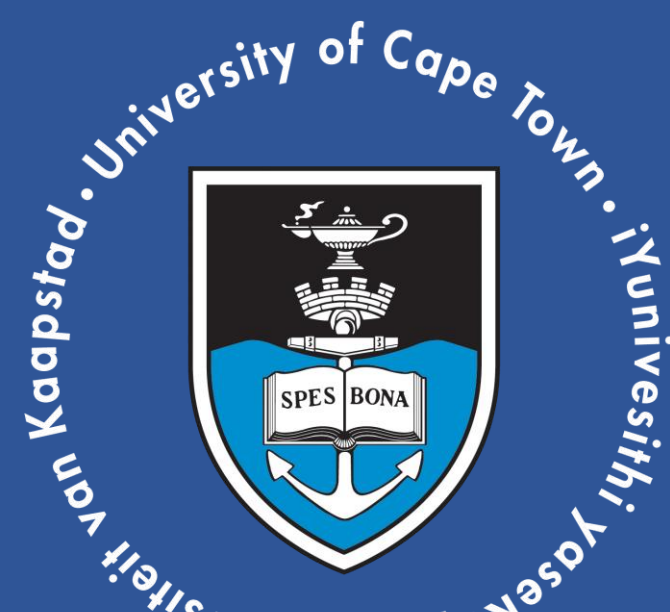# Investigation of brain-ageing in HIV-positive individuals using a neural network

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Introduction

- Over the last few decades research has explored the applications of ML models, and more recently neural networks, to the task of brain age prediction (e.g. [1], [2])
- HIV impacts approximately 38.4 million individuals around the world, as of 2021 [3], and has been a significant health care issue [4]
- Being able to determine and monitor the progression of HIV in the brain is important to assess factors such as treatment efficacy
- There is a question of whether HIV accelerates brain ageing and what factors may affect this accelerated ageing [4]
- The use of neural networks to investigate brain ageing in HIV+ individuals is relatively unexplored
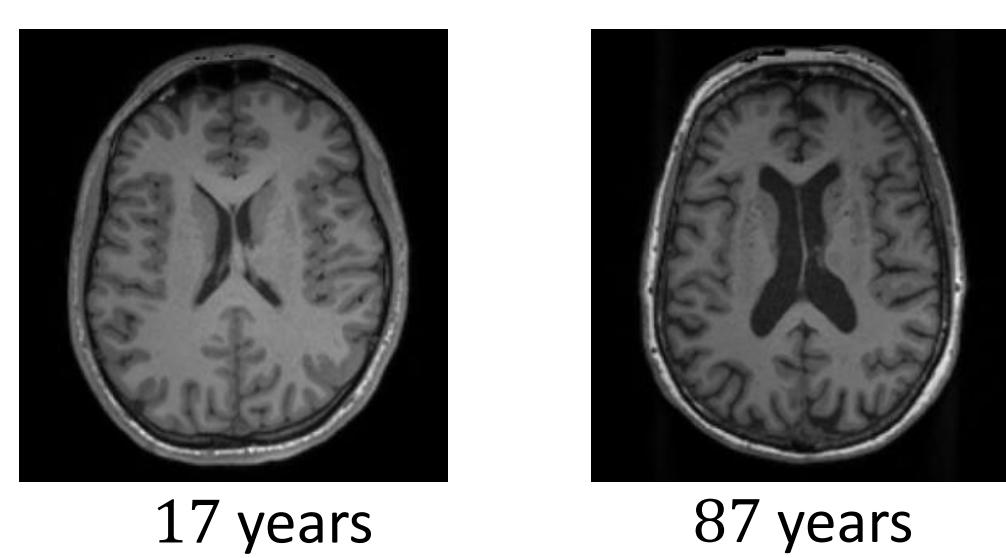
Research Questions

- Does HIV lead to an acceleration in brain ageing?
- Is this accelerated brain ageing correlated to an individual's CD4 count, nadir CD4 count, ART status and AIDS status?

