Detecting Dynamical Changes in Vital Signs using Switching Kalman Filter

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***Abstract*— Vital signs contain valuable information about the health condition of patients during their stay in the ward, when deterioration process begins. The use of methods to predict and detect regime changes such as switching models can help to understand how vital sign dynamics are altered in health and disease. However, time series of vital signs are remarkably non-stationary in these scenarios. The objective of this study is to quantify the potential bias of the switching models in the presence of non-stationary time series, when the inputs are spectral, symbolic and entropy indices. To distinguish stationary periods from non-stationary, a stationarity test was used to verify the stability of the mean and variance over short periods. Then, we compared the results from a switching Kalman filter (SKF) model trained using only indices obtained over stationary periods, with a model trained using indices obtained solely over non-stationary periods. It was observed that the indices measured over stationary and non-stationary periods were significantly different. The results were highly dependent of what indices were used as input, being the multi-scale entropy (MSE) the most efficient approach, achieving an average correlation coefficients of 38%.**

I. INTRODUCTION

Recent technological developments in wearable sensor technologies have the potential to impact patient monitoring in general wards. Although hospital wards require the use Early Warning Scoring (EWS) systems to monitor patients vital-signs, they are often paper-based and measured every 2-4 hours by nursing staff. The patient is considered to be at risk of deterioration if these scores exceed pre-defined thresholds. The deterioration is directly related to the concept of rescue failure, that is, the idea that although not all complications of medical care are avoidable, health systems must be able to identify and treat complications quickly when they occur. However, it is recognized that hospitals may have difficulty in detecting and responding to early signs of patient deterioration, leading to late intensive care referrals, excess mortality and morbidity, and increased hospital costs. During the last years, the efficacy of vital signs routinely measured as a tool to detect deterioration and adverse events was a controversial subject where conflicting evidence existed [1]. However, recent studies have provided evidence of quantitative studies indicating that abnormalities in vital signs occur in patients several hours before deterioration [2], some examples include changes in respiratory rate (RESP), heart rate (HR) and blood pressure [3], [4]. Although these results suggest the clinical relevance of routine measures of vital signs, it is unanimous that the subject is poorly studied [1].

The use of methods to predict and detect regime changes can help to understand how vital-sign dynamics are altered in health and disease, revealing potential patterns of physiological deterioration. Some examples include neonatal condition monitoring studied by the means of factorial switching models that involve the analysis of systems with hidden factors that "switch" between different models of operation, i.e. baby's health state [5] and, an approach of dynamic linear switching system to study several functional components of autonomic regulation [6].

Spectral, symbolic and entropy variables are some examples of analysis tools capable to extract relevant physiological information from the analysis of vital signs that have been used in different medical contexts. However, there are some studies that draw attention to the significant differences caused by non-stationarities in these indices, mainly if the experimental conditions are not kept under control [7], [8].

The objective of this study is to quantify the potential bias of switching models due to the presence of non-stationarities. The analysis focused HR and RESP indices obtained during patients' stay in general wards, when patients are subject to physiological changes (internally and externally induced) and is not possible to conduct a controlled trial. We assumed that although the dynamics of clinical configuration are mainly non-linear, these dynamics can be well approximated by a mixture of linear dynamical models that alternate between them. The Kalman filter was trained assuming as inputs, spectral, symbolic and entropy indices and two different setups were compared, a first one where only the values obtained over stationary periods were used, and another one where the inputs were obtained solely over non-stationary periods. The paper is organized as follows: an overview of the methodology used is presented in Section 2, the results and conclusions are presented in Section 3 and 4, respectively.

II. METHODS

A. Cardiorespiratory dynamics to model initialization

Special attention should be given to the initialization of the model, depending on the dynamics of interest, where a single dynamic regime may represent a particular clinical procedure taking place, a particular state of health or, as used in this work, shared cardiorespiratory dynamics. The Markov switch regression model [9] was used for this purpose, being the mean and/or variance of HR and RESP the switching variables, considering two different states ($M = 2$).

*Research supported by Marie Curie Actions under the project IPSIBiM (Grant number 656737 - H2020-MSCA-IF-2014).

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This non-linear model is able to capture complex dynamic patterns being the switching mechanism controlled by an unobservable state variable that follows a first-order Markov chain. Considering a univariate case, the two model states can be represented as:

$$y(t) = \mu_1 + \varepsilon(t), \quad \varepsilon(t) \sim (0, \sigma_1^2) \tag{1}$$

$$y(t) = \mu_2 + \varepsilon(t), \quad \varepsilon(t) \sim (0, \sigma_2^2) \tag{2}$$

where (1) and (2) can be treated as linear regression models, referring to states 1 and 2 respectively. The expectations of each state are given by μ_1 and μ_2 and the different volatilities σ_1^2 and σ_2^2 represent the uncertainty in vital signs measurements. It was implemented using MS Regress package [10].

