FROM MOLECULES TO MOTILE CHEMICAL SYSTEMS – SETTING CHEMISTRY IN MOTION

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From chemical reactions to microscopic motility

In the man-made world, motion is caused by mechanical forces that operate at the macroscopic length-scale. In contrast, it is the combination of physical and chemical mechanisms, involving molecules and their interactions, that sets living matter in motion. Whether biogenic movement is fueled by chemical transformations, or whether it is directed by the complex operation of molecular machines, (supra)-molecular interactions are ultimately responsible for any and all biogenic movement and associated purposeful motility.[1]

On the way to unravelling some of the rules that govern motion at all length scales,[2] we investigate the fundamental rules that impart purposeful motion to active supramolecular compartments – that is, to microscopic objects that are also chemically active. One main motivation for this, is that the cell is the unit structure of life thus its motile behaviour is also essential to its function; e.g. the motility of white cells for immunity, the motility of red blood cells for respiration, and the concerted movement of many cells contracting muscles. Further motivation comes with the possibility of a plausible link between evolutionary advantages and the motility of chemically active prebiotic cells. Finally, achieving control over the motile behaviour of compartments would give us greater control over mass transport in complex and dynamic molecular environments, at length scales between those of molecules and materials.

Hereafter, I will discuss how chemistry can set supramolecular compartments in motion, and conversely, how motion can alter the chemistry of these compartments. The reciprocal (mutualistic) interaction between chemistry and motion has implications for a variety of chemistry fields, including bio-industrial applications with the development of membrane-free artificial organelles, smart carriers, neuromorphic materials, and any other processes that involve controlling mass transport in complex supramolecular systems and at microscopic length scales.

Physical chemistry of droplets out of equilibrium

It is remarkable how little systemic complexity is required for purposeful movement to emerge, though only within a limited range of parameter space. In a heterogeneous oil-in-water system, the presence of a minimal concentration of lipids in water is sufficient to confer motility to oil droplets (Figure 1). Hereafter, I refer to this mechanism of motility as Marangoni propulsion, and one of its distinguishing characteristics is its relevance to a wide range of systems and environments.

Once oil droplets are immersed in a lipid-containing aqueous solution, the lipids organize at the droplet interface, and stabilize the droplet by decreasing the liquid-liquid interfacial tension. Above a minimal concentration, lipids also self-assemble into micelles. At even larger concentrations, these micelles can set a droplet in motion: the micelles take up oil molecules into their hydrophobic core, and this pinching sets the droplets out of their equilibrated organization. In particular, the disruption of the lipid coverage at the interface induces the formation of a flow both inside and outside the droplet, and the combination of these flows propels the droplet forward. The droplets move towards higher concentrations of micelles that sustain the interfacial tension gradient and hence motion. Therefore, this movement is chemotactic towards sources of micelles.[3]

Flows created as a response to gradients in interfacial tension, are known as Marangoni flows,[4] and therefore, when applied to droplets, the mechanism is best described as Marangoni propulsion. In this motile system, small gradients in interfacial tension drive substantial displacements. The movement stops once the lipid distribution on the droplet is homogenous and the droplet reaches equilibrium– which happens either when there are no empty micelles in the system anymore, or once the droplet diameter becomes too small.

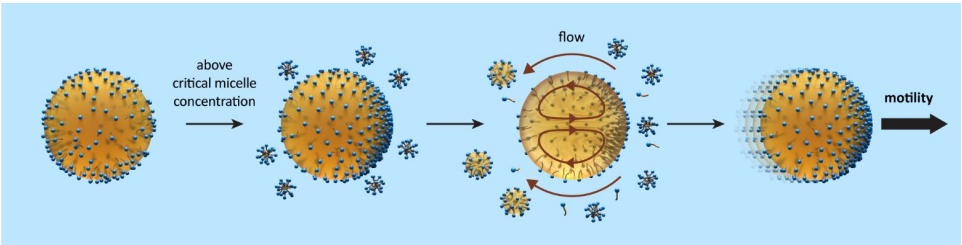

Fig. 1. Motile behavior of droplets in lipid-rich aqueous solutions. Above critical micellar concentration, and in the presence of micelles, the uptake of oil from the droplet causes local instabilities in the interfacial tension. Gradients of interfacial tension lead to mass transport and eventually to the establishment of Marangoni flows, that propel the droplet forward.

