Research area in the Strategic Objective “Innovation of Bio-Sensing, Elucidation of Dynamics and Interactions between Biomolecules by using Quantum Technology”

Creation of Life Science Basis by using Quantum Technology

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**Overview**

The aim of this research area is to apply the knowledge of quantum science and its technologies to biomolecule measurements through the collaboration between quantum science and life science researchers. In recent years, quantum technologies including quantum beams, quantum spin, light quantum sensors and quantum electronic, etc., has progressed markedly based on quantum science. These technologies have also realized quantum computing and time crystals. Japan has cutting-edge quantum technologies, or in a sense, seeds technologies capable of leading the research field in the world. These technologies are expected to advance the development of new biotechnologies for detecting dynamics and interactions of biomolecules, as well as the discovery of quantum phenomena in biological phenomena. At present, however, the application of quantum technologies to life sciences has not so progressed. The program of this research area will encourage applying quantum technologies to biotechnologies to develop new life sciences dramatically.

**Research Supervisor’s Policy on Call for Application, Selection, and Management of the Research Area**

1. **Background**

   In recent years, quantum cryptography communication and elemental technologies of quantum computing have become closer to a reality. Under such circumstances, in Europe and the U.S., investments as large as several trillion yen have been made in the application of quantum technologies, including applications in life sciences. In comparison with these advanced countries, our country, while leading the world in the fields of quantum sensor production, advanced quantum beam, and other quantum technologies, is currently far behind in the application of quantum technologies to life sciences.

   Recently as well in Japan, the application of technology seeds to life sciences is starting gradually. Quantum sensor technology, with diamond NV center, etc., has enabled high-sensitivity observations
of the temperature, magnetic fields, electric fields, etc., in living bodies that used to be impossible so far, and it is thus attracting attention around the world. In addition, by combining quantum-entangled photons with super-resolution microscopes, the development of new in-vivo imaging technology has advanced enough to capture states that have never been visualized so far at a high spatial resolution. Furthermore, in biomolecular structural analysis technology, the enhancement of quantum beams etc., has enabled ultra-precision structural analysis with resolutions at the level of quanta, which can capture the electron densities and positions of hydrogen that are the keys for biomolecules to perform their functions. However, it can hardly be said that these endeavors have matured sufficiently for applications. As obstacles, it is said that researchers in life science feel uncomfortable with and are resistant to quantum technologies, and researchers in the field of quantum science have only a vague awareness about their applications to life science.

2. Policies of Project Invitation and Selection

In this research area, on the basis of the background described in Section 1, we invite researchers to submit proposals for the three main themes in the last (third) call: ① "Clarifying biological phenomena through the application of quantum technologies," ② "Developing measurement technologies applicable to life sciences using quantum technologies," and ③ "Understanding of biological phenomena from a quantum science perspective."

In this call for proposals, we place great importance on how persuasive a proposal's description is based on the point-of-view of quantum technology or quantum science. Furthermore, we will look favorably upon novel and challenging proposals that may achieve great things after the end of the three-and-a-half-year period of the PRESTO project. In particular, we highly anticipate even more unique and challenging proposals for the development of quantum technologies that will further advance their conventional concept and apply for life sciences, and studies to try to find a genuine quantum mechanism as a biological function in life phenomena. Shown below are some examples of the points. We are looking forward to your unique and challenging proposals.

We call for proposals, considering, in particular, the following points.

● In the proposals to solve life phenomena in items ① and ③, consider the principles and physiochemical functions in life phenomena and optimize and introduce the quantum technology necessary for the solution. The quantum technology introduced here includes photon technology and nuclear medicine technology.
Some of you in the field of biology may feel something unusual in the expression "quantum." On the other hand, it is you who feels something interesting in the life phenomena. We are highly expecting such proposals that make challenges to solve life phenomena with respect to the current problems under the assumption of a mechanism as the level of molecules such as what kind of ingenuity reveals the symptom that is not visible with respect to an available technology that uses the nature of atoms, electrons, photons, and spins.

Shown below may be several examples of research topics. Do not confine yourself to these examples. We accept a wide range of unique ideas that have not even thought of by the research supervisor who has prepared these policies, and the research advisors.

(1) Clarifying biological phenomena through the application of quantum technologies

We are assuming that the main applicants may be researchers from the fields of biology, agriculture, dentistry and pharmacology who study specific biological phenomena. This objective is not the discovery of technology but the discovery of biological phenomena, principles, substances, and elucidation of disease pathologies.

We hope to invite research proposals considering the biological phenomena and the physiochemical functions in the research subject, which lead to applicants' unique ideas and optimization for the quantum technologies applied.

