# General Theoretical Aspects of Cell Mechanics from Circadian Oscillator Point of View Based on Higher Order Logic(HOL) – A Short Communication to Develop Informatics Framework Involving Bio-Chemical Concepts of Cells and Mobile Computing Environments.

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**Abstract :**

We observe the “internal clock” that man possesses in common with animals,plants and protists has drawn the interest of scientists and researchers from diverse fields of science and technology. Performing R&D in this promising and challenging domain of circadian rhythms is very much useful to those engaged in research in general,industrial and aerospace medicine.It is in this context it was decided to work on topics involving circadian rhythms and formalisms based on Higher Order Logic(HOL) using Dynamic Architecture concepts to further evaluate the theories involved and to come up with certain informatics frameworks. To the best of our knowledge this paper is one of the pioneering topics in the domain of “Circadian Systems” and its informatics.

**Key words :** Circadian Systems,HOL,Informatics,Cell Mechanics,Internal Clock.

## I. Introduction :

By definition “Circadian Rhythms” are physical, mental and behavioral changes that follow a roughly 24-hour cycle, responding primarily to light and darkness in an organism's environment.They are found in animals, plants and many tiny microbes.The study of circadian rhythms is called “chronobiology”. Our biological clocks drive our circadian rhythms.”The biological clocks that control circadian rhythms are groupings of interacting molecules in cells throughout the body.Researchers have already identified genes that direct circadian rhythms in people,fruit flies, mice, fungi and several other model organisms used for studying genetics.Circadian rhythms are produced by natural factors within the body, but they are also affected by signals from the environment. Light is the main cue influencing circadian rhythms, turning on or turning off genes that control an organism's internal clocks.Circadian rhythms can influence sleep-wake cycles, hormone release,body temperature and other important bodily functions”. [1-11].Figures I- IV explain the R&D work illustrated in this paper.

## II. Design of Informatics Framework Based on HOL :

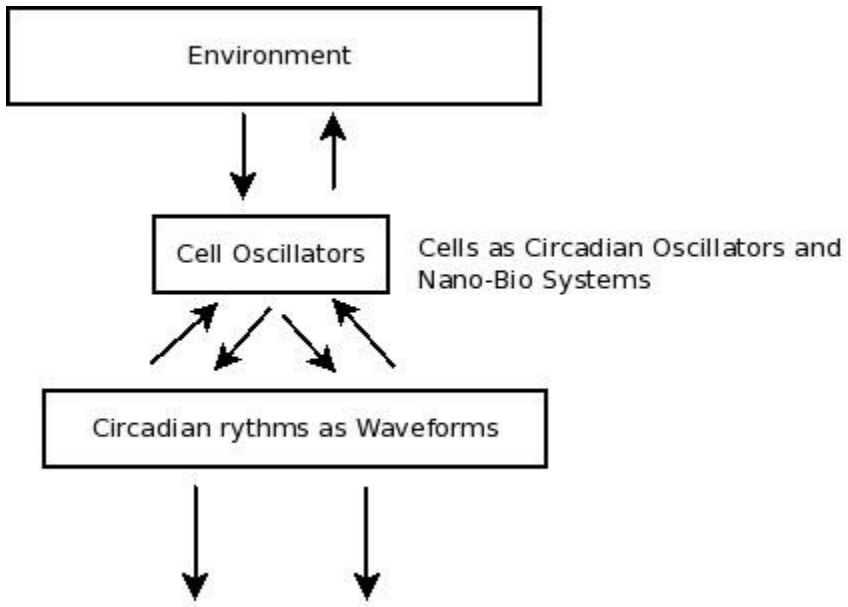


**Figure I. Simple/Basic Block Diagram Representing Environment interaction with Cells and finally producing the Circadian Rythms as waveforms for further display and analysis.Circadian oscillators are controlled through a common mechanism.**

“Although circadian rhythms are endogenous ("built-in", self-sustained), they are adjusted (entrained) to the local environment by external cues called zeitgebers (from German, "time giver"), which include light,temperature and redox cycles.Light resets the biological clock in accordance with the phase response curve (PRC). Depending on the timing,light can advance or delay the circadian rhythm. Both the PRC and the required illuminance vary from species to species”.[5-11]

