Decadal Survey on Biological and Physical Sciences Research in Space 2023-2032

Topical White Paper

Title: What follows is **Chapter 6**,

Soft matter, bioscience, and biotechnology—evolution and the marginal stability of life

from the Report from the APS Division of Soft Condensed Matter Physics
DSOFT, NASA sponsored Workshop on:
Grand Challenges in Soft Matter Science: Prospects for Microgravity Research,
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Executive Summary

The worldwide community of soft matter has grown rapidly in size, impact, and scope since the last NASA report in 2003 as evidenced by the organization of the new Division of Soft Matter (DSOFT) at the American Physical Society, and the arrival of a dedicated international journal "Soft Matter" published by the Royal Society of Chemistry. At the suggestion of NASA's Physical Science Research Program in the Space Life and Physical Science Research and Application Division[1] for an update of the 2003 report on the NASA Soft and Complex Condensed Matter Workshop, Paul Chaikin, Noel Clark, and Sidney Nagel, organized a focus session and workshop for the 2020 American Physical Society (APS) March meeting under the auspices of the DSOFT. Due to the COVID–19 pandemic, the March meeting was canceled and the workshop "Grand Challenges in Soft Matter and Opportunities for Microgravity Research" was reincarnated as a remote Zoom (Zoom Video Communications, Inc.) meeting convened Thursday, March 26, 2020, from 11:30 a.m. to 1:30 p.m. EST. After a brief introduction, the ~100 participants (mostly from the United States with several joining from the European Union) separated into eight breakout sessions on

1. Self-organization only possible far from equilibrium—machines making machines
2. Instrumentation—from neuromorphic computing to large-scale self-assembly
3. Suspensions, foams, emulsions, colloids, and granular materials—self-healing, tuning gravity, and life support for exploration
4. Packings, simulation, and big data—artificial intelligence emulation of soft matter
5. Mechanical metamaterials and topological soft matter: allostery and auxetics—distributed energetics and mutation upon deployment
6. **Soft matter, bioscience, and biotechnology—evolution and the marginal stability of life**
7. Active patterning and structure formation—self-limiting assembly, actuation, and integration
8. Fluids: liquid crystals—self-assembly of the superlarge and superweak active clothing

The participants then reassembled for a presentation of conclusions and general discussion. Three overarching themes emerged from this workshop and are presented with additional details:

- Machines made out of machines
- Scalable self-sustaining ecosystems
- Active materials and metamaterials

[1] Space Life and Physical Science Research and Application Division has moved to the Science Mission Directorate and is now the Biological and Physical Sciences Division.

2.6 Soft Matter, Bioscience, and Biotechnology

The field of soft matter began with early humans learning to deal with the soft, which apart from air and water, were largely the materials of life: hierarchical assemblies and composites spanning the full range of structural behaviors from liquid to solid, driven and evolved into active information-rich nonequilibrium states and structures by solar power. After millenia, the emergence of modern science was finally able to disentangle the science of soft matter from the science of life, and pursue the physics and chemistry of polymers, gels, emulsions, surfactants, colloids, and LCs as fields of materials research. Consequently, the cross-fertilization between soft matter and biology has been extensive, and now, in a turnaround, moves toward imbuing the broad range of soft materials with more lifelike properties, an emergence largely evolved by the ingenuity of chemists. The building blocks now have properties such as activity; recognition capability; chemical, temperature, or light sensitivity; and the ability to change shape.

One theme that arose in the workshop was why not go one step further and let them "think" and communicate. A basic question then is how to understand, control, and use such a complex dynamical system, so that it does not destroy itself chaotically (Wu et al., 2017). It appears that such questions will drive much of 21st-century soft matter science. While 19th-century science invented equilibrium thermodynamics and statistical mechanics, and the 20th century learned to apply these methods to understand the equilibrium properties of soft matter, the focus of the 21st century is nonequilibrium statistical mechanics, phenomena, and dynamics, ranging from the physics of swimming to understanding the origin of life.

