34th Annual International Conference of the IEEE EMBS
San Diego, California USA, 28 August - 1 September, 2012

Instantaneous Estimation of High-Order Nonlinear Heartbeat Dynamics by Lyapunov Exponents

Luca Citi⋆, *Member, IEEE*, Gaetano Valenza⋆ and Riccardo Barbieri, *Senior Member, IEEE*

Abstract— **This paper introduces a novel methodology able to provide time varying estimates of the Lyapunov Spectrum within a point process framework. The algorithm is applied to ECG-derived data to characterize heartbeat nonlinear dynamics by using a cubic autoregressive point process model. Estimation of the model parameters is ensured by the Laguerre expansion of the Wiener-Volterra kernels along with a maximum local log-likelihood procedure. In addition to the instantaneous Lyapunov exponents, as well as indices related to higher order dynamic polyspectra, our method is also able to provide all the instantaneous time domain and frequency domain measures of instantaneous heart rate (HR) and heart rate variability (HRV) previously considered. Experimental results show that our method is able to track complex cardiovascular control dynamics during fast transitional gravitational changes.**

I. Introduction

Physiological systems are often considered having nonlinear behavior. Due to the complexity of the sinus node activity modulation mechanisms, the study of heartbeat variations has been regarded by many scientists as highly suitable for application of computational nonlinear techniques. It has been shown that the electrical properties of the human heart undergo many complex transitions as important quantifiers of complexity of cardiovascular control in normal and diseased states [1]–[3]. Heart rate variability (HRV) has been the subject of intense investigation using a wide range of methodologies including time-domain, frequency-domain, geometric, and nonlinear methods (see [4], [5] for reviews). The Lyapunov exponents (LEs) [6] have been particularly proven to be a useful tool for the characterization of complex dynamics in a nonlinear system. They were first defined by Lyapunov [6] in order to study the stability of nonstationary solutions of ordinary differential equations (ODEs), and for more than fifty years they have been extensively studied in many other disciplines. Specifically, they refer to the average exponential rates of divergence or convergence of neighboring trajectories in phase space. In a stable deterministic nonlinear system with no stochastic inputs, a positive LE reflects sensitive dependence to initial conditions and can be taken as a definition of a chaotic system [7]. Nevertheless, a small amount of noise in a limit cycle oscillation could yield a positive LE if the trajectory has regions with large slopes. To this extent, we prefer not to address the issue related on the chaotic behavior of HRV, and rather follow the approach suggested by Chon et al. [8] and, later, by Armoundas et al. [9], suggesting that physiological control systems such as cardiovascular regulation are neither purely chaotic nor stochastic, but rather both. This concept is in agreement with current physiological knowledge, since the normal HRV is the output of a nonlinear deterministic system (the pacemaker cells of sinus node) being forced by a high-dimensional input (the activity in the nerves innervating the sinus node). Recently, point process theory has been used for modeling human heartbeats [10]–[14]. The point process framework primarily defines the probability of having a heartbeat event at each moment in time. A parametric formulation of the probability function allows for a systematic, parsimonious estimation of the parameter vector in a recursive way and at any desired time resolution. Instantaneous indices can then be derived from the parameters in order to quantify important features as related to cardiovascular control dynamics. In this work, we applied this approach to estimate the instantaneous values of the LEs by fitting the model to the observed data and applying the Fast Orthogonal Search (FOS) algorithm [15] followed by an estimation of the LEs. In order to retain most of the past information during LEs tracking, we have expanded the NAR kernels with the Laguerre functions [16] to devise a novel nonlinear autoregressive Laguerre (NARL) model. This method reduces the number of unknown parameters that need be estimated and ensures a good estimation even with short tracking time windows.

Manuscript received March 29, 2012. This research was supported in part by NIH Grant R01-HL084502.

L. Citi, G. Valenza and R. Barbieri are with the Neuroscience Statistics Research Laboratory, Harvard Medical School, Massachusetts General Hospital, Boston, MA 02114 USA, and also with the Massachusetts Institute of Technology, Cambridge, MA 02139 USA (e-mail: {lciti,barbieri}@neurostat.mit.edu).

G. Valenza is also with the Interdepartmental Research Center E. Piaggio and also with the Department of Information Engineering, University of Pisa, Pisa, Italy (e-mail: g.valenza@ieee.org).

⋆L. Citi and G. Valenza equally contributed to this work.

