

# Dynamical Landscape of Heart Rhythm in Discerning Erratic Rhythm in Elderly People

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## Abstract

*We hypothesize that increase with age of short-term measures of heart rhythm [a way in which accelerations and decelerations appear], especially dynamical pattern indices [Transition Rates ( $S_T$ ) or self-Transfer Entropy ( $sTE$ )], provide indicators for unhealthy autonomic activity or cardiac tissue remodeling in elderly people. Hence they can help in early recognition of arrhythmogenesis processes.*

*Based on properties of heart rhythm of 190 healthy persons, grouped into their age decade, we have found that both  $S_T$  and  $sTE$  are efficient separators for discerning elderly people with erratic rhythm. The values in minimum in  $S_T = 2.4$  and minimum in  $sTE = 0.27$ , obtained by square function approximation, have been used to divide subjects of 70s and 80s into two groups. For all entropic measures these groups are different ( $p < 0.001$ , in  $t$ -test or Man-Whitney in case normality test failed). The fragmentation metrics [based on statistics of signs of heart rate changes] PPP and PAS also distinguished these groups though at greater  $p$ -value, and PSS yielded that the groups are identical. The minima of these function did not give satisfactory division of elderly into groups.*

*Concluding, frequent changes in heart rate acceleration sign and size are the best signature for anomalous levels of short-term heart rate variability in elderly people.*

## 1. Introduction

The healthy human heart remains under the permanent influence of both branches of the autonomic neural system (ANS): the parasympathetic (considered to slow down heart rate) and the sympathetic (considered to speed up heart rate). Many measures estimating heart rate variability (HRV) have been proposed in order to quantify the regulatory function of the ANS, see [1–3]. Intensive healthy

population studies have found a correlation between an increase in age and a decrease in many HRV indices, including indices such as RMSDD, pNN50 and HF, which are known to describe the short-term HRV (ST-HRV) [4–10]. Therefore, higher values of HRV have been attributed to better organization of feedback reflexes driving the organism's response to actual body needs. However, there are observations suggesting that abnormal levels of short-term HRV indices should be related to erratic rhythms, i.e., rhythms resulting from remodeling of the cardiac tissue due to disease or aging [10–13].

In the following, we hypothesize that increase of short-term measures of dynamical patterns in elderly provides indicators of unhealthy autonomic activity, or possible erratic rhythm resulting from degradation of cardiac tissue, or both. Such erratic rhythms might be the first stage of silently developing arrhythmogenesis.

The term "dynamical landscape of heart rhythm" was proposed in [14] to collect HRV indices focused on quantifying differences in the subsequent heart periods: decelerations and accelerations, the so-called RR-increments. Standard ST-HRV indices: RMSDD, pNN50 and HF are also considered to belong to the set of the dynamical landscape measures.

Erratic rhythms are episodic and often develop when the heart slows down, as it naturally happens during the nocturnal rest. Therefore long series of nocturnal recordings are investigated by us.

## 2. Methods

Twenty-four hour ECG Holter signals were recorded from 190 healthy participants. All of them gave the written permission of informed consent which received approval by the Ethic Committee of Medical University of Gdansk. The participants were grouped according to their age decade: 20's (35 subjects: 18 women), 30's (23 sub-

jects: 11 women), 40's (33 subjects: 13 women), 50's (31 subjects: 13 women), 60's (27 subjects: 12 women), 70's (22 subjects: 10 women), 80's (18 subjects: 11 women).

The signals were analyzed on a Del Mar Reynolds system. The sampling rate of ECG was 128 Hz which ensured 8 ms accuracy for time identification of R-peaks in QRS-complexes. Quality of ECG recordings and accuracy of R-peak detection were verified by visual inspection by experienced cardiologists. All normal beats were carefully annotated, so that only sinus rhythms were considered.

The period of nocturnal rest was assigned individually, in each recording separately, according to the appearance of consecutive hours with the low rate. The non-normal beats were edited (replaced by the median of the last 7 normal beats). For each person 20000 subsequent normal-to-normal RR-intervals were extracted.

