

# **Affinity selection in germinal centers: cautionary tales and new opportunities**

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## **Abstract-**

**Our current quantitative knowledge of the kinetics of antibody-mediated immunity is partly based on idealized experiments throughout the last decades. However, new experimental techniques often render contradictory quantitative outcomes that shake previously uncontroversial assumptions. This has been the case in the field of T-cell receptors, where recent techniques for measuring the 2-dimensional rate constants of T-cell receptor&ndash;ligand interactions exposed results contradictory to those obtained with techniques measuring 3-dimensional interactions. Recently, we have developed a mathematical framework to rationalize those discrepancies, focusing on the proper fine-grained description of the underlying kinetic steps involved in the immune synapse. In this perspective article, we apply this approach to unveil potential blind spots in the case of B-cell receptors (BCR) and to rethink the interactions between B cells and follicular dendritic cells (FDC) during the germinal center (GC) reaction. Also, we elaborate on the concept of &ldquo;catch bonds&rdquo; and on the recent observations that B-cell synapses retract and pull antigen generating a &ldquo;retracting force&rdquo;, and propose some testable predictions that can lead to future research.**

**Index Terms-** antibody-antigen binding; kinetics; mathematical modeling; catch-bond; allostery

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