A Thesis

entitled

Kidney Compatibility Score Generation for a Donor – Recipient pair Using Fuzzy Logic

by

Sampath Kumar Yellanki

Submitted to Graduate Faculty as partial fulfillment of the requirements for The Master of Science Degree in Engineering

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An Abstract of

Kidney Compatibility Score Generation for a Donor – Recipient pair Using Fuzzy Logic

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This thesis, proposes and implements a Fuzzy Logic based Hierarchical model to address the problem of filtering the donor recipient pairs by predicting a kidney compatibility score. Donor – Recipient pair incompatibility is one of the major problems encountered in Renal Transplantation. Kidney Paired Donation is a barter system where the pairs exchange the donor organs to overcome the disadvantage of incompatibility. Identification of such pairs requires a Kidney Transplant Surgeon to evaluate the compatibility of swapped pairs. Unfortunately, such incompatible pairs run into huge numbers which is a herculean task for a surgeon and can prone to human fatigue.

This work presents a Hierarchical System developed based on Fuzzy Logic to determine the quality of a Kidney Transplant based on various input parameters. A surgeon’s expertise in selecting the incompatible pairs is
captured and embedded in this model in the form of rules. Fuzzy membership functions are designed to reflect the characteristics of input parameters. This model has been tested on several data sets. The pairs selected based on the kidney compatibility scores matched with the surgeon’s choice in most of the cases. This application provides many options to explore in future.
I dedicate this thesis to all the kidney transplant surgeons worldwide.

“Stay Hungry Stay Foolish” – Steve Jobs
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Chapter 1

Introduction

1.1 Problem Statement

Kidney Transplant is one of the major organ transplants. Unfortunately the gap between demand and supply is undesirably high. In United States of America in 2005, 4,052 people died waiting for a life-saving kidney transplant. During this time, almost 30,000 people were added to the national waiting list, while only 9913 people left the list after receiving a deceased donor kidney [1]. The waiting list currently has over 80,000 people, and the average waiting time varies from 2 to 5 years, depending on blood type. This list is growing year by year. An alternative is to find an Altruistic Donor who is willing to donate a kidney without wishing any financial compensation. In 2005, there were 6,563 altruistic donations in the US [1]. Number of altruistic donations is hard to match the demand.

Paired Kidney Donation is an Exchange Program designed for Donor – Recipient pairs who are incompatible for a Kidney Transplant. In Past, the incompatible donor was sent home and recipient was asked to wait for a matching deceased donor kidney or for an altruistic donation. In this case
they are added to a pool of all such incompatible Donor – Recipient pairs. They are compared against all existing pairs to check for a possibility of swapping. Therefore there is a need to develop an automated intelligent technique to evaluate Donor – Recipient pairs. This method should mimic the reasoning of the kidney transplant expert and take into consideration all the factors which a real surgeon would consider to evaluate the Donor – Recipient pairs.

In this thesis, this issue has been addressed and an application based on fuzzy logic has been developed to generate a numerical score for the quality of Donor – Recipient pair match.

1.2 Literature Review

A recent research paper discusses the importance of live donor kidney exchange program (a barter system of exchanging donor organs) where a donor’s kidney is not suitable for corresponding recipient due to ABO blood type incompatibility or because of positive cross matches [2, 7, 8, 9]. Live kidney exchange is of two types List Paired Donation (LPD) and Kidney Paired Donation (KPD). In List Paired Donation, intended donor’s kidney is traded with a deceased donor kidney for the incompatible recipient. In Kidney Paired Donation, incompatible recipients go for an exchange of their intended donors for kidney transplant. This is done carefully by selecting the
in incompatible pairs which result in successful transplants upon exchange of donor organs [3].

A recent study used Edmonds Matching algorithm to determine the potential impact of matching algorithms on the number of quality transplants achieved through Kidney Paired Donation. This algorithm was used to identify the incompatible pairs for an exchange of donor organs. From the results, it was concluded that the combination of KPD program and an optimized matching algorithm yields more matches and affords patients the flexibility of customizing their matching priorities and the security of knowing that the greatest number of high-quality matches will be found and distributed equitably. However, the results were generated using cycles of length 2 only. Allowing cycles of length 3 would yield significantly better results [1, 4].

In another prominent research done at Carnegie Mellon University, a directed graph was used to denote a barter exchange process. Cycles in the graph indicate a chain of transplants. Each directed edge was given a weight indicating the quality of transplant. Total weight of an exchange cycle is the sum of its cycle weights. Column generation algorithm was used to identify the cycles with maximum sum of weights when the maximum length of cycle is fixed [1]. Results proved that Column Generation technique outperformed the CPLEX algorithm, an existing market clearing algorithm for the Alliance for Paired Donation.
Existing matching algorithms deal with Donor – Recipient pairs having ABO blood type incompatibility and Positive Cross Match. This thesis aims at providing an algorithm which would generate kidney compatibility score for a Donor – Recipient pair by evaluating various parameters related to Recipient like Recipient Age, Recipient PRA etc and related to Donor – Recipient pair like Age Difference, Travel Distance etc. Thus generated score will be helpful for market clearing algorithms in identifying qualitative optimized chain of transplants.

1.3 Objectives of Kidney Compatibility Score Generation Technique

An Artificial Intelligence technique, Fuzzy Logic, is used to generate the kidney compatibility score by evaluating the input parameters of incompatible donor – recipient pairs.

The following are the goals of this thesis:

- Get a general understanding of Fuzzy Logic and Fuzzy Inference System
- Study the characteristics of input parameters responsible for generating the kidney compatibility score
- Design a model based on the Fuzzy Inference System
- Develop the application using the proposed model
- Run the application against the input data supplied
- Analyze the results with a Kidney Transplant Surgeon
1.4 Thesis Organization

This thesis is divided into 6 chapters. Chapter 2 gives an overview of Fuzzy Logic and Fuzzy Inference System. Chapter 3 discusses the designing of a Hierarchical Model based on the inputs which contribute in Score Generation. Chapter 4 describes the implementation of proposed Hierarchical Model. Analysis of results generated using the Hierarchical Fuzzy Inference System by a Kidney Transplant Surgeon is presented in Chapter 5. Finally in Chapter 6, conclusions are drawn and possible future work is presented.
Chapter 2

Understanding Fuzzy Logic

In this chapter, Fuzzy Logic (a concept from Artificial Intelligence) is explained in detail. Later in section 2.2, the topic Fuzzy Inference System and the steps involved are discussed.

2.1 What is Fuzzy Logic

Fuzzy logic is an Artificial Intelligence technique which has the ability to mimic human mind in terms of approximate reasoning rather than being exact. In general, computing techniques deal with crisp values like ‘True’ or ‘False’, ‘1’ or ‘0’, ‘Black’ or ‘White’, whereas Fuzzy Logic, also deals with the grey values which lie in between ‘Black’ and ‘White’.

A Classical Set has values with either full membership or with no membership. A Fuzzy Set has values with partial membership along with the crisp values. Classical Set is represented as \{x\}, where ‘x’ is an element from a classical set. A Fuzzy Set is represented as \((x, \mu_A(x))\) where ‘x’ is an element from a fuzzy set and \(\mu_A(x)\) is its membership value on A. Membership value denotes the degree to which an element belongs to a given set. Membership value \(\mu_A(x)\) of an element x lies in the range 0 to 1. General linguistic terms
like hot, cold, difficult, easy, frequent, rare, etc. are used to represent the values of a Fuzzy Set. Fuzzy Sets are useful in establishing conditions which are imprecise in definition through partial membership values. Elements in Fuzzy Set can overlap, so a given crisp value can belong to multiple fuzzy sets with different membership degrees in each set.

As shown in Figure 2.1, according to Classical Boolean Logic if the temperature is greater than equal to 100°F then it is defined as ‘Hot’ and if the temperature is less than 100°F then it is defined as ‘Normal’.

![Diagram showing temperatures of Day 1 and Day 2 in Boolean Logic](image)

**Figure 2-1: Temperatures of Day1 and Day2 in Boolean Logic**

As shown in Figure 2.1 the temperature of Day1 is 90°F and is less then 100°F temperature is said to be ‘Normal’. And temperature of Day2 is 100°F temperature is said to be ‘Hot’.
Figure 2.2: Temperatures of Day1 and Day 2 Fuzzy Logic

However, according to Fuzzy Logic, temperatures of Day1 and Day2 are expressed in membership degrees of each fuzzy set as shown in Figure 2.2. As the temperature of Day1 is 90°F it is said to be ‘Normal’ with membership degree 0.7 and ‘Hot’ with membership degree 0.3. And the temperature of Day2 is 100°F it is ‘Hot’ with membership degree 1 and ‘Normal’ with membership degree 0.

2.2 What is Fuzzy Inference System

Fuzzy Inference System (FIS) is a process of mapping Input data onto an Output using a set of Fuzzy Rules. Figure 2.3 gives an overview a Fuzzy Inference System.
Following are the steps of Fuzzy Inference System.

- Fuzzification
- Rule Evaluation
- Rule Aggregation
- Defuzzification

2.2.1 Fuzzification

Fuzzification is the first step in Fuzzy Inference System. It is the process of mapping a crisp value of an input to membership degrees in different Fuzzy Linguistic variables.

As shown in Figure 2.4, 90°F temperature of a day (Day1) is fuzzified as ‘Normal’ with membership value 0.3 and ‘Hot’ with membership value 0.7.
2.2.2 Rule Evaluation

In Rule Evaluation step the antecedent part of the If – Then rules are evaluated using the membership values obtained. Rules which satisfy the condition are fired with the appropriate rule strengths.

2.2.3 Rule Aggregation

Rule Aggregation is a process of unifying the output of the rules fired, for a given set of inputs.

2.2.4 Defuzzification

Defuzzification is inverse process of Fuzzification. It is the process of combining the fuzzy outputs of all the rules to give one crisp value.
Membership functions are defined for each input and output variable by identifying the degree to which it corresponds to each fuzzy set. Rule Base is a repository of If – Then rules where the antecedent belongs to fuzzy input variables and the consequent belongs to fuzzy output variables. It is also known as Knowledge Base since the expert knowledge is stored in those rules. When a Crisp Input is fed to the Fuzzy Inference System, several rules from the Rule Base are fired. Using the rules fired, Output is calculated.

This basic Fuzzy Inference System is used as building blocks to build a system which can generate kidney compatibility score a donor – recipient pair. Next chapter discusses this process of building in great detail.
Chapter 3

Design of Hierarchical model to generate Kidney Compatibility Score

In this chapter, firstly the input parameters which are required in evaluating a donor – recipient pair are carefully analyzed. Later, a fuzzy based hierarchical model for generating Kidney Compatibility Score for a donor – pair is explained.

3.1 Analysis of Input Parameters

Kidney Compatibility Score denotes the quality of a Kidney Transplant. Several factors are involved in calculating a kidney compatibility score. Some are solely dependent on Recipient and some are dependent on the Donor – Recipient pair. These include Biological, Physical and Geographical factors. They are

- Panel Reactive Antibody (PRA)
- Human Leukocyte Antigen B (HLA-B) Mismatches
- Human Leukocyte Antigen DR (HLA-DR) Mismatches
- Age Difference between Donor and Recipient
• Travel Distance
• Recipient being a Donor before
• Recipient Age
• Cytomegalovirus (CMV)
• Epstein-Barr Virus (EBV)
• Recipient Waiting Time

Descriptions of each input parameter listed above are provided in the following sections.

3.1.1 Panel Reactive Antibody (PRA)

Panel Reactive Antibody (PRA) is a measure of a person’s affinity to accept another person’s organ. It is an integer value with the range of [0,100]. If a person’s PRA is 70 then it denotes that out of 100 people, the recipient body is not compatible to accept an organ from 70 people. Recipient’s body will be compatible with only 30 people. People with higher PRA are given preference over others since it is rather difficult to find a donor for them.

