7．点検評価と課題

2022 年 4 月から研究顧問をお引き受けいただいている James M. Lisy 教授（イリノイ大学）と北川　進教授（京都大学），産学連携研究アドバイザーに就任いただいている菊池　昇博士（(株) トヨタコンポン研究所所長）と福田伸博士（(株) 三井化学分析センター技術顧問）に 2023 年 5 月開催の IMS Presentations 2023 に現地参加頂き，所全体の研究評価，研究体制，産業界の視点からの研究評価などについての提言をいただいた。

マンチェスター大学 David A. Leigh 教授が 2023 年 12 月に来所し，協奏分子システム研究センターを中心に，関連する研究分野の 2 名を加えてヒアリングが実施され，各グループの研究内容の評価をいただいた。また，2024 年 2 月，ハイデルベルグ大学の Matthias Weidemüller 教授に来所いただき，理論･計算分子科学研究領域と計算科学研究センターを中心にヒアリングが実施され，各グループの研究内容の評価をいただいた。

2023 年 4 月，新たに石田　美織博士（三菱ケミカル（株）Science & Innovation Center 所長），高田　昌樹教授（東北大学国際放射光イノベーション・スマート研究センター），谷口　功博士（国立高等専門学校機構理事長）の 3 名が運営顧問に就任されたことに伴い，2024 年 2 月に開催された運営顧問会議では分子科学研究所全体の活動の詳しい紹介を行い，研究活動の状況や運営上の課題について議論頂いた。

（渡辺芳人）

7-1　運営顧問による点検評価

運営顧問から第 4 期中期計画期間での運営方針のためのアドバイスをいただくことを目的として，3 名の運営顧問を招いて運営顧問会議を開催した。

分子科学研究所の第 3 期中期計画期間の活動については，2019 年 12 月から 2021 年 7 月にかけて一連の機関点検・評価が行われた。その結果については，分子研リポート 2019 において，7-1 国際諮問委員会による点検評価，また分子研リポート 2020 において，7-1 大学共同利用機関の教育研究等の検証，7-2 国際諮問委員会の答申リポートとして公開されている。これらを踏まえ，分子科学研究所の抱える課題とそれらへの対応状況を，渡辺所長から運営顧問に説明した。会議当日には，第 4 期中期計画期間での研究所機能強化に向けた機関運営方針の提案・検討事項について運営顧問から意見をいただき，分子研が行っている研究の卓越性や人材育成・共同利用への貢献などが高く評価された。また，そうした活動を外に向けて発信していくことの重要性などのアドバイスが表明された。

1. 日　時：2024 年 2 月 6 日（火）14:00 ～ 2 月 7 日（水）11:30
2. 会　場：研究棟 201，202，各研究施設
3. 出席者：

運営顧問

石田　美織（三菱ケミカル株式会社 Science & Innovation Center 所長）
高田　昌樹（東北大学国際放射光イノベーション・スマート研究センター 教授）
谷口　功（国立高等専門学校機構 理事長）

分子科学研究所

渡辺　芳人　所長
山本　浩史　教授（研究総主幹，装置開発室長）
石﨑　章仁　教授（理論・計算分子科学研究領域主幹）
大森　賢治　教授（光分子科学研究領域主幹）
横山　利彦　教授（物質分子科学研究領域主幹，機器センター長）
飯野　亮太　教授（生命・錯体分子科学研究領域主幹）
解良　聡　教授（極端紫外光研究施設長）
秋山　修志　教授（協奏分子システム研究センター長）
岡本　裕巳　教授（メゾスコピック計測研究センター長）
江原　正博　教授（計算科学研究センター長）

4. 議論内容：

研究活動・共同利用・人材育成の現状について
大学院生・技術職員の人材獲得・人材育成について
分子研の活動の「見せ方」について

7-2　理論・計算分子科学研究領域の評価

7-2-1　Matthias Weidemüller 外国人運営顧問

Report on the visit to the Institute for Molecular Science (IMS), Okazaki

7–9 February 2024

Matthias Weidemüller (Heidelberg University)

