Understanding The codebase

Back_shap - A series of image transformations are defined using MONAI, including loading, preprocessing, and augmentation steps for MRI images. - Minmax normalisation function to normalise image data - The code sets up an `MCExplainer` that is monte carlo based shapley analysis to compute shap values for the model prediction - In the `if __name__ == '__main__':` block: - The test dataset is loaded and transformed. - Label distributions are calculated and printed. - The model is initialized and loaded from a checkpoint. - A DataLoader for the test set is created. - The SHAP explainer is initialized and used to compute SHAP values for the test set.

Imaging_shap - An IMaging model is loaded from a checkpoint using densenet as the backend - The code loads MRI Information from json files for both NACC and other cohorts - A custom `FilterImages` class is defined to apply MONAI transformations to the MRI images, including resizing, normalization, and filtering out problematic images. - The code selects a sample MRI (index `smp_idx`) and runs it through the model to get predictions. - The samples are randomly selected - Shapley analysis is done using shap.DeepExplainer to generate saliency maps(area of focus maps) for selected values -

Imaging_train.py

- A dictionary `mri_emb_dict` is created to map patient IDs to their MRI file paths and connect them to the file location in the directory
- Labels distributions and fractions are calculated for the classification task
- An `ImagingModel` is initialized with various parameters, including model architecture details, training settings, and paths to checkpoints.This is a transformers based model with various parameters initialised
- `self.vld_transforms` = Compose performs image segmentation cropping and other augmentation techniques
- `mdl.fit(trn_list, vld_list, img_train_trans=trn_filter_transform, img_vld_trans=vld_filter_transform)` is used for fitting the model and starting training steps

img_embeddings.py

- A dictionary `mri_emb_dict` is created to map patient IDs to their MRI file paths. again connecting the csv paths to the files (3D data)

- `tst_filter_transform = FilterImages(dat_type='tst')` is defined to apply MONAI transformations to the MRI images, including resizing, normalization, and filtering out problematic images.
- An `ImagingModel` is loaded from a checkpoint file.
- For each MRI in the datasets:
    - It checks if the embedding already exists to avoid redundant computation.
    - If not, it loads the MRI, applies transformations, passes it through the DenseNet model, and extracts the features (embeddings)
    - The embeddings are then saved as numpy files in the form of matrices
    - A for loop ios initialised to keeps track of the number of MRIs processed for each cohort (NACC, ADNI, etc.).

skullstrip.py

- Minmax normalisation is used to normalise the image in the minmax range (0,1)
- A composition of MONAI transformations is defined in `tst_transforms`, including loading, resizing, and normalization operations.
- A `CSVDataset` is initialized with the test data file and the defined transformations.
- The script extracts file paths of MRI images from the dataset, filtering out certain types of images
- It checks that if there is a `_stripped.nii` prefix at the end of the file to check if threr is already stripped files to avoid redundant processcing
- SysnthStrip is used to perform skull stripping if already not performed
- Skull Stripping is a process that removes non-brain tissue from brain scans, such as those acquired using magnetic resonance imaging (MRI)

train.py

- Script for final training of ADRD classification such as MCI NC and Dementia
- A `minmax_normalized` function is defined for image normalization
- Multiple transformation functions and libraries imported from monai for image augmentation
- FilerImage class for cretaring and applying these transformations one function to apply transformation with the images and validate the same images with the self.val_trasnforms
- `mdl = ADRDModel(` starts and initialises the multimodal transformer with all the parameters

