〈活動報告〉

第 13 回 高度医療都市を創出する未来技術国際シンポジウム 複雑な課題を解決する イノベーションを生む鍵

妹尾昌治[*1]

The 13th International Symposium for Future Technology Creating Better Human Health and Society

The key to innovation that solves complex problems

Masaharu Seno[*1]

1. はじめに

令和４年２月３、４日に第 13 回 目となる「高度医療都市を創出する未来技術国際シンポジウム」をオンラインで開催させていただいたので報告する。今回のテーマは「複雑な課題を解決する イノベーションを生む鍵」とし、各発表者には専門を通じてテーマに沿った内容で話題を提供いただいた. 参加者は、演者、視聴者を含め 76 名、国別ではエジプト、インド、バングラデッシュ、マレーシア、インドネシア、中国、日本、カナダとかなりの時差を克服して、広範な地域からの参加を得ることができた.

ちなみに、開会のご挨拶はヘルスシステム統合科学学域長五福明夫教授、閉会の辞は同副学域長徳光浩教授にいただくと共に、全参加者に向けて歓迎のメッセージを研究担当理事那須保友副学長にいただいた。本シンポジウムのために作成したポスターを図１に示す。

2. プログラム

本シンポジウムでは二日間にわたって計15の講演が以下のプログラムにしたがって行われた。

2.1 ２月３日 (February 3)

9:55 – 10:00 am Opening Remarks Dr. Akio Gofuku, Ph.D., Dean, Okayama University

10:00 – 10:35 am

Chair, Dr. Kazuhiko Demura, Ph.D., Okayama University

1. History of Advanced Practice in a Hospital: a case report in our Graduate School. Dr. Yoshimi Hyodo, Ph.D. & Dr. Mizuki Morita, Ph.D., Okayama University

10:35 – 11:10 am

Chair, Dr. Masaharu Seno, Ph.D.

2. Augustinian Philosophical Anthropology of Heart and the Innovation of Health Systems. Dr. Kazuhiko Demura, Ph.D., Okayama University

11:10 -11:45 am

Chair, Dr. Kenji Sakai, Ph.D.

3. Driver drowsiness from perspective physiological approaches. Dr. Mahfuzah Binti Mustafa, Ph.D., Universiti Malaysia Pahang

11:45 am – 1:30 pm Break

1:30 pm

Welcome Remarks. Dr. Yasutomo Nasu, M.D., Ph.D., Vice President, Director of Research, Okayama University

1:40 – 2:15 pm

Chair, Dr. Hafizah Mahmud, Ph.D., Universiti Teknologi Malaysia

4. Bioprocess platform development for the production of fungal immunomodulators for pharmaceutical and nutraceutical industries. Dr. Hesham Ali El-Enshasy, Ph.D., Universiti Teknologi Malaysia

2:15 – 2:50 pm

Chair, Dr. Apriliana Cahya Khyrani, Ph.D., Universitas Indonesia.

5. Turning oil palm wastes into valuable chemicals. Dr. Misri Gozan, Dr.Eng., Universitas Indonesia.

2：50 – 3:05 pm Break

3:05 – 3:40 pm

Chair, Dr. Mona Mehruba, MBA, Ph.D., Okayama University

6. Digitalization of COVID-19 Vaccine Management in a Country of 170 Million People: The Way Forward. Dr. Shah Ali Akbar Ashrafi, M.D., Directorate General of Health Service, Bangladesh

3:40 - 4:15 pm

Chair, Dr. Sumauli Pyne, Ph.D., Sister Nivedita University,

7. Improving human lives with materials – A reality check. Dr. Argha Chakraborty, Ph.D., Sister Nivedita University, India

4:15 - 4:50 pm

Chair, Dr. Maram Zahra, Ph.D., Okayama University

8. A Journey in Design, Synthesis and Development of Novel

*1: 岡山大学学術研究院ヘルスシステム統合科学学域
*1: Faculty of Interdisciplinary Science and Engineering in Health Systems, Okayama University

Anticancer and Antimalarial Agents. Dr. Ibrahim El-Tantawy El-Sayed, Ph.D., Menoufia University, Egypt

2.2　２月４日（February 4）

11：00 – 11:35 am

Chair, Dr. Toshihiko Kiwa, Ph.D., Okayama University

9. Intense terahertz-matter interaction for advanced manufacturing of DNA nano materials. Dr. Tsuneyuki Ozaki, Ph.D., Énergie, Matériaux et Télécommunications, Institut national de recherche et de sécurité, Canada

11:35 – 12:10 am

Chair Dr. Kenji Sakai, Ph.D.

10. Characterization Techniques of Magnetic Nanoparticles: Instrumentation & Magnetic Properties Extraction. Dr. Mohd Mawardi Bin Saari, Ph.D., Universiti Malaysia Pahang

12:10 am – 1:15 pm　Break

1:15 – 1:50 pm

Chair, Dr. Jin Wang, Ph.D.

11. AC magnetic response of magnetic nanoparticles for biomedical application. Dr. Kenji Sakai, Ph.D., Okayama University

1:50 -2:25 pm

Chair Dr. Toshihiko Kiwa, Ph.D., Okayama University

12. Building Better Healthcare with Advanced Terahertz Chemical Microscope. Dr. Jin Wang, Ph.D., Okayama University

2:25 – 3:00 pm

Chair, Dr. Hiroshi Tokumitsu, Ph.D., Okayama University

13. Flexible way of thinking: practical, logical, theoretical, or traditional approach to cancer. Dr. Masaharu Seno, Ph.D., Okayama University

3:00 – 3:15 pm　Break

3:15 – 3:50 pm

Chair, Dr. Masaharu Seno, Ph.D.

14. A Systematic Approach to Find the Area of Contributions by Analyzing Different Influencing Factors using System Thinking. Dr. Soma Datta, Ph.D., Sister Nivedita University, India

3:50 – 4:25 pm

15. Digitization and low cost indigenous technologies to address health problems in India. Dr. Gargi Lahiri, Ph.D., Sister Nivedita University, India

4:25 – 4:30 pm

Closing Remarks　Dr. Hiroshi Tokumitsu, Ph.D., Associate Dean

3.　講演要旨

それぞれの講演要旨は以下のとおりであった。

3.1　History of Advanced　Practice in a Hospital: a case report in our Graduate School

The Graduate School was established in 2018 to set up a multidisciplinary research field, taking the advantage of the diverse educational environment of Okayama University. In the program, students are expected to see things from a wide range of perspectives, and create new knowledge through flexible ideas with originality [1].

