NONLINEAR METHODS IN HEART RATE VARIABILITY

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Abstract: In recent years, analysis of heart rate variability (HRV) has become a common tool for prediction of cardiac mortality. The universal rule is that a reduced variability is a signature for enhanced risk. However, the clinical value of the usual methods (the calculation of averages, standard deviations and variances of RR interval subsets, analysis of the power spectra in frequency domain) is very limited: false positive results cut the positive predictive value down to about 30%.
We applied a net information flow method of determination of complexity in deterministic chaos (associated with nonlinear dynamics) to 24 hour recordings of beat-to-beat heart-rate. It is likely that analysis of HRV by the means of nonlinear dynamics may open a way for a new classification of HRV.

Introduction

Since the first report on spontaneous oscillations in blood pressure associated with the respiratory cycle made by Hales in 1773 [1], physiologists and clinicians have recognized the presence of variation in cardiovascular signals. Modern digital computer techniques made it feasible to record and analyse such signals precisely. In recent years the clinical importance of HRV was first established by Hon and Lee in 1965 [2, 3, 4]. Since then HRV analysis has been developed and used as prognostic nonivasive technique to study many diseases: coronary heart disease, autonomic neuropathy associated with diabetes mellitus, monitoring graft rejection in cardiac transplant patients [5, 6, 7].

The R-R interval signal contains information which was used to produce a quantitative estimate of the autonomic nervous system control and the balance between its parasympathetic and sympathetic components. HRV analysis is divided into time domain and frequency domain analysis [8, 9, 10]. In the time domain several indices have been used: (mean of all R-R intervals between normal beats; standard

deviation of all R-R intervals; standard deviation of R-R interval of successive 5 min segments of Holter data; root mean squared successive difference which considers the sequence in time of the R-R intervals; percentage of successive normal R-R intervals that differ by more than 50 ms over a defined period). The frequency domain analysis requires that the R-R interval file undergoes either fast Fourier transformation (FFT) or autoregressive analysis (AA, it overcomes the problem of pseudoperiodicity which invalidates one of the main criteria for applying the FFT). By these analyses it is possible to obtain the power spectrum of HRV, which typically presents three bands of increase in oscillations: high frequency (HF) component, above 0,15 Hz, that reflects respiratory sinus arrhythmia, mediated predominantly by the vagus nerve and may reflect cardiac vagal activity; low frequency (LF) component, below 0,15 Hz, can be mediated by both the vagus and the cardiac sympathetic nerves; very low frequency (VLF) component, below 0,03 Hz, of unclear origin.

However, the clinical value of the above methods is very limited: false positive results cut the positive predictive value down to about 30%. A possible reason for this disappointing value might be found in data analysis technique [11].

Now we know that the heart rate variability is characterized by periodical and non-periodical oscillations. Thus, more recently an alternative approach to the time domain analysis of HRV has been proposed - the chaos theory [12]. Deterministic chaos is a subject associated with nonlinear dynamics: the study of behavior of systems that respond disproportionately to applied stimuli. It is not the same chaos as chaos in common sense of complete randomness. It refers to a constrained kind of randomness.

A tool often used for analyzing the dynamics of complex nonlinear systems is „phase space" representation. This technique tracks a number of independent variables. For many complex systems, including phase space representation of heart beat rate, all of the independent variables cannot be freely measured or even identified. For such a system a substitute phase space representation can be constructed using the method of delay maps (sometimes called Poincare plots). For the simplest delay map each point corresponds to the value of some variable at a given time plotted against the value of the same variable after a fixed delay. One can repeat this procedure a few times for a given point and obtain a multidimensional delay map.

A number of quantitative parameters may be used to estimate the chaotic complexity of the system. The more common examples are: correlation dimension, Kolomogorow entropy and scaling index [12]. In this paper we use net information flow introduced in [13].

Procedure

In this work we analyze a two-dimensional phase space constructed by the delay map method. First we coarse-grained it into subvolumes (marked by i, i=1 to imax) of the edge size of 48 ms. Then calculations of cell occupation probability P_i and transfer probability P_{ij} (probabilities of consecutive states occupying cell i and j respectively) were performed. The net information flow for given cell i is then calculated from [13]

$$\Delta = \sum_j P_{ij} \ln\left(\frac{P_i}{P_j}\right)$$

Δ_i can be positive (a „gain" in information) or negative (a „loss"), depending on the different transition probabilities. Although the algorithm of net information flow calculation is simple, due to large datasets from 24 hour RR recordings, the needed for computational power may be substantial. It is especially true in the case of multidimensional delay maps. After calculation of Δ in all cells we can determine the histogram $N(\Delta)$ by performing the appropriate sums.

When variability arises the information is created (positive Δ), when variability ceases the information is destroyed (negative Δ). Net information flow is believed to be well suited for biological systems, which are able not only to transmit and process information, but must also create and destroy it. There may be instances when the system is smoothly preceding within its normal operating range and only a small amount of information is created (or destroyed) in order to keep it going. The act of creating of information may be associated with a reaction to „special demand" or to pathological behavior. The act of destroying information can be associated with the return of the system into its standard operating mode.

