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To cite this version:

Jean-Louis Barrat, Emanuela del Gado, Stefan Egelhaaf, Xiaoming Mao, Marjolein Dijkstra, et al.. Soft Matter Roadmap. Journal of Physics: Materials, 2023, 10.1088/2515-7639/ad06cc . hal-04260533

HAL Id: hal-04260533

https://hal.science/hal-04260533v1

Submitted on 30 Oct 2023

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JPhys Materials

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Soft Matter Roadmap

To cite this article before publication: Jean-Louis Barrat *et al* 2023 *J. Phys. Mater.* in press https://doi.org/10.1088/2515-7639/ad06cc

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Soft Matter Roadmap

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Abstract

Soft materials are usually defined as materials made of mesoscopic entities, often self-organized, sensitive to thermal fluctuations and to weak perturbations. Archetypal examples are colloids, polymers, amphiphiles, liquid crystals, foams. The importance of soft materials in everyday commodity products, as well as in technological applications, is enormous, and controlling or improving their properties is the focus of many efforts. From a fundamental perspective, the possibility of manipulating soft material properties, by tuning interactions between constituents and by applying external perturbations, gives rise to an almost unlimited variety in physical properties. Together with the relative ease to observe and characterize them, this renders soft matter systems powerful model systems to investigate statistical physics phenomena, many of them relevant as well to hard condensed matter systems.

Understanding the emerging properties from mesoscale constituents still poses enormous challenges, which have stimulated a wealth of new experimental approaches, including the synthesis of new systems with, e.g., tailored self-assembling properties, or novel experimental techniques in imaging, scattering or rheology. Theoretical and numerical methods, and coarse-grained models, have become central to predict physical properties of soft materials, while computational approaches that also use machine learning tools are playing a progressively major role in many investigations.

This roadmap paper intends to give a broad overview of recent and possible future activities in the field of soft materials, with experts covering various developments and challenges in material synthesis and characterization, instrumental, simulation and theoretical methods as well as general concepts.

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Introduction

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Status Thirty years ago, in his 1992 Nobel Laureate lecture[1], PG de Gennes talked about a "sentimental journey in the wonderland of soft matter", characterized by complexity and flexibility. Indeed, the complex world of soft matter is probably better suited for such an impressionist journey than for a rigid roadmap. Nevertheless, in this roadmap, we have tried to find a compromise by gathering 26 contributions from leading groups worldwide, illustrating the many directions in which the field is presently developing. These contributions cover a very broad range, from fundamental aspects of statistical physics to engineering applications in fields as diverse as energy, biomaterials, or food science. In this field, and this is also a legacy of the "founding fathers" PG de Gennes and S Edwards, theory and experiment, fundamental and applicative research, are intimately linked, and the new experimental techniques and theoretical tools very rapidly find their ways to new applications. de Gennes and Edwards have often taken forward ideas and concepts developed in other areas such as quantum field theory and hard condensed matter, to build a more rigorous and insightful understanding of the properties of soft materials. Edwards' clear vision of how theoretical science can help resolve practical engineering and industrial problems has had a permanent imprint in soft matter science, bringing on many occasions theorists and industrialists to work together, a legacy still carried over through initiatives such as the Edwards Symposia in Cambridge among others[2]. How many of the topics highlighted in this roadmap could have been anticipated 30 years ago? Probably very few. Even if the basic ingredients of soft matter have not changed, surprising behaviours are still being discovered in fields that were considered as mostly understood, such as polymer networks[3]. The soft matter field once considered synonymous with "complex fluids" has evolved to encompass a growing number of "soft materials" such as dispersions, plastics, membranes, foams, active materials, metamaterials, biomaterials, as illustrated in various contributions of this roadmap. On a fundamental side, the study of soft matter systems has been essential in improving our understanding of major open issues in statistical physics with relevance for applications, such as the mechanism underlying the glass transition[4].

New building blocks, synthesis, and functionalities With the advent of well-defined model systems, systematic and quantitative experiments became possible[5,6] They were dedicated to, e.g., the equilibrium and non-equilibrium behaviour of colloidal, polymeric and surfactant systems and represented benchmarks for theoretical models. Over the years, systems were developed which

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possess a more complex architecture, show tunable properties, respond to external stimuli as well as their local environment, show a specific, e.g., chemical functionality, or use energy from their environment to sustain a directed motion. For example, introducing mechanophores or stress sensitive molecules[7] allows one to follow complex processes such as crystallization, deformation, and rupture of soft materials**.** Self-healing materials[8] with polymer or gel like properties can be achieved through supramolecular chemistry. Although many phenomena have already been observed to emerge from these properties, it is expected that additional, so far unexplored behaviour will be discovered and that the potential for modifications and extensions to the existing building blocks will be explored further. Recent developments and possible future directions in this area are illustrated with a few examples in this roadmap (Sections 1.1 to 1.6; Figure 1).

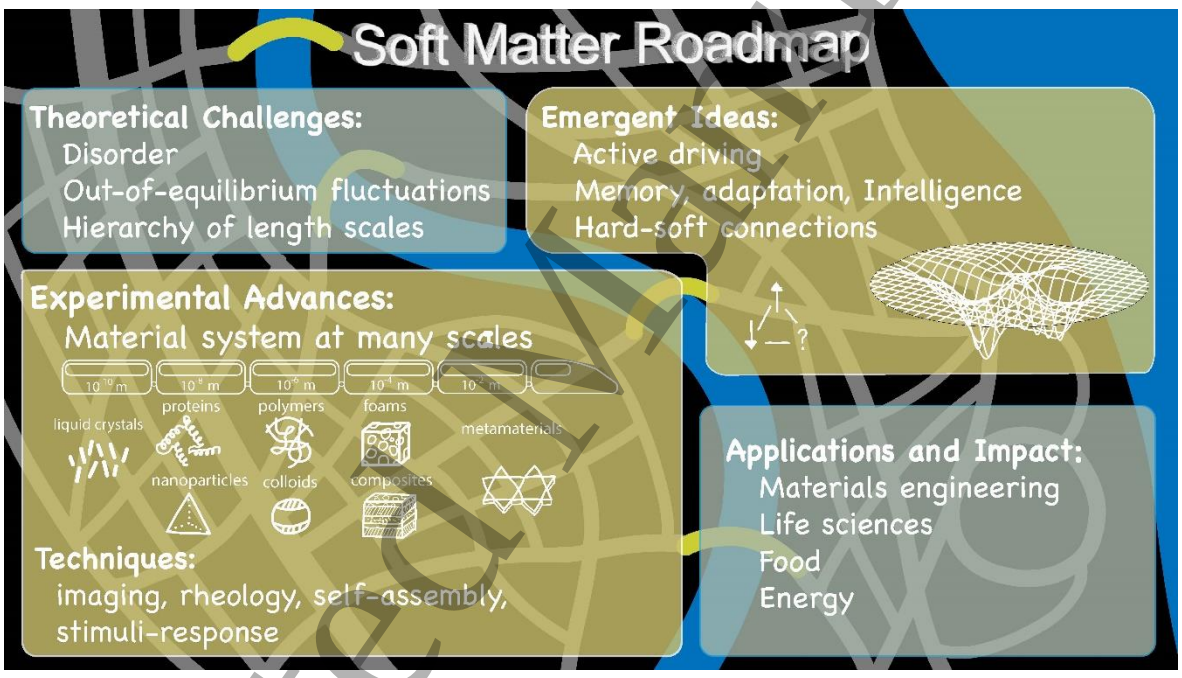

Figure 1 A graphic to demonstrate the areas covered within the Roadmap article

New experimental tools to characterize and manipulate soft materials To fully characterize soft materials, a broad range of length and time scales needs to be covered. During the last decades a range of experimental techniques have been developed, and are still being developed, specifically devoted to and motivated from the investigation of soft materials. The utilization of techniques has changed over the years: for example, to investigate the microscopic structure and dynamics of soft materials, scattering is more and more complemented and sometimes replaced by microscopy (in this case rather due to increasing computational power than developments of the measurement techniques). In addition, especially in non-equilibrium situations, a simultaneous determination of

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several parameters is advantageous to, e.g., link the microscopic structure and dynamics to macroscopic properties. This is reflected in the development of equipment and measurement procedures which combine different (existing or new) measurement techniques, a trend which is expected to continue in future. Moreover, combinations of distinct measurement techniques as such have been explored, a prominent and powerful example being Digital Fourier Microscopy, which benefits from advantages of microscopy and scattering experiments[9] (Sections 2.1 to 2.3; Figure 1). In addition, due to the susceptibility of soft matter to external fields, it is desirable to, on one hand, perform measurements while the samples are manipulated by, e.g., mechanical, electrical, magnetic, or optical fields, and, on the other hand, precisely set the sample conditions, ranging from temperature and other parameters to sample loading (Sections 3.1 to 3.6; Figure 1).

New theoretical concepts and modeling tools. Fundamental advances in theory and modeling as well as establishing new concepts have been an important component in the development of soft matter science. Indeed, soft matter is an exciting playground for new fundamental theories owing to the rich interplay between disorder, strong fluctuations, the hierarchy of length scales, as well as the excellent controllability of the building blocks of soft matter, e.g., nano, colloidal, and granular particles, where interactions can be fine-tuned to explore a plethora of new phases of matter. In the early days of theoretical studies of soft matter, concepts from statistical mechanics and hard condensed matter have been borrowed, ranging from renormalization, criticality, to frustrated interactions, which led to great successes in explaining basic phenomena of unique phases in soft matter. As our understandings of soft matter deepened, and more experimental probes became available in the past few decades, completely new fundamental notions are emerging from soft matter, from mesophases with partially broken symmetry, unique kinetics on rugged free-energy landscapes, nonlocality in rigidity transitions, to more recent advances in using artificial intelligence to understand and manipulate complex materials[10]. These new concepts are being shared with other branches of physics[11], leading to a much richer knowledge base of physics, mathematics, materials science and engineering, and biology (Sections 4.1 to 4.5; Figure 1).

New problems and emerging challenges Because of soft matter versatility, soft matter processes and concepts enter also non-soft materials, famous examples being water purification[12], batteries production[13] or self-assembly of photonic materials as well as building materials[14]. Beyond this, new questions related to the sustainability of material resources and of material processing, and to their environmental impact are emerging. Understanding how to recycle, repurpose and sustainably use plastics as well as biopolymer fibers present in, e.g., agricultural waste, how to reduce the use of toxic and polluting solvents, or, in general, to design more sustainable, stronger or more adaptable materials are all, in the end, soft matter problems and point to the key role that soft materials can play in reducing the human environmental footprint on our planet[15,16] as well as safeguarding a sufficient but also sustainable food production (Sections 5.1 and 5.2; Figure 1).

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Analyzing and sharing (huge amounts of) data Among the new challenges that the science of soft materials is facing, one of the most important and urgent is the sheer volume of data being produced, or to be produced, by advanced techniques, especially those combining different types of measurements. This renders it interesting to exploit the potential of AI based approaches (Section 4.5; Figure 1). In addition, how to share data properly and efficiently, how to develop shared benchmark soft materials, whose softness and frequently intrinsically non equilibrium nature make sample preparation and control particularly delicate, have become among the most pressing questions the soft materials community is working to address[17].

Conclusion In the beginning, soft matter systems were mainly studied in chemistry and chemical engineering. With the advent of well-defined, reproducible, and 'simple' model systems, physicists became interested in soft matter. Meanwhile, the range of systems has been extended to quite complex particles and samples as well as experimental conditions. Approaching the complexity of real-world systems, the developed concepts and models can hence be applied in chemistry, biology, and medicine as well as in material, food, and environmental science and in technological and industrial applications. Therefore, ideas developed in the context of soft matter systems can now be found in many other areas of science where they show a significant impact and relevance (Sections 6.1 to 6.4; Figure 1).

The 26 contributions to this roadmap are intended to illustrate the central position of soft matter science at the crossroad of disciplines, and to highlight recent developments and perspectives in the field, ranging from novel conceptual insights to modern applications. To help the reader navigate the breadth of materials, themes and disciplines covered, we have organized the content into 6 sections that highlight novelty in classical soft materials (1), connections with biomaterials and biological systems (2), applications and technology based on soft materials (3), new exploration tools (4), soft materials manipulation (5), and new concepts that have emerged in fundamental studies of soft materials (6).

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Section 1.1 – Complex colloidal materials

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Status The field of colloid science has undergone a revolutionary transformation in the 20th century. Advancements in the chemical synthesis and fabrication techniques have resulted in the creation of a dazzling variety of novel colloidal building blocks, while novel imaging, tracking, and manipulation techniques of colloidal particles have provided us with a wealth of fundamental insights into physical phenomena, such as melting, freezing, (de)mixing, glass transitions, nucleation, jamming, random packings, two-dimensional melting, and structure formation. These phenomena can be spontaneous or externally driven by gravity, templates, electric or magnetic fields, or other external forces.

From a theoretical point of view, not only the advent of computer simulations in the 1960s as a new scientific tool for studying highly correlated many-body systems, but also the exploitation of thermodynamics and statistical physics for predicting equilibrium properties of colloidal suspensions, have contributed significantly to our increased understanding and exploitation of colloids. Computer simulations enabled us to study with unprecedented microscopic detail the structure and phase behaviour of colloidal systems, whereas the high level of control in colloid synthesis resulted in well-defined experimental model systems, allowing for direct comparisons between experiments, simulations, and theory.

To illustrate the power of synergy between experiments, simulations, and theory, we refer to the freezing transition of hard-sphere fluids into face-centered cubic(fcc) solid phases, predicted theoretically in 1951 [1], and observed in early Molecular Dynamics and Monte Carlo simulations in 1957 [2, 3], but which was received with quite some scepticism at that time. The existence of such a phase transition was eventually proven once and forever by experiments on micron-sized sterically stabilized polymethyl methacrylate hard spheres in 1986 [4]. More interestingly, in contrast to atomic and molecular systems, the effective interactions between colloidal particles can be tuned by the addition of salt to a suspension of charged-stabilized colloids, giving rise to not only fcc but also body-centered cubic (bcc) phases for sufficiently long-range repulsive interactions [5]. Alternatively, an effective depletion attraction can be induced between the colloids by the addition of depletants or non-adsorbing polymer [6]. As the range and strength of the depletion interaction can be tuned by the size and concentration of the polymer, such mixtures serve as excellent model systems to test [7] the theoretical predictions on condensation of gases into liquids as laid down in the dissertation of Van der Waals in 1873 [8].

In addition, the field has shifted its attention from micron-sized colloids to nanometre-sized particles since the seminal work of Bentzon et al. who reported in 1989 the self-assembly of metaloxide nanoparticles into superlattice structures [9]. This study instigated a very active

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research field, driven by the potential of creating new nanostructured materials with unprecedented functionalities using colloidal self-assembly of for instance semiconductor, metal, perovskite, and metal organic framework particles [10].

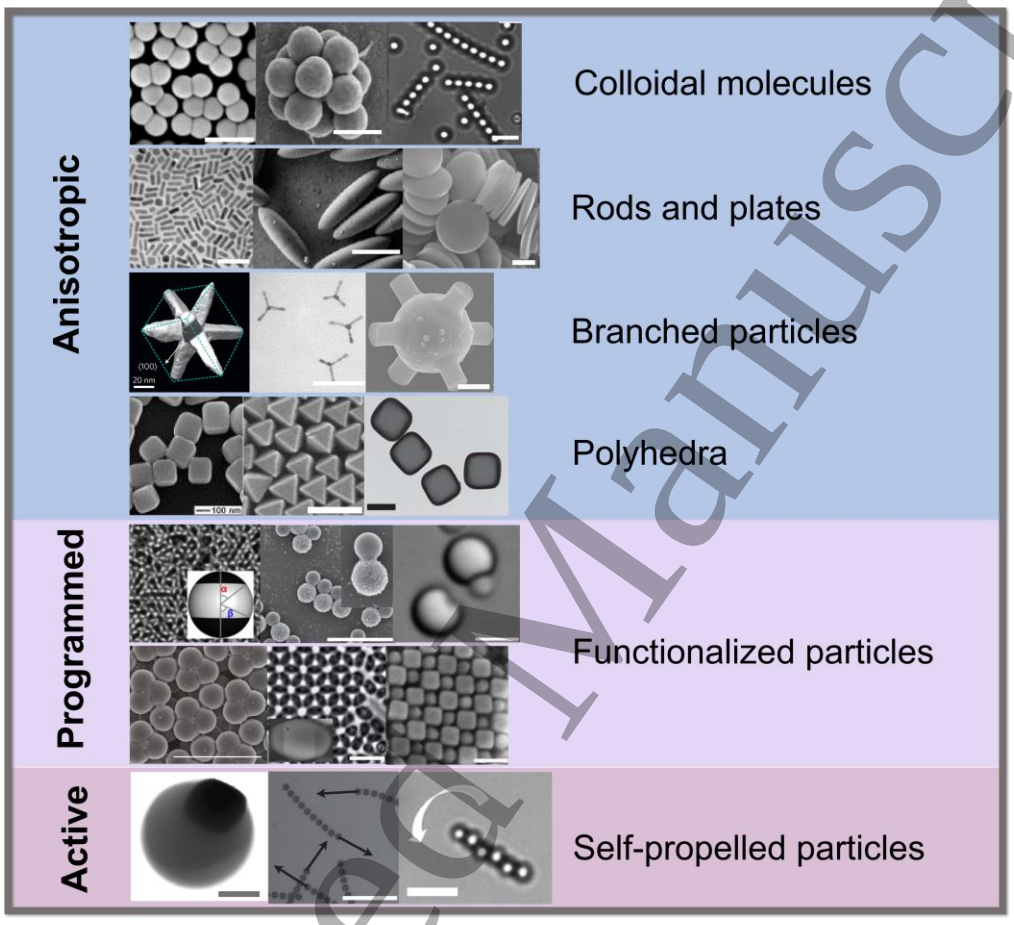

Figure 1 The dazzling variety of novel colloidal building blocks can be divided into A) anisotropic particles such as 1) colloidal molecules: colloidal silica dumbbells, scale bar 180 nm [11], colloidal clusters of polystyrene microspheres, scale bar 1 µm [12], colloidal (semi)flexible polystyrene bead chains, scale bar 4 µm [13], 2) rods and plates: Au nanorods, scale bar 100 nm [14], colloidal polymethylmethacrylate ellipsoids, scale bar 5 µm [15], colloidal polystyrene discs, scale bar 2 µm [16], 3) branched particles: colloidal CdS/CdSe octapod-shaped nanocrystals [17], colloidal CdTe tetrapod-shaped nanocrystals, scale bar 100 nm [18], branched cubic silica particle, scale bar 1 µm [19], 4) polyhedral-shaped particles: slightly truncated silver nanocubes [20], octahedral metal organic framework particles, scale bar 0.5 µm [21], hollow silica cubes, scale bar 1 µm [22], B) programmed functionalized particles: 2 µm silica triblock Janus spheres [23], polystyrene patchy dumbbells with different surface roughness, scale bar 10 µm [24], lock and key colloids, scale bar 2 µm [25], DNA functionalized tetrahedral polystyrene clusters, scale bar 5 µm [26], di-patch DNA functionalized colloids, scale bar 5 µm [27], DNA functionalized nanocubes and spheres, scale

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bar 100 nm [28] and C) active self-propelled particles: 3-methacryloxypropyl trimethoxysilane (TPM) polymer colloidal sphere with a protruding hematite cube, scale bar 1 µm [29], colloidal Quincke rollers, scale bar 50 µm [30], Pt-coated active polystyrene bead chains, scale bar 2 µm [31]

However, the self-assembly of colloidal spheres with isotropic interactions is limited to lattice structures with simple symmetries such as fcc and bcc. To increase the structural diversity, one may resort to binary mixtures that form surprisingly exotic crystal structures analogous to their atomic counterparts like NaCl, AlB2, NaZn13, MgZn2, MgCu2, MgNi2 phase [32, 33] or to mixtures of oppositely charged colloids forming colloidal analogues of ionic crystals like NaCl, CsCl, CuAu, but also novel structures that do not have an atomic or molecular analogue [34, 35].

Another way to increase the diversity of self-assembled structures is to develop novel classes of colloidal particles with anisotropic shapes and varying interaction potentials, see Figure 1. Over the past decades a spectacular variety of novel colloidal building blocks have been fabricated [10, 36, 37] from different materials like dielectric, metal, semiconductor, and combinations thereof, with sizes ranging from the nanometer to the micrometer scale, and with a plethora of shapes such as clusters of spheres, so-called ”colloidal molecules”, rod-like, platelike, branched particles, polyhedral-shaped particles, hollow objects, microcapsules, nanostars, etc. Theoretically, the effect of shape on the interaction of colloidal particles already started in the 1950s with the seminal work by Lars Onsager [38].

More recently, these particles can also be functionalized so that instructions for self-assembly are programmed in the shape, e.g., lock and key colloids [25] or shape-shifting particles [39], in the surface pattern, e.g., Janus colloids, triblock Janus colloids, and patchy particles using e.g., regioselective depletion [40] or surface functionalization by DNA or proteins. Especially, the hybridization of complementary DNA strands grafted on the surface of colloidal building blocks, pioneered by the works of [41, 42], has proven to be a successful and versatile route for programming the self-assembly of structures as complex as diamond and clathrates [26, 43]. In addition, the self-assembly can be aided or altered by the application of external fields such as electric fields, gravity, templates, and by the structure of the solvent. For instance, self-assembly of colloidal particles can be tuned in situ by solvent-mediated interactions upon approaching the critical point of a solvent mixture [44], bicontinuous gel networks are formed in the case of an arrested phase separation of the solvent mixture due to jamming of the adsorbed colloids at the liquid-liquid interface [45], and topological structures like strings, knots, and links are formed due to the anchoring of a (chiral) nematic solvent at the colloidal surfaces [46, 47]. This vast array of colloidal building blocks and self-assembly protocols can be exploited for the fabrication of nanostructured materials with interesting optical, mechanical, and catalytic properties. To accelerate the design of self-assembled nanomaterials, the experimental efforts can be guided by theory and simulations. Over the past decades, huge progress has been made in the development of algorithms to predict the candidate structures of these novel colloidal building blocks, determining the thermodynamically stable phases by calculating free energies, to the point where

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thermodynamic phase diagrams can be calculated in theory and simulations for any particle shape and interaction using the tools of thermodynamics and statistical mechanics.

Current and future challenges

(a) Designer soft matter

High throughput screening We have arrived at the brink of exciting times, where we can synthesize or fabricate colloidal building blocks with (nearly) any shape and interaction potential, from any material on demand. From a theoretical side, tremendous efforts have been devoted over the past decades to the "forward design" problem: Which structures with what properties are formed for a given colloidal building block under what circumstances? A major drawback of this approach is that the number of possible building blocks and thermodynamic conditions is vast, calling for the development of efficient high-throughput protocols to quickly conduct many experiments or simulations simultaneously and to test systematically many combinations of parameters. For instance, automated microfluidic and robotic synthesis platforms can be used to conduct many experiments in a high-dimensional parameter space in a very efficient way. On the other hand, surrogate models based on e.g., machine-learned many-body interactions can significantly accelerate the exploration of large search spaces in computer simulations [48]. Using these data-driven approaches, machine learning can be used to find a mapping between the input parameters, e.g., different thermodynamic conditions, on the one hand and the outcomes of the experiments on the other hand. Such machine-learned models can be used to make predictions for unexplored parameter combinations, thereby enabling rapid identification of promising building blocks, interaction potentials, and thermodynamic conditions for targeted self-assembly of colloidal structures with specific properties and functionalities. Additionally, the analysis of large amounts of data produced by high-throughput screening with novel machine-learning algorithms may result in the development of reliable and generic design rules that can be used to create soft advanced materials by design with certain electronic, optical or catalytic properties, or mechanical or rheological responses. A combined high-throughput screening and machine learning protocol can be used to provide suggestions for the next experiments/simulations to improve the machine-learned models or to optimize the conditions for a certain outcome. Very recently, a mobile robotic chemist was developed that could autonomously execute multiple experiments in a chemical lab and that uses machine learning to optimize a certain property based on the experiments done so far [49].

Inverse design The holy grail of designer soft matter is the development of a protocol for solving the so-called inverse design problem: What kind of colloidal building

blocks should we make and under what thermodynamic conditions should they self-assemble to realize a desired structure with a specific property? While state-of-theart computational and theoretical statistical mechanics methods have been very successful in solving the so-called "forward" design problem, a robust, versatile algorithm for solving the inverse problem remains a

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significant challenge. The lack of a reliable and efficient inverse design method remains a significant obstacle for the full exploitation of colloidal self-assembly in the development of next-gen materials. A variety of inverse-design approaches has been developed recently based on machine learning approaches or optimization techniques such as evolutionary strategies to optimize interaction potentials for targeted self-assembly, albeit often resulting into colloid interactions that are not always experimentally realisable [50]. This can be solved by restricting the search space to experimentally realistic potentials.

Kinetics Despite the availability of a wide variety of colloidal building blocks, the number of successfully self-assembled structures is still limited. To better understand and control the self-assembly, it is essential to also investigate the kinetic pathways for the formation of the thermodynamically stable phases, proceeding either via nucleation and growth or through spinodal decomposition.

Nucleation Homogeneous nucleation of colloidal particles has been the subject of many studies in the past decades. Several scenarios have been proposed in the literature such as one-step or two-step crystallization mechanisms, devitrification, spinodal-like processes, etc., but consensus has not been reached. Nucleation of the stable phase may also be hampered by the formation of competing polymorphs. To gain control over the formation of certain polymorphs requires a better understanding of the nucleation pathways and of the selection mechanisms that determines the pathway towards a certain self-assembled structure.

Vitrification Additionally, the self-assembly may be suppressed by kinetic effects such as vitrification, gelation, defects, stacking faults, and grain boundaries. Upon increasing the volume fraction, colloidal suspensions may undergo a glass transition where the viscosity increases by orders of magnitude and the system macroscopically behaves as a solid, yet its structure is still disordered. Despite the amount of research devoted to understanding glasses, the microscopic origin of the glass transition remains controversial and heavily debated. The main problem is that the structural relaxation time increases rapidly upon approaching the glass transition, making it difficult to unravel the physical phenomena underlying the glass transition. Recently, significant progress has been made in understanding the glass transition using machine-learning protocols to relate local structures hidden in the glass to the dynamics of the particles [51] as well as by employing algorithms that considerably speed up the equilibration deep in the glass [52]. It is clear that the kinetics and competition with other polymorphs, glass transitions, and gelation should be taken into account in the design and inverse design of self-assembly routes for specific target structures, e.g., by exploring the free-energy landscapes using data-driven methods and sculpting it towards the formation of the desired polymorph [53, 54].

(b) Soft materials and machines with lifelike properties The self-assembled materials mentioned so far are, however, passive. The next step would be to develop hierarchically structured soft materials and machines that can autonomously assemble, sense, respond, and reconfigure on demand. Nature displays a plethora of self-assembled dynamic materials that respond to external

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stimuli, e.g., Chameleons change colour for camouflage, plants have the ability to bend towards sunlight, pinecones can change shape for a sudden seed release, and geckos stick to surfaces and change adhesion due to a self-regulated cooperative motion of tiny hairs (setae) on their feet. In all these cases, the ability to respond and adapt is encoded in a hierarchically structured material, where active and passive components are coupled in a non-trivial way. The design of soft materials and machines that function far from equilibrium requires insight in the dynamical behaviour of self-organizing active elements.

Active matter In the last decade, a diversity of active or self-propelled particles [55] have been produced ranging from chemically fuelled phoretic swimmers, light activated self-propelled colloids, magnetic swimmers, Marangoni-driven active droplets, Quincke rollers, etc. The exact mechanism responsible for the self-propulsion of these particles varies with the details of the colloidal system, and may be driven by transport phenomena like electrophoresis, diffusiophoresis, or thermophoresis when the activity is generated by gradients in the electric field, concentrations of solutes, or temperature, respectively. A precise control of out-of-equilibrium active matter systems requires a thorough understanding of the self-propulsion mechanism. The collective behaviour of many interacting and self-propelling particles can give rise to fascinating phenomena and a plethora of self-organized structures, which are not observed in passive systems. Examples of such structures include clustering, motility induced phase separation, living crystals, dynamical superstructures of synchronized microgears, and chiral fluids, among others [55]. Since these particles incessantly convert energy into active motion, these systems are intrinsically out of equilibrium. In contrast to the collective behaviour of passive systems, which is well-described by the laws of equilibrium thermodynamics and statistical physics, there is no such framework yet for active matter. New theoretical approaches are required to describe the collective dynamic behaviour of active systems [56].

Hierarchical self-assembly Nature is rife of beautiful examples of hierarchically organized structures, where active and passive elements function in a cooperative way. For instance, macromolecules like lipids, DNA, and proteins self-assemble into cells, individual cells into tissues, tissues into organs, and organs into organisms such as birds and fish that can in turn dynamically organize into flocks and schools. These hierarchical, dynamical structures aspire researchers to also self-assemble colloidal matter hierarchically. A better insight in the laws and possibilities of hierarchical self-assembly will enable us to structure matter over multiple length scales and to add new (dynamic) properties and functionalities at each self-assembly step. Examples of hierarchically self-assembly include the fabrication of colloidal molecules [12], supraparticles [57], patchy particles [58], or the co-assembly of different colloidal particles in hierarchical multicomponent materials [59]. The ultimate aim is to create self-assembling micromachines [60, 61] that are motile, self-healing, responsive, and shapeshifting, which can autonomously assemble into complex and interesting dynamical structures.

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Concluding remarks The theoretical tools to understand the equilibrium behaviour of colloids were developed in the 19th and 20th century, before the advent of computer simulations in the 1960s and our ability to conduct controlled experiments since colloidal particles with accurately defined shapes, interactions, and surface functionalizations were only synthesized from the 1990s. However, applying the methods from statistical physics, thermodynamics, and liquid-state theory frequently led to equations that are too hard to solve analytically or numerically, and computer simulations gained ground over the past decades. While the equilibrium behaviour of colloidal matter is well described by equilibrium statistical physics, there is no such framework yet to describe out-of-equilibrium systems. The focus of the 21st century will be on the development of a theoretical framework that encompasses non-equilibrium statistical mechanics and non-linear dynamics. Recently, machine learning has become the fourth pillar of science, next to theory, experiments, and simulations. The use of machine learning as a scientific tool is picking up with an incredible speed. In the next years, we will see that large data sets from simulations and experiments will be combined to find mappings between input parameters, such as thermodynamic conditions, particle interactions, etc. on the one hand, and the macroscopic equilibrium or out-of-equilibrium behaviour on the other hand by training machine-learning algorithms with the available data. These machine-learned models can be used to make predictions for unseen input parameters and to optimize materials designs. An important question that arises is whether or not these machine-learning algorithms can deliver any scientific understanding, or should they solely be considered as black box models, and more provocatively, do we still need theory to obtain a physical understanding of the phenomena at hand. Time will provide us with an answer. What we do know is that the study of colloids has already provided us with a wealth of insights into physical phenomena such as freezing, nucleation, and glass transitions. In the coming years, this rapidly evolving field will turn its attention to the bottom-up self-assembly of bio-inspired complex materials and machines, where passive and active components function far from equilibrium together in an intricately cooperative and hierarchical way. Studying these new materials with life-like properties will lead to exciting new physics and will give us insights in the dynamic and collective behaviour of out-of-equilibrium systems, requiring the development of new theoretical frameworks to describe these fascinating systems with self-healing, responsive, and adaptive properties.

Acknowledgements Financial support from ERC Advanced Grant No. 884902 'SoftML' is acknowledged.

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Section 1.2 – Engineering colloidal particles

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Status Until recently, most synthetic colloidal particles were spheres that were suspended in a liquid and stabilized against aggregation by surface charges or by a polymer brush adsorbed or grafted to the particle surface. Such particles found widespread use in cosmetics, paints, medicine, and in fundamental studies of phase transitions and self-assembly. Interest in engineered colloidal particles was sparked in the mid-nineties by the realization that colloidal crystals might be useful for new optical applications including materials with photonic band gaps. Early work focused on close-packed FCC photonic crystals of spheres, but attention shifted to cubic diamond crystals, or structures with similar symmetry, which are needed to realize the large band gaps and the insensitivity to disorder required to achieve robust optical properties. This led to the development of particle clusters preassembled into dimers, tetrahedra, or other aggregates [1] that could serve as building blocks for assembling colloidal crystals more complex than the familiar FCC, BCC, and related structures. It also led to the development of patchy particles [2,3], especially 4-patch colloids that mimic the valence and tetrahedral bonding symmetry of diamond-forming atoms like carbon. However, patches alone proved inadequate to form cubic diamond crystals as they do not constrain the bond conformations of neighbouring particles. The requisite "staggered" bond conformations were achieved very recently by synthesizing patchy particles with tetrahedral lobes, which led to the first self-assembled cubic diamond colloidal crystals suitable for templating 3D photonic crystals [3].

Interest in colloidal self-assembly spurred several other innovations, including the development of Janus particles (particles with two dissimilar faces) that self-assemble into structures resembling those formed by molecular amphiphiles [1] and also into fascinating new structures like a 2D honeycomb lattice [4]. The development of oppositely charged ionic colloids stabilized by a thin polymer brush has produced colloidal crystals of unprecedented size and stability, with millimetre-size crystals in a variety of structures that can be permanently fixed, removed from aqueous suspension, and dried while maintaining their crystallinity [1].

The periodic spatial variation of the refractive index in colloidal crystals gives rise to structural colour that depends strongly on viewing angle due to Bragg scattering from different crystalline planes. The desire for colour independent of viewing angle thus led to intense activity on developing disordered arrangements of colloidal spheres with structural colour [5]. Hyperuniform arrangements of colloidal particles, which can be achieved through periodic shearing [6], also emerged as another significant idea for producing not only structural colour but also photonic band gaps from isotropic structures.

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Research on colloidal self-assembly focused on developing new attractive orthogonal programmable interactions between colloids, the most versatile being those derived from DNA-coated colloids, whose hybridizing sticky ends can be manipulated to control phase behaviour as well as to dynamically reconfigure colloidal structures using toehold displacement strands [7]. The development of roughness-controlled depletion attraction [8] as well has critical Casimir forces [9] also added to the expanding toolset for controlling self-assembly.

Another important direction was the development of lithographic methods form making structured particles, particularly hydrogel particles, which has led to a vast library of particle shapes and applications in photonics and medicine [10].

Current and Future Challenges Although a vast new toolset of colloidal interactions and particle shapes has been introduced recently, few new crystal structures have been realised. Ideally, one would like to be able to program virtually any multiparticle structure, crystalline or otherwise. The programmability and orthogonality of DNA-mediated colloidal interactions would seem to make this possible, but their potential has yet to be tapped. One problem is simultaneously controlling the relative melting (i.e., collective dehybridization) temperatures of many different complementary DNA sticky ends on differently functionalized particles [7]. This involves not only programming the DNA base-pair sequences of the sticky ends, but also controlling and understanding the role of areal grafting density, flexibility, and length of the polymers that tether the sticky ends. Some progress on this front has been made using DNA toehold displacement strands [1,7].

Making colloidal structures that dynamically reconfigure based on external cues like temperature or chemical environment is highly desirable. Here again, DNA toehold displacement strands [1,7] have been a powerful tool, with demonstrations of reentrant colloidal phase transitions and sequential self-assembly, but their potential for making colloidal micromachines remains largely unexplored.

While new particles with different shapes have been realized [1,3,10], many more will be required to realize complex non-crystalline structures such as fully three-dimensional quasicrystals. Moreover, of the particle shapes that can be realised, producing many of them in bulk quantities remains a challenge [1,10]. While there have been some notable advances in synthesizing patchy particles in bulk quantities [1,10], most remain difficult to produce in quantities needed for manufacturing [2,4,9].

A key challenge is fabricating patches, lobes, cavities, or other features with different functionalities so that different parts of a particle can interact with other particles, both through shape-specific lock-and-key interactions and chemically derived interactions. The challenge is to make arbitrary structures similar to those routinely realized with proteins in biological systems [1,7,10].

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Many applications in photonics, require control over structure—crystallinity, hyperuniformity—at long length scales; doing so remains a challenge. Current methods for annealing grain boundaries are crude and very slow. Creating hyperuniform colloidal structures over much more than a decade in length scale remains challenging [6].

Advances in Science and Technology to Meet Challenges Future progress requires advances on several fronts. Developing new approaches for the fabrication of multifunctional colloidal particles with control over patchiness and interactions is vitally important. Taking a cue from proteins, one promising approach is to develop the ability to make linear chains of different colloids in any desired sequence such that they subsequently fold in to a desired "globular" aggregate with preprogrammed patchy interactions. Such a project need not be overly ambitious: sequences from four to about a dozen particles would suffice to create multifunctional patchy particles significantly more complex and versatile than currently available. Using DNA origami to this end provides one approach [7], although the differences in length scales—micrometre vs. tens of nanometres—poses a challenge. Other developing approaches include using liquid colloidal particles (emulsions) or colloids with mobile DNA bound by a liquid bilayer to make flexible colloidal chains that can fold [11].

Developing quantitative models for the binding between DNA-coated colloids as well as a more quantitative understanding of their crystallization kinetics is needed, as crystallization is notoriously slow in these systems. Similarly, understanding the phase behaviour and kinetics of multifunctional patchy colloids could provide invaluable guidance for colloidal design.

A great deal of progress has been achieved is producing structural colour using colloidal glasses. Recent work suggests that modifying the packing protocol to control structural correlations and using core-shell particles to independently tune Mie scattering and structural correlations are important, but so are many other factors so that attaining maximal colour saturation while maintaining angle independence remains a challenge [5].

Concluding Remarks The field of engineered colloidal particles has exploded over the past decade with many new particles and fabrication techniques having been proposed and demonstrated. Lithographically manufactured hydrogel particles are finding ever-expanding medical applications. New colloidal crystals such as diamond have been fabricated for the first time, which could lead to the realization of materials with robust photonic band gaps. Understanding of structural colour and the means to produce it have moved forward significantly. New reconfigurable colloidal materials have been made. All of this opens up new opportunities for colloidal self-assembly. Many of these advances have been motivated by scientific curiosity. Going forward, the field will need to focus more of its efforts towards applications and do so more aggressively in order to realize them.

Acknowledgements DJP acknowledges support from the US Army Research Office (Award No. W911NF-17-1-0328) and the US Department of Energy (Award No. DE-SC0007991).

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Section 1.3 – Soft polymer materials

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Status Polymeric materials have been the focus of research for well over 100 years, and as in the case of many topics at the intersection of science and engineering advances are driven by and motivated by applications. Particularly germane examples today are the use of polymers in emerging energy technologies (carbon sequestration, battery applications, water purification membranes), in creating a circular economy (polymer upcycling), in understanding the context of biological relevant polymers (particularly the topic of coacervation relevant to membrane-less organelles; out of equilibrium – or active -materials) and in the bottom up creation of materials with desired properties (using for example DNA guided assembly of nanostructures). We elaborate on each of these aspects below but an important point we stress is that the future of polymer science and engineering are intimately related to the sustainability of life on this planet.

