

Liquefaction of Biopolymers: Solvent-free Liquids and Liquid Crystals from Nucleic Acids and Proteins

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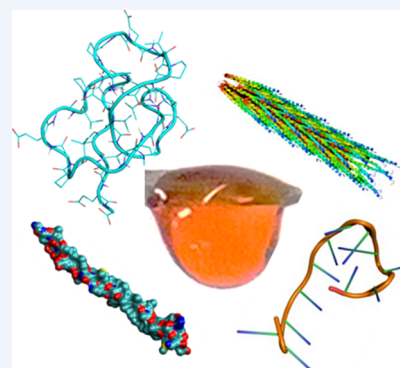
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CONSPECTUS: Biomacromolecules, such as nucleic acids, proteins, and virus particles, are persistent molecular entities with dimensions that exceed the range of their intermolecular forces hence undergoing degradation by thermally induced bond-scission upon heating. Consequently, for this type of molecule, the absence of a liquid phase can be regarded as a general phenomenon. However, certain advantageous properties usually associated with the liquid state of matter, such as processability, flowability, or molecular mobility, are highly sought-after features for biomacromolecules in a solvent-free environment. Here, we provide an overview over the design principles and synthetic pathways to obtain solvent-free liquids of biomacromolecular architectures approaching the topic from our own perspective of research. We will highlight the milestones in synthesis, including a recently developed general surfactant complexation method applicable to a large variety of biomacromolecules as well as other synthetic principles granting access to electrostatically complexed proteins and DNA.

These synthetic pathways retain the function and structure of the biomacromolecules even under extreme, nonphysiological conditions at high temperatures in water-free melts challenging the existing paradigm on the role of hydration in structural biology. Under these conditions, the resulting complexes reveal their true potential for previously unthinkable applications. Moreover, these protocols open a pathway toward the assembly of anisotropic architectures, enabling the formation of solvent-free biomacromolecular thermotropic liquid crystals. These ordered biomaterials exhibit vastly different mechanical properties when compared to the individual building blocks. Beyond the preparative aspects, we will shine light on the unique potential applications and technologies resulting from solvent-free biomacromolecular fluids: From charge transport in dehydrated liquids to DNA electrochromism to biocatalysis in the absence of a protein hydration shell. Moreover, solvent-free biological liquids containing viruses can be used as novel storage and process media serving as a formulation technology for the delivery of highly concentrated bioactive compounds. We are confident that this new class of hybrid biomaterials will fuel further studies and applications of biomacromolecules beyond water and other solvents and in a much broader context than just the traditional physiological conditions.



INTRODUCTION

Modern manufacturing of chemical products heavily relies on the tailor-making of molecules to combine desirable and discard undesirable material properties. Some of these properties, however, are almost exclusively associated with the molecules' state of matter. While, for example, porosity and crystallinity are generally attributed to the solid state, molecular mobility and flowability are characteristics mostly associated with liquids. Solvent-free liquids surpass this intrinsic limitation and combine advantageous and even create completely new properties from multiple aggregate states. Exciting examples are solvent-free liquids that enhance the performance of dyes,¹ create permanent liquid porosity,² or increase reaction yields by unprecedentedly high concentrations.³

Concerning biomacromolecules, the production of solvent-free liquids is a particularly challenging task as the basic requirement for self-organization and activity of DNA, RNA,

and proteins is the presence of water.^{4,5} Though biomacromolecular components are of increasing interest for the integration into artificial materials and devices,^{6–10} their processability is currently limited to methods primarily involving the aqueous phase due to their insolubility and structural (hence functional) destabilization in organic solvents. Concomitantly, solid state processing of freeze-dried powders obtained from aqueous biomacromolecular solutions suffers from safety issues in storage and manipulation. Consequently, also considering solvent-incompatible high- and low-temperature applications, the investigation of biomacromolecular liquids in a solvent-free environment expands their value beyond the traditional *modus operandi* of biology. The preparation of solvent-free liquids with high concentrations of intact biomacromolecules will have a

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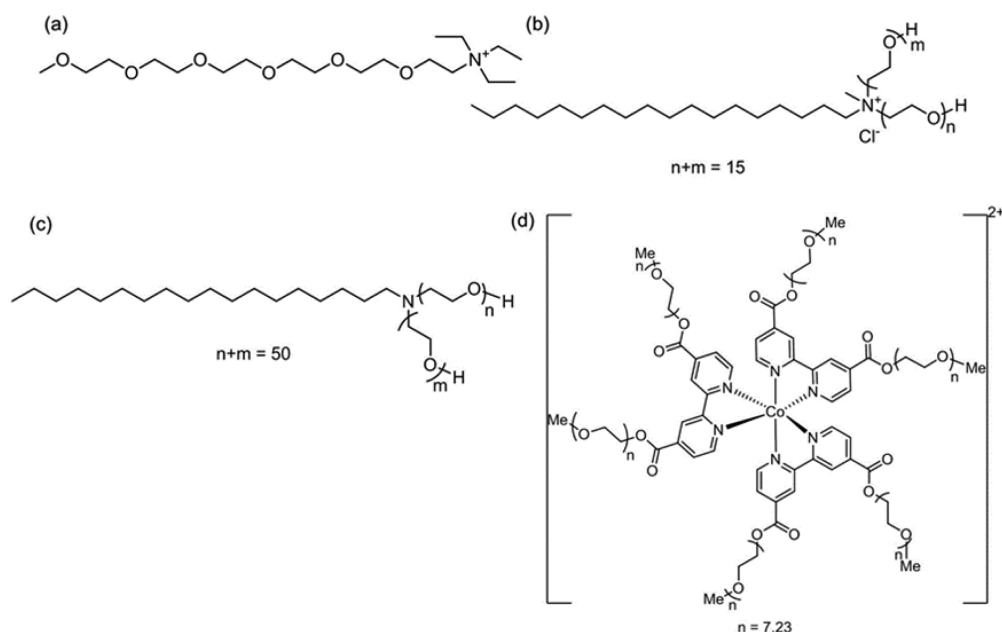


