Features of a Chronomics Analysis Toolkit (CATkit)

[1]Cathy Lee Gierke, [2]Jarmila Siegelova, [3]Yoshihiko Watanabe, [2]Kuniaki Otsuka, [4]Denis Gubin, [1]Germaine Cornelissen

[1]University of Minnesota, Minneapolis, USA; [2]Masaryk University, Brno, Czech Republic; [3]Tokyo Women's Medical University, Tokyo, Japan; [4]Medical Academy, Tyumen, Russia

University of Minnesota
Driven to Discover℠

Introduction

Chronomics, and the study of biological rhythms is a rapidly growing area of research. As the biological sciences embrace the impact of biological oscillators, and the vast network modulating genetic, molecular, physiological, and behavioral rhythms, there is increasing need for accessible tools to characterize rhythmicity. CATkit, an R package, provides rhythmic analysis, in exploratory and quantitative terms. It is free and ports to most platforms.

CAT Visualization & Quantitative Tools

Visual Assessment

- Actogram
- Smoothing
- Autocorrelation
- Crosscorrelation
- Periodogram by FFT

Only equidistant data

Quantitative Assessment

- Single-component cosinor
- Multiple-component cosinor
- Least squares spectrum
- Serial section cosinor
- Gliding spectrum

Model Building

Angina pectoris incidence by time of day and week 14 years of data stacked over 1 week

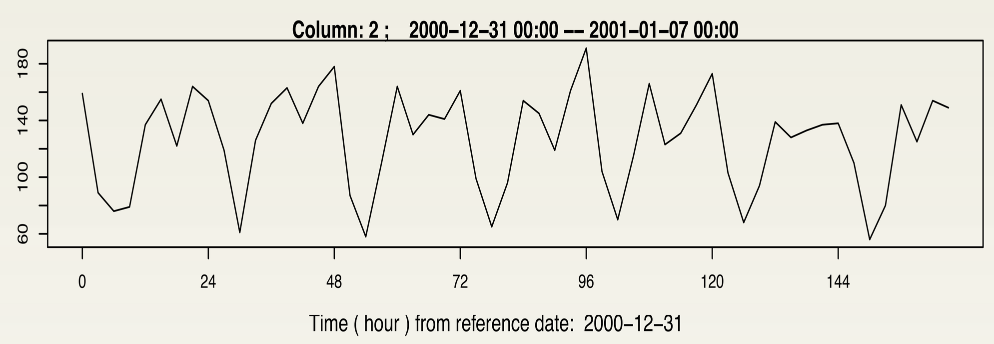

Figure 1: Raw data. Ambulance calls for angina pectoris in Khanty, Siberia, over 14 years. Wrapped over one week, Sunday to Saturday, in order to investigate weekly trends.

Least Squares Spectrum by Cosinor

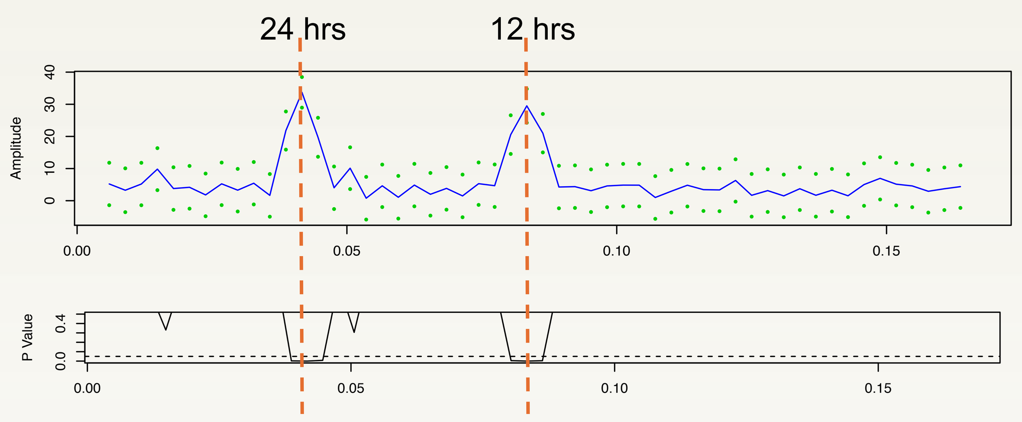

Figure 2: Results from spectral analysis to identify periodic components contributing most to the overall variance. Two periods show strongly: 24 and 12 hours.

