Fractal Dimension of In-vivo and Ex-vivo Rabbit HRV Series

[1,2]O. Janoušek, [1,2]M. Ronzhina, [1,2]J. Kolářová, [1,2]I. Provazník, [3]T. Stračina, [3]V. Olejníčková, [2,3]M. Nováková

[1]Brno University of Technology, Brno, Czech Republic,
[2]International Clinical Research Center, St. Anne´s University Hospital Brno, Czech Republic,
[3]Masaryk University, Brno, Czech Republic
Email: janouseko@feec.vutbr.cz

Abstract. *Fractal dimensions of beat-to-beat series have been estimated by box-count algorithm in five New Zealand white rabbits and five isolated New Zealand rabbit hearts. In-vivo hearts beat-to-beat series have fractal dimension value equal to 1.49±0.03, whereas fractal dimension for ex-vivo hearts series is equal to 1.45±0.14. The fractal dimension of in-vivo hearts beat-to-beat series does not statistically differ (α = 0.05) from those of the isolated hearts, indicating that fractal features of heart rate variability are probably predominantly affected by intrinsic behaviour of the heart.*

Keywords: HRV, box-count, fractal dimension, in-vivo and ex-vivo, rabbit heart

1. Introduction

The variability of RR-interval duration in beat-to-beat series has been recognized as characteristic attribute of vital heart [1]. The variability of RR-interval duration is affected by joint influence of sympathetic and parasympathetic branches of autonomous nervous system. Besides sympathetic-parasympathetic system activity, numerous intrinsic mechanisms of the heart may influence RR-interval duration, too. Cooperation of all abovementioned mechanisms gives rise to complex course of beat-to-beat time series.

There is a significant amount of variability in beat-to-beat series of isolated heart despite its complete denervation. Intrinsic mechanisms of the heart maintain the existence of beat-to-beat variability; however, the character of *ex-vivo* variability differs from the *in-vivo* one. The *ex-vivo* beat-to-beat series contain more quaziperiodic oscillations in comparison with *in-vivo* ones, resulting in a wavy shape of tachograms. Although the total amount of oscillations in *ex-vivo* tachogram is highly individual, one can visually differentiate *in-vivo* and *ex-vivo* beat-to-beat series by assessing of tachogram shape. Examples of *in-vivo* and *ex-vivo* tachograms are shown in Fig. 1.

In this article, the tachogram shape has been quantified by fractal dimension. We hypothesize that fractal dimension computed from sets of tachogram may be associated with influence of autonomous nervous system on heart rate variability (HRV). We investigated difference of fractal dimension between *in-vivo* and *ex-vivo* rabbit HRV series to discover, whether fractal dimension may serves as an indicator of autonomous nervous system activity.

2. Methods

The *in-vivo* ECG signals have been recorded from five New Zealand rabbits by SEIVA recording system. Body surface wire electrodes were attached to the skin with miniature clips. Location of electrodes did not restrict free posturing of the animal in sitting position.

