Adaptive Cardiac Resynchronization Therapy Device Based on Spiking Neurons Architecture and Reinforcement Learning Scheme

Rami Rom, Jacob Erel, Michael Glikson, Randy A. Lieberman, Kobi Rosenblum, Ofer Binah, Ran Ginosar, and David L. Hayes

***Abstract*—Spiking neural network (NN) architecture that uses Hebbian learning and reinforcement-learning schemes for adapting the synaptic weights is implemented in silicon and performs dynamic optimization according to hemodynamic sensor for a cardiac resynchronization therapy (CRT) device. The spiking NN architecture dynamically changes the atrioventricular (AV) delay and interventricular (VV) interval parameters according to the information provided by the intracardiac electrograms (IEGMs) and hemodynamic sensors. The spiking NN coprocessor performs the adaptive part and is controlled by a deterministic algorithm master controller. The simulated cardiac output obtained with the adaptive CRT device is 30% higher than with a nonadaptive CRT device and is likely to provide improvement in the quality of life for patients with congestive heart failure. The spiking NN architecture shows synaptic plasticity acquired during the learning process. The synaptic plasticity is manifested by a dynamic learning rate parameter that correlates patterns of hemodynamic sensor with the system outputs, i.e., the optimal AV and VV pacing intervals.**

***Index Terms*—Artificial neural network (ANN), cardiac resynchronization therapy (CRT), integrate-and-fire model (I&F), intracardiac electrograms (IEGMs).**

I. Introduction

SPIKING neural networks (NNs) architectures are a unique form of NNs that are similar to biological nerve system. Spiking neuron architectures, applications, and learning rules are reviewed by Maass and Bishop [1]. Natschlager and Ruf [2] have demonstrated the ability of spiking NN architectures to perform pattern recognition tasks, self-classification, and recognition of temporal sequences even in a noisy and disturbed environment.

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In this paper, we present a spiking NN architecture implemented by a field-programmable gate array (FPGA) chip for cardiac resynchronization therapy (CRT). The spiking NN architecture presented here employs spike-timing learning rule with both long-term potentiation (LTP) and long-term depression (LTD) components [3]. A short-term memory is implemented with a spiking NN architecture employing feedback by a reinforcement learning scheme, and a long-term memory capability is added by a second spiking NN that performs a pattern-recognition task and accordingly changes the learning rate parameter of the first spiking NN dynamically as described later.

CRT is an established therapy for patients with congestive systolic heart failure and intraventricular electrical or mechanical conduction delays. It is based on synchronized pacing of the two ventricles [4]–[6] according to the sensed natural atrium signal that determines the heart rhythm. The resynchronization task demands exact timing of the heart chambers so that the overall stroke volume is maximized for any given heart rate (HR). Optimal timing of activation of the two ventricles is one of the key factors in determining cardiac output. The two major timing parameters which are programmable in a CRT device and determine the pacing intervals are the atrioventricular (AV) delay and interventricular (VV) interval.

CRT device management and, more specifically, the management of the AV delay and VV intervals pacing parameters, is especially suitable for NN processing. The reason is the high variability of these parameters from patient to patient and with the same patient the variability of these parameters during regular daily activities. An NN is able to process the signals produced by hemodynamic sensors by using pattern-recognition techniques and to perform a feedback control scheme dynamically and online. The main novel feature of the spiking NN architecture, presented in [7]–[9] and here for the adaptive CRT device are as follows: 1) spiking NN architecture with Hebbian spike-timing learning and reinforcement-learning schemes; 2) additional spiking NN for pattern-recognition task that together with the first network adds synaptic plasticity based on dynamic learning rate to the spiking neuron architecture; and 3) the spiking neuron network consumes extremely low power that is crucial for implanted pacemakers and defibrillators devices that usually operate for 5–7 years with only a battery as a power source.

This paper is organized as follows. In Section II, we describe the spiking neuron architecture. The adaptive CRT device operational modes is presented in Section III and the Hebbian learning

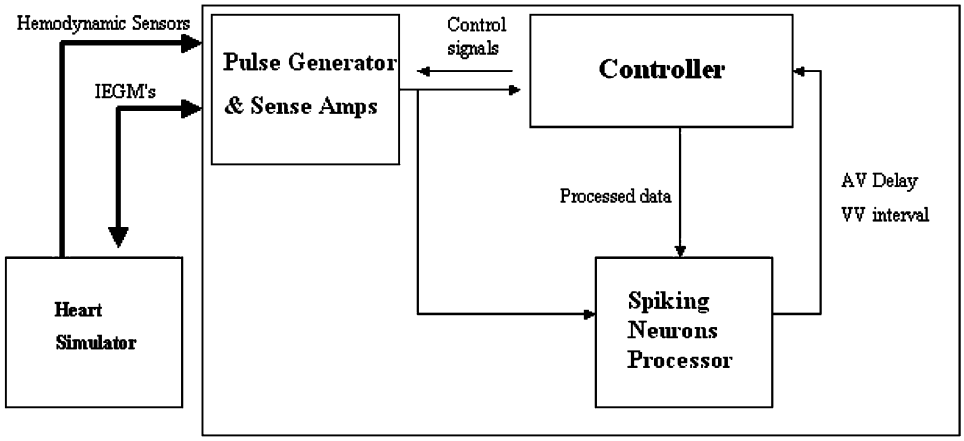

Fig. 1. Adaptive CRT device block diagram.

and reinforcement learning schemes with synaptic plasticity and stability are outlined in Section IV. In Section V, medical application and the prototype are discussed. Simulation results performed with the prototype and a commercial heart simulator is shown in Section VI.

