MAP ESTIMATION OF OXYGEN TENSION IN RETINAL VESSELS WITH PHOSPHORESCENCE LIFETIME IMAGING

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ABSTRACT

In phosphorescence lifetime imaging methods oxygen tension in retinal vessels has traditionally been indirectly determined from the estimates of intermediate variables whose noise-contaminated linear combinations are observed as phosphorescence intensity images. The classical least squares (LS) and regularized least squares (RLS) methods were used to obtain estimates of the intermediate variables. The estimates of the intermediate variables are then used to compute oxygen tension. The estimates of intermediate variables, however, do not yield an optimum estimate of oxygen tension due to its nonlinear dependence on the ratio of intermediate variables. Moreover, prior knowledge about the variables is very limited so that the level of noise cannot be reliably estimated, thereby affecting the automated choice of the regularization parameter in the RLS method. In this study the problem of optimally estimating oxygen tension in retinal vessels using the maximum a posteriori (MAP) criterion is addressed. For this purpose the conditional distribution of oxygen tension is derived given the phosphorescence lifetime imaging observations and model. The performance of MAP is compared with that of LS and the RLS methods using simulated data and its improved performance in the presence of different levels of noise is demonstrated.

Index Terms— Phosphorescence lifetime imaging, least squares, regularized least squares, maximum a posteriori, oxygen tension.

1. INTRODUCTION

In phosphorescence lifetime imaging methods oxygen tension in retinal vessels has traditionally been indirectly determined from the estimates of intermediate variables whose noise-contaminated linear combinations are observed as phosphorescence intensity images. The LS estimation discussed was initially used to estimate these intermediate variables [1-3]. Since phosphorescence intensity images are contaminated with noise, LS estimation suffers from high variance in oxygen tension maps that are manifested as spikes that adversely affect reliable analysis of retinal vasculature oxygenation. To overcome these shortcomings, we had, in an earlier study [4], proposed the use of spatial regularization of the least-squares estimates and showed the superior performance of the regularized LS (RLS) method by applying it to optimally estimate the intermediate variables for both simulated data as well as real image data acquired from rat retinas. These estimates of the intermediate variables are then used to compute oxygen tension.

The classical and the RLS estimates of intermediate variables, however, do not yield an optimum estimate of oxygen tension due to its nonlinear dependence on the ratio of intermediate variables. In this paper the problem of optimally estimating oxygen tension in large retinal vessels using the maximum a posteriori (MAP) criterion is first addressed. For this purpose the conditional distribution of oxygen tension is derived given the phosphorescence lifetime imaging observations and model. The performance of MAP is compared with that of LS and the RLS methods using simulated data and its improved performance in the presence of different levels of noise is demonstrated.

The derivation of MAP estimation method is provided next.

2. MAP ESTIMATION OF OXYGEN TENSION FROM PHOSPHORESCENCE IMAGES

The observed phosphorescence intensity vector in the presence of additive noise is modeled as

$$Y = SV + N \,. \tag{1}$$

where $V = \left[a_0 \; a_1 \; b_1 \right]^{\mathrm{T}} \in \Re^3$ denotes the vector of the parameters of interest, $Y \in \Re^L$ the vector of measurements,

$N \in \Re^L$ the vector of the additive noise, and $S \in \Re^{L\times 3}$ the system matrix defined according to the phosphorescence lifetime imaging model [4] .

Ideally, to estimate oxygen tension using the MAP criterion, the posterior density function of oxygen tension given the observed intensity vector should be derived and the values maximizing this function would be chosen as the optimum estimates of oxygen tension. Since all unknowns in the model parameters [4] cannot be expressed as functions of oxygen tension, the a posteriori density function of oxygen tension cannot be derived directly.

For notational simplicity, just y is used in the subscript throughout the paper instead of $Y=y$. Also R is used to denote oxygen tension to simplify the notation. The conditional probability density function $f_{R/y}$ is obtained by first defining the conditional distribution function of R ,

$$F_{R/y}(r) = P(R \le r / Y = y) . \tag{2}$$

Given constants τ_0 and K_φ, modulation frequency ω_0 and the theta correction angle θ_C [4], we obtain the conditional distribution function of R as follows:

$$F_{R/y}(r) = P(R \le r / Y = y) = P\left(\frac{\tau_0\omega_0(a_1 + b_1K) - (b_1 - a_1K)}{(b_1 - a_1K)K_\varphi\tau_0} \le r / Y = y \right), \tag{3}$$

where K equals to $\tan(\theta_c)$.

