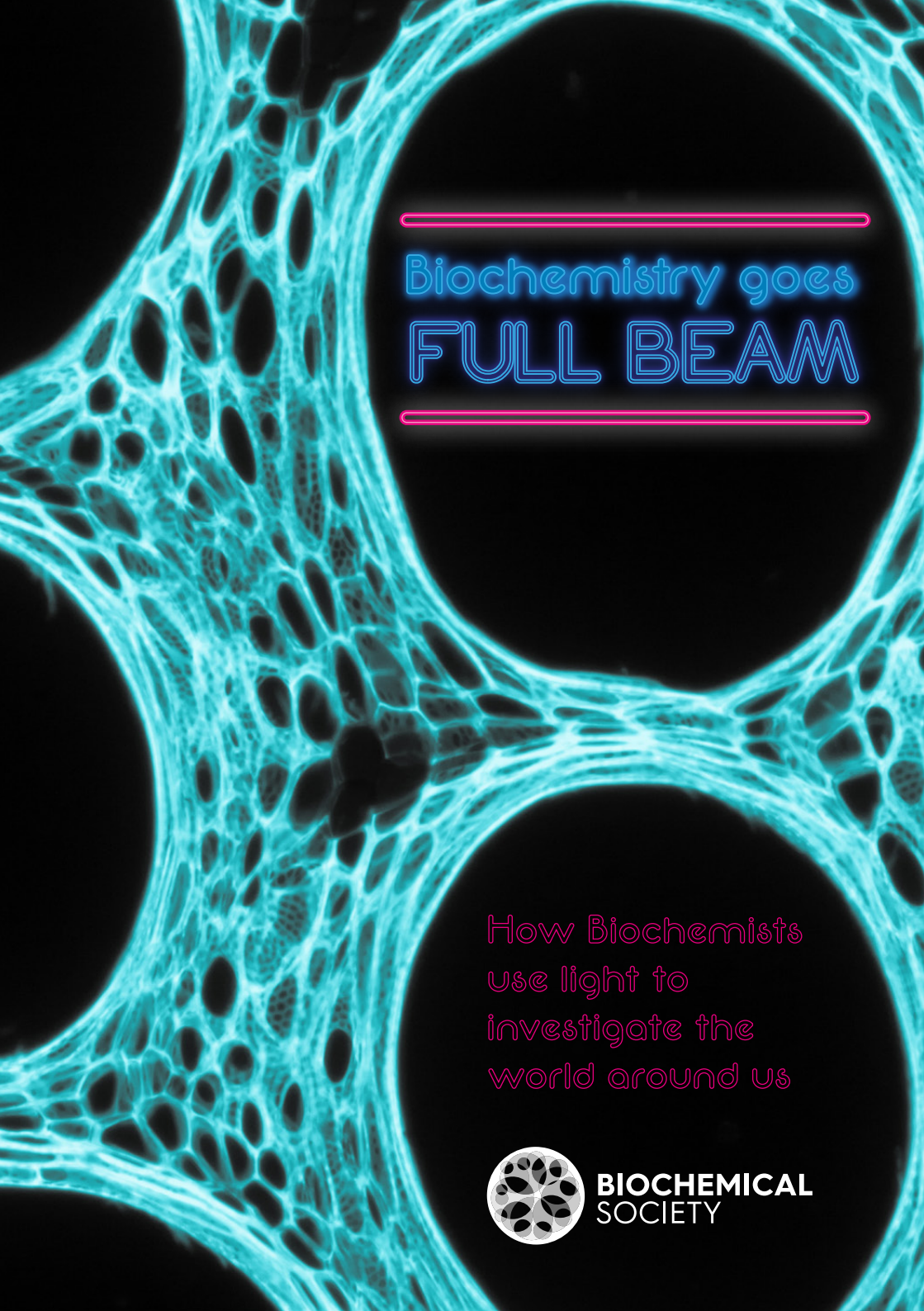
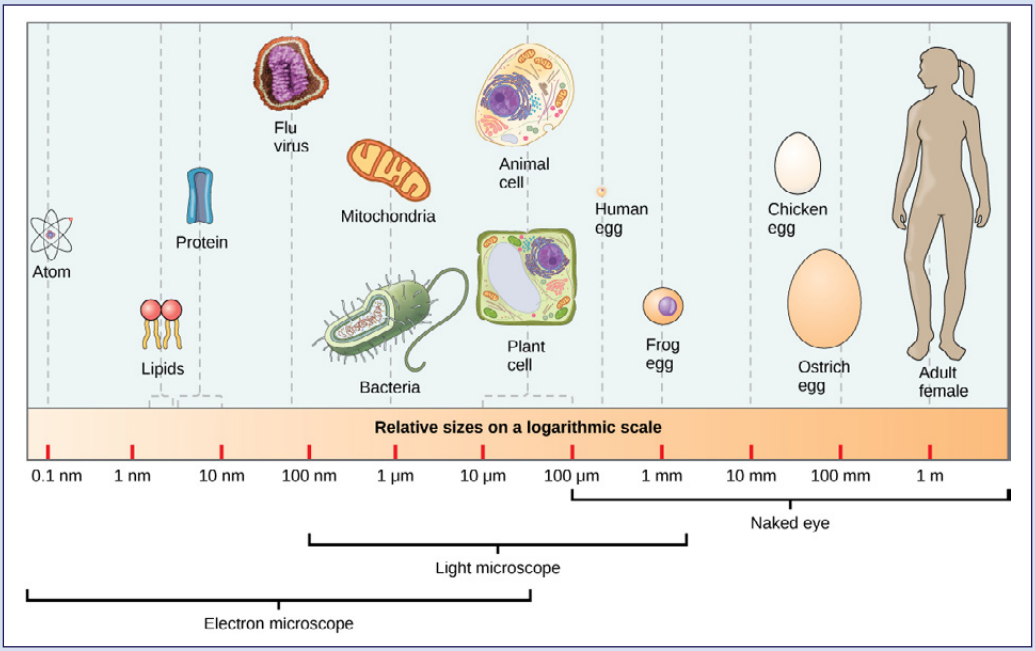

