USING INTERPRETABLE MACHINE LEARNING TO DIAGNOSE ALZHEIMER'S DISEASE THROUGH BLOOD-BASED IMMUNOLOGICAL BIOMARKERS

Minor - Collaborative Science for Biomedical Breakthroughs
Ellen Heck[1], **Madelon van Hoek**[2], **Tom Kitak**[3], **Clinten Mohan**[3 4]
[1] Maastricht University, [2] Leiden University, [3] TU Delft, [4] Erasmus MC

TUDelft

Erasmus MC

Background

Alzheimer's disease (AD) is a debilitating neurodegenerative disease characterised by a decline in cognitive functioning [3]. It is currently predicted that the prevalence of AD will double by the year 2050 [2,3]. This will have a great impact on society, as more resources will need to be allocated to mitigate the effects of the disease. While treatment plans are being developed, the way AD is diagnosed still leaves room for improvement in terms of costs and invasiveness. The goal of this project is to train a model intended to diagnose AD through the use of immunological biomarkers taken from blood samples - making diagnosis less invasive and less costly.

Diagnosis Now

Currently, two techniques can be used to diagnose AD:

- PET scan imaging [3]
  - Detects Amyloid-β42 plaques in brains
  - Cons: costly (up to €7000); radioactive tracer use
- Lumbar puncture [3,7]
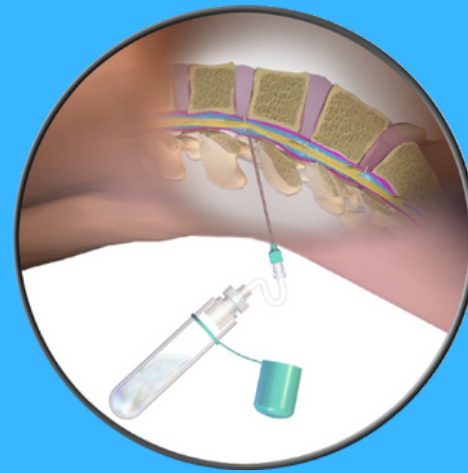 - Detects Aβ and p-Tau in Cerebral Spinal Fluid
  - Con: invasive

Figure 2: Lumbar Puncture Procedure. [b]

Established Biomarkers

- amyloid-β42 (Aβ42) [4]
- phosphorylated-tau protein (p-Tau)
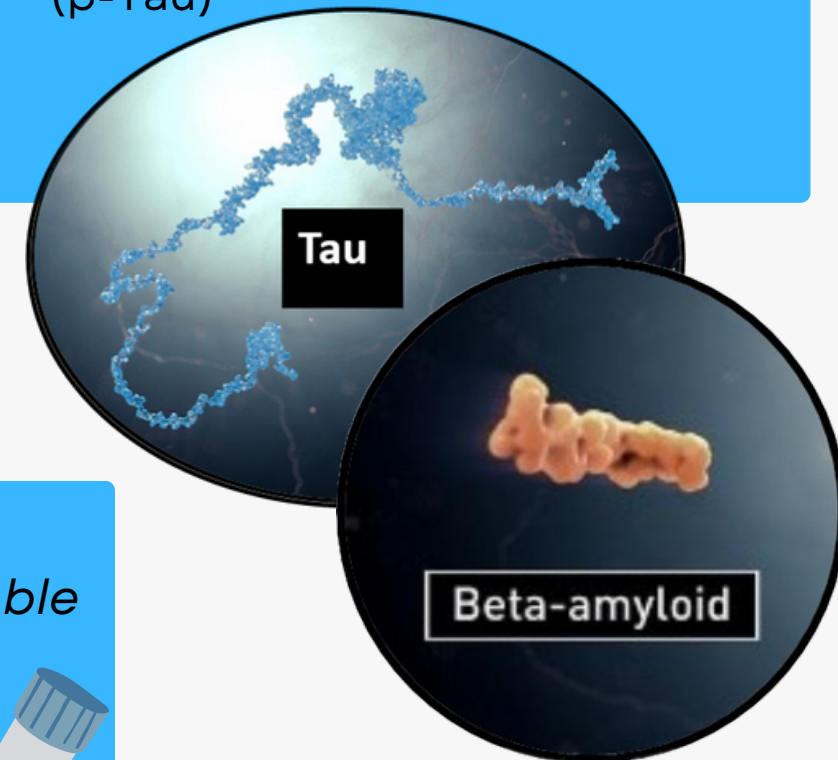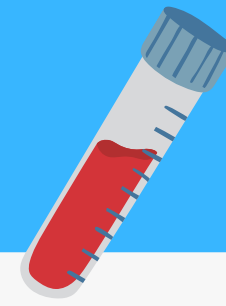
Tau

