Computational Intelligence for Digital Healthcare

Abdel-Badeeh M. Salem[0000-0001-5013-4339]

Faculty of Computer and Information Sciences, Ain Shams University, Cairo, Egypt
absalem@cis.asu.edu.eg, abmsalem@yahoo.com

Abstract. Digital healthcare (DH) is a multidisciplinary field of research, at the intersection of medical sciences, biology sciences, biochemistry neurosciences, cognitive sciences and informatics. In the last years, various computational intelligence (CI) techniques and methodologies have been proposed by the researchers in order to develop digital knowledge-based systems (DKBS) for different medical and healthcare tasks. These systems are based on artificial intelligence (AI) concepts and theories. Many types of DKBS are in existence today and are applies to different healthcare domains and tasks. The objective of the paper is to presents a comprehensive and up-to-date research in the area of DHI covering a wide spectrum of CI methodological and intelligent algorithmic issues, discussing implementations and case studies, identifying the best design practices, assessing implementation models and practices of AI paradigms in digital healthcare systems .This paper presents some of the CI techniques for managing and engineering knowledge in digital healthcare systems(DHS). Some of the research results and applications of the author and his colleagues that have been carried out in last years are discussed.

Keywords: machine learning, computational intelligence, Artificial Intelligence, knowledge engineering, digital healthcare informatics.

1. Introduction

Computational intelligence (CI) is the study of intelligent computer algorithms that improve automatically through experience. CI aims to enable computers to learn from data and make improvements without any dependence on commands in a program.CI is an inherently interdisciplinary, includes; neurobiology, information theory, probability, statistics, AI, control theory, Bayesian methods, physiology and philosophy [1,2].

In the recent years, various AI paradigms and CI techniques have been proposed by the researchers in order to develop efficient and smart systems in the areas of health informatics and health monitoring systems.AI and CI offers robust, intelligent algorithms and smart methods that can help to solve problems in a variety of health and life sciences areas [3, 4, 5, 6].

There are numerous examples of successful applications of CI in areas of diagnosis and prevention, prognosis and therapeutic decision making.

CI algorithms are used for the following tasks; (a) discovering new diseases, (b) finding predictive and therapeutic biomarkers, and(c) detecting relationships and structure among the clinical. CI contributes to the enhancement of management and information retrieval processes leading to development of intelligent (involving ontologies and natural language processing) and integrated literature searches.

Moreover, applications of CI in bioinformatics include the following areas of research ;(a) microarray analysis, chromosome and proteome databases, modeling of inhibition of metabolic networks(b) signal analysis (echocardiograph images and electroencephalograph time series). and (c) drug delivery and software for pattern recognition in biomedical data [7,8,9,10].

This paper discusses the potential role of the AI and CI approaches, techniques, which are used in developing the intelligent health informatics and health monitoring systems.

The paper discusses the following CI paradigms: (a) bio-inspired computing, (b) analogical reasoning computing, (c) vagueness and fuzzy computing, and (d) deep learning.

Also, the paper presents the challenges as well as the current research directions in the areas of digital health informatics.

Examples of the research performed by the author and his associates at Artificial Intelligence and Knowledge Engineering Research Labs, (ASU-AIKE labs) are also included.

The following cases and diseases are presented; cancer, heart, brain tumor, thrombosis diseases, Pandemic Influenza, Diabetics type-2, and volume visualization of the interior body.

The paper is organized as follows: Section 2 discusses the smart health monitoring paradigms. Section 3 reviews the bio-inspired computing approaches. In section 4, we discuss the analogical reasoning paradigms.

While section 5 discusses the vagueness and Fuzzy computing Section 6 presents our cases and applications, section 7 presents our future research directions and then we conclude in section 8.

2. Smart health monitoring systems (SHMS) models

SHMS involves deploying CI, information, and networking technologies to aid in preventing disease, improving the quality of care and lowering overall cost [10,11]. Currently, we have the following SHMS models;

- **Real-Time Monitoring Model**. In this model, sophisticated sensors and mobile devices can feed real-time medical data directly to patients and doctors via secure computing networks.
- **Computer-Aided Surgery Model**. In this model, advanced robotic devices make surgery more accurate and potentially less invasive
- **Telemedicine Model.** In which, automated tools in the home and on mobile devices are able help patients interact with providers remotely, enabling the patients to adjust their daily lives by better managing their own care.

- **Population-Based Care Model**. In which, monitoring devices enable collection of data from large populations with lower administrative and research costs than current method.
- **Personalized Medicine Model**. In this system, machine learning and predictive modeling will identify trends and causal relationships in medical data – leading to improved understanding of disease, development of new cures, and more accurate treatments tailored to each patient's specific needs
- **Ubiquitous Computing Model**. This model is characterized by improved security and privacy ensure the integrity of data stored in the "cloud," allowing stakeholders – patients, providers, and relatives – to access the right information at the right time from anywhere in the world
- **Decision Support Model**. In which, computer systems offer possible diagnoses and recommend treatment approaches, allowing doctors to quickly assess situations and viable options
- **Health 2.0 Model.** In which, Web-based tools such as wikis and social networks connect patients and clinicians to shared experiences, symptoms and treatments.

