the dynamics of water molecules bound to proteins to be unambiguously resolved for the first time.

The authors' key finding is that water molecules that have similar hydration dynamics form clusters across the protein surface (Fig. 1b). That is, the residence time of water on the surface is often similar at proximal regions of the protein. To understand the importance of this result, one should note that liquid water makes and breaks hydrogen bonds with other water molecules in a dynamic network[7]. The rapid molecular motions of liquid water result from cooperative rearrangements of this network — the water molecules can rearrange without going through transition states wherein one or several hydrogen bonds must break[7,9].

The presence of a protein can alter this network, however, changing not just the probabilities of the different structural rearrangements of solvent, but also the ease with which water molecules can interconvert between them (by altering the transition states of low-energy water arrangements). In principle, geometrical features on the protein surface can affect the residence times of individual water molecules[10,11]: if one or many hydrogen bonds must be broken to facilitate the movement of a molecule constrained by a particular feature, the probability of such an event will be decreased, and the water molecule will tend to stay where it is. One might therefore expect the residence times of individual water molecules at the protein surface to be determined by the precise structural features of the neighbourhood of each molecule, and to be independent of the residence times at other sites.

But this isn't what Nucci and colleagues' observed for ubiquitin[2]. Remarkably, they found that the protein confers regional effects on the solvent, so that rates of water-rearrangement processes vary by a factor of more than 10^{10} from one region of the protein's surface to another. In other words, the geometric constraints imposed by ubiquitin on the surrounding water molecules effectively create (to a first approximation) independent solvent networks around each region.

The water molecules in these regional networks seem to act cooperatively, but in a way that is blind to the behaviour of bulk solvent or of the other regions. Networks that require many hydrogen bonds to be broken in order to rearrange solvent molecules will reside longer at the surface than those that don't. Qualitatively, this observation is not altogether unexpected, as it is clear that several water molecules must be involved in any water rearrangement. It is the level at which these differences are manifested, however, that has broad implications for understanding protein function and evolution. Proteins function by recognizing and binding to ligand molecules such as cofactors, binding partners or enzymatic substrates[12]. Insight into the structural and energetic factors that make a

good binding site is central to an understanding of protein function, and to the development of *de novo* protein design[13]. The fact that hydration dynamics are regionally segregated across ubiquitin suggests that some protein surfaces are more conducive to rapid solvent rearrangement than others.

Are surface-hydration properties an evolutionarily selectable trait for proteins? Certainly it is easy to imagine why enzymes, which are optimized to accelerate catalytic processes, would benefit from the evolutionary selection of rapid hydration dynamics. But are regional patterns of hydration dynamics hard-wired into the folds of particular proteins, or are they tunable through mutation? Whatever the answer, Nucci and colleagues' study[2] forces us to think again about the ways proteins can manipulate not just their own structure and dynamics, but also the dynamics of their solvent environment[14].

It remains to be seen whether the regional patterns of hydration dynamics observed in ubiquitin also occur in other proteins. Currently, the main obstacle to applying Nucci and colleagues' analytical method[2] to other proteins is that preparing protein samples in reverse micelles is a non-trivial task. Nevertheless, the potential of this method to fundamentally alter our view of how proteins interact with their

solvent environment — and so also of how they function — makes the effort worthwhile. ∎

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CONDENSED-MATTER PHYSICS

The conducting face of an insulator

Stacking two oxide insulators together is known to yield a conducting system at the interface between the oxides. But the discovery that simply cleaving such an insulator yields the same outcome is unexpected. SEE LETTER P.189

ELBIO DAGOTTO

On page 189 of this issue, Santander-Syro et al.[1] report the discovery of a conducting two-dimensional electron system on the surface of an insulator, strontium–titanium oxide ($SrTiO_3$; or STO for short). The finding is unexpected, because STO has been much studied in the past and was believed to be fully understood; and it may have implications for all areas of research that routinely use STO, such as the rapidly growing fields of oxide superlattices and oxide electronics[2,3].

With its frequent discovery of new materials, condensed-matter physics is a dynamic field of research, full of surprises that regularly challenge our understanding of how electrons and atoms behave in solids. Well-known examples are high-temperature superconductors,

