



THE UNIVERSITY  
OF BRITISH COLUMBIA

# 3rd NanoLSI Symposium

at UBC in Vancouver

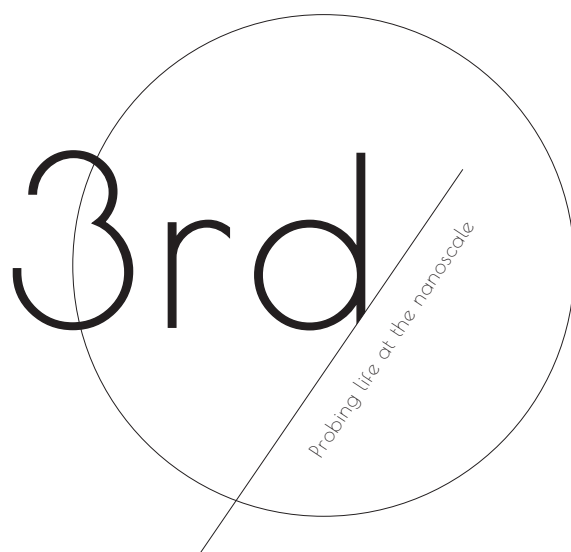
- Supramolecular Chemistry and Nanoprobes in Life Sciences -

Thursday, August 8, 2019



9:00 am

6:00 pm



# NanoLSI Symposium

## at UBC in Vancouver

- Supramolecular Chemistry and Nanoprobes in Life Sciences -

**August 8, 2019**

**Thursday**

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**9:00 am – 6:00 pm**

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**Department of Chemistry, The University of British Columbia**

- Symposium: Chemistry (CHEM) - D300

- Banquet: The Gallery Patio and Lounge, UBC Campus

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# PROGRAMME

	Speaker	Title	Chair
9:00		Opening remarks	
9:10	Takeshi Fukuma (NanoLSI)	Visualizing Subnanometer Structures at Nanobio-Interfaces by 2D & 3D-AFM	Hitoshi Asakawa (NanoLSI)
9:30	Sarah A. Burke (The University of British Columbia)	Chemistry atom-by-atom: Probing reactivity of surface-bound metal-terpyridine sites by STM and AFM	Hitoshi Asakawa (NanoLSI)
10:00	Noriyuki Kodera (NanoLSI)	Video imaging of bio-molecule in action by high-speed atomic force microscopy	Hitoshi Asakawa (NanoLSI)
10:20		Break	
10:35	Yasufumi Takahashi (NanoLSI)	Live cell functional imaging using scanning probe microscopy	Katsuhiko Maeda (NanoLSI)
10:55	Hitoshi Asakawa (NanoLSI)	Molecular-scale distribution and dynamics of host-guest complexes investigated by FM-AFM and HS-AFM	Katsuhiko Maeda (NanoLSI)
11:15	Shigehisa Akine (NanoLSI)	Design of new host molecules with open/close functions	Katsuhiko Maeda (NanoLSI)
11:35	Ramesh Jasti (University of Oregon)	Carbon Nanohoops as New Biological Imaging Tools	Katsuhiko Maeda (NanoLSI)
12:05		Lunch break	
13:30	Satoshi Arai (NanoLSI)	Visualization and Control of Cellular Activities by Thermodynamic Engineering	Mark MacLachlan (The University of British Columbia/NanoLSI)
13:50	Russ Algar (The University of British Columbia)	Not Everybody Dyes: Leveraging Quantum Dots and Other Luminescent Nanomaterials for New Opportunities in Bioanalysis	Mark MacLachlan (The University of British Columbia/NanoLSI)
14:20	David M. Perrin (The University of British Columbia)	One-step <sup>18</sup> F-labeling for PET Oncology	Mark MacLachlan (The University of British Columbia/NanoLSI)
14:50		Break	
15:05	Ratmir Derda (University of Alberta)	Genetically-Encoded Technologies for Discovery of Instructive Biomaterials	Russ Algar (The University of British Columbia)
15:35	Amy Szuchmacher Blum (McGill University)	Plasmonics with Viruses	Russ Algar (The University of British Columbia)
16:05	Kunio Matsumoto (NanoLSI)	Macrocyclic Peptides Targeting HGF-MET	Russ Algar (The University of British Columbia)
16:25		Break	
16:40	Satoru Okuda (NanoLSI)	Versatile modeling of three-dimensional multi-cellular dynamics: <i>in-silico</i> and <i>in-vitro</i> combined approach to self-organizing morphogenesis	Kunio Matsumoto (NanoLSI)
17:00	Satoshi Toda (University of California, San Francisco/NanoLSI)	Synthetic tissue formation: Programming multicellular self-organization	Kunio Matsumoto (NanoLSI)
17:20	Wendell Lim (University of California, San Francisco)	Learning to program cellular machines	Kunio Matsumoto (NanoLSI)
17:50		Closing remarks	
18:30		Banquet	

# ORAL PRESENTATION

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**P6** Takeshi Fukuma / NanoLSI

**P8** Sarah A. Burke / The University of British Columbia

**P10** Noriyuki Kodera / NanoLSI

**P12** Yasufumi Takahashi / NanoLSI

**P14** Hitoshi Asakawa / NanoLSI

**P16** Shigehisa Akine / NanoLSI

**P18** Ramesh Jasti / University of Oregon

**P20** Satoshi Arai / NanoLSI

**P22** Russ Algar / The University of British Columbia

**P24** David M. Perrin / The University of British Columbia

**P26** Ratmir Derda / University of Alberta

**P28** Amy Szuchmacher Blum / McGill University

**P30** Kunio Matsumoto / NanoLSI

**P32** Satoru Okuda / NanoLSI

**P34** Satoshi Toda / University of California, San Francisco/NanoLSI

**P36** Wendell Lim / University of California, San Francisco



# Takeshi Fukuma

Nano Life Science Institute (WPI-NanoLSI), Kanazawa University

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## Research Interests

Atomic Force Microscopy, Nanotechnology, Solid-Liquid Interfaces, Nanobio-science

## Education

2003 | Doctor of Engineering, Department of Electronic Science and Engineering, Kyoto University

## Professional Career

2001-2005 | Research Fellow, Kyoto University  
2005-2007 | Senior Scientist, Physics Department, Trinity College Dublin (Ireland)  
2007-2012 | Associate Professor, Frontier Science Organization, Kanazawa University  
2012 - present | Professor, Division of Electronic Eng. and Computer Sci., Professor, Kanazawa University  
2017 - present | Director/Professor, Nano Life Science Institute (WPI-NanoLSI), Kanazawa University

## Scientific Activities

1999 - 2003 | Instrumentation and applications of atomic-resolution ultrahigh vacuum AFM.  
2003 - present | Instrumentation and applications of atomic-resolution liquid-environment AFM.

## Honors

2011 | The Young Scientists' Prize, The Commendation for Science and Technology by the MEXT  
2017 | Hokkoku Bunka Award, Hokkoku Shinbun  
2018 | 15<sup>th</sup> JSPS Prize, Japan Society for the Promotion of Science

## Publications

1. T. Fukuma, R. Garcia, "Atomic- and Molecular-Resolution Mapping of Solid-Liquid Interfaces by 3D Atomic Force Microscopy", ACS Nano, 12 (2018) 11785-11797.
2. K. Miyata, J. Tracey, K. Miyazawa, V. Haapasilta, P. Spijker, Y. Kawagoe, A. S. Foster, K. Tsukamoto, T. Fukuma, Nano Lett., 17 (2017) 4083-4089.
3. K. Honbo, S. Ogata, T. Kitagawa, T. Okamoto, N. Kobayashi, I. Sugimoto, S. Shima, A. Fukunaga, C. Takatoh, T. Fukuma, ACS Nano, 10 (2016) 2575-2583.



# Visualizing Subnanometer Structures at Nanobio-Interfaces by 2D & 3D-AFM

Takeshi Fukuma

Nano Life Science Institute (WPI-NanoLSI), Kanazawa University

At a solid-liquid interface, water molecules interact with a surface to present non-uniform three-dimensional (3D) distribution referred to as hydration structures. In addition, atoms and molecules constituting the surface are not necessarily static but dynamically fluctuating or diffusing to induce various interfacial phenomena. Consequently, a solid-liquid interface is not two-dimensional but has a three-dimensional extent. However, such 3D fluctuating structures are very difficult to image, which has limited our understanding on various interfacial phenomena in biology, physical chemistry, electrochemistry, tribology, mineralogy and environmental sciences. To overcome this problem, we have been working on the development and applications of 3D atomic force microscopy (3D-AFM) [1]. In this technique, AFM tip is scanned in a 3D interfacial space and the force applied to the tip during the scan is recorded to produce a 3D force image. During the tip scan, the tip interacts with surrounding water and other flexible molecules so that the obtained force map represents their time-averaged distribution. So far, this method is mostly used for visualizing hydration structures on various minerals such as mica, calcite, fluorite and graphite. However, it is also shown that it can be used for visualizing hydration structures of softer materials such as biological molecules (e.g., bRs, GroELs and DNAs). One of these measurements, imaging of a lipid/water interface [2], suggests that the obtained force image reflects not only the hydration structures but also the 3D distribution of flexible molecular chains. This implies that 3D-AFM may allow us to visualize various 3D structures as long as the tip can penetrate into the subsurface area without causing irreversible damages. To explore this possibility, we have been working on visualization of various interfacial structures with different level of complexity and inhomogeneity.

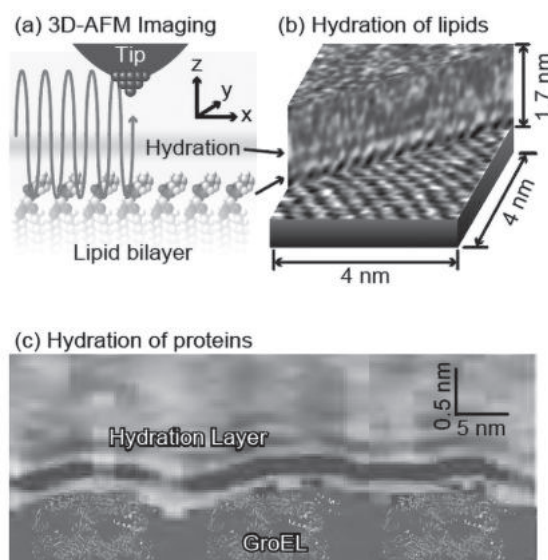


Fig. 1: 3D-AFM imaging of nanobio interfaces.

