

REDEFINING SPECTRAL UNMIXING FOR IN-VIVO BRAIN TISSUE ANALYSIS FROM HYPERSPECTRAL IMAGING

Hey Cynthia, have you heard of spectral unmixing?

A method to extract molecular composition of tissue from spectral measurements.

So I am not sure, but it seems I figured out how to make non-linear unmixing work...

Hah?!

Sounds very interesting! Do tell me more, Brunhilde...

Well... Excuse me, but, who the hell you are?

That's first. And second, the standard non-linear unmixing based on kernel methods is highly ill-posed, has no closed-form solution, and it can be sensitive to noise.

Pshhhh...



Hello ladies, I hear you wanna do some non-linear unmixing? How about the one based on kernel methods?



So, Bruni, where are we?

Hmm... So true...

The nature around us is highly non-linear. I fully agree. But how do you plan to address the limitations of non-linear solvers?

You know... I just thought one day that even though it is substantially simpler to solve the linear system compared to non-linear counterparts, the physical reality of the light-matter interaction can be far from linear.

We often resort to linear systems, but the use of linear descriptions can distance us from accurate molecular predictions...

It sounds appealing... In words... But do you have any theoretical support for it?

I designed a procedure to implicitly include the nonlinear character of light-matter interaction into the linear unmixing. Essentially, we can do this by redefining the unmixing problem via introduction of pseudo-endmembers extracted from Monte-Carlo simulations of light-matter interaction.

Sure thing... Look right here

So the effect of incoming light on the tissue can be mathematically described using the Beer-Lambert law (BLL):

$$I_R(\lambda) = I_0(\lambda)e^{-(\mu_a(\lambda)+\mu_s(\lambda))l}$$

Here, $I_0(\lambda)$ represents the intensity of the incident light, while $I_R(\lambda)$ is the intensity of the reflected light detected by the camera. The terms $\mu_a(\lambda)$ and $\mu_s(\lambda)$ correspond to the absorption and scattering coefficients, respectively. λ denotes the wavelength, and l is the optical pathlength. The absorption coefficient $\mu_a(\lambda)$ is, in the simplest case, defined as a linear sum over absorption characteristic of the considered tissue molecules, weighted by a molecular concentration c_i , ($\sum c_i \mu_a^i$). And we can actually rewrite it in a matrix form:

$$I_A = -\frac{1}{l} \ln \frac{I_R(\lambda)}{I_0(\lambda)} = M\alpha$$

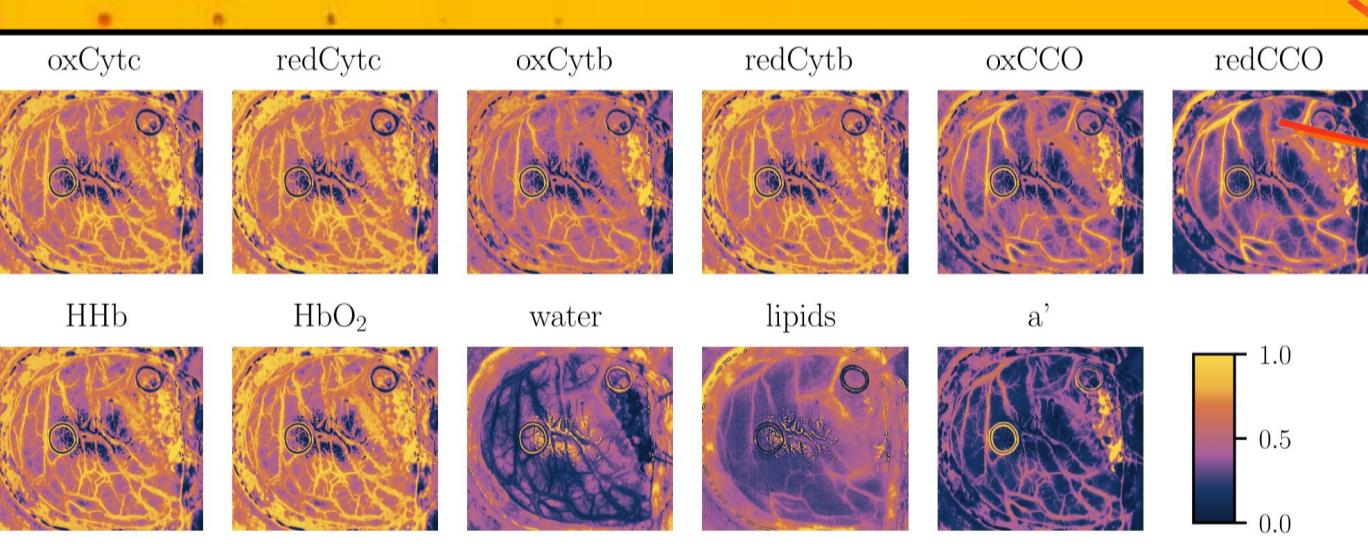
Here, M is a matrix of absorption and scattering spectra, and α is a vector of weights (a , and a - the scattering weight). Now let $I_A = I_A(c, a)$ be the light attenuation obtained using the nonlinear model. The partial derivative of I_A with respect to the concentration c , can be approximated by

