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Complex coacervate-based wet adhesives

van Westerveld, Larissa

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Introduction

In this chapter we introduce the field of adhesives with a special focus on pressure sensitive adhesives. We discuss the parameters that have an effect on the adhesion performance of polymeric materials. Then we concentrate on tissue adhesives and the challenges associated with wet/underwater adhesion. Inspiration from nature regarding underwater adhesion is discussed with a special interest for the mechanism of the sandcastle worm. This worm uses oppositely charged proteins to glue sand grains together underwater. This phenomenon of complex coacervation is then explained in more detail and lastly some examples of complex coacervates as underwater adhesives are discussed.

Adhesion

If you want to stick two objects together, an adhesive can be used to do the job. After you have applied the adhesive, you press the two objects together with some force to make good contact and to ensure optimal coverage of the adhesive joint. After you have put together the objects, you expect the glued pieces will remain stuck together.

To separate the bonded surfaces, the adhesive needs to resist the applied deformation though energy dissipation.[1,2] This means that energy has to be put in the separation of the surfaces. The adhesive bond can fail in two ways: adhesive failure or cohesive failure (Figure 1.1).[3] During the former, separation happens between the surface and the adhesive, with minimal residue of the adhesive left on the surface (Figure 1.1). Adhesive failure can result from poor contact between adhesive and substrate. Adhesive failure is, for example, desired for post-its, where no residue has to remain after removing it. On the other hand, when something has to stick permanently, the adhesion to the substrate is more important and it is of less importance if there is residue left on both surfaces when the adhesive fails. In this case, cohesive failure is desired, which happens within the adhesive, where adhesive residue is found at both surfaces (Figure 1.1). This points at weaker interactions within the adhesive compared to the interactions of the adhesive with the surface of the substrate.

Adhesive mechanisms/designs

In general, adhesives are applied in a liquid or fluid-like form to make good contact and cured to a solid state to increase the resistance to break the joint. For example, the well-known multipurpose superglue is applied as a monomer, which is liquid, and then quickly polymerizes fast upon contact with water.[4,5] So,

Adhesive failure   **Cohesive failure**

Figure 1.1   *Adhesive (left) and cohesive (right) failure if two surfaces are removed from each other.*

applying the adhesive as liquid monomers is one strategy, but most strategies already use polymers in their formulations.6 Hotmelts are an example of polymeric adhesives without any additional solvent.[6,7] The adhesive is heated to make it flow and once applied and cooled down it has formed a strong bond between substrates.[7,8] Solvents can also be added to the polymers to make them flow at room temperature, but then a curing step is needed to give the adhesive its final strength.[9] "Curing" can be done by evaporation of the solvent, UV-crosslinking, adding a crosslinking agent to the solution, or a combination of these.[9,10] Lastly, there is a class of adhesives that does not need to transition from a liquid to a solid. These adhesives are discussed in more detail in the next section.

Pressure sensitive adhesives

Pressure sensitive adhesives (PSAs) are designed to stick to almost any surface by only applying some pressure to form contact between two substrates.[11] PSAs must be soft enough to establish good contact with the substrate, but they must not be too soft that they cannot resist creep. To achieve this, PSAs usually consist of polymers that have a relatively low T_g and are often slightly crosslinked for better cohesion.[11]

PSAs rely on physical interactions such as hydrogen bonding, entanglements, electrostatic attraction and hydrophobic interactions as adhesive strategies (Figure 1.2).[12] They are commonly found in tapes, stickers, post-its etc. Thus, PSAs are usually processed as a thin layer deposited on a relatively large area compared to the thickness of the layer, which makes it highly confined.[13] Confinement is defined as the ratio between the area and the thickness, where a

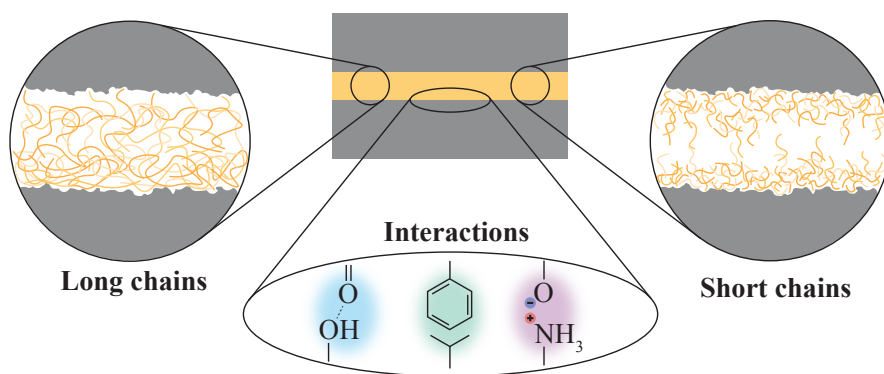**Long chains**   **Interactions**   **Short chains**

Figure 1.2   *Possible adhesive and cohesive interactions of a PSA and the effect of long and short chains on wetting and cohesion.*

large area and small thickness result in high confinement. The first PSAs were made from natural rubber, while nowadays acrylic polymers, styrene block copolymers, polyurethanes and polyesters are used as well.[11,14]

The molecular weight of the polymers that are used for the PSA are an important parameter to tune the rheological and adhesive properties (Figure 1.2). The molecular weight has an effect on the mechanical properties of the material, including: viscoelasticity, viscosity, stiffness, strength and toughness.[15,16] Often a broad molecular weight distribution is optimal because the shorter chains provide good surface wetting, due to their higher mobility.[9,11,15] Longer chains provide cohesion, because of their entanglements.[9,11,15] For example Jenkins et al. showed that mixing 3 different chain lengths outperformed the singular chain lengths and Siebert et al. showed that an increased polydispersity increased the adhesion for polymers with similar M_n.[15,16] Adhesives that are too viscous can be slightly crosslinked to increase adhesion and adhesives that are too stiff can be mixed with tackifier resins.[11,17] Tackifier resins are usually of low molecular weight and have a high Tg, so they will increase the molecular weight between entanglementels (i.e. create more distance between entanglements), while still maintaining the cohesive properties of the long polymer of the stiff adhesive.[11,18]