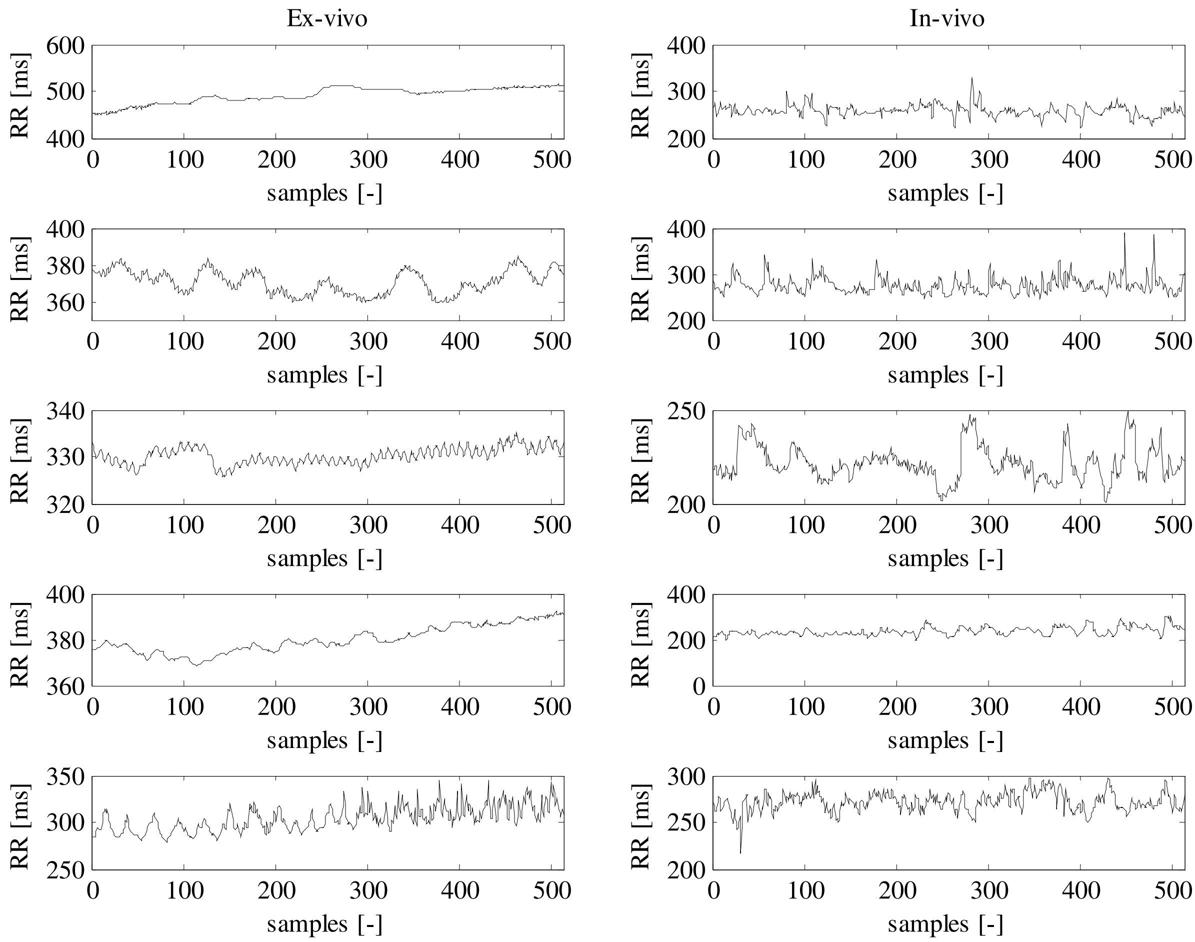

Fig. 1. Tachograms of *ex-vivo* (left) and *in-vivo* (right) hearts beat-to-beat series. Wavy shape of *ex-vivo* tachograms visually differs from sharp-edged shape of *in-vivo* tachograms.

The *ex-vivo* ECG signals have been recorded from isolated hearts perfused according to Langendorff in the mode of constant perfusion pressure (85mmHg). In deep anaesthesia with xylasin and ketamin, the hearts were excised and fixed on perfusion apparatus filled with Krebs-Henseleit solution (1.25mMCa^{2+}, 37°C) and placed in a thermostatically-controlled bath. After 30 minutes long stabilization period, the five minutes long ECG signals were recorded by touch-less method [2].

ECG signals degraded by arrhythmias were excluded from further processing. R-peaks were detected automatically by own R-wave detector designed in Matlab R2012b (MathWorks, USA). The results of automatic detection were reviewed and errors were corrected manually.

The fractal dimension has been estimated by box-count algorithm in custom made software in Matlab R2012b (MathWorks, USA). The box-count algorithm covers a beat-to-beat series with boxes of predefined size and the number of boxes required to cover the series is counted. In each subsequent step, the size of boxes is reduced, and the process of box counting is repeated [3]. Situation is illustrated in Fig. 2, where the tachograms covered by boxes of size 128 (upper part of figure), and 64 (middle part of figure), are shown. At each step, the number of boxes required to cover the curve and the size of box is kept in memory. When box size is reduced by factor of two in each step, resulting fractal dimension can be estimated as slope of ordinary least square regression fit of log(BoxCount) on log(BoxSize), where the BoxCount represents number of boxes required to cover the series, and BoxSize represents box size. The process of fractal dimension estimation is illustrated in bottom part of Fig. 2.

