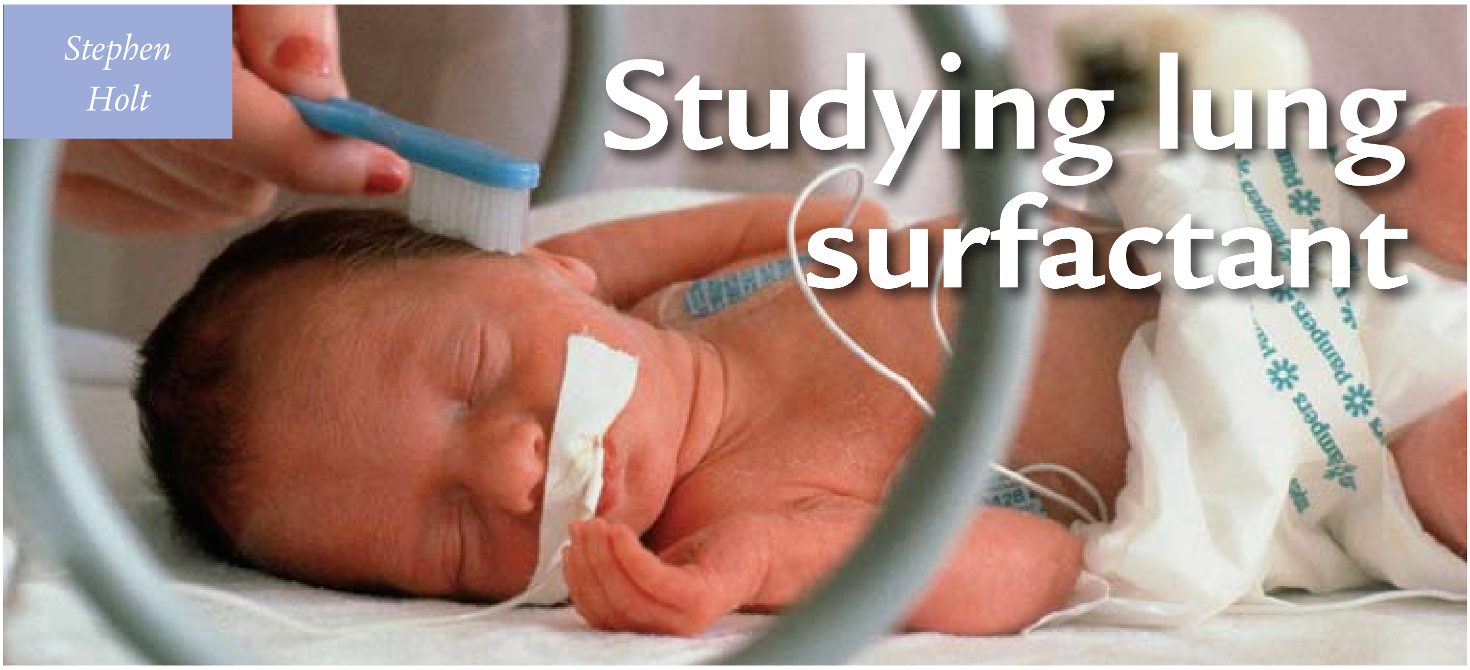
Stephen Holt

Studying lung surfactant



Joseph Nettis/SPL

This baby was born prematurely and is being supported in an incubator. It breathes oxygen-enriched air until its lungs are fully functional.

Our lungs have a specially designed coating on the inside and without it breathing would be impossible. This coating is called Natural Lung Surfactant and it reduces the work required to breathe. When babies are born very prematurely they can lack this surfactant, and this can make it very difficult for them to breathe. This is called Respiratory Distress Syndrome (RDS). This article looks at the background science of lung function, the development of treatments for RDS and future research directions.

Breathing is something that each of us does on average more than 20 000 times per day, every day of our lives. The breathing rate is even higher, more like 70 000 per day, for newborns. This is something that takes place without us having to think about it; in fact it is impossible for a healthy person to stop themselves breathing. The structure of the lungs is crucial to this process but so too is the surface which separates the lung tissue from the air breathed in.

The structure of the lungs

The internal surface of the lung is coated with a thin layer of liquid. It is the surface of this liquid which is in contact with the air and which the oxygen must cross to get from the lung sacs into the bloodstream. The composition of this liquid is vital because if it does not have the right properties then breathing cannot take place. One of the crucial factors is the **surface tension** of the liquid surface. The surface tension of water arises because water molecules attract each other strongly – more strongly than they attract molecules of the air. So molecules at the surface of water are pulled inwards, into the bulk of the liquid. This makes it much harder for any substances to cross into the water – see Box 1.

You can see the effect of surface tension if you look at water droplets. They adopt a shape which gives the minimum possible surface area, so drops of water and bubbles of air in water are spherical. This surface tension effect can also be seen when water is placed on a surface it doesn't like, such as a car that has been waxed or the outer surface of a tent.