II. The Heartbeat Interval Point-Process Nonlinear Model

Let us consider the Taylor expansion of a Nonlinear Autoregressive Model (NAR):

$$y(n) = \gamma_0 + \sum_{i=1}^{M} \gamma_1(i)\, y(n-i) + \sum_{K=1}^{\infty} \sum_{i_1=1}^{M} \cdots \sum_{i_K=1}^{M} \gamma_K(i_1,\ldots,i_K) \prod_{j=1}^{K} y(n-i_j) + \epsilon(n)\ . \quad (1)$$

where $\epsilon(n)$ are independent, identically distributed Gaussian random variables. We represent the nonlinear physiological system by taking into account up to the cubic nonlinear term, i.e. γ_0, $\gamma_1(i)$, $\gamma_2(i,j)$, and $\gamma_3(i,j,k)$ where the quadratic and the cubic kernels are assumed to be permutation invariant. This choice of a third order NAR system retains an important part of the non-linearity of the system and gives robustness against the presence of measurement noise in the data [8].

We use this framework to model the derivative RR series. Let $(0,T]$ denote the observation interval and $0 \leq u_1 < \cdots < u_k < u_{k+1} < \cdots < u_K \leq T$ the times of the events, in our case R peaks detected from the ECG. For $t \in (0,T]$, let $N(t) = \max\{k : u_k \leq t\}$ be the sample path of the associated counting process. Let define also a left continuous function $\widetilde{N}(t) = \lim_{\tau \to t^-} N(\tau) = \max\{k : u_k < t\}$. Let $\mathrm{RR}_j = u_j - u_{j-1} > 0$ denote the j^{th} R–R interval, or equivalently, the waiting time until the next R-wave event. This allows us to write the instantaneous mean RR as:

$$\mu_{\mathrm{RR}}(t, \mathcal{H}_t, \xi(t)) = \mathrm{RR}_{\widetilde{N}(t)-1} + \gamma_0 + \sum_{i=1}^{M} \gamma_1(i,t)\, \Delta\mathrm{RR}_i + \sum_{i=1}^{M}\sum_{j=1}^{M} \gamma_2(i,j,t)\, \Delta\mathrm{RR}_i\, \Delta\mathrm{RR}_j + \sum_{i=1}^{M}\sum_{j=1}^{M}\sum_{k=1}^{M} \gamma_3(i,j,k,t)\, \Delta\mathrm{RR}_i\, \Delta\mathrm{RR}_j \Delta\mathrm{RR}_k + \epsilon(t) \quad (2)$$

where $\Delta\mathrm{RR}_h = (\mathrm{RR}_{\widetilde{N}(t)-h} - \mathrm{RR}_{\widetilde{N}(t)-h-1})$. The choice of the derivative series improves the achievement of stationarity within the sliding time window W (in this work we have chosen $W = 90$ sec.) [17].

We used the Laguerre functions [16] to expand the kernels and reduce the number of unknown parameters in (2) that need be estimated. The j^{th}-order discrete time orthonormal Laguerre function is defined as follows:

$$\phi_j(n) = \alpha^{\frac{n-j}{2}}(1-\alpha)^{\frac{1}{2}} \sum_{i=0}^{j} (-1)^i \binom{n}{i}\binom{j}{i} \alpha^{j-i}(1-\alpha)^i,$$

where α is the discrete-time Laguerre parameter ($0 < \alpha < 1$) which determines the rate of exponential asymptotic decline of these functions, and $n \geq 0$. Thus, given the Laguerre function, $\phi_j(n)$, and the input signal, $\mathrm{RR}_{\widetilde{N}(t)}$, the i^{th}-order Laguerre filter output is:

$$l_i(t) = \sum_{n=1}^{\widetilde{N}(t)} \phi_i(n)(\mathrm{RR}_{\widetilde{N}(t)-n} - \mathrm{RR}_{\widetilde{N}(t)-n-1}) \quad (3)$$

The nonlinear Autoregressive Laguerre (NARL) model is devised by using the Laguerre expansion of the kernels, defining the instantaneous RR mean as:

$$\mu_{\mathrm{RR}}(t, \mathcal{H}_t, \xi(t)) = g_0(t) + \sum_{i=0}^{P} g_1(i,t)\, l_i(t) + \sum_{i=0}^{Q}\sum_{j=0}^{Q} g_2(i,j,t)\, l_i(t)\, l_j(t) + \sum_{i=0}^{K}\sum_{j=0}^{K}\sum_{k=0}^{K} g_3(i,j,k,t)\, l_i(t)\, l_j(t) l_k(t) \ . \quad (4)$$

After fitting the NARL model, the corresponding NAR representation can be found substituting (3) in (4).

