

## AFM force measurements in complex coacervate phases.

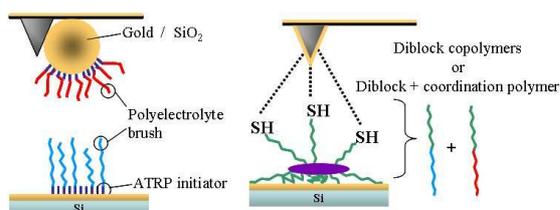
PhD-fellow: E. Spruijt, MSc (Evan)  
evan.spruijt@wur.nl  
Supervisors: Prof. Dr. M.A. Cohen Stuart (Physical Chemistry and Colloid Science, WU)  
Dr. Ir. J. van der Gucht (Physical Chemistry and Colloid Science, WU )  
Sponsors: Netherlands Organisation for Scientific Research (NWO)



### Introduction

Complex coacervation refers to the associative liquid-liquid phase separation in a solution of two oppositely charged colloids.<sup>[1]</sup> It is a frequently observed phenomenon in a solution of oppositely charged polyelectrolytes. When one or both of these polymers contain a second, uncharged and water-soluble, block this phase separation can become restricted to the colloidal domain, resulting in complex coacervate core micelles (C3Ms) of 10-100 nm.<sup>[2]</sup> These C3Ms are thought to be promising candidates as capsules for charged drug molecules (e.g. proteins, DNA) in the envisioned process of ideal controlled drug delivery.

However, no drug delivery systems based on micelles has reached a breakthrough yet. It appeared to be very difficult to design a complex that self-assembles (spontaneous formation of complex coacervate core) and remains stable for longer periods of time in the body, and that in addition releases its content at the desired location.<sup>[3]</sup> The largest problems are the extreme conditions under which C3Ms have to remain stable (stomach, intestine) and the dilution effect. This effect is a result of the large blood volume in which a small number of micelles are diluted. This calls for a better understanding of the interaction forces in complex coacervate phases in general and in C3Ms in particular, leading to more insight in making stable C3Ms.



**Figure 1:** (l) Complex coacervation by CP-AFM; (r) Interaction forces in C3Ms by single-micelle AFM.

### Complex coacervation by colloidal probe AFM

Using colloidal probe AFM, interaction forces between two polyelectrolyte brushes can be studied in the range of pN – nN. Polyelectrolyte brushes can be grown on gold and silica, using surface-initiated atom transfer radical polymerization (SI-ATRP).<sup>[4]</sup> By varying the initiator density, the brush grafting density can be varied, leading to grafted polyelectrolyte chains in the range of chains in a more or less unperturbed conformation at low grafting densities to highly stretched chains at the highest grafting densities.

Both grafting density, salt concentration and pH (in case of polyelectrolyte chains with ionizable groups) are expected to have big effects on the interaction forces. In addition, kinetic effects are expected to play an important role, based on the idea of 'stick at first contact' and in analogy to relaxation in concentrated polymer solutions.

### Interaction forces in polyelectrolyte micelles

Polyelectrolytes modified with thiol groups can be used to study interaction forces in C3Ms, using AFM force spectroscopy. The bonding between the polyelectrolytes and the AFM tip is based on the same gold-thiol bond as for the CP-AFM experiments. Again, strong dependence on salt concentration and pH is expected, but differences could be ascribed to the effects of the colloidal dimensions of the coacervate phase.

### References

- [1] Bungenberg de Jong, H.G., Kruyt, H.R., Proc. KNAW **1929** (32) 849.
- [2] e.g. Voets, I.K. et al, Macromolecules **2007** (40) 8476; Hofs, B. et al, Soft Matter **2008** (4) 1473.
- [3] Rijcken, C.J.F. et al, J. Contr. Release **2007** (120) 131.
- [4] Jones, D.M. et al, Langmuir **2002** (18) 1265.