Figure 1. Surfactants containing PEG tails for solvent-free DNA liquids. (a, b) Cationic quaternary ammonium surfactants.^{14,15} (c) Amine surfactant to complex acidified DNA by proton exchange.¹⁵ (d) Polypyridyl complex of Co decorated with polyether chains as cationic surfactants.¹⁴

significant impact on advancing the design and processing of biologically derived nanostructures and even might replace conventional polymeric ionic liquids¹¹ in applications requiring biocompatibility or degradability. Their use as injectable depots for drug delivery of highly concentrated bioactive compounds, for example, barrier dressings for wound healing or artificial skin,^{12,13} is also a promising prospect that may spawn development toward flexible, printable bioelectronics where water hampers device performance. Moreover and from a fundamental perspective, biomacromolecular liquids allow insights into the (vastly different) structural stability and functionality of biomacromolecules in the absence of any solvent.

This Account provides insight into the conceptual understanding of the formation of solvent-free biomacromolecular liquids whose popularity has been fast-tracked by the recent finding that they can be prepared conveniently through electrostatic complexation with surfactants containing flexible alkyl tails followed by dehydration.^{14–17} We will briefly outline design, preparation, and application of solvent-free liquids ranging from nucleic acids^{14–16} to proteins^{17–19} to whole viruses^{20,21} that have become accessible employing this simple and general protocol. In addition, this protocol has yielded access to solvent-free liquid crystals (LCs)^{21–24} introducing ordering and fluidity by ionic self-assembly while retaining biological function²⁵ for biocatalysis,²⁶ bioelectronics,^{27,28} and potentially biomedicine.

■ CONCEPT AND MECHANISM OF FORMATION OF BIOMACROMOLECULAR LIQUIDS

Many small molecules exhibit limited intermolecular interaction and hence can exist in all three common physical states of matter, that is, solid, liquid, and gas. However, with increasing molecular weight and presence of functional groups, forces, such as van der Waals (vdW), ionic interactions, or hydrogen bonds, restrict thermal motion limiting the adoption of different physical states in most pressure regimes.^{29–31} This is particularly true for biomacromolecules or large biological

complexes with sizes on the nanoscale as they strongly interact in the absence of solvent. Additionally, their phase behavior is limited as the size of the biomacromolecular features exceeds the range of the intermolecular force fields.³² Consequently, once a biopolymer powder obtained by freeze-drying is heated above a critical temperature, the material will not melt but degrade due to thermally induced bond scission. As this is a general feature, until recently biopolymeric properties and functions have almost exclusively been investigated in aqueous solution.

The implicit question arising is how folded biomacromolecules or even larger biopolymer complexes can be transformed to show a richer phase behavior. One way to approach this task is to sterically shield strong intermolecular forces by introduction of a surfactant or polymer surface layer physically separating the individual biomacromolecules. Though this method initially appears similar to solvation, the surfactants or polymers specifically bind via distinct electrostatic interactions forming well-defined hybrid structures.

The surfactants or polymers assemble into a defined corona around the biomacromolecule's surface and lower the intermolecular interactions twofold: First, they induce repulsion between the biomacromolecule–surfactant hybrids through the entropically unfavorable compression of surfactant or polymer chains.³² Second, vdW interactions are reduced due to similar electric moments (expressed in similar refractive indices) of the biomacromolecule and the surfactant.^{32,33} Heating these complexes overcomes their solid state positional order increasing volume and allows transition into the liquid state. Additionally to these effects, during the formation of biomacromolecular liquid crystals, the surfactants can also contribute to induce positional order of the included biopolymers.^{22,34}

