potent anti-HIV antibodies contain 40–100 somatic mutations[1,5,6,11] that span both the complementarity-determining region and the relatively constant, and mutation-resistant, framework regions. Experiments in which mutations in the framework regions were selectively reverted showed that these mutations are necessary for the evolution of broad and potent anti-HIV antibodies[6]. These structural alterations in the antibody were found to contribute to direct contacts with the virus and to enhanced flexibility of the antibody structure, both of which are required for optimal breadth and potency.

Combined with Liao and colleagues' findings, these data suggest a molecular explanation for why broadly neutralizing anti-HIV antibodies take 2–4 years to develop. Moreover, they indicate that an effective vaccine may require shepherding of B-cell responses through multiple rounds of the natural antibody maturation and mutation process, using naturally derived viral envelopes that induce the production of broad and potent antibodies in people with HIV. A recently suggested[7,8] alternative, non-mutually exclusive approach is to design specific 'immunogen' molecules that would bind to and activate B cells that produce the germline precursors of broadly neutralizing antibodies. Whether such roadmaps can be used to design effective vaccine strategies has yet to be determined, but they present a strong and testable route to addressing the main challenges of creating an antibody-based HIV-1 vaccine. ■

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IMAGING

Magnetic bacteria on a diamond plate

A new approach has been used to image magnetic fields in living cells of magnetotactic bacteria. The technique could be applied to study the dynamics of magnetism in other biological systems. SEE LETTER P.486

MIHÁLY PÓSFAI &
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Just as schoolchildren sprinkle iron filings on a sheet of paper placed over a magnet to visualize the magnetic field around the magnet, scientists who are interested in magnetism strive to image the magnetic fields within and around objects across a wide range of spatial and temporal scales. Although many different magnetic imaging techniques are now available, imaging micro- and nanoscale magnetic fields in living organisms is still challenging. On page 486 of this issue, Le Sage *et al.*[1] describe an advanced optical magnetic imaging technique which they use to study the three-dimensional magnetic fields that originate from chains of magnetic nanocrystals inside the living cells of magnetotactic bacteria.

Many organisms contain magnetic nanocrystals inside their bodies; some use them to navigate in magnetic fields, whereas others use them to harden or protect their tissues. Magnetotactic bacteria are the simplest organisms that are known to contain magnetic nanocrystals. Their delicate internal chains of tailor-made iron oxide or iron sulphide particles have attracted intense scientific interest since their discovery[2], and are often used as nanoscale natural laboratories to develop and test magnetic imaging techniques[3–6].

The fundamental principles of the technique that Le Sage *et al.* use have been known for some time[7] and have been applied to map magnetic-field variations on the nanoscale[8,9]. They involve detecting changes in the quantum spin states of crystallographic defects called nitrogen–vacancy centres in a diamond chip (a nitrogen atom and a vacancy substitute for two neighbouring carbon atoms in the diamond crystal lattice). The novelty of the authors' study lies in using this approach to image magnetic fields in living microorganisms.

"The study opens up the possibility of dynamic imaging of the development of magnetic fields in bacteria as their chains of magnetic crystals grow."

When the authors placed magnetotactic bacteria on a diamond surface, they found that the cells' magnetic fields affected characteristic signals, known as electron spin resonance frequencies, of the nitrogen–vacancy centres in the diamond. They detected such signals using an optical beam, and reconstructed all vector components of the magnetic field created by the chains of magnetic nanocrystals in the cells. Le Sage and colleagues' experimental set-up allowed them to simultaneously acquire magnetic maps and optical images of the bacteria. In this way, they could compare the recorded magnetic fields with the positions of the cells, map the positions of the chains of magnetic nanoparticles (see Fig. 4 of the paper[1]) and quantify the magnetic moments of the chains.

The importance of the technique for studying biomagnetic structures lies in the fact that both magnetic and optical images can be collected with a spatial resolution of about 400 nanometres from a population of cells across a wide field of view — spanning 100 μm × 30 μm. Although other approaches provide better spatial resolution for imaging magnetic fields in bacteria[3,5,10], at present these methods cannot be used under ambient conditions and for imaging multiple cells across such a large field of view in real time. Le Sage and colleagues' study opens up the possibility of dynamic imaging of the development of magnetic fields in bacteria as their chains of magnetic crystals grow.

Another potential application would be to screen non-magnetic mutant bacteria produced in genetic-engineering studies aimed at understanding the biological mechanisms that control the growth of magnetic nanocrystals inside cells[11]. The sharing of magnetic nanoparticles between daughter cells during cell division could also be studied. In addition to understanding magnetic nanocrystal formation by bacteria, it may be possible to use the method to reveal the presence and evolution of putative magnetic structures in the tissues of more complex organisms, including insects, birds and humans, under ambient conditions.

Some words of caution are warranted before making excessively bold predictions about

future uses of this imaging approach. First, the spatial resolution depends on the distance between the diamond surface and the source of the magnetic field. Submicrometre resolution in the recorded magnetic images was achieved only when the cells were dried (and necessarily dead) on the diamond surface. By contrast, when the bacteria were alive in a liquid environment, the cells were farther away from the nitrogen–vacancy centres and the resolution deteriorated.

Second, it may be possible to adapt several other magnetic imaging techniques, including SQUID microscopy, electron holography and magnetic resonance imaging, to achieve similar results in ambient conditions. These methods might provide higher-spatial-resolution alternatives to the optical magnetic imaging technique used by Le Sage and colleagues. Nevertheless, at the moment, the diamond-chip-based, optical magnetic imaging approach described by the authors is the only game in town that can be used to obtain quantitative, three-dimensional nanoscale information about magnetic fields originating from living microorganisms across a large field of view. ■

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GENOMICS

Zebrafish earns its stripes

The reported sequence of the zebrafish genome, together with the production of mutant strains representing more than one-third of all its protein-coding regions, will accelerate the characterization of human genes. SEE LETTERS P.494 & P.498

ALEXANDER F. SCHIER

Thousands of genes and gene variants are thought to contribute to human development, physiology and disease, but the functions of most of them are unknown. In the past 20 years, the zebrafish has emerged as a model system to investigate the function of human genes. Two papers in this issue[1,2], reporting the sequence of the zebrafish genome and the isolation of disruptive mutations in more than 10,000 protein-coding genes, add to other recent studies[3–7] in providing a strong boost to this effort*.

A common approach to studying gene function is to determine how a mutation changes an organism's phenotype, which includes its anatomy, physiology and behaviour. Zebrafish embryos and larvae are ideally suited for such studies: their small size, accessibility and transparency allow analysis of thousands of live animals at single-cell resolution. Most gene functions in zebrafish have been uncovered by 'forward genetics' approaches, in which genomic changes are induced randomly and resultant changes to phenotype are identified in later generations[8,9] (Fig. 1a). Identifying causative mutations using this strategy is laborious, but the approach has helped to uncover genetic pathways that control processes ranging from embryonic development to heart physiology. Many of these pathways are conserved in humans, which strengthens the use of zebrafish as a model system to study human gene function.

The high-quality zebrafish genome sequence reported by Howe *et al.*[1] (page 498) greatly facilitates the identification of mutations, because it makes possible a direct comparison of mutated and normal sequences. The genome sequence also reveals that more than 75% of human genes implicated in disease have counterparts in zebrafish, providing an opportunity to analyse their roles in this model system.

*This article and the papers under discussion[1,2] were published online on 17 April 2013.