

# Estimation of systolic time intervals among healthy subjects using cardiac electromechanical signals: a repeatability study

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## Abstract

Systolic time intervals (STIs) have been used to quantify the functionality of heart performance, particularly the left ventricle. STIs can be estimated through convenient and efficient techniques using cardiac electromechanical signals including electrocardiogram (ECG) and seismocardiogram (SCG). The STIs in our study included pre-ejection period (PEP), left ventricular ejection time (LVET), and their ratio (PEP/LVET). Despite numerous studies on using SCG and ECG for estimation of STIs, the repeatability of such an approach have not been thoroughly investigated. To address this gap, we conducted two repeatability experiments, consecutive (three consecutive measurements with a one minute interval in between) and 24-hour (two measurements with at least a 24-hour interval in between) on 21 healthy subjects. An expert annotated the aortic valve opening and closure characteristic points on the SCG, and Q wave on the ECG for all the measurements. For healthy subjects, it is not expected that STIs vary significantly between the measurements in any of the experiments. To quantify the repeatability, we considered the coefficient of variation (CV). Our results indicated small variation in STIs quantified by CV values. It can be concluded that STIs estimation through cardiac electromechanical signals is repeatable.

Keywords: systolic time intervals, repeatability, seismocardiogram, cardiac electromechanical signals

## 1. Introduction

Systolic time intervals (STIs) are critical timing parameters with diagnostic and prognostic implications in the assessment of heart performance, particularly the left ventricle. STIs have been used as a noninvasive technique in the evaluation of heart for suspected myocardial, coronary artery, and valve diseases [1]. One of the earliest investigation on the estimation of STIs

was conducted by Garrod in the late 19<sup>th</sup> century [2]. Since then, various methods have been proposed to estimate STIs such as concurrent electrocardiogram (ECG), phonocardiogram, and carotid pulse [3] [4], echocardiography (Echo) [5] [6], and impedance cardiography [7]. A brief review of these methods is presented by Tavakolian [8].

Among these methods, seismocardiography has gained popularity as a convenient and inexpensive method. The seismocardiogram (SCG) signal is collected by placing an

accelerometer on the sternum that captures the movement of the chest induced by heart vibrations. SCG provides information on mechanical aspects of heart, in contrast to ECG that indicates the electrical activities of heart. In this study, we refer to the SCG and ECG as heart's electromechanical signals, which can provide a more complete assessment of cardiac functions.

Crow, et al., in mid 90s used SCG for estimation of STIs, and compared their results with Echo as the gold standard. They concluded that both methods are equally accurate in the measurements of STIs [9]. Among different STIs, we considered pre-ejection period (PEP), left ventricular ejection time (LVET), and their ratio (PEP/LVET) for the purpose of this study. PEP can be estimated from Q-wave on ECG to the aortic valve opening (AO) characteristic point on SCG. LVET can be estimated from AO to the aortic valve closure (AC) characteristic point on SCG (Figure 1). It has been shown that PEP and LVET correlate with stroke volume and cardiac output [4]. PEP/LVET ratio has been reported to be correlated with the ejection fraction [1]. Also, this ratio is a more robust parameter with respect to the heart rate [1].

Our purpose in this study is to investigate the repeatability of STIs' estimation (test-retest reliability, [10]) among healthy subjects using heart electromechanical signals. Conducting such a study is important, because it indicates the ability of SCG and ECG in providing consistent and repeatable measurements of STIs.

The repeatability of STIs' estimation using other methods has been investigated. Reant, et al., [11] studied the Echo method, and obtained the averaged repeatability of 7.6% in PEP and 4.3% in LVET for two different Echo acquisitions over 20 subjects. They also conducted another experiment, in which the repeatability was obtained over 10 measures from one Echo acquisition. In this experiment, the average repeatability for PEP and LVET was 2% and 4%, respectively.

In another investigation, Kupari used arterial pulse tracing, ECG, and phonocardiogram to study the repeatability of STIs' estimation among 49 healthy subjects. He considered different periods of observation, (i) within 3 hour; (ii) within 24 hour; (iii) within 1 to 2 weeks; and (iv) within 14 to 18 months. The variability of STIs were the smallest in the measurements of period (i) and largest in the measurements of period (ii).

