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A generative deep learning approach for super-resolution microscopy

Super-Resolution Microscopy (SRM) surpasses the diffraction limit imposed by Abbe's law, enabling nanoscale cellular observation. Despite the improved resolution, SRM techniques suffer from long acquisition times. This is especially true for Single Molecule Localization Microscopy (SLML) techniques, such as Stochastic Optical Reconstruction Microscopy (STORM). To address this constraint, this study explores the use of the Enhanced Super-Resolution Generative Adversarial Network (ESRGAN) for super-resolution (SR) image reconstruction from low-resolution ones.
This approach is translated to microscopy imaging, aiming to generate SR images from widefield images, which can be acquired in a sensible shorter time.
The proposed procedure has been implemented in fluorescence microscopy imaging of subcellular tubulin filaments.

The ultimate goal is to enable improved measures of FLASH radiotherapy-induced effects, which is among the scientific goals of the PNRR THE project.
The available datasets to train and test the ESRGAN model were acquired at the Advanced Microscopy and Nanoscopy Laboratory of the Physics Department of Pisa University. It consists of 8-bit RGB image pairs (low and high resolution), stored in the Portable Network Graphics (PNG). They are classified by the specific protein employed and a quality score based on noise level and sharpness of tubulin filaments.

Due to limited datasets, different models were trained by means of transfer learning techniques, leveraging progressive fine-tuning in a step-wise fashion. The network in use is an example of a very deep structure, consisting of approximately 400 layers, totaling nearly 38 million trainable parameters. Around 30 different training sessions were conducted for this study, each with average execution times ranging between 30 and 120 hours, along with numerous performance validation tests. The entire work was carried out using the computational resources provided by the Computing Center of the Pisa Section of INFN, specifically employing 6x 10 cores Intel Xeon E5-2640v4 @2.40 GHz, 1x NVIDIA Tesla V100 with 16/32 Gb VRAM and 64 Gb RAM. Further developments of this work will involve the use of multiple GPUs, leveraging the potential of parallel computing to further reduce training execution times.
The results obtained prove that such a deep learning approach is suitable for microscopy imaging, demonstrating potential both in accelerating cellular analysis and improving the performances of conventional fluorescence microscopy towards super-resolution capabilities.

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