Metallomics

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The term “Metallomics” was coined in 2004 by Hiroki Haraguchi, an emeritus Professor of Nagoya University.¹ Metallomics involves integrated research for clarifying relationships between bio-metals to bio-function and life maintenance.²⁻⁴

Atomic emission spectrometry or mass spectrometry techniques, such as inductively coupled plasma-atomic emission spectrometry (ICP-AES), graphite furnace-atomic absorption spectrometry (GF-AAS), and inductively coupled plasma-mass spectrometry (ICP-MS), are widely used for the determinations of trace- and ultratrace elements due to their excellent analytical performances.^{5,6} Recently, a mass-spectrometry instrument, equipped with a multiple collector system has been recognized as a powerful tool for high-precision isotope analysis,⁷⁻⁹ which can be used to detect slightly isotopic fractionation in biological processes. Tanaka and Hirata reviewed the stable isotope composition of metal elements in biological samples as tracers for element metabolism.¹⁰ In their review, recent progress in determining isotope compositions for four essential elements (Fe, Cu, Zn, and Ca) in plant, animal, and human tissues were summarized. Fe, Cu and Zn exhibit large isotopic fractionations, reflected by changes in their oxidation states. The food habits of living organisms are related to the isotopic composition for zinc, which serves as an indicator of food habit. Calcium isotopic composition has a significant relationship with bone metabolism. These results strongly suggest that isotopic composition allows for acting as effective markers to assess health conditions. Sirataki *et al.* reported a method for the determination of arsenic in whole blood.¹¹ Polyatomic-ion

interferences against the detection of ⁷⁵As arise from Fe, Ca, and Cl, observed using a conventional single mass spectrometer (ICP-MS). They overcame these interferences by using ICP-QMS/QMS equipped with a collision/reaction cell and O₂ reaction gas.

The direct analysis of solid biological samples provides the distribution of metals in biological samples rapidly and simply without any tedious sample preparation. Highly sensitive direct analysis of metals has been performed by laser ablation methods, associated with plasma spectrometric methods.^{12,13} Recently femtosecond-laser ablation (fs-LA)-ICPMS has been used for metallomics because it provides imaging analysis and sensitivity with high spatial resolution. Makino and Hirata *et al.* reported on a protocol for quantitative elemental bio-imaging using fs-LA-ICPMS.¹⁴

Single-cell analysis by ICPMS has garnered considerable research attention for characterizing cell-to-cell variability.^{15,16} A high time-resolution and high-speed analysis of large amounts of data need to be established for single-cell analysis by ICPMS. Lin *et al.* have evaluated three different sample-introduction systems for single-particle (spICP-MS) applications, including a high-performance concentric nebulizer with a heated cyclonic spray chamber and a three-stage Peltier-cooled desolvation system (HPCN-APEX), a conventional sample-introduction system, and a total consumption (TC) system.¹⁷ The transport efficiencies of the HPCN-APEX and TC systems were almost 100% at sample uptake rates of 103 and 9.8 μL min⁻¹, respectively.

The biotic functions and toxicities of metals generally depend on their chemical states and species.^{18,19} Thus, both the determination and distribution of metals and species are required for understanding detailed mechanisms and functions related to metallomics. Narukawa *et al.* reported on a method for the determination of methylmercury (Me-Hg) and inorganic mercury (i-Hg) using HPLC-ICP-MS, assisted by alkaline extraction using tetramethyl ammonium hydroxide.²⁰ In this method, Me-Hg was completely separated from i-Hg on adamantyl-type and octadecylsilyl-type columns within 6 and 4 min using isocratic elution, respectively.

The recent progress in analytical techniques for the determination of metallic species in biological samples is mentioned above. However, many unsolved problems remain in the field of metallomics, such as pharmaceutical effects and the transportation of metallic species in cells and living subjects. Further efforts to improve the analytical performances of determination and separation methods for metallic species is essential to achieve detailed understanding of the biological roles of metallic species.

