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Regular Article

Entangled active matter: From cells to ants

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Abstract. Both cells and ants belong to the broad field of active matter, a novel class of non-equilibrium materials composed of many interacting units that individually consume energy and collectively generate motion or mechanical stresses. However cells and ants differ from fish and birds in that they can support static loads. This is because cells and ants can be entangled, so that individual units are bound by transient links. Entanglement gives cells and ants a set of remarkable properties usually not found together, such as the ability to flow like a fluid, spring back like an elastic solid, and self-heal. In this review, we present the biology, mechanics and dynamics of both entangled cells and ants. We apply concepts from soft matter physics and wetting to characterize these systems as well as to point out their differences, which arise from their differences in size. We hope that our viewpoints will spur further investigations into cells and ants as active materials, and inspire the fabrication of synthetic active matter.

1 Introduction

Active matter concerns the motion of self-propelling particles in both nature and the human-made world. In nature, examples include fish, birds, and ants, which often gather in large aggregations. In the built world, examples include modular robots and active colloids. In both worlds, it is common to see individuals that interact with each other following simple rules and, in spite of that, the emergence of complex collective behavior and spatial-temporal structures on the group level (Fig. 1) [1]. To put it more succinctly,"more is different," as once said by Princeton physicist Philip Anderson about social groups. But exactly how does adding more individuals change the collective? Solving this problem has been difficult. Many models have been proposed, but it remains difficult to validate models of such swarming active matter because the transfer of information between individuals is invisible. For instance, in

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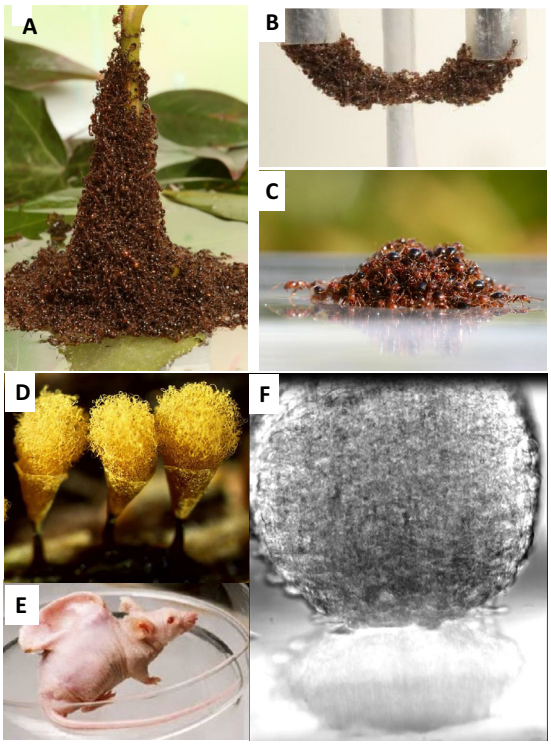

Fig. 1. Cells and ants self-organize to build structures. (A) Ants self-organize to build bivouacs to survive above ground [17], (B) bridges to cross gaps and (C) rafts to survive floods. (D) Slime mold cells build stalks to facilitate pick up by animals or rain to locations with more food. Photo courtesy of George Shepherd. (E) Reconstruction of an ear on a mouse back [22]. (F) A 3D aggregate of S180 Sarcoma cells.

flocks of birds and schools of fish, information can be transferred by vision, hearing, touch, or sensing of fluid wake signature. This invisibility makes it particularly difficult to characterize and test hypotheses on swarms of free individuals, where individuals remain unattached.

"Entangled active matter" has received less attention than free active matter, but provides new avenues for understanding how swarms work. Entanglement involves many individuals that are bonded to each other, as in long polymer chains. These links cause entangled active matter to be found in the form of three-dimensional aggregates, such as balls of cells or ants. Moreover, the transient nature of the links can lead to a variety of behaviors. Aggregates of cells and ants exhibit viscoelasticity: at shorter time, aggregates are elastic under compression and relax like a rubber. At longer time, they are viscous and flow like honey. Thus, living aggregates can be characterized by material properties that have only been seen up to now in inanimate materials. By characterizing these bulk material properties, we can obtain insight into the individual level of cooperation.

In this study, we will focus on two model organisms, cells and ants. Since the advent of microscopy in recent years, numerous examples have been found of cells linking together to build larger structures [2]. For example, the slime mold, genus Dictyostelium, comes together to build stalks in times of starvation (Fig. 1D). The cells in the stalk are rigid to increase the stability of the aggregate. Building these stalks increases the chance of being picked up by animals, washed away by rain

water, and eventually transported to a location with a greater food source. In this paper, we will focus on murine sarcoma (S-180) cells (Fig. 1F), which are a common model cell used in cancer research because they can be easily injected in mice to test various cancer treatments [3]. These cells generally link to each other in clumps but can also metastasize, in order to colonize new locations. In this review, we report a number of methods to predict when cells metastasize, and how cells behave on different substrates. These methods treat the cells as soft matter, made active by virtue of the change of their properties in response to external cues.

On the macroscopic level, there have been reviews of animal aggregates such observations of flocks of birds and schools fish [4]. In the 1840's, Savage was one of the first to record the aggregations made by driver ants or army ants of Africa [5]. Savage observed the formation of aggregations such as bivouacs, bridges, and rafts. Army ants form such structures because they are nomadic, and must build new homes in different locations as they search for food. Fire ants form rafts in response to flash flooding of their underground homes, a regular occurrence in the wet season in Brazil's Patanal. The ability to create aggregations enables the colony to stay near and protect the only reproducing member, the queen. In a flood, separation from the queen would mean certain death for the colony. In general, ants have become model subjects to study because of the variety of tasks they can accomplish in groups. Studies have shown that ants use simple rules to form many structures such as rafts, bivouacs, bridges, and foraging trails [1,6–17]. However, most of these studies treat ants discretely, and so do not consider their bulk properties. Material properties such as strength are important in determining the maximum height or size of such structures, in face of rising flood waters, wind and gravity. In this review, we will focus on the bulk material properties of ant aggregations, and compare these properties to those of cells.

The goal of this review is to develop clear analogies between cells and ants. We begin by enumerating the applications of studies of entangled active matter. We proceed with the biology of cells and ants, focusing on their various time scales, sensing, and connectivity. We then present methodology and results of mechanical tests that yield the bulk mechanical properties of cells and ants. Such tests are not possible with free active materials such as birds and fish. We then proceed to the dynamics of aggregates, going from the individual level of self-propulsion to bulk rates of spreading. We close with a few final thoughts and our perspective on the future of the field.

2 Applications

The study of a single cell, or ant, is an entire field in itself, and much still remains to be understood how such a complex organism works. Groups of individuals from beautiful striking patterns in ways that are simple to describe, but difficult to predict. Inspired by the elegance of such patterns, studies of aggregates of materials has found applications in a wide range of fields, including biology, medicine, agriculture, the food industry, and robotics. In this section, we discuss these applications.

Cellular aggregates are three-dimensional. Thus, they are good models for tissues and in vitro drug tests, because drugs active on a two-dimensional monolayer may be inefficient on three-dimensional tissue. Using cellular aggregates, prior to *in vivo* tests, saves the lives of millions of mice. Cellular aggregates can be formed in a number of ways, whose origins can be traced to other fields such as fluid mechanics or biology. One method, called "agitation", uses a snowball effect to permit individual cells to attach to a ball of cells of increasing size. Another method involves extrusion from a pipette such as in the pendant drop technique. This method generates a cellular aggregate whose size is given by the diameter of the pipette and adhesion of the cells.

In Sect. 4, we will show how pendant drops can also yield mechanical properties of the aggregate.

Another way to create aggregates is to proliferate cells in confined geometries. This technique was started by J. Bibette for the perfume and food industries [18]. Later, P. Nassoy developed a microfluidic method of fabrication of elastic, hollow micro-capsules in which to grow cells. As the cells reach confluence, they swell the elastic capsule up to a homeostatic state where the number of cells dividing is equal to the number of cells dying. From the deformation of the elastic capsule, one can estimate the homeostatic pressure [19]. Aggregates within capsules can be used to answer fundamental biological questions and enable testing of novel therapeutic approaches. For example, the encapsulation of proliferating cells in an alginate shell, one composed of a polysaccharide extracted from brown algae, is an important physical analogy. The work was first started at the Institut Curie for Cancer Research because tumors in the body are generally composed of cancerous cells surrounded by a matrigel membrane. The rupture of this membrane may lead to a dissemination of cells circulating into blood vessels or migrating into the tissues. This strategy of confined tissue growth is now used to mimic stem cells generated from embryonic, adult, and induced pluripotent stem (iPS) cells.

