JANE TAYLOR

Explaining inheritance

This year is a double anniversary in the hunt for an explanation of inheritance. The role of chromosomes was announced in 1903 and the structure of DNA was revealed in 1953.

Dr Yorgos Nikas/SPL

***Above:** Human sperm on the surface of an ovum during fertilisation*

GCSE key idea
Scientists, like other people, are reluctant to give up explanations that served them well in the past.

Since earliest times people have speculated about how features pass from generation to generation. A theory of **pangenesis** prevailed for centuries, from the time of Hippocrates (about 400 BC) onwards. This theory supposed that all parts of the body contribute some form of essence to the generative fluid or 'seed' of the male or female parent and that the essences of the parents are transmitted to the offspring at conception.

SPERMIST OR OVIST?

Things did not change much until the sixteenth century. Then **Anthony von Leeuwenhoek** ground some simple lenses with which he found tiny creatures swimming in seminal fluid. Until then no one knew that humans produced **eggs** and **sperm cells**. Leeuwenhoek thought he saw miniature individuals coiled up inside sperm cells, and this contributed to the idea that babies were pre-formed in sperm.

On the other hand **Marcello Malpighi** in Italy had seen a tiny embryo in a hen's egg and thought the egg carried the pre-formed individual. Two camps formed. The **ovists** favoured the egg as the source of the offspring, while **spermists** favoured sperm.

Sea urchins were useful for research because their large eggs and sperm can be observed in a cool Petri dish in a laboratory.

THE BIOLOGY EXPLOSION

By the mid nineteenth century new achromatic lenses gave a much better magnification and resolution, so that **Theodor Schwann** could see cell structure in detail. He suggested that **cells** were the basic unit of life. **Oskar Hertwig** watched the external fertilisation of sea urchin eggs and saw that the sperm penetrated the egg. He believed that sperm and egg nuclei fuse during fertilisation. Inherited material must therefore lie somewhere within both egg and sperm cells.

In 1882 **Walther Flemming** used Perkin's mauve to stain the nucleus and noticed a coloured material inside it that he called **chromatin**. Chromatin changed into threadlike strings, which became known as chromosomes, when the cell divided. He observed chromosome movement during cell division, which he called **mitosis**, but he did not connect it to inheritance.

FINDING OUT ABOUT CHROMOSOMES

Theodor Boveri also investigated what happened during fertilisation and the early development of sea urchins. By 1887 he had seen that maturing eggs lose half their nuclear material and that the sperm and egg nuclei do not fuse during fertilisation. Instead each contributes half the **chromosomes** which together make the normal number found in the cell. He saw that chromosomes stay as whole structures through cell division and this gives the continuity needed to pass information on to new cells. The idea that chromosomes were important in inheritance was unpopular.

Ten years later **Hugo de Vries** rediscovered Mendel's work on inheritance (see CATALYST Vol. 12, No. 4). Boveri spotted the match between Mendel's laws and what was known about chromosomes and suggested that chromosomes transmit hereditary characteristics. **Walter Sutton**, working on cell development, came to the same conclusion at the same time. Another clue was found at around the same time when it was realised that cells in females always have two X chromosomes while male cells have an X and a Y. This linked a feature (gender) to differences in chromosomes.

The Boveri–Sutton chromosome theory was hotly debated until **Alfred Sturtevant**, a student in Morgan's genetics laboratory, settled it in 1915. He realised that five characteristics of the fruit fly *Drosophila melanogaster*, on which he had been working, could be inherited as a cluster. Three other clusters of features were identified, making four groups that correlated with *Drosophila*'s four pairs of chromosomes. Further analysis confirmed that hereditary factors were carried on the four pairs of chromosomes. Morgan suggested that genes were arranged in a line in the chromosomes.

BIOCHEMISTRY

The biochemists had been busy too. **Friedrich Miescher** investigated the composition of white blood-cell nuclei in 1869. He extracted a new substance from them that he called **nuclein**. Nuclein had a different composition from other molecules, with high phosphorus and nitrogen content, and it resisted protease digestion so it wasn't a protein. Miescher thought that nuclein might be a store for phosphorus. Two forms of nuclein were eventually found but their structure and function were a mystery. **Albrecht Kossel** showed that a form of nuclein found in thymus cells contained four nitrogen compounds: adenine, guanine, cytosine and thymine. Other researchers found some carbohydrate and phosphorus.

Phoebus Levene showed that nuclein was different from proteins. In 1909 he found that the carbohydrate in a form of nuclein from yeast is a sugar, ribose. It took until 1929 to identify the carbohydrate in the thymus form of nuclein as a sugar called **deoxyribose**. Levene suggested a simple structure for the newly named **ribonucleic** and **deoxyribonucleic acids** (RNA and DNA). He proposed that there were units containing one molecule of each of the four bases, joined together by sugar and phosphate, and that these units were linked to make a polymer with bases in the same order repeating down the length.

This idea of a repetitive structure was a stumbling block in the search for the basis of inheritance. Scientists looking for something that could convey vast quantities of complex inherited information thought the simple structure proposed for nucleic acids was inadequate. The more complex and infinite structural variety of proteins had much more potential to encode such a diversity of information. The smart money looked for genes among proteins.

