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Not Just Going with the Flow: The Effects of Fluid Flow on Bacteria and Plankton

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Abstract

Microorganisms often live in habitats characterized by fluid flow, from lakes and oceans to soil and the human body. Bacteria and plankton experience a broad range of flows, from the chaotic motion characteristic of turbulence to smooth flows at boundaries and in confined environments. Flow creates forces and torques that affect the movement, behavior, and spatial distribution of microorganisms and shapes the chemical landscape on which they rely for nutrient acquisition and communication. Methodological advances and closer interactions between physicists and biologists have begun to reveal the importance of flow–microorganism interactions and the adaptations of microorganisms to flow. Here we review selected examples of such interactions from bacteria, phytoplankton, larvae, and zooplankton. We hope that this article will serve as a blueprint for a more in-depth consideration of the effects of flow in the biology of microorganisms and that this discussion will stimulate further multidisciplinary effort in understanding this important component of microorganism habitats.

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Contents

1. INTRODUCTION

Fluid motion is a prevalent feature of the physical environments inhabited by small organisms. Almost three quarters of the planet is covered by water, and these oceans, rivers, and lakes are characterized by the constant motion of water. In soil, water slowly seeps between soil grains, small rocks, and plant roots. In the human body, fluids flow in blood vessels, the urinary tract, the gut, the eye, and the mouth. In all these habitats, fluid flow exerts important controls over both the physical and chemical landscapes from the perspective of microorganisms. From the physical point of view, flow exerts forces on microorganisms, which induce changes to their motions and distributions. From the chemical point of view, flow sweeps molecules that signal the presence of nutrients, predators, or mates toward and away from microorganisms. In the absence of flow, molecules would drift more slowly, and as such, flow alters the concentration of chemicals in the surroundings of microorganisms. As a result, flow can have a broad range of effects on bacteria and plankton, altering their movement, behavior, resource acquisition, and signaling and thereby influencing their metabolic functions, spatial distribution, and diversity. Nonetheless, fluid flow is rarely considered when one is interpreting the biology of small organisms in aquatic environments.

In this review, we describe how flow influences the lives of bacteria and plankton, focusing on the effects of flow on their physical and chemical environments. We consider organisms ranging from a fraction of a micrometer to thousands of micrometers in size, both planktonic (i.e., free floating or swimming) and sessile (i.e., surface attached). To illustrate the diversity of the effects of flow on small organisms, we draw from different habitats and taxa, with a primary emphasis on bacteria and secondarily plankton inhabiting aquatic environments such as oceans and lakes. We divide the review into two parts, treating how flow shapes the physical and chemical environments of bacteria and plankton. We first illustrate how fluid flow affects small organisms by exerting forces and torques on them that can profoundly change their movement and spatial distribution. For example, we show that where phytoplankton end up in the water column depends heavily on the interaction between their shape and flow, an interaction that is purely passive. In addition, we describe how fluid flow can elicit intriguing behaviors in the plankton, that is, active responses. The latter is an exciting area of research because, historically, most interactions

Torque: measure of the force that can cause an object to rotate about an axis

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between bacteria or plankton and flow were assumed to be purely physical consequences of the forces exerted by the flowing fluid. However, it has recently become apparent that small organisms can sense and behaviorally respond to forces from the flow, adding both richness and new challenges to the study of organism–flow interactions. We then discuss how flow affects small organisms by altering their chemical landscape, including the distribution of resources, oxygen, and signaling molecules. We emphasize that we cannot here present either a complete review of the interactions of microorganisms with flow or a full treatment of the fluid mechanics involved. Instead, we offer a nontechnical and hopefully intuitive introduction to the effects of fluid flow on small organisms and their physical and chemical environment, illustrating recent progress in this field and highlighting promising avenues for future research.

2. PHYSICAL EFFECTS OF FLOW ON BACTERIA AND PLANKTON

Fluid flow takes on different forms in the wide range of environments inhabited by bacteria and plankton. In small liquid volumes, flow is often regular and organized, or laminar, such as in the transport systems of hosts; examples are water moving slowly through the roots of plants and human blood in capillaries. In aquatic systems, flow is often turbulent and easily observable at human scales but drives motion and creates forces down to the scales relevant to microorganisms, here referred to as the microscale. In soil, water motion through the pores between grains is again laminar but highly geometrically complex. In many compartments of the human body, such as the gut, urinary tract, and eye, liquids are in motion. In bioreactors, liquids are actively stirred, again leading to turbulent flow. In all these systems, flow can affect both the transport and physiology of the resident small organisms, and these can respond to flow with phenotypic and behavioral changes.

The appearance and effects of flow change dramatically as one moves from the human scale, at which our intuition is trained, to the microscale, at which microorganisms experience flow. Turbulent flow, for example, is often created at larger scales by some external forcing, such as wind and waves in aquatic systems and active pumping (e.g., pulsative or peristaltic motion) in the human body. An organism at large scales experiences this fluid flow as an intermittent, chaotic motion, such as when a fallen surfer is knocked about in a large wave, encountering rapid changes in flow speed and direction. However, to a smaller organism, this fluid motion appears slower and smoother, as the organism is embedded within a single whirl of the flow. For instance, a wave that knocks a surfer around (**Figure 1*a***, **subpanel *i***) will carry a small marine larva or bacterium much more smoothly, as the microorganisms are not large enough to be caught and tossed by the churning water (**Figure 1*a***, **subpanels *ii*,*iii***). They instead primarily experience turbulence as a fluid velocity that—at their scale—changes smoothly in space, here referred to as a shear flow (**Figure 1*a***, **subpanel *iii***). A shear flow occurs when different fluid volumes flow past each other at different velocities, such as in the case of a layer of warm surface water flowing on top of a layer of colder deeper water (**Figure 1*b***). Shear flows also develop when a moving fluid encounters a solid surface: In this case, the speed of the fluid gradually decreases so that its velocity in contact with the surface is zero (for an immobile surface). Surface shear flows affect the organisms moving near or living on those surfaces (**Figure 1*c*,*d***).

Shear is an important concept in the interaction of flow and small organisms: The fact that the velocity is different at different locations results in a torque that constantly rotates organisms (**Figure 2*a***, **subpanel *i*** and **Figure 2*b***, **subpanel *i***). This, as we present below, affects a host of processes from motility to attachment, which we illustrate using examples covering the interactions of bacteria, phytoplankton, and larvae with flow. Most of these examples (summarized in **Table 1*a***) constitute passive responses to flow: For instance, cell shape in bacteria and plankton species can lead to accumulation in high-shear regions. In this manner, organisms can end up in

Laminar flow: a flow in which fluid parcels move following regular paths, often in parallel layers. This type of flow is common for viscous fluids (like oil or mucus) and for aqueous fluids at very small scales

Turbulent flow: a highly disordered flow that is characterized by motion at many different scales and is variable in time and space. It typically results in rapid stirring and mixing

Shear flow: a flow in which the speed of the fluid varies between neighboring fluid parcels. Laminar flows in a conduit or close to a surface constitute examples of shear flow. Turbulent flow at the smallest scales is also a shear flow

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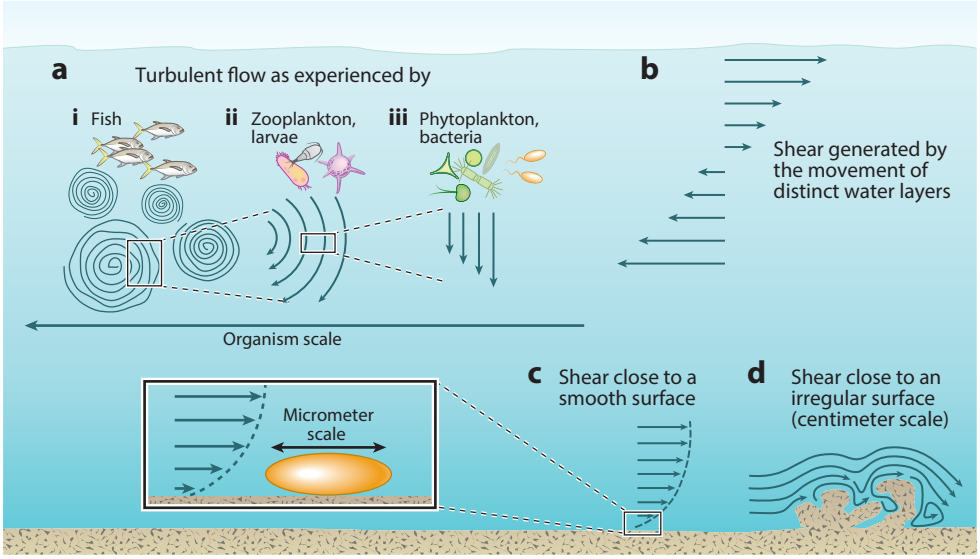

Figure 1

Types of flow experienced by bacteria and plankton in aquatic environments. (*a*) Turbulent flow. (*i*) At the scale of humans or fish, aquatic turbulence is experienced as a set of interacting whirls of different sizes; these whirls cause rapid changes in the direction and speed of flow. (*ii*) At the scale of zooplankton and larvae, turbulence is experienced as a smoother rotation, although sometimes also as strong shear, as organisms are approximately the size of the smallest whirls. (*iii*) At the scale of phytoplankton and bacteria, turbulence is experienced as a smooth change in flow speed over space, as these organisms are smaller than the smallest whirls. (*b*) Shear flow can occur in open water as different layers of water move past each other. Flow speed changes smoothly over space and can even change direction entirely. (*c*) Shear flows also occur near solid surfaces because water slows close to a surface. In all these cases, shear is felt right down to the scale of the smallest organisms, as shown in the inset. (*d*) Flows become more complex near rough bottom surfaces, causing changes in flow speed as well as direction.

specific regions of the flow without any active, behavioral response to the flow. The ecological outcome of these passive flow–organism interactions can be either positive or negative for the organisms, as we explore below. Additionally, some phytoplankton and many larvae also actively respond to flow (**Table 1*b***) and exploit flow conditions via behavioral responses to enhance transport and survival.

