An Insight to HIV-1 Assembly Through Normal Mode Analysis

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The human immunodeficiency virus type 1 (HIV-1) is a retrovirus that causes the acquired immunodeficiency syndrome (AIDS), a condition in humans in which the immune system progressively fails. The group specific antigen (Gag) protein is the fundamental building block of HIV, driving particle formation. The Gag protein is a dynamical object, where its flexibility is inherent for changes leading to assembly. Specifically, the SP1 domain undergoes a shift in conformation to become α-helical and that this shift is an essential early step in particle assembly [1]. Additionally the zinc fingers of the nucleocapsid (NC) are highly flexible, allowing different conformations of the protein to interact with almost any nucleic acid, with different specificity [2].

We have analyzed the vibrational modes of free NC and NC-RNA constructs, as well as free SP1NC and SP1NC-RNA constructs for different stem loops of Ψ RNA using an all-atom normal model analysis. We demonstrate that normal modes can be used to analyze how the movement of the protein changes when bound to specific RNA during HIV viral assembly. We find that SP1NC bound to SL3 Ψ produces the most rigid construct, agreeing with the high affinity binging of NC to SL3. Our results also suggest that SL3 binding promotes the helical conformational switch of the SP1 region, supporting the theory that changes in the local environment of SP1 occur when when Gag oligomerizes on nucleic acid [1].

References

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