Essay: Collections of Deformable Particles Present Exciting Challenges for Soft Matter and Biological Physics

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(Received 14 November 2022; published 30 March 2023)

The field of soft matter physics has expanded rapidly over the past several decades, as physicists realize that a broad set of materials and systems are amenable to a physical understanding based on the interplay of entropy, elasticity, and geometry. The fields of biological physics and the physics of living systems have similarly emerged as *bona fide* independent areas of physics in part because tools from molecular and cell biology and optical physics allow scientists to make new quantitative measurements to test physical principles in living systems. This Essay will highlight two exciting future challenges I see at the intersection of these two fields: *characterizing emergent behavior* and *harnessing actuation in highly deformable active objects.* I will attempt to show how this topic is a natural extension of older and more recent discoveries and why I think it is likely to unfurl into a wide range of projects that can transform both fields. Progress in this area will enable new platforms for creating adaptive smart materials that can execute large-scale changes in shape in response to stimuli and improve our understanding of biological function, potentially allowing us to identify new targets for fighting disease.

Part of a series of Essays which concisely present author visions for the future of their field.

DOI: 10.1103/PhysRevLett.130.130002

Characterizing emergent behavior and harnessing actuation in highly deformable active objects lie at the intersection of the fields of soft matter and biological physics. They pose challenges but also present many opportunities for physics discoveries and technological advancement. The extra degrees of freedom available when one allows changes to particle shape—alterations to the size, aspect ratio, or other geometric features of a particle—can generate beautiful results in largely unexplored realms.

Here *deformable particles* are defined as the constituent parts of a macroscopic material (composed of many such particles), where the small-scale particles can significantly change their shape over time or space, either due to interactions with other objects or actively according to some internal programming. Examples that may prove interesting are highly compliant gel beads, emulsion droplets, mammalian cells, molecules with multistable configurations, and some colloidal assemblies, to name a few. Because of their ability to change shape, these particles can adopt dynamics and behavior that resemble those of *liquid crystals*, *granular materials*, and *active matter.*

Since deformable particles can become elongated or disklike, their behavior resembles that of liquid crystals. The discovery that systems of molecules or particles with special, fixed geometries—such as ellipses, rods, or disks—would spontaneously develop phases in which some degrees of freedom exhibited crystalline order while others remained fluidlike was one of the first important successes in soft matter physics [1,2]. Using virial expansions and hydrodynamic theories combined with clever experiments, researchers were able to predict and verify phases, instabilities, and patterns and to understand how boundary conditions and curvature interact with underlying liquid crystalline order to generate defects and forces [3].

Moreover, the behaviors of dense deformable particles must also be related to glass physics and the jamming transition in granular matter. Dense emulsions and biological tissues composed of deformable cells both exhibit glassy dynamics [4] and rigidity transitions that occur while the system remains disordered. There is hope that deformable matter could be amenable to be described by the same theories that capture such transitions, including predictions for rigidity based on equating the number of constraints with the number of degrees of freedom, as well as replica symmetry-breaking theories for the mean-field behavior of glasses [5].

Deformable particles are also connected to active matter, which is composed of particles with energy injected at small scales. Active matter leads to phenomena that are not found in passive materials [6], including giant number fluctuations [7] and motility-induced phase separation [8]. More recently, scientists have begun to study materials with elements that engage in nonreciprocal interactions, where the force of particle a on particle b is not the same as b on a [9], and where the abrogation of Newton's third law also generally comes from energy injected at small scales [10]. The symmetries broken in these nonreciprocal systems allow all sorts of new mechanical phenomena, such a odd elasticity, where nonconservative interactions at the microscopic scale can allow energy to be injected or extracted from a material during a strain cycle [11]. Since a particle changing its shape over time in a dense field of other particles generally uses energy to perform work on the surrounding system, a collection of such particles can also be considered as active matter.

Importantly, almost all the existing research in the fields of active matter, jamming, and liquid crystals assumes that the constituent parts have fixed geometries. The big open physics questions, then, are the following: What happens if the particle shapes passively or actively change? What if their shapes can be tuned by environmental triggers or local feedback? What are the new possibilities for science and engineering, in terms of new types of physics, understanding features of biology, or making new materials? By addressing these questions, we could potentially design or self-assemble materials that take advantage of deformable particles to drive patterning or structures that are inaccessible with fixed particles. As many living systems take advantage of such functionality, we could design bioinspired actuatable materials with applications in fields like soft robotics or computing materials; we could identify new mechanisms that help drive morphogenesis in development and cancer tumor formation, possibly helping to identify unexpected targets for therapeutics.

One area that could be foundational is focused on developing a general Poisson-bracket formalism for a hydrodynamic theory of liquid crystals [12]. The authors of Ref. [12] explicitly retain a term, denoted $R(x)$, which represents the dynamics of the shape of the molecule, and they demonstrate that the standard expression for the nematic order parameter is a limit of this more general expression when there is no spatiotemporal variation in $R(x)$. In an extension of this article, a hydrodynamic theory for biological tissues [13] explored one specific biology-inspired coupling between shape and self-propelled polarization and found interesting pattern formation such as asters and stripes. A related body of work used a shape deformation tensor similar to $R(x)$ to describe *individual* self-propelled particles and investigated collective behavior for a few different choices of interactions between shapes and self-propulsion, identifying distinct patterns like crystals and global polarization [14]. Given the myriad patterns generated by these simple models, it might be worth exploring additional hydrodynamic theories with other nontrivial couplings between $R(x)$ and polarization.

