Diagnosing Alzheimer’s Disease using Early-Late Multimodal Data Fusion with Jacobian Maps

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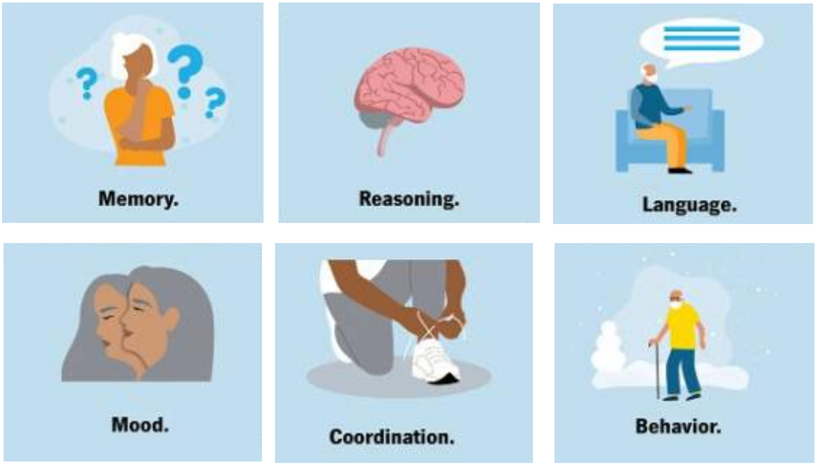
Alzheimer's Disease (AD)

- Risk for having Alzheimer's disease at age 45:

  1 in 5 women and 1 in 10 men.

- The number of AD patients **doubles** every 5 years, estimated to reach **14 million** by 2060.
- Mortality rate: AD kills more people than breast cancer and prostate cancer **combined**
- The symptoms of AD involve a decline in:

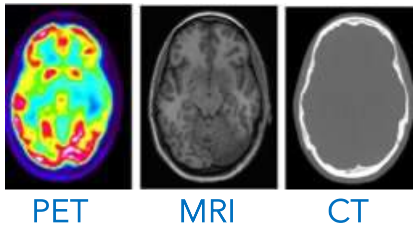


How to deal with it?

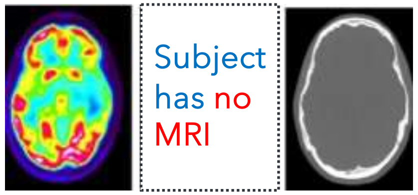
- Manual analysis of brain scans (CT, MRI, PET) is challenging
- Even more so for early detection of AD patterns

- Resorting to machine learning appears to be promising

Opportunities and Challenges

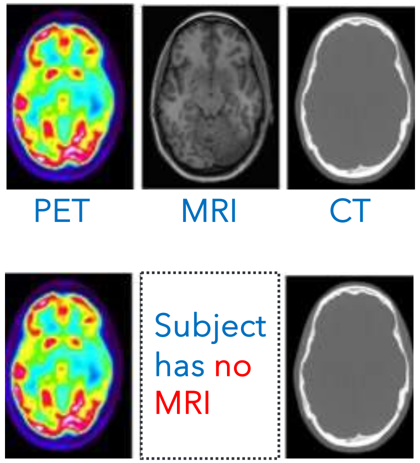


- Multimodal Learning:
  - Machine learning with multimodal data has promised to yield superior performance compared to relying on a single modality.
  - Yet it needs an effective fusion method



- Missing Modalities:
  - Can lead to biased or less accurate model predictions
  - Simply ignoring subjects with missing modalities is not advisable (medical data is scarce resource!)
- Imbalanced Datasets:
  - Medical datasets are often small (due to the difficulty in data collection), restricting models' ability to generalize
  - To make it worse, the dominant samples are healthy subjects, while AD has various stages (MCI, mild, moderate, severe)
- Preprocessing:
  - Directly learning on the raw data, even after cleaning, is not effective due to the very subtle differences to recognize in (early) AD detection

- Multimodal Learning
- Missing Modalities
- Imbalanced Datasets
- Preprocessing



Contributions

- **Early-Late Fusion Framework** (4)
- Hot Deck Imputation (HDI) (2)
- ADASYN + Reweighting (3)
- **Jacobian Maps** (1)