Characterization of pressure sensitive adhesives

Because PSAs generally do not use any hardening or chemical crosslinking mechanism upon application, the properties of the formulations are crucial for good adhesion performance. Bulk properties of PSAs can be determined with rheology experiments and the performance in specific applications can be tested with peel, lap shear, or probe-tack experiments (Figure 1.3).[19,20] We will first
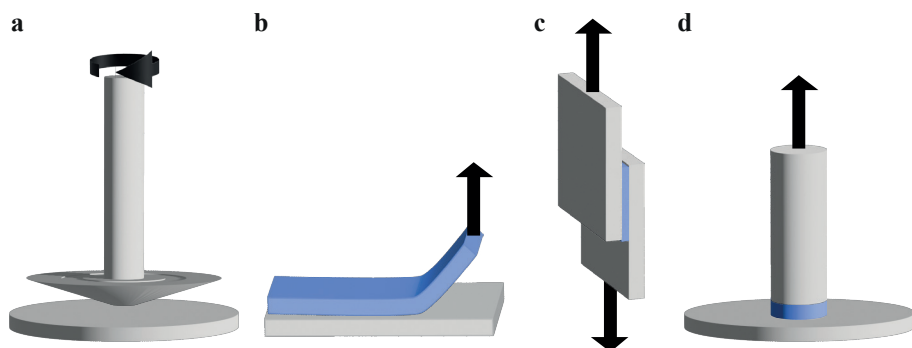

Figure 1.3   *Mechanical test methods: a) oscillatory rheology, b) peel test, c) lap shear test, and d) probe tack test.*

elaborate on the rheology before discussing peel and lap shear experiments and finally focus on probe-tack experiments.

Rheological requirements of PSAs

There are four important parameters to understand for rheology that are relevant to the development of PSAs:

1.   Storage modulus (G')
2.   Loss modulus (G")
3.   The ratio of G"/G': tan(δ)
4.   Frequency

The storage (G') and loss (G") modulus represent the elastic and viscous contributions of the sample, respectively. The moduli are measured over a defined frequency range, which means that the speed of the oscillation is varied during the measurement. Low applied frequencies are slow deformations, or in other words, a deformation over a long period of time. High applied frequencies represent fast deformations, which are deformations over a short period of time. Most samples contain both solid and viscous contributions. The ratio of G"/G', or tan(δ), indicates what the dominating response of the sample is and whether a crossover from viscous to solid or the reverse at a certain frequency can be observed. Viscoelastic materials, in general, display G" > G' at low frequencies, which means that tan(δ) > 1. Thus the material behaves as a liquid at long time scales. However, when the frequency is increased, the deformation becomes faster and viscoelastic materials then transition to show solid-like behaviour, because they cannot respond that fast to the applied deformation. Now G' > G" and tan(δ) < 1.

Some criteria have been defined to guide the development of PSAs. Due to the viscoelastic nature of PSAs the process of contact formation is important for the final properties of debonding.[13] In this regard, Dahlquist's criterion is often used as an empirical rule for contact formation. This criterion states that the storage modulus, G', should not exceed 10^5 Pa at a frequency of 1 Hz, which means that the material should exhibit enough flow to form good contact in the first second of application.[13,21] A second criterion, defined by Deplace et al., involves the formation of fibrils.[21] When the material is highly confined and subjected to high stresses, cavities can form that will eventually develop into fibrils when the material is pulled further apart.[2,3] To quantify the onset of fibrillation, the ratio of tan(δ)/G' at the debonding frequency was used. For the adhesive in their study a minimum ratio was found to be $0.5*10^{-5}$ Pa^{-1} for high energy surfaces and steel.

Which actually means that tan(δ) is close to 1 and that G' is close to the Dahlquist's criterion of 10^5 Pa.

Characterization of adhesion performance of PSAs

Peel, lap shear and probe tack experiments all explore a different aspect of adhesive debonding (Figure 1.3). Peel experiments use a backing to which the adhesive is secured and the force of detachment is subsequently measured when the backing is peeled of a substrate (although this can be done in a lot of different configurations) (Figure 1.3b). In general, peel tests are seen as fracture test, because a crack is propagating whilst peeling and the stress is localized at the peel front.[22,23] This is useful for steady state propagation of a crack, but the sample is subjected to a more complex geometry.[13] The results of peel tests are very system-dependent and therefore need careful interpretation of the data.[22] For a lap shear test, the adhesive is placed between two flat substrates that are partly overlapping (Figure 1.3c). In this test, the shear force is distributed over the whole area which is very different than the peel test.[23] Lap shear tests do not require complex instruments; they can be performed on a tensile tester, which is an easy and straightforward instrument to operate.

    In probe tack experiments, a well-defined geometry for loading is imposed by the cylindrical probe, but contrary to peel tests, steady state propagation cannot be observed here (Figure 1.3d).[13] During a measurement, the adhesive is (slightly) compressed, a fixed dwell time is waited before retraction at a constant velocity
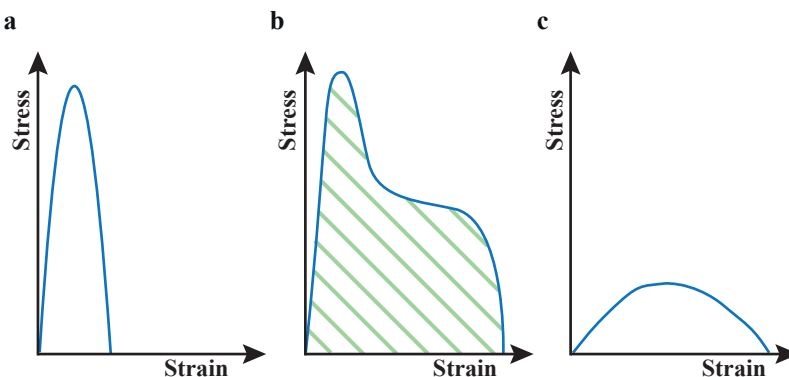

Figure 1.4   *Probe tack adhesion curves representing different material responses.*
a) brittle, ealstic material, b) good dissipative PSA, c) completely
viscious (liquid) material. Stripes in b are representative of the energy
needed to separate two surfaces, this is largest for the material in b.

while measuring the force. The resulting force-displacement curve is typically converted to a nominal stress versus nominal strain curve. The shape of this curve provides information about the peak stress, maximum extension and general debonding mechanism.[13] For example, a single high and narrow peak is a typical signature for adhesive failure and a too elastic material (Figure 1.4a). For a good PSA, a peak in the force is observed at the beginning, however the force does not go immediately to zero at larger strain values, due to fibril formation (Figure 1.4b). Finally, when the material is purely liquid, there is a low and broad force detected with strain values that are lower than for the viscoelastic case (Figure 1.4c). To know the energy that was needed to separate the two surfaces, the integral of the curve can be taken. Multiplied by the thickness of the sample, this calculation gives the work of adhesion (W_{adh}) or energy that was put in to separate the surfaces:

$$W_{adh} = h_0 \int_0^{\varepsilon_{max}} \sigma \, d\varepsilon$$

where h_0 is the initial thickness of the sample, ε_{max} the strain where the force was zero and σ the stress. It is clear that the integration of the stress-strain curves will result in the highest W_{adh} in the 'good PSA' case due to the larger strains that are needed to pull it apart (Figure 1.4b).

