



# Deceleration Capacity of heart rate: Two new methods of computation



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## ABSTRACT

Deceleration Capacity (DC) expresses the property of the neural control of the heart extrinsically to decelerate its rate. For the computation of DC a mathematical method has been proposed and used. Although this method was proved of significant prognostic value, it may produce meaningless negative values for DC, something in contradiction with the principle of inter beat deceleration. In this paper we propose two new methods of computation,  $DC_{sgn}$  (DC sign) and  $BBDC$  (Beat to Beat Deceleration Capacity), which not only give positive values for DC but could also improve the original method.  $DC_{sgn}$  modifies the filtering procedure by totally excluding from computation segments that include possible artifacts. It also uses information of four successive beats in order to detect deceleration (acceleration) segments and not only from the anchor points.  $BBDC$  bases all computations on two and not on four successive beats, detecting in this way shorter-term relationships. In order to evaluate the proposed methods, a dataset of 20 young and 20 elderly subjects, all healthy, has been used. Experimental results verify our theoretical claims and show that the proposed method can discriminate more efficiently healthy young and elderly subjects than the original method.

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## 1. Introduction

Heart rate variability (HRV) [1] originates as a physiological consequence of the Autonomic Nervous System (ANS) extrinsic control of heart rate on sinus node level. Parasympathetic Nervous System (PNS) and Sympathetic Nervous System (SNS) activity on sinus node level determine inter-cardiac cycles durations and its variations generating HRV. HRV reflects ANS influences on the heart and it is clinically applied on studies investigating mortality and arrhythmia prognosis in post myocardial infarction and heart failure patients. It is also used for detecting dysautonomia in diabetics.

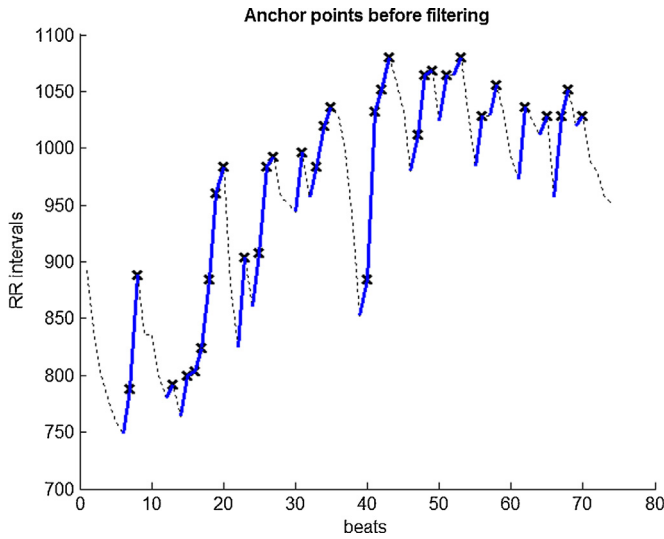
Deceleration Capacity [2] was proposed as a metric focusing on quantifying the decelerations of heart rate. Heart rate beat by beat regulation is achieved through the rapid vagus nerve activity which can change the heart rate substantially, even within one cardiac cycle [3]. As the PNS cardio protective role was proved experimentally a reduced vagal activity reflected from impaired DC values was linked to increased post myocardial infarction mortality [2].

Only a few published papers related to DC discuss the method itself while the rest of them applies the method in various problems. In [4] sinusoidal analysis is applied to elucidate the rationality of the improved PRSA (Phase Rectified Signal Averaging) and the validity of the modified DC is verified using databases of chronic

heart failure patients and a control group. In [5] the threshold of the filter is discussed and experiments have been made with filters with thresholds 5% and 10%, showing that 5% is the optimal filtering level. We also think that the work in [6] should be mentioned here, where monotonic runs or acceleration and decelerations are examined. Since 2006 the method has been used and evaluated several times. No significant changes have been proposed in the method all these years.

