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Characterising infant inter-breath interval patterns during active and quiet sleep using recurrence plot analysis

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Abstract—**Breathing patterns are characteristically different between active and quiet sleep states in infants. It has been previously identified that breathing dynamics are governed by a non-linear controller which implies the need for a nonlinear analytical tool. Further, it has been shown that quantified non-linear variables are different between adult sleep states. This study aims to determine whether a nonlinear analytical tool known as recurrence plot analysis can characterize breath intervals of active and quiet sleep states in infants. Overnight polysomnograms were obtained from 32 healthy infants. The 6 longest periods each of active and quiet sleep were identified and a software routine extracted inter-breath interval data for recurrence plot analysis. Determinism (DET), laminarity (LAM) and radius (RAD) values were calculated for an embedding dimension of 4, 6, 8 and 16, and fixed recurrence of 0.5, 1, 2, 3.5 and 5%. Recurrence plots exhibited characteristically different patterns for active and quiet sleep. Active sleep periods typically had higher values of RAD, DET and LAM than for quiet sleep, and this trend was invariant to a specific choice of embedding dimension or fixed recurrence. These differences may provide a basis for automated sleep state classification, and the quantitative investigation of pathological breathing patterns.**

I. Introduction

Sleep states in humans are a classification of the physiological features observed in human brainwave, and ocular muscular activity during the normal sleeping cycle. In adults, sleep states are classified as either awake, REM (rapid eye movement) sleep, or non-REM sleep stages. In infants sleep states are classified as awake (AW), active sleep (AS) or quiet sleep (QS). It has been widely observed that the respiratory patterns in humans vary throughout the defined sleep states, and the visual inspection of the respiratory patterns forms part of the criteria for sleep scoring in infants [1]. Investigations into infant breathing during sleep have shown that respiratory rate and minute volume was higher in active sleep than in quiet sleep, and the variability in respiratory rate, tidal volume and minute ventilation was higher in active sleep than in quiet sleep [2, 3]. In clinical practice, clinicians are able to qualitatively identify characteristic differences which go beyond measures of rate and variability. It is desirable to develop methods to quantify these characteristic differences. Such a methodology may allow the development of disease, and physiological state discriminators.

Recent developments in the field of non-linear mathematics have led to speculation that physiological systems, including breathing, may follow non-linear patterns. There have been a number of studies in human adults and infants which have investigated whether breathing patterns contain non-linear dynamics [4-6]. The overall conclusion suggests that human breathing patterns are non-linear and may express chaotic dynamics. Given that breathing patterns are non-linear, a number of studies have used non-linear approaches to compare breathing patterns during different sleep states. Studies in human adults have shown that the correlation dimension is higher in REM than in non-REM sleep, is lower in stage IV than stage I non-REM sleep [7], and that these changes also correlate to similar changes in the correlation dimension and approximate entropy of EEG patterns [8]. In a study of infants with broncho-pulmonary dysplasia (BPD), and healthy controls aged 37-54 days, breathing patterns were investigated using the correlation integral. In both controls and BPD subjects, the correlation integral was higher during active than quiet sleep [9].

The recurrence plot originally proposed by Eckmann [10], is a qualitative tool used to visualize non-linear patterns present in time series data. Recurrence plot analysis is used to quantify structures in the recurrence plot and therefore non-linear dynamics present in the original time series data. Webber [11] and Marwan [12] have proposed a number of different quantification variables. These include: radius (RAD) and recurrence (REC) which describe attractor size and structure; determinism (DET) which can estimate sensitivity to initial conditions; and laminarity (LAM) which quantifies the presence of laminar or invariant periods in the time-series data. The ability to quantify a number of different features, combined with no rigid requirements for data length and stationarity make it particularly applicable to exploratory studies of physiological systems.

The aim of this study is thus to apply recurrence plot analysis to infant inter-breath interval data. This is an exploratory study to investigate if there are characteristic differences in the non-linear features observed during infant active and quiet sleep states.

II. Method

A. Data

Overnight, lab based polysomnograms (PSG's) were obtained from 32 healthy infants aged between 19-153 days

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Table I: The recurrence quantification analysis (RQA) variables radius (RAD), determinism (DET) and laminarity (LAM) calculated for AS and QS periods at all combinations of embedding dimension (DIM) and fixed recurrence (REC). Median value across AS and QS periods, as well as P value calculated using Wilcoxon's sign-rank test are displayed.

