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**Tuesday, March 1st 2022, 10:00 s.t.**



MAX PLANCK INSTITUTE  
OF COLLOIDS  
AND INTERFACES



## Signal transmission and selectivity in T-cell receptor triggering

Abstract: Despite more than two decades of research, two central questions in T cell activation remain largely unanswered: (1) How is antigen recognition at the extracellular side of the T cell receptor (TCR) transmitted to the intracellular activation motifs of the TCR – CD3 complex? (2) And how do T cells discriminate selectively between antigenic peptides and self peptides despite rather small differences in binding affinities? In my talk, I will present recent results from atomistic simulations of the membrane-embedded TCR – CD3 complex [1] and from simulations of an elastic-membrane model of T cell adhesion [2]. Our atomistic simulations of the TCR – CD3 complex indicate that the extracellular (EC) domain of the TCR is highly variable in its orientation by attaining tilt angles relative to the membrane normal that range from  $15^\circ$  to  $55^\circ$ . The tilt angle of the TCR EC domain is both coupled to a rotation of the domain and to characteristic changes throughout the TCR – CD3 complex. Our simulations provide insights on conformational changes of the complex in response to tilt-inducing forces invoked by force-based models of T cell activation, and on tilt-induced variations in the membrane separation of bound TCR – MHC complexes that may be relevant for size-based segregation from TCRs. Our simulations of an elastic-membrane model of T cell adhesion illustrate a cooperativity of TCRs bound to antigenic or self peptides in stabilizing close-contact zones, which precede T cell activation according to size-based segregation models of T cell activation. The cooperative stabilization of close-contact zones in our simulations is sensitive to few foreign-peptide-MHC complexes and occurs at a rather sharp threshold affinity of these complexes, which implies selectivity.

[1] PR Pandey et al., eLife 2021, 10:e67195

[2] B Rozycki and TR Weikl, Cells 2021, 10:1023.

**Thomas Weikl** received his Ph.D. degree in physics from the University of Potsdam in 1999. In 2002, he became group leader at the MPI of Colloids and Interfaces in Potsdam.

All interested colleagues are welcome  
to this online seminar lecture  
(45 min. presentation followed by discussion)

> **ZOOM LINK**

Meeting ID: 996 4397 7328

Password: 5f5\$g@23

