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Biomechanics

Bacterial flagellar switching under load

Flagellated bacteria swim up gradients of chemical attractants by modulating the direction of rotation of their flagellar motors, but how this switching mechanism works is not understood. Here we show that the probability of the motor rotating in the clockwise direction increases under high load, when the motor spins slowly (at less than 50 Hz). We suggest that either the switch is responding to small changes in torque — the torque increases only fractionally between 50 Hz and stall — or it senses motor speed, perhaps by means of proton flux.

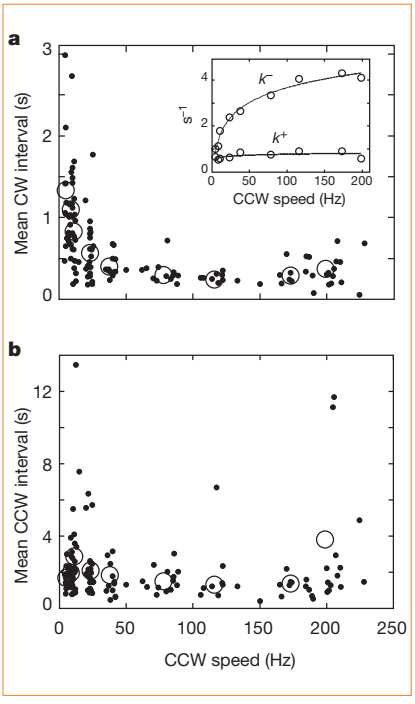

Figure 1 Behaviour of the flagellar switch of *Escherichia coli* under different loadings. **a, b,** Mean intervals for clockwise (CW; **a**) and counterclockwise (CCW; **b**) rotation of the flagellar motor, plotted as a function of mean CCW speed. Filled symbols, values measured for each cell; hollow symbols, averages over the ensemble of cells for beads of a given size, with the values for each cell being weighted equally. Bead diameters were 0.36, 0.54, 0.74, 1.03, 1.20, 1.44, 1.79, 2.13 and 2.60 μm (from right to left); the number of cells studied for each of these bead sizes was 12, 12, 7, 12, 12, 18, 18, 16 and 10, respectively. Each bead was monitored for 5 min at 20 °C. Inset, rate constants $k^- = 1/$(mean CW interval) and $k^+ = 1/$(mean CCW interval) were computed for each cell and then averaged over the ensemble of cells for beads of a given size, with the values for each cell being weighted equally.

Flagellar filaments of an *Escherichia coli* sticky-filament mutant[1], which is otherwise wild-type for chemotaxis, were shortened by viscous shear, and cell bodies were fixed to a polylysine-coated glass coverslip. Latex beads of various sizes were adsorbed to filament stubs and their rotation was followed in a weak optical trap with a quadrant detector[2].

Figure 1 shows clockwise and counterclockwise intervals for rotation plotted as a function of counterclockwise speed, together with rate constants for transitions between the clockwise and counterclockwise states. Clockwise intervals lengthened appreciably at high loading (k^- decreased), whereas counterclockwise intervals remained about the same for all loads (k^+ remained roughly constant).

A similar asymmetrical performance is seen under the action of fumarate[3]. However, when an attractant is added, the cells respond by shortening their clockwise intervals and lengthening their counterclockwise intervals[4]. From the results shown in Fig. 1, it follows that a motor that is spinning rapidly, as motors do in swimming cells, will spend a larger fraction of its time turning counterclockwise and will change direction more frequently than a motor that is spinning slowly, as motors do in tethered cells.

In a wild-type cell, the direction in which the motor spins depends on the degree of phosphorylation of a small signalling protein, CheY, which is activated by a kinase that is coupled to the chemoreceptors[5]. To determine whether this signalling pathway is involved in the load response, we repeated a number of measurements using cells in which this pathway had been disrupted. We used a strain in which *cheY*, *cheA* (which encodes the kinase) and *cheZ* (which encodes a phosphatase) were all deleted and which expressed $CheY^{13DK106YW}$ ($CheY^{**}$), a variant with fixed activity[1]. The response to different loadings was the same as that of wild-type cells, indicating that the motor's sensitivity to load is probably not due to feedback from the chemotaxis signalling network, but is instead an inherent property of the motor.

The bacterial flagellar motor is powered by protons moving down an electrochemical gradient and has a distinctive torque–speed relationship. At 20 °C, the relative torque falls gradually from unity at stall to about 0.9 at 120 Hz, and drops rapidly to zero at about 260 Hz (ref. 6); in the latter regime, the torque decreases markedly at lower temperatures or when H_2O is replaced by D_2O (ref. 7), indicating that the movement of mechanical parts and/or of protons becomes rate limiting.

We found switching to be particularly sensitive to load only during high-torque, low-speed operation, and mainly at speeds of less than about 50 Hz (Fig. 1). Over this speed range, the torque changes by about 5%. There is evidence that each revolution of the motor requires the passage of a fixed number of protons[8]. So, rather than sensing changes in torque, might the switch be monitoring proton flux?

Flagellated bacteria are sensitive to a variety of environmental factors, including mechanical stimuli. Swimming in viscous solutions or near surfaces can trigger developmental changes — for example, swarmer-cell differentiation in *E. coli*[9] or lateral flagellar synthesis in the marine organism *Vibrio*[10]. In the latter case, changes in gene expression occur in response to exposure to sodium-channel blockers, indicating that they might be caused by a reduction in motor ion flux[11]. It is possible that these different responses rely on a common mechanosensory mechanism.

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erratum

Rapid change in mouse mitochondrial DNA

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There is an error in the Volo Bog and Glenview components of Fig. 1 of this communication: two *Mw* haplotype mice were shown in the 1950–99 column of the former that should have been in the 1950–99 column of the latter. This mistake does not affect the conclusions, as the analysis was done with mice from the correct category. Sample sizes (left and right columns, respectively) for the different locations were: Volo Bog, 19 and 41; Glenview, 5 and 6; Illinois Beach, 8 and 5; Highland Park, 2 and 5; Palos, 1 and 8 (note that sample numbers were inevitably low for museum specimens).