This report is based on a visit to the Institute for Molecular Science from 7 to 9 February 2024. On 7 February, Director General Professor Watanabe provided me with general information, in particular concerning latest developments after my first visit in spring 2023. This year's focus was on the activities of the Department of Theoretical and Computational Molecular Science at IMS. The first meeting with Professor Saito and Associate Professor Okazaki was on the same day. On 8 February, I had meetings with Professors Okumura, Ishizaki and Ehara. Each of the meetings took about one hour, starting with presentations by the researchers followed by vivid and very insightful discussions on the research topics. We also briefly touched other issues related, *e.g.*, to the research environment offered by IMS. The scientists shared the files of their presentations with me, and they provided me with their most important publications from the last five years. The visit was closed by a review meeting with the Director General on 9 February. Further information for this report was extracted from IMS's Annual Report 2023.

General remarks

After having mainly met experimentally oriented researchers during my visit of last year, I now had the pleasure to discuss with five leading theoretical scientists at IMS. As a general impression, their research is of highest quality on an international scale. It addresses fundamental questions with regard to the emergence of complex dynamics in large molecular aggregates or condensed-matter systems. As far as I can judge, all researchers play a leading role in their respective fields of research. The research topics do not necessarily follow general mainstream, but indicate a large degree of independent scientific judgement of these outstanding scientists. Yet, all scientists consistently envisage applications of their research for, *e.g.*, material design or quantum control using external fields. The approaches are generally based on sophisticated theoretical and computational approaches well adapted to the intricacy of the systems under investigation. Providing insightful answers to subtle questions concerning the nature of complex molecular systems and the role of their environment is a characteristic, unique feature of IMS in general, and the research within the Department of Theoretical and Computational Molecular Science not only strongly supports this mission, but also positively contributes to IMS' outstanding reputation nationwide as well as internationally.

Unanimously, the important role of IMS' Research Center for Computational Science, headed by Professor Ehara, was emphasized by all researchers. The supercomputer facility and related infrastructure provide outstanding opportunities which are unmatched worldwide. They can be considered one important key element to the success of the theoretical groups at IMS.

All groups maintain broad collaborations with groups from other academic institutions in Japan or abroad. In most cases, theory and experiment work hand in hand. As a general feature, the theory groups at IMS are rather small in size, consisting essentially of the group leader and a small number of research staff including postdoctoral fellows. The number of graduate students in the groups is

rather small, in particular compared to the composition of typical research groups at a university. This feature is particularly striking as the topics of the research would, in my view, be ideally suited for successful PhD theses.

The following assessment follows the order of the presentations as given during the visit.

Shinji SAITO

The focus of Professor Shinji Saito and his group lies on the dynamics of condensed matter systems, especially with biological relevance. The studies comprise the excitation transport in light-harvesting complexes for photosynthesis, as well as structural and dynamical properties of supercooled water and other liquids. By using advanced computational methods including quantum chemical and molecular dynamics calculations, the research bridges the gap between microscopic models and macroscopic response functions. In this way, general conclusions on the nature of condensed matter and biophysical processes could potentially been drawn from the specific model systems under investigation, addressing the big question on how function follows structure. I was particularly impressed by his studies on the structure and dynamical slowdown of supercooled water, shedding new light on the largely unexplored region around 200 K.

Kei-ichi OKAZAKI

The group of Associate Professor Kei-ichi Okazaki addresses the fundamental processes of biomolecular machines in the cell with the goal to device possible control scenarios. In order to access long time scales, the group uses advanced molecular dynamics simulations and has develops novel methods such as coarsegrained models. These are applied to, *e.g.*, elucidate condition-dependent inhibitions mechanisms in ATP synthase. Modern techniques involving artificial intelligence such as structure predictions via AlphaFold are combined with molecular dynamics simulations to gain deeper insights into conformations in transporter proteins and other processes of biophysical relevance. The results on the conformational dynamics of oxalate transporters nicely highlight the added value of merging state-of-the-art approaches, including machine learning, with molecular structure calculations. In order to validate predictions of the theoretical models, the group maintains various cooperations with experimental groups at other places.

