



Z CARE



Yasmeen Saad Abdel-Fattah Mohamed Ashraf Ibrahim
Samuel Adel Azmy Shrouk Nasser Ali
Mohamed Yasser Ali

Supervised by: Dr.Esraa Elhariri
Dr.Asmaa Hashem

July 8, 2023

Acknowledgement

At first, at last, and all the time, for everything in our life. Nothing could be done without God's permission, and no success could be gained without his mercy. Thanks to Dr. Esraa M. Elhariri for her very much support and encouragement to accomplish this project in a professional and valuable way. She provided us with invaluable advice and helped us in difficult periods, her motivation and help contributed tremendously to the successful completion of the project. Thanks to Dr. Asmaa Hashem for her valuable help. Also, we want to thank DR. Samah Shehata from faculty of pharmacy fayoum university for her contribution and finally we would thank Dina Salah Saad for her contribution. Sincere thanks.

Abstract

Alzheimer's disease (AD) is a chronic, irreversible brain disorder, slowly causes a decline in memory affecting the patient's life, no effective cure for it till now. However, available medicines can delay its progress. Therefore, the early detection of AD plays a crucial role in preventing and controlling its progression. Advances in technologies produced high-dimensional data of different modalities including magnetic resonance imaging (MRI) and single nucleotide polymorphism (SNP). Understanding the complex association patterns among these heterogeneous and complementary data is of benefit to the diagnosis and prevention of AD. The main objective this project is to design an end-to-end framework for early detection of Alzheimer's disease and medical image classification for various AD stages.

ZCARE project aims to develop and investigate the performance of several Machine Learning (ML) models to develop an automated helpful system for AD diagnosis that can be useful for patients, caregivers, and physicians. It helps in the early diagnosis of Alzheimer's disease using multimodal data (SNPs and MRIs) and enables caregivers to monitor patients' life.

In our experiments, a dataset consists of 2 modals MRI and SNPs including 3 classes of different stages of Alzheimer's disease are used to train and evaluate **ZCARE**. A total of 1136 MRI-T2 slides and 690 samples of SNPs are divided into 80:20% training and testing datasets for multiclass and binary classification. For MRI Modality, the obtained experimental results demonstrate that the proposed method can yield better performance in both binary classification and multiclass classification tasks. Specifically, our proposed method achieves the accuracy of 95.61% and 92.98% for NC vs. AD vs. MCI using CNN with Attention and Reduced CNN, Respectively. While for binary classification CNN achieved accuracy of 89.47% and 91.55% for NC vs. AD and MCI vs. AD, respectively. Finally, for multimodality, ZCARE achieved an accuracy of 79.17 %.

ZCARE mobile application is proposed using the final qualified proposed architectures. It helps doctors and patients to check AD remotely. It also determines the AD stage of the patient based on the AD spectrum and advises the patient according to its AD stage with the aim of enhancing daily routine, observing and caring for the patient and finally, early diagnose by using deep learning.

Contents

Acknowledgement	1
Abstract	2
List of Abbreviations	10
1 Introduction	11
1.1 overview	11
1.2 Problem Definition	11
1.3 Project Motivation	12
1.4 Project Objectives	12
1.5 Organization	12
2 Preliminaries	13
2.1 Introduction	13
2.2 intelligent diagnose system	13
2.3 Data Preprocessing	15
2.3.1 MRI images	15
2.3.2 SNPs	19
2.4 Feature Engineering	21
2.4.1 Feature extraction	22
2.4.2 Feature Selection	22
2.4.3 Feature fusion	24
2.5 Deep Learning	24
2.5.1 Convolutional Neural Networks (CNNs)	25
2.5.2 The Used Deep Learning Models	29
3 Literature Review	35
3.1 Overview	35
3.2 A Deep learning-based approach to predict AD	35
3.3 A Traditional approaches to distinguish AD	39
3.4 Summarizes the Presented Exhaustive	41



Z CARE 2022/2023

4 Project Planning	43
4.1 Introduction	43
4.2 Project Plan	43
4.2.1 Gathering Requirements	43
4.2.2 System Analysis	43
4.2.3 System Design	43
4.2.4 Implementation	44
4.2.5 Project Schedule Gantt Chart	44
4.3 Feasibility Study	45
4.3.1 Focus	45
4.3.2 Strategies	45
4.3.3 Action Steps	45
4.3.4 KPIs	45
4.3.5 MOS	45
5 Proposed System	46
5.1 Overview	46
5.2 proposed framework	46
5.3 System Analysis	47
5.3.1 Process Modeling	47
5.3.2 Requirements	49
5.3.3 Use Case Diagrams	49
5.3.4 Use Case Scenario	52
5.3.5 Activity Diagram	58
5.3.6 Non Functional Requirements	63
5.4 System Design	64
5.4.1 Sequence Diagram	64
5.4.2 Class Diagram	65
5.4.3 Relational Database Diagram (ERD)	66
6 Experimental Results and Comparative Analysis	67
6.1 Experiment Specifications and Used Materials	67
6.2 Evaluation Metrics	67
6.3 Results of The System	68
6.3.1 Dataset description	68
6.3.2 Results and Discussion	71



Z CARE 2022/2023

7 System Development	77
7.1 Overview	77
7.2 App's architecture & design patterns	77
7.3 Methodological assumptions	78
7.3.1 User Requirements	78
7.3.2 System Requirements	78
7.4 Used Technologies	78
7.4.1 Dart	78
7.4.2 Flutter	78
7.4.3 Flutter Bloc	79
7.4.4 Flask	79
7.4.5 Google Cloud Platform	79
7.5 Mobile development	80
8 Conclusions & Future Work	102
8.1 Conclusions	102
8.2 Future work	103

List of Figures

2.1	General framework of intelligent diagnose system	14
2.2	TPM in MNI space	18
2.3	MRI Before and After Segmentation in MNI Space	19
2.4	4 Chromosomes responsible for AD	20
2.5	4 AD genes in the 4 mentioned chromosomes	20
2.6	whole genoem sequenced DNA (WGS)	21
2.7	Proposed workflow for genes	21
2.8	feature engineering	22
2.9	Embedded feature selection approach	23
2.10	An example of CNN architecture.	25
2.11	Sigmoid function	27
2.12	RELU Function	28
2.13	scaled dot product attention	30
2.14	multi head attention	30
2.15	batches of one slice in Z of MRI scan	31
2.16	Attention Block	31
2.17	MLP Block	32
2.18	Convolution Block	32
2.19	Reduced-CNN Model	33
2.20	Attention-CNN Model	33
2.21	Attention Block	34
3.1	Preprocessing results of (A) sMRI data and(B) fMRI data	39
4.1	Gantt Chart	44
4.2	Project Schedule	45
5.1	framework	46
5.2	Context Diagram	47
5.3	Doctor DFD	48
5.4	Patient DFD	48
5.5	CareGiver DFD	49
5.6	Patient, NormalUser, CareGiver Use case	50
5.7	Doctor UseCase	51



Z CARE 2022/2023

5.8	Normal User Activity Diagram	59
5.9	Patient Activity diagram	60
5.10	Doctor Activity diagram	61
5.11	CareGiver Activity diagram	62
5.12	Sequence diagram	64
5.13	Class diagram	65
5.14	ERD Diagram	66
6.1	CN status	69
6.2	MCI status	69
6.3	AD status	69
6.4	Full Framework	71
6.5	CNN from [7] Metrices	72
6.6	CNN Reduced Model Metrices	72
6.7	CNN-Attention Model Metrices	72
6.8	Comparing Between Image Models based on Confusion Matrix, Multi-Class	73
6.9	Metrices	74
6.10	Confustion Matrices	74
6.11	Metrices	74
6.12	Confustion Matrices	74
6.13	Metrices	76
6.14	Confusion Matrix	76
6.15	Metrices	76
7.1	Onboarding screen	80
7.2	sign up	80
7.3	Sign Up as Doctor	81
7.4	Sign Up as CareGiver	81
7.5	Sign Up as Patient	81
7.6	Verification	82
7.7	Login Screen	82
7.8	Login as Doctor	83
7.9	Login as CareGiver	83
7.10	Login as Patient	83
7.11	Forget password	83
7.12	Reset password	83
7.13	Doctor Home	84
7.14	Search for Patient	84
7.15	Upload Model	84
7.16	C.G-HomeScreen	85
7.17	C.G-LifeStyle	86
7.18	Plans	87
7.19	Routines	87
7.20	Plans Screen	87
7.21	Add Task	87



Z CARE 2022/2023

7.22 Medicine Type	87
7.23 C.G Emergency Screen	88
7.24 E-call Contacts	88
7.25 C.G Medicine Screen	89
7.26 C.G MedicineList	89
7.27 Tasks Screen	90
7.28 Tasks Edit	90
7.29 Account Screen	91
7.30 Edit Profile	91
7.31 Delete Account	91
7.32 E- call contacts	92
7.33 Contacts Edit	92
7.34 Patient History Screen	92
7.35 Add New Analysis	92
7.36 HomeScreenC.GPatient	94
7.37 C.GPatientMedicines	94
7.38 C.GPatientPlans	94
7.39 C.GPatientoutline	94
7.40 C.GPatientAccount	94
7.41 HomeScreen1	95
7.42 HomeScreen2	95
7.43 Notes Screen	96
7.44 Notes Add	96
7.45 Notes Save	96
7.46 Plans	96
7.47 Routine	96
7.48 Plans Screen	97
7.49 Add Task	97
7.50 Medicine type	97
7.51 Emergency Screen	98
7.52 E-call Contacts	98
7.53 Account Screen	99
7.54 Edit Profile	99
7.55 E- call contacts	100
7.56 Contacts Edit	100
7.57 Medicine List	101
7.58 Add Medicine	101

List of Tables

1	Glossary Table	10
2.1	Initially proposed structure for the workflow	16
2.2	Processing Steps	16
3.1	Summarizes the Presented Exhaustive	42
5.1	Patient Link to Caregiver Case Scenario.	52
5.2	Patient Registration Use Case Scenario.	53
5.3	Patient Take Test Use Case Scenario.	53
5.4	Patient Login Use Case Scenario.	54
5.5	Caregiver Registration Use Case Scenario.	54
5.6	Caregiver Login Use Case Scenario.	55
5.7	Caregiver tracks Patient Use Case Scenario.	55
5.8	Caregiver Choose Doctor Case Scenario.	56
5.9	Physician Registration Use Case Scenario.	56
5.10	Physician Login Use Case Scenario.	57
5.11	Physician searches patient Case Scenario.	57
5.12	Physician diagnoses patient Case Scenario.	58
6.1	Datasets (ADNI) description	70
6.2	Comparing between Models Multi-Class	73
6.3	SNPs discussion	75

List of Abbreviations

AD	Alzheimer's disease
CSF	Cerebrospinal fluid – the liquid in the brain filling the empty cavities in the skull
DARTEL	DARTEL is part of SPM package, used to make templates and flowfields.
GM	Grey matter – area packed with the neuronal cell bodies and synapses
MRI	Magnetic resonance imaging – a method for acquiring images of brain physiology
SNPs	single nucleotide polymorphism
NIFTI	Neuroimaging informatics technology initiative - refers to a related file format NIFTI-1.
NIPYPE	Neuroimaging in Python: Pipelines and Interfaces – a tool for automating workflows
ROI	Region of Interest
SPM	Statistical parametric mapping – a brain image-processing package for Matlab
T2	MRI technique for brain imaging, often utilised for capturing structural images
WM	White matter – brain area consisting mostly of myelinated axons
DNA	Deoxyribonucleic acid it's the carrier of genetic information

Table 1: Glossary Table

Chapter 1

Introduction

1.1 overview

Currently, more than 55 million people live with dementia worldwide "According to World Health Organization", and there are nearly 10 million new cases every year. Dementia results from a variety of diseases and injuries that primarily or secondarily affect the brain. Alzheimer's disease is the most common form of dementia and may contribute to 60-70% of cases. It is a brain disorder that slowly destroys memory and thinking skills and, eventually, the ability to carry out the simplest tasks. Typically, Alzheimer's symptoms mature after the age of sixty, affecting the patient's mental and physical condition. A person diagnosed with Alzheimer's could suffer from various syndromes including memory efficiency decreases, speaking difficulties, lack of attention, and a decline in the quality of lifestyle. More critically, the disease could develop to cause serious damage, and this could lead patients to start forgetting their family and friends. Currently, there is no available medication to fight and cure AD, hence the progression of this disease cannot be reversed. Thus, achieving an early diagnosis of AD can provide the patient with medication to slow the disease hence its symptoms of it. And for his family to be prepared for what the future is about.

1.2 Problem Definition

Alzheimer's disease makes you alive but not living and There is no medication for Alzheimer's disease, But healthcare providers have been successful in helping people maintain their mental function, control behavior, and slow the progress of the disease. Medicines are used to help people maintain mental function. And when symptoms start to appear we face another problem which is related to the caregiver. The caregiver needs to be with the patient all the time, give him medicine on time and make sure that the patient is fine, which is so stressful and with the daily routine, it becomes so hard.



1.3 Project Motivation

We believe that life is about helping others and giving back to our society! And we also believe in the power of technology and using it In this project could help patients to have more time. Being a human is about meeting new people, making new memories, and being with the ones that care about you and you care about them. Imagine that you can help someone and give him some more time with fewer symptoms of Alzheimer's by early diagnoses of the disease. You help a father to keep remembering his family, help a mother to remember to cook for her children and help a grandparent to remember the names of his grandchildren. Making it easier for caregivers to take care of their beloved ones. However, the proposed mobile application can determine an initial diagnosis whether the patient is healthy, potential, or diseased to help guide the physicians with how they will decide a treatment plan as soon as possible rather than taking multiple months.

1.4 Project Objectives

The main objectives of this project are to be accomplished within a timeline and with available resources are to Diagnose Alzheimer's disease in its early stages which would give us the ability to:

1. Slow the disease progression with medicine and exercises
2. Maintain mental function.
3. Make it easier for caregivers to take care of the patient.

1.5 Organization

We have structured the rest of this project as follows: Chapter(3) presents Related work including a brief history of some international Papers and their establishment, Chapter(4) presents the planning Phase is the fundamental process of understanding why a system should be built and also determining how the project team will go about building the system, Chapter(5) presents project analysis and reviews the Development methodology, the Agile Software Development Life Cycle also reviews the functional and non-functional requirements

Chapter 2

Preliminaries

2.1 Introduction

This chapter presents a brief idea concerning the core concepts of a smart AD caring mobile app, which can diagnose AD and determine its stage based on MRIs and SNPs, early diagnosis helps patients to slow the progression of the disease. Then it presents a brief idea about deep learning.

2.2 intelligent diagnose system

An intelligent diagnosis system is a new concept that makes a patient's life easier and slows the progression of the disease using advanced information technologies. The latest advancements in artificial intelligence help physicians to diagnose AD and caregivers to better monitor patients' lives. physicians, data scientists, and engineers continue to work on techniques that allow for optimizing the human labor required in diagnosing AD and tracking patient life. Alzheimer's disease makes you alive but not living and There is no medication for Alzheimer's disease, But healthcare providers have been successful in helping people maintain their mental function, control behavior, and slow the progress of the disease. Medicines are used to help people maintain mental function. And when symptoms start to appear we face another related problem to the caregiver. The caregiver needs to be with the patient all the time, give him medicine on time and make sure that the patient is fine, which is so stressful, and with the daily routine, it becomes so hard.

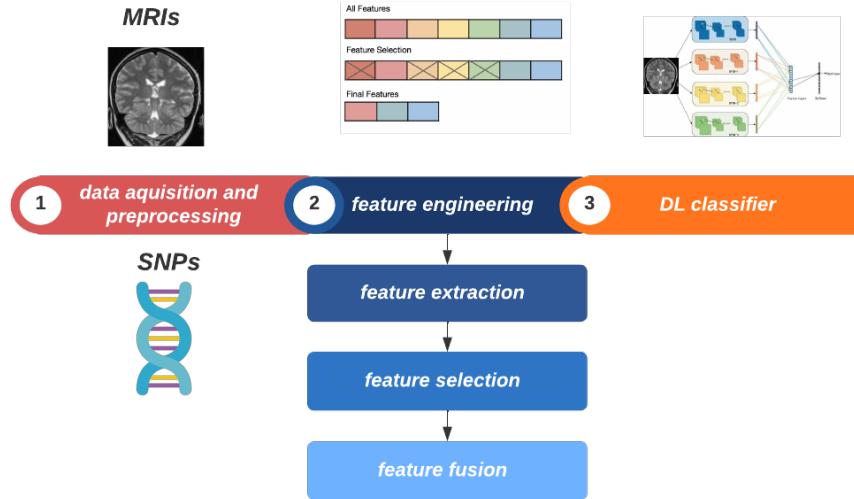


Figure 2.1: General framework of intelligent diagnose system

Moreover, Monitoring patients and diagnosis of AD is very important now to increase accuracy and reduce costs of time and money. Also, the Alzheimer's prognosis is one of the most worrying issues for AD as it has a high impact on patient life. An intelligent diagnose system comprises three major components as depicted in figure 2.1

Data acquisition and preprocessing phase

Constitute a very important phase of any intelligent diagnosis system and have a significant influence on the capability for diagnosis and assessment. It is responsible for data collecting using various sensors and preprocessing the collected data for the feature engineering phase. Preprocessing includes data cleaning, data transformation, and dimension reduction.

Feature engineering phase

Is the key component of a successful ML algorithm, contributing to their performance. It aims to extract features that better represent the underlying problem from raw data and transform them into a proper format for machine learning models.

Classification phase

Is responsible for classifying patterns into various categories using ML algorithms. These algorithms can be classified into three categories, namely, super-



vised learning, semi-supervised learning, and unsupervised learning based on the amount of required labeled data

2.3 Data Preprocessing

As mentioned above, ADNI dataset consists SNP data, and imaging data.

2.3.1 MRI images

Analysis Tools

- Nipype framework

Nipype - “a flexible, lightweight and extensible neuroimaging data processing framework in Python” (12) - is an open source, community-developed tool which enables integrated workflows among different neuroscience-related software packages. This allows automation and even batch execution of workflows, which can include multiple steps utilizing multiple different software packages and be run on the local machine or on special clusters. In the test environment Nipype was utilized to run the workflows and to coordinate the execution and parameters of other related software.

- SPM12 Standalone with Ocatve runtime

Statistical Parametric Mapping software package (open source), which is widely used in the field of neuroscience for the analysis of brain imaging data. It is designed to be used with the MATLAB programming language. SPM includes a variety of statistical methods and algorithms for the analysis of brain imaging data, including voxel-based morphometry (VBM), spatial normalization, and statistical inference.

SPM requires a commercially licensed version of MATLAB to run. For this reason, the Ocatve is used instance of MATLAB.

Ocatve is open-source numerical computing software package that is designed to provide many of the same features and capabilities as MATLAB.

- Other tools utilised

Other related tools in the area included DCM2NII converter for converting the original DICOM images to NIfTI-1 format.



Planned workflow

The initial workflow design consisted of running through all the tools observed to be relevant to the process, as described above. The workflow was initially planned to be based on Nipype framework, which would be used to automate and initiate the specific tools responsible for doing the actual processing for each step.

The Proposed Workflow
Converting to NIFTI
Preprocessing
Tissue Classification (Segmentation Core)
Postprocessing

Table 2.1: Initially proposed structure for the workflow

Preprocessing
Bias field correction
Skull Removing
Spatial normalization)
Spatial smoothing
Intensity normalization

Preprocessing
Bias field correction
Skull Removing
Spatial normalization)
Spatial smoothing
Intensity normalization

Table 2.2: Processing Steps

Segmenting white and grey matter

Segmentation is a process in neuroimaging that involves dividing an image into different regions or "segments" based on their intensity, texture, or other characteristics. In brain imaging, segmentation is often used to separate the different types of tissue in the brain, such as gray matter, white matter, and cerebrospinal fluid. The technique used for brain segmentation is tissue classification, which involves assigning each voxel in the image to a particular tissue type, such as gray matter, white matter, or cerebrospinal fluid. Tissue classification can be performed using automated algorithms that use a probabilistic atlas of the brain to assign each voxel to a particular tissue type.

SPM12 Multi-Channel-NewSegment

in SPM12 all preprocessing steps, Segmentation Process and postprocessing steps are combined to one module.

Preprocessing Steps

- Bias field correction

MRI images can have intensity variations across the image, which can



Z CARE 2022/2023

affect the accuracy of the subsequent segmentation. Bias field correction is a technique used to remove these intensity variations and make the image more uniform. SPM uses a bias field correction algorithm that estimates the intensity variations in the image and removes them.

- **Skull stripping**

The skull and other non-brain tissues in the image can interfere with the segmentation process, and so it is often necessary to remove them from the image. Skull stripping is a method used to isolate the brain from the rest of the image. SPM includes a skull-stripping algorithm that removes non-brain tissues from brain tissues.

- **Spatial normalization**

MRI data from different subjects can vary in size and shape, and so it is often necessary to bring all the images into a common coordinate space. Spatial normalization is the process of transforming the image from the subject-specific space to a standard space. SPM uses a nonlinear registration algorithm that warps the image to a standard space by deforming it to match a template brain.

- **Spatial smoothing**

MRI images can have high-frequency noise that can affect the accuracy of subsequent analyses. To reduce the noise and improve the signal-to-noise ratio, the image is often smoothed using a Gaussian filter. SPM includes a smoothing algorithm that applies a Gaussian filter to the image.

- **Intensity Normalization**

MRI images can have different intensity ranges, which can affect the accuracy of the segmentation. To account for this, the intensity of the image is often normalized to a standard range. SPM includes an intensity normalization algorithm that scales the intensity of the image to a specified range.

The Segmentation Process (Tissue Classification)

After preprocessing, the MRI data is classified into different tissue types using an automated algorithm. The most common approach is to use a tissue probability map, which is a probabilistic atlas of the brain that specifies the likelihood of each voxel belonging to a particular tissue type. The tissue probability map is generated using a large dataset of MRI scans that have been manually segmented into different tissue types, SPM has its TPM. The automated algorithm then uses the tissue probability map to classify each voxel in the MRI data into different tissue types, such as gray matter, white matter, and cerebrospinal fluid. and this compute the Probability Map for each Tissue, determining how much voxel belong to every type of tissue.

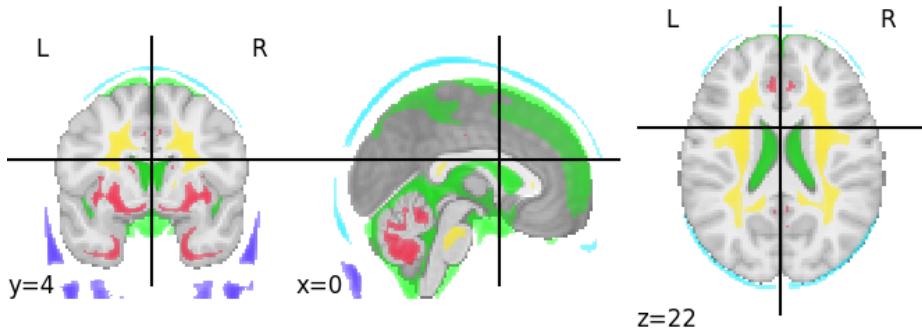


Figure 2.2: TPM in MNI space

Postprocessing Steps

Once the tissue classification is complete, the segmentation results are refined using post-processing methods. This includes removing any small or isolated regions of a tissue type that may be due to noise or other artifacts, smoothing the segmentation results to reduce noise, and correcting any inconsistencies in the segmentation results

- Removing isolated regions

The automated tissue classification algorithm used in SPM segmentation can sometimes produce small, isolated regions of a particular tissue type that are not part of the true structure of the brain. These regions can be removed from the segmentation results using post-processing methods. SPM includes a connected component analysis algorithm that identifies small, isolated regions of a particular tissue type and removes them from the segmentation results

- Filling holes

The automated tissue classification algorithm can sometimes produce holes or gaps in the segmentation results, where a particular tissue type is missing. These holes can be filled using post-processing methods. SPM includes a hole-filling algorithm that identifies gaps in the segmentation results and fills them in with the appropriate tissue type.

