A Graphical User Interface for an Automatic Rest-activity Cycle Detection and Dichotomy Index Computation

Racha Soubra[1], Aly Chkeir[1], Mohammad O. Diab[2], Majd Abdallah[1] and Jacques Duchene[1]
[1]University of Technology of Troyes, France
[2]Rafik Hariri University, Meshref, Lebanon

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Abstract: The success of chemotherapy treatment is achieved based on “Chronotherapy”: the concept of administering the correct drug at a precise time based on the circadian rhythm study. This paper aims to detect the rest/activity cycle and automatically calculate the dichotomy index (I<O), as both parameters have been proved to be reliable indices of the circadian rhythm. First, the DARC “Détection Automatique du Rythme Circadien” algorithm is used to segment the rest-activity phases automatically. Then, a Graphical User Interface (GUI) is used to calculate easily the I<O across several days of records and smooth the analysis. The outcome of this study provides an easy-to-use GUI that minimizes patients’ intervention, facilitates user involvement, and reduces the time required for analysis.

1 INTRODUCTION

The endogenicity of the circadian rhythm persists in constant environment in microorganisms, plants and in all kinds of animal species including man (Levi 2006). These endogenous rhythms manage daily events such as sleep, activity, hormonal secretion, cellular proliferation and metabolism (Levi 2006). Scientists have shown that the rest-activity cycle is a reliable marker of the circadian system function. locomotor activity dependably reflects the circadian clock function in several animal species like rodents and man. It is evident that researchers focus their work on examining the circadian rest-activity rhythm disturbances among patients with several diseases mainly cancer. For instance, Mormont, M. and Levi, F. documented the link between the rest-activity rhythm and the welfare of cancer patient (Mormont and Levi 2003). In their study, it was clear that the circadian rhythm tends to be lost in the rapidly growing or advanced stage of tumors. Similarly, in Levin, R. et al research study, the rest-activity circadian function differs significantly between patients with advanced non-small-cell lung cancer and control subjects (Levin, Daehler et al. 2005). Outcomes have shown that patients suffer poor sleep quality and high levels of fatigue. In addition, Mormont, M.et al found that patients with poor circadian rhythmicity had a 5-fold higher risk of dying within 2 years than the patients with a better circadian rhythm (Mormont, Waterhouse et al. 2000). Consequently, the rest-activity rhythm is a determinant of quality of life. Its level of disturbance can be set as a reference for anti-cancer efficacy and tolerability. Therefore, the rest-activity rhythm can provide additional prognostic information regarding patients’ response to treatment and maximum survival potential since it reflects tumor burden and patient general conditions (Mormont, Waterhouse et al. 2000, Mormont and Levi 2003, Rich, Innominato et al. 2005).

Moreover, the circadian or rest-activity disruption in patient with cancer is the result of chronic illness development and worsening of pre-existing conditions (Ortiz-Tudela, Martinez-Nicolas et al. 2010). However, these disruptions can resulted from a “wrongly timed or excessively dosed chemotherapy”. Scrully, C. et al proved that the circadian timing of anti-cancer medications improves treatment tolerability up to fivefold and doubles the efficacy in experimental and clinical studies (Scully, Karaboué et al. 2011). Therefore, the time-qualified chemotherapy, known as by “Chronotherapy”, is an essential element for cancer treatment. It guarantees improved cancer-treatment and optimizing the development of new anticancer or supportive agents (Mormont, Waterhouse et al. 2000, Levi 2001).

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Personalized cancer chronotherapeutics encourage the cell division cycle and the pharmacology pathways to improve patients' quality of life and survival (Lévi, Filipski et al. 2007). Thus, the circadian rhythm needs to be explored on large scale, and circadian biomarkers should be calculated to estimate the incidence of cancer-associated circadian-system alterations.

The most effective parameter that can correlates with the quality of life is the dichotomy index (I<O) (Mormont, Waterhouse et al. 2000, Innominato, Focan et al. 2009, Natale, Innominato et al. 2015). This latter represents the percentage of the activity counts measured when the patient is in bed that are inferior to the median of the activity counts measured when the patient is out of bed. This index can theoretically vary between 0 and 100%, where high I<O reflects a marked rest/activity rhythm.

