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The Promise of the State Space Approach to Time Series Analysis for Nursing Research

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Abstract

Background—Nursing research, particularly related to physiological development, often depends on the collection of time series data. The state space approach to time series analysis has great potential to answer exploratory questions relevant to physiological development but has not been used extensively in nursing.

Objectives—To introduce the state space approach to time series analysis and demonstrate potential applicability to neonatal monitoring and physiology.

Method—We present a set of univariate state space models; each one describing a process that generates a variable of interest over time. Each model is presented algebraically and a realization of the process is presented graphically from simulated data. This is followed by a discussion of how the model has been or may be used in two nursing projects on neonatal physiological development.

Results—The defining feature of the state space approach is the decomposition of the series into components that are functions of time; specifically, slowly varying level, faster varying periodic, and irregular components. State space models potentially simulate developmental processes where a phenomenon emerges and disappears before stabilizing, where the periodic component may become more regular with time, or where the developmental trajectory of a phenomenon is irregular.

Discussion—The ultimate contribution of this approach to nursing science will require close collaboration and cross-disciplinary education between nurses and statisticians.

Keywords

time series analysis; the state space approach; physiological nursing research

Change over time is universal to the human condition and therefore has key relevance to research by nurses, economists, social scientists, and epidemiologists. Nursing research,

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particularly related to physiological development, often depends on the collection of time series data for use in a variety of statistical models (Hepworth, Hendrickson, & Lopez, 1994; Thomas & Burr, 2008; Tsai, Barnard, Lentz, & Thomas, 2011). One approach to modeling physiologic change, the state space approach to time series analysis (Commandeur & Koopman, 2007; Durbin & Koopman, 2001; Harvey, 1989), has great potential to answer exploratory questions relevant to physiological monitoring but has not been used extensively in nursing, likely due to a lack of familiarity with the approach among nurse scientists and methodologists. The purpose of this article is to introduce the state space approach and to fuel newly productive research collaborations between clinical and statistical experts.

State space models, as will be shown in detail below, have benefits beyond those of more popular time series approaches in that they are flexible enough to capture phenomena that emerge with spurts or periods of high growth followed by plateaus. The parameters of state space models can vary with time, allowing the natural course of a phenomenon to emerge. The specification of state space models requires methodologists and nurse scientists to formulate and interpret an evolving model together. Therefore, the nurse scientist must know enough about the statistical model to provide interpretations, and the methodologist must know enough about the phenomena under study to propose appropriate statistical models. While a step-by-step procedural guide to fitting state space models is not provided in this presentation, the aim is to introduce enough of the statistical theory and application to illustrate how these models might contribute to nursing research.

Comparisons of state space models to other time series models used in nursing research, such as cosinor models and longitudinal models with mixed effects, are discussed in the fourth section, concluding in the fifth section with a number of potential challenges that lie ahead for nurse researchers interested in state space models of physiologic change.

Two data sets, both drawn from neonatal research, are used to illustrate the state space models below. In a study of temperature control in preterm infants (*the temperature study*, Knobel et al., 2011), researchers captured abdominal and foot temperatures every minute for the first 5 days of life in a neonatal intensive care unit, hypothesizing that mature temperature control would occur when abdominal temperature remained above the foot temperature for extended periods of time. A second data set consists of measured cerebral oxygenation in full term infants every 2 seconds over 90 minutes in a neonatal intensive care unit. In this *cerebral oxygenation study*, state space modeling was used to explore and describe variations in cerebral oxygenation in response to a variety of stimuli normally occurring in the neonatal intensive unit.

Basic Statistical Concepts

Time Series Models

Time series models are applicable to data collected at regular intervals for relatively long periods of time. Examples in the nursing literature include abdominal temperature collected every minute for 32 days in female adults (Padhye & Hanneman, 2007) and every minute for 24 hours in preterm infants (Thomas, 2001), and infant activity summarized every 15 seconds for 4 days (Thomas & Burr, 2008). Each empirical time series is conceived as the realization of a data generating process that governs the movement of variables over time (Shumway & Stoffer, 2006). Statistical models represent the data generating processes.