Other work has focused on developing and analyzing simulations for deformable particles. One set of papers represents deformable particles as a ring of springs (in 2D) [15] as shown in Fig. 1(a), or a mesh network with the topology of a sphere (in 3D) [19], with a macroscopic energy functional that depends on the perimeter (surface area) and the area (volume) of the particle. Another approach introduces an "active foam" model for cells in a 2D monolayer [16], shown in Fig. 1(b), which assumes each cell has a fixed area and a line tension associated with its perimeter. The models make different choices for effective friction, repulsion, and adhesion between particles; the rings are purely repulsive and have a jamming transition that shares some similarities with that of ellipses. The active foam is adhesive and exhibits a jamming transition at lower densities and adhesivity, while approaching a different type of rigidity transition in the limit of high densities and adhesions, where the particles become confluent with no gaps or overlaps between the cells. The confluent limit of the active foam model is nearly identical to vertex and Voronoi models for biological tissues. These models represent cells as polygons that are required to tile space, with only one edge to represent both cell interfaces, which means that it is not possible for cells to slide past one another.

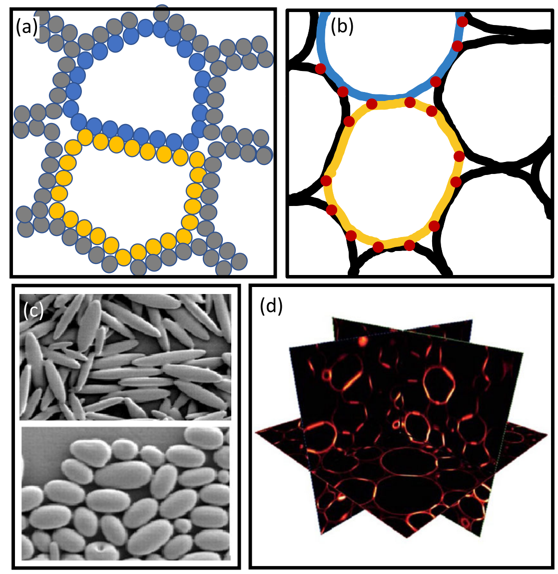

FIG. 1. Examples of deformable and actuatable particles in simulations and experiments. (a) Schematic of deformable particle model composed of beads connected by springs with additional energetic terms constraining the area and perimeter of particles. Adapted from [15]. (b) Schematic of active foam model for deformable particles with fixed area and specified tensions along each edge. Triple vertices are shown in red. Adapted from [16]. (c) PLGA particles that change the magnitude of ellipticity of their shape when exposed to stimuli such as temperature and pH. Adapted from [17]. (d) Three-dimensional reconstruction of an adhesive emulsion where adhesive molecules are fluorescently labeled. Adapted from [18].

While rigidity transitions in jammed particle systems are described by constraint counting, which arises from considering first-order perturbations to edge lengths or perimeters, the rigidity transition in vertex models typically occurs when there are fewer constraints than degrees of freedom, via a mechanism that depends on second-order perturbations to cell shapes [20–22]. Since many useful materials such as dense emulsions and most biological tissues are *nearly confluent* with small gaps between cells or particles, an interesting open question is how these systems interpolate between these two types of rigidity transitions. One hint comes from results for jammed ellipse packings, where one can enumerate the perturbations that cost energy to both first and second order and demonstrate that there is a generalized constraint counting for both types of perturbations that predicts rigidity [23,24]. Another hint comes from a theory for vertex models that uses a different constraint counting to predict how multifold-coordinated vertices alter the second-order rigidity transition [25].

The nature of the rigidity transition is also interesting from a design standpoint: in jammed systems one tunes the stiffness by pruning the number of bonds (possibly preferentially according to the stress along the bonds) [26], while in second-order rigidity systems like vertex models, the connectivity remains fixed and the stiffness can be tuned by changing the intrinsic shape of the particles (i.e. the preferred perimeter). One wonders if there is an interesting design space that uses interactions between network connectivity and shape in these systems to tune stiffness and fluidity.

Although many of these simulations and theories are inspired by biological cells, it is important to note that there are existing soft matter experimental systems that explore this design space. To investigate the effects of adhesion, emulsions can be coated with DNA or other adhesive molecules such that emergent properties of the emulsion can be tuned by the engineered adhesion, shown in Fig. 1(d) [18]. To explore the effects of shape, polymer-based particles have been designed that switch ellipticity in response to stimuli such as temperature and pH [Fig. 1(c)] [17]. More complex shapes are accessible in DNA-colloid systems that are folded into programmed patterns [27] and could be actuatable. Aqueous two-phase systems like DNA droplets or coacervates might be ideal for patterning via reaction-diffusion-advection systems. More design options for shape-changing particles are detailed in a recent review article [28]. In addition to these soft matter systems, the scientists working on developing synthetic cells for applications in understanding evolution and development [29] might be able to repurpose those systems to explore their collective physical behavior.

