

Molecularly Bridged Gold Nanoparticle Array for Sensing Applications

Hiroshi SHIIGI[†] and Tsutomu NAGAOKA

Department of Applied Chemistry, Graduate School of Engineering, Osaka Prefecture University, 1-2 Gakuen, Naka, Sakai, Osaka 599-8570, Japan

The fabrication of electronic devices using individual molecules necessitates an adept control of the placement of molecules and tuning the space between them. This paper provides an overview of sensing using molecularly bridged gold nanoparticles (AuNPs) with nanometer-sized space. We have attempted to form a nanometer-sized space in a two-dimensional network consisting of a repeated sequence of an AuNP-molecule-AuNP junction. It is possible to evaluate electron tunneling or electron transfer in an AuNP-molecule-AuNP junction by directly measuring the electrical resistivity of the two-dimensional network. The resistivity of the two-dimensional sequence, in turn, depends on the size and conducting states of the molecules in each junction. The molecular junction in such nanometer-sized structures can be moved and rearranged to any location, enabling the rapid development of miniaturized compact electronic devices.

Keywords Molecular bridging, nanogap, electrical resistance, molecular electronics, sensing

(Received August 20, 2013; Accepted September 26, 2013; Published January 10, 2014)

1 Introduction	89	6 Bridge Formed by Nanowiring	93
2 Molecular Bridging among AuNPs	90	7 Acid-base Switching	93
3 Nanogap on Microelectrode	91	8 Summary and Outlook	94
4 Electrical Detection of Hybridization	92	9 Acknowledgements	94
5 DNA Sensing	92	10 References	94

1 Introduction

Nanomaterials feature unique shape- and size-dependent physicochemical properties that can be of great use in the fabrication of miniaturized compact electronic devices. With recent developments in nanotechnology, several new technologies have emerged, relying on the use of nanometer-sized space created at the molecular level. Thus far, researchers have focused on exploiting the unique functionalities of

nanomaterials by precise structural control using top-down and bottom-up approaches. In addition, researchers have developed protocols needed to apply these strategies to molecular electronics, involving processors, switches, and sensors. Brought together and applied across a broad spectrum of analytical science disciplines, such as biotechnology, medicine, and environmental science, the challenge will lie in extending basic techniques to nanospace functions.¹

It is known that electrode pairs separated by nanometer-scale gaps are fundamental building blocks for the fabrication of



Hiroshi SHIIGI received his Ph.D. degree in Engineering from Yamaguchi University in 2000. He worked at Yamaguchi University as a Research Associate (2001–2003). He then joined Osaka Prefecture University as an Assistant Professor in 2003, and became an Associate Professor in 2008. At present, he is Assistant Professor at Graduate School of Engineering, Osaka Prefecture University. His current research interest is the development of nanobioelectronics and biosensors based on molecular recognition.



Tsutomu NAGAOKA received his D. Sc. degree from Graduate School of Science, Kyoto University in 1982, and became a Research Associate of Department of Applied Chemistry, Yamaguchi University. He became Associate Professor in 1990 and Professor in 2000. He moved to Osaka Prefecture University as Professor in 2003. At present, he is Professor at Graduate School of Engineering, Osaka Prefecture University. His research area includes the analytical application of molecularly imprint polymers and metal nanoparticle material science.

[†] To whom correspondence should be addressed.
E-mail: shii@chem.osakafu-u.ac.jp

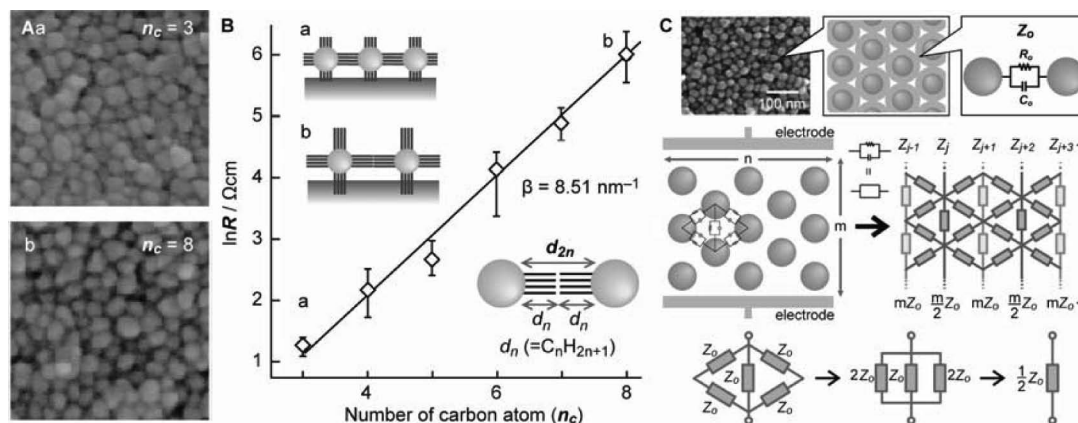


Fig. 1 (A) SEM images of AuNPs array fabricated on plastic substrate using (a) propanethiol and (b) octanethiol as bridging molecules. (B) Plot showing the dependence of $\ln(R)$ of an AuNP array on n_c . The inset represents a model of gap (d_{2n}) formed between adjacent AuNPs. (C) Illustration of a 2D network derived from SEM images and a model of electrical equivalent (Z_0) between adjacent AuNPs, expressed as capacitor (C_0) and resistor (R_0), and calculation process for deriving of Eq. (1). Copyright (2013) the Electrochemical Society.