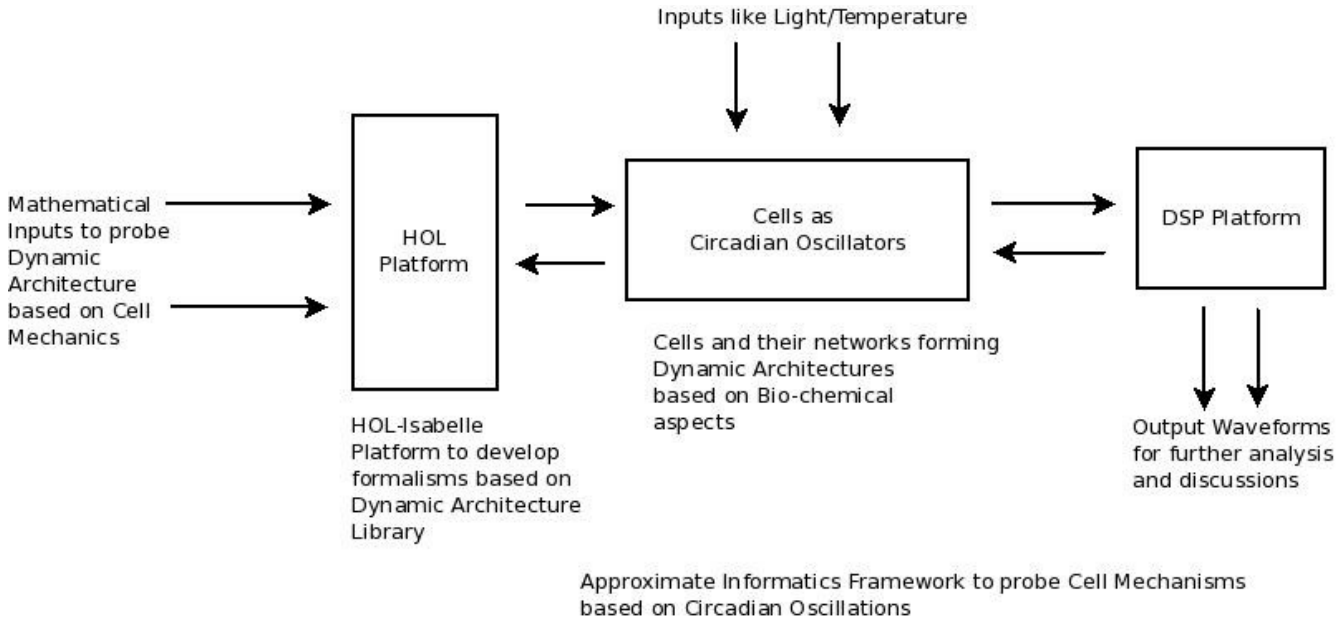


**Figure II. Approximate Informatics Framework describing the HOL – Dynamic Architecture of Cells as Circadian Oscillators.[[a-l] and [i-iii]]**

"Most circadian systems use a clock mechanism involving oscillators that are composed of positive and negative elements, which form feedback loops. In these loops, the positive elements activate the expression of the clock genes.The clock genes, as well as driving rhythmic biological outputs, encode negative elements that inhibit the activities of the positive element. These oscillators receive environmental input and, either alone or coupled to other oscillators, send signals through an unknown mechanism to the rest of the organism to control rhythmic behaviors".[7-11]

