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#### Abstract

Our team has been studying the maturation of temperature regulation in very low birth weight (VLBW) infants. The purpose of our simulation study was to determine if state space models could capture trends that followed a logistic curve in the presence of the high levels of variability and periodicity that we see in our empirical data sets. We simulated data that followed a state space process with stochastic level and irregular components, but where the slope was a logistic function of time. Fourteen simulation conditions varied the extent of level, irregular and cycle variance. Samples were analyzed with three types of state space models, two allowing slopes to be stochastic and one where the slope was fixed. Models with stochastic slopes provided trends close to the true logistic curve only when level and irregular variances were below that which we saw in our empirical data sets. Even when models had stochastic slopes, increasing amounts of irregular, level and cycle variance tended to produced trends which were straight lines. As compared to models with stochastic slopes, the one with a fixed slope performed worse, producing larger deviations of fitted trends from that based on the logistic curve.


## 1. Introduction

Our team has been studying the maturation of temperature regulation in very low birth (VLBW) infants (preterm infants weighing less than 1500 gms at birth) ${ }^{1,2 .}$ A mature response to hypothermia is said to occur when a VLBW infant can exhibit peripheral vasoconstriction, decreasing the peripheral temperature below the central temperature to shunt blood towards vital organs. When the infant is in a mature thermal state the central temperature should be warmer than the peripheral temperature. We utilized univariate state space models to capture trends in infant temperatures collected every minute for the first two weeks of life. ${ }^{2}$ In these analyses, the dependent variable was central (abdomen) vs. peripheral (foot) temperature difference (hereafter referred to as C-P difference). The independent variable was minutes since birth up to approximately two weeks of life. Our state space models consisted of a randomly varying ("stochastic") level, one or two cycles and a stochastic trend component. We expected the fitted trends to monotonically increase, and then level off, as in a logistic curve. The leveling off point would reveal the age at which these infants could maintain a mature thermal state keeping the abdomen warmer than the peripheral temperature, and thus maintain a positive C-P temperature difference. After fitting univariate state space models to the data for 26 infants, the fitted and smoothed trends in the C-P difference values across the first two weeks of life often were very slight and most never leveled off at any time during the two week period. See Figure 1. The fitted trends did not help us in identifying when the infant had attained the ability to keep the C-P difference consistently positive. There are many possible reasons why these fitted trends failed to facilitate our analysis of temperature maturation. One concern was that the state space models could not capture a logistic type trend, given the amount of variability and periodicity exhibited in the data. Therefore, we designed a set of simulations in which the process generating the data included a slope parameter that was a logistic function of time ( t ). Note that in the context of our research, t refers to the age of the infant in minutes since birth. Various amounts of level, irregular and cycle error variance were
generated along with the systematically varying slope parameter. The purpose of the simulations was to determine if univariate state space models could capture long terms trends that followed a logistic curve in the presence of increasing amounts of irregular, level and cycle variance. The organization of the paper is as follows. Section 2 describes how the conditions for the simulations were developed. In Section 3, the range of conditions studied is presented. The simulation results are presented in Section 4 and the discussion and conclusions in Section 5.

## 2. Development of Simulation Parameters

The logistic function of the slope parameter. Some literature on premature infants suggests that mature thermoregulation is apparent when an infant can exhibit a peripheral vasoconstriction response to hypothermia when the abdominal temperature exceeds the foot temperature by $2^{\circ} \mathrm{C}$ and when the C P difference remains positive. ${ }^{3,4}$ Therefore, if $v$ is a constant, non-time varying slope, then a logistic function of $v$ which systematically varies with time can be formulated as:

$$
\begin{aligned}
& f(t, v)=z^{*} e^{\left(v^{*} t\right)} /\left(x+e^{\left(v^{*} t\right)}\right), \\
& \text { Appendix A shows that } \\
& f(0, v)=z /(x+1) \\
& f(\text { infinity }, v)=z
\end{aligned}
$$

Note that the values of $f(t, v)$ when $t$ is 0 or as $t$ approaches infinity are independent of the value of $v$. They are dependent only on $z$ and $x$. Then setting $z=2$, and $x=3, f(0,2)=2 / 4=.50$, simulating the situation where at birth the infant is able to keep the abdominal temperature above the foot by .50 centigrade. Also, when $z=2$ (regardless of what $x$ or $v$ are), $f($ infinity, $v$ ) will approach 2 since $f($ infinity, $v$ ) $=\mathrm{z}$. For all simulations, v was set to .05 and t was an integer varying from 0 to 100 by 1 . The value of .05
was selected so as t approached 100, the function of $v$ would have enough time to "level off", as is shown in figure 2. The maximum value of $t$ was set relatively low in order to conserve resources. Placement of $f(t, v)$ in the state equation. When the expression $f(t, v)=\left(2^{*} e^{\left(.05^{*} t\right)} /\left(3+e^{\left(.05^{*} t\right)}\right)\right)$ replaces $v$ in the state space model of a local linear trend where variance of $v$ is 0 we have the following model for time points one to four ${ }^{5}$ :