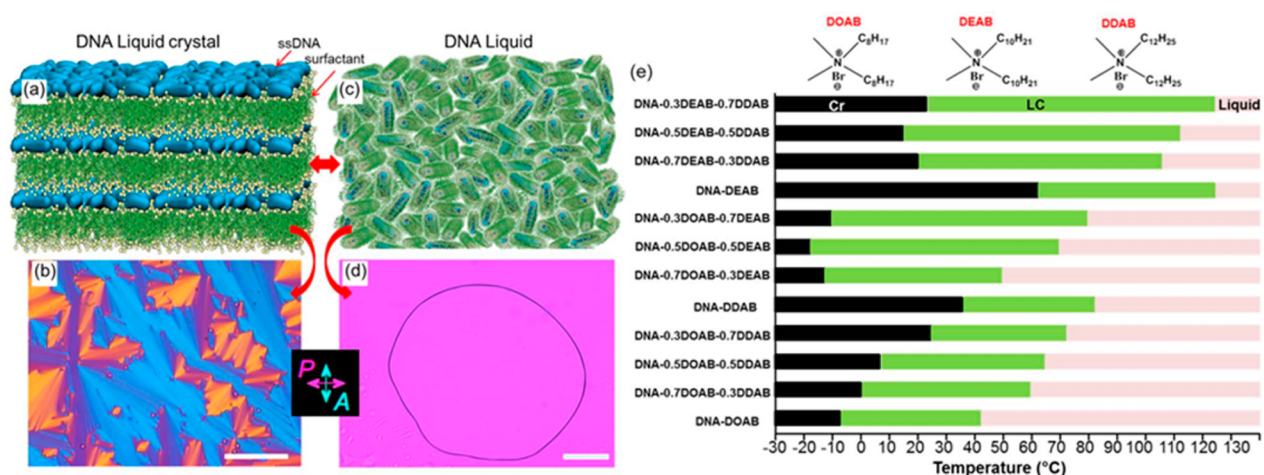


Figure 2. Solvent-free liquid crystals and liquids of DNA-surfactant complexes.¹⁶ (a) Lamellar structure in the LC phase. (b) POM image of the DNA-surfactant mesophases. (c) Schematic of disordered DNA-surfactant complex in the isotropic liquid phase, and (d) POM image of the isotropic liquid. The scale bar is 100 μm . (e) Phase-transition temperatures of DNA-surfactant complexes from crystalline (Cr) to liquid crystalline (LC) to isotropic liquid. Adapted with permission from ref 16. Copyright 2015 John Wiley & Sons, Inc.

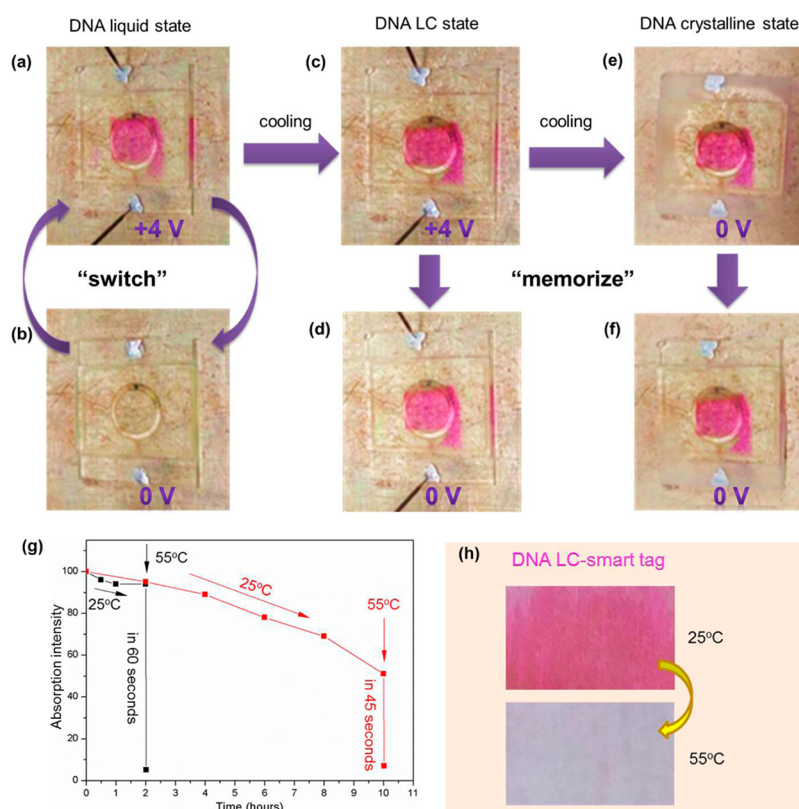


Figure 3. Phase-dependent electrochromic device based on solvent-free DNA-surfactant complexes.²⁸ (a, b) Switchable electrochromism in the isotropic liquid phase. (c, d) Optical memory of the liquid crystal as a persistent colored state. (e, f) Cooling the colored state to the crystalline phase further increases the relaxation time. (g, h) The activated device functions as time and temperature indicator. Adapted from ref 28. Licensed under CC BY 2016 Springer Nature.

DESIGN, PREPARATION, AND APPLICATION OF BIOMACROMOLECULAR LIQUIDS

Nucleic Acid Liquids and Liquid Crystals

Nucleic acid liquids can be prepared by the complexation of an oligonucleotide with a cationic surfactant. The groups of Thorp and Murray as well as Bourlinos pioneered this method and employed poly(ethylene glycol) (PEG) tail-containing quaternary ammonium surfactants (Figure 1a,b), which are electro-

statically complexed in a simple procedure including a final dehydration step.^{14,15} The integrity of the double stranded DNA is verifiable by a variety of methods including Fourier transform infrared (FTIR), UV/vis, and circular dichroism (CD) spectroscopy. Mechanical analysis confirms the DNA's liquid-like character as the loss modulus G'' is higher than the storage modulus G' .

