Singlet Oxygen Modeling for PDT Incorporating Local Vascular Oxygen Diffusion

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Abstract

Singlet oxygen (1O2) is the major cytotoxic agent that kills cells during photodynamic therapy (PDT). An energy diagram for type II PDT interaction is shown in Figure 1. Based on a previously developed model [Ref. 1] that incorporates the diffusion equation for the light transport in tissue and the macroscopic kinetic equations for the generation of the singlet oxygen, the distance-dependent reacted 1O2 can be numerically calculated using finite-element method (FEM), Fig. 2. We recently improved the model to include microscopic kinetic equations of oxygen diffusion from uniformly distributed blood vessels to the adjacent tissue, Fig. 3. In the model, the cylindrical blood capillary has a radius in the range of 2- 5 um and a mean length of 300 um. The blood vessel network is assumed to form a 3-D grid based on a single Krogh cylinder model with a varying vascular density, i.e., the spacing between vascular cylinders is varying between 20 and 60 um. The forward calculation is performed using COMSOL Multiphysics®. The resulting mean oxygen concentration vs. time during PDT from the improved formula is proportional to the ratio of the mean oxygen concentration [3O2] and the initial oxygen concentration [3O2]0, x=[3O2]/[3O2]0, and independent of light fluence rate; see Fig. 4. In conclusion, our model with microscopic oxygen diffusion proves the validity of the formulation of the oxygen perfusion term, g(1-x), used in the macroscopic singlet oxygen model.

Reference

1. Zhu TC, Finlay JC, Zhou X, Li J, Macroscopic Modeling of the Singlet Oxygen Production During PDT, Proc. of SPIE Vol 6427, 642708 (2007)

Figures used in the abstract

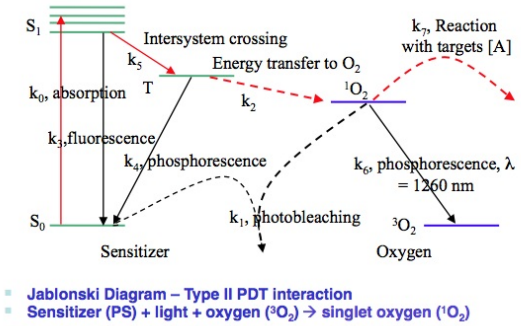

Figure 1: Jablonski Diagram

$$\mu_a\phi - \nabla\cdot\left(\frac{1}{3\mu_s'}\nabla\phi\right) = S$$ S: source term, Fluence rate: ϕ

$$\frac{d[S_0]}{dt} + \left(\xi\sigma\frac{\phi([S_0]+\delta)[^3O_2]}{[^3O_2]+\beta}\right)[S_0] = 0$$

$$\frac{d[^3O_2]}{dt} + \left(\xi\frac{\phi[S_0]}{[^3O_2]+\beta}\right)[^3O_2] - g\left(1-\frac{[^3O_2]}{[^3O_2](t=0)}\right) = 0$$

$$\frac{d[^1O_2]_{rx}}{dt} - \left(\xi\frac{\phi[S_0][^3O_2]}{[^3O_2]+\beta}\right) = 0$$

g is the maximum oxygen perfusion rate where there is no oxygen gradient

$\beta = k4/k2$ can be treated as constant.

$\xi = S_\Delta k5/(k3+k5)\varepsilon/h\nu/(k6/k7[A]+1)$

$\sigma = k1/(k7[A])$

$[S_0](t)$, $[^3O_2](t)$, and $[^1O_2]_{rx}(t)$ Equs. are function of β, σ, ξ, and g, and initial conditions of $[^3O_2]$ and $[S_0]$.

Figure 2: Coupled differential equation and 5 free parameters

• During PDT --Tissue

$$\frac{d[^3O_2]}{dt} + \left(\xi\frac{\varphi[S_0][^3O_2]\left(1+\sigma\left([S_0]+\delta\right)\right)}{[^3O_2]+\beta}\right) = \begin{cases} D_T\nabla^2[^3O_2] - q_0\dfrac{[^3O_2]}{[^3O_2]+[^3O_2]_m} & \Rightarrow \text{Krogh'smodel} \\ g\left(1-\dfrac{[^3O_2]}{[^3O_2]_{t=0}}\right) & \Rightarrow \text{Macroscopic} \end{cases}$$

Figure 3: Modified Equation that incorporate oxygen diffusion

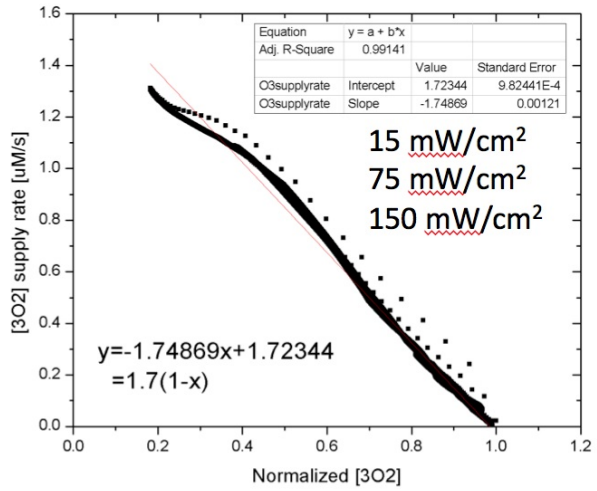

Figure 4: Relationship between oxygen supply rate (left side of Eq. in Fig. 3) and the normalized oxygen concentration, x = [3O2]/[3O2]0. Symbols: Solid line: 150 mW/cm2, Dashed line: 75 mW/cm2, Dotted line: 15 mW/cm2, Red line: linear fit, 1.7*(1-x).