PROFESSIONAL INTERNSHIP REPORT

Josué Pérez Sabater

100409398 · *josu.ps13@gmail.com*

Bachelor’s in Biomedical Engineering

Universidad Carlos III de Madrid

Neural Intelligence Systems Lab at Hanyang University

TABLE OF CONTENTS

DETAILS

Student

Name: Josué Pérez Sabater

NIA: 100409398

Contact: +34 607209428 / *josu.ps13@gmail.com*

Major: Bachelor's in Biomedical Engineering at Universidad Carlos III de Madrid

Company

Laboratory: Neural Intelligence Systems Lab at Hanyang University

Address: 222, Wangsimni-ro, Seongdong-gu, Seoul, Republic of Korea

Webpage: *https://www.anmokimlab.com*

Supervisors

Professional supervisor

Name: Professor Anmo J. Kim

Contact: *anmokim@hanyang.ac.kr*

Position: principal investigator

Other supervisors

Name: Sungyong Kim

Contact: *magicjet45@hanyang.ac.kr*

Position: graduate student

Internship

Period: from February 22nd, 2022 to July 26th, 2022

Schedule: 3 hours/day, Monday to Friday

Total number of hours: 330 (equivalent to 12 ECTS)

INTRODUCTION

During my biomedical studies at UC3M, I had the chance to learn about very diverse topics related to this field, such as medical image processing, biosensors and biomaterials, tissue engineering… However, spending my fourth year as an exchange student in Hanyang University (Seoul, South Korea) has provided me with the additional opportunity of exploring a new aspect of bioengineering not available in my home university: computational neuroscience. I assisted to the course Biomedical System Modeling imparted by Professor Anmo Kim, which focused on the use of differential equations and numerical methods as the basis to model the behavior of spiking neurons. Interested in this area, I talked to Prof. Anmo about the possibility of working as an intern in the laboratory he leads, Neural Intelligence Systems Lab (NISL). He accepted my proposal and put me in contact with Integrated PhD student Sungyong Kim, who has guided me during my work in the lab. The three of us agreed on the mission of my project, which consists on modeling a spiking neural network (SNN) and apply it to two different insect species, in order to study the differences in their behavior.

DESCRIPTION OF THE COMPANY

General description

The Neural Intelligence Systems Lab (NISL) combines the knowledge of three departments in Hanyang University: Biomedical Engineering, Electronic Engineering and Artificial Intelligence. With Prof. Anmo J. Kim as the lead investigator, this laboratory has the clear mission of understanding the neural circuit principles that govern sensorimotor systems in flying insects, with the aim of developing computational models that can be implemented in new engineering applications. In order to do so, the lab research focuses on reverse-engineering the brain of the fruit fly (*Drosophila melanogaster*), a widely recognized model organism. This insect species presents some impressive abilities regarding flight control, navigation and visual processing. Uncovering the underlying neural mechanisms responsible of these skills can help develop new algorithms with applications in predicted flight control, multimodal integration, object tracking and artificial olfactory sensors.

Activities

Hanyang's NISL has several projects that simultaneously work towards a common goal: develop computational models based on the complex circuit mechanisms of the fruit fly, and thereby bring new algorithms in visual processing and flight control with applications in man-made robots.

High-order visuomotor processing

There is an increasing industry around visual processing due to its useful applications in face recognition, full self-driving vehicles, medical image processing, etc. However, the simplest tasks such as recognizing people's expressions are not easy to accomplish, not even with the most state-of-the-art algorithms. Fruit flies dedicate over half of their brain to process visual cues from their surroundings and to respond to them. In NISL, research is done to understand how processes such as object tracking and avoidance, distance estimation, selective attention and more are represented in the neural circuits of the insect, and how the output is translated into a behavioral response.

Flight control via internal predictions

Flight abilities of the fruit fly are very impressive: they can make fast turns to avoid collisions, hover around a target and land on improbable places. All these flight maneuvers are possible thanks to the sensory feedback the insect receives from its visual system. However, research from NISL (*Nature Neuroscience, 2015* and *Cell, 2017*) has demonstrated that this input is modulated by internal predictions, which enable rapid flight turns. These internal predictions are being further studied in the laboratory, which aims to uncover the detailed mechanism that controls them.

Modeling brain-inspired predictive control

With the aim of developing new applications for man-made robots (such as unmanned air vehicles or the inverted pendulum), NISL is studying the "forward model" to predict sensory feedback caused by self-generated actions. The goal is to create a computational model of a mechanism that momentarily switches off the stabilization system and allows aggressive flight maneuvers, analogous to the internal predictions of the fruit fly.

Business model

The Neural Intelligence Systems Lab is a Hanyang University research facility that belongs to three different departments. As such, it receives part of its funding from the private finance of the university. The engineering departments are especially valuable not only within Hanyang University, but in all Korea due to their outstanding performance as a technological driving force (Electronic Engineering Dept.) and their efficiency in publishing peer-reviewed articles in high-impact factor journals (Biomedical Engineering Dept.).

Additionally, NISL receives financial support from two partners: the National Research Foundation of Korea (public) and the POSCO TJ Park Foundation (private). These organizations promote the nurturing of young talents in the fields of science and technology, and they support academic research infrastructures and strategic R&D projects with interest in the future of the country.