- The `fit` method of the `ADRDModel` is called to train the model on the prepared data.
- Multiple checkpoint and parallelism methods are used here
- CSV fgiles are loaded with model definition and other parametrs
- The loop iterates over a list of labels: `['NC', 'MCI', 'DE', 'AD', 'LBD', 'VD', 'PRD', 'FTD', 'NPH', 'SEF', 'PSY', 'TBI', 'ODE']`
- This loop counts how many time each of these occue and then the result is converted to a dictionary

tsne_visualisation.py

- The embeddings are standardized using StandardScaler to ensure all features are on the same scale.
- t-SNE stochastic neighber embeddings are applied to reduce the high dimensional embeddings to a 2D vis
- A scatter plot is created using the 2D t-SNE embeddings.
- Each point represents an MRI scan.
- Points are colored based on their class:
  - Red: NC (Normal Cognition)
  - Green: MCI (Mild Cognitive Impairment)
  - Blue: DE (Dementia)

1. Understand the different MRI sequences and what they tell about each other

Swin Transformer - Architecture

1. Like a vision transformer but with a heirachical way of dealing with things
2. Transformers with linearly scaled content can learn whole bunch of novels and text
3. VIT works with patches of 16X16 but that is not great if we want to go a bit more molecular and want semantic segmentation where algo needs to recognise objects of importance
4. SWIN transformer
5. Breaks the transformer into 4x4x3 features which is then translating to 48 entries
6. C is the capacity of the model or more like the dimension of the vector

7. C defines the parrameter size or the amount of hidden layers
8. Transformer block processes the patch vectors but not with the usual quadratically scaling but with the shifted window attention mechanism
9. This means that the attention span is limited over a limit of 2 patches
10. One patch does not communicate with other patches but only M neighbours
11. output - N
12. output is then merged by a merging layers that concatenates the vector of grp of 2x2 neighbouring patches
13. So from 4 of C dimensional vectors we have now one 4xC vector
14. From 4 patches to 1 patch
15. But the hidden represntation is been doubled in order to capture the information from a a larger region
16. Attention is shifted from one region to another
17. Different patches from layer one that could not communicate can now communicate in layer 2
18. Swin UTER is used for medical image segmentation
19. ◦ The primary use of CNNs in Swin UNETR is in the decoder part of the architecture. While the encoder is based on the Swin Transformer, the decoder uses convolutional neural networks.
20. Feature Reconstruction: CNNs in the decoder are responsible for reconstructing spatial features from the transformer embeddings. They help in upsampling and refining the features extracted by the Swin Transformer encoder.
21. The CNN decoder integrates features from different scales of the Swin Transformer encoder through skip connections. This allows the model to combine low-level and high-level features effectively.
22. CNNs are particularly good at preserving spatial relationships in the data, which is crucial for tasks like segmentation where precise spatial information is needed.

How we recognise impairement

- **Degree of Atrophy**: Progression from mild to severe atrophy correlates with cognitive decline.
- **Pattern of Atrophy**: Specific brain regions affected can suggest the type of dementia.
- **White Matter Integrity**: The extent and location of WMHs can differentiate vascular contributions from neurodegenerative processes.

- **Cortical Thickness Measurements**: Quantitative analysis provides precise assessment of cortical thinning.
- **Structural Connectivity**: Changes in the integrity of neural pathways assessed via diffusion tensor imaging (DTI).

Cortical thinning is ==a natural part of aging that occurs in the frontal and temporal regions of the brain==. It can also be accelerated in certain regions, which may be an early sign of neuropathologies like Alzheimer's disease.

MRI Data

2.2 Data Dimensions

- MRI data consists of **voxels** (3D pixels).
- Typical dimensions vary depending on the scan, e.g., 256×256×150 voxels.
- **Resolution**: The size of each voxel, e.g., 1×1×1 mm^3.

What each sequence tells you

MRI datasets are acquired using different MRI sequences, each highlighting different tissue properties:

- **T1-Weighted Imaging (T1w):** Good for anatomical detail and gray matter visualization.
- **T2-Weighted Imaging (T2w):** Highlights fluid-filled spaces; useful for detecting edema and lesions.
- **Fluid-Attenuated Inversion Recovery (FLAIR):** Suppresses cerebrospinal fluid (CSF) signals to detect white matter lesions.
- **Diffusion Tensor Imaging (DTI):** Assesses white matter integrity by measuring water diffusion.
- **Susceptibility-Weighted Imaging (SWI):** Sensitive to blood products, useful for detecting microbleeds.