For each period, he computed the coefficient of variation (CV) [12] for different STIs. For PEP, the average CV value was 3.6%, 8.7%, 5.6%, and 5.9% in periods (i) to (iv). For LVET, the average CV values were 1.4%, 3.5%, 2.6%, and 2%, respectively. For PEP/LVET ratio, the results were 3.7%, 9.9%, 5.7%, and 6.2%.

Barnes, et al., studied the repeatability of STIs using impedance cardiography [14]. They evaluated different hemodynamic parameters including PEP and LVET from 35 healthy subjects in two visits, separated by a 2-month interval. In each visit, day-time and night-time measurements were

obtained and averaged accordingly. The authors did not find a significant difference between the mean of PEP and LVET in the two visits.

Despite various investigations on cardiac electromechanical signals, the repeatability of STIs' estimation using such signals have not been thoroughly investigated. Therefore, our focus in this study is to address this gap as described in the following sections.

## 2. Method

### 2.1 Data collection

SCG and ECG signals were recorded from 21 healthy individuals (age:  $30 \pm 6$  years, height:  $172 \pm 6$  cm, weight:  $71 \pm 13$  kg, and sex: 13 males and 8 females). SCG was obtained by placing a triaxial accelerometer (Silicon Designs Inc. Model 2476, USA) on the sternum and collecting the acceleration signal in the dorsoventral direction ((Fig?)). A one-lead ECG was recorded simultaneously by the iWorx Systems, Inc., IX-BIO8-SA, NH, USA. All the recordings were transferred to a personal computer using the iWorx data acquisition system (iWorx Systems, Inc., IX-416, NH, USA) sampled at 1000 Hz with 16-bit resolution.

The risk of cardiovascular diseases (CVDs) among subjects was estimated by the age, sex, heart rate and rhythm, blood pressure, and cardiac hemodynamic parameters included ejection fraction, E/A ratio, and stroke volume obtained by echocardiography. We found the risk of CVDs to be low for all participants, whom are referred to as healthy subjects for the purpose of this study.

Ethics approval was issued by the Office of Research Ethics, Simon Fraser University (SFU), Burnaby, Canada. The data collection was conducted in the Aerospace Physiology Laboratory at SFU.

### 2.2 Repeatability experiments

Two repeatability experiments were considered in our study, consecutive and 24-hour. In the consecutive repeatability experiment, our objective was to assess if the estimated STIs derived from cardiac electromechanical signals of healthy subjects significantly change within a short period. Three consecutive measurements of 10 cardiac cycles, with a one minute interval in between, were used for comparison.

In the 24-hour repeatability experiment, the objective was to investigate if the STIs of the healthy subjects significantly change when the recordings are conducted under the same conditions over a period longer than 24 hours. To accomplish this objective, two 1-minute measurements were conducted at least 24 hours apart for each subject. The recordings were taken at exactly the same time each day to reduce the diurnal variation in the systolic intervals. Also, in the second

recording, the participants were examined again to be at low risk of CVDs (i.e. healthy).

In both of the these experiments, the subjects were advised not to drink caffeinated beverages, alcohol or smoke cigarettes four hours prior to data recordings.

### 2.3 Repeatability quantification

To obtain PEP and LVET, an expert annotated Q-wave on the ECG and AO and AC points on the SCG for at least 10 cycles in each recording. PEP, LVET, and their ratio were computed per cycle, and then their medians were considered as the final values for their pertinent recordings.

Repeatability was quantified by the coefficient of variation (CV) as [12],

$$CV = \sigma/\mu \quad \text{Eq. (1)}$$

where  $\mu$  is the mean and  $\sigma$  is the standard deviation of estimated STIs from SCG recordings.

## 3. Results and Discussions

((A table summarizing the average CV values for this study and potentially other studies))) Figures 2 and 3 show the values of STIs for different subjects in the consecutive and 24-hour experiments, respectively. As we can see in these figures, the values of STIs for different measurements in the consecutive and 24-hour experiments are close to each other. Even, the range of these values over various subjects are still close to each other. Such an observation was expected, because the subjects of this study were healthy, and thus their STIs were remained close to each other. In particular, the ratio of PEP/LVET in all the measurements and experiments did not exceed 0.4 that is a range for healthy subjects as indicated by prior studies [8] [13].