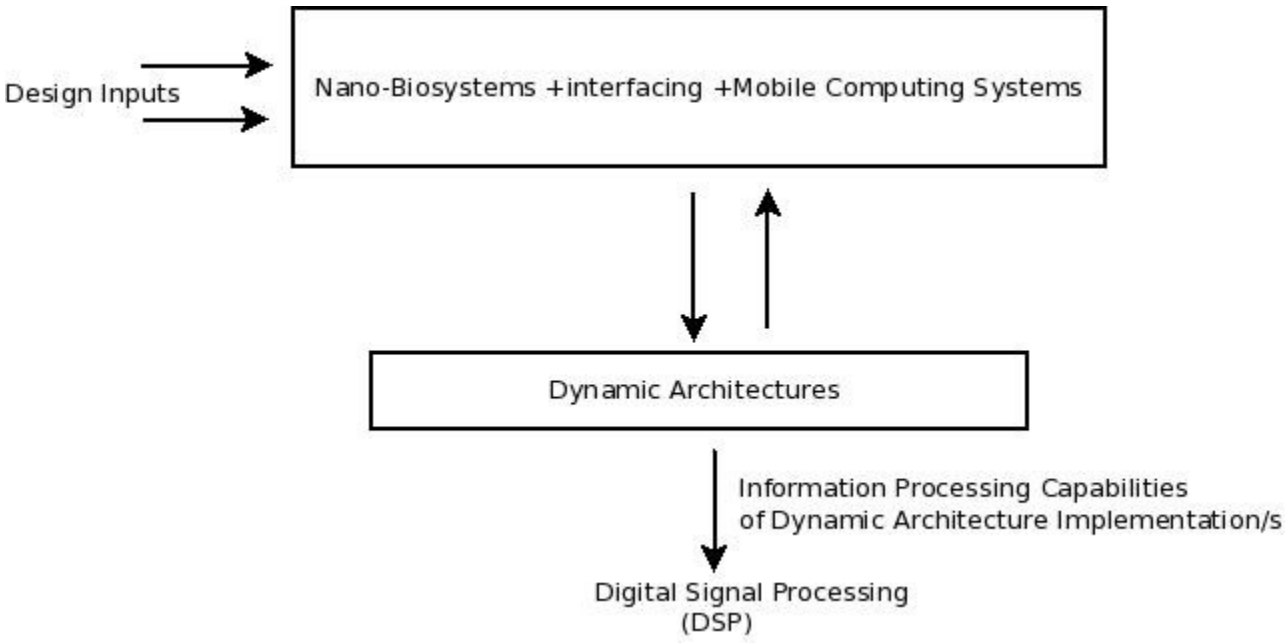


**Figure III. Approximate Schema of Dynamic Architecture Implementation.**

Dynamic architectures are needed for modeling reconfigurable systems or systems that adapt their behavior to changing environments. They are defined as the composition of dynamically changing architecture constraints offered by their constituent components. As a rule, using dynamic architectures may lead to more concise models to design and implement complex systems involving Cells.

