NeuroPET-M: A Multimodal PET Scan Platform as a Novel Diagnostic Tool for Neurodegenerative Diseases

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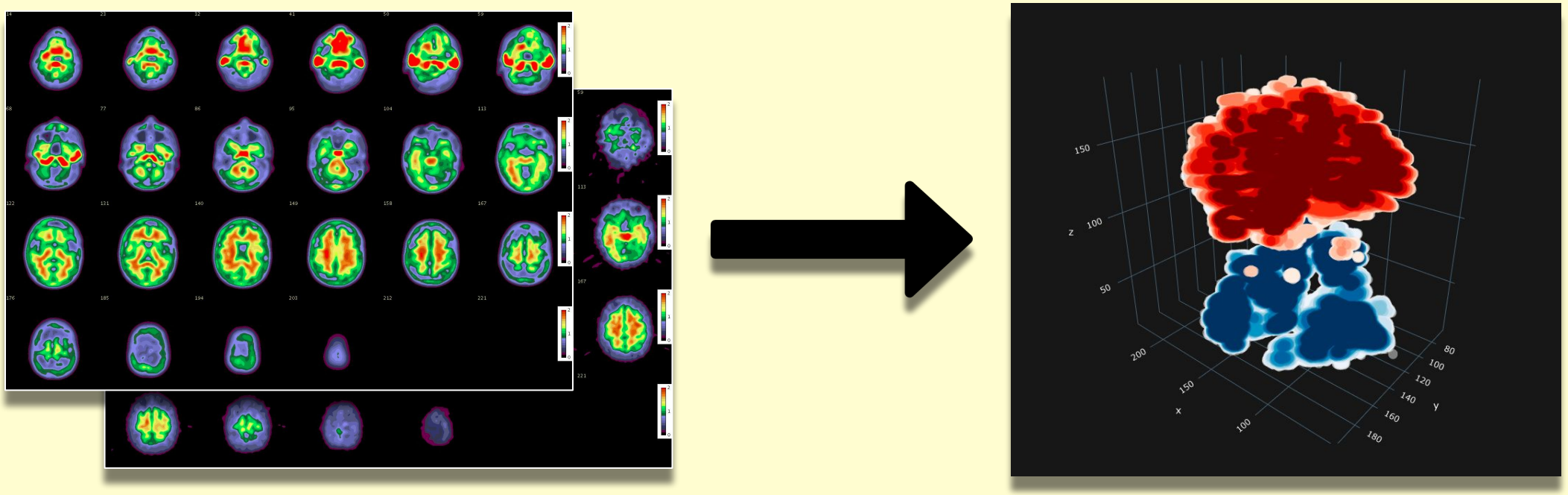


Introduction to the Current Medical Diagnosis Procedure

Neuroimaging is a powerful technique to study i) **brain function**, ii) **mechanisms of brain diseases** and iii) **to diagnose neurodegenerative diseases**.

- In this regard, **positron emission tomography** (PET) is a powerful imaging technique which enables **in vivo examination of brain function** and **disease diagnosis**.
- Neurodegenerative diseases can be diagnosed by **PET scans** of patient's brain region to **detect** and **diagnose complex brain diseases** such as Alzheimer's disease.

While diagnosing complex brain diseases such as Alzheimer's disease, there are numerous factors involved in the disease pathology such as i) **brain amyloidosis**, ii) **tau accumulation**, iii) **neuroreceptor changes**, iv) **metabolism abnormalities**, and v) **neuroinflammation**.

- Analysis of PET scans can provide **evidence** of abnormal biochemistry in the brain
- Physicians and/or neurologists will use this **evidence** to **predict** and **diagnose** neurodegenerative diseases such as AD for early detection
- This procedure is **inefficient** when there are **numerous** biomarkers analysed

Biological target	Radiotracer	Findings
Amyloid deposition	[^{11}C]PIB	Increased retention
Tau pathology	[^{18}F]T807	Increased retention
Glucose metabolism	[^{18}F]FDG	Low uptake
Neuroinflammation	[^{11}C]PK11195	Increased retention

PET Imaging signatures in Alzheimer's disease

Introduction to the Engineering Problem Statement & Goal

Engineering Problem Statement:

Since PET scans are primarily used to study a **single** biomarker at a time and is one of the most **versatile methods** of neuroimaging and yet its full potential has not been realized to study and **diagnose multiple biomarkers** in the 3D brain.