II. Adaptive CRT Device Architecture

Fig. 1 is a diagram of the adaptive CRT device. The inputs to the CRT device are three implanted electrodes that can sense and pace the right atria, right and left ventricles, and two Hemodynamic sensors signals from each ventricle that can be ventricle pressures or ventricle impedances that generate a measure of the ventricle volumes.

The outputs of the adaptive CRT device are stimulation pulses of the right and left ventricles combined with specific delays relative to the natural atrial depolarization wave. The controller manages the electrical system including the pulse generator delivering the stimulation to the heart. In addition, the controller manages the user interface allowing the programming of different CRT parameters such as AV delay and VV interval. Finally, the controller supervises the spiking NN learning schemes as detailed later.

The spiking neuron processor is working as a slave coprocessor in a master–slave architecture. This architecture assures operation within predetermined boundaries that are set by the master algorithmic processor. The master can either accept or reject the predictions made by the spiking NN processor [7]–[9].

The spiking neuron processor has three functional layers. The input stage synchronizer decoder is a predefined preprocessing stage where different subgroups of synapses are excited selectively according to the average heart rate and in each subgroup of synapses each synapse is excited with a fixed predefined increasing time delay measured from the synchronizing atrial event. The middle layer is composed of dynamic synapses modules where learning takes place by modifying the synaptic weights continuously during real-time operation according to a reinforcement learning scheme combined with Hebbian learning rule. The middle layer synaptic weights reach steady-state values that bring optimal performance, i.e., optimal AV delay and VV interval for a given heart condition characterized by the HR. The output layer is composed of two leaky integrate and fire neurons modules that accumulate postsynaptic responses from the middle layer synapses and together with the master controller manage the pacing of the right and left ventricles beat after beat.

The spiking neuron model is of the leaky integrate-and-fire (I&F) type [1], where the leaky I&F neurons and the dynamic synapses of the middle layer are implemented in an FPGA chip as digital state machines. The spiking neurons architecture presented here was chosen for the following reasons. 1) The learning task targets in both adaptive and nonadaptive CRT modes are time delays that are natural learning tasks for spiking neurons. 2) The spiking neurons architecture executes the learning and controls tasks with extremely low clock frequency of 1 kHz that translates to extremely low power dissipation from the battery of the implanted device. 3) The leakage characteristic of I&F neuron membrane potential plays an important role in the learning scheme of the time delays.

III. Operational Modes

The adaptive CRT device has two basic operational modes, adaptive and nonadaptive. With nonadaptive mode, the clinicians program the initial AV delay and the VV interval parameters as in the existing CRT devices, allowing the system to learn the programmed parameters values and to learn the hemodynamic sensor pattern as will be explained later. The adaptive CRT device starts operating in the nonadaptive mode, whereby the two I&F neurons of the output layer learn to fire at the programmed AV delay and VV intervals by using an error backpropagation scheme. When the I&F neurons have learned to fire at the programmed time intervals, the controller switches to adaptive CRT mode in which the AV delay and VV intervals are changed dynamically according to hemodynamic sensors that generate a measure of the ventricle stroke volumes. The stroke volumes, which depend on the changing pacing intervals, are obtained in each cardiac cycle and the synaptic weights of the spiking neurons network processor adapt accordingly with a local Hebbian and reinforcement learning schemes in order to deliver the optimal AV delay and VV intervals that result in maximal stroke volumes at a given HR.

IV. Hebbian Learning, Reinforcement Learning, and Synaptic Plasticity

The question as to whether information in the brain is coded in terms of the precise timing of individual spikes or in terms of mean spike rate is a central issue in neuroscience. The discovery of spike-timing learning rules in the brain provides a strong argument for the importance of coding in terms of spike timing [10]. Hebbian plasticity following pairing of individual spikes was first seen in recordings of cell pairs in layer V/VI of the mammalian neocortex by Markram *et al.* [11].

The spiking NN architecture learning rules presented here combines local Hebbian learning with a reinforcement learning scheme. The local Hebbian learning is performed at each synapse module concurrently according to the relative timings of the pre- and postsynaptic pulse inputs. The aim of synapse weight adaptation is to generate a coherent excitation of a group of three to five synapses that will excite the leaky I&F neuron, causing it to cross the internal membrane potential threshold and to emit a pulse at the target time.

The reinforcement learning scheme is implemented according to a global function calculated by the controller and extracted from the hemodynamic sensor signals (for example, the ventricle stroke volume affected by the varying pacing intervals).

