U3

GENETICS & NUCLEIC ACIDS

CELL DIVISION:

- It's hard to imagine, but the cells present in a tiny embryo ultimately generate all of the cells that make up the body of an adult human being.
- Four cells became eight; then eight became 16 individual cells with identical DNA.
- The cascade continued until several weeks later, millions of cells were dividing– powering the exponential pattern of growth that eventually formed all of the organs and tissues of your body.

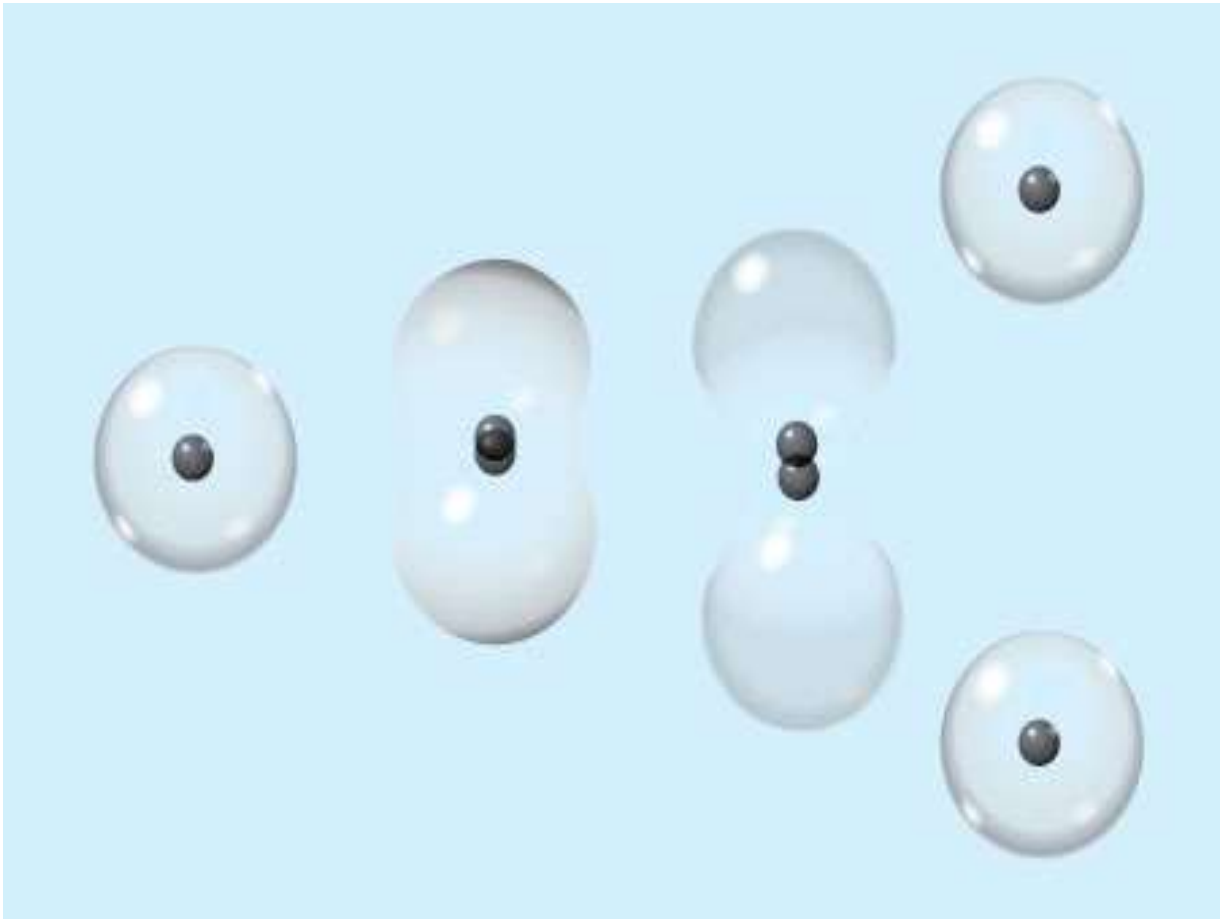


Figure 1:
Most plant and animal cells replicate by splitting into two identical daughter cells.

