



A computational investigation of folding free energy surfaces and structural characterization of Staphylococcal Protein A

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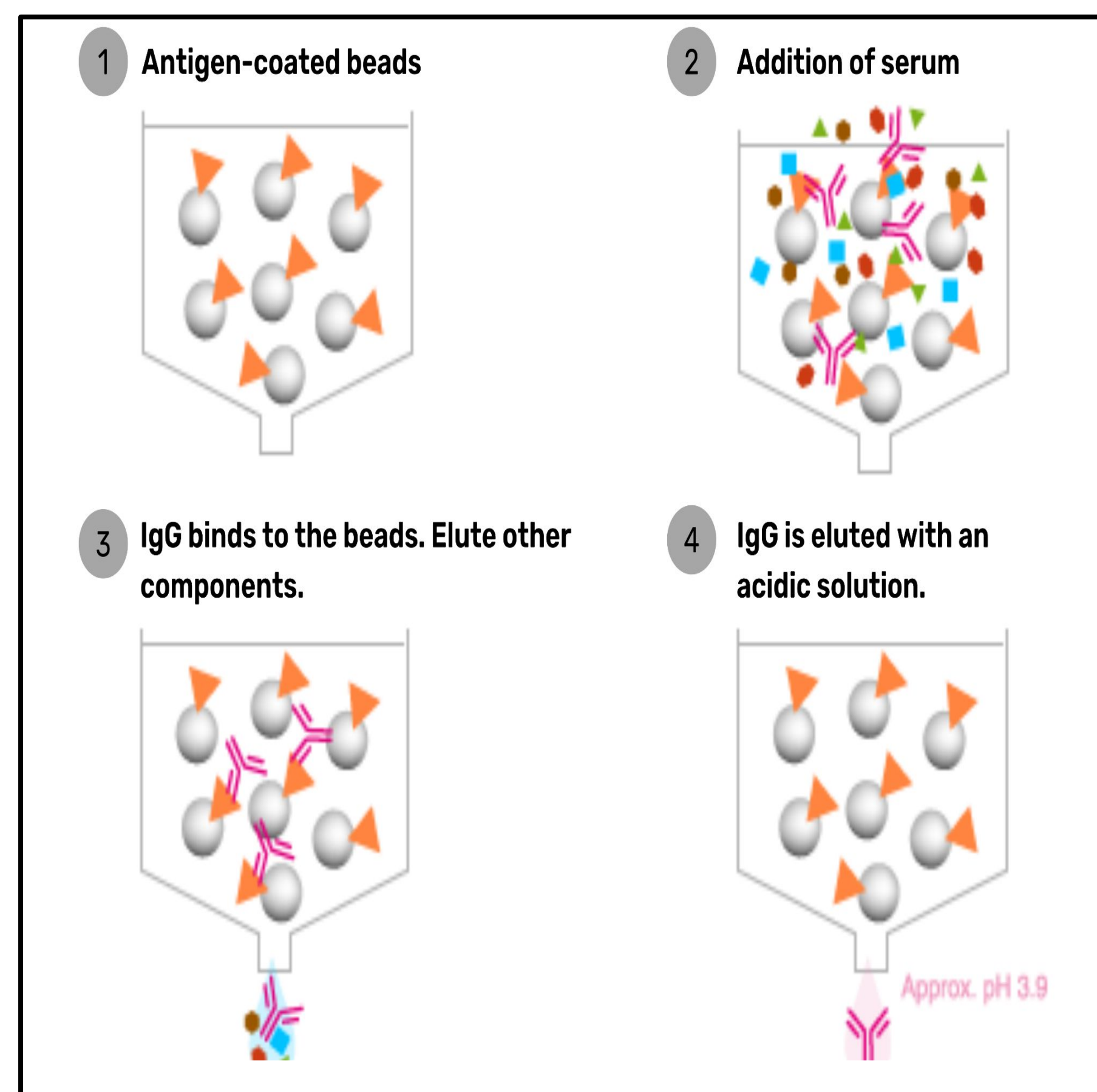
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What is Staphylococcal Protein A?

- SpA is a component of the cell wall of the bacteria *S. aureus*.
- The significance of SpA is its high affinity and exceptional specificity to antibodies IgG.
- SpA has 5 homologous domains that can bind to the Fc fragment of IgG.

Due to its affinity to IgG, Protein A is utilized in the Purification of Monoclonal Antibodies IgG



Protein A in Affinity Chromatography Purification of Monoclonal Antibodies IgG

However, we currently lacked a detailed structural and thermodynamic characterization of the full-length protein A.

While the individual domains are well-studied, a detailed structural and thermodynamic characterization of the full-length SpA has been elusive, due to the predominant intrinsic disorder between the folded domains.

