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Supplemental Information

Motor Adaptive Remodeling Speeds Up Bacterial Chemotactic Adaptation

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Supporting material

Further discussions about Eqs. 1 and 2.

Eq.1 in the main text consists in fact of the following two equations:

$$\frac{dN}{dt} = k_{on}(M-N) - k_{off}(N-N_{CW}), \text{for } t \in \text{CW intervals}, N_{CW} = 12, \quad [S1]$$

$$\frac{dN}{dt} = k_{on}(M-N) - k_{off}(N-N_{CCW}), \text{for } t \in \text{CCW intervals}, N_{CCW} = 34, \quad [S2]$$

where N_{CW} and N_{CCW} are the number of FliM molecules in the non-exchanging state for CW and CCW rotations respectively.

To take into account the fact that N may be smaller than N_{CCW}, more rigorously Eq. S2 should be written as:

$$\frac{dN}{dt} = \begin{cases} k_{on}(M-N) - k_{off}(N-N_{CCW}), & \text{for } N \geq N_{CCW}, \\ k_{on}(M-N), & \text{for } N < N_{CCW}. \end{cases} \quad [S3]$$

Under quasi-equilibrium approximation, the steady-state FliM number N_s (see Eq. 5) is always much larger than N_{NE} (i.e., $12\times B+34\times(1-B)$), so Eq. 2 in the main text is always valid. In our stochastic simulations not using the quasi-equilibrium approximation, Eq. S3 was implicitly used, as the "off" term ($k_{off}(N–N_{CCW})$ × the time step) was compared to a uniformly distributed random number in (0, 1) to determine whether N should be decreased by 1 (if it is larger than the random number, then N is deceased by 1). If $N < N_{CCW}$, the "off" term is negative and always smaller than the random number, so effectively this term is zero.

Derivation of dB/dt

Following a very small step of stimulus, B changes with time as the CheY-P level (Y) and the number of FliM molecules (N) change:

$$\frac{\mathrm{d}B}{\mathrm{dt}} = \frac{\partial B}{\partial Y} \times \frac{\mathrm{d}Y}{\mathrm{dt}} + \frac{\partial B}{\partial N} \times \frac{\mathrm{d}N}{\mathrm{dt}}. \quad [S4]$$

We start with the first term in the summation of Eq. S4. With a very small stepwise stimulus, the deviation from the steady state is very small, so all relevant equations can be linearized around the steady-state values. Near steady state, the CheY-P level (Y) is approximately proportional to the receptor activity a. Therefore

$$\frac{\partial B}{\partial Y}\times\frac{\mathrm{d}Y}{\mathrm{d}t}=\frac{\partial B}{\partial a}\times\frac{\mathrm{d}a}{\mathrm{d}t}\,. \qquad [S5]$$

Following a coarse-grained model of receptor cluster dynamics, three dynamic variables are defined(1): the ligand concentration L, the receptor activity a, and the receptor methylation level m. The receptor cluster can be either in the active or inactive state, with a free energy difference of $N_r(f(m)+g(L))$ between these states, where N_r is the number of receptor homodimers (i.e., ligand binding sites) in the cluster, and $f(m)$ and $g(L)$ are the free energy dependence on m and L respectively. The time scale for ligand binding/unbinding and receptor response is much faster than methylation/demethylation, so the dependence of a on L and m can be determined by a two-state model:

$$a=\frac{1}{1+\mathrm{e}^{N_r(f(m)+g(L))}}\,. \qquad [S6]$$

$f(m)$ is linear in m: $f(m) = \alpha(m_0-m)$ according to recent measurements(2), where α and m_0 are constants. As the network exhibits perfect adaptation, $\mathrm{d}m/\mathrm{d}t$ should depend explicitly only on a according to the linear integral feedback model(3), thus the kinetics of the methylation level can be described by a differential equation:

