News & views

impose known rules of protein biophysics or try to mimic the physical process of protein folding, as has previously been attempted[7,8]. Instead, it performs purely geometric refinements learnt from its repeated attempts to predict protein structures. In this sense, it exemplifies the learning-driven revolution that has swept the field of protein modelling[6,9].

In a companion paper, Tunyasuvunakool et al.[3] (page 590) report the use of AlphaFold2 to predict the structures of almost all human proteins that independently acquire well-defined 3D shapes, for a total of 23,391 proteins. Predictions at this scale were previously possible, but three features of the new system provide a big leap forward.

First, the accuracy of the predictions is sufficiently high to generate biological insights and hypotheses that can be tested experimentally. Second, a calibrated self-assessment of each prediction provides a reliable estimate of correctness at the level of individual amino-acid residues (Fig. 1), enabling biologists to make inferences about confidently predicted regions. Third, AlphaFold2 is applicable to whole proteins, including large ones that have multiple, independently self-assembling units – a common feature of mammalian proteins. The resulting resource 'confidently' predicts nearly 60% of all human-protein regions; most of the remaining regions might be unable to acquire well-defined structures, or be able to do so only in the presence of other biomolecules.

AlphaFold2 has already helped structural biologists to solve crystallographic protein structures[10] and refine ones derived from cryo-electron microscopy experiments. It provides biophysicists studying protein motion with starting (static) structures, and those studying protein interactions with hypotheses about how protein surfaces bind to each other. AlphaFold2 also presents opportunities to formulate new algorithms for bioinformatics based on protein structures, and might help systems biologists to understand the behaviour of cellular pathways and molecular machines on the basis of the structures that comprise them. And the study of evolution, which has long relied on genetic sequences, can now more readily be formulated in terms of the onset of new classes of protein structure (folds) and their relationship to cellular function and organismal fitness.

It is tempting to compare the scale of this advance to that of the Human Genome Project, but there are important differences. In contrast to the human genome sequence, the predicted structures have not been experimentally verified; it will take time for evidence of their correctness to emerge, so that scientists can gain confidence in the predictions. Of course, experimental measurements can also be affected by 'noise', bias and incompleteness – 20 years passed

between the publication of the first draft of the human genome and the complete sequence[11] – and modern structure-determination techniques routinely involve some computational inference. As predictions improve, disagreements between protein models and experiments could become difficult to resolve, a situation familiar to physicists[12] but largely unprecedented in biology.

Disordered protein regions, which do not have well-defined shapes but often encode functionally crucial parts of proteins, present an ongoing and fundamental challenge to AlphaFold2 and, therefore, to our understanding of protein structure. Future methods must take this disorder into account and begin to reflect the flexibility inherent in most proteins.

Other differences between the Human Genome Project and the present advance are in AlphaFold2's favour. Structure predictions are (relatively) cheap and will soon be available for all proteins, whereas genetic-sequencing technology took years to deploy and mature. Computational methods evolve rapidly, and it might therefore soon be possible to predict the structures of multi-protein complexes, alternative conformations of a protein (for proteins that adopt them) and the structures of designed proteins with a level of accuracy similar to that currently achieved by AlphaFold2. Finally, protein structures provide immediate biological insights, because they fit within established conceptual frameworks

that relate a protein's structure to its function – unlike genetic sequences, which were largely inscrutable at the dawn of the genomics era. The fruits of this revolution might thus be more swiftly reaped.

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Biogeochemistry

Carbon stocks of African montane forests assessed

Nicolas Barbier

The inaccessibility of African montane forests has hindered efforts to quantify the carbon stored by these ecosystems. A remarkable survey fills this knowledge gap, and highlights the need to preserve such forests. **See p.536**

On page 536, Cuni-Sanchez et al.[1] report the assembly of a large database of tree inventories for 226 mature montane-forest plots in 12 African countries. The authors analyse the data to determine the amount of aboveground biomass and carbon stored in these highly diverse and threatened ecosystems. Their results suggest that African montane forests store more carbon than was previously thought, and the findings should help to guide efforts to conserve these ecosystems.

