Timothy J. Pedley

Pedley is a fellow of the Royal Society (elected 9 March 1995) and Gonville and Caius College, Cambridge (1973–89 and 1996–present). His research has led to significant breakthroughs because of its relevance on studying fluid flow in critical components like arteries, veins and lungs, and his study in understanding fish and microorganism swimming.

Can you briefly tell us about your current research?

I am currently working on swimming of microorganisms in fairly concentrated communities in which some interesting patterns arise. Biologists assume that these patterns are a result of some chemical signalling or biological responses. On the other hand, physicists working on fluid dynamics seek a physical explanation for this phenomenon and work towards understanding it.

What got you interested in biological fluid mechanics?

I have been working in this field for about 50 years now. When I was a Ph D student, I went to the International Congress on Theoretical and Applied Mechanics in Munich, as my professor encouraged me to attend the conference. There was a lecture on the propagation of the pulse in arteries, and I thought it was quite interesting. I also read a book that was mentioned in the lecture, which was the only book at that time written on blood flow in arteries (by D. A. McDonald). Before I left for US for my postdoctoral studies, I told my professor that I would be interested in working on biological fluid mechanics if he heard of any opportunities coming up. While I was in the US, the Physiological Flow Studies Unit was founded in Imperial College London. I went back to England and took up a job there, and it was the beginning of it all. I began working on the physiological flow of blood and airflow in the lungs, and later moved on to studying the interaction of living organisms with their fluid environment, like swimming and flying.

Can you explain quorum sensing and biofilm formation in the context of fluid mechanics of microorganism swimming?

To explain in simple terms, bacteria of certain species function as individuals until the concentration of something particular in the fluid becomes high enough. It is hypothesized that all bacteria in the population produce a specific chemical, and they initiate collective behaviour when the concentration of that chemical is above a threshold. Biofilms are structures formed by bacteria that are usually attached to some solid surface and, apparently, the bacteria can resist antibiotics better when they are in a biofilm rather than swimming around as individual cells. It is not something I have studied, and I do not know if it is quorum sensing that triggers or halts biofilm formation.

What factors govern the movement of microbes outside and within the host?

The overall answer is the environment: Is the microbe free in the air, water, or in another fluid? In all these cases, the flow of the fluid, whatever its nature, will carry the microbe along with it unless it is adhering to a substrate, or the interface between two fluids, in which case a biofilm might form as explained in the previous answer.

Other aspects of the environment are the proximity of other organisms, of the same or different species; the concentration of chemicals, produced by themselves or others.

What factors or cellular signals are responsible when a body is moving through a fluid? What decides the role of the various cells (in the case of a multicellular organism)?

As it is understood, some cells respond to chemicals and gases in solution, and exhibit chemotaxis (moving up or down a concentration gradient); others respond to light (phototaxis). Movement in both cases is modulated by the flow of fluid in which they find themselves (both gases and liquids being fluids).

The second part of the question about the role of cells concerns: (a) how multicellular organisms evolved, and (b) how cell differentiation came about, i.e. the development of different types of cell in the same organism. The literature contains many hypotheses about such matters: to
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aid nutrient uptake since pure diffusion cannot give enough uptake unless the organism is extremely small, and a larger organism can afford to have some specialist swimming cells, for example; or to help avoid predators, etc.

These are major questions in evolutionary biology, to which physicists as well as biologists are seeking answers.

Can you shed some light on the phenomenon of bioconvection and gyrotaxis?

Consider a shallow dish in the lab with a population of swimming microorganisms: in particular, a suspension of single-celled algae which are the primary producers at the bottom of the food chain. You see patterns developing on the surface of the dish which are similar to those obtained when a shallow layer of liquid is heated from below. In that case, the liquid is cooler above and hotter below, which implies that it is denser above and less dense below. A stratified fluid with greater density above than below becomes unstable and generates overturning instability.

When investigating the apparently similar phenomenon in algae, we take into consideration two significant features. Like almost all swimming organisms (except for some fish), these algae are slightly denser than water; so if they were not swimming, they would all sediment down. Another fact is that they generally swim upwards. So this makes the top layer of the chamber denser than the layer below, and is unstable in the same way as in thermal convection. They swim upwards basically because they are bottom heavy. The centre of mass is behind the centre of buoyancy. Thus, if they were swimming at some angle to the vertical, the torque applied by gravity makes them go back to the vertical position, but not very quickly as the rotation is resisted by the viscosity of the fluid. There is always a balance between the gravitational torque tending to orient them upwards and the viscous torque resisting this rotation, and on average they swim upwards.

