Reliability Analysis of Healthcare Information Systems: State of the Art and Future Directions

Amjad Gawanmeh* and Hussam Al-Hamadi* and Mahmoud Al-Qutayri*and Shiu-Kai Chin¶ and Kashif Saleem♯
*Department of Electrical and Computer Engineering, Khalifa University, UAE, amjad.gawanmeh@kustar.ac.ae
¶Department of Electrical Engineering and Computer Science, Syracuse University, USA
♯Center of Excellence in Information Assurance, King Saud University, Saudi Arabia

***Abstract*—Testing and verification of healthcare information systems is a challenging and important issue since faults in these critical systems may lead to loss of lives, and in the best cases, loss of money and reputations. However, due to the complexity of these systems, and the increasing demand for new products and new technologies in this domain, there are several methods and technologies being used for testing these systems. In this paper, we review the state of the art on testing and verification of healthcare information systems, and then we identify several open issues and challenges in the area. We divide the exiting methods into three categories: simulation based methods, formal methods, and other techniques such as semi-formal methods. Then, we discuss challenging and open issues in the domain.**

I. Introduction

With the increasing population and aging society in several countries, healthcare providers aim to enhance the quality of the healthcare services while balancing the risk mitigation and service cost. Therefore, several new information technologies and innovative communication methodologies have evolved to improve the healthcare sector. These ICT-based technologies increase the quality of services and thus they help in decreasing the healthcare system overhead and increasing the quality of healthcare services. These technologies may include bio-sensors, computer aided diagnosis, Wireless Body Sensor Network (WBSN), mobile health, Radio Frequency Identification (RFID), cloud computing, communication protocols, electronic medical records, big data, and internet of things (IoT). Therefore, the complexity of healthcare systems has increased dramatically during the last two decades. However, the errors of integrating these technologies in healthcare systems cannot be compromised due to the possibility of losing lives and the huge cost associated with such errors. In addition, a considerable effort and time is consumed for system maintenance and recovery when errors occur in these systems. As a result, healthcare systems must go through rigorous testing before they are used.

In addition, and despite having several approaches developed for testing and verification of healthcare systems, ICT-related medical incidents that led into losses of money, time, reputation, and in certain cases, lives, still happen frequently. For instance, a serious incidents was caused by a radiation therapy device called Therac-25 [1] caused by several hidden malfunctions within the device, resulting in the delivery of lethal radiation to the patients that resulted in death. Another serious incident occurred in the National Cancer Institute, Panama City, where physicians and technicians misused an equipment without changing certain parameters in a software that was used to give a proper dosage of radiation for patients. This resulted in the death of eight persons and other 20 left suffering from significant health problems [2]. Investigators blamed the developing company for not providing a clear instructions and explanations on how to use the software [3].

In other incidents, a team of security researchers had successfully able to remotely control a pacemaker by re-instructing, shutting down, or delivering jolts to patient's body [4]. In spring 2012, 171 reports related to ICT problems were collected by ECRI Institute from different medical centers in the US during a nine-weeks period [5]. In one of these incident, a surgeon could not access a patient's radiology study during the surgery operation, which resulted in putting the patient under the anesthesia for extra time, which led into harmful complications [5]. Several other incidents led into privacy breaches [6], or exposal of patients' records [7]. These examples how that healthcare systems do not get enough testing and verification before being put into use, even though they are considered safety critical systems. This is due to the high cost of testing, short time to marker, and the lack of proper testing and verification techniques in the literature. In this paper, we provide a survey on existing methods for testing and verification of healthcare information systems, and then, we highlight open issues and challenges in the area.

II. Simulation-Based Verification

Simulation has been used heavily in testing and verification of several types of systems in several areas. It is well developed and practical method since it can be conducted on software models of systems. In this section, we survey simulation methods that has been used in testing and verification of ICT based healthcare system.

A. High Level Management and Security Issues

There are several high level issues in healthcare systems such as patient flow and allocating healthcare resources (manpower or facilities) that require thorough testing in order to reduce operations cost and increase efficiency. Therefore several solutions were proposed to improve the delivery of healthcare services. Some of these proposed methods were tested and

978-1-4673-8325-7/15/$31.00 ©2015 IEEE

verified using simulation. Koo *et al.* [8] and Taheri *et al.* [9] used on a baseline model with a pre-defined environment to validate their proposed approach that was intended to improve the patient flow at a hospital endoscopy unit. The authors in [10], [11] and [12] used simulation softwares such as Arena [13] and SIMIO [14] to validated their proposed method, and then they compared their simulation results with a real healthcare environment in the general hospital in Ningbo [10] and the NHS hospital in Landon ([11].

The authors in [8] examine four alternative solutions in rescheduling the doctors load rate to understand the patient bottleneck upon the doctors' schedule. The work in [9] simulated the shifting load in endoscopy unit to improve patients flow. Michael *et al.* [15] proposed a simulation model to evaluate multiple participant pathways effects on the flexibility of resource allocation. They evaluated their model by comparing it with data collected form a real healthcare environment during 20 months period. Wong *et al.* [12] developed a simulation model to mimic the emergency department workflow and observe the limitations in the used method for utilizing resources.

Discrete-event simulation (DES) was used by Raunak *et al.* [16] to simulate the patients flow in the emergency department, where they used a definition language called Little-JIL [17] and combined it with JSim simulation tool [18]. Alexander *et al.* [11] used DES to model the relationship between patient types, case-mix, and operating clinic allocation. The authors then used the model in order to predict and estimate the cost impact within various case-mix scenarios on patient throughput and utilization of clinics. The work in [19] and [20] used the agent technology to simulate different activities within the healthcare environments, while other authors improved the DES capabilities by integrating it with other techniques such as integer linear program [21] or the agent technology in [16].

