Fuzzy Logic in Clinical Decision Support Systems

The use of fuzzy reasoning in medical diagnostics

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Abstract

The diagnostic process is an important activity that is aimed at explaining and treating a patient's health problem. However, this process is subject to diagnostic errors that jeopardize patient safety and healthcare quality. In response to this, diagnostic clinical decision support systems (CDSS) have been developed to aid physicians in clinical reasoning and decision making. Diagnostic systems that have been successfully implemented employ fuzzy logic techniques.

The aim of this thesis is to examine how fuzzy reasoning can be used in these systems. This has led to the following research question: How can fuzzy logic be incorporated in diagnostic CDSS? In order to answer this question, literature on the operation of CDSS and the fundamentals of fuzzy logic has been reviewed. This literature has been used to create an example of a CDSS that uses fuzzy reasoning for the diagnosis of pneumonia (lung inflammation). Finally, the utility of using fuzzy logic in healthcare has been evaluated by discussing the difference between fuzzy and classical reasoning in CDSS.

The CDSS for pneumonia diagnosis has demonstrated that fuzzy logic can be incorporated in CDSS by employing a fuzzy expert system that executes the reasoning process. Furthermore, it has been found that fuzzy-based systems are characterised by robust outputs – which means that a change in input values will not cause a drastic change in the output. This feature is desirable in healthcare, as it should be prevented that minor alterations in symptoms, patient data or test results cause a major alteration in the diagnosis proposed by the CDSS. In addition, fuzzy CDSS are capable of handling contradictions. This property enables systems to alter their decisions as they obtain new information.

Further research could examine different techniques to implement a fuzzy CDSS. Additionally, the CDSS for pneumonia diagnosis could be expanded by entering more symptoms and patient data into the system and by extending the rules in the knowledge base. The accuracy of the CDSS could then be evaluated by comparing the results with existing medical data about pneumonia diagnosis in patients.

Keywords: medical diagnosis, clinical decision support system, healthcare, fuzzy logic, human reasoning, decision making, fuzzy expert system.

Contents

Chapter 1

Introduction

Making medical diagnoses is an important task performed by physicians in order to explain a patient's health problem and to provide the right treatment. The diagnostic process is a complex operation in which health professionals gather and interpret information from multiple sources, including a patient's clinical history, results of physical examinations and knowledge of medical specialists (Balogh, Miller, & Ball, 2015). This complexity makes the diagnostic process subject to diagnostic errors that occur when a diagnosis is missed, wrong or delayed (WHO, 2016). Healthcare research organization ECRI Institute has ranked diagnostic errors first place in their list of top ten patient safety concerns (2018; Papier, 2018). Furthermore, the U.S. National Academy of Medicine reported that almost every person will be faced with diagnostic errors at least once in their lifetime, sometimes causing severe harm to the patient (Balogh et al., 2015).

Research by Graber and Franklin (2005) shows that most diagnostic errors are caused by cognitive mistakes – faulty information synthesis, specifically. That is, physicians make mistakes in gathering medical data from multiple sources and analysing it as a whole. Among factors like faulty detection of symptoms and faulty estimation of the relevance of a finding, this mistake is particularly caused by failure in considering alternatives after an initial diagnosis was made (Graber & Franklin, 2005). Doctors have learned to recognize the most representative symptoms of a condition, leaving little room for exploring alternative diagnoses and rare manifestations of a disease (Papier, 2018). The physician uses this knowledge, along with practical experience, to make a diagnosis about a patient's health complaints. Unfortunately, this empiricism-based approach does not always yield the right diagnosis, leading to inappropriate treatments and poor healthcare quality (Papier, 2018).

The importance of reducing diagnostic errors combined with the computational power of modern computers has led to a growing interest in applying artificial intelligence (AI) techniques in healthcare. This has resulted in the development of clinical decision support systems (CDSS) that aid physicians in clinical reasoning and decision making processes. These systems use medical knowledge, a patient's medical record and results of physical examinations to generate an output – manifested as an alert, medication control, medical guideline or diagnosis (RIVM, 2018; Sutton et al., 2020). Various implementation techniques can be used in these systems, like artificial neural networks, decision trees and fuzzy logic (Hernández-Julio et al., 2019). A successful implementation of a CDSS that showed high accuracy in diagnosing nerve damage is created by Kunhimangalam et al. (2014) using fuzzy logic. Fuzzy logic is a many-valued logic that assigns degrees of truth to propositions – represented by any real number between 0 and 1. Fuzzy logic is able to handle approximate reasoning and is used to model the human ability to make effective decisions in an incomplete and vague environment (Dutta, 1988). Medical knowledge and clinical language tend to be vague and imprecise, as words such as "sudden, high, likely, fever and adult" often occur. Humans interpret the meaning of a phrase like "high fever" by considering the context in which it is used. However, computers have a hard time interpreting such vague linguistic phrases, as it is not clear what "high" denotes and what the concept of fever means. Research shows that fuzzy logic is able to deal with this vagueness and suggests that it is therefore an adequate technique for representing the language employed in medicine in a formal way (Tamir, Riche & Kandel, 2015).

This thesis focusses on the application of fuzzy logic in diagnostic CDSS. More specifically, it introduces rule-based CDSS along with fuzzy set theory and the operation of fuzzy expert systems. An example demonstrates how a fuzzy system can be incorporated into a diagnostic CDSS to determine the risk of pneumonia disease. Given the limited scope of this research, other CDSS functionalities and implementation techniques that have been shortly mentioned above are not discussed.

1.1 Research questions and methodology

As mentioned earlier, the fuzzy-based diagnostic CDSS designed by Kunhimangalam et al. (2014) has shown accurate results in diagnosing peripheral neuropathy – or damaged nerves. The results of the CDSS have been compared with the examination by a neurologist and showed about 93% accuracy. This raises the question how fuzzy logic and diagnostic CDSS can be merged together to successfully aid physicians in the diagnostic process. Therefore, this thesis answers the following research question:

> How can fuzzy logic be incorporated in diagnostic clinical decision support systems?

First, a theoretical framework is given that examines the two main components of the research question. This leads to the following two sub-questions:

1. What are rule-based diagnostic CDSS?
2. What are the fundamentals of fuzzy logic?

Literature on both topics is used for an example that demonstrates how fuzzy logic can be integrated into a diagnostic CDSS, thereby answering the research question. This example shows the design of a CDSS that determines the risk of having pneumonia by using a patient's symptoms, medical knowledge and a fuzzy inference mechanism.

Finally, the utility of fuzzy reasoning in CDSS has been compared to classical reasoning. The last sub-question is therefore:

3. How do fuzzy-based CDSS look different from classical CDSS?

This thesis is a literature review that demonstrates a way of implementing fuzzy logic in a diagnostic CDSS. For this purpose, extensive research on CDSS from the Dutch National Institute for Health and Environment (RIVM, 2018) and health professional Berner (2007) have been used, along with other research papers, to examine CDSS construction and operation. In addition, the pioneering paper on fuzzy logic by founder Lotfi A. Zadeh (1965) has been reviewed, among others, to introduce fuzzy set theory and fuzzy systems.

1.2 Relevance for the field of AI

Artificial intelligence (AI) is a branch in computer science that is concerned with creating technology that performs cognitive tasks associated with human intelligence. As AI techniques improve, their application in various fields is rapidly evolving. This has led to the development of information technology tools that support health professionals in diverse tasks.

