Chapter 2

Review of Related Research

2.1 Medical Diagnostic Protocol

The underlying intelligence of MAS is the domain specific protocol. For instance there is a medical diagnostic protocol that is used by caregivers and other healthcare practitioners to follow a systematic approach to categorize diseases or patients. Such a protocol can be used to embed intelligence in MAS.

In 2003, World Health Organization and Ministry of Health and Family have come up with a protocol called Integrated Management of Neonatal and Childhood, India (IMNCI)[16]. The aim of this protocol is to apply an organized approach to the children's health by defining the prevalent diseases and their respective treatment plans. This protocol is meant for treating outpatients at primary healthcare centers/ rural healthcare facilities. The most common illnesses among the children under 3 years of age include fever (27%), acute respiratory infections (17% ), diarrhoea (13% ) and malnutrition (43%). Keeping this statistics in mind, the protocol gives more emphasis on tackling these diseases. It also outlines the inequities of health care facilities in India.

The management of the children is divided into two parts:

- Young infants age up to 2 months
- Children age 2 months up to 5 year
Furthermore, the diagnostic process is again divided into two phases. During the first phase, the child is assessed and classified against a disease, whereas during the second phase the severity level of disease as well as the treatment plan is decided. The overall structure of the diagnostic process is depicted in Figure 2.1.

For all sick children age up to 5 years who are brought to a first-level health facility

ASSESS the child: Check for danger signs (or possible bacterial infection / Jaundice). Ask about main symptoms. If a main symptom is reported, assess further. Check nutrition and immunization status. Check for other problems.

CLASSIFY the child's illness: Use a colour-coded triage system to classify the child's main symptoms and his or her nutrition or feeding status.

IF URGENT REFERRAL is needed and possible

IDENTIFY URGENT PRE-REFERRAL TREATMENT(S)
Needed for the child's classifications.

TREAT THE CHILD: Give urgent pre-referral treatment(s) needed.

REFER THE CHILD: Explain to the child's caretaker the need for referral. Calm the caretaker's fears and help resolve any problems. Write a referral note. Give instructions and supplies needed to care for the child on the way to the hospital.

FOLLOW-UP care: Give follow-up care when the child returns to the clinic and, if necessary, reassess the child for new problems.

IF NO URGENT REFERRAL is needed or possible

IDENTIFY TREATMENT needed for the child's classifications: Identify specific medical treatments and/or advice.

TREAT THE CHILD: Give the first dose of oral drugs in the clinic and/or advise the child's caretaker how to give oral drugs and how to treat local infections at home. If needed, give immunizations.

COUNSEL THE MOTHER: Assess the child's feeding, including breastfeeding practices, and solve feeding problems. If present, advise about feeding and fluids during illness and about when to return to a health facility. Counsel the mother about her own health.

Figure 2.1 Overall structure of the IMNCI protocol

* Adopted from IMNCI protocol [16]
2.1.1 Infants Up to Two months of age:
During the first phase, the HCP follows the following step-wise procedure:

**Phase 1**
- Step 1: Assess and classify a young infant for bacterial infection
- Step 2: Assess and classify a young infant for jaundice
- Step 3: Assess and classify a young infant with diarrhea
- Step 4: Check for the feeding problem or malnutrition, assessing breastfeeding and classifying feeding and immunization

**Phase 2**
After assessing the infant for various sign-symptoms, healthcare practitioner then refers this protocol for administering the treatment. During this phase, the objective is to decide the treatment plans such as: giving antibiotics orally, treating local infection, or providing emergency treatment. The referral cases are also decided. Figure 2.2 shows the whole diagnostic process followed for young infants up to two months.

