A CONTINUOUS-TIME MODEL OF THE RESPIRATORY SINUS AR-RHYTHMIA: SIMULATION AND PARAMETER IDENTIFICATION

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Abstract: Models of the heart rate variability (HRV), and particularly of the respiratory contribution, called respiratory sinus arrhythmia (RSA) are usually either built in the frequency domain or as a discrete-time dynamic system. Nevertheless, the underlying mechanisms and signals involved are continuous in time, for example changes in the membrane potentials of the pacemaker cells in the heart or the autonomic inputs to them. This work proposes a continuous time model for the simulation of the RSA, and also a framework for its identification from the observed signals. An Integral Pulse Frequency Modulation (IPFM) system generates the heart beat timing having as input the respiratory flow filtered by a first-order low-pass filter with DC gain G and cutoff frequency Ω_c. Filter parameters are estimated by least-squares linear regression from the observed flow and signals obtained by interpolating a function of the heart beat times. The DC gain was recovered by the model with an overestimated mean error of $26.1 \pm 22.2\%$; the cutoff frequency Ω_c with a underestimated mean error of $19.7 \pm 14.5\%$. The model was able to represent RSA characteristics, but further research is needed to implement this technique.

Keywords: Heart rate variability, respiratory sinus arrhythmia, modeling, continuous-time model, integral pulse frequency modulation.

Introduction

Models of the heart rate variability (HRV), understood as the time changes of the interbeat intervals (commonly denoted as RR, the intervals between consecutive R waves of the ECG), also called cardiac tachogram, have been shown to provide useful information about the physiological processes involved in the generation of heart rhythm, such as autonomic activity, imbalance and baroregulation. Particularly, the respiratory portion of the HRV, called respiratory sinus arrhythmia (RSA), have been shown to convey information about the status of the autonomic system, reflecting changes due to factors such as disease [1] and affective state [2].

It is usual to employ frequency domain representations, for example the power spectral density (PSD), obtained either from the Fourier transform or from dynamic models, for the description, classification and diagnosis of the HRV. However, it is also usual that these models are built on a discrete-time basis, in which an evenly sampled RR signal is interpolated from the original series at a low sampling rate, for instance 4 or 5 samples per second.

Some limitations arise from this discrete-time approach. First, the assumption that there is a subjacent RR signal that is unevenly sampled by the actual heart beats does not correspond to the anatomical and physiological findings. Also, the mechanisms underlying the heart timing – changes in the membrane potentials of the pacemaker cells and its modulators such as the sympathetic and parasympathetic inputs – are of continuous nature. On the other hand, discrete-time models, although descriptive and useful, cannot provide one with the timing of the heart beats, that would be needed for some purposes, for instance in the study of the cardiorespiratory synchronization [3]. Hence, continuous-time models may be an alternative for the study of the HRV.

Among the continuous-time models available, those based on the integral pulse frequency modulation (IPFM) have been developed and presented in the literature as able to describe the HRV [4]. In the IPFM, the heart beats arise at the crossing of a threshold by the output of an integrator with reset, fed with a modulating signal that may represent the many inputs of the cardiac pacemaker. This model may be at the same time physiologically sound – since the pacemaker cells have an integrator-like behavior – and useful as a generator of the heart timing signal.

The purpose of the current work is to present simulations and a framework for the identification of parameters of a continuous-time model of the RSA portion of HRV, based on an IPFM system.

Materials and Methods

A description of the model, its simulation and the technique for the identification follows. All processing was performed with WinPython 2.7.5, using the DOPRI5 ODE solver from the Scipy package with de-

fault settings, under Windows 7 ® (Microsoft, USA) in a RF511 notebook (Samsung, Brazil). The algorithm is shown in appendix.