In many of these cases, the particles must be at quite high densities so that interactions between particles induce significant deformation. An important point is that active matter—even in nondeformable particles—has been relatively underexplored at very high densities, where motility-induced phase separation is largely inoperative.. In models of nondeformable self-propelled particles, activity can still induce nontrivial behaviors, including long-range velocity correlations [30], intermittent behavior [31], and avalanches that are more similar to those in sheared systems than to those in thermal systems [32].

Allowing variations in particle diameter is perhaps the simplest way to model shape change. Work exploring the effect of activity in dense active matter through oscillations of the particle diameter found a discontinuous transition between fluidlike and solidlike behavior as a function of the fluctuation magnitude [33]. In that work, the changes to particle diameter were decided *a priori*, but that raises the question of how one might design changes to particle radius or other shape parameters in order to achieve a desired property. By viewing cell shape as an extra tunable degree of freedom in configuration space in addition to particle positions, one could minimize an energy or cost function that depends on the shape variable, then freeze the shape variable, and arrive at a new type of configuration with properties that are distinct from the original. A recent article has studied this question for particle radii [34] and found that allowing radial degrees of freedom dramatically shifts the jamming point for spheres and creates ultrastable particle packings that are much more brittle under applied load. This can help explain the success of swap Monte Carlo methods in finding deeply quenched glassy states. Interestingly, allowing the particle stiffnesses to vary in the same way does not generate special states. Is particle shape especially good as a tuning parameter? If so, why?

In addition to the shape parameters, another important parameter that appears in many experiments, simulations, and theories is the effective friction and/or adhesion along interfaces between deformable particles. In one limit, the interfaces can slide past one another freely with no dissipation (or mean-field dissipation proportional only to the velocity of the particle), while in another limit studied, for example, in vertex models, the interfaces are perfectly adhered so there can be no relative slip and the dynamics occur via interfaces shrinking or growing only. In between, the nature and magnitude of dissipation could drive new types of instabilities or patterns.

A related question is how to characterize the different types of interfaces that occur in such systems. Do interfaces that touch other particles have different properties than those adjacent to free space? Is there a reasonable representation of the long-time particle shape as the minimum energy of a Hamiltonian, or must the description be inherently dynamic? More broadly, how should one parametrize the infinite space of particle shapes? Possible approaches include moments of the mass distribution, nondimensionalized ratios between the surface area and volume, or projections onto spherical harmonics. A good choice might allow systematic expansions, for example, in hydrodynamic theories. Further questions involve thinking about how to explore the design space of active, programmable shape deformations. Could one program the activity levels or shape changes to drive the system to execute a certain task? Are there extensions of gradient descent or autodifferentiation that might help identify local rules that could accomplish a task? More generally, are there time-varying protocols to drive the system to particular places in the energy landscape, such as those associated with recent discoveries in soft matter self-assembly [27,35]?

Overall, collections of deformable particles are interesting systems with behavior that is well understood in certain limits—jamming, liquid crystals, vertex models—and with a multitude of completely open questions outside those limits. These extra degrees of freedom allow new directions in a potential or free-energy landscape, opening up all sorts of fascinating possibilities for design and annealing. If local rules can be identified that minimize a specified cost function, these materials could execute adaptive learning protocols to achieve a design goal. Moreover, if one could couple other patterning systems, such as reaction-diffusion-advection chemical signaling, to particle shape, it may be possible to design large-scale material systems that can self-organize into quite complex morphological shapes and execute tasks.

These questions are immediately applicable in systems of current interest to physicists. Dense active matter naturally exists in this limit; real active matter particles are deformable as they are compressed; also, activity often induces changes to shape. Biological cells, especially animal cells, are highly deformable and active and are proof of principle that deformable particles can be programmed to generate extremely complex morphologies that perform functions.

Outside of physics, at the intersection of evolutionary and developmental biology, there is an "hourglass model" [36,37] that suggests that certain time points and length scales during development—the neck of the hourglass—are highly conserved, resulting in a rather standardized body plan in animals. Scientists have recently used similar ideas to suggest how developing organisms are able to convert a huge number of biomolecular inputs into a robust emergent morphology [38]. It is interesting to consider whether the mesoscale parameters that enter deformable particle models—friction, adhesion, shape change—could be the "neck" of such an hourglass that helps to integrate different aspects of biological signaling into a low-dimensional subspace that can drive tissue morphology and behavior.

Particles that deform and actuate represent an exciting avenue for the future of soft matter and biological physics research. They are an underexplored platform for the design and manufacture of advanced adaptive materials, and their collective behavior is a beautiful puzzle that will extend the fields of both physics and biology beyond their current limits.

M. L. M. would like to acknowledge discussions with Angus McMullen and Andrea Liu and funding from NSF-DMR-1951921 and Simons Foundation 04391.

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