Modern Vision Architectures Meet Alzheimer's Disease Diagnosis in sMRI

Javier Antonio Salazar Cavazos April 10, 2024

Preface

Presentation:

- Latex Typst is my new best friend
- My presentation: https://typst.app/project/ruQq-xBrGHMHYNQxrlfEEN

Myself:

- Research with others¹ on Alzheimer's disease in fMRI earlier this year
- Taking EECS542 (Adv. Topics in CV) so class project is on ADD in sMRI

Some info:

- 50 million people affected (2020) [1]
- This is a hard problem due to many factors...

¹Co-PIs: Scott Peltier & Zhongming Liu

Background²

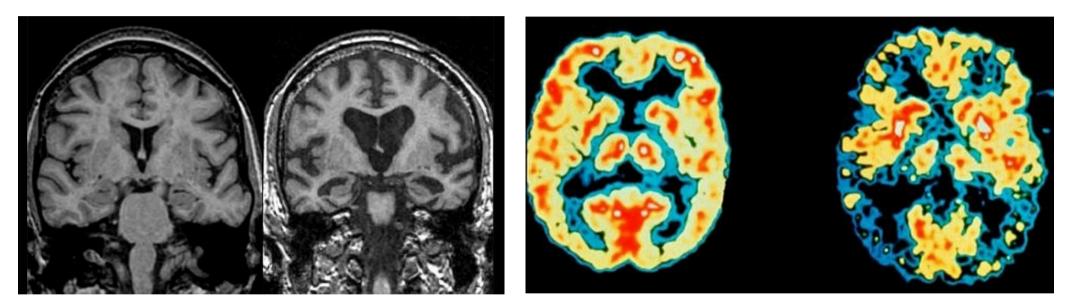
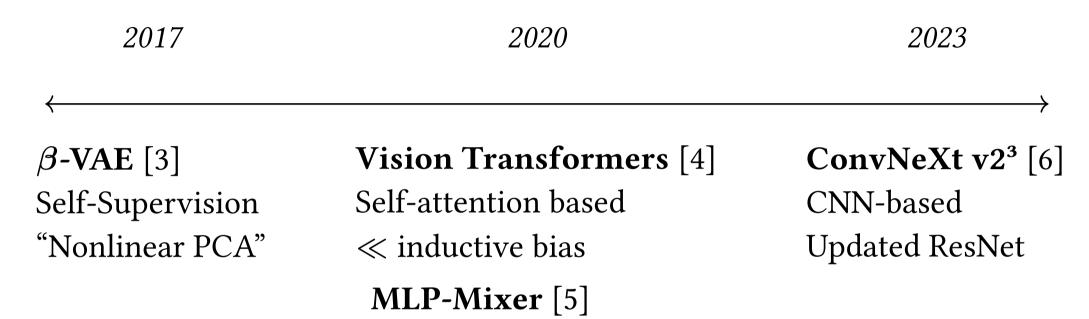


Figure 1: sMRI and fMRI scans (left/right) on CN and AD subjects (left/right).

²Figure adapted from [2]

Modern Vision Architectures



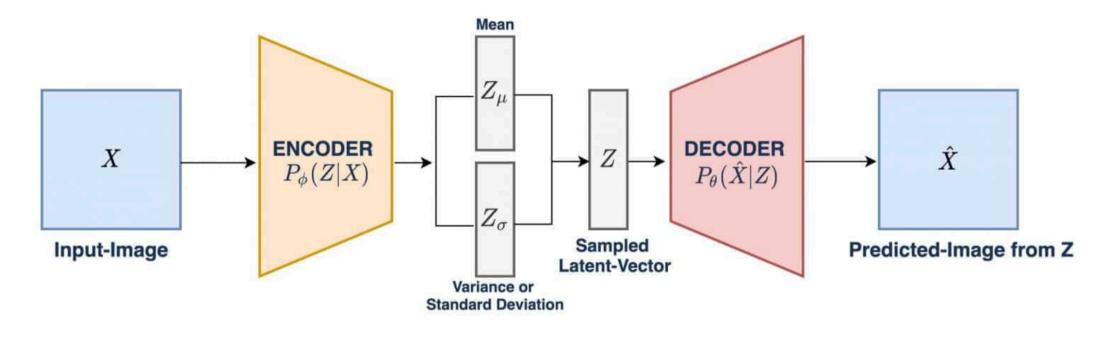
Make MLPs great again!

