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Using the Virtual Heart Model to Validate the Mode-Switch Pacemaker Operation

Zhihao Jiang

University of Pennsylvania, zhihaoj@seas.upenn.edu

Allison Connolly

Johns Hopkins University, aconnol2@jhu.edu

Rahul Mangharam

University of Pennsylvania, rahulm@seas.upenn.edu

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Abstract

Artificial pacemakers are one of the most widely-used implantable devices today, with millions implanted worldwide. The main purpose of an artificial pacemaker is to treat bradycardia, or slow heart beats, by pacing the atrium and ventricles at a faster rate. While the basic functionality of the device is fairly simple, there are many documented cases of death and injury due to device malfunctions. The frequency of malfunctions due to firmware problems will only increase as the pacemaker operations become more complex in an attempt to expand the use of the device. One reason these malfunctions arise is that there is currently no methodology for formal validation and verification of medical device software, as there are in the safety-critical domains of avionics and industrial control automation. We have developed a timed-automata based Virtual Heart Model (VHM) to act as platform for medical device software validation and verification. Through a case study involving multiple arrhythmias, this investigation shows how the VHM can be used with closed-loop operation of a pacemaker to validate the necessity and functionality of the complex mode-switch pacemaker operation. We demonstrate the correct pacemaker operation, to switch from one rhythm management mode to another, in patients with supraventricular tachycardias.

Keywords

Heart model, Pacemaker, close-loop, validation, verification

Disciplines

Computer Engineering

Comments

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Using the Virtual Heart Model to Validate the Mode-Switch Pacemaker Operation

Zhihao Jiang, Allison Connolly and Rahul Mangharam
Department of Electrical and System Engineering
University of Pennsylvania
{zhihaoj, allison and rahulm}@seas.upenn.edu

Abstract—Artificial pacemakers are one of the most widely-used implantable devices today, with millions implanted worldwide. The main purpose of an artificial pacemaker is to treat bradycardia, or slow heart beats, by pacing the atrium and ventricles at a faster rate. While the basic functionality of the device is fairly simple, there are many documented cases of death and injury due to device malfunctions. The frequency of malfunctions due to firmware problems will only increase as the pacemaker operations become more complex in an attempt to expand the use of the device. One reason these malfunctions arise is that there is currently no methodology for formal validation and verification of medical device software, as there are in the safety-critical domains of avionics and industrial control automation. We have developed a timed-automata based Virtual Heart Model (VHM) to act as platform for medical device software validation and verification. Through a case study involving multiple arrhythmias, this investigation shows how the VHM can be used with closed-loop operation of a pacemaker to validate the necessity and functionality of the complex mode-switch pacemaker operation. We demonstrate the correct pacemaker operation, to switch from one rhythm management mode to another, in patients with supraventricular tachycardias.¹

I. INTRODUCTION

Between 1990 and 2002, over 8,000 pacemakers were surgically explanted due to device malfunctions, and since 2002 over 200,000 pacemakers and implantable cardiac defibrillators (ICDs) were recalled[1]. While most recalls did not require device explantation, they still posed significant risk to the patient because of malfunctioning software. The software could be reprogrammed by a physician in the office, but this required physician time and resources which may prevent the correction of errors in all implanted pacemakers and put patients' lives at risk[2]. The use of a model as the platform for software *testing, validation and verification* has been shown to be useful because it provides a unifying point of reference for all brands of medical devices and a mathematical basis for software correctness. A spatio-temporal heart and device-in-loop model can provide a large variety of clinically relevant test cases, beyond the capability of synthetically generated signals[3]. The task of creating a realistic platform for the validation and verification of medical device software is complicated because the underlying physiology is not fully understood. Any model of the heart must be restricted to specific cases that are validated as *clinically relevant*. Thus, the major challenge is not in validating the medical device software, but in first validating the heart model itself for a sufficiently large number of cases.

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A. Virtual Heart Model Platform

A virtual heart model (VHM) has been developed as a basic platform for validation and verification of implantable medical device software[4]. The timing properties of the heart's electrical conduction system are extracted to create a timed-automata model. The refractoriness of tissues are modeled as node automata. Each node contains three states, the effective refractory period or blocking interval, the relative refractory period where preexcitation can occur, and the rest period. The conduction properties between nodes are modeled as path automata. Each path contains timers to model the antegrade and retrograde conduction of activation signals along that path.