In one of your papers, you pointed out oxygen to be a key factor in the movement of aerotactic bacteria. What happens in the case of anaerobic bacteria? Can this property be related to the virulence of the bacteria?

The phenomenon of bioconvection discussed previously is not restricted to aerotactic bacteria; it could operate for any chemotactic, free-swimming bacteria as long as there is a continuous supply of the chemical they like, at the top of the system.

As far as I am aware, this property is not commonly related to the virulence of bacteria.

Can you explain the bacterial movement when oxygen starts to deplete? Why is it that cell distribution cannot be determined if cell flux and oxygen consumption are zero?

Some species of bacteria we worked on, e.g. Bacillus subtilis, consume oxygen, and they also tend to seek out oxygen, i.e. they swim up a gradient towards higher oxygen concentration. Bacteria are not bottom heavy like algae, and they rotate their flagellum behind them to swim forward. A bacterial suspension in a dish open to the atmosphere on the top consumes oxygen. The oxygen concentration goes down in the bulk of the fluid; but at the surface, it is still atmospheric. The bacteria swim up this oxygen gradient generated by their own oxygen consumption. Therefore, when they are at the top, the top layer is denser compared to the bottom layer generating bioconvection. Mathematically, it is an interesting problem because we have to calculate not only the cell concentration and flow, but also the oxygen concentration.

How does the cell concentration profile vary with depth of the chamber? What is chemotactic cut-off point with respect to shallow and deep layers?

These refer to the discussion of chemotactic bioconvection discussed in the previous question. In sufficiently deep chambers, the cells near the bottom run out of oxygen before there is a sufficiently strong concentration gradient of chemotactant (oxygen) for them to sense and start swimming up. Therefore, there is a minimum in the cell concentration profile just where the oxygen first runs out, somewhere above the bottom of the chamber. When this depth coincides with the bottom of the chamber, then that represents the transition between ‘shallow’ and ‘deep’ layers in this context.

Can you explain the difference in hydrodynamics of land and sea animals? How is it that the swimming speeds of aquatic animals are higher than the muscle power required?

There was a hypothesis decades ago that dolphins could swim faster than their muscle mass, and the power associated with the muscle would suggest that they could. Dolphins are able to swim fast efficiently by reducing the drag, and they swim faster than engineers thought they should, but the hypothesis was based on incomplete understanding of fluid mechanics. What animals can do is largely governed by their physiology. It is about the efficient linkage between good muscles and streamlining.

Similarly, it has been considered that ‘bumblebees cannot fly’, but that was according to the steady-state aerodynamics that is applicable to fixed-wing aircraft with long wings. In fact, their wings are three-dimensional, and the beating is by no means approximately steady. The three dimensionality combined with the unsteadiness generates more lift, especially during hovering, for example.

How is pulmonary fluid dynamics altered in case of lung diseases? Especially in the context of the relation between wheezing and flow limitation. How does fibrosis affect the fluid exchange capabilities of tissues?

Different diseases affect different parts of the airways in the lungs. I worked on the fluid mechanics of airflow in the large airways. In asthma the large and middle-sized airways tend to contract, thus providing a high resistance to the air flow and consequently making it difficult to breathe through them. Bronchitis is inflammation of the airways, without muscular contraction, but with a similar effect. In emphysema, the peripheral air spaces are affected. The multi-generation series of airway branches leads to the alveoli, the air sacs on the periphery where the gas exchange takes place. In emphysema, the membranes between neighbouring alveoli are often damaged or broken and hence, even though volume is the same, gas exchange is markedly reduced. As for wheezing and flow limitation, when you breathe in, you stretch the lung and then on expiration, it elastically tends to contract again, aided by squeezing the chest or moving the diaphragm. When you breathe out, the pressure in the chest, outside the airways
and alveoli, is high compared to that in the mouth. As we come down towards the lung airways near the mouth, the pressure in the airways decreases because of viscous frictional resistance, but the pressure outside the airways is the same as that outside the alveoli. Hence, if you are driving flow fast enough, the internal pressure can fall below the external pressure.