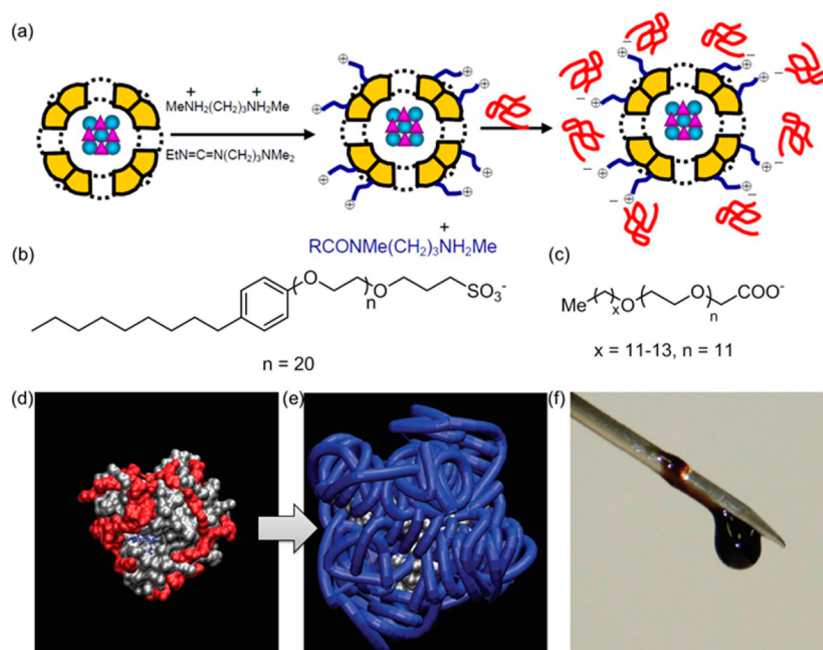


Figure 4. Fabrication of solvent-free protein liquids. (a) General route for the preparation of protein liquids:¹⁷ (i) EDC-initiated coupling of *N,N*-dimethyl-1,3-propanediamine to carboxylic acid surface residues of proteins; (ii) electrostatic complexation of cationized protein with anionic surfactants forming protein-surfactant hybrid. (b, c) Surfactants electrostatically bound to proteins. (d, e) Electrostatic binding of protein with surfactants.¹⁸ (f) Gravity-induced flow of a solvent-free protein-surfactant liquid. Adapted with permission from ref 17, Copyright 2009 John Wiley & Sons, Inc., and ref 18, Copyright 2010 Macmillan Publishers Ltd.

Besides relying on the exchange of the counterions, alternative pathways either make use of direct neutralization of acidified (i.e. protonated) high-molecular-weight DNA (>2000 bp) by tertiary amines (Figure 1c)¹⁵ or employ metal coordinated cationic complexes as surfactants (Figure 1d).¹⁴ Further functionality can be reached by blending hydrophobic molecules, such as the dyes coumarin or rhodamine 6G, into these DNA liquids yielding samples that may find application in DNA-based photonics.¹⁵

Inspired by previous work on electrostatic self-assembly of nucleic acid,^{35–39} we recently found that combining DNA or RNA with cationic surfactants can be exploited for the production of a series of liquid crystalline DNA or RNA fluids (Figure 2).^{16,21} Instead of PEG residues, we employed ammonium surfactants substituted with aliphatic alkyl chains yielding either DNA-surfactant liquids or mesophases. For the analysis of the DNA LCs, polarized optical microscopy (POM) can be used revealing the characteristic focal-conic textures of lamellar structures (Figure 2a,b). Typically, the DNA LCs transition into the disordered liquid state after heating above the clearing temperature (Figure 2c) losing their birefringence (Figure 2d). Long range ordering of the alternatingly intercalating lamellar layer structure can be confirmed by small-angle X-ray scattering (SAXS) measurements, while its topography is visualized directly employing freeze-fracture transmission electron microscopy (FF-TEM). The DNA-surfactant melts are thermally stable, and phase transition temperatures can be adjusted via the surfactant's alkyl chains (Figure 2e). These DNA thermotropic LCs are formed by virtue of their molecular shape, flexibility, and weak intermolecular interactions. This is in contrast to water-rich DNA LCs,^{40–42} in which the amphiphilic character of DNA molecules and the rigidity of Au nanorods stabilize the mesophases.

The anhydrous character, negligible volatility, high DNA content, and thermal stability of these DNA liquids render them ideal materials for the incorporation into microelectronic circuits utilizing DNA for both self-assembly and electronic connections.^{14,43} For example, the Co^{II} -containing DNA liquid (Figure 1d) can be oxidized electrochemically to Co^{III} while revealing a very low faradaic current as the rigid DNA helices impede transport of the metal surfactant complex to the electrode. Likewise, the electron transfer rate in the $\text{Co}^{\text{II}}/\text{Co}^{\text{I}}$ couple is also strongly reduced due to the low mobility of the DNA counterion.⁴³ The introduction of Fe^{II} into this system allows additional oxidation of the guanine base in the DNA through electrochemically generated Fe^{III} ,¹⁴ as observed in the DNA- $\text{Ru}(\text{bpy})_3^{3+}$ system.⁴⁴

Beyond acting as a scaffold, the nucleobases of DNA can be reversibly oxidized in pristine DNA-surfactant fluids giving rise to phase-dependent electrochromism (Figure 3).²⁸ While in the isotropic phase, the electric field-induced formation of highly colored nucleobase radicals^{45,46} vanishes in seconds (Figure 3a,b), a multiple hours long optical memory is observed in the smectic phase (Figure 3c,d). Cooling the DNA-LC material in the colored state to the crystalline phase extends this memory time (Figure 3e,f) implying that the memory volatility is controllable by changing the phase of the DNA-surfactant fluid.

