<u>Field:</u> Chemistry/Materials Science

Session Topic:

Nature's Chemistry: Exploring Synthetic Biology and Biogenic Materials

Introductory Speaker: YUZAWA Satoshi, Keio University

Title: Harnessing Synthetic Biology for sustainable production of chemicals and beyond

Synthetic Biology represents a dynamic interdisciplinary field at the intersection of Chemistry, Biology, and Engineering. This innovative research area seeks to fabricate artificial biological systems, characterized by two primary approaches: the topdown approach, involving the manipulation of existing natural systems, and the bottom-up approach, centered around the assembly of chemical and biological components (Fig. 1). In this lecture, I will provide a concise overview of the historical development of Synthetic including Biology, the first genome sequence of bacteria in



1995 [1], the first genome synthesis of bacteria in 2008 [2] and the first creation of artificial bacteria in 2010 [3]. Shifting focus, I will talk about instances of the top-down approach, highlighting the burgeoning interest in genome-engineered microbes for sustainable chemical production [4]. This includes the production of therapeutics, fuels, flavors, colorants, health supplements, and cosmetic ingredients from renewable nonfood biomass or carbon dioxide. The escalating demand for bio-based products is underscored by a total investment in Synthetic Biology startups surpassing \$50 billion (~\$20 billion in 2021). I will close my talk by introducing the bottom-up approach. Our session features two distinguished speakers: Satoshi Abe from the Tokyo Institute of Technology, Japan, discussing research related to the bottom-up approach, and a speaker from TBD, France, addressing topics aligned with TBD (either the top-down or bottom-up) approach. I invite you to engage in our session and explore the multifaceted future of Synthetic Biology. Your participation and insights are welcomed.

References:

[1] Fleischmann et al. Whole-Genome Random Sequencing and Assembly of

Haemophilus influenzae Rd. Science 1995, 269, 496-512.

[2] Gibson et al. Complete Chemical Synthesis, Assembly, and Cloning of a Mycoplasma genitalium Genome. Science 2008, 319, 1215-1220.

[3] Gibson et al. Creation of a bacterial cell controlled by a chemically synthesized genome. Science 2010, 329, 52-56.

[4] Li et al. Mining natural products for advanced biofuels and sustainable bioproducts. Curr Opin Biotechnol 2023, 84, 103003.

Background Review Article:

[1] Jones et al. Synthetic microbiology in sustainability applications. Nat Rev Microbiol 2024, doi: 10.1038/s41579-023-01007-9.

<u>Field:</u> Chemistry/Materials Science

Session Topic:

Nature's Chemistry: Exploring Synthetic Biology and Biogenic Materials

Speaker: Nicolas MARTIN, Centre de Recherche Paul Pascal

Title: Minimal models of synthetic cells

Living cells are extremely sophisticated compartmentalized chemical systems. They perform intricate tasks by dynamically coordinating matter and energy fluxes across space and time. Reproducing such complex behaviours in model systems could pave the way to the development of smart autonomous micro-machines. Driven by the promise of these advancements, recent years have witnessed a growing interest in constructing "synthetic cells", namely, artificial microcompartments that mimic the cellular organization. A major challenge in this vibrant field is imbuing synthetic cells with dynamic capabilities, including the ability to sense, respond and adapt to their environment, self-sustain and communicate with each other. In this presentation, I will show that micrometresized droplets formed by liquid-liquid phase separation of polymers in water, known as "coacervates", hold promise as platforms for creating minimal models of synthetic cells (Figure 1). Specifically, I will discuss how these droplets can be used as microreactors to promote simple reactions.^[1] I will highlight how the design of stimuli-responsive droplets enables precise spatiotemporal control over biomolecule localization. I will further showcase how microfluidics offers a robust approach to build structurally defined compartments and unravel physical mechanisms underlying droplet growth and dissolution. Last, recent directions toward constructing more advanced synthetic cells that integrate multiple functions in a drop will be discussed.^[2] Ultimately, these droplets provide new avenues for understanding cellular compartmentalization while shedding light on the transition from non-living to living matter.

References:

[1] T.P. Fraccia, N. Martin, Non-enzymatic oligonucleotide ligation in coacervate protocells sustains compartment-content coupling. *Nat. Commun.* **2023**, *14*, 2606
[2] C. Xu, N. Martin, M. Li, S. Mann, E Living material assembly of bacteriogenic protocells, *Nature*, **2022**, *609*, 1029-1037

Glossary:

- -*Synthetic cells*: micrometre-sized compartments that reproduce structural and/or functional features of living cells using a small set of biological or synthetic parts. -*Liquid-liquid phase separation*: spontaneous demixing phenomenon between two
- immiscible liquid phases.
- -*Coacervates*: micrometre-sized droplets formed in water by liquid-liquid phase separation between two immiscible aqueous solutions (that typically contain water-soluble polymers, surfactants or salts)

Background Review Article:

N. Martin, Dynamic synthetic cells based on liquid-liquid phase separation, *ChemBioChem*, **2019**, *20*, 2553-2568



Figure 1. Design of coacervate droplets for synthetic cells assembly.

<u>Field:</u> Chemistry/Materials Science

Session Topic:

Nature's Chemistry: Exploring Synthetic Biology and Biogenic Materials

Satoshi Abe, Tokyo Institute of Technology

Title: In-cell Protein Assemblies as Biomaterials

Proteins are the most critical functional molecules for biological activities with various structures and play essential roles in metabolism, such as signal transduction and catalysis. They form precise molecular assemblies that synthetic chemistry cannot form, making them exciting biomaterials both functionality and structurally. Among them, I focused on the phenomenon of protein crystallization in vivo (Figure 1).^[1] Protein crystals are often used to purify proteins and to elucidate their threedimensional structures. However, since the first protein crystals were reported in

human tissues in the 1850s, various proteins have been found to crystallize in natural environments and nonnatural cultured cells. In nature, protein crystals function as solid materials for immune activation, virus storage, and solid catalysts. Recently, functional development using these incell protein crystals has been underway, and rapid





Figure 2. Crystal engineering of in-cell protein crystals.

crystallization methods are expected to be applied to structure biology and biomaterials science. In this presentation, I will report on our recent research on applying in-cell protein crystals to biomaterials (Figure 2).^[2] Protein crystals encapsulating the target protein can be synthesized when in-cell crystals are

synthesized with an expression of the target protein. Solid catalysts with multiple immobilized enzymes in the single crystals and solid materials with immobilized protein caged assembly have been constructed. These studies are a method for synthesizing materials using the reaction system of living organisms and can be utilized to synthesize biofunctional materials encapsulating various functional molecules.

References:

[1] M. Kojima *et al. Biomater. Sci.* 2021, 10, 354-367., R. Schonherr *et al. <u>Biol.</u>* <u>Chem.</u> 2018, 399, 751-772 (2018)., C. N. Mudogo *et al. Traffic.* 2020, 21, 220-230.

[2] S. Abe *et al. Adv. Mater.* 2015, 27, 7951-7956., T. K. Ngyuen *et al. ACS Appl. Nano Mater.* 2021, 4, 1672-1681., T. T. Pham *et al. Nano Lett.* 2023, 23, 10118-10125.