A functional interface models probes to output electrograms, which can be used in closed-loop interactions with medical devices. Each probe monitors the antegrade and retrograde timers of neighboring paths and produces a spike according to the relative distance from these activations to the probe. The VHM also provides a formal interface for interaction with medical device software and for use in formal verification. Fig. 1 shows the principal conduction pathways within the heart modeled by a 30+ node and path automata model. The heart model is capable of generating clinically-relevant electrogram signals from the standard probing points across the heart wall. In addition, there is an interface for external pacing for electrophysiological testing. The synthetic electrograms for several case studies have been validated by an electrophysiologist.[4] The same model also executes on a programmable hardware (FPGA) platform for software-based and hardware-based device-in-loop evaluation.

We will use the VHM to investigate the different pacemaker operating modes during the onset and termination of complex cardiac arrhythmias involving the whole heart. Such spatio-

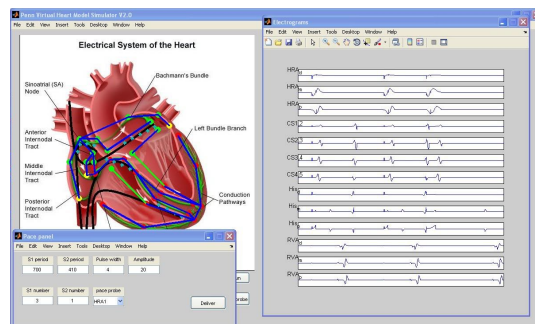


Figure 1. Virtual Heart Model Simulink environment. The network of nodes and paths is overlaid on an image of the heart. The right panel shows synthetic electrograms generated from VHM and the bottom panel controls programmed pacing.

temporal analysis requires a richer heart model to be used for closed-loop functional and formal validation of the pacemaker software prior to clinical trials.

II. MODELING A PACEMAKER

A. Basic Pacemaker Modes

In conjunction with the VHM, a model of an artificial pacemaker has been developed to investigate the closed-loop interaction between the physical system (heart) and the device (pacemaker) for correctness of operation across a range of cardiac arrhythmias. Pacemakers operate in different modes and these are labelled using a three character system (e.g. xyz). The first position describes the pacing locations, the second location describes the sensing locations, and the third position describes how the pacemaker software responds to sensing. For example, VDI mode paces only the ventricle (V) while it senses dually from both the atria and the ventricle (D) and the sensing in the ventricle inhibits pacing in the ventricle (I). The DDD mode paces both the atrium and ventricle (D), senses both (D), and sensing can both activate or inhibit further pacing (D). Pacemakers can have pace/sense leads in a single chamber or in two chambers (atrium and ventricle). These modes are referred to as low-level operations, as they perform the basic therapies necessary to maintain a baseline heart beat. They form a basis upon which more complicated therapeutic algorithms can be implemented.

The previously developed model[4] contained only the five basic timer components of a pacemaker to coordinate the sensing and pacing of the device software. The main timer component is the lower rate interval (LRI) which determines the slowest heart beat allowed by the pacemaker. With these five timer components, any mode of pacemaker from VVI (sensing and pacing in the ventricles only) to DDD can be modeled. Complex functionalities that exist in commercial pacemakers were not included in the previous model.

B. High-level Pacemaker Operations

Commercial pacemakers and other cardiac devices use counters, morphology detectors, and other attributes to detect arrhythmias before applying specialized pacing therapy[5]. For example, a dual chamber pacemaker can detect atrial tachycardias by counting the number of atrial beats with rate above a programmed threshold[6]. Once an arrhythmia has been detected, a high-level operation delivers specified therapy in order to deal with and in some cases terminate the arrhythmia. Examples of these high-level operations include atrial flutter response, rate hysteresis and rate smoothing to gradually quicken or slow pacing rates, and sudden bradycardia response.

III. MODELING ARRHYTHMIAS IN THE VHM

While simple pacemaker operations can be satisfactorily verified using pre-recorded electrogram signals, the high-level operations require a complex and interactive platform for validation and verification. The VHM provides this interactive device-in-the-loop environment, where pacing therapy from the pacemaker software will directly cause changes in the VHM, creating a more realistic testing environment. This also allows the testing parameters to cover a greater span of arrhythmias.