By defining

$W = a_1(\tau_0\omega_0 + K + KrK_\varphi\tau_0) + b_1(K\tau_0\omega_0 - 1 - rK_\varphi\tau_0)$ and $Z = b_1 - a_1K$, and using set partitioning, (3) can be written as:

$$F_{R/y}(r) = P(W \le 0 / Y = y)P(Z > 0 / Y = y) + P(W \ge 0 / Y = y)P(Z < 0 / Y = y) . \tag{4}$$

Here, the conditional distributions of W and Z containing random variables a_1 and b_1 which are equal to $V(2)$ and $V(3)$ in (1) are required. The derivative of $F_{R/y}(r)$ yields the conditional density function $f_{R/y}(r)$. Finally, the values of r that maximize the conditional density function will be chosen as MAP estimates of oxygen tension. To be able to derive the conditional distributions of W and Z, the conditional distribution of the parameter vector V is obtained by modeling the prior distributions of the parameter vector V and noise vector N using the linear model in (1).

The parameter vector V is modeled as Gaussian with mean and covariance (μ_V, Σ_v). The noise is also modeled as Gaussian with zero mean and a covariance matrix Σ_N. Therefore, the conditional distribution of Y given $V = v$ is Gaussian with mean Sv and covariance equal to the noise covariance Σ_N. Since both random vectors V and N are modeled as Gaussian and the observed intensity vector is the sum of linear combinations of the parameters and noise given in (1), the conditional distribution of V / y is also Gaussian with mean $\mu_{V/y} = \mu_V + \Sigma_{VY}\Sigma_Y^{-1}(y - \mu_Y)$ and covariance $\Sigma_{V/y} = \Sigma_V - \Sigma_{VY}\Sigma_Y^{-1}\Sigma_{YV}$. The priors are specified by the mean and the covariance of the parameter vector μ_V and Σ_V, as well as the covariance of the noise Σ_N. The terms in the mean and covariance of the conditional distribution of V / y depend on these through the following relations:

$$\mu_Y = S\mu_V , \tag{5-a}$$

$$\Sigma_Y = S\Sigma_V S^T + \Sigma_N , \tag{5-b}$$

$$\Sigma_{VY} = \Sigma_V S^T , \tag{5-c}$$

$$\Sigma_{YV} = S\Sigma_V , \tag{5-d}$$

where S is the system matrix in (1).

Since the conditional distributions of W and Z in (4) consists of a linear sum of the Gaussian random variables, they are also Gaussian random variables with mean and variance as follows:

$$\mu_{W/y}(r) = \mu_{V/y}(2)(\tau_0\omega_0 + K + KrK_\varphi\tau_0) + \mu_{V/y}(3)(\tau_0\omega_0K - 1 - rK_\varphi\tau_0) \tag{6-a}$$

$$\sigma^2_{W/y}(r) = (\tau_0\omega_0 + K + KrK_\varphi\tau_0)^2\Sigma_{V/y}(2,2) + (\tau_0\omega_0K - 1 - rK_\varphi\tau_0)^2\Sigma_{V/y}(3,3) + 2(\tau_0\omega_0 + K + KrK_\varphi\tau_0)(\tau_0\omega_0K - 1 - rK_\varphi\tau_0)\Sigma_{V/y}(2,3) \tag{6-b}$$

$$\mu_{Z/y} = \mu_{V/y}(3) - K\mu_{V/y}(2) \tag{6-c}$$

$$\sigma^2_{Z/y} = \Sigma_{V/y}(3,3) + K^2\Sigma_{V/y}(2,2) \tag{6-d}$$

From the conditional distributions of W and Z, (4) may be written as follows:

$$F_{R/y}(r) = \Phi\left(-\frac{\mu_{W/y}(r)}{\sigma_{W/y}(r)}\right)\left(1-\Phi\left(-\frac{\mu_{Z/y}}{\sigma_{Z/y}}\right)\right) + \left(1-\Phi\left(-\frac{\mu_{W/y}(r)}{\sigma_{W/y}(r)}\right)\right)\Phi\left(-\frac{\mu_{Z/y}}{\sigma_{Z/y}}\right), \quad (7)$$

where $\Phi(\cdot)$ is the normal distribution function. Finally, the conditional density function of oxygen tension given the observed intensity vector is obtained by taking derivative of (7) with respect to *r*:

$$f_{R/y}(r) = f\left(-\frac{\mu_{W/y}(r)}{\sigma_{W/y}(r)}\right)\frac{d}{dr}\left(-\frac{\mu_{W/y}(r)}{\sigma_{W/y}(r)}\right)\left(1-2\Phi\left(-\frac{\mu_{Z/y}}{\sigma_{Z/y}}\right)\right), \quad (8)$$

where $f(\cdot)$ is the normal density function. The maximum a posteriori (MAP) estimate of oxygen tension is then equal to:

$$\hat{R}_{MAP} = \arg\max_{r}\left\{f_{R/y}(r)\right\}. \quad (9)$$

3. RESULTS

The parameters a_1 and b_1 were created following the imaging model [4], which is assumed to be known a-priori. Based on the model, which calculates these parameters from the intensity values, intensity images of the simulated oxygen tension map containing a vein and an artery (bottom) shown in Figure 1 were generated from the model parameters, a_0, a_1 and b_1, associated with the simulated oxygen tension map. The thickness of retinal artery and vein was also carefully selected mimicking a realistic case when generating the data by choosing resolution of each image pixel as 3 by 3 micron. An i.i.d. Gaussian noise was added at different variance values to the intensity images to simulate the noise effect on the real measurements.

MAE performance of proposed method was compared with the currently existing methods. Monte Carlo simulations were conducted to compare bias and variance performances of the methods at a constant noise level. The simulated oxygen tension maps were estimated for 100 independent trials and the bias and variance of these 100 estimates were calculated.

The simulated oxygen tension map and its estimation by the LS, RLS, and proposed MAP methods in the presence of noise with variance 10^6 (resulting in an SNR of 12 dB) are shown in Figure 1. The effect of noise on LS estimates is clearly visible through the presence of spikes. Estimated oxygen tension map by the RLS method, on the other hand, is piecewise smooth and differs from the original map, especially in the artery although the spikes occurred in LS estimates are significantly suppressed and high variance is decreased. The MAP method further improves the RLS results and provides a very accurate estimate of the real oxygen tension map, which is almost unaffected by noise at all levels because of the accurate statistical model assumed to be known a-priori.

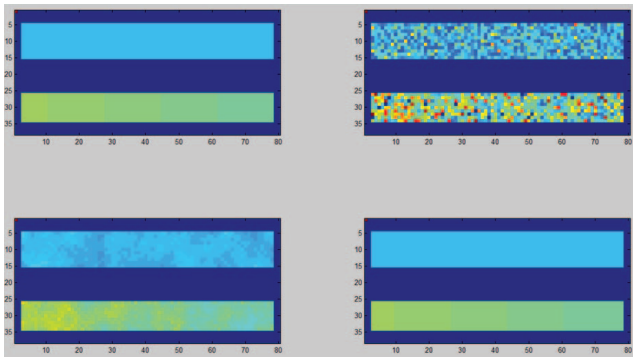


Figure 1: The original simulated oxygen tension map (left-top) and its estimates in the presence of noise with variance 10^6 using the LS (right-top), RLS (left-bottom), and MAP methods, respectively.