3.1.2 Human Leukocyte Antigen B (HLA-B) Mismatches

Human leukocyte antigen is a major human histocompatibility system. HLA typing is done before transplantation to determine the degree of tissue compatibility between donor and recipient.
Human Leukocyte Antigen B (HLA-B) is a class I alpha-chain gene in the human major histocompatibility complex. HLA-B is a gene which provides instructions for making protein that plays a critical role in immune system. The HLA complex helps the immune system distinguish the body’s own proteins from the proteins made by foreign invaders such as viruses and bacteria. For a quality transplant, it is preferable to have maximum number of HLA-B matches between Donor and Recipient. Calculation of number of matches is misleading whereas calculating the number of mismatches helps in identifying a quality match; hence number of mismatches is calculated.

3.1.3 Human Leukocyte Antigen DR (HLA-DR) Mismatches

Human Leukocyte Antigen DR (HLA-DR) is a major histocompatibility complex class II cell surface receptor encoded by the human leukocyte antigen complex on chromosome 6 region 6p21.31. The primary function of HLA-DR is to present peptide antigens, potentially foreign in origin, to the immune system for the purpose of eliciting or suppressing T-(helper)-cell responses that eventually lead to the production of antibodies against the same peptide antigen. For a quality transplant, it is preferable to have maximum number of HLA-DR matches between Donor and Recipient. Calculation of number of matches is misleading whereas calculating the number of mismatches helps in identifying a quality match; hence number of mismatches is calculated.
3.1.4 Age Difference

Age Difference between Donor and Recipient indirectly affects other biological factors. Pairs with less age difference are preferred for a quality transplant. Pairs with more age difference are given less preference.

3.1.5 Travel Distance

Travel Distance is the distance from Donor’s transplant centers to Recipient Transplant centers. Great Circle Formula is used to calculate the distances between transplant centers. Transplants involving minimal or no travel are given more importance.

3.1.6 Recipient being a Donor before

There could be a possibility for a Recipient being a Donor before. All such recipients are given more priority over others.

3.1.7 Recipient Age

Recipients whose age falls below 18 have more survival rate. They are given more preference. Recipients whose age is more than 18 are given less preference. Younger people are given more preference as compared to older people, other factors being similar.
3.1.8 Cytomegalovirus (CMV)

Cytomegalovirus (CMV) is one of the herpes viruses. CMV is a common infection that is usually harmless. Once CMV is in a person's body, it stays there for life. Among every 100 adults in the United States, 50 – 80 are infected with CMV by the time they are 40 years old.

CMV is a member of a group of large species-specific herpes-type viruses with a wide variety of disease effects. It causes serious illness in persons with human immunodeficiency virus, in newborns, and in people being treated with immunosuppressive drugs and therapy, especially after organ transplantation. It is preferable to have Donor and Recipient to be CMV negative.

3.1.9 Epstein-Barr virus (EBV)

Epstein-Barr virus (EBV) is also a virus which belongs to Herpes family that selectively infects human B cells by binding to complement receptor 2 (CR2, also known as CD21). EBV is one of the most common viruses in humans. People with EBV negative are given more preference for a quality transplant.
3.1.10 Waiting Time

Whenever a Donor – Recipient pair competes with another pair with better qualities, they are rejected. It reduces the chance of selecting for a transplant thereby increasing the Waiting Time. Hence people who are waiting for a longer time are given more preference over others.

3.2 Designing a Hierarchical Model

Input parameters discussed in section 3.1 contribute in generating compatibility score. Not all parameters make equal contribution in generating the score. The degree of importance varies for each factor along with the preference order in which they are evaluated. Some are preferred over the other as explained in the next page.

Although above given inputs can be loosely categorized into three groups. Grouping helps to evaluate those input parameters at different preference levels.

Grouping is done as shown below.

Group A

- Recipient PRA
- Human Leukocyte Antigen B
- Human Leukocyte Antigen DR
Group A consists of biological parameters which are primarily important in identifying the kidney compatibility of donor and recipient. Group A has the highest priority.

Group B has parameters which are of next importance in determining the compatibility. Group A and B can be collectively called as Primary Input Parameters as they make a major contribution in identifying the pair.

Group C has parameters which add more value to the compatibility score generated by Group A and B. These parameters can be considered as a bonus. Hence this group can be called as Bonus Input Parameters.
From the above analysis, evaluation order of inputs can be arranged in the following hierarchical manner as shown in Figure 3.1.

Figure 3-1: Hierarchical arrangement of Input Parameter
Chapter 4

Implementation of Hierarchical Model based on Fuzzy Inference System

In chapter 3, a hierarchical model was proposed. In this chapter, implementation details of hierarchical fuzzy inference system are discussed in great detail. The organization of this chapter is as follows.

A hierarchical fuzzy inference system based on hierarchical model proposed in chapter 3 is built. It first takes into consideration the highest priority biological parameters such as Panel Reactive Antibody, HLA B Mismatches and HLA DR Mismatches and develops fuzzy inference system FIS 1 as shown in Figure 4.1. Based on the expert knowledge, rules are designed to generate compatibility score of HLA_PRA_Compatibility_Score.

This HLA_PRA_Compatibility_Score is then combined with other parameter of Group B such as Age Difference, Travel Distance and Waiting Time to develop a fuzzy inference system FIS 2. These parameters along with the rules which capture the expert’s knowledge are used to predict the output Primary_Compatibility_Score using fuzzy inference system FIS 2 as shown in Figure 4.6.
Fuzzy Inference System FIS 3 is designed using the parameters of Group C such as Recipient Age, Recipient Was a Donor, CMV and EBV. Output Bonus_Compatibility_Score is predicted based on the rules incorporated in the fuzzy inference system FIS 3 as shown in Figure 4.12.

Finally fuzzy inference system FIS 4 is designed which uses Primary_Compatibility_Score and Bonus_Compatibility_Score to create the Final_Compatibility_Score which represents the extent to which recipients and donors match.
4.1 Defining Fuzzy Inference System FIS 1

Figure 4-1: Fuzzy Inference System FIS 1

Figure 4.1 gives overall view of fuzzy inference system FIS 1 used to represent Group A. List of parameters in Group A i.e. Panel Reactive Antibody, HLA B Mismatches, HLA DR Mismatches are passed as inputs to FIS 1 and the output HLA_PRA_Compatibility_Score is generated. In next section, how each input from Group A is represented in terms of fuzzy sets is discussed.

4.1.1 Defining Inputs and Output of FIS 1

The three inputs of FIS 1 PRA, Number of HLA B Mismatches, and Number of HLA DR Mismatches are represented as fuzzy sets in the following sections.
4.1.1.1 Input 1 (Panel Reactive Antibody) of FIS 1

Panel Reactive Antibody is a Continuous Function. Range of this input is [0 100]. As shown in Figure 4.2, this input is represented using five fuzzy sets \{Very Low, Low, Medium, High, Very High\}.

a) Sigmoid Function is used to represent the fuzzy sets ‘Very Low’ and ‘Very High’

b) Generalized Bell-Shaped Function is used to represent the fuzzy sets ‘Low’, ‘Medium’ and ‘High’

![Figure 4-2: Panel Reactive Antibody](image-url)
4.1.1.2 Input 2 (Number of HLA B Mismatches) of FIS 1

Human Leukocyte Antigen B is present in both donor and recipient. For good compatibility Number of Mismatches should be small. Number of Mismatches is a discrete variable and is represented as three singleton fuzzy sets of

a) 0 Mismatches
b) 1 Mismatch
c) 2 Mismatches

Singleton fuzzy sets of input HLA B are as shown in Figure 4.3.

Figure 4-3: Number of HLA B Mismatches
4.1.1.3 Input 3 (Number of HLA DR Mismatches) of FIS 1

Human Leukocyte Antigen DR is present in both donor and recipient. Less Number of HLA DR Mismatches is a sign of good compatibility. Number of Mismatches is a discrete variable and is represented as three singleton fuzzy sets of

a) 0 Mismatches
b) 1 Mismatch
c) 2 Mismatches

Figure 4.4 shows the Singleton fuzzy sets of input HLA DR

![Number of HLA DR Mismatches](image)

Figure 4-4: Number of HLA DR Mismatches
4.1.1.4 Output (HLA_PRA_Compatibility_Score) of FIS 1

The output of FIS 1 is HLA_PRA_Compatibility_Score. Its range is [0, 50]. It has been represented with five fuzzy sets {Very Low, Low, Medium, High and Very High} as shown in Figure 4.5. Output value thus generated is then defuzzified to obtain a crisp value.

a) Sigmoid function is used to represent fuzzy sets ‘Very Low’ and ‘Very High’

b) Generalized Bell-Shaped function is used to represent fuzzy sets ‘Low’, ‘Medium’ and ‘High’

Figure 4-5: HLA_PRA_Compatibility_Score
4.2 Defining Fuzzy Inference System FIS 2

Figure 4.6 represents a Fuzzy Inference System FIS 2. It takes the inputs of Group B along with HLA_PRA_Compatibility_Score (it will be passed as HLA_PRA) which was generated as an output of FIS 1. These inputs along with rules, through the process of fuzzy reasoning create an output Primary_Compatibility_Score.

In the next section, how each input from Group B along with HLA_PRA is represented in terms of fuzzy sets is discussed.

![Figure 4-6: Fuzzy Inference System FIS 2](image)

4.2.1 Defining Inputs and Output of FIS 2

The inputs of FIS 2 HLA_PRA, Age Difference, Travel Distance and Waiting Time are represented as fuzzy sets in the following sections.
4.2.1.1 Input 1 (HLA_PRA) of FIS 2

Output of Group A is fed as input to fuzzy inference system FIS 2 along with input parameters of Group B. Output of Group A is a Continuous function and it is scaled to range [0 100] from [0 50]. As shown in Figure 4.7 this input is represented using five fuzzy sets {Very Low, Low, Medium, High, Very High}.

a) Sigmoid function is used to represent the fuzzy sets ‘Very Low’ and ‘Very High’

b) Generalized Bell-Shaped function is used to represent the fuzzy sets ‘Low’, ‘Medium’ and ‘High’

Figure 4-7: HLA_PRA
4.2.1.2 Input 2 (Age Difference) of FIS 2

Age Difference between Donor and Recipient is a Continuous function. Age difference between a donor and a recipient can be from 0 yrs to 70 yrs. It is very rare to have donor – recipient pair with more than 70 yrs of age difference. As shown in Figure 4.8 this input is represented using four fuzzy sets {Very Low, Low, High, Very High}.

a) Sigmoid function is used to represent the fuzzy sets ‘Very Less’ and ‘Very High’

b) Generalized Bell-Shaped function is used to represent the fuzzy set ‘Less’

c) Gaussian Combination Function is used to represent the fuzzy set ‘High’

Figure 4-8: Age Difference
4.2.1.3 Input 3 (Travel Distance) of FIS 2

Travel Distance between Donor Transplant Center and Recipient Transplant Center is a Continuous function. It is assigned a range [-10 3000]. Longer distances requires kidney to be shipped or involves an airplane trip. To differentiate them, negative travel distance is used to represent Shipped Kidney and Airplane Trip is used for longer distances.

Figure 4-9: Travel Distance

As shown in Figure 4.9, six fuzzy sets {Home Transplant Center (HTC), Home City (H), Adjoining City (AC), One Day Drive (ODD), Airplane Trip (AT), Shipped Kidney (S)} are used to represent this input.

