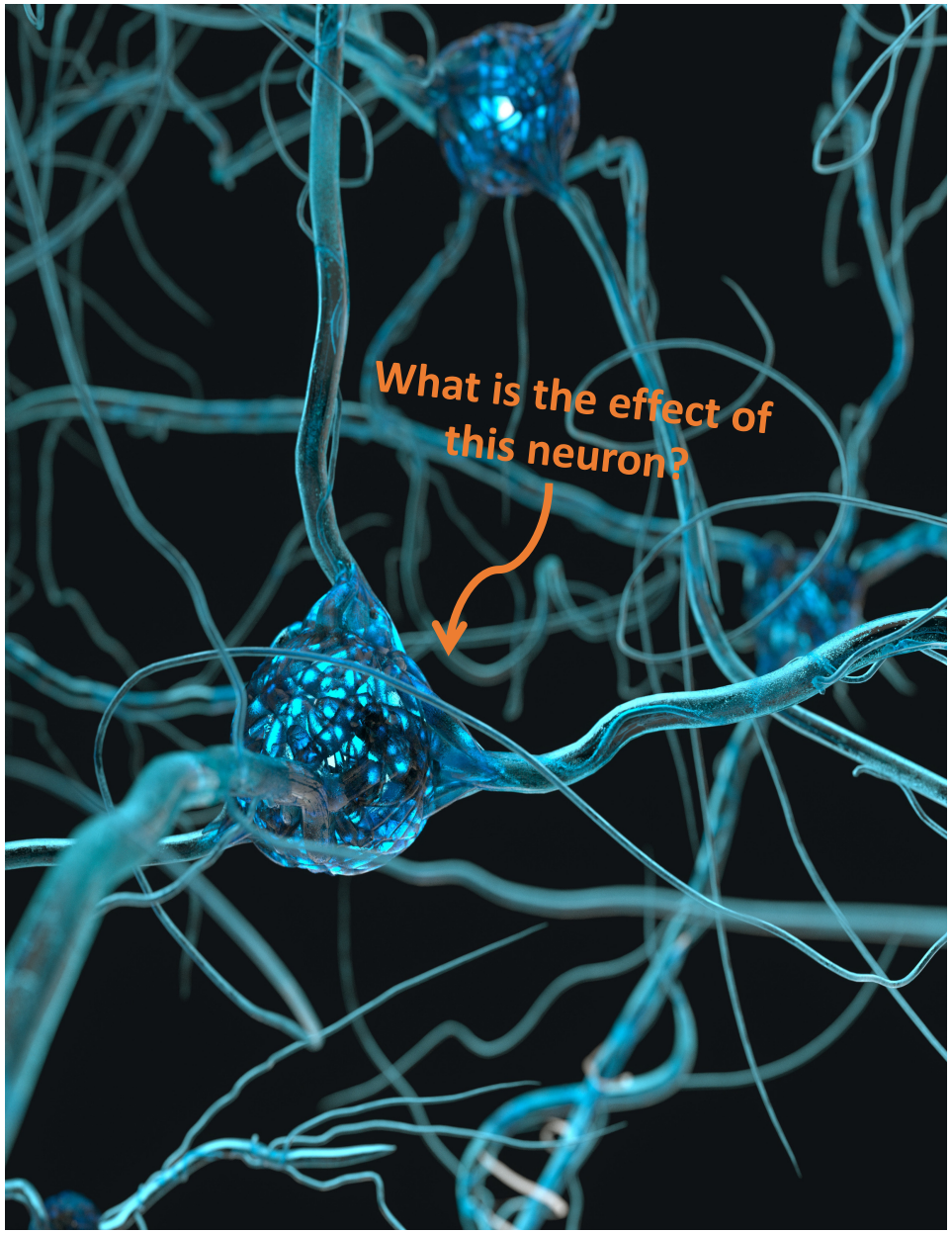
Optogenetics

A technique to change **particular** living cell activity **using a light**.

Gökhan Koçmarlı
22 May 2023

Outline

- The Problem Definition - why do we need that?
- General System Overview
- Detector Selection – Opsin molecules
- Light Source Selection – Scanning vs Parallel
- Other Applications & Specimens



Understanding the Brain

- Transcranial Magnetic Stimulation
- Transcranial Ultrasound Stimulation
- Transcranial Electrical Stimulation
- Deep Brain Stimultion

For spatial and temporal precise control:
Optogenetics

Extending Human Lifespan

If we would understand the behaviour of the brain deeply, we can treat some biological and visionary diseases.

