Circuits!

Using Light to Diagnose Lung Disease
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1. WHO ARE PROTEUS?

Proteus is a research group made up of scientists from various scientific fields who all work together towards the same goal. These scientists are doctors, biologists, chemists, physicists and engineers from three different universities: Edinburgh, Bath, and Heriot-Watt. They come from many different countries and they collaborate with universities from all over the world such as in India, France, the Netherlands and USA.

The goal of Proteus is to invent a new tool for detecting and diagnosing lung diseases for patients in critical care. These patients often have different types of lung diseases such as pneumonia, lung cancer or fibrosis. Sometimes these diseases can make it difficult for the patients to breathe, so doctors ventilate them: a machine is used to assist their breathing by moving air through a tube in and out of the lungs. The tool the Proteus team is developing also uses a tube that is inserted into the lung. This tube is made of glass that bends and lets the doctor see deep inside the lungs. Physicists call this an optical fibre. The optical fibre is passed into the windpipe in order to see the inside of the lung to diagnose disease and give treatment. In addition, a liquid made up of special molecules can be squirted into the lung that will make diseases glow. It also allows for measurements of properties such as acidity and oxygen levels. This gives the doctor important information about the health of the patient.

2. WHAT ARE THE LUNGS?

The lungs are the organ where gas exchange takes place. When you breathe in, the muscles of the rib cage pull up and expand the lungs, filling them with air. The oxygen from the air is transferred to the blood at something called the blood-air barrier. From there the oxygen is transferred to every part of the body through the bloodstream. The body uses the oxygen in a process that produces energy and carbon dioxide. The carbon dioxide is transported back to the lungs through the bloodstream and released into the lung. It then reaches the atmosphere when the muscles relax and bring the lungs into their resting position.

Humans have two lungs. The right lung is bigger than the left lung because the left lung shares space with the heart. The upper part of the lung is called the windpipe or trachea. It divides into airways, which are also called bronchi. The airways branch and get smaller and smaller until they are roughly the same size as one of your hairs. This branching structure is often compared to a tree.
and called the bronchial tree by doctors. At the end of these airways there are the air sacs, or alveoli, and this is where the gas exchange takes place.

3. WHAT LUNG DISEASES ARE THERE?

Lung diseases can affect anyone, not just smokers or the elderly. They are some of the most common diseases in the world and include asthma, bronchitis and pneumonia. The impact on a patient who is suffering from a lung disease can be very serious and in some cases life threatening. In this tutorial we will look at three different lung diseases; fibrosis, pneumonia, and cancer.

3.1. FIBROSIS

Fibrosis is a disease which causes scarring inside the lungs. Just like a scar on the skin which doesn’t move or look the same as healthy skin, this scar tissue doesn’t stretch like normal lung tissue, even after many years. This stiff tissue stops the lungs from expanding easily with each breath in, and this means you can’t take as much air into the lungs. Once in the lungs, it is also difficult for the oxygen in the air to diffuse across the scarred lung tissue and into the blood. Overall, less oxygen is able to get into the lungs and into the blood. It is important to have good oxygen levels in the blood so that it can be delivered to all of the organs in the body and keep them working efficiently. Having fibrotic lungs makes it difficult to
breathe out all the way because the lungs can’t go back to their original shape very easily. Some air can get trapped in the lungs. This trapped air does not have much oxygen content and is not useful to the body.

The scarring in fibrosis leads to symptoms including:

- Headache
- Dizziness
- Fast heart rate
- Shortness of breath
- Rapid breathing

These are all due to the lack of oxygen in the body. These symptoms can be similar to lots of other problems in the lungs and so it can be difficult for doctors to make a diagnosis. They often rely on special scans called CT (computerised tomography scans) to help them.

The only cure for fibrosis is lung transplant, which can only be offered in special circumstances. Other treatments only help with the symptoms and not the causes of the disease. These focus on improving breathing and fitness, stopping smoking or giving extra oxygen. For some types of fibrosis there is a medication available that can slow down the rate of scarring in the lung. The development of fibrosis is different for every patient and so each patient will need different treatment and support over a number of years.