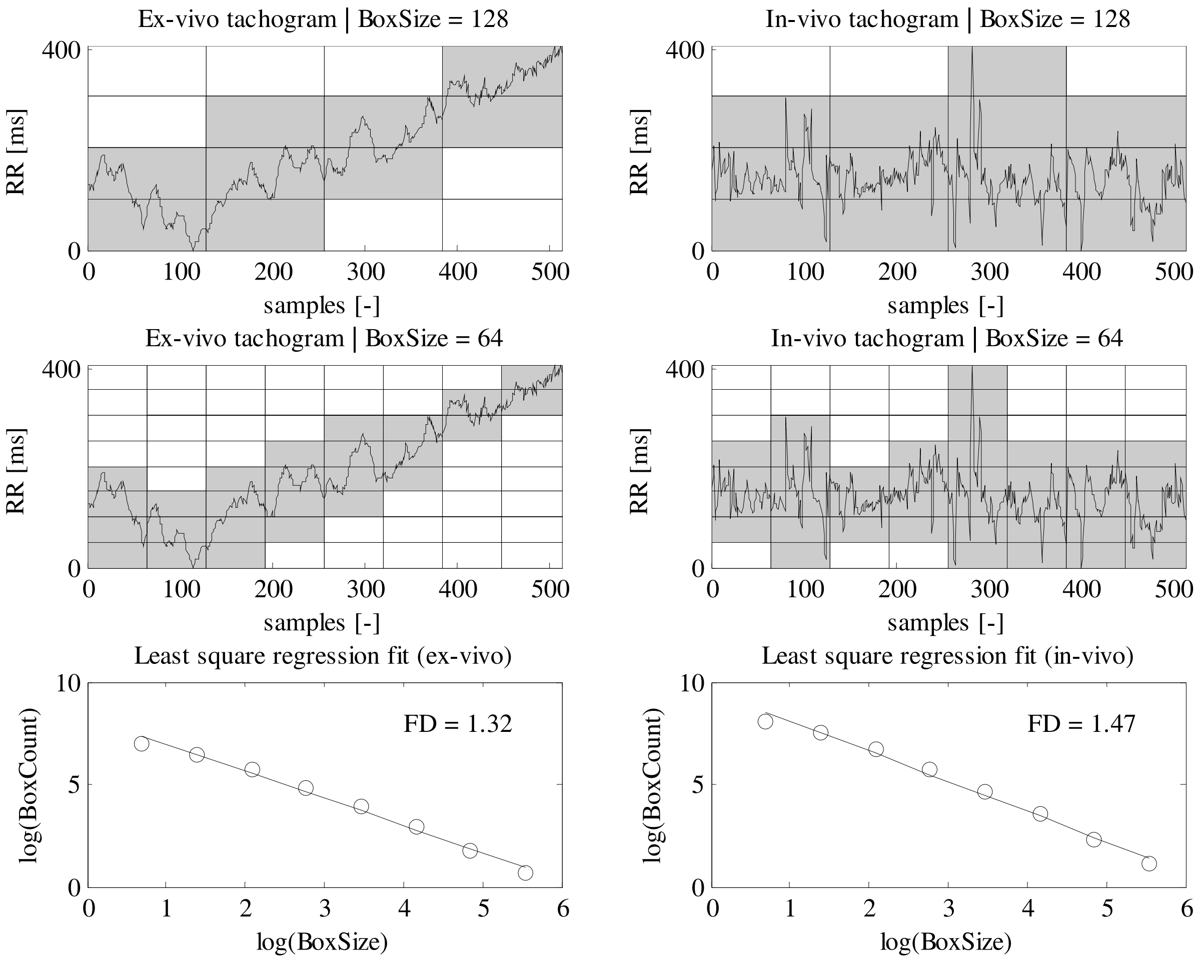

Fig. 2. Illustration of box-count algorithm. Upper part: tachogram is covered by boxes of size 128 and the number of boxes is counted. Middle part: the same situation with boxes of size 64. Bottom part: fractal dimension is estimated as the slope of least square regression fit of log(BoxCount) on log(BoxSize).

Wilcoxon rank sum test with $\alpha = 0.05$ has been used for evaluation of statistical significance of difference between in-vivo and ex-vivo fractal dimensions.

3. Results

Fractal dimension of *in-vivo* and *ex-vivo* beat-to-beat series has been estimated by box-count algorithm. The average value of estimated fractal dimension equals to 1.49±0.03 in *in-vivo* and 1.45±0.14 in *ex-vivo* beat-to-beat series. The difference between *in-vivo* and *ex-vivo* beat-to-beat series groups is not statistically significant. The least square regression fits of *ex-vivo* and *in-vivo* beat-to-beat series and the boxplot illustrating difference between *in-vivo* and *ex-vivo* groups are shown in Fig. 3.

The fractal dimension values of individual beat-to-beat series are close to each other in the *in-vivo* group. On the contrary, intra-individual value of fractal dimension in *ex-vivo* group is substantial.

4. Conclusions

The fractal dimension of *in-vivo* hearts beat-to-beat series is almost the same as of *ex-vivo* ones, indicating that the fractal features of HRV are probably predominantly affected by intrinsic behaviour of heart, not by sympathetic-parasympathetic branches of autonomous nervous system.