Strengths

When I first went to the laboratory, I noticed the diversity of students despite the relatively small facilities of the lab. Around a dozen people in total, NISL welcomes not only undergraduate, master's and PhD students, but also postdoc researchers and international students from exchange programs, as it was my case. Over a third of the people working in the lab during my stay were international, an indication of the open mindset of NISL. Thanks to this approach, the research facility can easily build ties with universities abroad.

Despite the short life of the research facility, several papers have been published by the lead investigator in important journals with high impact factor, such as *Nature Neuroscience*, *Journal of Neuroscience*, *Cell* and *Current Biology*. The publications focus on the mission of NISL and can be viewed as a result of the successful research progress made by the laboratory.

As I read in the laboratory blog, Prof. Anmo often organizes team-building activities outside of the University facilities, strengthening the relationships between members and creating a more comfortable and friendly atmosphere in the laboratory. Sometimes the lab members attend scientific conferences and meetings related to the work of NISL, where the achievements of the lab research can be showed to the public. Unfortunately, no activities were held during my stay in Hanyang University due to the restrictions imposed by the Government in relation to the global health crisis.

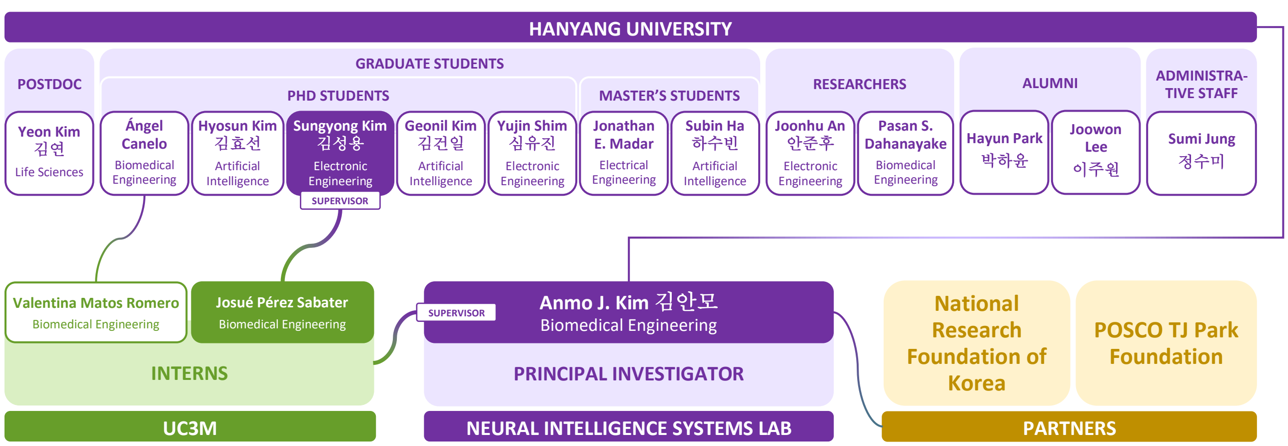
STUDENT TASKS

Description of the position

My project at NISL would be focused on the construction of a virtual network that simulates the spiking behavior of neurons in the central complex (CX) of flying insects. As an undergraduate research intern, I did not have any previous formation on computational neuroscience, which was essential for this task. Therefore, I first studied and commented some published papers related to the analysis of the CX and its modeling. Once I acquired the necessary knowledge, I started to build a spiking neural network based on the methods of the papers I had read, with the aim of reproducing the same results. Once the network was functional, my goal was to compare the CX of two insects (fruit fly and honeybee) and infer their differences in anatomy of the brain region, performance of the network and behavior of the real animals. An additional analysis consisted on adding noise to each connection to quantitatively measure their importance in the network.

Dependencies, interactions and responsibilities

Anmo Kim, leader of the laboratory NISL and associated professor at Hanyang University, was the tutor of my internship. However, he had a very tight schedule due to his several responsibilities and hence master's student Sungyong Kim acted as a closer supervisor of my work. Along my stay in the university, I had meetings with Sungyong (and often Anmo) in a regular basis in order to explain the progress of my work and receive feedback from them. I was lucky enough to work in a computer inside the facilities of the lab, where I could also meet the other research students at NISL. The organization chart below depicts the relationship between me and the rest of the members, highlighting the connections to my supervisors.



Input to the business model

My contribution to the laboratory is mostly represented by the usefulness of the MATLAB code I wrote during my internship. Near the end of my stay at the university, Sungyong revealed that the code could potentially help him on his own project, and he asked me to write a fully commented version so he could understand the complete script. Besides, my meetings with Sungyong were a great opportunity for both of us to practice our communication skills on English, and being my supervisor provided him with additional leadership skills. On top of that, the presence of foreign students in NISL is of great value for the laboratory since it strengthens ties between Hanyang and other universities or organizations abroad.

General objectives

The main objective of my internship was to learn the mathematical and programming tools to model a spiking neural network. This includes writing myself a MATLAB code containing the neural structure and connectivity of a brain region, simulate the input to the network and the response of the neurons to different stimuli, and display the results through meaningful graphs and visual representations.

I also improved my skills on research and bibliography evaluation through the study of papers published on the field and the investigation across scientific websites and other resources. Additionally, I acquired on the process some introductory knowledge about the biological structures of the brain, specifically the central complex of flying insects, and how to understand and examine the connections between neurons.

Lastly, I had the task of explaining the progress and results of my project to my supervisors through clear, concise presentations. To this end, Prof. Anmo organized several meetings throughout the internship period where I described the concepts I learned, the code I was developing and the results obtained, all with the help of PowerPoint presentations. As a result, I gained important skills on communication and delivery.