The Hebbian learning rule is similar to Klopf's drive-reinforcement model [12] with several differences that are mainly due to the leaky I&F neuron model used here. The leaky I&F neuron model includes a membrane potential that is grounded after a spike is emitted for a preprogrammed refractory period that is not part of Klopf's model. In addition, the reinforcement calculation and the learning rate parameter are used here differently as will be described later.

A. Nonadaptive CRT Mode Learning Scheme

The nonadaptive learning is an error backpropagation scheme with no feedback from the hemodynamic sensors that is used in the adaptive mode only. The Hebbian learning rule is as follows:

$$W_{ij} = W_{ij} + \eta * R_{ij} \tag{1}$$

where

$i = 1, 2$	I&F neuron index for the right and left ventricle neuron;
$j = 1, \ldots, 200$	synapse index for each spiking neuron; η is the learning rate coefficient;
T_i	firing time of the spiking neuron relative to the atrial depolarization wave;
P_i	programmed pacing interval which is also the supervised learning target time that is used with the error backpropagation scheme; according to the nonadaptive CRT mode, the pacing interval P_i can be changed only by the user and not by the device learning schemes;
R_{ij}	function of the relative timing of the firing of the I&F neuron T_i and the target time P_i, a hit or miss, which is determined by the absolute time difference, $\lvert T_i - P_i \rvert < 15$ ms is a hit and, otherwise, a miss and a local Hebbian state.

When the firing time of the I&F neuron occurs within a predefined interval Δ after the synapse was excited the synapse state is stored as a Hebb state. When the firing time of the I&F neuron occurs between Δ and 2Δ after the synapse was excited, the synapse state is stored as a post-Hebb state. When the firing time of the I&F neuron occurs within an interval Δ before the synapse was excited, the synapse state is stored as a pre-Hebb state. With these definitions of local synaptic states, R_{ij} in (1) is shown in

$$R_y = \begin{cases} +1 & \text{if } T_1 > P_p \text{ miss, post-Hebb} \\ & \text{if } T_1 > P_p \text{ hit, Hebb or post-Hebb} \\ & \text{if } T_1 < P_p \text{ hit, Hebb} \\ & \text{if } T_1 < P_p \text{ miss, pre-Hebb} \\ -1 & \text{if } T_1 > P_p \text{ miss, Hebb or pre-Hebb} \\ & \text{if } T_1 > P_p \text{ hit, pre-Hebb} \\ & \text{if } T_1 < P_p \text{ miss, Hebb or post-Hebb.} \end{cases} \tag{2}$$

Δ is typically 20 ms and the Hebbian states defined previously are stored locally at each synapse state machine at each heart cycle. Note that according to (2), the relative timings of the firing time T_i, the target time P_i, and the local synaptic Hebbian states determine if the synaptic weight is incremented (LTP) or decremented (LTD). When the time difference between the firing time and the target time is larger than 2Δ, there is no synaptic adaptation as was also shown to occur in biological system by Markram *et al.* [11].

The learning scheme described previously is understood better if we recall that the input stage synchronizer decoder excites the dynamic synapse every heart beat after the atrial IEGM is sensed (the synchronizing event) with a predefined delay sequence measured from the synchronizing event t_0, such that each synapse is activated at a different fixed delay time $t_0 + 30, t_0 + 35, \ldots, t_0 + 195, t_0 + 200$ ms. The learning task hence is to train the appropriate subgroup of synapses (about 5–7 synapses at a time) to have a dominant synaptic weights at the steady state at the optimal timing (the optimal AV delay and VV interval), to drive the I&F neuron membrane potential that accumulates postsynaptic responses from all the middle layer synapses beyond the threshold potential, and to fire at the right time at each HR.

The convergence of the I&F neurons to fire at the initially programmed value using error backpropagation supervised learning scheme is shown in Fig. 2(a) and (b).

Fig. 2(a) shows a histogram of the firing times of I&F neuron measured in milliseconds in nonadaptive CRT mode. The learning task target time in this example is 110 ms and, after 192 s, a distribution peak is already seen at the target time (in pink color) and, as the simulation proceeds to 258, 320, and 512 s, the histogram peak is enhanced showing that the supervised learning task in the nonadaptive CRT mode is achieved.

The function that is shown in Fig. 2(b) is the number of hits at the target time with ± 15-ms accuracy in a time frame of 32 heart cycles. After 3–5 min of operation, the I&F neuron learns to fire at the expected programmed time and the number of hits at the target time converges to the maximal value in a time frame of 32.