2.1. Vertical Migration of Phytoplankton in Flow

Persistent shear flows occur frequently in aquatic systems due to layering of water masses, proximity of flows to surfaces, and other physical drivers. The interactions of phytoplankton with shear flows have long interested oceanographers because they can affect the spatial distribution and competitive advantage of different phytoplankton species. Vertical swimming is a common behavior of motile plankton in aquatic systems, with many species making daily journeys between the surface and depth. Daily migration, often covering many meters or even tens of meters, allows photosynthetic phytoplankton to reside in well-lit surface waters during the day and to return to nutrient-rich depths at night (**Figure 2*a***, **subpanels *i,ii***). On this vertical journey, the phytoplankton encounter flow, which can affect their migration in surprising ways that have been only recently understood.

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The body shape of swimming phytoplankton affects how they are impacted by shear flows. Many motile phytoplankton have evolved to be bottom heavy (Roberts 1970), resulting from either pear-shaped morphologies (**Figure 2*a***, **subpanel *i***) or a higher density of organelles located on one end of the cell (e.g., the starch-rich chloroplasts). Many such phytoplankton swim by pulling or pushing themselves through the water, and the density asymmetry is a way to passively orient in their preferred, vertical swimming direction. For example, for upward migration, the wider end of a pear-shaped cell tends to fall below the narrower end of the cell, acting as a ballast to stabilize the organism in the vertical direction. This body asymmetry ultimately gives the cell an energy-efficient way to preserve the upward swimming direction in still water conditions. However, it confers a potential disadvantage when cells encounter shear flows, for example, due to ocean currents, which preferentially move along the horizontal direction. When an upward-moving cell enters a region of high shear, the change in flow velocity with height begins to tip the cell over,

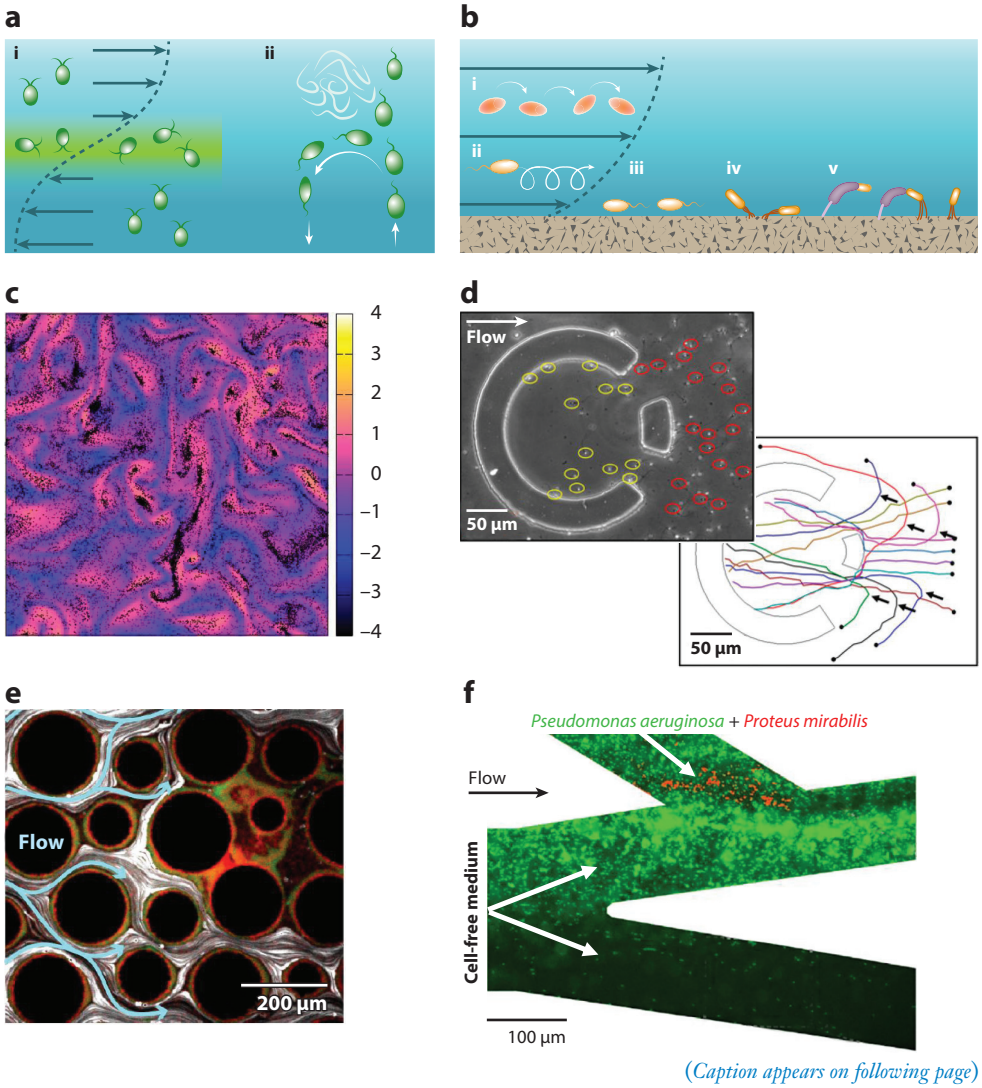

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Figure 2 (*Figure appears on preceding page*)

Physical effects of flow on bacteria and plankton. (*a*) Effects of flow on vertically migrating phytoplankton. (*i*) Upward-swimming phytoplankton encountering regions of high shear are rotated by fluid torques that deflect their intended swimming paths and trap them in thin layers in the water column. (*ii*) Upon encountering patches of strong turbulence during upward migration, some phytoplankton (e.g., *Heterosigma akashiwo*) can rapidly change shape to induce a change in swimming direction, allowing them to escape damaging and stressful turbulent conditions. (*b*) Effects of shear on bacteria in the water column and on surfaces. (*i*) In regions of shear, the torque from the shear rotates microorganisms as they are transported by the flow. (*ii*) Due to this mechanism, microorganisms move along periodic trajectories, termed Jeffery orbits. (*iii*) When cells use flagella to swim in the proximity of a surface, shear can orient the cells against the flow, causing cells to migrate upstream by swimming. (*iv*) With a similar mechanism, cells can migrate upstream by moving on a surface using pili. (*v*) Shear brings the piliated pole of curved stalked bacteria closer to the surface, increasing the attachment rate of the daughter cell after division. (*c*) Turbulence creates patchiness in the distribution of motile microorganisms. A numerical simulation of turbulent flow (*background color* denotes turbulence intensity) shows how simulated swimming phytoplankton (*black dots*) become trapped in regions of intermittent strong shear. Panel *c* adapted from De Lillo et al. (2014). (*d*) The effects of flow can be used to sort cells on the basis of motility, in this case for human sperm cells. Only motile sperm cells can reach the trap structure within a microfluidic channel by performing upstream swimming, and this principle can be used to sort these cells by motility. Panel *d* adapted from Zaferani et al. (2018). (*e*) Flow can lead to segregation within bacterial biofilms. In confined flow, weakly adhesive mutants of *Pseudomonas aeruginosa* (*red*) occupy locations protected from flow due to local clogging by the biofilms formed by strongly adhesive wild-type *P. aeruginosa* (*green*). Panel *e* adapted from Nadell et al. (2017). (*f*) Flow can lead to segregation on the basis of colonization ability. Surface colonization of a flow network by two bacterial species with different surface motility: Upstream twitching permits *P. aeruginosa* (*green*) to colonize all the branches of the flow network, whereas *Proteus mirabilis* (*red*) colonizes only the branch in which it is injected. Panel *f* adapted from Siryaporn et al. (2015).

away from its stable orientation (Durham & Stocker 2012, Durham et al. 2009). The cell is thus rotated by a fluid torque, and its path is deflected from its preferred vertical direction. If the shear is sufficiently large, the bottom heaviness is not sufficient to stabilize the cell, and the flow makes the cell tumble in the high-shear region, thus trapping the cell at that depth and preventing its vertical migration (**Figure 2*a***, **subpanel *i***). This trapping effect arising from shear flow has been proposed to be a mechanism for the formation of the frequently observed thin layers of phytoplankton in aquatic systems (Durham et al. 2009). These layers are accumulations of plankton in a narrow depth layer but extending over kilometers (Dekshenieks et al. 2001, Moline et al. 2010), reaching phytoplankton concentrations several times and potentially orders of magnitude higher than background levels (Ryan et al. 2008, Sullivan et al. 2010). Thin layers persist from hours to weeks (Durham & Stocker 2012) and represent important ecological hot spots in the ocean. The interaction between motile phytoplankton and shear flow thus offers a first example of how flow can change the spatial distribution of microorganisms on large scales.