In this paper we propose some modifications on the original method. Our motivation was our previous work [7], in which we observed that the original method was producing negative values for some patients. This was a paradox, since the method calculates the deceleration of a cardiac cycle compared to the previous one. The physical meaning of a negative value is that the heart accelerates and does not decelerate as assumed. Having that in mind, we modified the original method in the way with which four consecutive beat intervals are characterized as acceleration or deceleration. We also modified the way the filter is applied. According to the original method, some points are excluded from what is defined as *anchor* since they are considered as artifacts. However, these points are not totally excluded from the computations. We totally exclude these points and computations are based only on points that cannot be considered as artifacts. We also study the Beat to Beat Deceleration Capacity ( $BBDC$ ) focusing on the period in which the maximum effect of the vagus is expected.  $BBDC$  considers two instead of four beats and computations are done on successive beats only. This decision is based on physiology. From the physiology of the ANS we

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**Fig. 1.** Anchor points for a real recording before filtering. Anchors are marked with  $\times$  and the line segments before them (solid lines) show that heart decelerates the rhythm.

know that the variability of the heart rate mainly depends on the frequency with which the PNS releases acetylcholine to the sinus node. The maximum effect of this function of the vagus is expected in a short time period, less than 400 ms. We also compare the proposed modifications experimentally with the originally proposed method in order to support our theoretical claims.

The rest of the paper is structured as follows. Section 2.1 describes the original method. Section 2.2 describes the first of the two proposed methods while Section 2.3 the second one. Experimental evaluation is presented in Section 3 while the discussion and conclusions sections follow.

## 2. Materials and methods

### 2.1. The original method

A method for the computation of DC has been proposed in [2]. **Anchor points** are defined as RR intervals which are shorter than their preceding interval, when Acceleration Capacity (AC) is computed, or longer than their preceding intervals when DC is computed. For convenience and without loss of generality we will consider that we examine DC. In Fig. 1 we can see anchor points for a small part of a real signal.

Anchor points are marked with the symbol  $\times$ . Line segments before the  $\times$  marks always increase since the heart decelerates its rhythm at this moment (shown with solid lines in the figure).

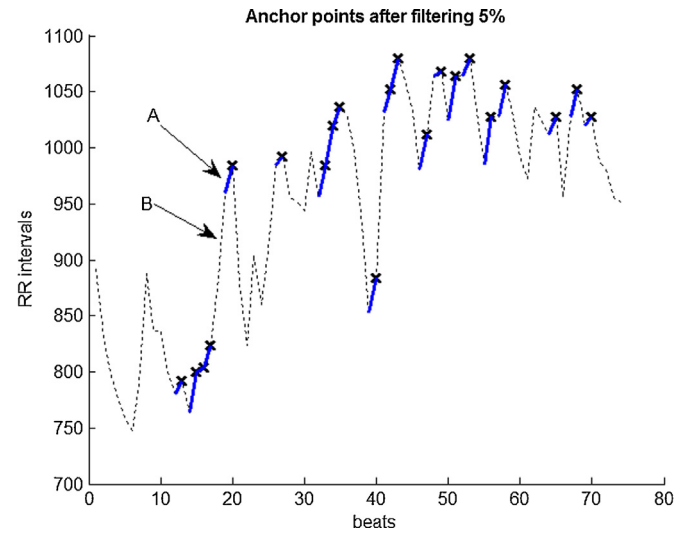
In order to avoid artifacts, intervals which differ more than 5% from their preceding intervals are excluded from computation. Fig. 2 shows anchor points and their preceding line segments for the same signal after excluding possible artifacts.

The line segments around anchor points are used for the computation of DC. We align those segments according to the anchor points (phase rectification [8,9]). Aligned segments are then averaged.

Suppose  $X(0)$  is the average for all anchor points.  $X(1)$  is the average of all points following an anchor point and  $X(-1)$  and  $X(-2)$  the corresponding average of the points preceding anchor points. Deceleration Capacity is given by the following formula [2]:

$$DC_{orig} = \frac{X(0) + X(1) - X(-1) - X(-2)}{4} \quad (1)$$

while Acceleration Capacity is computed in a similar way.



**Fig. 2.** Anchor points for a real recording after filtering. Anchors are marked with  $\times$  and the line segments before them (solid lines) show that heart decelerates the rhythm. Marked with A is a segment that was accepted by the filter and marked with B a segment which was rejected as possible artifact.

### 2.2. Deceleration Capacity characterized by the sign of the fraction

We examine here a variation of the method aiming to act complementary to the original proposed method. We propose two modifications (i) in the way we apply the filter which identifies possible artifacts and (ii) in the way we characterize series of consecutive intervals as deceleration or acceleration series.

Suppose the timeseries of RR intervals:

$$RR_i = RR_1, RR_2, \dots, RR_N$$

We define the series of vectors:

$$x_i = (RR_i, RR_{i+1}, RR_{i+2}, RR_{i+3})$$

where  $1 \leq i \leq N-3$ , i.e. we group consecutive RR intervals into quads, aligning, from the beginning, the line segments as done in [2] at a later stage.