Let $e_{t}$ be normally distributed with mean 0 and variance $\sigma^{2}{ }_{e}$ (the irregular component) Let $\eta_{t}$ be normally distributed with mean 0 and variance $\sigma_{n}{ }_{n}$ (the level component)
$y_{1}=u_{1}+e_{1}$

$$
u_{2}=u_{1}+\eta_{1}+f(1, v)
$$

$y_{2}=u_{2}+e_{2}$, substitute the above for $u_{2}$

$$
\begin{aligned}
& y_{2}=u_{1}+\eta_{1}+f(1, v)+e_{2} \\
& u_{3}=u_{2}+\eta_{2}+f(2, v) \\
& u_{3}=u_{1}+\eta_{1}+f(1, v)+\eta_{2}+f(2, v)
\end{aligned}
$$

$y_{3}=u_{3}+e_{3}$, substitute the above for $u_{3}$

$$
\begin{aligned}
y_{3}=u_{1}+ & \eta_{1}+f(1, v)+\eta_{2}+f(2, v)+e_{3} \\
u_{4} & =u_{3}+\eta_{3}+f(3, v) \\
u_{4} & =u_{1}+\eta_{1}+f(1, v)+\eta_{2}+f(2, v)+\eta_{3}+f(3, v)
\end{aligned}
$$

$y_{4}=u_{4}+e_{4}$, substitute the above for $u_{4}$
$y_{4}=u_{1}+\eta_{1}+f(1, v)+\eta_{2}+f(2, v)+\eta_{3}+f(3, v)+e_{4}$
Note that for each subsequent time point the expression for $u_{t}$ requires that the expression $2 \exp ^{\left(v^{* t}\right)} /(3+$ $\exp ^{\left(v^{*} t\right)}$ ) be summed $t-1$ times for each value of $t$. As $t$ increases, the value of $u_{t}$ will become very large, and will produce a trend that does not level off. This problem is eliminated if the first differences $\Delta y_{t+1}$ are modeled instead of $y_{t}$. This is shown in Appendix $B$. Therefore, for all conditions, $Y_{t}$ was generated as shown above with an irregular, a stochastic level, a slope parameter set to .05 and which
was a logistic function of $t$ as $\left(2^{*} \mathrm{e}^{\left(.05^{*} t\right)} /\left(3+\mathrm{e}^{\left(.05^{*} t\right)}\right)\right.$. Some simulations also had a cycle component with error variance as described in the following section. Then for analysis purposes, first differences of the series were computed.

In summary, the time series simulated (and before differencing) without cycles were similar to a local linear trend model but with the slope being a logistic function of time ${ }^{5}$ :
$y_{t}=u_{t}+e_{t}, \quad e_{t}$ is distributed normally with mean $=0$ and variance $=\sigma_{e}^{2}$
$u_{t+1}=u_{t}+\eta_{t}+v_{t}, \quad \eta_{t}$ is distributed normally with mean $=0$ and variance $=\sigma_{n}^{2}$
$v_{t+1}=2^{*} \exp ^{\left(.05^{* t}\right)} /\left(3+\exp ^{\left(.05^{* t}\right)}\right)$
The time series with a cyclic component was simulated as below where the periodicity was simulated as a sign wave with period of 30 minutes ${ }^{6}$. This value for the period was selected because it was observed in the empirical time series of the C-P difference for many of the 26 infants in the study.

$$
\begin{aligned}
& y_{t}=u_{t}+e_{t}+\psi_{t}, \quad e_{t} \text { is distributed normally with mean }=0 \text { and variance }=\sigma_{e}^{2} \\
& u_{t+1}=u_{t}+\eta_{t}+v_{t}, \quad \eta_{t} \text { is distributed normally with mean }=0 \text { and variance }=\sigma_{n}^{2} \\
& v_{t+1}=2^{*} \exp ^{\left(.05^{* t)}\right.} /\left(3+\exp ^{\left(.05^{* t)}\right)}\right) \\
& \psi_{t}=(.5 * \cos (.20943951 * t)+ \\
& \text { (.5*sin(.20943951*t) } \\
& +\gamma_{t} \quad \quad \gamma_{t} \text { is distributed normally with mean }=0 \text { and variance }=\sigma^{2}{ }_{v}
\end{aligned}
$$

## 3. Simulation Conditions

The primary manipulation in this study was the extent to which a given time series exhibited variation from sources other than the time varying slope. Simulation conditions were designed to contain increasing amounts of the stochastic level variance as compared to .05 which was the "trend - like" portion of the time varying level. The idea was to increase the stochastic level variance in relation to the extent to which the level was increasing systematically. Seven conditions were created where the level
variance was $.01, .101,5,10,50$ or 100 times the squared value of the slope parameter. The irregular variance was $25 \%$ of the level variance. This particular pattern of level and irregular variances was chosen because it roughly corresponds to the results of fitting state space models to our 26 very low birth weight infants as shown in Table 1. Note that in Table 1 the irregular variance is at most $25 \%$ of the level variance. The parameters of the seven simulation conditions are summarized in Table 2. Each of the seven conditions shown in Table 2 had a matching condition on which all parameters were repeated along with cycles with error variance of $50 \%$ of the level variance. Cycles had period of 30 . Again, these values for the cycle error variance and the period were selected because they were close to the characteristics of the cyclic component of the fitted models to the data from our 26 VLWB infants. Parameters for conditions with cycles are shown in Table 3. Each simulation consisted of 1,000 samples each of size 100 .