3. Bio-inspired computing

Figure 1 shows the different biological techniques of the bio-inspired computing this section presents a brief overview about the different bio-inspired techniques, namely; artificial neural networks, support vector machines, deep learning, genetic algorithms, evolutionary computing, and DNA computing.

3.1 Artificial Neural Networks (ANN)

ANN is a class of learning algorithm consisting of multiple nodes that communicate through their connecting synapses. ANN are inspired in biological models of brain functioning [10, 12].

They are capable of learning by examples and generalizing the acquired knowledge. Due to these abilities the neural networks are widely used to find out nonlinear relations which otherwise could not be unveiled due to analytical constraints. The learned knowledge is hidden in their structure thus it is not possibly to be easily extracted and interpreted. ANN can be used in the following medical purposes:

1. **Modelling**: simulating the functions of the brain and neurosensory organs.
2. **Signal processing:** Bioelectric signal filtering and evaluation
3. **System control and checking:** Intelligent artificial machine control and checking based on responses of biological or technical systems given to any signals.
4. **Classification tasks:** Interpretation of physical and instrumental findings to achieve more accurate diagnosis.
5. **Prediction:** provide prognostic information based on retrospective parameter analysis.

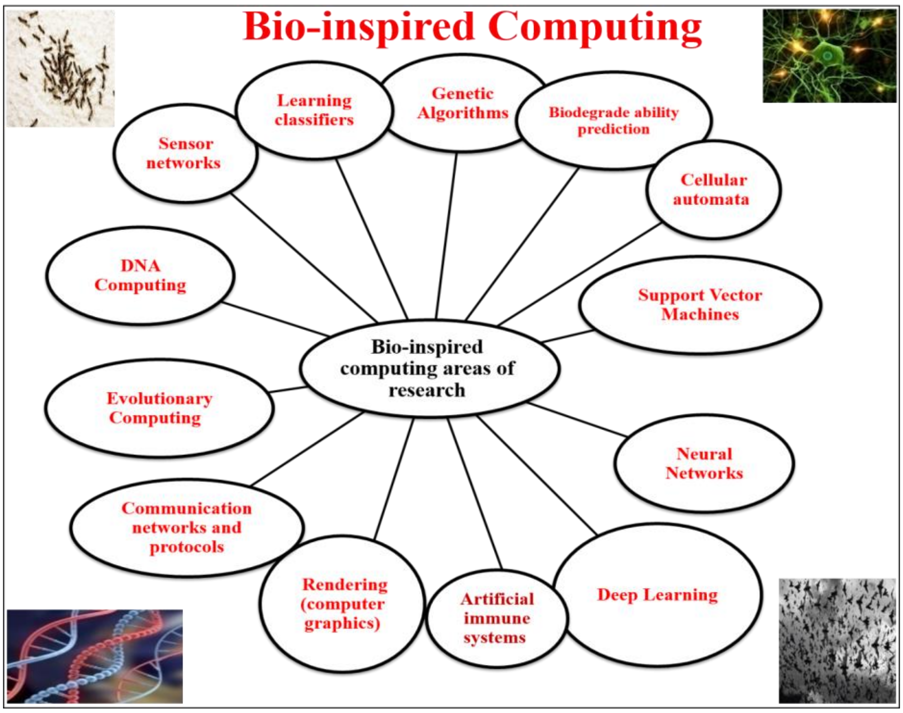

Fig.1. Bio-inspired computing

3.2 Support Vector Machines (SVM)

SVM are new learning-by example paradigm for classification and regression problems [10,13]. Their main advantage lies in the structure of the learning algorithm which consists of a constrained quadratic optimization problem (QP), thus avoiding the local minima drawback of NN. The approach has its roots in statistical learning theory (SLT) and provides a way to build "optimum classifiers" according to some optimality criterion that is referred to as the maximal margin criterion. An interesting development in SLT is the introduction of the Vapnik-Chervonenkis (VC) dimension, which is a measure of the complexity of the model. The trade-off between complexity and accuracy led to a range of principles to find the optimal compromise. Vapnik and co-authors' work have shown the generalization to be bounded by the sum of the training error and a term depending on the Vapnik-Chervonenkis (VC) dimension of the learning machine leading to the formulation of the structural risk minimization (SRM) principle. By minimizing this upper bound, which typically depends on the margin of the classifier, the resulting algorithms lead to high generalization in the learning process [10].

3.3 Deep Learning (DL)

Deep learning is a branch of AI covering a spectrum of current exciting research and industrial innovation that provides more efficient algorithms to deal with large-scale data in healthcare, recommender systems, learning theory, robotics, games, neurosciences, computer vision, speech recognition, language processing,human-computer interaction, drug discovery, biomedical informatics, act [14,15,16]. DL provides efficient algorithms to deal with large-scale data in many areas, see Figure 2.

