COURTESY S. L. BRAGG

Lawrence Bragg remains the youngest ever winner of a Nobel prize, aged just 25.

The birth of X-ray crystallography

A century ago this week, physicist Lawrence Bragg announced an equation that revolutionized fields from mineralogy to biology, writes **John Meurig Thomas**.

In the summer of 1912, a 22-year-old graduate student went on holiday with his parents to Britain's Yorkshire coast. There, his father, the physicist William H. Bragg, received a letter describing a dramatic lecture given by the German theoretical physicist Max Laue.

Laue's lecture reported the first observation by his colleagues Walter Friedrich and Paul Knipping[1] of the diffraction of X-rays by a crystal — the mineral zinc sulphide (ZnS). This proved that X-rays were waves, settling a controversy that had lasted the 17 years since their discovery. Bragg and his son Lawrence worked feverishly on X-ray diffraction all that summer at the University of Leeds, UK, where William was professor of physics.

On returning to the University of Cambridge at the end of the holiday, Lawrence had a revolutionary idea. Laue's results, he reasoned, could be interpreted simply as arising from the reflection of X-rays by planes of atoms in the crystal. He realized that X-ray observations, of the kind initiated by Laue, provide evidence from which the arrangement of atoms in the crystal could be inferred.

To explain the patterns they saw (pictured), Laue and his colleagues had assumed that their X-ray source was polychromatic — comprising six or seven distinct wavelengths — and that the structure of ZnS was a three-dimensional array of tiny cubes, with the zinc and sulphur atoms occupying each alternate corner.

Lawrence examined the X-ray photographs and noted that some of the diffraction spots were elliptical and that some had different intensities. In a paper read by his supervisor, J. J. Thomson, to the Cambridge Philosophical Society on 11 November 1912, Lawrence made two important proposals[2] to account for these features.

First, he suggested that Laue's results arose from the reflection of a continuous range of X-ray wavelengths by planes of atoms within the crystal. This interpretation yielded Bragg's law of X-ray diffraction: $n\lambda = 2d\sin\theta$, where θ is the angle of incidence of X-rays of wavelength λ, d is the separation of the reflecting planes and n is an integer. Second, he proposed that Laue's diffraction pattern from ZnS was characteristic of atoms located not only at the corners of the three-dimensional array of cubes, but also at the centre of the faces of each cube — a face-centred lattice.

So far, some two dozen Nobel prizes have been awarded for work related to X-ray crystallography, the technique Bragg set in train with his paper and used for his pioneering work on the structures of minerals, metals, their oxides and alloys. His colleagues were the first to use X-ray crystallography to determine the structures of a protein and an enzyme, and to formulate the model for the DNA double helix[3]. In my view, the technique is still the single most powerful analytical tool for scientists in physics, biology, medicine, materials and Earth sciences, as well as for many breeds of engineer.

VISIONARIES

In the audience in Cambridge in November 1912 was the physicist C. T. R. Wilson, whose work using cloud chambers to track cosmic rays earned him the Nobel prize in 1927. Wilson suggested that X-rays should also reflect from the external faces of crystals, provided the surfaces were sufficiently smooth. So Lawrence tested whether X-rays that reflected from the cleavage face of mica — known for its supposed flatness at the atomic scale — could be photographed. In December 1912, *Nature* published his paper on 'The Specular Reflection of X-rays'[4].

William Bragg quickly demonstrated that his X-ray spectrometer could detect diffracted monochromatic X-rays — not on photographic plate, but with a gas ionization detector. The power of Bragg's law, together with William's spectrometer for recording the intensities of reflected X-rays of fixed wavelength, was spectacularly demonstrated in two 1913 papers. Lawrence published one on the structures of crystals of sodium chloride, potassium chloride, potassium bromide and potassium iodide[5], and another with his father[6] on diamond.

The Braggs' approach provided a reliable way to determine the internal architecture of all crystalline solids, and thus to explain their properties. Once the structure of diamond was discovered — with its infinite array of carbon atoms bonded strongly to others in three dimensions — its hardness could be understood. Likewise, when X-ray crystallography revealed the structure of graphite in the 1930s, its softness made sense. Diamond and graphite have the same composition, but their structures make them mechanically, chemically and electronically very different.

Not until after the First World War did shock and exhilaration greet the publication of these papers, when their content filtered through to the textbooks. Shock, because Bragg had incontrovertibly established, contrary to what all chemists thought at the time, that there was no molecule of sodium chloride inside rock salt — simply an extended alternation of sodium and chloride ions. A particularly intemperate attack was mounted by Henry Armstrong, former president of the Chemical Society of London. Writing in *Nature* in 1927, he described the "chess-board pattern" of atoms in sodium chloride as "repugnant to common sense" and "absurd to the *n*… th degree"[7]. Others were exhilarated because the structure of diamond confirmed the tetrahedral coordination of carbon as envisaged by J. H. van't Hoff and others 40 years earlier.