2.1.2 Children age 2 months up to 5 years
The step-wise procedure that is followed at a rural dispensary is given below:

**Phase 1**
- Step 1: Asking the mother about the child's problem.
- Step 2: Checking for general danger signs.
- Step 3: Asking the mother about the main symptoms.
- Step 4: If the main symptom is present, then,
  a. Assess the child further for signs related to the main symptom
  b. Classify the illness according to the signs which are present or absent.
- Step 5: Checking for the signs of malnutrition and anaemia and classifying the child's nutritional status.
- Step 6: Checking the child's immunization status and deciding if the child needs any immunizations today, and finally
- Step 7: Assessing any other problems
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Figure 2.2 Structure of the IMNCI protocol for the Sick Young Infant up to 2 Months of Age

Phase 2

After completing the assessment and classification procedure, the next important step is to identify the treatment. The protocol gives more emphasis on the actions that need to be taken. All classifications are color-coded: pink calls for hospital referral or admission, yellow for the initiation of the treatment, and green means that the child can be sent home with a careful advice on when to return, as shown in Figure 2.3. If the patient is continuously convulsing, or suffering from severe pneumonia, or having complicated measles, or suffering from dehydration, or having persistent diarrhoea then

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b Adopted from IMNCI protocol [16]
Medical diagnostic protocol

he should be referred to a hospital. The referral patients are treated with the medications such as: Appropriate antibiotics, Quinine (for severe malaria), Vitamin A, Prevention of hypoglycemia with the breastmilk or sugar water, Oral antimalarial, Paracetamol for high fever (38.5°C or above) or pain, Tetracycline eye ointment, and ORS solution so that the mother can give frequent sips on the way to the hospital. Similarly, for non-referral patients, oral drugs are administered and where there are no-urgent cases, just monitor and counsel mothers.

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**Figure 2.3** Structure of the IMNCI protocol for the Sick Child from Age 2 Months up to 5 Years

Adopted from IMNCI protocol [16]
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This protocol is to be used for developing MAS wherein one agent will act on the part of HCP at rural center and another as a pediatrician. In the next section, various MASs in healthcare domain are discussed.

2.2 Multi-agent systems in Healthcare

Software agents are proving to be promising because of their reactive, proactive, autonomous, collaborative and knowledge-sharing capabilities.

In paper [17] the authors have discussed various challenges in the application of agent-based systems in health care environment. But they have argued that multi-agent systems have a set of characteristics that make them appropriate to be used to improve the provision of health care. To justify the point, they outlined the already developed application in this domain viz., agent-based appointment scheduling, patient information retrieval and workflow management, heterogeneous transaction workflow process among the people involved in the patient care management and the agent-based coordination of tissue or organ transplants across a hospital.

A browsing assistant agent called ‘Letizia’ has been developed [18]. It tries to find serendipitous connections when a user searches something related to medicine, and a software agent ‘Aria’ that has been developed to integrate the annotation and retrieval of images into a single, integrated application.

Research work [19] simulates an agent oriented environment for German hospitals with the objective to improve or optimize the appointment scheduling system, resource allocation and cost benefit of clinical trials. They introduced an agent that is a proxy “person” for a functional unit. It coordinates the incoming appointment requests and sends appointment proposals automatically. It acts as collateral for monitoring appointment schedule and starts executing rescheduling algorithm if discrepancies occur between the planned and actual schedules.
Researchers of [20] employ the Multi-agent system for providing diagnosis and advice to health care personnel dealing with the traumatized patients. An *Emergency Medical Assistant using Intelligent Monitoring agents* has been developed to demonstrate the system for the trauma environment with particular emphasis on types of shock and stabilization of arterial blood gases.

The author of [21] develops an agent based system to improve vaccination rates in Germany. The agents have been developed to maintain consistency of the patient's medical record at pharmacy level, specialist level and at the family doctor level. A 'personal medical agent' has been designed to mediate among several participants of the health service. Reactive and proactive behaviors are added to this agent in order to maintain consistency in the electronic records of the patients.

The research work reported in [22] demonstrates that the use of *emergent behavior* in a community of agents to produce self adaptive interface. MAS has been constructed in which a group of agents work at finding patterns that are combined together to produce an adaptive interface according to the users' demands. This system experiments with the accurate dosage advice for diabetic patients and aims to produce a Personal Digital Assistant (PDA) based system into which the patients enter various details about their diet and physical condition.

The authors of [23] discuss various applications of MAS in health care e.g., coordination of organ transplants among Spanish hospitals, patient scheduling, senior citizen care etc. They also present the reasons to justify the adequacy of MAS in healthcare.