Overview

- CNNs are a powerful tool in the field of computer vision
- ResNets have been successful in eliminating limiting training factors such as the degradation problem
- These networks are applicable to the brain age prediction task
- Brain components, such as the white matter, grey matter and ventricles change with age
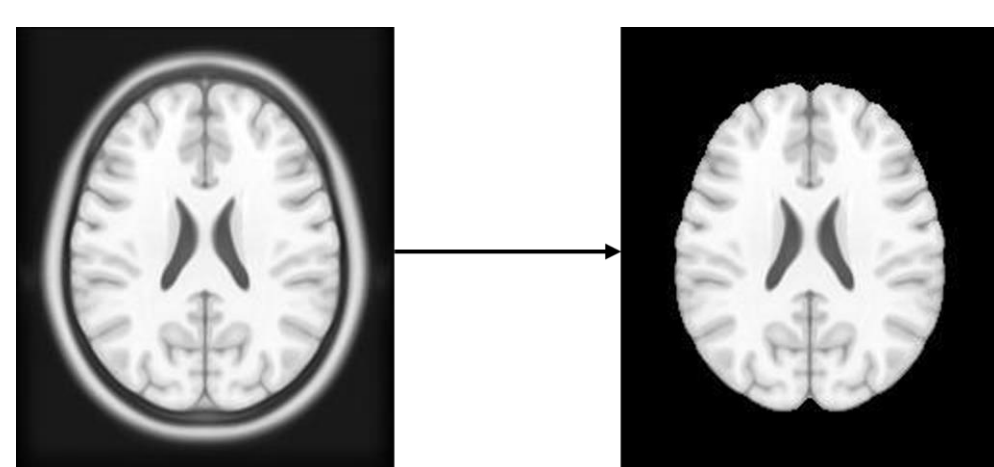
Brain changes with age [5]

17 years   87 years

- HIV may, for example, cause atrophy and lesions in the brain and have neurocognitive effects [4]
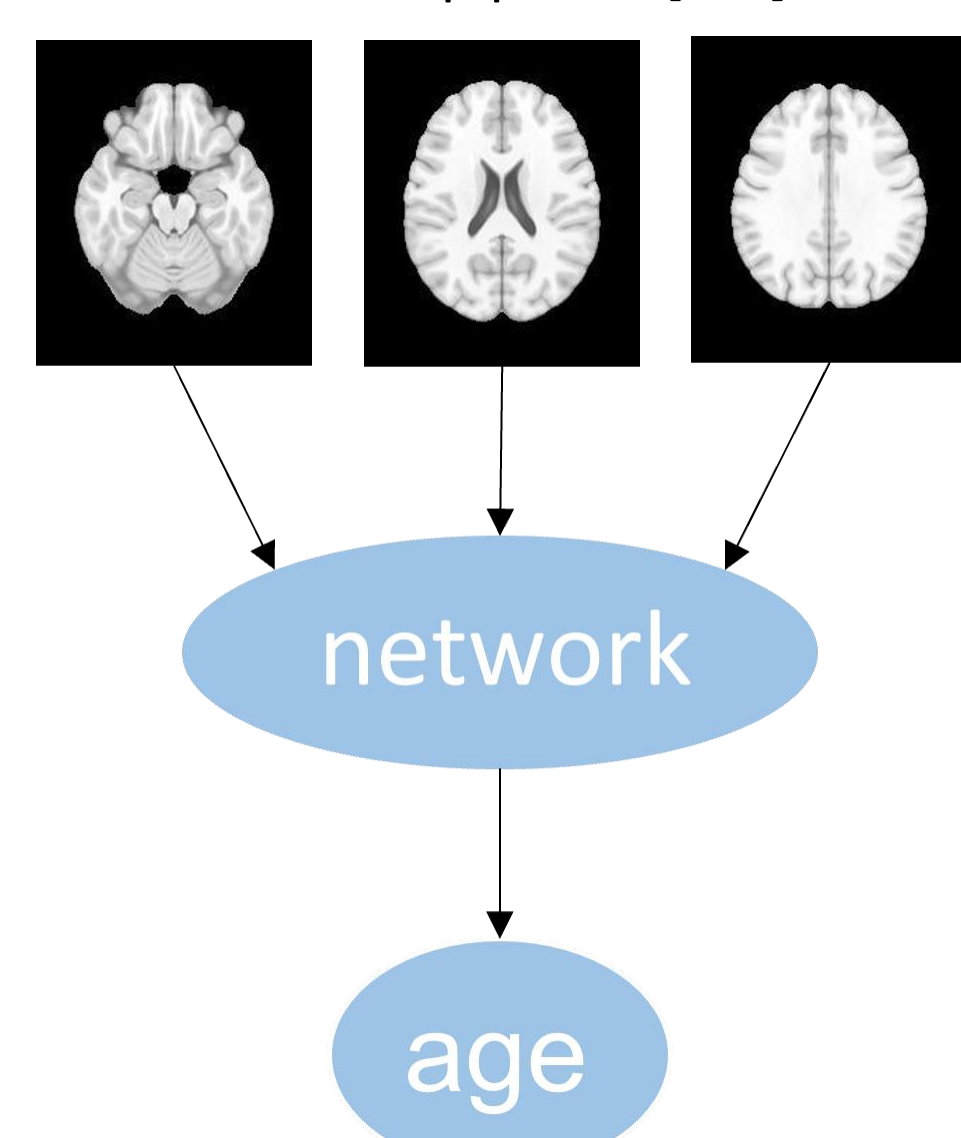
Methodology

