

Abstract Submitted
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The Role of gp120 Flexibility in Binding A.J. RADER, Indiana University-Purdue University Indianapolis — Current treatment of the human immunodeficiency virus (HIV) focuses on delivering several drugs to a few specific viral protein targets. A complementary antiviral therapy involves targeting the process of viral entry. Viral entry is a dynamic process which involves a series of conformational changes by the HIV envelope glycoproteins (gp120 and gp41). The extraordinary conformational flexibility, glycosylation and strain variability of these proteins complicate the development of an effective vaccine. We present results from the graph theoretical analysis of flexibility and rigidity using the Floppy Inclusion and Rigid Substructure Topography (FIRST) software for all known HIV-1 gp120 structures. Comparisons between structures using this mechanical stability and intrinsic flexibility is used to identify a consensus rigid region that might serve as drug targets in a pre-complex conformation. Furthermore, analysis of structures with various binding partners illustrates the differential partitioning of mechanical flexibility and strain. We relate these differences in mechanical stability to thermodynamic differences in binding and stabilizing mutations.

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