- Removing isolated regions

The automated tissue classification algorithm used in SPM segmentation can sometimes produce small, isolated regions of a particular tissue type that are not part of the true structure of the brain. These regions can be removed from the segmentation results using post-processing methods. SPM includes a connected component analysis algorithm that identifies small, isolated regions of a particular tissue type and removes them from the segmentation results.

- Normalizing to MNI space

It is important to align the images to a common coordinate space, which enables direct comparison of brain structures and functions across subjects. The Montreal Neurological Institute (MNI) space is a widely used standard coordinate space for brain imaging. One way to Normalize MRI to MNI space is using Affine Matrix Transformation, this matrix defines the operations (scaling, transition and rotation).

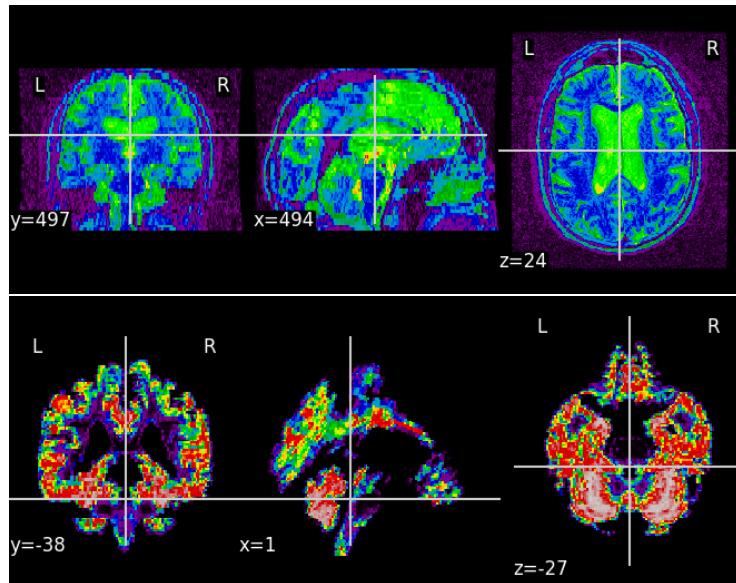


Figure 2.3: MRI Before and After Segmentation in MNI Space

2.3.2 SNPs

A chromosome is made of a very long strand of DNA and has many thousand genes. Every human cell has 23 pairs of chromosomes, for a total of 46 chromosomes in each cell. To detect AD, we search inside four definite chromosomes (chromosomes number 1, 14, 19, 21) shown in 2.4. In these chromosomes, we search inside them for four specific genes related to the detection of AD. Each chromosome contains a huge number of segments called genes and each gene has a particular location on the chromosome.

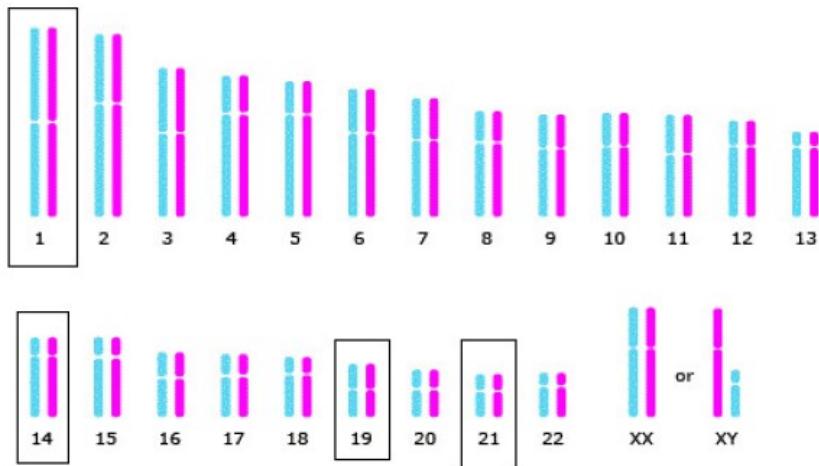


Figure 2.4: 4 Chromosomes responsible for AD

The four genes related to AD are: Amyloid precursor protein (APP), Presenilin-1 (PSEN-1), Presenilin-2 (PSEN-2), and Apolipoprotein (APOE4) shown in Figure

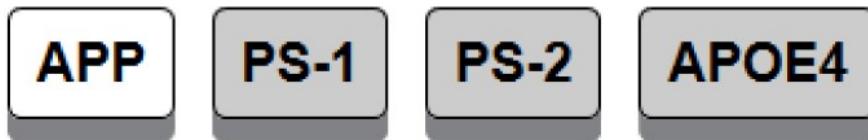


Figure 2.5: 4 AD genes in the 4 mentioned chromosomes

Each gene is made of a sequenced codons composed of three nucleotide represented by either one of the following four letters: Adenine(A), Thymine (T), Cytosine (C), Guanine (G). Each three characters represent an amino acid, that then linked together with peptide bonds to form a protein as shown in 2.6. If the sequence of the above mentioned genes is altered, then the patient will suffer from AD.

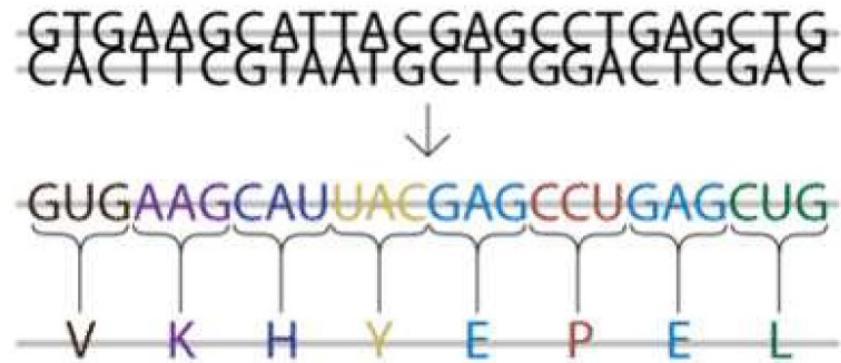


Figure 2.6: whole genome sequenced DNA (WGS)

Proposed work flow for genes

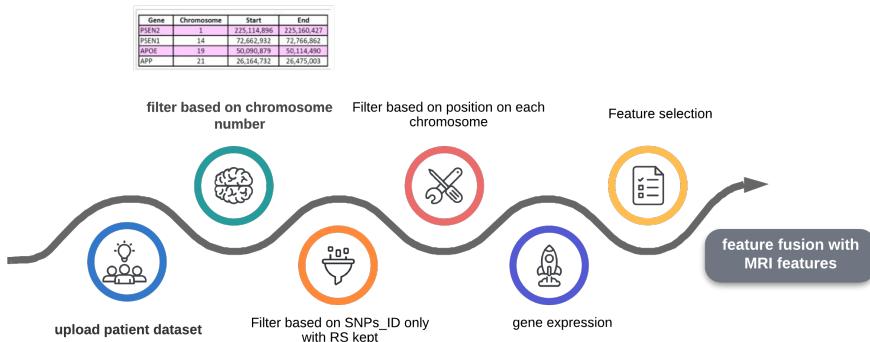


Figure 2.7: Proposed workflow for genes

2.4 Feature Engineering

Feature engineering is defined as the process of extracting features that better represent the underlying problem from raw data and transforming them into a suitable format for machine learning models, resulting in improving the performance of a trained model on unseen data. Feature engineering can be categorized into three categories, namely, feature extraction, feature selection and feature fusion as shown in 2.8 The main aim of feature extraction and selection is to:

1. Reduce high-dimensional feature space to low-dimensional representation
2. Focus on the most relevant data

3. Avoid overfitting the data
4. Improve the quality of feature space and hence the performance of machine learning algorithms such as learning time and accuracy .

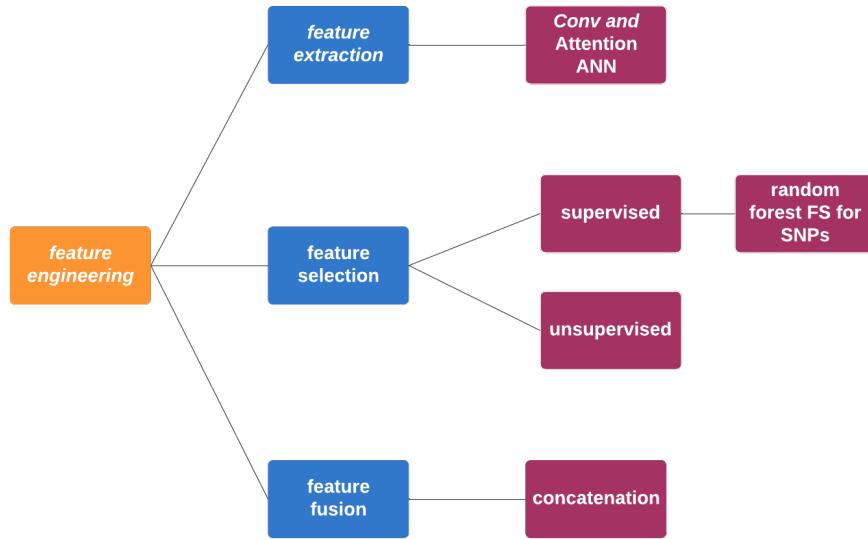


Figure 2.8: feature engineering

2.4.1 Feature extraction

Feature extraction is the process of transforming raw data into a set of meaningful and relevant features that can be used as input to a machine learning model. Neural Network is used to extract feature extraction

2.4.2 Feature Selection

Selecting the optimal subset of distinct features plays a key role in improving the performance of a classification model with lower computational effort, shorter learning time, data visualization, refined understanding of computational models, low risk of data overfitting, and lower dimensions of the problem. Feature selection picks out the subset of the features with maximum relevance to the target class and minimal redundancy from the original set to increase the classification accuracy . As shown in Figure 2.8, FS methods can be classified into:

1. supervised learning, class labels are specified beforehand, and the algorithms maximize some functions to select the relevant features, which are highly correlated with the class.

2. unsupervised learning, class labels are not given resulting in difficulty in finding relevant features simultaneously

Embedded methods

Embedded methods combine both filter and wrapper methods, where it is a built-in feature selection method embedding the feature selection in the learning algorithm and utilizing its properties to lead feature assessment. This makes the embedded method more efficient and tractable than the wrapper one, with similar performance and has a lower risk of overfitting. Similar to the wrapper method, they take into account the dependencies among features but is only specific to a given learning algorithm. Figure 2.9 shows the embedded feature selection approach.

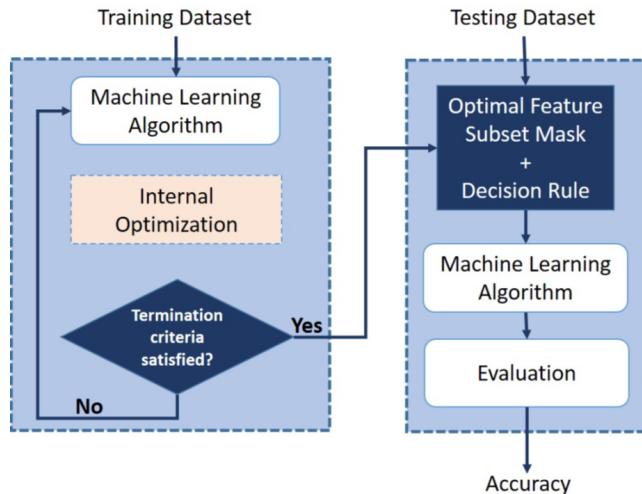


Figure 2.9: Embedded feature selection approach

Random forest

Feature selection using Random forest comes under the category of Embedded methods. Embedded methods combine the qualities of filter and wrapper methods. They are implemented by algorithms that have their own built-in feature selection methods. Some of the benefits of embedded methods are :

1. They are highly accurate.
2. They generalize better.
3. They are interpretable

How does Random forest select features?

Random forests consist of 4 –12 hundred decision trees, each of them built over a random extraction of the observations from the dataset and a random extraction of the features. Not every tree sees all the features or all the observations, and this guarantees that the trees are de-correlated and therefore less prone to over-fitting. Each tree is also a sequence of yes-no questions based on a single or combination of features. At each node (this is at each question), the tree divides the dataset into 2 buckets, each of them hosting observations that are more similar among themselves and different from the ones in the other bucket. Therefore, the importance of each feature is derived from how “pure” each of the buckets is.

- For classification, the measure of impurity is either the Gini impurity or the information gain/entropy.
- For regression the measure of impurity is variance.

Therefore, when training a tree, it is possible to compute how much each feature decreases the impurity. The more a feature decreases the impurity, the more important the feature is. In random forests, the impurity decrease from each feature can be averaged across trees to determine the final importance of the variable.

To give a better intuition, features that are selected at the top of the trees are in general more important than features that are selected at the end nodes of the trees, as generally the top splits lead to bigger information gains.

2.4.3 Feature fusion

Feature fusion, the combination of features from different layers or branches, is an omnipresent part of modern network architectures. It is often implemented via simple operations, such as summation or concatenation. Feature fusion attempts to extract the most discriminative information from several input features and eliminate redundant information. Feature Fusion may play an important role in improving the performance of classification tasks, in case of features Independence. To perform feature fusion, two or more different feature vectors are concatenated into one vector. Two main problems face the task of feature fusion; namely; the compatibility of different features and the high dimensionality. To solve the first problem, a normalization step is performed to transform the features within a range [0, 1].

2.5 Deep Learning

In the last few years, the deep learning (DL) computing paradigm has been deemed the Gold Standard in the machine learning (ML) community. Moreover, it has gradually become the most widely used computational approach in the field of ML, thus achieving outstanding results on several complex cognitive tasks, matching or even beating those provided by human performance. One of

the benefits of DL is the ability to learn massive amounts of data. The DL field has grown fast in the last few years and it has been extensively used to successfully address a wide range of traditional applications. More importantly, DL has outperformed well-known ML techniques in many domains, e.g., cybersecurity, natural language processing, bioinformatics, robotics and control, and medical information processing, among many others. Despite it has been contributed several works reviewing the State-of-the-Art on DL, all of them only tackled one aspect of the DL, which leads to an overall lack of knowledge about it.

2.5.1 Convolutional Neural Networks (CNNs)

Among the various deep neural network models, CNN is considered the most commonly used model for image classification. Standard CNN consists of several convolutional layers, pooling layers, and fully-connected (FC) layers. Figure 2.10 shows an example of CNN architecture. The main aim of the CNN is the automatic and adaptive learning of spatial hierarchies of useful features, from low-to high-level patterns. Figure 2.10 shows an example of CNN architecture.

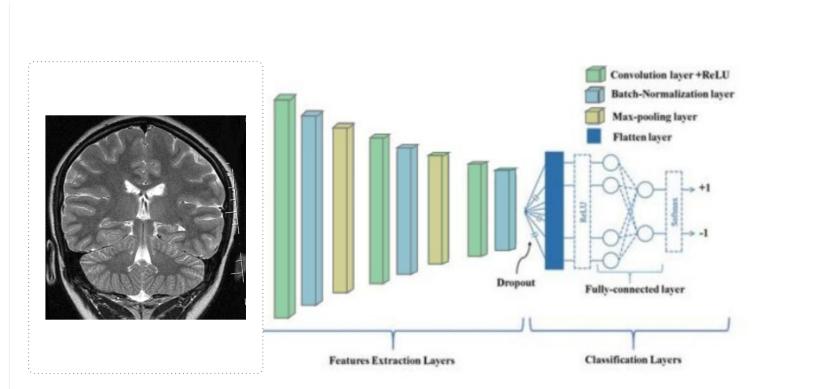


Figure 2.10: An example of CNN architecture.

1. Convolutional Layer:

The convolutional layer is the key aspect of CNN. Given an input array A of size I a receptive field, and stride step N , it operates by applying three steps. The first step is an element-by-element multiplication between a subarray of A , and a receptive field (both of size $N \times N$). The second step is the summation of the multiplied values and adding bias to the summed values. The final step adds the final values to the output array. The receptive field is also often called the filter, or kernel. The weight values of a receptive field are initialized randomly .

**2. Pooling Layer:**

Another key aspect of CNN is the down-sampling process performed by the pooling layer. It aims to achieve spatial invariance by reducing the resolution of the input feature map. Each pooled feature map corresponds to one feature map of the previous layer. Max and mean pooling are two types of pooling. The maximum values from an input array's sub-arrays are taken in max-pooling, while in mean pooling the mean values are taken. From the survey, max-pooling performance in image datasets outperformed mean pooling.

3. Activation Layer:

The activation layer is a non-linear transformation function, widely used in the standard Artificial Neural Networks (ANN). There are many different activation functions such as sigmoid, hyperbolic tangent (\tanh), Rectified Linear Unit (ReLU), etc. It is applied after the convolution operation is completed to enable CNNs to avoid learning trivial linear combinations of inputs. All non-linear functions are restricted to output values except ReLU, which has only restricted outputs for its negative inputs. The features of ReLU make computation faster and more accurate. ReLU is computed according to equation 2.1 .

$$R(z) = \max(0, z) \quad (2.1)$$

Where z is the input to a neuron.

4. Softmax Layer:

For classifying input image, having a layer for prediction is necessary matter. This layer is responsible for classifying input images and is located at the end of CNN model. It can be any machine learning algorithms such as support vector machine (SVM), multilayer perceptron (MLP), etc. To date, using softmax function given by equation 2.2 is the most outstanding method.

$$y_k = \exp(k) / (\sum_j \exp(j)) \quad (2.2)$$

Where y is the neural network outputs and y is the probability of belonging to a class.

5. Sigmoid / Logistic Activation Function

This function takes any real value as input and outputs values in the range of 0 to 1. The larger the input (more positive), the closer the output value will be to 1.0, whereas the smaller the input (more negative), the closer the output will be to 0.0, as shown in figure 2.11



Figure 2.11: Sigmoid function

Mathematically it can be represented as:

$$(x) = 1/(1 + \exp(-x)) \quad (2.3)$$

Here's why sigmoid/logistic activation function is one of the most widely used functions:

- It is commonly used for models where we have to predict the probability as an output. Since probability of anything exists only between the range of 0 and 1, sigmoid is the right choice because of its range.
- The function is differentiable and provides a smooth gradient, i.e., preventing jumps in output values. This is represented by an S-shape of the sigmoid activation function.

6. ReLU Function

ReLU stands for Rectified Linear Unit. Although it gives an impression of a linear function, ReLU has a derivative function and allows for backpropagation while simultaneously making it computationally efficient. The main catch here is that the ReLU function does not activate all the neurons at the same time. The neurons will only be deactivated if the output of the linear transformation is less than 0.

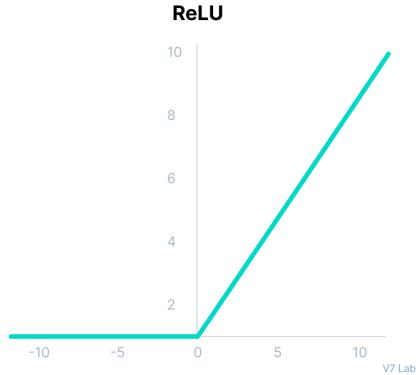


Figure 2.12: ReLU Function

Mathematically it can be represented as:

$$f(x) = \max(0, x) \quad (2.4)$$

The advantages of using ReLU as an activation function are as follows:

- Since only a certain number of neurons are activated, the ReLU function is far more computationally efficient when compared to the sigmoid and tanh functions.
- ReLU accelerates the convergence of gradient descent towards the global minimum of the loss function due to its linear, non-saturating property.

7. Dropout layer

Randomly sets input elements to zero with a given probability. At training time, the layer randomly sets input elements to zero given by the dropout mask

$$\text{rand}(\text{size}(X)) < \text{Probability} \quad (2.5)$$

X is the layer input and then scales the remaining elements by the Equation 2.6

$$1/(1 - \text{Probability}) \quad (2.6)$$

which helps prevent overfitting

8. Normalization

Normalization is a scaling technique in Machine Learning applied during data preparation to change the values of numeric columns in the dataset to use a common scale. It is not necessary for all datasets in a model. It is required only



when features of machine learning models have different ranges. Mathematically, we can calculate normalization with formula 2.7

$$X_n = (X - X_{\min}) / (X_{\max} - X_{\min}) \quad (2.7)$$

- X_n = Value of Normalization
- X_{\max} = Maximum value of a feature
- X_{\min} = Minimum value of a feature

2.5.2 The Used Deep Learning Models

Attention Block

1. Attention

The attention mechanism is a technique used in Deep Learning to focus on specific parts of the input data that are relevant to the task at hand. It allows the model to selectively concentrate on certain features of the input data while ignoring others. The attention mechanism is inspired by human attention, which is selective and focuses on important parts of the environment while ignoring irrelevant details.

2. How does Attention work

The attention mechanism works by assigning weights to different parts of the input data, based on their relevance to the task. These weights are then used to compute a weighted sum of the input data, representing the part of the input most relevant to the task. These are done by Input copies to 3 copies, a query Q , a key K , and a value V . Suppose we want to search YouTube for a specific video. The content of the video expresses the value, while the video title expresses the key. If the video title (key) is accessed, the video content (value) will be accessed, and the video will be accessed by the query (search clause). The most similar query to the key is searched, and the video (value) is accessed accordingly. The similarity between the query and the key for each part of the input (token or patch) is calculated by a cosine-similarity 2.8.

$$\text{score} = QK^T \quad (2.8)$$

Then scores will pass to softmax to make attention (probability of similarity), ensuring that the weights sum up to one and are scaled by the $\sqrt{-k-}$.

$$\text{attention} = (\text{softmax(score)}) / (|K|) \quad (2.9)$$

The value is filtered by the attention value.

$$\text{result} = V \text{attention} \quad (2.10)$$



Scaled Dot-Product Attention

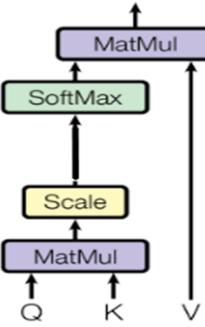


Figure 2.13: scaled dot product attention

2. Multi-Head Attention is the attention mechanism that is applied multiple times, each time with a different set of weights. This allows the model to learn different aspects of the input data.

$$\text{MultiHead}(Q, K, V) = \text{Concat}(\text{had}_1, \dots, \text{had}_h) \quad (2.11)$$

where $\text{head}_i = \text{Attention}(Q, K, V)$

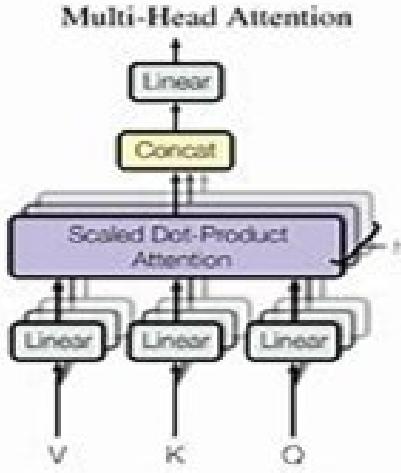


Figure 2.14: multi head attention

The attention can apply to different types of Applications. Commonly used in NLP but can use also in Computer Vision. Attention works on sequence data, to make image as sequence. The Image is divided into patches, then flattened.

