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Alzheimer's disease classification using deep learning from MR images

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By :

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I present to you this research, and I hope it will be to your satisfaction.

ACHOUR Dounia

Abstract

Alzheimer's disease (AD) is a neurodegenerative disease that causes memory loss. It can seriously affect a person's ability to carry out daily life activities. Alzheimer's Disease (AD) is the most common cause of dementia globally. Early diagnosis can help doctors to treat this disease and mitigate its symptoms. Deep learning methods have shown promising results in the field of healthcare. They have significantly improved medical imaging systems for AD by providing diagnostic performance close to the human level. Existing approaches have recently demonstrated significant performance in the automatic detection and classification of Alzheimer's disease from multi modality data such as MRI, CT, PET... The convolution neural network (CNN) is one of these techniques that has achieved better accuracy in diagnosing of AD from MRI images. In this work, we built a CNN model to automatically detect and classify Alzheimer's disease into three stages AD, MCI (mild cognitive impairment), and CN (cognitively normal). The dataset used in our study is 3D MRI scans of 298 subjects from the Alzheimer's Disease Neuroimaging Initiative (ADNI). We selected 20 slices from each plane (axial, coronal, sagittal), from which the result is shown to be the coronal plane with high accuracy. We obtained an accuracy around of 99.78% and 98.62% for binary classification and multi classification, respectively. The obtained results demonstrate the effectiveness of our model for the analysis of 3D MRI images in the detection and classification of AD and its earlier stages.

Key-words: Alzheimer's disease, Deep Learning, CNN, Classification, Detection, ADNI, MRI.

Résumé

La maladie d'Alzheimer est une maladie neuro dégénérative qui entraîne des pertes de mémoire. Elle peut gravement affecter la capacité d'une personne à accomplir les activités de la vie quotidienne. La maladie d'Alzheimer est la cause la plus fréquente de démence dans le monde. Un diagnostic précoce peut aider les médecins à traiter cette maladie et à atténuer ses symptômes. Les méthodes d'apprentissage profond ont montré des résultats prometteurs dans le domaine de la santé. Elles ont considérablement amélioré les systèmes d'imagerie médicale pour la maladie d'Alzheimer en fournissant des performances de diagnostic proches du niveau humain. Les approches existantes ont récemment démontré des performances significatives dans la détection et la classification automatique de la maladie d'Alzheimer à partir de données multimodales telles que l'IRM, le CT, le PET.... Le réseau neuronal à convolution (CNN) est l'une de ces techniques qui a obtenu une meilleure précision dans le diagnostic de la maladie d'Alzheimer à partir d'images IRM. Dans ce travail, nous avons construit un modèle CNN pour détecter et classer automatiquement la maladie d'Alzheimer en trois stages : AD, MCI (mild cognitive impairment), et CN (cognitively normal). La base de données utilisé dans notre étude est constitué à partir de scans IRM 3D de 298 sujets trouvés dans l'Alzheimer's Disease Neuroimaging Initiative (ADNI). Nous avons sélectionné 20 coupes dans chaque plan (axial, coronal, sagittal), le résultat étant le plan coronal avec une grande précision. Nous avons obtenu une précision d'environ 99.78% et 98.62% pour la classification binaire et la classification multiple, respectivement. Les résultats obtenus démontrent l'efficacité de notre modèle pour l'analyse des images IRM 3D dans la détection et la classification de l'Alzheimer dans ses stades précoces.

Mots-clés: La maladie d'Alzheimer, Détection, Classification, Apprentissage profond, CNN, ADNI, IRM.

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General introduction

Alzheimer's disease (AD) is a chronic, neurological brain disease which is caused by the damage of nerve cells in parts of the brain [1]. It leads to gradual loss of memory, thinking skills, difficulty in speaking a language and other basic functions. It can seriously affect a person's ability to carry out daily life activities.

Alzheimer's is the most common stage of dementia that requires extensive medical care. According to the World Health Organization, more than 55 million people live with dementia worldwide, and there are nearly 10 million new cases every year. Alzheimer's disease may contribute to 60–70 % of cases [2]. It is considered one of the six leading causes of death, with an estimated prevalence of nearly 30 million people worldwide [3]. In fact, there are three stages that lead up to AD as follows: normal healthy control (CN), mild cognitive impairment (MCI), and the final stage of Alzheimer's disease (AD). Hence, early diagnosis and detection of this disorder become crucial to the effectiveness of treatment, which requires good clinical assessment based on various techniques such as the Mini-Mental State Examination (MMSE), the patient's medical history, several neuropsychological tests, and the Global Deterioration Scale (GDS).

Machine learning approaches are more commonly employed in healthcare and are used to automate medical billing, clinical decision support, and the establishment of clinical care recommendations. The most popular among these approaches is the support vector machine (SVM) [4, 5, 6]. Deep learning algorithms are an alternative family of machine learning methods that perform automatic feature extraction without human intervention. Due to the availability of a greater number of hidden layers, deep learning approaches learn the high-level representation from the raw data. This is the reason behind its popularity in the computer vision domain.

Deep learning in radiology allows us to identify complicated patterns automatically and to assist radiologists in making intelligent decisions based on the insights obtained when evaluating pictures such as conventional radiography, CT, MRI, PET scans, and radiology reports. Recent studies have demonstrated significantly the performance of the automatic detection and classification of AD from multimodality data such as magnetic resonance imaging (MRI), positron emission tomography (PET), and computed tomography (CT), X-rays [7]. Although magnetic resonance imaging (MRI) is increasingly popular and more effective for carrying out Alzheimer's disease associated examinations when using conven-

tional machine learning. This is because the procedure is noninvasive and causes no pain to the patients. Further, MRI contributes a good contrast and a fine structural resolution [8].

Objective of the work

The objective of our work is to develop a two-dimensional convolution neural network model that can discriminate AD brains from Mild Cognitive Impairment (MCI) or Cognitively Normal (CN), and also be reliable, use less time, and achieve high classification accuracy.

- We develop classification models using 2D images rather than 3D MRI volumes for:
  - Binary classification (AD/CN, MCI/CN, and AD/MCI).
  - Multi-class classification (AD, MCI, and CN).
- Using the same dataset, we train our model in three planes (axial, coronal, and sagittal).

Dissertation Outline

The remaining sections of the dissertation are organized as follows:

— The first chapter consists of two main parts. We will start by providing a brief overview of human anatomy and Alzheimer's disease, with different approaches and techniques for diagnosing this disease. Then, we will present an overview of magnetic resonance imaging (MRI).

— In the second chapter, the background of our work is presented. We focus on convolution neural networks (CNN), machine learning and deep learning. Then, we will provide the CNN structure and the various layers. On the other hand, we will explain the data constraints and techniques for overcoming and combating the overfitting phenomena. In the end, a stat of art about deep learning and Alzheimer's disease is presented.

— The third chapter covers both the design and the implementation of our proposed system. We will start by presenting the general and detailed architectures, followed by the tools required and the code sources used in our work's implementation.

— The last chapter summarizes our results, analyzes the outcomes of the various plans, and includes a comparative section to highlight the differences between this work and earlier ones.

Chapter 1

Diagnostic Alzheimer's Disease in Brain MRI

Contents

1.1 Introduction

The brain is an incredible organ where its job is to take information from other areas of the body, analyze it, and figure out how to react to it. Also, memory, body movements, the senses, and pretty much everything else are all controlled by the brain.

The brain, being the body's most sensitive and master organ, is equally vulnerable to infections and other ailments of varying severity, such as brain cancer, tumors, and Alzheimer's disease, which is the focus of our project. Each of these disorders has a negative impact on brain processes. To detect these infections and problems, there are several clinical methods, such as medical tests, computer-aided diagnosis, etc.

Alzheimer's is from a family of diseases that can cause dementia, especially in elderly people. A diagnosis of dementia is considered a loss of memory and/or other mental disability. It can cause physical damage to the brain.

Alzheimer's disease is a progressive disease that begins with mild memory loss and possibly leads to loss of the ability to carry on a conversation and respond to the environment. It involves parts of the brain that control thought, memory, and language. It can seriously affect a person's ability to carry out daily activities.

In this chapter, we first briefly introduce the anatomy of the human brain, dementia, and Alzheimer's disease.

Then, different approaches and techniques proposed in literature for Alzheimer's disease diagnosis and detection are provided. After that, we focus on brain magnetic resonance imaging (MRI) image formation and techniques.

1.2 Anatomy of human brain

Since Alzheimer's is a disease of the brain, we need to present the various basic components of the brain. Where the cerebrum, cerebellum, and brainstem make up the cerebrum (see Figure 1.1). The cerebrum is made up of three main matters (tissues) which are the white matter (WM), the gray matter (GM), and the cerebrospinal (CSF) (see Figure 1.2).

1.2.1 The white matter (WM)

White matter is made up of bundles that connect various grey matter sections (where nerve cell bodies are located) of the brain to one another, carry nerve impulses between neurons, and include myelinated nerve fibers. It is whitish and glossy in appearance (color of myelin).

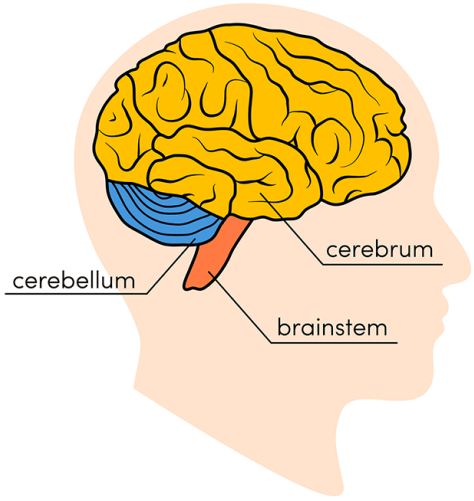

Figure 1.1 – Illustration of basic components of the Brain.

1.2.2 The gray matter (GM)

The other main component of the brain is the grey matter, which is composed of the cell bodies of neurons and glial cells. It appears darker in color compared with the rest of the tissues and is present mainly in the cerebral cortex, the cerebellar cortex, the central gray nuclei, the nuclei of the brainstem, and the inside of the medulla.

1.2.3 The cerebrospinal fluid (CSF)

It is a clear, colorless bodily fluid present in the tissue that surrounds all vertebrates' brains and spinal cord. The cerebrospinal fluid (CSF) acts as a cushion or buffer for the brain inside the skull, providing basic mechanical and immunological protection. The cerebrocerebrospinal fluid (CSF) also plays an important role in the cerebral autoregulation of cerebral blood flow.

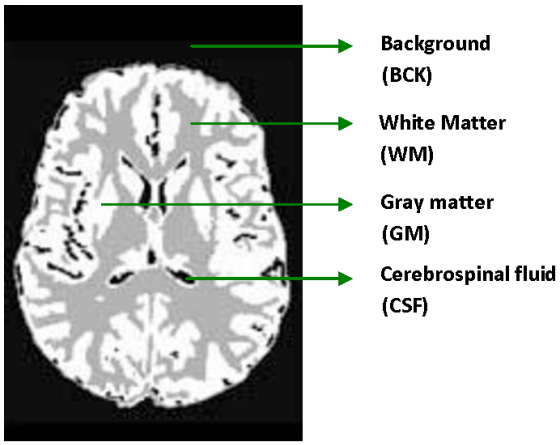

Figure 1.2 – Illustration of brain Tissues [9]

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1.3 What is dementia

Dementia is a condition in which a person's cognitive functioning (thinking, remembering, and reasoning) has deteriorated to the point where it interferes with daily living and activities. Some dementia patients lose control of their emotions, and their personalities shift. Dementia can range in intensity from the mildest stage, when it is just starting to damage a person's ability to function, to the most severe level, when the person is wholly reliant on others for basic daily activities. Worldwide, around 55 million people have dementia, this number is expected to rise to 78 million in 2030 and 139 million in 2050 [10]. Alzheimer's disease is the most common form and may contribute to 60-70% of cases (see Figure 1.3), but there are several other causes of dementia [10]. Dementia is now the 7th leading cause of mortality globally [11].

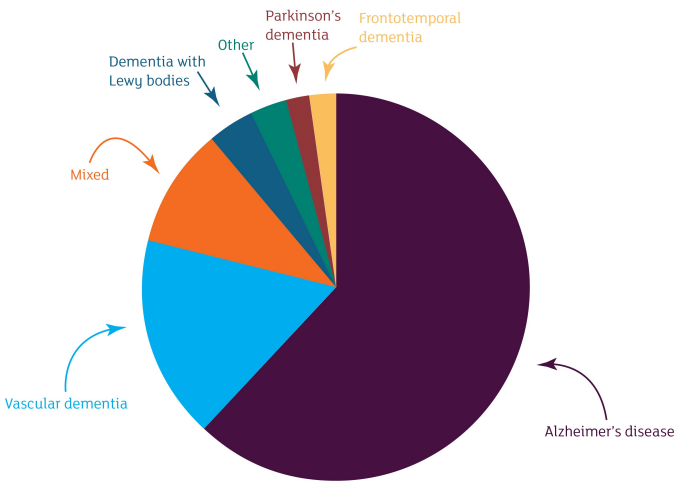

Figure 1.3 – Pie-chart of the leading causes of dementia.

1.4 Alzheimer's disease (AD)

Alzheimer's disease is the most frequent type of dementia, as shown in the statistics in Figure 1.3. It is considered a progressive brain disease that wreaks havoc on memory and thinking skills, as well as the capacity to carry out even the most basic tasks. As we know, Alzheimer's disease primarily affects adults aged 60 and up. The greatest known risk factor is aging [12]. The cause of Alzheimer's disease (AD) is closely related to the aggregation of a normal protein, β-amyloid (Aβ), within the neocortex [13].

The following Figure 1.4 shows the difference between a normal brain and an Alzheimer's brain, where the brain with Alzheimer's shrinks, ventricles enlarge, and atrophy (shrinkage) of the hippocampal.

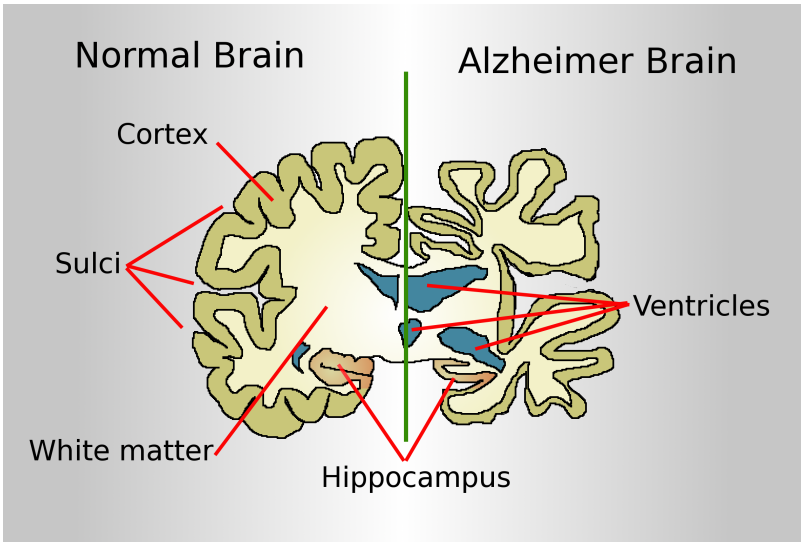

Figure 1.4 – Alzheimer's brain vs.Normal brain.

- **Most important Alzheimer's statistics & facts in 2021**
  - 50 million people are living with Alzheimer's and other dementias worldwide [14].
  - Based on updated calculations ,an estimated of 6.2 million americans age 65 and older are living with Alzheimer's dementia in 2021[11].
  - One in three seniors die with Alzheimer's Disease, every 65 seconds someone develops AD in the United States. In addition, the AD kills more people than the breast cancer and the pros-tate cancer [11].
  - Alzheimer's Disease is the six leading cause of death with an estimated prevalence of nearly 30 million people worldwide [3].
  - Presently, the drugs available for AD treatment, including cholinesterase inhibitors and an antagonist of the N-methyl-D-aspartate receptor, can only in-

hibit dementia symptoms for a limited period of time but cannot stop or reverse disease progression [15].

1.5 Alzheimer's disease stages

Alzheimer's disease progresses slowly in three general stages as follow: Mild Alzheimer's disease, moderate Alzheimer's disease, and severe Alzheimer's disease. Alzheimer's affects people in different ways, where each person may experience symptoms (or progress through the stages) differently.

1.5.1 Early-stage Alzheimer's (mild)

A person with Alzheimer's disease can function independently in the early stages. He can continue to drive, work, and participate in social events. Despite this, the person may experience memory lapses, such as forgetting common words or where ordinary things are located. Problems include wandering, getting lost, trouble handling money, repeating questions, and taking longer to do normal daily tasks [12]. Although the symptoms may not be obvious at this point, close people may detect a shift.

1.5.2 Middle-stage Alzheimer's (moderate)

Middle-stage Alzheimer's disease is the most advanced stage, and it can endure for many years. The dementia symptoms are more evident in the middle stages of Alzheimer's disease compared to the previous stage. Words may be misunderstood, the person may become upset or furious, and the individual may act in unexpected ways. Damage to nerve cells in the brain can make it difficult for a person to express their thoughts and carry out ordinary tasks without help. Where the person in this stage needs more care.Longitudinal studies reveal that not all patients diagnosed with MCI develop Alzheimer's disease. It is estimated that only 10-15% of people with MCI might develop dementia and then convert over time to AD[16].

1.5.3 Late-stage Alzheimer's (severe)

Dementia symptoms are severe during the end of the disease. The patients lose their ability of answering to their environment, converse, and eventually regulate their behavior. As memory and cognitive abilities deteriorate, substantial personality changes may occur, necessitating extensive care. In the advanced stage, the prevalence of cells decrying to other regions in the brain reaches a state where the patient becomes unable to complete the daily activities. At this level, the patient is considered (converted) to AD condition [16].

The Figure 1.5 illustrated the progression of Alzheimer's disease and the state of the brain in each stage.

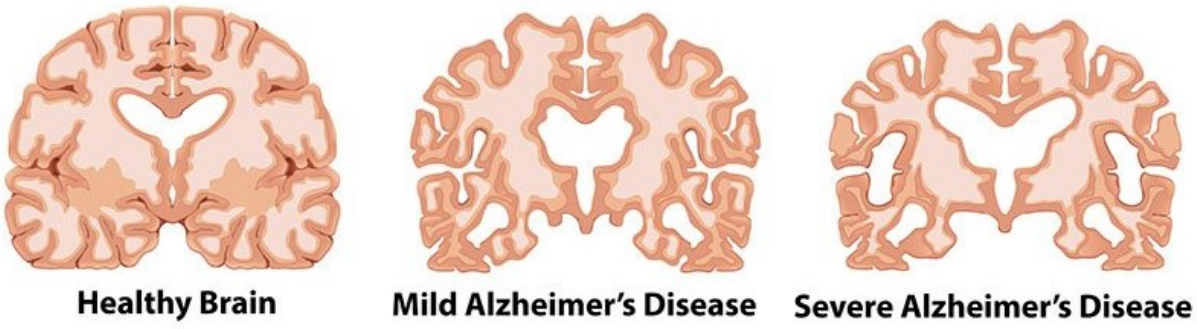

Figure 1.5 – Progression of Alzheimer's disease.