Student activities

Biological introduction

Since I did not have any background education on neuroscience, I started my internship with some literature review about the topic. As a first step, Sungyong compiled a short list of scientific papers related to the analysis of the central complex (CX) in different insect species.

Paper 1. Prueba Ioannis Pisokas, Stanley Heinze, Barbara Webb (2020). The head direction circuit of two insect species. *eLife*, 9:e53985. *https://doi.org/10.7554/eLife.53985*

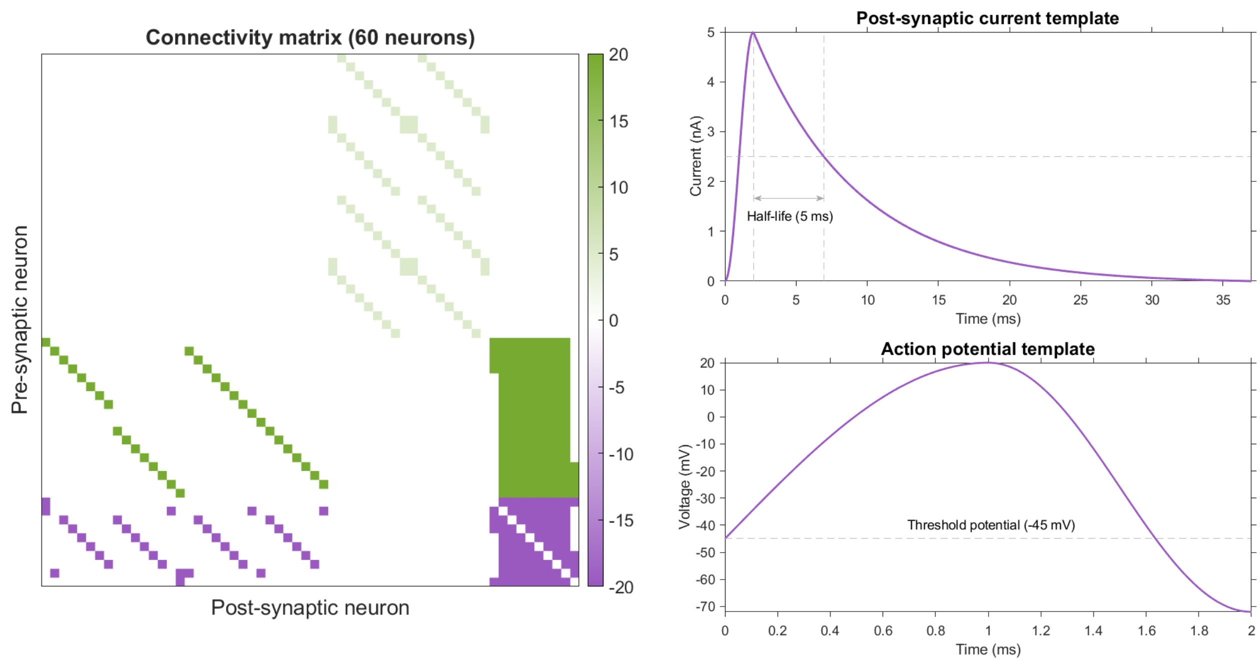
Paper 2. Marcel Ethan Sayre, Rachel Templin, Johanna Chavez, Julian Kempenaers, Stanley Heinze (2021). A projectome of the bumblebee central complex. *eLife*, 10:e68911. *https://doi.org/10.7554/eLife.68911*

Paper 3. Johannes Seelig, Vivek Jayaraman (2015). Neural dynamics for landmark orientation and angular path integration. *Nature*, 521(7551), 186–191. *https://doi.org/10.1038/nature14446*

Paper 4. Kakaria Kyobi, Benjamin de Bivort (2017). Ring attractor dynamics emerge from a spiking model of the entire protocerebral bridge. *Frontiers in Behavioral Neuroscience*, 11, 1662-5153. *https://doi.org/10.3389/fnbeh.2017.00008*

My first approach to the topic was to study those papers and learn about the biological aspect of the matter: what is the CX and how it works, the main structures and neurons involved, inputs to the system, differences between species… Understanding these concepts would be essential for my project and to explain the results of the code. The main and most important notions can be summarized as follows:

- The CX is a region in many insects' brain that works as an internal compass, that is, it encodes the head direction of the animal.
- In order to do so, the connection between cells is such that the network behaves as a "ring attractor", where each neuron represents a given angular direction.
- There are three main types of excitatory neurons and one inhibitory. The head direction is directly encoded by E-PG neurons as an activity "bump" that moves around the ring.
- Input to the system can be of two types: visual cues provided to the E-PG neurons or internal signals representing angular velocity when the insect turns its head, which are delivered to P-EN neurons.
- Anatomical differences across species lead to differences in behavior and capabilities of the animals.



