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Sustainable and Energy Efficient Computing Paradigms for Society

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Preface

This book intends to provide an insight into recent trends and innovation on technologies, mechanisms, and approaches to provide solutions to real life societal issues and problems using sustainable and energy-efficient computing approaches. The book is organized into nine chapters and includes several domains, such as: the pharmaceutical, medical sector and education. The book also examines technologies and systems such as: blockchain, value chain, Human Activity Recognition, Neural Networks, Internet of Things, and routing algorithms, among others.

The first and second chapters focus on the pharmaceutical industry, the first focusing on the value chain using blockchain technologies; and the second on proposing and discussing a computing paradigm to manage the entire pharmaceutical sector information system, ensuring its sustainability. The third chapter focuses on the education sector and how it can benefit from fostering entrepreneurship in its students. The fourth chapter focuses on Human Activity Recognition as a case study to make it more useful in real life by tolerating the heterogeneity of the types of smart devices. The fifth chapter targets the health sector and merges Internet of Things, databases, mobile apps, and stochastic geometry theory to address emergency medical situations where there is limited time and resource to handle a given medical condition. The sixth chapter addresses sustainable computing thematic and presents an analysis of the performance of the neoteric ZRP-RA technique with ZRP and SHART – two hybrid routing algorithms. The seventh chapter refers to personalized health and how it can benefit from IoT and ML techniques and algorithms. The eighth continues the focus on the health domain and attempts to encompass Internet of Things (IoT) and in-silico approaches to address various healthcare components including predictive analytics. Finally, the ninth chapter addresses security issues when storing patient's data as an Electronic Patient Record.

This book attracted contributors from all over the world, and we would like to thank all the authors for submitting their works. We extend our appreciation to the reviewers for their review work. We gratefully acknowledge all the authors and publishers of the books quoted in the references.

New Delhi, India — Mohd Abdul Ahad
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New Delhi, India — Sherin Zafar

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All the authors who have contributed to this book need a special acknowledgement. The reviewers, who took time from their busy schedules to help in reviewing the contributions of the authors, also need a special mention. With deep gratitude and love, we would like to acknowledge the university staff members, seniors and other colleagues both from India and Portugal who helped in this project.

We would like to thank our families as they are the true source of inspiration to us. Special thanks to our kids, parents, wives and husbands for being understanding and supportive throughout the project.

We are also blessed for every single person who came into our lives as all of them have taught us something. A word of appreciation also to all our friends and colleagues we worked with for the last 11–15 years at Instituto Politécnico de Viana do Castelo, Portugal, and Jamia Hamdard, New Delhi, and all researchers with whom we cooperate around the world, namely the ones we share the edition of this book with.

Last but not least by any means we would like to thank Almighty God for protecting and giving us the strength and courage to stand tall in this challenging time of COVID-19 pandemic.

Dr. Mohd Abdul Ahad
Dr. Sara Paiva
Dr. Sherin Zafar

Contents

Chapter 1
Traceability and Detection of Counterfeit Medicines in Pharmaceutical Supply Chain Using Blockchain-Based Architectures

Mohd Majid Akhtar and Danish Raza Rizvi

1.1 Introduction

1.1.1 Problem Description

Our problem will be serving a general business model that is supply chain. In general, a supply chain contains all the different checkpoints involved in manufacturing and distribution of goods. Nowadays, a supply chain can potentially involve hundreds of stages and many geographical locations. This makes it very difficult to track events happening in a supply chain and investigates any incidents as there are information losses and barriers in every step. Buyers and sellers need to have a reliable system to validate the true value of a product or service purchased. When an actor in the supply chain conducts illicit activities, investigation becomes very hard and often no one is held accountable.

Each industry faces problems due to lack of regulations in supply chain. Many got complaints with fake products and many with damaged ones. Pharmaceuticals industry face many of the same challenges as faced by any other brand owners, and what exactly is the problem that they are facing? The answer is simple, counterfeit products entering into the markets. But in this case, counterfeiting is quite more serious than other industries. In this section, we will understand what counterfeit drugs are by definition, what is the real danger of using counterfeit drugs, how big is this market, why is this happening, and finally some existing solution to solve it using case studies.

A picture of two medicines is given in Fig. 1.1, and you can clearly see there is hardly any difference between the two. You might have guessed correctly which is

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Fig. 1.1 Fake and real drugs | Photo Source: usp.org

50% right, but there is also a chance of getting 50% wrong and here wrong can be deadly in Fig. 1.1.

1.1.2 Problem Description

A drug is considered counterfeit when it either doesn't have all the good stuff that it promises or it replaces all the good stuff with the bad stuff.

That's it really; it is not a rocket science. It is a problem that is very easy to describe but very hard to fix.

Let's take a look at high-end sophisticated manufacturing plants where some of these fake pills are made in Fig. 1.2.

Now this can be someone's kitchen, garage, or a place built just for producing counterfeiting medicines under such contaminated conditions. The drugs produced here have never seen the insights of a testing lab and just as you saw earlier probably look identical to the original medicine with the naked eye but then contain completely different ingredients at its core.

1.1.2.1 Real Danger of Using Counterfeiting Drugs

Let's take two scenarios, one for the best case and other for worst case to understand the impact of using such counterfeiting drugs.

Fig. 1.2 A raided counterfeit drug lab in China | Photo Source: Pfizer

- **Best Case Scenario**

A fake drug would be filled with a substance that is relatively harmless. This would be something that passes through the body like chalk or even plastic (capsule heads), is relatively harmless, and does not damage the body, but who want to eat chalk and plastic right?

- **Worst Case Scenario**

A counterfeit drug would be filled with something that is more toxic, and this would be something like floor wax or boric acid. In some cases, it is found to be rat poison. These can cause allergic reaction to serious injury to death. Sometimes, these counterfeit drugs or substandard drugs carry one enzyme that makes bacteria resistant to antibiotics and it is named as NDM-1 (New Delhi Metallo Beta Lactamase 1).

1.1.2.2 How Big Is This Market?

Now, here are some facts and figures that are authentic and provided by known trusted institutions. The figures may vary according to different surveys and reports. But still a common statement can be made from it [1].

- **World Customs Organization (WCO)** estimates counterfeit drug market worth is $200 billion dollars annually. But more than that 700,000 people die annually due to malaria and tuberculosis alone and that will be equivalent to four fully packed jumbo jets crashing every day. Now that will make headlines all around the world as they will be obvious.
- **World Health Organization (WHO)** estimates that 35% of the fake drugs sold all over the world comes from India, and it occupies the counterfeit drug market of nearly Rs 4,000 crore. Twenty percent of the drugs sold in India are counterfeit or spurious. Drugs prescribed for cold and cough or a headache are mostly either fake or of poor quality *[Report by Think Change India, 2017].* And other report by WHO in 2017 said, 1 out 10 medical products are falsified products.
- **Department of Food Safety and Drug Administration** seized around 5150 drug samples in Uttar Pradesh (India) in 2015, and they were sent to laboratory for investigation. Five hundred six samples were found to be fake drug which establishes that more than 10% drugs found in the market are fake drugs.
- According to the **World Trade Organization**, the United Nations Office on Drugs and Crime (UNODC), India manufactured most of the counterfeit drugs worldwide in 2006, followed by China and Thailand.
- **ASSOCHAM** paper shows that Delhi-NCR is the biggest center for spurious drugs which includes Gurgaon, Faridabad, and Noida. Estimates indicate that fake medicines constitute nearly one-third of all drugs sold in NCR. In India, "Bhagirath Palace," Chandni Chowk, New Delhi, is the hub for counterfeit and spurious drugs in India.
- **ACG Report 2003** has defined this issue as the "The Crime of 21st Century.". According to **BASCAP**, "Pharmaceutical industry is the most counterfeited industry in India."

1.1.2.3 Why Is It Happening?

- **Drug counterfeiting industry** is deeply lucrative. Its global market is around $200 billion dollars. From Low level to high level, all types of mafia, and smugglers are involved.
- **Fake drugs are hard to see**. Many a time, if patient doesn't get any problem or allergy, he is never likely to doubt on the fake medicine he has taken. They look exactly like the original. Those fraud groups even have the latest technology, and can copy any hologram stickers. Even lab technician many times cannot tell the difference between the two products, and the only way he can tell is by tasting it whether it is bitter or not. The manufacturing sites' picture shown earlier of these fake drugs don't have to spend much money on the production sites as they spend all the money on packaging to imitate as close to the original. And when you as a customer see the drug, it is the packaging that counts right.
- **Low awareness**, because we don't hear it in news. If you are purchasing it online, at lower price, chances are its fake.

- Other various reasons such as growing pharmaceutical industry, poor pharmaceutical regulation, high drug prices. Many a times, it is customers who are creating demand for these activities unknowingly, because medicines for headache, painkillers, cold, and cough are generally taken directly from a pharmacy without any prescription. A criminal Mario Bogo caught smuggling these fake drugs from India to the USA said, "In India, you can literally manufacture anything, there is no limit." For criminals, this industry is seen as low risk and high profit.

[Fun Fact]: In Sept 2017, Sun Pharma popular medicine brand "Pantaocid" and "Pantaocid DSR" failed test when a sample at random pharmacy were taken to test. But later it was found that it was actually the counterfeit drug that regulators tested *[Source Economic times].*

1.1.2.4 Existing Solution Analysis Apart from Blockchain Domain

– **RxAll Inc**.

This company combats counterfeit medicine using artificial intelligence and molecular spectroscopy. This testing device shines radio frequency waves on the drug itself so that it reflects back the chemical composition of the product, and this chemical composition is called as the medical spectra or medical signature. A customer can scan the medicine and compare the signature with authentic signatures in the cloud and will immediately receive notifications in 10 s on patient's phone.

Limitations of this system: No accountability: It is good that patient is able to identify the drug as fake or not, but who will be responsible if the drug is fake and who is the culprit in the whole pharma supply chain.

- What about all the new drugs and all the levels of medicines, how much signature can we produce. India's generic industry is the largest exporter in the world. How many different products can we get with this medical signature?
- Accuracy of spectrometer device is the main issue. Even if the device is 90% correct, chances are 10% to fail, which means still there are some risks involved.
- Costly, every household will have to buy it unless it is as cheap as a thermometer which in this case is not. It is nearly around $20,000, and other cheaper version is $1000, i.e., 70,000 INR.

– **Scratch labels or some unique 14 digits number**

Just like phone recharge scratch labels, this will also serve the same purpose. You scratch it and SMS the scratch card number to a number given on the label. The result obtained will tell you whether it is fake or not. If it is found to be counterfeit, then the government will shut down the pharmacy as happened in West Africa.

Limitations of this system: Another method of no accountability. It is a system where whoever holds fake drugs at last gets caught.

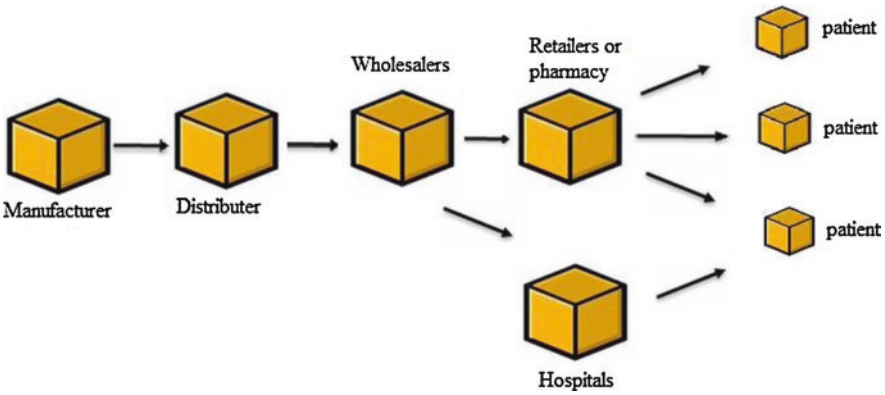

Fig. 1.3 How a basic supply chain looks like

- Pharmacies don't accept this system as viable, because many times it is found they are unaware of the fake drugs that are in their shelves because of other big players like distributors, etc. Using this scratch label there is no way for the pharmacy to get assure of the product before handing to the customer.

  Supply chain of pharmacy must look like in Fig. 1.3.

  But in reality, it is a more complex process; hence no proper accountability can be established, as shown in Fig. 1.4.

1.1.2.5 Proposed Methodology

Originally, the blockchain technology (BCT) was designed for its best-known implementation in the field of economics and crypto currencies, but today its utility is expanding in several other areas including the biomedical [2]. The revolutionary technology behind the famous Bitcoin, which is cryptographically secured and decentralized, hence, can act as the liberator for the detection of counterfeit drug. But it easy said than done. Let's understand what Blockchain is and can it really solve the issue?

Blockchain is a tamper-proof, distributed database that stores blocks of transaction bound together cryptographically over a peer-to-peer network. The blockchain architecture gives participants the ability to share a ledger that is updated, through peer-to-peer replication, every time a transaction occurs. Peer-to-peer replication means that every time a participant (node) in the network performs a transaction, then that data is synchronized across the whole network, i.e., other nodes receive a copy of that transaction. There is no need of a central authority to validate transactions as any transaction between participating entities is visible to all the participating nodes of the network. Every transaction is stored in blocks and linked together like a chain, hence, the name blockchain. So, when a transaction happens, the blocks are just added to the network confirming the time and sequence of transactions.

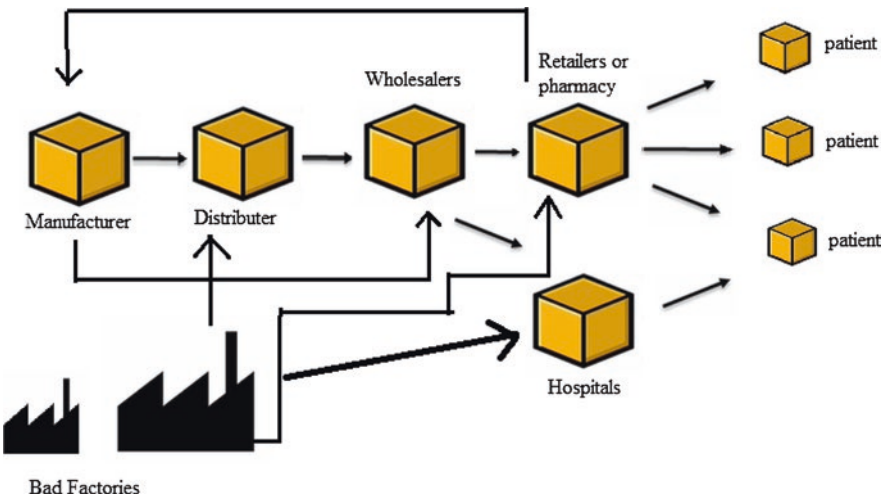

Fig. 1.4 How it actually looks like

Each block has a hash, timestamp, and the hash of the previous block. Previous hash prevents from altering blocks in between. Because of this, the network is tamper proof, transparent, and immutable.

Blockchain in short is distributed immutable ledger that maintains the integrity of the network by achieving consensus through algorithms like Proof of Work or Proof of Authority or own custom consensus algorithms.

To summarize, following features make Blockchain an ideal solution:

- Immutability
- Transparency
- Verification of information
- Secured by cryptography

Secondly, there are two types of blockchain, i.e., **Public Blockchain** and **Private Blockchain**. Both have some advantages and disadvantages.

These all give a base to solve the accountability issue. Now, whenever goods will exchange hands, it will be recorded and stored on blockchain for authenticity and verification.

Now, our base trust will be based on manufacturing companies. Raw materials supplied to them by the supplier will be tested in the lab and after testing manufacturing process will start.

The **first process** of these manufacturing companies like Sun Pharma, Abbott, Pfizer, Cipla, etc. is to generate a **unique QR code label** that will contain name of the manufacturer, expiry date, and transaction number or block number on the medicine pack itself. When the medicine is manufactured, they will be stored and their QR code will be scanned, and it will act as the authentication of the medicine from their side.

Now when this medicine will leave the factory, the distributor must scan the medicine to know that it is coming from the manufacturing factory plant and not from other fishy places. They will then add his signature details and further send it to different wholesalers, retailers, etc. With this technique we will achieve **FTP** (**Factory to Pharmacy**)**,** and all the transactions will be recorded on the blockchain and the customer can simply verify this by scanning the QR code at the local pharmacy story or in hospitals. All the stages will be recorded on the blockchain and it will solve the issue for counterfeit medicines.

1.2 Literature Survey

Blockchain is built with some benefits. But out of many, only few can be gained at this point of time, due to being in infancy state of development of blockchain. Hence, **performance element** for accountability in our literature survey will be based on the following:

- **Decentralization or centralization?**

To be honest, why you won't trust your Government or Ministry of Health to keep your data secured? Blockchain, in theory, states to decentralize institutions by giving no central authority. But we are not interested in the decentralization particular. If we are using any platforms like [3], we will simply let nodes and miners do the work without getting deep into centralization vs. decentralization. So if a solution is centralized or decentralized, both will be considered as equal.

- **Transparency**

Are transactions transparent for anyone to verify on the blockchain. This will be an important factor.

- **Security and Privacy**

Yes, the system will be secured always, and we can also trace back the supply chain to identify who interchanged right drugs with the counterfeit ones.

- **Scalability**

Who can participate, and are there any restrictions? What will be the size of blockchain after some time?

The survey is presented for ease of reading in Table 1.1.

Table 1.1 Literature survey matrix

Author and year	Short description of work	Techniques used	Performance	Source of publication
Asad Ali Siyal[1], Ayesha Zahid Junejo[2], Mohammad Zawish[2], Kainat Ahmed[3], published in **Jan 2019** [4]	They gave a theoretical model of how blockchain can be useful, no POC is given, and they mostly worked on PHR record (personal health record)	On-chain and off-chain is the used methodology with ML where user history is present, and using ML, it can more accurately tell about problems	1. Transparent, yes 2. Security/ privacy, no 3. Scalability no	**MDPI Journal, under cryptography** as "Applications of Blockchain Technology in Medicine and Healthcare: Challenges and future perspectives"
Soundarya K.[1], Priyanka Pandey[2], R. Dhalakshmi[2] published in **April 2018** [5]	They discussed terms of blockchain and supply chains, told how big this problem is, analyzed competitors like Modum.Io, and also gave theoretical model	Ethereum as backend and server having smart contract as the medium to interact with the blockchain	1. Transparency no, as no identity management system 2. Security, yes 3. Scalability, no	**EAI Endorsed Transactions on Cloud Systems** as "A counterfeit solution for pharma supply chain"
R. Y. Garankina, E. R. Zakharochkina, published in **2018** [6]	In Russia, Blockchain is called DLT (distributed ledger technology). They showed growth of BT in Russia, how many companies working, major is MediLedger by Pfizer, etc.	Discussed more about Ethereum Blockchain platform as the backbone	1. Transparency, yes 2. Security/ privacy, not much 3. Scalability, not much	Journal of Pharmaceutical Sciences and Research, **JPSR, ISSN: 0975–1459,** as "Blockchain technology and its use in the area of circulation of pharmaceuticals"
Ijazul Haq[1], Published in **March 2018** [7]	Discussed how deep the network of counterfeit drugs is	Permissioned Ethereum is needed	1. Transparency, yes 2. Security/ privacy, yes 3. Scalability, not much	**Research Gate Publication**, as "Blockchain Technology in Pharmaceutical Industry to prevent counterfeit drugs"

(continued)

Table 1.1 (continued)

Author and year	Short description of work	Techniques used	Performance	Source of publication
Yezhuvath Vinesh Balkrishnan, TCS Whitepaper, **2019** [9]	Discussed the application of IoT in Blockchain, more focused on finance part of the supply chain which is important too	Suggested own architecture of blockchain interactions between different parts of the supply chain logistics	1. Transparency, yes 2. Security/ privacy, yes 3. Scalability, no 4. Cost, high	**TCS Whitepaper** on TCS website as "Blockchain for a robust and efficient supply chain"
Patrick Sylim[1], Fang Liu[1], Alvin Marcelo[2], published in **Sept 2018** [8]	They described all the assumptions taken and scenarios of how a customer will verify medicine	Used both Ethereum and Hyperledger fabric as its theoretical model	The proposed system will be developed and tested in a controlled simulated network. Therefore, results may not be reflective of actual performance when deployed in real-world setting	**JMIR Publications Inc.,** as "Blockchain technology for detecting falsified and substandard drugs in distribution: Pharmaceutical supply chain intervention"
Faisal Jamil, Lei Hang, published in **May 2019** [10]	Showed the similar study of these counterfeit drugs and stated a novel fictitious solution by Hyperledger Fabric for complex scenario from point of verification of medicine to patient sharing data of health record	Complete Hyperledger Fabric architecture	1. Complexity, high 2. Privacy, secured 3. Transparency, low due to much permissioning 4. Scalability, yes 5. TPS (transactions per seconds are better)	**Research Gate Publication**, as "A novel medical Blockchain model for drug supply chain integrity Management in a Smart Hospital"

Table 1.2 Software and hardware used

Name of software	Purpose and version
PuTTY	To access AWS Cloud Server using public IP and .Ppk Auth file
Amazon Web Service EC2 (Ubuntu 16.04 LTS, 8GB RAM)	To set up Hyperledger Fabric v1.1 locally
Browser	Google Chrome
IDE	Remix IDE and Composer-playground
Node and npm	v8.16.2 and 6.4.1 respectively
Composer CLI Tool	Composer-rest-server
Docker Engine and Docker Composer	v19.03.5 and v1.13.0 respectively
Ethereum Network	Ropsten Test Net or Rinkeby Test Net

1.3 Report on the Present Investigation

1.3.1 Software and Hardware Used Information (Table 1.2)

1.3.2 Architecture and Working Flow

Any supply chain model in general involves many in between parties, but in our work flow, we have restricted it to be in a rigid model of only having four actors to reduce the complexity. These actors can belong to different organization but are mostly categorized into *Manufacturers*, *Distributors*, *Pharmacy/Hospital*, and *Customers* at the end of the Pharma supply chain receiving the output.

Manufacturers are actually the ones responsible for creating the medicine, and along with creating, adding different criteria to it like expiry date, price, and a field of current owner with the primary key attribute known as *medicine id*. Once a medicine is created by an organization's manufacturer, which then add that medicine to the storage of blockchain and is available whenever any actor holding the medicine wants to know the history of that medicine. These medicine ids play key role in identifying fake medicine with regard to real ones. Preventing these medicine ids from getting copied is a different aspect which is not in the scope of this chapter. The initial owner of the medicine should always be the manufacturer, and these data must always be retrieved back from the same blockchain network and not from any other nonreliable sources or databases present on the internet. After that, a manufacturer can transfer commodity/medicine to other actor of the blockchain network which can be a distributor or any other actor in the supply chain. Many questions pop up considering these basic initial tasks, and those are keenly taken into focus and looked into in order to solve it before this solution comes into practice.

1.3.3 Analysis of Solution Using Ethereum

Pharmaceutical supply chain needs *transparency* as well as *traceability for accountability*. Building a solution for such problem is time consuming and research oriented. The above sections of this chapter has already laid basis for the background understanding behind the *Blockchain* adoptive approach. Despite being the trendiest topic in the last decade, some negative market reaction got associated along the way related to cryptocurrency hype, i.e., the first Blockchain worldwide use case. Russia often use term "Blockchain" as *Distributed Ledger Technology* (DLT) to establish market status differently for the same technology. However, blockchain is a newbie technology, and daily innovations and evolution are contemplating into its era. Blockchain is a catalyst for change.

This section attempts to explore two fundamental platforms of blockchain and tries to distinguish key difference between their architectures and best fit use cases while showing the "do-how" of it with the specification of the system and network for the supply chain use case. Market in 2020 is very warming for the applications involving a layer of blockchain architecture.

Creating, maintaining, and securing a blockchain network from scratch is hard. So in late 2013, a developer Vitalik Buterin created a new blockchain called Ethereum to make it easy for anyone to create blockchain application on top of it without having to bootstrap a blockchain network themselves. Ethereum has its own built-in programming language that is Turing complete. **Ethereum** came in 2014 and is booming ever since. Developers and communities all around the world are exploiting the open-source platform for building different types of *Distributed Applications (Dapps)* [11]. In the later section of this chapter, the solution is assessed based on gas, cost, and network throughput. Ethereum is expensive and dependent on the type of consensus used based on which network you choose to deploy your smart contract. For example, at the time of development of this chapter, Ethereum Main Network was still using Proof of Work (PoW) consensus as its main protocol but soon will switch to Proof of Stake (PoS) because of efficient computing achieved by using PoS over PoW.

1.3.3.1 Implementation Using Smart Contract on Ethereum

Smart Contracts was first introduced in 1991 when two physicists wanted to preserve "History" and keep past "safe." They published a paper on cryptographic secured blocks. Then later in 1997, Nick Szabo developed the **Smart Contract** [12]. Smart contracts allow us to write logic and then the networks will operate on the logic it states for the functioning. Smart contract is written in "Solidity" language in case of Ethereum Blockchain. Bitcoin blockchain too provides feature for writing a contract but the programming language is more like assembly language and a bit complex.

Before going in the contract, let's understand what gas really is. Gas is a unit that measures the amount of computational effort that it will take to execute transactions. Solidity is very sensitive related to Gas. Each line of code requires some gas amount for its execution. Hence, while writing codes we must keep our gas amount as low as possible. Gases are given to incentivize nodes and to protect Spam abuse or infinite loops.

We have explained the basic concept of how one can interact with the supply chain contract based on the functions in Fig. 1.5. To deploy this Smart Contract, Remix IDE can be used. Before, deploying the contract, raise the gas limit from the default value of 30,00,000 to 32,00,000. This is done to successfully deploy the contract as the gas used in deploying the "datetime" contract is approximately 7,26,417 and for "supply chain contract" is approximately 23,95,276, and in total it is approximately 30,79,354. Hence, we need 32,00,000 as new gas limit. Reason for why gas limit is higher is given in the below section of findings and also some measurable steps to curb it are provided as well.

In this contract, two structures are used, i.e., *record_struct* and *stored*. In record_ struct, we have an array that hold the medicine ID's record corresponding to the addresses. In this, if we pass address of any account, it will tell us back what medicine they currently possess with them. This feature is achieved by mapping that helps to get value of type 2 when asked type 1. Code snippet is given below.

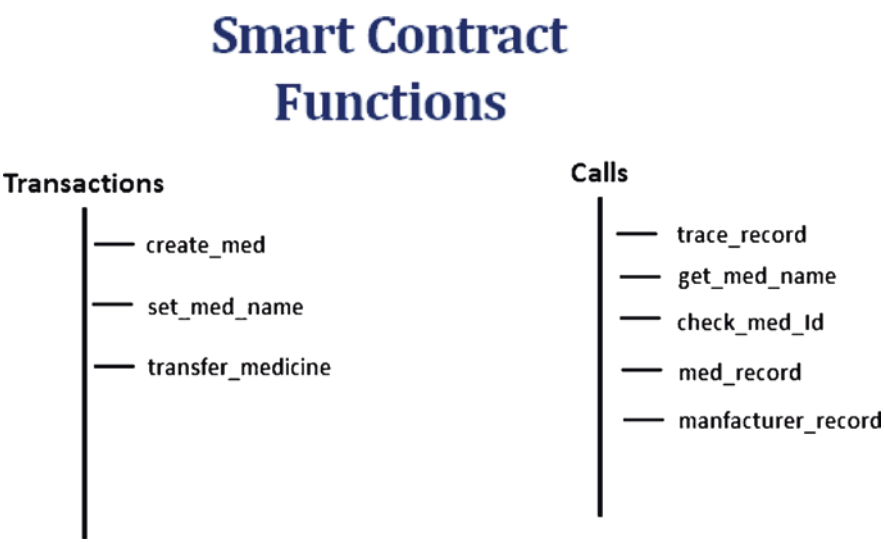

Fig. 1.5 Smart Contract functions

```
//Array for medicine
 string [] med_ids;

//Mapping used to get type 2 by giving type 1, type 1 is //
before =>
 mapping (address => record_struct) record;
 mapping (string => stored) public manufacturer;

 address public owner;


 struct record_struct
 {
 string [] record_array;
 }

 struct stored
 {
 string id;
 string med_name;
 uint256 index;
 address current_owner;
 string [] trace;
 }
```

Out of five demo accounts that we have in Remix IDE for testing the smart contract, we have given access to three accounts further to act as Manufactures by making our own Modifier named *onlyManufacturers* and only they can create new Medicines by using a function *create_med*.

```
modifier onlyManufacturers
 {
     require(msg.sender      ==      0xCA35b7d915458EF540aDe6068d-
Fe2F44E8fa733c ||
 msg.sender == 0x14723A09ACff6D2A60DcdF7aA4AFf308FDDC160C ||
 msg.sender == 0xdD870fA1b7C4700F2BD7f44238821C26f7392148);
 _;
 }
```

In the code in Fig. 1.6, a new medicine can be created by these three accounts only and then they can further provide other information like medicine name, expiry date, price, etc., by using either separate functions or by giving value in this function all together. In this, you can observe a variable *tracing_data*, which is an array that is actually binding the timestamp according to UTC (Universal Time Converter) along with the current owner. So whenever, any transfer of medicine takes place,

```
function create_med(string memory med_id) onlyManufacturers public returns(bool){

    bool check = check_med_Id(med_id);
    if(check == false)
    {
        check = true;
        med_ids.push(med_id);
        manufaturer[med_id].id=med_id;
        manufaturer[med_id].index = record[msg.sender].record_array.push(med_id) - 1;
        manufaturer[med_id].current_owner=msg.sender;
        uint noow = block.timestamp;
        string memory tracing_data = string(abi.encodePacked("[",check_time(noow)," => ","0x",toAsciiString(msg.sender) ,"]"));
        manufaturer[med_id].trace.push(tracing_data);
        return true;
    }
    return false;
}
```

Fig. 1.6 create_med function call written in Solidity

that transaction will be recorded in the *trace* function and each medicine will have its own trace record detailing who had this medicine at what timestamp.

```
function transfer_medicine(address vendor, string memory med_id,
address receiver) public returns(bool)
 {
 require(msg.sender == vendor);
```

Gas Used Approximately for this transfer_medicine Function: 1,93,321

Here, transfer of medicine takes place, which takes three parameters as address of *vendor*, *med_id*, and the *address of receiver*. Also there is a check to see that only person having medicine can transfer medicine, and this is done by inbuilt function *require*. We have skipped the logic part of transfer medicine, but in summary, this *med_id* will be added in the record of receiver's and the *trace_record* will be updated for this *med_id* with timestamp and the new owner. Also, medicine record for the vendor's record should not have that *med_id* anymore with him after once the *transfer_medicine* is successful. Hence, medicine under the vendor record is deleted.

```
//delete medicine under vendor record
 record[vendor].record_array.pop();
```

Interaction Steps with the Contract

Initially, the contract must be compiled by Solidity compiler version 0.5.1 or above. After compiling, proceed to the **deploy and run transactions** section and then click on the "deploy" to deploy the supply chain contract.

You will notice the amount of gas used in deploying the contract will be more than 30,00,000. *Create_ med* and *trace_record* are given in Fig. 1.7 and in Fig. 1.8.

The "med003" is being created by the demo account which is already given by RemixIDE for testing purposes 0xCA35b7d915458EF540aDe6068dFe2F44E8fa733c

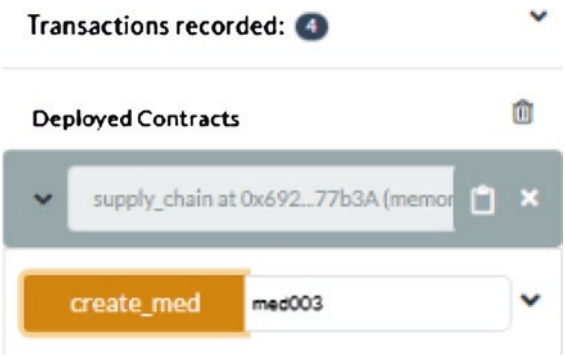

Fig. 1.7 create_med after deployment

Fig. 1.8 Manufacturer and med_record check

Fig. 1.9 trace_record call example 1

and then it gets stored in the *med_record* function. *Manufacturer* function gives the data about medicine with its name and who is the current owner.

Before transfer_medicine function is used, the trace_record only had one value in Fig. 1.9 which was timestamp and current owner as (0xCA35b…), but after *transfer_medicine* function is used (Fig. 1.10), the *trace_record* had one new timestamp along with the current owner (0x14723A…) which is when the transfer of

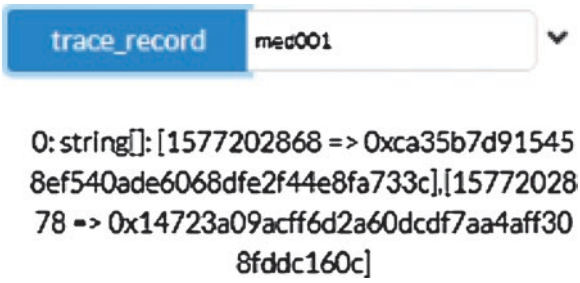

Fig. 1.10 trace_record call example 2

Fig. 1.11 Checking trace_record call

medicine happened. Here, it must be noted that this timestamp is the raw timestamp which is given in seconds. This data in seconds can be decoded at the client side to save gas amount, but if we insist on decoding it in the same contract, then **DateTime** library contract will be used. The result after decoding looks more presentable after using a function *check_time(uint timestamp)* and passing timestamp is shown as follows (Fig. 1.11).

One last thing to notice is that in solidity, as shown in Fig. 1.5, transactions and call functions are listed, and only transactions (shown in orange color) in Fig. 1.12 like *create_med* or *transfer_medicine* cause some fees or gas amount for execution as they are updating blockchain state storage, but the call functions on the other (shown in blue color) like *trace_record* do not require any gas fees to get deducted from the account as they are only reading from the blockchain state storage and not updating anything.

Challenges Faced in Implementation

- Smart Contract charge some fees for each transactions to happen, and this fees is given to miners for executing the transaction and maintaining the Ethereum network. To keep this amount as low as possible smart contract should be defined well on what data to store on on-chain and what to be stored on off-chain. For example, having raw timestamp saves much computation power and gas amount

Fig. 1.12 All deployed transactions and call functions

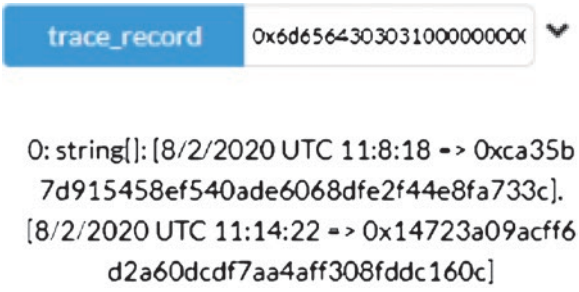

Fig. 1.13 trace_record check with byte32

than decoding the timestamp in the smart contract itself. Raw Timestamp can be converted into much presentable form on the client side or the front end easily. If we don't use the library DateTime for conversion of raw timestamp to "DD/MM/YYYY and hr:mn:sec," then 7,26,417 gas amount can be saved (Fig. 1.13).

- Strings are big issue to deal with in Solidity. In earlier version of Solidity, strings were not included. Now the support for string is provided but still strings are gas eater. It is advised not to use strings much in the code, as it takes a lot of the

execution gas. It is advised to use byte32 if the string length is less than 32. If the string length is more than 32 then byte32 [] array is used. But, the complexity increases and readability while testing the contract is not very humanly. It is found that using byte32 is cheaper and saves much gas amount. Hence, there is no need to change the default gas limit. The gas used for byte32 instead of strings is approximately 27,34,210 which is acceptable. Byte32 can only incorporate 32 characters, and they are cheaper in execution from the point of view of smart contract. For example, string value "test" will look like ("0x7465737400000000000000000…") in byte32. Although this does not seem much readable, this is three times cheaper than using strings. Just like timestamp, byte32 can also be converted back to strings on the client side or front end. As "med001" is "0x6d65643030310000…." in byte32, the following contract snippet is shown in Fig. 1.14.

- It is difficult to compare two strings, because strings are dynamic arrays in solidity and we do not know how long it can be. In order to compare, we used hashes of the strings and then made them compare because hash is always of fixed size. For hashing, *Keccak256* is used.
- Although we are in Remix IDE, which gives simulated environment of the test network, the smart contract is not fast enough even in the Remix IDE. Hence, this may take slightly longer time when deployed on Rinkeby network or Ropsten Network for transactions to get signed and executed by miners. All versions and variations done in the smart contract and their respective gas amount used for execution are given in Table 1.3 with a helpful remark.

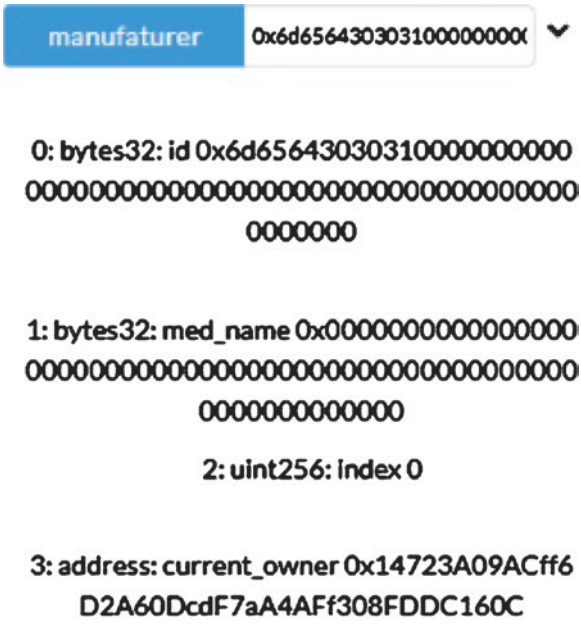

Fig. 1.14 Manufacture and med_record check with byte32

Table 1.3 Analysis of various Smart Contracts execution in Remix IDE

S. No.	Smart Contract behavior type	Gas used in Smart Contract execution	Remarks
1	Fully String Dependent + Full DateTime Conversion in Contract (example: DD/MM/YYYY UTC Hour:Min:Sec)	**30,79,354**	Have to raise or increase the initial default gas limit from 30,00,000 to 32,00,000 **(worst case)**
2	Fully String Dependent + No DateTime Conversion in Contract (just Unix imestamp, example: 1577202128)	**23,90,389**	Human readable due to string but timestamp is used instead of readable time format
3	Replacement of String with Byte32 + DateTime Conversion in Contract (example: "med001" is "0x6d656430303100000…")	**27,34,210**	Works with string for the outer interface part, but internally more suitable for machine as strings converted into byte32 before getting stored along with DateTime proper format. But still the gas limit is high
4	Replacement of String with Byte32 + No DateTime Conversion in Contract (just timestamp)	**20,14,904**	This works with all functionality except DateTime conversion. Only timestamp is given which is to be handle at the front-end **(best case)**

Result/Findings After Implementation in Ethereum

- Since, **Ethereum requires fees** for each write operation and transactions, it is not feasible for supply chain project where so many medicines have to be produced, and one has to pay fees for each transaction.
- **No KYC** (Know Your Customer) policy/module or Identity Management is present. There is no way to know who is operating the accounts. So while developing on Ethereum blockchain, we need external KYC module on the client side or the front end.
- To compare strings, hash has to be used. It is advised that strings must be avoided for use in Solidity. **Strings are expensive**; hence, we must replace strings with byte32 as they are three times cheaper than strings.
- **No date or datetime module** is present in Solidity as of now. So we need to create datetime externally which involves all the logic for finding DD/MM/YYYY and also the time HH/MM/SS from the raw Timestamp.
- Ethereum is also not suitable for production level deployment for Pharma supply chain, as it takes time for miners to select our transactions from transaction pool. And here we are referring about high rate of data when this solution will go to industry, which is not feasible for Ethereum to handle the request as it only does approximately **100 transactions per second (TPS)** which is very little as compared to what we want to achieve.

- Ethereum is a Public Blockchain. This means, there are several other data present on the blockchain of strangers. Apart from that, maintaining a full node is heavy task. Scalability is still one of the weakest factors of Ethereum because of the consensus protocol of Proof of Work (PoW). In future, we might see Casper or Plasma version of Ethereum.

1.3.4 Analysis of Solution Using Hyperledger

1.3.4.1 Hyperledger Composer Terminologies

Blockchain State Storage

- Ledger
- The state database: (i) level DB, (ii) couch DB

Connection Profiles

- It is in JSON Document, just like ID-Cards for the office, used for entering into the network and it is part of business Network card.