As the electrochromic switching time in the isotropic phase correlates with the DNA length, the rate of DNA oxidation is presumably limited by the rate of mass transport to the electrode. Concomitantly, the surfactant sublayers may act as insulating barrier preventing electron hopping thus slowing the reduction of the colored radical cations. As the clearing points of these materials can be tuned by employing different surfactant mixtures (Figure 3g,h), the temperature controlled

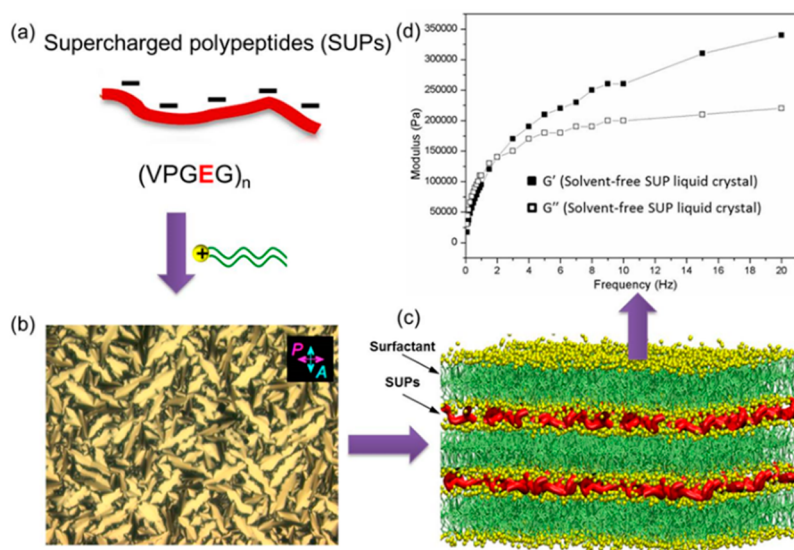


Figure 5. Solvent-free fluids based on SUPs.¹⁹ (a) Negatively charged SUPs combined with cationic surfactants. (b) POM image of SUP-surfactant smectic LC. (c) Lamellar bilayer structure of the LC phase. (d) Rheological investigation of the solvent-free SUP-surfactant fluids. Adapted with permission from ref 19. Copyright 2015 John Wiley & Sons, Inc.

decoloration is prospectively applicable in smart tags for packaging perishable food or medical products.

Protein Liquids and Liquid Crystals

The manufacturing of solvent-free liquids from proteins was pioneered by Mann and co-workers,^{17,18,25} inspired by previous work on nanoparticle liquids,^{47–49} and follows a three-step process (Figure 4). The resulting surfactant complexes melt around 25 °C (Figure 4f) and exhibit a typical water content corresponding to only 6 water molecules per complex.²⁵ This is drastically fewer than required to cover the solvent-accessible surface (526 H₂O per myoglobin (Mb)),⁵⁰ also fewer than the number of site-specific structural water molecules (36 H₂O per Mb) or those required for protein motion and function (60 H₂O per protein).^{51–53}

Additionally to the liquid phase, viscoelastic and smectic LC behavior are also observed, the latter of which can be confirmed by POM and differential scanning calorimetry (DSC).¹⁷ Interestingly, SAXS experiments on the LC phase indicate a lamellar structure with a layer spacing matching the external ferritin diameter. This is an unusual finding as ferritin is a spherical nanoparticle and hence not expected to assemble anisotropically implying that the cationization and subsequent complexation with surfactant may alter its shape to an ellipsoidal complex promoting LC formation.¹⁷

Conversely, Mb–surfactant liquids possess high structural integrity retaining their α -helical secondary structure with only minor perturbation, which is confirmed by attenuated total reflectance (ATR) FTIR and CD spectroscopy.¹⁸ Binding experiments show that the Mb–surfactant complex's affinity toward O₂ is comparable to results obtained for deoxy-Mb under physiological conditions underlining that structure and function of Mb are preserved even without solvent. Further study on this complex employing high-resolution synchrotron radiation as well as CD and UV/vis spectroscopy revealed that the surfactant-assisted solvent-free environment stabilizes the protein evidenced by an increase of the half denaturation temperature.²⁵ This preservation of the folded structure may stem from additional interactions (H-bonds, electrostatic, vdW) within the protein–surfactant complex caused by a decrease of

the protein interior's dielectric constant upon dehydration but also from restriction in translational mobility due to strong molecular crowding. Concomitantly, incoherent neutron scattering on deuterium labeled surfactants showed that the surfactant shell fulfills a similar function as the water hydration layer required for protein chain mobility and activity.⁵⁴

Aside from ferritin and Mb, solvent-free lysozyme–surfactant liquids were prepared employing the three-step procedure.⁵⁵ Studying such a complex with synchrotron radiation and CD spectroscopy while exploiting its increased thermal stability allows trapping an otherwise unobservable β -sheet-enriched intermediate unfolding state leading to a greater understanding of this transient analogue in aqueous environment. Molecular dynamics simulations allow a yet deeper insight into the atomistic structure suggesting that the mobility of the surfactant molecules is impaired and thus responsible for the retention and observability of the intermediate unfolding state.⁵⁶ In addition, anisotropic glucose oxidase–surfactant complexes can be synthesized exhibiting liquid, LC, and solid phase features while retaining the secondary structure.⁵⁷ As the conformational transition temperature of the enzyme correlates with the LC to liquid transition, it is likely that the shape anisotropy of the protein–surfactant building blocks plays a pivotal role in the formation of ordered structures of the complex. Beyond globular proteins, rod-like polypeptides, such as poly(L-lysine) or H-shaped hexapeptides, were transformed into solvent-free liquids and LCs employing lecithin or dodecylbenzenesulfonic acid as surfactants.^{23,24,58}

