Mathematical Models of Oxygen Flow in the Microcirculation

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The microcirculation is the body's network of its tiniest blood vessels – arterioles, capillaries, and venules. It supplies oxygen and nutrients to every part of the human body. We can describe transport in the microcirculation through the use of mathematical models, and, while these models are usually not completely accurate, they are quite useful in studying phenomena that are difficult to directly observe. Mathematical models can also effectively demonstrate the importance of the microcirculation in the transport of oxygen and nutrients throughout the body. The following paper will show, through the use of such models, the problems of transport via diffusion, and thus the importance of the microcirculation.

Diffusion, according the Merriam-Webster, is "the process whereby particles of liquids, gases, or solids intermingle as the result of their spontaneous movement caused by thermal agitation and in dissolved substances move from a region of higher to one of lower concentration." It is an important, albeit inefficient, mode of oxygen transport in the body. Fick's First Law of Diffusion defines the diffusion flux, J, through a substance. Fick's First Law of Diffusion is

$$J=-D\frac{\partial C}{\partial x}$$

where C is the concentration, x is the position, and D is the diffusivity, or diffusion constant, of the substance.

The concept of partial pressure is also important in studies of oxygen transport. Merriam-Webster defines partial pressure as "the pressure exerted by a (specified) component in a mixture of gases." Gases, such as oxygen, diffuse from areas of higher partial pressure to areas of lower partial pressure. Henry's Law

$$C=\alpha P$$

defines the concentration, C, of a gas in some medium, like tissue, in terms of partial pressure, P, and the solubility of the medium, ά. We can describe the total saturation, S, of a gas in a medium by the Hill Equation

$$S(P)=\frac{P^n}{{P_{50}}^n+P^n}$$

where P_{50} is the value of partial pressure for which the saturation is exactly ½. In tissue, $n\approx 2.4$. Using Henry's Law, the Hill Equation, and the knowledge that the maximum concentration of oxygen in red blood cells is approximately 0.4 $cm^3 0_2/cm^3$, we can construct a graph depicting the oxygen content of blood as a function of partial pressure. If we separate this graph into two curves, one representing the oxygen dissolved in blood and one representing the oxygen bound to hemoglobin, the importance of hemoglobin in oxygen transport becomes immediately apparent, as almost all of the oxygen in blood is bound to hemoglobin. This graph can be found on page 5.

With this knowledge of diffusion and partial pressure, we can begin to write models for oxygen transport in the human body. We will begin with simple one-dimensional models, which clearly demonstrate the inefficiency of diffusion for oxygen transport. Taking

$$D=1.5\times 10^{-5}\frac{cm^3}{s}$$

$$\alpha = 3\times10^{-5}\, cm^3 \frac{O_2}{(cm^3 . mmHg)}$$

which are reasonable approximations of the diffusivity and solubility of tissue, and the oxygen consumption, M = 0, and using Poisson's equation

$$\nabla^2 P = \frac{M}{D\alpha}$$

we see that

$$P = c_1 x + c_2$$

when M = 0. Given this equation and the initial conditions

$$x = 0\, cm\, ;\, P = 100\, mmHg$$
$$x = 0.1\, cm\, ;\, P = 0$$

which are also reasonable approximations of initial conditions in tissue, we can calculate the diffusion flux, J_x, of oxygen in tissue. After a few simple calculations, we find that

$$J_x = 4.5\times10^{-7} \frac{cm^3 O_2}{s.cm^2}$$

So, given an initial partial pressure of 100 mmHg, oxygen only diffuses 0.0045 μm per second. This is obviously a very short distance, and a clear demonstration that diffusion is an inefficient means of transport.