Subjects

In the current work we present analysis of 24 hour ECG Holter recordings of 2 male and 2 female patients. Their cardiovascular systems were assessed on the basis of anamnesis and status, as well as rest ECG and echocardiography. Two persons (in Table I no 1 and 2) recognized as free of cardiovascular diseases were directed for further tests of stenocardiac symptoms they complained of. The other two patients (no 3 and 4) were acknowledged as ill. One showed clinical signs of congestive heart disease in III/IV stage according to NYHA and congestive (dilated) cardiomyopathy was confirmed by echocardiography. The other patient verged on unstable coronary heart disease with congestive heart disease in stage I/II. These two patients were subjected to intensive treatment, they had the ischaemic-overloading changes in the rest-ECG and low ejection fraction. HRV analysis was based on ECG recording strips without any rhythm disturbances as supra- and ventricular ectopics, reticular tachycardia, pauses and bradycardia.

Time domain analysis consists of histogram of R-R values distribution, histogram of differences between successive R-R distances and Lorenz XY grip. Frequency domain analysis is presented in three frequency bands — very low (below 0,05 Hz), low (0,05 - 0,15 Hz), and high (0,15 - 0,5 Hz). ECG strips registered by FD-3 Medilog digital Holter recorder were processed by Oxford Instruments Excel 2 equipment using standard commercial software.

The very same HRV record strips were then analyzed by the net flow method described above.

Results

Table I displays the results of routine time domain HRV analysis for all subjects performed by commercially available software. One can see that the basic parameter values obtained from this analysis (mRR, pNN50) are not substantially different from case to case.

Table 1. *Basic parameters of HRV analysis in time and frequency domains*

	Patient code	*Age*	*Sex*	*ECG*	*LVDD*	*mRR [ms]*	*pNN50 [%]*	*WAW [ms]*	*VLF [ms]*	*LF [ms]*	*HF [ms]*
1	A.M.	40	F	(-)	Norm	793	16,732	75,3	56.7	42.8	24.9
2	J.B		F	(+/-)	Norm	863	4,633	60,4	24.6	23,1	21.3
3	W.K ZNK, MR	63	M	(+)	84 mm	892	5,302	198,9	189.3	33,8	50.9
4	K.S CW, ZNK	71	M	(+)	Norm	888	1,594	48	42.2	18,4	13.7

Legend: (+) features of pathology present in the recording; mRR — mean R-R interval; pNN50 — percentage of subsequent R-R difference larger then 50 ms; LVDD — left ventricular diameter diastole; WAW — Overall band deviation (0. 0 - 0. 5 Hz); VLF — very low frequency component (0.0-0. 05 Hz); LF — low frequency component (0,05-0,015 Hz); HF — high frequency component (0,15-0,5); CW — coronary heart disease; MR — dilated cardiomiopathy; ZNK — congestive cardiac failure

Figure 1 displays RR parameters plots in the time domain for healthy subject 1 (AM): RR interval histogram, RR difference histogram, mean of 3 RR intervals histogram and two dimensional delay map occupation (Lorenz XY grip). Some characteristic features present in those plots are common and usually considered representative for regular physiological RR variability. These include RR interval histogram which exhibits two wide maxima and a club shaped XY scatterplot of delay map occupation. Moreover, subsequent RR intervals difference histogram is relatively wide, which is usually judged a healthy symptom of well pronounced variability.

Figure 2 presents the same set of RR parameters plots for also healthy subject 2 (JB). The RR difference histogram shows significantly reduced variability if compared to subject 1. Furthermore, some features of HRV are better articulated in the case of ill subject 3 (WK, congestive heart disease in III/IV stage). This can be seen from Figure 3.

Figure 4 demonstrates HRV parameters in the time domain for subject 4 (KS). Despite the fact of a serious illness (unstable coronary heart disease with congestive heart disease in stage I/II) the picture is very similar to that of healthy subject 2 (JB) presented in figure 2. Consequently, it can be seen that two pairs of subjects 1-3 and 2-4 exhibit similar results of RR interval variability analysis in time domain, while the first subject in each pair was recognized as free of cardiovascular diseases and the second was acknowledged as very seriously ill.

The frequency domain analysis results are also presented in Table I. Power density was calculated by autoregression method in three usually considered frequency ranges: VLF - very low frequency component (0.0 - 0.05 Hz); LF - low frequ-

ency component (0.05-0.15 Hz); HF - high frequency component (0.15 - 0.5 Hz). Although significant differences are observable in power density, no link between magnitude of any of its components and existence of proper RR variability can be established.

Figure 5 presents plot of the net information flow in two dimensional phase space for subject 1 (AM). Although the variability itself is considerably profound, the netflow is small (near zero) in a large area of phase space. It indicates that only a small amount of fluctuation information is created and destroyed. The opposite situation can be seen in figure 7 presenting the net information flow for subject 3 (WK), where a lot of changes in information are observed in substantial part of phase space.