A research project, called PalliaSys is reported in [24]. It incorporates information technology and multi-agent systems to improve the care given to palliative patients. These patients suffer from an advanced-state terminal disease, and hence receive a symptomatic treatment of pain and other problems instead of a curative medicine.

The author of research paper [25] has developed *Telemedicine-Oriented Medical Assistant* which is used by each specialist to transfer microscopic images and
data of a patient for collaborative diagnosis in the department of pathology. He opines that the agent oriented approach is required because of various reasons, for example to arrange an appointment between two specialists is a matter of negotiation and collaboration, and can be taken through a collaborative effort of the two user agents. Similarly, the process of discussing a case history of the patient is related to the capability of communicating complex multimedia data with the specialized protocols. And adding new specialists or services is integration capability of the system.

An Intelligent Healthcare Knowledge Assistant who uses multi-agent system for dynamic knowledge gathering, filtering, adaptation and acquisition from Health care Enterprise Memory unit, has been reported in [26]. It states that the traditional medical systems do not sufficiently provide the necessary assistance to healthcare practitioners in the handling of critical situations. And the local knowledge bases often lack the required knowledge for problem solving. So it desired to have a system that assembles knowledge from different sources.

MAS that aims to enhance monitoring, surveillance and educational service of a Medical Contact Center (MCC) for chronic disease management in Greece is reported in [27]. In this system the role of the agents is to sense the MCC environment, percept about the environmental states, and act correspondingly. The main aim of the system is to effectively manage and interpret the large volume of medical data collected during the patient sessions with the system, and to provide a mechanism for evaluation of the educational process. It also aims at resource optimization.

The authors in [28] discuss a case study involving various agents for providing consultation and therapy to the patients suffering from diabetes. They conclude that the multi-agent system can be used in integrating the medical knowledge and clinical experience and can also help in decision making. Not only this, MAS adapts in accordance with the rapidly changing environment. Hence, this approach can also tackle the complexity of e-medicine system effectively.

The works mentioned above are domain specific, e.g. catering to special types of patients or providing assistance to the patients for the appointments or supporting the
Multi-agent decision system using probabilistic network

doctors in diagnosing specific diseases, etc. These systems are therefore, not capable of handling problems related with young infants/children, especially in Indian scenario. More precisely, the efficacy of the agents in this application area has yet not been explored.

The issue of intelligent behavior of MAS is still to be addressed. There is a need to explore intelligent decision making techniques that can be incorporated in MAS tackling childhood diseases in India. So, in the subsequent section Probabilistic Network based decision making systems are studied.

2.3 Multi-agent decision system using Probabilistic Network

Medical problems inherent uncertainty and Probabilistic Network (PN) provides a strong basis to deal with such problem as it is based on rigorous mathematical fundamentals. In fact, the usefulness of Bayes’s theorem has been accepted in this domain long time ago [29]. In this research work, uncertainty may arise when one agent needs to decide to ‘whom to contact while diagnosing a disease and correspondingly the treatment(s)’.

* Most of experimentation is undergoing to utilize BNs in diagnostic procedures. For example, discovering temporal-state transition patterns during hemodialysis has been discussed in [30]. It demonstrates the causal relationships between medical treatments and transitions of the patient’s physiological states in the hemodialysis process. The main advantage of discovering the hemodialysis clinical pathway is to provide better treatments, and to help medical professionals to react to the exceptions during the hemodialysis process. The basic fundamental of this process is to remove waste elements from the blood. This procedure is required in situations when kidneys do not work properly.

* Probabilistic Network and Bayesian Network (BN) terms are used interchangeably.
Similarly, [31] reports the usage of the BN to evaluate the accuracy of physicians in recommending ultrasound test to the infants to rule out pyloric stenosis. Mostly the results are negative. This suggests that there is a low accuracy of clinical assessment. It is concluded that the physicians using the BN, predict the probability of pyloric stenosis among the infants. They predict it better.

The Bayes’s theorem delivers sufficiently accurate results where specific manifestations have high frequency and high specificity [32]. For instance, if there is a high frequency of diastolic murmur at the cardiac apex then it’s a case of mitral stenosis. Bayes’ theorem can also predict the same disease as there is a high ‘posteriori’ probability of mitral stenosis available. And for other cardiac diseases low frequency is required.

