The team therefore decided to test whether termites of the *Cryptotermes domesticus* species might be able to discriminate between different sizes of wood. The team constructed experiments that presented termites with blocks of wood with a standard cross-sectional diameter of 20x20 mm but of either 20 mm or 160 mm length. The insects were placed in a gap between the two faces of the timber blocks so that they were not able physically to assess the length of each block.

The team found that the termites, when presented with a choice, preferred the shorter 20 mm block. To test whether the termites might be using vibration signal to assess the blocks, the researchers carried out two experiments. They recorded the vibration signals produced by termites placed in a hole in blocks of wood of lengths varying from 20 to 160 mm long. They then examined the influence of some of the recorded signals on termites faced with wood blocks of different sizes along with the influence of two artificially synthesized signals.

The team found that when they played the vibration signals recorded from the larger block into the smaller block, the termites' preference for the smaller block disappeared, but when the signal from the smaller block was played the preference was maintained. The termites did not change their behaviour in response to artificial noise signals.

The researchers believe the demonstrated preference for smaller pieces of wood may be a mechanism to avoid competition with larger species of termite attracted to larger pieces of wood.

But while individual termite species might be fussy, the news is not good for those whose home timbers have been deemed an ideal feast by whatever species finds this source and size of wood attractive.

**Q & A**

# Howard Berg

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***What turned you on to biology in the first place?*** I grew up in Iowa City in the shadow of the University of Iowa, where my father was a biochemist (metabolism of amino acids, notably tryptophan). I went to Caltech, expecting to become an electrical engineer, but started in physics, which I considered more fundamental. Linus Pauling taught me freshman chemistry (the year he got the structure of DNA wrong). That aroused my interest in chemistry. When I graduated, I got the idea that to do chemistry of merit, one needed medicine. I was admitted to the Harvard Medical School but postponed my entrance to work with Linderstrøm-Lang at the Carlsberg Laboratory in Copenhagen, a mecca for protein chemists. Then, upon arriving at the medical school, I realized that medicine was not for me. I spent two years learning the pre-clinical vocabulary and a lot about myself (both valuable) and withdrew. I returned to physics and earned a PhD at Harvard under the tutelage of Norman Ramsey, working on the atomic hydrogen maser (an atomic clock).

***How then biology?*** The frontier in experimental physics at that time (1964) was high-energy particle physics, which was carried out on a gigantic scale. I wanted to do experiments on a tabletop. A stint in Harvard's Society of Fellows gave me a chance to shop around and an appointment in Biology at Harvard a chance to settle down. I worked on a new kind of centrifuge (sedimentation field-flow fractionation) with Ed Purcell (of NMR fame), on the distributions of proteins in the human red cell membrane, and finally on bacterial chemotaxis. The latter subject goes all the way back to Antony van Leeuwenhoek, who saw bacteria swim in 1676. Elegant work was done in the late 19th century by Theodore Engelmann in Utrecht and by Wilhelm Pfeffer in Tübingen. The modern era began in the 1960s with Tetsuo Iino and Sho Asakura in Mishima and Nagoya, who began work on the structure of flagellar filaments (thought then to be primitive bending machines), and with Julius Adler in Madison, who mapped the responses of motile cells to chemical gradients. Adler published a classic paper in *Science*, December, 1969, "Chemoreceptors in bacteria" showing that the bacterium *Escherichia coli* responds to spatial gradients of certain amino acids and sugars for reasons of aesthetics rather than material gain.

***What does that mean?*** Chemotaxis evolved so that cells can locate nutrients, but Adler found that cells lacking permeases required for transport, or enzymes required for metabolism of specific substrates, still liked their taste. He modernized an assay due to Pfeffer, in which cells respond to a point-source of a chemical contained in a thin capillary tube, first accumulating near the mouth of the tube and later swimming inside. I got interested in the strategy that *E. coli* uses to navigate such gradients. Inspired by Max Delbrück, who told me that he might abandon *Phycomyces* for bacteria if he only knew how to 'tame' them, I built a microscope that tracked individual cells in three dimensions.