Hisashi OKUMURA

Associate Professor Hisashi Okumura and his group study the structure and dynamics of disease-related biomolecules, in particular aggregated amyloid-β (Aβ) peptides. Calculations are based on advanced replica molecular dynamics methods developed by the group. As a particular highlight, predictions concerning the Aβ peptide aggregation and behavior at interfaces extracted from these simulations are tested and validated in a cooperations with Prof. Kato's group at IMS. This successful internal collaboration impressively indicates the great potential of IMS's bundled expertise in theoretical as well as in experimental molecular science. The group also theoretically investigates possible scenarios for the breaking of amyloid fibrils in water solution through external ultrasonic or laser fields.

Akihito ISHIZAKI

The research of Professor Akihito Ishizaki and his group applies theoretical concepts from modern quantum optics and quantum open systems to a large variety of complex systems. Recent examples of such cross-disciplinary investigations are time-resolved

spectroscopy with entangled photons, a quantum-theoretical approach to processes in photosynthesis, non-Markovian effects in organic photovoltaic systems, or control of electron transfer reactions via techniques from cavity-QED. A characteristic feature of his research is that the chemical, condensed matter or biomolecular systems under investigation are not oversimplified, but relevant degrees of freedom are carefully selected and included into the models. In this way, one can identify which of these degrees of freedom are essential for certain dynamical processes in complex systems. Thus, this research offers an intriguing approach to the fundamental question how complexity arises from microscopic principles. A nice example is the cooperative effort with Prof. Minagawa's group at the National Institute for Basic Biology (next door to IMS) showing how advanced graph methods from network science and quantum dynamics of open systems can be combined with sophisticated analyses of molecular structure to gain deeper insights into the functionality of light-harvesting complexes in photosynthesis. At the same time, the unique approach of Prof. Ishizaki combining methodologies from different fields allows one to devise novel ways to use quantum techniques to control complex many-body systems.

Masahiro EHARA

Professor Masahiro Ehara and his group develop theoretical approaches to accurately describe large molecular aggregates. It was fascinating to see, that the group not only applies state-of-the-art computational approaches to tackle important problems, but also plays a leading role in developing new computational methods with large impact also in other fields of research. As a prime example, they devised an innovative inverse design method which was demonstrated by developing functional 1D molecular aggregates and moleculenanoparticle systems. The activities also comprise applications of advanced computational methods to an impressive breadth of studies on electronic structure to better understand and control technologically relevant materials and photo-induced processes. These include functional materials, such as modified single-wall carbon nanotubes, metal nano clusters, and heterogeneous catalysts. The investigations are performed in a larger framework of national and international collaborations.

Conclusion

In conclusion, the Department of Theoretical and Computational Molecular Science at IMS performs science at the highest international level. Each of the different research groups have achieved impressive results in the past years, contributing to a better understanding how functionality of complex molecules emerges from their microscopic structure, how these aggregates interact with their environment or with external fields, and how a deeper understanding of the underlying principles can be used for applications in material design and quantum control. The research environment offered by IMS to these scientific activities is truly exceptional, one the one hand side due to the critical density of exceptional researchers in theory and experiment at IMS, but also by the available infrastructure, in particular the supercomputer facility. The research of the theory groups is embedded into larger national and international collaborative networks, and there is even a nice example of an internal theory-experiment collaboration within IMS. Overall, my visit at IMS was outermost enjoyable and offered ample positive intellectual impressions to me as a non-expert in most of the presented research areas. Like last year, my warm thanks go to Director General, the scientists and the organizational team for the hospitality and for making my stay such a pleasant one.

Heidelberg, 8 May 2024

7-3　協奏分子システム研究センターの評価

7-3-1　David A. Leigh 外国人運営顧問

Prof. Dr. Yoshihito Watanabe

Director General

Institute for Molecular Science

Okazaki

Japan

14th December 2023

Dear Director Watanabe,

Evaluation of Various Groups of the NINS Institute for Molecular Science, Okazaki, Japan

Many thanks for the warm and kind hospitality of you and your colleagues during my on-site visit to the NINS Institute for Molecular Science on 3–8 December 2023. During my visit I discussed with you the response to my previous Report (April 2023) and was given in-depth presentations by Prof. Shuji Akiyama, Director of CIMoS, and other members of CIMoS and other parts of IMS. I also attended an excellent interdisciplinary workshop on molecular machines with leading researchers from all over Japan (and online from Strasbourg), organized by Prof. Iino.

