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Minimal modeling of two-oscillator circadian systems under conflicting environmental cues

Multiple coupled oscillators have been presumed to constitute the circadian system of many organisms. In some cases the different oscillators are driven by diverse environmental cues (*zeitgebers*), as suggested by the light- versus food-entrainable oscillators in mice and the light- versus temperature-entrainable oscillators in *Drosophila*. In order to survey the spectrum of dynamics that could emerge from the interaction of potentially conflicting *zeitgebers* with a multi-oscillator circadian system, we assume a minimal model consisting of two mutually coupled oscillators, each being exclusively driven by a periodic environmental signal. Mathematically we represent the circadian system by 2 mutually coupled phase oscillators [1], A and B, each with an arbitrary individual period. As the two environmental signals are assumed to have the same period (24 h) and are only separated by a phase shift DELTA , the environment can be represented by a third phase oscillator, which is unidirectionally coupled to oscillators A and B, respectively, with the DELTA being reflected in a delayed coupling to oscillator B. Performing numerical studies of the system as a function of DELTA , and the balance of the environmental and intra-oscillator coupling strength, rich dynamic behavior like bistability and hysteresis, as well as loss of entrainment and quasi-periodicity is observable. Our study provides insight into the structure of the putative coupling network required to maintain the organism in a stable phase-relation with the environment, even in the face of contradictory signals. Furthermore, our results can indicate appropriate experimental strategies to evaluate the strength of inter-oscillator coupling and the relative *zeitgeber* strength, which have been performed in the past, but mostly lacked guidelines for correct design and interpretation of the results. We finally compare our minimal model with a more complex model, using limit-cycle oscillators [2], showing that the principal dynamics are not altered by the inclusion or exclusion of more details.

REFERENCES

- [1] Kuramoto, Y. (1984) Chemical oscillations, waves and turbulence. Springer-Verlag, Berlin, DE.
- [2] Oda, G.A. and Friesen, W.O. (2002) A model for splitting of the running wheel activity in hamsters. *J. Biol. Rhythms* 17(1): 76-88.