Figure 4 shows the STIs' CV values for different subjects in the consecutive and 24-hour experiments, respectively. There is no unique and predefined value for CV that indicates the acceptable repeatability of STIs' estimation using cardiac electromechanical signals. In this study, all the CV values in the consecutive experiment were less than 5%, except for subjects 11 and 12 (Top plot, Figure 4). In the 24-hour experiment, the CV values were larger, as we expected, because of longer duration between the recordings (at least 24 hour), which could potentially impose higher variations in the STIs (what are the physiological reasons?). As the bottom plot in the Figure 4 indicates, all the CV values in the 24-hour experiment were less than 15%, except for subject 2. In this experiment, about half of the subjects had the CV values of less than 5%. Despite the variation among the estimated STIs, their values never exceeded the reference range of healthy subjects, particularly for the ratio of PEP/LVET. For instance,

the maximum and minimum values of PEP/LVET for subject 11 in the consecutive experiment were 0.24 and 0.27, respectively (bottom plot, Figure 2); which indicates an acceptable range for a healthy subject. As an example of the 24-hour experiment, the maximum and minimum values of PEP/LVET for subject 2 were 0.24 and 0.30, respectively (bottom plot, Figure 3); which do not exceed the ratio threshold of healthy subjects (i.e. 0.4).

The closest study to our work was conducted by Crow, et al., [9], in which the repeatability of PEP was investigated using SCG and ECG. In their study, an average CV value of 5.4% was obtained after 10 consecutive recordings per 39 subjects. Their result is comparable to the obtained PEP's CV in the consecutive experiment of our study, in which the maximum and average values of CV over 21 subjects were 5.15% and 1.71%, respectively. Also, it should be mentioned that, their study did not include similar investigations to our 24-hour repeatability experiment.

One interesting point about Crow's study is that a lower CV value was reported for PEP when it was estimated by SCG and ECG, compared to Echo. Currently, there is a consensus among experts that Echo is the gold standard for estimation of STIs. Therefore, a possible explanation for their result can be the technology of Echo, which was based on chart recorders that involved plotting on papers and marking the characteristic points. Such a procedure is very prone to error and bias that potentially can reduce the accuracy.

((All these CV values are comparable to our values)))

*In this study, we did not focus on the challenges of SCG annotations, which are addressed on other studies. Rather, we assumed to have the correct annotation, and then estimating the STIs*

the results of repeatability study for the consecutive and 24-hour experiments, respectively. As we can see in Figure 7, the CV values of STIs for different subjects are relatively small. The maximum CV for PEP, LVET, and their ratio was 5.2% (Subject 11), 3.7% (Subject 12), and 6.7% (Subject 11), respectively, which indicates good repeatability of the the consecutive measurements.

The CV values in Figure 8 are also small for most of the subjects.

The repeatability quantified by CV was better for the consecutive experiment (within the same day) than the 24-hour experiment (in two different days). This result is consistent with the results of previous studies such as ... ..

The accurate estimation of STIs is dependent on precise annotation of Q on ECG and AO and AC on SCG. In this study, we assumed

((The sources of variation in the duration of the systolic time intervals fall into three broad categories: physiological, technical, and interpretative)) [KUPARI 1983]

You may test if the mean of consecutive tests are significantly differ from each other (t-test, ANOVA, etc.)

((Add the mean+-SD for the ejection fraction))

((pooled variances were calculated as the sum of squares of the individual SDs divided by the number of subjects))

Although for the 24-hour experiment, in Subject 2, a CV of 18.1% was obtained, but when we looked at the values for two days recordings, we noticed that both the PEP/LVET ratios were less than 0.4 (i.e. healthy range

Subjects 4 and 11 have larger CV values though. In subject 4, particularly PEP has larger variations in consecutive measurements (CV = 20.1%). To find the possible reasons for this variation, we looked at the PEP values in each of the 3 consecutive measurements, which were

Under identical experimental conditions, it was expected for estimated STIs to show a degree of sameness.