$$\frac{\partial I_A}{\partial c_i} \approx \frac{1}{\Delta c_i} [I_A(c_1 + \Delta c_1, c_2, \dots, c_n, a) - I_A(c_1, c_2, \dots, c_n, a)] = m'_i$$

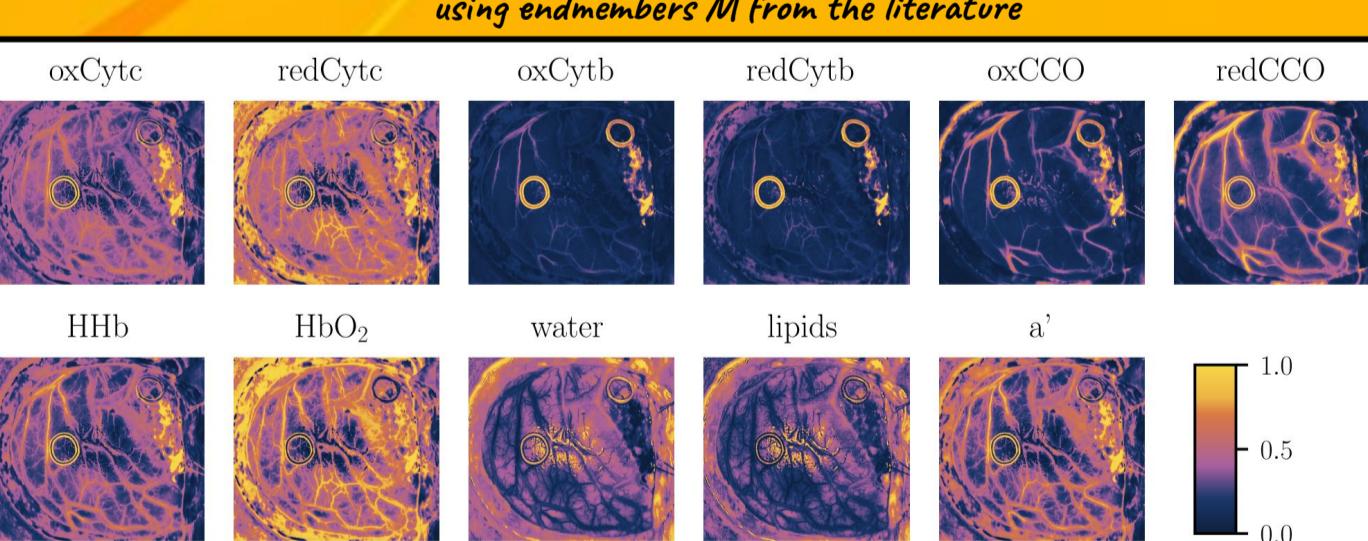
The gradient of I_A with respect to the whole concentration vector c (and similarly for the scattering weight a) can therefore be approximated by

$$\frac{\partial I_A}{\partial c}^T \approx [m'_1, m'_2, \dots, m'_n]$$

and thus, in the first approximation, the partial derivatives can be interpreted as endmembers for the following linear model: $\Delta I_A = M\Delta p$ where $\Delta I_A = I_A - I_A^{ref}$ is the relative spectrum with respect to a reference spectrum I_A^{ref} with fixed endmember abundances, $M' = [m'_1, m'_2, \dots, m'_n, m'_{scat}]$, and $\Delta p = [\Delta c_1, \Delta c_2, \dots, \Delta c_n, \Delta a]$ is the unknown differential abundance vector. In simple terms, our approach implies, first, computing the change of light attenuation upon the change of abundance of a particular endmember according to a realistic non-linear model. After computing it individually for every endmember, we then use these changes of attenuation $m'_i = \partial I_A / \partial p_i$, to define a new set of pseudo-endmembers M' .