⇒ Therefore, we performed advanced-sampling molecular dynamic simulations of full-length SpA to investigate the folding free energy surfaces and the behaviors of the flexible regions of SpA.

1. Simulation 1: We run the simulation of the full-length SpA to analyze the behavior of SpA as a whole.
2. Simulation 2: We restrained the folded domains for the duration of the simulation to observe the behavior of the flexible regions.

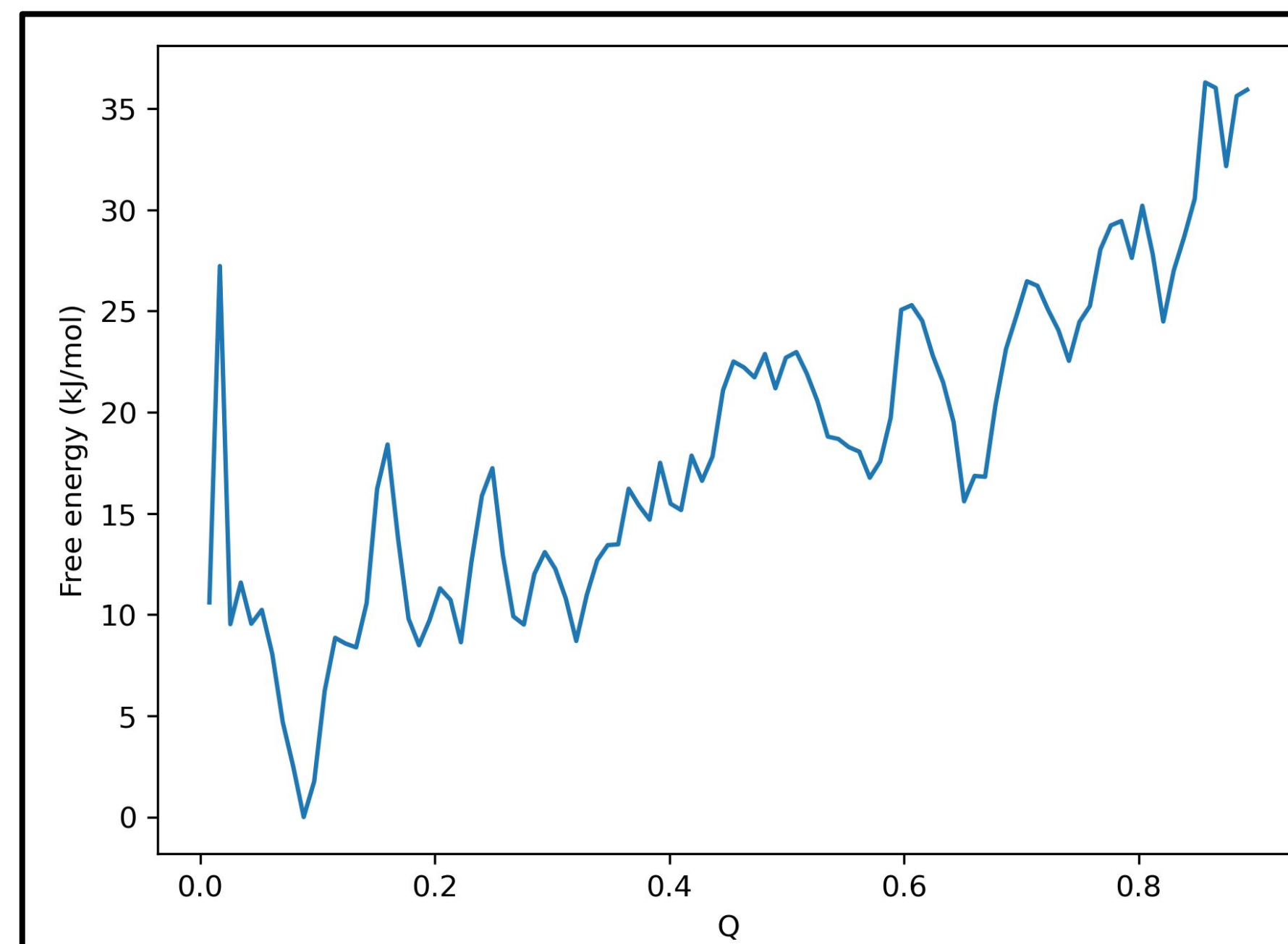


Fig 1. Free Energy (kJ/mol) as a Function of Q. Q is a measure of similarity between the conformation of the sampled SpA and the AlphaFold predicted structure of SpA.