The model – The IPFM model, including the first-order transfer function postulated to describe the respiratory modulation of the heart period, is depicted in Figure 1.
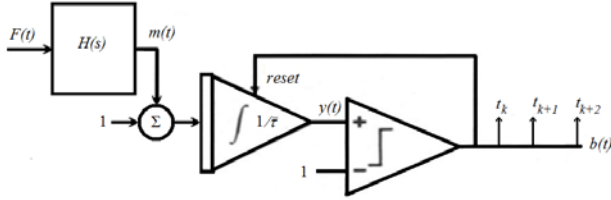

Figure 1. The transfer function of RSA coupled to the IPFM model. $F(t)$ is the respiratory flow, $H(s)$ is the transfer function between $F(t)$ and $m(t)$, the modulating function; $1/\bar{\tau}$ is the gain of the integrator, $y(t)$ is an intermediary signal and $b(t)$ is a signal with pulses at times t_k, t_{k+1} and t_{k+2} representing the instants of the heart beats.

The flow signal $F(t)$ is filtered by a low-pass first-order filter with transfer function $H(s)$ given by:

$$H(s) = \frac{G}{sT_c + 1} \qquad (1)$$

where G is the DC gain of the filter and $\Omega_c = 1/T_c$ is its cutoff frequency. The filter output, the dimensionless signal $m(t)$, is a modulating signal that is added to 1 and fed into an integrator through a gain $1/\bar{\tau}$, where $\bar{\tau}$ is the mean heart beat period. The output of the integrator is continuously compared to the unity; when it reaches this value, at time t_k, the integrator is reset and the k-th heart beat is issued. The series of heartbeat times is thus produced. Thus, the following equation hold:

$$k = \int_0^{t_k} \frac{(1+m(t))}{\bar{\tau}} dt \qquad (2)$$

that leads to equation (3):

$$k\bar{\tau} - t_k = \int_0^{t_k} m(t) dt \qquad (3)$$

Simulations – There were three simulations. Flow was represented by a sinusoidal wave, with period RP and inspiratory-to-expiratory time ratio of 1:1. Amplitude was set for a tidal volume of 0.5 L. Flow was filtered through the first-order low-pass filter, in equation (1). The resulting signal, $m(t)$, as well as the mean heart period $\bar{\tau}$ were fed into the IPFM model, which yielded the series of heart beat times t_k. The simulation time span was of 60 s, with a time step of 1 ms. Only the last 30 s were processed for parameter identification, to avoid transient effects. Table 1 presents the parameter values employed in this study, chosen to generate $F(t)$

and RR intervals roughly similar to those obtained from representative subjects in another study [5].

Table 1: Parameters values employed in the simulations (S1 to S3).

Parameter	S1	S2	S3
RP	4.5	7.5	4.5
Ω_c	0.1	0.2	0.2
G	5.0	5.0	2.0
$\bar{\tau}$	0.8	0.7	1.0

Parameter identification – The simulated signals were segmented from the first to the last available heart beat. Time origin was set at t_0 by subtracting this value from all t_k. The observed mean heart period, $\bar{\tau}$, was calculated as:

$$\bar{\tau} = (t_n - t_0)/(n - 1) \qquad (4)$$

where $n+1$ is the number of heart beats. Then, the series $k.\bar{\tau} - t_k$ was calculated and interpolated with a cubic spline as an estimate of the time integral of $m(t)$, see equation (3). The analytically differentiated spline rendered $m(t)$. From the integral of the inverse Laplace transform of the $H(s)$, the time-domain relationship between $F(t)$ and $m(t)$ at a given time t_i is found as:

$$m(t_i) = \frac{G \int_0^{t_i} F(t) dt - \int_0^{t_i} m(t) dt}{T_c} + C \qquad (5)$$

where C is a constant accounting for the initial conditions. The values of G/T_c and $-1/T_c$ are estimated by linear regression, using the integral of $F(t)$ estimated with the trapezoidal method and the integral of $m(t)$ and $m(t)$ obtained by the aforementioned spline interpolations, at the same time points of $F(t)$. The estimated parameters are calculated directly from these values. The first 10% of the signals were discarded, again to avoid transient effects.