However, the investigation of the exact debonding and failure mechanisms cannot be done solely with probe tack experiments. Additionally, visual information on how the debonding happens during probe tack experiment can add valuable information. For example, recording the debonding from below a glass substrate gives more information about how debonding starts and how defects grow and/or cracks propagate in the adhesive.[24]

Underwater/wet adhesion

PSAs work well on dry and clean surfaces, but you might have noticed yourself that Scotch tape does not stick when there is dust or sand on the surface, or when the surface is wet. Especially wet surfaces are the key obstacle in medical applications for use of adhesives. But also many other applications could benefit from underwater adhesives, such as: membranes for blue energy,[25] sea weed farms[26,27] and biomedical sensors or implants could all benefit from an underwater adhesive. All these applications have in common that: 1) they are in a dynamical environment, 2) usually one of the substrates is soft and/or flexible and 3) water is present.

Tissue adhesives

Nowadays, the most common method for closure of wounds is the use of sutures or staples. Though very effective, these methods damage the tissue, are not able to prevent leakage of fluids and cannot be applied during minimal invasive surgeries.[28] Tissue adhesives are promising in circumventing these problems. However, current commercial surgical adhesives fail in their application on different levels; they are either cytotoxic, adhere weakly, have poor mechanical properties or are unable to stick in wet surroundings.[28,29] A tissue adhesive should satisfy several requirements[28]:

- Biocompatibility and no toxicity
- Strong adhesion to tissue
- Similar mechanical properties as the adhered tissue
- Mechanical strength to cope with movements of the tissue
- Similar biodegradability as the rate of healing

We will briefly explain two existing tissue adhesives, fibrin glue and cyanoacrylates, to provide some context on where the field currently is and what the major points to improve are.

The first combination of solutions of fibrinogen with thrombin started being used halfway the 1940s for skin grafts.[28,30] Due to low concentrations, this fibrin glue did not show sufficient adhesion. In the 1970s it was possible to concentrate the active components and fibrin glue became more widely used in surgeries. The glue is prepared by mixing fibrinogen and factor XIII with an
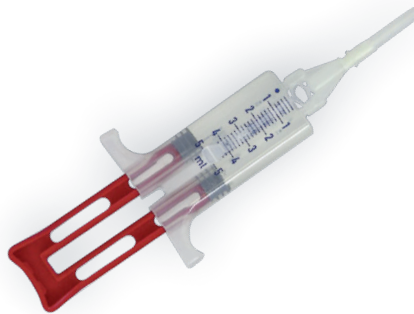

Figure 1.5   *Dual syringe for application of fibrin glue.*

aprotinin solution and by mixing thrombin with a $CaCl_2$ solution. These two mixtures are put in a dual syringe system with a common outlet and plunger (Figure 1.5).[31] When pressing the piston, both solutions are thoroughly mixed in the common outlet before application onto the wound. Within 10 minutes, 70% of the final strength is achieved.[31] Fibrinogen needs to be sourced from human blood plasma and is therefore biocompatible and biodegradable and does not cause any inflammation reaction.[28] However, this human derived material also imposes the risk of transmission of blood related diseases. The mechanical properties of fibrin glues are weak, which makes them suitable for softer tissues, although reinforcement with for example collagen makes it more suited for other tissue applications.[28]

Cyanoacrylates have been used since the end of the 1950s.[32] These type of adhesives rapidly polymerize upon contact with blood or water (in the range of 10 seconds).[32,33] This is both an advantage and disadvantage, because application is quick, but the presence of water may also limit good contact with the tissue.[28] Another important issue is the toxicity of some of the cyanoacrylate glues. The monomer and degradation products may have a toxic effect on the cell or tissue level.[28] Furthermore, the cured cyanoacrylate adhesive is a strong and brittle material which is not very compatible with most soft tissues of the body.

Challenges for underwater adhesion

To adhere substrates together underwater has become more and more interesting over the years. Besides all the challenges/requirements for PSAs in dry conditions (surface spreading, good contact, high energy dissipation) the main obstacle for underwater adhesives is, of course, water.[11,34,35]

Water can hinder an adhesive in several ways. The most evident is the hindering of good contact formation.[34,35] When an underwater adhesive is making contact with a substrate, it first has to remove or penetrate through water that is bound to the surface. This can be done by introduction of hydrophobic groups in the adhesive that repel water or by absorbing the interfacial water.[28,36,37] Even when contact is made, the risk of trapping water between surface and adhesive still exists. Secondly, the adhesive should not disperse or mix in the surrounding environment, because this will dilute the adhesive and reduce adhesion.[34,35] Lastly, as mentioned for the cyanoacrylates, the adhesive should not react (too fast) with water, as this can result in preliminary curing.[32,33]
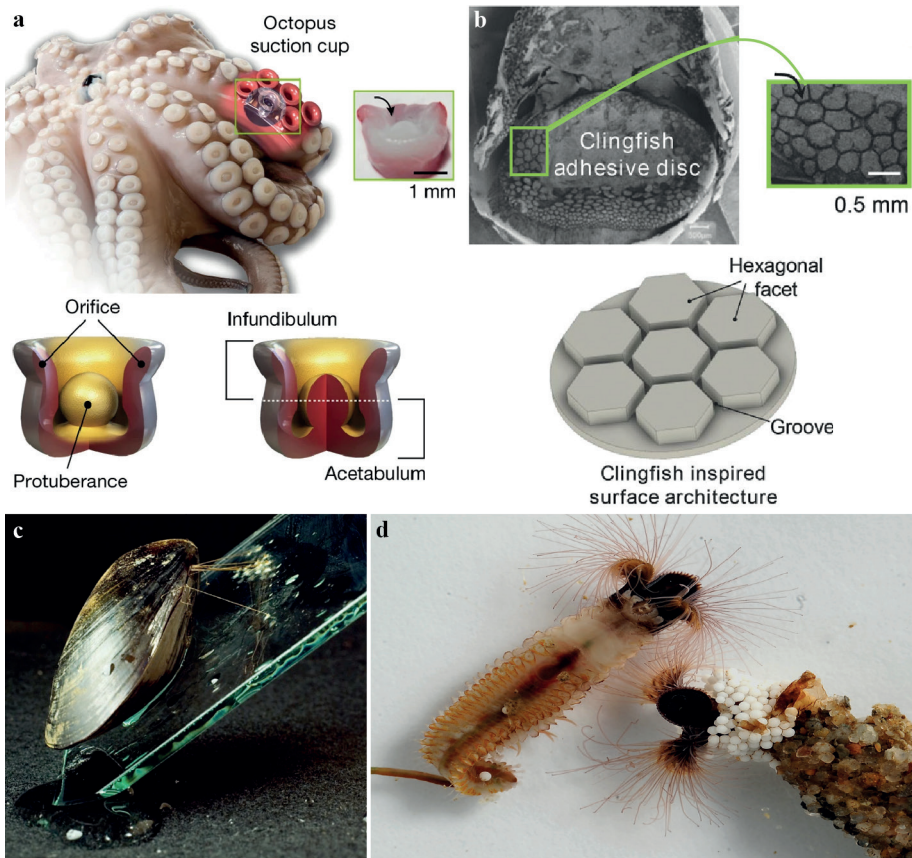
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Figure 1.6   *Nature inspired methods of adhesion. a) Suction cups of an octopus. Reprinted with permission of ref. 38. b) Canals of the adhesive disk of a clingfish. Reprinted with permission of ref. 39. c) A mussel attached with its byssal threads to a glass slide. Reprinted with permission of ref. 15. d) Sandcastle worms and a tube they build for themselves. Courtesy of Russell Stewart.*