## References

- [1] T. Fukuma, Y. Ueda, S. Yoshioka, H. Asakawa, "Atomic-Scale Distribution of Water Molecules at the Mica-Water Interface Visualized by Three-Dimensional Scanning Force Microscopy", *Phys. Rev. Lett.*, 104 (2010) 016101.
- [2] H. Asakawa, S. Yoshioka, K. Nishimura, T. Fukuma, "Spatial Distribution of Lipid Headgroups and Water Molecules at Membrane/Water Interfaces Visualized by Three-Dimensional Scanning Force Microscopy", *ACS Nano*, 6 (2012) 9013-9020.
- [3] T. Fukuma, R. Garcia, "Atomic- and Molecular-Resolution Mapping of Solid-Liquid Interfaces by 3D Atomic Force Microscopy", *ACS Nano* 12 (2018) 11785-11797.



# Sarah A. Burke

Dept. of Physics & Astronomy, and Dept. of Chemistry  
Quantum Matter Institute  
University of British Columbia

Contact : [saburke@phas.ubc.ca](mailto:saburke@phas.ubc.ca)

## Research Interests

Electronic structure, surface chemistry, light-matter interactions, scanning probe microscopy

## Education

2002	BSc(Hons.) Physics, Dalhousie University, Halifax, NS
2005	MSc Physics, McGill University, Montreal, QC
2009	PhD Physics, McGill University, Montreal, QC

## Professional Career

2009 - 2010	NSERC Postdoctoral Fellow, UC Berkeley
2010 - 2017	Assistant Professor, University of British Columbia
2017 - present	Associate Professor, University of British Columbia

## Honors

2010 - 2020	Canada Research Chair (tier 2) in Nanoscience
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## Publications

1. Agustin Schiffrin, Martina Capsoni, Gelareh Farahi, Chen-Guang Wang, Cornelius Krull, Marina Castelli, Tanya S. Roussy, Katherine A. Cochrane, Yuefeng Yin, Nikhil Medhekar, Adam Q. Shaw, Wei Ji\*, and **Sarah A. Burke\***, "Designing optoelectronic properties by on-surface synthesis: formation and electronic structure of an iron-terpyridine macromolecular complex", *ACS Nano*, 12(7) (2018); 6545-6553
2. K. A. Cochrane, T. S. Roussy, B.-K. Yuan, G. Tom, E. Mårzell, **S. A. Burke\***, "Molecularly Resolved Electronic Landscapes of Differing Acceptor-Donor Geometries", *Journal of Physical Chemistry C*, 122(15) (2018); 8437-8444
3. K. A. Cochrane, A. Schiffrin, T. Roussy, M. Capsoni, **S. A. Burke\***, "Pronounced polarization-induced energy level shifts at boundaries of organic semiconductor nanostructures" *Nature Communications* 6 (2015): 8312

# Chemistry atom-by-atom: Probing reactivity of surface-bound metal-terpyridine sites by STM and AFM

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Sarah A. Burke

Department of Physics & Astronomy, Department of Chemistry, and the Quantum Matter Institute,  
University of British Columbia, Vancouver, BC, Canada

Heterogeneous catalysts play a vital role in numerous industrial chemical processes, yet their complexity – involving interfaces and a distribution of reactive sites – can hamper mechanistic understanding and efforts towards rational design. Surface-bound molecular catalysts offer the potential to create identical reactive sites – especially by exploiting high fidelity self-assembly methods – bringing the benefits of molecular design from homogeneous catalysts to heterogeneous systems. Scanning tunneling microscopy (STM), spectroscopy (STS) and non-contact atomic force microscopy (ncAFM) provide unique atomistic views of surface structures and the frontier molecular orbitals that give rise to reactivity.

I will describe our recent work investigating the reactivity of self-assembled surface-bound Fe-terpyridine (tpy) species [1,2] with small-molecule gaseous reagents using STM, STS, and ncAFM at low temperatures (4-40K) in ultrahigh vacuum. STM and ncAFM images indicate that both CO and ethylene react with the undercoordinated Fe-tpy sites via a surface-bound intermediate step prior to forming a chemical bond with the Fe site. STS of the nascent and bonded species shows a distinctive signature for each reactant, indicative of changes in the frontier orbitals responsible for further reactivity. Statistical analyses show that subsequent annealing steps up to 40K lead to ensemble progression through these reaction stages and towards higher-order structures, indicating that reactivity can be induced at low-temperature through minimal heating, and revealing the reaction pathway. The ability to probe individual components of the distribution while also building ensemble data allows us to identify and characterize intermediate reaction steps, providing detailed reaction pathway information about this novel well-defined surface-bound reactive site.

## References

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- [1] Agustin Schiffrin, Martina Capsoni, Gelareh Farahi, Chen-Guang Wang, Cornelius Krull, Marina Castelli, Tanya S. Roussy, Katherine A. Cochrane, Yuefeng Yin, Nikhil Medhekar, Adam Q. Shaw, Wei Ji\*, and Sarah A. Burke\*, "Designing optoelectronic properties by on-surface synthesis: formation and electronic structure of an iron-terpyridine macromolecular complex", *ACS Nano*, **2018**, 12(7) 6545-6553
- [2] Cornelius Krull, Marina Castelli, Prokop Hapala, Dhaneesh Kumar, Anton Tadich, Martina Capsoni, Mark T. Edmonds, Jack Hellerstedt, Sarah A. Burke, Pavel Jelinek and Agustin Schiffrin\* "Iron-based trinuclear metal-organic nanostructures on a surface with local charge accumulation", *Nature Commun*, **2018**, 9, 3211





# Noriyuki Kodera

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## Research Interests

Biophysics, molecular motors, cytoskeletons, atomic force microscopy

## Education

Mar. 2001	B. Sci., Dept. of Phys, Fac. of Sci., Kanazawa Univ.
Mar. 2003	M. Sci., Div. of Math. & Phys. Sci., Grad. Sch. Nat. Sci. & Tech., Kanazawa Univ.
Sep. 2005	Ph.D., Div. of Basic Sci., Grad. Sch. Nat. Sci. & Tech., Kanazawa Univ.

## Professional Career

2005-2010	Research Fellow (DC2 & PD), JSPS and Postdoctoral Fellow, CREST, JST
2010-2018	Assistant Professor & Associate Professor, Bio-AFM Frontier Research Center, Institute of Science and Engineering, Kanazawa University
2013-2017	PRESTO Researcher, JST
2018 - present	Professor, Nano Life Science Institute (WPI-NanoLSI), Kanazawa University

## Scientific Activities

2000-2008	Development of high-speed atomic force microscopy (HS-AFM)
2008 - present	Biological application studies using HS-AFM and improvement of HS-AFM

## Honors

2012	Young Researcher's Nanoprobe Technology Prize (JSPS Nanoprobe Technology 167)
2013	Prize for Science and Technology (Development Category), The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology
2017	JSPS Prize

## Publications

1. Terahara N, **Kodera N**, Uchihashi T, Ando T, Namba K, Minamino T, "Na<sup>+</sup>-induced structural transition of MotPS for stator assembly of the *Bacillus* flagellar motor", **Science Advances** **3**, eaao4119 (2017).
2. Ngo KX, **Kodera N**, Katayama E, Ando T, Uyeda TQ, "Cofilin-induced unidirectional cooperative conformational changes in actin filaments revealed by high-speed atomic force microscopy", **eLife** **4**, 04806 (2015).
3. **Kodera N**, Yamamoto D, Ishikawa R, Ando T, "Video imaging of walking myosin V by high-speed atomic force microscopy", **Nature** **468**, 72-76 (2010).

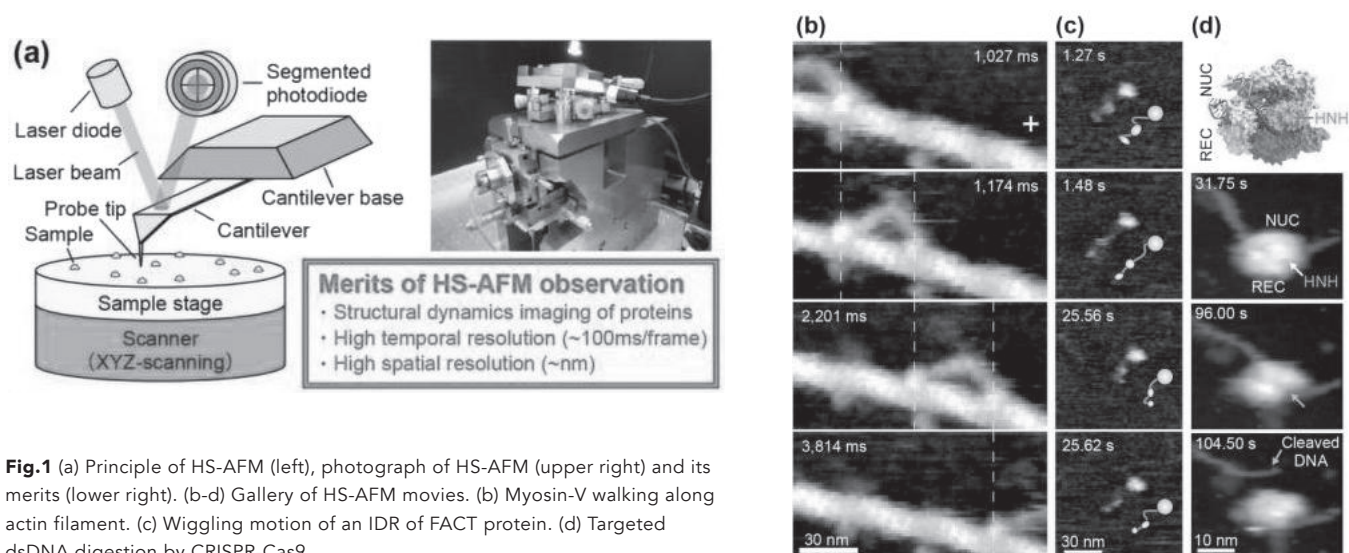
# Video imaging of bio-molecule in action by high-speed atomic force microscopy

Noriyuki Kodera

Nano Life Science Institute (WPI-NanoLSI), Kanazawa University

We have been developing a high-speed atomic force microscopy (HS-AFM) that can directly observe biological molecules in action at nanometer spatial and sub-second temporal resolution (Fig.1a) [1]. The unique performance of HS-AFM has been demonstrated by direct observations of proteins, protein-protein complexes (Fig.1b), protein-nucleic acid complexes (Fig.1d), and cellular surface [2]. Importantly, HS-AFM can even resolve thin and flexible features of intrinsically disordered regions (IDRs), single polypeptide chains with height of  $\sim 0.5$  nm, in a protein that could not be analyzed by any techniques at single molecule level (Fig.1c). In some cases, dynamic structural transitions in IDRs between ordered- and disordered-conformations can be directly visualized [3-5].

