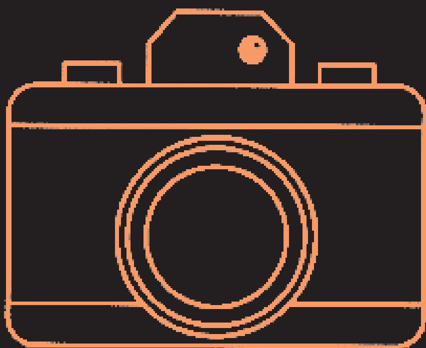
METABOLIGHT

Updates from UCL's ground-breaking project using light to monitor brain activity

02: The engineering issue



Welcome to our second edition of *MetaboLight* publications. Following the Science edition, this is the Engineering edition. Here the MetaboLight team introduces some key engineering advances and concepts that are extremely important in the development of our instruments and research.

This edition also offers the opportunity to see how physics and engineering can work together to produce devices and components such as the digital camera and the laser.

The third and last edition will be about our research within the hospital.

Enjoy!

Ilias Tachtsidis
Reader in Biomedical Engineering and Senior Wellcome Trust Fellow

Produced by the MetaboLight team from the UCL Department of Medical Physics and Biomedical Engineering; and funded by the Wellcome Trust

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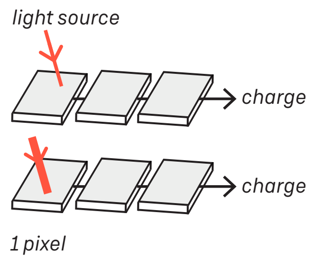
A brief history of digital cameras

by Ilias Tachsidis, Biomedical Engineer

1969

BOYLE & SMITH

Charge-couple device (CCD) image sensor developed at Bell Laboratories. Rows of pixels turn light intensity into a charge.



1970–1973

BELL LABORATORIES

First solid state video camera using CCD developed. Fairchild Semiconductors, USA improves the CCD.

© Bell Labs

1975

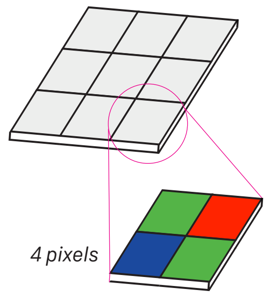
SASSON, KODAK

First digital camera (100 × 100 pixels) made. The image was recorded onto a cassette tape and this process took 23 seconds.

1975

BAYER

Digital cameras capture colour images using the Bayer Colour Filter Array. Each coloured pixel records one of the primary colours of light.



1981

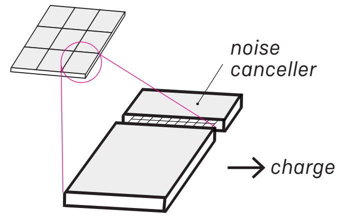
SONY

Introduces 'Mavica' – a camera that record images on a 'floppy disk' (ask your parents!).

Mid 1990s–today

ERIC FOSSUM, NASA

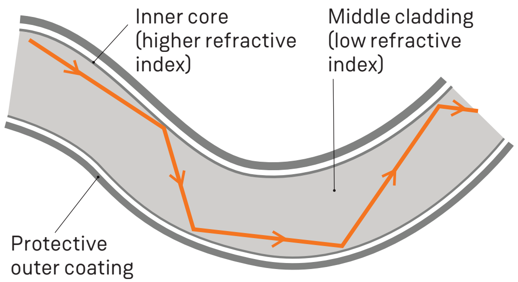
Complementary Metal Oxide Semiconductor (CMOS) invented to reduce the size of cameras on spacecraft. Today, most consumer products with cameras (like your mobile) use this.



Bending light

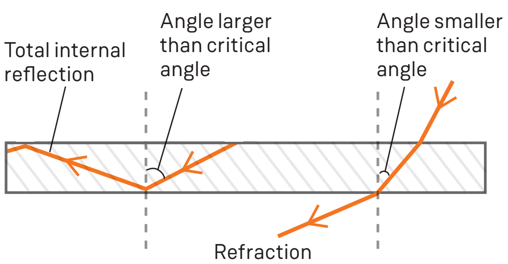
by Paola Pinti, Biomedical Engineer

Fibre optics are made of thin strands of glass or plastic – slightly thicker than a human hair. They can send signals for long distances detected through patterns of light, and can transmit more information than conventional cables with the same diameter.



STRUCTURE

Fibre optic cables consists of 3 parts: an inner core through which the light travels, middle cladding to keep the light inside the core, and an outer coating to protect the fibres. Light can travel through this structure for long distances and around curves without losing much intensity by bouncing repeatedly off the core's walls.



CRITICAL ANGLE

Light travels in straight lines until it reaches an object. If light reaches an object at an angle more than the critical angle (this angle depends on the material) it reflects on itself (total internal reflection). If it reaches an object below this angle it will pass through the object and bend (refract). Fibre optics works when the angle of light is always greater than the critical angle.

APPLICATIONS

Fibre optics are most commonly used for radio, TV broadcasting, internet and medicine. We use fibre optics in our MetaboLight devices to shine light into the brain and to measure the light coming out after travelling through the brain.

