Research Proposal: Monitoring optimization of Artificial Neural Network stability undergoing modelled neuroplastic effects of serotonergic psychoactives

Furaha, Damien
McGill University

Michael, Phelan
McGill University
{furaha.damien, michael.phelan2}@mail.mcgill.ca

Abstract

This research article proposes a possible framework for the exploration of the network effects of serotonergic drugs in the central nervous system. In particular, we explore how previous work done by Zenke et. al[1] can be leveraged to model neuroplasticity under the effects of common psychoactive substances. This would first be performed by mathematically modelling the pharmacodynamic effects of psychoactives with regards to spiking neural network plasticity, then by experimenting with network behaviour before and after this modification. Finally, we expand upon the cognitive and behavioural changes that are experienced in human neural networks and compare with the network behavioural of our artificial neural networks.

1 Introduction

In the past, several research groups[2] have explored the area of serotonergic psychoactives and their impact on different neurological pathways, including neuroplasticity. In a similar theme, there have been a number of studies that have looked at creating mathematical and computational algorithms that model the learning process in the human brain[1]. In recent research and industry, there is increased interest in using serotonergic psychoactive chemicals for treatment of various mental illnesses, including depression[3]. Thus, we propose to study the effects of psychoactive drugs on the central nervous system using modified artificial neural network models of plasticity.

1.1 Supporting topics

1.1.1 Neuroplasticity and Neurobiology of serotonergic Psychoactives

Neuroplasticity can be seen as the ability of a given network (typically biological) to grow and rearrange the connections between its nodes. Serotonergic psychoactives, including Lysergic acid diethylamide (LSD), N,N-Dimethyltryptamine (DMT) and Psilocybin are proposed in related literature [4] to have active effects on the neuroplastic ability of certain neurons.

Many studies have looked at the impact of psychoactive drugs on different pathways in the brain. Calvin Ly, et al.[4] observes that Psychedelics promote plasticity via evolutionary conserved mechanism and that 5-HT2A signalling underlie psychedelic-induced plasticity. They observe that structural changes induced by psychedelics result from the stimulation of 5-HT2A signalling pathway. Moreover, these researchers, as well as many current media markets, propose that there is therapeutic potential of psychoactive drugs in treating depression and related disorders, particularly due to the neuroplastic effects of these molecules.

1.1.2 Neural Networks as Biological Models

Biological neural networks were largely the inspiration for deep learning, the revolutionary machine learning framework that has led to an unprecedented interest and investment in artificial intelligence [5]. While the similarities in overall network theory exist, it is typically much easier to mathematically study and evaluate artificial neural networks (ANNs) than their natural counterparts, particularly at the neuronal level. Moreover, many researchers believe [6] that biological and artificial neural networks are subject to similar overarching rules in terms of computational ability, memory storage, network structure, etc. As such, in the absence of a complete analytical model for the human nervous system, many scientists have turned towards using ANNs as models of the brain [7]

1.1.3 Network Optimization

In traditional models of neural networks widely used in machine learning applications, a cost function is established with regards to a training objective that allows for network optimization via backpropagation [5]. However, our research aims not to create a learning machine, but to emulate the stabilizing network environment present in biological systems that has the ability to model memory formation and recall. Then, we propose to model how this network is affected in the events of exposure to serotonergic psychoactive drugs. To do this, we consider that networks subject to various homo-and-heterosynaptic mechanisms of neuroplasticity may have varying performance in their ability to:

1 - Produce a stable network
2 - Create and retain memories
3 - Minimize overall network activity

Thus we may establish cost functions with regards to the performance of our network that can create a comparative analysis for the scenarios with and without the addition of serotonergic drugs. In other words, our analysis seeks to view network performance in terms of meta-learning (or capability to learn), as opposed to performance on a particular learning task. Moreover, we seek to analyze network optimization when manipulated by serotonergic drugs, in order to abstract the potential network-level effects of these drugs in vivo.