4. MRI Modalities and Their Uses

4.1 T1-Weighted Imaging

- **Purpose:** Provides high-resolution images of brain anatomy.

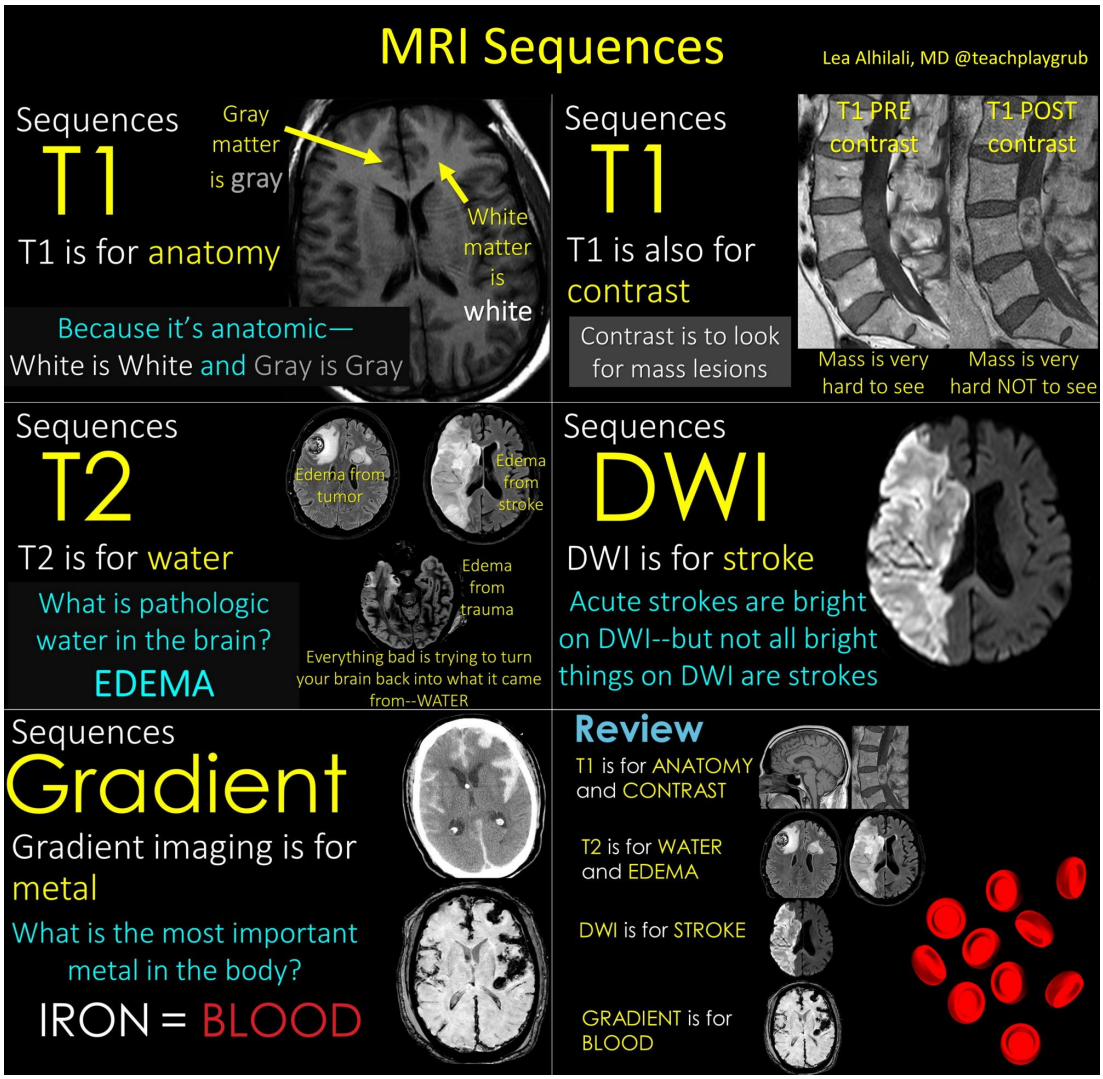
- **Use in Dementia:**
  - Measuring cortical thickness and volume.
  - Assessing hippocampal atrophy.

