The Guide through "Optogenetics"



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Advancements

Over the last couple of decades, growing advancements in the formation of technological devices had played a dramatic effect as it transformed many fields. This had deeply impacted factors such as health care in many ways. This would further impact our approach towards understanding parts of the human body, medical treatments, and even diagnosis. The idea of optogenetics has offered us one of the most promising breakthroughs as it requires the technique of using light and flashing it to the neurons to regulate, manipulate, and control them. Additionally, this would also transfigure the method when it comes to treatments of psychiatric and other neurological disorders.



Image Courtesy: Alcimed.

<u>Topic 1.1-Challenges and problems of the</u> <u>Optogenetics</u>

Even though the optogenetics had mostly been applied towards animal models and research, potential therapeutic applications of the optogenetics brings on a great amount of possibility towards having treatments towards diseases such as:

- Parkinson's disease and Bradykinesia.
- Alzheimer's disease.
- Depression and anxiety.
- Epilepsy.
- Post-Traumatic Stress Disorder (PTSD).
- Chronic pain.

Although the optogenetics hold great amount of promises into providing methods of treatments, but its potential is also filled with many challenges on the global scale. There are several hurdles that remain significant cost, training, accessibility, and ethical considerations. All these things are fundamental to take into consideration because they are all key factors in factors of having the most effective performance. These factors also influence behind how it can provide benefits towards many individuals all around the world. Despite the challenges and issues, the optogenetics still continues to tackle and provide treatments through some of the most urgent diseases. Let's delve deeper and see some specific examples and the health crisis that are happening globally.

<u>Topic 1.2-Health crisis of Neurological</u> <u>disorders</u>

In terms of the safety of individuals around the world, neurological disorders are an extremely dangerous factor. It is something that causes multiple amounts of disabilities and deaths worldwide and this ends up leaving a big impact to people from all ages. According to the World Health Organization (WHO), the amount of people which are impacted with neurological disorders are more than 3 billion people as shown on the results of the year 2021.

Focussing more particularly, the degenerative neural disorders such as the Alzheimer's disease and Parkinson's disease are the roots towards causing a global challenge. For example, the Parkinson's disease itself has caused over 10 million people to be affected as the number is continuing to increase due to the rising amount of population.

The Alzheimer's disease is most significant towards older adults and this type of condition is concerning many people globally as its impact continues to increase as time passes by.

The table below shows the increasing possibility of how much people can be influenced with Dementia or

Alzheimer's disease, according to the report of Alzheimer's Disease International (ADI).

Year	Estimated amount of people impacted
2010	The report showed 35.6 million people who had been impacted with Dementia or Alzheimer's disease.
2030	By the year 2030, the amount almost doubles and shows that there would roughly be 35.6 million people.
2050	Around the year of 2050, the amount of people with Dementia almost triples the amount of people that were impacted during 2010, as the report estimates 115.4 million people.

The main reason why these diseases occur so much is because of the degeneration of neuron cells in our body and that causes, and it causes some weakening symptoms like memory loss. While these certain types of conditions often makes devastating impacts for the quality of life an individual gets to have, it also leaves a lasting concern in the healthcare system, especially in the countries with high growing amounts of populations. The treatment alternatives and options for these certain types of conditions are limited and typically aren't active or effective enough in order to slow down the progression of a disease. Diseases like the Parkinson's disease are mainly managed with the help of certain types of medicines such as Levodopa. The Levodopa's purpose is to reduce the impact of the motor symptoms which are part of the disease. However, it cannot address any issues which represent the underlying causes of the disease.

In a similar approach, the Alzheimer's disease can also be acted towards with medicines that will have the ability to manage some important symptoms such as memory loss. But again, no cure for the Alzheimer's disease exist.

These are some limitations that occur in treatment

alternatives and options as they also highlight the urgency and significance of needing newer therapy methods which would further indicate the root causes of these diseases.

Image Courtesy: Alzheimer's Los Angeles



<u>Topic 1.3-Conditions and Disorders of the</u> <u>Mental Health</u>

Another global health crisis which affects millions of people from all over the world is about the topic of Mental Health Disorders. According to statistics of the World Health Organization (WHO), one in four people will go through some sort of mental health disorder in their lifetime. Some of the conditions that include Mental Health disorder are:

- Post-Traumatic Stress Disorder (PTSD).
- Anxiety.
- depression.
- Schizophrenia.

These are among the significant conditions which are leading the path for the amount of people having disabilities worldwide.

One example for instance is depression, according to the WHO, it shows that roughly 280 million people worldwide are experiencing depression. Studies also show that depression is more common in women, with the chance of 50%. Anxiety disorders are another condition of mental health, and it had impacted over 300 million people globally, this is estimated to be 4% of the world population. However, the amount of people impacted with these disorders has a chance to increase over the next few years because of the rise in population. Thus, it causes the need towards having a more advanced technology that would provide treatments to these diseases as many countries are currently struggling for having a more advanced healthcare system. Particularly in countries with lower income or economy.