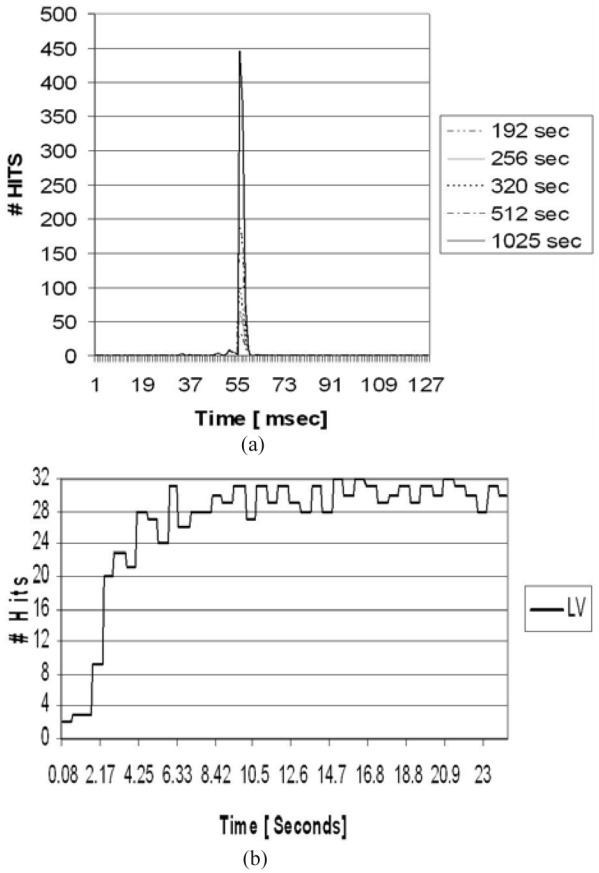

Fig. 2. (a) I&F neuron histogram. (b) I&F neuron hit count.

B. Adaptive CRT Mode Learning Scheme

Manual optimization of a CRT device using hemodynamic sensor was reported by Braunschweig *et al.* [13]. With the adaptive CRT mode presented here and in [7]–[9], a step further is taken relative to [13], where optimization is performed online via pacing intervals that are changing dynamically. The hypothesis of the dynamic optimization scheme relies on the fact that the AV delay and VV interval are physiologic parameters that have an optimal value, a bell-shape curve exists as a function of the pacing interval, where the maximum of the bell shape corresponds to the optimal pacing interval. The expected bell-shape curve should be the result of two opposite physiological phenomena that occur during a heart cycle, i.e., filling time and mitral regurgitation. If the filling time of the ventricle during diastole is too short, the ventricle volume will not be maximal. On the other hand, if contraction occurs too late, a blood backflow from the ventricle to the atria (namely, mitral regurgitation) will occur.

The bell-shape curves described previously are shown, for example, in [14, Figs. 5(b) and 6(b)], in an acute animal experiment. Hence, the task with the adaptive CRT mode is to converge to the optimal pacing intervals at the center of the bell shape. The optimal pacing intervals are expected to vary with HR and heart condition in general, thus the bell-shape curve is not expected to be static. With the present architecture, a dedicated registers, the Pi registers, store the dynamically changing AV delay and VV pacing interval. These parameters play an important part in the adaptive CRT device dynamic optimization scheme.

1) Pacing Register Management: The pacing register adaptation rule is as follows. When the I&F neuron firing time Ti is shorter than the stored pacing interval Pi, the value is decremented. When the I&F neuron firing time Ti is longer than the stored pacing interval Pi, the value is incremented [see (3)]. The increment/decrement parameter value Δp is typically 10 ms, and the pacing interval physiologic range forced by the master controller is 50–200 ms

$$Pi = Pi + \Delta p * \text{Sign}(Pi - Ti). \tag{3}$$

2) I&F Neuron Firing Distribution: The firing times of the I&F neurons, measured from the sensed atrial event at each cardiac cycle, are distributed equally below and above the stored values in the pacing register. However, it is not *a priori* known whether at the next cardiac cycle the firing time will be below or above the stored value. Hence, the firing events are used as a random parameter that dictates the dynamics and the exploration characteristics of the spiking NN architecture.

3) Reinforcement Learning According to State Selection: The ventricle stroke volume (SV), which is the volume ejected by the ventricle at each heartbeat, is calculated in every heartbeat. The last beat stroke volume and the pacing intervals are stored and compared with the current stroke volume and pacing interval. Accordingly, one condition out of four possible states is selected as shown in a flow diagram in Fig. 3. When the current stroke volume SV($P + \Delta$) is bigger than the last heartbeat stroke volume SV(P) and the spike timing T is longer then the value stored at the pacing register P, the state selected is state 1, as shown in Fig. 3 as an example for the state selection.

According to the state selection rule defined previously and the stored Hebbian states, the adaptation of the synaptic weights takes place locally according to (1) and with reinforcement learning factor R_{ij} given in

$$R_{ij} = \begin{cases} +1 & \text{if in state } 1 \text{ or } 3, \text{ pre-Hebb} \\ & \text{if in state } 2 \text{ or } 4, \text{ Hebb or post-Hebb} \\ -1 & \text{if in state } 1 \text{ or } 3, \text{ Hebb or post-Hebb} \\ & \text{if in state } 2 \text{ or } 4, \text{ pre-Hebb.} \end{cases}$$

Note that according to (4) the combination of state 1 or 3 and a pre-Hebb state, or states 2 or 4 and a Hebb or post-Hebb states leads to the increment of the synaptic weight, i.e., LTP, while the combination of state 1 or 3 with a Hebb or a post-Hebb states, or states 2 or 4 with a pre-Hebb state leads to the decreasing of the synaptic weight, i.e., LTD.