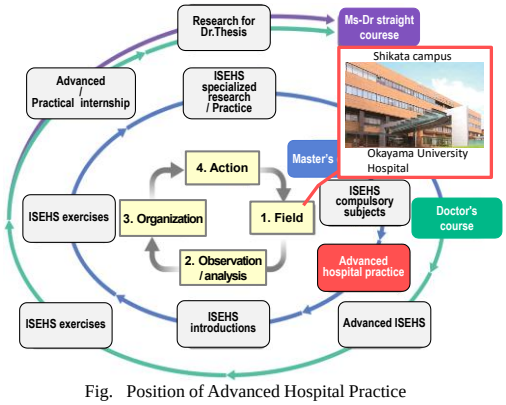


Fig.　Position of Advanced Hospital Practice

To achieve this goal, we are implementing unique education (Fig.) based on a new discipline called "integrated science". The "Advanced Hospital Practice" is one of the typical practices in our education.

The Advanced Hospital Practice is given in the medical field of each section in Okayama University Hospital. Students are divided into several groups to learn how the people and mechanisms work in the medical scene in each section. Students are to develop understanding it through discussion thoroughly within each group and/or the students as a whole, together with the faculty and staff in the medical field.

Focusing on group work, we discuss issues discovered from the various viewpoint of patients, families, medical devices, and healthcare professionals. After that, simulations are conducted to create products and ideas that can be used to solve problems in cooperation with others within or beyond the groups. Through this process, students are supposed to experience and learn practical approaches.

This year marks the fourth year of this practice. However, since the beginning of the 2020, in response to the spread of COVIT-19, the program has been switched to remote training. We describe four years of the progress, including how the practice has been switched from face-to-face to remote one.

3.2　Augustinian Philosophical Anthropology of Heart and the Innovation of Health Systems

As is defined in the Constitution of the WHO in 1948, “health is not merely the absence of disease or infirmity but the state of the complete physical, mental, social well-being”. And this WHO’s definition was once considered to be revised as “Health is a dynamic state of complete physical, mental, spiritual and social well-being and not merely the absence of disease or infirmity” in 1998. After some tough discussion among the delegates from the countries and areas which have various cultural religious and historical backgrounds, the World Health Assembly had not reached the conclusion, however, to understand the importance of the dimension of spiritualty has been shared since then among the people who are making effort to realize the integrated human well-being and complete health. The third goal of SDGs focusing on the physical, mental, and social dimension of the health and well-being, requires, of course, the innovation of the health systems, and the spiritual dimension of them should be paid attention, but the difficulty of dealing with the spiritual dimension of the health and well-being laid on the people’s cultural and/or religious preoccupations.

In this paper, I would like to introduce the philosophical anthropology of heart of Augustine of Hippo (354-430), who lived in the late antique North Africa and tried to make a bridge between self-understanding on human beings of Greco-Roman culture and the Scriptural tradition. His insight into the human conditions would have some contribution towards integrating the way of thinking on the health systems beyond the difference of the cultural, religious and historical backgrounds and establishing some integrated and interdisciplinary science and mutual understanding on health systems.

3.3 Driver drowsiness from perspective physiological approaches

Road accident is a crash relating to vehicle-vehicle, vehicle-pedestrian and vehicle-object. Lack of attention while driving likely one of factor cause of accident. Driver vigilance is the ability of the driver to sustain attention and to remain alert in perform the tasks in

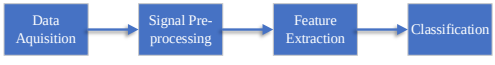


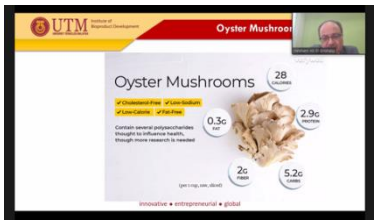
Figure 1

period of time. Drowsiness is the example of the causes that can decline driver vigilance. Drowsiness refers to excess sleepiness, can be accompanied by lethargy, weakness, and lack of mental agility. Feeling abnormally sleepy or tired during the day is also known as drowsiness. There are two main causes of driver drowsiness; lack of quality or quantity of sleep and driving at times of the day when you would normally be sleeping. In addition, sleepy driver may cause from driving on a limited speed, driving monotonous roads, driving in a long time and fatigue [2,3]. Some symptoms of driver drowsiness are troubling on focusing, inability to keep eyes open, constant yawing or rubbing eyes and drifting in the lane. Detection of driver drowsiness seems to be a major concern in road safety. One of the detections, called self-rating assessments through the questionnaires [4]. There is also another technique, vehicle-based measures such as

acceleration, lateral position, change in steering wheel rotation, lane-tracking, speed of vehicle and braking [5]. Another popular technique, is to use camera or known as video-based measure [6] which is non-invasive to detect driver drowsiness. Another promising technique, physiological measures extract feature from physiological signals such as galvanic skin response (GSR), electrocardiogram (ECG), electroencephalogram (EEG) and electromyogram (EMG). The general process flow for capturing data from physiological signal shown in Figure 1. The process starts with data acquisition from physiological sensor to subject. Then, the signal will be pre-processed to remove any artifacts. Processing of the signal which the features will be extracted. Finally, to get an output the further analysis such as classification will be implemented. This study used EMG signal from bicep brachii from 16 subjects while playing game Need for Speed (NFS) game for two hours. Prior experiment, the subject need to answer a questionnaire and the score were calculated. The pre-processed EMG signal were analyzed using time domain, frequency domain and time-frequency domain analysis. Finally, to evaluate the performance measure of the feature selection method and classify the driver’s condition, Artificial Neural Network (ANN) and Support Vector Machine (SVM) was used. Based on Figure 1, feature selection (FS) method was added after feature extraction in order to improve performance of ANN and SVM. As a result, ANN accuracy without FS 87.5%, with FS 93.8%. Whereas SVM accuracy without FS 68.8%, with FS 87.5%.