nanometer-sized electronics.²⁻¹⁴ They also act as important tools in the characterizing the properties of molecules and materials at the nanometer scale. In the past decade, researchers have reported several techniques for the fabrication of nanogap electrodes, and demonstrated their potential applications in the analysis of molecules and nanomaterials. This has opened up a new paradigm beyond the capability of traditional microfabrication technologies. Thus far, several effective methods have been considered to provide promising results for the fabrication of nanogap electrodes, including mechanical break junctions,¹⁵ electromigration,^{16,17} electron-beam lithography,¹⁸ electrochemical plating,^{19,20} focused ion beam lithography,²¹ shadow mask evaporation,^{22,23} and nanoparticle arrays.²⁴⁻²⁷ In particular, the combination of top-down and bottom-up approaches has been a successful strategy for providing the desired configuration, placement of molecules into the nanospace, and realizing promising molecular recognition results.^{12-14,28-34} In principle, bottom-up fabrication is achieved through the binding, interaction, self-assembly, and self-organization characteristics of molecules and materials as building blocks.³⁵⁻³⁹ Precise control of the spacing between the fabricated electrodes for specific molecules is expected to allow ultrasensitive sensing. Nanogap devices provide a sufficient level of sensitivity, as few as a single molecule to a small number of molecules, with the direct transduction of molecule-specific binding events into electrical signals.

In the present work, we made an effort to develop a sensor based on molecular recognition within a nanogap, controlled by a nanometer-sized space. The nanogap is an important key to the development of a new field within analytical science, and has become a prominent and continuously expanding field of research. Therefore, we discuss promising strategies for enhancing the performance, as well as the key challenges associated with the development of ultrasensitive sensors, especially from the viewpoint of molecularly bridged nanogap technologies, as applied to electrical sensing.

2 Molecular Bridging among AuNPs

Recently, inorganic nanoparticles and their arrays have attracted

the attention of researchers as important materials for nanoelectronics, owing to their unique physical and chemical properties.⁴⁰⁻⁴³ The self-assembly technology is an effective bottom-up technique to assemble well-organized one- to three-dimensional structures, wherein the interparticle connections can be controlled at the single-particle level.⁴⁴⁻⁴⁷ From the application standpoint, metal nanoparticles are one of the most frequently studied inorganic materials because of their distinct combination of properties, which impart unique functionality to the nanotechnology-based devices.^{48,49} We previously reported on the synthesis of a gold nanoparticle (AuNP) array prepared *via* a single-step procedure, wherein alkanethiols were self-assembled to deposit AuNPs on a plastic substrate, as shown in Fig. 1A.^{25-27,50} Scanning electron microscope (SEM) images of the AuNPs-deposited substrate represented a uniformly covered surface without any overlap of AuNPs. These results indicate the formation of a single layer of AuNPs on the plastic substrate, without aggregation or integration. The logarithmic electrical resistivity (R) of the AuNP layers thus obtained clearly depends on the length of the gap between AuNPs (d_{2n}) based on the alkyl chain, as shown in Fig. 1B. This phenomenon is attributed to be the predominant mechanism of electron transport through a self-assembled monolayer (SAM) in metal-insulator-metal (MIM) junctions.⁵¹⁻⁵⁷ So far, several studies have concluded that the electrical properties of the MIM junction formed through a SAM between the electrodes can be determined by considering it as a parallel circuit composed of a resistor and a capacitor.⁵⁸⁻⁶⁰ Because each AuNP is separated from the other AuNPs by alkanethiols, adjacent AuNPs electrically act as capacitors and resistors, as shown in Fig. 1C.⁶⁰ Consequently, the equivalent (Z_0) of the two AuNPs can also be expressed as a resistor (R_0) and a capacitor (C_0) connected in parallel, and the entire network (Z_{total}) can be considered as a parallel circuit composed of a resistor and a capacitor:

$$Z_{\text{total}} = \left(\frac{2m}{3n} \right) Z_0. \quad m, n = \text{positive integer.} \quad (1)$$

The proposed circuit scheme is substantiated by the Nyquist plot of a single hemisphere and the excellent agreement between the DC and AC measurements.²⁶ Therefore, considering a pair

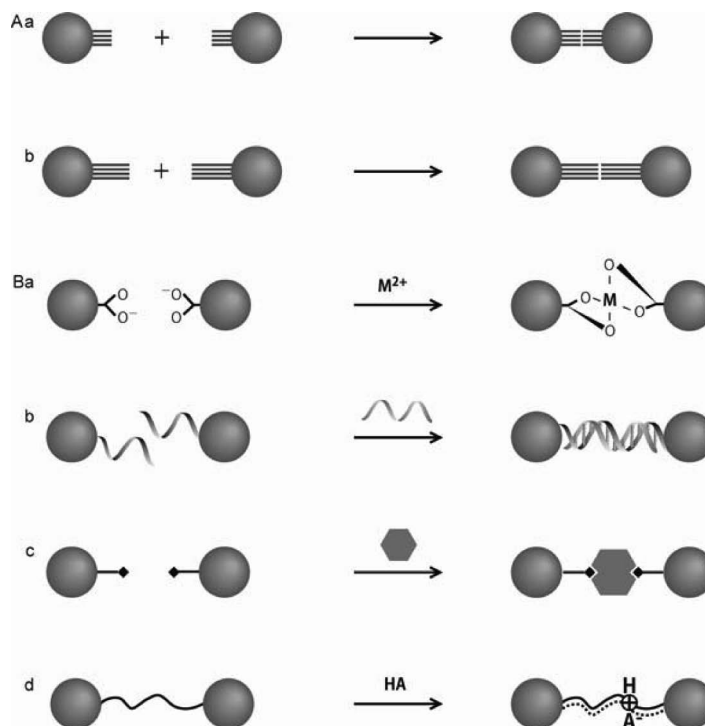


Fig. 2 Illustration of the nanogap between adjacent AuNPs. (A) Model of molecular bridging based on molecular size and (B) molecular recognition.⁶³

of AuNPs, it is possible to discuss the electrical characteristics of the layer formed by depositing AuNPs on a substrate. Electron transport in the AuNP-alkyl chain-AuNP junction is dominated by the tunneling barrier or, in other terms the resistivity, which decays exponentially with the distance according to the following equation:

$$\ln(R_0/R) = -\beta d_{2n}, \quad (2)$$

where β is the decay constant, which reflects the strength of electronic coupling across a particular molecular bridge (tunneling coefficient), and d_{2n} is twice the length of alkanethiol (d_n) along the tunneling pathway, as shown in the inset of Fig. 1B. The slope of the plot of $\ln(R)$ vs. d_{2n} , which has a y-intercept of $\ln(R_0)$, was found to be 8.51 nm^{-1} , which is consistent with the value of β reported for tunneling through alkanethiols.^{51-54,57-64}