We used metrics which are based on probability that particular RR-increments

$$\delta RR(i) = RR(i) - RR(i - 1) \text{ for } i = 1, 2, \dots, N$$

occur in a signal. Subsequently, probability for two-event patterns  $(\delta RR(i), \delta RR(i + 1))$  and three-event patterns  $(\delta RR(i), \delta RR(i + 1), \delta RR(i + 2))$  is also estimated.

For detail description of indices used we refer to [14]. Here we only provide their brief description to introduce the notation:

- $\Delta_I \in \{\Delta_{min}, \dots, 0, \dots, \Delta_{max}\}$  is any RR-increment ;
- $p()$  denotes probability of events enclosed in brackets ();
- $ShEn1 = -\sum_I p(\Delta_I) \ln p(\Delta_I)$  ;
- $ShEn2 = -\sum_{I,J} p(\Delta_I, \Delta_J) \ln p(\Delta_I, \Delta_J)$  for a pair  $(\Delta_I, \Delta_J)$  of consecutive in time events;
- $ShEn3 = -\sum_{I,J,K} p(\Delta_I, \Delta_J, \Delta_K) \ln p(\Delta_I, \Delta_J, \Delta_K)$  for a triple  $(\Delta_I, \Delta_J, \Delta_K)$  of consecutive in time events;
- $S_T = ShEn2 - ShEn1$ ;
- $sTE = (ShEn2 - ShEn1) - (ShEn3 - ShEn2)$  ;
- a: any acceleration:  $\Delta_I < 0$ ;
- d: any deceleration:  $\Delta_I > 0$ ;
- $PIP = \sum_{ad} p(ad) + \sum_{da} p(da)$  : probability of abrupt changes in the sign of two subsequent RR-increments
- $PSS = 1 - [\sum_{aaa} p(aaa) + \sum_{ddd} p(ddd)]$  : complement to the probability of short monotonic accelerations or decelerations;
- $PAS = \sum_{ada} p(ada) + \sum_{dad} p(dad)$  : probability of alternative three-event patterns.

As the qualification whether  $\delta RR(i) \neq 0$ , hence if  $\delta RR(i)$  is an acceleration or deceleration, depends on signal resolution, we performed estimates for the resolution of a signal, i.e., with 8 ms and with doubled resolution of 16 ms.

Changes in a short-term index are often described as being of letter *J* shape. Therefore, we used a square function approximation to find the index dependence on age decade. The nonlinear regression provided us with values which then allowed us to discern elderly people not affected by

erratic rhythms (called OK group) and people with erratic rhythms (called NOK group). For these groups we present the mean of the tensor of self-transfer entropy, for details see [15], estimated as follows

$$TsTE(\Delta_J, \Delta_K) = p(\Delta_K) \ln p(\Delta_K) - 2p(\Delta_J, \Delta_K) \ln p(\Delta_J, \Delta_K) + \sum_{\Delta_I} p(\Delta_I, \Delta_J, \Delta_K) \ln p(\Delta_I, \Delta_J, \Delta_K) \quad (1)$$

All statistical tests and approximations have been performed with SigmaPlot13 software.

### 3. Results

The square function approximations were estimated for all the quantities listed above. However, only for  $S_T$  and  $sTE$  these findings obtained the statistical significance. Namely the coefficient of determination how well the regression model describes the data was  $R^2 > 0.3$ . Similarly high though lower  $R^2$  values were obtained for  $ShEn1, ShEn2$ , and  $ShEn3$ . For  $PIP, PSS$ , and  $PAS$   $R^2 \approx 0.12$ .