In analogy to the definition of DC the four elements of vector  $x_i$  are referred as  $x_i(1)$ ,  $x_i(2)$ ,  $x_i(3)$ ,  $x_i(4)$ . We define a vector  $v_i$  as valid if:

$$\left| \frac{x_i(4) - x_i(3)}{x_i(3)} \right| \leq 0.05, \quad \left| \frac{x_i(3) - x_i(2)}{x_i(2)} \right| \leq 0.05, \quad \left| \frac{x_i(2) - x_i(1)}{x_i(1)} \right| \leq 0.05 \quad (2)$$

and we assign the value 1 to valid vectors:

$$v_i = \begin{cases} 1, & \left| \frac{x_i(4) - x_i(3)}{x_i(3)} \right| \leq 0.05, \left| \frac{x_i(3) - x_i(2)}{x_i(2)} \right| \leq 0.05, \left| \frac{x_i(2) - x_i(1)}{x_i(1)} \right| \leq 0.05 \\ 0, & \text{otherwise} \end{cases}$$

In other words, we exclude from computation all quads for which the criterion of 5% does not hold at least for one pair of consecutive elements. This is a simple generalization of the filter proposed in [2] where the filter is applied only to anchor points, i.e. only using the second inequality of inequalities (2). By using only the second inequality the criterion of 5% is applied only between anchor points and their preceding intervals, allowing a segment for which the criterion does not hold to participate in the computation of  $X(1)$ ,  $X(-1)$  and  $X(-2)$  in Eq. (1). In Fig. 2 the segment marked with A corresponds to an anchor point and satisfies the criterion of 5%, allowing the segment marked with B to participate in the computation of the averaged signal, even though this segment does not satisfy the criterion. For the filter proposed in this paper the line

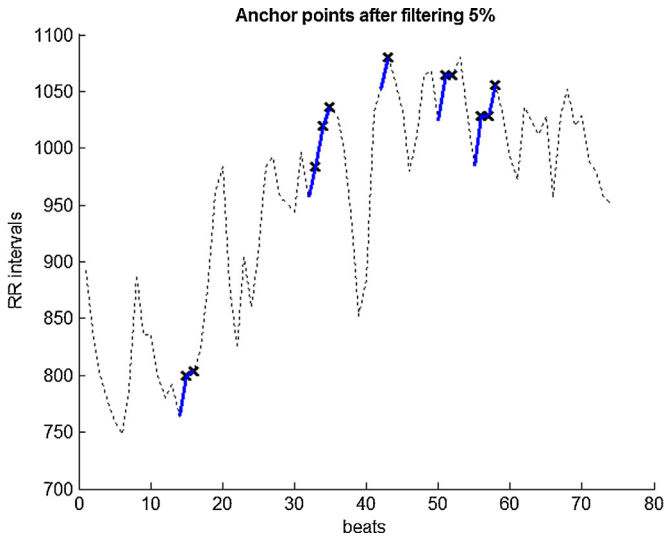


Fig. 3. Application of filtering when using  $DC_{sgn}$ .

segments participating in the computation of the averaged vectors for Deceleration Capacity are shown in Fig. 3.

Next, we compute  $acdc_i$  for each vector as:

$$acdc_i = \frac{x_i(4) + x_i(3) - x_i(2) - x_i(1)}{4} \quad (3)$$

and then we characterize each vector as acceleration or deceleration period:

$$ac_i = \begin{cases} 1, & \text{if } acdc_i < 0 \\ 0, & \text{otherwise} \end{cases}$$

$$dc_i = \begin{cases} 1, & \text{if } acdc_i > 0 \\ 0, & \text{otherwise} \end{cases} \quad (4)$$

We also compute the averaged vectors:

$$\overline{dc} = (\overline{dc_i * v_i * x_i(1)}, \overline{dc_i * v_i * x_i(2)}, \overline{dc_i * v_i * x_i(3)}, \overline{dc_i * v_i * x_i(4)})$$

and:

$$\overline{ac} = (\overline{ac_i * v_i * x_i(1)}, \overline{ac_i * v_i * x_i(2)}, \overline{ac_i * v_i * x_i(3)}, \overline{ac_i * v_i * x_i(4)})$$

and finally we calculate AC and DC with formulas similar to Eq. (1):

$$DC_{sgn} = \frac{\overline{dc}(4) + \overline{dc}(3) - \overline{dc}(2) - \overline{dc}(1)}{4} \quad (5)$$

$$AC_{sgn} = \frac{\overline{ac}(4) + \overline{ac}(3) - \overline{ac}(2) - \overline{ac}(1)}{4} \quad (6)$$

