Takeshi Asakawa
System Technologies Laboratories , SONY Corporation
e-mail: Takeshi.Asakawa@jp.sony.com
Satoshi Koinuma
Koh-hei Masumoto
Mamoru Nagano
Yasufumi Shigeyoshi
Department of Anatomy and Neurobiology, School of Medicine, Kindai University

Mathematical model of the mammalian circadian center as a many-body system of the limit cycle oscillators

In the present study, we propose a mathematical model of the mammalian circadian center, or the suprachiasmatic nucleus (SCN), which is described as a many-body system composed of limit cycle oscillators. Each oscillation unit in the SCN was described as a limit cycle oscillator based on a negative autoregulation of per genes by its protein product PER previously reported (Goldbeter 1995, Leloup & Goldbeter 1998, Kurosawa et al. 2002, Gonze et al. 2006). We adopted another assumption that oscillators interacted with each other only through a humoral factor, and ignored other possible neural interaction or network. Then, their nonlinear equations were reduced to the Stuart Landau equation forms (Kuramoto, 1996). Our present model was also constructed on the recent finding that most of oscillating neurons in the SCN shows damping under the isolated environment (Webb et al. 2009). Therefore, we assumed that most of oscillating neurons in the SCN were damping oscillators but have potential to generate limit cycle oscillators by appropriate external forces. In addition, we supposed a phase-dependent gate in the oscillators in the VLSCN which shut out the photic input to the SCN during the day, which had been recognized in the VLSCN of mammalians. We examined whether the model reproduced the asymmetrical resynchronization process associated with the abrupt shift of light: dark cycle (LD cycle; L:D=12h:12h). An abrupt shift of the LD cycle yielded internal desynchrony between VLSCN and DMSCN transiently which caused a jet lag syndrome (Nagano et al. 2003). The asymmetry appeared in the way of resynchronization; it took five days to restore synchronization after 10-hour delay and took more than 10 days after six-hour advance. The present model reproduced the asymmetrical expended time spent in resynchronization process after the rapid shift of the LD cycle. The model also reproduced the intrinsic phase wave shown in the SCN. The phase wave is propagated from the medial regions to the lateral regions in the SCN. By placing a small region containing short period oscillators (short period region: SPR: $\tau < 24h$) and remaining large region containing long period oscillators (long period region: LPR: $\tau > 24h$), the phase wave appeared, being initiated at SPR and propagated to LPR. Moreover, the phase response curve (PRC) generated from the present model by using the pulse-like input considerably corresponded to empirical PRCs obtained from locomotor activities of rats and mice.