With the VHM, we can create multiple arrhythmias to test the interactions between different features of the pacemaker.

Cavotricuspid-Isthmus-Dependent (CTI) Atrial Flutter (AFL) is a commonly seen supraventricular arrhythmia. The physiology of the right atrium, shown in the right panel of Fig. 2, lends itself to forming conduction pathways along pathological tracks. Slow conduction through the CTI, the area bounded by the inferior vena cava and the tricuspid valve annulus, creates a long cycle length in the tissue and allows for the reentry circuit to form[7]. Typical AFL occurs in the counter-clockwise direction, with activation following the posterior atrial wall through the CTI, along the inter-atrial septum, back across the anterior wall, and down the exterior wall. Clockwise direction conduction, known as reverse AFL, is also seen but is not as common. AFL encompasses a large portion of the atrium in a reentry circuit with rates up to 350 beats per minute. It is associated with significantly high morbidity rates because it occurs in transition from a regular rhythm to atrial fibrillation[8].

A dual chamber pacemaker is normally prescribed for patients with chronic bradycardia, or slow heart rate. These patients can have additional arrhythmias, including atrial flutter. The AFL rate of 240 to 350 bpm dominates the intrinsic slow rate of the SA node, and causes activation to conduct to both atria. Commonly, this rapid activation in the atria causes the conduction properties of the tissue downstream towards the ventricles to slow[9]. This blocks several activations from conducting to the ventricles and results in a 2:1 atrium to ventricle conduction ratio (shown in Fig. 3). The atrial rate is very fast while the ventricular rate remains relatively normal, around 100 beats per minute. When the AFL terminates on its own, the diseased heart returns to a bradycardia state.

The reentry circuit for AFL is modeled in the VHM by placing additional nodes and paths in the right atrium connected to the SA node. In order to model the reentry circuit with cycle length 226 msec, the sum of conduction timers for all

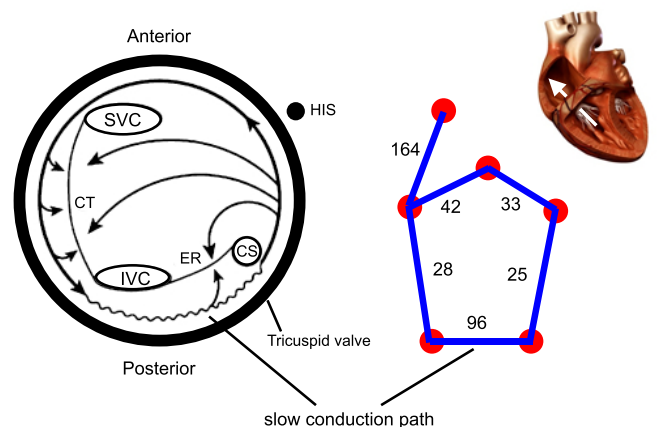


Figure 2. Left: View of the atrial flutter circuit from the right ventricle through the tricuspid valve into the right atrium. The wavy line shows slow conduction through the CTI, bounded by the inferior vena cava (IVC) and the coronary sinus (CS) (Adapted from [7]). Right: AFL circuit in the VHM. The numbers show the values of conduction timers in the paths, with corresponding slow conduction path on the bottom.

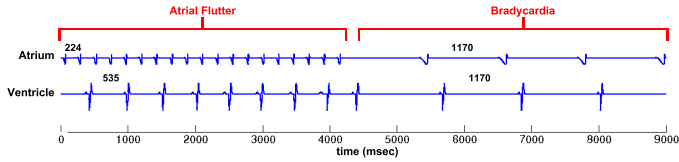


Figure 3. The VHM has intermittent AFL with nearly 2:1 conduction. The AFL terminates at 4000 ms and reveals the underlying bradycardia with extended beat-to-beat intervals and slow rate.

paths along the circuit equals the cycle length. The effective refractory timers for the nodes in the circuit were set to 150 msec, which allows the conduction to continue through the nodes without encountering block. However, the effective refractory timer for the AV node is known to be 500 msec. This means that every other activation signal conducted through the atria will be blocked at the AV node and not conduct to the nodes and paths in the ventricles, causing 2:1 conduction. The underlying bradycardia is modeled by setting the rest timer of the SA node to be 1000 msec.

