Chapter-1

Drug Delivery and Administration

1.1 Introduction

The fields of electronics and computer science jointly coined a term known as the Internet of Things (IoT) (Kulkarni & Sathe, 2014). IoT enables all the objects that have been assigned an IP address to communicate over the network. The ultimate goal of any social development is to improve human health (PANG, 2013). The emerging technology of IoT tremendously improves the quality life of patients and also reduces the cost of care (Niewolny, 2013). IoT has a great impact in the field of healthcare for collecting and processing the patient-related data (Mora, Gil, Terol, Azorin, & Szymanski, 2017). Patient monitoring through IoT allows healthcare professionals to take diagnostic decisions. This study aims to design feedback controlled dynamic drug delivery interface using hybrid computing technique. Drug delivery is concerned with quantity and duration of the drug in the patient's body. Therefore, drugs have been used to improve health and extend the life of a critically ill patient. The role of computer-controlled drug delivery plays a vital role in the recovery of a patient because the desired amount of drug is delivered to the patient. Therefore, the drug effect should be measured effectively.

In this process, vital signs of the patient play a vital role to know the exact status of a patient. The bedside monitors help to view the physiological data of the patients locally. The technology like body sensor network helps the researchers to transmit the vital information of a patient to the doctor at a remote location. Concerning the remote monitoring of a patient from a remote location, many researchers have demonstrated the transmission of the
physiological data of the patient in real time. Thus, continuous monitoring in real view not only improves the life quality of a patient, but also helping the family member of a patient to monitor the physiological signals from the remote location (Inform, Aminian, & Naji, 2013). In the proposed model a hybrid model is proposed to access the vital parameters of the patient from local and remote locations. This chapter focuses on the basics of drug delivery and administration of drug delivery, which are described in section 1.2 and 1.3 respectively. Outlines of the thesis have been presented in section 1.4.

1.2 Drug Delivery System

Drugs have been used to improve the health of a patient; therefore, drug delivery is an essential factor for an admitted patient. Drug delivery is a route to control the therapeutic effects of human beings (Wen, Jung, & Li, 2015). The essential task of the drug delivery system is to calculate the exact amount of drug and deliver it to the target area in the body. Therefore, the precise amount of drug must efficiently reach to the target area. Drugs can be delivered to the body through multiple paths. These paths may be a mouth, intravenous, intramuscular, nebulization, eyes, ear, skin, etc. Each route has its advantages and disadvantages. Finding a suitable path through which a drug is to be delivered to a target area is known as drug administration. The drug can be administered through either enteral routes or parenteral routes. Drug administration through enteral route is a slow process as it takes time to reach to the destination, e.g. oral drug delivery. On the other side drug delivery through parenteral route is quick, e.g. drug delivery through intravenous, intramuscular, ointment, inhalation, etc.

Drug delivery systems ensures that drug must reach into the destined area; therefore, the rate and the amount of dose in the body must be carefully calculated. In the traditional drug delivery methods where the dose rate is
calculated and delivered manually any mishandling can lead to certain complications in a patient (Arney et al., 2010). As both overdosing and underdosing may be harmful to the patient. So, it is necessary to administer an accurate amount of the drug.

In traditional methods, the drug is delivered through oral route or intravenous routes in the form of injections, where the drug is distributed through the blood circulation system. However, only a small portion of the drug reaches the destined area in the body, which results in the slow recovery of the patient. Drug delivery system ensures that drugs reach to the area, where they are needed. The clinician must take care of the amount of the dose to be delivered so that the body can effectively use the drug, which thus requires a drug system that allows for accurate dosing. In this process, the computer-controlled drug delivery system is playing a vital role to deliver precise amounts of the drug.

1.3 Administration of Drug Delivery

Administration of drug delivery is extensively improved in the past decade due to progression in the IoT, primarily due to telemonitoring, embedded technology, wireless sensor, and an ad-hoc network. Therefore, technology is playing an effective, important and vital role in the field of the healthcare industry. Healthcare professionals can administer the drug in a better way due to advancement in technology, which leads to advanced medical devices that assists health care professionals.

