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Abstract

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Abstract

Extracting pathology information embedded within surface optical properties in Spatial Frequency Domain Imaging (SFDI) datasets is still a rather cumbersome nonlinear translation problem, mainly constrained by intrasample and interpatient variability, as well as dataset size. The β -variational autoencoder (β -VAE) is a rather novel dimensionality reduction technique where a tractable set of latent low-dimensional embeddings can be obtained from a given dataset. These embeddings can then be sampled to synthesize new data, providing further insight into pathology variability as well as differentiability in terms of optical properties. Its applications for data classification and breast margin delineation are also discussed.

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Deep variational autoencoders for breast cancer tissue modeling and synthesis in SFDI

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ABSTRACT

Extracting pathology information embedded within surface optical properties in Spatial Frequency Domain Imaging (SFDI) datasets is still a rather cumbersome nonlinear translation problem, mainly constrained by intrasample and interpatient variability, as well as dataset size. The β -variational autoencoder (β -VAE) is a rather novel dimensionality reduction technique where a tractable set of latent low-dimensional embeddings can be obtained from a given dataset. These embeddings can then be sampled to synthesize new data, providing further insight into pathology variability as well as differentiability in terms of optical properties. Its applications for data classification and breast margin delineation are also discussed.

Keywords: Deep learning, modulated imaging, optical properties, spatial frequency domain imaging, breast cancer, variational autoencoder, turbid media

1. INTRODUCTION

Modulated imaging, i.e. the estimation of surface absorption and scattering properties of turbid media via pattern projection, is an already mature imaging technique in the field of Biomedical Optics. Modulation Transfer Function (MTF) data can be obtained through a series of simple demodulation algorithms and it can provide information with notable molecular and structural specificity.¹ These well-known procedures have been evaluated on biological tissue samples in the past five years, with significant results.² Obtaining some relationship between tissue pathology and surface (and subsurface) optical properties would then be ideal, allowing the use of standardized numerical margin delineation algorithms. There are, unfortunately, a few caveats to this next step. First, it is still unclear whether molecular or structural properties provide more information on tissue pathology. Second, local structure as well as polarization properties seem to be relevant as well. Third, and last, is the current lack of large SFDI pathology datasets, despite current efforts, that could be sufficient for deep learning implementations. Solving this problem requires finding a nonlinear dimensionality reduction method that can find a low-dimensionality embedding or feature space, under the hypothesis that different pathologies will have different optical properties. The β -variational autoencoder (β -VAE) is a non-linear system based on the implementation of variational Bayes probability estimation through neural networks.³ This algorithm can be introduced in any signal processing pipeline and, through random sampling, synthesized data can be obtained and exploited for further deep learning applications. To the authors' knowledge, this work describes the first application of a β -VAE on SFDI data.

2. MATERIALS AND METHODS

Spatial frequency domain imaging dataset The dataset consists of a total of 62 resected breast tissue samples, imaged at the Thayer School of Engineering at Dartmouth College, with custom-built imaging equipment, following standard protocol.² Each SFDI image is a $1024 \times 1024 \times 4 \times 4$ tensor, namely 1024×1024 pixel measurements at four wavelengths ($\lambda = 490.0, 550.0, 600.0$, and 700.0 nm) and four spatial frequencies

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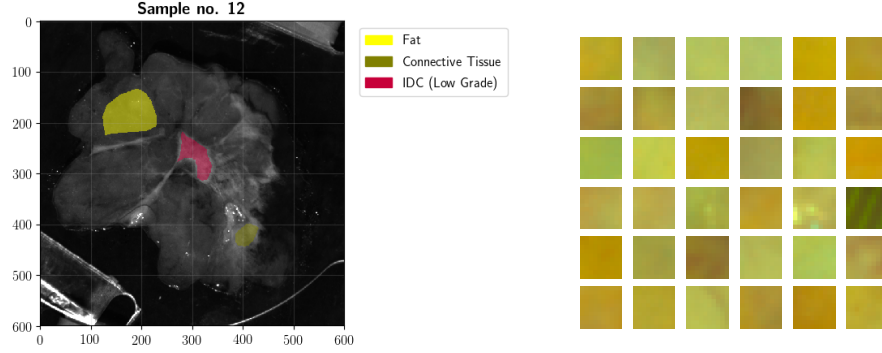


