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Many Weak Interactions Make a Difference – from "Fuzzy" Biomolecular Self Assembly to Superselectivity

Multivalent interactions are frequent in biological systems. They are key to the regulation of many biomolecular recognition events and to the self-organization of biomolecules into materials. This is particularly so at surfaces and interfaces, because these naturally provide a platform for the multivalent presentation of binding partners. Despite their importance, multivalent interactions remain poorly understood.

In this lecture, I shall present results of our efforts to better understand the role of multivalent interactions in two biological systems that involve biological polymers: (i) the nuclear pore permeability barrier, a meshwork of intrinsically disordered proteins that fills the nuclear pores and makes nucleo-cytoplasmic transport selective, and (ii) the interface between polysaccharide-rich extracellular matrix and the cell surface which is key to the communication of cells with their environment.

To study these systems directly on the supramolecular level, we have developed an approach that draws on knowledge from several scientific disciplines. Exploiting surface science tools, we tailor-make model systems by directed self-assembly of purified biomolecules (proteins, lipid and polysaccharides) on solid supports. With a toolbox of biophysical characterization techniques – including quartz crystal microbalance, spectroscopic ellipsometry, atomic force and optical microscopy – these model systems are then investigated quantitatively and in great detail. The experimental data, combined with soft matter physics theory, allow us to develop a better understanding of how the properties of the individual molecules and interactions translate into supramolecular assemblies with distinct physico-chemical properties. The insights gained help us to uncover physical mechanisms underlying biological functions (*e.g.* 'superselectivity' in the targeting of cell surfaces or the permeability of membranes) and may also lead to novel applications in the life sciences.