![Healthy Pneumonia and Fibrosis](image)

3.2. PNEUMONIA

Pneumonia is an inflammation of the lung tissue. Often the inflammation is caused by an infection with bacteria, viruses or fungi. It occurs deep down in the lung where the air sacs or alveoli become inflamed and fill up with liquid. The developing pneumonia can happen in the community or in the hospital and mostly affects people with weakened immune systems. Another type of pneumonia is ventilated associated pneumonia. This occurs in hospital when a patient in critical care (such as in the intensive care unit) develops inflammation in the lung after being on a ventilator machine for a long period of time.
The symptoms include:

- Coughing
- Fever
- Headache
- Aches
- Sweating
- Shortness of breath
- Shivering

As these are very similar to the symptoms of flu it is sometimes difficult to diagnose pneumonia. Cough samples and X-rays can be used to help the diagnosis, but these aren’t always reliable.

Depending on the cause of the pneumonia it can be managed by the GP at home and treated with antibiotics, antifungals, rest or drinking a lot of water. In more serious cases the patient needs to be treated in a hospital and seen by a specialist.

### 3.3. LUNG CANCER

Lung cancer is the second most common type of cancer and most common cause of cancer death in the world. It mostly affects older people; most commonly it is diagnosed in people aged 70–74 and it is rare in people under the age of 40. Smoking is the main cause of lung cancer. However, people who do not smoke can also develop lung cancer.

It is very difficult to diagnose lung cancer at an early stage.

Common symptoms are:

- Coughing
- Coughing of blood
- Shortness of breath
- Pain when breathing
- Unexplained tiredness
- Weight loss

Treatment of lung cancer depends on various factors. The size of the cancer and how far it has spread in the lung may determine which treatment a patient receives. If only a small area is affected, the tumor can be removed through surgery. If the cancer has spread to a large area, additional radiotherapy and chemotherapy might be necessary. Radiotherapy uses radiation to kill the cancer cells. The radiation can be delivered from outside the body with a focused beam or from inside the body with a radioactive capsule allowing the radiation to seep out into the cancer. In chemotherapy, medication is given through the veins or as a tablet, which stops the cancer cells from reproducing and growing further.
4. HOW CAN LUNG DISEASES BE DIAGNOSED?

Diagnosis of respiratory conditions is slow and imprecise. This can result in delays in providing treatment, which can be particularly problematic for severely ill patients. It can also lead to an over-prescription of anti-inflammatory drugs or antibiotics. This is harmful to patients and is a growing global concern as antibiotic resistance increases. Antibiotics are medicines such as penicillin that destroy or slow the growth of a microorganism, e.g. bacteria. Microorganisms can develop resistance to these drugs over time and this effect is worsened if antibiotics are prescribed incorrectly. If antibiotic resistance continues to rise it will mean that simple infections and minor injuries become untreatable.

It is therefore very important that doctors understand the disease of their patients so that they can prescribe only the correct antibiotic. Here, we look at two common procedures doctors carry out when they are trying to diagnose patients with suspected lung disease.

4.1 X-RAY

Lung diseases are hard to diagnose, but doctors will often take an image of the chest using X-rays. X-rays are part of the electromagnetic spectrum and they can pass through your body. An image taken with X-rays will show dense regions (such as bone) as white and less dense regions as black. An X-ray image may tell the doctor there is an area of dense tissue within the lung, which may be an indication of the type of disease the patient is suffering from. However, these images often don’t give the doctor enough information to make a confident diagnosis.

4.2 LAVAGE

If the doctor believes that their patient has lung disease they may perform a procedure called a lavage. This involves squirting a fluid down a small tube into the lung and then extracting it. The extracted fluid is then sent to a lab where scientists can figure out what is wrong with the patient. However, this test can take two to three days and might not even be accurate.
5. PHYSICS

You may think of physicists as people who study space and work with telescopes. However, physicists often work with doctors to help improve medical care. Some examples of physics at work in the hospital are; MRI, ultrasound, X-rays, radiotherapy.

