Temperature-modulated Bioluminescence Tomography

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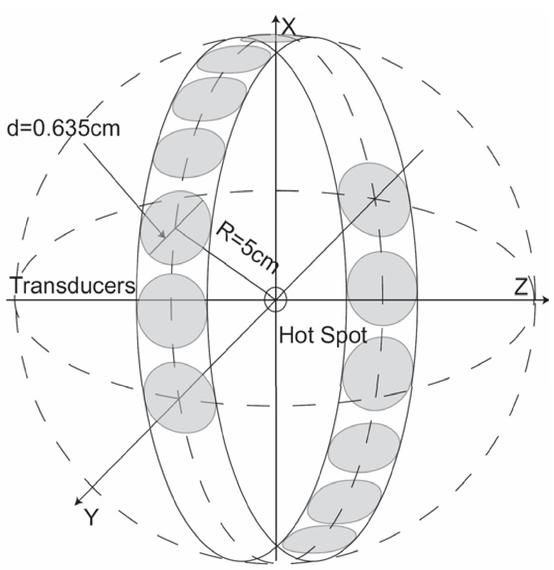
Introduction

Zhao et al. reported that the emission spectra of luciferase enzymes from firefly (FLuc), click beetle (CBGr68, CBRed), and Renilla reniformins (hRLuc) depend on temperature. With a change from 25° C to 39° C, the brightness increases in general, and FLuc has a 34 nm red shift as well. We recognize this phenomenon as a major opportunity to overcome the inherent ill-posedness of bioluminescence tomography (BLT).

Here we propose temperature-modulated bioluminescence tomography (TBT) to utilize the temperature dependence of bioluminescence for superior BLT performance. Specifically, we employ a focused ultrasound array to heat small volumes of interest one at a time, and induce a detectable change in the optical signal on the body surface of a mouse. Based on this type of information, the BLT reconstruction can be improved.

Ultrasound Heating

We propose an ultrasound focusing array mounted on a ring. It can generate a hot spot as small as 2x2x8 mm at the center of the ring.



The ultrasound pressure field at position X can be expressed as:

$$p(X) = \frac{i\rho c}{\lambda}\int_{S'} u\frac{e^{-(\alpha+ik)|X-X'|}}{|X-X'|}dS$$

where S' denotes the total surface area of the transducers, ρ medium density, c phase velocity, u velocity amplitude, λ wavelength, k wave number, and α attenuation coefficient. The induced temperature distribution T is governed by the steady state bioheat transport equation:

$$\kappa\nabla^2 T - c_b\omega(T-T_a) + Q = 0$$

where κ denotes thermal conductivity, c_b specific heat of blood, ω blood perfusion rate, and Q the absorption power density.

TBT Reconstruction

We use a finite element method to solve this inverse source problem Φ=BS, where Φ represents the photon density on the mouse body surface, S the source vector in a permissible source region, B a system matrix depending on the mouse anatomy and its optical properties. The original and heated signals can be expressed as

$$\Phi = BS_I + B'S_o, \qquad \Phi_H = tBS_I + B'S_o$$

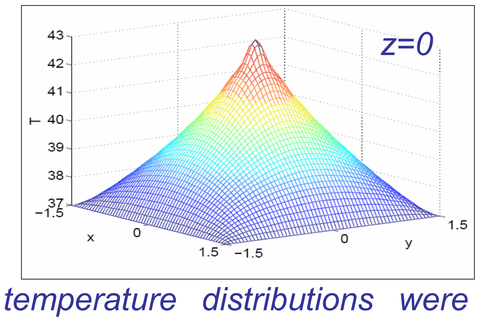
where S_I and S_o are the source vector inside and outside the heated region, t is the ratio between the heated source energy and the reference source energy. Then,

