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

By Aditya Keerthi

Objective

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**. 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**.

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 that enables **in vivo examination** of **brain function** and disease diagnosis. PET scans help neurologists to **visualize** the brain's biochemical levels by injecting a radioactive tracer. Radioactive tracers are essentially molecules that are labelled with a **positron-emitting isotope** that have an **affinity** toward neurotransmitter sites, specific proteins, and neurochemicals in certain brain regions. A PET scan can **project** the brain areas where the radioactive tracers can bind, which results in **producing an image** that presents the location and concentration of the neurotransmitters or proteins of interest.

Neurodegenerative diseases can be **diagnosed** by PET scans of a patient's brain region to detect and **diagnose diseases**. While diagnosing **complex brain diseases** such as Alzheimer's disease (AD), there are **numerous factors** involved in the disease pathology such as brain amyloidosis, tau accumulation, neuroreceptor changes, metabolism abnormalities and neuroinflammation. Analysis of PET scan images provides evidence of **abnormal biochemistry** in the brain. Physicians and Neurologists can use this evidence to predict and diagnose **neurodegenerative diseases** such as AD for **early detection**.

Depending on the disease state, **multiple biochemical changes** can happen in the brain. PET scans are primarily used to study a single **biomarker** or **neurotransmitter** at a time and are one of the **most versatile techniques** and yet its full potential has not been realized to study and diagnose multiple biomarkers and neurotransmitters in the brain. I am proposing a **novel software platform** called "NeuroPET-M" which will **optimize** PET-based neuroimaging by providing a **ground-breaking diagnostic tool for neurologists**. In theory, the process would require a set of multiple PET scans for different **biomarkers** and create an **interactive three-dimensional space** of the **patient's brain**, mapping **multiple biomarkers** and **neurotransmitters** in the brain. 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.

Relevant Application

There are **three main applications** that this **disruptive innovation** can immediately be implemented in both the research and practical field:

1) It will allow 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.

2) It will 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.

3) It can be implemented in **practical usage** at hospitals for an earlier and **more accurate diagnosis** to aid lives suffering from neurodegenerative diseases. 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**.

Experimental Design

The main design criteria for the proposed software platform is that: it 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).

However, there were multiple concepts that were utilized to **optimize** the software platform such that it meets the design criteria:

1. Multithreading in Python
    1.1. used to concurrently process through multiple PET scans to optimize the software program

2. Cython
    2.1. allows us to write Python-like code which gets translated into C/C++ code

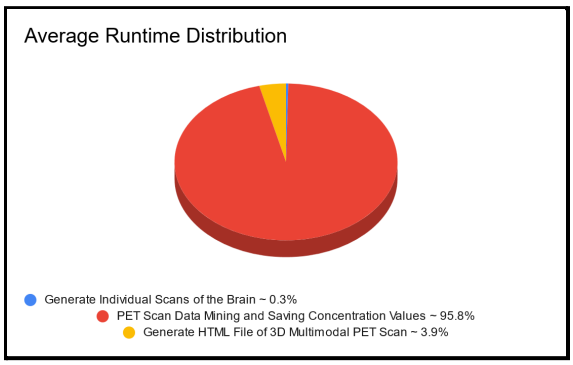
3. Image Processing in Python with OpenCV
    3.1. ability to extract the RGB values of pixels on a set image

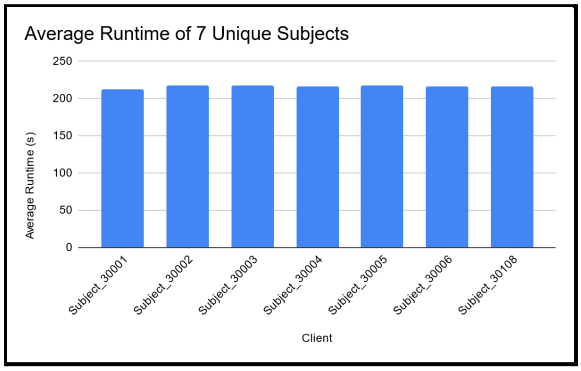
4. Data Visualization in Python with Plotly
    4.1. used for data visualization of the multimodal PET scan

5. Colour Difference
    5.1. used to calculate the concentration of a biomarker given a RGB value representing the levels of radioactivity of that specific biomarker

Results and Interpretation

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%**.



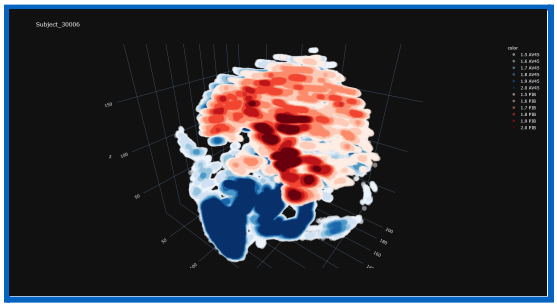


The average runtime distribution of the software program is as follows:

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%

A list of hyperlinks of each produced NeuroPET-M Scan:

Subject_30001, Subject_30002, Subject_30003, Subject_30004, Subject_30005, Subject_30006, Subject_30108.



Appendices

Materials:

- 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.

The main procedure that each client (doctors or neurologists) follows is very straightforward and minimalistic:

1) Setup environment (initialize directory & config files)
2) Input PET scans as snapshots in their according folders
3) Edit thresholds of concentration for each biomarker and create a title
4) Produce a NeuroPET-M Scan
    a) Concurrent image data mining
        i) Crop PET scans into individual scans of the brain
        ii) Concurrently data mine each image and save concentration values
    b) Use data visualization to create an HTML file that produces a widget
5) Access scan through your respective browser

Timeline of Project

Approximately 4-months will be used to complete this proposal. The first month (November/December) will be used to conduct a thorough literature review related to the project and another three months (December to March) will be used to design, develop and optimize software platforms and to document the results obtained.

Mentorship Support

I would like to give very special thanks to my mentor, Doctor Praveen Nekkar Rao and my supervising teacher, Matthew Klis for providing superb mentorship throughout this project.

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