Please note that  $DC_{sgn}$  reveals different information than  $DC_{orig}$ .  $DC_{orig}$  characterizes a set of consecutive beats as deceleration based on the anchor and its preceding interval. Then it checks if the anchor point is shorter (accelerates) or longer (decelerates) than its preceding interval and takes averages of successive differences. This could lead to negative values for Deceleration Capacity. Negative values indicate that the signal accelerates at this point, even though it was expected to decelerate based on the anchor point.  $DC_{sgn}$  looks directly at the four beat window and decides if the signal accelerates or decelerates considering all four beats. Then it characterizes the four beat sequence as acceleration or deceleration. The information extracted from these two metrics is different and seems that both should be taken into consideration and not the one replace the other, something also verified by the different but similar experimental results collected by the two methods and presented in Section 3.

Looking deeper in the above paragraph, one could see that there is some more information which has not been studied. What happens if we characterize a period as acceleration or deceleration using two beats, but without checking if the preceding and succeeding intervals follow or not? Let us see the next section which introduces *BBDC*.

### 2.3. Beat to Beat Deceleration Capacity – *BBDC*

We consider in this section one more method which could act complementary to the methods presented in Sections 2.1 and 2.2. It is a variation of those methods which computes the Beat to Beat Deceleration Capacity (*BBDC*). *BBDC* is based on Eq. (1) (suggested in [2]) limiting the window in two beats. This measure also corresponds to  $DC(1,1)$  that has been reported in [10]. However, in both papers it has not been suggested clearly that this measure is of special interest or even investigated experimentally. We move one step ahead and base it on the physiology.

The *BBDC* metric describes different information than  $DC_{orig}$  and  $DC_{sgn}$ . The effect of sympathetic stimulation on heart rate starts with a latency of approximately 5 seconds with the maximum response within 20–30 s [11]. In contrast, the maximum effect for the vagal stimulation occurs rapidly, within 400 ms [12]. In other words parasympathetic control of heart rate is faster than sympathetic control of heart rate. The information extracted from a window of two beats analyzed in this section with *BBDC* probably reflects more accurately the instant PNS influences on sinus node than a longer window of four beats. In the four beats window multiple vagal discharges may occur. Thus, there is much information hidden in a window of two beats and this information is different than that extracted from a window of four beats.

The procedure is similar to that presented in Section 2.1. Anchor points are defined as RR intervals longer than their preceding ones, excluding those differing more than 5% from their preceding intervals as possible artifacts. Next, the difference between the anchors and their preceding intervals is averaged and the *BBDC* is given by the formula:

$$BBDC = \frac{X(0) - X(-1)}{2} \quad (7)$$

where  $X(0)$  is the average of all intervals selected as anchors and not excluded by the filter, and  $X(-1)$  the average of their preceding intervals.

Please note that the segments participating in the computation of *BBDC* are always ascending and all differences between anchors and their preceding points are always positive. Please also note that the filter of 5% is applied only to line segments between the anchor points and their preceding intervals and is not necessary to decide about the participation of other segments as happens in the computation of  $DC_{orig}$  and  $DC_{sgn}$ .