and transition-metal oxides (TMO) that have large magnetoresistance[4] — a material's ability to change its electrical resistance when placed in a magnetic field. In TMO, and in bulk materials in general, the total energy of the system is minimized as a result of the atomic ions and electrons adopting a specific crystal arrangement, for example the perovskite structure, and by modifications to low-temperature properties such as their magnetic states. But it is hard to predict how a certain property will change without first preparing a sample of the compound and investigating it. And if a particular property is needed for a specific application, it is difficult to anticipate which chemical composition will produce the desired outcome. Thus, the crystal structure of bulk TMO, and its associated properties, cannot be easily controlled.
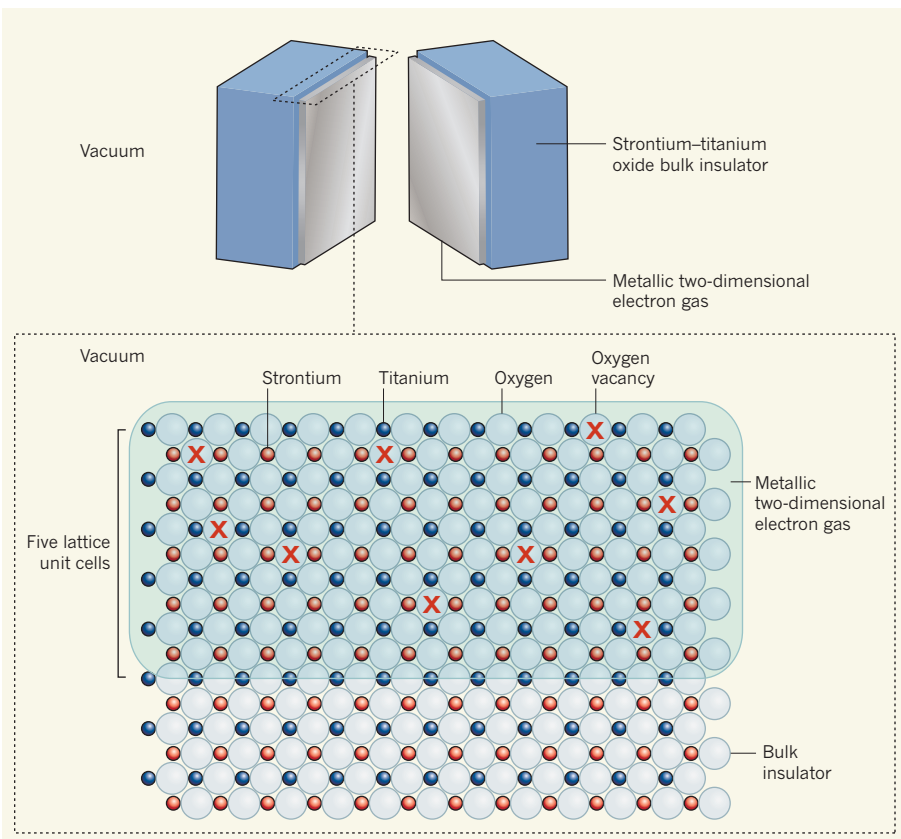
For this reason, the artificial preparation

Figure 1 | Cleave the oxide. Santander-Syro *et al.*[1] create a metallic, two-dimensional electron gas on the surface of a strontium–titanium oxide ($SrTiO_3$) bulk insulator simply by cleaving the material in an ultrahigh vacuum. The conductivity of the electron system, confined within a depth of merely five lattice unit cells below the surface, arises from the oxygen vacancies (here arbitrarily distributed) that are created by the fracture process.

of new TMO is receiving considerable attention. These days, it is possible to prepare, with atomic precision, materials made from a combination of other materials by growing layers of a particular oxide over layers of another oxide, and repeating the process in a variety of arrangements to create superlattices. The range of combinations that can be produced is enormous, with each one leading to a novel material. The stacking of two insulating TMO, one of them being STO, has already led to the discovery[5–7] of metallic (conducting) and even superconducting interfacial states.

At first glance, the existence of metallic states at the interface between two insulators may seem puzzling. But according to some researchers, a mechanism known as a polar catastrophe can take place that explains those metallic states. For instance, when lanthanum–aluminium oxide ($LaAlO_3$; LAO), which is made up of alternately charged layers of $(LaO_2)^-$ and $(AlO)^+$, is stacked on top of STO, which is composed of charge-neutral layers of TiO_2 and SrO, polar catastrophe arises[8] from the $(LaO_2)^-$–$(AlO)^+$ electric dipoles in the LAO structure. The dipoles give rise to an electric potential difference across the LAO structure that increases with the material's thickness. When the LAO structures are sufficiently thick, a sudden electronic reconfiguration — the polar catastrophe — occurs to compensate for the large potential difference generated, conferring conductivity on the LAO/STO interface.

But what about Santander-Syro and colleagues' observation[1] of a conducting state on the surface of STO, the thin portion of the material in contact with vacuum at the top of the crystal? How can a conducting system be created on the surface of an insulating bulk compound? STO is made of electrically neutral — not charged — TiO_2 and SrO layers, preventing polar catastrophe from taking place.

In their study, Santander-Syro *et al.* investigate the properties of the surfaces of a number of STO crystals. To obtain clean surfaces, they fractured each of the crystals in an ultrahigh vacuum. The remarkable result is that the properties of the surfaces of all samples examined are those of a metallic, two-dimensional electron gas — one that is estimated to be confined within a depth of merely five lattice unit cells below the surfaces (Fig. 1). What's more, despite the fact that the samples' low electronic densities in the bulk spanned a large range of values, the authors observed the same high electronic density at the metallic surface of all samples.

These results are surprising. Santander-Syro and colleagues argue that the fracture process creates a large number of oxygen vacancies on the material's broken surface (Fig. 1). Because oxygen in the crystal adopts an ionic state (O^{2-}), the removal of each oxygen atom effectively 'returns' two electrons back to the lattice — in the sense that the ion's two excess electrons remain in the material close to the vacancies, and thus close to the surface, and are therefore available for conduction. Although the samples had quite different numbers of bulk charge carriers (introduced via impurity doping), all samples were fractured in a similar manner — implying that the samples' resulting density of oxygen vacancies might be similar and account for the observed, universal behaviour.

With a view to applications in oxide electronics[2,3], the properties of the conducting states present at the surface of STO and at interfaces such as LAO/STO should now be compared to clarify their origin. In addition, and as was done for LAO/STO, field-effect transistors — the building blocks of electronic chips — based on the new conducting state at the surface of STO should be considered and implemented.

Perhaps the most important implication of Santander-Syro and colleagues' results is that a new conducting, two-dimensional electron system on a familiar and popular substrate is now available by simply cleaving it — or, more generally, by producing oxygen vacancies right at its surface. This simple approach is an attractive alternative to the techniques of growing superlattices, which are complex and expensive. The procedure brings to mind analogies to the way in which the field of graphene electronics started — with the discovery that graphene (a one-atom-thick, honeycomb-like lattice of carbon) could be produced simply by exfoliating graphite using a common adhesive tape. An interesting challenge for the future of oxide electronics is to understand and control the vacuum-fractured oxide conducting system described here, and to learn how to preserve it. ∎

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