Emerging Energy Technologies Polymer membranes are critical to the efficient separation of gas mixtures, carbon capture, the separation of ions and in water purification. Despite their widespread use, important challenges remain in the use of membranes in this context - primarily the need to selectively improve the transport of different mixture components while enhancing strength and aging behaviour. The important figures of merit here are the flux of the desired component, which is proportional to the permeability, $\mathrm{P_i = D_i \times S_i}$ ($\mathrm{D_i}$ is the gas diffusivity and $\mathrm{S_i}$ its solubility coefficient) and selectivity (i.e., gas purity) which is defined as $\alpha_{ij} = \mathrm{P_i/P_j}$. The goal is to maximize both $\mathrm{P_i}$ and α_{ij}. Most of the research in this area has empirically targeted the development of new polymers with improved separation performance.[1-3] Additionally mechanical robustness is critical, e.g., having mechanically strong materials to stand the pressure driven flows typically encountered, the ability to resist lithium dendrite formation in batteries, and the ability to minimize aging effects which typically unfavourably affect performance. The ability to *a priori* design polymers with enhanced separation and mechanical properties remains open. In this context we point to the new direction of creating mixed matrix membranes (mixed of MOF particles with polymers[4]; using polymer grafted nanoparticles[5, 6]) as superior constructs for such separations. Other cutting-edge technologies, and their underpinning science, need to be developed in this rapidly evolving field.

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Circular Economy While plastics use grows, US recycling rates have stagnated at 10%. There is thus a need to develop the science that will facilitate the difficult deconstruction of polymers into value-added small molecules.[7, 8] These small molecules can be independently useful, or, alternately, they could be repolymerized into value added polymers ("circularity"). Depolymerizing plastics requires sizable energy inputs because this process has to overcome the very favourable free energy of the forward process of polymerization. The polymer ceiling temperature, $T_{ceiling}$, is a convenient proxy for this important metric. For $T<T_{ceiling}$, the free energy of polymerization $\Delta G = \Delta H(1 - T/T_{ceiling})$, is negative, with typical enthalpies of polymerization being ΔH~50-100 kJ/mol of monomer depending on the particular chemistry in question. For polymers with low $T_{ceiling}$ (e.g., PET, PS, PMMA, Table 1), ΔG is moderately favorable and hence breaking them down into monomers is relatively inexpensive – this is why a large body of research has focused on those particular materials.[9] In contrast, a large fraction of ubiquitous, engineering polymers have high $T_{ceiling}$, e.g., polyolefins, polyisoprene (rubber tires), polyurethanes, polyimides, polyamides and most thermosets, the breakdown pathway is inherently energetically expensive. The free energy to depolymerize polyethylene (≈ 60 kJ/mol ~ 25RT) is high. Since this free energy is large, concurrently the activation barrier, E_a, to go from polymer to monomer is even larger. Thus, reaction rates to go from polymer to monomers are very small, even with the use of catalysts. To alleviate this major bottleneck, we hypothesize that external field(s) need to be judiciously used to flatten the free energy surface so that the polymer and monomer's free energy become closer; further, the activation energy between the two states can also be reduced by this external field. When combined with suitably chosen catalysts, such external drivers can be used to dramatically increase depolymerization rates and thus make recycling pathways viable. Of course, one cannot overcome basic thermodynamic constraints, and hence the external field, which flattens the free energy surface provides the energy that is required to raise the free energy of the polymer and makes it easier to depolymerize.

Table 1: Ceiling Temperature for Select Polymers

Monomer	$T_{ceiling}$
α-Methylstyrene (PαMS)	66^0 C
Isobutylene (PIB)	175^0 C
Methylmethacrylate (PMMA)	198^0 C
Ethyleneterephthalate (PET)	300^0 C
Styrene (PS)	395^0 C
Isoprene (PI)	466^0 C
Ethylene (PE)	610^0 C
Tetrafluoroethylene (PTFE)	1100^0 C

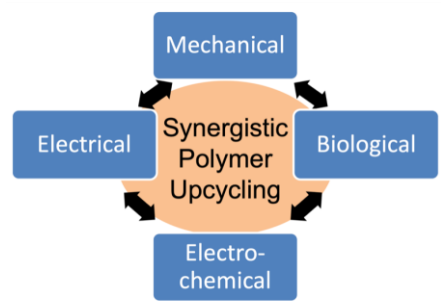

Figure 1 Schematic illustration of external forces that can aid in polymer upcycling.

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Coacervation The ability to understand how living organisms emerged provides fundamental insight into life on earth and paves the way for polymer scientists and engineers to mimic the emergent properties of cells and organisms to create more sustainable materials. For example, understanding how cells originally delineated self and other and gained the ability to grow, divide, and self-replicate could guide the design of autonomous polymeric materials capable of both healing and self-destruction as needed. Recent evidence has shown that short oligomers and polyions can form a condensed phase with a distinct chemical environment than the surroundings – providing a potential mimic of original protocells.[10] These condensed droplets can be imbued with catalytic activity, which makes their formation and dissolution sensitive to the presence of chemical fuel.[11] Theoretical efforts have also demonstrated the potential of droplets of condensed phases, fuelled by chemical reactions, to grow and divide[12] or control their size.[13] In addition to the potential role of oligomer and biopolymer phase separation in the origins of life, the condensation of biomacromolecules plays a key role in both bacterial and eukaryotic cell biology. The formation of these intracellular biomolecular condensates has received extensive attention over the past decade with numerous condensed compartments identified[14, 15] and more recently their functional implications on biomolecular and cellular activity revealed.[16] As understanding of the design rules for the formation of cellular condensates has improved, condensates have been engineered with specificity and metabolic activity.[17, 18]

Active Soft Matter Living matter performs complex functions such as force generation, energy conversion, and information processing that rely on complex biopolymer materials animated by chemical reactions.[19] These dynamic functions are characterized by flows of energy and matter, which are notably absent from passive equilibrium materials. Inspired by biological systems, the pursuit of synthetic soft matter operating outside the constraints of thermodynamic equilibrium aims to advance our fundamental understanding and deliver new material capabilities (e.g., artificial muscles,[20] colloidal robots.[21, 22] There are several strategies for driving materials out of equilibrium. Arguably the simplest relies on initializing the system in an otherwise improbable configuration—for example, glass formation by melt. Alternatively, control variables such as external fields can be modulated in time on scales commensurate with that of material relaxation as to stabilize (or destabilize) new structures.[23, 24] The use of time-dependent drivers that break time reversal symmetry enables steady currents underlying ratcheted transport and force generation. Another route to nonequilibrium uses multiple reservoirs to drive currents of mass, energy, and momentum that couple to and direct material organization. Common examples include polymer systems subject to mechanical shear, ionic currents, or gas fluxes. In addition to external currents and fields imposed at material boundaries, distributed energy input to the individual components of a material system (e.g., via chemical reactions) provides a basis for new phenomena known as active matter.[25] Experimental realizations include nematic liquid crystals with internal stresses powered by molecular motors[26, 27] as well as self-propelled colloids driven by phoretic flows.[28, 29] The latter highlight yet another route to nonequilibrium whereby non-conservative forces that do not derive from a global potential give rise to non-reciprocal interactions that violate Newton's third

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law of action-reaction symmetry.[30, 31] In the context of self-assembly, the use of chemically fuelled reactions to activate components for assembly enables active polymers[32, 33] and droplets[34, 35] inspired by the cytoskeleton and condensates of living cells.

Bottoms Up Assembly of Functional Materials Various nanomaterial classes can spontaneously self-assemble into ordered nanostructures, including nanoparticles (NP), polymers, and biomolecules. The ability to guide self-assembly processes through DNA-based methods stand out due their ability to encode information for specificity and directionality of interactions, which is critical for enabling *designability* of self-assembled nanomaterials. Starting from the early ideas of DNA organization of nanoscale matter[36] and DNA motifs for linking inorganic particles[37, 38], DNA-based assembly methods[39-41] have provided an ability to assemble nanoscale structures, including planar[42, 43] and isolated DNA architectures[41, 44 45, 46], and NP clusters[47, 48]. However, establishing methods for forming the *desired complex 3D organization* of inorganic NPs (*functional payloads*), has met a fundamental challenge: an inevitable coupling between the nature of NP (size, shape, interactions, grafted ligands) and the self-assembly process. Although a rich diversity of 3D inorganic NP lattices[49-51] have been demonstrated, the organizations are typically limited to: (i) mimicking atomic systems, (ii) mono and binary compositions, (iii) single-scale periodicity, and a simple architecture. Thus, a new fabrication platform that incorporates wet-chemistry derived payloads, offers means for creating designed nano-organizations with control on multiple scales and provides integration of different nanomaterial types is needed.

Recent demonstrated integration of polyhedral DNA frames with encoded NP into "material voxel"[52] open possibilities for rational assembly of though directional and encoded interaction of voxels. This assembly strategy permits us to assemble different types of lattice organization in a completely rational way[52]. Moreover, it allows us to decouple a nano-object nature form assembly process that is fully governed by directional bonds of voxel, thus, we built lattices form inorganic NP, proteins and enzymes using practically the same voxel assembly process[52]. Importantly, this realization promises a practically realizable assembly platform that will use inverse design strategy for creating targeted 3D nanoscale organization through the coordination of between voxels based on the encoding of their bonds.

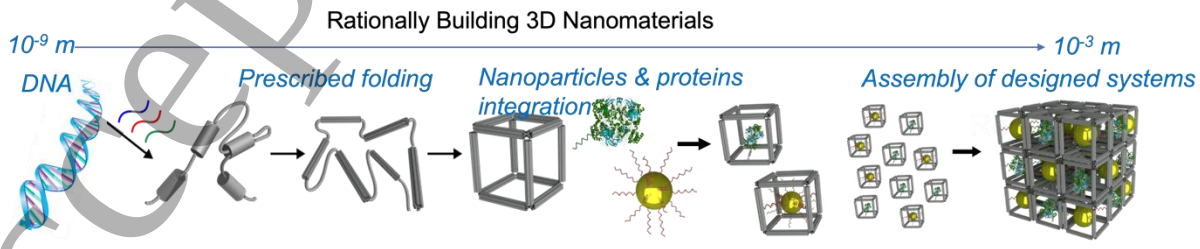

Figure 2 Programming material formation from DNA folding to nanoparticles and protein integration and to large-scale architectures.

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Section 1.4 - Complex Polymer Hydrogels

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Status Complex polymer hydrogels are ubiquitous, the most prominent example being the oxygen-permeable soft contact lenses invented in 1960, that consist of hydrophilic and hydrophobic block copolymers. They are significantly more versatile than the classical simple hydrogels, which consist of one type of water-soluble polymers that are cross-linked chemically and/or physically, typically retain a large amount of water and are mechanically soft [1]. The term 'complex hydrogel' does not only refer to a combination of building blocks having different properties, but also to their diverse functionalities, including the constituents they carry, e.g., payloads such as magnetic nanoparticles, quantum dots or stem cells. Network architectures that feature superior properties compared to classical polymer hydrogels, e.g., enhanced toughness, are based on, e.g., slidable, or high-functionality cross-links or on double interpenetrating networks (Figure 1a-c), and on cross-links having tunable strength (Figure 1d-f, [2,3]). Complex polymer hydrogels featuring multiple physical interactions may have extraordinary mechanical properties, such as high toughness (Figure 1g).

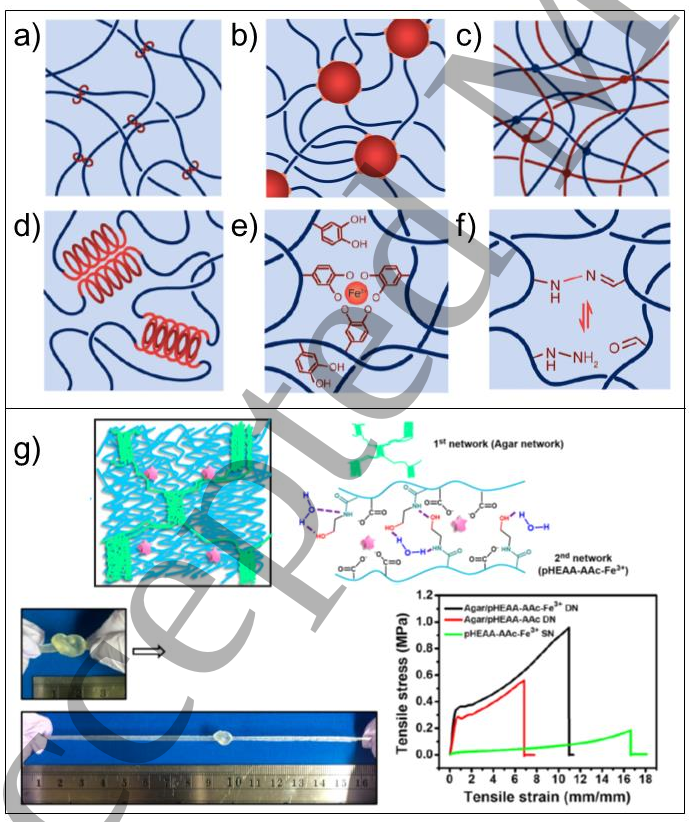

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Figure 1 Crosslinks in complex polymer hydrogels: Types of crosslinks: (a) slidable crosslinks, (b) high-functionality crosslinks and (c) interpenetrating polymer networks. Examples for strong physical crosslinks: helical association (d), weak physical crosslinks: coordination complexes (e), and dynamic covalent crosslinks: hydrazine bonds (f) Reprinted with permission from [2]. Copyright 2021 American Chemical Society. (g) Double network featuring multiple physical interactions. Upper left: Design principle. The first network is a physically cross-linked hydrogel from agar, while the second network is formed by a water-soluble polyanion with Fe^{3+} counterions. Green lines: Agar, forming double helix structures; blue lines: water-soluble polymer; magenta stars: Fe^{3+}. Upper right: Physical interactions at play in the second network. Bottom left: Mechanical behaviour under stress. Bottom right: Stress-strain curves proving the high toughness of the double network with ionic interactions (black curve). Reprinted with permission from [6]. Copyright 2020 American Chemical Society.

Motivated by healthcare needs and other modern technologies, such as robotics, immense progress on network design has been made in recent years through various disciplines, namely advanced chemistry including computational methods, macromolecular engineering, and recombinant DNA technologies. Synthetic model macromolecule precursors prepared by advanced polymerization techniques, such as "living", controlled polymerization, comprising various repeating units and functionalities, introduced via post-polymerization reactions, and featuring various architectures, such as linear, star or graft polymers, have been designed to satisfy combined requirements, namely dynamic association self-assembly, dynamic covalent bonding and multi-responsiveness to various environmental stimuli. The specific design of these polymeric species (e.g., amphiphilic 4-armed star block copolymers, [4]) can lead to well-defined "ideal" networks with tunable structures, mechanical response, and stimuli responsiveness [5]. A multitude of recent developments results in novel multifunctional hydrogels, that combine several properties and are perfectly tailored to the specific application, such as specific mechanical properties with sensing capability (Figure 1g, [7-9]).

Current and Future Challenges For several applications, hydrogels are needed, that not only feature appropriate mechanical properties, such as extremely high fracture toughness and tensile strength, but also particular physical properties, such as high electrical conductivity [2]. In addition, the interfacial properties, like adhesion, are of importance, especially when complex hydrogels are used together with other materials [6]. Hydrogels having multiple combined mechanical, physical, chemical and biological properties can only be achieved by designing complex networks. For instance, portable and wearable electronics require materials for energy storage that are highly stretchable [7-9]. Sensors in soft robotics require gels with high stretchability and sensing capability [10]. For long-term applications in rough environments, these gels need to be highly durable, i.e., self-healing. For applications as components of, e.g., drug delivery systems, microfluidic devices, tissue implants, contact lenses, chemo-mechanical sensors and actuators, materials are needed that mimic artificial muscles, i.e., they are supposed to swell, shrink, or bend in response to environmental stimuli [11]. Tunable hydrogels were proposed for the use in clean water production by solar desalination and in solar desalination and atmospheric water harvesting [9].

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Network design principles targeting modern biomedical applications require additional combined properties like biocompatibility, biodegradability, and bioactivity. Natural polymers, namely polysaccharides, polypeptides, hydrophobically modified peptides (self-assembled to nanofibers) and protein-like motifs, combined with biocompatible synthetic polymers are well-suited as network precursor biomaterials for the rational design of advanced, tailor-made complex networks, devoted to specific healthcare applications, such as drug/gene delivery, wound healing, and regenerative medicine.

For tissue engineering, adaptable hydrogels [12] formed by reversible crosslinks of more than one crosslinking mechanism, e.g., dual crosslinking [13], have been accomplished. This kind of networks, that have mechanical properties adapted to the specific tissue and create a suitable dynamic microenvironment (4D biology) approaching the natural extracellular matrices, allow cellular functions to take place, such as adhesion, migration, and proliferation [14]. For non-invasive or minimally invasive methods into the body, injectable and self-healable hydrogels have been proposed [15], that have specific mechanical properties during injection (protecting cells) and at rest in the host tissue along with suitable stress relaxation and controlled erosion rates. To provide these properties, responsive dynamic linkages based on a combination of triggers like shear or change of temperature or pH have been integrated to the network structure [16].

Hydrogels have been also designed as high-loading, multi-drug carriers for therapeutic purposes [17]. Particularly for cancer therapies, they can cause less severe side effects than systemic chemotherapy and can achieve sustained controlled delivery of drugs at tumour sites. However, these systems are faced with additional challenges related to clinical applications namely long-term biocompatibility, release rates and metabolism in vivo, specificity to patients and tissues [18].

Advances in Science and Technology to Meet Challenges A multitude of recent developments result in novel multifunctional hydrogels, that combine several properties and are perfectly tailored to the specific application. For instance, complex polymer gels have been proposed to be part of electroluminescent devices [7], supercapacitors [8] or in sensors in soft robotics [10]. The use of (interpenetrated) double networks, for instance, ensures the durability of the gels, which is of importance in long-term applications in rough environments. Design principles to achieve high electrical conductivity comprise hydrogels with percolated electrically conductive fillers, e.g., carbon nanotubes, hydrogels with ionically conductive salt solvents serving as electrodes, and hydrogels based on conducting polymers, that may be used as stretchable sensors in prosthetics [2]. Combination of properties is possible in an orthogonal way, e.g., by using a stretchy polymer network and percolating electrically conductive phases [2]. A synergistic way of combining properties could be to use stiffening elements, such as micro- or nanofibers that feature high electrical conductivity themselves [2].

Hydrogels have attracted particular attention as materials, that can change shape following an external stimulus, since they can exhibit complex swelling behaviours triggered by variations of

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external parameters, such as pH, temperature, light, electric fields, ionic strength, antigens, and glucose [19]. Due to such unique responsiveness, good biocompatibility and degradability, hydrogels have gained substantial interest and attention for a variety of potential applications, such as components of drug delivery systems, microfluidic devices, tissue implants, contact lenses, chemo-mechanical sensors and actuators.

The further development of dynamic hydrogel multifunctional platforms for basic and translational biomedical applications is faced with new challenges. The complexity of the emerging novel network platforms increases as to fulfil all the required structural, biocompatible, and final functional properties. This might generate some contradictions. For instance, microscopic structural dynamics and macroscopic long-term stability need to be balanced. Other important issues are the real-time characterization under microscopic resolution and the monitoring of the structural and physical properties along with the cell behaviour during long periods of time, requiring the development of advanced methodologies and novel techniques. In some applications, the hydrogel erosion rates must be rationally designed. The programmable orthogonal hydrogel erosion through distinct triggers, e.g., by sonication or light, targeting dissociation of specific crosslinks might be a solution. Although a plethora of promising network systems devoted to specific applications have been developed and studied in vivo with model animals, not many of them have reached clinical trials [20], which constitutes the final criterion for real biomedical applications and emerges as a new challenge.

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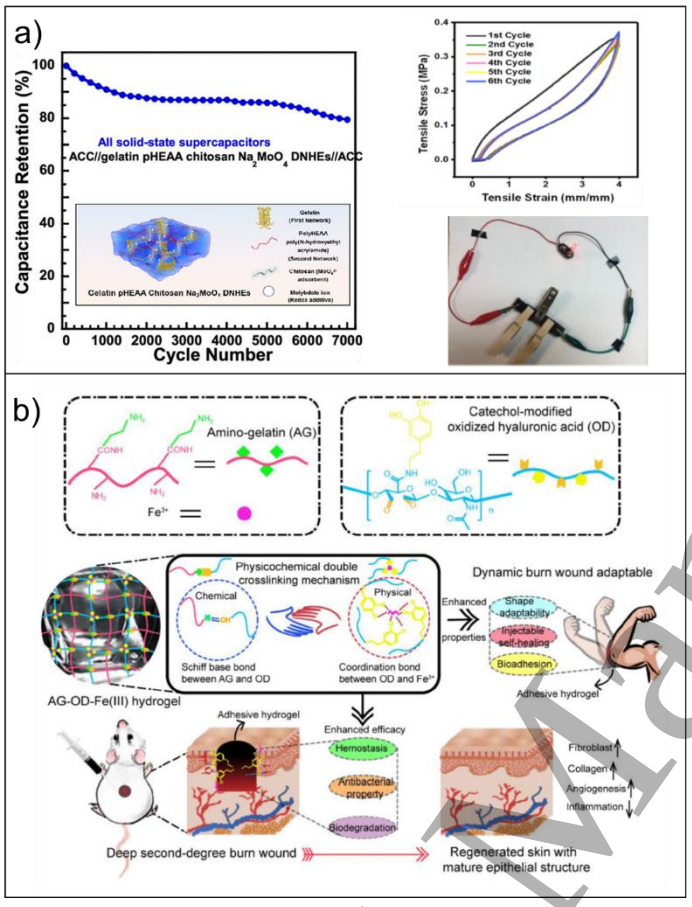

Figure 2 Complex hydrogels for (a) energy applications and (b) biomedical applications. (a) A flexible supercapacitor incorporated with solid-state double network hydrogel electrolytes. Loading-unloading testing cycles show that, while the first network breaks during the first cycle, the second network is rapidly recovered. After 7000 charge/discharge cycles, 80 % of the initial capacitance is retained. A light-emitting diode can be lightened up. Reprinted with permission from [8]. Copyright 2021 American Chemical Society. (b) Schematic representation of the design strategy of the physicochemical double cross-linked multifunctional hydrogel prepared by Schiff base and catechol-Fe^{3+} chelation bonds, capable of healing deep second-degree burn wounds. The hydrogel shortened the healing time of burn wounds to 13 days and accelerated the reconstruction of skin structure and function. Reprinted with permission from [21]. Copyright 2021 Elsevier.

Concluding Remarks Complex networks in the form of hydrogels have been systematically developed the recent years due to the vast variety of promising applications in various fields of technology. Unambiguously there are still several challenges that must be addressed to achieve real and safe applications. The increasing complexity of hydrogels needed to meet the different requirements in daily life applications, raises both fundamental and technological questions, which motivate further interdisciplinary developments of these soft materials. Systematic advancement and optimization of design principles combined with specialized implementation bottom-up strategies are expected to emerge in the years to come.

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Acknowledgements C. M. P. gratefully acknowledges Deutsche Forschungsgemeinschaft for funding (PA 771/19-1). C. M. P. and C. T. thank DAAD and IKY for funding within the IKYDA program.

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Section 1.5 - Liquid crystalline materials

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Status Early documented observations of liquid crystals (LCs) go back some 160 years [1], when they provided evidence of LC phase behaviour in cholesterol derivatives extracted from animals. Nowadays, LCs form a basis of many advanced technologies, ranging from displays to electro-optic, photonic and biomedical devices. These states of soft condensed matter combine various degrees of orientational and partial positional order with fluidity and exhibit structural diversity exceeding that of solid crystals. They can have uninhibited fluidity combined with orientational order alone, like in the so-called nematic LC phases, or exhibit one- or two-dimensional partial positional order or quasi-crystalline organization co-existing with fluidity, like in smectic and columnar phases, respectively. Being highly experimentally accessible, LCs often serve as model systems to understand behaviour of less accessible physical systems, ranging from elementary particles to the Early Universe cosmology [2].

With nearly two centuries of research history and LC-enabled technologies all around us, the LC research field recently exhibits a renaissance of its development [2-12]. For example, more nematic LC phases have been discovered over the recent period of about 10 years than during the rest of LC history. New application opportunities promise a means of addressing the global energy demand and climate-related challenges [3]. Old-textbook classifications need re-writing as entire new classes of LCs continue emerging, including the ones previously thought to be impossible. Recent breakthroughs in nanoscience enable molecular-colloidal LCs that combine thermotropic and lyotropic sub-classes [4,5], where rich phase behaviour stems from stimuli-tuneable molecular and colloidal interactions at the hierarchy of length scales ranging from angstroms to micrometres [4-9]. These LCs reveal unexpected combinations of order and fluidity, like the monoclinic and orthorhombic symmetries [4,5], uniaxial and monoclinic ferromagnetic and other polar LCs [8,9], twist-bend and splay-bend nematic phases [10], etc. Materials with ferroelectric LC fluid phases have been synthesized [11,12] and are actively studied [13-15]. A series of recent breakthroughs in LC elastomers, polymers and gels promise revolutionizing soft robotics, biomimetic smart window films [3], as well as various sensors and actuators. LC sub-classes of active and driven matter exhibit particularly intriguing behaviour of topological defects [16]. On the other hand, LCs are found hosting zoos of topological solitons with particle-like behaviour manifesting in the formation of solitonic crystals and unusual forms of active and driven matter [2,17]. From yet another perspective, manifestations of LC behaviour continue being observed in various biological and active matter systems, as well new biomedical applications such as biodetection, drug delivery and cancer treatment [18-22].

Current and Future Challenges While structure of crystalline solids is fully classified in textbooks, the diversity of structures of LC fluids is still being explored. Much like in the Planer's experiment [1], LCs were often discovered accidentally. To increase the odds of discovery, a common recipe

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was to design building blocks with symmetries of anticipated LC phases and hope that interactions between them will lead to such phase behaviours. Yet, recent findings reveal more complex relations between symmetries of building blocks and those of LC phases. For example, organic molecular dimers of building blocks of conventional uniaxial nematic phases organize into very different mesophases, the so-called twist-bend and splay-bend nematic states [10]. While brick-like molecules commonly exhibited high-symmetry uniaxial rather than highly thought after orthorhombic nematic LCs, an emergent behaviour of high-symmetry disc- and rod-like colloidal and molecular building blocks led to not only orthorhombic but also monoclinic nematic phases (Figure 1a) [4], where the molecular and colloidal subsystems order along obliquely oriented directions in the latter case. Could there be ways of discovering LCs by design? Hypothetically, fluid-like orientational order of colloidal nanoparticles within a molecular nematic host could lead to a series of symmetry-breaking transformations (Figure 1b), but one needs to discover the physical design rules to make these molecular-colloidal assemblies the energetic ground states.

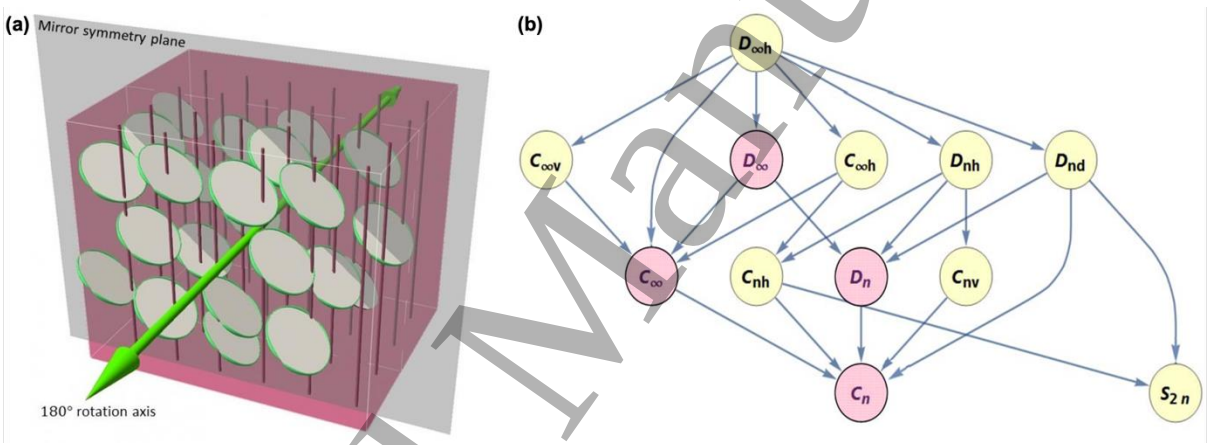

Figure 1 Demonstrated and anticipated diversity of molecular-colloidal LC fluids. (a) Monoclinic nematic formed by thin colloidal discs dispersed in a common molecular nematic host with molecular ordering direction depicted by magenta lines. The symmetry plane and axis are marked; green regions next to particle edges show the localized regions where nematic order of the molecular host medium is perturbed by the colloidal disc surfaces with conically degenerate surface anchoring. (b) Point group symmetries and transformations of orientational order that can emerge in mesostructured nematic LCs formed by a uniaxial $D_{\infty h}$ molecular nematic host doped with colloidal particles with various geometric shapes. Chiral and nonchiral phases are depicted with magenta and yellow colours, respectively.

While topology recently plays important roles in phase discovery in hard condensed matter, blue phases of chiral LCs show how topologically nontrivial field configurations can arise in soft matter, enriching behaviour beyond that of a chiral nematic (cholesteric) LC phase (Fig.ure2a). Cubic blue phases comprise periodic arrays of fractional skyrmions (double twist tubes) and disclinations [2]. 3D particle-like topological solitons can be building blocks of exotic phases too [2]. Figure 2 shows examples of crystalline arrays and phases of the so-called "heliknotons" [12], a type of 3D topological solitons with a dual nature of being a non-singular Hopf soliton in the material director field $\mathbf{n}(\mathbf{r})$ and a vortex (disclination) knot in the immaterial fields of helical axis $\boldsymbol{\chi}(\mathbf{r})$ and $\boldsymbol{\tau}(\mathbf{r})\perp\mathbf{n}(\mathbf{r})\perp\boldsymbol{\chi}(\mathbf{r})$. Such heliknotons form various crystalline lattices, open and closed, including triclinic crystals [12]. Curiously, like blue phases, under appropriate conditions, these heliknoton states can emerge in LC materials with "old" chemical composition, including the ones extracted from animals

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[1], showing how exotic LC states with nontrivial topology could have been overlooked. In a similar way, for many years, polar LC phases with uninhibited 3D fluidity were assumed to be impossible, but several different embodiments of such phases in purely molecular [11-15] and molecular-colloidal [8,9] systems were recently discovered. Technological needs and fundamental curiosity call for research to reveal LC materials with different symmetries, topological diversity and varying combinations of order and fluidity.

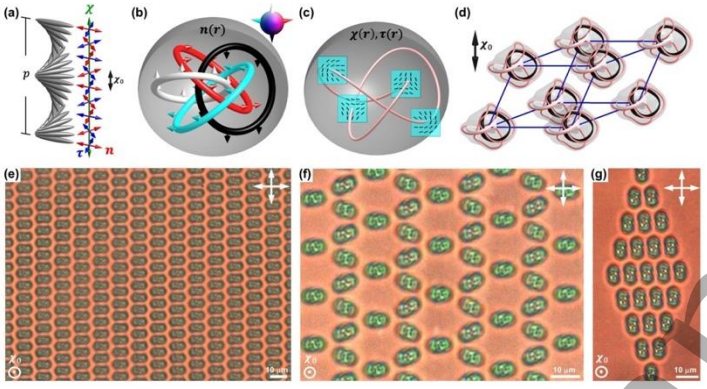

Figure 2 Topology and self-assembled crystals of heliknotons. (a) Helical field comprising a triad of orthonormal **n**(**r**), **χ**(**r**) and **τ**(**r**). (b) Preimages in the smoothly vectorized **n**(**r**) of a heliknoton coloured according to their orientations on $\mathbb{S}^2$ (inset). (c) Knotted skyrmionics structure in the director field **n**(**r**) is co-located with knots of vortex lines in **χ**(**r**) and **τ**(**r**). Gray isosurfaces in (b,c) show regions of distorted helical background. (d) Primitive cell of a triclinc heliknoton crystal. Isosurfaces (gray) of heliknotons with distorted helical background are co-located with vortex knots (red) & preimages of antiparallel vertical **n**(**r**) orientations (black & white). (e,g) closed & (f) open heliknoton lattices, respectively.

Advances in Science and Technology to Meet Challenges The design rules for obtaining molecular-colloidal hybrid LCs with various unusual symmetries of orientational order and fluidity, like triclinic nematics (with uninhibited fluidity and low-symmetry order that has no symmetry operations apart from trivial ones), remain to be revealed. For example, the emergent order with various symmetries can arise from a thermal self-reconfiguration of relative orientations of the molecular and colloidal subsystems, supplemented with competing anisotropic elastic, steric and electrostatic colloidal interactions [4]. Unlike in solids, where symmetries of the crystal basis are required to be compatible with crystallographic lattices, no such constraints apply to nematic fluids that can adopt even a larger variety of symmetries yet to be discovered [4]. The diagram in Fig. 1b shows different symmetries, and transitions between them, which all potentially are realizable in the molecular-colloidal hybrid LCs.

Approaches of recent LC discovery can be combined to open even more opportunities. For example, one can imagine dispersing anisotropic colloidal nanoparticles in twist-bend and splay-bend LCs and stabilizing various topological soliton and defect arrays within them. For example, particularly interesting high-dimensional order parameter spaces are SO(3)=$\mathbb{S}^3/\mathbb{Z}_2$ of the monoclinic biaxial colloidal ferromagnets [4,9] and SO(3)/D_2=$\mathbb{S}^3/Q_8$ of orthorhombic biaxial nematics [4,5]. The allowed topological solitons in these systems are understood based on homotopy theory, but little is known about their stability and interactions. What types of solitonic knotted field configurations can exist in these soft matter systems? For example, $\pi_3(\mathbb{S}^3/Q_8)=\mathbb{Z}$ and $\pi_3(\mathbb{S}^3/\mathbb{Z}_2)=\mathbb{Z}$ topological solitons in biaxial nematic and ferromagnetic LCs would be rather interesting analogues of the $\pi_3(\mathbb{S}^3)=\mathbb{Z}$ Skyrme solitons in high energy physics, but can they emerge as global or local free energy

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minima in these soft matter systems and can they form space-filling crystalline or other arrays, like in the LC blue phases?

New symmetries could impart designable ferroelectric, ferromagnetic, piezoelectric, and other properties on the ensuing LC materials, expanding the scope of technological and fundamental science utility even further. Promising significant new discovery, these emergent LC materials require dealing with a hierarchy of length and time scales as well as with creation of entirely new concepts, laws, and generalizations. LC discovery requires an interdisciplinary research effort that is not purely physics, chemistry, biology, or material science, nor that is a subfield of engineering, but rather is an intrinsically interdisciplinary mixture of these, a pursuit in which substantial progress is made simultaneously in the context of all these fields.

Concluding Remarks LCs with novel structure and physical properties are essential for reducing energy demand, slowing down climate change and improving quality of life. The future LC research will need to focus on understanding and control of molecular and nanoparticle self-assembly, as well as on material behaviour arising from their ordered mesoscale co-organization and self-alignment. The LC research transcends the traditional disciplinary boundaries of physics, topology, chemistry, engineering, and materials science, advancing the knowledge of self-organization of importance to advancing the emergent new technologies. While the examples above touched only the state of art and prospects for new discoveries in LCs of the nematic type, with uninhibited 3D fluidity and orientational order only, similarly exciting opportunities exist for other sub-classes of LCs, like smectics and columnar phases with partial one- and two—dimensional positional order co-existing with fluidity. The road of LC discovery ahead of us is promising entirely new worlds of these beautiful and technologically useful states of condensed matter.

Acknowledgements I.I.S. is grateful to students and postdocs in his research group who worked on liquid crystals and colloids. I.I.S. acknowledges the support by the U.S. Department of Energy, Office of Basic Energy Sciences, under contract DE-SC0019293, and the National Science Foundation grant DMR-1810513.

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Section 1.6 - Solid foams, interface-based materials

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Status Characterised by their remarkably rich properties, solid foams are exploited in a vast range of applications, ranging from food foams, mechanical protection, thermal and acoustic insulation, filtering and lightweight applications to electromagnetic shielding or tissue engineering (Figure 1). Despite their longstanding use, these aerated materials continue to raise many challenging scientific questions and offer great potential for innovation. Solid foams are a specific sub-class of cellular- and macro-porous materials. They consist of a close-packed assembly of gas pores in a solidified matrix whose morphology is determined during an initially fluid-like state where interfacial energies play a decisive role in fixing the pore shapes [1]. This is particularly evident when foams are obtained through "liquid foam templating", whereby a liquid foam in mechanical equilibrium is solidified [2]. Other pore-shaping energies enter into the foaming process when an initially viscoelastic matrix is foamed. The resulting gas fractions of solid foams are commonly above 0.64, with closely packed spherical pores at the lower limit and polyhedral pores for gas fractions close to one (Figure 1). Typical pore sizes range from micrometers to millimeters (Figure 2), with pores being closed (Figures 2a,b) or connected (Figures 2c,d). Pores can be polydisperse and disordered (Figures 2a-d) or monodisperse and ordered (Figures 2e-j).

The astounding properties of solid foams are governed by a complex interplay between the foam morphology, the gas fraction, and the properties of the solid matrix (Figure 1 & Figure 2). Amongst the wide range of modern materials, foams stand out due to their unique multi-scale nature, ranging from the molecular scale of the interfaces (potentially containing stabilising agents) and thin films, to the macro-scale of the full hierarchical material. A vast variety of materials is already routinely foamed, including bio- and synthetic polymers, metals, ceramics, concrete, or glass. Many different techniques have been developed for foam generation, relying on physical or (electro)chemical mechanisms for pore formation [3]. Increasingly, bi-liquid foams (emulsions) are used as templates, resulting in solid foams after removal of the dispersed phase.

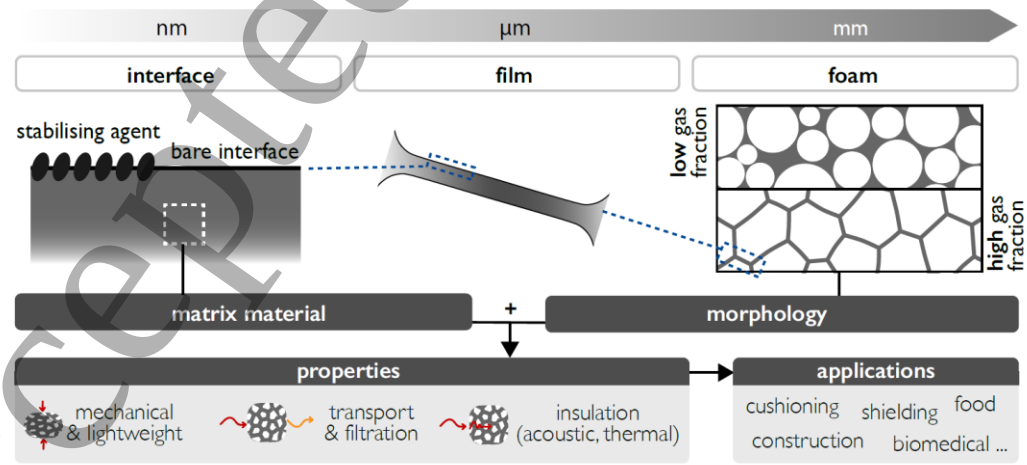

Figure 1 Foams are multi-scale materials, whose rich properties are governed by a complex interplay between the matrix material and the morphology.

