A drawback of the Zhu *et al.* study, and of biophysical studies of HIV generally, should be noted. Under typical experimental conditions, most HIV particles are either not infectious or very slow to infect, and electron microscopy cannot distinguish between infectious and non-infectious particles. It could be that the only virus particles that do effectively infect are those with the highest number of spikes (up to 35 spikes per particle are described by Zhu *et al.*) and/or those particles with particular clustering patterns that are rarely seen.

Nonetheless, Zhu *et al.* provide some stunning images, particularly those of a tripod shape where a head composed mostly of three gp120 molecules balances on three gp41 legs, deduced by averaging data from a large number of SIV spikes. The image is not unlike depictions of menacing aliens that recur in films and books (for a selection try searching Google Image using 'tripods'). The legs are well separated, in contrast to most representations so far. This may help to explain the observation that the external parts of gp41 near the membrane are accessible to neutralizing antibodies, and will encourage vaccine designers to target these regions. The gp120 molecules sit atop the legs, with a sugar-coated face upwards and the variable loops along the side of the spike, probably restricting antibody access to the crucial CD4-binding site.

What next? Independent corroboration of the tripod structure from different strains and differently treated HIV and SIV preparations is highly desirable. Atomic force microscopy studies have given a different view of the HIV envelope spike[8], so determining which view is more likely in infectious particles is an important next step. Also, vaccine designers crave a high-resolution structure of an intact native HIV envelope trimer, and this is surely one of the most important unsolved structures in biomedicine. ■

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MATERIALS SCIENCE

Oxygen breaks into carbon world

Pulickel M. Ajayan and Boris I. Yakobson

When oxygen atoms bind to a graphite surface, they fall into line and make bridges across carbon atoms. This is the spearhead of a chemical attack in which the atomic arrangement of solid carbon is torn apart.

What happens when we burn carbon? Combustion seems such a simple reaction, but at an atomic scale it is the result of several steps. When graphite burns, for example, an intermediate stage is the formation of a graphite oxide[1]. This process destabilizes the ordered arrangement of carbon atoms, so that cracks begin to form and the structure breaks up. Controlled oxidation reactions are useful for the preparation of very thin graphite flakes, or for chopping carbon nanotubes into shorter lengths, but the details of how oxygen attacks carbon bonds to break up the atomic structure of graphite have never been understood. Writing in *Physical Review Letters*, Je-Luen Li *et al.*[2] provide an explanation for this fundamental process.

The carbon atoms in graphite are arranged in a hexagonal lattice like a honeycomb, with each carbon bonded to three others, forming flat sheets held together by weak van der Waals forces. The bonds between the atoms are chemically inert, so unless there are flaws in the lattice, such as missing carbon atoms, the interaction of oxygen gas with a graphite surface is weak. During oxidation, the graphite oxide that forms is a complex structure[1] in which oxygen-containing groups are randomly attached to the honeycomb lattice. These groups, which can take part in varied surface chemistry, mainly attach at defects or edge-atom sites in the lattice, where the carbon atoms are not fully bonded to other atoms. So far so good, but how do the surface-bound oxygen-containing groups trigger the break-up of the carbon lattice, ultimately destroying the entire graphitic structure?

One kind of chemical group that forms on the graphite surface is known as an epoxy bridge, where a single oxygen atom bonds to two adjacent carbon atoms, forming a triangle. In their paper, Li *et al.*[2] describe how the stress generated by these epoxy bridges leads to unravelling of the graphite lattice. Each epoxy bridge is severely strained, because the geometry of the incorporated carbon atoms has changed. Where the bridged atoms were once only bound to other carbon atoms in a planar, hexagonal honeycomb arrangement, they are now bound to an oxygen atom sitting above the lattice surface, in place of a lattice carbon atom, and adopt an almost three-dimensional, distorted form. This new geometry doesn't fit well in the remaining lattice — it's like trying to fit a square peg into a round hole.

