Modeling Disability Progression in Multiple Sclerosis using Fully Convolutional Siamese Networks for Biomedical A.I Alignment

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Abstract— **Multiple Sclerosis (MS) is a potentially disabling condition and is a disorder of the central nervous system. Diagnosing MS is a difficult task if the patient has unusual and progressive symptoms. Another aspect of why this disease is difficult to diagnose is due to its variable symptom nature. A patient might have symptoms or no symptoms at all with some patients experiencing difficulty in walking and having no remissions. While there is no definite method for the diagnosis of the disease, healthcare professionals utilize MRIs (Magnetic resonance imaging) and blood tests to rule out and discover potential repercussions of the disease. Advances in Biomedical Artificial Intelligence, Data Science, and Computer Vision have led to remarkable performance in diagnosing and identifying computational biomarkers.**

In this study, (1) we propose to extend Siamese Neural Networks (Fully Convolutional Neural Networks and their variants) to model the disability progression in patients with MS utilizing neurological image modalities such as 3D Brain MRI scans. (2) The field of Computational Biomedicine suffers from medical data scarcity, both synthetic and medical annotated data, to rectify this, we propose the integration of an LLM (Large Language Model) to aid in generating synthetic medical descriptions that can be used as data modalities for representation learning to accelerate the biomedical annotation process.

Index Terms— **Biomedical AI, Siamese Networks, Large Language Models, Synthetic Data Generation**

I. INTRODUCTION

Multiple Sclerosis (MS) is a complex neurological disorder affecting the brain and the spinal cord. According to [1], early referral, diagnosis, and treatment are some of the key aspects to recover and control this disease effectively. To maximize recovery, neurologists often rely on comprehensive Brain MRI scans and this serves as the primary diagnostic method for a patient with MS. The annual or periodic review of these Brain MRI scans serves as the major diagnostic and consultation method as set forth by the healthcare provider for patients with MS and this plays a key role in identifying demyelination and predicting disability progression.

Advances in representation learning have allowed A.I researchers and engineers to build world-class and state-of-the-art computer vision systems that can effectively and accurately perform object detection/tracking and segmentation. According to a study [4], Deep Convolutional Neural Networks were applied to diagnose the Plus Disease in Retinopathy of Prematurity, ROP is one of the leading causes of blindness in infants. Current advances in representation learning and an influx of high-grade, easy-to-use, and customizable Deep Learning tools have advanced the field of Biomedical A.I exponentially give rise to new ideas and frameworks every year.

In this study, we propose to extend Siamese Neural Networks to model the disability progression in patients with MS (Multiple Sclerosis) utilizing neurological image modalities such as Brain MRI scans [5]. We aim to model disability progression via the Expanded Disability Status Scale (EDSS) score [6], a popular metric for quantifying disability. Additionally, we propose extending Siamese Neural Networks as an intermediary tool to generate comprehensive medical image descriptions through integration with a Large Language Model specialized in Biomedicine.

II. PREVIOUS WORKS

Siamese Networks are a class of neural networks that have shown good performance within areas where there is a data scarcity issue. One such example from the manufacturing industry is fault diagnosis [2]. This makes Siamese Networks a perfect candidate for medical applications. Computational Biomedicine encompasses the development of algorithms ranging from patient care to disease diagnosis. One such crucial area is disease severity/progression detection. ROP (Retinopathy of prematurity) is one of the leading causes of blindness in infants. A class of Siamese Networks was utilized to detect disease severity prediction. Retinal images contain blood vessels that are vital for predicting change and act as a feature for the Siamese Networks [12] were used to detect a great deal of medical applications. Due to the versatile nature of these networks and the ability to attach custom modalities, these networks have also been utilized in medical question matching [2].

III. A.I ALIGNMENT PROBLEM IN BIOMEDICINE

A.I alignment is defined as specifying the purpose of the A.I system and ensure that it achieves all the prescribed specifications accurately [7]. In current foundation models, alignment is often accompanied by pretraining on a large corpus of text and followed by Reinforcement Learning from Human feedback (RLHF). Current systems like ChatGPT undergo fine-tuning using RL (Reinforcement Learning) where the reward function is learned via human feedback. In the case of ChatGPT, the reward function was modeled after ranking by human labelers and then optimizing the model via PPO (Proximal Policy Optimization).