Assets

- Tangible or intangible goods or services
- Unique ID

Participant

- Create Asset
- Registry for participants or assets or users

Identities and Certificates

- Business card: contains the Identity, Certificate, and the connection profile, metadata for a participant

Queries

- To return back data from the blockchain world state
- Sent by Hyperledger Composer API
- Written in Bespoke Query Language

Events

- Indicate change has taken place

Access Control

- Set of rules

.bna (Business Archive File) comprises of

- .cto (Model File)
- .js (Script File)
- .qry (Query File)
- .acl (Access Rule File)

As it is clear, that Hyperledger composer is a tool used for the framework Hyperledger Fabric. For developing *.bna* (Business Archive File), it incorporates four sub files. In order to develop these files, we can use online editor/IDE just like Remix IDE in the case of Ethereum; here the online IDE is composer playground or we can install it locally from the documentation provided on Hyperledger website. So we first create a network, name it, and then we can use the interface for writing our chaincode or *.bna file* which is another name for smart contract in Hyperledger environment. While writing codes, namespaces are very important. Each file need namespace on the top and using it we can access anything between these four files. In our case, *namespace org.supplychain.network* is the namespace that is being followed in each of the file (Fig. 1.15 and Fig. 1.16).

1.3.4.2 Implementation in Hyperledger

1. In our *.cto* (Model File), it involves asset, participants, and transactions. Hence, we have two assets, i.e., commodity and PO (purchase order). Here commodity is alias for medicine which is used for creating new asset of type commodity (medicine), in which it is having complete detailed values like name, price, expiry date, issuer, owner, etc. Then we have four kinds of participants in our

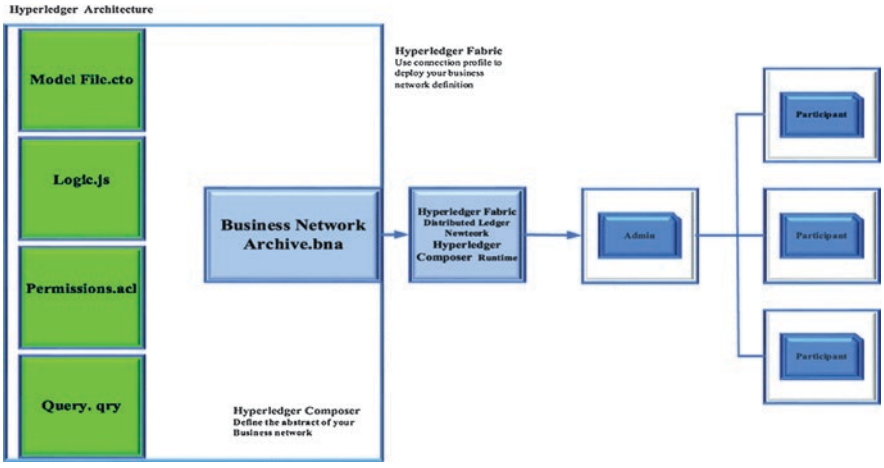

Fig. 1.15 Hyperledger Architecture | Source: Hyperledger Org

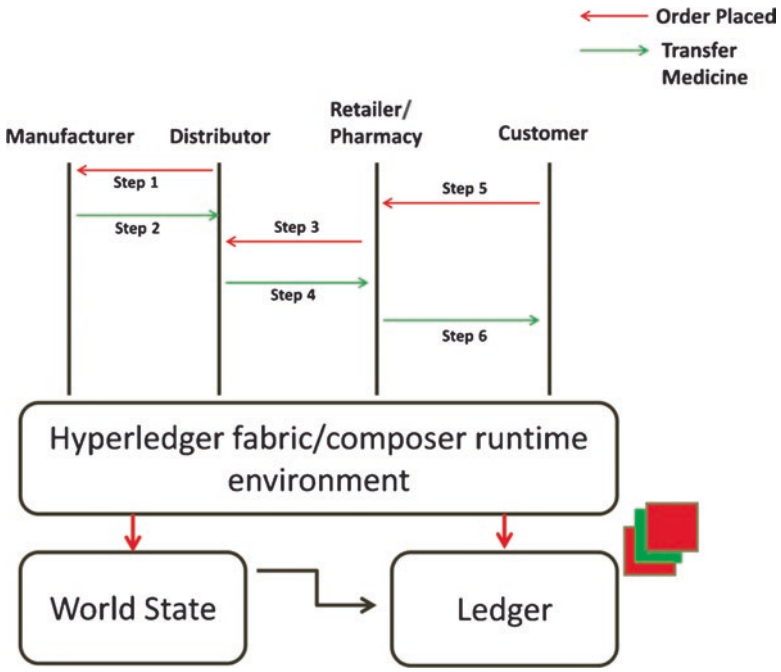

Fig. 1.16 Flow chart of implementation in Hyperledger

network to keep the network simpler, i.e., manufacturer, distributor, retailer, and customer/patient. Each of them is identified with a primary key in the form of manufacturer ID, Aadhaar number, Pharmacy ID, etc., and they act as users in the network to interact, create medicine, or transfer medicine. In the transaction part, we have two kinds of transaction functions, i.e., InitiatePO and TransferCommodity. One is used for placing a purchase order from orderer to vendor and the other is to transfer medicine from vendor to orderer. Code snippet is given below and the syntax might look different as it is modeling language in Fig. 1.17.

2. In our *.js* Transaction Function (Script file), we write logic to the two transactions described in the *.cto* file. In this section, we give backbone to the function InitiatePO and TransferCommodity. The syntax followed here is JavaScript. The transaction logic to InitiatePO is given in Fig. 1.18. On the other hand, TransferCommodity logic has something worth noting. It has a feature for tracing the record of medicine, by adding the information of new owner with the timestamp which is shown in Fig. 1.19. from line 42 to 46.

Model File models/model.cto

```
/*
 * Pharma Supply Chain Project Implementation by Majid
 */

namespace org.supplychain.network

/*
* Code for Assets
*/

concept Trace {
o DateTime timestamp
o Address location
--> Trader company
}

asset Commodity identified by commodityid {
o String commodityid
o String name
o Double mg
```

Everything looks good!
Any problems detected in your code would be reported here

Fig. 1.17 Model file .cto

Script File lib/script.js

```
/**
 * Initiate PO from one trader to another
 * @param {org.supplychain.network.InitiatePO} InitiatePO - the InitiatePO is to be processed
 * @transaction
 */
function initiatePurchaseOrder(InitiatePO) {
  console.log('Start of InitiatePO Function');
  var factory = getFactory();
  var NS = 'org.supplychain.network';

  var me = getCurrentParticipant();

  var order = factory.newResource(NS, 'PO', InitiatePO.orderId);

  order.orderStatus = 'INITIATED';
  order.orderer = me;
  order.vendor = InitiatePO.vendor;

 return getAssetRegistry(order.getFullyQualifiedType()).then(function (assetRegistry) {
```

Everything looks good!
Any problems detected in your code would be reported here

Fig. 1.18 Script File .js file

```
42    var newTrace = factory.newConcept(NS, 'Trace');
43    newTrace.timestamp = new Date();
44    newTrace.location = trade.shipperLocation;
45    newTrace.company = me;
46    trade.commodity.trace.push(newTrace);
```

Fig. 1.19 Trace function in Hyperledger

```
rule CreateOwnResourceOnlyToManufacturer {
    description: "Grant all Manufacturers to create its own resource"
    participant(p): "org.supplychain.network.Manufacturer"
    operation: CREATE
    resource(r): "org.supplychain.network.Commodity"
    condition: (r.owner.getIdentifier() == p.getIdentifier())
    action: ALLOW
}
```

Fig. 1.20 Access control rules example shown

3. In our *.acl* (access control file), we have provided some rules for different participant's on who can create medicine, who can read their own medicine record or public record, etc. For example, only manufacturer is allowed to create medicine and no one else can create asset of type commodity shown in Fig. 1.20. Other example is we can only transfer those medicines which we have with us, etc.
4. At last we have *.qry* file (Query file). This is used for reading data from blockchain storage and more useful with Composer API's if one would like to build as shown in Fig. 1.21.

In our project, we have shared some glimpse on how we can now take this *.bna* file and deploy on the Amazon Web Service hosted for Ubuntu platform where our local Hyperledger fabric is running.

1.3.4.3 Interaction Steps with the .bna File

The online composer playground has both **Define**, i.e., "code" part as well as the **Test** part. Also on the left side, all the asset, participation, and transactions are given. On the right-hand side, we have feature to switch between the accounts of manufacturers, customers, or even admin shown in Fig. 1.22.

Here, if we login from the manufacturer account, we can create medicine, which can further be transferred to different distributor or Pharmacy. But as soon as any transaction or transfer of medicine takes place, it is recorded down in the blockchain with information of a new owner and timestamp at the time it got successful. After new owner for example distributor had got the medicine, distributor can now give it to retailer/pharmacy or the customer and again the same updation follows. Finally customer can have the medicine and they will also be able to trace the history of the medicine back to the manufacturer stating whether it is genuine or not. Trace array is to be noted in Fig. 1.23.

After testing has been done, the *.bna* file can be deployed on the AWS server which is already configured and is ready for deployment and Composer API generation. The AWS EC2 instance can be connected from the local machine using PUTTY and live credentials (the .pem file) from anywhere around the globe.

```
query selectAllCommodities {
  description: "Select all commodties"
  statement: SELECT org.supplychain.network.Commodity
}
```

Fig. 1.21 Query example in .qry file

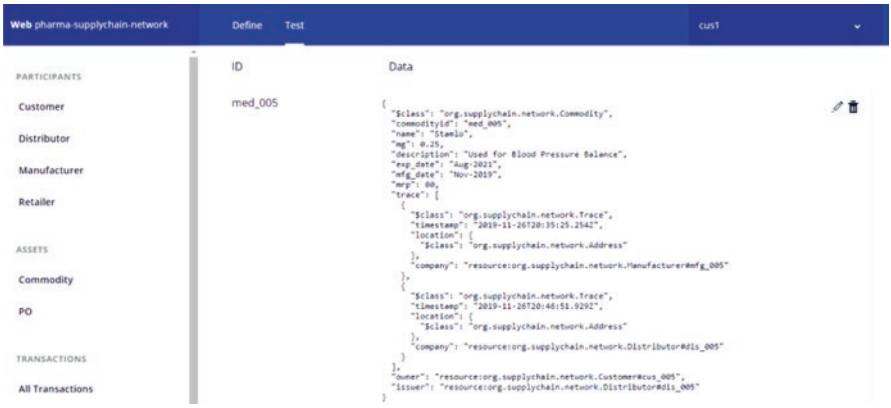

Fig. 1.22 Interface of composer-playground

med_005


```
{
  "$class": "org.supplychain.network.Commodity",
  "commodityid": "med_005",
  "name": "Stamlo",
  "mg": 0.25,
  "description": "Used for Blood Pressure Balance",
  "exp_date": "Aug-2021",
  "mfg_date": "Nov-2019",
  "mrp": 80,
  "trace": [
    {
      "$class": "org.supplychain.network.Trace",
      "timestamp": "2019-11-26T20:35:25.254Z",
      "location": {
        "$class": "org.supplychain.network.Address"
      },
      "company": "resource:org.supplychain.network.Manufacturer#mfg_005"
    },
    {
      "$class": "org.supplychain.network.Trace",
      "timestamp": "2019-11-26T20:46:51.929Z",
      "location": {
        "$class": "org.supplychain.network.Address"
      },
      "company": "resource:org.supplychain.network.Distributor#dis_005"
    }
  ],
  "owner": "resource:org.supplychain.network.Customer#cus_005",
  "issuer": "resource:org.supplychain.network.Distributor#dis_005"
}
```


Fig. 1.23 Medical record of medicine with Med_id med005

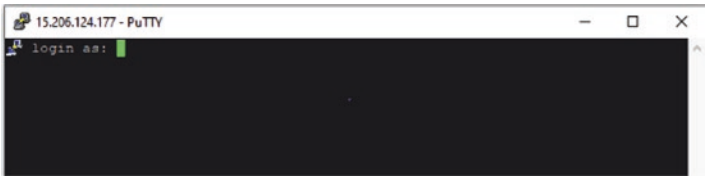

Fig. 1.24 Connection to AWS Cloud via PuTTY

We can notice the trace array in this and get history of the medicine med005 from starting. Below, we have shown some snapshots on how we access the server using PuTTY (Fig. 1.24).

After deployment is complete which is shown in Figs. 1.25 and 1.26, we can generate Rest API for this in Fig. 1.27.

Composer tools also provide feature to automatically generate Angular-based App using some in-built commands. App interface is show in Figs. 1.28 and 1.29.

1.3.4.4 Result/Findings After Implementation in Hyperledger

- **Hyperledger Platform does not require fees** for each transaction. Here, each transaction gets accepted as it is.
- **KYC** (know your customer) policy/module or **Identity Management is present** in Hyperledger Composer and Fabric environment. It provides inbuilt feature to generate certificate for the concerned people in the network, and this is given from CA (Certificate Authority). CA distributes connection profiles just like office punch cards or I-Cards.
- **No such issue of string** is there. It easily handles strings.
- Hyperledger **has inbuilt timestamp** feature which automatically displays time in format of DD/MM/YYYY, etc. Hence, no external care has to be taken on the client side.
- Hyperledger does take care of **throughput and transaction per second (TPS)** easily and it is more. Here our transaction gets accepted fast as compared to Ethereum. Also there is less chance of fail transactions.
- Hyperledger is a **Private Blockchain**. This type of blockchain is best suited for business model and enterprise projects. Here all the concerned authority has the power to control the network which in our case can be pharma manufacturers.

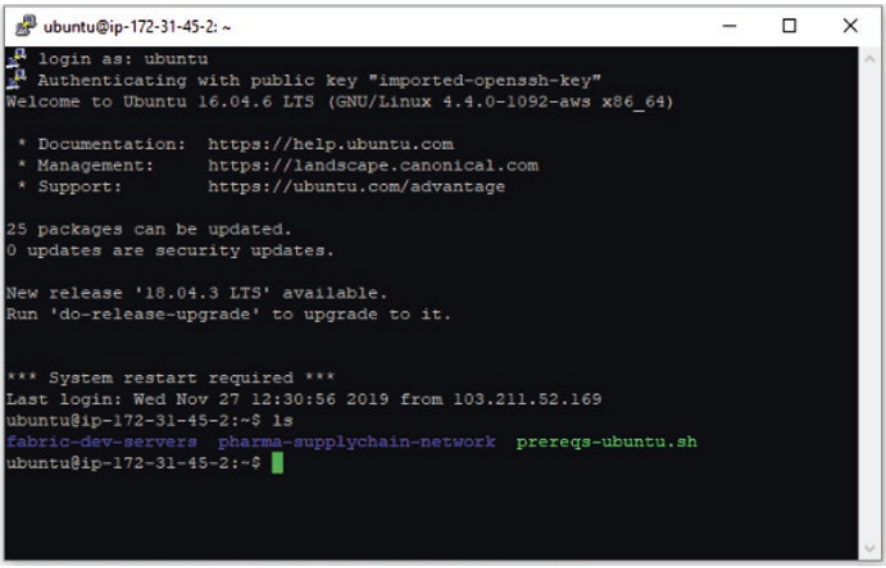

Fig. 1.25 Content of AWS Cloud for deployment

Fig. 1.26 File directory after deployment

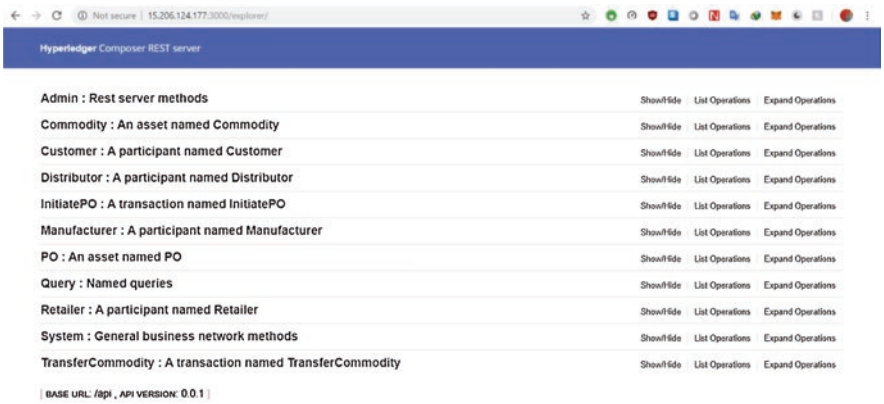

Fig. 1.27 Hyperledger composer REST server

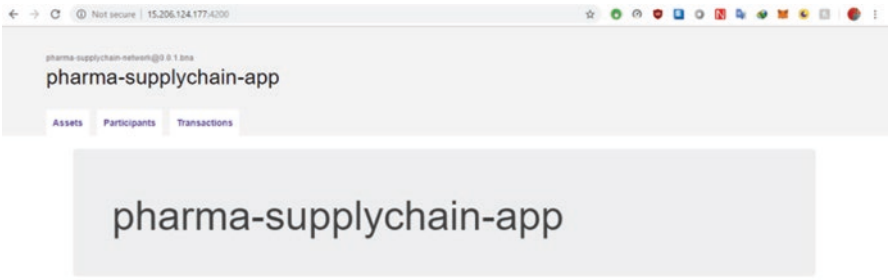

Fig. 1.28 Angular-based app interface

Fig. 1.29 App interaction

1.4 Conclusion

Pharmaceutical Supply Chain remains a very delicate aspect in India especially, because counterfeit drugs are very hard to find. Blockchain does help in finding the fake drugs and prevent it from getting into the vicious circle of supply chain and keep the customer or intaker of the medicine away from harmful state that could happen because of the fake drugs. In this chapter, we have described two approaches of using Blockchain (one with Ethereum and the other with Hyperledger) for the same pharma supply chain. It is found that Hyperledger-based approach is more efficient in number of ways for this particular cause. Hyperledger-based solution is better in scalability, TPS, and more enterprise friendly, authentication is handled, and accountability is achieved which was very difficult to track in public blockchain like Ethereum (Table 1.4).

Many aspects like security are fairly same in both the platforms. Also in Hyperledger, one is not liable to pay anything to the network in the form of fees. Blockchains are new to this era. Their boom arises due to cryptocurrencies, but as soon as people saw downfall of cryptocurrency, they assumed downfall of blockchains, which is not the case. Blockchains are here to stay and give fruitful result in many areas to come.

Table 1.4 Drawing out differences between both approaches

Parameters	Ethereum solution	Hyperledger Fabric and Composer solution
Latency	High (because of transaction pool and POW done by miner's take time)	Low (because here only endorsement policy is enough)
Transparency	Yes	Yes, and controlled way
Security	ECC, and SHA256	ECC, and SHA256
Scalability	Not scalable with more users	Stable, even with more users
Success rate	Low (not always succeed)	High
Transaction per second (TPS)	Low (due to mining)	Comparatively very high
Resource consumption	High (CPU) High (memory)	Low (CPU) Medium (memory)

1.5 Future Scope

Although many features were implemented and discussed in our chapter, some aspects are still left. For example, prevention of cloning of Quick Response (QR) codes and live tracking with IoT enabled devices are left for future prospects of the chapter. Quick Response (QR) code integration with the blockchain can be very handy and useful for making things to happen more smoothly. Other important factor that needs to be increased is scalability as right now blockchains are not as scalable as VISA or other transaction platforms. Other DLTs (Distributed Ledger Technology) like IOTA can be helpful for supply chain with more IoT enabled devices to make the process smooth and faster. Other main advantage of system like this could be in each sector of supply chain apart from pharma to even land registries, etc. Camera integration feature will open more doors for blockchain to be widely used.

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Chapter 2
Pharmaceutical Management Information Systems: A Sustainable Computing Paradigm in the Pharmaceutical Industry and Public Health Management

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2.1 Introduction

A comprehensive part of the healthcare sector is the analysis of supply chain and inventory control. The principle objective of this chapter is to scale down on costs without sparing the standard of service to the customers. A major component of health care is pharmaceuticals which contributes to relatively 10% of the healthcare sector's expenses in the USA and 600$ billion on a global scale in 2009. Though pharmaceutical goods are quite expensive, the lack of imperative medicines or the inaccurate usage of them can have adverse effects on the consumer and will also be a huge waste of resources. There are numerous reasons for pharmaceuticals to have power when it comes to inventory. Owing to the current economic situation, there is a lot of concern for the increase in costs in the healthcare sector, in particular toward pharmaceuticals. There is a direct relationship between the efficient management of pharmaceuticals and how a nation can tackle the concerns regarding its public health. According to Aptel and Pourjalali, the control of pharmaceutical supplies is a crucial issue in the healthcare sector. Nonetheless, a great number of healthcare corporations encounter hardships while handling their pharmaceutical commodities. The designing of a Pharmaceutical Supply Chain (PSC) is the process of consolidating the tasks involved in the transformation of raw materials to drugs that are consumed and also the processes that include the knowledge flow and improvement of processes to get better outcomes. The PSC involves three fundamental factors: producers, purchasers, and pharmaceutical providers. The producers comprise of

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the pharmaceutical organizations, firms that produce medical or surgical products, and manufacturers of the devices, important raw materials, and information system. The purchasers comprise of the group purchasing organizations (GPOs), wholesalers in the pharmaceutical sector, distributors of medical surgical goods, distributors who are independently contracted, and representatives of the product. The providers consist of hospitals and their subunits, integrated delivery networks (IDNs), and other site care facilities [1]. An efficient PMIS is able to analyze large amounts of data developed by the pharmaceutical processes and convert them into usable information that can be applicable to plan activities, estimate demands, resource allocations, monitoring, and to evaluate the operations. The information is usually in the manner of crucial factors that must be aimed at employers at all levels of the organization. This is done in order for them to supervise both, their own performance and that of the department they are answerable for. Another crucial aspect of a PMIS is the enhancement of liability. Most documentation and reporting in a PMIS is done in order to formulate an effective audit trail for commodities that go through the supply system [2].

2.2 Pharmaceutical Management Information Systems: A Sustainable Computing Paradigm

Sustainability can be defined as meeting the needs of the present without compromising the future generation's ability to meet their own needs. This section intends to help understand how Pharmaceutical Management Information Systems ensure sustainability in the processes and businesses in pharmaceutical industries [3].

Medicinal compounds are mainly derived from two main sources: synthetic and natural and rarely semi-synthetic compounds. In today's world, efforts have been made to produce the required drugs with efficient processing and less toxic compounds hence reducing energy consumption and generating fewer waste products. To meet future healthcare needs, the adoption of new technologies is required to ensure drugs as a sustainable commodity. This chapter discusses enhancing and sustaining the availability of drugs using pharmaceutical management information systems. With the rise of databases systems there is a possibility to collect knowledge for global healthcare benefit [4].

Pharmaceutical manufacturing processes involve huge energy consumption causing high greenhouse gas emissions and generation of waste. The industry spends an estimated $1 billion a year on energy to run its facilities apart from consuming huge amounts of water and material input. Due to increasing awareness about the environmental harm caused by chemical-based manufacturing plants and the advent of green chemistry, pharmaceutical companies are turning to environmentally, economically and socially sustainable technologies [3].

Pharmaceutical Management Information Systems (PMIS) is a computing paradigm that is integral to this transition in manufacturing. PMIS gives the pharmaceutical sector the ability to optimize manufacturing and distribution by providing the

tools to meticulously track inventory levels of raw materials, manufacturing processes, market demand and distribution, and patient consumption, enabling the transformation into a pull-based green manufacturing business model which is demand driven and built to order. This continuous measuring, monitoring, and improvement of all aspects of the pharmaceutical industry ensures sustainable product development with minimal consumption and maximum utilization of raw materials or resources and waste-minimization. These aspects of PMIS have also contributed to economic sustainability in the industry.

Figure 2.1 illustrates how the pharmaceutical industry can incorporate sustainability [3]. In the case of pharmaceutical industries, sustainable practices can be incorporated with the aid of Pharmaceutical Management Information Systems, as a way to help their growth, risk management, and the returns pertaining to their capital investment. (1) Growth: Sustainable practices, when incorporated by the pharmaceutical management information system, helps the company to come up with new and innovative products, find new dynamic markets, and most importantly, to come up with green products which are environmentally sustainable. (2) Risk Management: Sustainable practices could change the way pharmaceutical companies deal with risk management. It helps the company's information system come up with a framework for the processes involved, keeps track of the carbon footprint of the company, and even helps manage its reputation, regarding their practices. (3) Return on Capital Invested: The pharmaceutical management information system, on being incorporated with sustainable practices, can help with marketing, in a clean green way, to reduce its harmful environmental effects. It also helps create sustainable value chains and operations.

Fig. 2.1 Sustainability model in the pharmaceutical industry [3]

An efficient Pharmaceutical Management Information System (PMIS) also contributes to social sustainability by improving public health management during crises like epidemics and pandemics as illustrated in the case studies outlined in this chapter. A PMIS can analyze the data generated by various pharmaceutical management operations. The data is processed into information that is used in planning, demand estimation, resource allocation, monitoring, and evaluation of pharmaceutical processes. This information can be used to allow healthcare professionals at all levels to monitor performances of themselves and the units that they are handling. A good PMIS system also helps in identifying various problems and also takes actions against them. The system also helps in keeping an account on the number of patients being admitted, treated, and cured. A PMIS also ensures social stability by enabling healthcare improvement and access in isolated or rural areas and preventing addiction by monitoring drug consumption.

2.3 Organization and Management of Pharmaceutical Companies

Observing an information system as a pyramid helps us understand the system better. The base of the pyramid consists of the operational systems that comprise the subsystems that handle data at a transactional level involving procurement, financial management, distribution, and the medicine's uses. There must be a track of every item that enters or leaves the system and a decision based on the situation must be taken about supplying, reordering, and billing. This part of the pyramid is represented by large volumes of data that has to be documented and processed, commonly on a daily basis and at the time of transaction. The documenting of data must be done with precision, as it is crucial at this step owing to the fact that every medication is crucial. The proceeding part of the pyramid consists of management information systems (MIS). These are system units that recurrently generate reviews of the operational data (e.g., on a monthly or quarterly basis) to aid managers of different units, to supervise the progress of their respective departments (Fig. 2.2).

The annual reports usually encapsulate the information regarding the key indicators from various operational subsystems, like acquisition, personnel, financial management, or the control of stocks.

The information at this level may be of less precision owing to the errors that might have been made during the compilation of data; hence, an extent of variation is predictable. The executive level is at the top of the information systems' pyramid. The system consolidates management data to use for various policy and strategic plans. It develops a program-wide information about the missions that the organization has succeeded in. The systems at this stage monitor lesser indicators, less frequently. They make tools available to the users, namely, cost analysis and price comparison analysis, in order to execute recurring enquiries about the data at every level of the information system. This is done to either examine the root of the issues or to execute the "what if" test that examines the effectiveness of the alterations implemented [2].

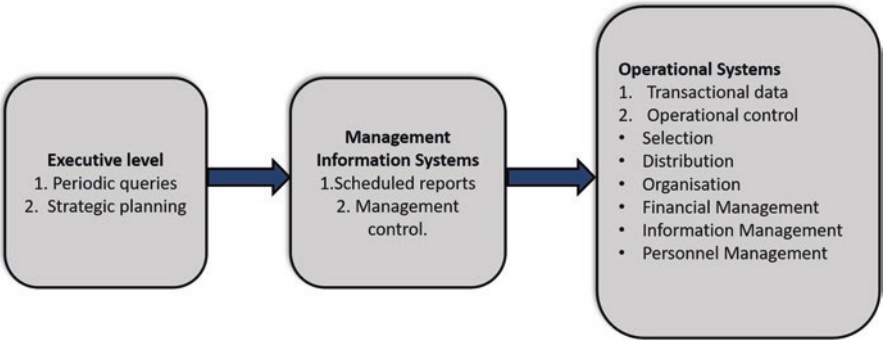

Fig. 2.2 Information system pyramid in a pharmaceutical company [2]

2.4 Workflow and Knowledge Flow in a Pharmaceutical Company

It is evident that pharmaceutical organizations that are based upstream of the value chain in the health care sector need to cautiously handle information from the upstream part of the chain which has the demanded data regarding the market, and also the technical information from the downstream flow of data that helps create demand.

A closer look at how firms regulate their supply chain shows us that there are two paths:

1. A path that delivers the materials, wherein the products, information regarding the order, and the information regarding financial properties are disclosed.
2. A demand creating path, which delivers the information regarding the medicines to the physicians. Figure 2.3 illustrates the two paths.

In the first path, i.e., "the material delivering path," "sell-in" depicts the inflow of products to the medicine stores and "sell-out" represents outflow of the products to patients, for which the demand is created by the doctors.

The stocks of drug stores report a disparity between "sell-in" and "sell-out," and ratio of sell-in/sell-out for effective inventory management. The order in which the information flows in the "material delivering path" begins from consumers to medical stores and eventually to the pharmaceutical company. Technical information flows downstream in the chain which is the "demand creating" path. The information flows from the companies to the physicians. The flow of information is complex in both paths having specific features that are difficult to manage. For example, "demand information" is received by the pharmaceutical companies via drug stores and key indicators play a role when it comes to ethical drugs, which is the ratio of prescription/sell-out, that explains the demand brought about by doctors, which is transformed into patient sales. A ratio less than 100% may be due to the inability of the patient to find the prescribed drug at the store due to, for example, stocking-out.

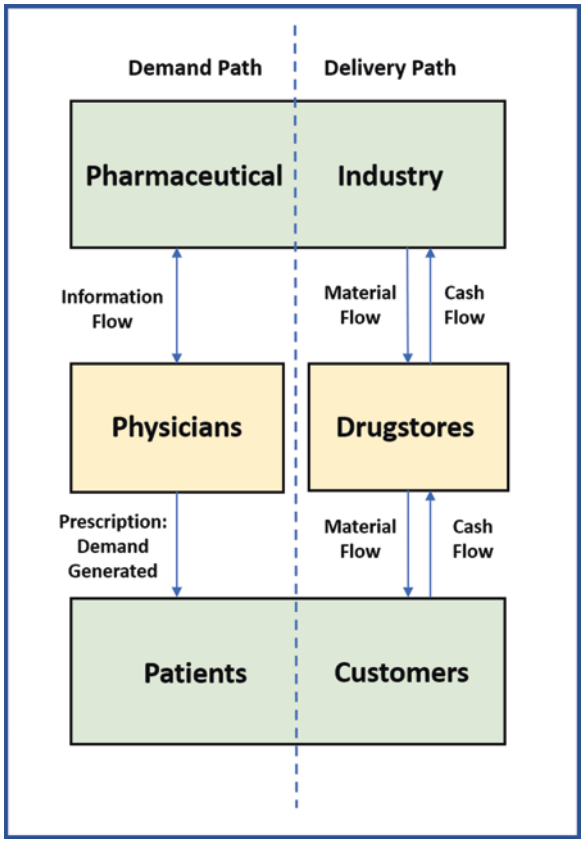

Fig. 2.3 Demand generation and sales in pharmaceutical companies [5]

The companies deliver information regarding the technical aspects to the market, ahead of the products hitting the stores. When a new molecule is deemed viable, a new product for commercial use and clinical trials come to the final stage (which will still take a few years), pharmaceutical firms begin working on building pipelines for technical information. A crucial procedure to guarantee a fruitful product is obtaining technical information early on during the new product development (NPD) process. Figure 2.4 illustrates the NPD procedure of medical firms and the processes of marketing, communication, and product auditing (alias pharmacovigilance).

A physical relations manager is also hired aside from the sales team, at the time of pre-launch in order to oversee the information reaching the market or to the physicians to be more precise, who will ultimately be prescribing the new drug. The first duty of a PRM is to form an Advisory Board, consisting of a group of professionals, doctors who are researchers as well and renowned experts of the field. The board is briefed about the process of development and is welcome to give guidance and advice about the product being developed. Key opinion leaders are also

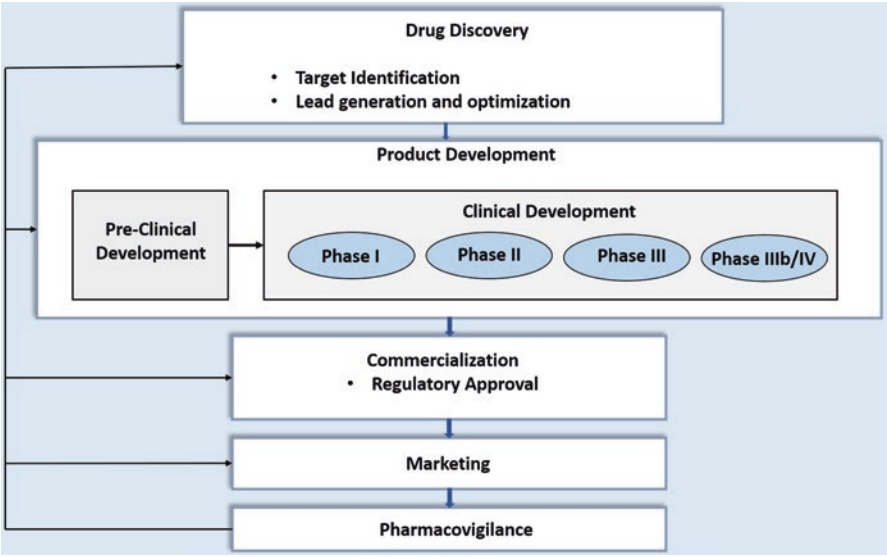

Fig. 2.4 Pharmaceutical company operations [5]

identified by the PRMs, who are mainly doctors from esteemed hospitals and experts from honored medical institutions. PRMs are in touch with the KOLs by updating them on the process of development. PRMs look forward to getting guidance from the KOLs and look to build stronger relationships with them, by funding their attendance to conferences. As the launch of the medicine gets closer, the work gets divided among the PMRs and managers of the sales department. The former group focuses on the Advisory Board and KOLs, while the latter group takes charge of the flow of medicine information to the market: doctors, hospitals, drugstores. Sales managers are supported by the PRMs, specifically at the time of pre-launch and launch periods, in aiding the transmission of information to the doctors. Post-launch, PRMs continue working in order to keep the KOLs informed and the Advisory Board may be dissolved. Figure 2.5 depicts a diagram that shows that the information flow regarding technical aspects to doctors, is crucial to handle the consumer's drug demand: doctors generate the need for the drug by prescribing them to the patients in need. This affirms the part of pharmaceutical firms. The diagram only depicts the flow of ethical drugs, as the process of flow for non-prescription drugs are different, as it is similar to consumer goods. The pharmaceutical companies' strategy is to direct sales to those who have an influence like traders and to retail stores that have a passive part in the process of demand definition. Nonetheless, if in case the middle stages had the ability to make decisions for demand, and these decisions were made on the basis of certain technical issues, they also should be considered in the communication strategy [5].

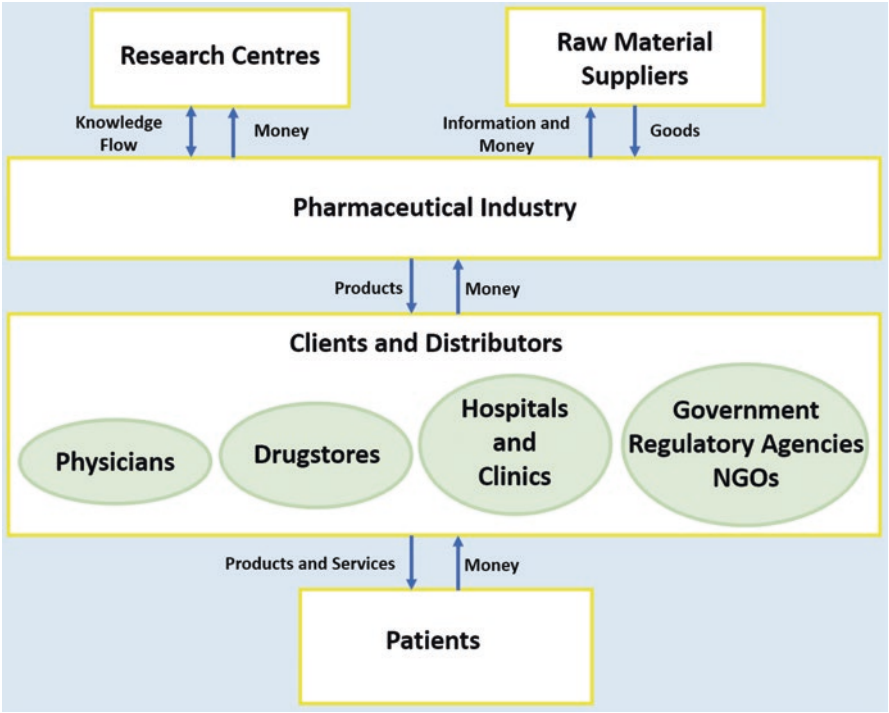

Fig. 2.5 Information and knowledge flows in pharmaceutical companies [5]

2.5 Pharmaceutical Management Information Systems (PMIS)

The PMIS collects, processes, reports, and makes decisions using the information. The process of planning for a new version of the pharmaceutical supply system should consist of a pharmaceutical management information system (PMIS), which could be used to supervise the information about patient adherence, resistance to drug, medicine availability, laboratory provisions and supplies, safety of the patient, post market intelligence, registration of the product, quality of the product, financing of the process, and program management, among the other problems (Fig. 2.6).

2.5.1 Features of a PMIS

The combination of collecting not just product-related data but also patient-specific data (Fig. 2.7).

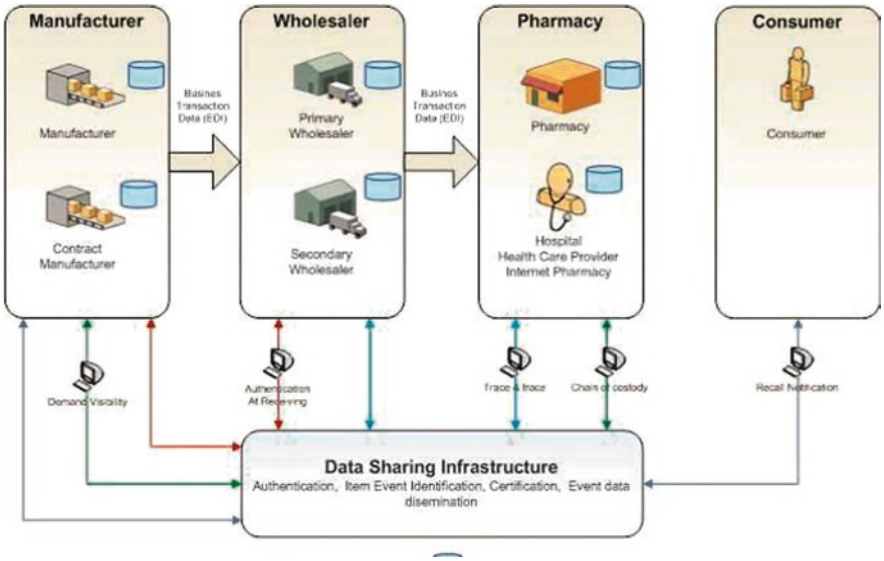

Fig. 2.6 Pharmaceutical Management Information System

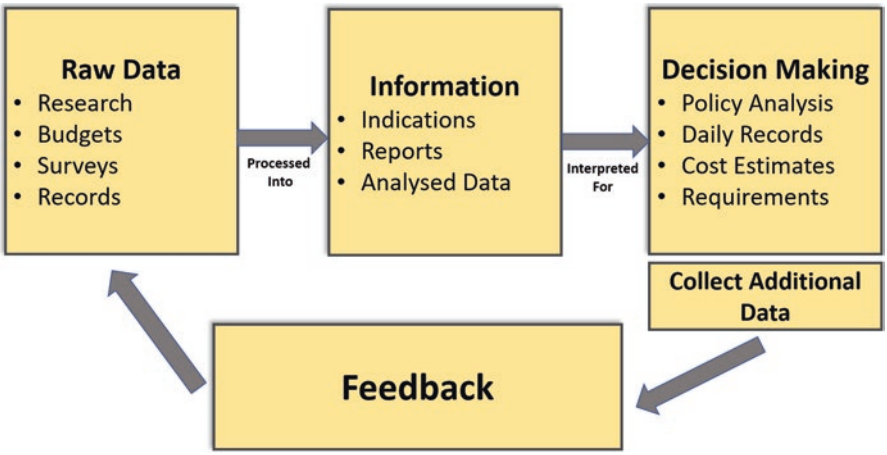

Fig. 2.7 Stages of a PMIS [2]

- Decision making for pharmaceutical services
- Information like adherence, adverse drug reactions, pharmacovigilance, individualized treatment options
- Data pertaining to the pharmaceutical industry like distribution of facilities and personnel

2.5.2 Components of PMIS

It usually has four subsystems which are selection, procurement, distribution, and use. Information can be stored in record-keeping documents, information-reporting forms, and feedback reports (Fig. 2.8).