Multiple-component cosinor

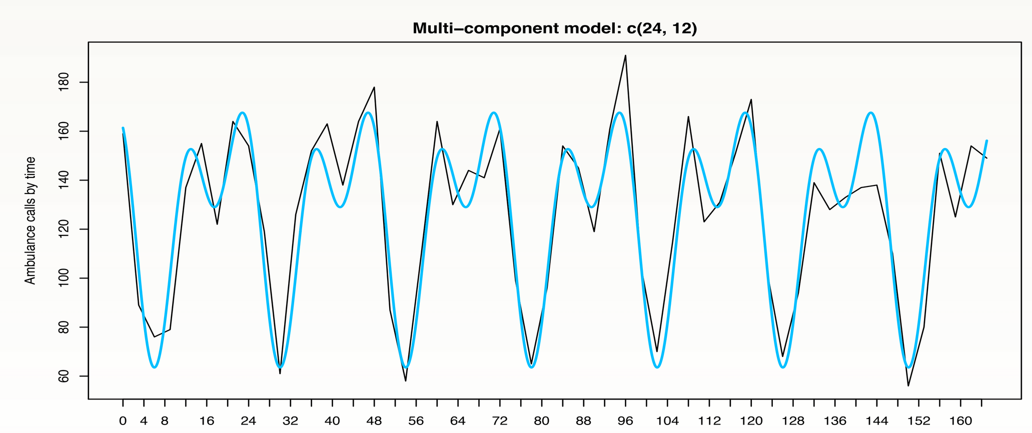

Figure 3 :A multiple-component model, built with both 24- and 12-hr cosines. Numeric results are provided from which conclusions can be derived regarding extent of predictable variation and timing of maxima/minima

Exploring the data: newborn HR

Smoothing: first 40 days of newborn HR

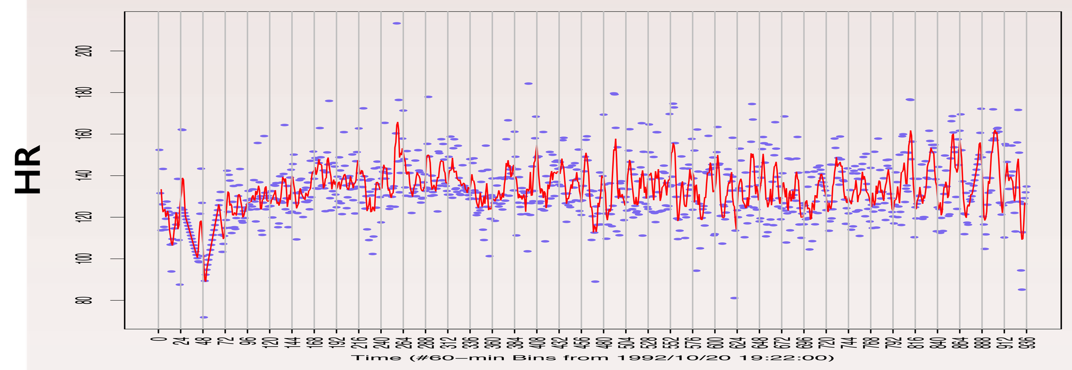

Figure 6: CATkit Smoothing averages a user-specified number of points. Data can be binned. Non-equidistant data have been interpolated. Here a 24-hr pattern can be seen near the end of the record.

Periodogram: HR days 33-40

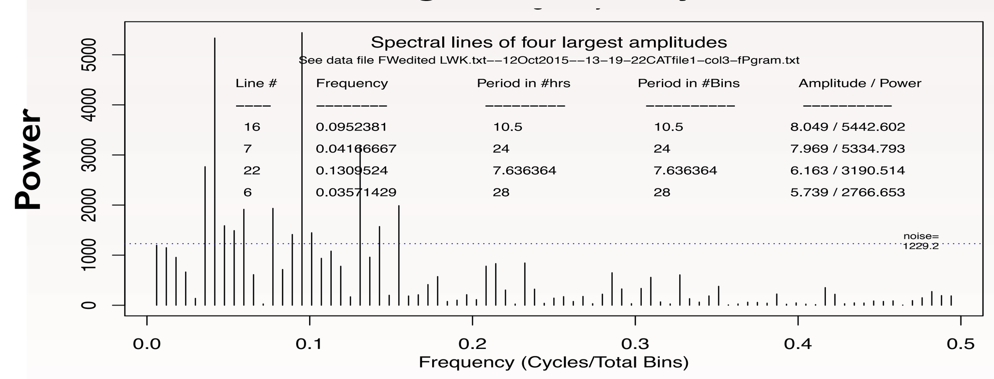

Figure 7: Days 33- 40 of the infant HR show strong 24-hr and 10.5-hr rhythms. Compare this to Figure 8. (A Least Squares Spectrum by cosinor will obtain the same results as a periodogram, in this case.)

