

1. FINAL PUBLISHABLE SUMMARY REPORT

TRASNADE has been designated for the study of the transport properties of nanoscale assemblies and devices fabricated from polymers and polyelectrolytes, such as polyelectrolyte multilayers, polyelectrolyte brushes, polymer micelles, and polymersomes. Transport properties are fundamental for the rational design of delivery devices since the mechanism of transport will finally define release properties. For most of the mentioned nanodevices, transport properties are adjusted in an empirical way. A deeper understanding of the underlying principles and mechanisms of transport of matter is highly desirable for the optimization of drug delivery. Polymer nanoassemblies in aqueous environments are heterogeneous and at least partly random systems. A complex scenario of interactions for the diffusing species with the nanomaterial can be expected resulting in unusual transport properties. Measuring transport properties at the nanoscale requires novel experimental and theoretical approaches. A multidisciplinary approach was needed, ranging from synthesis, self-assembly, to physical chemistry and theoretical physics.

TRASNADE has been formed by an international team with the required and complementary expertise. The expertise of Prof. Gao's group, from Zhejiang University (China), in synthetic chemistry and self-assembly together with the expertise of the group of Dr. Moya, from CIC biomaGUNE (Spain), in materials science has been fundamental in the design and fabrication of supramolecular assemblies and their characterization. Polyelectrolyte multilayers based on poly(styrene sulfonate) (PSS) and poly allyl amine chloride (PAH), or PSS and poly(diallyldimethylammonium chloride) (PDADMAC) have been fabricated on planar and colloidal particles. Assembly on planar surfaces was followed by the Quartz Crystal Microbalance with Dissipation (QCM-D). Water content in the multilayers was determined by combination of QCM-D with ellipsometry.

Polymer brushes of poly(N-isopropylacrylamide) (PNIPAM) / poly[2-(methacryloyloxy)ethyl]trimethylammonium chloride (PMETAC)/ poly(sulfo propyl methacrylate) (PSPM) were synthesized by Atomic Transfer Radical Polymerization from planar and colloidal surfaces. Polymer brush growth was followed by QCMD and the water content determined by QCMD and ellipsometry. Brush thickness has been determined by Atomic Force Microscopy imaging as a function of the loading force at different ionic strengths. An empirical model analogous to that of a compressible fluid was applied to describe the dependence of the apparent thickness of the brush with loading force. The z-potential of spherical brushes of PMETAC and PSPM was almost constant with values between +30 mV to +20 mV, and -30 mV and -25 mV respectively for ionic strengths between 10 mM and 200 mM NaCl. This unusual weak dependence of the z-potential on ionic strength is explained on the basis of the responsiveness of brushes and the specific hydrodynamics of the hairy brush solution interface.

Polymer vesicles were prepared by the so-called solvent-switch technique using polybenzyl methacrylate-*block*-poly(dimethylamino)ethyl methacrylate copolymer (2.6 kDa-1.9 kDa) as building blocks. Polymer vesicles were assembled alternating with PSS applying the Layer by Layer technique on planar and colloidal particles.

The group of Prof. Donath from the University of Leipzig (Germany) developed a novel reaction-diffusion approach for diffusion measurements in nanoassemblies. The idea is based on the quenching of fluorescently labeled polyelectrolytes by an oxidizing molecule, dithionite. The multilayers were assembled on colloidal particles and the changes in fluorescence were recorded by flow cytometry. Dithionite diffusion in the PEMS was studied

as a function of the layer thickness for PAH/PSS and PDADMAC/PSS PEMs, as a function of the salt concentration, and of the position of the labeled polyelectrolytes in the PEM. The fluorescent intensity decay curves show a very sharp decrease of fluorescence intensity addition of dithionite, which continuously slows down not reaching a plateau until 10 min. The fluorescence decay can be fitted assuming that the square of the displacement being proportional to t^α , where $\alpha < 1$, which is characteristic of a subdiffusional process. From the point of view of physics subdiffusion represents a major deviation from Einstein's law of diffusional transport and a qualitative change from a Markov process to a non-Markovian behavior, where the dependence on time becomes non-local. In this case diffusion cannot be considered as a completely random process.

Electrochemical measurements of transport have been performed by the groups of Dr. Omar Azzaroni and Prof. Claudio Gervasi, from INIFTA (Argentina).

The transport of the $[\text{Fe}(\text{CN})_6]^{3-/4-}$ redox couple through PAH/PSS and PDADMAC/PSS multilayers was studied by means of cyclic voltammetry and impedance spectroscopy. Cyclic voltammetry shows that the total current is reduced with the increasing of the layers in the PEM. The impedance relative of charge transfer increased with layer number in the PEM. Imbalances between cathodic and anodic currents could be observed as a result of the complexation of the the redox probe with the polyelectrolytes.

The effect of the grafting density on the molecular transport of the $[\text{Fe}(\text{CN})_6]^{3-/4-}$ redox couple through thin thermoresponsive brushes of PNIPAM was investigated using voltammetry and impedance spectroscopy. PNIPAM brushes with low grafting densities show the same transport properties as the initial self-assembled monolayer before brush synthesis. For higher grafting densities, the diffusion coefficients, D , is 7 orders of magnitude smaller than those typically measured in aqueous solutions. The collapse of the PNIPAM brush with temperature results in a hydrophilic/hydrophobic transitions, with smaller values of D . The effect of temperature on diffusion and electron-transfer processes for the electrochemical reaction of the $[\text{Fe}(\text{CN})_6]^{3-/4-}$ redox couple at a Au electrode modified with (PMETAC) brushes was also studied. Arrhenius-type dependences of the kinetic constant and the diffusion coefficient with temperature were determined in NaCl and NaClO₄. A thermal transition for the PMETAC brush in the presence of ClO₄ ions at near-ambient temperature (~ 17 °C) was detected electrochemically. Activation energies for electron-transfer and diffusion processes become twice as large as those for temperatures above the thermal transition.

The group of Prof. V. Arakelyan from the Yerevan State University (Armenia) together with the group of Prof. Donath worked in the modelling of experimental data to establish a mechanism for transport describing anomalous diffusion in polyelectrolyte multilayers. A complete toolbox of theoretical equations and computer programs was developed allowing for a systematic analysis of anomalous diffusion processes in polyelectrolyte at the nanoscale. An appropriate description of the rate constant of diffusion limited reaction in the case of subdiffusion was identified as an important open question. Studies are underway to find the extension of Smoluchowski expression in the case of subdiffusion

All the work performed at TRASNADE was based on the continuous exchange of Early and Experienced researchers among the European and non-European countries, sharing resources, knowledge and ideas.