Natural systems

Looking at nature for inspiration can give valuable information about how to solve the problems associated with underwater adhesion. Some animals use patterned surfaces to control underwater adhesion. Two examples are suction cups of octopuses,[38] and the adhesive discs of clingfishes.[39] The octopus suction cup mechanism is based on pressure difference (Figure 1.6a).[38] When a suction cup approaches a surface, first a seal is formed at the edge of the cup. Then, low pressure is created which keeps the cup in place, regardless of substrate chemistry. The design of the adhesive disc of a clingfish provides a solution for hydrogel-

based adhesives (Figure 1.6b).[39] The disc consists of hexagonally shaped structures that are separated by channels. These channels allow for the drainage of excess water during the underwater attachment to a surface.

Alternatively, instead of patterns, specific chemistry is used by other animals. Since the 1980s, the mussel species of *Mytilus edulis* have been studied for their wet adhesive properties (Figure 1.6c).[40] The mussel establishes its adhesion via a byssal thread in which a viscous proteinaceous solution is secreted that transitions into a solid foam.[40] The modified tyrosine amino acid, 3,4-dihydroxyphenylalanine (DOPA), was soon recognized to be abundantly present in the mussel foot and turns out to be one of the most important moieties for wet adhesion.41 The functional group of DOPA is called a catechol and it can have a large set of interactions like; hydrogen bonding, π-π interactions, cation-π interactions and metal complexation (Figure 1.7).[42–44] The proteins of the mussel are stored in an acidic and reducing environment, because the catechol moieties can be oxidized when exposed to a high pH or oxidizing agents. The oxidized form of DOPA, a quinone, is thought to be essential in crosslinking the material, which provides it with a better cohesion.[41,45] But, converting all catechols to quinones will decrease all the aforementioned interactions with the surface and reduce the adhesive properties.

About two decades later, the adhesive secreted by the sandcastle worm *Phragmatopoma californica*, was investigated (Figure 1.6d).[46] Again, the proteinaceous secretion formed a foam upon curing.[47] Special interest was displayed for the delivery mechanism of the worm, because the worm uses granules
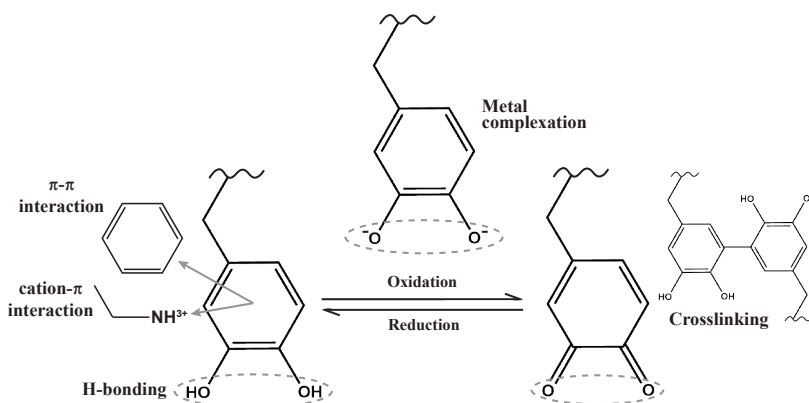

Figure 1.7   *Catechol (DOPA) interactions. The catechol can form π-π interactions, cation-π interactions and H-bonding, while oxidation promotes crosslinking and metal complexation.*

that consist of charged proteins to glue sand grains together.[48] This secretion does not dissolve in the sea water and sufficient adhesive strength is achieved within 30 seconds.

It is not feasible to let mussels or sandcastle worms produce their glue components (proteins) on a large scale.[49,50] Therefore, science has started its search for synthetic mimics for these components. The challenge is to select the most important components of the proteins and translate them into synthetically relevant molecules. The first step in mussel mimicked adhesives was to identify the different mussel foot proteins (MFPs).[51] Also the DOPA moiety has been extensively incorporated in adhesive formulations. The only drawback is the sensitivity to pH of this group.[43] The group of Stewart were one of the first to take inspiration from the sandcastle worm and design a polymer with similar functionalities. One of their polymers contained a phosphate and a DOPA analogue and the other polymer contained a primary amine.[52] With this formulation the researchers were able to bond two pieces of bone together, underwater.

Polyelectrolytes and complex coacervation

Next to adhesion promotors, such as catechol groups, several other interactions play a key role in both adhesive and cohesive properties. Recently, it was identified that charged proteins, i.e. electrostatic interactions, also seem to play a key role in adhesives of natural organisms. Charged proteins can be classified as polyelectrolytes, which are charged polymers and can be either strong or weak, depending on the pK_a of the charged repetitive units (Figure 1.8a). The number of charges on strong polyelectrolytes is not dependent on the pH of the solution, at least for a wide range of pH.[53,54] In contrast to strong polyelectrolytes, the number of charges on weak polyelectrolytes is influenced by the pH.[54,55] This gives the advantage to tune the ionization degree of weak polyelectrolytes. Since the charges on weak polyelectrolytes are not fixed, but depend on their environment, the charges are considered mobile.[54,56] For example, charges can localize more towards a charged object to reduce the charge there, but keep the flexibility in the chain elsewhere.