Only recently solvent-free liquids and LCs of unfolded polypeptides have been discovered in our laboratory. We produced supercharged polypeptides (SUPs) with the glutamic acid-containing pentapeptide repeat motif (VPGE)_n by gene multimerization through recursive directional ligation.^{59,60} Expression in *Escherichia coli* yielded unfolded monodisperse polypeptide chains with a well-defined number of negative charges (Figure 5).^{19,21} These SUPs were then complexed with cationic surfactants generating anhydrous, thermally stable SUP-surfactant complexes after dehydration that exhibit non-Newtonian (smectic LC) and Newtonian (isotropic liquid) fluid behaviors. Mechanical analysis indicated that viscoelastic

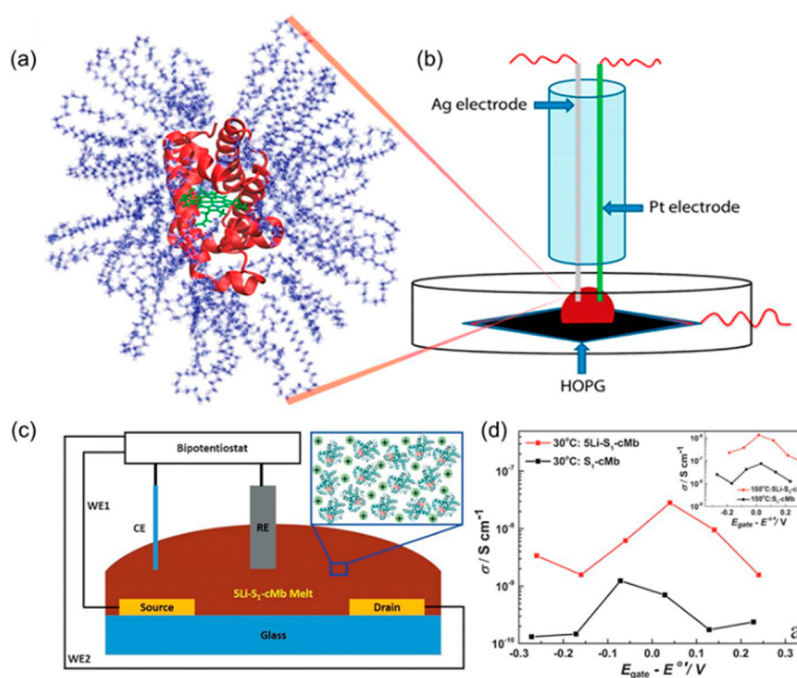


Figure 6. Electrochemical investigation of solvent-free Mb-surfactant liquids.²⁷ (a) Molecular model of the Mb-surfactant complex. (b) Diagram of the three electrode cell configuration. (c) Structure of electrochemical FET used for conductivity measurements. (d) Conductivity measurements for the Mb-surfactant melt blended with $LiPF_6$ (red) and pristine Mb-surfactant melt (black). Adapted with permission from ref 27. Copyright 2015 John Wiley & Sons, Inc.

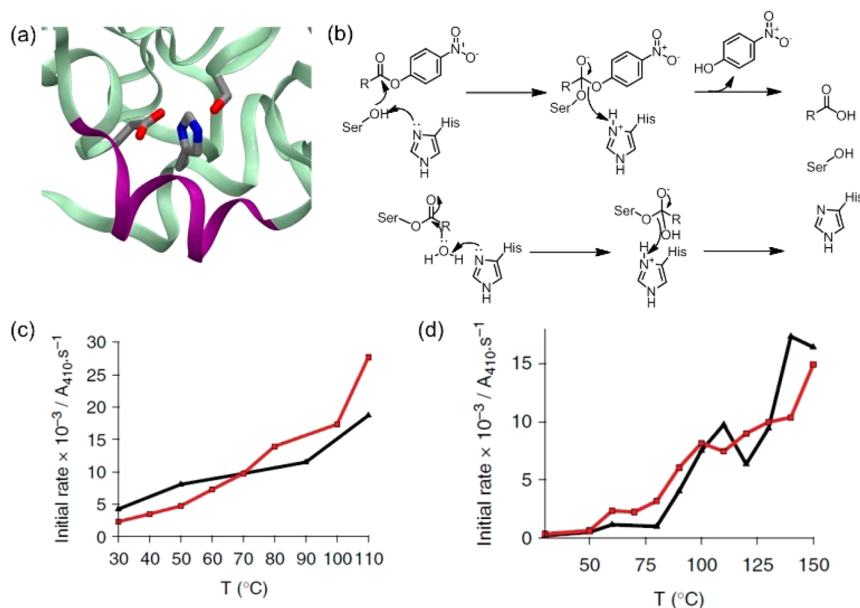


Figure 7. Hydrolysis of fatty acid esters in solvent-free lipase-surfactant liquids.²⁶ (a) 3D model showing the Ser144-His257-Asp203 catalytic triad of the lipase and the helical lid motif. (b) Two-step mechanism for lipase-based hydrolysis of $pNPPal$ and $pNPB$. Initial rate of reactions of $pNPB$ (c) and $pNPPal$ (d) within solvent-free lipase-surfactant liquids as a function of temperature (RML black; TML red). Adapted by permission from Macmillan Publishers Ltd.: ref 26, copyright 2014.

properties dominate in the LC phase while Newtonian behavior prevails in the isotropic liquid state. Notably, the elastic moduli of the SUP-surfactant LCs are in the megapascal-range uncovering their extraordinary elasticity (Figure 5). Moreover and in contrast to the sole components, that is, SUPs as well as cationic surfactants, the mechanical properties are recoverable even after multiple phase transitions indicating their origin in the spatially segregated lamellar structure. Variation of

surfactant alkyl chain length and molecular weight of the SUP backbone fine-tunes the mechanical response in the LC phase.