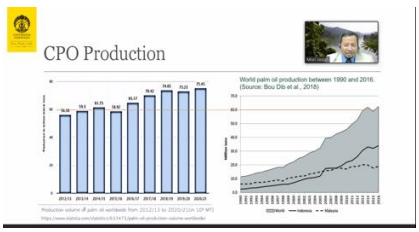
3.4 Bioprocess platform development for the production of fungal immunomodulators for pharmaceutical and nutraceutical industries

Immunomodulators are natural products of immune system in almost all living organisms to keep the body homeostasis conditions. In a big picture, nowadays, immunomodulator may be defined as a substance of biological or synthetic origin, which can stimulate, suppress or modulate any of the components of the immune system including both innate and adaptive arms of the immune response. In clinical point of view, immunomodulators are classified into three main categories: Immunosuppressors, Immunostimulators, and Immunoadjuvants. All these three are equality important for human life. Nowadays, the market value of immunomodulator products reached USD 161.57 billion in 2019 with almost equal market share between immunostimulators and immunosuppressors. Driven by the emerge of COVID-19, the market grew by 15.12% and reached 186.12 billion in 2020. It's also expected that the market will continue to grow at a CAGR of 6.3% in period 2020-2027, reaching USD 285 billion by 2027. In this presentation, a comprehensive information about the key immunomodulators products currently used in the world of fungal origin will be provided. Examples of two important immunomodulators of fungal origin will be presented. Cyclosporin A as immunosuppressor and mushroom immunostimulant polysaccharides will be presented in more details from strain cultivation in lab. scale up to large scale production platform for biopharmaceutical industries.



3.5 Turning oil palm wastes into valuable chemicals

Indonesia has more than 14 million hectares of palm oil land with more than 40 billion tons of palm oil (CPO). Solid palm waste produced is around one and a half times the volume of CPO production which can be in the form of the midrib, stem, empty fruit bunches (TKS), palm kernel shell (PKS) and mesocarp fiber (MF). All of the biomass contains lignocellulosic, which can be converted into higher-value products through Biorefinery. This concept integrates biomass conversion processes and equipment to produce biofuels, energy, and various valuable chemicals. This study presents the results of the author's research related to products from oil palm biomass which are expected to increase the sustainability and profitability of the palm oil industry.



Levulinic acid and furfural are chemical compounds produced by acid hydrolysis of EFB biomass and are high in added value. Levulinic acid can be applied, among others, as a polymer resin, pet food, perfume industry, textiles, additives, fuels, disinfectants, herbicides and plasticizers. Levulinic acid can be used as a platform chemical in producing alternative energy, namely biodiesel. The price of levulinic acid range from 5 – 10 USD per kg.

Furfural is a colourless liquid with an almond-like odour. Furfural production is generally carried out by initial hydrolysis of hemicellulose into pentoses (five-carbon sugars) which are then dehydrated to furfural. Furfural is used in the pharmaceutical, cosmetic, resin, and cleaning compound industries. Furfural is also widely used as an extraction agent, solvent, vulcanization agent, flavouring agent, the commercial component of pesticides, antiseptics, disinfectants, etc. The need for furfural increases continuously every year. The furfural prices range from 2,500 – 3,500 USD per ton.

Cellulose consisting of C6 (a hexose sugar) can be hydrolyzed to 5-hydroxymethylfurfural (HMF) and dehydrated to levulinic acid and formic acid. On the other hand, C5 (pentose sugar) of hemicellulose can be decomposed into xylose which can be dehydrated to furfural. Formic acid as a weak acid can be used for energy storage and chemical synthesis having unique properties such as non-toxicity, favourable energy density, and biodegradability. Many industries use FA such as textiles, pharmaceuticals and food chemicals. Due to its unique properties, formic acid has the potential for hydrogen storage that can be used as a fuel for fuel cell technology. The formic acid price is around 400 – 600 USD per ton.

Bioethanol is a fuel that is relatively compatible with gasoline-fueled car engines. Bioethanol used in fuel mixtures for vehicles must be anhydrous not to cause problems in phase separation, distribution, storage and use, so bioethanol must have a purity grade of 99.35% by volume. The price of ethanol ranges from 0.5 – 1.5 USD per kg.

Bioethanol is produced through a series of steps of enzymatic hydrolysis and fermentation of EFB. Bioethanol production alone is an uneconomical process, but this problem can be overcome by integrating the production of furfural and levulinic acid into the production of bioethanol in the Biorefinery concept [7-10].

3.6 Digitalization of COVID-19 Vaccine Management in a Country of 170 Million People: The Way Forward

Bangladesh is a country of South Asia. Total population of the country is 170.31 million. Population density per Sq kilometers is 1265. Average life expectancy at birth is 72.6 years [11]. Being a densely populated country, Bangladesh is always on a threat of spreading any contagious disease rapidly. Since inception of COVID-19 pandemic, Bangladesh was in high risk as it has contact with China for various purposes. In Bangladesh, the first COVID-19 case was detected on 8 March 2020. Till now, more than 17.31 million confirmed cases and more than 28,000 deaths have occurred. On March 22, 2020 Government of the People's Republic of

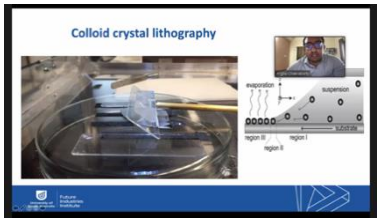
Bangladesh declared a 10-days shut down effective from 26 March to 4 April. This was later extended up to 30 May, 2020. Early detection and quarantine are one of the key steps combating Pandemic. To avoid public gathering during COVID-19 testing and report collection, we deployed a web-based approach. A one stop COVID-19 information website was launched: www.corona.gov.bd. Symptomatic individuals got registered through the website. After that, Health workers went to the house of individuals. Individuals can download the test report from online. As COVID-19 cases were increasing testing centers and labs had been increased. In May 2020, COVID-19 lab number increased to 48. One report has to complete 5 stages: Profile creation or registration, Clinical assessment, Specimen Collection, Lab Result and Notification, Vaccination Information. Directorate General of Health Services (DGHS) created a COVID-19 dashboard & Corona Corner for circulating info & Government orders.