Most of the fuzzy sets are crowded in the range [-10 100], to give a clear view Figure 4.10 is drawn.
a) ‘HTC’ (Home Transplant Center) and ‘SK’ (Shipped Kidney) are constants. Singleton function is used to represent them.

b) Sigmoid Function is used to represent fuzzy set ‘AT’ (Airplane Trip)

c) Gaussian Combination Function is used to represent the fuzzy set ‘HC’ (Home City).

d) Generalized Bell-Shaped Function is used to represent the fuzzy sets ‘AC’ (Adjacent Cities) and ‘ODD’ (One Day Drive)
4.2.1.4 Input 4 (Waiting Time) of FIS 2

This input is not a part of fuzzy inference system but is evaluated independently. Number of points for Waiting Time is calculated and is added to the output of Group B fuzzy inference system. Recipient’s rank in the list of recipients is also used for calculating the points for Waiting Time.

Calculating the Points for the Recipient’s Waiting Time

- Let $Y$ be the number of full years since the recipient was initially registered.
- Let $N$ be the number of recipients currently in the pool.
- Let $R$ be the recipient’s rank in the list of recipients when they are put in order from the person with the most recent registration date to the person with the earliest registration date.
- Then the waiting time bonus is $Y + (R / N)$.

For example, if a recipient has been in the pool for more than 1 but less than 2 years, and if the recipient’s registration date currently ranks in position 75 out of 100 recipients in the pool, then the waiting time bonus would be $1 + (75 / 100) = 1.75$ points.
4.2.1.5 Output of FIS 2 Primary_Compatibility_Score

Output of FIS 2, Primary_Compatibility_Score is generated in the range [0 100]. Primary_Compatibility_Score is a Continuous function. It is represented with five fuzzy sets {Very Low, Low, Medium, High and Very High} as shown in Figure 4.11. Output value thus generated is then defuzzified to obtain a crisp value.

a) Sigmoid function is used to represent fuzzy sets ‘Very Low’ and ‘Very High’

b) Generalized Bell-Shaped function is used to represent fuzzy sets ‘Low’, ‘Medium’ and ‘High’

![Figure 4-11: Primary_Compatibility_Score](image-url)
4.3 Fuzzy Inference System FIS 3 of Group C

Figure 4.12 gives overall view of fuzzy inference system FIS 3 for the parameters of Group C. Parameters of Group C i.e. Recipient Age, Recipient was a Donor, Cytomegalovirus and Epstein - Barr virus are passed as inputs to the fuzzy inference system and Bonus_Compatibility_Score is generated as output. In the next section, how each input from Group C is represented in terms of fuzzy sets is discussed.

![Figure 4-12: Fuzzy Inference System FIS 3](image)

**4.3.1 Defining Inputs and Output of FIS 3**

The inputs of FIS 3 Recipient Age, Recipient Was a Donor, Cytomegalovirus, Epstein – Barr virus. Later sections discuss the representation of inputs of FIS 3 with fuzzy sets.
4.3.1.1 Input 1 (Recipient Age) of FIS 3

Input 1 of FIS 3, Recipient Age is a Continuous function. Its range is [0, 100]. 0 yrs and 80 yrs are considered as lower and upper bounds of age of the recipients respectively. It is very rare to find a recipient with an age above 80yrs. Input Recipient Age is represented using two fuzzy sets {Less, High} as shown in Figure 4.13.

a) Sigmoid Function is used to represent the fuzzy sets ‘Less’ and ‘High’

Figure 4-13: Recipient Age
4.3.1.2 Input 2 (Recipient was once a Donor) of FIS 3

Recipient could be a Donor in the past. It has discrete values ‘Yes’ or ‘No’. This input is not a continuous function and cannot be represented in terms of fuzzy sets. Hence Singleton function is used to represent them as shown in Figure 4.14.

Figure 4-14: Recipient was once a Donor
4.3.1.3 Input 3 (Cytomegalovirus) of FIS 3

Cytomegalovirus could be present in Donor and/or Recipient. Both donor and recipient are expected to be negative. Hence this input has 2 discrete values {At least one is Positive, Both are Negative}.

This input is not a continuous function and cannot be represented in terms of fuzzy sets. Hence Singleton function is used to represent them as shown in Figure 4.15.

Figure 4-15: Cytomegalovirus
4.3.1.4 Input 4 (Epstein – Barr virus) of FIS 3

Epstein-Barr virus could be present in Donor and/or Recipient. Both donor and recipient are expected to be negative. Hence this input has 2 discrete values {At least one is Positive, Both are Negative}.

This input is not a continuous function and cannot be represented in terms of fuzzy sets. Hence Singleton function is used to represent them as shown in Figure 4.16.

![Figure 4-16: Epstein – Barr Virus](image)

Figure 4-16: Epstein – Barr Virus
4.3.1.5 Output (Bonus_Compatibility_Score) of FIS 3

Output of FIS 3, Bonus_Compatibility_Score is generated in the range [0 100]. Output of FIS 3, Bonus_Compatibility_Score, is a Continuous function. Bonus_Compatibility_Score is represented with three fuzzy sets {Low, Medium, and High} as shown in Figure 4.17. Output value thus generated is then defuzzified to obtain a crisp value.

a) Sigmoid function is used to represent fuzzy sets ‘Low’ and ‘High’

b) Gaussian Combination function is used to represent fuzzy set ‘Medium’

Figure 4-17: Bonus_Compatibility_Score
4.4 Fuzzy Inference System FIS 4

Figure 4.18 gives overall view of fuzzy inference system FIS 4 which generates the Final_Compatibility_Score as output. Output of fuzzy inference system FIS 2 Primary_Compatibility_Score and Output of fuzzy inference system FIS 3 Bonus_Compatibility_Score are passed as inputs to FIS 4. In the next section, how each input is represented in terms of fuzzy sets is discussed.

![Fuzzy Inference System FIS 4](image)

Figure 4-18: Fuzzy Inference System FIS 4

4.4.1 Defining Inputs and Output of FIS 4

Output of FIS 2 (Primary_Compatibility_Score) is passed with the name Primary Input and Output of FIS 3 (Bonus_Compatibility_Score) is passed with the name Bonus Input. Later sections discuss the representation of inputs of FIS 4 with fuzzy sets.
4.4.1.1 Input 1 (Primary Input) of FIS 4

Input 1 of FIS 4, Primary Input is a Continuous function and its range is [0 20]. As shown in Figure 4.19 a single fuzzy set {'Primary Input'} is used to represent this input. Triangular Function is used to represent the fuzzy set ‘Primary Input’.

Figure 4-19: Primary Input
4.4.1.2 Input 2 (Bonus Input) of FIS 4

Input 2 of FIS 4, Bonus Input is a Continuous function and its range is [0 20]. As shown in Figure 4.20 a single fuzzy set {Bonus Input} is used to represent this input. Triangular Function is used to represent the fuzzy set ‘Bonus Input’.

Figure 4-20: Bonus Input
4.4.1.3 Output (Final_Compatibility_Score) of FIS 4

Output of FIS 4, Final_Compatibility_Score is generated in the range [0 41]. Fuzzy sets \{Prime_Output, Bonus_Output\} are used to represent the output as shown in the Figure 4.21. Triangular Function is used represent the above fuzzy sets.

Figure 4-21: Final_Compatibility_Score
4.5 Design and Analysis of Rules for Fuzzy Inference Systems FIS 1, FIS 2, FIS 3 and FIS 4

In this section, Rules are designed for fuzzy inference system FIS 1 shown in Figure 3.1, FIS 2 shown in Figure 4.6, FIS 3 shown in Figure 4.12 and FIS 4 shown in Figure 4.18 using the expert’s knowledge. A Rule is an If – Then statement where Antecedent belongs to input fuzzy sets and Consequent belongs to output fuzzy sets. Antecedent is a logical combination of input fuzzy sets. Consequent is a fuzzy set from output. For each combination of input fuzzy sets, an output fuzzy set is predicted using expert’s knowledge. Maximum number of rules of a Rule Set is given by the product of the number of fuzzy sets of each input.

For example, input X has 3 fuzzy sets, Y has 5 fuzzy sets and Z has 4 fuzzy sets then the maximum number of rules will be $3 \times 5 \times 4 = 60$.

When input parameters are passed to a fuzzy inference system, antecedents of If – Then rules are evaluated. Rules which satisfy the condition are fired.
4.5.1 Calculation of Maximum number of Rules for FIS 1, FIS 2, FIS 3 and FIS 4

Total number of rules of a rule set of a fuzzy inference system with ‘M’ number of inputs and ‘N’ number of fuzzy sets for each input is \( N^M \) (N raised to the power of M).

4.5.1.1 Maximum number of Rules for FIS 1

Table 4.1 shows the number of fuzzy sets used by each input of FIS 1.

<table>
<thead>
<tr>
<th>SNo.</th>
<th>Input</th>
<th>Number of fuzzy sets</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Panel Reactive Antibody</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>Number of HLA B Mismatches</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>Number of HLA DR Mismatches</td>
<td>3</td>
</tr>
</tbody>
</table>

Number of Rules of FIS 1 = \( 5 \times 3 \times 3 \)

\[ = 45 \]

The rules generated will be of the following format

IF (Panel Reactive Antibody is Very High) and (Number of HLA B Mismatches is 0 Mismatches) and (Number of HLA DR Mismatches is 0 Mismatches) THEN (HLA_PRA_Compatibility_Score is Very High)
IF (Panel Reactive Antibody is Very Low) and (Number of HLA B Mismatches is 2 Mismatches) and (Number of HLA DR Mismatches is 2 Mismatches) THEN (HLA_PRA_Compatibility_Score is Very Low)

4.5.1.2 Maximum number of Rules for FIS 2

Number of fuzzy sets used by each input of FIS 2 is as shown in Table 4.2

Table 4.2: Number of input fuzzy sets of FIS 2

<table>
<thead>
<tr>
<th>SNo.</th>
<th>Input</th>
<th>Number of fuzzy sets</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HLA_PRA</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>Age Difference</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>Travel Distance</td>
<td>6</td>
</tr>
</tbody>
</table>

Number of Rules of FIS 2 = 5 x 4 x 6

= 120

The rules generated will be of the following format

IF (HLA_PRA is Very High) and (Age Difference is Very Less) and (Travel Distance is Home Transplant Center) THEN (Primary_Compatibility_Score is Very High)

IF (HLA_PRA is Very High) and (Age Difference is Very Less) and (Travel Distance is Home Transplant Center) THEN (Primary_Compatibility_Score is Very High)
4.5.1.3 Maximum number of Rules for FIS 3

Table 4.3 lists the number of fuzzy sets used by each input of FIS 3.

Table 4.3: Number of input fuzzy sets of FIS 3

<table>
<thead>
<tr>
<th>SNo.</th>
<th>Input</th>
<th>Number of fuzzy sets</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Recipient Age</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>Recipient Was a Donor</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>Cytomegalovirus</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>Epstein - Barr virus</td>
<td>2</td>
</tr>
</tbody>
</table>

Number of Rules of FIS 3 = 2 x 2 x 2 x 2

= 16

The rules generated will be of the following format

IF (Recipient Age is Low) and (Recipient Was a Donor is True) and (Cytomegalovirus is Both are Negative) and (Epstein – Barr virus is Both are Negative) THEN (Bonus_Compatibility_Score is High)

IF (Recipient Age is High) and (Recipient Was a Donor is False) and (Cytomegalovirus is At least One is Positive) and (Epstein – Barr virus is At least One is Positive) THEN (Bonus_Compatibility_Score is Low)
4.5.1.4 Maximum number of Rules for FIS 4

Number of fuzzy sets used by each input of FIS 4 is listed in Table 1.4.