$$\frac{\mathrm{d}m}{\mathrm{d}t}=F(a). \qquad [S7]$$

At the steady state activity of a_0, $F(a_0) = 0$. Following a very small stepwise stimulus, the deviation of the activity from a_0 is small such that the equation can be linearized: $\mathrm{d}m/\mathrm{d}t \approx F'(a_0)(a - a_0)$, and

$$\frac{\mathrm{d}a}{\mathrm{d}t}=\frac{\partial a}{\partial m}\frac{\mathrm{d}m}{\mathrm{d}t}=\alpha N_r a(1-a)\frac{\mathrm{d}m}{\mathrm{d}t}\approx\alpha N_r a_0(1-a_0)F'(a_0)(a-a_0)\,. \qquad [S8]$$

so $\mathrm{d}a/\mathrm{d}t$ can be written as $-(a-a_0)/\tau_m$, where $\tau_m = -1/\alpha N_r a_0(1-a_0)F'(a_0)$. Therefore

$$\frac{\partial B}{\partial Y}\times\frac{\mathrm{d}Y}{\mathrm{d}t}=-\frac{\partial B}{\partial a}\times\frac{1}{\tau_m}\times(a-a_0)$$

$$= -\frac{\partial B}{\partial Y} \times \frac{1}{\tau_{\mathrm{m}}} \times (Y - Y_0)$$
$$= -\frac{B - B_0}{\tau_{\mathrm{m}}} + \frac{\partial B}{\partial N} \times \frac{N - N_0}{\tau_{\mathrm{m}}} \ . \qquad [S9]$$

Next we consider the second term in the summation of Eq. S4. The time rate of change of *N* (i.e. Eq. 2 in the main text) is

$$\frac{\mathrm{d}N}{\mathrm{d}t} = k_{\mathrm{on}}(M - N) - k_{\mathrm{off}}(N - (B \times 12 + (1 - B) \times 34)). \qquad [S10]$$

Linearizing the right hand side at (N_0, B_0) leads to

$$\frac{\mathrm{d}N}{\mathrm{d}t} \approx \left.\frac{\mathrm{d}N}{\mathrm{d}t}\right|_{\mathrm{N_0,B_0}} - (k_{\mathrm{on}} + k_{\mathrm{off}}) \times (N - N_0) - 22 \times k_{\mathrm{off}}(B - B_0)$$
$$= -(k_{\mathrm{on}} + k_{\mathrm{off}}) \times (N - N_0) - 22 \times k_{\mathrm{off}}(B - B_0), \qquad [S11]$$

where d*N*/d*t* at steady state equals 0, and 22 is the difference in the number of non-exchanging FliM molecules for a motor in CCW and CW states. Using the dependence of *B* on *N* and *Y* (i.e. Eq. 3 in the main text):

$$B = \frac{1}{1 + \mathrm{e}^{N \times \mathrm{G}(Y) + \varepsilon}}, \qquad [S12]$$

$\partial B / \partial N$ can be expressed as

$$\frac{\partial B}{\partial N} = -\mathrm{G}(Y)B(1 - B) \approx -\mathrm{G}(Y_0)B_0(1 - B_0). \qquad [S13]$$

Combining with Eq. S11 leads to

$$\frac{\partial B}{\partial N} \times \frac{\mathrm{d}N}{\mathrm{d}t} = -\frac{\partial B}{\partial N} \times (k_{\mathrm{on}} + k_{\mathrm{off}}) \times (N - N_0) - \frac{B - B_0}{\tau_{\mathrm{N}}}, \qquad [S14]$$

where τ_{N} is the adaptation timescale due to motor adaptation:

$$\tau_{\mathrm{N}} = -\frac{1}{\mathrm{G}(Y_0)B_0(1 - B_0) \times 22 \times k_{\mathrm{off}}}. \qquad [S15]$$