WAS IT PROTEIN OR WAS IT NUCLEIC ACIDS?

The idea of proteins carrying genes was overturned in 1944. **Oswald T. Avery** and his colleagues had been puzzling for years over a substance from killed bacteria that could give new abilities to living bacteria. By 1936 they felt that it must be a nucleic acid. It was pure DNA, and a series of tests eliminated any alternatives. In 1952, **Alfred Hershey** and **Martha Chase** provided the final proof that DNA carries genes when they showed that the DNA in bacteriophages (viruses that attack bacteria) is the part that directs the making of new virus particles, including their protein coats (see Box 1 on page 18).

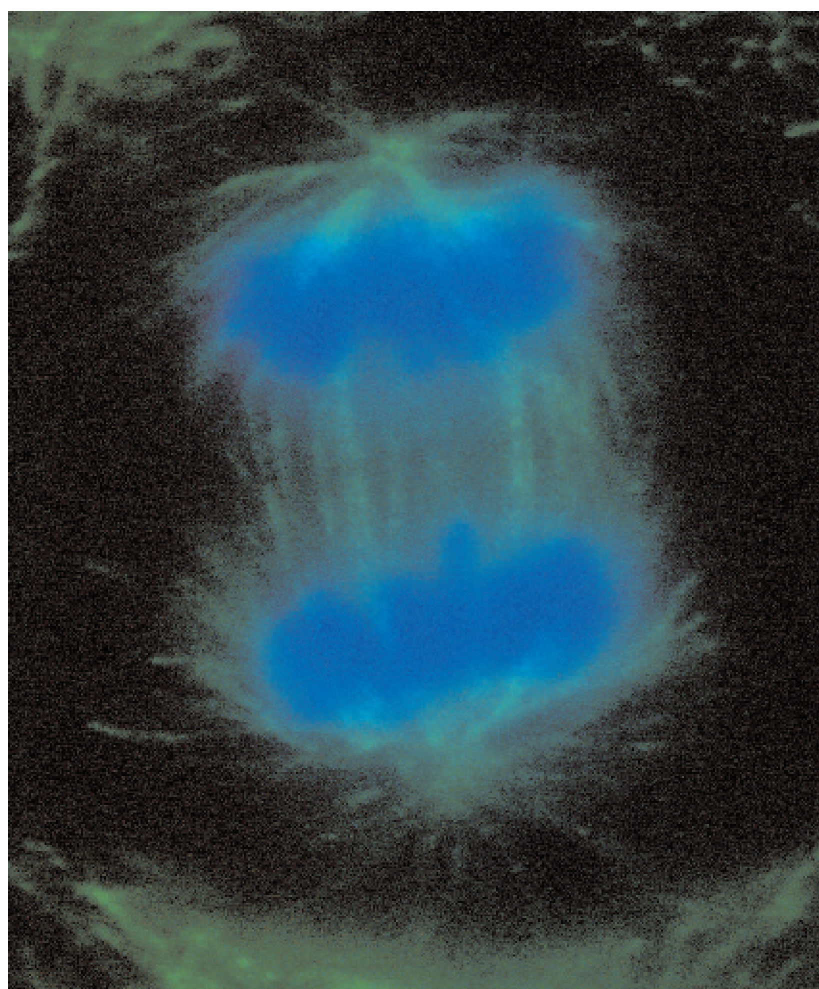
This work revived interest in DNA and people looked at its structure again. **Erwin Chargaff**'s observations disproved the idea of a simple DNA

***Drosophila melanogaster* is the tiny fruit fly often seen in summer.**

Gregor Mendel worked in relative isolation and his work was unknown to scientists working on inheritance for many years.

Many bacteria pass DNA into other bacteria. This is a normal way for bacteria which reproduce asexually to exchange genes.

***Below:** A cell during mitosis. The chromosomes (blue) have divided and are moving towards positions in which new nuclei will form*



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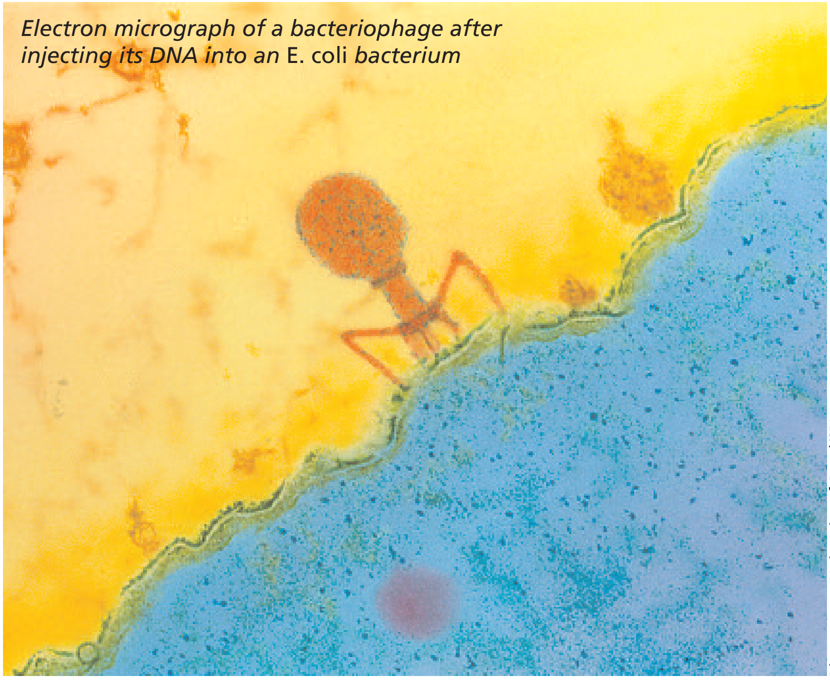