Specialized statistical models for time series data are needed because the observations in a series are most often highly related to one another, violating assumptions of many popular linear models. This very strong relationship to neighboring observations is obvious in nursing when, for example, infant temperature is captured every 5 seconds. Another reason

that specialized statistical models are required to model time series data is the complexity of what is being modeled. Many phenomena do not unfold over time in a monotonically increasing or decreasing manner. Instead, phenomena may appear and disappear until some particular developmental milestone. Additionally, there may be a number of forces at work to produce variations seen in one empirical series, especially if the data are collected in a strictly observational manner with no experimental controls. For example, in infant studies conducted in neonatal intensive care units, minute-to-minute fluctuations in temperature may reflect a variety of internal processes as well as environmental events (Knobel, Holditch-Davis, Schwartz & Wimmer, 2009; Knobel et al., 2011). This complexity requires highly flexible statistical models.

Stochastic versus systematic variation

Time series models represent two basic types of influences. Stochastic influences are those that vary randomly from time point to time point. Examples of stochastic influence would be that due to random electric surges in a machine recording heart rate or minute-to-minute variation in an infant's temperature due to random variation in air temperature. A second type of influence is hypothesized to occur due to systematic variation. Examples of systematic influence might be infant abdominal temperatures immediately after the start of a blood transfusion (Knobel & Holditch-Davis, 2007) or changes in an infant's cerebral oxygenation levels after an intraventricular hemorrhage. Specification of a model's component as systematic or stochastic depends on what one thinks is generating the variation (Zeger, Irizarry, & Peng, 2006).

Two types of stochastic variation

Two theoretical processes play an important role in all time series models--white noise and a random walk--both of which are governed entirely by random fluctuations. In time series models, these processes represent the background upon which more systematic processes are overlaid. Additionally, they play a central role in statistical model fitting because they represent residual variation in an empirical time series after removing variability from a properly fit statistical model. The statistical model for white noise is shown in Equation 1:

$$y_t = \varepsilon_t \quad (1)$$

where ε_t is a normally distributed random variable with mean of 0 and variance of σ^2_ε and the number of observations in the series is N , $t = 1$ to N .

In any realization of a white noise process, the dependent variable of interest y_t captured at any given point in the series is drawn from a normally distributed random variable with mean of 0 and variance of σ^2_ε . Each y_t is independent of any other y_t in the series. Figure 1a is a realization of a white noise process generated by drawing computerized random numbers, each from a normal distribution of mean of 0 and variance of 1. In the state space models presented below, the white noise component will be referred to as the *irregular* component.

A random walk is only slightly more complex than white noise. The statistical model for a random walk is shown below in Equation (2):

$$y_t = \varepsilon_1 + \varepsilon_2 + \varepsilon_3 + \dots + \varepsilon_t$$

$$y_t = y_{t-1} + \varepsilon_t \quad (2)$$

where ε_t is defined as in equation (1).

The random variable y_t at time t is equal to y_t at the previous time point plus white noise. Unlike the white noise process, in a random walk, y_t is related to past values since they are composed of them. Figure 1b shows a realization of a random walk where e_t was distributed normally with mean of 0 and variance of 1. In realizations of a random walk process of relatively small n , seemingly upward or downward trends emerge when there is a number of consecutive e_t with the same sign. However, when a random walk is generating the data, such trends are entirely due to random processes rather than to any systematic influences.

State Space Models

The defining feature of the state space approach is that the series of data can be decomposed into components that are functions of time (Harvey & Koopman, 1996) as shown below in Equation (3):

$$y(t) = \mu(t) + \gamma(t) + \varepsilon(t) \quad (3)$$

where y_t is the variable of interest at time t , $\mu(t)$ is slowly varying level, potentially with variance of σ^2_η , $\gamma(t)$ is faster varying periodic component, potentially with variance of σ^2_γ , and $\varepsilon(t)$ is the irregular component with variance of σ^2_ε .

State space models facilitate an understanding of the phenomena of interest rather than simply serving as a prediction tool for future values that y_t might assume. These models provide a conceptual framework for understanding the dynamics of a phenomenon. Within this framework, researchers specify mathematically how a process changes over time. Knowledge about the phenomena is gained through relating the aspects of the statistical model to the biological process under investigation. For example, in the developmental sciences, the long-term variation in a physiological measure early in life might reflect maturational processes. Very often, such long-term variation will not present as a straight line on a longitudinal plot, but rather will appear to *wobble* and even stabilize over certain periods of time. State space models simulate this process because the parameter reflecting long-term variation (the *level* in Equation 3) is allowed to vary over time. Similarly, cycles reflected in physiological measurements may represent random fluctuations along with an underlying systematic periodicity. State space models can capture this by allowing the cycle parameters to vary across time. Herein lays the beauty as well as the challenge of these models. On the one hand, the time-varying nature of these parameters allows the models to describe complex phenomena. On the other hand, researchers and methodologists must decide whether or not the fluctuations in trend or cycle from one time to the next are due to strictly random variation or to an underlying systematic process; hence, the need for nurse scientists and methodologists to work very closely together when specifying these models.