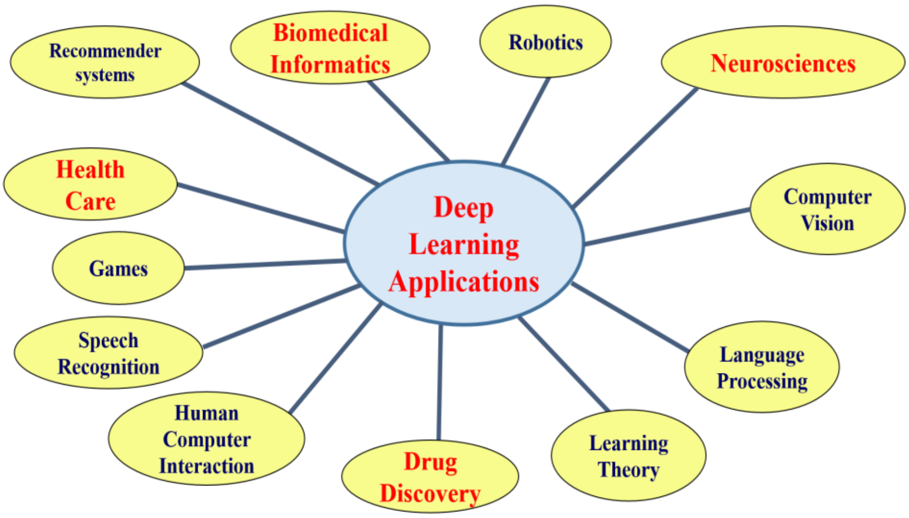

Fig.2. Deep learning applications

3.4 Genetic Algorithms (GA)

GA follows the lead of genetics, reproduction, evolution and the survival for the fittest theory by Darwin. GA is a class of machine learning algorithm that is based on the theory of evolution [10, 17]. Genetic Algorithms (GA) provide an approach to learning that based loosely on simulated evolution. The GA methodology hinges on a population of potential solutions, and as such exploits the mechanisms of natural selection well known in evolution. Rather than searching from general to specific hypothesis or from simple to complex GA generates successive hypotheses by repeatedly mutating and recombining parts of the best currently known hypotheses. The GA algorithm operates by iteratively updating a poll of hypotheses (population). One each iteration, old members of the population are evaluated according a fitness function. A new generation is then generated by probabilistically selecting the fittest individuals form the current population. Some of these selected individuals are carried forward into the next generation population others are used as the bases for creating new offspring individuals by applying genetic operations such as crossover and mutation.

3.5 Evolutionary Computing (EC)

EC is an approach to the design of learning algorithms that is structured along the lines of the theory of evolution. A collection of potential solutions for a problem compete with each other. The best solutions are selected and combined with each other according to a kind of ‘survival of the fittest’ strategy. GA are a well-known variant of evolutionary computation [10, 17].

3.6 DNA Computing

DNA computing is essential computation using biological molecules rather than traditional silicon chips. In recent years, DNA computing has been a research tool for solving complex problems. Despite this, it is still not easy to understand. The main idea behind DNA (Deoxyribo Nucleic Acid) computing is to adopt a biological (wet) technique as an efficient computing vehicle, where data are represented using strands of DNA. Even though a DNA reaction is much slower than the cycle time of a silicon-based computer, the inherently parallel processing offered by the DNA process plays an important role. This massive parallelism of DNA processing is of particular interest in solving NP-complete or NP-hard problems [18,19].

It is not uncommon to encounter molecular biological experiments which involve 6 × 1016/ml of DNA molecules. This means that we can effectively realize 60,000 Tera Bytes of memory, assuming that each string of a DNA molecule expresses one character. The total execution speed of a DNA computer can outshine that of a conventional electronic computer, even though the execution time of a single DNA molecule reaction is relatively slow. A DNA computer is thus suited to problems such as the analysis of genome information, and the functional design of molecules (where molecules constitute the input data) [20].

DNA computing will solve that problem and serve as an alternative technology. DNA computing is also known as molecular computing. It is computing using the processing power of molecular information instead the conventional digital components. It is one of the non-silicon-based computing approaches. DNA has been shown to have massive processing capabilities that might allow a DNA-based computer to solve complex problems in a reasonable amount of time [20].

4. Analogical reasoning computing (ARC)

ARC provides both a methodology for problem solving and a cognitive model of people [21, 22, 23, 24]. Case-Based Reasoning (CBR) is the most common technique of the ARC oaradigms.CBR means reasoning from experiences or “old cases” in an effort to solve problems, critique solutions and explain anomalous situations. The case is a list of features that lead to a particular outcome; e.g. The information on a patient history and the associated diagnosis. We feel more comfortable with older doctors because they have seen and treated more patients who have had illnesses similar to our own. CBR is an analogical reasoning method provides both: a methodology for building efficient knowledge-based reasoning systems (CBRS), and a cognitive model for People. CBR is a preferred method of reasoning in dynamically changing situations and other situations where solutions are not clear cut [22].

Most commonly application of CBR used in developing expert systems technology. In CBR expert systems, the system can reason from analogy from the past cases. This system contains what is called “case-memory” which contains the knowledge in the form of old cases (experiences). CES solves new problems by adapting solutions that were used for previous and similar problems [22]. The methodology of CBR directly addresses the problems found in rule-based technology, namely: knowledge acquisition, performance, adaptive solution, maintenance.