Thermodynamics of complex coacervation

Complex coacervates are formed when two solutions, containing well-soluble oppositely charged polyelectrolytes, are mixed together (Figure 1.8b). The complex coacervate is the polymer-rich viscoelastic phase that is formed after

mixing and the subsequent liquid-liquid phase separation. The main driving force for the formation of a complex coacervate is the entropy gain when counterions are released.[46,48,57,58] This entropy gain depends on the salt concentration; an increased salt concentration results in a decreasing entropy gain.[57–59] Consequently, an increased salt concentration leads to a decrease in density of the coacervate phase, until there is only a single phase left (Figure 1.9). This point, where no phase separation is observed anymore, is known as the salt resistance of a complex coacervate (Figure 1.8c). The value of the salt resistance depends, amongst others, on the type of polyelectrolytes, polyelectrolyte concentration and the type of salt. The peak of the binodal phase diagram is the critical salt concentration, which is the absolute highest salt concentration where phase separation can be observed (Figure 1.8c). Although complex coacervates are immiscible with water, they still contain a high amount of water (typically more than 60% in weight), together with ions and other molecules that may have been present during mixing.[60–62]

> Besides salt, other factors also have a distinct effect on the thermodynamics of complex coacervates. Firstly, low chain lengths have a lower salt resistance than higher chain lengths, due to their higher translational entropy gain compared to longer chain lengths (Figure 1.10).[63,64] Secondly, when using weak polyelectrolytes, the charge is dependent on the pH of the medium. Using a pH where not both polyelectrolytes are fully ionized decreases the charge density, reduces the salt
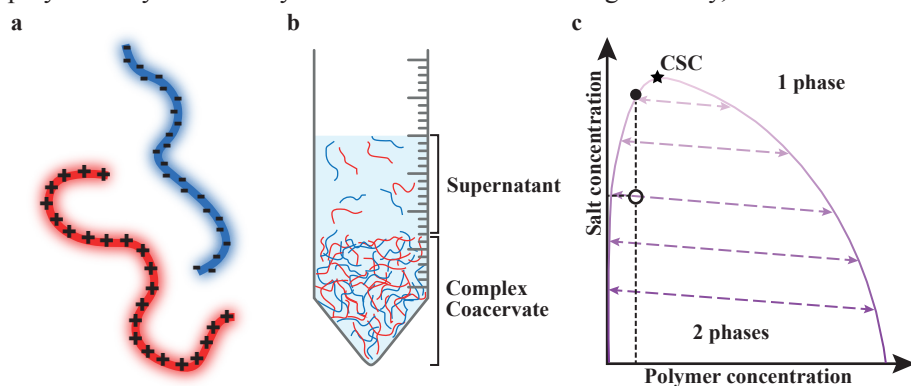
Figure 1.8   *a) Polyelectrolytes can be either positively or negatively charged. b) A complex coacervate forms when oppositely charged polyelectrolytes are mixed in water, with a polymer-depleted phase (supernatant) on top. c) Phase diagram when mixing polyelectrolytes at a chosen salt and polymer concentration (open circle). The salt resistance at that polymer concentration is represented by the solid circle and the critical salt concentration (CSC) is represented with the star. Any value within the curve will result in two phases with a compositions as on the curve.*

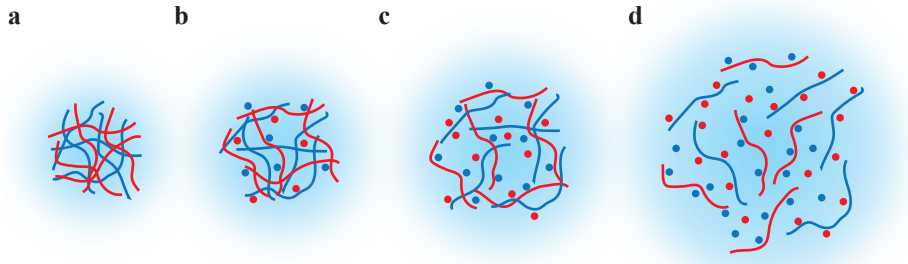**Figure 1.9**   *Effect of salt concentration on polyelectrolytes in solution. Starting from a precipitate with no salt (a), to make it a gel-like material with a little salt (b), to a complex coacervate (c) and finally a single phase polyelectrolyte solution (d), where the chains do not interact anymore.*

resistance and changes the rheological response.[65] Finally, additional interactions such as hydrogen bonding or hydrophobic interactions can provide an additional driving force for phase separation of the complex coacervate.[65–67]

Viscoelastic properties of complex coacervates

Complex coacervates are commonly characterized with rheology. Usually the terminal regime is probed at high salt concentrations, where G" is above G', and at low salt concentrations a crossover between the moduli can be observed.[68,69] The dynamics are often referred to as Sticky Rouse dynamics where the charges are seen as electrostatic 'stickers' that slow down the dynamics of the polymers.[70,71] Salt has been shown to influence the phase diagram, but also the dynamics are
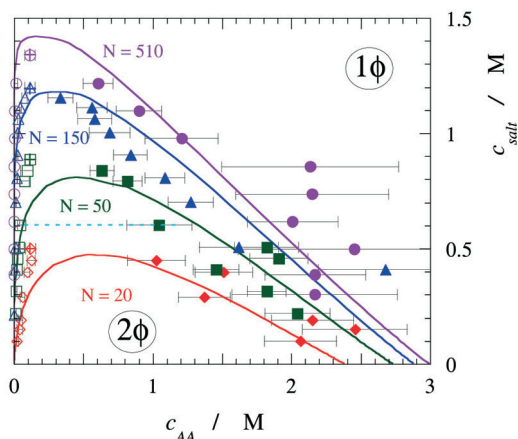

Figure 1.10   *Phase diagram where height and width of the graph are influenced by the chain length. Reprinted with permission of ref. 63.*

altered by the presence of salt. More salt in the complex coacervate screens the 'stickers' from each other and therefore speeds up the dynamics of the polymers, which means a more liquid-like material. Thus by only changing salt, complex coacervates can transition from gels to honey-like viscous liquids, or even be as fluid as water. Even though different salt concentrations result in different rheology responses, these data can be shifted horizontally. This is possible because salt only influences the rate of the dynamics, but not the underlying relaxation mechanism of how the polyelectrolytes interact.[72] The formed master curve spans a wider range of moduli and frequencies for the reference condition.

(Complex) coacervate-based underwater adhesives

Here we will give a selection of examples of underwater adhesives that are based on the principle of (complex) coacervation.

The group of Stewart were the first to show the applicability of complex coacervates as underwater adhesives.[73] They created a polymer that was analogous to one of the proteins found in the sandcastle worm, which contained phosphate groups and catechol groups. The oppositely charged polymer was a copolymer of acrylamide with a few percent of amine side chains. The complex coacervates were formed with divalent cations and different amine/ phosphate and cation/ phosphate ratios were studied. The best formulation was used to glue two bone pieces together underwater with a peak stress around 100 kPa.

Dompe et al. developed multiresponsive complex coacervate-based adhesives that were responsive to a change in salt concentration and/or an increase in temperature.[74] Side chains of poly(N-isopropylacrylamide) (PNIPAM) exhibit a temperature dependent solubility where the chains collapse at elevated temperatures. The achieved adhesion stress of a combined temperature and salt switch was around 30 kPa with an adhesion energy of 7.2 J/m2. Due to the fluid nature of the complex coacervate at high salt concentrations, it could be applied with a syringe and curing could happen at physiological salt concentrations and body temperature.

