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Comparison of experimental vs simulated data to train neural networks for speckle imaging data analysis.

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ABSTRACT

Multiple Laser Speckle contrast Imaging (MESI) is an imaging method that provides relative blood flow maps from the statistical analysis of the dynamic speckle patterns observed when a coherent source is used to illuminate a tissue that contains moving scatterers. The gold standard analysis of MESI data is done by pixelwise regression of the experimental images to a theoretical function of the contrast K as a function of the exposure time T and decorrelation time τ_c . This approach is computer intensive, and the duration required to obtain a single flow map is too long for "real-time" analysis of in vivo hemodynamics. In addition, the mathematical model used relies on assumptions that oversimplify the local flow within the object of study. We have evaluated as an alternative a method based on Convolutional Neural Networks (CNN) to directly infer blood flow maps from MESI data, bypassing the model based fitting procedure. The CNN approach is model-free and delivers blood flow maps several orders of magnitude faster than the classical pixelwise non-linear regression. Here, we have evaluated two different datasets of annotated speckle contrast images to train the neural networks. One is composed of simulated time integrated speckle while the other one is composed of experimental data acquired for microfluidic channels with controlled geometries and flows. The study aims at discussing the assets and limits of both approaches.

Keywords: Laser Speckle Contrast Imaging, blood flow, multiple exposure, Convolutional Neural Network, microfluidics flow phantoms, speckle patterns simulations

1. INTRODUCTION

Laser speckle imaging (LSI) has been used in the past decades to image the blood flow at the surface of tissues either in preclinical or clinical applications^{1,2}. Light from a laser diode is used to illuminate biological tissues and the backscattered light is recorded by a camera, providing an image of a interferometric pattern called speckle. When the object under illumination contains moving scatterers, the speckle pattern changes with time. Acquiring images of this time-varying patterns at a given exposure time leads to a blur, that is related to the rate of change of the pattern. To quantify the blur, LSI relies on the computation of the local speckle contrast K , which is defined as the local standard deviation divided by the local mean of the pixel's intensities. It has been shown that K is related to the decorrelation time τ_c of the moving scatterers, which in turn is inversely proportional to the velocities of the scatterers¹. Multiple exposure speckle imaging (MESI) is a significantly improved variant of LSI. It consists in acquiring sequentially images at increasing exposure times and rely on a model of $K(T, \tau_c)$ that includes the relative contribution of the static scatterers³. MESI was demonstrated to better account for the static scatterers contribution thus increasing the ability of the technique to estimate accurate changes of the flow over a wider range of flows⁴. However, MESI requires a more complex instrumentation to modulate the laser in both time and amplitude and the analysis is based on computer-intensive pixelwise non-linear fitting of the MESI-model to the data. This approach suffers from several flaws. First, the method is incompatible with short analysis times required by clinical protocols. Indeed, processing the MESI data acquired during a dynamic reperfusion protocol such as a post occlusive reactive hyperemia test at high spatial resolution would require at least several minutes. Second, the underlying mathematical MESI model is based on strong assumptions on the nature of the flow (ordered, unordered) and on the number of scattering events the detected photons (single, multiple). These assumptions cannot be verified *a priori* and it was shown experimentally in mice that in biological tissues, there exists a mix of flow regimes locally⁵. To

overcome these issues, the use of machine learning has been proposed for fast, model-free MESI data analysis. The rationale is to bypass the non-linear fitting by using a neural network to directly infer the relative flow maps from MESI data^{6,7}. The developed neural networks have been trained in a supervised manner using either simulated data or calibrated experimental data. Simulated data are fully characterized by nature and allow to consider many configurations. However, some experimental aspects are particularly difficult to simulate accurately because they are not known or well described. Contrarily, experimental data incorporate all instrumental aspects but are necessarily limited in terms of geometries and flows to few configurations. We investigate in this study the assets and drawbacks of each training method of CNN dedicated to MESI analysis.

2. METHODS MESI IMAGER AND MICROFLUIDIC EXPERIMENTAL DATA

The MESI imaging system is composed of a 634 nm laser diode (Shanghai laser, China) with a maximum output power of 400 mW and sCMOS camera (Orca Flash Hamamatsu, Japan). MESI data are acquired in the synthetic exposure approach with careful subtraction of noise contributions⁸. The microfluidic channels and set-up were described in detail previously⁹. Speckle images used to train the network were recorded for microfluidic channels with a rectangular section of 40,60,80,100, 300 and 500 μm of widths and 75 μm of length¹⁰. The exposure times were set to 1, 2, 3, 5, 10, 15, 25, 50 ms. We used 2% intralipid as the flowing media. Flows from 1 $\mu\text{l}\cdot\text{min}^{-1}$ up to 7 $\mu\text{l}\cdot\text{min}^{-1}$ (corresponding to velocities between 0.05 and 20 $\text{mm}\cdot\text{s}^{-1}$) were controlled using a pressure controller (Fluigent, France). An inline flowmeter allowed to assess the real flow in the channels and provide feedback to the controller, ensuring highly stable and controlled flows. A database of experimental speckle contrast for different channels, flow and exposure times was built. For supervised learning, target images of local velocities were associated to each experimental image based on the measurement of the average flow in the channel during the experiment and the Poiseuille's law⁷.

Simulated time integrated speckle data.

