The ability to perceive and respond appropriately to environmental cues is an essential prerequisite to the survival and adaptation of microorganisms to changes in their surroundings. One of the best-understood responses involves the chemotaxis two-component signal transduction system in Escherichia coli, which functions to relay sensory information about the surroundings to the flagellar motility apparatus (11, 23). Although the protein components of the E. coli chemotaxis signal transduction pathway have been characterized in molecular detail, the exact role that chemotaxis plays in the ecology of the organism remains poorly understood. A priori, the ability to sense and navigate toward a particular ecological habitat provides motile microorganisms with a competitive advantage; chemotaxis has been suggested, and often demonstrated experimentally, to be important in host recognition by various pathogenic and beneficial microorganisms (2, 9, 13, 27). An article in this issue by Schweinitzer et al. (18) provides new pathogenic and beneficial microorganisms (2, 9, 13, 27). An article in this issue by Schweinitzer et al. (18) provides new insight into how the gastric pathogen Helicobacter pylori monitors changes in its environment, suggesting a mechanism through which bacterial chemotaxis may direct and maintain H. pylori within a narrow zone deep in the gastric mucus, leading to persistent colonization and infection.

**Chemotaxis and niche adaptation.** Motile bacteria are capable of navigating in gradients of oxygen, light, ions, and nutrients by constantly monitoring their environment for change in order to occupy a position that is optimal for survival and growth. The ability to modulate (increasing or decreasing) the probability of random changes in swimming direction allows motile bacteria to navigate in chemical gradients, resulting in chemotaxis (3, 23).

In chemotaxis, sensory input to the flagellar apparatus is provided by a set of membrane-bound chemoreceptors. Chemoreceptors are comprised of two functional domains, namely, an N-terminal sensory domain and a conserved C-terminal signaling domain that interacts with the cytoplasmic signal transduction machinery (11, 23). The N-terminal sensing domains of chemoreceptors can be located in either the periplasm or the cytoplasm and are generally not conserved. Variations in the sensory specificity of the N-terminal domains of chemoreceptors reflect the diverse cues that a motile microorganism can detect and to which it may respond (25). Environmental cues may be detected either directly, by binding of a ligand to the sensory domains of chemoreceptors (metabolism-independent chemotaxis), or indirectly, by causing a change in the intracellular energy level that itself is detected by a redox-sensitive cofactor within the sensory domain of the chemoreceptor or by a proton motive force (PMF)-sensitive domain. Metabolism-dependent behavior is known as energy taxis, in which the signal for a behavioral response originates within the electron transport system, where a change in the rate of electron transport (or a related parameter) is detected by a signal transduction system (19). Effectors for energy taxis affect the bacterial redox potential and PMF and include compounds such as terminal electron acceptors, redox chemicals (including inhibitors of the electron transport system), and metabolizable substrates (donors of reducing equivalents to the electron transport system). Experimental evidence for the ability of cells to monitor intracellular energy levels has been obtained with E. coli, which possesses two membrane-bound chemoreceptors, Aer and Tsr, that sense different parameters related to intracellular energy levels (redox potential for Aer and probably the PMF for Tsr) and signal to the flagellar motors via the chemotaxis signal transduction pathway (8, 16), thus functioning in energy taxis.

The human gastric pathogen Helicobacter pylori utilizes a set of five sheathed polar flagella that provide optimum motility in the viscous environment of the gastric mucosa (6). Flagellar motility is a virulence factor in that nonmotile or nonflagellated mutants are attenuated in colonization of the stomach in animal models (7, 14). Although chemotaxis has been described for H. pylori in vitro and in vivo (2, 4, 5, 9, 26), the importance of this behavior in the ability of this pathogen to locate its niche within the stomach mucus was recognized only recently (17, 24). Schreiber et al. (17) used a microdissection method that allowed them to establish that H. pylori colonizes and persists in the stomach in a very narrow zone close to the gastric epithelial surface and away from the lumen, where the acidic pH would inhibit growth and motility. These findings suggested that H. pylori cells were capable of actively orienting in this environment so that they could reside within this narrow zone despite active mucus turnover. Furthermore, sensing and navigating along the pH gradient in the mucus were found to be key determinants in the establishment and persistence of H. pylori in its preferred niche (17). Considering the effect that environmental pH has on the proton gradient component of...
the PMF, two mechanisms were invoked for pH taxis, including direct sensing of the proton gradient and sensing of the effect that a decrease in the proton gradient across the bacterial membrane has on intracellular energy levels. A dedicated chemoreceptor(s) was also suggested to be a sensor for pH taxis in *H. pylori* (17), which is consistent with the previous observation that two of the *E. coli* chemoreceptors (Tsr and Tar) could mediate pH taxis in gradients of permeant weak acids (Tsr) and bases (Tar) (22). The genome of *H. pylori* encodes four putative chemoreceptors, three of which are membrane bound (TlpA, TlpB, and TlpC) and one of which is cytoplasmic (TlpD) (1, 21). The N-terminal sensory domains of the *H. pylori* chemoreceptors do not have detectable sequence similarity to any sensory domains of known function, and the exact sensory specificities of these chemoreceptors have remained unknown, until recently. One of the *H. pylori* chemoreceptors, TlpB, was recently found to be essential for temporal pH sensing in this species (5). Notably, TlpB mediated a repellent response (negative chemotaxis), which allows cells to escape environments where the pH is too low to support growth or motility. However, such a tactic response may not be sufficient to ensure that cells persist in dynamic environments, where other gradients (that may result from active local metabolism) or limiting factors for growth may be present.