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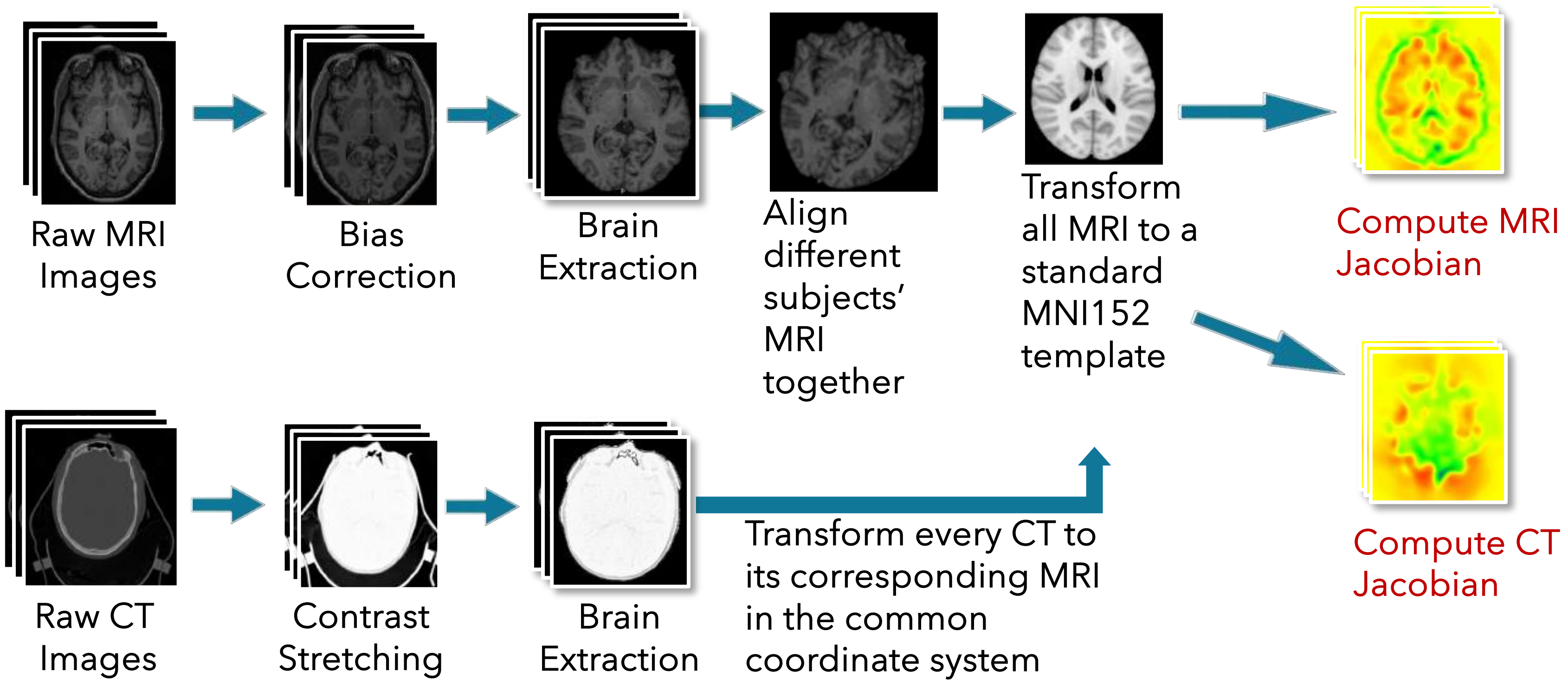
Data

- Participants included 755 cognitively normal adults and 622 individuals at various stages of cognitive decline, ranging in the age of 42-95 yrs.
- MRI and CT 3D images (depth=256)
- We re-labeled them based on clinical dementia rating (CDR) scores:

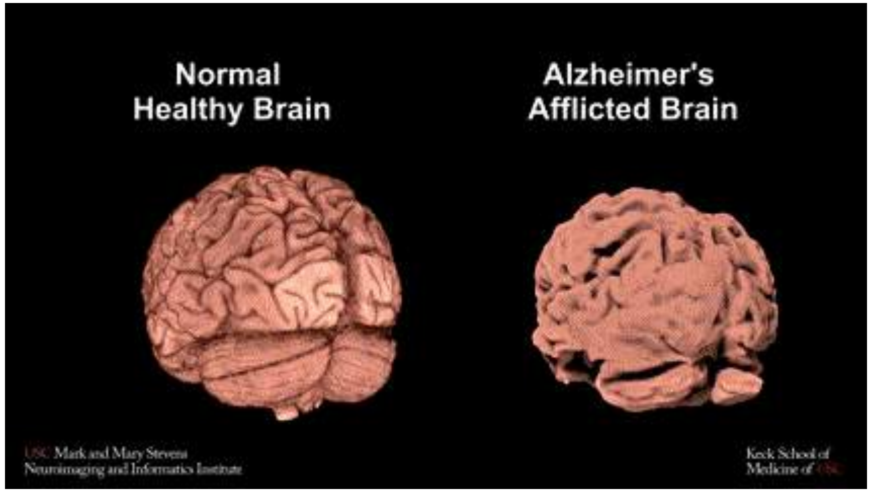
CDR	Class
0	Normal
0.5	MCI
1	Mild
2	Moderate
3	Severe