Using Poisson's equation again, with M = 1/600 $cm^3 O_2/cm^3.s$, given an initial partial pressure of 100 mmHg at x = 0 cm, we can easily calculate the distance that oxygen will diffuse until the diffusion flux and the partial pressure are both zero. Integrating Poisson's equation twice, we obtain

$$D\alpha \frac{\partial P}{\partial x} = M\, x + c_1$$

and

$$D\alpha P = \frac{M\, x^2}{2} + c_1 x + c_2$$

Applying the initial conditions x = 0 and P = 100, we find that

$$c_2 = D\alpha(100)$$

Taking x = L_D to be the distance that oxygen will diffuse until diffusion flux and partial pressure are zero, we can solve for c_2.

$$c_1 = \frac{\frac{M\, L_D^2}{2} - 100\, D\alpha}{L_D}$$

Now, solving for x = L_D when

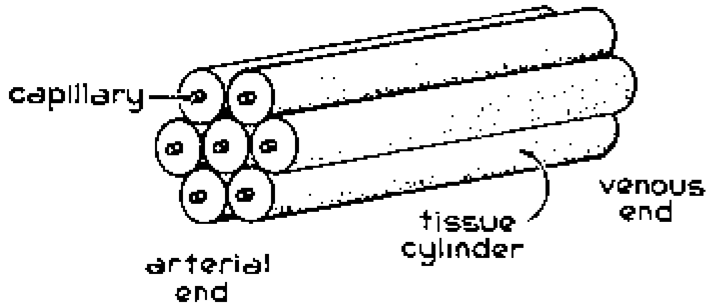
$$D\alpha \frac{\partial P}{\partial x} = 0$$

we see that

$$L_D = 73.5\, \mu\, m$$

So oxygen will only diffuse 73.5 μm through tissue until it stops. This is why the microcirculation is so important in supplying nutrients to the body. Vessels must always be extremely close to each other, or diffusion will not be an adequate means of supplying oxygen to all the necessary parts of the body.

In order to formulate a model of oxygen transport that is more representative of actual phenomenon in the human body, we must consider three dimensions. Not all tissue regions show geometrical regularity. “It is nevertheless tempting,” says Stanley Middleman, a chemical engineer at the University of Massachusetts, “to introduce the concept of a repetitive 'unit structure' as a representation of the capillary-tissue region." One popular geometrical model of microvascular patterns, according to Middleman, is the Krogh cylinder arrangement, pictured below:



The use of this model, however, implies that any particular section of capillary supplies to only one particular section of tissue, which is an oversimplification of what actually happens. In reality, many capillaries supply to one area of surrounding tissue. However, Middleman says that this simplification aids the process of developing mathematical models for blood-tissue exchange as long as three assumptions are made. First, we must assume that the Krogh cylinder arrangement is, in fact, an appropriate model. Second, we must assume, says Middleman, "that the tissue surrounding the capillary is actually a heterogeneous composite of materials," where "metabolic chemical reactions take place," and these reactions are continuously distributed. Finally, we must assume that the axis of the cylinder is symmetrical. This last assumption implies that there exists a "no-flux" cylinder where transport from surrounding capillaries is the same as transport toward these capillaries. Once we make all of these assumptions, we can begin to develop mathematical models of oxygen transport.

In one dimensional models, we know that

$$\nabla^2 C = \frac{\partial^2 C}{\partial x^2}$$

In three-dimensions, we have

$$\nabla^2 C = \frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial C}{\partial r}\right)$$

After some calculations, we obtain

$$\frac{\partial P}{\partial r} = \frac{rM}{2D\alpha} + \frac{c_1}{r}$$

and

$$P = \frac{r^2 M}{4D\alpha} + c_1 \ln r + c_2$$

Using these equations we can write a general formula for the partial pressure of oxygen as a function of the radius of the cylinder.

$$P = P_0 + \frac{M}{2D\alpha}\left[\frac{r - r_c^{\,2}}{2} - r_t^{\,2}(\ln r - \ln r_c)\right]$$