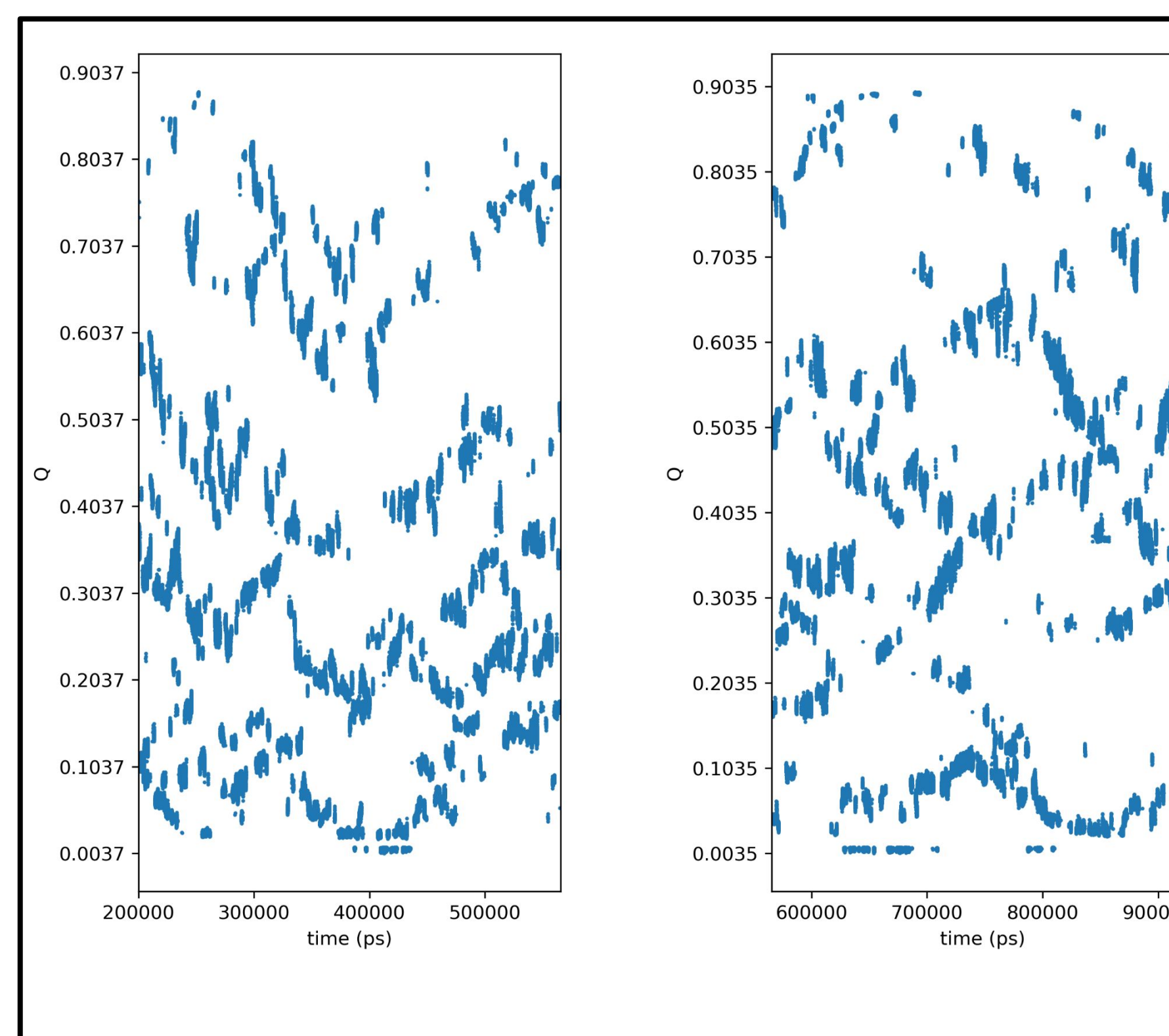


Fig 2. Q as a Function of Time in Simulation 1