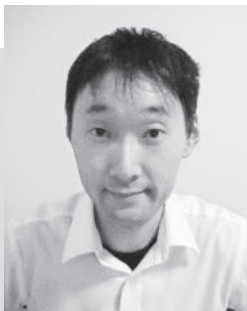
In this presentation, we will overview the principle and current performance of HS-AFM, and then show recent activities on improvement of scanning performance (super high-speed Z-scanner and high-speed amplitude detector for cantilever oscillation) and functional extensions (PDMS-based concave-convex substrate, high-speed scanner with a manipulator, and HS-AFM system combined with patch clamp) of HS-AFM.



**Fig.1** (a) Principle of HS-AFM (left), photograph of HS-AFM (upper right) and its merits (lower right). (b-d) Gallery of HS-AFM movies. (b) Myosin-V walking along actin filament. (c) Wiggling motion of an IDR of FACT protein. (d) Targeted dsDNA digestion by CRISPR-Cas9.

## References

- [1] T. Ando, T. Uchihashi, and N. Kodera, *Annu. Rev. Biophys.*, **2013**, 42, 393-414.
- [2] T. Ando, T. Uchihashi, and S. Scheuring, *Chem. Rev.*, **2014**, 114, 3120-3188.
- [3] M. Hashimoto, N. Kodera, Y. Tsunaka, M. Oda, M. Tanimoto, T. Ando, K. Morikawa, and S. Tate, *Biophys. J.*, **2013**, 104, 2222-2234.
- [4] N. Kodera, K. Uchida, T. Ando, and S. Aizawa, *J. Mol. Biol.*, **2015**, 427, 406-414.
- [5] N. Terahara, N. Kodera, T. Uchihashi, T. Ando, K. Namba, and T. Minamino, *Sci. Adv.*, **2017**, 3, eaao4119.



# Yasufumi Takahashi

Nano Life Science Institute (WPI-NanoLSI), Kanazawa University

Contact : yasufumi@se.kanazawa-u.ac.jp

## Research Interests

Live cell functional imaging, chemical sensing, scanning probe microscopy

## Education

2004	B.Sc. in Engineering, Tohoku University
2006	M.Sc. in Environmental science, Tohoku University
2009	Ph.D. in Environmental science, Tohoku University

## Professional Career

2011 - 2013	Research Assistant, Tohoku University
2013 - 2015	Assistant Professor, Tohoku University
2015 - present	Associate Professor, Kanazawa University

## Scientific Activities

2004 - 2009	Development of high resolution scanning electrochemical microscopy for live cell imaging
2009 - 2011	Development of SECM-SICM for live cell imaging
2011 - present	Development of nanoscale chemical sensor for live cell metabolite detection

## Honors

2016	Young Scientists' Prize of the Commendation for Science and Technology by the Minister of Science and Technology
2017	Bioindustry Award

## Publications

1. Zhou, Y. S.; Saito, M.; Miyamoto, T.; Novak, P.; Shevchuk, A. I.; Korchev, Y. E.; Fukuma, T.; Takahashi, Y., *Anal Chem* **2018**, 90 (4), 2891-2895.
2. Zhang, Y.; Clausmeyer, J.; Babakinejad, B.; Cordoba, A. L.; Ali, T.; Shevchuk, A.; Takahashi, Y.; Novak, P.; Edwards, C.; Lab, M.; Gopal, S.; Chiappini, C.; Anand, U.; Magnani, L.; Coombes, R. C.; Gorelik, J.; Matsue, T.; Schuhmann, W.; Klenerman, D.; Sviderskaya, E. V.; Korchev, Y., *Acs Nano* **2016**, 10 (3), 3214-3221.
3. Nashimoto, Y.; Takahashi, Y.; Zhou, Y. S.; Ito, H.; Ida, H.; Ino, K.; Matsue, T.; Shiku, H., *Acs Nano* **2016**, 10 (7), 6915-6922.

# Live cell functional imaging using scanning probe microscopy

Yasufumi Takahashi

Nano Life Science Institute (WPI-NanoLSI), Kanazawa University

Dynamic visualization of extracellular chemical concentration profile around the live cell is important for understanding the cell metabolic state, cell-cell interaction, and relationship between chemical concentration and cell function. However, still it is not established chemical sensor for detect the chemical around the single cell.

Scanning ion conductance microscopy (SICM) uses a less than 50 nm radius nanopipette for detecting ion current and is an effective tool for non-contact live cell nanoscale topography imaging, local chemical delivery, and cytosol collection (Fig.1). We have developed miniaturized electrochemical sensor and mounted the sensor on SICM probe to achieve chemical (oxygen, catecholamine, H<sub>2</sub>O<sub>2</sub>) and topographical simultaneous imaging.<sup>1,2</sup> To improve the electrochemical imaging resolution and sensitivity, we developed nanoscale electrode<sup>3</sup> and chemical sensing field-effective transistor (FET) probe<sup>4</sup>. These probes are effective to visualize nanoscale chemical distribution and  $\mu$ M level of the chemicals detection.

The local cytosol collection is also important technique to reveal the localization of mRNAs at a single cell level. We have developed a hybrid system of SICM and electrochemical syringe to collect the localized mRNA of single living cells. The system uses double-barrel glass nanopipette as a probe.<sup>5</sup> This system successfully detected local differences in *Actb* mRNA expression levels in single mouse fibroblast cells.

High speed SICM is effective to visualize the cell surface dynamic change.<sup>6</sup> To reduce the scanning time, we selected next scanning area at the specific region by using previous obtained topography information (Patent 2016-188803). By using this scanning mode, we visualized the volume change of neurites, transport of cargo molecule transport, and the structure change of growth cone.

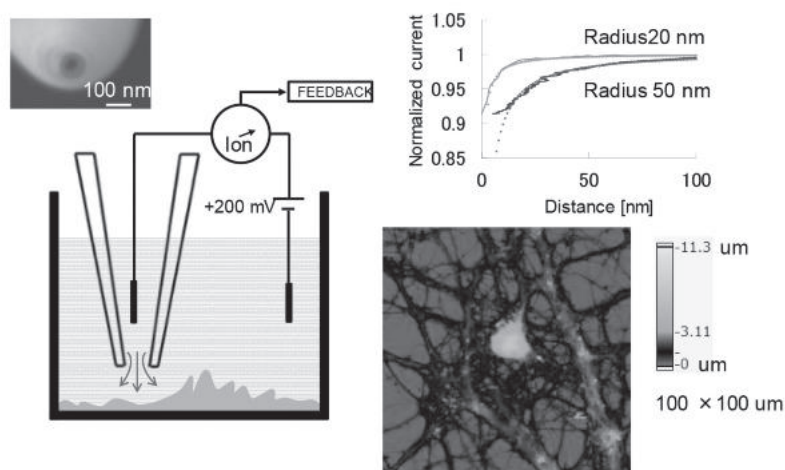


Figure 1 Schematic illustration of SICM and hippocampus neuron topography image.

## References

- [1] Takahashi, Y.; et al. *J. Am. Chem. Soc.* 2010, **132** (29), 10118-10126.
- [2] Takahashi, Y.; et al. *Angew. Chem. Int. Ed.* 2011, **50** (41), 9638-9642.
- [3] Takahashi, Y.; et al. *Proc. Natl. Acad. Sci. U. S. A.* 2012, **109** (29), 11540-11545.
- [4] Zhang, Y. et al. *Acs Nano* 2016, **10** (3), 3214-21.
- [5] Nashimoto, Y.; Takahashi, Y. et al. *Acs Nano* 2016, **10** (7), 6915-22.
- [6] Ida, H.; et al. *Anal. Chem.* **89**, 6015-6020, (2017).



# Hitoshi Asakawa

Nanomaterials Research Institute, Kanazawa University, Japan

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## Research Interests

Atomic force microscopy in liquid

Direct measurement of intermolecular interactions at the single molecular level

Self-assembly of chemical and biological molecules at solid/liquid interfaces

## Education

2007 | PhD in Biological Functions Engineering, Kyushu Institute of Technology, Japan

## Professional Career

2008 - 2010 | Postdoctoral Fellow, Frontier Science Organization, Kanazawa University, Japan

2010 - 2016 | Assistant Professor, Bio-AFM Frontier Research Center, Kanazawa University, Japan

2016 - present | Associate Professor, Division of Material Chemistry, Kanazawa University, Japan

2017 - present | Associate Professor, Nano Life Science Institute (WPI-NanoLSI), Kanazawa University, Japan

2018 - present | Associate Professor, Nanomaterials Research Institute (NanoMaRi), Kanazawa University, Japan

## Honors

2013 | Nanoprobe technology young scientist award from No. 167 committee of Japan society for the promotion of science (JSPS)

2019 | The young scientist prize from the ministry of education, culture, sports, science and technology (MEXT)

## Publications

1. Asakawa, H.; Holmström, E.; Foster, S. A.; Kamimura, S.; Ohno, T.; Fukuma, T., *J. Phys. Chem. C*, **2018**, 122, 24085-24093.
2. Asakawa, H.; Inada, N.; Hirata, K.; Matsui, S.; Igarashi, T.; Oku, N.; Yoshikawa, N.; Fukuma, T., *Nanotechnology*, **2017**, 28, 455603.
3. Asakawa, H.; Yoshioka, S.; Nishimura, K.; Fukuma T., *ACS Nano*, **2012**, 6, 9013-9020.