When it comes to the treatments towards these disorders, some of they are very difficult to manage with and have a very complicated system of functioning. These include Antidepressant and Antipsychotic medications. They offer therapeutic solutions towards effecting and promoting the amount of sleep a person gets. However, it does impact the sleep timing for the upcoming days if the medicine is taken at a mismatched time, making the medicine risky to take. Therefore, even certain types of medicines such as the Antidepressants and Antipsychotic may have actions on side effects and may not have an impact towards effectively tackling the root of the disorders.

Adding on to the sources and alternatives for treatment, having the access to talk to professionals of the mental health and having good therapy opportunities has limitations in our world.

Therapies include the Cognitive-Behavioural Therapy (CBT) and it is a psychotherapy which has a purpose of reducing certain mental health condition symptoms such as Anxiety, Depression, and PTSD. Because of the limitation of these treatments, millions of people around the world continue to be left untreated from these diseases, this causes people to not live their best quality of life as they should.



Image Courtesy: BrainFacts

Topic 1.4-Chronic Pain

According to many research reports, the Chronic Pain is one of the most influential and common health problems of the world, with the number of 1.5 billion people impacted globally. This is 20% of the world's population. It is a type of pain which includes some conditions such as:

- Arthritis.
- Nerve Damage.
- Back Pain.

Just like most others, the Chronic Pain may become dangerous to handle with and may impact daily performances as well as the quality of life for individuals if it's left untreated.

Topic 1.5-Global Scale of the Optogenetics

In our world, there are a bunch of health related problems that people are facing every day. The optogenetics may have the potential to address some of the ongoing issues that are in our world and help press against the healthcare systems. But even after realizing the global scale of optogenetics, our world would still have to put in countless amount of efforts and significantly research all threats and needs. This is in order to put the optogenetics into a perspective where it can overcome against diseases and conditions and have much more therapeutic applications. This also means that the Optogenetics should be more widely available or accessible, affordable, and ethical. By following these guidelines, we have to be able to make the optogenetics perform in a very precise manner towards developing the treatment systems in our world.

Topic 2-Purpose:

Optogenetic monitors are crucial and useful when it comes to the terms of the somatosensory system. It takes action when generating and processing such as the feelings of temperature, pain, and touch. The Optogenetic is active enough to make the specific neuron cells in the body have better activity, this is done by using light. This is the main reason why they are a very significant tool for our daily neuroscience investigation. Delving more deeply in the ways of how it exactly functions, the primary action that the optogenetic monitor will take is that it will aim towards specific neuron cells by shining light to it. Keep in mind that the cells are already genetically modified (GM) meaning that those cells and the DNA are changed by using some other technology. Doing this will make scientists activate or deactivate the neuron cells and investigate those cells, and they would record the information for how the cells are behaving at the time. This would also make better study methods in order to study the brain in a more complex way. This deep study of the brain would further help scientists to put cells that are light-sensitive proteins. If we are talking about the main key which leads to this action, it's light. This is because when it comes to tracking a person's neuron cells, optogenetic monitors often provide unique ways to observe and record data about the behaviour of the neuron cells. Shining light at the neuron cells would further test cells' reaction to interact to different situations, which would explain to us the results, and it would ensure that our bodies are capable of tackling such situations. Overall, the purpose of Optogenetic monitors and its power further provides us with explanations of gaining critical knowledge of the functioning cells in our body. It is a beneficial tool in the terms of the somatosensory system, as well as the things that are related to it.



Image Courtesy: ScienceDirect.com

Topic 3-Rationale of the optogenetics

Neither these two techniques, electrophysiology nor imaging, serve as a complete substitute for the perfect ability to control or manipulate one neural subpopulation at a time while simultaneously observing its activity; an optogenetic monitor really does bring both together. It offers real-time feedback loops where the experimenter can trigger and register outcomes of neural manipulation through light. Neural circuit study: To unravel the complexities of intricate brain circuits, it is required to manipulate the activity of specific neurons with a high temporal and spatial resolution. An optogenetic probe does this by combining optogenetic-light-based means of manipulation-with any kind of monitoring, such as calcium imaging, EEG or Electroencephalogram (measures brain electrical activity), or FMRI (Functional Magnetic Resonance Imaging). It can derive information about how much each neuron or circuit contributes to cognitive functions, memory, locomotion, and emotional responses.

1. **Personalized Medicine**: Coupling Optogenetic Control and Monitoring: Thus, this leads to the availability of a highly personalized treatment strategy. At last, the improved therapies targeted at individual patients suffering from neurological impairments could be made feasible by the ability of watching how a particular individual's brain reacts to various interventions.