3 Nanogap on Microelectrode

As mentioned above, the nanogap formed in the AuNPs layer self-assembled onto substrates could be connected covalently in series using organic thiol molecules. The electrical characteristics of the nanogap reflect the size of the alkanethiol in Fig. 2A. This signifies that the nanogap can be effectively used to sense molecules. Recently, the Murray group has reported that the electrical conductivity of the monolayer of AuNP coated with carboxylate alkanethiolate monolayers, linked together by carboxylate-Cu²⁺-carboxylate bridges, depended on the vapor pressures.⁶⁵ In this case, the presence of organic vapor induced a swelling of the flexible network-linked AuNPs by changing either the size or chemical nature of electron tunneling pathways, accompanied by a decrease in the

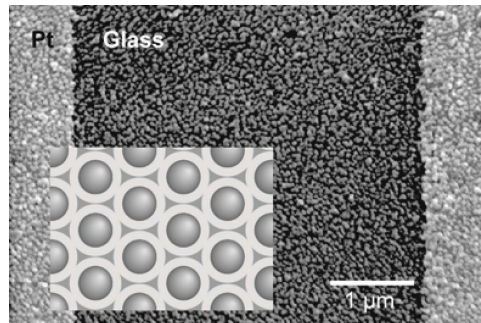


Fig. 3 SEM image of an AuNPs array formed on a microelectrode.

electrical conductivity. Similarly, Zhong *et al.* have also reported that the resistance of the AuNP film depends on the sorption of vapors by molecular interactions, such as hydrophobicity, polarity, and hydrogen bonding.⁶⁶ In the same manner, molecular bridging in the nanogap system will allow sensing for various molecules (Fig. 2B).⁶⁷

A monolayer of AuNPs deposited onto microelectrodes could be connected covalently in series using organic thiol molecules, as shown in Fig. 3. Therefore, the monolayer formed from the repeated sequences of a two-dimensional AuNP-organic molecule-AuNP arrangement, which have been fabricated by a self-assembling technique based on spontaneous Au-S binding, has an electrical nanogap between adjacent AuNPs that could be used for ultrasensitive detection.^{68,69} A decanedithiol was adsorbed onto the electrode by dipping it into a binder solution, and for self-assembly of AuNPs with the sulfur group of the binder molecule. This dip-coating procedure was repeated to produce an array with an equally spaced interval between each

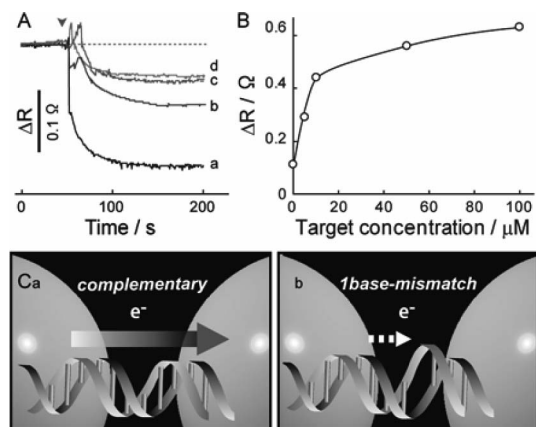


Fig. 4 (A) Resistance changes from the hybridization of a probe (12-mer, 5'-HS-TCT CAA CTC gTA-3') with: (a) complementary oligonucleotide (3'-AgA gTT gAg CAT-5'); mismatch sequences, (b) 1-base (3'-AgA gTT gAg CCT-5'), (c) 4-base (3'-AgA gTT AAC TCT-5'), and (d) 11-base (3'-CCC CCC CCC CCC-5') mismatched strands. Sample addition is indicated by arrow. (B) Dependence of sensor response on the concentration of target complementary DNA. (C) Model illustrations for electron transfer in molecular bridging with: (a) complementary, (b) 1-bp mismatched strands. Copyright (2005) American Chemical Society.

particle created by the binder (*ca.* 1.3 nm), which can be adjusted using the length of the alkyl chain. The resistance of the array was consistent with the value reported by Zhong *et al.* (nonanedithiol, *ca.* 1.1 nm).⁶⁶

4 Electrical Detection of Hybridization

The AuNP array was modified with a single-stranded (*ss*) DNA probe, whose amount required for probe modification was estimated to be approximately 5.4 pmol using an electrochemical intercalator.⁷⁰ Once the resistance became stabilized, a tris-EDTA (TE) buffer involving the sample *ss*DNA was added over the array for hybridization, as shown in Fig. 4A. Upon sample addition, an immediate decrease occurred in the resistance with the signal-to-noise (*S/N*) ratios being above 40, followed by a steady state within 90 s. The magnitude of the response depended on the number of mismatched base pairs (bp) in the double-stranded (*ds*) DNA. The largest response amongst the samples corresponded to the sample with the complementary strand (a, 0.19 Ω). An increase in the number of mismatches led to a decrease in the magnitude (b - d), with the 11-bp mismatched DNA (d) showing the smallest response (0.05 Ω). It should be noted here that the resistance change exhibited a nonlinear behavior with respect to the number of mismatches. A response was found in the complementary DNA concentration with a range of 5 - 100 μM (25 - 500 pmol), as shown in Fig. 4B.^{70,71} According to the results obtained from an impedance analysis, ionic migration has only minor effects on DNA sensing. Therefore, the resistance changes can be due to the conductivity of the *ds*DNA wire, which can be explained in terms of π overlapping between adjacent base pairs, as shown in Fig. 4C.⁷²⁻⁷⁶ The presence of a mismatch would produce a defect in electron transfer, which arises in the localization of electrons to reduce the electron-transfer rate. The molecular bridging system that utilizes the nanogap makes it possible to respond to a change in the electrical characteristics because of