4.2 T2-Weighted Imaging and FLAIR

- **Purpose:** Highlights differences in water content.
- **Use in Dementia:**
  - Detecting white matter hyperintensities (WMHs).
  - Identifying lesions associated with vascular dementia.

4.3 Diffusion Tensor Imaging (DTI)

- **Purpose:** Maps the diffusion of water molecules.
- **Use in Dementia:**
  - Evaluating white matter tract integrity.
  - Detecting microstructural changes.



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5. Preprocessing Steps

Preprocessing is essential to prepare MRI data for analysis:

5.1 Reorientation and Alignment

- **Purpose:** Ensure all images are in a standard orientation (e.g., MNI space).
- **Tools:** FSL's `FLIRT`, SPM's `Coregister`.

5.2 Skull-Stripping (Brain Extraction)

- **Purpose:** Remove non-brain tissues (e.g., skull, scalp) to focus on brain structures.
- **Tools:** FSL's `BET`, FreeSurfer's `mri_watershed`.

5.3 Intensity Normalization

- **Purpose:** Adjust intensity values to account for variability across scans.
- **Methods:** Histogram matching, z-score normalization.

5.4 Segmentation

- **Purpose:** Classify voxels into tissue types:
  - **Gray Matter (GM)**
  - **White Matter (WM)**
  - **Cerebrospinal Fluid (CSF)**
- **Tools:** SPM's `Segment`, FSL's `FAST`, FreeSurfer.

5.5 Registration to Standard Space

- **Purpose:** Align individual brains to a common template for group analysis.
- **Templates:** Montreal Neurological Institute (MNI) template.

5.6 Smoothing

- **Purpose:** Apply a Gaussian filter to reduce noise and enhance signal-to-noise ratio.
- **Considerations:** Balance between smoothing extent and spatial resolution.

7. Usage in Classification Tasks

MRI features are used as inputs to machine learning models for classification:

7.1 Feature Selection

- **Purpose:** Reduce dimensionality and focus on the most informative features.
- **Methods:** Statistical tests, recursive feature elimination, principal component analysis (PCA).

7.2 Model Input

- **Input Data:** Structured as feature vectors per subject.
- **Labels:** NC, MCI, Dementia (and subtypes if available).

7.3 Machine Learning Models

- **Traditional Models:**
  - Support Vector Machines (SVM)
  - Random Forests
  - Logistic Regression
- **Deep Learning Models:**
  - Convolutional Neural Networks (CNNs): Directly process MRI volumes.
  - Transformers (e.g., Swin UNETR): Capture spatial relationships in 3D data.

7.4 Multimodal Integration

- **Combining MRI features with other data:**
  - Clinical assessments
  - Genetic data
  - Neuropsychological test scores

Libraries for MRI 1. Nibabel for MRI data in python 2. Pytorch for deep learning 3. For Neuroimaging -**SPM (Statistical Parametric Mapping):** MATLAB-based analysis.