IV. PACEMAKER MODE SWITCH OPERATION

AFL is significant not only because of its high rate of occurrence, but also because it presents a complex situation that requires complex pacemaker rhythm therapy. AFL on its own is not life-threatening, because the tachycardia happens only in the atria. The delay and block properties of the AV node can maintain relatively normal ventricle rates. However, when supraventricular tachycardias such as AFL occur in patients with an artificial pacemaker, complications can arise if the pacemaker follows the timing sequence for simple bradycardia. In DDD mode, the pacemaker will pace the ventricles for every sensed atrial event, which induces a ventricular tachycardia and compromises proper pumping function. The mode-switch operation needs to be introduced so that the pacemaker can switch from DDD mode to VDI mode during supraventricular tachycardia. This prevents over-pacing the ventricles by decoupling the atrial and ventricular sensing. The VDI pacemaker paces the ventricles at the programmed LRI instead of once for every sensed atrial event.

In order to validate the necessity and functionality of the mode-switch operation, we implemented the mode switch pacemaker model in closed-loop simulation with the VHM with bradycardia and transient AFL. The following section illustrates how the DDD mode pacemaker produces undesired over-pacing and induces a ventricular tachycardia, while the pacemaker with mode-switch operation ensures appropriate therapy.

A. AFL with VVI pacemaker

A single chamber pacemaker, ventricle only, can better treat a heart with supraventricular arrhythmia than a DDD mode pacemaker. Because the atria are beating very fast on their own, atrial sensing is not necessary. The VVI pacemaker will keep the ventricles contracting at the desired LRI rate. While this is not optimal for pumping efficiency, it is sufficient, as the ventricles are the chambers that drive blood throughout the whole body. No pacemaker mode can slow down the atrial rate, so focusing on maintaining the ventricular rate is the best that can be done. Fig. 4 shows the VHM operating with a VVI

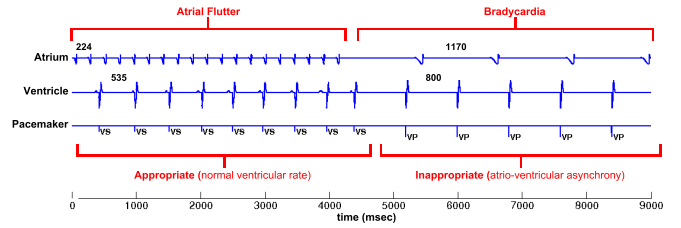


Figure 4. VVI Mode: The top two panels show the atrial and ventricular electrograms sensed by the pacemaker. The bottom panel shows the labelled pacemaker operation, with ventricular sensed (VS) and paced (VP) events. The ventricles are paced at appropriate rates in both AFL and bradycardia, but optimal function is not maintained as the atrium and ventricles are out of sync.

mode pacemaker. While the atrial electrogram shows very fast excitation, the ventricular electrogram shows how the pacemaker maintains a steady interval of 800ms, or 75 beats per minute, in the ventricles during AFL. This rate is also maintained during bradycardia, but the atria and ventricles are decoupled and contract asynchronously, which produces inefficient pumping.

B. AFL with DDD pacemaker

In many cases, patients require a dual chamber pacemaker to maintain synchrony between atria and ventricles, such as in bradycardia with heart block. The Post Ventricular Atrial Refractory Period (PVARP) is a period after each ventricle event that no atrial event should happen. In DDD mode pacemaker, atrial events sensed during PVARP will be marked as AR and will not trigger ventricular pacing[4]. Fig. 5 illustrates the situation where a DDD pacemaker can cause more harm than good. Although some atrial events fall into the PVARP period of the pacemaker and are ignored (AR in the figure), the ventricles are still paced for every sensed atrial event (AS in the figure), which results in rapid and irregular pacing of the ventricles with rates up to 150 beats per minutes, creating a ventricular tachycardia. At rates this fast, the ventricles do not have enough time to fill between contractions, and pumping efficiency suffers.

