Obituary

Alfred Hershey (1908–97)

One of the founding fathers of molecular biology

The 1940s saw the origins of molecular biology and the beginnings of a proper understanding of living systems. Until then, biological phenomena were either reduced to questions of chemistry or treated in abstract. There seemed to be no middle ground between the solidities of biochemistry and the abstractions of genetics, and it was not customary to ask how cells knew what they were doing. So the great leap forward largely depended on scientists who were not wedded to the technologies of an established discipline, and could focus their attention on the simplest possible system — the bacterium *Escherichia coli* and its viruses. Delbrück, Luria and Hershey (a physicist, a physician and a microbiologist) played a crucial part in these developments, and for this they shared a Nobel prize in 1969. With the death of Al Hershey on 22 May, the last of the three has gone and an era has come to an end.

Hershey spent the first 16 years of his career as an instructor in bacteriology at Washington University, St Louis. The head of the department was Bronfenbrenner who, like many people in those days, believed that viruses were proteins that somehow triggered their host cell into making more of the same so were not in any sense alive. Bronfenbrenner's influence ensured that Hershey's early publications (on bacterial growth and virus–antibody interactions) were rather undistinguished. Certainly, they gave no hint of what was to come.

But in 1943 Hershey met Max Delbrück, just at the time when Delbrück and Salvador Luria were struggling with the mathematics of mutation in bacteria. Three years later, at the age of 38, Hershey reported that bacterial viruses contain genetic determinants which occasionally undergo spontaneous, inheritable changes (mutation). Shortly afterwards, he showed that these determinants display genetic linkage and form linear arrays — just like the chromosomal genes of higher organisms. This established that bacterial viruses are a simple version of all living creatures and, as Delbrück had imagined, that they could be used to investigate the nature of the gene.

In 1950 Hershey moved to the Carnegie Institute of Washington's unit at Cold Spring Harbor and he remained there for

the rest of his career. His studies on linkage and recombination in the genes of the T2 bacteriophage became increasingly complicated and, some years later, culminated in a review of almost impenetrable obscurity; privately, he admitted that the review was his way of saying that he could not understand what was going on. So, he changed to studying the chemical components of phage, and their fate during infection of a bacterium. Within a year, he and his assistant, Martha Chase, had shown that it is the DNA — not the protein — that carries the viral genes and is responsible for the transfer of information from one generation of particles to the next. This came to be known as the 'blender' experiment, because they had used an ordinary kitchen blender to separate the empty protein shells of the infecting virus particles from the infected bacteria.

Hershey's evidence that genes are made of DNA rather than protein was less precise than Oswald Avery's (for the bacterial transforming principle). However, Hershey's experiment identified the chemistry of a group of conventional genes, whereas Avery's result applied to a single obscure trait (the ability of a bacterium to make a particular surface polysaccharide). For that reason many people found Hershey's experiment more persuasive. But together, the two sets of results inaugurated the science of molecular biology. As Hershey wrote, the development of molecular genetics showed repeatedly that "some redundancy of

evidence was needed to be convincing" and "diversity of experimental materials was often crucial to discovery".

His next eight years were spent filling in the biochemical and genetic details of the life-history of bacteriophage T2. Finally, following the discovery by Pete Davison that DNA molecules are fragile in solution, Hershey set about developing a way to work out the size of native, unbroken molecules. It was a desperately difficult project, but his studies were the essential precursor for much easier work by others.

Al Hershey was, in many ways, the perfect experimentalist. No project was too difficult for him to tackle single-handedly, no thought too much effort. Right to the end of his career he carried out his own experiments — he would even spend hours washing up the laboratory glassware (because, as he said, it temporarily spared him the burden of thought). It was, perhaps, an extension of this principle that made him say that 'Hershey heaven' was to find an experiment that worked, and then to do it again and again.

He seemed to feel the responsibility of the world on his shoulders: only if he laboured to the utmost of his ability could everyone else avoid being misled. He divided every day in half; one half usually starting at 9 a.m. and the other at about 9 p.m., with dinner, sleep and breakfast interposed between each half. At almost any time of day or night, therefore, you might find him either sitting motionless in his chair, thinking and gazing at the ceiling, or cocooned in the privacy of some experiment or blissfully cleaning up afterwards. His powers of concentration tended to make him taciturn and absent-minded. But when he did talk, it was as if a searchlight were being trained on a dark landscape. He seemed to approach every subject, serious or trivial, as if he had never thought about it before (or, sometimes, even heard of it). This gave his utterances a penetrating originality, which often caused a gap in the conversation while his listeners desperately revised their opinions and reordered their thoughts.

His final project was perhaps the hardest. Various circumstances forced him to retire in his mid-60s, and make space for younger scientists. Typically, he made that final transition without a murmur and, for 20 years, sought satisfaction in other versions of Hershey heaven — the clearing of forest to make a vegetable garden, and a search for the underlying meaning of Western music.

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