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Open Source Modeling of Cardiovascular System: A Brief Overview

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The open source movement, which can be traced back to the launch of the GNU Project in 1984 [1], has gained momentum since early 1990s when Linus Torvalds wrote the Linux kernel. Since then, numerous open source software (e.g., Mozilla Firefox, OpenOffice, etc.) has gained popularity, and the movement has spread outside the software industry. One of the beneficiaries is the biomedicine.

Biomedicine has increasingly become information oriented science. Fueled by the internet expansion and various initiatives, the past decade has witnessed growing interests in developing public databases and open source programs in biomedical research. While public databases allow open access of data for developing and testing new computer models and algorithms, open source programs share the source code of the computer models and algorithms, and permit users to copy, modify, and redistribute the source code – usually under a public domain license (e.g. the GNU General Public License). By tapping creativity in a much larger scale, biomedical research has greatly benefited from the global collaboration. In particular, tremendous progress has been made in open source modeling of cardiovascular system, likely reflecting the clinical significance of cardiovascular diseases, which are the No. 1 cause of death in the United States [2] and in the world [3]. While there are several tiers of computer models that simulate the cardiovascular system ranging from micro level (e.g., cells) to macro level (e.g., organs) and up to system level, multi-level integration of cardiovascular models are also gaining momentum.

Several integrated web platforms have been created to support the open source development in biomedicine, and many of them include open source computer models that simulate electrophysiology and/or hemodynamics of the cardiovascular system. One popular website is the PhysioNet (http://www.physionet.org/), which offers free access via the web to large collections of recorded physiologic signals and related open source software [4]. One key component of PhysioNet is the PhysioToolkit, which provides a large and growing repository of open source software for physiologic signal visualization, processing and analysis, biomedical models and simulation (with focus on cardiovascular modeling), etc. Another highly visible project is the Physiome (http://www.physiome.org/), which is the quantitative and integrated description of the functional behavior of the physiological state of an individual or species. The Physiome Project attempts to provide a comprehensive framework for modeling the human body using computational methods that incorporate biochemical, biophysical and anatomic information on cells, tissues, and organs [5, 6]. Other popular websites, just to name a few, include Simtk (http://www.simtk.org/), part of Simbios which focuses on multi-scale modeling and simulation of biological structures and functions [7]; and SBML (http://www.sbml.org/) which uses Systems Biology Markup Language (SBML) as a computer-readable format for representing models of biological processes [8, 9]. In addition to these integrated platforms, many stand alone open source models have also been developed that target specific applications in cardiovascular engineering. One representative example is the ECGSIM model (http://www.ecgsim.org/), which provides an interactive environment that simulates the relationship between the electric activity of the ventricular myocardium and the resulting potentials on the thorax [10].

To promote collaboration in open source modeling and accelerate synergy capture, the Open Pacing, Electrophysiology & Therapy Journal (TOPETJ) makes a timely publication of this special issue with the central theme of *Open Source Modeling of Cardiovascular System*. This special issue represents a collection of papers – including both review articles and original contributions – from the leading researchers in the field. These papers are certainly not exhaustive, but are intended to provide a snapshot of the state-of-the-art research on open source modeling in cardiovascular system.

This special issue starts with a review paper on fetal ECG (fECG) signal processing by Sameni and Clifford [11]. In this paper, the authors reviewed the fetal heart development and the etiology of the fECG, and then provided a comprehensive overview of the data collection, signal processing, and modeling techniques for fECG analysis. In particular, the paper highlighted the recently developed synthetic fECG model [12], which was developed based on the open source ECGSYN model [13] that is available at PhysioNet (http://www.physionet.org/physiotools/ecgsyn/). In addition, a collection of fECG data and open source codes for ECG generation, processing, and filtering are also available from the author's website (http://ee.sharif.edu/~ecg/). The authors concluded by highlighting the limiting factors and challenging signal processing issues pertaining to fECG, and making recommendations for promising future directions in signal processing, and database creation.

The next paper by Janusek *et al*. [14] studied the T-wave alternans (TWA) magnitude distribution over the body surface by using the open source ECGSIM model [10] developed by van Oosterom and Oostendorp. The ECGSIM model allows the interactive changing of the timing of depolarization and repolarization as well as the magnitude of the upstroke of the local transmembrane potentials. By solving the forward problem, the ECGSIM can calculate the resulting surface ECG and the body surface potential maps at different time instants. Based on the ECGSIM model, the authors developed a toolbox that allows user to modify the action potential duration of specific heart node (cell) over two consecutive beats, and then displays the calculated TWA amplitude distribution over the torso surface. Moreover, the authors compared their simulation results with the TWA maps constructed from experimental data that were collected from four patients with confirmed TWA, and similar patterns were observed. The findings not only hint the possibility of estimating the location of action potential disturbances in the heart cells, but also suggest alternative ECG lead configurations for optimally detecting TWA.