- Alzheimer’s Disease
- Parkinson’s Disease
- Epilepsy
- Stroke
- Vision
- ... and many more!

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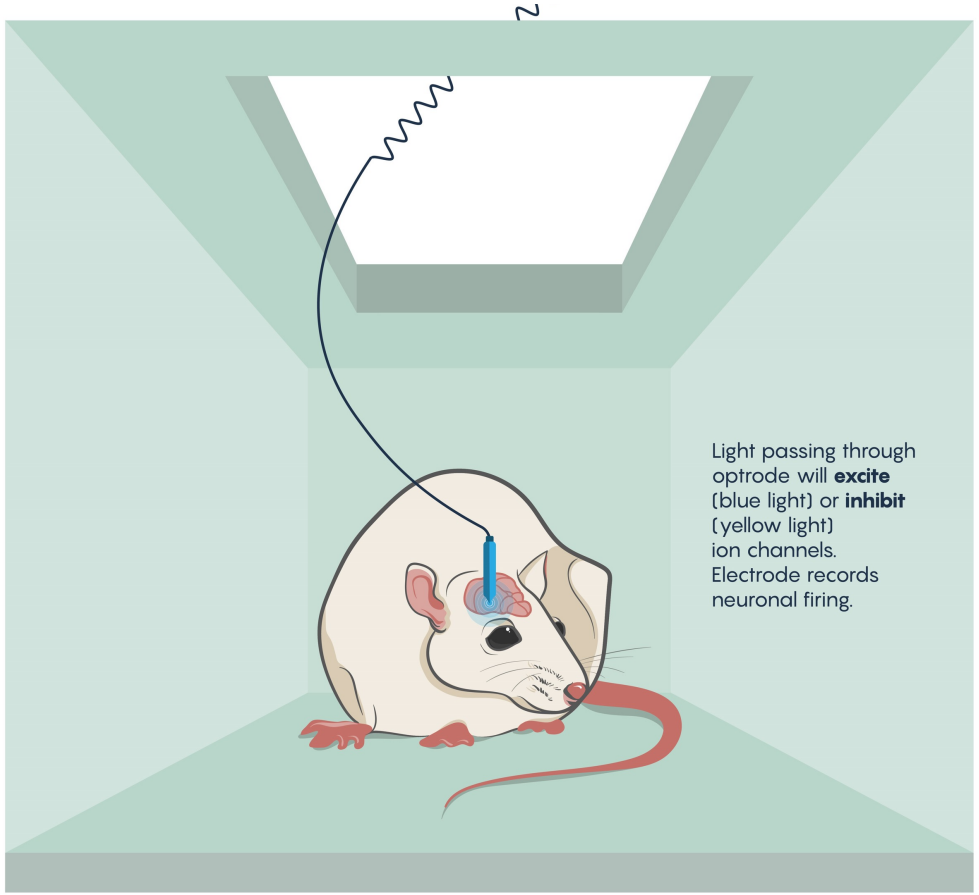
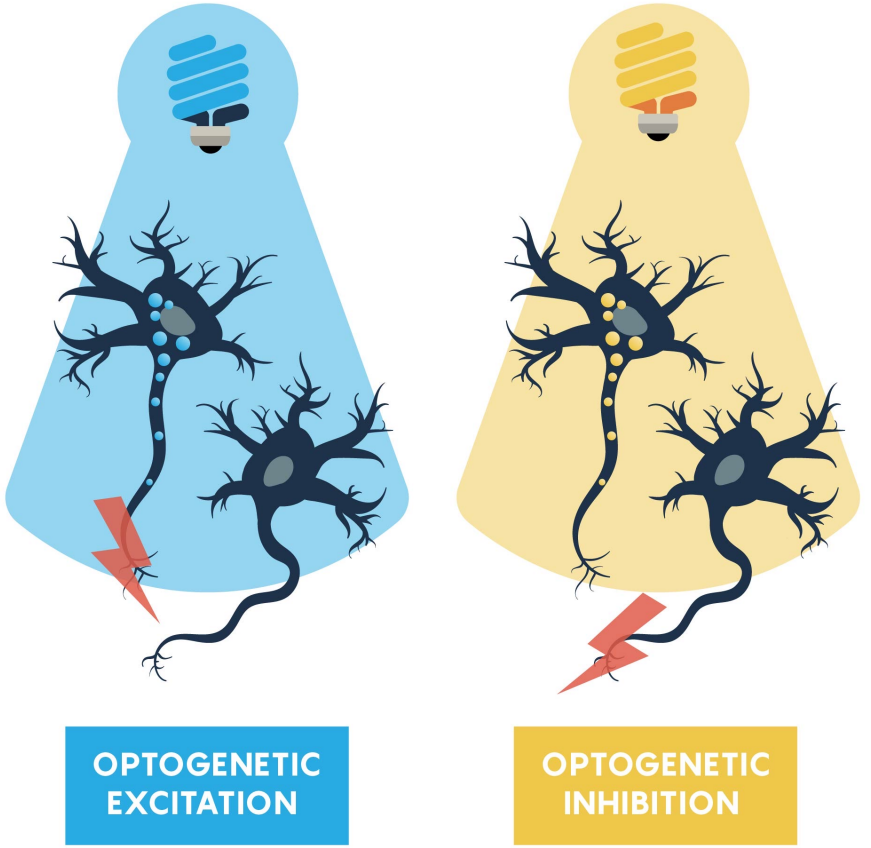
Other Applications & Specimens

