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13 Epilogue

What We Have Learned

I have told you some things about a free-living organism only one micron in size. It is equipped with sensors that count molecules of interest in its environment, coupled to a readout device that computes whether these counts are going up or down. The output is an intracellular signal that modulates the direction of rotation of a set of rotary engines, each turning a propeller with variable pitch. Each engine (or motor) is driven, in turn, by several force-generating elements (like pistons), powered by a transmembrane ion flux. In addition to a gear shift (labeled forward and reverse but prone to shift on its own) there is a stator, a rotor, a drive shaft, a bushing, and a universal joint.

We know a great deal about what all this machinery does for the bacterium, a fair amount about the structures of the molecular components involved (particularly those that have been crystallized), and even how the organism programs their syntheses. We know less about the precise ways in which these components function.

Levels of Amazement

Some wonder how the flagellar motor possibly could have evolved. The problem here is that we do not know about earlier states. What was the flagellar motor doing, for example, before the acquisition of the propeller (if, indeed, that was the sequence of events)? Perhaps it was winding up DNA. Or maybe it was injecting toxins into other cells as part of a program of conquest. In any event, it must have been doing something that promoted the survival of the organism. Evolution is opportunistic: it builds on components already at hand. One can not turn off the organism in order to redesign it, because that means extinction. You have to modify the machinery while it is running.

A Caltech friend, John Allman, an expert on the evolution of primate brains, once marveled to me about the similarity between circuits in brains and those in a Los Angeles power plant. When he visited the power plant, he discovered a hierarchy of control devices utilizing components ranging from antique to modern (e.g., mechanical relays, vacuum tubes, transistors, integrated circuits, and computers). The reason was simple: it was desirable to improve the design without interrupting the service. In biology, this is imperative.

The flagellar motor, albeit amazing, is no more so than a number of other molecular machines. Among these are enzymes used to make RNA copies of DNA templates, that is, RNA polymerase, or macromolecular ensembles used to translate these copies into sequences of amino acids, that is, the ribosome. The latter is particularly remarkable, because it dates from an ancient era in which catalytic functions were carried out by RNA rather than protein. The structures and functions of these machines are currently being examined in atomic detail. But unless you work in a chemical plant, everyday analogs of these devices are not readily at hand. However, everyone knows about rotary motors, including those with propellers. The speed of the flagellar motor is much faster than that of the motor of a boat, something like the speed of a table saw. And if you studied Chapter 6, you will know that the physics used by the flagellar filament is rather different from that used by the propeller of a boat—it shears water rather than accelerates it. Also, the flagellar motor is very small. Richard Feynmann once offered a prize to anyone who could build a rotary motor smaller than 1/64-inch on a side. The winning model is displayed behind glass in the hallway of one of Caltech's physics buildings. The flagellar motor is more like 1/640,000 of an inch on a side! That's a million million times smaller in volume.

Where We Go from Here

Our next task is to understand a number of things more quantitatively. We are trying to develop better ways of monitoring the concentration of the signaling molecule CheY-P in living cells, with the aim of understanding more about receptor function. Why is the gain of the chemotaxis system so high, and why does adaptation work so well? As noted earlier, detailed understanding of the force-generating and switching mechanisms of the flagellar motor probably awaits crystal structures. Might it be possible to crystallize the entire machine? And more needs to be learned about the precise way in which the transport apparatus decides what components are sent along the channel leading, ultimately, from the cytoplasm to the filament cap. At the genetic level, we need to know a great deal more about the mechanisms that up- or downregulate flagellar synthesis. How, for example, does the cell decide to make many flagella and swarm over surfaces?

Motivation

Is any of this knowledge practical? The reading of the external environment by cells of all types, leading to responses in growth or motility, is fundamental to life. Bacterial chemotaxis provides a model for learning how such processes can work. However, this is not what has motivated me. I have wanted to know, simply, how such a tiny creature does its thing. How, for example, has it solved the problem of finding greener pastures within the constraints imposed by physics? This is a matter of curiosity. Curiosity is the driving force of basic science.