1. *Documents to keep a track of information flow:* This involves ledgers, filing systems, and registers to document data relating to the businesses of a particular organizational department or unit. An efficient system to keep records lets users instantly retrieve information regarding the businesses and makes it easier to aggregate data for the purpose of reporting.
2. *Information gathering tools:* These are tools that are specifically formatted to facilitate the processing of data. Examples of these tools: summary registers, computer programs to compile data, and tally sheets.
3. *Data-reporting forms:* Forms used to report information are different from the records discussed above, as they are used to transmit data to other departments in an organization. Multiple copies at different organizational locations in the distribution network, establish an audit trail used to track the flow of drugs and funds.
4. *Feedback reports*: The data reported from other units is used to make an analytical report which is the feedback report. Processes to monitor and control the flow of information through the supply network is one of the key features in a good information system. The processes usually consist of details on how and when to gather data, on how to schedule the reporting of the collected data and to whom they must be sent to. There are different ways to gather data in a PMIS. The periodic collection of information from all departments and levels in firms to generate monthly or annual reports is typical, but at the same time rapid apprais-

Fig. 2.8 Components of PMIS

als, sentinel reporting systems, and sample surveys are important as well. In many situations, data provided by these means are used for decision making more frequently than the data collected by routine collection means [6].

2.5.3 Steps Involved in Designing a PMIS

While designing a new pharmaceutical supply agenda or when revising an older agenda, establishment of a complete information system is very important. As much as possible, PMIS should work on the present reports and processes. The addition of a few elements to the existing data and deleting the unwanted elements would make the system more efficient. Worksheets may be used to consolidate data obtained from the records to generate a summary report. The staff or user must be trained appropriately to analyze the data, comprehend the key components in their department, and make decisions based on it. Dependency on the reports generated from the top management may not help with efficiency due to their lack of local unit understanding and delays. Staff working at the site could have inputs to better the process or point out what part is not working. Consumers could be a part of the designing and testing process as the usefulness and viability of a PMIS betters with the involvement of consumers. In order to accept and use the system, consumers must know how the PMIS can solve the problem. For instance, reporting the amount of pharmaceuticals that are not in stock at a precise moment would be more logical than knowing the days when the medicine would be out of stock. Indicators are commonly put in areas of selection, efficiency of procurement, quality of product and service, efficiency of distribution, financial management, human resources management, and reporting compliance with the PMIS. Comprehensive datasets may seem to produce more accurate information, but data represented statistically could give information that is equitably good at a much cheaper cost in a short period of time.

Data collection: Forms of data collection include focus group, patient interviews, analytical observation, and surveys.

A crucial component in computerization is to adopt from standard coding systems in the areas of medicine, health facilities, diseases, and geographic locations. Consumers or users must be educated about the graphics techniques that are used with 2–4 important factors and they must use them to judge their own performance. Collaborating manual and computer systems in a balanced manner is important and so is making sure that they are completely integrated so that the departments that are not computerized can generate manual reports.

The utilization of software that fits the requirements: The software requires a PMIS, the size of which depends on the data set's size and the complexity of the analysis. A spreadsheet is easy to set up and to understand, but it is mainly devised to manipulate numbers and for calculations. Nonetheless, a spreadsheet commonly needs more redundancy while entering data, which is difficult to handle as there is

a gradual increase in records. Furthermore, querying data sets is challenging on a spreadsheet. A database program is constructed in order to gather, store, and organize data. It has better query aspects that aid in the handling of compound data. The proper designing of the database structure is very important in order to have an efficient system, which may require expert advice. Creation of graphics like charts and other resources must be possible by any system. Software development in-house seems tempting when an off-the-shelf package does not fit the criteria. The development of a software in-house needs accurate planning. To make sure that the information is effectively communicated, important decisions have to be made on what, how, and how often the data collected will be conveyed to higher authorities.

The technical knowledge required depends on the system. Aside from this the user must have knowledge on the design principles of information systems [6].

2.6 Supply Chain Management

A supply chain is a network of suppliers of raw materials, manufacturers, distributors, retailers, and consumers. The drugs manufactured by pharmaceutical companies are distributed by drug wholesalers to hospitals and finally to patients. With the employment of SCM systems, the process of handling of materials can be enhanced by combining the supply chain and the flow of materials, information, and resources in a unified manner. The most crucial success component of the SCM is the effective information sharing in the chain. Important SCM applications include direct ordering by the consumer, computer and internet-aided ordering, sharing of capacity and inventory data, vendor inventory, and continuous replenishment of goods. EHCR (Efficient Healthcare Consumer Response) is the SCM effort in the field of healthcare to manage the healthcare supply chain and effectively cut down on costs. The goal of EHCR is to scale down on the total healthcare costs and to improve the quality by bettering the supply chain's effectiveness. The EHCR Report states that the healthcare industry could greatly enhance its ability to provide reliable products and services to its users [6] (Fig. 2.9).

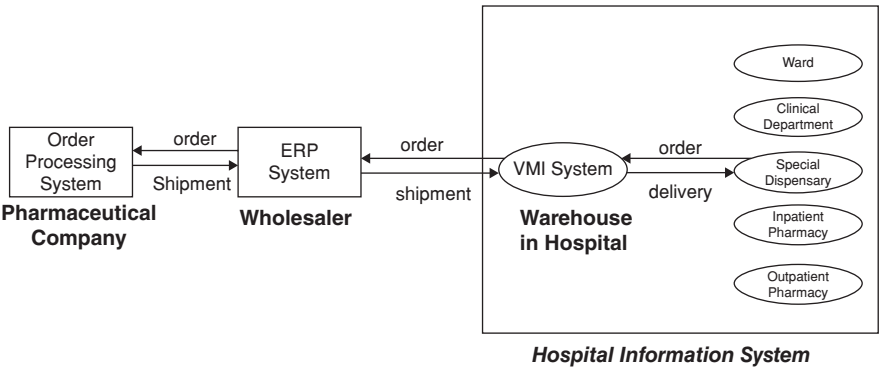

Fig. 2.9 Pharmaceutical supply chain management system [6]

2.7 Strategies Employed to Implement Effective Pharmaceutical Management Information Systems

2.7.1 Cold Supply Chain Management

Cold chain management is very important in effective transportation of insulin, vaccine, blood, and other fluids. The management of a cold chain requires the storage of the product within a specific temperature range throughout the whole supply chain. This poses a number of challenges for the government, health agencies, health care practitioners, and especially pharmaceutical companies [7].

Factors considered in the design of a cold chain:

- Efficient tracking of temperature – Temperatures may differ in different refrigerated units. Tracking temperature is therefore crucial to confirm the proper temperature.
- Choice of containers – The container chosen will influence the change in temperature inside the unit.
- Transportation ability – It is important to analyze the processes the transportation company implements.
- Distribution route – A few routes taken for transportation see a greater temperature change than others. A suitable outside temperature affects the viability.
- Contingency plans – Certain decisions about route, service provider, container, and tracking services contribute to the production of proper contingency plans, as it is important to have a backup plan [7].

2.7.2 RIFD: Radio Frequency Identification Technology

An RFID has four items, a reader, tags, computer, and encoder. Tags are produced from microchips with sizes of 0.2 mm or 0.4 mm, with bendable antennae. An encoder printer can be used to write information onto the tags, which a reader converts electromagnetic wave patterns from tag into measurable digital signals. These signals are then transmitted using computer systems. This data is stored on the tag in an Electronic Product Code (EPC) [8].

RFID in healthcare

(a) Automatic retrieval of patient history and deletion of mistakes made due to erroneous manual entries.
(b) The continuous monitoring of patient location and medication status can improve their safety.
(c) The elimination of the need for manual entry of data and enabling of authorized staff to precisely access patients data anywhere, increases efficiency and cut down overall costs.

Fig. 2.10 RFID [8]

(d) The tracking of RFID equipment allows instant access to the assets and timely service is ensured.
(e) In order to secure against fraud, a detailed electronic pedigree based on RFID/EPC technology has the ability to make criminal drug diversion difficult [8] (Fig. 2.10).

Multiple Reads: The technologist scans the barcode of each vial as information about billing, patient name, etc. is recorded. Inaccurate inventory records and billing may be caused due to scanning mistakes and omissions which may lead to unfortunate drug events. The RFID technology is wireless and allows the determination of complete content of vial cabinets at the same time, which makes logging automatic and no need for human involvement.

Data Storage Capacity: The capacity of data storage of the RFID is huge, which allows coding and documentation of information about an item explicitly. An exclusive code for an item can give access to the complete tracking, which aids in recalling and reduction of shrinkage, patient injuries, and adverse drug events. The more space available for storing data, information regarding date, time of manufacturing and expiration date, shipping, and dosage level can be stored in one RFID tag. One disadvantage is that counterfeiting of these tags can be done easily. RFID tags can be attached to the inside of the caps of vials which makes them completely durable unlike barcodes which can easily be damaged.

RFID provides real-time visibility as automatic counting and reordering decreases administrative costs [9].

Fig. 2.11 Electronic Product Code

2.7.3 EPC: Electronic Product Code

The Electronic Product Code (EPC) is a unique universal identifier of a particular object. EPCs are encoded onto RIFD tags to keep track of drugs and medicines, although they are not explicitly designed to be used with RIFD carriers (Fig. 2.11).

2.8 Case Study

2.8.1 Case Study 1: Management Information System Built for MDR-TB Surveillance in Brazil

The Hélio Fraga National TB Reference Centre, Rational Pharmaceutical Management Plus Program and National TB Program in Brazil, developed a novel information system to monitor multidrug-resistant tuberculosis (MDR-TB). This PMIS tracks the diagnosis, treatment, care, and medicine intake of affected patients. Since the information system is internet based, all tools and reports are available online ensuring accessibility to users at all levels. This program was designed to be integrated into the existing government health surveillance system. Major components of this system include patient case datasheets, follow-up datasheets during and after treatment, order for medicines, quarterly stock turnover reports, and data extraction tools [6] (Fig. 2.12).

The treatment of MDR-TB: The five drugs currently used in the intensive phase of the treatment regimen are ethambutol, levofloxacin, streptomycin, pyrazinamide, and terizidone, and the three drugs used in the maintenance phase are ethambutol, levofloxacin, and terizidone. Streptomycin or amikacin is used 5 days a week for the first 2 months and later three times a week for the next 4 months. The duration of the treatment is a period of 18–24 months with treatment monitored in the reference unit closest to the patient's home [10] (Fig. 2.13).

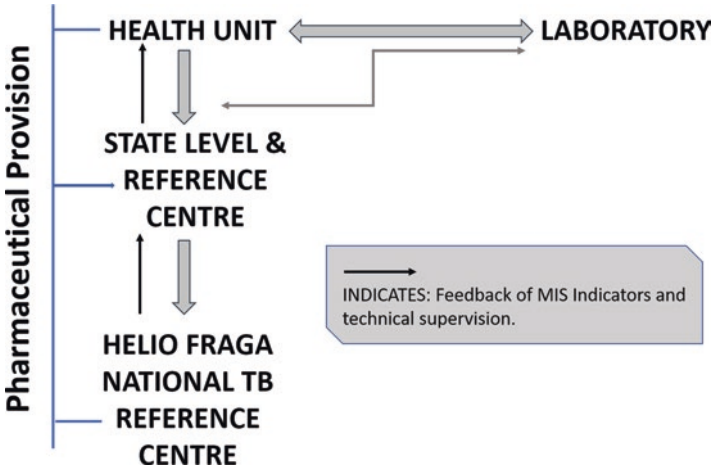

Fig. 2.12 MDR-TB surveillance program [2]

REGIMEN	DRUG	MONTHS
INTENSIVE STAGE 1	Streptomycin Ethambutol Terizidone Levofloxacin	2
INTENSIVE STAGE 2	Streptomycin Ethambutol Terizidone Levofloxacin	4
MAINTENANCE STAGE	Ethambutol Terizidone Levofloxacin	12

Fig. 2.13 Treatment regimen [10]

2.8.2 *Case Study 2: Electronic Dispensing Tool (EDT) in the Management of Pharmaceutical Information in the Healthcare System*

Antiretrovirals (ARVs) medicines require special care because they are expensive and due to the fact that healthcare professionals from developing countries do not have a lot of experience with them. For lifetime treatments, patients are to be supervised carefully to check their compatibility to the medication. In order to continue a constant supply of ARVs, staff working in the pharmaceutical field are to gather periodic information on the medicine consumed and of the patients' response to them so that an accurate forecast about the quantity of medicine needed can be predicted.

In Namibia, Togo, and 10 other countries, management sciences for healthcare (MSH) paid the groundwork for the Electronic Dispensing Tool, which is the leading-edge information system which treats the patient as the main point of interest and gathers critical information required to make decisions about a person's drug regimen. It also creates a stock inventory and summarizes the patient's statistics (Fig. 2.14).

The Rational Pharmaceutical Management Plus Program devised an uncomplicated, Microsoft access-based electronic tool to track patients and an inventory was designed for the pharmacy staff. This electronic dispensing tool keeps track of basic

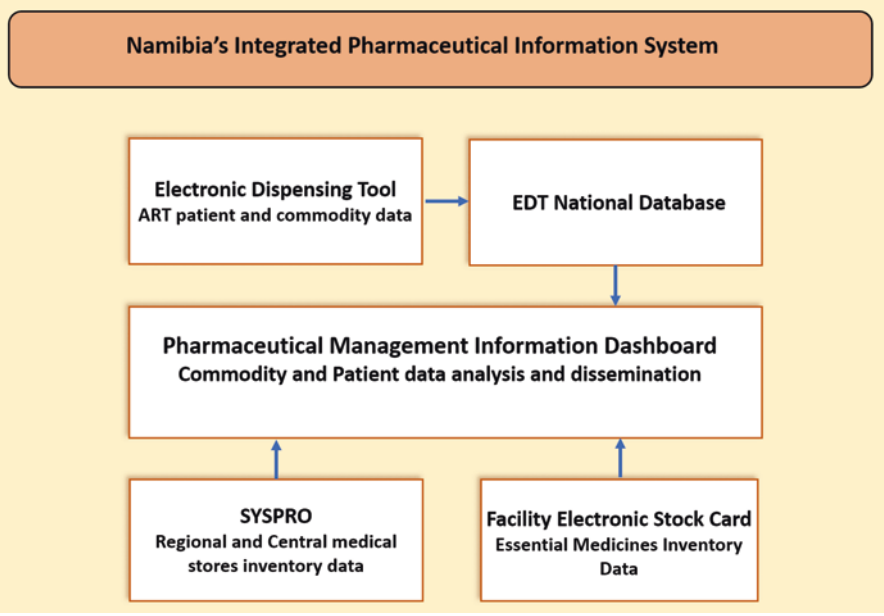

Fig. 2.14 Electronic dispensing tool [2]

patient profile, medicine use history, and other treatment parameters. It maintains consumption records as well, which are required to evaluate the pharmaceutical needs and for other program management decisions.

Advantages

- It lists the number of patient visits and the products given or administered to the patients.
- This tool tracks the batch and expiry of the medicines dispensed.
- It creates an adherence report which consists of the eight indicators validated by WHO.
- It has three different calendars for use (English, Ethiopian, Nepali).

2.8.3 Case Study 3: Overcoming of Barriers in the Implementation of Pharmacy Bar

2.8.3.1 Code Scanning System for Medicine Dispensing

This study shows the barriers and facilitators of the implementation of a pharmacy bar code scanning system in order to decrease medication dispensing errors at a large academic medical center in Boston, MA, where about 5.9 million doses of medication is dispensed every year from the pharmacy.

In November and December of 2003, the hospital's pharmacy shifted to a medication dispensing system. Ten of the pharmacy's staff were questioned about the implementation and the notes were reviewed to determine common themes. Three important barriers were determined: process (training requirements and issues in process flow), technology implementation (software and hardware), and resistance (communication problems, role definitions, and perceptions about technology). The strategies to solve these problems were identified as training and refining of the workflow process. The resistance from the staff was rectified using these measures [11].

2.9 Conclusion

Pharmaceutical Management Information Systems thus play an integral role in drug discovery, medicine production, distribution, and tracking. This ensures efficient distribution and utilization of drugs to tackle various public health concerns. Effective use of PMIS in the health industry can help cut costs and ensure ethicality in medicine production and consumption. The industry has also adopted various innovative strategies to optimize supply chain management and tracking systems. Nationwide implementation of information systems in pharmaceutical distribution can enable the government to efficiently provide for the nation's medical needs,

especially in rural settings in developing and underdeveloped countries. Use of this computational tool thus has the potential to revolutionize public healthcare and disease management.

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Conflict of Interest The authors listed in this chapter have no conflict of interest known best from our side. There was also no problem related to funding. All authors have contributed equally with their valuable comments which made the manuscript to this form.

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Chapter 3
Impact Factors Affecting Entrepreneurial Intention of Jordanian Private Universities Students: A Mediation Analysis of Perception Toward Entrepreneurship

Khalid Alkhatib, Ahmad Al-Aiad, Malik Mustafa, and Sharf Alzubi

3.1 Introduction

Entrepreneurship encompasses a process of generating and of recognizing values for entrepreneurs Henry et al. [14] and Dahlstedt and Fejes [5]. Activities associated with entrepreneurship are significant in the promotion of economic and social development, and therefore, many scholars and policy makers have been showing their concerns over the issues associated with entrepreneurship in the last few decades. Relevantly in China, the development of mass higher education has exacerbated the problem associated with employment among university graduates, and as a solution, the Chinese government is currently focusing on employment by entrepreneurship, and encouragement and support toward own business creation among university graduates. Nonetheless, entrepreneurship among Chinese graduates is still low, and Walter and Block [26] and Kyrö [17] accordingly highlighted the need to explore the entrepreneurial intentions of university students and their influencing factors in promoting entrepreneurship of graduates while also driving employment through entrepreneurship.

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3.1.1 Problem Statement

In the case of Jordan, entrepreneurial intention among students has not been explored [12, 22]. The reason for which has been highlighted in Barba-Sánchez and Atienza-Sahuquillo [2] who found only little such studies in the country as at year 2010. Hence, this chapter is aimed at Jordan as the study setting for the subject in question. As a developing Middle Eastern country, Jordan is also going through fast-paced entrepreneurship growth, and as reported in Kyrö [17] and Moloney et al. [21] which began in 2012.

In order to facilitate the understanding of the impact of the variables employed, this study proposed a model. This model is appropriate for the context of developing countries. Consequently, this study will contribute in increasing the level of entrepreneurial intention of the Jordanian private universities students.

The organization of the chapter is as follows: the following section discusses the literature review. Section three comprises research model and hypothesis. Research methodology and hypotheses were proposed in section four. Section five reveals research results of the study. The benefits of the study to society were elaborated in section six. Finally, major contribution and conclusion were discussed in sections seven and eight, accordingly.

3.2 Literature Review

3.2.1 Entrepreneurship Education

Enterprise and entrepreneurship education are the most commonly employed terms in the domain. Enterprise education is mainly employed in the UK, encompassing the broad focus on personal development, mindset, skills, and abilities [19, 23]. Comparatively, entrepreneurship education which is commonly used in the USA [11] concentrates on the specific context of the establishment of a venture and becoming self-employed [19, 23]. The terms enterprise and entrepreneurship education are used among researchers [13]. Such term is clearer but viewed as unpractical. Notably, the use of just entrepreneurship education term in deliberating the concept of enterprise and entrepreneurship education can lead to misunderstanding. Hence, referring entrepreneurial education as both enterprise and entrepreneurship education proposed in Erkkilä [11], and in order to prevent confusion, the term will be comprehensively utilized in this chapter. In addition, this chapter will refer the word “student” as learners in all education levels for an overview of terms.

3.2.2 Proactive Personality

Bandura [1] discussed the impact of person, environment, and behavior toward one another, and as indicated in [20], all the aforementioned aspects interact with one another in a vibrant manner. Bowers [6] and Schneider [10] explained that within the context of psychology and organizational behavior, behavior is controlled internally and externally, whereas situations are the function of persons, and vice versa. As such, it is clear that individuals are receptive toward the environmental forces [3]. Accordingly, people have the ability to impact their own environment, especially in the following manners: firstly, by manipulating their interpersonal environment, through modifying or changing it [3, 4]; secondly, by evocating, that is, by responding to the behavior of others [3, 9]; and thirdly through cognition, that is, through perceiving and construing their environments. All the aforementioned become the prerequisites of proactive behavior. White [27] and Langer [18] explained that the proactive dimension of behavior stem from the needs of individuals in manipulating and controlling the environment.

3.2.3 Prior Entrepreneurial Experience

Krueger [16] stated that entrepreneurial intentions of an individual may be influenced by previous entrepreneurial experiences, because these experiences establish the entrepreneurial intentions while also accumulating the experiences and skills for the coming entrepreneurial activities. However, there are those who found only a slight impact of past entrepreneurial experiences on individual's knowledge of entrepreneurship and have no significant effect on the individual's entrepreneurial attitudes [8].

3.2.4 External Environment

External environmental scanning and forecasting is known as "trend spotting," and scanning the external environmental during the formation of an institution's strategic plan can facilitate the organization in defining its preferred future, in comparison to merely responding to an imposed future [7]. The future cannot be predicted with certainty, but external environmental scanning and forecasting can decrease some uncertainty level in organizational planning, while allowing the organization to decrease its susceptibility to unseen change. For an organization, the provision of an advanced warning system for changes will generate a competitive edge.

3.2.5 Perceived Feasibility

Self-efficacy according to Bandura [1] is core to nearly human functioning, and according to the author, self-efficacy is more grounded upon what is believed, rather than what is true factually. Accordingly, perceived self-efficacy has been determined in various studies as a major factor in the determination of human agency and those who strongly believe that they can carry out certain task are more likely to pursue and persevere in that task. Hence, increased levels of self-confidence on the attainment of entrepreneurial tasks can be regarded as increased volitional control.

3.2.6 Perception Toward Entrepreneurship

This chapter examines the potential correlation between independent variables and entrepreneurship intention through the attitude factors, with attitude toward the entrepreneurship as mediating factor. Relevantly, a given act will be performed if the doer feels that the anticipated resulting total utility from the act is higher or greater than other substitutes. In the context of this study, it reveals that respondents who believe that they could achieve greater benefits from the execution of certain behavior will have a positive attitude toward that behavior. Moreover, in the context of the subject of this study namely entrepreneurship, respondents who suffer loss from entrepreneurship will demonstrate a negative look toward it and vice versa [25]. Hence, attitude toward entrepreneurship is classable into positive and negative perception.

3.2.7 Entrepreneurship Intention

In Katz and Gartner [15], entrepreneurship intention refers to the expanding conscious state of mind of which a given individual desires to initiate a new enterprise or generate new core value in the present organization. Remeikiene et al. [24] accordingly indicated that people execute their business with intent and that these people become entrepreneurs because they have decided so. In getting entrepreneurship intention and further behavior, the mind of humans governed by a number of psychological processes, which led to the importance of "pre-organizational phenomena."

3.3 Research Model and Hypothesis

The present study proposed the use of a research model comprising the variables as follows: entrepreneurship education, personal traits, prior entrepreneurial experience, external environment, and perceived feasibility as independent variables,

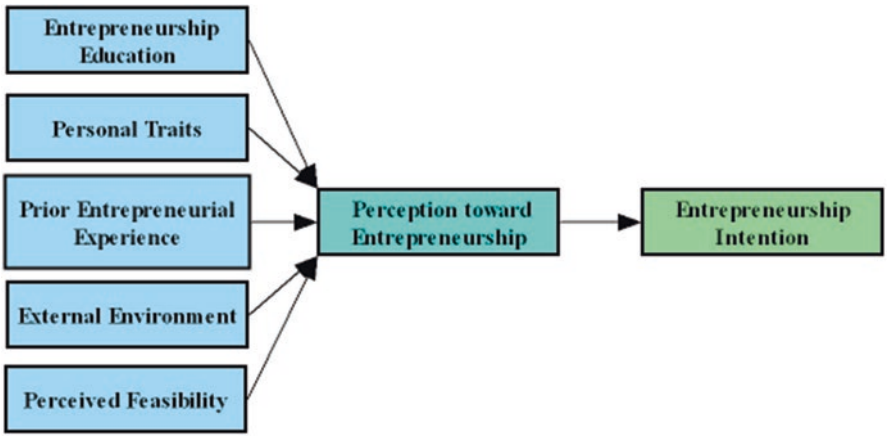

Fig. 3.1 Research model

positive perception toward entrepreneurship, negative perception toward entrepreneurship as mediating variables, and entrepreneurship intention as dependent variable. The research model is accordingly displayed in Fig. 3.1.

As depicted in the model above, our research has the following hypotheses:

H1: Entrepreneurship education has a direct impact on perception toward entrepreneurship.
H2: Personal traits perception has a direct impact on toward entrepreneurship.
H3: Prior entrepreneurial experience perception has a direct impact on toward entrepreneurship.
H4: External environment perception has a direct impact on toward entrepreneurship.
H5: Perceived feasibility perception has a direct impact on toward entrepreneurship.
H6: Perception toward entrepreneurship has a direct impact on entrepreneurship intention.
H7: Entrepreneurship education has a direct impact on entrepreneurship intention.

3.4 Research Methodology

3.4.1 Data Collection Method and Sampling Framework

The use of a research methodology facilitates the description, explanation, and prediction of a given phenomenon. In addition, it presents researcher with the research plan. Identifying the research type is important, and hence, the researcher needs to recognize the research and its contents. For the purpose of this study, a descriptive and analytical approach has been selected. A questionnaire was distributed to 334

Table 3.1 Sample characteristics

Measure	Frequency (%)	Percentage (%)
Gender		
Male	120	31.6%
Female	260	68.4%
Age		
<25	230	60.5%
25–35	100	26.3%
More than 35	50	13.2%
Educational level		
Secondary level	75	19.8%
Diploma degree	45	11.8%
Bachelor's degree	200	52.6%
Higher degree	60	15.8%
Experience		
<4 years	75	19.8%
4–9 years	155	40.8%
10–15 years	135	35.5%
More than 15 years	15	3.9%
Total	380	100%

private university students who were selected using the convenient sampling techniques, and 325 usable responses were analyzed. The sample characteristics are presented in Table 3.1.

3.4.2 Instrument Design

A questionnaire was the instrument used in gathering the needed data; it was ascertained in terms of its face validity and contents validity. The answers to the items in the questionnaire were classed using five Likert scale. There were two parts to the questionnaire: the first part includes four items covering personal information, while the second part includes 50 items covering the research variables. Smart PLS software was used for running PLS. PLS was employed in two stages comprising of measurement and structural model testing.

3.5 Research Results

3.5.1 Measurement Model

The evaluation made to the measurement model involved the scrutiny of the model's reliability, convergent validity, and discriminate validity. In this regard, reliability relates to the internal consistency of the model.

3.5.2 *Structural Model*

PLS analysis was carried out in this study in testing the structural model and the hypothesized relationships. Further, the procedure of bootstrapping with 5000 iterations was carried out to examine the statistical significance and the path coefficients of the relationships, the results are displayed in Fig. 3.2, Tables 3.2 and 3.3 in summary form.

- Path Diagram of Entrepreneurship Intention

The total causal effects result implies the significant effect of all the surveyed factors on the EI of Jordanian private universities students. Nevertheless, EE ($\beta = 0.291$, $p = 0.000$) appears to be the one independent variable with a direct impact on dependent variable. Hence, EE is the strongest determination of EI. Path analysis was carried out in this study, and it determined the indirect impacts of independent factors, namely PF, EE, PEE, EE, and PT with β index of 0.187, 0.171, 0.114, 0.112, and −0.242 respectively, which impact intention indirectly, following the order of the strongest to the weakest influences.

As mentioned earlier, the mediating factor in this study is attitude toward entrepreneurship and the results are as follows: PPTE ($\beta = 0.251$, $p = 0.000$), and NPTE ($\beta = -0.195$, $p = 0.000$). From the results, it can be said that the construct significantly affects entrepreneurship intention. These factors have a total effect on EI at 0.784.

The attained results show that the model elucidates a variation of 56.1%, 43.9%, and 0.459 in positive perception toward entrepreneurship, negative perception toward entrepreneurship and entrepreneurship intention correspondingly.

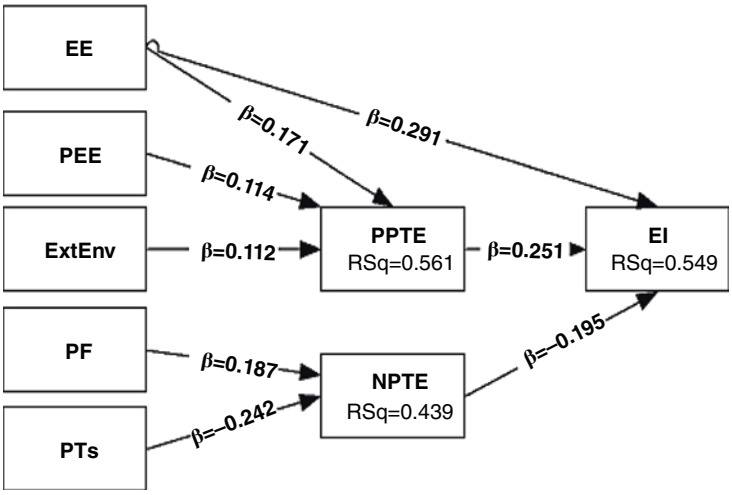

Fig. 3.2 Path coefficients of the structural equation for hypothesis testing

Table 3.2 Result of construct assessment

Constructs	Items	Factor loading	Mean ± SD	CR	Cronbach's α	AVE
Entrepreneurship education	EntE1	0.787	3.815 ± 0.926	0.928	0.815	0.521
	EntE2	0.786	3.816 ± 0.921			
	EntE3	0.787	3.817 ± 0.936			
	EntE3	0.785	3.715 ± 0.826			
	EntE4	0.784	3.712 ± 0.976			
	EntE5	0.883	3.855 ± 0.926			
Personal traits	PT1	0.882	3.686 ± 1.081	0.784	0.865	0.621
	PT2	0.881	3.676 ± 1.031			
	PT3	0.883	3.688 ± 1.019			
Prior entrepreneurial experience	PEE1	0.784	3.886 ± 1.031	0.897	0.874	0.638
	PEE2	0.886	3.646 ± 1.071			
	PEE3	0.787	3.623 ± 1.021			
	PEE4	0.789	3.671 ± 1.052			
	PEE5	0.885	3.685 ± 1.067			
External environment	EE1	0.783	3.972 ± 0.971	0.814	0.981	0.576
	EE2	0.882	3.712 ± 0.825			
	EE3	0.784	3.713 ± 0.974			
	EE4	0.881	3.854 ± 0.923			
	EE5	0.786	3.686 ± 1.082			
Perceived feasibility	PF1	0.884	3.675 ± 1.032	0.965	0.875	0.651
	PF2	0.782	3.716 ± 0.821			
	PF3	0.785	3.713 ± 0.979			
	PF4	0.786	3.871 ± 0.955			
	PF5	0.785	3.715 ± 0.921			
	PF6	0.787	3.716 ± 0.923			
	PF7	0.787	3.717 ± 0.932			
	PF8	0.786	3.815 ± 0.822			
	PF9	0.785	3.612 ± 0.975			
	PF10	0.784	3.775 ± 0.921			
	PF11	0.783	3.676 ± 1.082			
	PF12	0.889	3.686 ± 1.033			
	PF13	0.889	3.687 ± 1.018			
	PF14	0.895	3.885 ± 1.032			
	PF15	0.874	3.647 ± 1.072			
	PF16	0.758	3.624 ± 1.024			
	PF17	0.874	3.675 ± 1.053			

(continued)

Table 3.2 (continued)

Constructs	Items	Factor loading	Mean ± SD	CR	Cronbach's α	AVE
Positive perception toward entrepreneurship	PPTE1	0.874	3.686 ± 1.068	0.854	0.984	0.641
	PPTE2	0.754	3.971 ± 0.972			
	PPTE3	0.712	3.713 ± 0.822			
	PPTE4	0.796	3.715 ± 0.971			
	PPTE5	0.857	3.855 ± 0.926			
	PPTE6	0.841	3.687 ± 1.083			
Negative perception toward entrepreneurship	NPTE1	0.872	3.674 ± 1.031	0.817	0.843	0.658
	NPTE2	0.873	3.719 ± 0.823			
	NPTE3	0.842	3.714 ± 0.978			
	NPTE4	0.876	3.872 ± 0.956			
Entrepreneurship intention	EI1	0.874	3.813 ± 0.928	0.967	0.821	0.642
	EI2	0.812	3.815 ± 0.922			
	EI3	0.873	3.716 ± 0.931			
	EI4	0.814	3.733 ± 0.823			

AVE average variance extracted, *SD* standard deviation

Table 3.3 Direct, indirect, and total effect

	Causal effects		
Variables	Direct	Indirect	Total
Entrepreneurship education	0.291	0.171	0.462
Prior entrepreneurial experience		0.114	0.114
External environment		0.112	0.112
Perceived feasibility		0.187	0.187
Personal trait		−0.242	−0.242
Positive perception	0.251		0.251
Negative perception	−0.195		−0.195
Total	0.642	0.342	0.784

3.6 Study Benefits to Society

This study is beneficial to society through providing major implications for educational and political transformation. This allows the establishment of higher level of entrepreneurship with greater level of quality and knowledge. Simultaneously, students were provided with the basis for entrepreneurial future success. For policy makers, this study could assist them in providing the entrepreneurial training and increasing knowledge. Primarily for new business founders in the entrepreneurship domains, this study is of value as well since it connects with society through creating employment opportunities and increase knowledge workers.

The obtained results demonstrate the presence of correlations between task environment and independent variables. In regard to start-up intention, the results show

that general environment (e.g., economic indicator, regulatory environment, legal system, or political stability) does not considerably influence the intent of youngster to start up. However, several hurdles students had to deal with, and these hurdles were comparable to those faced by newly established firms in conducting their business. Among the hurdles is the lack of information concerning how to access to capital and financing their enterprise.

In addition, profit and nonprofit bodies with the willingness in supporting young entrepreneurs appear to be limited in terms of scale and quantity. Insufficient human and intellectual capital is another problem, causing difficulty to these youngsters in finding partners and supporting employees. For these young entrepreneurs, having to do all on their own, from searching for working space, profitable or ideal products, market demands to target customers or suppliers, etc. intensifies their intent in becoming entrepreneurs. Moreover, the supporting policies for entrepreneurship for the youth are generally passive and primitive at all levels. Hence, policy makers should consider the following:

Firstly, provide students with the foundation that allows them to obtain information on start-ups from the market, attain greater amount of access to capital and opportunity for practice for their business ideas. In addition, establish business-encouragement centers to allow the meetings of youngsters and newcomers for discovering prospects throw ideas and deliberate their shared desire in the initiation of a new business ventures. At the same time, should allow students to share stories, get inspired, and search for business partners or find human resources.

Secondly, the government could also facilitate these students through the provision of more start-up workshops and competitions or leagues at national level. All these could persuade investors and benefactors in transforming both ideas and innovations into reality.

3.7 Major Contribution

Several relevant issues are discussed in this chapter, particularly those that require the application of the fitting enhanced Impact factors that affecting Entrepreneurial Intention of the Students of Jordanian Private Universities: A Mediation Analysis of Perception Toward Entrepreneurship. Accordingly, this study adds to the knowledge body as follows:

- This study enriches the constant debate concerning the Impact factors affecting Entrepreneurial Intention of the Students especially in developing countries.
- This study enriches knowledge regarding the benefits and requirements for Entrepreneurial Intention of the Students areas.
- This study presents a model that illustrates the factors affecting Entrepreneurial Intention of the Students in Jordan.

This study looked into the Impact factors that affecting Entrepreneurial Intention of the Students of Jordanian Private Universities, and the proposed model involves

the Mediation Analysis of Perception Toward Entrepreneurship in developing countries particularly. These are the significant contributions of this study.

3.7.1 Contributions to Knowledge

This study is of value to the domain of entrepreneurship, as it provides the important theoretical knowledge. Therefore, a new model was proposed, and the model includes various variables with limited or other of variables. The study discussed several prominent factors to be considered in the implementation of entrepreneurial intention of the students; it proposed the attainment of full knowledge about entrepreneurship within the context of Jordan, while also identifying the specific factors affecting entrepreneurship intention in the country. Meanwhile, the measurements and the conceptual framework that illustrate the link among personal traits, past entrepreneurial experience, the external environment, and the perceived feasibility factor of Ajzen's model with entrepreneurship spirit were established in this study, through attitude perception toward entrepreneurship as mediator.

3.7.2 Model Contribution and Research Outcome

The use of a model in this study significantly contributes to the domain of entrepreneurship. The model highlights the advantages of entrepreneurship, while also demonstrating consistency for increased efficiency in the employed ideas of entrepreneurship that inevitably experience many challenges.

The model proposed in this study implemented, tested, and evaluated. The resultant outcome demonstrates the need to understand the Impact factors that affecting Entrepreneurial Intention of the Students of Jordanian Private Universities: A Mediation Analysis of Perception Toward Entrepreneurship.

3.8 Conclusion

A comprehensive understanding of entrepreneurship domain in Jordan was presented in this study, and clearly, the Jordan factors affecting entrepreneurship intention was highlighted. The measurements and the conceptual framework illustrating the relationship among personal traits, past entrepreneurial experience, the external environment, and the perceived feasibility factor of Ajzen's model with entrepreneurship spirit through the inclusion of attitude perception toward entrepreneurship as mediator were provided in this study. This study demonstrates the significant impacts of surveyed factors on the entrepreneurship intention of students. Equally, this study provides significant implications for educational and political transforma-

tion. This allows the establishment of higher level of entrepreneurship with greater level of quality. At the same time, students could be provided with the foundation for entrepreneurial success in future. For policy makers, this study could assist them in providing the entrepreneurial training. For new business founders in the entrepreneurship domains, this study is of value as well. Lastly, this study is a valuable addition to the extant literature as it presents fresh information on the factors affecting the Entrepreneurial Intention of the Students of Jordanian Private Universities.

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Chapter 4
Investigating the Classification of Human Recognition on Heterogeneous Devices Using Recurrent Neural Networks

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4.1 Introduction

The enormous capabilities and the low cost of smart devices have enabled consumers to purchase and use them for their daily activities. Smart devices that are most widely used these days are smartphones and smart-watches of different brands and manufacturers. In these smart devices, the most widely used embedded sensors are accelerometer, gyroscope, GPS, and compass sensors [1]. The accelerometer and the gyroscope sensors can be used to capture motion information of the users carrying the smart devices. This provides the ability to capture and recognize the various activities of a person in real time with very low power requirement over an extended period of time [2].

The ability to capture and recognize human activities out of the data produced from these motion sensors has played an important role in many fields and applications. The medical field has the highest number of applications using these data to provide health and fitness information for the users [3]. These data have been also used for detecting the health risk of falling that may occur among elderly people [4].

Daily activity tracking has been also of a great interest for both industry and research purposes [5, 6]. Different researchers have been working on beating the state-of-the-art results on different HAR datasets that are publicly available online. The Opportunity dataset (Opp) [7], PAMAP2 dataset [8], and Daphnet Gait dataset (DG) [9] are examples of such well-structured datasets that are publicly available for researchers. Despite the enormous work done by the researcher in the field, we believe that the results obtained were very optimistic compared to real-life scenarios as they were tested on homogeneous data created from similar devices.

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Different approaches, methods, and techniques have been used by researchers to build models for HAR classification problems [10]. These include KNN and Naive-Bayes classifiers [5], Multi-class Support Vector Machine (MC-SVM) [11], and many other traditional classification approaches. Nevertheless, deep learning methods have outperformed all those traditional methods in almost all HAR domains as well as in other domains [12].

On the other hand, deep learning techniques have not yet been implemented and tested on a heterogeneous HAR dataset such as the Heterogeneity Human Activity Recognition (HHAR) dataset [13].

In this chapter, we implement a deep learning framework that deals with a HAR system on heterogeneous data. The heterogeneity of the data may come from the heterogeneity of the devices that collect the data, the heterogeneity of the users who used the devices, and the heterogeneity of the locations of the devices on the user's body. To deal with the heterogeneity of the data, a statistical feature vector is generated out of the raw data using a sliding window technique. The number of feature vectors produced by each device may come out to be different. For this reason, an alignment technique is proposed to align those feature vectors with respect to their class values. This is also required to merge the feature vectors of both the accelerometer and gyroscope data with common labels for each smart device. Finally, these aligned and concatenated features are fed into a simple RNN architecture with two stacked Long Short-Term Memory cells (LSTM).

