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Hughes and Shelton: the fathers of fish respiration

David Randall discusses George Hughes and Graham Shelton's classic paper 'Respiratory mechanisms and their nervous control in fish', published in *Advances in Comparative Physiology and Biochemistry* in 1962.

George Hughes and Graham Shelton were members of the Cambridge University group of experimental biologists applying physical and chemical principles to the understanding of biological function. Hughes was Shelton's PhD supervisor and Shelton was mine when they published their review 'Respiratory mechanisms and their nervous control in fish' in 1962 (Hughes and Shelton, 1962). Hughes was, in my opinion, the more classical biologist whereas Shelton was more mechanistic and analytical in his approach to biological problems. The review is now more than 50 years old but is still refreshing to read and was clearly a major step forward in our understanding of respiratory mechanisms in fish, bringing together a disparate set of observations into a summary of respiration in fish that formed a framework for future work in the area. Their description of the respiratory apparatus, in terms of both the skeleton and musculature and the pumping mechanism, remains the basis for a more detailed knowledge of an extensive range of fish today. Pressure changes in the buccal and opercular chambers were recorded and analyzed, showing that fish maintain a unidirectional but oscillating flow of water countercurrent to gill blood flow.

Water contains only small amounts of dissolved oxygen. The amount of oxygen carried in the blood is usually far greater than that in an equivalent volume of water. Hughes and Shelton concluded, therefore, that water flow over the gills must be much higher than blood flow through the gills to deliver the required rate of oxygen transfer for metabolism. Hughes and Shelton introduced the term 'capacity rate ratio' (ratio of flow × oxygen content of blood and water) and analyzed the effects of this on oxygen transfer. They also introduced the term 'effectiveness of transfer', defined as the actual rate of oxygen transfer in relation to the maximum possible rate of transfer. There were insufficient data for a detailed analysis, but what they pointed out was that effectiveness depended on the capacity rate ratio of blood and water and the conditions for transfer across the gills as well as the countercurrent flow of blood and water.

The amount of oxygen removed from water flowing over the gills (percent utilization) had been observed to be as high as 70–80% in resting fish. Experiments presented in the review showed that increased flows of water across the gills were associated with a decrease in the amount of oxygen removed. Assuming that the cost of breathing might be as high as 20% of total energy output in resting fish and might increase with increases in ventilation, Hughes and Shelton concluded that with increasing gill ventilation and the associated decreasing oxygen percent utilization, the cost of breathing could limit maximum swimming activity. However, their assumption of the costs of breathing was too high and active fish are able to maintain oxygen percent utilization from water. Also, they did not consider ram ventilation, i.e. the ventilation of the gills due to forward movement of the fish with its mouth open, and in addition, many fish supplement oxygen uptake by exchange across their skin. Despite that, the systems approach promulgated by Hughes and Shelton did facilitate the development of concepts such as symmorphosis (Weibel et al., 1998). Subsequent model analysis of gas exchange in bony fish (Piiper and Scheid, 1984) and studies of gas exchange in elasmobranchs and birds also owe much to the analysis by Hughes and Shelton. As fish gas exchange systems became better understood and described, mammalian terms such as V (ventilation), Q (blood flow) and the V/Q ratio were adopted to facilitate comparison between different gas exchange systems so that the terms 'capacity rate ratio', and 'effectiveness of transfer' have largely disappeared from discussions of gas exchange.

At the time of the review, knowledge of the blood circulation in fish was limited. Fish had been placed in sealed chambers and the extent to which oxygen could be removed from the water assessed. Goldfish could remove almost all of the oxygen from the water even if haemoglobin oxygenation was blocked by adding carbon monoxide to the water. From these experiments, Hughes and Shelton concluded that fish could maintain standard oxygen consumption at low temperatures without the use of haemoglobin. This observation presaged the discovery of icefish, which lack haemoglobin and have a very high cardiac output to maintain capacity rate ratio. There was only limited discussion in the review of CO_2 transfer and no discussion of the third respiratory gas, ammonia, reflecting the paucity of data on transfer of these gases at that time. The next 50 years would see a large increase of our understanding of CO_2 and ammonia transfer in fish. It is now clear that gills play an important role in ion as well as gas transfer, and that they are a very complex structure, not simply a barrier between blood and water.

The extensive and elegant discussion of the neural control of breathing, along with the modelling of oxygen exchange across the gills, is probably the most important component of the review. Recording from the central nervous system was difficult and, at that time, the equipment was often made by the investigator. Signal to noise was a large problem. In the early 1960s, when I was a graduate student, Shelton and I were recording activity from a fish brain and

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as we lowered the electrode into the brain we heard music from a radio station in Germany. We recorded the event but made no special conclusions regarding the fish brain. I find that the Hughes and Shelton discussion of problems of defining a central respiratory centre is still valuable reading. They agreed with Kinkead (Kinkead, 2009) that 'current data indicate that respiratory rhythmogenesis is a phylogenetically ancient function that was highly conserved throughout evolution and that a comparative approach remains important to derive broader biological principles and a more comprehensive view.' The review by Hughes and Shelton of respiratory mechanisms and their control in fish was much more than a synthesis of work to date. It generated a greater interest in the subject and was a springboard for many subsequent studies (see Milsom and Perry, 2012).

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