According to Kolodner [21], CBR from the computational perspective refers to a number of concepts and techniques (e.g. data structures and intelligent algorithms) that can be used to perform the following operations; (a) record and index cases, (b) search cases in the case-memory to identify the ones that might be useful in solving new cases when they are presented, (c) modify earlier cases to better match new cases, and (d) synthesize new cases when they are needed, see figure 3.

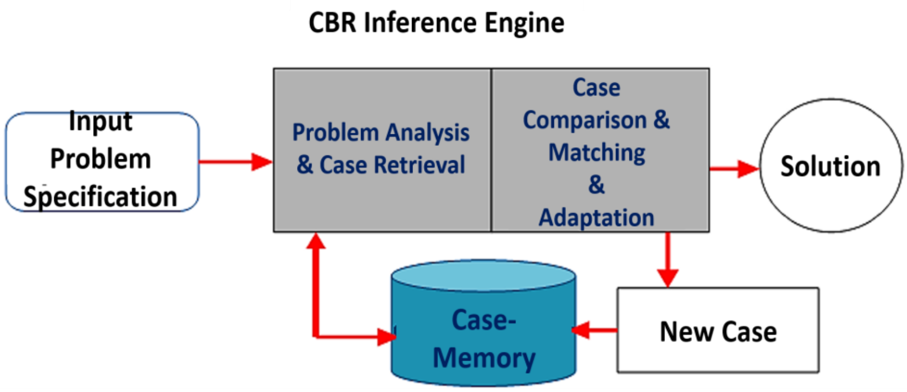

Fig. 3. Case-based reasoning methodology

5. Vagueness and fuzzy computing

5.1 Rough sets

Rough set theory was proposed as a new approach to vague concept description from incomplete data. The rough set theory is one of the most useful techniques in many real-life applications such as medicine, pharmacology, engineering, banking and market analysis. This theory provides a powerful foundation to reveal and discover important structures in data and to classify complex objects. The theory is very useful in practice, e.g. in medicine, pharmacology, engineering, banking, financial and market analysis [25]. In what follows, we can summarize the benefits and advantages of rough set theory:

1. Deals with vagueness data and uncertainty.
2. Deals with reasoning from imprecise data.
3. Used to develop a method for discovering relationships in data
4. Provides a powerful foundation to reveal and discover important structures in data and to classify complex objects.
5. Do not need any preliminary or additional information about data.
6. Concerned with three basics: granularity of knowledge, approximation of sets and data mining

5.2 Fuzzy Rules

Fuzzy logic allows one to express knowledge in a rule format that is close to a natural language expression. The difference between this fuzzy rule and the Boolean-logic rules we used in our forward- and backward-chaining examples is that the clauses "temperature is hot" and "humidity is sticky" are not strictly true or false. Clauses in fuzzy rules are real-valued functions called membership functions that map the fuzzy set "hot" onto the domain of the fuzzy variable "temperature" and produce a truth-value that ranges from 0.0 to 1.0 (a continuous output value, much like neural networks).

Reasoning with fuzzy rule systems is a forward-chaining procedure. The initial numeric data values are fuzzified, that is, turned into fuzzy values using the membership functions. Instead of a match and conflict resolution phase where we select a triggered rule to fire, in fuzzy systems, all rules are evaluated, because all fuzzy rules can be true to some degree (ranging from 0.0 to 1.0). The antecedent clause truth values are combined using fuzzy logic operators (a fuzzy conjunction or and operation takes the minimum value of the two fuzzy clauses).Next, the fuzzy sets specified in the consequent clauses of all rules are combined, using the rule truth values as scaling factors. The result is a single fuzzy set, which is then defuzzified to return a crisp output value. More technical details and applications can be found in the recent book of Voskuhl [26].

6 Case studies and applications

6.1 CI for Thyroid Cancer Diagnosis

Cancer is a group of more than 200 different diseases. From the medical point of view, Cancer occurs when cells become abnormal and keep dividing and forming either benign or malignant tumors. Cancer has initial signs or symptoms if any is observed, the patient should perform complete blood count and other clinical examinations. To specify cancer type, patient needs to perform special lab-tests. In our research Labs, we have performed an interesting research for developing intelligent systems for thyroid cancer diagnoses. .This research are based on using case-based and rule-based reasoning, ontological engineering, and artificial neural networks [27, 28, 29].

Figure 4 shows an examples for the encoded rules for cancer diagnosis..

Rule1:
IF the symptom is changes in bowel habits,
or The symptom is unusual bleeding,
or The symptom is thickening lymph
Then cancer is infecting

Rule2:
IF cancer is infecting,
and The symptom is severe headaches,
and The symptom is seizures
Then brain cancer

Fig. 4. Example for the encoded rules for cancer diagnosis.

6.2 Heart Disease Expert System

Heart disease is a vital health care problem affecting millions of people. Figure 5 shows Types of Heart Diseases. Expert system (ES) is a consultation intelligent system that contains the knowledge and experience of one or more experts in a specific domain that anyone can tap as an aid in solving problems.