A similar interaction between flow and organism shape occurs when flow is turbulent. The small turbulent whirls that microorganisms are embedded in exert torques on them; that is, the whirls reorient the microorganisms. This reorientation is again resisted by the bottom heaviness of the organisms. The competition between destabilizing torques due to turbulence and stabilizing torque due to bottom heaviness results in swimming phytoplankton accumulating in certain high-shear regions of the turbulent flow, causing patchiness in the population distribution at millimeter scales (Breier et al. 2018, De Lillo et al. 2014, Durham et al. 2013, Gustavsson et al. 2016) (**Figure 2*c***). Because the spatial distribution of organisms is a key determinant of encounter rates between organisms, these effects of flow can have far-reaching consequences for plankton and aquatic ecology. One consequence of accumulation in layers or patches is enhanced predation. In this respect, it is well established that thin phytoplankton layers are preferential foraging grounds for higher trophic levels; the larvae of some fish species do not make it to adulthood unless they

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Table 1 Summary of (*a*) passive flow–organism interactions and (*b*) active flow–organism interactions related to the physical effects of flow on bacteria, phytoplankton, and larvae (described in Section 2), highlighting the mechanisms and ecological consequences of these interactions

Organism type	Mechanism	Ecological consequences	Section
(*a*) Passive flow–organism interactions			
Phytoplankton or larvae, motile but weakly swimming, with nonuniform shape or density	Top-heavy or bottom-heavy cells are passively reoriented, thus swimming downward or upward, respectively. Organisms are vulnerable to overturning in high shear.	Organisms accumulate in patches or layers, which can make them more vulnerable to predation, can disrupt their vertical migratory patterns, and can favor cell–cell encounters for sexual reproduction.	2.1, 2.4
Bacteria, elongated	Cells undergo periodic rotations (Jeffrey orbits) due to torque exerted by shear, preferentially aligning with the flow direction due to their elongated shapes.	For nonmotile helical bacteria, this preferential alignment can cause the bacteria to drift perpendicular to the flow direction, leading to accumulation.	2.2
Bacteria, elongated and motile	Jeffery orbits and swimming contribute to the trapping of cells in high-shear regions (shear trapping).	Motile bacteria accumulate near surfaces, enhancing surface colonization, but their chemotactic migration is hampered.	2.2
Bacteria, elongated and flagellated, and sperm cells	Flow reorients swimming cells near a surface around their flagella, directing the cells upstream (upstream swimming).	By migrating upstream, bacteria can more effectively infect catheters and medical devices. Upstream swimming can also be exploited to separate motile sperm.	2.3
Bacteria, motile on surfaces via pili (twitching motility)	Flow reorients cells using twitching motility on a surface around the cell poles, directing the cells upstream (upstream twitching).	Like upstream swimming, upstream twitching can favor infection and colonization of flow networks.	2.3
Bacteria, elongated and/or curved, on surfaces	Bacterial shape enhances surface adhesion in flow by increasing the probability of contact of daughter cells with the surface.	There is increased surface colonization in flow by elongated and/or curved cells relative to nonelongated cells.	2.3
Bacterial biofilms	Flow influences biofilm initiation, structure, and mechanical resistance.	Biofilms show increased surface attachment, biofouling, and potentially infection.	2.3
(*b*) Active flow–organism interactions			
Phytoplankton, motile with nonuniform shape or density	Bottom-heavy cells rapidly adjust their shape to be top heavy in response to overturning in flow, thus shifting from upward to downward swimming.	Cells can avoid deleterious turbulence patches during vertical migration.	2.1
Larvae, strongly swimming	Larvae increase swimming speed in response to flow, swim against the prevailing vertical current, or sink/dive in response to flow.	Larvae regulate their vertical position in the water column to exploit differential transport and favorable horizontal currents, impacting dispersal and settlement success.	2.4
Larvae, specifically of the urchin *Strongylocentrotus purpuratus*	High-flow conditions accelerate development in urchin larvae to induce competence to settle.	Larvae leaving calmer open ocean conditions and approaching more turbulent near-shore regions can settle in and be recruited to preferred coastal sites.	2.4

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encounter a thin layer (Durham & Stocker 2012). The formation of patches can also have positive consequences for phytoplankton. For phytoplankton species whose life cycle includes a sexual stage, patch formation increases encounter rates. Furthermore, we speculate that patch formation may provide a means to enhance the local concentration of chemicals exuded by plankton, such as allelopathic compounds aimed at deterring other organisms. In general, however, much about the consequences of these prevalent plankton accumulations remains to be investigated.

The examples so far illustrate some of the consequences of microorganisms being redirected in their swimming by the torques caused by fluid shear. In these examples, shape plays a fundamental role in that it mediates the interaction between motility and flow. This role of shape, however, can be considered passive in that it involves no active response of the organisms to the flow. Recently, it was found that some phytoplankton are not simply passively at the mercy of flow—as had long been held—but can behaviorally respond to cues from the flow (see Section 4, titled Mechanisms of Flow Sensing, below). *Heterosigma akashiwo*, among other motile phytoplankton, can actively respond to flow cues by rapidly changing shape and thereby changing their swimming behavior (Sengupta et al. 2017). A small change to the shape asymmetry allows a fraction of the cells in a population to switch from bottom heavy to top heavy, thus passively reorienting the cells to swim downward rather than upward. The shape change is concurrent with a build-up in oxidative species in the cell, likely due to stress, but the biological mechanism of the shape change is unknown and represents fertile ground for investigation by cell biologists. This rapid and active physiological shift in response to flow may allow vertically migrating phytoplankton to alter their migratory strategies and to swim away from regions of high turbulence; such turbulence is physiologically deleterious for many species of motile phytoplankton (Sengupta et al. 2017) (**Figure 2*a***, **subpanel *ii***). This, therefore, represents an example of how plankton can actively control their shape, in response to cues from flow, to modulate their macroscale migratory behavior.

Viscosity: measure of a fluid's resistance to flowing when exposed to shear. A high-viscosity fluid is viscous

Jeffery orbit: rotational trajectories that particles (or microorganisms) undergo when exposed to a shear flow. The rotation speed typically varies with orientation relative to the flow (except for spheres, for which it is constant)

Microfluidics: technology that allows for the manipulation of liquids in the microliter to picoliter range, in networks of channels with micrometric or submicrometric dimensions

2.2. Spatial Distribution of Bacteria in Flow

Like phytoplankton, bacteria are transported by flow. If the flow is uniform, it has the simple effect of bringing bacteria to a different region in space. However, flow is rarely uniform and is often associated with spatial variation in velocity (i.e., shear) (**Figure 1*b–d***). Shear is the principal factor in the interaction between bacteria and flow and, as for phytoplankton, is mediated by the shape of the microorganisms. The shape of bacterial cells ranges from spheres and spheroids to triangles, squares, teardrops, and helices (Young 2006), some of which may have evolved to maximize the fitness of cells in their typical fluid dynamic environment, as discussed in Vogel (1996). A striking example in a quiescent fluid environment is the helical shape of the gastric pathogen *Helicobacter pylori*, which increases the ability of cells to move in the viscous stomach mucus, causing inflammation (Sycuro et al. 2012). In a shear flow, bacteria—like passive particles—undergo periodic rotations (Jeffrey 1922). These rotations, termed Jeffery orbits, arise because, while the center (more precisely, the centroid) of the bacterium moves exactly with the flow, the body rotates due to the torque exerted by the shear flow. Spherical bacteria, such as cocci, rotate with constant rotation rate. In contrast, elongated shapes, such as bacilli, rotate at a rate that fluctuates over time: more rapidly when they are oriented transverse to the flow and more slowly when they are aligned with the flow (**Figure 2*b***, **subpanels *i,ii***). This effect can be very strong, causing bacteria that have an aspect ratio like that of *Escherichia coli* or *Bacillus subtilis* to spend the vast majority of time aligned with the flow and to periodically flip (**Figure 2*b***, **subpanel *ii***). For nonmotile helical bacteria, this preferential alignment can cause the bacteria to drift perpendicular to the flow direction, leading to their accumulation around the center of a channel or other flow conduit, as observed with *Leptospira biflexa* in microfluidic experiments (Marcos et al. 2009).