Although not as evident as in the situation above, similar conclusion appears when comparing the net information flow plots for subjects 2 and 4 which are presented in figures 6 and 8 respectively. The difference in nonzero netflow is perhaps more visible in the histogram which is presented in pictures 9 and 10 respectively. What is important, the change in fluctuation information appears to be large and more spread over the whole phase space even in the case of subject 4 (KS), where fluctuation itself is very slightly pronounced.

We can see that the netflow information analysis has a capabillity to separate cases which feature similar results of conventional heart rate variability analysis in the time domain.

Conclusion

It is likely that the analysis of HRV by the means of nonlinear dynamics may open a way for a new classification of variability. It has a capacity to individualize cases with similar results of conventional variability analysis in the time and frequency domains. It seems that methods of chaos complexity analysis, borrowed from nonlinear dynamics, will prove fruitful.

The applied net flow method needs much of further work on large datasets in order to verify its usefulness as a diagnostic tool. We have to be aware that this picture may depend on the delay map dimension. It is important to make sure that the selected dimension is sufficiently large to represent the differentiate states in the phase space. This can be achieved by performing and comparing analysis in spaces of various dimensions.

Future studies are planned to describe better the picture of net information flow and other parameters of chaos complexity in HRV variability.

The opportunity to perform numerical calculation in TASK Computer Center is kindly acknowledged.

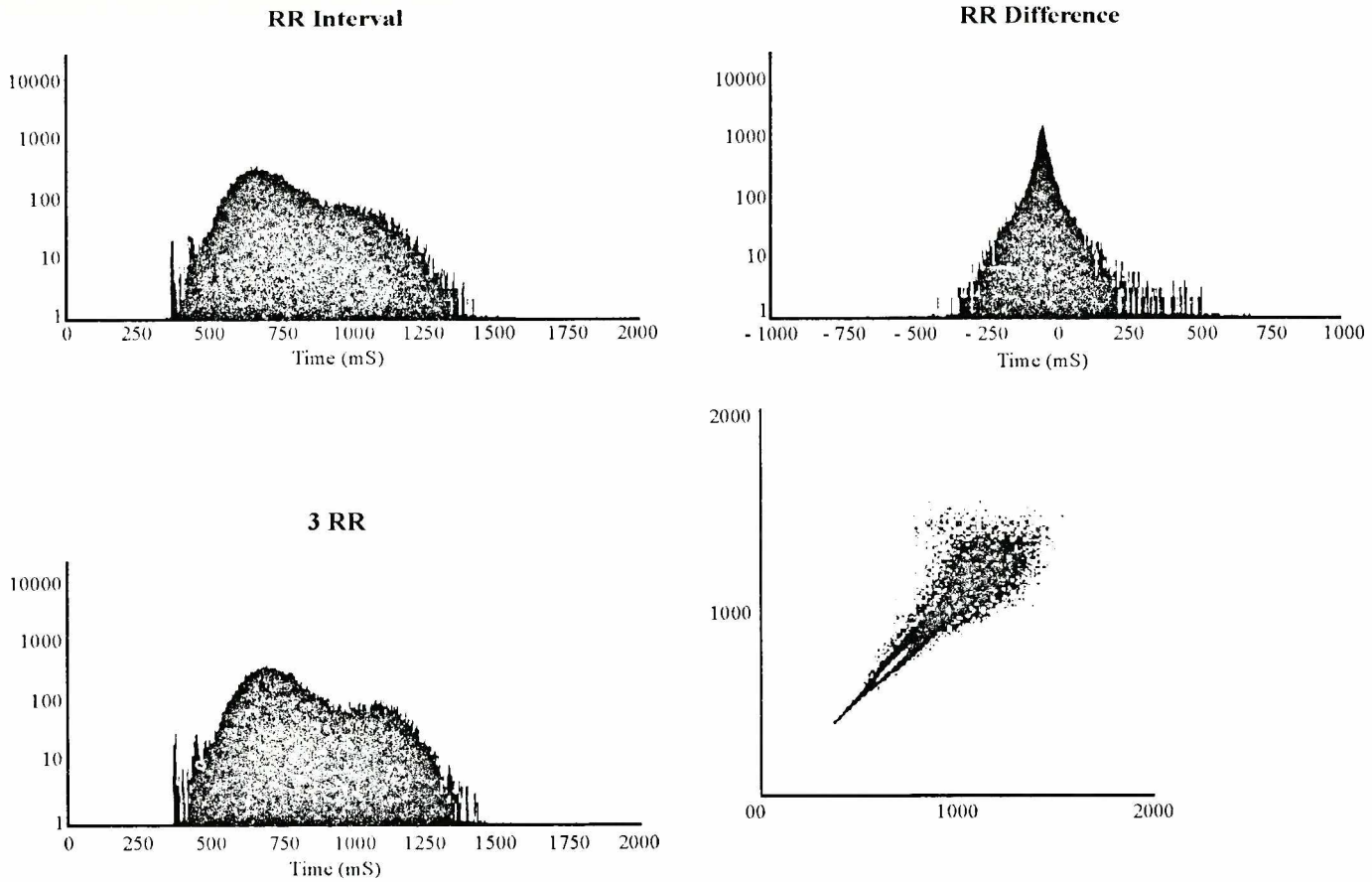

Figure 1. *RR plots in time domain for subject 1 (AM): RR interval histogram, RR difference histogram, mean of 3 RR intervals histogram and two dimensional delay map occupation (Lorenz XY grip)*

