THE EMBO JOURNAL

Have you seen . . . ?

The EMBO Journal (2010) 29, 3435–3436 | © 2010 European Molecular Biology Organization | All Rights Reserved 0261-4189/10
www.embojournal.org

Classifying chemoreceptors: quantity versus quality

Eric S Underbakke[1] and Laura L Kiessling[1,2,*]

[1]Department of Biochemistry, University of Wisconsin, Madison, WI, USA and [2]Department of Chemistry, University of Wisconsin, Madison, WI, USA
*Correspondence to: kiessling@chem.wisc.edu

The EMBO Journal (2010) **29,** 3435–3436. doi:10.1038/emboj.2010.246

Advances in genomic and proteomic methods provide the means to ascertain not only what receptors are present in a given cell but also how prevalent they are. While it is reasonable to assume that receptor concentration has a critical role in cell physiology, a new study published in this issue of *The EMBO Journal* suggests that the more relevant parameter can be a receptor's molecular mechanism. The findings arose from studies focused on bacterial chemotaxis. Chemotactic bacteria sense their chemical environment through a battery of transmembrane chemoreceptors. Previously, these receptors were grouped into two categories: high and low abundance. Neumann *et al* (2010) postulated that an alternative classification might be more apt. They note that chemoeffectors can bind their chemoreceptor either directly or indirectly through a periplasmic-binding protein (BP) intermediary, and they provide evidence that these distinct sensing mechanisms have different properties: indirect binding offers the opportunity to control sensitivity while direct binding gives responses over a wider concentration range. These different sensing mechanisms may be exploited by bacteria to survive in diverse niches.

Bacteria can pursue favourable niches through chemotaxis—they bias their swimming behaviour in response to their extracellular environment. The bacterial chemotaxis-signalling system has emerged as a paradigm for transmembrane signalling and molecular information processing (Hazelbauer *et al*, 2008; Sourjik and Armitage, 2010). The system has been studied extensively in *Escherichia coli*, the signalling components are known, and their general roles have been elucidated. Indeed, we are poised to understand this bacterial system from the level of atomic interactions to emergent decision-making behaviour. Nevertheless, features of the chemotaxis system remain paradoxical. Chemotaxis signalling is surprisingly economical yet capable of exquisite sensory performance. Chemotactic *E. coli* can both respond and adapt to stimuli using a collection of chemoreceptors and only six other gene products. This apparent simplicity belies

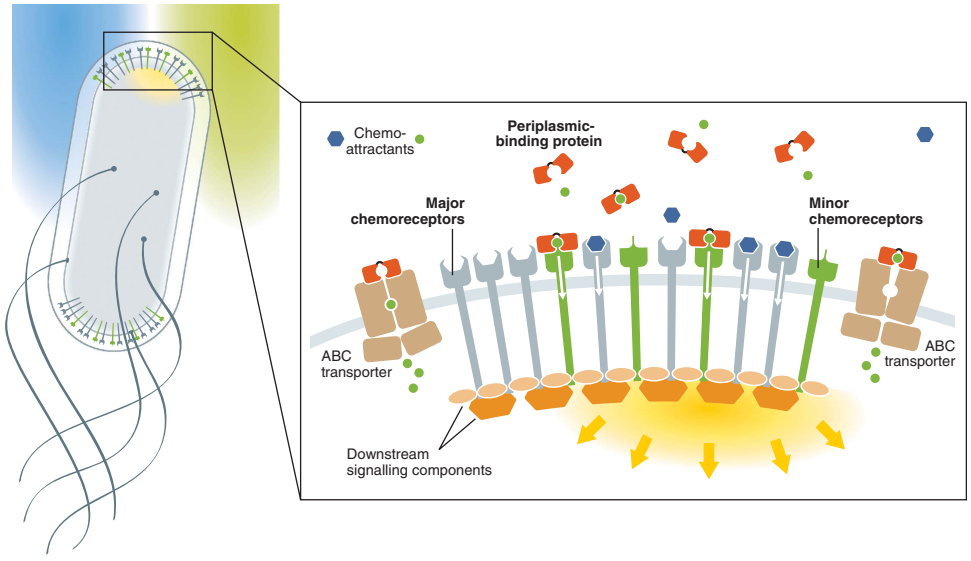

Figure 1 In a physiological niche, bacteria encounter diverse chemotactic signals that influence their behaviour. Chemotaxis signalling is mediated by a collection of transmembrane chemoreceptors. *E. coli* possess chemoreceptors (light blue) that can bind ligand directly, as well as those that (green) sense ligand indirectly via binding proteins (brown). Signalling responses from both classes are amplified and integrated in an inter-connected array of mixed chemoreceptors and downstream signalling components.

impressive sensory performance. For instance, the system can respond to as few as 10 molecules of chemoreceptor-bound ligand and adapt precisely to chemoeffector concentrations spanning 4–5 orders of magnitude (Mesibov *et al*, 1973; Segall *et al*, 1986). Moreover, in complex environments, the chemotaxis system integrates and reconciles diverse, contradictory stimuli (Figure 1).

