TRANSIENT EFFECTS ON THE INITIAL RATE OF OXYGENATION OF RED BLOOD CELLS

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The rate-controlling process in the oxygenation of red blood cells is investigated using a Roughton-like model for oxygen diffusion and reaction with hemoglobin. The mathematical equations describing the model are solved using two independent techniques, numerical inversions of the Laplace transform of the equations and numerical solutions via an implicit-explicit finite difference form of the equations.

The model is used to re-examine previous theoretical models that incorporate either a red cell membrane that is resistive to oxygen diffusion or an unstirred layer of water surrounding the cell. Although both models have been postulated to be equivalent, the results of the computer simulations demonstrate significant differences between the two models in the rate of oxygenation of the red cells, depending upon the values chosen for the diffusion coefficient for O2 in the membrane and the thickness of the water layer. The difference is apparently due to differences in the induction and transient periods of the water layer model relative to the membrane model.

1. Introduction. Determination of the rate of uptake of oxygen by red blood cells was pioneered by Roughton (1932) and later reviewed by him (1959). Using a rapid mixing apparatus, Roughton and his associates compared the rates of oxygen uptake of hemoglobin in solution and that of red cells. The results demonstrated a marked decrease in the rate of oxygen uptake by the cells compared with hemoglobin in solution. This finding was attributed to two diffusion factors; the additional time required for oxygen to diffuse through the finite thickness of the red cell, and to a small oxygen diffusion coefficient through the membrane. Roughton determined that neither factor alone was sufficient to reconcile the experimental observations and theoretical calculations.

The magnitude of the oxygen diffusion coefficient through the membrane has been since investigated. Comparisons of rates of oxygen uptake between equal layers of packed red cells and concentrated...
hemoglobin in solution were made by Kruezer and Yahr (1960). The rates were found to be similar and they suggested that the oxygen diffusion coefficients through the membrane and interior did not significantly differ. Kutchai and Staub (1969) noted similar findings with steady-state diffusion through packed red blood cells vs. concentrated hemoglobin solution. Fishkoff and Vanderkooi (1976) observed the oxygen quenching of pyrene fluorescence in membranes and concluded that the diffusion coefficient of oxygen in the hydrocarbon core of the membrane was similar to that in aqueous solution. Nuclear magnetic resonance studies of oxygen diffusion in artificial phospholipid membranes (McDonald et al., 1979) indicated that oxygen freely penetrated the hydrocarbon core and that the oxygen concentrations increased towards the center of the membrane. The above findings all seem to contradict Roughton's conclusion that the membrane resistance is a principal factor in reducing the rate of oxygen uptake by the red cells over that of hemoglobin in solution.

An alternate hypothesis to explain the difference in the rates of oxygenation of cells and solutions, suggested by a number of investigators (Middleman, 1972, Gad-el-Hak et al., 1977), is that in rapid mixing studies a stagnant water layer engulfs the red cell and acts as a barrier to oxygen diffusion and that little or no additional resistance is due to the red cell membrane. Middleman based his hypothesis on the work of Koyama and Mochizuki (1969), who looked at oxygenation of blood flowing in a tube and stated that the rate of oxygen uptake by the red cell was related to the velocity of flow. This observation suggested to Middleman that a water layer, of which the thickness was a function of the velocity of the cell relative to the surrounding fluid, could surround the red cell and impede the flow of oxygen inward. Gad-el-Hak and co-workers (1977) observed the light scattering of red blood cells in a rapid mixing apparatus. They determined that in the developed turbulence, eddies up to 1 mm in diameter existed in the flow, inside which a smaller diameter could be oxygen depleted (due to incomplete mixing of the eddies). The eddies were observed to mix on time scales similar to the time scale of oxygen uptake by red cells. Additional evidence of an unstirred layer of water around the red cell was obtained by Sha'afi et al. (1967), who looked at water transport in the red cell using a stop-flow apparatus. A 5.5 μm unstirred water layer was calculated to explain their results.

Theoretical models have been advanced to further investigate the role of the membrane or water layer in the rate of oxygenation of the red cell. Kutchai (1975) used a finite difference technique to obtain the rate of oxygenation of the red cell. The method, developed by Saul'yev (1964)