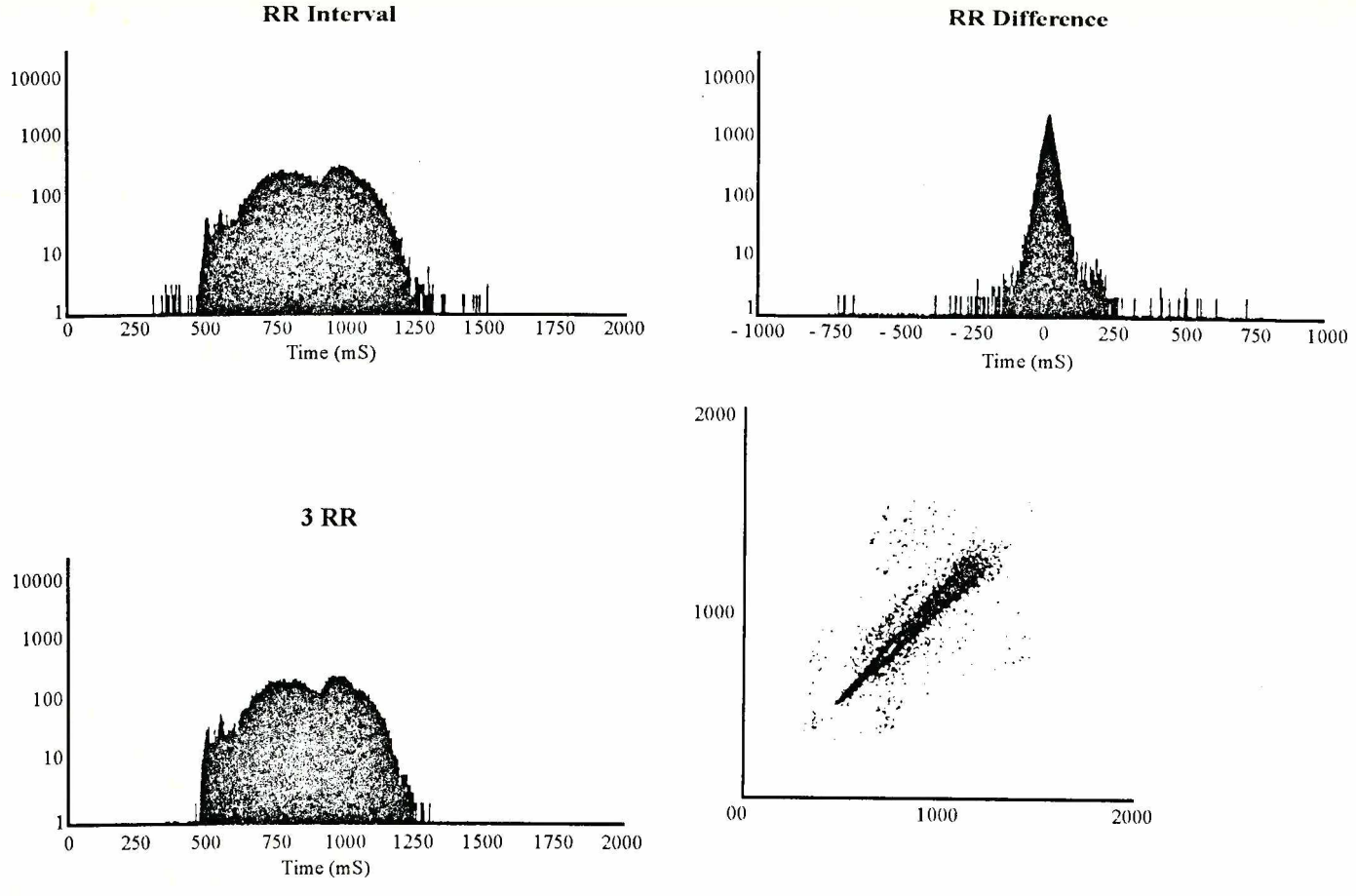

Figure 2. *RR plots in time domain for subject 2 (JB): RR interval histogram, RR difference histogram, mean of 3 RR intervals histogram and two dimensional delay map occupation (Lorenz XY grip)*

