



# Maternal and infant activity: Analytic approaches for the study of circadian rhythm



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## ABSTRACT

The study of infant and mother circadian rhythm entails choice of instruments appropriate for use in the home environment as well as selection of analytic approach that characterizes circadian rhythm. While actigraphy monitoring suits the needs of home study, limited studies have examined mother and infant rhythm derived from actigraphy. Among this existing research a variety of analyses have been employed to characterize 24-h rhythm, reducing ability to evaluate and synthesize findings. Few studies have examined the correspondence of mother and infant circadian parameters for the most frequently cited approaches: cosinor, non-parametric circadian rhythm analysis (NPCRA), and autocorrelation function (ACF). The purpose of this research was to examine analytic approaches in the study of mother and infant circadian activity rhythm. Forty-three healthy mother and infant pairs were studied in the home environment over a 72 h period at infant age 4, 8, and 12 weeks. Activity was recorded continuously using actigraphy monitors and mothers completed a diary. Parameters of circadian rhythm were generated from cosinor analysis, NPCRA, and ACF. The correlation among measures of rhythm center (cosinor mesor, NPCRA mid level), strength or fit of 24-h period (cosinor magnitude and  $R^2$ , NPCRA amplitude and relative amplitude (RA)), phase (cosinor acrophase, NPCRA M10 and L5 midpoint), and rhythm stability and variability (NPCRA interdaily stability (IS) and intradaily variability (IV), ACF) was assessed, and additionally the effect size ( $\eta^2$ ) for change over time evaluated. Results suggest that cosinor analysis, NPCRA, and autocorrelation provide several comparable parameters of infant and maternal circadian rhythm center, fit, and phase. IS and IV were strongly correlated with the 24-h cycle fit. The circadian parameters analyzed offer separate insight into rhythm and differing effect size for the detection of change over time. Findings inform selection of analysis and circadian parameters in the study of maternal and infant activity rhythm.

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## 1. Introduction

Establishment of a typical 24-h, diurnal pattern of activity is an essential developmental accomplishment during infancy that facilitates the “fit” among infant, parents, and family home environment (de Graag, Cox, Hasselman, Jansen, & de Weerth,

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2012; Feldman, 2006, 2007; Guedeney et al., 2011). The expression of rhythm is dependent on neurological maturation and is a gauge of brain development (Rivkees, 2003). Infant circadian rhythm is centrally linked with regulation of developing sleep–wake pattern and resultant impact on mother and household member sleep. Infant rhythm is consequently associated with maternal outcomes, including depression, fatigue, and wake disturbance, and is a significant health concern (Wells & Vaughn, 2012). The consequences of chronodisruption and sleep loss are varied and extensive (Cermakian et al., 2013; Goel, Basner, Rao, & Dinges, 2013; Grandner, Sands–Lincoln, Pak, & Garland, 2013; Kahn, Sheppes, & Sadeh, 2013; Penev, 2012; Reiter, Tan, Korkmaz, & Ma, 2012). Sleep regulation is a consequence of the interplay between circadian rhythm and homeostatic mechanisms (Achermann, Dijk, Brunner, & Borbely, 1993; Borbely, Achermann, Trachsel, & Tobler, 1989). However few studies characterize development of infant rhythm and examine the maternal and infant rhythm. Among these studies varied analytic approaches have been used to characterize maternal and infant rhythm decreasing ability to interpret findings.

The natural context of infant and maternal nycthemeral activity rhythm is the home environment. Instrumentation and analysis of rhythm are two related challenges posed by this area of study. Circadian measurement in the home requires approaches that are unobtrusive, acceptable to participants, suited to continuous long term recording, and encompass the complete 24-h period. While various approaches have been used to capture activity, actigraphy monitoring is a commonly used instrument meeting these requirements. Actigraphy monitoring, the measure of activity based on motion and movement, is suited to rhythm determination (Ancoli-Israel et al., 2003; Van Someren, 2011). Benefits of actigraphy monitoring include high acceptability and adherence as well as low subject burden. Actigraphy data are employed predominantly in the coding of sleep–wake state and a number of validation studies of infants, children, and adults confirm this usage (Martin & Hakim, 2011; Sadeh, 2011; So, Buckley, Adamson, & Horne, 2005), however actigraphy underestimates wake after sleep onset and should be used carefully in sleep research (Sadeh, 2011; So, Adamson, & Horne, 2007). Actigraphy raw activity counts may also be utilized to portray biorhythm aside from algorithm-driven coding of sleep and circumvent the limitation of rhythm derived from sleep–wake coded actigraphy records.

