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

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## ABSTRACT

The current medical diagnosis procedure for neurodegenerative diseases utilizes neuroimaging, and more specifically, PET scans. However, the constant analysis of PET scans by doctors will provide evidence to diagnose diseases such as Alzheimer's disease. Since PET scans are primarily used to study a single biomarker at a time, this procedure becomes inefficient when there are numerous biomarkers analysed. This innovation examined the effectiveness of using an optimized approach with the aid and speed of technology whilst visualizing numerous biomarkers in the brain. A multimodal PET scan platform acting as a novel diagnostic tool was implemented to visualize the location of multiple biomarkers in the brain through a software application that takes a set of patient's PET scans as input and relays a widget consisting of a 3D interactive brain output. PET scans will be separated into individual brain scans and then processed through an algorithm which calculates the levels of radioactivity within each radiotracer located in the brain. This data will be quantified to correlate with concentration levels of biomarkers by comparison of healthy and unhealthy PET scans. This disruptive innovation has been optimized such that the time allocated to create a multimodal scan has been decreased by 99%, tallying up a total of 2 minutes per biomarker being analysed. There has been little to no work reported on combining PET scans, and this research project will open up a new chapter in medical diagnosis procedures. With the broad-spectrum of applications, this novel diagnostic tool will be able to decrease the margin of error and provide a surplus of earlier accurate diagnoses, ultimately introducing new technology and saving millions of lives.

## INTRODUCTION

**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.



***Figure 1:*** *A set of 2D PET Scans from one patient. Left (AV45 radiotracer). Right (PIB radiotracer).*

*Each PET Scan shows the affinity of each radiotracer to specific neurotransmitting sites in the brain.*

- PET scan outputs generated from the computer software are displayed either as a horizontal or vertical cross section of the brain
- Color coding scheme is used to interpret the intensity of radioactivity
  - Rainbow colours, with red representing the highest level of radioactivity and blue or violet or black representing low levels of activity

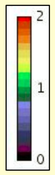



***Figure 2:***

*Colour scheme representing radioactivity levels.*

- PET Scans are primarily used to study a single biomarker one at a time
- They have recently become one of the most versatile methods of neuroimaging
- However its full potential has not been realized to study and diagnose numerous biomarker

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 |

## OBJECTIVE

The objective of this project is 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.

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).

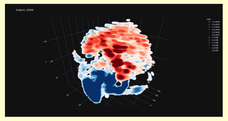


***Figure 3:*** *A visualization of the 3D brain through NeuroPET-M.*

## APPARATUS

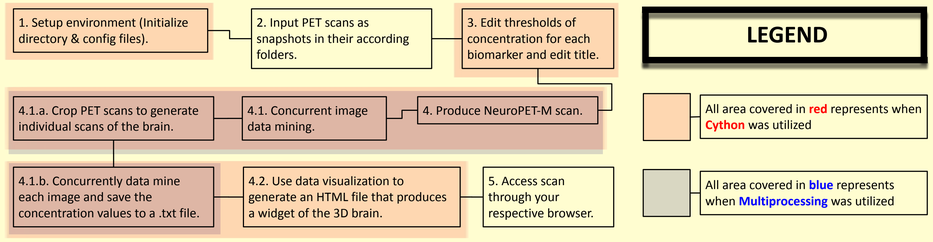
- A **workstation** with the following recommended specifications:
  - **Processor**: 3rd Generation Intel® Core™ i7-3520M (3.60 GHz, 4MB L3, 1600MHz FSB), or later generations
  - **Operating System**: Windows 8 (64-bit or 32-bit) and **higher generations** or any Linux distro
  - **Memory**: 4GB or higher is acceptable
  - **Storage**: 128GB SSD or higher is acceptable
- A **data set** of brain PET scan images obtained from **healthy volunteers** and **patient samples** available from publicly available resources
- An **internet connection** with (at minimum) 25 Mbps for download speed and 5 Mbps for upload

## CONCEPTS USED FOR OPTIMIZATION OF THE APPLICATION

| Concept | Importance of Concept Explained |
|---|---|
| **Multithreading** | • allows the program to utilize the hardware of the client to perform multiple tasks concurrently<br>• used to concurrently process through multiple PET scans to optimize the software program |
| **Cython** | • allows us to write Python-like code which gets translated into C/C++ code<br>• when paired with multithreading, our initial program receives a monumental speedup |
| **Image Processing** | • ability to extract the RGB values of pixels on a set image<br>• was crucial towards when we iterated through each pixel in an inputted PET scan |
| **Data Visualization** | • allows us to plot points onto the 3D coordinate system<br>• 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<br>• allows us to extrapolate the levels of radioactivity through the gradient of colour on the scan |