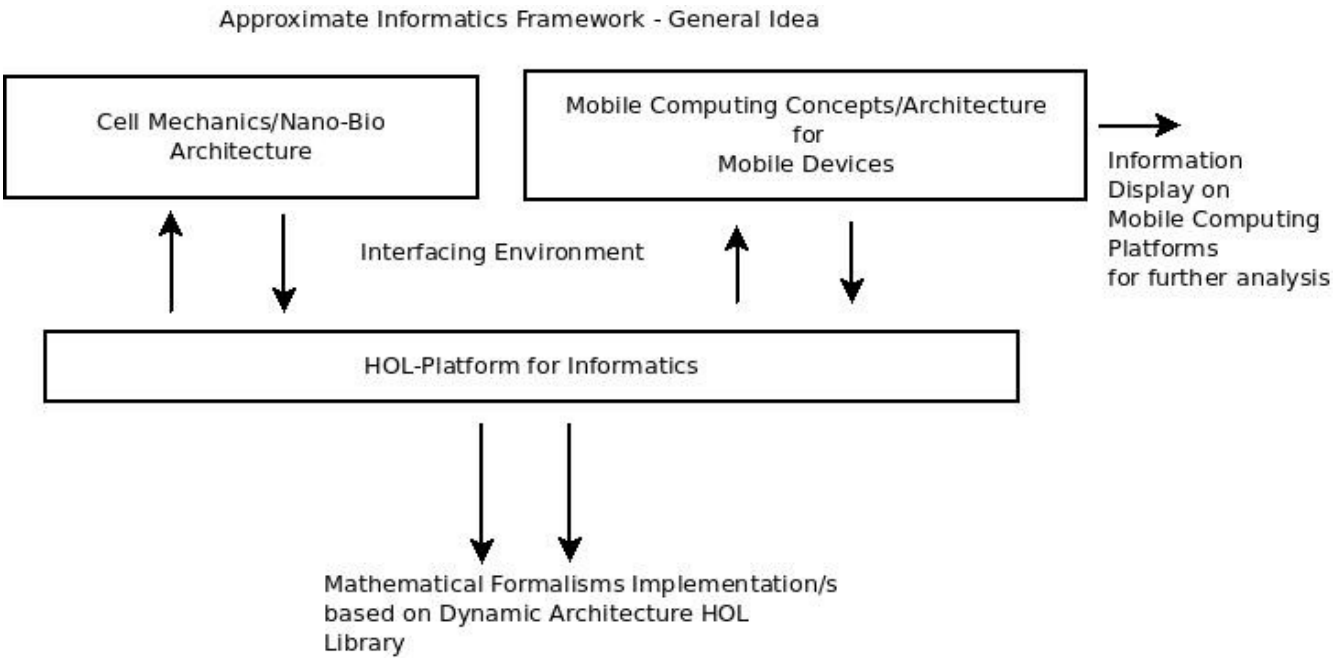


**Figure IV. Approximate Informatics Framework – General Idea about HOL Based Formalisms. Nano-Bio Systems Interfacing with Computing Platforms.**

**Algorithm could be designed on the following factors :**

1. Definition of a logic for the description of architecture constraints. The specified logic is expressive and amenable to analysis and reasonable implementation.

2. Study of a feasible model and a modeling methodology for writing architecture constraints associated with specified inputs.

3. Implementation principles for informatics frameworks handling symbolic architecture constraints.

4. Experimental results and benchmarks showing benefits from using dynamic architectures.

***** Please make a note :** The actual implementation/s both theoretical as well as practical could vary.Depends upon the R&D aim/s of the project in question.

## III. Discussion & Analysis :

The Informatics Framework and its architecture of a system describes the system's overall organization into components and connections between those components. With the emergence of mobile computing platforms involving nano-bio systems, dynamic architectures have become very much promising and increasingly important. In such architectures, components may appear or disappear, and connections could change over time.It is in this context,we propose a feasible computing and informatics platform based on HOL by considering the related mathematical formalisms.Since the nature of this paper is short communication it is not possible to discuss the implementation on an in-depth basis.[1-11]

## IV. Conclusions with Future Perspectives :

To finally conclude,many aspects of biological function are governed by circadian rhythms, including metabolism, ingestive behaviors, and sleep-wake cycles. Further,it is possible to observe that certain pathological processes are also affected by circadian rhythms.HOL based formalisms were proposed to probe circadian rythms from a “Dynamic Architecture” point of view involving “Cells” as Nano-Bio scale Systems or Machines with out going into too much details in the context of “Mobile - Computational Environments”.Current research work could serve as an inspiring paper for researchers in this challenging and promising field based on Higher Order Logic(HOL) as an informatics tool.During the past five years or so we have seen a remarkable set of interesting discoveries concerning the circadian clock mechanism in mammals.An important goal for our future work is to define novel regulatory pathways within the clock mechanism, to understand the bio-chemical mechanisms of the above mentioned concepts.

## V. Additional Information on Mathematics & Software Used :

“Isabelle is a generic proof assistant. It allows mathematical formulas to be expressed in a formal language and provides tools for proving those formulas in a logical calculus. Isabelle was originally developed at the University of Cambridge and Technische Universität München, but now includes numerous contributions from institutions and individuals worldwide. See the Isabelle overview for a brief introduction.” Please see the sources/references cited below.