Creating light

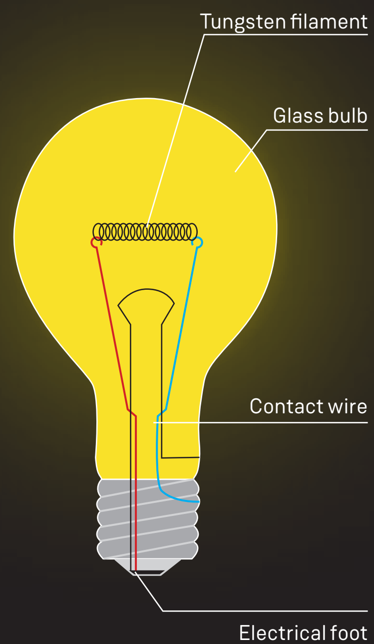
by Luca Giannoni, PhD student in Medical Physics

Light sources come in many different shapes and sizes. Here are the ones most commonly used in near infrared spectroscopy (NIRS).

1. INCANDESCENT LAMPS

These include the traditional tungsten light bulbs that used to be common in homes. The bulb contains an inert gas or vacuum. A metal filament within the bulb is heated up by an electric current to such a high temperature that it glows with visible and infrared light.

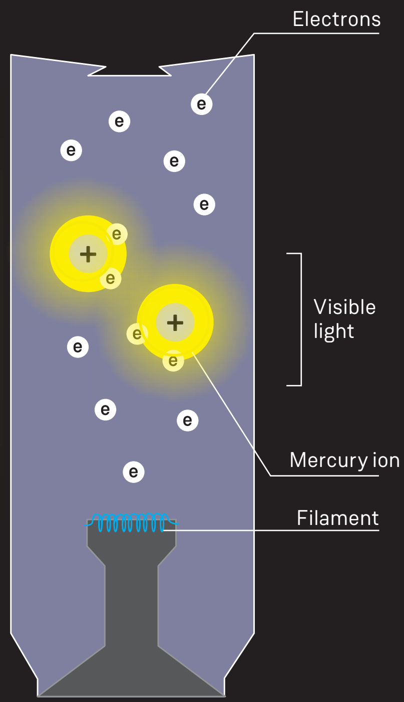
Halogen lamps, widely used in NIRS, are a type of incandescent lamp. They contain a mixture of inert gas and halogen gas (such as iodine). This produces a chemical reaction that increases the operating life of the filament, as well giving a brighter light.



2. GAS-DISCHARGE LAMPS

These generate light by sending an electric discharge through a gas, ionising it and creating a plasma.

The high-temperature plasma emits light photons at a specific range of wavelengths, depending on the type of gas (usually a noble gas such as argon, neon, krypton or xenon). Gas-discharge lamps are more efficient than incandescent lamps, but more expensive and complex to manufacture.

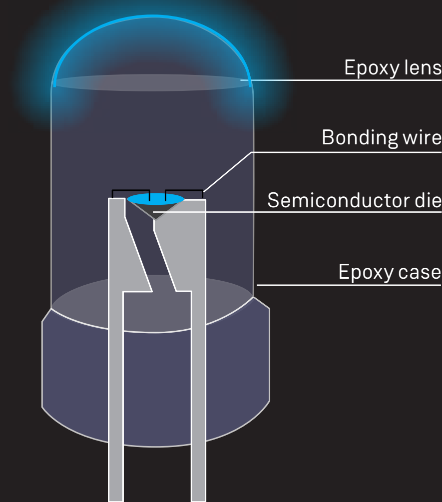


3. LIGHT-EMITTING DIODES (LED)

LEDs use semiconductors to produce light via electroluminescence – a physical phenomenon involving emission of light in response to the passage of an electric current.

Depending on the type of semiconductor used, LEDs can produce different wavelengths (colours) of light, within very small wavelength ranges. White light can be made by mixing together individual LEDs of different colours.

The main advantages of LEDs are their low cost, small size, low energy consumption and long operating life.



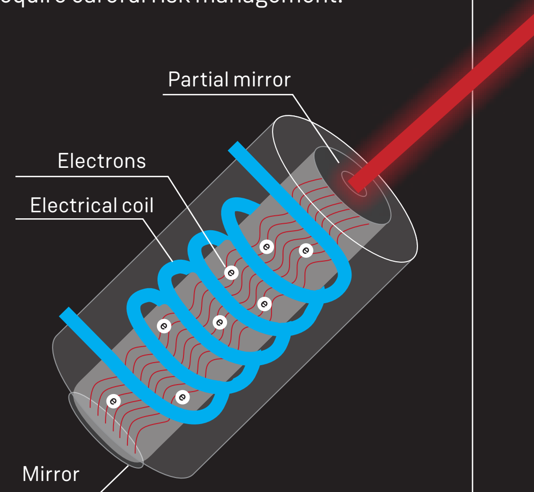
4. LASER

Stands for: Light Amplification by Stimulated Emission of Radiation. The light is released by electrons, which have been excited by energy from an electrical current.

The electrons give out light at a very specific wavelength (colour); it is *monochromatic*. Importantly, the light is also *coherent*, meaning the wave peaks are all in step. This allows it to be focused very precisely over long distances, which is one of the reasons it can be so dangerous. Lasers can also create very short bursts of light (as short as one millionth of a billionth of a second!)

