2016

HIROSAKI UNIVERSITY
RESEARCH HIGHLIGHTS

Establishing a Global Identity
Creating with the Community

HIROSAKI
UNIVERSITY

Activity on Radiation Emergency, Environment and Medicine in Hirosaki University - For Safety and Security on General Public

Purpose and Background of the Research

Following the Fukushima Daiichi Nuclear Power Plant (FDNPP) accident, assessment of the influences of the FDNPP accident in support of various research studies in other institutes has been conducted. However, information on the influences of the FDNPP accident are rarely available now. Therefore, the general public is still concerned with radiation exposures.

In August 2015, Hirosaki University was designated as two types of national centers in Japan: (1) an Advanced Radiation Emergency Medicine Support Center and (2) a Nuclear Disaster Medical Care/General Support Center.

It is expected that Hirosaki University will be able to develop a database related to radiation exposure to relieve anxieties among the general public and provide correct data on radiation exposures.

To carry out its responsibility, Hirosaki University carried out the following studies.

① Development of database on dose estimation under three different exposure situations.

② Investigation of impact of X-irradiation on the repair of DNA double-strand breaks

Research Results

① Development of database on dose estimation under three different exposure situations

A database was developed by compiling the measured results as well as referring to literature (Figure1). The database mainly consists of two parts, which are "dose estimation system" and "database".

In the part of the "dose estimation", the users can utilize a program for calculating effective dose to general public intake of radioactive materials. In the part of the "database", the users can utilize fundamental data such as dose coefficients, decay constants.

② Investigation of impact of X-irradiation on the repair of DNA double-strand breaks

By the trypan blue dye test and DNA double-strand breaks analysis, it is confirmed that mouse neuros show radio-resistant. Radiation-induced gamma-H2AX and 53BP1 expression, a marker of the DNA double-strand break response, were observed immediately after exposure to X-rays and gradually decreased over 48 hours. Neurons were survived even with 4, 7Gy exposure, while the frequency of mEPSCs was significantly reduced.

Future Prospects

① Development of database on dose estimation under three different exposure situations

One pattern of exposure situation on dose estimation is now available for the database developed at Hirosaki University. In order to estimate dose on other patterns, there is a need for updating the database and gathering new data. Hirosaki University will continue to develop the database and make it a goal to provide the scientific knowledges to the general public.

② Investigation of impact of X-irradiation on the repair of DNA double-strand breaks

Though X-ray irradiation to neuron cells does not cause cell death and severe DNA damage, there is a possibility that the synaptic networks are affected.

Further study of the dendritic spine morphology analysis and behavioral analysis will be required to clarify these mechanisms.

Funding

Figure 1. Outline of database on dose estimation
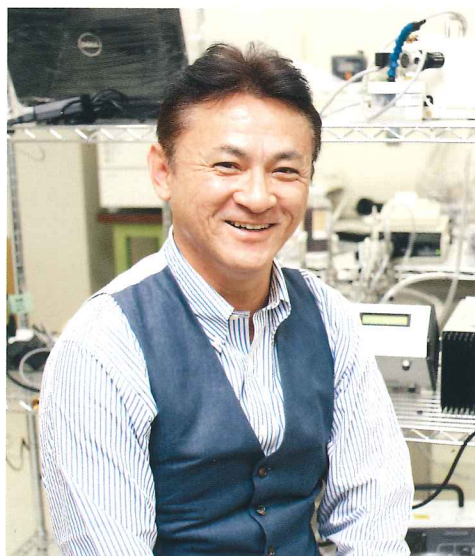
PROFILE

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Evaluation of Function and Reliability of Materials Systems - Development of Tactile Sensors for the Human Body and Simulation of Failure in Electronic Devices -

Purpose and Background of the Research

I am studying the Evaluation of Function and Reliability of Materials Systems. The research subjects are material systems such as the human body, medical systems, electronic devices and thermoelectric generators, which consist of several materials and show a function. Although information about mechanical stress in the human body is useful for medicine and development of medical systems, it remains very difficult to measure the mechanical stress applied to the human body. On the other hand, in electronic devices reliability becomes an issue because electronic circuits are exposed to high current density, high temperature and high mechanical stress as a result of the electronic device's miniaturization via nanotechnology. Collision of electrons with metallic atoms in a very fine circuit line leads to fatigue of the metal line, in otherwords degradation of circuit. Prediction of lifetime and failure site of circuit line is required in not only electronic industries such as mobile phone and computer manufacturings but also car and airplane industries which use a lot of electronic devices.