2.6.1 Polymers

There is a major difference between synthetic polymers such as polystyrene and polyethylene in solution and biopolymers such as polypeptides and nucleic acids (NAs); the bonds keeping the chains intact are stable for the synthetic ones but only metastable for those that occur in biology (Dobry et al., 1952). This is evident given that there are nonactive enzymes that are able to cleave the peptide or sugar linkages in biopolymers. Polymer theory should be reexamined for this class of metastable, living polymers. In particular, the entanglements of the polymers will be essentially different and needs to be worked out in detail. This has been partially investigated for somewhat similar cylindrical microemulsions. More specifically the rheological behavior, especially in the presence of the cleavage enzymes, should be investigated both in vitro and in vivo. This presents one significant challenge for the field.

The metastability of the biopolymers could be even more significant for the case of intrinsically disordered proteins (IDPs), which are often polyampholytes. IDPs exhibit many biologically relevant instances of protein-protein phase separation. This has been well documented in the last few years (Yongdae and Brangwynne, 2017). These molecules provide a whole set of new degrees of freedom where the polymers could become shorter or longer by breaking as well as by stretching. The field needs to be revisited in detail. The metastability coupled to active substrates, motors, chemical reactions, and other energy-dissipating processes may lead to a rich landscape of phase behaviors from equilibrium (no active elements) to dynamic (in the presence of active elements).

2.6.2 Prospects

Hierarchical assembly has been an active area of research for decades (see the Nation Research Council report "Hierarchical Structures in Biology as a Guide for New Materials Technology" (1994) for example). However, multiscale active biological structures such as microtubules, chromatin, or neurofilaments have not yet to our knowledge been achieved in synthetic systems. One of the

experimental constraints is that gravitational sedimentation or creaming limits them to nanosize objects. However, in microgravity, one can make much larger entities. Thus, an important challenge with many potential applications is in the direction of self-assembly of large objects where microgravity could play a pivotal role.

Over the last few years, it has become increasingly clear (Smith, Lee, and Perkin, 2016) that the range of validity of Debye-Hückel theory of electrolyte solutions (i.e., salty water) is limited to tens of millimolar concentrations for even one to one salts (e.g., NaCl). This calls for new methods to measure electrostatic screening such as the use of x-ray and neutron scattering (both elastic and inelastic) to probe ion-ion correlations in polar solvents. The theoretical situation also remains murky. While an established field, it is crucial for the control of biomolecular assembly, and merits clarification. For example, the old problem of the ionic-strength dependence of the polyelectrolyte persistence length is very likely associated with this issue.

It is important to emphasize that there are many basic aspects of soft matter equilibrium that have not yet been fully developed. These include Debye screening and electrostatics, for example, where behavior at high ionic strength is a dynamic current research field. Likewise, there are many unanswered questions regarding hierarchical self-assembly, of artificial microtubules, for example. In addition, the physics of protein-protein phase separation, IDPs and multiple structures, and issues having to do with polymer solutions, polyampholytes, and polyelectrolytes need more clarity.

Another very broad challenge has to do with dealing with systems, with or without activity, that are far from equilibrium. In the context of biology, this emphasizes complex (in charge and sequence) polymers and includes understanding motility-induced phase separation (Cates and Tailleur, 2015).

2.6.3 Soft Matter and the Origin of Life

The advance of biology in the 19th century fostered an intense scientific interest in understanding the origin of life, which developed in the 20th century with the flowering of biochemistry and cell biology, principally around the notion that the mystery of life's emergence was a problem in chemistry. Some remarkable insights were gained in this effort, not the least of which was that in the universe and early Earth, there were amino acid, NA, and lipid components, as well as accidental chemical reactions that could produce them from primitive molecular species. As this work progresses in the new century, the understanding of the physical states and collective soft matter organization of prebiotic systems have received increasing attention as key parts of the story.