Visualization of Patches

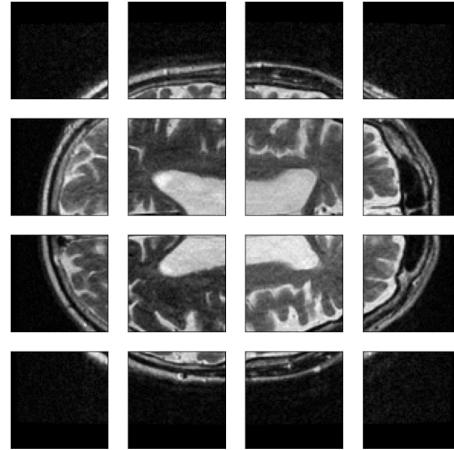


Figure 2.15: batches of one slice in Z of MRI scan

Then is added positional embedding to patches to make the patch unique, by apply the equations 2.12 , 2.13

$$PE(pos, 2_i) = \sin(pos10000^{(2i/|_m|)}) \quad (2.12)$$

$$PE(pos, 2(i+1)) = \cos(pos/10000^{(2i/|_m|)}) \quad (2.13)$$

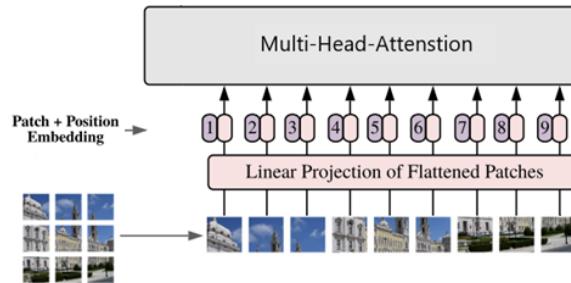


Figure 2.16: Attention Block



Z CARE 2022/2023

General Deep Learning Architecture

Common Blocks Multi-Layer Perceptron Block

MLP Block is used in all models to extract new features on Images after passed to CNN Block or Attention Block on 1D level.

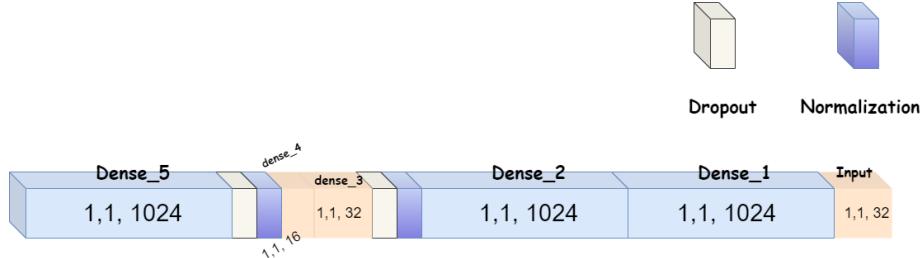


Figure 2.17: MLP Block

Convolution Block

This Block is used in CNN-Attention Model and Reduced-CNN Model

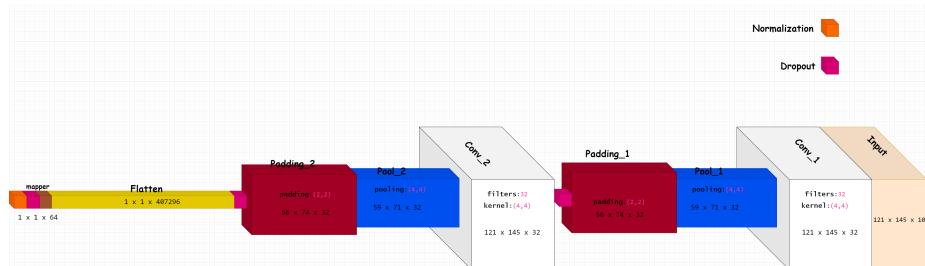


Figure 2.18: Convolution Block

Reduced CNN Model

This model differs from the [7] in the number of Conv-Blocks [Conv-Pooling-Padding], where this model uses 2 Conv-Blocks instead of 5.



Figure 2.19: Reduced-CNN Model

CNN and Attention

To take advantage of the advantages of Attention as well as Convolution, in this model the Image input passed to the Attention Block and Convolution Block in parallel and the output of each Block are concatenated, then passes to MLP Block and finally pass to Classifier layer.

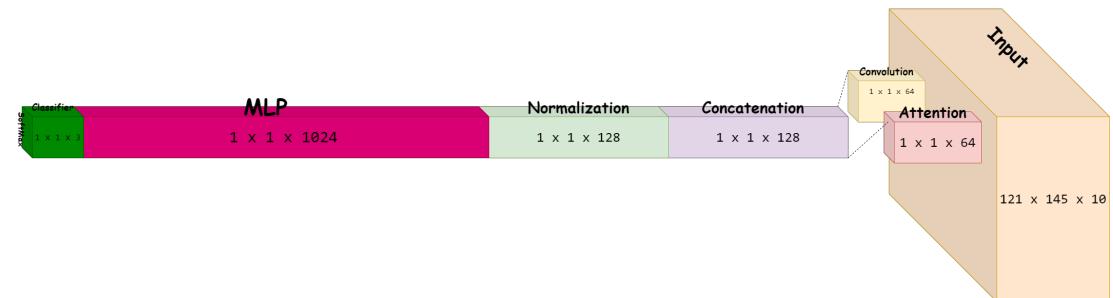


Figure 2.20: Attention-CNN Model



Z CARE 2022/2023

Attention Block

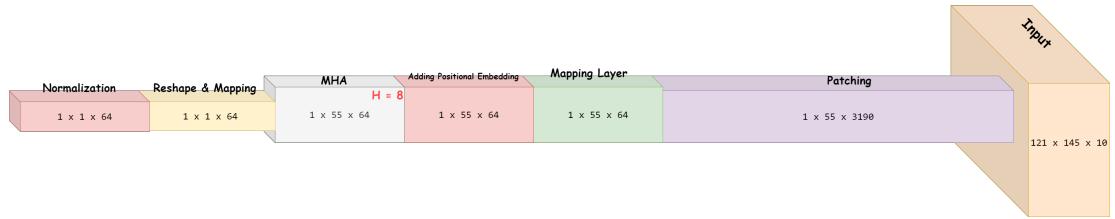


Figure 2.21: Attention Block

Chapter 3

Literature Review

3.1 Overview

This chapter includes a brief history of some international Papers and their establishment, the technology involved in improving and facilitating the advising and enrollment processes, what problems happen and what they reach and their limitations, and references.

As discussed in the previous chapter, this project presents:

1. Used a deep learning-based approach to predict an early diagnosis of AD(Alzheimer's Disease).
2. Employed Traditional algorithms to distinguish AD.

3.2 A Deep learning-based approach to predict AD

Shen et al. proposed a deep learning-based approach to distinguish Alzheimer's disease (AD) from mild cognitive impairment using PET data, as presented in [1]. The authors utilized DBNs as a feature selection technique to identify key features from the regions of interest (ROIs) in PET images. The support vector machine (SVM) model was employed to distinguish AD from mild cognitive impairment, which is a popular machine learning method for detecting AD with structural MRI data. The study reported that the proposed DBN-based method achieved good performance in differentiating between AD and mild cognitive impairment, with an AUC of 0.908.

However, the study only examined single-modal brain imaging data, namely PET images, and may have disregarded other likely morphological changes from multimodal brain image data. Additionally, the study did not compare the performance of DBNs with other deep learning algorithms such as CNNs, or with other machine learning algorithms such as random forests. Furthermore,

the study did not consistently use AUC as a standard evaluation metric for comparison.

Despite these limitations, the main contribution of the study is that it was the first to apply the concept of DBNs to distinguish AD from mild cognitive impairment using PET data. This approach has the potential to provide more accurate and reliable diagnoses of AD, which is crucial for early detection and timely intervention.[1].

Zhou, P. et al. In their study presented in [], authors proposed a deep learning-based approach to predict Alzheimer's disease (AD) using PET and MRI images. The approach utilized sparse-response Deep Belief Networks (DBNs) to extract features from the images, followed by the Extreme Learning Machine (ELM) model for classification. The study benchmarked their approach against support vector machines and Convolutional Neural Networks (CNNs).

The proposed approach achieved superior performance compared to benchmarking models, with an AUC of 0.87 for distinguishing AD from normal controls (NC), surpassing CNNs (AUC = 0.77) and DBNs (AUC = 0.83). The approach also outperformed CNNs (AUC = 0.60) and DBNs (AUC = 0.73) for distinguishing mild cognitive impairment from normal controls, achieving an AUC of 0.79. Furthermore, the proposed approach (AUC = 0.71) surpassed CNNs (AUC = 0.60) and DBNs (AUC = 0.68) for distinguishing AD from mild cognitive impairment.

However, the study did not compare the performance of the proposed approach with other deep learning algorithms such as GANs (Generative Adversarial Networks) or other machine learning algorithms, such as random forests. Despite this limitation, the main contribution of the study is that it was the first to utilize sparse-response DBNs for predicting AD using multimodal brain image data such as PET and MRI images. This approach has the potential to improve the accuracy and reliability of AD diagnosis, which is essential for early detection and intervention.[2].

Multimodal deep learning models for early detection of Alzheimer's disease stage:

May D.Wang.Pre-processing, the data analysis for EHR (electronic health record) data, the combination of the three data modalities, and the writing of the manuscript. Contributed to the pre-processing and analysis of the SNP (single-nucleotide polymorphism) data, and the writing of the manuscript. Contributed to the image processing pipeline and writing of the results of image processing. Contributed to the study design, result evaluation, and extensive relevant revision of the manuscript.[3].

In this study, conducted by Shangran Qiu, a deep learning framework was developed to assess Alzheimer's disease dementia using multiple modalities. Specifically, the framework was designed to accomplish two diagnostic steps, identifying individuals with normal cognition (NC), mild cognitive impairment (MCI), Alzheimer's disease (AD) dementia, and non-AD dementias (nADD)

due to other etiologies. The study demonstrated that the deep learning framework performed comparably to neurologists and neuroradiologists in terms of diagnostic accuracy. To aid in the interpretation of the model, three separate models were created, including an MRI-only model, a non-imaging model, and a fusion model. Furthermore, SHAP (Shapley Additive exPlanations) analysis was conducted on brain MRI and other features to reveal disease-specific patterns that corresponded with expert-driven ratings and neuropathological findings. Overall, this study highlights the potential of multimodal deep learning approaches for improving the accuracy and efficiency of Alzheimer's disease dementia assessment. The statement is written professionally and effectively summarizes the key findings of the study.[4].

Weiming Lin. Multiclass diagnosis of stages of Alzheimer's disease using linear discriminant analysis scoring for multimodal data: In this study, we proposed a latent Dirichlet allocation (LDA) based scoring strategy approach for AD multiclass diagnosis in the presence of four modalities, i.e., Magnetic Resonance Imaging (MRI), fluorodeoxyglucose (FDG-PET), Cerebrospinal fluid (CSF), and genetic features. The LDA was used to calculate a score representing the pathological information from each modality, and the scores from different modalities ensured that the classifier could easily discriminate between different groups. LASSO and PCA were used to exclude irrelevant and inferential components before LDA, and a binary ELM-based tree decision classifier was built for multiclass classification. The experimental results indicated that the LDA scoring significantly improved the multiclass diagnosis. [5].

Benefiting from the information obtained from multiple modalities and the scoring strategy, we achieved a promising performance with an accuracy of 66.7 %, an F1-score of 64.9 percent for three-way diagnosis, an accuracy of 57.3 %, and an F1-score of 55.7 % for four-way diagnosis, which was significantly better than the original method. When compared to other studies, the proposed approach also showed a better performance. Although multimodal data help to improve the performance of AD diagnosis, the requirement of too many modalities would limit the practical usage of this approach. However, this study's more efficient multimodal fusion approach is still useful for further AD studies, such as AD longitudinal trajectory modeling.[5].

Taeho Jo. Multimodal neuroimaging data have been used to identify structural and molecular/functional biomarkers for AD. deep learning approaches have been applied to AD diagnostic classification using original neuroimaging data without any feature selection procedures. If the data is imbalanced, the chance of misdiagnosis increases and sensitivity decreases. Multimodal neuroimaging data such as MRI and PET have commonly been used in deep learning: MRI for brain structural atrophy, amyloid PET for brain amyloid- β accumulation, and FDG-PET for brain glucose metabolism. The performance in AD/CN classification and/or prediction of MCI to AD conversion yielded better results in PET data compared to MRI.[6].

Hybrid Machine Learning Approach Using Deep Learning for the Prediction of AD Using Genome Data: Most machine learning approaches developed for the prediction of disease progression are either single-task or single-modality models, which cannot be directly adopted to our setting involving multi-task learning with high-dimensional images. Moreover, most of those approaches are trained on a single dataset, which cannot be generalized to other cohorts we propose a novel multimodal multi-task deep learning model to predict AD progression by analyzing longitudinal clinical and neuroimaging data from multiple cohorts. Our proposed model integrates high-dimensional MRI features from a 3D convolutional neural network with other data modalities, including clinical and demographic information, to predict the future trajectory of patients. Our model employs an adversarial loss to alleviate the study-specific imaging bias, in particular the inter-study domain shifts. In addition, a Sharpness-Aware Minimization (SAM) optimization technique is applied to further improve model generalization. The proposed model is trained and tested on various datasets to evaluate and validate the results. Our results showed that 1) our model yields significant improvement over the baseline models, and 2) models using extracted neuroimaging features from 3D convolutional neural networks outperform the same models when applied to MRI-derived volumetric features.[8].

A Robust Deep Learning Model of AD Progression for Real-World Clinical Applications” focused on developing a deep learning model for the classification of Alzheimer’s disease (AD) subtypes based on age of onset. Specifically, the study identified two subtypes of AD based on age of onset: Early-onset AD (EOAD) and late-onset AD (LOAD), with LOAD being more prevalent. The study utilized hybrid machine learning algorithms for the classification of LOAD and showed promising results. Artificial neural networks (ANN) were found to perform slightly better than convolutional neural networks (CNN). The study also employed a two-stage feature selection process, utilizing logistic regression to identify the most significant single-nucleotide polymorphisms (SNPs) associated with the disease and Random Forest to further reduce the number of SNPs, making the classification task computationally efficient. To the best of our knowledge, this work represents the first application of these models for AD. The study highlights the potential of deep learning models for real-world clinical applications in the classification of AD subtypes based on age of onset. The statement is written professionally and effectively summarizes the key findings of the study.[9].

Assisted Diagnosis of Alzheimer’s Disease Based on Deep Learning and Multi-modal Feature Fusion” utilized 3D convolutional neural networks and autoencoders to capture AD biomarkers. The study employed a multiscale residual neural network to collect multiscale information on a series of image slices and classify AD, mild cognitive impairment (MCI), and normal cognition (NC). The study improved the VGG-16 network for constructing a classification model of AD, MCI, and NC. Moreover, the study proposed a method for classifying migraine patients and normal people using stacked automatic encoders and functional connection matrices. The study proposed a dynamic time normalization

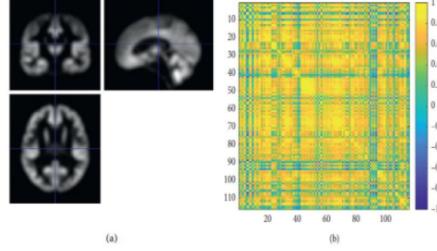


Figure 1: Preprocessing results of (a) sMRI data and (b) fMRI data.

Figure 3.1: Preprocessing results of (A) sMRI data and(B) fMRI data

distance matrix, Pearson correlation coefficient matrix, warping path distance matrix, and convolutional neural network to realize AD-assisted diagnosis. The method was used to preprocess MRI images, including segmentation, generating specific template generation, flow fields generation, and normalization, all implemented using Statistical Parametric Mapping (SPM8) software. Additionally, medical image processing software Data Processing Analysis of Brain Imaging (DPABI) was used to preprocess fMRI images, including data removal of the first 10 time points, slice timing, realignment, normalization, smoothing, detrending, filtering, and extracting time series to calculate function link matrix. The study fused sMRI features extracted by the 3DShuffleNet network with fMRI features extracted by the principal component analysis network (PCANet). Compared to a single modality, better classification results on multiple modalities were obtained. The study highlights the potential of deep learning and multimodal feature fusion for assisted diagnosis of Alzheimer's disease and other related diseases. The statement is written professionally and effectively summarizes the key findings of the study.[10].

Diagnosis of AD disease (Classification problem), Distinguish between 4-stages of AD:

- Huntington's disease (HD)
- Normal
- minor Alzheimer's disease (MAD)
- AD

A hybrid model of DBN CNN is better than traditional approaches. Datasets from Alzheimer's Disease Neuroimaging Initiative(ADNI) contain:

- MRI magnetic reverberation imaging
- EEG electroencephalography signal

The methodology is:- Median Filtering for EEG preprocessing. - Gaussian filtering for MRI preprocessing. - Gray level co-occurrence matrix GLCM Feature Extraction.- Classifiers o Support Vector Machine SVM. o Multi-Layer Perceptron MLP. o Deep Belief Network DBN. o Conventional Neural Network CNN. [11].

3.3 A Traditional approaches to distinguish AD

Auto-Encoders with MRI Images: using MRI (Magnetic resonance imaging) data. An auto-encoder is an artificial neural network for encoding purposes, where

the input layer serves the original MRI data, layers, and the previous multiple hidden layers provide nonlinear transformations from the output layer reconstructs MRI samples. In their study, various widely used machine learning methods, such as linear discriminant analysis, logistic regression, and support vector machines, were utilized for benchmarking.[1].reported that the proposed auto-encoder method ($AUC = 0.916$) surpassed various benchmarking models such as linear discriminant analysis ($AUC = 0.710$), and logistic Int. of 20 regression ($AUC = 0.765$), and support vector machines ($AUC = 0.789$) to predict an early stage of AD using MRI images. The main disadvantage of the study. is that only single-modal brain imaging data, namely MRI images, was examined, and thereby other likely morphological changes from multimodal brain image data may be disregarded? Moreover, other deep learning algorithms such as CNNs, and other machine learning algorithms such as random forests were not utilized for comparison. On the other hand, the main advantage of their study is that their approach was the first to exploit the concept of auto-encoders to predict an early diagnosis of AD using MRI data.[1].

AD is an irreversible, progressive brain disorder marked by a decline in cognitive functioning with no validated disease-modifying treatment. Much effort has been made to develop strategies for early detection, especially at pre-symptomatic stages, to slow or prevent disease progression. One weakness of deep learning is that it is difficult to modify potential bias in the network when the complexity is too great to guarantee transparency and reproducibility. Progress will be made in deep learning by overcoming these issues while presenting problem-specific solutions. form of learning that adapts to changes in data as it makes its own decision based on the environment, may also demonstrate applicability in the field of medicine. Machine learning generally requires four steps: feature extraction, feature selection, dimensionality reduction, and feature-based classification algorithm selection. Well-known pattern analysis methods, such as linear discriminant analysis (LDA), linear program boosting method (LPBM), logistic regression (LR), support vector machine (SVM), and support vector machine recursive feature elimination (SVM-RFE), have been used and hold promise for early detection of AD and the prediction of AD progression When deep learning is used together with traditional machine learning methods, i.e., SVM as a classifier, it is referred to as a “hybrid method”. [6].

Hybrid deep learning approach for classifying Alzheimer’s disease based on multimodal data: Distinguishing between the 4 stages of Normal, minor Alzheimer’s disease(MAD), AD, and Huntington’s disease(HD), the Hybrid model of DBN CNN are better than traditional approaches. [11].



3.4 Summarizes the Presented Exhaustive

Table (2.1) summarizes the presented exhaustive survey of state-of-the-art studies related to AD(Alzheimer's Disease) approaches based on deep Learning.

Table 3.1: Summarizes the Presented Exhaustive

Author	Objectives	Model	Data Modality	Dataset	Performance Accuracy %
Ju et al.2017 [1]	predict an early diagnosis of AD	Autoencoders	MRI	ADNI	91
Shen et al.2019 [1]	distinguish AD From mild cognitive impairment	DBNs	PET	ADNI	86
Zhou,P.et al.2020 [2]	To predict AD	Sparse-response DBNs	• PET + MRI	ADNI	87
May D. Wang.2021. [3].	Distinguish between 3-stages of AD • Normal (CN) • MCI • AD	• CNN • Shallow Models	• MRI • SNPs • HER	ADNI	78
Shangran Qiu.(2022) [4].	Differential diagnosis of Alzheimer's disease, differentiating between normal cognitive aging, NC, MCI, AD, and nADD, and other dementia etiologies	CNN	• MRI • Non-Imaging	ADNI • AIBL • NACC • NIFD • OA-SIS • PPMI • FHS • LBDSU	69.2
Weiming Lin.2021.[5]	propose a framework that can diagnose AD	Hybrid (CNN - RNN)	• MRI • FDG-PET • CSF • genetic features	ADNI	66.7
fnagi.2019.[6].	Early detection of AD - Prediction of AD progression	SAE - DBM - SVM	• MRI • PET • CSF	ADNI	91
jancen et al.2019.[8].	To predict the progression of Alzheimer's Disease 12 months from the first patient visit (baseline visit)	CNN architecture	Genetic data	ADNI	87
May D. Wang.2021. [3].	Distinguish between 3-stages of AD • Normal (CN) • MCI • AD	• CNN • Shallow Models	• MRI • SNPs • HER	ADNI	92
Yu Wang et al.2021.[9].	Making correct diagnoses of AD disease	ShuffleNet - PCANet	• sMRI • fMRI	ADNI	92

Chapter 4

Project Planning

4.1 Introduction

Project management is a process of planning and controlling the development of a system within a specified time frame with the right functionality, and define Project Focuses, Strategies, and Action Steps, and measuring progress and performance.

4.2 Project Plan

The planning Phase is the fundamental process of understanding why a system should be built and also determining how the project team will go about building the system

4.2.1 Gathering Requirements

The analysis of this information leads to the development of a concept for a new system

4.2.2 System Analysis

- functional and non-functional requirements
- (Data flow diagram) DFD
- Use Case

4.2.3 System Design

- Sequence diagram
- Class diagram
- Activity diagram
- context diagram



4.2.4 Implementation

- ML model
- Back-end
- Mobile Application

4.2.5 Project Schedule Gantt Chart

A gantt chart is a horizontal bar chart used in project management to visually represent a project plan over time.

