Silicon Heart: An Easy to Use Interactive Real-Time Baroreflex Simulator

Michael Menzel¹, Christopher Schölzel¹, Gernot Ernst ², Andreas Dominik¹

¹ THM University of Applied Sciences, Germany
² Kongsberg Hospital, Department of Anesthesiology, Kongsberg, Norway

Abstract

A simulator of the baroreflex loop is implemented as a distributed system, including independent functional units with each of them running without synchronisation and in real-time. Individual components are build from extended equations of the well established Seidel-Herzel-model.

The system includes five small computers representing five independent sub-models. Each component has a computer mouse connected that allow for real-time manipulation of simulation parameters in the respective part of the model. This way, numerical values of variables, such as neurotransmitter concentrations or breathing frequency, can easily be altered by turning the associated adjusting wheel.

Virtual administration of drug substances and virtual disease simulations are performed and show that the asynchronous simulation is robust enough to be used as an intuitive model to study heart rate dynamics.

1. Introduction

The baroreflex loop is a well researched field of physiology, but reliable prognosis and finding truly objective diagnostic criteria for baroreflex-related heart diseases is still difficult.

The required level of objectivity can probably only be achieved with the help of mathematical models. There are already numerous examples of such models in literature; however, to use them for diagnosis we must enable physicians to understand and use these models. Most existing models only allow to set parameters before execution while not providing any live feedback of the stimulus responses. This is not sufficient in order to analyse the dynamic behaviour of a living system.

Therefore we use extended equations of the well established Seidel-Herzel model of the baroreflex loop to build a simulator that runs in real time, and allows live monitoring and manipulation of physiological parameters.

2. Seidel-Herzel Model

The Kotani model is a well established model of the human baroreflex. It is based on a model first published by Seidel and Herzel in 1995[1] with the main purpose of analyzing heart rate variability (HRV). It was later extended by Kotani et.al. including a noise model and an additional feedback loop that enables the model to display cardiorespiratory synchronization. We chose this model for our research because although it is rather compact, it is in good agreement with measured data regarding heart rate characteristics including respiratory sinus arrhythmia (RSA), Mayer waves, bifurcations and the simulation of diseases such as baroreceptor hypersensitivity, congestive heart failure and primary autonomic failure[1–4].

In this paper we use an extended version of the model published in 2005 by Kotani et.al.. It includes the function of baroreceptors, the lung, the autonomic nervous system, the sinus node, AV node, the heart itself and the Windkessel arteries. The baroreceptor model assumes that there is a constant minimal pressure at which the baroreceptors start firing. The firing rate increases both with the static blood pressure level as well as with the dynamic increase in blood pressure. The baroreceptor signal is then passed on to the autonomic nervous system (ANS) and to the lung. The lung model assumes a constant breathing rate that is only modulated by the baroreceptor signal during expiration, as experimental results have shown that high baroreceptor activity can lengthen the period of expiration. As an additional influence, we added a term for the mechanical respiratory influence on the contractility. The ANS is effectively modeled as a black box. Seidel and Herzel assume a linear connection between the baroreceptor signal and the ANS that decreases sympathetic (SNS) activity and increases parasympathetic (PNS) activity and a second linear connection to the respiratory neurons that modulates the SNS and PNS response with a simple sine wave. The ANS is the second part of the model where Kotani et.al. include a noise term that changes on a beat-to-beat interval. The transmitter kinetics for the SNS neurotransmitter Norepinephrine are modeled explicitly as two different concentrations at the sinus node (as neurotransmitter) and
in the vascular system (as hormone) while the faster kinetics of the PNS neurotransmitter Acetylcholine are modeled by a delay of the raw neural signal. Both the concentration of Norepinephrine and the delayed PNS signal are modulated with a saturation term before they reach the sinus node, which is described as a simple integrate-and-fire model. In addition to the sinus node, we also modeled the function of the AV node by simply issuing a heartbeat and resetting the sinus phase prematurely when no sinus signal has been received for 1.7 seconds. The strength of the contraction depends both on the time that has passed since the last contraction (via the Frank-Starling mechanism) and on the Norepinephrine concentrations that increase both the contractility and the venous return to the heart. After a fixed time period of 0.125 seconds has passed, the heart model switches from the systole to the diastole where the decrease of blood pressure is determined by the vascular concentration of Norepinephrine.

3. Distributed simulation and analysis

In order to implement the extended model of the baroreflex a system with five separated computers is set up. Each computer solves the differential equations belonging to one component of the baroreflex model. The components are sinus node and Windkessel arteries, sympathetic, parasympathetic, baroreceptors and lung. The computers are five Raspberry Pis, which are fully functional small computers. For communication, the computers are attached to a local area network (LAN). Each computer runs multiple threads to both calculate new values and send and receive values from other computers.

Except of the explicit communication the computers are independent. This setup leads to an asynchronous behaviour: Components are not waiting for others to run in the same step. The distributed simulation is even able to run with one or more parts missing.

The asynchronous setup and network communication has side effects on the behavior. Calculated values can get omitted while calculating new values, or the new values can be calculated before the previous are sent. This introduces an additional noise into the system, present in real living organisms, too.

A standard computer mouse is attached to each computer. The scroll wheel allows to manipulate parameters of the components simulated on the respective computer while the model is running. Modifiable parameters include concentrations of neurotransmitters, PNS or SNS influence breathing frequency as well as the hypertension factor of the Windkessel arteries.