Biochemistry goes
FULL BEAM
How Biochemists use light to investigate the world around us
BIOCHEMICAL SOCIETY

Biochemistry goes FULL BEAM

Light – illuminating life

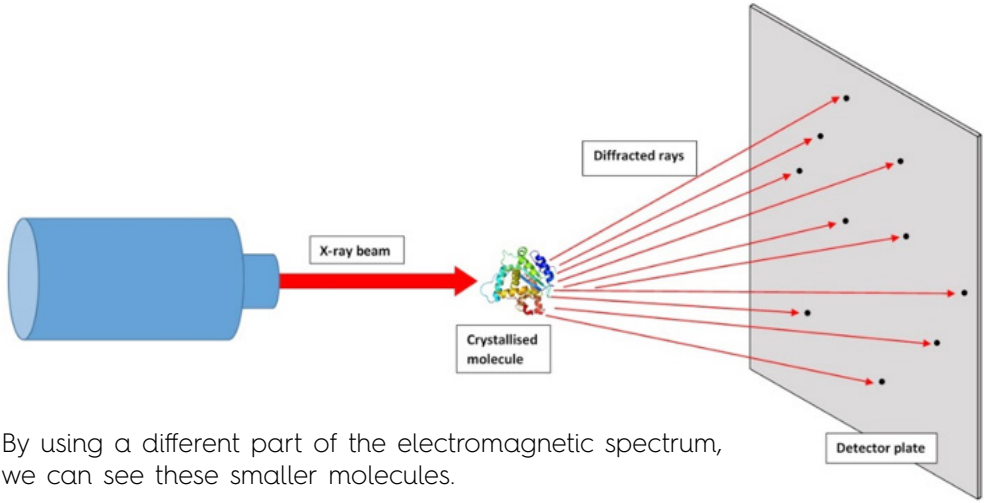
Much of biochemistry involves investigating things which are too small to see with the naked eye. Light microscopes use lenses to help us see things like cells which are fractions of a millimetre across. Lenses bend the light rays to make the object appear bigger. With a light microscope we can see individual cells and some of their larger components. Most human cells range from 0.1mm to 0.005 mm.