Glossary:

Background Review Article:

M. Kojima, Satoshi Abe and Takafumi Ueno. Engineering of protein crystals for use as solid biomaterials. *Biomater. Sci.* 2021, 10, 354-367. DOI: 10.1039/D1BM01752G

<u>Field:</u> Social Sciences/Humanities

Session Topic:

New Standards of Visualizations in Social Sciences

Introductory Speaker:

Vivien PHILIZOT, Universté de Strasbourg

Title: Visualization in the Humanities and Social Sciences: Epistemic Perspectives

As the American historian of science Matthew Norton Wise puts it, « much of the history of science could be written in terms of making new things visible – or familiar things visible in a new way. » (Wise 2006, 75). If much of science is about making the invisible visible, it is because there is a close connection between knowledge and the forms in which it is expressed. Such connections have been the subject of much research over the past forty years in the fields of laboratory studies and anthropological approaches to laboratory work (Latour and Woolgar 1979; Woolgar 1982; Lynch 1982), science studies (Lynch 1985, Hacking 1985), media studies (Bredekamp, Dünkel, and Schneider 2015) and visualization and information studies (Tilling 1975; Tufte 1983, Friendly et al. 2006). These contributions attest to a growing interest in visualization in science and in the materiality of the visual representations that mediate knowledge. This lecture will introduce the epistemological issues raised by visualization as they arise at the intersection of knowledge and materiality. It will also highlight the contribution of the humanities to practices of visualization, using an approach drawn from visual culture studies, science studies, and information studies.

References:

- Bredekamp, Horst, Vera Dünkel, and Birgit Schneider, eds. 2015. *The Technical Image: A History of Styles in Scientific Imagery*. Chicago: The University of Chicago Press. Daston, Lorraine, and Peter Galison. 2007. *Objectivity*. Mass: Zone Books.
- Drucker, Johanna. 2014. Graphesis Visual Forms of Knowledge Production. Harvard University Press.
- Drucker, Johanna. 2020. *Visualisation: l'interprétation modélisante*. Translated by Marie-Mathilde Bortolotti-Burdeau. Collection Esthétique des données 03. Paris: Éditions B42.
- Friendly, Michael, C Chen, W Härdle, and A Unwin. 2006. "A Brief History of Data Visualization." In *Handbook of Computational Statistics: Data Visualization*, 1–34. Springer-Verlag. <u>https://www.datavis.ca/papers/vita/Friendly06hbook.html</u>.
- Friendly, Michael, and Howard Wainer. 2021. A History of Data Visualization and Graphic Communication. Illustrated edition. Cambridge, Massachusetts: Harvard

University Press.

- Funkhouser, H. Gray. 1937. "Historical Development of the Graphical Representation of Statistical Data." *Osiris* 3:269–404.
- Galison, Peter. 1997. Image and Logic: A Material Culture of Microphysics. Chicago: University of Chicago Press.
- Hacking, Ian. 1985. "Do We See Through a Microscope?" In *Images of Science: Essays* on *Realism and Empiricism*, edited by P. M. Churchland and C.A. Hooker, 132–52. Chicago: University of Chicago Press.
- Hall, Peter. (2011) 2018. "Bulles, Lignes et Fils. Comment La Visualisation de l'information Façonne-t-Elle La Société ?" *Back Office*, no. 2, 58–73.
- Kittler, Friedrich. (1990) 2017. "Real Time Analysis, Time Axis Manipulation." Translated by Geoffrey Winthrop-Young. *Cultural Politics* 13 (1): 1–18. <u>https://doi.org/10.1215/17432197-3755144</u>.
- Larkin, Jill H., and Herbert A. Simon. 1987. "Why a Diagram Is (Sometimes) Worth Ten Thousand Words." *Cognitive Science* 11 (1): 65–100. https://doi.org/10.1111/j.1551-6708.1987.tb00863.x.
- Latour, Bruno. 1985. "Les 'Vues' de l'esprit. Une Introduction à l'anthropologie Des Sciences et Des Techniques." *Culture et Technique*, no. 14, 5–29.
- Latour, Bruno. (1987) 1989. La Science En Action. Introduction à La Sociologie Des Sciences. Paris: La Découverte.
- Latour, Bruno. 1991. *Nous n'avons Jamais Été Modernes. Essai d'anthropologie Symétrique*. Paris: La Découverte.
- Latour, Bruno. 1993. "Le Topofil de Boa Vista Ou La Référence Scientifique Montage Photo-Philosophique." *Raison Pratique*, no. 4, 187–216.
- Latour, Bruno. (1999) 2007. "Sol amazonien et circulation de la référence." In *L'espoir de Pandore: pour une version réaliste de l'activité scientifique*, 33–82. Paris: Éditions La Découverte.
- Latour, Bruno. 2014. "The More Manipulations, the Better." In *Representation in Scientific Practice Revisited*, edited by Catelijne Coopmans, Janet Vertesi, Michael E. Lynch, and Steve Woolgar, 347–50. MIT Press.
- Latour, Bruno, and Steve Woolgar. (1979) 1988. *La Vie de Laboratoire. La Production Des Faits Scientifiques.* Paris: La Découverte.
- Lynch, Michael. 1985. "La Rétine Extériorisée : Sélection et Mathématisation Des Documents Visuels." *Culture Technique*, no. 14, 37–66.
- Lynch, Michael. 2006. "The Production of Scientific Images. Vision and Re-Vision in the History, Philosophy, and Sociology of Science." In *Visual Cultures of Science: Rethinking Representational Practices in Knowledge Building And Science Communication*, edited by Luc Pauwels, 26–40. Hanover: Dartmouth College Press.
- Lynch, Michael E. 1982. "Technical Work and Critical Inquiry: Investigations in a Scientific Laboratory." *Social Studies of Science* 12 (4): 499–533. <u>https://www.jstor.org/stable/284826</u>.
- Morton, Timothy. 2013. *Hyperobjects: Philosophy and Ecology after the End of the World*. Posthumanities 27. Minneapolis (Minn.): University of Minnesota press.
- Schneider, Birgit. 2012. "Climate Model Simulation Visualization from a Visual Studies Perspective." WIREs Climate Change 3 (2): 185–93. <u>https://doi.org/10.1002/wcc.162</u>.
- Schneider, Birgit, and Thomas Nocke, eds. 2014. *Image Politics of Climate Change: Visualizations, Imaginations, Documentations.* Image, volume 55. Bielefeld: Transcript.
- Tilling, Laura. 1975. "Early Experimental Graphs." *The British Journal for the History* of Science 8 (3): 193–213.
- Tufte, Edward R. 1983. *The Visual Display of Quantitative Information*. Cheshire: Graphic Press.

Wise, M. Norton. 2006. "Making Visible." *Isis* 97 (1): 75–82. https://doi.org/10.1086/501101.

Wittgenstein, Ludwig. (1953) 2009. Philosophical investigations. Translated by G. E. M. Anscombe, P. M. S. Hacker, and Joachim Schulte. Rev. 4th ed. Chichester, West Sussex, U.K.; Malden, MA: Wiley-Blackwell.