Supercontinuum lasers have an additional step that spreads wavelengths across a broader spectrum, including the visible and infrared. Filters may then be used to select the desired wavelengths.

Laser are normally more bulky and expensive than other light sources, and require careful risk management.



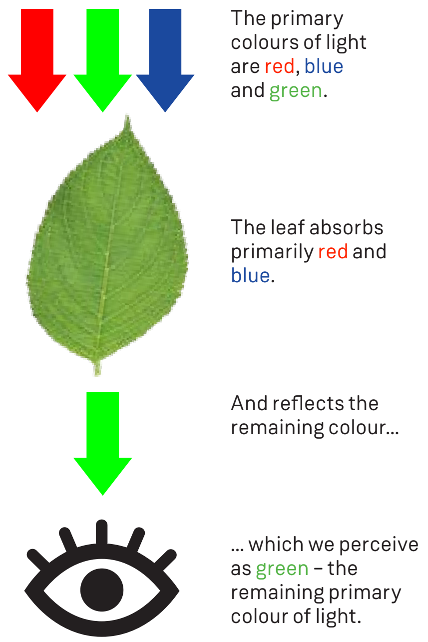
Measuring colour

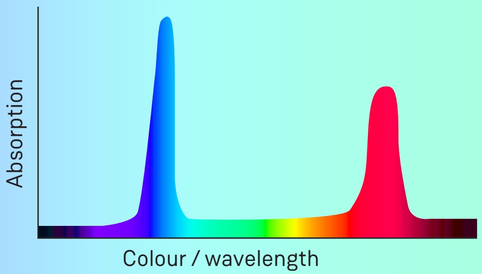
by Gemma Bale, Medical Physicist

Spectroscopy is the study of the interaction of light with matter. Understanding how specific wavelengths of the electromagnetic spectrum interact with matter lets us work out its specific structure and properties.

SPECTROSCOPY AND COLOUR

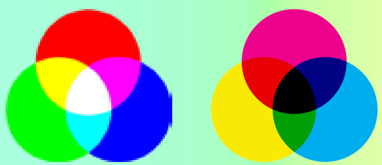
White light is made up of all the colours of the rainbow. Different objects have different colours because of the different colours of light, or wavelengths, they absorb or reflect. We perceive colour as the combination of the colours that aren't absorbed – the colours that are absorbed are the colours that we don't see. This can be shown on an absorption spectrum like the one of a leaf, below – note the peaks in absorption levels of blue and red light.





DID YOU KNOW

Light and pigment colour models are different! Light colour models are made of red, green, blue (RGB) and combine to made white. Pigment colour models are made of cyan, magenta and yellow, which combine to make black (CMYK).



light colour model (RGB)

pigment colour model (CMYK)

SPECTROSCOPY IN THE LAB

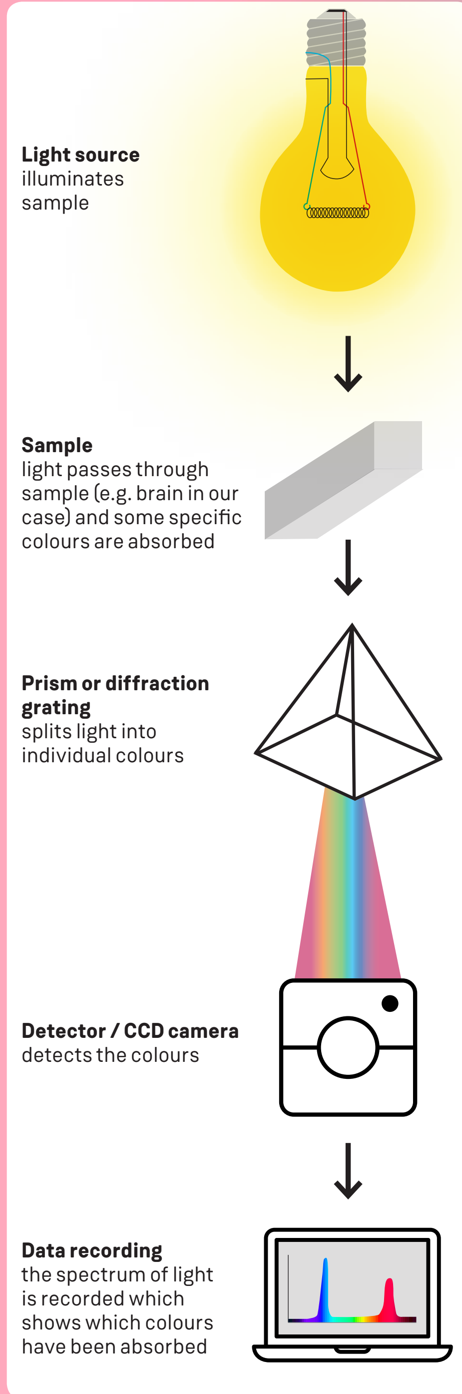
We use spectroscopy to measure the spectra (plural of spectrum) of objects we know, like the leaf. But in the lab, we also work backwards to identify unknown objects by matching them with known spectra. We use devices called spectrometers to do this.