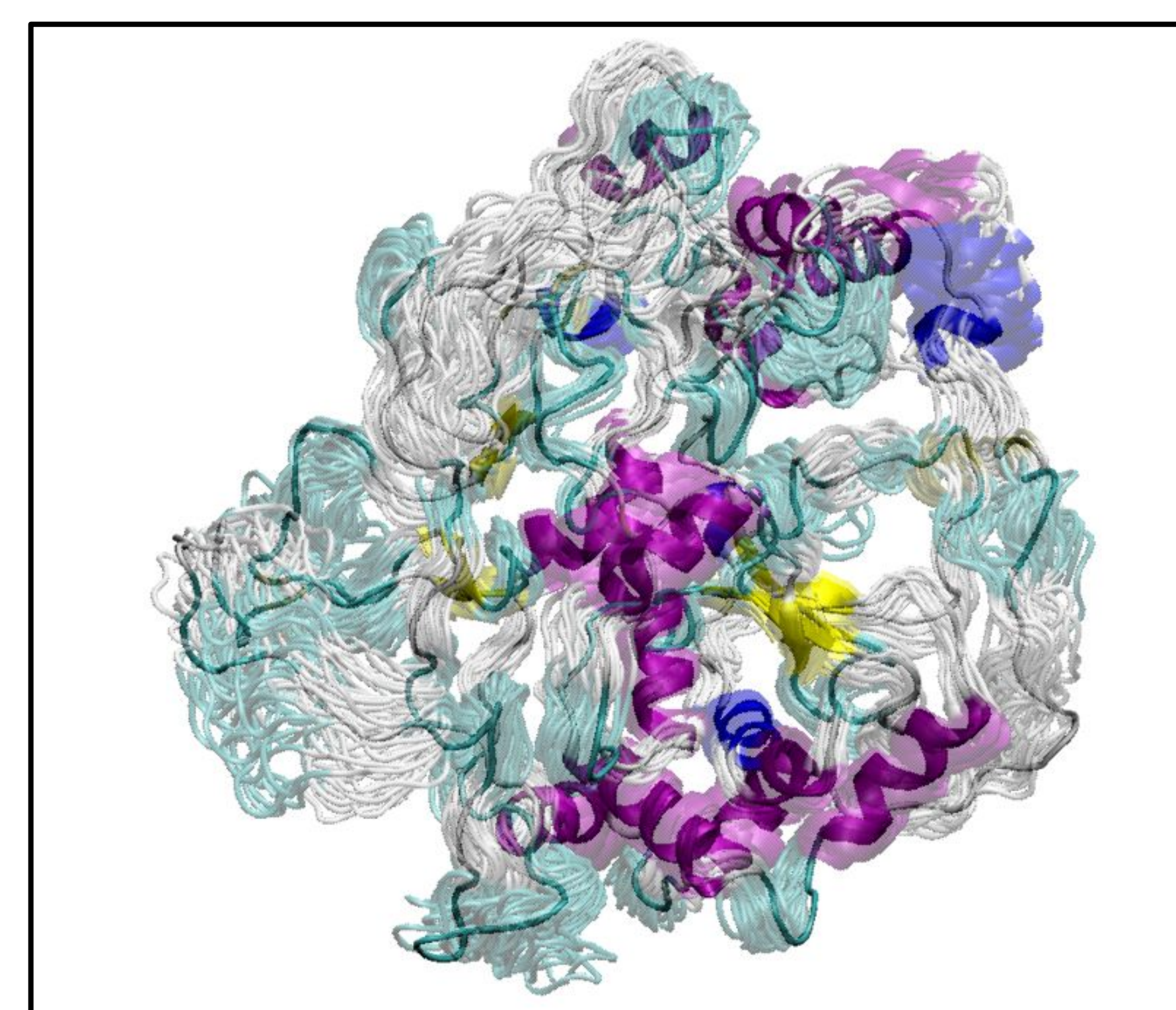


Fig 3. The Most Predominant Conformation of SpA in Simulation 1.