In order to record rest-activity cycle, the majority of recent studies used wrist actigraphy; a wearable device used to measure the activity motors. On the other hand, various techniques were used to calculate the I<O. For instance, in Mormont, M. et al study, the calculation was done manually where each patient had kept a diary for times of rising and retiring during the diagnosis (Mormont, Waterhouse et al. 2000). Scrully, C. et al and Ortiz-Tudela, E. et al have used square and mean waveform techniques respectively which resulted as a poor biomarkers (Innominato, Focan et al. 2009, Ortiz-Tudela, Martinez-Nicolas et al. 2010). In Ortiz-Tudela, E. et al study, patients were requested to give an informed consent and to complete a sleep and feeding log during the days of recording (Ortiz-Tudela, Iurisci et al. 2014). Finally, some patients were demanded to push an event-marker button on the wearable device to mark occurrences of time in and out of bed such as Natale, V. et al research (Natale, Innominato et al. 2015).

In this study, we aim to detect the rest- activity cycle automatically and calculate the I<O while minimizing the intervention of patients and smoothing the interference of physicians. After data acquisition, I<O was calculated automatically based on DARC algorithm. Then, a graphical user interface (GUI) was performed to detect and calculate automatically rest-activity cycle and I<O.

2 METHODOLOGY

2.1 Database

Our study is based on 9 control subjects (5 females and 4 males) aged 40 ± 10.6 years. After receiving a detailed description of the objectives and requirements of the study, the participants wore the infrared sensor "Movisens GmbH - move II". The move II sensor consists of a tri-axial acceleration sensor (adxl345, Analog Devices; range: ±8 g; sampling rate: 64 Hz; resolution: 12 bit) and a temperature sensor (MLX90615 high resolution 16bit ADC; resolution of 0.02°C). This sensor was patched onto the participants' upper right anterior thoracic areas by means of a hypoallergenic patch for a minimum of three consecutive days. It only weighs 32 g, and measures 5.0 x 3.6 x1.7 cm3. The recorded data is saved on a memory chip inside the sensor and transferred to a server via the General Packet Radio Service (GPRS). Three signals were available:

- Zero Crossing Mode (ZCM) signal: representing the human activity in function of time, with 1 record per minute
- Body Position: representing the human body slope with respect to the vertical x-axis, with 1 record per minute
- Body Temperature: representing the human body temperature, with 1 record every 5 minutes

2.2 Rest/Activity Cycle Detection

In this study, the automatic detection of rest/activity cycle is achieved based on the "Détection Automatique du Rythme Circadien" (DARC) algorithm (Chkeir et al. 2017). Six phases summarize our work, and for confidential reasons, it will be discussed generally in a brief way.

First, as we have one record of body temperature each 5 minutes and one record per minute for each of body position and ZCM signals, the Polynomial Cubic Spline method is used to interpolate the temperature signal, so we get an equal number of records between signals. The interpolated temperature signal intervenes as a reference to check if the sensor is worn or not. The algorithm will directly eliminate the body position and ZCM records when sensor is not worn. In case the sensor is worn upside down, the algorithm will correct the Body Position signal: when X is greater than 90, the value will be replaced by 180-X.

Subsequently, all outlier points that could appear in the signals will be eliminated based on the median filter techniques. After that, the method cited in the DARC Brevet automatically operates to separate between rest/activity phases for both signals.

After detecting the indices for each of the rest and activity phases, the ZCM and body position signals are converted into binary signals, where 1 represents the activity cycle and 0 represents the rest cycle. The “AND” logical operator is applied to combine the two binary signals, so new indices can state accurately the starting and ending point of each phase.

2.3 Graphical User Interface

Graphical user interface, abbreviated by GUI, is a software interface that works at the point of contact between a computer and its user. It allows the user to interact with computers through graphical elements, such as dialog boxes, pointing devices, push-buttons, menus, and scroll bars. By selecting one of these visual elements, either by mouse, pen or other selection from menu, the user can manipulate what is on screen and control commands to run a program without writing a text characters.