Woolgar, Steve. 1982. "Laboratory Studies: A Comment on the State of the Art." Social Studies of Science 12 (4): 481–98. <u>https://www.jstor.org/stable/284825</u>.

Glossary:

Background Review Article:

<u>Field:</u> Social Sciences/Humanities

Session Topic:

New Standards of Visualizations in Social Sciences

Speaker: OTSUKA, Jun, Kyoto University

Title: Changing Ideals of Science in the Age of AI

Scientific justification is an essential component of research activities. Researchers are tasked with the responsibility of justifying their hypotheses to various stakeholders, such as peer reviewers, policymakers, and the general public, to gain acceptance and implementation of their findings or proposals. This process of justification involves demonstrating that research outcomes are derived from objective and rational methodologies. Key elements in this endeavor include data encoding, visualization, and statistical inference, which collectively ensure that research conclusions are grounded in objectively verifiable evidence and logical reasoning. Historical studies [1-3] have shown that the evolution of these justificatory methods—for instance, the introduction of photography, the quantification of evidence, and the advancement of mathematical statistics—has been crucial in fostering objectivity and rationality within modern science.

However, the emergence of machine learning and AI-driven technologies presents the potential to significantly alter the nature and role of scientific justification. The widespread presence of big data makes manual data encoding obsolete and unnecessary. Furthermore, the complexity and high dimensionality of contemporary data and models challenge traditional methods of visualization and interpretation. Additionally, the shift from conventional theory-based statistical procedures to large-scale neural networks, whose reliability is primarily evaluated through empirical benchmark tests, marks a significant departure in scientific inferences [4].

These transformations might enhance the objectivity and rationality of scientific processes but at the cost of making them less accessible and comprehensible to human understanding. The presentation will examine the potential impacts of these changes on the ideals that have historically directed scientific inquiry from a philosophical perspective.

References:

Daston, L. & Galison, P. *Objectivity*. (Princeton University Press, 2007).
 Porter, T. M. *Trust in Numbers*. 324 (Princeton University Press, 1996).
 Porter, T. M. *The Rise of Statistical Thinking*, 1820–1900. (Princeton University Press, 1986).

[4] Otsuka, J. *Thinking About Statistics: The Philosophical Foundations*. (Routledge, 2022).

<u>Field:</u> Social Sciences/Humanities

Session Topic:

New Standards of Visualizations in Social Sciences

Speaker:

Pedro RAMACIOTTI MORALES, Institut des Systèmes Complexes de Paris Île-de-France

Title: Mapping politics in social media

Political opinions underlie a vast number of studies in several disciplines. Public opinion, political psychology and political sociology, political competition and voting behavior, polarization, agenda setting, and political communication studies often rely on data on individual political opinions. Newer and important fields of study also rely on individual political variables: the study of social media, misinformation, algorithmic biases, online polarization, online social networks, and opinion dynamics also rely on individual political opinions as explanations or control.

Political opinion has traditionally been studied using surveys: asking individuals where they stand on issues of relevance in politics. Some important limitations of survey research include the cost of administration (limiting frequency and reach, impacting cross-sectional and longitudinal studies), reliance on the truthfulness in responses (related for instance to social desirability), and framing.

In this presentation, I will present a method for inferring multidimensional political position estimates for large online populations using social media data (Ramaciotti et al., 2022). This method mixes Bayesian inference on interactional data and political expert survey data. Because it builds on expert surveys, it enables inference along the cleavage and strategic ideology and issue dimensions that are relevant for different national settings. Due to independence from text data, this method enables language-independent analysis suited for comparative studies. Relying on interactional data traces and not elicited answers, this method overcomes some limitations of survey research related to framing and respondent truthfulness. Finally, because estimation is done at the level of users, these political variables can be used jointly with other data traces enabling a diversity of studies. I will illustrate this method using Twitter data collected from debates in several countries, showing its application to the study of the spread of misinformation (Ramaciotti et al., 2023).

References:

Ramaciotti, P., Cointet, J. P., Muñoz Zolotoochin, G., Fernández Peralta, A., Iñiguez, G., & Pournaki, A. (2022). Inferring attitudinal spaces in social networks. *Social Network Analysis and Mining*, *13*(1), 14.

Ramaciotti, P., Berriche, M., & Cointet, J. P. (2023, June). The geometry of misinformation: embedding Twitter networks of users who spread fake news in geometrical opinion spaces. In *Proceedings of the International AAAI Conference on Web and Social Media* (Vol. 17, pp. 730-741).

<u>Field:</u> Mathematics/Informatics/Engineering

Session Topic: Reliability of Modern Technologies in Society

> Introductory Speaker: OSEKI Yohei, University of Tokyo

Title: Reliability of Artificial Intelligence in Society

Modern technologies have widely spread in society, thanks to the rapid development of Artificial Intelligence (AI) and related technologies like machine learning and big data. Importantly, modern AIs have outperformed humans in various downstream tasks such as natural language processing (e.g. machine translation) and computer vision (e.g. image recognition). However, those AIs, despite their super-human performance, have been regarded as not reliable due to several issues with (1) interpretability, (2) generalizability, and (3) efficiency [1], thus generating a barrier towards a human-centric AI society where humans and AIs can cooperate with each other [2].

- 1. Interpretability: AIs cannot be interpreted due to their "black box" nature.
- 2. Generalizability: AIs cannot be generalized to unforeseen environments.
- 3. Efficiency: AIs cannot be trained efficiently from the small amount of data.

In this session, we will address various aspects of the reliability of AIs in society from the interdisciplinary perspective. Specifically, the introductory speaker first reviews the reliability of AIs in general and illustrates them in the field of natural language processing (NLP). Then, two speakers present state-of-the-art results on the reliability of AIs and future directions to make AIs more reliable in the fields of human-computer interaction (HCI) and cognitive robotics, respectively. In addition, the reliability of AIs in academia like natural sciences and social sciences/humanities will also be discussed.

References:

[1] Lake, Ullman, Tenenbaum, & Gershman. (2017). Building machines that learn and think like people. *Behavioral and Brain Sciences* 40: e253.

[2] Cabinet Office, Government of Japan. (2019). Social Principles of Human-Centric AI. https://www.cas.go.jp/jp/seisaku/jinkouchinou/pdf/humancentricai.pdf.