Mainly in the major or the biggest airways inside the chest, where there is a high pressure outside, but they are not supported by surrounding tissue in the way the smaller ones are, the internal pressure is less than the external pressure, which for elastic tubes tends to drastically change their shape. This is the subject of collapsible tubes which I worked on for a long time. In the circumstances when a fairly thin-walled elastic tube is collapsing, you do not need much pressure change to create a relatively significant change in cross-sectional area and therefore a change in airflow resistance. This change in cross-sectional area is what is referred to as collapse. By collapse we do not mean total closure, we mean partial collapse. In these circumstances, not only is there an interesting balance between the mean pressure and the cross-sectional area, but it also tends to be unstable, and a flow-structure instability develops, which can lead to high-frequency oscillations which are almost certainly the mechanism by which some people wheeze when exhaling. There is a manner of hoarseness when exhaling, which is associated with high-frequency vibration of the walls.

The effect is not known to me yet.

**What is negative effort dependence?**

Forgetting the instability for a moment, let’s go back to the fact that when you exhale forcefully, there tends to be a change in the cross-sectional area of some airways and therefore, an increase in resistance. It usually has the result that when you try to exhale beyond a certain degree of effort, it will just make the airways collapse more, and you will be unable to get any more flow rate out. This is flow limitation.

There are examples of subjects in which above a certain point, the flow rate does not just level-off with an increase in effort; it can actually fall. This is negative effort dependence. The harder you try, the less successful you are when breathing out, especially in patients who are subjected to certain diseases. It occurs, but the reason for its occurrence in some people and not in others is yet unexplained.

**What is the role of boundary conditions in steady and unsteady solutions?**

When solving differential equations, there need to be boundary conditions to ensure your solution is relevant to the physical problem under investigation. This is a question about mathematics. I am not sure if there is anything to be gained by going into much more detail here.

**What is unique about fluid conduction in plants, especially tall trees? How do they accomplish it?**

Yes, it is undeniably an interesting phenomenon. I first read about it 30 years ago. The driving force for the sap rising up a big tree comes from the evaporation of water through the leaves via the stomatal openings, called transpiration. This evaporation is a suction force and roughly speaking, this is the driving force. However, if there were just a single tube going all the way from bottom to top, it would not work beyond a certain height because of cavitation – when the pressure in the liquid becomes so low that the dissolved gases come out of solution forming bubbles. The mechanism revolves around how the liquid and the solutes generate the pressures within the cell. Flow primarily occurs in the active region just inside the tree bark and the way the cells are constructed and connected and how they inhibit cavitation.

**What are your research goals for the coming year? Are there any projects you are planning to collaborate with the Indian labs you visited?**

I am now working mostly on populations of swimmers and rather less on internal flow dynamics. I am getting collaboration with my friend Sriram Ramaswamy, who is the current Director of TIFR, Centre for Interdisciplinary Sciences, Hyderabad. He is interested in pattern formation in populations of active individuals, whereas we have worked on continuum models of suspensions of swimming microorganisms generating bioconvection, as we discussed earlier. He along with one of his students (Simha) published an interesting paper in 2002, demonstrating the consequences in generating instabilities of the force/stresses that swimming exerts on the fluid. In our studies of gyro tactic bioconvection, the cells interact with the fluid and with gravity, but not with each other. They do not exert stress on water, apart from being heavier than water, and if they are swimming in water with the same density as themselves, they are not sedimenting. However, if they are making active breaststroke swimming motions, like certain algae, they are applying force to the fluid, a thrust force in front, and their body generates a drag at the back, forming a force dipole or a force pair with one sign. If they swim by waving or rotating their flagella behind, like sperm or bacteria, this produces thrust at the back and the drag of the body on the front; then a similar force dipole is formed, but with opposite sign. Simha and Ramaswamy showed that if you add and average the force dipoles or stresses that are generated by the swimmers over the entire population, you can generate interesting patterns without the gravitational instabilities that we had been working on. Ramaswamy believes that more interesting outcomes can occur in rather bigger organisms, and I agree. He works on the physics end while I work in the fluid mechanics end, but we might come together.

Also, my previous work on collapsible tubes was closely related to some of the work carried out by V. Kumaran, from the Department of Chemical Engineering at IISc. This was the major reason for my trip to Bengaluru two years ago, to attend a conference organized by him on flow and instability in elastic tubes.

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