$$V(t) = \begin{cases} V_{thr} + (V_{max} - V_{thr})\,\text{Normpdf}\left(0{,}1, -1 + \dfrac{t}{t_{AP}/2}\right), & 0 < t < \dfrac{t_{AP}}{2} \\ V_{min} + (V_{max} - V_{min})\sin\left(\left(t - \dfrac{t_{AP}}{2}\right)\dfrac{2\pi}{t_{AP}} + \dfrac{\pi}{2}\right), & \dfrac{t_{AP}}{2} < t < t_{AP} \end{cases} \qquad \text{(Equation 1)}$$

$$I(t) = \begin{cases} I_{PSC}\sin\left(\dfrac{t\pi}{2} - \dfrac{\pi}{2}\right), & 0 < t < 2 \\ I_{PSC}2^{-(t-2)/t_{PSC}}, & 2 < t \leq 2 + 7t_{PSC} \end{cases} \qquad \text{(Equation 2)}$$

$$\frac{dV_i}{dt} = \frac{1}{C_m}\left(\frac{V_0 - V_i}{R_m} + I_{stm\,(i)} + \sum_{j=1}^{60} M_{(j,i)} I_{PSC\,(j)} + I_{ect}\right) \qquad \text{(Equation 3)}$$

Figure 1. Above, an example of connectivity matrix can be seen (**left**) with each connection colored according to its weight (negative weight means inhibition). On the **right**, the templates of the action potential and the post-synaptic current are plotted. Below the graphs, the equations followed by the templates and the membrane potential are shown. **Equation 1** and **Equation 2** correspond to the voltage of the action potential and the current of the post-synaptic current, respectively. **Equation 3** is used to model the graded potential of the membrane. Graphs are produced with my own code.

Computational introduction

Learning about the computational aspect of the topic would be the next step in my formation. To do so, I used the fourth paper previously mentioned (*Paper 4*) as my main source to understand the mathematical algorithms that eventually build a spiking neural network (SNN). This step gave me a lot of insight into computational neuroscience, and I was able to gather the basic information needed to program a SNN, such as the equations to model the cell potentials and currents and the general structure that the code should follow.

Model construction

For the construction of the model, I mostly used *Paper 4* as a guide together with additional searches on the Internet when the concepts were not very detailed in the paper. The whole process of building the model was done with the programming language MATLAB. It should be mentioned that the publication of this paper included the MATLAB codes that the authors developed in their study, but I never used those codes to do my project. Instead, I followed my own design and received help from Sungyong. As a result, the process was difficult at some times because only the theory was explained in the original paper, not the actual implementation as MATLAB code.

I decided to start the script of the code by building the connectivity matrix, which is probably the most fundamental element when trying to translate a biological neural network into artificial code. It can be explained as a simplified representation (*Figure 1*) of the connections between all relevant neurons, obtained by analyzing the synapses between them. In the papers I read, electron microscopy images were used to determine the matrix.

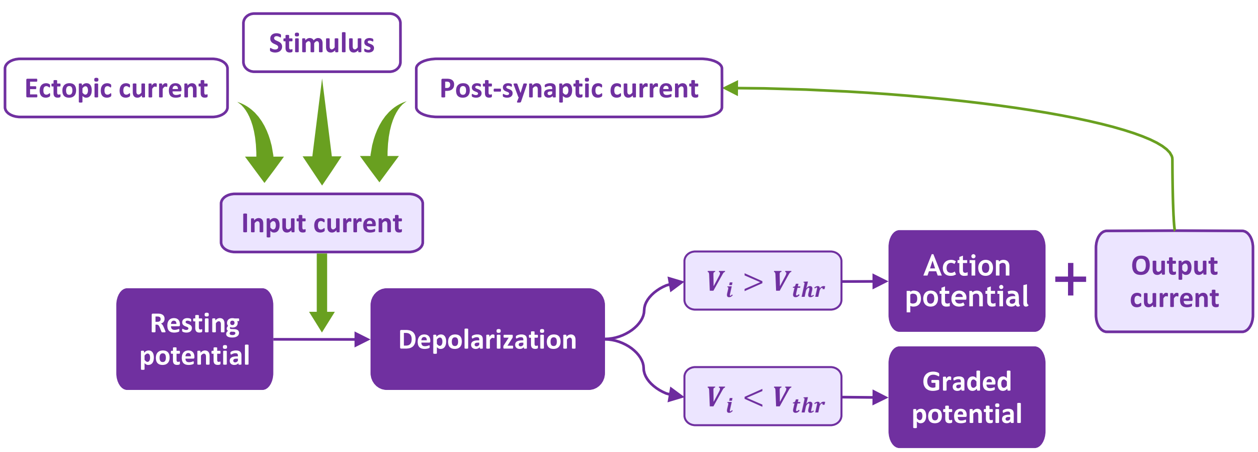


Figure 2. Diagram explaining how the cell membrane potential is built. Three different currents affect the depolarization of the membrane, one of them being the post-synaptic current created when an action potential occurs. The strength of depolarization will dictate whether the threshold potential is reached (an action potential is triggered) or not (a graded potential following *Equation 3* is used).

The next thing I coded were the mathematical equations defining cell behavior. The membrane potential of neurons is modeled with a differential equation that can be solved through numerical methods. Whenever the membrane potential of any neuron reaches a threshold voltage, an action potential is triggered together with a post-synaptic current. I defined these two events with two templates using the same cell parameters as the original paper. Once the equations were clearly coded, I started to build the time loop where the membrane potential is computed for each time step, following Euler's method. *Figure 2* shows the general structure of the loop. The input to a neuron comes in the form of three different currents: the one created by the stimulus, the post-synaptic current from other neurons that connect to this neuron, and the ectopic current. When the loop has finished, the membrane potential of all neurons at all time instants is stored in a single matrix.