Table 4.4: Number of input fuzzy sets of FIS 4

<table>
<thead>
<tr>
<th>SNo.</th>
<th>Input</th>
<th>Number of fuzzy sets</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Primary Input</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Bonus Input</td>
<td>1</td>
</tr>
</tbody>
</table>

Number of Rules of FIS 4 = 1 x 1 + 1 x 1 = 2

Rules generated for FIS 4 are

IF (Primary Input is Primary Input) THEN (Final Output is Primary Output)

IF (Bonus Input is Bonus Input) THEN (Final Output is Bonus Output)

Total number of rules = number of rules of FIS 1 + number of rules of FIS 2 + number of rules of FIS 3 + number of rules of FIS 4

= 45 + 120 + 16 + 2

= 183
4.6 Combinatorial Rule Explosion

In general, as the number of inputs and their fuzzy sets increase then the number of rules increases. It is called Combinatorial Rule Explosion or the Curse of Dimensionality.

For example, a Fuzzy Inference System with ‘M’ inputs and each input being defined using ‘N’ fuzzy sets, then the number of possible rules is $N^M$. As the values of M and N increase, number of rules becomes very large.

Fuzzy Inference Systems FIS 1, FIS 2, FIS 3 and FIS 4 use 183 rules for processing the inputs to predict the output. Generating 183 rules is huge and experts do not have such fine grained knowledge to represent 183 rules. Therefore it is a big challenge to reduce the number of rules and yet have enough rules to capture the expert knowledge and reduce the computational time.

To reduce the number of rules, Combs Method was chosen, which is explained in the following section.

4.7 Combs Method

William E. Combs and James E. Andrews proposed a method to tackle the problem of Combinatorial Rules Explosion in 1998 [5]. Combs Method reduces the number of Rules of Fuzzy Inference System dramatically. It is based on the logic presented in (1)
\[(a \land b) \Rightarrow c) \iff ((a \Rightarrow c) \lor (b \Rightarrow c)) \quad (1)\]

If a and b implies c then it is equivalent to a implies c or b implies c.

Table 4.5 provides a proof for above equivalence

<table>
<thead>
<tr>
<th>a</th>
<th>b</th>
<th>c</th>
<th>a \land b</th>
<th>(a \land b) \Rightarrow c</th>
<th>a \Rightarrow c</th>
<th>b \Rightarrow c</th>
<th>(a \Rightarrow c) \lor (b \Rightarrow c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T</td>
<td>T</td>
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</tr>
</tbody>
</table>

Using Combs Method a rule set with \(N_1 \times N_2 \times N_3 \times \ldots \times N_M\) rules can be reduced to \(N_1 + N_2 + N_3 + \ldots + N_M\) number of rules. Where \(N_i\) is the number of fuzzy sets used by \(i^{th}\) input (where \(i = 1\) to \(M\)).

Consider a fuzzy inference system having the following rule set

**Rule 1**: If Food is Good and Service is Good Then Tip is Good

**Rule 2**: If Food is Good and Service is Average Then Tip is Good

**Rule 3**: If Food is Good and Service is Bad Then Tip is Average

**Rule 4**: If Food is Average and Service is Good Then Tip is Average

**Rule 5**: If Food is Average and Service is Average Then Tip is Average

**Rule 6**: If Food is Average and Service is Bad Then Tip is Average

**Rule 7**: If Food is Bad and Service is Good Then Tip is Bad
Rule 8: If Food is Bad and Service is Average Then Tip is Bad

Rule 9: If Food is Bad and Service is Bad Then Tip is Bad [6]

Using Combs Method rules can be rewritten as

Rule 1: ((If Food is Good Then Tip is Good) or
    (If Service is Good Then Tip is Good))

Rule 2: ((If Food is Good Then Tip is Good) or
    (If Service is Average Then Tip is Good))

Rule 3: ((If Food is Good Then Tip is Average) or
    (If Service is Bad Then Tip is Average))

Rule 4: ((If Food is Average Then Tip is Average) or
    (If Service is Good Then Tip is Average))

Rule 5: ((If Food is Average Then Tip is Average) or
    (If Service is Average Then Tip is Average))

Rule 6: ((If Food is Average Then Tip is Average) or
    (If Service is Bad Then Tip is Average))

Rule 7: ((If Food is Bad Then Tip is Bad) or
    (If Service is Good Then Tip is Bad))

Rule 8: ((If Food is Bad Then Tip is Bad) or
    (If Service is Average Then Tip is Bad))

Rule 9: ((If Food is Bad Then Tip is Bad) or
    (If Service is Bad Then Tip is Bad))
In the next step, each rule with multiple antecedents is written into multiple rules with single antecedent. For example consider Rule 1 from the above rule set, it can be written as

- If Food is Good Then Tip is Good
- If Service is Good Then Tip is Good

Then rules with similar antecedents are merged into a single rule by taking the majority of the consequents. For example consider the rules with similar single antecedents which are formed from Rules 1, 2 and 3

- If Food is Good Then Tip is Good (from Rule 1)
- If Food is Good Then Tip is Good (from Rule 2)
- If Food is Good Then Tip is Average (from Rule 3)

Two rules give the result as Good and one is giving the result as Average. So the above 3 rules are reduced to “If Food is Good Then Tip is Good”. Similarly all remaining rules are reduced. The reduced rule set is given as follows

**Rule 1:** If *Food is Good* then *Tip is Good*

**Rule 2:** If *Food is Average* then *Tip is Average*

**Rule 3:** If *Food is Bad* then *Tip is Bad*

**Rule 4:** If *Service is Good* then *Tip is Average*

**Rule 5:** If *Service is Average* then *Tip is Average*

**Rule 6:** If *Service is Bad* then *Tip is Average*
Rule sets for fuzzy inference systems FIS 1 and FIS 2 are generated using Combs Method and listed in the next section. Combs Method is not required to generate the rule set for FIS 3 and FIS 4 as the size of rule set is small compared to rule sets of FIS 1 and FIS 2.

4.7.1 Rule Set generated for FIS 1 using Combs Method

Rule set size is reduced from $3 \times 3 \times 5 = 45$ to $3 + 3 + 5 = 11$. Rule set for FIS 1 is listed below

1. If (Number of HLA DR Mismatches is 2)  
   Then (HLA_PRA_Compatibility_Score is Very Low)

2. If (Number of HLA DR Mismatches is 1)  
   Then (HLA_PRA_Compatibility_Score is High)

3. If (Number of HLA DR Mismatches is 0)  
   Then (HLA_PRA_Compatibility_Score is Very High)

4. If (Panel Reactive Antibody is Very High)  
   Then (HLA_PRA_Compatibility_Score is Very High)

5. If (Panel Reactive Antibody is High)  
   Then (HLA_PRA_Compatibility_Score is High)

6. If (Panel Reactive Antibody is Medium)  
   Then (HLA_PRA_Compatibility_Score is Medium)

7. If (Panel Reactive Antibody is Low)  
   Then (HLA_PRA_Compatibility_Score is Low)
8. If (Panel Reactive Antibody is Very Low)
   Then (HLA_PRA_Compatibility_Score is Very Low)

9. If (Number of HLA B Mismatches is 0)
   Then (HLA_PRA_Compatibility_Score is Very High)

10. If (Number of HLA B Mismatches is 1)
    Then (HLA_PRA_Compatibility_Score is Medium)

11. If (Number of HLA B Mismatches is 2)
    Then (HLA_PRA_Compatibility_Score is Very Low)

4.7.2 Rule Set generated for FIS 2 using Combs Method

   The size of rule set used by FIS 2 is reduced to $5 + 4 + 6 = 15$ from $5 \times 4 \times 6 = 120$. Following is the list of rules used by FIS 2

1. If (Age Difference is Very High)
   Then (Primary_Compatibility_Score is Very Low)

2. If (Age Difference is High)
   Then (Primary_Compatibility_Score is Low)

3. If (Age Difference is Less)
   Then (Primary_Compatibility_Score is High)

4. If (Age Difference is Very Less)
   Then (Primary_Compatibility_Score is Very High)

5. If (Travel Distance is Home Transplant Center)
   Then (Primary_Compatibility_Score is Very High)
6. If (Travel Distance is Home City) 
   Then (Primary_Compatibility_Score is High)

7. If (Travel Distance is Adjoining Cities) 
   Then (Primary_Compatibility_Score is Average)

8. If (Travel Distance is One Day Drive) 
   Then (Primary_Compatibility_Score is Low)

9. If (Travel Distance is Airplane Trip) 
   Then (Primary_Compatibility_Score is Very Low)

10. If (Travel Distance is Shipped Kidney) 
    Then (Primary_Compatibility_Score is Very Low)

11. If (HLA PRA is Very High) 
    Then (Primary_Compatibility_Score is Very High)

12. If (HLA PRA is High) 
    Then (Primary_Compatibility_Score is High)

13. If (HLA PRA is Medium) 
    Then (Primary_Compatibility_Score is Average)

14. If (HLA PRA is Low) 
    Then (Primary_Compatibility_Score is Low)

15. If (HLA PRA is Very Low) 
    Then (Primary_Compatibility_Score is Very Low)
4.7.3 Rule Set generated for FIS 3

Combs Method is not used for this fuzzy inference system. Rules used by fuzzy inference system FIS 3 are listed below

1. If (Recipient Age is Less)
   And (Recipient Once A Donor is No)
   And (Cytomegalovirus is Both Are Negative)
   And (Epstein - Barr virus is Both Are Negative)
   Then (Bonus_Compatibility_Score is High)

2. If (Recipient Age is Less)
   And (Recipient Once A Donor is No)
   And (Cytomegalovirus is Both Are Negative)
   And (Epstein - Barr virus is At least One Is Positive)
   Then (Bonus_Compatibility_Score is Medium)

3. If (Recipient Age is Less)
   And (Recipient Once A Donor is No)
   And (Cytomegalovirus is At least One Is Positive)
   And (Epstein - Barr virus is Both Are Negative)
   Then (Bonus_Compatibility_Score is Medium)

4. If (Recipient Age is Less)
   And (Recipient Once A Donor is No)
   And (Cytomegalovirus is At least One Is Positive)
And (Epstein - Barr virus is At least One Is Positive)
Then (Bonus_Compatibility_Score is Medium)

5. If (Recipient Age is Less)
   And (Recipient Once A Donor is Yes)
   And (Cytomegalovirus is Both Are Negative)
   And (Epstein - Barr virus is Both Are Negative)
   Then (Bonus_Compatibility_Score is High)

6. If (Recipient Age is Less)
   And (Recipient Once A Donor is Yes)
   And (Cytomegalovirus is Both Are Negative)
   And (Epstein - Barr virus is At least One Is Positive)
   Then (Bonus_Compatibility_Score is High)

7. If (Recipient Age is Less)
   And (Recipient Once A Donor is Yes)
   And (Cytomegalovirus is At least One Is Positive)
   And (Epstein - Barr virus is Both Are Negative)
   Then (Bonus_Compatibility_Score is High)

8. If (Recipient Age is Less)
   And (Recipient Once A Donor is Yes)
   And (Cytomegalovirus is At least One Is Positive)
   And (Epstein - Barr virus is At least One Is Positive)
   Then (Bonus_Compatibility_Score is Medium)
9. If (Recipient Age is High) 
   And (Recipient Once A Donor is No) 
   And (Cytomegalovirus is Both Are Negative) 
   And (Epstein - Barr virus is Both Are Negative) 
   Then (Bonus_Compatibility_Score is Medium) 

10. If (Recipient Age is High) 
    And (Recipient Once A Donor is No) 
    And (Cytomegalovirus is Both Are Negative) 
    And (Epstein - Barr virus is At least One Is Positive) 
    Then (Bonus_Compatibility_Score is Low) 

