# Advisory Council Report

on

# RIKEN Quantitative Biology Center (QBiC)

**November 2013**

**Meeting Program**

The Advisory Council (AC) of the RIKEN Quantitative Biology Center (QBiC) met in Kobe from November 24-27 to discuss the progress and scientific directions of this new Center (established April 2011). The meeting opened with a tour of OLABB in Osaka and visits to individual laboratories. Following the return to Kobe, RIKEN Executive Director Dr. Maki Kawai summarized the history, current missions and organization of RIKEN. She drew attention to the Terms of Reference from the President Noyori to the ACs of each Center, including specific points relating to the management policy of the QBiC (see Appendix).

The QBiC Director Dr. Yanagida gave an overview of the QBiC. He described the overall mission of QBiC, which is to model whole cells so as to predict and control living systems. He outlined the organization of the Center. He presented QBiCs 10-year roadmap comprising four steps: quantitative measurement, modeling and design; the elucidation of common principles; the prediction of systems behavior; and, finally, the control of systems behavior. Further information about the overall goal of QBiC and the individual investigators was included in a White Paper, copies of which were distributed to the AC before the meeting. Dr. Yanagida also presented his own terms of reference for the AC (see Appendix).

The specific research topics were presented on days 2 and 3. Following an introduction by QBiC Deputy Director Dr. Taiji, the AC heard presentations on the main research topics - cell polarity, differentiation, techniques, structure and design. The presentations were made by up to three group leaders and there was ample time for discussion. On day 2 there were two short presentations on collaborative research, and an evening poster session summarizing work from each of the labs. Formal presentations were concluded on the afternoon of day 3 with an overview of QBiCs Future Plans led by Team Leader Dr. Takahashi, with participation from several of the group leaders, and lively discussion with the AC. Overall, the written materials, presentations and posters were of the highest quality.

Ample time was available on the afternoons of days 2 and 3 for internal discussions of the AC. On the morning of day 4, the AC drafted its report on the Center and evaluations of the individual groups. Afterwards, the AC presented its report and recommendations to Dr. Kawai, Dr. Yanagida and the group leaders.

During the review, the AC met only with group leaders. ***The AC recommends that in future it meet with representatives of the graduate students, postdoctoral fellows and research scientists*** to enable the AC to evaluate the scientific and working environment for junior researchers.

## Summary

QBiC is a highly interdisciplinary Institute at the interface between biology, engineering and physics. It focuses on developing new, quantitative approaches to biology—especially through single-molecule and single-cell techniques, together with systems theory. This research topic is timely and should significantly strengthen biological research in Japan. Despite being only 2.5 years old, QBiC has established a state-of-the art infrastructure with technological developments at the highest international standards. The institute has clear direction from strong management. There are many collaborations both within and outside of RIKEN, and internationally.

## Progress

Given that QBiC has only been operating for 2.5 years, progress towards meeting the long-term goals has been excellent. QBiC has already established itself as a world-class Center for quantitative measurement, modeling and design.

1. Microscope development takes place in several laboratories. This concerted effort is not redundant, but rather the concentration brings QBiC to the very highest international level. There is a high level of innovation, which is evidenced, for example, by patent applications. To complement the new microscopes, such as the new light-sheet-based single-molecule microscope and the ultrafast super-resolution microscope, there has been considerable effort in image processing and the development of new imaging tools. What is particularly impressive is that technical contributions are being made by several labs, indicating that the environment is supportive and collaborative.
2. There are several theory and simulation groups. This effort ranges from atomic modeling through to single-molecule modeling, the modeling of network behavior, and the beginning of whole-cell modeling. The Center takes advantage of its close ties with the K supercomputer.
3. Advanced tools in molecular and cell biology - mass spectrometry, molecular genetics and micro-devices - are also ground-breaking and at the highest international level. Particular mention is made to single-cell metabolomics, CMOS chips and new site-specific gene manipulation and knock-out tools.
4. There is close collaboration between theorists and experimentalists. It is particularly noteworthy that the stem-cell dynamics project is led by a theorist who has enlisted the help of experimentalists to test his hypothesis that “stemness” is associated with oscillatory network behavior.

The presentations clearly demonstrated that the combination of experiment and theory has already led to major discoveries. These include

1. The role of molecular number fluctuations in the dynamic variation of polarization during cell motility, and the potential roles of these fluctuations in the searching strategies of locomoting cells.
2. The role of feedback between motor activity and microtubule state in the dynamic decision-making process by which a neurite differentiates into an axon.
3. The role of network dynamics in determining the states of stem cells, and the measurement of fluctuations in stem cell transcription factors during early mouse development.
4. The roles of network dynamics in circadian rhythms.

Despite the relative newness of the Center and the fact that some of the groups have only just set up their labs, there was a feeling from the AC that some of the groups had not published as much as they could have. With the infrastructure established and exciting results now being produced, ***the AC recommends that increased emphasis be given to the publication of high-quality papers and the dissemination of the results at international meetings.***

Support from external grants is generally strong, another indication that the Center is progressing well in its early phase.

**Objectives**

The roadmap (2011-2020) vision of Dr. Yanagida was clear and most investigators are on board. Indeed, it was remarkable how often the same themes recurred in the different presentations. The long-term goal is whole-cell modeling to be achieved through four steps: quantitative measurement, modeling and design; the elucidation of common principles; the prediction of systems behavior; and, the control or steering of systems behavior. Two themes are prominent: the bridging of scales (reducing dimensionality) through the study of system behavior, and the role fluctuations (yuragi).