# Molecular-scale distribution and dynamics of host-guest complexes investigated by FM-AFM and HS-AFM

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Hitoshi Asakawa

Nanomaterials Research Institute, Kanazawa University, Japan

The reversible association-disassociation process is one of the critical molecular systems in biology and chemistry. For example, environmentally responsible materials are often developed based on the reversible association properties of host-guest complexes. To investigate the properties of complex formations, several analytical methods have been well established with spectroscopies and calorimetry such as XRD, NMR, and ITC. However, direct observation of host-guest complexes is very challenging, even with such established methods. Hence, the spatial distribution of host-guest complexes and their dynamics remain unclear. Frequency-modulation atomic force microscopy (FM-AFM) has proven to be a powerful technique for investigating surface structures with subnanometer resolution in liquid [1]. Besides, recent advances in high-speed AFM (HS-AFM) have enabled us to determine molecular dynamics with a frame rate of over 10 frames/s [2]. Here, we present a molecular-scale investigation on the distribution of host-guest complexes and their dynamics in liquid using both FM-AFM and HS-AFM.

A macrocyclic host structure referred to as pillar[5]arene (P[5]A) and n-alkanes with anionic headgroups were used as a host structure and guest molecules, respectively. P[5]A is known to capture n-alkane moieties of guest molecules by CH/ $\pi$  interactions with high selectivity [3]. Recently, we reported that cationic P[5]A molecules form self-assembled monolayers with a hexagonal molecular arrangement on mica [4]. In this study, structural changes by the formation of host-guest complexes were investigated by FM-AFM. The FM-AFM images show that subnanometer-scale particle-like contrasts become clearer with increasing the concentration of anionic guest molecules. We found that the association constant of P[5]A-guest complexes is able to be determined from the obtained FM-AFM images. The association constant was a reasonable value even compared with the expected from other analytical methods. In addition, dynamic reversibility of P[5]A-guest complex formation was also visualized by FM-AFM and HS-AFM imaging. The results suggested that the AFM techniques should contribute to the molecular-scale understanding of association-disassociation process not only host-guest complex but also various molecular systems in chemistry and biology.

## References

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- [1] Fukuma, T., *Rev. Sci. Instrum.*, **2009**, 80, 023707.
- [2] Shibata, M.; Yamashita, H.; Uchihashi, T.; Kandori, H.; Ando, T., *Nat. Nanotech.*, **2010**, 5, 208-212.
- [3] Ogoshi, T.; Yamagishi, T., *Chem. Commun.*, **2014**, 50, 4776-4787.
- [4] Ogoshi, T.; Takashima, S.; Inada, N.; Asakawa, H.; Fukuma, T.; *et al.*, *Commun. Chem.*, **2018**, 1, 29.



# Shigehisa Akine

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## Research Interests

1. Coordination-based functional systems for molecular recognition and chirality control
2. Dynamic structural conversion of multi-metal complexes

## Education

1991 - 1995	B. S. Department of Chemistry, Faculty of Science, The University of Tokyo
1995 - 1997	M. S. Department of Chemistry, Graduate School of Science, The University of Tokyo
1997 - 2000	PhD Department of Chemistry, Graduate School of Science, The University of Tokyo

## Professional Career

2000 - 2004	Research Associate, Department of Chemistry, University of Tsukuba
2004 - 2008	Assistant Professor, Graduate School of Pure and Applied Sciences, University of Tsukuba
2008 - 2013	Associate Professor, Faculty of Pure and Applied Sciences, University of Tsukuba
2013 - 2017	Professor, Graduate School of Natural Science and Technology, Kanazawa University
2017 - present	Professor, Nano Life Science Institute (WPI-NanoLSI), Kanazawa University

## Honors

2011	DIC Award in Synthetic Organic Chemistry Japan
2011	HGCS Japan Award of Excellence

## Publications

1. "Ligand Exchange Strategy for Tuning of Helicity Inversion Speeds of Dynamic Helical Tri(saloph) Metallocryptands"  
Sakata, Y.; Chiba S.; Miyashita, M.; Nabeshima, T.; Akine, S. *Chem. Eur. J.* **2019**, *25*, 2962–2966.
2. "A Closed Metallomolecular Cage that can Open its Aperture by Disulfide Exchange"  
Akine, S.; Miyashita, M.; Nabeshima, T. *Chem. Eur. J.* **2019**, *25*, 1432–1435.
3. "Anion-capped metallohost allows extremely slow guest uptake and on-demand acceleration of guest exchange"  
Sakata, Y.; Murata, C.; Akine, S. *Nat. Commun.* **2017**, *8*, 16005.
4. "A Metallo-molecular Cage That Can Close the Apertures with Coordination Bonds"  
Akine, S.; Miyashita, M.; Nabeshima, T. *J. Am. Chem. Soc.* **2017**, *139*, 4631–4634.

# Design of new host molecules with open/close functions

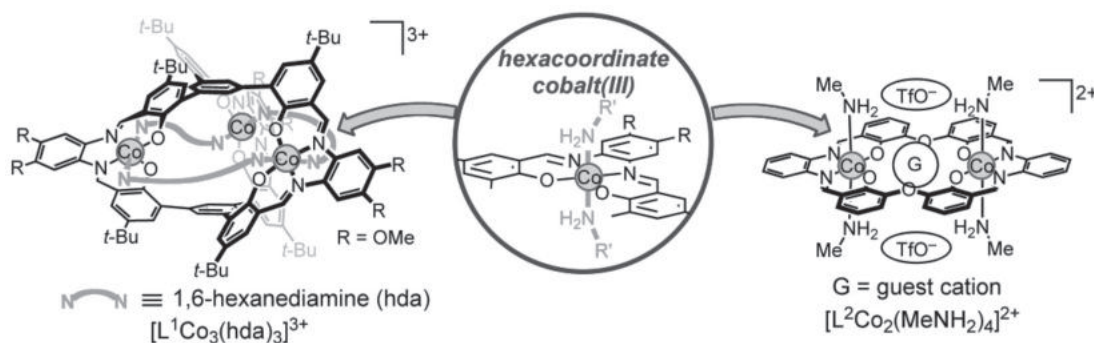
Shigehisa Akine

Nano Life Science Institute (WPI-NanoLSI), Kanazawa University  
Graduate School of Natural Science and Technology, Kanazawa University

Macrocyclic compounds and molecular cages are known to act as a good host molecule. Usual host molecules easily and quickly take up a guest species in the cavity, but some molecular cages can permanently confine the guest species in the cavity. This confinement effect depends on the guest size compared with the cage structures, because only the guest species that are smaller than the cage portal can enter and exit the cavity. If we introduce a cap function into the host compounds, we can switch the guest confinement effect; the guest is confined in the cavity when the cap is closed, while the guest freely enters and exits when the cap is open. In order to achieve this open/close function, we designed two new molecular scaffolds based on oligo(salen)-metal structures.<sup>[1]</sup> In this lecture, guest recognition control behavior of the macrocyclic and cage-like oligo(salen) structures will be presented.

**1. Cage-like metallocryptand that can close the aperture.**<sup>[2]</sup> A tricobalt(III) metallocryptand  $[L^1Co_3(hda)_3](OTf)_3$ , which has 1,6-hexanediamine (hda) ligands at the apertures of the molecular cage, was synthesized. This complex selectively recognized  $Cs^+$ , but it took more than 50 h for the complete conversion to the  $Cs^+$  complex. The uptake rate was more than 2000 times slower than that of the open cage analogue. The closed-cage structure with diamine ligands efficiently slowed down the guest uptake.

**2. Anion-capped macrocyclic metallohost.**<sup>[3]</sup> A macrocyclic dicobalt(III) metallohost  $[L^2Co_2(MeNH_2)_4](OTf)_2$  recognized various cations ( $Na^+$ ,  $K^+$ ,  $Rb^+$ ,  $Ca^{2+}$ ,  $La^{3+}$ ) to give the inclusion complexes, in which the binding site was capped with two triflate anions. The guest uptake became significantly slow due to the capping effect so that we could obtain kinetically trapped state where a disfavored guest was taken up prior to a favored guest. Based on the fact that the capping effect depends on the type of anions, we achieved an on-demand guest exchange triggered by replacing the anion caps starting from the kinetically trapped state.



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[2] S. Akine, M. Miyashita, T. Nabeshima, *J. Am. Chem. Soc.*, **2017**, 139, 4631.  
[3] Y. Sakata, C. Murata, S. Akine, *Nat. Commun.*, **2017**, 8, 16005.



# Ramesh Jasti

University of Oregon

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## Research Interests

The organic synthesis of precision carbon nanomaterials with unique properties and applications.

## Education

1998	B.S. with Honors at the University of North Carolina, Chapel Hill
2006	PhD at the University of California, Irvine

## Professional Career

2009-2014	Boston University
2014 - present	University of Oregon

## Scientific Activities

2009-2014	Assistant Professor of Chemistry, Boston University
2014-2019	Associate Professor of Chemistry and Biochemistry, University of Oregon

## Honors

NSF Career Award, Alfred P. Sloan Fellowship, Camille Dreyfus Teacher-Scholar Award

## Publications

1. Jasti, R.; Bhattacharjee, J.; Neaton, J. B.; Bertozzi, C. R. "The Synthesis, Characterization, and Theory of [9]-, [12]-, and [18]Cycloparaphenylene: Carbon Nanohoop Structures." *J. Am. Chem. Soc.* **2008**, *130*, 17646-17647.
2. Sisto, T. J.; Golder, M. R.; Hirst, E. S.; Jasti, R. "Selective Synthesis of Strained [7]Cycloparaphenylene: An Orange-Emitting Fluorophore." *J. Am. Chem. Soc.* **2011**, *133*, 15800-15802.
3. Evans, P. J.; Darzi, E. R.; Jasti, R. "Efficient Room-Temperature Synthesis of a Highly Strained Carbon Nanohoop Fragment of Buckminsterfullerene." *Nat. Chem.* **2014**, *6*, 404-408.

# Carbon Nano hoops as New Biological Imaging Tools

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Ramesh Jasti

University of Oregon

In their simplest form, nano hoops can be thought of as short slices of carbon nanotubes. In this lecture, I will describe my research group's impetus for developing synthetic methods to prepare a wide range of these types of structures. I will also detail the unique size-dependent optical properties of these molecules, which are direct manifestations of the unusual radially oriented  $\pi$ -systems. Finally, I will share our most recent results to elaborate this new class of nanoscale building blocks into materials useful for biological imaging.[1,2,3]



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# Satoshi Arai

Nano Life Science Institute (WPI-NanoLSI), Kanazawa University

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## Research Interests

My research background comprises expertizes such as chemical biology, polymer chemistry, and biophysics. Our great hope is to visualize and manipulate cellular events in all living organism from viewpoint of thermodynamics. To achieve this, we generated fluorescent sensors to light up cellular elements such as temperature and ATP. Recent years, we further focused on the development of "thermodynamic engineering technology", where temperature could be controlled at nano/microscale quantitatively.