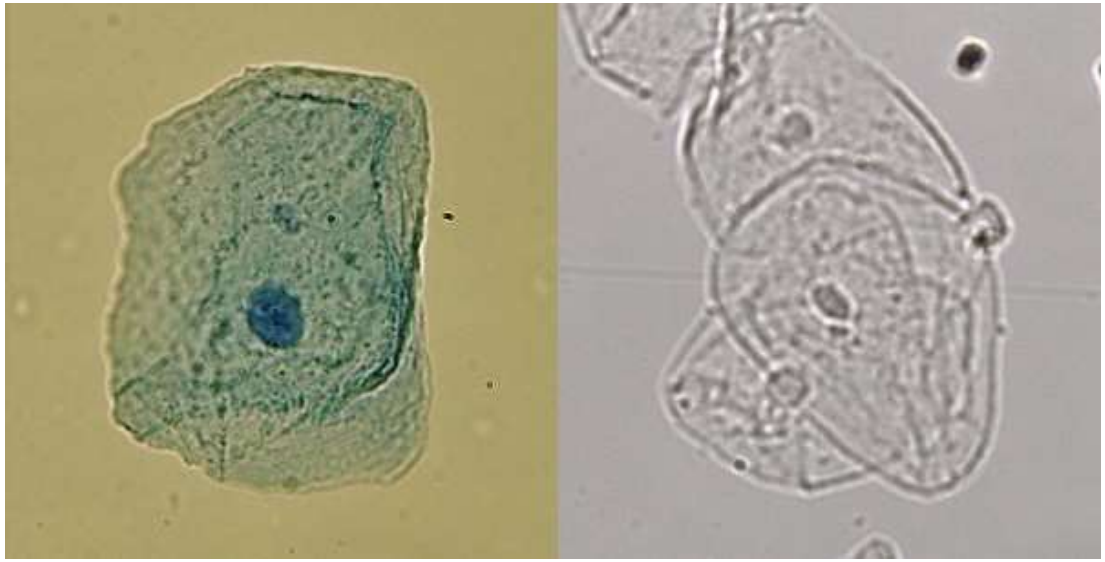
THE DISCOVERY OF CELL DIVISION

Walther Flemming, a 19th century professor at the Institute for Anatomy in Kiel, Germany, was the first to document the details of cellular division. The use of microscopes to study biological tissues was an emerging technology in Flemming's day, and he was highly regarded as an innovator in the field.

Figure : Walther Flemming

Kiel, Flemming experimented used dyes to color the specimens he wanted to examine under a microscope. Due to unavailability of good light source light todays electric bulbs, so dying the specimens allowed him to see them in greater detail.

Aniline dyes found particularly useful as different types of tissues absorbed the dyes at varying intensities depending on their chemistry.



Unstained (right) versus stained cells (left)image © Judith Beekman

Flemming found that a particular mass of material inside the nucleus of cells absorbed the dye quite well. He didn't have a name for it at the time, but later came to call the material "chromatin," from chroma, the Greek word for color. Flemming drew pictures of what he saw under his microscope to illustrate various publications he produced in his research (Figure).