- 2. **Finger Injuries:** It would not be too difficult for professional athletes to break their fingers from time to time, owing to the nature of their jobs. Despite the injury, they tend to play on successfully. Most of the time, the joint from which the fingers fracture is the proximal phalanx.
- 3. Human to Human Communication: With the current trends of research in virtual reality and artificial intelligence, the ideas of developing strategies for human-computer or human-to-machine interfaces have attracted interests. One of these theories has also matured into the emergent concept of user interface through pure kinesthetic inputs.
- 4. **Mirror Therapies:** An easy, ready-to-use, and effective example of psychophysics is the mirror therapy. Mirror therapy has already made a lot of differences in the general preferences of many therapy patients. "Look in the mirror," says one therapist, "either with attention or relaxedly, to enhance the effects on the limbs," according to the therapist.
- 5. Therapeutic Applications: Mapping the aberrant neural activity in several neurological disorders to manipulate it via optogenetic tools would provide relief in symptoms. An optogenetic monitor would help create seizure-controlling strategies, since certain areas in the brain become hyperactive during seizures and can more efficiently govern neuronal firing patterns.

- 6. **Kinesthetic Interference Settings:** When kinesthetic interference buildings have been completed for some time, the following features may emerge. Kinesthetic interference settings are tied down and "grounded," rough, not very vertical or horizontal, and not roughly very stiff or loose.
- 7. Proprioceptive Spatial Orienting: Proprioceptive spatial orienting, or static and dynamic limbs, can inform one thoroughly about the surrounding space. Proprioceptive spatial orienting refers to the proper use of limbs in relation to how a person is handling an object. This can be used in describing movements while standing or lying in a relaxed position with muscle deformities.

Topic 4.1-When was the optogenetics introduced?

The idea of optogenetics had been introduced by famous scientist Francis Crick, who was well-known to be a molecular biologist. The idea of this concept traces back to 1979, where he had originally established the idea of providing the supply of light to specific neuron cells. The ideas which he had come up with at the time were quite instinct. One factor which held neurologists back is the fact that they didn't have much understanding about such project and how exactly the method should be in order to succeed it.

There is someone who had identified a method on how optogenetics can be refined from connections of the brain, that man is Karl Deisseroth, an American scientist, professor of bioengineering, and a psychiatrist. He was considered to be the **Father of Optogenetics.** He and his team had cooperated together and came across the idea of putting an optogenetic monitor, without any invasiveness, to track the brain activities of mice. The results they had found out were that *tachycardia*, a medical term which refers to heartbeats above 100 bpm, is advantageously enhancing the behaviours of that mice related to anxiety. This was the process of how the optogenetic monitor was first tested.

<u>Topic 4.2-Functioning of the</u> <u>optogenetic-explained by Karl Deisseroth</u>

The actions of the optogenetics are fundamental in terms of controlling the neurons due to the process of stimulating the neuron cells. This is because magnetic and electrical interventions had enhanced the behaviours of the depolarizing cells, referring to the change, which effectively evolves overtime, as factors of the neural activity grow at a rapid pace according to science. A downside of these interventions is that they cannot detect and identify every single type of neuron cells located in the area. Instead, most of them look very identical according to the intervention. This is where optogenetics comes in, its job is to put antennas or sensitizers in order to bring along the external sources needed for each type of neuron cell. This process is fundamental because this is how light-sensitive neuron cells can be produced, from those light-sensitive antennas. The theme of optogenetics had shown a much easier way into these neuron methods. One aspect that appears a little off regarding the functioning of the optogenetics was its multicomponents. This refers to its ability towards overcoming obstacles in order to effectively target each variety of neurons.

Topic 5.1-Somatosensory system applications

The human body has a somatosensory system which detects sensations of touch, pressure, pain, temperature, and position in space. These sensations receive signals to the brain to effect these actions. Here are the numerous instances where somatosensory system practical applications are seen in everyday life. The touch and protection somatosensory system enables you to feel the heat of, for example, a stove and jerk away your hand. Therefore, this essential aspect is meant to protect the skin from trauma. The special nerve endings that your skin has, which detect temperature changes and send signals to your brain, all contribute to making the skin aware of the danger. Balance and Movement It is also from your somatosensory system that you know the position of your body in space; for example, when you are on a bike, your body is determining the position of your arms, legs, and head to help balance. It sends information from muscles, joints, and skin to ensure smooth movement and balance. Pain is also one part of the somatosensory system. When you step on a nail or cut your skin, pain receptors in your skin send messages to your brain saying that there is something wrong. This enables a reflex action of withdrawing your hand before any further damage can happen.

Examples of applications connected with the topic of optogenetics and others like the somatosensory system are:

— Typing and Texting.

Ever stopped to ponder about how one types on the keyboard or sends a text message on a keyboard or even texting on your phone? This is where the somatosensory system comes in, it is the reason we can feel the keys located beneath our fingers. When you press a key, the sensory nerves are responsible to send the detailed information to your brain which gives you the ability to write accurately.

— Touch and Protection.

An example of how the somatosensory system can help with the touch and protection factor is when you come in close contact with something hot, such as a stove. Whenever you go near it and try to touch it, your somatosensory system feels the warmth and pulls your hand away as a sign of cautiousness. This action from the somatosensory system is very important because it ends up protecting your hand from further injury. This occurs because specialized nerve endings situated all around a person's body because the sensory nerves responsibly send the detailed-information to your brain. Thus, making you be aware of the upcoming danger.