At our research unit, we have developed two versions of expert systems for heart diseases diagnosis.

The first one uses the rule-based reasoning while the second one uses case-based reasoning. The first version is composed of three components: knowledge base, user interface and computational model.

The knowledge was gathered from expert doctors in EL-Maadi Military Egyptian hospital, Egyptian Health Insurance Institute and medical books. We have built the system's knowledge base for the 24 heart diseases and it is composed of 24 facts and 65 rules.

The system is implemented in Visual Prolog and has been tested for 13 real experiments (patients). The experimental results have shown 76.9% accuracy in estimating the right conclusion [30].

The Second version of the expert system uses CBR methodology. We have represented the knowledge in the form of frames and built the case memory for 4 heart diseases namely; mistral stenosis, left-sided heart failure, left-sided heart failure, stable angina pectoris and essential hypertension.

The system has been implemented in visual prolog for Windows and has trained set of 42 cases for Egyptian cardiac patients and has been tested by another 13 different cases.

Each case contains 33 significant attributes resettled from the statistical analysis performed to 110 cases.

The system has been tested for 13 real cases. The experimental results have shown 100% accuracy in estimating the correct results for using nearest neighbor algorithm and this percentage is dropped to 53.8% in case of using the induction algorithm. The systems are able to give an appropriate diagnosis for the presented symptoms, signs and investigations done to a cardiac patient with

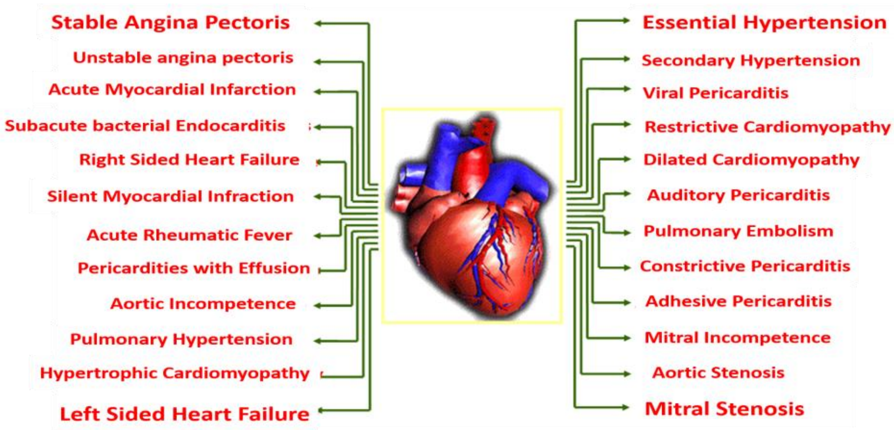

Fig. 5. Types of heart diseases

the corresponding certainty factors. It aims to serve as doctor diagnostic assistant and support the education for the undergraduate and postgraduate young physicians.

6.3 Mining Patient Date for Determining Thrombosis Disease using Rough Sets

At our research unit, ASU-AIKE labs, a rough set-based medical system for mining patient data for predictive rules to determine thrombosis disease was developed [31,32] this system aims to search for patterns specific/sensitive to thrombosis disease. This system reduced the number of attributes that describe the thrombosis disease from 60 to 16 significant attribute in addition to extracting some decision rules, through decision applying decision algorithms, which can help young physicians to predict the thrombosis disease.

6.4 Genetic Algorithms Approach for Mining Medical Data

In our research group we developed a hybrid classifier that integrates the strengths of genetic algorithms and decision trees. The algorithm was applied on a medical database of 20 MB size for predicting thrombosis disease [33]. The results show that our classifier is a very promising tool for thrombosis disease prediction in terms of predictive accuracy.

6.5 An Agent-Based Modeling for Pandemic Influenza in Egypt

Pandemic influenza has great potential to cause large and rapid increases in deaths and serious illness. The first major pandemic influenza H1N1 is recorded in 1918-1919, which killed 20-40 million people and is thought to be one of the most deadly pandemics in human history. In 1957, a H2N2 virus originated in China, quickly spread throughout the world and caused 1-4 million deaths worldwide. In 1968, an H3N2 virus emerged in Hong Kong for which the fatalities were 1-4 million [34]. In recent years, novel H1N1 influenza has appeared. Novel H1N1 influenza is a swine-origin flue and is often called swine flu by the public media.