Diffusion Models

Only FC layers

³I implement v2 but will only discuss v1, don't worry about it

 β -VAE⁴

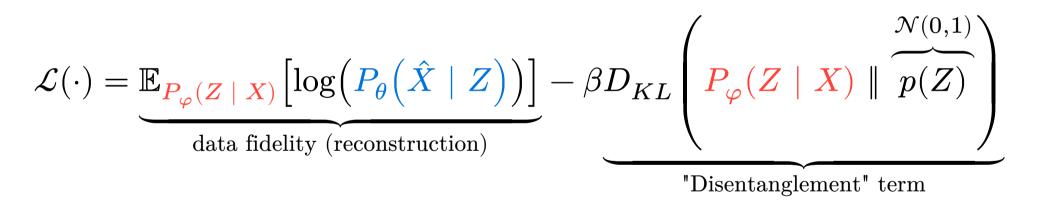


 $Z=Z_{\mu}+Z_{\sigma}\odot\varepsilon,\quad \varepsilon\!\sim\!\mathcal{N}(0,1)$

⁴Figure from [7]

β -VAE II

X = data, Z = latent variables $P_{\varphi}(Z \mid X) = \text{encoder}, P_{\theta}(\hat{X} \mid Z) = \text{decoder}$



Vision Transformers

What are vision transformers?

Well if we ask chatGPT, we get the following:

Vision Transformers

What are vision transformers?

Well if we ask chatGPT, we get the following: Just kidding!

Transformers I - Word Embedding

Let us tokenize⁵ the following sentence: "Javier ate an apple"

Javier $\rightarrow 12$

ate \rightarrow 38

an $\rightarrow 5$

apple $\rightarrow 27$

D = Dictionary Length d_k = Embedding Dim.

 $M = nn.Embed(D, d_k)$

$$\begin{pmatrix} \leftarrow M(12,:) \rightarrow \\ \leftarrow M(38,:) \rightarrow \\ \leftarrow M(5,:) \rightarrow \\ \leftarrow M(27,:) \rightarrow \end{pmatrix}$$

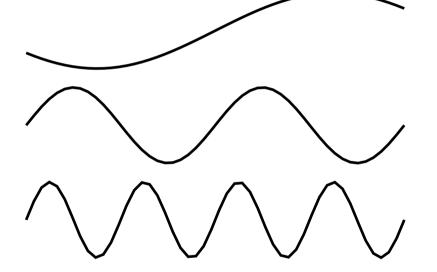
sequence of tokens

⁵Simpliest scheme is per word tokens but in practice "Huffman coding" is used here

Transformers II - Positional Encoding

Transformers are not RNNs! They don't really understand positions.

$$\begin{pmatrix} \leftarrow M(12,:) \rightarrow \\ \leftarrow M(38,:) \rightarrow \\ \leftarrow M(5,:) \rightarrow \\ \leftarrow M(27,:) \rightarrow \end{pmatrix}$$



T = Token matrix

Positional encoding matrix

Transformers III - Attention⁶

 $\begin{aligned} & \text{Attention}(Q,K,V) = \\ & \text{Softmax} \Big(QK^T \div \sqrt{d_k} \Big) V \end{aligned}$

⁶Figure from [8]. Note that this is self-attention, cross-attention is also useful.

Transformers III - Attention⁷

 $\begin{aligned} & \operatorname{Attention}(Q,K,V) = \\ & \operatorname{Softmax} \Bigl(QK^T \div \sqrt{d_k} \Bigr) V \end{aligned}$

T = ``Javier ate an apple'' $W_Q, W_K, W_V = \text{learnable params.}$ $\rightarrow Q, K, V = W_Q T, W_K T, W_V T$

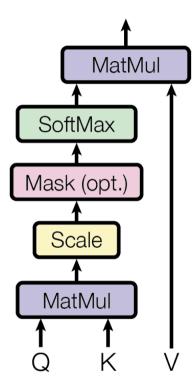
⁷Figure from [8]. Note that this is self-attention, cross-attention is also useful.