The emergence of early life, by definition, requires feedback: molecular selection and replication self-organized around some purpose, which in the earliest stages must be the stabilization and protection of active soft matter self-assemblies: "Soft matter" because it permits the coexistence of structure and chemistry, and "active" because the overall process is inherently nonequilibrium. Hierarchy develops as complementary feedback systems begin to interact, and all this evolves in the realm of marginal solubility, where the insoluble molecules are lost, the readily soluble are just part of the solvent, and the action is among molecules that must collectively interact into order to stay in solution. Figure 8 and Figure 9 show this in action for lipids and NA oligomers in which, for the latter, LC columnar ordering strongly promotes NA ligation and thereby the stability of the columnar phase (Fraccia et al., 2015). The grand challenge is to advance the science of templating and molecular replication by soft matter (He et al., 2017) to the state in which the regime of accidental chemistry can be connected with that in which autocatalysis stabilizes and evolves collective ordering.

2.6.4 Microgravity

Several problems related to biological activity such as hierarchical self-assembly, particularly from activity, would profit from making isolated model systems. This recalls the question of MIPS discussed earlier in this report. So far, this has only been investigated in two dimensions because of gravity, for example, due to sedimentation of the active swimmers. Microgravity allows experiments in the appropriate three dimensions. We now have some artificial systems that show templated self-replication

and exponential growth (He et al., 2017). When extended to the colloidal scale, it will be interesting to compare two-dimensional (2D) versus 3D growth. It would also be interesting to use microrheology to study the rheological behavior of polymers in the presence of cleavage enzymes in mesoscopic samples unsettled and undisturbed for long periods in microgravity.

