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Tasked-based quantification of measurement utility for *ex vivo* multi-spectral Mueller polarimetry of the uterine cervix

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Abstract: Significant contrast in visible wavelength Mueller matrix images for healthy and pre-cancerous regions of excised cervical tissue is shown. A novel classification algorithm is used to compute a test statistic from a small patient population.

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1. INTRODUCTION

Early detection through screening plays a major role in reducing the impact of cervical cancer on patients. In prior work a proof-of-concept study demonstrated significant contrast in Mueller polarimetric images acquired for healthy and pre-cancerous regions of excised cervical tissue [1]. To quantify the ability of this modality to differentiate between healthy and pre-cancerous tissue, polarimetric Mueller images of seventeen cervical specimens were compared to results from histopathology; excised tissue shown in Fig. 1. The sensitivity and specificity of the new polarimetric technique were calculated for images acquired at 450nm, 550nm, and 600nm, aiming to differentiate between high-grade cervical intraepithelial neoplasia (CIN 2-3) and healthy squamous epithelium. In this prior work an optimized value of 83% was achieved for both sensitivity and specificity for images acquired at 450nm and for a threshold scalar retardance value of 10.6.¹

In this work we aim to improve this detection performance by using a novel classification algorithm designed to compute quadratic classifiers from high-dimensional image data.² This J-optimal channelized quadratic observer (J-CQO) is an algorithm that can incorporate all polarimetric, spectral, and local spatial measurements into the classifier. Fig. 2 is a simple diagram of the algorithm. This detection problem is high dimension low sample size (HDLSS) since each pixel contains sixteen polarimetric and three spectral measurements and the classifier must be estimated from only seventeen patients. To form robust statistics the measurements are linearly combined; the novelty of the algorithm is computing the linear transform that is optimal for the detection task by using a non-linear manifold optimization. Detection performance will be compared among subsets of measurements that are down-sampled spectrally to test the usefulness of individual measurements. In this work the detection performance using only 600 nm measurements is very similar to using 450, 550, and 600nm wavelengths for the detection task.

Fig. 1: Masks overlay on 16 specimens: red (CIN 2-3), gray (healthy).

2. MATHEMATICAL METHODS

Consider the relationship between an image and an object as $\mathbf{g} = \mathcal{H}f + \mathbf{n}$. Here $\mathbf{g}$ is an $M \times 1$ vector of measurements made by an imaging system that is represented as a continuous-to-discrete operator $\mathcal{H}$. The measurements of the continuous object f are corrupted by measurement noise $\mathbf{n}$. We will consider post-processing signal detection. That is to say the forward imaging model $\mathcal{H}$ is fixed and can even be unknown since only the statistics of the image data $\mathbf{g}$ will be used. We are interested in linear combinations of the image data of the form $\mathbf{v} = \mathbf{T}\mathbf{g}$ where $\mathbf{T}$ is an $L \times M$ channel matrix and compression is achieved since $L < M$. Using terminology from the perception literature, each row of $\mathbf{T}$ is referred to as a channel and $\mathbf{v}$ is the channelized data.

Given a fixed set of L channels the optimal classifier will compute the channelized log-likelihood

$$\lambda(\mathbf{T}, \mathbf{g}) = \ln[p_1(\mathbf{T}\mathbf{g})] - \ln[p_2(\mathbf{T}\mathbf{g})] \quad (1)$$

and compare this decision variable λ to a threshold to sort the image data into one of two classes. For notational purposes the classes are denoted by $i = 1, 2$. This observer maximizes the area under the receiver operating characteristic (ROC) curve, otherwise known as the AUC, as well as other task based figures of merit (FOM). To measure detection performance of a classifier AUC is the gold standard FOM. In this work we assume the channelized likelihoods $p_i(\mathbf{T}\mathbf{g})$ are Gaussian. Since channelized data are weighted sums of the image data they may be at least approximately Gaussian distributed, as long as the image data are sufficiently independent, even if the original data are not.⁴ On top of the dimensionality reduction this is another critical benefit of channelized data. Under the normality assumption the log-likelihood ratio depends quadratically on the image data and is given by

$$\lambda_{CQO}(\mathbf{T}, \mathbf{g}) = Q_2(\mathbf{T}\mathbf{g}) - Q_1(\mathbf{T}\mathbf{g}) \quad (2)$$