C. AFL with Mode Switch

For patients who require dual chamber pacing due to bradycardia and have intermittent supraventricular tachycardias, a more advanced mode of pacemaker operation is necessary. The mode switch operation can disable the atrial pacing function of a DDD mode pacemaker and turn it into a VDI mode pacemaker during supraventricular tachycardias while switching back to DDD mode when the AFL terminates. Fig. 6 illustrates how a mode-switch would occur in closed-loop operation with the VHM. The pacemaker starts in DDD mode. The pacemaker

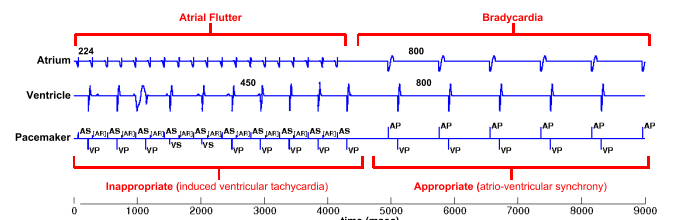


Figure 5. DDD mode: When the VHM is in AFL, the pacemaker induces a ventricular tachycardia which inhibits pumping. In bradycardia, the pacemaker can maintain atrio-ventricular synchrony and provides optimal pumping.

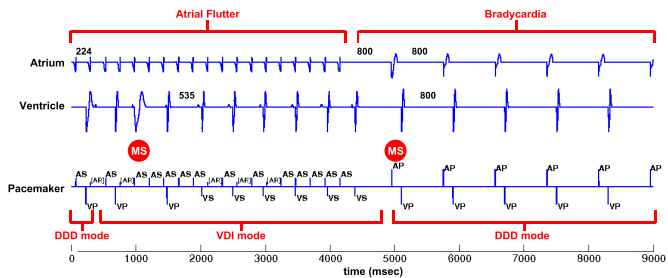


Figure 6. Mode switch: When the VHM is in AFL, the pacemaker can switch modes (MS) to VDI and slow the ventricular rate, preventing ventricular tachycardia. When the VHM switches to bradycardia, the pacemaker switches modes back to DDD and maintains proper rates as well as A-V synchrony.

constantly monitors the atrial beat-to-beat interval and records the number of intervals shorter than 500ms. When there are five consecutive short intervals in the atrial channel (both AR and AS), mode-switch occurs from DDD to VDI mode. In VDI mode, the pacemaker decouples atrial sensing and ventricular pacing. The ventricles are paced at the LRI of 800ms and only when a ventricular event has not been sensed.

Most supraventricular tachycardias are transient and eventually terminate on their own. The pacemaker must be able to mode-switch out of VDI mode to regain its normal operation when the tachycardia terminates. The pacemaker continues to monitor the atrial rate in order to detect when the AFL terminates, characterized by an interval recorded to be longer than 500ms. This triggers the reverse mode switch from VDI to DDD. If the interval length exceeds the LRI interval, the pacemaker will switch to DDD mode and simultaneously deliver an atrial pace to maintain natural conduction pattern.

V.RELATED WORK

Many researchers have previously tackled the problem of modeling cardiac arrhythmias. [10] and [11] have used a three-dimensional discrete element mesh to model supraventricular tachycardias, while [12] and [13] modeled the activity of individual ion channels to simulate arrhythmias. These models were created for research or diagnostic purposes and do not have the capability to have closed-loop interaction with medical devices. Currently, the FDA leaves the responsibility of software testing to the medical device companies, who use a series of pre-recorded cardiac signals to test the software operations. Medtronic's Virtual Interactive Patient simulator can be used in closed-loop operation with real medical devices, but the sophistication of this signal generator allows it to be used as a training tool only and not during the testing of device software itself[14]. [15] also extracted the timing properties of the cardiac conduction system to model the heart. Their model was able to do close-loop simulation with pacemaker software for several clinically-relevant cases and produce template-based ECG signals. The VHM platform builds upon this modeling technique and allows for cardiac device verification and interaction with real devices.

VI.DISCUSSION

As the algorithms used in implantable medical devices become more complex, the design of bug-free medical device

software is becoming an increasingly difficult problem. The high-level diagnostic and therapeutic operations of artificial pacemakers requires a dynamic and interactive testing platform to fully validate their functionality. The VHM provides closed-loop interaction with both medical device hardware and software implementations. We presented a case study to demonstrate how this closed-loop interaction can be used to show the necessity and validate the high-level pacemaker mode-switch operation. The basic pacemaker modes VVI and DDD are successful in managing individual cardiac arrhythmias. In reality, the human heart is not restricted to a single arrhythmic state and consequently requires a variety of therapeutic modalities. In the future, the VHM will be extended to validate other high-level operations such as rate hysteresis, rate smoothing, and atrial flutter response.

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