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Parameter Optimization for FEM based modeling of singlet oxygen during PDT using COMSOL

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Outline

- Introduction
- Theory for PDT dosimetry model
- Optimization results
- PDT dosimetry quantity prediction for prostate using COMSOL
- Conclusions

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Introduction

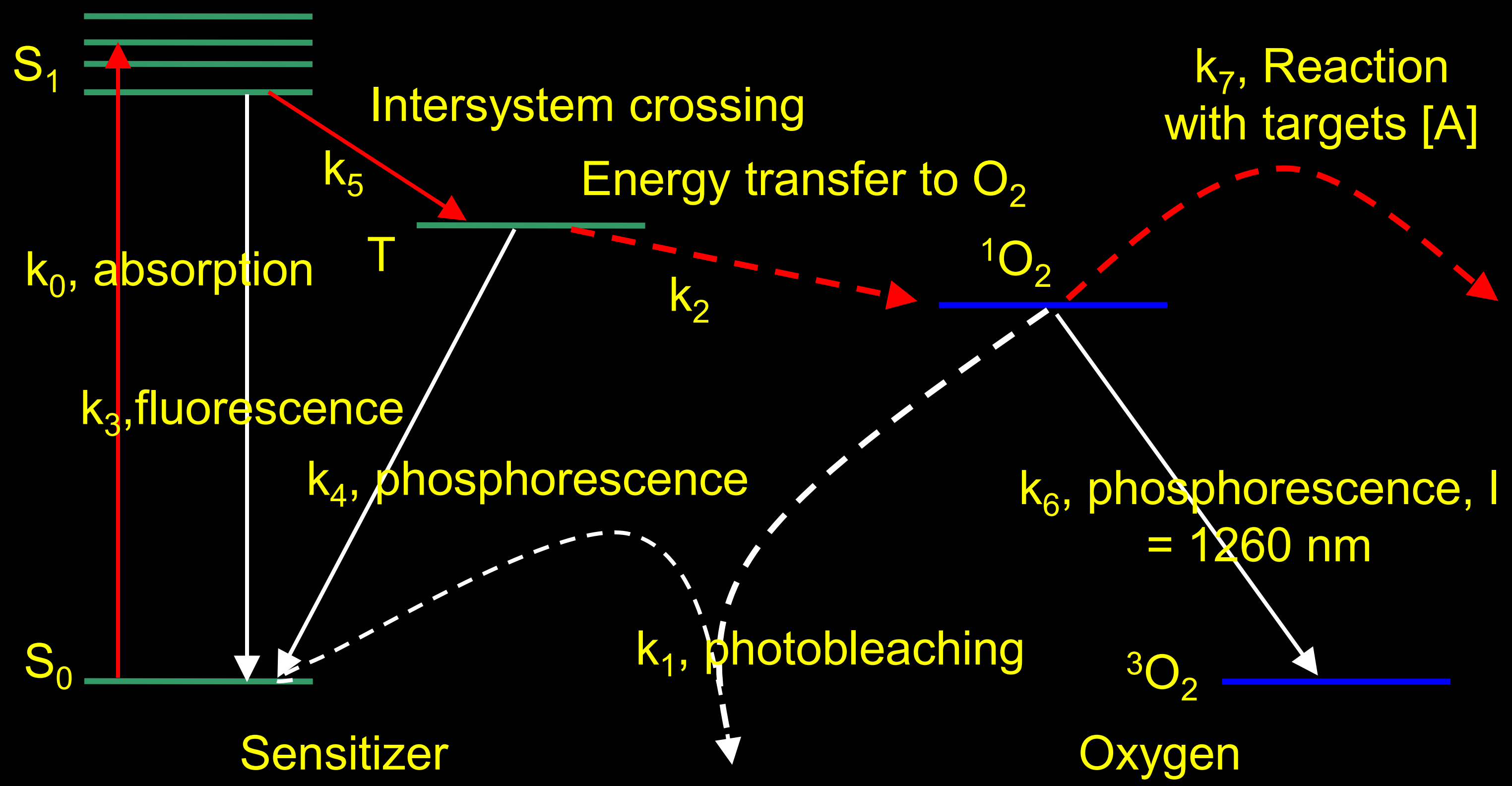
- Photodynamic therapy (PDT) is an important treatment modality for cancer and other localized diseases.

- In PDT, **photosensitizers** excited by **light** react with ground state **oxygen**, which leads to generation of singlet oxygen - the major cytotoxic agent - to kill the surrounding tissues and cells.

- Compared with other treatment modalities, PDT has advantages including non-ionizing, localized photon delivery and better cosmetic outcome.