In the absence of reliable pandemic detection systems, computational intelligence techniques and paradigms have become an important smart software tools for both policymakers and the general public [35, 36,27]. In our application, we propose a stochastic multi-agent model to mimic the daily person-to-person contact of people in a large-scale community affected by a pandemic influenza (novel H1N1) in Egypt. The developed multi-agent model is based on the modeling of individuals' interactions in a space time context. The model involves different types of parameters such as: social agent attributes, distribution of Egypt population, and patterns of agents' interactions. Analysis of the results leads to understanding the characteristics of the modeled pandemic, transmission patterns, and the conditions under which an outbreak might occur. In addition, model is used to measure the effectiveness of different control strategies to intervene the pandemic spread. More technical and computing aspects can be found in reference [36, 37]

6.6 Daily Meal Planner Expert System for Diabetics Type-2 in Sudan

Actually, recent estimates place the diabetes population in Sudan at around one million – around 95% of whom have type 2 diabetes and patients with diabetes make up around 10% of all hospital admissions in Sudan [38,39]. Mostly, Type 2 diabetes is strongly connected with obesity, age, and physical inactivity [39]. Most medical resources reported that 90 to 95% of diabetic is diagnosed as type 2. So, a successful intelligent control of patient food for treatment purpose must combines patient interesting food list and doctors' efficient treatment food list. In addition, many rural communities in Sudan have extremely limited access to diabetic diet centers. People travel long distances to clinics or medical facilities, and there is a shortage of medical experts in most of these facilities. This results in slow service, and patients end up waiting long hours without receiving any attention. Hence the expert systems paradigm can play a very important role in such cases where medical experts are not readily available. At our research ASU-AIKE labs, Ain Shams University, Egypt, we design and implement of an intelligent medical expert system for diabetes diet that intended to be used in Sudan [38,39]. The expert system provides the patients with medical advices and basic knowledge on diabetes diet. The development of such system went through a number of technical stages, namely; requirements analysis, food knowledge acquisition, formalization, design and implementation. Visual prolog was used for designing the graphical user interface and the implementation of the system. The system is a promising helpful smart tool that reduces the workload for physicians and provides a more comfort for diabetic patients.

6.7 CI in Medical Volume Visualization (MVV)

MVV brings profound changes to personal health programs and clinical healthcare delivery. It's seeks to reveal internal structures hidden by the skin and bones, as well as to diagnose and treat disease. Visual representation of the interior body is a key element in medicine. There are many techniques for creating it; such as magnetic resonance imaging, computed tomography, and ultra-sound [40]. The past few decades have witnessed an increasing number of new techniques being developed for practical clinical image display. One approach is to render the data interactively using a specialized multi-processor hardware support. Since these devices are not cheap, they are not widely used in practice. Another alternative is to use volume visualization [41]. In our research labs, we performed a comprehensive study for the recent intelligent techniques and algorithms used for medical data visualization [41]. These techniques cover filtering, segmentation, classification and visualization as well as the intelligent software supporting medical volume visualization. The study reveals hybrid techniques are the best approach for medical image segmentation is the best. In our future, work we are looking to develop mobile based intelligent system using direct volume rendering texture mapping technique with bones data sets.

7. Future research directions

Currently, we are working on the following applications;

(a) Determining the appropriate computational intelligent paradigm and model capable to classify Alzheimer disease and to build computer aided diagnostic system capable of detecting Alzheimer's at any stage [42.43].

(b) Big medical data analytics of intensive care unit data using machine learning and computational intelligence techniques [44,45].

(c) Developing an intelligent medical imaging evaluation system to help doctors diagnose pneumonia caused by the novel corona virus. The system capable of detecting corona at any stage.

8. Conclusions

The development of robust intelligent medical decision support systems is a very difficult and complex process that raises a lot of technological and research challenges that have to be addressed in an interdisciplinary way. The development of robust intelligent healthcare systems is a very difficult and complex process that raises a lot of technological and research challenges that have to be addressed in an interdisciplinary way. This paper analyzes the main paradigms and applications of the computational intelligence (CI) in healthcare from the artificial intelligence perspective.

The main results based on our analysis. CI offer potentially powerful tools for the development a novel digital healthcare system. The variety of such techniques enabling the design of a robust and efficient IHS. The key to the success of such systems is the selection of the CI technique that best fits the domain knowledge and the problem to be solved. That choice is depending on the experience of the knowledge engineer. And, digital medical decision support systems can benefit from systematic knowledge engineering and structure using techniques from the different disciplines artificial intelligence. AI technologies and techniques play a key role in developing intelligent tools for medical tasks and domains.CI Techniques (e.g. CBR, Data Mining, Rough Set, Ontology) can cope with medical noisy data, sub symbolic data, and complex structure data. In addition, CI offer intelligent computational methods for accumulating, changing and updating medical knowledge in IHS, and in particular learning mechanisms that will help us to induce knowledge from medical information or data. From our comprehensive analysis, one can recommend the following recommendations:

1. The cooperation between physicians and AI communities is essential to produce efficient computing systems for medical purposes. The physicians will have more information to deliver a better service and dynamic guidelines to improve quality and reduce risks.
2. Mobile devices can feed real-time medical data directly to patients and doctors via secure computing networks and IoT. The web based and IoT medical systems can enhance the online education/ learning/training processes.
3. The use of ICT technologies also improves the quality of patient care and reduces clinical risk. At the same time, the patient will be part of the healthcare process, having more information about diseases and access to his/her electronic health record.
4. Public health authorities can get more accurate information and develop dashboards to make better and fast decisions.
5. Hospital management benefits from a more updated meaningful data. This data is used by management systems to delivery KPI (Key Performance Indicators).