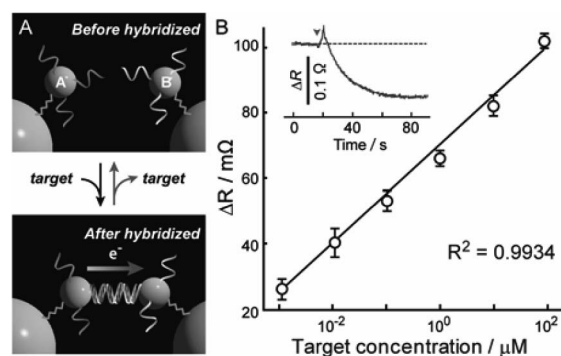


Fig. 5 (A) Model illustrations for electron transfer in an open-bridge system before and after hybridization. (B) Dependence of the sensor response on the concentration of target complementary DNA. Probes A, B and target DNA sequences were 5'-SH-poly(T)₁₂-3', 5'-poly(T)₁₂-SH-3', and 3'-poly(A)₂₄-5', respectively. Copyright (2008) American Chemical Society.

the structural change, based on the DNA hybridization.

5 DNA Sensing

To achieve DNA sensing using a nanogap, an open bridge-structured electrode was fabricated by repeatedly depositing the AuNP-*ss*DNA(A)-*ss*DNA(B)-AuNP sequence. Here, the gap between the AuNPs was precisely controlled using the probe sequence, as shown in Fig. 5A.⁷⁷ Using the combination of this electrode and conductive DNA, we were able to measure very small changes in the electrical properties of DNA with a high *S/N* (>30) and a detection limit of 5.0 fmol. A remarkable difference was observed even between the 1-bp mismatched DNA and the complementary DNA. We were able to amplify the detection limit of the 1-bp mismatch in the DNA sequence using the described system. The inset of Fig. 5B shows the time course of the array resistance after applying the target 24-mer DNA, which carries two complementary sections for probes A and B. In this case, the target is poly(A)₂₄, and both of the probes are poly(T)₁₂. After reaching a steady state, an aliquot of the target DNA was applied to the array. Consequently, the resistance decreased immediately, and became constant within 60 s. The ΔR value, defined as the difference in the resistance before and after the hybridization, was observed to be 100 m Ω , with an *S/N* ratio >30. The sensor exhibited responses over a wide range of concentrations with a detection limit of 5.0 fmol, as shown in Fig. 5B.

Electrical measurements were conducted using the described array having equivalent electrical resistance, and repeated in triplicate. The results presented in the previous section imply that the AuNPs separated by a gap of 1.3 nm were effective in detecting the hybridization event. However, their effectual concentration range was limited (detection limit of ~25 pmol), because not every probe could hybridize with a target strand in the gap between the particles.⁶⁸⁻⁷¹ Thus, the probes were not entirely responsible for the formation of conductive paths on the surface of AuNPs. In addition, opening bridge hybridization also occurred between adjacent AuNPs. Accordingly, the altered conductivity can be explained not only by the molecular conductivity of DNA, but also by the reduced structural distance between the parent AuNPs with attached 12-mer probes owing to this bridging by hybridization. The binder thiol (~1.3 nm)

was used to attach child AuNPs (12 nm) to parent AuNPs (46 nm), anchoring them to the parent and at the same time leaving a flexible tail free for target binding. When one side of the target DNA (24-mer) is hybridized to the 12-mer probe, for example probe A, the hybridization of the other half of the target DNA sequence with the other probe (probe B) leads to a decrease in the electrical resistance.⁷⁷ The distance between the child AuNPs was decreased compared to the distance before hybridization. A greater distance between the child AuNPs make it impossible to hybridize both halves of the target DNA, preventing the formation of a conducting pathway at the nanogap. These results suggest that the efficient formation of the conductive path increases the detection limit by 10^3 when compared to the detection limit achieved by using the single-AuNP array system.⁷⁰

Furthermore, we verified the effectiveness of this system for the identification of DNA mismatches by using complementary, 1-bp, 2-bps, and 24-bps mismatched sequences.⁷⁷ The results indicated that the response was highest for the complementary DNA ($\Delta R > 0.1 \Omega$), and decreased with an increase in the number of mismatched bases. Finally, the smallest ΔR was observed with the fully mismatched sequence ($\Delta R < 10 \text{ m}\Omega$). Furthermore, the response to each target sequence was consistent, regardless of whether the measurements were performed using the complementary or fully mismatched sequence. In this series of experiments with repeated hybridization and denaturing, the measured response to the complementary strand was stable. The resistance was accurate within $\pm 4.2\%$ in a given series of experiments, and the S/N value remained constant. The response was nonlinear with respect to the number of mismatches, and a clear difference ($>50 \text{ m}\Omega$) was observed between the complementary DNA and the 1-bp mismatch, suggesting that this system can be effectively used for the detection of single nucleotide polymorphism.