For the PEP measurements, it was shown that the median PEP recorded by considering the interval of ECG Q to the midpoint between SCG isovolumic moment (IM) and aortic valve opening (AO) lay within the interval defined from Q to the median of the start and end of aortic valve opening for all 23 individuals. Furthermore, it was demonstrated that the maximum difference between the median PEP/LVET derived from seismocardiography and echocardiography was 2.3%.

In three consecutive recordings one minute apart, it was demonstrated that the PEP/LVET was in the healthy range for all the 22 individuals. The maximum change of the median of PEP/LVET between the recordings was 3%. In other words, the PEP/LVET parameter extracted from seismocardiogram is reproducible over short periods of time .

For the 21 individual recordings, it was demonstrated that the PEP/LVET varied by a maximum of 5% for 19 individuals and by less than 10% for the next two candidates. Moreover, the ejection fractions for all 21 individuals were above 55%,

indicating a normal range with less than 5-10% change for two days of recordings.

Signals from 23 subjects were recorded on two different days and PEP/LVET was calculated for these subjects using SCG and the coefficient of variation (CV) was calculated for these measurements. The CV value was calculated to be 5% for SCG recorded over two different days while it was only 2.5% for the signals recorded on different session but in the same day. The CV was also calculated to be 4.8% for the ejection fraction values of the same subjects measured by echocardiography.

Sometimes, the morphology of the signal disturbed so that, the correct annotation becomes challenging, which can causes error in estimations of STIs.

CV has also been used to assess repeatability of STIs measurement in other modalities such as Echo, [REF], ICG, etc.

**1.1.1 Subsubsection heading.** In in nunc. Class aptent taciti sociosqu ad litora torquent per conubia nostra, per inceptos hymenaeos. Donec ullamcorper fringilla eros. Fusce in sapien eu purus dapibus commodo. Cum sociis natoque penatibus et magnis dis parturient montes, nascetur ridiculus mus. Cras faucibus condimentum odio. Sed ac ligula. Aliquam at eros.

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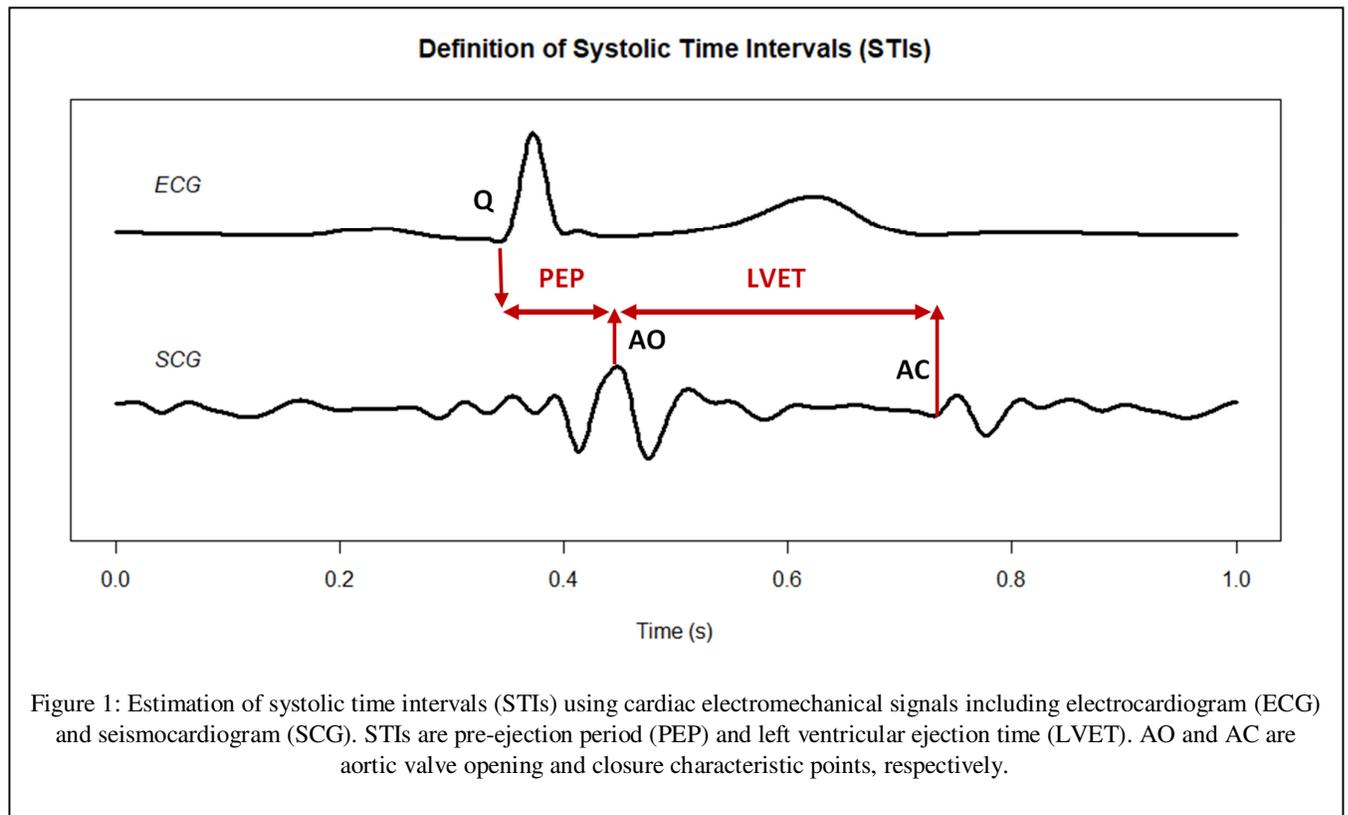
## Acknowledgements

