CONVOLUTIONAL NEURAL NETWORKS FOR FCS DATA FITTING

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KEY WORDS: FCS, Autocorrelation, Diffusion, CNN, Machine learning

Fluorescence Correlation Spectroscopy (FCS) utilizes the fluctuations of intensities to measure the dynamics of fluorescent particles of interest through spatial and temporal statistical analysis [1]. An intensity trace is recorded over long time scales to obtain sufficiently robust statistics, and correlated at a semi-logarithmic timescale to obtain an autocorrelation function (ACF) corresponding to the observed region. By fitting the ACF to a model function using least-squares fitting, we can parametrize particle dynamics. The use of a mechanistic human-designed model function motivates our exploration of supervised machine learning approaches, specifically neural networks. The universal approximation theorem shows that multilayer feedforward neural networks are capable of approximating any function given sufficient hidden units and an appropriate activation function [2]. In recent years, convolutional neural networks (CNNs) have been successfully applied to biologically-relevant problems, notably medical image segmentation [3] and protein structure prediction [4]. The key strength of CNNs is feature extraction, where consecutive layers learn progressively more abstract features. As the CNN model is trained through gradient backpropagation from the output, weights within each layer are tuned to minimize the error between the model output and the ground truth, corresponding to the learning of underlying features of our function. In this work, we train a convolutional neural network to predict diffusion coefficients using simulations of freely diffusing particles. We show that a simple CNN architecture manages to outperform least-squares fitting on simulated datasets. We then compare the CNN model performance to least-squares fitting on real plasma membrane measurements, and show that the CNN performs comparably. Finally, we show that a CNN trained with a large gap in the training set can still interpolate to ranges between the two extremes, indicating the generalizability of the CNN model.

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