B. Stationarity test

A stationarity test proposed by Porta et al. [11] was utilized to distinguish stationary periods from non-stationary ones. The stability of the mean and variance was checked over short HR and RESP periods (300 points). Three parameters were assigned: the number of samples N, the number of patterns M and the pattern length L. From the set of $N - L + 1$ possible patterns, M patterns were randomly selected (considering that all the patterns had the same probability to be selected). Then, the test checked whether the mean and variance remained constant over the M patterns. The Kolmogorov-Smirnov goodness-of-fit test was used to evaluate the normality of the distribution. If the null hypothesis of a normal distribution was rejected, the mean stability test was performed by the Kruskal-Wallis test. Otherwise, it was performed through analysis of variance (F-test statistic). If the null hypothesis of a normal distribution was rejected, then the variance stability test was performed by the Levene test, otherwise by the Bartlett test. The parameter values used were similar to the used by other studies [7], [12], N was set equal to 300, L was set to 50, M was set equal to 8. A confidence level of ($p < 0.05$ was set for all the steps).

C. HR and RESP indices

The vital signs indices were computed using symbolic (SA), spectral, multi-scale entropy (MSE) and kernel entropy (KE) analysis using the same 300 samples used in section II-B. The values obtained within non-stationary periods were compared to those obtained within stationary periods. Unpaired t-test and F-test were used to evaluate the differences in the mean and variance of each index. A $p < 0.05$ was considered as significant.

1) Symbolic Analysis (SA): Symbolic analysis was performed according to the approach described in Porta et al. (2001) [13]. Time series were transformed into a sequence of symbols using a coarse graining approach based on a uniform quantization procedure. The set of indices included: (i) patterns without variation, where all the symbols were equal (0V); (ii) patterns with one variation, i.e. two consecutive symbols were equal (1V); (iii) patterns with two likely variations, meaning that the three symbols formed an ascending or descending ramp (2LV); (iv) patterns with two unlike variations (2UV), e.g. (3,1,4).

2) Spectral Analysis: The power spectral density was also calculated. Very low frequencies were considered in the range from 0 to 0.03 Hz, low frequency (LF) from 0.03 to 0.15 Hz and high frequency (HF) from 0.15 to 0.40 Hz. The spectral components were analysed using the ratio between low and high frequency (LF/HF).

3) Multi-scale entropy (MSE): MSE method evaluates the entropy of a signal on different scales. Firstly, multiple coarse-grained time series were constructed by averaging the data points within non-overlapping windows of increasing length and then Sample Entropy (SampEn) was calculated for each coarse-grained time series [14]. In this work only the first scales (1 to 3) were used.

4) Kernel Entropy (KerEnt): KerEnt is obtained by incorporating the quadratic Renyi entropy [15] into the concept of entropy rate. The values were computed considering Gaussian kernels for specific time scales (m) and distribution width. The choice for m was similar to other entropy measures, where $m = 1$ or $m = 2$ are common values [16]. Different methods can be used for choosing appropriate distribution width, being the Metropolis-Hastings algorithm used in this work [17].

D. Kalman Regime Switching

Let $y(t)$ be a K-dimensional vector of physiological variables at time t (as described in Section II-C). An autoregressive (AR) model was used to describe these variables:

$$y(t) = \sum_{i=1}^{p} h(i) y(t-i) + v(t) \tag{3}$$

where p is the order of the model, $h(i)$ the KxK matrix of AR parameters capturing linear dynamics between $y(t-i)$ and $y(t)$ and $v(t)$ the Gaussian noise with zero mean and variance σ^2.

Then, M dynamical linear models are established based on a Kalman filter, considering a particular switch setting. Under this setup, non-linear dynamics are approximated by a mixture of models that alternate between them and, non-Gaussian noise is approximated using a mixture of Gaussians. The vector AR models are described in a state-space form:

$$s(t) = A\mathbf{s}(t-1) + \mathbf{q}(t) \quad q \sim N(0, Q) \tag{4}$$

$$y(t) = C\mathbf{s}(t) + \mathbf{r}(t) \quad v \sim N(0, R) \tag{5}$$

where $\mathbf{s}$(t) is the state vector at time t, $y(t)$ is the observations vector, A is the AR coefficients matrix, C is the state-observations matrix, Q and R are noise covariance matrices. Each one of the models M is characterized by a set of parameters A, C, Q, R. The switching Kalman filter (SKF) algorithm assumes $\mathbf{s}$(t) follow a Markov chain with transition matrix Z (MxM) and initial distribution vector π ($1xM$).