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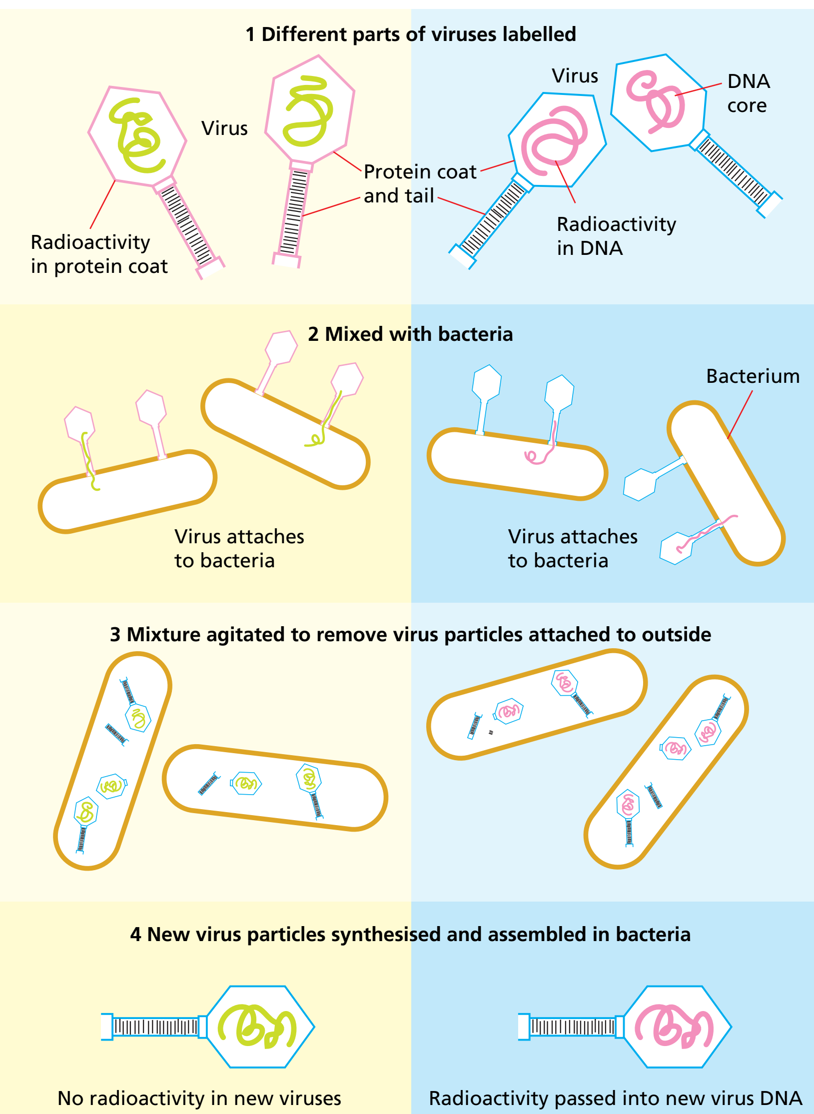

Figure 1 The Hershey–Chase experiment

BOX 1 HERSHEY AND CHASE

Hershey and Chase investigated the genetic material of a bacteriophage. Bacteriophages are viruses which attack bacteria and multiply inside them, before killing them. They are very simple in structure, consisting of a protein coat surrounding DNA. Hershey and Chase showed that bacteriophages containing radioactive DNA passed it on to the next generation of bacteriophages. But bacteriophages with radioactive protein did not pass it on to the next generation (see Figure 1).

structure. He noticed that there are the same numbers of molecules of adenine (A) as of thymine (T), and that cytosine (C) matches guanine (G) in the DNA of a given species, although he did not find out why. Many groups of scientists tried to work out the structure of DNA.

WHAT WERE THE VITAL CLUES?

A number of vital clues led the way to understanding the structure of DNA:

- The A–T/C–G base-pair system was deduced.
- In 1948, **Linus Pauling** discovered that many proteins take the shape of an alpha helix, spiralled like a coiled spring.
- **Rosalind Franklin**'s X-ray diffraction pictures of DNA suggested a helix to her and provided several of the vital helical parameters.

On 28 February, 1953, Francis Crick is said to have walked into the Eagle pub in Cambridge and announced, 'We have found the secret of life.' That morning, Watson and Crick had figured out the structure of deoxyribonucleic acid, DNA.

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