

P027 Forced rupture of the neural cell adhesion molecule complex
**Venkat Maruthamuthu, Klaus Schulten and
Deborah E. Leckband**

University of Illinois, Urbana-Champaign

We use steered molecular dynamics simulations to dissociate the complex formed between the outermost two Ig domains (Ig12) of the Neural Cell Adhesion Molecule (NCAM), a member of the Ig super family of cell adhesion molecules (IgSF CAMs). We consider the Ig12-Ig12 complex present in the crystal structures of both the Ig12 and Ig123 NCAM fragments. We find that the force response consists of two distinct stages: (i) an initial stretching phase, wherein the end-to-end length of the complex (5 nm) increases by as much as 100% due only to a change in the relative orientation of adjacent domains on the same molecule and (ii) dissociation of the complex. We find that the initial stretching phase involves the rupture of only one of the two intra-molecule, inter-domain H-bond linkers – E16-K98, and not E11-R177. We also show that a low constant force of 50 pN is sufficient to stretch the complex by 60% of its end-to-end length. Analysis of the unbinding trajectories shows that, among the aromatic residues identified from the crystal structures as important, F19 sustains a greater tensile force than Y65. In addition to the atomistic details of NCAM complex rupture, this work reveals how a multi-domain IgSF CAM complex responds to near-physiological tensile forces.