References

1. Russell, S. J., Norvig, P.: Artificial Intelligence: A Modern Approach (Second Edition). Prentice Hall (2003).
2. Borzemski, L., Świątek, J., Wilimowska, Z. (eds): Information Systems Architecture and Technology: In: Proceedings of 39th International Conference on Information Systems Architecture and Technology. Advances in Intelligent Systems and Computing, vol 85 DOI https://doi.org/10.1007/978-3-319-99981-4_1, Springer, Cham, Print ISBN978-3-319-99980-7, Online ISBN978-3-319-99981-4 (2018).
3. Cook, D.: Health monitoring and assistance to support aging in place. JUCS, **12**(1),15–29 (2006).
4. Salem, A.-B. M., Shendryk, V., Shendryk, S.: Exploiting the Knowledge Computing and Engineering in Medical Informatics and Healthcare. International Journal of Computers http://www.iaras.org/iaras/journals/ijc, **3**, ISSN: 2367-8895, pp. 130-139 (2018).
5. Salem, A.-B. M.: Knowledge Engineering Paradigms in the Intelligent Health Informatics and Medical Knowledge-Based Systems. Journal of Global Research in Computer Science, ISSN: 2229-371X.
6. Salem, A.-B. M., Aref, M. M., Moawad, I. F., Alfonse, M., AL Marzoqi, G.: Ontological Engineering in Medical Informatics. International Journal of Genomics, Proteomics, Metabolomics & Bioinformatics (IJGPMB), SciDoc Publishers, Infer, Interpret & Inspire Science, **1**(2), 9-13 (2016).
7. Said, H.M., Salem, A.-B. M.: Exploiting Computational Intelligence Paradigms in e-Technologies and Activities. Elsevier Procedia Computer Science 65 iii–vii, pp. 396-405 (2015).

8. Dix, A., Finlay, J., Abowd, G. D., Beale, R.: Human–Computer Interaction 3d edition. PRENTICE HALL (2003).
9. Cios, K. J., Kurgan, L. A., Reformat, M.: Machine Learning in the Life Sciences How it is Used on a Wide Variety of Medical Problems and Data. IEEE Engineering in Medicine and Biology Magazine, pp. 14-16 (2007).
10. Mitchell T.: Machine Learning, New York:McGraw-Hill (1997).
11. Noorbakhsh-Sabet, Nariman, et al.: Artificial intelligence transforms the future of healthcare." *The American journal of medicine*, **132**(7), pp. 795-801 (2019).
12. Neural Networks and Learning Machines , 3rd Edition, Originally published: 1993, Author: Simon S. http://dai.fmph.uniba.sk/courses/NN/haykin.neural-networks.3ed.2009.pdf
13. Cortes, C., Vapnik, V.:Support vector networks, Machine Learning, **20**, pp. 273-297 (1995)
14. Miotto, R., et al.: Deep learning for healthcare: review, opportunities and challenges. Briefings in bioinformatics **19**(6), pp. 1236-1246 (2017).
15. Rajkomar, A., et al.: Scalable and accurate deep learning with electronic health records. NPJ Digital Medicine, **1**(1), pp. 18 (2018).
16. KWAK, GLORIA HYUN-JUNG, and PAN HUI. "DeepHealth: Deep Learning for Health Informatics reviews, challenges, and opportunities on medical imaging, electronic health records, genomics, sensing, and online communication health." *arXiv preprint arXiv:1909.00384* (2019).
17. Salem, A.-B. M., Mahmoud, A. M.: A Hybrid Genetic Algorithm-Decision Tree Classifier. In: Proceedings of the 3rd International Conference on New Trends in Intelligent Information Processing and Web Mining, Zakopane, Poland, pp. 221-232, June 2-5 (2003).
18. Paun GH., Rozenberg G., Salomaa A.: DNA Computing: New Computing Paradigms. Yokomori T (Translated Ed) Springer (1999)
19. Steele, G., Stojkovic, V.: Agent-oriented approach to DNA computing. In: Proc. Of Computational Systems Bioinformatics Conference, pp. 546-551 (2004).
20. Huang, Y., He, L.: DNA computing research progress and application. The 6th International Conference on Computer Science & Education, pp. 232-235 (2011).
21. Kolodner, J.: Case-Based Reasoning. Morgan Kaufmann (1993).
22. Lopez, B., Plaza E.: Case-based planning for medical diagnosis. (1993).
23. Voskoglou, M. Gr., Salem, A.-B. M: Analogy-Based and Case-Based Reasoning: Two sides of the same coin. International Journal of Applications of Fuzzy Sets and Artificial Intelligence (ISSN 2241-1240), 4, pp. 5-51 (2014).
24. Pethuru Raj ,Jyotir Moy Chatterjee ,Abhishek Kumar and B. Balamurugan, Internet of Things Use Cases for the Healthcare Industry, ISBN 978-3-030-37525-6 ISBN 978-3-030-37526-3 (eBook) , Springer Nature Switzerland AG 2020
25. Pawlak, Z.: Rough Sets: Theoretical Aspects of Reasoning about Data, Kluwer Academic Publishers, Dordrecht (1991).
26. Voskoglou, M.: Special Issue Fuzzy Sets, Fuzzy Logic and Their Applications. published in *Mathematics* (2020), ISBN 978-3-03928-520-4 (Pbk); ISBN 978-3-03928-521-1 (PDF) https://doi.org/10.3390/books978-3-03928-521-1
27. Salem, A.-B. M., Nagaty, K. A., El-Bagoury B. M.: A Hybrid Case-Based Adaptation Model For Thyroid Cancer Diagnosis. In: Proceedings of 5th International Conference on Enterprise Information Systems, ICEIS 2003 ,pp. 58-65 , Angres, France (2003).
28. Salem, A.-B. M., El-Bagoury B. M.: A Case-Based Adaptation Model For Thyroid Cancer Diagnosis Using Neural Networks. In: Proceedings of the 16th International FLAIRS Conference, pp. 155-159, Florida, U.S, (2003).

