Does Sample Entropy Reflect Nonlinear Characteristics of Cardiovascular Murmurs?

SE Schmidt[1], M Græbe[2], E Toft[3], JJ Struijk[4]

[1]Medical Informatics Group, Department of Health Science and Technology, Aalborg University, Denmark
[2]Department for Vascular Surgery, Copenhagen University Hospital, Denmark
[3]Center for Sensory-Motor Interaction, Department of Health Science and Technology, Aalborg University, Denmark

Abstract

Sample entropy has been applied successfully for quantification of cardiovascular murmurs, but does sample entropy reflect nonlinear and chaotic characteristics of the murmurs? Seven digital audio recordings from subjects with audible carotid murmurs were recorded. Sample entropy was calculated from periods with and without murmurs and compared with sample entropy from surrogates with linear properties. None of the sample entropy measures from the recordings differed significantly from the surrogates with known linear properties. The sample entropy increased significantly in periods with audible murmurs compared to periods without. A similar difference was found between the surrogates of periods with and without murmurs. This confirms that sample entropy is suited for quantification of cardiovascular murmurs, but there is no evidence that nonlinear signal components of the murmursare present or affect the sample entropy.

1. Introduction

Analysis of cardiovascular murmurs is a recurrent topic in biomedical signal processing. The challenges includes the detection of murmurs, differentiation between murmurs from different pathologies, estimation of the degree of stenosis, estimation of blood flow velocity, and estimation of pressure drop across a stenosis [1,2]. A typical focus is on signal processing methods that assist clinicians in diagnosing cardiovascular disease such as heart valve defects [1].

The current paper examines murmurs or bruits from the carotid arteries to gain deeper understanding of the nature of cardiovascular murmurs. At a first look, cardiovascular murmurs seem stochastic without determinism and the majority of the studies apply linear signal processing methods, although the origin of the murmurs is turbulent flow, which is characterized by nonlinear and chaotic behavior [3]. Consequently, several recent studies have implemented methods for analysis of nonlinear signals [4,5]. One such measure is sample entropy, useful for quantifying complexity of dynamic systems. Ahlstrom et. al [6] found that the presence of aorta stenosis increases sample entropy for systolic heart sounds and that sample entropy correlates to the blood flow velocity through aorta valves.

But are nonlinear and chaotic characteristics actually present in cardiovascular murmurs? Is sample entropy influenced by these characteristics? Or does the observed change in sample entropy just describe the degrees of randomness in a linear stochastic process, which might be fully described by the power spectrum? It is well accepted that recorded signals do not necessarily reflect the nonlinear and chaotic behavior of the underlying system [5]. This is a likely scenario in the case of the murmurs, since murmurs measured at the body surface are the sum of pressure fluctuations through tissue caused by a large number of eddies in the artery beneath the recording point.

The aim of the current study was to test if sample entropy is affected by nonlinear or low dimensional chaotic components in digital recordings of murmurs from stenosed carotid arteries.

2. Methods

The null hypothesis of the study was that murmurs are not different from a stationary linear Gaussian process. This was evaluated by comparing sample entropy from murmurs to sample entropy from surrogates. In addition, the difference between silent periods in the recording and murmurs were compared with the difference between surrogates of murmurs and surrogates of silent periods.

2.1. Data collection and pre-processing

Digital audio recordings were collected with an

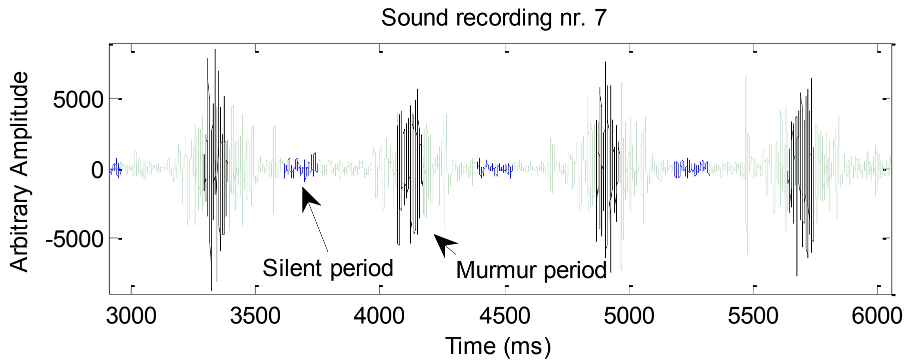

Figure 1. Sound recording example. The extracted murmur and silent periods are indicated.

electronic stethoscope (3M/Littmann E4100) from stenosed carotid arteries in patients referred to an ultrasound examination of the carotid arteries because of prior symptoms of cerebral ischemic events. The sample rate was 4 kHz and the recording duration 8 seconds. To ensure good data quality 7 recordings with clearly audible murmurs were selected amongst recordings from 14 patients prior to the data analyses. The degree of stenosis was between 50% and 99% estimated from peak systolic and end diastolic blood velocities measured using Doppler ultrasound (Philips iU22,) according to Polak et. al. [7].