Beta-amyloid

Figure 3: B-amyloid and Tau protein models. [c]

Our Solution

Create a more cost-effective, less invasive, and interpretable diagnostic method

- Make use of blood samples
- Identify immunological proteins involved in AD
- Train an algorithm for AD diagnosis with these proteins

Figure 1: Cardiovascular and Nervous Systems superimposed. [a]

Research plan

Objective 1: Data Collection

- Blood sample collection and analysis
- Use LC-MS for molecule identification
- Calculate their concentration

Objective 2: Data Validation

- Preventing false positive in objective 1
- Use of ELISA

Objective 3: Machine Learning Model

- Utilize Logistic Regression for its clarity and cost.
- Benchmark with tau and amyloid-β42 markers.
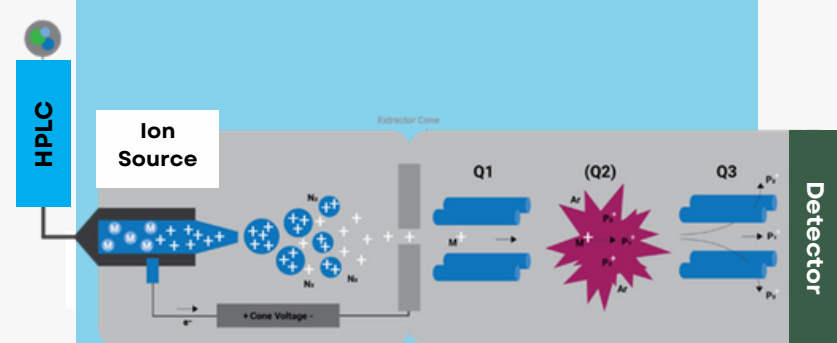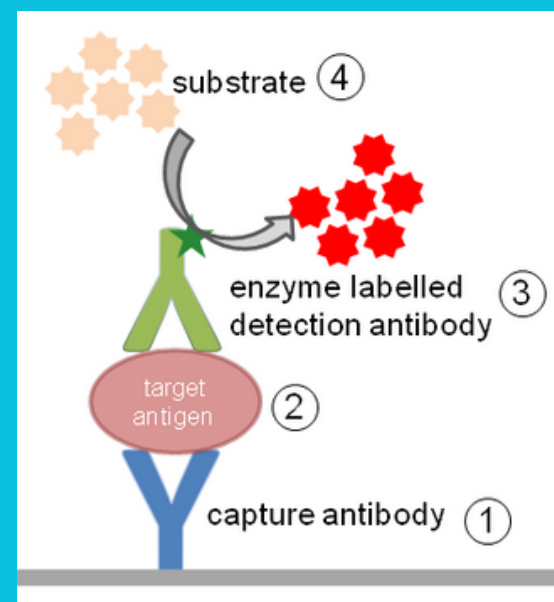- Analyze importance of immunological markers for future research directions.

Recruit Participants

Figure 4: Diagram of LC-MS machine. [d]

substrate ④
enzyme labelled detection antibody ③
target antigen ②
capture antibody ①

Figure 5: Sandwich ELISA method. [e]

Y-axis / X-axis

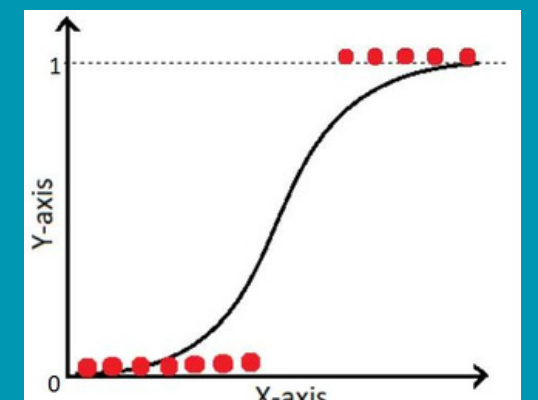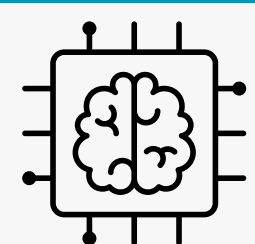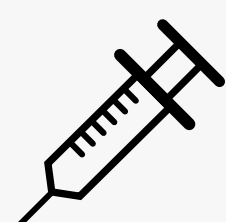**Figure 6:** Logistic regresssion. [f]

References

Innovation

Identifying immunological biomarkers in AD could point to the root cause of the disease.
This method will be less invasive than a lumbar puncture.
Taking blood is less expensive than PET scans.