1. Response to my Previous (April 2023) Report

I note the significant steps you have taken in response to the recommendations of my April 2023 report. These include:

1. To address the relatively small size of IMS groups compared to international competitors you are (i) allowing PIs to hire (through funding from their own grants) associate and/or junior associate professors for research; and (ii) the SOKENDAI (graduate school) is being reorganised which you hope will make it more attractive to PhD applicants.

   I hope that these measures prove successful. I believe that the best way to get access to potential graduate schools is to foster closer relationships with universities, as I outlined in my previous Report. But I accept there are practical, and perhaps institutional, reasons why this may be difficult to achieve.

2. To address the substantial gender imbalance amongst PIs I was delighted to learn that you are making three cross-appointment positions at Associate/Full Professor level and that two of these have already been agreed upon. That is a fantastic response and I'm sure will provide role models that will demonstrate to female PhDs and postdocs that a career for them is possible in academic research. I hope that in time that you might also reconsider the removal of the 'no internal promotion' rule for female scientists, in recognition of the unique burden of women in bearing children, as recommended in my previous report. I'm aware that female PhD students and postdocs have mentioned the importance of stability during their late-20s and 30s, when they would (or could) be starting and raising young families. Knowing that they would have to change institution to be promoted is a reason they may not seek a position at IMS.

3. I was also delighted to hear that you intend to offer a PI position to a foreign colleague to establish a satellite lab at IMS. This is a great initiative to bring cultural diversity in the way of thinking at PI level to IMS. I think it will be great for Japanese science generally. I am sure that leading scientists in Europe and the US will follow this development closely!

4. The cross-appointment with the University of Tokyo of Prof. Makoto Fujita, one of the world's leading scientists, is certainly a boost for the international recognition of IMS.

5. I was also impressed with the new multidisciplinary projects you are proposing to bring strengths from different parts of IMS (and elsewhere) together to tackle major scientific problems: Spin-Bioscience—which ranges from the development of novel molecular probes for MRI to magnetic resonance imaging on living organisms— and a project that seeks to leverage IMS's great strengths in photonics and bioscience.

2. Overall impressions

My overall impression of IMS in two visits has been over-whelmingly positive: It is an influential and highly respected institute in the field of the molecular sciences. It is globally renowned for carrying out high quality innovative research, its strong faculty, an excellent research environment, and collaborations with other institutions and universities, all of which make it a leading centre for research internationally. The Institute and Department strengths include that the staff are well motivated and perform at the highest level. The leadership is outstanding. The level of equipment and instrumentation is well above that of many world class laboratories in the USA and Europe. This gives the groups at IMS a significant advantage over competitors worldwide in terms of their ability to tackle the toughest problems in science today. I will not repeat here the other observations discussed in my previous Report.

3. Evaluation of Various Individual Groups of the NINS Institute for Molecular Science

On this visit I had research presentations from 3 members of CIMoS and 2 from other parts of IMS. Two were primarily associated with studies on the molecular basis and mechanisms of biological systems (Akiyama, Okazaki), one working on aspects of materials (Yamamoto) and two working on the application of state-of-the-art spectroscopy to molecular problems (Kuramochi, Kumagai). All of these groups are of very high quality; they tackle important fundamental problems in creative ways and publish their findings in the best international journals.