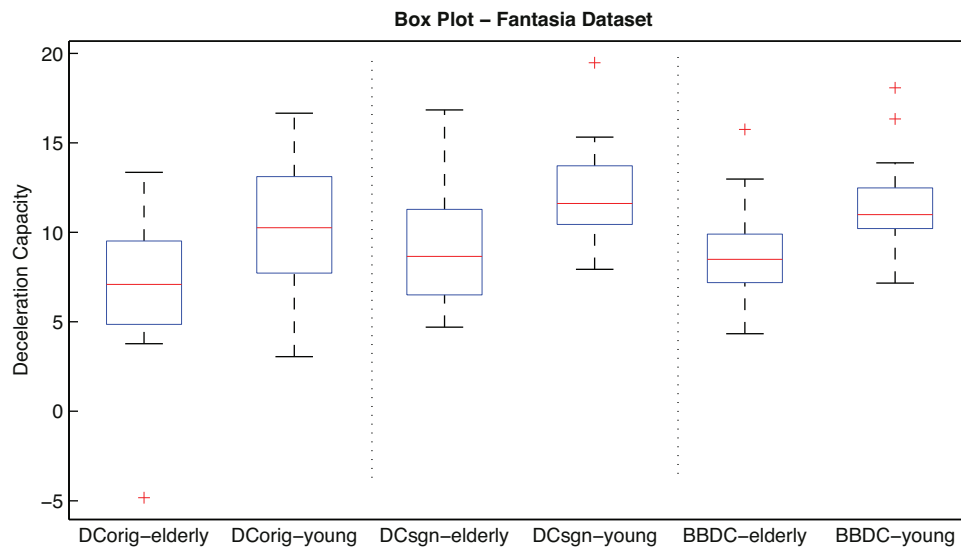
Anchor points before and after filtering are the same with those selected by  $DC_{orig}$  and are shown in Figs. 1 and 2.

Beat to Beat Acceleration Capacity (*BBAC*) can also be defined in a similar way.

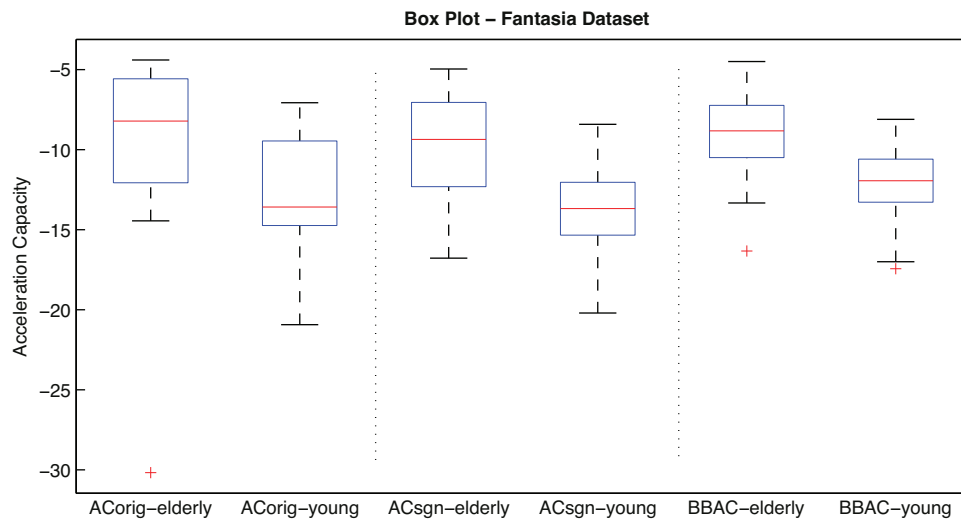
### 3. Experimental evaluation

We used a public dataset from physionet to evaluate all three methods:  $DC_{orig}$ ,  $DC_{sgn}$  and *BBDC*. For the computation of  $DC_{orig}$  we used and analyzed the software kindly provided to us by Prof. Georg Schmidt.

We also used the *fantasia* [13,14] dataset, which consists of 40 recordings, 20 from young subjects (21–34 years old) and 20 from elderly (68–85 years old), all were healthy. Each subgroup includes equal numbers of men and women. All subjects remained in a resting state in sinus rhythm during recording while watching



**Fig. 4.** Box plots presenting the results of the application of Deceleration Capacity analysis for the *fantasia* dataset and the three examined metrics:  $DC_{orig}$ ,  $DC_{sgn}$ ,  $BBDC$ .



**Fig. 5.** Box plots presenting the results of the application of Acceleration Capacity analysis for the *fantasia* dataset and the three examined metrics:  $AC_{orig}$ ,  $AC_{sgn}$ ,  $BBAC$ .

the movie *Fantasia* (Disney, 1940) to help maintain wakefulness. The continuous ECG signals were 120 min long and digitized at 250 Hz. Each heartbeat was annotated using an automated arrhythmia detection algorithm, and each beat annotation was verified by visual inspection.