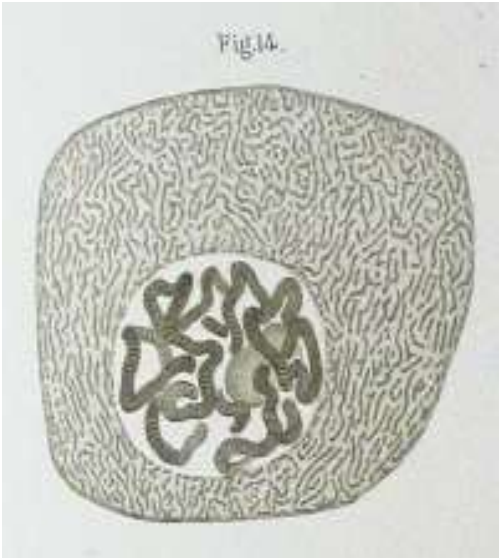


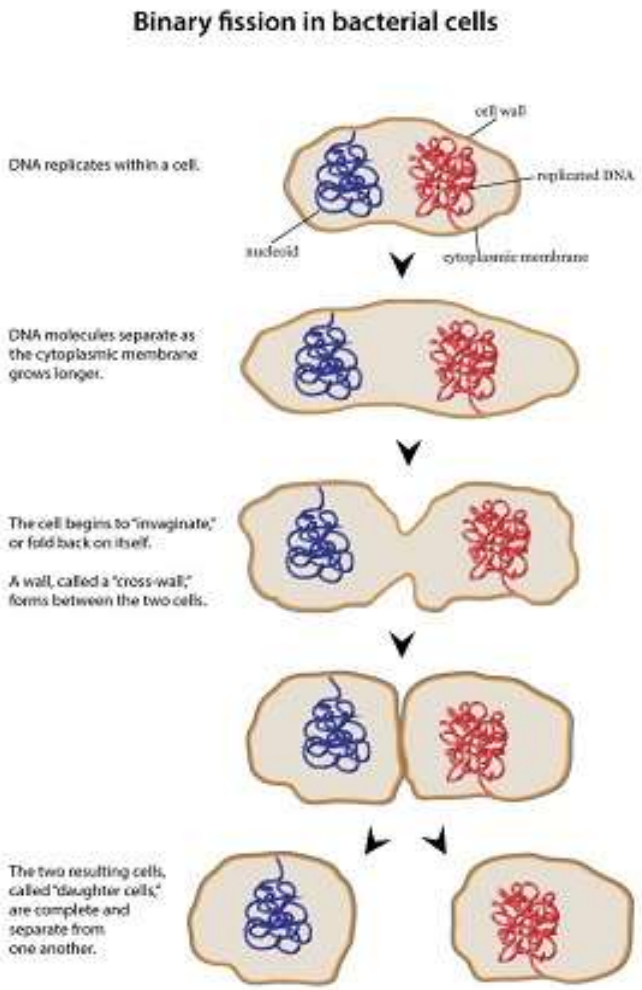
Figure 4: Flemming's drawing of an insect cell treated with an aniline dye as he saw it under the microscopeimage © Wikimedia Commons

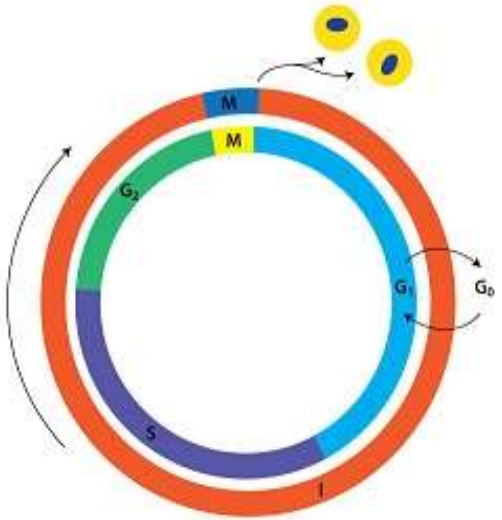
- After many hours of observation, Flemming began to see a pattern whereby cells would periodically transition from a resting stage to a period of frenzied activity that turned one nucleus into two, and then pulled the entire cell apart creating two identical cells – each with its own complement of chromatin enveloped within its nucleus.
- **Today we call the process of the nucleus splitting into two nuclei *mitosis*, and the cell split itself, *cytokinesis.* The terms came into use years after Flemming's discovery**.
- He described the process fully in ***his book Zur Kenntniss der Zelle und ihrer Theilungs-Erscheinungen (To the knowledge of the cell and its phenomena of division) (Flemming, 1878).***

Cell Division

- ✓ While all living cells are remarkably similar, cell division is one of those areas where eukaryotic cells (plants, animals, fungi, and protists) are very different than bacteria and other prokaryotes.
- ✓ This is because bacteria and other simple cells do not have a nucleus, so the process can be much simpler. In effect, bacteria simply grow and divide continuously with no distinguishable phases between one division and the next.
- ✓ The process by which prokaryotes divide is called binary fission, and the term "mitosis" never applies to them.
- ✓ Another difference between prokaryotes and eukaryotes is that prokaryotes have one main circular chromosome, while eukaryotes typically have many linear chromosomes.

