February 28, 2013

Final Review Report

Initiative Research Scientist

Song Changyong

Kohei Tamao, Chair

Initiative Research Scientist Program Promotion & Review Committee

This is a report on the final review, conducted by email and carried out in accordance with Article 13 (Evaluation) of the RIKEN Regulations for the Initiative Research Unit Program, of the Song Initiative Research Unit, which is scheduled to end its 5-year term on February 28, 2013.

Research topic: Atomic Resolution Coherent X-ray Diffraction Imaging

utilizing the Japan XFEL

Term : March 1, 2008 to February 28, 2013

Final email review

1. Date: February 26, 2013
2. Review committee:
   Chair : Kohei Tamao, Director, RIKEN ASI

   Deputy Chair : Masaki Takada, Deputy Director, RIKEN SPring-8 Center

   Members : Yoshiyuki Amemiya, Professor, Graduate School of Frontier Science, University of Tokyo

   : Masayoshi Nakasato, Professor, Department of Physics, Faculty of Science and Technology, Keio University

   : Katsumi Midorikawa, Deputy Director, ASI
3. Review process:
   Reviewers were asked to comment by email on the unit's final report, submitted on January 31, 2013. Reviewers were also given a list of review criteria and a self-evaluation as reference. The reviewers' comments were summarized in a one-page report.
4. Review results:
   The final review report and comments of individual reviewers are attached.

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This document summarizes the comments provided by peer reviewers on the project, "Atomic Resolution Coherent X-ray Diffraction Imaging utilizing the Japan XFEL" conducted by the Song Changyong Initiative Research Unit. This unit is scheduled to end its research activity on February 28, 2013.The reviewers are listed separately in the appendix.

The Song Initiative Research Unit was launched within the RIKEN Frontier Research System (FRS) in March 2008, and immediately thereafter moved to the RIKEN Advanced Science Institute, which was established in April 2008. In October 2009, the unit was moved again to the RIKEN SPring-8 Center (RSC). Over the past five years, this unit has worked to achieve coherent X-ray diffraction imaging (CDI) for atomic resolution, making full use of SPring-8 and the RIKEN XFEL facility SACLA. The unit has a number of major achievements, among them:

(1) New wet-CDI imaging technique enabling high-resolution imaging of live cells
(2) Multiple-application x-ray imaging chamber (MAXIC) for single-particle imaging, pump-probe ultrafast imaging, nano-crystallography, and other diverse applications making use of the SACLA X-ray pulses and coherence.
(3) Liquid-jet and aerodynamic-jet injectors enabling single-particle CDI structural analysis
(4) New CDI scheme for surface and thin film observation
(5) Fixed target, single-particle CDI imaging

The originality, creativity and academic significance of these successful achievements have already been highly evaluated in the unit's 2011 Interim Review, and the unit has made further progress since then. In addition, Initiative Researcher Song has chaired a number of international workshops for SACLA utilization, expanding the user network and leading the way for research making use of this key national technology. The lab's management was also highly evaluated at that time and we have seen no need to add new

evaluation criteria in this regard.

This Initiative Research Unit has consistently achieved excellent results, despite its frequent change in affiliation from one RIKEN organization to another, and we are pleased that Song will stay at RIKEN as a team leader within the RSC where he will be able to continue his work in research and development.

The comments of the individual review committee members which were submitted to the review committee chair are attached to this report. These comments are based on the Review Criteria distributed to the committee members prior to the review.

[Appendices]

Comments from individual review committee members

● Dr. C Song has made effort on the research program of x-ray diffraction imaging at SACLA (single-shot imaging), Spring-8(3D bio-imaging) and SCSS.

He constructed computer facilities with reconstruction algorithms for rapid data analysis and versatile imaging platform at single-pulse SACLA by introducing Multiple Applications X-ray Imaging Chamber (MAGIC) in order to host many domestic and foreign users.

He also developed liquid jet single particle-injector with 3 microns diameter, which is required for live cell imaging and nano-crystallography. He is currently developing gas-jet injector.

In addition to the construction of the above infrastructure, he has performed the following experiments and published the results in the scientific journals.

1. 3D imaging of a mouse nucleus with a resolution of better than 50 nm at SPring-8, which will be a basis for the 3D imaging of human nuclei and immune-labeled human chromosomes.
2. Demonstration of single-shot diffraction of DNA molecules using SCSS, including the assessment of FEL radiation damage for the first time.
3. Proof-of-principle experiments on single-shot diffraction imaging in reflection geometry at SCSS with an aim to transplant the technique at SACLA for high resolution.
4. CDI experiment of wet specimens with a resolution of better than 40 nm, which will be a basis for high-resolution bio-imaging in native conditions.
5. R&D experiment of ultrafast pump-probe x-ray diffraction imaging at SACLA using MAXIC, with an aim to pursue ultrafast phenomena in materials science and life science.