Mechanistically, the oxygen atom acts as a minuscule wedge, pushing apart the bridge's carbon atoms and stretching the carbon–carbon bond. The epoxy groups do not act individually, but cooperate. The authors' extensive calculations[2], based on density functional theory, show that side-by-side parallel positioning of the epoxy bridges is energetically favoured, so that they tend to line up on the graphite surface (Fig. 1). As a result, they collectively induce enough tension in the underlying lattice to break the native carbon bonds.

The feedback guiding such organized attachment of oxygen to graphite resembles generic brittle fracture, where the site of the next bond failure is determined by the existing crack as it propagates through the material. Having broken up carbon bonds, the bridging oxygen atoms go on to hold the fractured graphite sheet together, forming a seam between the separated lattice fragments. These fragments are held together at an angle to each other, to comply with the chemically preferred obtuse angle at the oxygen joints. The emerging network of such oxygen-zipped ridges results in the crumpling of a single graphite layer, known as a graphene sheet. This sheet flakes away from the stack of solid graphite, breaking the weak van der Waals forces that once bound it (Fig. 1).

The emerging picture of isolated epoxy groups falling into ranks, to take part in a well-orchestrated serial bond-breaking process, is rather appealing. But the kinetics require further explanation. Randomly bound epoxy groups are unaware of the energetic benefits of forming lines. The epoxy groups can only find such stable alignments as a result of rapid hopping around, but this is not easy to reconcile with the high energy barriers to such hopping. Further study is also required to determine exactly how visible faults or crack discontinuities emerge. Whatever the details may be, the lines of epoxy groups predetermine the tear pattern, like a perforation line directs the tear in a sheet of postage stamps. The resulting fault lines become clearly visible in optical microscope images of oxidized graphite[2].

A similar sequence of events can also be expected in the oxidation of carbon nanotubes. These share the same bonding as in graphite, except at the end caps where defects are present. Oxidation treatment in strong acids has led to the selective removal of end caps[3] and the breaking of long nanotubes into small pieces[4]. One would expect epoxy groups to line up circumferentially in a nanotube, leading to its transverse fracture into shorter segments, in a useful cutting process. On the other hand, uncontrolled oxidation can severely compromise the strength of nanotubes[5].

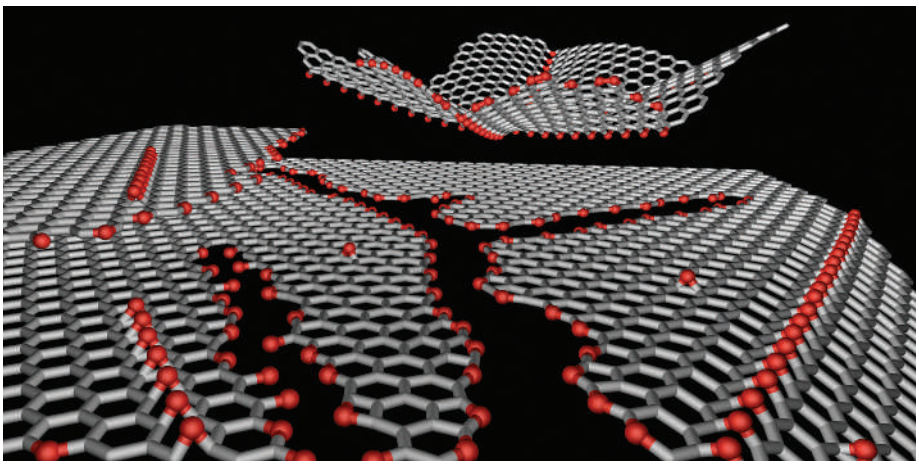

Figure 1 | Oxygen attack on graphite. Li *et al.*[2] show that when oxygen atoms (in red) bind to a graphite surface, they form two-legged epoxy bridges, which line up to lower their energy. This exerts a collective tension, breaking the underlying carbon–carbon bonds. Structural relaxation around the emerging ridges results in crumpling of the initially flat graphite sheets. This eases their separation, giving rise to distorted flakes of graphite, such as the one at the top of the figure. Faults along the oxygen trails lead to further mechanical fractures.