Gantt charts typically show the timeline and status

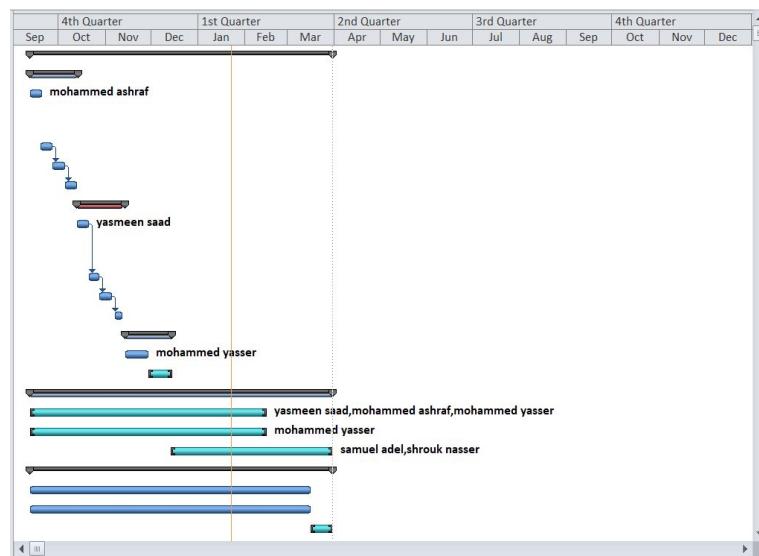


Figure 4.1: Gantt Chart



Z CARE 2022/2023

Start	Task Name	Duration	Start	Finish	Predecessors	Resource Names
Mon 6/12/22	ZCARE mobile app	144 days	Mon 9/12/22	Thu 3/30/23		
2	- Planning	24 days	Mon 9/12/22	Thu 10/13/22	mohammed ashraf	
3	Collect Advantages and Disadvantages of mobile app	6 days	Mon 9/12/22	Mon 9/19/22	mohammed ashraf	
4	Check Data Availability	6 days	Mon 9/19/22	Mon 9/26/22		
5	Identify stakeholders	6 days	Tue 9/27/22	Tue 10/4/22	4	
6	Set & prioritize goals.	6 days	Wed 10/5/22	Wed 10/12/22	5	
7	= System Analysis	23 days	Thu 10/13/22	Sun 11/13/22	yasmeen saad	
8	Functional & non Functional Requirements	6 days	Thu 10/13/22	Thu 10/20/22	yasmeen saad	
9	Context diagram	5 days	Fri 10/21/22	Thu 10/27/22	8	
10	DFD Level 0	6 days	Fri 10/28/22	Fri 11/4/22	9	
11	Use Case	5 days	Mon 11/7/22	Fri 11/11/22	10	
12	= System Design	23 days	Mon 11/14/22	Wed 12/14/22	mohammed yasser	
13	Sequence diagram	11 days	Mon 11/14/22	Mon 11/28/22	mohammed yasser	
14	Activity Diagram	12 days	Tue 11/29/22	Wed 12/14/22		
15	= Implementation	144 days	Mon 9/12/22	Thu 3/30/23	yasmeen saad,mohammed ashraf,mohammed yasser	
16	ML Model	112 days	Mon 9/12/22	Tue 2/14/23	mohammed yasser	
17	Backend	112 days	Mon 9/12/22	Tue 2/14/23	samuel adel,zhrouk nasser	
18	Mobile App	77 days	Wed 12/14/22	Thu 3/30/23	mohammed ashraf,mohammed yasser,samuel adel,zhrouk nasser,yasmeen saad	
19	= testing	144 days	Mon 9/12/22	Thu 3/30/23		
20	Component Testin	133 days	Mon 9/12/22	Wed 3/15/23		
21	System Testing	133 days	Mon 9/12/22	Wed 3/15/23		
22	Acceptance Testing	11 days	Thu 3/16/23	Thu 3/30/23		

Figure 4.2: Project Schedule

4.3 Feasibility Study

The feasibility study outlines and analyzes several alternatives or methods of achieving business success.

4.3.1 Focus

Helping Alzheimer's disease patient

4.3.2 Strategies

- Build a recommendation system that recommends activities to help Alzheimer's patients through Mobile Application.
- Create a Business Model
- lunching Application

4.3.3 Action Steps

- team members are familiar with technology to create an app easy to use.
- team members will get educated more about Alzheimer's disease
- create Business Plan which includes Marketing, Financial plans.

4.3.4 KPIs

- Model Classify Patients Correctly.
- API works properly with Mobile APP.

4.3.5 MOS

- Application has been launched and a lot of patients use it

Chapter 5

Proposed System

5.1 Overview

This chapter reviews the Development methodology also reviews the functional and non-functional requirements. It also discusses System analysis through the life cycle and its requirements showing the USE-CASE Diagram which is a list of actions or events steps typically defining the interactions between a role (known in the Unified Modeling Language as an actor) and a system to achieve a goal, Activity diagram which is a graphical representation of workflows of stepwise activities and actions and process modeling.

5.2 proposed framework

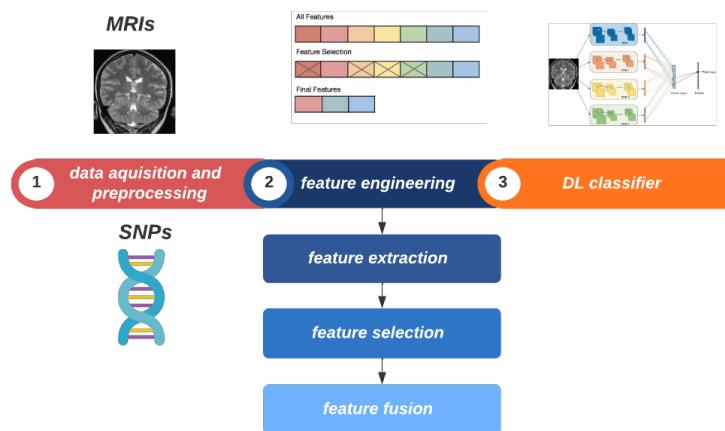


Figure 5.1: framework



5.3 System Analysis

Through this chapter we are going through the project requirements that the system must satisfy are of two types, which are functional and non-functional requirements. Functional requirements are the requirements that define a function of the software that runs on the system. Non-functional requirements are the requirements that specify criteria that can be used to judge the operation of the system, rather than specific behaviors. In the following subsections, both functional and non-functional requirements of the proposed system are listed.

5.3.1 Process Modeling

Context Diagram

The Context Diagram shows the system under consideration as a single high-level process and then shows the relationship that the system has with other external entities

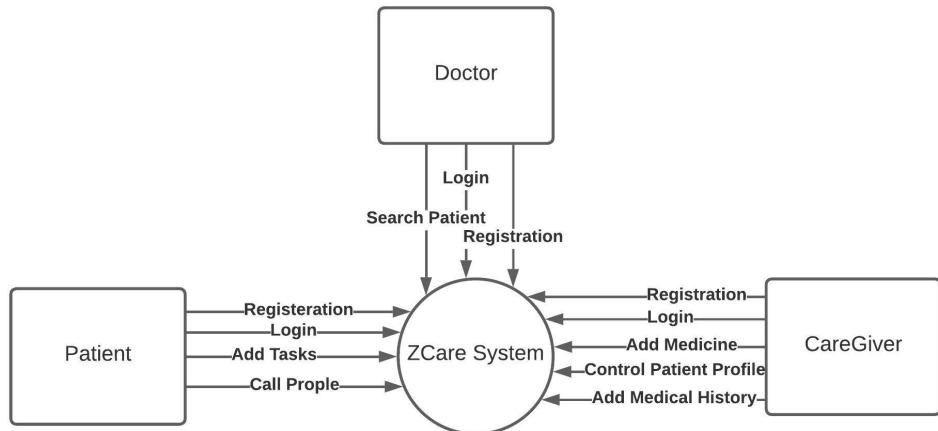


Figure 5.2: Context Diagram

Data Flow Diagram

A data flow diagram (DFD) illustrates how data is processed by a system in terms of inputs and outputs. As its name indicates its focus is on the flow of



Z CARE 2022/2023

information, where data comes from, where it goes, and how it gets stored It provides an overview of :

- What data is the system process?
- What transformations are performed?
- What data are stored?
- What results are produced, etc.

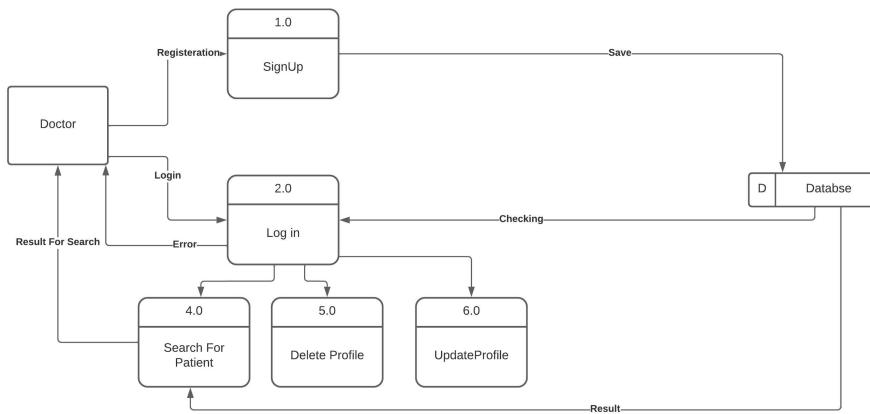


Figure 5.3: Doctor DFD

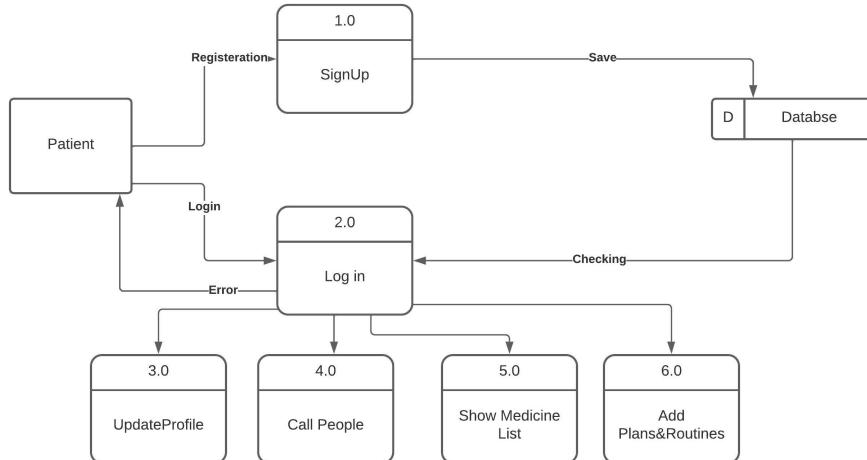


Figure 5.4: Patient DFD

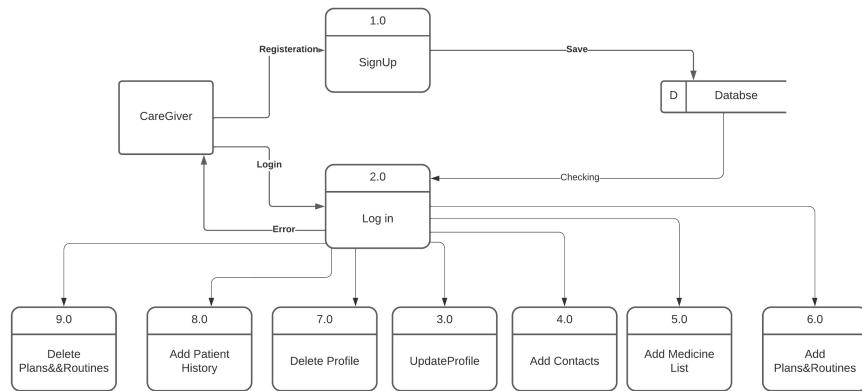


Figure 5.5: CareGiver DFD

5.3.2 Requirements

Functional Requirements

Functional requirements are features that allow the system to function as it was intended. Put another way, if the functional requirements are not met, the system will not work. Functional requirements are product features and focus on user requirements. Functional requirements are features that allow the system to function as it was intended. Put another way, if the functional requirements are not met, the system will not work. Functional requirements are product features and focus on user requirements.

5.3.3 Use Case Diagrams

- it represents system functionality from the user's perspective
- describes who will use the system and in what ways the user expects to interact with the system.
- represents the interactions between use cases and actors.

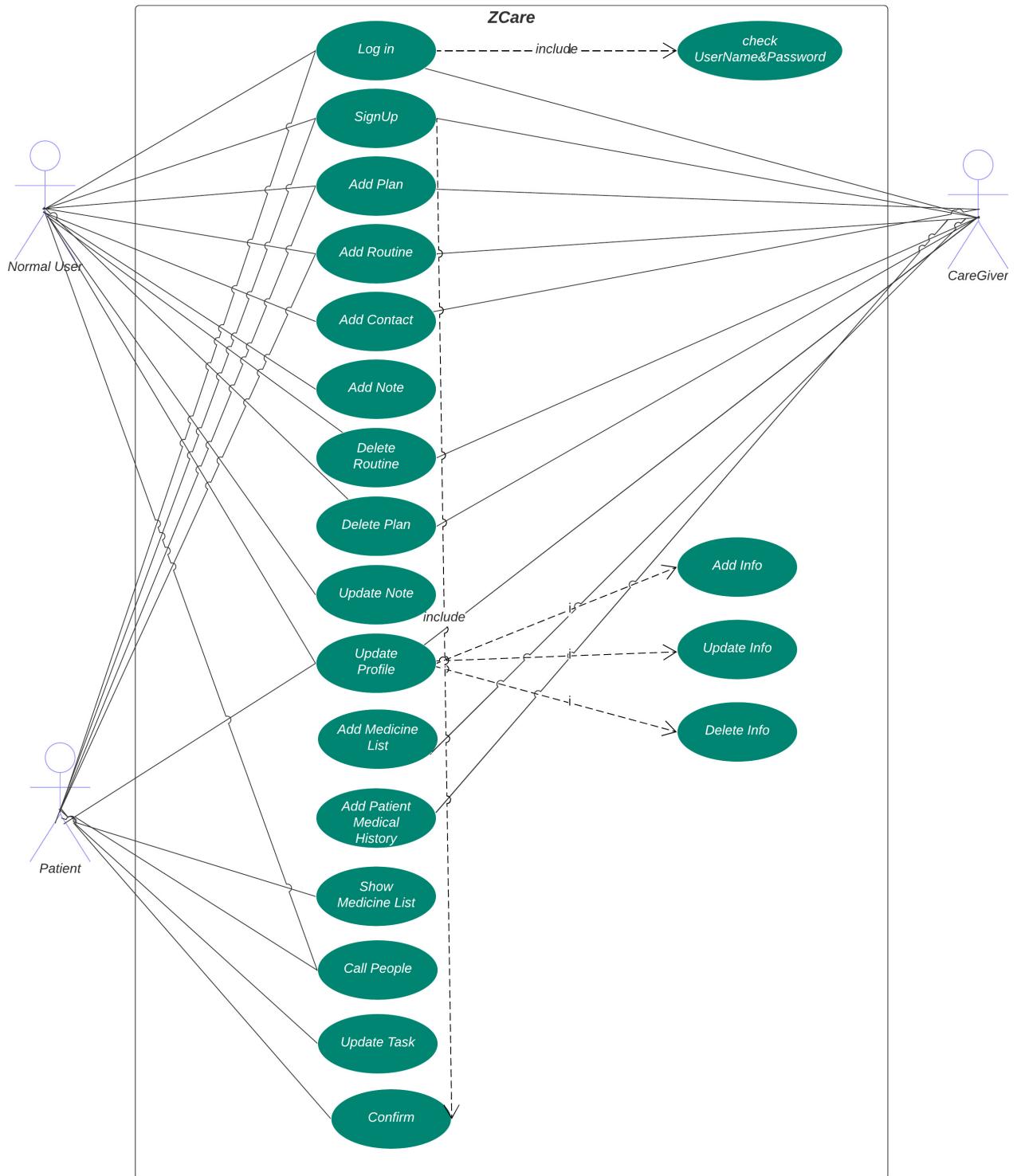


Figure 5.6: Patient, NormalUser, CareGiver Use case

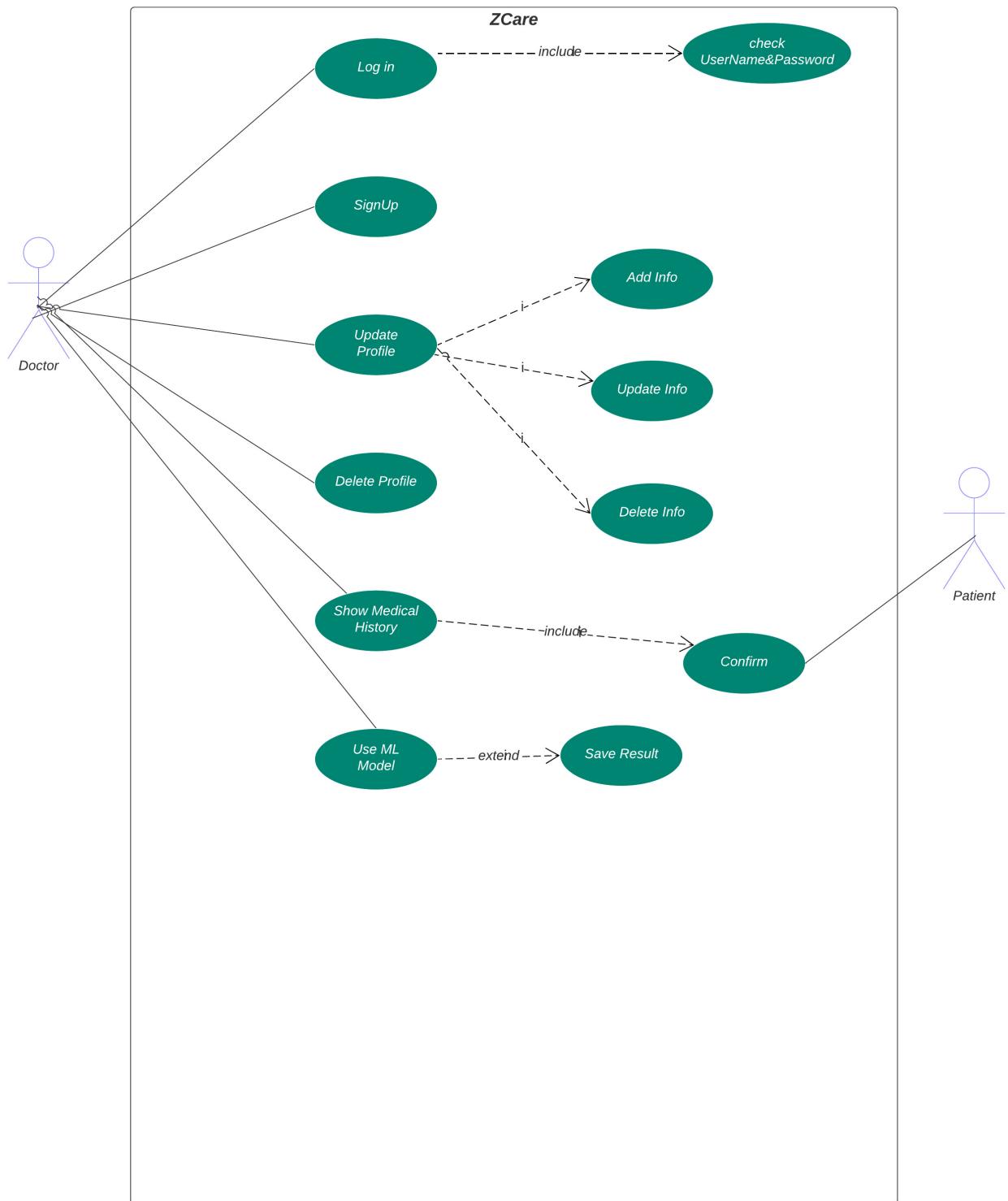


Figure 5.7: Doctor UseCase



Z CARE 2022/2023

5.3.4 Use Case Scenario

A use case Scenario represents the sequence of events along with other information that relates to this use case. A typical use case specification template includes the following information:

- Description
- Pre- and Post- interaction condition
- Basic interaction path
- Alternative pat

Patient use cases

Use case name	Link to Caregiver	
Actor(s)	Patient	
Description	steps for link to Caregiver.	
Typical of Events	Actor action	System Response
	1. enter caregiver username	2. search about caregiver username
Alternative	3. link to the caregiver, in case the username is found. otherwise shows a message error.	
Precondition	No Precondition	
Postcondition	Registration	

Table 5.1: Patient Link to Caregiver Case Scenario.



Use case name	Patient Registration	
Actor(s)	Patient	
Description	the Registration steps for a Patient to our Application.	
Typical of Events	Actor action	System Response
	1. a form appears to the patient-user, to fill in his information.	2. confirms with a message.
Alternative	3. shows a message error, in case something happened.	
Precondition	Link to the Caregiver	
Postcondition	Take Test	

Table 5.2: Patient Registration Use Case Scenario.

Use case name	Patient Take initial Test	
Actor(s)	Patient	
Description	steps of take test	
Typical of Events	Actor action	System Response
	1. answer some initial questions	2. determine is the patient need to the doctor or not
Alternative	3. in case the patient needs to the doctor, alarm his caregiver. otherwise suggest strategy to maintain his life	
Precondition	Registration use case	
Postcondition	System Create Patient File.	

Table 5.3: Patient Take Test Use Case Scenario.



Z CARE 2022/2023

Use case name	Patient Login	
Actor(s)	Patient	
Description	how patient open the Application	
Typical of Events	Actor action	System Response
	1. use Face ID or Finger ID from mobile.	2. determine the identity.
Alternative	3. in case the identity doesn't determine, show a help message.	
Precondition	Mobile has FaceID or FingerID	
Postcondition	No Postcondition	

Table 5.4: Patient Login Use Case Scenario.

Caregiver use cases

Use case name	Caregiver Registration	
Actor(s)	Caregiver	
Description	the Registration steps for a Caregiver to our Application.	
Typical of Events	Actor action	System Response
	1. a form appears to the caregiver-user, to fill in his information.	2. confirms with a message.
Alternative	3. shows a message error, in case something happened.	
Precondition	No Precondition	
Postcondition	create Caregiver file	

Table 5.5: Caregiver Registration Use Case Scenario.



Use case name	Caregiver Login	
Actor(s)	Caregiver	
Description	how caregiver open the Application	
Typical of Events	Actor action	System Response
	1. use Face ID, Finger ID from mobile or Password. 2. determine the identity.	
Alternative	3. in case the identity doesn't determine, show an error message.	
Precondition	No Preconditions.	
Postcondition	No Postcondition	

Table 5.6: Caregiver Login Use Case Scenario.

Use case name	Track Patient	
Actor(s)	Caregiver	
Description	steps of get patient information	
Typical of Events	Actor action	System Response
	1. Enter Patient username 2. search about the username	
Alternative	3. in case the username is not found shows a message error.	
Precondition	Login to the system	
Postcondition	Retrieve the patient file	

Table 5.7: Caregiver tracks Patient Use Case Scenario.



Z CARE 2022/2023

Use case name	Choose Doctor	
Actor(s)	Caregiver	
Description	steps to choose doctor.	
Typical of Events	Actor action	System Response
	2. choose the desired Doctor.	1. list the available Doctors in the system.
Alternative	3. take an appointment and send confirm message.	
Precondition	Log in	
Postcondition	No Postcondition	

Table 5.8: Caregiver Choose Doctor Case Scenario.

Physician

Use case name	Physician Registration	
Actor(s)	Physician	
Description	the Registration steps for a Physician to our Application.	
Typical of Events	Actor action	System Response
	1. a form appears to the physician-user, to fill in his information.	2. confirms with a message.
Alternative	3. shows a massage error, in case something happened.	
Precondition	No Precondition	
Postcondition	No Postcondition	

Table 5.9: Physician Registration Use Case Scenario.