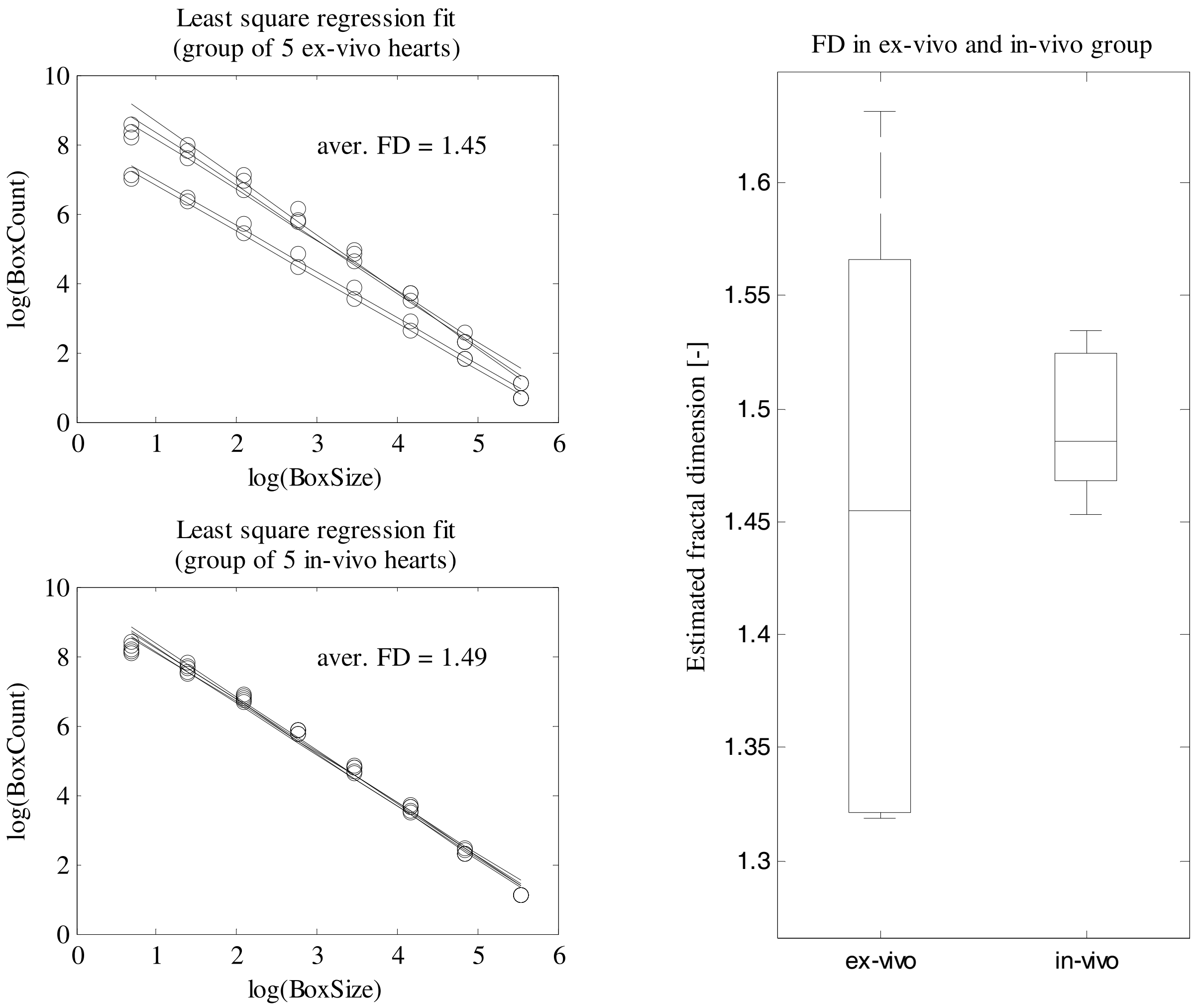

Fig. 3. Left: Slope of individual least square regression fits in *ex-vivo* (upper) and *in-vivo* (bottom) hearts. Right: boxplots of estimated fractal dimensions (FD) in *ex-vivo* and *in-vivo* heart groups.

Acknowledgements

The work was supported by European Regional Development Fund - Project FNUSA-ICRC (No. CZ.1.05/1.1.00/02.0123), grant projects of the Grant Agency GACR 102/12/2034, and MUNI/A/0957/2013.

References

[1] Berntson GG, Bigger JT Jr, Eckberg DL, Grossman P, Kaufmann PG, Malik M, Nagaraja HN, Porges SW, Saul JP, Stone PH, van der Molen MW. Heart rate variability: origins, methods, and interpretive caveats. *Psychophysiology*, 34(6): 623-48, 1997.

[2] Kolářová J, Fialová K, Janoušek O, Nováková M, Provazník I. Experimental methods for simultaneous measurement of action potentials and electrograms in isolated heart. *Physiological Research*, 59(S1): 71-80, 2010.

[3] Gneiting T, Ševčíková H, Percival DB. Estimators of Fractal Dimension: Assessing the Roughness of Time Series and Spatial Data. *Statistical Science*, 27(2): 247–277, 2012.