National COVID-19 Surveillance System was created using District Health Information System-2 (dHiS-2) to provide test certificate within 24-72 hours of sample collection. Patients are receiving their COVID-19 test results via SMS. A separate online complaint receiving system was developed to address patient complaints. DGHS launched more than 25 apps and web portal to help people doing self-test, risk assessment and for getting necessary info. Bangladesh submitted the EOI to GAVI to be included in the AMC (Advance Market Commitment) country list of COVAX in July 2020. At national level 3 committees were formed: Vaccine Management Taskforce- led by Hon'ble Prime Minister, Vaccine Management Working Group- led by Additional Secretary (PH), HSD, MoHFW, Vaccine Preparedness and Deployment Core Committee- led by Additional Director General (Planning and Development) of Directorate General of Health Services (DGHS). To combat the pandemic, mass vaccination is the one of the solution. However, vaccinating everyone in a week or month was not practicable. Vaccines were in short supply across the world. We needed to decide who should receive immunizations first. We would have produced a chaotic situation if we had done it manually. We launched a web-based Android app called 'Surokkha' and a web portal called 'www.surokkha.gov.bd' for the COVID-19 immunization campaign. More than 87 million individuals have signed up for the Surokkha system, with approximately 95 million having received their first dosage of the COVID-19 vaccination. It was not easy to work with a completely digital vaccine management system. We needed to teach statisticians from 493 Upazila health complexes and 64 district offices and 12 City Corporations quickly. We needed to hire data assistants right away. Adult education is a challenging process. We used the online platform Zoom to train many of health care workers in surokkha. MIS gathered data from numerous categories according to the government's priorities (frontliners). After that, it was transferred to the ICT division to be whitelisted. Citizens can get themselves registered using an android phone. For registration we used three identities e.g., NID, Passport & Birth ID. After registration scheduling for vaccine is done from surokkha system and citizens get notified by SMS. Then, they go to the vaccine centre and our data assistants update the vaccine info in surokkha system. Soon after getting the vaccine citizens can download the certificate from surokkha app/website. The certificate is verifiable online.

3.7 Improving human lives with materials - A reality check

The advancement of material science has played a crucial role in improving the lifestyle of people with impaired hip, knee, limb, eye or any other body parts that have been replaced with a prosthetic biomaterial implant [12]. With the advancement of materials science, synthetically manufactured or naturally occurring materials can be tailored into fully functioning biomaterials that can be implanted within the human body [13]. To be precise, functionality of materials can be tailored on demand by introducing nano-topographies and nano-chemistries on substrate surfaces with which the substrate can modulate their ability to interact with organic cells and tissues to replicate the natural functionality of an impaired organ or body part [14,15].

However, after implanting biomaterials into the patients, growing cases of infections oozing out from the implanted biomaterials have concerned patients, doctors, scientists and the community worldwide [16]. These infections can spread throughout the body and can even result in death. In the US alone, there are 55,000 annual deaths occurring from biomaterial infections [17]. This also results in a huge financial burden on the healthcare systems of a country. Around $27 billion is spent annually to circumvent the expenditures due to biomaterial infections in the US [17]. Although in the literature, out of the plethora of scientific publications detailing strategies on how to overcome biomaterial associated infections, very few publications exist that have actually been translated as a clinical solution by healthcare systems [18].



Recent studies highlighting this "blockade" of anti-infective technologies which are being actively pursued but are not translated clinically, provides some recommendations to all the stakeholders including regulatory bodies, clinicians, health-care payers, doctors, patients, scientists and think-tanks for improving the regulatory practices involved in clinical translations of the available anti-infective technologies [19]. In order to create anti-infective

biomaterials, antimicrobial surface coatings should address a clinical need to combat polymicrobial biofilms. While much attention has been paid towards ways to combat bacterial cells, strategies for combatting fungal cells, which are an important contributor to biomaterial infections, have not been given due attention [20]. Given the rise in biomaterial associated infections and lack of translatable counter measures to circumvent biomaterial associated microbial infections, this talk addresses the question of identifying necessary counter measures to fight-off microbial infections on biomaterial surfaces.

3.8 A Journey in Design, Synthesis and Development of Novel Anticancer and Antimalarial Agents

Malaria and cancer are a major cause of morbidity and mortality worldwide, especially in developing countries where they have serious economic and social costs [21]. The disease is present in over 100 countries and threatens half of the world‘s population. The main reason for the recent dramatic increase in deaths from malaria and cancer are attributed to the spread of Plasmodium falciparum (Pf) strains and cancer cells ability to gain resistance to the mainstay antimalarial chloroquine and anticancer drugs [22,23]. To date, an effective therapeutic option for the treatment of resistant malaria is represented by the natural endoperoxide artemisinin and its semisynthetic derivatives, although there are concerns that artemisinin tolerant plasmodia are emerging.4 As a consequence of drug resistance, the present situation is alarming and new drugs are urgently needed. As part of a larger project for developing more potent and safer antimalarial and anticancer lead compounds based on natural product alkaloids, we have developed robust and efficient synthetic method for the natural alkaloid, neocryptolepine (Figure 1) isolated from the shrub Cryptolepis sanguinolenta used in Central and West Africa in traditional medicine for the treatment of malaria and cancer [24,25]. A lead optimization program was started to modify the compound and a wide range of neocryptolepine analogues with diversified frameworks and drug-like properties were synthesized. Potent and selective analogues against malaria and cancer, with IC50 in the low nanomolar range were obtained. The green synthetic routes of these molecules, their biological activities and proposed mechanism of action will be presented.

