Abstract Submitted for the MAR13 Meeting of The American Physical Society

A Binding Model and Similarity for Flexible Modular Proteins¹ GABRIELL MÁTÉ, CHRISTOPH J. FEINAUER, ANDREAS HOFMANN, Institute for Theoretical Physics, Heidelberg University, Germany, SEBASTIAN GOLDT, Fitzwilliam College, Cambridge University, Cambridge, England, LEI LIU, DIETER W. HEERMANN, Institute for Theoretical Physics, Heidelberg University, Germany — Modular proteins are one of the most commonly found disordered protein motifs. An example is CTCF, a protein that has been named the master waver of the genome i.e., the organizer of the 3D structure of the chromosomes. Using NMR and numerical simulations, much progress has been made in understanding their various functions and ways of binding. Modular proteins are often composed of protein modules interconnected by flexible linkers. They can be imagined as "beads on a string." We argue that when the number of beads is small, these structures behave like a self avoiding random walk. Nevertheless, when binding to a target, linkers can fold in more ordered and stable states. At the same time, folding can influence functional roles. We show that the flexibility of the linkers can boost binding affinity. As a result of flexibility, the conformations of these proteins before and after binding are different. So this implies that generic binding site prediction methods may fail. To deal with this we introduce a new methodology to characterize and compare these flexible structures. Employing topological concepts we propose a method which intrinsically fuses topology and geometry.

¹GM gratefully acknowledges support from the HGS-MathComp and the RTG 1653.

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Date submitted: 06 Nov 2012

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