Challenges in MRI - 1. Dataset is large and complex along with high dimention - can be solved by dimentianality reduction using PCA or maybe find the latent variables with VAEs 2. Differences in MRI scanners and protocols can introduce variability. - solved by Harmonization techniques, scanner-specific **preprocessing** 3. Datasets may have unequal numbers of NC, MCI, and Dementia subjects. **Solution:** Oversampling minority classes, using weighted loss functions. 4. Risk of models capturing noise instead of meaningful patterns. - cross validation and regularisation techniques

```
graph TD
   A[Obtain MRI Data] --> B[Preprocess MRI Scans]
   B --> C[Data Augmentation]
```

```
    C --> D[Split Dataset]
    D --> E[Train SWIN UNETR Model]
    E --> F[Validate Model]
    F --> G{Performance Satisfactory?}
    G -->|No| H[Tune Hyperparameters]
    H --> E
    G -->|Yes| I[Test Model]
    I --> J[Deploy Model]

    subgraph Preprocessing
    B1[Skull Stripping]
    B2[Intensity Normalization]
    B3[Spatial Normalization]
    B4[Noise Reduction]
    end

    B --> B1
    B1 --> B2
    B2 --> B3
    B3 --> B4

    subgraph Data Augmentation
    C1[Rotation]
    C2[Flipping]
    C3[Scaling]
    C4[Elastic Deformation]
    end

    C --> C1
    C --> C2
    C --> C3
    C --> C4

    subgraph Model Training
    E1[Initialize SWIN UNETR]
    E2[Forward Pass]
    E3[Calculate Loss]
    E4[Backpropagation]
    E5[Update Weights]
    end

    E --> E1
    E1 --> E2
    E2 --> E3
    E3 --> E4
    E4 --> E5
    E5 --> E2

    subgraph Validation
    F1[Evaluate on Validation Set]
    F2[Calculate Metrics]
    end

    F --> F1
    F1 --> F2

    subgraph Testing
    I1[Evaluate on Test Set]
    I2[Generate Final Metrics]
    I3[Analyze Results]
```

```
    end

    I --> I1
    I1 --> I2
    I2 --> I3
```

Some Info

1. Normal Cognition (NC)

In individuals with normal cognition, MRI scans typically show:

- **Intact Brain Structure**: No significant atrophy (shrinkage) in brain regions.
- **Normal Hippocampal Volume**: The hippocampus, crucial for memory formation, maintains its typical size.
- **Minimal White Matter Changes**: Little to no white matter hyperintensities (WMHs), which are lesions appearing as bright spots on T2-weighted images.
- **Symmetric Brain Structures**: No asymmetry or focal lesions.

2. Mild Cognitive Impairment (MCI)

MCI represents a transitional stage between normal aging and dementia. MRI features that may indicate MCI include:

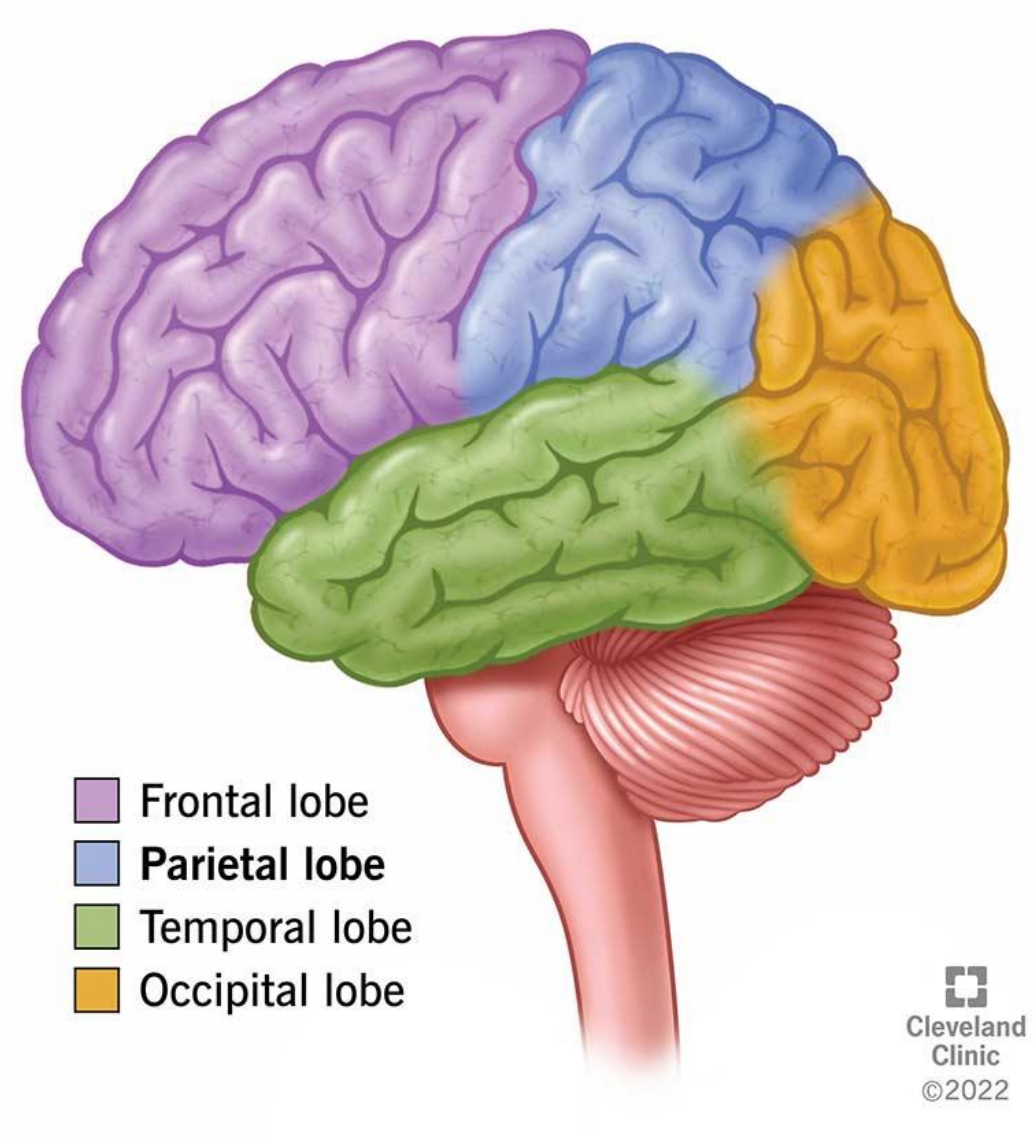
- **Mild Hippocampal Atrophy**: Early shrinkage of the hippocampus detectable through volumetric analysis.
- **Cortical Thinning**: Slight thinning in the cerebral cortex, especially in areas associated with memory and executive functions.
- **Increased White Matter Hyperintensities**: WMHs become more apparent, indicating small vessel disease or demyelination.
- **Changes in Brain Connectivity**: Subtle alterations in the structural connectivity between brain regions.
- **Enlarged Ventricles**: Slight increase in ventricular size due to surrounding brain tissue loss.

3. Dementia

In dementia, especially Alzheimer’s disease (AD) and other types, MRI scans reveal more pronounced changes:

- **Significant Hippocampal Atrophy**: Marked shrinkage of the hippocampus and medial temporal lobes.
- **Global Cortical Atrophy**: Widespread thinning of the cerebral cortex, particularly in the temporal and parietal lobes.
- **Enlarged Ventricles**: More pronounced ventricular enlargement due to extensive brain tissue loss.
- **Extensive White Matter Hyperintensities**: Increased presence and severity of WMHs, which may contribute to cognitive deficits.
- **Regional Specific Atrophy**:
  - **Alzheimer’s Disease**: Atrophy in the temporal and parietal lobes.
  - **Frontotemporal Dementia**: Atrophy in frontal and temporal lobes.
  - **Vascular Dementia**: Multiple infarcts or extensive WMHs in subcortical regions.
- **Posterior Cortical Atrophy**: In some dementias, the occipital lobe is affected, leading to visual disturbances.

Atrophy is the decrease in size of tissue or body part


Parietal Lobe
Frontal lobe
Parietal lobe
Temporal lobe
Occipital lobe
Cleveland Clinic
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hello