1.2 Related work

Artificial neural networks can be represented as a composition of differential equations to give an output that models certain cognitive functions in the human brain. A similar application has been studied by Zenke, et. al [1] to help simulate the synaptic plasticity in the process of memory formation and recall. In their work, they present a mathematical model that uses a set of differential equations to combine both Hebbian and non-Hebbian plasticity in networks called cell assemblies. In the model, they show how using a combination of both hebbian and non-hebbian plasticty they are able to create a network that simulates a simplified model of learning and memory retention processes in the human brain. Our study aims to leverage the approach brought forward by Zenke, et. al[1] as a starting point for the simulation of artificial neural network exposure to serotonergic chemicals.

$$\Delta\omega_{ij}(\text{t}) =$$
$$A(pre)_j X(post)_i^2 - B_i pre)_j X(post)_i \text{ (i)}$$
$$- \beta X(\omega_{ij} - \omega'_{ij}(post)_i^4 \quad \text{(ii)}$$
$$+ \delta(pre)_j \quad \text{(iii)}$$

Zenke, et. al[1] model for memory recall and formation where (i) is Hebbian(STDP), (ii) is Heterosynaptic and (iii) is Transmitter-induced plasticity.

2 Proposal

2.1 Hypothesis

This proposal focuses on the ability of artificial neural networks to model biological neural network processes in the human brain. In particular, we expect that our model may be used to further understanding of serotonergic drugs on memory processing and learning, particularly in showing novel mathematical notions as to the network-wide effects of these chemicals and the resulting biological analogies.

2.2 Research Objectives

In developing experiments targeting the research objective, we hope to explore and progress the following topics:

2.2.1 Serotonergic drugs at the neuronal level

Before making network-wide conclusions, we must create a synaptic-level modification to our chosen artificial neuron model in order to represent the addition of serotonergic chemicals. We expect that a localized increase in modelled homosynaptic plasticity results from the chemicals. However, the drug is also subject to pharmacodynamic metabolism, thus representing a temporally decaying element in our model. In sum, our first tasks are to:
1 - Mathematically integrate the individual synaptic effects of serotonergic drugs into our network 2 - Include a biologically realistic decay element of the drug's influence in order to represent the temporal concentration of chemicals.

2.2.2 Network framework

Given that we aim to create test and control subjects for our research, it important that create a network model that looks at both networks simulating exposure to psychoactive and those that don't.

Thus, we want to first study how we can simulate the brain without any exposure to psychedelics. This is will hep us develop a control for all the resulting experiments in the study. As mentioned above, we plan to leverage one of the previous attempts at a similar topic, that of Zenke, et. al [1]. The idea is to develop this model further to encompass possible brain regions that are susceptible to psychedelics.

We would then use this analysis as a comparison with the serotonergic drugged network. Some questions of intrigue include how we will Combine Hebbian and non-Hebbian plasticity in the network? Will we have to add a Homeostasis plasticity term to the model? How will we determine optimal parameters and what will be the initialization parameters to begin with? Can we add new activation functions to the model in addition to the ones tried by the original authors? Does parameter tuning for different plasticity terms help/hurt the network? How do these drugs affect different plasticity mechanisms? If we are able to build a network simulation how does the exposure to drugs affect the stability of the network. Are we able to achieve a better fixed point in terms of various network efficiency parameters than the one(s) observed without drugs?

2.2.3 Repeating procedures for additional conclusions in diverse brain regions

Our study aims primarily to model the effect of serotonergic drugs in the hippocampus, in order to expand on behavioural and cognitive network effects on neuroplasticity. However, as an additional interest, we also propose modelling a diverse set of brain regions in order to compare and contrast different network morphologies. We predict that the changing distribution of inhibitory vs. excitatory synaptic connections, in particular, will result in significantly different network stability. Of particular interest is modelling certain distinct physical effects of serotonergic chemicals and determining if these effects are regulated by similar neuroplastic effects, or if they act via additional pharmacological mechanisms. Specifically, this would be in comparing cognitive and visual processes, two commonly distorted elements under human experiences of psychoactive drugs.

Moreover, as an additional point of research beyond the scope of this proposal, it would be of interest to model the brain-wide effects of serotonergic psychoactives via this same model. Much work has been done recently [8] in imaging these effects; we propose that it would be interest to develop a high-level network model to review communicative effects between diverse brain regions.

3 Research Plan

3.1 Experimental Tools

As earlier indicated, we intend to first reproduce the model that was developed by Friedmann Zenke, et. al [1]. This will give use a baseline for our research. The source code used to develop their network is open sourced on GitHub. Our aim is to use their source in the study. Given the licence of the software, we will be able to edit the source code to suit out experimental needs. This will allow us to easily scale the depth and the width of the network in the quest to achieve high accuracy. Give that we aim to explore other brain regions that were not looked at by their model, having their open-source code will allow us to easily add new terms to the model to simulate the unstudied regions and mechanisms.