The signal to noise ratio was improved by filtering with a 1st order Butterworth high pass filter with a 60 Hz cut-off frequency, applied both forward and backward to prevent phase distortion. The murmurs were identified manually and only the middle segment of the murmurs were used to ensure approximate stationarity. To ensure homogeneity from beat to beat, the timing between the first heart sound (S1) and the initialization of the selected murmur segments was the same throughout the recording. The mean segment duration was 139 ms. In a similar way silent periods were collected from diastolic periods (where no murmurs are expected).

2.2. The surrogates

The construction of the surrogates builds on the fact that the characteristics of a stationary linear Gaussian process is fully describe by its power spectrum [8,9]. The surrogates were generated to represent a stationary linear Gaussian process with the same properties of the amplitude spectrum as the murmurs. This was obtained by Fourier transforming the murmurs, subsequently randomizing the phase of the spectrum, and finally, inverse Fourier transforming the result. Consequently, if the murmurs can be fully described by the power spectrum, then the surrogates and the murmurs are realizations of the same process.

2.3. Phase space representation

According to the Takens embedding [10] term, the phase space of a multi dimensional dynamic system may be reconstructed from single-dimension time series using the delay method, where each point in the reconstructed phase space consists of a vector of m signal points, sampled from the signal at intervals τ:

$$X_i = [x(t_i), x(t_{i+\tau}), \dots . x(t_{i+(m-1)\tau})]^T \qquad (1)$$

To fully represent the dynamic system, the embedding dimension, m, and embedding delay, τ, must be estimated from the data or from prior knowledge of the system. In the current study both approaches were examined. Sample entropy was calculated with recording specific embedding parameters, using the method of mutual information for τ [11] and the modified false nearest neighbors method for m [12].

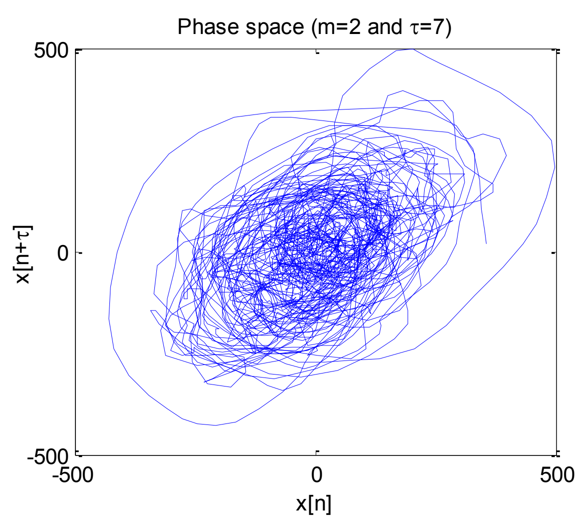

Figure 2. Two-dimensional phase space representation of murmurs from recording 2.

The mean embedding dimension was m=9.1 and the mean embedding lag was τ=7.4. In addition sample entropy was calculated using fixed embedding values at *m=2* and τ=7.

To compensate for the short duration of the murmur segments, a phase space was constructed by collecting the embedding matrices from each cycle into one embedding matrix, thereby constructing one phase space including all heart cycles from the current recording. The rationale was that each heart cycle is a realization of the same process.

2.4. Sample Entropy

Sample entropy is the negative logarithm of the conditional probability that a point which repeats itself within a tolerance of ϵ in an *m* dimensional phase space will repeat itself in an *m+1* dimensional phase space.

$$SampEn(m,\epsilon) = -\log\left(\frac{C(m+1,\epsilon)}{C(m,\epsilon)}\right) \quad (2)$$

C(*m*, ϵ) is number of repeating points in the *m* dimensional phase space. Repeating was defined as points closer in a Euclidean sense than ϵ to the examined point. The allowed tolerance ϵ was 0.6 and 0.2 times the standard deviation of the signal for recording specific embedding parameters and fixed embedding parameters respectively.

2.5. Statistics

To avoid assumptions about the sample entropy distribution, the non-parametric rank-order test was used as statistical test between the surrogates and the recordings [9]. 199 surrogates were generated to each recording and sample entropy was calculated from each. Consequently, the rank of sample entropy from the recording must be lower than 6 or higher than 195 to reject the null hypothesis.
The comparison between sample entropy in silent periods and sample entropy in murmur periods was evaluated using a Mann–Whitney U test ($\alpha = 0.05$ significance level). To evaluate if nonlinearity influenced the difference between silent periods and murmur periods a Mann–Whitney U test was applied to compare the difference between the surrogates simulating periods with and without murmurs with the difference between real periods with and without murmurs. In addition, the correlation coefficient (r) between the median sample entropy from surrogates and sample entropy from recordings was estimated.

Table 1. Sample entropy from recordings and their ranks within the set of surrogates. The 95% ranks were 6-195.