Introduction

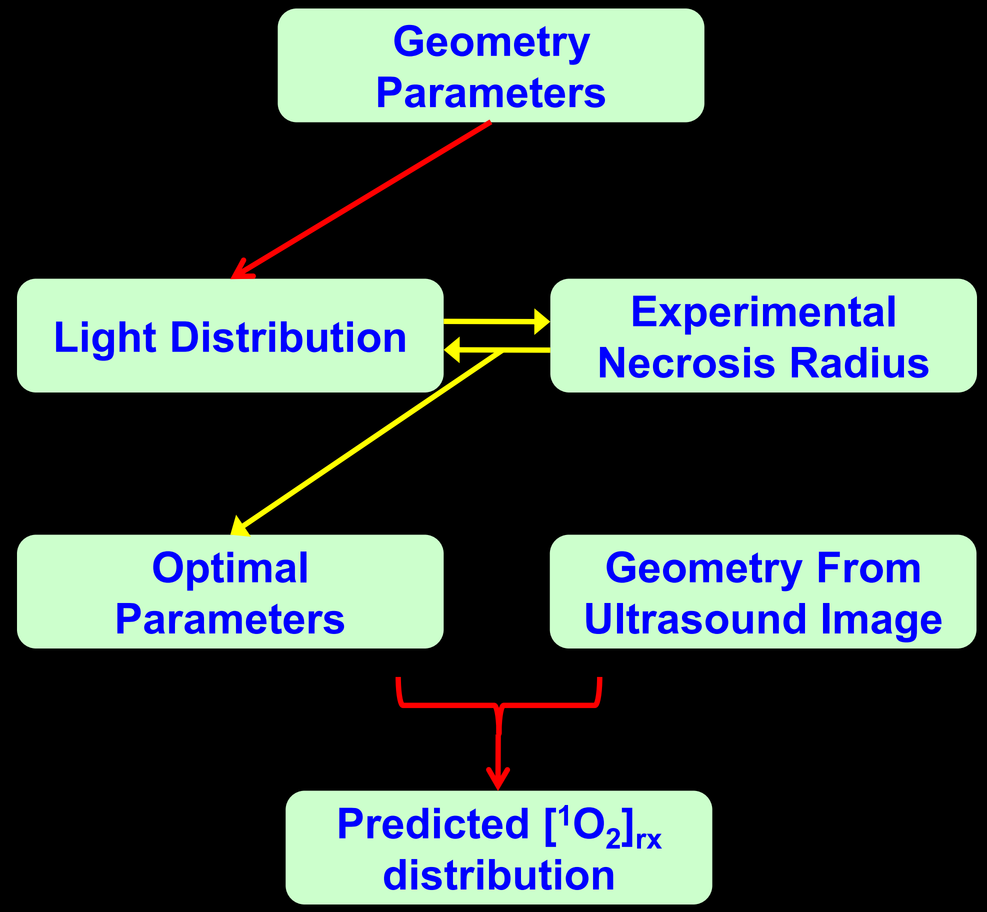
Jablonski Diagram for Type II PDT interaction



Sensitizer (PS) + light + oxygen ($^3O_2$) → singlet oxygen ($^1O_2$)

Introduction

Apparent reacted singlet oxygen $[^1O_2]_{rx}$ was introduced as a PDT dosimetry quantity to better predict the PDT treatment outcome than PDT dose



→ By COMSOL

→ By COMSOL + MATLAB

Flow chart for PDT photophysiological parameter optimization and dosimetry prediction

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Theory for PDT dosimetry model

Light diffusion equation

$$\mu_a \varphi - \nabla \cdot \left(\frac{1}{3\mu_s'} \nabla \varphi \right) = S$$