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Current and Future Challenges One of the key challenges in foam research remains to establish a predictive understanding of their complex, multi-scale structure-property relations (Figure 1) with emphasis on their largely non-linear response. This requires the development of efficient and reliable structural analysis tools and reverse engineering approaches to predict and design optimal foam morphologies. While foam morphologies in the limit of high and low gas fractions are now routinely treated, important challenges subsist in the description of intermediate gas fractions.

The dominant role of interfacial effects in the initially fluid-like matrix puts important constraints on the foam morphology which limits the accessible range of material properties. Recent advances in 3D printing (Figure 2q) have shown the value of a more flexible control of cellular architectures - yet with limitations for producing large volumes of multi-scale materials at low cost. Solid foams will therefore remain the material of choice for many applications, although they need to be pushed beyond their current limits, for example, to turn them into acoustic/electromagnetic (Figures 2g,q) or mechanical (Figure 2k) metamaterials. Researchers are therefore actively working on developing new strategies to enlarge the range of accessible foam morphologies, either by explicitly controlling the interactions between bubbles in the assembly process (adhesion, friction, interfacial viscoelasticity) (Figures 2g-j), or by exploring the use of hybrid foams of initially liquid-solid composites, involving elastocapillary interactions (Figures 2m,n). Foams with intriguing properties are also obtained using controlled property gradients (Figure 2o), by combining different characteristic length scales (Figure 2n), or by shaping them into simple (Figure 2p) or into complex forms through 3D printing (Figure 2r). Last but not least, better morphology control also involves the need to reach nanoscale pore sizes (Figure 2l) for extraordinary thermal insulation and ultra-large surface to volume ratios.

One of the major challenges in the effort to foam new materials arises from the fact that the mechanisms which control foam stability in the initially fluid-like template remain far from understood [4]. Moreover, each new material requires the development of an appropriate foaming process. Other open questions concern the mechanisms arising at the different material scales during the fluid-solid transition. For example, to control the pore opening process, a better understanding of the thinning and stability of the solidifying thin films is required (10-1000 nm), evoking timely questions related to fluid dynamics and solidification in the presence of complex interfaces and under (soft) confinement. In the race towards high-performance and smart materials, future progress on foams must be intimately linked with the rapidly growing fields of stimuli-responsive materials, soft robotics, and life-like materials, of particular relevance for biomedical applications.

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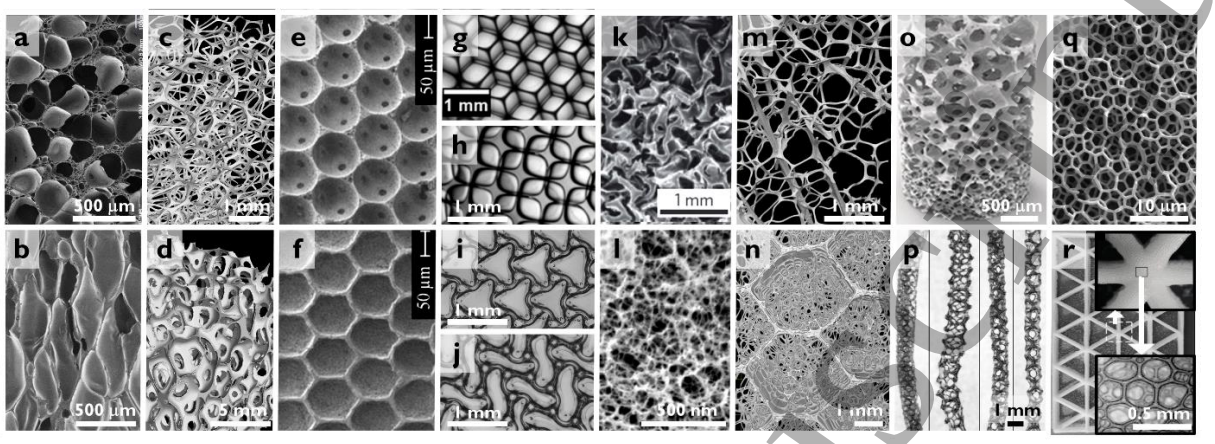

Figure 2 Modern foams come in a wide range of morphologies: Isotropic (a) and non-isotropic (b), closed-cell polymer foams. Low- (c) and high density (d) open-cell polyurethane foams. Periodic open- (e) and closed-cell (f) polystyrene foams obtained by emulsion-templating [5]. Unbuckled (g,h) and buckled (i,j) periodic hydrogel foams of interest for acoustic/electromagnetic metamaterials. (k) Re-entrant foam for mechanical metamaterials [6]. (l) Nano-foam/sponge[7]. Hybrid polyurethane foams containing fibres (m) or a second foam (n). (o) Graded foam [8] and (p) foamed fibres. (q) 3D-printed foam structure as optical metamaterial [9]. (r) 3D-printing with foamed resin [10]. [Credits: a,b,c,d,g,h,l,j,m,n,p – courtesy of ICS MIM team (C. Gauthier, D. Favier, A. Egele, T. Roland, H. Pelletier, A. Hourlier-Fargette, S. Andrieux, W. Drenckhan)]

Advances in Science and Technology to Meet Challenges The evolution of the strongly market-driven research on foam materials is an excellent example that a close link between applied and fundamental research encourages rapid progress. The inherently interdisciplinary nature of this research area requires convergence of diverse communities from academia and industry (mechanics, physics, physical-chemistry, chemistry, biomedical/chemical engineering, etc.) and between different emerging fields (metamaterials, extreme mechanics, soft robotics, …). Improving the interactions between these communities and providing high-quality training of scientists at their interfaces is thus essential to ensure efficient progress. To accompany this progress, advances in experimental, computational, and theoretical tools are crucial to understand and optimise structure-properties relations of multi-scale materials – and to push them beyond current limits with a reverse engineering approach. Computational tools need to cover the multiple length, time and energy scales naturally present in foams, often with strong out-of-equilibrium elements. An example is the efficient coupling of molecular-dynamics-type simulations with finite elements, which remains a challenging issue. Computational and experimental foam research will greatly profit from the rapidly growing progress in Artificial Intelligence tools. For example, they will provide important input in the optimisation of complex formulations and structure/property relations. The development of sufficiently complete mean field theories remains a particularly difficult exercise and its usefulness is sometimes questioned in the light of rapidly evolving computational tools. Experimentally, advances in chemistry and physical chemistry need to provide new stabilising agents and responsive materials suitable for foaming, while advances in the development of new foaming processes need to allow the production of large foam volumes with fine control over the foam morphology. Simpler tools to characterize reliably static and dynamic properties of complex thin films and interfaces need to be developed and their use needs to be

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harmonised across the different research laboratories. Efficient 3D-characterisation of the foam morphology needs to be ensured through technological innovations including lab-based, multi-scale X-ray tomography and associated software for image analysis. The exploitation of large-instrument facilities (X-ray/Neutron scattering and tomography) remains a heavy exercise and hence restricted to a small group of experts despite its unequalled analytic power. Dedicated structures may be put in place to accompany researchers with more ready-to-use solutions.

Concluding Remarks Even though mankind started producing solid foams more than a thousand years ago, progress in the optimisation and exploitation of these "interface-driven", aerated materials will continue to require high-quality, innovative research. Solid foams provide an excellent scientific playground to advance our fundamental tools and our understanding of systems with complex, multi-hierarchical structure-property relations, while providing a natural access to industrial applications in the search for solutions to societal problems.

Acknowledgements We acknowledge discussions with numerous researchers from academia and industry. We acknowledge funding from an ERC Consolidator Grant (agreement 819511 – METAFOAM), from the region Grand Est (Young Investigator Grant), and from the Interdisciplinary Institute "Hierarchical Functional Materials" supported by IdEx Unistra (ANR-10-IDEX-0002) and SFRI (STRAT'US project, ANR-20-SFRI-0012) under the framework of the French Investments for the Future Program.

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Section 2.1 – Rheo-SANS: Small Angle Neutron Scattering (SANS) with in situ rheometry

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Status Development of "structure-property" relationships in colloid, polymer, and surfactant science is a central concept for understanding both equilibrium and non-equilibrium complex fluids and soft materials. The need to understand these structure-property relationships drove the development of neutron scattering sample environments capable of measuring the flow of complex fluids and viscoelastic polymers at the nanoscale[1]. In comparison to X-rays or polarized light, the unique ability of neutrons to penetrate many materials and to provide contrast (isotope substitution) opened fundamentally new avenues of research. The first flow-SANS instrumentation was developed in the 1980's at neutron scattering facilities in France (ILL)[2] and the US (NIST).[3] Investigators quickly recognized the need for simultaneous measurements of rheological properties and *in situ* structural changes to address ever more complex systems showing memory, thixotropy and hysteresis. As shown in Figure 1, the application of a shear field breaks structural symmetry. Consequently, measurements in all three scattering planes defined by the shear flow are needed to reconstruct the flowing microstructure.[4] A commercial Rheo-SANS instrument from Anton Paar is now widely available as a neutron scattering sample environment for the radial and tangential experiments.[5] However, the velocity-velocity gradient plane (1-2 plane, Fig. 1) is the most informative, yet challenging, configuration to measure, and current access to the 1-2 plane is restricted to flow-SANS without simultaneous rheometry.[6, 7]

Significant advances in neutron scattering instruments, increases in neutron flux, broader q-range, and time-resolved data acquisition now enable Rheo-SANS methods to probe materials across a wide range of shear flow conditions, over length scales spanning nanometres to micrometres, and under time scales down to 10 ms.[8] New scientific opportunities in soft matter, biology, and materials development are driving the improvement of scattering environments that can cover greater ranges of shear rate (Fig. 2), broader temperature ranges, complementary *in situ* methods such as dieletric spectroscopy,[9] and more complex flows with extensional components.[10, 11]

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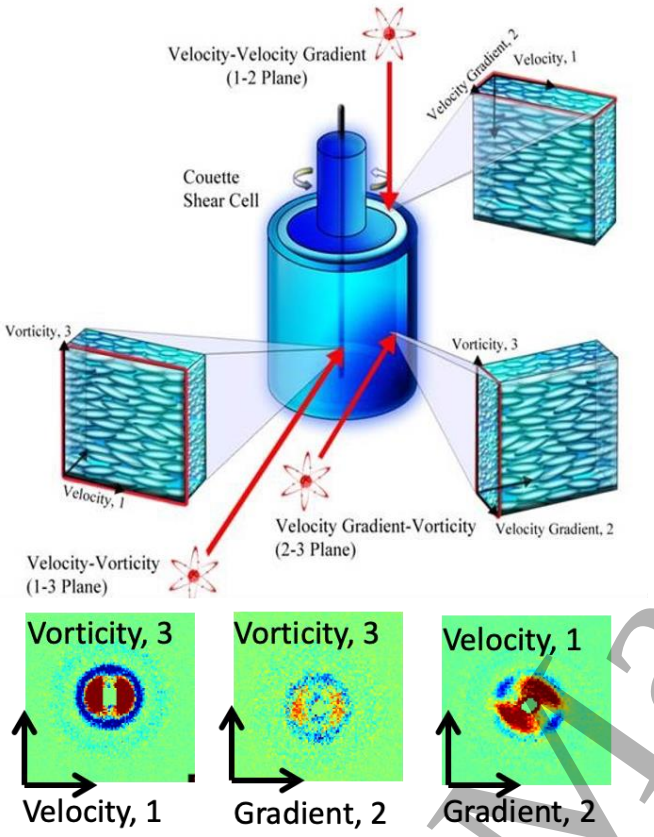

Figure 1 Rheo-SANS schematic (courtesy of Dr. Keyi Xu) showing the planes of flow accessed by neutrons (red arrows). The SANS patterns shown reflect the highly non-equilibrium, highly anisotropic microstructure of a shear thickening colloidal suspension. These spectra are combined with Stress—SANS theory to elucidate the underlying mechanism of the continuous shear thickening phenomenon. SANS data from Ref. 4, used with permission of Cambridge University Press.

Current and Future Challenges One current challenge being addressed is to develop a single Rheo-SANS device capable of measuring the structure and rheology in all three orthogonal flow planes as a function of time. A "4D Rheo-SANS" instrument must be able to easily change orientation with respect to the stationary neutron beam path, as well as provide accurate stress measurements and thermal control to fully characterize the behaviour of sheared materials. Improvements must also be addressed to quantify the time-dependent behaviour of various materials, including their memory effects, relaxations, and hysteresis. Increasing rheometer complexity and higher neutron fluxes requires the ability to synchronize rheological and neutron scattering data across long sequences of repeated experiments for higher time resolution. For instances where the sample microstructure becomes inhomogenous under flow,[12] it is still challenging to measure and verify the structure of highly nonlinear, shear-banding materials where the local concentration,

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microstructure, rheology and flow-field are coupled. Also, it is of significant interest to understand mechanisms by which yield stress fluids transition from elastic gels to flowing liquids.[13]

Another challenge is to measure complex fluids at extreme shear rates and under industrially relevant pressure driven flows. Generating shear rates up to 10^6 s^{-1} and beyond necessitates high flow velocities, high pressures, and precision geometries on micrometre scales. Pressure-driven flows also produce additional complexity in data analysis, as the projected scattering pattern is inherently convoluted by multiple scattering planes.

Additional advances in Rheo-SANS environments are required for limited biological sample volumes, as well as for samples that require specialized environmental conditions, such as humidity or evaporation control, extreme temperatures and pressure, electric fields, or magnetic fields. Integrating additional metrology with Rheo-SANS, such as dielectric and light scattering methods, can widen the length scale of structures probed, measure dynamic processes on the micro to millisecond scale, and detect flow instabilities.

As instrumentation upgrades continue to generate larger datasets more rapidly, new, and faster data analysis methods will be critical. The growing data size requires integration of new simulation tools for designing experiments, on-the-fly analysis of 2D scattering data sets, and tomographic reconstruction of the full 3D microstructure obtained from multiple 2D scattering projections. Standard procedures and calibrations for Rheo-SANS sample environments would also promote consistency across different beamlines, providing a more user-friendly and accessible experiment for the Rheo-SANS user community.

Advances in Science and Technology to Meet Challenges Development is underway to build a true 4D Rheo-SANS sample environment capable of measuring stress and microstructure in all three plans of flow (Fig.1) with the same instrument and with time resolution down to 10ms. A key goal is to provide the Rheo-SANS user community with a commercial 4D Rheo-SANS instrument that is integrated with beamline data acquisition software (SBIR Phase II DE-SC0019595).

Recently, various other Rheo-SANS environments have been developed with different advantages. Capillary Rheo-SANS (CRSANS) measures complex fluids at high shear rates up to 10^6 s^{-1}.[14] The high-shear capillary geometry, together with traditional concentric cylinder Rheo-SANS geometries, can now provide structural and rheological signatures across eight orders of magnitude in shear rate. Dielectric spectroscopy methods have already been integrated *in situ* with Rheo-SANS,[9] and more complex flows with extensional components have also been recently developed.[10, 11] Orthoganol integration of optical microrheology methods, such as diffusing wave spectroscopy, together with SANS can provide linear rheological characterization under extreme temperatures and pressures or under applied electric or magnetic fields.

The recently developed Very Small-Angle Neutron Scattering (VSANS) instrument at NIST provides unique neutron collimation and detector options that will help address challenges in measuring

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hierarchical materials from the nanometre to micrometre scales.[15] Multiple detectors are positioned at different distances to capture a broader q-range within a single measurement. In addition to accessing a lower q-range with a 2D detector, VSANS will be particularly advantageous for time-resolved rheological measurements, low volume geometries, reacting systems, and stopped-flow mixing experiments.

Ongoing developments in community-driven software tools such as SasView (www.sasview.org), computational power, and recent statistical methods to determine orientation distribution functions from anisotropic scattering data[16] will help the broader scattering community extract more structural information from two-dimensional scattering projections and with different applied flow fields. Advances in computing, machine learning algorithms, AI pattern recognition, and 3D data visualization will help meet challenges in extracting, analyzing, and presenting data-rich Rheo-SANS measurements.

Finally, advances in complementary methods, such as rheo-NMR, [17] rheo-light scattering, [18] rheo-X-ray scattering[19, 20, 21], and rheo-confocal microscopy,[22] provide additional information for some systems that can be combined with Rheo-SANS to extend the range of length scales covered or to examine different species within the structure due to differences in scattering contrast. A more extensive review of measurements of microstructure under flow can be found in a recent monograph. [23]

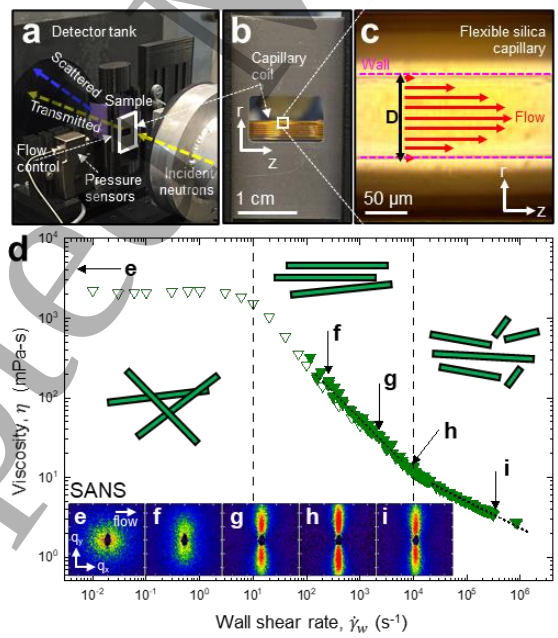

Figure 2 Capillary Rheo-SANS instrument for measuring the rheology and nanostructure of complex fluids at high shear rates. (a) Capillary rheometer setup on a SANS beamline at NIST, (b) capillary coil scattering cell composed of (c) fused silica capillary. (d) Shear-dependent viscosity of worm-like micelles (sodium lauryl ether

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sulfate in brine) as measured with traditional Rheo-SANS (open symbols) and Capillary Rheo-SANS (closed symbols). (e-i) Inset 2D SANS patterns correspond to different shear rates designated by arrows. Reproduced and adapted from Ref. 14 with permission from the Royal Society of Chemistry.

Concluding Remarks The user community and beamline facilities are advancing neutron scattering sample environments for Rheo-SANS. Instrument commercialization promises wider availability and standardization of metrology. Advances in simulation and theory enable mechanistic interpretation of structure-property relationships for flowing systems. Extensions of the Rheo-SANS method to a broader range of shear rates, extreme pressures and temperatures, broader time and length scales, more complex flows, and confined flows are ongoing developments desired by the user community. Opportunities for full 3D structure-under-flow reconstruction with time resolution (4D Rheo-SANS), paradigm changes in data analysis afforded by advances in machine learning, and the coupling with complementary *in situ* metrologies, will improve structure-property relationships and help verify theory and simulation. Increased neutron flux and SANS instrumentation such as VSANS, coupled with advanced data acquisition and analysis methods, will increase user accessibility to address broader scientific challenges in soft matter and biology.

Acknowledgements This manuscript was prepared under cooperative agreements 70NANB20H133 & 370NANB17H302 from NIST, U.S. Department of Commerce, as well as DOE SBIR/STTR RPM acknowledges support from the Center for High Resolution Neutron Scattering (CHRNS) which is jointly funded by the NCNR and NSF under Agreement No. DMR-2010792. Identification of commercial equipment or materials in this work does not imply recommendation or endorsement by the National Institute of Standards and Technology.

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Section 2.2 – Imaging Microscopic Processes

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Status In March 2022, for the first time the American Physical Society March Meeting featured a "Gallery of Soft Matter" to showcase the visual beauty of soft matter systems. While some fraction of the submitted images were from simulations, many came from experimental images. And while soft matter science is known for beautiful static images such as fractal gels and dry foams, there are equally pleasing images and movies of dynamical processes such as colloidal suspensions undergoing phase transitions (Fig. 1A,B) and flowing soft materials (Fig. 1C).

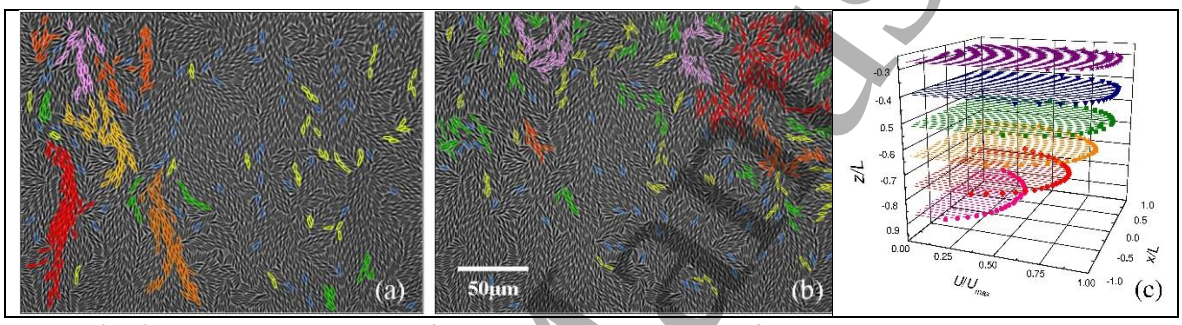

Figure 1 (A,B) Video microscopy image from dense colloidal sample of ellipsoids with aspect ratio = 6 at area fraction ϕ = 0.70. The most mobile 8% of the particles are highlighted in color for translational (A) and rotational (B) motion. (A) and (B) reprinted with permission from Zheng, Wang, and Han, *Phys. Rev. Lett.* **107**, 065702 (2011) [1]. Copyright 2011 by the American Physical Society. (C) Velocity profile of a flowing colloidal gel, exhibiting plug-like flow. The gel is at volume fraction ϕ = 0.27. Data are taken with confocal microscopy. L = 25 μm is the half-width of the capillary tube, which has a square cross-section. Reprinted with permission from Conrad and Lewis 2008, *Langmuir* 24 7628-7634 [2]. Copyright 2008 American Chemical Society.

A starting point for visualizing soft materials is video microscopy, which became useful once inexpensive CCD cameras became available in the 1990's. Video microscopy uses a conventional optical microscope to view samples. From this starting point, important developments for soft matter included the use of fast confocal microscopes to take three-dimensional images (reviewed in [3]) and holographic microscopy as an alternative method of fast 3D imaging [4]. Some soft matter scientists now use super-resolution microscopy to directly image nm-sized objects [5]. The main advantage of microscopy is that it allows localized study of spatially heterogeneous samples, and in many cases also temporally heterogeneous processes.

A now-classic method for turning microscope movies into quantitative measurements is multiple particle tracking, launched in the soft matter community by the 1996 work of Crocker and Grier [6]. Their open-source particle tracking code has since been translated into several different programming languages. The original algorithm is optimized for particles that move via Brownian motion. Several groups have modified the algorithm for flowing situations [7] or active particles which have a directional bias to their motion. Other codes have arisen for specific purposes such as tracking live cells [8] or tracking polydisperse objects (reviewed in [9]). Nowadays the main challenge an experimentalist faces is identifying the particle tracking method that is easiest to use,

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is written in a desired programming language, and/or is optimized for the particular experimental needs [9-12].

Current and Future Challenges Recent developments in imaging microscopic processes in soft materials can be roughly divided into two buckets: software and hardware.

The software side consists of clever ways to squeeze more information out of images. Particle tracking specifically requires particles that can be easily seen and distinguished against the background. This visibility constraint is circumvented by Differential Dynamic Microscopy (DDM). This method uses any microscopy technique one likes to take a movie, and then Fourier analysis of the sequence of images allows one to obtain dynamical data like that measured by dynamic light scattering [13]. This method works on quite challenging samples; for example, the original article demonstrates a measurement of the diffusivity of particles that are much smaller than the optical resolution limit of the microscope. The method also works for highly scattering samples where there is an index of refraction mismatch between the particles and the solvent. A fascinating variety of other analysis techniques for microscopic movies are reviewed in [9], which also makes the point that analysis techniques are cheaper than investing in new microscopy hardware.

The hardware side starts with new and/or more widely available microscopy techniques, such as the above-mentioned confocal microscopy and holographic microscopy methods. The next step is combining instruments and techniques. An excellent illustration is boundary stress microscopy [14]. The method starts by combining a rheometer and a confocal microscope, as shown in Fig. 2; this combination has been used by several groups [7]. The rheometer uses a transparent bottom plate atop an inverted microscope, so that the microscope looks upward into the rheometer. The sample thus can be sheared by the rheometer, allowing for precise control over strains and simultaneous measurements of stresses, while the sample is imaged by the confocal microscope (potentially even in 3D for slow strain rates). To visualize boundary stresses, an additional idea from traction force microscopy is added. Directly on the transparent bottom plate, a thin gel substrate is added with embedded tracer particles. The sample then contacts this gel substrate, rather than directly the bottom plate. When the sample is sheared, stresses are transmitted to the gel substrate which responds elastically (see Fig. 1B). The elastic displacements of the tracer particles reveal the stresses exerted on the substrate.

Advances in Science and Technology to Meet Challenges Challenges for the future, then, are to devise clever new analysis techniques, and to find new ways to merge experimental hardware techniques. Progress is most likely to come from collaborations that bring together ideas and complementary expertise.

For example, one could imagine a colloidal chemist designing novel tracer particles that allow one to measure new properties inside a sample. DNA-based mechanosensors can be sensitive to pN-scale tension forces, for example [15], and other mechanosensitive molecules are even more sensitive [16]. Might colloids coated with such sensors be useful to soft matter scientists? Colloids

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of a wide variety of shapes are possible (as reviewed in [17]) and have led to observations of rotational diffusion (for example [18]); what might one do with more exotic shapes?

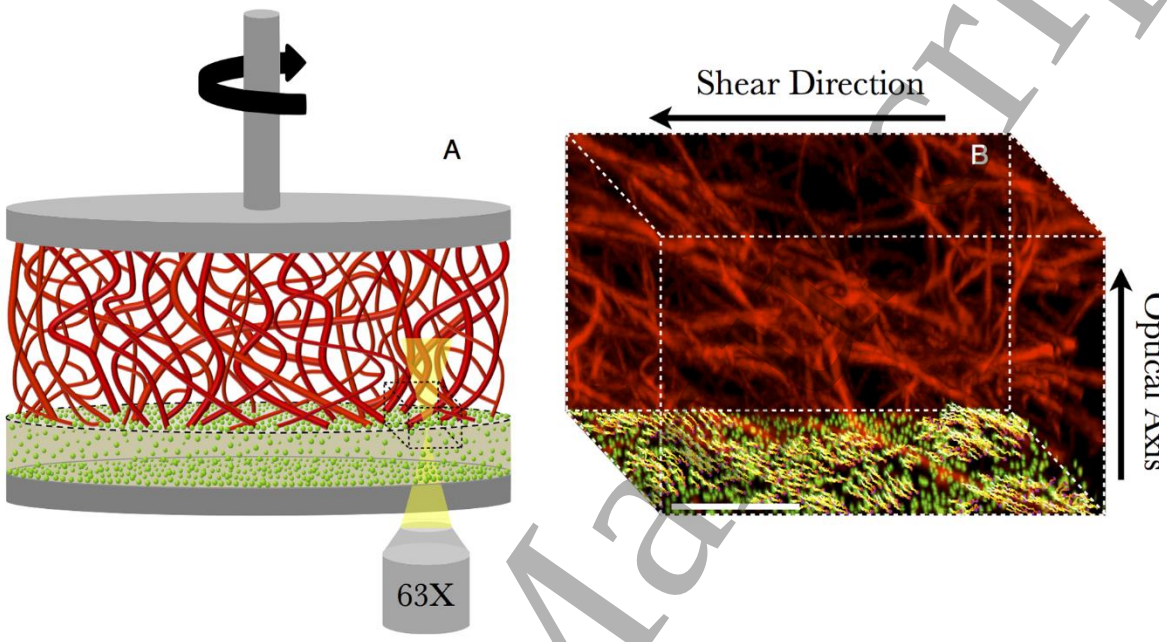

Figure 2 (A) Illustration of the boundary stress microscopy method, using a "rheoscope" that combines a rheometer and a confocal microscope. In this sketch the red tendrils represent a collagen network. (B) A confocal image of sheared collagen fibers along with yellow vectors representing boundary displacements which indicate boundary stresses. Scale bar = 25 μm. Image from [14], copyright 2015, open access under the Creative Commons Attribution License.

The above example of boundary stress microscopy challenges us to consider new mergers of experimental techniques. One needs to find appropriate techniques to match to interesting scientific questions in soft matter science. Indeed, one way to state the challenge is the need to stay aware of the increasing variety of clever experimental techniques.

An additional challenge is to implement real-time analysis of microscopy images with real-time feedback. This has been done in many cases, but the speed is limited based on computer speed and the complexity of the analysis required. One can speculate that as computer speeds continue to improve, and as faster algorithms are developed, that there is room for new science to be done where the computer is an important component to the experimental instrument beyond just storing data for later analysis.

Concluding Remarks Imaging dynamical processes in soft matter systems often starts with your eye and brain. You see something interesting, and then you try to quantify it; to show that what you see is not just an accidental event. Other times one starts with imagination: if we could design the

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proper instrument or engineer the right sample, what might we be able to image and measure? Ambitious experimentalists should read broadly, look for techniques that one can bring to soft matter (whether hardware or analysis ideas), and be open to collaborations especially outside one's own field.

Acknowledgements This work was supported by the National Science Foundation under Grant No. CBET-1804186. The author thanks Y. Han, J. C. Conrad, and D. L. Blair for providing copies of their figures and for helpful discussions, and J. C. Crocker for introducing him to the joys of microscopy a while ago.

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Section 2.3 – New microscopy techniques

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Status Optical microscopy is a prominent technique to study soft matter structure and dynamics: it is easily implemented, and it matches the relevant spatiotemporal scales. Despite early applications, such as the study of Brownian motion by Jean Perrin, the urge of increasing the spatiotemporal resolution toward the molecular scales have relegated optical microscopy in the underwood of qualitative methods for quite some time, with light, x-ray, and neutron scattering techniques dominating the scene of quantitative tools for soft matter characterization.

Starting from the 1970s, the invention and development of CCD cameras, in combination with the introduction of a plethora of novel microscopy techniques (e.g., confocal, light-sheet, super-resolution…) brought optical microscopy back to the stage as a major player for the quantitative characterization of soft matter. Nowadays, soft matter experimentalists can use light to observe samples in direct space with various techniques and contrast mechanisms (e.g. absorption, scattering, fluorescence…) to perform accurate quantitative experiments [1]–[3]. Alternatively, static and dynamic light scattering (SLS and DLS) remain unbeatable tools to capture fast dynamics or to obtain robust ensemble information, at the expense of losing access to a space-resolved characterization of the sample.

An intermediate approach, known as Digital Fourier Microscopy (DFM) [4], obtains scattering information from Fourier analysis of images acquired in direct space, transforming a microscope into a light scattering instrument, while at the same time retaining the original movies for alternative analyses. DFM techniques - and in particular Differential Dynamic Microscopy (DDM) that is based on Fourier transforming differences between images acquired at different times [5], [6] - are increasingly gaining popularity, with applications covering classical soft matter systems such as polymers, colloids and liquid crystals, as well as biological ones, including proteins, bacteria and eukaryotic cells [7].

Besides representing a convenient and accessible alternative to light scattering, DDM has several key qualities, among which special mention goes to its capability to probe dynamic entities that are abundantly smaller than the wavelength of light. Compared to DLS, DDM is more robust against optical imperfections and multiple scattering. One main drawback is the heavy post-processing of large stacks of images.

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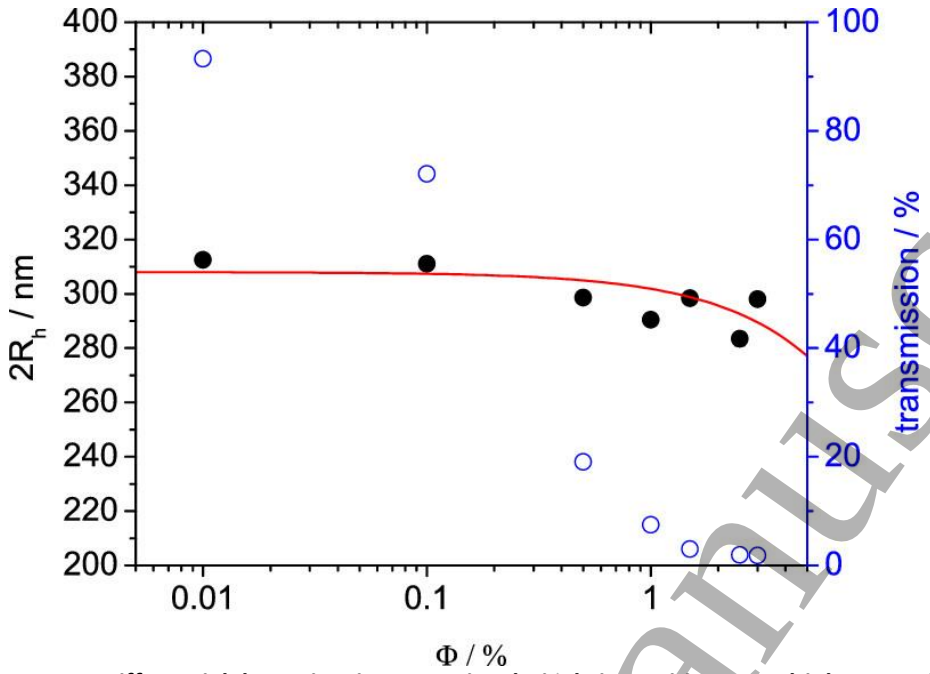

Figure 1 **Differential dynamic microscopy is relatively insensitive to multiple scattering**: Hydrodynamic diameter (closed symbols) measured by DDM and optical transmission (open symbols) of a sample of PMMA particles dispersed in water as a function of particle concentration. The red line is a fit to the data using a model that accounts for particle interactions. Reprinted with permission from Kathrin Eitel, Gary Bryant, and Hans Joachim Schöpe Langmuir 2020 36 (35), 10307-10320 DOI: 10.1021/acs.langmuir.0c00709. Copyright 2020 American Chemical Society.

Current and Future Challenges Robustness of DDM against multiple scattering makes it the tool of choice to study optically dense samples, such as the interior of living cells or non-dilute colloids [7]. A case in point is shown in Figure 1, where Eitel et al. [8] prove that for optical transmission conditions under which DLS would fail, DDM can correctly size colloidal particles suspended in a liquid. However, beyond a generic consensus that the relative insensitivity of DDM to multiple scattering is due to the partial limited spatial and temporal coherence of the typical light source used (e.g halogen lamps or LEDs), a systematic study of the optimal working conditions is still lacking.

Other challenges that researchers will need to face are related to the wide spatiotemporal range that needs to be accessed when studying soft matter. Theoretically, the smallest accessible timescale in DFM experiments is the inverse of the acquisition frame rate, whereas the largest one is typically the duration of the experiment. Similarly, the pixel and the image size (including optical magnification) set the lower and upper spatial scales, respectively, with the additional degree of freedom that the magnification can be changed in a wide range (typically from 1x to 100x).

Once a camera is chosen, the brute force approach to cover a wide range of space and time scales implies performing very long, fast image acquisitions of megapixel images obtained with different magnifications. Clearly, this approach becomes very rapidly unfeasible: for instance, modern

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sCMOS cameras acquiring 3200x3200 8-bits images at 500 fps produce about 5 GB/s (~17 TB/h) of data to be saved on disk and later analysed, where the images are post-processed to compute suitable correlation functions at different Fourier wave vectors q.

Extracting maximum information would thus benefit from: 1) accessing fast dynamics with slow cameras; 2) accessing slow dynamics and large spatial scales with minimal disk occupancy; 3) shortening the computational time needed to analyse large amounts of data, possibly in real-time; 4) automating image analysis to reach the level typical of commercial DLS instruments. Progress in all these areas would tremendously favour the massification of DFM techniques.

Advances in Science and Technology to Meet Challenges As far as multiple scattering is concerned, some progress has been made by using DDM in combination with spatially-selective fluorescence microscopy techniques, such as light sheet [9] and confocal [10], [11]. It would be crucial to understand whether multiple scattering suppression schemes typical of DLS and based on cross-correlation, can also be extended to DDM, which would further push the range of applicability to strongly scattering systems normally studied only with Diffusing Wave Spectroscopy or x-ray scattering.

The development of novel image acquisition protocols is a very promising area. For example, access to dynamics faster than the inverse acquisition rate has been obtained by Philippe et al. with a variable-delay temporal scheme [12], by Arko and Petelin with two randomly triggered cameras acquiring two sequences of images of the same region in the sample [13], and by You and McGorty, who used a color camera to acquire images obtained by sequentially pulsing blue and then red light separated by a variable lag time much smaller than the camera's exposure time [14] (see Figure 2). Some of these protocols also lead to a reduction of the disk occupancy [12].

To hopefully bring DDM closer to real-time analysis as in DLS, optimization of the image processing algorithms is also desirable. Using GPUs instead of CPUs can lower the time to complete image analysis by two orders of magnitude [10], [15]. Without resorting to GPUs, one can employ a Fourier transform in time instead of performing differences of images (as in the original DDM algorithm) to reach speed-up factors up to 300 [16]. Adopting a probabilistic approach to downsample the imaging data before processing can lead to a dramatic reduction (up to a factor of ~100) of the computational load, with virtually no loss of information on the estimated, physically relevant, quantities [17]. Further progress is likely and will allow us to run DDM in real time minimizing or cancelling the need to store the images, paving the way to its massive use as standard technique in every soft matter laboratory.