Use case name	Physician Login	
Actor(s)	Physician	
Description	how Physician open the Application	
Typical of Events	Actor action	System Response
	1. uses Face ID, Finger ID from mobile or Password.	2. determines the identity.
Alternative	3. in case the identity doesn't determine, show an error message.	
Precondition	No Preconditions.	
Postcondition	No Postcondition	

Table 5.10: Physician Login Use Case Scenario.

Use case name	Patient Search	
Actor(s)	Physician	
Description	steps search about patient.	
Typical of Events	Actor action	System Response
	1. Enter a patient username.	2. in case the username is not found shows a message error.
Alternative		
Precondition	Physician logs in.	
Postcondition	Retrieve the patient file	

Table 5.11: Physician searches patient Case Scenario.



Z CARE 2022/2023

Use case name	Patient Diagnosis	
Actor(s)	Physician	
Description	steps to use ML model.	
Typical of Events	Actor action	System Response
	1. Enter model parameters.	2. display results.
Alternative		
Precondition	1. doctor logs in. 2. patient in the system (patient search use case).	
Postcondition	add results to Database	

Table 5.12: Physician diagnoses patient Case Scenario.

5.3.5 Activity Diagram

An activity diagram gives a graphical representation of how data move around an information system based on data flows.

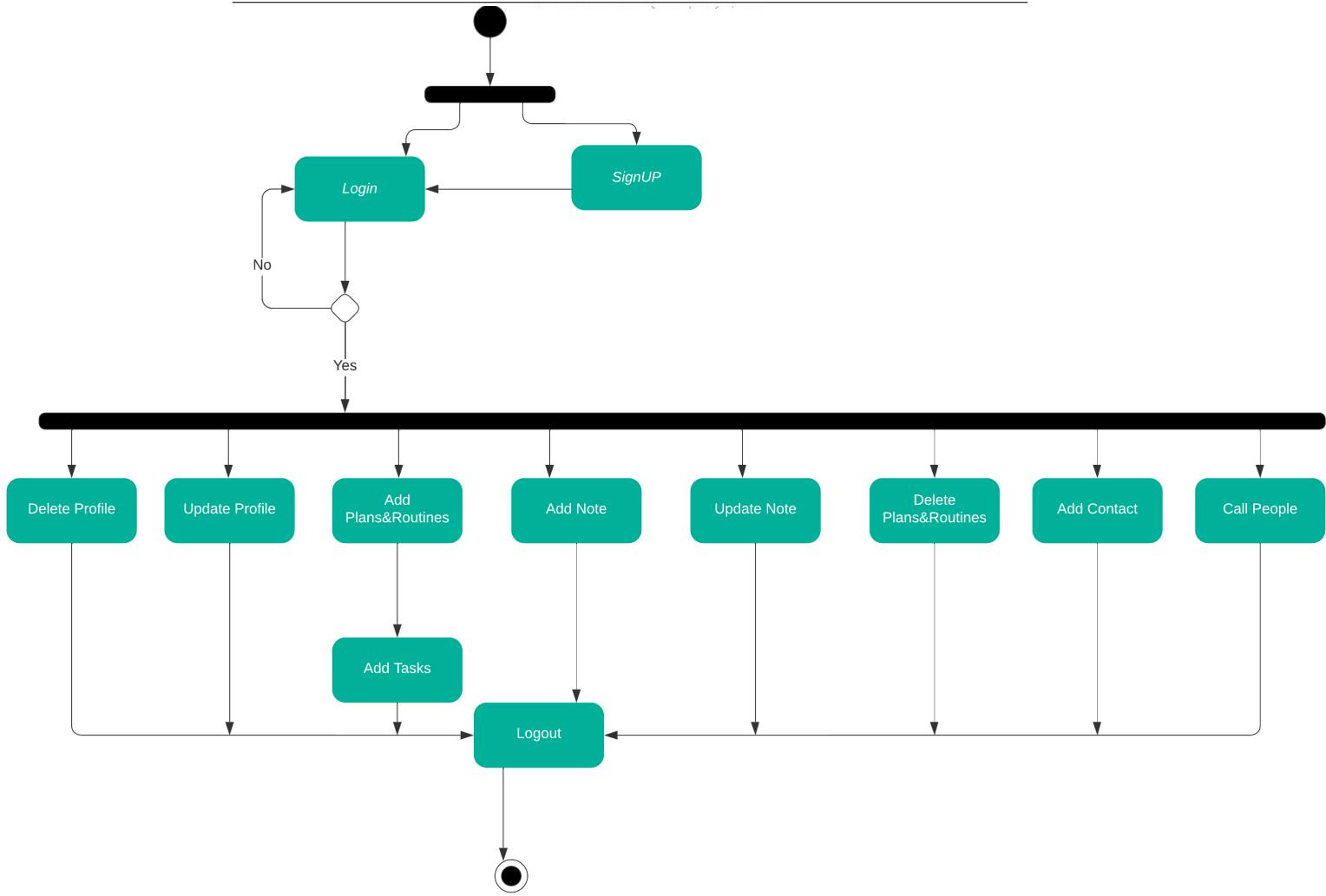
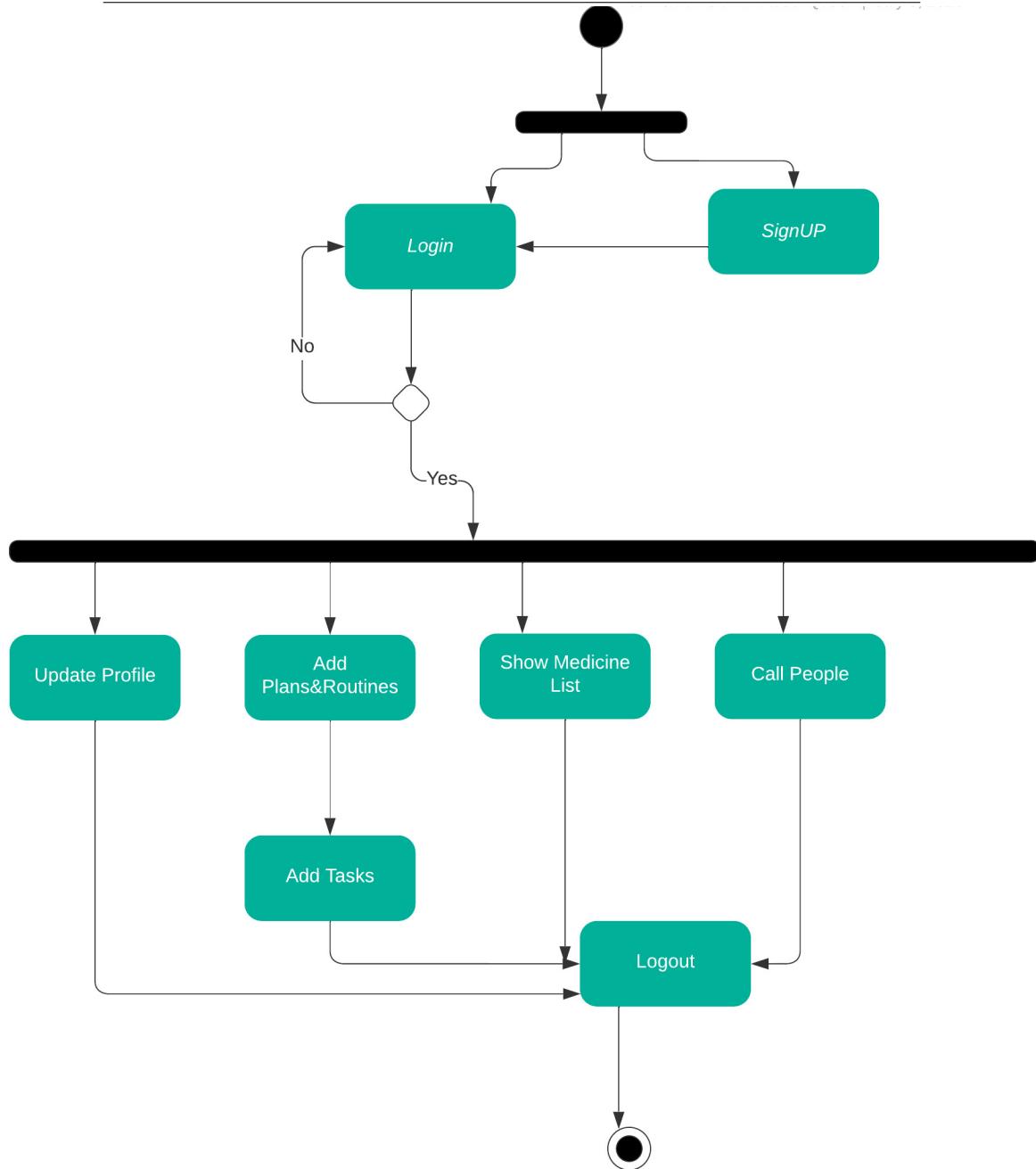


Figure 5.8: Normal User Activity Diagram



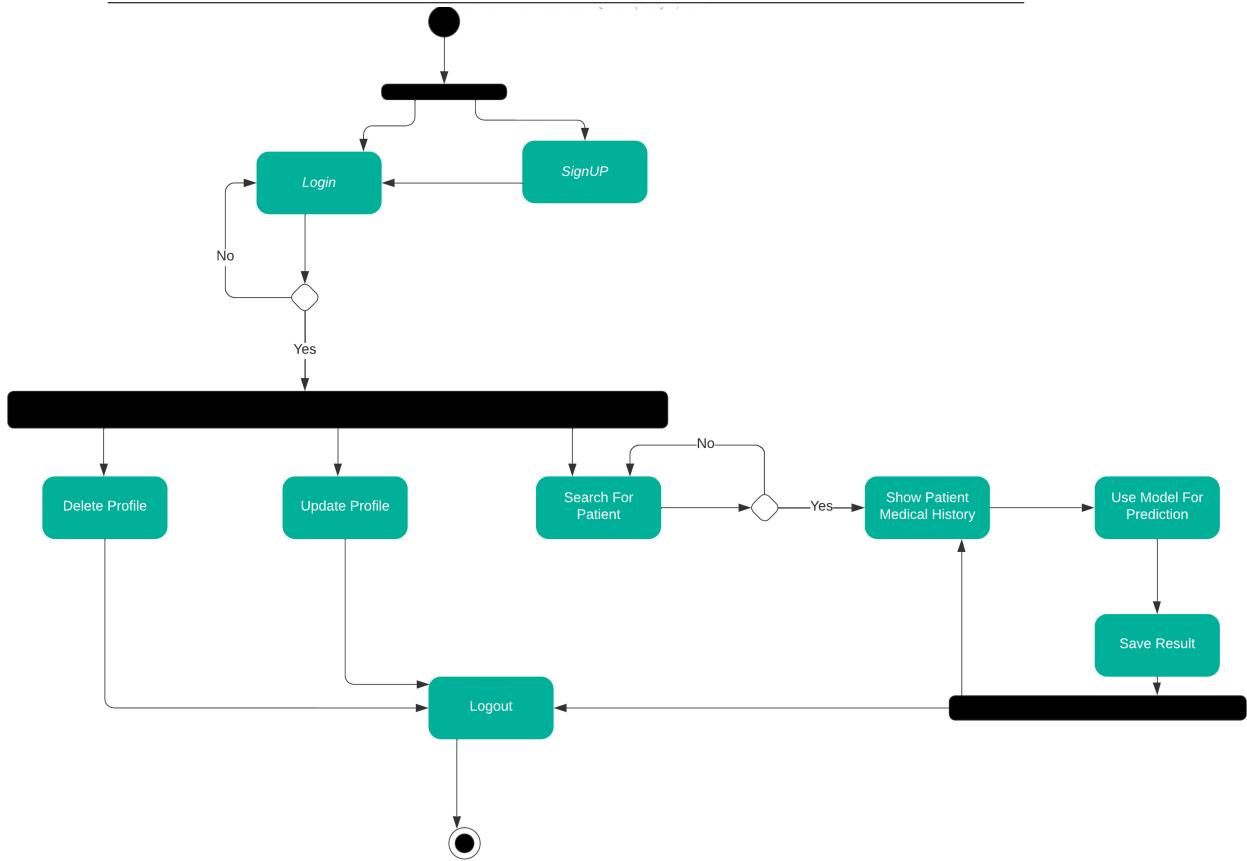


Figure 5.10: Doctor Activity diagram

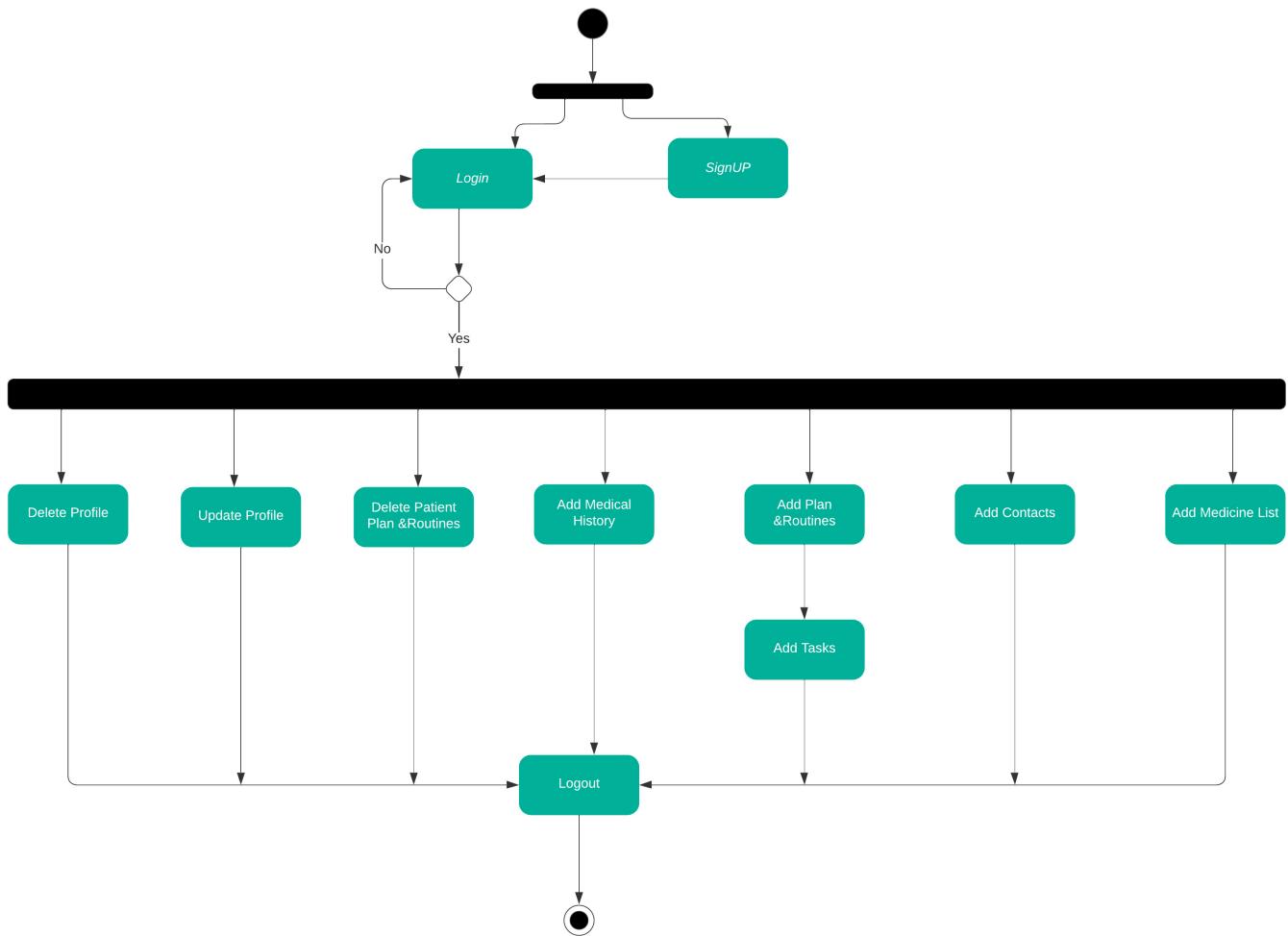


Figure 5.11: CareGiver Activity diagram



5.3.6 Non Functional Requirements

Non-functional requirement (NFR) is a requirement that specifies criteria that can be used to judge the operation of a system, rather than specific behavior. They are contrasted with functional requirements that define specific behavior or functions.

- Usability: The Mobile Application cart should be easily usable by the Patient.
- Accessibility: the caregiver will receive the Call
- Performance: The main function must have specific real-time to be executed for each operation to not delay the whole system
- Security: The patient must be sure that all his details will be secured in the App options.
- User-friendly: Easy to use and manipulate every proposed feature

5.4 System Design

Systems design is the process of defining elements of a system like modules, architecture, components and their interfaces, and data for a system based on the specified requirements

5.4.1 Sequence Diagram

sequence diagram given is used to show the interactive behavior of the system

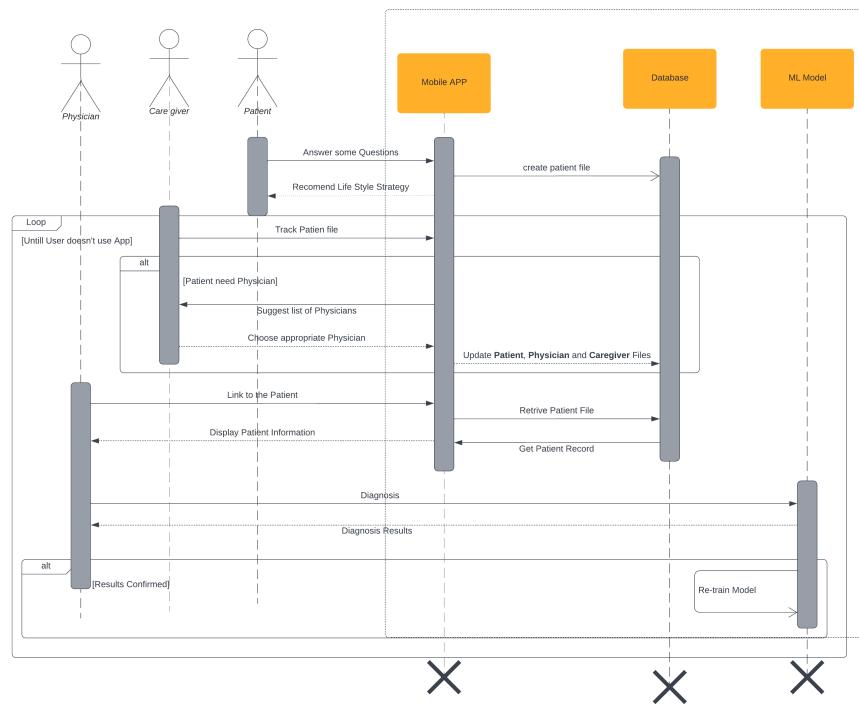


Figure 5.12: Sequence diagram



Z CARE 2022/2023

5.4.2 Class Diagram

A class diagram in the Unified Modeling Language (UML) is a type of static structure diagram that describes the structure of a system by showing the system's classes, attributes, operations (or methods), and relationships among objects.

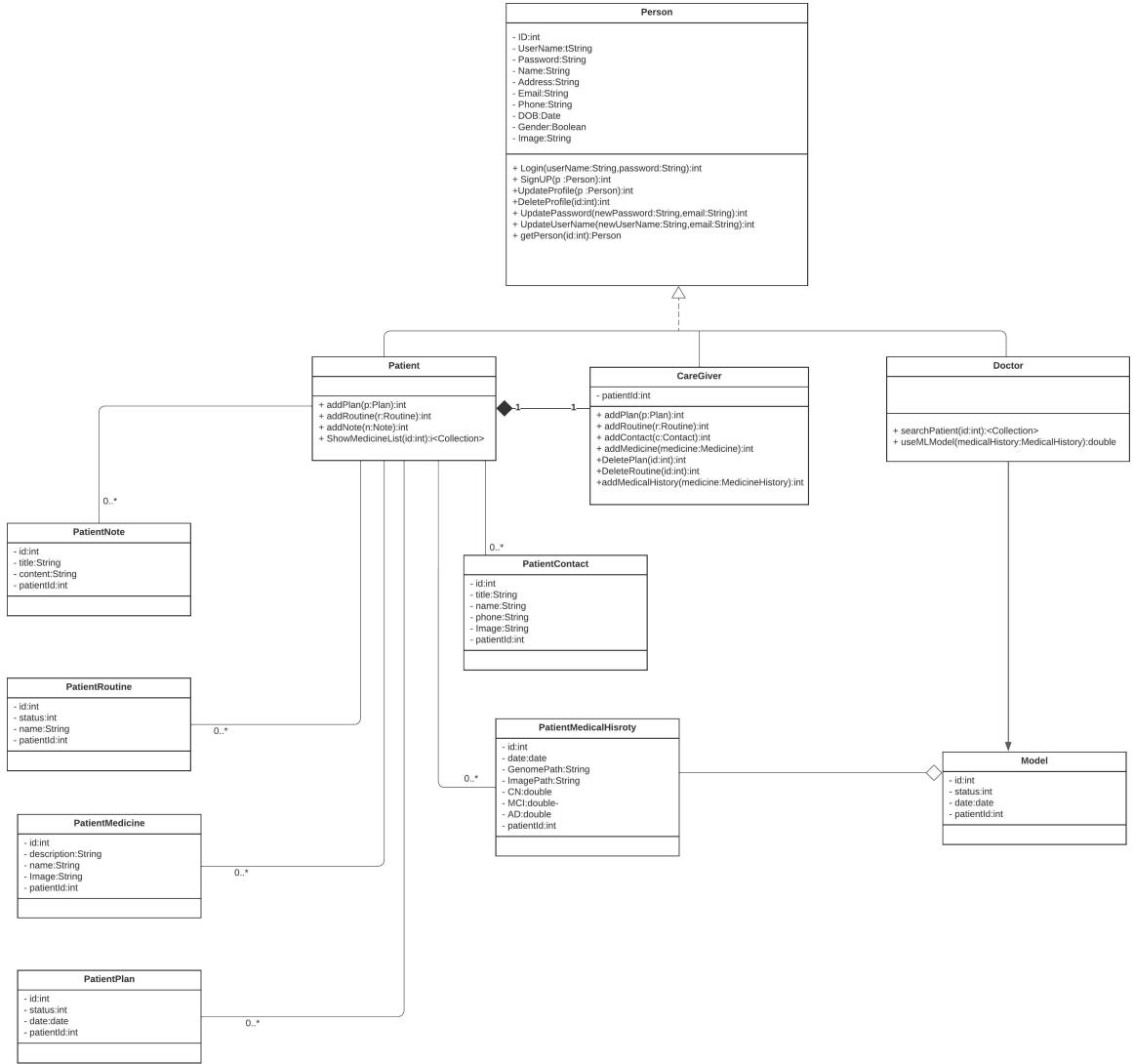


Figure 5.13: Class diagram

5.4.3 Relational Database Diagram (ERD)

An entity-relationship model (ERM) is an abstract and conceptual representation of data. Entity-relationship modeling is a database modeling method, used to produce a type of conceptual schema or semantic data model of a system, often a relational database, and its requirements in a top-down fashion