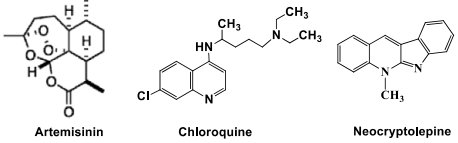


Figure 1. Structures of artemisinin, chloroquine and neocryptolepine

3.9 Intense terahertz-matter interaction for advanced manufacturing of DNA nano materials

Terahertz (THz) radiation science is expected to significantly impact a wide variety of disciplines that are bound to shape people’s lives in the 21st century. THz waves, whose frequency range is defined roughly to be from 0.1 to 10 THz (or wavelengths from 30 μm to 3000 μm), lies between optics and microwaves. T-ray imaging and diagnostics have tremendous potential for applications in non-destructive testing and imaging, medical diagnosis, health monitoring, and chemical and biological identification. Over the past two decades, there has been massive progress in THz technologies, mainly propelled by the rapid advancement in ultrafast laser technology and microelectronics fabrication. For example, recent advances in the generation of intense THz pulses are stimulating new studies in nonlinear THz optics. We have studied the interaction of intense THz pulses and microwave radiation with DNA nanostructures. These nanostructures are formed from three single-stranded DNA (ssDNA) strands that can assemble into several possible structures [26]. Thermal annealing results in two predominant double-stranded DNA (dsDNA) structures, that is, a “CUBE” and a “NINJA STAR”, along with a few other fully complementary thermodynamic constructs. These DNA structures were suspended in 180 μL of solution, which were first irradiated by high-intensity THz pulses with peak electric fields of ~70 kV cm-1 at focus and 2.5 kHz repetition rate from a tilted-pulse-front lithium niobate source. Interestingly, a 10 min exposure of the mixture to THz radiation resulted in □96% randomly assembled, small DNA structures (Fig. 1) [27]. These data not only provide the first direct experimental evidence for an effect of intense THz radiation on DNA nanostructures in solution but also confirm that this interaction provokes the opening of the double-helical structure of dsDNA.

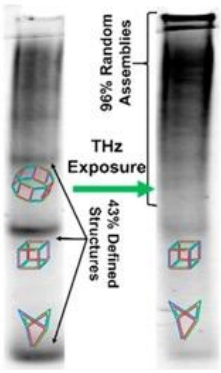
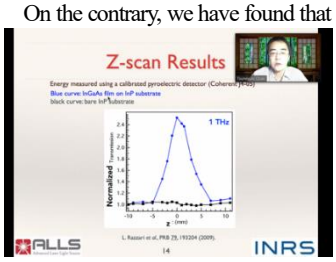


Fig. 1 Gel electrophoresis of thermally assembled DNA nanostructures before and after irradiation of intense THz pulses

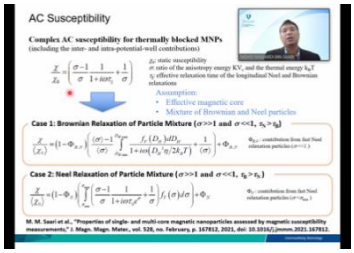
On the contrary, we have found that the irradiation of microwave radiation promotes the assembly of the same DNA nanostructures [27]. We used a DiscoveryTM single-mode microwave reactor from CEM (Matthews, NC, USA) with attached Coolmate® temperature control companion module



employing perfluoropolyether (PFPE HT-55, Kurt J Lesker Company, Toronto, Canada) as the circulating. Sample temperature, pressure, and microwave power were controlled/recorded using the Synergy software (vide infra). In the experiments, the sample's temperature was maintained at 20 °C while being irradiated with 85 to 105 W of microwave power. After such microwave irradiation, we have found that 82 ± 8% of the DNA structures consisted of assembled, thermodynamic structures, while the control sample not exposed to microwaves possessed 20.6 ± 0.6% of such species. Understanding the differences in the underlying mechanisms for THz and microwave irradiation would significantly merit from access to advanced, real-time biomedical and molecular imaging techniques.

3.10 Characterization Techniques of Magnetic Nanoparticles: Instrumentation & Magnetic Properties Extraction

Characterization of structural and magnetic properties of MNP assembles is crucial in tailoring MNP responses for each biomedical application, such as high responses of magnetic moment in the high-frequency region is desired for the Magnetic Particle Imaging technique. To characterize MNPs, DC and AC susceptibilities have been used to derive MNPs' properties, such as geometrical characteristics. For this reason, we have reported the development of a DC magnetometer utilizing a high critical temperature



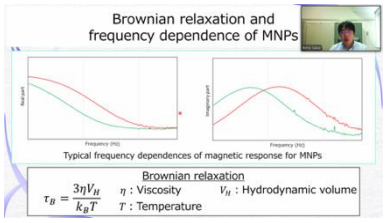
superconducting quantum interference device (high-Tc SQUID) and a flux transformer composed of an induction coil [28]. The high-Tc SQUID is used in order to realize high sensitivity, compact, and low-running cost magnetometer. A flux transformer with a first-order planar gradiometer was used as the detection coil to achieve a high sensitivity and cancellation factor. For the AC susceptibility characterization, we have reported an improved simple, wideband, and sensitive AC magnetometer using an induction coil [29]. The sensitivity and usable frequency range of six pickup coil geometries were compared. A low noise instrument amplifier circuit (AD8429, Analog Devices, USA) was designed and fabricated on a printed circuit board to amplify the weak signal from the pickup coil. A generalized Goertzel algorithm was used to achieve fast signal amplitude and phase extractions. The developed AC magnetometer showed a sensitivity of 10-8 Am2/√Hz at 6 Hz and a frequency range of 158 kHz.

Using the developed DC and AC magnetometers, we measured the magnetization curves and frequency responses of commercial magnetic nanoparticles [30]. The size distribution of magnetic cores in single- and multi-core nanoparticles in water suspension was derived from their magnetization curves and compared with the geometrical size from transmission electron microscopy (TEM), which ranges from 8.3 to 40.2 nm. A reasonably good agreement was obtained between the magnetic core size derived from the magnetization curve and the geometrical size from the TEM image. The reduction of effective magnetic core size was observed in the magnetic moment distribution, and this could be inferred due to the magnetization degradation in cores. The hydrodynamic size and average anisotropy energy ratio were estimated from the AC susceptibility response of MNPs from 5 Hz to 100 kHz, where a non-negative least square method was used to construct the complex distribution of relaxation time. An AC susceptibility model that incorporates the inter- and intra-potential-well contributions was proposed and used in the construction. It is demonstrated that the proposed AC susceptibility model was able to fairly estimate the average anisotropy energy ratio for MNP ensembles dominated by thermally blocked particles. Moreover, it can be suggested that besides the geometrical core size, the degree of core aggregation also plays an essential role in determining the anisotropy energy ratio and effective magnetic moment.