Table I below summarizes the verification of different high-level properties in healthcare system, where P1: represents patient Flow, P2 represents length of stay, P3 represents patient waiting time, P4 represents medical doctor load rate, P5 represents medical doctor overtime rate, P6 represents staff scheduling, P7 represents resource allocation, and finally, P8 represents operation cost.

TABLE I: Simulation methods of high level healthcare issues

Ref	Properties								Method	Tools
	1	2	3	4	5	6	7	8		
[8]	√		√	√	√				DES	Arena
[9]	√		√		√				DES	Simio
[10]	√						√		DES	Simio
[11]	√						√	√	DES	Arena
[12]	√		√				√		DES	Arena
[15]		√					√		Grid	N/A
[16]	√	√							DES	JSim
[21]		√		√		√			DES-LIP	Arena
[19]		√					√	√	Agent	N/A
[20]								√	Agent	Teema
[22]			√			√			N/A	Simul8

Testing and verifying security related properties in healthcare systems has received some attentions recently. The authors in [23], [24] developed their own simulation model to test and validated their approach that enabled different actors in the e-Healthcare society to interact in a secure manner. Table II shows security properties that were addressed in healthcare systems, where the developed approach was tested for related performance issues using simulation methods.

TABLE II: Security requirements addressed in healthcare systems

Ref	Security Requirements				
	Authentic.	Confidentiality	Integrity	Privacy	Availability
[23]					
[24]				√	
[25]		√	√	√	
[26]	√	√	√		
[27]		√			
[28]	√	√	√		
[29]	√			√	√
[30]	√	√	√		
[31]	√	√		√	
[32]	√	√		√	
[33]				√	
[34]				√	

B. Low Level Performance Issues

ICT based healthcare systems are developed using several types of technologies related to communication, electronics, and medical data. Therefore, there are several performance parameters that affect its operation. For instance, in several performance issues are important in Wireless Body Sensor Networks (WBSN), such as Bit-Error Rate (BER), Signal to Noise Ratio (SNR), packet loss, and energy consumption. When ICT based healthcare systems are designed, several design parameters are optimized in order to enhance the performance of the system, hence, the designed need to be tested thoroughly before it is implemented and put into use.

The authors in [35] used a method to measure SNR in data collected by medical sensors by measuring pulse width, transmission power, data rate, and antenna gain. The authors in [36] and [37] provided a compressed sensing (CS) algorithm and a Block Sparse Bayesian Learning (BSBL) framework to enhance sampling of electrocardiogram (ECG) signals, which in turn can reduce power consumption. They used simulation to show a better root-mean-square, SNR, sampling-rate, and power consumption. In other approaches such as the work in [38] and [39], Matlab tool was used to measure power consumption, while other authors such as [25] and [26] customized their own simulator to measure the message size effects and the encryption technique on the power consumption.

Other works have focused in the ECG sensor design in order to reduce the power consumption. For instance, the authors in [40] proposed an asynchronous method to transmit data from an ECG front-end that is designed with a 2-bit level-crossing Analog-to-Digital Converter (ADC) combined with a pulse encoder circuit. In the same ADC concern, the authors in [41] presented a predictive sensing-based ADC architecture that has improved energy efficiency, compared to a conventional ADC, by predicting the next input sample, based on previous samples. In [42] the authors used simulation to show that their new hardware architecture for ECG sensors can reduce power consumption.

There is considerable work in testing medical sensors, such as the ECG sensor. Mukhopadhyay *et al.* [43] used an ECG database to test their proposed compression method that is intended to speed uo the sensing operations and reduce the amount of data storage when recording ECGs. Swamy *et al.* [44] used number of recorded ECGs taken from 12-lead ECG equipment to test their proposed algorithm to calculate the heart rate from ECG signals. Josko *et al.* [45] developed a technique to simulate ECG signals in order to test of an ECG identification algorithm, and thus enhance the algorithm design to detect the specific ECG segments accurately. Yalcinkaya *et al.* [46] presented a mathematical model of human heart to produce ECG waveforms. They relied on clinical experiments to examine the validity the functionality of the generated ECG signals. Touati et*et al.* [47] presented an ECG simulator to test the quality between the high-resolution wired sensors and a Labview model of three wireless sensors connected to an edge router. The authors validate their proposed system by comparing it with commercial system, then with theoretical system using Matlab simulation. Furthermore, Chen *et al.* [27] presented an ECG generator to test a cryptography system model. Their proposed model aims to utilize the ECG signal in order to secure the communication in wireless body sensor network. Therefore, the authors highlight the need of choosing an appropriate ECG generator to evaluate their security methodology. Balasubramanian *et al.* [28] used simulation method to measure the reliability percentage, number of error packet, percentage of battery discharge and throughput of the sensor node while being used to implement their proposed security protocol for WBSNs. Other authors such as Liang *et al.* [29] used a traditional paper and pencil method to verify security protocols in used in WBSNs.

