Symposium report: understanding biological systems with quantum science and technology

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Recent years have witnessed remarkable progresses in quantum technologies based on quantum science, and these technologies and viewpoints are expected to bring innovations to measurement technologies and interpretations of biological phenomena. However, its application to life science is still in its early days and further leaps are expected in the future. To explore the future prospects of the fusion of quantum science and biology, a symposium on quantum biology was organized in the 57th Annual Meeting of the Biophysical Society of Japan in Miyazaki City on September 25th Wednesday. The authors organized this symposium with support from the Japan Agency of Science and Technology (JST).

In this symposium, we invited seven speakers to showcase their state-of-the-art research achievements. All authors are working under the Precursory Research for Embryonic Science and Technology (PRESTO) project of JST to explore new directions of quantum biology in Japan. This project, “Quantum Bio,” is led by the supervisor Dr. M. Setou (International Mass Imaging Center, Hamamatsu University School of Medicine) who presented the opening remarks in this symposium. Each researcher has a diverse background

such as synthetic chemistry, material science, laser physics, neuroscience, structural biology, and philosophy, but all share the same aim to develop novel technologies that incorporate quantum-mechanical concepts and technologies and ultimately apply them to biology (Fig. 1). In order to facilitate the discussion about the applicability and future direction of quantum biology in the field of biophysics, we asked all speakers to give their thoughts on “how the viewpoints and techniques based on quantum science and technology that they use in their own researches can contribute to biophysics.”

Our first speaker was Dr. N. Yanai (Kyushu University), who gave a talk entitled “Materials chemistry of photo-excited triplet state for dynamic nuclear polarization.” He introduced application of quantum technology to enable imaging dynamics of biological molecules by nuclear magnetic resonance (NMR) and magnetic resonance imaging (MRI). NMR and MRI spectroscopy are one of golden-standard tools in modern chemistry, biology, and medical fields. However, they suffer from intrinsically limited sensitivity due to low nuclear spin polarization at ambient temperature. The speaker proposed and realized a novel technique using dynamic nuclear polarization based on photo-excited triplet (triplet-DNP) to achieve hyperpolarization at room temperature with a better accessibility and feasibility (Nishimura et al. 2019). He showed the first example of triplet-DNP of nanoporous metal-organic frameworks (MOFs), which allows the accommodation of biology-relevant target molecules (Fujiwara et al. 2018). He also showed the first example of air-stable and high-performance polarizing agent for triplet-DNP (Kouno et al. 2019).

Dr. H. Watanabe (Keio University) gave a talk entitled “Incorporation of quantum chemical effect of solvation into molecular dynamics simulation and the applications to biomolecules,” where he introduced a new concept and technique for simulating dynamics of solutes and solvents in biological systems. Water molecules play important roles in protein functions and thus understanding quantum chemical effects of

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Fig. 1 Schematic overview of the symposium

water and solutes is critical in biology. However, the present molecular simulations cannot incorporate these effects into dynamics-based analysis because of solvent diffusion. To overcome the problems, he proposed the size-consistent multi-partitioning (SCMP) method (Watanabe et al., 2014), and successfully demonstrated that the SCMP method can achieve stable simulations by effectively taking into account quantum chemical effects of solvation (Watanabe 2018, Watanabe and Cui, 2019). He introduced the basic concept and the latest progress in further development of the SCMP method.

Next, Dr. Y. Maruyama (Kyoto University) gave a talk entitled “Contextuality and non-locality in quantum physics and cognitive science.” He is a mathematical philosopher, and has been aiming to figure out the applicability of quantum physics on biological phenomena such as cognition, and to clarify the mathematical laws shared by physics and life/cognitive science. Utilizing the fundamental connection, he asks if and how the concept of quantum science helps explain cognition and gain insights that contribute to understanding various phenomena of life sciences. Since this symposium was held in an annual meeting of biophysics where most of the audience was biologists, we asked the speaker to spend more time for introduction to the basic part of his research so that they can follow his presentation. In the presentation, he demonstrated similarities and dissimilarities between contextuality of reality and that of reason by showing some real-life cases, and nicely introduced the audience with a new theoretical approach of quantum biology that can be further exploited to various topics in biophysics (Maruyama 2019).