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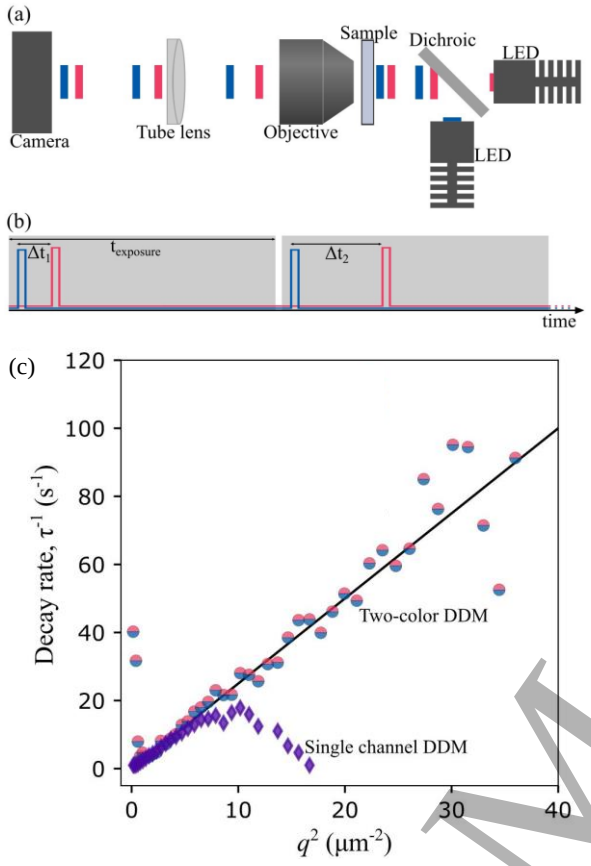

Figure 2 **Two-colour DDM for capturing fast dynamics**: (a) Schematic of an optical microscope showing two LED light sources (one with a peak wavelength of 625 nm, the other 455 nm) used to illuminate an aqueous suspension of 180 nm diameter polystyrene particles prepared at 0.02% mass fraction. A 40× objective and tube lens image the sample onto a colour CMOS camera. (b) Images are acquired at 10 Hz and, within a single exposure time of the camera, each LED is pulsed for about 1 ms. The time interval between pulses is varied and, for the data shown in (c), ranges from 3 to 91 ms. (c) The relaxation rate, τ^{-1}, characterizing the particle dynamics is determined with standard DDM plotted versus the squared wave vector q^2. The solid line shows a diffusive dynamics $\tau^{-1} = Dq^2$, with $D = 2.48\ \mu m^2/s$. Data from the standard DDM method (violet diamonds) starts deviating from this straight line just after the expected decay rate exceeds 10 s^{-1}, as anticipated given the images were acquired at 10 Hz. Data from the two-color DDM method follows the expected linear relationship up to around 70 s^{-1}. In the low-q region, the two- color method does not accurately detect data fluctuations slower than about 10 s^{-1}. (Figure panels are reproduced and adapted under CC BY 4.0 license from arXiv:2101.12147)

Concluding Remarks The incessant advances in microscopy, combined with the development of novel experimental schemes, and with the constant technological progress leading to faster, less noisy, and more sensitive image detectors, will ensure further development of DFM methods in the next years. It is not difficult to imagine a near future in which users without a strong background in optics and image processing will be able to run real-time, high-throughput, automated DFM experiments on a variety of samples that would be hardly accessible with other techniques. At the

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same time, new possibilities will arise from combining DFM with other experimental tools, such as rheology, electrophoresis, chromatography, microfluidics, to perform a characterization of the microscopic dynamics of externally manipulated soft matter. Finally, applications to biology have been many, and initial successes point to a possible wider use for the characterization of crowded biological systems ranging from the cell interior to cellular tissues.

Acknowledgements
I acknowledge useful and inspiring discussions with Fabio Giavazzi.

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Section 3.1 - Phase transition studies in colloids

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Status Soft materials serve as powerful platforms for studies of phase transition because they exhibit rich phase behaviours. For example, liquid crystals exhibit various phases absent in atomic systems. Instead of focusing on discovering new phase transitions in soft materials, in this work, we focus on phase transition studies by using colloidal systems. Colloidal micro-particles move much slower than atoms and can be directly visualised by optical microscopy, even inside dense three-dimensional crystals or liquids (Figure 1a [1]). Single-particle kinetics can hardly be observed in atomic systems, making colloids important model systems of large atoms for the study of phase transitions [2]. The use of imaging analysis to track colloidal particles, which began in the 1990s, has afforded researchers important insights into microscopic structures and kinetics during phase transitions.

Most colloid phase-transition studies have focused on crystallisation [1,3] and glass transitions [4], and less studies have explored other transitions such as crystal melting, solid–solid transitions, and transitions of liquid crystal phases. The kinetic transition pathway depends on various factors and exhibits rich behaviours on complicated free-energy landscapes. Moreover, classical nucleation theory, which is based on certain oversimplified assumptions, can often be problematic in real systems. These make room for publications about kinetics of first-order transitions such as crystallization. Besides the initial nucleation stage, nuclei growth and coalesce, defects and stress effects, and transition of interfaces such as roughening have been explored. Some results obtained in colloids can guide studies of atomic systems; for example, the two-step nucleation in solid–solid transition from a parent crystal to a liquid to a product crystal was first observed in colloids and subsequently confirmed in metals.

New colloids, phases, and assembly and observation techniques (Figures 1b–d) have afforded additional opportunities for phase-transition studies. In particular, transitions between non-equilibrium steady states, which occur widely in nature, are much less understood than transitions between equilibrium phases. Specifically, the general theoretical framework and the categorisation of these transitions are unclear. Colloids can be controlled and observed at the single-particle level, rendering them an important research avenue.

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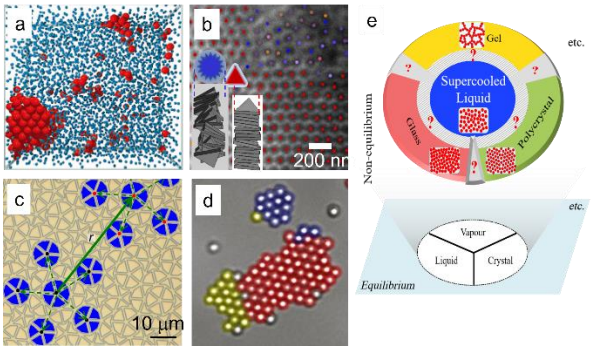

Figure 1 Examples of phase studies on colloids.
(a) Nucleation in crystallisation [1].
(b) Nano-triangles forming a crystal, as observed by liquid electron microscopy [5].
(c) Colloidal quasicrystal by lithography [6].
(d) Crystal formed by active colloidal particles [7].
(e) Transitions between non-equilibrium states.

Current and Future Challenges Phase transitions occur under various conditions and have many aspects worth to study. For example, transitions in curved or confined spaces; in translational, rotational or other degrees of freedom; induced quasistatically or abruptly by changing effective temperature, pressure, shear or particle properties; and phase transition precursors (such as premelting and prefreezing). Finding poorly explored topics can be just a matter of combination of these aspects. For example, the structure of a phase can be ordered or disordered; while particles' motions can be liquid-like or solid-like. These produce 2x2=4 states: fluid, crystal, glass, and structural fluid with active particle swapping on a lattice. The last state has not been found in passive atomic systems but can nevertheless be formed by active particles.

Perhaps the most important topic is the non-equilibrium transitions such as the following:
(1) Transitions between metastable states such as conventional supercooled-liquid-to-glass transition. 'What is the nature of the glassy state? -- Where and why does liquid end and glass begin?' is ranked as the 125 most important scientific questions by *Science*. This question can be generalised to other non-equilibrium phases which similarly have blurry boundaries, e.g., between fine-grained polycrystals and glass [9] and between dense gels and glasses (Figure 1e).

(2) Transitions induced by athermal macro-parameters (e.g., shear-induce yielding transition).

(3) Transitions in systems with non-reciprocal interactions (i.e., breakdown of Newton's 3rd third law), for example, in some active matters [10]. Active particles form rich states such as active nematic, crystal (Fig. 1d), and hyperuniform states. Their transitions have not been explored in conventional atomic or molecular systems.

Combinations of (1-3) can yield topics such as shear-induced polycrystal–glass transition in active systems. Combination of (1-3) with other aspects of transitions can produce even more topics; for example, glass melting in orientational degrees of freedom. Challenges are often in the fabrication

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of high-quality samples with a large uniform phase and the tunability to quasi-statically drive the phase transition.

Advances in Science and Technology to Meet Challenges Many topics are yet to be explored using conventional repulsive colloidal spheres, which have been used in most previous phase-transition studies. New techniques of colloid fabrication, assembly, control, and imaging certainly provide additional opportunities. Recently synthesised novel colloids include particles of various shapes, soft deformable spheres, Janus, or patchy spheres with anisotropic interactions, oppositely charged particles without agglomeration, particles with anisotropic long-range interactions in liquid crystals, and active particles with ballistic translational or circular motions. In particular, arrays of arbitrarily shaped 2D colloidal platelets can be printed by photolithography and their designed structure can be maintained after dissolved into a solution (Figure 1c [6]). The study of phase behaviours on the free surfaces of solids or liquids requires attractive particles. Tunable attractions have been achieved by coating DNA molecules, adding thermal-sensitive depletants or dyes, using solvents near the phase separation point, and applying high-frequency magnetic fields. Electric, magnetic, optical, and ultrasonic fields can be used to manipulate individual particles or a group of particles and are helpful in testing related theories.

High-resolution optical microscopy and liquid-phase transmission electron microscopy (Figure 1b [5]) can resolve nm-sized particles. Smaller particles have relatively longer-range interactions and thus can form more types of crystalline phases. Particles of various shapes can be fabricated relatively more easily for nanoparticles. Their stronger Brownian motions are helpful for exploring slow dynamics in glasses and solid–solid transitions.

The recent non-reciprocal generalisations of synchronisation, flocking, and pattern formation provide a theoretical framework for transitions in active matters [10], which can guide further experimentation and simulation. Since the parameter space is too big to explore, we should focus on searching for the general features and providing a clear classification of non-equilibrium transitions.

Concluding Remarks Combination of various aspects of phase transitions can produce many topics that are yet to be well explored. Metallurgy is also a source of open questions. For example, the mechanisms of various mechanical transitions in crystalline and amorphous alloys are not clear. Transitions between non-equilibrium states are the least understood and most important. Colloids might provide valuable insights into the general features of non-equilibrium phase transitions in physical and biological systems.

Colloidal experiments have revealed important microscopic kinetic details of known phenomena (e.g., nucleation) and even discovered new phenomena (e.g., pre-solid-solid transition) which can guide the future studies in atomic systems. We should take advantage of the strengths of colloids, such as their tailorable size, shape, interaction, and self-propulsion. For example, colloidal solids are soft and thus can be used to explore transitions under ultrahigh pressure or shear levels inaccessible in atomic solids research.

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Acknowledgements
This work was supported by the Hong Kong RGC grant (CRF-C6016-20G). We thank Huijun Zhang for developing Figure 1e.

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Section 3.2 – Large mechanical deformation

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Status The very term 'Soft Matter' indicates why we should care about large mechanical deformation (LMD): soft systems are easily deformed by even a modest stress. Thus, the LMD regime is of paramount importance in one or more steps of the life cycle of virtually all industrial and technological soft systems, in food production and sensory experience, as well as in active matter and biological systems (Fig. 1). Here, we use LMD as a proxy for the non-linear regime, where stress and strain, or strain rate, cease to be mutually proportional. Depending on the materials, the onset of non-linearity may occur for extremely large strain or strain rate. While LMD is relevant for both fluid- and solid-like systems (Fig. 1A), we shall focus mainly on soft solids, providing a (necessarily partial) glimpse of the research in the field.

Most early work addressed macroscopic quantities only (e.g. stress and strain). The pioneering investigation of bubble rafts by L. Bragg and J.F. Nye [1], by contrast, nicely exemplifies a research approach that is extremely up-to-date: the use of soft matter as a model system for hard condensed materials (in [1], the foam simulated the behaviour of a metal under strain), and the search of the microscopic origin of the macroscopic behaviour under LMD. The bubble rafts of Ref. [1] were crystalline, making it easy to identify structural changes, e.g. due to defect migration or annihilation. By contrast, most soft systems are amorphous, and detecting and quantifying structural changes is more arduous. Concepts such as the 'shear transformation zones' [2] have been introduced to address this challenge.

Other popular research lines include designing materials with outstanding properties under LMD (see the next section) and leveraging on transitions induced by a LMD to obtain new materials. Examples of the latter approach range from extrusion and spinning of polymers to manufacturing meat replacement by creating protein fibre, e.g. by electrospinning or mechanical elongation [3].

Theoretical work on LMD is very abundant and ranges from approaches drawing analogies with equilibrium statistical physics by introducing phase or state diagrams (jamming and shear banding transitions [4,5]), to models at the mean field level (soft glassy rheology [6], fluidity models [7]) or, on the contrary, emphasizing spatio-temporal fluctuations (rheo-chaos [8], viscoelastic instabilities [9]), to more microscopic approaches as in the Mode Coupling Theory [10]. As discussed below, such diversity reflects in part our lack of a general framework for the LMD regime.

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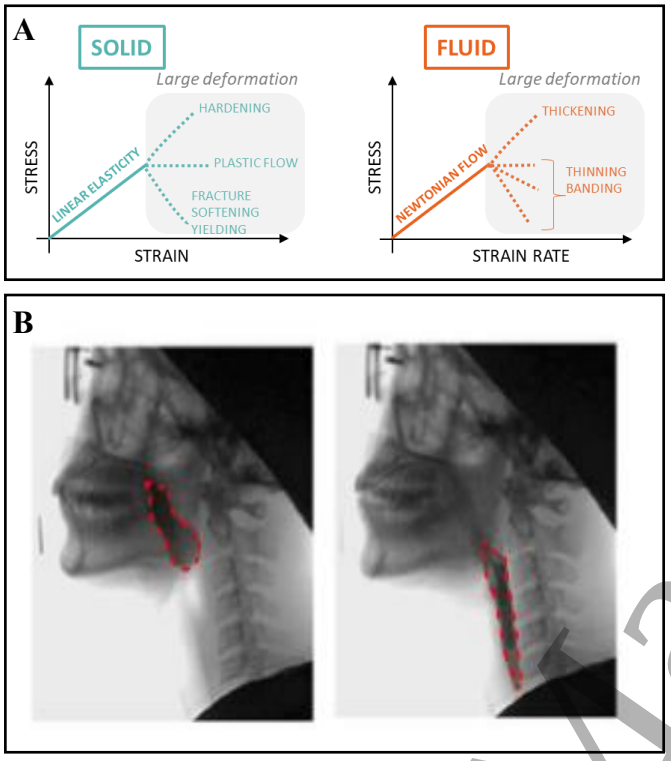

Figure 1 (A) Schematic behavior of a solid and a liquid under a mechanical load and definition of the large deformation regime. (B) X-ray images showing the large extension of the bolus (highlighted by the dashed red lines) during swallowing. Adapted from [11]. This is just one example of the large deformation of soft materials occurring in a variety of soft materials, from red blood cells in small blood capillaries, to wheat dough used in preparing pizza, to extrusion in the processing of polymers-based materials.

Current and Future Challenges

For small deformations, statistical physics tells us, even if it is generally not trivial and straightforward, how to relate the microscopic structure and dynamics to the macroscopic mechanical properties. Establishing an analogous link for systems under a LMD and, more generally, for systems driven out of equilibrium, is arguably one of the greatest challenges in modern material science and statistical physics. It also has implications for biology and medical science where the behaviour of the cell cortex, the extracellular matrix or of tissues under LMD is crucial. To reach this goal, several challenges must be addressed:

1) The most relevant quantities to be monitored experimentally or numerically and to be included in a theoretical approach need to be identified. In rheology, stress and strain often change smoothly across the linear/non-linear transition, while other quantities, e.g. extracted from Lissajous plots or inharmonicity analysis may carry more information. At the microscopic level, changes of the structure or the dynamics under LMD may be subtle, especially for amorphous, dense systems.

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2) Several phenomena in LMD occur randomly in space and time (think e.g. of crack nucleation), or encompass a wide range of time- and length scales (e.g. in avalanche-like failure), or exhibit complex spatio-temporal patterns (e.g. due to flow and elastic instabilities). This complexity must be tracked.
3) Existing statistical mechanics tools and concepts developed for equilibrium systems need to be extended to the non-linear regime of LMD; new theoretical tools and paradigms will be likely required.

A thorough understanding of the relationship between the macroscopic mechanical behaviour and the microscopic structure and dynamics under LMD is a very ambitious and long-term goal. Closer on the horizon, challenges that are attracting an intense research effort include (but are not limited to):

1) Predicting failure: soft solids often exhibit sudden failure after a long induction time, e.g. under a constant load, as in creep, or as a result of cycling loading, as in fatigue. Identifying signals of failure as early as possible is of great practical importance. While rheological quantities exhibit little if any precursors of macroscopic failure, recent work has shown that changes at the microscopic level, e.g. in the dynamics, significantly anticipate material failure [12].
2) Designing new materials with outstanding mechanical properties under LMD, e.g. high extensibility coupled to a large stress at failure or self-healing capabilities. Ref. [13] discusses advances in various strategies deployed at this end, from interpenetrated networks to systems based on dynamic, reversible bonds.
3) Developing guidelines to design systems with a prescribed range of properties under LMD, which is of paramount importance, e.g., for mechanical metamaterials [14] or in the food industry [15,16] .

Advances in Science and Technology to Meet Challenges To reach the goals outlined in the previous section, several technological and scientific advances are needed.

1) Most mechanical tests are performed under shear or traction. Other deformation geometries will be required to reach a general understanding of LMD and to test driving modes closer to those in technological applications. Examples include indentation, extensional flow or flow in constrictions, and drop impact (Fig. 2A). Geometries of this kind often allow for measuring the strain or strain rate, e.g. by imaging methods: a concomitant measurement of the stress will be a major advance. Advanced rheological methods will be needed to cope with the non-linear and time-varying response of soft matter under LMD. Recent improvements include fast mechanical spectroscopy via 'chirp rheometry' [17] and the popularization of orthogonal superposition rheometry, where a small-amplitude deformation is superimposed to a primary large deformation to probe non-linear moduli [18].
2) Experiments probing the microscopic structure and dynamics simultaneous to mechanical measurements are gaining momentum. Optical or confocal microscopes provide snapshots of the system with sub-micron resolution, but they are limited in terms of size of the field of view and viable samples (mostly particle-based and optically transparent). Advanced

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scattering methods [19] allow for time- and space-resolved measurements of the structure and dynamics on macroscopic portions of the sample and for a large variety of systems (Fig. 2C). However, spatial mapping is coarsened over tens of microns and data interpretation is less straightforward than for imaging. Ultrasonic velocimetry maps the flow field with resolution 20-100 µm [20] (Fig. 2B). Mechanophore molecules incorporated in the system can report optically the local stress [21] (Fig. 2E) or bond breaking events in networks [22] (Fig. 2D), but they require system-specific, sophisticated synthesis. Future developments will likely involve combining several of these methods.

3) Advances are also needed in sample design and preparation. Model systems allow for easier data interpretation and comparison with theory and simulations. For example, DNA-based systems afford great control on the interactions among constituents and the resulting architecture, e.g. in DNA hydrogels [21], but it is still difficult to synthesize them in amounts suitable for mechanical tests. A related issue is that of sample initialization: most soft solids are out-of-equilibrium and their LMD behaviour depends greatly on sample history, as exemplified by recent simulations of amorphous packings of soft particles, whose failure behaviour (ductile *vs* fragile) depend on the degree of annealing [23] (Fig. 2F).
4) In numerical works, a major challenge is to cover the wide range of time- and space- scales relevant to LMD. A promising approach consists in coupling different methods, from molecular dynamics or Monte Carlo at the molecular level, to mesoscopic finite-element models based on a visco-elasto-plastic formalism [24]. The ability of dealing with hydrodynamic interactions is also a key advance [25].
5) On the theoretical side, current approaches are mostly phenomenological [7], or restricted to a mean field approach, e.g. as in soft glassy rheology [6], making the connection with the microscopic level difficult. Strategies to go beyond these approaches include drawing analogies with well-known statistical physics models, e.g. likening yielding to a phase transition in the random field Ising model [23].

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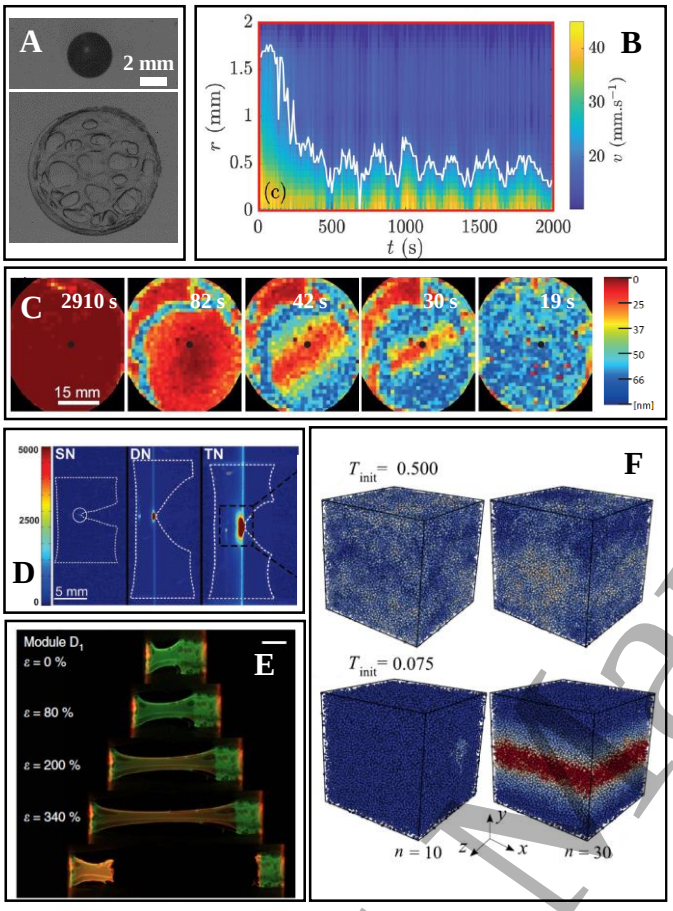

Figure 2: (A) Impact of a drop of viscoelastic fluid on a repellent surface, yielding a large and fast deformation of the material (bottom image). (courtesy of Carole-Ann Charles, L2C, CNRS & U. Montpellier). (B) Experimental spatiotemporal map of the flow velocity of a colloidal gel sheared at a fixed rate in a Couette cell, as measured by ultrasonic velocimetry [20]. (C) Experimental maps of the local dynamics over 1 s for a biopolymer under creep, measured by time- and space-resolved dynamic light scattering. Labels: time before failure. Adapted from [26]; (D) Bond breaking events reported by fluorescent mecanophores in (multiple) elastomer networks [22]; (E) Fluorescent signal reporting the local strain in DNA-based hydrogels [21]; (F) Color maps of the one-cycle nonaffine deformation after 10 and 30 shear cycles, for two different sample preparations, as obtained by molecular dynamics simulations of a dense packing of spheres. Adapted from [27].

Concluding Remarks While many key questions are still open, the recent progress in experimental tools, numerical methods and theoretical approaches suggests that this field should develop vigorously in the forthcoming years. Drawing a common scenario by unveiling the common features across different systems and driving modes will be, in our view, the greatest challenge in the field.

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Acknowledgements We thank the French CNES and ANR (grants No. ANR-14-CE32-0005, FAPRES, and ANR-20-CE06-0028, MultiNet) for financial support. LC acknowledges support from the Institut Universitaire de France.

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Section 3.3 – Suspension Rheology: A Smooth Past, Rough Present and Sticky Future?

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Status Thomas Kuhn famously describes fundamental shifts in perspective in science as changes in *paradigm.*[1] Paradigm changes share certain features. For example, one-time heresies become orthodoxy and previously unrelated areas become unexpectedly unified. After a new paradigm is seen to bring new insight in understanding to one or more exemplars, the members of the relevant community begin to rethink their entire field under the new perspective. There has been a recent paradigm shift in suspension rheology. Previous orthodoxy says that suspended particles do not touch, because lubrication forces between closely-approaching particles diverge and keep them apart.[2] The same forces render it difficult for nearby particles to separate, giving rise to 'hydroclusters' that cause shear thickening in suspensions.

The 'no touching' rule is true for perfectly smooth particles with ideal stick boundary conditions. However, the surfaces of two suspended spheres (radius R) in shear can approach[3] to where the simplification of 'smoothness' must break down in practice, *e.g.*, due to roughness at $\lesssim 10^{-4}\mathrm{R}$. In the new paradigm, the (previously unthinkable) frictional interactions between contacting particles dominate suspension rheology, especially in the non-Brownian size regime.[4] This realisation partly emerged from the insight that aspects of the physics of dry granular materials could be 'borrowed' for wet suspensions. This led to a rather unexpected, and fruitful, convergence of these two hitherto unrelated areas.[5] There followed an intense effort to understand the exemplar of shear thickening. The emerging picture is coherent enough that the new frictional paradigm has won widespread acceptance, and its wider implications are now being explored. Below, we review this paradigm shift and indicate key areas of suspension rheology that need to be re-thought in its light to move towards a predictive understanding of this industrially relevant class of materials, found in the processing of chocolate[6] through to cement.[7]

For dry monodisperse spherical grains, it is long known that if interparticle contacts are frictionless, mechanical stability requires each particle to contact on average $\mathrm{Z} = 6$ neighbours. At this 'isostatic point' with volume fraction $\phi = \phi_{rcp} \approx 0.64$, or random close packing, the system is jammed. With static friction coefficient $\mu \to \infty$, jamming occurs at $\mathrm{Z} = 4$ and $\phi \approx 0.55$, sometimes identified as random loose packing (ϕ_{rlp}). The transition from $\mathrm{Z} = 6 \to 4$ as μ increases essentially occurs over the range $\mu \approx 0.1$ to 1.[8] In 2014, Wyart and Cates (WC)[9] 'borrowed' this physics to explain shear thickening in wet hard-particle suspensions. They assume that suspension viscosity diverges as $\phi \to \phi_J$, a *stress-dependent* jamming point. As the applied stress increases, particles transition from having lubricated ($\mu = 0$) contacts to having frictional ($\mu \gtrsim 1$) contacts at some characteristic 'onset stress' σ^*. (This is in principle a local tensorial quantity, but in the scalar WC model it is typically taken to be the external applied shear stress, σ.) At $\sigma \ll \sigma^*$, $\phi_J = \phi_{RCP}$, while $\phi_J \approx \phi_{rlp}$ at $\sigma \gg \sigma^*$. At a fixed ϕ, the suspension viscosity therefore increases as the system moves closer to jamming at higher σ.

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Quantitatively, one uses a phenomenological expression for the relative viscosity of the suspension (*i.e.*, normalised by that of the solvent) such as $\eta_r = [1 - \phi/\phi_J(\sigma)]^{-2}$ and a linear ansatz $\phi_J = f(\sigma)\phi_{rlp} + [1 - f(\sigma)]\phi_{RCP}$, with some interpolating expression $f(\sigma)$ for a changing fraction of frictional contacts to connect the two endpoints. Shear thickening data from sterically-stabilised polymethyl methacrylate (PMMA)[4] and charge-stabilised silica suspensions[10] can be fitted using $f(\sigma) = \exp[-(\sigma/\sigma^*)^{-\alpha}]$ with $\alpha \approx 1$. The WC model correctly predicts that above some ϕ_{DST} just below ϕ_{rlp}, $\sigma(\dot{\gamma})$ becomes S-shaped, so that the viscosity jumps discontinuously, potentially by orders of magnitude, when a critical shear rate ($\dot{\gamma}$) is reached: the phenomenon of discontinuous shear thickening (DST). At ϕ_{rlp}, there is no flow above some maximum applied stress; such shear jamming can be observed transiently in experiments.[11]

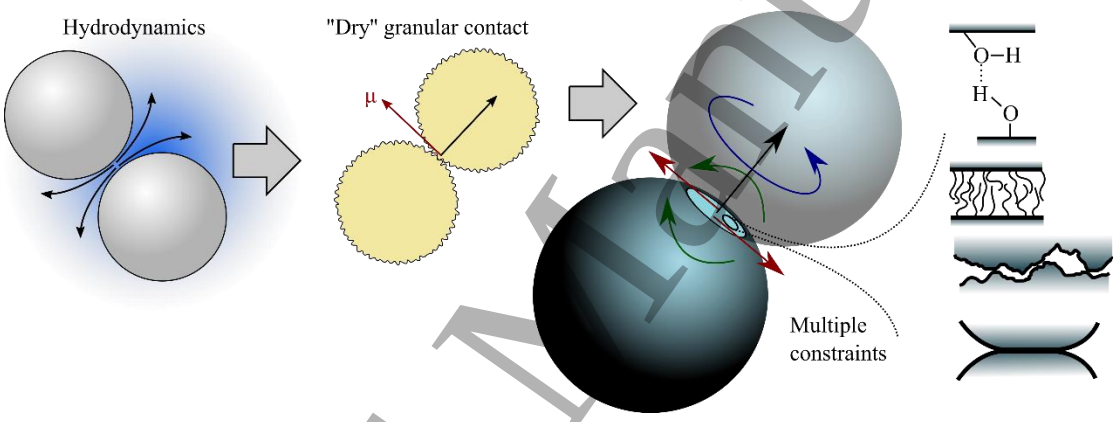

Figure 1 A schematic of the paradigm shift in suspension rheology from hydrodynamic lubrication to contact mechanics. The latter was first 'borrowed' for suspension rheology from dry granular mechanics in the WC model, which then inspired the consideration of multiple coarse-grained constraints on inter-particle motion that are agnostic to microscopic mechanisms at multiple length scales (hydrogen bonding, polymer interdigitation, surface asperities, particle softness, …

The onset stress, σ^*, for PMMA suspensions corresponds to the right order of magnitude of the force needed to collapse their stabilising 'hairs'. Importantly, $\sigma \sim R^{-2}$, so that for non-Brownian particles with $R \gtrsim 10$ μm, all practical stresses will drive the particles into frictional contact, and the suspension will respond as a shear-thickened system. It is therefore almost impossible to pack non-Brownian suspensions to ϕ_{RCP}: they will almost always jam at the lower ϕ_{rlp}. Simulations[12] confirm that the viscosity divergence in a suspension in which particles always interact frictionally occurs at a ϕ_J that smoothly varies from ϕ_{RCP} to ϕ_{rlp} as μ varies from 0 to ∞, giving a whole family of viscosity plots $\eta_\mu(\phi)$. Shear thickening is then a transition from the lowest branch of this family to one of the higher branches at fixed ϕ. Simulations also reveal compressional 'force chains' in thickened suspensions comparable to jammed dry granular materials.[12]

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The role of friction has been verified by a variety of more[13] or less[14] direct experiments, and many aspects of the rheology of shear-thickening suspensions beyond steady shear, *e.g.*, shear reversal[15] or sudden stress[11] (key for 'running on cornstarch') are being investigated under this new paradigm. Behaviour beyond the frictional jamming point ($\phi_{rlp} < \phi < \phi_{rcp}$) is also being elucidated, such as the response to vibration that allows flow at high ϕ[16] or granulation (where boundary interactions due to a confining surface tension prevent flow).[17]

Current and future challenges The phenomenology of shear thickening is robust. Similar $\eta_r(\phi)$ plots are reported in suspensions of quasi-monodisperse spheres[4,10], bidisperse spheres,[18] irregularly-shaped mineral crystals,[19] and mixtures of glass spheres and shards.[17] Interestingly, the WC model is able to account for data and deliver physically-meaningful fit parameters whenever the particle size distribution is single-peaked. However, it fails badly for highly bidisperse (large-small) suspensions. This is because WC is a mean-field model that treats large-large, large-small and small-small particle contacts 'democratically', while in fact the large-large contacts dominate the rheology and force transmission.[18] Similarly, in mixtures of bumpy and smooth particles, a small number of smooth particles have a disproportionate effect in breaking up the force network.[20] Indeed, mean field models should not work for suspensions, because $\mathcal{O}(10)$ nearest neighbours do not justify averaging out local details. A theory including these details that treats local stress propagation tensorially is still to be developed. Progress is being made through considering local force balance[21] and contact anisotropy.[22] In parallel, the transition at ϕ_{DST} has been fruitfully compared to classical critical phenomena.[23]

So far, we have not defined 'friction' beyond specifying that it should be *static* friction that prevents relative sliding and lowers the number of contacts needed to reach mechanical stability (= jamming) due to a 'constraint counting' argument. Precisely how sliding constraints generate extra dissipation is the subject of ongoing research. These constraints may act on the molecular level, *e.g.*, hydrogen bonding;[24] mesoscopic surface 'bumpiness' much larger than tribological asperities also suffice,[20] Fig. 1. Even hydrodynamic interactions under special conditions[25] will give essentially the canonical shear-thickening phenomenology, with DST at $\phi \approx \phi_{rlp}$. As hydrodynamic interactions disappear in the strict static limit ($\dot{\gamma} \to 0$), this raises the question as to whether enhanced tangential interaction at $\ll \dot{\gamma}R$ suffices for 'static friction'. Indeed, measurement of 'static' friction remains outstanding, requiring either a reanalysis of existing dynamic techniques[13,20] or new methods. Such measurements may resolve the apparent discrepancy that dynamically measured friction coefficients are too low to explain observed values of ϕ_{rlp} that consistently suggest $\mu \gtrsim 1$.

The possibility of constraints other than sliding arising from a variety of interactions, Fig. 1, is now being explored.[26] Stress-activated constraints that prevent rolling in addition to sliding could enhance shear thickening and lead to shear jamming at $\phi \ll \phi_{rlp}$.[27] Alternatively, adding *adhesive* constraints to inter-particle rolling that are operative at zero applied stress, but are broken beyond some characteristic stress predicts a 'zoo' of experimentally-realistic flow curves.[26] In this scenario, a finite yield stress emerges above some 'adhesive loose packing', $\phi_{alp} < \phi_{rlp}$, and then increases to divergence at ϕ_{rlp}. Significantly, this yield stress is not due to adhesive forces alone,

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but such forces stabilising frictional contacts along force chains,[19] so that studying yield-stress suspensions may illuminate the role of rolling resistance.

To date, information on rolling has come from optical-trap measurement of the critical bending moments of particle chains in a strong colloidal gel. Such experiments suggest that mechanical contacts between micron-sized suspended particles may strengthen with time.[28] This raises intriguing possibilities. For example, under prolonged stressing, nominally hard particles may be pushed beyond 'frictional contact' into softer, even adhesive, contact. A transiently jammed state may no longer be 'fragile', *i.e.* only load-bearing in the direction in which the suspension was originally shear jammed,[15] with softness leading to the possibility of fully (or isotropically) jammed states.[29] This would profoundly influence how a jammed region behaves in unsteady flow, where currently a variety of system specific behaviours are seen in spatially-resolved experiments measuring density[30] or velocity.[31] This suggests combining such tests with transient rheological protocols, *e.g.*, shear reversal, to probe the nature of jammed regions. Recent large amplitude oscillatory shear work on local stresses already points in this direction.[32]

Concluding remarks Once contacts are admitted, wide-ranging research topics emerge. Consider, *e.g.*, issues raised by the move away from non-contacting *attraction* arising from potential interactions (Van der Waals, Coulomb) to contact *adhesion*; the origin for static sliding friction; the nature of various kinds of stress-dependent rolling resistance that enhances shear thickening; and how to control the response of the inhomogeneous DST state. Resolving these issues may finally give the ability to predict and tune the rheology of non-Brownian suspensions in industrial settings. Beyond such developments, the extension of frictional rheology to suspensions of highly anisotropic particles such as flexible rods[33] will considerably increase its range of applicability, *e.g.*, to cellulose suspensions, a sustainable alternative additive to synthetic polymers in certain products.[34]

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Section 3.4 – Driven liquid to solid transitions

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Status Search the internet, and you fill find hundreds of videos showing people running, jumping, and even riding bicycles on the surface of liquid mixtures of cornstarch and water. These fun demonstrations illustrate a ubiquitous property of nearly all dense suspensions, the tendency to undergo a liquid to solid transition when driven at high enough stresses [1] (Figure 1 Left). Such transitions continue to be industrially important for numerous applications including high-throughput processing of dense suspensions such as cement and concrete, 3D printing, and conching during the production of chocolate.

A seminal advance in this field has been the discovery that, in addition to hydrodynamic coupling between the suspension particles that causes a relatively minor increase in viscosity, the onset of thickening is stress dependent and arises from the repulsion, frictional interactions, and/or interdigitation between the particle surfaces [2,3] (Figure 1 Right). Indeed, studies have shown that thickening can be controlled by modifying the particle surfaces to be more or less frictional, smoother or rougher, more or less chemically attractive etc. The origin of these interactions continues to be a very active area of research and has obvious ties to many decades of activity in the field of surface science. Theoretically, the importance of stress dependent surface interactions was intuitively summarized by the Wyart and Cates model, which postulated that the fraction of frictional interactions between particles increases with stress, capturing the idea that for stable suspensions, there is barrier that must be overcome before surface interactions can arise [5].

More recently, attention has been turned towards abstracting away the specific origins of these interactions and thinking of them in terms of the physical constraints they impose on the particle motions. In this approach one becomes agnostic about the origin of say frictional interactions and simply acknowledges that the suspension particles are subject to sliding constraints [6]. This abstraction has focused the community on formulating questions about and addressing a different scale in the thickening problem: the formation, structure, and manipulation of the force network formed by the suspension particles exhibiting these surface interactions [7].

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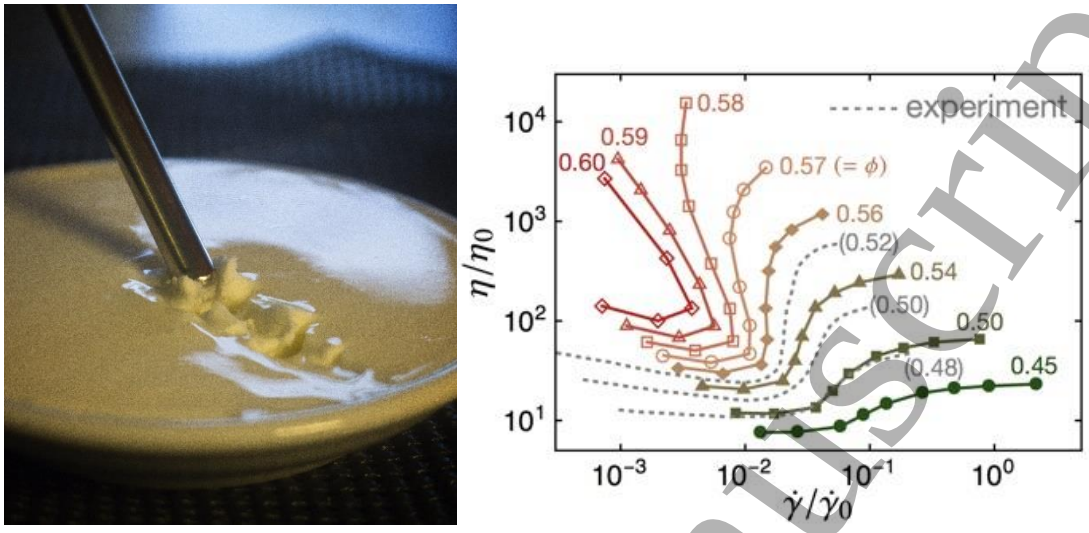

Figure 1 Shear thickening suspension of cornstarch and water. Left, photograph illustrating the liquid to solid transition as the surface is scraped (Image curtesy of Neil Lin). Right, normalized viscosity versus shear rate in experiments and numerical simulations adapted from [3] and [4].

Current and Future Challenges A major challenge for the field is to develop experimental techniques, models, and theories that can accurately address various properties of the force network including heterogeneity, anisotropy, and its evolution under imposed flows. In the Wyart and Cates model, for example, such effects are ignored and the suspension is assumed to be isotropic with a viscosity that is related to the suspension's proximity to a stress dependent jamming volume fraction: as surface interactions increase, isotropic particle networks can support themselves at lower volume fractions and the system is driven closer to a solid phase. To address this challenge in experiments, it will be necessary to move beyond standard rheometery, and develop approaches capable of measuring the heterogeneity of the stress response and its full tensorial nature. Techniques such as angle resolved rheometry where the suspension is strained along a primary flow direction, to set up the force network, and then probed at various angles are quite promising in this regard. Simulations capturing hydrodynamic, frictional, and interdigitation interactions have played a major role in elucidating the origins of thickening. Moving forward, however, it will be necessary to abstract some of these interactions to simulate larger systems, suspension states that are closer to shear jamming, and the evolution of the force networks in 3D. Finally, there is a desperate need for statistical theories that can elucidate the formation and evolution of the force network.