## Education

2004	M.S., Polymer Chemistry, Waseda University
2007	PhD (D. Eng.), Polymer Chemistry, Waseda University

## Professional Career

2007 - 2009	Research Associate, Department of Life Science and Medical Bioscience, Waseda University
2009 - 2010	Postdoctoral Fellow, Cooperative Bio Science Research Institute, Waseda University
2011 - 2012	Research Fellow, National University of Singapore (prof. Chang Young-Tae Lab)
2012 - 2016	Senior Research Fellow, WASEDA Bioscience Research Institute in Singapore
2016 - 2019	Assistant Professor, WASEDA Bioscience Research Institute in Singapore, Waseda University
July. 2019 - present	Associate Professor (Tenure-track), Nano Life Science Institute (WPI-NanoLSI), Kanazawa University

## Scientific Activities

2015 - present	PRIME Researcher (Japan Agency for Medical Research and Development, AMED)
2019 - present	Visiting Researcher (Nanyang Technological University)

## Honors

2014	The Award for Encouragement of Research in IUMRS-ICA2014
2014	Tanaka Kikinzoku Kogyo, MMS award
2018 - 2019	JSPS-LEADER (candidate)

## Publications

1. RGB-Color Intensiometric Indicators to Visualize Spatiotemporal Dynamics of ATP in Single Cells, S. Arai, R. Kriszt, K. Harada, L-S. Looi, S. Matsuda, D. Wongso, S. Suo, S. Ishiura, Y-H. Tseng, M. Raghunath, T. Ito, T. Tsuboi, T. Kitaguchi, **Angew. Chem. Int. Ed.**, vol.57, pp.10873-10878 (2018).
2. Gold Nanoshell-Mediated Remote Myotube Activation, A. Marino, S. Arai, Y. Hou, A. Degl'Innocenti, V. Cappello, B. Mazzolai, Y-T. Chang, V. Mattoli, M. Suzuki, G. Ciofani, **ACS Nano** vol.11, pp.2494-2508 (2017). Highlighted at "Gold nanoparticles: A warm-up for muscle cells" Nature Nanotechnology 12. 188 (2017).
3. A Molecular Fluorescent Probe for Targeted Visualization of Temperature at the Endoplasmic reticulum, S. Arai, S-C. Lee, Z. Duaning, M. Suzuki, Y-T. Chang, **Sci. Rep.**, vol.4, 6701 (2014).

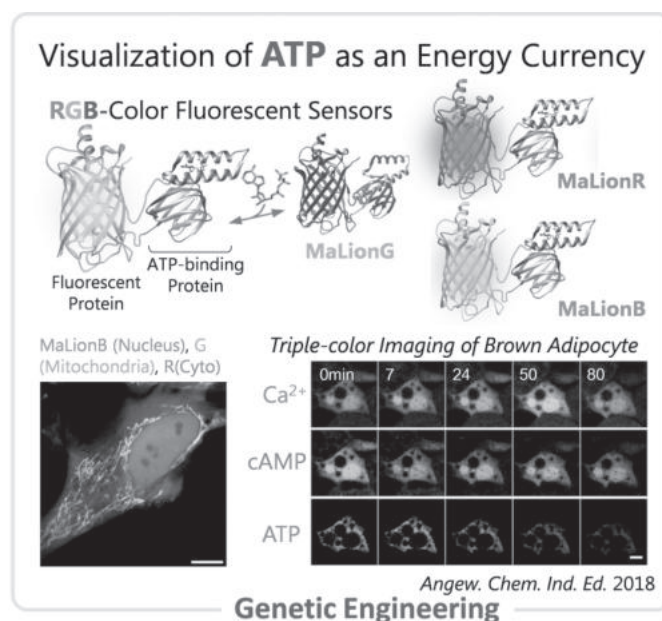
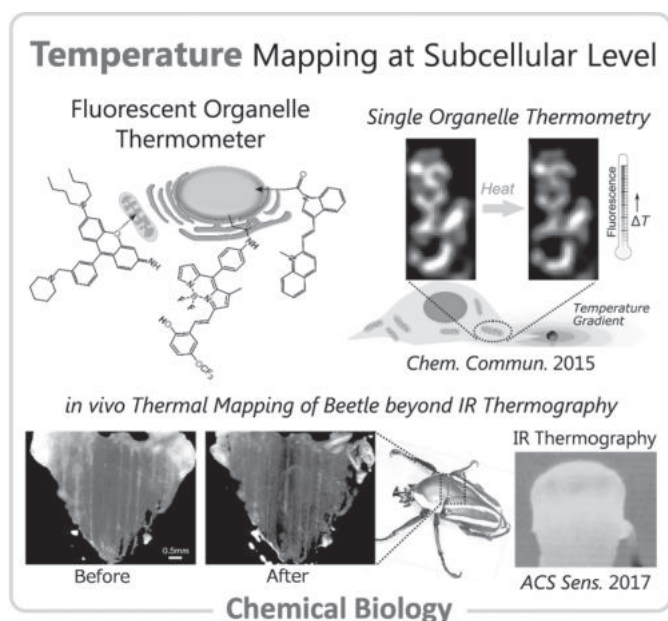
# Visualization and Control of Cellular Activities by Thermodynamic Engineering

Satoshi Arai

Nano Life Science Institute (WPI-NanoLSI), Kanazawa University

Very recently, it was discovered that a certain fish, the opah, generates heat by themselves in order to warm up his body for predation activities in the deep sea (Wegner et al, 2015). Recent studies also revealed that dinosaur seems reasonable to be categorized between warm and cold blooded animals (Grady et al, 2014). These findings are likely to give fresh surprises for those who understands generating heat (thermogenesis) to be the unique property in only mammals and birds. At the same time, they would teach us how important temperature is as an inherent parameter to drive chemical reactions in all living systems.

Our research is focused on the visualization of an energy flow in living cells, where key elements are temperature and ATP. To date, we have developed various fluorescence sensors to visualize intracellular temperature and ATP [1,2]. Recent achievement also includes "Thermodynamic Engineering Technology", enabling to measure and control temperature at nano/microscale using photothermal materials and temperature sensing dyes [3]. Using this technology, we attempted to induce the rapid apoptosis in cancer cells and muscle contraction. In this talk, we are going to share the tips of these topics and more than welcome for fruitful discussion.



## References

- [1] RGB-Color Intensiometric Indicators to Visualize Spatiotemporal Dynamics of ATP in Single Cells, S. Arai, R. Kriszt, K. Harada, L-S. Looi, S. Matsuda, D. Wongso, S. Suo, S. Ishiura, Y-H. Tseng, M. Raghunath, T. Ito, T. Tsuboi, T. Kitaguchi, **Angew. Chem. Int. Ed.**, 2018, 57, 10873-10878.
- [2] Nanosized Optical Thermometers, **Smart Nanoparticles for Biomedicine** (ed. by Gianni Ciofani), Elsevier, \*S. Arai, M. Suzuki, 2018, Chapter 14, 199-217.
- [3] Gold Nanoshell-Mediated Remote Myotube Activation, A. Marino, S. Arai, Y. Hou, A. Degl'Innocenti, V. Cappello, B. Mazzolai, Y-T. Chang, V. Mattoli, M. Suzuki, G. Ciofani, **ACS Nano**, 2017, 11, 2494-2508.



# Russ Algar

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Vancouver, V6T 1Z1, Canada.

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## Research Interests

My research group is interested in the development of luminescent materials for applications in bioanalysis and bioimaging, including but not limited to point-of-care diagnostic devices, multiplexed probes, molecular photonic logic, new materials development, and fundamental studies of photophysics and how nanomaterials interact with biological molecules and systems.

## Education

2005	Hon.B.Sc. University of Toronto
2010	Ph.D. University of Toronto

## Professional Career

2010- 2012	NSERC Postdoctoral Fellow, Center for Bio/Molecular Science and Engineering, US Naval Research Laboratory, Washington, DC, USA
2012- 2018	Assistant Professor, University of British Columbia
2018- present	Associate Professor, University of British Columbia

## Scientific Activities

2012- present	Canada Research Chair in Bio/Chemical Sensing
2014- present	Michael Smith Foundation for Health Research Scholar
2019- present	Features panel member, <i>Analytical Chemistry</i> (ACS)

## Honors

2017	Canadian Society for Chemistry (CSC) Fred Beamish Award in Analytical Chemistry
2017	<i>Spectroscopy</i> magazine Emerging Leader in Molecular Spectroscopy
2017	Alfred P. Sloan Foundation Research Fellowship
2018	The Power List 2018: Top 40 Under 40 by <i>The Analytical Scientist</i> magazine

## Publications

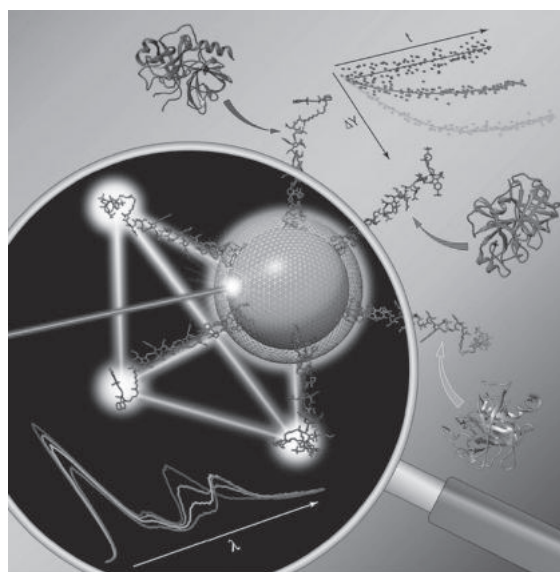
1. E. Petryayeva, W.R. Algar\*, *Analyst*, **2015**, 140, 4037-4045.
2. M. Massey, I.L. Medintz, M.G. Ancona, W.R. Algar\*, *ACS Sensors*, **2017**, 2, 1205-1214.
3. M. Massey, H. Kim, E. Conroy, W.R. Algar\*, *J. Phys. Chem. C*, **2017**, 121, 13345-13356.