6 Bridge Formed by Nanowiring

As mentioned above, the nanogap allows highly sensitive detection of the electrical property of DNA molecular bridges.^{68-71,77} However, the DNA used for detection is either a polymer or an oligomer, rather than a molecule. Therefore, we made an attempt to create a nanogap by using a conducting polymer in order to bridge the nanogap. Among the conducting polymers, polyaniline (PANI) is the material of considerable scientific interest because of its unique electrical behavior and potential as an environmentally stable conducting polymer. An emeraldine-type PANI becomes electrically conductive when doped with an acid, wherein the doping level can be tuned simply by an adept control of the oxidation-reduction or acid-base chemistry.⁷⁸ Therefore, PANI is considered to be a technologically important and stable conducting polymer. In addition, its reversible conductivity, achieved by a suitable doping, makes it a promising material for many applications, including chemical sensors and biosensors.⁷⁹⁻⁸¹ In our previous studies, we demonstrated a new synthetic strategy for the self-assembly of AuNPs to form raspberry-like aggregates. Forming three-dimensional AuNP-PANI-AuNP repeated sequences could further help in the realization of nanoscale electronics and molecular devices.⁸²⁻⁸⁵

Figure 6A shows TEM images of AuNPs prepared using aniline as a reducer, showing a raspberry-like aggregated structure. The AuNPs in this aggregated structure had a particle diameter of 5.52 nm with a standard deviation of 0.83 nm. It is well known that the diameter of a particle strongly depends not

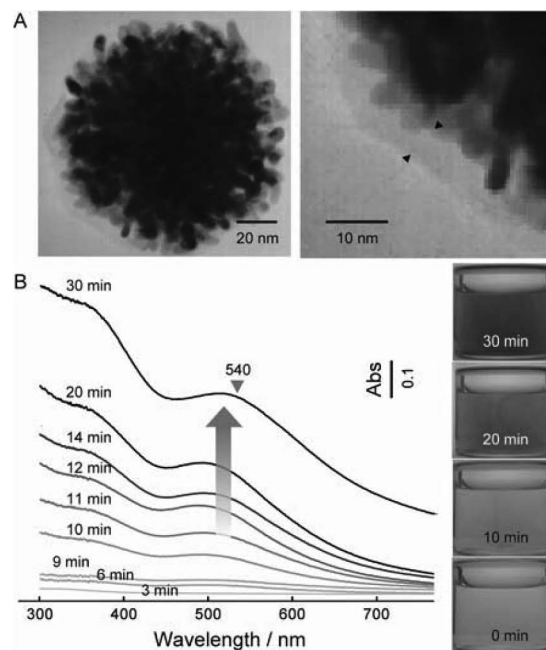


Fig. 6 (A) TEM images of raspberry-like aggregation. Arrows indicate a 4.0-nm-thick passivation layer. (B) UV-Vis spectra of the generation and growth of aggregation. Copyright (2012) the Electrochemical Society.

only on the reaction time and temperature, but also on the initial ratio of the reactants, which in this case are aurate and reducer. The AuNPs synthesized by aniline reduction were nearly dispersed spheres, whose sizes were controlled by the initial concentrations of aurate and the reducer.⁸²⁻⁸⁷ Therefore, the diameter was controlled solely by the reaction time at a constant temperature (333 K). The UV-Vis spectra of the AuNPs changed drastically over 10 min, as shown in Fig. 6B. Finally, a broad peak at 540 nm, which could be attributed to the surface plasmon resonance (spr) of the AuNPs, and a background absorbance were observed. In addition, we could observe a red shift of 20 nm, compared to that of the generally reported AuNPs coated by surfactants. This signifies the spr coupling between the closely spaced AuNPs, and also that the AuNPs were coated with a monolayer having a larger dielectric constant.^{82,88}

7 Acid-base Switching

Furthermore, to confirm the composition of the passivation layer, the resulting raspberry-like aggregated structure was stirred in a strongly acidic medium (a). New absorbance peaks were observed at around 445 and over 700 nm. On the other hand, the spectrum (b) possessed a peak intensity at around 540 nm, which could be attributable to spr because of dedoping in an alkaline medium, as shown in Fig. 7A. The new absorbance peaks, which were not based on the aggregation of AuNPs, could be attributed to the localized and delocalized polaron of PANI, respectively.^{89,90} This observation indicates that the origin of the structural change in the oxidized aniline was caused by acid doping, where it was transformed from an insulating base to a conducting salt-type PANI. The difference between the spectra (a) and (b) was attributed to the absorbance based on the existence of the oxidized aniline. Consequently, a

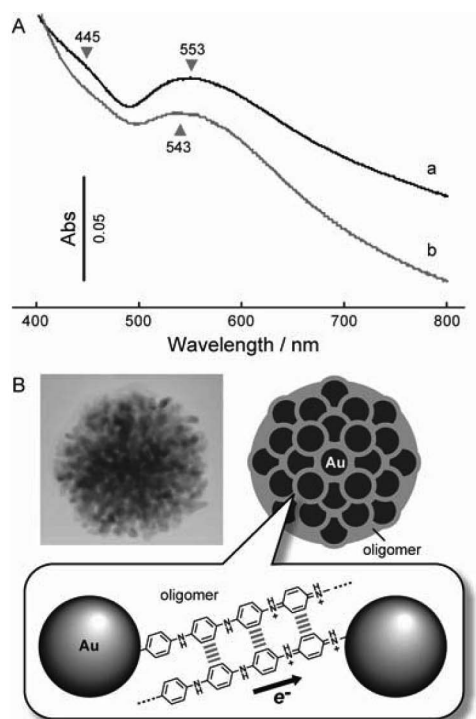


Fig. 7 (A) UV-Vis spectra of raspberry-like aggregation after (a) doping and (b) dedoping processes. (B) Model illustration of an enlarged view of an aniline oligomer between adjacent AuNPs. Copyright (2011) the Electrochemical Society.

thick aggregation was postulated as follows: a 4.0-nm-thick passivation layer, indicated by the arrows in Fig. 6A, corresponded to the oxidized aniline formed during the reduction of aurate. The resulting size was calculated from the molecular length with at least one octamer of aniline (4.1 nm), because pH 4.1 of the solution mixture constitutes a limiting factor for the growth of PANI. It was assumed that interactions such as π -stacking of the respective aniline oligomer, coated to the AuNPs, lead to the raspberry-like aggregation. Therefore, the overlapping of oligomers produces a polymer, as shown in the spectroscopic results in Fig. 7A. The electrical properties of the raspberry-like aggregation, cast on a microelectrode, significantly changed with the doping and dedoping processes. The aggregation, which resulted from doping, revealed a good conducting property of $3.1 \times 10^{-2} \text{ S cm}^{-1}$. This is similar to the conductivity of the generally reported salt-type PANI.^{78,91} On the other hand, the conductivity of the base-type PANI reduced dramatically to $10^{-8} \text{ S cm}^{-1}$. This observation implies the formation of molecular bridges of the overlapped aniline oligomers between the adjacent AuNPs. Therefore, this system could act as a molecular switch, characterized by a transformation from the conducting (salt-type) to insulating (base) oligomers, and sensitively determining the concentration of acids.