11. If (Recipient Age is High) 
    And (Recipient Once A Donor is No) 
    And (Cytomegalovirus is At least One Is Positive) 
    And (Epstein - Barr virus is Both Are Negative) 
    Then (Bonus_Compatibility_Score is Low) 

12. If (Recipient Age is High) 
    And (Recipient Once A Donor is No) 
    And (Cytomegalovirus is At least One Is Positive) 
    And (Epstein - Barr virus is At least One Is Positive) 
    Then (Bonus_Compatibility_Score is Low) 

13. If (Recipient Age is High) 
    And (Recipient Once A Donor is Yes)
And (Cytomegalovirus is Both Are Negative)
And (Epstein - Barr virus is Both Are Negative)
Then (Bonus_Compatibility_Score is High)

14. If (Recipient Age is High)
And (Recipient Once A Donor is Yes)
And (Cytomegalovirus is Both Are Negative)
And (Epstein - Barr virus is At least One Is Positive)
Then (Bonus_Compatibility_Score is Medium)

15. If (Recipient Age is High)
And (Recipient Once A Donor is Yes)
And (Cytomegalovirus is At least One Is Positive)
And (Epstein - Barr virus is Both Are Negative)
Then (Bonus_Compatibility_Score is Medium)

16. If (Recipient Age is High)
And (Recipient Once A Donor is Yes)
And (Cytomegalovirus is At least One Is Positive)
And (Epstein - Barr virus is At least One Is Positive)
Then (Bonus_Compatibility_Score is Low)
4.7.4 Rule Set generated for FIS 4

Combs Method is not used reducing the rule set for the fuzzy inference system FIS 4. Following rules are used for FIS 4 are listed below

1. IF (Primary Input is Primary Input) THEN (Final Output is Primary Output)
2. IF (Bonus Input is Bonus Input) THEN (Final Output is Bonus Output)

Total number of rules, number of rules for FIS 1 + number of rules for FIS 2 + number of rules for FIS 3 + number of rules for FIS 4 used is reduced from $45 + 120 + 16 + 2 = 183$ to $11 + 15 + 16 + 2 = 44$ by applying Combs Method. These rule sets are added to the fuzzy inference systems FIS 1, FIS 2, FIS 3 and FIS 4. Then the output of each fuzzy inference system FIS 1, FIS 2 and FIS 3 is analyzed to see if it makes right sense, if not then rules or the input membership functions need to be tweaked. Observations and their analysis are discussed in the next section.

4.8 Observations

In this section, relation between input and output is studied. To study the relation, one input is varied at a time by keeping all other inputs constant and the outcome is observed. Then the process is repeated for the remaining inputs. Inputs which are discrete functions have fixed number of points hence inputs which are continuous functions are varied to observe the output.
4.8.1 Studying Input – Output relation of FIS 1

In this section input – output relation of FIS 1 is studied. Inputs, Number of HLA B Mismatches and Number of HLA DR Mismatches are discrete functions, whereas input Panel Reactive Antibody (PRA) is a continuous function. Hence only input 1(PRA) – Output relation is studied.

4.8.1.1 Input 1(PRA) – Output relation of FIS 1

Figure 4.22 is a graph obtained by setting Number of HLA B Mismatches and Number of HLA DR Mismatches to a constant value ‘1’ and ‘1’ respectively. And PRA is varied from 0 to 100 with an interval of 0.1.

![Graph showing HLA_PRA_Compatibility_Score Vs Panel Reactive Antibody](image-url)

Figure 4-22: HLA_PRA_Compatibility_Score Vs Panel Reactive Antibody
When the input parameter PRA is varied from 0 to 100, it is desired that HLA_PRA_Compatibility_Score should either increase or remain constant but not decrease. But from the Figure 4.22 it is observed that in the interval’s [0 10] and [13 20], HLA_PRA_Compatibility_Score is decreasing as the PRA increases. This is a deviation from the regular pattern given by experts and need to be fixed.

4.8.2 Studying Input – Output relation of FIS 2

In this section input – output relation of FIS 2 is studied. Inputs of FIS 2, HLA_PRA, Age Difference and Travel Distance are all continuous functions. To test the output at one time, only one input is varied in its range by keeping other inputs constant. The same is repeated for the remaining inputs.

4.8.2.1 Input 1 (HLA_PRA) – Output relation of FIS 2

A graph is plotted between input HLA_PRA and output Primary_Compatibility_Score of FIS 2 as shown in Figure 4.23. Graph is generated by keeping the inputs Age Difference at 70 and Travel Distance at 1000.

When the inputs Age Difference and Travel Distance are constant and input HLA_PRA is varied in the range 0 to 100 and the output of FIS 3, Primary_Compatibility_Score, is expected to be increasing or remain
constant. As shown in Figure 4.23 a slight decrease in output is observed in the interval [50 55] and a great decrease in output is seen in the interval [65 75]. This is an anomaly which is to be corrected.

![Figure 4-23: HLA_PRA Vs Primary_Compatibility_Score](image)

**4.8.2.2 Input 2 (Age Difference) – Output relation of FIS 2**

Inputs of FIS 2, HLA_PRA and Travel Distance are kept constant at 100 and 1000. The variation in output (Primary_Compatibility_Score) is observed by varying the input Age Difference from 0 to 70.

Figure 4.24 is the graph plotted between the input Age Difference and output Primary_Compatibility_Score. When the input parameter Age Difference is varied from 0 to 70, it is expected that output should remain
constant or decrease. But from the Figure 4.24, in the intervals [5 10] and [50 60] a slight increase in the output is observed as the input Age Difference increases. It is not in agreement with the expert’s knowledge and needs to be fixed.

![Figure 4-24: Age Difference Vs Primary_Compatibility_Score](image)

**4.8.2.3 Input 3 (Travel Distance) – Output relation of FIS 2**

HLA_PRA is kept constant at 100 and Age Difference at 70 and change in output (Primary_Compatibility_Score) is observed by varying the Travel Distance as shown in Figure 4.25. Range of Travel Distance is [-10 3000]. Negative value (-10) is used to represent Shipped Kidney which is a constant
and values above 400 are also constant and give same output. Hence Travel Distance is varied in the range [0 400] in the intervals of 0.1.

Figure 4.25 is the graph plotted between input Travel Distance and output Primary_Compatibility_Score. As the input Travel Distance varied from 0 to 400, output Primary_Compatibility_Score should decrease or remain constant. But from the Figure 4.25 it is observed that output increases as input is increases in the interval [275 375]. This is not congruent with the expert’s knowledge and it has to be tweaked.

![Figure 4-25: Travel Distance Vs Primary_Compatibility_Score](image)

**Figure 4-25: Travel Distance Vs Primary_Compatibility_Score**
4.8.3 Studying Input – Output relation of FIS 3

In this section input – output relation of FIS 3 is studied. Inputs of FIS 3, Recipient Once a Donor, Cytomegalovirus and Epstein – Barr virus are discrete functions and input Recipient Age is a continuous function.

4.8.3.1 Input 1 (Recipient Age) – Output relation of FIS 3

Recipient Once a Donor, Cytomegalovirus and Epstein – Barr virus are kept constant at 1, 1 and 0 respectively. Recipient Age is varied to observe the output, Bonus_Compatibility_Score. Range of recipient age is [0 100]. When recipient age is varied from 0 to 20 and 40 to 100, output remains constant. Hence recipient age is varied from 20 to 40 to observe the change in output.

![Figure 4-26: Recipient Age Vs Bonus_Compatibility_Score](image)

Figure 4-26: Recipient Age Vs Bonus_Compatibility_Score
A graph is plotted between Recipient Age and Bonus_Compatibility_Score as shown in Figure 4.26. As the Recipient Age increases from 20 to 40, output should decrease or remain constant. But in Figure 4.26 it is observed that output increases in the range [30 38].

A deviation from regular pattern is observed in the outputs of FIS 1, FIS 2 and FIS 3 when inputs of corresponding fuzzy inference systems are varied by keeping remaining inputs constant. The cause for this deviation is analyzed in the next section.
4.9 Analysis of Inconsistencies in Output

In section 4.8, outputs of FIS 1, FIS 2 and FIS 3 are observed to be deviating from the desired pattern when the corresponding inputs are varied in certain range. The deviation occurs because of overlapping of fuzzy sets in inputs and outputs. This section discusses the overlapping problem and a method to overcome it.

4.9.1 Inconsistencies in Output due to Overlapping of Fuzzy Sets

In this section, how overlapping of fuzzy sets leads to deviation of output from the desired pattern is discussed. To explain this problem a generalized fuzzy inference system, FIS 5, with two inputs (input1 and input2) and one output (output) is proposed as shown in Figure 4.27.

![Figure 4-27: Overview of Fuzzy Inference System FIS 5](image)
Input1 is defined in the range [0 100] using two membership fuzzy sets ip1mf1 and ip1mf2 as shown in Figure 4.28.

Figure 4-28: Input1 membership functions of FIS 5

Input2 is defined in the range [0 100] using one membership fuzzy set ip2mf1 as shown in Figure 4.29.

Figure 4-29: Input2 membership functions of FIS 5
Output is defined in the range [0 100] using three membership fuzzy sets opmf1, opmf2 and opmf3 as shown in Figure 4.30.

![Figure 4-30: Output membership functions of FIS 5](image)

Input1 of FIS 5 is used to represent the inputs which were varied to check the output of the corresponding fuzzy inference system. Input2 is used to represent the inputs which were kept constant while varying an input of the fuzzy inference system for observing the output. Output is defined using three fuzzy sets in which two are defined for input1 and one is defined for input2.

Following are the rules defined for FIS 5 using combs method

1. If (input1 is ip1mf1) then (output is opmf1)
2. If (input1 is ip1mf2) then (output is opmf2)
3. If (input2 is ip2mf1) then (output is opmf3)
Now input1 is varied by keeping input2 constant at 50 and output is observed. Output is expected to decrease or remain constant as input1 decreases. An inconsistent pattern of output is observed when the input1 is varied in the range [67 75] as shown in Figure 4.31 and Figure 4.32.

Figure 4-31: Output of FIS 5 as input1 is varying
When input1 is in the interval [67 75], this range lies in the overlapping region of two input fuzzy sets ip1mf1 and ip1mf2. In this region, the output does not agree with the expected output. This is because, in this range, the fuzzified input which lies in two fuzzy sets ip1mf1 and ip1mf2
results in a fuzzified output which lies in two fuzzy sets $\text{op1mf1}$ and $\text{op1mf2}$ with different membership degrees which when defuzzified to a crisp value does not agree with the experts’ knowledge.

Blue area in the output indicates the fuzzified output in terms of membership fuzzy sets $\text{opmf1}$, $\text{opmf2}$ and $\text{opmf3}$. Thick red line in the output is the crisp value of result obtained by defuzzifying the values in blue area. As the input1 value varied from 75 to 67 the output crisp value should move towards 0 or remain constant. In Figure 4.31 output crisp value is shifted towards 0 which is desired. But in Figure 4.32 output crisp value shifts away from 0 which is not desired. This shift is caused because of overlapping of fuzzy sets in input and output.

The deviation of output in FIS 1, FIS 2 and FIS 3 is the shift caused by overlapping of fuzzy sets. To rectify this anomaly, input1 and output of FIS 5 must be represented using fuzzy sets which have minimum overlapping area or with zero overlapping area.

In view of the generalized explanation of abnormality in FIS 5, same solution can be applied to FIS 1, FIS 2 and FIS 3 by defining membership fuzzy sets with no/minimal overlapping area without losing the essence of input/output as defined by experts. Next section discusses the redefinition of input and output membership fuzzy sets of fuzzy inference system FIS 1, FIS 2 and FIS 3 to overcome the inconsistency of output.
4.10 Redefinition of Input and Output Membership Fuzzy Sets

This section discusses the redesigning of membership fuzzy sets of inputs and output of fuzzy inference systems FIS 1 (Figure 4.1), FIS 2 (Figure 4.6) and FIS 3 (Figure 4.12). Depending on the characteristics of inputs/output, a single fuzzy set or multiple fuzzy sets with minimal overlapping area are redefined.

