

## **Probing the Structure and Dynamics of Antigen-Antibody Interactions Using Synchrotron Radiation and Mass Spectrometry**

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Antibodies raised in response to immunization with a native antigen tend not to react with denatured preparations of the same protein. This supports the view that the interaction between antibody and antigen is a highly conformation-dependent process. Yet our understanding of these interactions in the humoral B-cell response is largely based on crystallographic studies that are not amenable to widespread use given the time necessary to acquire and interpret such data and the requirement that the antigen-antibody complex must be isolated in a pure crystalline form. We are developing a new technique capable of studying the interactions between antigens and antibodies in solution with high structural resolution and on millisecond timescales using synchrotron radiation and mass spectrometry. Radiolysis of aqueous solutions of protein antigens or their complexes results in the production of a high flux of hydroxyl radicals that have been found to oxidize certain reactive amino acid residues. The site and extent of reaction, determined by mass spectrometry, is influenced in part by the accessibility of these residues to the bulk solvent. This enables a three-dimensional "footprint" of the surface of interaction between antigen and antibody to be identified from studies of their complex and the antigen alone. Initial studies for a model protein are being extended to a number of other important antigens, among them the surface antigens of the influenza virus.