8 Summary and Outlook

This review delineates recent advancements in the development of sensing methods based on the arrangement of AuNPs. Using this approach, a molecular electronic device could be fabricated, with electrodes spaced at the nanoscale. The use of a nanogap electrode has enabled the detection of very small electrical signals, which could be utilized in highly sensitive and

label-free sensing applications.

The proposed molecular recognition using the nanogap is based on molecular bridging, with binding and interactions between a target molecule and a recognition site. Therefore, two important points must be considered for molecular recognition. Firstly, the chemical reaction or the interaction between the probe and target occurring in the nanogap must be defined. Secondly, a probe must be placed into the nanogap. These points are easily achieved by the technique proposed in this review, because it is possible to reliably place the probe in the nanogap using the probe-modified AuNPs.

The techniques proposed in this study could further help in the realization of a high-density and high-throughput sensing platform for molecular sensors. We believe that the findings will hold the key to the future development of nano-bioscience and associated technologies. We anticipate the formation of a uniform array of AuNPs and direct translation of the activity of a single molecule into an electrical signal. Moreover, two-dimensional arrangements of nanoparticles have also evolved with respect to their pathognomonic optical characteristics, because metal nanoparticles have distinctive optical characteristics. Some promising results have suggested that such arrangements and nano-spacing may be useful in optical applications.

9 Acknowledgements

We gratefully acknowledge financial supports provided by Ministry of Agriculture, Forestry and Fisheries through a Science and Technology Research Promotion Program for Agriculture, Forestry, Fisheries and Food Industry, and the Japan Society for the Promotion of Science through a Grant-in-Aid for Scientific Research (B) (JSPS KAKENHI, 25288039).

10 References

1. H. Shiigi, S. Tokonami, Y. Yamamoto, and T. Nagaoka, *Anal. Sci.*, **2012**, *28*, 1037.
2. C. Zhou, C. J. Muller, M. R. Deshpande, J. W. Sleight, and M. A. Reed, *Appl. Phys. Lett.*, **1995**, *67*, 1160.
3. D. L. Klein, P. L. McEuen, J. E. Bowen Katari, R. Roth, and A. P. Alivisatos, *Appl. Phys. Lett.*, **1996**, *68*, 2574.
4. D. L. Kleina, R. Roth, A. K.L. Lim, A. P. Alivisatos, and P. L. McEuen, *Nature*, **1997**, *389*, 699.
5. T. Junno, S.-B. Carlsson, H. Xu, L. Montelius, and L. Samuelson, *Appl. Phys. Lett.*, **1998**, *72*, 548.
6. M. A. Reed, C. Zhou, C. J. Muller, T. P. Burgin, and J. M. Tour, *Science*, **1997**, *278*, 252.
7. S. J. Tans, A. R. M. Verschueren, and C. Dekker, *Nature*, **1998**, *393*, 49.
8. D. Porath, A. Bezryadin, S. de Vries, and C. Dekker, *Nature*, **2000**, *403*, 635.
9. J. Park, A. N. Pasupathy, J. I. Goldsmith, C. Chang, Y. Yaish, J. R. Petta, M. Rinkoski, J. P. Sethna, H. D. Abruna, P. L. McEuen, and D. C. Ralph, *Nature*, **2002**, *417*, 722.
10. T. Dadosh, Y. Gordin, R. Krahn, I. Khivrich, D. Mahalu, V. Frydman, J. Sperling, A. Yacoby, and I. B. Joseph, *Nature*, **2005**, *436*, 677.
11. J. Zhang, X. Wang, X. Wang, H. Ma, K. Cheng, Z. Fan, Y. Li, A. Ji, and F. Yang, *Appl. Phys. Lett.*, **2010**, *96*, 213505.
12. S.-F. Shi, X. Xu, D. C. Ralph, and P. L. McEuen, *Nano Lett.*, **2011**, *11*, 1814.

