Individualized on-line monitoring tool to analyse the complex physiological signal of heart beat fluctuations in pigs

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Abstract

Quantifying and understanding the complex fluctuations of physiological signals is the focus of many research. The complexity of physiological signals reflect the ability of organisms to adapt and function within an ever changing environment. The most studied physiological signal to reflect the autonomic imbalance in cases of disease, chronic stress and impaired welfare, in both human and animals is Heart Rate Variability (HRV). Given the limitations of current HRV analyses, like spectral or total entropy analyses, it is suggested to improve our understanding by decomposing the heart rate fluctuations with a dynamic model, based on a Bayesian approach for time series analysis.

The model consists of three components describing the interbeat-intervals dynamics: (1) level and trend, (2) autoregressive process of order 2 and (3) observation error (white noise). The analysis also detects abrupt changes and slightly growing deteriorations. A dataset with continuous ECG recordings from 2 pigs was analysed. The model decomposed total Heart Rate dynamics successfully in the time domain. So, it was possible to detect abrupt changes and slightly growing deteriorations in RR-interval in terms of the moments of occurrence, the magnitude, the duration and recovery.

Key words: Dynamic modelling, Bayesian forecasting, inter-beat interval, heart rate variability, autonomic nervous system

Introduction

Early detection of alteration in health status is of great importance in farm animals, as early intervention after e.g. infection can minimize symptoms, may shorten the recovery period and diminishes production losses due to disease. Most early warning systems in animals focus on the early detection of disease symptoms or infectious agents. When a certain population of pathogens is present, it is uncertain whether, when and to what extent animals will get ill or how capable the animals are to cope with the present pathogenic load without showing symptoms. This is caused by differences in the capability to maintain a certain health state under varying conditions.

The complexity of cardiovascular dynamics has been studied as an indicator for autonomic balance or health state. To describe the variations in both instantaneous heart rate and fluctuations in RR-intervals over time, the term that has become conventionally accepted is "Heart Rate Variability" (HRV) (Malik 1996). In both humans and animals, high complexity of HRV is associated with good health and high adaptive capacity. Low complexity of HRV has become a popular marker for autonomic imbalance in cases of disease, chronic stress and impaired welfare (Malik 1996; Goldberger, Challapalli et al. 2001; von Borell, Langbein et al. 2007) and has gained widespread acceptance as a clinical and investigational tool (Billman 2011).

HRV is usually measured under one of the two common settings: short term measurements under controlled laboratory conditions, or long term measurements derived from 24 hour ECG-recordings made while performing daily activities. The current methods used to describe HRV deliver conventional time domain measures, spectral measures, geometric measures, and a variety of nonlinear variables. Each single variable derived from the different methods reflects a different aspect of HRV. They all show significant associations with physiological outcome or state, but it is still unclear which is the best variable to describe and assess HRV (Kleiger, Stein et al. 2005). Therefore, the clinical utility and predictive value of the existing HRV measurements is under discussion, which focusses on (1) the relationship between the autonomic nervous system (parasympathetic and sympathetic effects) and the descriptive variables of HRV and (2) the substantial variance in HRV within and between normal individuals (Goldberger, Challapalli et al. 2001; Peng, Costa et al. 2009). It can be concluded that we still lack an effective reconstruction method for the phenomenon of interbeat fluctuations in heart rate, that is characterized by a non-stationary process and a degree of stochasticity (Ghasemi, Sahimi et al. 2006).

The goal of this paper is to show the first experiences with an adaptive dynamic model that is able to analyse the non-stationary and non-linear heart rate fluctuations in the time-domain in terms of fast and slow variation. We used the model to analyse time series of ECG recordings (RR-intervals) of 2 pigs to show that it reveals the non-stationary complexity of the cardiac function both in terms of fast and slow variation simultaneously, as well as the detection of the moment of occurrence and extent of changes in its dynamics. Results are presented and it is discussed whether this model can be used in longitudinal on farm settings as an online monitoring tool to detect process disturbances in early stage.