RQA Variable	REC	DIM=4			DIM=6			DIM=8			DIM=16		
		AS Median	QS Median	P value	AS Median	QS Median	P value	AS Median	QS Median	P value	AS Median	QS Median	P value
RAD	0.50%	0.23	0.10	p<0.01	0.40	0.17	p<0.01	0.55	0.23	p<0.01	1.10	0.45	p<0.01
	1%	0.28	0.12	p<0.01	0.47	0.20	p<0.01	0.63	0.26	p<0.01	1.22	0.48	p<0.01
	2%	0.35	0.14	p<0.01	0.54	0.22	p<0.01	0.72	0.29	p<0.01	1.35	0.53	p<0.01
	3.50%	0.41	0.17	p<0.01	0.63	0.25	p<0.01	0.82	0.32	p<0.01	1.51	0.57	p<0.01
	5%	0.46	0.17	p<0.01	0.70	0.27	p<0.01	0.90	0.35	p<0.01	1.61	0.59	p<0.01
DET (%)	0.50%	48	46	p<0.01	66	64	p<0.01	76	73	p<0.01	89	87	p<0.01
	1%	56	54	p<0.01	71	69	0.010	80	77	p<0.01	91	89	p<0.01
	2%	63	61	p<0.01	76	75	p<0.01	83	81	p<0.01	93	91	p<0.01
	3.50%	69	67	p<0.01	81	79	p<0.01	87	85	p<0.01	94	92	p<0.01
	5%	74	72	p<0.01	83	82	p<0.01	89	87	p<0.01	95	93	p<0.01
LAM (%)	0.50%	14	6	p<0.01	23	9	p<0.01	30	11	p<0.01	44	17	p<0.01
	1%	24	12	p<0.01	36	16	p<0.01	43	19	p<0.01	57	26	p<0.01
	2%	36	21	p<0.01	49	25	p<0.01	57	29	p<0.01	68	39	p<0.01
	3.50%	49	29	p<0.01	60	36	p<0.01	65	40	p<0.01	75	49	p<0.01
	5%	56	36	p<0.01	66	42	p<0.01	70	46	p<0.01	78	56	p<0.01

(16 male, 16 female) from the Collaborative Home Infant Monitoring Evaluation) CHIME dataset [13]. This data was sleep staged by an expert clinician using defined criteria [1] as AS, QS, or AW. The PSG signal source of interest in this study is respiratory inductive plethysmography (RIP). The RIP measures chest or abdominal wall excursions with breathing. The raw data used in this study was sampled at 10Hz, with 8 bit resolution. This data was further processed to calculate successive respiratory period, or inter-breath interval (IBI) series using a tidal amplitude threshold algorithm [14].

From each of the 32 sleep scored healthy infant PSG's, the 6 longest periods each of active and quiet sleep were identified, and the abdomen channel of Respiratory Inductive Plethysmography (RIP) data extracted. In total 192 periods each of active and quiet sleep were extracted. The RIP data for each period was converted to inter-breath intervals (IBI's), and the middle 400 IBI's extracted. If the total length of the series was less than 400 breaths, the whole series was discarded to avoid using datasets of different lengths. After shorter periods were discarded, 125 periods of active sleep and 173 periods of quiet sleep remained.

B. Non Linear Analysis of Breathing Data

Recurrence plot analysis is a phase space technique and requires the selection of an embedding dimension and time delay. In the application of phase space techniques to human respiratory data, embedding dimension in the range of 2-20 have been used, with 4-10 being the most common range [4-6, 8, 15, 16]. In this experiment it was chosen to explore embedding dimensions (DIM) of 4, 6, 8 and 16. A time delay of 1 was chosen due to the discrete nature of IBI data.

Each period of AS and QS data was analysed using recurrence plot analysis at a dimension of 4, 6, 8 and 16, and for each dimension at a fixed recurrence values (REC) of 0.5, 1, 2, 3.5 and 5%. The following recurrence plot analysis variables were calculated:

- Radius (RAD)
- Determinism (DET)
- Laminarity (LAM)

For the variables DET and LAM a line (diagonal and vertical respectively) is defined as 2 or more recurrent points in length.

III. RESULTS

Table 1 presents the results for recurrence plot analysis across all periods of AS and QS IBI data. For each combination of DIM, and REC, the median value of that variable for AS and the median value for QS periods are presented. A paired sample Wilcoxon signed rank test was applied with a confidence level of alpha=0.01 to determine whether the differences between AS and QS results were statistically significant.

For all three variables, RAD, DET and LAM, the median result calculated for AS periods was higher than the median result for QS periods for each combination of REC and DIM. For almost all embedding combinations, the difference between AS and QS medians was statistically significant, with $p<0.01$ allowing the null hypothesis to be rejected and the alternate hypothesis to be accepted. The only exception was for DET at DIM=6, REC=1%. Figure 1 shows box-plots for a subset of the results, for DIM=8. The trends in table 1 may be observed with results for RAD, DET and LAM typically higher for AS than QS.