Assuming history dependence, the probability distribution of the waiting time $t - u_j$ until the next R-wave event follows an inverse Gaussian model:

$$f(t|\mathcal{H}_t, \xi(t)) = \left[\frac{\xi_0(t)}{2\pi(t-u_j)^3}\right]^{\frac{1}{2}} \times \exp\left\{-\frac{1}{2}\frac{\xi_0(t)[t-u_j-\mu_{\mathrm{RR}}(t,\mathcal{H}_t,\xi(t))]^2}{\mu_{\mathrm{RR}}(t,\mathcal{H}_t,\xi(t))^2(t-u_j)}\right\} \quad (5)$$

where $j = \widetilde{N}(t)$ is the index of the previous R-wave event occurred before time t, $\mathcal{H}_t = (u_j, \mathrm{RR}_j, \mathrm{RR}_{j-1}, ..., \mathrm{RR}_{j-M+1})$, $\xi(t)$ is the vector of the time-varing parameters, $\mu_{\mathrm{RR}}(t, \mathcal{H}_t, \xi(t))$ represents the first-moment statistic (mean) of the distribution, and $\xi_0(t) = \theta > 0$ denotes the shape parameter of the inverse Gaussian distribution. By definition, $f(t|\mathcal{H}_t, \xi(t))$ is characterized at each moment in time, at the beat as well as in-between beats. The use of an inverse Gaussian distribution to characterize the RR intervals occurrences is motivated both physiologically (the integrate-and-fire initiating the cardiac contraction [11]) and by goodness-of-fit comparisons [12]. Given the proposed parametric model, the nonlinear indices of the HR and HRV will be defined as a time-varying function of the parameters $\xi(t) = [\theta(t), g_0(t), g_1(0,t), ..., g_1(P,t), g_2(0,0,t), ..., g_2(Q,Q,t), g_3(0,0,0,t), ..., g_3(K,K,K,t)]$. Concerning the parameter estimation, a local maximum likelihood method [11] using a sliding window of duration W is used to estimate the unknown time-varying parameter set $\xi(t)$. The proper order $\{P, Q, K\}$ for the proposed NARL model was determined according to the Akaike Information Criterion (AIC) by fitting a subset of the data using a local likelihood method [11], [18]. The goodness-of-fit of the point process model is based on the KS test [11], [19]. Autocorrelation plots are also considered to test the independence of the model-transformed intervals [11].

III. Lyapunov Exponents Estimation

The Lyapunov exponent of a real valued function $f(t)$ defined for $t > 0$ is defined as:

$$\lambda = \limsup_{t \to \infty} \frac{1}{t} \log(|f(t)|) \quad (6)$$

More specifically, let us consider a n-dimensional linear system in the form $y_i = Y(t)p_i$, where $Y(t)$ is a fundamental solution matrix with $Y(0)$ orthogonal, and $\{p_i\}$ is an orthonormal basis of $\mathbb{R}^n$. Then, the corresponding λ_i are straightforward defined. When the sum of the λ_i is minimized, the orthonormal basis $\{p_i\}$ is called "normal" and the λ_i are called the Lyapunov exponents [20]. One of the key theoretical tools for determining Lyapunov exponents is the continuous QR factorization of $Y(t)$ [21], [22]:

$$Y(t) = Q(t)R(t) \quad (7)$$

where $Q(t)$ is orthogonal and $R(t)$ is upper triangular with positive diagonal elements R_{ii}, $1 \leq i \leq n$, leading to an easier formulation of the LEs, i.e. [20]–[22]:

$$\lambda_i = \lim_{t\to\infty} \frac{1}{t} \log \|Y(t)p_i\|$$
$$= \lim_{t\to\infty} \frac{1}{t} \log \|R(t)p_i\| = \lim_{t\to\infty} \frac{1}{t} \log \|R_{ii}(t)\| \,. \quad (8)$$