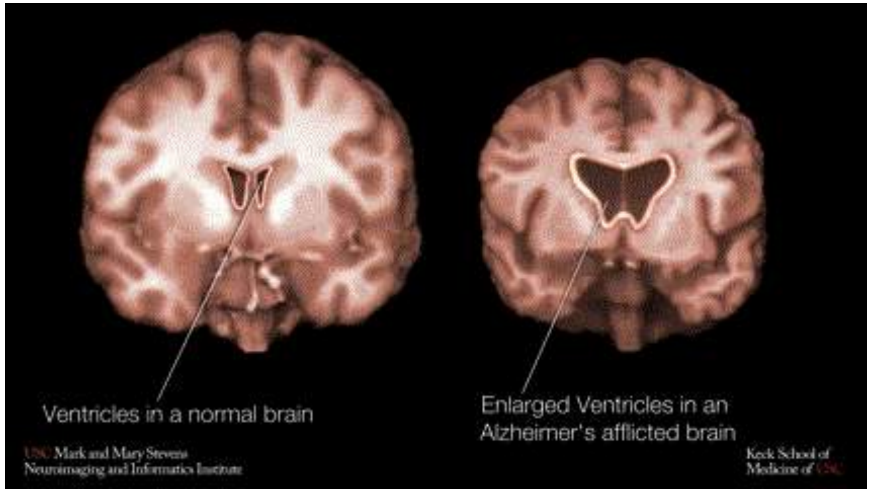
Combined (too few samples each)

Preprocessing Pipeline



Brain Volume Changes
Indicating Dementia





1) Jacobian Maps

- Capture subtle brain volume changes
- Provide informative representations for feature learning
- Highlight local brain morphometry

$$J(v) = \begin{bmatrix} \frac{\partial v_x}{\partial x} & \frac{\partial v_x}{\partial y} & \frac{\partial v_x}{\partial z} \\ \frac{\partial v_y}{\partial x} & \frac{\partial v_y}{\partial y} & \frac{\partial v_y}{\partial z} \\ \frac{\partial v_z}{\partial x} & \frac{\partial v_z}{\partial y} & \frac{\partial v_z}{\partial z} \end{bmatrix}$$