Four scenarios are tested to evaluate the effect of heterogeneity. The first scenario uses phone data for training and watch data for testing. The second scenario merges phone and watch data for each user and then uses the data of a set of the users for training and the data of the other set of the users for testing. The third scenario deals with only phone data. In this, we use a subset of the phone users for training and the rest of the users for testing. The fourth scenario is the same as the third scenario, but it deals with watch data instead. The results show how RNN models tolerate the heterogeneity on each of the given scenarios.

The rest of the chapter is organized as follows. Section 4.2 covers some related work on different HAR classification approaches as well as various neural network architectures used in similar problems. Section 4.3 explains the methodology this work is based on. After that, the results are shown in Sect. 4.4. Finally, Sect. 4.5 presents our conclusion based on the achieved results and Section and discusses the future work that can be built on this research.

4.2 Related Work

Many efforts were spent in the literature to study the accuracy of smartphone-based HAR systems. Such studies tend to give optimistic results that are proven to be unrealistic when deploying a HAR system in a real-world environment [13]. Stisen et al. suggested two reasons for the accuracy differences between research work and real-world deployment [13]. The first reason is that different devices contain sensors

that vary in their specifications such as the frequency rate and these sensors are also prone to inaccurate readings. The second reason is the fact that the number of training devices is very limited when compared to the variety of devices in the real world.

To address such challenges, a Heterogeneity Human Activity Recognition (HHAR) dataset that is publicly available at the UCI Machine Learning Repository which is considered to benchmark human activity recognition algorithms in real-world contexts [14]. The dataset was gathered with different device models and use scenarios to reflect sensing heterogeneities that are expected in real deployments.

The HHAR dataset contains the readings of accelerometer and gyroscope sensors in smartphones and smart-watches. The readings were sampled at the highest frequency the respective device allows. Readings were recorded while the users, carrying these devices, were executing activities in a random order. Those activities are walking, standing, sitting, stair up, stair down, biking, and some null values between the mentioned activities. To assure user heterogeneity of the dataset, nine different users carried out the mentioned activities. Moreover, four different smartwatches (two LG watches, two Samsung Galaxy Gears) worn on user's arms were used. And, eight different smartphone devices (two Samsung Galaxy S3 mini, two Samsung Galaxy S3, two LG Nexus 4, two Samsung Galaxy S+) were worn on the user waists.

In their work, Stisen et al. [13] have clustered the devices with similar sensor characteristics to enable a trained model to deal with unknown devices according to such characteristics to overcome the data heterogeneity. Moreover, they have used interpolation to increase the number of training devices by synthesizing new ones from the existing data. They have supported their argument using KNN, C4.5, SVM, and Random Forest classifiers. The results obtained from all the given techniques had lower accuracies than what is suggested by the literature. However, they suggest that their results are more realistic when compared to real-world HAR deployments.

Despite the good performance that the standard classification techniques offer in this field, deep learning has become of a great importance in different application domains [15]. And of course, HAR is one of those domains where deep learning substitutes handcrafted feature extraction techniques that require expert knowledge.

Lipton et al. [16] have reviewed the breakthrough that Recurrent Neural Networks (RNN) have achieved in the past three decades, which is due to its ability to retain a state that represents information from an arbitrarily long context window, which makes it a best choice for modeling time-series data, such as HAR sensor data. The authors also covered the advantages for LSTM and Bidirectional RNN (BRNN) architectures over the vanilla RNN implementations.

A further research that evaluated different types of recurrent units in RNN has been introduced by Chung et al. [17]. In their work, they have compared between LSTM units and Gated Recurrent Unit (GRU) which is much simpler than an LSTM unit. Their work confirms the previous findings of researchers that both advanced recurrent units are better than the traditional RNN units. And they have also found that GRU performance is comparable to LSTM performance on many tasks. GRU units have shown great performance in the experiments done by Tang et al. for question detection in speech applications [18]. They have used GRU units to build

different RNN and BRNN models to extract efficient features at segment and utterance levels. They claim that GRU units can determine a proper time scale to extract high-level contextual features.

Moreover, Graves et al. have found that LSTM is much faster and more accurate than both standard RNN and time-windowed Multilayer Perceptron's (MLPs) [19], because they are designed to avoid the diminishing gradients through many layers time in RNN. The same fact was obtained by Gers et al. in their work with context-free language benchmarks [20].

Sak et al. have also confirmed the same fact again in their work with large-scale acoustic modeling [21]. Graves et al. proved that Bidirectional LSTM (BLSTM) significantly outperforms unidirectional ones [19]. That is because they contain two parallel recurrent layers that stretch both to the future and the past. They are then followed by a layer that concatenates their internal states for the given time-step. Thus, to utilize the benefits of deep learning methods, Ordóñez et al. have proposed a generic deep framework for HAR systems that is based on convolutional and LSTM recurrent units which model both the spatial and temporal dynamics from raw sensor inputs [22]. Their results have outperformed other non-recurrent network architectures. However, they have mentioned in their work that their proposed framework can be applied to homogeneous modalities.

On the other hand, Park et al. used RNN for a depth camera-based HAR system. Unlike sensor-based HAR systems, their work uses joint angles from multiple body joints that are changing in time representing outperforming Hidden Markov Model (HMM) and Deep Belief Network (DBN) systems [23].

Finally, in their work, Hoos et al. provided a systematic exploration of the performance of three neural network architectures, namely, Deep, Convolutional, and Recurrent Neural Networks [24]. That exploration was done on three different HAR benchmark datasets using the fANOVA analysis framework. Their study shows the impact of hyper-parameters on the neural network performance in HAR like datasets. And it has also shown that bi-directional LSTM cells outperform all other deep learning techniques for HAR datasets.

4.3 Proposed Deep Learning Activity Prediction

To be able to deal with the HHAR dataset, the authors of this chapter started visualizing the data to get insights about its content. There exist four files of 10 attributes and different number of tuples in each file as shown in Table 4.1. The attributes in each file are the same, and they are explained in Table 4.2.

Figure 4.1 shows the uniform distribution of the class labels inside the watch gyroscope file. It also shows that the amount of null values in the dataset is as equal as the other class labels. Furthermore, Fig. 4.2 shows the typical order of activities in a single experiment in the file and shows the distribution of null values between the different activities. Since these null values will signify different types of

Table 4.1 Number of tuples of the four files using 4 s sliding window with 2 s overlap

	Accelerometer		Gyroscope	
File names	Phone	Watch	Phone	Watch
Original file tuples	13,062,475	3,540,962	13,932,632	3,205,431
After removing nulls	11,279,275	3,020,605	12,063,005	2,735,002
Generated windows	50,345	8614	34,728	7919
After alignment	27,782	7799	27,782	7799

Table 4.2 Description of the attributes in the four files

Attribute	Description
Index	The index for each experiment of a combination of a user, a model, and device. It starts with zero for every experiment in the file
Arrival_ Time	Timestamps in nanoseconds assigned by the operating system of the device
Creation_ Time	Timestamps in microseconds assigned by the sensor hardware of the device
X	Floating number for the x coordinate of the sensor
Y	Floating number for the y coordinate of the sensor
Z	Floating number for the z coordinate of the sensor
User	A letter (a–i) for the corresponding user carrying out the experiment.
Model	Name of the device in use
Device	Different devices of the same model
Gt	A class attribute (walk, stand, sit, stairs up, stairs down, bike, and null)

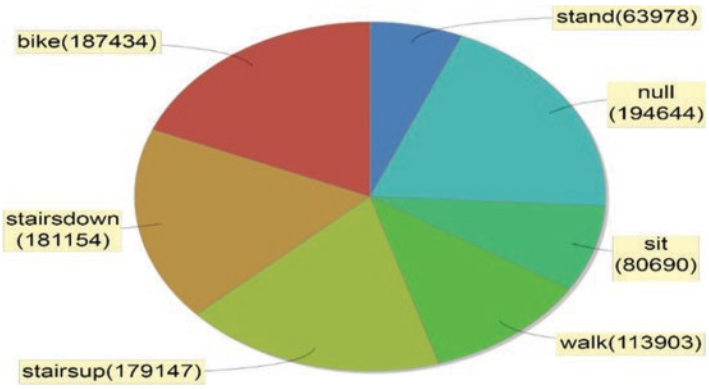

Fig. 4.1 Class labels' distribution inside the watch gyroscope data file

movements between the given activities, they are excluded as the first preprocessing step in all our experiments.

And to decide between using creation or arrival time for the sliding window process, Fig. 4.3 shows that the creation time is much smoother – has non-repetitive timestamps – than the arrival time in a single experiment in the file. And that is

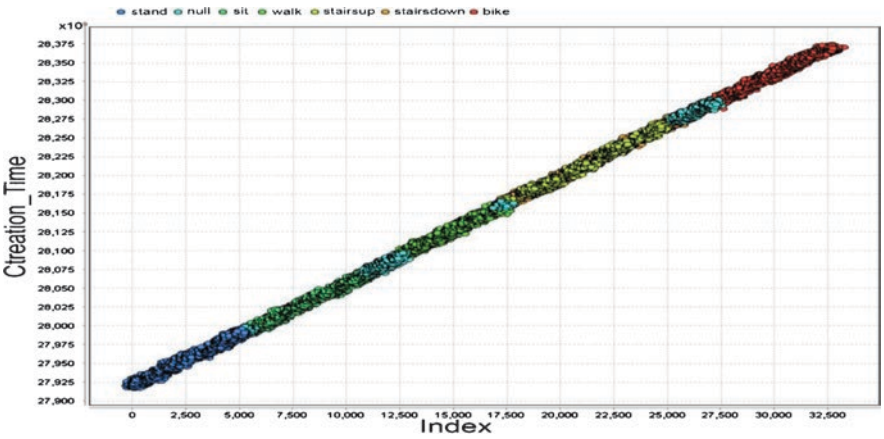

Fig. 4.2 The distribution of the activities in a single experiment inside the watch gyroscope file

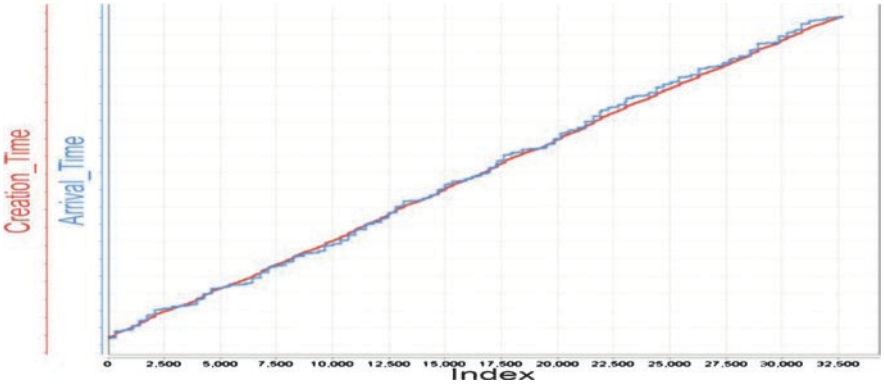

Fig. 4.3 Creation versus arrival timestamps in a single experiment inside the watch gyroscope file

because the arrival time is affected by the different CPU loads in the operating system, which makes the creation time more suitable for the sliding window process.

Figure 4.4 shows that the index value starts with zero to some upper limit for each new experiment in the file. It shows also that the creation and arrival times are not monotonically increasing throughout the whole file. And that should be taken into consideration while performing the sliding window on the file. That is simply done by avoiding overlaps between different experiments in a single file.

After understanding the data to be worked on, preprocessing could be started followed by the training and testing process, where preprocessing includes a sliding window of a given file. Followed by an alignment process to combine the windows from the accelerometer and gyroscope files of either the phone or watch data. The working environment for all the work done in this chapter is described in Table 4.3.

Four scenarios were implemented corresponding to each of the combinations shown in Fig. 4.5. The first scenario uses the phone files (accelerometer and gyro-

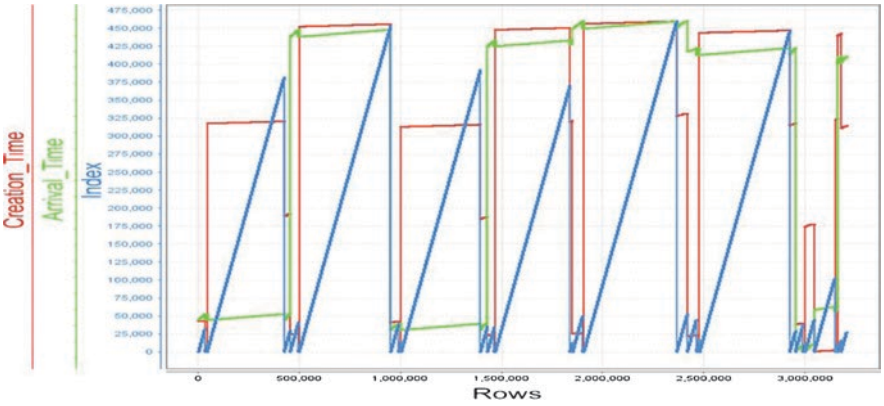

Fig. 4.4 Index values, creation, and arrival timestamps in the watch gyroscope file

Table 4.3 Work environment

Item	Description
Device	Dell Inspiron (15–7559) laptop
Processor	Intel(R) Core(TM) i7-6700HQ @ 2.60GHz
RAM	16.0 GB DDR-3
Hard disk	128GB SSD SanDisk Z400s
GPU	NVIDIA GeForce GTX 960 M
GPU CUDA compatibility	5.0
CUDA cores	640
Operating system	64-bit windows 10
Implementation software	TensorFlow 1.7

scope) for training and watch files for testing. While the second one combines the phone and watch data together, producing an accelerometer file and a gyroscope file for phones and watches merged together. They are then split into training (for the first five users) and testing (for the last four users) files during the sliding window process. The third scenario uses only the phone files split into training and testing based on the users as in the second scenario. And similarly, the fourth scenario uses only the watch files split into training and testing in the same way.

After the sliding window process, the produced accelerometer and gyroscope feature windows need to be aligned to merge their labels' files into a single common file. Two window sizes have been implemented for each scenario with 2 and 4 s and 50% overlap between consecutive windows considering nonoverlapping of class values (activities) and Index values (experiments). After removing the tuples with the null class, the sliding process starts maintaining a minimum of 20 tuples per window for feature extraction to ensure meaningful statistical information out of those numbers. If the threshold was higher, we will lose many tuples at the end of each activity, and if it was lower, we might get errors from some functionals, and we

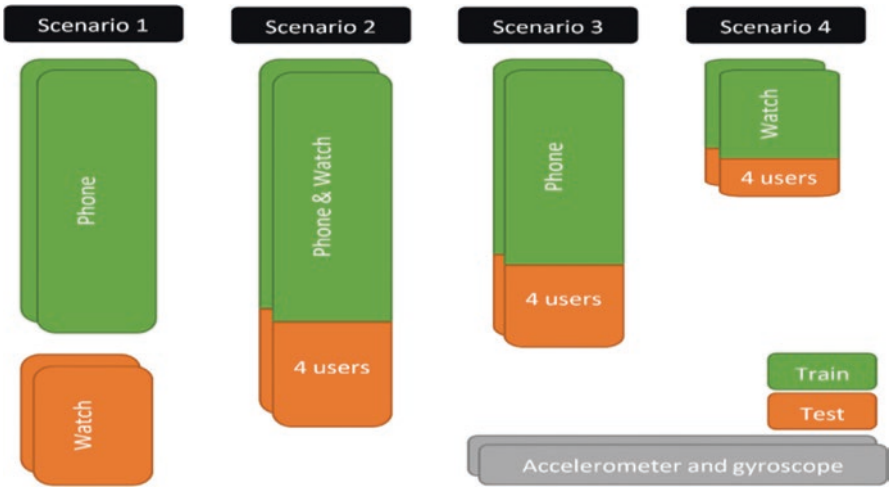

Fig. 4.5 The four different combinations for the four original files

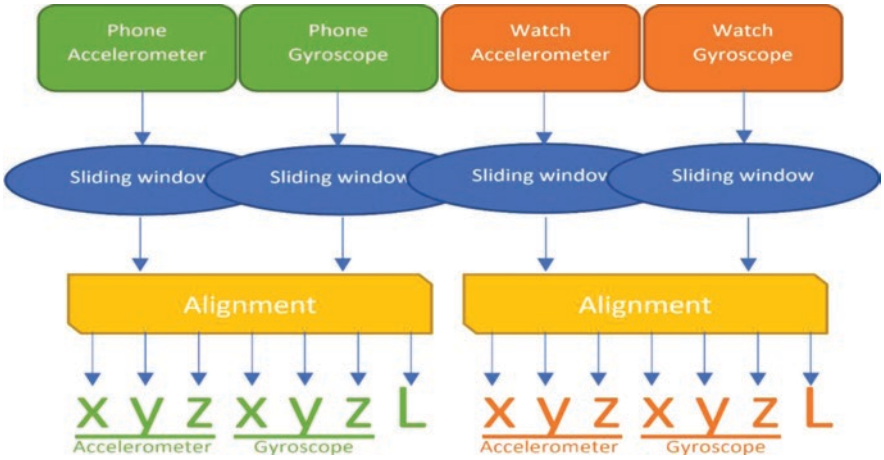

Fig. 4.6 Sliding and alignment process produces training (green) and testing (orange) files for scenario 1

might get meaningless statistical information since the consequent numbers are very close to each other. The sliding window process then obtains 128 statistical features for each of the x, y, and z windows. After an activity is split into multiple windows, each window is associated with the class label for that activity to be classified to the same activity.

Figure 4.6 shows the preprocessing steps for the first scenario. It starts by doing a sliding window for each one of the original four files separately. That creates four intermediate files for each input file (x, y, z, and labels). After that, the phone files (three accelerometer and three gyroscope) are aligned based on their labels' files to

Algorithm 1: Align *File*1 and *File*2 based on their `Labels`

```
Align (File1, File2)
    inputs: File1 and File2 of different number of rows, each containing X, Y, Z features and their Labels
    output: X, Y, Z features for both files and a single Labels file
    i ← 0 ;                          // Initialize a pointer for the beginning of both files
    while not the end of either files do
        if File1.labels[i] ≠ File2.labels[i] then
            // If the labels in this row do not match, a row or two should be deleted
            if file.labels[i] == file.labels[i − 1] then
                // If this row's label is the same as the previous one, delete it
                Delete the row(file[i]) ;                                  // In File1 or File2
            else if file.labels[i] ≠ file.labels[i + 1] then
                // If this row's label is NOT the same as the next one, delete it
                Delete the row(file[i]) ;                                  // In File1 or File2
            else
                // otherwise, simply delete that row from both files
                Delete both rows(File1[i] & File2[i])
            end
        end
        i ← i + 1 ;                                  // Increment the pointer to the next row
    end
    return 6 Feature files and 1 labels file ;                    // 3 Features for each file
```

Fig. 4.7 Algorithm 1 for the alignment procedure

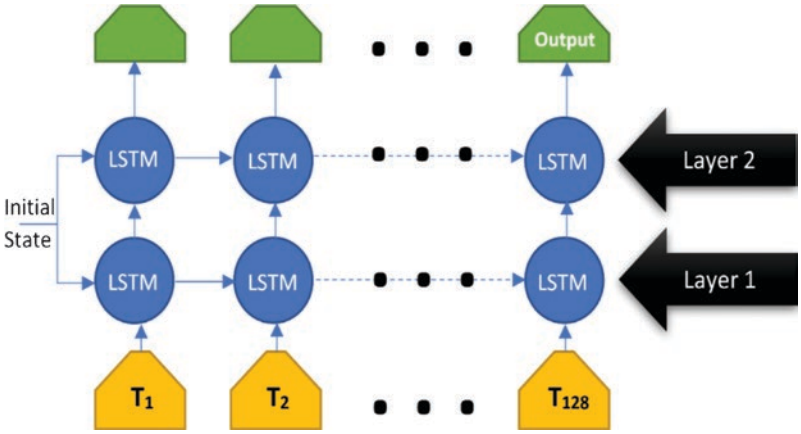

Fig. 4.8 Unfolded view of a single multilayer (two stacked layers) LSTM unit

have a single common label file. The alignment process can be seen from the naïve but effective implementation of algorithm 1. That produces six feature files aligned with a single label file for training (phone) and the same thing for testing (watch) (Fig. 4.7).

After the alignment process, six files are ready to be used as an input to the RNN network to be classified to the seventh – labels – file. Three hundred epochs of training were maintained for all the given scenarios. A simple LSTM architecture is used with two stacked LSTM cells over 128 time-steps. The number of time steps correspond to the number of extracted statistical features out of each window as can be seen from Fig. 4.8.

4.4 Results

The first expected observation was resulted from the first scenario, where the phone data was used for training while the two different places on the user body creating significantly different motions on the devices. The phone devices were placed on the waist of the user, while the watch devices were placed on their arms. Hence, different types of motion data are going to be captured for each of these two devices.

That can be seen in Fig. 4.9 with the test accuracy almost having no improvement while the training accuracy is getting improved. This result was expected, and hence, the placement of a specific device by the users in real-life situations should be considered when implementing a HAR system for this kind of a device.

With that observation from the results of the first scenario, researchers and practitioners should pay attention to this type of heterogeneity in the dataset. And that is because this kind of heterogeneity should be handled in two different applications in real-life situations as the placement of the device on the human body generates different types of movements for the same kind of activity. Hence, generating HAR heterogeneity should be carefully done based on the device placement on the human body to produce robust and realistic models.

Furthermore, Fig. 4.10 shows the performance of the testing data that is created with every scenario. In the last scenario, the watch data was used alone by splitting it into training (for the first five users performing the experiments) and testing (for the last four users). The results show that its performance was far less those of the second and third scenarios. And the main reason for this low performance is the small size of the data in the watch files, which is around 3 million tuples compared to around 12 million tuples in the phone files. This observation suggests that increasing the dataset size is directly correlated with the obtained accuracy of the generated model, keeping in mind that the data is correctly heterogeneous as mentioned earlier.

Moreover, the second and the third scenarios show the highest testing accuracies, which is first due to the large size of the training data. And, because the testing

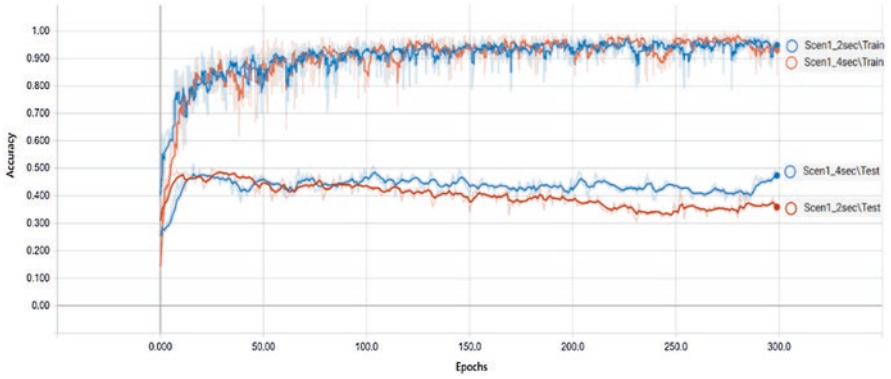

Fig. 4.9 Training and testing accuracy for the first scenario

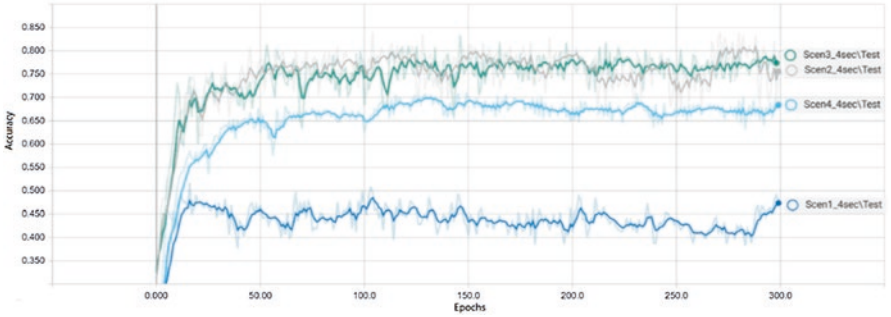

Fig. 4.10 Testing accuracies for all the scenarios using 4 s sliding window

process was done on device models and types that were considered during the training process. The highest testing accuracies (Scenario2 = 84% and Scenario3 = 83.36%) are comparable to the state-of-the-art results (from 55% to 86%) using interpolation techniques. Those accuracies were obtained using a 4 s sliding window with 50% overlap, which indicates that considering a longer motion period is better than a shorter one. And that shows the movement dependency over time for a given type of activity.

At last, it can be seen from the obtained results that the accuracies achieved are far less than the state-of-the-art for any HAR system in the literature, which can jump up to 95% in a nonheterogeneous HAR dataset. That is caused by the huge amount of heterogeneity for a single device and the heterogeneity of adding multiple devices in the dataset. However, increasing the amount of heterogeneous data for training, like for the second and third scenarios, significantly enhances the network performance to adapt with this heterogeneity. Hence, to provide a robust, realistic, and heterogeneous dataset, it should have a huge amount of data that the models should learn from. And that data can be either real data gathered from devices in real experiments, or it can be augmented using interpolation or different augmentation techniques to increase the amount of data samples in the dataset.

4.5 DEEP Learning Benefits for HHAR

In this section, healthcare field will be discussed on how the filed will customize our approach to be used effectively in the predication of serious health problems.

HAR determines the activities of an object based on the collected data from the object movements. This captures various activities of an object in real time. The major benefits of our approach discussed in this chapter to different fields in the real life can be customized to meet the fields requirements.

Since the HHAR includes heterogeneous of different smart devices, our approach has an ability to contribute solutions to be used in these environments, where the device placement, the size, and the heterogeneity of the data can significantly affect

the performance of HHAR applications. In addition, many applications can benefit from the approach where the placement of the device on the human body generates different types of movements for the same kind of activity.

An important factor for development health care is to understand the activities done by the human. The approach in this chapter uses smartphones which are considered the most appropriate devices that can be used easily and efficiently to help in the healthcare sector. Most smartphones have three components including collecting data components, model usage, and activity recognitions. Sensory components utilized accelerometer and gyroscope, which are built in the smartphones to collect data. The patients usually use these phones to help them in recording their activities and then can be used in serious health problems and predict falling elderly people. In the model training, our approach uses deep learning methods then the activity recognition components used the trained model component for prediction. These components can be used in a client-server design or any simple model. The designers can utilize the best scenario that suitable to the application.

4.6 Conclusion

In this work, we have provided a very important investigation on the impact of the heterogeneity of smart devices on any HAR system, which was done using the huge Heterogeneity Human Activity Recognition (HHAR) dataset. Essential steps of sliding windowing and files' alignment were implemented as a preparation step for the Recurrent Neural Network Training.

The alignment process was done in a very simple way that achieves reasonable results, and the same thing for the simple RNN architecture that only uses two stacked layers of LSTM cells. The results obtained show how real-life implementations should consider the device placement on the human body in real-life scenarios. They show also how the size and heterogeneity of the data can significantly affect the overall performance of the model. Finally, the work shows that the realistic heterogeneous HAR system performance is far less than the optimistic homogeneous HAR performance proposed in the literature even when using the state-of-the-art deep learning tools, such as LSTM networks.

As a future work, we propose building a sophisticated BRNN architecture to be trained on the second and third scenarios. A further investigation on the performance of the most complex BRNN architecture on this data will further confirm the results obtained in this work. On the other hand, a similar dataset can be created again by placing both the phone and watch devices on the same place on the body of the user performing the experiment. This way, we can eliminate the reason of having two different types of motions on these devices.

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Chapter 5
Toward an IoT-Based Solution for Emergency Medical System: An Approach to *i-medical* in Bangladesh

Md. Arif Uz Zaman, Saifur Rahman Sabuj, Romana Yesmin, Sadman Sakib Hasan, and Asif Ahmed

5.1 Introduction

An epitome of high living standards would include convenient and updated medical treatment throughout an individual's lifetime. In Bangladesh, there are approximately three physicians and one nurse per 10,000 population [1]. In more depth, the density of doctors, nurses, dentists, physicians, and other health-related workforce who are qualified and registered as Healthcare Providers (HCP) is 7.7 per 10,000 populations. Thus, Bangladesh has the lowest number of HCP compared to other Southeast Asian countries. Likewise, they also fall short of the MDG targets projected by WHO. In more general term, there is only 0.58 HCP per 1000 population with a health workforce of 2.3. Therefore, it can be assumed that Bangladesh lacks over 60,000 doctors and 280,000 nurses [2]. As this is a poor ratio, we can see how it leads to a crisis whenever there is a demand for medical experts. Thus, Bangladesh suffers from a lot of incidents where immediate health support is required. And for this, the medical system needs a major renovate in our country.

As this is the era of growing wireless paradigm, wireless technology and the embedded system have been developed a lot. The number of Internet of Things (IoT) enabled devices worldwide is 26.66 billion in 2019; gradually it is increasing, and in 2025 it will be 75.44 billion approximately [3]. In health industry this system can do a lot. This IoT system can face new challenges with improved solutions, providing medical treatment during the emergency situation in the several parts of

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the world. As a result, the life of the people around the world will be easier to survive during any emergency period.

A developed country like Canada has the doctor to patient ratio of 220 doctors per 100,000 people, a statistic from the year 2013 [4]. Moreover, it is said that it is improving. Likewise, when it is compared to Bangladesh we can see the severity of the difference. However, it was stated in 2002 how Canada was suffering proper medical health treatment due to long unique geographic, population, and political challenges and other challenges. It was compensated by using e-Health and the help of the Canadian Government through ICT [5]. Moreover, due to geographical and location challenges, Canada is benefitting a lot. An example would be of Michael Humber, who has saved six million kilometers of traveling for patients, by providing health care through telehealth for 8 years to over 8000 patients [6].

Most of the work that has been done so far which is related with the IoT for medical purposes involves data collection with the help of IoT-enabled devices that are connected to the subject's body. This enables to control many purposes like remote monitoring and data collection from several locations which can improve the emergency medical facilities. In this chapter, we will focus on a group of people in Bangladesh. In Bangladesh, approximately 6.23% of its population is aged above 60 years [7] who lives in rural area. Moreover, 70% of the total population of Bangladesh lives in rural area [1]. They are unaware of the government medical facilities which are reserved for them. For example, there is a telemedicine facility for the people of Bangladesh provided by the government. At present, there are 43 telemedicine centers and these telemedicine centers are equipped with high Internet bandwidth, good quality telemedicine camera, large screen displays, and telemedicine peripherals [8]. The usage of IoT devices can change their living standards. They basically depend on their family members for their health care. The IoT devices have the potentiality to add the independence to take care of their health by a doctor on a regular basis from any locations of Bangladesh.

In this research, we would focus on the possibilities of combining e-Health IoT and GSM technology. Our research is based on the notion of improvement of existing technology using IoT and makes it cost effective for a developing country like Bangladesh. The overall aim of this research is to design a medical emergency system by leveraging the concept of crowdsourcing in order to:

- Establish an IoT-based network to improve existing e-Health monitoring system
- Develop a mathematical model for uplink and downlink scenario and evaluation of our proposed *i-medical* system
- Develop a mobile application for practical simulation in the context of Bangladesh

The organization of the chapter can be summarized as Sect. 5.2, literature review which talks about the current researches or the research that has been done on the topic. Next is Sect. 5.3, called the problem and the solution approach which gives an overview of the problem and the criteria which will be used to solve them. Furthermore, Sect. 5.4 which is the system model explains the architecture of the methodology. Likewise, Sect. 5.5, system implementation, describes in detail about

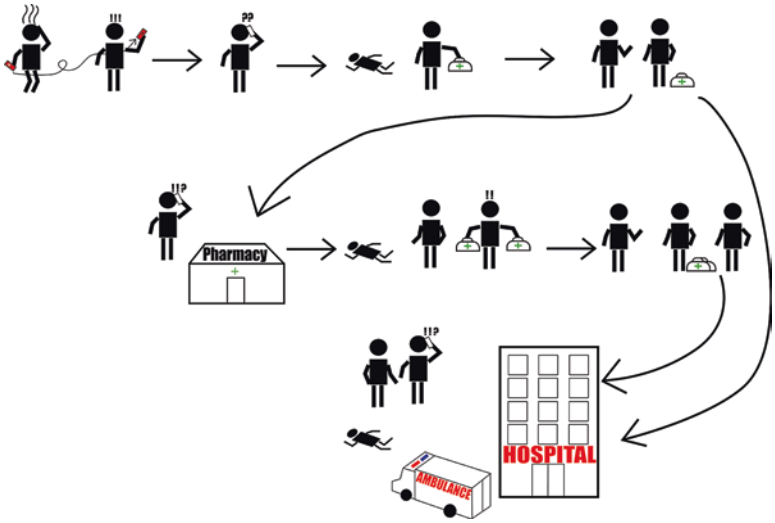

Fig. 5.1 Working steps for *i-medical* in physical layer

the methodology for implementing the system. In addition to that, mobile application integration describes how mobile application can help the overall procedure. For analysis and evaluation, the section system evaluation is involved. Finally, conclusion is added to give a brief overview of everything that has been done and will be planning to do in the future (Fig. 5.1).

5.2 Literature Review

Several kinds of research have been done in IoT-based technology to bring emergency medical support in the period of emergency. One such significant research is [9] where the researchers come up with a solution focusing on privacy by accessing the patient's Personal Health Information and caring chronic patients combining with the IoT, medical sensors, and wireless communication to monitor the health-related parameters of the patients to give the best medical solutions in emergency situations and also having a record of their conditions. Again, in [10] the authors developed an IoT-based remote well-being checking framework where the elderly people can take care of themselves by staying at home, and this system contains multiple independently functioning layers (CoAP-based IReHMo implementation). While in [11] the authors discuss an IoT device for rehabilitation and elderly monitoring system with the help of IoT considering two functions – Activity Recognition and Movement Recognition that detect the idleness and illness of the patients. This [12] survey paper discusses an energy proficient and dependable e-Health observing system that focuses on presenting an architecture system to portray the complete

checking life cycle and highlight fundamental benefit components and give some potential solutions on patient remote monitoring system. In [13] there is an architecture of an unused e-Health stage consolidating humanoid robots linked with IoT to a web-centric Diseases Management Hub that supports people to get treatment on diabetes. In [14] authors demonstrate a process on how to coordinate and apply IoT system in a big network.

In [15] authors focused most important perspective of novel IoT innovations for shrewd healthcare-wearable sensors, progressed inescapable healthcare framework, and big data analytic to identify unused points of view and highlight compelling investigate issues and challenges like device-network human interfaces, scalability, and security. In [16] the researchers propose a novel approach to improve IoT-based medical records security by watermarking it using algorithm which is composed of Daubechies-3 and Daubechies-9 wavelet transform in IoT-based Hospital Information System. In [17] researchers developed a multilayer architecture of an integrated medical platform that allows to monitor patient's medical condition by biomedical data during transfer by an ambulance.

In [18] the researchers promised to build a multilayer architecture of IoT e-Health ecosystem which requires a move from the clinic-centric treatment to patient-centric treatment where hospitals, patients, and other related things will be benefited and connected with each other. In the research paper [19], the authors developed a comprehensive response crowdsourced framework that reduced the reaction time as well as the operating cost during emergency medical services. In article [20] the authors introduced a smart urban city, which collected data through energy consumption model, a new generation of sensing fabric is also introduced as a part of smart urban city. In survey paper [21] the authors proposed a model of distinct IoT that monitor the biological signal using WBANs technology. It uses wearable sensors to collect data to work with WBAN. In [22] the researchers proposed an effective health monitoring system that supervised the health status of the patients very carefully with the help of IoT and data monitoring system and using that data a decision-making system is designed. In [23] the authors proposed an IoT-based Case-Based Learning methodology for medical students that can help to store patient's data and analyze the imperative signs by using IoT. In [24] the authors described a smart IoT system for real-time health monitoring system using multiple heterogeneous wearable sensors. In [25] the researchers studied a medical control system based on IoT that improves the conditions of medical care and effective medical treatment and also the researchers designed to characterize challenges occurred by technological tools in making strides the conditions of well-being structures and to recreate the working of the framework. In [26] the authors offered an embedded system and IoT-based solution for continuous and noninvasive measuring of cardiac values by using a technology named Pulse Oximetry and also they have made a wearable cardiac monitoring and alert system that can be patients specific and helps to reduce heart-related accidents. They also used embedded system to build their device and make it wireless so anytime people can use it. They came up with a system that uses IoT and other wireless system to get heart-related various data. This data helped them to take medical decisions. Lastly, in [27] the author for

this paper describes the possibility of the 5G technology in the mobile well-being system. The author also proposed a small cell 5G-based mobile technology-based medical system.

It can be observed from the papers that they have not associated and combined technologies like IoT, use of Database, and deployment of smart healthcare system which can improve the overall healthcare system. This paper converges those technologies and it also includes mobile application. These ensure that the nearest ambulance, pharmacy, hospital, and neighbors are connected, so they can be reached out any time when an injured person requires help immediately. Likewise, in paper [9] and paper [10] patients cannot be assisted by neighbors in times of emergency. Other than that, in paper [11] a cousin is alerted however; the alerted person can be far away from the patient, hence, providing emergency medical care might be hindered. Similarly, in paper [12] there is a life cycle of the device used; however, there is no network simulation involved or association of IoT. Our work's significant improvement can help assist the problem of poor doctor to patient ratio in Bangladesh. Also inclusion of IoT can be useful in Bangladesh. In paper [28], the author introduced a telemedicine system that uses ICT and IoT technology to identify patients with intractable diseases. This paper describes reliable alarm system and expected medical IoT features for those patients. In 2020 the world has observed a severe disease called "Covid-19" which is very contiguous and deadly. World was not prepared for it and thus many death occurred. In paper [29] the author discussed about a service-oriented smart medical system which can be established to prevent such an event. In this paper they developed an IoT-based medical system which would allow them to proper resource allocation, utilization and efficiency. This management system can be promoted to an intelligent system which would be able to manage the resource more efficiently.

5.3 Problem and Solution Approach

As Bangladesh is yet to develop, expectation of quality medical services is low. Moreover, the integrity of handling medical emergency is yet to grow. As per definition, an emergency situation is such that, it can occur at anyplace or at any time. On that possibility, the researcher must develop a system which would be available at low cost and without the slightest intervention of time.

5.3.1 Problem

In Bangladesh, one of the major problems is unplanned urbanization. Moreover, due to the living condition in Bangladesh, the medical services cannot be provided swiftly. In different cases, it has been observed that medical care could not reach the place due to lack of time and manpower.

To solve this problem, this chapter introduces IoT-based e-Health monitoring system and connect it with mobile application. Similar kind of solution has been proposed in numerous research papers [9, 19, 20, 25].

The goal of this chapter has been set and specified as to introduce an IoT-based medical emergency system for Bangladesh. In this chapter, the system is called *i-medical*. Bangladesh is the second largest economy in South Asia and the 41st largest economy in the world [30]. The country went through various milestones to finally achieve this position. Despite Bangladesh developing a lot in the last 5–10 years, the emergency medical alert system has not been implemented. Thus, in this chapter, the major target would be solving to

- Not provide low-quality medical treatment on emergency situation
- Provide low cost medical service
- Provide medical services in adverse situations

As mentioned earlier the unplanned urban city is a major problem for the emergency medical system. Moreover, there are other problems which also aggregate like inflated population density and lack of basic emergency treatment knowledge. Furthermore, those who have knowledge due to lack of communication adversities cannot provide treatment to the person in need. Thus, using the latest technology and mobile network this chapter proposes a solution to the problem.

5.3.2 Solution Approach

As mentioned earlier, this paper is proposing a solution with IoT and mobile network. Figure 5.2 shows the detail process of the overall methodology.

In Fig. 5.2 it is possible to observe how the system would work. In the first block, it can be observed that the emergency initiation starts To start an emergency from the patient side the mobile application would be observing if anything is wrong. A physical button (e.g., Volume button or Power button) would be assigned as an emergency button. By pressing that an emergency alert would be observed in IoT network. Through that network, data would be served to database Thingspeak. The Thingspeak would save these new data accordingly. In the Physical Layer, the main work would be done. Patient, Neighbor, Pharmacy, and Ambulance to the hospital all are connected with the network so that communication happens very rapidly. The mobile application would be responsible to do the task. Likewise, all the system would work simultaneously.

5.4 System Model

In [31] the author describes that the emergency response system is divided into four segments. This chapter is the extension of the previous work of the research [31].