In spectroscopy, a light source produces white light which is shone onto a sample. Different wavelengths (colours) of the white light are either absorbed by the sample or transmitted through it. The transmitted colours can be detected by a spectrometer which splits the light into its many colours with a prism or diffraction grating, and then detects this spectrum of light with a camera. We can also use wavelengths beyond the visible spectrum of light, known as near infrared spectroscopy (NIRS).

MEASURING OXYGEN IN BLOOD

In our devices, we use a spectrometer to measure brain activity. We can measure a brain's metabolism and its level of oxygenation, as different levels of oxygenation have different spectra.

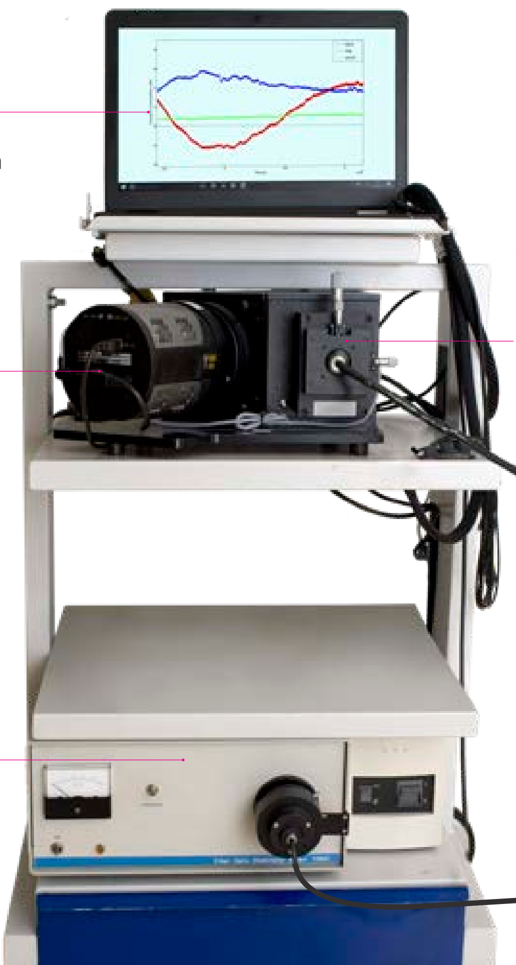
See our *Science* issue for more details: metabolight.org/resource/metabolight-magazine-issue-1-science/



Visualising brain health

by Isabel de Roever, PhD student in Biomedical Optics
Find out more at metabolight.org/resource/cyril/

CYRIL stands for CYtochrome Research Instrument and appLication. It's a **near-infrared spectroscopy system** that measures changes in oxygenation and metabolism in the brain. These measurements can monitor the severity of brain-injury in babies so doctors can understand and give the most appropriate treatment.



6. LAPTOP
controls all the components of CYRIL. Software converts the light intensity collected by the camera to concentration data of oxygenation and metabolism.

5. CAMERA
charge-coupled device (CCD) collects the separated light that has returned from the brain.

1. LIGHT SOURCE
CYRIL uses a broadband (over a hundred wavelengths) white light source with a high intensity in the NIR region. It is a tungsten halogen light bulb.

4. SPECTROMETER
separates the incoming light from the brain into its different wavelengths

2. OPTICAL FIBRES
connect the light source to the subject (using source fibres) and the subject to the detector (using detector fibres).

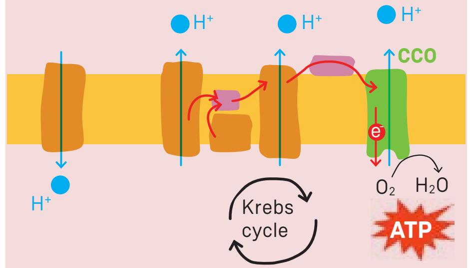
3. OPTODE HOLDER
securely holds the source and detector fibres in place on a person's head.

MONITORING BRAIN OXYGENATION

CYRIL can distinguish between oxygenated and deoxygenated blood as they are different colours. Haemoglobin, the protein in the blood that carries oxygen, is redder in oxygenated blood, and more purple in deoxygenated blood.

MONITORING METABOLISM

Metabolism (how much energy cells are producing) can be measured by monitoring the colour change of an enzyme called cytochrome-c-oxidase (CCO). CCO is found in the mitochondria, or 'powerhouse', of cells.



ENGINEERING FOR HOSPITALS

Designing for hospital use is no easy feat! CYRIL has several features that makes it suitable for patients and doctors. The light source has specific colour filters to block out any light outside the wavelengths needed to prevent unnecessary heating of the patient's head. To maximise patient comfort, the 'patient ends' of the optical fibres are light-weight plastic, and the optode holder is soft and flexible. It was designed using computer-aided design and manufactured using 3D printing. The laptop's software also has a user friendly design so doctors can start and stop measurements, and view oxygenation and metabolism changes in real-time.

See our *Science* issue for more about metabolism and NIRS.

Catching photons

by Frederic Lange, Biomedical Engineer
Find out more at metabolight.org/resource/cyril/

Alongside CYRIL, we built a system call MAESTROS*, It uses **time resolved NIRS** (TR NIRS), which means it measures the time taken for light particles (photons) to travel through the brain.