But there has been criticism of Bayesian based probabilistic systems also. The main limitation is to obtain realistic prior probabilities. This can be tackled by involving the domain experts for deciding probabilities or utilizing statistical data as it is being done in [33], for diagnosing hypertension. The aim of this system is to determine the hypertension and five types of secondary hypertension. It takes into account the blood pressures, general information and general biochemical data for decision making.

As discussed in previous section, software agents are proving to be promising solution in medical domain because of their reactive, proactive, autonomous, collaborative and knowledge-sharing capabilities. For instance, [34] discusses management of diabetic patient, and [35] highlights a case study for community surgery where the agents need to collaborate for appointment scheduling, monitoring and recording data, etc.

To make the agents demonstrate the requisite behaviors, probabilistic networks, rule based system and Markov decision making process can be utilized. But probabilistic networks are more appropriate as probabilistic networks have a clear semantics that allow them to be processed in order to do diagnosis, learning, explanation, and many other inference tasks necessary for intelligent systems. For instance, [36] models a real world
scenario, where a smart agent performs daily diagnosis on the hydration state of kidney disease patients.

In MAS, automatic negotiation mechanism is often required. This is because of the fact that the agents usually have incomplete information. To deal with this problem, a Bayesian learning algorithm is proposed in [37] and compared with reinforcement learning negotiation and non-learning negotiation. The results suggest that the BN based algorithm is more efficient. This is particularly important in medical domain since, the agents have incomplete information about the capabilities of other agents.

With passage of time, the behavior of an agent tends to modify. To tackle such a case, influence diagrams and the BNs have been used in [38]. This paper describes a methodology that utilizes Bayesian-net model to build new MAS. A framework is presented in which the agents try to learn the model of other agents in a MAS system based on their observed behavior. The agents maintain a number of possible models and assign the probability of being correct. Such a construction of MAS model is required in medical domain too, as the diagnostic systems also tend to change with the time.

The other competing decision making techniques are: Markov Model (MM), Contract Net protocol and Artificial Neural Networks. The rest of this section deals with applicability of MM and contract net protocol.

One application of MM is presented in [39]. This system tries to assist elderly people suffering with the disease called dementia. These people often cannot remember how to complete activities of daily living and require a caregiver to aid them through the steps involved. The system is designed to provide prompts to a user with dementia for guidance through the activity of the hand-washing. Hence it reduces the dependency on a caregiver. Results from the study suggest that MM can be applied effectively to this type of guidance problem. Generally, it is stated that Markovian model is a special case of the BN. So, variation in the BN can also be effective in medical decision making system. This is reported in [40] too. In this research paper, authors present a new framework for combining logic with probability, and demonstrate the application of this framework to the breast cancer prognosis.
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The Contract Net Interaction protocol [41] specifies communication protocol among the agents. One agent behaves as an initiator and others as participants. The initiator broadcasts a requirement that can be met by one or more agents. This negotiation concludes with the initiator behaving as a server and the most promising agent as a client. Such kind of interaction is not very feasible in medical domain. For instance, if one agent broadcasts ‘Constipation’ as a sign symptom then number of agents say; Surgeon agent, Cardiologist agent, Endocrinologist agent, etc. would respond, sensing the probable sign-symptom in their own respective branch.

The above discussion concludes that the BNs can work well in the Multi-agent systems environment for health care domain. In the next section, Neural Network (NN) based decision making systems are reviewed to understand the applicability of NNs in MAS.

2.4 Multi-agent decision making based on Neural Networks

It is considered that Artificial Neural Networks (ANN) or simply Neural Networks based systems are producing the promising results in the decision making systems in general and particularly well in medical domain. This is because of the fact the NN techniques are capable of modeling nonlinear relationships, which are frequently observed in medical datasets.