Cuni-Sanchez and colleagues measured trunk diameters and heights of the trees in plots, and identified the botanical species

to deduce wood density – an approach that constitutes the gold standard for estimating the biomass, and thus the amount of carbon, contained per unit of forest area. This method involves the use of general statistical equations for describing tree form, called allometric models, and considers only the aboveground parts of trees. It therefore disregards several other pools of carbon, notably in the roots and soil. The overall approach might seem crude, but recognizing and measuring the many hundreds of tree species found on steep, cloud-shrouded slopes (Fig. 1), let alone the underground carbon, without visiting the sites,

Figure 1 | Montane forest in Boginda, Ethiopia. Cuni-Sanchez *et al*.[1] use data from a survey of montane tropical forests in Africa to quantify the amount of carbon stored above ground in these ecosystems.

will long remain difficult, even with the best drones and satellite systems.

Anyone who has conducted field inventories in tropical mountains knows that measuring and identifying 72,336 trees, often just a few steps away from the void, is an amazing feat. For comparison, a previously reported study[2] based its estimates of the carbon stored in montane African forests on as few as seven plots. The study also brings together contributions from numerous researchers and institutions, including many in Africa, to greatly increase the size of the data set, which is also a remarkable achievement. Even so, the total area of forest studied is less than 150 hectares, whereas African montane forest covers about 100,000 times that area, inevitably raising questions about how representative the inventory is.

Statisticians might raise their eyebrows at the sampling design. As is usually the case in meta-analyses, the data set was neither homogeneous (for example, there is a roughly tenfold variation in the plot sizes), nor were the sites selected at random. However, the authors did their best to rule out possible biases induced by sampling artefacts.

Cuni-Sanchez *et al*. chose not to discuss one tricky aspect of surveys of this sort (extensively discussed elsewhere[2]): how should the land area of a steep slope be measured? The authors followed standard practice, which is to measure the extent of forest plots and of land-cover types in reference to horizontal, planimetric areas (that is, the areas that would be represented on a 2D map, as if seen from the air). This tends to overestimate aboveground carbon because the sloped surface area is greater than that of the planimetric area — which means that the tree density of the planimetric area is higher than it is on the slope. By contrast, the use of planimetric areas underestimates total montane-forest area (by about 40%; see ref. 2). These two biases should roughly cancel each other out when estimating carbon stocks, or changes to stocks, for a region or country. But care should be taken not to combine data acquired using planimetric and non-planimetric areas in future meta-analyses, because the resulting estimates could end up well off the mark.

One might expect that trees in mature African montane forests would be, on average, shorter — and therefore store less carbon — than their lowland counterparts, because of their lower environmental temperatures and shallow soils, frequent landslides and strong winds. However, this is not what Cuni-Sanchez *et al*. report. Instead, they find that average aboveground carbon stocks are not significantly different from those of mature lowland forests. This contrasts with the situation in the neotropics and southeast Asia, where montane forests store, on average, less carbon than do lowland forests.

However, the new results fit with the 2016 discovery that the tallest African trees (81.5 metres) grow on Mount Kilimanjaro[3], the highest mountain in Africa. African forests, in general, tend to contain fewer but larger-statured tree stands than does, for example, Amazonia[4]. The current study confirms that this peculiarity applies even at high altitudes.

The authors investigate several possible drivers for the variations in biomass observed at different sites in their study, including topography, climate, landslide hazard, and even the presence of elephants or certain conifers (Podocarpaceae), but were unable to identify any clear pattern. Many environmental, historical and biological effects probably interact, with each of these effects varying greatly in ways that are poorly captured by available data sets. These effects must therefore be disentangled before a predictive model of African montane carbon distribution can be developed.

Nevertheless, Cuni-Sanchez and colleagues' study underlines a crucial message: African

montane forests are immensely valuable, and not only because they host the source of the River Nile, mountain gorillas and ecosystems such as mysterious lichen-covered forests. They also store vast amounts of carbon, and thereby have a key role in tackling climate change. Of course, this immense intrinsic value does not preclude intense human exploitation of these ecosystems, which can lead to rapid degradation and deforestation. For instance, on the basis of satellite monitoring, Cuni-Sanchez and colleagues report that Mozambique lost nearly one-third of its montane forests between 2000 and 2018.

There is, however, the faint hope that putting a financial value on carbon, and the establishment of economic incentives to avoid deforestation in tropical countries, might help to check the flood of damage[5]. The aim is to reward African countries – for which montane forest sometimes constitutes the last remaining forests – for their conservation endeavours, and for renouncing efforts to access the timber and ore in these ecosystems, even when such resources are otherwise desperately lacking. By gathering the best-available data to provide precise, country-level estimates of average aboveground carbon content in African montane forests, Cuni-Sanchez and colleagues' study will add weight to such efforts – not least because the new estimates are, on average, two-thirds higher than the values reported by the Intergovernmental Panel on Climate Change[6].