The NAR model (2) can be rewritten in an M-dimensional state space canonical representation:

$$\begin{aligned} r_n^{(1)} &= r_{n-1}^{(2)} \\ \vdots \;&\vdots\; \vdots \\ r_n^{(M-1)} &= r_{n-1}^{(M)} \\ r_n^{(M)} &= F\left(r_{n-1}^{(M)}, r_{n-1}^{(M-1)}, \cdots, r_{n-1}^{(2)}, r_{n-1}^{(1)}\right) \end{aligned}$$

where $F(\cdot)$ directly arises from (2). The matrix $Y(t)$ in (7) corresponds to the Jacobian of this system [9]:

$$J(n) = \begin{pmatrix} 0 & 1 & 0 & 0 & \cdots & 0 \\ 0 & 0 & 1 & 0 & \cdots & 0 \\ 0 & 0 & 0 & 1 & \cdots & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & 0 & 0 & \cdots & 1 \\ \frac{\partial F}{\partial r^{(1)}} & \frac{\partial F}{\partial r^{(2)}} & \frac{\partial F}{\partial r^{(3)}} & \frac{\partial F}{\partial r^{(4)}} & \cdots & \frac{\partial F}{\partial r^{(M)}} \end{pmatrix}.$$

As described above, by evaluating the Jacobian over the time series, it is possible to determine the LE by means of the QR decomposition:

$$\begin{aligned} J(1)\, Q_{(0)} &= Q_{(1)}\, R_{(1)} \\ J(2)\, Q_{(1)} &= Q_{(2)}\, R_{(2)} \\ &\cdots \\ J(n)\, Q_{(n-1)} &= Q_{(n)}\, R_{(n)} \\ &\cdots \end{aligned}$$

This decomposition is unique except in the case of zero diagonal elements. Then the LE exponents λ_i are given by

$$\lambda_i = \frac{1}{\tau H} \sum_{j=0}^{H-1} \ln R_{(j)ii} \quad (9)$$

where H is the available number of matrices within the local likelihood window of duration W, and τ the sampling time step. The estimation of the LEs is performed at each time t from the corresponding time-varying vector of parameters, $\xi(t)$. This provides us with a time-varying vector, $\lambda_i(t)$, able to track the Lyapunov spectrum in continuous time. We set forth the first LE, $\lambda_1(t)$, as the instantaneous dominant Lyapunov exponent (IDLE).

IV. Experimental Results

In order to validate the proposed algorithms' performance on real physiological dynamics, we have considered an experimental RR datasets which was fully described in [11]. Physiological variables were recorded from 10 healthy subjects whose cardiovascular and autonomic regulation were studied using a tilt-table protocol. Subjects were first placed horizontally in a supine position, with restraints used to secure them at the waist, arms, and hands. Then, they were tilted from the horizontal to the vertical position and returned to the horizontal position. Each subject performed six tilt sessions remaining in each tilt state for 3 min. The protocol lasted 55–75 min (3300–4500 s). A single-lead ECG was continuously recorded for each subject during the study, and the RR intervals were extracted using a curve length-based QRS detection algorithm [23]. The nonlinearity test [24] applied to the RR series showed that the level of nonlinearity of the considered RR intervals is significant for all but one of the considered subjects (see Table I). The performance of the proposed NARL model was measured by the KS distance: the smaller the KS distance, the better the model fit. It can be observed that the NARL always shows a good model fit, with a KS distance smaller than 0.06 in all cases. A representative IDLE identification is shown in Fig. 1. The relative KS plots and the autocorrelation function of the residuals are also reported in Fig. 2 As shown in the representative case (Fig. 1), after a 30s transient dynamic the IDLE sharply decreases to negative values (<-0.1) and stabilizes at around -0.1 along the sympathetic driven compensatory action to the gravitational stimulus. The significant decrease of the IDLE to negative values is confirmed by group statistics, as indicated by the time-varying average in the right panel of Fig.1. Statistical analysis by means of the non-parametric rank-sum test confirms a significative difference between the 'rest' and the 'fast-tilt' epochs ($p < 0.001$).

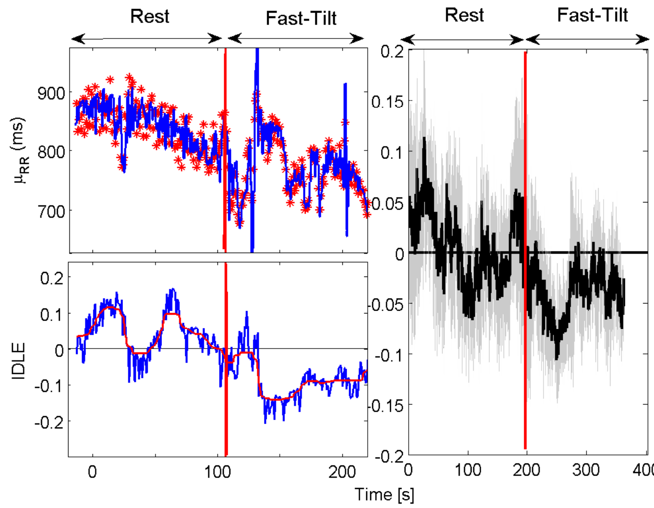

Fig. 1. (Left) Instantaneous heartbeat statistics computed from a representative subject using the cubic NARL model. On the top panel, the estimated $\mu_{\mathrm{RR}}(t)$ is superimposed on the recorded RR series. On the bottom panel, the corresponding IDLE dynamics are reported. (Right) IDLE dynamics averaged for all 10 subjects. The vertical red line indicates the transition from the supine to the upright position.