The paper by Lian *et al.* described a framework for open source modeling of intrinsic heart rhythm and extrinsic cardiac pacing [15]. In this paper, the authors explained detailed model structure and software implementation of the Integrated Dual-chamber Heart and Pacer (IDHP) model, which is capable to simulate intrinsic heart rhythm under both normal and pathological conditions, and its interactions with extrinsic dual-chamber cardiac pacing [16]. The IDHP model is an extension and enhancement of the AF-VP model, which is another open source computer model that was developed to elucidate the effects of ventricular pacing (VP) on ventricular rhythm in atrial fibrillation (AF) [17, 18]. The open source IDHP model can be freely downloaded from the Physiome website (http://nsr.bioeng.washington.edu/jsim/models/webmodel/NSR/-NON_JSIM_MODELS/Lian_Mussig_2009_IDHP/index.html), and the AF-VP model has been freely available from the PhysioNet (http://www.physionet.org/physiotools/afvp/).

Besides cardiac electrophysiology, open source modeling of cardiovascular hemodynamics has also drawn significant interests and efforts from researchers in the field. One representative work is the CVSim, which is a lumped-parameter model of the human cardiovascular system that has been developed and used for research and for teaching quantitative physiology courses at MIT and Harvard Medical School since mid-1980s [19-22]. In this issue, Heldt *et al.* [23] reviewed the development of major versions of CVSim over a 25-year period of the CVSim model, and described the features and differences of four different versions of CVSim, all freely available in open-source form via the PhysioNet (http://www.physionet.org/physiotools/cvsim/). The authors further discussed their experience of using CVSim as a teaching tool and summarized its research applications.

Another open source model on cardiovascular pressure-flow dynamics, SimPower Toolbox, was independently developed by Barnea' lab [24]. The model was written in Matlab and Simulink, and can be freely downloaded from the group's website (http://www.eng.tau.ac.il/~barneao/CVT.ZIP). In this issue, Barnea [25] reviewed the theoretical background of simulating cardiovascular hemodynamic, and described the key elements of the SimPower toolbox, including a model of contracting heart chamber, a model of a heart valve, and a model of a blood vessel.

The Physiome Project maintains a CellML archive, which consists of a large collection of CellML models on cardiovascular circulation and cardiac electrophysiology (http://www.physiome.org/jsim/models/cellml/index.html). The CellML language is an open standard based on the XML markup language [8]. The purpose of CellML is to store and exchange computer-based mathematical models. CellML allows scientists to share models even if they are using different model-building software. It also enables them to reuse components from one model in another, thus accelerating model building. OpenCell (formerly the Physiome CellML Environment) is a complete environment for working with CellML models. In this issue, Reeve *et al.* [26] described a newly attractive feature of the OpenCell, which allows exporting CellML modules to different programming languages including Matlab.

This special issue is concluded by a paper contributed by Professor Jim Bassingthwaighte, the originator of the Physiome Project, who provided an insightful overview of the history, progress, and future direction for predictive modeling and integrative physiology [27]. The Physiome Project is a worldwide effort to define the physiome, or the "*life as a whole*", through the development of databases and open source models which will facilitate the understanding of the integrative function of cells, organs, and organisms. Bassingthwaighte emphasized the three pillars of Physiome Project: constructing databases, developing standards, automating aggregated multi-scale models. In particular, he shared his vision of the Physiome Project, and outlined the modeling strategy that starts from the middle level, the well defined cell and tissues, zoom out to the highly integrated organism level and zoom in to the finely detailed gene level.

In summary, open source modeling of cardiovascular system has generated substantial interests in the past decade. Researchers around the world, from both academic institutions and biomedical industries, have contributed to and/or benefited from this movement. This focus issue of TOPETJ, which represents the first collection of scientific papers on open source modeling of cardiovascular system, is by no means a comprehensive review of the progress in the field, and many outstanding research projects on this topic are not covered. On the other hand, it shall be realized the trend has just started, most work still stay in the grassroots level, the values and potentials of open source modeling have not been fully realized. As Bassingthwaighte pointed out, the scope of the open source modeling in biomedicine requires not only international collaborations within the scientific community, but also the support from sociological and political dimensions. It is my hope that this special issue may be helpful to those seeking to contribute to and/or learn more about this exciting field, and stimulate more synergistic collaborations in the cardiovascular research community.

Finally, I would like to acknowledge the Bentham Science Publishers for giving me opportunity to organize this focus issue, and the TOPETJ editorial board for providing excellent support. Moreover, my special thanks go to all contributing authors who have enthusiastically participated in this project, and to all reviewers who have provided constructive comments and invaluable suggestions.

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Received: May 11, 2010 Accepted: May 19, 2010