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When bacteria are motile, the preferential alignment caused by Jeffery orbits has strong and rapid effects on their spatial distribution. This was recently demonstrated in microfluidic experiments (Rusconi et al. 2014) with suspensions of *B. subtilis* and of *Pseudomonas aeruginosa*. In those experiments, bacteria in flow accumulated preferentially in the low-velocity but high-shear regions close to the microchannel sidewalls, creating a depletion in cell concentration of up to 70% in the central region of the channel, characterized by high velocity but low shear. This phenomenon, termed shear trapping, has also been predicted on theoretical grounds (Ezhilan & Saintillan 2015) and is likely of broad occurrence, as it depends only on the elongated shape of the bacteria, their motility, and the presence of shear. Shear trapping can directly affect fundamental microbial functions. First, since this mechanism causes cells to move to high-shear regions that often arise near surfaces, it increases the encounter and attachment rate of cells with surfaces, possibly promoting biofilm formation and infections. As shown with *P. aeruginosa* (Rusconi et al. 2014), the surface coverage (i.e., the fraction of the surface covered by bacteria) can increase by up to 125% as shear increases relative to quiescent conditions. This mechanism is solely regulated by the local hydrodynamics and is due neither to an active response of the bacteria nor to the specifics of their interaction with the surface. Second, shear trapping hampers the ability of bacteria to actively move in response to chemical stimuli (chemotaxis), a fundamental mechanism to find nutrients and infect hosts, as shown by experimental observations (Rusconi et al. 2014) and numerical modeling (Bearon & Hazel 2015). By trapping *B. subtilis* in regions where shear is high, flow can reduce the ability of this bacterium to move toward higher oxygen concentrations in an oxygen gradient (aerotaxis) by up to 85% relative to flow-free conditions (Rusconi et al. 2014). These effects depend only on the morphology of the bacteria and are independent of other traits or physiological conditions, so these interactions likely affect a very broad range of bacteria across different habitats. While the ecological consequences of this recently discovered mechanism remain to be investigated, one can speculate that certain animals may use this mechanism to prevent chemotaxis of pathogens toward the animals' surfaces. Corals, for example, generate strong flows, and therefore high shear, in the vicinity of their surfaces by means of cilia on their outer surfaces (Shapiro et al. 2014). Moreover, bacterial pathogens of corals use chemotaxis toward the mucus secreted by the coral animal, likely to facilitate coral colonization and potentially infection (Garren et al. 2014). The trapping induced by high shear rates may thus serve a function analogous to the function of a simple immune system in corals by hampering pathogens from landing on the coral.

Gradient: the rate at which a quantity (e.g., chemical concentration) changes with distance

Shear trapping is an example of how flow controls bacterial distribution and concentration. At the same time, the concentration of bacteria can influence the flow. In dense suspensions, i.e., bacterial suspensions with cell density higher than approximately 10^9 cells/mL, the motility of bacteria creates turbulence-like flow patterns on a spatial scale of 100 μm (Dombrowski et al. 2004, Secchi et al. 2016) and can create flows (Wioland et al. 2016) that can substantially accelerate the transport of objects suspended in the fluid (Kaiser et al. 2014). This bacterial turbulence can cause bacteria to move two to three times faster than individual cells can swim (Dombrowski et al. 2004). Bacterial densities of this magnitude may occur in the gut (Dukowicz et al. 2007), and while more work is required to determine whether these flow structures are present, their occurrence would affect the mixing regime of the gut as well as the access of individual bacteria in the microbiome to the different gut regions. If present, bacterial turbulence could be beneficial for the host by increasing the mixing and transport of microbiota-generated metabolites, which play a crucial role in immune and metabolic disorders (Lee & Hase 2014).

2.3. Surface-Associated Behaviors of Bacteria in Flow

Near surfaces, bacteria encounter a hydrodynamic environment that is substantially different from the one they experience in bulk, and in this environment, the forces generated by the motion of

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the fluid impact their transport and behavior (**Figure 1*c*,*d***). In an otherwise quiescent fluid, motile bacteria accumulate near solid surfaces due to a force—arising from the flow generated by their swimming—that attracts the bacteria to the surface (Berke et al. 2008, Molaei et al. 2014). In the presence of flow, this interaction with the surface can instead trigger bacterial movement in the direction opposite to the flow, or upstream swimming (**Figure 2*b***, **subpanel *iii***). This behavior is observed in flagellated bacteria with an elongated body; such bacteria swim very close to a surface (i.e., within a body length) by using the flagella to propel themselves (**Figure 2*b***, **subpanel *iii***). The front part of the body acts as a pivot point around which fluid shear rotates the cell and orients it facing upstream, like a weather vane orienting in the wind. This effect, well studied in *E. coli* (Hill et al. 2007, Kaya & Koser 2012), can lead to an upstream migration speed that is much larger than the speed at which a bacterial colony spreads by growth (Hill et al. 2007), with important implications for the spreading of infections in catheters and medical devices. Incidentally, upstream swimming also occurs in sperm cells (Miki & Clapham 2013), potentially the result of coevolution of sperm flagellar motility and the flow rate in the female reproductive tract (Tung et al. 2015). This upstream swimming behavior can be exploited to separate motile sperm from samples for the treatment of infertility, as recently demonstrated in microfluidic experiments (Zaferani et al. 2018) (**Figure 2*d***).

In bacteria, upstream migration can be achieved not just by flagellar motility but also by surface motility. Such migration has been observed for *P. aeruginosa* (Shen et al. 2012), *Xylella fastidiosa* (Meng et al. 2005), and *Mycoplasma mobile* (Miyata et al. 2002), all of which move on surfaces by the extension and retraction of type IV pili, a type of motion termed twitching (**Figure 2*b***, **subpanel *iv***). Pili are located predominantly at one pole of the cell, and the cell periodically extends and retracts them to pull itself along the surface. The torque exerted by the shear flow next to the surface flips the cell around the pole so that the latter points upstream, triggering a preferential twitching migration against the flow (Shen et al. 2012). Although migration speeds by upstream twitching are 100-fold lower than for upstream swimming with flagella, dispersal by upstream twitching can still grant growth advantages. Such upstream migration can drive a cyclical process to colonize flow networks, termed dynamic switching, in which cells move upstream on the surface, detach, and are transported downstream by flow (Kannan et al. 2018). Microfluidic experiments recently revealed that, by using upstream twitching, *P. aeruginosa* gains a competitive advantage over its natural competitor *Proteus mirabilis*. *P. mirabilis* grows more rapidly and moves considerably faster on surfaces but is not able to migrate upstream. Thanks to upstream twitching, *P. aeruginosa* can segregate by moving upstream from a coculture with *P. mirabilis* and can thrive in flow regions that cannot be reached by *P. mirabilis*, which would otherwise outgrow *P. aeruginosa* in the absence of flow (Siryaporn et al. 2015) (**Figure 2*f***).

Shear can favor surface colonization not only by increasing the encounter rate of bacteria with surfaces (Rusconi et al. 2014) but also by increasing the residence time of bacteria on surfaces. In *P. aeruginosa*, larger shear rates caused longer residence times of cells on microfluidic surfaces independently of the specific surface chemistry (Lecuyer et al. 2011). The exact mechanism remains unknown, but a reduced effect in mutants lacking polar type I and IV pili (cupA1 and pilC), flagella (flgK), or the ability to synthesize certain matrix components (pelA) suggests the involvement of multiple adhesive structures (Lecuyer et al. 2011). Shear-enhanced adhesion also occurs in other bacterial species. In *E. coli*, it is a consequence of specific catch bonds formed between an adhesion protein present on type I pili (FimH) and mannose adsorbed on the surface: Enhancement of adhesion is triggered by a conformational change of FimH under load (Thomas et al. 2008). Similar conformational changes of fibers under load are responsible for shear-enhanced adhesion in *Staphylococcus epidermis* (Weaver et al. 2011) and *Staphylococcus aureus* (Pappelbaum et al. 2013).

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Fluid flow can further enhance surface colonization through interaction with the shape of bacteria. The curved, elongated shape of *Caulobacter crescentus* was recently found to enhance colonization of surfaces in flow upon cell division, whereby flow orients the piliated pole of the arched daughter cell toward the surface to which the mother cell is attached (Persat et al. 2014) (**Figure 2*b*, subpanel *v***). This mechanism increases the frequency of daughter-cell attachment to the surface after cell division relative to the case of a nonarched mutant, favoring the spreading of colonies in environments with flow. More generally, elongation assists bacteria in withstanding shear forces on surfaces, as elongation reduces the area exposed to the shear force when the cell is oriented with one pole facing the incoming flow (Young 2006).

