Nanoscale films of biomolecular hydrogels – a novel platform to interrogate the relationship between supramolecular organization and dynamics, and biological function

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Nature has evolved complex materials that are exquisitely designed to perform specific functions. Certain proteins and glycans self-organize *in vivo* into soft and dynamic, strongly hydrated gel-like matrices. Illustrative examples of such biomolecular hydrogels are cartilage or mucus. Even though biomolecular hydrogels are ubiquitous in living organisms and fulfill fundamental biological tasks, we have today a very limited understanding of their internal organization, and how they function. The main reason is that this type of assemblies is difficult to study with conventional biochemical methods.

In order to study biomolecular hydrogels directly on the supramolecular level, we have developed an unconventional approach that draws on knowledge from several scientific disciplines. Exploiting surface science tools, we tailor-make model films with thicknesses in the nanometer range by directed self-assembly of purified components on solid supports. With a toolbox of biophysical characterization techniques, these model systems can be investigated quantitatively and in great detail down to the nanometer scale. The experimental data, combined with polymer theory, allow us to develop a better understanding of the relationship between the supramolecular organization and dynamics of biomolecular hydrogels, their physico-chemical properties and their biological function. To illustrate this concept, I will present two examples of our recent research. They relate to (i) a nanoscopic protein hydrogel that is responsible for the regulation of all macromolecular transport between the nucleus and the cytosol of eukaryotic cells [1] (Figure 1), and (ii) a microscopic glycoconjugate hydrogel that is involved in fertilization as well as cancer progression [2, 3].

References

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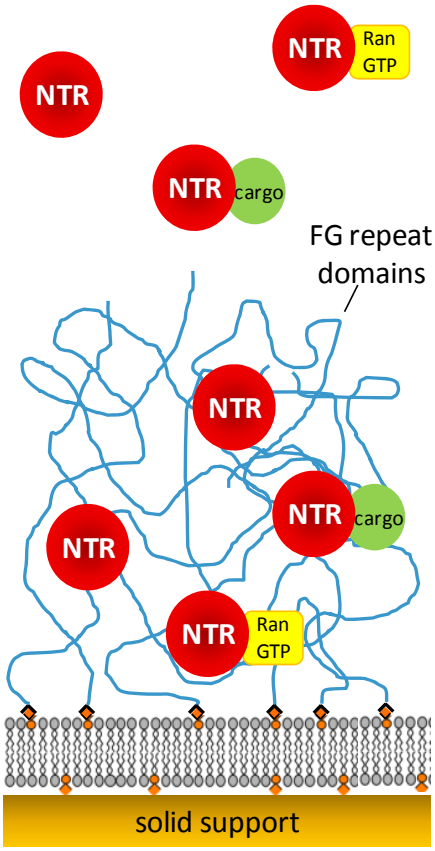

Figure 1: Macromolecular transport between the cell's nucleus and the cytosol occurs through nuclear pore complexes (NPCs). The transport is selective: objects (cargo) beyond a certain size (30 kDa) need to attach to soluble nuclear transport receptors (NTRs) in order to be channeled efficiently through the pore. A supramolecular assembly of specialized and natively unfolded protein domains within the NPC is thought to be the key component of the NPC´s permeability barrier. The mechanism behind transport selectivity is at present only poorly understood. We have developed ultrathin FG repeat domain films as a surface-confined model system of the permeability barrier. In this contribution, we will present how such model systems can provide insight into the mechanism of transport across the permeability barrier.