where

$$Q_i(\mathbf{v}) = (\mathbf{v} - \mathbf{T}\mathbf{g}_i)^\dagger (\mathbf{T}\mathbf{K}_i\mathbf{T}^\dagger)^{-1} (\mathbf{v} - \mathbf{T}\mathbf{g}_i) \quad (3)$$

and the subscript stands for Channelized Quadratic Observer (CQO). Note that if $\mathbf{K}_1 = \mathbf{K}_2$ the observer reduces to a linear dependence on the image data and this observer is known as the Hotelling observer or linear Fisher discriminant. When the first- and second-order statistics of each class are different the relationship between the log likelihood ratio and the image data is quadratic; this is called a quadratic observer.

Fig. 3: AUC and J evaluated at channel matrix solutions versus iteration, these trends indicate J is a useful surrogate figure of merit for AUC.

Fig. 2: Diagram of J-CQO methodology. The novelty is computing an optimal linear transform (*i.e.* channels) using a figure of merit that trends with detection performance.

What solution for $\mathbf{T}$ is best for a quadratic observer? The J-CQO computes a channel matrix $\mathbf{T}$ that optimizes Jeffrey's divergence (J).³ When the means are equal (*i.e.* $\mathbf{g}_1 = \mathbf{g}_2$) but the covariances are different we presented a new result in:² that the same optimal $\mathbf{T}$ solution is achieved by maximizing the Bhattacharyya distance, J , or the AUC. Therefore, under this equal-mean condition, J is an exact surrogate figure of merit (SFOM) for ideal observer AUC, since J has the same optimum channel matrix and is much easier to compute. In this work we demonstrate J as a SFOM under more general conditions since this dataset of multi-wavelength polarimetric images differs in both first- and second-order statistics.

Note that the J -divergence is invariant under the replacement of $\mathbf{T}$ with $\mathbf{M}\mathbf{T}$, where $\mathbf{M}$ is an invertible $L \times L$ matrix. This means that J does not depend on the exact value of the channel matrix $\mathbf{T}$, just on the subspace spanned by the rows of $\mathbf{T}$.

A Grassmannian manifold parameterizes all L -dimensional linear subspaces of an M -dimensional vector space.⁵ Therefore J is a function on the Grassmannian manifold $\mathbf{Gr}(L, M)$ of L -dimensional subspaces in $\mathbb{R}^M$. To compute the channel matrix we populated $\mathbf{T}$ with random numbers as a starting solution and used the Matlab function `fmincon` with a user-supplied gradient. Fig. 3 is an example of J and AUC evaluated at the matrix $\mathbf{T}$ as a function of iteration. Both J and AUC increase with each iterate indicating empirically that J is an appropriate SFOM.

3. RESULTS

The area under the receiver operating characteristic curve (AUC) is computed to quantify J-CQO performance. To ensure an unbiased estimate of AUC statistical independence in each step of the computation is required. The 17 patients are divided into three non-overlapping groups: patient data to solve for the optimal linear transform, patient data to train the quadratic classifier (*i.e.* estimate $\mathbf{K}_i$ and $\mathbf{g}_i$ in Eq. 3), and patient data to test the performance of the J-CQO classifier (*i.e.* value of $\mathbf{v}$ in Eq. 3 is evaluated). These three non-overlapping groups form six unique combinations of testing and training which are reported as six colored ROC curves in Fig. 4 and AUC mean and $\pm$ one standard deviation are reported. The subplots in Fig. 4 are: (a) 450, 550, and 600 nm; (b) 450 nm only; (c) 550 nm only; (d) 600 nm only. Patient variability is a large source of uncertainty in the classifier. The standard deviation in AUC amongst these combinations ranges from 0.05 to 0.20 over different wavelengths. Fig. 4(d) shows that detection performance using only 600 nm measurements is very similar to Fig. 4(a) using all three wavelengths for the detection task. This analysis yields insights into measurement utility and informs future imaging protocols.

Fig. 4: Receiver operating characteristic (ROC) curves for (a) 450, 550, and 600 nm measurements, (b-d) is using only 450, 550, and 600; respectively. The different colored lines represent different selections of testing and training amongst patient population; AUC mean and $\pm$ one standard deviation are reported. The mean AUC values increases with increasing wavelength. Detection performance using only 600 nm measurements is very similar to using all three wavelengths for the detection task.

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