One avenue for developing such theories entails adopting ideas from equilibrium critical phenomena to the inherently out-of-equilibrium flows associated with thickening. Towards this end, a recent analysis of experiment data showed it is possible to collapse the viscous response of different suspensions (cornstarch in glycerol and silica in glycerol), over a range of volume fractions (0.16 to 0.58) onto a single universal curve with two separate scaling regimes [8]. The collapse

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indicates that thickening is a transition from a regime where suspension properties are governed by isotropic frictionless jamming to one where they are governed by frictional shear jamming. The analogous process in thermodynamic systems is crossover scaling between two critical points belonging to different universality classes. Should this analogy hold, it may be possible to bring over 50 years of developments in the statistical mechanics of phase transitions to bear on the problem of thickening.

Advances in Science and Technology to Meet Challenges Developing a satisfying analogy between the statistical mechanics governing thermally equilibrated systems and those governing shear thickening non-thermal suspensions will require addressing several critical issues. For example, it will be necessary to determine how ergodicity, the ability of a system to explore a high dimensional phase space in a uniform fashion, must be modified to address driven non-thermal systems. It remains a deep and fascinating question whether trajectories between points in the phase space associated with different geometric contact networks in thickening systems are analogously ergodic, more akin to hopping between local attractors in a process governed by Levy statistics, or are characterized by some new, yet to be discovered, mode of phase space sampling. Moreover, given the steep potentials associated with the particle interactions, it will be necessary to confront the problem that for nearly identical particle configurations, the stress distribution could be completely different. As such, there may be important analogous questions relating to the way-imposed flows allow non-thermal systems to explore constraint landscapes associated with *each* geometric contact network. It is possible, therefore, that understanding thickening may require solving for system trajectories through a nested phase space.

The development of such theories will undoubtedly benefit from experiments that enable manipulation of these phase space trajectories and the resulting suspension properties. Several promising techniques for dramatically tuning the shear viscosity of thickened suspension have recently been developed. These include orthogonal shear perturbations [9] enabled by biaxial rheometers and the application of acoustic perturbations via attached piezos [10] (Figure 2). It is likely that additional techniques due to chemical, electrical, and magnetic activity will enable similarly powerful manipulations. Many of these techniques are applicable in more complex flow geometries and could be combined to enable important technical applications. As the number of parameters necessary to control the resulting flows increases, it will become useful to incorporate the latest advances in measurement science and even machine learning to determine how to efficiently scan an increasingly unwieldy parameter space to achieve the desired suspension properties.

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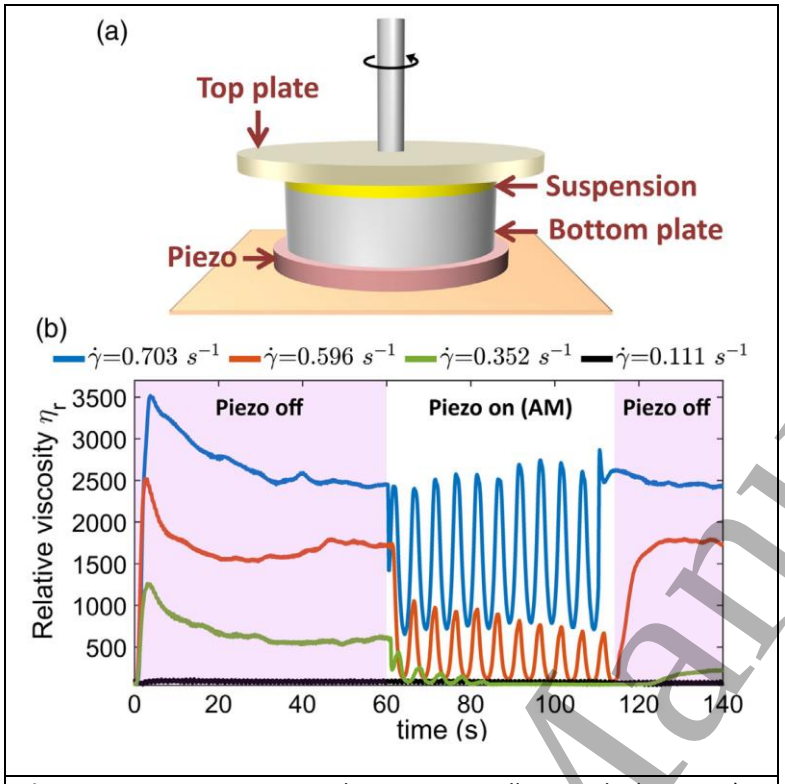

Figure 2 Using acoustic perturbations to rapidly tune thickening. a) A Piezo is used to apply amplitude modulated (AM) acoustic perturbations. b) The instantaneous viscosity response of a suspension with 53% volume fraction at four different strain rates. As the amplitude of the acoustic perturbations is increased, the viscosity rapidly decreases. Taken from [9].

Concluding Remarks The rapid pace with which the understanding of this driven liquid to solid transition has advanced, points to a future where we could have full control over the resulting suspensions properties in arbitrarily complex flow geometries. Such control could, in addition to reducing the stresses associated with thickening suspensions, enable the development of completely new materials. For example, if we can manipulate the resulting suspension viscosity on a time scale smaller than that associated with the global flows, it may be possible to create viscosity metamaterials, where the average viscosity arises from a suspension that is only thickened for part of the time. More broadly, the breadth of technological applications, new experimental geometries, and deep analogies rooted in statistical theories of phase transitions speak to the richness of the thickening problem and its importance to the cannon of soft matter phenomena.

Acknowledgements This work was supported by NSF CBET award numbers: 2010118, 1804963, 1509308, and an NSF DMR award number: 1507607

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Section 3.5 – Electric and magnetic field control

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Status External fields affect the flow behaviour, the transmission of electromagnetic energy, or the ultimate organization of a soft material (whether equilibrium or non-equilibrium). The scientific and engineering interests in external field control include magneto- and electrorheology, ferrofluid flow in magnetic fields, magnetic microfluidic mixers, and the rapid optical switching in liquid crystal and e-ink display technologies. Other applications of fields and field control relevant to soft materials include processing using external fields, such as electrospinning polymer nanofibers and the magnetic or electric directional ordering of nanoscale structure in block copolymers and polymer-based nanocomposites. It is clear from these examples that electric and magnetic fields drive a material's underlying nano- or micro-structure—externally and often rapidly relative to thermal or solvent annealing, drying, or changes in temperature or other physical chemical conditions. But phenomena that occur in field-driven soft materials are rich and sometimes unexpectedly universal, like the analogy between the Landau-Peierls fluctuation-driven interactions of polarizable particle chains and those of Abrikosov vortex lines in high-temperature superconductors. [1] Interesting analogies also exist with the behaviour and assembly of particles in nematic liquid crystals (see section 1.5) and on curved fluid interfaces. [2]

A few of the most exciting recent developments use electric and magnetic fields to *direct* self-assembly, realize new methods of *dissipative* self-assembly, and drive emergent dynamics and organization in active soft matter by *dynamic* self-assembly (Figure 1). [3] In directed self-assembly, fields nudge or guide the kinetics of self-assembly through nonequilibrium states to an equilibrium structure. Its aim is to provide direction and control without losing the scalability of thermodynamically driven self-organization. Using directed self-assembly, one can organize the direction of block co-polymer nanoscale structures by weak diamagnetic forces [4] or guide anisotropic nanoparticles to form close-packed crystals in electric fields. [5] Entirely new forms of non-equilibrium assembly, termed dissipative self-assembly, occur when fields are used to rapidly oscillate interaction energies, especially in dispersed materials like suspensions. [6, 7] Similarly, the energy input by oscillating or periodic fields can drive motion in a soft material that leads to self-organization—a form of the dynamic self-assembly of active matter (see section 3) which resembles the organization of insect swarms, bird flocks, and schools of fish.

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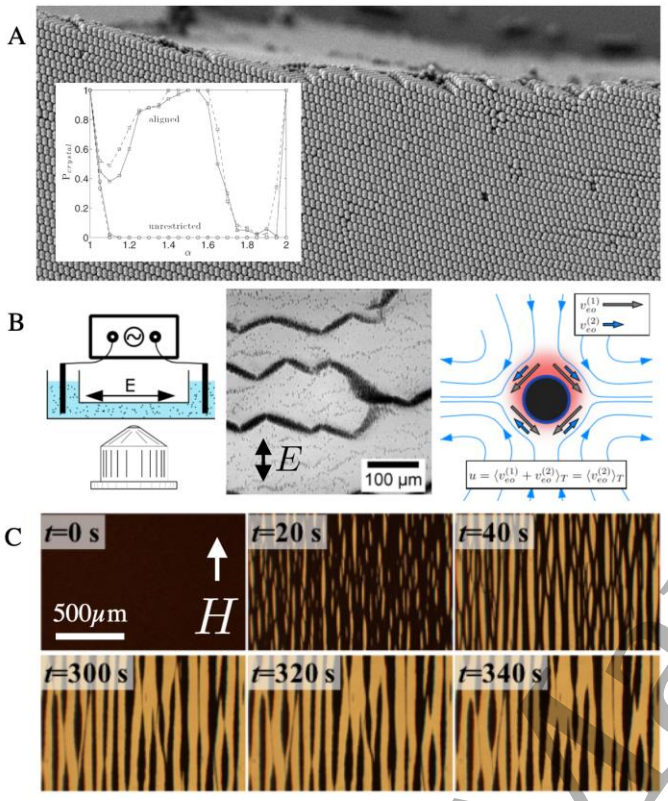

Figure 1 Electric and magnetic fields are used to drive directed, dynamic, and dissipative self-assembly. (A) Dumbbell nanoparticles assembled into close-packed crystals through a directed self-assembly process. The inset shows the probability of crystallization with alignment for different aspect ratio particles. Adapted with permission from J. D. Forster et al., "Assembly of Optical-Scale Dumbbells into Dense Photonic Crystals," ACS Nano, vol. 8, pp. 6695–6700–6700, 2011. Copyright 2011 by the American Chemical Society. (B) Organized, rotating bands of silica particles in an ac electric field. This dynamic assembly is attributed to secondary electrokinetic flows around each particle. Adapted with permission from F. Katzmeier, et al., Phys. Rev. Lett., vol. 128, no. 5, p. 58002, 2022. Copyright 2022 by the American Physical Society. (C) Phase separation during the dissipative assembly of paramagnetic colloids in a toggled magnetic field. Adapted with permission from H. Kim, et al., Langmuir, vol. 36, pp. 9926--9934, 2020. Copyright 2020 by the American Chemical Society.

Current and Future Challenges Despite its promise—scalable assembly, potentially new morphologies, and dynamical responsiveness and control—there are several key challenges in the field. For one, there is a general lack of design rules for directed, dissipative, and dynamic self-assembly by electric and magnetic fields. Little is still understood about these processes, and much work remains in experiment, theory, and simulation. Perhaps the greatest challenge of electric and

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magnetic field control of soft matter lies in the inverse design problem: given a desired functional structure, what are the fundamental building blocks and processes to achieve them?

In both *directed* and *dissipative* self-assembly, knowledge of thermodynamic states—including mechanical and thermal equations of state—are necessary. As a case in point, for the directed assembly of dispersions a significant design challenge is the need to know the equilibrium phases and nonequilibrium states, especially for complex particle shapes with field-mediated interactions. Relaxation timescales should be known, too, to capture the kinetics of transitions and select favorable assembly conditions. For some shapes, like highly anisotropic or asymmetric particles, the existence of multiple phases and dynamic modes (rotation, translation) complicate this theoretical understanding, and few modeling efforts have described the interactions between even more complex metallo-dielectric and patchy particles that are designed to couple to fields. [8, 9] Magnetic and electric interactions are long-ranged and subject to mutual polarization. Properly incorporating these interactions is challenging and in simulations requires sophisticated algorithms. [10] The computational expense of computing long-range interactions limits both the system size and simulation duration.

Where external fields have been used to guide particles into close-packed configurations, they orient anisotropic particles and move them from low concentrations to high concentrations through gradients [11]. With dumbbell nanoparticles (Fig. 1A), the role alignment is clear and explained by the low probability that particles form close-packed structures in the absence of a directing field because of combined arrest in their translational and rotational motion at high concentrations. [12] Without alignment, the suspension particles get trapped in a glassy, disordered state. For now, though, this process of field-guided assembly is entirely empirical. Nor is it clear whether the equilibrium close-packed structure is really achieved, or what controls the type and frequency of defects. Theoretical studies of dumbbell nanoparticles identified their glass lines, but what is the corresponding state diagram for particles *aligned* by a field? Furthermore, fields induce polarization and interactions, so there must be a trade-off between alignment and other field-driven microstructural transitions (even gel-like states) found in electro- and magneto-rheological fluids.

Advances in Science and Technology to Meet Challenges There are several immediate investments that can be made to meet the above challenges. First, better, and more accessible computational tools, simulations, and theories are needed. Experimentalists need theoretical and computational models that accurately capture the physics of directed, dissipative, and dynamic self-assembly.

In recent years, several groups produced encouraging results toward a theoretical basis of dissipative assembly (Figure 2). Tagliazucchi et al. developed a first principles understanding of suspensions with particles interacting by periodic, oscillatory potentials. [6] In the limit of fast oscillations, the resulting distribution of dissipative self-assembling states is exactly equivalent to that created by time-averaged effective potentials. These potentials have no equilibrium counterparts. But their work demonstrated that, in some cases, dissipative self-assembly can be predicted and analyzed in terms of equilibrium self-assembly. Sherman and co-workers studied

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nanoparticle suspensions with periodic *toggled* interactions that led to structures that are not near the global minimum in free energy, and they found that toggling can stabilize nonequilibrium phases. [7, 13] Their brilliant use of the sticky hard sphere model connects equilibrium with toggled steady-state structures. [7] Both research groups provide clear design rules for experimental work—target oscillation frequencies, field strengths, and duties (for toggled fields) that optimize the assembly kinetics and control structures; both also lay the groundwork for more robust non-equilibrium thermodynamic theory.

Second, investigators need rational design and synthesis of field-responsive molecular and colloidal building blocks, especially those that use first-principles designs aided by computer modeling. Some part of these materials could be dedicated to a functional property while the other is optimized purely for the ability to align the functional domains, as described for field-responsive block copolymers. [4] For both polymeric and colloidal soft materials, there has been little optimization to enhance the efficacy of field direction and control, although there are promising studies that use metallodielectric patchy particles, noted earlier.

There have been few studies using combinations of fields, or combining fields and other driving forces, such as flow. The parameter space is vast, and there is plenty of opportunity to advance the experimental and theoretical work in the area. In related studies, investigators used orthogonal oscillatory fields to generate "isotropic" potentials (analogous to a Keesom dipole-dipole interaction) between paramagnetic colloids. [14] This effect relies on the short Néel relaxation time of the magnetic nanoparticles used to produce paramagnetic responses in otherwise large (and slow) polymer latex particles.

Finally, fabricating materials on a commercial scale by bottom-up self-assembly requires well-characterized and efficient manufacturing techniques. How these processes will be scaled up or incorporated into existing or new manufacturing is an open question. This is closely tied to the "inverse design" problem highlighted at the beginning of this survey. Possibly the most pressing need is to develop a strong feedback loop from simulation and theory to aid the design of new field-responsive materials that achieve targeted, functional structures.

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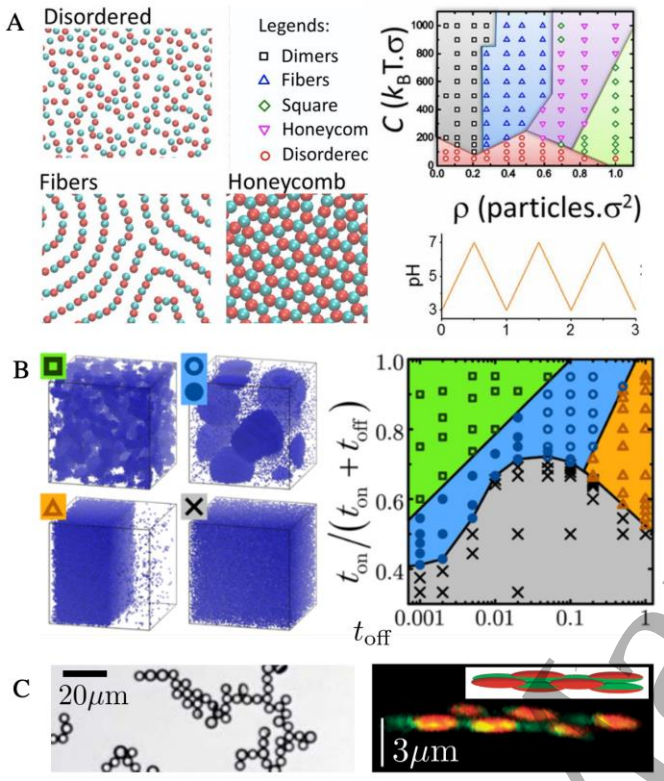

Figure 2 Developments toward a theory of dissapative assembly include (A) nonequilibrium structures formed in an oscillatory potential modeled by changes in pH. The parameter C denotes a strength of interaction. Adapted with permission from ref [6]. (B) Nonequilibrium phases due to similar toggled attractive interactions are sensitive to frequency and duty. Reprinted with permission from Z. M. Sherman and J. W. Swan, "Dynamic, Directed Self-Assembly of Nanoparticles via Toggled Interactions," ACS Nano, vol. 10, pp. 5260–5271, 2016. Copyright 2016 American Chemical Society. (C) Spherical (left) and ellipsoidal (right) metallo-dielectric particles designed to couple and respond to electric fields. Adapted with permission from ref. [8] Copyright 2009, Royal Society of Chemistry and adapted by permission Springer Nature: Nature Materials, "Actuation of shape-memory colloidal fibres of Janus ellipsoids," A. Shah, B. Schultz, W. Zhang, S. C. Glotzer, and M. J. Solomon, 2014.

Concluding Remarks The use of electric and magnetic fields in soft matter much holds significant promise by enabling new modes of directed, dissipative, and dynamic assembly into functional materials. Fields can improve the speed of assembly, quality of the final product, and ease of control, while also leading to new and useful nonequilibrium structures. The focus of this survey is

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on self-assembly, but new functional soft materials are also being developed as extensions of magnetorheology, including magnetic elastomers. [15] Intriguing and important applications of these composites include the development of controllable soft actuators—grippers or artificial cilia; open questions abound, such as the role of the interphase region between magnetic particles and the surrounding matrix. Further advances in magnetic and electric field control will require investments in experiment, simulation, and theory.

Acknowledgements This material is based upon work supported by the National Science Foundation under Grant No. CBET- 1637991.

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Section 3.6 – Stimuli-responsive materials

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Status The term "stimuli-responsive" (SR) refers to materials that undergo a meaningful change in properties (the response) when subjected to a change in external environment (the stimulus). The term is intrinsically redundant – a response by definition has a stimulus that triggered it, and the delivery of energy or matter is only a stimulus if it triggers a response. The broad, if linguistically uneconomical, use of "stimuli-responsive" likely reflects a desire to emphasize the breadth available on either side of the stimulus-response relationship. Stimuli include various forms of energy (e.g., thermal, photons, electromagnetic waves and fields, or mechanical) and the introduction or removal of matter (e.g., solvents, reagents, acids/bases, salt, or electrons), and each can in principle be coupled to an ever-increasing range of responses (e.g., change in shape, assembly, colour, luminescence, mechanical properties, thermal transport, material transport, conduction, or uptake/release of cargo). The interest in, and study of, such materials has captured commercial and academic interest for decades. Excellent reviews of stimuli-responsive materials are available [1-3].

The ability to change properties differentiates SR materials from those whose properties are largely static. As a result, for a couple of decades it has been fashionable to refer to such materials as "smart" [4]. A more appropriate term for the state-of-the-art, however, is probably "obedient" [5]. The scientist wants a material that exists in state *A* under condition *a*, and in state *B* under conditions *b,* and any "smarts" come into play by finding the material compositions in which *A*/*B* switching occurs at a desired *a*/*b* threshold. The material is instructed through chemical synthesis as to how it should respond. The complexity of the approach, and the range of applications for which it is relevant, can be extended by introducing additional states to form a "multi-stimuli-responsive" material. Each state has its own corresponding stimulus thresholds which can be simultaneously or independently addressed. This form of multi-stimuli-responsive material engineering is likely to remain an active area of research.

Current and future challenges Material systems with spatially distinct, individually responsive components hold the potential for a different level of "smarts," because of the combinational possibilities of spatially distributed SR events. Further, when the right feedback loops are incorporated, materials might become capable of adapting their structure to arrive at a final system-wide state that meets the challenge of a given environmental condition, even when the optimum final state is not known in advance. That is, the material is "smarter" than the scientist who created it, creating a complexity in response that can be guided by machine learning models in the future.

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Here, we illustrate examples that employ SR elements on both the macro and molecular scale, with mechanical properties chosen for illustrative purposes.

On the **macro** scale, microstructured materials (metamaterials) include those with novel quasi-static and dynamically responsive mechanical properties [6], and there a few emerging examples of their intersection with SR materials, such as those made from magnetically response material components [7]. For the case of mechanical properties, the combination of metamaterials and SR materials holds the possibility of highly amplified system-level changes in mechanics due to a change in properties of only a small fraction of the overall object. An example can be seen in Maxwell lattices, where the removal of a single edge can have a dramatic impact on lattice mechanics (Fig. 1). An SR response in an edge can similarly trigger a similar transition from a stable to a floppy lattice across large length scales, even though the region of SR change is comparatively small. The local responses can, in principle, be used to switch between multiple stable lattice states, including extreme properties brought about by non-linearity. Opportunities include the potential for directional response(s) depending on which location(s) within the lattice is triggered – the exact same material response can give a dramatically different metamaterial response depending on the relative orientation of the triggered edge.

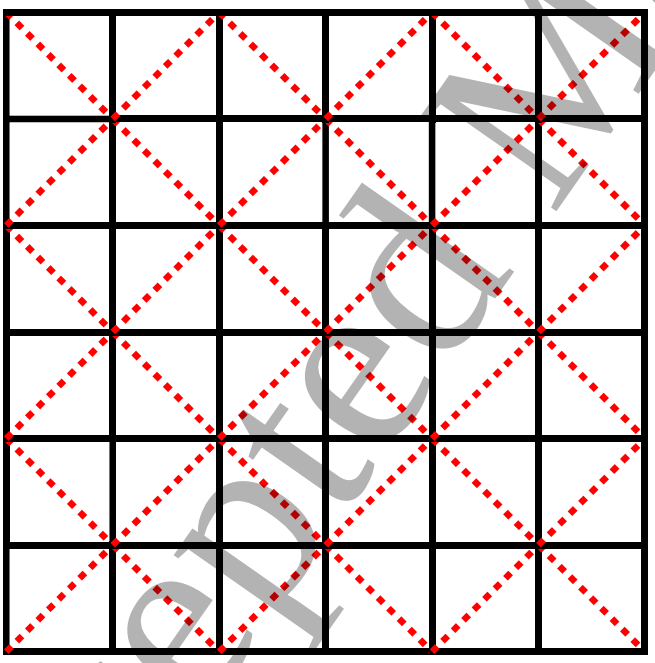

Figure 1 The Maxwell lattice shown is rigid under shear when SR components (red) are intact and stiff, but the entire lattice becomes soft in shear when those components disappear or soften.

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On the **molecular** scale, consider polymer networks, in which the edges of a lattice are replaced by the spring-like behaviour of fluctional non-crystalline (disordered) polymer strands. The ultimate strength of polymer materials is <1% of the potential collective strength in their strands, and evenly distributing load across all strands in a network could increase ultimate strength of the material by over 100-fold (e.g., rubber bands or even hydrogels that are as strong as steel but still easily stretched). The challenge in achieving those properties arises from the fact that as a network is strained, a few strands within the broad distribution act as stress concentration sites that initiate failure. The "statistical distribution problem" cannot be overcome with traditional strand or network synthesis; purely monodisperse and fully reacted strands still have a Gaussian distribution of initial end-to-end lengths. One can envision, however, how a mechanically triggered response that irreversibly lengthens a single strand at a critical force of tension [8] might rectify the molecular force imbalances (Fig. 2) to create "self-perfecting" networks.

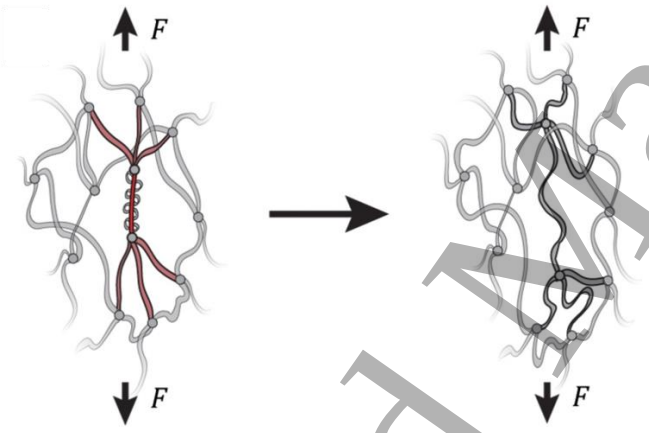

Figure 2 Areas of high tension (red) in a polymer network are sites of likely damage initiation on the molecular level. Mechanoresponsiveness at the molecular level, however, might lead to the irreversible release of stored length that redistributes and balances the tension.

Advances in science and technology to meet challenges

1. *Modeling of topological metamaterials as a function of the range of properties available in SR material components*. Such models should account for variations in properties that might arise from incomplete switching in real systems, any imprecision in the dimensions of the fabricated components, and the dynamics of switching.

2. *Molecularly precise synthesis of SR materials and improved fabrication of SR metamaterials.* Opportunities abound from the macro and molecular scales, as advances in the breadth and precision of additive manufacturing [9] enable the pursuit of the former, while advances in precision synthesis and characterization enable an informed approach to the latter. Continued

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expansion of these techniques to SR materials will provide an opportunity to test and refine the development of multi-scale models.

3. *Robust strategies for complex feedback loops.* The range of available SR input and output combinations continues to increase. Mechanical property changes, for example, can be induced by swelling, light, redox, temperature, electromagnetic fields, etc… A particularly exciting opportunity is found, however, when the trigger mediates a change in the way its associated form of energy/matter is processed by the material/metamaterial, such as when the SR elements respond to mechanical signals by changing mechanical properties. It has been shown that the resulting feedback loops can lead to signal amplification, system-wide dynamic responses to local actions, and autonomous homeostasis [10].

4. *Data structures that capture chemical complexity, characterization, and metadata.* With increasing complexity, machine learning strategies may play a pivotal role in the development of these systems. A machine learning based design approach could accelerate the identification and optimization of SR input/output combinations with a fewer number of physical experiments.

Concluding remarks Mechanical properties are presented here only as an example of the broad possibilities. Related opportunities exist at the topology-SR material nexus for optical properties (responsive light traps, lenses, filters, or absorbers), electrical conductivity, thermal regulation, or the transport of diffusing species. Overarching questions include: when topology can be controlled precisely (e.g., in metamaterials), how can it be optimized to take greatest advantage of local switching in SR elements? Or when topology is intrinsically uncontrollable (e.g., in polymer networks made via random polymerization), how can responses at the molecular level be optimized to ameliorate performance limitations brought about by the topological disorder? These emerging opportunities will only be strengthened by continued development in traditional areas of SR material research, such as multi-response, faster and more complete switching, and continuing to increase the magnitude of property change available in an SR event.

Acknowledgments This work was supported by the NSF Center for the Chemistry of Molecularly Optimized Networks (MONET), CHE-2116298. We thank X. Mao and S. Wang for providing the graphics in Figures 1 and 2, respectively.

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Section 4.1 – Linking Hard and Soft Matter Physics

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Status Any reasonable attempt at a roadmap linking the physics of hard and soft matter cannot possibly begin without bringing to the fore the landmark 1972 paper by de Gennes that brought out the striking analogies between the normal-to-superconducting transition in metals and the nematic-smectic A transition of mesogens [1]. In the absence of spatial inhomogeneities, the Ginzburg-Landau Hamiltonians describing both these transitions are similar, and the expulsion of the external magnetic field in the Meissner phase is analogous to the expulsion of twist in the smectic A phase. Building on this observation, Renn and Lubensky would later predict the twist-grain-boundary (TGB) phase - the liquid-crystalline analogue of the Abrikosov flux lattice of type-II superconductors [2]. Experiments on ferroelectric liquid crystals (LCs) observed the TGB phase just a year later [3]. Such striking analogies between hard and soft matter are not limited to superconductors and LCs; see, for instance, the mapping of polymer chain confirmations due to excluded volume interactions to a magnetic system [4], again due to de Gennes, or the Kovacs memory effect that was first observed in polyvinyl acetate and then in numerous other systems, including molecular glasses [5].

The link between soft and hard materials has further strengthened in the past two decades from the clever use of colloidal suspensions to investigate numerous physical phenomena encountered in atomic/molecular matter. Despite being ruled by entropy, the phase behavior of colloidal suspensions shares striking similarities with hard matter, where energetics dominates [6]. Furthermore, colloidal particles, being micrometer-sized, are amenable to particle resolved imaging of dynamics in real-space; particle shape and interactions can be tuned at will, and individual colloidal particles can also be manipulated. Probing physical phenomena in real-space with 'colloids as big atoms' presents a clear advantage over scattering-based approaches, which are ensemble-averaged, and has indeed been well-leveraged to test theory and numerical predictions [7]. See, for instance, the first observation of dynamical heterogeneities in supercooled liquids [8], the direct observation of thermal capillary waves [9], premelting at grain boundaries [10], observation of solid-solid phase transitions [11], kinetic roughening of driven grain boundaries [12], and recently, devitrification [13], to name a few.

Given the many bridges between soft and hard matter, each of which merits a detailed discussion, here, we restrict ourselves to three areas that we anticipate will continue to draw researchers.

Exploiting parallels between atomic, nanoparticle, and colloidal epitaxy for self-assembly Advances in understanding atomic epitaxial growth processes have hugely enhanced our ability to fabricate functional surface nano and microstructures [14]. More than two decades ago, van Blaaderen and co-workers extended these concepts to colloidal systems [15]. Subsequent studies found that while the island growth laws governing atomic and colloidal homoepitaxy were similar, there were also subtle differences [16]. For instance, the Ehrlich-Schwoebel step-edge barrier (ESB), which decides the ease of interlayer mass transport and the morphology of the

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growing film, has an energetic origin in atomic systems. In contrast, in colloidal systems with short-range interactions, it is a purely kinetic barrier. Recent studies have found that for large molecules like C60, whose range of interactions is intermediate between atoms and colloids, both the energetic and kinetic ESB have a role during film growth [17].

Even while atomic homoepitaxy concepts carry over to colloidal systems [18], whether this is also the case with heteroepitaxy, i.e., when there is also a lattice misfit between the growing film and the substrate, remains largely unexplored. Exploiting strain-relief mechanisms in heteroepitaxy to organize matter on surfaces is extensively used in atomic and molecular systems; with nanoparticle and colloidal ones, the first steps have just been taken (see Fig. 1) [19-23]. The range of interparticle interactions is a crucial parameter in deciding how strain-relief occurs; for instance, with DNA-grafted nanoparticles, where the interactions are long-ranged, film growth remains pseudomorphic with the substrate even for very large misfits and is quite unlike in atomic systems [21]. On the other hand, for colloids with sticky interactions, Mondal et al. find striking parallels between the strain-relief mechanisms in colloidal and atomic systems for compressive misfits [22]. However, the level of self-organized growth seen in atomic systems remains unrivalled. See, for instance, the spectacular self-organized growth of metal nanostructure arrays on a strain-relief dislocation network achieved in the late 1990s [24]. If this level of self-organization with nanoparticle and colloidal systems is attained, one can then only envisage the richness that particle valence and shape can further bring [25].

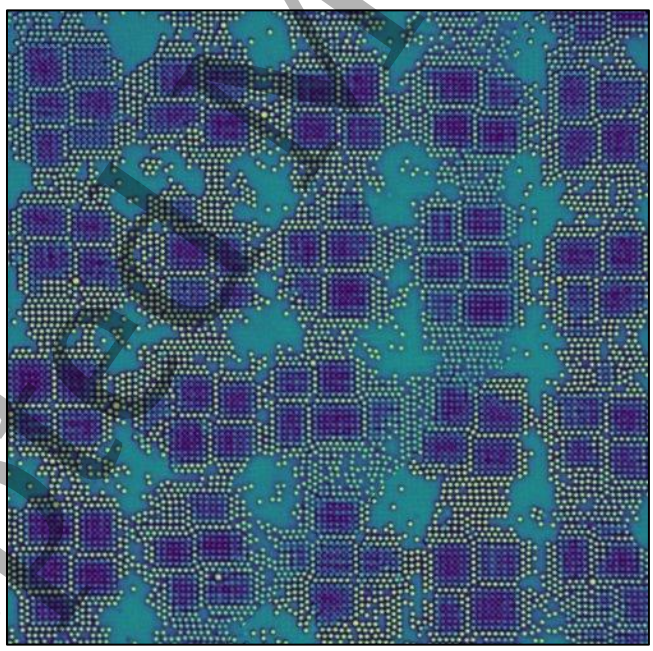

Figure 1 Hierarchically organised colloidal crystal arrays obtained in colloidal heteroepitaxy. Picture used with permission from Manodeep Mondal, Soft Matter Lab, Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore 560064, India. See Ref. [22] for details.

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Glass Transition Understanding how liquids turn into glassy solids on quenching is one of the grand challenges in condensed matter physics [26]. Theories of the glass transition are many, experiments that directly test theoretical predictions are few, and experiments that pit theories against each other, even fewer. The contribution of colloid experiments in gaining insights into glassy dynamics cannot be overstated (see the many Review Articles [27-28]). While helping visualize dynamics, the large size of the colloidal particles also means that the system falls out of equilibrium before reaching the deeply supercooled regime, which is also the dynamical regime of interest. The first steps towards overcoming the sample equilibration bottleneck have just been made. Using the Stimulated-Emission-Depletion (STED) microscopy technique, Royall and co-workers imaged nanoparticle liquids, where relaxation is substantially sped-up due to the smaller particle size [29]. This study provided real-space evidence of structural relaxation beyond the mode-coupling singularity and a direct link between the growth of locally favoured structures and dynamics. Competing glass theories remain untested in this newly accessible dynamical regime. Experiments that capitalize on the latest advances in imaging techniques to shed light on glass physics are bound to pay huge dividends.

As has been the case in the past, identifying the role of static structure in glassy dynamics will continue to remain a key research avenue. The numerical isoconfigurational ensemble (ICE) approach [30], which first identified an underlying structural basis of dynamical heterogeneities, remains untested in experiments, and for a good reason [31]. However, the difficulties plaguing colloidal systems may not apply to two-dimensional dense granular liquids, which is an avenue worth exploring. The causal link between structure and dynamics in supercooled liquids and amorphous solids has been made more robust with the advent of machine-learning-based approaches [32-33]. Moving forward, obtaining physical intuition into the machine-learned (ML) structure and determining how these fit within the various glass physics theories will be essential.

Linking quiescent and driven soft and quantum matter While much of our discussion hitherto has largely focussed on systems with a rather steep repulsion between the constituent particles, the link between hard and soft matter is equally rich when the particles are extremely squishy. There is now experimental evidence that soft matter systems made of highly deformable particles, such as DNA-based dendritic triblocks, form cluster crystals [34, 35]. These, as the name suggests, are spatially ordered arrangements of particle aggregates. What is even more remarkable is that these soft matter systems appear to share similarities with many quantum phases of matter [36,37].

Driving soft matter out of equilibrium is actively pursued due to fundamental science issues arising from the violation of equilibrium concepts like time-reversal symmetry and detailed balance and its relevance in industrial applications. Shearing soft matter as one of the many ways to drive the system has a rich history of fascinating phenomena like shear-thinning and -thickening, shear-jamming, unsteady chaotic flows [38], random organization separating the steady and fluctuating states [39], memory formation [40], to name a few. These findings have parallels in electrical current-driven vortex lattices [41], charge density wave, and skyrmion systems.

One future direction in linking soft and hard matter is the nonequilibrium physics of quantum soft matter, a state of correlated electron fluids that can exhibit electron nematic and smectic phases [42]. The former refers to a metallic phase that is translationally invariant with spontaneously

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generated spatial anisotropy, whereas the latter has spontaneous breaking of both the symmetries. Recent experiments [43] have shown that the high mobility two-dimensional electron gas in a perpendicular magnetic field exhibits zero resistance state when driven by microwave radiation (ZRS). Interestingly, it has been shown [44] that the ZRS in the limit of zero magnetic field and short-range electron-electron interactions is identical to flocking transitions seen in the context of active soft matter. The connection between active matter and open quantum systems -- in particular between non-reciprocal interactions and non-Hermitian systems -- is a promising frontier [45,46]. We anticipate that microwave or terahertz radiation-driven quantum soft matter will be an exciting future direction with parallels to driven soft matter.

Conclusions The link between the physics of soft and hard matter is stronger than ever before, but there is room for more. This roadmap identifies potential problems in three subareas where a synergistic exchange of concepts between hard and soft matter systems is already present. At the same time, we acknowledge that these subareas are by no means representative. Yet another fascinating avenue of research bridging soft and hard materials, which we expect to thrive in the years to come, is unravelling the role of intermediates during crystallization, solid-solid phase transitions, and even devitrification.

Acknowledgements RG thanks Jawaharlal Nehru Centre for Advanced Scientific Research and the Department of Science and Technology (DST), Govt. of India (Swarna Jayanti Fellowship Grant and DST-Nanomission Grant) for financial support. RG also thanks members of the Experimental Soft Matter Research group at JNCASR for many discussions over the years. AKS thanks the DST, Govt of India for support under the Year of Science Professorship. AKS acknowledges gratefully the contributions of his group members over the years and Prof Sriram Ramaswamy for most enjoyable collaboration over the last 30 years.

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Section 4.2 – Glasses and Gels

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Status Dynamically arrested disordered colloidal systems, either glasses or gels, are fairly common soft matter materials. With a small change in control parameters (either temperature, composition, concentration, shear stress) these systems transform from a fluid of diffusive particles to a material in which excluded volume (glass) or bonding (gels) freezes particle mobility. Arrested states provide additional structural and functional possibilities beyond those offered by crystalline states. At the same time, they also act as unwanted kinetic bottleneck in the self-assembly of a desired ordered lattice. This schizophrenic role mirrors recent and ongoing research, dedicated both to understand the conditions under which arrested disordered states are stable and to understand how to avoid kinetic arrest to facilitate the formation of ordered structures.

Colloidal solutions (Fig. 1) have provided model systems for theoretical investigations of the glass transition [1], starting from the paradigmatic hard-sphere case and progressively evolving with the modulation of the repulsive interaction, as in soft and in charged colloids. Goetze's mode coupling theory for the glass transition [2] (the progenitor of a long list of approaches [3–5] that seek to extend the theory to more realistic conditions or to clarify the underlying uncontrolled approximations) has the merit to highlight the important role of the self-reinforcing caging process on the increase in packing.

