7-3　生命・錯体分子科学研究領域の評価

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

24th April 2023

Dear Director Watanabe,

Evaluation of the Department of Life and Coordination-Complex Molecular Science

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 6–8 March 2023. During my visit I was given in-depth presentations by Prof. Ryota Iino, Director of the Department of Life and Coordination-Complex Molecular Science, and other members of the Department and IMS. I also received presentations from Prof. Masahiro Ehara, Director of the Research Center for Computational Science (RCCS), Prof. Satoshi Kera, Director of the UVSOR Synchrotron Facility, Prof. Koichi Kato, Ex-Director of the Exploratory Research Center on Life and Living Systems (ExCELLS) and Distinguished Professor Makoto Fujita of the Division of Advanced Molecular Science. For reasons of clarity I have organised my report in 4 Sections, plus a Summary at the beginning.

Summary

The Department of Life and Coordination-Complex Molecular Science at IMS is a center of research excellence that is tackling some of the most important and profound challenges in the molecular sciences today. Its success and performance is reflected not only in the outstanding research outputs (in terms of journal publications, invited lectures and prizes) of the current PIs, but also in the remarkable number of high quality scientists that have started their independent careers at IMS and then moved to be highly successful Associate or Full Professors at other universities.

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. However, the IMS groups are considerably smaller than those of international competitors, which means that they simply do not have the human resource to exploit breakthroughs as quickly or as well as larger competitor groups internationally. A contributing reason for the small group sizes is the available budget for personnel, which is perhaps half that of competitors in the USA and Europe. Another factor may be poor access to the best students for recruitment purposes because of a general lack of integration and cooperation for mutual benefit with universities. A striking weakness in terms of staffing is the lack of diversity in gender at PI level. In my opinion, it is important for IMS, and for the future of Japanese science in general, that this is addressed as quickly as possible.

1. Overall impressions

My overall impression of IMS, and the Department of Life and Coordination-Complex Molecular Science in particular (one of the four Departments of IMS), is over-whelmingly positive: It is an influential and highly respected institute in the field of the molecular sciences. The Department of Life and Coordination-Complex Molecular Science 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.

2. The role of IMS in the national scientific landscape

The Institute for Molecular Science was founded in 1975. I believe that one reason for establishing national research institutes at that time was to support and supplement the national research effort of universities by being a focal point for 'big' facilities that individual universities could neither afford to purchase nor to run. This remains a compelling need today, for example few universities would be able to run a synchrotron. Nevertheless, the scientific era we live in now is very different from the 1970s, and many universities have large instruments and facilities that serve as resources for others researchers in Japan and worldwide. Within this changing scientific climate, research institutions and their position in national and international science strategies benefit from growth and revaluation of purpose. In particular, the role and interaction of research institutions with other national bodies, such as universities, should evolve. In this regard, I note that IMS has undergone a healthy number of changes in structural organisation over its lifetime, including the establishment of many new, highly successful and internationally important, research centers.

A key part of IMS's Mission Statement is that it should '…*enhance the progress of molecular science covering broader research areas via mutual exchange of human resources among all the universities in this country*…'. IMS fulfils this role admirably by providing an opportunity for researchers to be fully independent at a much earlier stage (associate professor) than is traditional in Japanese universities. For a dramatic example of the impact that independence at a young age can have in the chemical sciences, one need look no further than the 2021 Nobel Prize in Chemistry, awarded to Ben List and David MacMillan for the development of asymmetric organocatalysis. The two seminal papers that led to that Nobel Prize were the first (List) and second (MacMillan) papers of the recipients as independent PIs. Perhaps because they have no scientific program of their own to build on initially—or perhaps because of the impetuosity of youth(!)—young PIs are often less conservative than more established PIs and more inclined to explore radically new concepts and ideas that can lead to breakthroughs, and even completely new fields of science. The consequences of this aspect of IMS's employment policy must be taken into account in any objective consideration of the impact and success of IMS.

Since IMS was founded in 1975, more than 60 IMS associate professors have been promoted to full professors or similar positions at other institutions, including the following researchers who are particularly relevant to the research area covered by the Department of Life and Coordination-Complex Molecular Science: Tatsuya Tukuda (Professor, University of Tokyo; https://www.chem.s.u-tokyo.ac.jp/users/chemreact/index-e.html); Takeaki Ozawa (Professor, University of Tokyo; https://analyt.chem.s.u-tokyo.ac.jp/en/); Hirokazu Tada (Professor, Osaka University; http://molectronics.jp/en/); Hidehiro Sakurai (Professor, Osaka University; https://www-chem.eng.osaka-u.ac.jp/~sakurai-lab/en/index.html); Donglin Jiang (Professor, National University of Singapore; https://blog.nus.edu.sg/chmjd/professor/); and Shigeyuki Masaoka (Professor, Osaka University; http://www.chem.eng.osaka-u.ac.jp/masaoka_lab/english/index.html).

