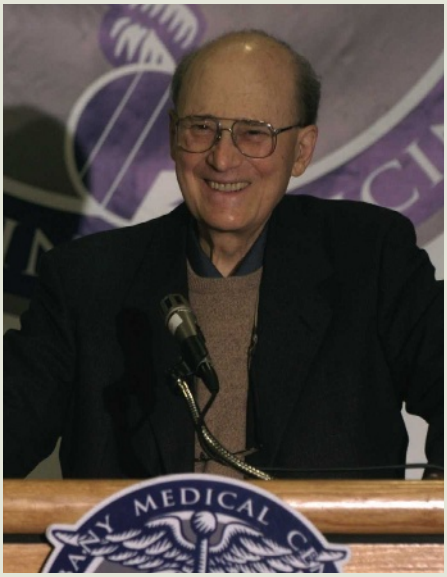
OBITUARY

Seymour Benzer (1921–2007)

Restless spirit, and pioneer in molecular genetics.



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Seymour Benzer, one of the giants of twentieth-century biology, died on 30 November. Benzer, who maintained an active laboratory until the time of his death, was a unique figure who made seminal contributions to physics, molecular biology and behavioural genetics.

He was born in New York to immigrant Jewish parents from Poland, and grew up in Brooklyn. After graduating from Brooklyn College, he obtained his PhD in physics from Purdue University in 1947, where his discoveries in solid-state physics contributed to the development of the transistor. Relentlessly curious, Benzer possessed both a single-minded fascination with the mysteries of nature and the intellectual talent to unravel them. Purdue hired him as a physics professor, but almost immediately he began working in biology, taking the 'bacteriophage course' at Cold Spring Harbor Laboratory, followed by a two-year postdoc with Max Delbrück at the California Institute of Technology (Caltech). Benzer's style was to pioneer a new area, and then to move on to something new once the hordes had rushed in. As he said: "I like to take things that are fuzzy, and turn them into something tangible."

Benzer next took a series of sabbaticals, wandering the world of phage genetics to sojourn with François Jacob in Paris and Francis Crick in Cambridge, UK. It was during this period that he made some of his most important contributions to what is now viewed as the golden era of molecular genetics — the period following the publication of James Watson and Crick's double-helical structure of DNA that witnessed a feverish race to understand the mechanisms underlying the molecular basis of heredity.

Using bacteriophage T4, Benzer developed a technique to select for rare genetic-recombination events in organisms carrying different mutations in the *rII* locus, and showed that mutations can occur at many different sites in the same gene. By generating a fine-structure genetic map, he proved that genes are not indivisible units, but are composed of a linear array of chemical building-blocks, or bases, each of which can be subject to alteration. Moreover, by a simple argument, he deduced that the minimum unit of mutation is probably a single base pair of DNA. This idea was fundamental to connecting the structure of DNA to the reality of genetics. And, together with Fred Sanger's discovery that proteins are composed of precise sequences of amino acids, this work laid the foundations of the new science of molecular biology.

Most scientists would have been content to continue in this exciting field, but Benzer became characteristically restless. For him, once it became obvious how a problem could be solved, it was time to move on to another. This time, he was attracted to a far more formidable question: how genes influence behaviour. Traditional approaches to this problem had included studying how complex behavioural traits could be enhanced by selective breeding or altered by intercrossing. But Benzer had a different approach in mind: he would look for a model organism in which it would be possible to define single-gene mutations that altered specific behaviours. This strategy was clearly linked to his previous work on bacteriophage, and it established what he called genetic dissection as a valid method for analysing complex biological processes.

In search of such an organism, Benzer took a sabbatical with Roger Sperry at Caltech, where he tinkered with various animal models. Eventually, he chose the fruitfly *Drosophila*, and although his colleagues in the Sperry lab were not convinced, Benzer was undeterred. He once said: "If everyone you talk to says you shouldn't do something, you probably shouldn't do it, and if everyone says you should do something, you should also probably not do it; but if half the people you talk to tell you to do it and half say you're crazy, then you should definitely go ahead."

Benzer turned his sabbatical at Caltech into an indefinite stay and never touched a phage again. He founded the modern field of *Drosophila* neurogenetics and explored this area in his peripatetic style from 1967 until his death. His work showed not only that it is possible to dissect behaviour with single-gene mutations, but also that fruitflies are capable of far more sophisticated behaviour than had previously been thought possible. They could learn, they had a sense of time, and they showed complex, stereotyped courtship rituals.

To quantify these behaviours, Benzer built simple but ingenious devices, such as his counter-current apparatus for measuring phototaxis (an organism's movement in response to light). Using such tools, Benzer screened large numbers of flies to discover rare mutants with specific behavioural defects. This work, among his other achievements, laid the foundations for cloning genes controlling circadian rhythms and encoding potassium channels — crucial regulators of neuronal excitability — that had resisted all efforts at identification. Throughout, Benzer retained his arch and often ribald sense of humour, for example naming his learning and light-avoiding mutants dunce and photophobe, respectively. Almost 40 years later, hundreds of scientists continue in this experimental tradition, and entire meetings are devoted to neurogenetics.

In later years, Benzer turned his attention to the genetic control of ageing, discovering mutations that cause degeneration of the brain (Swiss cheese) or extended lifespan (Methuselah) in *Drosophila*, and opening the way to using the fruitfly as a model system in which to study neurodegenerative diseases such as Alzheimer's or Parkinson's.

Benzer remained active until his last days. A food-lover, he led expeditions to exotic ethnic restaurants, and into his eighties participated in matzoh-ball or potato-latke cook-offs with his friends. Watching him trundle tirelessly down the corridor of his laboratory draped in a smudged lab coat, pockets heavy with tools and packets of notes scrawled in his near-illegible, crabbed handwriting; holding court with his lab members around a small steel table in his cramped conference room, while sipping hot tea and munching Fig Newtons; and asking rare but razor-sharp questions well into his mid-eighties, it was difficult to escape the conclusion that Benzer had discovered some magical elixir of youth in *Drosophila* and was experimenting with it on himself — but not telling. Benzer was an original, a scientist's scientist, and his death in many ways marks the end of an era.

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