Multiple-component cosinor model

SBP variation over 7 days: 24 & 12 hours

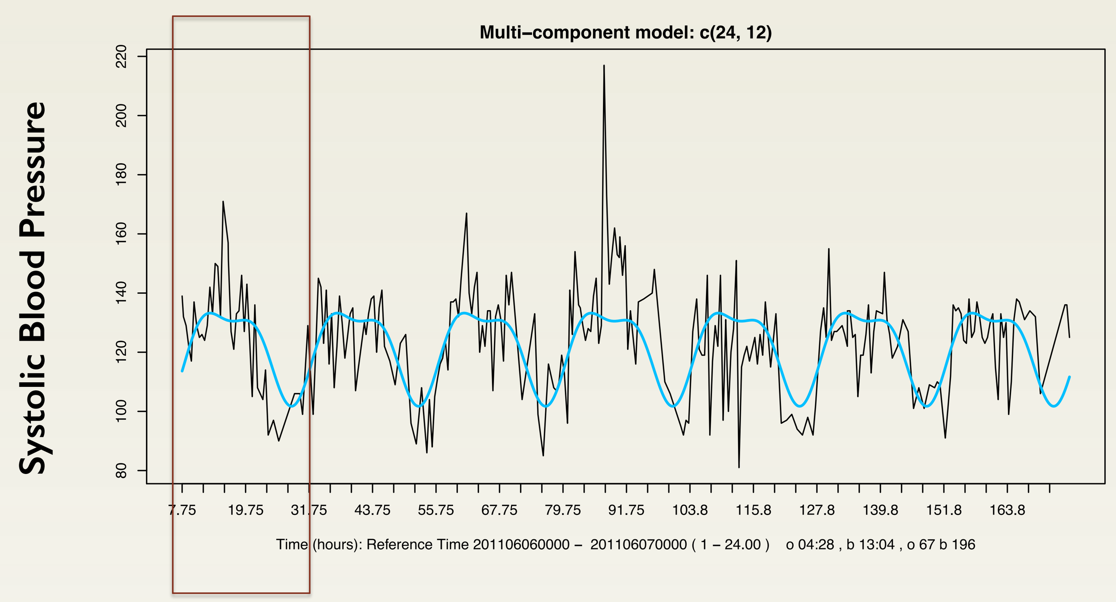

Figure 4: Two cosine curves, of 24 and 12 hours, are fitted to one week of data, Sunday to Saturday. Forty to fifty measurements were taken daily. One full cycle is shown in the red box. Seven full compound cycles can be seen in the 7-day plot. SD of 7-day MESOR of SBP is 6.7 mmHg.

Notice that the multiple-component model conforms nicely to the structure of the data. Multiple-component cosinor models can comprise any number of frequencies, and combine to produce complex waveform models.