TIMING PHOTONS IN THE BRAIN

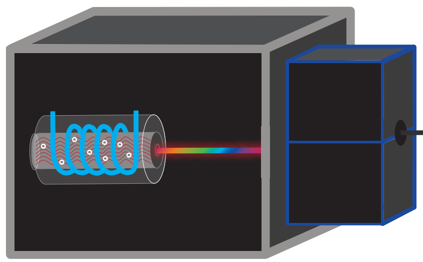
Like CYRIL, MAESTROS can investigate metabolism and oxygenation states in the brain. Unlike CYRIL, MAESTROS records the time of flight of photons in the head, and can tell us whether light is absorbed or scattered at specific depths of the brain by measuring the travel time of light. The four main components needed fo this particular detection in MAESTROS are:

- a pulsed laser source
- a very sensitive detector able to detect just one photon
- a photon counting card that will record the arrival time of each detected photons and sort them accordingly.

1

THE PHOTON CATCHING RACE BEGINS!

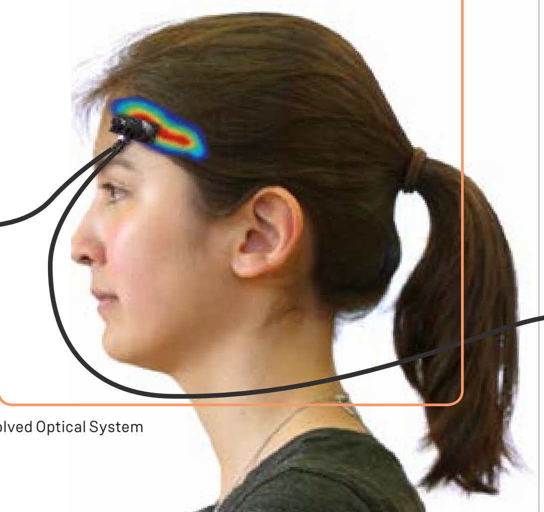
The **SUPERCONTINUUM LASER** produces a rapid pulse of light of all wavelengths, made up of photons. Specific wavelengths of light are then selected by **TUNEABLE FILTERS**. There are two filters in MAESTROS, which means we can study two parts of the brain at a time.



2

PHOTONS TRAVEL THROUGH THE BRAIN

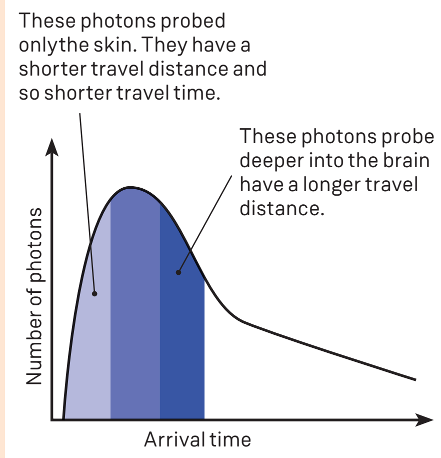
The filtered photons are directed to the head via optical fibres. When they get to the head, each photon takes a different path through the brain (due to scattering) or gets absorbed.



*Metabolism and hAemoglobin Evaluation via a Spectroscopic Time Resolved Optical System

ANALYSING PHOTONS

To analyse the data, we plot a histogram of the distribution of the photons' travel time by grouping the photons that arrive at the same time. The shape of that distribution depends on the absorption and scattering properties of the tissue.



To build up a picture of what happens to different colours of light, we repeat this experiment multiple times using different wavelengths by changing the filters. From this information we can calculate the level of oxygenation of the blood, and separate the contribution from each depth of the brain.

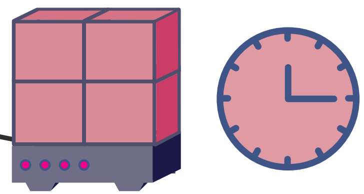
DID YOU KNOW

Only a single photon can be detected between each burst of light, but we need millions of photons to create the histogram. To solve this problem, we produce millions of bursts of light every second!

3

PHOTONS ARE DETECTED

A complex **PHOTON DETECTION SCHEME** detects how long it has taken for the photon to travel through the head. It's made up of four **PHOTOMULTIPLIERS** that transform the detected photons into an electrical current, a **ROUTER** that tags the signal from each of the photomultipliers and identifies its source and a photon counting card that acts as a **CLOCK**, which measures the number and arrival time of photons for each detector.



4

DATA IS COLLECTED

Finally, we use a computer to control all the components of the systems, and setup all the data acquisition. The data is then processed off line by another computer.

A day in the life: Nico Chen

We spoke to Nico Chen, the **biomedical engineer** who built the MetaboLight hand scanner, to find out what he does day to day.

What do you do to get ready for the day?
I start off early with the gym followed by breakfast in the office with colleagues. I enjoy having a sense of accomplishment even before starting my work schedule, and hitting the gym helps kick my mind off to a fresh start. Chatting with colleagues is also an essential part of the morning routine as I love a cheerful friendly environment to start work!