Research Results

Regarding evaluation of mechanical stress on the human body, a wearable tactile sensor has been developed using a conductive polymer. The sensor is able to measure contact pressure and friction stress in the human body and act as an interface between the human body and medical systems since it is very thin and flexible. Measurement systems for swallowing pressure, pressure distribution on human joint surfaces, interface pressure distribution between an amputee and the socket of lower extremity prosthesis, between articular cartilage and artificial joints, between the buttocks and seat of a chair ski, between lower limbs and compressive stockings were developed. Two related patents have been registered.

Regarding evaluation of reliability in electronic devices, a prediction method of lifetime and failure site was developed utilizing numerical simulation. The reliability in high power circuits using wide interconnected metal lines and very fine circuits using nano-sized metal lines can now be evaluated accurately. Also an evaluation method of allowable input electric current which will not damage the circuit was developed using numerical simulation. Using these methods one can predict the reliability during the circuit design process, and avoid unexpected accidents. Eight patents related to this, which include three foreign patents, have been registered.

Future Prospects

The tactile sensor will be adapted to the visualization of expert skills, such as blood collecting technique, and to tactile operation in haptic interfaces such as a touch panel. The evaluation method of circuit reliability will 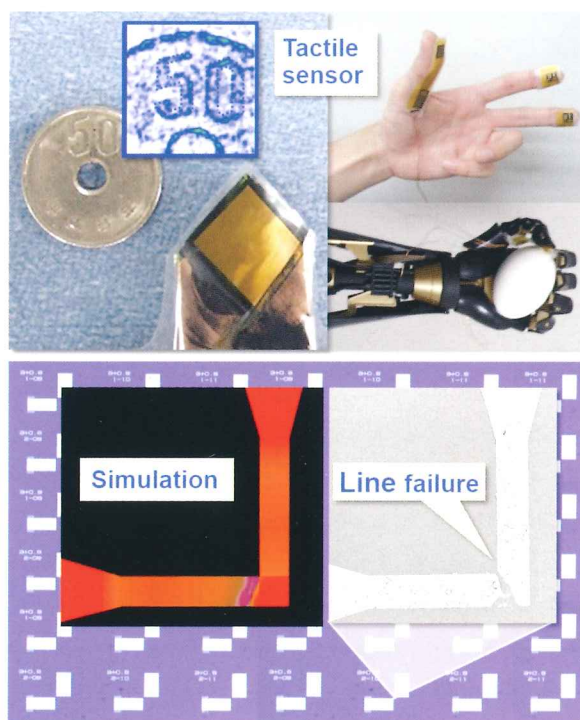be expanded for novel electronic materials, such as carbon nanotubes and metallic nanoparticle and nanowire. A simplified evaluation method for circuit reliability, which is easy to use in the design process, will be developed instead of numerical simulation.
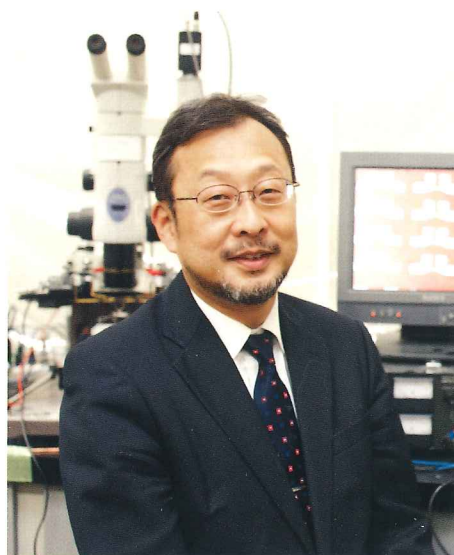
Funding

A very thin and flexible tactile sensor (top) and reliability evaluation of electronic circuit using numerical simulation (bottom)

PROFILE

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Identification of host factors involved in flavivirus infections

Purpose and Background of the Research

Positive-strand RNA viruses can dramatically rearrange the intracellular membranes of the host cell and produce unusual organelle-like structures called "replication organelle". These membrane structures appear in close proximity to the endoplasmic reticulum and likely serve as a scaffold for the assembly of replication machinery by providing an organization and environment facilitating viral propagation. These structures also serve as shells that protect the viruses against various cellular stress responses and allow persistent viral replication in the cytoplasm.

Our group has focused on the molecular mechanisms involved in the formation of these replication complexes to determine the dynamic state of viral and/or host factors during the viral propagation cycle. We had successfully purified replication complexes from cells infected with flavivirus and performed quantitative mass spectrometry analyses. In these studies, we identified several cellular factors that were specifically recruited to viral replication complexes. We are currently focusing on the molecular functions how these newly identified cellular factors are involved in the biosynthesis of the viral replication organelle. These studies may contribute to the development of novel antiviral therapies against for the human pathogenic flaviviruses including Dengue virus, Zika virus that have significant impacts on the public health of the world.