# Not Everybody Dyes: Leveraging Quantum Dots and Other Luminescent Nanomaterials for New Opportunities in Bioanalysis

W. Russ Algar

Department of Chemistry, University of British Columbia, Vancouver, BC, Canada.

Fluorescent dyes and proteins are great—except when they're not. Colloidal semiconductor quantum dots (QDs) are excellent alternatives for fluorescent dyes—except when they're not. With the wide and growing variety of luminescent materials available, no single material is best-suited to every application [1]. This presentation will overview our research in developing methods of bioanalysis that leverage QDs and other luminescent nanomaterials to achieve capabilities that are both suited to the nanomaterial and not possible with fluorescent dyes or proteins alone. These include smartphone-based platforms for biomolecular and cell-based assays [2-4], as well as single-vector multiplexed concentric FRET probes toward cellular sensing [5-7]. Special attention will be paid to our ongoing development of multifunctional composites of QDs and magnetic or plasmonic nanoparticles. The optical properties of these composites overcome the deficiencies of a smartphone for fluorescence measurements without requiring sophisticated engineering. With the composite nanoparticles and a simple 3D-printed device, we are able to isolate and count HER2-positive cancer cells against a background of HER2-negative cells. This work is now moving toward barcoded assays for multiplexed cell detection, cell-surface antigen profiling, and single-analyte detection on a smartphone. A primary goal of our research is to develop materials and devices that make molecular medicine more accessible, whether at the bedside or in remote or low-resource settings.



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- [2] E. Petryayeva, W.R. Algar\*, *Analytical Chemistry* **2014**, *86*, 3195-3202.
- [3] E. Petryayeva, W.R. Algar\*, *Analyst* **2015**, *140*, 4037-4045.
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# David M. Perrin

Chemistry Department – University of British Columbia

Contact : dperrin@chem.ubc.ca

## Research Interests

Bioorganic Chemistry, Chemical Biology, DNAzymes, PET imaging agents, Peptide natural products

## Education

1990	BA Biochemistry UC Berkeley
1995	Ph.D. Biological Chemistry, UCLA

## Professional Career

1995 - 2000	Postdoctoral Fellow
2000 - present	Professor, UBC

## Publications

1. A densely modified  $M^{2+}$ -Independent DNAzyme capable of efficient all-RNA cleavage and mammalian cell membrane penetration, Yajun Wang, Er kai Liu, Curtis H. Lam, and **David M. Perrin\*** *Chemical Science* **2018** 9: 1813-1821.
2.  $^{18}F$ -Organotrifluoroborates as Radioprosthetic Groups for PET Imaging: From Design Principles to Preclinical Application, **David M. Perrin\***, *Acc. Chem. Res.* **2016** 49: 1333-1343.
3. Synthesis of the death-cap mushroom toxin  $\alpha$ -Amanitin, Kaveh Matinkhoo, Alla Pryma, Mihajlo Todorovic, Brian O. Patrick, and **David M. Perrin\*** *J. Am Chem. Soc.* **2018** 140: 6513-6517.

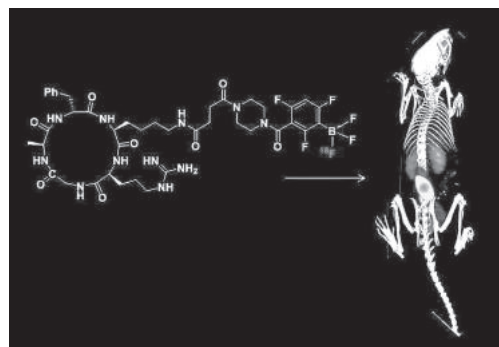


# One-step $^{18}\text{F}$ -labeling for PET Oncology

David M. Perrin

Chemistry Department, University of British Columbia

The American oncology tracer market will grow annually at >8% to >\$8B. Driving this growth are peptides that detect specific molecular targets whose dysregulation and presence leads to cancer.<sup>1</sup> While several PET-useful isotopes exist,  $^{18}\text{F}$ -fluoride is the only isotope with a track-record of FDA clearance and which can be produced at Curie-levels, on-demand.<sup>2</sup> Nevertheless, the challenges for  $^{18}\text{F}$ -labeling large molecules are considerable; these include a short half-life and the need to work in anhydrous conditions.<sup>3</sup> Hence most peptide labelings require 2-4 steps including a preliminary drying step, various steps related to precursor synthesis, and an HPLC step to remove unreacted peptide in a radiosynthetic process normally requiring 70-180 min.<sup>4</sup> In seeking a water-friendly reaction, we developed several organotrifluoroborates that can be conjugated to peptides to provide precursors that are  $^{18}\text{F}$ -labeled by isotope exchange in a single aqueous step.<sup>5</sup> Because the unlabeled  $^{19}\text{F}$ -precursor and  $^{18}\text{F}$ -labeled product are chemically inseparable (they differ by only a neutron), a final HPLC step may often be avoided. This allows for an exceptionally time-efficient radiolabeling method of a single step. We believe this method will be generalizable to many peptides as we have successfully labeled RGD, bombesin, octreotate, and bradykinin.<sup>6-10</sup> Preclinical animal data with  $^{18}\text{F}$ -RBF<sub>3</sub>-octreotate provide a comparable profile to that seen with  $^{68}\text{Ga}$ -DOTA-TATE. In pursuit of dual-mode fluorescent PET tracers, we have conceived of a "radiosynthon" that lets researchers graft any peptide and a fluorophore of choice to provide tracers that combine the sensitivity of PET with the brilliance of fluorescence.



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9. Zhang, C.; Zhang, Z.; Lin, K.-S.; Lau, J.; Zeisler, J.; Colpo, N.; Perrin, D. M.; Benard, F., Melanoma Imaging Using  $^{18}\text{F}$ -Labeled alpha-Melanocyte-Stimulating Hormone Derivatives with Positron Emission Tomography. *Mol. Pharm.* **2018**, *15* (6), 2116-2122.
10. Liu, Z. B.; Radtke, M. A.; Wong, M. Q.; Lin, K. S.; Yapp, D. T.; Perrin, D. M., Dual Mode Fluorescent F-18-PET Tracers: Efficient Modular Synthesis of Rhodamine-[cRGD](2)-[F-18]-Organotrifluoroborate, Rapid, and High Yielding One-Step F-18-Labeling at High Specific Activity, and Correlated in Vivo PET Imaging and ex Vivo Fluorescence. *Bioconjugate Chem.* **2014**, *25* (11), 1951-1962.



# Ratmir Derda

University of Alberta

Contact : Ratmir@ualberta.ca

## Research Interests

Molecular recognition and receptor-ligand interactions, genetically-encoded technologies in chemistry and biology, discovery trajectories and reproducibility of molecular discovery, chemistry-information interface, emergence of complexity.

## Education

2001	B.Sc. in Physics, Moscow Institute of Physics and Technology
2008	Ph.D. in Chemistry, University of Wisconsin-Madison

## Professional Career

1997 - 2001	Postdoctoral fellow, Harvard University, Wyss Institute of Biologically Inspired Engineering
2006 - 2011	Assistant Professor, Department of Chemistry, University of Alberta
2011 - present	Associate Professor, Department of Chemistry, University of Alberta

## Scientific Activities

2017- present	Founder and CEO 48Hour Discovery INC
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## Honors

1997	Gold Medal at the XXIX International Chemistry Olympiad, Montreal, Canada.
2011	Canadian Rising Star in Global Health (from Grand Challenges Canada)
2014	Boulder Peptide Society Young Investigator Award
2016	Rising Star in Chemical Biology from International Chemical Biology Society
2017	Martha Cook Piper Research Prize from University of Alberta
2018	David Gin Award in Carbohydrate Chemistry from American Chemical Society
2018	Melanie O'Neill Young Investigator Award in Biological Chemistry from CSC

## Publications

1. S. Ng, *et al.* Genetically-encoded Fragment-based Discovery of Glycopeptide Ligands for Carbohydrate-binding Proteins, *J. Am. Chem. Soc.*, **2015**, 137, 5248–5251
2. W. Matochko, S.C. Li, S.K.Y. Tang, R. Derda, Prospective identification of parasite sequences in phage display screens, *Nuc. Acid. Res.* **2014**, 42, 1784-98

# Genetically-Encoded Technologies for Discovery of Instructive Biomaterials

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Ratmir Derda

University of Alberta

Interaction between extracellular ligands and cell-surface receptors is a fundamental mechanism for control of cellular responses, homeostasis and differentiation. Discovery of new ligands that actuate cell surface receptors interaction is the starting point for development of drugs and instructive biomaterials. Genetically-encoded (GE) molecular libraries, such as Nobel prize-winning phage display technology, are poised to become the major source of discovery of biological drugs and development of ligands. We employ organic chemistry to upgrade canonical GE-polypeptide libraries restricted to 20 natural amino acids [1] and expand the use of GE-technologies to drug and material discovery. Such discoveries necessitate development of new chemical scaffolds that do not break down in aggressive proteolytic environment encountered in extracellular environment, serum or GI-tract. Using GE-libraries of peptides as a starting material for multi-step organic synthesis [1], we produce GE-libraries of novel cyclic [2] or bicyclic [3] architectures that exhibit remarkable stability to proteolytic degradation. We show that libraries of phage-displayed peptides can be applied to discover ligands for receptors on the surface of cells. Ligand discovered in such campaigns can be immobilized on 3D [4-5] or 2D substrates [6-8] to give rise to materials that control adhesion, growth, differentiation and self-renewal of stem cells.