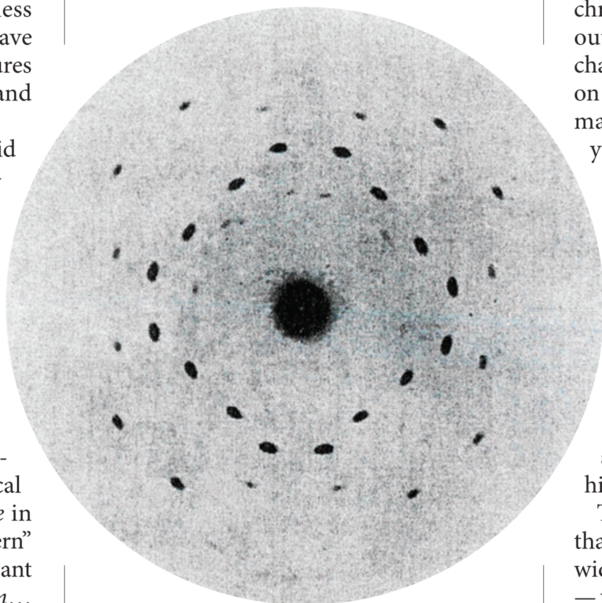
For the next several decades, the Braggs' equation and spectrometer became the cornerstones of X-ray crystallography, largely supplanting Laue's polychromatic X-ray diffraction procedure. (Some experimentalists used both methods — notably, Linus Pauling in his determination of the structures of haematite and corundum in 1925.)

NOBEL HAUL

At 25, Lawrence Bragg is still the youngest ever recipient of the Nobel prize, which he shared with his father in 1915 "for their services in the analysis of crystal structure by means of X-rays". He kept working at a prodigious pace for some 50 more years[8]. Laue was awarded the Nobel prize in 1914 for the discovery of X-ray diffraction by crystals but, unlike Lawrence, he largely ceased to work on its consequences, turning to relativity and other pastures in theoretical physics.

In 1919, Lawrence succeeded Ernest Rutherford as chair of physics at the University of Manchester, UK. Using techniques that flowed from his 1912 and 1913 papers, he accounted for the chemical and physical properties of silicates, the dominant members of the mineral kingdom, which traditional chemistry had not explained in satisfactory atomic terms. He explained, for example, why mica and talc are so soft, but beryl is tough.

He showed that many minerals, especially silicates, are dominated by essentially space-filling, negatively charged oxygen atoms. He found that other, smaller (cationic) atoms are lodged in the interstices, and discovered a constant tetrahedral coordination of four oxygen atoms, whatever the ratio of silicon to oxygen. At Manchester he also solved the structures of γ-brass, magnetic alloys and many others fundamental to the development of the modern theory of metals.



SOURCE: REF. 1

Max Laue's photo of X-ray diffraction from ZnS revealed spots of varying shape and intensity.

In 1938, Bragg again replaced Rutherford, this time as Cavendish professor at the University of Cambridge. Here, after the Second World War, he encouraged his protégés Max Perutz and John Kendrew in their fiendishly difficult X-ray crystallographic determination of the proteins haemoglobin and myoglobin. Later, he gave free reign to Francis Crick and James Watson's X-ray work on DNA.

SEEING IS BELIEVING

In 1953, Bragg became director of, and Fullerian professor at, the Royal Institution of Great Britain (RI) in London, where he appointed David Phillips, Tony North and others to investigate biological structures, with Perutz and Kendrew as honorary readers. A special automated, linear X-ray diffractometer built at the RI enabled Kendrew, Phillips and others to produce the first structure of a protein — myoglobin. It also helped Phillips and Louise Johnson to establish the structure and mode of action of lysozyme, the first enzyme to yield to Bragg's X-ray technique. While at the RI, Bragg had the satisfaction of hearing, in 1962, of the award of Nobel prizes to his acolytes Perutz, Kendrew, Crick and Watson.

The Braggs' method of structure determination is still at the heart of modern X-ray crystallography. It is now almost completely automated by sophisticated, ultra-sensitive X-ray detectors and associated algorithms for data analysis of hundreds of thousands of diffraction intensities.

Meanwhile, the advent of accessible synchrotron radiation sources and rapid read-out detectors is especially well suited to charting structural changes that take place on sub-picosecond timescales in biological macromolecules such as the photoactive yellow protein PYP[9]. A striking example is the work of an international team of researchers[10], almost exactly a century after the pioneering papers by Bragg and Laue. The team aimed femtosecond synchrotron pulses at a stream of droplets containing biologically significant macromolecules such as photosystem I, which is central to photosynthesis. The X-ray pulses are short enough to avert radiation damage, but sufficiently intense to produce high-quality diffraction data.

The seminal work begun in Yorkshire that summer of 1912 still resonates worldwide. Just this week, Venki Ramakrishnan — who shared the Nobel Prize in Chemistry in 2009 for unravelling the structure of the ribosome, which catalyses protein synthesis — was scheduled to lecture the Cambridge Philosophical Society. His theme? "Seeing is believing: how a century after its discovery, Bragg's law allows us to peer into molecules that read the information in our genes." ■

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