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## References

- [1] R. P. Lewis, S. E. Rittogers, W. F. Froester, and H. Boudoulas, "A critical review of the systolic time intervals," *Circulation*, vol. 56, no. 2, pp. 146–158, 1977.

- [2] A. H. Garrod, "On some points connected with the circulation of the blood, arrived at from a study of the sphygmograph-trace," *Proc. R. Soc. London*, vol. 23, no. 156–163, pp. 140–151, 1875.
- [3] L. N. KATZ and H. S. FEIL, "Clinical observations on the dynamics of ventricular systole: I. Auricular fibrillation," *Arch. Intern. Med.*, vol. 32, no. 5, pp. 672–692, 1923.
- [4] A. Weissler, W. Harris, and C. Schoenfeld, "Systolic time intervals in heart failure in man," *Circulation*, vol. 37, no. 2, pp. 149–159, 1968.
- [5] M. Stefadouros and A. Witham, "Systolic time intervals by echocardiography," *Circulation*, vol. 51, no. 1, pp. 114–117, 1975.
- [6] S. Hirschfeld, R. Meyer, D. C. Schwartz, J. Korfhagen, and S. Kaplan, "Measurement of right and left ventricular systolic time intervals by echocardiography," *Circulation*, vol. 51, no. 2, pp. 304–309, 1975.
- [7] V. Balasubramanian, O. Mathew, A. Behl, S. Tewari, and R. Hoon, "Electrical impedance cardiogram in derivation of systolic time intervals," *Br. Hear. J.*, vol. 40, no. 3, p. 268, 1978.
- [8] K. Tavakolian, "Systolic time intervals and new measurement methods," *Cardiovasc. Eng. Technol.*, vol. 7, no. 2, pp. 118–125, 2016.
- [9] R. S. Crow, P. Hannan, D. Jacobs, L. Hedquist, and D. M. Salerno, "Relationship between seismocardiogram and echocardiogram for events in the cardiac cycle," *Am. J. Noninvasive Cardiol.*, vol. 8, no. 1, pp. 39–46, 1994.
- [10] W. M. K. Trochim, J. P. Donnelly, and K. Arora, *The research methods: The Essential knowledge base*. 2016.
- [11] P. Reant et al., "Systolic time intervals as simple echocardiographic parameters of left ventricular systolic performance: correlation with ejection fraction and longitudinal two-dimensional strain," *Eur. J. Echocardiogr.*, vol. 11, no. 10, pp. 834–844, Dec. 2010.
- [12] H. Abdi, "Coefficient of variation," *Encycl. Res. Des.*, vol. 1, pp. 169–171, 2010.
- [13] H. Boudoulas et al., "Assessment of ventricular function by combined noninvasive measures: factors accounting for methodologic disparities," *Int. J. Cardiol.*, vol. 2, no. 5–6, pp. 493–506, 1983.
- [14] V. A. Barnes, M. H. Johnson, and F. A. Treiber, "Temporal stability of twenty-four-hour ambulatory hemodynamic bioimpedance measures in African American adolescents.," *Blood Press. Monit.*, vol. 9, no. 4, pp. 173–177, Aug. 2004.



