DTU Compute
Department of Applied Mathematics and Computer Science

MSc Thesis Project: Circadian Rhythm in Neural Networks and in Social Networks

Section for Dynamical Systems (DYNSYS)

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TAGS (projektbank.dtu.dk, section web-site): DYNSYS, eama, CIRCADIANRHYTHMS

Primary study lines: Math. Modeling & Computing, Physics & Nanotech., Applied & Eng. Math. (N5T), Biomed. Eng.

Project background. In the human or in mammals, the sleep/wake cycle (circadian rhythm) is mainly regulated by the supra-chiasmatic nucleus (SCN, see Figure): a network consisting of $N \sim 10^4$ neurons. Neurons in the SCN oscillate with a period typically around 24.5 h, and synchronize their phases so that they exhibit a common rhythm so that they act like one giant clock: the SCN serves as a *primary master clock* to control physiological processes in our body that adhere to a circadian rhythms. Such processes are vital and occur at the level of the body, organs, hormone production and individual cells, where they control body temperature, blood pressure, stress hormone release etc. Without external stimuli, cells in the SCN is slightly longer than 24.5 h, and a human will go through a sleep/wake cycle that is out of phase with the natural day/night cycle. However, under the sun's (or other) influence, the SCN's rhythm is locked to an exact 24 h cycle and matches the sun's cycle. – *Why is this important?* The absence of a regular daily activity or night work occurs in particular for shift workers, but may also for people who are exposed to frequent jet lag [2]. Entrainment to a regular circadian 24 h rhythm may be compromised by jet-lag or shift work. Failure to maintain a regular circadian rhythm *increases risk for disease* including clinical depression and cancer among other. While the solar activity is a primary effect entraining the circadian clock to an exact 24 h cycle, other important influences exist, in particular, *social interactions*. Thus, the social network and its interactions may greatly affect the ability to synchronize individual person's day/night rhythm.

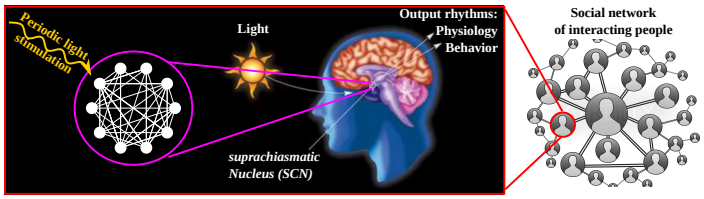

Figure 1: Left: A network of neurons (SCN) controls our human day/night rhythm and is reset by the sun's activity. Right: The day/night rhythm is also influenced via social interaction.

Model I. We formulate a model of the SCN rhythm based on individual neurons's dynamics, i.e. the rhythmic gene expression of N individual neurons is modeled via phase oscillator model [3],

$$\frac{d\theta_j(t)}{dt} = \underbrace{\omega_j}_{\text{uncoupled freq.}} + \underbrace{\frac{K}{N}\sum_{l=1}^{N}\sin\left[\theta_j(t)-\theta_i(t)\right]}_{\text{coupling from other neurons}} + \underbrace{F\sin\left[\sigma t-\theta_j(t)+p(t)\right]}_{\text{24 hr periodic external driving (sun)}} \tag{1}$$

where θ_j is the dynamic phase of neuron $j = 1, \ldots, N$. This N-dimensional microscopic dynamics can be reduced and studied to an effectively 2D problem in the phase plane [4].

Model II. A similar but more general macroscopic model can be formulated for the wake/sleep phases ϕ_j of interacting people in a social network, where a node j represents one individual, and $K_ij(t)$ models a (time dependent) social interaction:

$$\frac{d\phi_j(t)}{dt} = \underbrace{\omega_j}_{\text{uncoupled freq.}} + \underbrace{\frac{1}{N}\sum_{l=1}^{N}K_{ij}(t)\sin\left[\phi_j(t)-\phi_i(t)\right]}_{\text{influence from other people}} + \underbrace{F\sin\left[\sigma t-\phi_j(t)\right]}_{\text{24 hr periodic external driving}} \tag{2}$$

Project aims and questions. The project builds and extends on existing literature [1, 3].

1. **Model 1**: What is the dynamic behavior of neurons with periodic forcing? What is the transient dynamics during re-synchronization after a one-time perturbation (such as jet lag)? Optimized methods to boost the re-synchronization process in terms of speed, e.g. via specially designed light devises?
2. **Model 2**: What has a stronger impact on resetting the circadian clock to $T = 24$ h, the sun's activity or stimuli from social interaction? How and when do people in a social network synchronize their day/night rhythms? How do model predictions match social network data?

Methods: bifurcation theory, dynamical systems theory, data analysis, simulation, dimensional reduction, network theory.

[1] L M Childs and S H Strogatz. Stability diagram for the forced Kuramoto model. *Chaos (Woodbury, N.Y.)*, 18(4):043128(1–9), 2008.

[2] B Hald and E A Martens. *Circadian Rhythms. Lecture notes in Mathematical Physiology.*

[3] Z Lu, K Klein-Cardeña, S Lee, T M Antonsen, M Girvan, and E Ott. Resynchronization of circadian oscillators and the east-west asymmetry of jet-lag. *Chaos*, 26(9), 2016.

[4] E Ott and T M Antonsen. Low dimensional behavior of large systems of globally coupled oscillators. *Chaos*, 18(3):037113, 2008.