Balance and Movement.

Your somatosensory system helps you sense what are your surroundings and helps you know which space your body is in. An example of this is riding a bike. When you are doing an activity such as riding a bike, your somatosensory system makes you know where your arms, legs, and head need to be in order to balance it out. This is why this system then transports the information from muscles, joints, etc, to the brain and coordinates. This is how we can perform our daily activities smooth and balanced.

— Pain Detection

In terms of the somatosensory system, pain is one of the most crucial because it represents the actions that the nerve endings in your body do and send the information to the brain. This is why your brain triggers them as pain and sends signals to other parts in order to act upon its best to try to protect you. Examples of this can be things like stepping on something sharp (nails) or cutting yourself, all these pain sensors get the brain involved in order to inform you that something may be wrong and actions need to be taken.

Medical Devices (Prosthetics)

The word prosthetics refers to an artificial device which covers one of the missing or disabled body parts a person may have. For example, a person who has a broken limb can use prosthetics to replace it with an artificial because it can still be part of the somatosensory system. This is how those individuals can "feel" sensations such as pressure and temperature, which still gives them the ability for more control and remain in a good condition.

Topic 5.2-Optogenetic application

The terms of the methods of optogenetics can have applications which extends beyond the subject of physiology, and in many fields of neuroscience. The optogenetics can be applied towards many situations, which would further help us gain a deeper understanding about them. Not only them, optogenetics can also effectively cure diseases. Having is cure to these diseases is very fundamental as these diseases are often very dangerous and can lead to certain progression of degenerating neurons.

Some examples of the diseases that can be cured by the optogenetics are:

 Epilepsy-The development of optogenetics had significantly impacted the topic of epilepsy. In many research studies, there shows plenty of animal models which provide evidences of having epilepsy. These animals were mostly rodents such as mouses and rats. In these particular animal models, the optogenetics immensely focusses on regulating the amount of neuron cells which would be present and have connections to the organisms' brain in order to manipulate and control the seizure activity. Diving more deeply, a study shows and demonstrates how the optogenetic monitor can also stimulate the neurons around the area of the hippocampus and that can deal with the seizure that takes place. In general, this approach towards dealing with seizures using the help of optogenetics will also help towards developing more therapeutic strategies in order to fully be able to manage epilepsy.

2. Parkinson's disease-Although the Parkinson's disease has no cure for it, there are several treatments that are available for it. Some characteristics that the Parkinson's disease has to do with having difficulties on certain activities, such as the ones that involve balancing and coordination. Other common characteristics are shaking and having a stiffness on your body. In our brain, one of the harsh parts of it called the substantia nigra, and it contains of the type of neuron cell called the dopaminergic neuron (Chinta et al.). The Parkinson's disease associates with the degeneration of the dopaminergic neurons (Mamelak 2018). The Parkinson's disease also has terms such as motor symptoms which refers to things like dizziness, slowness, weak, etc. The use of optogenetics would further selectively stimulate the dopaminergic neurons and it functions in order to reduce the motor symptoms towards the Parkinson's disease in the animal models. Furthermore, this would provide a more advanced treatment towards neurological disorders such as the Parkinson's disease. Additionally, the term associated with Parkinson's disease is called Bradykinesia. Bradykinesia is the cardinal symptom which actually

refers to the slowness towards movement and having difficulity with doing things within a certain or regular motion. Just like Parkinson's disease, the role that optogenetics play in the symptom of Bradykinesia is that it had stimulated the D1-SPNs in resulting of reducing the impact of the symptom towards the animal models (Gittis et al.). The D1-SPNs are known as the type D1 dopamine receptor (Al-Muhtasib et al.) and it is responsible for keeping the neurons continuing to develop even after hormones of dopamine being in tight with them (Bhatia et al).

3. Alzheimer's disease-When the Alheimer's disease occurs, it leads to to the degenration of neurons that are in our brain, especially in the hippocampus. This often leads to problems relating to memory loss. Here's where the part of optogenetics come in, they are used to manipulate circuts of the hippocampus in the animal models. This means that the optogenetics also has the ability to rearrange and lessen the impact of neural circuit and impairments towards memory (Mirzayi et al.). Research studies also show that the optogenetics had been used in certain pathways of the Alzheimer's disease and had a better overall memory performance in the models.

Topic 6-What are Microbial Opsins?

The optogenetic is something that is very fundamental and there are many other topics which also apply to its significance. These topics include genetical components or proteins that are used, such as Microbial Opsins. "Species from multiple branches of the animal kingdom have evolved mechanisms to sense electromagnetic radiation in their environments" (Fenno et al.). It mainly describes the function of how the animal species had developed with light-activated with certain purposes such as equalizing the impact of vision when the organism is in different areas. It also plays a major role behind the manipulation of the various types of cells involved during the process of optogenetics.