→ COMSOL

Photo chemical equations

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

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

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

} MATLAB

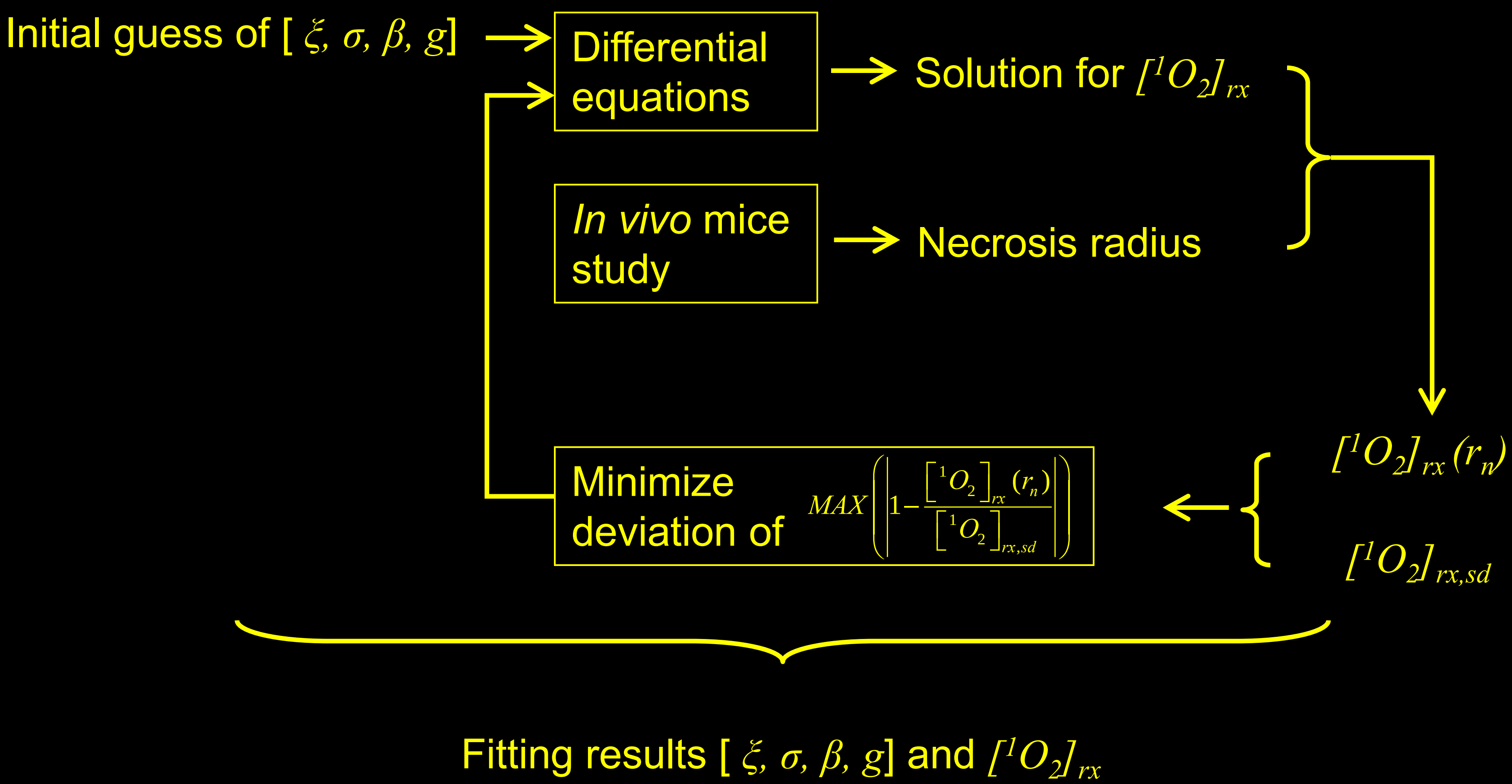
φ Light fluence rate

$[S_0]$ Ground sensitizer concentration

$[^3O_2]$ Ground triplet oxygen concentration

$[^1O_2]_{rx}$ Reacted singlet oxygen concentration

Theory for optimization model



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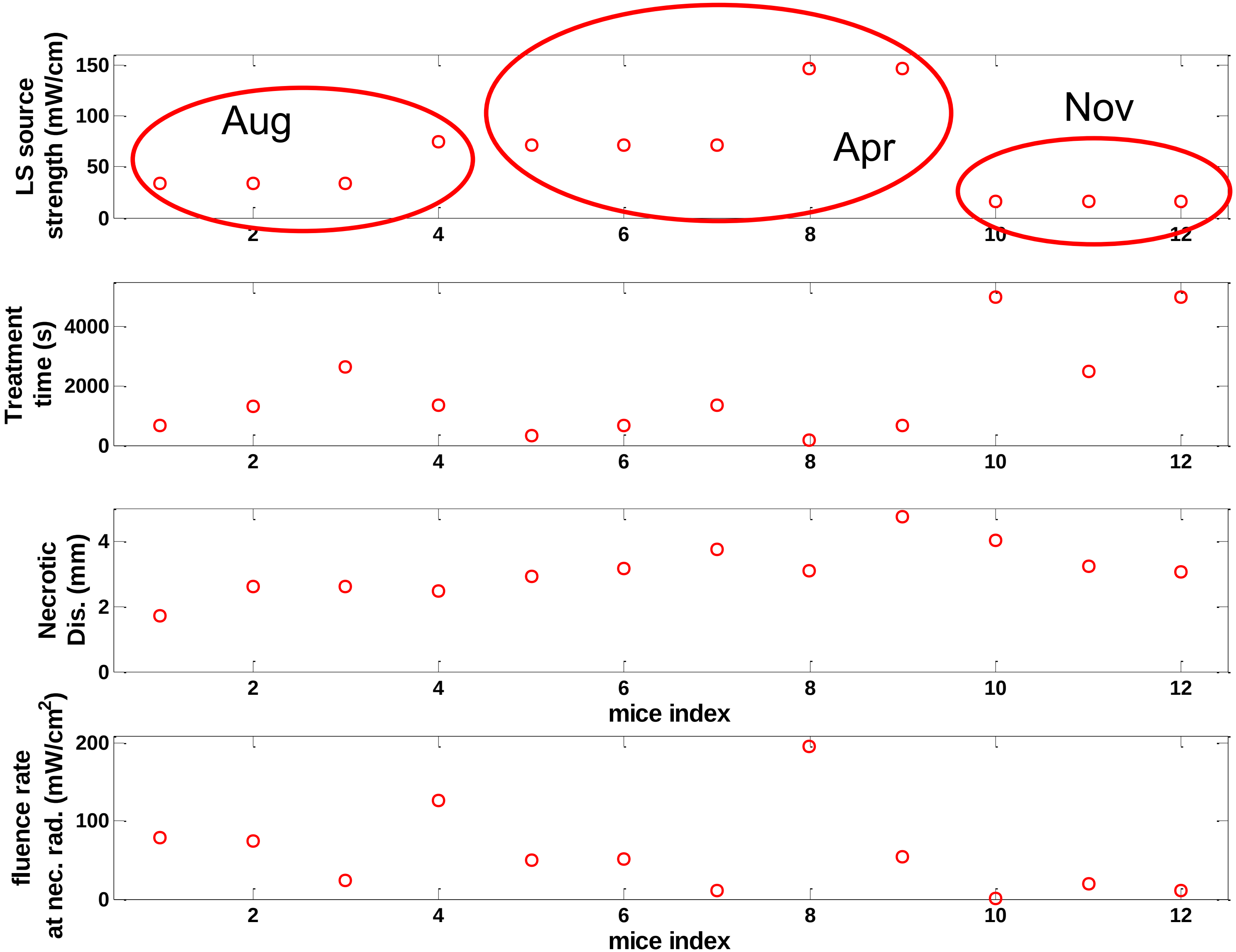
Optimization results