- Neuron cells,
- Stem cells,
- (etc.)

- Intensity
- Wavelength
- Multi- or single-processing

- Arkeorhodopsins,
- Channelrhodopsins,
- (... other opsins)





Figures taken from [Neuroscience: Canadian 1st Edition Open Textbook] by Dr William Ju.

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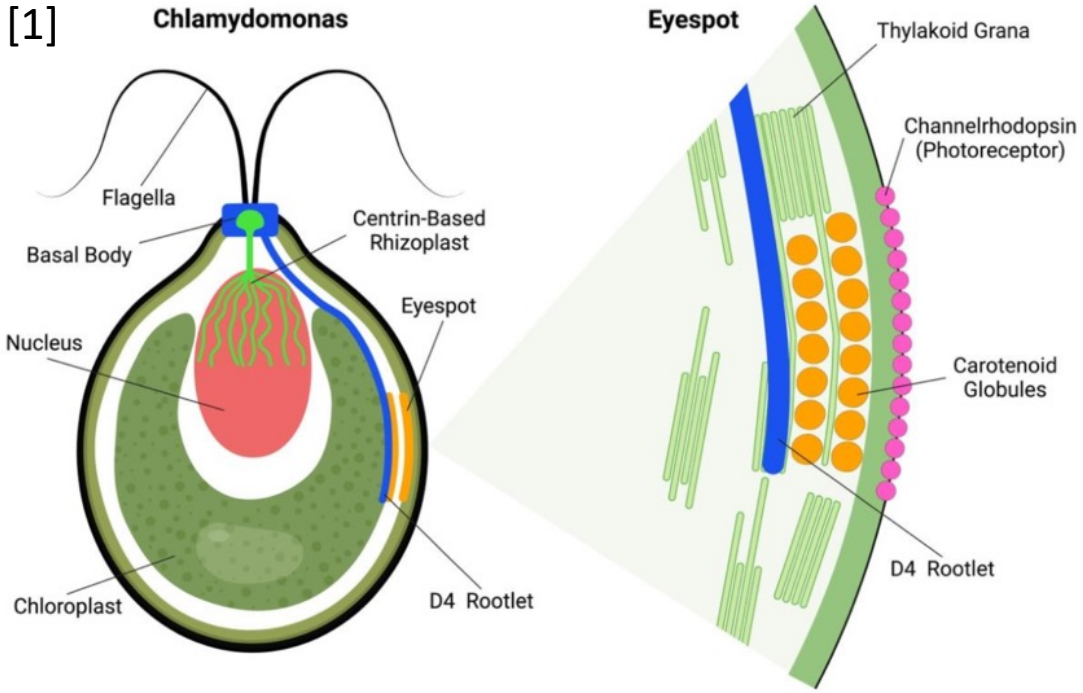
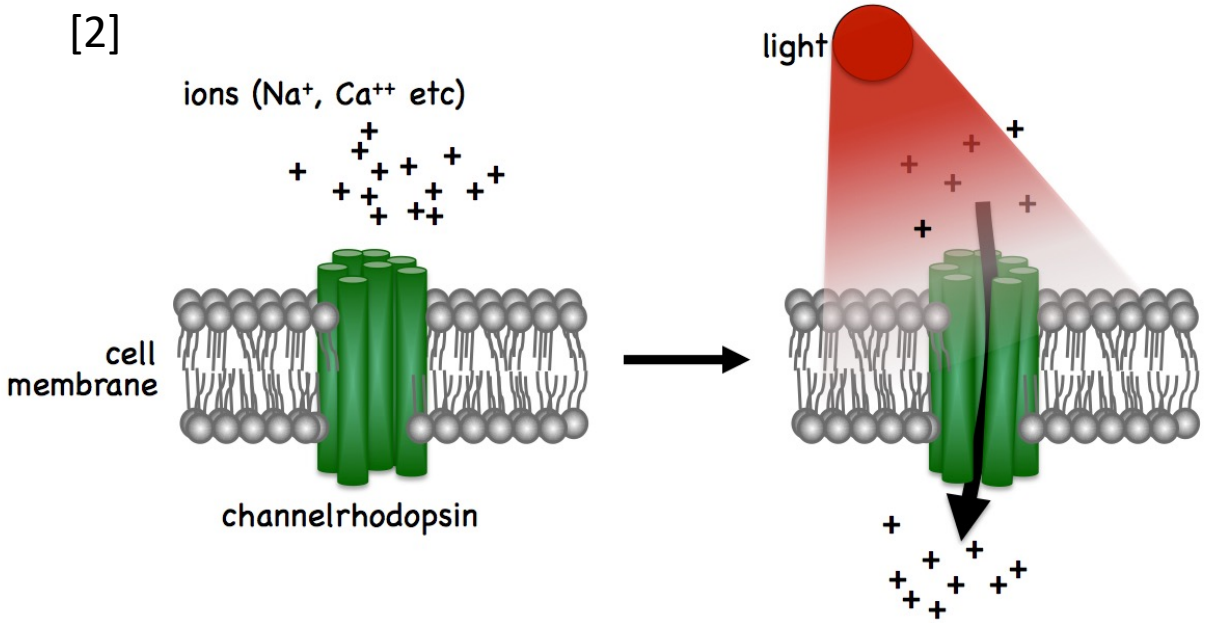
Opsins: Creates Voltage from Light

