provide approved data for final viewing through an elaborate website[6].

The resulting Allen Brain Atlas (ABA) allows one to view all the locations at which any of the 21,500 genes in the mouse brain are activated, down to cellular-level resolution. The site allows one to search any anatomical region of the brain for any gene or combination of genes. The activated genes can be viewed with tools that can zoom from a whole-brain section down to a single cell while retrieving data at multiple levels of resolution — itself a masterly stroke of informatics. The site is also linked to many gene banks around the world, allowing researchers to zoom into the building-blocks of each gene.

The ABA team also constructed a three-dimensional brain viewer, which maps the location and intensity of gene expression onto a reference atlas. The viewer can manipulate the atlas in three dimensions while moving a slider to virtually slice through any location in the brain and focus on areas of interest (Fig. 1).

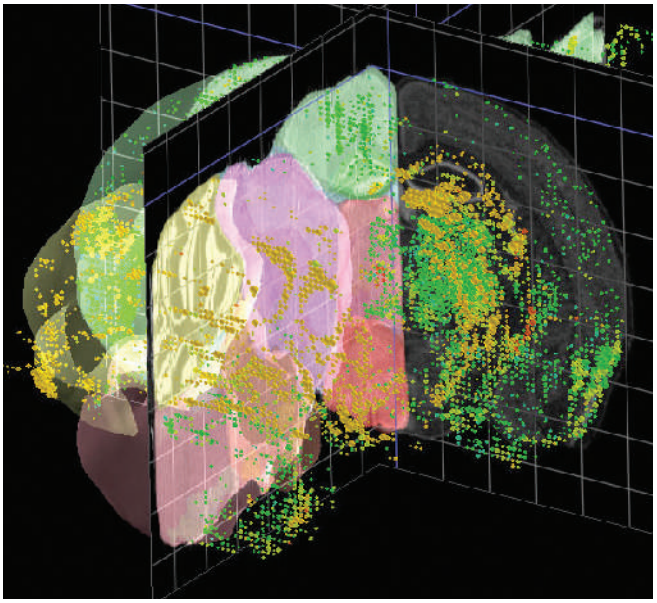

Figure 1 | Three-dimensional gene expression in the mouse brain. The model shows the expression of the gene encoding a G-protein-coupled receptor (GPCR12) mapped onto a reference atlas. On the left side are three-dimensional structures of different brain regions (in different colours). The expression of GPCR12 is indicated by the dots on both sides of the brain. The colour of the dots indicates the expression level — green (low expression) through to red (high expression). The squared planes can be moved along the *x* and *y* planes to focus on different parts of the brain.

Overall, the ABA provides unprecedented insight into how gene expression is orchestrated throughout the brain. The study does not determine specifically how sensitive the method is, but it was sensitive enough to yield a major surprise: that most of the genome is activated in the building of the brain. Expression of nearly 80% of the genes was detected, much higher than expected[7]. This is unlikely to be the case for body cells, as they do not require neuron-specific proteins (such as those encoding synapses and ion channels, and those regulating neuronal plasticity). Individual brain cells, however, express a much smaller percentage of genes (about 15%), which still allows for an enormous molecular diversity of neurons, connections and brain regions. Theoretically, the potential molecular diversity is greater than $10^{4,000}$, which should indicate that such gene-expression atlases will only be properly understood in combination with expression rules that make up the biologically viable solution — the choices made in evolution to focus on a minute subset of possible expression combinations.

The real power of the ABA, therefore, lies in its ability to pinpoint the anatomical locations of expressed genes. Taken together, these expression brain atlases provide the recipe of genes that are most needed to construct each brain region. On the other hand, each individual expression atlas highlights the different brain regions where the gene is used and reveals that some fundamental genes are activated in almost all regions, whereas other more specialized genes are activated only in specific locations — an essential guide for future transgenic experiments.

When such expression atlases are combined with functional studies on the proteins produced, we may begin to understand the essential functions that each gene has in different brain regions, and understand why certain genes are not expressed in certain brain regions and in certain types of cell. By analysing the overall correlation between anatomical locations for all 21,500 genes, it may be possible to get a glimpse of the role played by the 'conductor' that orchestrates gene expression throughout the brain. If such atlases could be built for each step taken in development, through adulthood and into ageing, we could capture the entire 'symphony' as genes are switched on and off in different parts of the brain during the life of an animal, and begin to understand the expression rules.

The ABA's main shortcoming is that any given cell in the brain is tested for only one expressed gene. The ideal case would be to determine the expression of all 21,500 genes for each neuron in the mouse brain — a task that is some 100-million-fold larger. With improved technology, such a feat may become possible in the future. The potential of such data would be incredible. By comparing how the transcriptomes of different types of neuron are correlated with their emergent properties, the secrets of how different neurons are built and connected might reveal themselves at the genetic level.