Another great challenge is cellular therapy for the treatment of hair loss and skin reconstruction. For instance, the aggregation of adult human hair-follicle dermal papilla cells in 3D spheroids enables partial reprogramming sufficient to initiate hair follicle induction in recipient human tissue [20]. Recent findings by intracutaneous transplantation of bioengineered follicle aggregates indicate that it is possible to not only restore a hair follicle but also to reestablish successful connections with the recipient skin. This process can regenerate and sustain hair cycles [21]. Another important application of cell spheroids research is repair and eventually replacement of damaged organs by permitting stem cells to grow and restore the damaged areas inside the body. A recent example is the growth of a human ear on a mouse [22]. iPS cells are thought by many researchers to have a bright future to repair worn out tissues and to replace entire diseased or damaged body parts. Recently, a miniature brain-like organ, called the cerebral organoid, was made of stem cells aggregates and recapitulates some of the complex features of a growing brain [23]. Another application in the food industry: it is possible to grow a synthetic burger using stem cells from cows [24].

In this review, we primarily consider aggregates of murine sarcoma (S-180) cells transfected to express E-cadherins at their surface. S180 are fibroblasts taken from a mouse's epithelial sarcoma [25] that does not normally express cell adhesion molecules on its surface. We consider clones that are S180 cells stably transfected to express different levels of E-Cadherins. The transfection is made with the pCE-Ecad eukaryotic expression vector and pAG60 as described in [26]. Generation of these cells and their observation require a microscope and often more sophisticated equipment. In contrast, ants are easier to visualize and to maintain in a lab. Thus, ant aggregates constitute a natural alternative to improve our understanding of the collective behaviors of living active matters.

Studies of fire ants have application in agriculture and in robotics. Fire ants earned their name with the pain of their venomous sting. They are an invasive species to the United States, and are considered a pest. They cause losses of over one billion dollars annually due to the combined damage to crops, injury by fire ant stings, and destruction of property [27]. Fire ants are attracted to and aggregate in the electrical wiring of traffic signals, dying in such large numbers that they create clusters that short-circuit the wires [28].

The cooperation of ants has inspired much of modular robotics, the design and construction of robots that can link their bodies together and form larger, more

capable robots. Indeed, as technology advances, robots are built smaller and smaller, and more resembling ants in their abilities. In fact, discovering the principles of modular robotics was one of the Grand Challenges of Robotics in 2007 [29]. Modular robotics has potential applications in exploration of challenging terrain. For example, a modular robot might separate itself into small pieces so it can more easily pass through the grate of a sewer. The robot could then reconstruct itself into a snake-like configuration to then clear the drain pipe [30–33]. Modular robots are also being considered for use in extraterrestrial exploration where the price of payload transport requires robots to be brought up piecemeal.

Currently, modular robots have a number of limitations, making studies of fire ants useful in inspiring ideas to improve modular robots. First, modular robots can reliably connect to each other in relatively small numbers from 2 to 1,000 individuals [34], which is small compared to the several hundred thousands of ants that make up a colony [35]. Larger numbers of modular robots are difficult to study because as the number of robots increases, so does the probability of encountering a non-operative robot. Thus, the manufacturing precision of modular robotics necessitates special algorithms to control them in large numbers. In contrast, because cells and ants must adhere to each other actively, only live individuals remain in aggregations, where-as the dead ones fall away. Lastly, modular robots are also generally stiff and connect to each other in a cubic lattice. As we will see in the next section, cells and ants do not connect randomly. This method represent an entirely new way to adhere together from the engineering point of view, and provides an inspiration for building more dependable large-scale structures [36].

3 Biology

Although ant and cell aggregations may look similar (Fig. 1), the length and time scales of their motion vary greatly. This size difference affects life as these organisms know it. As a result, both cells and ants have different means of sensing, connecting to each other, and moving. While ants have legs, cells must use molecular "legs" to propel themselves. In this section, we present the biology of cells and ants.

3.1 Time scale

The body lengths of cells and ants are orders of magnitude apart. Animal cells are in the range 10–100 microns while fire ants are in the range 2–4 mm [37,38]. Consequently, cell masses are of the order of 500 femtograms (5×10^{-13} g), which is 10^{-10} times smaller than an ant, of characteristic weight 1 mg [37,39]. Despite their size difference, both organisms can create both 2D and 3D aggregates. This confluence of abilities is striking, and suggests that forming such entities is useful from an evolutionary point of view.

The fundamental size difference results in a difference of propulsion speed, 0.6–6 body length/hour for a cell and 30,000–70,000 body length/hour for a free (non-entangled) ant [40–42]. The ratio of body length to walking speed can be expressed by a time scale τ_s of 10–100 minutes for a cell and 0.5–1 seconds for an ant. The high speed of ants is further evident when considering groups. The time scales of spreading are 35–50 hours for cells and 2–3 minutes for ants, upon considering comparable numbers of individuals (from 3,000–10,000) [41,43]. The difference in speed is due to the difference in motile mechanisms at each length scale. Cells take significantly longer time to move and sense their environment due to the reliance on spreading of extracellular matrix (EC). Ants, on the other hand, have adapted to moving on a

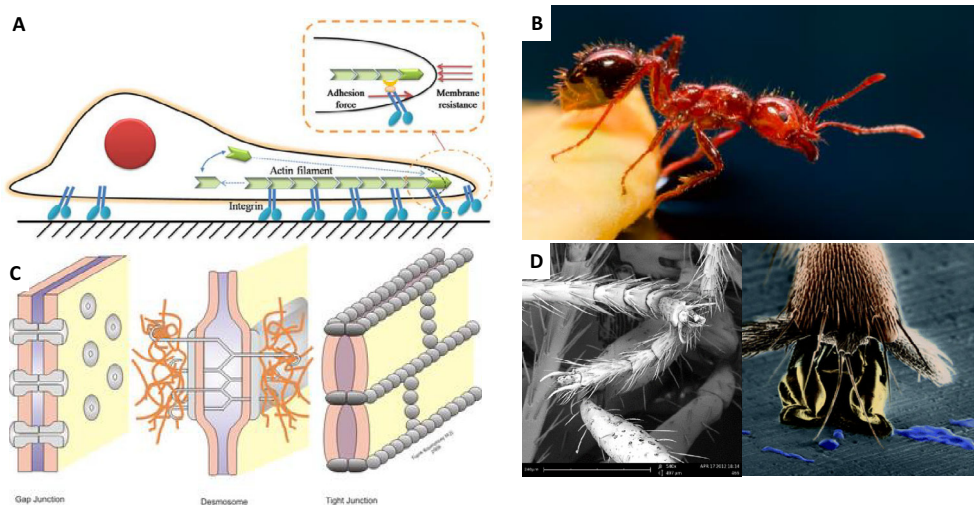

Fig. 2. (A) Schematic of a cell attaching to a substrate by using extracellular matrix (ECM) such as the integrin shown here. Cells connect and disconnect these proteins along with extending and contracting their bodies to walk on surfaces [98]. (B) Ants walk by using the six legs on their thorax. (C) Schematics of the three ways cells can connect to each other. From left to right: gap junctions, desmosomes, and tight junctions. Photo courtesy of Boumphreyfr. (D) Ants use hooks and sticky pads at the end of their legs to connect to each other. Photos courtesy [99].

variety of surfaces. Their legs and sticky feet allow them to navigate around and over obstacles.

3.2 Self-propulsion

The migration of single cells is relatively well understood. A keratocyte migrates on a plane by the expansion of a lamellipodia, or "membraneous foot" in the front, and a retraction of the cell body in the back (Fig. 2A). In confined geometries, corresponding to the migration of cells in the extracellular matrix, the cell velocity is much faster and the mechanism is completely different, with a molecular motor building a pressure gradient along the cell body responsible for the motion [44]. The motion of cells inside an aggregate is less studied. It is known that they divide at the periphery and die in the center, giving rise to a flow of cells towards the center. Many cell types are thus frozen in the center. However, cells, such as S180 celss, which do not secrete extracellular matrix are motile in the center [19]. Ants, in contrast, are generally more entangled in the center of structures. Mobility in ants is restricted mostly to the surface of their rafts and other built structures. We have observed a slow downward creeping flow within the ant towers, of speed 0.38 ± 0.21 mm min^{-1} due to the tower slowly being disassembled at the bottom and rebuilt at the top [17].

Ants usually propel themselves by walking. They have six legs, and the tip of each leg has a claw used to hook onto asperities in the underlying substrate (Fig. 2B). Each leg also has an arolium, an inflatable balloon that extrudes a combination of a hydrophobic and hydrophilic fluid. As ants take footsteps they excrete fluids, leaving a trail of footprints that is only 10 microns thick. This fluid adhesion is the basis for ants walking on all kinds of surfaces, the waxy surfaces of pitcher plants walls and ceilings, and even on carpets of other ants, such as on the ant raft [45,46].