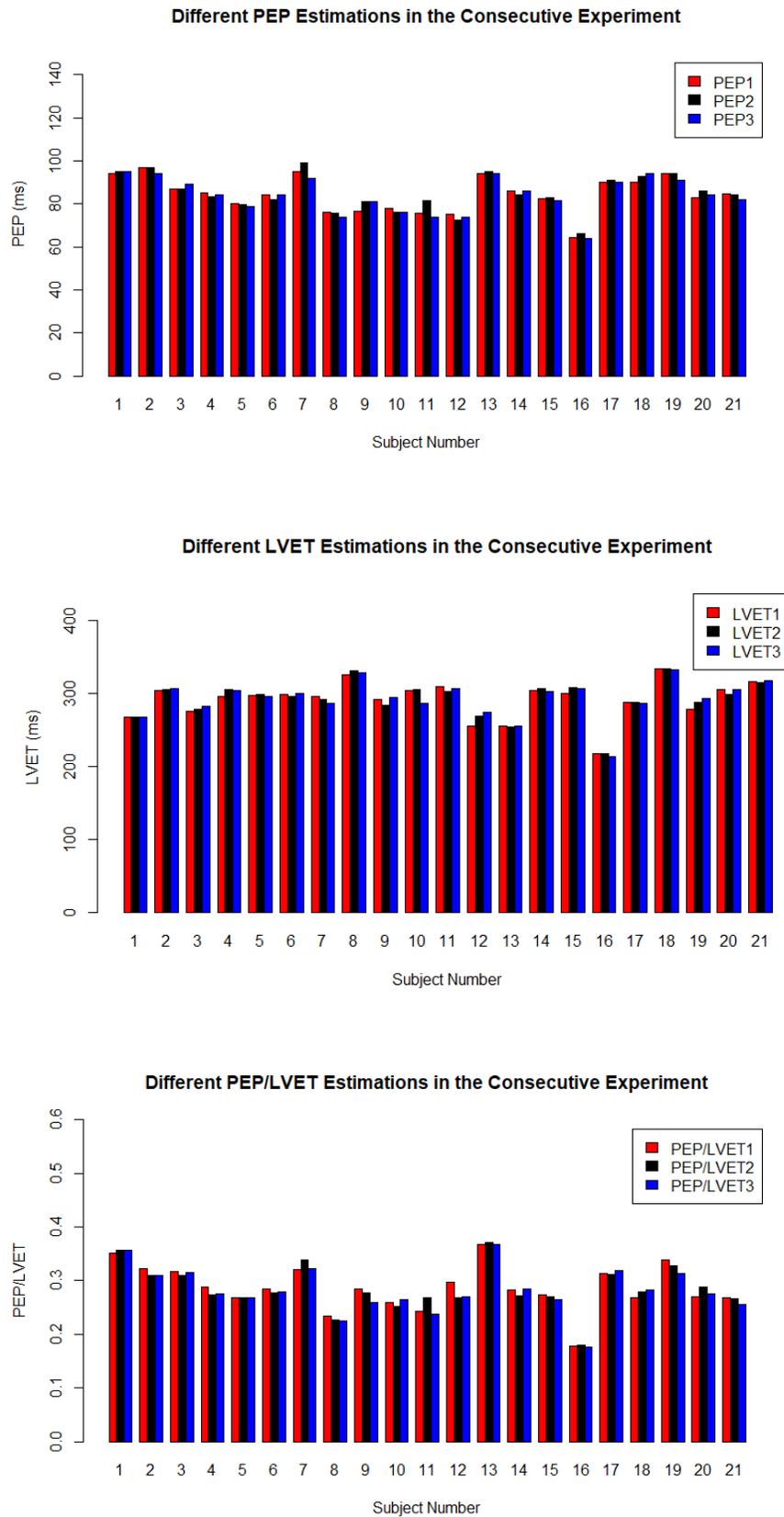


Figure 2: The values of systolic time intervals (STIs) for different subjects in the consecutive experiment.