**Navigating along “energy” gradients.** Energy taxis was put forward as an additional or alternative hypothesis to explain the movement of *H. pylori* in pH gradients. Schweinitzer et al. (18) found that the swimming motility bias of *H. pylori* wild-type cells was affected by growth conditions that impacted energy yields. In order to accurately describe a taxis mechanism, sensitive behavioral assays must be used to quantitatively measure tactic responses. This is not a trivial issue, since very often chemotaxis assays that work well in the model organism *E. coli* do not provide insightful information for microorganisms that have a different type of motile behavior. Schweinitzer et al. (18) used a set of sensitive spatial and temporal assays to obtain convincing evidence for energy sensing in *H. pylori* by demonstrating that two electron transport inhibitors that reduce the intracellular energy levels can trigger a concentration-dependent change in the swimming motility bias. Restoring the electron flow through the respiratory chain (and thus increasing energy production) by using artificial electron donors also restored the swimming motility bias. The demonstration that *H. pylori* is capable of energy sensing is significant because it suggests that by coupling sensing of the intracellular energy to motility, swimming *H. pylori* cells may navigate toward niches that support optimal energy generation, thus integrating sensory information about all nutrient and pH gradients into a single response.

In addition to characterizing energy taxis in *H. pylori*, Schweinitzer et al. (18) have attributed most of the energy-sensing capabilities to a single putative chemoreceptor, TlpD. They used the set of behavioral assays described above, a defined *tlpD* mutant, and a triple *tlpABC* mutant to determine that TlpD is the major chemoreceptor responsible for sensing perturbation of the electron transport system (energy sensing) and initiating a repellent response. However, the mechanism(s) by which this proposed chemoreceptor might sense an energy-related parameter remains to be determined. TlpD is a cytoplasmic chemoreceptor-like protein that possesses a short N-terminal sensory domain that does not have any apparent homolog that could be indicative of a sensing mechanism. Furthermore, unusual features of TlpD are intriguing and, if confirmed, may provide significant insight into the mechanism(s) related to the energy-sensing functions of TlpD. First, under conditions of overexpression from a plasmid, TlpD localizes to the cytoplasmic face of the membrane, but no distinct preferential localization can be identified. This is highly unexpected, since in *E. coli* as well as other species studied so far in this respect, chemoreceptors are clustered, typically at the cell poles, and this organization is essential to chemotaxis in *E. coli* (10–12). It is noteworthy that the *H. pylori* chemotaxis signal transduction pathway is significantly divergent from that of *E. coli* in that it includes chemotaxis proteins that are not present in *E. coli* (9, 15, 20) and could account for this unusual (although preliminary) observation. Second, TlpD mediated a stronger response under conditions where cells generated relatively lower energy, suggesting that sensing via TlpD is dominant under these specific conditions. This effect could be correlated with a change in the expression of TlpD itself, a potential energy-transducing interacting partner(s), or even some of the other chemoreceptors or chemotaxis proteins. To date, two (TlpB and TlpD) of four chemoreceptors have been found to monitor energy-related parameters in *H. pylori*, underscoring the likely advantage that this behavior provides to the organism with restricted metabolic capabilities. How the cues sensed by TlpD and TlpB are integrated into a response and how each cue can modulate adaptation to the gastric mucosa remain to be understood. The work by Schweinitzer et al. (18) paves the way for the design of experiments that could directly address the contributions of these behaviors to niche adaptation.

I thank Calvin Green, Amber Bible, Zhihong Xie, Beth Mullin, and Christine Josenhans for useful comments on the manuscript.

Research in my laboratory on chemosensory transduction in plant-associated bacteria is supported by an NSF career award (MCB-0622277).

**REFERENCES**


The views expressed in this Commentary do not necessarily reflect the views of the journal or of ASM.