Differences in Cell Division





1. In the more complex eukaryotic cells, the G_1, S, and G_2 phases are collectively referred to as ***interphase***.
2. These phases cannot be under the microscope. Cells in our bodies spend approximately 78% of their lives in interphase.
3. During interphase, eukaryotic cells double in size, synthesize new strands of DNA, and prepare for mitosis and cytokinesis.

When was meiosis and mitosis discovered? .

- ***Mitosis*** **-**Walter Flemming observed and described chromosome behavior during animal cell division in **1879**. Flemming was one of the first cytologists and the first to detail how chromosomes move during mitosis, or cell division.
- **Meiosis** was discovered and described for the first time in sea urchin eggs in **1876** by the German biologist Oscar Hertwig.
- It was described again in **1883, at the level of chromosomes**, by the Belgian zoologist Edouard Van Beneden, in Ascaris roundworm eggs.

Chromosomes the carrier of Heridity

- Thomas Hunt Morgan discovers that **genes are located on chromosomes.**
- Working on fruit flies, he concludes that certain traits are linked to gender and that those traits are probably carried on one of the sex chromosomes (X or Y).
- He hypothesizes that other genes are also carried on specific chromosomes.
- Using chromosome recombination, he and his students map the locations of genes on chromosomes.
- Morgan and his students write the seminal book The Mechanism of Mendelian Heredity.