[1]



[2]



[1] Algal Ocelloids and Plant Ocelli - Scientific Figure on ResearchGate [accessed 18 May, 2023]

[2] Using Drosophila to demonstrate optogenetic tools on IndianaEdu [accessed 18 May 2023]

Opsins Used in Optogenetics

Cation Channels (activators)

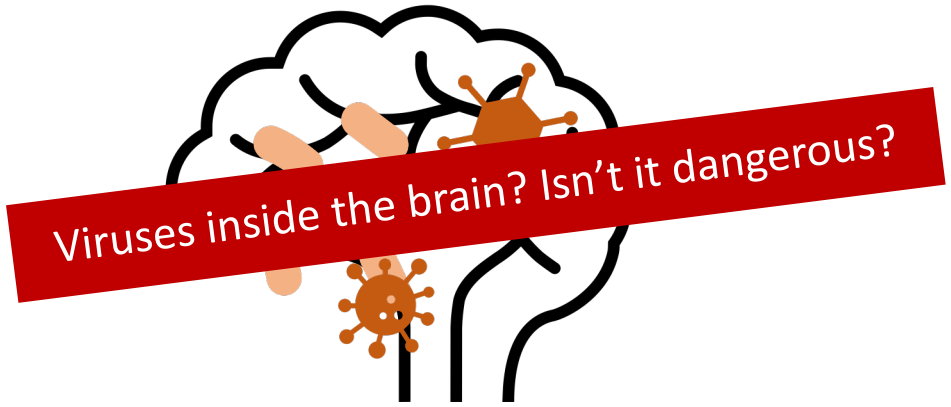
Molecule	Wavelength Needed
ChR2	**470 nm**
C1v1	560 nm
bReaChES	590 nm
Chrimson	590 nm
ReaChR	620 nm

Spike Freq up to 30 Hz
nearly real-time!

Anion Channels (inhibitors)

Molecule	Wavelength Needed
GtACR2	470 nm
ArchT	540 nm
NpHr	**590 nm**
JAWS	620 nm

Delivering Opsins to Neuron's: **Gen Threapy with Viruses**



1. Select a virus type that is suitable for your group of interest.
2. Add the opsin's genetic code into virus.
3. Give the virus into the region of interest and wait for the neuron to produce opsins.
4. The opsins will be on the walls of the cells.

