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Weaker is better: how weak transient molecular interactions give rise to robust, dynamic immune protection

The longstanding view in chemistry and biology is that high-affinity, tight-binding interactions are optimal for many essential functions, such as receptor-ligand interactions. Yet, an increasing number of biological systems are emerging that challenge this view, finding instead that low-affinity, rapidly unbinding dynamics can be essential for optimal function. These mechanisms have been poorly understood in the past due to the inability to directly observe such fleeting interactions and the lack of a theoretical framework to mechanistically understand how they work. In fact, it is only by tracking the motion of effector nanoprobe that afford detection of multiple such interactions simultaneously, coupled with inferences by stochastic modeling, Bayesian statistics, and bioimaging tools, that we recently begin to obtain definitive evidence substantiating the consequences of these interactions. A common theme has begun to emerge: rapidly diffusing third-party molecular anchors with weak, short-lived affinities play a major role for self organization of micron-scale living systems. My talk will demonstrate how these ideas can answer a longstanding question: how mucosal barriers selectively impede transport of pathogens and toxic particles, while allowing diffusion of nutrients.