Mirzayi, Parsa et al. "Optogenetics: implications for Alzheimer's disease research and therapy." Molecular brain vol. 15,1 20. 23 Feb. 2022, doi:10.1186/s13041-022-00905-y

The image that is placed above represents how the brain can be controlled with the help of optogenetics and show the movement and behaviour of neural circuits.

Topic 7.1-Neuron Cell Activities

This picture below details the reasoning and the actions of the stimulated neuron cells. These cells can be classified into two categories: Hyperpolarized and Depolarized. In terms of neuron activities, hyperpolarized cells represent how negative potentiality of the membrane increases. In other words, hyperpolarized cells can also indicate that the membrane potentiality is less positive. It is the opposite for the depolarized cells because it represents the membrane potentiality becomes more positive. However, both of them are crucial because they are mutual, and their balance is also important.



Damercheli et al. Transcranial Direct Current Stimulation (tDCS) for the treatment and investigation of Phantom Limb Pain (PLP). Psychoradiology. 22 Apr. 2022 <u>https://pmc.ncbi.nlm.nih.gov/articles/PMC10917199/</u>.

Topic 7.2-Action Potential



The graph shown above is created by us based on what we had learned about the behaviour of neuron cells or any activities that is recorded. The membrane potential energy also has sudden changes as the time of milliseconds (ms) pass by. This graph had been designed several times by others. We had taken inspiration from those people and made our own similar version. The one below is an example of what we had taken to learn about the graph.

Let's break down the information of these graphs. On the y-axis of the graph, we have the potential energy of the membrane or the voltage, which is measured in the unit of millivolts. More specifically, the typical resting potential is at -70 millivolts. Another influential thing that is mentioned in the graphs are about the threshold. The threshold occurs when the depolarizing cells reach somewhere in between -50 to -55 mV. When it does, the neuron will fire, something known as the action potential.

When it comes to the depolarizing cells that would be approaching the threshold, there is one part that remains as key. That is called the stimulus. The stimulus from a sensory neuron cell go into action as it makes the targeted cell to depolarize more towards the threshold potential. Reaching the threshold potential would cause the membrane of the cell to open up, which leads to the entrance of sodium ions (Na+). The next thing that would happen is that because the sodiums ions (Na+) are positively charged, it would take action quickly as shown on the graph. This means that if the millivolts are currently more on the negative side, the sodium ions which are rushing into the cells would cause less negative millivolts and bring it more towards the positive side.

This event also matches the graph, as we can see that the amount of millivolts rose a lot more positively right after the action of the stimulus. After this, the depolarizing cells will stop going up and reach its peak, which is usually 30-40 mV.

After it reaches the peak, the potassium ion K⁺ channel opens up, and it causes K⁺ to leave the channel. However, at the same time, Na+ channels begin to close. This would lead to the step of hyperpolarization, which causes the amount of mV to get towards the negative side. This is the refractory period, as it cannot fire any more action potential.

As the hyperpolarization process ends, the potassium channels will begin to close up and form a natural balance, which bring it back to the resting potential at -70mV.



Image Courtesy: Differencebetween.com

<u>Topic 8-Steps and processes of the</u> <u>optogenetics</u>



Image Courtesy: <u>Optogenetics: Controlling the Brain with Light | by Shabana</u> <u>Khan | Medium</u>

Now let's take a look at how the neuron cells can be manipulated through the steps of optogenetics and how it can be done. The image shown above explains a fundamental process behind how the neuron cells can be manipulated by harnessing the power of light. During this task, genetical engineering is required for a very effective performance.

This process begins the initial and crucial step, which is to gather all the required and appropriate materials. This will include things like genetic contracts and viral vector, which is a fascinating process of a modified virus entering the cells and changing the gene. The optogenetic process may require any other material that remains as a key during the manipulation. To increase the effectiveness even more, it is vital to ensure that the materials that are being used are in their highest quality so it can be more suitable for its applications. Proper performance setup is also a big thing that strengthens the reliability. In terms of the genetic construct, the first thing that you would have to attach is the gene that encodes the Opsin, or the protein. Then, attach another piece of DNA which resembles as the Promoter. This step is very fundamental as it sets up the rest of the procedure.

The next step in the process includes the conversion of the genetic construct into a modified virus. This is another essential part of the procedure as the virus will be the key source behind the transportation of the genetic material to the organism, for example: mice. The viral vector that was discussed earlier is responsible for carrying the genetic construct in a way that allows the targeting of different cells in the organism. After this process is prepared, then the

virus situated in the organism will become the key tool behind manipulating and controlling the genetical expression of the organism. The main role that the virus plays here is that it is trying to ensure that the genetic material is accurately introduced and expressed because it's critical for the control of cellular activities. Also, this step requires diligent precision as the virus must be optimized to ensure the efficiency and delivery and a step towards minimizing any unexpected occurrences of effects.