Vahdati et al. used polymer chains that were much shorter than in the work of Dompe et al. was presented.[75] Therefore, they had the possibility to make a viscoelastic complex coacervate at much lower salt concentrations. The complex coacervate made at physiological salt concentration was stronger than a coacervate that was switched from high to physiological salt concentration. This was attributed to the tan(δ) which was close to one (G' and G" are equal), which is

also called the critical gel point. An adhesion energy of 16.4 J/m2 could be reached with the complex coacervate at physiological salt concentration compared to 3.5 J/m2 for the switched complex coacervate.

The group of Joy developed a self-coacervating polymer (so no complex coacervation) that contained moieties with LCST behaviour, catechols for good adhesion and UV crosslinkable units for cohesion.[76] Above 7 °C the polymer would self-associate and form the coacervate. The observed adhesion strength for the best ratio of catechols and UV crosslinkers (6:14) was 66 kPa, which is in the same range as the group of Stewart has reported.

Aim of this research

In the previous paragraphs general knowledge is provided which can be used for the rational design of complex coacervates as wet PSA-like adhesives. Both requirements for PSAs and underwater adhesion have to be taken into account and can be verified with rheology and probe-tack tests. In this thesis we aim to extend the fundamental understanding of complex coacervate-based underwater adhesives via numerical simulations and systematic studies in which charge density and hydrophobic content are varied. In particular these systematic studies provide more insights into the influence of polymer chemistry and water content on the adhesion of these materials.

In Chapter 2, a numerical simulation approach is used on complex coacervation. Starting from viscosity experiments that determined the radius of gyration of the polyelectrolyte, we tried to develop a model that in the end would be able to predict complex coacervate behaviour. This chapter provides guidelines and considerations when designing a model from the bottom up. This chapter ends with the calibration of the single polyelectrolyte chain and gives some prospects on the simulation of complex coacervation.

In the following two chapters we look more fundamentally how adhesion of complex coacervates is affected by charge density (Chapter 3) and hydrophobic interactions (Chapter 4). The charge density is varied on the polyanion via copolymerization of 3-isobutoxysulphopropyl methacrylate with oligo(ethylene glycol) methyl ether methacrylate in different ratios. After deprotection, the copolymers are complexed with poly(4-vinylpiridine) at different salt concentrations. Subsequently, water content, salt resistance, rheology and adhesion are measured as a function of charge density and salt concentration.

Chapter 4 has a similar approach, but with a slightly different polyanion.

Here, 3-isobutoxysulphopropyl methacrylate is polymerized at two chain lengths. The hydrophobicity is tuned by the partial deprotection of the isobutyl group. The two chain lengths of these polymers are again complexed with matching poly(4-vinylpiridine) chain lengths at different salt concentrations. The same experiments as in chapter 3 are performed here. Additionally, the shifted frequency sweeps of the longer chains were fitted with the sticky Rouse model, which could capture the rheological behaviour well.

In the last chapter, Chapter 5, we present how complex coacervates made from biopolymer polyelectrolytes can be used as a medical adhesive. The polymers are added mixed at high concentrations, resulting in a complex coacervate phase with a larger volume. The complex coacervate is dispersed again in the supernatant, freeze dried and grinded into a powder. The rehydration of the powder is studied for a range of added volumes of water. Water content, rheology and adhesion are determined for the powder that was rehydrated fast with a centrifuge. Lastly, the powder was applied to pieces of chicken meat and the adhesion strength was determined with a tensile tester.

1

References

1.   Zosel, A. The effect of fibrilation on the tack of pressure sensitive adhesives. Int. J. Adhes. Adhes. 18, 265–271 (1998).

2.   Creton, C. and Lakrout, H. Micromechanics of Flat-Probe Adhesion Tests of Soft Viscoelastic Polymer Films. J. Polym. Sci. Part B Polym. Phys. 38, 965–979 (2000).

3.   Shull, K. R. and Creton, C. Deformation Behavior of Thin , Compliant Layers Under Tensile Loading Conditions. 42, 4023–4043 (2004).

4.   Shantha, K. L., Thennarasu, S. and Krishnamurti, N. Developments and applications of cyanoacrylate adhesives. J. Adhes. Sci. Technol. 3, 237–260 (1989).

5.   Rajesh Raja, P. Cyanoacrylate adhesives: A critical review. Rev. Adhes. Adhes. 4, 398–416 (2016).

6.   Fan, H. and Gong, J. P. Bioinspired Underwater Adhesives. Adv. Mater. 33, (2021).

7.   Malysheva, G. V. and Bodrykh, N. V. Hot-melt adhesives. Polym. Sci. - Ser. D 4, 301–303 (2011).

8.   Sandoval, A. J., Fernández, M. M., Candal, M. V., Safari, M., Santamaria, A. and Müller, A. J. Rheology and Tack Properties of Biodegradable Isodimorphic Poly(Butylene Succinate)-Ran-Poly(ε-Caprolactone) Random Copolyesters and Their Potential Use as Adhesives. Polymers (Basel). 14, (2022).

9.   North, M. A., Del Grosso, C. A. and Wilker, J. J. High Strength Underwater Bonding with Polymer Mimics of Mussel Adhesive Proteins. ACS Appl. Mater. Interfaces 9, 7866–7872 (2017).

10. White, J. D. and Wilker, J. J. Underwater Bonding with Charged Polymer Mimics of Marine Mussel Adhesive Proteins. Macromolecules 44, 5085–5088 (2011).

11. Creton, C. Pressure-sensitive adhesives: an introductory course. MRS Bull. 28, 434–439 (2003).

12. Yang, J., Bai, R. and Suo, Z. Topological Adhesion of Wet Materials. Adv. Mater. 30, 1–7 (2018).

13. Creton, C. and Ciccotti, M. Fracture and adhesion of soft materials: A review. Reports Prog. Phys. 79, (2016).

14. Czech, Z. and Milker, R. Development trends in pressure-sensitive adhesive systems. Mater. Sci. Pol. 23, 1015–1022 (2005).

15. Jenkins, C. L., Meredith, H. J. and Wilker, J. J. Molecular weight effects upon the adhesive bonding of a mussel mimetic polymer. ACS Appl. Mater. Interfaces 5, 5091–5096 (2013).

16. Siebert, H. M. and Wilker, J. J. Improving the molecular weight and synthesis of a renewable biomimetic adhesive polymer. Eur. Polym. J. 113, 321–327 (2019).

17. Sun, S., Li, M. and Liu, A. A review on mechanical properties of pressure sensitive adhesives. Int. J. Adhes. Adhes. 41, 98–106 (2013).