As it happens that $k_{\mathrm{on}} + k_{\mathrm{off}}$ approximately equals $1/\tau_{\mathrm{m}}$ in value, the second term in the right-hand side of Eq. S9 cancels out the first term in the right-hand side of Eq. S14. Thus combining Eq. S9 and Eq. S14 leads to

$$\frac{\mathrm{d}B}{\mathrm{d}t} \approx -\left(\frac{1}{\tau_{\mathrm{m}}} + \frac{1}{\tau_{\mathrm{N}}}\right) \times (B - B_0) \, . \qquad [S16]$$

Both τ_{m} and τ_{N} contribute to the overall adaptation timescale τ_{T}:

$$\frac{1}{\tau_{\mathrm{T}}} = \frac{1}{\tau_{\mathrm{m}}} + \frac{1}{\tau_{\mathrm{N}}} \, . \qquad [S17]$$

Supporting References

1. Tu, Y., Shimizu, T. S., and H. C. Berg. 2008. Modeling the chemotactic response of *Escherichia coli* to time-varying stimuli. Proc. Natl. Acad. Sci. USA 105:14855-14860.
2. Shimizu, T. S., Y. Tu, and H. C. Berg. 2010. A modular gradient-sensing network for chemotaxis in Escherichia coli revealed by responses to time-varying stimuli. Mol. Syst. Biol. 6.
3. Yi, T. -M., Huang, Y., Simon, M. I., and J. Doyle. 2000. Robust perfect adaptation in bacterial chemotaxis through integral feedback control. Proc. Natl. Acad. Sci. USA 97:4649-4653.