Ants possess a number of traits that permit them to be robust in a variety of conditions in which cells would surely perish. Ants can use their legs to swim both on and underwater. They survive immersion in water by carrying with them small air bubbles collectively called a plastron, or underwater gills. The surface area of the plastron is so high that the diffusion of oxygen into the bubble exceeds the ant's metabolic rate, permitting them to breathe underwater nearly indefinitely [47]. The plastron enables ants on the bottom of rafts to avoid drowning. The legs of ants even enable them to glide through the air. Ants that inhabit the canopies of trees sometimes fall off the trees as they are moving about. In response to falling, the ants perform directed aerial descent, using their spread legs and bodies to generate aerodynamic forces that guide them back to the tree [48].

3.3 Sensing

Since many species of ants are partially or totally blind, information from their immediate surroundings and other ants are critical for navigation through new environments. Ants are believed to use tactile sensing and sensing of pheromones to prevent separation from the group [35,49,50]. Information found by select individuals can dictate behaviors that in turn propagate throughout the group. Such communication enables finding the shortest path to the nest or developing traffic flows that minimize congestions [51]. Studies have shown that certain ant species have memory and use physical cues to navigate [52,53]. These cues help to translate the baseline stochastic behavior of individual ants towards organized movement of the aggregation.

Single cells have receptors on the cell surface that allows them to respond to external cues by controlling their fate and behavior. Indeed, chemical factors and the mechanical properties of the cellular environment as well as gradients have been shown to dictate morphogenesis by changing cell shape and contractility, cell proliferation, survival, differentiation and cell migratory properties. When connected, cells communicate with each other using chemical pathways formed between cells [54,55].

3.4 Adhesion

Figure 2C–D shows the adhesive methods of cells and ants, which we discuss in turn. Cellular adhesion consists of the binding of one cell to another using cellular adhesion molecules, or binding of a cell to a substrate decorated with extracellular matrix. Extracellular matrix is a complex network of macromolecules, including collagen, bronectin, laminin and proteoglycan, whose main function is to form a supporting framework for cells and tissues. Cell adhesion is essential to all forms of life. By adhering to other cells or substrates, cells not only obtain physical support, but also can communication with the environment and neighboring cells through both chemical and mechanical means. Adhesion enables regulation of their own activities, such as cell shape, differentiation, migration, proliferation, and even survival [56].

Cell adhesion is mediated by events occurring at the cell surface, a zone that includes three major components including: the plasma membrane itself, the nearby extracellular space, and the underlying subcortical cytoplasm. Each of these areas contains molecules involved in cellular adhesion. In particular, the so-called Cell Adhesion Molecules (CAMs) are proteins located on the cell surface that enable binding to other cells or to the extracellular matrix (ECM). These proteins are typically transmembrane receptors and are composed of three domains: an intracellular domain that interacts with the cytoskeleton, a transmembrane domain, and an extracellular domain that interacts with other CAMs of the same kind (homophilic binding), with

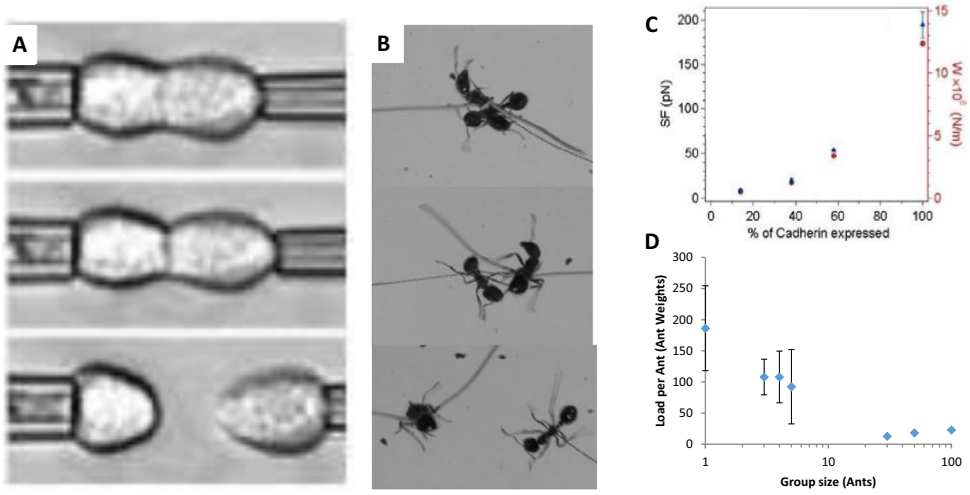

Fig. 3. Adhesion of cells and ants. (A) Dual micropipette assay. Left cell is held firmly by the micropipette and the aspiration pressure is increased gradually in the right micropipette until the adherent cells are separated when the pipettes are pulled apart. (B) Sequence of ants being pulled apart by human hairs courtesy of T. Dave [61]. (C) Relationship between both separation force (pN) and adhesion energy (N/m) as a function of relative cadherin content (%). Adapted from [60]. (D) Separation force between ants of increasing group size. Force per ant lowers when group size increases.

CAMs of a different kind, or with the extracellular matrix (heterophilic binding). In this review, we focus on the Integrins and the Cadherins: Integrins are a family of heterophilic CAMs that bind to extra-cellular proteins via short amino acid sequences [57–59].

Cadherins are a family of homophilic CAMs. The most important members of this family are the E-cadherins (epithelial), which bind cells to each other in several ways as shown in Fig. 2B. Gap junctions transfer ions and molecules directly between cells. The gap is wide compared to other junction types, but nonetheless, cells use gap junctions to resist shearing. In comparison, tight junctions are close and strong connections used by cells found in vertebrate organisms. Cells using this type of connection join together their membranes to create an impermeable wall. In Fig. 3A,C, the force to separate two cells is measured by the dual pipette technique. The separating force (SF) is proportional to the cell-cell adhesion energy, and increases with the level of E-cadherin expression at the surface [60]. Similar to the level of E-cadherin in cells, the adhesion force of an ant aggregation increases with increasing number of ants. However, the contribution of each ant decreases as group size increases, as shown in Fig. 3B,D [61].

In foraging and other behaviors, the specialization of ants is evident. However, in our work, we have not observed specialization to affect ant location and tasks within rafts or towers. As such, ants can easily interchange their bodies without sacrificing function of the aggregate. Several features of the ants allow them to connect and change location within structures. Many species of ants use their tarsal claws to climb and their arolia to navigate on even moving and shifting surfaces such as a raft of ants. These tarsal claws and arolium are also used to cling to one another, an important trait for building aggregations. We performed tensile tests with fire ants and found that each leg-to-leg link (using their tarsal claws) can hold up to 200 ants, and each leg to body link (using their arolium) can hold up to 70 ants.

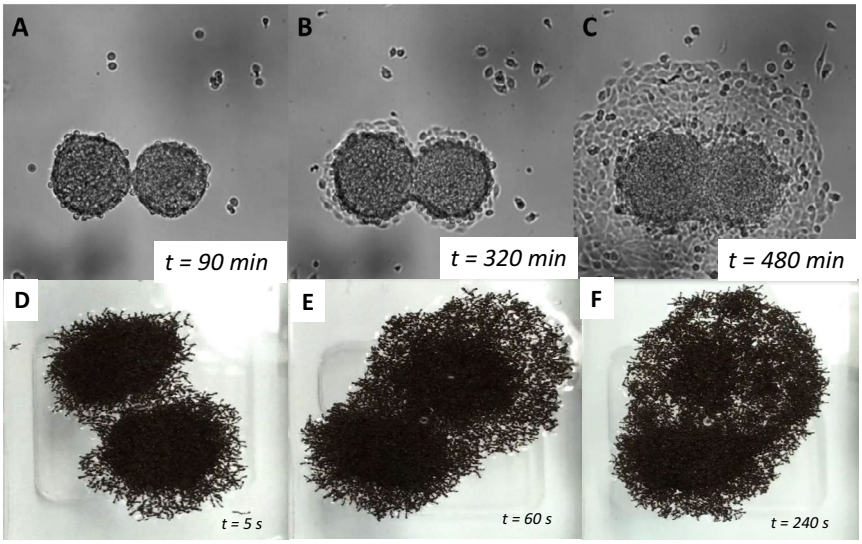

Fig. 4. Fusion of cellular aggregates. (A) Two aggregates in contact. (B) A neck connects the aggregates and (C) spreading and fusion of the aggregates. Scale bar corresponding to 100 microns. Photos courtesy of Stéphane Douezan. (D-E) Two ant rafts contact, fuse, and spread.

When in aggregates, ant linkages become a complex highly-interconnected network. Ants within aggregates have an average of 4.8 neighbors and 8.5 connections [62] which is contributed mostly by the leg connections. Moreover, the polymorphism (difference in body size) can increase the average number of connections per individual. For instance, small ants can fill in the spaces around a big ant, increasing solid volume fraction of an aggregation.

Figure 4 shows two aggregations coming into contact, making clear the rapidity that individuals can make and break connections. Here, two rafts connect via ants on the edge of the structure. Ants on the raft boundary use their tarsal claws to link the rafts. In the meantime, ants on the top roam around looking for new connections to make. A similar behavior is observed when two groups of cells fuse.