Simulated data sets were analyzed with three different univariate state space models: stochastic level and stochastic slope (SS), fixed level and stochastic slope (FS) and stochastic level and fixed slope (SF). For each of the three models, we computed the difference between the "true" level predicted by the logistic function of t with a slope of .05 and the smoothed trend fit by the model (true - smoothed level). We used the SAS UCM procedure to generate the fitted trends and resulting smoothed level values. Statistical summaries of (true - smoothed level) across the sample of 100 data points for each of the three models were the primary dependent variables of interest. These included the mean, median and the standard deviation of the 100 values of (true - smoothed level) on each simulation for each of the three models. Summary statistics of the distribution of these sample values, across the 1,000 simulations were also computed. Statistics summarizing the fit of the trend to the logistic curve across all 100 "time points" are global indicators with the mean measuring bias (over or under the logistic curve) and the standard deviation reflecting variability. On each simulation we also stored the value of (true - smoothed level) at time points 10, 60 and 90 for conditions without cycles and on 10, 40, 50 ,60
and 90 for conditions with cycles. The logistic curve that we studied has decreasing slope beginning near 50. Therefore we thought it particularly important to look at the (true - smoothed level) values in this region and compare them to those at the beginning and end of the time series.

## 4. Results

Conditions without cycles Results indicated increasing standard deviations of (true - smoothed level) as conditions went from 1 to 7 as shown in Table 4 and Figure 3. Of the three models the stochastic level and fixed slope consistently exhibited the largest standard deviations, indicating the poorest global fit with the logistic curve generating the data. Details regarding how well the trends fit the logistic curve at selected time points are provided in Tables 5 through 7 and Figures 4 through 6. They show average values of (true - smoothed level) by time point for each condition and model. The pattern of fit for both the (SS) and the (FS) models are similar. Almost no deviations from the logistic in all three time points occur in conditions 1 through 3 . However beginning with condition 4, the fitted trends are too high at the beginning and the end of the time period and too low in the middle. In other words, the fitted trends are not following the curve to level off. This pattern of deviations is consistent with the fitted trend being a straight line. When considering the condition in which the slope is fixed, a different pattern of fit emerges for the conditions 1 through 3. In these conditions, the fits appear on average to be too low at all three time points. Then with larger amounts of variance the bias disappears, and instead the fitted trend is too high at either end of the series and too low in the middle as was the case with the SS and FS models.

In summary, for SS and FS models, and conditions 1 through 3, the fitted trends follow the logistic curve well. For the SS and FS models there is some (but small) systematic departure from the logistic curve in conditions 5,6 and 7 indicating that it is too low at the ends and too high in the middle. The fit of the
trends for the SF model was worse than the other two models in all conditions, especially conditions 1 through 3. In those, the fit was consistently low across time points.

Conditions with Cycles The average value of the standard deviation of (true - smoothed level) deviations by matched conditions (for those with and without cycles) and model are presented in Table 8. Interestingly, the addition of cycles only minimally affected these standard deviations when the state space model fitted included a stochastic slope. When the model specified a fixed slope the effect of cycles under all conditions was to increase the variability in this index. This is shown in table 8 by the ratios of the average standard deviation for the condition with cycles to the same statistic from the matching condition without cycles (i.e., std of data with cycles/std of data without cycles). For the fixed slope conditions these ratios ranged from 5.2 to 8.7. Except for the standard deviations from the SS model under condition 1, the other ratios range from 1.0 to 1.5. See also Figure 7.

As expected then, the average value of (true - smoothed level) across selected time points by condition showed very similar patterns to those revealed by the no cycle conditions when model SS or model FS was fit to the data. See Tables 9 and 10 and Figures 8 and 9. Very different patterns of the average value of (true - smoothed level) emerged over these time points by condition when the SF model was fit. In conditions 5, 6 and 7 the average value of (true - smoothed level) is between . 4 and .8 at each of the selected time points (see Table 11 and Figure 10). This result however, was due to the presence of a very few but extremely large values of (true - smoothed level) for these conditions. For example, two were near 54 , and another was 16 . Recall that the data were generated with a logistic curve which has a value of 2 as $t$ approaches infinity. This must have been due to something in the fitting algorithm because the same data was fit with SS and FS models. If this outlier was due to a very large value of y being generated then it should have appeared in the other conditions as well. The median values of (true - smoothed level) by time point and condition for the SF model are shown in Table 12 and Figure
11. These median values show a very similar pattern to the average values of (true - smoothed level) by condition and time point generated without cycles shown in Table 7 and Figure 6. That pattern is for conditions 1 through 3 to generate trends which are slightly but consistently too low. For conditions 4 through 7, the familiar pattern of a fit which is too high at either ends but too low in the middle is approximated.

In summary the effect of adding cycles to the data was to increase the standard deviations of (true smoothed level) by a small amount for the fitted trends provided by the SS or the FS models and by a larger amount for those provided by the model with a fixed slope.

## 4. Discussion

In this section we first discuss the implications of these results for our program of research in temperature control. Next we discuss some limitations of this study. Finally we suggest further methodological research regarding the analysis of "noisy" data similar to high frequency physiological measurements collected in acute care settings.

