New method to obtain spontaneous baroreflex gain curve as a function of the systolic pressure

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Abstract. We present a non invasive new method based on the analysis of blood pressure and heart rate variability[1] to obtain baroreflex gain as a function of the systolic pressure. This method can explain certain results obtained in orthostatic tolerance studies, such as great variations of the baroreflex sensitivity[2, 3]. This approach help to understand the behavior of the baroreflex and to place some results in a more complete context.

1. Introduction
The baroreflex is a well-known system to stabilize arterial blood pressure by means of negative feedback. The baroreceptors are placed in the carotid sinus and the aortic arch.
In a laboratory environment the stimulation pressure can be controlled, and the RR interval changes response registered. In this way the entire baroreflex function can be computed.
This is an open loop estimation because we control the pressure instead of the natural control, which is the autonomic system. This invasive method can be very risky if we wish to reach curve boundaries.

Fig. 1 - Baroreflex curve
This has been done in early 1930, and as many other biologic functions, its shape is sigmoid. We can therefore distinguish three important points, the threshold, the saturation and the mid level.

The baroreflex has a minimal value of pressure to work named threshold, and beyond a determined value (saturation) the response is not increased. In the neighborhood of the mid level the sigmoid is almost linear and its derivative is constant. For this reason it is accepted to use that value as a unique characteristic of the baroreflex function. This value is called baroreflex sensitivity (BRS) and is measured in ms/mmHg.

Gain can be estimated by computing the derivative of the sigmoid function. We can also assume that real baroreflex gains should have similar shapes. If these hypotheses were true we can expect that points extracted from baroreflex sequences could have good correlation with these curves. Different mid values and pressure ranges before saturation had been simulated to mimic variability between subjects, this is shown in Fig. 2.

![Fig. 2 The parameters of each subject make the curve more flat or acute](image)

The baroreflex gain remains within certain boundaries in a certain subject in different physiological situations, and changes will be result of distinct modulation mechanism of the Autonomic Nervous System. Therefore the BRS is function of the operation point having it’s maximum at a certain arterial pressure which can be assumed as the reference value to be stabilized. With the subject at rest operation points are near the mid values and we don’t commit great errors assuming linear relationship, but if our interest is to study the behavior of the system in situations where the work points are far from the mid level we have to abandon this simplification. This is the case of tilt test, a widely used technique in orthostatic intolerance studies.

The tilt test push patient from equilibrium and usually produces an arterial pressure fall, and in case of inadequate compensation leads the patient to syncope. Subject is registered in a tilt bed at rest and next at 70 degrees. In this case new points from the curve are detected. These points have lower values of BRS and now have no sense average them. We are presenting a new method to reconstruct this curve from spontaneous techniques. We cannot obviously reconstruct the whole curve, but instead we can reconstruct it in the zone of work.

### 2. Data Acquisition

All of the subjects participating in this study were selected from patients of the Fernandez Hospital. We used a commercial isolated amplifier with acquiring software, a Colin non-invasive blood pressure monitor, and a computer, which records the signals. Both channels are digitized at 1200 samples/sec.
3. Preprocessing

Signal acquisition during tilt test includes electrocardiogram (ECG) and continuous blood pressure curve (CBPC). Baroreflex action is evaluated by studying correlations between heart rate (HR) and blood pressure (BP) changes. Two signals must be available as digital data for computer processing: beat to beat interval and beat to beat systolic and diastolic BP. They are obtained respectively from ECG and CBPC. This implies detection of R wave on ECG to compute intervals between them and determination of maximum and minimum BP for every heart beat on CBPC.

4. Method description

The tilt test has two stages, the first lasts twenty minutes with the patient at rest, this bring us a cloud of spots near the maximum of the baroreflex curve, each of these spots corresponds to different gains of baroreflex sequences. The second stage has a maximum duration of forty five minutes, and is associated with lower arterial pressure values, in some cases very far from mid level. Another test like to sit and stand up may produce similar effects in pressure. These changes in pressure induces compensation by the baroreflex.