Optimization results

Parameters	Final fit	Apr Fit	Apr and Aug Fit	Previous fit [1]	Published values
ξ (cm^2/s/mW)	**2.0×10^{-3}**	5.0×10^{-3}	3.9×10^{-3}	2.1×10^{-3}	3.7×10^{-3} [2]
σ (1/μM)	**11.2×10^{-5}**	6.6×10^{-5}	11.5×10^{-5}	7.6×10^{-3}	7.6×10^{-3} [2]
β (μM)	**11.9**	11.9	11.9	11.9	11.9 [3]
g (μM/s)	**0.8**	0.62	0.56	0.69	_
$[^1O_2]_{rx,sh}$ (mM)	**0.41**	0.46	0.41	0.74	_

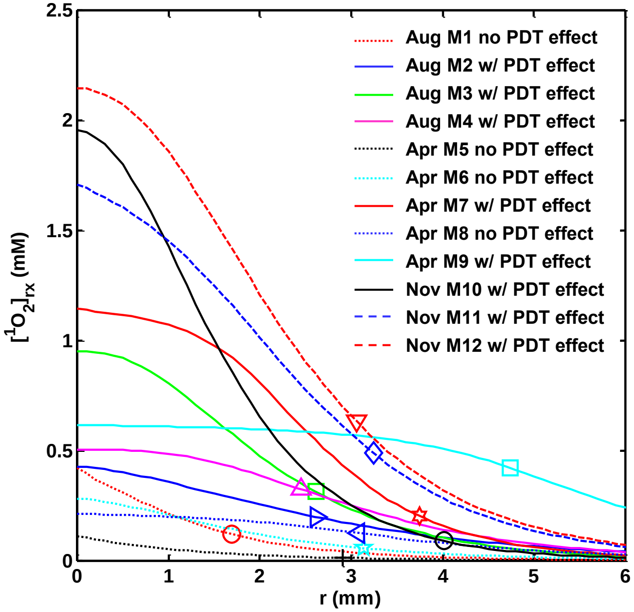
[1] Wang et al., J. Biophoton, 2010.

[2] Mitra et al., Photochem. Photobiol, 2005.

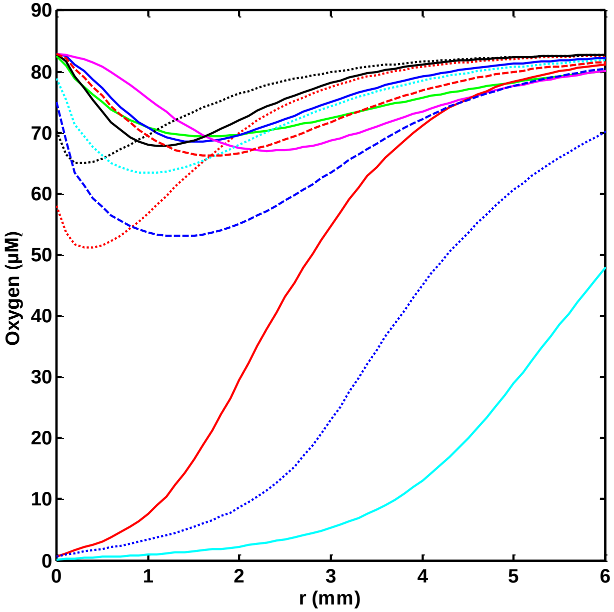
[3] Georgakoudi et al., Photochem. Photobiol. 1997.