29. Salem, A.-B. M., Alfonse, M.: Ontological Engineering Approach for Breast Cancer Knowledge Management, Proceeding of Med-e-Tel The International eHealth, Telemedicine and Health ICT for Education, Networking and Business. Luxembourg. March 30 – April 5 (2009).
30. Salem, A.-B. M., Roushdy, M., HodHod, R. A.: A Case Based Expert System For Supporting Diagnosis Of Heart Diseases. International Journal On Artificial Intelligence and Machine Learning, AIML, Tubungen, Germany, **1**, pp.33-39, Dec. (2004).
31. Salem, A.-B. M., Roushdy, M., Mahmoud, S. A.: Mining Patient Data Based on Rough Set Theory To Determine Thrombosis Disease. International Journal On Artificial Intelligence and Machine Learning, AIML, Tubungen, Germany, **1**, Dec., pp.27-31 (2004).
32. Salem, A.-B. M., Mahmoud, S. A.: Mining patient Data Based on Rough Set Theory to Determine Thrombosis Disease. In: Proceedings of First Intelligence conference on Intelligent Computing and Information Systems, pp 291-296. ICICIS 2002, Cairo, Egypt, June 24-26 (2002).
33. Salem, A.-B. M., Mahmoud, A. M.: Applying the Genetic Algorithms Approach for Data Mining Classification Task. In: IFIP WG12.6, First IFIP Conference on Artificial Intelligence Applications and Innovations, Toulouse France, August, 22-27 (2004).
34. World Health Organization, http://www.who.int/en/.
35. Timpka, T., Eriksson, H., Gursky, E. A., Nyce, J. M., Morin, M., Jenvald, J., Strömgren, M., Holm, E., Ekberg, J.: Populationbased simulations of influenza pandemics: validity and significance for public health policy. Bull World Health Organ. 87(4), pp. 305-311. ISSN 0042-9686, (2009).
36. Perez, L., Dragicevic, S. An agent-based approach for modeling dynamics of contagious disease spread. International Journal of Health Geographics, 8:50, (2009).
37. Khalil, K. M., Abdel-Aziz, M., Nazmy, T. T., Salem, A.-B. M.: An Agent-Based Modeling for Pandemic Influenza in Egypt. In: INFOS2010: 7th International Conference on Informatics and Systems, Cairo, Egypt, AOM 24-30, (2010).
38. Ahmed, I. M., Mahmoud A. M.: Development of an Expert System for Diabetic Type-2 Diet. International Journal of Computer Applications, (IJCA), 107(1), pp 13-21, December (2014).
39. Ahmed, I. M., Alfonse, M., Aref, M. M., Salem, A.-B. M.: Daily Meal Planner Expert System for Diabetics Type-2. E-Leader International Journal, 10(2), New York, USA, July (2015).
40. Balazs, C.: Interactive volume-rendering techniques for medical data visualization. Institut fur Computer graphik und Algorithme (2001).
41. Abdallah, Y., Abdelhamid, A.-A., Elarif, T., Salem, A.-B. M.: Intelligent Techniques in Medical Volume Visualization. Procedia Computer Science 65, 546 – 555 (2015).
42. Kruthika, K. R,et al.: Multistage Classifier-Based Approach for Alzheimer's Disease Prediction and Retrieval. Informatics in Medicine Unlocked, doi: 10.1016/j.imu.12.003 (2018).
43. Solimana, S. A., Mohsen, H., El-Dahshan, S. A., Salem, A.-B. M.: Exploiting of Machine Learning Paradigms in Alzheimer's disease. International Journal of Psychiatry and Psychotherapyhttp://www.iaras.org/iaras/journals/ijpp , ISSN: 2535-0994, 4, pp. 1-11 (2019)
44. Rayan, Z., Alfonse, M., Salem, A.-B. M.: Machine Learning Approaches in Smart Health. Procedia Computer Science 154, pp. 361–368, ScienceDirect (2019). Available online at www.sciencedirect.com www.elsevier.com/locate/prodedia.
45. Rayan, Z., Alfonse, M., Salem, A.-B. M.: Intensive care unit (icu) data analytics using machine learning techniques. ITHEA® Int. Journal "Information Theories and Applications", 26(1), pp. 69-82 (2019) http://www.foibg.com/ijita/vol26/ijita-fv26.htm.