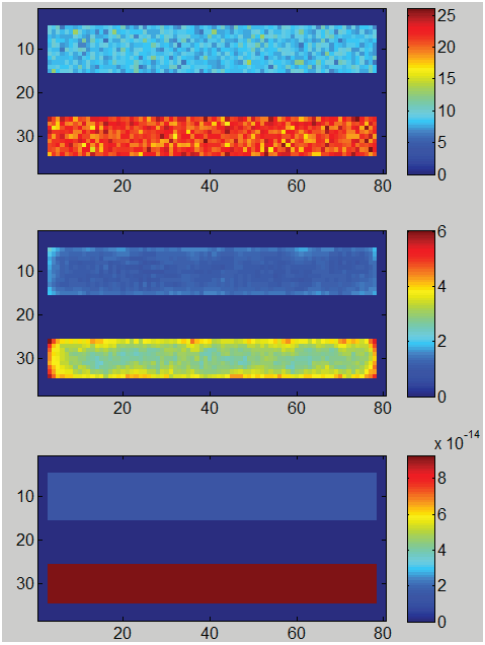


Figure 2: Bias comparison of the LS (top), RLS (middle), and MAP methods. The colorbar represents bias values.

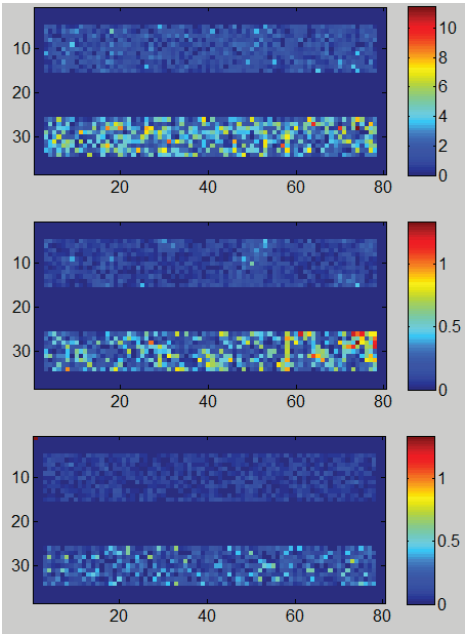


Figure 3: Standard deviation comparison of the LS (top), RLS (middle), and MAP methods. The colorbar represents standard deviation values

The bias and variance performance of the methods obtained from 100 independent estimates were compared and the results are shown in Figures 2 and 3, respectively. The proposed method generated the smallest bias and variance values as expected. The RLS method significantly decreased variance of the LS estimates but not to the same extent as the proposed method.

For different noise variance values in the ranges between 10^4 and 10^7 (SNR between 42 dB and 12 dB), MAE performance of the methods are also compared. The proposed method provided very accurate results, which are most robust to noise as shown in Figure 4. MAE at 22 dB SNR decreased from 10.8 to 2.3 when RLS is used instead of LS and from 2.3 to 0.12 when MAP estimation is used instead of RLS.

4. CONCLUSION

We proposed an optimum estimation method in maximum a posteriori (MAP) sense for the estimation of oxygen tension values based on phosphorescence lifetime imaging. The method was motivated by the need to estimate oxygen tension values directly using the priors and measurements unlike the previous approaches that obtained oxygen tension values indirectly by estimating the model parameters. We

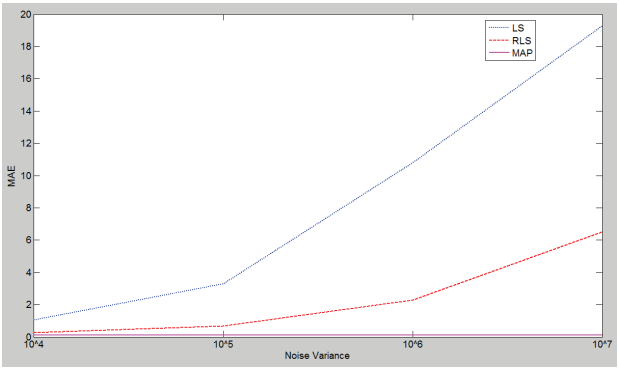


Figure 4: The mean absolute error (MAE) of the oxygen tension maps estimated by using the LS, RLS, and MAP methods.

tested the performance of the proposed method comprehensively by comparing it with the currently available methods.

It was shown that the proposed method produced improved estimates compared with the results of the existing approaches, which obtained oxygen tension values indirectly from the estimates of intermediate parameters. In the future work, the estimating of priors in our MAP estimation model will be investigated and the proposed method will be tested by applying it to the experimental data obtained from rat retinas.

5. REFERENCES

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