Abstract for an Invited Paper
for the MAR09 Meeting of
The American Physical Society

**How T lymphocytes see antigen**

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Complex organisms, like humans, have an adaptive immune system that enables us to do battle with diverse pathogens. This flexible system can also go awry, and many diseases are the direct consequence of the adaptive immune system failing to discriminate between markers of self and non-self. The orchestrators of adaptive immunity are a class of cells called T lymphocytes (T cells). T cells recognize minute numbers of molecular signatures of pathogens, and T cell recognition of these molecular markers of non-self is both specific and degenerate. The specific (yet, cross-reactive), diverse, and self-tolerant T cell repertoire is designed in the thymus. I will describe how an approach that brings together theoretical and computational studies (rooted in statistical physics) with experiments (carried out by key collaborators) has allowed us to shed light on the mechanistic principles underlying how T cells respond to pathogens in a digital fashion ("on" or "off"), and how this molecular machinery coupled with frustration (a la spin glasses) plays a key role in designing the special properties of the T cell repertoire during development in the thymus.