- Re-orientate, skull strip and register T1-weighted brain MRI scans for input pre-processing

Skull stripping pre-processing step [6-8]

- Regression problem – age falls along continuous spectrum
- Network takes axial brain slices as input and outputs a predicted brain age

Network pipeline [6-8]

- Train, validate and test on dataset of healthy controls from UK Biobank [9]
- Apply trained network to testing dataset from ENIGMA-HIV Working Group [10] of HIV+ individuals
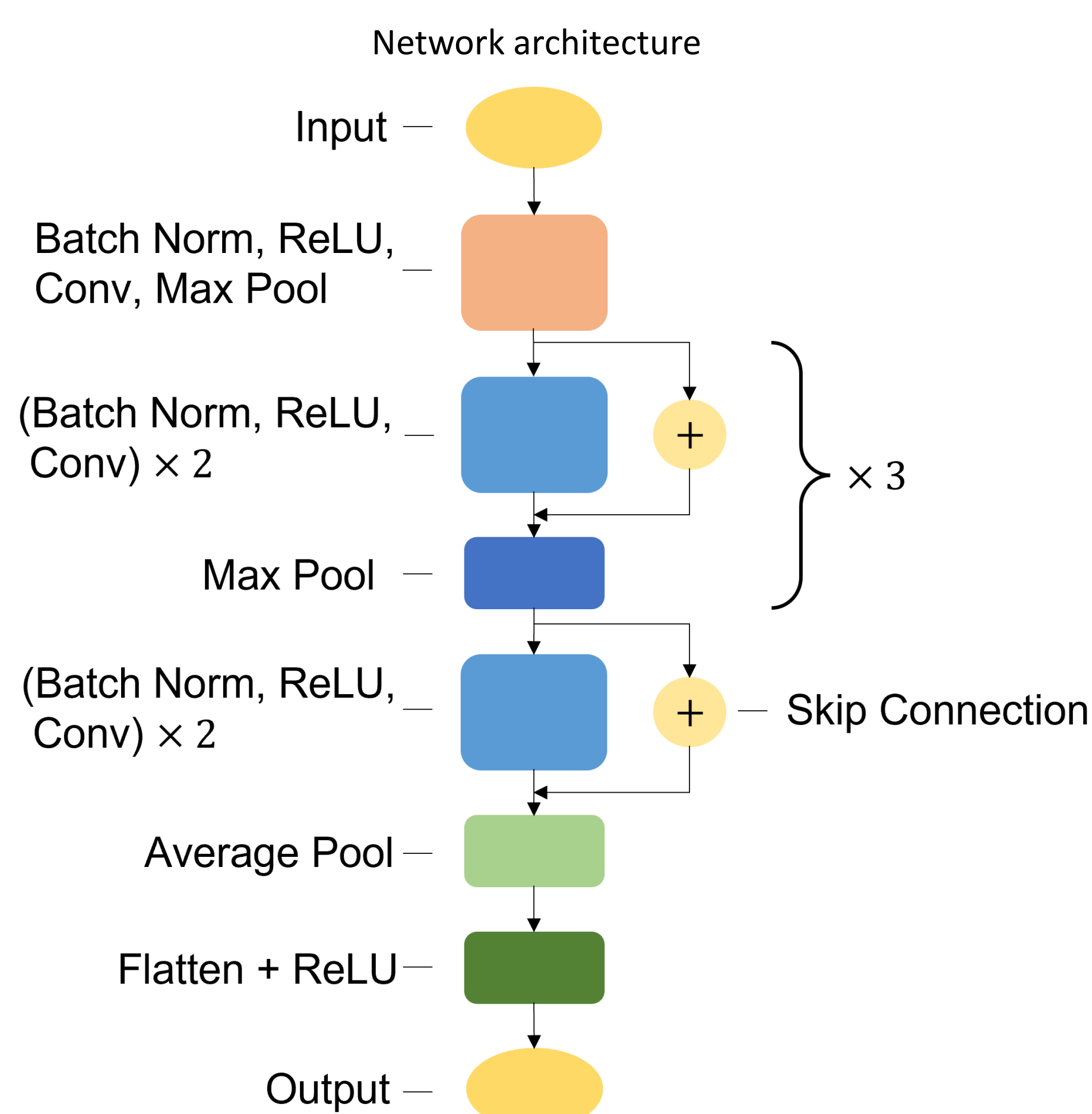
Datasets