Due to their small size and lack of inertia, direction of travel does not affect the motion or metabolic rate of an ant [63–65]. An ant expends as much energy per step as it moves along a floor, up a wall, or across a ceiling. Cell and ants both have strong adhesion to each other and their environments. Non-dimensionalized by body weight, cells adheres 2–3 orders of magnitude stronger than ants to both each other and on substrates as shown in Table 1 [66–68]. Presumably, this strong adhesion also affects the time scale that cells can de-adhere and flow.

4 Mechanics

4.1 Mechanical properties

The linkages between cells enable an aggregate to be treated as a single entity whose bulk material properties can be measured. The same is the case for ants, although because ants have a large amount of air spaces between them, bulk properties also

depend on their packing fraction. Since the time and length scales vary, a number of different techniques are used to characterize cells and ants. In this section, we review their mechanical properties.

We begin with Table 1, which lists material properties of cell and ant aggregates. Since ant properties depend on density, we set the density of ants to be $0.34\,\mathrm{g\,cm^{-3}}$, that of ants found at atmospheric pressure and room temperature [69]. The elastic modulus of an aggregate is measured using a rheometer or pipette. Surprisingly, cells and ants have nearly the same range of elastic modulus, with cells having 0.2 to 20 kPa [70], and ants 1–2 kPa. This finding may be related to the fact that other intensive variables, such as pressure, are also independent of body size [71]. This measurement does not include tendon and cartilage cells which can be much stiffer.

There is no agreed-upon measurement method for ant surface tension, so we consider $\gamma = EL^{-1}$ where E is the Young's modulus and L is the length scale of an ant. Using this method, we find the surface tension of ants is in the range of 10^3 dyne cm^{-1}, while the surface tension of soft tissue is much smaller, at 1.6–20.1 dyne cm^{-1} [41,72]. The surface tension of ants seems to be 10 times larger than water and even slightly larger than mercury. We find the high surface tension of ants to be surprising, but the surface tension is consistent with the large size of ant balls that we can make by hand, about 2 cm in diameter, suggesting a much large capillary length compared to that of water, which has a capillary length of 2.3 mm.

The viscosity of these aggregates indicates how easily they flow and dissipate energy. B cells and ants flow slowly, indicating their viscosities are both very large. The viscosity is 10^8–10^9 cP for cells as compared to 10^6 cP for ants [41,73]. The higher viscosity of cell aggregates can be attributed to their higher packing fraction of 0.64 (quite similar to a random close packing of balls) as compared to ants of 0.2–0.4 [62,74]. Elastic modulus and surface tension are the fundamental variables used in the mechanics in this section. In the next section, we discuss how mechanics can be used to infer forces from these variables.

4.2 Physical picture

Since the pioneering work of Malcolm Steinberg who was the first to claim that tissues are liquids [75], the mechanical properties of cellular tissues are still debated. Analogies with soft matter bring valuable insights into the rheological properties of tissues. At first sight, cell packing in a tissue is similar to the packing of bubbles in foams. If this analogy has been fruitful to describe the statics properties of cell configuration in tissue development, it does not hold for the dynamics of tissues. Foams are solid, and flow only above a yield stress σ_y. Tissues, on the other hand, are ultra-viscous liquids similar to polymer melt: below a tissue relaxation time τ ($\sim$ few hours) they behave like a rubber with an elastic modulus E. Above τ, they flow like a liquid, with a viscosity $\eta = E\tau$. This is a common feature for both cells and ants: cell aggregates and ants swarms squeezed between two plates behave as a rubber and quickly round up again after compression (Fig. 5). These aggregates are also named spheroids because, as liquid droplets, they minimize their surface energy adopting a spherical shape. Given time, these same aggregates will spread like liquid drops.

The difference between foams and tissues is due to the noise produced by the living cells. Thermal agitation is not strong enough to reorganize the structure of foams to relax mechanical stresses. The energy barriers corresponding to the reorganization are much larger than thermal agitation energy. Thus, the foam system is frozen. On the other hand, cells and ants are active and produce a large noise, which explains why they can flow.

Table 1. A table showing some measurable properties of both cell and ant aggregates.

			Cells	Ants	References
Individual	Size	L	10–100 μm	2–4 mm	Pruves et al. (2013), Tschinkel (2006)
	Mass	m	5×10^{-10} mg	1 mg	Goodin et al. (2007), Tschinkel (2006)
	Walking speed	u	0.06–6 L/h	$30 \times 10^5 - 70 \times 10^5$ L/h	Dimila et al. (1991), Mlot et al. (2011)
Rates	Building Rates	r	35–50 h	3 min	Beaune et al. (2014), Mlot et al. (2011)
	Time scale	τ =L/u	1–16 h	$2 \times 10^{-7} - 6 \times 10^{-7}$ h	
Material Properties	Young's Modulus	E	0.2–20 kPa	1–2 kPa	Wells et al. (2008), Tennenbaum et al. (under reivew)
	Surface Tension	σ	1.6–20.1 dyne/cm	103 dyne/cm	Foty et al. (1996)
	Viscosity	μ	10^8–10^9cP	10^6cP	Forgacs(1998), Mlot (2011)
	Packing Fraction	Φ	0.63	0.25-0.44	Martin (1997), Foster (2014)
Adhesion Force (Nondimensionalized by body weight)	Agent-to-Agent		50×10^{-12} N (0.1 N/mg)	3×10^{-3}N (0.003 N/mg)	Puech (2006)
	Agent-to-Substrates		30×10^{-12} N (0.06 N/mg)	$10^{-5} - 3 \times 10^{-3}$N (0.00001-.003 N/mg)	Pelham (1997), Dejean (2010)

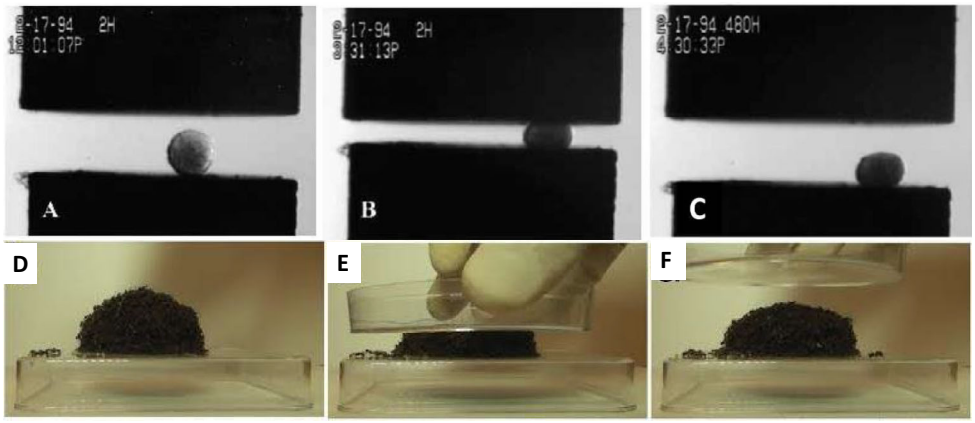

Fig. 5. (A-C) Cell aggregates (top) are elastic at short time and behave like a rubber. At long time $t > 1$h, they flow like a liquid. Photos adapted from [76] (D-F) Ants swarm (bottom) also behave like Silly Putty paste for short times.

Back in the sixties, Malcolm Steinberg was the first to find this unexpected behavior and to measure the surface tension of organs [75]. Mixing cells of two tissues, he observed cell sorting. As liquid droplets, the tissue with lower surface tension engulfs the tissue with higher surface tension γ [76]. Steinberg's hypothesis that cell sorting in tissues arises from differences in surface tension between different cell populations has gathered extensive experimented support [77]. The most widely used technique to characterize tissue properties has been parallel-plate compression introduced by Steinberg and co-workers [73]. Compressed between two plates, aggregates behave as viscoelastic droplets. From the measurement of the time course of force, one can derive the elastic modulus at short times and the surface tension at long times [78], but this technique is difficult to use and cannot be applied in vivo.

We have developed a novel method based on aspiration by micropipette to investigate tissue mechanical properties [79]. The aggregate is aspirated at a constant suction pressure Δ–P into a micropipette (Fig. 6), larger than $\Delta P_c = 2\gamma(R_p^{-1} - R^{-1})$ where R_p and R are the micropipette and aggregate radii, respectively. We use this technique to measure the viscosity η and observe cell activities due to change in Δ–P.

First, the surface tension γ increases with ΔP (Fig. 6C), showing that cells stretched in the capillary react by reinforcement of the cortex, which is a layer of the cytoplasm that supports the plasma membrane. Second, in a narrow range of pressure ΔP, we observe pulsed contraction or a "shivering" of the aggregate: a signature of the molecular motor activity induced by external forces. It has also been observed that forces exerted between cells in a developing tissue under stress are not always monotonically varying, but can also be pulsatile [56]. Although arising from different kinds of forces, that behavior is reminiscent of the intermittency observed in certain flow regimes of dry granular matter when moving through an hourglass-type constriction (called tickling effect) and also the intermittent motion of ants trying to escape through a constriction [80].