These models can be applied to data collected in either an observational or an experimental setting. They are particularly well-suited to observational studies where many uncontrolled factors are known to influence the dynamics of a process. Because of the flexibility of state space models, they can extract a number of influences allowing the few of interest to be examined more clearly. For example, in the temperature study, infants were premature and ill simultaneously. In addition, they were in an acute care setting and exposed to many medical procedures. Amidst all of these influences, capture of developmental trends was attempted. In the models, the time varying level was interpreted as the developmental signal, while the cyclic and irregular components were interpreted as noise and other phenomena irrelevant to the scientific question.

In any given sample, the parameters of a state space model are estimated through a process called the Kalman filter (Harvey, 1989). Through this process each time-varying component is estimated in a stepwise manner beginning with that for the first time point and ending

with the last. For example, to estimate the slowly varying level for the 10th time point, $u_{(9)}$ (the estimated level for the 9th time point) is compared to $y_{(9)}$ (the actual observation at the 9th time point). If the estimate $u_{(9)}$ was too high, the estimate for $u_{(10)}$ is adjusted down from $u_{(9)}$. If it was too low, the estimate is adjusted up from $u_{(9)}$. These estimates are further refined by a smoothing process, working from the parameter for the last time point backwards to the first (see chapter 2 in Durbin & Koopman, 2001). Both the filtering and the smoothing processes produce parameter estimates that reflect the natural course of the phenomena over time, regardless of regularity or shape. This flexibility provides exceptional promise for contributing to nursing research, particularly developmental physiology.

Another aspect of state space models is its de-emphasis on statistical hypothesis testing in the service of facilitating scientific inquiry. As pointed out by Harvey and Koopman (1996), the analytic process used in state space modeling is one of fitting components to the data using a combination of criteria only some of which are statistical. An acceptable state space model should have accounted for all systematic variability based on statistical tests for normality, heteroscedasticity and serial correlation in residuals (see chapter 2 in Durbin & Koopman, 2001). However, there may be several acceptable models for a given data set and there is no specific test to indicate the scientific value of one model over another. The optimal state space model of a given phenomenon is ultimately one proposed by the nurse scientist and methodologist based on both clinical and statistical evidence.

Even though not emphasized in this article, there are statistical tests of the null hypothesis that a particular fixed effect within a specified state space model is zero. For example, if a univariate state space model includes a fixed slope, there is a way to test the hypothesis that the population value of that parameter is equal to 0. Similarly there is a test associated with the amplitude of a cycle, if it is specified as fixed and for a shift in the level. These tests provide valuable aids, along with scientific theory or clinical judgment, in determining the components to include in a final state space model. For example, including a fixed slope in a final model would be justified only if one could reject the null hypothesis that this parameter was equal to zero in the data generating process. See chapter 10 in Koopman, Harvey, Doornik, and Shephard (2009) for details regarding these tests.

Univariate State Space Models

Univariate models simulate the dynamics of a single variable. They are similar to the regression of a variable on time. Although beyond the scope of this article covariates can be incorporated into these models; see chapter 3 in Durbin and Koopman (2001), as well as chapters 5, 6, and 8 in Commandeur and Koopman (2007).

The Local Level Model

The local level model is the simplest of state space models, consisting of a time-varying level plus white noise. This model is analogous to a randomly varying intercept (Commandeur & Koopman, 2007). In algebraic form the model is:

$$Y_{(t)} = \mu_{(t)} + \varepsilon_{(t)} \quad (4)$$

where $\mu_{(t+1)} = \mu_{(t)} + \eta_{(t)}$, $\varepsilon_{(t)}$ = time-varying irregular component, variance of irregularity = σ^2_{ε} , $\eta_{(t)}$ = time-varying component of level, variance of level = σ^2_{η} , and $\mu_{(t)}$ = level at time t .