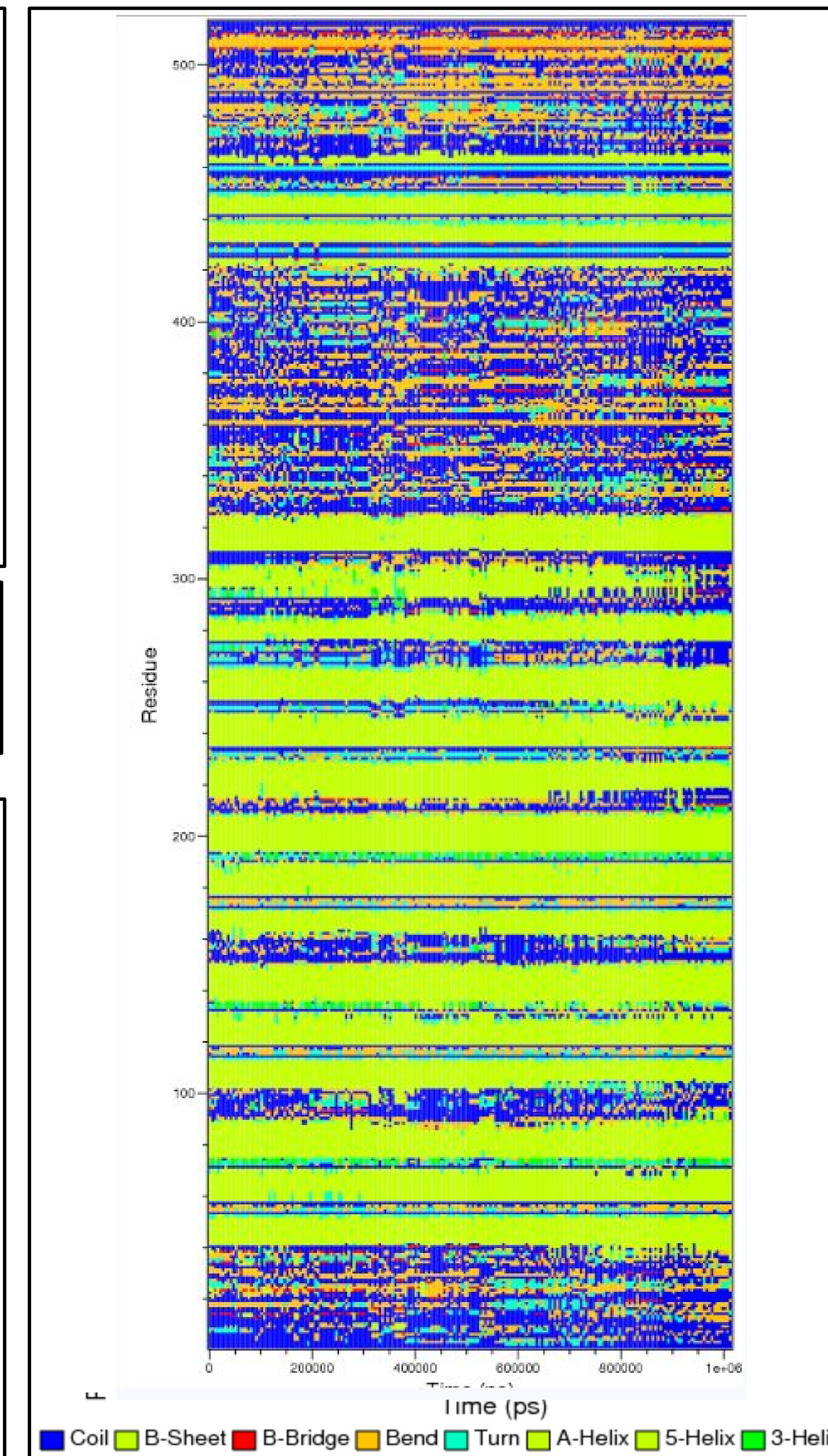


Fig 4. Secondary Structure of