The main reason from creating a GUI is to make things simple for the program end-users. In order to accomplish a task, users do not have to edit the command line interface, create a script command, or even understand the details of how tasks are performed. Applications that are based on GUI are simple to learn and run.

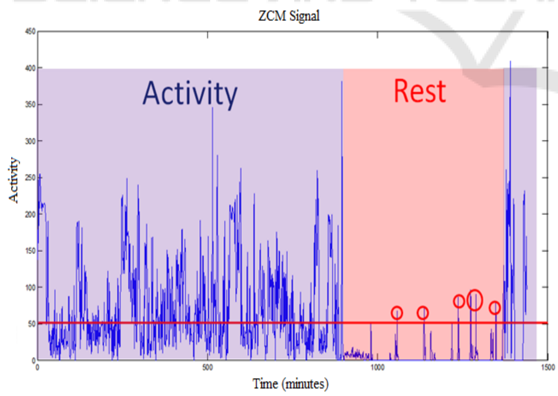

Figure 1: Segmentation of Rest/Activity cycle and application of I<O formula.

Accordingly, in order to automatically calculate the I<O and facilitate the intervention of users (physicians, clinicians, researchers…), we aimed to perform an easy-to-use GUI. The goals of this GUI were to: (i) Detect the rest/activity cycle either automatically through the DARC algorithm or manually by user involvement and (ii) Calculate automatically the I<O while applying the following formula:

$$I{<}O = (1 - NB\_L/NB\_C) \times 100 \quad (1)$$

Where NB_L represents the number of activities recorded during the day and NB_C represents the number of activities recorded during the rest period that are greater than the median of NB_L.

3 GUI RESULTS

In this section, we demonstrate the GUI usage shown in Figure 2.

First, users import the Patient Excel File (xls, xlsm, xlm…).

Then, they could choose between ‘Manually’ and a ‘Graph’ radio-button to select the starting time of the day. If the ‘Manually’ option is chosen, a Time Panel will appear on the screen. Users select the appropriate time and then press ‘Set’. If the ‘Graph’ option is chosen, the select cursor will be available and ZCM signal will be plotted. So, users select a starting point from the graph. Time will be displayed on the screen with an option of Reset.

At this time, users will have the opportunity to edit ‘threshold’ and ‘filter’ values as convenient.

To segment rest-activity cycle, users can choose an ‘automatic’ and/or ‘manual’ detection methodology. If ‘Automatic Detection’ is chosen, users can press ‘Activity/Position’ to plot signals segmentation and ‘Average’ buttons to get I<O results. Once the ‘Activity/Position’ button is pressed, ZCM and position signals will be plotted in graphs 1 & 2 respectively showing the rest/activity phases. ‘Next’ and ‘Previous’ buttons are available to show the plots across each day. If ‘Manual Detection’ is chosen, a ‘help window’ will be displayed asking the users to select the intervals of sleep across each day plotted separately in graph 1. If users select the sleep intervals wrongly, a ‘warning window’ will be displayed requesting the repetition of the manual detection procedure. If both ‘automatic’ and ‘manual’ detection techniques are chosen, the ‘Auto/Manual Activity’ button can be pressed to plot the difference of segmentation between both techniques and for each day.