3.11 AC magnetic response of magnetic nanoparticles for biomedical application

Magnetic nanoparticles (MNPs) have received great attention for their promising applications in biomedical field. As the AC susceptometry of MNPs is employed in the biomedical applications, such as magnetic hyperthermia, magnetic particle imaging (MPI), and magnetic immunoassay (MIA), the AC magnetic response of MNPs is one of important factor for biomedical applications. In our group, magnetic measurement systems for the evaluation of MNPs have been developed [31, 32] and the AC magnetic response for MIA has been investigated. Using the developed systems, we clarified the effect of some factors on AC magnetic response which is caused by the phenomenon during immunoassay process except for immunoassay reaction [33, 34]. In this presentation, our developed measurement system for evaluating the AC magnetic response of MNPs is introduced and the effect of viscosity, aggregation of MNPs and dispersion method for MNPs on AC magnetic response is discussed.

The developed system consists of two induction and detection coil units. The induction coils are connected in series while the detection coils are reversely connected in series. Therefore, the same magnetic field is applied to two samples (one is a measurement sample and the



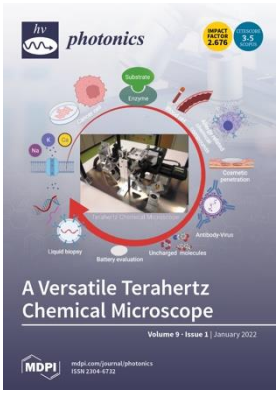
other is reference sample) and a differential magnetic signal from two samples can be detected. This

enables to eliminate the magnetic signal of solution and obtain only the signal from MNPs. These coil units are connected to gain phase analyzer and the frequency dependence of real and imaginary part for measured magnetic signal was obtained.

In this study, a commercially available MNPs dispersed in solution was used. To avoid the aggregation of MNPs, MNPs were generally dispersed by vibration, such as ultrasonic dispersion. However, some MNPs showed a different AC magnetic response after ultrasonic dispersion. This result indicates some polymeric coating was damaged and the hydrodynamic diameter of MNPs which determines the AC response of MNPs changed. Next, the viscosity of solution was changed and when the viscosity of solution increased, the AC magnetic response changed owing to the increase in Brownian relaxation time which is related to the viscosity. However, when the serum was added to solution of MNPs, the AC magnetic response was changed drastically. Although the viscosity of solution increased when the serum was added in the solution, it was found that the AC magnetic response is mainly affected by the aggregation of MNPs. From these results, the AC magnetic response was found to change owing to some factors other than immunoassay reaction and these effects on AC magnetic response should be considered in MIA.

3.12 Building Better Healthcare with Advanced Terahertz Chemical Microscope

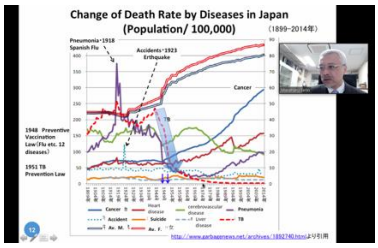
Terahertz waves have gained increasingly more attention because of their unique characteristics and great potential in a variety



of fields. In this study, we introduced the recent progress of our versatile terahertz chemical microscope (TCM) in the detection of small biomolecules, ions, cancer cells, and antibody–antigen immunoassaying. We highlight the advantages of our TCM for chemical sensing and biosensing, such as label-free, high-sensitivity, rapid response, non-pretreatment, and minute amount sample consumption, compared with conventional methods. The new application in detection of histamine that released from allergic response for fast screening of allergen was also explored. Very low concentration of histamine (nM level) could be measured. These features demonstrate that TCM has a great potential in future chemical sensing and biosensing. More impressive progress is that TCM is now being developed and applied to detect SARS-CoV-2, liquid biopsy, and neurotransmitters, as well as other biological substances, which aims to provide an effective and accurate method to fight against diseases and environmental threats around us [35-37].

3.13 Flexible way of thinking: practical, logical, theoretical, or traditional approach to cancer

Cancer is one of the most serious diseases in the world. In Japan,



the death rate of cancer is the top during the 4 decades, and almost the same in the developed countries. The death number has still been increasing in Japan despite the huge progress of science and technology since the last quarter of 20th century. Especially, the advancement in molecular biology, biotechnology, and medicine has appeared magnificent completing the genome projects on life including humans, developing the therapeutic procedures for such as regeneration and immune system. This contradiction may be due the traditional theory long lasting for 100 years. Since this theory is essentially based on the genomic mutations, cancer is currently believed as the genetic disease [38]. It is true because familial mutations and oncogenic infection of retroviruses are well known to induce cancer. However, it is also true that 80% of the cause of cancer is still sporadic. In this context, it seems necessary to revisit the mechanism of cancer initiation.

Looking back into 100 years ago almost at the same time of the mutation theory was proposed, we notice that a Japanese professor at Tokyo university artificially developed the cancer on rabbit ears [39]. His work was so respected that nominated as a Nobel prize laureate. But unfortunately, not so many descendent apparently followed his work. Probably due to the lack of suitable methods and resources at that time unlike the research activity in the molecular biology coupled with genetic engineering and biotechnology.

However, it was clear that he demonstrated the induction of cancer by the chronic inflammation. On the other hand, in 1990's cancer stem cell (CSC), of which existence were proposed in the late of 19th century, were first identified in leukemia [40]. Then CSCs gradually became focused by some scientists. However, the population of CSCs in cancer tissues are so small (less than 1%) and the resource of study is so limited by the number of patients that the growth of the field of study has been slow.

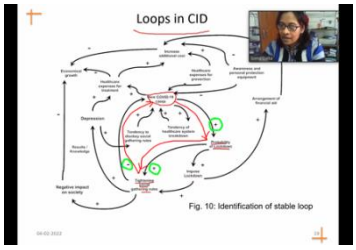
In this situation, we fortunately encountered the finding of cell reprogramming technology, that is the establishment of induced pluripotent stem cells (iPSCs) [41]. I thought it might be possible to induce cancer because the cells were pluripotent. And we found it

was possible almost 10 years ago [42]. We are currently working on the CSCs developed from iPSCs without

introduction of mutations or foreign genes. These procedures and the developed CSCs inspired us in many ways to think about cancers and found how important to be flexible to work with the unknown or unsolved problems. I will summarize our unique studies on CSCs during the last decade.