The next step should be to extend measurements in these forests, particularly by continuing to support national forest-inventory efforts. These inventories target all vegetation types, rather than just the most intact forests, and all carbon pools, using standardized protocols and systematic sampling methods. Remote sensors, both in the sky and in space, should also be used to fully map the detailed spatial variation of forest diversity, structure and dynamics. But there is no excuse for delaying policymaking – we already know enough to justify immediate decisive action to preserve yet another of Earth's threatened treasures.

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Quantum technology

# Single proton cooled by distant ions

Manas Mukherjee

Laser-cooled ions have been used to substantially lower the temperature of a proton located several centimetres away. This technique could be useful in ultraprecise measurements of the properties of antimatter particles. **See p.514**

On page 514, Bohman *et al.*[1] (the BASE Collaboration) report the cooling of a single proton by a cloud of laser-cooled beryllium ions. Remarkably, the ions were separated from the proton by a distance of about 9 centimetres – which is too far apart for the charges on the ions to have interacted with that of the proton. This means that the ions could not have exerted a direct cooling effect on the proton. Instead, the researchers used an indirect cooling process, mediated by an electric circuit that established an effective interaction. This approach has potential applications in studies of antimatter particles and in the field of quantum information.

A wealth of knowledge about nature's inner workings comes from studies of fundamental particles, such as electrons and protons. Currently, the most accurate theoretical model of the forces of nature is the standard model of particle physics, which describes how fundamental particles interact with each other and thereby build up the macroscopic world. The standard model has passed many stringent tests using various experimental tools, at particle energies that range from 10^{11} electronvolts in particle accelerators[2] to only about 0.0001 electronvolts in ion traps[3]. However, it is widely accepted that the standard model does not explain some natural phenomena, such as the fact that the Universe is made up of only matter. It also does not account for the existence of dark matter – the invisible and largely unaccounted for mass of the Universe.

High-precision measurements of fundamental particles and their corresponding antiparticles provide opportunities to verify the standard model, and maybe even to find evidence of new physics that goes beyond the currently accepted model[4,5]. Two conditions must be met to perform such measurements: the particles must be spatially confined; and they should be very nearly at rest (that is, the particles must be cooled to almost zero kelvin, to minimize their kinetic energy). The first of these requirements can be solved using a combination of static electric and magnetic fields in a device called a Penning trap.
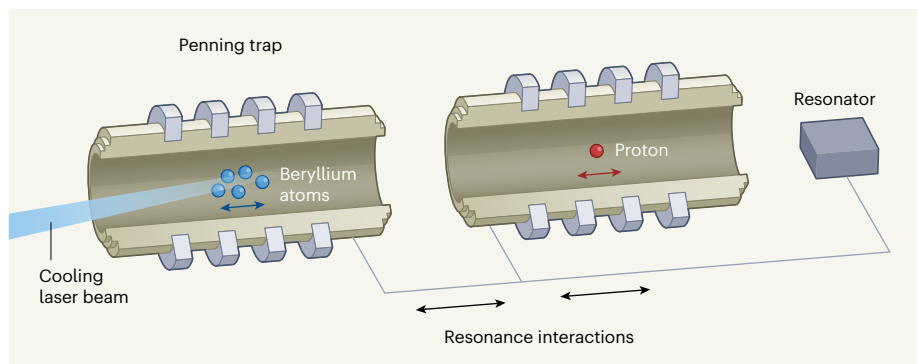
Figure 1 | Sympathetic cooling at a distance. Bohman *et al.*[1] used devices called Penning traps to capture a proton at 17 kelvin and a cloud of beryllium ions, which was continuously cooled by a laser to a much lower temperature. The traps were connected by a wire to a circuit known as a resonator. Oscillations (coloured arrows) of the proton and of the ions generate electrical currents (not shown) in the electrodes of their respective traps; these currents oscillate at the same frequency as the particles that generate them. If the natural oscillation frequency of the proton is the same as that of the ions and of the electrical current in the resonator circuit, a phenomenon called resonance allows the currents in the system to interact. The ions therefore cool the resonator, which, in turn, cools the proton. Such indirect cooling of the proton by the ions is called sympathetic cooling through the resonator.