In addition, nearly 130 IMS assistant professors have been promoted to full professors or similar positions at other institutions. Outstanding examples include: Mitsuhiko Shionoya (Professor, University of Tokyo; https://www.chem.s.u-tokyo.ac.jp/~bioinorg/indexE.html); Hiroshi Kitagawa (Professor, Kyoto University; http://kuchem.kyoto-u.ac.jp/ossc/index.html); and Hajime Ito (Professor, Hokkaido University; https://itogrouphp.eng.hokudai.ac.jp/).

These are staggeringly successful numbers. Although Japanese universities are increasingly allowing full independence of PIs earlier in careers, I believe that this is still one of the most important factors that makes IMS stand out as an attractive institution for outstanding young researchers wanting to start their independent academic career.

However, the very success of this role of IMS disadvantages the institute in terms of metrics such as citations and international awards. Since promotions in IMS are prohibited, all of your (very successful) young staff have to leave to be promoted elsewhere. It is at the Full Professor stage that one gets the full benefit, in terms of citations, recognition and funding, of having built an internationally important research program. The tremendous success of IMS is thus reflected in these 190(!) staff that have been promoted to positions elsewhere in the 48 years since it was founded. That is, on average, nearly 4 staff members a year for an institution that currently numbers 36 Full, Associate and Project Professors and 40–50 Assistant Professors.

3. Gender imbalance and lack of international diversity at PI level

IMS currently has 18 Full Professors (including Distinguished Professor Fujita), 16 Associate Professors and 2 Project Professors. Of these 36 senior academic staff, just one (Assoc. Prof. Momiyama) is female. This extremely poor gender imbalance at PI level is a weakness for many reasons: First of all it means that IMS is missing out on a huge amount of talent; secondly, it means there is a lack of senior role-models in IMS that would showcase to female young researchers that IMS is well set up for women to succeed in a scientific career. In contrast, the junior positions (PhD and Post-Doctoral Fellows) in all of the research groups I met with had good gender balance (typically 30–50% female). There are no doubt many reasons—historical, cultural, social and practical—that contribute to the gender imbalance at PI level, but it is a problem that I strongly suggest you start solving immediately.

Of course, it would be wrong to suggest that IMS is unique in having a gender imbalance problem; my own Department has only 15 women PIs out of 80 faculty, which is probably typical of UK Chemistry Departments. It is an issue in science academia that many western countries struggled with. My advice is to start by asking female professors and female PhD students what they think are the issues involved and what would make a difference to them. Then it will be up to men and senior leadership to take the lead in implementing solutions that women feel would make a difference. If, for example, young women scientists tell you that the non-promotion of Assistant or Associate Professors within the Institute is an issue because it is desirable to have stable roots for starting or growing a family then, in my view, that rule should be *very publicly* removed for women scientists. Other ways of supporting women professors, such as giving them a PDRA for a year any time they give birth to help them run their group during this important time, should be considered if, again, young female scientists tell you that they are reluctant to pursue academic careers because of the difficulty of juggling a young family with establishing their research program. These are examples of the sort of initiatives that might help make IMS an institute that women PIs really want to join. Let me reiterate that in my opinion the role of men in this should be to put into place initiatives that women say they want; it is not for men to concoct plans that they *think* women want.

Also on the issue of diversity, although less important, it feels to me like a missed opportunity that all 36 of the professors in IMS are Japanese. There is some international diversity within research groups—Prof. Iino's group is an excellent example of this—it is at PI level that it is lacking. As with gender, diversity in terms of origins, ethnicity, upbringing and education brings different ways of thinking, not just with regards as to how to tackle scientific problems, but also in the way institutes and laboratories are organised and run. Europeans and Americans love Japan: The people, the culture, the country and the food. Although there may be cultural and language issues with attracting outstanding foreign PIs of the quality that would benefit the institute to move full time to Japan, I suggest it would be easy for IMS to attract outstanding foreign PIs to have satellite labs at IMS. Many leading chemists (including Fraser Stoddart, Ben Feringa and myself in the molecular machines field) have satellite labs in China, for example. I believe the Chinese have found that our presence (and that of many others) gives them insight into how leading US and UK scientists think and run their research programs and labs and that has benefitted Chinese science in their ways of thinking and scientific culture. Perhaps this is something that IMS could consider, maybe through participating in or leading bids in the WPI program, which could provide funding for such cross-national appointments.