Our measurement of mechanical properties using pipette aspiration is now widely used. All in all, the main conclusion is that aggregates behave like "living" viscoelastic liquids: they reinforce their mechanical properties with pressure, showing a mechanosensitive active response of the acto-myosin cortex. Acto-myosin cortex is a layer of protein on the cell membrane that controls the cell shape.

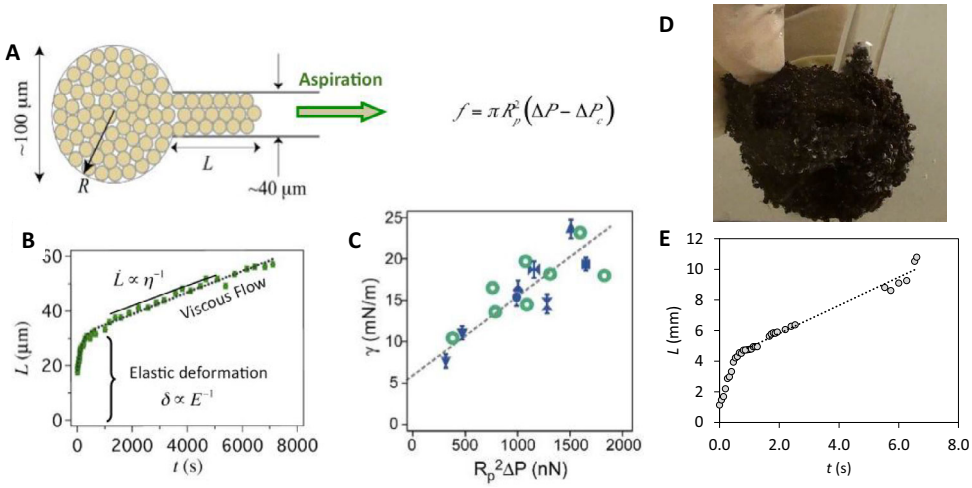

Fig. 6. Aggregate aspiration. (A) Illustration of micropipette aspiration of spherical cellular aggregate. $\Delta P_c = 2(1/R_p - 1/R)$ is the threshold aspiration pressure. (B) Aspiration cycle for an aggregate $\Delta P = 1180$ Pa, with $R_0 = 175$ microns, and $R_p = 35$ microns (C) surface tension η (mN) as function of applied force $R_p^2\Delta P$. Adapted from [87] (D) image of the aspiration of a spherical ant aggregate. (E) Aspiration cycle of an ant aggregate.

The aspiration method can also be used for ants held underwater. The results show similar regimes compared to cells: an elastic regime and viscous regime as seen in Fig. 6 from which we can extract the viscosity. In the experiment showed in Fig. 6D–E, the viscosity was found to be 4.3e5 cP which is close to the value found by Mlot et al. [41]. However, further investigations show that ants are shear thinning: so their viscosity decreases with applied stress.

The mechanical properties of ants was measured in an experimental study by Tennenbaum et al. [69]. The rheometer setup is shown in Fig. 7A–B, where velcro is used to ensure no-slip. In a variety of conditions, ants were shown to be able to both store and dissipate energy. Controlled shear rate experiments were performed in which we measured the stress required to maintain a constant shear rate. Aggregations of 3000 ants were used. For a wide range of strain rates (10^{-2} to 10^{1} s^{-1}), there is a plateau of stress. This stress shows that ants are indeed resisting the rotation of the rheometer. Moreover, this plateau is reminiscent of the plateau of polymer melts [81,82], which may indicate that the stress is due to the disentanglement of the connections of both ants and polymer melts. The ants flow according to the constitutive relation for ant stress, $\sigma = \eta\dot{\gamma}$, where σ is the stress, $\dot{\gamma}$ is strain rate. The viscosity η decreases with strain rate according to $\eta = \sigma_0\dot{\gamma}^{-1}$. The constant σ_0 of 70 Pa is consistent with a dissipation due to the high friction within the joints of ants, which have friction coefficients is three orders of magnitude higher than in human joints [83,84]. This 70 Pa is consistent with a shear stress of 7 ants pulling on one ant. Both live and dead ants satisfy the same constitutive relation, indicating that live ants "play dead" when forced to flow.

We also perform creep tests in which we apply a constant stress and measure the strain rate. This test describes how willing the ants are to release each other under duress. We find that ants do not behave like a simple fluid. For applied stresses between 40 and 70 Pa, we observe periods where strain is linear with time and others where strain is constant. The ability of ants to hold themselves stationary indicates that they are able for brief periods to store elastic energy.

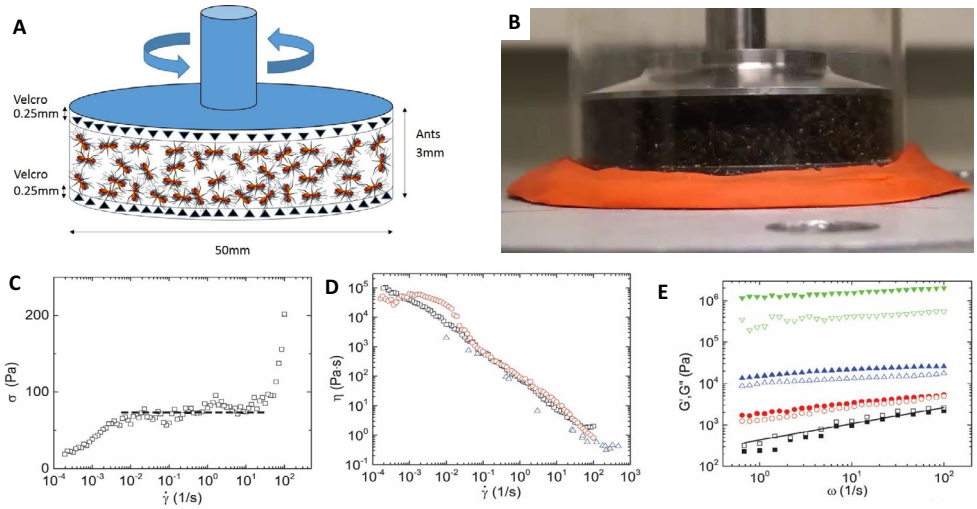

Fig. 7. (A) Schematic of ants inside the rheometer. Velcro is attached on the top and bottom walls to create a no slip boundary. (B) Image of the rheometer set up. (C) Shear stress, σ, as a function of applied shear rate, $\dot{\gamma}$. For a large range of shear rate, 10^{-2} to 10^{2} s^{-1}, the stress remains at a constant 70 Pa. (D) Viscosity, η, as a function of shear rate. The squares are the viscosities that result by dividing the stress and the shear rate shown in a. The circles correspond to a similar experiment where the shear rate is progressively increased from 2×10–$4\,s^{-1}$. The triangles correspond to viscosities taken from creep experiments where a stress is applied and the strain is measured as a function of time. The ant density in all these experiments is $0.34\,g\,cm^{-3}$. (E) Frequency sweep in the linear regime for live ants at a density of (squares) $0.34\,g\,cm^{-3}$, (circles) $0.68\,g\,cm^{-3}$, (triangles) $1.02\,g\,cm^{-3}$, and (upside-down triangles) $1.36\,g\,cm^{-3}$. G′ (closed) and G″ (open) are shown. As the ant density is increased the congruence observed for $\rho = 0.34g/cm3$ disappears and G′ progressively becomes larger than G″ and becomes more frequency independent. Photos and chart adapted from [69].

For applied stresses above 250 Pa, ants are torn apart, indicating that the stress which they resist during flow is only 4 times less than their maximum.

We also perform oscillatory tests in the linear regime to further understand the ability of ants to store and dissipate energy. Figure 7D shows the strain rate dependency of the viscosity. In addition, Figure 7E shows the elastic modulus G′ (closed circle) and storage modulus G″ (open circle) as a function of frequency. As ant density increases, there is a clear separation between G′ and G″. Moreover, as density increases, the two moduli become frequency independent. For low densities, ants behave like a critical gel, in which G′ and G″ are equal. For high densities, live ants are primarily elastic and have a similar G′ to dead ants.

The mechanics of entanglement shares some similarities with linkages of u-shaped particles. Gravish et al. find that the entanglement due to the bent ends of *u*-particles increases the stability of the pile [85]. Franklin shows how entanglement of *u*-shaped particles can resist extension. During extension, there is a stick-slip inside the pile in which weak links break but the links rearrange, maintaining a cohesive pile [86]. There is also a similar behavior when ant aggregates undergo constant extension. More work is needed to understand how ant aggregations exhibit this range of mechanical behaviors.

