50 Years Ago

The Liberal conference which took place last week afforded the now familiar sight of the Young Liberals adopting a more radical and militant approach than that of the parent body, and being subsequently chastised for it. But the motion which had the greatest bearing on science and technology, on European unity, was largely their work. This motion commits the Liberal Party to press not only for entry into the EEC but also for a "United States of Europe" with common economic, technological and foreign policies. The Liberals see this as the only effective way to combat the increasing American dominance of European technology and consumer markets … The motion was carried by an overwhelming majority, and this makes the Liberal Party the foremost advocate of joining the Common Market among the political parties.

From *Nature* 27 September 1969

100 Years Ago

Dr. Victor E. Shelford writes in the *Scientific Monthly* … on the general question of the waste involved in the discharge of domestic and industrial sewage into the sea and rivers. Experimental methods for testing the effect on fishes of various substances in solution have been devised … The sensibility of fish to such compounds as occur in waste material is thus shown to be greater than has hitherto been supposed, thus an increase in carbon dioxide of 2 c.c. in one litre above the normal content caused the turning-away reaction. A low oxygen content was also detrimental, and this was usually found to accompany a high carbon dioxide content. The waste substances resulting from gas-production works and from munitions processes were also studied, and it was shown that these substances … had very marked effects on fish-life.

From *Nature* 25 September 1919

When the authors superimposed an available structure of a pMHC bound to a TCRαβ heterodimer onto their TCR structure, the TCRαβ heterodimers were similar in both structures. This is unsurprising, because force application is probably the major cause of structural changes driving TCR subunit rearrangements, and these structures were obtained in the absence of force, and thus capture a compact state of the TCRαβ heterodimer. The force-based TCR–pMHC recognition process differs from typical receptor–ligand interactions such as antibody–antigen interactions, which are force-independent. Harnessing energy for mechanosensing from cellular motions could explain how, unlike in force-independent interactions, TCRs can discriminate so sensitively between very similar antigens, differing by just one amino acid.

It has been suggested that the subunit rearrangements that occur when force is applied to the TCR might foster CD3 dimer dissociation, starting with CD3ζζ, and that this contributes to T-cell activation[8]. The authors' structure confirms that CD3ζζ dissociation would indeed cause changes to the TCR structure in the transmembrane region.

Dong and colleagues' work provides a basis for future studies. Could structures of other αβ-type TCRs of defined antigen specificities, with or without the relevant pMHC, be obtained? Might it be possible to obtain high-resolution structures of the transmembrane segments of a TCR in a natural lipid-membrane environment to visualize the cytoplasmic tails of TCR proteins? Could conformations of the TCR complex under the application of force be imaged if new structural-analysis methods are developed?

Given the importance of the TCR for understanding immune-cell function and the use of T cells in immunotherapy to tackle cancer, information about TCR structure might bring improvements in TCR design for medical purposes. Dong and colleagues' work is an urgent summons to immunologists interested in tumour biology and to others to consider bio-forces when assessing T cells *in vitro* to gauge the potential of their TCRs *in vivo*. Great opportunities lie ahead to make more progress in developing high-quality TCRs for clinical use. ■

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CONDENSED-MATTER PHYSICS

X-rays glimpse solid hydrogen's structure

Little was known about the properties of hydrogen under extreme pressure. Experiments now reveal key details about the arrangement of molecules in several of the element's high-pressure phases. SEE LETTER P.558

BARTOMEU MONSERRAT & CHRIS J. PICKARD

Hydrogen is the most abundant element in the Universe. Our knowledge of celestial bodies such as the Sun, which is about 75% hydrogen[1], relies on understanding the properties of this element at extreme temperature and pressure. Replicating these conditions in the laboratory is exceptionally challenging, and even the structure of high-pressure phases of hydrogen at low temperatures has been an open question. On page 558, Ji *et al.*[2] report experiments that probe this structure at unprecedented pressures, revealing a hexagonal close-packed arrangement of molecules.

The simplicity of the hydrogen atom, which comprises a single proton and a single electron, does not prevent the high-pressure phases of the element from being rich and complex. Hydrogen is an electrical insulator at ambient conditions, but becomes a metal under extreme compression[3] — a state that could, for example, help to generate Jupiter's magnetic field. Additionally, theoretical work suggests

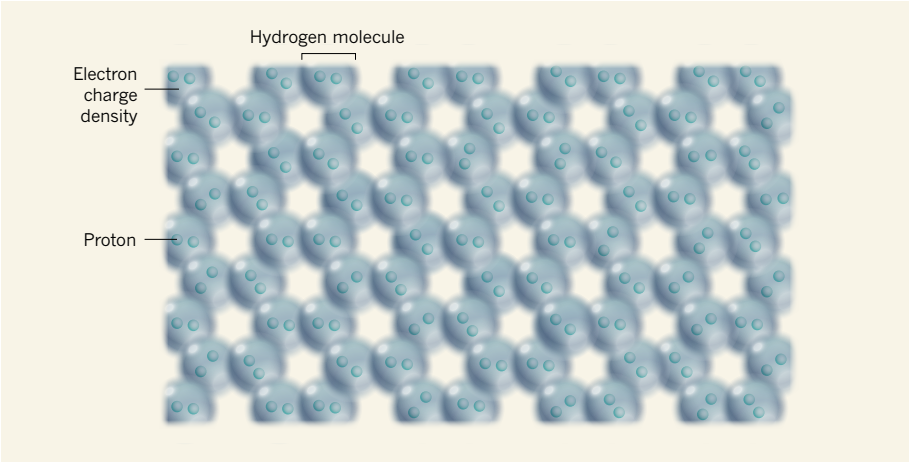

Figure 1 | Structure of hydrogen under extreme pressure. Ji *et al.*[2] demonstrate that the molecules in three high-pressure solid phases of hydrogen adopt a hexagonal close-packed structure. The drawing is a snapshot of where the two constantly moving protons in each molecule might be located. It also shows the charge density of the two electrons in each molecule, averaged over many snapshots.