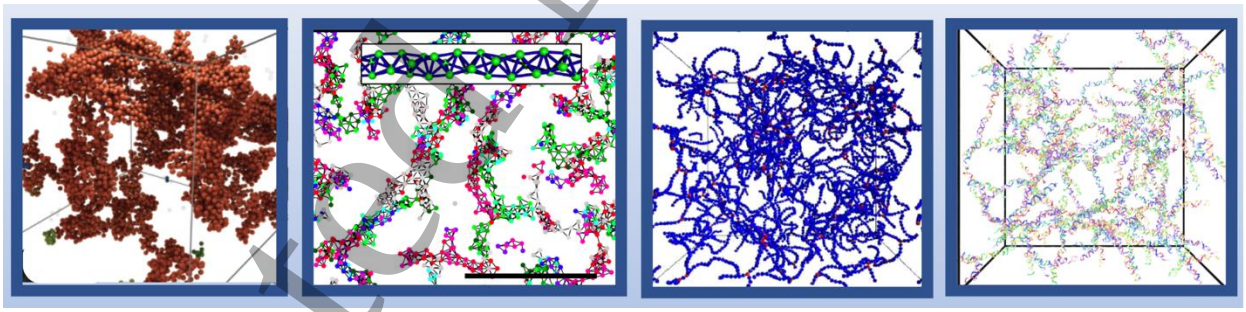

Figure 1 Experimental and numerical images of colloidal gels: From left to right: a confocal microscope image of a depletion gel [9] and of a competing interaction gel (with the characteristic Bernal spiral in the inset) [10]. A simulation image of a low valence particle gel [13] and of a DNA-nanostar gel [27].

Depletion interactions have added a new twist to colloidal systems, making it possible to complement repulsive interaction with an attractive tail of tuneable strength and, more important, interaction range. Guided by mode-coupling predictions [6], the experiments demonstrated the important role played by the combination of short-range attraction and hard-core repulsion [7]. At low packing, colloidal depletion gels originate from spinodal decomposition interrupted by glass formation [8, 9]. Similarly, the combination of a short- range attraction with a

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long-range repulsion has provided a framework for understanding cluster phases and one-dimensional cluster growth [10, 11].

The synthesis of colloidal particles with specific binding sites on their surface (patchy colloids [12]) has opened the possibility of framing gel-formation in colloidal systems from a thermodynamic perspective. Gels of patchy particles — as opposed to glasses which are mainly driven by excluded volume interactions — are characterised by a network of bonds that is progressively formed with cooling. It has been shown that the ability to form such an equilibrium gel phase is made possible by the emergence of an intermediate density region between the density of the coexisting liquid and the that of the glass as the valence of the patchy particles decreases [13] (Fig. 2).

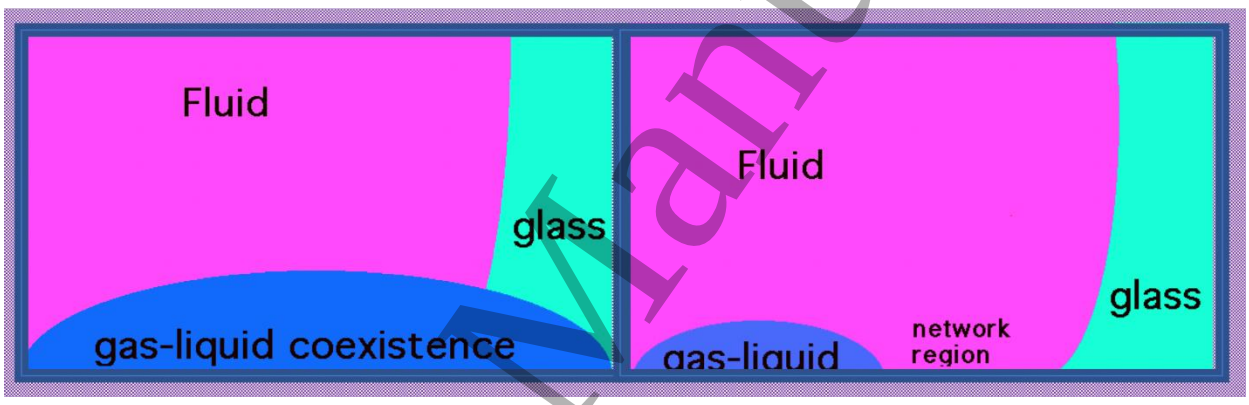

Figure 2 Cartoon of the (disordered states) phase diagram in the temperature-density plane of isotropically attractive colloidal particles (as in depletion interactions [9]) and of the phase diagram of limited valence colloids (as in the DNA-nanostar case [27]). Note that in the last case, the phase-separation region is disjunct from the glass region, offering the opportunity to explore a window of densities in which the liquid progressively turns into an equilibrium gel (the network region).

Current and Future Challenges Future theoretical research on colloidal glasses will focus on how to include hopping effects [14, 15] and non-gaussian dynamics [16, 17] in a quantitative way, improving our pre- dictions on the long-time decay of the correlation functions, both in equilibrium and during aging. A comparable theoretical challenge in colloidal gelation is instead the formulation of a theory (with a predictive power similar to what mode-coupling can do for glasses, i.e., a prediction of the behaviour of the collective density correlation for different wave-vectors) for the gel dynamics, both approaching the gel state as well as in the fully developed gel. The difficulty arises from the much more complex dynamics that originates from bond-cages as compared to excluded-volume cages. In addition, clustering and network formation takes place in dilute solutions and requires a combined description of cluster diffusion as well as network breathing modes. While some attempts have been formulated for the self-dynamics, quantitative predictions for collective observables are largely unexplored.

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Routes to gel formation are multiple. While we have now a clear understanding of depletion and equilibrium colloidal gels [18] (and for gels based on competing interactions [19, 20]), other gelation routes have been significantly less investigated. Particularly relevant, for their biological applications, are gels made by largely anisotropic particles and gels made by growth and branching of fibres. The thermodynamic stability and the spatial and temporal homogeneities of equilibrium gels [21] have been investigated in detail. It has been shown that limited valence gels can be the thermodynamic stable state even at quite low temperatures [22]. Now work is required to understand how these ideas can find applications to gels formed with other routes.

How to design particle interactions to self-assemble desired structures, avoiding kinetic traps will also be a prominent research theme. Up to now the bottom-up self-assembly, a powerful method, has been successful in important but limited cases. A general strategy for self-assembly into a well-defined crystal (avoiding polymorphs) or a precise finite-size structure [23] is clearly needed [24–26].

Finally, the connection between different forms of dynamic arrest (gel, glasses, jammed states) and the mechanical properties of the corresponding material and its response to external perturbations (yielding transition, shear-banding, viscoelasticity) are topics which are receiving (and will continue to receive) a significant attention. Diversity in dynamic arrest in gels and glasses surely leads to a rich variety of elastic and rheological behaviours relevant for industrial processes and products.

Advances in Science and Technology to Meet Challenges Understanding slow dynamics in colloidal solutions has proceeded step by step with both instrumental development as well as novel chemical synthesis. In the last years, particle with complex shapes and surface patterning have become available, significantly enlarging the arsenal of elementary building block. Among others, DNA functionalized particles [27], DNA constructs and DNA origami are emerging as examples of colloids with exquisite control of both particle shape and binding selectivity. Unfortunately, sometime the yield of these interesting novel colloidal particles is quite limited, optimized for academic application. The availability of bulk quantities of mono-disperse colloidal particles is often fundamental to precisely control theoretical predictions. An effort needs to be made to scale up synthesis and availability of the particle themselves. From the experimental side, several novel techniques [28, 29], mixing scattering and imaging, have been developed providing accessibility to longer time scales and larger distances. Super-resolution microscopy, a method based on photo-activatable fluorescent probes, allowing for a detailed picture at the nanoscale is also expected to significantly contribute to detailed characterization of soft-matter systems. From the computational side, efforts are ongoing to include hydrodynamic interactions in the computer models, an interaction which has a non-relevant role in the dynamics and in the coarsening of out-of-equilibrium gels.

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Concluding Remarks Colloidal gels and glasses are central to material science (pastes, paints, foams), food preservation, household applications. The ability to encode in the particle (or in the chemical physic properties of the solvent) information about the desired material properties offers countless application possibilities. Understanding dynamic arrest will provide an important handle to control material properties from the bottom up. Despite significant efforts in the last decades (dynamic arrest in colloidal science has been central to soft-matter research), our current understanding of particle slowing down (resulting from a combination of experiments, numerical and theoretical studies) requires further efforts to unambiguously link particle properties to dynamic behaviour.

Acknowledgements I acknowledge the support from MIUR PRIN 2017 (Project 2017Z55KCW).

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Section 4.3 – Memory in soft matter

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Status Memory effects in the properties of materials are abundant in nature, particularly in soft materials. Obvious examples are the properties of glasses, microstructure in metals, melt memory in polymers, the shape memory in some alloys, as well as the magnetization state of magnetic materials, each of which exhibit history dependence. In this road map we will use the term memory broadly to refer to the dependence of material properties on their past history (for a more extended discussion, see [1], and articles in a special collection on memory formation [2]). Such memory phenomena typically emerge in materials whose energy or free-energy landscape consists of multiple locally stable structures or states. Their dynamics is often associated with slow or glassy relaxation, characterized theoretically by concepts such as hysteresis, kinetic arrest, metastability and plasticity. Research in the past has focused primarily on understanding better the underlying physics (*e.g.* memory effects in glasses) and on improving upon performance (*e.g.* shape memory materials). There has been a renewed interest in memory effects in soft matter in recent years, with new perspectives which we attempt to highlight here.

These new directions of research have focused on understanding how specific memories are encoded in the properties of materials, how they can be accessed, and how the ability to do so can be harnessed towards the design of devices with targeted, often multiple, functionalities. Viewed from the perspective of designing such novel materials, these developments highlight the increasing role played by information and information processing, establishing relations with similar themes in the areas of self-assembly (see also Sections 1.1, 1.2, 3.6 and 4.4 of this roadmap) and learning networks [3], as well as machine learning inspired approaches in soft matter design [Section 25 of this roadmap]. The emphasis has been on systems whose properties can either be designed in detail through theoretical analysis [4,5,6] or tuned through accessible training protocols [7 – 15] (Fig. 1a). Some of these investigations, motivated by machine learning approaches, aim to develop physical alternatives to *in silico* learning platforms [3,15]. Many studies have focused on model systems investigated only computationally. However, there have also been several experimental investigations into fabricating, synthesizing or training soft materials that realize some of these ideas [4,5,6,7,9,10,14] (Fig. 1b). Such experimental explorations have established valuable proofs of principle and point the way to exciting future directions in soft matter physics.

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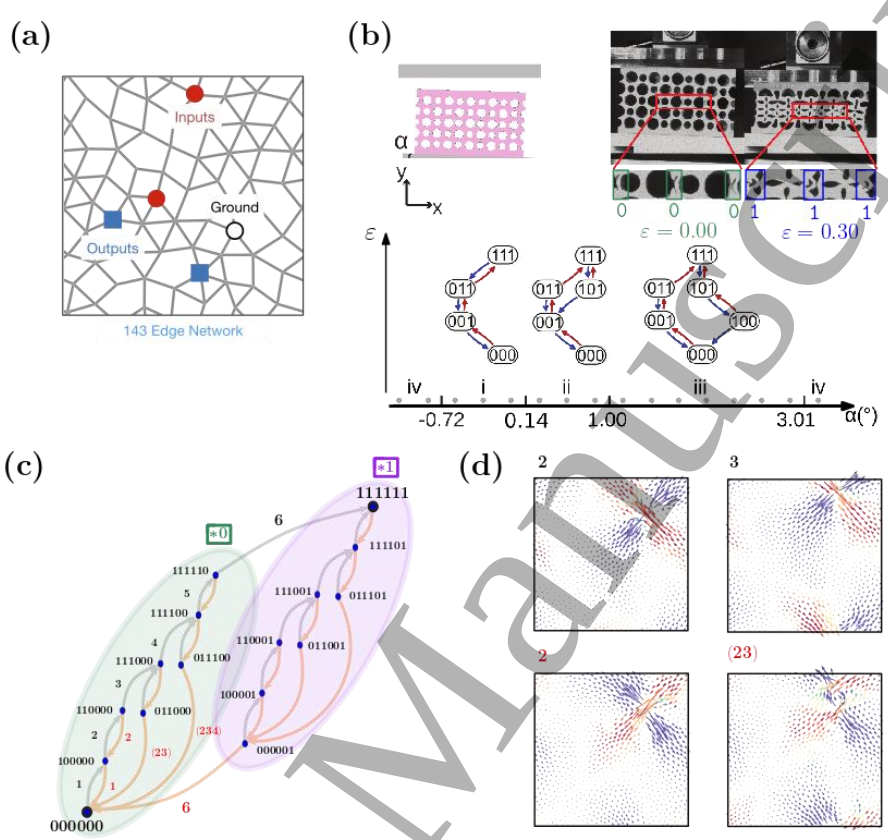

Figure 1(a) (**Physics-driven learning network)** A network of resistors is allowed to evolve by changing values of the resistors based on local rules so that it can generate specified voltages at a set of target nodes (blue boxes), given input voltages at input nodes (red circles). Figure from ref. [15]. **(b) (Programmable meta-material)** A holey metamaterial has three mechanically bi-stable elements with hysteresis, called hysterons, embedded in its centre, indicated by the red box in the top right part of the panel. The material is subjected to compression ε. Denoting the states of each bi-stable element by 0 and 1, the transition graphs show the configuration changes as the compression is increased/decreased just enough to trigger a transition (blue and red arrows, respectively). By varying the relative angle α between the top and bottom plates, the hysteresis response of individual hysterons can be altered, giving rise to different history-dependent response to compression, as described by the different transition graphs at the bottom of the panel. Figure adapted from ref. [5] **(c) and (d) (Transition graphs and hysterons)** The microscopic states traversed by a sheared amorphous solid can also be represented through transition graphs which exhibit nested structure (c). Here the transitions are due to mechanical instability that trigger spatially localized particle rearrangements termed soft spots. Such soft spots act like hysterons and the configurations of the amorphous solid can be represented in terms of the individual hysteron states, as indicated by the binary sequences in (c). The state changes of individual soft sports are identified by numerals in black (forward transitions) or red (backward

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transitions), and the corresponding particle rearrangements are shown (d). Soft spots do interact, however, as in the coordinated '23' reverse transition in panel (d), which leads to the presence of transients and coordinated avalanches. Such features are not present in the idealized Preisach model which assumes that hysterons are non-interacting. Figure adapted from [8]

Current and Future Challenges An example of a system in which memory encoding and retrieval have been analyzed in detail is an amorphous solid subjected to cyclic shear deformation [8]. Under such deformation, the solid evolves until eventually reaching limit-cycles consisting of microstates through which the system makes transitions in a periodic fashion and by repeatedly triggering a set of spatially localized mechanical instabilities called soft-spots, as shown in Figs. 1c and d. The limit-cycles encode information about the deformation they are subjected to. An idealized picture is given by the Preisach model of hysteresis which regards the system of soft-spots as non-interacting, bistable, hysteretic elements, called hysterons [16]. The Preisach model can help rationalize several aspects of memory behavior, as also observed, for example, in a metamaterial [5] shown in Fig. 1b, or in stacks of origami bellows [17]. It omits, however, the role played by interactions between the soft spots, which is important for understanding key aspects, such as the evolution of systems under repeated external perturbation to achieve memory encoding states. This type of evolution can be observed experimentally, *e.g.*, in the mechanical response of crumpled elastic sheets to cyclic shear [9]. The interactions between hysterons also leads to more complex mechanisms, where the periodic response spans multiple driving cycles [18]. A satisfactory understanding of general mechanisms governing the evolution towards memory encoding cyclic response and the role of hysteron interactions is still lacking.

Another direction in exploring memory effects has aimed at the design of mechanical networks is to achieve desired properties or response, such as large negative Poisson ratios [10], or allosteric response [11]. Such properties have been achieved through computational design exploiting specific material properties [5,6], or through the evolution of the mechanical properties of network components under loading, for example through a process that has been described as *directed ageing* [10]. Such mechanical networks are capable of retaining multiple memories, such as multiple allosteric responses. Analogous approaches carry over to flow and electrical networks [13,15], with corresponding physical cost functions that the system may optimise, as well as (design) cost functions which represent the design goals. The ability to encode desired memories, however, requires specific properties of the network components – for example, encoding memories sequentially without erasing already existing ones has been shown to require nonlinear springs [12]. The properties of network components, and training protocols that will lead to the desired macroscopic behavior, are the subject of ongoing research.

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Another important and recurring theme is that of memory capacity, which is the number of distinct memories that may be stored and retrieved. For systems described reasonably by noninteracting hysterons, the relationship with the nesting depth of the limit cycles, number of hysterons, and memory capacity has been investigated [16,19]. The standard point of reference for discussing memory capacity, the Hopfield model of associative memory, has also been the subject of recent investigations. Past, as well as recent work [20] has addressed the role of the learning rule in determining memory capacity in the Hopfield model. Interestingly, the nature of the dynamics associated with memory retrieval also appears to play a significant role, with active dynamics leading to enhanced memory capacity [21].

Advances in Science and Technology to Meet Challenges We outline some open questions and desirable directions to build upon recent progress along two broad themes:

(i) By taking advantage of the bistability underlying the mechanical response of the hysterons, features of the mechanical loading history can be digitally encoded. Such systems act therefore as analog-to-digital converters which sense aspects of their changing loading environment, which are digitally represented as hysteron configurations and thereby form memories. This type of memory is a consequence of the (loop) return-point memory property which gives rise to a hierarchical organization of configurations into cycles and sub-cycles of transitions [16]. It has been demonstrated in systems like the sheared amorphous solids [8] and crumpled elastic sheets under cyclic shear [9]. Common to both is their programmability under cyclic loading which can be understood as a process of self-organization leading to the establishment of a persistent system of interacting hysterons. Understanding better how the emergent system of interacting hysterons and the memory created thereby depends on the loading protocol, and how such information can be accessed and harnessed to create programmable materials, is a future challenge. Although powerful in the contexts mentioned, the mapping to discrete hysteron states is not obviously available for systems such as colloidal suspensions [7], gels [14] (and even mechanical networks), which nevertheless exhibit similar memory formation phenomenology. Useful alternate descriptions of memory encoding in these systems are thus highly desirable.

(ii) Several approaches have been explored to design [4,5,6] or train [10,11,12,13,15] networks (or metamaterials) with desired properties, starting from network elements with given properties, and a given network topology. The simplest formulation of the problem is through a (design) cost function whose minimization would correspond to achieving the design goal. Such an approach, easy to implement *in silico*, does not easily lend itself to experimental realization. An appealing alternative explored has been that of *directed ageing*, wherein the properties of network elements (*e.g.*, stiffness) co-evolve with the state of the system (*e.g.*, extensions) in response to a training protocol, optimizing a physical cost function (*e.g.*, elastic energy). Such an approach has been shown

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to be effective in several examples [10], but its generality remains to be further understood. An alternative approach [13,15], combines optimization of a cost function with *local* updates of network properties through feed-back. Exploration of the relative merits of these approaches and of possible other approaches forms an exciting direction of future research.

Concluding Remarks We have described recent work exploring memory in soft matter along two broad themes: (i) Realizing hysteretic systems composed of identifiable bistable elements, or hysterons, and investigating interactions among them, and transitions between different states. (ii) Training of various networks to have desired properties, typically responses to specific stimuli. Work along theme (i) has been concerned with a system of hysterons whose presence is established *a priori* through design or training, and there has been relatively less attention to the transient behavior that leads to the memory encoding states. In theme (ii) the emphasis is on the transients and the microscopic properties of final states have been analyzed to a lesser degree. In several such cases, a discrete representation of the state of the system and memory formation in terms of hysterons is not applicable. How these two themes, related yet developing along parallel tracks, may be combined is a challenge for future work. As alluded to above, the research themes discussed here have obvious and exciting connections with active areas of self-assembly design, machine learning and neural networks, to name a few, which we hope will be explored more deeply in the future.

Acknowledgements S. S. acknowledges support through the JC Bose Fellowship (JBR/2020/000015) SERB, DST (India). MM was funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) under Projektnummer 398962893, Projektnummer 21150405, and Projektnummer 390685813.

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Section 4.4 – Soft Metamaterials: Adaptation and Intelligence

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Status Mechanical metamaterials are composite structures whose collective mechanical properties go beyond those of their individual constituents [1]. For example, auxetic materials, which contract in all directions when squeezed, can be engineered via appropriate arrangements of flexible bonds. *Topological* meta- materials are those that use notions from topology (such as winding numbers or other topological invariants) to ensure the existence of a particular feature, typically a localized deformation mechanism or vibrational mode [1]. For in- stance, the lattice in Fig. 1a is rigid everywhere, except near the colored defect where there is a soft mechanical mode protected by topology. Beyond materials with fixed properties, *programmable* metamaterials use elastic multistability to encode specialized responses to external actuation. In Fig. 1b, a pattern (e.g., a smiley face) is programmed to appear when the metamaterial is compressed. *Trainable* metamaterials turn programmability into a process that emerges from a sequence of experiences [2]. For instance, the elasticity of the network in Fig. 1c is tuned through a process called directed aging, during which bonds are strengthened and weakened in response to external stress, a phenomenon that may also occur in colloidal glasses and gels. The individual building blocks can also have an internal source of energy [3]. This is the case for the *active* and *robotic* metamaterial shown in Fig. 1d, in which a wall of motorized hinges steers the outgoing direction of a projectile. In such active media, the familiar symmetries and conservation laws of passive matter need to be revisited to write down effective elastic models [4, 5]. The concepts behind mechanical metamaterials, such as topology or continuum mechanics, often apply across length scales. For example, the world's smallest origami bird in Fig. 1e is a *deployable* metamaterial that uses minimal actuation along with geometric constraints to guide its global shape change. One can even envision metamaterials that build themselves - a possibility particularly interesting at small scales - like the *self-assembled* colloidal structure in Fig. 1f that mimics the atomic arrangement of diamond

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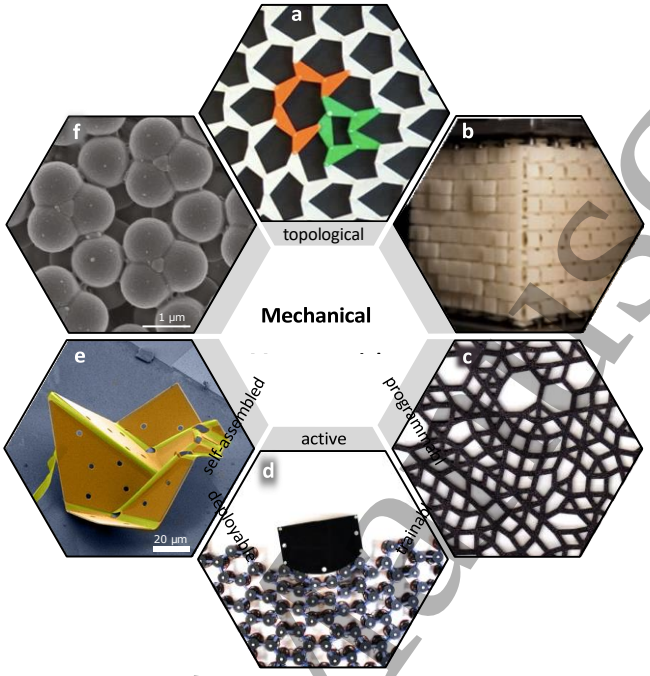

Figure 1: **Mechanical metamaterials. a.** A topological metamaterial exhibiting a robust soft mode bound to a crystalline defect, adapted from Paulose, et al. Nat. Phys. (2015). **b.** A programmable metamaterial using multistability to create a desired post-buckling form, adapted from Coulais, et al. Nature (2016). **c.** A disordered network of foam bonds can be trained via repeated compression and directed aging, adapted from Pashine, et al. Sci. Adv. (2019). **d.** An active metamaterial consisting of robotic building blocks with distributed energy sources, adapted from Brandenbourger, et al. arXiv:2108.08837 (2022). **e.** A deployable metamaterial undergoing dramatic, but controlled, shape changes using folding constraints and minimal actuation, adapted from Liu, et al. Sci. Robot (2021). **f.** A colloidal diamond exemplifies self-assembly at the micron scale, adapted from He, et al. Nature (2020).

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Current and Future Challenges The design of trainable, deployable, or self-assembled metamaterials exploits dynamic pathways. Yet, the functionalities targeted by such dynamic pathways are often encoded in static structures (e.g., buckled or self-assembled states) with desired mechanical properties (like rigidity or a certain vibrational spectrum). Programmable active or robotic elements embedded in the metamaterial allow us to envision inherently dynamical functionalities such as self-sustained motion and learning.

Metamaterials as dynamical systems. A first challenge consists in engineering functionalities rooted in the nonlinear dynamics of the metamaterial. Figure 2a-c illustrates this objective: when stimulated, an initially homogeneous and undifferentiated piece of metamaterial transitions to a deployed state (dolphin- or bird-like states in panels a and c) that depends on the stimulus (purple and blue light in panel b). Crucially, this deployed state is not a static fixed point but a dynamic state that allows the metamaterial to act like a robot: it repeatedly performs actions that do work on their surroundings (swimming and walking). Formally, these dynamic states are limit cycles or more complex attractors in configuration space. This is shown in Fig. 2d-f, in which each axis represents a dynamical degree of freedom. Reaching this goal requires designing dynamical states that perform the required tasks, ensuring that they can be dynamically reached, and implementing them at the appropriate scales.

Metamaterials as computers. A second challenge consists in conceptualizing and implementing some amount of intelligence in metamaterials. The non-linear dynamics of the metamaterial can be harnessed to perform simple calculations in situ, learn and perform a variety of tasks from the same undifferentiated form, and adapt to external fluctuations. Materials that change over time, such as shape-memory alloys and spin glasses, naturally store representations of their previous experiences [2]. A key objective consists in creating materials that can manipulate and act upon this information in desired ways. Figure 2g-i illustrates the end goal: as the metamaterial is externally deformed under a colored light, it learns to perform a desired motion. This level of complexity could be achieved by metamaterials that effectively perform simple machine learning algorithms using only distributed physical processes. For instance, Hebbian-like learning strategies, similar to that used in Hopfield networks, could be applied to interparticle interactions in order to train an ensemble of particles to perform tasks by showing them examples of the desired dynamics [6]. Such a form of distributed intelligence would lead to materials that are truly adaptive, like army ants forming and maintaining a bridge with their bodies

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Fabrication and programming. Three main goals include miniaturizing and mass-producing small elements that can be combined into a material-like structures; decentralizing control to remove the need of an external computer; and integrating computation and actuation so that part of the computation is delegated to the underlying physics. To achieve these goals, advances in manufacturing will need to be combined with the design of decentralized algorithms tailored to the limited abilities of the building blocks. Ideally, these building blocks should be able to repair and replicate themselves. In that respect, biology is a power- ful source of inspiration: neural tissues (Fig. 2j) are able to form and process complex representations, while in-vitro reconstitution of cytoskeletal proteins forming an active gel produce large-scale deformations (Fig. 2k). Integrating both the computation and actuation into a single metamaterial could be done using bio-inspired systems, such as engineered DNA molecules capable of implementing algorithms [7] and acting as robots that perform complex tasks [8]; or using micro-robots: small, electronically integrated machines, which can now be manufactured by the millions at the micron scale [9].

Effective theories of adaptive dynamics. Adaptive metamaterials are com- plex: they can adapt over long-time scales while sustaining continued microscopic motions at very short time scales. This presents a challenge in describing the intermediate time scales relevant to material functionalities. Hence, de- scribing adaptive metamaterials requires going beyond approaches relying on the simple separation of time scales characteristic of hydrodynamic theories. Model reduction techniques developed in the context of statistics and dynamical systems, such as dimensionality reduction and invariant manifold reduction, can serve as a basis for developing such effective theories of adaptive dynamics. These effective theories must rise to the challenge of describing phenomena such as physical learning [6] and back propagation [10], which occur in non-linear glassy model systems. When these learning processes occur, the material effectively produces a representation of its past experiences which can be leveraged to perform some of the computations necessary to achieve desired functionalities.

Machine learning for material intelligence and design. Finally, machine learning can be used to accelerate and automate the inverse problem of design: how to go from target functionalities to the basic building blocks. For instance, machine learning can help establish relationships between tunable physical parameters and the dynamical attractors that define the dynamic functionalities of adaptive materials. Moreover, machine learning can facilitate dimensionality re- duction techniques for forming effective theories, thereby offering the possibility of starting directly from experimental data.

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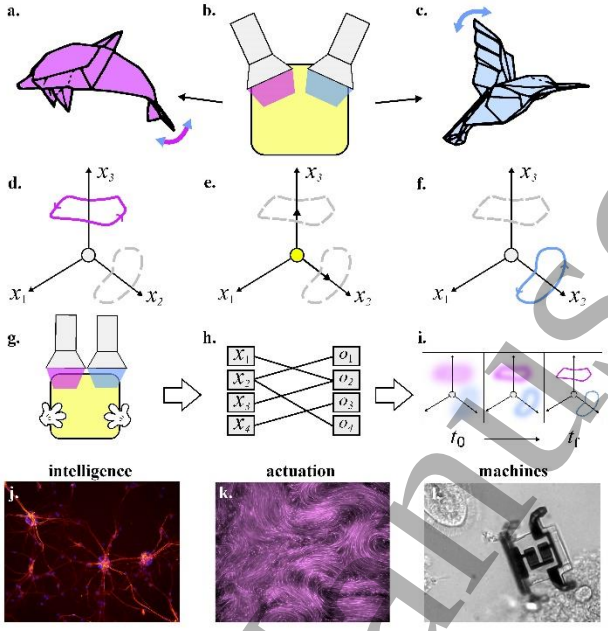

Figure 2: **Adaptive and intelligent metamaterials. a-c.** Schematic picture of a dynamic and intelligent metamaterial. When exposed to a stimulus (represented by light), the metamaterial performs a computation, actuates, and reaches a dynamical steady-state that serves a function such as swimming or flying. **d-f.** From the point of view of dynamical systems, these dynamical steady-states are attractors (such as limit cycles). Functionalities emerge by engineering suitable attractors and bifurcations. **g-i.** An adaptive metamaterial performs computation and learns. For example, physical stimulation (panel g) is processed by the material, which acts as a distributed machine-learning algorithm (panel h). The outputs of this process are, for instance, adapted dynamical states (panel i). **j.** Neurons are biology's solution for intelligent distributed materials, reproduced from [https://www.flickr.com/photos/nichd/21086425615]. CC BY 2.0. **k.** Physicochemical processes such as ATP consumption by kinesin motors power large-scale motion like active nematic flows, adapted from Duclos, et al. Science (2020). **l.** Micromachines the size of a single-cell organism provide a platform for intelligent and adaptive metamaterials, adapted from Miskin et al. Nature (2020).

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Concluding Remarks. Adaptive and intelligent metamaterials raise the prospect of merging matter with computers, and hold promise for applications ranging from medical science to space exploration. Reaching these promises will require tackling conceptual and practical challenges in fabrication at the nano and microscales [7, 9] as well as answering theoretical questions about the nature of information storage and learning in systems out of equilibrium [5, 6, 8, 7].

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Section 4.5 – Machine learning for soft matter learning

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Status Machine learning (ML) and soft matter have many natural connections [1-2]. ML can be used to analyze or augment soft matter data or evaluate models for describing data [3-9]. Soft matter ideas have also proven invaluable for understanding ML [10-11]. Here we concentrate on three other areas of connection that have received less attention in reviews. We focus on how ML can be useful for physical insight into soft matter problems.

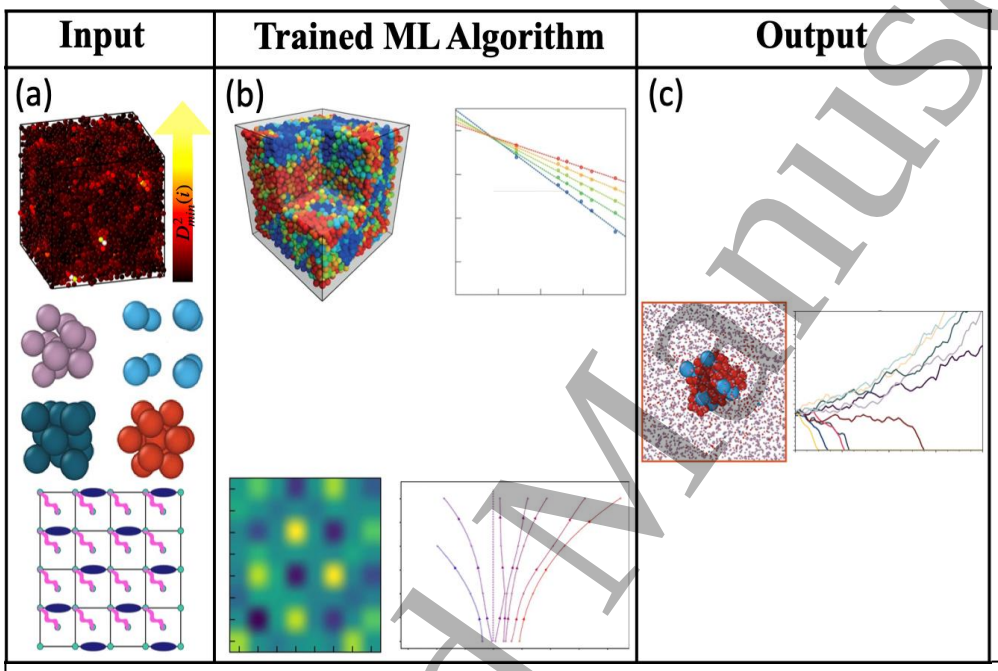

Figure 1 (a) Input data, such as the mobility of particles (top left) or the probability of observing certain microstates (center left [14] and bottom left [13]), may be fed into an ML algorithm to construct a model of the data. (b) In some applications, the structure of the model is directly analyzed to gain understanding, *e.g.* identifying a structural variable strongly correlated with dynamics in a glassy liquid, whose behaviour may then be studied (top center) [12], or identifying an RG transformation in lattice models (bottom center) [13]. (c) In other cases, the actual ML output (prediction) is used as an order parameter, as in the study of crystallization (right) [14].

Identifying key variables or equations A primary aim in soft matter is to understand the microscopic origins of collective behaviour. Statistical physics is the workhorse for distilling immense amounts of microscopic detail into distributions of a few key variables or governing equations of motion to capture and explain emergent properties. However, many soft matter problems have resisted solution, often because they are far from equilibrium, exhibit highly nonlinear response, possess complex structure/behaviour over multiple length or time scales, and/or lack characterized forms of order. It is natural to turn to ML for help since it is designed for dimensional reduction. However, it is not easy to extract insight from it, either from the output or from the trained algorithm itself (Fig. 1) [12-19].

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Solving inverse design ML is a logical choice of tools for designing systems with desired properties because training a neural network to perform tasks is itself an inverse problem. Conventional approaches to inverse design require expensive repeated solution of the forward problem in the high-dimensional space of "learning degrees of freedom," namely adjustable microscopic interactions/properties. ML can optimize the choice of forward problems for efficient solution of the inverse problem [20-21]. Alternatively, ML-inspired approaches adjust learning degrees of freedom to minimize a cost function whose global minimum corresponds to attainment of the desired property [22-23].

Soft-matter learning machines In addition to using machine learning to understand soft matter, one can use soft matter to understand machine learning by developing soft matter systems that solve machine learning tasks by evolving each learning degree of freedom independently according to direct physical influences [24-30] so that the system minimizes the desired cost function on its own (Fig. 2). Such systems, while currently less powerful than computational or biological neural networks, combine the adaptability and parallelization of the latter with the mathematical simplicity of the former, providing a novel window into how systems can learn [30,31].

Current and Future Challenges

ML is a new tool for physicists to use in order to gain physical understanding. Learning how to use it most effectively towards this goal is an important challenge.

Symmetries In applying ML, some architectures and models, due to their inductive biases, as in [32], may be more effective than others for a given problem. For example, algorithms that encode certain symmetries are more effective for problems that obey those symmetries [33]. In soft matter, building in such symmetries can be more challenging since the symmetries can be complex and different at different length and/or time scales. For example, block copolymer systems can be disordered at short and long length scales but have different symmetries at intermediate length scales. As another example, phase transition kinetics can lead to nuclei with structures of different symmetries at different timescales.

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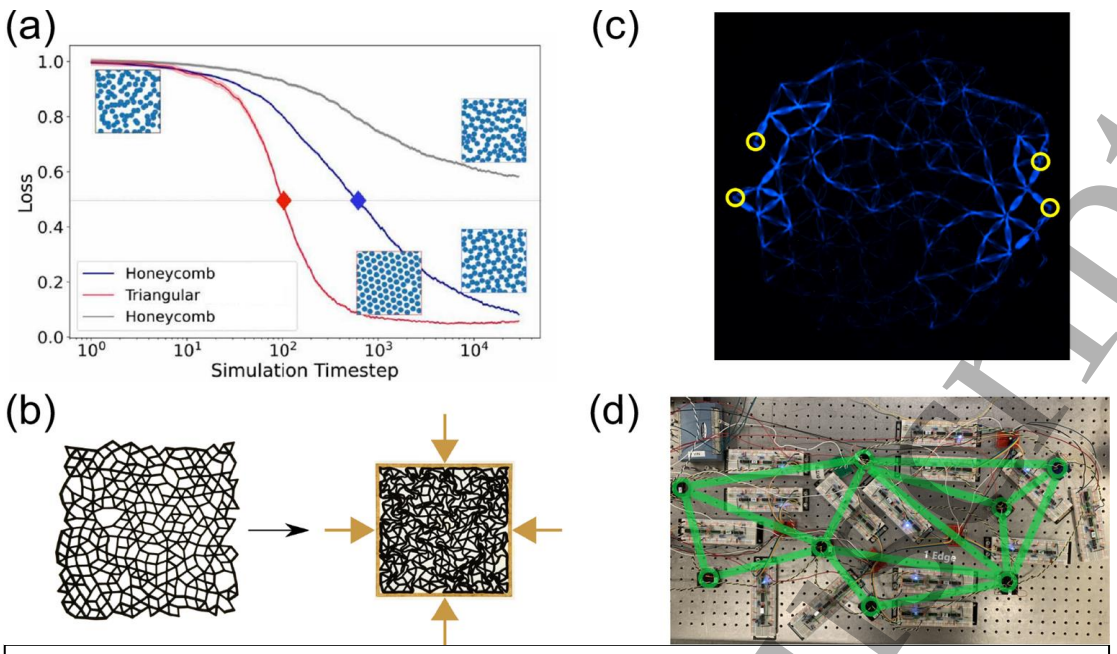

Figure 2 Machine learning inspires inverse design of metamaterials and learning machines. (a) High-yield self-assembling lattices can be obtained via numerical optimization of a cost function [23]. (b) Directed aging allows materials to adopt desired properties by lowering the energy cost of such properties [25]. (c) Local "learning rules" allow materials to be modified to minimize a general cost function and adopt desired properties [28]. (d) Such learning rules can be embedded in the physical dynamics of active matter systems, giving rise to learning machines [29].