Optimization results

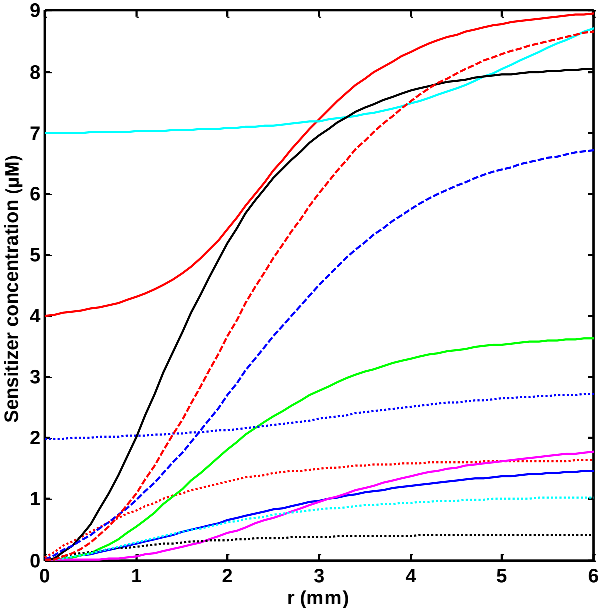
Final fitting results including experimental data from All data



Apparent reacted singlet oxygen concentration



Oxygen concentration

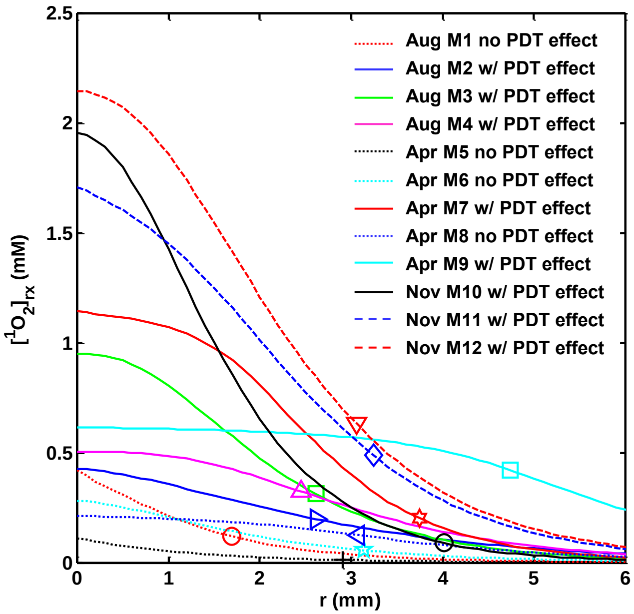


Photosensitizer concentration

Optimization results

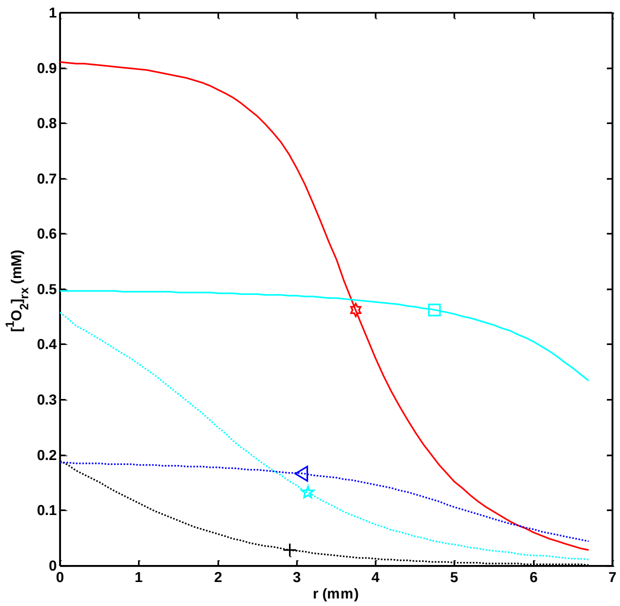
Fitting results: apparent reacted singlet oxygen concentration

All data



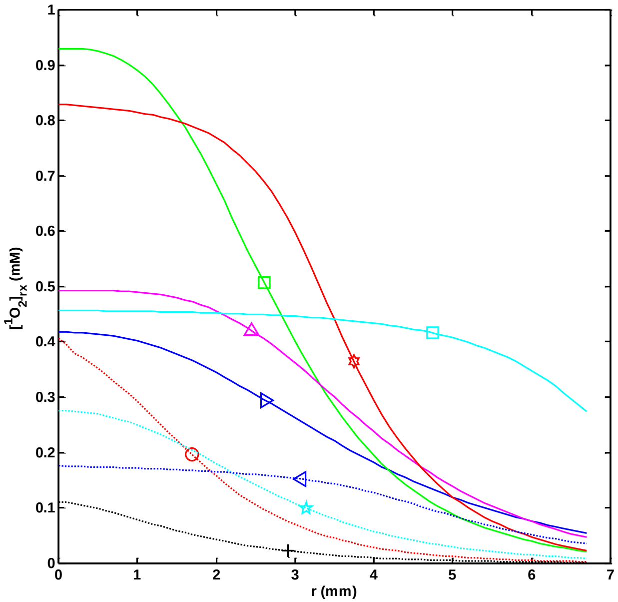
g = 0.8 μM/s
ξ = 2.0 x 10^{-3} $cm^2mW^{-1}s^{-1}$
σ = 11.2 x 10^{-5} μM^{-1}
$[^1O_2]_{rx,sh}$ = 0.41 mM