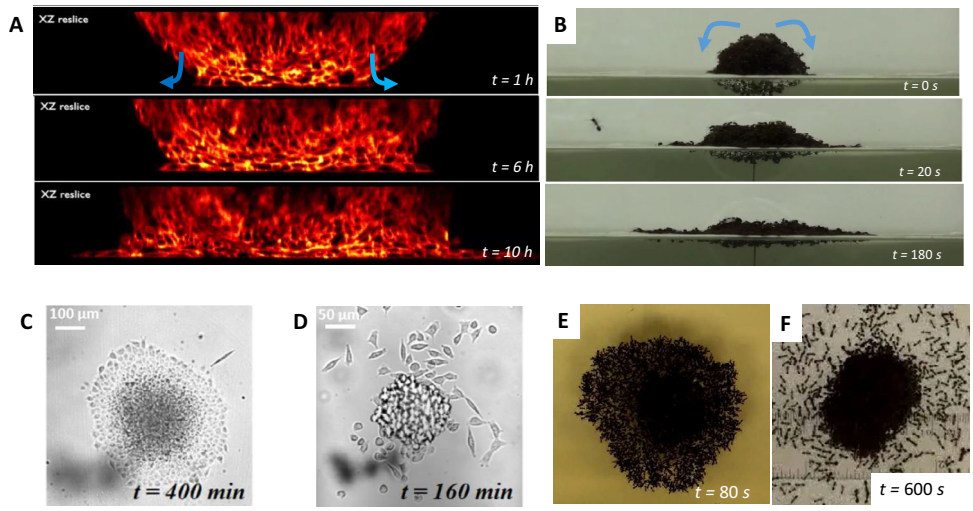

Fig. 8. The spreading of cell and ant aggregates from a ball to a pancake shape. (A) An image sequence of ball of S-180 cell spreading on a substrate over a period of 10 hours [43] (B) an image sequence of nearly 3,000 ants spreading on top of water over a period of 3 minutes. Free ants on the surface walk and attach to the edge of the raft, thus growing it laterally [41]. (C–D) Cell Aggregate Spreading: Liquid (C) and Gas phase (D) of the precursor film [87]. (E-F) Top view of the spreading of ants on water which shows the cohesiveness (E) vs. land which shows the looseness (F) of the aggregates.

5 Dynamics

Analogies between living tissue mechanics and dynamical phenomena involving liquid interfaces known as wetting phenomena have been used to explain several ubiquitous tissue behaviors. A striking analogy between tissue mechanics and liquid wetting is found in tissue spreading. For instance, when two aggregates of cells or ants are brought into contact, they coalesce to form a single larger spheroid [56]. One can see the spreading and the fusion of two aggregates of cells and ants of radius R in Fig. 4. From γ and η measured with the pipette aspiration for cells [79] and γ and η measured by Mlot et al. for ants [41], we can define the capillary velocity $V^* = \gamma\eta^{-1}$ ($\sim 10^{-8}$ ms^{-1} for cells and $\sim 10^{-3}$ ms^{-1} for ants). A scaling relationship ($V^*t = R$) leads to spreading times t of order 6 hours for cells and 3 minutes for ants. We also show in Fig. 8A-B a striking analogy between the spreading of ball of cells and ants.

When a cell aggregate is put into contact with the substrate, we find two regimes of spreading. At short times, the aggregate flattens. The spreading area follows a universal law interpreted in analogy with the spreading of a viscoelastic droplet [87]. At long times, a precursor film made of one cell monolayer spreads around the aggregate. We interpret the dynamics of the precursor film from a balance between the gain of surface energy, and the viscous losses associated with the permeation of cells from the 3D aggregate into the 2D film [43,88]. The slippage of the surrounding monolayer is negligible. On patterned substrates with adhesive strips separated by non-adhesive PLL-PEG bands, we observe a spreading of the monolayer on the stripe at constant velocity V^* ($V^* \approx 7.9\ 10^{-9}$ ms^{-1} on glass coated with fibronectin), demonstrating that permeation is the factor limiting the spreading [88].

We have studied the spreading of balls of cells that express a tunable level of cadherins. These balls are placed on various substrates, such as glass substrates and polyacrylamide gels decorated with extracellular matrix (ECM) protein fibronectin. In particular, the physics of wetting has been applied to describe the tissue's wetting transitions in term of a single spreading parameter S, which, for liquids, measures the difference between cell-cell affinity and cell adhesion to the substrate. If S is negative, corresponding to large cell-cell adhesion (controlled by a high level of cadherin expression), the living drops do not spread. This regime is called "Partial Wetting". If S is positive, corresponding to a strong adhesion with the substrate, the wetting is complete, with a precursor film (a cell monolayer) escaping from the drop. A wetting transition can be induced by using tunable adhesive substrate (PEG-Fibronectin surface treatment or substrate rigidity). In complete wetting, we observed two states of the precursor film. For strong cell-cell adhesion, the precursor film is in a cohesive liquid state. For weak cell-cell adhesion, the film is in a gas state, and so cells escape from the aggregate individually. This liquid-gas transition corresponds to the epiyhelial-mesenchymal transition introduced in biology for cancer metastasis and processes in embryonic development. Remarkably, this behavior is also observed in ants. When ants spread on water, they form a cohesive film. On land, they do not stay connected but begin to escape from the aggregate in a gas state. Therefore, they spread in manners similar to cells, as shown in Fig. 8C–F.

The gas state of these individuals can also be referred to as the "dilute limit." Much of ant activity is performed in this dilute limit, especially for species that do not form aggregates. For example, foraging activity may occur either by individual random walks (or perhaps Levy flights), or by means of well-organized foraging trails where ants move most of the time without touching each other with the exception of short inter-antennal contacts [89–91]. Even in experiments where leaf-cutting ants are constrained into a 2-dimensional Hele-Shaw cell and excited by an insect repellent fluid, the individuals try to avoid entanglement among them, and behave even "politely" if they need to escape through a narrow door, as illustrated in Fig. 9A–B: this behavior, different from the common attitude of humans in panic, prevents clogging at the door.

In another experiment, a Hele-Shaw cell with two symmetrical exits is filled with leaf-cutting ants [92]. When ants are excited by a repellent fluid in the middle, they tend to follow each other. The resulting crowd eventually breaks the symmetry by using preferentially one of the two doors. While that phenomenon increases the total escape time from the cell, it does not mean that ants jam at the selected door, endangering their lives: they try to avoid entanglement, and even retreat from the door if other ants are already trying to get out at the same time. Then, ant-ant entanglement occurs only in the "high density limit" of certain species of ants which results in a unique soft matter phase on which this review is basically focusing. From the experimental point of view, it is worth mentioning that, even in the "dilute limit", tracking of ants based on videos is a difficult task as soon as bodies touch each other.

There remains much work to be done to understand how cells and ants sense and respond to their environments. We know cells are sensitive to the surrounding environment; they feel the rigidity and the forces applied on them. Our living drops can therefore be described as "active" viscoelastic pastes, able to react to the forces applied on them by a reinforcement of their mechanical properties. Ants are also sensitive to their environments. On land, they don't stay in a cohesive cluster but spread out avoiding direct mechanical contact with other individuals. On water, they stay connected while they spread. Only in this bulk state can we obtain measurable properties to compare to cell aggregates.

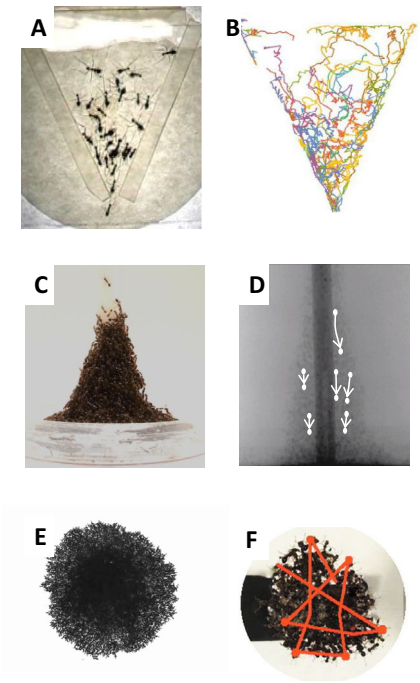

Fig. 9. Ants in dilute and in high density limits. (A) A snapshot from a video of *Atta insularis* into a triangular, two-dimensional Hele-Shaw cell. Ants try to escape but never jam or connect during the escape. (B) The colored lines in the picture are ant trajectories associated to the whole video, which reveal that loops and intermittent motion are typical of escaping ants in a "panic" situation (Picture courtesy of E. Altshuler, J. Ferněndez, F. Tejera and A. Reyes). (C) A snapshot of the side view of an ant tower. (D) X-ray of the ant tower shows that ants inside the tower also sink over time [17]. (E) Top view of an ant raft spreading over water. (F) Tracks of ants moving on top of a raft over the duration of the spreading.