***How did you do that?*** It was a three-dimensional DC servo system. Build a mechanical stage that can rapidly move a small chamber containing a suspension of swimming cells about 1 mm in

any direction; design a detector that can dissect the image of a single cell; add electronics to compute errors in position and move the stage so that the image remains locked on the detector; then write down the displacement of the chamber. This tells you the displacement of the cell relative to the medium in which it is suspended. The accelerations of the chamber are so small that the bacterium does not know that it is being manipulated.

***Was it worth the trouble?*** Yes. We found that *E. coli* executes a three-dimensional random walk. A cell picks a direction at random, counting molecules of interest as it goes along. If it is in a gradient of an attractant and that count goes up, then it tends to keep going. If the count goes down, then it tries a new direction, with the frequency that it would in the absence of a stimulus (once per second, on average). So the random walk is biased, and the bias is positive: if life is getting better, enjoy it more; if it is getting worse, don't worry about it! This was surprising, because it had been thought since the work of Engelmann that cells retreat in response to unfavorable stimuli.

***What have you learned since?*** That bacterial flagella rotate, rather than wave or beat; that cells compare counts made over the past second to those made over the previous three seconds and respond to the difference; that the flagellar motor has several pistons and a novel torque-speed relationship; that one can visualize the motion of flagellar filaments and their polymorphic transformations by fluorescence; and that the prodigious gain of the signal transduction pathway is due to receptor–receptor interactions. At the moment, we are using fluorescence resonance energy transfer (FRET) to look at the dynamics of signal transduction at the single-cell level.

***Have you had much help?*** Yes, from a number of very able students and postdoctoral fellows. Colleagues at other institutions have used genetics to identify genes and gene products, biochemistry to purify proteins and study their interactions, X-ray crystallography and cryo electron microscopy to determine near-atomic and atomic structures, and mathematics and computer science to model the signaling network and the behavior of the flagellar motor.

***Do you have scientific heros?*** Ed Purcell for one. We had a lot of fun thinking about bacterial behavior. To glimpse the workings of his mind, see E.M. Purcell, "Life at low Reynolds number", *Am. J. Physics*, January, 1977. This was a talk given in honor of Viki Weisskopf. Ed shared the stage with several high-powered theorists, so he referred to his bit as comic relief. Francis Crick is at the top of the list. I admire his view that life is chemistry and physics: we don't need religious fanaticism.

***What advice would you give someone interested in biophysics?*** Learn analytical subjects as early as you can: applied mathematics, electricity and magnetism, statistical mechanics, and the like. Do more descriptive subjects later on: biochemistry, molecular biology, genetics. If you are a physicist, learn some biology, and if you are a biologist, learn some physics. Don't count on someone from a different culture to do your thinking for you.

***Is the gap between biology and physics large?*** Yes, but not insurmountable. It is a matter of language. On the one hand, there are basic biological facts — physicists do not like facts — and on the other, mathematical manipulations — biologists prefer to name things. At Harvard, the physics curriculum is largely devoid of biology, and the biology curriculum is backwards. Instead of sharpening their analytical talents on physics and then applying this armament to other subjects, many biology students put off physics until their senior year. It is reduced to a requirement for admission to medical school.

***Is your work well funded?*** I had a hard time early on. Study sections did not know what to do with me. The Research Corporation came to my rescue, and then the National Science Foundation, where I was funded by their biochemistry program. More substantial support came later from the National Institutes of Health, once bacterial chemotaxis became fashionable. NIH has been very supportive. The trend these days seems to be for interdisciplinary collaborations, where to compete you need to find principal investigators from different disciplines (biology, chemistry, physics, mathematics). Is one allowed to collaborate with oneself? I think it vital that we maintain support for individual investigators.

***What intellectual challenges remain in your field?*** We hope to understand how bacterial chemotaxis works, every nut and bolt. Who would have imagined: receptor complexes that count molecules and make temporal comparisons; activation of a diffusible signal that couples receptors to flagella; reversible rotary engines that drive propellers of variable pitch; force generators, rotors, drive shafts, bushings, and universal joints; a system with prodigious sensitivity, with amplification generated by receptor–receptor interactions? The biggest black box is the motor. We know a great deal about its electromotive and mechanical properties (torque, speed, changes in direction, and so forth) but we do not really know how it works. We need more structural information. This is hard, because essential components are membrane embedded. But even in an age of systems biology, one should not be embarrassed to focus on an isolated network controlling a particular molecular machine.

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