Introduction of Computational Models to PhysioNet

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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) on-line 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 1) it stimulates new investigations of physiologic systems; 2) it provides computational tools for use by experimentalist; 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 Computational 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 (*RCVSIM*). Indeed, we have previously utilized *RCVSIM* 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 [6], 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

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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 (*1/f* exogenous disturbance to heart rate). Thus, *RCVSIM* is capable of generating reasonable human pulsatile hemodynamic waveforms, cardiac output and venous return curves, and spontaneous beat-to-beat hemodynamic variability.

The hemodynamic data simulated by *RCVSIM* 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 *RCVSIM* 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 *RCVSIM* 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 *RCVSIM*. 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 *RCVSIM*. 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

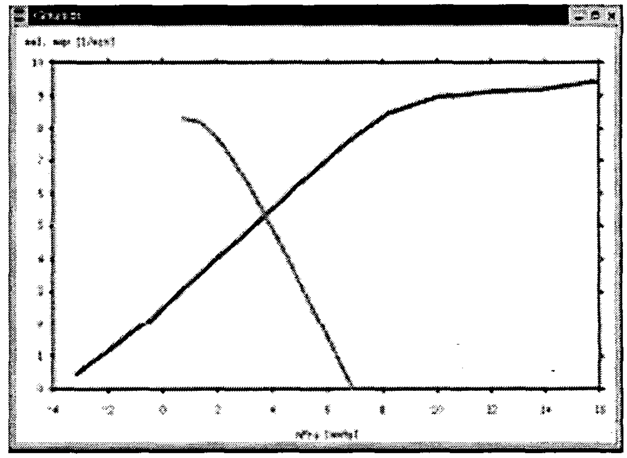

Figure 2. Gnuplot window of simulated cardiac output and venous return curves. mPra denotes effective mean right atrial pressure; mql, mean left ventricular flow rate; and mqv, mean systemic venous flow rate.

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

The *RCVSIM* software is open-source and heavily commented so that it can be extended and modified by the physiologic modeling community. The *RCVSIM* 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 *RCVSIM* 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 *RCVSIM* 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 *RCVSIM* 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 [8]. 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.

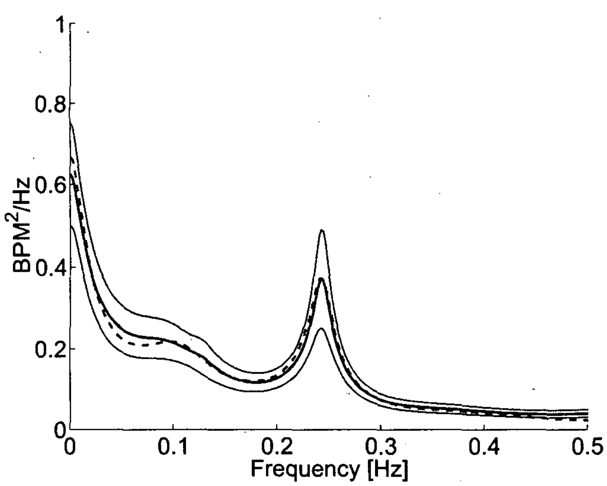

Figure 4. Model (dashed) and averaged human (solid; mean ± 95% confidence intervals) heart rate power spectra. See text for details.

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

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[8] `http://www.physionet.org/physiobank/`.