The ABA marks the beginning of an era in neuroscience in which such tasks become possible. We will see the production of hitherto unimaginable volumes of precisely standardized data, which will allow bottom-up reconstruction and eventual modelling of the brain in exquisite biological detail. ■

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1. International Human Genome Sequencing Consortium *Nature* **409,** 860–921 (2001).
2. Venter, J. C. *et al. Science* **291,** 1304–1351 (2001).
3. Lein, E. S. *et al. Nature* **445,** 168–176 (2007).
4. www.alleninstitute.org
5. Visel, A., Thaller, C. & Eichele, G. *Nucleic Acids Res.* **32,** D552–D556 (2004).
6. www.brain-map.org
7. Sandberg, R. *et al. Proc. Natl Acad. Sci. USA* **97,** 11038–11043 (2000).

MATERIALS SCIENCE

Displaced by radiation

Rodney C. Ewing

The mineral zircon suffers more structural damage from the α-decay of plutonium present in its crystal than was thought. That could have a knock-on effect on strategies for managing nuclear waste.

On page 190 of this issue, Farnan, Cho and Weber[1] describe how nuclear magnetic resonance (NMR) spectroscopy can be used to assess the damage caused to a solid's structure by α-decays of an emitter incorporated into its crystal. The authors test their technique on the mineral zircon ($ZrSiO_4$), and find that each α-decay event displaces significantly more atoms than simulations had predicted.

Zircon is an important material for two reasons. First, its trace content of long-lived α-emitters, combined with its ubiquity and high chemical durability in Earth's crust, has made it the mineral most often used in geological dating. Second — and this lends Farnan and colleagues' work its most immediate significance — zircon has been proposed as a material in which to immobilize the plutonium isotope

^{239}Pu over geological timescales. This α-emitter, of half-life 24,110 years, is the environmentally and politically awkward waste product of uranium-fuelled nuclear reactors. An accurate assessment of how its decay — as well as those of other members of the group of elements known as actinides[2], among them neptunium, curium and americium — might compromise the long-term chemical durability of surrounding materials is essential.

Such α-decays can lead to the slow accumulation of 'damage domains' and the eventual complete loss of periodic structure in a solid crystal, causing changes in the material's physical and chemical properties[3–6]. As long ago as 1815, the Swedish chemist Jöns Berzelius noted a rapid, and at the time inexplicable, release of heat from minerals that had accumulated such radiation damage. In 1893, the Norwegian mineralogist Waldemar Brøgger coined the term 'metamict' to describe amorphous materials that had, judging by their well-formed crystal faces, clearly at some point been crystalline.

With the construction of the first nuclear reactors during the Second World War, larger-scale radiation effects were seen in solids. The intense neutron flux from the production reactors at Hanford, Washington state, which were used to produce fissile material for the first nuclear bombs, displaced atoms in the surrounding graphite moderator and reactor fuel, causing both to swell. This effect was termed 'Wigner's disease', after Eugene Wigner, the theoretical physicist who first predicted these radiation effects.

The damage from an α-decay event comes from two different particles. First, there is the α-particle itself. This has a relatively low mass — it is a helium nucleus of two neutrons and two protons — and dissipates most of its energy (around 5 megaelectronvolts, MeV) through electronic excitations along its path, which is just a few tens of micrometres long. Only near the end of its trajectory does it interact with the crystal atoms in billiard-ball fashion, causing a few hundred displacements.

Second, there is the 'recoil nucleus' that is left after the emission of the α-particle, for example uranium-235 following the decay of plutonium-239. This particle has a much lower energy, just 86 keV, but deposits nearly all of it through ballistic interactions along a path of just a few tens of nanometres. This "cannon ball awry through a crowded dance floor" — to use chemistry Nobel laureate Roald Hoffmann's metaphor[7] — can cause several thousand atomic displacements. Energy deposition in this recoil cascade is high, at a few electronvolts per atom, and temperatures in its core can exceed 5,000 K for some picoseconds (a picosecond is 10^{-12} s).

The damage comprises a complex combination of isolated defects caused by the α-particle and branching collision cascades from the recoil nucleus (Fig. 1). The exact extent of the damage depends on the temperature of the irradiation. As they accumulate, the defects and collision cascades interact and finally overlap, producing an amorphous material. This is accompanied by significant changes in the material's physical properties: zircon's density, for example, decreases by some 17% at a dose of 10^{19} α-decay events per gram (ref. 8).