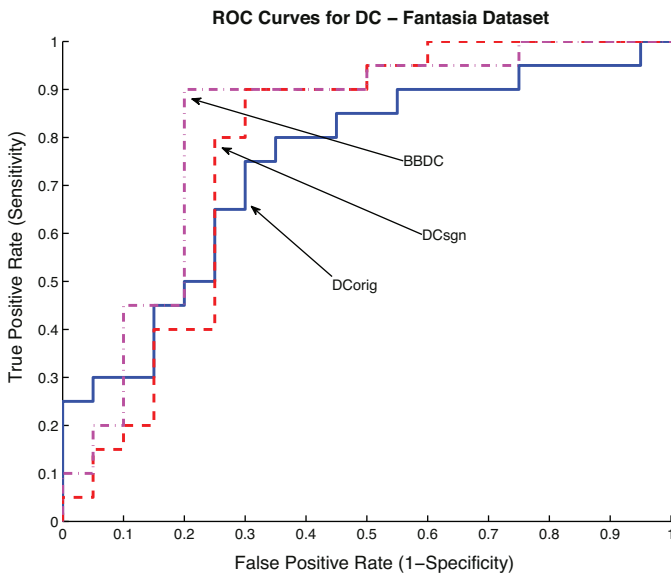
Since the heart of a younger subject is expected to be able to accelerate and decelerate more effectively than that of an elderly subject, we expected to observe a statistical significant discrimination when using Acceleration and Deceleration Capacity in order to

discriminate the two groups of subjects, for all examined metrics. The results are presented in Table 1. In the first column we present  $p$ -values for the achieved discrimination, while in the rest two columns the means and standard deviations for each group of subjects. We can observe that all three measures present remarkable discrimination power. We can easily see that both methods proposed in this paper present lower  $p$ -values than the original method. For the estimation of  $p$ -value  $t$ -test and  $anova$  tests were used after checking that the distributions are normal using the

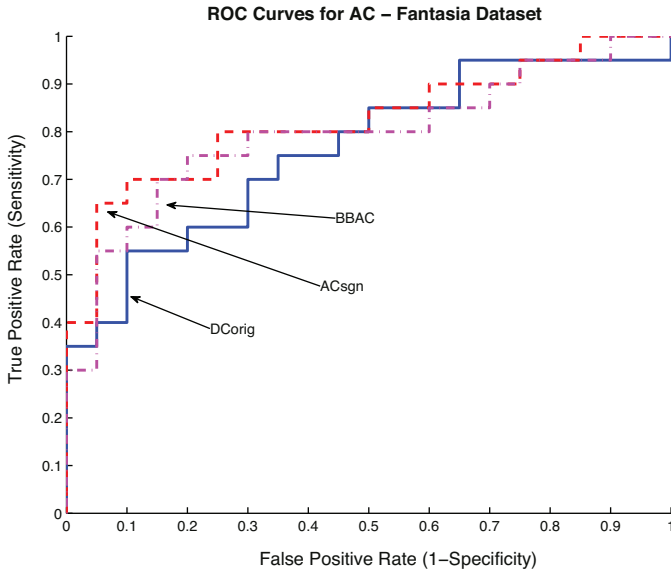
**Table 1**

Discrimination results when computing Deceleration Capacity and Acceleration Capacity for young and elderly subjects.

	$p$ -Value	Mean $\pm$ std Elderly subj. (in ms)	Mean $\pm$ std Young subj. (in ms)	Area under ROC (AuC)	std for AuC (bootstrap test)
$DC_{orig}$	0.01230	$7.03 \pm 4.06$	$10.17 \pm 3.47$	0.745	$0.75 \pm 0.031$
$DC_{sgn}$	0.00448	$9.24 \pm 3.37$	$12.16 \pm 2.70$	0.775	$0.78 \pm 0.032$
$BBDC$	0.00203	$8.84 \pm 2.78$	$11.60 \pm 2.49$	0.818	$0.82 \pm 0.029$
$AC_{orig}$	0.05519	$-8.54 \pm 5.67$	$-11.47 \pm 3.41$	0.762	$0.77 \pm 0.030$
$AC_{sgn}$	0.00027	$-9.71 \pm 3.46$	$-13.88 \pm 3.08$	0.822	$0.82 \pm 0.027$
$BBAC$	0.00153	$-9.24 \pm 2.97$	$-12.16 \pm 2.40$	0.795	$0.80 \pm 0.029$



**Fig. 6.** ROC curves comparing the three examined methods when Deceleration Capacity is computed:  $DC_{orig}$ ,  $DC_{sgn}$ ,  $BBDC$ . Young subjects are considered as *positives*.



**Fig. 7.** ROC curves comparing the three examined methods when Acceleration Capacity is computed:  $AC_{orig}$ ,  $AC_{sgn}$ ,  $BBAC$ . Young subjects are considered as *positives*.