4.10.1 Redefining Inputs and Output of FIS 1

Inputs Number of HLA B Mismatches and Number of HLA DR Mismatches are discrete and have non overlapping membership fuzzy sets, hence they are not redefined. Whereas input Panel Reactive Antibody (PRA) and Output HLA_PRA_Compatibility_Score have overlapping membership fuzzy sets hence they need to be redefined.

4.10.1.1 Redefined Input 1 (Panel Reactive Antibody) of FIS 1

In section 4.1.1.1, fuzzy sets {Very Low, Low, Medium, High, Very High} were used to define the input PRA. All the above fuzzy sets were removed and replaced with one customized fuzzy set PRA as shown in Figure 4.33.
The customized fuzzy set, PRA, is a combination of Triangular Function and Gaussian Function. At any given value of x, PRA is the maximum of Triangular Function value and Gaussian Function value. For example in Fig 3.32, at x = 50 value of Triangular function T1 is 0.35 and value of Gaussian function G1 is 0.2 then the value of PRA is 0.35 (Maximum of 0.2 and 0.35).

In Fig 4.33 at x = 87 value of Triangular function T2 is 0.5 and value of Gaussian function is 0.85 then the value of PRA is 0.85 (Maximum of 0.5 and 0.85). Hence the resultant customized fuzzy set PRA is as shown in Fig 4.34 in next page.
Figure 4-34: Input 1(PRA) of FIS 1
4.10.1.2 Redefined Output (HLA_PRA_Compatibility_Score) of FIS 1

Output HLA_PRA_Compatibility_Score had five membership fuzzy sets {Very Low, Low, Medium, High, Very High} as mentioned in section 4.1.1.4. These membership fuzzy sets are now replaced with new membership fuzzy sets \{op1mf1, op1mf2, op1mf3, op1mf4, op1mf5, op1mf6\} as shown in Figure 4.35.

![Membership function plots](image)

**Figure 4-35: Output (HLA_PRA_Compatibility_Score) of FIS 1**

- Fuzzy set op1mf1 is a combination of Triangular and Gaussian Combination functions. It is defined similar to PRA (Input1 of FIS 1) as shown in Figure 4.33

- Fuzzy sets \{op1mf2, op1mf3, op1mf4, op1mf5, op1mf6\} are Singleton functions
4.10.2 Redefining Inputs and Output FIS 2

Inputs Age Difference, Travel Distance and HLA_PRA and output Primary_Compatibility_Score have overlapping membership fuzzy sets hence they need to be redesigned. Redesigning of inputs and output of FIS 2 is explained in the next section.

4.10.2.1 Redefined Input 1 (Age Difference) of FIS 2

In section 4.2.1.2, four membership fuzzy sets \{Very Low, Low, High, Very High\} were used to define input Age Difference. As shown in Figure 4.36 these membership fuzzy sets are replaced with a single membership fuzzy set, \(AD\), which is defined using Gaussian Combination function.

![Figure 4-36: Input 1 (Age Difference) of FIS 2](image)
4.10.2.2 Redefined Input 2 (Travel Distance) of FIS 2

Input Travel Distance, as mentioned in section 4.2.1.3, had six fuzzy sets {Home Transplant Center (HTC), Home City (H), Adjoining City (AC), One Day Drive (ODD), Airplane Trip (AT), Shipped Kidney(S)}. To overcome the overlapping problem, input 2, travel distance, is redesigned using new fuzzy sets as shown in Figure 4.37.

Figure 4-37: Input 2 (Travel Distance) of FIS 2

Input Travel Distance is in the range [-10 3000] as shown in the Figure 4.37, the membership fuzzy sets TD1, TD2 and TD4 are concentrated in the left corner and are not very well visible.
In order to give an expanded view of membership fuzzy sets TD1, TD2 and TD4, a new Figure 4.38 is drawn with travel distance in the range [-10 30].

![Figure 4-38: Membership Fuzzy Sets TD1, TD2 and TD4 of Input 2](image)

A brief description of membership fuzzy sets TD1, TD2, TD3 and TD4 are given below.

- TD1: Singleton function is used to define this fuzzy set. It is used to represent the case Donor and Recipient are from Same Transplant Center
- TD2: Triangular function is used to define this fuzzy set. It covers the case Donor and Recipient transplant centers are in Same City
• TD3: Trapezoidal function is used to define this fuzzy set. It covers the cases Donor and Recipient Transplants are in Adjoining Cities or Within One Day Drive or Airplane Trip

• TD4: Singleton function is used to define this fuzzy set. It is used to represent the case of when Kidney needs to be shipped (Shipped Kidney)

4.10.2.3 Redefined Input 3 (HLA_PRA) of FIS 2

In section 4.2.1.1, five fuzzy sets {Very Low, Low, Medium, High, Very High} were used to represent input HLA_PRA. To overcome the problems associated with the membership as explained in section 4.8, many membership fuzzy sets were tried. After a great deal of fine tuning keeping in consideration the expert knowledge, a linear function was proposed as shown in Figure 4.39 which gave the best results.

Figure 4-39: Input 3 (HLA_PRA) of FIS 2
4.10.2.4 Redefined Output (Primary_Compatibility_Score) of FIS 2

Output Primary_Compatibility_Score had five fuzzy sets \{Very Low, Low, Medium, High, Very High\} as mentioned in section 4.2.1. A single fuzzy set cannot be used to redefine the output; hence more than one fuzzy set are used as shown in Figure 4.40.

![Figure 4-40: Output (Primary_Compatibility_Score) of FIS 2](image)

Following are the fuzzy sets used to define Primary_Compatibility_Score

- op2mf1, op2mf3 and op2mf4 fuzzy sets are redefined using Gaussian Combination function
- op2mf2, op2mf5 and op2mf6 fuzzy sets are redefined using Triangular function
4.10.3 Redefining Inputs and Output of FIS 3

Inputs Recipient Once a Donor, Cytomegalovirus and Epstein – Barr virus are discrete and have non overlapping membership fuzzy sets hence they need not be redesigned. Whereas input Recipient Age and Output Bonus_Compatibility_Score have overlapping fuzzy sets hence they need to be redesigned. Later section discusses the redesigning of inputs and output of FIS3.

4.10.3.1 Redefined Input 1 (Recipient Age) of FIS 3

In section 4.3.1.1, input Recipient Age was defined using two fuzzy sets {Less, High}. A single fuzzy set, RA, is used to represent input Recipient Age as shown in Figure 4.41. A Sigmoid function is used to define the fuzzy set RA.

Figure 4.41: Input 1 (Recipient Age) of FIS 3
4.10.3.2 Redefined Output (Bonus_Compatibility_Score) of FIS 3

Output Bonus_Compatibility_Score was defined using three fuzzy sets {Low, Medium, High} as mentioned in section 4.3.1.5. A single fuzzy set cannot be used to represent the output hence multiple fuzzy sets {op3mf1, op3mf2, op3mf3, op3mf4, op3mf5, op3mf6, op3mf7} are used to represent the output as shown in Fig 4.42.

![Graph showing membership function plots for fuzzy sets](image)

Figure 4-42: Output (Bonus_Compatibility_Score) of FIS 3

- All membership fuzzy sets are defined using Triangular functions
4.11 Transformation of Rules of FIS 1, FIS 2 and FIS 3

In section 4.10 Inputs and Output of FIS 1, FIS 2 and FIS 3 are redefined with new fuzzy sets. Rules of fuzzy inference systems FIS 1, FIS 2 and FIS 3 defined in sections 4.7.1, 4.7.2 and 4.7.3 with old fuzzy sets will be updated with new fuzzy sets. As the number of fuzzy sets used by inputs and output of FIS 1, FIS 2 and FIS 3 are reduced, number of rules used by each fuzzy inference system is automatically decreased.

For example in section 4.7.3, following were the rules used for input Travel Distance of FIS 2 were

1. If (Travel Distance is Home Transplant Center) Then (Primary_Compatibility_Score is Very High)
2. If (Travel Distance is Home City) Then (Primary_Compatibility_Score is High)
3. If (Travel Distance is Adjoining Cities) Then (Primary_Compatibility_Score is Average)
4. If (Travel Distance is One Day Drive) Then (Primary_Compatibility_Score is Low)
5. If (Travel Distance is Airplane Trip) Then (Primary_Compatibility_Score is Very Low)
6. If (Travel Distance is Shipped Kidney) Then (Primary_Compatibility_Score is Very Low)
Since the membership fuzzy sets of input 2 (Travel Distance) and output (Primary_Compatibility_Score) of FIS2 are redefined with new fuzzy sets \{TD1, TD2, TD3, TD4\} and \{op2mf2, op2mf3, op2mf4, opemf5\} respectively, the above rules will be changed to

1. If (Travel.Distance is TD3)
   Then (Primary.Compatibility.Score is op2mf4)
2. If (Travel.Distance is TD1)
   Then (Primary.Compatibility.Score is op2mf2)
3. If (Travel.Distance is TD2)
   Then (Primary.Compatibility.Score is op2mf3)
4. If (Travel.Distance is TD4)
   Then (Primary.Compatibility.Score is op2mf5)

Similarly rules defined for FIS 1 in section 4.7.1 will be modified to

1. If (HLA.B is 0) then (HLA.PRA.Compatibility.Score is op1mf4)
2. If (HLA.B is 1) then (HLA.PRA.Compatibility.Score is op1mf3)
3. If (HLA.B is 2) then (HLA.PRA.Compatibility.Score is op1mf2)
4. If (HLA.DR is 0) then (HLA.PRA.Compatibility.Score is op1mf6)
5. If (HLA.DR is 1) then (HLA.PRA.Compatibility.Score is op1mf5)
6. If (HLA.DR is 2) then (HLA.PRA.Compatibility.Score is op1mf4)
7. If (PRA is PRA) then (HLA.PRA.Compatibility.Score is op1mf1)
Rules defined for FIS 2 in section 4.7.2 will be changed to

1. If (Age.Difference is AD)
   Then (Primary.Compatibility.Score is op2mf1)

2. If (Travel.Distance is TD3)
   Then (Primary.Compatibility.Score is op2mf4)

3. If (Travel.Distance is TD1)
   Then (Primary.Compatibility.Score is op2mf2)

4. If (Travel.Distance is TD2)
   Then (Primary.Compatibility.Score is op2mf3)

5. If (Travel.Distance is TD4)
   Then (Primary.Compatibility.Score is op2mf5)

6. If (HLA.PRA is HLA.PRA)
   Then (Primary.Compatibility.Score is op2mf6)

Rules defined for FIS 3 in section 4.7.3 will be updated to

1. If (Recipient.Age is RA)
   Then (Bonus.Compatibility.Score is op3mf1)

2. If (Donor? is Donor.Yes)
   Then (Bonus.Compatibility.Score is op3mf3)

3. If (Donor? is Donor.No)
   Then (Bonus.Compatibility.Score is op3mf2)

4. If (CMV is CMV.Both.Negative)
   Then (Bonus.Compatibility.Score is op3mf5)
5. If (CMV is CMV.Atleast.One.Positive) 
   Then (Bonus.Compatibility.Score is op3mf4)

6. If (EBV is EBV.Both.Negative) 
   Then (Bonus.Compatibility.Score is op3mf7)

7. If (EBV is EBV.Atleast.One.Positive) 
   Then (Bonus.Compatibility.Score is op3mf6)

Fuzzy inference systems FIS 1, FIS 2 and FIS 3 are updated with new fuzzy sets and new rules. These fuzzy inference systems, FIS 1, FIS 2 and FIS 3, are then updated in Hierarchical Fuzzy Inference System defined in section 3.2. Kidney Compatibility Score for a Donor - Recipient pair is generated when a set of input parameters are passed to hierarchical fuzzy inference system. Next section discusses the process of extracting the data in suitable format which can be passed to the hierarchical fuzzy inference system from the Input Data provided by the Kidney Transplant Surgeon.
Chapter 5

Comparative Analysis of Results of Hierarchical Fuzzy Inference System with the decision of Kidney Transplant Surgeon

In this chapter, results are generated by passing input parameters to the hierarchical fuzzy system redefined in section 4.10. The output generated is the Kidney Compatibility Score given to a Donor – Recipient pair. This compatibility score is used for selecting the pairs which are eligible for a quality transplant.