SpA in Simulation 2

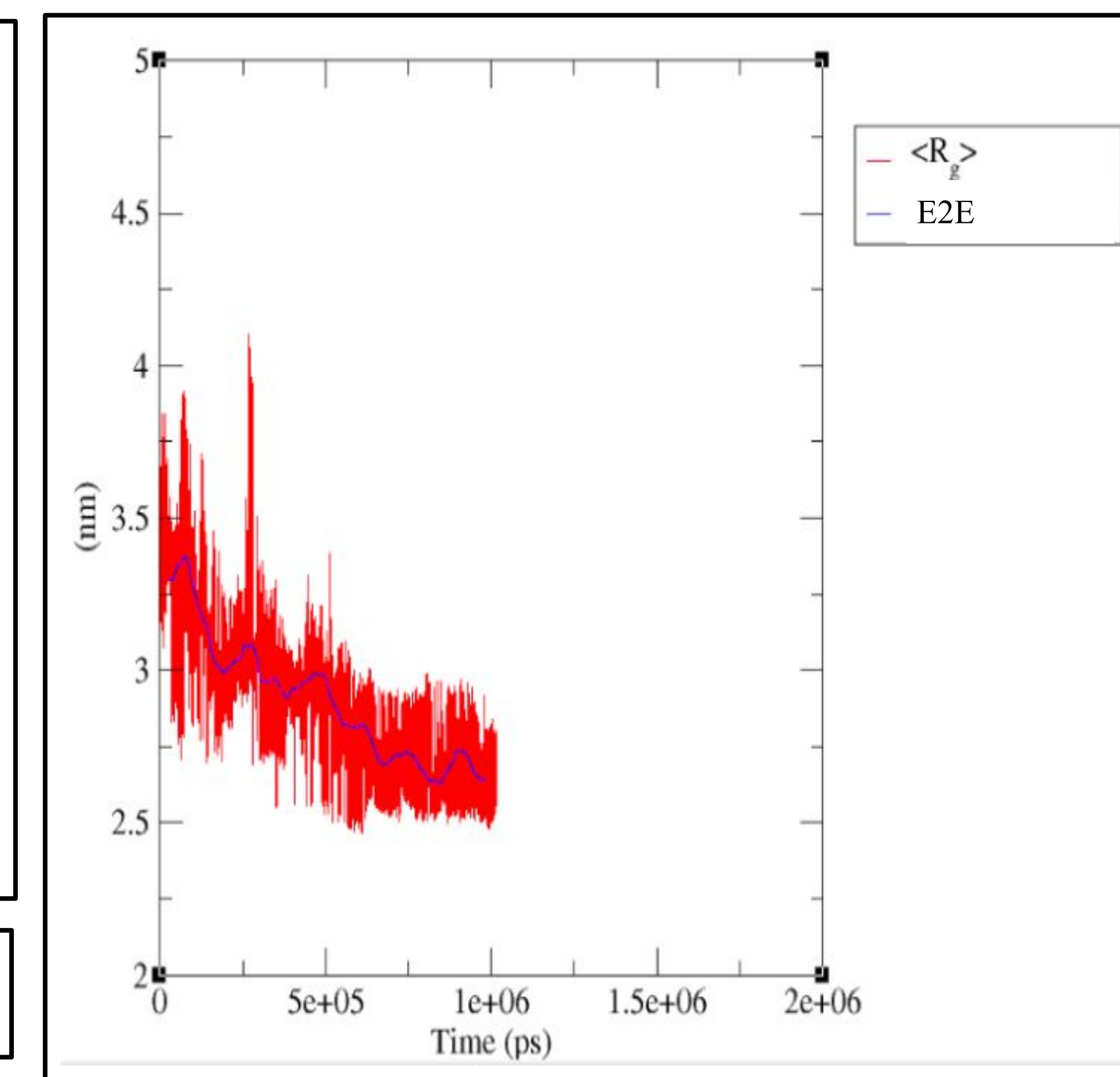