With respect to achieving these goals, it is clear that the first two are progressing well: the quantitative measurement, modeling and design and the elucidation of common principles. The AC feels that despite this progress it is very important to really “nail” the finding that have been already made - for example, that molecular number fluctuations play a fundamental role in variation in dynamic behavior. Therefore, the studies should not move too quickly to the prediction and control phases. Likewise, the development of new techniques should not be abandoned.

The AC felt that it in order to be successful in the control phase of the objectives, it was going to be necessary to focus on a limited number of systems. The committee suggests that the Center choose three areas - such as the immune system, stem cells and the brain - to focus on. One strategy would be to bring several QBiC group leaders to collaborate in each of these areas. **The AC recommends that QBiC recruit three additional team leaders to bring in biological expertise to the projects.** In this way, QBiC can be in the driver's seat with these projects (rather than playing secondary roles to outside collaborators). These projects would constitute a "strike zone" and maximize the chance of making a truly huge impact, i.e. a home run. The hiring of these new groups will require additional budget support and space.

**Fostering young talent, diversity and internationality within QBiC**

It is highly commendable that 40% of the group leaders were recruited while in their 30's. This no doubt contributes to the innovation, collaboration and general excitement within the Center. However, given that most positions in RIKEN are of limited duration, it is especially important that these groups are given advice from their senior colleagues to prepare them for future positions in academia, research or industry. ***Therefore the AC recommends establishment of a mentoring program for unit and team leaders.*** For example, a group of more senior group leaders including the Director and a group leader not closely collaborating with the unit or team leader, provide periodic advice on publications, grants, personnel management and ultimately help with job applications.

To increase the internationality, ***the AC recommends that QBiC establishes an International PhD program***, for example modeled after the IMPRS of the Max Planck Society***.*** Key aspects of this program are international advertising, common recruitment mechanism for all labs, on-campus interviews of short-listed candidates, a minimum of 50% foreign student intake, an international office to help moving to Japan (apartments, banks etc.), and student organized events such as special lectures, retreats, opportunities to develop soft-skills such writing manuscripts, making presentations, and applying for grants.

To bring in the top postdocs and foster collaborations, especially between experimental and theory groups, ***the AC recommends the establishment a Postdoctoral Fellows program*** modeled after e.g. the Lewis-Sigler program at Princeton, the Bauer program at Harvard or Elbe program at MPI-CBG in Dresden, Germany.

The gender diversity of QBiC is very low with only one female group leader. ***The AC r****ecommends that more female scientists be recruited at all levels.* This requires

concerted attention from upper management including the Director of the QBiC and the RIKEN administration. We were disappointed that this subject was not addressed in the opening presentations and no data was made available to the AC about the numbers of female scientists in QBiC. Attention should be given to practical issues such as child care and family leave.

**Maintaining and improving diversity of approaches, fostering collaborations**

There are a strong collaborations within QBiC, with other institutes inside and outside RIKEN and also international collaborations.

One difficulty identified by the AC is that the Center is split between several sites. This makes collaborations difficult. To facilitate collaborations within the Center, ***the AC recommends that additional space be made available adjacent to the new building at Osaka University***.

**Budget and other issues**

The Center is strongly supported by RIKEN administrative staff, and the AC strongly supports the maintenance of this level of support.

Technology transfer is important for an Institute developing new techniques and should be a priority for QBiC and RIKEN. The AC were unable to evaluate the procedures for technology transfer. The QBiC Director and the RIKEN administration need to make sure that appropriate and effective measures are taken in this regard.

**Summary of recommendations**

1. The AC recommends that additional space be made available adjacent to the new building at Osaka University.
2. The AC recommends that QBiC recruit three additional team leaders to bring in biological expertise to the projects.
3. Now that the QBiC has successfully established itself, the AC recommends that emphasis now be given to the publication of high-quality papers and the dissemination of the results at international meetings.
4. The AC recommends the establishment of a mentoring program for unit and team leaders.

5. The AC recommends that more female scientists be recruited at all levels.
6. The AC recommends that QBiC establishes an International PhD program
7. The AC recommends the establishment a Postdoctoral Fellows program.
8. The AC recommends that in future it meet with representatives of the graduate students, postdoctoral fellows and research scientists.

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Chair of the Advisory Council
8 December 2013

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**Appendix: Terms of Reference**

*Terms of reference (QBiC)*

*Direction of QBiC*

- *Objectives 2011-2020*
- *Progress*

*Fostering talent and diversity within QBiC*

- *Recruiting young talent*
- *Maintaining and improving diversity of approaches*

*Current collaborations within RIKEN, Japan and internationally*

*Terms of reference (President)*

*Up to international standards?*

*Management policy*

- *roadmap*
- *attracting top international talent*
- *personnel turnover*
- *collaboration inside and outside RIKEN (including globally)*

*RIKEN Missions (Dr. Kawai)*

*Strategic, problem-solving research to meet national and social needs*

*Develop, maintain and share state-of-the-art infrastructure*

*Interdisciplinary research*

*Collaboration within and outside RIKEN for industrial and medical applications*

*Training outstanding scientists*