1.6 Diagnosis of Alzheimer's disease

Alzheimer's disease progresses slowly over time. People with AD proceed at varied rates, ranging from mild Alzheimer's when symptoms first appear to severe Alzheimer's when they are fully reliant on others for care. An early and precise diagnosis is advantageous. While there is no cure for Alzheimer's 100 %. Starting treatment early in the disease process may help you maintain daily function for a longer period of time. The majority of drugs are most effective for those who are in the early or middle stages of an illness[17]. In the following, we mention some approaches to Alzheimer's disease diagnosis.

1.6.1 Medical tests for diagnosing Alzheimer's

Doctors employ a variety of approaches and technologies to evaluate whether a person suffering from memory or cognitive problems has Alzheimer's disease. Alzheimer's disease is diagnosed using a series of tests.

- **Medical history :** this method inquires about the overall health and well being of the person having symptoms, as well as a family member or friend. It is based frequently on asking questions which include the use of prescription and over-the-counter medications, as well as previous medical issues.
- **Physical exam and diagnostic tests :** it consists to check diet, blood pressure, temperature and pulse. Blood test can predict presence of beta-amyloid in the brain [18].
- **Neurological exam:** during a neurological exam the doctor will look for issues that could indicate a brain illness other than Alzheimer's.

- **Mental cognitive status tests:** these tests check memory, reasoning, and simple problem-solving abilities are assessed during the mental cognitive status assessment. Such tests can determine whether or not a person: Knows the date, where he is, and do simple calculations.

  The most often utilized tests are briefly described below:

  1– **Mini Mental State Evaluation (MMSE) :** the MMSE is the most extensively used cognitive assessment instrument for testing and evaluating a variety of mental functions in patients. A health practitioner asks a patient a series of questions meant to assess a variety of ordinary mental skills during the MMSE. It has a maximum score of 30 points. Patients are categorized accordingly to a range of intervals: A score of 20 to 24 indicates mild dementia, 13 to 20 indicates moderate dementia and less than 12 indicates severe dementia [19].

  2– **Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog):** is the gold standard for evaluating anti-dementia medication efficacy. ADAS-cog can detect changes at earlier stages of AD progression [20]. It includes eleven tasks that assess the cognitive domains of memory, language, word recall,word recognition,orientation, naming objects and fingers, commands, constructional praxis,ideational praxis, orientation, word recognition, and comprehension [21].

- **Brain imaging:** if the doctor suspects that the patient has Alzheimer's, he asks for more accurate diagnoses, such as computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET), in order to confirm a diagnosis of Alzheimer's disease or rule out other probable sources of symptoms. These tests are mostly used to decide out other illnesses that have symptoms and similar to Alzheimer's but require different therapy. The understanding of the anatomy and function of the living brain has been transformed because to advances in imaging technology. Recent studies have demonstrated significantly the performance of the detection and classification of AD from multimodality data (brain imaging) as magnetic resonance imaging (MRI), positron emission tomography (PET) and computed Tomography (CT), X-rays [7]. We can briefly explain various brain imaging techniques as follows (see Figure 1.6):

  1– **Computed tomography (CT):** a CT scan is a type of imaging that employs X-rays to create cross-sectional images of your brain.

  2– **Magnetic resonance imaging (MRI):** an MRI creates a precise image of your brain using strong radio waves and magnets. where our dataset contains a collection of MRI images

  3– **Positron emission tomography (PET):** a PET scan detects compounds in the body by using a radioactive material known as a tracer. PET scans that

identify clumps of amyloid proteins (plaques) linked to Alzheimer's disease have recently been created, however, this form of PET scan is typically employed in the research setting.

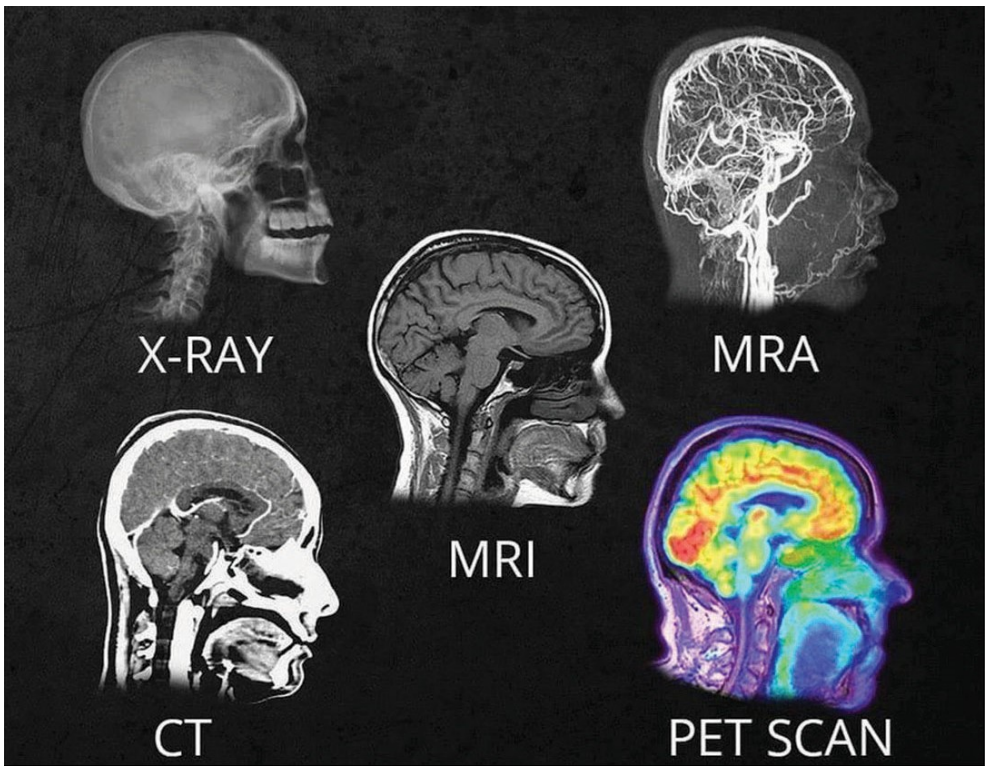

Figure 1.6 – Illustration of various brain imaging technique.

1.6.2 Computer-aided diagnosis

Computer-Aided Diagnosis (CAD) systems aid clinicians and radiologists in detecting and diagnosing diseases. They provide the support and information that medical professionals require to better comprehension of diseases and their progression in a short period of time. CAD is a collection of technologies that combine artificial intelligence (AI) and computer vision with image processing in radiology and pathology. The requirement for precise and seamless Alzheimer's disease diagnosis led to the integration of intelligent modules to organize and interpret medical data allowing health practitioners to make more dependable decisions. Computer-aided diagnosis (CAD) systems can help detect metastases in bone scans, X-rays, CT, PET, and/or MRI[22]. Traditional machine learning algorithms such as Support Vector Machines (SVM), Decision trees, linear and logistic regression, and artificial Neural Network (ANN) were extensively investigated in AD detection and classification.

- **Logistic regression:** it is a powerful supervised machine learning approach for binary classification issues. The best way to think of logistic regression is as a type

of linear regression that is used to solve classification difficulties. Logistic regression has been applied to AD classification in several studies [23, 24, 25].

- **Support vector machine :** is a set of supervised learning methods used for classifying, predicting, and detecting outliers. The objective of the support vector machine algorithm is to find a hyperplane in an N-dimensional space (N — the number of features) that distinctly classifies the data points [26]. In a large number of research, SVM has been used to classify Alzheimer's disease [27, 28, 29]
- **Random forest :** is a machine learning technique used to solve classification and regression problems consisting of many decisions trees (see Figure 1.7). It makes use a set of learning, which is a technique for solving complex problems by combining multiple classifiers. Random Forest strength to overcome the overfitting problem, makes it better than the others, and achieves high accuracy [30].

  Some of the random forests that have been used for AD classification are [31, 32, 33]

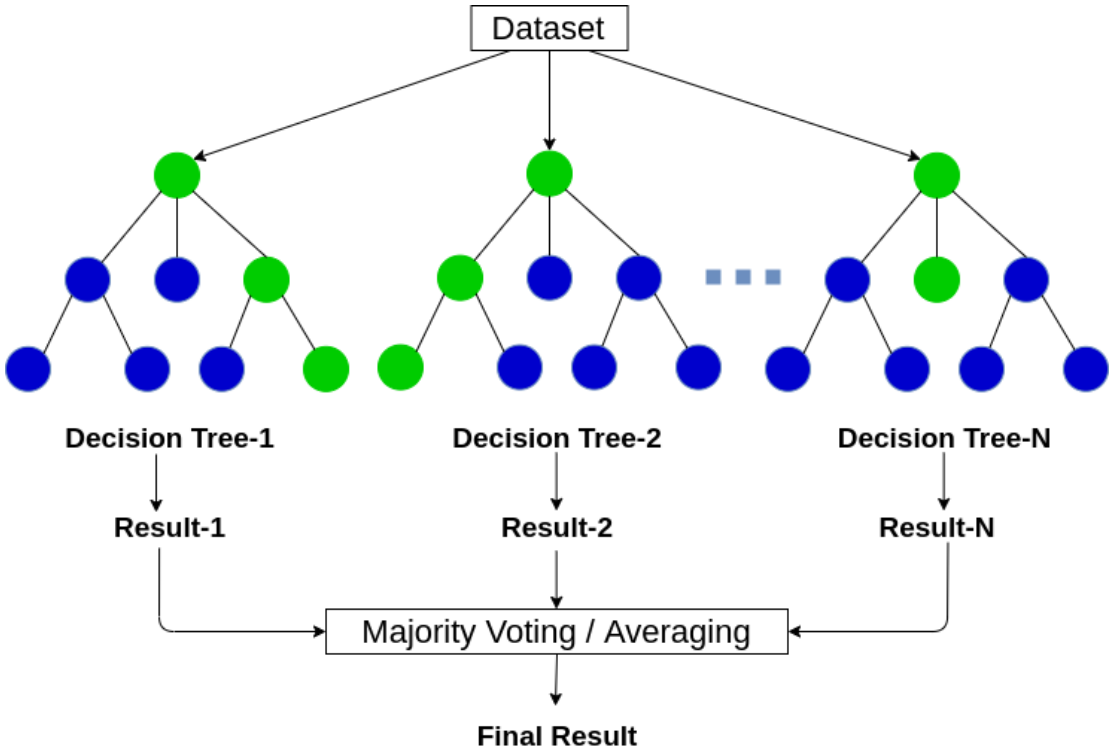

Figure 1.7 – Illustration of random forest approach.

1.7 Magnetic Resonance Imaging (MRI) image formation

Magnetic Resonance Imaging (MRI) is a painless, noninvasive diagnostic examination that uses a strong magnetic field and radio waves to create two or three-dimensional images of the structures inside your body (see Figure 1.8). A magnetic resonance imaging (MRI) scan provides detailed images of organs, tissues, and the skeleton, which can be used to detect, diagnose, and monitor a number of medical diseases. It employs radio frequency (RF) radiation in the presence of carefully controlled magnetic fields in order to produce high quality cross-sectional images of the body in any plane[34].

MRI is considered the best when the images need to be very detailed, for example to look at cancer, causes of dementia or neurological diseases, or places where bone might interfere[35]. An MRI scan differs from a computed tomography (CT) scan, which produces images using X-rays rather than magnets. Both tests produce images of your body's components. MRI contributes to good display contrast and features of soft tissue such as the brain, muscles, tendons, ligaments, nerves, and spinal cord, whilst a CT scan is better at imaging bones and blood arteries. Further, magnetic resonance imaging (MRI) is increasingly popular and more effective for carrying out Alzheimer's disease associated examinations [8].

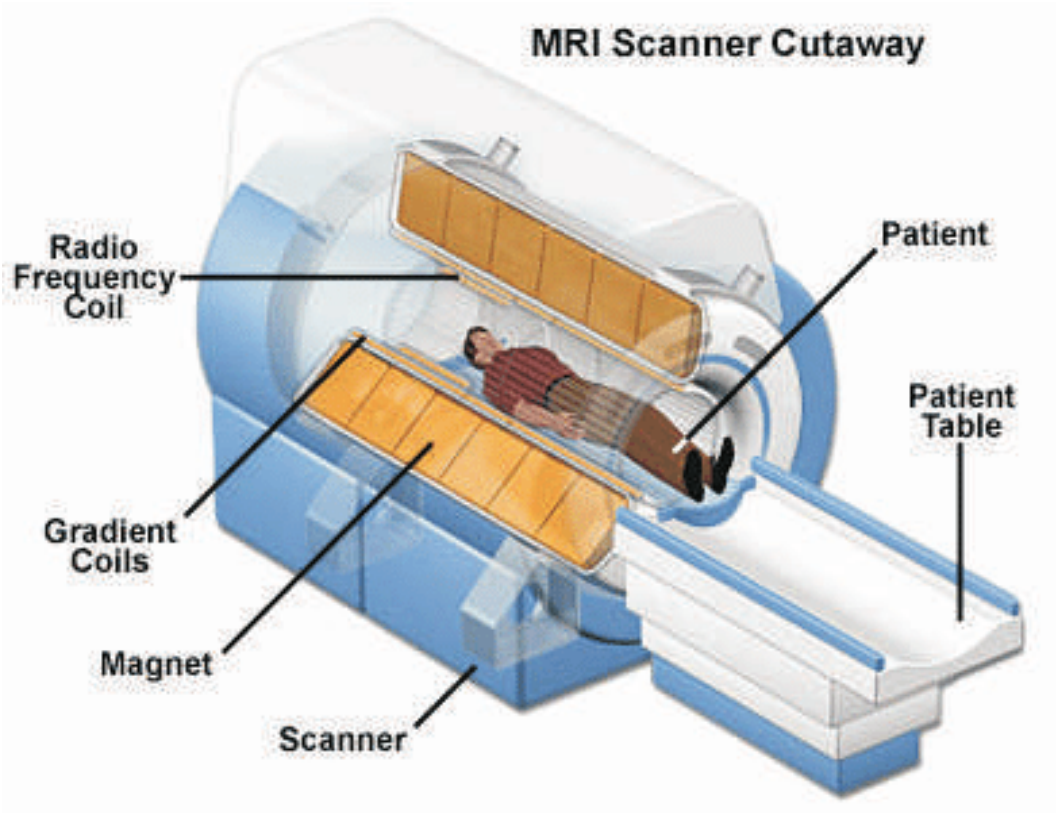

Figure 1.8 – Magnetic Resonance Imaging (MRI) scanner system.

There are three other gradient magnets termed x, y, and z inside the MRI scanner system, each orientated with a different projection of the body and all of them significantly less powerful than the main magnet (as illustrated in Figure 1.9).

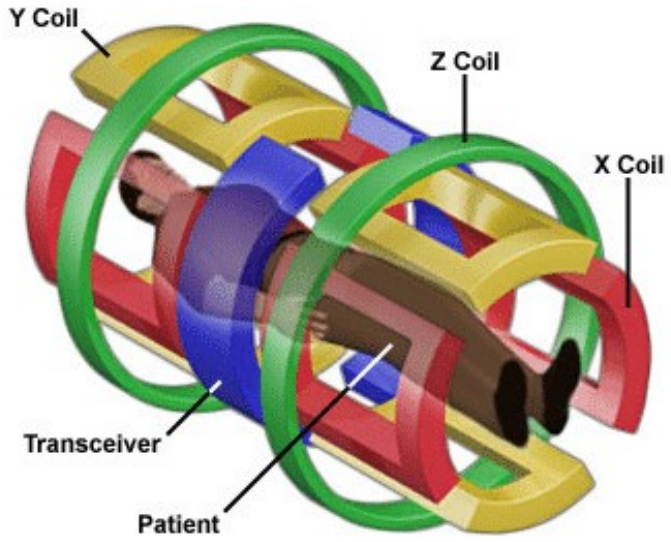

Figure 1.9 – MRI scanner gradient magnets.

1.7.1 MRI sequences

Before presenting the different types of sequences MRI, we need to define two important parameters in the MRI sequences such as:

— Repetition Time (TR): the amount of time between subsequent pulse sequences given to the same slice is called repetition time (TR).

— Time to Echo (TE): is the period between when the radio frequency (RF) pulse is delivered and when the echo signal is received.

Let us now presenting the different MRI sequences:

- **T1-weighted (short TR and short TE):** the rate at which stimulated protons return to equilibrium is controlled by the time constant T1 (longitudinal relaxation time). It is the time token for spinning protons to realign themselves with the external magnetic field. Gray matter (dark gray) and white matter (lighter gray) tissues have strong contrast. However, cerebrospinal fluid (CSF) is devoid of signal (black). They are believed to be the best of all MRI protocols because they produce the most anatomical images, which closely resemble the appearances of tissues.
- **T2-weighted(long TR and long TE):** the time constant T2 (transverse relaxation time) governs the rate at which excited protons attain equilibrium or move out of

phase with one another. It creates a good contrast between the bright (CSF) and the dark (brain tissue), with GM being light gray and WM being dark gray. Due to the superior determination of water content in T2-weighted images, radiologists can see abnormalities within the ventricles and cerebral cortex better than on T1-weighted images.

- **Fluid Attenuated Inversion Recovery (Flair) (very long TE and TR):** the Flair sequence is similar to the T2-weighted image. The anomalies remain visible, but the normal CSF fluid is dimmed and darkened. This sequence is extremely sensitive to disease, making it much easier to distinguish between CSF and an abnormality.

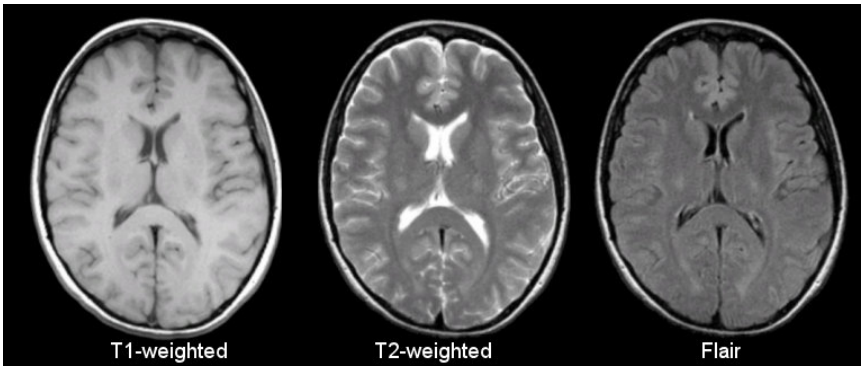

Figure 1.10 – Example: Axial slices of T1-weighted , T2-weighted , and Flair images of brain tissue.

In the Table 1.1, we summarize the difference between the tissues in each MRI sequences.

Tissues	**T1-Weighted**	**T2-Weighted**	**FLAIR**
CSF	Dark	Bright	Dark
White Matter	Light	Dark Gray	Dark Gray
Cortex	Gray	Light Gray	Light Gray

Table 1.1 – Comparison between T1, T2 and FLAIR.

1.7.2 MRI different planes

MR scanner can produce three different human head positions, which are Axial (a), Coronal (b), and Sagittal (c). The following are the basic terms for a body MRI. Where,

a sagittal plane would be viewed from the side, a coronal plane from the front, and a transverse plane from the top down.

