MOLECULAR RECOGNITION IN ANTIBODY–ANTIGEN COMPLEXES

BY ERIC J. SUNDBERG AND ROY A. MARIUZZA

Center for Advanced Research in Biotechnology,
University of Maryland Biotechnology Institute, Rockville, Maryland 20850

With the numerous detailed molecular descriptions of antibody–antigen interfaces, the structural study of these molecular interactions has evolved from an attempt to understand immunological function to their use as model systems for protein–protein interactions. In this chapter, we describe the structural aspects common to antibody–antigen interfaces and discuss the roles they may play in antibody cross-reactivity and molecular mimicry. More detailed analysis of these interfaces has required the marriage of structural studies with extensive mutagenesis and thermodynamic analysis efforts. Here, we discuss the thermodynamic mapping of interfaces for two model antibody–antigen complexes, including the identification of thermodynamic hot spots in binding and the various mechanisms used to accommodate interface mutations. We also discuss the functional roles for protein plasticity in antigen recognition, including the entropic control of antibody affinity maturation and the use of induced fit mechanisms of different types and to varying degrees by mature antibodies in binding their specific antigens.

I. Introduction

The ability of proteins to form specific, stable complexes with other proteins is fundamental to most cellular processes, including signal

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