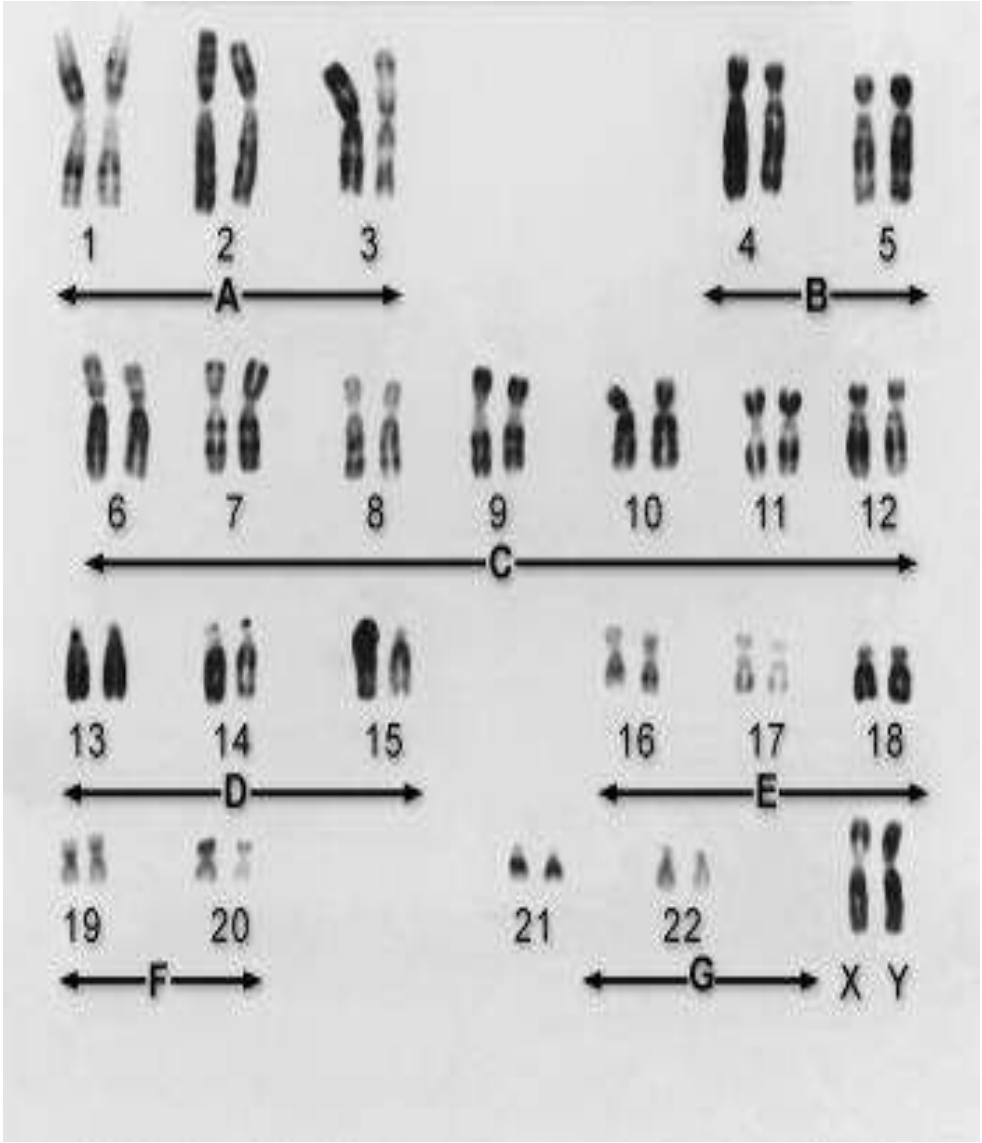
Chromosomes

- Eukayotic cells display condensed bodies periodically just before cell division which is visible under a light microscope.
- These bodies appear in the central area where the nucleus was located, but now disappeared or transformed into these bodies
- In a resting cell a chromosome is made of a very long strand of DNA and contains many genes (hundreds to thousands).
- The genes on each chromosome are arranged in a particular sequence, and each gene has a particular location on the chromosome (called its locus). In addition to DNA, chromosomes contain other chemical components that influence gene function.

Pairing (e.g., Human cells)

- Except for certain cells (for example, sperm and egg cells or red blood cells), the nucleus of every **human cell contains 23 pairs of chromosomes, for a total of 46 chromosomes. Normally, each pair consists of one chromosome from the mother and one from the father.**
- There are 22 pairs of nonsex (AUTOSOMAL) chromosomes and one pair of sex chromosomes. Paired nonsex chromosomes are, for practical purposes, identical in size, shape, and position and number of genes. Because each member of a pair of Autosomal (nonsex) chromosomes contains one of each corresponding gene, there is in a sense a backup for the genes on those chromosomes.
- The 23rd pair is the sex chromosomes (X and Y).

Karyotype of Human Chromosomes



Chromosomal involvement, DNA level of involvement.

- **Genes are segments of deoxyribonucleic acid (DNA) that contain the code for a specific protein that functions in one or more types of cells in the body. Chromosomes are structures within cells that contain a person's genes.**
- Genes are contained in chromosomes, which are mainly in the cell nucleus.
- A chromosome contains hundreds to thousands of genes.
- Every human cell contains 23 pairs of chromosomes, for a total of 46 chromosomes.
- A trait is any gene-determined characteristic and is often determined by more than one gene.
- Some traits are caused by abnormal genes that are inherited or that are the result of a new mutation.

NUCLECIC ACIDS-GENETIC MATERIAL

- **Introduction**

  That the chromatin of the cell nucleus is the physical basis of inheritance was rather widely accepted by scientists in the late 1800s.

  Nägeli in 1884 had hypothesized that the stuff of inheritance resided in a cellular material he named **idioplasm**.

  Soon followed the proposal independently from several scientists, including Weismann, Strassburger and Hertwig, that Nägeli's hypothetical idioplasm was the nuclear chromatin detected by cytological observations.

Support for this concept came from studies of sexual reproduction of plants and animals, where it was noted **that both male and female parents contribute nuclei** to the fertilized egg, while the cytoplasm is derived almost entirely from the female.

Even more important, Roux had shown as early as 1883 that mitosis involves the accurate equal division of the nuclear material to the two daughter cells.

In contrast, the mass fission of the cytoplasm is not necessarily an equal division of the individual parts.

In 1871, Miescher extracted nuclear material of cells and called this material nuclein said to be rich in phosphorus; Altmann, in 1889, and subsequent analysis of Hoppe-Seyler, Kossel drew the *conclusion that what the cytologists designated as chromatin contains nucleic acid and various amounts of the nuclear proteins*

- Since nucleic acids were limited to the chromosomes of the nucleus, they were generally accepted as the material basis of inheritance.
- In the 1920s, nucleic acid structure were subjected to chemical analysis, and deoxyribonucleic acid (DNA) was interpreted to be a monotonous repeating polymer of only four nucleotides.