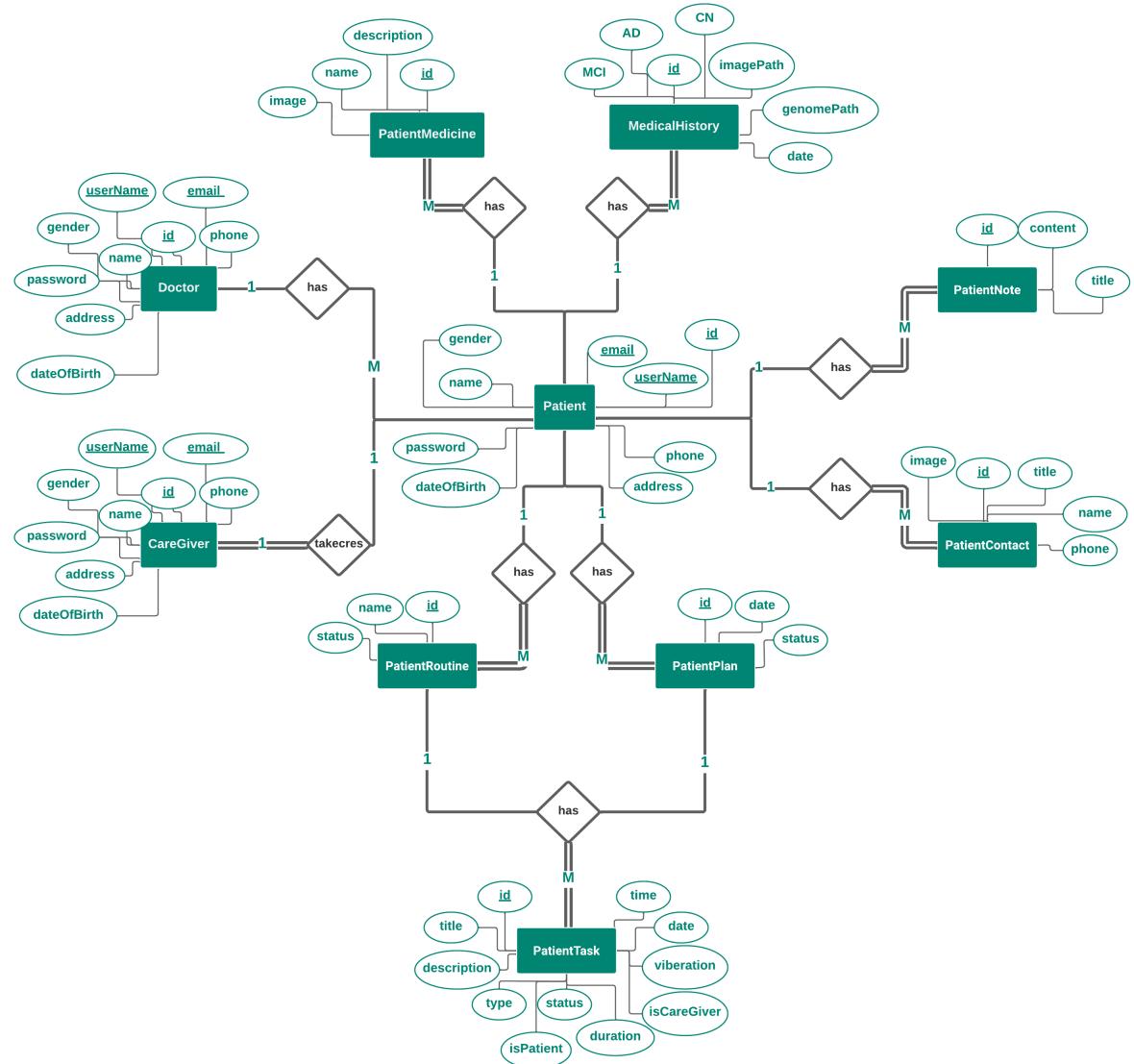


Figure 5.14: ERD Diagram

Chapter 6

Experimental Results and Comparative Analysis

6.1 Experiment Specifications and Used Materials

This section presents and discusses all the details related to the experiments carried out to investigate and evaluate the performance of the proposed approaches. In this project, simulation experiments were performed on Google Colab with A100 GPU and 12 GB memory and a 16 GB RAM, Intel Core i7-4610M CPU (8.00 GHz, 1600 MHz, 4 MB L3 Cache, 2 cores, 37W). The proposed approach is designed with Tensorflow and Keras using Python, and Octave and SPM on Ubuntu OS.

6.2 Evaluation Metrics

To evaluate the performance of the proposed system, several performance metrics, namely, Accuracy, Recall (Sensitivity), Precision, and loss function, were calculated according to equations 6.1,??,?? , 6.2 respectively. where TP is the true positive value, FP is the false positive value, TN is the true negative value, FN is the false negative value, and N is the total number of observations.

$$Accuracy = (TP + TN) / (TP + FN + TN + FP) \quad (6.1)$$

$$L = -(y \log^y + (1 - y) \log(1 - y)) \quad (6.2)$$

Also, the Area Under Curve (AUC) separability measure is calculated. The AUC metric is commonly used as a performance measurement for classification problems using various threshold settings. It represents a measure of the model's separability or distinguishability between classes. TP, FP, TN, and FN terms in Confusion Matrix are defined as follows:



Z CARE 2022/2023

-
- True Positive (TP): the image is X and is classified as an X.
 - False Positive (FP): the image is Y and is classified as an X.
 - True Negative (TN): the image is Y and is classified as Y.
 - False Negative (FN): the image is X and is classified as Y.

6.3 Results of The System

6.3.1 Dataset description

Data obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data. A complete listing of ADNI investigators can be found at: http://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_Acknowledgement_List.pdf

The primary goal of ADNI has been to test whether serial magnetic resonance imaging (MRI), positron emission tomography (PET), other biological markers, and clinical and neuropsychological assessment can be combined to measure the progression of mild cognitive impairment (MCI) and early Alzheimer's disease (AD). Determination of sensitive and specific markers of very early AD progression is intended to aid researchers and clinicians to develop new treatments and monitor their effectiveness, as well as lessen the time and cost of clinical trials.

This dataset consists of 2 modals including 3 classes of different stages of Alzheimer's disease withtotal number of images, 690 sample of SNPs AD ,MCI and CN images and 360 have both images and SNPs . It is also openly available on the internet with requested access . Each class contains approximately 195 of CN ,337 of MCI and 158 of AD images and 426 of CN ,535 of MCI and 175 of AD samples of genes. Figures 6.1, 6.2, 6.3 shows samples of CN, MCI, AD respectiviley . The description of classes used in the system from this dataset is given in the table 6.1.

Z CARE 2022/2023

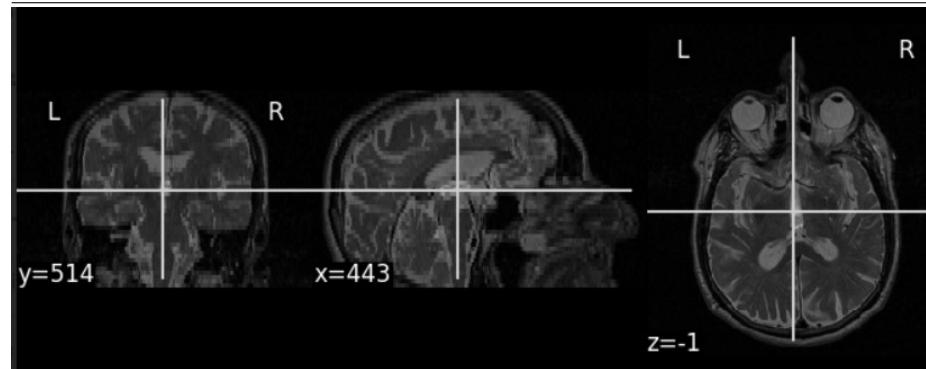


Figure 6.1: CN status

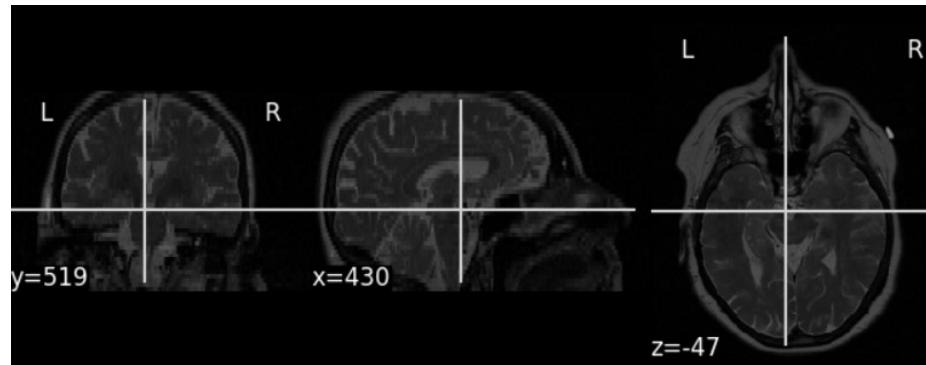


Figure 6.2: MCI status

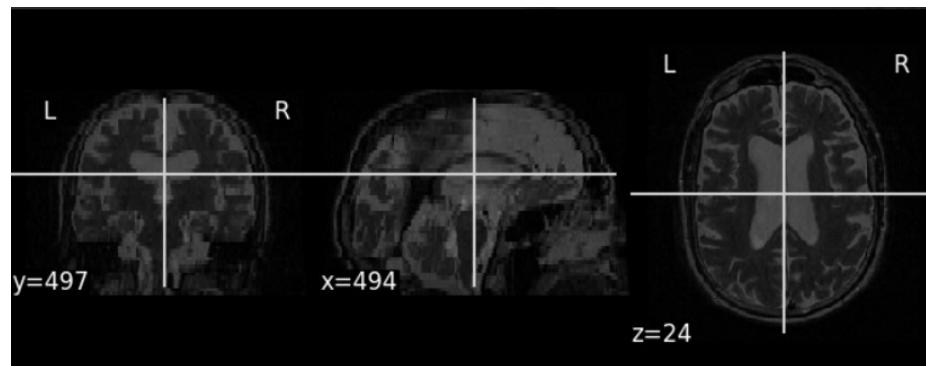


Figure 6.3: AD status



Z CARE 2022/2023

ADNI DATASET			
Class	Disease name	SNPs number	image number
0	CN	195	426
1	MCI	337	535
2	AD	158	175

Table 6.1: Datasets (ADNI) description

6.3.2 Results and Discussion

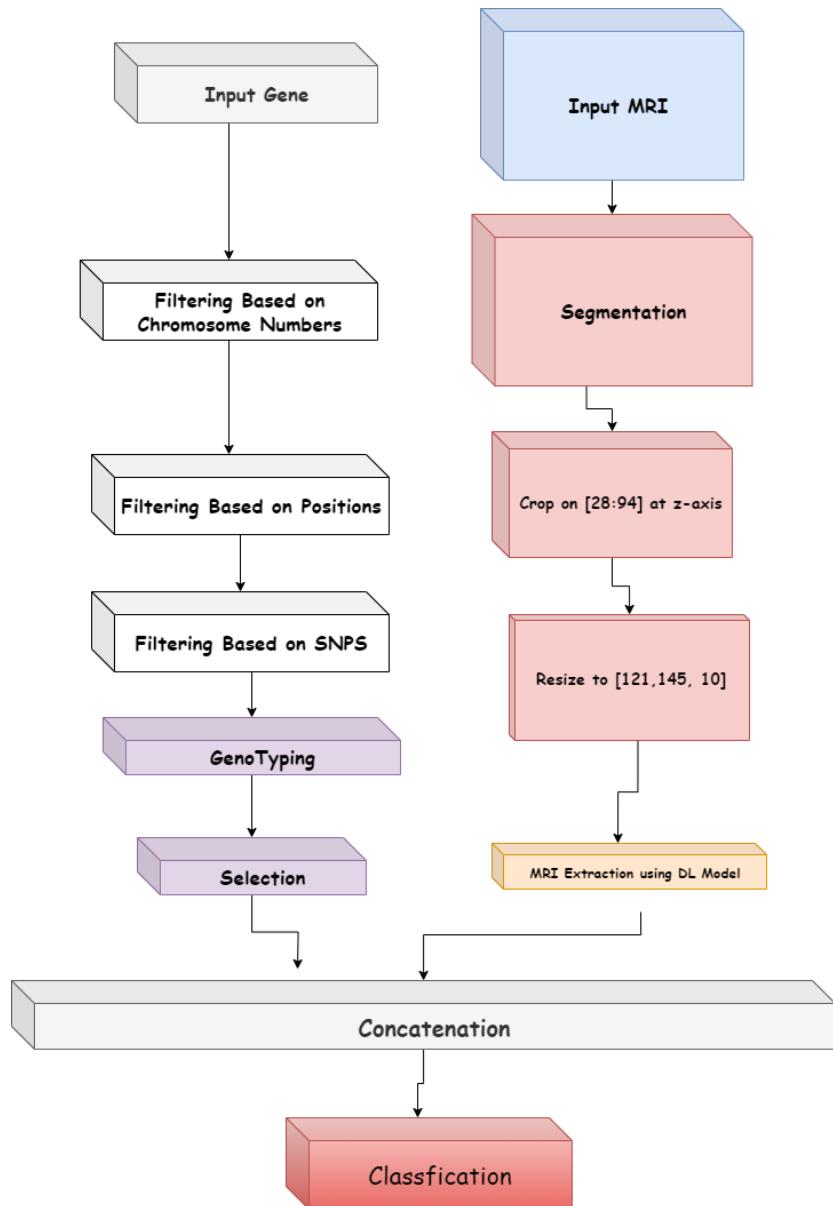


Figure 6.4: Full Framework



Z CARE 2022/2023

MRI Discussion

In our experiment we used 1136 MRI-T2 slides. We split the image data into 80:20 train and test. the train set is split into 70:30 train and validation set. We used this data set for multiclass and binary classification and the data set is summarized in 6.1.

After Preprocessing on MRI. The MRI is cropped on [28:94] at the z-axis, where the most important information of the brain can be found in this region. and then resize to (121, 145, 10).

The Activation Function in Classification Layer, in Multi-Class Classification, is **SoftMax** and in Binary Classification **Sigmoid**. During training, the model is activated to classify MR brain images for 64 epochs. and The best epochs are saved based on validation Loss, to begin from it on the next try.

Muli-Class Classification

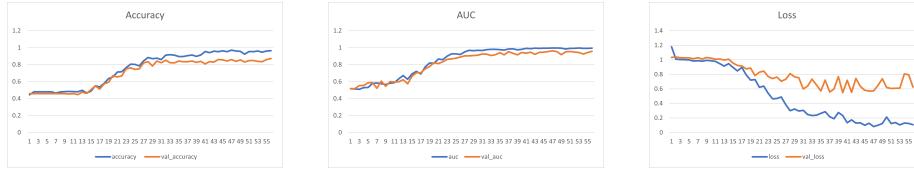


Figure 6.5: CNN from [7] Metrices
Multi-Class Classification

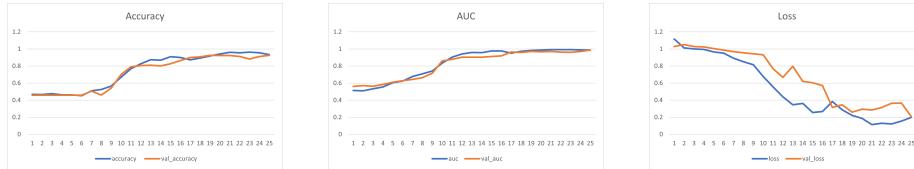


Figure 6.6: CNN Reduced Model Metrices
Multi-Class Classification

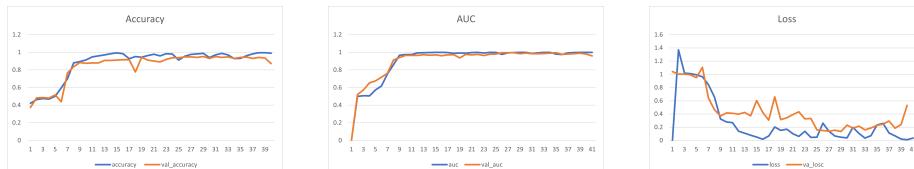
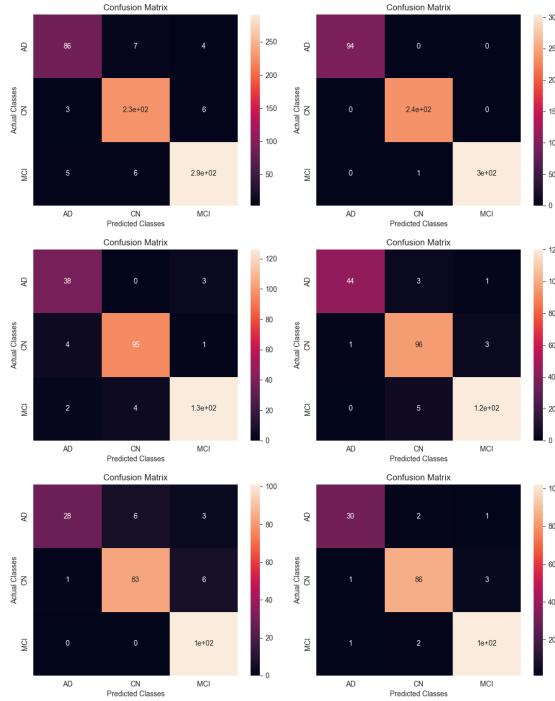


Figure 6.7: CNN-Attention Model Metrices
Multi-Class Classification



(a) CNN-Reduced (b) CNN-Attention

Figure 6.8: Comparing Between Image Models based on Confusion Matrix, Multi-Class

The first Row represents Training.

The Second Row represents Validation.

The Third Row represents Testing.

As shown the CNN-Atten is performed will over the CNN-Origin and CNN-Reduced.

Model	Accuracy		AUC		Loss	
	Train	Test	Train	Test	Train	Test
CNN 1	0.9661	0.9298	0.9938	0.9810	0.1083	0.2655
CNN Reduced	0.9511	0.9298	0.9912	0.9834	0.1400	0.2014
CNN with Attention	0.9984	0.9561	1.0000	0.9897	0.0101	0.1348

Table 6.2: Comparing between Models Multi-Class



Z CARE 2022/2023

Binary Classification These Models have the same Architecture of CNN-Reduced 6.9

- CN vs All

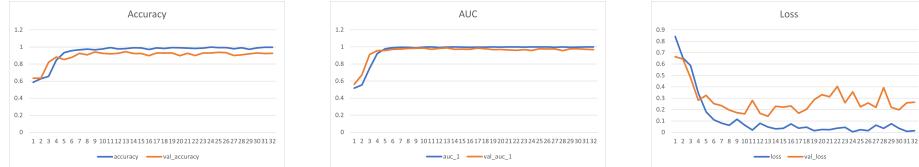


Figure 6.9: Metrices

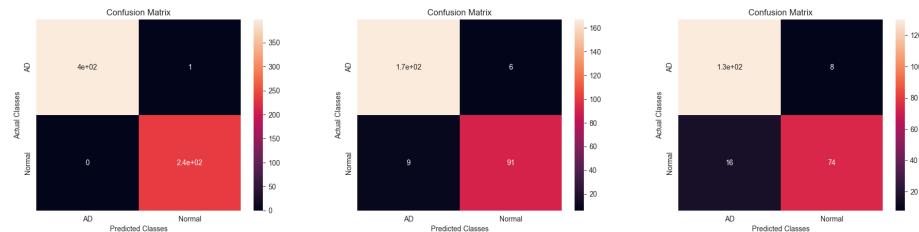


Figure 6.10: Confustion Matrices

- MCI vs AD

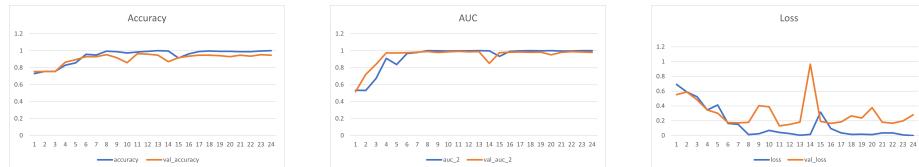


Figure 6.11: Metrices

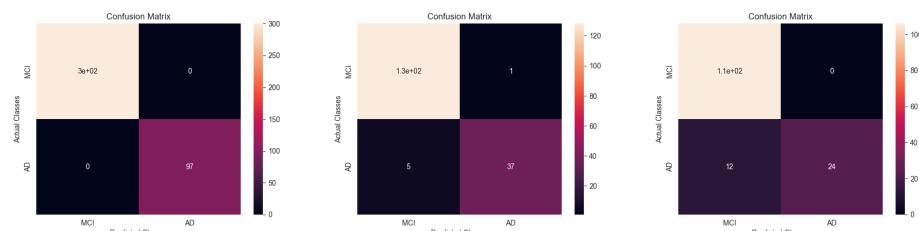


Figure 6.12: Confustion Matrices



Gene Discussion

In genes we intended to select set of features which achieve best accuracy. in order to do that we used many feature selection techniques like BORUTA and random forest feature selection techniques, random forest achieved best results and select 43 feature out of 96 which reduce dimensions to increase accuracy and remove overfitting, which accuracy increase from 67.6 for 96 column to 71.09 for 40 columns CN VS. MCI/ AD ,which will be explained in detail in the following table 6.3

ADNI1GWAS data				
Approach	Training acc	Testing acc	modality	Shape
After FS Xg boost	100	71.09	CN VS. MCI/ AD	690 rows × 39 columns
After FS Random forest	73.5	61.2	CN VS. MCI/ AD	690 rows × 39 columns
After FS ANN 4 layer	94.43	67.05	CN VS. MCI/ AD	690 rows × 39 columns
After FS Xg boost	100	62.9	AD VS. MCI	690 rows × 39 columns
After FS Random forest	70.8	50.8	AD VS. MCI	690 rows × 39 columns
After FS Xg boost	100	76.4	AD VS. CN	690 rows × 40 columns
After FS Random forest	74.6	67.4	AD VS. CN	690 rows × 43 columns

Table 6.3: SNPs discussion

NOTE: highlighted result id the best one which we build our model on it after using feature selection by random forest which this features achieve 74.6 training accuracy and 67.4 testing accuracy which is acceptable.

this features is the most affecting features which we can use to detect is this patient has Alzheimer disease or not CN VS. AD

most affecting features

```
[rs1150895, rs12126925, rs12405469, rs1295640, rs16846644, rs1783016, rs1783025, rs2014146, rs2073489, rs2156079, rs216762, rs2234983, rs2256331, rs2313007, rs2802268, rs2829973, rs2829997, rs2830000, rs2830008, rs2830012, rs2830028, rs2830033, rs2830036, rs2830038, rs2830044, rs2830052, rs2830088, rs362350, rs362393, rs373521, rs3787620, rs380417, rs439401, rs440666, rs452987, rs466448, rs466609, rs7276036, rs7278838, rs8006497, rs8106922, 'Sex', 'Age']
```

Fusion Classification Discussion

After Passing the MRI on Image prepare baseline and Gene on Gene prepare baseline as shown in 6.4. the fusion (concatenated data) passes to Classifier. The Classification phase is split into two ways, multi-class Classification and binary-class Classification.

