Introduction of Computational Models to PhysioNet

R Mukkamala, GB Moody, RG Mark

Harvard-MIT Division of Health Sciences and Technology, Cambridge, USA

Abstract

PhysioNet is a national research resource that provides experimental data sets and open-source software for their analysis. Computational modeling can complement studies of these experimental data sets so as to facilitate the advancement of physiologic research. Thus, in order to introduce computational models to PhysioNet, we have developed and posted a cardiovascular model designed for research that generates reasonable human pulsatile hemodynamic waveforms, cardiac output and venous return curves, and beat-to-beat variability. Some of the key features of the software include: 1) compatibility with PhysioNet's open-source data analysis software; 2) online viewing and parameter updating as the data are being calculated; 3) off-line viewing after completion of the simulation; 4) pre-compiled Linux binaries; 5) open-source code that may be compiled on other platforms; and 6) an extensive user's manual and software guide.

1. Introduction

PhysioNet is an NIH-funded national research resource that currently provides, through its web site [1], well characterized, experimental data sets of complex physiologic signals and open-source signal processing and display software for their analysis [2, 3]. This project is generally about extending PhysioNet to provide open-source computational models of physiologic systems as well.

The principal motivation underlying this project is that computational modeling and simulation studies can complement research with the experimental data sets provided by PhysioNet. Through computational modeling studies, the researcher may formulate hypotheses which may be subsequently tested through experimental data analysis. Computational modeling studies may also aid the researcher in the development and evaluation of inverse modeling algorithms for determining important cardiovascular parameters from the experimental data, since the gold standard model parameter values are precisely known. The experimental data studies, in turn, improve the researcher's understanding of the physiologic system in question thereby permitting him or her to construct more accurate computational models. Thus, the researcher's ability to devise new experimental hypotheses and inverse algorithms will be improved. Note that a potential by-product of this project may be the enhancement of the teaching of physiology, since professors and teachers world-wide would have free access to the models which could be utilized to complement their current methods for teaching physiology.

The general objective of this project is to introduce computational models of physiologic systems to PhysioNet by developing and posting a user-friendly, open-source computational model of the human cardiovascular system. A cardiovascular model is a sensible choice for satisfying this objective, since PhysioNet currently provides a wealth of cardiovascular data. Note that this project is much in the spirit of the original benefits and aims of PhysioNet in that it 1) it stimulates new investigations of physiologic systems; 2) it provides computational tools for use by experimentalists; 3) it protects the integrity and reliability of the computational tools; and 4) it avoids the need for redundant modeling efforts thereby providing a foundation for future work [2, 3]. Although there are numerous other national research resources for biomedical simulation and computation (e.g., Biomedical Simulations Resource [4], National Biomedical Computation Resource [5]), to our knowledge, none of these resources provide the types of computational models that could complement studies with the experimental data sets currently available on PhysioNet.

2. Research cardiovascular simulator

The computational model that we have developed and posted on PhysioNet is intended for research and is thus referred to as the Research CardioVascular Simulator (RCV SIM). Indeed, we have previously utilized RCV SIM in cardiovascular research specifically for the development and evaluation of system identification methods aimed at dynamically characterizing autonomic regulatory mechanisms and the mechanical properties of the heart and circulation [6].

The model, which is described in more detail and validated in [5], includes three major components. The first component is a lumped parameter model of the pulsatile heart and circulation with ventricular, systemic, and pulmonary compartments. This model may be

0276-6547/01 $17.00 © 2001 IEEE

Computers in Cardiology 2001;28:77-80.
implemented as an intact preparation, a heart-lung unit
preparation, or a systemic circulation preparation. The
second component is a short-term regulatory system
model which includes an arterial baroreflex system, a
cardiopulmonary baroreflex system, and a direct neural
coupling mechanism between respiration and heart rate.
The final component is a model of resting physiologic
perturbations which includes respiration, autoregulation
of local vascular beds (exogenous disturbance to systemic
arterial resistance), and higher brain center activity
impinging on the autonomic nervous system (if exogenous
disturbance to heart rate). Thus, RCYSIM is capable
of generating reasonable human pulsatile hemodynamic
waves, cardiac output and venous return curves, and
spontaneous beat-to-beat hemodynamic variability.

The hemodynamic data simulated by RCYSIM are stored
in a format that is identical to the experimental data sets of
PhysioNet. As such, the open-source data analysis software
also provided by PhysioNet may be readily applied to the
simulated data as well. The data generated by RCYSIM
may be viewed on-line as they are being calculated or off-
line any time after the completion of the simulation with
PhysioNet’s WAVE display system [7] as well as Gnuplot.
(Off-line viewing may be desired when the data required
for analysis is very time consuming to generate, as would
be the case with Monte Carlo simulations.) Moreover, the
parameter values characterizing the human cardiovascular
model may be adjusted off-line in batch mode or on-line
in the midst of a simulation period. Examples illustrating
both these software features and the hemodynamic data
simulated by RCYSIM are provided below.