Following the step behind the viral preparation, the next thing in the procedure is to inject the prepared virus into the organisms' brain. This procedure is also quite delicate because the virus needs to be deliberately administrated to further ensure that it is reaching the correct location. The main reason why the brain of the organism is a vital point is because it stores the neurons which would ultimately express the Microbial Opsin, which resembles as the protein responsible for the effect of optogenetics. Furthermore, the injection of the virus that goes in the brain is a key step that plays significant roles in precise control and target towards specific neuron cells.

After injecting the virus, the next step in the process is to insert the optrode with other components such as Fibre-Optic cable included with the electrode. "The combination of optical and electrical elements in one single probe is referred to here as an optrode" (Dufour et al.).



Dufour, Suzie, and Yves De Koninck. "Optrodes for combined optogenetics and electrophysiology in live animals." *Neurophotonics* vol. 2,3 (2015): 031205. doi:10.1117/1.NPh.2.3.031205

Topic 9.1-What is ChR2?

ChR2 is short for Channelrhodopsin-2 and its main role plays in the topic of optogenetics. The ChR2 is a type of blue light from the algae protein of Chlamydomonas reinhardtii, and it is a cation channel which is light-activated (Britt et al.). The Cation channels are responsible for creating a more open flow of the cations of sodium, magnesium, potassium, etc. It also includes other cellular and intracellular membranes (Brown et al.).

<u>Topic 9.2-Optrode Application.</u>

For this part of the fundamental process, the optrode along with the Fibre-Optic and usually a metal electrode is something that needs to be set up very carefully because it is significant for the transformation of light signals. Along its path, there are several sensors which act as the monitor for regulating its behaviour. The main purpose of this is that the Optical Fibre that is located in the Optrode is responsible for delivering the light to certain areas of the brain as the electrode proceeds to record any electrical activity.

From here, a laser light is used to provide activation of that had been genetically modified with opsins which are light sensitive. There are numerous reasons why the laser light is used in the process of optogenetics instead of other variations. These reasons include:

- Low heat generation-Generates less heat and delivers a higher quality of performance.
- Specific wavelengths-Describes the corresponding waves of light. Laser has a very exceptional performance, which is why it's crucial in the terms of opening the ion channel in an organism's neuron system. "Neuronal ion channels are gated pores whose opening and closing is usually regulated by factors such as voltage or ligands" (Mathie et al.). This can also involve through other terms, such as Neuron circuits.

- Intensity-One advantage of the laser light being used in optogenetics is that its intensity performance can be manipulated, as it is significant because of how different intensity levels can affect the psychological behaviour of the organism. Thus, it is important to know which intensity level the light should be at to have the most effective performance towards achieving the goal.
- Non-invasiveness-When it comes to optogenetics, invasiveness is something that is very indispensable to consider, especially because it may cause a lot of harm to whatever organism it is being applied on. This is also something to be cautious about, as invasiveness may cause significant tissue damage (Pouliopoulos et al.).



Image courtesy: CNI Laser.

Conclusions

We are accepting our hypothesis because the optogenetics had undergone through major developments and advancements as it became a more effective device. Particularly in the field of neuroscience. These developments not only reorganize the understanding behind neural circuits and brain functions but also paved the groundbreaking rationale and application for medical research as well as potential health treatment. Because of its fundamental process with harnessing the power of light, the optogenetic monitor is responsible for stable control over neuron cells and offering a high level of manipulation as these cells can be controlled. This process is a fine refinement of what scientists had been experimenting with, investigating newer techniques behind these discoveries of unparalleled insights. The optogenetic monitor remains as a complex mechanism for further investigation of behavioural patterns or even diseases.

The idea of optogenetics had been changing overtime as it had increased its quality of performance overtime. As this device continues to evolve, the more deeply it could sense information based upon the nervous system. It may also stand out as an excellent method towards detecting mental health disorders such as Parkinson's disease, which describes the brain condition of going through mental health problems. Other than detecting diseases, the advanced optogenetic monitor can guide us through therapies which remain as a long-term solution against challenging conditions. Thus, this can bring on the betterment towards many people, and it will be life-saving for countless amount of individuals in our world.

Furthermore, the optogenetic monitor will continue to evolve with stronger cooperations among different groups of people including engineers, biologists, and others. These collaborations should continue to embrace the changes and make the optogenetic monitor continue to stand out in the newer generation of personalized medicine, which allows the treatments to be even more customized. With that being said, the optogenetics would also bring a more comprehensive impression towards healthcare.

Therefore, we are truly fascinated by the overall topic of optogenetics not only because of its wonderful capabilities in the present, but also because of its remarkable changes and applications, as they all apply to the activities in our world. Looking back to its history, the optogenetics was known as a method to study the neural activities. It had now become an essential technology for the future medical applications, with immense promise of developments throughout its journey. Additionally, this not only drives us through a better understanding of neuroscience, but also remarks the entire path towards groundbreaking innovations and an upgraded healthcare system set for the future generations.