The sophisticated sensory performance arises from the inter-connectivity of the chemoreceptors (Bray *et al*, 1998). Chemotaxis signalling is amplified, tuned, and integrated by communication between coupled teams of chemoreceptors (Ames *et al*, 2002; Gestwicki and Kiessling, 2002; Sourjik and Berg, 2004; Mello and Tu, 2005). In *E. coli*, these signalling teams are composed of receptor combinations that can respond to a unique set ligands. Responses are elicited either via direct binding to the chemoreceptor (e.g. Tsr, Tar) or through an intermediary periplasmic-BP (Tap, Trg) (Figure 1). Earlier estimates of chemoreceptor concentrations identified the direct-binding receptors as major and those chemoreceptors that act in conjunction with BPs as minor. Interestingly, the BPs also shuttle their chemoeffector ligands to the ATP-binding cassette transporters responsible for nutrient uptake. The apparent link between the indirectly signalling chemoreceptors and the nutrient uptake system inspired Sourjik and Berg (2004) to reexamine the oft-overlooked BP-dependent chemoreceptors. Their study notes that the concentration of the 'minor' receptors depends upon growth conditions. Moreover, a comparison of sensing by direct and indirect chemoeffector interaction reveals that each molecular mechanism for signal recognition has a significant effect on signal sensitivity, integration, and response range.

Sourjik and Berg (2004) used a FRET assay to monitor the signalling responses of both classes of chemoreceptor in live bacteria. The authors determined signal strength and dynamic response range for attractants sensed either directly (serine or aspartate) or indirectly (galactose, ribose, or Pro-Leu dipeptide). Consistent with previous reports, bacteria managed to respond and adapt to directly sensed ligands at ambient concentrations ranging from 4 to 5 orders of magnitude (Mesibov *et al*, 1973). In contrast, ligands sensed by the BP intermediaries elicited responses over a narrower concentration regime; the dynamic sensitivity range for the indirectly sensed ligands was limited to 2 to 3 orders of magnitude. What could account for the discrepancy? When normalized to their relative representation in signalling teams, the minor chemoreceptors signalled just as potently as their major peers. The authors conclude that the minor, indirect chemoreceptors are constrained by the expression levels of the BP. Chemoreceptors that sense ligands directly are responsive to the intracellular adaptation mechanisms that dampen responses. The BPs, however, do not adapt directly and remain susceptible to ligand saturation. Thus, for cells to tune responses to signals that act indirectly, they must change their BP production level.

If direct ligand-binding confers such an expansive response range, why deploy BPs as signalling intermediaries? The authors propose an intriguing evolutionary possibility. The BPs serve dual roles as both chemotaxis receptors and nutrient transporters. Navigating to nutrient-dense niches is profitable only to the extent that the bacterium can absorb and use the resources. By coupling chemosensing and uptake through BP intermediaries, bacteria pursue transported nutrients until their ability to import them is saturated. Beyond saturation, the cell is free to pursue alternative resources sensed by the more widely responsive direct-binding chemoreceptors. In the meantime, expression of BPs and metabolic systems can be upregulated to concomitantly pursue and capitalize on the nutrient resources. In this way, indirect ligand sensing may be another deceptively simple, functionally sophisticated chemotaxis optimization that couples motility with nutrient utilization.

Acknowledgements

LLK acknowledges support from the NIH (GM55984). ESU was supported by the NIH Molecular Biosciences Training Grant (GM07215).

Conflict of interest

The authors declare that they have no conflict of interest.

References

Ames P, Studdert CA, Reiser RH, Parkinson JS (2002) Collaborative signaling by mixed chemoreceptor teams in *Escherichia coli*. *Proc Natl Acad Sci USA* **99:** 7060–7065

Bray D, Levin MD, Morton-Firth CJ (1998) Receptor clustering as a cellular mechanism to control sensitivity. *Nature* **393:** 85–88

Gestwicki JE, Kiessling LL (2002) Inter-receptor communication through arrays of bacterial chemoreceptors. *Nature* **415:** 81–84

Hazelbauer GL, Falke JJ, Parkinson JS (2008) Bacterial chemoreceptors: high-performance signaling in networked arrays. *Trends Biochem Sci* **33:** 9–19

Mello BA, Tu YH (2005) An allosteric model for heterogeneous receptor complexes: understanding bacterial chemotaxis responses to multiple stimuli. *Proc Natl Acad Sci USA* **102:** 17354–17359

Mesibov R, Ordal GW, Adler J (1973) Range of attractant concentrations for bacterial chemotaxis and threshold and size of response over this range—Weber law and related phenomena. *J Gen Physiol* **62:** 203–223

Neumann S, Hansen CH, Wingreen NS, Sourjik V (2010) Differences in signalling by directly and indirectly binding ligands in bacterial chemotaxis. *EMBO J* **29:** 3484–3495

Segall JE, Block SM, Berg HC (1986) Temporal comparisons in bacterial chemotaxis. *Proc Natl Acad Sci USA* **83:** 8987–8991

Sourjik V, Armitage JP (2010) Spatial organization in bacterial chemotaxis. *EMBO J* **29:** 2724–2733

Sourjik V, Berg HC (2004) Functional interactions between receptors in bacterial chemotaxis. *Nature* **428:** 437–441