How and why did you get your job?
I studied a degree in Biomedical Engineering – applying a mixture of mathematical theories and practical knowledge to biological environments, such as healthcare. During my A-Levels, I was interested in so many subjects – mathematics, physics, chemistry, biology, computing. I wanted to know more about science as a whole, not just a single particular branch. Hence I studied the most interdisciplinary subject offered in the engineering department – Biomedical Engineering.

What does your typical day look like?
It consists of me doing one of two things: either building and developing new devices, or organizing outreach events.

Developing devices starts off with planning what functions the device should have and what it needs to illustrate – a process which I personally feel is the most important when building new instrumentation. For instance, when I designed the hand scanner, it needed to demonstrate how different colours of light can travel through the body so I had to decide which colours to use for demonstration, and what components would be needed to show the specific colours.

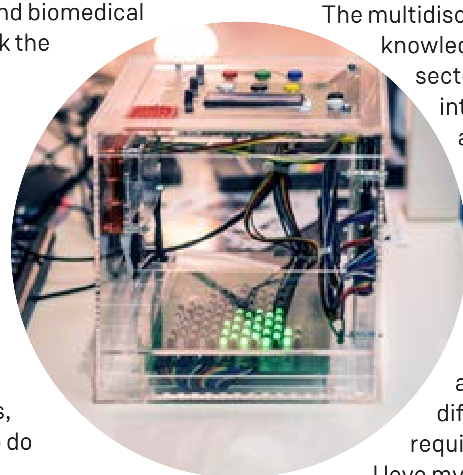
During the building stage, many things do not go as planned and compromises have to be made, hence it is crucial to set a direction to work towards. There are times when components do not work as intended, which means I have to try to figure out how to make it work smoother.

I also organise events to educate the public about medical physics and biomedical engineering. I try to break the stereotypical stigma of medical physics being an incredibly difficult subject open only to certain demographics. The faces that people make when seeing light penetrate through their hand and how this technology can be used to monitor their brain activity is priceless, and this motivates me to do my job better!

What's the most challenging part of your work?
Perhaps when things do not go as planned. There is much truth in Murphy's Law when it comes to engineering: whatever can go wrong, will go wrong. From planning and coding the microprocessors, to soldering and debugging the electronic circuit boards, to 3D drawings and cutting acrylic sheets. Every component has its specific function, and they all rely on one another to work in harmony to achieve a final functioning device. This is the beauty of engineering – you have to be creative and delegate a specific function for each part of the system, yet not overwhelmingly rely on one single part to sustain the whole system.

"I TRY TO BREAK THE STEREOTYPICAL STIGMA OF MEDICAL PHYSICS BEING AN INCREDIBLY DIFFICULT SUBJECT OPEN ONLY TO CERTAIN DEMOGRAPHICS"

What's the best thing about being a biomedical engineer?
The multidisciplinary nature – knowledge from different sectors are required and integrated to approach a problem. Biomedical engineers are especially important for integrating expertise from different fields. I cannot stand doing repetitive work and am always in search of different activities that require me to use my brain. I love my job as a biomedical engineer – nothing beats the sense of accomplishment when everything works in harmony.



Above: handscanner built by Nico.

QUIZ

Metabolight crossword

Test your knowledge!

ACROSS

1 A plot of the distribution of photon arrival times

2 A process in which a photon changes the direction of flight when incident on a larger particle

3 An elementary particle that carries electromagnetic force

4 A camera in CYRIL that detects light

5 Cables that can transport light

6 Metabolight's TR NIRS system

7 Visible light colour with the shortest wavelengths

8 Type of gas used in incandescent lamps

9 A meteorological phenomenon when drops of water disperse, reflect and refract light

10 Total internal reflection occurs when the incident light ray is at an angle larger than the ____ angle in an optic fibre