Citations

Deisseroth, Karl. "Optogenetics." *Nature methods* vol. 8,1 (2011): 26-9. doi:10.1038/nmeth.f.324

Guru, Akash et al. "Making Sense of Optogenetics." *The international journal of neuropsychopharmacology* vol. 18,11 pyv079. 25 Jul. 2015, doi:10.1093/ijnp/pyv079

Addgene-optogenetics guide.

Sciencedirect-Neuroscience.

Joshi, Jyotsna et al. "Optogenetics: Background, Methodological Advances and Potential Applications for Cardiovascular Research and Medicine." *Frontiers in bioengineering and biotechnology* vol. 7 466. 29 Jan. 2020, doi:10.3389/fbioe.2019.00466

Chen, Wenqing et al. "The Roles of Optogenetics and Technology in Neurobiology: A Review." *Frontiers in aging neuroscience* vol. 14 867863. 19 Apr. 2022, doi:10.3389/fnagi.2022.867863

Xiaobu interprets Nature: Karl Deisseroth, the father of optogenetics, tells you that being too excited can cause anxiety.

Fenno, Lief et al. "The development and application of optogenetics." *Annual review of neuroscience* vol. 34 (2011): 389-412. doi:10.1146/annurev-neuro-061010-113817

Hogan, Matthew K et al. "Neural Stimulation and Molecular Mechanisms of Plasticity and Regeneration: A Review." *Frontiers in cellular neuroscience* vol. 14 271. 14 Oct. 2020, doi:10.3389/fncel.2020.00271

Targeting Neural Circuits - ScienceDirect

Liu, Bao-hua et al. "Intervening inhibition underlies simple-cell receptive field structure in visual cortex." *Nature neuroscience* vol. 13,1 (2010): 89-96. doi:10.1038/nn.2443

Glover, Gary H. "Overview of functional magnetic resonance imaging." *Neurosurgery clinics of North America* vol. 22,2 (2011): 133-9, vii. doi:10.1016/j.nec.2010.11.001

Yang, J., Cumberbatch, D., Centanni, S. *et al.* Coupling optogenetic stimulation with NanoLuc-based luminescence (BRET) Ca⁺⁺ sensing. *Nat Commun* 7, 13268 (2016). https://doi.org/10.1038/ncomms13268

<u>The Anatomy and Physiology of Pain - Pain and Disability - NCBI</u> <u>Bookshelf</u>

Central Pain Syndrome (CPS): Symptoms & Treatment

Zhang, Feng et al. "The microbial opsin family of optogenetic tools." *Cell* vol. 147,7 (2011): 1446-57. doi:10.1016/j.cell.2011.12.004

Duebel, Jens et al. "Optogenetics." *Current opinion in ophthalmology* vol. 26,3 (2015): 226-32. doi:10.1097/ICU.00000000000140

Warnock, James N et al. "Introduction to viral vectors." *Methods in molecular biology (Clifton, N.J.)* vol. 737 (2011): 1-25. doi:10.1007/978-1-61779-095-9_1

Manfredsson, Fredric P. "Introduction to Viral Vectors and Other Delivery Methods for Gene Therapy of the Nervous System." *Methods in molecular biology (Clifton, N.J.)* vol. 1382 (2016): 3-18. doi:10.1007/978-1-4939-3271-9_1 Travieso, Tatianna et al. "The use of viral vectors in vaccine development." *NPJ vaccines* vol. 7,1 75. 4 Jul. 2022, doi:10.1038/s41541-022-00503-y

Dufour, Suzie, and Yves De Koninck. "Optrodes for combined optogenetics and electrophysiology in live animals." *Neurophotonics* vol. 2,3 (2015): 031205. doi:10.1117/1.NPh.2.3.031205

Pouliopoulos, Antonios N et al. "Non-invasive optogenetics with ultrasound-mediated gene delivery and red-light excitation." *Brain stimulation* vol. 15,4 (2022): 927-941. doi:10.1016/j.brs.2022.06.007

Damercheli S, Ramne M, Ortiz-Catalan M. transcranial Direct Current Stimulation (tDCS) for the treatment and investigation of Phantom Limb Pain (PLP). Psychoradiology. 2022 Apr 22;2(1):23-31. doi: 10.1093/psyrad/kkac004. PMID: 38665143; PMCID: PMC10917199.

Dufour, Suzie, and Yves De Koninck. "Optrodes for combined optogenetics and electrophysiology in live animals." *Neurophotonics* vol. 2,3 (2015): 031205. doi:10.1117/1.NPh.2.3.031205

Depolarization, hyperpolarization & neuron action potentials (article) | Khan Academy

Neuron action potentials: The creation of a brain signal (article) | Khan Academy

Ferenczi, E., Vierock, J., Atsuta-Tsunoda, K. *et al.* Optogenetic approaches addressing extracellular modulation of neural excitability. *Sci Rep* 6, 23947 (2016).