4. The Department of Life and Coordination-Complex Molecular Science

The Department has 8 research groups, four primarily associated with studies on the molecular basis and mechanisms of biological systems (Iino, Kato, Aono and Nakamura) and four motivated by unsolved problems in chemical synthesis (Uozumi, Kusamoto, Momiyama and Segawa). 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. Ryota IINO

Professor Iino's research focuses on the study of biomolecular motors using advanced imaging techniques. He is a world leader in the use of super-resolution microscopy to investigate the operational and design principles of molecular motors. These include the visualisation of fast dynamics of motor-molecules such as V-ATPase, kinesin, chitinase and dynein by single-molecule imaging. In the last few years he has expanded his group's program to include the development of new cutting-edge single-molecule techniques for angstrom-precision tracking and high-speed tracking. This is a highly competitive area trying to answer profound questions regarding the way that biology works at the molecular level. Recent highlights include "*Direct observation of stepping rotation of V-ATPase reveals rigid component in coupling between V_o and V_1 motors*," *Proc. Natl. Acad. Sci. USA* **119**, e2210204119 (2022) and "*Combined approach to engineer a highly active mutant of processive chitinase hydrolyzing crystalline chitin*," *ACS Omega* **5**, 26807–26816 (2020).

Prof. Yasuhiro UOZUMI

Professor Uozumi is a highly respected international leader in the development of highly effective heterogeneous catalysts, particularly for applications in green chemistry. In recent years he has developed highly active ppb-catalysts with turnover numbers >3 million for various coupling reactions and developed polymer supported asymmetric Pd-catalysts that work in water. He has recently applied his expertise in polymer supported reagents to photoredox catalysis in water, bringing a 'green' perspective to one of the hottest areas of synthetic organic chemistry today. Recent highlights include "*Photocatalytic carbinol cation/anion Umpolung: Direct addition of aromatic aldehydes and ketones to carbon dioxide*," *Org. Lett.* **23**, 7194–7198 (2021) and "*Production of bio hydrofined diesel,* *jet fuel, and carbon monoxide from fatty acids using a silicon nanowire array-supported rhodium nanoparticle catalyst under microwave conditions*," *ACS Catal.* **10**, 2148–2156 (2020).

Assoc. Prof. Norie MOMIYAMA

Associate Professor Momiyama is well known for her significant, original and important contributions in asymmetric organocatalysis. She continues to use halogen bonding as a recognition element in new organocatalysts and polymer catalysts. She has recently started a highly ambitious program on the digitisation of chemistry which seeks to take organic synthesis to the frontiers of what is chemically possible. Recent highlights include "*Three-center-four-electron halogen bond enables non-metallic complex catalysis for Mukaiyama–Mannich-type reaction*," *iScience* **25**, 105220 (2022) and "*Chiral counteranion-directed catalytic asymmetric methylene migration reaction of ene-aldimines*," *J. Org. Chem.* **87**, 9399–9407 (2022).

Assoc. Prof. Tetsuro KUSAMOTO

Associate Professor Kusamoto's group create photofunctions based on stable radicals. These include luminescent systems based on photostable triaryl radicals and magnetoluminiscent systems. His group have a series of papers in the top journals in the field, such as *JACS* and *Angewandte Chemie*. Recent highlights include "*An open-shell, luminescent, two-dimensional coordination polymer with a honeycomb lattice and triangular organic radical*," *J. Am. Chem. Soc.* **143**, 4329–4338 (2021) and "*Radical-based coordination polymers as a platform for magnetoluminescence*," *J. Am. Chem. Soc.* **143**, 5610–5615 (2021).

Assoc. Prof. Yasutomo SEGAWA

Associate Professor Segawa is widely regarded internationally as a rising star in the field of organic chemistry. His research focuses on the development of new synthetic methods and strategies for constructing topologically complex carbon-rich molecules. He has published the synthesis of a series of extraordinary catenanes and knots and Mobius strip molecules. His research achievements have been published in the highest impact, most visible, journals, including *Science*, *Nat. Chem.*, *Nat. Synth.*, *JACS* and *Chem*. Recent highlights include "*Synthesis of a Möbius carbon nanobelt*," *Nat. Synth.* **1**, 535–541 (2022) and "*Topological molecular nanocarbons: All-benzene catenane and trefoil knot*," *Science* **365**, 272–276 (2019). In addition, he has started a research program on microcrystal electron diffraction structure determination which offers the potential for revolutionising structure determination of organic molecules.

Assoc. Prof. Akihiko NAKAMURA (cross-appointment)

Associate Professor Nakamura is a cross-appointment with Shizuoka University and his group's research interests include protein engineering, heterogeneous enzyme catalysis, and single-molecule analysis. His research program is involved in developing and improving plastic degrading enzymes which have the potential to solve critical environmental problems related to plastic degradation. Recent highlights include "*Positive charge introduction on the surface of thermostabilized PET hydrolase facilitates PET binding and degradation*," *ACS Catal.* **11**, 8550–8564 (2021) and "*Domain architecture divergence leads to functional divergence in binding and catalytic domains of bacterial and fungal cellobiohydrolases*," *J. Biol. Chem.* **295**, 14606–14617 (2020).