Bacterial attachment to surfaces is often the first step toward the formation of biofilms. Biofilms are communities held together by a self-secreted matrix of extracellular polymeric substances and represent a widespread mode of life of bacteria (Hall-Stoodley et al. 2004). Biofilms grown in high-shear conditions have a dense monolayer (flat) structure, which resists shear due to its compactness, whereas in low shear, biofilms develop a multilayer (fluffy) structure, which allows for better nutrient exchange relative to the flat structure but cannot withstand the same mechanical stimuli (Paul et al. 2012, Salek et al. 2009, Stoodley et al. 1999). Local flow conditions associated with the presence of obstacles, constrictions, or corners can even more dramatically affect the structure of biofilms, leading to the formation of long, filamentous structures termed streamers (Rusconi et al. 2010). The systematic study of microscopic streamers has only recently begun with the advent of microfluidic systems (Autrusson et al. 2011; Rusconi et al. 2010, 2011). Often characterized as biofilm filaments suspended in the flow, streamers can have a greater impact on the flow relative to classic biofilms, for example, by causing rapid clogging of artificial and natural conduits, porous media, and medical devices (Drescher et al. 2013, Hassanpourfard et al. 2015). In the context of the effects of flow on biofilm architecture, a largely open question is the extent to which flow affects the microstructure and the mechanical properties of these cell consortia. In some studies, flow was reported to increase the adherence and cohesion of biofilms (Klapper et al. 2002, Rodesney et al. 2017, Rupp et al. 2005, Stoodley et al. 2002), whereas other studies reported no effect (Galy et al. 2012, Kundukad et al. 2016). These discrepancies may be due to the diversity of growth conditions and of the bacterial species considered. In addition, flow control and quantification of the biofilm development are challenges that we are only recently beginning to overcome, using advanced microfluidic technologies (Yawata et al. 2016) and sophisticated imaging techniques (Drescher et al. 2016). Further research in this domain may have important implications for combating biofouling on medical devices, filtration membranes, and other devices (Conrad & Poling-Skutvik 2018).

The flow environment can significantly affect population dynamics within growing biofilms by generating feedback between flow conditions, spatial architecture, and interspecies competition. For example, the presence of regions with different velocity in a flow can trigger the spatial segregation of bacterial communities on the basis of their adhesiveness (Martínez-García et al. 2018, Nadell et al. 2017). As an example, in surface-attached communities, high-velocity flow detaches weakly adhesive cells, favoring their dispersal and the formation of smaller colonies, whereas low-velocity flow does not affect the attachment of highly adhesive cells, promoting the formation of larger colonies (Martínez-García et al. 2018). There is also feedback: By forming large and stiff biofilm structures that can withstand considerable hydrodynamic forces, more adhesive cells create areas protected from flow that favor the growth of less adhesive cells, which would otherwise be detached by shear (Nadell et al. 2017) (**Figure 2*e***).

2.4. Dispersal and Settlement of Larvae in Flow

Many species of aquatic invertebrates are meroplanktonic; i.e., they spend part of their lives in the plankton (that is, suspended), interacting with flows in the bulk. The adult often lives on

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a surface but releases larvae in the water column. To transition to adulthood, the larvae must eventually settle on surfaces; some larvae do so by sensing and responding to flow signals near surfaces (**Figure 1*c*,*d***).

Diffusion: flux of molecules along a concentration gradient driven by molecular interactions. The motion is directed from high-concentration to low-concentration regions

Advection: transport of a substance by fluid flow, i.e., a net motion of the fluid

Vertical migration and the regulation of vertical position in the water column are important to larvae during their free-swimming planktonic phase. Some highly asymmetrically shaped, weakly swimming larvae, such as the echinoderms *Hemicentrotus pulcherrimus* and *Dendraster excentricus*, are passively oriented swimmers (Chan 2012, Mogami et al. 2001), like the phytoplankton described in Section 2.1, and such larvae have bottom-heavy morphologies that induce upward swimming in still water. Many stronger-swimming larvae, however, can actively change their swimming behaviors in the presence of the uniform or turbulent flows that characterize their coastal environments. Diverse larvae (e.g., the blue crab *Callinectes sapidus* and the urchin *Arbacia punctulata*) increase swimming speeds (Welch & Forward 2001, Wheeler et al. 2016), the barnacle *Semibalanus balanoides* swims against prevailing flows (DiBacco et al. 2011), and the oyster *Crassostrea virginica* sinks or dives (Fuchs et al. 2015, Wheeler et al. 2015). Such behaviors—among others—allow larvae to regulate their vertical position in the water column. Such positioning, in turn, affects how larvae are transported and dispersed by flow at large scales: Larvae higher in the water column are carried further by strong surface currents (Dekshenieks et al. 1996, North et al. 2008), and vertically moving larvae can swim into and exploit depth-dependent horizontal currents that transport these larvae toward coastal settlement sites (Helfrich & Pineda 2003). This depth-dependent dispersal of larvae offers an example of how organisms can affect their dispersal by flow over large scales by regulating their behavior and flow interactions at small scales.

As larvae seek a surface to settle onto the ocean floor, the flow cues that they experience change, and their responses to these cues may facilitate settlement in suitable locations. Near rough bottom topographies where, for example, oyster or coral larvae settle, flow is highly complex, changing speed and direction frequently (**Figure 1*d***). Swimming larvae then experience rapid, intermittent fluctuations in flow that increase closer to the bottom surface (Pepper et al. 2015). Rapid behavioral responses to flow may thus help larvae settle. *C. virginica* larvae, for instance, respond to rapid fluctuations in flow velocity by arresting their swimming, permitting them to dive-bomb toward surfaces owing to their excess density over seawater (Wheeler et al. 2015). In addition to inducing behavioral responses, flow cues can induce developmental acceleration, as shown in the larval urchin *Strongylocentrotus purpuratus*. This accelerated development causes a transition from precompetence to competence to settle following exposure to high-turbulence conditions (Gaylord et al. 2013), although the physiological underpinnings of this transition remain unknown (Hodin et al. 2018).

3. EFFECTS OF FLOW ON THE CHEMICAL LANDSCAPE EXPERIENCED BY BACTERIA AND PLANKTON

Beyond directly affecting small organisms by exerting forces and torques that change their migration and surface behaviors, flow can also indirectly affect these organisms by shaping the landscape of their nutrient and signaling cues. Nutrient uptake, respiration, detection of predators and prey, and signaling rely upon the transport of dissolved chemicals. In the absence of flow, molecules are transported solely by molecular diffusion (**Figure 3*a***, **subpanel *i***). In the presence of flow, molecules are instead transported primarily by advection (**Figure 3*a***, **subpanels *ii–iv***), which is typically much faster than diffusion. The spatial scale, the rate of diffusion of molecules, and the speed of the flow determine which of the two processes is dominant, with considerable impact on life at the small scale. As we describe below, much like for the physical effects of flow on organisms, organismal size and shape play a fundamental role in determining the flow-mediated chemical landscape that organisms experience.

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The region surrounding an organism that is chemically altered by its presence is known as the diffusion boundary layer. For example, in the case of nutrients, the diffusion boundary layer is the region depleted in nutrients because of uptake by the organism. By transporting nutrient molecules more effectively toward the organism, fluid flow can make the diffusion boundary layer thinner. A thinning of the boundary layer is thus, in general, the mechanism by which flow enhances transport to and from an organism. Motility has a similar effect as flow in thinning the boundary layer—both motility and flow are driven by the relative motion of the organism and the surrounding fluid—and can thus similarly enhance transport.

Diffusion boundary layer: region near a solid boundary (such as a cell) where fluid velocity decreases to the point at which any transport is governed by diffusion, such as the localized region around cells absorbing nutrient molecules

Chemical resources in aquatic environments often occur as localized or point sources, for example, a phytoplankton cell or a marine particle releasing amino acids that act as nutrients for bacteria. In the absence of flow, such chemicals diffuse away from the source symmetrically (i.e., equally in all directions; **Figure 3*a*, subpanel *i***), and if the release is not constant, concentrations rapidly become homogeneous (within minutes, at the microscale). In the presence of a laminar flow, for example, the sinking of a particle, chemicals again diffuse away from the source but are also advected downstream so that the source and its diffusing profile are carried along in the flow