Supporting figures

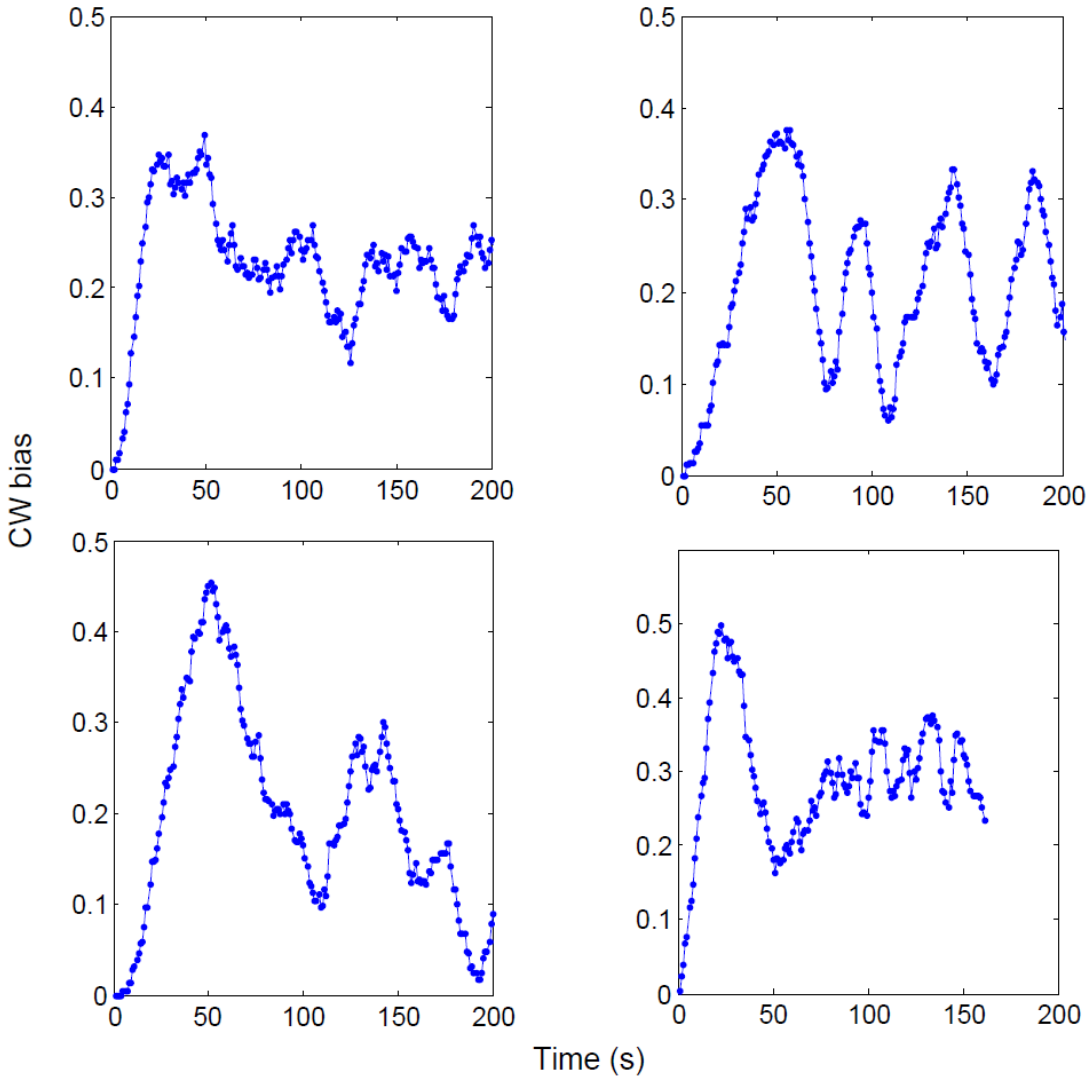

Fig. S1. Example traces (un-normalized) of four motors for cells with single typle of receptors (Tar) subjected to a stepwise stimulus of 2.5 μM MeAsp at time 0. Due to large fluctuations, twenty traces have to be averaged to demonstrate the overshoot phenomenon clearly in Fig. 1a.