Prof. Koichi KATO (ex-Director of ExCELLS)

The ambitious aims of this group are to understand how chemistry becomes biology, the origin of life. This is one of the contemporary 'Grand Challenges' of science, involving chemistry, physics and biology. Professor Kato collaborates with many groups around the world and has been hugely successful in establishing major consortia, such as ExCELLS. His group's own research program is aimed at answering fundamental questions such as what is the blue print for protein glycosylation? and what are the design principles for protein assembling systems? Recent highlights include "*Key residue for aggregation of amyloid-β peptides*," *ACS Chem. Neurosci.* **22**, 3139–3151 (2022) and "*An embeddable molecular code for Lewis X modification through interaction with fucosyltransferase 9*," *Commun. Biol.* **5**, 676 (2022).

Prof. Shigetoshi AONO

Professor Aono is a bioorganic chemist whose research interests revolve around metalloproteins and sensor proteins. His group are working to establish the protein machinery responsible for the active site assembly and maturation of NiFe-hydrogenases and also the molecular mechanism of O_2 sensing and signal transduction by the HemAT/CheA/CheW complex. Recent highlights include "*Crystal structural analysis of aldoxime dehydratase from Bacillus sp. OxB-1: Importance of surface residues in optimization for crystallization*," *J. Inorg. Biochem.* 230 (2022) and "*Heme controls the structural rearrangement of its sensor protein mediating the hemolytic bacterial survival*," *Commun. Biol.* **4**, 467 (2021).

There are a number of successful collaborations between groups in the Department of Life and Coordination-Complex Molecular Science and other groups in IMS that clearly add value: For example, the Uozumi group with Prof. Ehara (Dept. Theoretical Comp. Mol. Sci.); Prof. Momiyama working with Prof. Suzuki (Instrument Center) on the design and understanding of complex catalysts; a series of highly successful collaborations between the Iino group and Prof. Okazaki (Dept. Theoretical Comp. Mol. Sci.) on simulations of chitinase, with Prof. Koga (ExCELLS) and Kosugi (CIMoS) on computational engineering of PET hydrolase and redesigning of V_1-ATPase, and with Profs. Kumagai and Nishida (Mesoscopic) on single protein vibrational spectroscopy; as well as a series of collaborations between the Kato group and various groups that bring both experiment and theory to bear on problems relating to amyloid formation mechanisms.

The quality of equipment in each group's laboratories in the Department of Life and Coordination-Complex Molecular Science, and in the institute in general, is outstanding and significantly better than almost all university laboratories worldwide. The Segawa laboratories, in particular, are one of the best equipped labs for cutting-edge organic synthesis that I have ever seen. They are better equipped than my own lab, which is one of the best equipped labs in the UK! This gives the groups at IMS a significant advantage over competitors worldwide in terms of their ability to tackle the toughest problems in the molecular sciences today.

However, although they are highly productive, the groups tend to be significantly smaller than that of their international competitors (my own group, for example, is 30–35 researchers, equally split between PhD students and postdoctoral scientists). The small size of the groups in the Department inevitably means that they do not have the person-power necessary to capitalise on conceptual breakthroughs as quickly as others around the world would do.

I think that there are several ways that IMS could consider addressing this issue:

(i) The first is that, in my opinion, there needs to be an increase in budget. I realise that it is always easy to say ‘give more money’ but, in this case, it is clear that the groups are underfunded in terms of personnel by a factor of 2 compared to their international competitors. This is a key disadvantage when one is in competition to find answers to important scientific problems.

(ii) A second approach that might be useful could be to reconsider your relationship with universities. As I noted earlier, you have more and better laboratory equipment than universities, but they have more—and better access to—young researchers in the form of students. I suggest you consider the possibility of having more cross-appointments with universities, perhaps having IMS staff teach courses at the universities (which would give potential PhD students exposure to IMS staff as well as easing teaching loads for staff at universities). In this way universities would benefit by having easier access to more equipment and extra staff who would teach, while IMS would benefit from having better access to a larger pool of potential researchers. However, if this is done, care must be taken to ensure that cross-appointments are done properly. If I recall correctly, the cross-appointment of Prof. Nakamura requires him to teach a full teaching load at Shizuoka University. That appears from the outside to be completely inappropriate; if it is a cross-appointment then I would expect half his salary should be paid by the university (and half by IMS) and he should have, at most, a 50% teaching load and no administration at the university so as to take into account all the additional travel and work he has to do in order to play a substantial role in two locations.

I hope that this short report proves 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. Thank you for this opportunity.

Best wishes,

David A. Leigh FRS
Royal Society Research Professor & Sir Samuel Hall Chair of Chemistry, University of Manchester, UK
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