The **engineering problem** that *NeuroPET-M* aims to solve is that: current PET-based neuroimaging is limited to a **unimodal** technique, which prohibits the ability to **diagnose complex brain conditions** with multiple biomarkers, such as **bipolar disorder**.

Currently, a mental health professional diagnoses bipolar disorder based on their observation of symptoms, which can be **biased** or **inaccurate**. *NeuroPET-M* aims to solve this **problem** so there is **less of a margin of error** and **earlier accurate diagnoses**.

There has been **little to no work** reported on combining PET scans, and my research project will open up a new chapter in medical diagnostic procedures.

Engineering Goal:

1. To **visualize** the location of multiple (two or more) **biomarkers** in the brain through a **software application** that takes a set of patient's **PET images** as input and relays a **widget** consisting of a **3D interactive brain output**.

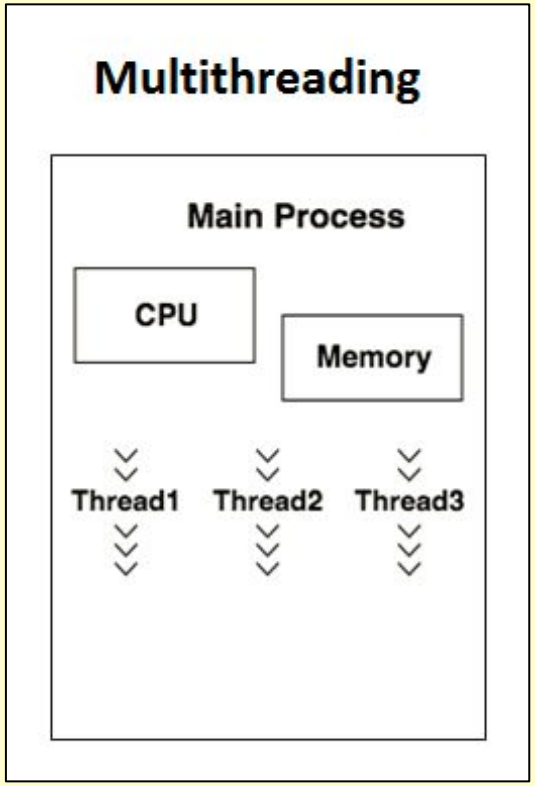
Design Criteria & Concepts Utilized & Optimization

Design Criteria:

- The proposed software platform will be a **modularized, object-orientated, lightweight** program in **terms of time and memory**, and **user friendly** to any end user (eg: physicians or nurses or nuclear medicine technologists).

Concepts Utilized:

1. Multithreading in Python (concurrent.futures library)
2. Cython (Superset to the Python programming language)
3. Image Processing in Python (OpenCV library)
4. Data Visualization in Python (Plotly library)
5. Colour Difference (Red Mean Euclidean method)



Optimization & Runtime:

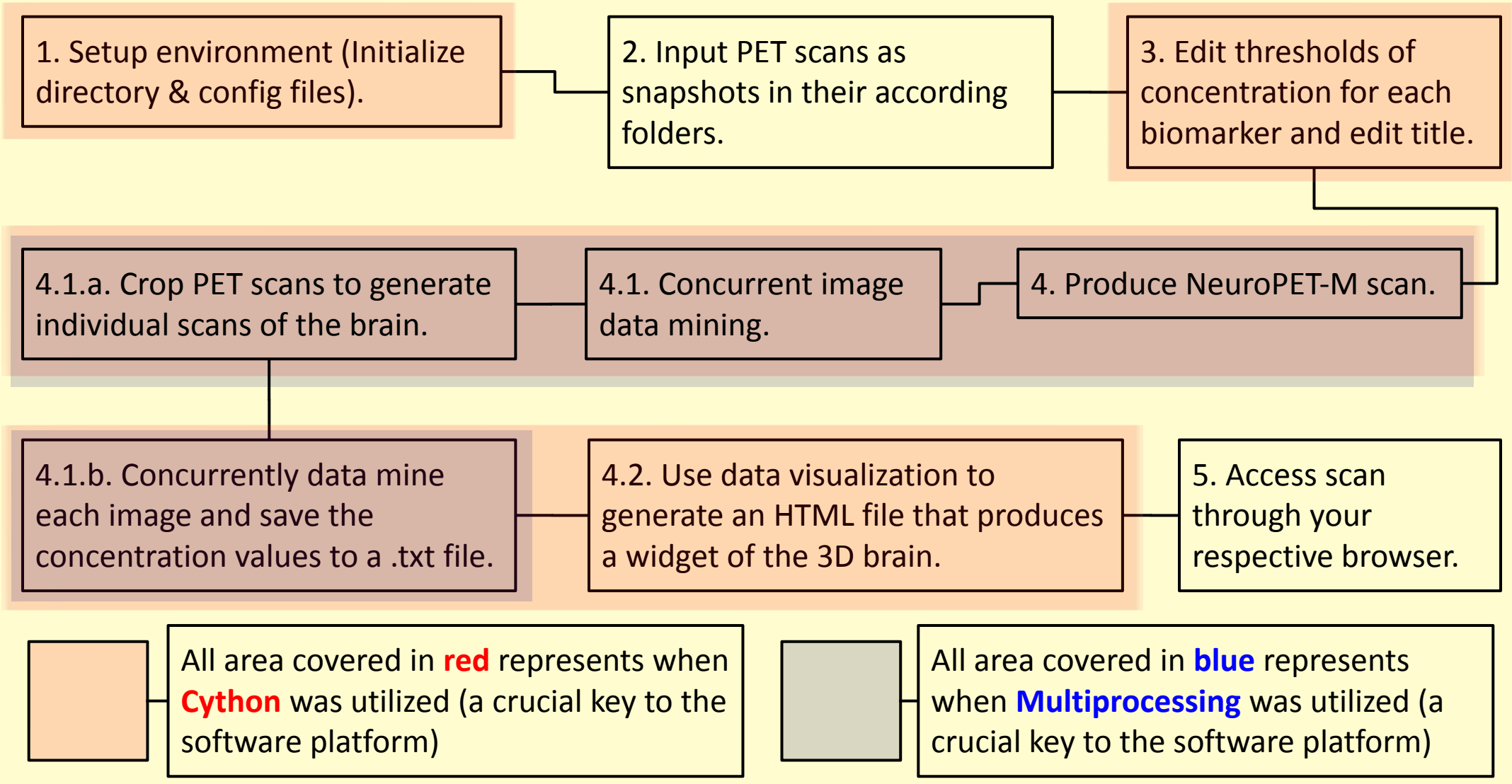
Before NeuroPET-M was optimized to the core, the average runtime was approximately **50 000 minutes per biomarker**. After multiple optimized software platforms and variations, the current version of NeuroPET-M has an average runtime of approximately **2 minutes per biomarker**. With the beauty of the concepts listed above, the average runtime was decreased by approximately **99%.**

Important Concepts Utilized Cont'd

The table below outlines the importance of five concepts utilized in this project, to achieve the goal.

Concept	Importance of Concept Explained
Multithreading in Python	- allows the program to utilize the hardware of the client to perform multiple tasks concurrently - used to concurrently process through multiple PET scans to optimize the software program - some memory will be sacrificed for each thread created in the main process.
Cython	- was used to attain more than 30 times speedup on the initial code - allows us to write Python-like code which gets translated into C/C++ code - when paired with multithreading, our initial program receives a monumental speedup
Image Processing in Python with OpenCV	- required library that was used for image processing - ability to extract the RGB values of pixels on a set image - was crucial towards when we iterated through each pixel in an inputted PET scan
Data Visualization in Python with Plotly	- another crucial library that was used for data visualization of the multimodal PET scan - allows us to plot points onto the 3D coordinate system - view the graph on a widget that can be accessed with any browser
Colour Difference	- was used to calculate the concentration of a biomarker given a RGB value - calculating the colour difference allows us to extrapolate important information from the PET scan - information such as the levels of radioactivity through the gradient of colour on the scan

Flowchart & Step-by-Step Procedure

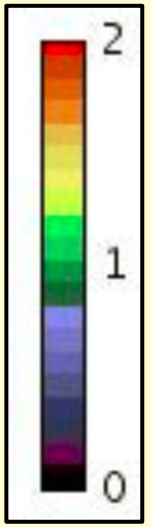


PET Scan Analysis & Testing Procedure

PET Scan Analysis:

The **input** consists of a set of **2D PET scan data** of **multiple** biomarker locations in the brain.

- In practice, brain PET scan outputs generated from the computer software are displayed either as a horizontal or vertical cross section of the brain.



The location of biomarkers is mapped onto the **3D plane** based on the **radioactivity** observed. A **colour coding scheme** is used to interpret the radioactivity levels in the brain.

The image data mining of brain PET scans will be conducted by measuring the location of the biomarker and the **gradient of colour** at that location.

This will be quantified to correlate with concentration levels of biomarkers and/or neurotransmitters with a comparison of healthy PET scan data. To conclude, this information will be used by **mapping the localizations of each biomarker** into 3D space, this is the **output**.