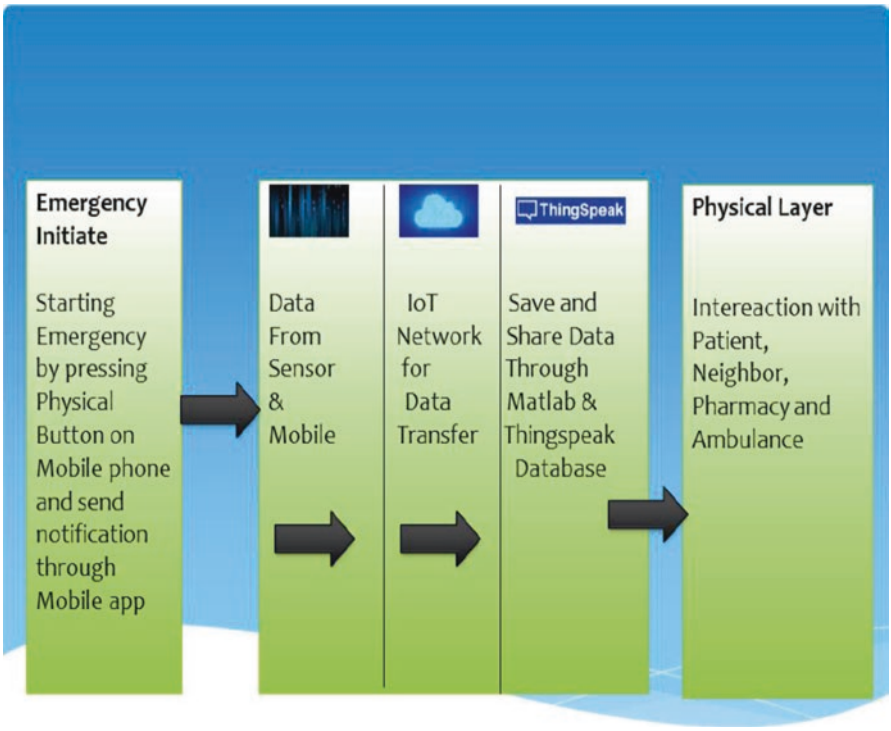

Fig. 5.2 Proposed solution for *i-medical*

The complete work is shown through a flowchart. Flowchart in Fig. 5.3 describes the working diagram.

In Fig. 5.3 the first phase of the system is shown. Likewise, in Fig. 5.4 the second phase of the system is shown.

In the first phase of an emergency situation, this system explains how patient and neighbor interact with each other. When a person has a medical condition, he or she uses his or her mobile phone to send an emergency notification. There would be a mobile application to govern all the actions. After initiating emergency, mobile takes the location data of the patient from the GPS and sends this information to the database (Thingspeak). Thingspeak saves this information and actuates a notification to all the neighbors near to the location of the patient. This updates the data on Thingspeak. After this, the database sends a push notification to all the neighbors nearby of that patient. Mobile application in neighbor's mobile would then show a notification along with the emergency sound. This would happen only to the nearest neighbors. The first neighbor who would accept the emergency would get the location data along with a specific direction to the patient. Neighbor would go to the location and start treatment for the patient. This includes checking the patient (i.e., checking blood pressure, pulse system, etc.). The neighbor would give primary treatment with first aid. With this, the first phase of the system ends.

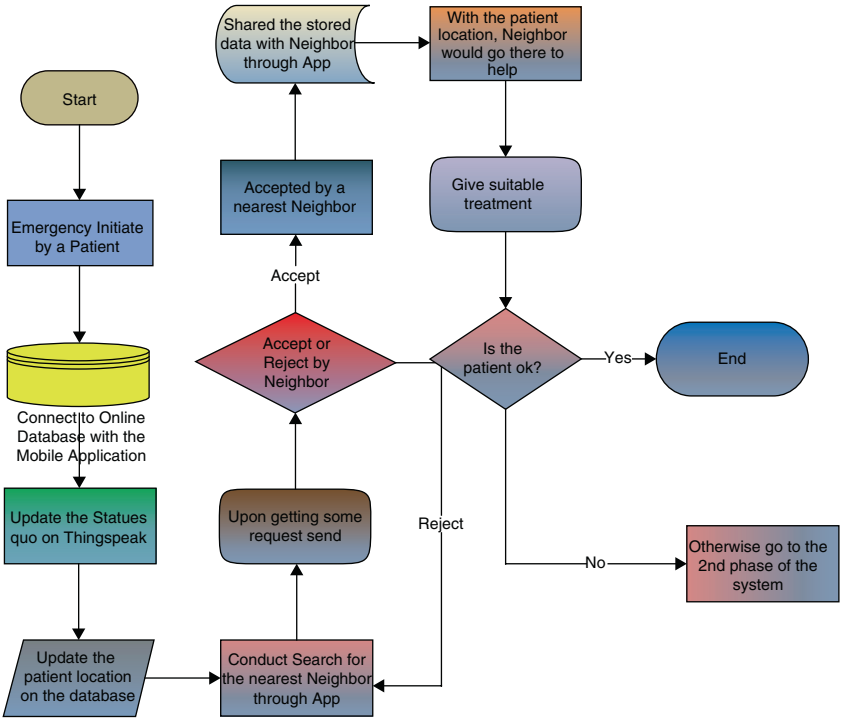

Fig. 5.3 System model and working plan first phase

In the second phase, the neighbor would take the treatment to the next step. If the first aid treatment is not sufficient, then neighbor would take the decision on what to do next. If the neighbor thinks the patient needs further examination, the neighbor should call pharmacy for help. Otherwise, if the patient is very sick, then neighbor would call for an ambulance to take the patient to the nearest hospital. If the neighbor calls for pharmacy, then the mobile app would take the location and send it to the database. With the help of the IoT network, it would launch a search for the nearest pharmacy. It would send an emergency notification to all the nearest pharmacies. When a pharmacy accepts the emergency, the pharmacy would get the necessary data uploaded by the neighbor. With the data, the pharmacy person would know what is necessary to the neighbor for the treatment. The pharmacy would take all medicines and equipment to patient's location. The neighbor would use those to give proper treatment to the patient.

If the neighbor thinks that the help from the pharmacy would not be significant, then the neighbor would go for the ambulance service. The ambulance would take the patient to the adjacent hospital. Lastly, the hospital doctor would take the rest of the responsibility.

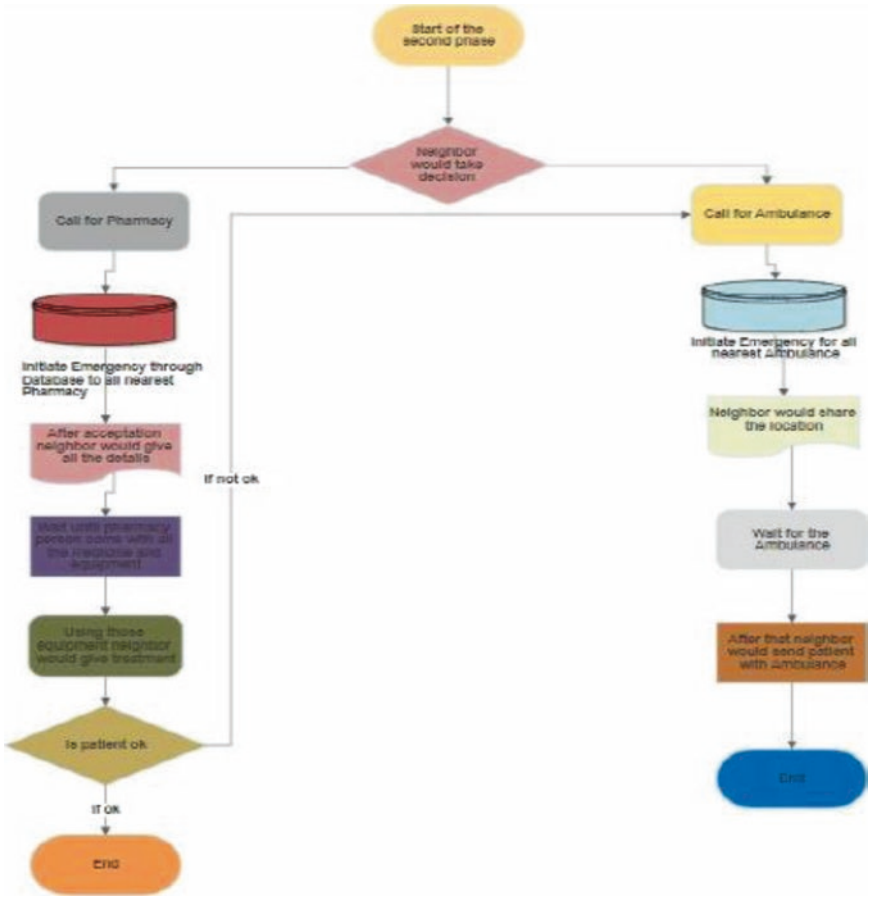

Fig. 5.4 System model and working plan second phase

5.5 System Implementation

5.5.1 Device Description

We have used some devices that have given us the best results for analyzing the emergency medical situation. For our device implementation, we have used SIM808 made by Simcom. Along with that, Arduino pro mini, GPS, and GSM antennas were also used. Thus, our experimental setup basically consists of four parts: (i) A Arduino Pro mini, (ii) SIM808, (iii) GPS antenna, and (iv) GSM antenna (Fig. 5.5).

Arduino Pro-mini is a microcontroller board based on ATmega328 with 14 digital input/output pins [32]. We have considered this device as the brain of our system. It contains the program that runs the system to collect and transfer the data.

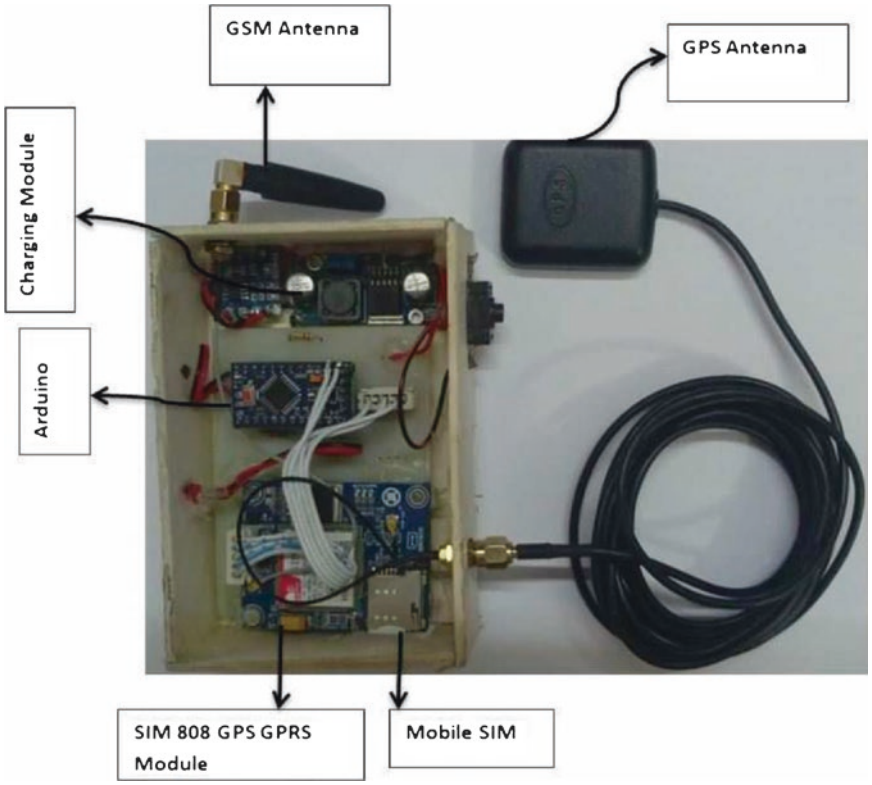

Fig. 5.5 Device description

SIM808 is a complete Quad-Band GSM/GPRS module that combines GSM technology. It has GPRS multi-slot class 12/10 [33]. It is controlled by AT commands which are similar for every model. This device requires a cellphone SIM. In our experimental setup, we have used a 4G enabled SIM from the mobile network operator Grameenphone and used their coding schemes (e.g., CS 1, 2, 3, 4) [33]. SIM808 can connect with the database with FTP or HTTP and uses TCP/UDP protocol. We have also imbedded two antennas GPS and GSM. For these reasons, we selected to use this module. These antennas assist to link and obtain the data from the servers [34].

We have used a GPS antenna that is associated with the SIM808 module for gathering the various location data in the form of latitude and longitude. The latitude and longitude we received are in the mathematical floating point value. Later, this data was sent to the server which was created beforehand and the data would be stored there. Then the stored data was sorted into an excel sheet [35].

GSM antenna is used for Internet connection and mobile network. In our research, we connect this device with the mobile network to transfer the data.

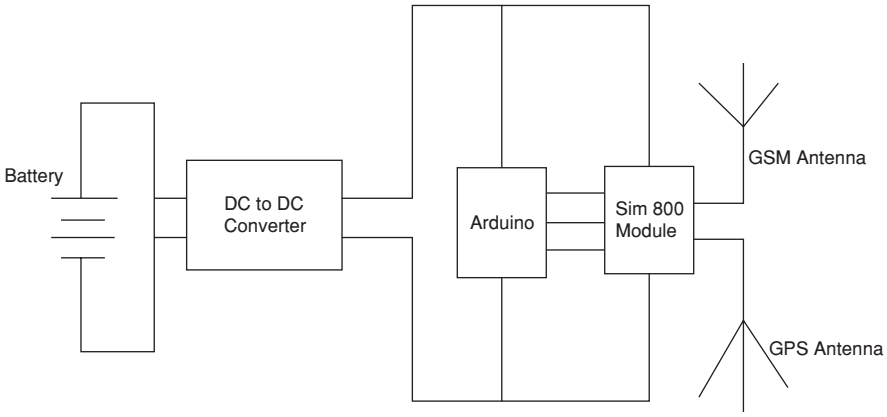

Fig. 5.6 Circuit diagram

5.5.2 Circuit Diagram

In Fig. 5.6 the circuit diagram is shown to represent how the components are connected inside the device.

5.5.3 Data Collection

With the help of the device, data have been collected from various locations within Dhaka city of Bangladesh. Table 5.1 shows some of the sample data for the simulation.

5.5.4 Database

Thingspeak is an online platform for researcher, scientist, and other people to work with numerous data from sensors.

IoT is a system where different sensors send data to the cloud server for analysis. In this chapter, the research was conducted using IoT. To save the data, online platform Thingspeak was used [36]. Thingspeak specializes in IoT connectivity. Also, it helps to monitor the data in real time and analyze it as per need. In Fig. 5.7 we can see the connectivity between computer, smart device, and cloud service (Thingspeak). A number of smart devices are connected with each other. A router is connected which controls the flow of data within the network. Using the network, the data is transferred to the cloud server Thingspeak.

In this research, our device is used to collect data and send it to Thingspeak. This data is monitored by Thingspeak. Thingspeak is a free database for storing sensor

Table 5.1 Sample dataset from our experiment

Patient		Neighbor		Pharmacy		Ambulance	
Latitude	Longitude	Latitude	Longitude	Latitude	Longitude	Latitude	Longitude
23.602572	90.167521	23.102468	90.167635	23.102448	90.967658	23.902477	90.167567
23.602533	90.167533	23.102492	90.167568	23.202422	90.867572	23.802377	90.936756
23.602497	90.167625	23.202425	90.236757	23.302338	90.736757	23.702332	90.267572
23.180243	90.167652	23.202397	90.267565	23.488745	90.676615	23.602572	90.836752
23.148025	90.267583	23.302332	90.367572	23.602422	90.467572	23.402372	90.767562
–	–	–	–	–	–	–	–
23.180246	90.267663	23.888025	90.476915	23.706922	90.372725	23.387523	90.477173
23.602452	90.267756	23.991217	90.475582	23.879087	90.275763	23.202468	90.667635
23.702422	90.267592	23.502477	90.567567	23.150523	90.906702	23.169575	90.138914
23.280242	90.267673	23.602422	90.667572	23.259528	90.189118	23.906922	90.972725
23.772417	90.267772	23.602377	90.636756	23.357523	90.877173	23.279087	90.275763
23.702442	90.167565	23.502448	90.567658	23.902492	90.167568	23.102425	90.536757
23.702372	90.177562	23.780693	90.772718	23.450523	90.206702	23.869575	90.838914
23.702372	90.177592	23.780088	90.770975	23.559528	90.789118	23.306922	90.372725
23.280237	90.787562	23.890183	90.876052	23.667523	90.377173	23.779087	90.775763
–	–	–	–	–	–	–	–
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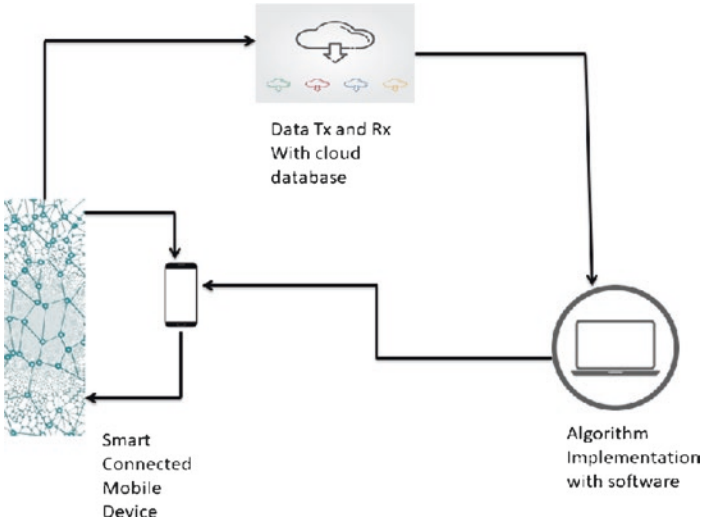


Fig. 5.7 Thingspeak connection with proposed network

data for IoT connection. Also, it is directly connected with MATLAB. MATLAB can fetch data from Thingspeak directly. So we can analyze the data through Thingspeak or MATLAB. It helps to develop algorithm in MATLAB that would make the simulation. Simulation results would help us to understand the data in the real world. Also simulation would show us visually how it would work in the real world. The data flow is shown in Sect. 5.6.

5.5.5 *Collaboration with Google Map, Google Earth*

To see the location, we have used Google Earth plot [37]. This plot shows us how the location is spread throughout the Dhaka City. Figures 5.7 and 5.8 represent the normal view and satellite view of Google Earth (Fig. 5.9).

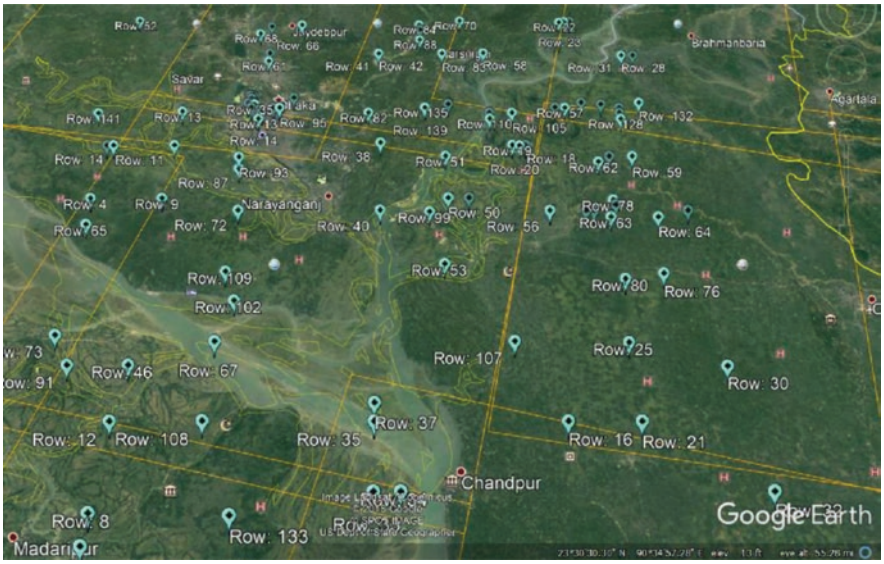
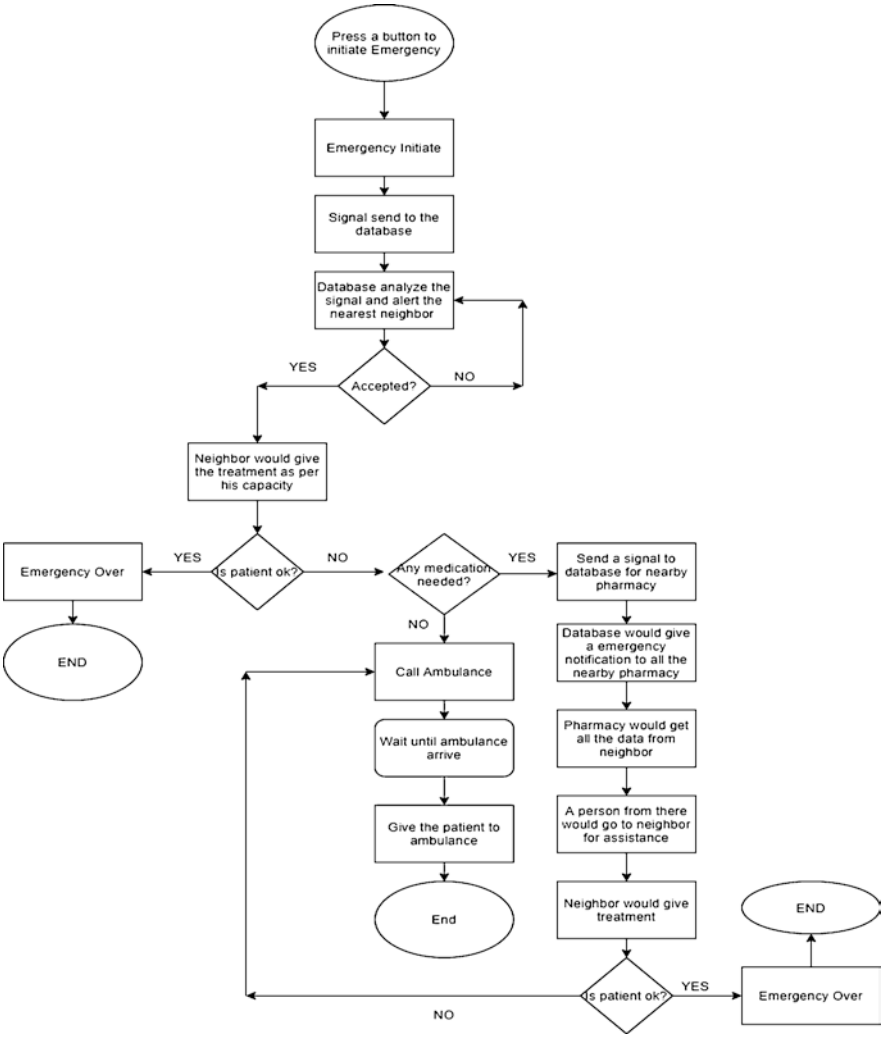


Fig. 5.8 Google Earth plot (normal view)

Fig. 5.9 Google Earth plot (satellite view)

5.5.6 *Algorithm Flowchart*

The flowchart of our proposed algorithm is given below [38].



5.6 Mobile Application Integration

This section discusses the mobile application that was developed for this system. For user-friendly experience, mobile application is the best option. For this research, two mobile apps which would work collectively are described. One app is called "Patient Helper" and the other is "FindMyPatient."

Table 5.2 Work flow diagram for mobile application

Emergency initiate by a patient	↓
Data uploaded to the Thingspeak	↓
Neighbor app sets alarm for nearest emergency call	↓
Neighbor would go to the person for giving treatment	↓
For better treatment neighbor would ask for help from pharmacy	↓
For better treatment neighbor would ask for help from ambulance	

The first application is responsible for sending the emergency notification if anyone is in a medical emergency. This app would track the location of the person, and upon emergency initiation, it would send it to the database. The second application is used by Neighbors. A neighbor would get the emergency signals from the nearest patient. Among the signals, the neighbor would take the decision which one to attend (Table 5.2).

For developing the current application, the model is implemented in the Android operating system. The application was developed using Android Studio which is the official Integrated Development Environment, which is established upon IntelliJ IDEA [39, 40]. After development, the file was in Android Package (APK) format and not published in Google Play Store [41].

Figure 5.10 shows the first application developed for the patient's convenience, namely "Patient Helper." Patient Helper requires location access and Internet access to be functioning properly. If at any moment, a patient is in inconvenience, Patient Helper can easily help that person achieve treatment. When the person clicks on the Button in Fig. 5.11, FIND MY LOCATION, the application requests for the last known location of the patient or requests for the location update. In the next step, the person should click on GET HELP as soon as their location is successfully updated which they can see on the screen. In Fig. 5.12, the description of the location is shown in Latitude and Longitude. When GET HELP is pressed, the information is passed to thingspeak.com [36], using the RESTFUL API provided by the thingspeak.com. In Thingspeak, the location of the patients is saved in a database, which is then sent to another application named FINDMYPATIENT for further purposes.

Showing the location of the patients is imperative for this project. Hence, achieving it in an easier way seemed to be by an application. Likewise, this application is developed for Android operating system for experimental purpose and named, FINDMYPATIENT. Initially, the data were fetched from an API which is sent by thingspeak.com. The API sends the file in JSON Array. A JSON Array is similar to JavaScript [42]. The JSON Array consists of four types of data which are being sent: longitude, latitude, the data type, and the date of the entry. At the same time, the Google Map API is called, for displaying the map. When the map has all the data of the markers, the map animates to display all markers of different colors zoomed in the Google Map in Fig. 5.12. For displaying the location of the patient, the orange marker was used; for displaying neighbor's location, the yellow marker was used; for displaying pharmacy's location blue marker was used, for displaying hospital green marker was used; and for displaying ambulance red marker was used. The

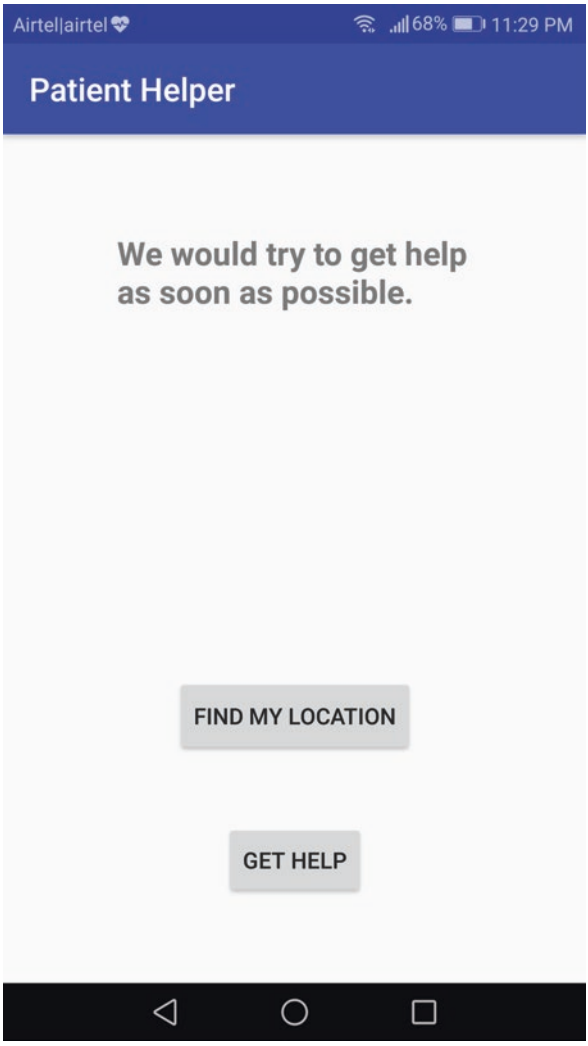


Fig. 5.10 Interface of the application, Patient Helper

user is given the ability to zoom in any interesting location to see more details around his point of interest in Fig. 5.13. Moreover, if he/she clicks on the marker, the option to see the direction and the time it will take to reach his interested location using Google Map Services are given (Fig. 5.14).

Moreover, this mobile application is also going to be used by ambulance service so that they can get the news instantly. In addition, the researcher suggests the pharmacy to use web application to get the information. A web application is suitable for pharmacy as they are not moving.

After the treatment, all the information regarding treatment would be uploaded to the server for future reference.

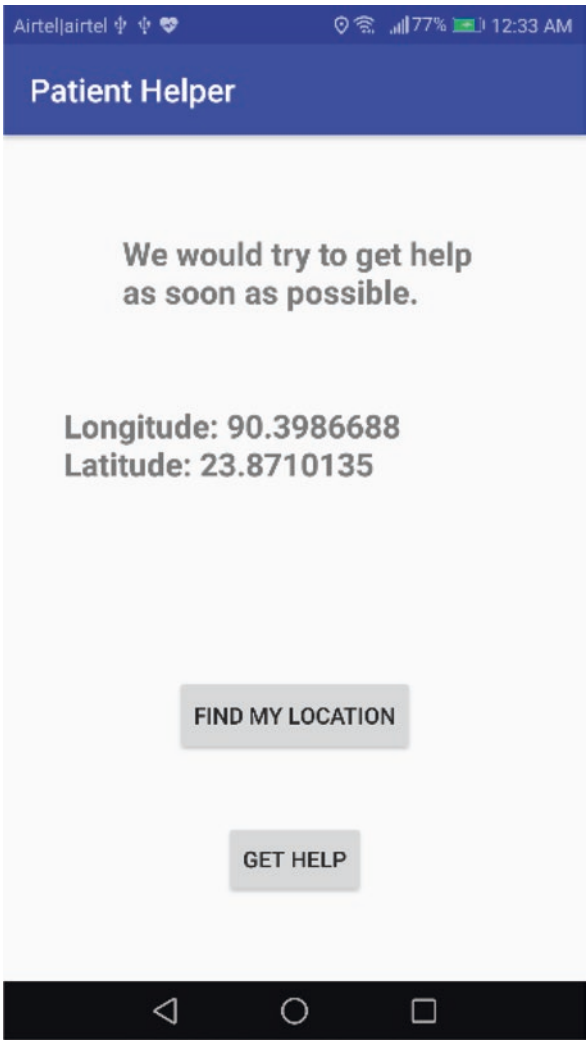


Fig. 5.11 Patient Helper displaying the longitude and latitude of the patient

This information is significant to analyze the patient's health. If enough information is gathered, then an AI system can be implemented by training and using machine learning algorithms.

5.7 System Evaluation

International Telecommunication Union has divided 5G communication into ultra-reliable and low latency communication (URLLC), massive machine-type communication (mMTC), and enhanced mobile broadband (eMBB). To understand the

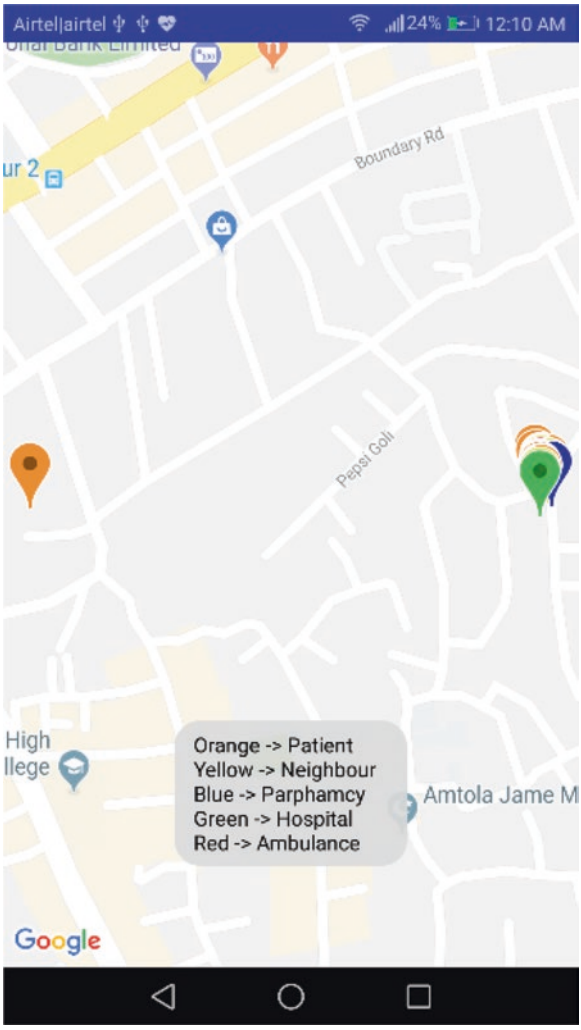


Fig. 5.12 Google Map displaying all the partaker from the application, FindMyPatient

diversified communication system ITU has introduced these various systems. mMTC is a new type of service to assist the access of a large number of machine-type devices where mMTC-based services, for example, sensing, monitoring, tagging, and metering are included for high connection density and better energy efficiency. IoT devices are in part of mMTC where latency is not an important factor [43].

This system is considered to be a random network [44, 45]. Every point on the system (e.g., patient, neighbor, pharmacy, and ambulance) is situated on different locations on the system. All the random points are used by mMTC devices. For the purpose of this research, these random points are generated using the device described in device description (Sect. 5.5.1).

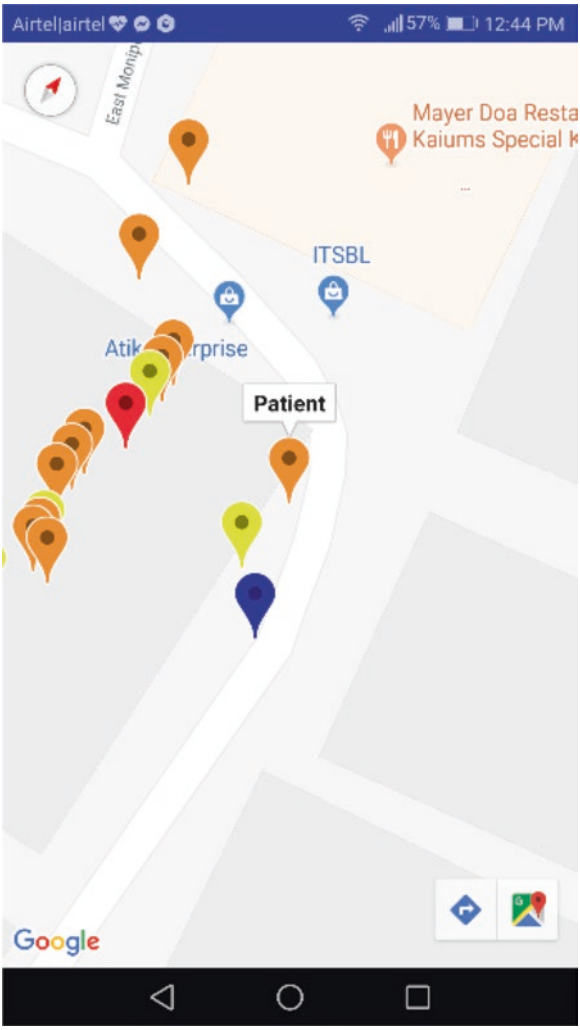


Fig. 5.13 Displaying all the partaker zoomed in FindMyPatient

In Fig. 5.15, the location of the simulated position is shown. Plotting longitude and latitude of the patient, neighbor, pharmacy, ambulance, and base station (BS) is there. Only pharmacy and BS position would be fixed in place every time. Other than pharmacy and BS, location of everything changes. Thus it becomes a random wireless network. This IoT network works the same as a 5G wireless network system. Connectivity between all these would be analyzed in this section. It is necessary to evaluate the performance of this network in a random situation.

From Fig.5.15 it is easily understandable that there are a lot of mMTC devices working simultaneously. When mMTC device of the patient is communicated with BS, another mMTC device creates interference. This interference signal can be described as [44–46]:

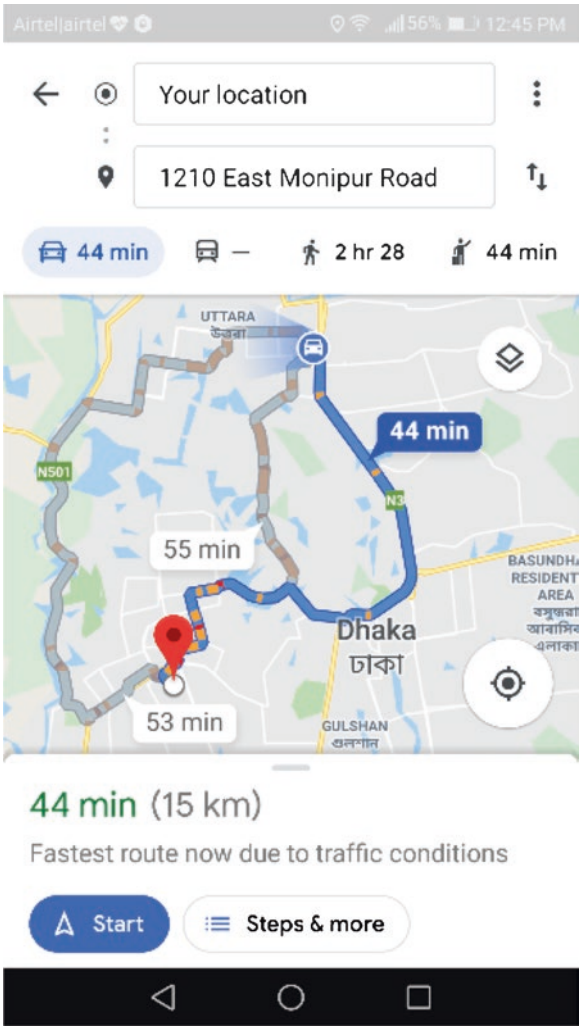


Fig. 5.14 Showing the fastest route to the patient using Google Map

$$\mathrm{I}_o = \sum_{d_i \in \varphi \setminus d_o} p_i h_i d_i^{-n} \tag{5.1}$$

Where p_i the transmission is power from mMTC device of the patient and h_i is the channel gain from the intended patient's device to BS. The distance between the intended patient's device to BS is denoted by d_i. And n denotes pathloss exponent in wireless environment.

Outage probability is a significant feature to assess the 5G network. The outage probability of BS (uplink scenario) or mMTC devices (downlink scenario) can be represented as [44]:

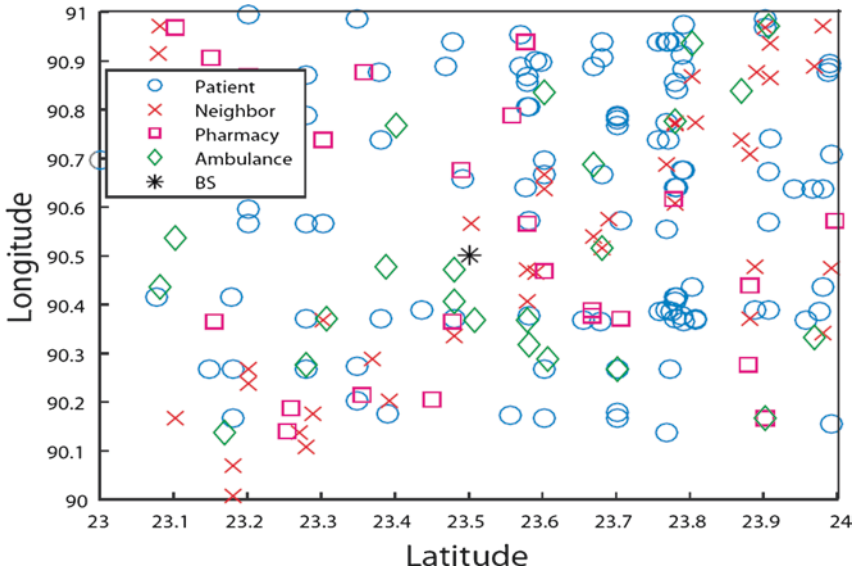


Fig. 5.15 Simulated location for patient, neighbor, pharmacy, ambulance, and BS

$$O_p = \Pr\left[SIR_o < \theta\right] = 1 - \Pr\left[SIR_o > \theta\right] \tag{5.2}$$

Where SIR_o is signal-to-interference ratio represented as $SIR_o = p_o/I_o$. p_o Represents signal power of intended mMTC device (uplink scenario) and BS (downlink scenario). I_o is the interfering power from adjacent mMTC devices where intended mMTC device is not included. θ denotes intended SIR threshold. Signal does not recover when SIR_o is lower than target SIR threshold. For the simulation of outage probability, we consider that all transmit powers of mMTC or BS are same (i.e., $p_o = p_1 = p_2 = \ldots = p$) [44].

BS is the main station which would be responsible to maintain the connection between mMTC stations. This research has proposed a mobile application along with an online database. This online database is user-friendly and all mMTC devices are connected everywhere with different level of capability, 5G has always maintained security to secure the sheer volume of data across a diverse set of platforms. An algorithm would be responsible for controlling the connection between mMTC devices.