By CNX OpenStax - http://cnx.org/contents/GFy_h8cu@10.53:rZudN6XP@2/Introduction, CC BY 4.0, https://commons.wikimedia.org/w/index.php?curid=49923763

Cells are great, but the really interesting stuff is even smaller – too small to see even with the most powerful light microscopes because they are smaller than light rays.

Proteins, fats, sugars, and amino acids are all found inside cells and it is these chemicals that do all the work inside the cell. The largest proteins in a cell are less than 0.001mm and single amino acids can be down to 0.000001mm or even smaller. DNA, the genetic code that acts as our bodies' instructions for how to operate, is only 0.000002mm across – far too small to see with a light microscope.



By using a different part of the electromagnetic spectrum, we can see these smaller molecules.

One way to do this is to turn the molecules into crystals and then fire X-rays at them. This, unsurprisingly, is known as X-ray crystallography. The image we see is a sort of shadow caused by the molecules; this is called a diffraction pattern. By using maths, we can work out what shape the molecules must be to cause that sort of pattern.

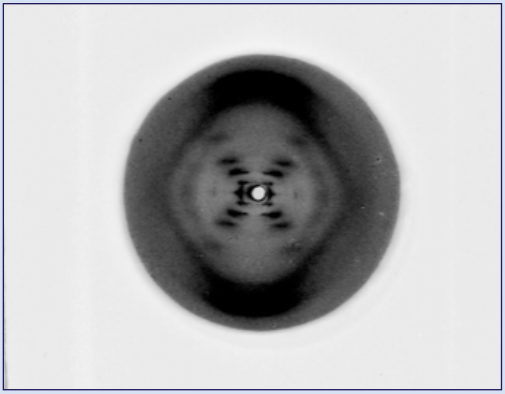


Photo 51, the X-ray diffraction pattern caused by DNA. King's College London Archives License: CC-BY-NC

Rosalind Franklin

One of the most famous of these X-ray diffraction patterns is Rosalind Franklin's 'photo 51' which led to the working out of the structure of DNA.

This tells us what these molecules look like, but because we had to turn them into crystals first, they are 'fixed' samples and we cannot see them in action in the cell.

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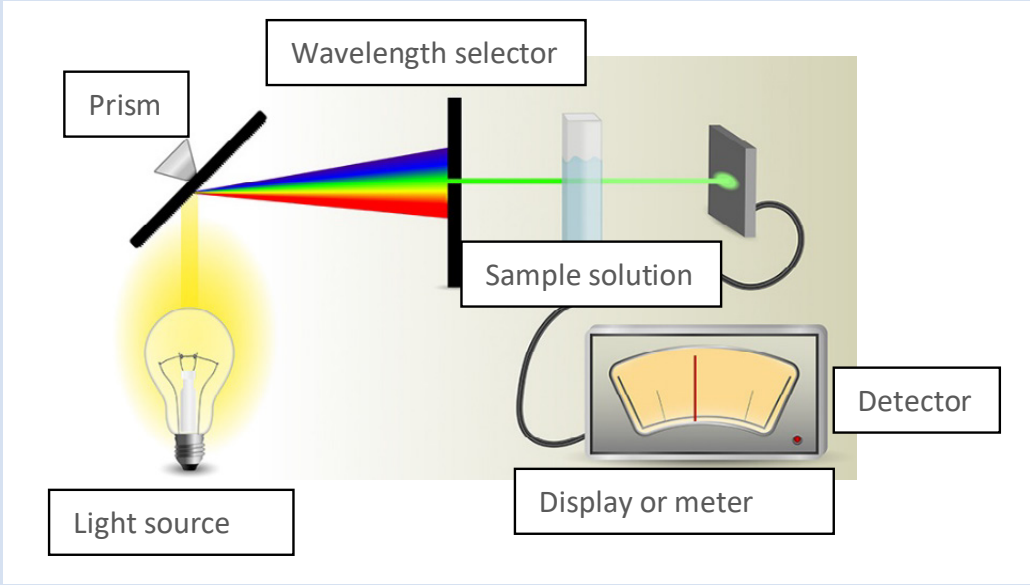
Spectrophotometry – measuring with light

One of the most common pieces of equipment in a biochemistry lab also uses light to investigate molecules. A spectrophotometer shines a particular wavelength of light at molecules and measures the effect the molecules have on the beam of light.