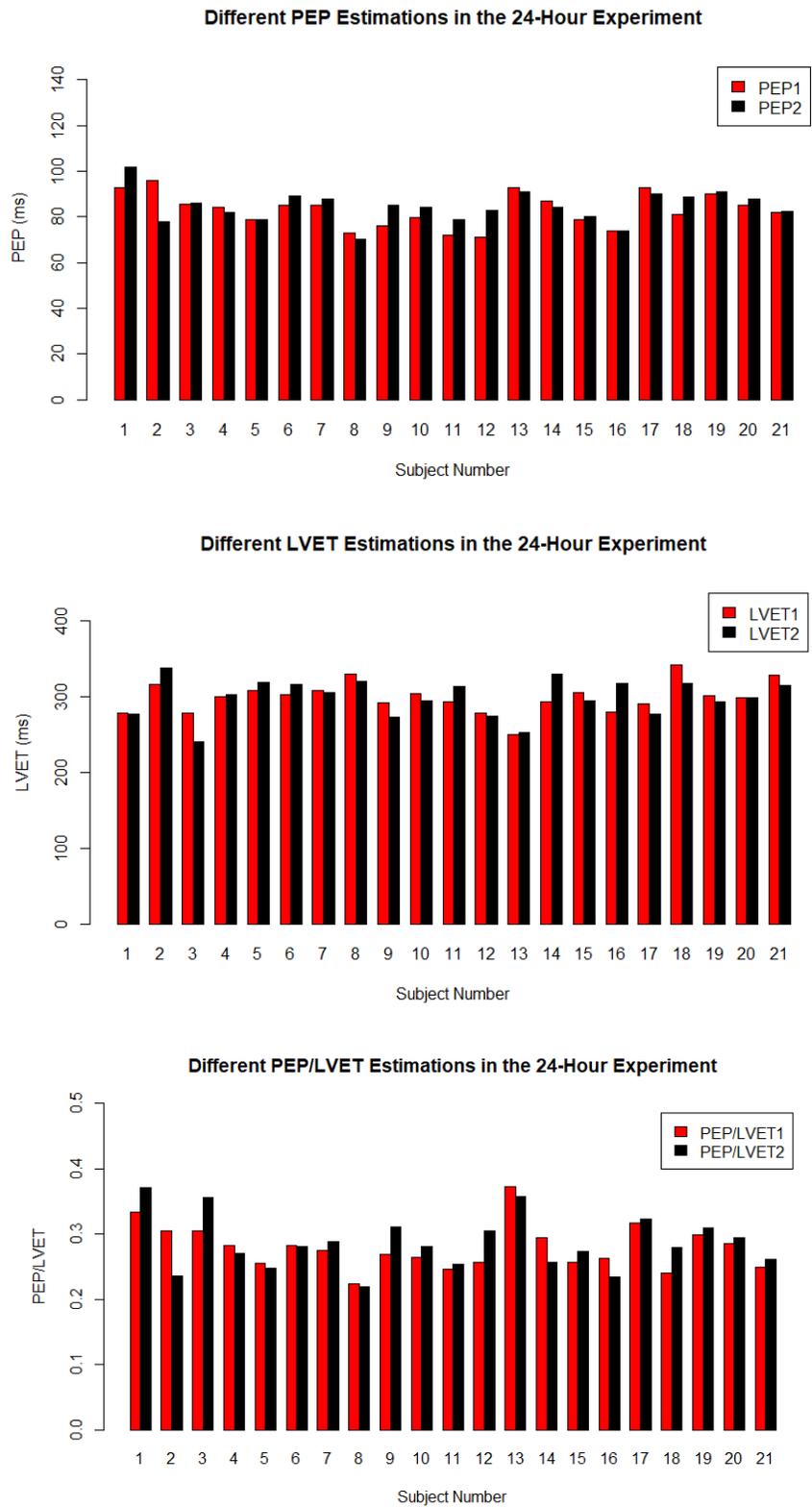


Figure 3: The values of systolic time intervals (STIs) for different subjects in the 24-hour experiment.