As shown in Fig. 5.16, we see that the outage probability has a notable outcome on the SIR threshold (θ). Here pathloss exponent is considered 4 ($n = 4$). As θ increases, the outage probability of BS increases, and this implies that low θ is better. For $\theta = 0$ dBm, the outage probability is 0.2329 which is an acceptable level for uplink communication.

Figure 5.17 shows the outage probability for the downlink scenario of various mMTC devices' consideration of $n = 4$. mMTC device of an ambulance is lower outage probability than mMTC device of neighbor and pharmacy. Because the

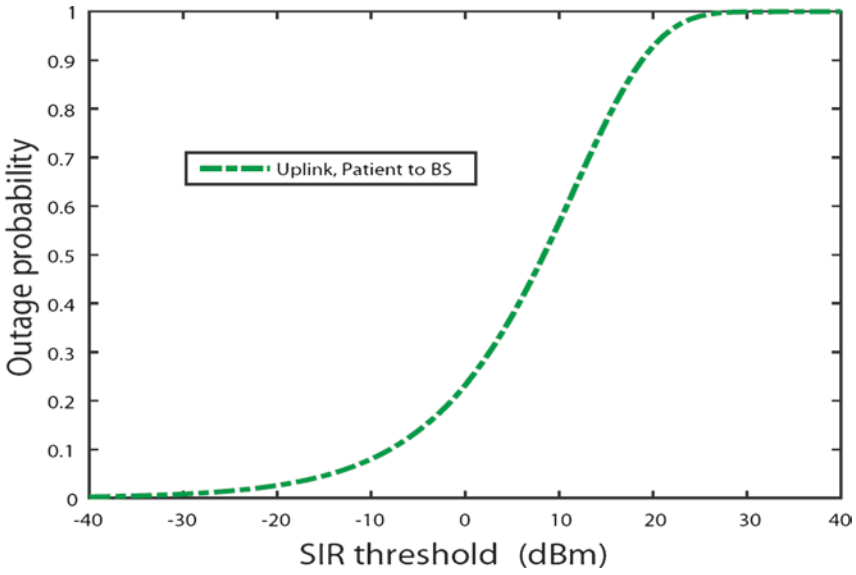


Fig. 5.16 Outage probability versus SIR threshold (θ) for uplink connection

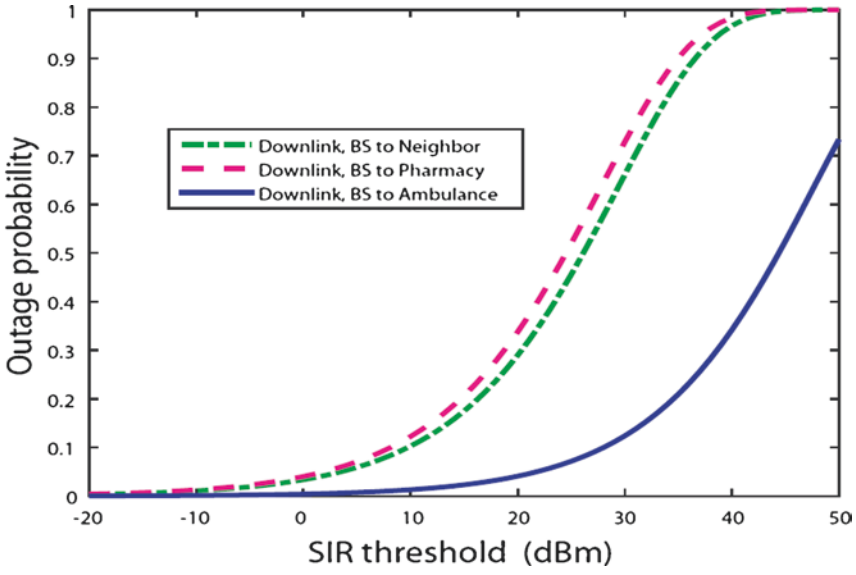


Fig. 5.17 Outage probability versus SIR threshold (θ) for downlink connection

distance of mMTC device of ambulance and BS is lower than other mMTS devices shown in Fig. 5.15, there is a line of sight communication between mMTC device of ambulance and BS. For $\theta = 0$ dBm, the outage probability of ambulance, neighbor, and pharmacy is 0.01314, 0.1026, and 0.1223, respectively.

5.8 Conclusion and Future Work

Despite the poor doctor to patient ratio and below standard medical service, Bangladesh is a developing country with a huge potential. With the rapid growth of technology and innovation, a system can be implemented which can mitigate the medical services and poor doctor to patient ratio. In this chapter, a research has been done deeply by combining IoT, GSM, and mobile application. Moreover, a real-time database is introduced which will be connected with the IoT device, and mobile application thus will update and provide information about location of the patient, pharmacy, ambulance, and hospital. From the simulation results, it can be concluded that the performance will be lower in highly populated areas, having high numbers of patient, pharmacy, ambulance, and hospital. In the future, this system would be upgraded for better performance. The database would include artificial intelligence and automation. This inclusion would make the system swift and help IoT to make its own decision. Also, there is a plan to use a body sensor to detect problems more quickly and properly.

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Chapter 6
Collation Analysis of ZRP-RA Accompanying ZRP and SHARP for Sustainable Computing

Sherin Zafar, Deepa Mehta, Samia Khan, Nida Iftekhar, and Siddhartha Sankar Biswas

6.1 Introduction

Ad hoc networks [17] are accustomed to not hinge on any existing infrastructure. The participating nodes are accountable for the transmission of data packets within the network. For the nodes to get familiar with the arrangement of the network also called topology and further take a decision of which way to route, the packets within the computing devices are controlled by the ad hoc routing protocol [7]. The various distinctive ad hoc network application sectors such as military applications and emergency rescue operations are characterized by highly varying temporal and spatial boundaries. Flexibility is a peculiar feature of an ad hoc network; by virtue of its dynamic nature, the highly mobile nodes have freedom to join in and leave the network in case their power gets exhausted or may rejoin from some other location, hence changing the topology of the network autonomously resulting in a rapid change in the network arrangement. The wireless nature of the network also poses challenges wherein the interference and fading affect the bandwidth and error rate of the link. Thus, the pivotal obstacle in the efficient functioning with respect to an ad hoc network is the design of a protocol adapting perfectly and delivering optimal performance braving the obstacles owing to the frequently and quickly changing topology of the network.

Ad hoc routing protocols proposed heretofore are proactive [1, 4, 10], reactive [3], and hybrid routing [6]. Proactive protocols, such as DSDV and OLSR, maintain a table for all the available paths to all the destinations within the network which are also updated constantly. Unlike proactive, reactive protocols, such as AODV, DSR,

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and TORA, only trigger a mechanism of route discovery whenever a route to a particular destination is required, and thus routes are discovered when demanded, hence introducing delays in route determination.

One of the stumbling blocks in case of efficient performance of highly reliable and low latent proactive protocols is the poor scalability and generation of supplemental control traffic in an attempt to maintain the current routes, some of which may never be required, such stale route when repaired results in a wastage of scarce resources such as bandwidth, these control packets also utilize the space in the queue and as a consequence, results in the loss of data owing to congestion introducing delays because the lost data is retransmitted resulting in supplemental congestion. Proactive protocols thus will perform better in case of static networks. Whereas the reactive protocols are characterized by reduced routing overhead, one of its limitations is the latency caused as a result of the route discovery and maintenance process. It can hence be inferred that the characteristics of the network are crucial role players in altering the performance of both reactive and proactive protocols. In conditions, favorable to given protocol, it may perform better than the other. Hybrid protocols, [9] such as ZRP [12–14], ZHLS, HARP, and SHARP, efficiently amalgamate the proactive and reactive functionalities into a single algorithm to deduce a new set of protocols called the hybrid protocols. This paper discusses and analyzes three algorithms pertaining to the hybrid routing protocols ZRP, ZRP-RA, and SHARP in Sect. 2 followed by collation analysis of the abovementioned hybrid protocols in Sect. 3 through packet delivery ratio. Last sections of the paper consist of conclusion and references.

6.2 Sustainable Computing and Hybrid Routing Protocols

Sustainable systems are a kind of system with manageable vitality. They comprise of parts and sensors that work in an agreeable way. Multi-way steering improvement is a promising stage in MANET with execution parameters that are application explicit. Right now sensor hubs create huge measure of information in the applications like occasion observing, object following, and so on. These sensor information are sent to the hub assigned as sink that devours part of vitality. It relies upon factors like throughput, average end-to-end delay, jitter, packet delivery ratio, average energy consumption, normalized routing load, and packet loss ratio. Past investigations on ideal multipath steering in MANET are confined to create the ideal way utilizing increasingly number of irregular parametric qualities. There is constrained work concentrating on classifying the ways that are utilized to course the basic information like deals identified with continuous and non-ongoing. Hybrid routing protocols have gained high popularity owing to the mode of operation, incorporating the reactive and proactive strategies. The various proposed hybrid protocols are discussed below.

6.2.1 Zone Routing Protocol (ZRP)

ZRP [15] capitalizes on the advantages of proactive as well as reactive routing protocols and utilizes in its operation both the procedures effectively. The functioning is based on the amalgamation of the two, proactive and reactive strategies, into a single protocol architecture. The proactive routing is restricted among a particular group of nodes within the network with the help of zones. The network is divided into zones with each node creating its own zone within a set of nodes around it as most of the communication happens by hops so the nearest hop neighbor forms the participants in the zone. The zone area is defined by a set radius within which the routes are determined proactively. The nodes with hop distance less than the radius form interior nodes, and nodes distant at a hop distance exactly the same as the radius are called border nodes (Fig. 6.1).

For any data transmission with the source, destination shares the same zone. The routes are prestored in the link state tables with the help of two protocols: NDP (neighbor discovery protocol) [11, 18, 19] which is responsible for sending the periodic beacons, enabling the recognition of new neighbors, and forming of link state table and updates in case of link failures and with the information from the NDP, the proactive set of protocol used in ZRP [2], i.e., the IARP (intrazone routing protocol) [21, 22, 24, 26], which maintains the link state table proactively carrying the route metrics for all the nodes within the zone. Thus, the source with the help of IARP sends data to the destination in the same zone.

For data transfer to the nodes which lie outside each other's zone, IERP (interzone routing protocol) [27] is employed by ZRP and takes responsibility of the reactive routing. The route discovery initiation is triggered by sending a route request to the border nodes, a process called border-casting [16], and proves better than broadcasting (Fig. 6.2).

The border-casting resolution protocol (BRP) [25] is responsible for providing the "border-casting" service for delivering the message, i.e., IERP route requests. A border-cast tree determines the routing of message from a border-casting node to its

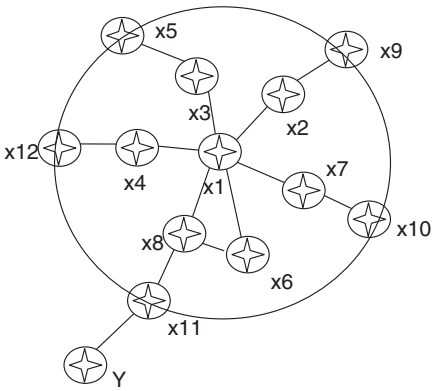

Fig. 6.1 Example of routing zone with radius = 2

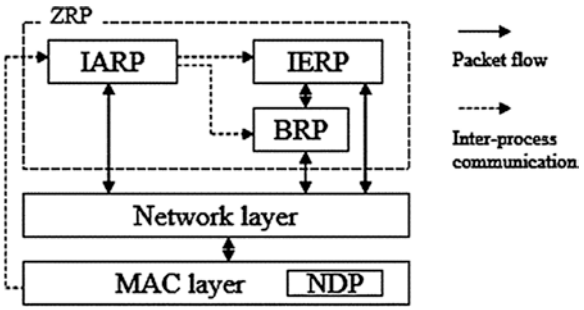

Fig. 6.2 Architecture of ZRP

peripheral nodes. It is also responsible for query control mechanisms [23]. If the destination exists in the zone of the recipient node, a route reply is sent back to the source, and thus the data packet is transmitted along the same route. ZRP thus proves to be better than pure reactive and pure proactive routing protocols, but it suffers from a lot of disadvantages limiting its performance [28] under different network conditions.

6.2.2 Sharp Hybrid Adaptive Ad hoc Routing Protocol (SHARP)

SHARP [20] adapts effectively and smoothly from proactive to reactive routing mechanism. This adaptation is dependent on the network characteristic which is measured and is directed to optimize QOS parameters. The metrics involved can be routing overhead, delay, jitter, and loss rate. The adaptation is possible by dynamically changing the extent of information to be shared in proactive manner. It is done by choosing hot destinations, i.e., the nodes receiving maximum data from multiple sources and thus creating zones around these destinations, and the data within the zone is shared proactively. The routes are maintained within the zones only to the zone which is central. The zone is characterized by a radius specific to every node (destination). The radius of the zone at every destination can be varied dynamically; for popular destinations, the radius is more, covering larger zones. For destinations drawing small amount of traffic, radius is small leading to smaller proactive zones. SHARP thus offers a flexibility of varying radius and control parameters according to requirement. A decrease in the radius can render majorly reactive routing within the network with a reduced routing overhead but ends up increasing the loss rates, jitter, and delay. The opposite will reduce delay but will increase the overhead. SHARP, however, is capable of controlling the trade-off efficiently.

1. SHARP Proactive Routing

SHARP proactive routing is possible through a protocol derived with strategies from two separate protocols: DSDV and TORA. Since the working process only demands routes to a lone node (destination) in every zone, making it possible for the

protocol to engage some strategies for incurring low overhead in order to create and sustain routes offering predictable overhead, reduced loss of data, SPR involves the use of two subprotocols: construction protocol and update protocol. Construction protocol works by generating and broadcasting a DAG construction packet which triggers the construction process. The packet contains radius pertaining to the zone, a sequence number which helps differentiate between the old and the new DAG, and it also contains the TTL field limiting the scope to the proactive zone only. DAG is formed by taking height as the measure of distance of the node from the destination. Every node after receiving a construction packet adds the link to the DAG and after incrementing the height by 1 rebroadcasts the packet. After receiving packets from various nodes, every node makes a note of height information pertaining to all the nodes.

Update protocol enables the beaconing and maintaining of the DAG in case there are link failures. Update packets serve as beacons if the new links are formed. It also involves the periodic broadcasting of the height information of every node which helps updates in case of link failures. The proactive routing involves the transmission of data packet arrived at the node to the downstream neighbor with the least height. The next best route is chosen in case of link failures.

2. SHARP Reactive Routing

SHARP reactive routing is derived from ad hoc on-demand distance vector (AODV) routing protocol by involving certain optimizations mainly route caching. In case the destination does not lie in the same zone as the source, it triggers the broadcast of route request packets from the AODV. When the request reaches the nodes in the proactively functioning zone of the destination, the request is responded by *route reply* by the node in the proactive zone which assigns its distance from destination as zero. Thus, data from the reactive routing is collected by the proactive set of destination zone. And the packets are routed efficiently by the protocol (Fig. 6.3).

6.2.3 Route Aggregated ZRP (ZRP-RA)

ZRP-RA focuses on the shortcomings faced by ZRP and attempts to eradicate them by using the concept called route aggregation [5, 8]. The performance of ZRP is majorly impacted due to the overlapping zones causing the flooding of redundant route requests. Although query control mechanisms are able to combat the issue to a great extent, ZRP-RA attempts to improve the performance of ZRP by aggregating the routes into a single-line route, thus saving scarce resources in many ways. ZRP-RA commences the process by first making additional bigger zones involving member's nodes apart from their own routing zones. These bigger zones also choose a Zone Head for that particular zone on a random basis, and a route aggregation algorithm is then applied at the head which aggregates all the routes available in the bigger zone into the Zone Head.

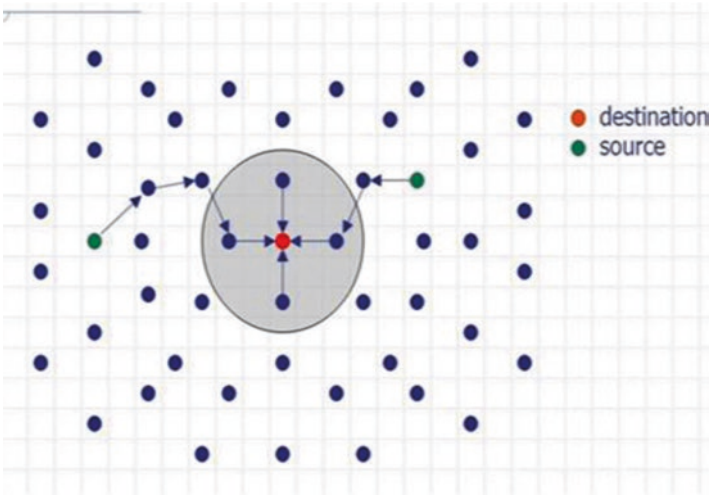

Fig. 6.3 SHARP reactive routing

The packet delivery for a destination lying in the same zone as the source happens proactively, as in the case of ZRP but in case of a packet intended for a destination outside the zone of as the Route Request is border-casted the recipient node checks its Zone Head at first for the destination thus, saving several border-casting of requests. ZRP-RA also involves mechanisms to update the Zone Head in case of link failures or other node leaving the network, so the packet delivery ratio of ZRP-Ra is quite better than the other discussed hybrid routing protocols the source, as the Route Request is border-casted the recipient node checks its Zone Head at first for the destination thus, saving several border-casting of requests. ZRP-RA also involves mechanisms to update the Zone Head in case of link failures or another node leaving the network. The Zone Head in those cases are updated and formed afresh with the entire process happening again. It thus is able to bring the routing information closer to the nodes and thus save time and bandwidth resources (Fig. 6.4).

6.3 Simulation for Collation Analysis of ZRP-RA Accompanying ZRP and SHARP

NS2 simulator has been utilized to simulate SHARP, ZRP, and ZRP-RA taking packet delivery ratio (PDR) as one of the QOS (quality of service) parameters. The calculation of packet delivery ratio (PDR) is based on the received and generated packets as recorded in the trace file. In general, PDR is defined as the ratio between the received packets by the destination and the generated packets by the source. Figures 6.5, 6.6, and 6.7 depicts the collation analysis of hybrid routing protocols.

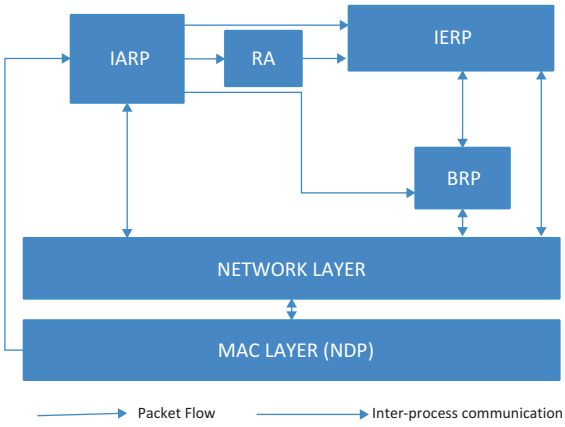

Fig. 6.4 RA application between IARP and IERP

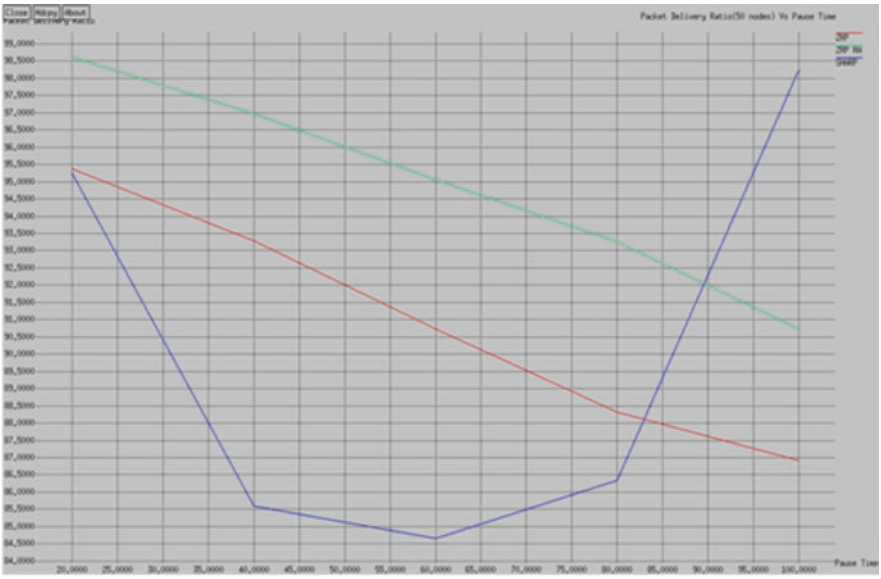

Fig. 6.5 Packet delivery ratio analysis of ZRP, ZRP-RA, and SHARP with 50 nodes

Figure 6.5 depicts packet delivery ratio analysis of ZRP, ZRP-RA, and SHARP with 50 nodes validating ZRP-RA through fluorescent green line (Table 6.1).

Figures 6.6 and 6.7 depict packet delivery ratio analysis of ZRP, ZRP-RA, and SHARP with 75 and 100 nodes validating ZRP-RA over ZRP and SHARP. Simulation analysis of SHARP, ZRP, and ZRP-RA specifies the effectiveness of the proposed ZRP inculcating route aggregation approach. Since in ZRP-RA the packet delivery for a destination lying in the same zone as the source happens proactively, as in the case of ZRP but in case of a packet intended for a destination outside the zone of the source, as the Route Request is border-casted the recipient node checks its Zone

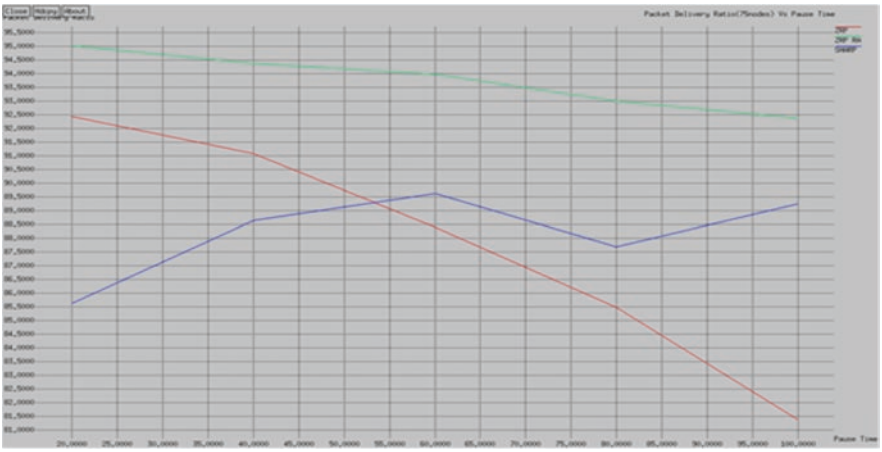

Fig. 6.6 Packet delivery ratio analysis of ZRP, ZRP-RA, and SHARP with 75 nodes

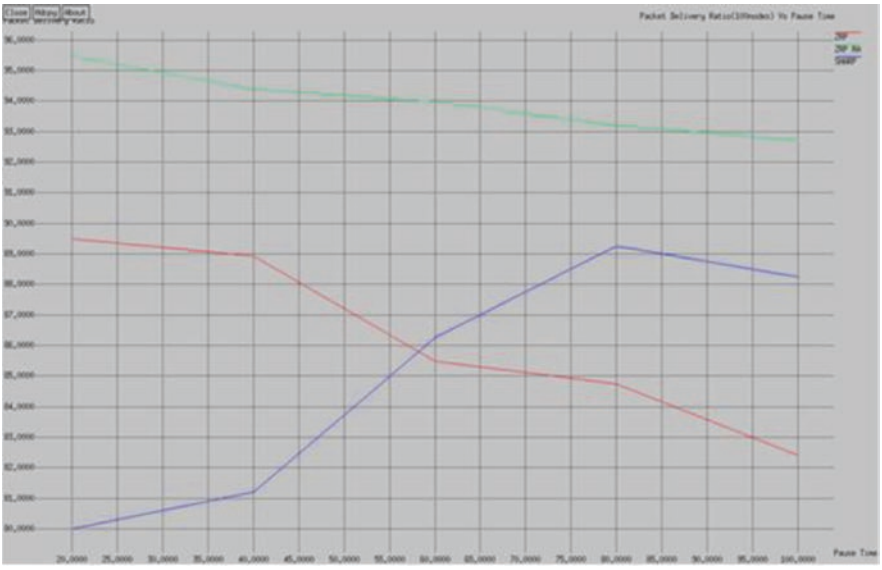

Fig. 6.7 Packet delivery ratio analysis of ZRP, ZRP-RA, and SHARP with 100 nodes

Head at first for the destination thus, saving several border-casting of requests. ZRP-RA also involves mechanisms to update the Zone Head in case of link failures or other node leaving the network so the packet delivery ratio of ZRP-RA is quite better than the other discussed hybrid routing protocols.

Table 6.1 Simulation parameters

Parameter	Value
Network area	400 × 400
Velocity	10 m/s
No. of nodes	50, 75, 100
Packet size	512 byte
Traffic type	CBR
Number of connection	20
Packet rate	2 P/s
Pause time	20,40,60,80,100
Simulation time	100

6.4 Conclusion

Section above depicts the collation analysis of SHARP, ZRP, and ZRP-RA through NS2 simulator taking packet delivery ratio as a comparison parameter which is considered one of the most important parameters for comparison analysis. ZRP-RA focuses on the shortcomings faced by ZRP and attempts to eradicate them by using the concept called route aggregation. The performance of ZRP is majorly impacted due to the overlapping zones causing the flooding of redundant route requests. Although query control mechanisms are able to combat the issue to a great extent, ZRP-RA attempts to improve the performance of ZRP by aggregating the routes into a single-line route, thus saving scarce resources in many ways and hence making ZRP-RA quite effective over its other counterparts. The ZRP-RA-based random cluster selection energy enrichment approach helps in reducing the various control and routing overheads involved in the functioning of ZRP. It also reduces the number of route requests to be sent, and thus superfluous route requests can be avoided, and thus saving bandwidth is achieved. Also the reduction in the routing and control overhead reduces the probability of collisions, and thus the data is effectively forwarded to the destination. This also helps improve latency and packet delivery ratio as the queuing up of data packets is lessened owing to the less overhead which validates the sustainability of hybrid routing protocols for real-time applications.

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Chapter 7
Recent Machine Learning and Internet of Things (IoT) Applications for Personalized Healthcare: Issues and Challenges

Md Tabrez Nafis, Aksa Urooj, and Siddhartha Sankar Biswas

7.1 Introduction

This paper firstly gives us ideas about machine learning and IoT. They have become increasingly more fundamental in these days. We will also discuss the various issues and challenges related to personalized healthcare with ML and IoT.

7.1.1 IoT

Sensory intelligence that holds sensory information is also processed by algorithms and converted into useful information so that computers have an improved understanding regarding actual human environment. Computers must somehow cope with human reasoning at this period. What's more and most significant, we are able to initiate additional useful technologies, products and services that transform our lives mechanically and dramatically. For several years, systems are developed for particular functions with restricted flexibility. It suggests that it cannot be continuously and dynamically updated until one machine is operating. The present initiative on implementing the IoT (or in addition generally the longer term of the Internet) calls for software application, product and repair systems that might collect, store, connect, use and exchange knowledge from the physical environment, particularly communication within the Earth. This can produce new prospects in a wide range of realms, such as sensible health, distribution, producing inexperienced resources, sensible homes and additionally customized end-user applications.

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https://doi.org/10.1007/978-3-030-51070-1_7

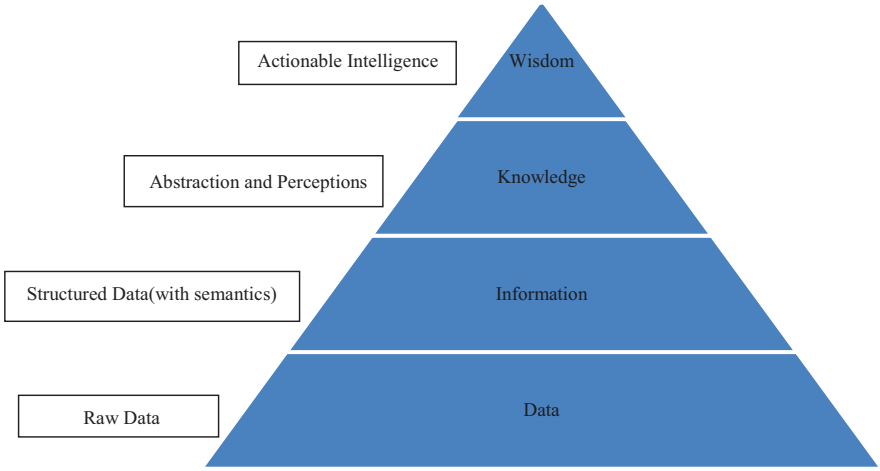

Fig. 7.1 Knowledge hierarchy in the context of IoT [1]

7.1.1.1 Knowledge Hierarchy

The layer at the bottom indicates the huge quantity of knowledge generated by the IoT devices, most typically in metallic element. The layer at the middle creates organized and machine understandable information from immense data. But humans and high-level applications don't need the data. It's the knowledge hidden behind the data that gives human a more robust understanding to the information and machine comprehensible insights of the big data. Using this hidden data, machines will forecast what is going to happen in the future. This style of knowledge is designed to some end-to-end product, and therefore, the main purpose of IoT is that the data hierarchy is mechanically summed up by machines (Fig. 7.1).

7.1.2 Machine Learning

In the late 1950s, AI (ML) was introduced as a computerized logic technique. After some period of time, its centre advanced and moved towards calculations that are computationally suitable and powerful. Recently, AI methods are being utilized broadly for a large scope of errands including regression, grouping and thickness prediction in various regions, for example, speech recognition, bioinformatics, PC vision, spam identification, fraud recognition and product advertisements [2–4]. The algorithms and methods come from a number of fields like statistics, neuroscience, mathematics and computer science and, nowadays, used even in broader or more machine-related areas.

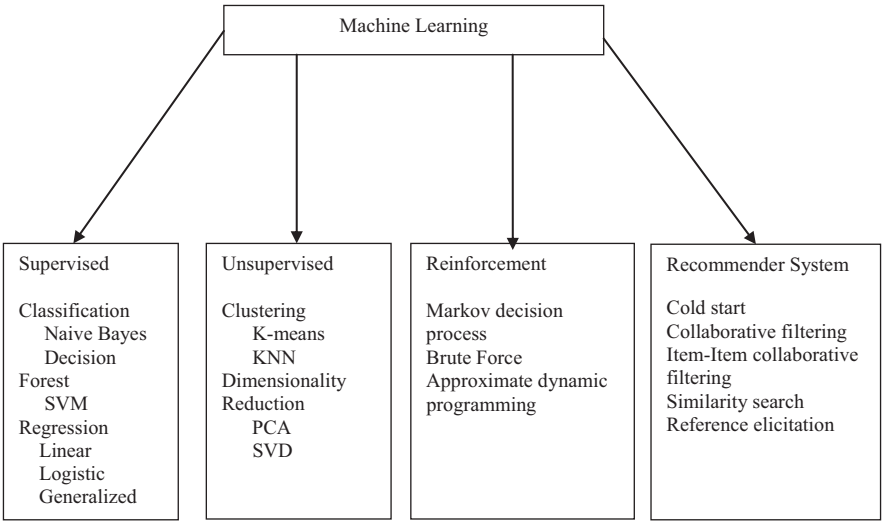

Fig. 7.2 Machine learning algorithms [5]

7.1.3 Machine Learning Algorithms

Machine learning assignments are usually ordered into two general categories, contingent upon whether or not there's a learning "flag" or "criticism" accessible to a learning framework. The kinds of learning algorithms are shown in Fig. 7.2 and discussed in (a), (b), (c) and (d).

Supervised learning: During this sort of learning, the information is tagged and might be calculated. In cases wherever the labels are unknown, their operational information are accessible.

Semi-supervised learning: It relies on a group of unknown data that is usually incomplete.

Reinforcement learning: An agent receives penalty/reward based on previous action.

Unsupervised learning: In this type of learning, the data is unlabelled. We have input data but no corresponding output data.

7.2 Personalized Healthcare

The ongoing trend is that much of the time doctors inflict medicines through trial and error, using a one-size-fits-all method, although every person's feedback to a medicine isn't identical. While most of the people might feel better after taking a specific drug, others may have fewer effects or may have side effects from the same

medicine. As per certain reports, patients complete and take medications just 50% of the time as advised [6]. There are several possible causes, including an increasing community of doubt about medications and side effects and an increasing climate of medical systems mistrust [7]. Hydrogen ion concentration will improve the standard of care and simultaneously decrease prices. It can even facilitate us to predict the proper medical therapy with least side effects for the patients.

Personalized diabetic management is one among hydrogen ion concentrations with IoT and machine learnings in case studies [8]. Each person's food habit and hormone response are totally different. The body's response to food intake conjointly varies from individual to individual. Bluetooth-activated glucose observation offers the patient nutritional guidance about the quantity of food that can be consumed as well as dietary advice on the effects of uncontrolled feeding. This information is displayed on the patient's personal mobile device.

PH conjointly plays an important role in readmission to hospital. One-fifth of the postsurgery patients are readmitted to hospital, as per a survey. Among those, a huge fraction of these readmissions may be avoided if enough personalized care is set up and proper monitoring was in place [9]. Studies also reported that insufficient continuity of treatment is liable for unnecessary payment of $25 billion to $45 billion through evitable complications and needless patient readmissions in US local hospitals [10, 11].

The idea of the implementation of the IoT and the Internet of Nanothings (IoNT) became feasible due to the advent of affordable smaller computing tools. Additionally, for healthcare applications, the advantage of these technologies is realized. IoT and IoNT's little sensory devices will communicate with one another, forming a personal area network (PAN), body area network (BAN) and other different network varieties.

The three fields in which ML and IoT contribute toward PH can be seen in Fig. 7.3.

These are:

1. Diagnostic care
2. Assistive care
3. Monitoring and alarming

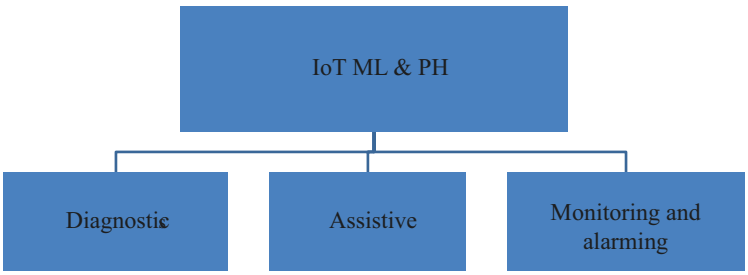

Fig. 7.3 Uses of IoT and machine learning in personalized healthcare [12]

The bio-module devices will facilitate the patient perform some medical specialty in diagnostic care. For example, there aren't any qualified doctors out there in remote areas. In remote and semi-remote areas, there's additionally a scarcity of pathological employees and medical device operator. These challenges are often overcome by intelligent and automatic medical specialty. Hence, diagnostic service through the IoT and metric capacity unit will vastly advance the PH.

The assistive PH programs focused on ML and IoT now have an effect on many lives. The influence is additionally increasing because of advances in technology. But assistive hydrogen ion concentration would still have to be tackled regarding its accessibility and affordability issues [13].

In addition, the issue of security and safety for the little devices may pose serious questions as they can be misused if not properly protected [13]. Remote monitoring has an important role to play in hydrogen ion concentration service. Patients discharged from the hospital, individuals residing in backward areas and the aged people living in residential care will make the most of remote watching as a part of hydrogen ion concentration. Through remote watching of health standing via IoT devices, personal health data of patients is pushed into the cloud server. Additionally, cloud primarily based huge knowledge services will perform good prognostic analysis supported the hydrogen ion concentration will keep knowledge. The medium of contact had to be involved in this model so as to pass data about the actual person.

7.3 Issues and Challenges

Personalized healthcare isn't resistant against scrutiny and downsides. It derives the prevailing basic IoT and cubic centimetre issues. The subsequent explains a situation in which a senior is employing a sensor-based pH device.The device gathers varied data like pulse rate, pressure, EEG, glucose, etc. and delivers it to a database. The collected data is used by the concerned people. Simultaneously, the database runs some ML algorithms to assess the gathered information so as to calculate patient's risk score and health recovery and regarding that recommend additional precautionary measures. The architecture in Fig. 7.4. depicts a design identical to this. Also in this basic example, each of the phases entails different problems and concerns. The sensory tools ought to resolve problems of data transfer and packet delivery, secrecy and authentication.

7.3.1 IoT-Related Issues in PH

By and large, the utility to the consumer will decide the performance of the system. BAN utilizes sensors to gather user's health data relating to the body. BAN must successfully communicate and turn sensed anomalies into useful data, and it has to make sure that it satisfies alternative device necessities like energy potency.

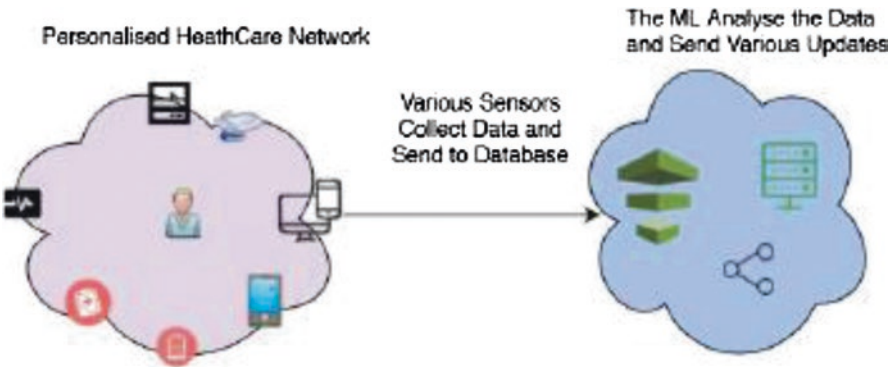

Fig. 7.4 Data flow in personalized healthcare network [12]

Moreover, the capacity to selectively store and transmit data at accuracy standards and speeds relevant to the destination of the data, be it to a runner who is concerned about her pulse or to a doctor who wants a patient's ECG. These various technology necessities imply the flexibility to combination stratified knowledge and disintegrate BAN structures into the current data architecture [14]. To sum up, it is important to confirm the information integrity, energy efficiency of the sensors and capacity to connect with current systems in order to get the maximum value of the BAN for PH.

7.3.2 ML-Related Issues in PH

The machine learning is deeply connected to applied mathematics, taking choices from current knowledge and predicting from past expertise. The ML-based methodology can analyse the case consistent with the trained dataset if a patient is monitored. Most of the time, the coaching knowledge set plays an important role in estimating the long-run pattern of a new issue. Typically this dataset could also be skewed and will not be specific to hide several situations. Dirty data, noisy data and insufficient knowledge may lead to a lower likelihood for detection and predicting diagnosis associated with health safety. Sleeping schedule and habits will vary from one individual to another depending on various factors such as age and health condition. Therefore, to record sleep patterns, an entire dataset of all case studies might not be available and this might lead to incorrect estimate of pH scale.

If the IoT and cubic centimetre enable hydrogen ion concentration to be used, the system may have to make a decision for the user to be diagnosed, expected and alerted. There are some instances wherever a call-supported cubic centimetre might be wrong, and it's difficult to suggest why a selected call has been created. For instance, few accidents occurred within the case of autonomous driving automobile because of the autonomous car's wrong call.

Table 7.1 IoT- and ML-related issues in PH

IoT-associated issues in PH	ML-associated issues in PH
Data integrity	Data may be biased and diverse
Energy efficiency of the sensors	Data may be noisy, dirty and incomplete
BAN must be able to integrate with existing infrastructure	Complete dataset may not be available
BAN needs to relay and efficiently turn perceived anomalies into useful knowledge	May lead to wrong estimations
It must be able to deliver information at appropriate rates	Data transmission loss

The important question, however, was to perceive associate AI machine's call once victimization unsupervised learning. This results in moral question on *who* is accountable for the event of a misconduct and the way to spot or correct that flaw is beneath the decision-making method. These disadvantages will limit the employment of cubic centimetre in hydrogen ion concentration for sensitive applications like custom medication.

Predictive analysis will assist patients discharged from the hospital UN agency and might have to be readmitted to the hospital whereas victimization ML-based pH service prophetic analysis is convenient to make a model of risk stratification within which further effort is employed to manage bound patients with higher risk. This includes, however, isn't restricted to, further watching devices and continuous monitoring.