Materials & Methods

Experimental protocol

Four crossbred pigs (Yorkshire x Landrace) were kept together in a pen with rubber flooring (150 cm wide and 120 cm deep) from 11 days until 86 days of age. Milk replacer (Sprayfo Pork, Husdyr Systemer as, Mosby, Norge) was provided *ad libitum* with an automatic wetfeeder (Mambo, Husdyr Systemer as, Mosby, Norge). Milk replacer was slowly reduced until the Mambo was removed at 46 days of age. Solid piglet feed (pellets) were available *ad libitum* from the start of the experiment. Water was provided *ad libitum* during the experimental period. The pigs were exposed to a 12h light (6am until 6 pm) - 12 h dark (6pm until 6 am) photoperiod. Temperature was kept at 28^{o} C from start until 35 days, at 25^{o} C until 64 days age and at 24^{o} C until the end of the experiment. Average relative humidity of the air was 55% during the experiment. The pigs had 2 weeks for acclimatization to the housing facility and weaning regime. At the age of 26 days, two of the four pigs were surgically equipped (intra-abdominal) with implantable telemetry transmitters (Data Science International, DSI, St Paul, MN) to record continuously temperature, activity and cardiac activity (ECG) until the end of the experiment. When the pigs were 35 days old, the two pigs without implants were removed from the pen to enlarge individual space. The growth curve of the two pigs with implants was similar to the curves of the animals that did not have surgical treatment. One pig at the time was monitored during 24 hours (weekdays) and 72 hours (weekends). Every day the pens were cleaned and the animals were inspected clinically. During the experimental period no signs of illness appeared.[1].

Data acquisition telemetry system & video recording

The telemetry system (Data Science International, DSI, St Paul, MN, USA) consisted of implantable transmitters with two bio-potential leads (positive and negative) for measuring ECG signal, a temperature sensor to measure body temperature and one blood pressure fluid filled catheter (model TL11M2-D70-PCT; 49 grams, 33cc), a data exchange matrix and receivers (DSI PhysioTel® Receivers - RMC-1 Model for Large Animals). Only the ECG recordings were analysed in this paper. Signal strength between transmitter and receiver was recorded and expressed in a physical meaningless number ranging from 0 to 51 units. No data were recorded when signal strength dropped below 17 units. During the experimental period video recordings were made with a Sanyo (type RC506CH) camera and Samsung SHR-2040 digital recording system of the complete pen during the light period (6am until 6pm). Telemetry data of the implants were collected with DSI Dataquest A.R.T.™ version 4.31. The ECG signal was measured and stored at 1 kHz.

Data pre-processing

The length (time in msec) of the RR-interval was derived from the raw ECG data with the Ponemah Physiology Platform version 5.0 software (Data Science International, DSI, St Paul, MN, USA). Due to weak radio or transfer signal or high noise some R-peaks were incorrectly detected, resulting in extreme RR-intervals ($RR \leq 200$ msec or $RR \geq 700$ msec). These RR-intervals (denoted as extreme RR-intervals), together with sections where no PQRS complex could be detected (denoted as missing RR-intervals), were omitted from the data series. Subsequently, equidistant time series were formed by averaging the RR-intervals per second (further indicated as averaged or observed RR-intervals). Missing values in the time series were replaced by interpolated data and weighted zero in the analysis.

[1] The established principles of laboratory animal use and care were followed as well as the Dutch law on animal experiments. The Wageningen University Animal Care and Use Committee (Lelystad Department) approved the experiment under number 2011040.f.

Data selection

From the experiments we randomly selected and analysed one hour of one pig (pig #231 from 15:00 until 16:00 on the 23d of January 2012). For detailed explanation of the Bayesian model for analysis of HRV, two periods of 5 minutes were selected within this hour. The two periods of 5 minutes were selected, one with high and one with low activity of the pig based on the video recordings.