13. B. K. Duan, J. Zhang, and P. W. Bohn, *Anal. Chem.*, **2012**, *84*, 2.
14. L. Rassaei, K. Mathwig, E. D. Goluch, and S. G. Lemay, *J. Phys. Chem. C*, **2012**, *116*, 10913.
15. H. Park, A. K. L. Lim, A. P. Alivisatos, J. Park, and P. L. McEuen, *Appl. Phys. Lett.*, **1999**, *75*, 301.
16. W. Liang, M. P. Shores, M. Bockrath, J. R. Long, and H. Park, *Nature*, **2002**, *417*, 725.
17. L. D. L. S. Valladares, L. L. Felix, A. B. Dominguez, T. Mitrelias, F. Sfigakis, S. I. Khondaker, C. H. W. Barnes, and Y. Majima, *Nanotechnology*, **2010**, *21*, 445304.
18. W. Chen, H. Ahmed, and K. Nakazoto, *Appl. Phys. Lett.*, **1995**, *66*, 3383.
19. A. F. Morpurgo, C. M. Marcus, and D. B. Robinson, *Appl. Phys. Lett.*, **1999**, *74*, 2084.
20. Y. Kashimura, H. Nakashima, K. Furukawa, and K. Torimitsu, *Thin Solid Films*, **2003**, *438* - 439, 317.
21. T. Nagase, T. Kubota, and S. Mashiko, *Thin Solid Films*, **2003**, *438*, 374.
22. S. Kubatkin, A. Danilov, M. Hjort, J. Cornil, J. L. Bredas, N. Stuhr-Hansen, P. Hedegard, and T. Bjørnholm, *Nature*, **2003**, *425*, 698.
23. Y. Naitoh, T.-T. Liang, H. Azechara, and W. Mizutani, *Jpn. J. Appl. Phys.*, **2005**, *44*, L472.
24. T. Ogawa, K. Kobayashi, G. Masuda, T. Takase, and S. Maeda, *Thin Solid Films*, **2001**, *393*, 374.
25. H. Shiigi, Y. Yamamoto, H. Yakabe, S. Tokonami, and T. Nagaoka, *Chem. Commun.*, **2003**, 1038.
26. Y. Yamamoto, H. Shiigi, and T. Nagaoka, *Electroanalysis*, **2005**, *17*, 2224.
27. Y. Yamamoto, N. Yoshi, H. Shiigi, and T. Nagaoka, *Solid State Ionics*, **2006**, *177*, 2325.
28. S. Roy, X. Chen, M.-H. Li, Y. Peng, F. Anariba, and Z. Gao, *J. Am. Soc. Chem.*, **2009**, *131*, 12213.
29. S. Roy and Z. Gao, *Nano Today*, **2009**, *4*, 318.
30. X. Chen, Z. Guo, G.-M. Yang, J. Li, M.-Q. Li, J.-H. Liu, and X.-J. Haung, *Materials Today*, **2010**, *13*, 28.85
31. M. Löhndorf, U. Schlecht, T. M. Gronewold, A. Malavé, and M. Tewes, *Appl. Phys. Lett.*, **2005**, *87*, 243902.
32. U. Schlecht, A. Malavé, T. M. A. Gronewold, M. Tewes, and M. Löhndorf, *Biosens. Bioelectron.*, **2007**, *22*, 2337.
33. V. Haguët, D. Martin, L. Marcon, T. Heim, D. Stiévenard, C. Olivier, O. El-Mahdi, and O. Melnyk, *Appl. Phys. Lett.*, **2004**, *84*, 1213.
34. H. J. Park, Y. S. Chi, I. S. Choi, and W. S. Yun, *Appl. Phys. Lett.*, **2010**, *97*, 033701.
35. A. E. Nel, L. Mädler, D. Velegol, T. Xia, E. M. V. Hoek, P. Somasundaran, F. Klaessig, V. Castranova, and M. Thompson, *Nat. Mater.*, **2009**, *8*, 543.
36. M. Oyama, *Anal. Sci.*, **2010**, *26*, 1.
37. N. Uehara and O. Yoshida, *Anal. Sci.*, **2012**, *28*, 1125.
38. K. Tomita, T. Ishioka, and A. Harata, *Anal. Sci.*, **2012**, *28*, 1139.
39. Y. Takahashi, N. Miyahara, and S. Yamada, *Anal. Sci.*, **2013**, *29*, 101.
40. L. Li, J. Hu, W. Yang, and A. P. Alivisatos, *Nano Lett.*, **2001**, *1*, 349.
41. C. A. Foss, G. L. Hornyak, J. A. Stockert, and C. R. Martin, *J. Phys. Chem.*, **1994**, *98*, 2963.
42. K. Yakushiji, F. Ernult, H. Imamura, K. Yamane, S. Mitani, K. Takanashi, S. Takahashi, S. Maekawa, and H. Fujimori, *Nat. Mater.*, **2005**, *4*, 57.
43. Y. Azuma, M. Kanehara, T. Teranishi, and Y. Majima, *Phys. Rev. Lett.*, **2006**, *96*, 016108.
44. H. Nakao, H. Shiigi, Y. Yamamoto, S. Tokonami, T. Nagaoka, S. Sugiyama, and T. Ohtani, *Nano Lett.*, **2003**, *3*, 1391.
45. H. Nakao, H. Hayashi, H. Shiigi, and K. Miki, *Anal. Sci.*, **2009**, *25*, 1177.
46. H. Nakao, T. Taguchi, H. Shiigi, and K. Miki, *Chem. Commun.*, **2009**, 1858.
47. H. Nakao, S. Tokonami, T. Hamada, H. Shiigi, T. Nagaoka, F. Iwata, and Y. Takeda, *Nanoscale*, **2012**, *4*, 6814.
48. I. D. Walton, S. M. Norton, A. Balasingham, L. He, D. F. Oviso, D. Gupta, P. A. Raju, M. J. Natan, and R. G. Freeman, *Anal. Chem.*, **2002**, *74*, 2240.
49. C. C. Chen, Y. P. Lin, C. W. Wang, H. C. Tzeng, C. H. Wu, Y. C. Chen, C. P. Chen, L. C. Chen, and Y. C. Wu, *J. Am. Chem. Soc.*, **2006**, *128*, 3709.
50. H. Shiigi, S. Shirai, T. Fujita, H. Morishita, Y. Yamamoto, T. Nishino, S. Tokonami, H. Nakao, and T. Nagaoka, *J. Electrochem. Soc.*, **2013**, *160*, H630.
51. K. Slowinski, R. V. Chamberlain, C. J. Miller, and M. Majda, *J. Am. Chem. Soc.*, **1997**, *119*, 119101.
52. M. A. Rampi and G. M. Whitesides, *Chem. Phys.*, **2002**, *281*, 373.
53. M. L. Chabinyc, X. Chen, R. E. Holmlin, H. Jacobs, H. Skulason, C. D. Frisbie, V. Mujica, M. A. Ratner, M. A. Rampi, and G. M. Whitesides, *J. Am. Chem. Soc.*, **2002**, *124*, 11730.
54. R. L. York, P. T. Nguyen, and K. Slowinski, *J. Am. Chem. Soc.*, **2003**, *125*, 5948.
55. T. Lee, W. Wang, J. F. Klemic, J. J. Zhang, J. Su, and M. A. Reed, *J. Phys. Chem. B*, **2004**, *108*, 8742.
56. A. Salomon, D. Cahen, S. Lindsay, J. Tomfohr, V. B. Engelkes, and C. D. Frisbie, *Adv. Mater.*, **2003**, *15*, 1881.
57. E. A. Weiss, R. C. Chiechi, G. K. Kaufman, J. K. Kriebel, Z. Li, M. Duati, M. A. Rampi, and G. M. Whitesides, *J. Am. Chem. Soc.*, **2007**, *129*, 4336.
58. K. Slowinski, R. V. Chamberlain, R. Bilewicz, and M. Majda, *J. Am. Chem. Soc.*, **1996**, *118*, 4709.
59. R. L. York and K. Slowinski, *J. Electroanal. Chem.*, **2003**, *550* - 551, 327.
60. K. Slowinski and M. Majda, *J. Electroanal. Chem.*, **2000**, *491*, 139.
61. K. Slowinski, H. K. Y. Fong, and M. Majda, *J. Am. Chem. Soc.*, **1999**, *121*, 7257.
62. S. Sek, R. Bilewicz, and K. Slowinski, *Chem. Commun.*, **2004**, 404.
63. R. E. Holmlin, R. F. Ismagilov, R. Haag, V. Mujica, M. A. Ratner, M. A. Rampi, and G. M. Whitesides, *Angew. Chem., Int. Ed.*, **2001**, *40*, 2316.
64. R. E. Holmlin, R. Haag, M. L. Chabinyc, R. F. Ismagilov, A. E. Cohen, A. Terfort, M. A. Rampi, and G. M. Whitesides, *J. Am. Chem. Soc.*, **2001**, *123*, 5075.
65. F. P. Zamborini, M. C. Leopold, J. F. Hicks, P. J. Kulesza, M. A. Malik, and R. W. Murray, *J. Am. Chem. Soc.*, **2002**, *124*, 8958.
66. L. Han, D. R. Daniel, M. M. Maye, and C.-J. Zhong, *Anal. Chem.*, **2001**, *73*, 4441.
67. T. Nagaoka, H. Shiigi, and S. Tokonami, *Bunseki Kagaku*, **2007**, *56*, 201.
68. H. Shiigi, S. Tokonami, H. Yakabe, and T. Nagaoka, *J. Am. Chem. Soc.*, **2005**, *127*, 3280.
69. S. Tokonami, M. Iwamoto, K. Hashiba, H. Shiigi, and T. Nagaoka, *Solid State Ionics*, **2006**, *177*, 2317.
70. S. Tokonami, H. Shiigi, and T. Nagaoka, *Electroanalysis*, **2008**, *20*, 355.
71. S. Tokonami, H. Shiigi, and T. Nagaoka, *J. Electrochem. Soc.*, **2008**, *155*, J105.