TABLE III: Simulation methods of low level healthcare issues

	Properties				
Ref	SNR	BER	Energy	Test Bench	Tools
[26]			√	TC	N/A
[28]		√	√	N/A	j-sim
[30]			√	ECG DB	N/A
[35]	√			N/A	MatLab
[36]	√			ECG DB	C++
[37]	√	√	√	ECG DB	N/A
[38]			√	Gaussian	MatLab
[39]			√	TC	MatLab
[40]			√	TC	N/A
[41]			√	N/A	MatLab & CMOS
[42]			√	ECG DB	MatLab & CMOS
[43]			√	N/A	C Lang.
[44]	√			ECG DB	N/A
[45]	√			Real ECG	LabWindows/CVI
[46]	√			TC	MatLab
[47]			√	TC	LabView
[48]	√	√	√	Fading Channels	MatLab
[49]			√	N/A	QualNet
[50]			√	ECG DB	MatLab
[51]	√	√		Fading Channels	MatLab
[52]	√	√	√	N/A	MatLab
[53]			√	N/A	ADS

Table III summeriness the properties reflated to the lower level of healthcare design, along with the method and tool used to verify them. In addition, table II shows a list security requirements that some paper try to ensure in their systems, however due to the lack of available simulation framework, they intend to verify them using paper and pencil analysis.

III. Formal Verification Methods

Formal methods [54] use mathematical models for the analysis of computing, communication, and industrial systems in order to establish system correctness with mathematical rigor. Formal methods are highly recommended verification techniques for safety critical systems. Research in formal methods has recently led to the development of promising verification techniques that facilitate the early detection of defects and hence enhance the design quality. These techniques are accompanied by powerful tools that can automate various verification steps which have been successfully used for the analysis of a variety of complex systems [55]. The most commonly used techniques in formal methods are theorem proving [56] and model checking [57].

Formal methods techniques have been used for the verification of several healthcare aspects such as efficiency, security, reliability of WBSN, computer aided diagnosis, medical devices, access polices, and finally, ECG algorithms. The authors in [58] used the Communicating Sequential Processes (CSP) to model and verify properties about the workflow consistency, checking against timed specifications, and resource scheduling. The work in [59] applied formal method to verify the reliability of the software of a medical infusion pump, where they used model checking to verify different properties about the correct operation of the pump. The authors then conducted a forensic analysis using a tool called Program Slicing to detect which line code may cause system failure [60]. In the same context, the authors in [61] used CSP to model and verify software of various application for medical devices at Philips Healthcare like X-ray machines. They concluded that developing software using formal method produces a more reliable application than the traditional development methods. The authors in [62] used on hybrid automata to developed a formal model for a rate-adaptive pacemaker that which contains sensors for controlling the heart rate. The authors in [63] proposed an ECG based human verification system for both healthy and cardiac irregular conditions using the heartbeat level and segment level information fusion.

Masci *et al.* [64], [65], [66] used the PVS [67] theorem prover to formalize and verified safety requirements in a commercial PCA infusion pump to avoid accidental tampering of the infusion pump's settings. Based on this work, Paolo *et al.* [68] extended the model to translate the software implementation into a formal specification and thus create a behavior model, and then used the specifications in PVS to verify the human factors properties, and then extract design issues that might be detected in the user interface level. Then, those extracted design issues are applied on a real system implementation to conclude the efficiency of the verification approach. Mery *et al.* [69][70] used Event-B [71] for modeling the behavioral of heart nodes and verifying the functionality of a pacemaker controller. They modeled eight nodes in heart and generate the ECG to feed it inside the pacemaker and observe the output. Finally, the FHIR standard based e-Health system was modeled and verified using PRISM probabilistic model checker [72].

The authors in [73], [74] presented a method for automated verification the controller of a biosensor structure that is used in WBSN at a high level of abstraction. The sensor is used for reading the ECG and diagnosing the *QRS* characteristic to detect if the heart system suffers from abnormal behaviors. Then, in [75], They refined the block to a lower level of abstraction at the ECG wave specification level, where we formalized ECG signal components and then defined and validated several properties about it. Next, in [76], they presented a lower level of refinement for ECG signals and then, use the ECG model to further provide another lower level refined model for the *QRS* wave, which is considered fundamental component in ECG based diagnosis. Recently, the work in [77] used HOL theorem prover [78] for reasoning about molecular pathways in biological regulatory networks (BRNs), where the utilization and effectiveness of the proposed development has been shown by presenting the automatic analysis of reaction involving TP53 degradation and metabolic pathway known as Glycolysis.

In security domain, the authors in [79] utilized the formal model to measure the trust metric of U-healthcare systems' entities and their relationship using a model that consists of three layers; trust engine, security manager and security analyzer. The authors in [80] presented a formal specification model for producing a metric of measuring the survivability of the services inside any pervasive system. The authors evaluated the survivability degree based on the critical service operations. Table IV below summaries the work on using formal methods in verify healthcare system.

TABLE IV: Formal methods for verification of healthcare systems

Ref.	Verif. Field	Formal Tech.	Language	Medical Field	Support
[58]	Func.	M.C.	CSP	EMR	-
[59]	Func.	M.C.	C $\rightarrow$ Model	Device S/W	TCG
[61]	Func.	M.C.	CSP	Device S/W	-
[62]	Func.	T.P	Automata	Pacemaker	-
[68]	Func.	T.P.	PVS	Device S/W	TCG
[64]	Func.	M.C.	PVS	Infusion Pump	-
[69] [70]	Func.	T.P.	Event-B	Pacemaker	-
[73] [75] [76]	Func.	T.P.	Event-B	ECG Sensor	Sim.
[79]	Sec.	Other	N/A	EMR	-
[80]	Func.	Other	N/A	μ-Health	-
[81]	Func.	M.C.	CSP	CAD	Sim.
[82]	Sec.	Other	N/A	μ-Health	Sim.
[83]	Func.	M.C.	PRISM ML	DT	Sim.
[72]	Func.	T.P.	PRISM	FHIR	-
[77]	Func.	T.P.	HOL	BRNs	-

IV. Semi-Formal and Other Techniques

Semi-formal verification methods are based on formal syntax and allow informal semantics. There are several semi-formal languages and supporting tools that have been used for modeling and verification both in academia and industry. For instance, UML and Object Constraints Language, Petri Nets and its variation, and assertion based verification. Semi-formal methods have been used recently in testing healthcare systems. For instance, the authors in [84] used UML to formalize and translate the specification of operations in the Pulmonology Department (PD) into Timed Petri Net (TPN). They used a PD database to evaluate several timing properties in order to optimize the department and coordination of the patient flow by reducing the cost and patient waiting time according to available resources.