The examples of biological phenomena in our targets are: cell biology on the biomolecular behavior and state changes of in cells, biochemistry on the activation of proteins that govern biomolecular functions, neuroscience or metabolic physiology, brain functions, etc., at the individual level, pharmacological research such as the resolution of the functions in chemical reactions based on the acquisition of the chemical bond information of protein molecules etc., in blood vessels and cancers, as well as the resolution of the relationship between biological reactions and diseases, the resolution of intermolecular interactions in living bodies and the reaction mechanisms with chromosomes, chromatin, oxidoreductase, metalloenzymes, or the like by introducing information on the motions of hydrogen atoms and/or water molecules based on the linked usage of neutrons and X-rays, the understanding of temporal changes in protein structures or the like using X-ray free-electron lasers, the relationship between the drive
mechanism and the energy conversion mechanism in biomolecular structures based on the linked usage of a cryo-electron microscope and X-rays, the resolution and/or inhibition of biomolecular functions such as for proteins based on the understanding of the behaviors of the peripheral electrons and the functions of the hydrogen bonds etc. (or the enhancement of medical applications based on the aforementioned), electron transfer mechanisms in photosynthesis, cellular functions with the intervention of the membrane potential, and other fundamental biological research. We are assuming a wide variety of biological studies. As for examples of quantum technologies, we can mention ① beam and optical technology used for structural biology, ② bio-imaging technology and sensor technology, and ③ the applications of different types of probes. More specifically, they can be microscopes using cryo-electron microscopy, X-rays, neutrons and X-ray free-electron lasers, proton/heavy particle beams or other quantum beams, multiphoton microscopy or other light quantum processes, single molecule imaging visualization technology using atomic force microscopy (AFM) and/or AFM in ultra-resolution liquids, the measurement of temperatures and magnetic fields using diamond vacancy, PET and other quantum sensors, single molecular imaging visualization technology that uses fluorescent molecules, Qdot (quantum fluorescent molecules), or the like, tag and/or probe technology to track down fluorescent and/or light-emitting probes and other biomolecules, etc, some of which were adopted in the first and second call. In the third call, we are expecting, besides the above-mentioned, the proposals for research in the fields of spin control, specifically, the fields of MRS, fMRI, and diffusion tensor, and those of PET probes.

(2) Developing measurement technologies applicable to life sciences using quantum technologies: We are assuming that the main applicants may be the researchers from the fields of applied physics or chemistry. We are also assuming the measurement technologies can be applied to the life sciences and has not been studied, and the development of probes for this purpose. We, of course, welcome proposals for introducing quantum technologies made by highly experienced researchers with knowledge of the development of measurement technologies in the field of biotechnology or medical engineering. The purpose is not to discover but to invent. We are assuming the researches may apply the technologies that have attained some achievements in the fields of quantum electronics, quantum optics, etc., to living bodies. It is not necessary to arrive at the phase where the technology can cope with any specific problems in the field of biology or medical science within the research period of the PRESTO project. However, applicants need to describe what is the biological phenomena and/or molecular mechanisms of the measurement technology and/or probe applicants are trying to develop, and what technological superiority lies on the basis of the aforementioned.

As for examples of the technologies are: the development of a biomolecular interaction
detecting system using quantum sensors, the measurement of quantitative inner-cellular temperatures, magnetic fields, electric fields, etc., with nanometer-length spatial resolution based on the enhancement of the sensitivity of quantum sensors, the development of multi-modal imaging in the physical field of a specific inner-cellular location, application to the fields of industry and/or medical treatment based on the measurements of the magnetocardiogram, magnetoencephalography, or the like, the development of NMR and/or MRI for single molecules using electron spin resonance, the development of a minimally invasive imaging technology for the deep inner parts of living bodies based on the introduction of quantum entanglement to fluorescent microscopy, the development of a new imaging technology for the inner parts of living bodies based on ultra-resolution microscopy, multiphoton microscopy, and/or other optical and/or quantum technologies, the development of an observation technology for the inner walls of blood vessels based on quantum-entangled light, the development of an operating system using single state or small number-of-states individual biomolecules by applying laser cooling and/or other atomic and/or molecular cooling technologies, application to ultra-high speed symptom analysis in the reactions of living bodies using attosecond light pulses and/or attosecond magnetic field pulses, application to the life sciences of high-resolution optical measurements using an optical frequency comb, the application of silicon photonics and atomic layer science (graphene, two-dimensional substance), the application of topological superconductivity through majorana particles, to the field of living body measurements, etc.

(3) Understanding of biological phenomena from a quantum science perspective:

As for the applicants, we are assuming mainly researchers on quanta from science departments, researchers from the field of information science, mathematics and physiochemistry, scientists in the field of structural science that use SPring-8, cryo-electron microscopy, NMR, and/or the like, researchers in the fields of theoretical biology, computational science, so-called quantum biology in a narrow sense, and so forth. Our purpose is not to invent but to discover or understand. More specifically, it is to understand living things based on quantum science. Our tools do not necessarily have to be from quantum technology. For instance, an approach using a computational simulation may be acceptable. The case where quantum coherence, quantum entanglement, or some other effect is closely and directly related to a function of a living thing, namely, the case where there is no classical macro-model (coarse-grained model) involved, is at the forefront of these discussions. We are involved a wide range of subjects, including very fundamental approaches: whether any such things exist in the first place, if so how to judge the existence. We expect that a new path will be generated from this research area which will provide important suggestions and research directions to the themes
of ①" Clarifying biological phenomena through the application of quantum technologies", ②"Developing measurement technologies applicable to life sciences using quantum technologies,"

As specific examples are: light absorption/optical response to visual substance based on crystal structural analysis at a super-high resolution, research on the electron transfer systems, energy transfer, or similar in relation to the photosynthesis of plants, the respiration of mitochondria, and the like, research on the terrestrial magnetism sensing system of migratory birds, research on the resolution of quantum effects in the activation and/or structure of biomolecules using heavy water and/or stable isotopes, etc.