This thesis focusses on fuzzy logic and its application in healthcare. Fuzzy logic is an AI technique that stems from the field of soft computing, which is dedicated to techniques that enable computers to work with uncertainty, vagueness and imprecision (Massad, Ortega, de Barros, & Struchiner, 2008). The application of fuzzy logic in CDSS might amplify the diagnostic reasoning process of medical specialists as it is able to handle vague linguistic terms that are often used in healthcare. It is therefore very promising to further investigate fuzzy-based CDSS as an attempt to improve healthcare quality. This thesis explains the fundamentals of CDSS and fuzzy logic and demonstrates how they can be merged into one system. This review contributes to a better understanding of the implementation and underlying reasoning process of fuzzy-based diagnostic CDSS.

1.3 Thesis structure

This thesis provides a theoretical framework on the two main topics, CDSS and fuzzy logic, before answering the research question. Chapter 2 is dedicated to the operation and components of CDSS. Chapter 3 discusses fuzzy logic by introducing fuzzy set theory and the operation of fuzzy expert systems. Chapter 4 answers the research question by demonstrating through an example how fuzzy logic can be incorporated in a CDSS. Chapter 5 evaluates the difference between fuzzy-based and classical CDSS. Chapters 6, 7 and 8 are dedicated to the results, conclusion and discussion, respectively.

Chapter 2

Diagnostic clinical decision support systems

Clinical decision support systems (CDSS) are health information technology tools designed to assist health professionals in making clinical decisions (Sutton et al., 2020). These systems are intended to improve healthcare quality by linking medical knowledge with a patient's health record and results of physical examinations (Pearlman, 2013). CDSS have been designed to fulfil various tasks in healthcare – including drug control, prescribing medicine, diagnosing diseases and sending out alerts – and have positively influenced healthcare (Sutton et al., 2020). This thesis mainly looks at diagnostic CDSS.

Diagnostic CDSS are not stand-alone systems that are expected to perform the diagnostic process autonomously or to come up with the right disease. Rather, these systems have been developed to work with health professionals side by side. The system provides suggestions and insights that guide the clinician in the complex diagnostic process (Berner & La Lande, 2007). Physicians make diagnoses by interacting with the CDSS, thereby combining their medical knowledge with information provided by the system (Sutton et al., 2020). The physician is expected to carefully analyse the results and to either select useful information or dismiss faulty suggestions. In this way, CDSS may provide a second opinion on medical decisions and may propose alternative diagnoses physicians would not have considered otherwise (Papier, 2018).

General CDSS are usually classified as knowledge-based and non-knowledge-based systems. The latter is involved in complex tasks based on machine learning, like recognizing patterns in clinical data and looking for abnormalities in scans (RIVM, 2018). Knowledge-based systems are frequently used for patient treatment and diagnostic purposes. As this thesis is focused on diagnostic CDSS, only knowledge-based systems are discussed in this chapter.

2.1 Knowledge-based CDSS

Many knowledge-based CDSS are derived from earlier expert systems (ES). ES help to solve problems that require expert knowledge (Kunhimangalam et al., 2014). These systems reason through bodies of knowledge, rather than using procedural code. Most knowledge-based CDSS consist of three main parts: a knowledge base (KB), inference engine and communication mechanism.

The KB operates as a source of medical knowledge. It may contain information about drug interactions, relationships between diseases and symptoms, and probabilities of disease occurrences (Berner & La Lande, 2007). This information is usually formatted in IF-THEN rules or expressed as facts. An example of a rule might be "IF the patient's blood pressure value is above 140 mmHg THEN the patient has high blood pressure". As new diseases and medicines are discovered, new medical knowledge is gained. It is therefore necessary to regularly update the KB with new information (Berner & La Lande, 2007).

The second part is the inference engine, which executes the reasoning process. It combines the medical knowledge in the KB with patient data to produce an output (Sutton et al., 2020). An alert, a treatment suggestion and a potential diagnosis are examples of outputs a CDSS might produce.

Lastly, the communication mechanism is necessary to insert patient data into the system and to extract information from the system (Berner & La Lande, 2007). The mechanism presents the final output to the physician.

Diagnostic CDSS have been designed to provide a set of potential diagnoses or to determine the risk of having a certain disease (Berner & La Lande, 2007). In chapter 4, an example is illustrated of a CDSS that uses fuzzy reasoning to determine the risk of having pneumonia.

Chapter 3

Fuzzy logic

Fuzzy logic is a many-valued logic that is used for reasoning about inherently vague concepts (Massad et al., 2008). As opposed to classical binary logics that use the absolute values of 0 (false) and 1 (true) to express the truth of a proposition, fuzzy logic uses degrees of truth represented by any real number between zero and one inclusive.

The notion of fuzzy logic was introduced by professor Lotfi A. Zadeh in 1965 when he was working on the theory of fuzzy sets. At the time, Zadeh was concerned with natural language comprehension of computers (Zohuri & Moghaddam, 2017). He noticed that human reasoning involves concepts that cannot be categorized in precisely defined classes (1965). Rather, human reasoning includes a range of possibilities between two ends of a spectrum. For instance, logical statements can be true or false, but also "almost certain, possibly, possibly not and very unlikely". Fuzzy logic considers possibilities between two extremes and therefore approaches human reasoning in a different way than classical binary logics.

3.1 Motivation for using fuzzy logic

The development of fuzzy logic was inspired by a human's remarkable ability to solve complex problems in an imprecise environment (Nikravesh, 2007). Humans use heuristics to quickly and efficiently make decisions in a world where information can be missing or hazy (Todd, 2001). Natural language enables humans to describe and reason about their surroundings. However, it contains many linguistic terms of which most people have a general idea of what they mean, but their exact meaning is open to one's own interpretation. To get a better understanding of the term, humans usually consider the context in which they are used, but computers have a hard time interpreting these concepts (Hoffman, 2019).

Fuzzy logic enables systems to handle imprecise reasoning that is important for making efficient decisions in an incomplete environment (Dutta, 1988). The following example illustrates the difference between fuzzy and classical logic in their approach to human reasoning:

What exactly do we mean when a patient's blood pressure is high? According to medical literature, high blood pressure is characterized by values from 140 mmHg and up (IQWiG, 2010). In classical logic, a blood pressure value of 139 mmHg is not high. However, fuzzy logic could consider it as a fairly high blood pressure, thus classifying it somewhere between "not high" and "high". Considering values between two ends resembles human reasoning more closely, as we reason in terms of falsity, partial truths and higher truths (Zohuri & Moghaddam, 2017).

The utility of this approach to reasoning quickly became apparent in medicine – a field where observations and knowledge are often described in vague linguistic terms (Godil et al., 2011). Medical terms have vague definitions that complicate the classification of medical data. Research by Kazem Sadegh-Zadeh (2012) suggests that fuzzy logic is capable of adequately representing the language employed in medicine, as fuzzy sets – that have imprecise boundaries – could offer a more suitable representation of vague linguistic terms.