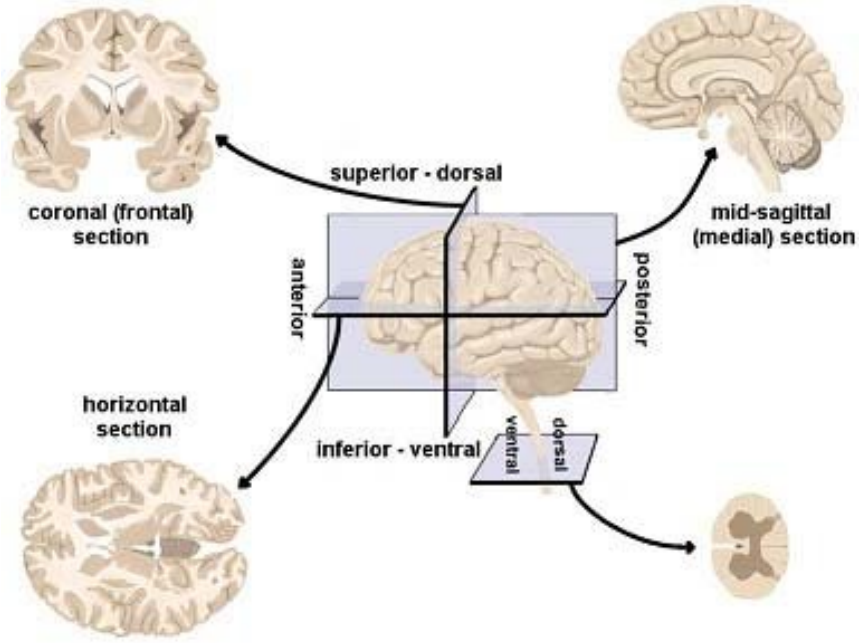

Figure 1.11 – Different planes of MRI brain image[36]

- **Axial plane (X-Y):** (also known as a transverse or horizontal plane) is a plane parallel to the ground separates the superior and inferior hemispheres of the brain. It's made by slicing the brain perpendicular to the body's long axis.
- **Sagittal plane (Y-Z):** (also known as the median plane) is a plane perpendicular to the ground that divides the brain into two separate halves (right and left). A mid-sagittal plane is a sagittal plane that runs across the center of the brain.
- **Coronal plane (X-Z):** (also known as a frontal plane) is a plane perpendicular to the ground that separates the anterior and posterior parts of the brain. It's made by slicing the brain parallel to the body's long axis.

1.7.3 Diffusion Tensor Imaging (DTI)

Peter Basser was the first to introduce DTI technology in 1994. It is a relatively new imaging technology that can be used to evaluate the brain's white matter. It's a better form of traditional MRI, in which signals are generated exclusively by the movement of water molecules. Diffusion is a word that refers to the random thermal mobility of water molecules. DT Image Representation by The tensor's information is either condensed into one number (scalar) or four numbers. To display the image with a R (red), G (green), B (blue) color and a brightness value like the Figure 1.12. Reduced fractional anisotropy

may indicate dementia [37]. Studies have shown that DTI is a powerful method for distinguishing Alzheimer's patients from healthy people.

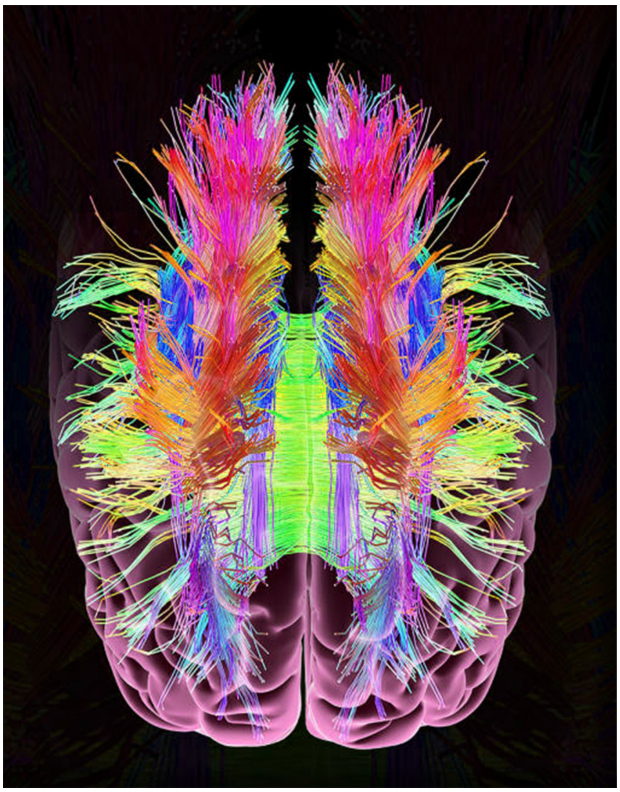

Figure 1.12 – Representation of DT images

1.7.4 The MRI magnet

As the name implies, magnetic resonance imaging (MRI) would not be possible without the magnet. Similarly, the scanner's magnetic field would not exist without the magnet. Magnetic resonance (MR) scanners are sometimes referred to as 1.5T or 3.0T scanners by medical practitioners, but there are varied strengths below 1.5T and, more recently, up to 7.0T. This refers to the strength of a scanner's magnetic field.

— **1.5T**: for most routine scans, is the standard imaging method. Longer sequences at 1.5T can greatly improve the quality of images, while 3.0T provides clarity and better detail [38].

— **3T :** is more likely to have artifacts caused by noise[39]. Because of the higher signal strength, 1.5T scans take longer to produce clear images, but 3.0T scans take less time.

1.8 Conclusion

In this chapter, we provided an overview of Alzheimer's diseases and different methods for diagnosis. We have also described the MRI methods, the different sequences and planes of MRI imaging. Deep learning methods allow building robust models for AD classification. so, in the next chapter we will try to detail it starting from an artificial neural network to a deep CNN network, we cover practically all of the fundamental principles, including the main modules and functions used to construct architectures.

Chapter 2

Deep learning for Alzheimer disease classification

Contents

2.1 Introduction

Artificial intelligence has been widely used in a various fields. Machine learning, and mainly deep learning, is one of its branches that has received a lot of attention in the recent years. Advanced algorithms based on deep learning methods are now included in computer-aided diagnostic (CAD) systems for neuroimaging. Where, many studies are relevant to neurodegenerative illnesses. In this context, the classification, detection, and segmentation are specific high-level tasks that have been engaged in several studies. One of the most important is the detection and the classification of Alzheimer's disease (AD).

This chapter provides an overview of deep learning methods which we will utilise to develop our work. We are focus on the Convolutional Neural Network (CNN) architecture where firstly, we start by presenting machine learning, and its different types of algorithms until we get to the deep learning and the algorithm used. Then, we introduce the main layers and elements used in the CNN approach. In the follow up, we describe the different standard components of CNN networks. Besides, we present an overview about the most popular techniques for overfitting. Finally, a brief state of the art is provided concerning the different works produced in the classification of Alzheimer's disease using deep learning.

2.2 Machine learning

Machine learning is an area of artificial intelligence (AI) and computer science that focuses on using data and algorithms to mimic the way humans learn, with the goal of getting better accuracy. According to Arthur Samuel (1959), machine learning is a "Field of study that gives computers the ability to learn without being explicitly programmed." In other words, it is concerned with the subject of how to build computer programs that develop themselves over time.

Tom M. Mitchell proposed a more formal definition of the algorithms explored in machine learning: "a computer program is said to learn from experience E with respect to some class of tasks T and performance measure P, if its performance at tasks in T, as measured by P, improves with experience E". This is in response to Alan Turing's proposition in his paper "Computing Machinery and Intelligence" [40], which asks: "Can machines think?". Machine learning, from our perspective, is a set of techniques that allow a machine to learn, solve problems, and perform tasks. This collection of techniques also enables machines to perform analysis and conception in order to solve difficult or even impossible to execute algorithms. The relationship between artificial intelligence (AI), machine learning (ML), and deep learning is represented in Figure 2.1.

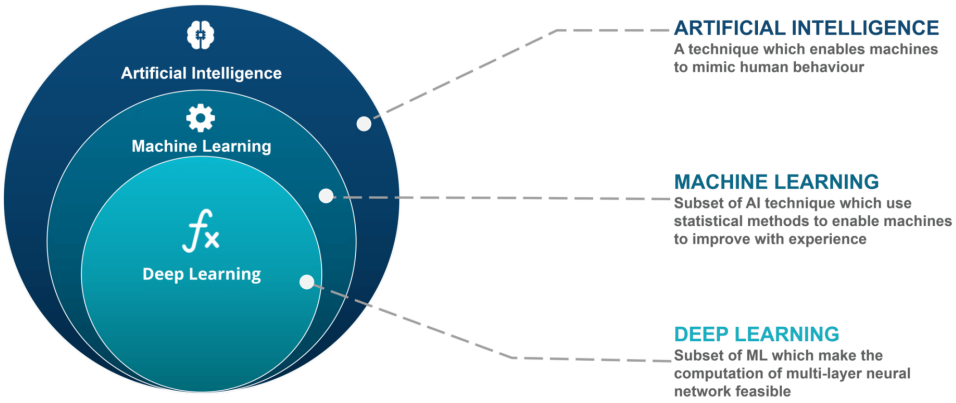

Figure 2.1 – Relationship between: AI, ML, and DL.

2.2.1 Types of machine learning algorithms

Depending on the type of the signal or feedback available to the learning system, machine learning systems are generally divided into three major categories:

2.2.1.1 Supervised learning

The supervised learning consists of using labeled data sets to train algorithms in classifying and predicting data results. Organizations can use supervised learning to tackle a range of real-world problems at scale. The figure (see Figure 2.2) shows an example of supervised machine learning. Some frequently used algorithms in supervised learning are linear and logistic regression, random forest, and support vector machine (SVM).

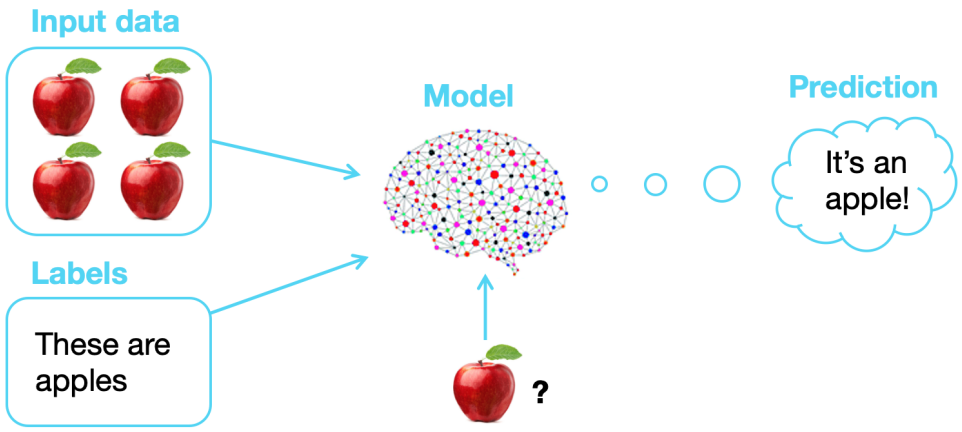

Figure 2.2 – Illustration of supervised learning example.

2.2.1.2 Unsupervised learning

Machine learning algorithms are used to analyze and cluster unlabeled datasets in unsupervised learning. These algorithms uncover hidden patterns or data groupings. Its ability to discover similarities and differences in information make it the ideal solution for exploratory data analysis, cross-selling strategies, customer segmentation, image and pattern recognition [41]. It is also used to reduce the number of features in a model through the process of dimensionality reduction, principal component analysis (PCA) and singular value decomposition (SVD) which are the two common approaches for this task [41]. Some frequently used algorithms in unsupervised learning are k-means, Apriori Algorithm for learning association rule.

In Figure 2.3 we fed the model by unlabeled data, and after training, the model was able to distinguish between the three classes, as well as build classes based on sample similarities.

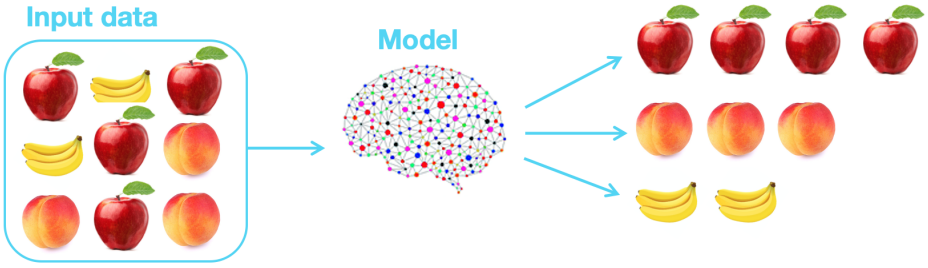

Figure 2.3 – Illustration of unsupervised learning example.

2.2.1.3 Semi-Supervised learning

Semi-supervised learning is a middle ground between supervised and unsupervised learning. It guides categorization and feature extraction from a larger, unlabeled data set using a smaller labeled data set during training. The basic procedure involved is that first, the programmer will cluster similar data using an unsupervised learning algorithm and then use the existing labeled data to label the rest of the unlabelled data [42] (see Figure 2.4).

2.3 Deep learning

Deep learning is a subdomain of machine learning that consists of more than three layers. These neural networks aim to mimic the activity of the human brain by allowing it to learn from enormous amounts of data, although they fall far short of its capabilities. While a single-layer neural network may produce approximate predictions, additional hidden layers can help to optimize and improve accuracy.

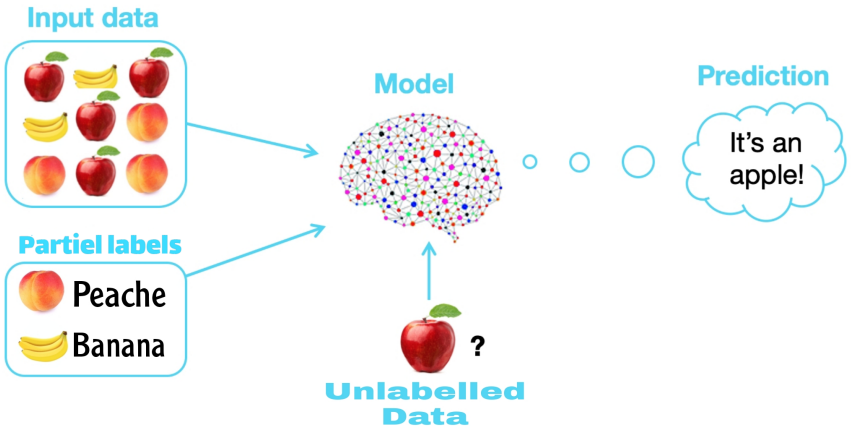

Figure 2.4 – Example of semi-supervised learning.

The deep learning algorithm passes the data through several layers. Each layer is capable of extracting features progressively and passing them to the next layer. Initial layers extract low-level features, and succeeding layers combine features to form a complete representation [43] .

2.3.1 The main difference between machine learning and deep learning

Before knowing the difference, let us first have an example of how machine learning (see Figure 2.5) and deep learning work (see Figure 2.6).

The workings of machine learning models can be illustrated using the example of classifying a cat or dog image. So, the machine learning model takes images of both cats and dogs as input, extracts various features from the images, such as shape, height, nose, eyes, and so on, applies the classification algorithm, and predicts the result.

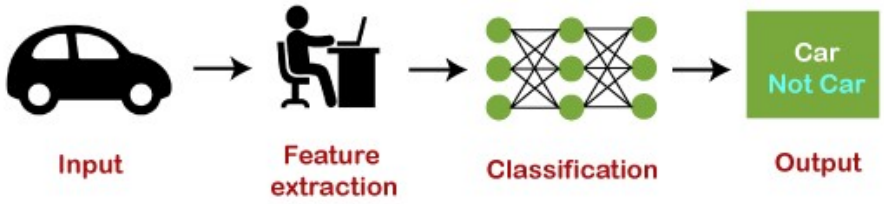

Figure 2.5 – Machine learning example.

With the same example of recognizing cat vs. dog, we can understand how deep learning works. The images are fed directly to the algorithms by the deep learning model, which eliminates the need for a manual feature extraction step. The images are passed through the artificial neural network's layers, which predict the ultimate output. after we know

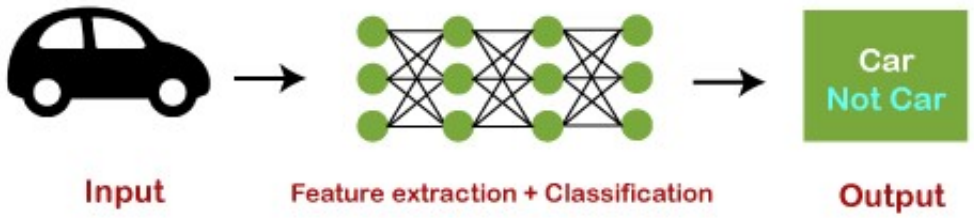

Figure 2.6 – Deep learning example.

how both deep learning and machine learning work we can say now the primary distinction between deep learning and machine learning algorithms is that deep learning algorithms automatically learn features. Whereas, machine learning requires us to manually extract features.

2.3.2 Deep learning applications in MRI image processing and analysis

In recent years, many deep learning algorithms for MRI image processing and analysis have been proposed, including image detection, image registration, image segmentation, and image classification.

All of these may be considered as feature representation problems, which can be solved well by employing deep learning techniques to identify an appropriate set of features.

2.3.2.1 Image detection

It is a type of computer technology that analyzes images and recognizes items within them. In computer-assisted detection routines, image detection is crucial. Its primary goal is to locate the tissues of interest, then measure and assess whether or not they generate lesions. Among the deep learning algorithms for MRI image detection that have been proposed in literature, we can cite: Shin et al.[44] which proposed a deep learning model using a stacked sparse autoencoder to perform organ diagnosis from a given complicated dataset with abnormalities, for which it is difficult to determine the labels of the samples in the dataset. Dou et al.[45] suggested an autonomous 3D convolutional network method to detect cerebral microbleeds (CMBs) from MRI data. Ghafoorian et al.[46] proposed an automated two-step deep convolutional network method for detecting lacunes of suspected vascular origin.

2.3.2.2 Image registration

Image registration is the process of combining several image files into a single coordinate system with matched imaging components, and it has numerous medical uses. Registra-

tion may be necessary when analyzing a pair of images that were acquired from different viewpoints, at different times, or using different sensors/modalities [47]. The spatial relationships between these images can be rigid (translations and rotations), affine (shears for example), homographies, or complex large deformations models [48].

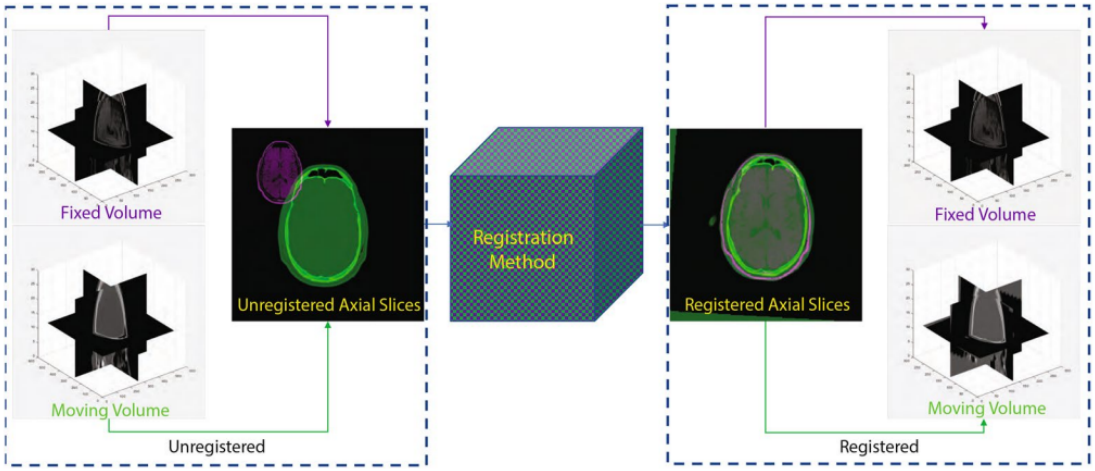

Figure 2.7 – The process of 3D medical image registration. [49]

2.3.2.3 Image segmentation

In computer vision, image segmentation is a crucial step. It consists segmenting a visual input to make image analysis easier. The regions segmented are made up of groupings of pixels, or super pixels, that depict things or sections of objects.