SBP variation on days 4 & 6: 24 & 12 hours

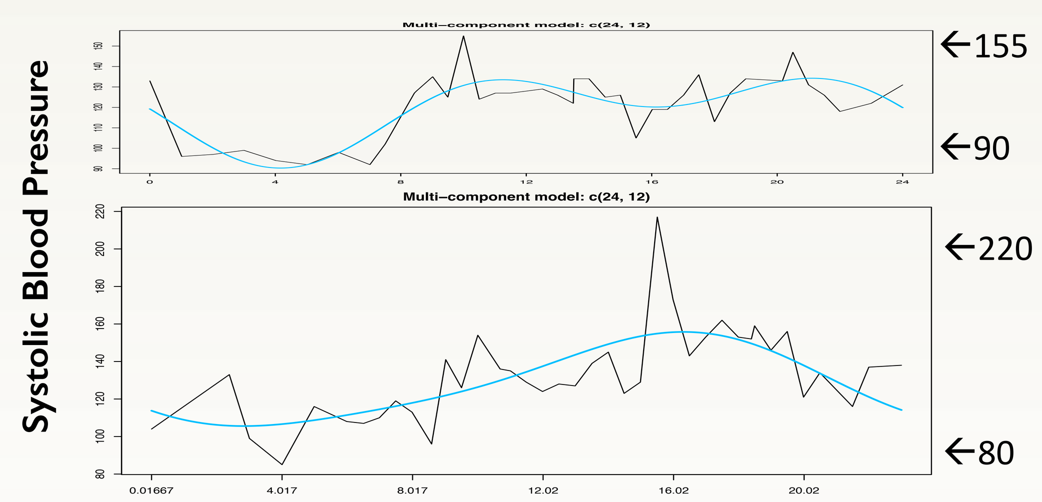

Figure 5: Days 4 and 6 are here fitted separately, instead of as a full week. Note the variation between days. The curve for day 6 goes up where is goes down on day 4. Among 39 subjects, SD of daily MESOR of SBP varies from 1.3 to 7.7 mmHg between days.

In this study, SBP values in any individual record varied in a range around 100 mmHg. The resulting uncertainty from sparse individual measurements can make a large difference in terms of the decision to treat. For the diagnosis of hypertension and other abnormalities in BP patterns, BP should be monitored around the clock for longer than 24 hours to obtain a reliable estimate of BP and BP variability.

Analysis of non-stationary data: newborn HR

Analysis of non-stationary data requires special treatment.

First 40 days of newborn HR

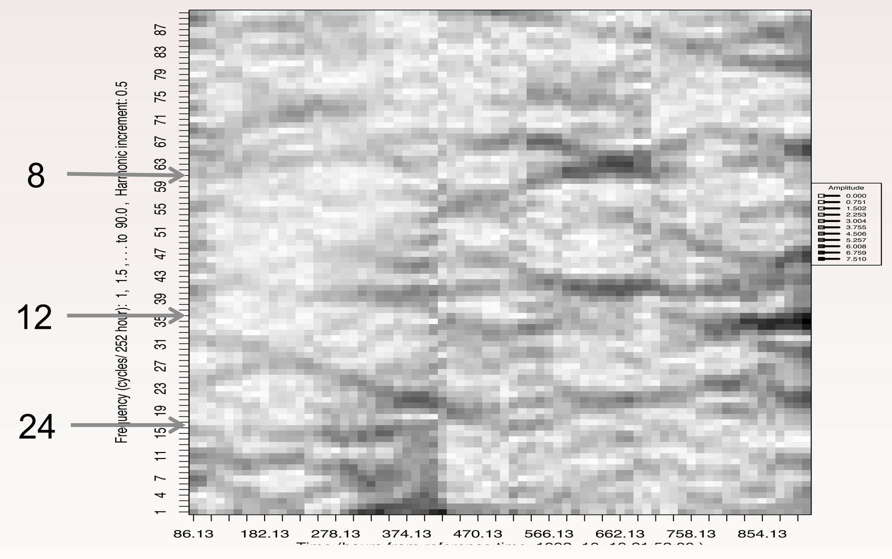

Figure 8: Figure 6 shows us the data are changing a great deal over time – the time series is non-stationary. A gliding spectrum analyzes progressive subsections of data (X-axis) at a spectrum of frequencies (Y-axis), giving us a breakdown of changes over time. Amplitude is represented by shading, with higher values being darker. The infant HR is seen to resolve to a 24-hr rhythm over the first 40 days

Analysis of non-stationary data: phase shift

Transatlantic flight shifts circadian activity rhythm

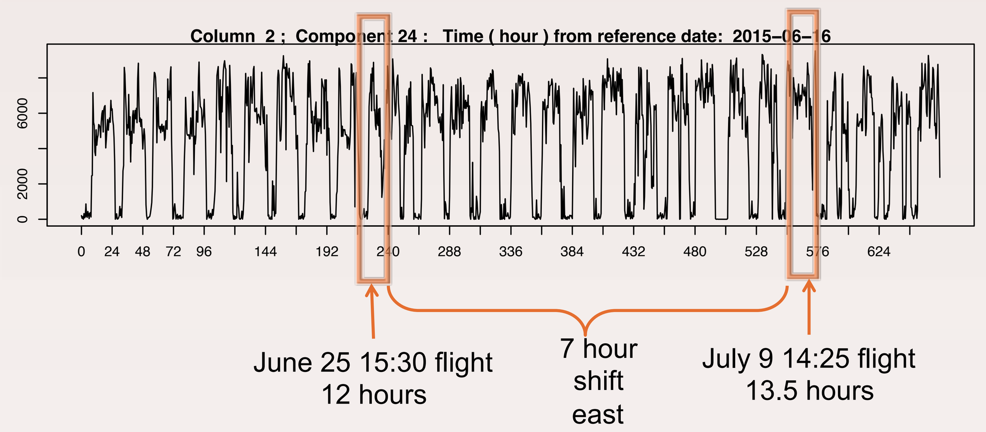

Figure 9: Activity data collected over a month, before, during and after a transatlantic shift in time zones of 7 hours. Boxes delineate transatlantic flights where shifts in phase are to be expected.

