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DESIGNING MICROPOROUS HOLLOW FIBRE BLOOD OXYGENATORS

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Extracorporeal blood oxygenators are used to oxygenate the blood during open-heart surgery. Today the vast majority of these blood oxygenators use hydrophobic microporous hollow fibre membranes to separate the blood and gas phases. Oxygen diffuses from the gas phase through the gas-filled membrane pores into the blood. Oxygen in the blood plasma binds to haemoglobin present in the red blood cells. Consequently the rate of oxygen transfer is enhanced compared to the oxygenation of water where the oxygen does not react in the liquid phase. Here mass transfer and friction factor correlations developed for nonreactive Newtonian and non-Newtonian fluids are used to predict results for blood. Characteristic parameters such as the Reynolds and Schmidt numbers and the friction factor have been modified to account for the shear-thinning behaviour of blood. A mass transfer enhancement factor has been developed based on film theory which accounts for the reaction between oxygen and haemoglobin. These equations may be used to predict the performance of a blood oxygenator based on results for simple systems such as the oxygenation of water. Consequently in the initial stages of new blood oxygenator designs, experiments may be conducted using water rather than blood to save time and money.

Keywords: blood oxygenators; cardiopulmonary bypass; friction factor; mass transfer; microporous membranes.

INTRODUCTION

Extracorporeal blood oxygenators (BOs) have been used for 50 years to oxygenate the blood during open-heart surgery. Gibbon (1937, 1954) performed the earliest successful open-heart operation using a film oxygenator. Though the blood surface area in contact with the oxygen in these devices was large, the gas transfer efficiency was often compromised by channelling of the blood flow (Kirklin and Dushane, 1955; Livesey and Lennox, 1992; Wegner, 1997). The next generation of BOs were known as bubble oxygenators. In these devices the gas exchange efficiency was increased by dispersing bubbles of oxygen in the blood resulting in significantly reduced priming volumes compared to film oxygenators. Since bubbling gas through blood lead to foam formation, silicone compounds were used as defoaming agents (Clark *et al.*, 1950). While increasing the gas flow rate (i.e., the number of gas bubbles) lead to an increase in the gas transfer efficiency, it also lead to greater blood damage and microemboli formation.

In order to improve the haemocompatibility of BOs, and avoid direct contact between the blood and gas, a nonporous membrane was placed between the blood and gas phases giving rise to membrane BOs (Kolff and Balzer, 1956; Clowes *et al.*, 1956). Since the diffusion coefficient of oxygen and carbon dioxide in air is about four orders of magnitude higher than in blood, the gas side mass transfer resistance is negligible. Major resistances to the transfer of respiratory gases were due to the membrane and liquid side concentration boundary layer.

The next major advance in the development of membrane BOs came with the introduction of hydrophobic microporous membranes. In these membranes, the pores are gas filled. The respiratory gases pass through the membrane pores rather than the membrane material. Consequently the major resistance to transfer of the respiratory gases is the blood side concentration boundary layer. Further, low rates of carbon dioxide removal due to low permeabilities of the nonporous membrane to carbon dioxide are also eliminated (Dantowitz and Borsanyi, 1969; Lautier *et al.*, 1969; Gille *et al.*, 1970).

In 1980, microporous membrane BOs accounted for only 20% of all BOs sold in the United States (Voorhees and Brian, 1996). During the early 1980s the designers of membrane BOs started to focus on incorporating passive mixing of the blood in order to reduce the blood side resistance to gas transfer. For example, the Cobe CML

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(Cobe Cardiovascular) contained a microporous flat sheet membrane with a screen in the blood channels to induce mixing (Elgas and Gordon, 1984). The membrane surface area was reduced to 2.5 m^2. The Johnson and Johnson Extracorporeal Maxima used cross-wound hollow fibres where the blood flowed outside the fibres (Iatridis *et al.*, 1985). By increasing the gas transfer efficiency of these devices, the membrane surface area and priming volume were reduced. As a consequence of these improvements, by 1986, membrane BOs accounted for more than 60% of all BOs sold in the United States.

Today over 99% of BOs sold in the United States contain microporous membranes. Flat sheet and hollow fibres are used though the latter geometry is much more popular. Devices with very low membrane surface areas (e.g., Sarns Turbo and Cobe Optima have surface areas of 1.9 m^2 and 1.7 m^2, respectively) have been built using carefully spaced mats of woven hollow fibres (Baurmeister, 1990, 1992). These woven hollow fibres provide uniform flow channels which minimize channelling of the blood.