Many molecules absorb light at certain wavelengths and so by shining a beam of light through a sample and measuring how much of the beam comes out the other end, we can calculate the amount of that type of molecule there is in a sample. This can be used to measure the concentration of molecules, the rates of reaction and the way that molecules change under different conditions.

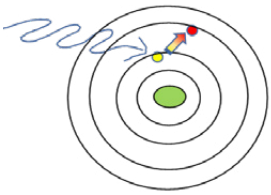
Spectrophotometry is a very precise, accurate and fast technique which is relatively cheap and easy to carry out.

Fluorescence – tagging your cells

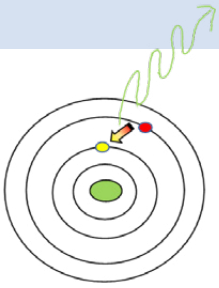
Fluorescence is a naturally occurring process. Some natural fluorophores include tonic water, egg shell and cumin. It occurs when the molecule absorbs light of a particular wavelength and then emits light of a different wavelength.

Everyday objects that naturally fluoresce. From left to right: (under UV/black light): olive oil; vitamin B2 (in water); turmeric (in alcohol); Irish Spring soap; canola oil; tonic water; laundry detergent. Picture by Professor Brian Wagner, UPEI

One of the best ways to see what molecules are doing inside a living cell is to 'tag' them with a marker which will show us where they are. Fluorescent tags give out light under the right conditions, meaning we can see where a molecule is. Using a fluorescent microscope, we can create the right conditions for these tags to 'shine out' so that we can see them clearly.



Light of a particular wavelength is absorbed by the atom and 'excites' an electron to a higher energy level.



The excited electron drops back to its original energy level and emits light at a different wavelength.

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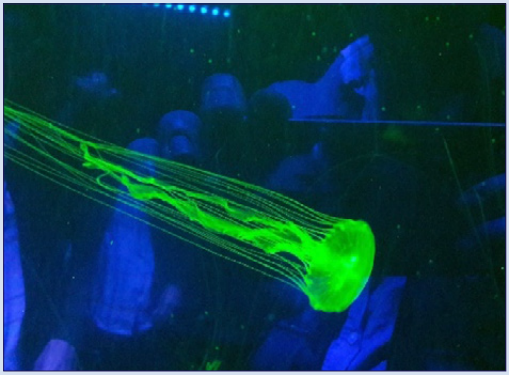
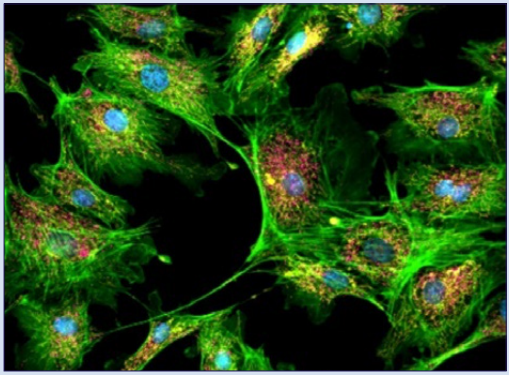
Fluorescence – tagging your cells (cont)

There are a number of ways to add fluorescent tags into a cell. We can use dyes which will only stick to particular types of molecules, or we can genetically engineer proteins so that they are made able to fluoresce. This is done by inserting a small piece of DNA which creates something called Green Fluorescent Protein, or GFP for short. This was discovered in Jellyfish and is the protein which makes them naturally fluorescent under UV light.





There are different colours of fluorescent tags and we can attach them to different molecules to see where they are, how they interact, where they move to/from, and even how many of them there are.

By doing this we can tell how much of a protein is made under different conditions by looking at the amount of light given off. The more protein produced, the brighter the glow.

The big advantage of using fluorescent markers is that it can be done in living cells, or even in whole organisms so that we can see how the cells work in real-time.

Bioluminesence – way to glow!

We may rely on external sources for all our light needs, but there are many living things which are able to create their own light using their natural biochemistry. This is called bioluminescence and occurs in glowworms and fireflies as well as some types of bacteria, fungi and marine creatures. This is used in everything from bacteria communicating with each other, to angler fish luring prey and from adaptive camouflage to attracting mates.