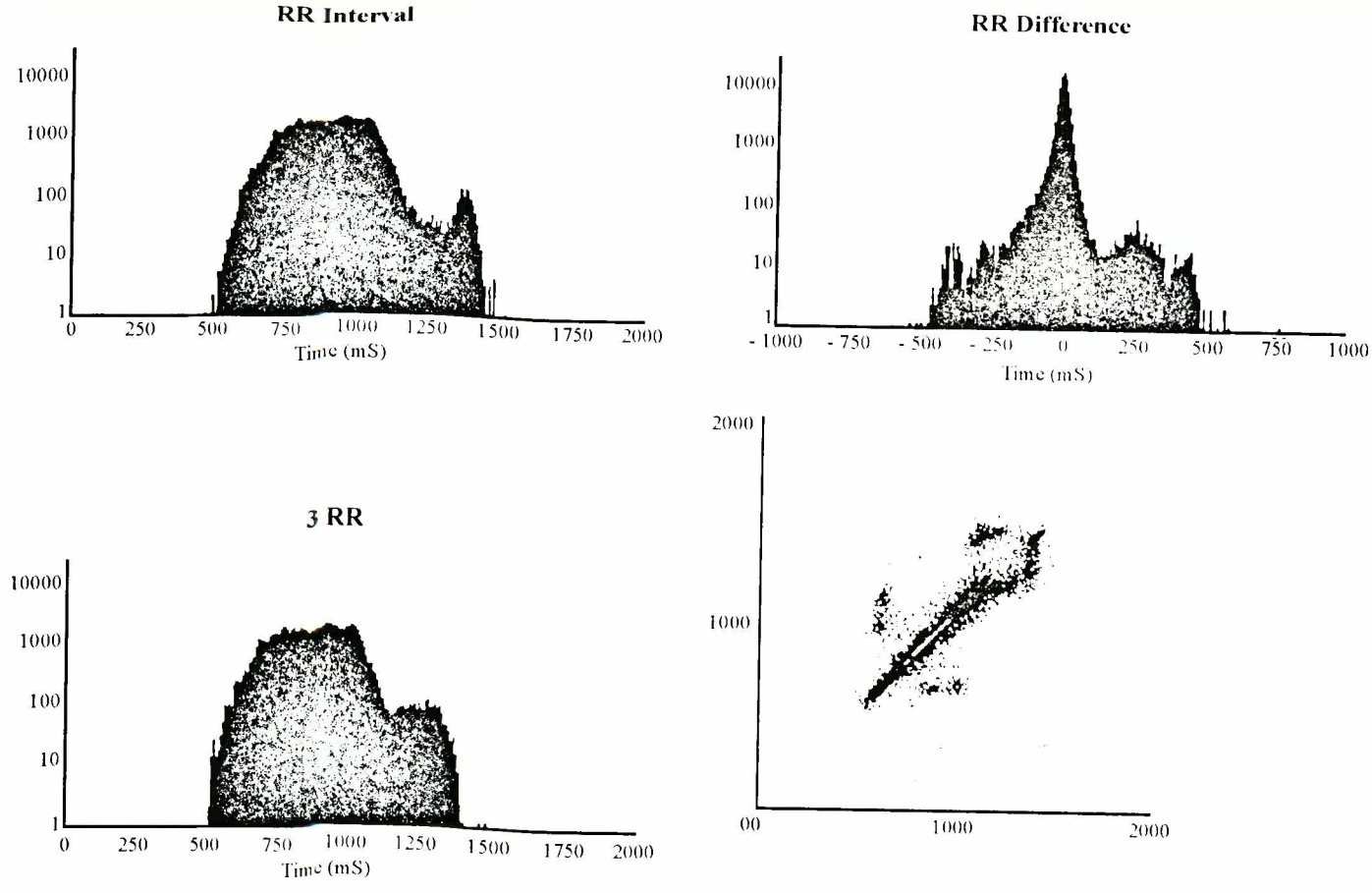

Figure 3. *RR plots in time domain for subject 3 (WK): RR interval histogram, RR difference histogram, mean of 3 RR intervals histogram and two dimensional delay map occupation (Lorenz XY grip)*

