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3D single-molecule detection using CNNs and semiconductor nanowires

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Semiconductor nanowires are successfully used as a biosensing substrate due to their ability to enhance the fluorescence of bound fluorescently labeled molecules. This enhancement, which combines excitation, quantum yield, and collection enhancement, is influenced by nanowire diameter, refractive index, and the wavelength of the bound fluorophore. Combined with a large surface-to-volume ratio and high throughput in the field of view, nanowires allow the quantification of molecular concentrations as low as 100 fM and the observation of single-molecular binding processes over time [1, 2]. However, information about a bound molecule's position along the nanowires'z-axis has not been available to date.

Here we extend the capabilities of nanowire-based single-molecule detection to include information about the molecule's position along the z-axis. For this purpose, we utilize the image formation asymmetries observed for fluorophore emission wavelengths where fluorescence enhancement is sigificant and depend on the fluorophore binding position (fig 1b). We used numerical solutions of Maxwell's equations to simulate fluorophore excitation and emission enhancement by nanowires, followed by image creation [3] (fig. 1 a-c). These axial position-dependent images were then used to train convolutional neural networks to predict the binding position with 50 nm step-size. The ability to simulate images for specific nanowires and microscopes enables these trained networks to be applied to real microscopy images. High prediction accuracies suggest that more advanced neural networks can be implemented to track single-molecules' motion along the nanowire axis, and even opening a possibility to track the full molecular motion in three dimensions.

Our results indicate that waveguiding semiconductor nanowires can detect single-molecules in 3D, allowing the investigation of molecular processes such as the diffusion of a single molecule or molecular motor movements with simple widefield microscopy without any modifications in experimental setup.

Image simulation pipeline (image)

1 D. Verardo et al, "Nanomaterials," 11(1), 227 (2021).
[2] J. Valderas-Gutiérrez, et al, ACS Appl. Nano Mater. 5, 9063–9071(2022)
[3] N. Anttu, 2024. doi: https://doi.org/10.48550/arXiv.2403.16537.

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