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- [2] R. Mukherjee, J. Y. K. Wong, V. Triana, M. Miskolzie, A. Henninot, J. J. Dwyer, R. Derda\* "Aqueous Biocompatible Bicyclization of Peptides with Two-fold Symmetric Linchpin", **in review**
- [3] S. Kalthor-Monfared, M. R. Jafari, J. T. Patterson, P. I. Kitov, J. J. Dwyer, J. J. Nuss, R Derda "Rapid Biocompatible Macrocyclization of Peptides with Decafluorosulfone" *Chem. Sci.*, **2016**, 7, 3785-3790
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# Amy Szuchmacher Blum

McGill University

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## Research Interests

Self-assembly, plasmonics, nanoparticles, iron oxide, metamaterials

## Education

1994	B.A. Chemistry ( <i>cum laude</i> ) Princeton University
2000	Ph.D. Physical Chemistry University of Washington

## Professional Career

2001 - 2003	National Research Council Postdoctoral Fellow, US Naval Research Laboratory
2003 - 2008	Research Chemist, US National Research Laboratory
2008 - 2014	Assistant Professor, Department of Chemistry, McGill University
2014 - present	Associate Professor, Department of Chemistry, McGill University

## Scientific Activities

2012 - present	Director, McGill QCAM AFM User Facility
2018 - 2020	ESF College of Expert Reviewers

## Publications

1. *Iron oxide surface chemistry: the effect of chemical structure on binding in benzoic acid and catechol derivatives*, **Katalin V. Korpany, Dorothy D. Majewski, Cindy T. Chiu, Shoronia N. Cross**, and Amy Szuchmacher Blum\*. *Langmuir*, **33 (12)**, 3000-3013 (2017).
2. Nanoring formation via in-situ photoreduction of silver on a virus scaffold, **Serene S. Bayram, Omar K. Zahr, Julia Del Re**, and Amy Szuchmacher Blum\*. *Nanotechnology*, **27**, 485603 (2016).
3. Quick and Spontaneous Self-Assembly of Silver Nanoparticles into Highly Anisotropic Superstructures. **Serene S. Bayram**, Klas Lindfors, and Amy Szuchmacher Blum\*. *Beilstein Journal of Nanotechnology*, **7**, 1219-1228 (2016).

# Plasmonics with Viruses

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**Amy Szuchmacher Blum**

McGill University

Although there have been many advances in synthesizing nanoparticles, the assembly of these materials into deterministic and controllable patterns remains a major challenge. Biological systems operate at the nanoscale, building structural components with great chemical specificity that enable the processes of life. These successes result from billions of years of evolution. By adapting them to our needs, it is possible to utilize well-defined and well-controlled scaffolds to produce materials with novel properties that result from precise ordering on the nanoscale, such as a negative index of refraction, signal enhancement for spectroscopy, or evanescent wave focusing for superlenses. Utilizing viruses and viral proteins as templates is a relatively new idea that could have a large impact in nanotechnology and bioengineering. This approach offers the promise of exquisite control for positioning on the nanoscale, since the position of each coat protein within a virus-like particle is precisely defined, and self-assembly into homogenous micron-scale particles occurs spontaneously.

We use tobacco mosaic virus (TMV) coat protein as a template to self-assemble nanoparticles. This approach uses spatial arrangement instead of nanoparticle size, shape, or composition to control optical properties through the collective interactions between neighboring nanoparticles. Surface plasmons are resonant oscillations in the free electrons of a metal that are excited through interaction with light at the resonant wavelength. The effect of these plasmons is to focus incident light at the resonant wavelength into very small volumes near metal surfaces, leading to very intense local fields. In addition, these plasmonic oscillations can couple together, giving rise to more complex modes like plasmonic ring resonances that can be used to tune their response to incident light.

Here, we present robust covalent techniques using TMV coat protein as a template to produce nanostructured materials with novel properties. By exploiting the self-assembling properties and chemical addressability of TMV coat protein, we can utilize site-directed mutagenesis and bioconjugation strategies to produce highly symmetrical plasmonic nanorings, as evidenced by transmission electron microscopy (TEM). Theoretical models suggest that these rings may display an induced magnetic response at optical frequencies, and ensemble spectroscopic measurements reveal intriguing optical properties. Optical effects can be tuned by the introduction of a nanoparticle in the center of the rings through a pH dependent electrostatic interaction. Preliminary dark field scattering data, obtained for individual surface bound ring structures, is remarkably consistent with ensemble measurements, demonstrating that the observed optical properties arise from the ring structures. Thus, we show the utility of biotemplates in generating nanostructured building blocks for advanced materials.



# Kunio Matsumoto

Nano Life Science Institute (WPI-NanoLSI), Cancer Research Institute,  
Kanazawa University

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## Research Interests

HGF-MET pathway in regeneration and cancer progression, drug discovery by macrocyclic peptide, structural base of MET receptor activation

## Education

1981	Faculty of Science, Kanazawa University
1983	Graduate School of Science, Kanazawa University
1986	Graduate School of Science, Osaka University (Ph.D.)

## Professional Career

1987-1990	Assistant Professor, Department of Dermatology, Osaka University
1990-1993	Assistant Professor, Department of Biology, Kyushu University
1993-1994	Assistant Professor, Biomedical Research Center, Osaka University
1994-2007	Associate Professor, Graduate School of Medicine, Osaka University
2007- present	Professor, Cancer Research Institute, Kanazawa University
2017- present	Professor, Nano Life Science Institute (WPI-NanoLSI), Kanazawa University

## Honors

1992	Academic Incitement Award of Japanese Industrial Hygiene Dermatology Association
1996	JB Award of the Japanese Biochemical Society
1997	Incitement Award of the Japanese Cancer Association
2001	The 3rd Bio Business Competition JAPAN, The Special Award
2006	Nature Medicine-AnGes MG BioMedical Award (Main Award)
2014	The Commendation for Science and Technology by MEXT, Prizes for Science and Technology

## Publications

1. Sakai K, Passioura T, Sato H, Ito K, Umitsu M, Takagi J, Kato Y, Yano S, Furuhashi H, Shibata M, Suga H<sup>§</sup>, Matsumoto K<sup>§</sup>. Macrocyclic peptide inhibits hepatocyte growth factor by capturing its flexible multi-domains in a static conformation. **Nat Chem Biol**, 15: 598-606, 2019.
2. Miao W, Sakai K, Ozawa N, Nishiuchi T, Suzuki Y, Ito K, Morioka T, Umitsu M, Takagi J, Suga H, Matsumoto K. Cellular signaling and gene expression profiles evoked by a bivalent macrocyclic peptide that serves as an artificial MET receptor agonist. **Scientific Rep**, 8: 16492, 2018.
3. Matsumoto K, Umitsu M, De Silva DM, Roy A, Bottaro DP. HGF-MET in cancer progression and biomarker discovery. **Cancer Science**, 108: 296-307, 2017.
4. Adachi E, Sakai K, Nishiuchi T, Imamura R, Sato H, Matsumoto K. Cell-autonomous changes in Met receptor expression regulate the growth and metastatic characteristics in malignant melanoma. **Oncotarget**, 7: 70779-70793, 2016.
5. Ito K<sup>†</sup>, Sakai K<sup>†</sup>, Suzuki Y, Ozawa N, Hatta T, Natsume T, Matsumoto K<sup>§</sup>, Suga H<sup>§</sup>. Artificial human Met agonists based on macrocycle scaffolds. **Nat Commun**, 6: 6373, 2015.



# Macrocyclic Peptides Targeting HGF-MET

Kunio Matsumoto

Nano Life Science Institute (WPI-NanoLSI), and Cancer Research Institute, Kanazawa University

HGF (Hepatocyte Growth Factor), a bioactive protein composed of 697 amino acids, binds and activates its receptor MET (Fig. 1, 2). Activation of MET receptor drives mitogenesis (cell proliferation), motogenesis (cell migration), morphogenesis (3-D tubulogenesis), and cell survival, thereby participates in regeneration of damaged tissues. Clinical trials using recombinant HGF protein are ongoing for treatment of spinal cord injury and amyotrophic lateral sclerosis. On the other hand, aberrant activation of MET is associated with progression of cancer, particularly drug resistance and invasion-metastasis. Therefore, promotion of HGF-MET pathway become regeneration-based medicine, while the detection and inhibition of HGF-MET pathway become anti-cancer diagnosis and therapeutics.

By RaPID (Random Peptide Integrated Discovery), an innovative drug discovery platform, we obtained macrocyclic peptides that specifically bind to HGF or MET with 1-10 nM Kd values. The cross-linking of MET-binding macrocyclic peptides conferred them an ability to selectively activate MET [1-3]. These artificial MET-ligands exhibited mitogenic, motogenic, and morphogenic activities that are comparable to native ligand HGF. On the other hand, we obtained HGF-inhibitory peptide-8 (HiP-8) (Fig. 2) [4]. HiP-8 selectively recognizes and inhibits two-chain active HGF but not single-chain precursor HGF. High-speed atomic force microscopy analysis indicated that the binding of HiP-8 to HGF suppress dynamic domain movement of HGF. Using HiP-8 as a molecular probe, accumulation of tHGF in cancer tissue could be detected by PET (Positron Emission Tomography) imaging. Selective detection and/or inhibition of tHGF by HiP-8 is expected to be better diagnosis and/or therapeutics for drug discovery approach targeting HGF-MET.

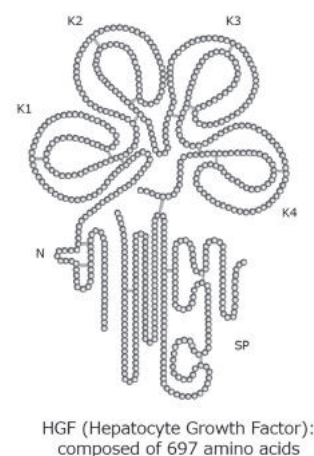


Fig. 1. Outline structure of HGF.

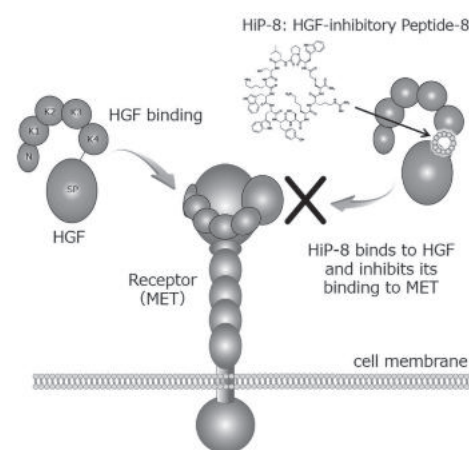


Fig. 2. Structure and outline action of HiP-8.