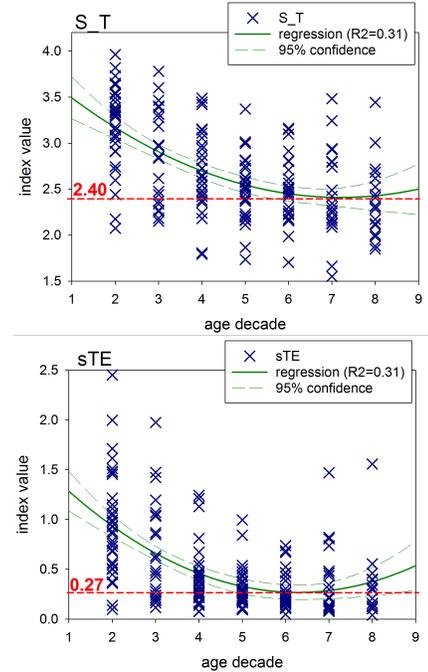


Figure 1. Results of  $S_T$  and  $sTE$  for all signals grouped in age decades are presented together with the square function regression. The minimal values in these approximations, namely 2.40 for  $S_T$  at 70's (the upper) panel and 0.27 for  $sTE$  at 60's (the bottom) panel serve further as the group delimiters.

Fig. 1 presents the method in which the separators for the groups of elderly people OK and NOK were defined.

Table 1. Central values (mean or median) and dispersion (SEM or first and third quartiles) in groups OK and NOK for dynamical landscape indices considered by us.

Index name	group name	mean or median	$\pm$ SEM or [.,]quartiles	OK vs NOK p-value
<b>Shannon entropy based measures:</b>				
$S_T$	OK	2.10	$\pm 0.05$	< 0.001
	NOK	2.84	$\pm 0.08$	
sTE	OK	0.13	[0.13, 0.15]	< 0.001
	NOK	0.46	[0.40, 0.79]	
ShEn3	OK	6.3	$\pm 0.14$	< 0.001
	NOK	8.2	$\pm 0.17$	
ShEn2	OK	4.3	$\pm 0.10$	< 0.001
	NOK	6.0	$\pm 0.18$	
ShEn1	OK	2.25	[2.1, 2.3]	< 0.001
	NOK	3.0	[2.8, 3.3]	
<b>fragmentation indices:</b>				
PIP	OK	0.39	$\pm 0.012$	< 0.001
	NOK	0.50	$\pm 0.017$	
PAS	OK	0.177	$\pm 0.013$	0.012
	NOK	0.250	$\pm 0.019$	
PSS	OK	0.928	[0.904, 0.951]	NS
	NOK	0.933	[0.908, 0.960]	
p(ad)	OK	0.196	$\pm 0.007$	< 0.001
	NOK	0.251	$\pm 0.009$	
p(da)	OK	0.192	$\pm 0.006$	< 0.001
	NOK	0.251	$\pm 0.008$	
p(aa)	OK	0.122	$\pm 0.007$	0.005
	NOK	0.159	$\pm 0.009$	
p(dd)	OK	0.118	$\pm 0.008$	NS
	NOK	0.134	$\pm 0.009$	
p(aaa)	OK	0.038	[0.022, 0.046]	NS
	NOK	0.037	[0.020, 0.054]	
p(ddd)	OK	0.036	$\pm 0.004$	NS
	NOK	0.030	$\pm 0.005$	
p(ada)	OK	0.091	$\pm 0.007$	0.020
	NOK	0.131	$\pm 0.012$	
p(dad)	OK	0.087	$\pm 0.007$	0.016
	NOK	0.119	$\pm 0.009$	
<b>standard STV indices:</b>				
RMSSD	OK	20.6	[17.2, 24.3]	< 0.001
	NOK	43.6	[37.4, 70.8]	
pNN50	OK	1.21	[0.67, 2.1]	< 0.001
	NOK	18.0	[11.4, 28.4]	
HF	OK	96.6	[67.3, 131.4]	< 0.001
	NOK	462.6	[318, 1113]	
<b>Other HRV indices:</b>				
mean(RR)	OK	870	$\pm 14$	0.002
	NOK	976	$\pm 23$	
SDNN	OK	67.2	[58.7, 80.5]	NS
	NOK	78.8	[66.8, 112.3]	