Figure 1 (see last page) illustrates a WAVE window
depicting the beat-to-beat variability in the systemic arterial
pressure (Pa), instantaneous lung volume (Qlu), and heart
rate (F) waveforms generated by RCYSIM. The WAVE
window here also depicts annotations which indicate the
times of ventricular contractions.

Figure 2 illustrates a Gnuplot window depicting the
cardiac output and venous return curves simulated by
RCYSIM. Again, this window and the WAVE window of
Figure 1 may be displayed on-line as the data are being
calculated or off-line any time after the completion of the
simulation.

Figure 3 (see last page) illustrates a WAVE window
depicting an on-line parameter update. This window
shows the systemic arterial pressure (Pa) and volume (Qa)
waveforms simulated with the nominal parameter values
of the model and following a 50 percent step decrease in
systemic arterial compliance. Note how systemic arterial
pressure transiently increases at the time of the systemic
arterial compliance step decrease in order to preclude an
instantaneous change in systemic arterial volume. Also note
that the parameter update is annotated (with parameters.1)
so that the simulation is fully documented. Thus, the

researcher can retrospectively review all the simulation
experiments that he or she has completed.

The RCYSIM software is open-source and heavily
commented so that it can be extended and modified
by the physiologic modeling community. The RCYSIM
software includes pre-compiled Linux binaries which may
be executed at either the Linux or MATLAB prompts.
It should also be possible to compile the source code to
create executables that may run on the other platforms
in which WAVE is fully supported (e.g., Solaris, SunOS).
Note that MATLAB and its compiler are required for
compiling the source code. Researchers who port RCYSIM
to other platforms are encouraged to contribute binaries
to PhysioNet so that they may be used by others who do
not have access to MATLAB. The RCYSIM software also
includes an extensive user’s manual that explains how to
install, compile, and use the software with many examples
and further describes the source code.

3. Research examples

In order to understand better how RCYSIM may be
employed in conjunction with the open-source software
and experimental data sets of PhysioNet, we provide here
a simple research example. The aim of this example is
to illustrate how the experimental data can be utilized to
permit the model to behave realistically in terms of the
heart rate power spectrum that it generates. In order to
address this aim, it was necessary to obtain both software
to compute the heart rate power spectrum and experimental
data sets against which the model spectrum could be
compared (that is, the gold standard heart rate power
spectrum). Both the software and experimental data sets are available from PhysioNet.

Establishing the gold standard heart rate power spectrum was achieved as follows. First, the QRS annotations of the 14 human subjects in the metronomic breathing group of the Exaggerated Heart Rate Oscillations Database of PhysioNet were downloaded [3]. Then, a heart rate tachogram was computed from the QRS annotations for each of the subjects with the PhysioToolkit application tach (WFDB Software Package [7]). Next, the maximum entropy power spectrum of each heart rate tachogram was computed with the PhysioToolkit application memse (WFDB Software Package [7]). The gold standard heart rate power spectrum was then established by averaging the power spectra over the group of subjects. Finally, parameters of the model were tuned such that its heart rate power spectrum, also computed with tach and memse, would match the averaged human power spectrum.

The results are illustrated in Figure 4 which demonstrate that RCVSIM is capable of generating a realistic heart rate power spectrum; note the correspondence between its power spectrum (dashed line) and the averaged human heart rate power spectrum (solid lines). In fact, because RCVSIM can generate reasonable beat-to-beat hemodynamic variability, we utilized this simulator as a basis for developing an algorithm for monitoring systemic arterial resistance changes from the beat-to-beat variations in the systemic arterial pressure waveform [6]. We subsequently demonstrated the promise of this algorithm with experimental data obtained from the MIMIC database of PhysioNet[6, 8]. Note that this is another example of how RCVSIM can be utilized to complement research with the experimental data sets of PhysioNet.

![Figure 4](image_url)

**Figure 4.** Model (dashed) and averaged human (solid; mean ± 95% confidence intervals) heart rate power spectra. See text for details.

4. Summary

The RCVSIM software that we have presented here is currently available on PhysioNet at the following URL: www.physionet.org/physiotools/rcvsim/

We invite the physiology research community to download it, try it out, and provide us with your feedback. We would also like to encourage other researchers to contribute their computational models of physiologic systems to PhysioNet as well. Our ultimate vision is a comprehensive library of open-source, computational models that are freely provided by PhysioNet. Such a library will stimulate the advancement of research in physiology. For example, the models might be interfaced together to understand better the interaction between distinct physiologic systems or they might be utilized to complement studies of all of the experimental data sets that are and will be available on PhysioNet.

Acknowledgements

The authors would like to thank Isaac Henry for his systems software support. This work was supported by a grant from the National Center for Research Resources of the National Institutes of Health (P41 RR13622).

References


Address for correspondence:
Ramakrishna Mukkamala
MIT Room E25-505, Cambridge, MA 02139 USA.
mukkamala@MIT.edu
Figure 1. WAVE window of simulated pulsatility and beat-to-beat variability. See text for details.

Figure 3. WAVE window illustrating an on-line parameter update. See text for details.