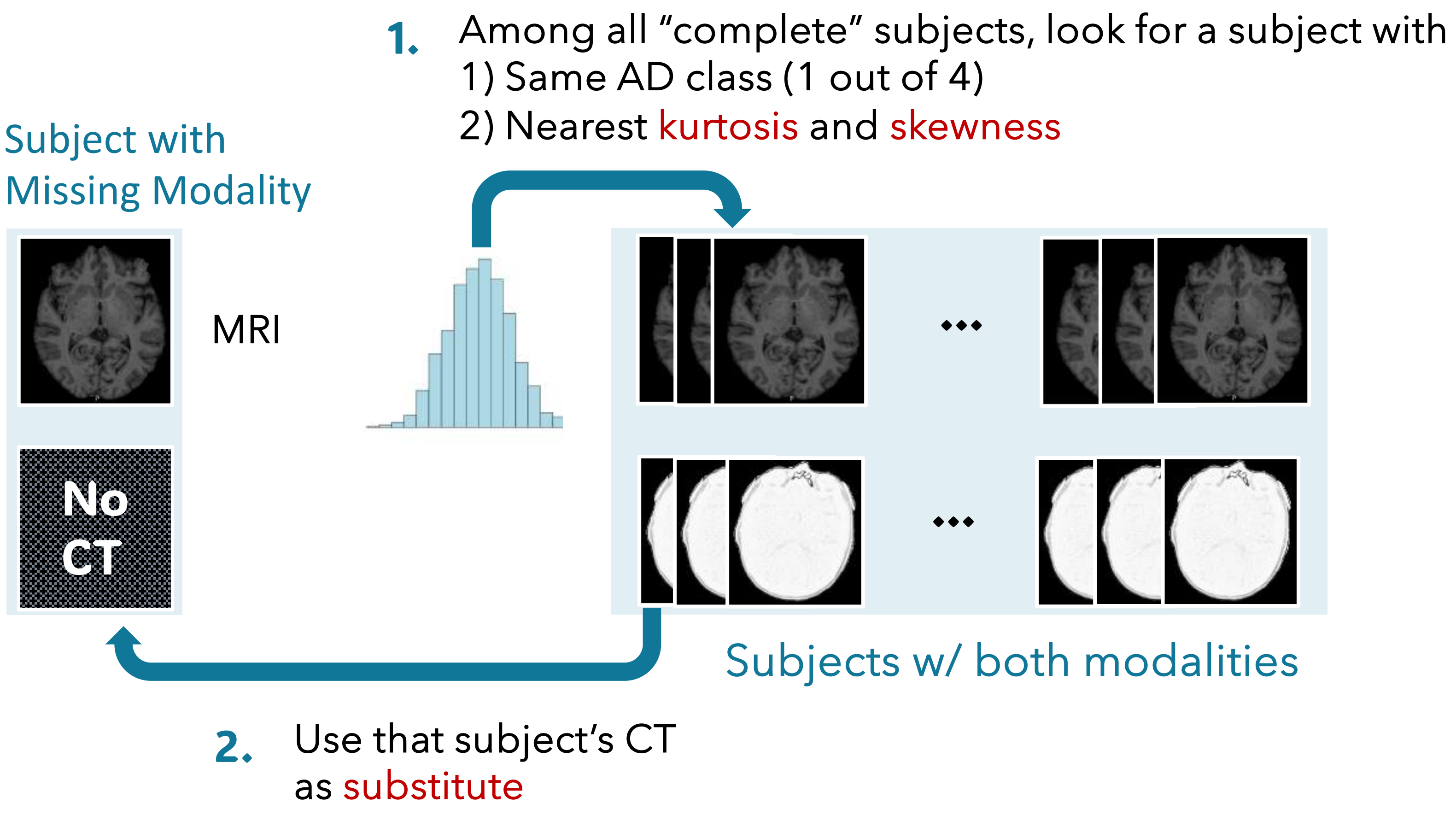
$$\boldsymbol{v}(x, y, z) = \phi(x, y, z) - (x, y, z).$$

Displacement Transformation Original voxel

$$J_{map}(M) = \begin{bmatrix} & \vdots & \\ \dots & Det(J(v(x,y,z)) & \dots \\ & \vdots & \end{bmatrix}_{\substack{x = 1 \dots W \\ y = 1 \dots H \\ z = 1 \dots D}}$$

$$\text{At each voxel:} \begin{cases} \text{volume expansion} & \text{if } Det(J) > 1 \\ \text{no change} & \text{if } Det(J) = 1 \\ \text{volume compression} & \text{if } Det(J) < 1 \end{cases}$$

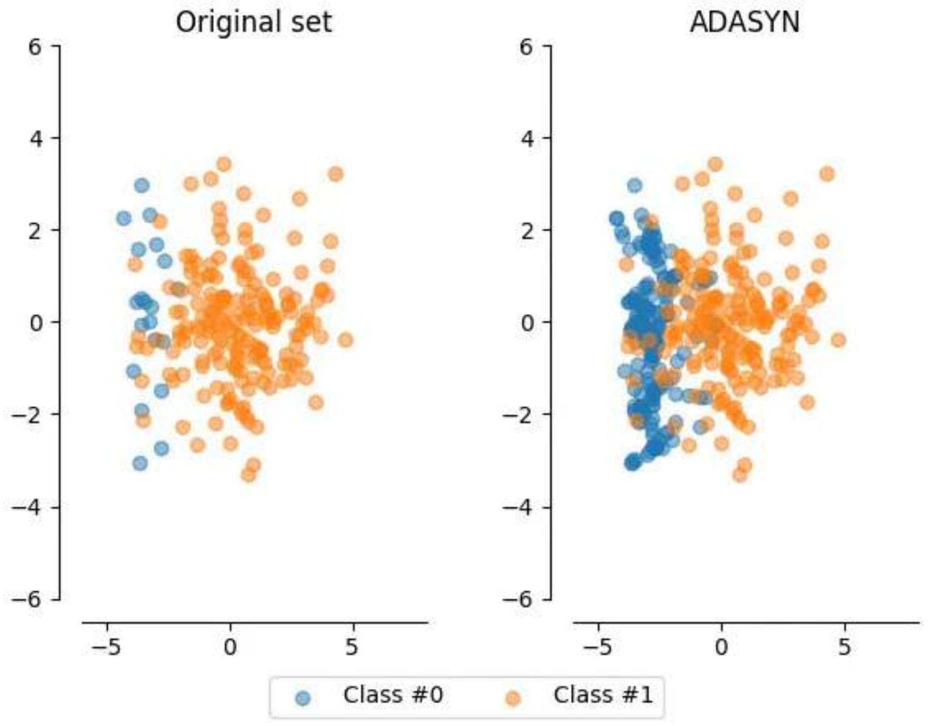
Handling Missing Modalities: 2) Hot Deck Imputation