The authors in [85] used the Architecture Analysis and Description Language (AADL) integrated with their own tool chain to formally describe the architecture's components and generate a semi-formal model of the wireless system architecture. Then, they also used simulation to test several relevant functional and security properties in the WBSN. The authors in [86] proposed an automatic test generation tool with from UML specifications in order to improve the verification level of transforming the requirement of mHealth systems. The authors in [87] used the Structured Object-Formal Language (SOFL) to specify a brain tumor treatment system. Other authors developed an insulin pump system using the SOFL method [88] and used it to validate the specifications of the software embedded into the insulin pump system. Table V summarizes use of semi-formal methods in testing and verification of healthcare systems.

TABLE V: Semi-formal methods for testing healthcare systems

Ref.	Technique	Language	Healthcare Field	Support
[84]	M.C	TPN & UML	PD	Sim.
[85]	Other	AADL	WBSN	Sim.
[86]	M.C	UML	WBSN	TCG
[87]	Other	SOFL	DT	-
[88]	Other	SOFL	Device S/W	Sim.

V. Discussion and Open Issues

We found that there is a lack for a single verification framework for healthcare systems, where different types of properties can be tested, since they are considered hybrid systems with several technologies being used at the same time. Therefore, we identify potential open issues in the area of testing and verification of ICT based healthcare systems:

Test Case Generation. When conducting simulation, input test cases are required in order to test the system under different scenarios. Practically, it is impossible to cover all possible scenarios due to the huge number of cases required. Therefore, guided test case generation is a well known method for providing test cases. In several aspects of healthcare systems, there is a lack of availability of data that can be used for testing. For instance, in order to test ECG based algorithms, researchers rely on the recorded ECG data, which can be difficult to achieve due to privacy. In addition, these recorded data cannot provide good coverage in testing due to the lack of diversity and corner cases coverage. In this context, TCG can be conducted from formal or semi-formal specifications of ICT based systems.

Probabilistic Verification. In formal methods, most researchers used model checking technique in their verification, due to the nature of properties verified, while there are several complex features that requires more expressive formal languages than the ones used in model checking. For instance, the behavior of the medical system exhibits probabilistic features since workflow transitions occur with certain probabilities. Hence, it is essential to analyze the reliability of the overall medical system using probabilistic theorem proving techniques and model checking techniques.

Verifying of Trust in Healthcare Systems. There are several formal trust models in the literature, however, there is no standard reference that could have been adopted in implementations of healthcare systems. Therefore, proving a formal model for trust in healthcare domain is an appealing subject. This will help in addressing several security issues such as access control in the context of healthcare.

Verifying Privacy in Healthcare Systems. Several security techniques were reused in the context of healthcare systems, which have led into undesired breaches into private records. Therefore, it is essential to pay more attention into the verification of security aspects when they are integrated into of healthcare systems.

Verifying Data Integration. Data integration is the effort of linking independent data elements from different sources in order to create new useful information. It includes data collection, processing, storage, quality assurance, compilation, and analysis. Practically, there is a lot of data omission, transcription and computational errors at the primary collection source at the clinic level. Therefore, data obtained and collected by health facilities often lack quality, suffer from bias and missing values and, sometimes have computation errors. Hence, this data must be assessed and validated properly before put into analysis and use [89].

Modeling and Verification of Big Data in Healthcare

Big data [90] concept refers to the practice of collection and analysis of huge data sets and the algorithms, tools, and data centers that are used to analyze the massive information associated with this data. ICT based healthcare systems are good candidate for big data applications due to the large amounts of healthcare records and genomic data. In addition, the processing of this data requires complex resource and software configuration tasks [91], which adds more challenges to big data manipulation in this domain. On the other hand, several emerging issues are currently being integrated into the cloud, for instance, the development frameworks for cloud based medical images processing [92] is a new prominent subject where formal methods can be used in order to enhance the trust in such newly developed systems [77]. Verification of such algorithms is considered costly and challenging due to the huge amount of associated information. Hence, formal methods can provide the necessary background to be able to handle such challenge. In particular, several developed abstraction techniques that have supporting tools in both model checking and theorem proving can be used in this context.

Several cloud-based healthcare applications have been proposed recently [93], therefore, several security and privacy issues have been raised. For instance, the integrity of big data in the cloud has been highlighted as a challenging research problem [94]. Despite that existence of several data integrity verification methods, the healthcare owner may still be able to verify their data, that is stored remotely in the cloud, this, however, is a very complex process due to the huge amount of data and communication overhead. While proposed solutions suggest to apply mechanisms such as digital signatures on distributed cloud servers to verify healthcare realted data integrity, instead of retrieving the whole data, this methods can be subtle to several critical security problems if the method is not designed properly. In this context, there exists several model checking tools for security protocols that can effectively be used to verify such distributed algorithms. In addition, the processing of large amounts of genomic data requires complex resource and software configuration tasks [91], which adds more challenges to big data manipulation in the cloud. Finally, several emerging issues are currently being integrated into the cloud, for instance, the development frameworks for cloud based medical images processing [92] is a new prominent subject where formal methods can be used in order to enhance the trust in such newly developed systems [77].