Figure 1. Example spatial frequency domain image of Sample 12 (left), as well as some color-reconstructed, randomly selected patches from the complete dataset (right), corresponding to different tissue categories. RGB patches are extracted from spectra via CIE 1931 color matching functions (CMFs) from the sample's multispectral data, i.e. $R(f_x, \lambda)$ with $f_x = 0.0 \text{ mm}^{-1}$.

($f_x = 0.0, 0.15, 0.61$, and 1.37 mm^{-1}). Each sample contains a set of 15 binary masks, corresponding to benign, malignant, and normal tissue regions of interest (ROIs), histologically cross-referenced, described and labeled by a pathologist. In order to generate a statistically significant population of patches, random coordinates within the ROI of each sample were generated. A subset of these points were randomly selected to produce a dataset with 20×10^3 patches. The dimensions of these patches are 10×10 pixels in space, with their corresponding spatial and spectral properties per pixel.

β -Variational Autoencoder (β -VAE) A variational autoencoder (VAE) can be understood as a nonlinear dimensionality reduction method, where an input vector $x \in \mathbb{R}^n$ is forced to be reconstructed through a symmetrical neural network with a bottleneck at its middle, namely layer $z \in \mathbb{R}^m$, $m \ll n$. The result of this operation is a reconstruction, $\hat{x} \in \mathbb{R}^n$. While a standard autoencoder simply attempts to minimize the reconstruction error $\frac{1}{2}\|x - \hat{x}\|^2$, a VAE also forces the distribution of latent feature space z to resemble a multivariate Gaussian normal distribution $\mathcal{N}(0, I)$. This is achieved by applying the loss function $l_i(\theta, \phi) = \frac{1}{2}\|x_i - \hat{x}_i\|^2 + \mathcal{D}[q_\theta(z|x_i) \|\mathcal{N}(0, I)]$, where θ are the parameters of the encoder $q_\theta(z|x_i) : x_i \rightarrow z_i$, ϕ represents the parameters of the decoder $p_\phi(x_i|z) : z_i \rightarrow \hat{x}_i$, and $\mathcal{D}[q \|\mathcal{N}(0, I)]$ is the Kullback-Leibler distance between the distribution of the latent space and that of a multivariate normal Gaussian distribution.³ This additional constraint forces the feature space to be centered around 0 and have unit variance across all its dimensions, while at the same time obtaining sufficiently good reconstruction. In a β -VAE, hyperparameter $\beta \in \mathbb{R}^+$ simply multiplies the Kullback-Leibler distance in the loss function, therefore establishing a tradeoff between reconstruction quality and latent space Gaussianity.⁴ Once the loss function has been minimized up to the capacity of the neural network, synthesis can take place by providing a point in feature (or pathology) space, namely z_0 , to the neural network's bottleneck. The decoder will generate a representation $\hat{x}(z_0)$ from feature (pathology) space and synthesize a patch of tissue with its corresponding properties.

3. RESULTS

After a total of 10^6 epochs, the VAE is considered to have converged to its optimum and can be dissected into an encoder and a decoder (4×200 tanh units each). The encoder translates any SFDI patch given spectral, spatial frequency and inherent textural properties into a *latent* or *feature* space, where pathology can be differentiated (Figure 2, left). With the given dataset we can assess differentiability between benign tissue (in shades of green), malignant tissue (in red and grey), and adipose tissue (in yellow), with 2 latent space dimensions (z_1 and z_2 ; more dimensions will provide better representations). Feature/pathology space, given its Gaussian properties, will be sufficiently sampled by a uniform grid in the range $[-4, 4] \times [-4, 4]$. The result of synthesizing patches for a uniform grid of 40×40 points in feature space is displayed in Figure 2 (right). In other words, each of the 1600 squares in the plot is a color reconstruction of the reflectance properties of a patch tissue with pathology-space coordinates (z_1, z_2). Synthesis can be performed for all other spatial frequencies as well (Figure 3), showing a visually significant variation in tissue frequency response as a function of pathology. Applying β -VAE has certain potential not only on machine translation of optical properties into understandable pathology spaces, but also