Results

The identified parameters are compared to the original in Table 2.

Table 2. Comparison between parameters employed and estimated in simulations.

Parameter	S1		S2		S3	
	Orig	Est	Orig	Est	Orig	Est
G	5.00	6.24	5.00	5.23	2.00	2.98
Ω_c	0.100	0.0800	0.200	0.19	0.200	0.132

Interbeat intervals obtained with the model are presented in Figure 2, together with the tachograms of representative subjects from the referred experimental study.
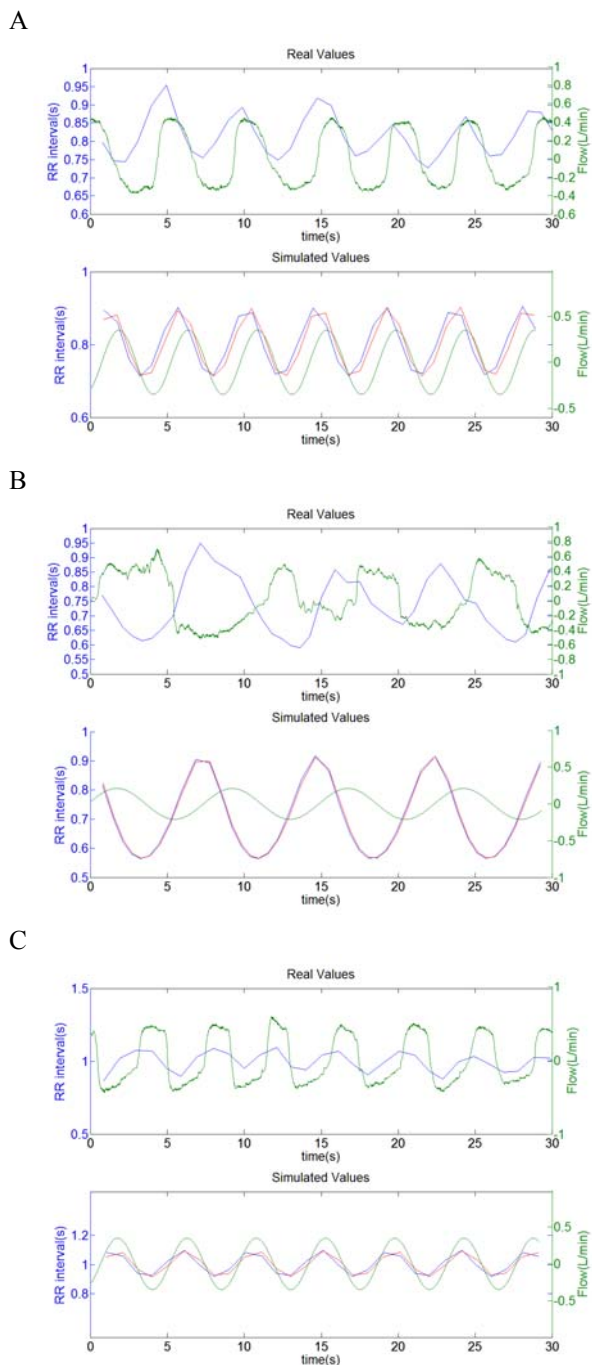
A

B

C

Figure 2. A, B and C are the plots of the three simulations (S1, S2 and S3, respectively). The upper panel of each graph represents measured values of flow and tachogram; the lower panels show simulated flow and tachograms obtained with the original and estimated parameters (blue and red, respectively).

Discussion

The model was able to generate tachograms with reasonable characteristics. Parameters were estimated with low error in some cases, although loss of accuracy occurred.

Data from other works, for instance that of Angelone and Coulter [6], suggest that a low-pass process may be in course between respiration and RSA. On the other hand, at very low respiratory frequencies the RSA seems to vanish. The current model meets qualitatively some of these experimental observations.