Glossary:

- Natural language processing: AI in the domain of "language" (e.g. machine translation)
- Computer vision: AI in the domain of "vision" (e.g. image recognition)
- Human-computer interaction: a field to investigate how humans and AIs can interact
- Cognitive robotics: a field to simulate human cognition in real world with AIs/robots

<u>*Field:</u>* Mathematics/Informatics/Engineering</u>

Session Topic: Reliability of Modern Technologies in Society

Speaker: Baptiste CARAMIAUX, Institut des Systèmes Intelligents et de Robotique

Title: Interactive AI: Bringing Technology closer to People

Résumé

Machine learning and artificial intelligence systems have shown remarkable results over the last ten years. However, their successes have gone hand in hand with the development of a less open technology, more oriented towards a black-box model, i.e. one with little transparency. This evolution has had important repercussions on society, where black-box models were deployed in applications even though they showed significant biases. In the field of Human-Computer Interaction (HCI), the discipline that studies the contextualized uses of technology and how to design technology to facilitate its use, more and more work is seeking to introduce more interactivity into AI in order to provide a means of preventing these problems (Amershi et al., 2014; Gillies et al., 2016). More specifically, the so-called interactive AI approach aims to involve users more closely in the development of AI systems, giving them more influence over the data and the model in order to audit the model or customize it according to their needs. However, this approach brings with it a number of challenges. On the one hand, these challenges are technical, such as designing a more efficient model that can be refined and customized on the basis of small datasets (Mishra et al. 2021). On the other hand, these challenges are linked to the definition of evaluation measures adapted to this system. In this presentation, I will focus on the latter. Using two examples (Sungeelee et al, 2024; Scurto et al. 2021), I will illustrate how the evaluation of an AI system needs to be considered differently from the usual methods of AI development (e.g., based on accuracy, confusion matrix or f-score metrics) when considering in interaction with users. In addition, I will use this AI evaluation problem as a means of triggering more fundamental questions about AI design and its impact on society and science. This presentation, I hope, will therefore highlight problems at the frontiers of different sciences and with significant societal impacts.

References

Amershi, S., Cakmak, M., Knox, W. B., & Kulesza, T. (2014). Power to the people: The role of humans in interactive machine learning. *AI magazine*, *35* (4), 105-120.

Gillies, M., Fiebrink, R., Tanaka, A., Garcia, J., Bevilacqua, F., Heloir, A., ... &

Caramiaux, B. (2016). Human-centred machine learning. In *Proceedings of the 2016 CHI conference extended abstracts on human factors in computing systems* (pp. 3558-3565).

- Mishra, S., & Rzeszotarski, J. M. (2021). Designing interactive transfer learning tools for ML non-experts. In *Proceedings of the 2021 CHI Conference on Human Factors in Computing Systems* (pp. 1-15).
- Scurto, H., Kerrebroeck, B. V., Caramiaux, B., & Bevilacqua, F. (2021). Designing deep reinforcement learning for human parameter exploration. *ACM Transactions on Computer-Human Interaction (TOCHI)*, 28(1), 1-35.
- Sungeelee, V., Jarrassé, N., Sanchez, T., & Caramiaux, B. (2024, March). Comparing Teaching Strategies of a Machine Learning-based Prosthetic Arm. In *Proceedings of the 29th International Conference on Intelligent User Interfaces* (pp. 715-730).

<u>Field:</u> Mathematics/Informatics/Engineering

Session Topic:

Reliability of Modern Technologies in Society

Speaker: Hiroki Mori, Future Robot Organization, Waseda University

Title: Meaning of Meanings: Embodied structure of language

Large Language Models (LLMs) like ChatGPT are socially impactful technology, resulting in decreased freelance jobs and income [1]. Raj et al. suggests that high-income professions like teachers and magistrate judges are notably affected by LLMs [2]. Another notable instance is a Japanese novel incorporating ChatGPT winning the Akutagawa Prize, a prestigious Japanese literary award. The author revealed that about 5% of its sentences were generated by the model. This signifies the growing acceptance of artificial intelligence even in creative activities.

The question arises: Is it safe to allow generative AI, such as LLMs, to distribute society? To address this, we must consider whether generative AI understands "meaning." The widely used word2vec technology, based on the "distributional hypothesis" in which a meaning of a word is determined by the surrounding words. This means that different words that have similar words distributed around them are considered to have similar meanings and are placed in closed locations in a multidimensional continuous space (embedded space). However, based on this idea, words such as "right" and "left," "fast" and "quick," etc. would be placed close to each other even though they have opposite meanings.

Our study investigated "embodied semantics" based on word allocation in the embedded space after integrating a robot's behavior and linguistic descriptions [3]. We found that words with similar meanings as actions moved closer together, while those with different meanings moved further apart. This highlights the importance of physicality in meaning comprehension.

Ultimately, the result suggests that for reliable artificial intelligence, models need to exhibit human-like semantic understanding based on body and behavior. Concepts like cognitive developmental robotics [4] and human-in-the-loop [5] are deemed crucial for achieving reliable AI.



References:

[1] Xiang Hui, Oren Reshef, Luofeng Zhou, The Short-Term Effects of Generative Artificial Intelligence on Employment: Evidence from an Online Labor Market, SSRN: 4527336

[2] Ed Felten, Manav Raj, Robert Seamans, "How will Language Modelers like ChatGPT Affect Occupations and Industries?," arXiv:2303.01157

[3] Minori Toyoda, Kanata Suzuki, Hiroki Mori, Yoshihiko Hayashi, and Tetsuya Ogata, Embodying Pre-Trained Word Embeddings Through Robot Actions, IEEE Robotics and Automation Letters, Vol. 6, No. 2, 2021

[4] Minoru Asada, Koh Hosoda, Yasuo Kuniyoshi, Hiroshi Ishiguro, Member, Toshio Inui, "Cognitive Developmental Robotics: A Survey," IEEE Transactions on Autonomous Mental Development, Vol. 1, Issue 1, pp.12 – 34, 2009

[5] Eduardo Mosqueira, Elena Hernández, David Alonso, José Bobes, Ángel Fernández, "Human-in-the-loop machine learning: a state of the art," Artificial Intelligence Review, Vol. 56, pp.3005–3054, 2023

<u>Field:</u> Physics/Astrophysics

Session Topic:

Time Domain Astronomy -from long time to short time-

Introductory Speaker: Pierre MAGGI, Observatoire astronomique de Strasbourg

Title: *Time Domain Astronomy -from long time to short time- and from ancient times to modern times*

Abstract:

In this introductory talk, I will offer a panorama of time-domain astronomy. This is the study of time-variable or transient celestial phenomena, which, I will argue, also fits the definition of astronomy in general. I will start with an historical perspective, showing that analysing such phenomena always lead to a change of world view in our understanding of the Universe. Fast-forwarding to recent times, I will present the advent of the recent era of time-domain astronomy and how it affected and drove the development of modern radio, optical, and high-energy astronomy. I will discuss the observational challenges of the field, and (some of) the many scientific prospects of the field.

References:

Grindlay, Tang, Los, and Servillat, IAUS 285 29, 2012 Klebesadel, Strong, and Olson, ApJL 182 L85, 1973 Pietka, Fender, and Keane, MNRAS 446 3687, 2015 Polzin, Margutti, Coppejans, et al., ApJ 959 75, 2023 Stratta, Ciolfi, Amati, et al., AdSpR 62 662, 2018 Clark and Stephenson, "The Historical Supernovae" 1977 (Oxford)

Glossary:

GRB : Gamma-ray bursts : A brief flash of high-energy gamma rays lasting less than a few seconds, followed by an afterglow extending from gamma-ray to radio on timescales of minutes to weeks. Occurs either when a massive star collapse with the ejection of a collimated jet ("long" GRBs), or upon the merger of two neutron stars in a binary ("short" GRBs)

NS: Neutron Star; the collapsed remnant of a massive stellar core, consisting mostly of neutron packed together at ~nuclear density

Pulsar: Contraction of pulsating-star; a neutron star that emits a narrow radio beam periodically visible from Earth, with periods ranging from a few milliseconds to a few hours. Sometimes visible as X-ray pulsars

SN: Supernova; a bright event marking the gravitational or thermonuclear disruption of some stars

TDE: Tidal disruption event : When stars in the central region of galaxies get too close to the central supermassive black holes, they may be destroyed by tidal forces. Matter from the disrupted star is then accreted onto the black hole, leading to enhanced emission that is visible as a slow "flash" on timescales from weeks to years.

