Soft Matter Biomimetics Symposium
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Abstracts poster presentations

1. Nelda Antonovaite, VU Amsterdam

Depth-controlled indentation mapping for soft tissues and cells

There are many factors that influence the outcome of a measurement of mechanical properties of soft biological tissues and cells, including sample preparation and preservation, testing protocols, and scale of testing. Previous studies have reported that biological samples are heterogeneous, viscoelastic and exhibit nonlinear responses already at small strains. To analyze these features in more details, we have recently introduced the so-called *oscillatory indentation-depth controlled mapping* indentation approach, which is capable of capturing both the viscous and elastic component of the material at various depths, for different frequencies, and at various locations over the sample. Using this method, we have gathered high resolution (~50 μm) maps of storage and loss modulus of mouse brain tissue (hippocampus and cerebellum), and of mesoderm of *in vivo* HH10-11 chicken embryos obtained at 5.62 Hz for strains up to 10%. Our measurements show that structurally distinct regions come with different mechanical properties, indicating the existence of a clear structure-stiffness relationship. Furthermore, we applied the same method to study primary mixed glial cells where we found that the nucleus of an astrocyte is softer than its cytoplasm. Importantly, our data shows that astrocytes undergo both strain and frequency stiffening, proving that dynamic (rather than static) indentation methods should always be used to study single cells. Taken together, our study shows that our novel indentation method is able to capture nonlinear viscoelastic nature of various biological samples, from single cells to complex tissues, enabling new findings when studying the role of mechanics in biology.

Declaration of interest: Davide Iannuzzi is founder, shareholder, and advisor of Optics11.

2. Marie-Eve Aubin-Tam, TU Delft

Bacterially-produced, nacre-inspired composite materials

Biomaterials in nature are a source of inspiration for the design of high-performance materials. Nacre, a biomineralized material lining seashells, shows impressive mechanical properties due to its layered nanoarchitectures. While chemical approaches aim to mimic nacre, most involve toxic chemicals, high temperatures and/or high pressures, our approach is to use bacteria for an eco-friendly production of nacre-like materials in ambient conditions.

We use Sporosarcina pasteurii to precipitate calcium carbonate layers. In between those layers, we deposit polyglutamate produced by Bacillus licheniformis. These layered composites show a higher toughness than the same materials without polyglutamate. At the nano-scale, the bacterially-produced materials show a characteristic granular structure and nano-asperities, similar to those found in nacre and likely involved in improving mechanical properties.

3. Lennard van Buren, AMOLF

Mechanical stabilization of giant vesicles

Cellular life lives in containers that mechanically protect them from the outside world. Here, we aim to investigate this mechanoprotection in a bottom-up approach by probing the influence of a reconstituted actin cortex on the lipid bilayer membrane of giant unilamellar vesicles. We develop multiple techniques to measure the cell's mechanical properties, such as micropipette aspiration, tether pulling and FRAP.

4. Federica Burla, AMOLF

Revisiting the extracellular matrix: effect of internal stress on fibrous biopolymer networks

The extracellular matrix is a biopolymeric network which supports cells and provides them with mechanical cues. This scaffold shows a remarkable adaptiveness to external deformations, as it is able to dramatically stiffen at high strains, thereby guaranteeing tissues' integrity. The response of

tissues to external mechanical deformation was extensively addressed and understood in reconstituted, one-component systems of collagen. However, an equally important role in a tissue's response to strain is played by internal stresses, which can be generated, for example, by the intrinsically composite nature of living matter. Here we set to investigate the role of internal stresses in two model systems of tissues. The first, mimicking cartilage, reveal that the presence of hyaluronic acid in a tissue plays a crucial role on the collagen networks' response to strain. The second, mimicking a healing tissues composed of fibrin and collagen, seems to reveal that these two interpenetrating networks are exerting mutual stresses onto each other, with potential implications in tissue remodelling.

5. Henri de Gagny, University of Amsterdam/Unilever Research Center Vlaardingen

Mechanical properties of soft semi solid composites

Fat based products are an essential part of food industries. Examples include chocolate spread, margarine, biscuits or bouillon cubes. Such materials are made of a continuous fat phase in which solid particles are dispersed. Phenomena such as yield and fracture occur in those materials and depend heavily on the composition of the samples.

The crystallization of fat is altered in presence of particle, which leads to products with different properties. However, very little work has been done to characterize the influence of the solid particles on the final product. In these studies, small amplitude oscillatory rheology is often used to characterize the stiffness of the materials. But processed products might not meet the desired geometry necessary to perform measurements with proper boundary conditions and in absence of wall slip.

This poster covers various mechanical properties of materials consisting of hard fat mixed with solid particles, such as salt and the way to measure them. We study the influence of the volume fraction of the inclusions on the linear deformation of the samples, but also on non linear phenomena such as the fragmentation of the materials. Finally, we also show that the addition of water in the mixture can have a dramatic influence on the hardness of the samples by forming capillary bridges between inclusions and thus forming a coherent structure.