## References

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# Satoru Okuda

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PRESTO, Japan Science and Technology Agency

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## Research Interests

Biomechanics, Multi-cellular dynamics, Multi-scale simulation, Morphogenesis, Collective cell motion

## Education

2008	School of Engineering Science, Faculty of Engineering, Kyoto University
2010	Department of Mechanical Engineering and Science, Grad. School of Engineering, Kyoto University
2013	Department of Micro Engineering, Grad. School of Engineering, Kyoto University

## Professional Career

2010 - 2013	Pre-Doctoral Fellow DC1, Japan Society for the Promotion of Science
2013 - 2016	Research Scientist, RIKEN Center for Developmental Biology
2016 - 2017	Special Postdoctoral Researcher, RIKEN Center for Developmental Biology
2016 - present	PRESTO Researcher, Japan Science and Technology Agency
2019 - present	Associate Professor, Nano Life Science Institute (WPI-NanoLSI), Kanazawa University

## Honors

2017	Yamaguchi Medal, Asian-Pacific Association for Biomechanics
2017	Encouragement Award, Japan Society of Mechanical Engineers

## Publications

1. Okuda, et al, "Apical junctional fluctuations lead to cell flow while maintaining epithelial integrity," *Biophysical Journal* 116 (6): 1159-1170 (2019)
2. Okuda, et al, "Strain-triggered mechanical feedback in self-organizing optic cup morphogenesis," *Science Advances* 4(11): eaau1354 (2018)
3. Okuda, et al, "Combining Turing and 3D vertex models reproduces autonomous multicellular morphogenesis with undulation, tubulation, and branching," *Scientific Reports* 8: 2386 (2018)

# Versatile modeling of three-dimensional multi-cellular dynamics: *in-silico* and *in-vitro* combined approach to self-organizing morphogenesis

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**Satoru Okuda**

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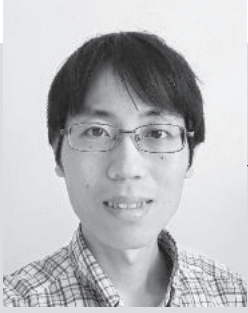
Organogenesis is a self-organizing process of multiple cells in three-dimensional (3D) space. This process is driven by intrinsic mechanisms of individual cells; nevertheless, macroscopic 3D tissue deformations are robustly regulated during morphogenesis. While such robust regulation of multicellular dynamics requires feedback from tissue deformations to cellular force generations, however, it is still unclear how individual cells sense 3D tissue deformations during morphogenesis. To address this issue, we developed a versatile 3D vertex model that enables the computational simulation of 3D multicellular dynamics at the single-cell resolution. We then combined it with the unique culture system of pluripotent stem cell-derived optic-cup organoids. This *in vitro* system recapitulates the step-wise process of optic-cup formation. We measured several mechanical properties *in vitro* and introduced them into the model to perform quantitative simulations. Remarkably, computational simulations for unknown parameters predicted several key cell behaviors. Based on the predictions, we carried out mechanical and pharmacological assays *in vitro*, which revealed the crucial role of mechanical force in signaling between distant cells to trigger their next-step behaviors in the sequential tissue deformations. We hereby conclude that 3D tissue deformation is fed back to cellular force generation via mechanosensing, where mechanical force plays a key role in signaling between distant cells to robustly regulate self-organizing morphogenesis [1].

In this talk, I will present the versatile 3D vertex model and its applications to the embryonic stem cell-derived optic-cup formation and several other biological phenomena [1,2,3].

## References

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- [1] Okuda, et al, "Strain-triggered mechanical feedback in self-organizing optic cup morphogenesis," *Science Advances* 4(11): eaau1354 (2018)
- [2] Okuda, et al, "Apical junctional fluctuations lead to cell flow while maintaining epithelial integrity," *Biophysical Journal* 116 (6): 1159-1170 (2019)
- [3] Okuda, et al, "Combining Turing and 3D vertex models reproduces autonomous multicellular morphogenesis with undulation, tubulation, and branching," *Scientific Reports* 8: 2386 (2018)



# Satoshi Toda

Department of Cellular and Molecular Pharmacology, Center for Systems and Synthetic Biology, University of California San Francisco  
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## Research Interests

I am interested in how the systems of molecular or cellular networks can achieve biological functions such as tissue development. To address this question, I take a bottom-up approach: design, build and test molecular/cellular networks to understand how they work and create useful products for applications.

## Education

2009	B.Sc., Engineering (Kyoto University)
2011	M.Sc., Life science (Kyoto University)
2014	Ph. D., Medical science (Kyoto University)

## Professional Career

2014-2015	Postdoctoral fellow, Kyoto University
2015 - present	Postdoctoral fellow, University of California San Francisco
2019 - present	Cooperative Researcher, Nano Life Science Institute (WPI-NanoLSI), Kanazawa University
Oct. 2019-	Assistant Professor, Nano Life Science Institute (WPI-NanoLSI), Kanazawa University

## Scientific Activities

2015-2016	Japan Society for the Promotion of Science (JSPS) Overseas Research Fellowship
2016-2019	Human Frontier Science Program (HFSP) Long-Term Fellowship

## Honors

2009	Hatakeyama Award (The Japan Society of Mechanical Engineers)
2012	KMYIA Young Investigator Award (Kyoto University Faculty of Medicine)
2013	Suzuki Koichi memorial award (The Japanese Biochemical Society)

## Publications

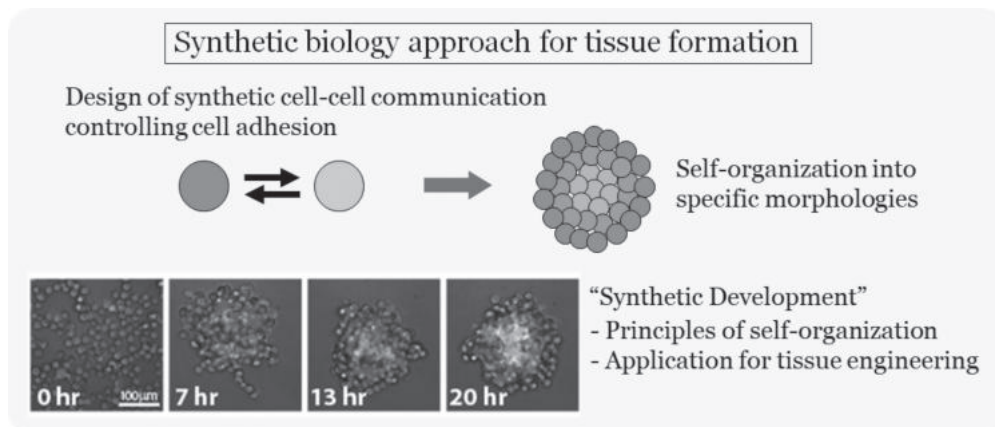
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2. Toda S, Blanch LR, Tang SKY, Morsut L, Lim WA. Programming self-organizing multicellular structures with synthetic cell-cell signaling. **Science**. 361, 156-162 (2018)

# Synthetic tissue formation: Programming multicellular self-organization

Satoshi Toda

Department of Cellular and Molecular Pharmacology, Center for Systems and Synthetic Biology, University of California San Francisco  
Nano Life Science Institute (WPI-NanoLSI), Kanazawa University

Multicellular animals emerge from a single fertilized cell that can differentiate into a multitude of diverse cell types that spatially self-organize into 3D tissue architectures. All the necessary genetic circuits to develop complex tissues and organs are written and stored as genomic DNA programs in the single cell. To understand how such compact genetic programs can encode algorithms that allow individual cells to build complex macroscale structures by themselves, we need to rewrite and test genetic programs. A common theme in the self-organization of multicellular tissues is the use of cell-cell signaling networks to induce morphological changes. We have recently developed a synthetic Notch receptor (synNotch) system that allows us to engineer new orthogonal cell-cell signaling to control transgene expression [1]. Using the modular synNotch platform, we engineered artificial genetic programs in which specific cell-cell contacts induced changes in cadherin-based cell adhesion. Despite their simplicity, these minimal intercellular programs were sufficient to yield multicellular assemblies with hallmarks of natural developmental systems: robust self-organization, well-choreographed sequential assembly, cell type divergence, symmetry breaking, and regeneration upon injury [2]. These results demonstrate the flexibility and power of the modular synthetic system to program self-organizing structures. I will present a series of experiments to design and test synthetic self-organizing structures and discuss next research directions towards constructive understanding of tissue formation.



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[2] Toda S, Blauch LR, Tang SKY, Morsut L, Lim WA., *Science.*, **2018**, 361, 156–162.



# Wendell Lim

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Howard Hughes Medical Institute

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## Research Interests

My research focuses on the design principles of molecular circuits that govern cell decision-making and responses.

## Education

1986	Harvard University, Cambridge, MA	AB	Chemistry
1991	MIT, Cambridge, MA	PhD	Biochemistry and Biophysics
1992 - 1996	Yale University, New Haven, CT	Postdoc	Biophysics and Biochemistry

## Professional Career

1996 - 2000	Assistant Professor, Department of Cellular & Molecular Pharmacology, UCSF
2000 - 2003	Associate Professor, Department of Cellular & Molecular Pharmacology, UCSF
2003 - present	Professor, Department of Cellular & Molecular Pharmacology, UCSF
2008 - present	Investigator, Howard Hughes Medical Institute, San Francisco, CA
2015 - present	Chair, Department of Cellular & Molecular Pharmacology, UCSF

## Honors

1992 - 1994	Helen Hay Whitney Foundation Postdoctoral Fellowship
1997	Burroughs Wellcome Fund New Investigator in the Pharmacological Sciences
1997	Searle Foundation Scholar
1997	David and Lucille Packard Fellow in Science and Engineering
2010	Hans Neurath Award, Protein Society
2012	Wired SmartList: 50 people who will change the world
2018	Feodor Lynen Medal, German Society for Biochemistry and Molecular Biology

## Publications

1. Morsut et al., Engineering Customized Cell Sensing and Response Behaviors Using Synthetic Notch Receptors. *Cell*, 2016.
2. Roybal et al., Precision Tumor Recognition by T Cells With Combinatorial Antigen Sensing Circuits. *Cell*, 2016.
3. Toda et al, Programming self-organizing multicellular structures with synthetic cell-cell signaling. *Science*, 2018.



# Learning to program cellular machines

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**Wendell A. Lim, PhD**

University of California, San Francisco  
Howard Hughes Medical Institute

Living cells are remarkable machines capable of complex sensing, decision making and cooperation. We have been pioneering synthetic biology approaches in which we ask how we can use simple molecular components to construct and rewire cellular regulatory networks to engineer cells that perform novel functions, with the same precision and robustness of evolved systems. We have been applying these approaches to the challenge of engineering therapeutic immune cells that can precisely recognize cancer (or other diseases) and execute robust and controlled therapeutic programs.



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