Specificity vs. universality (transferability) In soft matter we often search for insight that transcends a given system and desire common ways of understanding phenomena across different systems. ML solutions are typically designed for specific tasks over narrow domains, so that different training is required for different conditions or systems. Understanding phenomena across conditions or systems requires transferring what is learned from training for one task to another task. Ref. [34] shows a successful example in which a ML model predicts nonlinear composition-structure relationships for glass compositions outside its training set.

Prediction vs. model building ML algorithms are typically used for prediction, not physical insight. While prediction is the aim for some soft matter problems, and some insight can be gained from prediction, more typically the aim is to construct a model as a caricature that captures only the essential features for understanding a system or phenomenon. It can therefore be more useful to use ML to identify key variables, and then construct models based on those variables. One example is a model that yields insight into microscopic mechanisms controlling ductility of disordered solids, built upon a machine-learned structural variable that predicts the propensity of constituent particles to change neighbours [35]. Another approach is to use an algorithm that directly learns a model in the form of a set of differential equations [36,37].

Explainability Most tools used in soft matter allow for straightforward physical interpretation, but many ML tools do not. Using the most interpretable (usually the simplest and least powerful) ML approach possible is helpful, but identifying what a machine learning algorithm learns to perform a task remains a major stumbling block. Insight into explainability in soft matter problems has been gained using dimensional reduction techniques like autoencoders [19] or physical representation learning [38].

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Physical learning While physical learning machines show much promise [29] for smart metamaterials and for machine learning in hardware (neuromorphic computing), they are hard to realize experimentally in specific physical media. Physical learning machines that exploit contrastive learning need to be able to compare physical states with different boundary conditions (requiring memory and changing sign for weight updates) [24, 27, 29]. It is likely that each different system, be it an elastic network, flow network, etc., will require very different engineering solutions to implement the appropriate version of learning dynamics for that system.

Advances in Science and Technology to Meet Challenges Several advances are needed to harness machine learning more effectively towards our own ends in soft matter. ML methods [39-41] can be useful for performing computer simulations. Autodifferentiation is also powerful for inverse design [23]. Technological ML advances such as methods to accelerate automatic differentiation or optimization, or to train algorithms with less data can certainly benefit soft matter, especially for experiments [3]. In addition, technical advances that allow algorithms to build in varying symmetries across scales are needed.

For the challenge of transferability, we note that the ability to apply parameters learned from one task to another task varies among ML algorithms. The subfield of "transfer learning" in learning theory is devoted to developing methods that allow a computational neural network to retain memory of how to perform one task while adding memory related to a new task. Progress on developing highly transferable algorithms could potentially allow physical insight gained from ML applied to one system to be applied to another, enabling quantitative study of connections across phenomena and across systems.

The greatest challenge in wringing physical understanding from ML remains explainability. Fortunately, the difficulty of understanding what a trained ML algorithm has learned bedevils ML practitioners across all fields so there are widespread and well-funded efforts to address it. New mathematical tools are needed to understand precisely what algorithms—particularly those involving neural networks--pick up on when they learn a task. Approaches that have been applied to simple tasks [31] may be useful for neural networks, but this has yet to be determined.

While improving explainability is necessary, it is not sufficient to reach the level of understanding we typically aim for. Physical understanding requires an "all of the above" approach, guided by physical insight to formulate a useful question, determine whether ML will be helpful, choose the best ML algorithm, and use it and interpret it most effectively.

Concluding Remarks Machine learning is not a panacea for solving all of our soft matter problems, but neither should it be shunned as a temporary fad incapable of providing understanding to serious researchers. It is here to stay. Like any other good set of tools, machine learning is most effective when wielded with physical insight to answer well-posed questions.

While explainability remains a major hurdle, soft matter researchers can also contribute to overcoming this challenge through, for example, the development of learning machines [27,29] and new analysis approaches [31].

The use of ML for going beyond prediction to gain understanding of soft matter is still in its infancy. In coming years we will discover the extent to which ML can be used to tackle long standing challenges, particularly in inverse-design problems such as non-equilibrium processes that avoid kinetic traps or that lead to desired equilibrium or metastable states, as well as recalcitrant far-from-equilibrium problems such as the glass problem, friction, fracture and turbulence.

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Acknowledgements The Flatiron Institute is a division of the Simons Foundation, which also supported this work through the collaboration "Cracking the glass problem" via Grant No. 454945 (SAR and AJL) and Simons Investigator Grant No. 327939 (AJL). This work was also supported by the U. S. Department of Energy, Office of Science, DE- DE-SC0020963 (AJL), and the National Science Foundation via NSF-DMR-2005749 (MS and IT), and the UPenn MRSEC NSF-DMR-1720530 (GZ).

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Section 5.1 – Soft Materials for Energy

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Status The generation, transduction, storage and deployment of energy rely on physical and chemical phenomena operating in materials. Conventionally, our attention first falls to hard condensed matter, or hard materials. The roles of metals, semiconductors and ceramics in energy lie in plain sight – for example, copper as a universal conductor for the transmission of electricity, silicon as the quintessential photovoltaic material for solar cells, and ceramics, whether employed for their dielectric strength in capacitors and insulators, or for lossless transport in superconducting heavy metal oxides in magnets. Soft materials however also play critical roles. Polymeric insulators for example are key enablers of low cost, safe electricity transmission and usage. That said, the growing impetus for improving sustainability in energy has brought with it a growing interest in developing and utilizing new soft materials.

Today, a broad variety of soft materials are the subject of research for energy applications. Here, the term "soft materials" is used to encompass solid polymers, gels, complex fluids (e.g., multicomponent particulate slurries), organic-inorganic hybrid nanomaterials, and molecular materials such as liquid crystals. Both small molecule and polymeric organic photovoltaics (OPVs) remain highly visible examples of soft materials used in energy (Figure 1).[1] A burst of activity over roughly 10-15 years saw the power conversion efficiency (PCE) of polymer-based bulk heterojunction devices increase over an order of magnitude from ~ 0.6% to more than 7% in the 2010s. These devices feature an interpenetrating network, a nanocomposite, of a p-type polymer donor and a n-type acceptor, as the active layer. The canonical materials were poly(3-hexylthiophene) (P3HT) and derivatives thereof, and a functionalized carbon nanomaterial, [6,6]-phenyl-C61-butyric acid methyl ester (PC61BM). Improvements driven largely by empirical optimization of nanostructure through processing, including the use of additives, eventually saturated. Subsequent efforts focused more deliberately on improving PCE through molecular engineering to optimize donor band gaps and band-alignment. So called "push-pull" conjugated polymers which rely on alternating electron-rich and electron-poor segments are now the current state of the art in low bandgap conjugated polymers and offer PCEs above 18%. Roughly comparable PCEs (~15% and higher) have been demonstrated in state-of-the-art small molecule OPVs. Significant progress has been made in the development of all organic solar cells that do away with the need for inorganic acceptors such as PC61BM.[2] Finally, the field has focused in recent years on amorphous or near-amorphous conjugated polymers that display high charge carrier mobilities despite their disordered structure. This represents something of a paradigm shift given the traditional association of poor electronic transport with poor structural order.

Beyond OPVs, three areas of particular interest regarding soft materials in energy are polymer membranes, ionic gels, and energy harvesting materials, Figure 2. Polymer membranes have been developed and used for a few decades in a variety of energy technologies and energy-adjacent applications, including water purification, gas separations, and as separators in batteries (e.g., Celgard™, a microporous polypropylene) and fuel cells (Nafion™, a sulfonated fluoropolymer, developed in the 1960s). There is a strong need however for improved performance of such membranes, particularly regarding the ability to design membranes with tailored high selectivity. Cost is also an issue, as seen with Nafion in fuel cells and other electrochemical devices. The use of membranes for harvesting energy from salinity gradients is at a nascent stage. Its potential future viability is reliant on the development of high-performance polymer membranes. Energy harvesting using soft materials and ionic gels is at a relatively early stage of development by comparison with polymer membranes, and by comparison with OPVs. The ability to realize stretchable soft materials that are simultaneously electrically and ionically conducting is a topic of contemporary interest,

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particularly in the context of bioelectronics. While we do not cover complex fluids here in detail, it is worth noting that they have a substantial footprint in energy. The flow behaviour and thermophysical properties of particulate slurries are important as they affect both the manufacturing and performance of batteries, including current (e.g., Li-ion) and emerging (e.g., redox flow batteries) technologies (Figure 2). As dense, disordered suspensions, these materials are typically non-Newtonian and viscoelastic systems. They also may exhibit jamming, and time-dependent behaviour that are subjects of current scientific inquiry.

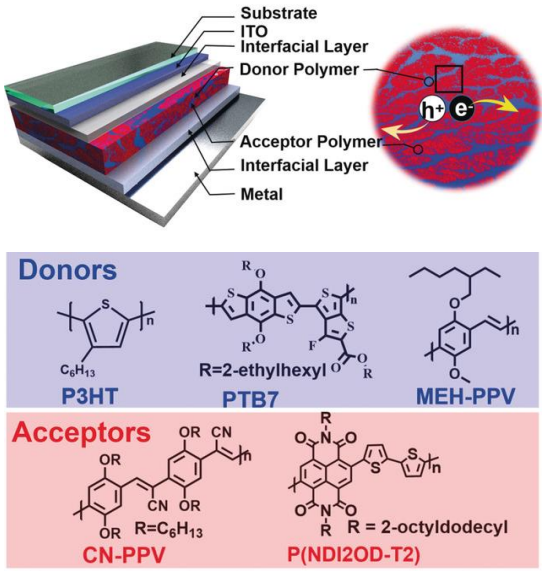

Figure 1 Current state of the art all-polymer solar cells. Top: Cell composition. Bottom: Chemical structures of polymer donors and acceptors. Adapted with permission from Ref. [2].

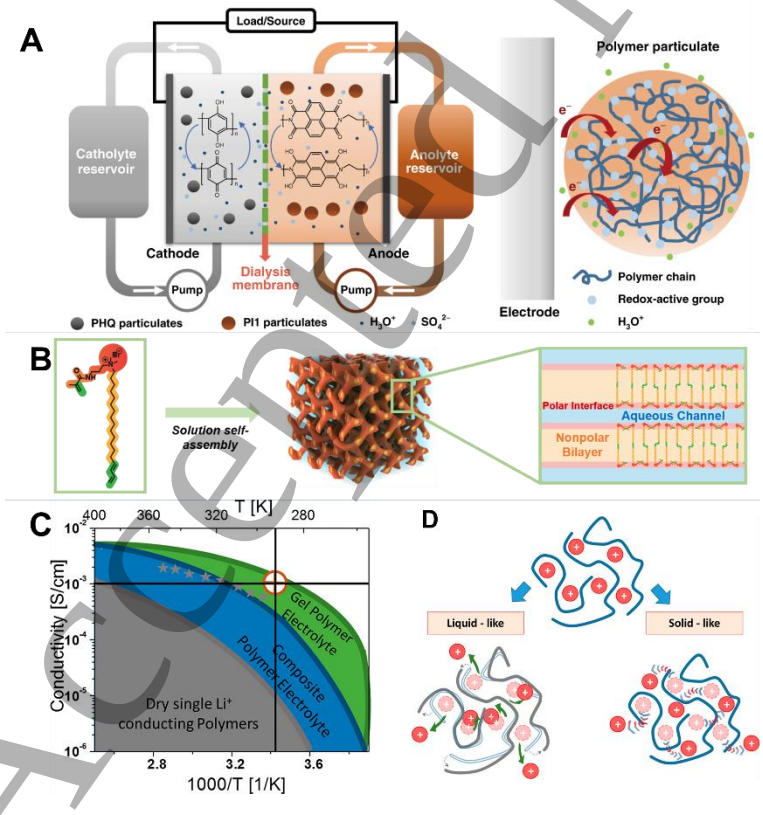

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Figure 2 A: A redox flow battery based on particulate-polymer slurry. Adapted with permission from [3]. B: Nanoporous membranes made by self-assembly of crosslinkable amphiphiles into bicontinuous double gyroid structures. Adapted with permission from Ref. [4]. C, D: Conductivity performance of polymer electrolytes with desired room temperature performance indicated, and segmental vs. hopping motion of ions in polymers in liquid vs solid-like regimes. Adapted with permission from Ref. [5]

Current and Future Challenges On the basis of PCE alone, it is apparent that OPVs have experienced significant maturation. Nevertheless, challenges remain, particularly regarding durability of materials during extended use in non-inert conditions. Concerning polymer membranes, there are also challenges associated with durability under challenging environments, as well as persistent challenges to sharpen selectivity. For example, one of the principal impediments to the development of practical alkaline fuel cells is the poor performance of hydroxide ion-selective membranes. Many polymer membranes exhibit good OH- conductivity (> 100 mS/cm at < 90 °C), but their durability at high pH and elevated temperatures is poor.

Concerns regarding stability are also present in the field of organic solvent nanofiltration, which has attracted considerable interest as a means of circumventing the large energy footprint of conventional thermal hydrocarbon separations. In other contexts, such as gas separations and water purification, the acute need is to break the permeability-selectivity trade-off that is ubiquitous in the operation of current materials.[6] This calls for the development of membranes with ideal nanostructure – with a high degree of uniformity in the transport limiting feature sizes and chemistry. Such materials are also of interest in electrochemical applications such as redox flow batteries, to facilitate ion transport while preventing harmful crossover of relevant species by size and/or electrostatic exclusion. Self-assembly of soft materials provides an attractive route to achieving the desired nanostructure uniformity. Membranes derived from block copolymers, lyotropic surfactant mesophases and small molecule liquid crystals are of interest in this respect, in addition to systems employing discrete nanomaterials such as carbon nanotubes or transmembrane proteins (e.g. aquaporin) as transport structures.[7] There are significant challenges in this space associated with scalable fabrication of the relevant soft materials. Recent advances have been made however in highly-ordered membranes derived from self-assembled direct hexagonal lyotropic mesophases.[8] There are also non-trivial challenges associated with our still incomplete understanding of nanoscale transport under strong confinement in the presence of charge – molecular transport under nanoscale confinement and in the presence of electrostatic interactions is poorly understood from a fundamental perspective. There are numerous open questions regarding the impact on transport, and ultimately selectivity, due to pore wall dynamics, roughness and local structure, suppression and anisotropy of local dielectric permittivity, and ion-pairing, to name a few. Our ability to rationally design nanoporous ion selective materials for energy applications depends on developing new principles that can accurately describe such situations.[9] Such principles will provide clear insight regarding phenomena in nanoscale transport for which we currently lack satisfactory explanations and which we generically refer to as anomalous.[10]

Some of these same concerns regarding nanoscale transport apply to nanoporous inorganic materials used as electrodes in electrochemical devices. While these electrodes are made of hard materials, soft materials provide an attractive route for creating well-controlled high specific surface area constructs that are useful as templates to produce electrodes. Methods include the pyrolysis or carbonization of self-assembled soft mesophases, and the use of co-continuous bijel structures as templates for hard material deposition.[11] Polymers can be incorporated into conventional electrode materials to improve mechanical properties. They provide resilience against repeated volume changes during charge/discharge cycles and thereby increase the durability of the electrode.[12, 13] Significant challenges remain in terms of molecular design to realize electrochemically stable polymers and self-

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healing systems that can lead to not just more durable static electrodes, but potentially also stretchable batteries.

Ion conducting gels, or gel polymer electrolytes (GPEs) have been employed in batteries and supercapacitors for energy storage.[14] In comparison to liquid electrolytes, they bring improved mechanical stability without overly compromising transport properties. Many of the challenges here are associated with molecular engineering to provide the required transport and electrochemical stability, as is also the case for liquid electrolytes. For example, for Li-ion batteries, a conductivity > 1 mS/cm at 25 °C is typically sought (Figure 2). Additionally, the landscape is still evolving regarding the ability of computational approaches and theoretical polymer/soft matter physics to accurately describe the thermodynamics and dynamics of ion containing polymers and gels.[15-18] There is intellectual synergy here with efforts on coacervation in polyelectrolytes and other charged macromolecular systems.[19] Methods to improve mechanical properties, such as the use of double network architectures, or the incorporation of high strength nanomaterials are topics of current interest.

Polymers and (electrolyte-impregnated) polymer gels incorporating stable radicals provide a rich landscape for new research in soft materials for energy, with the stable radicals providing redox-based electronic conduction mechanism.[20] The development of organic radical polymers (ORPs) has been driven by their potential as electrode materials in organic radical batteries (ORBs)[21] based on their high stability and fast redox kinetics. Ease of synthesis and processability, as well as optical transparency are key benefits, and ORBs offer performance that is competitive with Li-ion batteries in many respects (e.g. capacity ~ 140 mAh/g), but absent the adverse environmental impacts, highlighted for example by a recent report on biodegradable ORPs.[22] While the principal focus is on electrochemical energy storage in batteries and supercapacitors, applications of ORPs in biomedicine, as organic magnets, and as electrochemical transistors are also under study. Current and future challenges include processing and molecular engineering to improve conductivity, understanding dopant interactions, and improved first-principles prediction of properties.

There is an emerging class of devices, ionic diodes, that lies at the intersection of ionic membranes and GPEs. Appropriately engineered ionic heterojunctions – of membranes with asymmetric pore geometry and charge, or GPEs of differing charge – lead to rectification of ion currents, in a manner that is strongly reminiscent of biological ion channels. This is a compelling area of research that has challenges regarding fundamental nanoscale electrokinetics, as well as material and process development. GPEs or other stretchable soft materials that exhibit simultaneous ionic and electronic conductivity are of interest in bioelectronics – biological signals are communicated by ionic currents, while device logic is handled electronically.

Energy harvesting devices have been engineered from ion diodes, using osmotic gradients. Other energy harvesting mechanisms have also been leveraged from soft materials, involving triboelectric, piezoelectric and thermoelectric generation.[23] The use of thermomechanical actuation for locomotion, or the realization of artificial muscles has been a topic of interest, particularly given the large coefficients that can be obtained in soft materials such as semi-crystalline polymers and liquid crystal elastomers. A coupling of thermomechanical effects in shape memory soft materials and bimorphs with piezo/pyroelectric devices provides a route to energy harvesting.

Advances in Science and Technology to Meet Challenges Addressing the challenges described above requires progress in both fundamental and applied research. As highlighted, some challenges are associated with gaps in fundamental knowledge regarding physico-chemical phenomena in new situations. Molecular transport under tight confinement in the presence of charged species represents

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one such scenario. Here there is a need for advances in theory and computational approaches, as well as a need for high quality statistically meaningful experimental data against which theory and computational results can be evaluated. Properly elucidating molecular structure-function relationships in charge- and stable-radical containing soft materials is also reliant on advances in computational and theoretical approaches. In other areas, efforts aimed at scalability are needed to enable large area/volume processing of materials at low cost. Methods to effectively guide self-assembly of soft materials used in nanostructured membranes are needed. Finally, advancements are required to accelerate the rate at which new soft materials can be discovered and developed. Scaling up computational and experimental efforts to generate large high-dimensional data sets that can accelerate materials discovery through machine learning of other methods is notoriously difficult. Advances that enable (smart/directed) higher throughout experimentation, such as autonomous experimentation, are expected to be greatly enabling.

Concluding Remarks The increasing emphasis on sustainability is opening up new directions for soft materials in energy and accelerating already ongoing efforts. OPVs will continue to command attention in this regard, but this is alongside concerted efforts in other areas. A few key topics were discussed here. Conceptually, ion-containing and radical-containing soft materials represent a very rich landscape in aggregate – including charged nanoporous membranes, ion gels, polymerized ionic liquids, and related systems. There are important contributions to be made regarding the fundamental materials science, transport phenomena and physical chemistry of these materials, as well as in the development of new chemistries and processing methods to control their properties. These materials have the potential for significant societal impact in numerous energy and energy-adjacent applications.

Acknowledgements C.O.O. acknowledges financial support from NSF through DMR-1945966 and DMR- 2223705

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Section 5.2 – Soft Materials and Food Structure

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Status Soft matter includes soft materials and complex fluids found in everyday life, soft materials whose dynamics are governed by timescales of seconds. These include structured fluids, semi-solids, colloids, polymers, foams, emulsions, gels, and granular materials, which are all relevant to a wide range of naturally occurring and manufactured foods and beverages that contain hierarchical structures and multiple phases. Many of the building blocks in foods are polymeric and colloidal in origin. Considering soft matter theory in relation to soft materials and food provides a coherent basis from which to interpret complex structural and rheological properties occurring across several length, time, and energy scales. The relevance of soft matter physics to all classes of macronutrients (protein, fat, and carbohydrates) supports the development of causal relationships with food sensory perception that go beyond changes in food composition.

The definition of food as soft matter comes fundamentally from the physical and mechanical perspective [1] that differentiates them from pure, low-viscosity fluids and rigid solid materials. This is because the structural entities (such as proteins, polysaccharides, starch, microgels, micelles, colloidal fat, plant cells, and plant fibres) and included phases in foods form complex microstructures via self-assembly, thermal treatment and mechanical processing. The dynamics of the resultant structure is arrested because the interaction between entities makes them unable to move freely within a fluid phase. This generally leads to solid-like rheology that includes a yield stress and elasticity [2] to stabilise multiple phases (e.g., emulsions, particles). Typical physical structures in foods and soft materials include gel and soft glasses (Figure 1), at which structural entities are arrested by a percolated network or jamming, respectively. This definition covers a vast array of foods, such as yoghurt and cheese that may be considered densely packed suspensions of proteins in a microgel-like state; molten chocolate that is a concentrated suspension of solid particles (sugar, cocoa and milk solids) in cocoa butter; and potato chips and apple that are a packed array of plant cells. In addition, even foods that may not appear to follow this structural definition are transformed during oral processing into a swallowable bolus, which is typically a soft material in the form of a densely packed particle suspension in an aqueous physiological fluid, i.e., saliva.

Donald [3] has commented that many foods are complex self-assembled composites that demonstrate behaviours following soft matter physics laws. She also emphasises that, despite our familiarity with food and the plethora of empirical knowledge, research from the perspective of soft matter physics and chemistry is worthy and necessary to meet the 21st century challenges of sustainably producing nutritious, safe, and convenient foods. In addition to societal challenges, scientific challenges remain in fundamental soft matter physics and chemistry and their application to food design, synthesis, and characterisation. For example, due to the complexity of foods, they are often found far from equilibrium; despite this, universal structural scaling laws may still apply [2]. As such, the investigation of food within the framework of soft matter physics remains a rich research area with exciting opportunities for applying fundamental science to complex food structures and behaviours for translation into food manufacture and design. Future research directions include:

I. Understanding of food structures as basic soft matter states such as gels, liquid crystals, biopolymer complexes, foams, emulsions, and colloidal dispersions [1, 4]. Such interpretations of food structure help create model food systems to investigate the underlying mechanism of food functionality and perception, ultimately enabling the design of novel food structures for the delivery of sustainable nutrition.

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II. Advanced techniques in characterising food structures and their soft matter behaviour. These include, for example, scattering [5], rheology [2], tribology [6] and microscopy/fluorescence.
III. The relationship between food structure, oral processing and sensory texture perception [6, 7]. This assists in elucidating the influence of whole and masticated food structure on sensory texture and flavour during oral processing to enable the application of fundamental soft matter models and theories in rational food product design. This includes consideration for the transformation of food structure during oral processing.

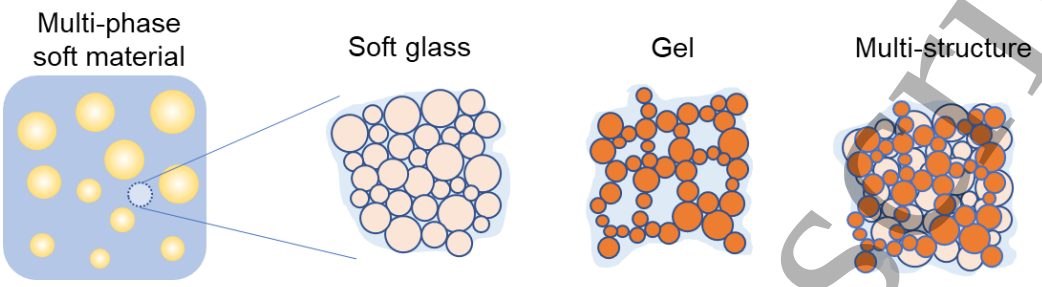

Figure 1 Schematics of soft glass and/or gel microstructure required to physically stabilise macroscopic phases (e.g. oil droplets) as generally observed in foods, building on ref. [2]. The circles indicate nano- and micro-scale structural entities. The multi-structure represents a situation where multiple structural entities give both soft glass and gel characteristics.

Current and Future Challenges Natural and processed foods are complex compositionally, structurally, and rheologically, which presents a significant challenge in rational structure design, evaluation and manufacturing. This complexity occurs across time and length scales at the molecular-to-nano scale (e.g. protein molecular structure), microscopic or meso-scale (e.g. protein aggregation) and macroscale (e.g. phase separation). This is the case for even seemingly simple soft materials and foods; for example, butter is a water-in-oil emulsion derived from cream, and the oil phase is structured via a complex multi-dimensional fractal network made from self-assembly of fat crystalline nanoplatelets over a range of length scales [8], which is also a non-equilibrium structure resulting from varying degrees of lipid crystallisation that is a function of time and temperature [5]. Food can be challenging to characterise into a single fundamental classification, such as a simple gel or soft glass. Many manufactured food products are formulated as a combination of several physical states. Unlike many model systems studied in soft matter literature, foods may have a multi-structured state (Figure 1) where it is often unclear whether they have a soft glass or gel microstructure or both. Many foods have the closely packed structure of a soft glass yet also contain strongly interactive particles or polymers (proteins, polysaccharides) that form a gel; one example is mayonnaise products that have a dense suspension of oil droplets structured within an egg protein network[2]. Thus, the compatibility and interaction between components and phases complicates the structure and behaviour of soft matter foods.

"Soft" is not a definitive term from a physical and mechanical perspective, i.e., a material is considered soft only relative to a reference state and over a specific time scale. A challenge thus comes as the measured rheological properties of foods and soft materials are time-dependent [2], such that measurement of rheological parameters over a time scale may insufficiently represent the behaviour of food during processing and consumption. The microstructures within foods and soft materials are typically shear-sensitive. Thus, the structural state alters with any imposed shear, and microstructures may be unrecoverable and rheologically thixotropic. These issues also impose difficulties correlating the properties obtained from static (e.g., scattering) and dynamic (e.g., rheology) measurements.

Early progress in food research has related food structures with fundamental colloidal, polymeric, and physical sciences. However, recent works increasingly realise that the inherent properties such as

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viscosity, density and stability cannot completely describe the behaviour of soft materials and foods under conditions they may encounter. For example, oral processing exposes soft foods to a combination of shear and squeeze flow, which causes the confinement of particulates and fluids to thin films between oral surfaces and exposure to saliva, as shown in Figure 2. Under these 'thin film' conditions, the continuum assumption in rheology measurement is no longer valid and complementary characterisation such as micromechanics, soft-tribology and interfacial properties are required. 'Micromechanics' refers to the mechanical analysis of composite or heterogeneous materials on the level of the individual constituents.

Plant-based substitution of animal products is a growing food research area, which needs investigation using a soft matter framework to design microstructures emulating those from animal components. For meat analogues, the key challenge is creating a soft matter matrix that exhibits multi-scale mechanical properties and textures close to their natural meat rivals to be accepted by consumers [9], which may require greater control over structural and mechanical anisotropy and other factors. The key challenge in replacing animal-based ingredients with plant-based equivalents, particularly proteins, is matching their techno-functional properties, including their interfacial and colloidal properties that contribute to stability and texture, whilst avoiding the negative sensory properties arising from poor solubility. Incomplete understanding of the relationship between food structure, mechanical/physical properties, and sensory textures makes this challenge more profound. Addressing this challenge is required to improve sustainability in food processing.

Advances in Science and Technology to Meet Challenges The hierarchical structure of foods is now widely accepted in food research. However, it is still more common to alter food composition rather than investigate food's hierarchical structures in the context of fundamental soft matter science. Food researchers and manufacturers also recognise that formulation, manufacturing, storage, and oral processing of foods is dependent on the physical/mechanical properties over a range of length and time scales. Below, we highlight how recent advances in science and technology empower researchers to measure and characterise multi-dimensional properties and the response of foods as soft matter systems.

Small angle scattering (SAS) is a powerful tool in soft condensed matter physics and is highly applicable to food research. The setup of SAS experiments and data interpretation can be complicated, as reviewed by Gilbert [5]. However, by selecting the proper radiation source, such as X-ray or neutrons, and experimental setup, SAS provides spatial information regarding how entities, from nanometre to micron length scales, are located relative to others within the material. Successful interpretation of SAS results requires complementary techniques to assist in determining mathematical form factors and structure factors. This multidimensional structure studied by SAS corresponds to the multiple scales of self-assembly within soft matter foods, such as the study of lipid self-assembly and lipid digestion. Thus, SAS provides unique value in food structure research.

Investigation into the mechanical and rheological response of soft materials and foods in the non-linear regime and under confinement forms another area in which progress has been made on model soft matter systems. Soft materials are characterised by their non-linear and time-dependent rheology, e.g. the measured yield stress and viscoelastic parameters are not definitive to the material but apparent over a certain deformation and time spectra [2]. These extremes of rheology are relevant to the high-shear environment and confinement experienced by foods during oral processing between tongue and palate or tongue and teeth and offer opportunities to understand the mechanisms driving sensory perception. Large amplitude oscillatory shear (LAOS) [10], gap-dependent rheology [6], and squeeze flow rheology are three such techniques.

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Soft contact tribology is emerging as a valuable tool in the design of foods and beverages due to its relevance to oral processing and sensory perception [6]. This involves rubbing two highly deformable bio-mimetic surfaces with a soft matter or complex fluid phase as a lubricant. The soft lubrication behaviour of foods is a system variable strongly dependent on lubricants' rheology but further impacted by the speed, substrate elasticity, surface roughness and interfacial properties. Therefore, it provides complementary information to rheological measurements in efforts to correlate the physical properties of foods with their sensory texture (Figure 2).

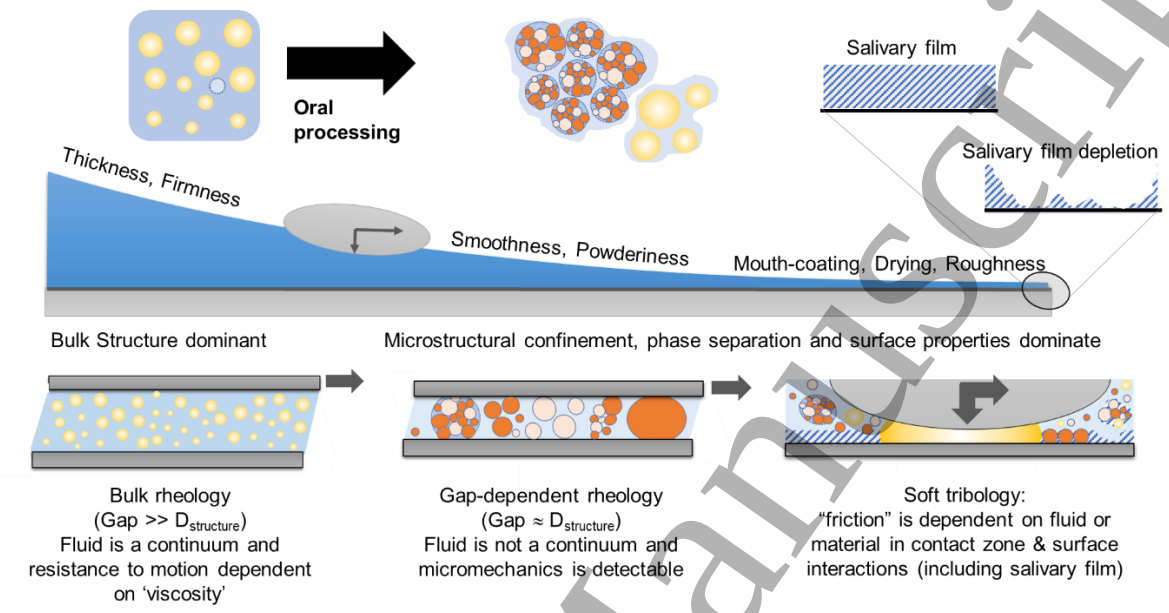

Figure 2 Multi-scale mechanical/rheological analysis techniques of soft matter foods. The length scale of each method and its 'correlation' with sensory textures are indicated. Builds on ref. [6].

Concluding Remarks The research into food structure and its relationship with physical/mechanical properties is closely related to fundamental soft matter physics and colloidal science. Challenges in soft matter physics are also common in food research, e.g., formulation, synthesis, and advanced characterisation of soft materials with multi-dimensional structures and tailored properties under complex physiological and mechanical environments. The predominant approach in food science is to build empirical correlations between physical properties and sensory attributes of whole foods, which does not provide mechanistic understanding. The use of soft matter theory as a fundamental basis for food research promotes a focus on the relevant physics occurring in-mouth to provide insights to interpret and mechanistically predict and design products for desired performance, and sustainable food processing.

Acknowledgements Contributions to this article have been made possible due to research funded by the Australian Government through the Australian Research Council (ARC) Grants DP180101919 and LP160100239.

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Section 6.1 – Active Biological Materials

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Status The field of active matter physics arose almost 30 years ago from the desire to better understand the collective and dynamical properties of living systems. Most of the time, researchers have set out to better understand how many, equally behaving, energy-consuming agents can organize across different scales, e.g., molecules into cytoskeletal gels, cells into tissues, and animals into swarms.

Here, we focus on active biological materials, which we define as living biological systems for which material properties such as a viscosity or elastic moduli can be reasonably defined. This is often not the case for "dry" systems where active agents propel themselves with respect to a common substrate. Instead, this usually applies to "wet" active systems such as the cytoskeleton, swarms of bacteria, and biological tissues.

Despite this vast diversity of active biological materials, many fundamental properties have been understood from a theoretical perspective, using simulations of agent-based models, explicitly coarse-graining such models, and analyzing the resulting hydrodynamic descriptions (Marchetti et al., 2013). Experimentally, these properties have been demonstrated in many *in-vitro* and *in-vivo* systems (Sanchez et al., 2012; Duclos et al., 2018). So far, connecting between theories and experiments has, in most cases, only been possible in simplified setups, such as 2D reconstituted gels or cultured epithelial monolayers.

Despite this progress, our understanding of active biological materials is still limited. In some cases, active matter theory even opened new fundamental questions. For instance, active anisotropic tissue deformation is a key process during animal morphogenesis. However, the orientationally ordered state in wet active matter is generally unstable, consistent with in-vitro experiments (Duclos et al., 2018). How oriented tissue deformation can be robust during morphogenesis despite this instability is still unclear (Ibrahimi and Merkel, 2023). More generally, much remains to be done to bridge between active material theories and the full complexity of living organisms.

Current and Future Challenges Current theories focus on the description of idealized systems, which fail to capture several key aspects of the complexity of *in vivo* active matter. We discuss here three of these aspects.

First, many of the active matter systems studied so far had a flat 2D geometry (reconstituted cortices, motility assays, cell monolayers, etc.). However, both intracellular structures and living tissues *in vivo* can be bulk 3D structures (e.g. connective tissue, cytoplasm; Duclos et al., 2020), curved 2D structures (e.g. epithelia, membranes; Maroudas-Sacks et al., 2021; Randriamanantsoa et al., 2022; Bell et al. 2022; Gehrels et al., 2023), or combinations of both (e.g. embryos, organs, organoids; Tao et al., 2019; Brandstätter et al., 2023), each embedded in a complex 3D environment. For instance, in many systems, taking into account the curvature and its temporal dynamics is experimentally and mathematically challenging. Furthermore, the environment of active materials *in*

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vivo often deforms in response to the forces exerted by the active material. This adds the challenge of dissecting the interplay between active matter mechanics, geometry, and mechanics of the environment.

Second, much of the past work studied average behavior of active biological materials, even though fluctuations can play a physiological role, e.g., in tissue fracture (Sonam et al., 2023). In addition, fluctuations can also be harnessed to extract more information about the dynamics driving the system. For equilibrium systems the fluctuation-dissipation theorem (FDT) paved the way to micro-rheology, allowing to extract rheological parameters from observed fluctuations. For active systems, weaker generalizations of the FDT exist (Rupprecht and Prost, 2016), and micro-rheology has been successful for some systems (Lau et al., 2003). However, additional measurements are generally required to extract the material rheology (Turlier and Betz, 2018). While a limited number of key material parameters can often be directly extracted from fluctuations (Blanch-Mercader et al., 2018), a deeper understanding of fluctuations in active materials will allow us to better harness the information contained in fluctuations.

Third, both *in vitro* and artificial active matter systems tend to be designed to be as clean, i.e., homogeneous and monodisperse, as possible, and most often, theories for active materials have been tested on such systems. But *in vivo* materials are not clean. The cytoskeleton is a heterogeneous, highly composite structure, while biological tissues contain multiple cell types, arranged in complex structures. Taking the “dirtiness” of *in-vivo* systems into account will be a major challenge.

Finally, an overarching difficulty in accounting for more complexity is the proliferation of parameters required to describe the systems. Keeping the number of parameters in check while moving towards a more realistic yet intelligible description of living materials is a key future challenge (Brunton et al., 2016).

Advances in Science and Technology to Meet Challenges To address these challenges, one must bridge between the complexity of living organisms and theories of active materials. We distinguish here four steps.

Step 1 - from living organisms to images. Significant progress has been made recently in imaging 3D systems, where light-sheet and two-photon microscopy have become standard techniques over the last decades (Wan et al., 2019). However, challenges remain such as light scattering, phototoxicity, and a limitation in the number of fluorophores for live imaging of protein dynamics.

Step 2 - from images to data. Image data often needs to be segmented and objects tracked over time before it can be compared to theoretical models. For such data analysis, new tools, including deep learning tools (Weigert et al., 2020), are emerging to analyze the local material structure. However, so far system-specific solutions are often required, but universal tools are starting to emerge (Pachitariu, 2022; Kirillov, 2023). Image analysis is also important for techniques to measure forces and rheological properties of living systems (Roca-Cusachs et al., 2017). While these techniques are currently being adopted more broadly, we believe that they should be combined more often with techniques to experimentally manipulate the 3D environment, such as microfluidics and micro-confinement.

Step 3 - from data to models. To compare data to a theoretical model, problem-specific data analysis tools often need to be developed. For noisy or incomplete data, the calibration of theoretical models

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requires the use of statistical inference techniques (Frishman and Ronceray, 2020). Another example are theoretical tools to connect dynamics across different length scales, which allow calibrating macroscopic models using microscopic data (Merkel and Manning, 2017).

Step 4 - from models to theories. Finally, quantitative models for specific systems are not the end-goal; the goal is to understand what unifying principles underlie the complexity of life. For 3D systems, general theoretical descriptions (Salbreux et al., 2022) and simulation tools (Okuda et al., 2018; Bächer et al., 2021; Borja da Rocha et al., 2022) have recently been developed. However, new theoretical developments are needed to account for the "dirtiness" of real biological materials. This includes, for instance, the combination of active matter physics with existing high throughput "omics" techniques (La Manno et al., 2018), to better understand, e.g. how cell type heterogeneity interacts with active mechanics during morphogenesis.