3.2 Fuzzy set theory

Fuzzy logic is derived from the theory of fuzzy sets and is used to model human reasoning about inherently vague concepts. Fuzzy set theory can be seen as an extension of classical set theory as it deals with possible values between the conventional true and false (Godil et al., 2011). A classical set, or crisp set, contains a strict boundary that separates the objects that are in the set from the objects that do not belong to the set. Classifying objects takes place through a binary process that either accepts (1) or rejects (0) an object as belonging to the set (Massad et al., 2008). On the contrary, fuzzy sets have imprecise boundaries that relax the strict separation between membership and non-membership of an object in a set (Klir & Wierman, 2013). Fuzzy set theory allows for “degrees of membership”, meaning that an object can be partially in a set. To illustrate this, again consider the example of high blood pressure.

According to classical logic, a value of 139 mmHg is ”not high”, thus the membership degree of this value to the set ”high” is equal to 0. This is illustrated in Figure 3.1 on the left. Anything below 140 mmHg is definitely not in the set, anything above it is definitely in the set. In fuzzy logic, this strict boundary is relaxed by considering possibilities other than high (1) and not high (0). The value of 139 mmHg belongs to a certain degree to the set ”high”, i.e. a degree of 0.9. As can be seen in Figure 3.1 on the right, the higher the blood pressure value, the greater the extent to which it belongs to the fuzzy set ”high”. In what follows, fundamental concepts of fuzzy logic are explained.

3.2.1 Linguistic variables and linguistic terms

Linguistic variables represent natural language concepts. A linguistic variable can take on various values, called linguistic terms. Consider the linguistic variable body mass index (BMI), denoted u. Then its set of linguistic terms could be $T(u) =$ {underweight, normal, overweight, obese}.

Linguistic terms are used to express concepts in everyday communication, think of “cold weather” and “crowded boulevard”. The meanings of “cold and crowded” are usually dependent on the context in which they are used. In the medical field, linguistic terms as “moderate, decreased, low, sometimes and never” are frequently used to describe observations and results of laboratory tests (Massad et al., 2008).

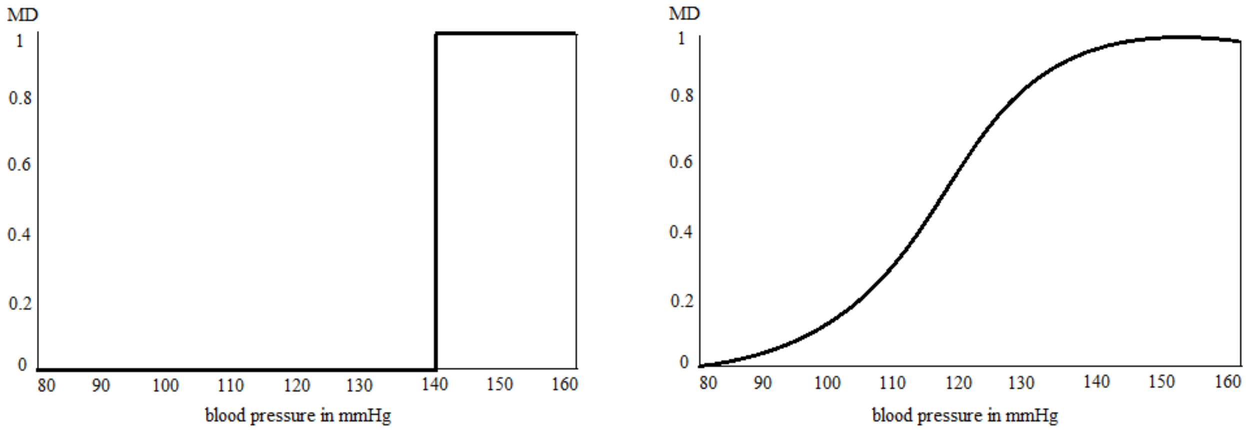


Figure 3.1: Membership degrees in a classical set (left) and fuzzy set (right)

3.2.2 Fuzzy sets and membership functions

Linguistic terms are represented by a fuzzy set. A fuzzy set is characterised by a membership function that determines the degree to which an object belongs to the fuzzy set. Consider the example mentioned above. Let fuzzy set O represent the linguistic term "obese". The membership function of O is denoted $\mu_O(x) : X \rightarrow [0, 1]$, which assigns to element x a real number between 0 and 1 inclusive. This number represents the degree of membership of element x in O. For example, a BMI value of 31 may belong to set O with a degree of 0.9. Formally, a membership function is defined as follows (Zadeh, 1965):

Let X be the universe of discourse and $x \in X$. Let A be a fuzzy set, where A is a subset of X, then

$$\mu_A(x) = \begin{cases} 1 & \textit{if } x \textit{ is totally in } A \\ 0 & \textit{if } x \textit{ is not in } A \\ 0 < \mu_A(x) < 1 & \textit{if } x \textit{ is partly in } A \end{cases}$$

3.2.3 Fuzzy rules

A fuzzy rule is a conditional statement of the form "if x is A, then y is B" where x is the input variable, y is the output variable and A and B are the linguistic terms (thus, fuzzy sets) defined on x and y, respectively.

An example of a fuzzy rule might be: "if respiratory rate is high, then breathing difficulty is severe". This rule is activated when the antecedent is satisfied with a degree that is higher than 0. This means that the membership degree of the respiratory rate value in the fuzzy set "high" is greater than 0. If the antecedent contains multiple conditions, then the AND/OR operators are applied to obtain a single value. The AND operator takes the minimum value of the operands, the OR operator takes the maximum value. The operators are further explained in section 3.3. The single value that is obtained in the antecedent determines the membership degree of the output variable in the consequent. The following example illustrates how a fuzzy rule works. The membership degrees are made up for this example, indicated between the parentheses:

IF respiratory rate is high (0.7) AND fever is moderate (0.6), THEN breathing difficulty is severe (0.6).

The antecedent is evaluated by using the AND operator that takes the minimum value of the operands, thus 0.6. This value determines the membership degree of the output, thus the breathing difficulty value belongs to the fuzzy set “severe” with a degree of 0.6.

3.2.4 Operators

Operations can be applied over fuzzy sets that are similar to the standard classical operations for classical sets. The elementary fuzzy operations for union, intersection and complement are defined in terms of their membership functions (Zadeh, 1965; Mendel, 1995). Let X be a non-empty set and $x \in X$.

Union

The union operator is applied when the OR operator is used in a fuzzy rule. It takes the maximum value of two operands. This is formally defined as follows:

Let A and B be two fuzzy subsets in universe X, and $\mu_A(x)$ and $\mu_B(x)$ their respective membership functions. The union of A and B is defined by $\mu_{A\cup B}(x) = Max[\mu_A(x), \mu_B(x)]$, for all $x \in X$.

Intersection

The intersection operator is applied when the AND operator is used in a fuzzy rule. It takes the minimum value of two operands. This is formally defined as follows:

Let A and B be two fuzzy subsets in universe X, and $\mu_A(x)$ and $\mu_B(x)$ their respective membership functions. The intersection of A and B is defined by $\mu_{A\cap B}(x) = Min[\mu_A(x), \mu_B(x)]$, for all $x \in X$.

Complement

The complement of a fuzzy set A, denoted $\neg A$, is defined by $\mu_{\neg A}(x) = 1 - \mu_A(x)$ and represents objects that belong to $\neg A$ to a certain degree.

3.2.5 Fuzzy expert systems

Fuzzy reasoning often takes place in fuzzy expert systems (FES) that are a form of knowledge-based systems (Hassanzad et al., 2017). These systems assist human decision making and problem solving by reasoning through entities of encoded knowledge in the form of IF-THEN rules, rather than procedural code (Senthil, 2014).