- Dataset to develop a trained, validated and tested model from the UK Biobank (N = 21369 healthy controls) [9]
- Dataset of HIV+ individuals to test model from ENIGMA-HIV Working Group (N ≈ 1700) [10]

Age distribution of UKB dataset

Age distribution of subset of ENIGMA-HIV dataset

- ENIGMA-HIV dataset contains subset of HIV- controls which can be used to further train the model
- Datasets span different age ranges – further training on HIV-controls beneficial for improving accuracy on HIV+ testing dataset

Experimental Design

- Implement a CNN with four residual blocks
- Input of spatial dimensions $225 \times 225 \times 225$
- Output scalar age value
- Max pooling for downsizing of spatial dimensions
- Feature maps increase in order $32, 64, 128, 256$
- NVIDIA Tesla V100 SXM2 GPU used for computations

Network architecture

Input

Batch Norm, ReLU, Conv, Max Pool

(Batch Norm, ReLU, Conv) × 2

Max Pool

} ×3

(Batch Norm, ReLU, Conv) × 2   + — Skip Connection

Average Pool

Flatten + ReLU

Output

Output Analysis

- Network predicted age used to calculate brain age delta

$$\delta = age_{pred} - age_{chron}$$

- Correlation between δ and CD4 count, nadir CD4 count, ART status and AIDS status to be analysed
- Confounding factors include lack of information on duration of disease, treatment timeline, and date of nadir CD4 count measurement
- Not all individuals in the dataset have details on ART and AIDS status

Preliminary Results

- Use of subset ($N_{train} = 1500$, $N_{val} = 320$, $N_{test} = 320$) to explore regularisation and optimisation

Results prior to implementation of dropout

MAE loss function log plot

Correlation plot on testing dataset

Test set MAE = 3.76 years
Pearson correlation coefficient $r = 0.78$

Results post implementation of dropout

MAE loss function log plot

Correlation plot on testing dataset

Test set MAE = 3.51 years
Pearson correlation coefficient $r = 0.8$

- Post-dropout shows less overfitting
- Fine-tuning to further improve MAE and correlation coefficient
- Neural network brain age prediction SOTA, held by [1], achieved MAE = 2.14 years – subset results indicate comparative potential

