Singlet Oxygen Modeling of BPD Mediated-PDT Using COMSOL

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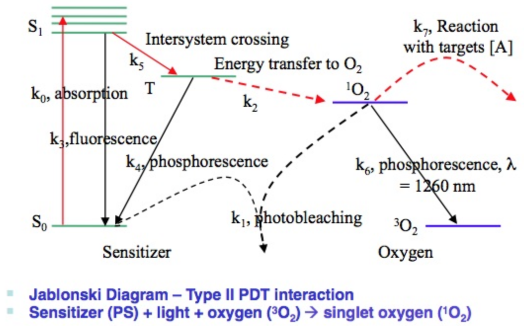
Abstract

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). The formula of reacted 1O2 concentration involves 5 photophysiological parameters which can be determined explicitly to predict the generation of reacted 1O2, see Fig. 2. We have improved an algorithm developed previously to solve the inverse problem to determine the 5 parameters. The optimization is performed using MATLAB® and dynamically linked with COMSOL for the forward calculation. The sensitivity of the model parameters to the necrosis depths and treatment conditions are examined. We have shown the results of applying this algorithm on a new photosensitizer drug, BPD, which does not have previously published results for these parameters in-vivo [Ref. 2]. The results are compared with in-vivo experiments performed in mice, see Figs. 3&4. In conclusion, our method can successfully extrapolate critical photochemical parameters in vivo for singlet oxygen based dosimetry of PDT.

Reference

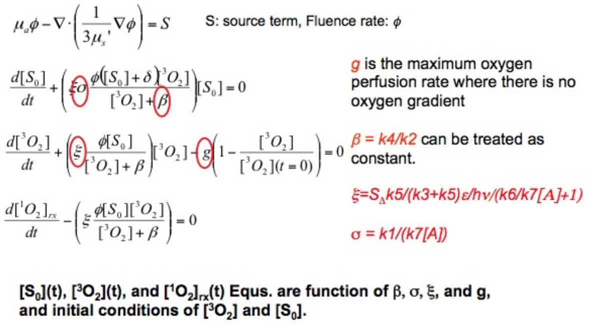
1. Zhu TC, Finlay JC, Zhou X, Li J, Macroscopic Modeling of the singlet oxygen production during PDT, Proc. of SPIE Vol. 6427, 642708, (2007).
2. Mitra S and Foster TH, Photochem & Photobiol 81, 849-859 (2005).

Figures used in the abstract



- **Jablonski Diagram – Type II PDT interaction**
- **Sensitizer (PS) + light + oxygen ($^3O_2$) → singlet oxygen ($^1O_2$)**

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

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

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

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

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

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

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

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

$[S_0](t)$, $[^3O_2](t)$, 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.

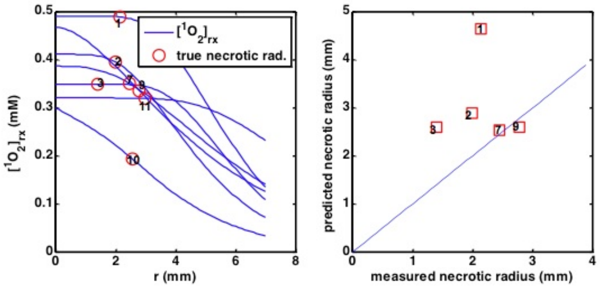
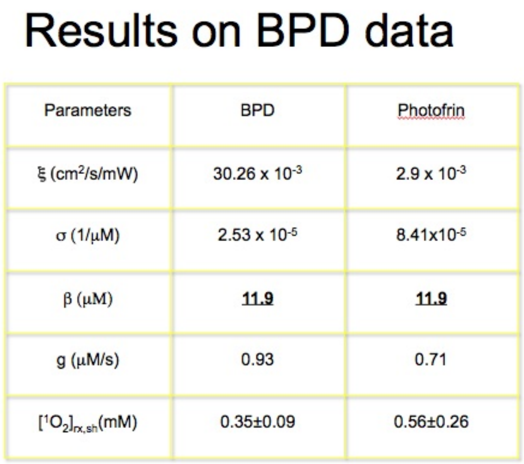


Figure 3: Fitting results for BPD.



Results on BPD data

Parameters	BPD	Photofrin
ξ (cm^2/s/mW)	30.26 x 10^{-3}	2.9 x 10^{-3}
σ (1/μM)	2.53 x 10^{-5}	8.41x10^{-5}
β (μM)	**11.9**	**11.9**
g (μM/s)	0.93	0.71
$[{}^1O_2]_{rx,sh}$(mM)	0.35±0.09	0.56±0.26

Figure 4: Results for BPD parameters.