VI. Conclusions

Testing and verification is essential in based on ICT healthcare systems due to the losses in lives and cost associated with bugs and errors in these systems. However, verifying the correctness of a healthcare system is not straightforward, due to their complexity and wide range of technologies used in their design. Therefore, several efforts were put into the area of testing and verification of these systems. In this paper we reviewed the state of the art on this subject, where we grouped methods into three categories: simulation based methods, formal methods, and semi-formal and other methods, and identified aspects of healthcare systems that were tested.

We concluded that the incorporation of recent technologies, such as cloud systems and big data, into health care systems have created several challenging problems. For instance, data integration creates considerable testing and verification issues, on the other hand, healthcare systems have several practical applications in the domain of big data, hence, integrating new methods developed to process big data may also impose several new challenges in testing these methods within healthcare systems. We have shown that there is a wide scope of existing methods being used for testing healthcare systems, while at the same time several challenging issues are being raised. Therefore, an up to date review on the state of the art on the subject can be beneficial to researchers.

REFERENCES

[1] T. Taylor, G. VanDyk, L. W. Funk, R. Hutcheon, and S. Schriber, "Therac 25: A new medical accelerator concept," *IEEE Transactions on Nuclear Science*, vol. 30, no. 2, pp. 1768–1771, 1983.

[2] "History's worst software bugs," 2005. [Online]. Available: http://www.wired.com/software/coolapps/news/2005/11/69355

[3] I. A. E. Agency, *Investigation of an Accidental Exposure of Radiotherapy Patients in Panama: Report of a Team of Experts*. Int. Atomic Energy Agency, 2001.

[4] B. J. Feder, "A heart device is found vulnerable to hacker attacks," *The New York Times*, Mar. 2008.

[5] "Ways EHRs can lead to unintended safety problems - amednews.com," 2013-06-27. [Online]. Available: http://www.amednews.com/article/20130225/profession/130229981/4/

[6] "Privacy incident - mount sinai medical center | miami beach, FL," 2013-06-27. [Online]. Available: http://www.msmc.com/privacy-incident

[7] "3 health incidents in breach roundup," 2013-06-27. [Online]. Available: http://www.databreachtoday.asia/3-health-incidents-in-breach-roundup-a-5403

[8] P.-H. Koo, J. Jang, K. Nielsen, and A. Kolker, "Simulation-based patient flow analysis in an endoscopy unit," in *IEEE Workshop on Health Care Management*, 2010, pp. 1–6.

[9] J. Taheri, Z. Gellad, D. Burchfield, and K. Cooper, "A simulation study to reduce nurse overtime and improve patient flow time at a hospital endoscopy unit," in *Simulation Conference*, 2012, pp. 1–12.

[10] Q. Zheng, J. Shen, Z.-q. Liu, K. Fang, and W. Xiang, "Resource allocation simulation on operating rooms of hospital," in *IEEE Int. Conf. on Industrial Engineering and Engineering Management*, vol. 3, 2011, pp. 1744–1748.

[11] A. Mousavi, A. Komashie, and S. Tavakoli, "Simulation-based real-time performance monitoring (simmon): A platform for manufacturing and healthcare systems," in *Simulation Conference*, 2011, pp. 600–611.

[12] S. Wong, K. Tsui, K. Chin, and M. Xu, "A simulation study to achieve healthcare service quality improvement in accident amp; emergency department," in *IEEE Int. Conf. on Quality and Reliability*, 2011, pp. 259–263.

[13] N. Collins and C. Watson, "Introduction to ArenaTM," in *Simulation Conference Proceedings*, 1993, pp. 205–212.

[14] C. Pegden and D. Sturrock, "Introduction to simio," in *Simulation Conference (WSC)*, 2009, pp. 314–321.

[15] M. Thorwarth and A. Arisha, "A simulation-based decision support system to model complex demand driven healthcare facilities," in *Simulation Conference*, 2012, pp. 1–12.

[16] M. Raunak and L. Osterweil, "Resource management for complex, dynamic environments," *IEEE Transactions on Software Engineering*, vol. 39, no. 3, pp. 384–402, Mar. 2013.

[17] A. Wise, *Little-JIL 1.5 Language Report*. University of Massachusetts Amherst: Amherst, MA, 2006.

[18] A. Wise, "JSim agent behavior specification language," University of Massachusetts Amherst, Tech. Rep., Jul. 2013. [Online]. Available: http://laser.cs.umass.edu/documentation/jsim/language.html

[19] C.-h. Choi and W. Cheung, "A multi-agent resource allocation framework for patient journey shortening," in *IEEE Int. Conf. on Bioinformatics and Biomedicine Workshops*, 2010, pp. 481–486.

[20] R. Paranjape and S. Gill, "Agent-based simulation of healthcare for type II diabetes," in *Int. Conf. on Advances in System Simulation*, 2010, pp. 22–27.

[21] M. Centeno, R. Giachetti, R. Linn, and A. Ismail, "A simulation-ILP based tool for scheduling ER staff," in *Simulation Conference*, vol. 2, 2003, pp. 1930–1938.