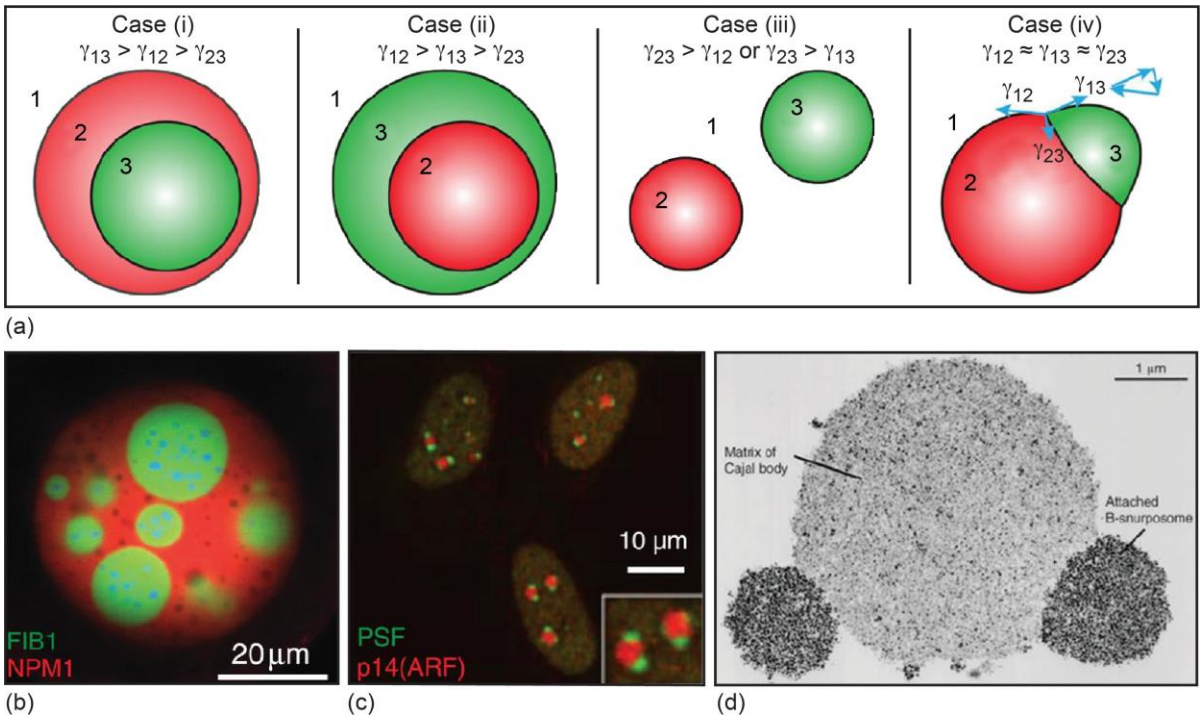

Figure 8.—Surface tension and multiphase droplet architecture. (a) Relative surface tensions among different possible interfaces (g_{ij}) dictate droplet architecture. Minimizing free energy of system requires minimizing energetically costly interfaces. For example, in Case (i) the costly 1–3 interface (g_{13} large) is avoided by phase 2 enveloping phase 3, whereas Case (ii) achieves opposite. For Case (iii), interface between the two droplets is costly (high g_{23}), and thus, droplets do not contact one another. When relative energetic costs are comparable, all three phases can have shared interfaces, as shown in Case (iv). Surface tensions from three interfaces are balanced, forming Neumann's triangle. (b) Multiphase nucleolus after actin disruption in *Xenopus laevis* nucleoli. (c) Transcription inhibition leads to reorganization of nucleolar architecture, forming perinucleolar caps bound to nucleolar bodies in HeLa nucleoli. (d) Electron micrograph showing *X. laevis* Cajal body with attached B-snurposomes. Adapted from Yongdae and Brangwynne, 2017.

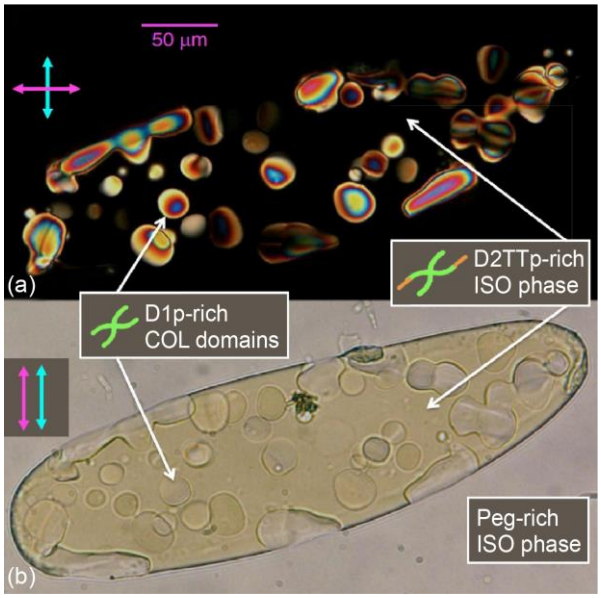

Figure 9.—Aqueous microdroplet reactor for liquid crystal (LC) autocatalysis of ligation of the deoxyribonucleic acid (DNA) 12-mers D1p (brightly birefringent under crossed polarizers). Duplex 12-mers D1p and D2TTp phase separate from polyethylene glycol (PEG) solution, forming yellow drop and then further separated into columnar (COL) LC domains of D1p (brightly birefringent under crossed polarizers) and dark isotropic (ISO) domains of non-LC-forming D2TTp. Having distinct LC and non-LC DNA phases enables comparison of ligation efficiency at same DNA density. Ligation is much more rapid in D1p LC fraction. Second phase transition takes place within DNA-rich droplet after it was already separated from PEG-rich ISO phase, appears from continuous and smooth interface with PEG-rich phase that enclose both DNA ISO and DNA LC domains. (a) DNA-rich droplet imaged under crossed polarizers. (b) DNA-rich droplet imaged under parallel polarizers. Adapted from Fraccia et al., 2015.

References

Extensive references are provided for NASA/CP-20205010493, pp. 26-29, at https://ntrs.nasa.gov/api/citations/20205010493/downloads/CP-20205010493%20Final.pdf.