The input to the network representing visual stimuli is delivered to E-PG neurons and the input imitating angular velocity is provided to P-EN neurons. At first, I programmed the stimuli as a constant input either of value zero for the neurons that do not receive it, or equal to one for the neurons that do receive it. This simple depiction was changed into a more complex and accurate method to deliver action potentials at a Poisson process of 120 Hz whenever neurons were stimulated. The Poisson process made it possible to create more natural and random inputs. I designed a set of stimulus types (*Figure 3*) that became very useful to test the performance of the code. For example, using the *constant bar* helped me detect if the network could respond steadily to a fixed stimulus, *rotating bar* enabled the study of the system efficiency when the angle changes continuously, and *competing bars* allowed to analyze whether the system chose just one candidate when several stimuli appear at the same time. Also, I added background noise to all neurons, characterized as action potentials provided with a frequency of 5 Hz.

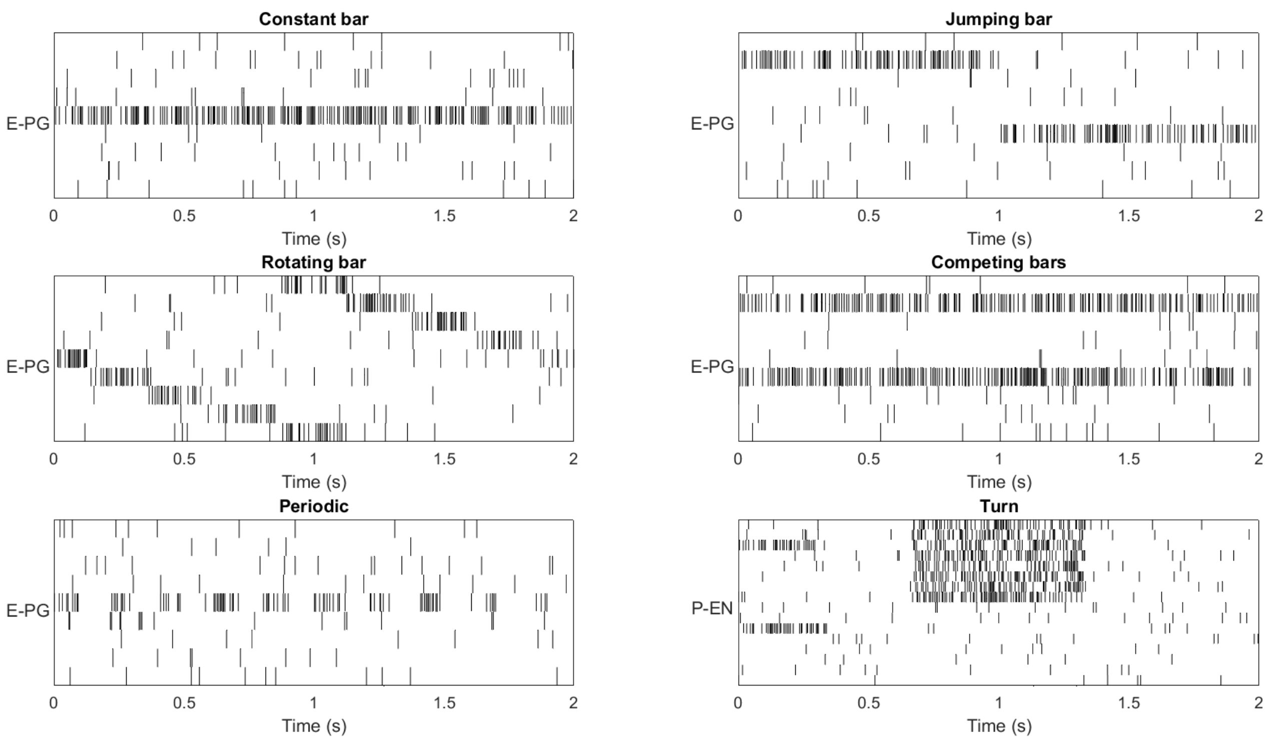


Figure 3. Raster plot of the different types of stimulus provided to the network with a Poisson process of 120 Hz. Each vertical line represents an action potential that was simulated and given to specific neurons, indicated in the y axis. On top of the stimuli, noise is also added with a Poisson process of 5 Hz.

I combined the noise and the stimulus to create a single matrix containing the information on when action potentials are provided to the network. This matrix, together with the one obtained after the simulation with the membrane potential of all neurons in the network, were very important for my next step:

visualize the results of the network, in order to study its performance. Sungyong explained me the concept of a raster plot, a type of graph where action potentials of each neuron are plotted as vertical lines. I used this type of visualization to check if the response produced by the network was coherent. The outcome of the first trials was quite disappointing, but with Sungyong's help I managed to find some appropriate values of the membrane capacitance and resistance that induced a result similar to the expected behavior: an activity bump representing the direction of the head, conditioned by the stimulus delivered. *Figure 4* displays several simulations where I changed the parameters to explore their effect on the network.

