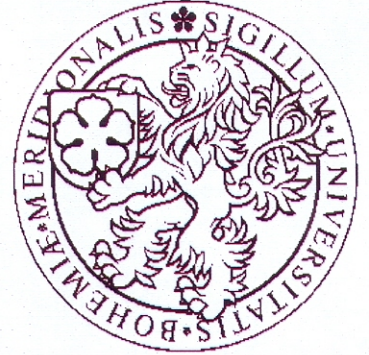


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**Review of dissertation thesis by Serhiy Sosniyenko entitled: “Entrainment of the Circadian System in Rodents”.**

Presenting dissertation thesis is focused on the biochemical and molecular characterization of the SCN entrainment in mice and rats. The entrainment abilities and dynamics of the circadian clock were tested under various, well-defined lighting conditions and in animals at different stages of their ontogenesis. The studies of circadian timing systems and their molecular properties, especially in mammalian model systems, are very relevant for current biology and medicine. It is well documented that circadian variations affect virtually all aspect of human physiology and disruption of circadian rhythms can contribute to many serious pathophysiological stages including sleep disorders, schizophrenia, onset of Parkinson and Alzheimer diseases, and even cancer. Thus, increased understanding of the fundamental mechanisms of biological clock function will facilitate the development of better treatment for a wide range of human disorders.

The presented thesis consists of Abstract, brief Introduction, Review of our current knowledge of the mammalian circadian biology, Aim of the Work, Methods, Results and Discussion, Conclusions, Summary, References, and five original research articles included in the Attachment. The Review chapter with its 35 pages represents the most extensive part of the thesis. Here the author summarizes the current understanding of the chronobiology field including the general introduction into biological rhythms, circadian systems, molecular and genetic bases underlying the circadian rhythmicity, as well as synchronization and development of the circadian clock machinery.

The following chapter of the thesis, the Results and Discussion, presents results of the research that are further described and discussed in detail in the five attached papers. The Conclusions section synoptically summarizes the major achievements of the author's results. All the aforementioned chapters are supplemented by more than 130 references of cited literature documenting the Ph.D. candidate's ability to work with the original scientific resources. Finally, as already mentioned above, the last part of the dissertation thesis consists of five attached original articles. All five papers in the Attachment section were already published in international scientific journals with IF ranging from 1.5 to 4.2. This fact makes my task as a reviewer of this thesis much simpler, because each of the published research article had to undergo a rigorous international peer-review process before the publication, and there is no need for me to question its quality and objectivity.

I have the following, mostly minor, comments and/or questions to the presented dissertation thesis:

1. I appreciate that the specific aims of the presented research are clearly stated at the beginning of the dissertation thesis. This makes the orientation of the thesis reader through the conducted research much easier.
2. The reproductions of some color Figures (e.g. Fig. 2 and Fig. 3) are rather of poor quality, some of the text in the figures is unreadable or at least difficult to read.
3. In the Review part of the thesis (pages 21-26), the encyclopedic list of known circadian genes and description of their functions in the molecular clock machinery, taken out of the "whole dynamic clock picture" contents, is quite redundant and for "non-clock" reader quite difficult to follow. I believe the following sub-chapter 2.3.3. describing our current understanding of the molecular mechanism underlying the mammalian circadian clock is sufficient for the purpose of the thesis, and it is much more useful and easier to understand.
4. I also believe that the chapter 5. Overview of the Results and Discussion could be significantly abbreviated since virtually all the results are included and discussed in great details in the attached research articles.
5. One sentence on the page 18 (top line) is not completed; but otherwise I found only few misprints and typing errors in the entire thesis.
6. My final question is as follow: In several experiments in the thesis the transcriptional regulation of *c-fos* gene is measured/monitored in the SCN. The *c-fos* is a proto-oncogene, one of the canonical genes (transcription factors) involved in the eukaryotic cell cycle regulation. I would like to ask the author, what is the actual molecular action, if any, of the c-Fos in the mammalian clock machinery. Also, is the dimerization partner of c-Fos, the c-Jun protein also expressed in the SCN? And finally, is it known whether the *c-fos* knock-out/knock-down mice have any alteration in their circadian timing system?

In the summary of this review I would like to state that the presented dissertation thesis fulfils, according to my opinion, all postulations imposed upon the Ph.D. thesis and I recommend it to be accepted as a partial fulfillment of the requirements for the degree of Doctor of Philosophy at the Faculty of Medicine of the Charles University in Prague.

In Ceske Budejovice, September 15, 2010

Ivo Šauman