Biomedical engineering plays a vital role here to deal with these advance medical devices, thus bridging the gap between research and execution. Progression in telecommunication allows healthcare professionals to monitor a patient from a remote location. Therefore, the physiological data of a patient can be monitored and recorded from a remote location to assist the patient.
Evolution of embedded system provides health care professionals to control the medical devices in an improved way.

Infusion pumps are helpful to overcome the effects of over-dosing and under-dosing. It is an electro-mechanical device which is used to deliver liquid drugs to a patient through intravenous route. These pumps are controlled through an advanced micro-controller. There are several types of infusion pumps such as manual, semi-automatic and fully automatic. In manual infusion pumps, the flow control is dependent on the gravitational force whereas phototransistors control the flow control in a semi-automatic pump. The fully automatic infusion pumps are different from the other two because its flow control is independent of gravity. These pumps are used when high precision is required. Therefore, the infusion pumps are required under those conditions where low flow and high accuracy is necessary. Drug delivery can be classified as:

1. Manual drug delivery
2. Semi-automatic drug delivery
3. Automatic drug delivery

1.3.1 Manual Drug Delivery:
This is a kind of traditional drug delivery, where the drug is calculated and delivered manually. The chances of miscalculations in such type of drug delivery are more. Any miscalculation either in the form of under-dosing or over-dosing may have adverse consequences for the patient. Medication error is a significant drawback of a manual drug delivery system. According to a study conducted by (Arney et al., 2010) 33 incidents involving medication errors were analyzed, where the most common error (36%) was due to incorrect dosage (over or underdose), and 30% cases of incorrect medication found. Although development in this era is going on due to enhanced demand for patient safety. So, this type of drug delivery is still used by the doctors. In
general, medicines, when the drug is to be delivered through any of the enteral routes (oral, nasal, gastric, rectal, injections, etc.) then this type of drug delivery is adopted by the doctors.

1.3.2 Semi-automatic drug delivery

This type of drug delivery is a step ahead to manual drug delivery system. As the name suggests, it is a semi-automatic system, where human intervention is required. Open loop drug delivery is a type of semi-automatic drug delivery system. An open loop system directly controls the output without getting any input from the output. Therefore, pre-programmed infusion pumps are used for this purpose which are predicted to have desired effects. This prediction depends on the prior information of pharmacokinetics of the drug (Biebuyck, O’hara, Bogen, & Noordergraaf, 1992).

A clinician has to make continuous adjustments, which put an extra workload on the clinician who has to perform multiple tasks in the operating room (Michel M.R.F. Struys, Mortier, & De Smet, 2006; Soltesz & Heusden, 2012). Based upon their experience the clinician sets the Target Concentration (TC) and let the system adjust the infusion rate automatically (Stephane Bibian, Dumont, & Black, 2015). The major drawback of open loop drug delivery systems is the lack of feedback mechanism.

In the case of physiological changes in the patient, the doctor has to make manual adjustments. However, where self-administration of a patient has required, the manual drug delivery system always delivered a fixed amount of drug. For example, many diabetic patients administer a bolus of insulin, where changes of bolus must be according to the insulin requirements of the body. Therefore, an open loop drug delivery system may release overdose or underdose (Shaw & Francisco, 2014). As clinician who has to perform multiple tasks in the operating room, therefore, the chances of drug dosing
errors are increased (Soltesz & Heusden, 2012) because more human intervention is required in case of an open loop drug delivery system.