18. Abbott, S. Adhesion Science: Principles and Practice. (DEStech Publications, Inc, 2015).

19. Lindner, A., Lestriez, B., Mariot, S., Creton, C., Maevis, T., Lühmann, B. and Brummer, R. Adhesive and rheological properties of lightly crosslinked model acrylic networks. J. Adhes. 82, 267–310 (2006).

20. Callies, X., Fonteneau, C., Pensec, S., Bouteiller, L., Ducouret, G. and Creton, C. Adhesion and non-linear rheology of adhesives with supramolecular crosslinking points. Soft Matter 12, 7174–7185 (2016).

21. Deplace, F., Carelli, C., Mariot, S., Retsos, H., Chateauminois, A., Ouzineb, K. and Creton, C. Fine tuning the adhesive properties of a soft nanostructured adhesive with rheological measurements. J. Adhes. 85, 18–54 (2009).

22. Bartlett, M. D., Case, S. W., Kinloch, A. J., Dillard, D. A., Bartlett, M. D., Case, S. W., Kinloch, A. J. and David, A. Peel Tests for Quantifying Adhesion and Toughness : A Review. Prog. Mater. Sci. 101086 (2023) doi:10.1016/j.pmatsci.2023.101086.

23. Wang, Y., Yin, T. and Suo, Z. Polyacrylamide hydrogels. III. Lap shear and peel. J. Mech. Phys. Solids 150, 104348 (2021).

24. Creton, C., Hooker, J. and Shull, K. R. Bulk and interfacial contributions to the debonding mechanisms of soft adhesives: Extension to large strains. Langmuir 17, 4948–4954 (2001).

25. Yip, N. Y., Brogioli, D., Hamelers, H. V. M. and Nijmeijer, K. Salinity Gradients for Sustainable Energy: Primer, Progress, and Prospects. (2016) doi:10.1021/acs.est.6b03448.

26. Kerrison, P. D., Stanley, M. S. and Hughes, A. D. Textile substrate seeding of Saccharina latissima sporophytes using a binder: An effective method for the aquaculture of kelp. Algal Res. 33, 352–357 (2018).

27.   Umanzor, S., Li, Y. and Yarish, C. Effect of direct "seeding" binders and embryonic sporophyte sizes on the development of the sugar kelp, Saccharina latissima. J. Appl. Phycol. 32, 4137–4143 (2020).

28.   Nam, S. and Mooney, D. Polymeric Tissue Adhesives. Chem. Rev. 121, 11336–11384 (2021).

29.   Li, J., Celiz, A. D., Yang, J., Yang, Q., Wamala, I., Whyte, W., Seo, B. R., Vasilyev, N. V., Vlassak, J. J., Suo, Z. and Mooney, D. J. Supplemtary Materials: Tough adhesives for diverse wet surfaces. Science (80-.). 357, 378–381 (2017).

30.   Brennan, M. Fibrin glue. Blood Rev. 5, 240–244 (1991).

31.   MacGillivray, T. E. Fibrin Sealants and Glues. J. Card. Surg. 18, 480–485 (2003).

32.   Jenkins, L. E. and Davis, L. S. Comprehensive review of tissue adhesives. Dermatologic Surg. 44, 1367–1372 (2018).

33.   Ryou, M. and Thompson, C. C. Tissue adhesives: A review. Tech. Gastrointest. Endosc. 8, 33–37 (2006).

34.   Shao, H. and Stewart, R. J. Biomimetic underwater adhesives with environmentally triggered setting mechanisms. Adv. Mater. 22, 729–733 (2010).

35.   Zhu, X., Wei, C., Zhang, F., Tang, Q. and Zhao, Q. A Robust Salty Water Adhesive by Counterion Exchange Induced Coacervate. Macromol. Rapid Commun. 40, 1–7 (2019).

36.   Yuk, H., Varela, C. E., Nabzdyk, C. S., Mao, X., Padera, R. F., Roche, E. T. and Zhao, X. Dry double-sided tape for adhesion of wet tissues and devices. Nature 575, 169–174 (2019).

37.   Peng, X., Xia, X., Xu, X., Yang, X., Yang, B., Zhao, P., Yuan, W., Chiu, P. W. Y. and Bian, L. Ultrafast self-gelling powder mediates robust wet adhesion to promote healing of gastrointestinal perforations. Sci. Adv. 7, 1–14 (2021).

38.   Baik, S., Kim, D. W., Park, Y., Lee, T. J., Ho Bhang, S. and Pang, C. A wet-tolerant adhesive patch inspired by protuberances in suction cups of octopi. Nature 546, 396–400 (2017).

39.   Rao, P., Sun, T. L., Chen, L., Takahashi, R., Shinohara, G., Guo, H., King, D. R., Kurokawa, T. and Gong, J. P. Tough Hydrogels with Fast, Strong, and Reversible Underwater Adhesion Based on a Multiscale Design. Adv. Mater. 30, 1–8 (2018).

40.   Waite, J. H. Nature's underwater adhesive specialist. Int. J. Adhes. Adhes. 7, 9–14 (1987).

41.   Strausberg, R. L. and Link, R. P. Protein-based medical adhesives. TIBTECH 8, (1990).

42.   Moulay, S. Dopa/catechol-tethered polymers: Dioadhesives and biomimetic adhesive materials. Polym. Rev. 54, 436–513 (2014).

43.   Waite, J. H. Mussel adhesion - Essential footwork. J. Exp. Biol. 220, 517–530 (2017).

44.   Hofman, A. H., van Hees, I. A., Yang, J. and Kamperman, M. Bioinspired Underwater Adhesives by Using the Supramolecular Toolbox. Adv. Mater. 30, (2018).

45.   Burzio, L. O., Burzio, V. A., Silva, T., Burzio, L. A. and Pardo, J. Environmental bioadhesion: themes and applications. Curr. Opin. Biotechnol. 8, 309–312 (1997).

46.   Jensen, R. A. and Morse, D. E. The bioadhesive of Phragmatopoma californica tubes: a silk-like cement containing L-DOPA. J. Comp. Physiol. B 158, 317–324 (1988).

47.   Stevens, M. J., Steren, R. E., Hlady, V. and Stewart, R. J. Multiscale Structure of the Underwater Adhesive of Phragmatopoma California : a Nanostructured Latex with a Steep Microporosity Gradient. 280, 5045–5049 (2007).

48.   Stewart, R. J., Wang, C. S., Song, I. T. and Jones, J. P. The role of coacervation and phase transitions in the sandcastle worm adhesive system. Adv. Colloid Interface Sci. 239, 88–96 (2017).