Transformers III - Attention⁸

$$\begin{aligned} &\operatorname{Attention}(Q,K,V) = \\ &\operatorname{Softmax} \left(QK^T \div \sqrt{d_k} \right) V \end{aligned}$$

T = "Javier ate an apple" $W_Q, W_K, W_V = \text{learnable params.}$ $\rightarrow Q, K, V = W_Q T, W_K T, W_V T$

 QK^T = affinity matrix $sm(QK^T)V$ = new embedding

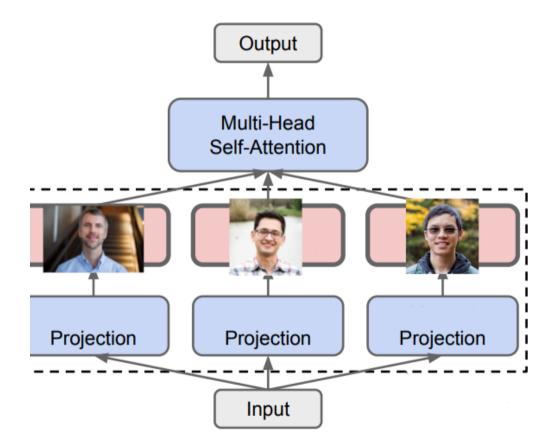


⁸Figure from [8]. Note that this is self-attention, cross-attention is also useful.

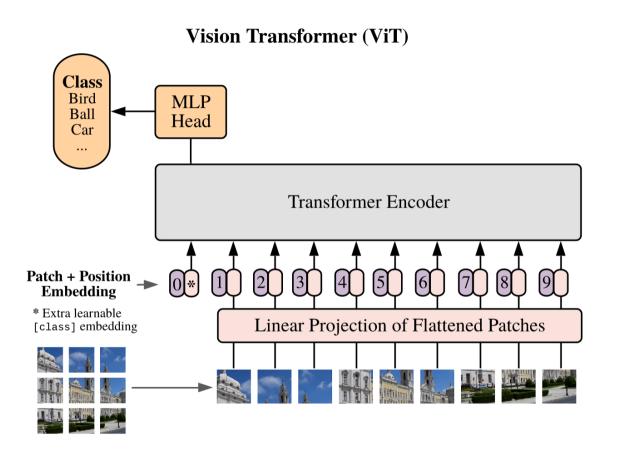
Transformers IV - Multi-Head Self-Attention

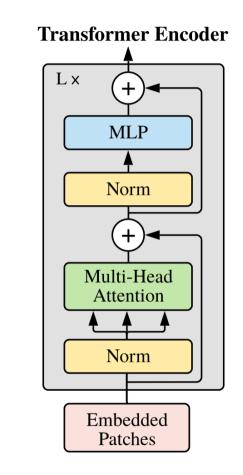
```
\begin{split} & \text{MultiHead}(Q,K,V) = \\ & \text{Concat}(\text{head}\_1,\dots,\text{ head}\_3) \ W^O \end{split}
```

Jeff/Javier/...