![Figure 1.1 Open Loop Drug Delivery System](image)

**1.3.3 Automatic Drug Delivery**

Automatic drug delivery is an upshot of advanced technology. During the past decade due to innovation in the area of mobile telecommunication systems, high bandwidth, wireless sensor network, and microcontroller not only affect the daily life of a person but, also bring revolution in the healthcare industry. Now hospitals are equipped with advanced medical devices such as a bedside monitor to view, physiological data of the patients, an infusion pump to deliver a precise amount of drug to the patient, scanning devices, etc. Therefore, administration of drug delivery improved due to automation. The infusion pump is used to deliver a precise amount of drug(s). An infusion pump is an electro-mechanical device, used for delivering drugs to the patient with less human intervention. Closed loop drug delivery system is a type of automatic drug delivery system.
Closed loop drug delivery system is a form of automatic drug delivery system (Agarwal, Puri, & Mathew, 2009). Automation in the field of drug delivery help the clinician to limits the effects of individual patient variability related to the quality of the drug, utilize the time for the desired clinical state. Therefore, automation improves safety measurement to provide quality care (Stephane Bibian et al., 2015). The idea of feedback was severely formulated in 1934 by Harold Black with the invention of the feedback amplifier (Dumont & Ansermino, 2013). This invention leads to a revolution in the field of telecommunication industry. The concept of the closed loop is also used effectively for drug delivery. Closed loop drug delivery system senses the level of output, compares it and sends this information as feedback to a set point.

This feedback helps to calculate the new rate. Here feedback is known as a control variable. The status of the control variable is checked before calculating the new rate of infusion. Closed loop system can make the decisions at their own and try to achieve and sustain the defined target. The efficiency of the closed-loop system depends upon the reliability of the variable to be control as well as optimization of the control algorithm (M. M R F Struys, De Smet, & Mortier, 2002). The best part of a closed-loop system is that they can make decisions at their own to maintain a defined target because they are computer programme and are designed to maintain a target effect (Michel M.R.F. Struys et al., 2006). A closed-loop system senses the output, compares it with the set point and accordingly calculates the new rate of infusion. This kind of system is also known as a feedback control system. The difference between the feedback signal and the set point is known as an error, which may be positive or negative. The negative error shows the excessive amount of drug, whereas positive error shows insufficient medication (Biebuyck et al., 1992). Main components required for
administration using closed loop (Struys, Mortier, & De Smet, 2006) drug delivery system are:

- A control variable
- Setpoint (target value as per control variable)
- An actuator (Microcontroller)
- Actuator Controller (Infusion Pump)

- **Control Variable:** Control variable in closed loop drug delivery system must be measured sensibly. Therefore, an ideal sensor should be chosen for effective dose response (Dumont & Ansermino, 2013).

- **Set Point:** Setpoint is used as a target value by the controller. The clinician selects this value based on the population mean data and individual data.

- **Actuator:** Actuator is used to convert rotary motion into linear motion, which actually helps to deliver infusion.

- **Actuator Controller:** Infusion pump acts as an actuator controller, which delivers the infusion as per feedback mechanism.

![Figure 1.2 Closed Loop Drug Delivery System](image)

Figure 1.2 Closed Loop Drug Delivery System
1.4 Thesis Outline

The research work has been achieved to meet the four main objectives as depicted in section 2.9 of chapter 2. Where the findings and outcomes of each research objective have been framed and documented in the form of chapters (3-6). The outline of the thesis has been listed below.

In chapter 2, drug administration, traditional and modern drug delivery systems, challenges in the computer-controlled drug delivery systems; Internet of Things in healthcare; role of expert system in healthcare and telemonitoring have been detailed. The first research objective of the study "to explore various types of drug delivery systems available and to make the comparative analysis," is presented in chapter 3. This study was conducted through a survey.

Second research objective which is to design and develop the architecture of dynamic drug delivery interface system that will be able to deliver accurately calculated drug(s) as per the vital sign-based interface system with least human intervention by using hybrid technique has been proposed in chapter 4. For vital signs, dataset recorded from patients undergoing anesthesia at the Royal Adelaide Hospital is used (Liu, Görges, & Jenkins, 2012). Algorithm for data communication and flow charts has been proposed.

Chapter 5 consists of the third research objective which is to merge the expert system facility and analyzer database within the dynamic drug delivery interface. Algorithms and flow charts to store and retrieve patient information have been proposed. The fourth research objective has been contributed in chapter 6 of the thesis, which is an implementation of an IoT based hybrid drug delivery interface. Chapter 7 of the thesis is focused on the conclusion and future scope followed by references.