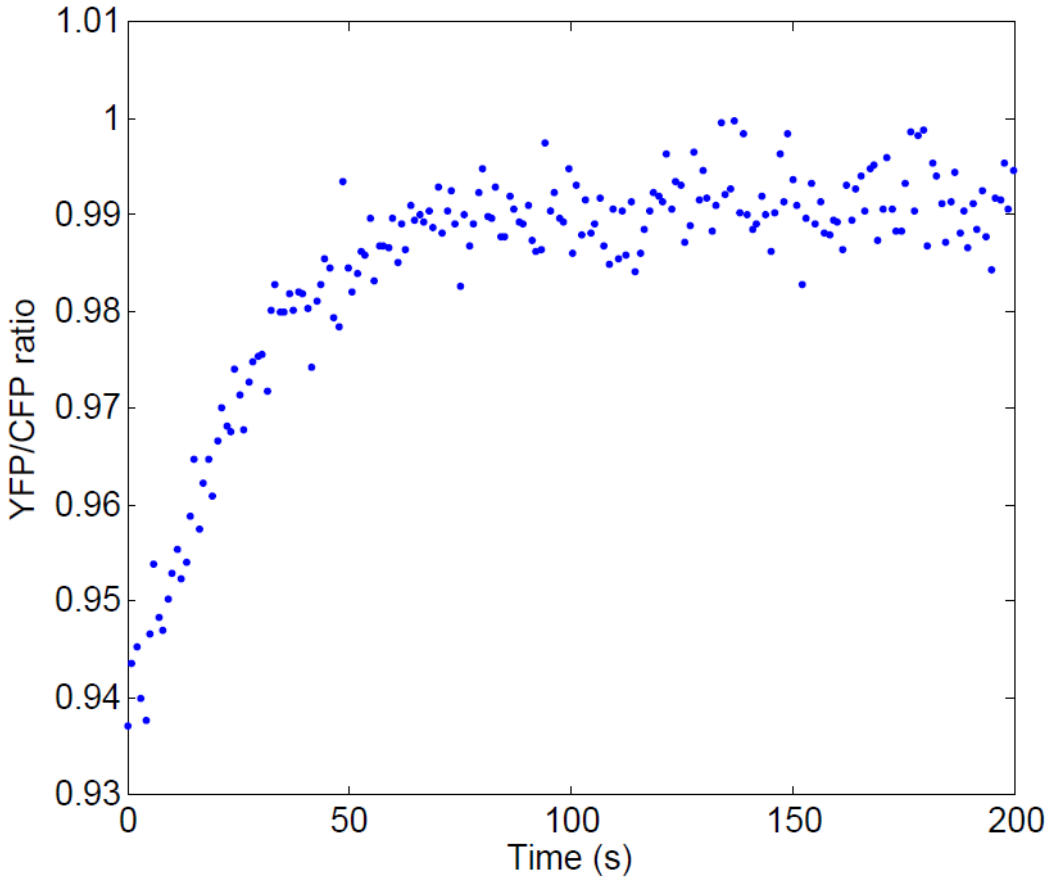

Fig. S2. No overshoot at the level of CheY-P concentration measured by FRET between CheZ-eCFP and CheY-eYFP. The ratio of YFP/CFP is shown without normalization.

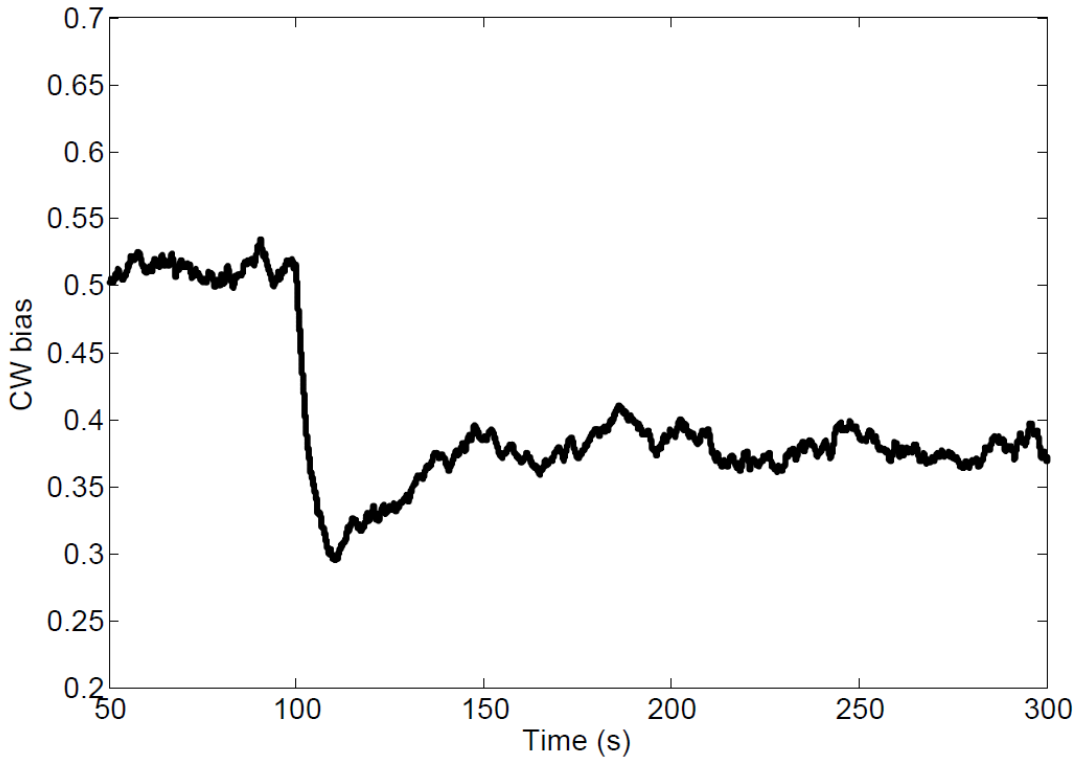

Fig. S3. The motor partial adaptation trace generated by stochastic simulation of the motor dynamics. The CheY-P level was reduced from 2.90 μM to 2.60 μM at t = 100 s with no recovery, mimicking a *cheRcheB* deletion strain used in motor adaptation experiments. The trace was the average of 10 repeated simulations.