Current base foundational models can also be modeled

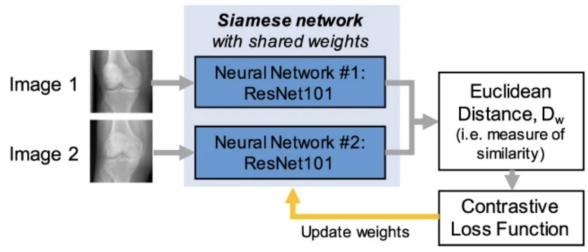

Fig. 1. Siamese Network Architecture[11]

using supervised fine-tuning, where the base model can use the supervised dataset to alter the model's distribution. This approach is effective when the specified or prescribed task is not that complex. An example would be aligning a model to chat in the style of a movie character.

In the field of computational biomedicine and medicine in general there exists a notable limitation— the availability of such medical datasets. For text-based systems, this might mean having to deal with a lot of regulations, and for multi-modal models, this means having to deal with a complex and expensive annotation process. To improve performance in computer vision systems, techniques such as transfer learning [8] have been effective but there is still a significant lack of accurate textual medical data

IV. Modeling Disability Progression using Siamese Networks

Siamese networks are a class of neural networks representing twin networks capable of learning the similarity between pairs of modalities. These networks have shown successful results in object tracking [9] change detection [10] disease severity [11] and skin medical captioning [12]. Siamese networks are extremely effective in learning similarity between two classes as its loss is modeled using a contrastive loss where similar inputs are optimized to have similar embeddings and dissimilar inputs are optimized to have different embeddings.

Siamese networks, due to their one-shot classification behavior, are robust to class imbalance and perform effectively if there are minimal samples for each class. For modeling disability progression, this serves as the perfect candidate due to the lack of a large-scale MS (Multiple Sclerosis) Dataset. Siamese networks allow us to compare two medical images or MRIs for MS by learning the similarity instead of just classifying the disability score. For predicting severity or disability, an A.I automated diagnosis system can potentially save both money and time for a clinical expert while accelerating the diagnosis process[11].

A. Loss function and Measure of Similarity (EDSS)

EDSS (Expanded Disability Status Scale) scores are used for evaluating and quantifying disability over time for MS patients [6]. Each MRI scan of a patient is processed with an EDSS score that signifies the disability level. An EDSS score of 10.0 refers to death. For modeling disability progression, we select two patient MRIs with a score difference of 0.0 such that for similar EDSS scores, we model Brain MRI scan similarity and vice versa.

TABLE I
EDSS Score and their interpretation

EDSS Score	Interpretation
1.0 to 4.5	Refers to people with MS who are able to walk
5.0 to 9.5	Refers to people with the impairment to walking

$$L(y,d) = \frac{1}{2N}\sum_{i=1}^{N} y \cdot (d)^2 + (1-y)\cdot(\max(\text{margin} - d, 0))^2 \tag{1}$$

Fig. 2. Constrastive Loss Function for Siamese Network

When patient MRI scans are dissimilar but EDSS scores are similar then the loss will increase. Patients with similar image features will have similar EDSS scores and vice versa.

B. Dataset Description

We leverage 3D Brain MRI data from the cross-sectional study done on patients with white matter lesion segmentations [5]. MRI scans were collected from 30 MS patients rated by 3 expert raters. All samples have three views:

- Coronal: Shows the left and right hemisphere
- Sagittal: Shows the cerebellum
- Axial: Top View, shows cerebral hemisphere (We use this)

According to the National Institutes of Health, MS affects the cerebral cortex and this is the reason why we use the Axial View paired with FLAIR imaging. For each patient, a total of six columns are presented with the most notable one being the EDSS score.