The reinforcement learning synaptic weights adaptation rule is shown in Fig. 4 schematically. The stroke volume has a bell-shape curve as a function of the paced AV delay, and the optimal AV delay corresponds to the maximal stroke volume. Note that the position of the maximal stroke volume changes from patient to patient and also changes dynamically in each patient with the HR and stress conditions and, hence, the control task calls for dynamic optimization as presented here.

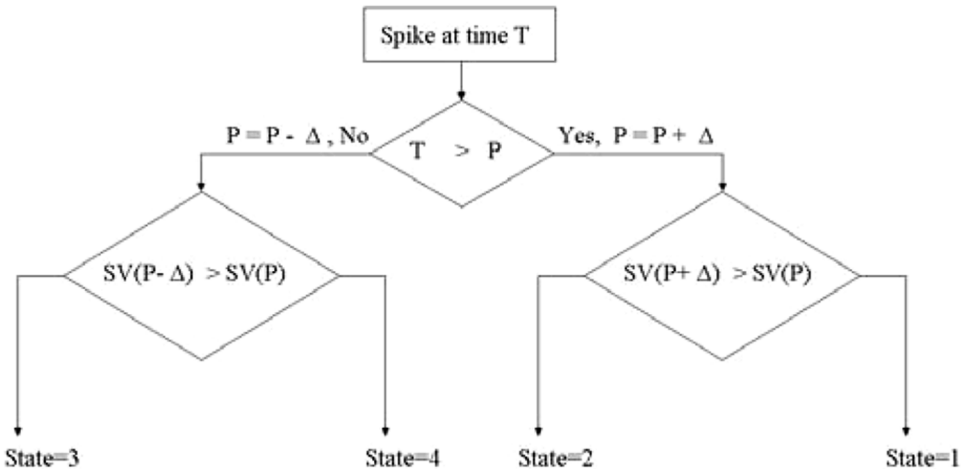

Fig. 3. State selection in a flow diagram.

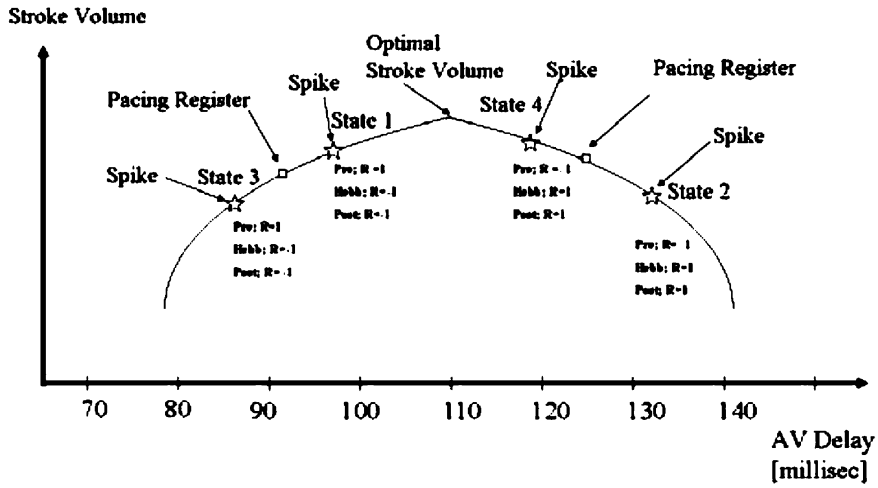

Fig. 4. Stroke volume bell-shape curve.

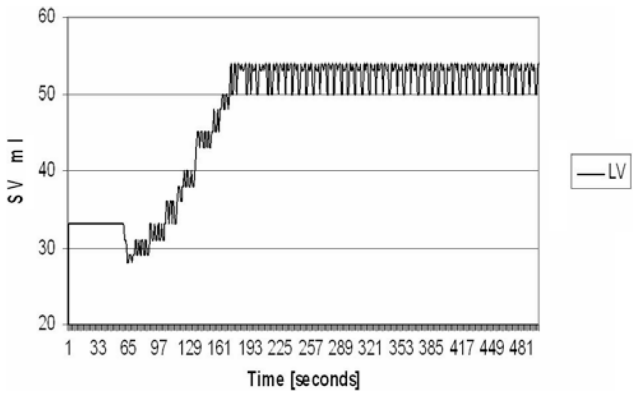

Fig. 5. Responder to CRT curve.

The initial stroke volume depends on the initially programmed AV delay and VV interval. After switching to adaptive CRT mode, the adaptive CRT device dynamically optimizes the AV delay and VV interval pacing parameters and achieves a higher stroke volume as shown in Fig. 5 with adaptive CRT mode. The convergence to a higher stroke volume values is an indication to the positive response to CRT and can be used to identify responders to CRT in the procedure room [8].