6 Conclusion

Cells and some ant species show remarkable resemblances in their collective behaviors that call for interdisciplinary studies to strengthen the analogies between the two sets of organisms. We showed that even though cells and ants communicate and self-propel in different manners, there are some common underlying behaviors. They have means to connect to each other and to substrates, communicate with each other, and navigate their environment. In addition to these basic features, the rules that governs both of these organisms results in complex motions that arise through interactions with their peers. We also showed that, when individuals are in an entangled state, we can characterize their bulk properties. Although they interact in different scales and have large differences in their physical properties, there is still a need to find common test methods to characterize mechanical properties of these two organisms. These studies involve the fields of collective motion, active matter, and soft matter.

One of the big challenges in the study of ants and cells is their opacity. We still do not have an easy way to see inside the structures they form. How ants move inside an aggregate has yet to be systematically studied. Ants are accustomed to moving in small spaces, such as within tunnels. Their legs, which are fully extended as they walk on flat substrates, are also capable of propelling the ants within tight spaces. As the packing fraction of ants is increased, the inherent motion decreases. We call

for the need of methods to effectively track ants inside their structures in real time. Certain ant species build 3D structures such as bridges and bivouacs whose internal structures are not easy to visualize. Methods such as the one used by Foster et al. are useful for looking into snapshots of ant structures [62] but better methods of data collection are needed to study the construction, maintenance, and disassembly of these structures in real time. One possibility is using x-ray to track the activity of ants inside their nest, that is otherwise obstructed from view [93]. Similarly, new methods such two photons microscopy are being developed for visualization of cells within aggregates [43].

It remains difficult to track the individual motion of large groups of ants, but there have been some progress in the last years. Vision based tracking of multiple objects has improved over several years and can be useful in applications where ants are set up in a 2D environment [94,95]. However, it is still difficult to track the activity in ants at the colony level. Noda et al. developed a device that can track long term activity of ants as they get out and into their nest with great accuracy, and during extended periods of time [96]. This device could prove useful in tracking the activity of the colony in nature. More recently, however, ant tracking has reached a qualitatively new level by implanting tiny radio tags on individual ants, which has allowed, for example, to understand the collective decision-making process in ants [97].

Both cells and ants have much to reveal about the behavior of active matter. Moreover, concepts of soft matter and wetting have been fruitful in unveiling striking analogies between the physics of inert soft matter, such as polymer, viscous pastes, silly putty, and the behavior of biological tissues and swarms of ants. The comparative study of these cells and ants aggregate could lead to new experimental methods and modeling techniques that may have applications from tissue engineering to robotics.

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References

1. S. Camazine, *Self-organization in Biological Systems* (Princeton University Press, 2003)
2. N.J. Mehdiabadi, C.N. Jack, T.T. Farnham, T.G. Platt, S.E. Kalla, G. Shaulsky, D.C. Queller, J.E. Strassmann, Nature **442**, 881 (2006)
3. Z. Cui, M.C. Willingham, A.M. Hicks, M.A. Alexander-Miller, T.D. Howard, G.A. Hawkins, M.S. Miller, H.M. Weir, W. Du, C.J. DeLong, Proc. Nat. Acad. Sci. **100**, 6682 (2003)
4. W.C. Allee (Chicago: The University of Chicago Press, 1931)
5. T.S. Savage, Trans. Royal Entomol. Soc. London **5**, 1 (1847), ISSN 1365-2311
6. C. Anderson, N.R. Franks, Adv. Study Behav. **33**, 1 (2003), ISSN 0065-3454
7. C. Anderson, G. Theraulaz, J.L. Deneubourg, Insectes Sociaux **49**, 99 (2002), ISSN 0020-1812
8. W.R. Ashby, J. Gen. Psychol. **37**, 125 (1947)
9. E. Bonabeau, G. Theraulaz, J.L. Deneubourg, S. Aron, S. Camazine, Trends Ecol. Evol. **12**, 188 (1997), ISSN 0169-5347
10. E. Bonabeau, G. Theraulaz, J.L. Deneubourg, A. Lioni, F. Libert, C. Sauwens, L. Passera, Phys. Rev. E **57**, 5904 (1998)

11. A. Colorni, M. Dorigo, V. Maniezzo, et al., *Distributed Optimization by Ant Colonies*, in *Proceedings of the First European Conference on Artificial Life*, Vol. 142 (Paris, France, 1991), p. 134
12. S. Garnier, J. Gautrais, G. Theraulaz, Swarm Intell. **1**, 3 (2007), ISSN 1935-3812
13. J. Halley, D.A. Winkler, et al., Complexity **14**, 10 (2008)
14. B. Hölldobler, E.O. Wilson, *The Superorganism: The Beauty, Elegance, and Strangeness of Insect Societies* (WW Norton & Company, 2009)
15. D.J. Sumpter, Philosophical Trans. Royal Society B: Biol. Sci. **361**, 5 (2006), ISSN 0962-8436
16. G. Theraulaz, E. Bonabeau, C. Sauwens, J.L. Deneubourg, A. Lioni, F. Libert, L. Passera, R. Solé, Bull. Math. Biol. **63**, 1079 (2001)
17. S. Phonekeo, N. Mlot, D. Monaenkova, D.L. Hu, C. Tovey (in preparation) (2015)
18. J. Bibette, L.Y. Chu, E.S. Carreras, A. Royere, N. Bremond, *Method for Manufacturing Capsule Series, and Related Capsule Series* (2009), US Patent App. 13/131, 971
19. K. Alessandri, B.R. Sarangi, V.V. Gurchenkov, B. Sinha, T.R. Kießling, L. Fetler, F. Rico, S. Scheuring, C. Lamaze, A. Simon, et al., Proc. Nat. Acad. Sci. **110**, 14843 (2013)
20. C.A. Higgins, J.C. Chen, J.E. Cerise, C.A. Jahoda, A.M. Christiano, Proc. Nat. Acad. Sci. **110**, 19679 (2013), ISSN 0027-8424
21. K.E. Toyoshima, K. Asakawa, N. Ishibashi, H. Toki, M. Ogawa, T. Hasegawa, T. Irié, T. Tachikawa, A. Sato, A. Takeda, et al., Nat. Comm. **3**, 784 (2012)
22. Y. Cao, J.P. Vacanti, K.T. Paige, J. Upton, C.A. Vacanti, Plastic Reconstructive Surgery **100**, 297 (1997), ISSN 0032-1052
23. M.A. Lancaster, M. Renner, C.A. Martin, D. Wenzel, L.S. Bicknell, M.E. Hurles, T. Homfray, J.M. Penninger, A.P. Jackson, J.A. Knoblich, Nature **501**, 373 (2013), ISSN 0028-0836
24. C. van der Weele, in *Encyclopedia of Food and Agricultural Ethics* (Springer, 2014), p. 1219
25. L.J. Dunham, H.L. Stewart, J. National Cancer Inst. **13**, 1299 (1953), ISSN 0027-8874
26. B. Boyer, S. Dufour, J.P. Thiery, Exper. Cell Res. **201**, 347 (1992), ISSN 0014-4827
27. D. Pimentel, R. Zuniga, D. Morrison, Ecological Econom. **52**, 273 (2005), ISSN 0921-8009
28. W.P. MacKay, S. Majdi, J. Irving, S.B. Vinson, C. Messer, Jo. Kansas Entomol. Soc., p. 39 (1992), ISSN 0022-8567
29. M. Yim, W.M. Shen, B. Salemi, D. Rus, M. Moll, H. Lipson, E. Klavins, G.S. Chirikjian, Robotics & Automation Mag., IEEE **14**, 43 (2007), ISSN 1070-9932
30. G. Beni, J. Wang, in *Robots and Biological Systems: Towards a New Bionics?* (Springer, 1993), p. 703
31. Y.U. Cao, A.S. Fukunaga, A. Kahng, Autonomous Robots **4**, 7 (1997), ISSN 0929-5593
32. M. Dorigo, V. Trianni, E. Ahin, R. Gro, T.H. Labella, G. Baldassarre, S. Nolfi, J.L. Deneubourg, F. Mondada, D. Floreano, Autonomous Robots **17**, 223 (2004), ISSN 0929-5593
33. R. Groß, M. Bonani, F. Mondada, M. Dorigo, Robotics, IEEE Trans. **22**, 1115 (2006)
34. M. Rubenstein, A. Cornejo, R. Nagpal, Science **345**, 795 (2014), ISSN 0036-8075
35. B. Hölldobler, E.O. Wilson, *The Ants* (Harvard University Press, 1990)
36. R. Pfeifer, M. Lungarella, F. Iida, Science **318**(5853), 1088 (2007), ISSN 0036-8075
37. W.R. Tschinkel, *The Fire Ants* (Harvard University Press, 2006), ISBN 0674022076
38. W.K. Purves, G.H. Orians, D. Sadava, H.C. Heller, *Life: The Science of Biology: Volume III: Plants and Animals*, Vol. 3 (Macmillan, 2003), ISBN 0716758105
39. M. Godin, F.F. Delgado, S. Son, W.H. Grover, A.K. Bryan, A. Tzur, P. Jorgensen, K. Payer, A.D. Grossman, M.W. Kirschner, Nat. Meth. **7**, 387 (2010), ISSN 1548-7091
40. P. DiMilla, K. Barbee, D. Lauffenburger, Biophys. J. **60**, 15 (1991)
41. N. Mlot, C. Tovey, D.L. Hu, Proc. Nat. Acad. Sci. **108**, 7669 (2011), ISSN 0027-8424
42. N. Mlot, C. Tovey, D.L. Hu, Comm. Integr. Biol. **5**(6), 590 (2012)