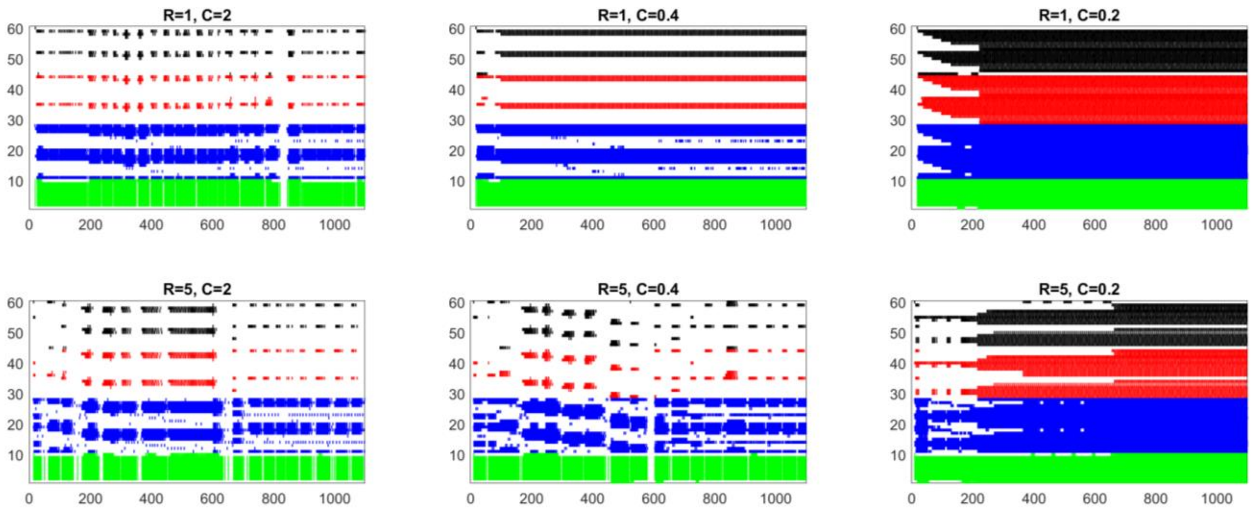


Figure 4. Six simulations showing the activity of the network in response to a combined stimulus: rotating bar followed by competing bars. Different colors correspond to different neuron types. The head direction is encoded by E-PG neurons (blue). The values of the resistance and capacitance of the cell membrane were modified to find the best behavior. After several trials, the best results were yielded by a resistance of 8 MΩ and a capacitance of 1 µF.

Results and analysis

Following Sungyong's instructions, I designed a new way of analyzing the results: rather than plotting the activity of all neurons in the system, I estimated the angle of the head direction in degrees. This value was somehow encoded in the output of the network, so I processed this signal to obtain an approximation of head direction that could be displayed together with the angle of the original stimulus (*Figure 5*). The difference between these two signals would be the error of the simulation, which can then be used to compare the accuracy of different network configurations.

The stimulus was further developed to allow more flexibility and better accuracy: I added the possibility of combining several types of stimuli together, as it can be viewed in *Figure 5*, and I changed how the neurons receive the stimulus (*Figure 6* clearly depicts the difference between the two methods). These modifications improved the quality of the results, and the stimuli represented the reality more faithfully.

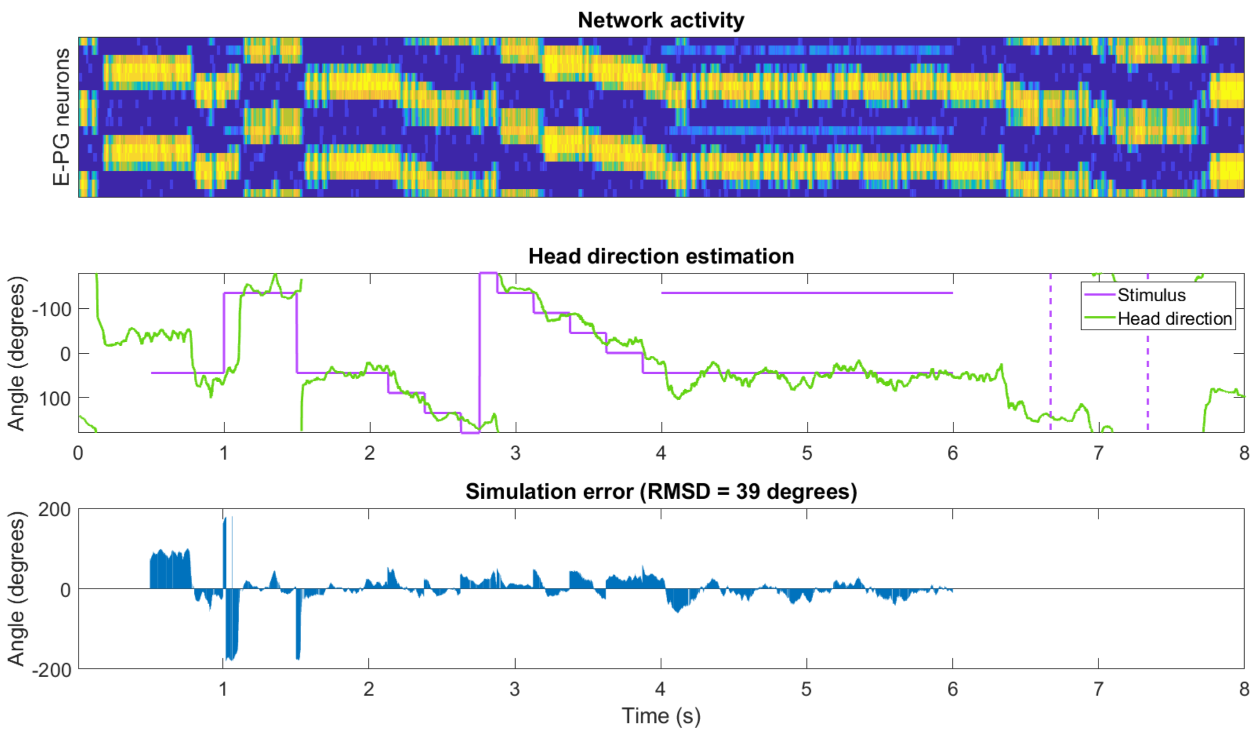


Figure 5. Results of a simulation, displayed as in the final version of the MATLAB code. The input used for this graph is a combination of different stimulus: dark, constant bar, jumping bar, rotating bar, competing bars and finally turn. The head direction encoded by the network followed closely the original input, proving its successful performance.