When two Donor – Recipient pairs (A1, B1), (A2, B2) are considered, it is not possible to compare the relevance of their scores, as there is no commonality between the two pairs (A1, B1), (A2, B2). Therefore following two different cases are analyzed.

- Fixed Donor Multiple Recipients (For example: (A1, B1), (A1, B2))
- Multiple Donors Fixed Recipient (For example: (A1, B1), (A2, B1))

In case 1, Fixed Donor Multiple Recipients, donor is fixed and all possible recipients to whom the donor can give his kidney are considered as a set. In case 2, Multiple Donors Fixed Recipient, recipient is fixed and all
possible donors from whom the recipient can accept the kidney are considered as a set. By keeping either Donor or Recipient constant comparison of two pairs becomes easier. Later sections discuss the above mentioned cases in detail.

5.1.1 Fixed Donor Multiple Recipients

In this section, five sets of fixed donor multiple recipients are tested. In each set, donor is fixed and all possible recipients for that donor are listed. Output of each set is reviewed by an expert.

Due to the space limitation, column names of input data tables and output tables are represented using alphabets and their description is provided in Table 5.1 and Table 5.2 respectively.

Table 5.1: Column Description of Input Data Tables

<table>
<thead>
<tr>
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Table 5.2: Description of Columns of Output Tables

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5.1.1.1 Analysis of Test Set 1

In this section, all possible recipients who can receive kidney from a donor whose DonorID (an identifier used to identify a Donor uniquely) is 10006125 are considered. Each Donor – Recipient pair is uniquely identified by Case ID. Input parameters for each pair are listed in Table 5.3.

Table 5.3: Input Values of Fixed Donor (10006125) - Multiple Recipients

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Each row (all columns except column A) in Table 5.3 represents a set of input parameters of Donor – Recipient pair with Case ID present in column A. They are passed as input to the hierarchical fuzzy inference system. Output values generated are listed in Table 5.4. Descriptions of columns of Table 5.4 are given in Table 5.2.

Table 5.4: Output values of Fixed Donor (10006125) - Multiple Recipients

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Column ‘A’ of Table 4.4 is the Case ID which helps in identifying each row uniquely. Columns E, J, O and P are the outputs of fuzzy inference systems FIS 1, FIS 2, FIS 3 and FIS 4 respectively.

From Table 5.4 it is observed in column P, the highest three scores are 7.4, 6.98 and 6.34 and they belong to Donor – Recipient pair Case ID’s 243, 1 and 337 respectively.

To verify the validity of score generated by hierarchical fuzzy inference system, an expert’s opinion was taken. The expert, a Kidney Transplant Surgeon, was asked to evaluate the input data which is in Table 5.2 and asked to select the best three choices.

Surgeon’s choice was 337, 243 and 1. Case ID 337 picked as his first choice because the values 62 and 0 of PRA and HLA DR mismatches respectively were more important than 1.61 years of waiting time of Case ID 243.

5.1.1.2 Analysis of Test Set 2

In this section, a donor whose DonorID is 10006570 is fixed and all possible recipients are considered. Input parameters for each Donor – Recipient pair are listed in Table 5.5 and the column descriptions were provided in Table 5.1.
Table 5.5: Input Values of Fixed Donor (10006570) - Multiple Recipients

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Each row in Table 5.5 except column ‘A’ are the input parameters passed to hierarchical fuzzy inference system. Output values generated are listed in Table 4.6. Column descriptions of Table 5.6 are listed in Table 5.2.

Columns E, J, O and P of Table 5.6 are the outputs of fuzzy inference systems FIS 1, FIS 2, FIS 3 and FIS 4. Column P is the final output score given to the Donor – Recipient pairs.
As seen from column P 9.45, 7.88 and 6.99 are the highest three scores which belong to Case ID’s 314, 33 and 342. After analyzing input data table 5.5, his top three picks were 18, 160 and 294. Following comments were given after analyzing the results generated by the hierarchical fuzzy inference system. The system favors Donor – Recipient pairs who are from the same Transplantation Center and implies that Panel Reactive Antibody is more important than HLA B matching.
5.1.1.3 Analysis of Test Set 3

This section discusses the test set whose DonorID is 10006395 and all its possible recipients. Input parameters of Donor – Recipient pairs of this test set are listed in Table 5.7. Column descriptions are provided in Table 5.1.

Table 5.7: Input Values of Fixed Donor (10006395) - Multiple Recipients

| A | B | C | D | E  | F  | G  | H   | I  | J  | K 
|---|---|---|---|----|----|----|-----|----|----|---
| 3 | 3 | 1 | 1 | 2.7 | 582 | 1.95 | 61.08 | 0  | 0  | 0 
| 19 | 37 | 2 | 2 | 0.17 | 582 | 1.97 | 58.55 | 0  | 0  | 0 
| 34 | 0 | 1 | 1 | 12.67 | 529 | 1.88 | 71.05 | 0  | 0  | 0 
| 51 | 0 | 2 | 1 | 1.22 | 468 | 1.68 | 59.6  | 0  | 1  | 0 
| 73 | 0 | 2 | 2 | 11.98 | 178 | 1.89 | 70.36 | 0  | 0  | 0 
| 74 | 0 | 2 | 2 | 11.98 | 178 | 1.89 | 70.36 | 0  | 0  | 0 
| 110 | 0 | 1 | 2 | 1.96 | 5  | 0.05 | 56.42 | 0  | 0  | 0 
| 127 | 0 | 2 | 2 | 6.39 | 933 | 1.82 | 51.99 | 0  | 0  | 0 
| 144 | 0 | 2 | 1 | 2.76 | 567 | 1.83 | 61.14 | 0  | 0  | 0 
| 161 | 24 | 2 | 2 | 12.76 | 582 | 2    | 71.14 | 0  | 0  | 0 
| 179 | 0 | 1 | 2 | 6.7  | 1112 | 1.71 | 65.08 | 0  | 1  | 0 
| 196 | 0 | 2 | 1 | 6.75 | 178 | 1.91 | 51.63 | 0  | 1  | 0 
| 213 | 19 | 1 | 2 | 5.57 | 567 | 1.85 | 52.81 | 0  | 0  | 0 
| 248 | 0 | 1 | 2 | 7.83 | 1630 | 1.5  | 66.21 | 0  | 0  | 0 
| 278 | 0 | 2 | 2 | 17.71 | 567 | 0.36 | 76.09 | 0  | 0  | 0 
| 302 | 10 | 2 | 2 | 13.82 | 5  | 0.35 | 44.56 | 0  | 1  | 0 
| 315 | 10 | 2 | 2 | 18.83 | 529 | 0.33 | 39.55 | 0  | 0  | 0 
| 338 | 62 | 2 | 2 | 15.34 | 370 | 0.3  | 43.04 | 0  | 0  | 0 
| 343 | 17 | 2 | 2 | 6.8  | 529 | 0.27 | 65.18 | 0  | 0  | 0 
| 355 | 0 | 1 | 1 | 3.57 | 406 | 0.21 | 61.95 | 0  | 0  | 0 
| 384 | 57 | 1 | 1 | 11.08 | 139 | 0.15 | 47.3  | 0  | 0  | 0 
| 399 | 0 | 1 | 2 | 7.97 | 49  | 0.2  | 66.35 | 0  | 0  | 0 
| 416 | 0 | 1 | 2 | 1.09 | 1630 | 0.18 | 57.29 | 0  | 1  | 0 
| 444 | 0 | 2 | 2 | 3.78 | 49  | 0.12 | 62.16 | 0  | 0  | 0 
| 461 | 0 | 2 | 2 | 4.71 | 49  | 0.11 | 63.09 | 0  | 0  | 0 

97
Columns B through K of Table 5.7 are the input parameters which are passed to hierarchical fuzzy inference system and the output values are listed in Table 5.8. Column descriptions of Table 5.8 are listed in Table 5.2.

Output of FIS 1, FIS 2, FIS 3 and FIS 4 are in columns E, J, O and P of Table 5.8 respectively. Output of FIS 4 is the final compatibility score given to Donor – Recipient pair with Case ID listed in Column A.

Table 5.8: Output values of Fixed Donor (10006395) - Multiple Recipients

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</tbody>
</table>

98
Hierarchical Fuzzy Inference system picks pairs with Case ID’s 196, 51 and 179 as best three choices with scores 8.16, 8.12 and 7.11 respectively as listed in Column P of Table 5.8.

Kidney Transplant surgeon is asked to pick his best three choices by evaluating the data provided in Table 5.7. His best three choices were 384, 19 and 3. The selection of pairs was different because the Hierarchical Fuzzy Inference system was giving more priority for CMV negative for both Donor and Recipient. Whereas Surgeon feels 1 HLA B match or 1 HLA DR match or 3 months of Waiting Time have more priority than CMV negative.

5.1.1.4 Analysis of Test Set 4

In this section a Donor with DonorID 10047734 is fixed and all possible Recipients for this donor are analyzed. Input parameters are listed in the Table 5.9 and its column descriptions are provided in Table 5.1.

Table 5.9: Input Values of Fixed Donor (10047734) - Multiple Recipients

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
<th>H</th>
<th>I</th>
<th>J</th>
<th>K</th>
</tr>
</thead>
<tbody>
<tr>
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<td>57.62</td>
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<td>0</td>
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<tr>
<td>2</td>
<td>266</td>
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<td>1</td>
<td>1</td>
<td>11.68</td>
<td>1291</td>
<td>1.52</td>
<td>58.88</td>
<td>0</td>
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<tr>
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<td>270</td>
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<td>1</td>
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</tr>
</tbody>
</table>

Columns B through K of Table 5.9 are passed as inputs to the hierarchical fuzzy inference system and output values are listed in Table 5.10 and their column descriptions are provided in Table 5.2. Columns E, J, O and P of Table 5.10 are the outputs of FIS 1, FIS 2, FIS 3 and FIS 4 respectively.
Table 5.10: Output Values of Fixed Donor (10047734) - Multiple Recipients

<table>
<thead>
<tr>
<th></th>
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<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
<th>H</th>
<th>I</th>
<th>J</th>
<th>K</th>
<th>L</th>
<th>M</th>
<th>N</th>
<th>O</th>
<th>P</th>
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<td>0.68</td>
<td>2.01</td>
<td>0.5</td>
<td>1.64</td>
<td>0.68</td>
<td>4.83</td>
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</tr>
<tr>
<td>266</td>
<td>5.9</td>
<td>0.5</td>
<td>1</td>
<td>7.38</td>
<td>1.89</td>
<td>0.5</td>
<td>1.52</td>
<td>7.38</td>
<td>11.29</td>
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<td>0</td>
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<td></td>
</tr>
<tr>
<td>270</td>
<td>4.5</td>
<td>0.5</td>
<td>1</td>
<td>6</td>
<td>2.61</td>
<td>0.75</td>
<td>0.38</td>
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<td>9.74</td>
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</tr>
</tbody>
</table>

Using Column P, final compatibility score given to a Donor – Recipient pair, Hierarchical Fuzzy Inference system ranks the pair 266 with score 11.29 in first place, pair 270 with score 9.74 in second place and pair 233 in third place with score 4.83.