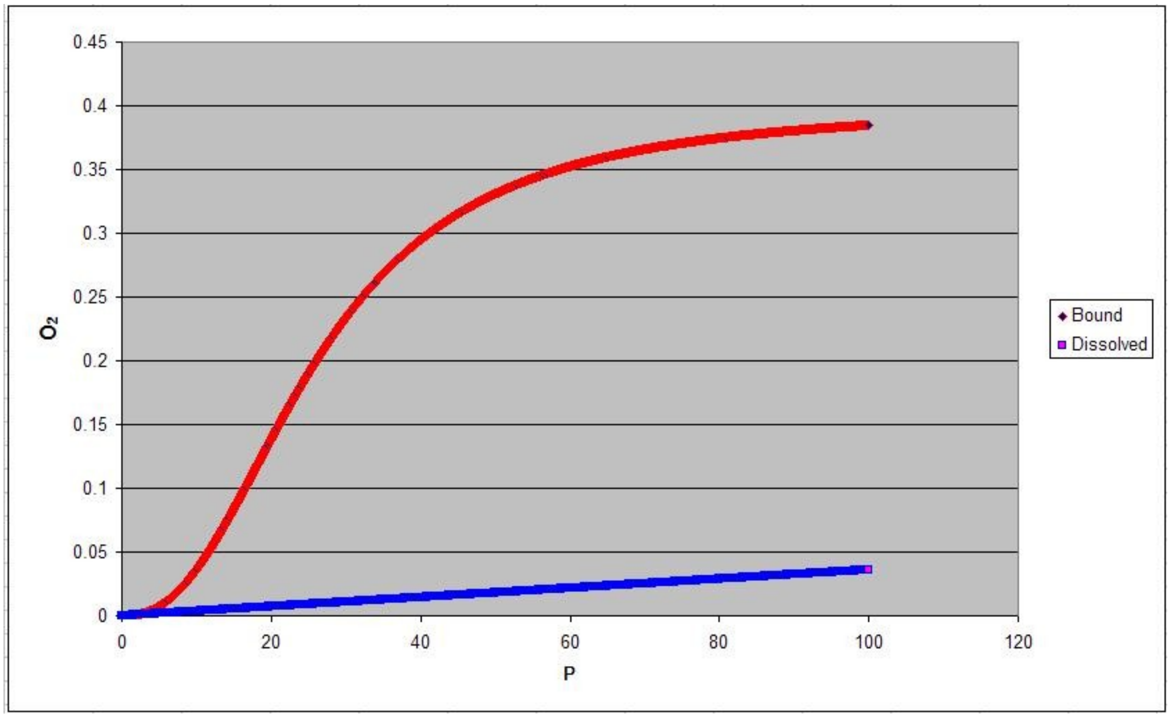
In this equation, P_0 is the initial partial pressure at the center of the cylinder, r_c is the radius of the capillary, r_t is the radius of the tissue surrounding the capillary, and r is the total radius of the Krogh cylinder.

From the preceding models, we can clearly see that diffusion is an inefficient means of oxygen transport. This is why the microcirculation is so important. Without it, oxygen could not be transported to all parts of the body. The Krogh cylinder arrangement is an excellent geometrical model to use when studying oxygen transport, despite its inherent flaws, as it is often far easier to make these sorts of calculations rather than directly observe such phenomena.

In this paper, I only analyzed models of oxygen transport with initial partial pressure of 100 mmHg and an oxygen consumption rate of either 0 or 1/600 $cm^3 O_2/cm^3$. Really, these values can change depending on certain conditions. For example, the partial pressure of oxygen will be less in people with lung disease or people at high altitudes. Further research could lead to a better understanding of the effects of lung disease by studying models of oxygen transport with lower initial partial pressure. Oxygen consumption can change significantly depending on where oxygen is being supplied or how much work a person is doing. In skeletal muscle $M \approx 1/6000$ at rest but increases to 1/600 at moderate exercise, and to 4/600 or high levels of exercise. Next, I plan to study how changes in these parameters, P and M, affect oxygen transport in the microcirculation. I will attempt to answer the question of what capillary density is needed to supply oxygen at these different rates of consumption.

Mathematical models of oxygen transport can be much more sophisticated than the models analyzed above. Obviously, oxygen transport in the human body is much more complicated than simple diffusion. Microvascular networks often change their structure when they are growing and in response to functional demands, such as changes in metabolic requirements. Such structural adaptations, says Dr. Secomb, can be modeled with systems of differential equations. I intend to study these models in an attempt to understand how specific changes in functional demands of the microcirculation affect mass transport and what conditions allow for a stable network structure. Such findings would describe what conditions are necessary for all parts of the body to receive adequate oxygen, which is essential for maintaining good health.

Oxygen Content of Blood



References

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Picture of the Krogh Cylinder arrangement from: "The Krogh Cylinder." Retrieved 3 Dec 2006 from http://www.owlnet.rice.edu/~chbe402/proj04/seli/CENG402_Project_Files/Blank%20Page%202.htm

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