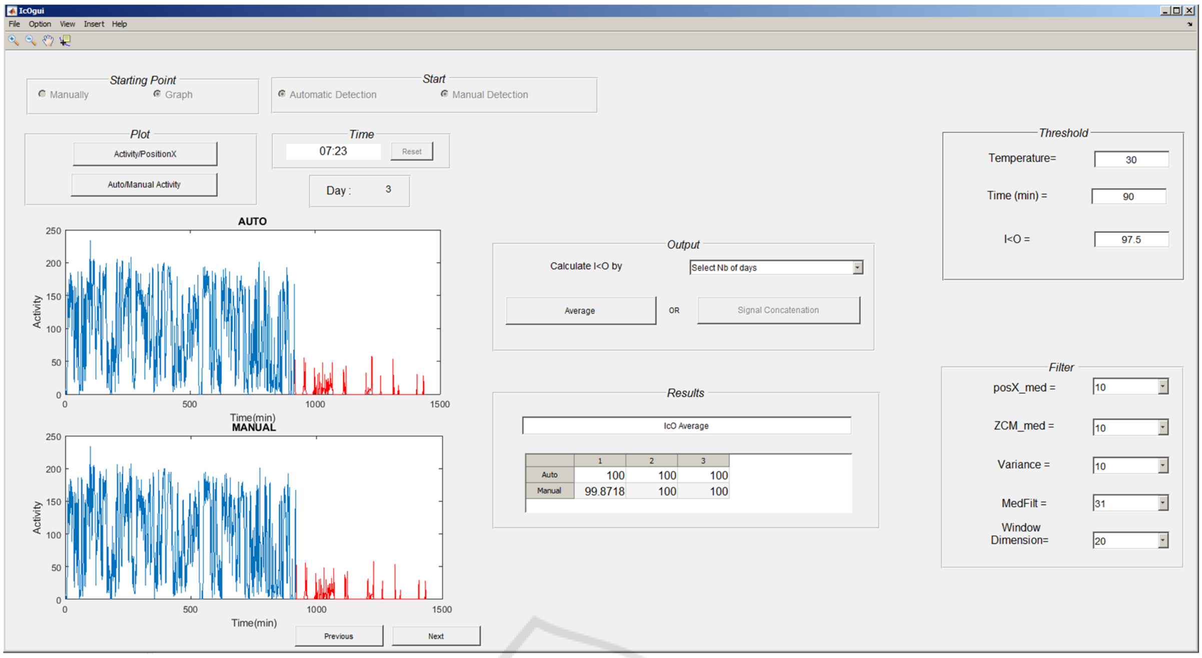

Figure 2: Graphical User Interface.

After the rest-activity detection, users can press the 'Average' button to examine the I<O results of each day coordinated in a table. Additionally, they can select the number of days (X) to calculate the I<O average of each X consecutive days.

To save the plotted figures and results, users have the option of selecting a folder and the excel filename. For each day, figures and I<O results will be plotted on a separate sheet titled by the day number. Moreover, the I<O table will be copied to 'I<O Results' sheet.

A 'Restart' button is available to repeat the process. Once this button is clicked, a message box will appear to ensure the restarting process. Similarity for the 'Exit' button, once it is clicked, a message box will appear to ensure the closing.

In order to validate our method, the student-test and mean squared error (MSE) measurements were evaluated. High correlation was found between I<O calculated automatically and those calculated manually, giving an R of 0.95 and MSE of 0.022.

4 DISCUSSION

The I<O, a reliable marker of rest/activity cycle, has been used frequently in order to identify the optimal time of the chemotherapy. In addition, it was demonstrated that this parameter can give physicians supplementary information for about the patients' quality of life. Therefore, an automatic detection of the rest and activity phases can minimize the patient's intervention, reduce the time required for I<O calculation and encourage more related studies. Additionally, a GUI can facilitate the users' intervention and reduce the time of analysis.

In the first part of our study, patients intervened only by wearing the Movisens. Data was directly saved on a memory chip and transferred to the server via GPRS. The I<O of each subject was calculated automatically. Then, a comparison of I<O results was performed.

Next, a GUI was performed. Several options and advantages encourage its usage. For instance, the user has the option of segmenting rest-activity cycle automatically and/or manually. Accordingly, a comparative study can be performed between the two techniques. Moreover, several parameters are set as "variable data" such as I<O threshold, temperature reference value, median filter and others. Therefore, these factors can be changed based on the user analysis and depending on each subject. Then, segmented graphs, stating each of the rest and activity phases, can be plotted for each recorded day. Therefore, physicians can see the relation between rest-activity cycle and I<O results for both manual and automatic detections and save outcomes on Excel File. Last but not least, a clear demonstration is available with the GUI to smooth

the user interface and explain other supplementary options.

5 CONCLUSION

In this paper, we provide physicians and researchers with a new technique to detect the rest-activity cycle and calculate the dichotomy index automatically. This work provides an easy-to-use graphical user interface. It incorporates our listed purposes with several analysis options that vary according to the user requirements for an enhanced I<O study and an improved chronotherapy. Physicians can detect the optimal time for a chemotherapy treatment so that a better quality of life and less disturbance of circadian rhythms can be achieved.

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