

# A BACKGROUND ON ALZHEIMER'S

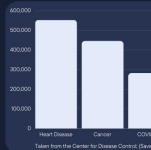
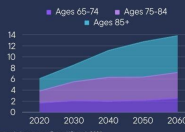


As of 2023, an estimated **6.7 million** Americans age 65 and older suffer from Alzheimer's.

In other words, about **1 in 9** people age 65 and older are diagnosed with the disease.

Taken from the Alzheimer's Association, Alzheimer's Association, 2023.

By **2060**, the population could grow to **13.8 million** barring the development of medical breakthroughs to prevent, slow or cure the disease (Alzheimer's Association, 2023)



Within the elderly population, Alzheimer's remains as the **fifth-leading cause of death** (Alzheimer's Association, 2023)

Taken from the Center for Disease Control, Global Health, Understanding Causes of Death, 2018-2022 Single Rank, (CDC 2023, 14)

"The vast majority of [Alzheimer's] studies have used a **'one-size-fits-all'** approach to targeting diet, exercise, and other lifestyle factors **without** accounting for **any** individual genetic variables." (Berezowitz et al., 2018)

As of 2020, Alzheimer's Disease has been considered a **WORLD HEALTH CONCERN**. (Bielzyk et al., 2020)

"Current therapies for Alzheimer's disease **do not** modify the course of the disease and **are not** universally beneficial." (Muller, 2018)



# Developing a Predictive Model to Compute the Progression of Alzheimer's Disease via a Neural Apoptotic Marker



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## APOPTOTIC MARKER RESEARCH

### Cytochrome C

- ◆ A special type of protein that is normally found in the *intermembrane space* (IMS) of mitochondria, released into the cytosol when the cell *initiates* apoptosis (Naniche et al., 2011)
- ◆ *Activates* caspases which *ideally* result in the definite event of cell death (Naniche et al., 2011)

VS.

### Caspases

- ◆ A type of *endoprotease* that plays a *major role* in the process of cell death (McIlwain et al., 2013)
- ◆ *Initiator*: Caspase -9 (McIlwain et al., 2013)
- ◆ *Executioner*: Caspase -3, -7 (McIlwain et al., 2013)
- ◆ A study conducted via the *HeLa cell line* deduced that caspase -3 *could not* accurately predict cell death vs. survival (Nano et al., 2023)

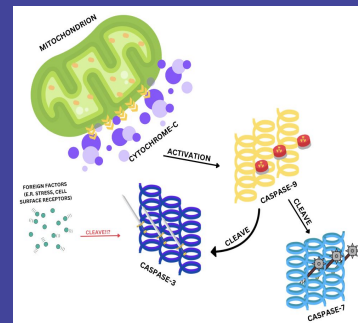


Figure 1. A diagram visualizing the interactions of Cytochrome C and the focused caspases in a cell body.

Take note of the foreign factors that could cleave caspase -3 instead.

The following model was created using a dataset of fMRIs of rats treated with **streptozotocin**, found through OpenNeuro.

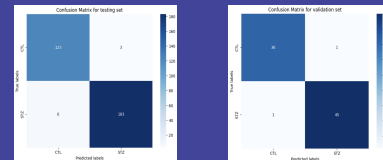
## MODEL RESULTS

### CLASSIFICATION (KNN)

Classification Report for testing set:					Classification Report for validation set:				
	precision	recall	F1-score	support		precision	recall	F1-score	support
CTL	0.95	0.98	0.96	126	CTL	0.97	0.97	0.97	32
STZ	0.98	0.97	0.98	189	STZ	0.98	0.98	0.98	46
accuracy				315	accuracy				83
micro avg	0.97	0.97	0.97	315	micro avg	0.98	0.98	0.98	83
weighted avg	0.97	0.97	0.97	315	weighted avg	0.98	0.98	0.98	83
Accuracy: 0.97					Accuracy: 0.98				
F1 Score: 0.98					F1 Score: 0.98				

Figure 2. Classification reports of the testing process (left) and the validation confirmation (right)

Figure 3. Confusion matrices of the testing process (left) and the validation confirmation (right)



### PREDICTION (PIXEL-BY-PIXEL ANALYSIS)



Figure 4. An example of a visualization of a slice of an fMRI scan of a rat treated with streptozotocin, through pixel-by-pixel color value metrics

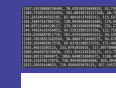


Figure 6. Example snippet of raw fMRI pixel-value data, obtained through the NIBabel library.

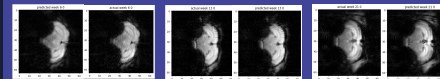
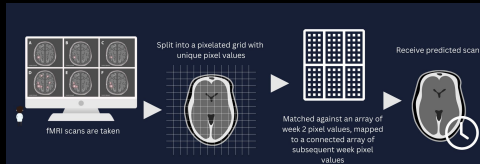


Figure 5. Actual fMRI scans compared to the model's prediction over the course of 6(left), 13(middle), and 21(right) weeks.



## ANALYSIS

### Classification

- ➔ Achieved a **significant** accuracy of **97%** for the testing data
- ➔ Achieved an accuracy of **98%** for the **validation** set
  - ◆ **Highly** reliable, could pose to be a **new tool** in regards to *diagnosis in medical settings*

### Prediction

- ➔ Image comparison score (comparing pixel values in actual vs. predicted arrays) achieve **similarity of 95%**
  - ◆ **Monumental** in **bioinformatics**
    - Pixel-by-pixel analysis is a **first** for *prediction* in a medical setting

## DECISION MATRIX

Criteria	Lvl	Weight	Created Model	Existing Methods
Differentiation between Stages	9	4	8	8
Early Detection	8	3	9	5
Informational Capability	10	4	8	6
Convenience	6	2	9	6
Reliability	7	3	7	9
TOTAL			130	110

## FUTURE STEPS

- ➔ Specificity: Obtain the apoptotic marker activation fMRI dataset to allow for a **higher level of precision medicine**.
- ➔ Establish significance further: Gain **public approval** in the medical field by ascertaining the model's **adequacy and practicality**.

➔ Doctors **do not** have access to enough information to create precision treatment plans.

➔ This project aimed to use **apoptotic marker activation** detected by **fMRI scans**.

- ◆ Conversations with **Dr. Nils Henning** of UMass Chan resulted in a realization of the **difficulty** in obtaining these scans given the timeframe.

## THE GOAL

- ❑ Establish a deeper understanding of **apoptotic markers** and choose likely candidates for further exploration
- ❑ Create a working **classification and prediction** model trained on **general fMRI scans**, optimizing for a **≥90% accuracy**.