We will consider adopting the proposals in which researchers create experimental or theoretical challenges to find, discriminate, or search for the physiological significance in quantum symptoms in life phenomena such as the quantum tunnel effect and quantum coherence. For this purpose, an excellent logic is expected to be constructed.

3. Selection of Proposals

We place great importance on how persuasive a proposal's description is from the point-of-view of quantum science or quantum technology. Furthermore, we highly value challenging proposals that may result in great achievements at the end of the three-and-a-half-year period of the PRESTO project.

We select proposals in cooperation with the research advisors. The advisors include experts who span the fields of quantum science, biology, chemistry, and spectroscopy to cope with the selection of a variety of research proposals.

4. Addition of Cooperative Plans

In this research area, from the point-of-view of promoting the exchange of ideas among researchers from different research fields, it is allowed for the researchers in the life sciences and for the researchers in quantum technology to add any plans in cooperation with each other (cooperative plans). In such a case, ① consult with the other researcher (one researcher) who makes a proposal in this same research area and "add" the joint proposal with the researcher to your proposal. Alternatively, in your joint proposal, you can add a proposal in cooperation with ② a researcher (one researcher) whose proposal has been adopted in this research area.

(Note: Any joint research or the like other than ① or ② is not included in the cooperative plans described here.)
However, the purpose of the "PRESTO" project is to promote the individual research based on concepts and/or ideas unique to the researcher and to create a source of scientific and technological innovation. For this purpose, in this research area, even in the case where cooperative plan is added, we place great importance on the proposals in relation to individual research proposal, which is the foundation of the "PRESTO" research project.

We do not include, in the scope of our assessment, proposals that cannot be made without a cooperative plan for individual research.

If you wish to add cooperative plans, fill in Form 1 and Form 3 to clarify the organization, full name, and name of the work of the researcher you will cooperate with and describe how you will enhance the contents of the proposal for your individual research through such cooperation. It is not necessarily the case that your proposal will not be adopted unless both proposals are approved in our selection process in the case of ①; there will be a lot of cases where either one of the proposals is adopted.

Of course, as has previously been the case, an individual researcher who has expertise in the fields of both the life and quantum sciences can apply to this project as an individual. In this research area, we also recommend that a researcher should maintain a positive attitude towards cooperation with other individual researchers, research advisors, and so forth. The researchers who aim at the application in the field of life science measurement as a researcher in the field of quantum science and the researchers who aim at the solution of life phenomena by using a quantum technology as a researcher in the field of life science will be finding a partner in this research area someday if their proposal is adopted even in the case where they do not presently have any partner for cooperation.

In the "PRESTO" project, the research funds are allocated only to the individual researchers whose proposals are adopted. Note that no funds will be allocated to your partner or joint researcher who is involved in a proposal that is not adopted. Furthermore, "PRESTO" is a program that allows the researchers to participate as dedicated researchers. We welcome novel proposals that are free from the research themes of the laboratory to which the researcher belongs (we have an internal JST examination to adopt a researcher as a dedicated researcher).

* The research proposal form for applying for this research area is different from that of other research areas, so to apply, download the correct form from the JST website for Invitation of Research Proposals.

5. Principles of Management

In the management of this research area, we place great importance on the exchange of ideas among researchers from different fields. We are also considering providing some "technology/analysis base" as a platform and, in addition, considering a system in which the researchers in the life sciences and
the researchers in quantum science and technology can continue their research in one research area. Furthermore, besides establishing a system in which the advisors in the fields different from that of an individual researcher whose proposal is adopted will supervise so that the researcher can learn a variety of knowledge, we are considering some ideas to enable researchers in the field of life science and technology and researchers in the field of quantum science and technology who can cooperate to be flexibly matched with other researchers inside and outside their research areas.

In this research area, we do not intend to assess the achievements by the number of theses or by the number of presentations in academic societies that are made in the three-and-a-half-year period of the PRESTO project. We do not expect that such achievements will come so quickly. As for the social applications of the research achievements, it cannot be helped that they will take a much longer time to appear. We want the researchers to feel safe to bring positive attitudes towards challenging, high-risk themes. We are certain that some achievement that goes beyond our imagination today will come up in this research field someday. If even one more researcher who is involved in such achievement comes from this research area, we, the research supervisors, will find greater satisfaction than we could possibly find in anything else.

The upper limit of the research expenses is 40 million yen in total (excluding indirect expenses). The research period begins in the fiscal year of 2019 and ends at the end of the fiscal year of 2022 (three-and-a-half years or shorter).