In modern medical research and clinical practice, automatic organ and tissue segmentation in MRI images is a challenge. Many medical image segmentation challenges, such as ischemic Stroke Lesion Segmentation, Multimodal Brain Tumor Image Segmentation, MR Brain Image Segmentation, and cardiac MR Left Ventricle (LV) segmentation, that have been organized to encourage the development of automatic segmentation systems. In this context, MRI brain images is one of the most common image segmentation field. It consists to segment the brain MR image to various tissues which are the gray matter (GM), white matter (WM), and cerebrospinal Fluid (CSF) [50].

2.3.2.4 Image classification

Deep neural networks have recently made a huge step forward in image classification systems. Image classification is useful in automatic disease diagnosis and cognitive identification, such as the classification of various disease severity and the recognition of various brain processes. Many deep learning algorithms for accomplishing image classification tasks in MRI images have also been proposed [51], such as:

✓ Alzheimer's disease classification

✓ Schizophrenia classification

✓ Brain activity classification

There are various classification approaches that have been developed and widely used However, there are two broad types of classification procedure and each finds application in the processing of remote sensing images: one is referred to as supervised classification and the other one is unsupervised classification [52].

In this context, our study are interested to the classification of Alzheimer's disease MRI images using deep learning methods.

2.4 Artificial Neural Networks (ANN)

The term artificial neural network is derived from biological neural networks, which define the structure of the human brain. The ANN have neurons in multiple layers that are connected one to another as the human brain where the neurons are referred to nodes (see Figure 2.8). Therefore, an artificial neural network is frequently modeled as an algorithm and its output is mostly determined by the activation functions and weights of the neural network.

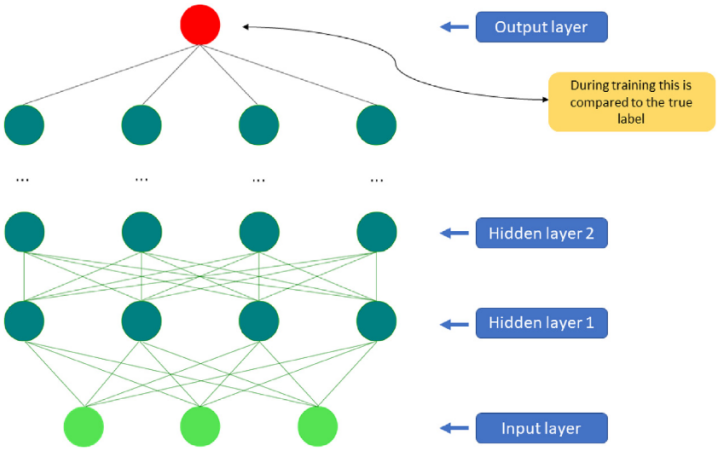

Figure 2.8 – Artificial neural network.

2.4.1 Biological neuron

Neurons generate electrical signals called action potentials, which allow them to quickly convey information over large distances. They are the basic functional components of the nervous system. A nerve cell neuron is a special biological cell that processes information. According to an estimation, there are huge number of neurons, approximately 10^{11} with numerous interconnections, approximately 10^{15}[53]. It composed of:

- **Dendrites :** are tree-like branches that receive messages from other neurons and transmit them to the cell body.
- **Cell body (or Soma) :** is the cell body of the neuron, and it is responsible for processing information received from dendrites.
- **Axon :** is a type of cable that transmits information from neurons.
- **Synapses :** are the connections between the axon and the dendrites of other neurons. Rather than a structure, it's a space where specific chemical interactions can take place.

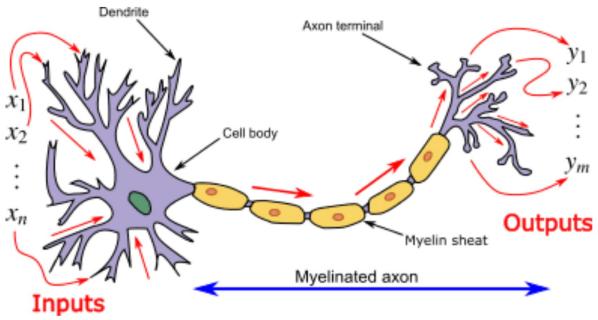

Figure 2.9 – Biological neural.

2.4.2 Artificial neuron

The basic unit of a neural network is the artificial neuron, often known as a perceptron. It's a mathematical function that's based on a biological neuron model. It can be viewed as a binary-output logic gate (see Figure 2.10). It composed of:

- **Input layer :** we can said also input values or one input layer. we pass input values which represent a number of variables $X = x1, x2, x3, ..., xn$ in order to a neuron using this layer.
- **Weights and bias :** each artificial neuron's input has a weight w that represents the value of the connection. The weighted sum is the sum of input values multiplied to the weight $\sum_{i=1}^{n} w_i * x_i$. A bias value is added to get the final value for prediction .
- **Activation layer:** it is a node that is placed at the end or in the middle of a neural network. The activation function is a non-linear transformation that we apply to the input before passing it to the next layer of neurons or transforming it to output. Some of the activation layer functions applied in CNN are presented as follows:
  - **Sigmoid :**

$$Sigmoid(x) = \frac{1}{(1 - e^{-x})} \tag{2.1}$$

— **ReLU :**

$$ReLU(x) = max(0, x) \tag{2.2}$$

— **Tanh :**

$$Tanh(x) = \frac{2}{(1 - e^{-2x})} - 1 \tag{2.3}$$

— **Softmax :**

$$Softmax(\vec{z})_i = \frac{e_i^z}{\sum_{j=1}^{K} e_j^z} \tag{2.4}$$

- **Output layer :** it provides a neuron's final output, which can later be transferred to other neurons in the network or used as the ultimate output value after being compared to a threshold value.

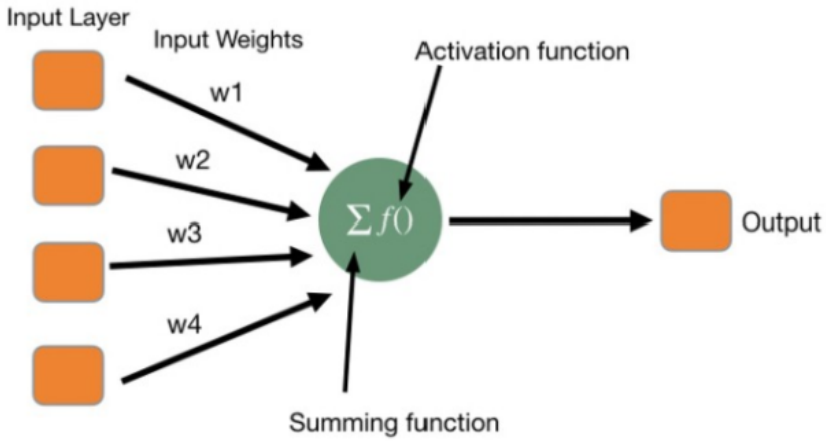

Figure 2.10 – Artificial neuron.

After explaining both biological neurons and artificial neurons, we can summarize the comparisons between them in the following Table 2.1:

Artificial neuron	**Biological neural**
Input	Dendrites
Node	Soma
Output	Axon
Interconnection	Synapse

Table 2.1 – Biological neuron vs. artificial neuron.

2.5 Convolutional neural network

A Convolutional Neural Network (CNN), often known as CNN or ConvNet, is a deep feed-forward artificial neural network that is commonly used to analyze visual input. It's the most popular deep learning algorithm. Their operation is based on the mathematical operation of convolution. A CNN architecture is made up of several layers. All of these layers are stacked together in some way in order to construct a complete CNN model. The main benefit of CNN compared to its predecessors is that it automatically identifies the relevant features without any human supervision[54].

There are multiple hidden layers in a convolutional neural network where the most important layers in CNN are:

- ✓ Convolutional layer
- ✓ Activation layer
- ✓ Pooling layer
- ✓ Fully-connected layer
- ✓ Dropout

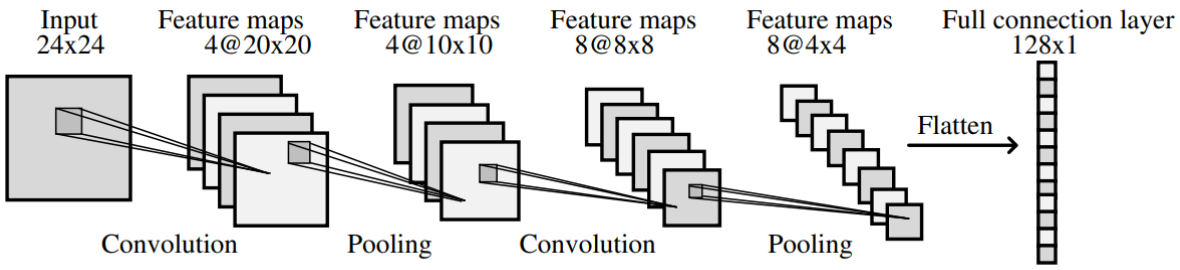

Figure 2.11 – An general architecture of the convolutional neural network [55]

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2.5.1 Convolutional layer

The core and first layer of a CNN's building component, the convolutional layer, is where the majority of computation takes place. In fact, the image is abstracted to a feature map, also known as an activation map, after passing through a convolutional layer. The convolution operation is performed by many filters in a convolution layer. Each image is viewed as a pixel value matrix.

In the convolutional layers, we use a kernel size of $m \times m \times C$, where C is the depth of a filter and m is the size of convolutional kernel [56]. The convolution operation can be denoted as:

$$x_j^l = \sum_{l=1}^{n} x_i^{l-1} * k_{ij}^{l-1} * b_i^l \tag{2.5}$$

where x denotes convolution, x_j^l is the j^{th} output map in layer l, the convolutional kernel k_{ij}^{l-1} (also called weight) can be updated while training the network. It connecting the i^{th} output map in layer l1 and the j^{th} output map in layer l. b_i^l is the trainable bias parameter of the j^{th} output map in layer l [56].

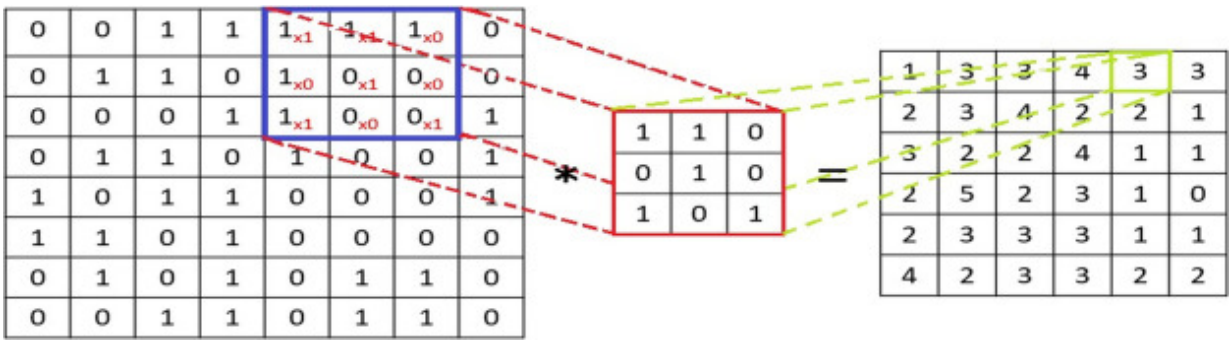


Figure 2.12 – Illustration of a simple example of the computing activation map. [57].

2.5.2 Pooling layer

Another layer of convolutional neural networks is the pooling layer. The function of this layer is to reduce the spatial dimensions (W and H) while keeping the same depth as the previous layer (C'). The pooling layer summarizes the features found in a specific region in the feature map generated by the convolution layer. In most cases, a pooling layer is located between two convolutional layers. There are different types of pooling operations such as the maximum pool, minimum pool, average pool and adaptive pool. The maximum pool and Average pool are the most used.

- **Max pooling :** is a pooling that selects the maximum element from the region in the feature map covered by the filter. As a result, the output of the max-pooling layer would be a feature map with the most prominent features from the previous feature map (see Figure 2.13).
- **Average pooling :** it computes the average of the items present in the region of the feature map covered by the filter. As we said before, the max-pooling returns the most prominent feature, while average pooling returns the average of all features present in that patch (see Figure 2.14).

2.5.3 Fully-Connected layer

Each neuron in the fully-connected layer is connected to every other neuron in the previous layer, similar to how neurons are arranged in a standard neural network (see Figure 2.8). This layer performs classification based on the features retrieved by the previous

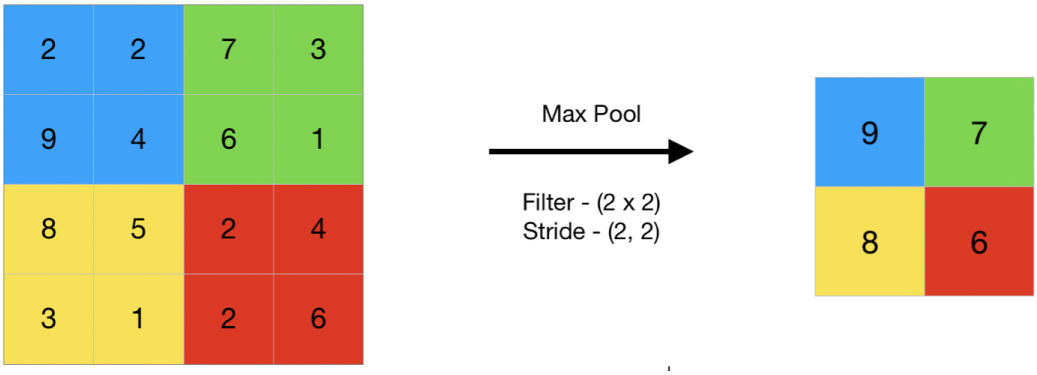


Figure 2.13 – Simple example of max pooling.

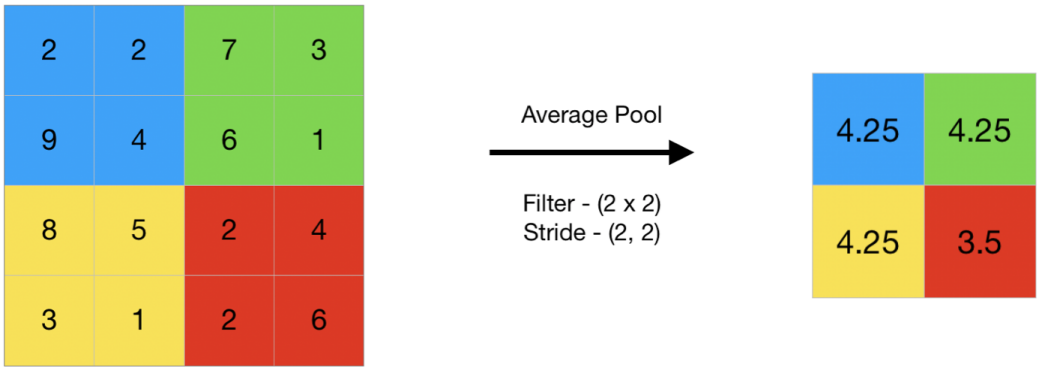


Figure 2.14 – Simple example of average pooling.

layers (convolutional and pooling layers), as well as their different filters. These are the most parameters used with the CNN within these layers, and take a long time in training [58].

2.6 Deep learning and data limitation constraint

In deep learnig approaches, we can find many limitations of data. The most known problem is the over-fitting. So, before presenting the different solutions proposed to solve this phenomena, we try to provide a brief explication of it.

2.6.1 Over-fitting phenomena

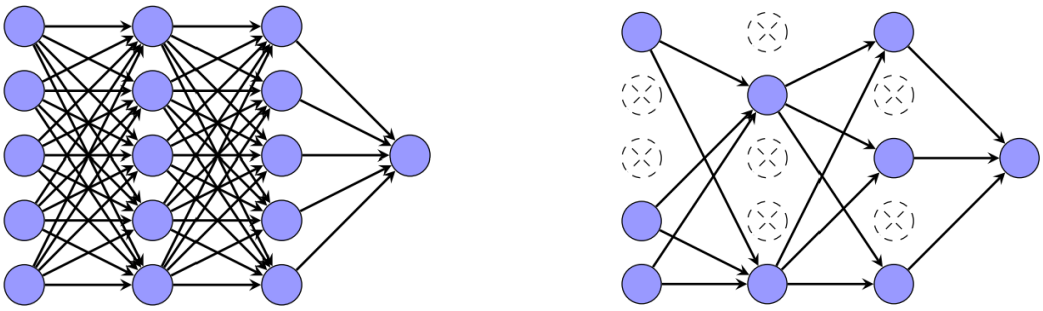
Overfitting is a statistical term for a modeling error that occurs when a function fits a set of data too closely. As a result, overfitting may fail to fit new data, lowering the accuracy of future prediction. Because of the presence of noise, the limited size of training set, and the complexity of classifiers, overfitting happens [36]. There are specialized techniques known as regularization methods, such as dropout, artificial data augmentation and transfer learning, that can be used to solve the problem in the context of CNNs. There are

other methods that can be used to prevent over-fitting that we did not explain in detail, which are : early stopping, train with more data and batch normalization.

2.6.2 Dropout layer

Dropout is an example of a regularization method and for dealing with both of Over-fitting and computational consumption problems. Where it prevents overfitting and allows for the efficient combination of exponentially many different neural network topologies.

The idea of dropout is to drop out units (neurons) in a neural network in which the dropping units are chosen by random with probability $q = 1p$. When any unit is dropped out, all its incoming and outgoing connections will be neglected [59] as illustrated in Figure 2.15. In the simplest case, each unit is retained with a fixed probability p independent of other units, where p can be chosen using a validation set or can simply be set at 0.5, which seems to be close to optimal for a wide range of networks and tasks. For the input units, however, the optimal probability of retention is usually closer to 1 than to 0.5 [60].



(a) (b)

Figure 2.15 – Illustration of an example of dropout method : (a): Standard neural network. (b): Result after applying dropout method.

2.6.3 Data augmentation

The quantity and diversity of training data determine the success of most machine learning models and deep learning models in particular. However, one of the most prevalent problems in applying machine learning is the limited data available.

Data augmentation is a set of techniques for producing additional data points from actual data in order to artificially increase the amount of data available. Making small modifications to data or applying deep learning models to create additional data points are examples of this. These modifications are: padding, random rotating, re-scaling, vertical and horizontal flipping and zooming, etc.

The figure (see Figure 2.16) below shows some modifications in the image of the cat by using rotation and clipping. From one image, we were able to extract six images using only two methods: Crop and Rotate.