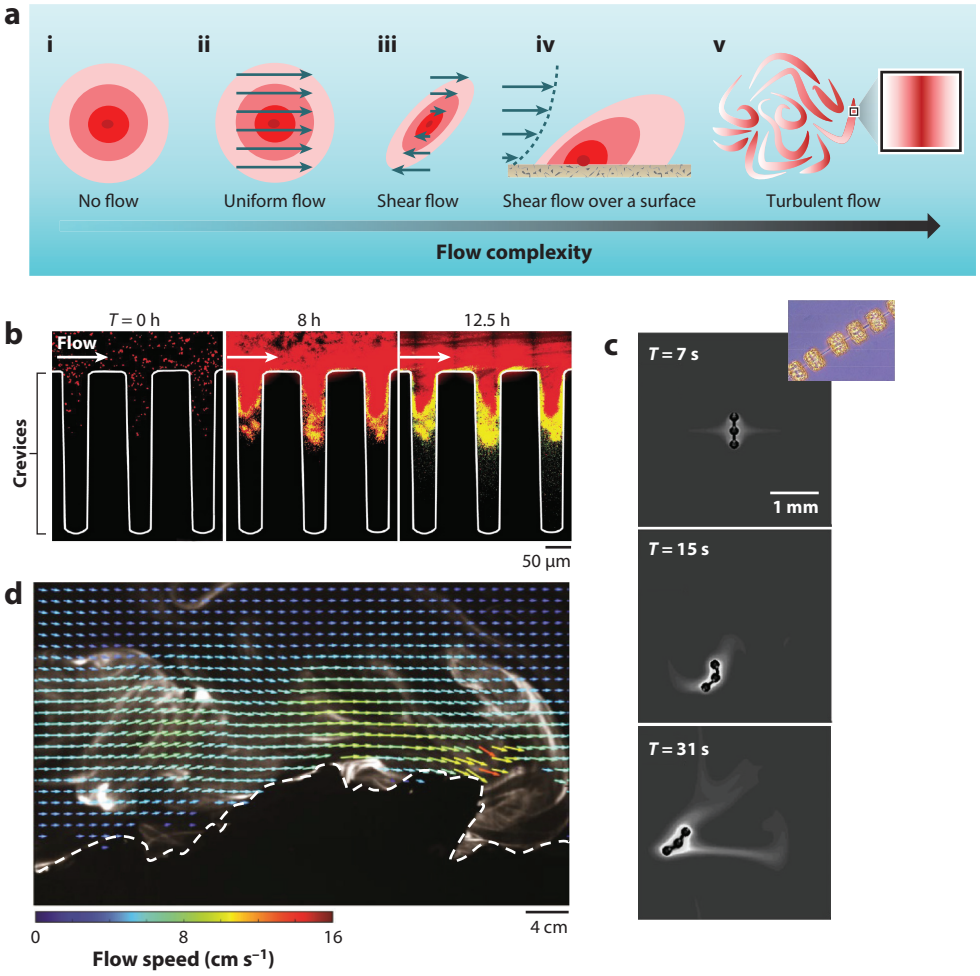

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Figure 3 (*Figure appears on preceding page*)

Effects of flow on the chemical landscape experienced by bacteria and plankton. (*a*) Propagation of a chemical signal in flow environments of increasing complexity. The color intensity denotes chemical concentration, with high concentrations in dark red and low concentrations in light red. (*i*) In no-flow conditions, molecules diffuse away symmetrically from a point source, with the highest concentrations at the source and concentrations decreasing with distance until they are indistinguishable from the background. (*ii*) A uniform flow does not alter the shape of a chemical cloud, because all molecules are transported with the same flow velocity. (*iii*) In a shear flow, the chemical cloud is stretched into a diagonal plume by the different flow velocities across the size of the plume. (*iv*) In a shear flow over a surface, the plume is stretched away from the surface. (*v*) In turbulent flow, a plume is stretched and deformed into filaments, which have higher chemical concentrations near their centers (*inset*) that diffuse away toward their edges. (*b*) In *Staphylococcus aureus* biofilms, quorum sensing (QS) can occur in crevices—which mimic complex topographies such as cracks in rocks, tooth cavities, intestinal crypts, and corrugated pipes—even when it is quenched in the external flow, because crevices prevent washout of secreted autoinducer molecules. Panel *b* adapted from Kim et al. (2016). In this panel, merged images of *S. aureus* QS-off (*red*) and QS-on (*yellow*) cells are shown. (*c*) Uptake rates in flow by phytoplankton depend on cell size and morphology, as these factors determine the thickness of the diffusion boundary layer around cells. Large diatoms and small chain-forming diatoms (such as *Thalassiosira*, *inset*) benefit most from flow due to a larger deformation of their boundary layer relative to the deformation experienced by small cells. A numerical simulation of a diatom chain in flow (*connected black points*) shows the complex, time-dependent deformation that the diffusion boundary layer (*white regions*) can undergo. Panel *c* adapted from Musielak et al. (2009). (*d*) Rough bottom biological communities like oyster or coral reefs, or biofouled landscapes (under the *dashed white curve*), generate complex near-bottom flows (*overlaid arrows*), with areas of high velocity (*red*) and low velocity (*blue*). Chemicals (*white patches*) exuded from the surface are swept and distorted into filaments by the turbulent flow, giving swimming larvae a complex map of chemical cues to interpret when they seek to settle. Panel *d* adapted from Koehl & Hadfield (2010).

(**Figure 3*a***, **subpanel *ii***). In the presence of a shear flow, where the flow speed—and thus the advection—is different on different parts of a point source, a stretched plume forms (**Figure 3*a***, **subpanel *iii***). When the point source is on a surface, shear flow stretches the plume away from the surface (**Figure 3*a***, **subpanel *iv***). In the presence of turbulent flow, the diffusing chemical plume is warped and stretched into thin filaments (**Figure 3*a***, **subpanel *v***), which in the ocean can become as thin as a few tens of micrometers. Finally, entire surfaces can act as chemical sources, such as a seafloor biological community releasing chemical signals for bacteria and plankton in the bulk. The presence of flow near the bottom mixes these chemical signals and produces complex chemical fields for small organisms swimming nearby. Bacteria and plankton thus navigate chemical fields that are frequently influenced by flow, simultaneously interpreting perturbations to their own local chemical fields while responding to signal sources that are disguised by the motion of the fluid. We now illustrate this process in more detail with examples drawn from biofilms, bacteria, phytoplankton, and larvae.

Quorum sensing: cell-cell communication process by which bacteria release and detect chemical molecules, termed inducers, thereby obtaining a measurement of the local population density

3.1. Quorum Sensing in Flow by Bacteria and Biofilms

Bacterial populations can orchestrate their collective behavior through a mode of communication termed quorum sensing that relies upon the release of diffusible chemical signals, the inducers. Once the concentration of inducers reaches a threshold, diverse bacterial behaviors can be triggered, ranging from light production in marine *Vibrio* inhabiting the squid light organ (Bassler et al. 1997) to extracellular matrix production and expression of virulence factors in human pathogens such as *S. aureus*, *Vibrio cholerae*, and *P. aeruginosa* (O'Loughlin et al. 2013, Stoodley 2016).

Fluid flow can modulate quorum sensing by affecting the transport and thus the local concentration of inducer molecules. For example, genetically identical cells of *S. aureus* and *V. cholerae* under flow do not exhibit a uniform quorum sensing response throughout the thickness of a

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biofilm (Kim et al. 2016, Stoodley 2016). Under flow, only cells at the base of the biofilm exhibit quorum sensing, whereas stopping the flow triggers quorum sensing in the upper layers as well (Kim et al. 2016). Microfluidic experiments have revealed that flow washes away inducer molecules in communities growing on planar surfaces, whereas bacteria growing in narrow cavities that mimic natural environments such as cracks in rocks and dental cavities are sheltered and can still perform quorum sensing even in the presence of a strong ambient flow (Kim et al. 2016) (**Figure 3*b***). A similar effect occurs in *P. aeruginosa* biofilms, in which a thick extracellular matrix reduces the washout of inducer molecules and confers resilience to quorum sensing up to moderate flows (Emge et al. 2016, Kirisits et al. 2007). In fact, fluid flow is in general not able to penetrate inside the biofilm matrix, where molecules are transported preferentially by diffusion (Stewart 2003). Similar principles thus apply to the transport of nutrients and oxygen, whereby cells residing deep within the biofilm receive only those nutrients capable of diffusing through the matrix, whereas cells residing in the outermost layers experience much higher supply rates due to flow (Stoodley et al. 1999, Thomen et al. 2017).

Taxis: active directional motion of organisms in response to an ambient stimulus, for example, a chemical stimulus (chemotaxis) such as a nutrient or a physical stimulus (e.g., light, giving phototaxis). Taxis can be attractive or repulsive

Run-and-tumble: motility strategy in which bacteria alternate straight-swimming runs with brief, nearly random reorientation events (tumbles)

Run-and-reverse: motility strategy in which bacteria alternate straight-swimming runs with nearly instantaneous reversals of direction

3.2. Chemotaxis in Flow by Bacteria

Bacteria can sense chemical gradients and tune motility accordingly: Chemotaxis allows them to swim toward beneficial chemicals or away from harmful ones. Flow can decrease the ability of bacteria to perform chemotaxis and, similarly, other forms of taxis. For example, shear trapping (Rusconi et al. 2014), described above, prevents bacteria from turning effectively in the direction of the gradient. Flow can also trick bacteria to move in incorrect directions, as shown on the basis of a mathematical model of taxis (Locsei & Pedley 2009): When the timescale over which a bacterium measures the local chemical concentration is similar to the timescale over which flow reorients the cell, the cell moves in an incorrect direction, in extreme cases even causing negative chemotaxis (i.e., migration in the direction opposite to the chemoattractant source). We speculate, however, that the negative taxis is not sufficiently robust to be exploited, for example, by animals to prevent bacterial colonization and infection.