[22] S.-J. Weng, T. Wu, G. Mackulak, and J. Fowler, "Distributed resource allocation for healthcare systems," in *IEEE Int. Conf. on Service Operations and Logistics, and Informatics*, vol. 1, 2008, pp. 1078–1083.

[23] K. Saleem, A. Derhab, J. Al-Muhtadi, and B. Shahzad, "Human-oriented design of secure machine-to-machine communication system for e-healthcare society," *Computers in Human Behavior*, 2014.

[24] K. Saleem, A. Derhab, and J. Al-Muhtadi, "Low delay and secure m2m communication mechanism for ehealthcare," in *e-Health Networking, Applications and Services (Healthcom), 2014 IEEE 16th International Conference on*. IEEE, 2014, pp. 105–110.

[25] L. Chen, Z. Cao, R. Lu, X. Liang, and X. Shen, "EPF: an eventaided packet forwarding protocol for privacy preserving mobile healthcare social networks," in *Global Communications Conference*, 2011, pp. 1–5.

[26] M. Majidi, R. Mobarhan, A. Hardoroudi, A. H-Ismail, and A. Parchinaki, "Energy cost analyses of key management techniques for secure patient monitoring in WSN," in *IEEE Open Systems*, 2011, pp. 111–115.

[27] X. Chen, Y. Zhang, G. Zhang, and Y. Zhang, "Evaluation of ECG random number generator for wireless body sensor networks security," in *Biomedical Engineering and Informatics*, 2012, pp. 1308–1311.

[28] V. Balasubramanian, D. Hoang, and T. Zia, "Addressing the confidentiality and integrity of assistive care loop framework using wireless sensor networks," in *Int. Conf. on Systems Engineering*, 2011, pp. 416–421.

[29] X. Liang, R. Lu, L. Chen, X. Lin, and X. Shen, "PEC: a privacy-preserving emergency call scheme for mobile healthcare social networks," *Journal of Communications and Networks*, vol. 13, no. 2, pp. 102–112, 2011.

[30] Z. Zhang, H. Wang, A. Vasilakos, and H. Fang, "ECG-Cryptography and authentication in body area networks," *IEEE Trans. on Information Technology in Biomedicine*, vol. 16, no. 6, pp. 1070–1078, 2012.

[31] R. Lu, X. Lin, and X. Shen, "SPOC: a secure and privacy-preserving opportunistic computing framework for mobile-healthcare emergency," *IEEE Transactions on Parallel and Distributed Systems*, vol. 24, no. 3, pp. 614–624, 2013.

[32] S. Avancha, A. Baxi, and D. Kotz, "Privacy in mobile technology for personal healthcare," *ACM Computing Surveys*, 2009.

[33] M. Kumar, "Security issues and privacy concerns in the implementation of wireless body area network," in *Int. Conf. on Information Technology*, Dec 2014, pp. 58–62.

[34] M. Rushanan, A. Rubin, D. Kune, and C. Swanson, "SoK: Security and privacy in implantable medical devices and body area networks," in *IEEE Symposium on Security and Privacy*, May 2014, pp. 524–539.

[35] H. Shaban, M. El-Nasr, and R. M. Buehrer, "Toward a highly accurate ambulatory system for clinical gait analysis via UWB radios," *IEEE Transactions on Information Technology in Biomedicine*, vol. 14, no. 2, pp. 284–291, 2010.

[36] M. Balouchestani, K. Raahemifar, and S. Krishnan, "A high reliability detection algorithm for wireless ECG systems based on compressed sensing theory," in *Int. Conf. of the IEEE Engineering in Medicine and Biology Society*, July 2013, pp. 4722–4725.

[37] M. Balouchestani, K. Raahemifar, and S. Krishnan, "New sampling approach for wireless ECG systems with compressed sensing theory," in *IEEE Int. Symposium on Medical Measurements and Applications Proceedings*, May 2013, pp. 213–218.

[38] V. Karira, S. Kharidehal, and D. Das, "Selective multicast protocol for wireless body area networks (WBAN) for power conservation," in *Annual IEEE India Conference*, 2009, pp. 1–4.

[39] B. Otal, L. Alonso, and C. Verikoukis, "Highly reliable energy-saving mac for wireless body sensor networks in healthcare systems," *IEEE Journal on Selected Areas in Communications*, vol. 27, no. 4, pp. 553–565, 2009.

[40] A. Mansano, Y. Li, S. Bagga, and W. Serdijn, "An asynchronous event-driven data transmitter for wireless ECG sensor nodes," in *IEEE Biomedical Circuits and Systems Conference*, Oct 2014, pp. 404–407.

[41] J. Van Rethy, M. De Smedt, M. Verhelst, and G. Gielen, "Predictive sensing in analog-to-digital converters for biomedical applications," in *Int. Symposium on Signals, Circuits and Systems*, July 2013, pp. 1–4.

[42] M. Zare and M. Maymandi-Nejad, "A fully digital front-end architecture for ecg acquisition system with 0.5 v supply," *IEEE Transactions on Very Large Scale Integration Systems*, vol. PP, no. 99, pp. 1–1, 2015.

[43] S. Mukhopadhyay, M. Mitra, and S. Mitra, "An ECG data compression method via R-peak detection and ASCII character encoding," in *Int. Conf. on Computer, Communication and Electrical Technology*, Mar 2011, pp. 136–141.

[44] P. Swamy, S. Jayaraman, and M. Chandra, "An improved method for digital time series signal generation from scanned ECG records," in *Bioinformatics and Biomedical Technology*, 2010, pp. 400–403.