Research Results

We identified several ESCRT (Endosomal Sorting Complexes Required for Transport) components as factors that are recruited to sites of flavivirus replication. We found that depletion of several unique sets of ESCRT factors, e.g. CHMP2s and CHMP4s, exerted a strong inhibitory effect on viral propagation. This unique ESCRT requirement implies the existence of ER-specific features for ESCRT-mediated membrane rearrangement (Tabata et al. Cell Reports 16:2339-2347, 2016).

Another cellular factor that we identified is VCP complex. We found that the addition of pharmacological inhibitors for VCP ATPase, as well as siRNA depletions for VCP complex, strongly inhibits virus propagations. Currently we have several cases of evidence proving that viruses utilize VCP complex to minimize cellular stress responses for efficient viral replication.

Future Prospects

Considering the low mutation rate in the interface of cellular protein, the virus-host interaction inhibitors are assumed to avoid driving the emergence of resistant viruses. We are going to develop screening systems to identify small compounds that inhibit interactions between virus and cellular factors that we identified.

Funding

1. Grant for Hirosaki University Young Institutional Research FY2015-2016 6,000,000 Yen
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3. JSPS KAKENHI Grant Number 26460555 FY2014-2016 3,800,000 Yen
4. Health and Labour Sciences Research Grants for Research on Emerging and Re-emerging Infectious Diseases, Grant Number 12103320 FY2012-2014   13,776,000 Yen
5. JSPS KAKENHI Grant Number 23790503 FY2011-2012 2,000,000 Yen
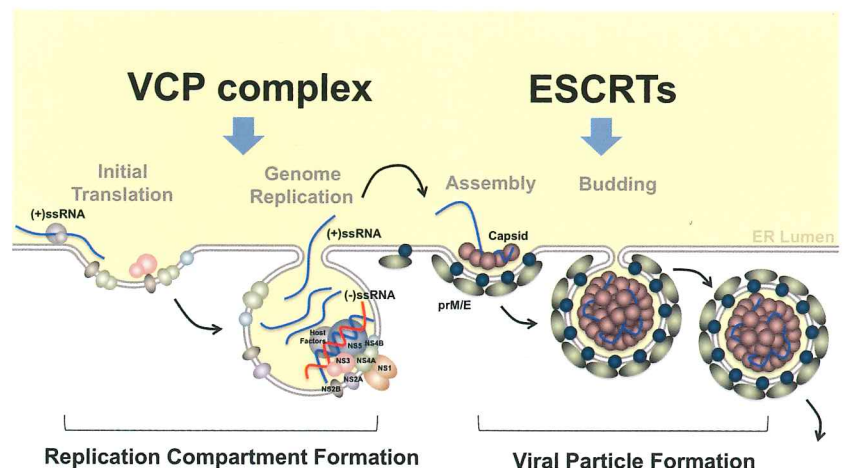
Model of membrane dynamics in viral replication organelle.

PROFILE

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Study on Ezochi from the Middle Ages to early modern times and northern trade

Purpose and Background of the Research

Recently, the public is full of the images of Ainu who lived together with nature and built a rich inner space, by a reaction against historical view that had been cultivated in Hokkaido reclamation after the Meiji era. On the other hand, the history that *Wajin* are migratory from the main island to Hokkaido, called the *Ezochi*, is downplayed. The history in the *Ezochi* has been formed by Ainu and *Wajin*, and with the relationships between Japan and China and/or Russia. Ainu did not have a character, and their history has been studied by the ancient documents which *Wajin* recorded exclusively. However, true history of Ainu may be not uncovered only from those ancient documents including prejudice and the misunderstanding for Ainu by *Wajin*. In this study, I researched archaeology documents, ancient documents and stone monuments, and discussed multidirectionally about the process that the *Ezochi* was incorporated from the land of the Ainu race into Japan based on those researches.

Ceramics excavated from the Yafurai-date site at Hokuto-city, Hokkaido
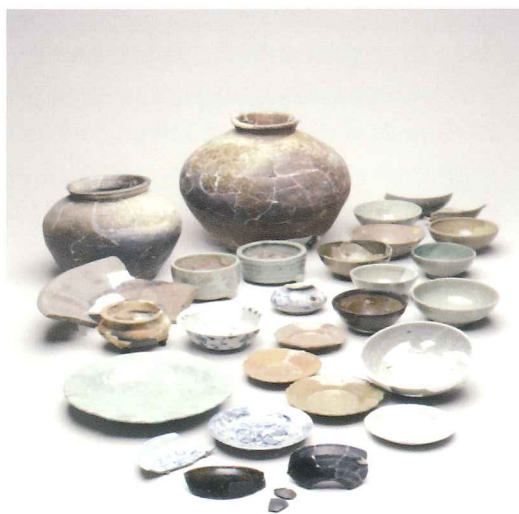
Research Results

