Available online at www.sciencedirect.com
SCIENCE DIRECT®
Journal of Theoretical Biology 232 (2005) 545–549
Journal of Theoretical Biology
www.elsevier.com/locate/yjtbi

Nonlinear modeling of the atrioventricular node physiology in atrial fibrillation

Armin Rashidi*,[1], Iman Khodarahmi

Tehran University Medical School, Tehran, Iran

Received 15 January 2004; received in revised form 26 July 2004; accepted 31 August 2004

Abstract

A nonlinear model of the atrioventricular (AV) node physiology in atrial fibrillation (AF) is proposed based on three assumptions: (1) normal distribution of atrial impulses, (2) right-skewed distribution of R–R intervals, (3) increase in the refractory period of the AV node due to rapid bombardment from the atria. Simulation resulted in the following conclusions, all of which are in agreement with previous experience: (1) the entry speed of atrial impulses into the AV node in AF is inversely proportional to the ventricular rate, (2) the autocorrelation function of R–R intervals is zero at all delays, (3) a newly introduced index, sign of first difference, has a negative autocorrelation function at the first delay and zero ones at all others. In spite of its simplicity, the model is able to explain what happens in atrial premature complexes, sinus tachycardia and sinus bradycardia. Different rhythms, some of which rarely seen clinically, can be reproduced by changing input patterns or by slightly manipulating the model parameters. In order to make possible a long irregular time series of R–R interval, aperiodic changes in atrial signals are shown to be necessary. In conclusion, we proposed a simple model for the AV node physiology capable of explaining the previously known facts about AF as well as predicting interesting properties of some other supraventricular arrhythmias.

Keywords: Logistic; R–R interval; Right-skewed; Time series; Autocorrelation

1. Introduction

Atrial fibrillation (AF) is a supraventricular arrhythmia, famous for its electrocardiographic markings of P-wave loss and R–R irregularity. Clinically, the patient with AF has an irregular pulse. The current belief about the pathophysiology of the disease is that many sites in the atria (instead of the single sinus node in the normal heart) set the atrial rhythm, but to a very rapid irregular pattern. Because of the atrioventricular (AV) node refractory period, these signals are filtered so that only those reaching the node after the refractory period will pass to the ventricles. Lack of a single atrial contraction is responsible for P-wave loss, while irregularly filtered atrial signals make R–R intervals irregular (Josephson and Zimetbaum, 2001). Spatial mapping of atrial signal production as well as properties of R–R intervals have been studied extensively (Kadish et al., 1999; Luo et al., 2003; Stein et al., 1999). However, little work has been done on the AV node, itself (Billette et al., 1975; Hashida et al., 1978).

How does the AV node filter the signals? The AV node is a network of interconnected differentiated cardiac muscle fibers with similar electrical properties. So, modeling the entire network as a single unit makes it easier to study the behavior of the AV node. Both linear and nonlinear modeling of the AV node has been attempted. The stochastic differential equations approach is an interesting example (Zeng and Glass, 1996).

Based on two previous studies (Hashida et al., 1978; Hashida and Tasaki, 1984), R–R intervals have a

*Corresponding author. No.12, Aramesh Alley, Mellat Park, Tehran, Iran. Tel.: +98 21 2042595.
E-mail address: rasidiarmin@yahoo.com (A. Rashidi).
[1]Alternate address: 4607 Fairfield Drive, Corona Delmar, Zip code 92625, USA.

0022-5193/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jtbi.2004.08.033

unimodal right-skewed histogram and the autocorrelation function of the corresponding time series is zero at all delays. Also, the refractory period of the AV node is believed to increase by rapid entry of atrial signals to the node. During this period, no signals can pass to the ventricles (if the atrial rate is sufficiently rapid, i.e. when the interatrial interval is less than 0.25) (Ross, 1990). With the assumption that atrial signals come independently from a common normal distribution (Zeng and Glass, 1996), we will try to develop a nonlinear model for the AV node, which is in agreement with our aforementioned knowledge about AF. Moreover, we will look for the abilities of the model to provide additional information about some other cardiac problems.