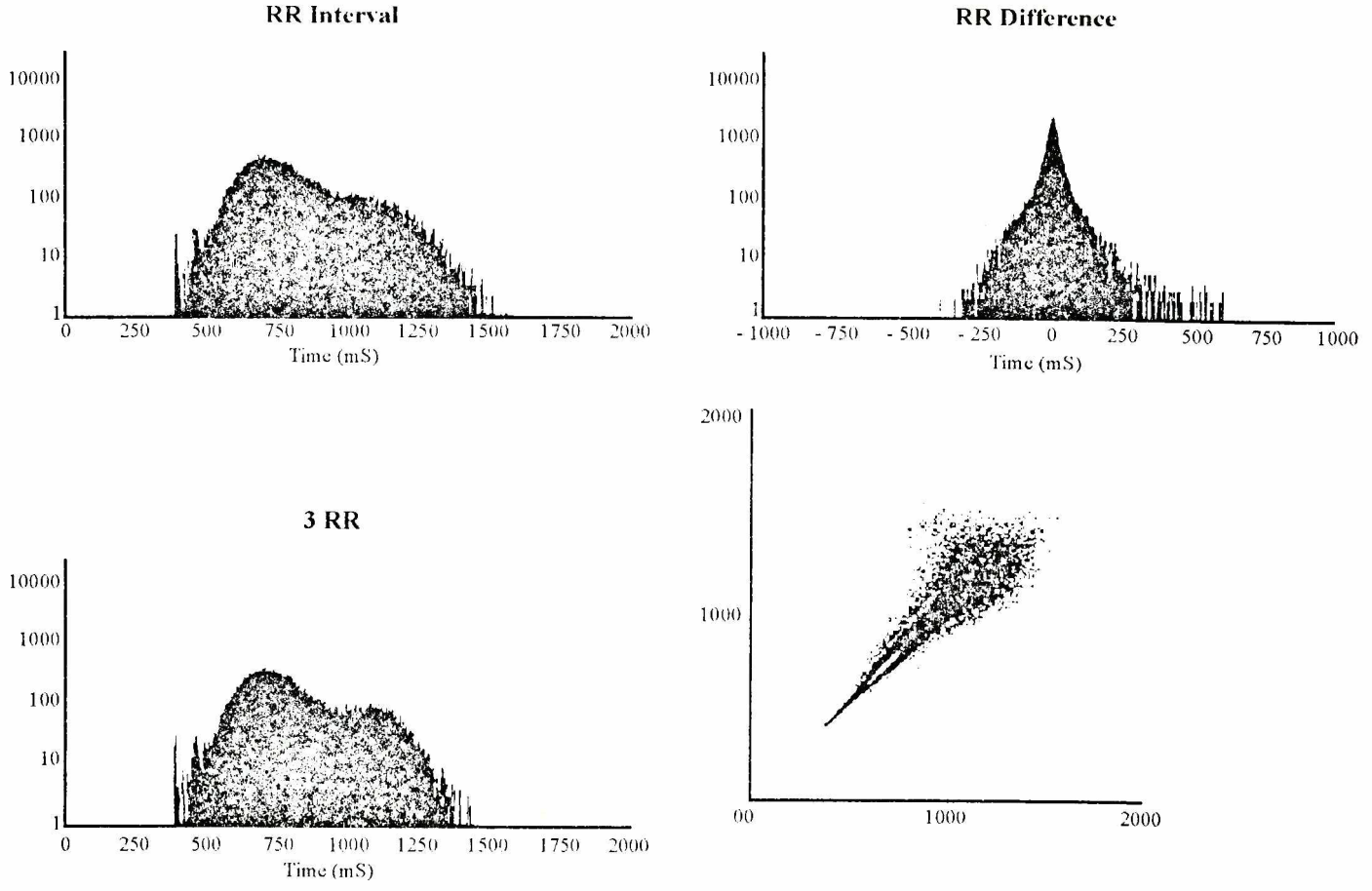

Figure 4. *RR plots in time domain for subject 4 (KS): RR interval histogram, RR difference histogram, mean of 3 RR intervals histogram and two dimensional delay map occupation (Lorenz XY grip)*