**Source/s :**

[i] https://www.cl.cam.ac.uk/research/hvg/Isabelle/

[ii] https://www.isa-afp.org/entries/DynamicArchitectures.html

[iii] https://www.isa-afp.org/browser_info/current/AFP/DynamicArchitectures/document.pdf

**VI. Chronobiological Resources on the World Wide Web :**

[a] http://www.nwu.edu/ccbm/ - Web site of Northwestern University's Center for Sleep and Circadian Biology

[b] http://www.sleepquest.com/ - Information site of William Dement's Sleep Research Center

[c] http://www.med.stanford.edu/school/ - Narcolepsy site created by Emmanuel Psychiatry/narcolepsy Mignot at Stanford University USA

[d] http://www.sleepfoundation.org/ - Web site of the National Sleep Foundation

[e] http://www.srbr.org/ - Web site of the Society for Research on Biological Rhythms

[f] http://www.cbt.virginia.edu/ - Web site of the Center for Biological Timing at the University of Virginia USA.

[g] http://www.hhmi.org/grants/lectures - Web site providing Howard Hughes Medical Institute Holiday Lectures ;

[h] http://www.hhmi.org/research/molecular-and-genetic-analysis-mammalian-circadian-clocks

[i] http://millar.bio.ed.ac.uk/Downloads.html ;

[j] http://wsbc.warwick.ac.uk/software/

[k] http://www.research.ed.ac.uk/portal/files/28252291/paper_16.pdf

[l] http://www.dana.org/Media/GrantsDetails.aspx?id=38920

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No competing financial interest/s is/are declared in preparing this manuscript. This manuscript is meant to inspire others to develop more advanced circadian software and its applications in this demanding area of sleep studies using novel methodologies based on HOL. The Authors strictly abide by all copyright agreements in using open source software or other such technologies used in this paper. Special thanks to all who made this happen.We thank FAPESP R&D funding via Versor Innovations/Tech 4 People Project,Santo Andre,SP,Brazil for generously supporting our research work.

**References :**


[1]. PITTENDRIGH, C.S. Circadian rhythms and the circadian organization of living systems. Cold Spring Harbor Symposia on Quantitative Biology: Volume XXV. Biological Clocks. New York: Cold Spring Harbor Press, 1960. pp. 159-184.

[2]. ASCHOFF, J. Exogenous and endogenous components in circadian rhythms. Cold Spring Harbor Symposia on Quantitative Biology: Volume XXV. Biological Clocks. New York: Cold Spring Harbor Press, 1960. pp. 11-28.

[3]. KING, D.P., AND TAKAHASHI, J.S. Molecular genetics of circadian rhythms in mammals. Annual Review of Neuroscience 23:713-742, 2000.

[4]. LOWREY, P.L., AND TAKAHASHI, J.S. Genetics of the mammalian circadian system: Photic entrainment, circadian pacemaker mechanisms, and post-translational control. Annual Review of Genetics 34:533-562, 2000.

[5]. WAGER-SMITH, K., AND KAY, S.A. Circadian rhythm genetics: From flies to mice to humans. Nature Genetics 26:23-27, 2000.

[6]. DEMENT, W.C. History of sleep physiology and medicine. In: Kryer, M.H.; Roth, T.; and Dement, W.C., eds. Principles and Practice of Sleep Medicine. 3d ed. Philadelphia: W.B. Saunders, 2000

[7]. https://pubs.niaaa.nih.gov/publications/arh25-2/85-93.htm – Overview of Circadian Rythms.

[8]. D. A. Rand, B. V. Shulgin, D. Salazar & A. J. Millar (2004). Design principles underlying circadian clocks. Journal of The Royal Society, Interface. 1(1): 119-130

[9].Rand DA, Shulgin BV, Salazar D, Millar AJ. (2006) Uncovering the design principles of circadian clocks: mathematical analysis of flexibility and evolutionary goals. J Theor Biol, 238:616-635. Published online August 2005..

[10].D. A. Rand. Mapping the global sensitivity of cellular network dynamics: Sensitivity heat maps and a global summation law. J. R. Soc. Interface (2008) doi:10.1098/rsif.2008.0084.focus.

[11]. https://en.wikipedia.org/wiki/Circadian_rhythm