6. Eliane van Dam, AMOLF

Correlation of molecular water dynamics and visco-elastic behavior in a biomolecular hydrogel

Hyaluronic acid is a biopolymer that shows a fascinating pH-dependent macroscopic response: it changes from a liquid to an elastic state in a narrow pH range around pH 2.5. We study the role of water in the formation of this elastic state by measuring the dynamics of water in solutions of hyaluronic acid in the liquid and elastic state with polarization-resolved infrared pump-probe spectroscopy. We observe that a fraction of the water molecules shows much slower reorientation dynamics ($\tau or > 10$ picoseconds) than bulk water ($\tau or = 2.5$ picoseconds). These slow water molecules are interacting with the hydrophobic parts of the hyaluronic polymers. Interestingly, the fraction of slowed-down water decreases substantially upon the formation of the elastic state, which shows that the formation of the elastic state involves the expulsion of water from the surfaces of the hyaluronic acid polymers, leading to hydrophobic aggregation of the polymer chains into a macroscopically connected network.

7. Mani Diba, Eindhoven University of Technology

Development of Light-Responsive Hydrogels Using Plasmonic Nanoparticles

Hydrogels are three-dimensional interconnected networks dispersed in an aqueous phase. Hydrogel systems that are dynamic and can alter their properties in response to external stimuli are highly attractive for various biomedical applications. Consequently, this study aims to investigate the development of light-responsive hydrogels using gold nanoshells (GNSs) and supramolecular hydrogelators as building blocks. To this end, GNSs were synthesized using silica cores through a seeded growth strategy, and supramolecular hydrogelators were synthesized by functionalizing poly(ethylene glycol) with four-fold hydrogen bonding ureido-pyrimidinone (UPy) units.

Supramolecular hydrogels could be successfully prepared containing various concentrations of GNSs. The GNSs were uniformly dispersed within the hydrogel matrix, and individual GNSs could be tracked using dark-field microscopy, even at high GNS concentrations (3*10^10 GNSs/mL). The supramolecular hydrogel matrix confined the GNSs in place, and impeded their intrinsic Brownian motion. Further investigations will focus on the evaluation of the response of GNSs-hydrogel nanocomposites to light illumination.

8. Jan Maarten van Doorn, Wageningen University

Strand Plasticity Governs Fatigue in Colloidal Gels

The repeated loading of a solid leads to microstructural damage that ultimately results in catastrophic material failure. While posing a major threat to the stability of virtually all materials, the microscopic origins of fatigue, especially for soft solids, remain elusive. Here we explore fatigue in colloidal gels as prototypical inhomogeneous soft solids by combining experiments and computer simulations. Our results reveal how mechanical loading leads to irreversible strand stretching, which builds slack into the network that softens the solid at small strains and causes strain hardening at larger deformations. We thus find that microscopic plasticity governs fatigue at much larger scales. This gives rise to a new picture of fatigue in soft thermal solids and calls for new theoretical descriptions of soft gel mechanics in which local plasticity is taken into account.

9. Giulia Giubertoni, AMOLF

Molecular origin of the elastic state of aqueous hyaluronic acid

Biological hydrogels have an extraordinary ability to respond to environmental cues by tuning their mechanical properties, which is important in their function of regulating the mechanical properties of cells and tissues. Although the macroscopic mechanical properties of biological hydrogels are broadly studied and successfully mimicked in synthetic materials, little is known about the precise molecular interactions that mediate these properties. Two-dimensional infrared spectroscopy (2D-IR) is ideally suited track interactions at the molecular scale. Here we use 2D-IR to study the pH-induced gelation of hyaluronic acid, a ubiquitous biopolymer, which undergoes a transition from a viscous to an elastic state in a narrow pH range around 2.5. We find that the gelation originates from the enhanced formation of strong inter-chain connections, consisting of a strong double amide-COOH hydrogen-bond and a strong N-D-COO- hydrogen bond on the adjacent sugars of the hyaluronan disaccharide unit. The enhanced inter-chain connectivity in the elastic state is confirmed by AFM measurements that reveal the association of hyaluronan into thick strands in this state.

10. Fabiola Gutierrez, Wageningen University

Development of Poly (Arginine) grated gelatine-colloidal silica composites

In this work we present the development of composites of Gelatine-Silica. These composites can be used as additives for encapsulation and as drugs and nutrients carriers and therefore are of high interest for food and pharmaceutic applications. In particular we present a system consisting of methacrylate gelatine and colloidal silica.