Proof of DNA as Genetic Material

- The experiments of Griffith, in 1928, were one of the first steps toward proof that nucleic acids are the genetic material.
- He used different strains of the bacterium pneumococcus to demonstrate a genetic 'transformation' of one strain type into another.
- Different strains of pneumococcus can be distinguished by the type of polysaccharide found in the cell capsule. The capsule type is a constant, inherited characteristic of each strain.
- Occasionally some cells may lose the ability to form a capsule, but such unencapsulated cells do not change strain type.
- Encapsulated cells are deadly when injected into mice, while Sunencapsulated cells have lost their virulence.

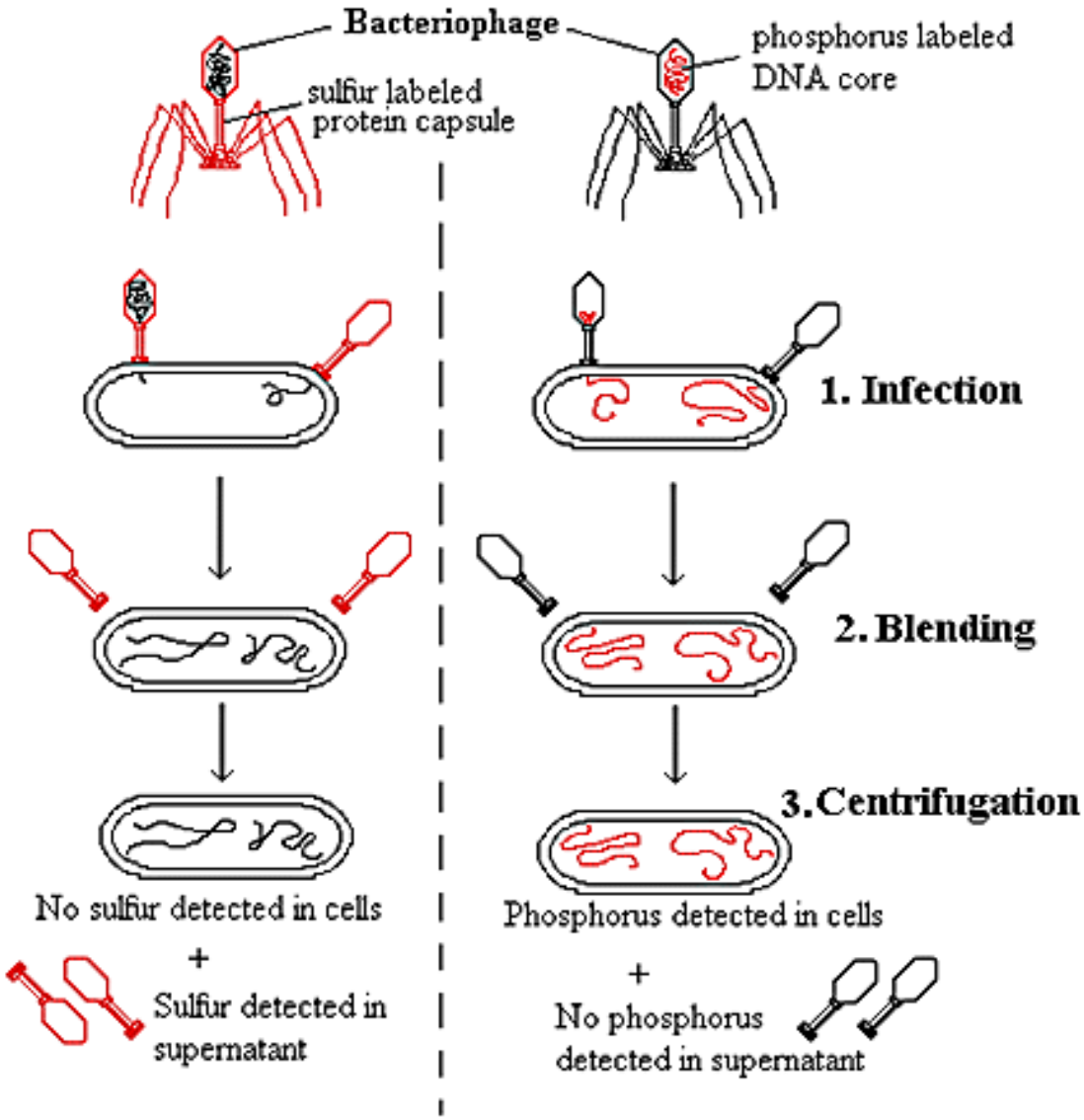
Griffiths Experiment

Experiment:

- Griffith carried out a series of experiments on mice injected with various combinations of pneumococcus strains.
- He discovered that mice injected with unencapsulated, avirulent cells mixed with an extract of heat-killed encapsulated cells generally died, just as if they had received live virulent cells.
- Clearly, the extract of heat-killed cells was somehow conferring virulence to the live unencapsulated cells.
- The crucial observation came from mice injected with live unencapsulated cells of one strain mixed with the extract of heat-killed encapsulated cells of a different strain.
- Griffith noted that bacteria recovered from the dead animals proved to be encapsulated with the genetically determined polysaccharide characteristic of the heat-killed strain.
- Repeat experiments, with all of the necessary controls, indicated not only that association with an extract of dead encapsulated bacteria could in some way restore virulence to the unencapsulated cells, but that those cells were actually genetically transformed into the heat-killed encapsulated strain type.
- **That this was indeed an inherited transformation, and not just the result of coating avirulent cells with the polysaccharide capsule material, was clear from culturing the cells to show that the capsule type was transmitted to daughter cells.**

Hershey and Chase 'Waring blender' experiments

- The demonstration that DNA is the genetic material of a particular type of virus was provided by the elegant 'Waring blender' experiments of Hershey and Chase in 1952 (Figure).