Designing improved BOs is complex given the interdependence of the important design variables. Increasing the rate of gas transfer per priming volume of the device will minimize the transfusion requirements. This is particularly important clinically, given the risk of contamination of the patient's blood by pathogens associated with the donated blood. Further, in the past the patient's body temperature was lowered by cooling the blood during cardiopulmonary bypass (CPB) in order to reduce the oxygen requirement. However in modern practice there is a trend towards normothermic coronary perfusion which increases the oxygen requirement. In addition, reducing the membrane surface area present will reduce the cost of the device. Finally, ideal designs are ones which disrupt the blood side mass transfer boundary layer thus enhancing the rate of gas transfer yet minimizing damage to the blood components.

More recently, computational fluid dynamics (CFD) models have been developed to guide the development of new BO designs (Goodin *et al.*, 1994; Bludszuweit, 1997; Gartner *et al.*, 2000). While these models are helpful, a large number of experimental studies are still necessary. Conducting experiments using human blood is costly and time consuming. A number of safety procedures are required when using human blood in order to minimize the risk of transmission of pathogens from the blood being tested to the operator. Consequently sheep and bovine blood have been used as models for human blood (Bellhouse *et al.*, 1973; Mockros and Leonard, 1985; Vaslef *et al.*, 1994). While animal blood is far safer than human blood, the large amount of biological variability between units of blood can make comparison of experimental results for different units of blood difficult in research and development studies.

Here, mass transfer and friction factor correlations for commercially available hollow fibre BOs have been developed. We focus on hollow fibre BOs as these are far more popular than flat sheet BOs. The correlations developed here may be used to predict the rate of gas transfer and the pressure drop for blood, using nonbiological, nonpathogenic blood analogue fluids. Blood is rheologically complex. It is a shear-thinning viscoelastic fluid. Blood shows thixotropic properties due to its slow recovery from shear degradation and displays an apparent yield stress (Thurston, 1979).

Blood rheology is often described in terms of two basic phenomena (Chien *et al.*, 1966): red cell deformation and red cell aggregation. During CPB, addition of fluids such as anticoagulants leads to a reduction in the haematocrit (percentage by volume red blood cells) of the blood. Typically the haematocrit is less than 35% (Voorhees and Brian, 1996). Brookshier and Tarbell (1993) showed that under these conditions, the elastic properties of the blood do not play a significant role in its flow behaviour. Further, due to the low haematocrit, cell–cell interactions are likely to be less important. In microporous membrane BOs the average shear stress on the blood is about 5–20 Pa (Voorhees and Brian, 1996). Under these conditions blood may be modelled as a shear-thinning fluid. Consequently the friction factor correlations developed for blood analogue fluids must account for the shear-thinning behaviour of blood.

In human and animal blood, oxygen diffuses into the plasma and binds to haemoglobin whereas in the nonbiological blood analogue fluids studied here, no reaction of the dissolved oxygen occurs. Thus in order to predict the rate of gas transfer to and from blood, the effects of the oxygen haemoglobin reaction must be accounted for in the mass transfer correlation developed for the blood analogue fluids. Predicting the rate of gas transfer and the pressure drop for blood flowing through a BO using nonbiological, nonpathogenic fluids could lead to significant cost savings when designing new BOs. Initial experiments conducted to screen potential new BO designs may be carried out using blood analogue fluids.

THEORY

Newtonian Blood Analogue Fluids

Newtonian blood analogue fluids consisting of deionized water and mixtures of glycerol and deionized water have been tested. Mass transfer and friction factor correlations for these fluids have been described in earlier publications (Goerke *et al.*, 2002; Wickramasinghe *et al.*, 2002a). Since the mass transfer and friction factor correlations for bovine blood are based on these results for blood analogue fluids, the results are summarized in Table 1 and briefly described below.

The transfer of oxygen to Newtonian blood analogue fluids may be described by the following equation (Cussler, 1997),

$$N = K\Delta C \tag{1}$$

where N is the total molar flux, ΔC is the overall concentration difference and K is the overall average mass transfer coefficient. A mass balance over the liquid phase results in the following expression for the overall average mass transfer coefficient,

$$K = \frac{Q}{A}\int_{C_I}^{C_O} \frac{dC}{C^* - C} \tag{2}$$

where Q is the Newtonian fluid flow rate, A is the membrane surface area and C_I, C_O and C^* are the inlet and