Although silica particles (negatively charged) can interact electrostatically with some (positively charged) groups in gelatine and hydrogen bonding, it is not very clear which conditions are needed to form stronger composites. Here we propose a model system to enhance the affinity of the gelatine to the silica using peptides. We graft the gelatine (Type A) with positively charged polypeptides (Poly Arginine, n= 30); by varying the grafting density, we aim to increase systematically the electrostatic interactions of the gelatine with the silica particles and thereby to reinforce que mechanical properties of the composite. We prepare composites with different %w of colloidal silica (Ludox, 25 nm) at a stable pH 8. After 15% silica content, the composites phase separate. We are interested in analysing a continues phase.

11. Stefan Kooij, University of Amsterdam

Fragmentation of Prince Rupert's drops

Fragmentation is involved in a great number of phenomena and applications and covers a large range of length scales. Prince Rupert's drops (also known as 'Dutch tears') undergo an explosive fragmentation process due to their huge internal stresses: we find that a millimeter-sized object fragments into more than 20,000 pieces. To identify the underlying statistical process, the distribution of fragment sizes was determined using micro-CT analysis. We find that the fragment sizes are exponentially distributed, which compares favorably to finite-element simulations, and demonstrates the random nature of the fragmentation process. This contrasts with power-law distributions, often observed for sequential breaking events.

12. Cristina Martinez Torres, AMOLF

Elucidating the physical basis of blood clot stability

Fibrin, the main structural component of blood clots, provides a highly extensible scaffold that stiffens several orders of magnitude upon deformation, conferring the clot with the mechanical durability it needs to withstand blood flow and tissue remodelling. When the clot is no longer needed, the fibrin scaffold needs to rapidly and completely disappear to ensure normal blood circulation, showing an 'all-or-nothing' behaviour not found in any other biomaterial. But how does the molecular system 'know' when the fibrin scaffold is needed and when it must disappear? Interestingly, clots under mechanical strain have been shown to be protected against enzymatic degradation, suggesting that clot stability may be regulated by a physical mechanism involving the mechanical regulation of protein activities.

We use a quantitative and multiscale biophysical approach to elucidate the role of mechanical strain in clot stability, allowing to distinguish between the mechanisms involving strain-induced changes in the structure at the network scale which modify the access of proteolytic enzymes, from mechanisms involving strain-induced structural changes of the fibres.

Given the natural functions of fibrin, understanding the mechanisms that regulate its lifespan is of particular relevance for the design of clinical products employed in wound healing and in tissue engineering, offering the possibility to design smart and fully biocompatible scaffolds.

13. Melle Punter, AMOLF

Clogged mayonnaise - pushing low yield stress mayonnaise through a semi-permeable membrane

To have a better understanding of the expulsion of fluid from light mayonnaise, low yield stress mayonnaise was pressed through a semi-permeable membrane by the hydrostatic pressure of a mayonnaise column. We explain the measured expulsion of fluid using Darcy's law, mass conservation, and by considering the experimental setup as a sequence of a horizontal region, connecting the semi-permeable membrane to the mayonnaise column, and a vertical region, representing the mayonnaise column. The observed linear dependence of the rate of fluid expulsion to the height of the mayonnaise column, turns out to be a consequence of high fluid velocity in the horizontal region and low fluid velocity in the vertical column. Finally, we find the relative size of the horizontal and vertical region, and the permeability of the oil droplet layer blocked by the semi-permeable membrane.

14. Joep Rouwhorst, University of Amsterdam

Colloidal gelation as a nonequilibrium continuous phase transition

A new view on gelation as a second-order nonequilibrium phase transition is presented using combined experiments on critical Casimir colloidal suspensions, simulations, and analytic solutions to a simplified master kinetic equation. The experiments and simulations show cluster sizes and correlation lengths diverging with exponents 1.6 and 0.8, respectively, consistent with growth exponents in percolation theory. Cluster masses exhibit power-law distributions with exponents -3/2 and -5/2 before and after gelation, respectively, as predicted by the master kinetic equation with single-bonded particle detachment. Because detailed balance is violated in this process, our results

univocally point to gelation as a nonequilibrium continuous phase transition (nonequilibrium percolation). This makes gelation, where fluid particles aggregate and percolate into rigid structures, an analogue, mirror-image process of yielding, where emerging fluid-like particles percolate within a rigid matrix.