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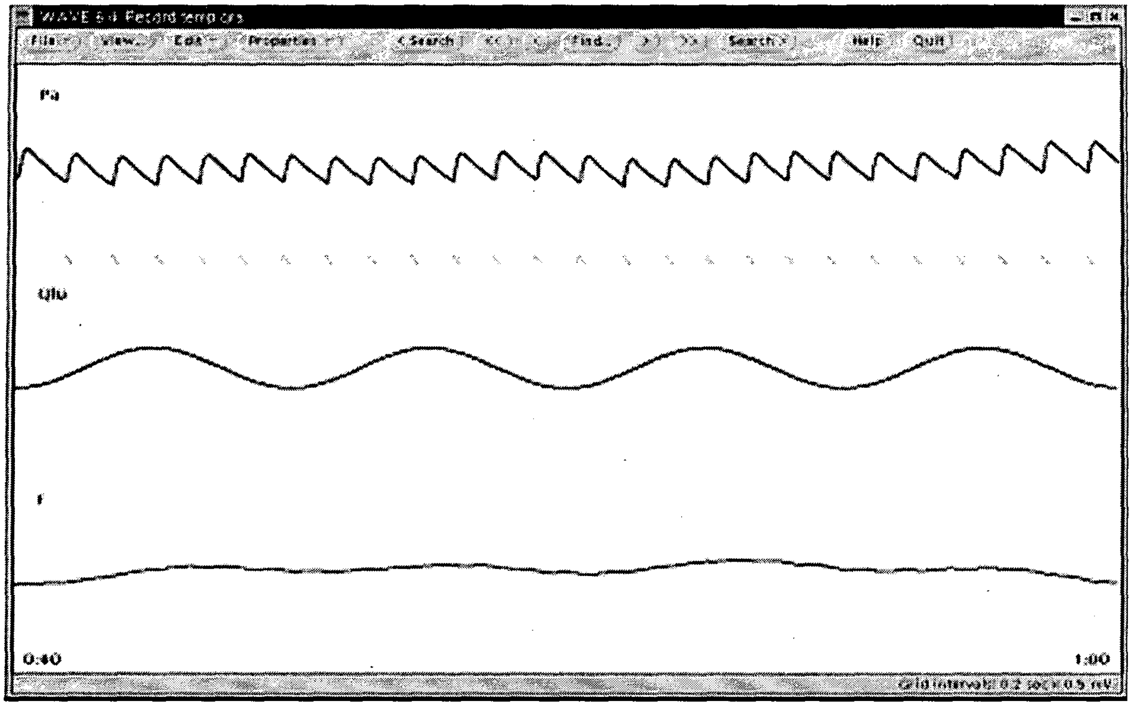

Figure 1. WAVE window of simulated pulsatility and beat-to-beat variability. See text for details.

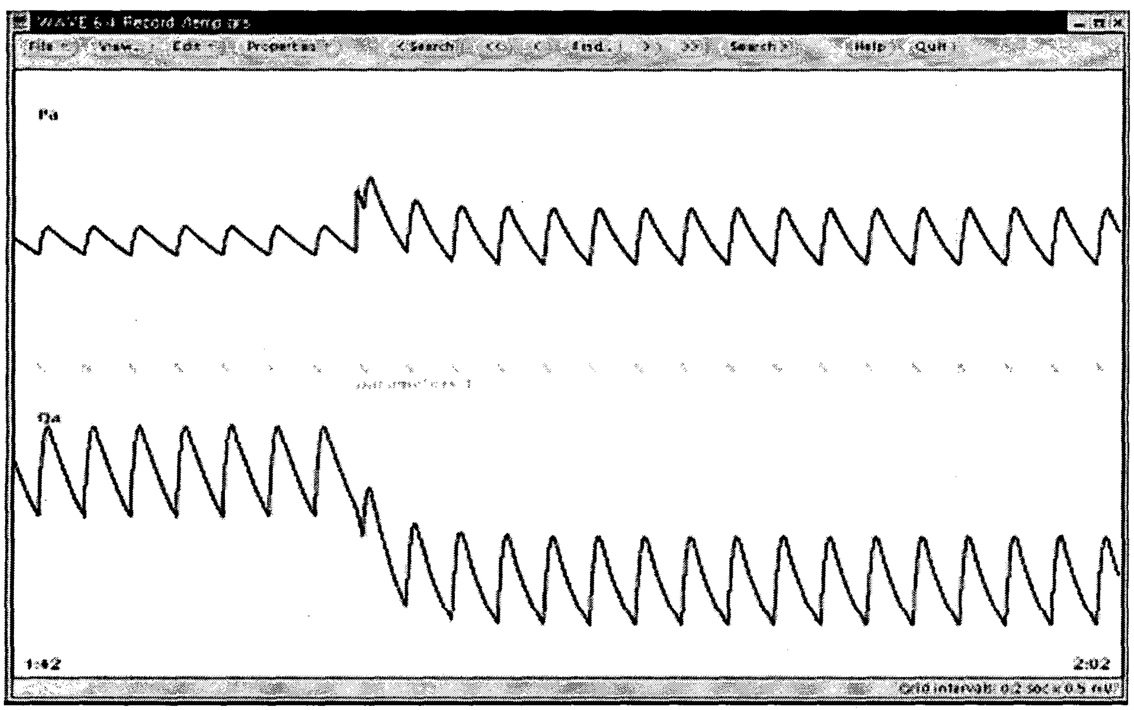

Figure 3. WAVE window illustrating an on-line parameter update. See text for details.