Emergence of complex motility in the course of chemical reactions

In a heterogeneous environment, the rate of chemical reactions can be enhanced by active supramolecular motion (Figure 2). The thio-Michael reaction between 1-hexanethiol and water-soluble 2-methacryloyloxyethyl phosphorylcholine (MPC) produces a surface-active lipid that self-assembles into micelles. This system installs micellar auto-catalysis, where the products of the reaction form micelles, and the presence of the micelles accelerates the reaction further.[5,6] Octanol droplets added to the reaction medium are initially stationary, but later, once the reaction produces enough lipids to create an asymmetry in the interfacial tension, they start moving chemotactically. We observed that the rate of the bond-forming reaction was enhanced (Figure 2b). We hypothesise that this acceleration results from two complementary effects: i) the droplets actively and chemotactically attract the reactive interfacial areas to the reagents, and ii) after solubilization, the resulting filled micelles are larger than the empty micelles. As the surface area of a sphere scales quadratically with radius, filled micelles may be able to provide a greater interface for micellar catalysis.[7]

Overall, a lipid-producing chemical reaction initiates the chemotactic movement of droplets and, reciprocally, the chemotactic motion of these droplets enhances the production of lipids. In this symbiotic relationship between chemistry and motion, droplet motility can catalyze bond-forming chemical reactions –we call this phenomenon kinematocatalysis.

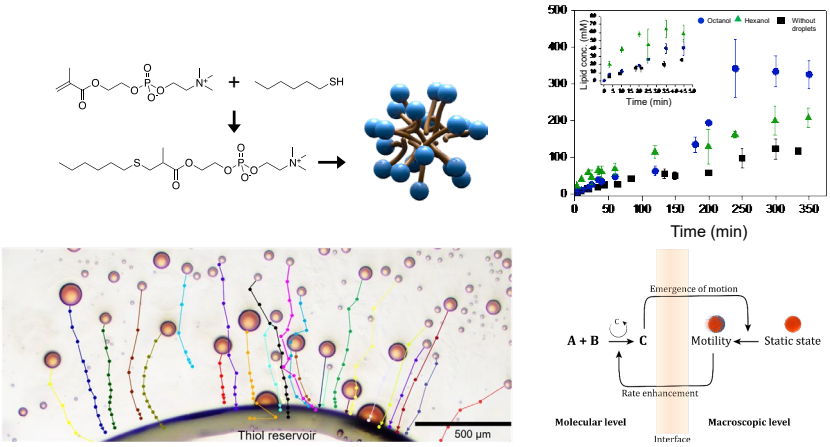

Fig. 2. Mutualism between lipid reproduction and microscopic motion.[7] a) The reaction between 1-hexanethiol and 2-methacryloyloxyethyl phosphorylcholine (MPC) yields a surface-active lipid, which self-assembles to form micelles in water. b) The rate of the lipid-forming reaction is enhanced in the presence of motile droplets. The kinetics are reported in the presence of motile droplets (150 µm, circle), in the presence of stationary droplets of hexanol (~132 µm, triangle) and in the absence of droplets (square). c) The rate enhancement is attributed to the fact that octanol droplets move chemotactically towards regions of high micelle concentration, which also corresponds to regions of high thiol concentration. d) Mutualism between chemistry and motion.