April data



g = 0.62 μM/s
ξ = 5.0 x 10^{-3} $cm^2mW^{-1}s^{-1}$
σ = 6.6 x 10^{-5} μM^{-1}
$[^1O_2]_{rx,sh}$ = 0.46 mM

April and August data



g = 0.56 μM/s
ξ = 3.9 x 10^{-3} $cm^2mW^{-1}s^{-1}$
σ = 11.5 x 10^{-5} μM^{-1}
$[^1O_2]_{rx,sh}$ = 0.41 mM

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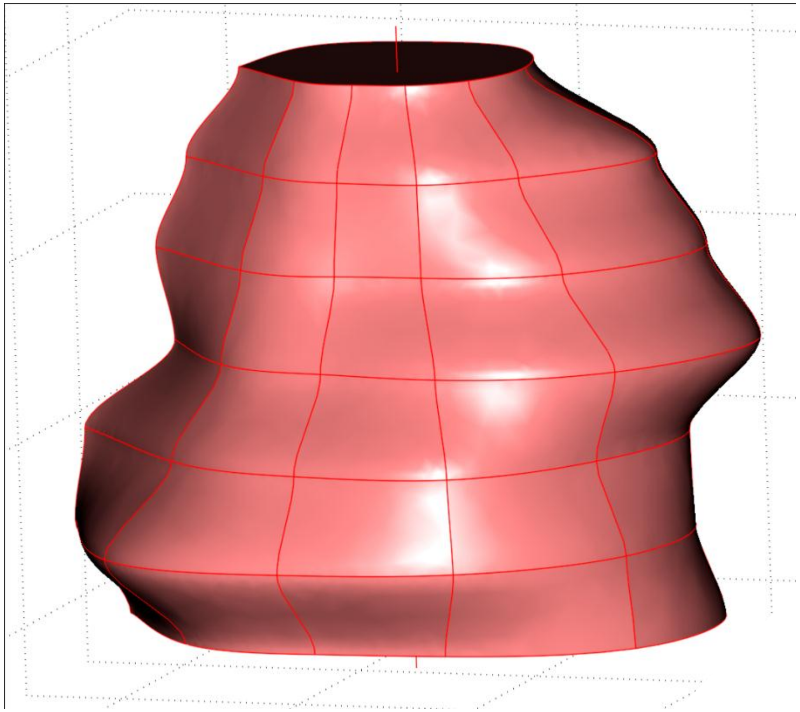
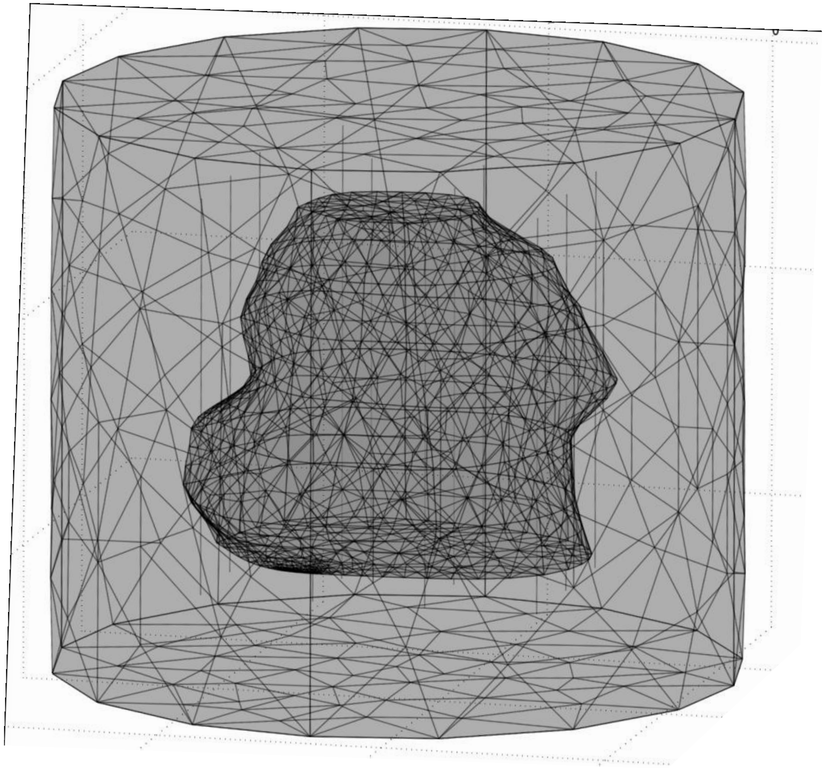
$[^1O_2]_{rx}$ prediction using COMSOL

