GENETICS

Winding road to DNA

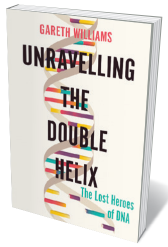
Jan Witkowski lauds an account of the half-obscured scientists whose work helped to reveal the double helix.

Long before the double helix was discovered in 1953, biochemists vied to determine the enigmatic nature of DNA. As early as 1914, chemist Walter Jones wrote (in his monograph *Nucleic Acids*) that the macromolecules "constitute what is possibly the best understood field of Physiological Chemistry". Cytologists, geneticists and even physicists, however, also co-authored the story of DNA.

In *Unravelling the Double Helix*, medical historian Gareth Williams illuminates key research in the 85 years between the discoveries of nuclein, as it was first known, and the double helix. He refreshes a familiar chronicle by ending there, rather than using it as a stepping stone to the Human Genome Project, epigenetics or gene editing. Moreover, he eschews the 'mountain top' approach — featuring individuals synonymous with major advances. Instead, he shines a light on lesser-known scientists struggling, as philosopher Bertrand Russell put it, to bring into the world "some little bit of new wisdom".

Williams starts in 1868, the beginning of a biochemistry golden age. Biologist Friedrich Miescher, working with physiologist Felix Hoppe-Seyler in Tübingen, Germany, was then developing a technique for isolating cell nuclei from the white blood cells in pus. He extracted a strange, fluffy substance from the nuclei, dubbing it nuclein. Moving to Basel in his native Switzerland, he determined its chemical formula using nuclei from salmon sperm. A decade later, cytologist Walther Flemming was studying division in salamander cells by staining them with dyes; he revealed coloured threads that he called chromatin (chromosomes). In 1882, he showed with great clarity their behaviour in the replication processes of mitosis and meiosis.

Genetics enters the picture in 1900, when abbot-scientist Gregor Mendel's research on principles of inheritance was rediscovered



Unravelling the Double Helix: The Lost Heroes of DNA
GARETH WILLIAMS
Weidenfeld & Nicolson (2019)

by botanists Hugo de Vries, Carl Correns and Erich Tschermak. Williams adds immediacy to the tale of pea plants and heredity by starting with an encounter between Mendel and C. W. Eichling, whose story was new to me. A German seller of exotic flowers, he visited Mendel in Brünn, Austria, in 1878, looking for new varieties. He later published a verbatim account of his conversation with Mendel — the only one in existence (C. W. Eichling *J. Hered.* **33**, 243–246; 1942).

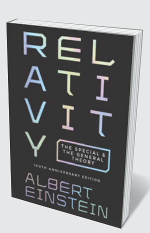
The contributions of cytology continued in the early twentieth century with the work of Walter Sutton. (Williams could also have mentioned Nettie Stevens and William Cannon.) They recognized that the distribution of chromosomes during mitosis and meiosis mirrored what was expected of Mendel's hereditary 'factors', and showed that specific chromosomes were associated with sex. The fusion of genetics and cytology came in the 1910s, when Thomas Hunt Morgan and his colleagues mapped the chromosomal locations of fruit-fly mutations.

Physicists' work in the field was at first theoretical. In 1944, Erwin Schrödinger published *What Is Life?*, which built on work by biophysicist Max Delbrück to suggest that genes were "aperiodic crystals". This influenced physicists including Francis Crick and Maurice Wilkins (see P. Ball *Nature* **560**, 548–550; 2018). But physics really entered the fray when X-ray crystallography was harnessed to study biological macromolecules.

That field was tiny in the 1920s. William Astbury, J. D. Bernal and Kathleen Lonsdale worked at the Royal Institution in London

NEW IN PAPERBACK

Highlights of this season's releases.



Relativity: The Special and the General Theory — 100th Anniversary Edition
Albert Einstein, Hanoch Gutfreund & Jürgen Renn PRINCETON UNIV. PRESS *(2019)*
First published in English in 1920, Albert Einstein's popular introduction to his world-shaking theories reveals what he dubbed his "step-motherly" approach. This authoritative centenary edition is a fitting tribute to Einstein's efforts to make his concepts accessible — in turn, helping to raise the profile of basic science and modern physics on a global scale. Insightful commentaries and excerpts from Einstein's original manuscript of the book provide context.

under physicist and Nobel laureate William Henry Bragg, studying small molecules such as tartaric acid. Moving to the University of Leeds, UK, in 1928, Astbury probed the structure of biological fibres such as hair. His colleague Florence Bell took the first X-ray diffraction photographs of DNA, leading to the "pile of pennies" model (W. T. Astbury and F. O. Bell *Nature* **141**, 747–748; 1938). Her photos, plagued by technical limitations, were fuzzy. But in 1951, Astbury's lab produced a gem, by the rarely mentioned Elwyn Beighton. Using wet DNA fibres, he took images revealing the black-cross diffraction pattern characteristic of helical molecules. They were never published, and Astbury did not follow up on them; if he had, the story of DNA might have been very different.