The three Hebbian states are defined similarly as in the nonadaptive mode as defined previously. When a postsynaptic pulse occurs (firing of the I&F neuron), the synapse state machines locally stores the state as it occurred. Later, when the gradient of the stroke volume is calculated and a state is selected, the synaptic weights are updated locally at each synapse according to (1) and (4), the flow diagram in Fig. 3, and the bell-shape curve shown in Fig. 4.

4) Learning Rate Parameter: Hebb [15] suggested that long-term memory is related to structural changes in the nervous system that was later termed synaptic plasticity. With no structural changes, he argued that the nervous system could have had only short-term memory. As for the nature of the structural changes, he proposed that if one cell repeatedly assisted in firing another, the knobs of the synapse between the cells could have grown so as to increase the area of contact. Synaptic plasticity was shown to occur as part of a learning process in many experiments with two leading examples as follows: a sea slug [16] and rabbit hippocampus [17].

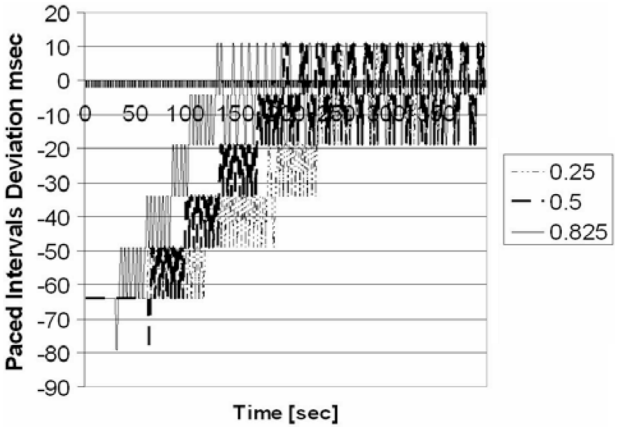

Fig. 6. Dependence on the learning rate parameter.

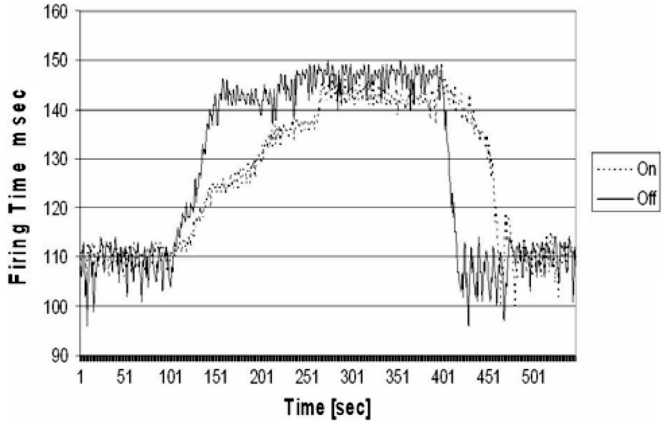

Fig. 7. Dynamic versus fixed learning rate.

η in (1) is the learning rate parameter that defines the synaptic weights steps size in the learning scheme [(2) and (4)]. In Fig. 6, the deviation from the exact solution of the pacing AV interval is shown in a simulation with three different values of learning rates $\eta = 0.2$, 0.5, and 0.825. The convergence time to the exact solution (160 ms in this simulation with HR of 60 beats per minute (BPM) is seen in the figure. With $\eta = 0.2$, the time to converge is about 225 s, with $\eta = 0.4$, it is 175 s, and with $\eta = 0.825$, it is about 125 s. After convergence is achieved, the pacing interval oscillates below and above the exact solution and the solution is stable as shown in Fig. 6.

5) Dynamic Learning Rate Parameter According to Heart Condition Seen Through Hemodynamic Sensor: We suggest to modify the learning rate parameter dynamically according to the heart condition as obtained by temporal input patterns of a hemodynamic sensor that reflect the heart condition. An additional spiking NN performs a pattern-recognition task implemented for the sensor temporal input pattern. According to the firing hit count at a target time [similar to the plot shown in Fig. 2(b)] the learning rate parameter η is modified. When the hit count is low, the input pattern does not match a learned pattern, and the learning rate parameter is assigned a higher value ($\eta = 0.825$, for example). When the hit count is high (the input signal matches a learned pattern), the learning rate parameter is assigned a lower value (e.g., $\eta = 0.2$). Hence, the dynamic learning rate parameter that is changed according to a pattern-recognition NN I&F neuron hit count is a result of a learned correlation between the input temporal patterns of the hemodynamic sensor that reflect heart condition and the appropriate optimal pacing intervals obtained by the reinforcement learning spiking NN.

6) Synaptic Plasticity–Stability With Spiking Neuron Architecture: The dynamic learning rate parameter is used to add synaptic stability by reducing the synaptic plasticity of the spiking neuron architecture. With a small learning rate parameter η, the adaptation to a new optimal value of pacing interval is slower. With a larger learning rate parameter, adaptation is faster as shown in Fig. 6.