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%.**

## FLOWCHART WORKFLOW & STEP-BY-STEP PROCEDURE




## RESULTS & ANALYSIS

### Prototype Validation:

- 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%

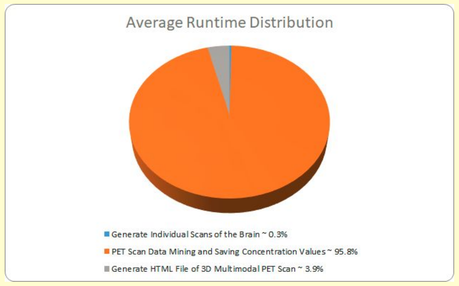



***Figure 4:*** *Graph representing the runtime distribution of each process*

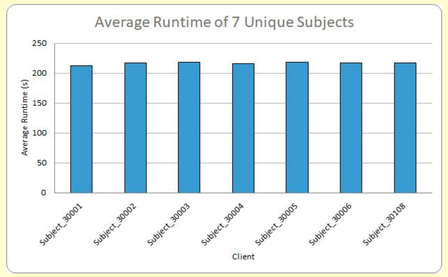



***Figure 5:*** *Graph showing the average runtime of different subjects*

## RESULTS & SNAPSHOTS OF PRODUCED SCANS

- The following snapshots are produced NeuroPET-M Scans from a publicly available dataset provided by the Open Access Series of Imaging Studies (OASIS) Brains

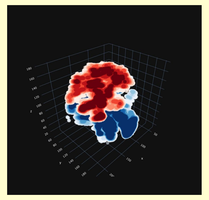


***Figure 6.1:*** *Snapshot of Subject_30001*

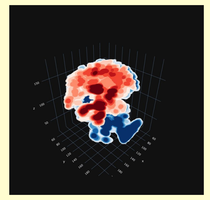


***Figure 6.2:*** *Snapshot of Subject_30002*

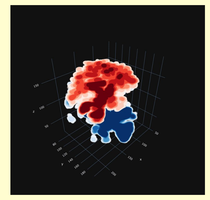


***Figure 6.3:*** *Snapshot of Subject_30003*

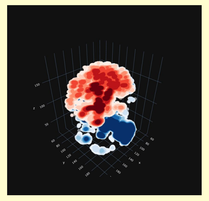


***Figure 6.4:*** *Snapshot of Subject_30004*

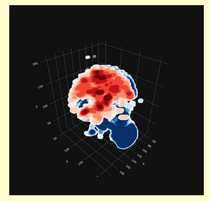


***Figure 6.5:*** *Snapshot of Subject_30005*

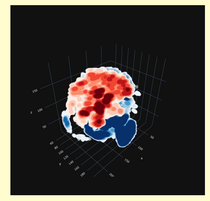


***Figure 6.6:*** *Snapshot of Subject_30006*

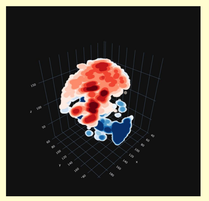
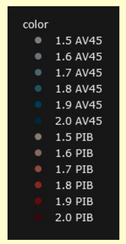


***Figure 6.7:*** *Snapshot of Subject_30108*




- in comparison to the first iteration of NeuroPET-M, there is a drastic improvement in runtime and quality of visualization of the 3D brain
- unique compatibility of HTML files allows clients to share new findings amongst each other
- 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

## CONCLUSION

- 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.)
- A 3D multimodal PET scan is generated with ease of access and the ability to distinguish between different biomarkers
- Evidence will be presented such that we can view the abnormalities in biochemistry in certain brain regions, leading to a proper and easier diagnosis

## RELEVANT APPLICATIONS

- Allows researchers to study and create biomarkers for complex conditions such as bipolar disorder
- Enable the development of open access PET scans used to the location of multiple biomarkers.
- Practical usage at hospitals for an earlier and more accurate diagnosis to aid lives suffering from neurodegenerative diseases.

## 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.

## ACKNOWLEDGEMENTS

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