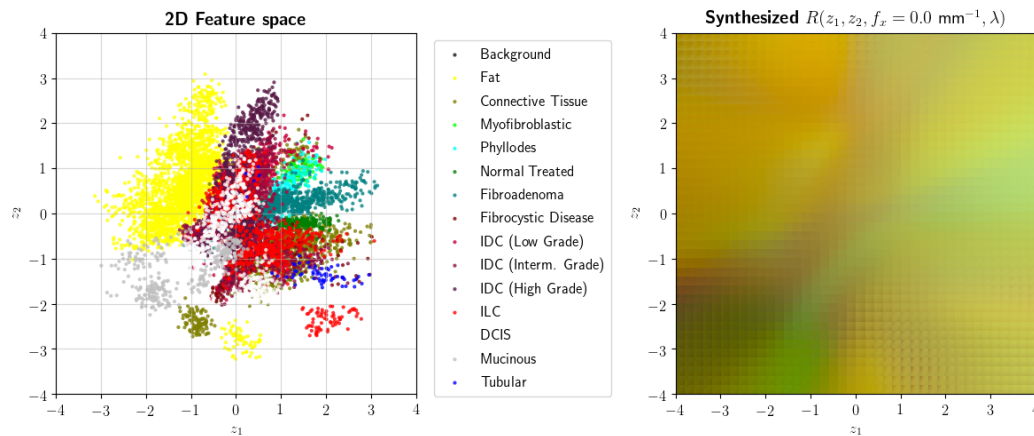


Figure 2. General overview of training results for a 2-dimensional feature latent space. The left scatter plot represents every labeled patch as a point in feature space. Color indicates the type of pathology specified in its corresponding ROI. On the right subplot, this feature space is sampled in a uniform 40×40 grid, synthesizing all possible DC reflectance values for breast tissue. Note both plots have the same frame of reference, i.e. feature space. Patch color is obtained via CIE 1931 CMFs.

in training deep learning algorithms –as well as traditional machine learning methods– for breast margin tumor delineation, as well as quantification of optical properties. These applications will be discussed as well.

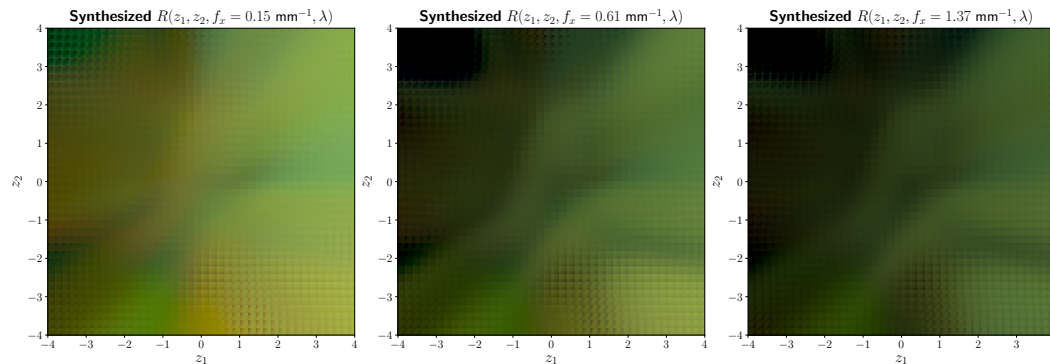


Figure 3. Left to right, 1600 synthesized patches for three spatial frequencies: $f_x = 0.15$, 0.61 , and 1.37 mm^{-1} . As expected, different pathologies respond differently to modulated light.

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