Such models are created on the premise of claims and past historical information in several cases. The dynamic pH system that might assist with admission shunning initiatives conjointly has to leverage the patient's dynamic information associate degree, use it to forecast possible prospects and make an attempt to minimize possible complications. Rothman et al.'s studies have shown that it is valuable to predict readmissions by incorporating clinical variables and important signs [15]. You'll use the PH system for this situation. However, it's necessary to handle the problems of loss of knowledge transmission, noise in information and incomplete data (Table 7.1).

7.4 Conclusion

Machine learning mostly relies on the accessible dataset and algorithms to divide the information into certain classes either by supervised learning or unattended learning. When we tend to rely upon our noninheritable information to form a choice, human beings make wrong choices. The choice we tend to build someday involves feeling while as computers won't understand it. Human beings may be selective to form a choice that supported our moral beliefs, global interpretation, political and nonsecular price and self-identity.

Such considerations will appear within the offered dataset that the computers may use to learn to form a choice. Therefore, it's a task to confirm the dataset that can be used for machine learning is clear of human prejudices the maximum amount as double. To improve personal interest, it is important to get rid of these limitations in cubic centimetre and IoT.

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Chapter 8
New Age Approaches to Predictive Healthcare Using In Silico Drug Design and Internet of Things (IoT)

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8.1 Impact on Society and Sustainability

The advancement of technology has resulted in an improved way of life. The healthcare industry which is one of the largest and most complex has also witnessed the results of improved technology. With the implementation of techniques like in silico methods, predictive and big data analytics and Internet of Things IoT has led to rapid and long-lasting evolutions. Digital solutions have managed to make the drug development process more cost- and time-effective. Aspects that were once extremely challenging are no longer that challenging. Technological advancements have resulted in enhanced patient experience and safety. In this fast data-driven era, technologies like predictive analytics are taking the front seat by predicting and forecasting outcomes of a process, thereby helping in taking the necessary preventive actions well in advance. Risk assessment has managed to make the process more reliable, by eliminating many untoward incidents. IoT has enabled remote monitoring of patients more realistic. Real-time collection of patient data has now become more seamless. In silico techniques, employed during the early phases of drug development, have made it possible to shrink the timeline of drug development. This has not only made drug development less time-consuming but also less expensive. All these advancements have significantly contributed to enhancing the quality of results, reliability and reproducibility. This is in direct correlation with the enhance quality of patient life. Improvement in healthcare has resulted in increased life expectancy and better diagnosis and treatment than ever before. These technologies have also enhanced the ease of access to treatment for a larger population. The healthcare sector has also improved the economy by being one of the major contributors to economic development. It wouldn't be wrong if it is concluded that the

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development of mankind is directly influenced by improvement in healthcare. Advancements in technologies like in silico techniques, analytics and IoT have made healthcare more efficient and treatments more effective.

8.2 Introduction

8.2.1 Motivation

The traditional methods in conventional approaches are used to make use of trial and error methods to design a new drug. A project would never start as there were very few or no adequate assays to look into testing for the proper functioning of compounds. These approaches were so weak that the development effort for a drug would be very costly and that used to become a liability for some rare diseases. The conventional drug discovery process is complicated, time-consuming and costly, and some of the main drawbacks are lack of effectiveness, adverse reactions, poor pharmacokinetics and marketable reasons. Even as traditional medicine products have been used for centuries, less amount of work has been done on its developmental aspect.

8.2.2 Organization of the Chapter

Primary healthcare systems from ancient times relied on traditional medicines, but even though it was present for so many centuries, very less work was done on its developmental aspect. Now with emerging technologies, the problems associated with the discovery of a new drug have effectively been tackled. Now that molecular structure of a drug can be visualized by various databases, various computer programs have been developed which can be used to check whether a particular chemical can be identified which earlier could not treat a disease within a specified amount of time. The entire drug development process takes around 10–15 years to come into the market. Time is the only reason why very few new drugs come into the market; it also speaks why the drugs are so costly.

The drug development process involves various steps where the first step involves choosing molecules like protein, which is a selection of a biochemical mechanism for a disease condition. The next step involves in vitro and in vivo testing. In vitro is based on examining the interaction of drug molecules on living cell cultures, while in vivo is based on examining the interaction of drug molecules on animal models and in other living cell cultures. Investigational new drug application has to be submitted to the FDA. This is done prior to the clinical trials. FDA during this step scrutinizes the results which were obtained after preclinical testing. Clinical studies (phase I) and tolerance around study agents are determined in the case of normal healthy participants. Clinical studies (phase II) check safety and efficacy involved

with the drug. For clinical studies (phase III), the data which were collected during earlier trials are expanded in this step. They are at first confirmed and then expanded by conducting trials again. The next step is application filing (new drug) which is done so that the new drug can be filed for approval from the FDA. Then comes the decision about whether it has been approved or not. Last step the clinical trial phase IV involves general post-market trails. These are conducted to get data such as quality-of-life data, adverse events.

The healthcare industry, however, is evolving at a fast pace to accommodate the new changes and is trying extensively to tackle these new challenges. The huge influx of high-quality data from advanced technologies has created the room for its analysis and utilization. And one such area, which has outgrown other areas, is predictive analytics. Predictive analytics along with in silico drug discovery and the Internet of Things (IoT) has helped create better treatment and care for patients. The use of predictive analytics in the process of clinical trials and regulatory aspects has enabled faster and better outcomes. Designing experiments, patient recruitment and predicting drug safety have resulted in reduced risks and increased efficacy of the processes. These new approaches have also made things faster and less expensive.

Thus the chapter mainly focuses on past and present practices in healthcare ranging from conventional drug development practices to new age approaches. The chapter also deals with the importance of big data analytics in predictive healthcare which is helpful for real-time clinical decision-making which has enhanced patient experiences and reduced costs of healthcare. We also discuss one of the major aspects of clinical trials and the impact of IoT-enabled services and permissions on such a crucial step of the drug discovery process on how this approach is making a significant reduction in time and costs. It also gives an account of some IoT applications in the devices which have been made for remote patient monitoring like glucose metres for patients having diabetes and blood pressure cuffs for monitoring the patients with high blood pressure. Furthermore, with the use of communication means such as sensors, the manufacturers under a service contract have been able to monitor the status of equipment which has led to an improvement in efficiency and also has increased profit margins.

8.2.3 Key Contributions

Predictive healthcare has enabled patient self-monitoring and treatment through the use of smart devices [4]. The data being generated every day in hospitals is being used to create models involving various factors. Data mining helps in the easy study of patterns around a complicated dataset. High quality of information can now be obtained in various forms with the help of text mining. Since digital storage is cheaper and plenty, the information can now easily be stored and studied with various software. IoT-based devices provide digital results in no time which has enabled self-monitoring easy and also has cut down the time and money which used to be spent earlier. In silico approaches are been found to be effective in these new approaches have made the healthcare system smarter, cheaper and more effective as a result.

Table 8.1 Comparison of conventional and modern drug discovery approach [4]

Parameter	Conventional approach	Modern approach
Process for management	Difficult	Easy
Process for transparency	Less	More
Communication between disciplines	Complicated	Generally uncomplicated
Cost for drug development	Very high	About one third
Time for drug development	10–16 years	6–8 years
Disciplines involved	May be incompatible	Compatible
Execution of steps involved	Sequential	Parallel
Process	Trial and error	More logical
Basis	Blind screening	Specific and target-based

8.3 Conventional Drug Discovery and Traditional Medicines

Traditional approaches for drug designing were based on the primary objective of finding compounds that would easily bind to a target with a lot of affinities. The drug discovery process involving conventional approaches requires a lot of time and has many complications associated with it like they are less effective and have a higher amount of problems associated with marketing. These approaches also have too many side effects and very weak pharmacokinetics. Conventional drug discovery and its development had an imperceptive screening approach, which involved a lot of investment in labour. Rational drug design as a concept started growing in 1960s due to many disadvantages associated with conventional approaches. For example, CADD (computer-aided drug design) was developed as there was a need to understand the structure and biological activity relationship (quantitative) which was not achievable through traditional approaches. A comparison of conventional and modern drug discovery approach is given in table below (Table 8.1).

Even as traditional medicine products have been used for centuries, less amount of work has been done on its developmental aspect. To develop these products, carrying out validation studies becomes necessary. To carry out research using traditional medicines, it is essential that some basic ethical requirements are followed. There are eight necessary requirements for clinical research using traditional medicines which were shown by studies done by Emanuel et al. With the current requirements of these types of medicines growing, it is essential that safety and quality aspects are improved. This can be achieved by the integration of some fields such as traditional medicines, basic sciences and most importantly modern sciences.

8.4 Predictive Analytics in Healthcare

Analytics can simply be defined as an approach of developing insights through the systematic use of data and its application for qualitative and quantitative analysis. It typically includes big data analytics, data mining and text mining. In healthcare,

such technology plays a vital role in aiding the healthcare personnel in disease diagnosis as well as its prediction and treatment, furthermore enhancing the quality of service provided at a faster rate and economical cost [13]. With an abundance of numbers, words, voices and images, there is this parallel rapid growth of data. This humongous repository of data is big data. The concept of big data is virtually new, and the way big data is defined has been changing constantly. Different efforts have been made at defining big data. Its speed, size, variety and complexity have compelled one to design innovative hardware and software mechanisms capable of effectively storing, analysing and visualizing the data.

Big data in healthcare can primarily be regarded as an illustration of the three Vs: data velocity and its volume and variety, which are innate aspects of data as it is produced [2]. The volume of data can be the entire collection of data stored in an organization. Dependent on diverse factors, it can also be transactional data generated over the years or on grounds of data flowing in social media. The data produced in an organization or institute rises regularly at an unforeseeable rate, which can usually range from petabytes to zeta bytes, however, completely centred on production activities and the category of the organization. The entirety of data that is transmitted in an organization or currently in movement is given by the data velocity. The rapid increase in the pace of generation and analysis of data has an impact on the transfer of the data between ends, which is highly time-sensitive. The complication of different forms and origin of the data, as well as its frequency, is the data variety. The data can exist in multiple forms ranging from structured data which includes data like business information, traditional data systems and numerical databases to semi-structured data (like the JSON) and unstructured data which generally includes pictures, audios and videos [16].

Data mining study enables identifying patterns inside massive and complex datasets to obtain useful information and develop insights thereby becoming a very valuable tool for the healthcare providers providing for better healthcare services and reduction in costs.

Text mining or text data mining is an equivalent of text analytics and is the course of obtaining high-value information from text. Statistical pattern learning helps in the procurement of high-value data by the formulation of patterns and movements. Big data in healthcare typically requires special software designed to analyse the digitized clinical data generated at a rapid rate by healthcare organizations throughout the scale. Additionally, apart from the three Vs, big data also speaks about its power. The huge volume and complexity of the datasets pose a challenge for the present techniques to analyse, visualize and obtain useful outcomes. The substantially developing healthcare business sector requires better decision-making through big data analytics to identify hidden patterns understand previously unidentified correlations and the market variations [16]. The healthcare analytical tools can be predictive which helps to smoothen customer experience and improve outcomes in comparison to traditional business tactics through large datasets allowing to process large chunks of structured and unstructured data all at once and also predicting the future outcomes, whereas descriptive analytics is useful in illustrating the picture about the previously stored data and it uses business intelligence and data mining.

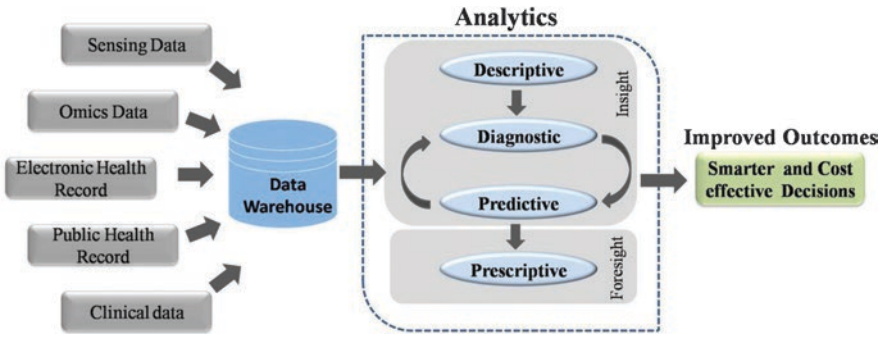

Fig. 8.1 Workflow of big data analytics [17]

Figure 8.1 describes the workflow of big data analytics in healthcare. The input data can be from EHR which includes medical imaging, socio-behavioural, and environmental data, omics data clinical data and sensing data. Data warehouses are a repository of large volume of data collected from multiple sources. Analytical pipelines are used to process and analyse this data and finally resulting in smarter and inexpensive healthcare options.

8.4.1 Application of Predictive Analytics in Healthcare

There are numerous noteworthy applications of predictive analytics. It is possible to predict individualized patient outcomes. Using this information, one can calculate if a patient is at greater risk of any disorder or the probability of the patient to readmit post-surgery, as well as predict the chances of survival post-surgery. The information obtained through predictive analytics has been revolutionary for the medical practice. Big data analytics can be used to transform the way healthcare professionals use technologies to analyse and improve decision-making using the clinical and other data repositories. Healthcare industries are using predictive health analytics to obtain a complete picture of the patient's health along with included risk factors by combining information from a wide range of sources. This information can assist in proactive care management and improve operational cost efficiency by predicting patients that require specialized healthcare or are at a high risk of infection and identifying if a patient has to be readmitted. Some of the objectives of big data analytics are clinical decision support (CDS) which aims at increasing the service quality provided by healthcare and improving the outcomes. Disease management helps to analyse diverse diseases and its evolution by the tests conducted at the laboratory. Patient matching uses the patient-centric model approach utilizing prescriptive big data analytics and treat a patient on the account of symptoms rather than disease-based management approach, lifestyle analytics, data matching, etc. [16]. The software systems such as electronic healthcare predictive analytics (e-HPA) can

differentiate between risk and prediction models. These can perform data retrieval from electronic data repositories like electronic health records (EHRs), wearable technologies or medical devices; cleaning and synchronization of the data; calculating the risk of an event; informing of risk prediction models using the new data; and the activation of clinical or other pathways, directly by alerting the patient's or provider's devices [15].

8.5 Drug Development Process: Key Steps

The drug development process involves various scientists and researchers, statisticians and physiologists. In recent years with developing technology, various other specialists also assist in drug development like biochemists are into studying the chemistry associated with life processes. Toxicologists look into whether a particular chemical can be harmful. On average it takes more than a billion dollars to develop a drug. Food and drug administration (FDA) is responsible for approving it, and then it has to regulate the development of the concerned drug. Different types of new drugs that in recent times are being developed are for diseases such as AIDS and cancer, diabetes and arthritis. The health crisis around Ebola and Zika has led to an urgent need for the development of drugs for these diseases. The drug development process generally involves many stages to get a product that is effective and safe. The process also has to meet standard regulatory requirements. Some of the steps followed in the USA are discussed below [7]:

Drug Discovery and Target validation Discovery work is the first step that involves choosing molecules like protein, which is a selection of a biochemical mechanism for a disease condition. The protein or drugs are selected to the target. Drug developers confirm whether or not the particular molecule identified is relevant to the disease being targeted. After testing the diverse molecules, the best among them is selected.

Testing(Pre-clinical) This step is classified into in vitro and in vivo testing. In vitro is based on examining the interaction of drug molecules on living cell cultures. It also involves examining the drug molecules' interactions in test tubes. In vivo is based on examining the interaction of drug molecules on animal models and in other living cell cultures. FDA does not allow preclinical studies into the human trials unless it finds it completely safe. This step generally takes many years as thousands of drug molecules are tested and only two to five drug molecule candidates are selected.

New Drug (investigational application filing) Investigational new drug application has to be submitted to the FDA. This is done prior to the clinical trials. FDA during this step scrutinizes the results which were obtained after preclinical testing. They then look into other aspects like knowing the side effects, the chemical structure

of the drug is examined and then it looks into safety features around the new drug. Later on, they also look into the process of manufacturing a particular drug. Once FDA approves this, drug developer can start with human trials.

Clinical studies (phase I) Study and tolerance around study agents are determined in the case of normal healthy participants. This is done with the exception of rare diseases such as HIV and cancer. Sometimes they are also called "first in man" studies as this is the first time that drug is introduced into a man. Various things which are analysed are drug-disease interaction and physiological side effects. The drug-drug interaction and bioavailability data are collected and analysed for a population of around 100 people (study group).

Clinical studies (phase II) Safety and efficacy involved with a drug are sought here. They are conducted for a particular disease or are done on a specific targeted population. They can be classified into pilot and pivotal. The pilot is basically about getting information involving efficacy. Pivotal is done for both safety and efficacy. These are done so that the new drug can be included in the new drug application. Phase II studies generally are conducted on larger populations (few hundred). Same types of data which was collected in phase I have collected here also.

Clinical studies (phase III) The data which were collected during earlier trials are expanded in this step. They are at first confirmed and then expanded by conducting trials again. The marketing approval can be obtained only after it is confirmed that the new drug has therapeutic benefits. These trials are conducted on thousands of people, where there is a specific control group involved. This control group is present so that the trails can be done on multiple treatment groups. This is also the appropriate time where drug developers start thinking of increasing the productions if phase III studies have been successful. By assuming that the drug will have a primary endpoint and it has been demonstrated to be safe, then the next step forward is to look for its approval by filing the application.

Application filing(new drug) This is the simplest step. This is done so that the new drug can be filed for approval from the FDA. They can have a large number of pages such as around 100,000 or more. The application contains all data related to safety and research. These data were collected from the earlier steps. This is not the step where FDA approved or disapproves a particular drug, but this is the step where it is promised that the application can be reviewed over the next 10 months. Once NDA is accepted as PDUFA (prescription drug user fee act), date is given for approval of the FDA. At this point, the FDA has to decide whether to accept or decline. Sometimes FDA postpones it due to several reasons around a drug.

The date for PDUFA and decision FDA has mainly three choices after the date has been sought. They can either deny or approve a drug. It can also ask for more information by dispatching a response letter, or it can also send CRL. Information about what is missing and how the remedy can be done is provided by CRL. Often the drug developers have also been asked to have further studies or have been asked to

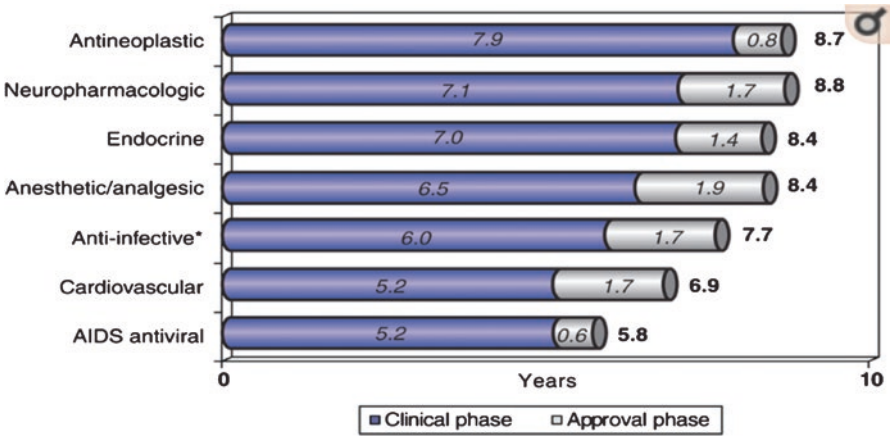

Fig. 8.2 Clinical development times. (From IND filling to NDA submissions and regulatory approval times for new molecular entities approved by FDA [7])

look into the manufacturing process properly and to have changed in the process. Once the FDA approves it, the drug can now be used for commercial production. FDA for most of the time has to wait for the PDUFA date and then can give its decision.

Last step: clinical studies (Phase IV) These are in general post-market trails. These are conducted to get data such as quality-of-life data, adverse events. They are conducted on a population of thousands. It's not uncommon that FDA can sometimes request long-term studies. If requested then the drug developers have to submit reports where they have to give details on whether there were any adverse events. These reports can report on whether there are any long-term side effects with these drugs. *Time (Fig.8.2) is the only reason why very few new drugs come into the market; it also speaks why the drugs are so costly.*

Predictive analytics has found tremendous applications in the clinical healthcare area. Right from the first step of patient recruitment for clinical trials to the last step of gaining approval, predictive analytics and in silico drug design have made a huge impact on the field.

8.6 Clinical Trials

Clinical trials are intended to assess the new drug intervention on the target recipient. It is composed of mainly three stages, although a prior phase called the preclinical trials and the post-phase called the phase IV clinical trials are normally considered part of clinical trials. The drug is normally given to a small group which

consists of healthy volunteers during the phase I trials. The study mainly emphasizes drug safety. During phase II the drug is assessed for both safety and effectiveness, on a small group of patients. If satisfactory results are obtained, phase III trials are initiated where a large group of patients are studied in detail for the drug efficacy and safety. After gaining regulatory approval, the drug enters phase IV trial which is primarily post-marketing surveillance, wherein the long-term safety of the molecule is assessed.

8.6.1 Clinical Trial Size Design and Study Population

Any population associated with clinical trials is made up of the test group and control group. Intervention is given to the test group, whereas the test parameters are evaluated for the control group. Depending on the study, the control group may be administered either with a placebo or no intervention at all. In some cases, the control group might receive an intervention that is already prevalent for that particular condition. A number of parameters affect the size of the population group. A number of people affected by a particular disease, social and economic conditions, additional eligibility criteria like age, sex and the severity of the disease condition and the number of people with the willingness to participate in the trial, etc. play a key role in the selection of participants. Phase III clinical trials are normally conducted on a large population of diseased patients (a few hundred). However, a smaller population is acceptable in cases like (a) the number of people affected by the disease is very small, (b) the disease is very lethal or fatal, (c) absence of existence of any potential treatment for the disease and (d) the intervention under test is highly effective and shows extremely little toxicity. Therefore the choice of the population for the study is a critical step, and the design of the entire study very well depends on it. Hence in order to get study right, specific predefined criteria should be set for eligibility of patients [6].

8.6.2 Patient Eligibility for Clinical Trials

Randomized clinical trials play an important role in producing evidence-based and reliable treatments, wherein the participants are categorized into the test and the control group randomly without any bias. However, there are certain limitations to it, like the benefit of the drug received being missed by certain participants. Also, the effective results derived turn out to be the statistical average. Predictive analytics can be a definite answer to the long-standing issue of improving the efficiency of patient recruitment. Being the most important step of clinical trial design, utmost care and accuracy are required in this stage. With the advancement in technologies and improvement in the quality and quantity of the data being produced in recent times, the use of predictive analytics seems promising. The main challenge with the

implementation of predictive analytics for determining patient eligibility is contained basic data.

During the past, the primary source of data pertaining to healthcare had been claims data. But the main drawback was that claims data could not provide the overall well-being or health or disease-specific functioning of the patient. On the other hand, clinical data was often written by hand, incomplete, spoken or dictated. Therefore, the corresponding datasets were relatively small, contained limited variables and of poor quality. The resulting predictive model worked only marginally and was unreliable. Recent advancements and technological growth has resulted in the use of EMR (electronic medical records) that has generated diverse and huge data digitally. Clinical data from different sources and organizations can be linked and aggregated remotely for analytics to be enabled. For the data that is unstructured, NLP (natural language processing) can be used to access it. With such high-quality clinical and claims data, predictive analytics has reached new heights. Predictive analytics utilizes statistical and mathematical approaches to the outcomes of the future. It comprises of a wide range of machine learning, modelling and data mining techniques to predict outcomes based on the historical facts. Therefore the overall ability of the model to divide the population to test and control group based on the probability of the future outcome is increased, which is best explained by the goodness of fit method. Different models and prototypes in recent times were developed which were established with respect to the requirements of the project.

Among the best methods is the clinical trial simulators (CTRSS). It is a decision support technology that considers all the possible variables and gives practicable data of the performance of the clinical trials and how it is affected by patient recruitment, thus making the tool more effective and reliable in decision-making. Many of the challenges regarding the eligibility of patients and performance of prototype for different system configurations can be addressed on the basis of its feasibility. Another critical parameter of comparison of studies between test and control samples can also be addressed. A combination of biomarker studies and predictive modelling could be a potential solution. A biomarker can be said as a measure of the biological state. According to the definition, a biomarker is "a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes or pharmacological responses to a therapeutic intervention". Parameters like blood pressure and cholesterol levels act as biomarkers by indicating the health state of an individual. Such biomarkers can be a basis for performing clinical assessment and relevant therapeutic intervention is decided. Early detection biomarker, endpoint biomarker, prognostic biomarkers and predictive biomarkers are some of the types of biomarkers currently prevailing. A study conducted to assess the advantages of node-negative oestrogen and breast cancer patients from cytotoxic chemotherapy with Oncotype-Dx scores. Sadly, incorrect results were obtained when conventional statistical tools like regression analysis, ANOVA and t-tests were used.

The erroneous identification of patients for chemotherapy could have been due to:

(a) Increased number of genes when compared to the number of cases.
(b) The insignificance of regression coefficients in the prediction of accuracy.
(c) Overdependence on inference problems.
(d) The goodness of fit model not practically applicable in predictive accuracy.
(e) Hazards and odds ratio not being an appropriate measure of prediction accuracy.
(f) The data used to develop the model, when fitted with the same model will not provide evidence of prediction accuracy for independent data.

Compound covariate the predictor was used to build a predictive model from the log-ratios of ten differentially expressed genes. It could also concentrate on a diverse group of heterogeneous molecules and the oncogenic mutations which cause their responsiveness to specific drugs.

Implementation of predictive analytics in clinical trials, finds the best use when patient eligibility for a particular trial needs to be done quickly and thoroughly. New bioinformatics and biostatistical techniques have been a result of the advancement of biotechnology and genomics research. These new techniques have aided in the development and validation of new diagnostic tests and genomic biomarkers which make choosing the appropriate treatment for patients relatively easy. The varied range of diseases based on genomic biomarkers leads to the development of new methods and paradigms of clinical trial analysis and design with enhanced criteria for patient eligibility and reliable predictive personalized medicine on the basis of biomarkers.

8.6.3 Experimental Design and Population

Another big challenge during clinical trials is to identify the most optimal and best fitted experimental design. Many times, designing a study during randomized clinical trials (RCT) is the most critical and deciding factor of the entire clinical trial. This issue can be addressed by simulation studies. A group of virtual patients are simulated in environments of potential randomized clinical trials. The effects of the intervention are modelled using dose-effect relationship, and the qualitative and quantitative outcomes are noted. Estimation of therapeutic effect with precision, size of the sample, duration of the trial and power are some of the specific criteria that are considered for comparison. Performance of different designs in different models is taken into account and compared. The most suitable design can be obtained after a rigorous simulation of more than a thousand clinical trials for a modelled disease condition. After the finalization of the RCT design among several different designs, it is used to improve the evaluation of the drug in specific patients, as in the case of personalized medicine or in specific fields, as in the case of rare diseases.

8.6.4 Observational and Interventional Studies

Before commencement of any clinical study, it is highly imperative that a thorough risk-benefit ratio is assessed. It becomes very crucial that study design, endpoint and all the necessary details are decided upon. Study designs can broadly be categorized into interventional and observational types. With its own advantages and limitations, each design presents its own dimension to arrive at right conclusions for the study.

Observational designs tend to rely upon historical data. They are often retrospective in nature and generally called epidemiological study designs. These studies mostly glorify the cause-effect relationships, resulting in identifying the potential causes of an outcome. These studies mostly exemplify the exposure-resultant relationships and diagnostic study designs which evaluate the accuracy of the procedures. Observational designs include diagnostic randomized controlled trials, diagnostic accuracy designs and diagnostic cohort designs, which are of high importance. This study type includes cross-sectional, case-crossover, case-control, ecological designs and prospective and retrospective cohorts.

Interventional studies are usually prospective in nature. So more often they are used in the prediction and/or evaluation of preventive measures of a condition. These studies are used to directly assess the impact of a treatment on a disease. This study design is gaining more and more popularity lately, owing to its common observational and preventive conclusions [10].

8.6.5 Clinical Trials Guided by Next-Generation Sequencing

With the improvements in the field of genetics and genomics, NGS (next-generation sequencing) has also seen a lot of growth. There has been an increase in awareness about personalised medicine as a result. Scientists are on their toes, for incorporating genetic information for the study of the drug effectiveness and interaction. Enhanced knowledge in the areas of mutation and polymorphism analysis has made targeted drugs much easier. An extension of the same has been applied to the eligibility criteria for participants of clinical trial studies. Especially in cases like cancer, clinical treatment studies, where the source of malignancy in each participant, may not be the same. Also the cause and location of mutation are widespread, making the intervention not-so-effective. The specific target mutation being present in only a minority of a population is also a setback. With the introduction of advanced technologies like parallel genomic sequencing and increased availability of targeted molecules for these abnormalities, oncological research sees a new ways for improving cancer treatment. To ensure the treatment reaches the right beneficiary during clinical trials, eligibility criteria just based on stage and histology are not sufficient. Additional categories like genomic analysis, mutation and polymorphism studies are necessary. In recent times, the above-mentioned criteria are taken into

consideration for the design of several clinical trials for targeted treatment. However, a number of setbacks stand in the way of its implementation like tumour heterogeneity, choice of assay, identification of resistance mechanism, levels of evidence regarding gene variants, the need to screen large number of patients, collaboration of industry and investigators and infrastructure needs. Consequently, a number of disadvantages also could be noted based on the sole dependency of molecular variants as the criteria of eligibility [8].

8.6.6 Predicting Drug Safety

The main focus of any clinical trial study is to prove drug safety and efficacy. Although a large number of drugs clear the clinical trial studies and make it to the market, a larger number of drug molecules fail during this stage, causing immense losses. Hence it would be better if we could predict the safety of a drug before clinical trials is conducted on a large scale to reduce the therapeutic risks. A number of models have been developed for the same and they use a combination of structure-activity relationship and topology analysis along with a number of other tools. Cheminformatics measurements along with integrated network topology analysis are a key tool. A thorough comparison of the intended drug with the information from a database could help in predicting the safety of an intended drug. The safety indications are predicted by measuring the similarity between the intended drug's target with other existing molecules. When a drug with the same target is confirmed to be discontinued or withdrawn in certain regions of the world, further investigations take over before the start of clinical trials. Pharmacovigilance and activity of natural products could also be predicted by 2D chemical fingerprint similarity calculations from a traditional database. Hence this tool can be applied to a number of compounds even if the target is not known and acts as a great tool for safety surveillance [12].

8.7 Regulatory Aspects

In silico predictive methods have become a handy tool not only for the drug discovery process but also in regulatory processes to keep a check on product quality and safety. Strategic support risk-based approaches are adopted by regulatory authorities to like FDA (Food and Drug Administration). Computational models closely working with chemically intelligent systems using structure-based assessment are the methods used for predicting safety liabilities and toxicity data. Necessary steps have been taken by the FDA to enhance innovation in the field of regulatory science by utilising in silico predictive models and developing medical toxicity databases. The most recent application of predictive modelling in regulatory aspect is in the prediction of mutagenicity of drug impurities. Another case is the cardiovascular

drug safety modelling based on the data of clinical trials. Computational toxicology program has been initiated by FDA and CDER (Centre for Drug Evaluation and Research) in collaboration with private companies across the world. Safety assessments of food additives have also been stepped up by the use of toxicology modelling by FDA and CFSAN (Centre for Food Safety and Applied Nutrition). Currently in silico predictive models are used by regulatory authorities to support decision-making based on scientific evidence in terms of approval of the drug molecules. When it comes to dug impurities used, ICH (International Council for Harmonisation) has provided quality guidelines Q3A and Q3B for different classes of drug impurities permitted for use. FDA draft guidelines use QSAR (quantitative structure-activity relationship) implemented in predictive approaches for the identification of potentially carcinogenic and genotoxic impurities [9].

8.8 Drug Testing

Choosing compounds that have a lower chance of causing toxicity can help in getting higher attrition rates during before drug discovery and development process. Some predictions involving toxicity can be given to chemists so that they are well in advance aware of the compounds which have been proposed. Many approaches are used to balance the toxicity potentials. Toxicity can cause increased attrition rates and cost which can, in turn, lead to market withdrawals. Data from 2006–2010 from the FDA has shown that 22% of drug candidates entering clinical development failed due to toxicity.

Knowledge-based prediction-predictive systems have been made in a way to make the process of decision-making with the knowledge which is based on facts and is used to make predictions by inferring from a process called reasoning. Expert systems can help in making predictions of toxicity from various mechanisms. This is usually done when there are incomplete datasets available. Predictions of the chemical causing harm can be done through in silico systems. The analysis requires proper knowledge of the dosing regimen and also some pertinent biological details such as sex and age. Derek for windows application can give active and inactive predictions for the toxicity endpoint. No report is returned when there is no evidence of toxicity. In the drug discovery process for the selection and design of compounds, predictions based on toxicity hazards have to be balanced against other available properties. A project team can define property criteria as a profile which is needed in an ideal compound by methods for MPO (multiparameter optimization) like probabilistic scoring. When compared to others, it has an edge as it has a knowledge-based approach for toxicity prediction is that increased likelihood of toxicity is identified. This is usually associated with the structural features of a compound. By focusing this alert on the structure of a compound, it can be very important to chemists who are associated with medicines and who want to optimize it. MPO method associated with predictive models of other properties in an

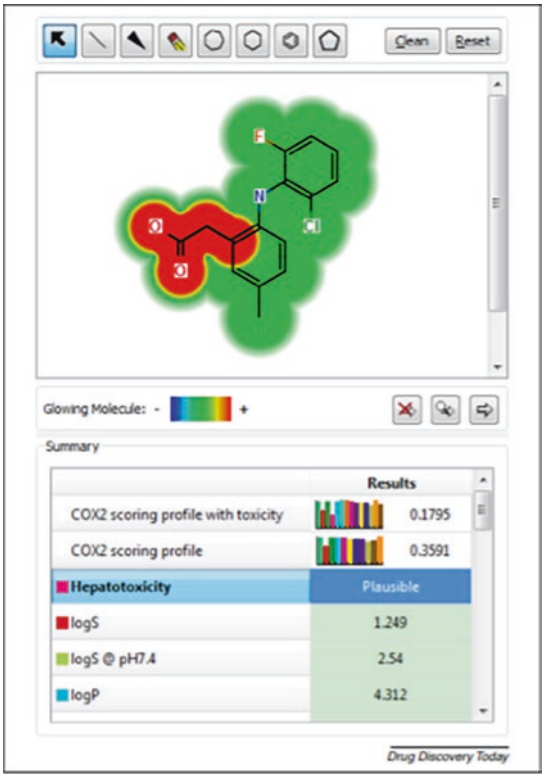

Fig. 8.3 An example of an interactive designer in which the structural alert giving rise to the prediction of an increased chance of hepatotoxicity for lumiracoxib is highlighted in red [11]

environment which is interactive can be used in alternative compounds as it can guide in designing them.

The risk associated with toxicity can be avoided or reduced without that making a negative impact on the other required properties. The figure shown below gives an example of such an "interactive designer" (Fig. 8.3).

8.8.1 Drug Approval Analysis

Small molecule drugs that have been approved can be analysed with the help of Derek Nexus module for star drop with available endpoints. The predictions generally cover a range of things such as hepatotoxicity, mutagenicity (in vitro) and some other things that are involved. It also involves prediction of activity which is linked to structural alert. This alert is identifying motif which is triggering the prediction (positive), along with likelihood. The level of confidence can be understood as likelihood since it can be easily equated to the accuracy of prediction (Fig. 8.4).

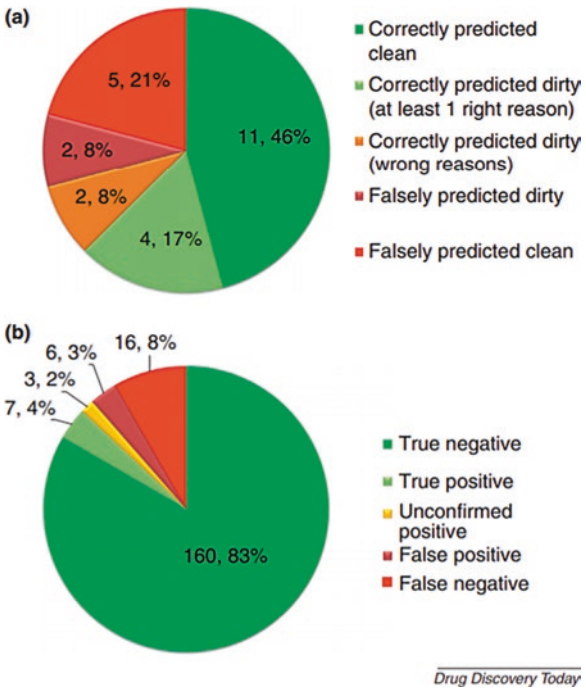

Fig. 8.4 Results of predictions from Derek Nexus module from starDrop on the compounds approved by FDA in 2012. (**a**) Analysis on per compound basis, (**b**) analysis on per endpoint basis [11]

In short, these analyses suggest that often toxicity can be predicted by a knowledge-based prediction which can be a very effective tool. Potential toxicities can be identified by this effective tool before a compound is sent to a clinic. Flagging the potential toxicities before the drug development process can help in screening the hazards before investments are done. MPO analysis can help in balancing these risks. This was shown when carfilzomib had six alerts, yet it was accepted for the treatment of cancer as other treatments were unsuccessful. Knowledge-based predictions of toxicity can help in guiding the selection and later on optimization of the compound. This is done when in vivo and in vitro data are not available.

8.9 IoT-Enabled Clinical Trials

With the operational costs as high as four million USD for phase I, eight million USD for phase II and 21 million for phase III on an average, the cost of compliance is a direct correlation. In this competitive era, cost and time are the key drivers to any clinical research, technology being the major influencer. IoT provides feasible solution to many cumbersome difficulties faced in clinical trials. Increased availability of smartphones and other smartphone-enabled devices has managed to pave way for a whole new dimension.

IoT-enabled devices can contribute in a number of ways to simplify the process of clinical trials. Right from checking the eligibility of patients to the trials, to governing the dosing regimen, to enhancing the communication of any adverse events to the investigators in real-time, technology has changed the way things are done. Mobile applications connected to smart pills or blisters provide reminders and keep a track of the consumption of medication, which helps reduce the manual data entry errors. It also helps enhance the assessment of patient adherence to the study protocol. It also increases the efficiency of telephonic or remote visit assessment, thereby reducing the time and costs associated with travel and other test procedures. It also helps create a closed network of patients, investigators and other stakeholders for better communication. In a nutshell, technological advancements are aiding to address the long-standing challenges of clinical trials and improving the quality for reduced time and costs [14].

8.9.1 Related Permissions and Its Importance

Implementation of IoT and other in silico techniques has not only revolutionized the process of clinical trials but also created an amendment in the existing processes and regulatory requirements. Just like in the conventional way, IoT-enabled clinical research also demands an informed consent obtained from the potential subject before their enrolment into the study. An informed consent form (ICF) is a form that declares the willingness of the patient to be participating in the study. This form is also an acknowledgement that the potential subject is fully aware of the process and understands the medical and legal consequences of being a part of the study. This ICF also ensures the participants gain access to the schedules, procedures and clinical appointments. In case of IoT-enabled studies, ICF is a way clinicians seek permission from the subjects to gain visibility to patient data in real time from the subjects' smartphones and other IoT devices.

A few untoward incidents in the past have led to major frameworks that govern the ethical aspects of clinical research. The Declaration of Helsinki, 1964, and the Nuremberg Code were drafted by the medical authorities to guide the conduction of trials in an ethical manner. Informed consent is a major resultant of it. According to the governing authorities, all the study-related documents like the protocols, study design, Clinical Trial Agreements (CTA), Investigator brochure, informed consent forms are to be reviewed by an Institutional Review Board (IRB) or the Ethics Committee (EC) to ensure ethical conduct of the trials. The IRB contains members of all walks of the society, like medical practitioners, legal practitioners, common people, people associated with any non-governmental organizations (NGO) and people representing government agencies or authorities. This committee reviews all the documents associated with the process and ensure rights the participants are protected and the procedures adhere to the guidelines. Along the same lines, the review board ensures that documents that require an understanding of the participant like the ICF are explained in simple terms. The intention of ICF is to convey to

the potential subjects the procedures, risks and benefits (medical and monetary) involved and consequences of the study. It also describes in detail the data and the biological samples that shall be collected and the rights of the subject over it. Regulations require that the consent of the patient is voluntary and not influenced by any sort of pressure or monetary benefits. It is also highly imperative that the subject is made aware of all the terms and conditions of the study and that the subject is free to withdraw his/her consent at any point of time during the course of the study. Regulations also demand that the informed consent is obtain well before the subject is enrolled into the study and that consent is provided in the presence of principal investigator or an authorized personnel involved in the study. These regulations help draw a line between the rights of an investigator and a study subject, making sure no rights are violated [3].