Our next speaker was Dr. T. Ideguchi (The University of Tokyo), who gave a talk “Label-free molecular vibrational

spectro-microscopy.” He is a laser-physicist who has been actively developing high-speed spectroscopy and imaging techniques based on novel laser technology using advanced quantum physics. In this talk, he introduced and compared a family of novel techniques for vibrational spectro-microscopy that are used in life sciences. While fluorescent probes provide molecular selectivity in microscopy at the expense of some drawbacks such as photo-bleaching or cytotoxicity, vibrational spectro-microscopy is a label-free counterpart molecular-sensitive technique, where one can have image contrast on molecular vibrations without staining specimens. His technique achieved vibrational spectro-microscopy of biological specimens based on Raman scattering or infrared absorption with highly improved speed, spatial resolution, and sensitivity (Hashimoto et al. 2019, Tamamitsu et al. 2019, Toda et al. 2019, Kinogawa et al. 2019).

Dr. M. Nuriya, one of the authors of this article, also gave a presentation as a symposiast with a title of “Imaging dynamics of molecules inside the brain tissue by the application of multiphoton microscopy.” He is a neuroscientist and has been applying advanced optical microscopy to neuroscience. In the presentation, he introduced his attempts to utilize multimodal multiphoton microscopy to reveal dynamics of molecules inside the living brain tissues, with special focus on water molecules. Dynamics of molecules inside the brain are the key determinants of its physiology and pathophysiology and thus visualization of these molecules is critical in neuroscience. He realized deep-tissue imaging using multiphoton microscopy with high three-dimensional resolution. In addition to the two-photon excitation of fluorescence molecules, other multiphoton events including coherent Raman scattering were also applied to various biophysical research projects (Nuriya et al. 2019).

The second last speaker was Dr. H. Ishiwata (Tokyo Institute of Technology), who talked on “Nanoscale thermometry and magnetometry in biology using NV center in diamond.” Nitrogen-vacancy (NV) center in diamond is a powerful tool as a local environment sensor in nanoscale through the quantum interaction between the NV center and the chemical/physical environment. His talk focused on magnetometry and thermometry at subcellular level by using special preparations, and their applications to analysis of biological processes. High sensitivity of shallow ensemble NV center enables novel magnetometry technique such as nanoscale NMR for localized NMR analysis in $\sim (20 \text{ nm})^3$ volume (Ishiwata et al. 2017). Quantum thermometry has also been demonstrated with sub-degree temperature resolution by detection of the zero-field splitting for the NV center. Detection of the nuclear spin combined with a thermometer capable of sub-degree temperature resolution should provide a powerful new tool in many areas of biological research.

Our last speaker was Dr. T. Ono (Osaka University) who gave a talk “Electrical biosensing beyond the Debye screening

length using graphene field-effect transistor in femtoliter microchamber”. Graphene is a 2D material which has extraordinarily high carrier mobility. Graphene field-effect transistor (G-FET) has a potential for electrical biosensing, because it transduces the carrier modulation by charged targets to a large conductivity change. The speaker developed a novel technique for high-sensitivity electrical biosensing (Ono et al. 2019). In physiological ionic strength, electrical field around the target is confined by Debye screening into 1 nm in proximity, which makes it difficult to detect the target in realistic use. To overcome this issue, he detected the target by detecting its reaction products encapsulated and accumulated in a microdroplet. He demonstrated that his G-FET sensor can detect ammonia production of urease in real-time. Its application to *Helicobacter pylori* detection through urease reaction was realized with the sensitivity at the level of single bacterium.

In the two-and-half hours of symposium, there were around one-hundred people listening to the talks in the room. As could be inferred from the summaries above, the research topics introduced by the speakers were diverse, covering wide fields of science that may not seem to be directly related to biophysics at the first glance. However, through the symposium, we could easily understand that quantum science and the quantum-based technologies underlie all of the diverse presented research topics, and their relationship to biophysics was both clear and immediate. Indeed, for all the talks, we had many active questions and comments from the audience. Therefore, despite the challenging and ambitious aim to explore the application of quantum science/technology to previously unexplored field of biophysics, we believe that the symposium was a great success and proceeded with great excitement in the bright and fruitful new field of biophysics shared by all the participants.

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