QPO: Quasi-periodic oscillations : A variable signal found in the light curve of many accreting sources from NS to stellar mass or supermassive black holes, characterised by a broad line in frequency space.

<u>Field:</u> Physics/Astrophysics

Session Topic:

Time Domain Astronomy -from long time to short time-

Speaker: Motogi Kazuhito, Yamaguchi University

Title: Time-domain studies on a massive protostar beyond angular resolution

Time-domain astronomy stands as one of the final frontiers in the field. Typically, astronomical events, like star/galaxy births and cosmic element evolution, unfold over timescales far exceeding human lifetimes. Conversely, astronomers delve into rapidly variable phenomena under the stellar scale, measured in nanoseconds for neutron star rotations and milliseconds to several tens of minutes for stellar explosions. These events remain spatially unresolved even with modern telescopes. Until now, such short and long timescale studies have progressed independently within distinct communities. This talk introduces a new midtimescale phenomenon that bridges these short and long timescale studies. Our monitoring observations of a very young massive protostar [1] over ~ 10 years have unveiled, for the first time, a periodic variation in protostellar luminosity (Fig 1). The observed periodicity of ~ 1 year suggests potential stellar pulsations [2], likely resulting from an extremely swollen atmosphere. The expected stellar radius is approximately 400 solar radii, similar to that of a red supergiant star. Theoretically, such pronounced swelling critically influences protostellar evolution [3]. While suggestions from time-domain data alone remain inconclusive, the next-generation radio inteterferometers, such as ngVLA and SKA, could resolve the protostellar surface, giving more direct and critical verification. Unraveling the evolutionary process of massive stars is crucial for comprehending the cosmic synthesis of heavy elements, the origins of the solar system, and the formation of neutron stars/black holes which cause various physical phenomena such as pulsars and gravitational waves. We anticipate that time-resolved astronomy will shed light on the evolutionary journey of massive stars from an u n p r e c e d e n t e d perspective



Figure 1: (Left) The highest-resolution image of the circumstellar disk around massive protostar G353 observed by Atakama Large Millimetr/submillimeter Array (ALMA). The color points indicate locations of gas clumps emitting methanol maser emission and Doppler velocities along the line-of-sight. The size of the solar system is shown in the upper-left corner. (Right) Integrated light curve for methanol maser clumps near the protostar from MJD 59000 to 60000.

References:

- [1] Motogi et al. 2019, ApJL, 877, L25
- [2] Inayoshi et al. 2013, ApJL, 769, L20
- [3] Haemmerle et al. 2016, A&A, 585, A65

Glossary:

Neutron star: An extremely high-density star made of neutrons.

Protostar: A young, contracting star before the ignition of nuclear burning in the stellar core.

Massive star:

A star with a stellar mass exceeding 8 times of the sun, which eventually die in an explosion called supernova. The stellar core turn into the neutron star or black hole, because of strong compression by backlash of the supernova. Almost all heavy element in the universe had synthesized by massive star via nuclear burning, supernova, and merger of binary neutron stars.

Solar radius: 7×10⁵ km.

Red supergiant star:

An extremely swollen massive star such as Betelgeuse. They are just before their death (~last 10 per cent of their lifetime).

Radio interferometer:

The synthesized telescope consists of multiple radio telescopes. Its angular resolution is obtained by observing radio wavelengths over each telescope's maximum separation (baseline length), while its sensitivity is determined by the total surface area of the telescopes.

Methanol maser:

An astronomical maser is a strong line emission analogous to a laser in optical wavelength. Several interstellar molecules, such as methanol and water, show maser activity in a limited volume of the circumstellar gas. Methanol molecules cause maser activity excited by infrared emission from a massive protostar. Therefore, a methanol maser is used as an indirect sensor of stellar luminosity.

Integrated flux:

Radio energy flux integrated over the observing frequency band. It has the same dimension with luminosity per unit area.

MJD: Modified Julian Date

<u>Field:</u> Physics/Astrophysics

Session Topic: Time Domain Astronomy -from long time to short time-

Speaker: Cherry NG-GUIHENEUF, Laboratoire de physique et chimie de l'environnement et de l'Espace

Title: Digitizing the radio transient sky

The recent technological advancement has enabled astronomers to digitize large areas of the radio sky with remarkable resolutions. This unprecedented capability provides sensitivity to transient phenomena to which we would have otherwise been blind. We will discuss the case of Fast Radio Bursts (FRBs), which are bright, millisecond-duration radio bursts from extra-galactic distances. First discovered in 2007 [1], our knowledge of FRBs was initially limited since only a few tens of cataclysmic FRBs were observed. The large field-of-view and the commensal beamforming capability of the CHIME radio telescope [2] have been a game changer for the study of FRBs. Thanks to the development of a real-time GPU beamforming algorithm [3], CHIME has made thousands of FRB discoveries in the last few years which has revolutionized the landscape of Fast Radio Burst research. We are beginning to populate the short-timescale variability region of the radio transient parameter space (see Fig. 1) which has until now been under-explored. It is now apparent that FRBs are prolific, with high event rate of >5000 bursts/sky/day. FRBs have by now been detected by 16+ radio telescopes (between 110 MHz – 8 GHz). However, there is so-far no conclusive detections of



Figure 1) Radio pseudo-luminosity vs the product of observing frequency (v) and variability timescale (W) (plot from $[\underline{4}]$). The frequency-time spectrum of the first FRB discovered by $[\underline{1}]$ is shown as an inset.

multi-wavelength counterparts, except an FRB-like burst from the Galactic magnetar SGR1935+2154 [5].

Despite the yet unknown origin(s) of FRBs, the fact that FRBs are the most compact known extragalactic sources of electromagnetic radiation means that there are high hopes that we might be able to employ FRBs as cosmological probes [6], for example, to locate the missing baryons and to map the intergalactic medium, which are extremely hard to probe otherwise. To do that, we will need tens of thousands of well-localized FRBs. Large-scale telescope projects such as the \$2-billion, multi-national Square Kilometre Array¹(SKA) is expected to come online before 2030. The SKA will be the most sensitive radio telescope ever constructed and can discover many FRBs at the intermediate redshift range, providing an orthogonal cosmological tool that will complement the existing picture of the history of the Universe.