Upcoming Tasks

- Fine-tune network
- Optimise computational efficiency and expand to full dataset
- Explore scaling of number of feature maps at each stage of network
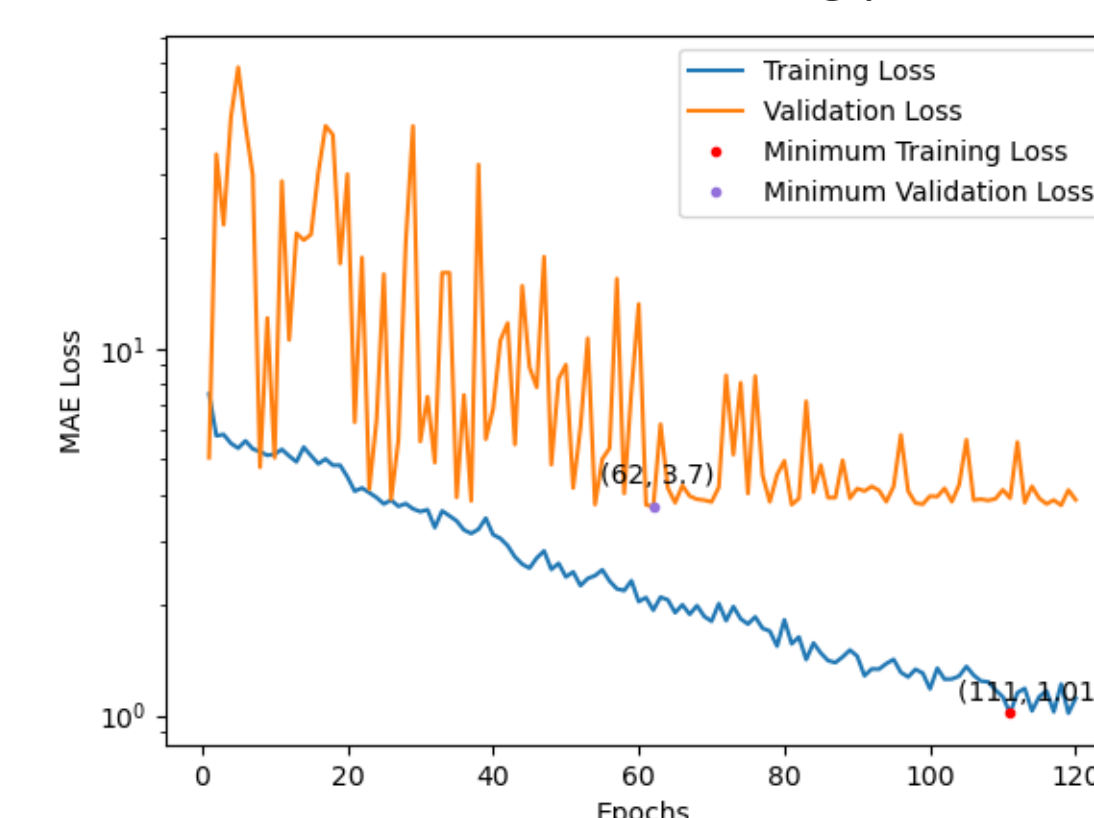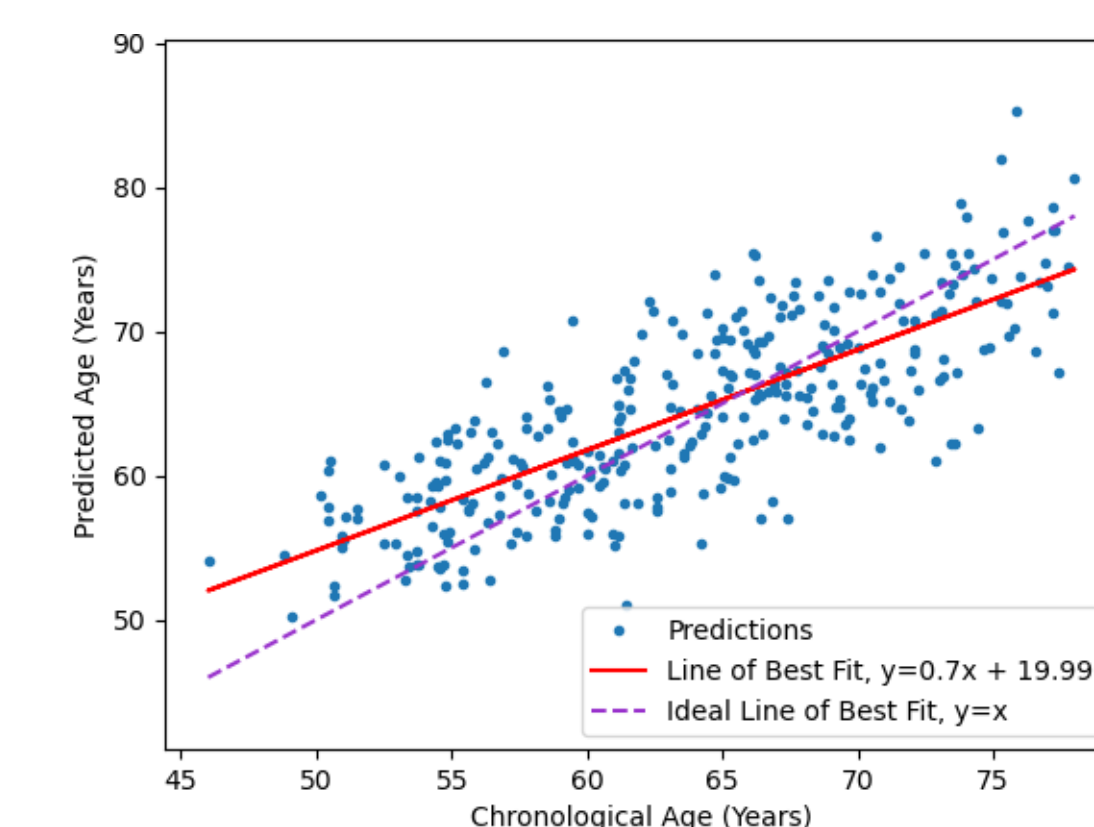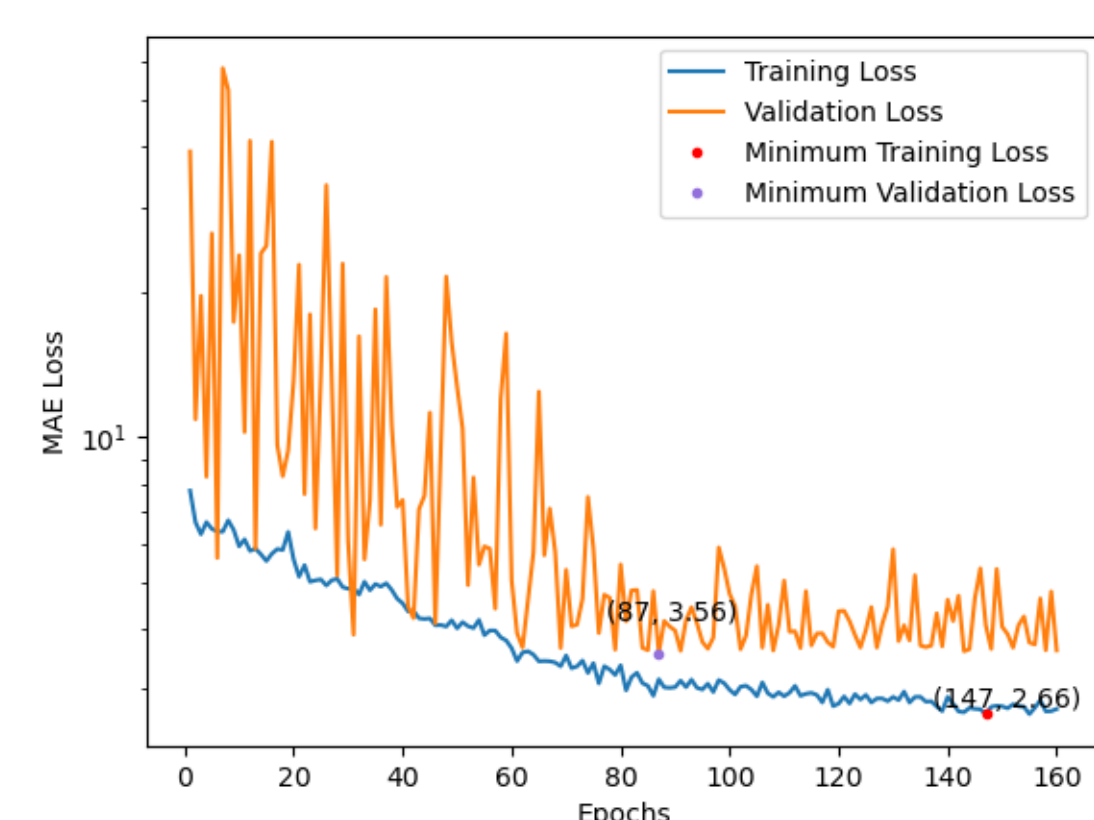