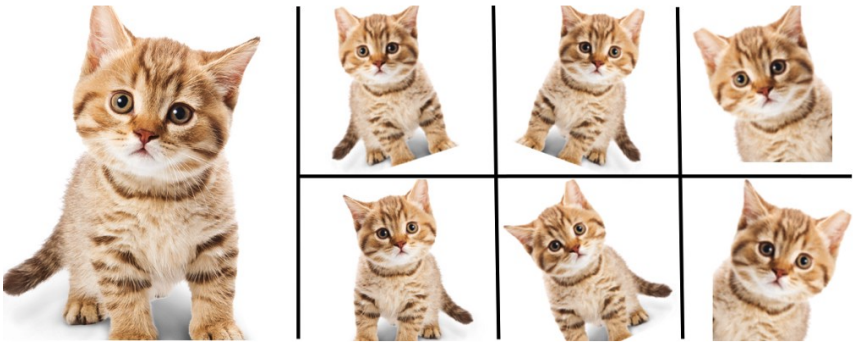


Figure 2.16 – Example of data augmentation.

2.6.4 Transfer learning and fine-tuning

In reality, learning a model from scratch is a difficult process in real-life situations. The training algorithms may not function properly, training time frames may be excessive, or training data may be insufficient. One of the approaches for facilitating training is transfer learning. The developer can take a pre-trained model and apply it to a similar task with a few modifications. Transfer learning can be defined as a fine-tuning process [16]. It has a number of advantages, the most important of which are reduced training time and higher neural network performance (in most cases)(see Fig 2.17).

- **Fine-Tuning :** is when the weights of all the layers of pre-trained neural networks (on dataset A) except the penultimate layer are frozen, and the neural network is trained on dataset B. This allows us to fine-tune the fundamental model's higher-order feature representations to make them more relevant for the task.
- **Pre-trained models :** AlexNet, GoogleNet, ResNet, Xception, VGG, Inception, InceptionResNet, MobileNet, MobileNet SSD ...

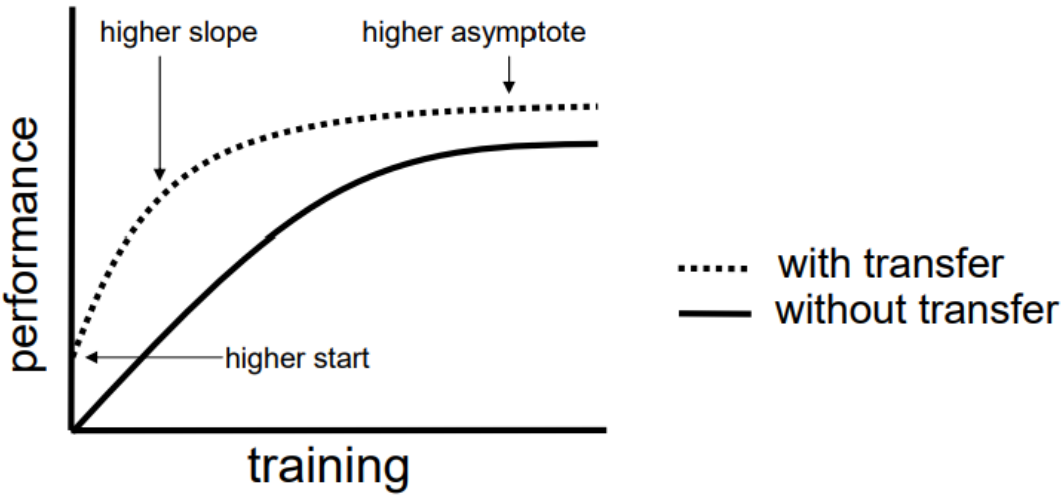


Figure 2.17 – Three ways in which transfer might improve learning [61]

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2.7 State-of-the-art about Alzheimer's disease classification in MRI images

Recently, the use of deep learning has been getting a lot of attention in the diagnosing of Alzheimer's disease. Several deep learning approaches have been proposed to help doctors in diagnostic and in making informed medical decisions for Alzheimer's disease. In this section, we present some of the works that are closely related to our study.

- **Ali Nawaz, et al.** [7]**:**
  Using an imbalanced three-dimensional MRI dataset of 160 patients, Ali Nawaz et al.[7] proposed a model based on a two-dimensional deep convolutional neural network (2D-DCNN). This model successfully classified MRI data into three categories: Alzheimer's disease (AD), mild cognitive impairment (MCI), and normal control (CN). They used initial preprocessing that contained Gradwarp, B1 non-uniformity, and N3 bias field correction for the dataset.

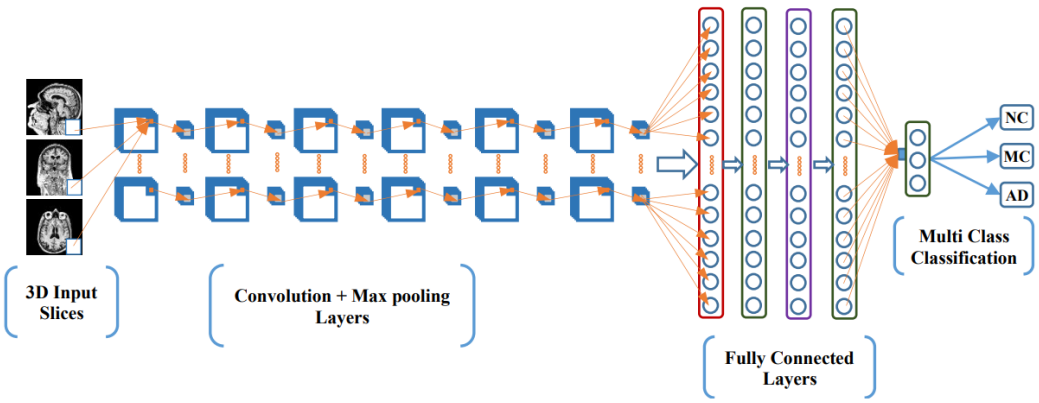


Figure 2.18 – The proposed convolutional neural network (CNN) model in this work.

- **Ahmad Waleed Salehi et al.** [62]:
  They employed the ADNI 3 class of images with a total of 1512 mild, 2633 normal, and 2480 AD to develop a Convolutional Neural Network (CNN) for the earlier diagnosis and categorization of AD using MRI scans. A level of accuracy of 99 percent was achieved.The input of the model is jpg image format, which was converted from nii using software called DICOM.
- **K A N N P Gunawardena et al.** [63]:
  Gunawardena et al. [63] proposed two experiments in order to the automatic prediction of Alzheimer's Disease from Structural MRI data. The first one is based on the use Support Vector Machines (SVMs) where they achieved 95% sensitivity, 71% specificity, and 84% accuracy. These obtained results were not successful. However, the second experiment, which was based on Convolutional Neural Network (CNN), achieved a high accuracy of around 96%. This proposed model was trained on 36 subjects divided into three classes: Alzheimer's disease (AD), mild cognitive impairment (MCI), and normal control (CN). They selected only the coronal plane for this study and used the Canny edge detection algorithm for extracting features (ventricles, hippocampal, and coretex) . Then they applied the segmentation using the Region of Interest (ROI) method.

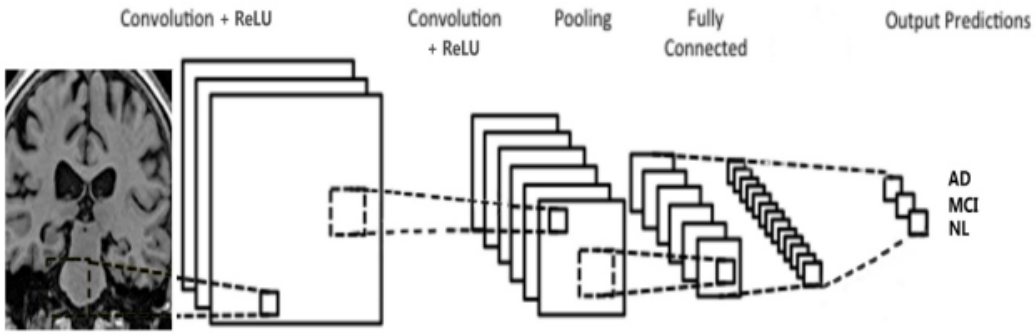


Figure 2.19 – Architecture of the CNN model.

- **Emtiaz Hussain** [64]:
  Emtiaz Hussain et al. [64] presented a model based on 12 layer convolutional neural network with different activation function (Sigmoid, ReLu, and Leaky ReLU) for binary classification indeed, to detect Alzheimer's disease using brain MRI data. They achieved an accuracy of 97.75%. To show the performance of this proposed model, they provided a side-by-side comparison between it and pretrained CNN models. The proposed model's results outperform pretrained CNN models, where the accuracy of InceptionV3, Xception, and MobileNetV2 was 90.62%, 84.37%, and 81.24%, respectively. The dataset used in this work is obtained from the Open Access Series of Imaging Studies (OASIS). They used function of library OpenCV3 to denoise images.
- **Ketki C. et al.** [65]
  In this work [65], Ketki et al built Deep CNN that achieved 97.98% accuracy. The used data is obtained from ADNI with a total of 13,733 images from 266 subjects. They used three convolutional layers, each followed by a maxpooling layer.
- **Lauge Sorensen et al.** [66]:
  They proposed a deep learning system that uses MRI and PET data from heimer's Disease Neuroimaging Initiative (ADNI), relying on hippocampal texture to identify distinct phases of Alzheimer's disease progression. They used the dropout strategy to improve classical deep learning by eliminating weight co-adaptation, a common source of deep learning overfitting. According to the obtained results of this work, the dropout methodology improved classification accuracy by 5%. For AD/NC, MCI/NC, and AD/MCI, the proposed technique achieved 91.4 percent, 77.4 percent, and 70.1 percent accuracy, respectively.

From all these studies, we conclude that the use of CNN achieved successful results for the diagnosis of Alzheimer's disease, not only here but in several other studies. This is what motivated us to rely on it in our study.

2.8 Conclusion

We presented an overview of the machine learning and deep learning approaches in this chapter. We also went over some of the basic concepts that are used to optimize models in the machine learning area, specifically Deep Neural Networks classifiers. After that, we went over CNN and its different layers. We next talked over some approaches for dealing with overfitting, such as artificial data augmentation and transfer learning.

In the next chapter, We will provide our AD classification systems and their implementations using CNN neural networks methods in MRI data.

Chapter 3

Design and implementation of Alzheimer's diseases classification system

Contents

3.1 Introduction

In our project, we want to build a convolutional neural network that can detect and classify Alzheimer's disease. In order to realise this aim we must do a will design assuring the best results. In this chapter, we present the design global and the detailed design of the proposed system, the implementation of our application for Alzheimer's diseases in MR images. The first part consists the presentation of the general and detailed architecture of our classification system. Where, the second one is about the implementation details

which are common tools, frameworks, and libraries used to realize the application. A swell as how we implemented our system.

3.2 Design of our Alzheimer's diseases classification system

In this section, both the conceptual study and the design of our system are provided. First, we present the general architecture that highlights the main processes of our system. Then, we will present the detailed one where each process will be independently explained.

3.2.1 General architecture

Our system will follow certain steps in order to construct a deep learning model for detecting and classifying Alzheimer's disease. The system begins by collecting the dataset, applying preprocessing on it, and splitting it, after which we input the split dataset to the CNN model, resulting in a model that is accurate, Then, our model can classify the new images into three classes: Alzheimer Disease (AD), Cognitively Normal (CN), or Mild Cognitive Impairment (MCI) as shown in the following Figure 3.1.

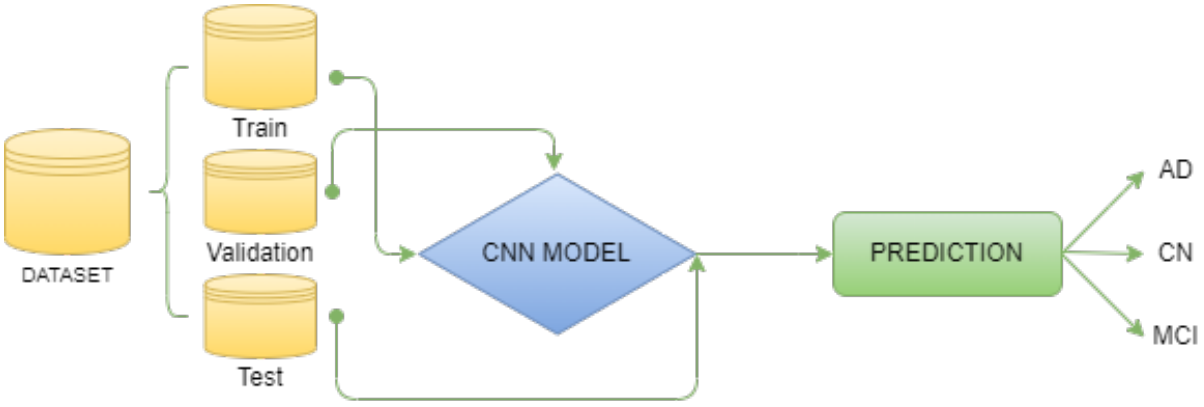


Figure 3.1 – The general architecture of our system.

3.2.2 Detailed architecture

In this part, we effectively get to the heart of our work with its detailed design in several steps starting from the loading and collecting data to the implementation (see Figure 3.2).

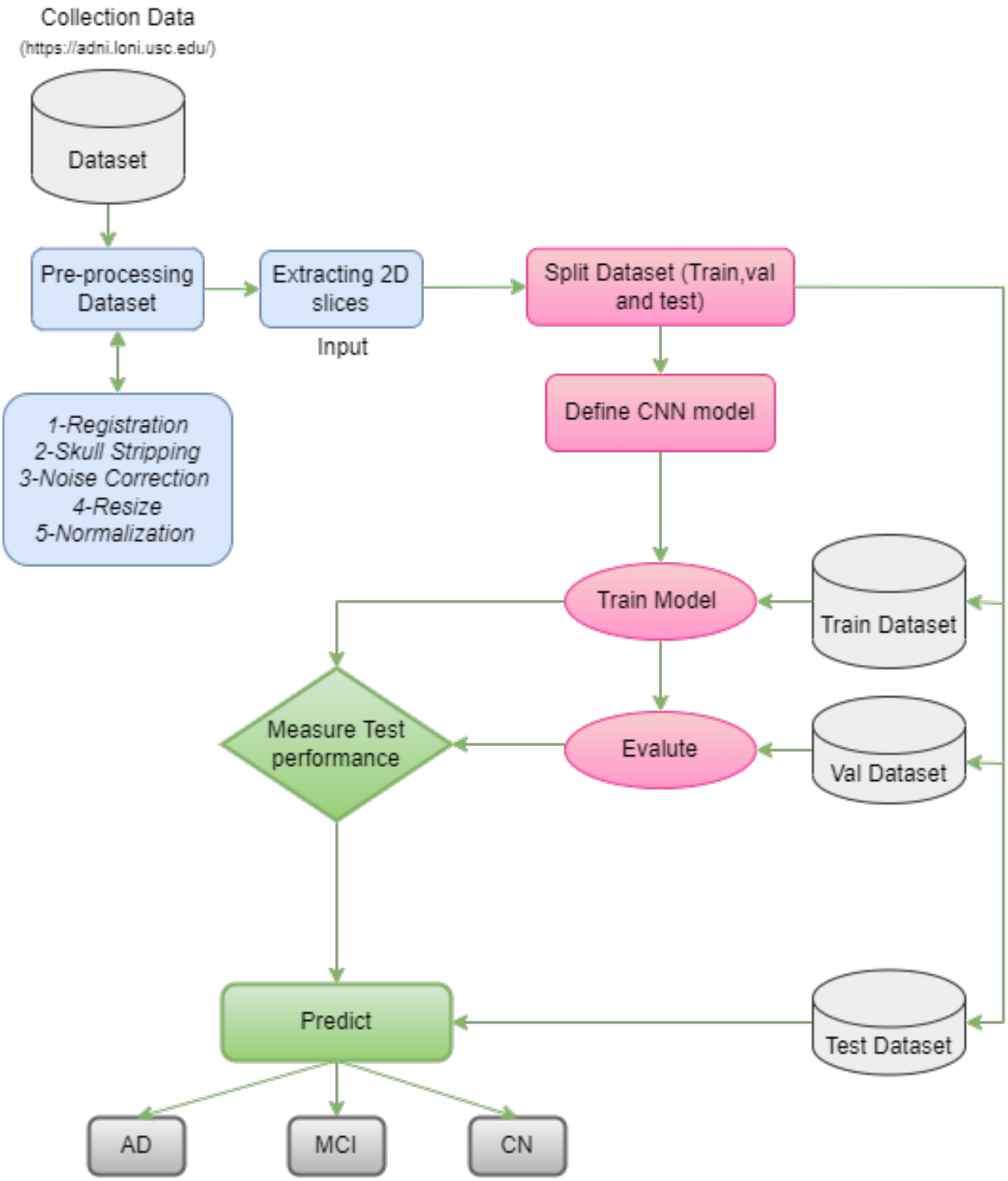


Figure 3.2 – Detailed architecture of our system.

3.2.2.1 Collecting data

The loading phase, which includes collecting data for both training and testing, is the initial step in our learning system. The dataset used in our study was collected from the Alzheimer's Disease Neuroimaging Initiative (ADNI) [67]. This one was established

in 2004 by the National Institute on Aging (NIA) as a multi-center longitudinal study to discover clinical, imaging, genetic, and biochemical biomarkers for the early diagnosis and tracking of Alzheimer's disease (AD). The ADNI dataset contains various modality data such as PET, functional MRI, MRI, genetic data, and clinical in- formation for thousands of patients. In particular, the subjects structural MRI volumes were obtained on 3T scanners during a multi-time period ranging one to three years. The images were in NII extension format (Neuroimaging Informatics Technology Intiative (Nifti)). After one, two, and three years, the same patient is scanned at different points in time on different visits. The study included 86 AD patients, 101 MCI patients, and 111 healthy controls. The demographics of the dataset are listed in Table 3.1.

Source	**Classes**	**Subjects**	**Age**	**Gender (F/M)**
ADNI	AD	86	[58 - 90]	(68 F/ 18 M)
	MCI	101	[56 - 89]	(31 F/ 70 M)
	CN	111	[71 - 88]	(46 F/ 65 M)

Table 3.1 – Illustration of the demographic description of the ADNI dataset group.

3.2.2.2 Pre processing

Before providing data to our model, certain image processing methods can be applied in order to prepare the data. In our work, the pre processing step includes affine transformation (registration) [68], skull stripping [68], bias field Correction, rescale intensity and denoise, resize and normalization.

- **Affine transformation (registration) :** one of the most fundamental and important procedures in biological image processing is image registration. The method is classified as an optimization method, with the purpose of determining the best spatial transformation (or deformation) parameters that align source images with the destination image or template (Figure 3.3). The registration method's goal is to align a series of images from a dataset to a common space in order to facilitate image processing and analysis while also improving performance and efficiency. There are many templates used in data pre-processing, especially for the registration process such as ICBM-152.
- **Skull stripping :** this phase was used to eliminate any non-essential information from the scans, leaving only the brain matter. This was done with FSL BET [68]. Because not all MRI data is acquired and preprocessed in the same way before being

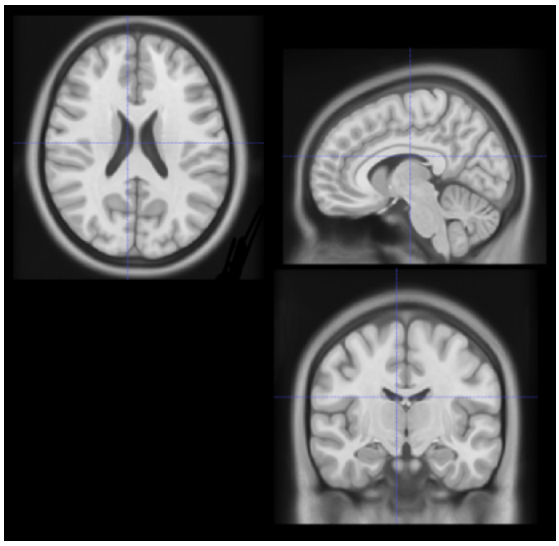


Figure 3.3 – The ICBM-152 template.

stored in the ADNI database, finding the ideal fractional intensity threshold for the entire dataset would be impossible. After several experiments, a threshold of 0.5 was chosen since it maintained a correct balance for the majority of photos.