Modelling and analysis

Variation in interbeat intervals was decomposed in three parts:

$$\begin{Bmatrix}\text{interbeat}\\ \text{interval}\end{Bmatrix} = \begin{Bmatrix}\text{level\&}\\ \text{trend}\end{Bmatrix} + \begin{Bmatrix}\text{autoregression}\\ \text{component}\end{Bmatrix} + \begin{Bmatrix}\text{white}\\ \text{noise}\end{Bmatrix}$$

Level and trend represent slow dynamic variation, the autoregression component and the white noise represent fast dynamic variation. The white noise represents the independent random residual error. Figure 1 shows a simulated series of 5 min (=300 sec) illustrating the 3 components of the model.

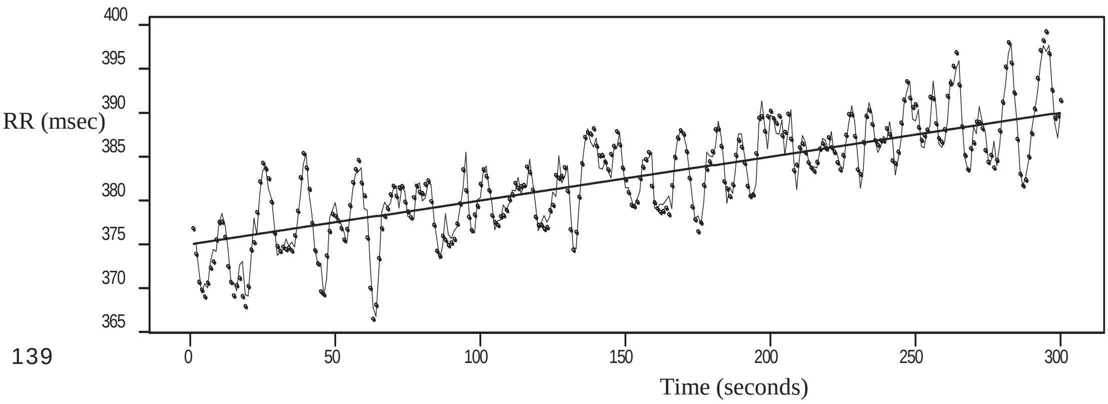


Figure 1: Simulated time series of RR intervals of 5 minutes (300 sec.) showing the 3 components: level and trend (thick straight line); auto-regression component (thin fluctuating line) and white noise scattered around the thin line (points).

A dynamic model was formulated for analysis of the time series of averaged RR-intervals per second Y_t. The dynamic model consisted of an observation and a system equation. The observation equation (1) described the relation between the observation and the parameters:

$$Y_t = \mu_t + Z_t + \nu_t \tag{1}$$

with the parameters: μ_t (level), Z_t (autoregression, AR2) and $\nu_t \sim N\left(0, k_t V_t\right)$ (observation error or white noise, with unknown variance V_t and weight k_t equal to the number of beats per second). The system equations (2) and (3) describe the evolution of the parameters over time:

$$\begin{aligned}\mu_t &= \mu_{t-1} + \beta_{t-1} + \omega_{1,t} \\ \beta_t &= \beta_{t-1} + \omega_{2,t}\end{aligned} \tag{2}$$

$$\begin{aligned}Z_t &= \phi_{1,t-1} Z_{t-1} + \phi_{2,t-1} Z_{t-2} + \omega_{3,t} \\ \phi_{1,t} &= \phi_{1,t-1} + \omega_{4,t} \\ \phi_{2,t} &= \phi_{2,t-1} + \omega_{5,t}\end{aligned} \tag{3}$$

