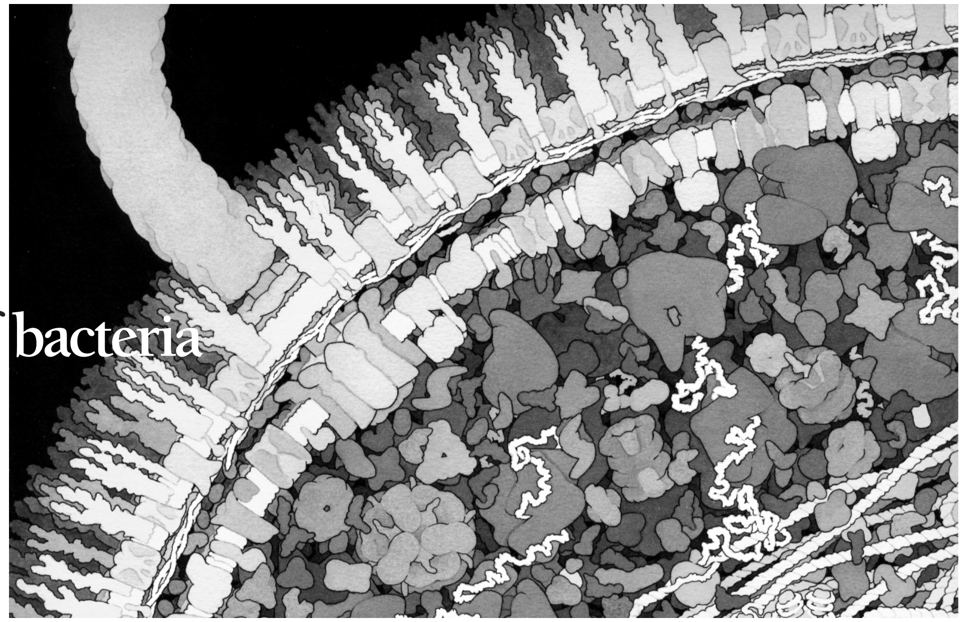
feature

Biological physics of bacteria



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BY **ANDREW RUTENBERG**

Abstract

Physicists, including Erwin Schrödinger, Max Delbrück, and Francis Crick, have a long and distinguished history of thinking about the problems of biology. A short overview of the physics of a simple bacterium, which is a self-assembled micromachine, is presented here.

Bacteria – self-organizing micromachines

Bacteria are self-organized reproducing micromachines, a few microns long and less than a micron wide. A bacterial volume of a cubic micron or two, compared to the volume of a single protein of around ten cubic nanometers, allows one million protein molecules per bacterial cell. Indeed, the cell interior is not so much water as a thick stew of hydrated protein and genetic material: a non-Newtonian fluid where diffusion dominates. This compactness is only possible with compressive pressures of several atmospheres applied by a strong network of peptidoglycan outside the bacterial inner-membrane.

Proteins are the machines of the cell, key parts of the mechanisms required to accurately move, grow and divide, and to ingest, excrete, while maintaining the cell structure. With a genome encoding several thousand proteins, there is only room for about one thousand molecules of each protein. As a result, each bacterial mechanism is poised on the edge of disruption by the noise inherent in so few molecules.

Nanotechnology done by nature

Energy, in the form of ATP within the cell or the 100–200 mV potential difference across the 6 nm thick bacterial inner membrane (tens of thousands of volts/metre), drives motors, pumps, and processes in the face of this noise. A few bacterial mechanisms, such as those for RNA transcription and protein translation, the rotary electric motor of the flagellum, or the calculations involved in hunting for food (chemotaxis), are relatively well-studied. Many others, such as the polymerized bacterial cytoskeleton, coordinated cell growth, and the detailed mechanisms of cell division, are not.

Consider the inner and outer lipid bilayers, sandwiching the peptidoglycan sheath, that characterize Gram-negative bacteria like *E. coli*. Only the inner-membrane is energized, yet the bacterium has to maintain the outer membrane and to import food and export enzymes across it. Little is yet known about these processes, but what is known is remarkable. Flagella are rooted in the inner membrane, and their rotation is driven by the electrical potential there. The flagellum itself is hollow, and is assembled by diffusing building-block proteins up its hollow core to its tip. Other protein export machines are also built on this principle and work somewhat like hypodermic syringes. Others are more like pistons, cyclically pushing enzymes out of the cell and then retracting to be reloaded. This is done by cyclically assembling and disassembling the piston *in situ*! Using a similar mechanism, pili are extended far beyond the cell, stick to a surface, and are reeled in to allow cells to "twitch" along a surface. This is nanotechnology done by nature, teetering between the amazing and the implausible.

To understand the behavior in quantitative detail

Understanding how geometry, diffusion, noise, force, elasticity, and the strong non-linearities inherent inside the cell combine to give regular behavior – and to understand that behavior in quantitative detail – is our goal. To modernize Rutherford: a simple but quantitative description of the world is the goal of physics, and is our goal with respect to the bacterial cell. Molecular microbiology gives us the parts list; we try to figure out how it all fits together in non-trivial ways. Biological physics is not a mature field, reduced to a short list of well-defined problems that everyone agrees upon. Given the enormity of nature, this is unlikely to change in our lifetimes.

There are millions of bacterial species, each solving the problem of efficient survival in many different and interesting ways. Only a dozen or so are well studied "model" organisms, and even *E. coli* (the model of model organisms) is still mostly a black box to us. Every year several undergraduate students join our group to help pin down a bacterial mechanism by creating and exploring simple yet realistic computational models of its function.

Physicists and the problems of biology

Physicists, including Erwin Schrödinger, Max Delbrück, and Francis Crick, have a long and distinguished history of thinking about the problems of biology. However, it is only recently that a significant number of physicists are working on biological problems from inside physics, both in Canada (see, *e.g.*, www.qbio.ca) and beyond.

If you are interested, have a look at three books: *The way of the cell* by Franklin Harold sketches how cells work, *The self-made tapestry: pattern formation in nature* by Philip Ball describes the sorts of rich physical processes that cells exploit. Finally, the more technical *Mechanics of motor proteins and the cytoskeleton* by Jonathan Howard overviews the physics of biomolecular machines. Or, you could chat with the next biological physicist you meet!

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