Prostate geometry for prediction model



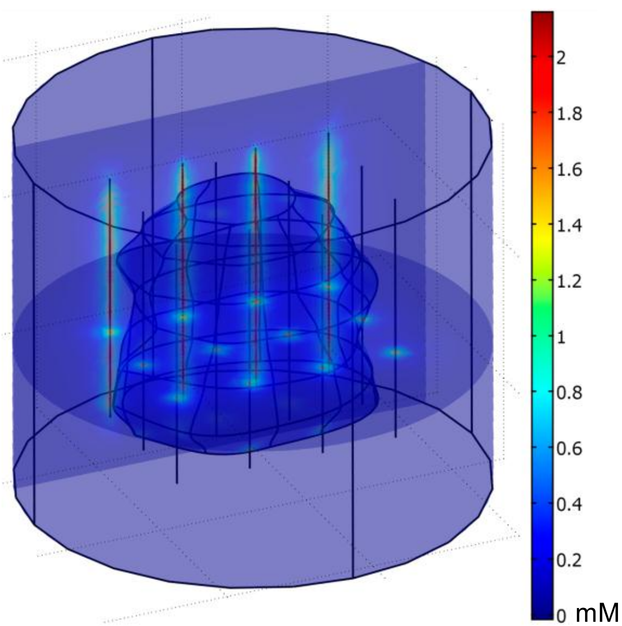
Geometry



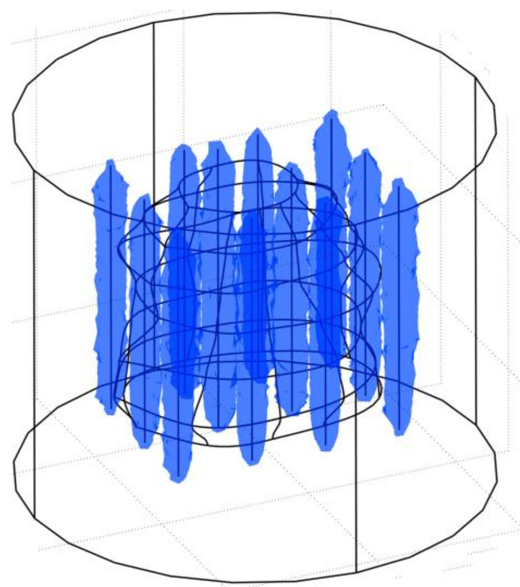
Meshing

$[^1O_2]_{rx}$ prediction using COMSOL

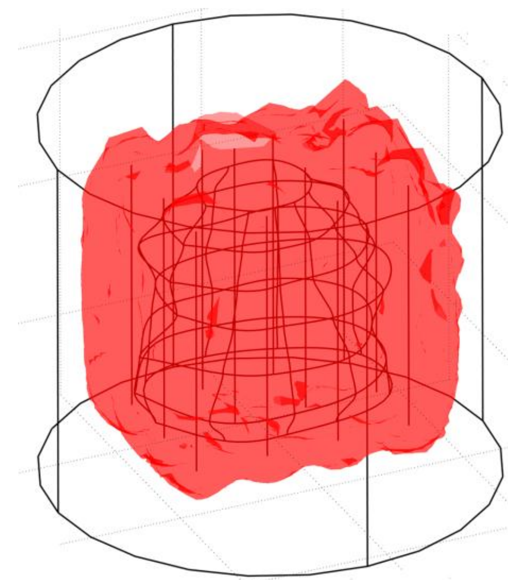
PDT dosimetry quantities for treatment up to 300 s in a homogeneous prostate