Their source code is written in C++. This is very great for computational and time resource optimization of the network. However, this will mean that any additional libraries needed will have to be build from scratch by ourselves, To this end, we intend to re-write the model in Python. This is very key because there has been a lot progress in this field of the last few years and a lot of Python libraries have been develop to tackle the field of artificial neural networks. Re-writing the code in python will allow us to leverage those libraries if need be while retaining the benefit of being able to customize the model.

Given the computational requirements of building a model like this, the study will requires state of the art computational power provided by cloud computing vendors or physical Graphical Processing Units(GPUs). In combination with our move to Python, we also can leverage many different cloud environments with increased ease, including platforms such as Google Collaboratory.

3.2 Summary and Approach

In our study, we aim to model the impact of psychoactive drugs on the brain via the development of artificial neural networks. We thus divide our tasks into the following:

1 - Proposing a neural model analogous to desired brain region:
Firstly, we must develop a framework on which we may perform our analysis. In particular, we build off of Zenke et al. with focus to better model the hippocampus. This will primarily be performed through literature review, particularly in implementing a network and cell assemblies with more tailoring into how best to represent traditional physical systems affected in the hippocampus.

2 - Developing a baseline:
The overarching aim is to present a network defined by partial equations that can simulate learning, memory formation and recall in the brain in the presence of psychoactives. In order to do so, we must first establish a baseline set of experiments with which we may compare our research. In this section, we aim to extend Zenke et al.'s network for a vastly increased number of neurons as well as more realistic hippocampus cell assemblies (specific groups with higher initial co-weights, so as to form groups within the network) and stimulus patterns.

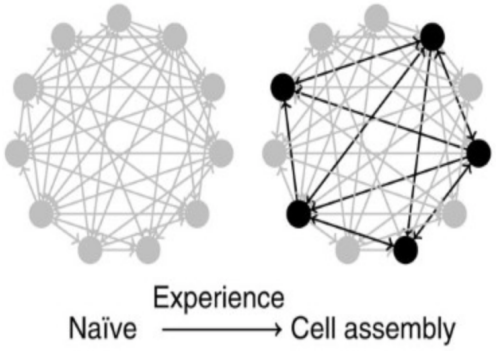

Figure 1: Artificial neural network
Zenke et al [1]

3 - Simulating adjusted neuroplasticity under the influence of serotonergic drugs:
This is also be performed through a literature review and experimentation with the network develop above. In particular, a pharmacodynamic approach will be taken to simulate exposure to the drug at various concentrations, then modelling the changes in neuroplasticity. Seeing as we expect some external instabilities in adjusting homosynaptic plasticity, we also propose a cyclical process to find the most realistic model for our network.

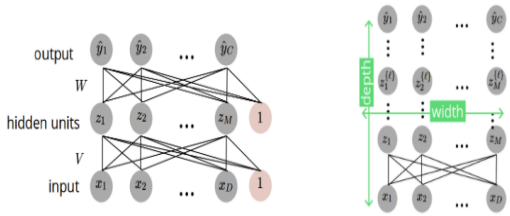

Figure 2: Artificial neural network[5]

The study will involve building an artificial neural network. The network will be such that in the hidden layers, the units will represent specific plasticity mechanism. This means that we can easily alter the activation function of the units to simulate different combinations of plasticity mechanisms. Scaling of the functions can also be done to ultimately silence or enhance a specific mechanism in the quest to simulate exposure to drugs.

Ideally, we hope that by carefully tuning the depth, learning rate and objective functions on units we can simulate plasticity mechanisms and consequently simulate the brains exposure to psychedelics.

3.3 Closing Notes

In pursuing this research, our goal is to simultaneously unearth the potential for artifical neural networks as models as drug activity in the central nervous system as well as specifically look at the effects of serotonergic drugs on neuroplasticity.

Overall, based on work of previous authors[9], we expect a higher instability in the networks overall, largely attributed to an decrease in neuroplastic organization. In other words, we expect the network to be less capable of sustaining initial cell assemblies. However, we also expect an increased time-to-stability as well as an increased ability to move between stable points.

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