References:

[1] Lorimer et al., 2007, Science, 318, 5851, 777

[2] The CHIME/FRB Collaboration et al., 2018, ApJ, 863, 48

[3] C. Ng, 2017, Proceedings of the IAU 337

[4] <u>N. Hurley-Walker et al., 2022, Nature, 601, 526–530</u>

[5] The CHIME/FRB Collaboration et al., 2020, Nature, 587, 7832, 54-58

[6] <u>V. Ravi et al., 2020, Astro2020 Decadal Survey white paper</u>

Glossary:

- Transient a temporary, non-permanent, time-varying phenomenon
- Extra-galactic Outside of and beyond our Milky Way Galaxy
- Cataclysmic one-off, non-repeating
- Field-of-view the angular extent of the observable sky seen at a given moment
- Commensal beamforming beamforming is a signal processing technique used in antenna arrays for directional signal reception. Commensal is the ability to beamform in parallel, simultaneously as other signal processing processes
- GPU Graphics Processing Unit
- Radio pseudo-luminosity the apparent brightness which is the product of flux density (S) and the distance of the object squared (d²). This provides a way to compare the apparent brightness of different objects, assuming they are all at the same distance.
- Observing frequency the window of the electromagnetic spectrum being studied
- Variability timescale the time duration of the transient phenomenon
- Busts/sky/day the average event rate across the entire sky in a single day
- Magnetar a type of neutron star with an extremely powerful magnetic field
- Cosmology the science of the origin and development of the universe
- Missing baryons the observed discrepancy of baryonic matter (composite subatomic particles, including protons and neutrons) detected shortly after the Big Bang with respect to more recent times.

¹ SKAO website: <u>https://www.skao.int</u>

- Intergalactic medium (IGM) the material found between galaxies which consists mostly of hot, tenuous hydrogen gas.
- Redshift describes how much light is shifted to longer wavelengths due to the expansion of the Universe. Combined with the Hubble relation, a distance can be calculated from a redshift value.

<u>Field:</u>

Earth Science/Geosciences/Environment

Session Topic:

Uncovering Paleo Disasters and Human Impacts on Modern Earth Science

Introductory Speaker: Ishimura Daisuke, Tokyo Metropolitan University

Title: *How do we know paleo-hazards and link them to future disaster risk assessment?*

The past is the key to the present as well as "the present is the key to the past". In particular, when considering present-day low-frequency disasters (e.g., earthquake, tsunami, volcanic eruption), the present instrumental record alone is not a sufficient period of observation to assess the frequency, intensity, and magnitude of the hazards in the geologic time scale. Therefore, we are trying to assess the disaster risk by uncovering past disasters (i.e. natural hazards). In an active margin like Japan, a variety of natural hazards have occurred from the past, and they have been regarded as disasters that have struck people. It is said that the history of Japan is also the history of disasters. In Japan, the history of how ancient peoples resist natural hazards has been preserved in documents and artifacts, and this knowledge has been handed down from generation to generation. At the same time, these natural hazards have greatly influenced the landscape and culture of Japan, and people have also had their benefits.

This session topic is to know past disasters and natural hazards for the benefit of earth science and future human activities. In this presentation, we will use Japan as an example to show how we can uncover past natural disasters and relate them to human activities. It will also introduce low-frequency disasters and increasingly severe meteorological disasters that have struck Japan in recent years. Through these stories, we hope to provide an opportunity to think about the global environment in the Holocene epoch, when the climate environment became the way it is today, and in the Anthropocene epoch, when modern industry began to influence the global environment.

References:

[1] [2]

Glossary:

- Active margin: A zone on the Earth's surface where crustal deformation and seismic activity are active. It locates along plate boundaries.

- Holocene: The most recent geological epoch from 11,700 years ago to the present. It follows the last glacial period and is the current warm period in the glacial-interglacial cycle.
- Anthropocene: It is a hypothetical geological epoch following the Holocene, proposed as the starting point for humans to have a significant impact on the Earth's geology and ecosystems.

Background Review Article:

<u>Field:</u> Earth Science/Geosciences/Environment

Session Topic: Uncovering Paleo Disasters and Human Impacts on Modern Earth Science

<u>Speaker:</u> Anaelle SIMONNEAU, ISTO, UMR 7327, Univ Orleans, CNRS, BRGM, OSUC, F-45071 Orléans, France

Title: Flash flood events as Paleo disasters & their effects on human societies

In the last 20 years, flooding has been the most common natural disaster by far, accounting for 43% of all recorded events. The IPCC (Intergovernmental Panel On Climate Change (Ipcc), 2023) report states that a flood event can be defined as "a complex interplay of hydrology, climate, and human management, and that the relative importance of these factors varies for different flood types and regions.". At the continental and regional scales, the projected changes in floods are uneven in different parts of the world, but there is a larger fraction of regions with an increase than with a decrease over the 21st century (Wilhelm et al., 2022). Researchers are however more confident at global than at regional scale which need today more investigations. A key feature of paleoflood records is variability in flood recurrence at centennial timescales, although constraining climate-flood relationships remains challenging.

Paleofloods can be reconstruct using documentary evidence (grape harvest data, religious documents. newspapers, logbooks); model-based analyses; or paleoreconstructions (i.e. natural archives such as speleothems (Denniston and Luetscher, 2017), spatial patterns of natural environment, lake sediments Simonneau et al., 2013). Reconstructing palaeo-floods in pre-instrumental information, reconstruct from lake sediment, can particularly help to put events occurring in the instrumental record (referred to as 'observed') in a longer-term context (Simonneau et al., 2013), especially over the last 2000 years (Wirth et al., 2013a), and examine climate and meteorological trends based on reference levels discussing natural (Wirth et al., 2013b) and human forcing (Brisset et al., 2017). Objectives are 1/ to determine quantitative information for specific events, such as the timing, peak discharge, and maximum stage of an individual flood or floods, and 2/ investigate more general spatial and temporal patterns of flooding, commonly to assess relations among climate, land use, flood frequency and magnitude, and geomorphic response. Methods consist in stratigraphic correlation and mapping, visual description of sediment cores, high-resolution imaging, but also based on destructive analysis to quantify particle size distribution, sediment density, magnetic properties, mineral and isotopic geochemistry of the sediment and organic matter content and composition.

References:

Brisset, E., Guiter, F., Miramont, C., Troussier, T., Sabatier, P., Poher, Y., Cartier, R., Arnaud, F., Malet, E., Anthony, E.J., 2017. The overlooked human influence in historic and prehistoric floods in the European Alps. Geology 45, 347–350. https://doi.org/10.1130/G38498.1

Büntgen, U., Tegel, W., Nicolussi, K., McCormick, M., Frank, D., Trouet, V., Kaplan, J.O., Herzig, F., Heussner, K.-U., Wanner, H., Luterbacher, J., Esper, J., 2011. 2500 Years of European Climate Variability and Human Susceptibility. Science 331, 578–582. https://doi.org/10.1126/science.1197175

Denniston, R.F., Luetscher, M., 2017. Speleothems as high-resolution paleoflood archives. Quaternary Science Reviews 170, 1–13. https://doi.org/10.1016/j.quascirev.2017.05.006

Intergovernmental Panel On Climate Change (Ipcc), 2023. Climate Change 2022 – Impacts, Adaptation and Vulnerability: Working Group II Contribution to the Sixth Assessment Report of the Intergovernmental Panel on Climate Change, 1st ed. Cambridge University Press. https://doi.org/10.1017/9781009325844