Fuzzy logic in FES can handle situations that involve uncertain and ambiguous data. FES are successfully applied in various tasks, including financial decision-making, medical diagnosis, planning, data classification and legal advising (Tavana & Hajipour, 2020). Most FES are generally comprised of four main components (Garibaldi, 2005; Massad et al., 2008):

1. Fuzzification module: transforms crisp input values into fuzzy sets by using the membership functions. Recall that membership functions map objects to a fuzzy set by determining their degree of membership to the set.

2. Knowledge base: can be split into two databases, namely a rule base that contains expert knowledge in the form of fuzzy IF-THEN rules, and another base that contains the membership functions for the input and output variables of the system. The rules in the rule base are written as fuzzy rules; thus, they are written in terms of fuzzy sets.

3. Inference engine: evaluates each rule in the rule base. The antecedent of the rules are compared to the set of input values. Rules are activated if the truth of the antecedent is greater than 0. The activated rules are aggregated to produce a single fuzzy output set.

4. Defuzzification module: transforms final fuzzy output set back into crisp value. This value is then communicated to the physician.

Now that the concept of fuzzy sets, membership functions, fuzzy operators and the architecture of FES are explained, the integration of FES in diagnostic CDSS is demonstrated in chapter 4.

Chapter 4

Incorporating fuzzy logic in CDSS

This chapter demonstrates how fuzzy logic can be incorporated in a CDSS by using a fuzzy expert system (FES) that executes the reasoning process. An example is given that shows the design of a fuzzy-based CDSS for the diagnosis of pneumonia (lung inflammation). Symptoms of other respiratory conditions – like bronchitis, asthma and common cold – are similar to those of pneumonia but might manifest less severe. The overlap between symptoms complicates the process of getting the right diagnosis. A CDSS that is aimed at determining the risk of having pneumonia might provide guidance for the physician in the search for the correct respiratory disease. Its result might give more reason to adopt further tests and treatments that target pneumonia or might indicate that the presence of pneumonia is not likely, whereby the physician may test for other respiratory conditions instead. The following description on pneumonia symptoms is found on the website from an American academic medical center that provides information about various diseases:

> The signs and symptoms of pneumonia vary from mild to severe, depending on factors such as the type of germ causing the infection, and your age and overall health. Mild signs and symptoms often are similar to those of a cold or flu, but they last longer. . . . See your doctor if you have difficulty breathing, chest pain, persistent fever of 102 F (39 °C) or higher, or persistent cough, especially if you're coughing up pus. (Mayo Clinic, 2020)

This passage exemplifies how disease symptoms are usually described. Humans have a general idea of what terms such as "mild, severe, overall, cold, longer, persistent and higher" mean. However, their meanings only become clear when one considers the context in which they are used. These terms show the inherent vagueness in natural language that humans employ to describe complex situations and observations.

The CDSS for pneumonia diagnosis shows how fuzzy logic deals with these kinds of vague linguistic terms that often occur in medicine. Recall that a general CDSS consists of three main parts: a knowledge base (KB), inference engine and communication tool. The fuzzy-based CDSS is built of the same parts but also includes the components of a fuzzy expert system, as can be seen in Figure 1. Its KB comprises a rule base that contains medical knowledge written in IF-THEN rules, along with the membership functions for the input and output values of the system. The fuzzifier converts crisp input values to fuzzy sets using the input membership functions.

The fuzzy inference engine evaluates each rule in the rule-base for a given input and produces a single fuzzy set. This set is then converted back to a crisp value in the defuzzifier using the output membership function. The resulting output value is then transmitted through the communication tool to the physician. The operation and details of these components are further explained in the rest of the chapter.

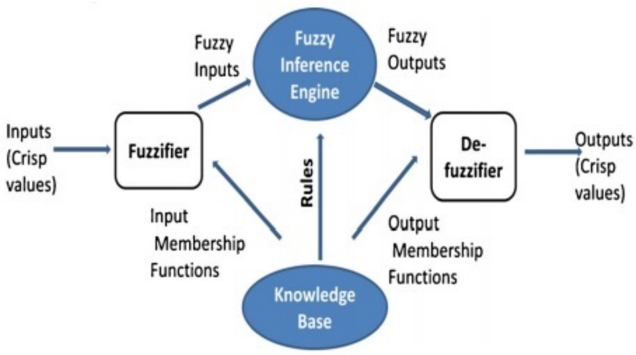


Figure 4.1: Architecture of a fuzzy-based CDSS

Note. Reprinted from "A Clinical Decision Support System with an Integrated EMR for Diagnosis of Peripheral Neuropathy", by Kunhimangalam, R., Ovallath, S., & Joseph, P. K., 2014, *Journal of Medical Systems, 38*, p. 4.

The input values of this CDSS comprise of three symptoms that might indicate the presence of pneumonia, these include fever, breathing difficulty and cough. These symptoms are fed into the system to determine the output value – the risk of having pneumonia. The system uses the Mamdani inference method to produce the output, as this technique is most often used in decision support applications and works well with rules that are based on human expert knowledge (Sari et al., 2016). This method uses the Min-Max operators for the evaluation of the rule base. The operation of the Mamdani inference technique is explained in section 4.3

The design of the fuzzy-based CDSS follows four phases that have been shortly introduced in section 3.3. In what follows, the implementation of the CDSS for pneumonia diagnosis is discussed in more detail by means of the following steps:

1. **Initialization**
   a. Define linguistic variables and terms
   b. Construct their corresponding membership functions
   c. Construct rule base
2. **Fuzzification** Convert crisp input values into fuzzy sets
3. **Inference**
   a. Evaluating each rule in the rule base
   b. Aggregate the rule outputs
4. **Defuzzification** Convert fuzzy output set into single crisp value

4.1 Initialization

(a) *Define linguistic variables and terms.* Recall that linguistic variables are meaningful concepts that can be qualitatively expressed by linguistic terms, and quantitatively expressed by membership functions (Massad et al., 2008). Each input and output value of the system is represented by a linguistic variable u, and their corresponding linguistic terms are denoted by *T(u)*. The input values are three symptoms, and the output value represents the risk of having pneumonia.

Input or output value	Linguistic variable u	Linguistic terms *T(u)*
Input	Fever	{absent, low, medium, high}
Input	Breathing difficulty	{absent, moderate, severe}
Input	Cough	{absent, intermittent, persistent}
Output	Pneumonia risk	{low, normal, high}

Table 4.1: Linguistic variables and their corresponding terms

(b) *Construct corresponding membership functions.* Membership functions (MFs) assign to each crisp value a degree to which it belongs to a fuzzy set. There are many functions that can be used as a MF, like triangular, trapezoidal, Gaussian and sigmoidal functions. There does not seem to be an objective way of choosing the right MF for a given situation. The choice depends on the problem that needs to be solved and is usually made by experts on the subject (Drossos, 2013). This CDSS uses triangular and trapezoidal functions because of their simplicity and wide use in fuzzy expert systems (Massad et al, 2008). The MF for each linguistic variable is defined and visualized in Figure 2. The membership degrees (MD) of each crisp value can be read from the graph or calculated through the definitions on the right. As also can be seen in Figure 2, fever, breathing difficulty and cough are measured by body temperature (°C), respiratory rate (breaths/minute) and cough frequency (coughs/hour), respectively. Pneumonia diagnosis is manifests as the risk of having pneumonia (%). The design of the MFs is based on the following medical knowledge:

– Fever is characterized by body temperatures above 37 °C. Depending on the rise in temperature, a patient can have a low, medium or high fever. Body temperatures between 37-38 °C indicate low fever, temperatures from 39 °C and up indicate high fever (Davis, 2020). Fever is absent if the normal body temperature of 37 °C is not exceeded.