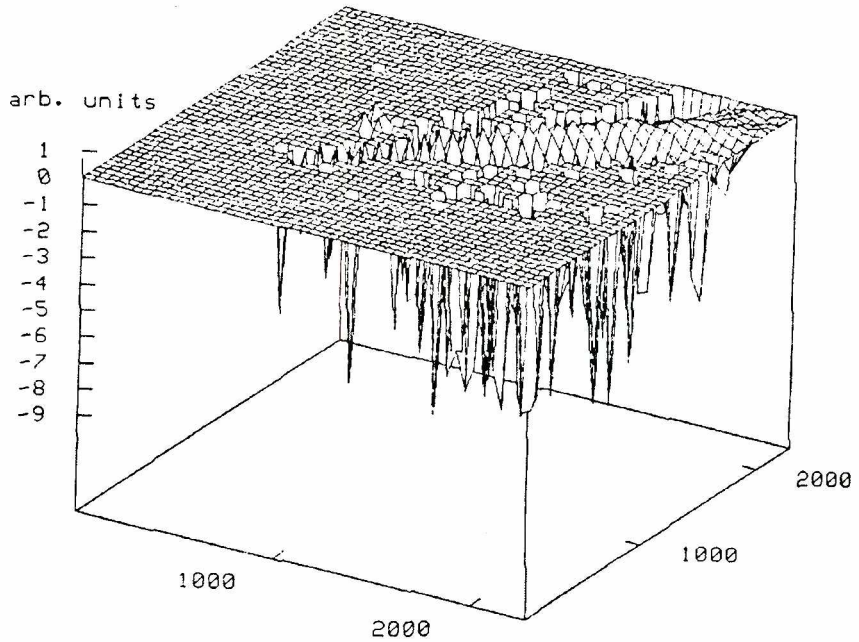

Figure 5. *Two dimensional net flow plot for subject 1 (AM)*

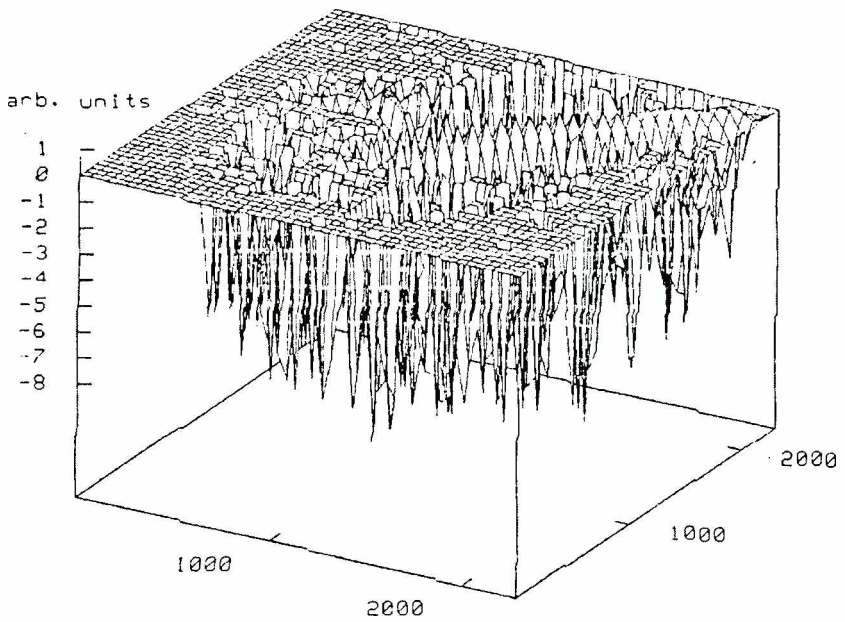

Figure 6. *Two dimensional net flow plot for subject 2 (JB)*

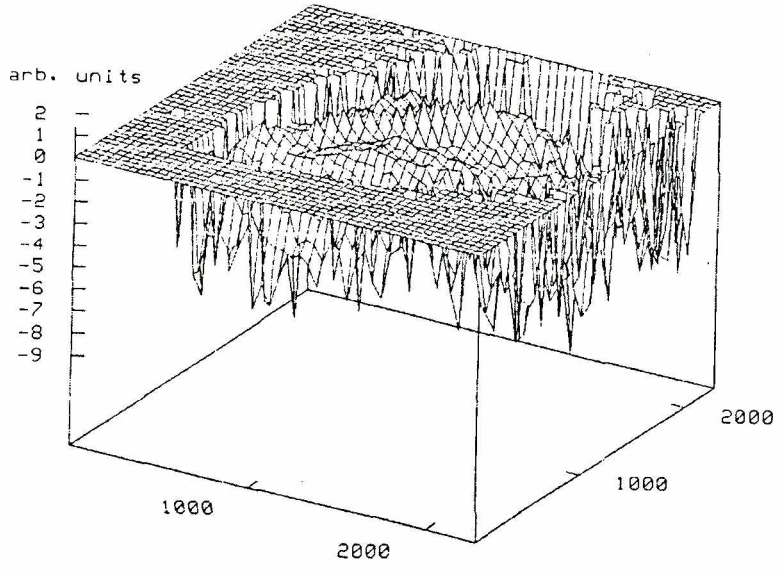

Figure 7. *Two dimensional net flow plot for subject 3 (WK)*

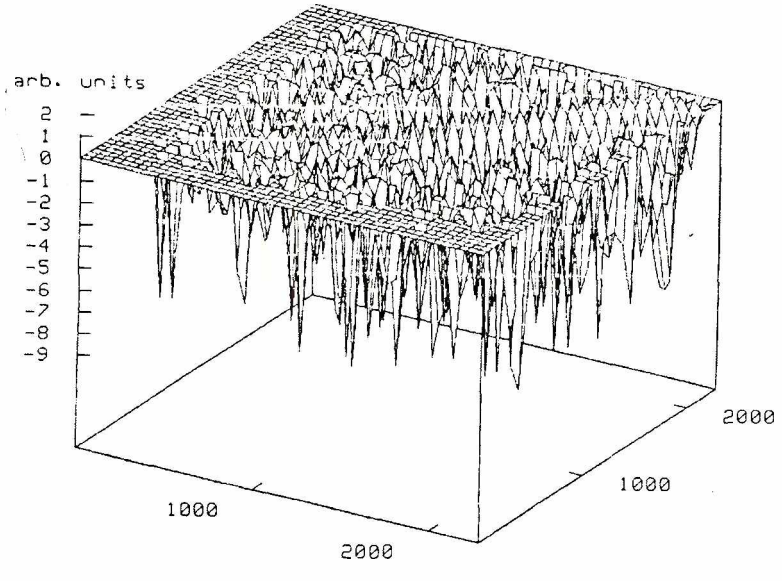

Figure 8. *Two dimensional net flow plot for subject 4 (KS)*

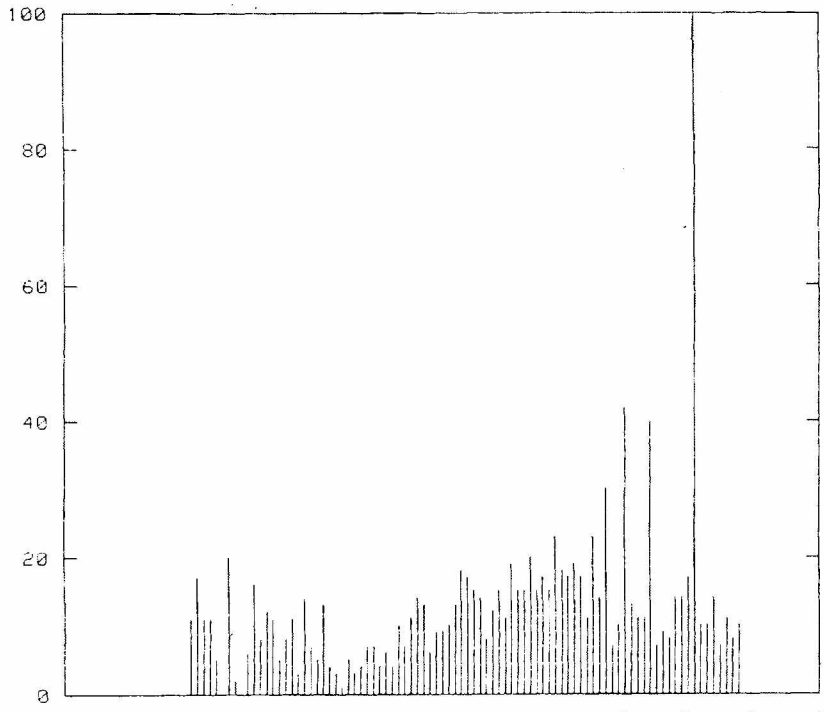

Figure 9. *Histogram of two dimensional net information flow for subject 2 (JB)*

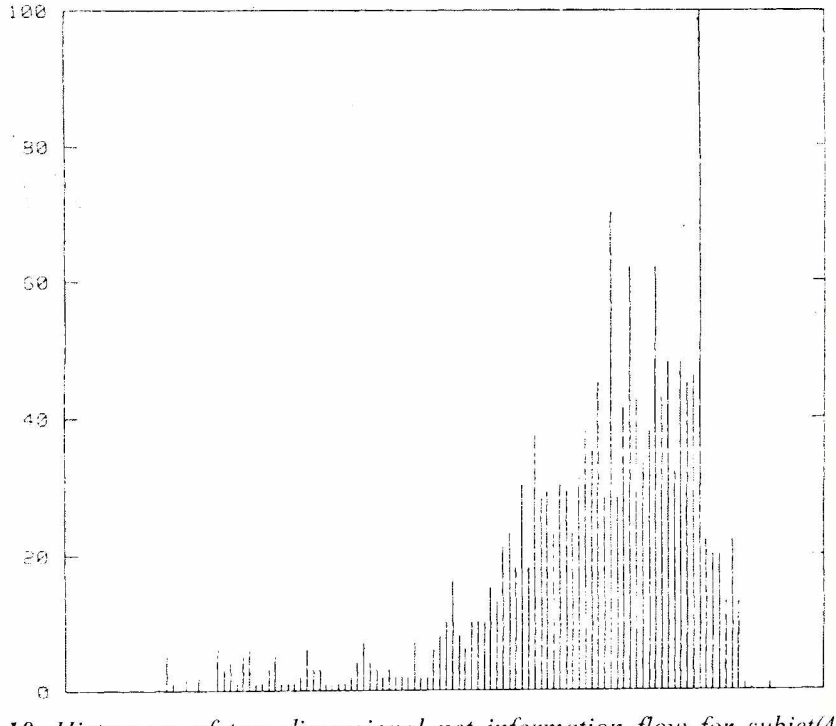

Figure 10. *Histogram of two dimensional net information flow for subjet(4KS)*

References

[1] Schlomka G.; Kreislaufforschung, 29 (1937) 510 (in German)

[2] Ori Z., Monir G., Weiss J., Sayhouni X., Singer D. H.; Cardiology Clinics, 10 (1992) 499-533

[3] Bieniaszewski L, Rynkiewicz A., Furmański J., Narkiewicz K., Krupa-Wojciechowska B.; Kardiologia Polska, 35 (1991) 165-169 (in Polish)

[4] Baranowski R.; Kardiologia Polska, 34 (1991) 190-194 (in Polish)

[5] Dąbrowska B.; Elektrofizjologia i Stymulacja Serca, 2 (1995) 65-73 (in Polish)

[6] Dąbrowski A.; Kardiologia Polska, 40 (1994) 41-45 (in Polish)

[7] Kjellgren O., Gomes J. A.; American Heart Journal, 125 (1993) 204-215

[8] Heart Rate Variability; Editor R. Piotrowicz; Wydawnictwo Medyczne Via Medica, Gdansk, 1995 (in Polish)

[9] Practical aspects of accurate spectral HRV; By the Staff of Oxford Instruments Medical System Division. November 94

[10] Heart rate/R-R interval variability. Clinical guide; Oxfords Instruments (UK) Ltd. 1994

[11] Malik M., Farrell T., Cripps T., Camm A. J.; European Heart Journal, 10 (1989) 1060-1074

[12] Goldberger A. L., Rigney D. R., and West B. J.; Sci. Am. 264(1990)35

[13] Schmidt G., and Morfill G. E.; Nonlinear Methods for Heart Rate Variability Assessment in Malik M., Camm A. J. (eds.): Heart Rate Variability; Futura Publishing Company, NY 1995