Shapiro–Wilk test for normality. The same results, from another perspective can be seen in the box plots of Figs. 4 and 5 for Deceleration Capacity and Acceleration Capacity respectively. These figures show graphically the discrimination achieved by each one of the three applied metrics. We can see that the proposed methods present less (almost no) overlap between the boxes representing the subjects of the two groups. Finally Figs. 6 and 7 compare all three methods using ROC curves. We can see that both  $DC_{sgn}$  and  $BBDC$  seem to discriminate the two groups more successfully. The *area under ROC curve* (*AuC*) is a quantitative measure of the discrimination achieved and is shown in Table 1 for both Deceleration Capacity and Acceleration Capacity.  $AC_{sgn}$ , providing the maximum area under the ROC curve, has the best discrimination power.

We also performed a bootstrap test to check the stability of our results. Since the number of recordings are relatively small, we performed bootstrap test repeating the experiment 1000 times, each times using 35 out of 40 recordings. The results are shown

**Table 2**  
*p*-Values and area under ROC curve for common statistical HRV indices [1].

	<i>p</i> -Value	AuC
Mean	0.275	0.382
sdnn	0.011	0.785
rmssd	0.219	0.665
pNN50	0.001	0.857
sdann	0.015	0.770
sdnni	0.007	0.790

in the last column of Table 1 and show the mean values and the standard deviations of the results of all experiments. For completeness, we also present in Table 2 *p*-values and the corresponding *AuC* indices for the most common statistical measures of HRV analysis. The discrimination power of all measures is lower than those of the methods examined in this paper with the exception of pNN50 which is something larger. pNN50 is a widely used method expressing the probability of two successive beats to differ more than 50msec and is an index of fast (beat–beat) RR changes and of parasympathetic activity.

All necessary software for analyzing the signal or statistical analysis has been developed by our team in Matlab.

#### 4. Discussion

The two new methods proposed in this paper for the computation of Deceleration Capacity were first examined and compared theoretically with the originally proposed method. We showed that filtering in a quad level rather than in an anchor level could lead to a more accurate selection of the points which should participate in the computations. We also showed that if we use information from the whole quad and not only from the anchor point in order to characterize segments as acceleration or deceleration, it is possible not to obtain negative values (indicating acceleration) in the computation of Deceleration Capacity. We proposed  $BBDC$  which computed Deceleration Capacity based on successive beats only. In order to support our theoretical claims we used all three metrics to discriminate young and elderly subjects and showed that the two new methods achieved a more accurate discrimination.

One of the main characteristics of  $DC_{sgn}$  is the use of stricter criteria for the selection of the quads which will participate in the computation. This may lead to a smaller number of legal quads compared to those used by  $DC_{orig}$ . The signals from *fantasia* are approximately 2 h long. The average number of quads left after filtering from each file in the computation of  $DC_{sgn}$  was approximately 1500, consisting a sufficient large set for stable and statistically significant results. The minimum number of quads per signal necessary to provide statistically significant results will be a study of a future paper.

The performance of  $DC_{orig}$  could be better if a proper filter had been applied before the application of the method, since this filter could reduce the number of artifacts that participate in the computations. However, such a filter does not solve the problem, since it is still possible points being characterized as possible artifacts and excluded from the anchors to appear in the computation of the averaged vector. From the recordings we selected only the NN (normal to normal beats) intervals and did not use any additional filtering apart from that embedded in the methods.

#### 5. Conclusions and future plans

In this paper we suggested some modifications in the way Deceleration Capacity is computed which seem to improve the originally proposed method. We propose modifications in the way the filtering is done and in the way we characterize four consecutive beats as acceleration or deceleration. We also studied the ability to extract



information examining beat to beat decelerations rather than using only a four beat window. We show theoretically, based on the physiology and with our experiments using a dataset of young and elderly subjects that the newly proposed methods improve the original method.

Since the original DC methodology was developed as a prognostic index for total mortality in post myocardial infarction patients [2], we plan to extend our evaluation on total mortality and arrhythmic sudden cardiac death risk stratification for post myocardial infarction patients and patients with dilated cardiomyopathy. For this purpose we will use our dataset also used in [15,16]. This database consists of more than 200 recordings acquired from heart failure patients and will soon be based on recent follow up information.