Key words
breathing
lungs
surface tension
hydrophobic
hydrophilic

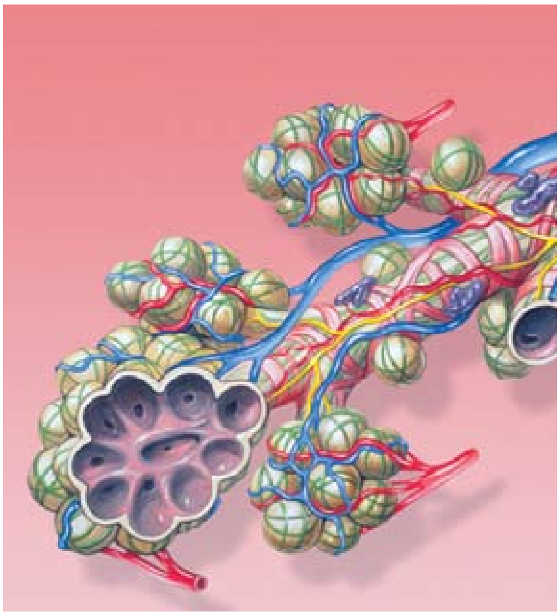
Box 1
The surface tension of water

Here's how to observe how the surface tension of water prevents transfer across the water air barrier. Take a small bowl or cup of water and float a pin on it. It is easy to do as the surface tension of the water is strong enough to prevent the pin from crossing the surface. This is the force that the lungs would have to overcome if they did not have lung surfactant. If a single drop of detergent is added to the water, the pin sinks straight away. In a similar way, lung surfactant makes it easier for oxygen to pass from the air in the lungs into the blood.

The surface tension of water pulls inwards on each droplet, preventing the water from wetting the entire surface.

The lungs are not two large empty chambers but consist of large numbers of bunches of alveoli. There are about 600 million of these very small circular chambers. It is these which are lined with liquid and which change their size during breathing. The strength of the surface tension over all the alveoli is so high that if they were lined with pure water breathing would be almost impossible. This is where Lung Surfactant (LS) comes in; one of its main roles is to reduce the surface tension of the lungs to enable breathing.

Respiratory Distress Syndrome (RDS), suffered by some premature babies, is a condition in which the lungs do not have sufficient LS. In a normal 9 month pregnancy, the lungs start to produce surfactants about 2 months prior to birth; babies born earlier than this are likely to have RDS because the strength of the surface tension forces makes it impossible for them to breathe. Prior to the development of treatments, RDS was a significant cause of death in premature babies.



When you breathe in, air enters the internal space in the alveoli; oxygen diffuses across into the blood vessels, while carbon dioxide diffuses in the opposite direction.

Box 2
How big are your lungs?

The total volume of air in your lungs is about 6 litres. However, the structure of the alveoli means that they have a large surface area.

Using the following information, you can calculate the surface area of a single alveolus and then the total surface area of the lungs.

600 million alveoli in lungs
Radius of one alveolus = 0.1 mm
Area = $4 \times \pi \times r^2$
1000 mm = 1 m

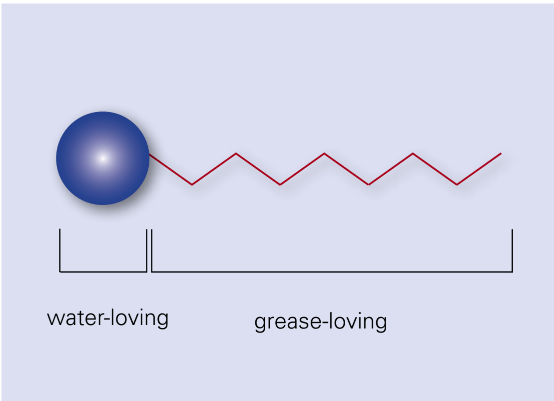
Is the total area closest to ...?

- **a** **A football pitch (about 4500 m^2)**
- **b** **A squash court (about 65 m^2)**
- **c** **A double bed (about 4 m^2)**

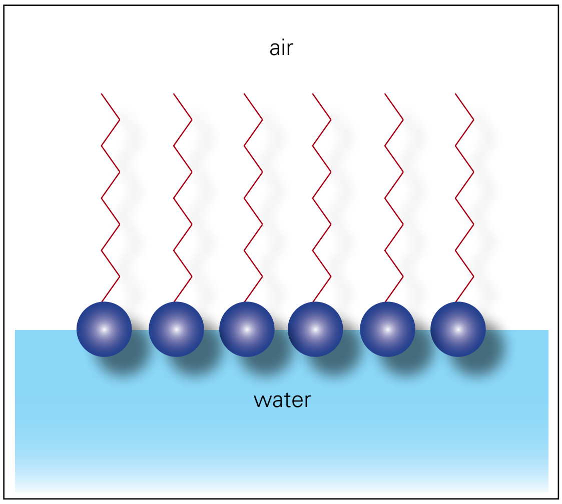
Answers on page 21.