The first part of the method we propose consist in detect baroreflex sequences from time series of both channels. To do this task we adopt the sequential method [4] and also identify three or more consecutive cycles of blood pressure increments coupled with RR interval concordant changes. Only values of correlation coefficient greater than 0.85 between both point series are included to assure linear relationship between point serial pairs. The quotient between segments is the gain. The minimum increment to be considered is 1 mmHg for the arterial pressure. For each ramp we register not only the gain but also the corresponding arterial pressure. The method also allows a lag of one beat between ramps.

![Fig. 3 -Concordant changes between arterial pressure and RR Interval](image)

The sequential method then averages all the gains from the selected ramps. The value obtained is the BRS. In our method instead of computing the average from all systolic arterial pressure points, pressure space is divided in non-overlapping windows of 10 mm of Hg wide. Then gain values corresponding to pressure values within each window are averaged. The abcissa will be the central pressure of the corresponding window. Each ramp of baroreflex detected contributes to approximate real points of the gain curve, for this reason we can only reconstruct part of the curve.

The philosophy upon this is to characterize the same phenomena by means of averaging the slopes obtained from each selected sequence. The biological signals have great variability and we will have different gain values at the same pressure range. To partially reconstruct the baroreflex curve covered we must interpolate between points, each points separated the following by 10 mm Hg. Cubic splines are used for this task.
5. Results

In Fig 3 we can observe results of the sequential method, where baroreflex sequences are detected and their slope shown. The segments are placed at a distance from the left margin coincident with the systolic arterial pressure at the beginning of the sequence. If we observe their slopes are very close when sequences have the same or similar arterial systolic pressure.

![Sequential method from one subject](image)

We are able to reconstruct important parts of the whole curve of baroreflex function of several subjects with only rearranging the data collected during tilt test studies. In the figure 4 we can see the results of curve fitting process of five of them. In many occasions the partially reconstructed curves are enough to give us an idea of how the entire curve could be. In some cases we cannot reconstruct the curve from impaired baroreflex subjects, but in this case other methods also fail. In other occasions only two points are extracted which represent a part of the curve. We have also tried other sizes for the systolic pressure windows to obtain better curve resolution, but due to the spontaneous characteristic of the method, when reordering the samples it can be noted that they are not evenly spaced. Therefore results are similar, but with higher distortions, and the conclusion is that it is not worth increasing the complexity. On the other hand when the window size is greater the gain is computed using more gain points and its value more confident and the reconstructed curve more smooth.

![Baroreflex gain curves from different subjects](image)
6. Conclusion

By rearranging the data collected doing standard procedures of assessing baroreflex gain in the time domain, the analysis of the results can be enhanced, incorporating new features like the central pressure to be stabilized, the width of the curve, and the part of the curve the subject has activated.

Those features are not obvious in a traditional analysis, but here are exposed and can be very useful in another studies of cardiovascular diseases.

We do not present numerical results, but we are trying to introduce this method in the analysis and discussions on this subject.

Recently it is viewing a growing interest in studying the baroreflex, since it has been proved its utility to assess various cardiological diseases. It is known that others diseases modify the baroreflex curves, for example diabetes and others neuropathies, so this method can also be applied.

In this context non-invasive methods like this are receiving great importance, and clinical acceptance because there is no risk to patient.

References:

1. Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology, 1996 Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Circulation, 93(5): p. 1043-65.

2. Bechir, M., et al., 2003 Dysfunctional baroreflex regulation of sympathetic nerve activity in patients with vasovagal syncope. Circulation, 107(12): p. 1620-5.

3. Pitzalis, M., et al., 2003 Enhanced reflex response to baroreceptor deactivation in subjects with tilt-Induced syncope. Journal of the American College of Cardiology, 2003. 41(7): p. 1167-1173.

4. Parati, G., M. Di Rienzo, and G. Mancia, 2000 How to measure baroreflex sensitivity: from the cardiovascular laboratory to daily life. J Hypertens, 18(1): p. 7-19.