3.14 A Systematic Approach to Find the Area of Contributions by Analyzing Different Influencing Factors using System Thinking

Most of the time, success in a work is stuck due to improper planning; it is also true for research works. Arbitrary selection in the area of contribution may lead to failure in the near future. It seems like the blockage of paths in a complex maze. Systematic analysis of different influencing factors is essential at the time of determining the area of contribution which may lead to success. When the volume of influencing factors is huge then it is quite difficult to manage. In these circumstances, systematic tools are helpful to manage different influencing factors. These tools assist for proper planning and determine the area of contribution. System thinking is one such tool that helps us to proceed in a systematic way. It could be used in any area of research and has been applied to the study of medical, environmental, political, economic, human resources, educational systems, and among many other research domains.



System Tools help us to innovate new thinking in our research domain. It also helps us to generate and organize information about our system – our situation of interest. System Thinking contains a total of thirty six different tools to handle different situations. However, here I would discuss some of the major tools. These are, 18 words, Affinity Diagram, Context Diagram, Input output Diagram, Systems Maps, Cybernetic Influence Diagram along with the case studies [43-49].

3.15 Digitization and low cost indigenous technologies to address health problems in India

India is a country with the second largest population in the world spread across rural and urban areas. About 75% of the country's health infrastructure and health manpower is concentrated in the urban areas where only 27% of the population resides. One of the major challenges for the Government is to ensure affordable access of the vast population to essential health care. Use of appropriate technology in healthcare can be an answer to solve challenges of accessibility, affordability and quality. In recent times, technology has percolated in the healthcare arena in a huge way in almost all countries of the globe and India is no exception. The Covid 19 pandemic has fueled the application of technology to a great extent and transformed healthcare in India. Technology in the form of Artificial Intelligence (AI), Internet of Medical Things (IoMT) etc. is in wide use in the country to solve health problems and create healthy individuals and community. More than WHAT of healthcare delivery, it is HOW the healthcare must be delivered to all, which is of concern in the country. This presentation will feature the commitment of the country to achieve the goals of National Health Policy, 2017 and the Sustainable Development Goals (SDGs) by establishing an integrated nationwide digital health system – the Ayushman Bharat Digital Mission (ABDM) and how the ABDM will expand the reach of digital health to reach persons in the remotest part of the country. India, often referred to as the global capital of TB is under a huge burden of the disease. The presentation would cover India's attempt to eradicate TB from the country through the development of NIKSHAY, an innovative IT application which has in store the database of all TB patients and also patients with Multi Drug Resistant TB across the country and this enables the grass root level health workers to track and monitor every TB patient. An exemplary approach to TB treatment in India is the Information Communication Technology (ICT) based approach called 99 DOTS. The presentation will cover the working principle of 99 DOTS in the treatment of TB. Equally important with the treatment is the early detection of the deadly disease since the disease claims a number of lives each year. The presentation will give an overview of the technology enabled cost-effective TB test the country has recently come up with and which has already received the WHO approval. TrueNat assay kit is a low cost indigenous portable kit capable of being used in the peripheral centers, running on a solar powered battery and able to detect TB and drug resistance TB in about 90 minutes, a much shorter time than the conventional tests. Another significant innovation in the diagnosis of TB is the paper based device by scientists of IISc, Bengaluru, which enables the detection of TB at the point of care. These technologies address the challenges of affordability, accessibility, ease of use in a developing country like that of ours. Another area in which the country has introduced digitization is the area of Maternal and Child Health. The presentation will cover The Mother and Child Tracking System (MCTS), which uses information technology to ensure that full spectrum of healthcare services and immunization is available to pregnant women and children up to 5 years of age. Such a tracking system will surely go a long way in order to reduce infant and maternal mortality rates in India. In addition, the presentation will highlight some innovative technological low cost approaches in remote and mobile

healthcare which will be helpful to reach the marginalized section of the population [50-52].

4. 演者の紹介

今回ご講演いただいた先生方を講演の順にしたがって簡単に紹介する.

4.1 兵藤好美 教授、森田瑞稀 教授

岡山大学学術研究院ヘルスシステム統合科学学域所属. 兵藤教授は研究科長補佐, 森田教授は大学病院のバイオバンクも担当されている. 兵藤教授の専門は看護学. 森田教授の専門はバイオインフォマティクス. 今回は大学院ヘルスシステム統合科学研究科における病院実習の研究科設置からこれまでの成果について紹介いただいた.

4.2 出村和彦 教授

岡山大学学術研究院ヘルスシステム統合科学学域所属. 研究科長補佐を担当されている. 専門は哲学. 今回は心や哲学的観点からイノベーションの講演をいただいた.

4.3 Dr. Mahfuzah Mustafa, Ph.D.

Assistant Professor, Faculty of Electrical and Electronics Engineering Technology, Universiti Malaysia Pahang（協定校）. 居眠り運転の生理システム的解析について講演をいただいた.

4.4 Dr. Hesham Ali El Enshasy, Ph.D.

Director of Institute of Bioproduct Development (IBD), and professor in bioprocess engineering, school of Chemical and Energy Engineering, Faculty of Engineering, Universiti Teknologi Malaysia (UTM), Skudai, Johor, Malaysia. 菌類の産生する免疫賦活物質の製薬および機能性食品の面からみた生物生産における現状と課題について講演いただいた.

4.5 Dr. Misri Gozan, Dr. of Ingineuer

Professor at Bioprocess Engineering Program, Chemical Engineering Department, Faculty of Engineering, Universitas Indonesia, Indonesia. He was the AFOB Vice President of the Indonesia region (2014-2020). ヤシ油の固形廃棄物からの有用な化学物質生産への利用について講演いただいた.

4.6 Dr. Shah Ali Akbar Ashrafi, M.D.

Chief, Health Information Unit, Management Information System, Directorate General of Health Services, Health Services Division, Ministry of Health and Family Welfare, Government of the People's Republic of Bangladesh. バングラデッシュにおける COVID-19 の現状と課題について講演いただいた.