Implications for research in temperature control. Probably the most basic question concerns the assumption that the temperature data yielded by the VLBW infants follow a state space process shown in the introduction of this paper. There, and in Appendix B, we demonstrated that if it did, the undifferenced series would produce extremely large values quickly. The range of values yielded by our simulated (un-differenced) series could not plausibly be C-P differences obtained from VLBW infants since they reached values of 40 to 50 . The differenced series however, does represent a very plausible model for these infants. This implies that for our temperature data we should not model the raw C-P differences but rather the first differenced series if we believe that maturation of C-P differences follows a logistic curve. It also implies that there are perhaps reformulated versions of state space models where the parameters themselves are differenced, rather than the data after the fact.

The level, irregular and cycle variances that we have obtained from the analysis of the C-P differences from our 26 VLWB infants most closely resemble condition \#5 of this study. In those conditions, even the models with stochastic slopes yielded some degree of systematic distortion of the logistic trends, fitting a linear rather than a curvilinear trend line. This was exaggerated in the presence of cycles. In terms of our research we need to determine methods for reducing level, irregular and cycle variance. We can think of level variance as very short term changes in the C-P difference. This variation might reflect the infant's responses to procedures where the incubator door is open for some time, or the infant's responses to blood transfusions or even feeding. In an intensive care environment some of these sources of variation reflect life supporting clinical practice and therefore will always be present. However, we believe that other influences existed that could be controlled, such as temperature probes falling off of the child. The results of these simulations show that if one wants to capture systematically varying long term trends with state space models, it is important to maintain other sources of variation at a low level. Another alternative is to identify those events most likely to be associated with large amounts of short term variation in C-P difference and include them as covariates while fitting the trend.

As one might expect, state space models with a fixed slope showed the most overall distortion in fitted trends. However, if theory dictated a logistic type trend, then a univariate state space model with a fixed slope might not be an appropriate choice and should probably be avoided.

Study limitations Our simulations were designed to mimic the maturation of temperature control as measured in VLWB infants in an intensive care unit. We hypothesized that the long term trend in our measurement of this underlying phenomenon would resemble a logistic curve. However, there are several variations of these curves and we studied only one. There are others we could have included such as those with steeper slopes, and those that are shifted so that C-P differences do not start to rise until some period after birth. Additionally, in our temperature study, the length of our time series was
much longer than 100. In our simulations, the slope of the maturation curve began to decrease half way through the series. Maturation curves with slopes that decrease at an earlier point in time (say at one tenth of the series length) may be harder or easier to capture with state space models.

From a more technical perspective, the cycles that we generated were fixed with amplitude of $1(.5+$ $.5)^{2}$, and frequency $=(.20944)$, period $=30$. Random error was built into the cycle by adding an independent component on each time point $t$. An alternative formulation of cycles is to have the amplitude of the cycle at time point $t$ be related to that of the cycle at time point $t-1 .{ }^{5,7}$ It was unclear to us which formulation would be most appropriate to mimic maturation in temperature. However, it is possible that the results of our simulations may have differed with this alternative formulation of cycle.

Future research In this study we focused on capturing logistic long term trends via state space models. However, we also suspect that short term variations in both cycles and level are important to model in the acute care setting for VLBW infants. We suspect that systematic trends in level and cycle variance may reflect maturation, or the ability of the neonate to respond to wide variations in the environment. This would by the case in our temperature study if in the first few hours following birth that exposure to extreme temperatures elicited small C-P variance reflecting the ambient temperature. Then as the infant matured there might be periods of high variability in C-P measures as the neural ability to control temperature develops. Finally, in the mature infant C-P variance would decrease to a steady amount. The existence of these changes in C-P variance may obscure the emergence of the long term trends in the C-P difference. Other time series models which capture systematic variations in level and/or cycle variance should be carefully considered. It might be possible to model level and cycle variances, remove systematic trends in them, then apply the "filtered" series to state space models to study longer term trends in levels less affected by bursts of variability.

## Appendix A

## Development of the logistic function of the slope parameter for the simulations

Below we present a logistic function of $t$ (time); $f(t, v)$. This logistic function $f(t, v)$ has two other parameters $z$ and $x$. We show that when $z=2, v=2$ and $x=3$ then when $t=z e r o$, the value of $f(0,2)$ is .50 and when $t$ approaches infinity the value of $f($ infinity, 2$)$ is 2 .
a. $f(t, v)=z^{*} \exp \left(v^{*} t\right) /\left(x+\exp \left(v^{*} t\right)\right)$,
i. Where $t=$ time
ii. $\exp (b)=e$ to the vth power
b. Let $t=0$, then
i. $f(0, v)=z^{*} \exp \left(v^{*} 0\right) /\left(x+\exp \left(v^{*} 0\right)\right)$
ii. $f(0, v)=z^{*} \exp (0) /(x+\exp (0))$
iii. $f(0, v)=z(1) /(x+1)$
c. Let $\mathrm{t}=$ infinity
i. $\quad f($ infinity,$v)=z * e\left(v^{*}\right.$ infinity $) /\left(x+\exp \left(v^{*}\right.\right.$ infinity $\left.)\right)$
ii. $f($ infinity,$v)=z^{*} \quad e(*$ infinity $) /(x+\exp ($ infinity $))$
iii. $f($ infinity,$v)=z^{*} \quad e(*$ infinity $) /(x+\exp ($ infinity $))$
iv. $f($ infinity,$v)=z$ * (infinity) $/(x+$ (infinity))
v. $f($ infinity,$v)=z^{*} \quad($ infinity $) /$ (infinity)
vi. $f($ infinity,$v)=z^{*} \quad 1$
vii. $f($ infinity, $v)=z$
d. let $v=2, z=2, x=3$
i. From (b) above