The Mb liquids containing folded polypeptide backbones exhibit remarkable thermal stability and retain their biological function even at high concentrations. Therefore, they are well-suited for bioelectrochemical applications. Consequently, Mann and co-workers deposited Mb onto a highly oriented pyrolytic

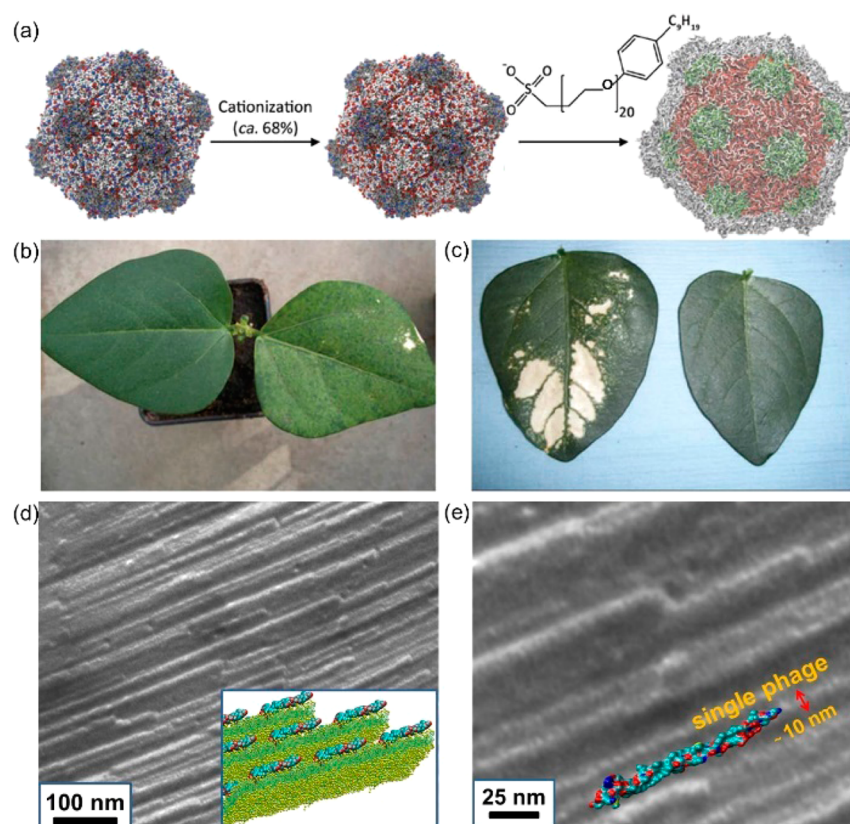


Figure 8. Solvent-free virus-surfactant fluids. (a) General route toward CPMV melt.²⁰ Optical images of symptomatic *Vigna unguiculata* plants after infection with aqueous dispersions of wild-type CPMV (b) and solvent-free CPMV-surfactant droplet (c). Pairs of leaves either treated or untreated are shown. (d, e) Bacteriophages used for solvent-free virus liquid crystals and liquids.²¹ Magnifications of FF-TEM images of the phage-surfactant LCs are shown. Adapted with permission from ref 20. Copyright 2012 John Wiley & Sons, Inc.

graphite (HOPG) electrode inserting Pt (counter) and Ag (pseudoreference) wires into the electrolyte-free, anhydrous protein droplet (Figure 6a,b).⁶¹ Cyclic voltammetry in combination with diffuse reflectance UV/vis, SAXS, and rheology measurements reveal that charge transport occurs via electron hopping between heme cofactors. Since charge transport is considerably lower than that reported for Mb dispersed in hydrated polyelectrolytes,⁶² LiPF₆ was added.²⁶ From this a field-effect transistor was constructed granting control over the redox state of the heme by tuning the gate potential difference between working and reference electrodes (Figure 6c). Two temperature-dependent charge transport mechanisms can be identified, one stemming from electron hopping between heme redox centers and the other from ion movement within the protein liquid (Figure 6d).

Enzyme catalysis in solvent-free protein liquids is an exciting prospect yet a considerable challenge as water or other solvent molecules regulate mass transfer of substrates, nucleophilicity, and proton transfer and dictate catalytically active conformations. Nevertheless, Mann and co-workers fabricated solvent-free lipase-surfactant liquids from the mesophile *Rhizomucor miehei* (RML) and thermophile *Thermomyces lanuginosus* (TML). With both liquids, hydrolysis of fatty acid esters was demonstrated (Figure 7) and by synchrotron experiments as well as CD and ATR-FTIR spectroscopy the conservation of the lipases' native states was shown.²⁶ Esterase activity was monitored hydrolyzing model substrates *p*-nitrophenyl palmitate (pNPPal) and *p*-nitrophenyl butyrate (pNPB) (Figure 7a,b). UV/vis spectroscopy reveals that lipase activity increases

with temperature (Figure 7c,d) yet reaction rates are much lower compared to catalysis in water at physiological temperatures due to the high intrinsic viscosity and hence unfavorable mass transport properties. However, enzyme activity in the solvent-free liquid state was maintained up to 150 °C allowing the investigation of biocatalysis at extreme conditions possibly providing new directions for industrial catalysis.