3) Handling Imbalanced Data

ADASYN

- Estimates a desired distribution based on the minority class to be oversampled.
- Then generates different number of samples according to the distribution.



Reweighting

- ADASYN does not make the class distribution even
- So we prioritize underrepresented classes to avoid bias towards majority classes

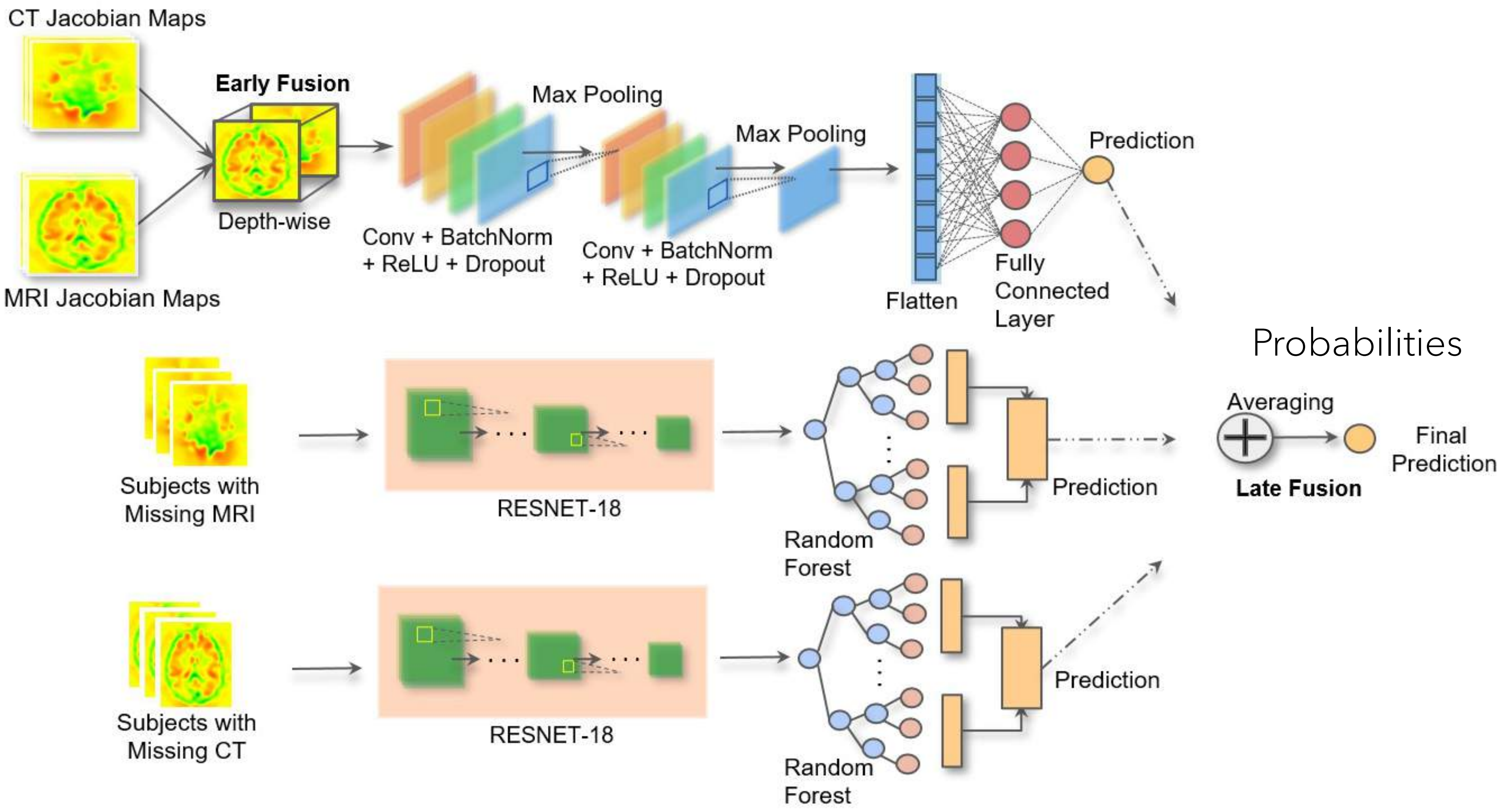
$$\text{freq}(c) = \text{count}\left(y_{train} = c\right), \text{for } c \in C$$