Many other "lost heroes" emerge in Williams's telling. Martin Henry Dawson and James Lionel Alloway made important contributions to Oswald Avery's demonstration that DNA probably made up genes. H. F. W. Taylor, C. J. Threlfall and Michael Creeth crucially participated in J. Masson Gulland's work showing that DNA solutions changed viscosity owing to the rupture of hydrogen bonds between nucleotides. All is scrupulously documented in more than 50 pages of notes.

Although there is little Williams can add to the intensely scrutinized narrative on the double helix itself, he clarifies key issues. He points out that the infamous conflict between Wilkins and chemist Rosalind Franklin arose from actions of John Randall, head of the biophysics unit at King's College London. He implied to Franklin that she would take over Wilkins' work on DNA, yet gave Wilkins the impression she would be his assistant. Wilkins conceded the DNA work to Franklin, and PhD student Raymond Gosling became her assistant. It was Gosling who, under Franklin's supervision, took the iconic X-ray diffraction 'Photograph 51'. Williams debunks the myth that Wilkins "stole" it; he clarifies how, before moving on to Birkbeck, University of London, Franklin gave her materials and data on DNA to Gosling, to pass on to Wilkins to use as he wished. It was after this that Wilkins showed Photograph 51 to James Watson, who, with Crick, used it to uncover the double helix.

There are a few errors — inevitable in a book of such scope. Williams writes, for instance, that biochemist Linus Pauling took a "surprisingly long time" to recognize that his proposed three-strand structure of DNA was wrong. In fact, at a meeting before the publication of the true, two-strand structure (J. D. Watson and F. H. C. Crick *Nature* **171**, 737–738; 1953), Pauling remarked that the discovery "may turn out to be the greatest development in the field of molecular genetics in recent years". And, on occasion, the scope is too broad. The tragic figure of Nikolai Vavilov, the great Soviet plant geneticist of the early twentieth century who perished in the Gulag, features prominently, but I am not sure how relevant his research is here. Yet pulling such figures into the limelight is partly what distinguishes Williams's book from others.

What of those others? Franklin Portugal and Jack Cohen covered much the same ground in the 1977 *A Century of DNA*, but that now seems dated. James Schwartz's *In Pursuit of the Gene* (2008) hardly touches on biochemistry, whereas Siddhartha Mukherjee's 2016 *The Gene* devotes little space to the backstory of the double helix.

Isaac Newton wrote to natural philosopher Robert Hooke that he had seen further than others only by standing on the shoulders of giants. *Unravelling the Double Helix* looks beyond giants to the many researchers, now half-forgotten, whose contributions paved the way for an icon of science. ■

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PARTICLE PHYSICS

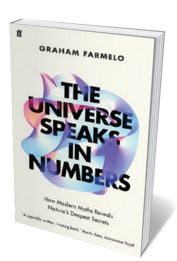
A singing, dancing Universe

Jon Butterworth enjoys a celebration of mathematics-led theoretical physics.

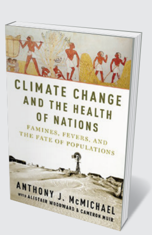
Mathematics is an immensely powerful tool for understanding the laws of the Universe. That was demonstrated dramatically, for instance, by the 2012 discovery of the Higgs boson, predicted in the 1960s. Yet an ongoing, often fervid debate over the direction of theoretical physics pivots on the relationship between physics and maths — specifically, whether maths has become too dominant.

The worry — expressed by a number of theorists and writers over several decades — is that theoretical physics has become a monoculture too focused on a small clutch of concepts and approaches. Those include string theory, overstated predictions of new discoveries, over-reliance on mathematical elegance as a guide and a general drift into what physicist and writer Jim Baggott, in *Farewell to Reality* (2013), called "fairy-tale physics", divorced from its empirical base. Notable critiques have come from theoretical physicists including Peter Woit, Lee Smolin and, more recently, Sabine Hossenfelder (see A. Ananthaswamy *Nature* **558**, 186–187; 2018). Science writer Graham Farmelo clearly intends *The Universe Speaks in Numbers* as a riposte.

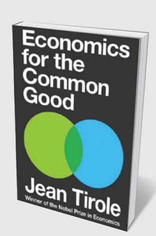
Farmelo takes us on a tour through the ▶



The Universe Speaks in Numbers: How Modern Maths Reveals Nature's Deepest Secrets
GRAHAM FARMELO
Faber & Faber (2019)



Climate Change and the Health of Nations
Anthony J. McMichael OXFORD UNIV. PRESS *(2019)*
In this posthumously published volume, epidemiologist Anthony McMichael journeys through the deep history of Earth's changing climate and its human implications — such as agricultural collapse resulting from shifts in temperature. A book with echoes for today.



Economics for the Common Good
Jean Tirole PRINCETON UNIV. PRESS *(2019)*
French economist Jean Tirole's deft study (translated by Steven Rendell) questions his discipline's role in society. Researchers, he argues, should become socially responsible, probing issues beyond the euro's stability, such as climate change and resource distribution.