Binary Classification

The Image will be Classified into a Normal Person or a Patient have AD, after this, the Genetic Data will be concatenated with the data extracted from MCI-AD-Image Extractor. and then pass to two Dense Layers with **relu** activation function with 100 and 50 Nodes, respectively. then the Classification layer

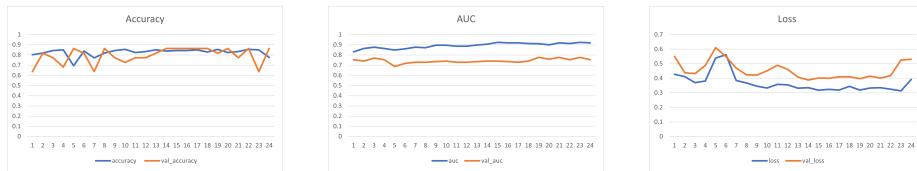


Figure 6.13: Metrics

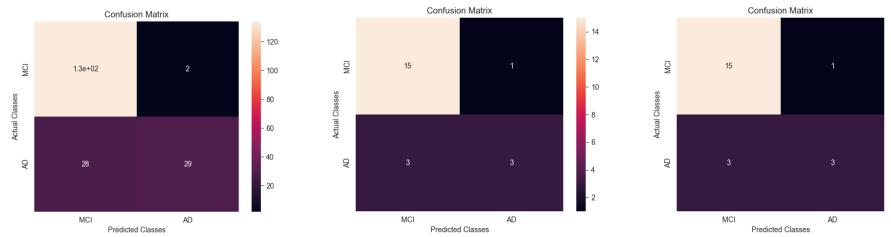


Figure 6.14: Confusion Matrix
 First Confusion for Training.
 Second Confusion for Validation. Third Confusion for Testing

Multi-Class Classification

the Genetic will be concatenated with the data extracted from CNN-Atten Image Extractor. and then pass to the Classification layer directly.

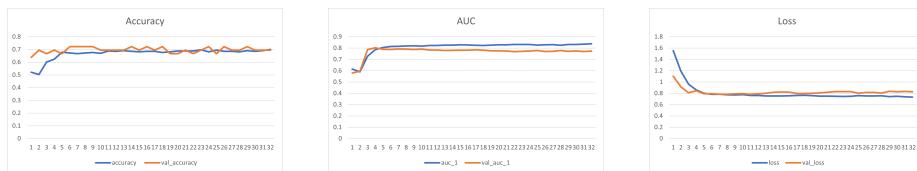


Figure 6.15: Metrics

Chapter 7

System Development

7.1 Overview

Our comprehensive solution is designed to assist Alzheimer's patients and their caregivers in managing day-to-day activities. The app is built using Flutter and a Java-based backend API for processing and managing data and offers three distinct interfaces tailored to different user roles.

The first interface is designed for healthcare professionals and enables them to leverage our machine-learning model to predict Alzheimer's disease based on patient genes and images, as previously mentioned in detail. The second interface is designed for patients and provides a range of features such as medication reminders, appointment scheduling, and task lists to better manage their daily life. The third interface is designed for caregivers, providing them with remote control over their patient's life and ensuring they have access to critical information and tools to provide the best possible care. Our app is designed to enhance patients' quality of life while also empowering caregivers with the necessary tools to support and have trust in their loved ones.

We are proud to offer our app in two languages, English and Arabic, to better serve our users and ensure they can access our app in the language of their choice. This feature is designed to make our app more accessible to users around the world and to ensure that language barriers do not prevent users from accessing critical healthcare resources.

7.2 App's architecture & design patterns

Our app uses a client-server architecture, with the Flutter app as the client and the Java-based backend API acting as the server. The app is built on a foundation of the Model-View-Controller (MVC) design pattern, which provides a clear separation of concerns and enables the effective organization of code. Furthermore, our app employs a RESTful API design, facilitating communication between the client and server via HTTP requests. This architecture and design



Z CARE 2022/2023

pattern combination ensures that our app is scalable, maintainable, and easily extensible.

7.3 Methodological assumptions

User and system requirements to activate the system.

7.3.1 User Requirements

- Users should have basic computer skills in operating systems and the internet browsers.
- Users must have a connection to access the internet.
- Users must be either university students or university staff members (Advisor, Administrator).

7.3.2 System Requirements

- Basic computer hardware such as core i3 processor, 4 GB RAM, and Microsoft Windows operating system.
- Internet Browser such as Internet Explorer, Mozilla Firefox, Google Chrome, etc.

7.4 Used Technologies

7.4.1 Dart

Dart is a programming language optimized for building fast apps on any platform. It aims to be a productive language for multi-platform development, with a flexible execution runtime platform for app frameworks. Dart is versatile and well-suited for a range of development tasks, providing tools for building fast, reliable, and high-quality applications.

7.4.2 Flutter

Flutter is an open-source UI framework by Google for building cross-platform applications from a single codebase. It enables developers to create responsive applications for Android, iOS, Windows, Mac, and Linux. Flutter's native performance, hot reload feature, and comprehensive set of widgets and APIs make it a versatile and powerful tool for building high-quality applications with ease.



7.4.3 Flutter Bloc

A state management library for Flutter that helps separate the UI from business logic.

7.4.4 Flask

Flask is a popular Python web framework for building web applications. It is a micro-framework, which means that it is designed to be lightweight and flexible, and can be extended with a wide range of third-party libraries and tools. used for ML model Deployment

7.4.5 Google Cloud Platform

Google Cloud Platform (GCP) is a cloud computing platform offered by Google that provides a wide range of cloud-based services and tools to help individuals and organizations build, manage, and deploy applications and services. such as VMs. Also, provide access to Google Products using APIs, such as accessing to Drive to get the patient data (medical history).



7.5 Mobile development

- In our App we provide you can set which language will use in the App, and you can change it again many times after creating an account.

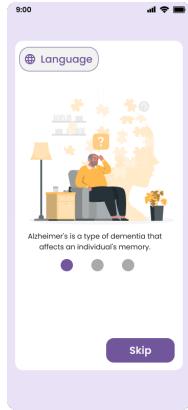


Figure 7.1: Onboarding screen

- First, You have to choose which interface you will sign up with.

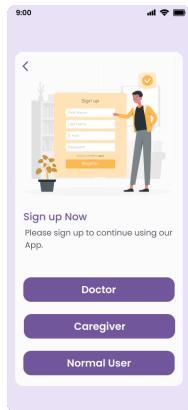


Figure 7.2: sign up

- Three distinct interfaces for Sign Up (Doctor - CareGiver - Patient).



9:00

Sign up as a Doctor

Name
Enter your name

User Name
Enter your user name

Phone Number
Enter your password

Email
Enter your email address

Password
Enter your password

Sign up

9:00

Sign up as a Caregiver

Name
Enter your name

User Name
Enter your user name

Patient ID
Enter your user name

Phone Number
Enter your password

Email
Enter your email address

Password
Enter your password

Sign up

9:00

Sign up as a Normal user

Name
Enter your name

User Name
Enter your user name

Phone Number
Enter your password

Email
Enter your email address

Password
Enter your password

Sign up

Figure 7.3: Sign Up as Doctor

Figure 7.4: Sign Up as CareGiver

Figure 7.5: Sign Up as Patient

- Verify Account: you have to receive a verification code from the mail/mobile to verify your account.

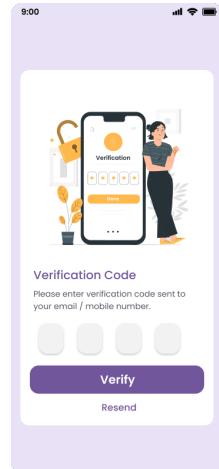


Figure 7.6: Verification

- If you already have an account, you can log in by choosing the interface first.

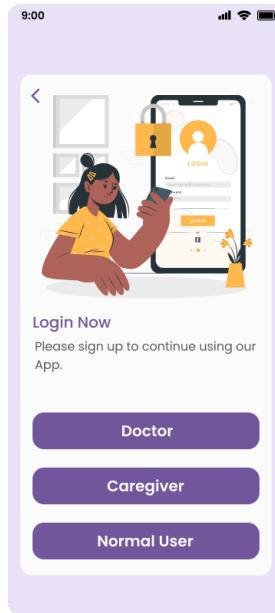


Figure 7.7: Login Screen

- Three distinct interfaces for Login (Doctor - CareGiver - Patient).

Z CARE 2022/2023

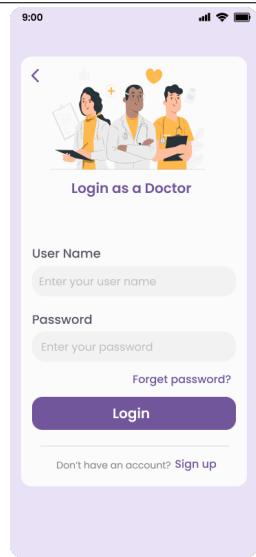


Figure 7.8: Login as Doctor

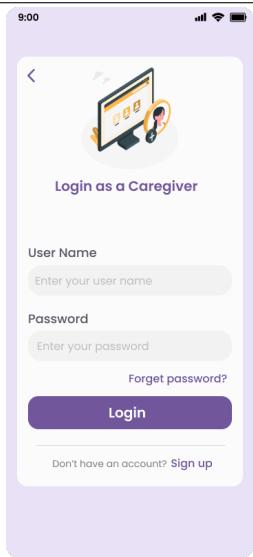


Figure 7.9: Login as CareGiver

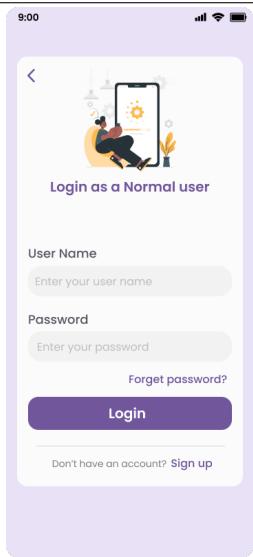


Figure 7.10: Login as Patient

- Password: Our App helps you if forgetting password by entering the address associated with your account then you can reset your password.

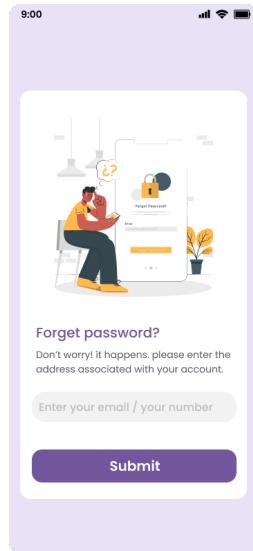


Figure 7.11: Forget password

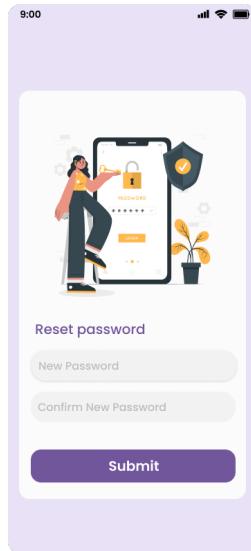


Figure 7.12: Reset password

Z CARE 2022/2023



- First interface as a Doctor: The doctor interface of our app is designed to provide healthcare professionals with the tools they need to manage Alzheimer's patients' health effectively.

1. Our app leverages a machine-learning model to predict Alzheimer's disease based on patient genes and images.
2. The interface is user-friendly and intuitive, providing easy access to the features doctors need to manage their patients' health. Doctors can use the app to search for patients' historical data by ID, enabling them to review critical information about their patient's health and daily activities.
3. Doctors can manage their profile information, including their profile image, name, username, email, and password. This feature enables doctors to keep their profile information up-to-date and accurate.

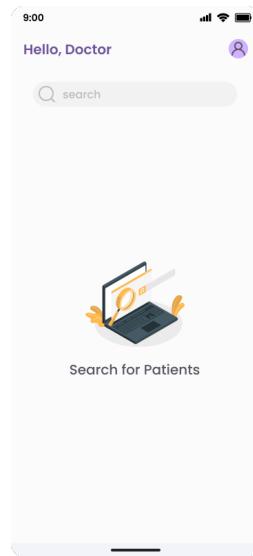


Figure 7.13: Doctor Home

Sample ID	Class	Date
1	2	00\00
2	2	00\00
3	2	00\00
4	2	00\00
5	2	00\00

Figure 7.14: Search for Patient

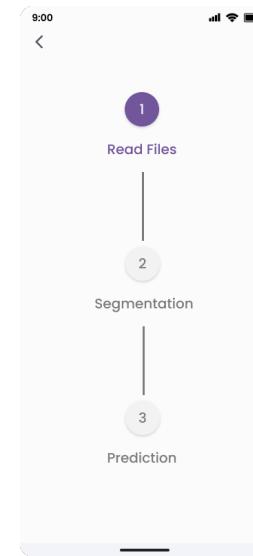


Figure 7.15: Upload Model

Our doctor interface is designed to empower healthcare professionals to provide the best possible care for Alzheimer's patients. By leveraging our machine-learning model and accessing patients' historical data, doctors can make informed decisions about their patients' health and well-being.

- Second interface as a Care Giver:

The caregiver interface of our app is designed to support Alzheimer's patients in managing their daily life. Caregivers play a crucial role in the lives of Alzheimer's patients(Hidden



Z CARE 2022/2023

Key), and our app is designed to provide them with the tools they need to provide the best possible care.

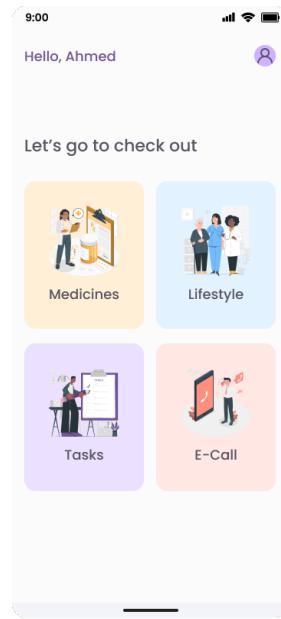


Figure 7.16: C.G-HomeScreen

1. The interface is user-friendly and intuitive, providing easy access to features such as managing the patient's Lifestyle as daily routine, setting plans, and creating task lists.

Z CARE 2022/2023

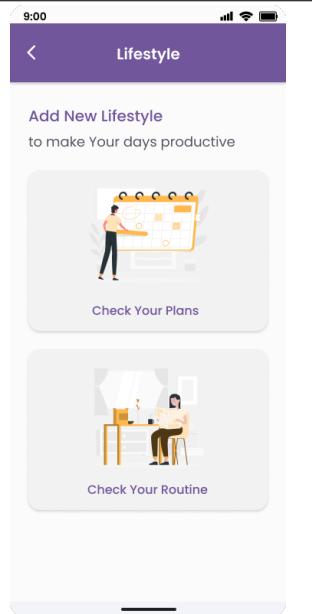


Figure 7.17: C.G-LifeStyle

- Caregivers can create new tasks and add them to the patient's existing schedules.
- Caregivers can set alarms for task due dates, specifying the day, month, year, and even hours, minutes, and seconds. They can also choose to enable or disable vibration alerts for their alarms.
- The caregiver interface allows tasks to be created with specific types, such as medication, exercise, or appointment. A pre-populated medication list is available for easy selection. Caregivers can also add a title and description to tasks for additional context.
- For routines, caregivers can create daily tasks that are repeated at the same time each day, ensuring that patients receive consistent care and support.

Z CARE 2022/2023



Figure 7.18: Plans

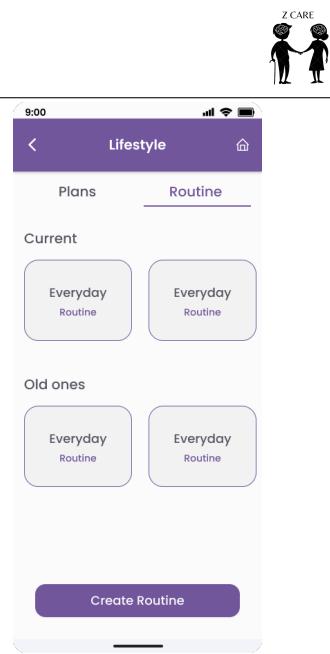


Figure 7.19: Routines

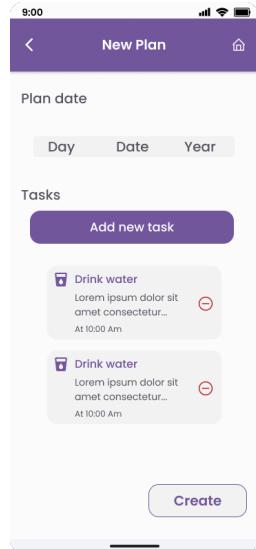


Figure 7.20: Plans Screen

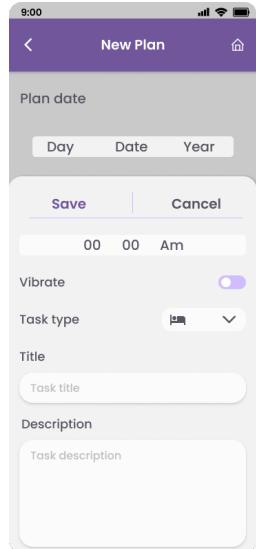


Figure 7.21: Add Task

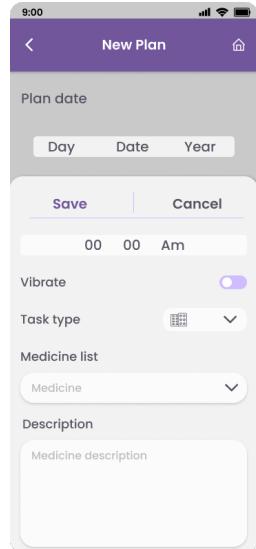


Figure 7.22: Medicine Type

2. The app includes tools to help caregivers manage the patient's health, such as managing emergencies,
The Emergency Call screens provide caregivers with an efficient and user-



Z CARE 2022/2023

friendly way to quickly contact emergency services on behalf of the patient. This feature is accessible from the main menu with just a few taps. Caregivers can also use the "find home location" option on the interface to locate the patient in case they are lost. This feature is particularly helpful for patients with mobility or cognitive impairments who may have difficulty navigating their surroundings.

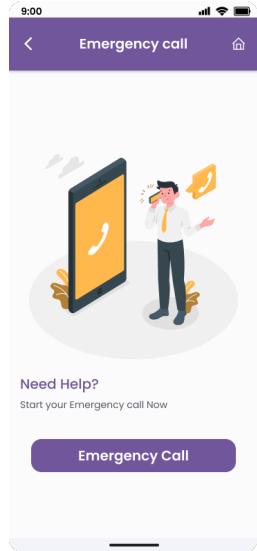


Figure 7.23: C.G Emergency Screen

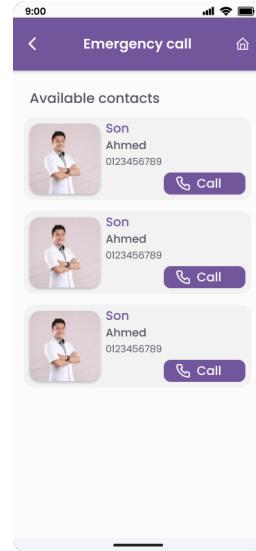


Figure 7.24: E-call Contacts

3. The caregiver interface's medicines screen is a comprehensive tool for remotely managing the patient's medication regimen. It allows caregivers to view, add, edit, or remove medications from the patient's list. This feature supports the patient interface and enables caregivers to remotely monitor and manage the patient's medication regimen, ensuring optimal healthcare management.

Z CARE 2022/2023

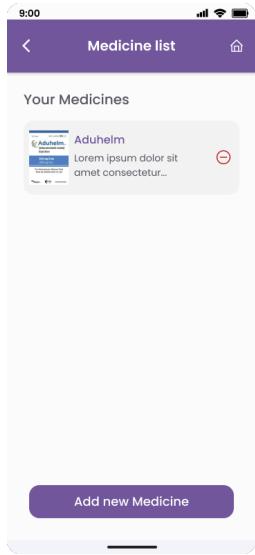


Figure 7.25: C.G
Medicine Screen

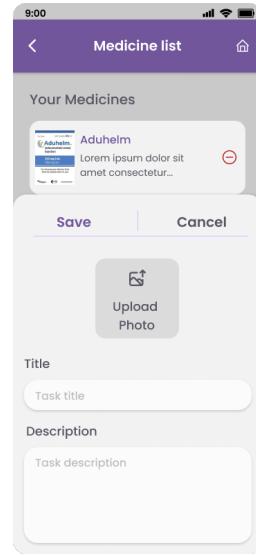


Figure 7.26: C.G
MedicineList

4. The caregiver interface's Tasks screen displays the patient's daily tasks and allows for editing if necessary. Caregivers can remotely manage the patient's task list and set reminders. This feature supports the patient interface by providing a clear list of daily tasks. Caregivers can also edit tasks if there are changes to the patient's schedule or care plan. The Tasks screen enables caregivers to remotely monitor and manage the patient's daily tasks, ensuring optimal healthcare management.

Z CARE 2022/2023

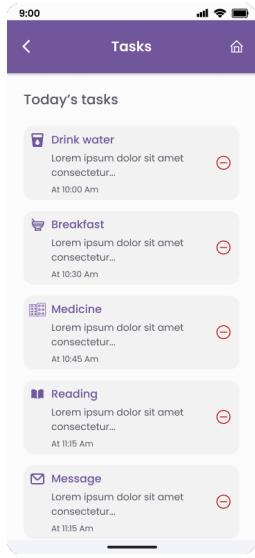


Figure 7.27: Tasks Screen

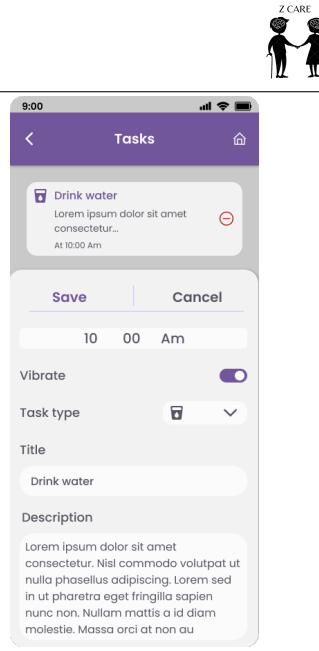


Figure 7.28: Tasks Edit

5. The Account screen is a comprehensive and customizable tool for managing personal information. Care Givers can edit their profiles, add emergency contacts, Add Patient History, Delete Accounts, and set a preferred language from the main menu.

Care Giver can update their personal information on the profile editing feature, including image, name, username, email, password, and phone number. This ensures the accuracy of personal information for effective healthcare management.

Care Giver can delete the Account if the patient doesn't need to have care giver anymore.

Z CARE 2022/2023



Figure 7.29: Account Screen

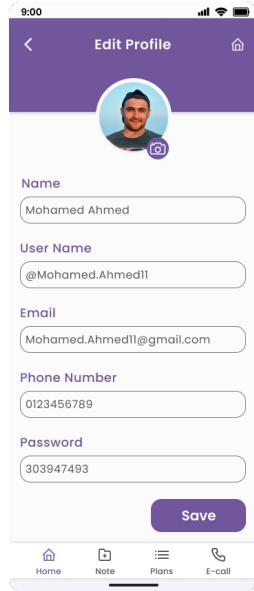


Figure 7.30: Edit Profile

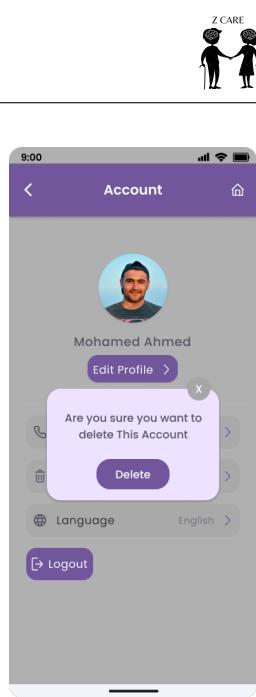


Figure 7.31: Delete Account

- The E-call contacts feature enables remote management of the patient's emergency contacts list. Caregivers can add or delete emergency contacts and input contact details such as name, phone number, and relationship. This feature ensures that the appropriate individuals are notified in case of an emergency, supporting the patient interface and providing a reliable and secure solution.