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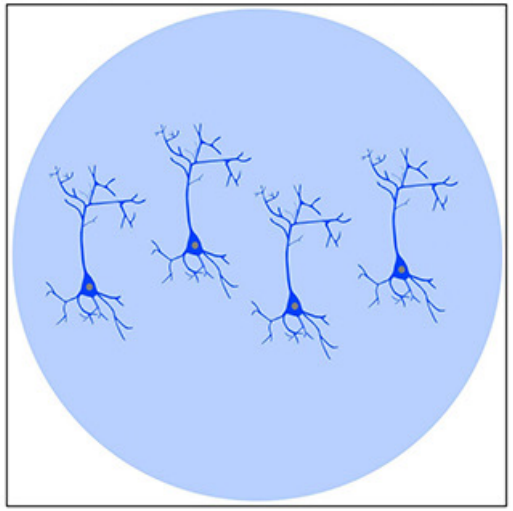
LEDs

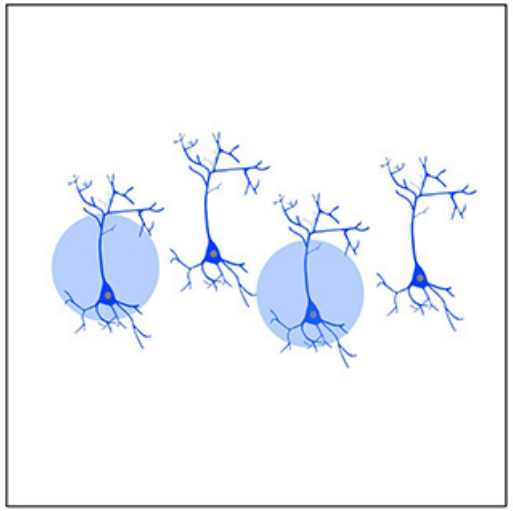
- Wide field-of-view
- Cheaper
- UV to NIR
- Fast response
- Low intensity

LASERs

- Narrow field-of-view
- Expensive
- Narrow spectral bandwith
- Slow responses
- High intensity