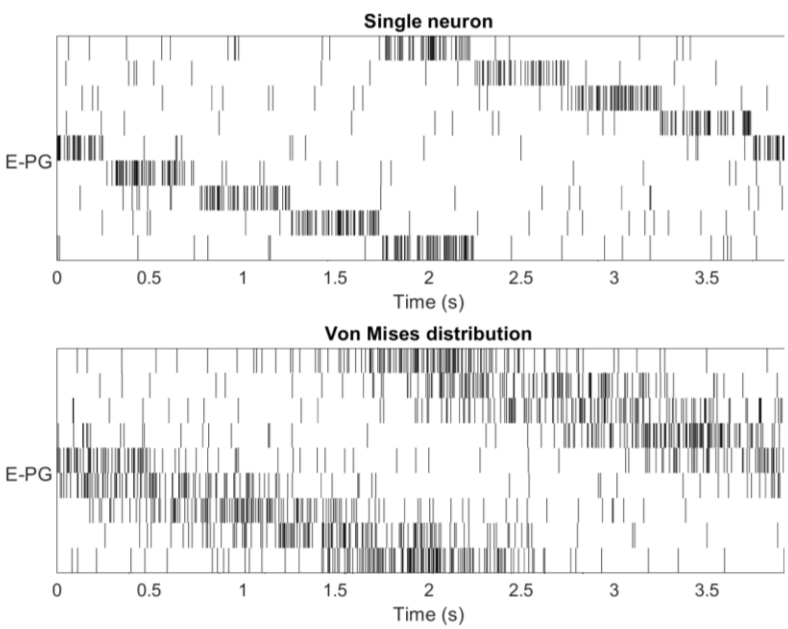


Figure 6. Comparison between two different approaches of stimulus delivery. **Above**, the stimulus is provided to only one neuron and it is confined to some specific angular values (discrete input). **Below**, the stimulus is divided across several neurons following a von Mises distribution, allowing any angle to be at the maximum stimulation (continuous input).

Sungyong also gave me the task of displaying the tuning curves of each neuron type. This graph was present in *Paper 1* and therefore he thought it would be a nice way of studying the characteristics of the activity bump. To do so, I first had to do some research with the aim of understanding what a tuning curve is and how it is created. I learned that in our case, the tuning curve allowed to visualize the width of the activity bump, which gives an idea of the precision of the signal. Therefore, I added an option in the code to compute and display a chart with this information. *Figure 7* shows the resulting plot.