V. Discussion and Conclusion

We present a novel methodology for the characterization of heartbeat nonlinear dynamics by means of continuous

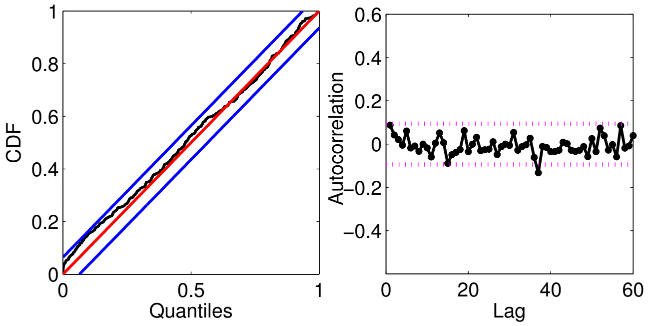

Fig. 2. KS plot (Left) and Autocorrelation plot (Right) of the NARL model computed for one representative subjects (subject 1). The dashed lines in all plots indicate the 95% confidence bounds

TABLE I

MEAN AND SD OF DLE FOR THE FAST TILT-TABLE EXPERIMENTAL DATASET.

Subject	P-Value	KS dist.	Rest	Tilt
1	0.032	0.0458	0.0518 ± 0.0227	-0.1165 ± 0.0326
2	0.034	0.0603	0.2226 ± 0.0988	0.0075 ± 0.0515
3	$< 1e^{-8}$	0.0355	-0.0222 ± 0.0662	-0.0313 ± 0.0574
4	0.030	0.0227	0.0649 ± 0.0785	0.0084 ± 0.0365
5	0.022	0.0451	-0.0137 ± 0.0595	-0.0388 ± 0.0226
6	0.002	0.0409	-0.0007 ± 0.0786	-0.0362 ± 0.0303
7	0.002	0.0458	0.0969 ± 0.0406	-0.0258 ± 0.1049
8	0.076	0.0408	0.0093 + 0.0518	-0.0612 + 0.0375
9	$< 1e^{-6}$	0.0571	0.0058 + 0.0394	-0.0042 + 0.0145
10	$< 1e^{-8}$	0.0572	0.2662 + 0.1708	0.0384 + 0.1653

P-values are obtained from the nonlinearity test.

estimation of the Lyapunov Spectrum within a point process paradigm. The use of the discrete Laguerre expansions of a cubic autoregressive Wiener-Volterra model gives several advantages, such as long-term memory, lower number of parameters, and improved goodness of fit. Once the model parameters are estimated by means of a maximum log-likelihood procedure, the LE is computed by means of the QR factorization. In this work we focus on the instantaneous dominant Lyapunov exponent (IDLE). Our experimental results demonstrate that the proposed point process model is able to clearly follow the transient dynamics and to characterize the time-varying inherent nonlinearity of the system. In all the subjects, in fact, we found a significant reduction of the IDLE index after tilt. Accordingly, the inference performed on the entire population showed prominent significance. This outcome is in agreement with previous findings that point at a remarkable presence of complex nonlinear heartbeat dynamics during rest states, amplified under vagal predominance and buffered after sympathetic-driven shifts. Given these findings and the strong mathematical foundation of our model, future works are aimed at further testing our novel measures on a wide range of experimental settings and at better understanding the physiological interpretation of our instantaneous nonlinear assessment.

ACKNOWLEDGMENT

We are grateful to Roger G. Mark and Thomas Heldt (Harvard-MIT Division of Health Sciences and Technology) for kindly providing the tilt-table data analyzed in this study.

REFERENCES

[1] "Special issues on nonlinearity on heart rate," *Chaos*, vol. 19, 2009.

[2] C. Poon and C. Merrill, "Decrease of cardiac chaos in congestive heart failure," *Nature*, vol. 389, no. 6650, pp. 492–495, 1997.

[3] L. Glass, "Dynamics of cardiac arrhythmias," *Physics Today*, vol. 49, p. 40, 1996.

