Label-free nanoscale optical metrology on myelinated axons *in vivo*

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1. Abstract

In the mammalian nervous system, myelin provides electrical insulation for the neural circuit by forming a highly organized, multilayered thin-film around the axon fibers. Here, we investigate the spectral reflectance from this subcellular nanostructure and devise a new label-free technique based on a spectroscopic analysis of reflected light, enabling nanoscale imaging of myelinated axons in their natural living state. Using this technique, we demonstrate 3-dimensional mapping of the axon diameter and sensing of dynamic changes in the substructure of myelin at nanoscale. We further reveal the prevalence of axon bulging in the brain cortex *in vivo* after mild compressive trauma. Our novel tool opens new avenues of investigation by creating unprecedented access to the nanostructural dynamics of live myelinated axons in health and disease.

2. Representative result

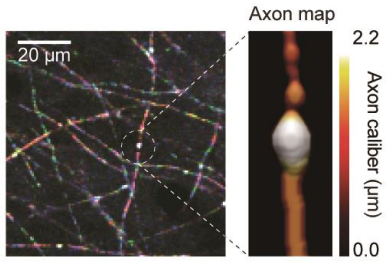

Figure 1: Traumatic brain injury imaged by SpeRe

We report that spectroscopic analysis of broadband light reflection from myelinated axons provides quantitative examination of the multilayered cytoarchitecutre at nanoscale precision [1]. The physical principle of this technique is based on spectral reflectometry (SpeRe), which is widely used in the state-of-the-art semiconductor industry to measure layer thicknesses of a multi-film stack with sub-nanometer accuracy [1]. By adopting and optimizing this technique to mammalian axons, we demonstrate label-free myelinated axon imaging at nanoscale precision and 3-dimensional the axon diameter map. We further conduct live measurements of nanoscale dynamics in myelinated axons in response to physiologic osmotic modulation and mechanical injury.

References

[1] Kwon J. Label-free nanoscale optical metrology on myelinated axons *in vivo*. Nat. Commun. 2017; 8(1): 1832.