Surgeon was asked to give his preference order by analyzing the input data table 5.9. His top three preferences were 266, 270 and 233 which is matching with the top three choices of Hierarchical Fuzzy Inference System.

5.1.1.5 Analysis of Test Set 5

In this section a Donor with DonorID 30001174 is fixed and all possible recipients of that donor are considered. Table 5.11 lists the input parameters for the above Donor – Recipient pairs. Table 5.1 provides the column descriptions of Table 5.11.

Table 5.11: Input Values of Fixed Donor (30001174) - Multiple Recipients

<table>
<thead>
<tr>
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<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
<th>H</th>
<th>I</th>
<th>J</th>
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<th>O</th>
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<td>2065</td>
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<td>0</td>
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<td></td>
</tr>
<tr>
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<td>1</td>
<td>0.23</td>
<td>457</td>
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<td>44.56</td>
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</tr>
<tr>
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<td>2065</td>
<td>0.18</td>
<td>57.29</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>
Hierarchical fuzzy inference system takes columns B through K of Table 5.11 as input parameters. Output values generated are listed in Table 5.12. Column descriptions of Table 5.12 are provided in Table 5.2. Outputs of FIS 1, FIS 2, FIS 3 and FIS 4 are listed in columns E, J, O and P of Table 5.12 respectively.

Table 5.12: Output Values of Fixed Donor (30001174) - Multiple Recipients

<table>
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<td>1.9</td>
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</table>

It is evident from column P of Table 5.12 that highest matching score is 7.71 which belongs to pair with Case ID 312. 5.42 is the next highest score which belongs to pair with Case ID 429 and pair with Case ID 261 stands last among three with score 3.84.

Table 5.11 is given to the Transplant Surgeon and asked to rank the pairs in decreasing order of his preference. His three choices were 261, 312 and 429. Case ID 261 was his first because 1.5 years of waiting time was more important than small Age Difference and CMV both Negative of Case ID 312. Case ID 261 also outweighs the combination of small Age Difference, CMV both Negative and HLA B Matches of Case ID 429.
5.1.1.6 Analysis of Test Set 6

In this section Recipient with RecipientID 10006395 is fixed and all possible Donors who can give their kidney to the above recipient are considered. Input parameters are listed in the Table 5.13. Column descriptions are provided in Table 5.1.

Columns B through K of Table 5.13 are the input parameters which are passed to hierarchical fuzzy inference system.

Table 5.13: Input Values of Multiple Donors - Fixed Recipient (10006395)

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<th>D</th>
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</tr>
</tbody>
</table>

Table 5.14 lists the Output values generated by the hierarchical fuzzy inference system. Column descriptions of Table 5.14 are given in Table 5.2.
Columns E, J, O and P of Table 5.14 are the outputs of FIS 1, FIS 2, FIS 3 and FIS 4 respectively.

Table 5.14: Output Values of Multiple Donors – Fixed Recipient (10006395)

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<th>C</th>
<th>D</th>
<th>E</th>
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The top three picks of the Hierarchical Fuzzy Inference system are 1, 3 and 13 with scores 6.98, 6.86 and 6.48 respectively. Selection is based on the pair compatibility scores listed in Column P of Table 5.14.

Surgeon’s choice after analyzing the table 5.13 was 1, 3 and 13 and it matches with the fuzzy system’s choice. His choice was mainly based on the inputs HLA B, HLA DR and Age Difference as inputs PRA, Waiting Time and Recipient Age were constant.
5.1.1.7 Analysis of Test Set 7

In this section all possible Donors for the Recipient with RecipientID 10006408 are considered. Their input parameters are listed in Table 5.15. Column descriptions of Table 5.15 are listed in Table 5.1.

Table 5.15: Input Values of Multiple Donors – Fixed Recipient (10006408)

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Inputs which are passed as parameters to the hierarchical fuzzy inference system are listed in Columns B through K of Table 5.15. Output values generated are listed in Table 5.16. Column descriptions of table 5.16 are provided in Table 5.2.

Output of FIS 1, FIS 2, FIS 3 and FIS 4 are listed in Columns E, J, O and P of Table 5.16.
Table 5.16: Output Values of Multiple Donors – Fixed Recipient (10006408)

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Based on Column P, final compatibility score given to the Donor – Recipient pairs, highest three scores given by the Hierarchical Fuzzy Inference system are 8.29, 8.11 and 8.08 which belong to Case ID’s 27, 30 and 29 respectively.

Transplant Surgeon was asked to pick his best three choices by analyzing the input data table 5.15. Pairs with Case ID’s 20, 27 and 30 were his three choices. Case ID 20 was his first preference because, Number of HLA DR Mismatches was 0 and Number of HLA B Mismatches was 1. Fuzzy System was not picking pair with Case ID 20 in top three choices because of 26.3 years of Age Difference.
5.1.1.8 Analysis of Test Set 8

In this section Recipient with RecipientID 30001717 is fixed and all possible donors are considered. Input parameters are listed in Table 5.17 and their column descriptions are provided in Table 5.1.

Table 5.17: Input Values of Multiple Donors – Fixed Recipient (30001717)

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Inputs which are passed as input parameters to hierarchical fuzzy inference system are present in Columns B through K of Table 5.17. Output values are listed in Table 5.18 and their column descriptions are listed in Table 5.2. Values in Column P of Table 5.18 are the final compatibility scores given to the Donor – Recipient pairs.

Table 5.18: Output Values of Multiple Donors – Fixed Recipient (30001717)

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As seen from Column P of table 5.18 it is evident that Hierarchical Fuzzy Inference system picks Case ID’s 441, 436 and 439 as three best pairs with scores 13.3, 11.54 and 9.57 respectively.

To compare the results generated by fuzzy system, Transplant Surgeon was asked to pick three most important pairs by analyzing input data table 5.17. Pair with Case ID 439 was his first choice. Both pairs with Case ID 441 and 436 were almost equally eligible for his second choice. Choice made by the surgeon is matching with the choice made by the fuzzy system but the preference order is different.

Cause for the difference in preference order is analyzed as follows. Hierarchical Fuzzy Inference system picked Case ID 441 in first place because Donor – Recipient pair are from same transplantation center. Case ID 436 in second place because CMV of both Donor and Recipient is Negative and the Age Difference between Donor and Recipient is small. And Case ID 439 in third place because of number of mismatches in HLA DR was 0. But according to surgeon HLA DR 0 mismatches should be of highest priority. Hence Case ID 439 was his first choice among three pairs. Surgeon was not able to make a choice between pairs 441 and 436 because the overall value of inputs was nearly same.
5.1.1.9 Analysis of Test Set 9

In this section all possible Donors for Recipient with RecipientID 30001458 are considered. Input parameters are listed in Table 5.19 and their column descriptions are provided in Table 5.1.

Columns from B through K of Table 5.19 are passed as input parameters to hierarchical fuzzy inference system

Table 5.19: Input Values of Multiple Donors – Fixed Recipient (30001458)

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<th>D</th>
<th>E</th>
<th>F</th>
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Output values generated by fuzzy system are listed in Table 5.20 and their column descriptions are provided in Table 5.2. Output of FIS 1, FIS 2, FIS 3 and FIS 4 are listed in Columns E, J, O and P of Table 5.20.
Table 5.20: Output Values of Multiple Donors – Fixed Recipient (30001458)

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It is observed from Column P of Table 5.20 that 7.08, 6.67 and 6.57 are the three highest scores given to the pairs with Case ID’s 394, 393 and 388 respectively by Hierarchical Fuzzy Inference system.

To cross check the selection made by the fuzzy system Transplant Surgeon is asked to pick three best pairs by analyzing input data table 5.19. His choice was 393, 384 and 387. Case ID 393 was his first choice as the Number of HLA DR Mismatches was 0 and Number of HLA B Mismatches was 1. Case ID’s 384 and 387 were second and third choice because of small Age Difference among the pairs with 1 HLA DR Mismatch and 1 HLA B Mismatch. Inputs HLA DR and HLA B mismatches were primarily used to make decisions. After that input Age Difference was used in selecting the pairs.
### 5.1.1.10 Analysis of Test Set 10

In this case Recipient with RecipientID 30000635 is fixed and all possible donors are considered. Input values are listed in Table 5.21 and their column descriptions are given in Table 5.1.

#### Table 5.21: Input Values of Multiple Donors – Fixed Recipient (30000635)

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</table>

Columns from B through K are passed as input parameters to the hierarchical fuzzy inference system and Output values are listed in Table 5.22 and their column descriptions are listed in Table 5.2. Columns E, J, O and P of Table 5.22 are outputs of FIS 1, FIS 2, FIS 3 and FIS 4.

#### Table 5.22: Output Values of Multiple Donors – Fixed Recipient (30000635)

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<th>E</th>
<th>F</th>
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After analyzing the values listed in Column P of Table 5.22, pairs with Case ID’s 299, 296 and 294 are the top three choices made by Hierarchical Fuzzy Inference system with scores 6.98, 6.92 and 6.17 respectively.

When the Transplant Surgeon was asked to analyze the table 5.21 and give his top three picks, his choice was 296, 299 and 294. Pairs picked by fuzzy system and surgeon are same but the first and second choice are different. Surgeon picked 296 as first choice because it is more worthy to pick the Case ID 296 with Donor – Recipient Age Difference of 1.23 years and Travelling Distance 985 miles rather than picking Case ID 299 with Age Difference of 0.18 years and Travelling Distance 2405 miles.

5.2 Summary

In this chapter, ten different data sets were analyzed. The best picks of our Hierarchical Fuzzy Inference system were compared with what a Kidney Transplant Surgeon would have picked without the help of Hierarchical Fuzzy Inference system.

It was found that in the majority of instances, the best picks were same, however, the ranking of the best picks were different. The possible explanation for this difference in choices was analyzed. Our fuzzy system is unbiased and once the rules are fixed then it evaluates all the cases according to those rules. Sometimes surgeon’s choice can be influenced by the individual preferences.
However, aim of our fuzzy system is not to finalize the pair for transplant, but to present the pairs which have highest priority from the pool of Donor – Recipient pairs to the Kidney Transplant Surgeons. Surgeons can use this filtered list to finalize the pairs for Kidney Transplant.
Conclusion and Future Work

This thesis tackled the problem of filtering the Donor – Recipient pairs from the pool of Donor – Recipient pairs who have been waiting over a period of time using an Artificial Intelligence technique based on Fuzzy Logic. The proposed approach is based on the evaluation of if – then rules to predict the quality of the Kidney Transplant.

In first phase, input parameters were grouped into Group A, Group B and Group C based on their priority. Group A had highest priority parameters and Group C with the lowest. A Hierarchical model was proposed based on the parameters listed in Group A, Group B and Group C.

In second phase, the proposed hierarchical model was constructed using Fuzzy Inference Systems. Fuzzy Inference Systems FIS 1, FIS 2, FIS 3 and FIS 4 were created by defining membership functions for inputs and outputs and by incorporating rules designed based on the expert’s (Surgeon) knowledge. Input data was passed to generate results using the hierarchical fuzzy inference system.
The results generated were compared against the choices made by the Kidney Transplant Surgeon. In most instances results generated were in agreement with the surgeon's decision. In few cases, choices made by the surgeon and fuzzy system were same but the preference were different. Feedback given by the expert (surgeon) leaves a room for improving the results in future. As the knowledge of the fuzzy inference system lies in its rules, rules can be tuned to improve the final output.
References