15. Maria Raquel Serial, Wageningen University

Selective oil-phase rheo-MRI velocity profiles to monitor heterogeneous flow behavior of oil/water food emulsions

Rheo-MRI is becoming an established technique in food soft matter research. Since NMR imaging (MRI) allows to acquire velocity profiles of the sample during shear, it is possible to determine the structure and rate of deformation of the material non-invasively1. In the past years, rheo-MRI has been successfully applied to the characterization of multi component food materials, in particular to assess their behaviour as shear thinning yield stress fluids. The velocity and density profiles obtained by rheo-MRI allow for unambiguous recognition of shear banding and non-local properties.
In the current work we have addressed the study of non-linear flow of oil/water and mayonnaise systems by means of rheo-MRI in a standard micro-MRI probehead of a wide bore 7 T system (1H NMR frequency of 300 MHz). At this high magnetic field oil/water food emulsions display well resolved NMR spectra with a 3.5 ppm separation between the main oil and water peaks. This provided the opportunity to specifically record the local density and velocity of the oil droplet phase. We have modified the standard spin-echo sequence to measure flow by adding chemical selective signal suppression pulses. In this way, suppression of the signal of the continuous water phase allowed to obtain rheo-MRI velocity profiles of the oil droplet phase with high signal to noise ratio. This approach was successfully applied to mayonnaises with distinct shear thinning yield stress properties.

16. Markus Weingarth, Utrecht University

New design parameters for tissue engineering scaffolds

Stem cells are actively regulated by the mechanical and nano-topological properties of their microenvironment, which provides critical cues for cellular migration, differentiation, and proliferation. This paradigm has critical implications for the design of biomimetic stem cell substrates which promise fascinating applications in tissue engineering and regenerative medicine. Tissue engineering scaffolds and their mechanical and morphological parameters are commonly probed with micro- or macroscale methods such as AFM or Rheology.
Here, we introduce a cutting-edge spectroscopic method with broadest applicability that provides unique high-resolution information on biomimetic tissue engineering scaffolds at physiological conditions. We demonstrate our high-resolution method on a series of functionalized peptidic-scaffolds and explain at the atomic-level the parameters that favour the viability of neural human stem cell (hNCS). Finally, we validate our findings with functional studies and compare them to macroscopic methods. Altogether, our high-resolution method provides unique insights for the design of tissue engineering scaffolds and other biomimetic materials.

17. Dan Jing Wu, Eindhoven University of Technology

Dynamic supramolecular thermoresponsive scaffold with controlled modularity and motion

3D processing techniques have been widely used for the development of biomaterials. However, the objects produced are rather static and inanimate. Therefore, stimuli-responsive materials for 3D processing are explored to induce motion due to external stimuli. An interesting example is the thermoresponsive polymer, poly(N-isoproylacrylamide) (PNIPAM), that swells or shrinks due to temperature dependent phase separation in water (lower critical solution temperature; LCST). However, these stimuli-responsive polymers lack modularity in the combination with bioactive components to create the desired biomaterial. Therefore, we propose to use supramolecular chemistry to produce a supramolecular thermoresponsive polymer to control scaffolds in a dynamic way.

This supramolecular thermoresponsive material can be used for a wide range of potential biomedical applications. The temperature change can induce efficacy, programmability and speed in transformation of material geometry. Supramolecular UPy-UPy system provides a modular approach to mix and match different polymers in a controlled manner and therefore versatile scaffolds for various applications can be produced.

18. Qimeng Wu, Wageningen University

Exploring the microscopic origin of elasticity in model low fat mayonnaise

Low fat food products often contain natural, edible polymers to retain the desired mouth feel and elasticity of their full fat counterparts. However, this type of product often suffers from syneresis; the densification due to the expulsion of fluid. Understanding the origin of the elasticity in such soft hybrid dispersions is crucial for product stability against syneresis. Due to the complexity of real food systems, we have developed a system comprising monodispersed copolymer droplets, mixed with three topologies of the same polymer, polyacrylic acid (PAA):linear coils, micrometer sized hydrogels, and sub-granular Carbopol. We use a suspending mixture of DMSO and water which refractive index matches the droplets while dissolving the PAA. For these samples, the particle coordination number and local mobility are analysed from 3D structure using confocal microscopy as the system is optically transparent. Additionally, the macroscopic elasticity of the mixtures is measured with rheology. We found that the droplets mixed with Carbopol are more mobile with higher coordination numbers compared to linear PAA at the same weight fraction of polymer; concurrently a lower storage modulus is measured with Carbopol than with linear PAA. This may indicate the presence of a colloidal network formed when mixed with linear PAA, while droplets form dense glassy pockets when mixed with Carbopol. Relationship between 3D microscopic structure and the macroscopic elasticity is discussed.

19. Florian Wruck, AMOLF

Force sensing by single molecules

Here we designed and constructed molecular force sensors that allow force readout via fluorescence, utilizing FRET for a range of different forces in the piconewton range. During development of these molecular force sensors we characterized them on the single molecule level using combined confocal fluorescence and correlated optical tweezers force spectroscopy. The physical constrains imposed by the utilization of confocal microscopy to measure fluorescence of a single fluorophore suspended on a tether between two optically trapped beads required the development of single molecular spacers with a length of several hundred nanometers that do not interfere with the physical characteristics of the molecular force sensor. These characterized molecular force sensors will be used to visualize forces in two and three dimensions within transparent polymer gels.