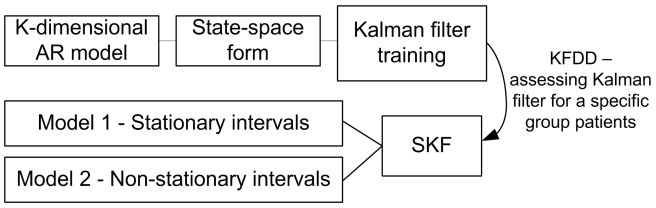

Fig. 1. Schematic representation of the methodology used in Kalman regime switching.

Based on the assumption that different patients share similar dynamical patterns, such as Nemati et. al demonstrated [18], physiological variables were grouped considering groups of 3 to 6 patients, that where used to train Kalman filter. It was trained based on the initial segmentation from Section II-A and the expectation-maximization (EM) algorithm was used to refine estimates for each state. For each group, to access how well the training was, we applied Kalman Filter Diagnostic Dashboard (KFDD) [19] that compares the innovation sequences, that is, the difference between the actual observations and the predicted values using the Kalman model, and the covariance of innovations under optimal conditions when applied to training data.

The SKF was then performed for a different group of patients, using Kalman model estimates achieved previously. Two different setups were tested, first using the estimates obtained when the Kalman model was trained using only indices measured over stationary periods and, in a second case when the observation vector included solely indices obtained over non-stationary periods. A schematic representation of the methodology used is depicted in Figure 1.

III. Results

This study includes data from 39 adult patients from the MIMIC II waveform database with at least 24h of minute-by-minute HR and RESP values. Thirteen patients were used to initialise and train the Kalman filter for each state. The remaining 26 patients were used to compare both SKF models.

Similar HR/RESP values were obtained in both training and testing sets, $77.72 \pm 12.95/22.26 \pm 5.53$ and $87.21 \pm 18.08/19.94 \pm 6.50$, respectively. Non-stationary series were found frequently in both datasets: $97.89 \pm 2.98\%$ and $87.63 \pm 7.22\%$ for HR and RESP, respectively. Table I reports *mean* $\pm$ *SD* of each index calculated over all the segments and over exclusively stationary series. It is also presented the result of the t-test and F-test. All the indices calculated over exclusively stationary periods were significantly different from the values observed from the analysis of non-stationary segments. The percentage of stationary periods was very low, around 3%, and as the focus of this paper remains on the role of stationary periods, we focused our attention on the analysis of RESP.

The state's initialization based on cardiorespiratory dynamics was performed using the method described in Section II-A. An example of RESP segmentation is presented in Figure 2, where the periods of stationarity are also indicated. In this figure, only RESP is represented, but in the segmentation process, both HR and RESP signals were considered, namely considering HR (mean) and RESP (mean and SD).

TABLE I

RESP INDICES FOR STATIONARY AND NON-STATIONARY GROUPS.

index	Stat. series	Non-stat. series	Comparison over the Mean	Comparison over the variance
0V	10.60 ± 6.02	22.54 ± 16.92	$p < 0.001$	$p < 0.001$
1V	50.18 ± 4.31	49.79 ± 9.44	$p < 0.001$	$p < 0.001$
2UV	15.47 ± 2.77	11.20 ± 4.29	$p < 0.001$	$p < 0.001$
2V	23.76 ± 5.40	16.47 ± 7.60	$p < 0.001$	$p < 0.001$
LF/HF	1.23 ± 0.83	2.02 ± 1.81	$p < 0.001$	$p < 0.001$
KerEnt	1.93 ± 0.20	1.76 ± 0.29	$p < 0.001$	$p < 0.001$
SEnt (1)	2.04 ± 0.43	1.59 ± 0.62	$p < 0.001$	$p < 0.001$
SEnt (2)	1.98 ± 0.40	1.54 ± 0.59	$p < 0.001$	$p < 0.001$
SEnt (3)	1.96 ± 0.41	1.54 ± 0.60	$p < 0.001$	$p < 0.001$

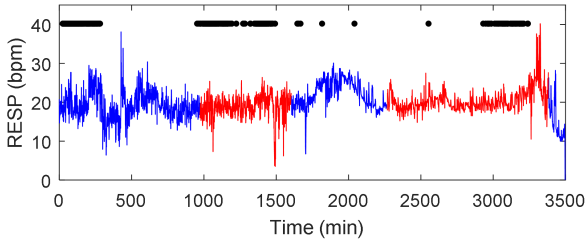

Fig. 2. Stationary and non-stationary periods are identified in the upper panel (black), and cardiorepiratory segmentation in the lower panel, state 1 (red) and state 2 (blue).