1. $f(0,2)=2 /(3+1)$
2. $f(0,2)=2 / 4$
3. $f(0,2)=.5$
ii. From c above
4. $f($ infinity, 2$)=z$
5. $f($ infinity, 2$)=2$

## Appendix B

The state space model for a stochastic level and fixed slope which is a logistic function of time
Review of the state space model when level is stochastic and slope fixed ${ }^{5}$
$Y_{t}=u_{t}+e_{t}$
$u_{t+1}=u_{t}+\eta_{t}+v_{t}$
Where $u_{t}$ is an unobserved level with variance at time $t$ of $\eta_{t}$
$v_{t}$ is the unobserved slope, or the change in level from time $t$ to time $t+1$.
$\eta_{t}$ is normally distributed with mean of 0 and variance $\sigma_{n}^{2}$
$e_{t}$ is normally distributed with mean of 0 and variance $\sigma_{e}^{2}$
$y_{1}=u_{1}+e_{1}$
where $e_{1}$ is drawn from a normal distribution with mean of 0 and variance of $\sigma^{2}{ }_{e}$
$u_{2}=u_{1}+\eta_{1}+v_{1} \quad$ (level and second time point = level at first time point plus error plus trend)
$\mathrm{v}_{2}=\mathrm{v}_{1}$ (trend component at all time points is the same)
$\mathrm{y}_{2}=\mathrm{u}_{2}+\mathrm{e}_{2}$
But $\mathrm{u}_{2}=\mathrm{u}_{1}+\eta_{1}+\mathrm{v}_{1}$
Then
$\mathrm{y}_{2}=\mathrm{u}_{1}+\mathrm{n}_{1}+\mathrm{v}_{1}+\mathrm{e}_{2}$
$u_{3}=u_{2}+\eta_{2}+v_{2}$
$u_{3}=u_{1}+\eta_{1}+v_{1}+\eta_{1}+v_{1}$
$u_{3}=u_{1}+\eta_{1}+\eta_{2}+2^{*} v_{1}$
$y_{3}=u_{3}+e_{3}$
But $u_{3}=u_{1}+\eta_{1}+\eta_{2}+2^{*} v_{1}$
Then $y_{3}=u_{1}+\eta_{1}+\eta_{2}+2^{*} v_{1}+e_{3}$

$$
u_{4}=u_{3}+n_{3}+v_{3}
$$

$$
u_{4}=u_{1}+\eta_{1}+\eta_{2}+\eta_{3}+v_{1}+v_{2}+v_{3}
$$

$$
\begin{aligned}
& \quad u_{4}=u_{1}+\eta_{1}+\eta_{2}+\eta_{3}+3^{*} v_{1} \\
& y_{4}=u_{4}+e_{4} \\
& y_{4}=u_{1}+\eta_{1}+\eta_{2}+\eta_{3}+3^{*} v_{1}+e_{4}
\end{aligned}
$$

Note that the fixed slope $v_{1}$ is multiplied by $t-1$ in the state equation for the $y_{t}$. In this way, the long term trend for $Y$ is fixed and linear, since the values of $\eta_{t}$ have expected value of 0 . When we substitute $f(t, v)$ for $v$, this property remains with the value of $f(t, v)$ entering into the state equation for $y_{t}$ a total of $t-1$ times. This produces a distortion of the logistic "curve" in that the values of $y$ as $t$ increases do not in fact level off and as $t$ approaches infinity f(infinity,t) does not approach a constant.

Let $f(t)=\exp \left(v^{*} t\right) /\left(1+\exp \left(v^{*} t\right)\right)$, where $v$ is constant from one time point to the next.
$y_{1}=u_{1}+e_{t}$

$$
u_{2}=u_{1}+\eta_{1}+f(v, 1)
$$

$$
f(v, 1)=\exp \left(v^{*} 1\right) /\left(1+\exp \left(v^{*} 1\right)\right)
$$

$$
\mathrm{u}_{2}=\mathrm{u}_{1}+\eta_{1}+\exp \left(\mathrm{v}^{*} 1\right) /\left(1+\exp \left(\mathrm{v}^{*} 1\right)\right)
$$

$$
\mathrm{y}_{2}=\mathrm{u}_{2}+\mathrm{e}_{2}
$$

$$
y_{2}=u_{1}+\eta_{1}+\exp \left(v^{*} 1\right) /\left(1+\exp \left(v^{*} 1\right)\right)+e_{2}
$$

$$
u_{3}=u_{2}+\eta_{2}+f(v, 2)
$$

$$
u_{3}=u_{1}+\eta_{1}+\exp \left(v^{*} 1\right) /\left(1+\exp \left(v^{*} 1\right)\right)+\eta_{2}+f(v, 2)
$$

$$
u_{3}=u_{1}+\eta_{1}+\exp \left(v^{*} 1\right) /\left(1+\exp \left(v^{*} 1\right)\right)+\eta_{2}+\exp \left(v^{*} 2\right) /\left(1+\exp \left(v^{*} 2\right)\right)
$$

$$
u_{3}=u_{1}+\eta_{1}++\eta_{2}+\exp \left(v^{*} 1\right) /\left(1+\exp \left(v^{*} 1\right)\right)+\exp \left(v^{*} 2\right) /\left(1+\exp \left(v^{*} 2\right)\right)
$$