- **Bias field Correction :** one of the most basic corrective approaches that must be applied to MRI data is bias field correction. For this situation, several image analysis data sets and corrections can be employed to reduce the influence of the signal that obscures the white/gray matter.
- **Rescale intensity and denoise :** working with a series of photos from a medical database requires the intensity normalization technique. This operation allows us to bring all of the database's elements intensities to a common standard scale. Researchers in the field have developed several image intensity normalization techniques, among which we found those that are appropriate for brain imaging. This method is based on the utilization of the image's histogram. In other words, the goal is for all photos in the database to have a similar intensity, allowing us to detect the same tissue.
- **Image resize :** the dataset contains images of different sizes which can cause the architecture to be inaccurate. So, in our model we resized each image to (224 × 224 × 224).
- **Image normalization :** it is a procedure for standardizing the range of independent variables or data characteristics (i.e., changing the range of pixel intensity values). It involves rescaling the range of image intensity values to a scale of [0, 1] according to the equation 3.1.

$$F(x) = \frac{x - min(x)}{max(x) - min(x)} \tag{3.1}$$

The following Figure 3.4 provide an overview of our proposed pre processing step.

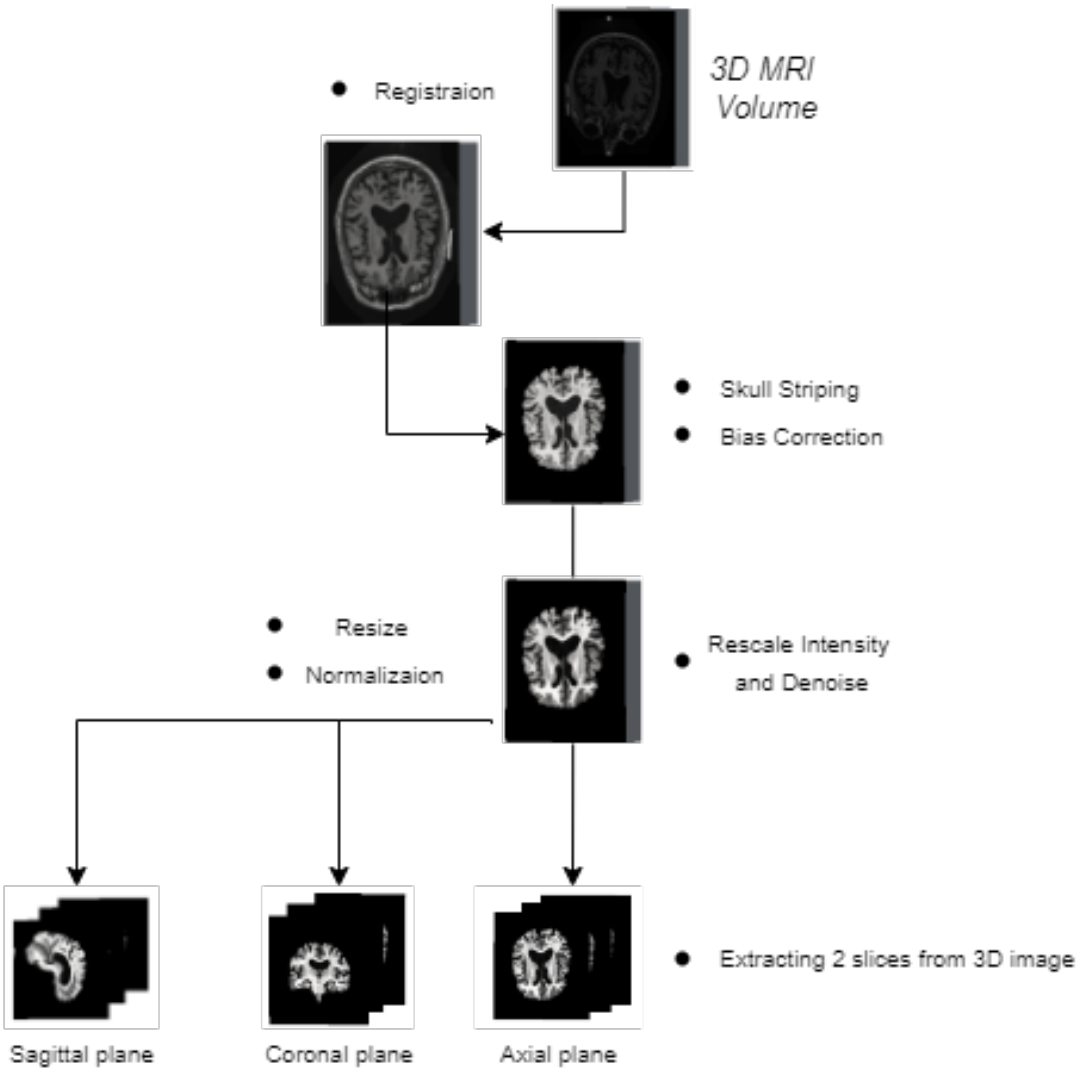


Figure 3.4 – An overview of our proposed preprocessing steps.

3.2.2.3 Data loading

- **Data labeling :**
  After the phase of preprocessing, we labeled our data into 3 classes: AD, MCI, and CN using a csv file provided with the ADNI dataset.
- **Data Split :**
  Based on random selection, we divided the dataset into an 8:1:1 ratio. That means 80% of the data is used for training, 10% is used for validation, and 10% is used for testing.
- **Extraction of 2D slices :**
  Each image is represented on a three-dimensional plane. First, we converted it into

two-dimensional images, represented by slices. The choice of slices is an essential process for the recognition of patterns in medical images, because if the slices are selected incorrectly, it may impair the learning of the algorithms. Therefore, for each examination, we selected 20 slices. The total quantity in this dataset is 5960 slices. It is the same number for each plane axial, coronal, and sagittal.

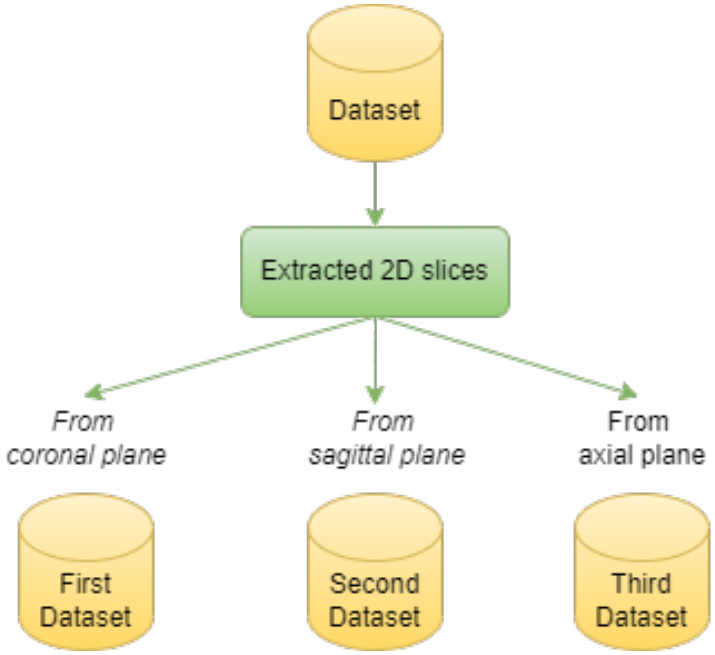


Figure 3.5 – Our proposed data structure.

3D-level: this method offers data in 3D volume and has a lot of features. However, some brain regions are included in this method that aren't always appropriate, especially if we wish to diagnose Alzheimer's disease early. Working with 3D volume also necessitates a lot of processing power (it needs a strong GPU capability and RAM).

Now we're ready to train our model, which will be broken down into three steps: training, testing, and prediction.

3.2.2.4 CNN learning

In order to create a CNN, we will need to first go over layer parameters, hyper parameters, optimizers, and other model parameters using the training and validation subsets.

The CNN is a mathematical structure with various levels (as seen in the previous chapter), each layer performing a task on the image or set of images in order to obtain characteristics that can be found anywhere in the image.

	Description
Layers	A CNN is made up of a stack of separate layers, such as convolution layers, pooling layers, fully connected layers, and dropout layers.
Optimizers	are techniques or approaches that adjust the characteristics of a neural network, such as weights and learning rate, to reduce losses. There are a variety of optimizers available, including SGD, RMSprop, adam, and others.
Loss function	The error value is defined as the difference between the actual and predicted values computed using loss functions (such as regression loss, binary classification, and multiclass classification loss functions).

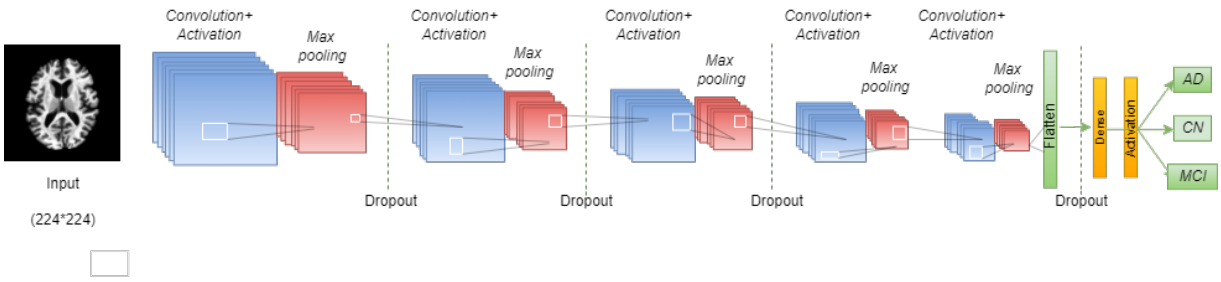


Figure 3.6 – Our proposed CNN architecture.

3.2.2.5 Prediction

Following the training phase, the prediction phase is when a CNN model is ready to classify images. We will utilize the third subset from the dataset splitting to test our CNN model.

3.2.2.6 Evaluation of a CNN model

In order to asses our deep learning CNN, we need to compute some metrics. Because the accuracy alone is insufficient to assess model performance, particularly for multi-class data, performance metrics like precision, recall, and F1-score were employed to assess test accuracy. The performance metrics are defined by four parameters: (1) true positive (**TP**): a data point labeled as positive by the model but is actually positive (correct). (2) false positive (**FP**): a data point labeled as positive but is actually negative (incorrect). (3)

true negative(**TN**): the model labels a data point as negative when it is actually negative (wrong), and (4) False negative (**FN**): the model labels a data point as negative when it is actually positive. The equations of accuracy, precision, recall, and f1-score are presented as follow:

$$ACCURACY = \frac{TP + TN}{TP + TN + FP + FN} \tag{3.2}$$

$$PRECISION = \frac{TP}{TP + FP} \tag{3.3}$$

$$RECALL = \frac{TP}{TP + FN} \tag{3.4}$$

$$F1SCORE = \frac{TP}{TP + \frac{1}{2}(FN + FP)} \tag{3.5}$$

3.3 Implementation of our deep learning model

3.3.1 Hardware configuration

Our hardware configuration is an Microsoft Surface pro laptop of the following characteristics:

— Processor : Intel(R) Core(TM) i5-7300U.

— Processor Frequency : 2.71 GHz.

— RAM: 8 Go.

— Hard drive: 256Go (Solid state drive (SSD)).

— Graphics: HD Graphics 620.

3.3.2 Frameworks , tools and libraries

- **Python :** is an open source programming language. It was designed to be both simple to read and effective. Python was created in 1991 by Guido van Rossum, a Dutch programmer.

Figure 3.7 – Python logo.

- **Google Colab :** also known as Google Colaboratory, is a free Jupyter notebook environment that runs on Google's cloud servers and allows users to take advantage of backend hardware such as GPUS and TPUS.

Figure 3.8 – Google colab logo.

- **TennsorFlow :** is a machine learning and artificial intelligence software library that is free and open-source. It can be used for a variety of applications, but it focuses on deep neural network training and inference.

Figure 3.9 – TensorFlow logo.

- **Keras :** Keras is an open source neural network library written in Python that runs on top of Theano or Tensorflow. It's built to be modular, quick, and simple to use. It was created by Google developer François Chollet.

Figure 3.10 – Python logo.

- **Matplotlib :** is a graphing package for Python with NumPy, the Python numerical mathematics extension. It provides an object-oriented API for embedding plots into applications utilizing GUI toolkits such as Tkinter, wxPython, Qt, or GTK.

Figure 3.11 – Matplotlib logo.

- **Numpy :** is a Python library for array processing. It includes a high-performance multidimensional array object as well as utilities for manipulating it. It is the most important Python package for scientific computing.

Figure 3.12 – Numpy logo.

- **OpenCv** (Open Source Computer Vision Library): is a free software library for computer vision and machine learning. OpenCV was created to provide a common infrastructure for computer vision applications and to help commercial goods incorporate machine perception more quickly.

Figure 3.13 – OpenCv logo.

- **FSL (FMRIB Software Library) :** is a comprehensive toolkit for the analysis of medical MRI brain imaging data. It provides tools for data preprocessing, brain extraction, image registration as well as a broad spectrum of statistical analyses.

Figure 3.14 – FSL logo.

- **NiBabel :** is the successor of PyNIfTI.This package provides read-only access to some common medical and neuroimaging file formats, including: GIFTI, NIFTI1, NIFTI2, etc.
- **Advanced Normalization Tools (ANTS) :** is an ITK-based suite of normalization, segmentation, and template-building tools for quantitative morphometric analysis.

3.3.3 Dataset preparation and preprocessing

- **Registration :** we used the template ICBM-152 in this step to perform the 3D affine transformation (see Figure 3.3). Where the parameters used are:
  flirt : (FMRIB's Linear Image Registration Tool)is a command for image regestration.
  -in : input
  -ref : template(ICBM-152)
  -out : output

```
import os
import subprocess
import matplotlib.pyplot as plt
from multiprocessing import Pool, cpu_count
def registration(src_path, dst_path, template):
    command=["flirt", "-in", src_path, "-ref",template,"-out",
   dst_path]
    subprocess.call(command, stdout=open(os.devnull, "r"),
                    stderr=subprocess.STDOUT)

```

Listing 3.1 – Registration

- **Skull-stripping :**
  After registration, a skull-stripping step has been carried out to remove irrelevant information from the images. As previously mentioned, FSL BET was used for this. The key here was to find the appropriate value for the main hyper-parameter: the fractional intensity threshold, which is 0.5.

```
import os
import subprocess
from multiprocessing import Pool, cpu_count
def strip_skull(src_path, dst_path, frac="0.5"):
    print("Working on :", src_path)
    try:
        bet(src_path, dst_path, frac)
    except RuntimeError:
        print("\tFailed on: ", src_path)
def bet(src_path, dst_path, frac="0.5"):
    command=["bet", src_path, dst_path, "-R", "-f", frac]
    subprocess.call(command)
    #-R: robust brain centre estimation (iterates BET several times)
    #-f: fractional intensity threshold (0->1); default=0.5;
```

Listing 3.2 – Skull-stripping

- **Bias field correction :**

  We have applied the N4 bias field algorithm of the ANTS package. N4 is a variation of the well-known N3 bias correcting method (nonparametric, nonuniform normalization).

```
import os
from multiprocessing import Pool, cpu_count
from nipype.interfaces.ants.segmentation import
    N4BiasFieldCorrection
def bias_field_correction(src_path, dst path):
    try:
        n4=N4BiasFieldCorrection()
        n4.inputs.input_image=src_path
        n4.inputs.output_image=dst_path
        n4.inputs.dimension=3
        n4.run()
    except RuntimeError:
        print ("\tFailed on: ", src_path)

```

Listing 3.3 – Bias field correction

- **Rescale itensity and denoise :**

  medflit :is function to perform a median filter on an N-dimensional array.

```
import os
import numpy as np
import nibabel as nib
from scipy.signal import medfilt
from multiprocessing import Pool, cpu_count
def denoise(volume, kernel_size=3):
    return medfilt(volume, kernel_size)
def rescale_intensity(volume, percentils, bins_num): #volume is the
    image
    obj_volume=volume[np.where(volume>0)]
    min_value=np.percentile(obj_volume, percentils[0])
    max_value=np.percentile(obj_volume, percentils[1])
   if bins_num=0:
        obj_volume=(obj_volume-min_value)/(max_value-min_value).
    astype(np.float32)
    else:
        obj_volume=np.round((obj_volume-min_value)/(max_value-
    min_value)*(bins_num-1))
    volume=volume.astype(obj_volume.dtype)
    return volume
```

Listing 3.4 – Rescale itensity and denoise

- **Resize and normalization :**

  Normalization of each image and resizing to (224 × 224 × 224).

```
import os
import numpy as np
import nibabel as nib
import matplotlib.pyplot as plt
from multiprocessing import Pool, cpu_count
from scipy.ndimage.interpolation import zoom
from dltk.io import preprocessing
def norm(data):
            data=data/float(np.max (data))
    return data
def process (src_path, dst_path):
    print("Wroking on: ", src_path)
    try:
        data=load_nii(src_path)
        data=preprocessing.resize_image_with_crop_or_pad(data,
   img_size=(224, 224, 224),mode='symmetric')
        data=norm(data)
        save_nii(data,dst_path)
    except RuntimeError:
        print("Failed on :", src_path)
```

Listing 3.5 – Resize and normalization

- **Splitting of dataset**

  To divide our dataset into three subsets, we used splitfolder.ratio.

```
import splitfolders
input="path/to/dataset"
output="path/to/new_dataset"
splitfolders.ratio(input,output,
                   seed=42,
                   ratio=(.8,.1,.1),#devide dataset to 80% training,
    10% validation, and 10% testing.
                   group_prefix=(None))
```

Listing 3.6 – Splitting dataset

- **2D Slice extraction :**

  In this step, we chose 20 slices between (100, 120) then we converted them to 2D images in png format. Therefore, we obtained 3 datasets where the first dataset is 2D axial slices, the second dataset is 2D sagittal slices, and the last one is 2D coronal slices.

```
import numpy as np
from skimage import img_as_ubyte
import nibabel as nib
```

```
from skimage import io
import os
import subprocess
from multiprocessing import Pool, cpu_count
def extract_2d_slices(data,path):
    image = nib.load(data)
    image = a.get_data()
    id=data.split('/')[-1]
    id=id.split('.')[-0]
    for i in range(100,120):
            img=image[:,i,:]
            id_name=id+"_"+str(i)+".png"
            io.imsave(os.path.join(path,id_name),img_as_ubyte(img))
```

Listing 3.7 – 2D slice extraction

- **Preparing dataset**

  After uploading the dataset to our account on Google Drive and mounting Google Colab with Google Drive, we will now prepare it for the CNN model.

```
from google.colab import drive
drive.mount('/content/drive')
```

Listing 3.8 – Mount Google Drive

Training dataset

```
import numpy as np
import cv2.cv2 as cv
import os
for label in LABELS:
        path = os.path.join("path/to/trainig_dataset", label)
        class_num = LABELS.index(label)
        for img in os.listdir(path):
            try:
                img_array = cv.imread(os.path.join(path, img))
                new_array = cv.resize(img_array, (224, 224))
                X_TRAIN.append(new_array)
                Y_TRAIN.append(class_num)
            except Exception as e:
                pass
```

Listing 3.9 – Preparing training dataset

Validation dataset

```
for label in LABELS:
        path = os.path.join("path/to/validation_dataset", label)
        class_num = LABELS.index(label)
        print(class_num)
```

```
        for img in os.listdir(path):
            try:
                img_array = cv.imread(os.path.join(path, img))
                new_array = cv.resize(img_array,(224, 224))
                X_VAL.append(new_array)
                Y_VAL.append(class_num)
            except Exception as e:
                pass
```

Listing 3.10 – Preparing validation dataset

3.3.4 Building our CNN model

1. **Import libraries and modules**

   In order to build a CNN model, we must use Keras. Firstly, we import the necessary libraries.

```
import numpy as np
import matplotlib.pyplot as plt
import os
import tensorflow as tf
from tensorflow.keras.models import Sequential
from tensorflow.keras.layers import Dense, Dropout, Activation,
    Flatten, Conv2D, MaxPooling2D
from keras.callbacks import ModelCheckpoint, EarlyStopping
```

   Listing 3.11 – Necessary imports for building a CNN model

2. **Creating CNN model**

   Table 3.2 contains the parameter specifications for both the binary classification and multi-class classification models. Loss provides the most accurate assessment of the model's fitness. For our dataset, the Adam optimizer provides the best accuracy with less loss.