We have simulated time integrated speckle patterns and the corresponding speckle contrast images for the same configuration as the experimental data. The simulation parameters are the decorrelation time of the scatterers, the exposure times considered, the dimensions of the channel. The decorrelation times were set according to previous calibration of data analyzed with the non-linear fitting approach. In such, we could associate for each flow value in each channel a decorrelation time. In the channel, the media was supposed to be purely dynamic (no static scatterers) while outside the channels it was supposed to be entirely static. On the basis of direct *in vivo* experimental measurements of the decorrelation functions in mice brain¹¹, the flow regime was assumed to be either unordered, with single scattering or ordered with multiple scattering, both resulting in the same decorrelation function $g_1(t)$. To match the experimental database, the number of pixels per speckle was set to 3. For both the experimental and simulated data an augmentation approach has been implemented, by rotating the data at different angles to avoid biasing the training if the vessel had always the same positioning within the annotated images.

3. RESULTS

The two types of speckle contrast databases obtained are illustrated on figure 1. Regarding the experimental data, some potential biases have been observed, such as reflection effects on the side of the channel leading to a "ghost channel" in the contrast image. In addition, some data could not be recorded for the smallest channel due to instrumental limitations. Indeed, it was not possible to record a stable flow in the 40 μm wide channel for the flows above 4 $\mu\text{l}/\text{min}^{-1}$. In addition, complementary experiments have shown the effect on the speckle contrast of instrument parameters such as the optical zoom used during the acquisitions. For the same flow in the same channel, changing the zoom modifies the depth of field and ultimately the corresponding speckle contrast values. Regarding the simulations, we simulated time integrated speckle contrast images with similar dimensions as the experimental ones (1920x1440 pixels). This process is computer intensive as millions of random numbers must be sampled and processed. On a standard computer, it took about 2 hours to simulate the time integrated patterns for all exposure times for one flow in one channel. For the same configuration, the simulated

data present systematically lower contrast values compared to experimental ones. It is likely that the experimental data capture more variability of the signal due to instrumental noises and instabilities.

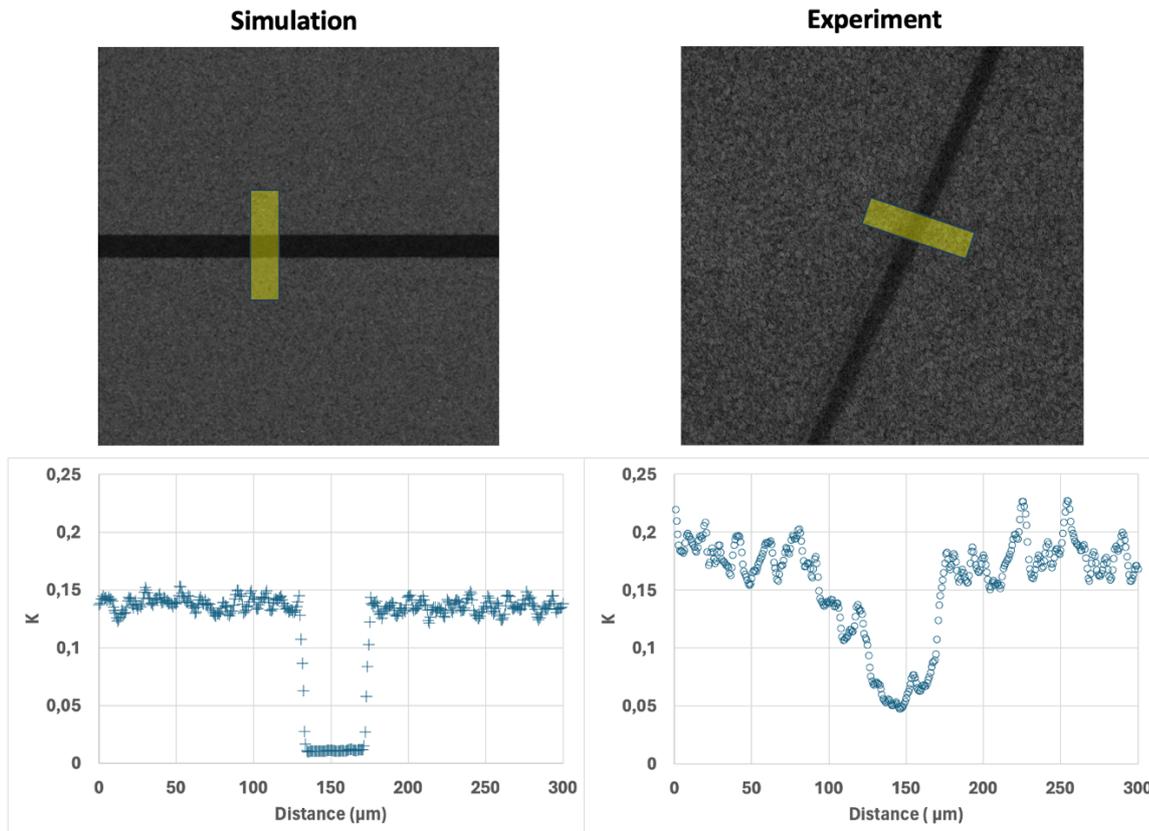


Figure 1. Comparison of simulated and experimental data for a 40 μm wide channel, an exposure time of 5 ms and laminar flow of 1 $\mu\text{l}\cdot\text{min}^{-1}$. Regions of interest in yellow on the images on top were used to plot corresponding profiles on the bottom.

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