BACTERIAL CHEMOTAXIS: USING COMPUTER MODELS TO UNRAVEL MECHANISM

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We have used both deterministic and individual-based stochastic programs to investigate the pathway of intracellular signals used by coliform bacteria in the detection of chemotactic stimuli. The function and formation of this pathway were examined by means of computer-based models based on physiological data collected from single tethered bacteria of over 60 mutant genotypes. Quantitative discrepancies between computer models and experimental data throw a spotlight on areas of uncertainty in the signal transduction pathway, highlighting the importance of spatial organization to the logical operation of the pathway. In particular they emphasize the function of a specific, well-characterized, cluster of proteins associated with the chemotaxis receptors which acts like a self-contained computational cassette.

We have investigated the possibility that the receptor cluster might show coordinated response because of the spread of conformational states from one receptor to its neighbours. A Monte Carlo simulation was developed in which receptor flipped in probabilistic fashion between active and inactive states. With conformational energies, dependent on ligand binding, methylation level, and activity of neighbouring receptors. The simulated system showed a greatly enhanced sensitivity to external signals compared to a set of uncoupled receptors and was operational over a much wider range of ambient concentrations. Recent atomic level models of the spatial arrangement of proteins in the cluster provide a possible mechanistic basis for the spread of conformation.