Widefield Optogenetics



Cellular-Resolution Optogenetics

2-Photon Microscopy

- Less scattering in deep tissues
- High resolution on 3D localization

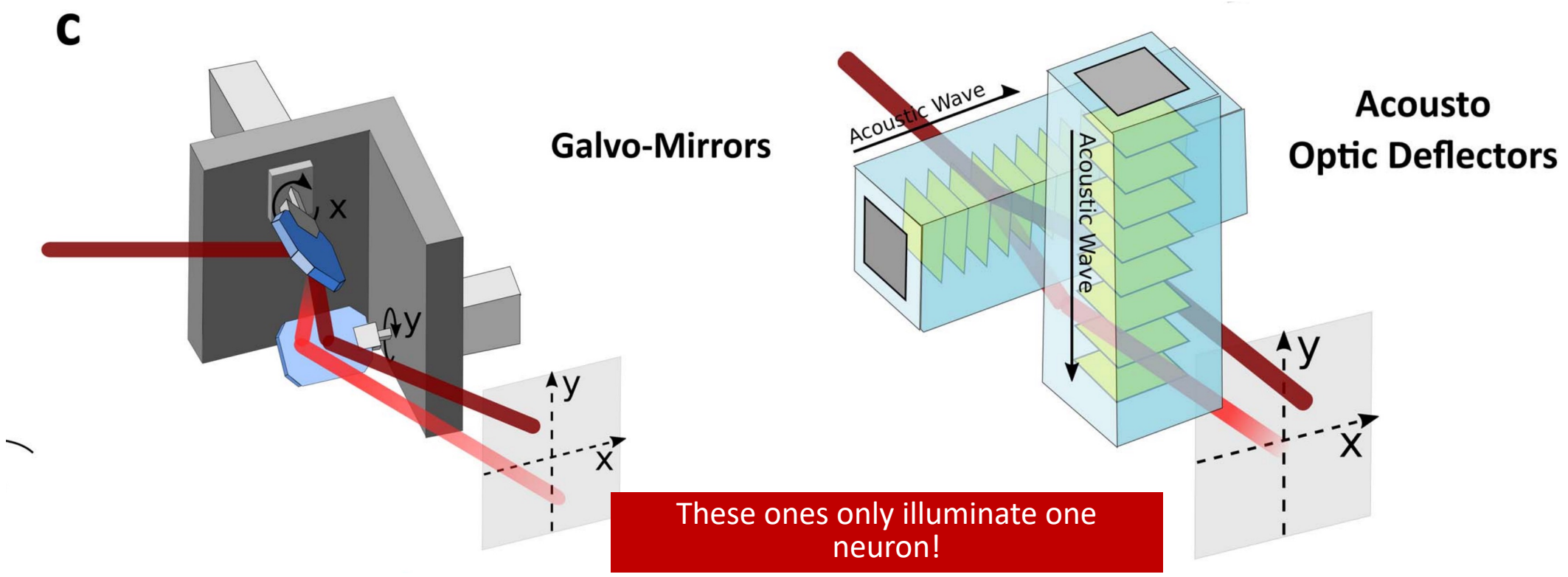
Approaches

- Scan-based: Longer time
- Parallel: Higher powered

Figure is taken from Mightex's blog on Optogenetics found here. [accessed 19 May, 2023]

Scan-based Techniques for Cellular-Resolution

Timing is the main drawback. $T_{total} = N_{neurons} \cdot T_{activation} + (N_{neurons} - 1) \cdot T_{change}$



These ones only illuminate one neuron!

Parallel Techniques for Cellular-Resolution

With Spatial Light Modulators

A **programmable** optics intensity and angle modulator. It includes **array of pixels** which all have different controllers.