TABLE II
Dataset Description

Number of Patients	EDSS score range
30	0.0 - 6.5

C. Dataset Development for Prediction

We leverage 3D Brain MRI data from the cross-sectional study done on patients with white matter lesion segmentations [5]. For each patient, we model the difference or similarity between their EDSS scores. Given two patients with the same or different EDSS score, we aim to learn a similarity function capable of differentiating the disability score. Scans that have the same EDSS score should have high similarity. For each patient, we are given the following image type:

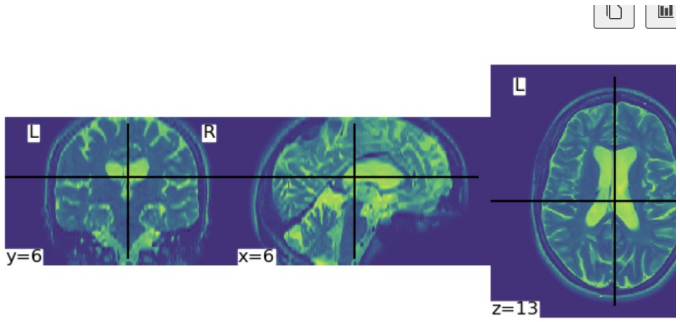

Fig. 3. Sample 3D (Left/Right/Combined)Neurological Image Modality[6]

- **FLAIR (Fluid-Attenuated Inversion Recovery)**: Useful for detecting white matter abnormalities and lesions
- **Gold Standard**: Reference Set
- **T1 and T1Post (Pre and Post-Contrast)**: T1 images are useful for anatomical detail. Post-contrast (T1Post) can highlight areas of active inflammation or breakdown of the blood-brain barrier.
- **T2**: Depicts acute and chronic lesions

For the dataset development, we extract the FLAIR (Fluid-Attenuated Inversion Recovery) due to its effectiveness in highlighting white matter lesions in the Brain, something that is of importance in detecting MRI. Additionally, these scans are correlated with disability as measured by the EDSS.In clinical practice, FLAIR imaging is a staple in MS imaging protocols, reflecting its widespread acceptance and trust in the medical community

- Step 1: **Create Dictionary:** Create a dictionary (edssScoresDict) mapping patient IDs to EDSS scores, based on patientsData.
- Step 2: **Extract Patient IDs:** Create a list of patient IDs (patientIds) from patientsData.
- Step 3: **Compute Cartesian Product:** Generate all possible pairs (cartesian product) of patient IDs.
- Step 4: **Create Data Frame:** Create a data frame (cartesianDataFrame) from the cartesian product with columns 'patient1' and 'patient2'.
- Step 5: **Assign Similarity Scores:** For each row in the data frame, assign a similarity score (isSimilar) of 1 if the EDSS scores of 'patient1' and 'patient2' are equal, otherwise 0.
- **Step 6: Filter Data Frame:** Create a filtered data frame (filteredDataFrame) by excluding rows where 'patient1' and 'patient2' are the same.

D. Identification of the slice for input to the Siamese Network

"Slices" are individual images taken at different levels (depths) of the brain. Each slice provides a detailed view of the brain structures at that specific level. By examining these slices, medical doctors detect abnormalities that might

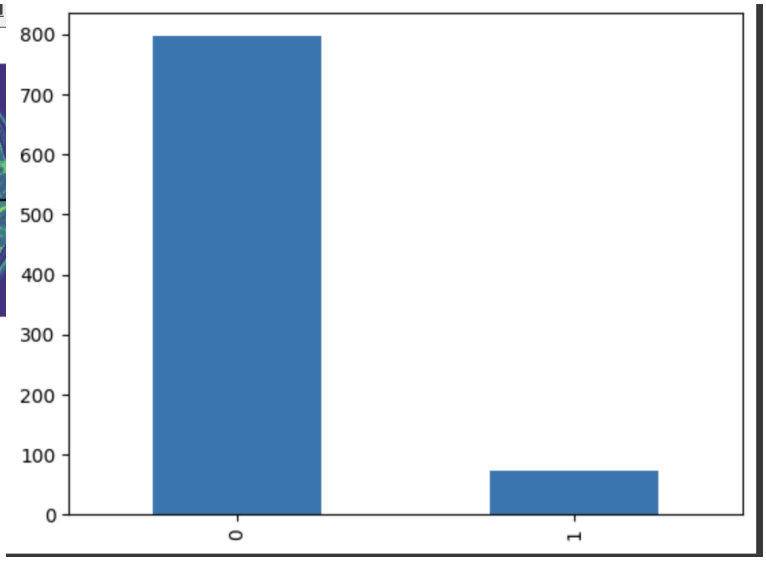

Fig. 4. Dataset Distribution (1 represents similar EDSS scores and 0 represents different EDSS scores)

	patient1	patient2	is_similar
1	patient01	patient02	0
2	patient01	patient03	0
3	patient01	patient04	0
4	patient01	patient05	0
5	patient01	patient06	0
6	patient01	patient07	0
7	patient01	patient08	0
8	patient01	patient09	0
9	patient01	patient10	0
10	patient01	patient11	0

