rest of the channel, as the authors show by comparison with another crystal structure, of segments S1 to S4 alone. This flexibility explains the difficulty that the authors encountered in crystallizing the protein; it also suggests a mechanism for voltage sensing. The paddle is a hydrophobic, charged particle that can move in the membrane interior, transporting its four positive charges from one membrane surface to the other (Fig. 1b).

It is the location of S4 — not embedded in the protein core, but loose in the membrane — that is the big surprise here. It explains an old puzzle, that small lipid-soluble molecules somehow have ready access to ion-channel voltage sensors. Such molecules include local anaesthetics, the alkaloid nerve toxins and the well-known insecticides allethrin and DDT. It is now easy to imagine them diffusing up to the voltage-sensor paddle from within the lipid membrane interior.

An X-ray crystal structure is like a posed photograph; in the KvAP crystal, for instance, the voltage-sensor paddle is held firmly in place by an antibody scaffold. What can be learned about the paddle's natural conformation and movements? A few years ago, Horn and colleagues[9] showed for sodium channels that a bulky moiety, attached by chemical modification to an S4 amino acid on the outside of the membrane, can actually be dragged through to the inner surface in response to an inside-negative voltage. In their second paper[3], MacKinnon and colleagues show that a much larger molecule — biotin plus a 17-Å linker — flips across the membrane in a voltage-dependent manner when it is attached to an S4 amino acid in KvAP. They conclude that the S3–S4 paddle moves through a quite unrestricted space. They go on to attach this biotin–linker molecule to various other sites in the paddle, to map its position relative to the membrane surfaces at positive and negative voltages.

After all this, MacKinnon and co-workers have still left a few questions to be answered. The actual conformation of the channel in the membrane will need to be clarified, because in the crystal the membrane is replaced by a blanket of detergent molecules. Questions also remain about the disposition of the amino-terminal end of the protein (thought to be intracellular) and of the loop between the S3 and S4 segments in related channels (in the well-studied Shaker potassium channel, this loop is always accessible from the outside surface). Moreover, details of the motions of the voltage sensor — in some channels the charge movement occurs in several discrete steps — remain to be worked out, as does the energetic issue of moving the quadruply charged paddle through the membrane interior. But the structure of KvAP's voltage sensor, so simple and, with hindsight, so obvious, is a wonderful end to a 50-year-old mystery. ■

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Optics

Positively negative

John Pendry

An artificially created material with negative refractive index has opened the door to new phenomena — and controversy. New work finally sets the seal of experimental confirmation on negative refraction.

As light crosses a boundary between different materials (such as between air and water), its speed changes and it refracts, or bends. On entering most materials, light refracts with a positive angle, as shown in Fig. 1. But some years ago, Veselago[1] suggested that some materials might produce 'negative refraction': light would refract the other way, through a negative angle. In 2001, the observation of negative refraction was reported in an artificially created material[2] — but not everyone was convinced. Now two papers in *Physical Review Letters*, one by Parazzoli *et al.*[3], the other by Houck *et al.*[4], report experiments at radio frequencies that confirm the existence of negative refraction.

The response of a material to electric and magnetic fields is characterized by its permittivity, ϵ, and its permeability, μ, respectively. Veselago argued that if both ϵ and μ were negative, it follows that the refractive index of the material, which determines the velocity of light within it, would also be negative. There matters rested, because, although there are natural materials with negative ϵ, there are none with both negative ϵ and negative μ. In the absence of any materials on which to experiment, the concept was purely theoretical.

But the situation changed with the publication of three papers. In the first, my own group showed[5] that it is easy to fabricate an artificial material with negative ϵ using a lattice of thin metal wires. We then showed[6] how to do the same thing for μ: the required magnetic response was obtained from a lattice of metal 'split rings' that resonate with magnetic fields of a given frequency; the induced currents give a negative magnetic response. The third paper, by Smith and colleagues[7], made the key advance. This team made a structure that combined these elements in a microwave experiment, the first demonstration of negative ϵ and negative μ in the same material. They went on to demonstrate negative refraction in their material[2].

This work sparked great interest in negative materials, but also a fair bit of controversy: one group of sceptics wrote[8] of "Wave Refraction in Negative-Index Media: Always Positive…". Others claimed, unfairly in my view, that the results were an artefact of losses in the system and observations taken too close to the sample. The challenge to experimenters was to reproduce the results and eliminate all areas of doubt.

Parazzoli *et al.*[3] and Houck *et al.*[4] follow the same basic design for the negatively refracting material: split rings of copper are

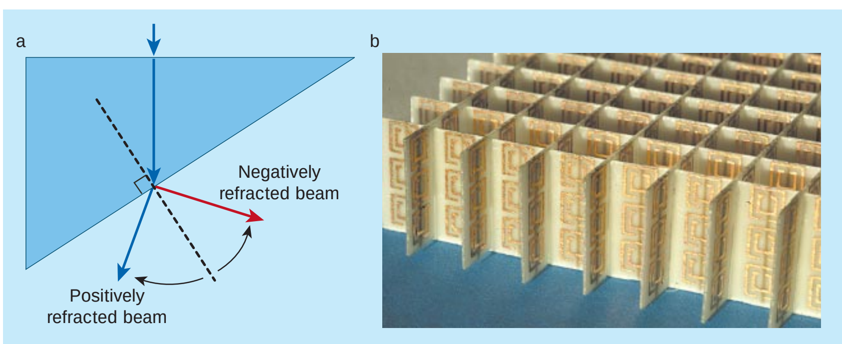

Figure 1 **Negative refraction.** a, **Light incident on a normal material refracts at a positive angle (blue), but in a negative-index material the refraction angle is negative (red). Negative refraction occurs only in specially engineered materials.** b, **This arrangement of fibreglass sheets (1 cm high) in which is embedded an array of copper loops and wires was the first 'material' for which negative refraction was seen[2].**