Testing Procedure:

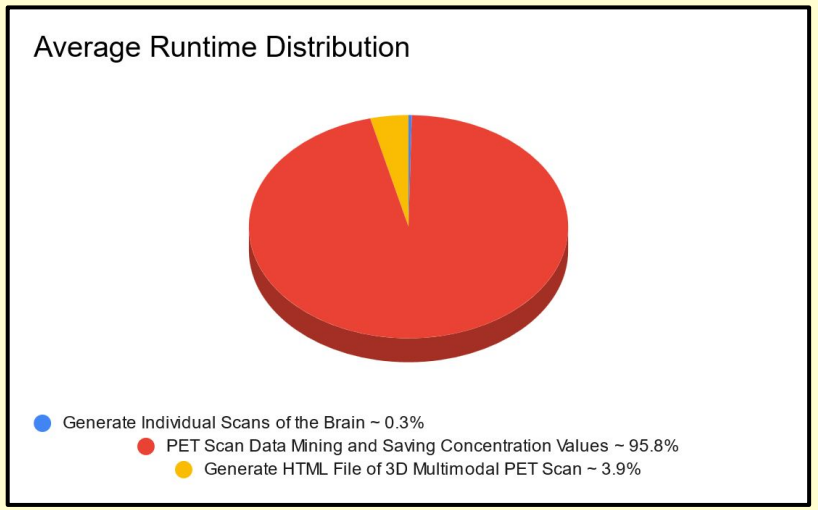
To test the **validity** and **functionality** of the software platform, a dataset of 2D PET scan data from Open Access Series of Imaging Studies (OASIS) Brains was received. The software platform ran on **seven** different snapshots five different times. Shortly after, a table of testing was created representing the runtime of each trial for each snapshot. Lastly, the average runtime for a dataset with **two different biomarkers** with **threshold values of 1.5 to 2.0**, was ≅ **3.6 minutes**.

Results: Prototype & Statistical Analysis of Data

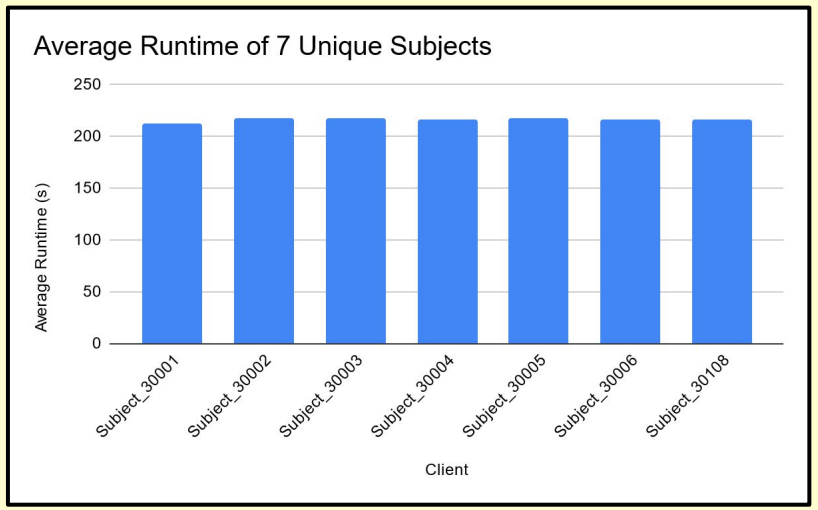
The **prototype** achieves the initial engineering goal and successfully visualizes the location of multiple biomarkers in the brain through a widget consisting of a 3D interactive brain.

Statistical Analysis of Data:

- average runtime of the software platform is ≅ 216 seconds, 108 seconds per biomarker
- standard deviation is ≅ 3.9 s
- runtime distribution is as follows i) Generate Individual Scans of the Brain ≅ **0.3%**,
  ii) PET Scan Data Mining and Saving Concentration Values ≅ **95.8%**,
  iii) Generate HTML File of 3D Multimodal PET Scan ≅ **3.9%**