– Breathing difficulty manifests as a high respiratory rate. Patients will breathe faster in order to get more oxygen into their blood. For adults, a respiratory rate of 12-20 breaths per minute is normal. High respiratory rates start from 25 breaths per minute (Whitworth, 2019).

– Cough may indicate that something is wrong with a patient's respiratory system or may give an indication of the severity of the complaints (Osborn, 2020). Cough could be absent, intermittent or persistent, depending on its frequency throughout the day.

(c) *Construct rule base.* The KB of the CDSS contains, among the membership functions, the rule base in which medical literature and expert knowledge is formulated in IF-THEN rules. In Mamdani inference, a rule (R) is of the following form (Garibaldi, 2006):

$$R_i \qquad \text{if } x_1 \text{ is } A_1 \text{ and ... and } x_r \text{ is } A_r \text{ then } y \text{ is } B.$$

where x_j (j = 1, 2,..., r) are the input variables, y is the output variable, and A_j and B are fuzzy sets. A sample of the rule base might be:

1. IF (fever is absent) AND (breathing difficulty is absent) AND (cough is absent) THEN (pneumonia risk is low).
2. IF (fever is medium OR high) AND (breathing difficulty is absent) AND (cough is absent) THEN (pneumonia risk is low).
3. IF (fever is low OR medium) AND (breathing difficulty is moderate) AND (cough is intermediate OR persistent) THEN (pneumonia risk is normal).
4. IF (fever is medium OR high) AND (breathing difficulty is severe) AND (cough is intermediate OR persistent) THEN (pneumonia risk is high).

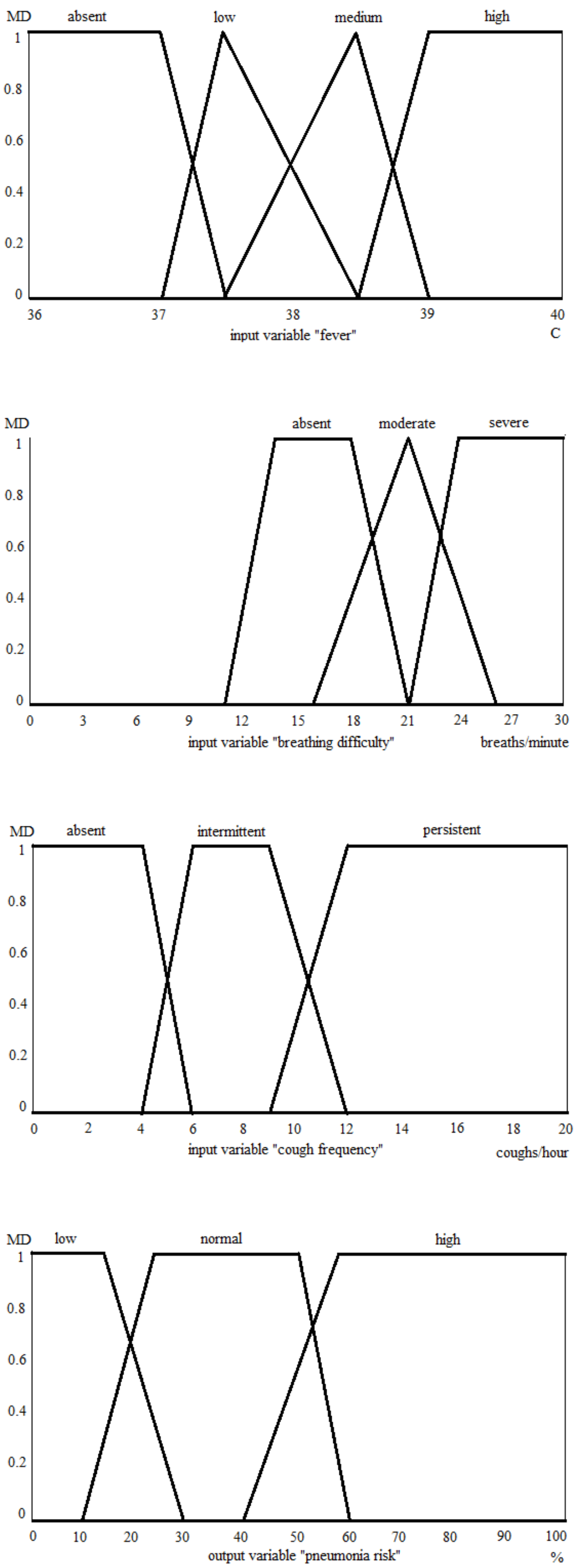
4.2 Fuzzification

Consider the following complaints from a patient P: "Patient P is a 34 years old female who has had high fever for the past three days. She has vomited once and is feeling tired. She regularly coughs throughout the day and experiences a burning sensation in her chest. The pressure and discomfort on her chest make it seem as if breathing takes more effort than usual."

Upon hearing this information, a physician might perform a few additional tests to retrieve more accurate data. The physician measures patient P's body temperature, respiratory rate and asks for her cough. The results can be found in Table 2 under "input value x". These crisp values need to be converted into fuzzy sets in order to be used in the fuzzy-based CDSS. For each crisp value, its MFs are used to calculate its membership degree (MD) for each fuzzy set, according to Figure 2. The MDs are given in Table 2.

Input value x	Fuzzy set	Membership degree
Body temperature: 38.8 °C	Absent	0.0
	Low	0.0
	Medium	0.4
	High	0.6
Breathing difficulty: 25 breaths per minute	Absent	0.0
	Moderate	0.2
	Severe	1.0
Cough: approx. 10 coughs per hour	Absent	0.0
	Intermittent	1.0
	Persistent	0.33

Table 4.2: Membership degrees for each input value



$$\mu_{abs}(x)=\begin{cases}1 & \textit{if } x<37\\ \frac{37.5-x}{0.5} & \textit{if } 37\leq x<37.5\\ 0 & \textit{if } x\geq 37.5\end{cases}$$

$$\mu_{low}(x)=\begin{cases}0 & \textit{if } x<37\\ \frac{x-37}{0.5} & \textit{if } 37\leq x<37.5\\ \frac{38.5-x}{1} & \textit{if } 37.5\leq x<38.5\\ 0 & \textit{if } x\geq 38.5\end{cases}$$

$$\mu_{med}(x)=\begin{cases}0 & \textit{if } x<37.5\\ \frac{x-37.5}{1} & \textit{if } 37.5\leq x<38.5\\ \frac{39-x}{0.5} & \textit{if } 38.5\leq x<39\\ 0 & \textit{if } x\geq 39\end{cases}$$

$$\mu_{high}(x)=\begin{cases}0 & \textit{if } x<38.5\\ \frac{x-38.5}{0.5} & \textit{if } 38.5\leq x<39\\ 1 & \textit{if } x\geq 39\end{cases}$$