Note that this model consists of two time-varying (or *stochastic*) sources of variability: one due to variations in the underlying level symbolized by σ^2_{η} and another due to the white noise (or *irregular*) component symbolized as σ^2_{ε} . The $\eta_{(t)}$ accumulate (sum) over the

preceding time points to produce a random walk of the level. At each time point an additional source of variance is the $\varepsilon_{(t)}$, each modeled as completely unrelated to each other over time. An example of a realized local level process, based on simulated data, is shown in Figure 1c. In the cerebral oxygenation study, the irregular component could plausibly represent instrument error while the variation in level could represent very short-term fluctuations in cerebral oxygenation due to a composite of physiological processes.

Trends

A trend can be thought of as a changing level. In state space models the trend of a series refers to the level when it contains a slope--when the level is changing systematically across time. The slope parameter can be specified as fixed or time-varying. If the slope is fixed, it is the same at each point in time. If the slope is specified as time-varying, it changes over time and has a variance. When the trend is specified as time varying it may reflect both systematic and random variation over time. The estimates of the slope parameters at each point in time provided by the Kalman filter minimize the difference between the one step ahead forecasts and the actual data one step ahead. In this way, they will reflect both systematic and random variation over time. It is up to the scientist and the methodologist to decide the extent to which variations in the modeled trend represents systematic rather than random variability.

Fixed slope

The equation for a state space model with a stochastic level, fixed slope, and white noise is shown below:

$$\begin{aligned} y_{(t)} &= \mu_{(t)} + \varepsilon_{(t)} \\ \mu_{(t+1)} &= \mu_{(t)} + \beta_{(t)} + \eta_{(t)} \\ \beta_{(t+1)} &= \beta_{(t)} \end{aligned} \quad (5)$$

where $\varepsilon_{(t)}$ = time varying irregular component, variance of irregularity = σ^2_{ε} , $\eta_{(t)}$ = time varying component of level, variance of level = σ^2_{η} , $\mu_{(t)}$ = level at time t, and $\beta_{(t)} = \beta_{(t+1)} = \beta$ = slope.

A realization of this process is shown in Figure 1d, using the same simulation program that produced the realization of the local level process but with the addition of a fixed slope parameter of $-.50$. In the temperature study, $\mu_{(t)}$ might represent the true temperature differential between the abdomen and the foot. The stochastic level might represent variation in this differential, possibly caused by normal fluctuation in internal physiological processes. The slope, if specified as fixed, would represent maturation occurring at a fixed rate. This might be a reasonable model over short periods of time such as one or two days. However, for longer periods of time, a constant rate of growth in this ability might be unreasonable, since at maturity a fairly constant temperature differential between the abdomen and the foot should exist. For these longer periods of time, such as 2 weeks, a model where the slope is allowed to decelerate to 0 might be a better fit.

Stochastic slope

The same model as shown in (5), but with a stochastic slope, is shown in Equation (6):

$$\begin{aligned} y_{(t)} &= \mu_{(t)} + \varepsilon_{(t)} \\ \mu_{(t+1)} &= \mu_{(t)} + \beta_{(t)} + \eta_{(t)} \\ \beta_{(t+1)} &= \beta_{(t)} + \xi_{(t)} \end{aligned} \quad (6)$$

where $\varepsilon_{(t)}$ = irregular component, variance of irregularity = σ^2_{ε} , $\mu_{(t)}$ = level at time t , $\eta_{(t)}$ = time varying component of level, variance of level = σ^2_{η} , $\xi_{(t)}$ = time varying component of slope, variance of slope = σ^2_{ξ} , and $\beta_{(t)}$ = slope at time t .

A state space model with a stochastic slope was fit to the abdominal-to-foot temperature differential data collected on an infant each minute for 5 days (Knobel et al., 2011). The actual differential between the abdominal and foot temperatures at each minute post birth in one infant and the modeled level are shown in Figure 2. The time-varying level, which now includes a slope, could be interpreted as the maturation in the ability to control central and peripheral temperature (vasomotor tone) for this infant. Full maturation is expected to be exhibited by the existence of a constant differential between the abdominal and foot temperatures of some positive number above 0 degrees Celsius. For this infant, these results imply that maturation is not monotonically increasing. There may be instances where the infant loses recently gained maturation of vasomotor tone, as shown by the modeled level beginning to trend towards zero on the far right hand portion of the plot (Knobel et al., 2011).