Slide view of $[^1O_2]_{rx}$



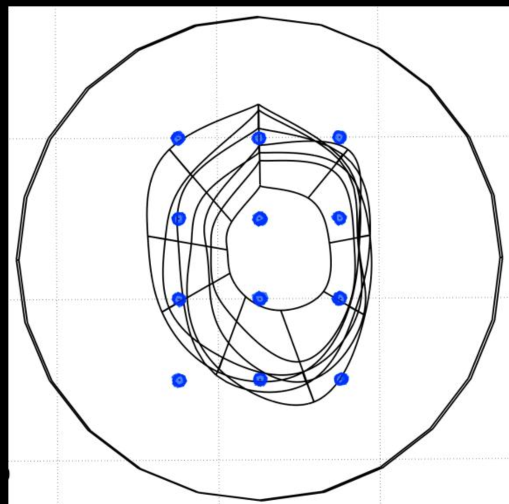
Isosurface of $[^1O_2]_{rx}$ at 0.41 mM



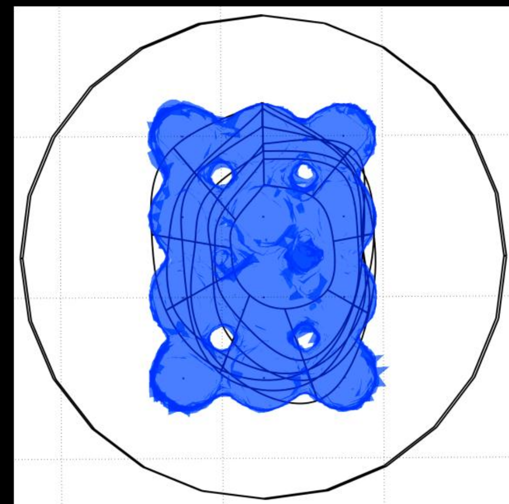
Isosurface of light flucence

$[^1O_2]_{rx,sh}$ prediction using COMSOL

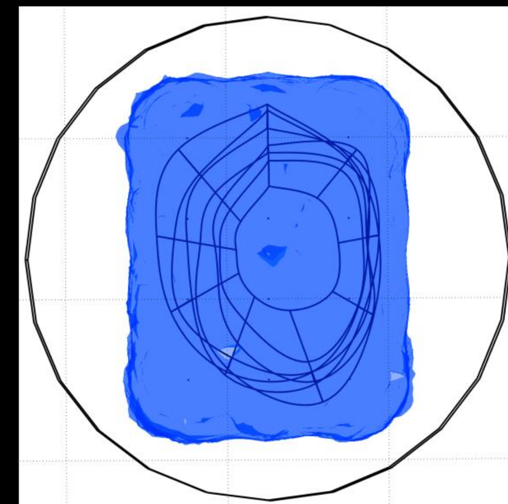
Top view of isosurface of $[^1O_2]_{rx}$ at 0.41 mM



200 s

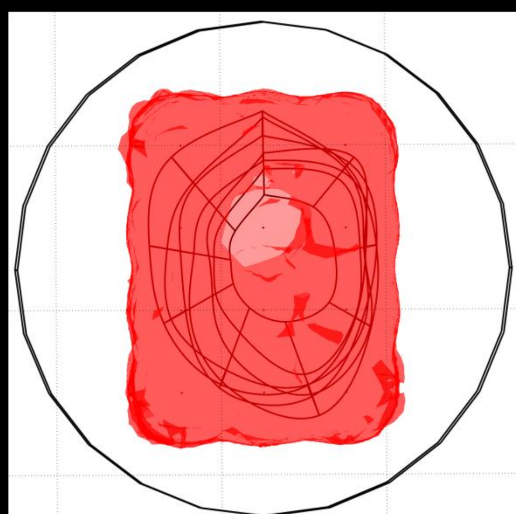


500 s

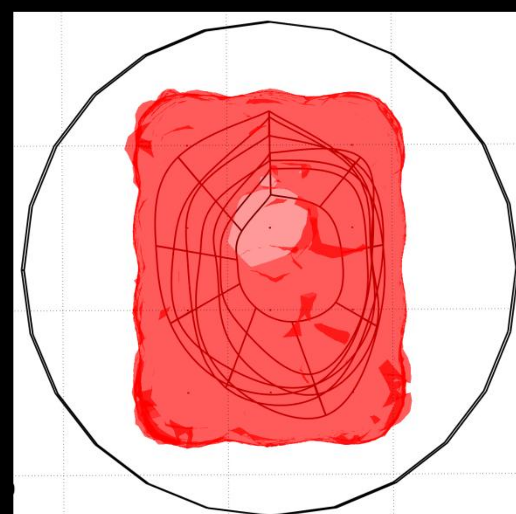


1000 s

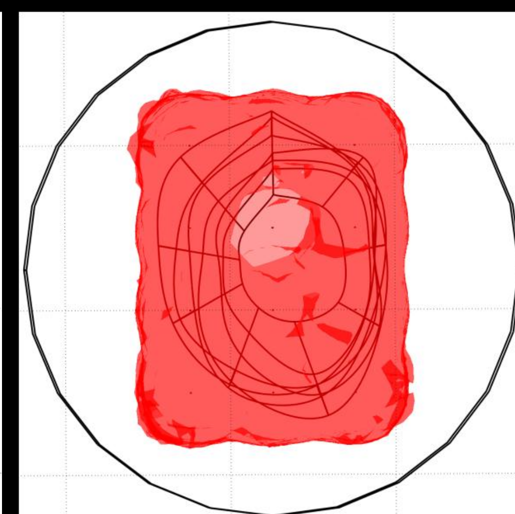
Top view of isosurface of light flucence



30 J/cm^2



75 J/cm^2



150 J/cm^2

Conclusions

- PDT model including light diffusion and PDT kinetics equations
- Optimized photo-chemical parameters in the PDT model
- PDT prostate model with homogeneous properties
- Prediction of PDT dosimetry quantities for treatment

Thank you!