学术报告

题 目: Variety of vibrational spectroscopy for probing amyloid fibrils: from UV Raman to VCD and TERS

报告人: Prof. Igor Lednev
University at Albany, State University of New York, USA

时 间: 5 月 4 日（周一）上午 10: 00

地 点: 卢嘉锡楼报告厅（202）

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固体表面物理化学国家重点实验室
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Abstract

In spite of the key medical importance of amyloid fibrils, the molecular mechanism of fibrillation is not fully understood. At least in part this is because amyloid fibrils are non-crystalline and insoluble, and thus are not amenable to conventional X-ray crystallography and solution NMR, the classical tools of structural biology. Together with our collaborators we have developed and applied novel experimental approaches based on advanced vibrational spectroscopy for characterizing structure and dynamics of amyloid fibril during the last decade. These include deep ultraviolet resonance Raman (DUVRR) spectroscopy, vibrational circular dichroism (VCD) and tip-enhanced Raman spectroscopy (TERS). In addition to hardware, we developed advanced statistical methods for analyzing spectroscopic data including two dimensional correlation spectroscopy (2DCoS). The application of these complimentary methods for amyloid fibril characterization will be discussed.

We established a detail fibrillation mechanism by detecting the structural intermediates at early stages of fibrillation and determining the sequential order of their appearance through 2DCoS analysis of DUVRR data. DUVRR spectroscopy combined with hydrogen-deuterium allowed us for characterizing the fibril core structure for various fibril polymorphs. A new protein folding-aggregation phenomenon, spontaneous refolding of one fibril polymorph to another was discovered. Fibril polymorphs prepared from the same protein under slightly different pH conditions exhibit opposite chirality according to VSD measurements. Overwhelming majority of structural information accumulated so far about amyloid fibrils are limited to its bulk or core properties. However, the fibril surface determines the biological activity and associated toxicity. TERS offers a unique opportunity to characterize the surface structure of an individual fibril due to a high depth and lateral spatial resolution of the method in the nanometer range. We utilized TERS for characterizing the secondary structure and amino acid residue composition of the fibril surface. It was found that the surface is strongly heterogeneous and consists of clusters with various protein conformations. The propensity of various amino acids on the fibril surface and specific surface secondary structure elements were evaluated.

Brief bio

Igor K. Lednev is a professor at the University at Albany, State University of New York. He graduated from Moscow Institute of Physics and Technology, Russian Federation, receiving his Ph.D. degree in 1983. Then Dr. Lednev worked at the Institute of Chemical Physics, Russian Academy of Sciences, as a group leader. As an academic visitor, he worked in several leading laboratories around the world including the United Kingdom, Japan, Canada and Germany. In 1997, Dr. Lednev came to the US and joined Prof. Sanford Asher laboratory at the University of Pittsburgh until he moved to the University at Albany in 2002. Dr. Lednev research is focused on the development and application of novel laser spectroscopy for biomedical research and forensic purposes. Dr. Lednev served as an advisory member for the White House Subcommittee on Forensic Science. He is a member of the International Steering Committee of the International Conference on Raman Spectroscopy and serves on editorial boards of four scientific journals including Journal of Raman Spectroscopy and Biochimica et Biophysica Acta. Dr. Lednev is a fellow of the Society for Applied Spectroscopy. He received the Research Innovation Award and the University President Award for Excellence in Research. He has co-authored over 160 publications in peer-reviewed journals, including 2009 article in Forensics Science International, which is the most downloaded and one of the most cited papers from this top journal in the field. His 2014 article in Biophysical Journal is one of the most read.