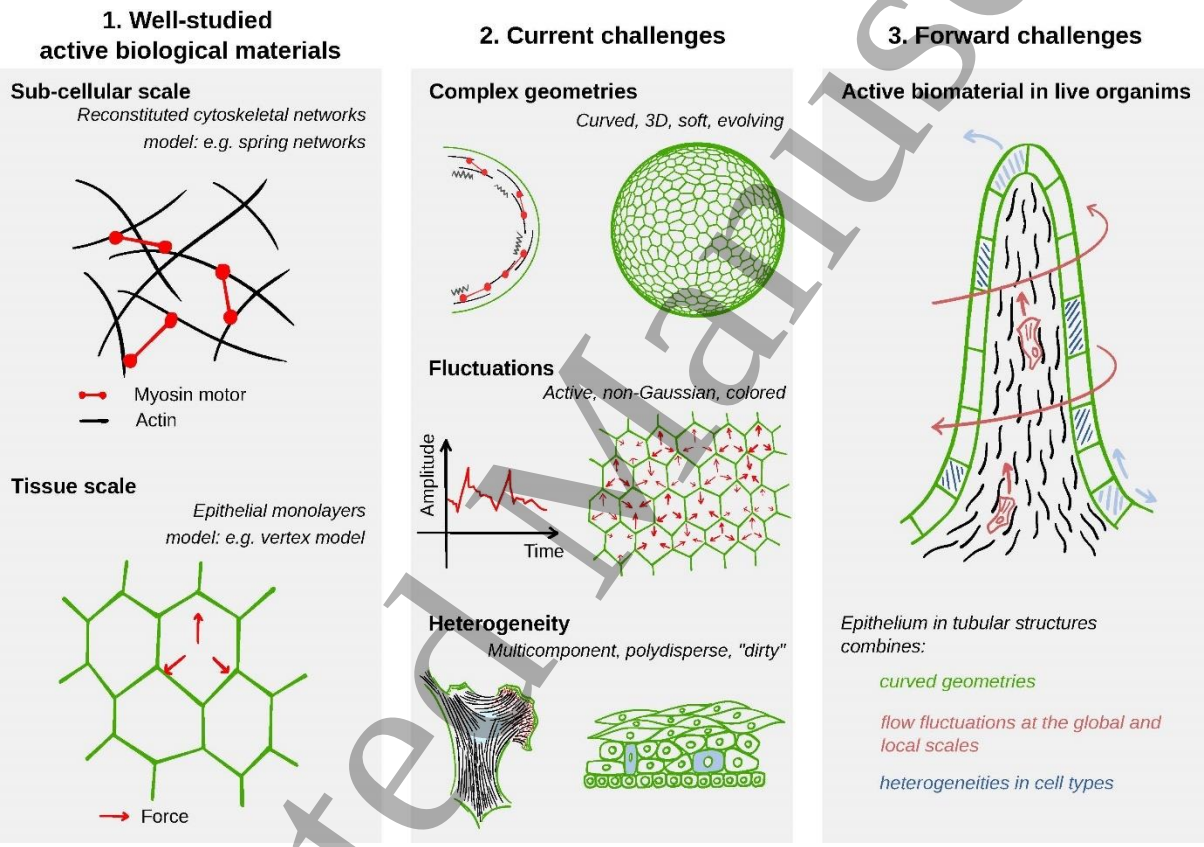

Figure 1 (1) Well-studied active biological materials include, at the sub-cellular scale, reconstituted cytoskeletal networks (which can be modeled as complex spring networks) and, at the tissue-scale, epithelial monolayers (which can be modeled for example using vertex models). (2) Current challenges include generalization to complex geometries (curved, 3D, soft, evolving surfaces), to fluctuations (that can be active, non-Gaussian and colored), and to encompass the heterogeneity of materials. (3) A forward challenge is to develop a framework to understand the properties of active biomaterials within live organisms. One example is the epithelium in tubular structures (such as the gut); it combines the challenge of curved geometries, of flow fluctuations at the global and local scales, and of heterogeneities in cell types. All illustrations by Alexander Brodovitch (curved tissue image in (2) adapted from Sussman, 2020).

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Concluding Remarks The field of active matter was created to better understand the collective and out-of-equilibrium properties of living systems. After almost 30 years, we have arrived at a theoretical and experimental characterization of many fundamental effects in the dynamics and structure of biological materials, from intracellular gels to multicellular tissues. These advances, however, concern mostly idealized systems: to move towards an active material description of *in vivo* systems such as live animals, progress must be made to include the complexity of these systems, for instance by looking at 3D systems, better understanding fluctuations, and try to include more and more of the "dirtiness" of real systems. This will require an even closer collaboration between biologists and physicists.

Finally, improving our quantitative understanding of the collective properties of active biological materials opens the way for the control of their dynamical and mechanical properties using global fields or local cues (Cohen et al., 2014).

Acknowledgements M.M. thanks the Centre Interdisciplinaire de Nanoscience de Marseille (CINaM) for providing office space. M.M., P.R. and J.-F.R. received funding from the «Investissements d'Avenir» French Government program managed by the French National Research Agency (ANR-16-CONV-0001) and from the Excellence Initiative of Aix-Marseille University - A*MIDEX.

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Section 6.2 – Protein Self-Assembly

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Status Processes of protein self-assembly are highly relevant in a broad range of research fields linked to soft matter, covering aspects from fundamental understanding of life to everyday applications and advanced biotechnology. While the individual protein molecule already presents a complex folded structure, assembly of proteins frequently governs biological function such as during enzymatic reactions, cyteskeleton formation, viral replication, and condensation of membraneless organelles [1-3]. This central role of protein assembly for life is also reflected in biomedical and pharmaceutical challenges. Examples are administrable (i.e., sufficiently low viscosity) antibody formulations, fibril formation in neurodegenerative diseases, and protein condensation linked to age-related eye cataract. In terms of essential research tools, structure determination of proteins is still mostly dependent on the controlled formation of protein crystals. Biomaterials represent another advanced application of protein assembly – often in a biomimetic spirit – [4], where specific material properties enable biomedical applications such as drug delivery and tissue engineering. Recent approaches based on established soft matter accounts in food science [5-7] aim for controlled assembly of plant proteins to produce sustainable alternatives to meat and dairy products. Besides these advanced applications from the last decades, protein assembly has been exploited in traditional food production (e.g., cheese and bread) for millennia.

As evident from these examples, protein self-assembly in a broader sense does not only imply the formation of selective, specific, and rigid protein structures, but also contributes to a dynamic picture of transient and disordered protein assemblies such as dense condensates which represent a growing research interest due to their role in cellular metabolic pathways. Currently, multiple key questions regarding protein self-assembly remain unsolved. For example, a detailed understanding of how molecular dynamics drives assembly processes is missing. Examples include the role of protein docking in metabolic regulation or responses of proteins to external stimuli, such as allosteric effects. On the level of macroscopic emergent phenomena, the link between protein phase behaviour and nucleation pathways of solid structures such as fibrils and crystals, as well as formation pathways of hydrogels, remain poorly understood. The role of thermodynamic driving forces giving rise to self-organisation, has been increasingly appreciated [2, 9-10].

In this context, a central question is whether control parameters, e.g., solvent conditions, salts, and other macromolecules, could be used to control protein assembly and phase behaviour [2,11,12], with the aim, inter alia, to provide cures to diseases [1] and to enable rational design of biomaterials [13,14].

Current and Future Challenges A first challenge to be understanding of protein assembly is its complex and hierarchical character on multiple length scales, ranging from the primary structure of the amino acid sequence, over secondary structure elements and the tertiary structure of protein domains on nanometer size, to the quarternary structure of multi-domain or multi-subunit proteins, and eventually supramolecular assemblies of different topology on micrometer length scale (see Figure 1).

A second challenge is linked to the soft matter nature of proteins: due to their inherent physico-chemical complexity, proteins comprise aspects of colloids, polymers and amphiphiles. Potential

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interaction modes include colloid-like molecular docking of anisotropic protein molecules; induced-fit assembly, i.e. a combined process of unfolding and assembling; and polymer/polyelectrolyte-like transient interactions, but all this for inherently anisotropic and inhomogeneous objects. These manifold interaction modes point toward a third challenge: Proteins not only flexibly respond to environmental changes on the molecular level – some proteins even have the potential to act as molecular motors or enzymatic facilitators of controlled assembly. A quantitative understanding of biological function of protein assembly and the functionality of biomaterials thus needs to go beyond a mere picture of multi-scale structure. Dynamical signatures on multiple relevant time scales (posing a formidable challenge to experimental methodology) as well as kinetic, non-equilibrium aspects are needed for a conclusive mechanistic understanding [8,15].

Studying protein assembly requires an interdisciplinary and multi-technique approach (see Fig. 2). Combining the appropriate techniques and reaching a comprehensive picture is of utmost importance and requires not only deep methodological knowledge, but also careful organization and cross-disciplinary communication. Very practical challenges start from the production and storage of a sufficient amount and purity of relevant proteins. To cover the plethora of processes on different time and length scales, prominent experimental methods include optical spectroscopy, scattering techniques, NMR, and fluorescence approaches [8]. In addition, theoretical models rooted in statistical physics and stochastic processes as well as molecular dynamics and coarse-grained simulations are valuable tools for mechanistic insights and hypothesis generation for experiments. Protein research thus strongly relies on interdisciplinary and integrative collaboration to translate soft matter approaches to biological systems with relevance for health and medicine.

Advances in Science and Technology to Meet Challenges The theoretical description of protein phase behaviour in terms of colloidal models has improved over the last years [16], e.g., by introducing patchy interactions matching real properties of the anisotropic protein molecules [17-20], promising more predictive schemes for future applications. In response to the huge interest in condensates of intrinsically disordered proteins (IDPs), theoretical concepts of polymer and colloid physics have been revisited and adapted [2]. These theoretical aspects are complemented by efforts in computer simulations to improve the force-fields for atomistic molecular dynamics simulations of IDPs and develop coarse-grained realistic models which capture the propensities of local secondary structure even for IDPs [21].

On the experimental side, advances in a range of research fields open new opportunities for complementary and comprehensive studies of protein assemblies. FRET provides specific local information on docking processes in dynamic structural ensembles [22]. New trends of NMR methodology enable the structural characterization of large specific protein assemblies [23]. Super-resolution microscopy emerges as a tool to study growth processes from surfaces using time-resolved real-space imaging [24].

In recent years, time-resolved small-angle scattering in combination with stochastic modeling has been used to unravel assembly pathways of proteins, e.g. by comparing the observed time trace of structural signatures during protein crystallization with rate-equation models [25], by using data-driven analysis methods to extract kinetic and structural information on intermediates in viral assembly [26], or exploiting contrast variation to study the dynamic multi-subunit protein structure [27].

Furthermore, even time-resolved measurements using dynamical scattering techniques are becoming applicable to protein solutions due to the recent instrumentation improvements for X-ray Photon Correlation Spectroscopy (XPCS) [28,29] and Quasi-Elastic Neutron Scattering (QENS) [8].

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Concluding Remarks Overall, it is becoming increasingly obvious that there is a strong trend towards interdisciplinary work and a pronounced "softening" of the boundaries between traditional research disciplines. Indeed, multi-technique and time-resolved characterization of biomaterials and a consistent combination of experiment and theoretical modeling are becoming more and more important. It is safe to assume that these trends will continue in the future.

Acknowledgements
The authors gratefully acknowledge financial support by the Deutsche Forschungsgemeinschaft (DFG), the German Ministry for Education and Research (BMBF), the Crafoord Foundation as well as various large-scale research facilities (in particular Diamond Light Source, the ISIS Neutron and Muon Source, the European Synchrotron Radiation Facility, the Forschungsreaktor München II, the Julich Center for Neutron Science, the Institut Laue-Langevin and Oak Ridge Neutron Laboratory) for beamtime allocation and excellent on-site support.

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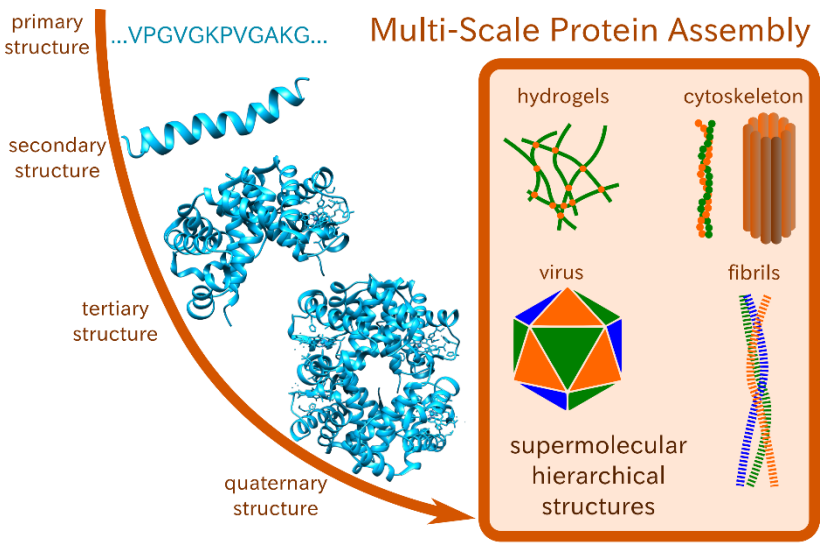

Figure 1 Protein assembly starts from multi-level macromolecular folding and extends to multi-scale and hierarchical structures.

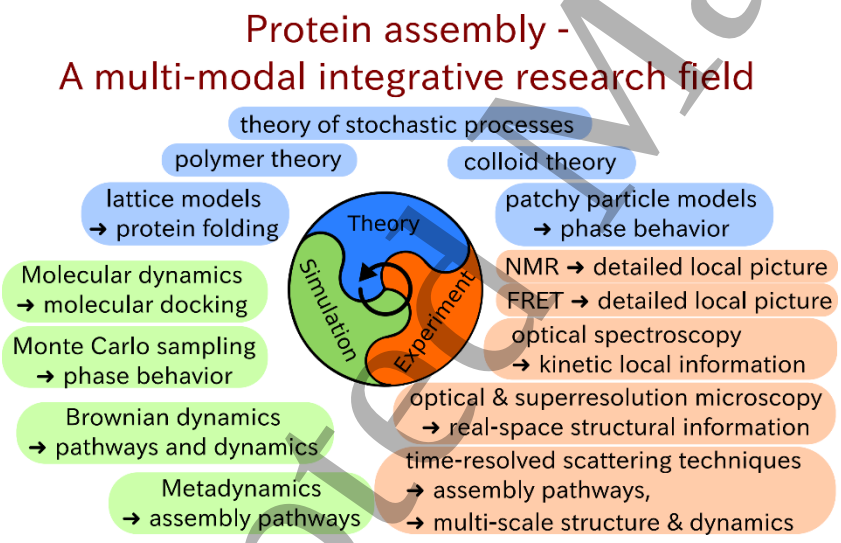

Figure 2 Protein assembly combines research approaches from a broad research field, integrating experimental techniques with theoretical and computational modeling.

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Section 6.3 – Biosourced soft materials

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Status Biosourced soft materials consist of soft materials derived from or manufactured (at least partly) by living organisms. They fall under the general term 'biomaterials', which usually refers to materials in three categories: [1] Biosourced materials, also called biological materials, which include for example polymers extracted from cells, food materials (see section 5.5 of this Roadmap), and active biological materials (see section 6.1). [2] Materials composed of chemically synthesized molecules identical, or similar to, macromolecules synthesized by living organisms. Examples include solid phase synthesis of nucleic acids or peptides, which can be building blocks for DNA or protein-based materials (see section 6.2 of this Roadmap). [3] Materials (biosourced or synthetic) used for a biological and/or medical application, such as scaffolds for mineralization for bone regeneration (see section 6.4).

Biosourced soft materials have a long history, going back to adhesives based on birch bark tar in the Paleolithic, papyrus in ancient Egypt, and the age-old use of leather and wool for clothing. Biological manufacturing is not limited to multicellular organisms like plants and animals. Bacterially produced polymers such as gellan gum are for instance popular rheology modifiers in the food industry. More recent "cell factories" include mammalian cells for biomedical materials, and microorganisms (yeast, bacteria, microalgae) for bioplastics, biominerals, and hierarchically structured composites [1, 2] (Figure 1). Recent developments in synthetic biology make it even possible to spatiotemporally control cells to produce materials on demand [3].

Biosourced materials have many advantages. A first obvious advantage is their high abundance. Cellulose for example constitutes >40% of the dry mass of plants. Second, they are inherently eco-friendly since biological organisms perform "green" chemistry. Third, their inherent biocompatibility makes them suitable for food and biomedical applications. Fourth, materials produced by living organisms often have superior material properties due to hierarchical structuring across multiple length scales [4]. Animal skins are for instance compliant yet resilient by virtue of a strain-stiffening fibrous collagen matrix combined with stretchy elastin, while bone and nacre are hard yet tough due to a layered structure with alternating soft protein polymer and rigid biomineral phases. Finally, many biosourced materials display additional features such as special optical or magnetic properties.

Engineered living materials, i.e., biosourced materials containing living cells, promise many additional advantages. Embedded motile microbes or contractile animal cells can serve as actuators that actively deform the material [5]. Cells can also render the material properties responsive to chemical cues or physical inputs, either naturally or through genetically engineered novel functionalities [3, 6]. Extracellular matrix synthesis by animal cells is for instance naturally mechanosensitive, as illustrated by the ability of bone to adapt its structure to mechanical load. Cells can endow materials with many additional life-like properties such as autonomous self-repair and programmed responses based on genetic circuits [3]. Such smart materials can open up many new applications, for instance as soft robots, intelligent food packages, recyclable bricks, and wearable bioelectronics[6].

Current and Future Challenges

1. Most commercial biosourced materials such as plant-based cellulose or animal-based collagen are obtained by processing and/or extraction from natural sources. Although the materials are themselves eco-friendly, their insolubility often requires processing steps that involve harsh

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chemicals and/or high energy input. Also, it can be challenging to ensure product purity, safety, and reproducibility; and especially animal-derived products raise ethical and cultural concerns.

2. These challenges can be overcome by sourcing biomaterials from wild type or engineered cell factories. Microbial fermentation is increasingly used for producing nucleic acids (DNA, RNA), proteins, polysaccharides, and biominerals [1]. However, it is not always straightforward to engineer novel pathways for materials production without compromising cell growth or viability [1]. Protein production yields are often lower than in endogenous organism and host organisms often lack the biosynthetic machinery needed to produce the correct posttranslational modifications. Polysaccharides can generally be produced in higher yields than proteins, but it is more challenging to engineer their production because our knowledge of their synthesis and processing pathways is incomplete [7]. Biomineral production is even more complex because it is environmentally sensitive.
3. Nucleic-acid-based materials are attractive because their properties can be programmed with rational computer-aided design of base-pairing DNA sequences. However, DNA-based materials are limited in their chemistry (4 DNA bases) and lack mechanical strength. Protein-based materials offer more versatile chemistry (20 amino acids, expandable with non-natural amino acids and posttranslational modifications) and higher mechanical strength. However, rational protein design is still hampered by our limited understanding of protein folding and self-assembly (see Section 6.2 of this Roadmap). Polysaccharides likewise offer versatility, but their physico-chemical properties are relatively poorly understood.
4. Current engineered living materials are far away from mimicking the complex shapes and internal structures of natural materials, although recent efforts to grow co-cultures of cells engineered to produce materials upon specific local triggers promise enhanced control [3]. Maintaining material production and performance over periods longer than a few days can be problematic due to nutrient and oxygen requirements and/or size constraints from cell growth. Some of these issues are also relevant in the field of tissue engineering [2].

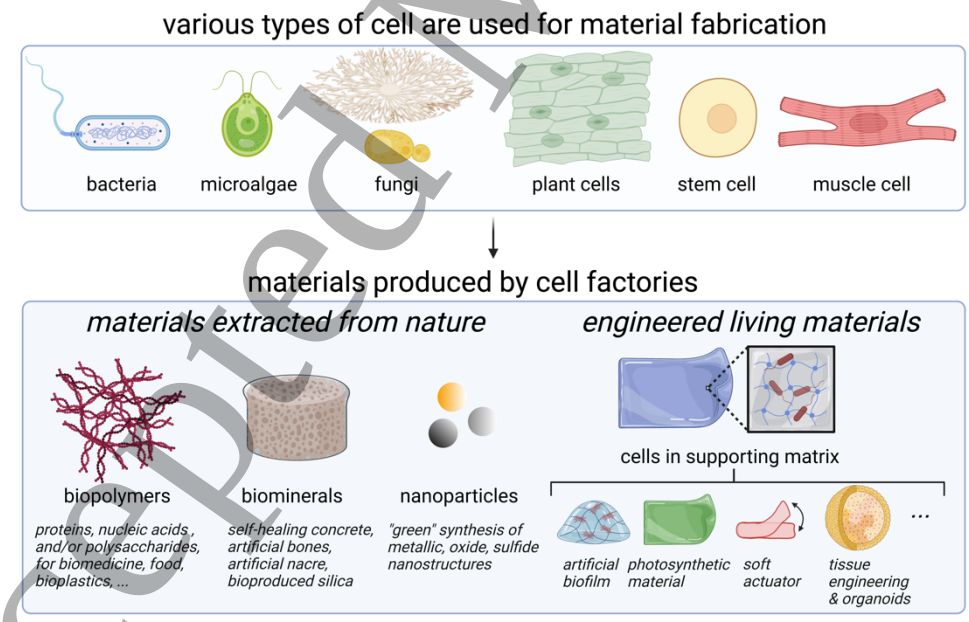

Figure 1 Schematic overview of the main biosourced cell and material categories.

Advances in Science and Technology to Meet Challenges

1. A promising route towards more eco-friendly material extraction from natural biological sources is **enzyme-mediated extraction** [8]. Many natural enzymes exist that are selective for particular

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biomacromolecules since living organisms depend on enzymes to dynamically sculpt their structure. Enzymatic processing proceeds under ambient conditions with low energy consumption, provides spatiotemporal control, and enzymes can add additional functionalities to the material [8]. Fundamental studies of the structure-degradation relationship for different materials are needed.

2. Production yields of cell factories can be enhanced by using synthetic biology tools to equip host cells with biosynthetic and secretory machineries from other organisms [1]. Directed evolution could further improve the performance of cell factories.
3. Achieving programmable material properties requires deep knowledge of the structure-property relation of biomolecules. Recent advances in artificial intelligence promise predictable protein folding from sequence. Advances in systematic coarse-graining computational approaches open the possibility to predict material properties from the underlying molecular properties, especially when combined with multiscale experiments exploiting new nanoscopic biophysical tools such as optical tweezers, atomic force microscopy, and molecular tension sensors [9]. Some of the new scattering and microscopy techniques developed for traditional soft matter systems would also be useful for studying biosourced materials (see sections 2.1 and 2.3 of this Roadmap).
4. New top-down fabrication processes such as molding, electrospinning, and 3D printing (Figure 2) provide a short-term strategy to achieve user-defined shape control of engineered living materials [10]. However, the holy grail in the field is autonomous cell-driven material assembly [3]. Synthetic biology makes it possible to achieve on-demand material synthesis by placing the corresponding gene(s) under the control of an inducible promotor and to pattern materials by fusing proteins with self-recognition motifs or by programming cell-material adhesion. Larger-scale patterning can be achieved by engineering cells that phase separate based on differential adhesion strengths or by using chemotactic responses of motile cells or stochastic reaction-diffusion mechanisms. Long-term performance stability of living materials will require a fundamental understanding of the behavior of cells confined within polymeric matrices.

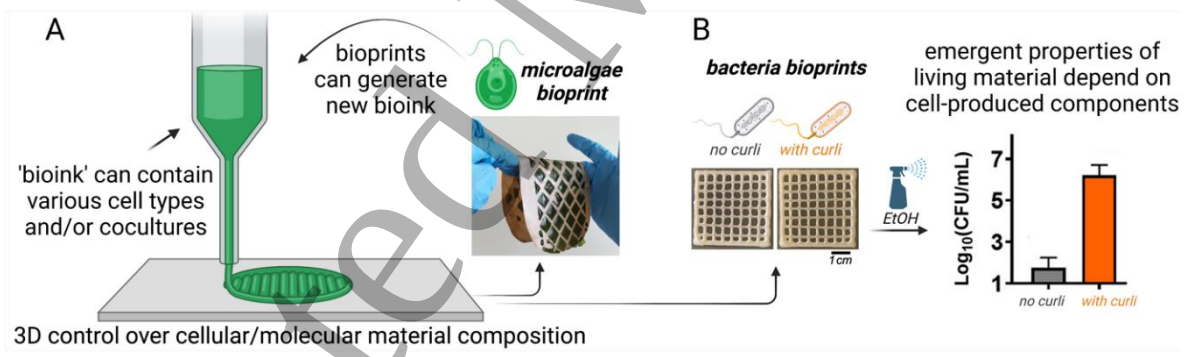

Figure 2 Examples of bioprinted engineered living materials composed of (A) microalgae or (B) bacteria, which demonstrate the possibility of controlling the 3D structure, cellular and molecular composition, and the functional properties of the printed living material. (A) Microalgae bioprints can survive several days off water and nutrients, and cells can be reused and grown to print additional living materials. (B) Emergent resistance of 7 day-old 3D-printed *E.coli* biofilms exposed to 70% ethanol during 10 min. The viability of bioprinted *E.coli* not producing (grey) and producing (orange) curli protein fibers is measured as colony-forming units (CFU) per mL. Parts of this figure are taken from Refs. [10, 11].

Concluding Remarks Biosourced materials have a bright future because they provide a sustainable solution for many urgent societal challenges that demand safe and environmentally friendly materials. New engineered living materials further promise revolutionary new applications, such as self-repairing

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construction materials or biologically active materials for personalized medicine. We expect many exciting future advances from the convergence of metabolic engineering and synthetic biology with (soft) materials science [3]. There are several important issues to address. The nomenclature in this new field is still being developed and would benefit from standardization. Recent papers have proposed a taxonomy for engineered living materials [12, 13]. Also, it is important to find ways to scale up fabrication methods to allow real-world applications. Finally, it is important to engineer the materials such that they are safe by design. To prevent release of the embedded cells to the environment, either the material can be designed to retain the cells by entrapment or adhesion, or the cells can be designed so they survive only inside the material.

Acknowledgements This publication is part of the project *How cytoskeletal teamwork makes cells strong* (with project number VI.C.182.004 of the NWO Talent Programme which is financed by the Dutch Research Council (NWO)), and the project *Light-responsive microalgal living materials* (ERC starting grant No. 101042612). Images are created with *BioRender.com*.

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Section 6.4 – Reinforced Hydrogels via Mineralization: Next Generation Bioscaffolds

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Status Reinforced hydrogels have the potential to address the growing need for biomaterials that can support the growth and differentiation of stem cells, deliver drugs to specific tissues or organs, promote tissue regeneration (1) and ultimately lead to improved clinical outcomes in regenerative medicine.(2) Many organisms direct mechanisms referred to as biomineralization to produce a wide array of organic–inorganic composites with a broad spectrum of mechanical properties, spanning from hard and fracture resistant to soft and tough (3, 4). This remarkable variety is mediated by cell-coordinated material assembly processes that govern the mineralization of (nano)structured macromolecular scaffolds. Organic scaffoldings may reduce the energetic barrier for nucleation, locally raise the supersaturation of the solution, and/or direct the growth and assembly of the crystals within the organic matrix(5). One outstanding example is bone, which exhibits high levels of precision yielding multi-scale hierarchical gradients between soft organic matter and mineral phase, *i.e.,* collagen and calcium phosphate. Bone growth appears to be templated by the collagen matrix, which leads to uniaxially oriented hydroxyapatite (HAP) nanocrystals parallel to the collagen fibers. The use of amorphous precursor phases is a widespread strategy in biomineralization(6, 7). In bone mineralization, it is proposed amorphous calcium phosphate (ACP) nanoparticles form first and gradually transform to hydroxyapatite (HAP) (8, 9). There is also recent evidence that amorphous calcium carbonate (ACC) may play a key role in mineralizing vertebrate tissues like bone (10).

Abiotic mineralization pathways have been intensively investigated aiming to gain control over material properties of nanostructured composites for biomedical applications. Hydrogels are often used to template mineralization. They possess a three-dimensional porous network, and therefore, microcavities, where the liquid composition can be controlled through both the polymer functional groups and the mesh size (11, 12). However, the relation between mineralization pathway, the microstructure of the mineralized hydrogels and their enhanced mechanical properties has only received attention recently. The projection is promising; a substantial reinforcement was achieved through the enzymatic precipitation of amorphous nanoparticles of calcium phosphate distributed homogenously within a hydrogel (13). The enhanced hydrogel toughness surpassed what can be achieved with (non-interacting) nanoparticles (fillers). It also proved the efficient coupling between mineral growth dynamics and polymer network mechanics (14). Moreover, this system promoted cell attachment, proliferation and differentiation and provided sites for bone osteogenesis (15, 16). Despite these advances, the fundamental principles dictating the relation between mineralization pathways in hydrogels, their microstructure, and mechanical reinforcement, and how it influences bone regeneration, remain greatly unexplored.

Current and Future Challenges Unrevealing this relation requires solving several challenges. The influence of the polymer concentration on nucleation is critical for the microstructure of the mineralized organic scaffold. This is intricate. On the one hand, it can lead to “shadow” effects –as the polymer may hinder collisions between clusters and prevent them from reaching a critical size. On the other one, it can provide low-surface energy nucleation sites that favour nucleation. In the context of non-classical nucleation, more studies are needed to fully understand how the assembly of minerals in the organic scaffold is affected or directed by the presence of highly ionic polymer-

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induced liquid precursors. Strong interactions between the mineral and the organic phase are believed to, e.g., disturb the typical spherulitic structure of HAP in abiotic studies. However, there is still a lack of knowledge of the underlying principles.

The overall toughening of hydrogel-like scaffolds goes beyond the effects of nucleation. A crystal surrounded by a supersaturated solution exerts a thermodynamic pressure against the polymer network. Crystal growth against the polymer happens only if the disjoining pressure between mineral and crystal is smaller than this thermodynamic limit. If the polymer resists, the mineral traps the polymer during its growth (11). This disjoining pressure results from Derjaguin-Landau-Verwey-Overbeek (DLVO) and non-DLVO forces, which are greatly unknown for mineral-organic systems and difficult to measure or predict (Figure 1)(17). Polymer and solution compositions alter the disjoining pressure and could be a control mechanism for the polymer-mineral interaction, including the polymer inclusion. How amorphous precursors might affect such interaction remains also to be examined. Perhaps nanodroplets coalescing along the polymer network form a wetting film first. This film could solidify into an amorphous phase and eventually crystallize, while retaining the shape delineated by the wetting film along the polymer.

Predicting strengthening of hydrogels via mineralization poses additional challenges. Rubber elasticity models using adequate network theories could help test various hypotheses, including the often ignored but expected interactions between polymer and mineral. Polymer/mineral affinity could justify a more prominent reinforcement than simple fillers.

Advances in Science and Technology to Meet Challenges Traditional hydrogels are often too weak to withstand the mechanical requirements of tissue engineering applications, which calls for new strategies for targeted reinforcement. Hydrogel mineralization can both improve mechanical support and maintain biocompatibility, and thereby promote the growth and differentiation of stem cells and tissue regeneration. Progress in this field requires the convergence of several disciplines, including (bio)mineralization, colloidal science, polymer physics, rheology, and cell biology. Figure 2 showcases recent developments in understanding the fundamental principles that guide the mineralization pathways in hydrogels. This work focused on calcium phosphate mineralization in agarose hydrogels via ACC precursors (18). It is important to realize that methods that rely on the drying of the composites need to be considered cautiously. Drying can alter both the mineral phase and the composite microstructure. Hence, *in situ* infrared or Raman spectroscopy are ideal to examine the (co)existence of amorphous and crystalline minerals in hydrated hydrogels. They can also be useful to reveal the chemical bonds between mineral and polymer. Environmental scanning electron microscopy and dynamic light scattering can reveal how nanoparticles grow, dissolve, and reaggregate inside hydrogels. This previous work (18) showed ACP nanoparticles were larger, and the number density smaller in the absence of ACC, reflecting that ACC promoted ACP nucleation. Small-angle X-ray scattering could reveal information about interparticle interactions. The observed particle aggregation can be compared with the stability ratio based on DLVO theory to understand the mechanisms that favour or hinder aggregation(19). However, accounting for non-DLVO phenomena, like charge reversal and adhesion from ion-ion correlations, will be more challenging. In colloidal science, a common strategy to elucidate colloidal stability is to vary ionic strength, ion valency and temperature, which could be applied in future research.

Figure 2c shows that the presence of ACC also changed the morphology of HAP precipitated in agarose hydrogels and strengthened the gel. Classical models to predict the strengthening of gels by fillers predict much smaller elastic moduli than the actual values (Fig. 2f), supporting the achieved

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strong mineral-polymer interaction. It is possible that the smaller size of the ACP nanoparticles in the presence of ACC slowed down HAP crystallization, enhanced the liquid-like behaviour of ACP, and its wetting properties. All this could justify the different morphology of HAP and the strong interaction with the polymer. Nevertheless, studies that relate mineralization pathways with microstructure and mechanical properties of hydrogels are still needed to prove these hypotheses.

Concluding Remarks While hydrogels functionality and biodegradability make them suitable as scaffolds for tissue engineering, the most prominent challenges are still their inadequate mechanical strength and insufficient bioactivity. Achieving control over the strengthening of hydrogel-like scaffolds via mineralization relies on elucidating the relation between polymer properties, mineralization pathways and microstructure, the effect of solution chemistry, and the strengthening mechanisms. A suite of characterization techniques is available to examine these relations and experiments can be designed to explore specific mechanisms. Nevertheless, the parameter space is wide as not only mineral and solution composition but also polymer properties like polymer functionality, crosslinking type and self-assembly could significantly alter the mineralization pathway and the strengthening mechanisms. The delineated roadmap will be valuable to advance the knowledge and, among others, the use of mineralized hydrogels as bioscaffolds for bone regeneration. Further research will be needed to relate the principles underlying mineralization of hydrogels to their bioactivity.

Acknowledgements This material is based upon work supported by the National Science Foundation under Grant Nos. CMMI-2035122, CMMI-1435920, and Convergence RAISE program IOS-1848671.

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Figures

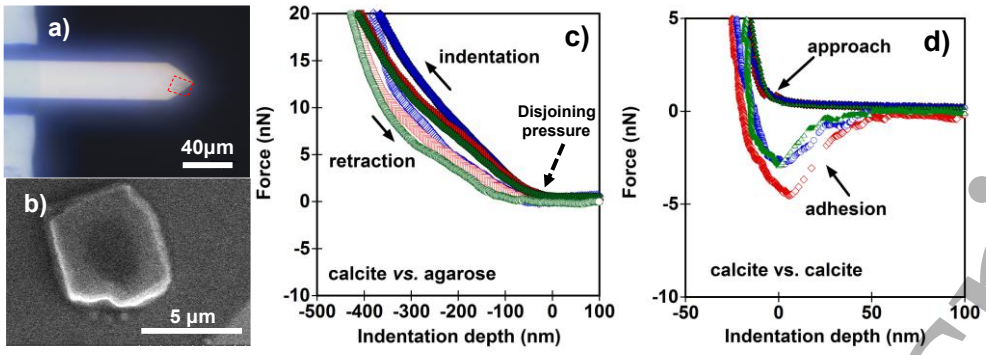

Figure 1 Measurement of mineral-polymer interactions. a) Light microscopy images of a calcite crystal glued to the AFM cantilever (red dashed square highlights the crystal) and b) SEM image of the calcite crystal glued to the cantilever. (c–d) Force–indentation curves upon extension (filled markers) and retraction (empty markers) at constant velocity of 20 nm/s measured with a calcite crystal glued to the AFM cantilever on (c) agarose hydrogels (1 wt %) and (d) a calcite crystal fixed to the AFM stage, both in a saturated calcium carbonate solution. The low adhesion energy between agarose and calcite (c) suggests the action of a disjoining force between them, which is also expected to exist during the growth of calcite within the hydrogel network. In comparison, this interaction becomes strongly attractive between two calcite crystals (d). Adapted with permission from Lopez-Berganza JA, Chen S, Espinosa-Marzal RM. Tailoring Calcite Growth through an Amorphous Precursor in a Hydrogel Environment. Crystal Growth & Design. 2019;19(6):3192-205. Copyright 2019 American Chemical Society.

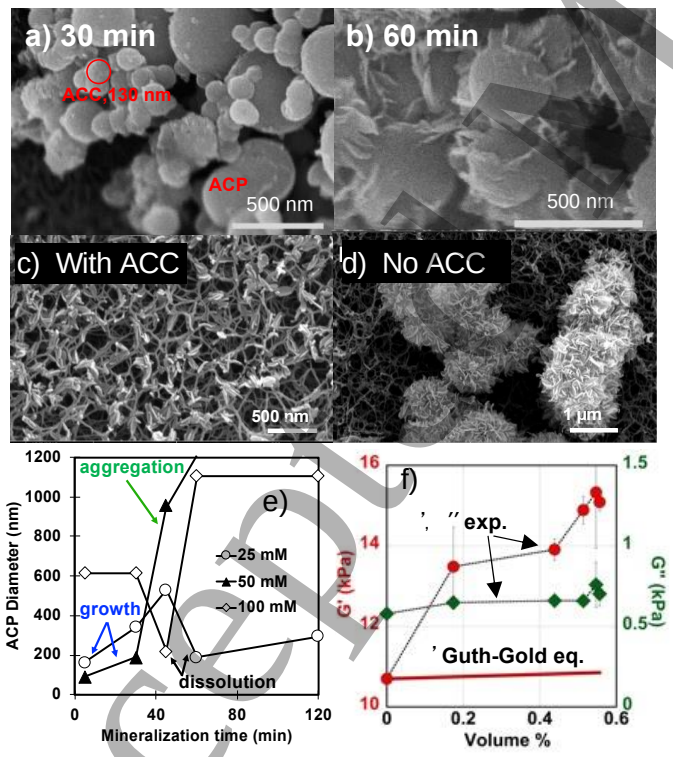

Figure 2 HAP mineralization in agarose hydrogels in the presence of ACC precursors. a-b) SEM images of coexisting ACP and ACC after 30 and 60 min mineralization, respectively. c-d) SEM images of the mineralized hydrogels; the morphology of apatite and its affinity to the polymer are altered upon mineralization via the ACC precursor. e) ACP nanoparticles growth, dissolution and aggregation in hydrogels, as measured by Dynamic Light Scattering at various equimolar concentrations of $CaCl_2$ and $NaCO_3$, Ca/P-ratio=1. f) Storage (G')

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and loss modulus (G'') as a function of HAP volume fraction. e-f) correspond to HAP mineralization via ACC precursor. ACC prolonged the stability of ACP and retarded the crystallization into HAP. Spherulitic HAP-clusters formed in the absence of ACC, while ACC led to the formation of HAP platelets deposited along the agarose network, reflecting the stronger interaction between agarose and HAP. a-e) Adapted with permission from J Lopez-Berganza JA, Fu B, Lee C-WJ, Rogers SA, Espinosa-Marzal RM. Mediating the Enhanced Interaction Between Hydroxyapatite and Agarose through Amorphous Calcium Carbonate. Crystal Growth & Design. 2020;20(10):6917-29. Copyright 2020 American Chemical Society.

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