Fig. 5. Dataset Representation

be obscured by CSF (Cerebrospinal fluid) in standard MRI sequences. MS (Multiple Sclerosis) affects the white lesions area i.e the area with the highest intensity. For the axial view, we extract the max. intensity slice. In the context of FLAIR (Fluid-Attenuated Inversion Recovery) imaging, a "slice" refers to a single cross-sectional image captured as part of a series that covers a specific region of interest in the body, typically the brain. These slices are essentially two-dimensional representations of a three-dimensional volume. Hence when processing these images, we first have to convert the 3D representation into a 2D representation and we achieve this by utilizing NiBABEL (A Neuroimaging library in Python)

V. Model Development and Training

We utilized the popular deep learning framework known as PyTorch for developing the Siamese networks. PyTorch contains DataLoaders and Datasets classes that make handling datasets and modifying very convenient. For an image

```
# Calculate the mean intensity of each slice
slice_intensities = image_data.mean(axis=(0, 1))

# Find the slice with the maximum mean intensity, which might indicate lesions
max_intensity_index = np.argmax(slice_intensities)
selected_slice = image_data[:, :, max_intensity_index]
```

Fig. 6. Intensity Computation

dataset, it also allows the addition of essential transform operators. For our data processing, we have applied the following transformations:

- Resizing: Resizing the image to a lower resolution makes the process computationally efficient. Given the compute bandwidth, increasing the size can yield better results.
- Gray to RGB: We convert the grayscale images to RGB due to the architecture requirement of ResNet.

Residual Networks are widely used in medical applications. ResNet is a deep-learning convolutional neural network that are based on the ResNet architecture and was exclusively designed for breast cancer detection. Due to the nature of medical applications where subtle features are extremely valuable, ResNets employ "skip connections" that limit the vanishing gradient problem[20]. Additionally, PyTorch supports many pretrained ResNets that Siamese networks can utilize as backbones.

With this, we create a "MSDataset" that takes in a Pandas Data Frame of pairs with its associated image data path.

Train/Test/Split	Split
870	556, 174, 140

A. Model Architecture

The model architecture comprises of two variants of the network. The first variant comprises simple dense layers where each output is passed through a layer of 64 and 32 units with the image being resized to 32. The loss function used for all networks is a contrastive loss function. The use of this loss function depends on the change detection i.e in our case, we want similar images to have lower loss and vice versa. The loss is designed to ensure that similar items have a small distance between them, and dissimilar items have a large distance. The margin is a hyperparameter

$$L(y,d) = \frac{1}{2N}\sum_{i=1}^{N} y \cdot (d)^2 + (1-y) \cdot (\max(\text{margin} - d, 0))^2 \tag{2}$$

Fig. 7. Constrastive Loss Function for Siamese Network

that defines how far apart the dissimilar items should be. For our case, the margin is 1. For Dissimilar Pairs (Y = 0): The loss is driven by the square of the distance D between the pair. The goal is to make the distance as small as possible for similar items. For Similar Pairs (Y = 1): The loss considers the distance D only if it is greater than the margin. For each network, we first calculate the composite features using the dense layers, followed by a Sigmoid layer to curb the output between 0 and 1. The second network comprises a

$$\sigma(x) = \frac{1}{1+e^{-x}} \tag{3}$$

Fig. 8. Sigmoid Function used in the Sigmoid Layer

similar functioning but with a ResNet50 backbone. ResNet50 is a neural network that is 50 layers deep and is highly suited for medical applications. In the context of Siamese Networks, the primary purpose of using a backbone is to allow for more granular feature representations. ResNet50 acts as a feature extractor with pre-trained weights. For a Siamese network, as each branch shares the same weights, this allows for a deeper understanding of the input images thus in our case, similarity learning.