With regard to chemotaxis, marine bacteria face several environmental challenges: Seawater is generally characterized by low concentrations of nutrients, frequently occurring as point-source events, and fluid flow is prevalent (Stocker & Seymour 2012). In this scenario, motility can confer an advantage (Stocker et al. 2008), and flow may favor specific motility adaptations. It has been proposed on the basis of a mathematical model that bacteria using the common run-and-tumble swimming pattern (best studied in the enteric bacteria *E. coli*) are poor at chemotaxis in a shear flow, whereas a run-and-reverse swimming pattern enables bacteria to stay close to a nutrient source even under high shear (Luchsinger et al. 1999). Experimental evidence shows that in a shear flow, *Pseudoalteromonas haloplanktis*, due to its run-and-reverse swimming, has a faster chemotaxis response and more intense accumulation relative to *E. coli*, leading to twice the nutrient exposure (Stocker et al. 2008). Consequently, run-and-reverse swimming has been proposed as an adaptive strategy adopted by marine bacteria to enhance chemotactic abilities under turbulent conditions (Stocker et al. 2008). In contrast, the run-and-tumble behavior of *E. coli*, mediated by many flagella, may be optimal in very viscous environments, such as the human gut, where multiple flagella generate a higher total torque to drill through the high-viscosity environment. Swimming speed is another crucial factor in increasing nutrient uptake but comes at a high energetic cost, with the trade-off being determined by flow conditions. Competition simulations in a turbulent flow typical of the oceans show that the optimal swimming speed is in the order of 60 μm/s (Taylor & Stocker 2012), in agreement with speeds typical of marine bacteria (Stocker & Seymour 2012).

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An important example of chemotaxis of bacteria in flow is that toward marine particles. These particles are responsible for a large flux of carbon from the surface ocean to the deep ocean as they sink (impacting global carbon cycling): The magnitude of this flux is determined by particle degradation by bacteria, which in turn is driven by how rapidly bacteria find particles. Bacteria can chemotax toward particles by sensing the gradients of dissolved organic matter emanating from them (Kiørboe et al. 2002). The flow associated with the sinking of the particle elongates the resulting chemical plume, which becomes a comet-like tail behind the particle at high sinking speeds (Kiørboe & Jackson 2001). Mathematical models (Kiørboe & Jackson 2001) and microfluidic experiments (Son et al. 2016, Stocker et al. 2008) have shown that motile marine bacteria, thanks to their fast swimming speed and the run-and-reverse swimming strategy, are very effective in using chemotaxis to take advantage of these chemical-rich plumes shaped by flow and in ultimately finding the particle from which they emanate.

3.3. Nutrient Uptake in Flow by Phytoplankton

Flow can have a considerable, size-dependent effect on nutrient uptake. Smaller phytoplankton cells have a natural advantage over larger cells because nutrient uptake rates per cell volume are largest for small cells (Karp-Boss et al. 1996; Kiørboe 1993, 2008). This results both from a small cell's greater surface area–to–volume ratio and from the fact that the thickness of the nutrient-depleted boundary layer increases with cell size so that small cells have relatively thin boundary layers and easy access to surrounding nutrients. The presence of flow reduces the advantage of small size: The boundary layers around large cells are more strongly deformed by flow than those of small cells, because of the relatively greater thickness of large cell boundary layers. This deformation increases nutrient concentration gradients near the cell and draws more nutrient-rich fluid from outside the boundary layer toward the cell surface, thus enhancing uptake (Barton et al. 2014, Karp-Boss et al. 1996). When cells become very large or the flow becomes turbulent, the diffusion boundary layer can be deformed into very complex shapes (**Figure 3*c***). Flow therefore produces nutrient environments local to cells whereby the preferential boost to larger cells may allow them to dominate communities. This picture of size-specific flow–uptake interaction is consistent with experiments on the diatoms *Thalassiosira* and *Coscinodiscus* in laboratory turbulence (Peters et al. 2006) and *Thalassiosira* species in turbulent mesocosms (Cózar & Echevarría 2005), where large diatoms grow preferentially over smaller competitors when flow is introduced.

Flow may also help explain the tendency of many phytoplankton species, primarily diatoms and some dinoflagellates, to form chains of multiple connected cells (**Figure 3*c***). In the absence of flow, chain formation may be disadvantageous for nutrient uptake because nutrient supply by diffusion alone is higher for single cells than for chains (Pahlow et al. 1997), and furthermore, individual cells compete with each other. However, in the presence of an oscillating shear flow, the increased size of chains confers an advantage through greater thinning of the boundary layer and thus a larger increase in nutrient supply, as indicated by numerical simulations (Musielak et al. 2009). Laboratory observations support the theory. Carbon uptake rates in chain-forming *Skeletonema* and *Chaetoceros* diatoms increase with flow, and the flow-enhanced uptake rates are greater for chains than for individual cells (Bergkvist et al. 2018). Mesocosm experiments also show that chain-forming diatoms (e.g., *Skeletonema* and *Thalassiosira*) dominate other species in the presence of flow (Cózar & Echevarría 2005).

3.4. Navigation of Turbulently Mixed Chemical Cues by Larvae

Large planktonic organisms, such as zooplankton and larvae, experience chemical signals in flow differently than bacteria and phytoplankton due to their greater size and swimming capabilities.

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These large plankton use chemical signals to find mates or prey, for example, by following pheromone trails (e.g., Yen 2000). In turbulence, these chemical signals take on a form that is substantially different from still water conditions (compare **Figure 3*a***, **subpanel *i*** and **Figure 3*a***, **subpanel *v***). As turbulence stretches and deforms a chemical source into filaments, large plankton experience rapid on/off changes in concentration when they enter/exit filaments, and as such, it is beneficial to these organisms to respond rapidly to sudden changes in their chemical landscape.

As larvae transition to adulthood and seek to settle out of the water column, the interplay of bottom boundary flow and chemical cues produces a complex map for larvae to follow. Many chemical signals induce changes to larval behavior to enhance contact with the seafloor, including those from adult conspecifics (Turner et al. 1994), prey (Hadfield & Koehl 2004, Koehl & Reidenbach 2010), and biofilms (reviewed in Hadfield 2011). There are two main chemical sensing strategies in larvae, waterborne and contact based, and these are impacted by bottom boundary flows in different ways. Larvae that sense waterborne cues, such as the oyster *C. virginica*, enhance downward swimming when exposed to solutions of adult metabolites in both still water and uniform flows (Tamburri et al. 1992, Turner et al. 1994). For the sea slug *Phestilla sibogae*, larvae rapidly cease swimming when exposed to millimeter-scale filaments of their prey exudate (Hadfield & Koehl 2004, Koehl & Reidenbach 2010), allowing them to rapidly sink when they encounter even weak chemical cues indicative of suitable settlement sites (**Figure 3*d***). This experimental evidence suggests that larvae have evolved to react on rapid timescales to intermittent and patchy chemical cues, like those generated in the bottom boundary flow.

Flow impacts contact-based chemical sensing differently. Unlike the sensing of waterborne cues, contact-based sensing relies on larvae sampling the chemical composition of a surface by contacting the surface directly with a sensory apparatus. The polychaete *Hydroides elegans*, for instance, cannot detect the chemical exudates of a surface biofilm from a distance (Hadfield 2011). While these larvae preferentially settle on surfaces covered in biofilms, they must directly touch a biofilm with apical cilia to induce a settlement response (Hadfield 2011). Flow determines how frequently larvae contact a surface to identify settlement-relevant biofilms, as in a near-bottom shear flow, larvae tumble at high flow rates when they cannot successfully reorient against the flow (Jonsson et al. 1991). Shear is thus likely to decrease the capacity of contact-based sensing larvae to sample a surface and to thus successfully settle.

4. MECHANISMS OF FLOW SENSING

Many examples discussed in this review detail the passive effects of flow on microorganisms, such as the redistribution of bacteria and plankton in shear due to motility and morphology. Sensing of flow by the organisms may not be involved in these instances, and these effects occur even for organisms that cannot sense flow. However, several examples demonstrate that higher organisms have relatively sophisticated flow-sensing mechanisms, such as larval swimming responses to turbulent cues, and this area has received considerable interest from biophysical researchers. Less studied are the capacities for direct flow sensing in phytoplankton and bacteria, a new and intriguing line of research from both a biophysical and a physiological perspective. Here, we summarize some potential flow-sensing mechanisms in larvae, phytoplankton, and bacteria.