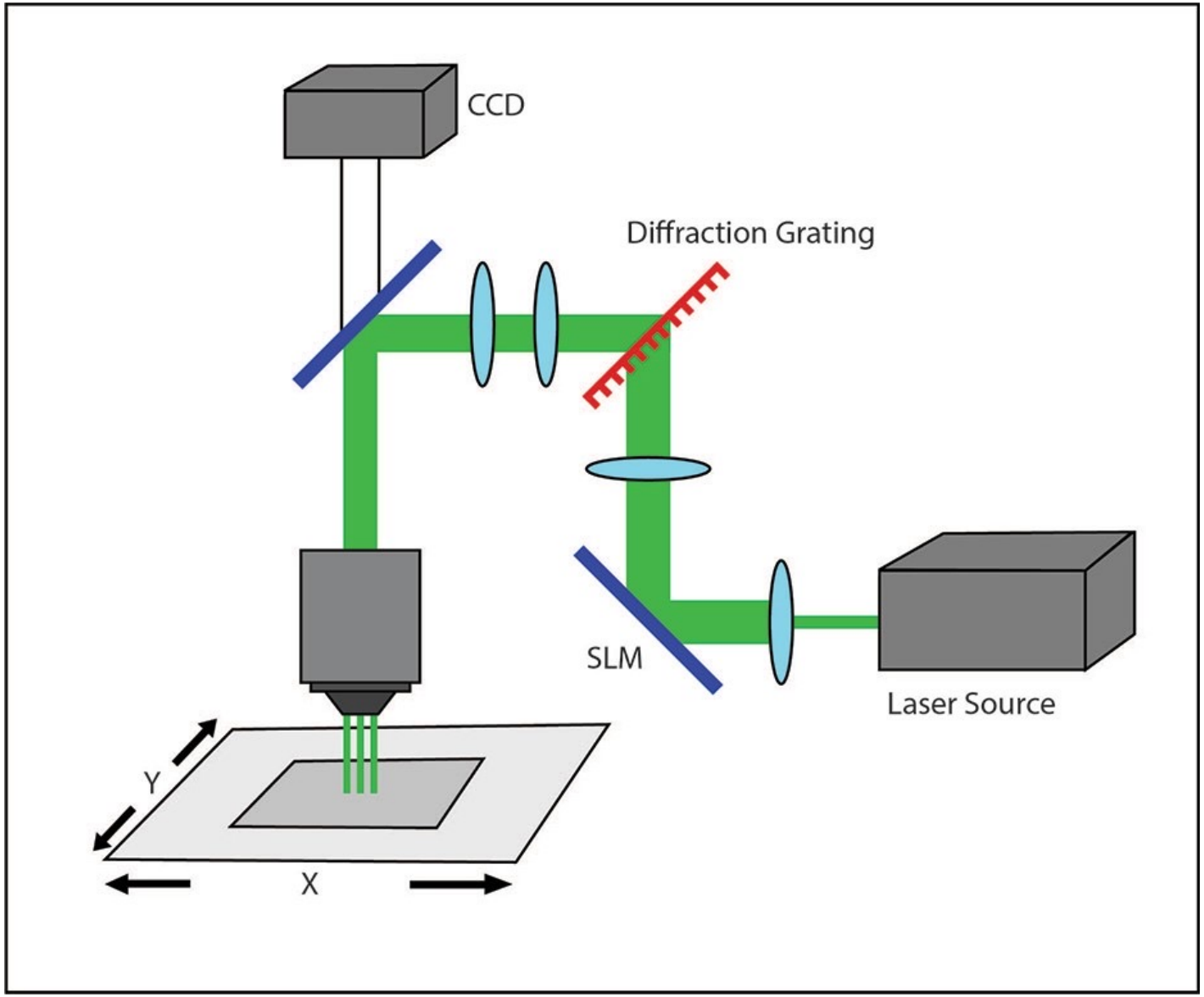
With Holography

Recording and re-construction of lights with their **interference pattern**.

Mixed Version

Save the pattern into a **computer generated holography**, and convert it to a form of SLM can understand. Afterwards, **contine with SLM technique**.

Mixed Version



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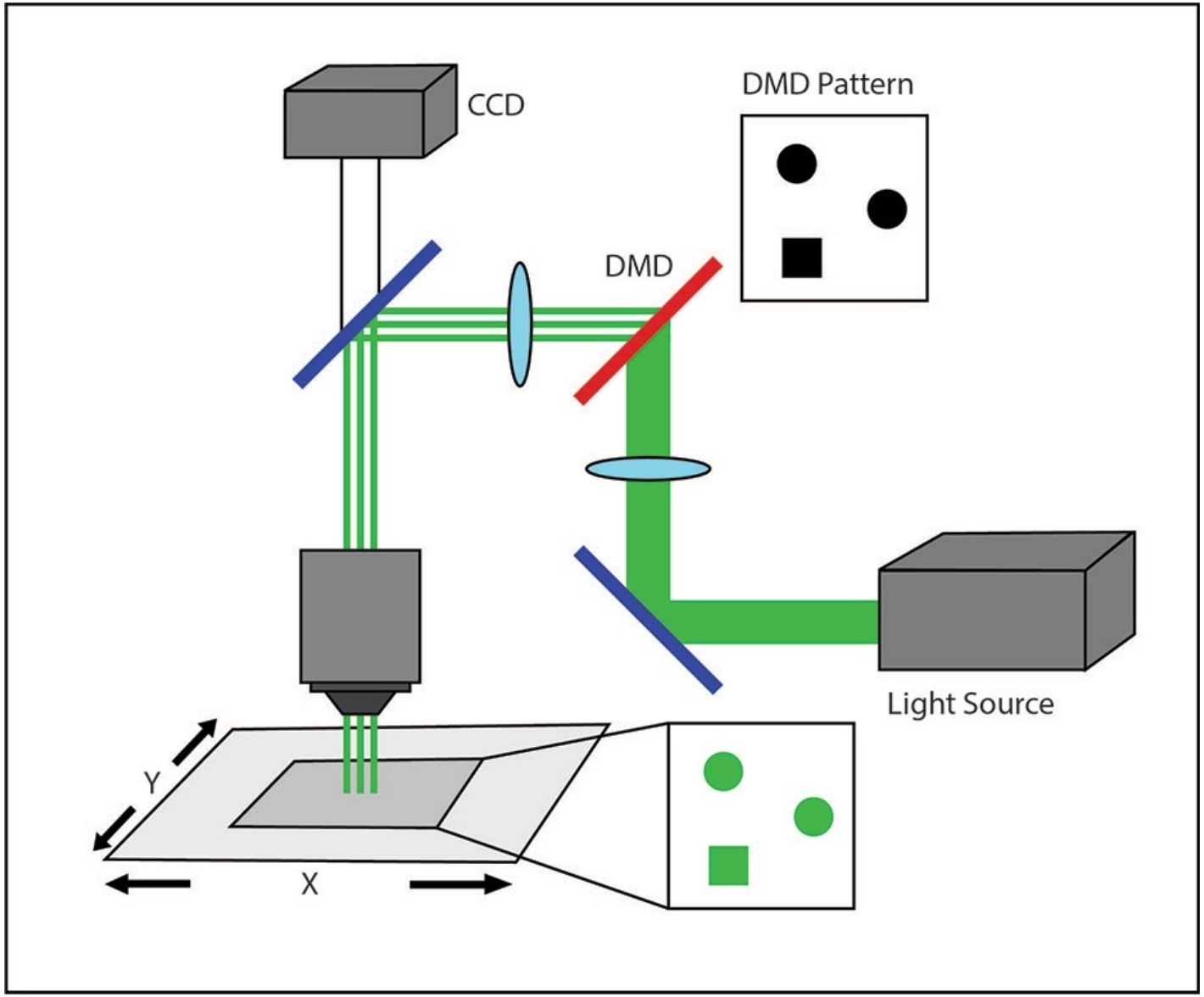
Microscopic Mirrors (DMDs)