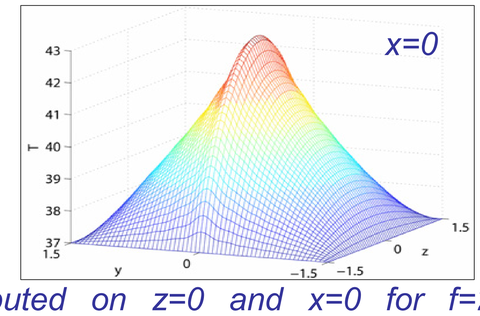
$$\Phi_D = \Phi_H - \Phi = (t-1)BS_I$$

where Φ_D is the difference between heated and original signals. Finally, the TBT reconstruction can be formulated as minimizing the object function:

$$\Theta(S_I) = (\Phi_D - \Phi_D^m)^T W(\Phi_D - \Phi_D^m) + \varepsilon\eta(S_I)$$

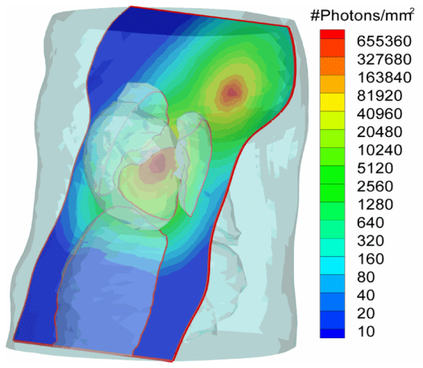
Numerical Results



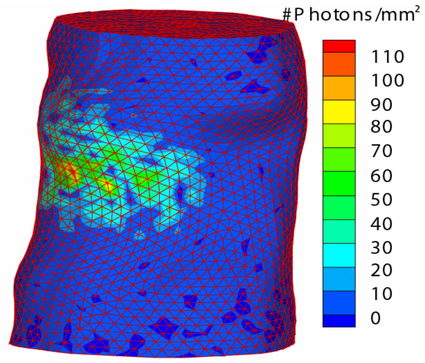


The temperature distributions were computed on z=0 and x=0 for f=2MHz, ω=1.5 $kgm^{-3}s^{-1}$, and W=0.008wattr.

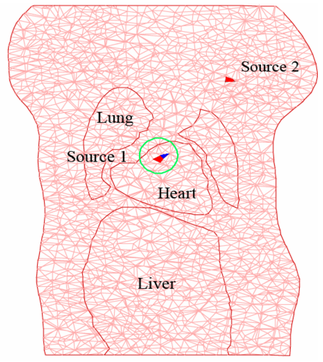
The TBT reconstruction was performed using a digital mouse phantom containing two sources. While the true source locations were indicated in red, the reconstructed source locations were marked in blue, and a heated region was circled in green below. Source 1 and 2 were inside and outside the heated region, respectively. In all the 80 groups of tests, it was found that the source localization and power estimation were done with < 1mm and < 25% errors, respectively.



Oblique section showing the photon density



Difference data after and before heating



Oblique section showing source locations.

Conclusion

By heating a small region and extracting the difference signal, the permissible region for BLT reconstruction can be reduced. This helps regularize an ill-posed BLT problem into a better-conditioned or well-posed TBT framework. Also, this idea is applicable in 2D bioluminescence imaging and computed optical biopsy (COB).

References

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2. *Wang G, Shen H, Cong W, Zhao S, Wei G: Temperature-modulated bioluminescence tomography. Optics Express 14:7852-7871, 2006*
3. *Wang G, Shen H, Cong W, Zhao S, Wei G: Temperature-modulated bioluminescence tomography. Patent disclosure filed with the University of Iowa Research Foundation; 2006*

Acknowledgments: *The authors thank Dr. Doyle (Stanford University) for discussion with Dr. Wang on the temperature-dependence of the bioluminescent spectra and permission for use of their data in [1], as well as Drs. Jiang (Peking University), Li and Henry (University of Iowa) for comments. This work was supported by NIH/NIBIB grant EB001685.*