It works by using a group of enzymes known as luciferases and light emitting molecules called luciferin which react together to create light. Biochemists can now use these bioluminescent systems to do all sorts of cool stuff. They can use them as markers in cells, in medical imaging, and as reporters to let us know a gene is working. There are also scientists working on using this process to create light sources for street lighting.

Photo of bioluminescent bacteria by Dr M Roberts.

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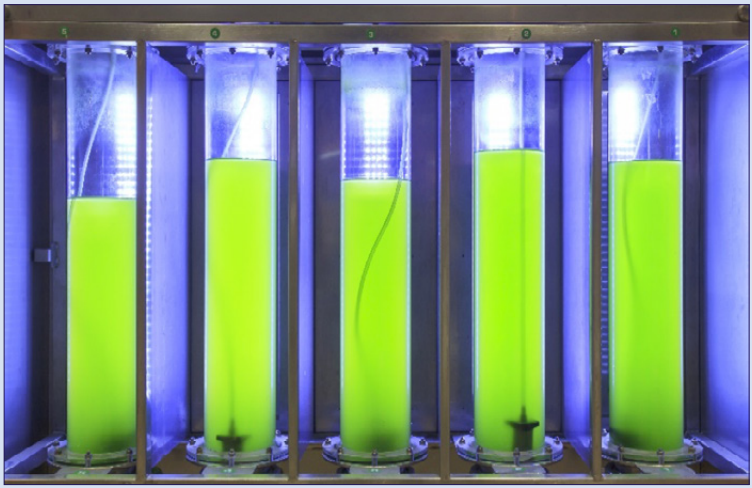
Photosynthesis – learning from plants

We may have figured out some ways to manipulate light, but that's nothing compared to how plants are able to make use of light.

The molecule chlorophyll is able to use energy from light to convert CO_2 and water into glucose and O_2 in a process called photosynthesis. Almost all life on earth is dependent on this reaction occurring.

If we could harness the Sun's energy like this, we might be able to produce sustainable, green energy.

Biochemists are investigating the photosynthetic reactions to see if we can manipulate them for our own ends.



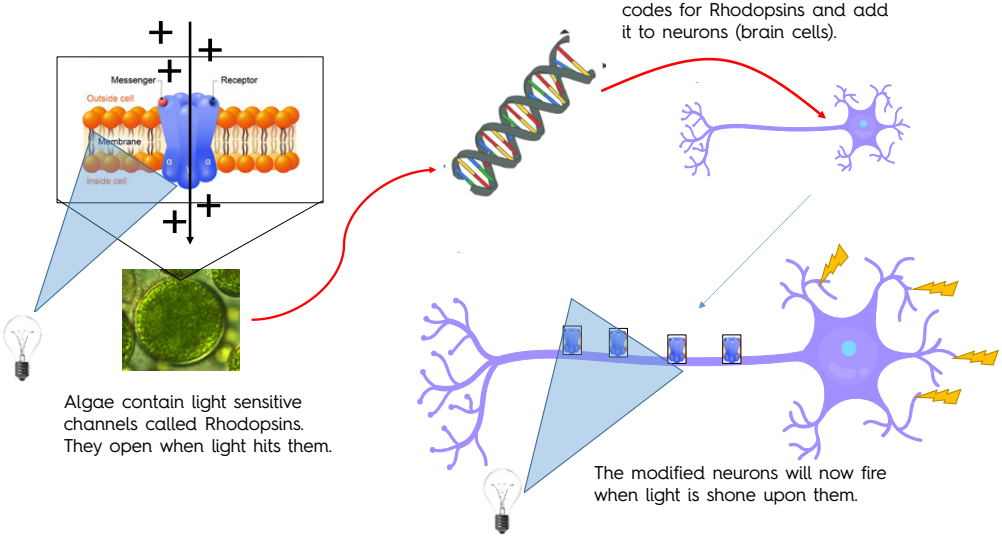
Algae being grown in a bioreactor. The oil inside the algae can be converted to biodiesel.

Photosynthetic algae can be used to produce biofuel which could act as a carbon neutral replacement for our rapidly disappearing fossil fuels such as petrol or diesel. Understanding the metabolism of algae will allow us to fine tune them to be as efficient as possible at making biodiesel.