$$\mu_{abs}(x)=\begin{cases}0 & \textit{if } x<11\\ \frac{x-11}{3} & \textit{if } 11\leq x<14\\ 1 & \textit{if } 14\leq x<18\\ \frac{21-x}{3} & \textit{if } 18\leq x<21\\ 0 & \textit{if } x\geq 21\end{cases}$$

$$\mu_{mod}(x)=\begin{cases}0 & \textit{if } x<16\\ \frac{x-16}{5} & \textit{if } 16\leq x<21\\ \frac{26-x}{5}0 & \textit{if } 21\leq x<26\\ 0 & \textit{if } x\geq 26\end{cases}$$

$$\mu_{sev}(x)=\begin{cases}0 & \textit{if } x<21\\ \frac{x-21}{3} & \textit{if } 21\leq x<24\\ 1 & \textit{if } x\geq 24\end{cases}$$

$$\mu_{abs}(x)=\begin{cases}1 & \textit{if } x<4\\ \frac{x-4}{2} & \textit{if } 4\leq x<6\\ 0 & \textit{if } x\geq 6\end{cases}$$

$$\mu_{int}(x)=\begin{cases}0 & \textit{if } x<4\\ \frac{x-4}{2} & \textit{if } 4\leq x<6\\ 1 & \textit{if } 6\leq x<9\\ \frac{12-x}{2} & \textit{if } 10\leq x<12\\ 0 & \textit{if } x\geq 12\end{cases}$$

$$\mu_{per}(x)=\begin{cases}0 & \textit{if } x<9\\ \frac{x-9}{3} & \textit{if } 9\leq x<12\\ 1 & \textit{if } x\geq 12\end{cases}$$

$$\mu_{low}(x)=\begin{cases}1 & \textit{if } x<15\\ \frac{x-15}{15} & \textit{if } 15\leq x<30\\ 0 & \textit{if } x\geq 30\end{cases}$$

$$\mu_{norm}(x)=\begin{cases}0 & \textit{if } x<10\\ \frac{x-10}{15} & \textit{if } 10\leq x<25\\ \frac{60-x}{10} & \textit{if } 50\leq x<60\\ 0 & \textit{if } x\geq 60\end{cases}$$

$$\mu_{high}(x)=\begin{cases}0 & \textit{if } x<40\\ \frac{x-40}{20} & \textit{if } 40\leq x<60\\ 1 & \textit{if } x\geq 60\end{cases}$$

Figure 4.2: Membership functions for the input and output variables

4.3 Inference

(a) *Evaluate each rule in the rule base.* Next, each rule in the rule base is evaluated by comparing the conditions in the antecedent with the input values. When the antecedent contains AND/OR operators, the Mamdani inference technique applies the Min/Max operators, respectively, as defined in section 3.2.2. A rule is activated if the antecedent can be partially fulfilled. This means that the value of the antecedent, after applying the necessary operations, is greater than 0. Consider the sample of four rules described above and the MDs in Table 2. Rules 2, 3 and 4 are activated, as at least one condition in the antecedent of each rule meets the input values. Rule 1 is not activated, as none of the conditions in its antecedent are met by the input values.

Consider the three rules of the rule base that have been activated. For convenience, the rules are stated below. Each input value (symptom) is described by a fuzzy set. The number between the parentheses indicates the degree to which the input value belongs to that fuzzy set. The OR operator takes the maximum value of two operands. This value has been underlined for each case. The AND operator takes the minimum value of two operands, indicated in bold font. The value of the antecedent is determined by applying the AND operator over all its conditions. The value of the consequent is equal to the value of the antecedent.

2. IF (fever is medium (0.4) OR high (<u>0.6</u>)) AND (breathing difficulty is absent (**0.0**)) AND (cough is absent (**0.0**)) THEN (pneumonia risk is low (0.0)).

3. IF (fever is low (0.0) OR medium (<u>0.4</u>)) AND (breathing difficulty is moderate (**0.2**)) AND (cough is intermediate (<u>1.0</u>) OR ongoing (0.33)) THEN (pneumonia risk is normal (0.2)).

4. IF (fever is medium (0.4) OR high (<u>**0.6**</u>)) AND (breathing difficulty is severe (1.0)) AND (cough is intermediate (<u>1.0</u>) OR persistent (0.33)) THEN (pneumonia risk is high (0.6)).

(b) *Aggregate the rule outputs.* Now that each rule has been individually evaluated, the results of the activated rules should be aggregated. This is done by clipping: for each activated rule, the membership function of the consequent is equal to the level of the antecedent truth. The clipped fuzzy sets of each activated rule are combined into one fuzzy set (see Figure 3).

4.4 Defuzzification

Finally, this single fuzzy set is converted into a crisp value. This is done by using the center of gravity (COG) method - a technique most often used in Mamdani inference. COG is the point where the final fuzzy set would be divided into two equal parts. COG is calculated as follows:

$$\text{COG} = \frac{\sum_{i=1}^{N}(\mu_i \cdot x_i)}{\sum_{i=1}^{N} *\mu_i} = \frac{(0+10)\cdot 0.0+(20+30+40)\cdot 0.2+(50+60+70+80+90+100)\cdot 0.6}{(0.0\cdot 2)+(0.2\cdot 3)+(0.6\cdot 6)} = \frac{288}{4.2} = 68.6\% \text{ risk.}$$

This fuzzy-based CDSS has reasoned about the symptoms of patient P and has concluded that there is a 68.8% risk that the patient has pneumonia. This result can encourage the physician to adopt tests and treatments that target pneumonia, since the presence of the disease for this patient is very likely.

This example has demonstrated how fuzzy logic can be incorporated in a diagnostic CDSS. The system relies on the membership functions and medical knowledge defined in the KB, and the inference mechanism that is used. It is important to note that this example is only one way of implementing a fuzzy-based CDSS. Creators of fuzzy-based systems might use different membership functions, inference mechanisms or definitions of the AND/OR operators. The choice depends on the problem that needs to be solved and the experience of the expert that creates the system and knowledge base.