Z CARE 2022/2023

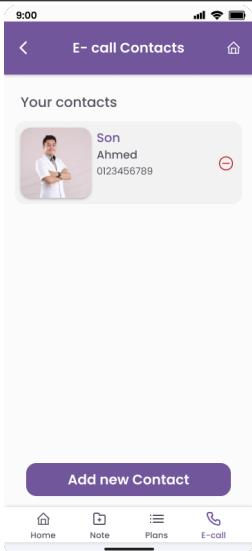


Figure 7.32: E-call contacts

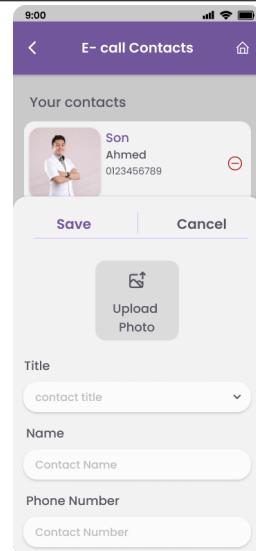


Figure 7.33: Contacts Edit

- Add Patient History screen is an essential tool for caregivers to manage and update the patient's medical history(Images & genes), ensuring the quality and continuity of healthcare services.

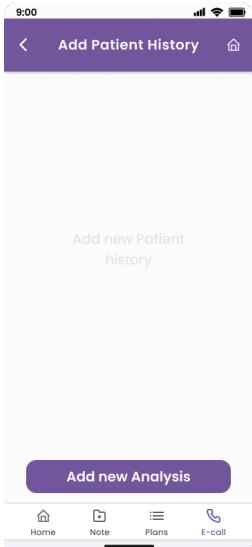


Figure 7.34: Patient History Screen

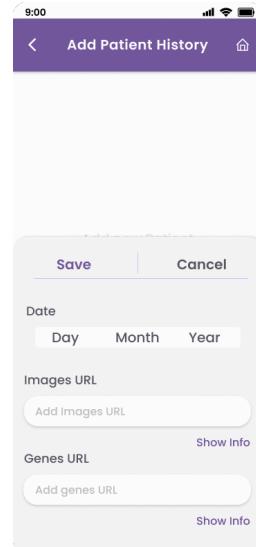


Figure 7.35: Add New Analysis



Z CARE 2022/2023

Our Care Giver interface is designed to empower caregivers to provide the best possible care for Alzheimer's patients. Caregivers are the hidden key to the patient's well-being, and our app is designed to support them in every aspect of their caregiving role. Whether managing the patient's daily routine, setting plans, or tracking medication, our app provides caregivers with the tools they need to ensure their patient's safety and well-being.

- Third interface as a Patient: The patient interface of our app is designed for Alzheimer's patients to manage their daily life.
Patient has two options:
 1. Patients can choose to have a caregiver who assists them with their daily lifestyle.
 2. They can manage their daily life on their own if they don't need a caregiver As a Normal User.
 1. The interface is user-friendly and intuitive, providing easy access to features such as medication reminders, appointment scheduling, task lists, etc.
 2. For patients who choose to have a caregiver, the app provides remote access to their caregiver and enables communication between patients and caregivers. Caregivers can access critical information about the patient's health and daily activities to provide the best possible care. However, patients with caregivers have limited access to certain features in the app. For example, patients cannot delete plans or routines by themselves, add medications or delete their accounts. These actions can only be performed by the caregiver to ensure the patient's safety and well-being.



Z CARE 2022/2023

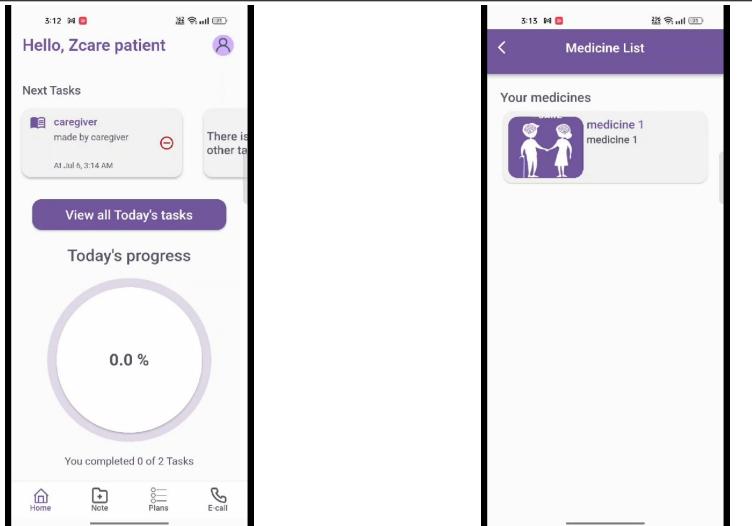


Figure 7.36:
HomeScreenC.GPatient

Figure 7.37:
C.GPatientMedicines

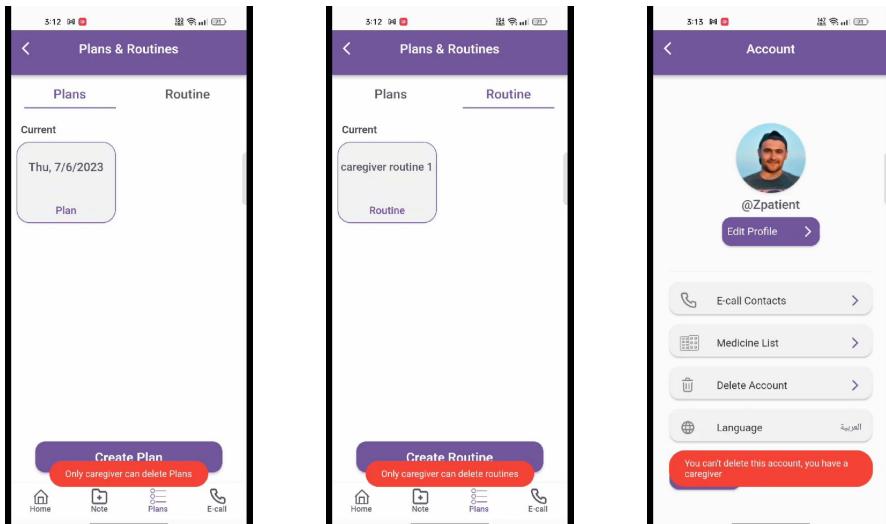


Figure 7.38:
C.GPatientPlans

Figure 7.39:
C.GPatientroutine

Figure 7.40:
C.GPatientAccount

Home Screen for a Patient(NormalUser) interface that has: today's progress, next recent tasks, and view all tasks.

Z CARE 2022/2023

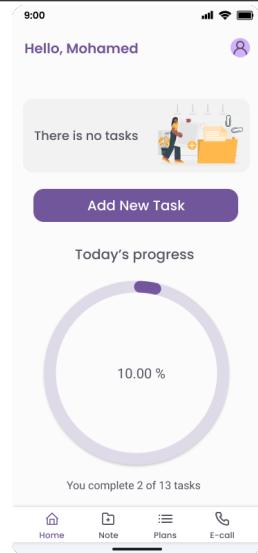


Figure 7.41: Home-Screen1

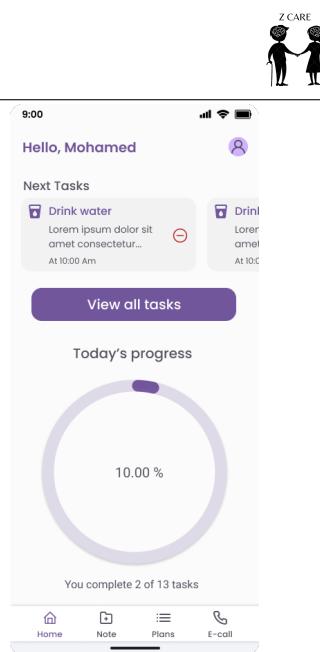


Figure 7.42: Home-Screen2

Notes Screen patient(With CareGiver or not) can Add his notes, Save, Edit, or Delete them.

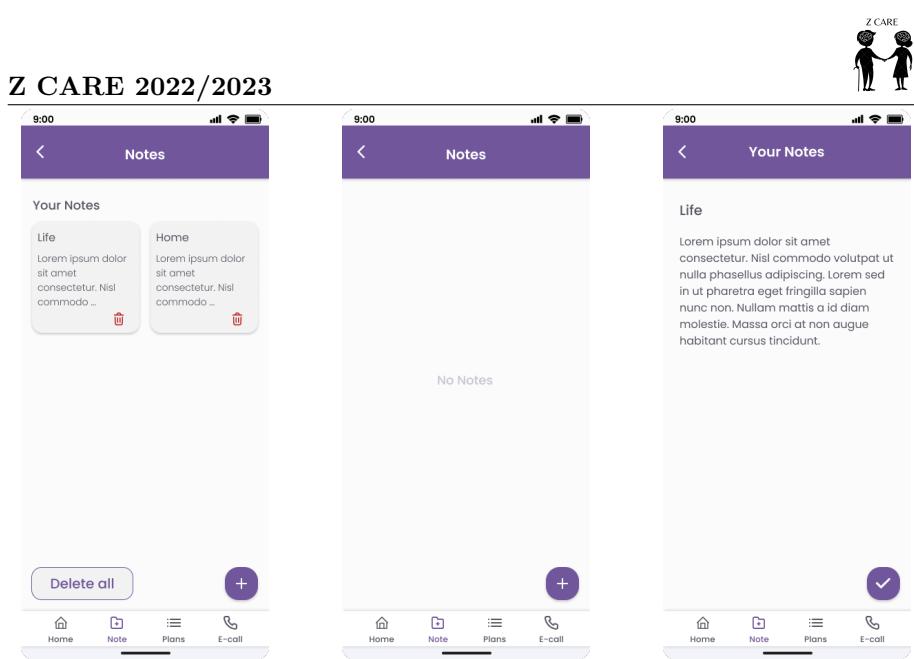


Figure 7.43: Notes

Figure 7.44: Notes Add

Figure 7.45: Notes Save

The patient(Normal User) interface provides users with a platform to manage their Plans and Routines.

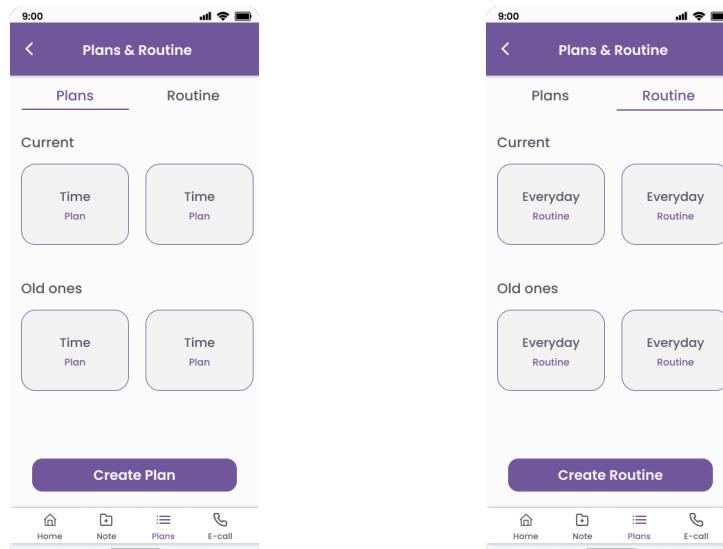


Figure 7.46: Plans

Figure 7.47: Routine

- Patients(Normal Users) can create new tasks and add them to their ex-



isting schedules.

- Patients(Normal Users) can set alarms for task due dates, specifying the day, month, year, and even hours, minutes, and seconds and can choose to enable or disable vibration alerts for their alarms.
- Patients can select the type of task they are creating, such as medication, exercise, appointment, etc...If patients choose the medication type, they can select from a pre-populated list of medications.
- Patients can add a title and description to their tasks to provide additional context and information.
- For Routines, patients can create daily tasks that are repeated at the same time each day.

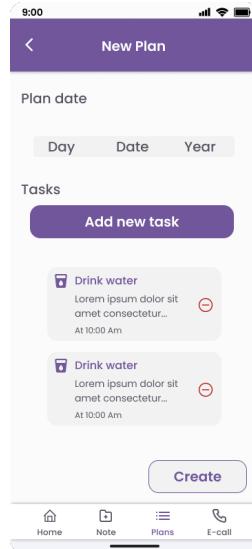


Figure 7.48: Plans Screen

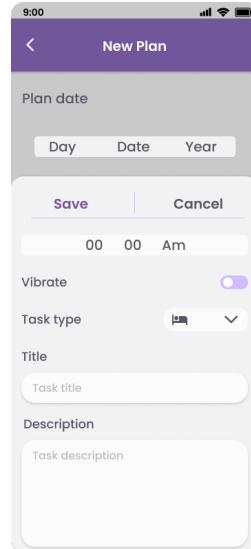


Figure 7.49: Add Task

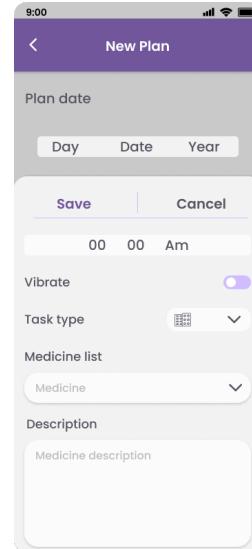


Figure 7.50: Medicine type

The Emergency Call screens offer patients an efficient and user-friendly way to quickly contact emergency services, accessible from the main menu with just a few taps.

The interface also offers a "find home location" option for patients who are lost, which is particularly helpful for those with mobility or cognitive impairments who may have difficulty navigating their surroundings.

Z CARE 2022/2023

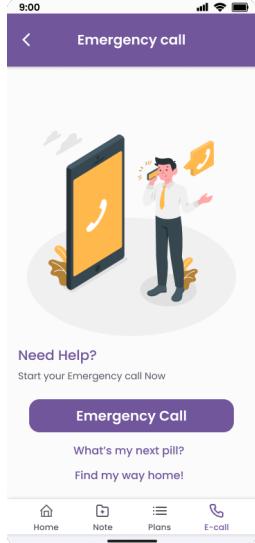


Figure 7.51: Emergency Screen

Figure 7.52: E-call Contacts

The Account screen is a comprehensive and customizable tool for managing personal information. Patients can edit their profiles, add emergency contacts, manage medicine lists, and set a preferred language from the main menu.

Patients can update their personal information on the profile editing feature, including image, name, username, email, password, and phone number. This ensures the accuracy of personal information for effective health-care management.

Z CARE 2022/2023



Figure 7.53: Account Screen

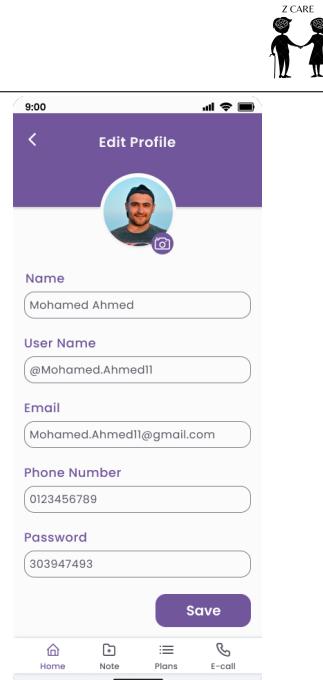


Figure 7.54: Edit Profile

- Patients can add or delete emergency contacts from the E-call contacts feature. This feature enables patients to add trusted contacts to be reached in an emergency. Patients can easily input contact details such as name, phone number, and relationship to the patient.

Z CARE 2022/2023

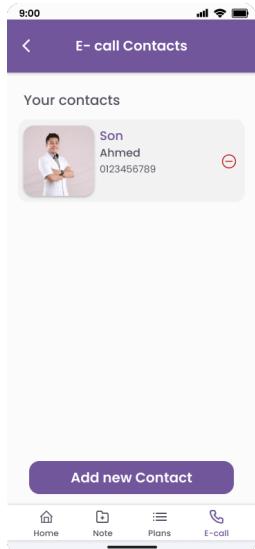


Figure 7.55: E-call contacts

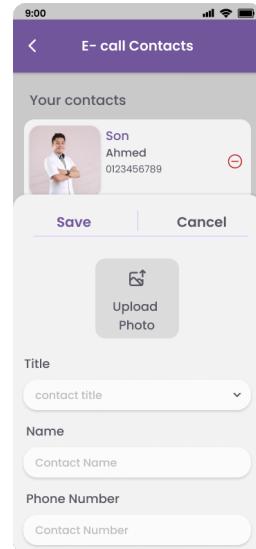


Figure 7.56: Contacts Edit

- Patients(With CareGiver only) have medicine lists on the account screen. This feature allows patients to add medication names, dosages, and frequency of use. Managing medicine lists ensures healthcare providers have accurate and up-to-date information. Patients can easily input medication details.

Z CARE 2022/2023

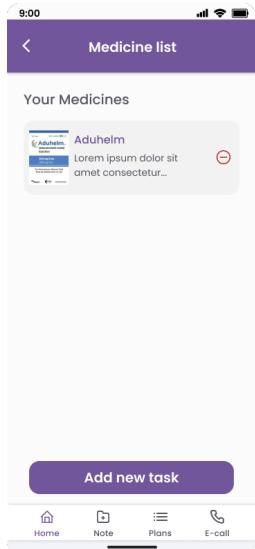


Figure 7.57: Medicine List

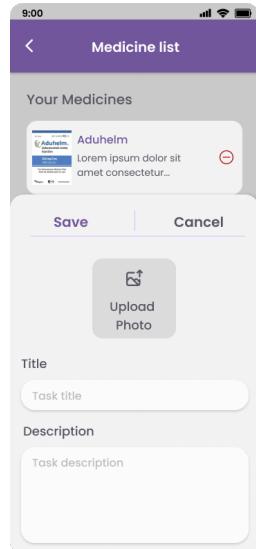


Figure 7.58: Add Medicine

Our patient interface is designed to empower Alzheimer's patients to take control of their daily life and enhance their quality of life, whether they choose to have a caregiver or manage their daily life on their own. 1

Chapter 8

Conclusions & Future Work

8.1 Conclusions

In this project, We have introduced the structure and assessment of a mobile application that uses a multimodal data (DNA, MRI) sample from the patient in order to be able to correctly diagnose the patient with AD, MCI, OR CN. And also to be able to associate the patient with one of three groups either being healthy (CN), potential (MCI), or diseased(AD) with AD. Our process starts with the (DNA, MRI) sample being uploaded to the mobile app, afterwards the application preprocesses it to ensure that it is in the same format and size that is needed to amply diagnose the patient. Subsequently, the data along with the patient's name and his DNA and MRI are loaded into our database and the physician can classify the sample using a model made with Deep Learning. Our models achieved(accuracy) respectively. Therefore, the choice of which data modal or both is left to the physician or the lab technician conducting the test.

Moreover, ZCARE allows the CAREGIVER to monitor patients' daily routine and know generally how it is doing about it by entering the id of the patient in the field search bar and the data for this patient will be displayed if this caregiver has access to this patient.

Finally, ZCARE can classify the Alzheimer's stages. The proposed system has three main stages; data acquisition and pre-processing, feature engineering, and AD diagnosis, The proposed classification approach was implemented. Then, feature extraction was applied to each pre-processed image and gene, this dataset consists of 3 classes of different stages of Alzheimer's (CN, MCI, AD) DL model is implemented for AD stage classification. Assessment, based on the obtained experimental results, demonstrate that the proposed method can yield better performance in both binary classification and multiclass classification tasks. Specifically, our proposed method achieves the accuracy of 95.61% and 92.98% for NC vs. AD vs. MCI using CNN with Attention and Reduced CNN, respectively. While for binary classification CNN achieved an accuracy



Z CARE 2022/2023

of 89.47% and 91.55% for NC vs. AD and MCI vs. AD, respectively. Finally, for multimodality, ZCARE achieved an accuracy of 79.17 %.

8.2 Future work

For Future work We aim to:

1. Increase SNPs samples
2. Insert personalized medicine with our study.
3. In addition to MRIs and SNPs we intend to use clinical data to improve accuracy
4. Suggesting suitable medicine for each person depending on personalized medicine.
5. Follow the stages of disease development.
6. Add an expert user to manage data and model.
7. Apply Time Series Analysis to understanding the progression of AD for the Patient

Bibliography

- [1] A Alatrany, Abir Hussain, Jamila Mustafina, and Dhiya Al-Jumeily. A novel hybrid machine learning approach using deep learning for the prediction of alzheimer disease using genome data. In *International Conference on Intelligent Computing*, pages 253–266. Springer, 2021.
- [2] Somaye Hashemifar, Claudia Iriondo, Evan Casey, and Mohsen Hejrat. Deepad: A robust deep learning model of alzheimer’s disease progression for real-world clinical applications. *arXiv preprint arXiv:2203.09096*, 2022.
- [3] Taeho Jo, Kwangsik Nho, and Andrew J Saykin. Deep learning in alzheimer’s disease: diagnostic classification and prognostic prediction using neuroimaging data. *Frontiers in aging neuroscience*, 11:220, 2019.
- [4] Eugene Lin, Chieh-Hsin Lin, and Hsien-Yuan Lane. Deep learning with neuroimaging and genomics in alzheimer’s disease. *International journal of molecular sciences*, 22(15):7911, 2021.
- [5] Weiming Lin, Qinquan Gao, Min Du, Weisheng Chen, and Tong Tong. Multiclass diagnosis of stages of alzheimer’s disease using linear discriminant analysis scoring for multimodal data. *Computers in Biology and Medicine*, 134:104478, 2021.
- [6] Shangran Qiu, Matthew I Miller, Prajakta S Joshi, Joyce C Lee, Chonghua Xue, Yunruo Ni, Yuwei Wang, Ileana De Anda-Duran, Phillip H Hwang, Justin A Cramer, et al. Multimodal deep learning for alzheimer’s disease dementia assessment. *Nature communications*, 13(1):3404, 2022.
- [7] M. Satya Sai Ramb Shaik Basheeraa. A novel cnn-based alzheimer’s disease classification using hybrid enhanced ica segmented gray matter of mr. <https://www.sciencedirect.com/journal/computerized-medical-imaging-and-graphics>.
- [8] Arifa Shikalgar and Shefali Sonavane. Hybrid deep learning approach for classifying alzheimer disease based on multimodal data. In *Computing in Engineering and Technology*, pages 511–520. Springer, 2020.



Z CARE 2022/2023

- [9] Janani Venugopalan, Li Tong, Hamid Reza Hassanzadeh, and May D Wang. Multimodal deep learning models for early detection of alzheimer's disease stage. *Scientific reports*, 11(1):1–13, 2021.
- [10] Yu Wang, Xi Liu, and Chongchong Yu. Assisted diagnosis of alzheimer's disease based on deep learning and multimodal feature fusion. *Complexity*, 2021, 2021.
- [11] Liuqing Yang, Xifeng Wang, Qi Guo, Scott Gladstein, Dustin Wooten, Tengfei Li, Weining Z Robieson, Yan Sun, Xin Huang, and Alzheimer's Disease Neuroimaging Initiative. Deep learning based multimodal progression modeling for alzheimer's disease. *Statistics in Biopharmaceutical Research*, 13(3):337–343, 2021.