S N BOSE NATIONAL CENTRE
FOR BASIC SCIENCES
Block JD, Sector III, Salt Lake, Kolkata 700 106

DEPARTMENTAL SEMINAR
Chemical and Biological Sciences

17th January, 2023 **4.00 PM** **ONLINE / FERMION**

SPEAKER

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TITLE OF THE TALK

Investigation of structure-dynamics-function relationship of biomolecules with microsecond time resolution

ABSTRACT

Biomacromolecules, such as DNA, RNA, and proteins, are molecular machines that perform various cellular functions. The functions are often realized due to the ability of these biomolecules to undergo structural changes on relevant time scales. Sometimes, "misfolding" of these biomolecules also generates structures that are toxic to the cells, leading to diseases. In this presentation, I will discuss my efforts toward understanding this structure-dynamics-function relationship of biomolecules using fluorescence spectroscopy and microscopy.

The first part of the presentation will focus on the biophysical mechanisms of protein aggregation diseases, especially on the aggregation of amyloid-β implicated in Alzheimer's disease. I try to address three major questions: (I) which earliest aggregate of amyloid-β is toxic?[1](II) why is it toxic?[2,3] and, (III) how is it toxic?[4,5] Our results show that a key structural change at the earliest step of aggregation possibly drives amyloid-β toward the toxic pathway. Next, I will introduce a new single-molecule fluorescence method called two-dimensional fluorescence lifetime correlation spectroscopy (2D FLCS),[6] which provides a microsecond time resolution for studying biomolecular structural dynamics. This method, recently developed at my postdoctoral laboratory, is currently one of the most advanced single-molecule techniques. I will talk about my contributions in further advancing this cutting-edge method,[7] and its application to biologically important macromolecules.[8] I will discuss the development of dynamic-qenching 2D FLCS, which can report microsecond-resolved local structural change of biomolecules with single dye labeling.[7] I will also discuss the application of 2D FLCS in elucidating the folding energy landscape of the ligand-binding "aptamer" domain of prequeosine riboswitch, which is a therapeutically important noncoding RNA. We propose that a microsecond structural change of the aptamer domain likely governs the biological function of the riboswitch, i.e., to regulate transcription in bacteria.[8]

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[4] B. Sarkar et al, Front. Physiol. 3 (414), 1 (2012).
[5] B. Sarkar# & A. Banerjee#et al. ACS Chem. Neurosci. 5(5), 329 (2014). (#equal contribution)
[6] K. Ishii, & T. Tahara, J. Phys. Chem. B 117, 11414 & 11423 (2013).
[7] B. Sarkar, K. Ishii, & T. Tahara, J. Phys. Chem. Lett. 10, 5536 (2019).
[8] B. Sarkar, K. Ishii, & T. Tahara, J. Am. Chem. Soc. 143, 7968 (2021).

HOST FACULTY

Dr. Suman Chakrabarty
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