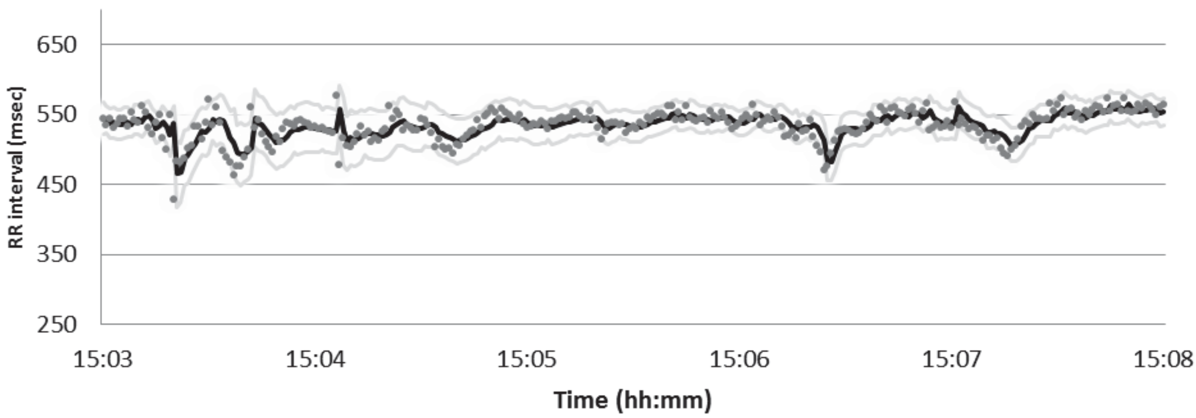
with level μ_t, trend or incremental change β_t, two autoregression coefficients $\phi_{1,t}$ and $\phi_{2,t}$ with system errors $\omega_{1...5,t}$ normally distributed with zero mean and variance matrix $\mathbf{W}_t$. The dynamic parameters are locally constant and follow a random walk. Two kinds of parameter estimates were achieved: online estimates, which were based on observations from the past only, and retrospective estimates, which were based on all observations from the whole time series. All parameters were recursively estimated following the Bayesian approach to the analysis of time series according to (West and Harrison 1997) including a monitoring procedure followed by automatic intervention to detect process disturbances.

The results describing variation in the time domain were linked to results in the frequency domain. Level and trend corresponded to ultralow frequency variation, the pseudo (or stochastic) cyclic behaviour, described by the autoregression AR(2) component corresponded with low frequency variation and the white noise (or random error) corresponded to the high frequency variation. From the parameter estimates at any point in time the correlogram, spectrum and variances were calculated (Diggle 1990).

Results and Discussion

Within the complete analysed hour, 147 RR-intervals were indicated as extreme values and left out of this analysis. Out of the 3600 averaged RR-intervals, 3480 intervals were classified by the monitoring routine as normal, 51 as warnings and 69 as outliers. According to the video recordings, between 15:00 and 15:30, the pigs were mostly resting/sleeping. After this period they awoke, stood up and started eating and drinking, at 15:44 the pigs lied down again.

The results of the analysis are shown in figures 2 to 5. Figures 2a and b show the observed (averaged per second) and forecasted RR intervals for the two periods of 5 minutes within the hour. Figure 2a shows the period of 5 minutes in which the pig was mostly resting and figure 2b shows a more active period where the pig was eating, drinking and playing with its pen mate. Even during these short periods a substantial variation in RR-intervals was detected.