49.   Kim, B. J., Oh, D. X., Kim, S., Seo, J. H., Hwang, D. S., Masic, A., Han, D. K. and Cha, H. J. Mussel-mimetic protein-based adhesive hydrogel. Biomacromolecules 15, 1579–1585 (2014).

50.   Stewart, R. J. Protein-based underwater adhesives and the prospects for their biotechnological production. Appl. Microbiol. Biotechnol. 89, 27–33 (2011).

51.   Hwang, D. S., Yoo, H. J., Jun, J. H., Moon, W. K. and Cha, H. J. Expression of functional recombinant mussel adhesive protein Mgfp-5 in Escherichia coli. Appl. Environ. Microbiol. 70, 3352–3359 (2004).

52.   Shao, H., Bachus, K. N. and Stewart, R. J. A water-borne adhesive modeled after the sandcastle glue of P. californica. Macromol. Biosci. 9, 464–471 (2009).

53.   Wang, J., Kareem, M. A., Kareem, R., Taylor, B., Lombardo, A. W. and Brigano, F. A. Formation and immobilization of small particles by using polyelectrolyte multilayers. (2017).

54.   Stornes, M., Linse, P. and Dias, R. S. Monte Carlo Simulations of Complexation between Weak Polyelectrolytes and a Charged Nanoparticle. Influence of Polyelectrolyte Chain Length and Concentration. Macromolecules 50, 5978–5988 (2017).

55.   Adamczyk, Z., Bratek, A., Jachimska, B., Jasiński, T. and Warszyński, P. Structure of poly(acrylic acid) in electrolyte solutions determined from simulations and viscosity measurements. J. Phys. Chem. B 110, 22426–22435 (2006).

56.   Barenbrug, T. M. A. O. M., Smit, J. A. M. and Bedeaux, D. Influence of charge mobility on the equilibrium properties of polyelectrolytes in salt solutions: a Monte Carlo study. Macromolecules 26, 6864–6872 (1993).

57.   Van Der Burgh, S., De Keizer, A. and Cohen Stuart, M. A. Complex Coacervation Core Micelles. Colloidal Stability and Aggregation Mechanism. Langmuir 20, 1073–1084 (2004).

58.   Gucht, J. van der, Spruijt, E., Lemmers, M. and Cohen Stuart, M. A. Polyelectrolyte complexes: Bulk phases and colloidal systems. J. Colloid Interface Sci. 361, 407–422 (2011).

59.   Priftis, D., Laugel, N. and Tirrell, M. Thermodynamic characterization of polypeptide complex coacervation. Langmuir 28, 15947–15957 (2012).

60.   Stewart, R. J., Wang, C. S. and Shao, H. Complex coacervates as a foundation for synthetic underwater adhesives. Adv. Colloid Interface Sci. 167, 85–93 (2011).

61.   Blocher, W. C. and Perry, S. L. Complex coacervate-based materials for biomedicine. Wiley Interdiscip. Rev. Nanomedicine Nanobiotechnology 9, 76–78 (2017).

62.   Liu, Y., Winter, H. H. and Perry, S. L. Linear viscoelasticity of complex coacervates. Adv. Colloid Interface Sci. 239, 46–60 (2017).

63.   Spruijt, E., Westphal, A. H., Borst, J. W., Cohen Stuart, M. A. and Van Der Gucht, J. Binodal compositions of polyelectrolyte complexes. Macromolecules 43, 6476–6484 (2010).

64.   Kayitmazer, A. B., Koksal, A. F. and Kilic Iyilik, E. Complex coacervation of hyaluronic acid and chitosan: Effects of pH, ionic strength, charge density, chain length and the charge ratio. Soft Matter 11, 8605–8612 (2015).

65.   Es Sayed, J., Caïto, C., Arunachalam, A., Amirsedeghi, A., van Westerveld, L., Maret, D., Mohamed Yunus, R. A., Calicchia, E., Dittberner, O., Portale, G., Parisi, D. ; and Kamperman, M. Effect of Dynamically Arrested Domains on the Phase Behavior, Linear Viscoelasticity and Microstructure of Hyaluronic Acid – Chitosan Complex Coacervates. Macromolecules (2023) doi:10.1002/ma-2023-00269f.

66.   Sadman, K., Wang, Q., Chen, Y., Keshavarz, B., Jiang, Z. and Shull, K. R. Influence of Hydrophobicity on Polyelectrolyte Complexation. Macromolecules 50, 9417–9426 (2017).

67.   Huang, J. and Laaser, J. E. Charge Density and Hydrophobicity-Dominated Regimes in the Phase Behavior of Complex Coacervates. ACS Macro Lett. 10, 1029–1034 (2021).

68.   Morin, F. J., Puppo, M. L. and Laaser, J. E. Decoupling salt- And polymer-dependent dynamics in polyelectrolyte complex coacervatesviasalt addition. Soft Matter 17, 1223–1231 (2021).

69.   Yu, B., Rauscher, P. M., Jackson, N. E., Rumyantsev, A. M. and De Pablo, J. J. Crossover from rouse to reptation dynamics in salt-free polyelectrolyte complex coacervates. ACS Macro Lett. 9, 1318–1324 (2020).

70.   Rubinstein, M. and Semenov, A. N. Dynamics of entangled solutions of associating polymers. Macromolecules 34, 1058–1068 (2001).

71.   Spruijt, E., Cohen Stuart, M. A. and van der Gucht, J. Linear Viscoelasticity of Polyelectrolyte Complex Coacervates. Macromolecules 46, 1633–1641 (2013).

72.   Spruijt, E., Sprakel, J., Lemmers, M., Stuart, M. A. C. and Van Der Gucht, J. Relaxation dynamics at different time scales in electrostatic complexes: Time-salt superposition. Phys. Rev. Lett. 105, 1–4 (2010).

73.   Shao, H., Bachus, K. N. and Stewart, R. J. A water-borne adhesive modeled after the sandcastle glue of P. californica. Macromol. Biosci. 9, 464–471 (2009).

74.   Dompé, M., Cedano-Serrano, F. J., Vahdati, M., van Westerveld, L., Hourdet, D., Creton, C., van der Gucht, J., Kodger, T. and Kamperman, M. Underwater Adhesion of Multiresponsive Complex Coacervates. Adv. Mater. Interfaces 7, (2020).

75.   Vahdati, M., Cedano-Serrano, F. J., Creton, C. and Hourdet, D. Coacervate-Based Underwater Adhesives in Physiological Conditions. ACS Appl. Polym. Mater. 2, 3397–3410 (2020).

76.   Narayanan, A., Menefee, J. R., Liu, Q., Dhinojwala, A. and Joy, A. Lower Critical Solution Temperature-Driven

Self-Coacervation of Nonionic Polyester Underwater Adhesives. ACS Nano 14, 8359–8367 (2020).

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