43. G. Beaune, T.V. Stirbat, N. Khalifat, O. Cochet-Escartin, S. Garcia, V.V. Gurchenkov, M.P. Murrell, S. Dufour, D. Cuvelier, F. Brochard-Wyart, Proc. Nat. Acad. Sci. **111**, 8055 (2014)
44. M.L. Heuzé, O. Collin, E. Terriac, A.M. Lennon-Duménil, M. Piel, in *Cell Migration* (Springer, 2011), p. 415
45. W. Federle, M. Riehle, A.S. Curtis, R.J. Full, Integrative Comparative Biol. **42**, 1100 (2002), ISSN 1540-7063
46. W. Federle, T. Endlein, Arthropod Struct. Dev. **33**, 67 (2004), ISSN 1467-8039
47. J.W. Bush, D.L. Hu, M. Prakash, Adv. Insect Physiol. **34**, 117 (2007), ISSN 0065-2806
48. S.P. Yanoviak, R. Dudley, M. Kaspari, Nature **433**, 624 (2005), ISSN 0028-0836
49. N.R. Franks, T. Richardson, Nature **439**, 153 (2006), ISSN 0028-0836
50. M. Möglich, U. Maschwitz, B. Hölldobler, Science **186**, 1046 (1974)
51. I.D. Couzin, N.R. Franks, Proc. Royal Society London B: Biol. Sci. **270**, 139 (2003), ISSN 0962-8452
52. R. Rosengren, W. Fortelius, Insectes Sociaux **33**, 306 (1986)
53. T.S. Collett, P. Graham, R.A. Harris, N. Hempel-De-Ibarra, Adv. Study Behavior **36**, 123 (2006), ISSN 0065-3454
54. R.O. Hynes, Cell **69**, 11 (1992), ISSN 0092-8674
55. J. Pearson, J. Fluid Mech. **4**, 489 (1958), ISSN 1469-7645
56. J. Solon, A. Kaya-Copur, J. Colombelli, D. Brunner, Cell **137**, 1331 (2009), ISSN 0092-8674
57. N.J. Armstrong, K.J. Painter, J.A. Sherratt, Bull. Math. Biol. **71**, 1 (2009)
58. M. Singh, C. Berkland, M.S. Detamore, Tissue Eng. Part B: Rev. **14**, 341 (2008)
59. F.G. Giancotti, E. Ruoslahti, Science **285**, 1028 (1999)
60. Y.S. Chu, W.A. Thomas, O. Eder, F. Pincet, E. Perez, J.P. Thiery, S. Dufour, J. Cell Biol. **167**, 1183 (2004)
61. S. Phonekeo, T. Dave, D.L. Hu, Soft Matter **12**, 4214 (2016)
62. P.C. Foster, N.J. Mlot, A. Lin, D.L. Hu, J. Exper. Biol. **217**, 2089 (2014), ISSN 0022-0949
63. J.H. Dirks, C.J. Clemente, W. Federle, J. Royal Society Interface p. rsif20090308 (2009), ISSN 1742-5689
64. P. Drechsler, W. Federle, J. Comparative Physiol. A **192**, 1213 (2006), ISSN 0340-7594
65. A. Lipp, H. Wolf, F.O. Lehmann, J. Exper. Biol. **208**, 707 (2005), ISSN 0022-0949
66. P.H. Puech, K. Poole, D. Knebel, D.J. Muller, Ultramicroscopy **106**, 637 (2006), ISSN 0304-3991
67. A. Dejean, C. Leroy, B. Corbara, O. Roux, R. Crghino, J. Orivel, R. Boulay, PLoS ONE **5**, e11331 (2010), ISSN 1932-6203, 09-PONE-RA-14396R3[PII] 20593032[pmid] PLoS One, `http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2892516/`
68. R.J. Pelham, Y.l. Wang, Proc. Nat. Acad. Scien. **94**, 13661 (1997), ISSN 0027-8424
69. M. Tennenbaum, Z. Liu, A. Fernéandez-Nieves, D.L. Hu, Nat. Mater. **15**, 54 (2016)
70. R.G. Wells, Hepatology **47**, 1394 (2008), ISSN 1527-3350
71. W. Kim, T. Gilet, J.W. Bush, Proc. Nat. Acad. Sci. **108**, 16618 (2011)
72. R.A. Foty, C.M. Pfleger, G. Forgacs, M.S. Steinberg, Dev. **122**, 1611 (1996), ISSN 0950-1991
73. G. Forgacs, R.A. Foty, Y. Shafrir, M.S. Steinberg, Biophysical J. **74**, 2227 (1998), ISSN 0006-3495, `http://www.sciencedirect.com/science/article/pii/S0006349598779329`
74. I. Martin, B. Dozin, R. Quarto, R. Cancedda, F. Beltrame, Cytometry **28**, 141 (1997), ISSN 0196-4763
75. M.S. Steinberg, Science **141**(3579), 401 (1963), ISSN 0036-8075 (Print)
76. R.A. Foty, M.S. Steinberg, Inter. J. Dev. Biol. **48**, 397 (2004), ISSN 0214-6282
77. M.S. Steinberg, Curr. Opin. Genet. Dev. **17**, 281 (2007), ISSN 0959-437X
78. R.A. Foty, G. Forgacs, C.M. Pfleger, M.S. Steinberg, Phys. Rev. Lett. **72**, 2298 (1994)

79. K. Guevorkian, M.J. Colbert, M. Durth, S. Dufour, F. Brochard-Wyart, Phys. Rev. Lett. **104**, 218101 (2010)
80. T. Le Pennec, K.J. Måløy, A. Hansen, M. Ammi, D. Bideau, X.l. Wu, Phys. Rev. E **53**, 2257 (1996)
81. F. Brochard, P. De Gennes, Langmuir **8**, 3033 (1992), ISSN 0743-7463
82. K. Migler, H. Hervet, L. Leger, Phys. Rev. Lett. **70**, 287 (1993)
83. F.C. Linn, J. Bone & Joint Surgery **49**, 1079 (1967)
84. Z. Dai, S.N. Gorb, Science in China Series G: Phys., Mechan. Astron. **47**, 99 (2004)
85. N. Gravish, S.V. Franklin, D.L. Hu, D.I. Goldman, Phys. Rev. Lett. **108**, 208001 (2012)
86. S.V. Franklin, EPL (Europhysics Letters) **106**, 58004 (2014), ISSN 0295-5075
87. S. Douezan, K. Guevorkian, R. Naouar, S. Dufour, D. Cuvelier, F. Brochard-Wyart, Proc. Nat. Acad. Sci. **108**, 7315 (2011)
88. S. Douezan, F. Brochard-Wyart, Eur. Phys. J. E **35**, 1 (2012)
89. A. John, A. Schadschneider, D. Chowdhury, K. Nishinari, Phys. Rev. Lett. **102**, 108001 (2009)
90. S.C. Nicolis, J. Fernández, C. Pérez-Penichet, C. Noda, F. Tejera, O. Ramos, D.J. Sumpter, E. Altshuler, Phys. Rev. Lett. **110**, 268104 (2013)
91. F. Tejera, A. Reyes, E. Altshuler, Eur. Phys. J. Special Topics **225**(4), 663 (2016)
92. E. Altshuler, O. Ramos, Y. Núñez, J. Fernández, A. Batista-Leyva, C. Noda, Amer. Nat. **166**, 643 (2005)
93. D. Monaenkova, N. Gravish, G. Rodriguez, R. Kutner, M.A. Goodisman, D.I. Goldman, J. Exp. Biol. **218**, 1295 (2015), ISSN 0022-0949
94. T. Balch, Z. Khan, M. Veloso, Proceedings of the fifth International Conference on Autonomous Agents (2001), p. 521
95. Z. Khan, T. Balch, F. Dellaert, *An MCMC-based Particle Filter For Tracking Multiple Interacting Targets* (Springer, 2004), p. 279, ISBN 3540219811
96. C. Noda, J. Fernández, C. Pérez-Penichet, E. Altshuler, Rev. Sci. Inst. **77**, 126102 (2006)
97. E.J. Robinson, T.O. Richardson, A.B. Sendova-Franks, O. Feinerman, N.R. Franks, Behav. Ecol. Sociobiol. **63**, 627 (2009), ISSN 0340-5443
98. J. Li, D. Han, Y.P. Zhao, Sci. Rep. **4** (2014)
99. J.H. Dirks, W. Federle, Soft Matter **7**, 11047 (2011)