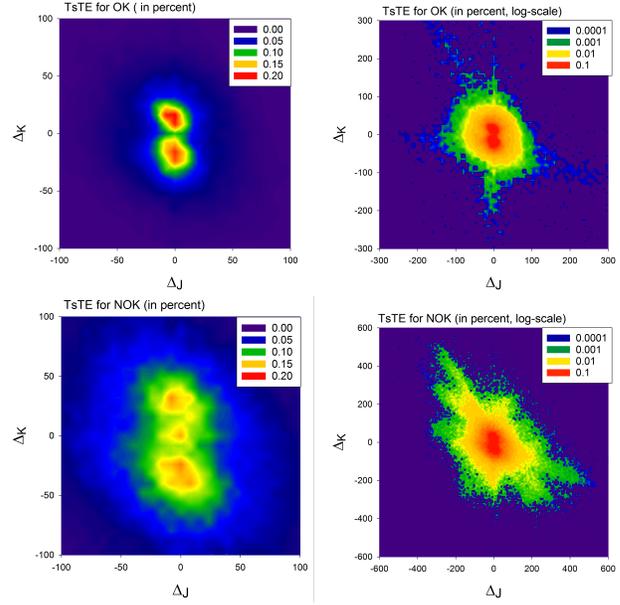


Figure 3. The mean tensor of self-transfer entropy (TsTE) for the considered groups OK and NOK. The left column is to show the main part of the tensors, the right columns shows rare events thanks to log-scale.

Then in Fig. 2 we show how these two separators, 2.40 for  $S_T$  and 0.27 for sTE, are related with each other for a given person. Consequently, the group OK consists of rhythms for which both indices are smaller than the minima (20 signals), and the group NOK contains signals for which both indices are greater than the minima (16 signals). The remaining four signals form a group of unclassified signals.

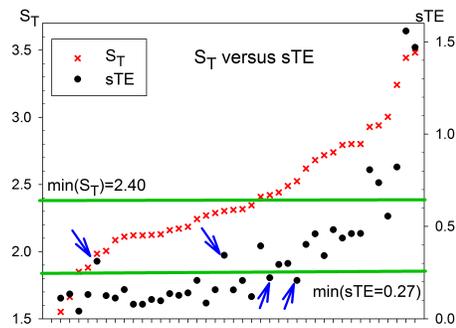


Figure 2. The group membership for signals of people in the age of 70's and 80's. By arrows four signals of the group unclassified are marked.

Then, in Table 1 the description of values for short-term HRV indices obtained for these groups is given. Together the result of the statistical test for difference between the groups OK and NOK is shown. It is noticeable that statisti-

cal significance ( $p < 0.02$ ) was attributed to the difference between unclassified signals and NOK for entropies  $ShEn_2$  and  $ShEn_3$  and for  $S_T$ .

The analogical estimates were performed for a signal resolution of 16 ms. All the results obtained, though quantitatively different, were qualitatively in agreement with the results obtained for resolution of 8ms.

Finally, in Fig. 3 we show the mean tensors of self-transfer entropy, see Eq. (1), calculated from tensors obtained for signals classified as OK and NOK. Notice that the contour plots are displayed in different ranges of  $(\Delta_J, \Delta_K)$  events. Each group results are presented twice: by values scaled linearly to concentrate on properties of core dynamics, and by logarithms of values to see the whole variety of events.

#### 4. Discussion and summary

Frequent changes in heart rate increments sign and size have proven to be the best signature for anomalous levels of ST-HRV in elderly people. The best discerning ability have been obtained for transition rates and self-transfer entropy. Perhaps it is because both measures are built on the concept of Shannon entropy. Shannon entropy quantifies the signal values following the logarithm of signal probability distribution function. So the entropy extracts and collects information across the scales in which the phenomenon operates. This way it enhances diversity in the probability distribution function. Fragmentation indices directly summarize probabilities of specially grouped dynamical patterns. The entropy based measures, while cumulating probabilities of events, scale them what provides evaluation both strength of given patterns and the pattern diversity.

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