$y_{3}=u_{3}+e_{3}$
$y_{3}=u_{1}+\eta_{1}++\eta_{2}+\exp \left(v^{*} 1\right) /\left(1+\exp \left(v^{*} 1\right)\right)+\exp \left(v^{*} 2\right) /\left(1+\exp \left(v^{*} 2\right)\right)+e_{3}$
In general,
$y_{t}=u_{t}+e_{t}$
$u_{t+1}=\Sigma \eta_{i}+\Sigma f(v, i), I=t-1, t=2$ to $T$ (where $T$ is the total number of time points in the series)

The state space model for the differenced time series however, has only 1 value of $f(v, t)$ contributing to each differenced value of $y_{t+1}-y_{t}$ for $t$ going from 2 to $T$. Continuing with the same example for $f(v, t)$, we show this for the state equation for $y_{3}-y_{2}$.

$$
\begin{aligned}
& y_{3}-y_{2} \\
& =\left(u_{1}+\eta_{1}+\eta_{2}+\exp \left(v^{*} 1\right) /\left(1+\exp \left(v^{*} 1\right)\right)+\exp \left(v^{*} 2\right) /\left(1+\exp \left(v^{*} 2\right)\right)+e_{3}\right)- \\
& \left(u_{1}+\eta_{1}+\exp \left(v^{*} 1\right) /\left(1+\exp \left(v^{*} 1\right)\right)+e_{2}\right) \\
& =\eta_{2}+\exp \left(v^{*} 2\right) /\left(1+\exp \left(v^{*} 2\right)\right)+e_{3}-e_{2}
\end{aligned}
$$

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Tables

Table 1. Variance components of fitted state space models to C-P differences captured by minute on very low birth weight infants. ${ }^{1}$

| Infant | Sample size | Variance Component |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | Level | Irregular | Irregular/Level | Cycle | Cycle/Level |
| t002 | 17722 | 0.0303 | 0.0059 | 0.1947 | 0.0133 | 0.4378 |
| t004 | 12356 | 0.0273 | 0.0007 | 0.0256 | 0.0153 | 0.5607 |
| t009 | 20370 | 0.0194 | 0.0050 | 0.2577 | 0.0196 | 1.0120 |
| t011 | 20325 | 0.0141 | 0.0033 | 0.2340 | 0.0142 | 1.0038 |
| t012 | 20425 | 0.0256 | 0.0058 | 0.2266 | 0.0135 | 0.5288 |
| t017 | 20525 | 0.0292 | 0.0049 | 0.1678 | 0.0072 | 0.2449 |
| t020 | 20658 | 0.0214 | 0.0023 | 0.1075 | 0.0070 | 0.3249 |
| t026 | 40629 | 0.0203 | 0.0016 | 0.0788 | 0.0014 | 0.0705 |
| t029 | 40348 | 0.0292 | 0.0073 | 0.2500 | 0.0105 | 0.3595 |
| Mean |  | 0.0241 | 0.0041 | 0.1697 | 0.0113 | 0.4702 |

${ }^{1}$ Each model contained a fixed level, a stochastic slope and one or more cycles.

Table 2. Simulation conditions without cycles

|  | Variance of level / (slope) ${ }^{2}$ where slope $=.05$ |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
|  | .0100 | .1000 | 1.0000 | 5.0000 | 10.0000 | 50 | 100 |
| Condition <br> Number | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Variance of <br> level | .000025 | .00025 | .0025 | .0125 | .0250 | .1250 | .250 |
| Measurement <br> error <br> (25\% of level <br> variance) | .00000625 | .0000625 | .000625 | .003125 | .00625 | .0312 | .0625 |

Table 3. Simulation design for conditions with cycles

|  | Variance of level / (slope) ${ }^{2} \quad$ where slope $=.05$ |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | . 0100 | . 1000 | 1.0000 | 5.0000 | 10.0000 | 50 | 100 |
| Condition number ${ }^{1}$ | 1c | 2c | 3c | 4c | 5c | 6c | 7c |
| Variance of level | . 000025 | . 00025 | . 0025 | . 0125 | . 0250 | . 1250 | . 2500 |
| Measurement error (25\% of level variance) | $\begin{aligned} & .000006 \\ & 25 \end{aligned}$ | . 0000625 | . 000625 | . 003125 | . 00625 | . 0312 | . 0625 |
| Cycle variance =50\% of level variance | $\begin{aligned} & \hline .000012 \\ & 5 \end{aligned}$ | . 000125 | . 00125 | . 00625 | . 0125 | . 0625 | . 125 |

${ }^{1}$ The " $c$ " with these numbers indicates that the condition includes a cycle with error variance.