B. Fine Tuning Process

Depending on the dataset and task, we might choose to fine-tune some layers of the ResNet50 model while keeping others frozen. Some tasks require training from scratch while maintaining the architecture requirements of ResNet. For our case, the second network consists of a pretrained ResNet50 architecture (trained from scratch) to capture intricate and granular features for disability progression. Additionally, we include both approaches in the code. We report a 72%-symbol on the test set

Parameter	Value
Backbone	Resnet50
Learning Rate	0.003
Epochs	100
Batch Size	16
Loss Function	Contrastive Loss

TABLE III
TRAINING PARAMETERS FOR THE SIAMESE NETWORK

VI. SIAMESE NETWORKS AS TOOLS TO GENERATE MEDICAL DESCRIPTIONS POWERED BY LARGE LANGUAGE MODELS

Siamese networks can express multiple modalities (image and text) given the right encoder. Given the ground truth for an image, a Siamese network can go beyond modeling similarity but can generate descriptive image descriptions. This process is called image captioning [12]. For an image-text pair, a siamese network can be modeled to learn the

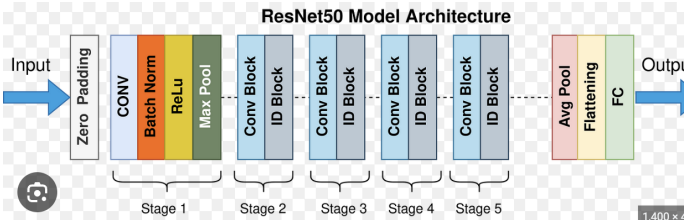

Fig. 9. ResNet50 Architecture

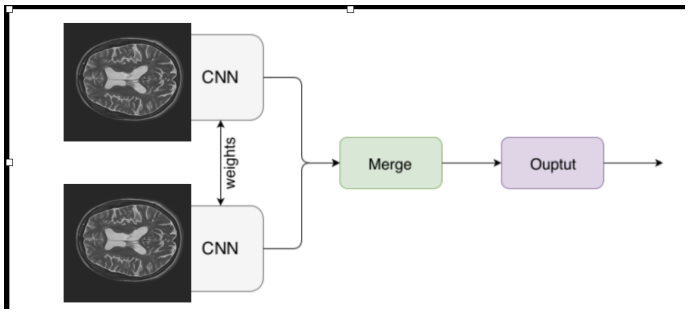

Fig. 10. Base Model Architecture

similarity between two modalities[13]. This capability aims to solve these critical problems in the field of biomedicine:

- Generation of a novel dataset (image-text) for Brain MRI scans i.e. addresses the data availability issue for medicine.
- Extending Siamese networks to synthesize multiple modalities given the image query (3D Image and medical description) and thus enriching disability progression detection with medical textual context.
- For a sufficiently trained Siamese network, this could essentially allow us to generate comprehensive MS image descriptions i.e. reduce clinical annotation burden.

A. Use of LLM (Large Language Model) as an annotator to generate synthetic image dataset

A major challenge in operating this pipeline is the lack of ground truth MRI description text. To rectify this, we aim to utilize a medical LLM (Large Language Model) capable of highlighting all the intricate details of an MRI scan. Multi-modal models such as LLaVA-Med[2] Visual med-alpaca[3] and GPT-4 [13] encode a great deal of medical knowledge and are a perfect candidate.

Additionally, due to the nature of siamese networks requiring fewer samples per class, enriching siamese networks with descriptions accelerates minimal clinical burden and thus acts as an intermediator tool to speed up the annotation process. Furthermore, techniques such as RAG (Retrieval Augmented Generation) [15] can also significantly increase the accuracy of these image description pairs.

TABLE IV
A LIST OF OPEN AND CLOSED LLMS (LARGE LANGUAGE MODELS)

LLM	Source and Availability
GPT-4 (Most Accurate)	Closed and Pay to Use
LlAVA-Med	Open Source
Visual Med Alpaca	Open Source and Free to use

B. Generation of a novel synthetic dataset for MS disability progression

To generate a novel synthetic dataset for MS Disability progression, we utilized state-of-the-art Prompt Engineering Methods coupled with RAG and human evaluation to verify the result. Additionally, most LLMs suffer from hallucination i.e. predicting something completely unrelated to what was searched for. Prompting is how the model locates certain tokens and can be thought of as a system to perform Bayesian Inference.

