Biomolecular hydrogels – from supramolecular structure and dynamics to biological function

Ralf P. Richter

I2BM, Department of Molecular Chemistry, J. Fourier University, Grenoble, France
CIC biomaGUNE, Biosurfaces Unit, San Sebastian, Spain
Max-Planck-Institute for Intelligent Systems, Stuttgart, Germany

rrichter@cicbiomagune.es

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 immobilize one or several types of biomolecules (proteins, lipids and carbohydrates) on solid supports (typically gold, silica or glass) – with tight control on the distribution, mobility and molecular orientation. The functionalized surfaces serve as templates to self-assemble model films with thicknesses in the nanometer range from purified components. With a toolbox of biophysical characterization techniques, including quartz crystal microbalance (QCM-D), spectroscopic ellipsometry (SE), atomic force microscopy (AFM) and reflection interference contrast microscopy (RICM), these model hydrogels can be investigated in aqueous environment, quantitatively and in great detail. 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 a few examples of our recent research. They relate to (i) a nanoscopic protein hydrogel inside living cells that is responsible for the regulation of all macromolecular transport into and out of the nucleus [1] (Figure 1), (ii) microscopic hydrogel-like assemblies that are made from polysaccharides of the glycosaminoglycans family and their binding partners and that are involved in various physiopathological process such as inflammation, fertilization, cancer progression and immune response [2, 3, 4]. Our results may ultimately prove useful for the development of novel bioinspired devices, such as size and species selective filtration devices, or advanced biosensors, and for the development of novel diagnostic or therapeutic methods.

References

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Figures

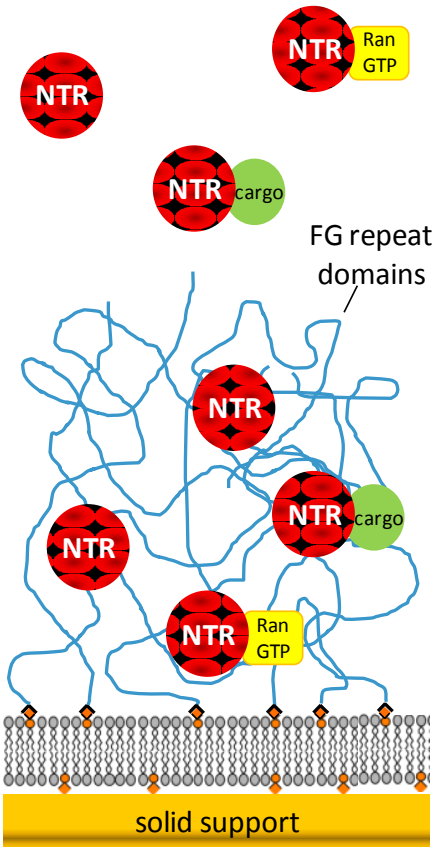

Figure 1: Macromolecular transport between the cell's nucleus and the cytosol occurs through nuclear pore complexes (NPCs). The transport is selective: objects (cargo) beyond a certain size (30 kDa) need to attach to soluble nuclear transport receptors (NTRs) in order to be channeled efficiently through 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.