Parameter	Binary classification	Multi-class classification
Input shape	(224,224)	(224,224)
Epochs	70	200
Batch size	32 (By default)	
Layer activation	ReLu	ReLu
Dense activation	Sigmiod	Softmax
Optimizer	Adam	Adam
Drop out	0.2	0.2
Loss	Binary Crossentropy	Sparse Categorical Crossentrop

Table 3.2 – Parameter specification of the binary and multi-class classification model.

```
model = Sequential()

model.add(Conv2D(filters =32 , kernel_size =(5,5), input_shape =
    (224,224,3)))
model.add(Activation("relu"))
model.add(MaxPooling2D(pool_size=(2,2)))

model.add(Dropout(0.2))

model.add(Conv2D(filters =32 , kernel_size =(5,5)))
model.add(Activation("relu"))
model.add(MaxPooling2D(pool_size=(2,2)))

model.add(Dropout(0.2))

model.add(Conv2D(filters =32 , kernel_size =(5,5)))
model.add(Activation("relu"))
model.add(MaxPooling2D(pool_size=(2,2)))

model.add(Conv2D(filters =32 , kernel_size =(5,5)))
model.add(Activation("relu"))
model.add(MaxPooling2D(pool_size=(2,2)))

model.add(Dropout(0.2))

model.add(Conv2D(filters =32 , kernel_size =(5,5)))
model.add(Activation("relu"))
model.add(MaxPooling2D(pool_size=(2,2)))

model.add(Flatten())
```

```
model.add(Dropout(0.2))
```

Listing 3.12 – CNN model architecture

There are two choices for the last layer, which is according to the type of classification (binary classification or multi-class classification).

Binary classification

```
model.add(Dense(1))
model.add(Activation("sigmoid"))
```

Listing 3.13 – Binary classification

Multi-class classification

```
model.add(Dense(3))
model.add(Activation("softmax"))
```

Listing 3.14 – Multi-class classification

3. **Compiling CNN Model**

   Binary classification

```
model.compile(optimizer='adam',
              loss=tf.keras.losses.BinaryCrossentropy(),
              metrics=['accuracy'])
```

Listing 3.15 – Compiling binary model

Multi-class classification

```
model.compile(optimizer='adam',
              loss=tf.keras.losses.SparseCategoricalCrossentropy
   (),
              metrics=['accuracy'])
```

Listing 3.16 – Compiling model

4. **Model summary**

   Now we can call the summary () method to show the contents and parameters of the model.

```
model.summary()
```

Listing 3.17 – Model summary

```
Model: "sequential"
_________________________________________________________________
 Layer (type)                Output Shape              Param #
=================================================================
 conv2d (Conv2D)             (None, 220, 220, 32)      2432

 activation (Activation)     (None, 220, 220, 32)      0

 max_pooling2d (MaxPooling2D  (None, 110, 110, 32)     0
 )

 dropout (Dropout)           (None, 110, 110, 32)      0

 conv2d_1 (Conv2D)           (None, 106, 106, 32)      25632

 activation_1 (Activation)   (None, 106, 106, 32)      0

 max_pooling2d_1 (MaxPooling  (None, 53, 53, 32)       0
 2D)

 dropout_1 (Dropout)         (None, 53, 53, 32)        0

 conv2d_2 (Conv2D)           (None, 49, 49, 32)        25632

 activation_2 (Activation)   (None, 49, 49, 32)        0

 max_pooling2d_2 (MaxPooling  (None, 24, 24, 32)       0
 2D)

 conv2d_3 (Conv2D)           (None, 20, 20, 32)        25632

 activation_3 (Activation)   (None, 20, 20, 32)        0

 max_pooling2d_3 (MaxPooling  (None, 10, 10, 32)       0
 2D)

 dropout_2 (Dropout)         (None, 10, 10, 32)        0

 conv2d_4 (Conv2D)           (None, 6, 6, 32)          25632

 activation_4 (Activation)   (None, 6, 6, 32)          0

 max_pooling2d_4 (MaxPooling  (None, 3, 3, 32)         0
 2D)

 flatten (Flatten)           (None, 288)               0

 dropout_3 (Dropout)         (None, 288)               0

 dense (Dense)               (None, 3)                 867

 activation_5 (Activation)   (None, 3)                 0

=================================================================
Total params: 105,827
Trainable params: 105,827
Non-trainable params: 0
_________________________________________________________________
```

Figure 3.15 – Illustration of our model summary.

5. **Training CNN model**

   We used fit, Modelcheckpoint, and EarlyStopping with the model to train it.This section will explain it.

```
early_stopping = EarlyStopping(monitor='val_accuracy',
                               min_delta=0,
                               patience=10,
                               verbose=1,
                               mode='auto')
model_checkpoint = ModelCheckpoint("model.h5",
                                   monitor='val_accuracy',
                                   verbose=1,
                                   save_best_only=True,
                                   save_weights_only=False,
                                   mode='auto',
                                   period=1)
model.fit(X_TRAIN,Y_TRAIN,
          epochs=number_of_epochs,
          validation_data=(X_VAL,Y_VAL),
          callbacks=[model_checkpoint,early_stopping])
```

Listing 3.18 – Fitting model

- **Modelcheckpoint**: is used in conjunction with training using model.fit() to save a model or weights (in a checkpoint file) at some interval, so the model or weights can be loaded later to continue the training from the state saved.
- **EarlyStopping**: this Keras callback function is used to pause model training in the middle. When your models get overfit. It's used to stop the model from becoming overfitted. While saving the model checkpoints, we defined what to monitor.
- **Model Fit**: we are first feeding the training data(X_TRAIN) and training labels (Y_TRAIN) and validation by (X_VAL,Y_VAL). We then use Keras to allow our model to train for 100 epochs on a batch_size of 32.

3.3.5 Testing our CNN model

In order to test our model on the third subset (test) we have used this code.

```
path = "path/to/test_dataset"
for img in os.listdir(path):
    try:
        img_array = cv.imread(os.path.join(path, img))
        new_img = cv.resize(img_array, (224, 224))
        predictions = model.predict(new_img)
```

```
7           print(predictions)
8           print(LABELS[np.argmax(predictions)])
9       except Exception as e:
10          pass
```

Listing 3.19 – Testning model

3.4 Conclusion

In this chapter, we explained in details the different steps of our system design, the tools, libraries, and frameworks that we are utilized, the implementation of a large section of our system, and our CNN model. The following chapter will go over various experiments and their results.

Chapter 4

Experimental Results and Discussion

Contents

4.1 Introduction

In the previous chapter, we discussed our system architecture, demonstrated the structures of the used dataset, and provided code source for each part of our classification system. In this chapter, We will explain our experimental results of the Alzheimer's disease classification into three stages AD, MCI (mild cognitive impairment), and CN (cognitively normal). Our results are divided into two parts. The first one describes the obtained results for the binary classification of Alzheimer's disease. Where the second one is devoted to present the multi-class calssification results. At the end, we will provide a comparison between our findings and those of other studies in the field.

4.2 The obtained results for binary classification of Alzheimer's disease

4.2.1 Binary classification AD vs. CN

In the case of binary classification of Alzheimer's disease (AD), we train our model in order to detect two classes: AD and CN (cognitively normal). Therefore, to construct our data base, the label YES AD represents the AD patients and NO AD represents the CN patients (cognitively normal) (see Table 4.1).

In this binary classification, we don't use the class MCI (mild cognitive impairment) because longitudinal studies reveal that not all patients diagnosed with MCI develop Alzheimer's disease.

Class	Number of images
AD	1720
CN	2220

Table 4.1 – Dataset structure.

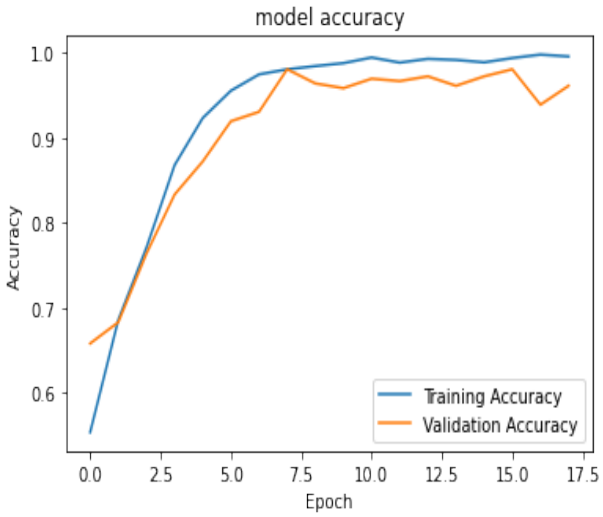
4.2.1.1 Model performance

The experiment results were carried out using 3,940 2D slices extracted from 3D structural MRI scans of 197 patients in the ADNI datasets. To asses our model in different planes (axial, sagittal, and coronal) of our dataset, we used training and validation accuracy and loss.

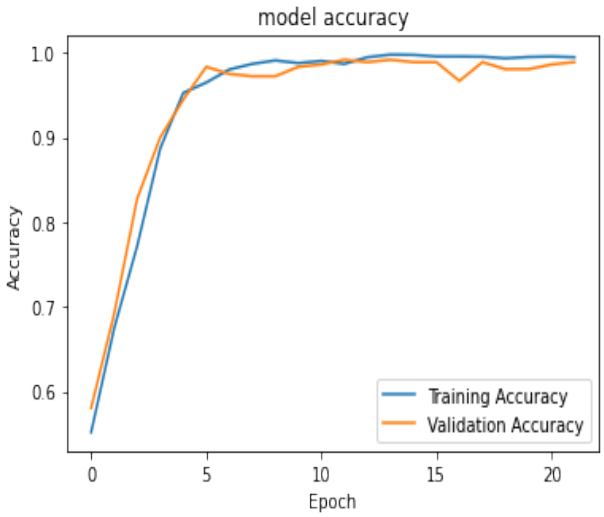
The Figure 4.1 shows a plot of training and validation accuracy over epochs for each plane. As we said before, we trained our model for 70 epochs using early stopping with a patience of 10. The cornal plane model stops at epoch 20, the sagittal plane at epoch 17, and the axial plane at epoch 25. As shown in these graphs, Our model provided a good performance in the coronal plane, which is close to **100 %**, and **98 %** in the sagittal and axial planes.

The Figure 4.2 illustrates the loss and validation loss values over epochs For each plane. We can see that the loss values in these plots is almost null. Where, the validation loss in the third dataset (axial plane) is higher than in the coronal and sagittal planes.

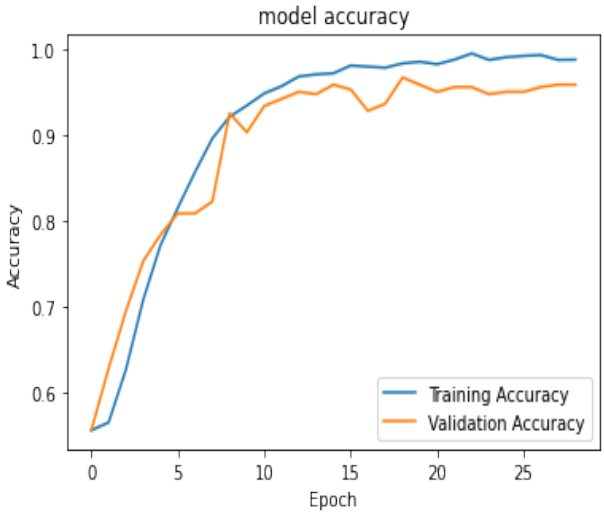
The Table 4.2 summarizes all the performances obtained (accuracy and loss) by our model in each plane for the binary classification of Alzheimer's diseases.



Sagittal Plane

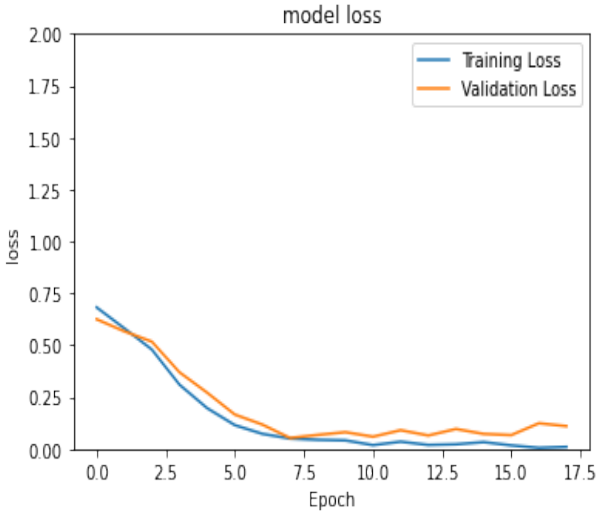


Coronal Plane

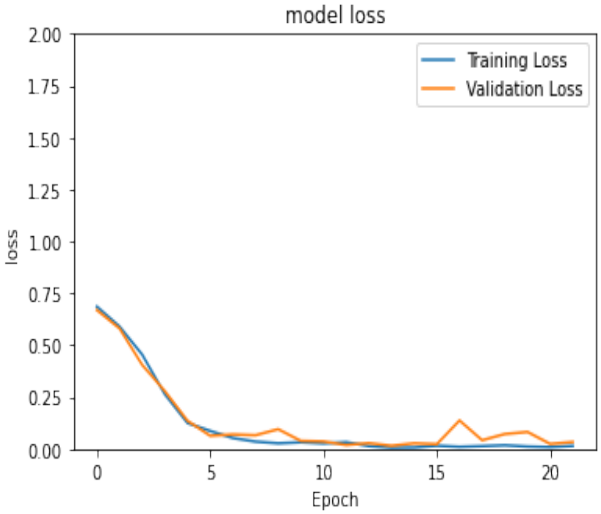


Axial Plane

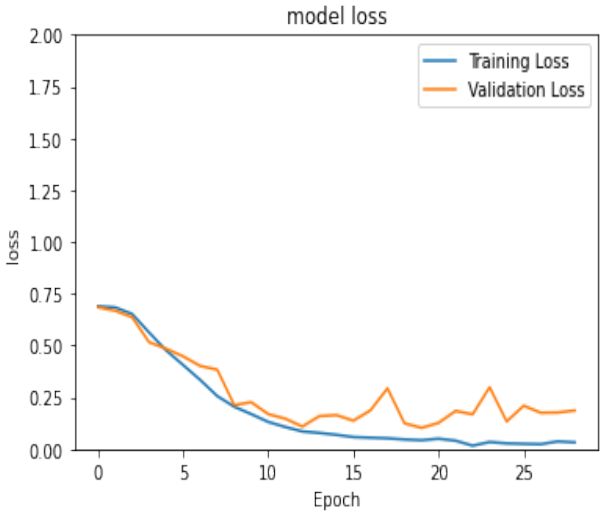
Figure 4.1 – Binary classification model accuracy.



Sagittal Plane



Coronal Plane



Axial Plane

Figure 4.2 – Binary classification model loss.

	Accuracy	**Loss**	**Validation accuracy**	**Validation Loss**
Coronal Plane	99.78%	0.006	99.17%	0.01
Sagittal Plane	98.05%	0.05	98.06%	0.05
Axial Plane	98.31%	0.04	96.67%	0.12

Table 4.2 – Illustration of binary classification performance of our proposed model.

— **Model results on Testing data**

The obtained result by testing our model demonstrate its ability to correctly predict all the images, which means that it achieved a perfect score of 100% in coronal plane as shown in the following Figure 4.7.

```
---------Test Model----------
13/13 [==============================] - 0s 25ms/step - loss: 0.0523 - accuracy: 0.9825
Accuracy  : 0.9825
Precision : 0.9833333333333333
f1Score : 0.9825940189226455
[[140   0]
 [  7 253]]
```

Sagittal Plane

```
---------Test Model----------
13/13 [==============================] - 0s 25ms/step - loss: 0.0031 - accuracy: 1.0000
Accuracy  : 1.0
Precision : 1.0
f1Score : 1.0
[[140   0]
 [  0 260]]
```

Coronal Plane

```
---------Test Model----------
13/13 [==============================] - 0s 27ms/step - loss: 0.0424 - accuracy: 0.9850
Accuracy  : 0.985
Precision : 0.985
f1Score : 0.985
[[137   3]
 [  3 257]]
```

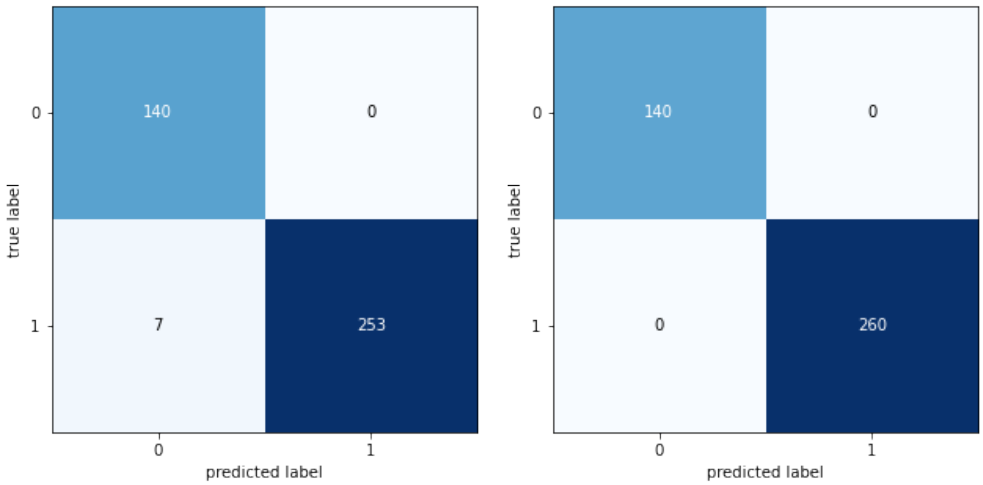
Axial Plane

Figure 4.3 – Illustration of model results on Testing data.