5.1. OPTICAL FIBRES

An optical fibre is a thin strand of high-quality glass. Light can be transmitted through it over very large distances. You may have heard of fibres before because we use them for high-speed internet. However, the fibres used in medicine can be specially made to see inside the body. They are cylindrical and narrower than a piece of spaghetti, which is thin enough to be fed through a patient’s mouth and into their lungs.

While all fibres vary in design slightly, the structure of the fibre is made up of the same primary parts. The innermost part is made of glass and is called the core. The core is surrounded by a different kind of glass, called the cladding.

Light is transmitted through a fibre by a process called total internal reflection. It is because of this process that you can sometimes see a reflection in the underside of the water when you are in a swimming pool. Instead of leaving the water or glass and refracting away at the boundary, all of the light is reflected back inside. Total internal reflection can only occur if the light is already in the material that it travels more slowly in, and only if the angle between the boundary and the light ray is small. The first condition is met when light is travelling from water towards air, or when the light moves more slowly in the glass in the core because a chemical element is added to that glass to change its properties.

When the light beam hits the surface beyond a certain angle, all light is reflected back and is trapped inside the slower material. This angle is called the critical angle. Only the light that travels along the fibre within the critical angle gets reflected on the surface between core and cladding and leaves the fibre at the other end. The light that travels outside this angle can refract into the cladding and comes out the sides of the fibre instead.

Figure 8. Left to right: Ultrasound during pregnancy of a developing foetus, X-ray of an adult skull, MRI of an adult head.

Figure 9. Optical fibres transmitting light from one end to the other. These kinds of fibres are used for high-speed internet but they can also be adapted to be used in medicine.
These fibres are used to illuminate the lung and also transmit the images back to a screen so that the doctor can see inside the lung. We use a specific type of light, called fluorescence, to investigate lung disease. These fibres can also deliver fluid to the area being imaged and can also carry out a lavage.

5.2. FLUORESCENCE

When certain molecules absorb light they emit light of a different colour. This is called fluorescence. Proteus make molecules that emit fluorescent light only when in the presence of disease. These are called Smartprobes. They consist of two parts; a dye and a recognition element. When the recognition element detects a disease molecule it attaches itself to it and the fluorescent dye starts lighting up. This is like a lightbulb for disease – when there is no disease the light is off but when there is disease the light is on.

Figure 11. Light travelling through a core of an optical fibre. The light is confined to the core because of a process of total internal reflection. This is basically a process whereby light repeatedly bounces off the walls of the core and it can only exit at the end of the fibre.

Figure 10. This is a microscope image of the face of the optical fibre that can go into the lung. The two dark round bits are holes, called capillaries, that allow doctors to squirt molecules in the lungs and sucked back up during a procedure called a lavage. The square part is an imaging fibre. This is like a tiny video camera which transmits images from the lung to the doctor.

Figure 12. A Smartprobe is a special molecule that has two important structures. The first is called a recognition element which detects signs of disease, such as bacteria, cancer or fibrosis. The second structure is a fluorescent dye which glows only when the recognition element detects disease in its environment.
6. PROTEUS’ LIGHT TOOL

Proteus have combined these ideas into one light tool that can inform doctors of their patient’s lung disease. This will allow doctors to deliver the right medicine and improve the chances that their patient recovers well.

- An optical fibre is passed into the patient’s lung. This gives the doctor a live view of the inside of the lung.

- The doctor then squirts Smartprobes into the lung which fluoresce only if there is disease. Each Smartprobe is for a different disease and each Smartprobe fluoresces a different colour.

This means that if the doctor sees fluorescence, they know that the patient has a disease. The colour of the fluorescence tells the doctor which disease the patient has and the correct treatment can be carried out.

Figure 14. This is what the inside of the lung looks like using fluorescence. The green sponge-like structure is the lung tissue while the red dots show bacteria labelled with Smartprobes. An image like this would tell the doctor that the patient has pneumonia and they need to prescribe antibiotics.
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<td>Bronchial tree</td>
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<td>Cancer</td>
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<td>Pneumonia</td>
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