72. D. Porath, A. Bezryadin, S. de Vries, and C. Dekker, *Nature*, **2000**, 403, 635.
73. H.-W. Fink and C. Schönberger, *Nature*, **1999**, 398, 407.
74. J. Richter, *Phys. E*, **2003**, 16, 157.
75. M. R. Arkin, E. D. A. Stemp, R. E. Holmin, J. K. Barton, A. Hörmann, E. J. C. Olson, and P. F. Barbara, *Science*, **1996**, 273, 475.
76. A. Kasumov, M. Kociak, S. Guéron, B. Reulet, V. T. Volkov, D. V. Klinov, and H. Bouchiat, *Science*, **2001**, 291.
77. S. Tokonami, H. Shiigi, and T. Nagaoka, *Anal. Chem.*, **2008**, 80, 8071.
78. S. W. Haug, D. B. Humphrey, and G. A. MacDiarmid, *J. Chem. Soc., Faraday Trans. 1*, **1986**, 82, 2385.
79. K. Ogura, H. Shiigi, T. Oho, and T. Tonosaki, *J. Electrochem. Soc.*, **2000**, 147, 4351.
80. K. Ogura, H. Shiigi, M. Nakayama, and A. Fujii, *J. Electrochem. Soc.*, **1998**, 145, 3351.
81. K. Ogura, A. Fujii, H. Shiigi, M. Nakayama, and T. Tonosaki, *J. Electrochem. Soc.*, **2000**, 147, 1105.
82. H. Shiigi, Y. Yamamoto, N. Yoshi, H. Nakao, and T. Nagaoka, *Chem. Commun.*, **2006**, 4288.
83. H. Shiigi, R. Morita, Y. Yamamoto, S. Tokonami, H. Nakao, and T. Nagaoka, *Chem. Commun.*, **2009**, 3615.
84. R. Morita, R. Inoue, S. Tokonami, Y. Yamamoto, M. Nakayama, H. Nakao, H. Shiigi, and T. Nagaoka, *J. Electrochem. Soc.*, **2011**, 158, K95.
85. H. Shiigi, R. Morita, Y. Muranaka, S. Tokonami, Y. Yamamoto, H. Nakao, and T. Nagaoka, *J. Electrochem. Soc.*, **2012**, 158, D442.
86. A. N. Shipway, E. Katz, and I. Willner, *ChemPhysChem*, **2000**, 1, 18.
87. H. Shiigi, Y. Muranaka, Y. Yamamoto, and T. Nagaoka, *Anal. Sci.*, **2013**, 29, 937.
88. I. D. Walton, S. M. Norton, A. Balasingham, L. He, D. F. Oviso, D. Gupta, P. A. Raju, M. J. Natan, and R. G. Freeman, *Anal. Chem.*, **2002**, 74, 2240.
89. A. A. Nekrasov, V. F. Ivanov, and A. V. Vannikov, *J. Electroanal. Chem.*, **2000**, 482, 11.
90. K. Ogura, R. C. Patil, H. Shiigi, T. Tonosaki, and M. Nakayama, *J. Polym. Sci., Part A: Polym. Chem.*, **2000**, 38, 4343.
91. A. Pron, F. Genoud, C. Menardo, and M. Nechtschein, *Synth. Met.*, **1988**, 24, 193.
-