Graph representing the Runtime Distribution of each process



Graph showing the Average Runtime of different subjects

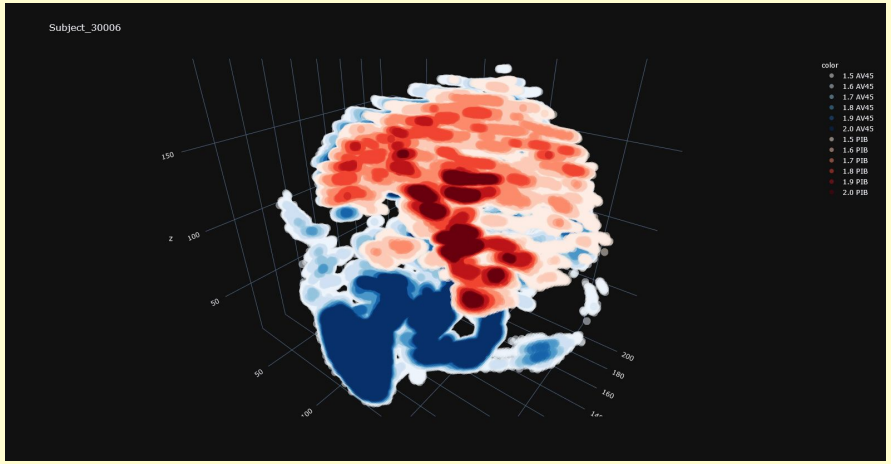
Produced PET Scan
Subject_30001
Subject_30002
Subject_30003
Subject_30004
Subject_30005
Subject_30006
Subject_30108

Hyperlinks to produced PET Scans

Discussion: Interpretation of Results & Improvement

Interpretation of Results:

- the proposed software platform is highly efficient, 99% faster than the naive approach
- the ability to study PET images by combining multiple PET scans enables further analysis in disease diagnosis advancing the field of neuroscience
- the most time-consuming segment of the algorithm entails in the image data mining portion, ≅ 95.8%



Produced 3D Multimodal PET scan from Subject_30006

Improvement:

- in comparison to the first iteration of *NeuroPET-M*, there is a drastic improvement in runtime and quality of visualization of the 3D brain
- currently, diagnosis of neurodegenerative highly depends on PET scans and the ability for the client (doctor or neurologist) to visualize multiple 2D PET scans
- due to the novelty of *NeuroPET-M*, clients no longer need to depend on their visualization skills, but can view the localization of biomarkers on this novel platform
- unique compatibility of HTML files allows clients to share new findings amongst each other

Conclusion: Reflection & Next Steps

Reflection:

The table below summarizes the comparison between the expectations four months ago, when this project began and the current state of the project.

Expectations	**Current**
The process of image data mining through multiple sets of PET scans would be efficient such that the runtime and memory usage is adequate in a practical environment (lab, hospital, etc.)	- image data mining exceeded expectations with a runtime of *108s * number of biomarkers* - memory usage is above expectations due to the immediate access of threads in each CPU
A 3D multimodal PET scan would be generated with ease of access and the ability to distinguish between different biomarkers.	- data visualization was genuine with a colour gradient associated to each biomarker - ease of access is high (e.g. HTML file is accessible)
Evidence will be presented such that we can view the abnormalities in biochemistry in certain brain regions, leading to proper and easier diagnosis.	- abnormalities are easily distinguishable meeting expectations - evidence is presented with many tools guiding diagnosis

Next Steps:

A self-diagnosis tool that studies the localization of biomarkers and predicts the chances of a specific neurodegenerative disease to occur, lifting the weight off doctors and neurologists.

Conclusion: Applications

Applications:

The table below outlines the four applications that this disruptive innovation can immediately be implemented in both the research and practical field.

Application	**Further Information regarding Application**
Allows researchers to study and create biomarkers for complex conditions such as bipolar disorder.	Many complex conditions involving the brain lack biomarkers for diagnosis, resulting in inefficient and inaccurate diagnoses from doctors. Researchers will utilize *NeuroPET-M* to create biomarkers by comparing PET scans from patients to non-patients.
Enable the development of open access PET scans used to the location of multiple biomarkers.	Similar to the application above, NeuroPET-M can be utilized to discover new localizations of biomarkers to advance the field of neurology. Researchers can utilize this tool to properly visualize and note discoveries regarding the location of neurotransmitter sites, specific proteins, and neurochemicals in certain brain regions.
Practical usage at hospitals for an earlier and more accurate diagnosis to aid lives suffering from neurodegenerative diseases.	The current medical diagnosis procedure has been proven to be inefficient and lacklustre in terms of accurate diagnoses. NeuroPET-M hopes that hospitals will use this tool to predict and diagnose diseases at high accuracy. This tool will also eliminate the need to properly visualize the brain, and instead allow the client (doctors or neurologists) to make accurate notes and diagnoses.

References & Acknowledgements & Extra Material

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Extra Material

Video Demonstration