- The virus T2 is a bacteriophage that infects Escherichia coli cells. It does so by attaching to the surface of the cell and injecting its core material into the bacterium. Many new viruses are produced inside the cell, causing it to burst (lysis), releasing new virus particles.
- Hershey and **Chase used radioactive isotopes to label two different components of T2. 32P, an isotope of phosphorus,** was incorporated into the DNA, and the radioisotope of sulfur, 35S, was used to label the protein.
- The double-labelled viruses were then used to infect bacteria. After the viruses had attached and injected their core material into the cells, the mixture was placed in a Waring blender. The rapid mixing removed most of the T2 protein coats that remained on the outside of the cells.
- Inside the cells the infection continued to produce many new copies of T2 DNA that was packaged into new protein coats.
- After lysis, the new T2 viruses were separated from the cellular debris and analysed for their isotope composition.
- **The results showed that almost all of the 32P was recovered but almost none of the 35S, demonstrating that it is the DNA that provides the genetic information necessary to produce new virus particles.**



The Hershey-Chase Experiment

Other Molecules as Genetic Material

RNA as the Genetic Material in Viruses

Many viruses have been shown to contain **ribonucleic acid (RNA)** as their genetic material. One of the early examples is the Tobacco mosaic virus (TMV), shown in the 1930s to be composed of protein and RNA.

No DNA is found in the particle. The protein can be easily separated from the RNA by mild alkali treatment. That it is the RNA that acts as the genetic material in such particles was demonstrated directly by Gierer and Schramm, in 1956, who showed that tobacco plants could be infected by inoculation with the RNA alone.

Non-nucleic Acid Information Vectors

Infectious proteinaceous particles called **prions** have been characterized by Prusiner as the basis for some cases of central nervous system degenerative disorders, such as Creutzfeldt–Jacob disease (CJD) in humans. Bovine spongiform encephalopathy (BSE), known as mad cow disease, and scrapie in sheep are also diseases attributed to prions.

CJD may occur as a sporadic, genetic or infectious illness, while **kuru**, a similar disease found in the Fore people in New Guinea, is known to be due to prion infection through ritual cannibalism of diseased brain tissue.