It is also possible to 'hack' photosynthesis to use it to produce electricity. Biophotovoltaic cells use plant biochemistry to produce a voltage and a small current. It is hoped that these could be used to power devices in remote locations with little need for maintenance and small environmental impact.

Optogenetics – laser brain control!

Algae have also been used to help us study the brain. Algae have proteins called channel rhodopsins which help them respond to light. These channel proteins act as gates which let ions in or out of the cell. These gates open and close in response to light. Conveniently for us, controlling the amount of ions that can go in and out of a cell is how our brain cells (neurons) work. Researchers realized that if they could genetically engineer neurons to have these channel rhodopsins, they could switch the brain cells on and off by shining a light on them. This is known as optogenetics.



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Optogenetics – laser brain control! (cont)

By using fibre optic lights, researchers can stimulate different types of brain activity, triggering things like movement, behaviour, sleep, or even memory.

Before this, neuroscientists could stimulate brain activity by using drugs or electrical probes. The problem was that drugs acted too slowly and electrical probes are not precise enough to only affect particular neurons. Using optogenetics, we can control specific cells instantly in living organisms. We can also use optogenetics to feed back information about what is going on in the brain at any exact moment.

It doesn't just have to be used in the brain either. Optogenetics is currently being used to study diabetes in the pancreas as well as other places where you might want to impact just a small selection of cells amongst many. It also looks like it may be possible to use optogenetics to help treat diseases such as epilepsy, Parkinson's, schizophrenia, Tourette's and others. One way to do this might be to use implants which can monitor brain activity and use flashes of light to modulate brain activity to prevent, say, an epileptic fit.

Further Reading:

biochemistry.org/Portals/0/Dec2016-Biochemist.pdf

biochemistry.org/ezine/355/index.html

essays.biochemistry.org/content/60/3/255

scientificamerican.com/article/optogenetics-controlling/

stem.org.uk/system/files/elibrary-resources/legacy_files_migrated/9579-catalyst_21_4_487.pdf

insight.mrc.ac.uk/2013/04/25/behind-the-picture-photo-51/

microscopyu.com/techniques/fluorescence/introduction-to-fluorescent-proteins

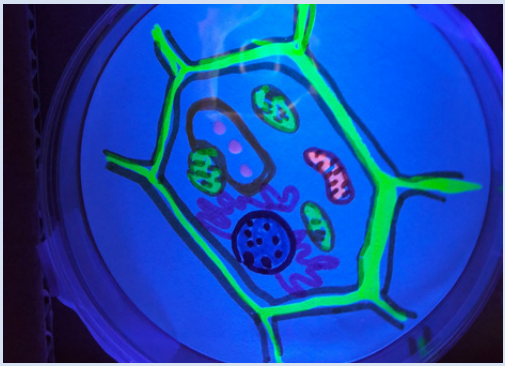
Do try this at home!

Have a go making your own fluorescent tagged cells. All you need are some colouring pens, some highlighter pens and an ultraviolet (UV) light source (these can be picked up for a few pounds online).

Draw your cell using the regular colouring pens and then use the highlighters to 'tag' the structures that you want to fluoresce. The ink in the highlighter pens absorb the UV light, which human eyes can't see, and then gives out regular light, which the human eye can see.

When biochemists do this in real cells, they use a protein called GFP (Green Fluorescent Protein), which does exactly the same thing. They can 'tag' different bits of the cell with GFP to study them more easily.

The molecular structure of GFP (Green Fluorescent Protein)



Highlighter pen under a UV light source

BIOCHEMICAL SOCIETY

THE **BIOCHEMICAL SOCIETY**

WHO ARE WE?

The Biochemical Society promotes the future of molecular biosciences; facilitating the sharing of expertise, supporting the advancement of biochemistry and molecular biology, and raising awareness of their importance in addressing societal grand challenges.

OUR EDUCATION PROGRAMME

The Biochemical Society's Education Programme aims to support the next generation of biochemists and provide opportunities for people of all ages to explore and discuss the issues raised by developments in molecular bioscience. We do this with our:

- Public Events
- Careers guidance resouces
- Materials for students, teachers and educators, scientists and the general public

biochemistry.org/education

For further information, please contact
E: education@biochemistry.org
T: 020 7685 2451

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