Multiple-component cosinor: 24-hr component

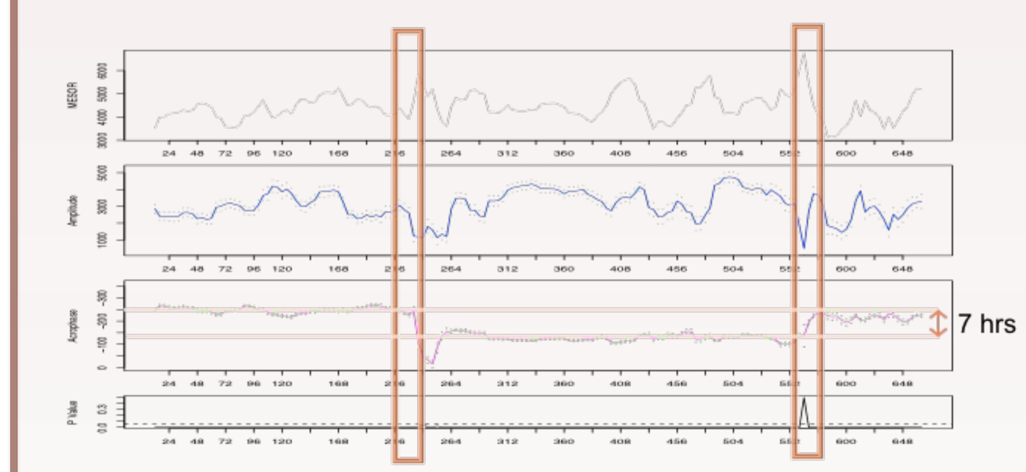

Figure 10: Because it is non-stationary, subsections of data are progressively analyzed and plotted to show the change over time of MESOR, Ampli-tude, Phase and P-value over time. A multiple-component cosinor of 24 and 12 hours was used. Only the 24-hr component is shown. A 7-hour phase shift is evident.

Multiple-component cosinor: 12-hr component

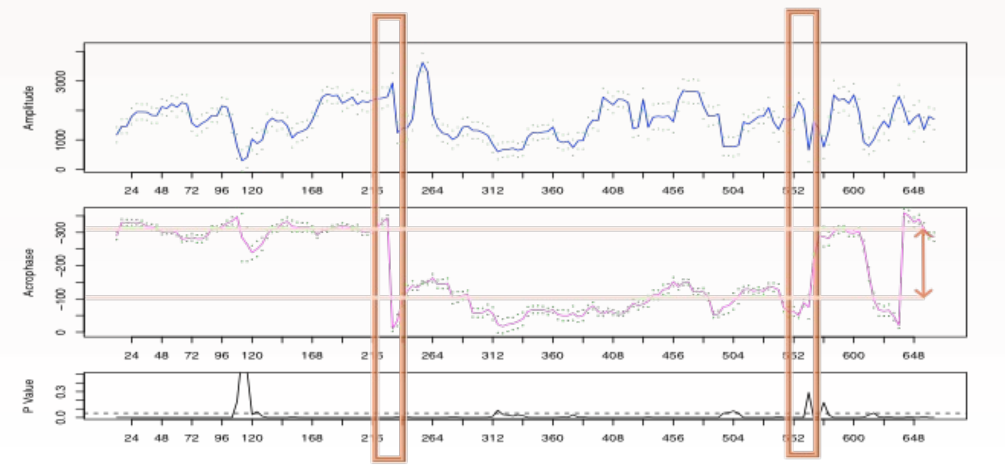

Figure 11: This is the same treatment as Figure 10, but only the 12-hr component is shown. A shift in phase of 7 hours is also evident here. It appears larger because the period is smaller. P-values are shown in lower plot.

Conclusion

There are few current packages providing an integrated suite of functions for rhythm analysis. A freely available, cross platform solution such as CATkit allows broader accessibility to key rhythm analysis tools. z.umn.edu/CATkit