

## P1 – Tracing Carbon Nanotube Uptake and Transport Inside Living Cells With Combined Fluorescence and Atomic Force Microscopy

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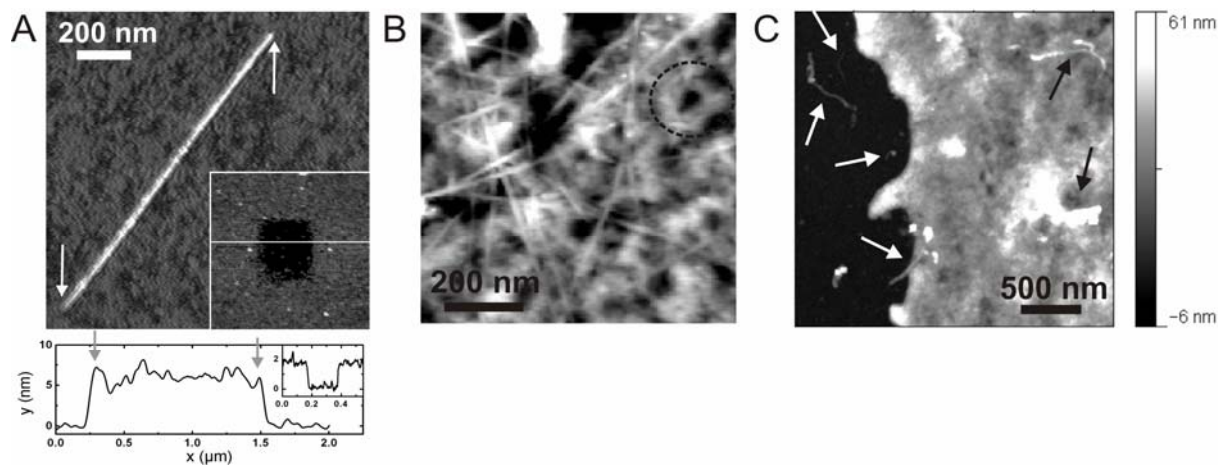
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Carbon nanotubes (CNTs) are considered to be promising for biomedical applications as their nano-size gives them access into various cellular compartments including the nucleus. They could be used for biosensing or act as multi-functional carrier systems for therapy and diagnosis at the cellular level. Functionalization of CNTs with biomolecules facilitates internalization into the cell. However, the exact uptake mechanism remains a controversial issue as it may well depend on cell type, bio-functionalization scheme, size of the nanotube and other factors. Cellular uptake of CNTs is commonly addressed with fluorescence microscopy but a direct and label free detection of CNT uptake is challenging. At present, atomic force microscopy (AFM) offers a unique solution to study biological specimens under (near-) physiological conditions without the need for rigorous sample preparation or labelling. We expect significant bio-physical insights into the delivery process and transport mechanism of CNTs in cells by employing the AFM in combination with fluorescence microscopy to study the internalization of differently bio-functionalized CNTs into living cells.

Here we present AFM as a useful tool for a simple and direct assessment of CNT surface bio-functionalization [1]. We further show high-resolution topographic AFM images of functionalized single walled carbon nanotubes (SWNT) and double walled carbon nanotubes (DWNT) immobilized on various relevant biological membranes, including nuclear membranes and cell surfaces. [2] Present experiments combine fluorescence and AFM imaging as well as simultaneous topographical and recognition (TREC) imaging to localize binding of functionalized carbon nanotubes and nanoparticles on different substrates. These preliminary studies will facilitate the investigation of the binding of CNTs to the cell and their possible internalization in a time resolved manner. We also show first results of studies addressing cellular uptake of fluorescently labelled CNTs, where we were able to trace individual carbon nanotubes internalized into living cells.



- A) Biotin-functionalized CNT on a dense layer of avidin.  
 B) RNA-coated CNTs on nuclear membrane. Dashed circle: individual nuclear pore complex.  
 C) RNA coated MWNT on cell membrane. (zoom-in)

- [1] C. Lamprecht, J. Danzberger, P. Lukanov, C.-M. Tîlmaciu, A.-M. Galibert, B. Soula, E. Flahaut, H. J. Gruber, P. Hinterdorfer, A. Ebner and F. Kienberger, *Ultramicroscopy* 109 (2009), p. 899-906
- [2] C. Lamprecht, I. Liashkovich, V. Neves, J. Danzberger, E. Heister, M. Rangl, H. Coley, J. McFadden, E. Flahaut, H. J. Gruber, P. Hinterdorfer, F. Kienberger and A. Ebner, *Nanotechnology*, in press.