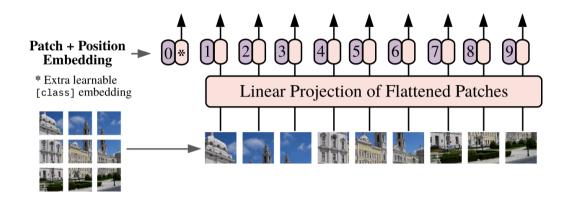
Vision Transformers I





1

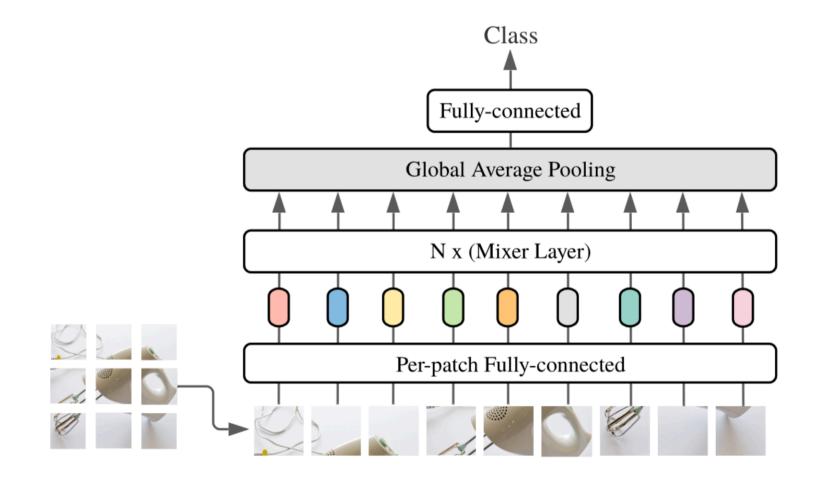
Vision Transformers II - Patch Embedding



1 def __init__():

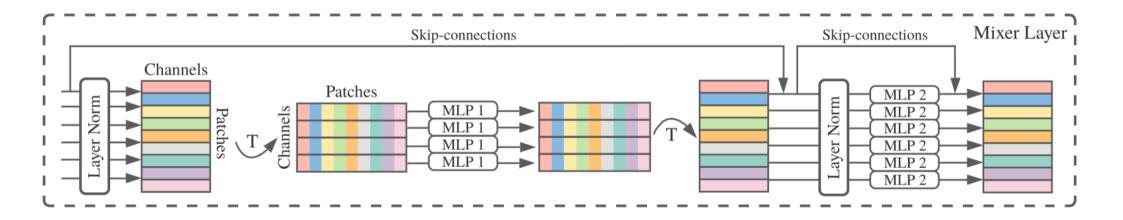
- 2 project = nn.Conv2d(C, d_k, kernel=1, stride=patch_size)
- 3 def forward(input):
- 4 o = project(input) # (d_k, Patch_x, Patch_y)
- 5 o = o.flatten(2).transpose(1, 2) # (Num_patches_total, d_k)

MLP-Mixer



Mixer Layers

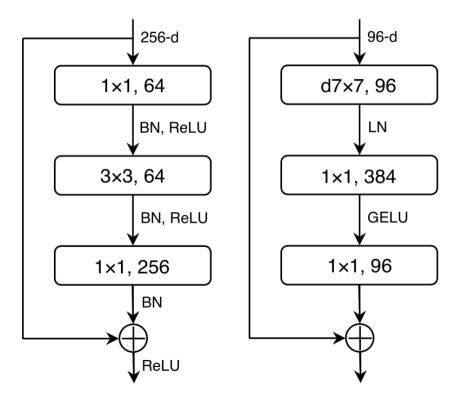
"Mixing" spatial information + channels



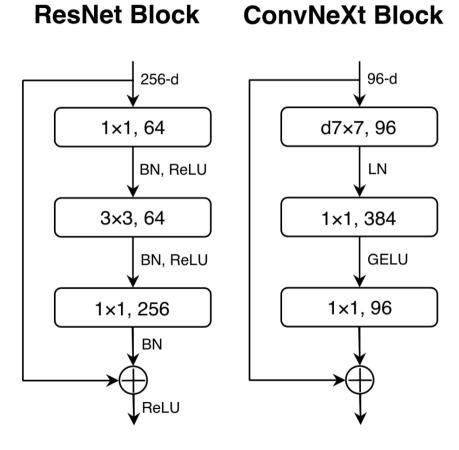
 $MLP \rightarrow [Linear, GELU, Linear]$