Limitations – Nonrespiratory portions of the signals, for example the low-frequency fluctuations of the tachogram and the heartbeat detection errors, were not represented. However, even in the absence of these and other possible departures from the proposed model, such as nonlinearities and higher order behaviors, estimation errors were observed. These may be due to some factors, such as the uneven and low sampling rate of the modulation function that is inherent to the nature of the heart beat fluctuation, and the spline interpolation technique, which may produce artifacts in both the integral of $m(t)$ as well as in its derivative, $m(t)$. Another important limitation is that, for the sake of simplicity, a sinusoid was chosen to represent the respiratory signal in the simulation. It has a poorer spectral content than their real counterparts. Broader spectra may enhance parameter estimation or cause undesirable effects, for instance aliasing due to low sampling rate by the heart beats. The test of these hypotheses, for instance by the evaluation of sensitivities to noise, mean heart rate and other parameters, require further investigation.

In conclusion, this model seems to be able to represent RSA characteristics. Further research is needed to assess whether the proposed model fits experimental data well and if the identification technique is able to deal with real-world nonidealities such as noise and artifacts.

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Appendix – listing of the simulation program with parameters according to the S1 model (see Methods).

```
from scipy.integrate import ode,cumtrapz
from scipy.interpolate import interpolate

def derivatives(t,states):
    dm = (G * F - states[0]) / Tresp
    dI = (1.0 + states[0]) / Taum
    return [dm,dI]


I = 0.0
m = 0.0
Taum = 60.0/80.0 # Selected values: [0.75 s]
Presp=60.0/15.0 # Selected values: [4 s]
A=0.5*2.0*pi/Presp/2.0 # Tidal volume = 0.5
G = 2.0 # Selected values: [2.0]
Tresp = 5.0 # Selected values: [5.0]
t0 = 0
t1 = 60.0
dt = 1.0/1000.0
states0=[m,I]

r = ode(derivatives).set_integrator('dopri5')
r.set_initial_value(states0, t0)
Mstates=zeros((1+int((t1-t0)/dt),len(states0)))
Flow=zeros((1+int((t1-t0)/dt)))
Vtime=zeros((1+int((t1-t0)/dt)))
tbat = array([0.0])
i=0
while r.successful() and r.t < t1:
    F=A*sin(r.t*2.0*pi/Presp)
    Flow[i]=F
    Mstates[i,:]=r.y
    Vtime[i]=r.t
    r.integrate(r.t+dt)
    if r.y[1]>=1.0:
        r.set_initial_value([r.y[0],0.0],t=r.t)
        tbat=hstack((tbat,[r.t]))
    i=i+1

q=find(tbat>t1/2.0)
tbat=tbat[q]
q=find((Vtime>=tbat[0]) * (Vtime<=tbat[-1]))
Vtime=Vtime[q]
Vtime=Vtime-Vtime[0]
Flow=Flow[q]
tbat=tbat-tbat[0]

Tm=(tbat[-1]-tbat[0])/(len(tbat)-1)
k=arange(0,len(tbat))
Vol=cumtrapz(Flow,axis=0,initial=0.0)*dt
S=interpolate.splmake(tbat,k*Tm-tbat,order=3)
Im=interpolate.spleval(S,Vtime,deriv=0)
m=interpolate.spleval(S,Vtime,deriv=1)
M=vstack((Vol,Im,ones(shape(Im)))).T
B=reshape(m,(len(m),1))
l=len(m)
M=M[int(l/10):,:]
B=B[int(l/10):]

pars=inv(M.T.dot(M)).dot(M.T.dot(B))

print 'Simulated: G='+format(G,".3f")+\
' ; Tau='+format(Tresp,".3f")
print 'Estimates: G='+format(float(pars[0]/-
pars[1]),".3f")+\
' ; Tau='+format(float(1.0/-pars[1]),".3f")
```