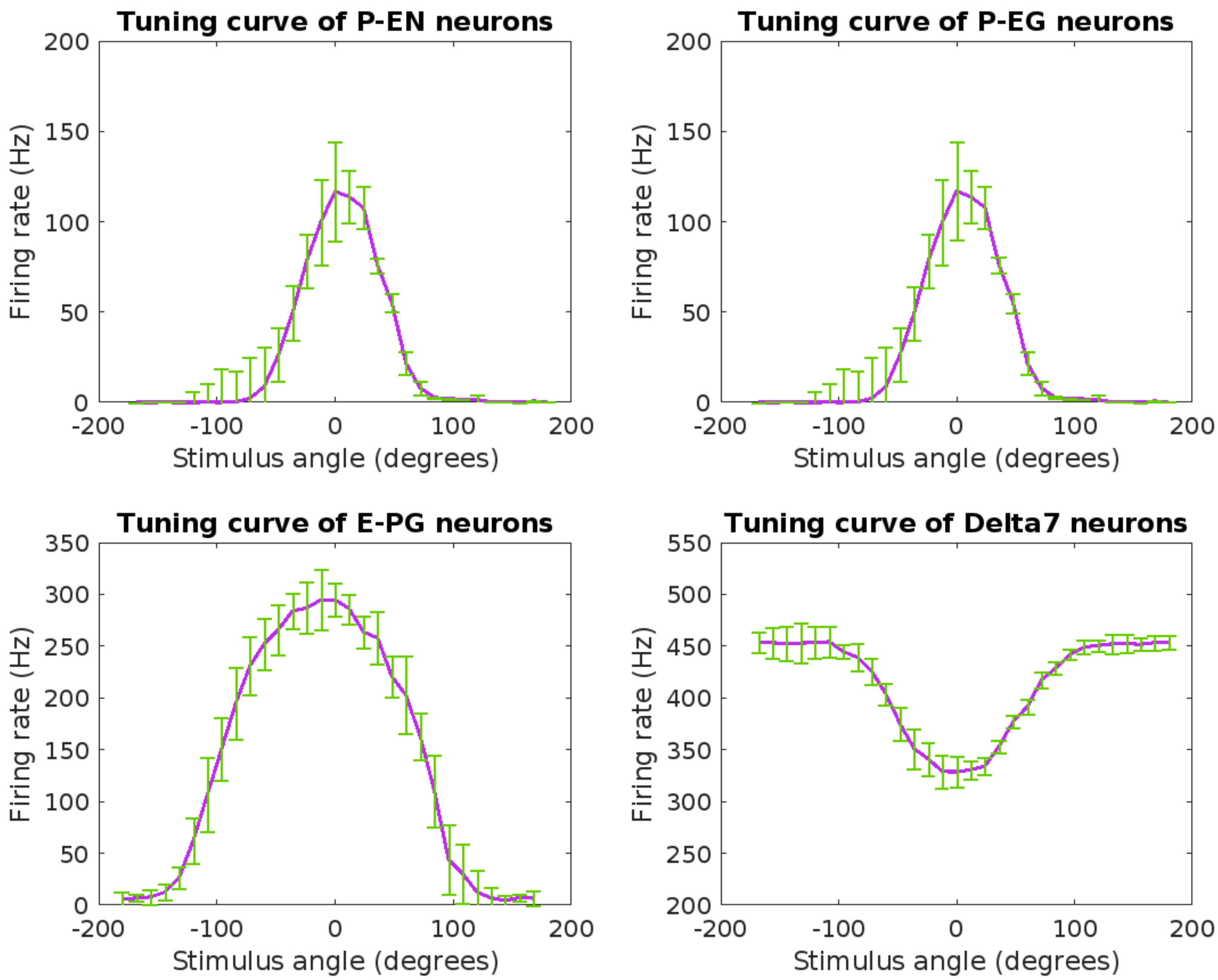


Figure 7. Tuning curves of all neuron types. Data is the average of 20 iterations and the bars indicate the standard deviation. The plots have been shifted to set the peak at the center. The E-PG curve represents the activity bump and its width is inversely proportional to the precision of the model.

Connectome comparison

Once the model of the SNN was functional, I moved to the next phase of my internship: compare different configurations of the connectivity matrix (or connectomes), corresponding to different insect species. The results should be consistent with the capabilities and behavior of each animal. The original plan proposed by Sungyong was to compare the fruit fly and the honeybee. However, exhaustive research revealed that the CX of the honeybee has not been translated into a simplified connectivity matrix and published. Therefore, we decided I would replicate the study made in *Paper 1*, which compares the performance of fruit fly and locust. Both models were tested with equivalent stimuli and the results showed important differences between them: the locust network was slower to follow the stimulus, and the activity bump was thinner. These characteristics are coherent with the nature of the two insects: fruit flies require a fast circuit to allow rapid changes mid-flight, while locusts need a network more robust against noise that helps maintain a constant direction in long journeys.

An additional analysis consisted of adding noise to each connection to quantitatively measure their importance in the network. However, constrains in time and computational power (the simulations necessary to do the study would take too long to run in a regular computer) prevented the realization of that analysis.

EVALUATION OF THE INTERNSHIP

Learning outcomes

This internship has taught me a lot on the fields of neuroscience and spiking neural network modeling. The introductory research at the beginning of the internship provided me with some basic notions on neural networks in flying insects, specifically the neurons in the central complex that are in charge of navigation and detecting head direction. I have learned the different structures and neuron types, their functions and how to map and simplify the connections. Likewise, I dedicated my time to comprehend the anatomical similarities and differences in the CX of different insects (fruit fly and locust), as well as how those disparities may affect their capabilities in navigation and orientation.

On the computational aspect, I have learned the concept of a ring attractor network and how it can be used to model the azimuthal heading direction of an insect. I have managed to implement with my own design this type of network as a SNN, using differential equations and parameters to represent the stimulation and inhibition between neurons. Through my own experience, I have understood how to imitate input (stimuli) to the network, and I have made use of several mathematical tools along the process (Poisson process, von Mises distribution, RMSD, tuning curve…). I also was able to implement all this knowledge in a MATLAB code, improving a lot my competences in this programming language.

Apart from getting new technical knowledge, I could also develop my soft skills. The initial research taught me the importance of keeping track of the bibliography used in a project, and the necessity of being organized with all the information collected. After the many meetings I had with my supervisors, I realized about the importance of not only doing a good job, but also being able to present it in a clear and concise manner. Additionally, I improved my organization, public speaking and time management skills as well as the ability to fulfill deadlines.

Company, supervision and interest

I really enjoyed my experience in Neural Intelligence Systems Lab. The atmosphere in the lab facilities was always friendly and relaxed. I liked how each student was working on their own independent project, but all of us had similar goals shared by the laboratory mission. Working with Sungyong was also great as he dedicated his time to guide me and teach me along the process. I feel very grateful to Prof. Anmo for kindly allowing me to work in his lab. Not only did he help me find an exciting project for my internship, but also paid interest on my progress and joined regularly to my meetings with Sungyong. All these people and their work have inspired me and fostered my interest in computational neuroscience and its applications.

Conclusion

This experience has been a great opportunity for me to learn from a promising field of biomedical engineering that is not readily available at my home university. In conclusion, I think of this internship as an enriching example of how investigation can be applied in bioengineering. The knowledge, skills and people I have met have changed my perspective and interest on computational biology and neuroscience. I definitely feel really proud of my accomplishments in this internship and I trust the code I've developed can be used in future projects I may encounter.