# Mechanistic studies of Nucleic Acid Chaperone activities of Retroviral Nucleocapsid Proteins

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Abstract:

The nucleocapsid (NC) proteins are small nucleic acid (NA)-binding proteins containing two functional and structural domains, a basic N-terminal domain and two CCHC-type zinc fingers. It has been observed, both in vivo and in vitro, that NC proteins behave as multifunctional viral proteins, which can stabilize the virion and chaperone several NA structural rearrangements, such as the genomic RNA dimerization, strand transfers in reverse transcription and proviral DNA integration, which are crucial to the retroviral life-cycle. Since NC may be a potential target for anti-viral therapy, it is essential to study the complicated dynamic NC-NA interactions. However, ensemble measurements only provide averaged information about the overall kinetics, and are thus incapable of resolving the heterogeneous kinetics and underlying reaction pathways involved in the NC-chaperoned NA strand transfers. Single molecule Fluorescence Resonance Energy Transfer (smFRET), which serves as a nanoscale spectroscopic ruler, can be used to study one molecule at a time, allowing us to develop detailed, molecular-level understanding of the NC chaperone activities. Furthermore, the local environment in the cytoplasm is quite different from the salted buffer solutions used in smFRET. In order to probe more physiologically relevant situations, we choose poly-ethylene glycol (PEG) as a model neutral polymer cosolute to study the macromolecular crowding effects on NC-chaperoned NA anealing.