A new model for O$_2$ dependent ATP signaling between erythrocytes and capillary endothelium

Hasan Al-Taee

Medical Biophysics Department

Western University

Wednesday April 13$^{th}$, 2012
Introduction

Oxygen supply and demand need to be matched at the microvascular level. Studies have shown that a decrease in oxygen saturation triggers ATP release by red blood cells (Bergfeld, 1992). The fact that ATP is released by red blood cells can be proven by testing this phenomenon in the presence and absence of carbon monoxide (CO) (Jagger, 2001). In the presence of carbon monoxide, which has a very high affinity for hemoglobin, the hemoglobin becomes bound to the CO and therefore cannot change to its deoxygenated state and hence ATP is not released from the red blood cells (Jagger, 2001).

There is also evidence that ATP released in blood vessels causes ascending vasodilation and increased blood flow (Ellsworth, 2009). These findings may be helpful in studying conditions such as hypoxia. The objectives of this 6-week-project were to develop a new model (based on an existing one) of oxygen dependent ATP release by red blood cells (RBCs) in capillaries and to determine if the new model increases ATP-based oxygen supply regulation in microvessels. The hypotheses are as follows:

- The new model demonstrate ATP release from RBCs in the capillaries at decrease saturation of oxygen
- New model will allow hematocrit, RBC velocity and RBC supply rate to regulate microvascular flow

Theory

The new model was based on an equation developed by Arciero et. al in a paper published in 2008. The equation developed by them is

$$\frac{d}{dx}[(1 - H_D)QC(x)] = \frac{\pi}{4} D^2 H_T R[S(x)] - k_s \pi DC(x)$$

where $H_D$ is discharge hematocrit, $H_T$ is tube hematocrit, $Q$ is volume flow rate in an
individual, C is saturation, D is vessel length, R is release rate, S is saturation and kd is rate constant.

The new model equation is \[ \frac{\pi}{2} v_{rbc} D \delta \frac{dC}{dx} = -\pi D k_d C + \frac{\pi}{4} D^2 H_r \rho \left( \frac{dS}{dx} \right) \] where \( \rho \) is the new release rate, \( v_{rbc} \) is RBC velocity and \( \delta \) is the plasma layer i.e. distance between RBC outer circumference and capillary wall. The release rate equations are, for the Arciero model and our model respectively:

\[ R = R_0 (1 - R_1 S) \quad \text{and} \quad \rho = \rho_0 - \rho_1 v_{rbc} \frac{dS}{dx} \]

The equations have analytical solutions.

**Methods**

Firstly, we need to solve for ATP concentration in a single capillary. We need to change ATP release rate to a function of rate of change of saturation with respect to time. Also, in the new model, we changed the control volume to plasma layer between RBC and vessel wall as opposed to the total plasma volume which was the case in the original (Arciero) model. Finally, analytical solutions are plotted under varying conditions using MATLAB.

**Results**

For the baseline case-where consumption, hematocrit and velocity factors are equal to one- we observed an initial increase in ATP release followed by a no further increase after about 1 mole/ml of ATP has been released (figure 1).
The second case is one in which consumption was increased by a factor of six while hematocrit and velocity remained the same. This resulted in a large decrease in O₂ saturation in comparison to the other results. In this case we observed a large increase in ATP release in the new model and a smaller increase in the Arciero model (figure 2).

When both consumption and velocity were increased by a factor of six, we also saw an increase in ATP release for the new model, albeit less than the second case. The Arciero model showed a slight decrease in this case (figure 3).

In the final case, consumption was increased by a factor of six whereas velocity and hematocrit were only increased by factors of three and two respectively. Both models showed an increase in ATP release but the increase in the new model was almost double that of the Arciero model (figure 4).
Figure 2
Discussion

Generally, a decrease in oxygen saturation will cause an increase in ATP release. This was not the case for the Arciero model in figure 2. A larger decrease in oxygen saturation causes a larger increase in the amount of ATP released by the red blood cells. The release of ATP results in an interaction between the ATP and receptors located on the endothelium (Ellsworth, 2009). The receptors, which are located on the endothelial cells, then release vasodilators such as Nitric oxide (NO) (Ellsworth, 2009). This causes dilation upstream in vessels and hence increased blood flow is achieved.
Results may not be very accurate because wall shear rate and blood pressure not taken into account. This might be a possible source of error.

Conclusion

Blood flow could perhaps be regulated by the ATP released in the capillaries, making the capillaries the main site of flow regulation.
References