Parkinson's disease — The Lancet

Geng, Yuanming et al. "Advances in Optogenetics Applications for Central Nervous System Injuries." *Journal of neurotrauma* vol. 40,13-14 (2023): 1297-1316. doi:10.1089/neu.2022.0290

Kim, TaeKen et al. "Thermal effects on neurons during stimulation of the brain." *Journal of neural engineering* vol. 19,5 056029. 7 Oct. 2022, doi:10.1088/1741-2552/ac9339

Mardinly, Alan R et al. "Precise multimodal optical control of neural ensemble activity." *Nature neuroscience* vol. 21,6 (2018): 881-893. doi:10.1038/s41593-018-0139-8

Leemann, Siri et al. "Cardiac optogenetics: shining light on signaling pathways." *Pflugers Archiv : European journal of physiology* vol. 475,12 (2023): 1421-1437. doi:10.1007/s00424-023-02892-y

Neuron action potentials: The creation of a brain signal (article) | Khan Academy

Vann, Kiara T, and Zhi-Gang Xiong. "Optogenetics for neurodegenerative diseases." *International journal of physiology, pathophysiology and pharmacology* vol. 8,1 1-8. 25 Apr. 2016

Wang, Yilin et al. "Animal Models of Epilepsy: A Phenotype-oriented Review." *Aging and disease* vol. 13,1 215-231. 1 Feb. 2022, doi:10.14336/AD.2021.0723

Chinta, Shankar J, and Julie K Andersen. "Dopaminergic neurons." *The international journal of biochemistry & cell biology* vol. 37,5 (2005): 942-6. doi:10.1016/j.biocel.2004.09.009

Luo, Sarah X, and Eric J Huang. "Dopaminergic Neurons and Brain Reward Pathways: From Neurogenesis to Circuit Assembly." *The American journal of pathology* vol. 186,3 (2016): 478-88. doi:10.1016/j.ajpath.2015.09.023 Mamelak, Mortimer. "Parkinson's Disease, the Dopaminergic Neuron and Gammahydroxybutyrate." *Neurology and therapy* vol. 7,1 (2018): 5-11. doi:10.1007/s40120-018-0091-2

Gradinaru, Viviana et al. "Optical deconstruction of parkinsonian neural circuitry." *Science (New York, N.Y.)* vol. 324,5925 (2009): 354-9. doi:10.1126/science.1167093

Duan, Liting et al. "Optogenetic control of molecular motors and organelle distributions in cells." *Chemistry & biology* vol. 22,5 (2015): 671-82. doi:10.1016/j.chembiol.2015.04.014

Gittis, Aryn H, and Eric A Yttri. "Translating Insights From Optogenetics To Therapies For Parkinson's Disease." *Current opinion in biomedical engineering* vol. 8 (2018): 14-19. doi:10.1016/j.cobme.2018.08.008

Al-Muhtasib, Nour et al. "Differential electrophysiological properties of D1 and D2 spiny projection neurons in the mouse nucleus accumbens core." *Physiological reports* vol. 6,13 (2018): e13784. doi:10.14814/phy2.13784

Bhatia A, Lenchner JR, Saadabadi A. Biochemistry, Dopamine Receptors. [Updated 2023 Jun 22]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-.

Mirzayi, Parsa et al. "Optogenetics: implications for Alzheimer's disease research and therapy." *Molecular brain* vol. 15,1 20. 23 Feb. 2022, doi:10.1186/s13041-022-00905-y

Tiwari, Prabhat, and Nicholas S Tolwinski. "Using Optogenetics to Model Cellular Effects of Alzheimer's Disease." *International journal of molecular sciences* vol. 24,5 4300. 21 Feb. 2023, doi:10.3390/ijms24054300 Psychiatry.org - What is Posttraumatic Stress Disorder (PTSD)?

<u>Neurological conditions now leading cause of ill health and disability</u> <u>globally, affecting 3.4 billion people worldwide|Health Data</u>

<u>Over 1 in 3 people affected by neurological conditions, the leading</u> <u>cause of illness and disability worldwide|World Health Organization</u>

Dementia statistics | Alzheimer's Disease International (ADI).

Anxiety disorders | WHO

Krystal, Andrew D. "Antidepressant and Antipsychotic Drugs." *Sleep medicine clinics* vol. 5,4 (2010): 571-589. doi:10.1016/j.jsmc.2010.08.010

Goldberg, Daniel S, and Summer J McGee. "Pain as a global public health priority." *BMC public health* vol. 11 770. 6 Oct. 2011, doi:10.1186/1471-2458-11-770

Britt, Jonathan P et al. "Use of channelrhodopsin for activation of CNS neurons." *Current protocols in neuroscience* vol. Chapter 2 (2012): Unit2.16. doi:10.1002/0471142301.ns0216s58

Brown, Brandon M et al. "Recent advances in our understanding of the structure and function of more unusual cation channels." *F1000Research* vol. 8 F1000 Faculty Rev-123. 30 Jan. 2019, doi:10.12688/f1000research.17163.1