EXPLOITING DIFFUSE REFLECTANCE MEASUREMENT UNCERTAINTY ESTIMATES IN SPATIAL FREQUENCY DOMAIN IMAGING

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Spatial frequency domain imaging (SFDI) is a wide-field, noncontact diffuse optical imaging technique that has garnered significant interest for a variety of applications, including the monitoring of skin and breast lesions in clinical settings, and the progression of Alzheimer's disease and drug delivery to the brain in mouse models. In most applications, diffuse reflectance measurements are used to quantify the optical absorption and reduced scattering coefficients of the turbid medium, and with these, chromophore concentrations of interest are extracted (e.g., hemoglobin in tissue). However, uncertainties in estimated absorption and reduced scattering values are rarely reported, and we know of no method capable of providing such uncertainties when look-up table-based inversion algorithms are used to recover the optical properties. Quantifying these uncertainties would have several important benefits. For example, they could be propagated forward to yield uncertainties in estimated chromophore concentrations, which could have profound implications for the interpretation of experimental results. They could also be employed to help guide the selection of spatial frequencies used for SFDI measurements, given the requirements of the specific application.

In this work, we make two novel contributions. First, we show how knowledge of the accuracy of diffuse reflectance measurements from an SFDI instrument (i.e., diffuse reflectance uncertainty estimates) can be transformed to yield quantitative predictions of uncertainties for recovered absorption and reduced scattering values. Second, we use diffuse reflectance uncertainty estimates directly in a new algorithm for the recovery of optical properties. This algorithm performs equivalently to a standard look-up table-based approach but is up to ~200X faster (per pixel).

To transform diffuse reflectance uncertainty estimates into uncertainty estimates for the absorption and reduced scattering coefficients, we employ the Cramer-Rao bound (CRB). The CRB is a lower bound that defines the best achievable precision (i.e., lowest variance) of any unbiased estimator for a given data model. It is often used in the statistical signal processing community, especially in the sonar and radar signal processing communities, to perform feasibility studies and system design. We calculate the CRBs for the absorption and reduced scattering coefficients and use them as our estimates of uncertainties for these parameters. We show that these estimates agree with results from Monte Carlo simulations to better than 0.1% for the common scenario where optical properties are computed with a look-up table using two spatial frequencies. We validate our simulations with tissue-mimicking phantom experiments and *in vivo* measurements on a human volunteer. This method of generating uncertainty estimates opens the door to several exciting possibilities. For example, the analytical form of the CRB calculation can be exploited to quickly generate "maps" of uncertainty estimates as a function of optical properties and spatial frequencies, thereby providing a tool that can be used to efficiently explore this trade space. The CRB-derived uncertainty estimates can also be propagated into chromophore uncertainty estimates. With knowledge of the spatial frequencies and wavelengths used for a given application, it is possible to pre-compute look-up tables of optical property and/or chromophore uncertainty estimates, which would be a significant advantage for applications requiring real-time performance.

Diffuse reflectance uncertainty estimates can also be used to speed up optical property recovery with no performance penalty. We have developed a new algorithm to do this that in simulation performs equivalently to a standard look-up table-based approach employing linear interpolation but is up to ~200X faster (per pixel).