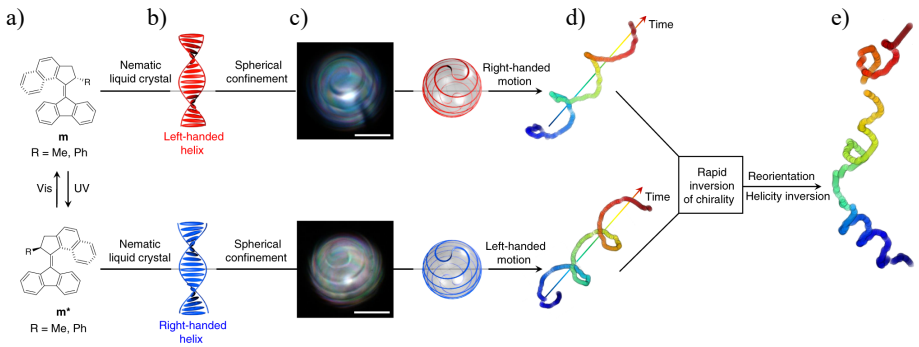

Fig. 3. Reorientation of light-responsive spiral droplets.[8] a) Under illumination with UV light, artificial molecular motor **m** converts into **m***, with opposite helical shape. b) In a nematic liquid crystal, both forms of the motor twist the liquid crystal and thus a supramolecular helix forms, with a mesoscopic handedness that is defined by the helical shape of the motor. c) In spherical confinement and with the liquid crystal molecules aligning perpendicularly to the interface, a double spiral disclination line forms at the surface of the droplet. d) These chiral droplets move along helical trajectories with a handedness that is opposite to that of the droplets. e) Once the molecular motor is illuminated, the photo-inversion of handedness reorients the helical trajectory and the new propagation direction correlates with the number of spiral turns on the droplet.

Although chemotactic, the movement of chemically propelled droplets lacks persistence – typically, it results in erratic motion, with a notable lack of control over rotational degrees of freedom. In contrast, swimming cells and bacteria exhibit persistent movement in fluid, turbulent, and chaotic environments by utilizing deterministic mechanisms to alter their propagation direction. Helical pathways are an evolutionary trait shared by these cells that actively move through water – in other words, they follow the threads of a screw. To explore their environment effectively, these cells have also evolved chirality-based reorientation processes, such as the run and tumble of Escherichia Coli[9] or even more intriguing mechanisms, such as the helical klinotaxis of sperm cells and chlamydobacteria, which is deterministic.[10] Overall it appears that helical trajectories are at the origin of the purposeful movement of swimming cells.

Chiral liquid crystal droplets also exhibit helical motility (Figure 3). We have shown that cholesteric liquid crystal droplets exhibit a distinctive spiral pattern.[11] We created such droplets by adding a small amount of molecular motors as dopants to a nematic liquid crystal. Using an artificial molecular motor as a dopant is obviously not without benefit, as we know that such liquid crystals undergo helix inversion.[12] These chiral droplets follow helical trajectories, with a handedness that is determined entirely by the handedness of the helix-shaped molecular motor dopants (Figure 3). As soon as the chiral droplet is irradiated, the droplet and its trajectory undergo chirality inversion and, also, the direction of propagation is modified dramatically. This deterministic reorientation is entirely encoded by a molecular process, and can be controlled by adjusting the concentration of dopant or the intensity of light.

Outlook

Active mass transport can be controlled by chemical reactions in supramolecular systems. This mass transport at the microscopic length scale can be harnessed to guide interactions between large ensembles of molecules with specific functions—what we refer to as complex molecular systems. In general, systems chemistry is concerned with approaching the chemistry of life. This step forward into complexity requires chemists to shift their focus from optimization and the tackling of independent problems, towards complex systems that integrate orthogonal, parallel-operating functions. Beyond diffusion, I argue that the future of systems chemistry will involve active mass transport, as remaining out of equilibrium necessitates transporting matter.

Controlling supramolecular motility may also prompt the development of new materials for brain-inspired computing. Motion at intermediate length scales serves as means of reorganizing molecules within supramolecular architectures, a crucial step in the evolution of artificial cognitive systems. The active transport of mass will be essential to the design and synthesis of complex and functional molecular systems, because if there is to be communication between two distinct compartments, it will be necessary to manipulate matter, alter its form, deliver fuel for chemical processes, remove waste, etc. In such complex systems, spatially separated molecular modules – compartmentalization – will be essential.

The emergence of movement by interfacial instability requires only an emulsion and surface-active molecules, both of which must have existed at the onset of life on Earth.[13] Consequently, the interplay between movement and chemical reactivity as we describe it is also relevant to prebiotic chemical evolution. Primitive compartments, whether droplets, coacervates, vesicles, or a combination of these, would have required motility to effectively exchange molecules and react with their environments. Current micro-organisms are propelled by entirely different mechanisms than early life compartments would have been, as molecular machines and protein motors have emerged much later. Nevertheless, there must have been a time when primitive life forms and movement mechanisms coexisted.

Overall, I argue that interfacial mechanisms set chemistry in motion. The generation of flows at interfaces is a primitive mechanism that can endow supramolecular systems with autonomous and directional movement. Such purposeful movement is fundamental to the mechanisms of life and will undoubtedly prove to be equally significant in designing increasingly complex and functional chemical systems.

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