$$\text{Inverse Class Frequencies:} \quad w(c) = \frac{1}{\text{freq}(c)}, \text{for } c \in C$$

$$\text{Normalized Class Weights:} \quad w_{\text{normalized}}(c) = \frac{w(c)}{\sum_{c \in C} w(c)}$$

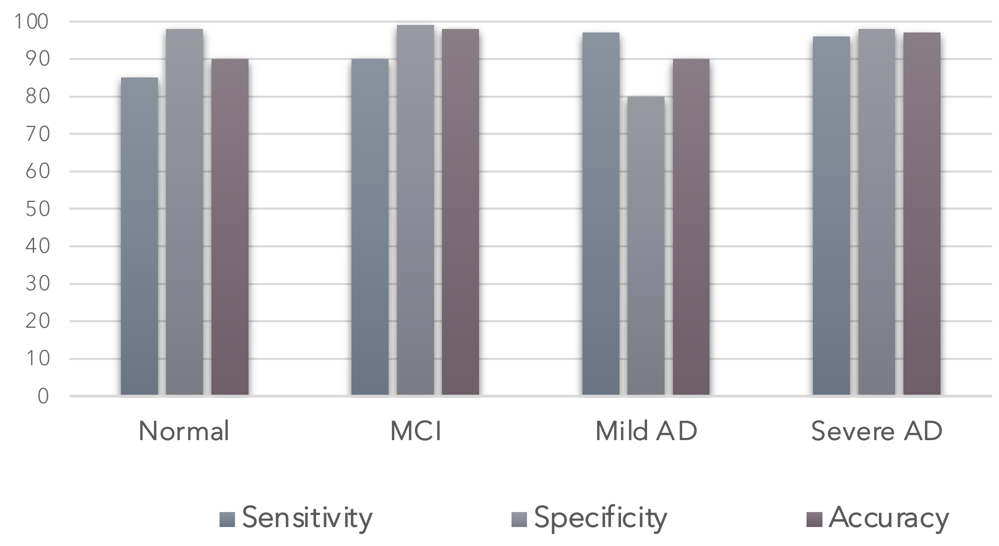
4) Early-Late Fusion Framework

preprocessing



Performance across four AD stages

Model	Accuracy	Sensitivity	Specificity
CNN	91.02	83.37	87.21
RF CT	94.26	86.79	90.52
RF MRI	89.35	83.14	94.47
ELF	**97.19**	**95.19**	**98.76**



Comparison with SOTA

Model	Modality	Classes	SENS	SPEC	ACC
Salami et al. 2022	MRI	AD, CN	86	85	87.7
Massalimova et al. 2021	MRI	NC, MCI, AD	96	96	96
Lazli et al. 2019	MRI, PET	AD, healthy	92	91.7	91
ELF	MRI, CT	Normal, MCI, mild AD, severe AD	95.19	**98.76**	**97.19**

Conclusion

- Proposed an Early-Late Fusion (ELF) framework to aggregate multimodal data for Alzheimer's disease diagnosis across four stages: normal, MCI, mild AD, severe AD.
- Jacobian domain transformation for better representation learning to capture (subtle) nuances
- Hot Deck Imputation to handle missing data modalities
- ADASYN + reweighting to handle imbalanced data
- Contributing towards more effective intervention and treatment of Alzheimer's disease.

"Diagnosing Alzheimer's Disease using Early-Late Multimodal Data Fusion with Jacobian Maps", Healthcom'23.

Thank You!

https://tluocs.github.io