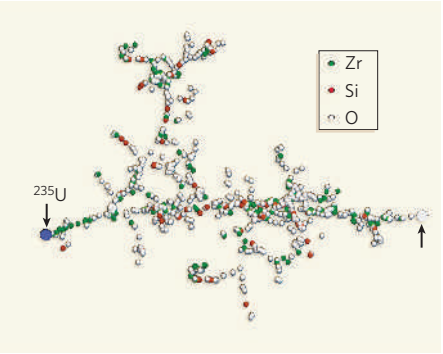

Figure 1 | Defect trail. The calculated spatial distribution of vacancies (colour-coded for zirconium, silicon and oxygen) produced by the recoil of a typical 86-keV uranium-235 nucleus in zircon following the α-decay of plutonium-239 (ref. 8). The arrow at the extreme right indicates the original position of the recoil nucleus. This simulation is based on a two-body collision approximation, which provides a good representation of the spatial extent of the cascade and the branching through the formation of sub-cascades. Farnan and colleagues' NMR experiments indicate that even more atoms are displaced along such recoil tracks than was thought — leading to the swifter formation of amorphous domains in the host material. (Figure courtesy of W. J. Weber.)

Farnan and colleagues' work[1] addresses two limitations that have plagued studies of radiation damage in zircon. First, there is the extent to which the experiments performed up to now produce results that are comparable to effects seen in natural zircon. Natural zircon contains the α-emitting actinides uranium and thorium, and has thus accumulated its radiation doses over many hundreds of millions of years. Synthetic phases doped with actinides such as the plutonium isotope ^{238}Pu (half-life 87.7 years), on the other hand, require just 5–10 years for irradiation, and materials irradiated with ion beams reach radiation levels of interest in less than an hour. But can these accelerated actinide-doping and ion-beam methods be used to simulate the long-term effects important for evaluating nuclear-waste containment strategies over hundreds of thousands of years? Does the rate at which the radioactive dose is administered really play no role?

The second problem that hampers studies of the evolution of damage structure is that, as the dose increases, so the length-scale of interest — and the appropriate tool to investigate it — changes. At low doses, techniques such as Raman spectroscopy are required that are sensitive to small-scale structural distortions in the crystal. At intermediate doses, methods such as X-ray diffraction measure the expansion of a crystal's unit cell as gaps accumulate between its component atoms, and high-resolution transmission electron microscopy shows the overlap of recoil cascades. At the highest doses, when the material is fully amorphous, X-ray absorption spectroscopy must be used to investigate the geometry of nearest neighbours. None of these methods alone can resolve the different types of defects and damaged domains.

Farnan *et al.*[1] measure the NMR spectrum of the silicon-29 isotope present in zircon doped with the long-lived ^{239}Pu and the shorter-lived ^{238}Pu using 'magic-angle spinning'. This technique enhances the resolution of an NMR spectrum by spinning the sample under investigation at high speeds at a certain angle to the applied magnetic field. Spinning highly radioactive samples at more than 200,000 rotations per minute is no mean feat and required elaborate safety procedures, including the triple containment of all the samples.

The improved resolution possible with magic-angle spinning means that even at low doses, before damage domains have overlapped, the nature of the individual damage events can be discerned. Furthermore, the NMR signal can be used to deconvolute the spectrum into the crystalline and amorphous fractions. The result that emerges is that around 5,000 atoms are displaced in each α-decay event. This is significantly more than the 1,000–2,000 predicted by standard simulations.

Comparison of these data from doped zircons with data from natural zircons[1], which are damaged over hundreds of millions of years, shows that the dose rate has no significant effect, despite its differing by a factor of 10^8. Thus, accelerated experiments using highly radioactive actinides can indeed be used to simulate long-term effects in forms of nuclear waste. That conclusion applies to the wide range of structure types and compositions that are currently under investigation to immobilize the actinide components of nuclear waste[9].

The increased damage observed by Farnan *et al.*[1] in each α-decay event means that the amorphous state will occur in radioactively doped zircon sooner, rather than later. Such information is vital in assessing the durability of such materials, and in informing the development of strategies for the safe encapsulation of actinides. ■

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1. Farnan, I., Cho, H. & Weber, W. J. *Nature* **445,** 190–193 (2007).
2. Ewing, R. C. *Proc. Natl Acad. Sci. USA* **96,** 3432–3439 (1999).
3. Weber, W. J. *et al. J. Mater. Res.* **13,** 1434–1484 (1998).
4. Robinson, M. T. *J. Nucl. Mater.* **216,** 1–28 (1994).
5. Hobbs, L. W. *et al. J. Nucl. Mater.* **216,** 291–321 (1994).
6. Ewing, R. C. *et al. Rev. Mineral. Geochem.* **39,** 319–361 (2000).
7. Hoffmann, R. in *The Metamict State: Poems by Roald Hoffmann* 101–102 (Univ. Central Florida Press, Orlando, 1987).
8. Ewing, R. C. *et al. Rev. Mineral. Geochem.* **53,** 387–425 (2003).
9. Ewing, R. C. *et al. J. Appl. Phys.* **95,** 5949–5971 (2004).