[4] E. T. F. of the European Society of Cardiology the North American Society of Pacing, "Heart rate variability : Standards of measurement, physiological interpretation, and clinical use," *Circulation*, vol. 93, no. 5, pp. 1043–1065, 1996.

[5] U. Rajendra Acharya, K. Paul Joseph, N. Kannathal, C. Lim, and J. Suri, "Heart rate variability: a review," *Medical and Biological Engineering and Computing*, vol. 44, no. 12, pp. 1031–1051, 2006.

[6] A. Lyapunov, "Problem general de la stabilite du mouvement," *Ann. Math. Stud*, vol. 17, 1949.

[7] D. Ruelle, "Where can one hope to profitably apply the ideas of chaos?" *Physics Today*, vol. 47, p. 24, 1994.

[8] K. Chon, J. Kanters, R. Cohen, and N. Holstein-Rathlou, "Detection of chaotic determinism in time series from randomly forced maps," *Physica D: Nonlinear Phenomena*, vol. 99, no. 4, pp. 471–486, 1997.

[9] A. Armoundas, K. Ju, N. Iyengar, J. Kanters, P. Saul, R. Cohen, and K. Chon, "A stochastic nonlinear autoregressive algorithm reflects nonlinear dynamics of heart-rate fluctuations," *Annals of biomedical engineering*, vol. 30, no. 2, pp. 192–201, 2002.

[10] R. Barbieri and E. Brown, "Analysis of heartbeat dynamics by point process adaptive filtering," *Biomedical Engineering, IEEE Transactions on*, vol. 53, no. 1, pp. 4–12, 2006.

[11] R. Barbieri, E. Matten, A. Alabi, and E. Brown, "A point-process model of human heartbeat intervals: new definitions of heart rate and heart rate variability," *American Journal of Physiology-Heart and Circulatory Physiology*, vol. 288, no. 1, p. H424, 2005.

[12] Z. Chen, E. Brown, and R. Barbieri, "Assessment of autonomic control and respiratory sinus arrhythmia using point process models of human heart beat dynamics," *Biomedical Engineering, IEEE Transactions on*, vol. 56, no. 7, pp. 1791–1802, 2009.

[13] ——, "Characterizing nonlinear heartbeat dynamics within a point process framework," *Biomedical Engineering, IEEE Transactions on*, vol. 57, no. 6, pp. 1335–1347, 2010.

[14] Z. Chen, P. Purdon, G. Harrell, E. Pierce, J. Walsh, E. Brown, and R. Barbieri, "Dynamic assessment of baroreflex control of heart rate during induction of propofol anesthesia using a point process method," *Annals of biomedical engineering*, pp. 1–17, 2011.

[15] M. Korenberg, "A robust orthogonal algorithm for system identification and time-series analysis," *Biological Cybernetics*, vol. 60, no. 4, pp. 267–276, 1989.

[16] V. Marmarelis, "Identification of nonlinear biological system using laguerre expansions of kernels," *Ann. Biomed. Eng.*, vol. 21, pp. 573–589, 1993.

[17] C. Granger and R. Joyeux, "An introduction to long-memory time series models and fractional differencing," *Journal of time series analysis*, vol. 1, no. 1, pp. 15–29, 1980.

[18] C. Loader, *Local regression and likelihood*. Springer Verlag, 1999.

[19] E. Brown, R. Barbieri, U. Eden, and L. Frank, "Likelihood methods for neural spike train data analysis," *Computational neuroscience: A comprehensive approach*, pp. 253–286, 2003.

[20] L. Dieci, R. Russell, and E. Van Vleck, "On the computation of lyapunov exponents for continuous dynamical systems," *SIAM journal on numerical analysis*, pp. 402–423, 1997.

[21] J. Holzfuss and U. Parlitz, "Lyapunov exponents from time series," *Lyapunov Exponents*, pp. 263–270, 1991.

[22] K. Geist, U. Parlitz, and W. Lauterborn, "Comparison of different methods for computing lyapunov exponents," *Prog. Theor. Phys*, vol. 83, no. 5, pp. 875–893, 1990.

[23] W. Zong and G. Moody, "Wqrs-single-channel qrs detector based on length transform," *Physionet. http://www.physionet.org/physiotools/wag/wqrs-1.htm*, 2003.

[24] A. Barnett and R. Wolff, "A time-domain test for some types of nonlinearity," *Signal Processing, IEEE Transactions on*, vol. 53, no. 1, pp. 26–33, 2005.