11 Light Amplification by Stimulated Emission of Radiation

12 A laser that emits broadband light

13 The carrier of oxygen in blood

14 A charged elementary particle

15 A leaf is green because it reflects green light and ____ light of other colours

16 A type of NIRS that measures the time of flight of photons

17 The material used to house LEDs

18 The place where CCO is found in cells

DOWN

3 Hot gas in which electrons are no longer bound

6 The production of energy in cells

10 CYRIL stands for _____ Research Instrument and appLication

11 Light of only one wavelength

20 An invisible part of the light spectrum following red wavelengths

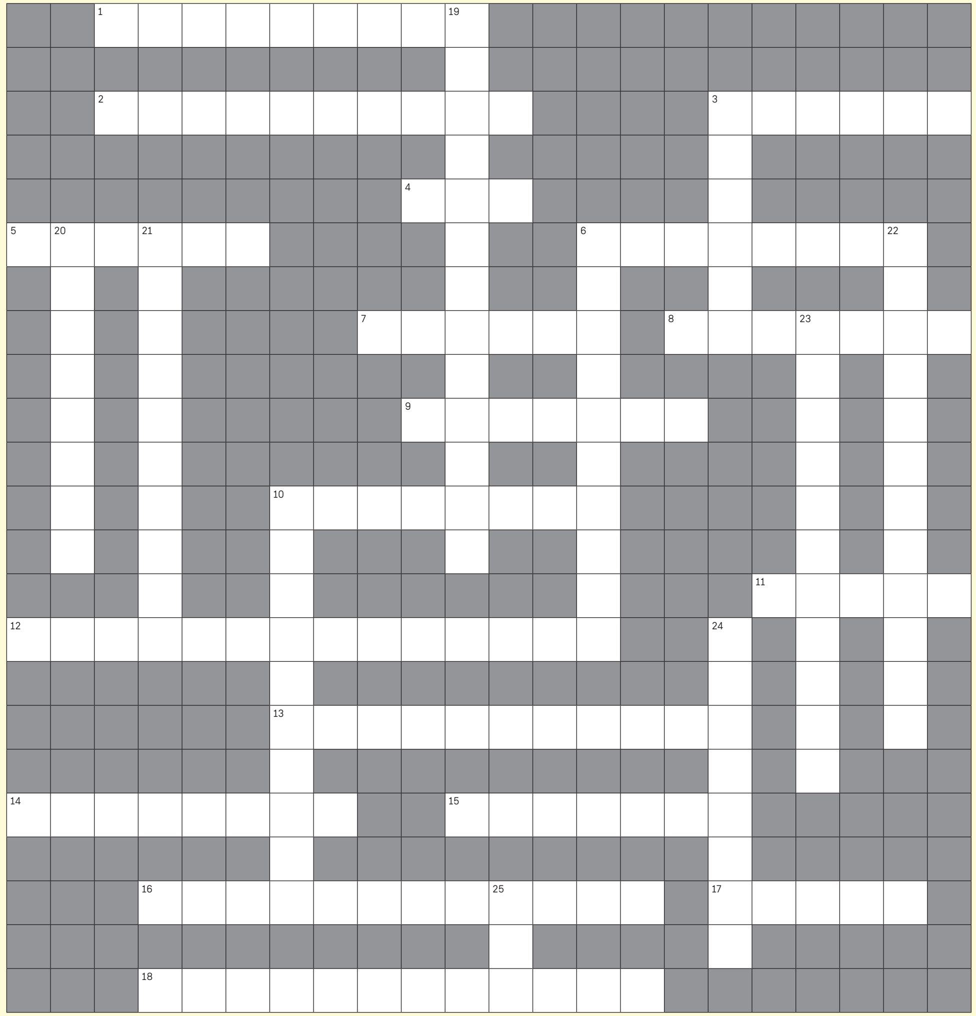
21 An index describing the reflection properties of a material

22 A device that separates light into its different wavelengths

23 The process of adding oxygen

24 A metal used to make filaments in light bulbs

25 A light source out of semiconductors



Answers available at: metabolight.org/resource/engineering-issue-answers

DIY SCIENCE

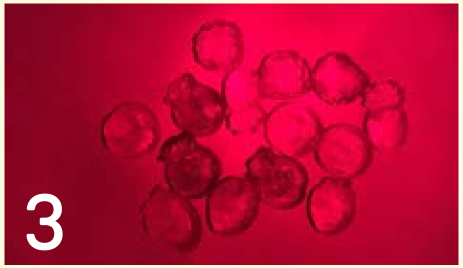
Gummy bear challenge

Sort the gummy bears into groups with same colour. This challenge uses the principles of light absorption and spectroscopy (see page 8)

TIP
Use clear, coloured sweet wrappers or a phone app that changes your screen colour, e.g. Screen or Flashlight, instead of LED lights

What you need: A dark room or box, gummy bears (mixed colours) and a white light LED and different coloured LEDs (ideally red, green and blue)

Make a pile of different coloured gummy bears – ideally a mixture of colours like red, green, yellow, orange and clear.



Shine the red light. It should be more difficult to tell the true colour of each gummy bear. Try separating the gummy bears into piles of the same colour.

Now use the green light, you should be able to see more colours in your piles.

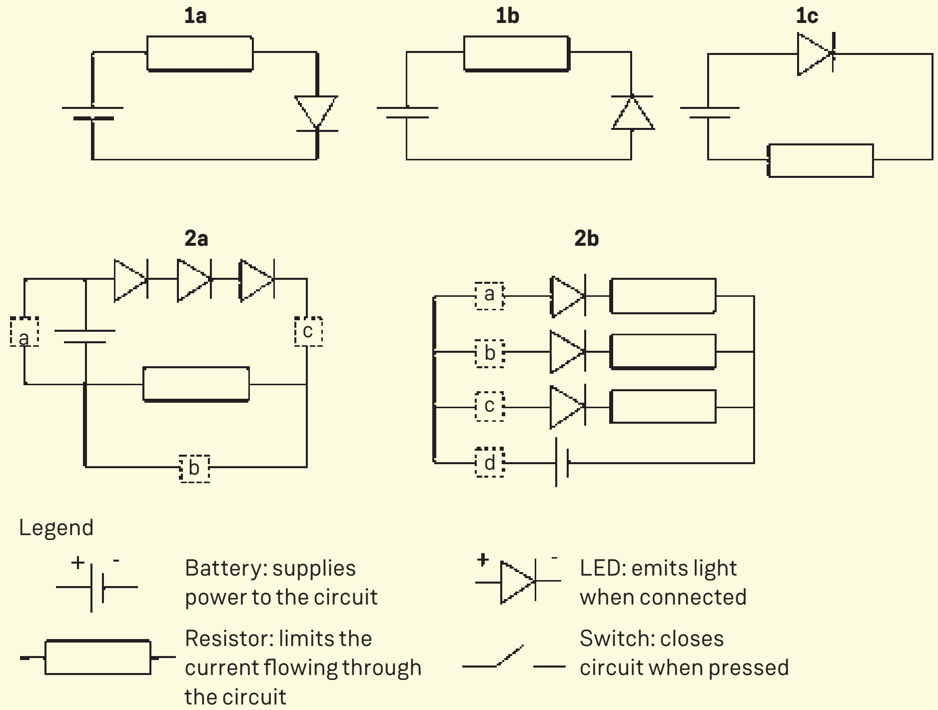
Finally, repeat step 3 with blue light.