Humans lack specific flow-sensing systems, but many aquatic species have dedicated flow sensory systems, like the lateral line in fish (Coombs & Van Netten 2006) and the hair-like setae in arthropods (Casas & Dangles 2010), or use gravity-sensing systems to detect and respond to flow. Many invertebrate larvae, particularly, have statocysts. Statocysts are fluid-filled cavities lined by sensory hairs and containing a calcareous statolith particle, and they act as gravity- and orientation-sensing systems (Budelmann 1988), analogous to the utriculus and otolith structures of

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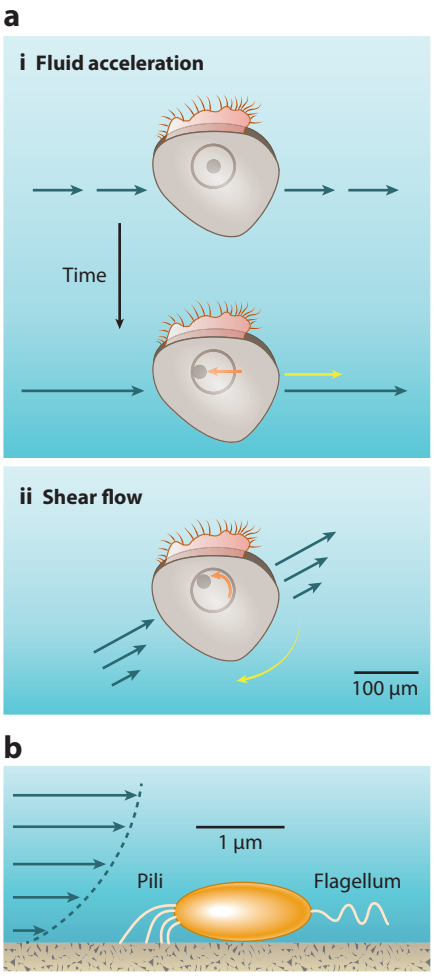

Figure 4

Potential flow-sensing mechanisms in bacteria and plankton. (*a*) Proposed larval detection of local hydrodynamics in (*i*) accelerating and (*ii*) shear flow. Flow (*dark teal arrows*) induces changes in the larval position (*yellow arrows*) and the position of the internal statolith (*orange arrows*). Both fluid acceleration and shear might displace the statolith, allowing larvae to sense these flow signals. (*b*) On surfaces, bacteria may sense mechanical cues—possibly due to hydrodynamic forces generated by shear flow on the surface—using flagella or pili. Flow-sensing mechanisms in bacteria and plankton remain an area in need of dedicated research.

the vertebrate ear. Because statoliths are denser than the surrounding fluid of the statocyst, gravity is sensed via the settling of a statolith onto receptor cilia (Wiederhold et al. 1989). It is speculated that larval motion due to fluid acceleration (**Figure 4*a***, **subpanel *i***) and shear forces (**Figure 4*a***, **subpanel *ii***) induces similar sensory transduction in larvae (Fuchs et al. 2015, Wheeler et al. 2015). Fluid acceleration would push a statolith back against the statocyst wall (**Figure 4*a***, **subpanel *i***), while a rotating shear would cause the statolith to roll along the statocyst wall (**Figure 4*a***, **subpanel *ii***). As such, this orientation-sensing organ may also have a role in flow sensing in larvae.

Little is known regarding the capabilities and mechanisms of flow sensing in phytoplankton. The question was recently raised as to whether phytoplankton sense flow directly or indirectly

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through other environmental signals (Amato et al. 2017). Larger phytoplankton, such as *Euglena gracilis*, use the entire cell body as a primitive statocyst-like structure. The dense cytoplasm settles to the bottom of the cell and exerts a force on the outer membrane as the cell swims upward, whereas when the cell is overturned in flow, the cytoplasm is displaced from the cell membrane, activating mechanosensitive ion channels via intracellular calcium concentrations (Häder et al. 2010). Smaller cells lack this ability, as the cytoplasmic gravitational pressure on the membrane of a small cell (<15 μm) is of comparable strength as thermal noise (Sengupta et al. 2017). Nonetheless, small phytoplankton exhibit physiological responses to flow such as rapid changes to cytosolic calcium concentrations (Falciatore et al. 2000)—much like larger cells—and exhibit changes in gene expression (Amato et al. 2017), fatty-acid accumulation (Amato et al. 2017, Chengala et al. 2013), and morphology (Sengupta et al. 2017). Yet despite evidence of rapid physiological responses to turbulence, our understanding of the sensing mechanisms employed by phytoplankton remains limited.

In bacteria, no direct evidence of flow sensing appears to be available, and information potentially relevant for flow sensing comes from experiments on mechanosensing of surfaces, as presented in detail by Gordon & Wang (2019). When bacteria transition from the planktonic to the sessile lifestyle, they disable flagellar rotation (Lele et al. 2013) and initiate the secretion of biofilm matrix (Guttenplan et al. 2010). This switch is determined by mechanical cues sensed by flagella or pili (**Figure 4*b***). The hydrodynamic load on the flagellum can trigger both the loss of motility and the initiation of matrix secretion (Belas 2014). Flagellar mechanosensing has been observed in bacteria living in diverse environments, including *E. coli* (Lele et al. 2013), *P. aeruginosa*, *V. cholerae*, *B. subtilis* (Guttenplan et al. 2010), *C. crescentus*, *Vibrio parahaemolyticus*, and *P. mirabilis* (Belas 2014). As the trigger for surface colonization, the flagellar mechanosensing mechanism is a potential target in the development of biofilm-inhibiting drugs. Pili can also act as mechanosensors, as shown in *P. aeruginosa*, which activates virulence upon contact with surfaces. By sensing mechanical cues with the PilY1 protein (Siryaporn et al. 2014) and type IV pili (Persat et al. 2015), *P. aeruginosa* activates cyclic-di-GMP signaling (a secondary messenger used by *P. aeruginosa* and many other bacteria to regulate the expression of genes associated with biofilm initiation), which was recently shown to increase proportionally to the magnitude of the shear force in the presence of flow (Rodesney et al. 2017). Bacteria may also sense surfaces using the mechanosensitive channels that protect the integrity of the cell wall upon osmotic shock (Cox et al. 2018); these channels may also be sensitive to mechanical deformation of the cell wall and trigger a cellular response, similar to that described above in phytoplankton. In principle, these mechanisms could also serve to sense flow (although this has not been demonstrated); however, the forces associated with flow are often smaller than those associated with surface contact. The possibility of direct flow sensing in bacteria thus remains an open question.

5. CONCLUDING REMARKS

Most microorganisms live in moving fluids, and many microorganisms have developed morphologies, behaviors, and physiological responses to flow. Flow is experienced differently by organisms of different sizes, as reflected in their behaviors. Zooplankton and larvae feel turbulence as a chaotic and rapidly fluctuating signal, whether in terms of forces or in terms of chemical cues, whereas smaller phytoplankton and bacteria experience the flow environment, including turbulence, as a more smoothly changing signal. Accordingly, zooplankton and larvae have adapted to react quickly to turbulent signals, as exemplified by the nearly instantaneous cessation of swimming by some larvae when they encounter rapid changes in flow velocity or chemical concentration. Bacteria and phytoplankton, in contrast, must detect and navigate smoother environmental

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changes, like chemotactic bacteria following the comet-like tail of a sinking nutrient particle. Despite this disparity in how flow is experienced across organismal scales, there are also fundamental commonalities in the physical effects of flow among aquatic species. For instance, elongated body shapes are rotated in shear flows on scales from bacteria to larvae, leading to many ecologically significant phenomena, such as the formation of thin layers and the shear-induced accumulation of organisms near surfaces.

We highlight several themes in this review. First, we argue that flows cause forces and torques on organisms, which can compete and interfere with their locomotion and migration behaviors, at times entirely impeding them. This interference directly affects the spatial distribution of organisms, which is a primary determinant of downstream processes, such as encounter rates with prey, predators, and conspecifics. Second, we describe how flows reshape the landscape of chemicals that many bacteria and plankton rely on for nutrient acquisition and communication, in ways that may enhance or hinder their ability to navigate that landscape. Third, we provide examples in which bacteria and plankton show active behavioral responses to flow. For larger organisms, such as larvae, this capacity has been known for some time. For smaller ones, such as phytoplankton, this capacity has been only recently discovered. This is an intriguing direction of inquiry that considerably enriches the palette of possible outcomes of flow–organism interactions at small scales. We illustrate these effects of flow through selected examples, which we trust can serve as blueprints to study the effects of flow on organisms in other systems. Finally, the consequences of flow for microorganisms remain in many cases to be elucidated because experiments are technically challenging. However, new methods, including microfluidics, that allow for the simultaneous manipulation of flow and observation of organisms at the microscale are increasingly available.

In this review, we consider only the tip of the iceberg: Given the diversity of flows and of species, there are a wide array of questions concerning the physiological underpinnings of flow–behavior interactions in microorganisms. How pervasive are passive and active responses to flow, and how do these responses impact microorganism physiology? How are such responses related to the mesmerizing diversity of shapes observed in bacteria, phytoplankton, and larvae? How are complex morphological features such as spines and adaptations such as chain formation related to behavior in flow? Which morphological features of biofilm structures are adapted to flowing environments? What fraction of plankton have evolved active responses to flow, and what are the underlying mechanisms? When active responses to flow are mediated by changes in shape, what are the biological mechanisms underpinning these shape changes? What is the range of timescales in the active responses to flow? Among the many different types of flow encountered by plankton in aquatic environments, have certain types of flow—for example, turbulence—resulted in the evolution of a great prevalence or diversity of flow responses? What are the costs and trade-offs of responding, passively or actively, to flow? To dive into these questions, we must cross the traditional boundaries between physical and biological disciplines and allow the interaction between biophysicists and cell and developmental biologists to flow freely. An ocean of discoveries awaits as we seek to understand the role of these fascinating organisms in the context of the flowing environments they inhabit.

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The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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