IV. DISCUSSION

The variable RAD calculated at fixed recurrence values quantifies how closely neighbouring phase space points are situated. Invariant to the embedding dimension and chosen fixed recurrence value, RAD was higher for AS periods than QS periods. It can be concluded that neighbouring phase

space points are clustered closer together in QS compared to AS periods. A compact phase space implies greater regularity of inter-breath intervals throughout the period.

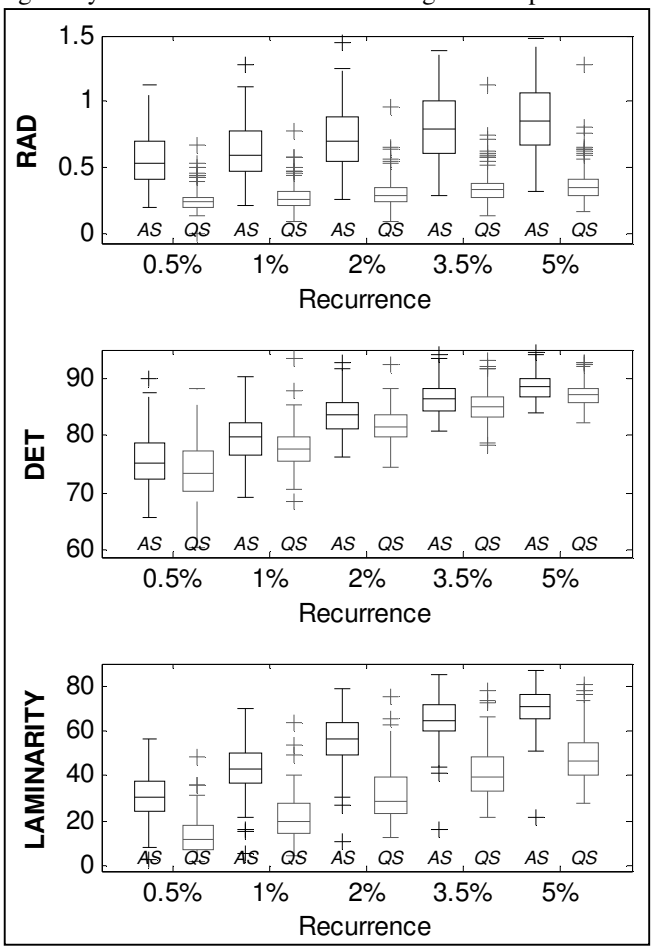

Figure 1: Box-plots of recurrence quantification analysis variables radius (RAD), determinism (DET) and laminarity (LAM) calculated at DIM=8, and REC=0.5, 1, 2, 3.5 and 5%, across all periods of AS and QS IBI data.

The variable DET quantifies the percentage of recurrent points which fall on diagonal lines. Diagonal lines represent times when phase space trajectories remain close for extended periods. Longer diagonal lines indicate greater predictability, whilst shorter lines indicate that the system is more sensitive to initial conditions. DET calculated at each embedding combination, was higher for AS than QS, and implying that AS inter-breath interval dynamics are less sensitive to initial conditions than QS breathing dynamics. This is somewhat counter-intuitive, because in clinical observation, the greater variation in AS IBI values appears less predictable than the more regular QS IBI time series. Although not using true measures of predictability, these results may be compared with studies by Rostig [17], where it was found using de-trended fluctuation analysis, that long range correlations are present in adult REM IBI data, but not non-REM IBI data. This greater predictability may be associated with the "memory" associated with long term correlation. One interpretation of this may be that although there is greater variation in AS breathing (quantified using RAD), it occurs in a more predictable manner relative to QS.

The variable LAM quantifies vertical lines in the recurrence plot. Vertical lines imply that the time series has reached some laminar, invariant state, or the presence of tangential motion [12]. LAM was higher in AS periods than QS periods. Once again, this is a somewhat counter-intuitive and surprising result, since when inter-breath interval time series is observed, QS breathing has more frequent, and longer periods of regular breathing compared to AS. However, it is necessary to consider calculations are being made at a fixed recurrence value, and therefore vertical lines imply periods of regularity relative to the normal phase space variation. Thus, in AS, where there is a large area of phase space explored, periods of time series data which are relatively invariant, are observed as vertical lines in the recurrence plot. When considered in this context, the results make more intuitive sense with the implication that AS IBI is highly variable, but with periods of relative invariance, compared to QS periods which have a more regular, low level of variation.