Table 4. Average standard deviation of (true - smoothed level) across 1,000
simulations by condition and model.

| condition | state space model $^{\mathbf{1}}$ |  |  |
| :---: | :---: | ---: | ---: |
|  | SS | FS | SF |
| 1 | 0.0017 | 0.0017 | 0.0106 |
| 2 | 0.0042 | 0.0042 | 0.0128 |
| 3 | 0.0108 | 0.0108 | 0.0196 |
| 4 | 0.0209 | 0.0208 | 0.0312 |
| 5 | 0.0264 | 0.0262 | 0.0385 |
| 6 | 0.0587 | 0.0580 | 0.0736 |
| 7 | 0.0813 | 0.0804 | 0.0950 |

SF = stochastic level and fixed slope.

Table 5 Average value of (true - smoothed level) by time point and condition for
SS models

| Condition | time point |  |  |
| :---: | ---: | ---: | ---: |
|  | $\mathbf{1 0}$ |  | $\mathbf{6 0}$ |
| 1 | -0.00034 | 0.00001 | 0.00008 |
| 2 | -0.00191 | 0.00015 | 0.00040 |
| 3 | -0.00502 | 0.00084 | -0.00002 |
| 4 | -0.00844 | 0.00384 | -0.00349 |
| 5 | -0.01187 | 0.00737 | -0.00640 |
| 6 | -0.02979 | 0.02717 | -0.02935 |
| 7 | -0.04560 | 0.04239 | -0.04371 |

Table 6 Average value of (true - smoothed level) by time point and condition For FS models

| Condition | time point |  |  |
| :---: | :---: | :---: | :---: |
|  | $\mathbf{t}=\mathbf{1 0}$ | $\mathbf{t}=\mathbf{6 0}$ | $\mathbf{t}=\mathbf{9 0}$ |
| 1 | -0.0003 | 0.0000 | 0.0001 |
| 2 | -0.0019 | 0.0001 | 0.0004 |
| 3 | -0.0050 | 0.0008 | 0.0000 |
| 4 | -0.0085 | 0.0039 | -0.0035 |
| 5 | -0.0113 | 0.0074 | -0.0066 |
| 6 | -0.0297 | 0.0272 | -0.0294 |
| 7 | -0.0459 | 0.0433 | -0.0441 |

Table 7 Average value of (true - smoothed level) by time point and condition for SF models

| condition | time point |  |  |
| :---: | ---: | ---: | ---: |
|  | $\mathbf{t}=\mathbf{1 0}$ | $\mathbf{t}=\mathbf{6 0}$ | $\mathbf{t}=\mathbf{9 0}$ |
| 1 | 0.0231 | 0.0115 | 0.0030 |
| 2 | 0.0227 | 0.0111 | 0.0032 |
| 3 | 0.0208 | 0.0138 | 0.0034 |
| 4 | 0.0149 | 0.0190 | -0.0013 |
| 5 | 0.0093 | 0.0237 | -0.0063 |
| 6 | -0.0223 | 0.0528 | -0.0409 |
| 7 | -0.0426 | 0.0715 | -0.0601 |

Table 8 Mean standard deviations of (true - smoothed level) by condition model and the presence or absence of cycles in the generated data. ${ }^{1}$

| condition | state space model |  |  |
| ---: | ---: | ---: | ---: |
|  | SS | FS | SF |
| 1 | 0.0017 | 0.0017 | 0.0122 |
| 1 c | 0.0224 | 0.0021 | 0.1066 |
| ratio of 1 c to 1 | 13.1882 | 1.2294 | 8.7051 |
| 2 | 0.0042 | 0.0042 | 0.0137 |
| 2 c | 0.0049 | 0.0049 | 0.1078 |
| ratio of 2c to 2 | 1.1571 | 1.1571 | 7.8428 |
| 3 | 0.0108 | 0.0108 | 0.0201 |
| 3 c | 0.0133 | 0.0160 | 0.1278 |
| ratio of 3c to 3 | 1.2352 | 1.4778 | 6.3550 |
| 4 | 0.0209 | 0.0208 | 0.0334 |
| 4 c | 0.0218 | 0.0217 | 0.2000 |
| ratio of 4 c to 4 | 1.0416 | 1.0409 | 5.9841 |
| 5 | 0.0264 | 0.0262 | 0.0509 |
| 5 c | 0.0318 | 0.0290 | 0.2656 |
| ratio of 5 c to 5 | 1.2034 | 1.1057 | 5.2197 |
| 6 | 0.0587 | 0.0580 | 0.0971 |
| 6 c | 0.0638 | 0.0629 | 0.5686 |
| ratio of 6 c to 6 | 1.0862 | 1.0845 | 5.8550 |
| 7 | 0.0813 | 0.0804 | 0.1198 |
| 7 c | 0.0896 | 0.0889 | 0.8003 |
| ratio of 7 c to 7 | 1.1020 | 1.1052 | 6.6805 |

${ }^{1}$ The "c" after the number indicates that in that condition cycles were simulated. Conditions with cycles were exactly the same as those without cycles except for the addition of the cycle.