Surfactants

Surfactants, an abbreviation of SURFace ACTive AgeNTs, are molecules that stabilise the surface between water and oil or water and air by lowering the surface tension. One part of the surfactant molecule likes water (hydrophilic) while the other does not (hydrophobic.) Because of this surfactants congregate at water/oil or water/air surfaces reducing the surface tension. Surfactants are key components of many everyday products such as detergents, fabric softeners, emulsions and foods like mayonnaise. In applications using these products the surfactant stabilises the surface where the oil and the water meet. In a detergent, one part of the molecule (the hydrophilic part) will interact with the water while the hydrophobic part interacts with an oily stain to help remove it from the item being cleaned.



A surfactant molecule: the long thin 'tail' is hydrophobic and will not dissolve in water. The spherical 'head' end is hydrophilic and so will dissolve.



On the surface of water, surfactant molecules have their hydrophilic 'heads' in the water and their hydrophobic 'tails' in the air.

Lung surfactant

LS is a very complex mixture of many components with the majority being phospholipids. Phospholipids are the molecules that make up most of the body's cell membranes and they can act as surfactants because they contain hydrophilic and hydrophobic regions. There are at least six different types of phospholipids in the LS mixture. There are also four different proteins which are a part of LS.

The behaviour of phospholipids has been extensively studied as they are a crucial component of every cell in the body. The Lung Surfactant Proteins have proved to be more difficult to study as purifying them from the lungs is a long process. Scientists have conducted experiments on the proteins to try to understand their size and shape at an air water surface and how this is affected by phospholipids. This is a difficult system to study so experiments started with protein and have progressed to simple mixtures of protein with one or two of the main phospholipids. These experiments are not carried out on people or animals but in a lab using a Langmuir trough (see Box 3) which provides a good model system for the fluid layer in the lungs.

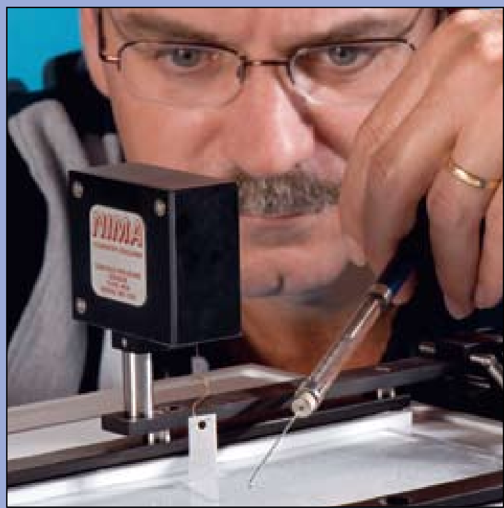
The Langmuir trough provides a way of controlling the amount of area at the air/water surface so we can simulate or model the difference between breathing in (large surface area) and breathing out (small area). Scientists then use a range of methods to study the different components as the area is changed to try to understand the location and possible role of each in the breathing process. As a result of experiments carried out over the years a number of treatments for infant RDS have been developed. These have resulted in a dramatic drop in the number of infant deaths from RDS.

A baby with RDS is usually helped to breathe in some way and given oxygen. If necessary, lung surfactant can be sprayed into the baby's lungs along with the oxygen. Most babies who develop RDS now make a full recovery.

Make your own Langmuir trough and use it to measure surface tension - see *Try this* on page 21.

Box 3
The Langmuir trough

A Langmuir trough consists of a reservoir and two barriers made of Teflon. The trough is filled with water and surfactant molecules or proteins can be placed on top of the water surface. The distance between the two Teflon barriers can be changed thereby changing the area of the water surface; this simulates the breathing process. This either squeezes the surfactant molecules together or gives them more room. The photo shows the drop of solution containing the LS molecules about to be placed on the surface and the device used for "weighing" the surface to determine the surface tension.



Stephen Kill, STFC

The author dropping solution on to the surface of water in a Langmuir trough.

Research goals

The proteins used in these treatments come from animal sources (mainly cows) and this can lead to problems. The goal of current research is to improve our understanding of the role of the main components of LS so that the simplest possible treatment mixture may be used until the premature baby's body can produce its own LS. The second aim is to work out how to synthesise the essential protein components, giving safer treatments which will be more widely available, particularly in the developing world.

***Stephen Holt** is a research scientist who works for the government funded Science & Technology Facilities Council. His own studies are aimed at understanding the behaviour of surfactants and proteins at surfaces.*

Look here!

Visit this Canadian website to see animations and to learn more about premature babies, RDS and lung surfactant.
http://tinyurl.com/yswwt4