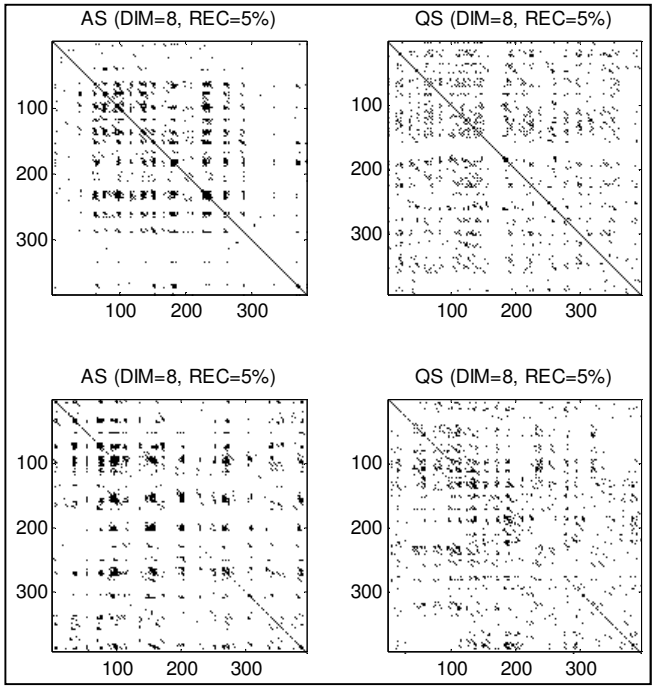

Figure 2: Recurrence plots generated for periods of AS and QS data from a single infant. These images show the characteristic differences in line structures between sleep states, with AS showing square blocks of recurrent point, while QS shows more distinct diagonal lines.

The clinical implication of diagonal and vertical line structures cannot be considered in isolation. When using a time delay of 1, vertical lines rarely appear as individual vertical lines, but rather appear as blocks of recurrent points. Blocks of recurrent points not only have vertical lines, but also diagonal lines, which will contribute to values of DET. This explanation is supported by figure 2 which shows recurrence plots for 2 sample periods each of AS and QS from a single infant. These plots are characteristic of the

plots seen across the dataset. It can be observed that whilst recurrence plots for AS periods, tend to have square blocks of recurrent points, the recurrence plots for QS periods tend to show more individual diagonal lines. The square blocks in AS result in both vertical and diagonal lines. This may explain the counter-intuitive result for DET.

Perhaps the most important conclusion that may be drawn from these results is that healthy infant IBI patterns are characteristically different between infant AS and QS states. This statement in itself is not new. It is well known that human infant breathing patterns observed in AS are different to those observed in QS. This has been documented in literature [2], and forms part of the definition for the sleep stage classification system [1]. These results are important because they quantitatively demonstrate that not only are there differences in the statistical distribution of IBI patterns between infant sleep states, but that there are characteristic differences in the non-linear dynamics of these patterns. Further, these differences were invariant to a specific choice of embedding dimension and fixed recurrence, meaning that the results are unlikely to be an artefact of specific non-linear methodology. The results support the findings in infants by Patzak [9], and adults by Burioka [8, 15] and Sako [7]. This study is also important, because it has used IBI patterns rather than digitally sampled respiratory movement waveform data. This experiment thus demonstrates that these differences in non-linear breathing dynamics may be detected using IBI data. The results provide further evidence to support the argument that respiratory control is governed by deterministic, non-linear dynamics [5, 6, 16]. It may be further speculated that the infant respiratory control system follows different attractor's in AS than in QS.

Observation of the box-plots in figure 1, shows distinctive differences in results recorded for AS and QS periods for the variables RAD and LAM. These distinctive differences suggest that these variables may be utilised as novel sleep state discriminators. Tools such as clustering, linear discriminant analysis and machine learning may be used to develop sleep state classification tools based on these features. The application of recurrence plot analysis may also have interesting applications in the investigation of pathological breathing patterns, perhaps with view toward developing automated disease state discriminators. This study has a number of limitations. Like all physiological data, there is likely to be artefacts. The infants were from an age range of 19-153 days, a period in which there is significant maturation. Both genders were present in this group. Further analysis should consider stratification of these variables to investigate whether the AS/QS relationships observed in this study vary with age or gender.

V. Conclusion

Non-linear features of infant breathing patterns are characteristically different between infant active and quiet sleep and these differences can be quantified using recurrence plot analysis of IBI data. The relative difference in results between active and quiet sleep was invariant to a specific choice of embedding dimension or fixed recurrence.

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