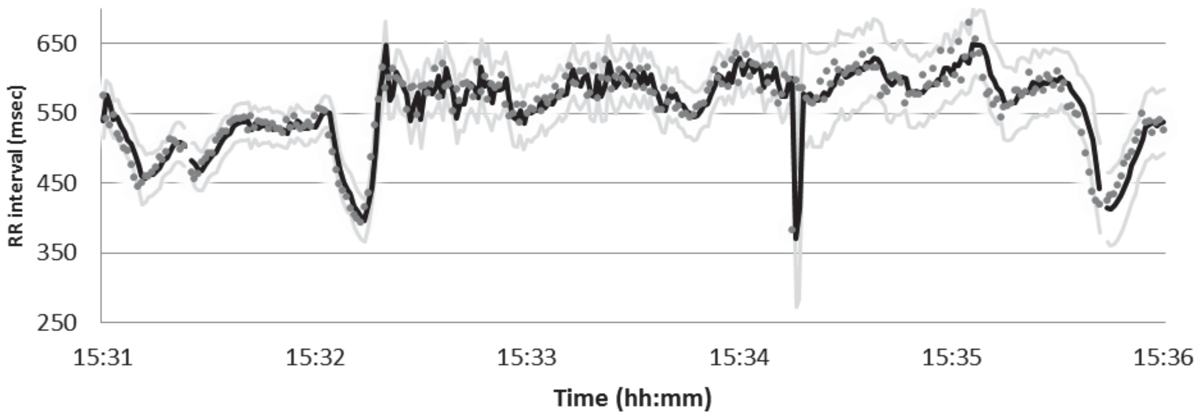
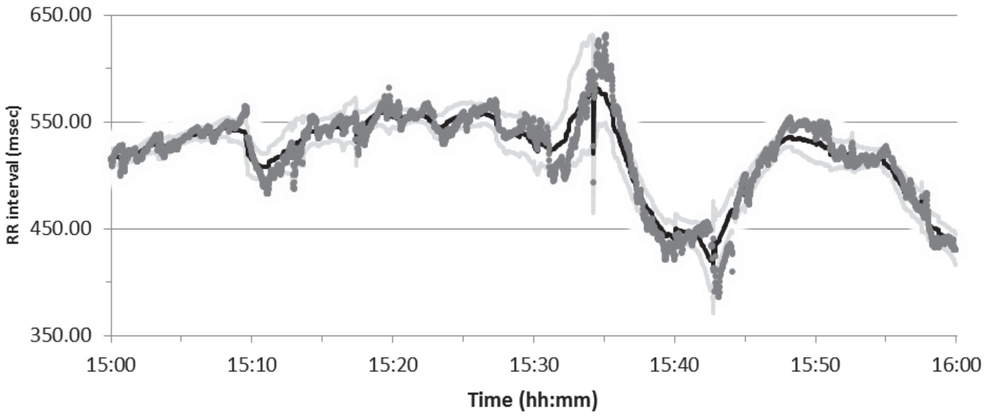


Figure 2a&b Observed and forecasted RR-interval; 2a: Selection of 5 min. period (resting): above and 2b (active): below; observed values (grey points), forecasts (black line), upper and lower level of 90% confidence interval (light grey lines).

Figure 3a and b show the estimated parameters for level (μ_t) and trend (β_t) for the selected hour, representing the slow changing dynamics. Level was accurately estimated at any point in time. More active periods were described by a shorter RR-interval and changes in level were easily picked up, even sudden changes. Figure 4b shows the trend β_t. In the first period of the hour, the trend was not significantly different from zero (the confidence intervals were not above or below zero). It resulted in a more or less constant level, which is shown in figure 3a. Only at t=15:36 a significant negative trend was seen, followed by a significant positive trend, which resulted in an temporary reduction of RR-interval. This is the period the pig was active and was detected by a change in level and trend by the model. Thus, the moment of occurrence of changes in trend of RR-intervals were properly detected by the analysis and could directly be related to the behaviour of the animals. Rapid changes (e.g. at t=15:10 and t=15:12) did not result in a change in level or trend. However, the variance of the process increased, which resulted in a larger confidence interval.



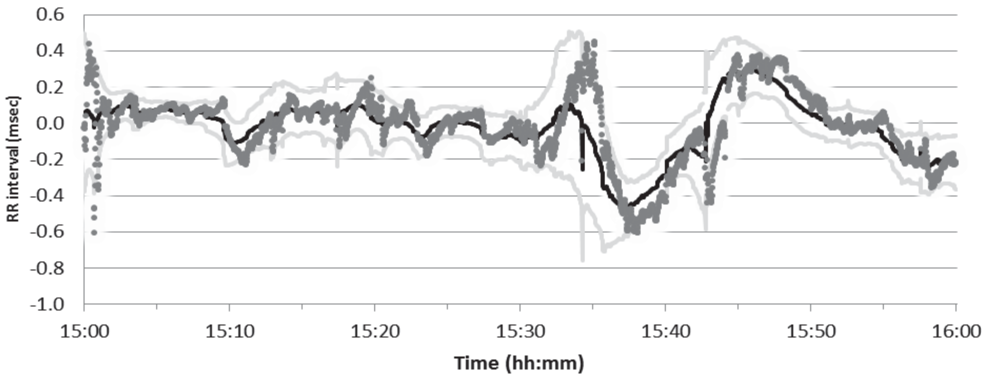


Figure 3a: Estimated level μ_t (above) and 3b: Trend β_t or incremental growth (below); online estimates (grey points); retrospective estimates (black line) incl. 90% confidence interval (light grey lines)

