Emergency cell swimming

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The study of cell locomotion is a branch of biophysics with a long history (1). One area that has been particularly successful at attracting the combined attention of theorists and experimentalists alike for more than 60 y is that of cell swimming, to the point of reaching textbook knowledge (2, 3). Most bacteria swim by inducing the passive rotation of helical flagella using rotary motors embedded in the cell wall. Swimming eukaryotes, such as spermatozoa or microalgae, generate propulsion by actively deforming flexible flagella in a wavelike fashion using the actuation of molecular motors along polymeric filaments. Ciliates, such as the protozoan *Paramecium*, swim under the coordinated deformation of a large number of cilia (short flagella) anchored on their surface. In PNAS, Hamel et al. (4) have experimentally measured the escape dynamics of *Paramecium* from a model aggression—specifically, a localized heating from a focused laser beam. Their results challenge the conventional physical picture for cell swimming in two ways, first by showing the unexpected role of inertial effects in unsteady swimming, and then by reporting on the discovery of a new swimming gait for *Paramecium*, not based on the use of cilia but on the rapid and directed discharge of organelles.

It's an Inertial World (After All)

Hamel et al. (4) experimentally probe the response of cells to three levels of aggression, referred to here as mild, intermediate, and severe. In the case of mild aggression, either because a low laser power was used or the laser was placed far from the cells, the cell response was observed to be undistinguishable from normal cilia-based swimming, but with the cell changing its swimming direction to move away from the aggression.

For an intermediate aggression level, the cells still used their cilia, but were able to generate rapid accelerations away from the aggression. In normal swimming conditions, cilia are known to beat collectively in so-called metachronal waves (5), in which each cilium beats with a finite phase difference with respect to the beating of its neighbor. In contrast, for the cells escaping intermediate aggression, the cilia near the laser location were observed to beat in synchrony, and displayed coordinated effective and recovery strokes. In essence, in response to an aggression of intermediate level, cilia switched their body

kinematics from that akin to a soccer stadium wave to a legion of synchronized viscous rowers.

That observation is puzzling at first because, on small scales, synchronous rowing should actually not work. The Reynolds number (Re) for the typical flows around the swimming *Paramecium* in this escaping regime never gets higher than $\rho UL/\mu \sim 0.1$, where L is the typical organism size, U its swimming speed, and ρ and μ the density and shear viscosity of the fluid.

Hamel et al. experimentally probe the response of cells to three levels of aggression.

As a result, the equation of motion satisfied by the fluid flow around the organism is the Stokes equation, which has the interesting property of being linear and time-reversible: as a rowing motion is time-reversible, recovery strokes should lead to swimming kinematics equal and opposite to that of effective strokes, and thus together should average to zero (6). For real cilia, of course, the kinematics of their deformation in the effective and recovery strokes are different (7); thus, on average, swimming can be obtained. However, if the cilia all beat in synchrony, at the very least, effective strokes should lead to forward swimming whereas recovery strokes should induce backward swimming. Instead, continuous forward swimming is observed with oscillations between cell acceleration and deceleration. How can this be understood in the context of low Reynolds number locomotion?

The key is the role of inertia, not of the surrounding fluid, but that of the cells themselves. After a recovery stroke, even if the cilia were to all instantaneously stop beating, the cells would be able to coast inertially for a small distance, just like olympic swimmers coast before doing a flip turn. As long as the time scale for the recovery stroke remained less than the time scale for significant coasting, then the cells would never actually stop moving forward. What is the typical value of this coasting time scale τ? During coasting, the cells experience viscous forces on the order of $\sim \mu UL$, which slow them down and, according to Newton law, balance the rate at which their momentum decreases,

which is on the order of $\sim (mU)/\tau$. With cell mass scaling as $m \sim \rho_s L^3$, where ρ_s is the cell density, the balance leads to the estimate for the coasting time $\tau \sim \rho_s L^2/\mu$, notably independent of the speed U during the effective stroke. For neutrally buoyant 100-μm *Paramecium* cells in water, one gets a coasting time scale of $\tau \sim 10$ ms. That time scale is precisely the deceleration time scale measured by Hamel et al. (4), and points to the important role played by cell inertia in the escape dynamics.

Viscous Ballasts

Beyond the two swimming-based escape responses described here, Hamel et al. (4) further show that to escape a severe aggression by the laser, the cells swim away using a completely new gait—one that does not involve cilia. In this "jumping" gait, the cells were able to undergo up to a 10-fold increase in velocity by rapidly ejecting a few so-called trichocysts into the fluid in the direction of the laser, leading to an escape systematically directed away from the aggression. Trichocysts are organelles bound to the plasma membrane, a few microns long, which are known to play a role in chemical defense mechanisms. The fact that trichocysts can also be used for cell locomotion offers a new twist on the hydrodynamics of small-scale swimming.

A detailed look at the cell dynamics offers further insight on the biophysics of cell escape. The trichocyst ejection was observed to occur on a small time scale (~3 ms), leading to a rapid acceleration of *Paramecium*. This fast motion was followed first by a decay of the cell velocity on the time scale τ estimated earlier, and then by normal cilia-based swimming. The sensitivity of the cells to severe aggression, and their ability to exploit the jumping gait to swim away from the laser in any direction, was further observed to be uniform around the cells.

One of the most interesting questions arising from the discovery of the jumping gait is the quantitative relationship between the aggression signal and the dynamic response of the cell. Hamel et al. (4) quantify the cell response by measuring

its initial acceleration. By plotting this acceleration against the magnitude of the signal (in this case, the distance between the laser and the cell), they demonstrate that the cells display an exponential response to the stimulus. Furthermore, the typical high speed ($U \sim 10$ mm/s) reached by the cell at the peak of its escape was found to be well predicted by a force balance argument, whereby the viscous drag force on the backward-moving trichocysts is in instantaneous mechanical equilibrium with the drag force on the forward-swimming *Paramecium*. The trichocysts can thus be thought of as viscous ballasts, released by the cells to induce drag on its environment, thereby gaining the same force as forward thrust.

Biomechanics Approach

Although addressing a different biological scale, the study of Hamel et al. (4) is reminiscent of classical biomechanics investigations at the whole-organism level, in which changes to the environment are used to prompt changes in locomotion gaits (8). A familiar example is the change from running to walking displayed by enthusiastic human bipeds upon entering an ocean; there, the forces from the environment change progressively from friction on the ground to drag forces from water, and ultimately renders traditional running impossible with a human musculature. Similarly, on land, quadrupeds can switch among walking, trotting, and galloping. In fluids (8, 9), some fish alternate between flapping of their fins to whole

body undulations, whereas certain squids swim slowly using fin undulation and switch to unsteady jet propulsion at higher speeds. For these types of large organisms, measurements of changes in locomotion gaits have allowed access to metabolic energetic tradeoffs, and often resulted in rationalizing gait choice as a solution to an optimization problem (8). The prospect of using similar tools to address open questions in the relationship between swimming cells and their environment (10), as done by Hamel et al. (4), is a compelling proposal. It is time to put cells on a treadmill.

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