Keywords Essential elements, single-cell analysis, laser ablation, speciation

Metallomics

Integrated metal science

Recent progress

Isotope analysis
Imaging analysis
Highly sensitive analysis
Hyphenated analysis for Speciation
Single cell analysis

H																	He																															
Li	Be											B	C	N	O	F	Ne																															
Na	Mg											Al	Si	P	S	Cl	Ar																															
K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr																															
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<table><tr><td>La</td><td>Ce</td><td>Pr</td><td>Nd</td><td>Pm</td><td>Sm</td><td>Eu</td><td>Gd</td><td>Tb</td><td>Dy</td><td>Ho</td><td>Er</td><td>Tm</td><td>Yb</td><td>Lu</td></tr><tr><td>Ac</td><td>Th</td><td>Pa</td><td>U</td><td>Np</td><td>Pu</td><td>Am</td><td>Cm</td><td>Bk</td><td>Cf</td><td>Es</td><td>Fm</td><td>Md</td><td>No</td><td>Lr</td></tr></table>																			La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu	Ac	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr
La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu																																		
Ac	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

Advancement of analytical techniques for metals promotes metallomics study.

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References

1. H. Haraguchi, *J. Anal. At. Spectrom.*, **2004**, *19*, 5.
 2. R. Lobinski, J. S. Becker, H. Haraguchi, and B. Sarkar, *Pure Appl. Chem.*, **2010**, *82*, 493.
 3. H. Haraguchi, *Metallomics*, **2017**, *9*, 1001.
 4. Y. Ogra and T. Hirata, “*Metallomics: Recent Analytical Techniques and Applications*”, **2017**, Springer Japan, Tokyo.
 5. F. Esaka, *Anal. Sci.*, **2017**, *33*, 1097.
 6. N. Yamada and J. Takahashi, *Bunseki Kagaku*, **2018**, *67*, 249.
 7. M. Ohata, Y. Zhu, and N. Nonose, *Anal. Sci.*, **2017**, *33*, 375.
 8. M. Tanimizu, K. Nagaishi, and T. Ishikawa, *Anal. Sci.*, **2018**, *34*, 667.
 9. T. Hirata, S. Yamashita, T. Suzuki, and M. Ishida, *Bunseki Kagaku*, **2019**, *68*, 81.
 10. Y. Tanaka and T. Hirata, *Anal. Sci.*, **2018**, *34*, 645.
 11. J. Shirataki, K. Fujisaki, K. Sakaguchi, and N. Sato, *Anal. Sci.*, **2018**, *34*, 735.
 12. D. Pozebon, G. L. Scheffler, V. L. Dressler, and M. A. G. Nunes, *J. Anal. At. Spectrom.*, **2014**, *29*, 2204.
 13. K. Ido, H. Obayashi, Y. Zhu, T. Hirata, A. Hokura, N. Nonose, and K. Inagaki, *Anal. Sci.*, **2018**, *34*, 693.
 14. Y. Makino, S. Ohara, M. Yamada, S. Mukoyama, K. Hattori, S. Sakata, Y. Tanaka, T. Suzuki, A. Shinohara, T. Matsukawa, Y. Yokoyama, and T. Hirata, “*Metallomics: Recent Analytical Techniques and Applications*”, ed. Y. Ogra and T. Hirata, **2017**, Springer, 93.
 15. H. Mizuno, *Anal. Sci.*, **2017**, *33*, 1209.
 16. S.-I. Miyashita, S.-I. Fujii, and K. Inagaki, *Bunseki Kagaku*, **2017**, *66*, 663.
 17. F. Lin, S.-I. Miyashita, K. Inagaki, Y.-H. Liu, and I.-H. Hsu, *J. Anal. At. Spectrom.*, **2019**, *34*, 401.
 18. D. M. Templeton, F. Ariese, R. Cornelis, L.-G. Danielsson, H. Muntau, H. P. van Leeuwen, and R. Lobinski, *Pure Appl. Chem.*, **2000**, *72*, 1453.
 19. T. Yabutani, S. Kishibe, M. Kamimura, K. Nozoe, Y. Yamada, and T. Takayanagi, *Anal. Sci.*, **2018**, *34*, 725.
 20. T. Narukawa, T. Iwai, K. Chiba, and J. Feldmann, *Anal. Sci.*, **2018**, *34*, 1329.
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