In fig 4a and 4b the parameter estimates that describe the fast dynamics changes are shown. These are the autoregression component Z_t the forecast variance Q_t and observation variance S_t. The variances fluctuated, even during both 5 minute periods. The variances increased, especially after abrupt changes. The two AR-parameters $\phi_{1,t}$ and $\phi_{2,t}$ described the properties of the AR(2)-process, i.e. the shape and rate of decay of random deviations from the base level. In figure 5 $\phi_{1,t}$ and $\phi_{2,t}$ are plotted for both selected periods of 5 minutes.

The AR-process is stable when the AR-parameters lie within the triangle (figure 5). If they lie outside the triangle, the process is unstable and the heart rate will exponentially grow or decline which is physiologically not possible in living organisms. When the AR-parameters lie within the triangle and below the parabola the decay of the deviations follows a decaying cycle, otherwise they follow a decaying curve.

The stochastic cycle during the resting and active period showed different characteristics. It appeared that when the pig was resting, the AR-parameters lied clustered together and more to the left in the upper part above the parabola. In this area, the fluctuations around the base level are characterized by a relatively fast exponential decay (dark grey cluster in figure 5). When the pig was more active, the estimated AR-parameters lied in a strip near to the right side of the triangle (light grey strip in figure 5) where the decay of fluctuations appear to be slower (light grey line in figure 5).

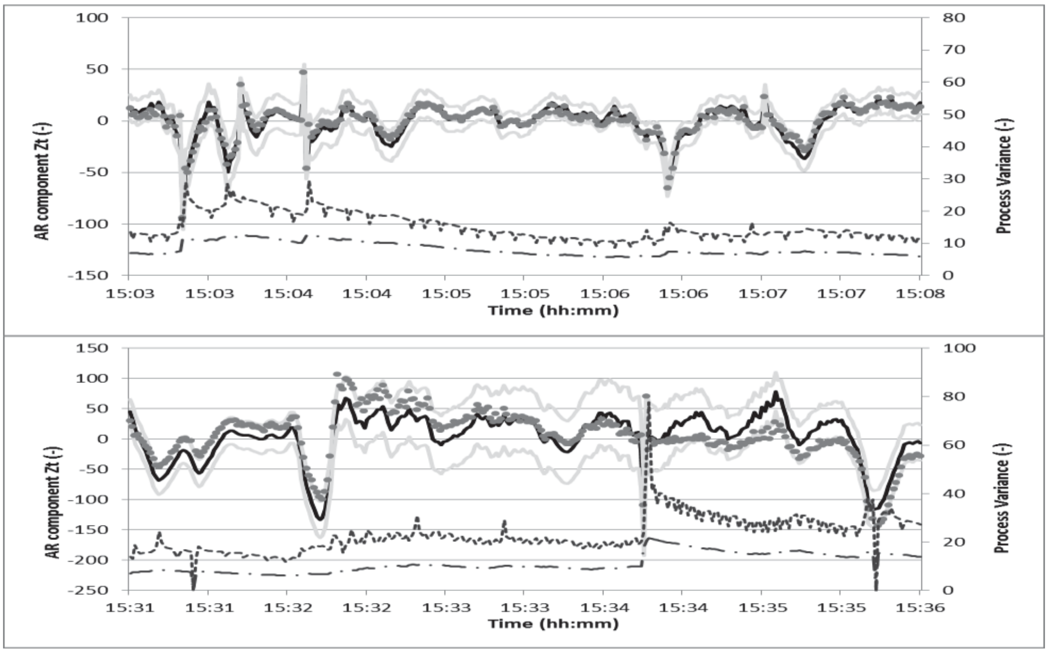


Figure 4a & b: Autoregression component Z_t and variances within the two selected periods of 5 minutes; 4a sleep (above) 4b active (below): Online estimates (grey points); retrospective estimates (black line) incl. 90% confidence interval (light grey lines).
Forecast variance Q_t (------) and observation variance S_t (white noise, - . -)