4.7 Dr. Argha Chakraborty, PhD

Assistant Professor at School of Health Sciences & Translational Technology, Sister Nivedita University （協定校）. 感染抵抗性を示す生物機能材料の応用と課題について講演いただいた.

4.8 Dr. Ibrahim El-Tantawy El Sayed, Ph.D.

Professor of Organo-Medicinal Chemistry & Head of Chemistry Department, Faculty of Science, Menoufia University（協定校）, Shebin El Koom, Egypt. 植物由来の化学物質ネオクリプトルピンを基本骨格とするの抗マラリア薬および抗がん剤の研究における現状と課題について講演いただいた.

4.9 Dr. Tsuneyuki Ozaki, Ph.D.

Professor at the Institut national de la recherche scientifique (INRS) （協定校）near Montreal, Canada, serving from 2006 to 2012 as the Director of the Advanced Laser Light Source (ALLS), an international laser user facility. テラヘルツを利用した DNA 関連ナノマテリアルの作成について講演いただいた.

4.10 Dr. Mohd Mawardi Bin Saari, Ph.D.

Lecturer at the Faculty of Electrical and Electronics Engineering Technology, Universiti Malaysia Pahang（協定校）, Malaysia. 磁気ナノ粒子の性質を測定する技術の開発と課題について講演いただいた.

4.11 堺 健司 准教授

岡山大学学術研究院ヘルスシステム統合科学学域所属. 専門は磁気工学. 交流磁場における磁気ナノ粒子の挙動を生物医学的に応用する技術の現状と課題について講演いただいた.

4.12 王 璡 助教

岡山大学学術研究院ヘルスシステム統合科学学域所属. 専門は磁気工学. テラヘルツを用いた化学顕微鏡の開発における現状と課題について講演いただいた.

4.13　妹尾昌治 教授

岡山大学学術研究院ヘルスシステム統合科学学域所属. 研究科長補佐を担当（本稿執筆者）. 専門は生物工学. 人工多能性幹細胞をがん研究へ応用する現状と課題について講演を行なった.

4.14　Dr. Soma Datta, Ph.D.

Assistant Professor of the Department of Computer Science and Engineering,, Sister Nivedita University（協定校）. COVID-19 パンデミックを例に、思考に影響する要素についてシステム的考察を行う方法を講演いただいた.

4.15　Dr. Gargi Lahiri, Ph.D.

Assistant Professor at the Department of Management, Sister Nivedita University（協定校）. インドにおける健康問題に対応するためのデジタル化と低価格な従来技術における現状と課題について講演いただいた.

図１　シンポジウム広報ポスター・チラシ

5.　おわりに

テーマの文脈に「やはり統合科学がその鍵」となることを意図して含ませた．今回も多方面からの話題を提供いただきその現状と課題について、短時間であったが議論し、統合科学的アプローチの重要性と課題解決に対する姿勢を考えることができる機会になったとすれば幸いである．以下に、那須先生からの歓迎メッセージと今回ご講演いただいた先生方に送らせていただいた参加証の範例を掲ておく．

5.1 那須副学長からの歓迎メッセージ

Dear ladies and gentlemen, it is our great pleasure to have “the 13th International Symposium for Future Technology Creating Better Human Health and Society” in our Okayama University organized by the Graduate School of Interdisciplinary Science and Engineering in Health Systems. In this symposium we are focusing “The key to innovation that solves complex problems”. During the two days, we have speeches crossing over basic through applied research from various fields and on a practice of interdisciplinary education in a hospital.

In this symposium we invited many professors, scientists, and directors, who are currently and actively working in their fields related to health systems, from abroad and the graduate school. We appreciate all the participants for their valuable contributions to this symposium. We hope this symposium would provide a great platform to demonstrate your recent successful achievements and to have some new insights and creative discussion.

Nowadays the complicated problems are incrementing day by day all over the world. It is still eagerly requested to develop or to discover effective procedures and solutions to help the people avert from the trauma that they endure in their lives. However, as everyone knows for example, drug discovery is neither simple nor an easy work even for a pharmaceutical company leading the world. As in the past previous symposia, many experts from different fields of science, technology, medicine, pharmacology, and philosophy are taking part in this meeting today. We would like to make this opportunity in both corroborating and collaborating various aspects of research work with one another. You may feel discussion contemporary and thought-provoking.

I hope this symposium may enlighten us more than ever to adopt some ingenious approach in our research and education. The strategies to find the keys to innovation that solves complex problems are getting so important that our contribution to help people, who are enduring the health problems, should be highly expected to solve the complex problems. We believe we can integrate our power to make a big driving force to innovate much more effective solutions.

5.2 参加証

今回ご講演いただいた方々には以下のような参加証を発行させていただいた.

Certificate of Appreciation

This certificate is awarded to

Dr. Ibrahim El-Tantawy El-Sayed

For your contribution as an invited speaker at the

13th International Symposium for Future Technology Creating Better Human Health and Society

The key to innovation that solves complex problems

3rd to 4th February 2022

Online

Organized by

Graduate School of Interdisciplinary Science and Engineering in Health Systems
Okayama University
Japan

Akio Gofuku, Ph.D.
Dean

Masaharu Seno, Ph.D.
General Chair

6. 謝 辞

今回のシンポジウムは，五福明夫学域長のご配慮により、ヘルスシステム統合科学研究科の機能強化経費を利用して開催させていただいた．また、各講演の座長をお引き受けいただいた先生方、シンポジウムの運営を支えてくれたスタッフに対して、お名前を挙げて謝意を表したい.

6.1 座長の先生方（担当講演順）

出村和彦 教授, 妹尾昌治 教授, 堺 健司 准教授（岡山大学）, Assistant Prof. Hafizah Mahmud (Universiti Teknologi Malaysia), Assistant Prof. Apriliana Cahya Khyrani (Universitas Indonesia), Mona Mehruba 助教（岡山大学）, Dr. Sumauli Pyne (Sister Nivedita University), Maram Zahra 助教, 紀和利彦 教授, 王 璡 助教, 德光 浩 教授（岡山大学）.

6.2 開催スタッフ

妹尾彬正 助教, Maram Zahra 助教, 公文一輝　技術職員, 三村真梨　事務補佐員.

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