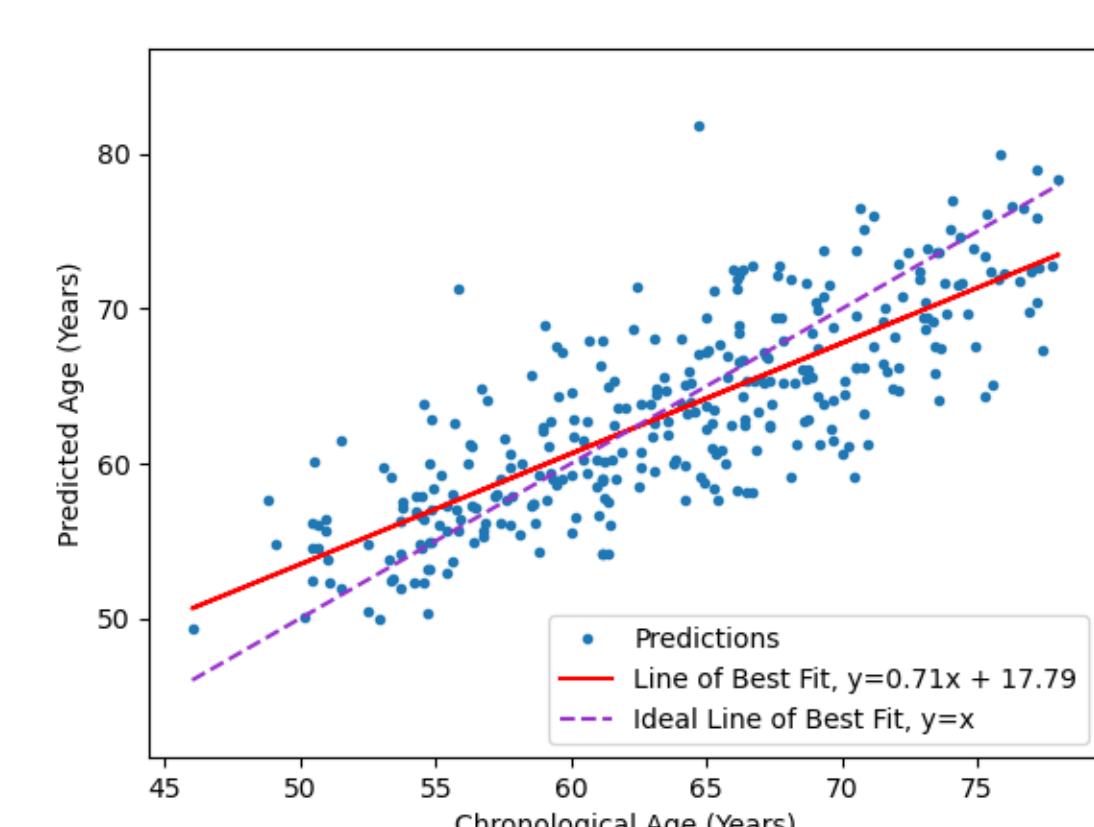- Apply trained network to HIV+ dataset and perform analysis

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