Table 9 Average of (true - smoothed level) by time point and condition (with cycles) for SS models.

| condition | $\mathrm{t}=10$ | $\mathrm{t}=40$ | $\mathrm{t}=50$ | $\mathrm{t}=60$ | $\mathrm{t}=90$ |
| ---: | ---: | ---: | ---: | ---: | ---: |
| 1c | 0.0279 | 0.0284 | -0.0104 | -0.0178 | -0.0178 |
| 2c | -0.0025 | 0.0008 | 0.0001 | 0.0004 | -0.0005 |
| 3c | -0.0011 | 0.0072 | 0.0020 | -0.0005 | -0.0056 |
| 4c | -0.0057 | 0.0096 | 0.0104 | 0.0074 | -0.0109 |
| 5c | 0.0028 | 0.0224 | 0.0195 | 0.0145 | -0.0123 |
| 6c | -0.0030 | 0.0494 | 0.0519 | 0.0439 | -0.0359 |
| 7c | -0.0221 | 0.0716 | 0.0806 | 0.0686 | -0.0567 |

Table 10 Average of (true - smoothed level) by time point and condition for FS models

| condition | $\mathbf{t = 1 0}$ | $\mathbf{t}=\mathbf{4 0}$ | $\mathbf{t}=\mathbf{5 0}$ | $\mathbf{t}=\mathbf{6 0}$ | $\mathbf{t}=\mathbf{9 0}$ |
| ---: | ---: | ---: | ---: | ---: | ---: |
| 1c | -0.0016 | -0.0009 | 0.0002 | 0.0010 | 0.0009 |
| 2c | -0.0025 | 0.0008 | 0.0001 | 0.0004 | -0.0005 |
| 3c | 0.0031 | 0.0112 | 0.0005 | -0.0032 | -0.0080 |
| 4 c | -0.0059 | 0.0094 | 0.0105 | 0.0075 | -0.0107 |
| 5c | -0.0071 | 0.0136 | 0.0164 | 0.0127 | -0.0169 |
| 6c | -0.0128 | 0.0415 | 0.0489 | 0.0414 | -0.0414 |
| 7c | -0.0332 | 0.0627 | 0.0742 | 0.0632 | -0.0636 |

Table 11 Average of (true - smoothed level) by time point and condition for SF models.

| condition | $t=10$ | $t=40$ | t=50 | $\mathrm{t}=\mathbf{6 0}$ | $\mathrm{t}=90$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 1c | 0.0174 | 0.0149 | 0.0219 | 0.0110 | 0.0050 |
| 2c | 0.0181 | 0.0166 | 0.0229 | 0.0101 | 0.0022 |
| 3 c | 0.0190 | 0.0235 | 0.0258 | 0.0104 | -0.0039 |
| 4c | 0.0169 | 0.0381 | 0.0327 | 0.0163 | -0.0183 |
| 5 c | 0.4635 | 0.5030 | 0.4813 | 0.4636 | 0.4085 |
| 6c | 0.4854 | 0.6207 | 0.6178 | 0.6000 | 0.4387 |
| 7 c | 0.5325 | 0.7155 | 0.7247 | 0.7054 | 0.4938 |

Table 12 Median value of (true - smoothed level) by time point and condition for SF models

| condition | $\mathbf{t = 1 0}$ | $\mathbf{t = 4 0}$ | $\mathbf{t}=\mathbf{5 0}$ | $\mathbf{t}=\mathbf{6 0}$ | $\mathbf{t}=\mathbf{9 0}$ |
| ---: | ---: | ---: | ---: | ---: | ---: |
| 1c | 0.0174 | 0.0148 | 0.0218 | 0.0110 | 0.0053 |
| 2c | 0.0181 | 0.0167 | 0.0228 | 0.0104 | 0.0016 |
| 3c | 0.0189 | 0.0236 | 0.0257 | 0.0106 | -0.0038 |
| 4c | 0.0150 | 0.0374 | 0.0338 | 0.0190 | -0.0188 |
| 5c | 0.0173 | 0.0572 | 0.0402 | 0.0242 | -0.0321 |
| 6c | -0.0146 | 0.1064 | 0.1051 | 0.0890 | -0.0691 |
| 7c | -0.0420 | 0.1348 | 0.1490 | 0.1255 | -0.0895 |

Figures

Figure 1. Actual C-P differences (red) and fitted state space trends (black by minute since birth for three VLBW infants.




Figure 2. The value of $y$ by $t$ where $y$ is the value of the logistic curve simulated:

$$
2 * \mathrm{e}^{(.05 * \mathrm{t})} /\left(3+\mathrm{e}^{(.05 * \mathrm{t})}\right)
$$



Figure 3. The mean value of the standard deviation of (true - smoothed level) by condition
And model.


Figure 4. The mean value of (true-smoothed level) by time point and condition for SS models.


Figure 5. The mean value of (true-smoothed level) by time point and condition for FS models.


Figure 6. The mean value of (true-smoothed level) by time point and condition for SF models.


Figure 7. The ratio of the mean standard deviation of (true - smoothed level) from simulations with cycles to matched pairs without cycles by condition and model


Figure 8. The mean value of (true-smoothed level) by time point and condition (with cycles) for SS models.


Figure 9. The mean value of (true-smoothed level) by time point and condition (with cycles) for FS models.


Figure 10. The mean value of (true-smoothed level) by time point and condition (with cycles) for SF models


Figure 11. Median value of (true - smoothed level) by time point and condition (with cycles) for SF models.