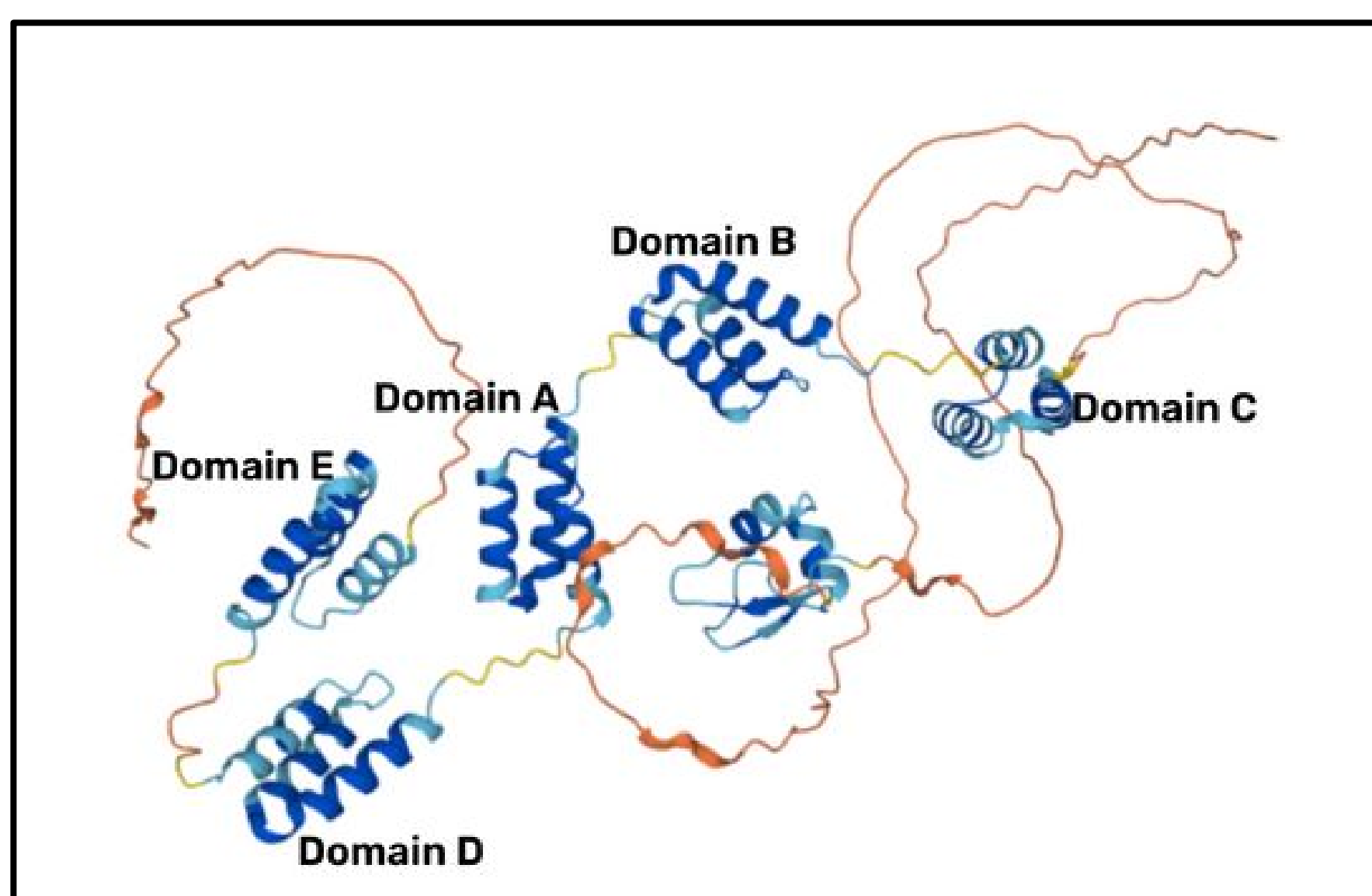
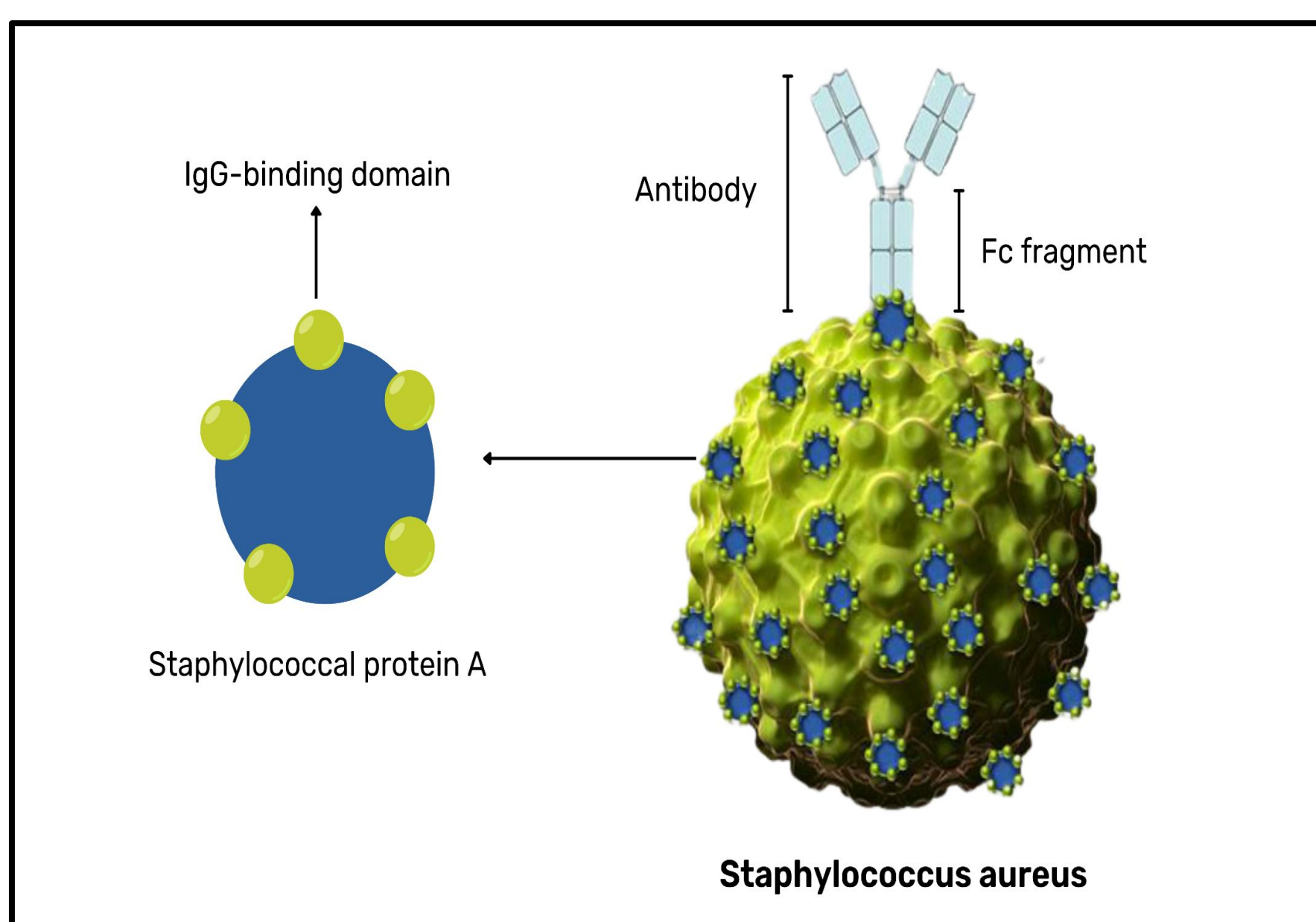