Fig. 7 compares simulations with a fixed learning rate parameter (titled "off") and a dynamic learning rate (titled "on"). The simulated scenario is based on an alternating value of an internal time delay between a paced stimulus and the resulting ventricle evoked response of the simulated heart. The internal delay parameter is set to 5 ms initially. After 400 s, it is changed to 45 ms and, after another 400 s, it is set back to 5 ms. This cycle is repeated several times. The optimal AV delay depends on the internal delay parameter. With 5-ms delay the optimal AV delay is 150 ms and with 45-ms internal delay the optimal AV delay is 110 ms. Hence, the task of the adaptive CRT device spiking NN architecture is to learn the two optimal solutions and to switch between them according to the input pattern from the simulated hemodynamic sensor. With fixed learning rate parameter the transition time is shorter and follows immediately after the change in the scenario takes place and, hence, does not show a learned stability. With dynamic learning rate parameter the system has a long-term memory in the form of the dynamic learning rate that is the result of the learned correlation between the hemodynamic sensor input patterns that reflect heart condition and the appropriate learned optimal pacing intervals. The system learned stability is seen through the rigidity to transients that occurs with some delay relative to the fixed learning rate transition and with longer transition time as seen in Fig. 7. With dynamic learning rate, the system is more stable and rigid to switching between the two solutions and the optimal pacing intervals are kept stable for longer time before the adaptive CRT device makes the transition.

To summarize this section, the synaptic stability is implemented by a dynamic learning rate parameter that correlates the input hemodynamic sensor patterns that reflect heart condition with the system outputs, i.e., the learned steady-state optimal pacing interval values. The dynamic learning rate parameter mimics, within the architecture presented in this paper, a structural changes needed for long-term memory, as suggested by Hebb [15].

7) Classical Conditioning With Spiking Neuron Architecture: Modeling studies have shown that networks which implement Hebbian spike-timing-based rules can learn to predict the next step in a sequence of inputs. Such a learning mechanism could be responsible for classical conditioning in which neuronal responses to conditioned stimuli predict the unconditional stimuli after a learning period in which the two stimuli are presented repeatedly in the same sequence [10].

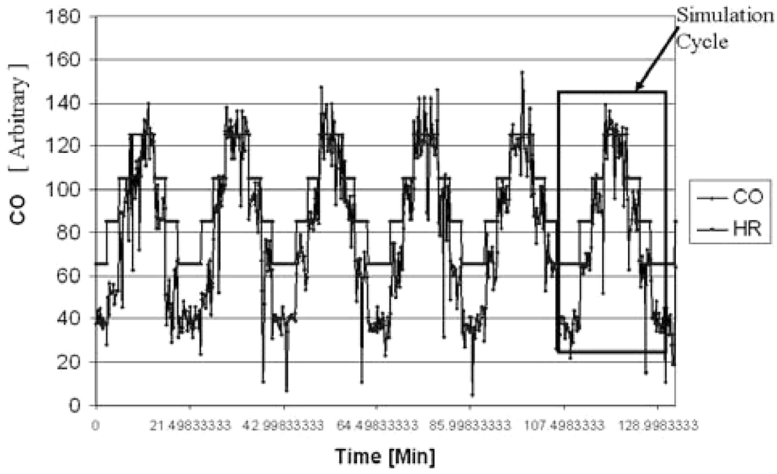

Fig. 8. Simulated cardiac output in exercise.

In this section, we describe the analogy between the adaptive CRT device spiking neurons architecture reinforcement learning task presented here and Klopf's drive-reinforcement model [12]. If the sensed atrial signal that is used here as a synchronization signal at each new heart cycle is counted as a conditional stimuli (CS), the target time stored at the pacing register [see (3)] as the unconditional stimuli (US), and the firing time of the I&F neuron is counted as the conditional response (CR), then the time interval between the CS and the CR is the information that is learned by the adaptive CRT device spiking NN architecture, i.e., the AV delay and VV interval (that can be either a preprogrammed value in a nonadaptive CRT mode or a dynamic value in the adaptive CRT mode), and, hence, the adaptive CRT learning of the optimal AV delay and VV interval for each heart condition is analogous to a classical conditioning and associative learning task, as described in Klopf's model for classical conditioning [12].

V. Adaptive CRT Device Prototype

The clinical hypothesis of the adaptive CRT device presented here highlights that changing the AV delay and VV interval dynamically according to hemodynamic sensors feedback scheme, managed by a combined controller and NN processor, may solve the major drawbacks of CRT devices [7]–[9], and, hence, significantly improve quality of life for patients with heart failure.

The spiking NN processor and the controller are both implemented with an Altera Stratix 80 FPGA. Additional active components such as operational amplifiers, analog-to-digital converters, serial communication chip, and pulse generators are implemented on a daughter board with additional passive electronic components (resistors, capacitors, and diodes).

VI. Simulation Results

Fig. 8 demonstrates the simulated cardiac output during an exercise scenario. The simulated cardiac output is calculated as the stroke volume extracted from the simulated impedance sensors multiplied by the simulated HR.