ConvNeXt

ResNet Block ConvNeXt Block



ConvNeXt



| | output size | • ResNet-50 | • ConvNeXt-T | | | |
|------|-------------|---|--|--|--|--|
| stem | 56×56 | 7×7 , 64, stride 2 3×3 max pool, stride 2 | 4×4 , 96, stride 4 | | | |
| res2 | 56×56 | $\begin{bmatrix} 1 \times 1, 64 \\ 3 \times 3, 64 \\ 1 \times 1, 256 \end{bmatrix} \times 3$ | $\begin{bmatrix} d7 \times 7, 96\\ 1 \times 1, 384\\ 1 \times 1, 96 \end{bmatrix} \times 3$ | | | |
| res3 | 28×28 | $\begin{bmatrix} 1 \times 1, 128 \\ 3 \times 3, 128 \\ 1 \times 1, 512 \end{bmatrix} \times 4$ | $\begin{bmatrix} d7 \times 7, 192 \\ 1 \times 1, 768 \\ 1 \times 1, 192 \end{bmatrix} \times 3$ | | | |
| res4 | 14×14 | $\begin{bmatrix} 1 \times 1, 256 \\ 3 \times 3, 256 \\ 1 \times 1, 1024 \end{bmatrix} \times 6$ | $\begin{bmatrix} d7 \times 7, 384 \\ 1 \times 1, 1536 \\ 1 \times 1, 384 \end{bmatrix} \times 9$ | | | |
| res5 | 7×7 | $\begin{bmatrix} 1 \times 1, 512 \\ 3 \times 3, 512 \\ 1 \times 1, 2048 \end{bmatrix} \times 3$ | $\begin{bmatrix} d7 \times 7, 768\\ 1 \times 1, 3072\\ 1 \times 1, 768 \end{bmatrix} \times 3$ | | | |
| | FLOPs | 4.1×10^{9} | 4.5×10^{9} | | | |
| # | params. | $25.6	imes10^6$ | 28.6×10^{6} | | | |

Model Comparisons

Given some input X,

Convolution: MLP:

 $K * X = \underbrace{\mathcal{F}(K)}_{\text{weights}} \odot \mathcal{F}(X)$

 $\underbrace{W}_{\text{weights}} X$

Transformer:

 $\operatorname{Sm}(QK^T)X$ weights

- Very different philosophies, yet very familiar
- Varying levels of inductive biases
- Unclear which approach works best given data

Moving on to Alzheimer stuff...

Datasets

Alzheimer's Disease Neuroimaging Initiative (ADNI):

- Develop biomarkers and advance understanding of pathophysiology
- Improve diagnostic methods for AD and improve clinical trial design
- Data: MRI, PET, genetics, cognitive tests, CSF, and blood biomarkers
- Posible additional data sources:
- AIBL (sMRI/fMRI)
- OASIS (sMRI/fMRI)
- MADC (sMRI/fMRI michigan data)
- HCP (sMRI/fMRI healthy patients only!)

Dealing with real data is pain 🙁

Data Preprocessing

Data Distribution

| | total (train/test) | | | | |
|--------------------|----------------------|------------------------|--|--|--|
| Class | Subjects | Sessions | | | |
| CN | 711 (568/143) | 711 (568/143) | | | |
| EMCI ⁹ | 326 (260/66) | 1814 (1414/401) | | | |
| MCI | 388 (310/78) | 928 (760/168) | | | |
| LMCI ¹⁰ | 177 (141/36) | 933 (743/190) | | | |
| DAT | 276 (220/56) | 756 (612/144) | | | |

⁹This class only exists for ADNI Phase 2 / GO, overlap with MCI ¹⁰Same as above

Data Processing / Augmentation¹¹

- 1 training_transform = tio.Compose([
- 2 tio.ToCanonical(),
- 3 tio.Resample(2),
- 4 tio.CropOrPad((96, 108, 96)),
- 5 tio.RescaleIntensity(out_min_max=(-1, 1)),
- 6 tio.OneOf({
- 7 tio.RandomAffine(scales=0.1, degrees=5): 1,
- 8 tio.RandomMotion(degrees=5, translation=5): 1,
- 9 tio.RandomNoise(std=0.05): 1, }),])

O Pytorch

¹¹TorchIO[10] library used for loading, preprocessing, augmentation of medical images

Training setup

Data:

model(sMRI $\in \mathbb{R}^{B \times 1 \times 96 \times 108 \times 96}$) \longrightarrow unnormalized logits $\in \mathbb{R}^{B \times \text{num_classes}}$ **Optimizer:** AdamW = Adam + Weight Decay

Cost function¹²:

P: true distribution, Q: model distribution

$$\underbrace{H(P,Q)}_{\text{Cross Entropy}} = \underbrace{H(P)}_{\text{Entropy}} + \underbrace{D_{KL}(P \parallel Q)}_{\text{KL divergence}} = -\sum_{x \in \text{ classes}} P(x) \log Q(x)$$

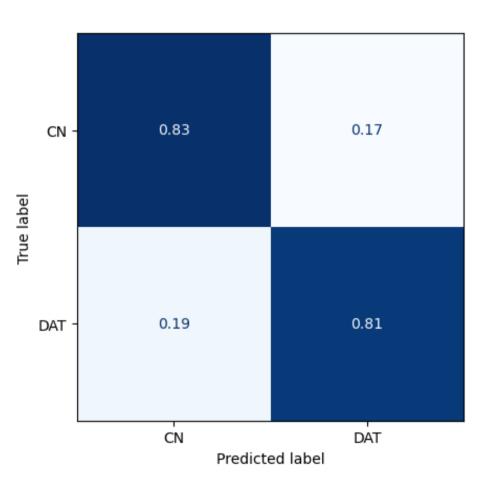
¹²I use weighted CE to handle class imbalances by using inverse frequencies as weights

Experiments¹³

- Model size
 - ► ConvNeXt ~30M vs. ~80M
- Spatial resolution
 - 1mm (~ 200^3) vs. (~ 100^3)
- 5-class classification
- Binary vs. 3-class classification
- Transfer learning
- Feature Maps
- VAE results

¹³Blue text indicates discussion, no additional slides

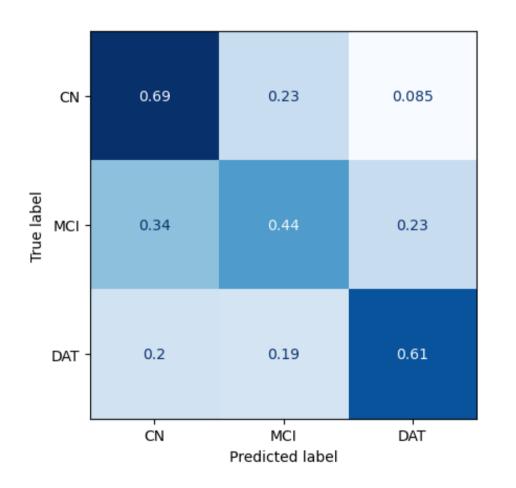
ConvNeXt - Binary Classification



| precision | recall | f1-score | | |
|-------------|--------|----------|--|--|
| CN 0.79 | 0.83 | 0.81 | | |
| DAT 0.85 | 0.81 | 0.83 | | |

accuracy 0.82

ConvNeXt - Multi-Class Classification I

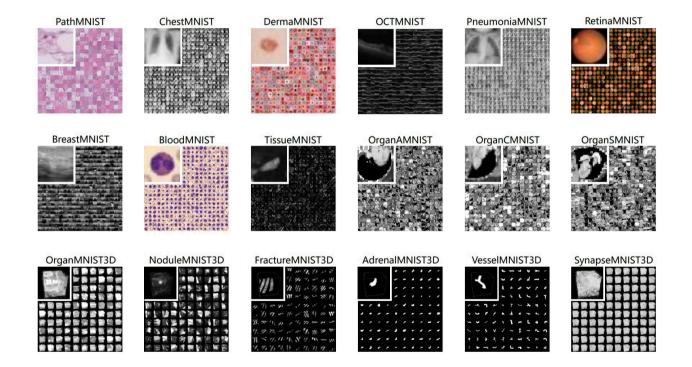


precision recall f1-score CN 0.52 0.69 0.60 MCI 0.53 0.44 0.48 DAT 0.67 0.61 0.64

accuracy 0.57

ConvNeXt - Transfer Learning

Can we use features from other problems to increase accuracy?¹⁴



¹⁴MedMNIST [11] contains 2D/3D medical data for classification from many modalities

