OXYGEN TRANSPORT IN RESTING AND EXERCISING SKELETAL MUSCLE

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It is well known that exercise causes skeletal muscle blood flow to increase dramatically. This is usually accompanied by an equally dramatic increase in the number of patent capillaries. This phenomenon appears to be the result of a local control mechanism designed to provide the increased oxygen needed during exercise. Actually this control mechanism is designed to insure that each muscle cell is always provided with the correct amount of oxygen. It thereby governs the oxygen transport system operating in muscle. In spite of its great physiological significance, this local control mechanism is poorly understood.

We are investigating quantitatively the dynamics of the tissue oxygen transport system using chemical engineering methods of analysis and treating the muscle tissue like a complicated chemical reactor. Our approach is to analyze the transient in the muscle following a step change in the input concentration of oxygen to the muscle in very much the same way that orthodox chemical engineers analyze standard chemical reactors. Ordinary dissolved oxygen is our tracer. We use the excess oxygen which passes through the muscle unconsumed and therefore behaves like an inert tracer. We hope eventually to develop a mathematical model for the complete oxygen transport system operating in the whole human body by integrating the separate systems operating in individual tissues. We also hope that our quantitative analysis of the microcirculation can be tested on, and eventually be useful in treating, such clinical conditions as shock.

Our input-output technique (1) involves exposing the gracilis muscle of an anesthetized (sodium pentobarbital) adult mongrel dog. The dog is then intubated and artificially respirated. The respirator stroke volume and rate are adjusted to wash out the lungs as rapidly as possible while at the same time maintaining normal blood gases. For a 20 kg dog we usually find the best balance when we set the stroke volume at approximately 400 ml and the rate at approximately 8 breaths/min. Calibrated needle oxygen electrodes are placed in the artery and vein supplying the gracilis muscle. These vessels are isolated so that only gracilis blood passes the electrodes. Otherwise the autoperfused gracilis, and the animal's circulation in general, are maintained in a normal condition. Calibration values for the electrodes are verified by sampling blood near the electrodes and measuring the PO_2 *in vitro* (Radiometer Blood Gas Analyzer). After perturbing the input arterial PO_2 by changing the animal's breathing gas, we continuously monitor the PO_2 in the gracilis artery as well as in the small vein draining the muscle. This method has the significant advantage that oxygen itself is used as the tracer.

The intravascular needle oxygen electrode, which was designed and constructed in this laboratory, is shown in Figure 1. It consists of a

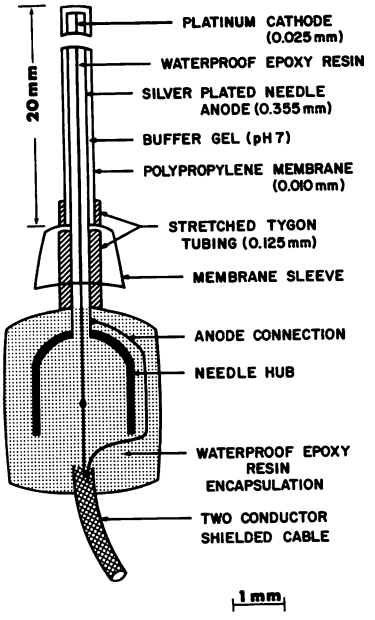

FIGURE 1: NEEDLE OXYGEN ELECTRODE

0.001" platinum cathode potted in epoxy resin (Microcast 200, Electroscience Laboratories, Philadelphia) inside a 28 gauge silver plated needle. The needle is encased in a tight, buffer filled, 0.0005" polyethylene membrane, shaped like the finger of a glove. The current from this electrode is amplified (Keithley Picoammeter #414S), recorded on an FM analog tape recorder (Midwestern Instruments #434), and eventually converted into a digital tape at a rate of 3 per second. This tape can then be processed on our digital computer (CDC 6400).

Figure 2 shows the Calcomp output for a typical set of experimental data obtained, in this case, after changing the animal's breathing gas from 100% oxygen to room air. The data are plotted as fractional change in oxygen tension, $(P - P_o)/(P_\infty - P_o)$, versus time. Actual values

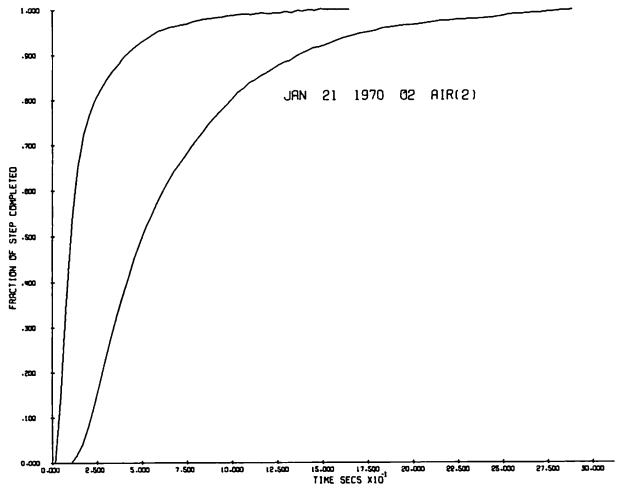

FIGURE 2: ARTERIAL AND VENOUS OXYGEN CHANGES FOLLOWING A CHANGE IN BREATHING GAS

for arterial PO_2 are usually 100 and 500 mm Hg on room air and 100% oxygen respectively while venous values are 40 and 50 mm Hg on these same gases. The lung washout time constant usually is approximately 20 seconds. The faster curve in Figure 2 is, of course, the arterial one.

Figure 3 shows the Calcomp plot of the derivative of the venous curve of Figure 2. Because of the noise inherent in the analog tape recorder, it was necessary to smooth the derivative data. Each point in Figure 3 is the mean of 10 derivatives, making the points approximately three seconds apart. Since the comparable arterial derivative curve is approximately a spike by comparison, and the system is linear, the venous curve is actually (2) the residence time distribution of oxygen molecules in skeletal muscle after the arterial spike. The arterial spike is marked by the arrow on Figure 3. The mean residence times at rest and during exercise are found on the digital computer. The effect of exercise on the tissue oxygen transport system is illustrated by comparing these times.

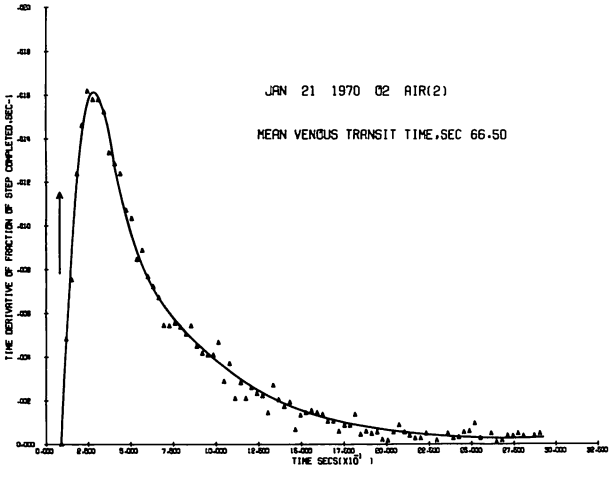

FIGURE 3: TIME DERIVATIVE OF VENOUS CURVE

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REFERENCES

1. Goldstick, T.K., Allen, B.J., and Fry, W.F., Oxygenation of Tissue Studied by an Input-Output Technique", Proceedings International Conference on Medical and Biological Engineering, 8, 1.2 (1969)

2. Levenspiel, O., "Chemical Reaction Engineering", Wiley, New York, 1962.