However, this process comes with a few hindrances. With the increasing ease of access to patient data remotely, the risk of data confidentiality breach has also increased significantly. The responsibility of data protection is a prime concern. Enhanced privacy policies and security frameworks are needed to ensure the conclusions, and results obtained are authentic, reliable and reproducible. Interference of some regulations like the General Data Protection Regulation (GDPR) and other related laws have in a way made the governance much easier.

Enforcement of these regulatory guidelines is overlooked by the US Department of Health and Services (HHS), Food and Drug Administration (FDA) and Office of Human Research and Protections (OHRP). "The Common Rule" often protects the rights of the patients enrolled in the study. 14 regulations laid down by the FDA perform a similar function although its relevance depends on the nature of the intervention. Section 8.11, 21 CFR is of great importance to clinical researches as this section mainly deals with the technical specifications of recording, storage, maintenance, transmission, modification, archival and retrieval of data in electronic form. It is also deals with electronic signatures and consents involved in clinical trials. HIPAA (Health Insurance Portability and Accountability Act) is one another act that protects the rights of human subjects involved in clinical trials. It ensures the conduction of the research in an ethical manner [18].

8.10 IoT and Its Applications

Remote health monitoring – Historically the first-ever recorded Doctor was Hippocrates. During 460 BCE doctor was a rare profession so he was called a medicine man. From that time to till the twentieth century, the world has been using traditional health monitoring. In traditional health monitoring, when any person used to suffer from any type of disease, they used to visit a place where many doctors used to do their medical practice, and that particular place was called the hospital. This method of health caring was nice but not perfect. There were many gaps in this method. A study done by the Institute of Medicine in 2012 shows an interesting result that "33% of hospital patients suffer some form of preventable harm

during their hospital stay…" IOM, 2012. This states that a hospital is no more a fun place and if anyone goes there, then there will be a good probability that anyone can end up with some quite unaware disease. The world is facing an acute shortage of trained doctors and nurses as the increasing rate of the trained doctors is very much less than the increasing rate of the patients and deadly diseases. The ratio of the number of beds available when compared to the number of people in India is very less; it's 1.3 beds for every thousand people. To overcome these problems, remote health caring methods are being used by which many non-chronic problems can be solved by the doctors without a face-to-face visit. By the help of the remote monitoring, good quality of healthcare can be expanded to the remote and aging peoples. India has a huge population of around 1.3 billion in which around 34% is contributed by the urban peoples. Urban people don't get proper healthcare, but by the remote monitoring, the geographical and physical barriers can be removed. Remote patient monitoring also called as RPM sensors work in several components; first the physiological parameters like blood pressure or glucose level, etc. are measured by the sensors, and then this data is stored locally which later sent to the third party basically healthcare provider. Then these healthcare providers process the collected data and analyse it; if any problem or any disease is detected, then the healthcare provider will notify the particular person. Devices for the RPM are like the glucose metres for the patients having diabetes, blood or heart rate pressure monitors and continuous surveillance monitors that detect patient conditions like dementia, and, also, it can help by alerting the healthcare professionals about an event like fall and sends help for them through emergency contacts, remote infertility treatment and monitoring, caloric intake and diet logging programs like fit bands.

8.10.1 Devices

IoT-Enabled Glucometer 7.2% of the Indian population is suffering with diabetes. Normally when the glucose level of the body increases human body releases insulin, this insulin acts as signalling molecules for the cells which tell them to take the nearby glucose by which the glucose level decreases. Diabetes is the disorder in which our body stops producing insulin. So every person suffering with the diabetes needs to know his or her glucose level in the body. Due to high level of the glucose in the body a person can fall, his bladder will fill quickly, feels hungry after every hour, etc. To do glucose testing, i.e. to know the amount of glucose present in the body, a diabetic needs to use a glucose testing metre. This glucometer gives the amount of glucose in the unit of mg/dl. To test the glucose level present in a person, a drop of blood is collected from a diabetic person. Then that drop is added to the glucometer strip; this glucometer strip has an enzyme called glucose oxidase, which will convert glucose to gluconic acid. This strip also has a chemical called ferricyanide. When ferricyanide and glucose react with each other, then they form ferrocyanide. Since ferrocyanide is ion, when little current is applied on the strip, ions start traveling. Amount of ions travelled is equivalent to the amount of glucose present in

there. This method comes under semi-traditional methods, as by this method we can only know about the amount of glucose present, it cannot analyse anything and every time we need to prick the blood. Therefore it's a major disadvantage.

The IoT-enabled glucometer is like a wrist band which has photothermal sensors and quantum cascade laser. Quantum cascade lasers are the semiconductors which release a mid-range of infrared rays of electromagnetic spectrum. Photothermal sensors sense the temperature and it is very sensitive. So when the quantum cascade lasers release the laser beam penetrates through the human skin and is absorbed by the glucose present in the bloodstream at a particular place. When glucose absorbs light, it emits little heat that changes in temperature that is detected by the photothermal sensors. During the trails they calibrated one machine learning linear regression algorithm by which just by knowing the change in the temperature value, we can estimate the amount of glucose present. This process works continuously by which we monitor the glucose level of the body; the data is then sent to the healthcare provider by which healthcare providers can notify the person in case of emergency. Even the wrist band can send the data to the physicians [5].

Automatic Blood Pressure Cuff One out of eight persons in India is suffering from either high or low blood pressure. Blood pressure can in general terms be understood as the pressure of the blood when it is in the circulatory system. It is usually measured to know the rate of the heartbeat and to know the radius and straggle of the arteries. According to the AHA (American Heart Association), normal reading of the blood pressure should be around 120/80 mm Hg, so here two readings are recorded. The (120 mm hg) upper reading is known as systolic reading, which shows the pressure exerted on arteries when the heart is beating, whereas the (80 mm Hg) lower reading is called diastolic reading, which indicates pressure exerted on arteries when the heart is resting. Cuff is placed around the upper arm, approximately at the same height where the heart is situated. Then pressure is increased in the cuff so that the blood will stop between the arteries, and then the physician takes a stethoscope to listen to any blood if flowing or not. Once it is made sure that no blood is flowing, then there is release of pressure. When pressure is released, then it makes some kind of noise. The noise should stop and until then everything is stopped. Once it stops making noise, then it is observed under the manometer that gives blood pressure values. The main drawback of this is that the manometer is made up of mercury which is not good for environment as it makes noise and we need to wait until it stops making noise, which means that it cannot be used at the noisy environment.

Automated cuffs are oscillatory-based devices that can give digital results, and they work on the principle that when the bloodstream is moving inside the artery, the diastolic pressure and systolic pressure lead to vibration in the arterial wall. These vibrations can be sensed by the sensors and transuded into electrical signals by transducers. This model follows a fuzzy model where the pressure in the cuff which is tied in the upper arm is given 20 mm Hg more than the systolic pressure as at this pressure there will be no blood flow. Then the cuff is deflated so that pressure

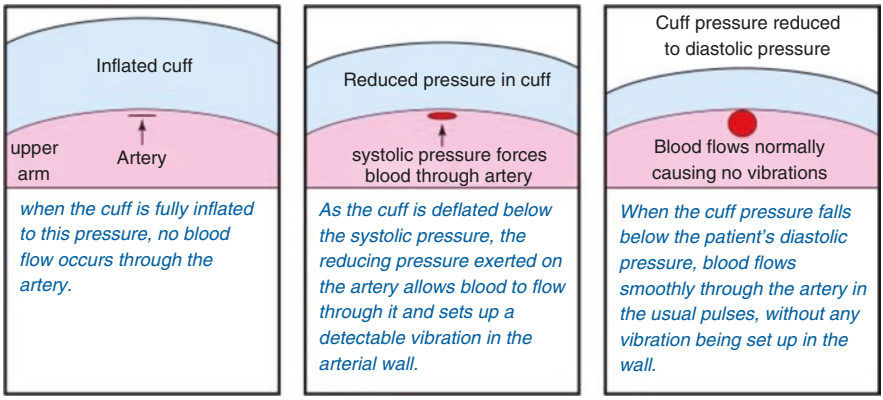

Fig. 8.5 Workflow of the automated cuff [1]

is decreased, and when the pressure of cuff becomes lower than the systolic pressure, then blood flows through arteries, and from the vibration of arteries' cell wall, we can detect the blood pressure. Once the cuff pressure is lower than the diastolic pressure, the blood present in the person moves freely at normal pressure without making any vibrations in the arteries' walls. The vibrations are placed away from the arterial wall, through the air which is inside the cuff, into the monitor. It is placed into transducer part of the monitor. Transducers as we know converts the measurements to the signals (electrical) [1] (Fig. 8.5).

8.11 Conclusion and Future Prospects

Traditional medicines for years have been used in primary healthcare systems. With changing economic scenes globally, there is a very high need to have research on efficacy involving traditional medicines as they are mainly based on the primary healthcare systems. Even as traditional medicine products have been used for centuries, less amount of work has been done on its developmental aspect. The entire drug development process takes around 10–15 years to come into the market. Drug developed will get the time off around a decade for selling the drugs once they have made it to market. Time is the only reason why very few new drugs come into the market; it also speaks why the drugs are so costly. New research avenues have opened up due to the availability of big data. In healthcare the big data analytics and related applications are at a very nascent stage [2].

Improving healthcare system worldwide is one of the main aims of predictive analytics. Some of the recommendations for future areas of research is the integration of domain-expert knowledge approaches to decrease prediction error and integration of predictive models in actual work environments. Facing diseases at an early stage can be achieved by data mining techniques. The companies providing

service for healthcare analytics and clinical transformation are indeed contributing to better and effective outcomes. Some problems associated with predictive analytics are privacy issues and fast rate at which technology and its impact on decision-making process, moral hazard and human intervention points with the machine and lack of regulation and algorithm. These risks are very old and are amplified with the help of decision-making process with the digital disruption.

In today's world of rapidly growing health-conscious people, the healthcare sector seems to be the industry to look forward to. With the increasing awareness about diseases among people, the requirement for its control and treatment has become the need of the hour. Increased awareness, on the other hand, has managed to shed light on some new problems and challenges. The healthcare industry, however, is evolving at a fast pace to accommodate the new changes and is trying extensively to tackle these new challenges. The huge influx of high-quality data from advanced technologies has created the room for its analysis and utilization. And one such area, which has outgrown other areas, is predictive analytics. Predictive analytics along with in silico drug discovery and the Internet of Things (IoT) has helped create better treatment and care for patients. The use of predictive analytics in the process of clinical trials and regulatory aspects has enabled faster and better outcomes. Designing experiments, patient recruitment and predicting drug safety have resulted in reduced risks and increased efficacy of the processes. These new approaches have also made things faster and less expensive. With the incorporation of genome analysis and next-generation sequencing, the participant screening technique has reached new dimensions. Drug safety and toxicity issues can be better addressed with outcomes of predictive modelling. Implementation of predictive analytics by regulatory authorities for decision support has made the approval process seamless.

The overall process of drug development and approval has improved by multiple folds with the use of computational methods. In the near future, the in silico techniques of drug development and predictive analysis can be used to improve personalized medicine for the better. By studying the genetics of a person, the suitability of a particular treatment can be predicted. This helps enhance patient care and experience. Post-market surveillance of a new product could be improved by predicting the long-term effects of a molecule. Drug safety can also be improved by monitoring adverse event data. This also helps predict any unexpected interactions of the drug by taking multiple parameters into consideration. Targeted drugs can become more practical and employable using in silico drug design and predictive analytics. It also paves the way for new approaches to respond to cancer treatment issues. Regulatory approvals can also be improved by predicting product quality parameters based on historic evidence. The recent trends in healthcare have pressurized healthcare device manufacturers to have a high amount of profit and be innovative to be in the market. With the use of communication means such as sensors, the manufacturers under a service contract have been able to monitor the status of equipment which has led to an improvement in efficiency and also has increased profit margins. Sensors, for example, can record everything such as fault in operations, environmental conditions, etc. As the global market is changing, there is a need to have a lot of research in the IoT field. Overall, vast amounts of high-quality

data, created as a result of advancements in technology and improvement in the field of analytics, have made healthcare more efficient and treatments more effective and less expensive. Thus, the healthcare industry is on its way to a big revolution.

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Chapter 9
A Novel Authentication Approach Towards Secured Storage of Electronic Patient Record Using 3D Dynamic Order Template

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9.1 Introduction

The expanding integration of profoundly empowered innovations in healthcare fields has essentially created a need to connect hospitals to procure and secure medical data in association with pharmaceutical companies to medical coverage organizations. The EPR of individuals is being hailed as a part of the big medical data that aids to provide better treatment plans and increase hospital profits [1]. Health informatics is ceaselessly advancing to make the existing electronic health record (EHR) better to support doctors in treating better and reduce medical errors [2].

The Health Information Technology for Economic and Clinical Health (HITECH) Act of 2009 in the Unites States has, to some degree, prompted 80% acceptance of implementation of EHRs in intensive care clinics. Since then, the rate of EPR selection across advanced EHR software and practice management software for therapy is in high demand around the world [3]. Despite the fact that the adoption of EPR and big data embeds numerous advantages, it also raises a few hindrances and difficulties in its implementation and usage [4]. The inappropriate choice of EPR software could also affect patient security and congruity of consideration. However, customizable open-source software (OSS) with a feature of interoperability between different healthcare providers provides a promising solution to bridge the gap between healthcare providers and facility for patients. The success of the chosen software tool is measured by the acceptance among doctors and hospital staff [5].

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The task of choosing the best one is tougher in today's world as there are large varieties of healthcare subfields [6, 7] complying different applications as noted in open Source Software (OSS) healthcare repositories online. Since OSS are inspected systems and licensed software, they are of zero cost except for commercial usage in exceptional cases [8–12]. A.A. Zaidan et al. [13] have compared the subjective usability, functionality, and features of the existing open-source EMR systems and have created a visual map to accomplish the best choice of OpenEMR based on easy installation, developer support, customizability, and user support. Study reveals that GNUmed and OpenEMR software are the most promising candidates for providing a good basis on ranking score records compared to other open-source EMR software packages.

Although the storage of EPRs proves to be secured, the interoperability between clinics and hospitals, remote systems administration, distributed computing, etc. paves a path toward concern of confidential information being hacked on networks. This leads to the most alarming medical data breach. The cyberattacks on healthcare industries and hospitals have been on the ascent in the recent past across the world [14–17]. The cybersecurity in healthcare segment normally focusses on safeguarding the secrecy, integrity, and accessibility of EPR, and it assures of not sharing recognizable confidential information in the wrong individuals [18]. The aftermath from the worldwide WannaCry ransomware assault in May 2017 is as yet settling; it allegedly influenced around 200,000 systems frameworks across 150 nations [19]. The ransomware attack has targeted technology frameworks but also claims cash [20–23]. From the survey of available EPR creation and storage types, it can be seen that a breach preventive and highly secured proactive measure must be taken by every healthcare organization to safeguard the EPR. Encryption, cloud storage, and password protection are different measures to make EPR more secure [24, 25].

With another information hiding technique, namely, digital watermarking [26, 27], privacy and reliability of the medical data could be doubled by ensuring authentication and security with imperceptibility, security, and capacity being the main attributes. A reversible watermarking method [28] applied on a database of medical images results in high peak signal-to-noise ratio and imperceptibility. Another approach based on 1D biomedical signal encoding allows embedding metadata, thereby securing the privacy, but is not currently supported by well-established signal standards (e.g., DICOM waveform 30, SCP-ECG), which makes it a promising alternative for the development of new and upgrade of existing e-health services [29]. A high-capacity and semi-reversible data hiding scheme based on Pixel Repetition Method (PRM) and hybrid edge detection is effective for electronic healthcare applications, but this work does not include the technique of having an authentication key for watermarking and dewatermarking of the EPR [30].

A keytagging technique [31] also hides the biomedical content of the image without the need for assessment, but this technique is not combined with any of the data hiding techniques. A combination of watermarking and a feature from biomedical signal as a key has been implemented in the paper [32]. Another technique with double security of the EPR has been presented in which the first level being the

usage of augmentation index (AI) from PPG signal [33] with a uniqueness of 95% by using augmentation index as password and the second being the watermarking with 98% reliability.

9.2 Motivation

From Sect. I, it can be noted that EPR with highly confidential patient information can be digitally transmitted usually over the Internet/intranet. This transmission requires immense security, and safeguarding the privacy and security of EPR is vital. Cloud storage, encryption, and password protection are different measures to make digital data more secured. Steganography, cryptography, and watermarking are the available methods in encryption. The systems also use biometrics, which have the rights to access medical proceedings, computer networks, medical image security, or watermark image security by recognizing approved individuals by perceiving passwords and ID cards. However, these systems could be outwitted using a person's picture and imitation of voice and also could be recreated using LaTeX, etc. Hence, a state-of-art but much more promising system with security of medical data is required. This technique, could provide not only an authentication key but also retrieval of medical information with minimum loss of information.

9.3 Prime Contribution of the Work

- Development of an integrated framework that emphasizes on creating a single platform to consolidate the patient data as an EPR
- Customization of HL7, GNUmed, and OpenEMR for Dental college and Hospital to securely store electronic patient data under one single platform
- Development of a novel hybrid algorithm to imperceptibly watermark the medical information into the facial image of the patient
- Creation of a unique 3D authentication key from the biomedical signal of the patient

9.4 Methodology of the Proposed Work

The methodology section includes four modules, which describe the patient demographic information mapping, biomedical signal acquisition, and EPR watermarking in Module 1, innovative key generation in Module 2, customizing the OpenEMR in Module 3, and statistical subject demographic information in Module 4.

9.4.1 Module 1: Patient Record Mapping

Module 1 involved obtaining the facial photograph of the patient along with his/her recognizable information and demographic information in a hospital registration desk in order to create a unique Electronic Patient Record [EPR] for the individual. The biomedical signals, namely, photoplethysmogram [PPG] and electrocardiograph, of the patient are acquired using the BIOPAC MP45 with SSL4 pulse photoplethysmogram transducer and three-lead ECG, respectively. These signals were acquired from 200 patients of Dental College and Hospital with prior permission from the Institutional Ethics Committee. The EPR is then further built with details such as orthopantomogram (OPG)/IOPAR, lab test reports, and so on. The watermarking procedure involved hiding of the EPR into the facial photograph (an RGB image) with photograph as the cover image and EPR as the host/watermark image. All the three planes of the cover image are utilized to watermark the EPR data.

To watermark the EPR, firstly, the aggregate size of the EPR information is ascertained and later compared with the size of the cover image so that the equivalent size would not as much as the cover image. Then EPR images to be watermarked are reshaped along the array to form a matrix of 10×10 and then transformed to 1×100 dimension vector. Then, the least significant bit of the cover image is replaced with watermark image data as given in Algorithm 9.1.

Algorithm 9.1 produces the watermarked image hiding the host EPR image information inside the cover image. The dewatermarking of the EPR is performed using Algorithm 9.2 to obtain the host EPR. The dewatermarking technique is briefed in Algorithm 9.2.

Algorithm 9.1 Patient record mapping

1	Let I_C be the cover image with size m, n, and p_C and I_H the host which has to be embedded inside I_C where $c \neq 0$
2	"I_H" the host image of DICOM format with a dimension of one plane I_{H1} and size k, r, and p_H
3	Check if $p_H = p_C$ and $(m \times n) > (k \times r)$, else $I_C \xrightarrow{\Delta} \sim I_C$ where $\sim I_C$ has dimension of k, r, and p_C
4	If the host image to be embedded is in DICOM format, then the patient information is retrieved and saved as a text file. Then the image format of the host is matched with the cover image Else, if the patient information is required, then it is embedded as text during watermarking
5	Transform "I_H" using wavelet transform, and then look for the pixel value which is maximum in the block and divide it by 2
6	Compare the blocks $I_{H1}\ldots_{Hn}$ of I_H. If the least pixel value obtained in these blocks is greater than from Step 5, then that particular block is chosen for embedding the host image information
7	Now, the HL and LH bands have the embedded information, and on performing inverse transform, the host images I_E could be retrieved

Algorithm 9.2 Dewatermarking technique

1	Apply wavelet transform on I_E, consider the maximum pixel value from the block, and then divide it by the value of 2
2	If the value of smallest pixel in the block is found to be greater than the value obtained from the above step, that block contains embedded data
3	The embedded data is computed from the difference in the pixel value
4	Inverse transform is applied to obtain original and embedded images

Implementation of Module 1 generates the embedded data, but the data is vulnerable to attacks and hence needs to be protected by a key which is explained in Module 2.

9.4.2 Module 2: 3D Secure Key Generation – An Innovative Key Generation Method

In Module 2, the watermarked data is protected by making certain that none of the unauthorized personnel can access the data. This is achieved using a 3D secure key generated using patient and diagnosis information which can be shared with only the authorized recipient. The information used in key generation are patient information like personal information (name, date of birth, age, sex), diagnosis information, and also vital information extracted from biological signal (ECG and PPG). The methodology of generating a 3D key using PPG acts as a biometric as shown in Fig. 9.1. A distinct parameter derived from the PPG signal called as augmentation index is set as rotational factor "θ" for converting a normal key into a 3D key and is depicted in Fig. 9.2, and the algorithm is explained using Algorithm 9.3.

Algorithm 9.3 results in a secured 3D authentication key. This key is used for securing watermark and dewatermarking the EPR from the facial photograph of the patient.

9.4.3 Module 3: Customizing the OpenEMR

The OpenEMR software is customized by framing the entity relationship diagram to store the demographic information, medical history of the patient and his/her relatives, medical reports of the patient obtained from any of the investigation, and the patient undergoes whether it would be blood investigation or any other investigation process as the doctor suggests. The option for saving, modifying, and deletion is also provided in the database so that the reports of the investigation can be updated when the patient visits the hospital for further checkup and treatment. Provision is also made to access the reports anywhere in the hospital through the Internet and intranet.

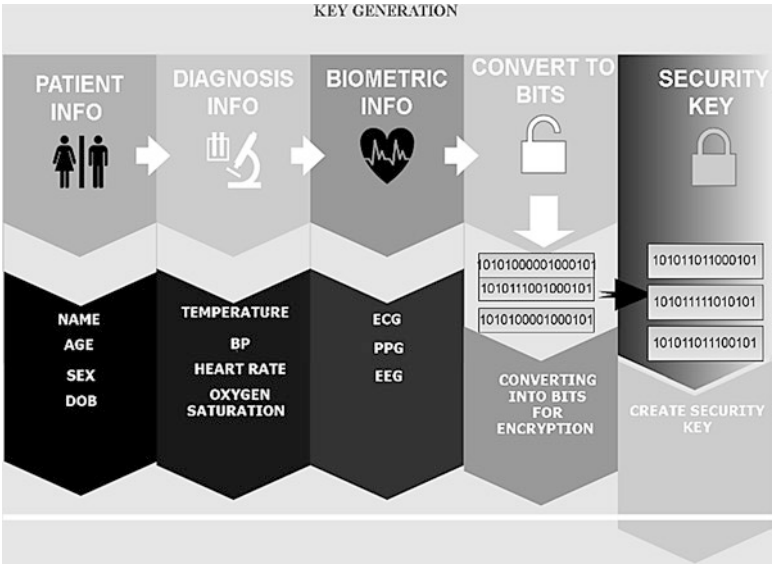

Fig. 9.1 Secured 1D key generation using vitals from the patient

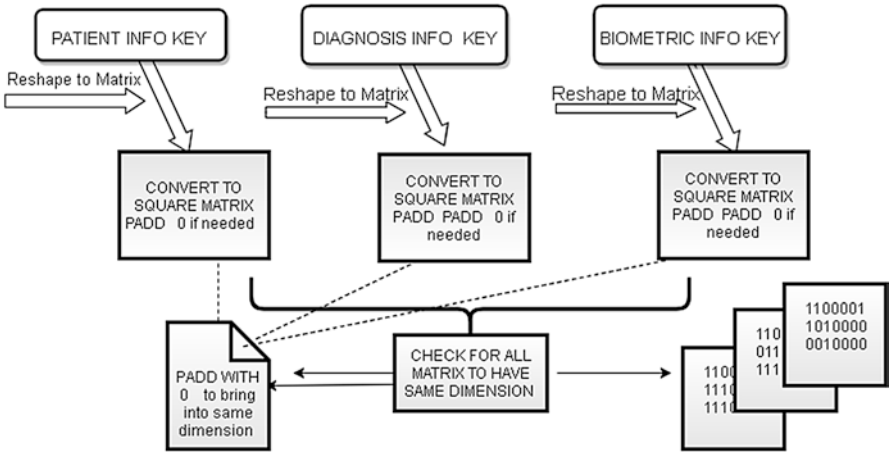

Fig. 9.2 Conversion of 1D key to secured 3D key

Algorithm 9.3 3D key generation

1	Let "X," "Y," and "Z" represent the binary value of the patient information
2	The binary value is reshaped into a matrix with padding zero if necessary to bring into a 3D structure so that all XYZ have similar structural order
3	Acquired PPG signal S is analyzed for augmented index and is obtained by $F(t)_p = \sum_{t=\text{length(S)}}^{t=2500} S(t) \geq S(t+1) \,\&\&\, S(t) \geq S(t-1)$ (9.1) where S is the PPG signal $F(t)_v = \sum_{t=\text{length(S)}}^{t=2500} S(t) \leq S(t+1) \,\&\&\, S(t) \leq S(t-1)$ (9.2) $D(t) = \left(\sum_{t=\text{length(s)}}^{t=2500} \frac{dy}{dx}(s(t)) \right)$ (9.3) $F(t)_n = \sum_{t=\text{length(s)}}^{t=2500} D(t) \leq D(t+1) \,\&\&\, D(t) \leq D(t-1)$ (9.4) $AI = \sum_{\text{length(F)}}^{t=1} \left(F(t)_v - F(t)_n \right) / F(t)_p$ (9.5)
4	The obtained AI is the rotational factor θ which is used to create a secured 3D key obtained by $\text{key} = \theta\left(\bar{X}\bar{Y}\bar{Z} \right)$ (9.6) θ_X = (AI/2) Round to ceil (9.7) θ_Y = (AI/3) Round to ceil (9.8) θ_Z = (AI/4) Round to ceil (9.9) The matrix XYZ is rotated with θ_X, θ_Y, and θ_Z in row vs column order so that the same order can be followed during extraction of information from key as shown in Fig. 9.4. Figure 9.4 shows transformation for one axis X with rotational factor θ_X as 4. Similarly, the transformation is performed on all axis
5	The obtained matrix key is transformed into its 3D matrix using Δ transformation as shown in Eq. (9.10) $\text{Key} \xrightarrow[\Delta]{} \text{3Dkey}$ (9.10) where Δ is the transformation that converts a 3D key into a QR code as shown in Fig. 9.3. This QR code is protected by a password as per the user, shown in Fig. 9.4

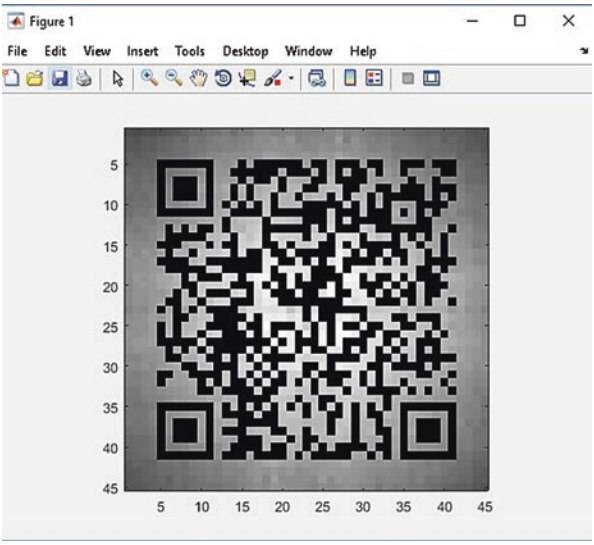

Fig. 9.3 QR protected code

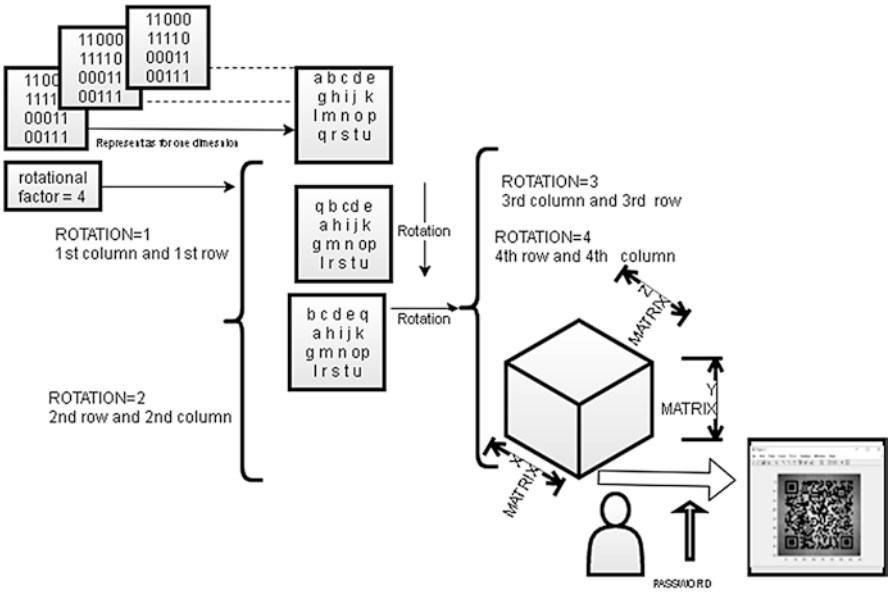

Fig. 9.4 Transformation of 3D key using rotational factor "θ"

Table 9.1 Statistics of subject demographic information of 102 males and 92 females

Characteristics	Count	Mean ± SD	Minimum	Maximum
Age (years)	200	26.80 ± 10.90	17	69
Height (cm)	200	165.28 ± 13.70	120	183
Weight (kg)	200	65.64 ± 7.01	56	89
Systolic BP (mmHg)	200	120.71 ± 10.15	105	145
Diastolic BP (mmHg)	200	76.81 ± 6.79	67	98
Body mass index (BMI)	200	25.10 ± 5.39	16.12	45.1

9.4.4 Module 4: Statistics of Subject Demographic Information

The biomedical signals PPG and ECG were acquired from 200 patients at the DAPM RV Dental College and Hospital, Bengaluru, Karnataka, India. The informed consent from the patient was taken prior to the acquisition of the data. The PPG signal was acquired using BIOPAC MP 36/45 Data Acquisition Unit. The patients for the acquisition involved 102 males and 92 females. The statistical information of patient-specific details is tabulated in Table 9.1.

From Table 9.1, it can be observed that the patients involved in the acquisition process were aged between 17 and 69 with blood pressure variation between 67/98 and 105/145 and BMI ranged from 16 to 45. Hence, from Table 9.1, it can be inferred that the signal acquisition and analysis involve patients of varied age group, with both hypertensive and hypotensive patients. Also, from the BMI obtained, it can be inferred that the sample size of 200 patients involves underweight to obese patients.

9.5 Results and Inferences

This section puts light on the results and the inference obtained during the acquisition of biomedical signals, its analysis, and watermarking and dewatermarking of images.

Figure 9.5 shows the PPG and ECG waveform obtained from Patient 1 using BIOPAC Data Acquisition. These signals were obtained for a duration of 3 min with the patient in supine position. The signals obtained were stored in .txt format and then the preprocessed in MATLAB to obtain the systolic peaks, diastolic peak, dicrotic notch, and augmentation index from PPG signal. Figure 9.6 shows the peaks of the PPG signal.

Figure 9.7 shows the sample EPRs (four in number: histopathology, dental cone-beam computed tomography (CBCT), intraoral periapical radiographs (IOPAR), orthopantomogram (OPG) images) to be watermarked inside the facial cover image. The facial image of the patient is not disclosed due to ethical issues. Figure 9.8 depicts the EPR stored in the OpenEMR database which is customized for Dental

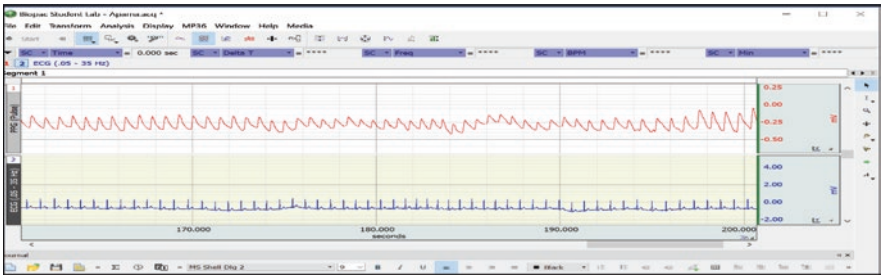

Fig. 9.5 PPG and ECG waveform obtained from BIOPAC MP45 DAQ

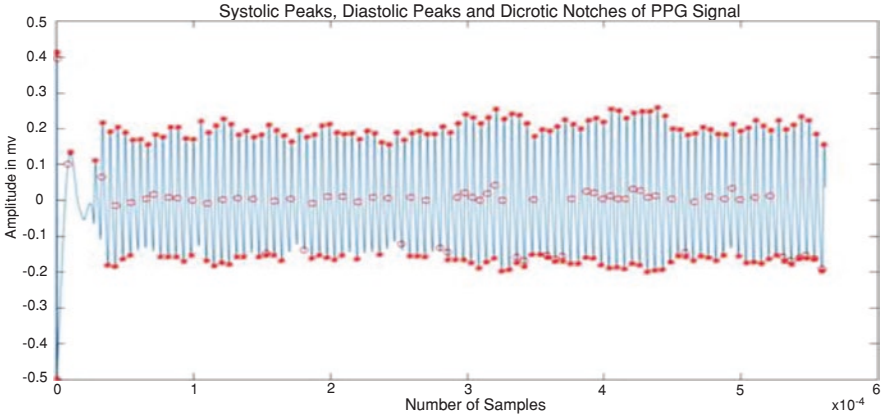

Fig. 9.6 Peaks of the PPG signal

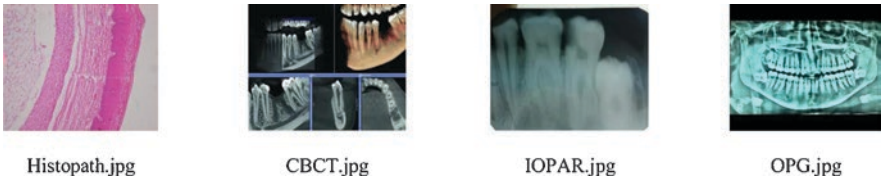

Fig. 9.7 Watermark images

College and Hospital. It can also be noticed that all the medical report can be categorized into different folders and stored easily. Figure 9.9 shows the PSNR and the time taken for the entire process for the watermarking and dewatermarking technique. The proposed novel algorithm can watermark multiple images inside a single cover image as shown in Fig. 9.10.

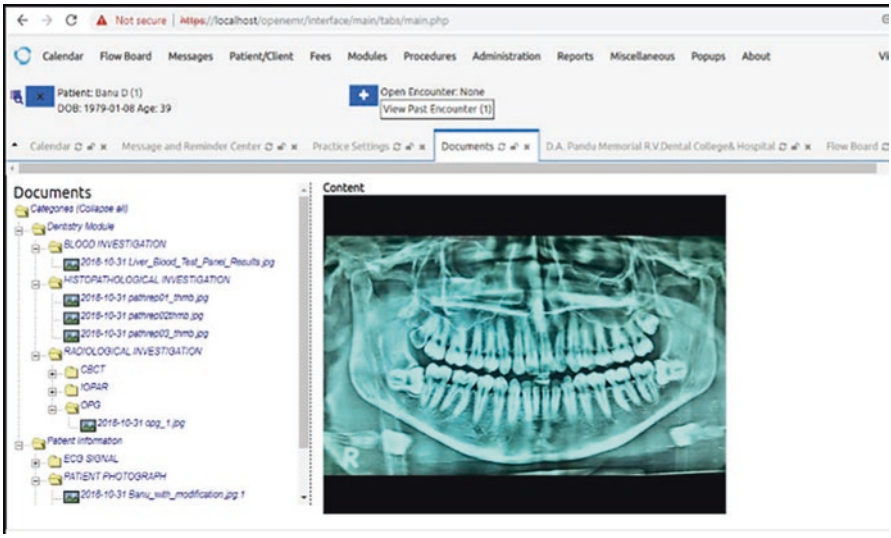

Fig. 9.8 EPR in openEMR

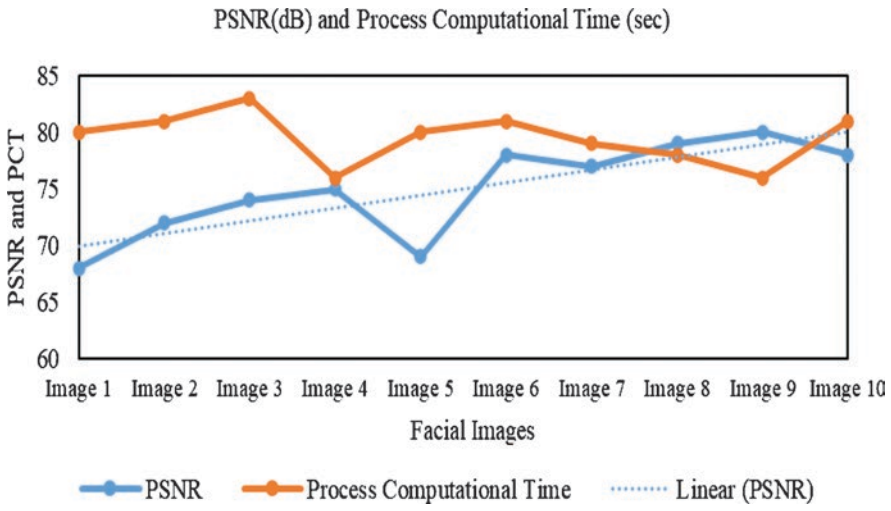

Fig. 9.9 PSNR and computational time

From Fig. 9.9, it can be inferred that maximum PSNR is 86 dB and the process computational time of 80 ± 4 agrees with acceptable limits for watermarking and dewatermarking. Figure 9.10 shows that AI is distinct for every patient and a maximum of five EPRs could be watermarked inside the facial image of the patient.

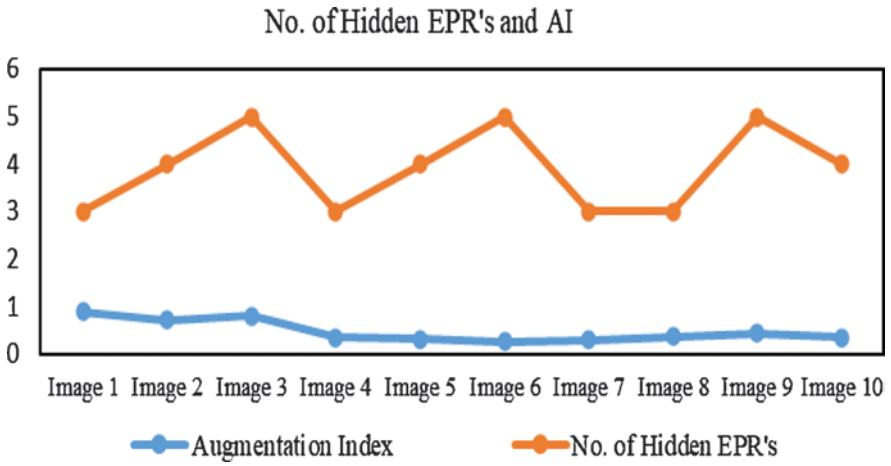

Fig. 9.10 No. of hidden EPRs and AI

9.6 Conclusion

In this chapter, the scheme makes use of watermarking with signal processing techniques to optimize the security of EPR stored inside the facial image of the patient. The 3D authentication key doubles the security since the rotation factor is dependent on the parameter derived from the biomedical signal. Also, watermarking of multiple EPRs in a single cover image proves that the proposed technique can be effectively used for healthcare applications using OpenEMR as an open-source solution.

9.7 Societal Benefits and Sustainability of the Proposed Concept

The proposed chapter ensures robust security and privacy protection of confidential information of both the patient and the hospital, thereby allowing this developed method to be applied in rural hospitals. The open-source OpenEMR customization for having a free licensed hospital management system in rural hospitals with low infrastructure is an added feature to cure and care facilities at all times with zero cost. Both these features suffice the sustainability as it has been tested for more than 200 patients in the dental hospital.

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Conflict of Interest The authors declare no conflict of interest.

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Index

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