Results

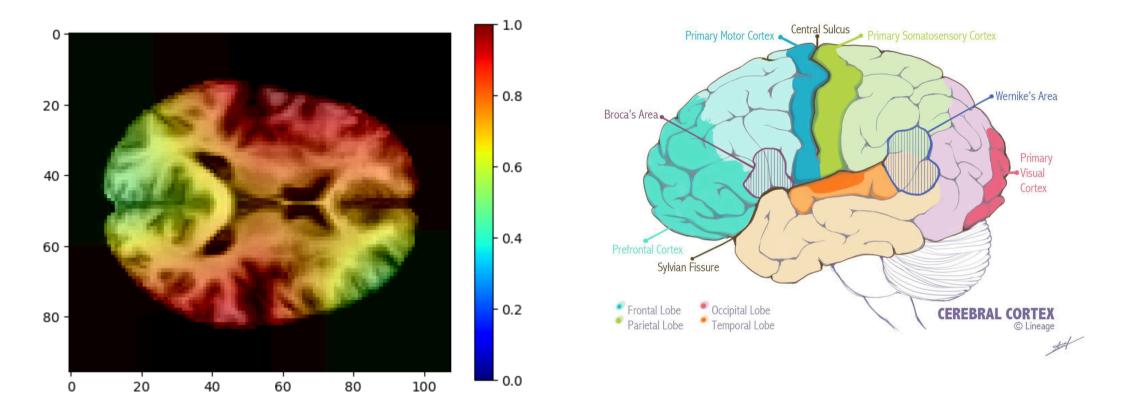
| Model | Precision | | Recall | | A a a 1140 a 114 | |
|-----------------------|-----------|------|--------|------|-------------------------|--|
| Model | CN | DAT | CN | DAT | Accuracy | |
| ConvNeXt | 0.79 | 0.85 | 0.83 | 0.81 | 0.82 | |
| ViT (p=8) | 0.79 | 0.76 | 0.69 | 0.84 | 0.77 | |
| MLP-Mixer (p=3) | 0.87 | 0.82 | 0.76 | 0.90 | 0.84 | |
| VAE (Self-Supervised) | 0.67 | 0.80 | 0.80 | 0.66 | 0.73 | |

Table 1: Binary Classification Results

| Model | Precision | | Recall | | | 1 | |
|-----------------------|-----------|------|--------|------|------|------|----------|
| Model | CN | MCI | DAT | CN | MCI | DAT | Accuracy |
| ConvNeXt | 0.52 | 0.53 | 0.67 | 0.69 | 0.44 | 0.61 | 0.57 |
| ViT (p=8) | 0.59 | 0.42 | 0.55 | 0.49 | 0.37 | 0.69 | 0.52 |
| MLP-Mixer (p=3) | 0.73 | 0.45 | 0.64 | 0.68 | 0.53 | 0.57 | 0.59 |
| VAE (Self-Supervised) | 0.47 | 0.45 | 0.57 | 0.64 | 0.40 | 0.46 | 0.49 |

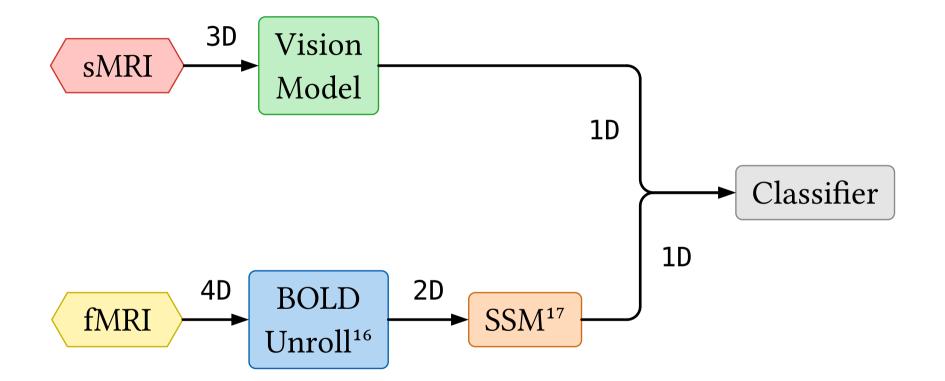
Table 2: Three-Class Classification Results

