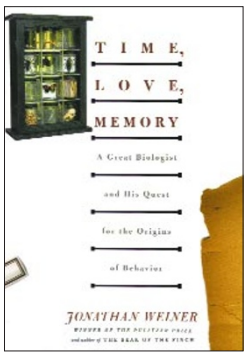
Flies by night



Time, Love, Memory: A Great Biologist and His Quest for the Origins of Behavior

By Jonathan Weiner
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Reviewed by Charles Jennings

As a young graduate student, I was once stumped by an off beat question from my departmental chairman: "How many Sturts between license and liberty?" Had I read Weiner's book, I would have known the answer. The term 'Sturt' was coined by Seymour Benzer, the central character in this story, in honor of Alfred Sturtevant and his method for mapping where genes act during development. My chairman's point, and Benzer's great insight, was that any behavior that is affected by a genetic mutation can be studied mechanistically, be it license or liberty, time, love or memory.

Benzer began his career as a physicist, and during the war made significant contributions to the development of the transistor. His deeper interest, though, was in biology, and a chance encounter with Salvador Luria led him to phage genetics and, by 1955, to the first map of an individual gene. This was a landmark study in that it established the connection between genetic maps and the newly discovered physical structure of the gene. Benzer spent the next ten years pursuing this work, but by the mid-1960s he felt that molecular biology was no longer the frontier it had once been, and that it was time for something new.

He chose the brain, and decided to use genetics to dissect behavior in the same way he had dissected phage genes. The biggest mystery was the role of heredity in human personality, but this was too much even for Benzer; he settled instead for fruit flies, thanks largely to his neighbors at Caltech, where he has remained to this day. His great contribution was the development of robust genetic screens that allowed the isolation of mutant alleles based on behavior rather than morphological traits. Using simple tests—responses to lights, odors or other flies—Benzer and his colleagues isolated a large number of mutants and thereby established behavioral genetics as a mainstream scientific discipline. Many of these mutants have now been characterized at the molecular level, yielding new insights into a whole range of biological phenomena.

Weiner recounts all this in lively and literate style. *Time, Love, Memory* is neither a textbook nor a scholarly biography, but the science is, for the most part, accurate and clearly explained. The book is aimed at the general reader, but it should interest any biologist curious about the evolution of this fascinating field. Weiner considers the rise of modern biology to be "the most towering accomplishment of the human mind in the last one hundred years", and it is remarkable how much intellectual history has been spanned in Benzer's career. Reading this account, one is left with great respect for his determination to confront the big scientific questions, and for his courage in following new directions despite his colleagues' skepticism.

Benzer himself emerges as a thoroughly likeable character, with many virtues and many eccentricities. Nocturnal in his habits (a circadian mutant, perhaps?), eclectic in his culinary tastes, a kindly if idiosyncratic mentor (how many lab chiefs will offer to cut their postdocs' hair?), his main fault seems to have been a reluctance to proselytize on behalf of his own field. As a teenager he was inspired by reading *Arrowsmith*, a novel about a young man for whom scientific curiosity was a near-religious calling. Yet the world of *Arrowsmith* has given way to that of *The Double Helix*, Watson's archetypal description of the ruthless competitiveness that now pervades so much of biology. Benzer was not like that. In one telling anecdote, a visitor to his lab sat and talked with them, and at the end joked that he'd "done his bit for Gerry Rubin" by keeping everyone away from their benches for over an hour. Rubin (who now heads the *Drosophila* genome project) had moved into Benzer's field and become a formidable rival, and in an era where races—and postdoc job prospects—could be won or lost in a matter of days, the joke wasn't altogether funny.

The main weakness of the book is that it never really attempts a critical evaluation of what fruitflies have contributed to our understanding of behavior. Have *Drosophila* geneticists succeeded in isolating 'atoms of behavior', as Benzer once hoped? For Weiner's three core examples—time, love and memory—I would answer no, not yet, and a tentative yes.

'Time' refers to circadian rhythms, and Benzer's contribution has been spectacularly validated in the last two years by the discovery that the molecules controlling rhythm generation are conserved between flies and vertebrates. Yet I do not think this is behavior; the clock mechanism is cell autonomous and is not confined to the nervous system, and we still have no idea how it regulates the daily cycle of activity. As for love, courtship mutants such as *fruitless* (which affects flies' sexual preference) have revealed how the fates of sex-specific neurons are determined during development, but we do not know how such neurons contribute to behavior, far less whether they hold any lessons for human sexuality. The cellular basis of memory would surely qualify as an 'atom of behavior', and Drosophila geneticists have established the transcription factor CREB as a regulator of long-term memory formation. This is a major advance, but the key question of whether fly memory mutations affect synaptic plasticity remains unanswered, mainly because of the difficulty of recording neuronal activity in such a tiny brain. Perhaps for that reason, Benzer has moved away from behavior in recent years to focus instead on the development of the fly nervous system.

Benzer has always been wary of extrapolating from insects to human behavior—in contrast to his contemporary, E.O. Wilson, whose attempt to draw broad lessons from the evolution of ant societies led to a storm of protest in the late 1970s. Human behavioral genetics will probably be a fertile source of controversies for decades to come, but its practitioners will do well to look to the fruitfly and to the tradition established by Benzer, with his insistence that behavioral genetics be grounded in mechanistic understanding of how genes build brains.

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