To assess how well trained was the Kalman filter for a specific group of patients, KFDD was applied. It allowed to evaluate if the innovations came from a Gaussian distribution with zero mean and a specific covariance, and if they were not correlated in time. In practice, this allowed to assess if the physiological states considered for the specific grouped patients was sufficiently consistent to be used in the analysis. Table II column KFDD-variance relates to the variance of the innovations considering the 5 different training groups, the values below 0.1 were considered acceptable. Maximum and minimum values ranged between 0.03 and 0.3.

The switching bias analysis comprised the comparison of the switch setting. The example presented in Figure 3 presents the original RESP time series (upper panel) and the switch setting considering both approaches (bottom panel), when SKF was trained using the values obtained over stationary periods (blue) and non-stationary periods (black). In this case correlation coefficient was 70%, which means that both models switch state at approximately the same time frequently.

Results from 5 different groups are presented in Table II. Given the significant differences observed between both groups we were not expecting a significant overlap between both approaches. It is visible, that the results are highly dependent of what indices are used as input, being the MSE the most efficient approach, achieving an average correlation coefficients of 38%. KerEnt only improved the results for the group G4 in comparison with MSE approach. The other

TABLE II

AVERAGE CORRELATION COEFFICIENT OBTAINED FOR THE SWITCH SETTINGS, CONSIDERING DIFFERENT INDICES AS INPUT AND 6 TRAINING GROUPS. TRAINING GROUPS ASSESSED THROUGH THE KFDD VARIANCE.

	KE&MSE	MSE	SA	LH/HF	All	KFDD-Variance
G1	0.362	0.464	0.098	–	0.148	0.067
G2	0.123	0.231	0.127	0.171	0.083	0.094
G3	0.315	0.478	–	0.107	–	0.047
G4	0.530	0.234	0.145	0.090	0.175	0.069
G5	0.319	0.608	–	0.085	0.227	0.069
G6	0.130	0.281	0.253	–	0.108	0.042

KerEnt-kernel entropy, MSE-multi-scale entropy, SA-symbolic analysis.

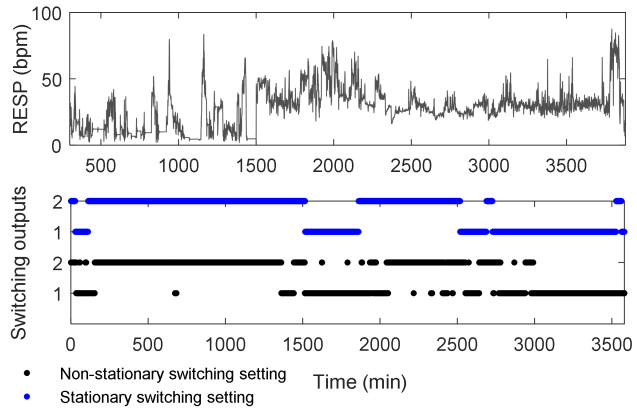

Fig. 3. RESP time series (upper panel) and inferred distribution of switch settings (lower panel) for stationary (blue) and non-stationary case (black) considering all the indices studied.

approaches performed significantly worse. Those results do not include switching setting that do not switch at least 10% between states, e.g. the entries (-) mean that none of the patients achieved a minimum switch of 10%.

IV. CONCLUSIONS

Vital signs time series cannot be considered stationary as a result of being acquired in non-controlled settings and so therefore subject to huge variations. This study focuses on the impact that non-stationary time series can have on switching systems. As expected, the measured indices over stationary and non-stationary periods are significantly different. However, the non-stationarity nature did not compromised the results as expected, when MSE was used as input, an overlap of about 50% was observed in three of the training groups.

The main drawbacks are: the fact that only two switching models were considered, e.g. Lehman et. al. [20] identified 9 models and, the fact that dynamical patterns discovered are not physiologically interpretable. However, these results are promising for the exploration of switching models in non-controlled clinical setting, such as general wards, where physiological deterioration may occur. In future, we intend to initialise the models based on physiological information related to particular states of health, aiming to understand how vital-sign dynamics are altered in healthy and non-healthy conditions.

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