This Week's Citation Classic®

Rusak B & Zucker I. Neural regulation of circadian rhythms. *Physiol. Rev.* 59:449-526, 1979.
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This paper provided a critical review of the neural mechanisms regulating daily physiological and behavioral rhythms in animals, as well as estrous and seasonal reproductive cycles in mammals. It reviewed information on rhythm generation and environmental synchronization in both invertebrate and vertebrate species. [The *SCI*® indicates that this paper has been cited in over 385 publications.]

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Until about 1970 research on animal biological rhythms had proceeded largely in ignorance of the physiological mechanisms that generated these pervasive rhythms and synchronized them to environmental time cues. The identification around that time of neural and neuroendocrine structures that acted as pacemakers regulating daily (circadian) rhythms in several species helped to transform the entire field. In particular, the identification of the hypothalamic suprachiasmatic nuclei (SCN) as a putative pacemaker for the mammalian circadian system[1,2] stimulated tremendous interest and opened up a whole new research area.

Seeing the need for a synthetic review of recent findings on the neural control of circadian rhythms, the editors of *Physiological Reviews* invited Irving Zucker to write one in 1975. He and I had written a review on biological rhythms, which had dealt briefly with neural mechanisms, while I was a graduate student in his laboratory at the University of California, Berkeley.[3] Writing that review had been both intellectually and personally satisfying and had the incidental advantage of delaying my graduation and departure from Berkeley for a year. By 1975 I had, however, finally left Berkeley for a faculty position at Dalhousie University.

Zucker invited me to coauthor the review on neural control of rhythms. I was reluctant to undertake a task I knew would require an enormous commitment of time and energy, especially while trying to cope with my recent abrupt transition to faculty responsibilities. But I was also attracted by the chance to renew the personal and intellectual interactions Zucker and I had enjoyed in Berkeley. After some debate, I agreed to do it, subsequently abandoned the project, and finally was somehow cajoled by Zucker into resuming work on it.

Collaborating across several thousand miles was more cumbersome and less satisfying than writing together, and it was more challenging to reconcile our radically different approaches to writing. I generated detailed, hierarchical outlines before beginning to write or even read papers on any subtopic, while Zucker read and wrote on various subjects as his interests shifted, with little regard for which pigeonholes these writings might eventually occupy. In the end, more than a year of steady work was required to read, annotate, and attempt to integrate over 800 papers (only about 400 of which appeared in our bibliography), as well as to repeatedly reorganize and rewrite each other's contributions. As in our earlier review, the work was shared so evenly that the decision on the order of authorship (which we left until the end) was quite arbitrary.

The paper has been heavily cited in part because it was the first, and probably the only, review that covered so many aspects of the neural mechanisms regulating daily rhythms in mollusks, crustacea, insects, amphibia, reptiles, birds, and mammals, as well as related seasonal and estrous cycles in mammals. One measure of the interest in this topic at the time the review was published is that we received more than 1,300 requests for reprints. Many of the citations refer to the large portion of the review dealing with the role of the SCN in mammalian circadian organization. These citations, however, are used occasionally to support statements with which we did not agree. I suspect, for example, that our discussion of the difficult problems of analysis and interpretation of lesion effects on rhythms may not be read and appreciated as often as it is cited.

Research on biological rhythms and their physiological regulation has expanded rapidly since the early 1970s, and it has been strongly influenced by the concurrent explosive growth of neuroscience. Given the current size of the literature, it is certain that we, and probable that others, will not attempt as comprehensive a review in the future. More recent reviews in this area have generally dealt with one taxonomic group or focused on a single topic.[4] Our review had shortcomings, for example, in our coverage of invertebrate systems, but I am generally satisfied that it was worth the effort we invested. It probably served to strengthen the links between biological rhythms research and neuroscience and provided a broad introduction to the physiology of rhythms for many scientists who entered the field during the last decade.

1. **Stephan F K & Zucker I.** Circadian rhythms in drinking behavior and locomotor activity of rats are eliminated by hypothalamic lesions. *Proc. Nat. Acad. Sci. USA* 69:1583-6, 1972. (Cited 345 times.)
2. **Moore R Y & Eichler V B.** Loss of a circadian adrenal corticosterone rhythm following suprachiasmatic lesions in the rat. *Brain Res.* 42:201-6, 1972. (Cited 375 times.)
3. **Rusak B & Zucker I.** Biological rhythms and animal behavior. *Annu. Rev. Psychol.* 26:137-71, 1975. (Cited 130 times.) [See also: **Zucker I.** Citation Classic. *Current Contents/Agriculture, Biology & Environmental Sciences* 19(9):18, 29 February 1988; *CC/Arts & Humanities* 10(9):18, 29 February 1988; and *CC/Social & Behavioral Sciences* 20(9):18, 29 February 1988.]
4. **Moore R Y.** Organization and function of a central nervous system circadian oscillator: the suprachiasmatic hypothalamic nucleus. *Fed. Proc.* 42:2783-9, 1983. (Cited 75 times.)

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