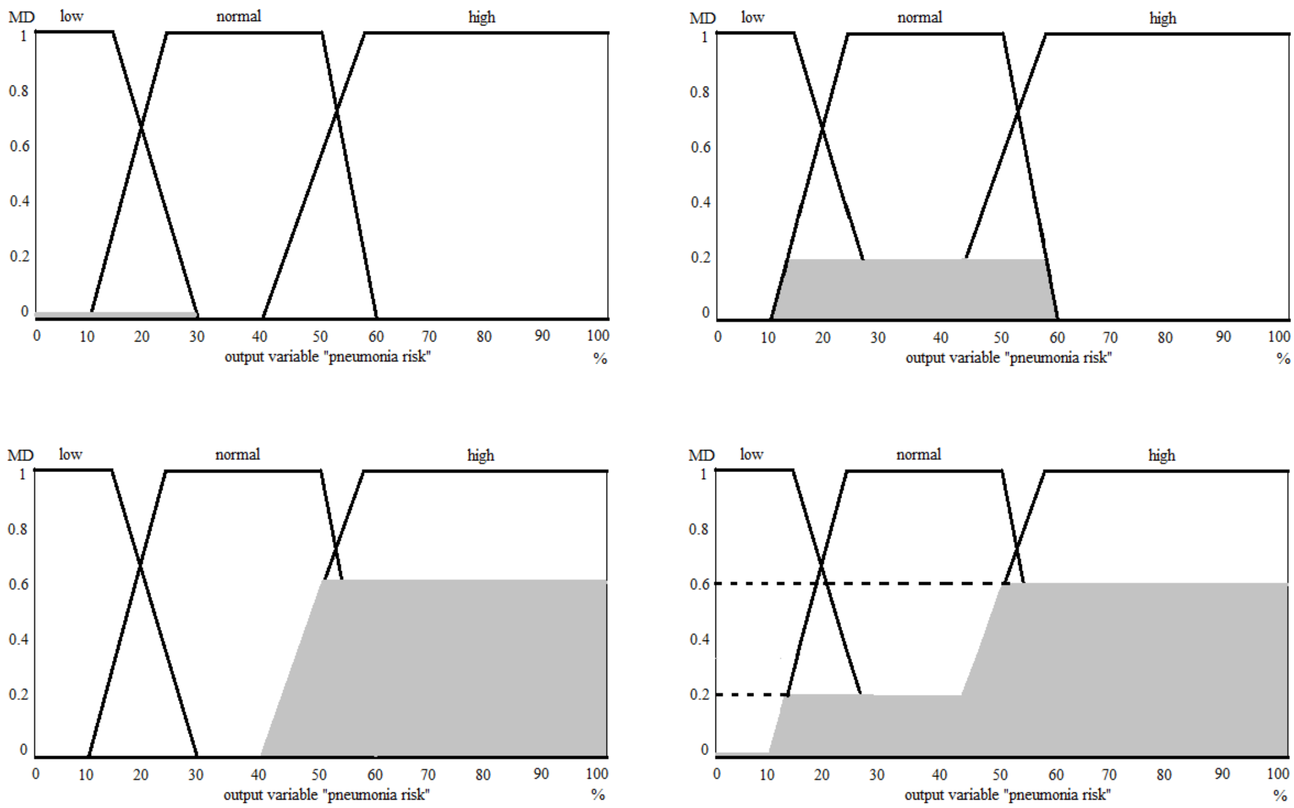


Figure 4.3: Clipped fuzzy sets are combined into one fuzzy set

Chapter 5

Evaluating fuzzy and classical CDSS

Now that a fuzzy-based CDSS has been created, this section evaluates how it differs from classical decision support systems. Reasoning processes of both systems are examined along the lines of output robustness and their way of handling contradictions.

5.1 Input sensitivity and output robustness

An important difference between a fuzzy and classical set is that the latter has strict boundaries that determine the (non)membership of an object. As can be seen in Figure 3.1, the membership function of a classical set is sharp-edged. This means that a classical set is sensitive to slight value changes, as this might cause a completely different classification of that value (Kayacan & Khanesar, 2016). To illustrate this, the following example shows how a fuzzy and classical CDSS handle small changes in input values. First, consider the fuzzy CDSS for pneumonia diagnosis described in chapter 4. Assume that the KB contains the following fuzzy rule:

IF (fever is medium) AND (breathing difficulty is severe) THEN (risk is high)

Consider the data from patient P described earlier; she has a body temperature of 38.8 °C and a respiratory rate of 25 breaths per minute. The membership degrees of these input values within their corresponding fuzzy sets – "medium" and "severe", respectively -– can be calculated with the mathematical definitions of the membership functions given in Figure 4.2. For readability, these calculations are not shown in this section. It follows that $\mu_{medium}(38.8) = 0.6$ and $\mu_{severe}(25) = 1$. Thus, value 38.8 belongs to "medium" with a degree of 0.6, and value 25 belongs to "severe" with a degree of 1. As we have seen in chapter 4, the membership degree of the output value in the consequent is then determined by applying the AND operator, thus $Min[0.6, 1] = 0.6$. This means that pneumonia risk belongs to fuzzy set "high" with a degree of 0.6.

What happens if the input values slightly change? Let's say that another patient P_2 has a body temperature of 37.8 °C and the same respiratory rate of 25 breaths per minute. By using the mathematical definitions in Figure 4.2, it can be calculated that $\mu_{medium}(37.8) = 0.3$ and $\mu_{severe}(25) = 1$. The membership degree of the output value in the consequent is then determined by $Min[0.3, 1] = 0.3$. Thus, pneumonia risk belongs to "high" with a degree of 0.3. When the truth of the antecedent decreases, so does the truth of the consequent. This shows that a change in input values leads to a corresponding change in membership degree of the output value.

Now consider a classical CDSS that is also designed for pneumonia diagnosis. The classical rules in the KB are also written in IF-THEN format, but do not contain fuzzy sets (thus, linguistic terms). Assume that the KB contains the following rule:

> IF (body temperature $\geq$ 38) AND (respiratory rate $\geq$ 25) THEN (diagnosis is pneumonia)

For patient P it follows that both conditions in the antecedent are met, thus patient P is diagnosed with pneumonia. For patient P_2 it follows that only the second condition in the antecedent is met, thus patient P_2 is not diagnosed with pneumonia.

This comparison shows that contrary to classical CDSS, slight changes in the input values of fuzzy CDSS will not abruptly cause a different output. Rather, input changes are accounted for by adjusting the membership degree of the output accordingly. This is desirable in healthcare, because generated outputs that are based on degrees might propose rare diagnoses or might enable the physician to better consider the importance of certain findings. It should be prevented that minor changes in symptoms, patient data or test results generate a potential disease that heavily deviates from the initial diagnosis.

5.2 Handling contradiction in human reasoning

One important law in classical logic is the Law of Contradiction, which states that an element can either be in one set or its complement, but not in both simultaneously (Mendel, 1995). This law is broken by fuzzy logic, which allows elements to (partially) belong to multiple sets. This implies that an element can be in a set and the complement of the set simultaneously. The following example illustrates what could happen when a fuzzy and classical CDSS encounter a contradiction in the KB. Consider the following rules for determining whether the risk of pneumonia diagnosis is high:

1. IF (respiratory rate is over 22 breaths per minute) THEN (pneumonia risk is high)
2. IF (respiratory rate is over 22 but below 25 breaths per minute) AND (fever is low) THEN $\neg$(pneumonia risk is high)

These rules seem to be reasonable to a physician who is determining whether pneumonia is present in patient P_3. Patient P_3 has a respiratory rate of 24 breaths per minute. This is a fairly high respiratory rate and might indicate the presence of pneumonia (rule 1). The physician then measures the body temperature of the patient and finds a value of 37.8 °C. This is only a slight increase in temperature, which indicates low fever. This new piece of information might change the physician's estimation of the risk, as pneumonia should manifests itself with high fever (rule 2). Something else could be causing the high respiratory rate. This short anecdote shows that physicians alter their decisions and treatment plans as they gather new information from sources like patient data, physical tests and knowledge from specialists. For humans it is reasonable to override a general statement with another statement that adds more detail (Covington, 2020).

Although these two reasoning steps seem very natural in human reasoning, they are contradictory in classical logic. For P_3 with a respiratory rate of 24 breaths per minute, both rules apply. Rule 1 says pneumonia risk is high, rule 2 says it is not. In classical expert systems, the creators of the KB try to keep the rules free from contradiction as it may cause a collapse of the system (Poulin, St-Vincent, & Bratley, 2005). However, such contradictory rules could be used in the KB of a fuzzy CDSS as the Law of Contradiction does not hold in fuzzy logic. Instead of collapsing, a contradiction might cause an alteration of the membership degree of the output variable. The same happens when new information is obtained, as explained in the previous section. For example, after evaluating the first rule, the pneumonia risk may belong to "high" with a degree of 0.70. But after measuring the patient's body temperature, this degree may decrease to 0.50.

