

## **The role of membrane-mediated interactions in the formation of membrane adhesion domains**

Oded Farago

*Department of Biomedical Engineering, Ben Gurion University of the Negev,  
Be'er Sheva 84105, Israel – ofarago@bgu.ac.il*

### **Abstract**

Cellular adhesion is achieved when specialized membrane proteins form specific receptor–ligand bonds with other molecules in the extracellular matrix, the cytoskeleton or other cells. These adhesion bonds often aggregate and form large adhesion domains that provide strong cell anchoring and play a vital role in many biological processes such as signal transduction, cell motility and embryogenesis. Over the past years, many studies have been conducted to better understand the biophysical basis that drives adhesion bond aggregation. One possible source of attractive forces between adhesion bonds is the membrane–mediated interactions. These originate from the increase in the membrane's fluctuation entropy and decrease in its curvature elastic energy, occurring upon bond condensation. We use exact statistical–mechanical results, novel mean–field theories and computer simulations to analyze these two membrane–mediated mechanisms. We demonstrate that the fluctuation entropy mechanism produces a long range potential of mean force (PMF) which eliminates approximately half of the bonds' mixing entropy. The curvature energy generates a pair PMF with a characteristic range of  $\xi \sim 50\text{--}100$  nm, and can induce formation of semi–dilute adhesion domains with density of about one bond per unit area  $\xi^2$ . Remarkably, such densities resemble the densities of adhesion bonds in the immunological synapse, suggesting that membrane-mediated interactions may have an important role in the formation of such biological structures.