[45] A. Josko and R. Rak, "Effective simulation of signals for testing ECG analyzer," *IEEE Transactions on Instrumentation and Measurement*, vol. 54, no. 3, pp. 1019–1024, June 2005.

[46] F. Yalcinkaya, E. Kizilkaplan, and A. Erbas, "Mathematical modelling of human heart as a hydroelectromechanical system," in *Int. Conf. on Electrical and Electronics Engineering*, Nov 2013, pp. 362–366.

[47] F. Touati, R. Tabish, and A. Ben Mnaouer, "Towards u-health: An indoor 6LoWPAN based platform for real-time healthcare monitoring," in *IFIP Wireless and Mobile Networking Conference*, April 2013, pp. 1–4.

[48] S. Ibrahim and G. Kang, "Error rate analysis and co-operative communication for ad-hoc and sensor network to combat rician fading based

on disaster healthcare," in *IEEE Int. Conf. on e-Health Networking, Applications and Services*, 2012, pp. 458–461.
[49] N. Nikzad, J. Yang, P. Zappi, T. Rosing, and D. Krishnaswamy, "Model-driven adaptive wireless sensing for environmental healthcare feedback systems," in *IEEE Int. Conf. on Communications*, 2012, pp. 3439–3444.
[50] A. Dixon, E. Allstot, D. Gangopadhyay, and D. Allstot, "Compressed sensing system considerations for ECG and EMG wireless biosensors," *IEEE Transactions on Biomedical Circuits and Systems*, vol. 6, no. 2, pp. 156–166, April 2012.
[51] M. Mahboob, "Signalling and detection of parallel triple layer wireless sensor networks with M-ary orthogonal modulation," in *IEEE Symposium on Communications and Vehicular Technology in the Benelux*, 2012, pp. 1–6.
[52] H. Shaban, M. El-Nasr, and R. Buehrer, "A framework for the power consumption and ber performance of ultra-low power wireles swearable healthcare and human locomotion tracking systems via UWB radios," in *IEEE Int. Symposium on Signal Processing and Information Technology*, 2009, pp. 322–327.
[53] S. Manjula and D. Selvathi, "Design of micro power CMOS LNA for healthcare applications," in *Int. Conf. on Devices, Circuits and Systems*, 2012, pp. 153–156.
[54] J. Abrial, "Faultless systems: Yes we can!" *IEEE Computer Journal*, vol. 42, no. 9, pp. 30–36, 2009.
[55] P. Boca, J. Bowen, and J. Siddiqi, *Formal Methods: State of the Art and New Directions*. Springer, 2010.
[56] T. Kropf, *Introduction to Formal Hardware Verification*. Springer, 1999.
[57] C. Baier and J.-P. Katoen, *Principles of Model Checking*. Cambridge, MA, USA: The MIT Press, 2008.
[58] J. Faber, "A timed model for healthcare workflows based on CSP," in *Int. Workshop on Software Engineering in Health Care*, 2012, pp. 1–7.
[59] R. Jetley, S. Purushothaman Iyer, and P. Jones, "A formal methods approach to medical device review," *Computer*, vol. 39, no. 4, pp. 61–67, Apr. 2006.
[60] C. Duanzhi, "Program slicing," in *International Forum on Information Technology and Applications*, vol. 1, 2010, pp. 15–18.
[61] J. Groote, A. Osaiweran, and J. Wesselius, "Analyzing the effects of formal methods on the development of industrial control software," in *IEEE Int. Conf. on Software Maintenance*, 2011, pp. 467–472.
[62] M. Kwiatkowska, H. Lea-Banks, A. Mereacre, and N. Paoletti, "Formal modelling and validation of rate-adaptive pacemakers," in *IEEE Int. Conf. on Healthcare Informatics*, September 2014, pp. 23–32.
[63] M. Li and X. Li, "Verification based ECG biometrics with cardiac irregular conditions using heartbeat level and segment level information fusion," in *IEEE Int. Conf. on Acoustics, Speech and Signal Processing*, May 2014, pp. 3769–3773.
[64] P. Masci, A. Ayoub, P. Curzon, M. D. Harrison, I. Lee, and H. Thimbleby, "Verification of interactive software for medical devices: PCA infusion pumps and fda regulation as an example," in *Symposium on Engineering Interactive Computing Systems*. ACM, 2013, pp. 81–90.
[65] P. Masci, P. Curzon, D. Furniss, and A. Blandford, "Using pvs to support the analysis of distributed cognition systems," *Innovations in Systems and Software Engineering*, vol. 11, no. 2, pp. 113–130, 2015.
[66] P. Masci, R. Ruksenas, P. Oladimeji, A. Cauchi, A. Gimblett, Y. Li, P. Curzon, and H. Thimbleby, "The benefits of formalising design guidelines: a case study on the predictability of drug infusion pumps," *Innovations in Systems and Software Engineering*, vol. 11, no. 2, pp. 73–93, 2015.
[67] N. Shankar, "PVS: combining specification, proof checking, and model checking," in *Formal Methods in Computer-Aided Design*, ser. Lecture Notes in Computer Science. Springer Berlin Heidelberg, Jan. 1996, no. 1166, pp. 257–264.
[68] P. Masci, Y. Zhang, P. Jones, P. Curzon, and H. Thimbleby, "Formal verification of medical device user interfaces using PVS," in *Fundamental Approaches to Software Engineering*, 2014, pp. 1–15.