Simonneau, A., Chapron, E., Vannière, B., Wirth, S.B., Gilli, A., Di Giovanni, C., Anselmetti, F.S., Desmet, M., Magny, M., 2013. Mass-movement and flood-induced deposits in Lake Ledro, southern Alps, Italy: implications for Holocene palaeohydrology and natural hazards. Clim. Past 9, 825–840. https://doi.org/10.5194/cp-9-825-2013

Soon, W., Velasco Herrera, V.M., Selvaraj, K., Traversi, R., Usoskin, I., Chen, C.-T.A., Lou, J.-Y., Kao, S.-J., Carter, R.M., Pipin, V., Severi, M., Becagli, S., 2014. A review of Holocene solar-linked climatic variation on centennial to millennial timescales: Physical processes, interpretative frameworks and a new multiple cross-wavelet transform algorithm. Earth-Science Reviews 134, 1–15. https://doi.org/10.1016/j.earscirev.2014.03.003

Wilhelm, B., Amann, B., Corella, J.P., Rapuc, W., Giguet-Covex, C., Merz, B., Støren, E., 2022. Reconstructing Paleoflood Occurrence and Magnitude from Lake Sediments. Quaternary 5, 9. https://doi.org/10.3390/quat5010009

Wirth, S.B., Gilli, A., Simonneau, A., Ariztegui, D., Vannière, B., Glur, L., Chapron, E., Magny, M., Anselmetti, F.S., 2013a. A 2000 year long seasonal record of floods in the southern European Alps: FLOOD SEASONALITY IN THE SOUTHERN ALPS. Geophys. Res. Lett. 40, 4025–4029. https://doi.org/10.1002/grl.50741

Wirth, S.B., Glur, L., Gilli, A., Anselmetti, F.S., 2013b. Holocene flood frequency across the Central Alps – solar forcing and evidence for variations in North Atlantic atmospheric circulation. Quaternary Science Reviews 80, 112–128. https://doi.org/10.1016/j.quascirev.2013.09.002

Glossary: N.D.

Background Review Article: (So

Büntgen, U., Tegel, W., Nicolussi, K., McCormick, M., Frank, D., Trouet, V., Kaplan, J.O., Herzig, F., Heussner, K.-U., Wanner, H., Luterbacher, J., Esper, J., 2011. 2500 Years of European Climate Variability and Human Susceptibility. Science 331, 578–582. https://doi.org/10.1126/science.1197175

Soon, W., Velasco Herrera, V.M., Selvaraj, K., Traversi, R., Usoskin, I., Chen, C.-T.A., Lou, J.-Y., Kao, S.-J., Carter, R.M., Pipin, V., Severi, M., Becagli, S., 2014. A review of Holocene solar-linked climatic variation on centennial to millennial timescales: Physical processes, interpretative frameworks and a new multiple cross-wavelet transform algorithm. Earth-Science Reviews 134, 1–15. https://doi.org/10.1016/j.earscirev.2014.03.003

<u>Field:</u> Earth Science/Geosciences/Environment

<u>Session Topic:</u>

Uncovering Paleo Disasters and Human Impacts on Modern Earth Science

Speaker: NAKANISHI Ryo, Kyoto University (Graduate School of Science)

Title: Reconstruction of paleo earthquakes from geological archives and modeling

Because M~9 earthquakes, which are called "giant earthquakes", are due to infrequent recurrence intervals with several hundred to several thousand years [1], it is difficult to understand their recurrence intervals and rupture zones of with the limited instrumentally observations and historical documents of the past hundred years. Therefore, it is necessary to extend the paleoseismic record to several thousand years using geological archives such as tsunami deposits and seismic turbidites. Tsunami deposits are mainly sand transported by tsunamis, and their distribution has been used to estimate the inundation area of paleotsunamis. Tsunami simulations can provide the rupture zone of earthquakes by inverting the tsunamigenic crustal deformation. Estimated faults based on the tsunami deposits suggest the maximum magnitude and the recurrence intervals of the giant earthquake, and their tsunami inundation area is the basis for disaster prevention and evacuation of residents.

Glacial sea-level fall over hundreds of meters constrains our understanding of the tsunami history on land; however, the seafloor sediments have the potential to reveal seismic history even more ancient ages. Turbidites formed by seismic motions may serve as "natural seismometer" [2].

The geological archives are the only evidence available to examine natural hazards prior to historical documents; however, the data available are limited due to artificial alterations and environmental changes. The combination of deep learning and numerical modeling has the potential to overcome problems such as little data and computational loads for inversion [3], and to advance paleoseismic reconstruction research to a new stage.

References:

[1] Philibosian, B., Meltzner, A.J., 2020. Segmentation and supercycles: A catalog of earthquake rupture patterns from the Sumatran Sunda Megathrust and other well-studied faults worldwide. Quaternary Science Reviews 241, 106390.

https://doi.org/10.1016/j.quascirev.2020.106390

[2] Hayward, B., Sabaa, A., Howarth, J., Orpin, A., Strachan, L., 2022. Foraminiferal evidence for the provenance and flow history of turbidity currents triggered by the 2016

Kaikōura Earthquake, New Zealand. New Zealand Journal of Geology and Geophysics 1–14. https://doi.org/10.1080/00288306.2022.2103157

 [3] Mitra, R., Naruse, H., Abe, T., 2020. Estimation of Tsunami Characteristics from Deposits: Inverse Modeling Using a Deep-Learning Neural Network. Journal of Geophysical Research: Earth Surface 125, e2020JF005583. https://doi.org/10.1029/2020JF005583

Glossary:

- Turbidite: A turbidite is the sediment by a turbidity current, which is a type of sediment gravity flow responsible for distributing vast amounts of clastic sediment into the deep ocean.

Background Review Article:

- Nakanishi, R., Okamura, S., Yokoyama, Y., Miyairi, Y., Sagayama, T., Ashi, J., 2020. Holocene tsunami, storm, and relative sea level records obtained from the southern Hidaka coast, Hokkaido, Japan. Quaternary Science Reviews 250, 106678. https://doi.org/10.1016/j.quascirev.2020.106678

 Nakanishi, R., Ashi, J., Miyairi, Y., Yokoyama, Y., 2022. Spatial Extent of Mid-To Late-Holocene Sedimentary Record of Tsunamis Along the Southern Kuril Trench, Hokkaido, Japan. Geochemistry, Geophysics, Geosystems 23, e2022GC010334. https://doi.org/10.1029/2022GC010334 **Field:** Biology / Life Sciences

Session Topic: Unlocking the Secrets: Exploring Neurotechnology

<u>Speaker:</u> Léa PILLETTE, Univ. Rennes, Inria, CNRS, IRISA, Rennes, France

Title: Neurotechnologies - From brain activity acquisition to neurofeedback

Advances in stem cell technology and advanced imaging of neuronal dendrites open new perspectives for neurotechnologies research and in particular for neurofeedback. Neuronal organoids derived from human stem cells enable the modeling of complex brain structures in vitro, providing a platform to study neural development and associated dysfunctions. Concurrently, the use of nonlinear 3D acousto-optic lens two-photon microscopes allows real-time observation of dendritic activity in awake animals, revealing specific modulations of neuronal activity in response to behaviors. These converging technologies can be integrated into the field of neurofeedback, where real-time measured neural signals are used to provide feedback to people in order to train them to modulate their brain activity [1]. Neurofeedback is often used to improve cognitive abilities in clinical applications such as improving the motor abilities of patients after a stroke [2] or people with Parkinson's disease [3]. An in-depth understanding of neuronal dynamics from organoids and animal models could enhance the precision and efficacy of neurofeedback protocols, paving the way for more targeted and personalized therapies for various neurological and psychiatric conditions.