With help of these manipulators different conditions, such as diseases or influence of medication can be simulated easily. The behavior under altered conditions can immediately be observed in the plots.

Multiple lights are connected to the sinus node computer to display each beat.

All components of the model are attached to a board for display. Figure 1 shows the board from the front view.

For logging purpose an additional part of the system is set up on a laptop. This optional passive unit is only receiving values.

4. Results

Baseline
Figure 2 displays the baseline behavior of the model. Beats per minute (BPM), shown in the upper right, variates only in a small frame. The blood pressure follows with the BPM. The influence of sympatheticus and parasympathicus, are shown in the lower plots.

Figure 2. Baseline plots for blood pressure, beats per minute and influence of parasympathicus and sympathicus.

In order to evaluate the characteristics of the distributed simulation, we performed multifractional analysis of the baseline heart rate as well of conditions that simulate medication.

Multifractal spectrum and singularity spectrum of the baseline simulation are displayed in figure 3 (a) and (b) respectively as black solid circles. The multifractal spectrum shows a change of slope of $\tau(q)$ and the singularity spectrum shows a dependency of the fractal dimension $D(h)$ from the local Hurst exponent $h$, similar to experimental data from healthy subjects [10, 11].

Virtual medication
Administration of a betablocker, such as metoprolol that suppresses SNS signals leads to a weak decrease in multifractal complexity of heart rate dynamics [10]. In order to simulate administration of a betablocker we turned the mouse-wheel of the sympathicus computer until the SNS gain is decreased to 80% of the baseline value. After a waiting time of 100s we recorded heartbeat intervals and analysed multifractal properties. The results are displayed as blue diamonds in figure 3 (a) and (b). The model shows a slight decrease in the curvature of the $\tau(q)$-spectrum and a narrowing of the $D(h)$-spectrum.

In a similar way virtual administration of atropine, as an example for a PNS blocking substance, is simulated by decreasing the gain of the parasympathicus to 80%. The results are displayed as red empty circles in figure 3. The almost linear curve of $\tau(q)$ and the reduced singularity spectrum $D(h)$ suggest almost monofractal signals. Both, the responses to blockade of SNS and to PNS activity are consistent with experimental data and indicate a realistic behaviour of the distributed simulation [10].

Virtual disease
Congestive heart failure (CHF) and primary autonomic failure (PAF) involve changes in long-range scaling properties of heart rate [12].

In CHF PNS activity is decreased and SNS activity is increased. According to Kotani et al. CHF can be simulated by decreasing the gain parameters for PNS influence and increasing the gain for cardiac and vascular branches of the SNS activity [4]. For disease simulation with the distributed simulator, we run the model in baseline condition for some minutes before PNS gain is decreased to 60% and SNS gain is increased to 120% by turning the respective mouse wheels. The resulting heart rate is shown in figure 4 (b). Both, the decrease of average heart beat interval and the decrease of multifractality are consistent with Konati’s results and with experimental data from CHF patients.

In PAF both, PNS activity and SNS activity are decreased due to neuronal degeneration. We performed the simulation in a similar way as for CHF by reducing PNS influence to 80% and SNS influence to 50%. Results are displayed in figure 4 (c). As reported by Kotani for his model [4], the multifractality is only slightly reduced while heart beat intervals and variability of heart beat intervals are significantly reduced.

5. Discussion

We have presented a new type of baroreflex simulator that is based on distributed simulation of the virtual functional units (i.e. organs) sinus node, windkessel arteries, lung, parasympathicus, sympathicus and baroreceptors. The simulations of these components run in an asynchronous manner and in real-time. Each individual part of the simulator re-implements a parts of the Seidel Herzel model. This way of simulation aims to be realistic, because the parts of the models only share information that
The local Hurst exponent is estimated by a sliding window algorithm and coded as a colour ramp from blue (minimum h=0.6) to green to yellow to red (maximum h=1.2). (a) Baseline simulation of a healthy subject. (b) Simulation imitating subjects suffering from CHF by blocking the parasympathetic influence by 40% and increasing the sympathetic influence by 20%. (c) Simulation imitating subjects suffering from PAF by blocking the parasympathetic influence by 20% and the sympathetic influence by 50%.

is also shared between organs in a living organism, such as blood pressure or neural activation. Although the distributed simulation adds several additional sources of noise to the model (because the independent components are not synchronised), the model seems to be robust and displays similar properties as Kotani’s implementation. Results are comparable for baseline simulation of healthy subjects as well as for virtual administration of drug substances (atropine and metoprolol) and disease conditions (CHF and PAF).

Modification of parameters in course of a running simulations additionally gives the opportunity to observe transitions from healthy to disease status, or the time-dependent effect of drug administration. Monitoring these time-dependent effects is only possible with an interactive simulator.

6. Conclusion

The proposed distributed baroreflex simulator shows realistic responses to virtual medication and virtual diseases. The influence of these virtual experiments can be intuitively monitored as change of heart rate dynamics. Furthermore the model can be intuitively operated without knowledge of the implementation. This can make the model a valuable tool to familiarise students and domain experts with the concepts of mathematical modelling.

References


Address for correspondence:
Andreas Dominik
THM - University of Applied Sciences
Department MNI
Wiesenstrasse 14
D-35390 Giessen Germany
andreas.dominik@mni.thm.de