C. Limitations for Medical Applications

Medical Applications of medical inference suffer a lot of hallucination and additionally, due to the way these proprietary models have been aligned, they refuse to answer a medical interpretation query. To rectify this, a context is required from where the model can ”pick” or estimate the impression of the image [21].

D. Synthetic Medical MRI MS impressions

- **Patient 1**
  - **File Name:** FLAIR (1).nii.gz
  - **Annotation:** This is an axial T2-weighted MRI brain scan displaying high signal intensity in the white matter regions, which may indicate demyelination, gliosis, or edema. The ventricles appear normal in size, suggesting no hydrocephalus or atrophy. There are no signs of mass effect or midline shift. The cortical gray matter shows normal differentiation from the white matter. There’s no evidence of acute infarct or hemorrhage in the parenchyma. The basal ganglia and thalami are intact, without signal abnormality. Overall, specific pathologies would require clinical correlation for accurate diagnosis.
- **Patient 2**
  - **File Name:** FLAIR (2).nii.gz
  - **Annotation:** The image appears to be an axial FLAIR MRI of the brain with increased signal intensity within the periventricular white matter, possibly indicating leukoaraiosis, demyelination, or chronic small vessel ischemic changes. The ventricles are symmetrical with no evidence of hydrocephalus. There is no apparent midline shift or mass effect. The sulci and gyri appear preserved without signs of significant atrophy. Further clinical correlation is required for diagnosis.

E. Metric to analyze medical image description similarity

To measure similarity in addition to human evaluation, we utilize Cosine Similarity[23] which works by checking if two documents/sentences are pointing in roughly the same direction in a multi-dimensional space. To achieve this, we require tokenizing or vectorizing the text. We utilized TFIDF

(Term Frequency-Inverse Document Frequency), a method that measures the frequency of the words.

$$\text{TF}(t,d) = \frac{\text{Number of times term } t \text{ appears in document } d}{\text{Total number of terms in document } d}$$

$$\text{IDF}(t,D) = \log\left(\frac{\text{Total number of documents in corpus } D}{\text{Number of documents containing term } t}\right)$$

$$\text{TF-IDF}(t,d,D) = \text{TF}(t,d) \times \text{IDF}(t,D)$$

$$\text{Cosine Similarity} = \frac{\sum_{i=1}^{n} A_i \times B_i}{\sqrt{\sum_{i=1}^{n} A_i^2} \times \sqrt{\sum_{i=1}^{n} B_i^2}}$$

For each entry with the same EDSS score (i.e those patients who are similar should have a high similarity score and those patients whose disability progressions are not similar should have a low similarity score. We assessed the mean cosine similarity across 10 patients. This shows that

Category	Mean Similarity
Same EDSS Scores	0.4203
Different EDSS Scores	0.3839

TABLE V
MEAN SIMILARITY FOR SAME AND DIFFERENT EDSS SCORES

those with the same report (i.e same disability progression impression) have a higher similarity.

VII. EVALUATION METHODOLOGY

- **Evaluation of the Siamese Nets for disability progression**: We report the model performance on the test set.
- **Evaluation of the synthetic dataset**: We evaluate this with a combination of human evaluation and cosine similarity.
- **[Optional] Expert evaluation of the synthetic dataset.**

VIII. CONCLUSION, LIMITATIONS AND FUTURE STEPS

In conclusion, we propose the adaptation of the Siamese Network for predicting disability progression projects. The use of 3D Brain MRI scans as a primary data modality, coupled with use of a Large Language to generate a novel synthetic medical description. This approach not only aids in modeling disability progression in MS patients but also addresses the issue of medical data scarcity. Furthermore, we show how the process of biomedical annotation can be accelerated while developing a metric and a pipeline to verify the synthetic dataset for MS disability progression detection. Additionally, (1) from a medical perspective, we cannot just rely on the accuracy but we need to test this on a wide range of M.S modalities and datasets that signify progression. (2) Compute Bandwidth also plays a significant role in accelerating performance (3) Expert evaluation of the medical annotations can also significantly accelerate the value of the dataset and plays an important role in the development of Brain MRI/MS Automatic Medical Description Generation.

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