Use the white light (or turn the room light on!) All the colours can be seen easily

QUIZ

Test your circuits knowledge

Can you answer the questions below about these electric circuits?



Q1

LEDs (light-emitting diodes) emit light when their positive end (+) is connected to the positive end of a power supply, and their negative end (-) is connected to the negative end of a power supply. Which LED(s) will light up?

Q2

Nico wants to turn on all three LEDs at the same time and came up with two configurations. Where should he put the switch in order to do this? Mark the location of the switches for each configuration and whether the remaining boxes should be open or closed circuits.

Q3

Nico finally decided to use configuration 2b instead of 2a. Can you figure out why? (Hint: think what happens when some equipment is damaged).

Answers available at: metabolight.org/resource/engineering-issue-answers

QUIZ SECTION

MetaboLight wordsearch

by Zuzana Kovacsova, PhD Student in Biomedical Optics

Can you find the following words? Words may be forward, backward, down or diagonal.

angle	iodine	cytochrome	detector	dispersion	energy
filter	research	frequency	physics	wavelength	interaction
laser	computer	mitochondria	orange	haemoglobin	programming
router	engineering	semiconductor	software	spectroscopy	transmission

A	C	I	M	P	R	H	S	P	A	M	A	L	A	S	E	R	E	N	R	G	Y	A	C	T	U
Y	Y	J	I	O	C	A	C	S	E	M	I	C	O	N	D	U	C	T	O	R	C	T	I	O	T
U	T	G	U	E	O	M	O	E	C	W	A	V	E	S	E	S	E	L	L	I	O	D	I	N	E
O	O	T	R	C	N	O	M	S	N	O	I	T	C	A	R	E	T	N	I	P	H	Y	S	C	X
A	C	W	A	T	P	G	F	D	C	F	R	E	Q	A	U	M	N	C	U	S	N	S	I	D	R
Q	H	U	N	V	H	L	T	I	T	H	O	E	I	S	O	I	P	R	A	C	T	I	O	H	O
P	R	Z	H	C	Y	O	Q	S	L	S	U	R	D	A	S	C	R	Y	A	V	B	D	A	A	U
M	O	A	E	O	S	B	D	P	Y	T	D	S	A	C	B	O	O	C	R	O	E	E	G	W	P
X	M	E	S	M	I	E	E	E	T	N	E	P	N	B	S	N	G	N	S	K	M	T	E	S	D
A	E	B	H	P	C	T	T	R	O	P	O	R	G	U	E	D	R	E	O	O	I	E	I	P	A
W	O	E	O	U	S	R	E	H	C	R	R	E	L	S	N	U	A	U	G	C	R	C	D	E	N
A	E	U	F	T	P	A	C	W	H	U	E	A	E	N	I	C	M	Q	M	H	O	T	L	C	G
V	Q	O	T	E	U	O	T	A	O	A	S	N	L	G	H	T	M	E	L	E	N	O	F	T	E
E	Z	F	W	R	T	S	Y	R	M	R	G	A	I	C	S	M	I	R	P	M	G	R	R	R	D
L	N	N	O	I	S	R	E	P	S	I	D	L	R	B	E	I	N	F	H	U	A	A	E	O	O
E	E	S	M	R	T	M	P	N	N	C	K	A	E	E	M	T	G	M	Y	S	E	N	I	S	W
N	M	R	O	U	T	E	R	E	L	H	E	B	N	A	I	O	Y	S	S	T	S	G	S	C	U
G	M	P	A	C	E	S	E	G	L	S	L	N	I	N	C	K	R	W	I	R	P	E	N	O	S
T	A	R	R	P	A	R	E	S	E	M	O	E	N	N	L	B	M	E	C	Y	A	H	D	P	N
H	R	O	E	S	I	O	Z	R	E	E	B	F	U	B	N	E	Y	N	N	A	B	U	Y	Y	J
P	G	G	Y	N	S	N	M	L	S	S	V	T	T	E	S	N	L	E	S	A	O	C	E	S	A
R	O	R	G	Y	E	X	E	A	H	D	E	N	G	W	A	I	O	R	A	N	G	N	A	E	I
J	R	A	S	A	M	A	I	E	M	I	N	R	A	V	A	G	V	G	T	G	E	E	P	W	S
D	P	H	A	E	M	O	G	L	O	B	I	N	E	E	E	R	E	Y	R	H	A	S	O	L	W
N	D	W	U	N	O	I	S	S	I	M	S	N	A	R	T	A	E	S	L	W	R	W	A	R	E