The paper by Li *et al.*[2] provides insight into the atomic-level mechanisms of oxidation in carbon. Graphite and its artefacts, such as carbon nanotubes, are materials with a wide range of uses, from lubrication to electronics. Controlled oxidative scission to extract nanoscale graphitic structures (for example, cut-to-size nanotubes[6] or nanosize graphene sheets[7]) from larger domains of these materials would be an extremely powerful technique for all sorts of applications. Understanding how oxygen breaks up the atomic structure of graphite could lead to a whole new area of nanotechnology based on nanoscale graphite origami[8]. ■

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NEURODEGENERATION

Good riddance to bad rubbish

Daniel J. Klionsky

Autophagy — cellular 'self-eating' — can be induced by stress, but it also acts continuously in a housekeeping role, disposing of unwanted proteins. Can it protect against neurodegenerative diseases?

Alzheimer's, Parkinson's and Huntington's diseases are names we hear with a certain dread. These devastating illnesses, typically associated with ageing, result from the death of neurons. The cause of cell death is not known, but the onset of the disease symptoms is often accompanied by the appearance of large aggregates of particular proteins, such as Aβ in Alzheimer's, α-synuclein in Parkinson's, or huntingtin in Huntington's disease[1]. These are normal proteins — everyone has them — although their function is not always clear. For years, the consensus theory has been that the aggregated proteins lead directly to cell death. But perhaps the cellular housekeeper that should get rid of the proteins is at fault? There have been hints that autophagy may have a role in protecting against neurodegeneration, based on studies with human cell lines or animals with mutations that predispose them to these diseases[1]. In this issue, Komatsu *et al.*[2] (page 880) and Hara *et al.*[3] (page 885) provide the first genetic evidence that the housekeeping role of autophagy is essential for preventing neurodegenerative disease in healthy animals.

Protein aggregates have long been considered the major culprits in neurodegenerative disease because of the linear correlation between the age of disease onset and the time of aggregate appearance. Furthermore, certain mutated forms of the implicated proteins are more prone to aggregation and/or resistant to degradation, and result in earlier onset of neurological symptoms. Accordingly, many scientists in the field of neurodegeneration have focused on these mutated proteins and the accompanying large aggregates or 'inclusions' in cells.

Cells have several mechanisms to dispose of proteins when they misfold, become damaged or are no longer needed. One of the main degradation systems is the proteasome, a multi-subunit enzyme that breaks down proteins that have been tagged with ubiquitin. The proteasome only degrades unfolded, monomeric proteins, however, so it cannot handle protein aggregates. In addition, some of the mutant neuronal proteins are not good substrates for the proteasome.

The other principal degradation system is macroautophagy (which we shall refer to here as autophagy). The hallmark of this process is the formation of double-membrane bubble-like 'vesicles' that sequester portions of the cell's cytoplasm and deliver them to an organelle called the lysosome, where they are broken down (Fig. 1, overleaf). Autophagy can be induced by starvation and various hormonal stimuli[4]. Autophagic vesicles, or autophagosomes, can engulf entire organelles as well as the large aggregates generated by misfolded neuronal proteins. So, there is potential therapeutic value in being able to regulate autophagy to prevent or ameliorate some diseases. Recent data indicate, however, that the large protein aggregates are not the toxic species in these conditions[5,6]. Rather, the soluble or micro-aggregated forms may be the ones that cause cell death. What, then, is the role of autophagy, and its capacity to sequester large structures, in protecting against neurodegeneration?

Komatsu *et al.*[2] and Hara *et al.*[3] have engineered mice that lack the *Atg7* and *Atg5* autophagy genes, respectively. Both groups have used a genetic trick to delete the gene only from neural cells and only during later stages of embryogenesis, in order to bypass developmental defects that would arise from the elimination of the corresponding gene products constitutively (that is, in all cells throughout development). In both cases, mice lacking the autophagy genes develop symptoms of neurodegeneration, including neuronal cell death.

One reason these studies are of such significance is that they examine mice that are not genetically prone to neurodegenerative disease — the genes encoding the various neuronal proteins in these mice do not have the mutations associated with early onset of disease symptoms. These are healthy animals in which autophagy cannot be acting as an induced cytoprotective response to damaged proteins. This implies that the basal, housekeeping