[69] D. Mery and N. K. Singh, "Closed-loop modeling of cardiac pacemaker and heart," in *Foundations of Health Information Engineering and Systems*, ser. Lecture Notes in Computer Science, J. Weber and I. Perseil, Eds. Springer Berlin Heidelberg, Jan. 2013, no. 7789, pp. 151–166.
[70] D. Mry and N. K. Singh, "Medical protocol diagnosis using formal methods," in *Int. Conference on Foundations of Health Informatics Engineering and Systems*. Springer-Verlag, 2012, pp. 1–20.
[71] J. Abrial, *Modelling in Event-B: System and Software Engineering*. Cambridge University Press, 2009.
[72] U. Pervez, O. Hasan, K. Latif, S. Tahar, A. Gawanmeh, and M. S. Hamdi, "Formal reliability analysis of a typical fhir standard based e-health system using prism," in *e-Health Networking, Applications and Services (Healthcom)*. IEEE, 2014, pp. 43–48.
[73] H. Al Hamadi, A. Gawanmeh, and M. Al-Qutayri, "A verification methodology for a wireless body sensor network functionality," in *IEEE-EMBS Biomedical and Health Informatics*, June 2014, pp. 635–639.
[74] H. Al-Hamadi, A. Gawanmeh, and M. Al-Qutayri, "Theorem proving verification of privacy in WBSN for healthcare systems," in *Int. Conf. on Electronics, Circuits, and Systems*. IEEE, 2013, pp. 100–101.
[75] H. Al-Hamadi, A. Gawanmeh, and M. Al-Qutayri, "Formalizing electrocardiogram (ECG) signal behavior in Event-B," in *IEEE Int. Conf. on e-Health Networking, Applications and Services*, Oct 2014, pp. 55–60.
[76] H. Al-Hamadi, A. Gawanmeh, and M. Al-Qutayri, "Formal validation of QRS wave within ECG," in *IEEE Int. Conf. on Information and Communication Technology Research*, May 2015, pp. 190–193.
[77] S. Ahmad, O. Hasan, and U. Siddique, "On the formalization of zsyntax with applications in molecular biology," *Scalable Computing: Practice and Experience*, vol. 16, no. 1, 2015.
[78] M. Gordon and T. Melham, *Introduction to HOL: A Theorem Proving Environment for Higher Order Logic*. Cambbridge Univ, Press, 1993.
[79] C. Subramaniam, A. Ravi, A. Nayak, and S. Thunuguntla, "Actor based domain specific privacy model for U-healthcare system," in *Int. Conf. on Digital Content, Multimedia Technology and its Applications*, 2010, pp. 381–385.
[80] A. Ayara and F. Najjar, "A formal specification model of survivability for pervasive systems," in *International Symposium on Parallel and Distributed Processing with Applications*, 2008, pp. 444–451.
[81] O. Faust, U. Acharya, and T. Tamura, "Formal design methods for reliable computer-aided diagnosis: A review," *IEEE Reviews in Biomedical Engineering*, vol. 5, pp. 15–28, 2012.
[82] A. Gawanmeh, "An axiomatic model for formal specification requirements of ubiquitous healthcare systems," in *IEEE Consumer Communications and Networking Conference*, 2013, pp. 898–902.
[83] A. Sorathiya, A. Bracciali, and P. Li, "Formal reasoning on qualitative models of coinfection of HIV and tuberculosis and HAART therapy," *BMC Bioinformatics*, vol. 11, p. S67, Jan. 2010.
[84] M. Fanti, A. Mangini, M. Dotoli, and W. Ukovich, "A three-level strategy for the design and performance evaluation of hospital departments," *IEEE Transactions on Systems, Man, and Cybernetics: Systems*, vol. 43, no. 4, pp. 742–756, 2013.
[85] K. Kang, M.-Y. Nam, and L. Sha, "Model-based analysis of wireless system architectures for real-time applications," *IEEE Transactions on Mobile Computing*, vol. 12, no. 2, pp. 219–232, 2013.
[86] V. Jones, "Model driven development of m-health systems (with a touch of formality)," in *IEEE Int. Conf. on Pervasive Computing and Communications Workshops*, 2006, pp. 580–584.
[87] A. Mat and A. Masli, "SOFL-based approach for requirements analysis of brain tumor treatment system," in *Int. Conf.on Computer Information Science*, vol. 2, 2012, pp. 885–888.
[88] J. Wang, S. Liu, Y. Qi, and D. Hou, "Developing an insulin pump system using the SOFL method," in *Asia-Pacific Software Engineering Conf.*, 2007, pp. 334–341.
[89] M. L. On, V. Bennett, and M. Whittaker, "Issues and challenges for health information systems in the pacific," *Pacific health dialog*, vol. 18, no. 1, p. 20, 2012.
[90] P. Russom, "Big data analytics," *TDWI Best Practices Report, Fourth Quarter*, 2011.
[91] P. Church and A. Goscinski, "Selected approaches and frameworks to carry out genomic data analysis on the cloud," *Scalable Computing: Practice and Experience*, vol. 16, no. 1, 2015.
[92] C. Jansen, M. Beier, M. Witt, J. Wu, and D. Krefting, "Extending xnat towards a cloud-based quality assessment platform for retinal optical coherence tomographies," *Scalable Computing: Practice and Experience*, vol. 16, no. 1, 2015.
[93] B. Calabrese and M. Cannataro, "Cloud computing in healthcare and biomedicine," *Scalable Computing: Practice and Experience*, vol. 16, no. 1, 2015.
[94] C. Liu, R. Ranjan, X. Zhang, C. Yang, and J. Chen, "A big picture of integrity verification of big data in cloud computing," in *Handbook on Data Centers*. Springer, 2015, pp. 631–645.