Review Article References:

[1] Batail, J. M., Bioulac, S., Cabestaing, F., Daudet, C., Drapier, D., Fouillen, M., ... & Vialatte, F. (2019). EEG neurofeedback research: A fertile ground for psychiatry?. *L'encephale*, 45(3), 245-255.

[2] Bai, Z., Fong, K. N., Zhang, J. J., Chan, J., & Ting, K. H. (2020). Immediate and long-term effects of BCI-based rehabilitation of the upper extremity after stroke: a systematic review and meta-analysis. *Journal of neuroengineering and rehabilitation*, 17, 1-20.

[3] Matzilevich, E. U., Daniel, P. L., & Little, S. (2024). Towards therapeutic electrophysiological neurofeedback in Parkinson's disease. *Parkinsonism & Related Disorders*, 106010.

<u>Field:</u> Biology / Life Sciences

Session Topic:

Unlocking the Secrets: Exploring Neurotechnology

<u>Speaker:</u>

SAKAGUCHI Hideya, RIKEN Center for Biosystems Dynamics Research

Title: Stem Cell-Derived Neural Organoids -History, Current Status, Future Perspectives, and Ethical aspects-

The advance of stem cell technology has enabled researchers to generate organoids: stem cell-derived three dimensional (3D) tissues with biological structures and functions(Eiraku et al. 2008, Kadoshima et al. 2013, Lancaster et al. 2013). By application of organoid technology with human pluripotent stem cells, organoids can provide a novel platform to study human biology in a dish. Using human embryonic stem cells, we have succeeded in the generation of 3D neural tissues including cerebral cortex, hippocampus, choroid plexus, and spinal cord (Kadoshima et al. 2013, Sakaguchi et al. 2015, Ogura and Sakaguchi et al. 2018, Sakaguchi et al. 2019). The neural organoid technology enables to study several aspects of neural development including neural function/dysfunction in human system. Thus, the neural organoids will bring us many advantages, such as facilitating disease modeling, drug discovery, and regenerative medicine in the future; on the other hand, the generation of human neural tissues with in vivo-like structures and functions may induce ethical concerns such as possible emergence of consciousness in cerebral organoids.

In this presentation, we first overview the history of neural organoid research, and then introduce our achievements of the generation of regionalized neural organoids with functional neural network. And lastly, we will share future perspectives of neural organoid technology from multiple viewpoints related to biology, medicine, and ethics.

References:

[1] Eiraku M, et al : Cell Stem Cell, 3, 519-532, 2008

[2] Kadoshima T, et al : Proc. Natl. Acad. Sci. USA, 110, 20284-20289, 2013

[3] Lancaster MA et al : Nature, 501(7467), 373-379, 2013

[4] Sakaguchi H, et al : Nature Communications, 6, 8896, 2015

[5] Ogura T & Sakaguchi H, et al : Development, 145(16):dev162214, 2018

[6] Sakaguchi, H, et al : Stem Cell Reports 13(3): 458-473, 2019.

Glossary:

- Organoid: Pluripotent/Tissue stem cell-derived structures generated in a dish that display features of 3-dimensional architectures and physiologies of the corresponding organ in vivo. Regarding neural organoids, cerebral, retinal, hippocampal, choroid plexus, thalamus, hypothalamus, pituitary, cerebellar, midbrain, spinal cord organoids as well as organoids which have some of the regions in one aggregate have been reported.
- Pluripotent Stem Cell: Pluripotent stem cells are cells that have the capacity to self-renew by cell division and to develop into the three primary germ cell layers of the early embryo which means all types of cells of the adult body. Embryonic stem cells and induced pluripotent stem cells are examples of pluripotent stem cells.

Background Review Article: Sasai Y : Cell Stem Cell, 12, 520-530, 2013 Sakaguchi H & Takata N, Handbook of Stem Cell Applications 1-19, 2023 Field: Biology / Life Sciences

Session Topic: Unlocking the Secrets: Exploring Neurotechnology

Speaker: Antoine VALERA, Institut des Neurosciences Cellulaires et Intégratives

Title: Decoding Activity Patterns Across Pyramidal Cell Dendritic Trees During Spontaneous Behaviors Using 3D Arboreal Scanning

Our understanding of how sensorimotor information is integrated across dendritic trees is limited by our ability to image these distributed 3D structures in awake animals. We overcome the existing limitations of rapidly measuring 3D dendritic activity and avoiding signal distortion by brain motion artefacts by utilizing our novel nonlinear 3D acousto-optic lens two-photon microscope with real-time 3D brain motion correction and innovative Ca2+ imaging analysis pipelines [1]. This enables the study of sensorimotor information representation in dendritic activity patterns of awake mice during natural behaviors. We imaged layer 2/3 neurons of primary motor cortex, a representationally rich sensorimotor integration hub that plays a key role in modulating primitive movements like locomotion and whisking. Consistent with previous work, we found that a strong, highly correlated cell-wide Ca2+ signal is the dominant activation mode in vivo. We find independent branch-specific local events are rare, and when observed, are largely accounted for by contaminating signals. Applying nonlinear dimensionality reduction techniques to the global signals, we discovered specific dendritic regions that covary with uninstructed spontaneous movements. These modulations (spread over >20 um compartments) were superimposed on the global signals. Dendritic modulations were dynamic across behavioral epochs including quiet-rest, exploration, active whisker touch, and unexpected sensory surprise. Remarkably, regression analyses suggest that these modulations in the activity of dendritic segments are more informative about specific behaviors than the activity at the soma in the majority of cells. Our results indicate that L2/3 pyramidal cell dendritic activity patterns are multidimensional and represent several innate behavioral features simultaneously

References:

 [1] Griffiths VA, Valera AM, Lau JY, et al. Real-time 3D movement correction for twophoton imaging in behaving animals. *Nat Methods*. 2020;17(7):741-748.
 Glossary: - Calcium Imaging: An optical technique that uses fluorescent indicators to visualize calcium ions in cells, often used as a proxy to study neuron electrical activity.

- Dendritic Tree: Neurons are made of compartments. Information enters the neuron from neighboring neurons through the dendrites, converges at the neuron soma, and is sent (or not) to downstream neuronal targets through the axon.

- Acousto-Optic Lens: A device that uses sound waves to control the direction of a laser beam, enabling precise focusing for imaging.

- Action Potential: A rapid rise and subsequent fall in voltage or membrane potential across a cellular membrane, the primary way neurons communicate.

- Back-Propagating Action Potential: An action potential that travels back into the dendritic tree of a neuron, rather than just along the axon.

Background Review Article:

Spruston, N. Pyramidal neurons: dendritic structure and synaptic integration. *Nat Rev Neurosci* **9**, 206–221 (2008).