that metallic hydrogen might exhibit many exotic phenomena, such as high-temperature superconductivity[4] (electrical conduction without resistance) or superfluidity[5] (fluid flow without friction).

Over the past few decades, multiple solid phases of hydrogen have been identified by increasing the pressure to well above that at the centre of Earth. These experiments make use of devices called diamond anvil cells, in which a hydrogen sample is placed in a thin-foil gasket, which is in turn screwed between two diamonds to achieve extreme pressures in the centre of the sample.

The main approaches for analysing the compressed samples involve studying how the constituent molecules absorb infrared light (infrared spectroscopy), or observing how they scatter light (Raman spectroscopy). Such methods provide insights into the molecular structure. They have revealed that, as pressure increases, hydrogen transitions from a crystalline solid in which all of the molecules have similar bond lengths, to a mixed phase in which molecules of different bond lengths coexist[6,7]. The results are consistent with theoretical models[8].

The predominant technique for examining long-range order in materials is X-ray diffraction, in which X-rays scattered by the electrons in a crystal interfere with each other. The resulting diffraction pattern contains bright spots, corresponding to waves that interfere constructively; and dark spots, coming from waves that interfere destructively. X-ray diffraction has been used to make many important scientific discoveries, including the double-helix structure of DNA.

Unfortunately, using this technique to study high-pressure hydrogen has, up to now, proved extremely challenging. A major difficulty is that the ability of X-rays to scatter off electrons decreases as the mass of the atoms that make up the material decreases. Hydrogen, being the lightest element, therefore gives rise to particularly weak signals. As a result, it is hard to distinguish between the X-rays scattered by the electrons in the hydrogen sample and those scattered by the surrounding gasket, which is typically made from heavy elements (such as tungsten or rhenium). A further challenge is that the diamonds that are used to pressurize the sample break easily when exposed to X-rays, leading to loss of pressure.

Because of these difficulties, X-ray diffraction studies of hydrogen had so far reached pressures of up to only 190 gigapascals[9] (about 1.9 million times standard atmospheric pressure). This is about half the pressure that hydrogen can be subjected to in diamond anvil cells, and is not high enough to study some of the element's most exotic phases, such as the mixed phase.

"The results provide evidence of the long-range structure of molecular hydrogen across three high-pressure solid phases."

Ji and co-workers have addressed these challenges in a tour de force, carrying out more than a hundred experiments over a period of five years at pressures of up to 254 GPa. To increase the signal arising from hydrogen compared with that from its surroundings, the gaskets used were made of elements lighter than tungsten and rhenium. The authors also designed the experiments to yield useful data in the short time available before the inevitable diamond failure.

The results provide evidence of the long-range structure of molecular hydrogen across three high-pressure solid phases, including the mixed phase. In all three, the molecules adopt a hexagonal close-packed structure (Fig. 1) in which they are symmetrically arranged in the shape of a hexagonal prism. Furthermore, increasing the pressure squeezes the prism, causing it to become flatter and fatter.

Some questions remain. Unlike all of the elements heavier than helium, hydrogen has no electrons tightly bound to its nucleus, and the electrons in a hydrogen molecule are situated in the molecular bond. As a result, the scattering of X-rays by these electrons cannot be used to directly probe the location of the nuclei in the molecule or the molecule's orientation, but instead the location of the bond.

Consequently, Ji and colleagues' X-ray results will need to be combined with those from other experimental techniques, such as infrared and Raman spectroscopy, and possibly also nuclear magnetic resonance spectroscopy, which has only in the past year become available at the extreme pressures being studied here[10]. Combining these experimental insights with theoretical models will make the full characterization of high-pressure hydrogen phases a reality.

The pressures reached in this X-ray study correspond to electrically insulating molecular hydrogen. In the next few years, experiments will probably focus on even higher pressures. However, it will prove a challenge for X-ray techniques to study the pressures at which the element becomes atomic and metallic. In this phase, the electrons are no longer in the molecular bond; instead, they are shared by all of the atoms in the structure, so it is unknown what the corresponding X-ray diffraction pattern would look like. Exciting times lie ahead for the study of the lightest and most abundant element in the Universe. ■

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CORRECTION

In the News & Views 'Gerrymandering in social networks' by Carl T. Bergstrom and Joseph B. Bak-Coleman (*Nature* **573**, 40–41; 2019), Figure 1c incorrectly stated the numbers of blue and orange nodes that influence each participant in the blue part of the diagram. This has been corrected in the online version of the article.