Cellular imaging and nanoanalytics to study neurodegeneration: From nanomechanical sensors to single cell visual proteomics.

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The three lectures present new methods for the biomedical imaging and nanoanalysis of cellular systems and their application to the study of neurodegenerative diseases.

The first lecture will provide a general overview of neurodegenerative diseases, the state of current research, and the limitations of present analytical methods. Neurodegenerative disorders such as Parkinson's disease (PD) and Alzheimer's disease (AD) mainly affect the elderly, and due to demographic shifts, they are afflicting an increasing number of people. Unusual intra- and extracellular aggregates are closely associated with PD and AD. These "plaques" are related to disease-specific misfolded proteins. A stereotypical spreading of these plaques throughout the brain is typical in these disorders. The model of the "prion-like spreading" of aggregates containing misfolded proteins provides an elegant explanation for this phenomenon. However, the detailed mechanism for this spreading is unknown, and different pathways have been suggested. The lecture will provide an overview of neurodegenerative diseases and ongoing research.

The second lecture will provide an overview of nanomechanical sensors and their application in biomedical research. Since the invention of the atomic force microscope by Binnig, Quate, and Gerber in 1986, many different applications have been invented. The lecture will provide a historical overview of the various modes of the atomic force microscope and its siblings, nanomechanical sensors. Whenever possible, the focus will be on biomedical applications for the study of neurodegenerative diseases.

The third lecture will provide an overview of microfluidic sample preparation methods for electron microscopy and the new opportunities arising thereof. During recent years, direct electron detection cameras for electron microscopes (EM) introduced a rapid and lasting advance to structural biology, and are now regarded as a standard method for the structural analysis of protein complexes to atomic resolution. However, protein isolation techniques and sample preparation methods for cryo-EM remain a bottleneck. For a high-resolution analysis of proteins by the cryogenic EM (cryo-EM) single-particle approach, only 10’000 to a few million individual protein particles must be imaged. Therefore, microfluidic techniques can provide enough protein complexes for the structural investigation by cryo-EM and the single-particle approach. We developed microfluidic methods for the sample preparation for electron microscopy, consuming only a few nanoliters of the specimen in total. The lecture will provide an overview over microfluidics and EM sample preparation in general and will highlight new experimental approaches for the single-cell analysis not possible before.

Prerequisites for attending the lecture: All three presentations will discuss basic concepts and no prior knowledge is needed.