Virus Liquids and Liquid Crystals

Besides solvent-free liquids based on nucleic acids or protein building blocks, liquids from bacteriophages and plant viruses are of particular interest for the development of storage and transport media as well as nonaqueous virus based nanotechnology. Cowpea mosaic virus (CPMV) or tobacco mosaic virus liquids, for example, can be engineered via a procedure comparable to that used for protein liquids (Figure 8a) and characterized by DSC and ATR-FTIR spectroscopy.²⁰ These methods reveal that dehydration and melting neither impede the secondary structure of the coat proteins nor remove the genetic material from the virus interior. The virus melt can directly be applied on plant leaves as the surfactant chains do not influence host processing of the viral RNA (Figure 8b,c). CPMV-surfactant complexes are soluble in a variety of low-boiling point organic solvents rendering aerosol delivery a viable option.

Moreover, our group recently prepared solvent-free liquids of even larger and anisotropic, monodisperse rod-like M13 bacteriophages.²¹ The negatively charged major coat protein of M13 allows complexing with mixed aliphatic ammonium surfactants yielding solvent-free liquids and LCs that can be

characterized employing POM and SAXS measurements. The observed long-range periodicity in the LC phase is confirmed by FF-TEM studies revealing individual phages globally aligned along a preferred direction (Figure 8d,e).

■ CONCLUSIONS AND FUTURE DIRECTIONS

In this Account, we introduced the concept behind biomacromolecular solvent-free liquids and liquid crystals and highlighted the most important synthetic pathways toward these materials. Moreover, we gave an outlook of the potential applications of this new class of biomacromolecular architectures. The wrapping of nucleic acids, polypeptides, proteins, and multiprotein complexes in a well-defined shell by complexing a surfactant electrostatically with the biomacromolecular component yields thermally stable, easy-to-process liquids with dimensions from the nanometer to the micrometer range. Phase transitions and order of these fluidic materials can be controlled over a broad temperature range granting access to functional liquid crystalline phases. While DNA melts provide a hydrophobic environment in the absence of water allowing the fabrication of DNA-based electrochemical devices, for example, control over the volatility of an optoelectronic state, protein liquids can retain the natural form of the enzyme enabling catalytic applications far outside the range of physiological conditions. Concomitantly, virus liquids prove worthwhile as concentrated, temperature resilient nanocarriers to infect biological targets.

The presented findings show that structure and function of most biomacromolecules can be retained during complexation with surfactants and subsequent transformation to the anhydrous state unleashing formerly unthinkable properties, such as extremely stiff liquid crystals employing noncovalently assembled supercharged polypeptides or biologically inspired charge transporting media relying on tunable myoglobin conductivity. These milestones in synthesis and material fabrication certainly will fuel further efforts employing the presented protocols for the preparation of solvent-free biofluids based on an even wider range of biomacromolecules and offer great opportunities to fabricate stimuli-responsive biological soft materials, thus providing new directions in technological applications including biosensing, biocatalysis, biomedicine, and the construction of bioelectronic devices.

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Notes

The authors declare no competing financial interest.

Biographies

Kai Liu studied chemistry at the University of Chinese Academy of Sciences and gained his master's degree in inorganic chemistry in 2010. He then pursued Ph.D. and postdoctoral studies at the University of Groningen in Netherlands under the supervision of Prof. Andreas Herrmann. From March of 2017, he has been working as a principle investigator at Changchun Institute of Applied Chemistry of Chinese Academy of Sciences and heading a laboratory with research on functional biomaterials.

Chao Ma received his master's degree in chemical biology in 2013 from the China Pharmaceutical University in Nanjing. He then joined the group of Prof. Andreas Herrmann at the University of Groningen to earn his Ph.D. degree. His research is dedicated to genetically engineered supercharged polypeptides and proteins.

Robert Göstl studied chemistry at the Humboldt-Universität zu Berlin, Germany, and has been researching organic photoswitches in the group of Prof. Stefan Hecht since 2009 where he obtained his diploma in 2011 and his doctoral degree in 2014. After his postdoctoral stay in the group of Prof. Rint Sijbesma at the Eindhoven University of Technology in the Netherlands, he took up a position as project leader working on mechanoresponsive (bio)materials at DWI–Leibniz Institute for Interactive Materials.

Lei Zhang received her master's degree in chemistry in 2010 from the University of Science and Technology of China in Hefei. In 2012, she started her Ph.D. studies in the group of Prof. Andreas Herrmann at the University of Groningen. Her research deals with peptide sledding on DNA.

Andreas Herrmann holds a chair for Polymer Chemistry and Bioengineering at the Zernike Institute for Advanced Materials, University of Groningen, The Netherlands. He studied chemistry at the University of Mainz (Germany). In 2000, he completed his graduate studies on dendritic macromolecules at the Max Planck Institute for Polymer Research in Mainz. After a short stay as a management consultant at Roland Berger, he returned to academia and worked as a postdoctoral researcher at the Swiss Federal Institute of Technology in Zurich on protein engineering. From 2004 to 2006, he was head of a junior research group at the Max Planck Institute for Polymer Research. Since 2007, he is full professor at the University of Groningen and his group is interested in nanobiomaterials with a focus on nucleic acid hybrids and supercharged polypeptides.

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