The above achievements are very important so as to make the best use of SACLA in the coming very near future. They also reflect Dr. Song's good leadership and governance of his team.

I am convinced that Dr. C. Song has played an important role in the research and development of CDI for use with SACLA and hope that his research will be further developed in collaboration with users at SACLA.

● 1. Scientific achievement

The mission of Song Initiative Research Unit (IRU) is the application of coherent X-ray diffraction imaging (CXDI) for non-crystalline particles using coherent X-rays provided by

SPring-8 and SACLA. Through 5-years project, the IRU has achieved significant advances in the methodology and application of CXDI, and provided key techniques to promote cutting-edge researches using SPring-8 and SACLA. The research results from the IRU open new venues in structural analyses of non-crystalline materials, which are never crystallized, from biological and material science field.

For instance, visualization of cells at a resolution of better than 50 nm under wet condition is a great advance in the CXDI field. Until mid-term review, Dr. Song succeeded in the visualization of spore yeast cell at a resolution of 50 nm. However, the sample was dried under non-physiological condition. Because biologists require the structures of cells and molecules in fully hydrated condition, Dr. Song and his collaborators developed a special CXDI chamber dedicated for experiments under wet condition necessary to maintain their functional structures. The equipment works well, and the research group succeeds in the visualization of some cellular imaging. The results will open new science and technology based on CXDI imaging of biological non-crystalline objects. Furthermore, Dr. Song developed the MAXIC chamber for single-shot diffraction imaging using XFEL pulse from SACLA. This chamber can mount the sample particles fixed on membrane films, single-particle liquid injectors developed in collaboration with Professor Mafune of The University of Tokyo.

Taking his contribution to the CXDI field, it is clear that Dr. Song is one of leaders in the world as indicated by the number of invited lectures in international symposium on CXDI (19 in 5 years), the six publications in top journals and one invited review paper. The experimental techniques including data analysis proposed by the IRU are unique and would be one of worldwide standard of CXDI researches.

2. Management

The IRU unit consists of PI, one research scientist, two post-doctoral researchers, one IPA student and one part-time technical assistant. Dr. Song recruited the research scientist and two post-doctoral fellows, who were expert in X-ray diffraction imaging using synchrotron X-ray. As a result of these recruitment, the well organized role-sharing arrangement in the IRU was possible in carrying out researches including collaborative projects with laboratories outside RIKEN. In addition, Dr. Song received competitive grants, Kakenhi from JSPS (2010-2011) and CELA/GIST fund of Korea (2011-2012).

The Unit has several collaborative projects with university laboratories of domestic and oversea countries. Regarding the application of well-established CXDI technique, Dr. Song promotes collaborative projects with sample suppliers to extend the possibilities of CXDI. On the other hand, for novel experimental techniques requiring R&D, the IRU interacts with the professionals. For instance, the collaboration with professor Mafune of the

University of Tokyo would be a key to develop the liquid injector method in SACLA single-shot CXDI experiments. Thus, two types of collaboration promoted by Dr. Song are quite effective to extend the methodology and application of CXDI.

3. Summary

In the past five years, Dr. Song and his staffs performed outstanding developments of equipments and data processing, CXDI experiments for wet biological samples and promotions of several collaborative projects in CXDI. The research progresses are being made timely, properly and nicely with high impacts. Thus, it is concluded that the Song IRU has made great contribution to the development and application of CXDI at SPring-8/SACLA.

● Dr. C Song engaged in researches on the x-ray diffraction imaging using synchrotron radiation at UCLA. Making full use of his carrier, he has been developing a variety of infrastructures including x-ray diffraction imaging devices specialized for SACLA, Spring-8 and EUV-FEL, computer facilities for data acquisition and analysis, and multiple-application X-ray imaging chamber to further pursue his research. It should be specially noted that those devices are contributing to the advancement of x-ray imaging research by SACLA and SPring-8. Especially, a single-particle injector is highly evaluated because this injector is indispensable for single-shot diffraction imaging and nano crystallography by SACLA, which are expected to bring a breakthrough for biology and drug design.

In parallel to the construction of infrastructures, he has achieved three remarkable research results, which are

- 3D imaging with 50 nm resolution
- Wet-CDI of fully hydrated biological specimens
- Single-shot diffraction imaging by FEL and assessment of radiation damage

These achievements are timely and published in high-impact, prestigious journals. He presented 19 invited talks in his tenure. These facts prove his high performance and excellent ability.

I am convinced that Dr. C. Song plays a key role of the future use of SACLA for x-ray imaging and hope that he continues his research activity at Spring-8 facility.