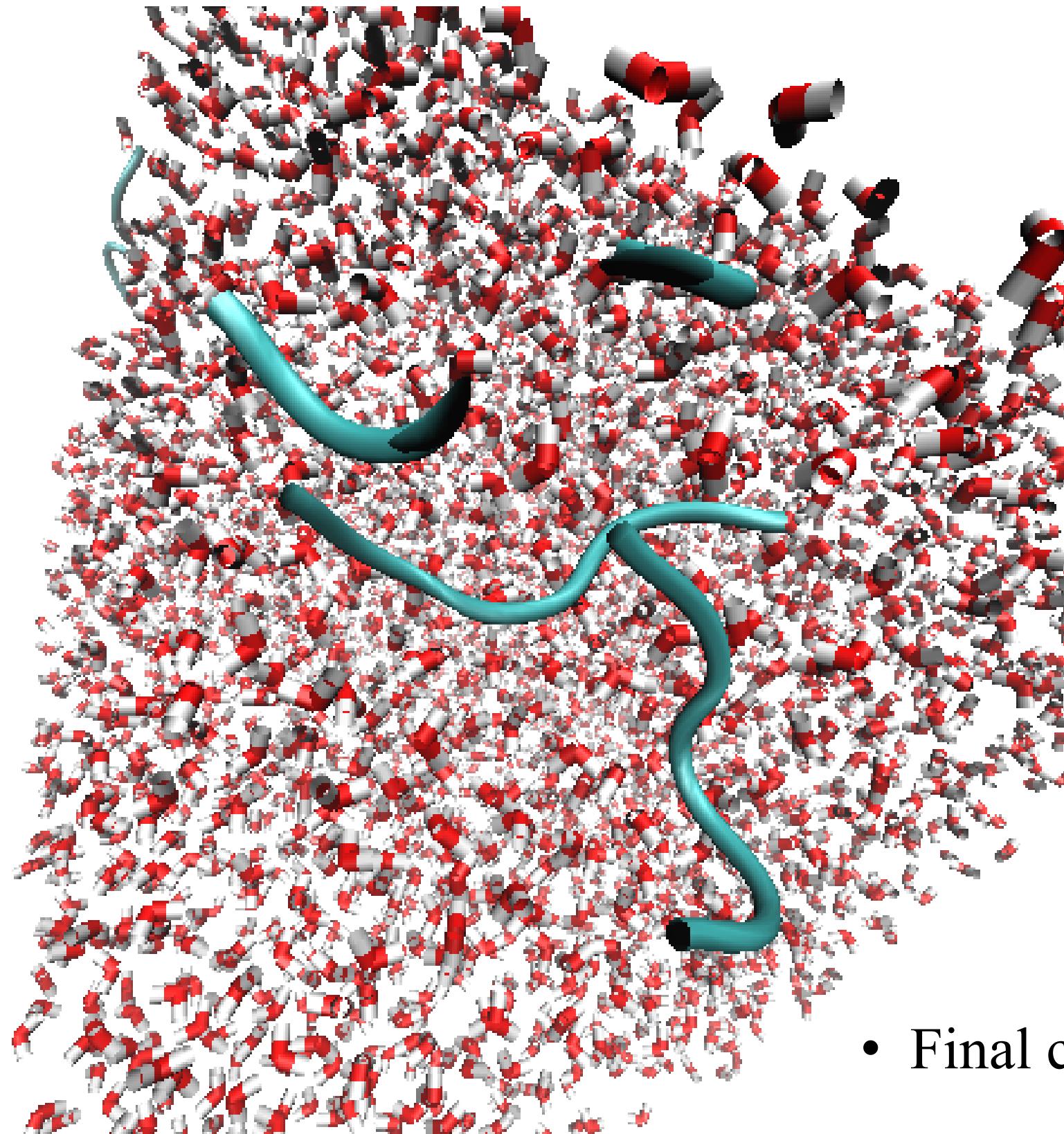
IFEADV RESULT



- Initial configuration



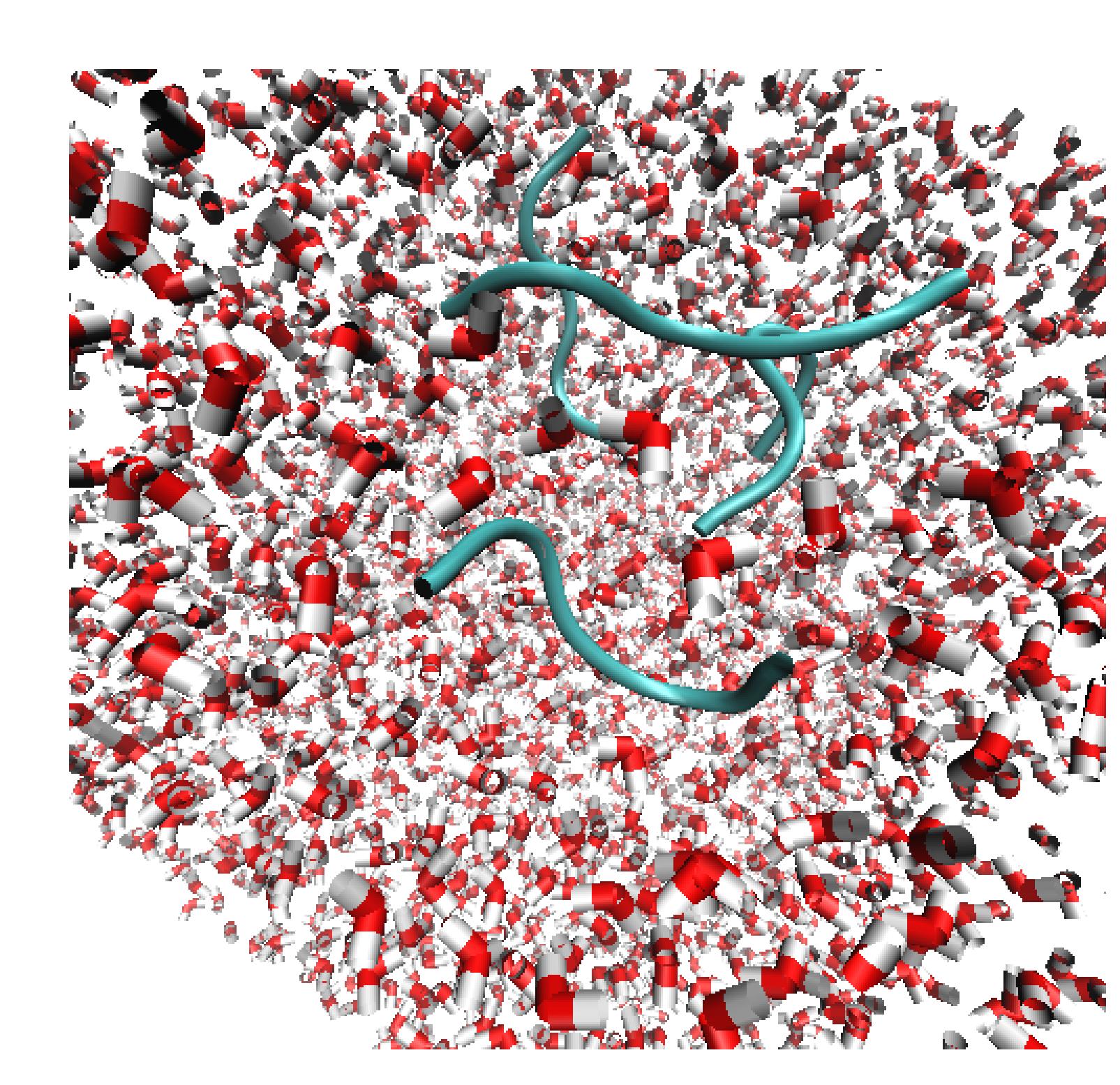
- At 45 nanoseconds



- Final configuration

Figure 2: IFEADV Simulation

IFEADV TAKEAWAY



- At 85 nanoseconds. The peptide structure did not retain its original form.

CONCLUSION

- Limitations:** The use of four amyloid proteins to run the simulation gives a less realistic view of the stability of the structure.
- Further research** should be done to include more amyloid proteins, so that it is a more realistic simulation of amyloid structures.

AKNOWLEDGEMENT

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REFERENCE

1. Ma, B., & Nussinov, R. (2006). Simulations as analytical tools to understand protein aggregation and predict amyloid conformation. *Current Opinion in Chemical Biology*, 10(5), 445-452.
2. Michael, R. S, et al (2007). Atomic structures of amyloid cross-β spines reveal varied steric zippers. *Nature*, 447(7143), 453.

ABBREVIATION

- VEALYL: Amyloid structure of insulin
- IFEADV: Amyloid Beta Polymorphic form 2
- MDS: Molecular Dynamics Simulations

Figure 1: VEALYL Simulation

Figure 2: IFEADV Simulation