The history of the *Ezochi* during the Middle Ages to early modern age was divided into 4 periods, as follows. Initial Ainu culture period was from the 13th century to the early 15th century before the fight of *Kosyamain*. Middle Ainu culture period was from the late 15th century to the late 17th century when *Wajin* place was set at the southwestern edge of Hokkaido by their migration and the economic relationship was strengthened among Ainu with *Wajin*. Late Ainu culture period was from the end of 17th century to the end of 18th century when armed uprisings of Syakusyain had been suppressed and the *Ezochi* place was incorporated into the economic zone in Japan. The *Ezochi* was incorporated into Japan and a nationalization policy was pushed forward for Ainu in the 19th century.

Metal products excavated from the Yafurai-date site at Hokuto-city, Hokkaido

Future Prospects

The problem of the Ainu race and the problem of base in Okinawa are the extremely important political items of Japan. These political problems seem to be caused by the historical background of the territory expansion in Japan. Addressing these political problems at the north and south ends of Japan also seem to be greatly differences between Hokkaido or Okinawa and other areas. I'm carrying on the historical research of both Okinawa and Hokkaido, and will find a lead to solve these political problems by comparison between both histories in the future.

Funding

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Quantum mechanics of general relativity (Construction of a basic formula that describes the whole Universe including its origin)

Purpose and Background of the Research

What was the birth of the Universe like? The origin of our existence has been a subject of great inquiry since ancient times. The evolution of the Universe is described by a solution of the Einstein equation of general relativity. If we go back to the birth of the Universe by using the solution, the Universe will become a point and general relativity will break down at the beginning. Actually, general relativity possesses a limitation of a theory, that is, it cannot describe a microscopic world. Quantum mechanics can describe such a microscopic world. Therefore, we need to construct quantum mechanics of general relativity to describe the birth of the Universe. Although the superstring theory is known to be quantum mechanics of general relativity, the superstring theory has not been completed yet.

Research Results

We proposed a three-algebra model of M-theory as a model for the complete superstring theory and obtained a relation between the model and the past superstring theory. After that, we obtained several evidences that the model is complete as follows:

1. We show that the model possesses N=1 space-time supersymmetry in eleven dimensions that consists of 16 kinematical and 16 dynamical ones. We also show that the model with a certain algebra reduces to the Banks-Fischler-Shenker-Susskind matrix theory if the discrete light-cone quantization limit is taken. (M. Sato, Journal of High Energy Physics 07(2010)026)

2. We show that the model is ghost-free even if the Lorentzian 3-algebra is applied. (M. Sato, Physical Review D85 (2012) 046003)

3. We applied the Zariski quantization to the model and show that the Zariski quantization preserves supersymmetries of the model. (M. Sato, Physical Review D85 (2012) 126012)

4. We find general complete independent bases of a volume preserving diffeomorphism algebra. (M. Sato, The European Physical Journal C (2014) 74, 2878)

Future Prospects

In order to answer what the origin of the Universe is, we have started to perform numerical simulations of the model by using supercomputers.

Funding
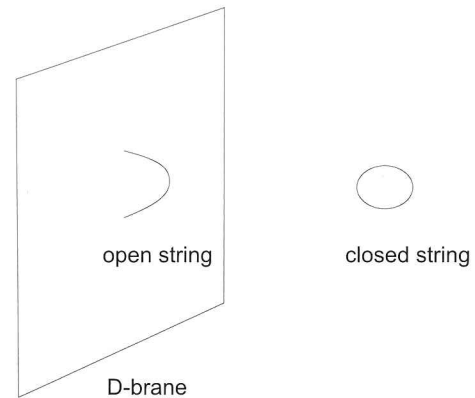
Fundamental objects in superstring theory.

$$S = \left\langle -\frac{1}{12}[X^I, X^J, X^K]^2 - \frac{1}{2}(A_{\mu ab}[T^a, T^b, X^I])^2 \right.$$
$$-\frac{1}{3}E^{\mu\nu\lambda}A_{\mu ab}A_{\nu cd}A_{\lambda ef}[T^a, T^c, T^d][T^b, T^e, T^f]$$
$$\left. -\frac{i}{2}\bar{\Psi}\Gamma^\mu A_{\mu ab}[T^a, T^b, \Psi] + \frac{i}{4}\bar{\psi}\Gamma_{IJ}[X^I, X^J, \psi] \right\rangle$$

The principle of the three-algebra model of M-theory.

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