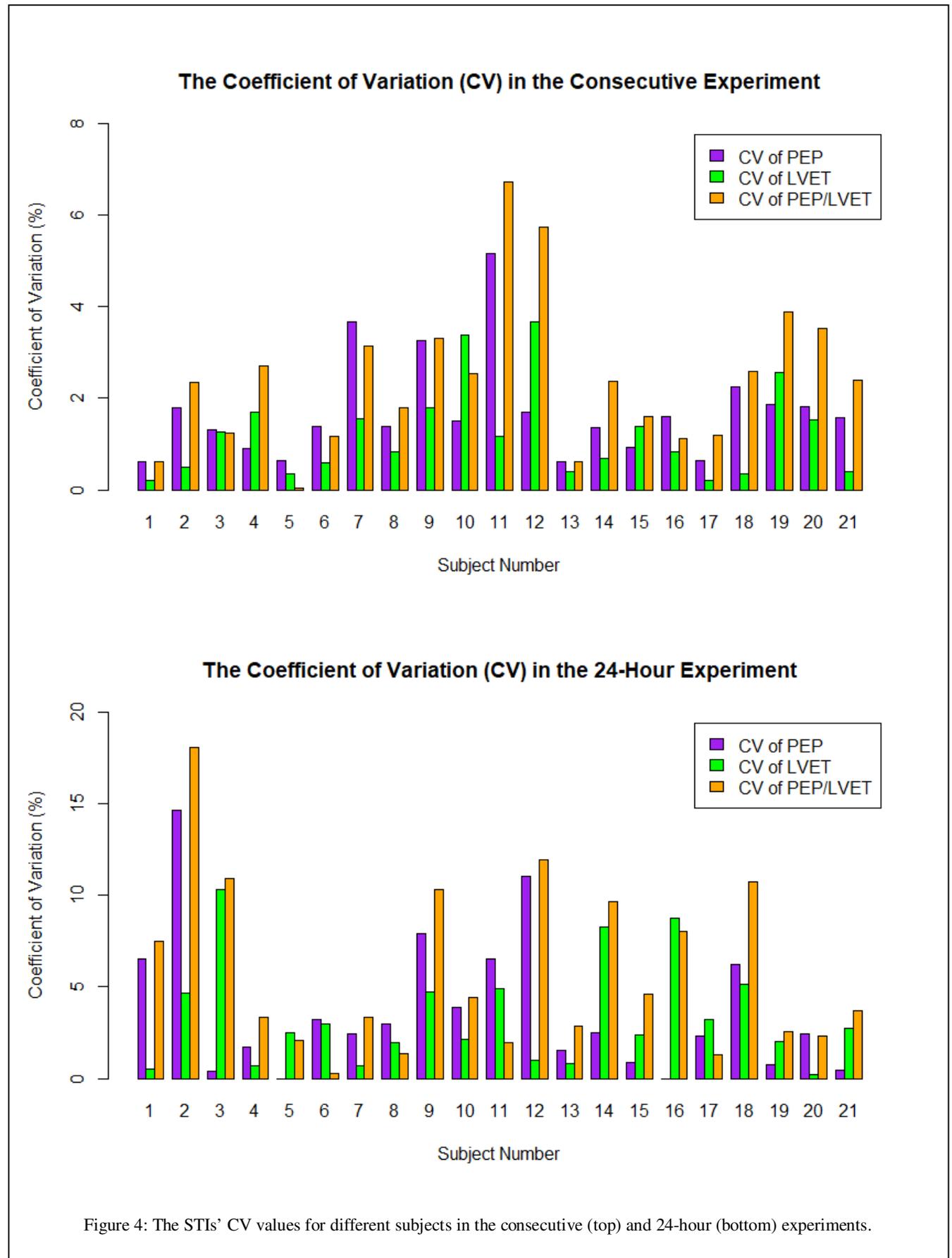


Figure 4: The STIs' CV values for different subjects in the consecutive (top) and 24-hour (bottom) experiments.