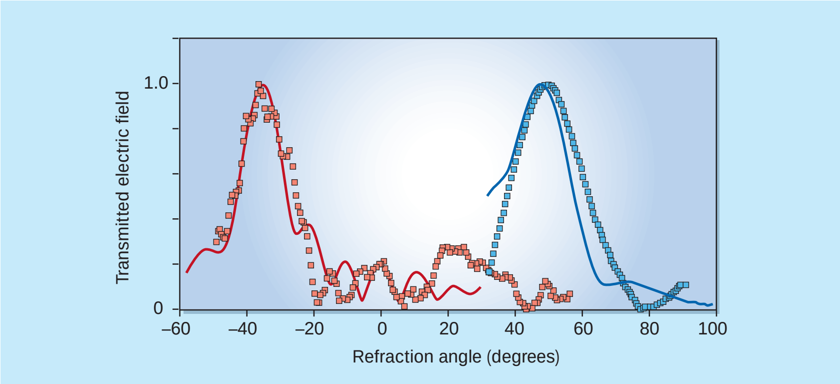

Figure 2 **Negative refraction confirmed. These data from Parazzoli *et al.*[3] compare refraction in their negative-index material (red points) with the response of a normal, positive-index material, Teflon (blue points). Moreover, the experimental data are in fair agreement with simulations (solid lines).**

held in place by fibreglass sheets, and current circulating in them produces a negative magnetic response; in addition, thin straight copper strips respond to electric fields, also in a negative manner (Fig. 1). The new ingredients, different in each of the two experiments, are in the manner the data are collected. Parazzoli *et al*. made their measurements in free space, up to 66 cm from their material sample. The data show a clear, well-defined, negatively refracted signal (Fig. 2). Houck *et al*. work within the confines of a planar waveguide, but sample the electromagnetic field at many points. They too observe unambiguous negative refraction. In most people's minds this will settle the long-running argument about the issue of negative refraction, which has also now been lent more theoretical support by extended computations[9].

Houck *et al.*[4] go on to tackle another, even more controversial issue. Veselago[1] observed that a slab of negative-index material would focus light, like a lens. Because they measured the transmitted light at many points around the sample, Houck *et al*. were able to verify some limited focusing capabilities of their material. This is an area in which further work can be expected.

It has been said that tackling a new scientific problem is like going into a darkened room. First you fall over the furniture, then you collide with other people in the room; arguments might develop. With time things settle down, as you learn where most of the furniture is and don't fall over so often. Eventually someone finds the light switch and everything becomes obvious.

I think I just heard the click of a switch. ■

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Genomics

Relative pathogenic values

Julian Parkhill and Colin Berry

The bacterium that causes anthrax has several close relatives. Comparison of their genome sequences should provide insight into the biology of these organisms as agents of disease — and of terrorism.

Particular notoriety has been accorded to *Bacillus anthracis* of late. As the causative agent of anthrax, this bacterium was used in the 2001 postal attacks in the United States[1], and it has reportedly been 'weaponized' as a warfare agent on at least one occasion[2]. On pages 81 and 87 of this issue, Read *et al.*[3] and Ivanova *et al.*[4] bring the power of genomics to bear on efforts to understand this pathogen and its close relatives.

Bacillus anthracis is a member of a group of closely related organisms that includes *B. cereus*, an opportunistic pathogen of humans, and *B. thuringiensis*, an insect pathogen that has been used worldwide as

NATURE

100 YEARS AGO

The discovery by Monsieur and Madame Curie that a sample of radium gives out sufficient energy to melt half its weight of ice per hour has attracted attention to the question of the source from which the radium derives the energy necessary to maintain the radiation; this problem has been before us ever since the original discovery by Becquerel of the radiation from uranium. It has been suggested that the radium derives its energy from the air surrounding it, that the atoms of radium possess the faculty of abstracting the kinetic energy from the more rapidly moving air-molecules while they are able to retain their own energy when in collision with the slowly moving molecules of air. I cannot see, however, that even the possession of this property would explain the behaviour of radium… I think that the absence of change in the radium has been assumed without sufficient justification; all that the experiments justify us in concluding is that the rate of change is not sufficiently rapid to be appreciable in a few months. There is, on the other hand, very strong evidence that the substances actually engaged in emitting these radiations can only keep up the process for a short time; then they die out… I have recently found that water from deep wells in Cambridge contains a radio-active gas, and I am anxious to see whether water from other sources possesses the same property. I should be greatly obliged if any of your readers who have access to deep level water would fill a clean two-gallon can with it and forward it to the Cavendish Laboratory. I should, of course, pay the carriage and return the can. J. J. Thomson

From *Nature* 30 April 1903.

50 YEARS AGO

***Royal Society: Foreign Members.* The following have been elected foreign members of the Royal Society: Louis Victor Pierre Raymond, Prince de Broglie (Paris), distinguished for his contributions to quantum theory; Marie Jules Constant Robert Courrier (Paris), distinguished for his contributions to endocrinology; Hermann Joseph Muller (Bloomington, Indiana), distinguished for his contributions to the chromosome theory of heredity; Wolfgang Pauli (Zurich), distinguished for his contributions to theoretical physics, in particular the formulation of the exclusion principle.**

From *Nature* 2 May 1953.