Multi-day actigraphic recordings can be approached using several different analysis methods in order to extract information about 24-h rest-activity rhythm properties. Historically, the most common methods were based on cosinor analysis, using computational procedures pioneered by Halberg, Tong, and Johnson (1967) and Nelson, Tong, Lee, and Halberg (1979) to explore rhythmic properties of a wide variety of physiological, behavioral, and cognitive measures. The basic single harmonic 24-h fixed period cosinor model, when fit to a multi-day time series of measurements using least squares model fitting methods, can describe three rhythm parameters: the mesor (cycle mean), magnitude (amplitude of the cycle), and acrophase (timing of the 24-h rhythm's peak). A fourth parameter,  $R^2$ , is often also reported to quantify the within-recording goodness-of-fit. The cosinor model is robust with respect to data distribution assumptions, resistance to outliers, applicability to unevenly sampled data, and tolerance of a very high percentage of missing/excluded data (Lentz, 1990; Monk, 1987; Monk & Fort, 1983; Naitoh, Englund, & Ryman, 1985).

The mathematical simplicity of the cosinor model, however, may mask scientifically important characteristics of the diurnal signal under study, possibly limiting the comparability of the estimated parameters under different conditions, across interventions, or over time due to development. Circadian variables, including actigraphic recordings, often express a shape over 24-h that is not well approximated by an idealized cosinor curve. The shapes of many measured diurnal variables deviate from a pure cosinor curve in a variety of other ways, including degree of flatness of the peaks and valleys and slopes of the transitions. The cosinor model also requires that the acrophase, the timing of the rhythm peak, be exactly 12 h before or after the nadir, the timing of the rhythm trough. Observed circadian patterns do not generally follow this constraint. When the cosinor model is fit to data that does not closely follow a pure cosinor curve, the  $R^2$ , a measure of model fit, is reduced.

Another approach to the parsimonious description of a 24-h diurnal pattern is the L5:M10 model (Witting, Kwa, Eikelenboom, Mirmiran, & Swaab, 1990), now considered part of the Nonparametric Circadian Rhythm Analysis (NPCRA) ensemble of methods that has been popularized by Van Someren et al. (1999). The least active (lowest average) contiguous 5 h segment in the 24-h pattern is located, and is described by its mean value (L5 value) and its timing (either L5 onset, or L5 midpoint). Similarly, the most active (highest average) contiguous 10 h segment in the 24-h pattern is located, and described by mean value (M10 value) and timing (M10 onset, or M10 midpoint). Then an empirical rhythm amplitude can be described as  $(M10 - L5)$ , as well as a relative amplitude ( $RA = (M10 - L5) / (M10 + L5)$ ), with a normalized value between 0 and 1. Note that the L5:M10 model can be viewed as a four parameter square wave model of the time sequence data, with two parameters describing the timing and average level of a constant value low segment, and two parameters describing the timing and average level of a constant value high segment. The model specifies the value of the rhythm for 15 h of the 24-h diurnal pattern, and treats the remaining 9 h as two “don't care” segments. This model is well-suited to diurnal patterns that are relatively flat on the top and bottom, have unbalanced diurnal cycle periods, and contain acrophase peaks and nadirs that are not exactly 12 h apart. For better or worse, this model ignores the transitions in the rhythm from low to high value, which generally occur in the “don't care” segments of the 24-h pattern. Because the mean estimates describing the levels of the L5 and M10 segments for multi-day actigraphy recordings are typically computed using hundreds or thousands of raw data points, the within-subject model tends (like the cosinor) to be reasonably robust, resistant, applicable to unevenly sampled data, and tolerant of a large percentage of missing data.

Two other components of the NPCRA toolkit of measures have also been very influential, both based on an empirical model of an arbitrary 24-h pattern constructed from hourly averages. The inter-daily stability (IS) measures the similarity of the diurnal pattern from day to day. The intra-daily variability (IV) quantifies fragmentation within the daily patterns (Van

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