DATE: Day 5 Month 7 Year 2020

SUMMARY of
2020 RESEARCH RESULTS REPORT
For International Collaborative Research with IPR, Osaka University

Research Title		Solid-state NMR Studies on Bone and other biomaterials
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	Affiliation	University of Michigan
	Present Title	Professor
Research Collaborator (Host PI)		Professor Toshimichi Fujiwara

Summary

Solid-state NMR provides structural information of biological systems such as biological membranes and fibers which are not amenable to X-ray crystallography owing to difficulties in forming well-ordered crystals. However, applicability of NMR to study biologically important macromolecular complexes is primarily limited by the sensitivity of NMR spectroscopy. Therefore, we apply recently developed technologies, such as high-field dynamic nuclear polarization (DNP) and high-speed magic angle spinning, to the sensitivity enhancement of solid-state NMR in collaboration with researchers at Institute for Protein Research, Osaka University. Conventional methods of structure elucidation, i.e. X-ray crystallography and solution-state NMR, often fail when applied to membrane proteins, which play very important roles in most diseases. We carried out multi-microseconds MD simulations to better understand the amyloidogenic peptide folding and aggregation in a lipid membrane environment. The parallel computing using IPR facilitated UV 3000 enable us to generate a structural model for membrane-bound, polymer-bound amyloid intermediates and de novo designing of polymer/peptide based nanodiscs. Although, this study is in progress and would need more simulations and calculations in the coming years, initial results obtained this work has been published (Sahoo et al. 2019; Lin et al. 2019, Sahoo et al. 2020). In addition, we are able to carry out coarse-grain and all-atom MD simulations to demonstrate the self-assembly process underlying the formation of lipid-nanodiscs by polymers, recently synthesized in our lab, using the parallel computing of IPR (*J. Phys. Chem. B (2019)*). These results, along with the reconstitution of membrane proteins in nanodiscs, have been reported in our recent publications: Sahoo et al. *J. Phys. Chem. B (2019), Chem. Sci. (2019) and J. Mol. Biol. (2020).* Four manuscripts are under preparations/revision that integrates NMR and MD calculation to report high-resolution structural details of amyloid peptides (amyloid-beta and human-IAPP). All of these publications and the presentations in scientific meetings/conferences acknowledged the collaborative and resource support from IPR. We look forward to carrying out solid-state NMR experiments on a variety of exciting biological systems in the coming years.

We take this opportunity to thank IPR (and Professor Fujiwara and the Director of IPR) for the continued support to our research.

***Deadline: May 15, 2020**
***Please submit it to E-mail: tanpakuken-kyoten@office.osaka-u.ac.jp.**
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