The HR was changed on the heart simulator from 65 BPM up to 125 BPM at steps of 20 BPM for several times (six simulation cycles are shown in Fig. 8 and the last simulation cycle is shown with a rectangle). The entire simulation lasted more than two hours. During the simulation, the internal heart simulator pace delay parameter (i.e., the evoked response time) for the right ventricle was kept constant (5 ms) and the pace delay parameter for the left ventricle was programmed to change as a function of the HR. With HR of 65 BPM, the left ventricle pace delay was 65 ms. With HR of 85 BPM it was 55 ms, at HR of 105 it was 45 ms, and with HR of 125 BPM it was 35 ms. The left ventricle pace delay was used to mimic a patient with left bundle branch block (LBBB) where the conductance to the left ventricle is slow relative to the right ventricle.

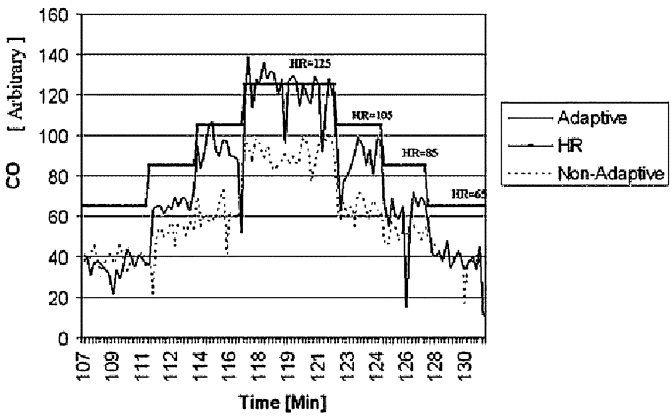

Fig. 9. Adaptive versus nonadaptive pacing modes.

Fig. 9 compares cardiac output during a simulation cycle using dynamic optimization of the AV delay and VV interval with constant intervals optimized at rest (65 BPM). Dynamic optimization produces 30% higher simulated cardiac output on average during a simulation cycle. The benefit of dynamic optimization is emphasized more at higher HRs where the AV delay and VV intervals differ mostly from their values at rest, as shown in Fig. 10.

PRV and PLV are the pacing interval timing relative to the sensed atrial event. The AV delay and VV interval are related

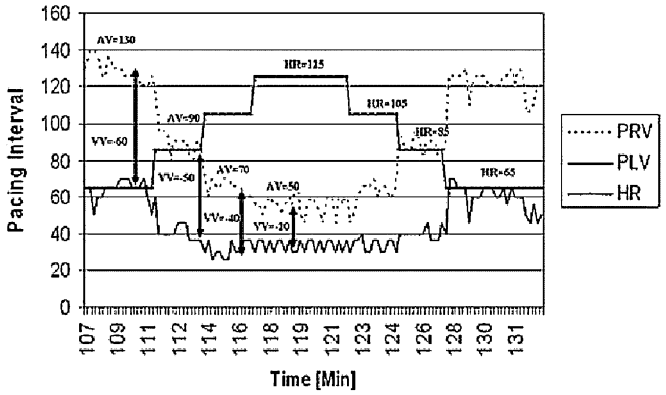

Fig. 10. Dynamic AV and VV pacing intervals.

to the pacing interval values PRV and PLV according to the following:

$$\text{AV Delay} = \text{PRV}$$
$$\text{VV Interval} = \text{PLV} - \text{PRV}.$$

Fig. 10 shows that the optimal AV delay was 130 ms at 65 BPM, reducing gradually to 50 ms at 125 BPM. The optimal VV interval was 60 ms at 65 BPM, reduced gradually to 20 ms at 125 BPM. In summary of Section IV, unlike the adaptive CRT device presented here, no other CRT device can change the AV and VV intervals dynamically according to hemodynamic sensors, resulting in 30% increase in cardiac output. Thus, this simulation demonstrates the potential benefit expected with dynamic optimization according to hemodynamic sensors in a closed-loop system.

VII. Conclusion

An adaptive CRT device with a spiking NN coprocessor has been presented. It performs dynamic optimization of the pacing intervals according to Hebbian and reinforcement-learning schemes using a hemodynamic sensors. The spiking NN processor operates in a master–slave architecture that allows complete operation of predetermined boundaries set by a master controller. The spiking NN processor synaptic weights adapt online according to a local Hebbian spike timing learning rule combined with a reinforcement learning scheme and with synaptic stability, acquired by pattern-recognition task, that adds rigidity to the overall behavior of the adaptive CRT system. The adaptive CRT prototype shows 30% increase in simulated cardiac output compared to a nonadaptive CRT device and is likely to improve the quality of life of patients with congestive heart failure. Preclinical and clinical experiments are needed to show similar results *in vivo*.

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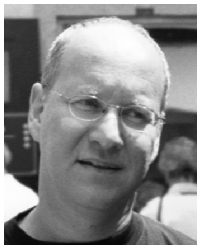

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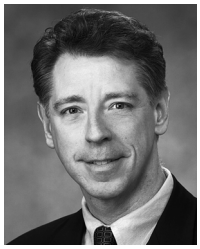

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