2. Materials and methods

Fig. 1 is the start point of our study.

Based on clinical evidence, the atrial rate in AF ranges from 300 to about 600 beats/min, so the interval between two successive atrial signals ranges from 0.1 to 0.2 s. A normal random number generator with a mean of 0.15 and a standard deviation of 0.0165 is all we need for this purpose. As seen in Fig. 1 which is the histogram of 1742 successive R–R intervals during AF, the model for the AV node is expected to convert the simulated atrial dataset to a smaller set (because of conduction blocks) of data within the range of 0.3–0.9 with a mean of about 0.45 to 0.5 and a standard deviation of about 0.1.

The main part of the model deals with the AV node. Suppose x_n stands for the interval between the nth atrial signal and the last signal conducted before it. Also, let t_n be the refractory period after the effect of the $(n-1)$th atrial signal on the AV node. Furthermore, suppose that the refractory period is limited to the range 0.3–0.9, which is reasonable considering the saturability of ionic channels. Now, if $x_{n-1} \geqslant t_{n-1}$, then the $(n-1)$th signal will pass and t_n will be set to 0.3. Otherwise, the signal is blocked and t_{n-1} will rise to t_n. This rise has been suggested previously (Ross, 1990), but to date, no serious attempt has been made to model it with an appropriate function.

Consider the logistic function

$$u_n = 1/1 + \exp(-k(z_n - q)),$$

where k and q are constants we will find by simulation and

$$z_n = (t_n - x_n)/t_n.$$

Then, we will calculate t_{n+1} by

$$t_n + 1 = t_n + u_n(0.9 - t_n).$$

Apart from being smooth which makes unpredictable changes of u_n impossible, the logistic function introduces the upper bound 0.9 to the refractory period because u_n is always less than 1.

Therefore, each time a signal is blocked, the refractory period rises toward saturation. Small values of x_n increase the refractory period more than larger ones. Also, longer refractory periods are affected less than shorter ones. When a signal is conducted to the ventricles, an R-wave appears. In this way, we can calculate the R–R intervals. We rounded these intervals to two decimal degrees for simplicity.

Finally, we constructed the first difference time series for R–R intervals. 1 and −1 substituted nonnegative and negative numbers in the new series, respectively. We named the resulting time series the "sign of first difference" (SFD) series. Then we proceeded to calculate the autocorrelation functions of the SFD series.

We developed the appropriate simulation program and used Matlab 6.5.1 for computations. Minitab 13.32 calculated the autocorrelation functions and drew the histograms.

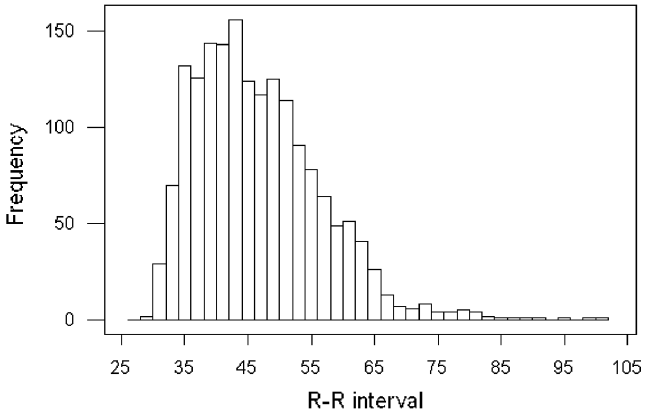

Fig. 1. Histogram of 1742 successive R–R intervals in a patient with AF.

3. Results

Five hundred atrial signals (with the properties mentioned earlier) were randomly generated and the R–R sequence was calculated with some initial values chosen for k and q and the assumption that $t_1 = 0.3$. Changing q and k shifts the diagram of the logistic function horizontally and manipulates the graph steepness around q, respectively. This way, we can determine how much the refractory period increases depending on its different points of collision with atrial signals. Fig. 2 shows the effects of changes in one variable while the other remains fixed.

By changing k and q, we obtained histograms of various shapes for R–R intervals. Unimodal, bimodal,