ConvNeXt - Feature Maps / Visualization¹⁵



¹⁵Grad-CAM++ method [12] used for saliency map generation

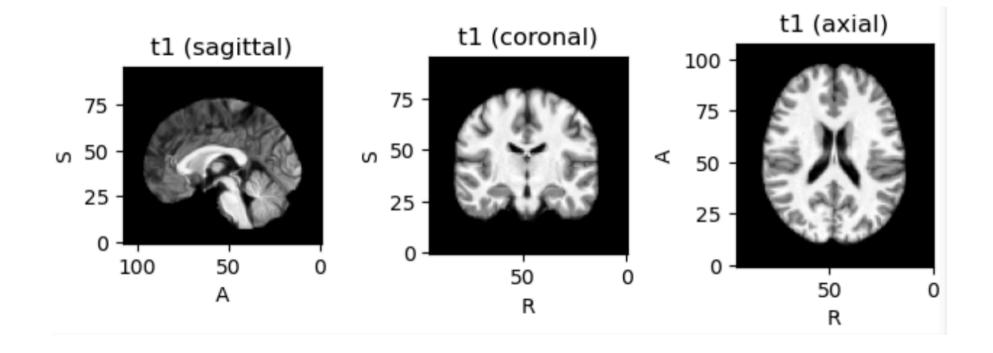
Future Work



¹⁶(my own notation) Generate BOLD matrix w/ PE for sequence modeling
¹⁷More on this in the fall

Conclusion

Javier's sMRI scan¹⁸



¹⁸Thanks to Luis Hernandez-Garcia and David Frey for the scan 😀

Conclusion

\rightarrow model \rightarrow [**cn: 0.99**..., mci: 10⁻⁴, ad: 10⁻⁶]

thanks for listening!

Bibliography

- [1] Z. Breijyeh and R. Karaman, "Comprehensive review on Alzheimer's disease: causes and treatment," *Molecules*, vol. 25, no. 24, p. 5789, 2020.
- [2] E. Dinesh, M. S. Kumar, M. Vigneshwar, and T. Mohanraj, "Instinctive classification of Alzheimer's disease using FMRI, pet and SPECT images," in 2013 7th International Conference on Intelligent Systems and Control (ISCO), 2013, pp. 405–409.
- [3] I. Higgins *et al.*, "beta-vae: Learning basic visual concepts with a constrained variational framework.," *ICLR (Poster)*, vol. 3, 2017.
- [4] A. Dosovitskiy *et al.*, "An image is worth 16x16 words: Transformers for image recognition at scale," *arXiv preprint arXiv:2010.11929*, 2020.

- [5] I. O. Tolstikhin *et al.*, "Mlp-mixer: An all-mlp architecture for vision," *Advances in neural information processing systems*, vol. 34, pp. 24261– 24272, 2021.
- [6] S. Woo *et al.*, "Convnext v2: Co-designing and scaling convnets with masked autoencoders," in *Proceedings of the IEEE/CVF Conference on Computer Vision and Pattern Recognition*, 2023, pp. 16133–16142.
- [7] "https://learnopencv.com/variational-autoencoder-in-tensorflow/," vol.0, no. , p. , 2024.
- [8] A. Vaswani *et al.*, "Attention is all you need," *Advances in neural information processing systems*, vol. 30, 2017.

- [9] O. Esteban *et al.*, "fMRIPrep: a robust preprocessing pipeline for functional MRI," *Nature methods*, vol. 16, no. 1, pp. 111–116, 2019.
- [10] F. Pérez-García, R. Sparks, and S. Ourselin, "TorchIO: a Python library for efficient loading, preprocessing, augmentation and patch-based sampling of medical images in deep learning," *Computer Methods and Programs in Biomedicine*, p. 106236, 2021, doi: https://doi.org/10.1016/j. cmpb.2021.106236.
- [11] J. Yang *et al.*, "Medmnist v2-a large-scale lightweight benchmark for 2d and 3d biomedical image classification," *Scientific Data*, vol. 10, no. 1, p. 41, 2023.
- [12] A. Chattopadhay, A. Sarkar, P. Howlader, and V. N. Balasubramanian,"Grad-cam++: Generalized gradient-based visual explanations for deep

convolutional networks," in *2018 IEEE winter conference on applications of computer vision (WACV)*, 2018, pp. 839–847.