Prof. Shuji AKIYAMA

PProfessor Akiyama's research focuses on the Circadian clock system in cyanobacteria, in particular the atomic-scale origin of slowness of the cycle and its rhythm, structure and diversity. He is a world leader in these areas, seeking answers to deeply fundamental questions from molecular mechanism to how these extraordinary systems evolved. The group is trying to answer profound scientific questions regarding the way that biology works at the molecular level. The breadth of science being undertaken is remarkable for a single research group, as they seek an understanding of (i) the self-sustained 24 hour oscillation of the system, (ii) the temperature compensation observed, and (iii) the synchronization of the clock. Recent highlights include "*Atomic-scale origins of Slowness in the cyanobacterial Circadian clock*," *Science* **349**, 312–316 (2015), "*Regulation mechanisms of the dual ATPase in KaiC*," *Proc.*

Natl. Acad. Sci. USA **119**, e2119627119 (2022) and "*Elucidation of master allostery essential for Circadian clock oscillation in cyanobacteria*," *Sci. Adv.* **8**, eabm8990 (2022).

Prof. Hiroshi YAMAMOTO

Professor Yamamoto is an international leader in the development of electronics based on π-systems in soft matter. In recent years he has exploited the low dimensionality of the π-electrons to generate materials with a range of different characteristics to silicon. The potential applications of this research range from nano-scale devices to superconductivity and quantum computing. Recent highlights include "*Giant spin polarization and a pair of antiparallel spins in a chiral superconductor*," *Nature* **613**, 479–484 (2023) and "*Highly durable spin filter switching based on self-assembled chiral molecular motor*," *Small* **19**, 2302714 (2023).

Assoc. Prof. Hikaru KURAMOCHI

Associate Professor Kuramochi is an exciting, relatively new, appointment (April 2020) who uses ultrafast spectroscopy to study chemical reaction dynamics. This includes ultrafast spectroscopy at the single molecule level, the development of novel light sources, and the use of advanced ultrafast spectroscopy to study ensembles. Recent highlights include "*Rapid-Scan Resonant Two-Dimensional Impulsive Stimulated Raman Spectroscopy of Excited States*," *J. Phys. Chem. A* **127**, 5276–5286 (2023) and "*Environment-Sensitive Fluorescence of Cot-Fused Perylene Bisimide Based on Symmetry-Breaking Charge Separation*," *Photochem. Photobiolo. Sci.* **22**, 2541–2552 (2023).

Assoc. Prof. Kei-ichi OKAZAKI

Associate Professor Okazaki was a Project Associate Professor at IMS from 2016–2020 and since 2020 has been an Associate Professor at the Research Center for Computational Science. Okazaki's group elucidate the dynamics of biomolecular machines through molecular simulations and other theoretical/computational methods. His growing standing in the field is reflected in his recent co-authorship of an opinion piece on protein folding and folds, from experts in the field ["*Opinion: Protein folds vs. protein folding: Differing questions, different challenges*," *Proc. Natl. Acad. Sci. USA* **120**, e2214423119 (2023)]. Other recent highlights include "*Molecular mechanism on forcible ejection of ATPase inhibitory factor 1 from mitochondrial ATP synthase*," *Nat. Commun.* **14**, 1682 (2023) and "*Structure and mechanism of oxalate transporter OxlT in an oxalate-degrading bacterium in the gut microbiota*," *Nat. Commun.* **14**, 1730 (2023).

Assoc. Prof. Takashi KUMAGAI

Associate Professor Kumagai is another recent appointment, arriving at IMS in 2020. His research focuses on advanced nano-spectroscopy with time- and spatially-confined light. While he continues to build new instruments in his lab, he has made good use of instruments from his previous post in Berlin. Recent highlights include "*Inelastic Light Scattering in the Vicinity of a Single-Atom Quantum Point Contact in a Plasmonic Picocavity*," *ACS Nano* **17**, 10172 (2023) and "*Nanoscale coherent phonon spectroscopy*," *Sci. Adv.* **8**, eabq5682 (2022).

I hope that this short report and my previous longer one are useful to you and your colleagues in thinking about how to continue to develop IMS. It is a truly fantastic institute with excellent scientists doing world class research. It has been a pleasure to visit and

interact with such inspiring people, from the young researchers to the thoughtful generous leadership. I hope to visit again and to collaborate with some of the groups there. I wish you and your colleagues much continued success!

Best wishes,

David A. Leigh FRS

Royal Society Research Professor & Sir Samuel Hall Chair of Chemistry, University of Manchester, UK

14 December 2023