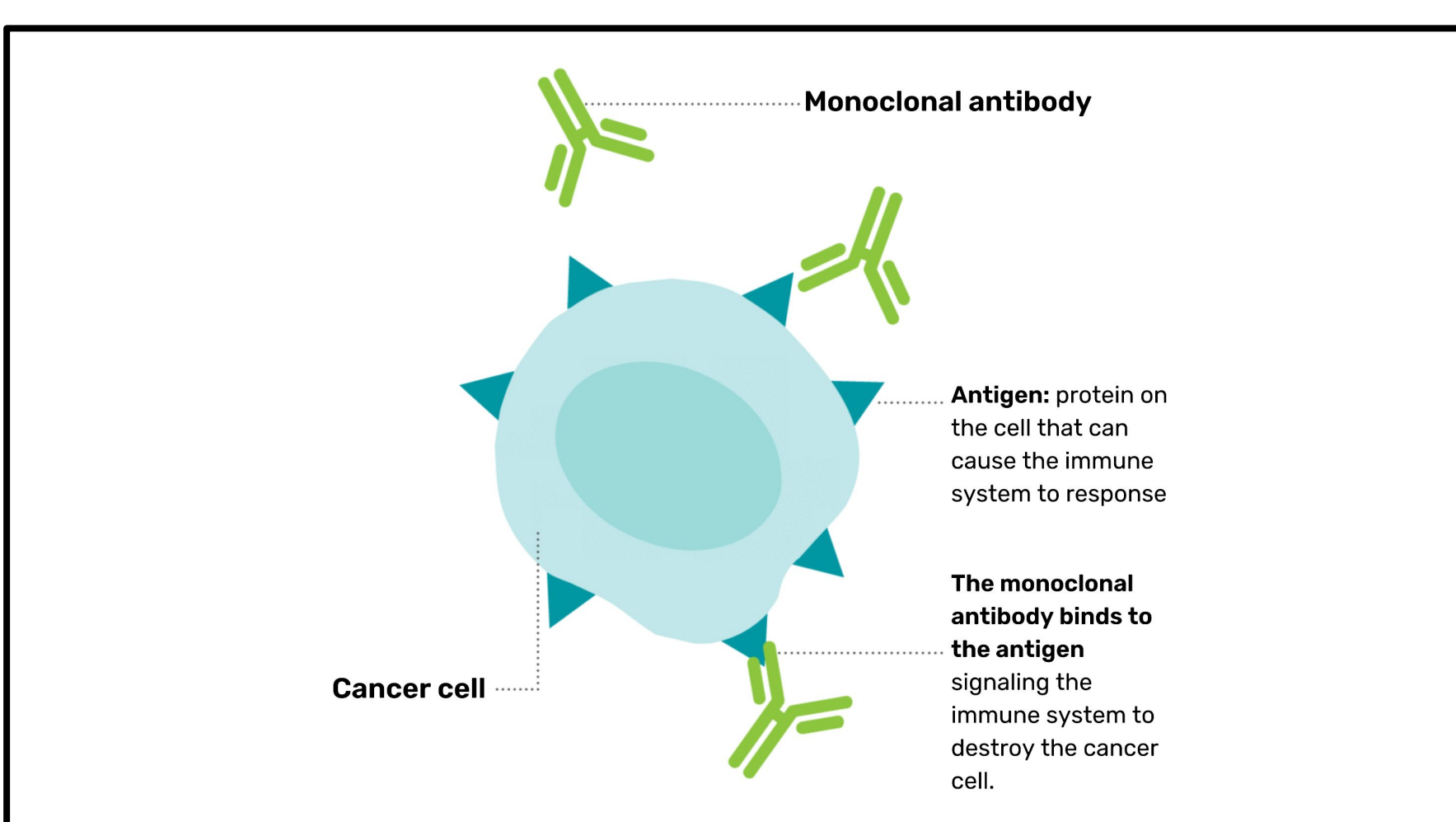
Fig 5. Radius of gyration and E2E of SpA in Simulation 2



AlphaFold Predicted Structure of Full-Length Protein A



SpA Binds to the Fc fragment of Antibody



Monoclonal Antibody Targets the Antigen Unique To Or Overexpressed By Tumor Cell