This example has shown the ability of human reasoning to change our minds after we have obtained new information. As fuzzy logic allows for contradictions, it enables CDSS to alter an initial diagnosis as new information is obtained, even if the new diagnosis contradicts the intial diagnosis.

Chapter 6

Results

Within this section, the results of the three sub-questions that have been presented in the introduction are answered.

Diagnostic clinical decision support systems (CDSS) are health information technology tools that aid health professionals in the process of medical diagnosis. Most diagnostic CDSS are derived from rule-based systems that comprise a knowledge base (KB) and inference engine. The KB contains medical knowledge that is used by the inference engine to reason about patient data. Patient symptoms and results of physical examinations are fed into the system to generate an output in the form of a potential diagnosis.

Successfully implemented diagnostic CDSS are based on fuzzy logic techniques. Fuzzy logic is a many-valued logic that is capable of reasoning with inherently vague linguistic concepts. It offers a different approach to human reasoning than classical logic, as it allows for degrees of truth rather than the conventional values of 0 and 1. In fuzzy set theory, linguistic variables are used to capture a linguistic concept. The set of corresponding linguistic terms represents possible values of the linguistic variable. A fuzzy set is characterised by a membership function that determines the degree to which an object belongs to the set, denoted $\mu_A(x) = [0, 1]$, where A is a fuzzy set and x the object. Objects can (partially) belong to multiple sets simultaneously. Fuzzy reasoning takes place in fuzzy expert systems that generate decisions based on vague and imprecise data.

For evaluation, the difference between fuzzy and classical CDSS has been discussed. One important difference is the robustness of outputs from fuzzy systems. The gradual change in membership of fuzzy sets prevents abrupt changes in classification of objects. This is desirable in healthcare, as diagnostic errors might occur when a minor change abruptly modifies a decision. Another distinction is the ability of fuzzy logic to handle contradiction in human reasoning. Whereas a classical system would collapse when a contradiction in the KB is encountered, a fuzzy system would adapt the membership degrees of the output value accordingly. This characteristic can be helpful in healthcare, because physicians alter their expectations and treatment plans as they obtain new information.

Chapter 7

Conclusion

The aim of this thesis has been to examine how fuzzy logic can be incorporated in diagnostic clinical decision support systems (CDSS). A literature review has been carried out that discusses the architecture of knowledge-based CDSS, the fundamentals of fuzzy logic and the difference between fuzzy and classical reasoning in diagnostic CDSS.

The literature on diagnostic CDSS and fuzzy logic has been used to create a CDSS for the diagnosis of pneumonia. This system demonstrates how fuzzy logic can be incorporated in a diagnostic CDSS by employing a fuzzy expert system that executes the reasoning process. As medical language often uses inherently vague concepts, we need a way of connecting concrete (numerical) values to this imprecisely described knowledge. It has been shown that these concrete values – that describe patient symptoms and test results – can be interpreted by converting them to fuzzy sets. The reasoning process uses the fuzzy sets and expert knowledge to reason about the patient data that has been fed into the system. During this process, rules in the rule base are activated when the conditions in the antecedent are (partially) met. The truth values of the outputs are then aggregated into one fuzzy set. This set is converted back into a concrete value by using the center-of-gravity method. The final output value indicates the risk of a patient having pneumonia. The height of the risk may indicate that the physician is searching in the right direction (if pneumonia risk is high) or may encourage the physician to look into other respiratory conditions (if pneumonia risk is not high), thereby redirecting the physician in the diagnostic process. Similar diagnostic CDSS might positively influence medical diagnostics by assisting health professionals in the search for the right diagnosis.

Chapter 8

Discussion

This section further discusses the utility of fuzzy reasoning in CDSS in comparison with classical CDSS, along with the implications of this review and suggestions for further research.

It has been demonstrated that fuzzy systems are less sensitive to small input changes compared to classical systems. This is because fuzzy sets relax the strict boundary between membership and non-membership of an object. The degree of membership of an object in a fuzzy set gradually changes according to the change in its value. This is in contrast to classical sets, in which slight input changes may abruptly cause a total different classification of an object. This might propose an issue for diagnostics, as it should be prevented that minor alterations in symptoms, patient data or test results cause major alterations in the diagnosis proposed by the CDSS. One could think of this as a certain threshold that needs to be exceeded before the CDSS proposes a different potential disease. If this threshold is low, then the system could too quickly propose a different diagnosis without carefully considering the importance of an input change. Thus, the robustness of fuzzy system outputs might be more suitable to generate accurate diagnoses.

Another difference between the systems is their way of handling contradictions. The Law of Contradiction does not hold in fuzzy logic, which implies that an object can to some extent belong to a set and the complement of the set simultaneously. Human reasoning often encounters contradictions. We are capable of overriding a general rule if there is another rule that provides more information, even if the new rule contradicts the old rule (Covington, 2020). This is very common in the diagnostic process. Health professionals alter patient treatment by iteratively reconsidering their decisions as new patient data is gathered. It would be useful if CDSS can mimic this feature, as the diagnostic process would then not be ceased by contradictions, but rather be expanded by a system that closely resembles the efficiency of human reasoning.

This review is an addition to existing studies on fuzzy-based CDSS. The focus has been on the theoretical details of the design of the fuzzy CDSS and has provided examples to illustrate what happens in each phase. It has explained in detail the design of the membership functions, the process of rule activation and aggregation, and the defuzzification calculation. This review has demonstrated a way of implementing fuzzy logic in a diagnostic CDSS. However, it is important to note that there are many other ways of implementing the four phases – initialization, fuzzification, inference, defuzzification – of a fuzzy-based system. In the initialization phase, different linguistic variables and terms could have been used to represent fuzzy sets. Also, different types of membership functions could have been defined to convert crisp inputs to fuzzy sets. This is mostly dependent on the experts that create the knowledge base of the system, as the design of the functions is based on medical knowledge. Also, a different inference technique could have been chosen to execute the reasoning process. This choice is dependent on the preference of the creator, the application of the CDSS and the desired computational efficiency of the system. The inference technique also determines how the fuzzy operators are defined and which defuzzification method is used. There are different techniques for using the AND/OR operators besides the Min/Max methods that have been used in this review. Lastly, there exist different methods to convert a fuzzy set back into a crisp value. As can be seen, there is not an objective way to implement a fuzzy-based system. The overall structure of fuzzy systems is similar, comprised of the four phases, but differ in implementation details.

Further research might explore these different techniques to implement a fuzzy CDSS. One could then observe what outputs are generated and how they differ from the designed CDSS in this thesis. Also, further research could expand the CDSS by entering more input values (symptoms and patient data) into the system and extending the knowledge base. The diagnostic accuracy of the system could then be evaluated by using existing medical data about patients that have been tested positive or negative on pneumonia. The number of correctly diagnosed cases by the CDSS can be obtained by comparing the results of the CDSS with the actual number of patients that were diagnosed with pneumonia. Comparing the results of the designed CDSS with existing medical data may give an indication of the diagnostic accuracy of the system.

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