Cycles

One of the most useful aspects of univariate state space models is the provision for extracting the cyclical from the trending component of a series. In many time series models periodic phenomena are modeled by cosine functions. The graph of the cosine function over time will look like a wave and is shown in Figure 3, where the values of the cosine of $(\text{minutes} * 2 * \pi) / 30$ have been graphed for minutes ranging from 1 to 80. The cycle is completed every 30 minutes.

When cycles are fit to time series data in the Structural Time Series Analyser, Modeller, and Predictor (STAMP) software version 8.2 (Koopman et al., 2009), a variety of statistics concerning the cycle are reported, two of which are the period and the variance of the cycle innovations. The period refers to the length of time required to complete one cycle, and the variance of the cycle innovations reflects how regular the shape of the cycle is over time with higher variance of innovations reflecting more irregularity.

A state space model with three cycles and a stochastic level was fit to the cerebral oxygenation measurements obtained from an infant at 2-second time intervals. The three cycles had distinctly different variances of innovations, as shown in Figures 4a, 4b, and 4c. In Figure 4a, the first cyclical component has no variability in innovations and is probably reflecting a process related to the machine used to collect the cerebral oxygenation measurements. Cycle 3 appears to be very irregular (with high variability in innovations). It was surmised that if cerebral oxygenation measurements were taken over longer periods of time, they might show more regularity as the neonate ages.

Interventions

A state space model can also specify shifts in the series by introducing a binary variable that takes on a value of 1 immediately following the point at which the intervention is hypothesized to occur. If the effects are thought to be lasting, then the binary variable is 0 for all time points leading up to the time of the intervention, with 1s for all time points afterwards.

The model for a local level plus an intervention is shown below in Equation (7):

$$\begin{aligned} y_{(t)} &= \mu_{(t)} + \lambda^* \omega_{(t)} + \varepsilon_{(t)} \\ \mu_{(t+1)} &= \mu_{(t)} + \eta_{(t)} \end{aligned} \quad (7)$$

where ε = time varying irregular component, variance of irregularity = σ^2_ε , η = time varying component of level, variance of level = σ^2_η , $\mu_{(t)}$ = level at time t , and $\omega_{(t)}$ is a variable taking on a value of 1 if $t \geq \tau$ where τ is the time point where the intervention begins. For example, if the intervention begins at time point 20 the value of $\omega_{(20)} = 1$ but the value of $\omega_{(19)} = 0$.

If the parameter λ is specified as fixed, then it represents the shift in the value of y from time $(t-1)$ to time point t , apart from both variations in level and the irregular portion of the model. Implicitly, this model specifies that the effect of the intervention is at a particular point in time and that its effect is constant for a particular length of time thereafter.

A realization of the local level plus intervention effect was simulated where the intervention effect was operative for the first 20 time points only (Figure 5). Other versions of this model (e.g., for investigation of several interventions occurring at different points in time) can be tested easily within the state space framework.

Relationship to Other Time Series Models

Cosinor Analysis and State Space Models

Nursing researchers have used cosinor analysis to describe the cyclic nature of physiological phenomena (Halberg, 1969; Lentz, 1990; Padhye & Hanneman, 2007; Thomas 2001; Thomas & Burr, 2008; Tsai et al., 2011). In this method, a cosine wave with some specified period (often 24 hours) is fit to measurements collected every minute (or second). Certain characteristics of the fitted wave pattern are then quantified such as the amplitude and the acrophase (time at which the maximum amplitude is reached). Thomas (2001) used cosinor analysis in the study of circadian rhythms in the temperature of preterm infants. Padyhe and Hanneman (2007) examined the use of cosinor analysis with a long time series of temperature data from both humans and animals. Thomas and Burr (2008) and Tsai et al. (2011) used the cosinor method to examine synchronicity in maternal and infant activity levels. Padhye and Hanneman (2007, p. 34), described the following cosinor model for one cycle:

$$y_t = M + \alpha \cos(2\pi t/b) + (\beta) \sin(2\pi t/b) + \varepsilon$$

where t = time, b = the period of the cycle (if t is in minutes and a 24 hour cycle is fit then $b = 1440$), α and β = parameters estimated by least squares, M = the average value of the cycle, and ε = an independent random component.