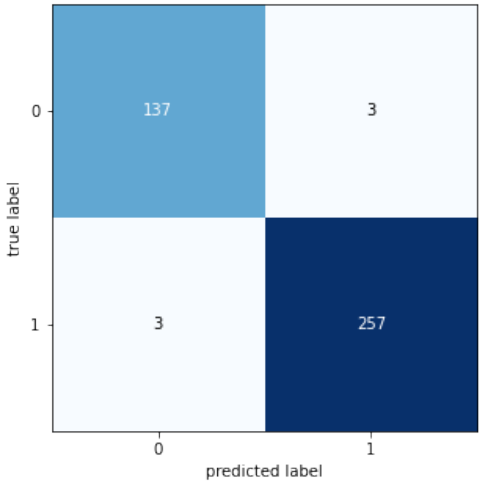
— **Confusion matrix**

The Figure 4.4 depicts matrix confusion, with label 0 representing YES AD and label 1 representing NO AD. The confusion matrix is a graph or table that summarizes the performance of a machine learning classification model. Confusion matrices are useful for predictive analysis and can be used to assess which functions a machine learning system performs correctly and which ones it performs incorrectly. As see in the following our model could predict:

1. 100% of YES AD and 100% NO AD in coronal plane.
2. 100% of YES AD and 97.30% NO AD in sagittal plane.
3. 97.86% of YES AD and 98.85% NO AD in axial plane.



Sagittal Plane Coronal Plane



Axial Plane

Figure 4.4 – Confusion matrix.

4.2.2 Binary classification (AD vs. MCI and MCI vs. CN)

Table 4.3 shows all the obtained results of our model in order to classify different classes (AD vs. CN, AD vs. MCI, and MCI vs. CN). Our model can differentiate between both AD vs. CN and MCI vs. CN with high accuracy. Whereas, in the case of AD vs. MCI, the validation accuracy is low compared to the other results.

	Accuracy					
	Axial Plane		**Coronal Plane**		**Sagittal Plane**	
	Training	**Validation**	**Training**	**Validation**	**Training**	**Validation**
AD vs.CN	98.31%	96.67%	99.78%	99.17%	98.05	98.06
MCI vs.CN	98.50%	97.73%	99.74%	99.62%	99.53	99.47
AD vs.MCI	99.05%	93.25%	98.98%	97.35%	99.34	95.29
	Loss					
AD vs.CN	0.04%	0.12%	0.006%	0.01%	0.05	0.05
MCI vs.CN	0.03%	0.06%	0.008%	0.01%	0.01	0.02
AD vs.MCI	0.05%	0.21%	0.02%	0.12%	0.01	0.20

Table 4.3 – Results of binary classification (AD vs. CN, AD vs. MCI, and MCI vs. CN).

4.3 The obtained results for multi-class classification

In this case, we trained our model in order to classify Alzheimer's disease into 3 stages (AD, MCI and CN). Where the AD stands for Alzheimer's disease patients, MCI stands for mild cognitive impairment, and CN stands for cognitively normal. AD, MCI (mild cognitive impairment), and CN (cognitively normal). As mentioned in the previous chapter, we divided the ADNI data into three datasets asee Figure 3.5). We just change the planes (axial, sagittal, and coronal).

The following Table 4.4 illustrates the general dataset structure as the number images in each stage.

Class	**Number of images**
AD	1720
MCI	2020
CN	2220

Table 4.4 – Dataset structure.

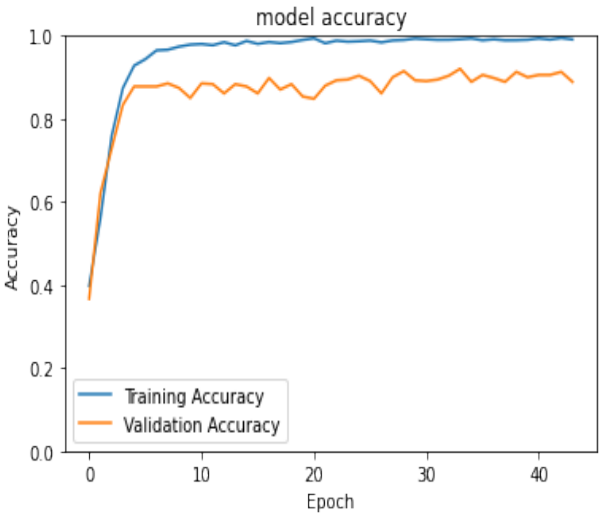
4.3.0.1 Model performance

The experiment results were carried out using 5,960 2D slices extracted from 3D structural MRI scans of 298 patients in the ADNI datasets, CN, and two AD severity images. To asses our model, we used training and validation accuracy and loss. Furthermore, the value of early stopping callbacks used during the training with a patience is 10.

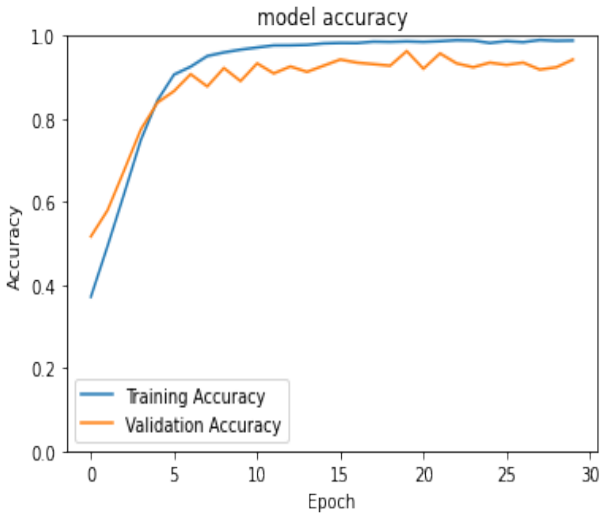
The Figure 4.5 shows a plot of training and validation accuracy over epochs for each plane. As we said before, we trained our model for 200 epochs using early stopping with a patience of 10. The cornal plane model stops at epoch 30, the sagittal plane at epoch 44, and the axial plane at epoch 39. The best obtained performance is in the coronal plane with **99%** training and **96%** validation accuracy, which means the features that can differentiate Alzheimer's disease in 3 stages are more clear in the coronal plane in our case. Then the sagittal plane with 99% training and 92% validation accuracy, and the last one is the axial plane with low accuracy (96% training and 90% validation).

The Figure 4.6 represents a plot of loss and validation loss during the training. In plots of sagittal and axial plane, there are times when loss is decreasing while validation loss is increasing (different from inequality of loss and validation loss), which means learning based on training data is done successfully, but this learning is not that generalized to be able to be applied to another data-set that hasn't been seen before (validation dataset). Reverse the coronal plane in which the loss and validation loss are decreasing to 0.

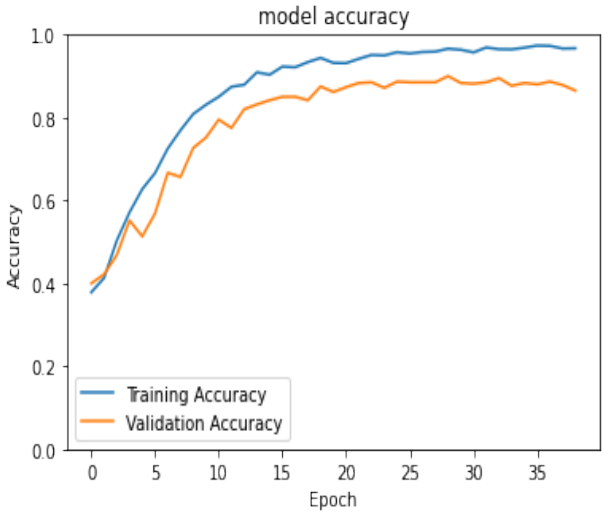
The Table 4.5 summarizes all our model performance (accuracy and loss) for each plane.



Coronal Plane

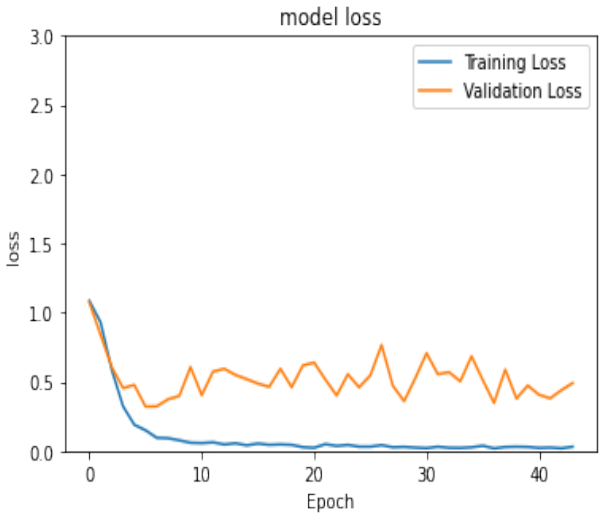


Sagittal Plane

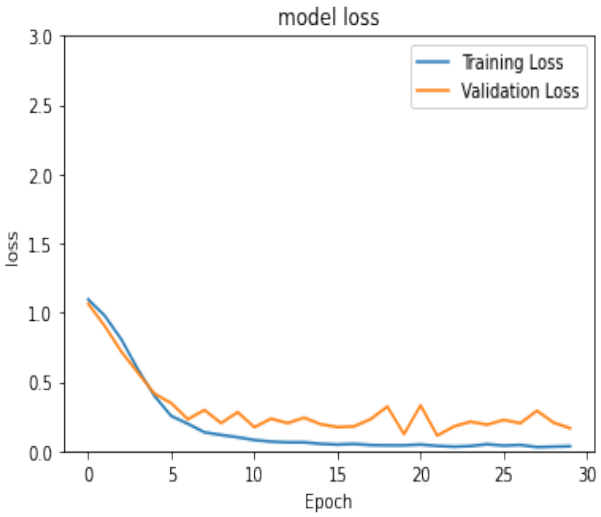


Axial Plane

Figure 4.5 – Multi-class classification model accuracy.



Sagittal Plane



Coronal Plane

Axial Plane

Figure 4.6 – Multi-class classification model loss.

	Accuracy	**Loss**	**Validation accuracy**	**Validation Loss**
Coronal Plane	98.62%	0.04	96.30%	0.12
Sagittal Plane	99.15%	0.02	92.04%	0.50
Axial Plane	96.61%	0.09	90.00%	0.69

Table 4.5 – Illustration of multi-class classification of our proposed model.

— **Model results on Testing data**

When we tested our model, we obtained the results shown in the figure below.

```
---------Test Model----------
20/20 [==============================] - 1s 25ms/step - loss: 0.3657 - accuracy: 0.9323
Accuracy  : 0.932258064516129
Precision : 0.9371539788236617
f1Score : 0.9327864093667297
[[139   0   1]
 [ 11 241   8]
 [ 15   7 198]]
```

Sagittal Plane

```
---------Test Model----------
20/20 [==============================] - 1s 28ms/step - loss: 0.0319 - accuracy: 0.9887
Accuracy  : 0.9887096774193549
Precision : 0.9887257690002281
f1Score : 0.9886923325037902
[[140   0   0]
 [  0 258   2]
 [  1   4 215]]
```

Coronal Plane

```
---------Test Model----------
20/20 [==============================] - 1s 25ms/step - loss: 0.2181 - accuracy: 0.9435
Accuracy  : 0.9435483870967742
Precision : 0.9472164122194301
f1Score : 0.9444629199550502
[[133   1   6]
 [  8 248   4]
 [ 16   0 204]]
```

Axial Plane

Figure 4.7 – Illustration of model results on Testing data.

— **Confusion matrix**

The Figure 4.8 shows the matrix confusion of our proposed model performance where label 0 represents the AD class, label 1 represents the CN class, and label 2 represents the MCI class.

- Labels 0, 1, and 2 represent our classes AD, CN, and MCI respectively.
- We can see here our model could predict:
  1. 100% of AD, and 99.23% CN, and 97.73% MCI in coronal plane.
  2. 99.28% of AD, and 92.69% CN, and 90% MCI in sagittal plane.
  3. 95% of AD, and 95.38% CN, and 92.72% MCI in axial plane.

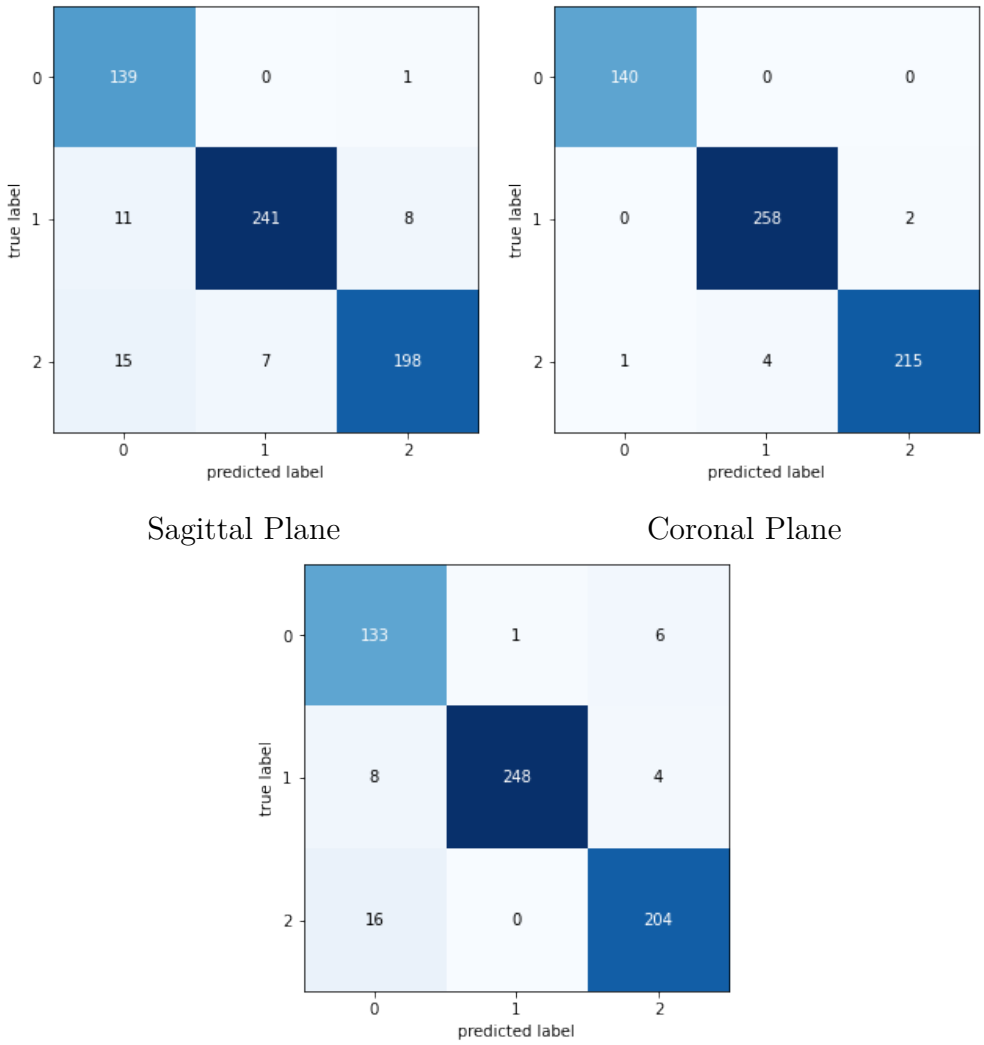


Figure 4.8 – Confusion matrix.

4.4 Results comparison

To evaluate our model's performance, we compare our obtained results to some existing deep learning-based approaches in the literature. In general, our approach performs well and provides good results compared to other proposed works in the same context.

We get a good accuracy of about **99.78%** in binary classification compared to 97.75% in [64]. Also, in multi-call classification, we get an accuracy of about **98.62%** compared to 96.25%, 98.57%, and 96% in [69], [65], and [63] respectively.

Models	Architecture	Modality	Type of classification	Accuracy
Our proposed	**CNN**	**298/MRI**	**Multi (3 classes)**	**98.62%**
Marcia Hon et al [69]	CNN	416/MRI	Multi (3 classes)	96.25%
Swathi S. Kundaram [65] and Ketki C. Pathak	DCNN	266/MRI	Multi (3 classes)	98.57%
Gunawardena et al [63]	SVM	36/MRI	Multi (3 classes)	84%
Gunawardena et al[63]	CNN	36/MRI	Multi (3 classes)	96%
P.R. Buvaneswari [8] and R. Gayathri	Res-Net-101	240/MRI	Multi (3 classes)	96.3%
Our proposed	**CNN**	**197/MRI**	**Binary (2 classes)**	**99.78%**
Emtiaz Hussain et al [64]	CNN	46/MRI	Binary (2 classes)	97.75%

Table 4.6 – Performance comparison of our proposed models with different models.

4.5 Discussion

After examining the outcomes of several plans, we conclude that the coronal plane provides the most discriminative results in binary classification. Indeed, our model can discriminate between AD brains and healthy control (CN) perfectly. As well, it holds true for the CN/MCI classification task. Nonetheless, there is no consensus on measurements in AD/MCI. Indeed, separating Mild Cognitive Impairment (MCI) from already present Alzheimer's disease is challenging even for medical experts, making AD/MCI the most difficult categorization endeavor.

In the multi-class classification, we also achieved the best results in the coronal plane. But in the axial plane and sagittal plane, our model is over-learned because in these planes there are not enough features (less representative data from the coronal plan) which can help the model to be able to distinguish stages of the Alzheimer disease.

4.6 Conclusion

In this chapter, we presented the general and the detailed design of our classification model. Also the different tools, packages and APIs required in our implementation.

In addition, we described the various parameters for both binary and multi-class classification. Also, all the experiments and the obtained results are displayed. The acquired results show exceptionally strong performance in the medical field.

General conclusion

Artificial intelligence (AI) has garnered the attention of a wide range of fields in recent years, including health. The development and deployment of AI in medicine is aided by the rise of computer hardware and software applications in medicine. One of the uses of deep learning in health care is decision-making and diagnosis. Alzheimer's disease is one of the most major challenges that medical industry clients are now dealing with. Deep learning is being used to diagnose Alzheimer's disease in its early stages, making treatment easier for clinicians, which has shown encouraging results. Where the diagnostics are being made more accurate and faster through deep learning.

In this context, we proposed in our study to use Convolutional Neural Network (CNN) architecture in order to detect and classify Alzheimer's disease in different stages: Cognitively Normal CN, Mild Cognitive Impairment (MCI), and AD brains. Our model is trained and validated using 2D images extracted from 3D MRI volumes providing in the Alzheimer's Disease Neuroimaging Initiative (ADNI) unites researchers ADNI [67] for:

— Binary classification (AD/CN, MCI/CN, and AD/MCI).

— Multi-class classification (AD, MCI, and CN).

— In three planes (axial, coronal, and sagittal).

Each 3D MRI scan has 256×256×160 slices, which makes it difficult to choose the slices correctly, and this decision requires a neurologist. Because we don't have a background in the field of medicine, we had to run a number of experiments in order to choose the slices properly. The result of these experiments is taking 20 slices for each plane and training it.

The obtained results demonstrated the effectiveness of our model in both binary classification and multi-class classification compared to some existing methods. We get a good accuracy of about **99.78%** in binary classification compared to 97.75% in [64]. Also, in multi-class classification, we get an accuracy of about **98.62%** compared to 96.25%, 98.57%, and 96% in [69], [65], and [63] respectively. Therefore, we can rely on it in the detection of Alzheimer's disease.

Perspectives

In this regard, our future works will focus more and more on:

— Improving the performance of our model by training more datasets from different sources such as the data set OASIS.

— On the other hand, using other methods for a diagnosis, such as region of interest (ROI) and 3D CNN.

— Finding the primary slice that allows us to distinguish between Alzheimer's phases.

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