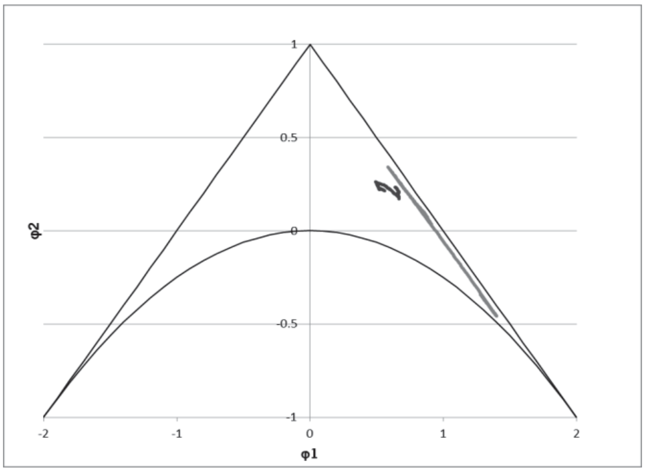


Figure 5 Retrospective estimated AR parameters $\phi_{1,t}$ and $\phi_{2,t}$ showing the two selected 5 minute periods while sleeping (dark grey line 15:03-15:08) and active (light grey line 15:31-15:36).

The first two components level (μ_t) and trend (β_t) adjust the base level of heart rate to the required set point according the behaviour and physiological demands at that moment.

Significant trends appeared whenever an increase or decrease in base level is required to meet the physiological needs. Changes in RR-interval at arousal were described by a decreasing trend, followed by a slow increasing trend to adjust to the desired level again. Sudden fast changes in level (mainly drops in RR-intervals) were not detected by trend since the process variance increased simultaneously. This indicates that the level and trend components of the model reflect the slow dynamic changes in RR-interval.

Within 5 minute periods substantial variation in interbeat interval can be seen. This actual, more subtle, variation in RR-intervals cannot be described accurately by models based on the assumption of a stationary process, like the Fast Fourier Transformation (FFT). They were, however, captured by the decomposing model, which moment by moment follows every fluctuation and any changes in dynamics. These fast dynamic fluctuations around the slowly changing base level is described by the autoregression and error components, corresponding to low and high frequency variation. The AR2-process ensured that the modelled RR-interval oscillated around the base level that was set by level and trend. This process with more or less decaying deviations can be seen as continuously fine-tuning towards the desired heart rate.

As expected, the random error component ν_t could not be captured within any pattern or related to any cause. This is the white noise component, which is shown as random scattering around the AR oscillations as shown in figure 1. As shown in figure 4 the variance of this white noise component was not constant within the 5 minute periods. So, the white noise variance is dynamically changing even within short periods.

The parameters were estimated online at each moment of the time series and together characterized the total dynamic variation in RR-interval and the dependency between successive observations in the actual situation. The accuracy of the online estimates was improved afterwards by the backward smoothing procedure, resulting in the retrospective estimates.

Conclusion

Our model is based on a beat to beat calculation, which is necessary for timely detection of the dynamical changes in HRV that apparently occur continuously over time. Techniques that cannot calculate on a beat to beat basis, such as other time or frequency domain techniques, overlook the dynamic changes when a mean value over a longer time period is calculated, and therefore provide less (detailed) information.

We concluded that the adaptive dynamic model is able to analyse the non-stationary and non-linear heart rate fluctuations in the time-domain in terms of fast and slow variation. The model detects sudden changes as well as slightly growing deteriorations.

These characterisations of dynamics will differ depending on the physiological state of the animal and may be individually different. Further research will focus on the relation between estimated parameter values and the physiological state of animals. After the physiological interpretation of the parameters with respect to the autonomic nervous system the model will be further developed as an online monitoring tool that can be used to detect early alterations in physiological state of animals in husbandry systems.

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