As discussed in section 2.3, there is a need to decide a ‘collaborating agent’. This is necessary because there are a number of competing agents and to select the most appropriate one involves high precision. In this section, Probabilistic Neural Network (PNN) and Back Propagation Neural Network (BPNN) based medical decision making system are discussed and finally it would be argued that the NN techniques can be useful in the MAS too.
The use of the PNN has been noticed in medical domain with the aim of classifying the intensity of the disease or monitoring of vital parameters. There is a discussion by the author of research work [47] on a system that implements a PNN to estimate mortality risk following cardiac surgery. The aim is to predict the patient’s survivability after open-heart surgery. The author also attempted to use variants of the BPNN to model cardiac surgery mortality. Even with multiple attempts with variable preprocessing and many network configurations, i.e. varying the numbers of hidden layers, connections and neurons, the BPNN models failed to meet the accuracy of the PNN architecture.

Similarly, [42] discusses the classification results for two types of acute leukemias and five categories of embryonal tumors of the central nervous system. They found the computation speed to be satisfactory and 100% recognition accuracy in classifying a type of leukemia cancer. They also demonstrated that the PNN is faster than other neural networks.

There is another system in medical sphere reported in [51] which utilizes the PNN for monitoring vital parameters of the patients for diagnosing purpose. This paper proposes a method to discriminate the vascular conditions from the biological signals by using the PNN, and develops the diagnosis support system to judge the patient’s conditions on-line.

A modified PNN for the brain tissue segmentation with Magnetic Resonance (MR) imaging is proposed in [54]. In their research, a new method is proposed which is based on a novel self-organizing map-weighted probabilistic neural network structure to estimate the probability density function of pixels from the brain MR images. It is a supervised learning algorithm.

In another research [55], the methods have been developed to integrate Independent Component Analysis (ICA) and neural network for Electrocardiogram (ECG) beat classification. The ICA is used to decompose the ECG signals into the weighted sum of the basic components which are statistically mutually independent. Two neural networks, the PNN and the BPNN, are employed as the classifiers. The ECG
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samples attributing to eight different beat types are sampled from the MIT-BIH arrhythmia database for the experiments. The results show high classification accuracy of over 98% with either of the two classifiers.

Similarly, in some researches expert system is also used along with the PNN, like in [44]. It utilizes Association Rule (AR) for reducing dimension of the breast cancer database and the NN is used for intelligent classification. This research demonstrated that the AR can be used for reducing the dimension of feature space and the proposed AR + NN model can be used to obtain fast automatic diagnostic systems for other diseases.

Other investigators in [45], describe the use of the NNs in decision making for surgery to the traumatic brain injury patients. This system aids physician and other medical professional in making uncertain medical decisions. It consists of three mathematical models for generating the traumatic brain injury medical decision support system on clinical database. The result suggests that the NN may be a better option for complex, non-linear medical decision support systems than conventional techniques.

In another study reported in [49], an object oriented ANN is used for dermatological decision making. It demonstrates the clinical decision making process to analyze the skin lipid data from the patients having microbial skin diseases.

The researchers in [57] report a tool on the decision making for health professionals based on the NN. It supports the Graphical User Interface (GUI) for visualizing 2-D and 3-D data for biomedical problems. Apart from this medical domain, the NN techniques are used in other fields too for decision making as discussed in [43, 46, 56, 59, and 60]. There are papers that report the usage of ANN in MAS. For instance, [50] develops an intelligent agent system to detect the fall events of elderly people automatically. The fall problem, among elderly is a crucial public health and clinical problem because the fall is the prime cause for the traumatic death and physical sequela of them. The system uses back-propagation neural network classifier to detect the fall events automatically.
2.5 Conclusion

The research works and the systems discussed in this chapter are efficient and effective. This encourages our belief that MAS can be really useful in our domain, i.e. providing medical help to rural infants and children. Moreover, no such endeavors have ever been made in this regard. To build knowledge base for agents, one can rely on a well defined protocol developed by World Health Organization (WHO) in collaboration with Government of India.

To embed decision making capability in multi-agent environment, one can think of Bayesian network or neural networks. The detailed review of literature is conducted to understand the already built decision making systems in MAS.

It is concluded that there is no MAS, specifically dealing with childhood diseases in the world and that decision making capabilities can be either be BN based or NN based.