Rec. Nr.	**Sample entropy**		**Sample entropy (m=2 and τ=7)**	
	Value	Rank	Value	Rank
1	0.645	49	1.800	147
2	0.637	10	1.956	35
3	0.848	106	2.020	172
4	0.747	129	1.931	125
5	0.861	124	2.076	80
6	0.821	130	2.014	33
7	0.901	113	2.032	124
Average	0.780	94.4	1.975	102.3

3. Results

Table 1 shows the sample entropy from the seven recordings calculated with either recording specific embedding parameters or with fixed embedding parameters. Moreover, their ranks within the Sample entropies of 199 surrogates are shown. None of the values ranks outside the interval 6 to 195 that is required for rejection of the null hypothesis that the murmurs are from a stationary Gaussian linear process.
In all recordings, sample entropy in murmur periods was had higher values than sample entropy in silent periods, see table 2. This increase in Sample Entropy was significant ($p<0.05$). The mean difference between silent

Table 2. Sample entropy in murmur periods versus silent periods

Rec. Nr.	**Murmur periods** Sample entropy (*m*=2, τ =7)	Rank	Median surrogate value	**Silent periods** Sample entropy (*m*=2, τ =7)	Rank	Median surrogate value
1	1.800	147	1.765	1.796	45	1.828
2	1.956	35	1.974	1.807	65	1.820
3	2.020	172	1.982	1.771	10	1.838
4	1.931	125	1.923	1.766	1	1.845
5	2.076	80	2.082	1.755	92	1.758
6	2.014	33	2.039	1.703	11	1.774
7	2.032	124	2.020	1.748	163	1.708
Average	1.975	102.3	1.969	1.764	55.3	1.796

periods and murmurs periods was 0.21 (95% CI: 0.11 - 0.32). The difference between median values of surrogates from murmur periods and median value of surrogates from silent periods was 0.17 (CI: 0.044 - 0.30). According to the Mann–Whitney U this increase in sample entropy from the surrogates was not significantly different from the increase in sample entropy from the recordings. The correlation coefficient between sample entropy from recordings and from the medians of the surrogates was r=0.952 (95% CI: 0.851 - 0.985) confirming a high degree of similarity between recordings and surrogates.

4. Discussion and conclusions

The sample entropy from murmurs was significantly higher than the sample entropy from the silent periods, which confirmings that sample entropy is suited for quantification or identification of cardiovascular murmurs. But similar differences were found between surrogate Sample Entropies from murmurs and silent periods, which in combination with the relative strong correlation between sample entropy from surrogates and recordings suggests that the sample entropy was not significantly influenced by nonlinear or chaotic components in the cardiovascular murmurs. Therefore, the changes observed in sample entropy under the presence of cardiovascular murmurs are due to changes in linear characteristics of the sounds. This is also fully reflected in the system's autocorrelation and power spectrum. Still, sample entropy can be useful as analytic feature in the analysis of cardiovascular murmurs, but it might not reveal any information which is not present in regular power spectrum. For instance, the degree of randomness of a linear random process is readable from the sharpness/flatness of the power spectrum.

Acknowledgements

This study was performed within the acoustic heart patch project, granted by the Danish National Advanced Technology Foundation and Coloplast A/S.

References

[1] Watrous RL. Computer-aided auscultation of the heart: From anatomy and physiology to diagnostic decision support. Proceedings of the 28th Annual International Conference of the IEEE Engineering in Medicine and Biology Society: IEEE, 2006.

[2] Delgado-Trejos E et. Al. Digital auscultation analysis for heart murmur detection. Annals of Biomedical Engineering 2009;37:337-53.

[3] Ruelle D, Takens F. On the nature of turbulence. Communications in Mathematical Physics 1971;23:343-4.

[4] Li BB, Yuan ZF. Non-linear and chaos characteristics of heart sound time series. Proceedings of the Institution of Mechanical Engineers. Part H, Journal of engineering in medicine 2008;222:265-72.

[5] Taplidou SA and Hadjileontiadis LJ. Nonlinear analysis of heart murmurs using wavelet-based higher-order spectral parameters. Proceedings of the 28th Annual International Conference of the IEEE Engineering in Medicine and Biology: IEEE; 2006.

[6] Ahlstrom Ast C, Hoglund K, Hult P, Haggstrom J, Kvart C, Ask P. Assessing aortic stenosis using sample entropy of the phonocardiographic signal in dogs. IEEE Trans.Biomed.Eng. 2008;55:2107-9.

[7] Polak JF. Carotid ultrasound. Radiologic clinics of North America. 2001;39:569-589.

[8] Oppenheim AV, Schafer RW. Discrete-Time Signal Processing 2nd Edition. Upper Saddle River: Prentice-Hall, 1999;730-1

[9] Schreiber T, Schmitz A. Surrogate time series. Physica D: Nonlinear Phenomena 2000;142:346-82.

[10] Takens F. Detecting strange attractors in turbulence. Lecture Notes in Mathematics 1981;898:366-81.

[11] Fraser AM, Swinney HL. Independent coordinates for strange attractors from mutual information. Phys.Rev.A 1986;33:1134.

[12] Cao L. Practical method for determining the minimum embedding dimension of a scalar time series. Physica D 1997;110:43-50.

Address for correspondence:
Samuel Emil Schmidt
Frederik Bajers vej 7, E1-209
9220 Aalborg Ø
sschmidt@hst.aau.dk