The model is fit using least squares regression, with y_t being the dependent variable and $\cos(2\pi t/b)$ and $\sin(2\pi t/b)$ being the two independent variables. Using estimates of α and β the fitted curve is plotted and the acrophase (time at which maximum of the cycle is reached) as well as the amplitude are obtained. In the state space framework, this is exactly the model fit to the data from a process consisting of one cycle plus white noise (see Harvey, 1989, p. 39).

If the focus of research is exclusively on the 24-hour cycle and not on development, then the cosinor approach is appropriate since it provides a detailed view of how well the data fit a specified cyclic form at one point in time. However, if the research question concerns human development, the state space approach provides the same information with at least one large advantage; it models cycles while controlling for other systematic effects in the data. For example, if it were hypothesized that variations in infant's temperatures become more synchronous with the 24-hour daily cycle as they age, then separate state space models

fit to infant temperature collected by minute over week 1, 2, and 3 of life should exhibit decreasing variation in innovations. Cosinor models could also be fit to the 3 weeks of data, and similar information might be obtained by examining the R^2 for the model fit to each week's data. However, the R^2 might be low because of either irregularity in the cyclic component or the presence of developmentally important trends occurring within each 1-week time period. The advantage of the state space approach is that the cyclical parameters will be independent of any trends or shifts occurring over any of the 1-week time periods.

Linear Mixed Models and State Space Models

Linear mixed models are a class of statistical models used for normally distributed longitudinal data where several measurements are collected on many individuals (Diggle, Heagerty, Liang, & Zeger, 2002). These models are employed often to describe the trajectory of some phenomenon over a time period. Holditch-Davis, Scher, Schwartz, and Hudson-Barr (2004) used mixed models to describe the growth trajectories of infant sleep-wake states. In most applications of mixed effects models, the primary interest is in the fixed portion--that is, the estimated mean of the dependent variable at each time point. The random portion of the model is included only to increase the accuracy of statistical tests about the fixed parameters (Diggle et al., 2002), rather than because of scientific interest in the way the random effects play out over time. State space models on the other hand not only allow for a specification of parameters as either fixed or stochastic (time-varying), as in the linear mixed model, but also show how a particular stochastic parameter evolves over time, which can be of substantive interest to nurse scientists.

Future Directions

The state space framework offers many additional features that have not been exploited fully. For example, in the cerebral oxygenation study, one plan is to model the relationship between cerebral oxygenation and additional explanatory variables such as heart rate and other vital signs within each infant. These bivariate relationships can be easily incorporated into each of the univariate state space models presented here. In addition, common factor state space models provide ways in which individuals can be clustered or grouped together based on their modeled parameters (Harvey & Koopman, 1996).

As in any data analytic endeavor, the challenge is always to obtain a thorough understanding of the statistical methods utilized. The current literature on the interpretations of state space models is underdeveloped, in stark contrast to the voluminous literature on longitudinal mixed models in the biostatistics literature. As state space models are adopted for use in nursing and medical research, the planning issues of sample size and power associated with certain tests of trend or shifts in level might be studied. Methodological research on tests for shifts in models of data collected from interrupted time series designs have appeared recently (see McLeod & Vingilis, 2008 and Zhang, Wagner, & Ross-Degnan, 2011).

Ultimately, the value of the state space approach for nursing research will be demonstrated as it is used in actual research projects. The potential to facilitate physiological nursing research is promising, but largely untapped. This manuscript is intended to motivate the nursing community to fill that gap by providing researchers with a fundamental understanding about the state space model in order to ensure that its potential can start to be realized.

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Figure 1.

- a. A realization of a white noise process
- b. A realization of a random walk process
- c. A realization of a local level process: A random walk plus white noise
- d. A realization of a local level plus fixed slope process

Figure 2.
Abdominal-to-foot temperature by minute since birth and modeled trend composed of stochastic level and stochastic slope

Figure 3.
A cosine function of minutes

Figure 4.

- a. Modeled cyclical component of cerebral oxygenation: Variance of innovations of 0.000
- b. Modeled cyclical component of cerebral oxygenation: Variance of innovations of 0.0258
- c. Modeled cyclical component of cerebral oxygenation: Variance of innovations of 0.1419

Figure 5.
A realization of a local level process plus an intervention