Inferred molecular maps for different brain tissue relevant molecules using endmembers M from the literature



Inferred molecular maps for different brain tissue relevant molecules using pseudo-endmembers M' from the literature



It seems so... Both qualitatively, when I compare inferred molecular maps for unmixing with and without the pseudo-endmembers; and quantitatively, when I use the maps as an additional channel for a downstream segmentation task.

Uhhh... That's quite mathy... But let's assume I got it. Does it work actually in practice?

That sounds awesome! I see you analysed brain tissue hyperspectral images. Do you think it can generalize to other spectral data and living tissues?

Good question... So by using pseudo-endmembers derived from Monte Carlo simulations, my method enhances molecular biomarker extraction and, as a result, improves the classification of brain tissue types. However, I used a general Monte Carlo simulator of light propagation in matter, and the methodology is applicable to other complex simulators. I thus envision that the wider optics research community will adopt this methodology and identify non-linear simulators providing more refined representation of light-matter interaction across various spectral data.

Hmm... Not sure... Weak reject!



Designed by anonymous authors from Technical University Munich, Freepik, and the newly elected Fellow of the UK Royal Society

Table 1: Mean and standard deviation of performance metrics (accuracy, precision, recall, specificity and F1 score) over test images across five folds.

Normal tissue (NT)				Tumor tissue (TT)			
BL	HM	OHM	NMC	BL	HM	OHM	NMC
Acc. 0.89 \pm 0.04	0.92 \pm 0.04	0.90 \pm 0.02	0.91 \pm 0.05	0.92 \pm 0.02	0.93 \pm 0.02	0.92 \pm 0.03	0.91 \pm 0.03
Prec. 0.82 \pm 0.09	0.89 \pm 0.01	0.85 \pm 0.08	0.87 \pm 0.11	0.51 \pm 0.22	0.52 \pm 0.26	0.38 \pm 0.26	0.41 \pm 0.27
Rec. 0.94 \pm 0.03	0.93 \pm 0.03	0.91 \pm 0.03	0.90 \pm 0.1	0.32 \pm 0.17	0.35 \pm 0.21	0.17 \pm 0.12	0.32 \pm 0.24
Spec. 0.87 \pm 0.06	0.93 \pm 0.06	0.90 \pm 0.05	0.92 \pm 0.06	0.98 \pm 0.01	0.98 \pm 0.01	0.99 \pm 0.02	0.97 \pm 0.04
F1 0.85 \pm 0.06	0.90 \pm 0.05	0.86 \pm 0.03	0.87 \pm 0.09	0.34 \pm 0.13	0.37 \pm 0.20	0.22 \pm 0.12	0.33 \pm 0.23
Blood vessels (BV)				Background (BG)			
BL	HM	OHM	NMC	BL	HM	OHM	NMC
Acc. 0.96 \pm 0.01	0.95 \pm 0.01	0.95 \pm 0.01	0.96 \pm 0.02	0.91 \pm 0.03	0.93 \pm 0.04	0.93 \pm 0.03	0.93 \pm 0.03
Prec. 0.80 \pm 0.10	0.80 \pm 0.18	0.86 \pm 0.18	0.82 \pm 0.16	0.97 \pm 0.03	0.96 \pm 0.04	0.94 \pm 0.07	0.95 \pm 0.05
Rec. 0.83 \pm 0.09	0.87 \pm 0.05	0.83 \pm 0.10	0.85 \pm 0.07	0.82 \pm 0.07	0.88 \pm 0.05	0.87 \pm 0.08	0.86 \pm 0.08
Spec. 0.98 \pm 0.01	0.96 \pm 0.01	0.97 \pm 0.02	0.97 \pm 0.01	0.97 \pm 0.03	0.96 \pm 0.03	0.95 \pm 0.02	0.95 \pm 0.02
F1 0.79 \pm 0.08	0.80 \pm 0.12	0.80 \pm 0.09	0.80 \pm 0.10	0.86 \pm 0.04	0.89 \pm 0.04	0.88 \pm 0.06	0.88 \pm 0.04

Some numbers...