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## References

- [1] Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, Heart rate variability: standards of measurement, physiological interpretation, and clinical use, *Circulation* 93 (1996) 1043–1065.
- [2] A. Bauer, J.W. Kantelhardt, P. Barthel, R. Schneider, T. Makikallio, K. Ulm, K. Hnatkova, A. Schomig, H. Huikuri, A. Bunde, M. Malik, G. Schmidt, Deceleration capacity of heart rate as a predictor of mortality after myocardial infarction: cohort study, *Lancet* 367 (9523) (2006) 1674–1681.
- [3] M.N. Levy, T. Yang, D.W. Wallick, Assessment of beat-by-beat control of heart rate by the autonomic nervous system: molecular biology techniques are necessary, but not sufficient, *J. Cardiovasc. Electrophysiol.* 4 (1993) 183–193.
- [4] Q. Pan, Y. Gong, S. Gong, Q. Hu, Z. Zhang, J. Yan, G. Ning, Enhancing the deceleration capacity index of heart rate by modified-phase-rectified signal averaging, *Med. Biol. Eng. Comput.* 48 (4) (2010) 399–405.
- [5] J. Sacha, J. Sobon, K. Sacha, A. Muller, G. Schmidt, Short-term deceleration capacity reveals higher reproducibility than spectral heart rate variability indices during self-monitoring at home, *Int. J. Cardiol.* 152 (2) (2011) 271–272.
- [6] J. Piskorski, P. Guzik, The structure of heart rate asymmetry: deceleration and acceleration runs, *Physiol. Measure.* 32 (8) (2011) 1011.
- [7] P. Arsenos, K. Gatzoulis, G. Manis, et al., Reduced deceleration capacity of heart rate risk stratifies patients presenting with preserved left, *Eurpace* 13 (Suppl. 3) (2011).
- [8] A. Bauer, J.W. Kantelhardt, A. Bunde, P. Barthel, R. Schneider, M. Malik, G. Schmidt, Phase-rectified signal averaging detects quasi-periodicities in non-stationary data, *Phys. A: Stat. Mech. Appl.* 364 (2006) 423–434.
- [9] L.M. Campana, R.L. Owens, G.D. Clifford, S.D. Pittman, A. Malhotra, Phase-rectified signal averaging as a sensitive index of autonomic changes with aging, *J. Appl. Physiol.* 108 (6) (2010) 1668–1673.
- [10] J.W. Kantelhardt, A. Bauer, A. Schumann, P. Barthel, R. Schneider, M. Malik, G. Schmidt, Phase-rectified signal averaging for the detection of quasi-periodicities and the prediction of cardiovascular risk, *Chaos* 17 (1) (2007) 015122.
- [11] C.M. Furnival, R.J. Linden, H.M. Snow, Chronotropic and inotropic effects on the dog heart of stimulating the efferent cardiac sympathetic nerves, *J. Physiol.* 230 (1973) 137–153.
- [12] M.N. Levy, P.J. Martin, T. Iano, H. Zieske, Effects of single vagal stimuli on heart rate and atrioventricular conduction, *Am. J. Physiol.* 218 (1970) 1256–1262.
- [13] N. Iyengar, C.K. Peng, R. Morin, A.L. Goldberger, L.A. Lipsitz, Age-related alterations in the fractal scaling of cardiac interbeat interval dynamics, *Am. J. Physiol.* 271 (4 Pt 2) (1996).
- [14] A.L. Goldberger, L.A.N. Amaral, L. Glass, J.M. Hausdorff, P.C. Ivanov, R.G. Mark, J.E. Mietus, G.B. Moody, C.-K. Peng, H.E. Stanley, PhysioBank, PhysioToolkit, and PhysioNet: Components of a new research resource for complex physiologic signals, *Circulation* 101 (23) (2000) e215–e220.
- [15] P. Arsenos, K.A. Gatzoulis, T. Gialernios, P. Dilaveris, D. Tsiachris, S. Archontakis, A.I. Voulitiotis, L. Raftopoulos, G. Manis, C. Stefanadis, Elevated nighttime heart rate due to insufficient circadian adaptation detects heart failure patients prone for malignant ventricular arrhythmias, *Int. J. Cardiol.* 172 (2014) e154–e156.
- [16] G. Manis, P. Arsenos, S. Nikolopoulos, K. Gatzoulis, C. Stefanadis, Details on the application of multiresolution wavelet analysis on heartbeat timeseries, *Int. J. Bioelectromagn.* 15 (1) (2013) 60–64.