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Applications on Other Fields

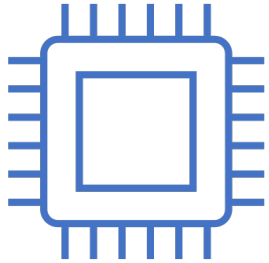
Cardiology: Control heart muscle cells, investigate arrhythmias.

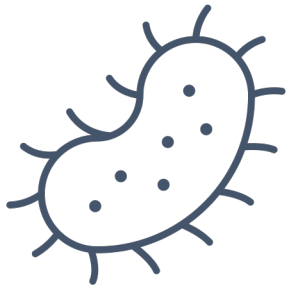
Endocrinology: Studies hormone secretion and regulation with light-signals.

Cell Biology: Investigates organelle dynamics and protein localization.

Bioengineering: Using light to create biosensors and bioactuators.

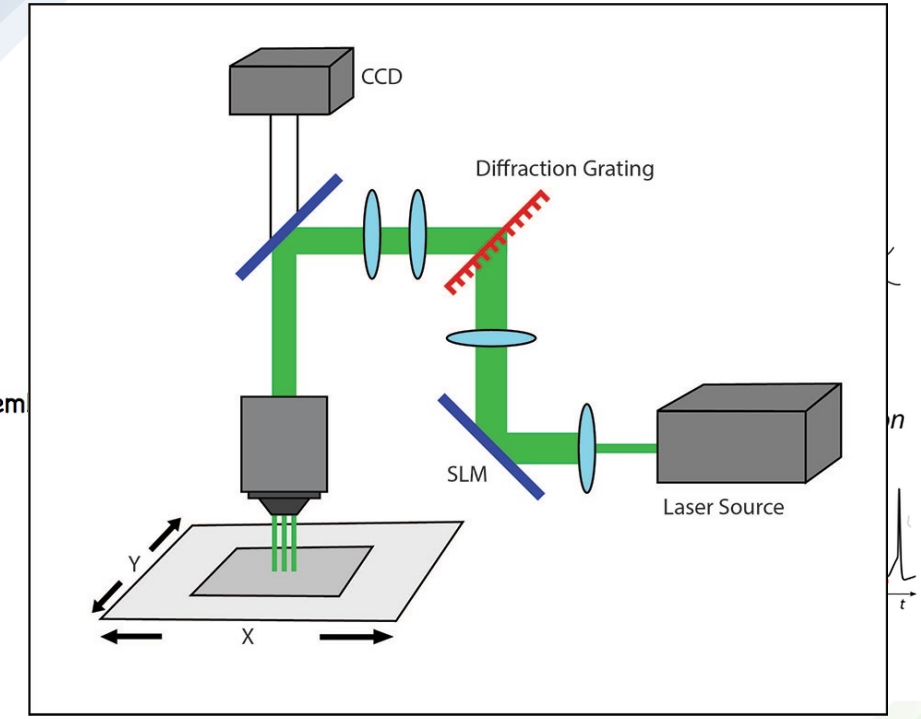
Ophthalmology: Regeneration of eye-sight with optogenetics.





The Outcomes

- Activate or inhibit specific neurons or tissues with light.
- It relies on light-sensitive proteins called **opsins**, which can be expressed in target cells through **genetic modification**.
- Optogenetics offers **high temporal precision**.
- Parallel activation of neurons is crucial for studying complex neural circuits: **Spatial light modulators** (SLMs) and **Holography.**
- Ongoing advancements are focused on **improving the tools**:
  - developing more efficient opsins,
  - expanding the range of wavelengths for activation,
  - enhancing the spatial precision of light delivery.



References and Further Reading

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Q&A Session

Feel free to ask me any question!

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EE4092: Advanced Biomedical Optics
Optogenetics