DNA Nanowires

DOI: 10.1002/anie.201202401

Surface "Click" Reaction of DNA followed by Directed Metalization for the Construction of Contactable Conducting Nanostructures

*Jan Timper, Katrin Gutsmiedl, Christian Wirges, Janine Broda, Michael Noyong, Joachim Mayer, Thomas Carell, and Ulrich Simon**

Dedicated to Professor Günter Schmid on the occasion of his 75th birthday

DNA has been recognized as a structure-guiding template for the construction of nanoscale assemblies owing to its outstanding self-recognition properties.[1] Research is currently directed towards enhancing its intrinsically low electric conductivity for potential use in electric circuitry.[2] A promising concept for the preparation of DNA-based electronically conducting nanostructures is the deposition of an ideally homogeneous metal coating, and different protocols for the metalization of DNA with, for example, Ag,[3] Pd,[4] Pt,[5] Cu,[6] and Co[7] have been developed. These routes mainly rely on the reduction of electrostatically bound metal ions, which serve as counterions for the negatively charged DNA backbone. In this process, small metal clusters are formed which act as seeds for a subsequent step, that is, the reductive deposition of metal from solution. In order to increase the selectivity of the metalization process, specific routes that rely on bimetallic coating,[8] the photoinduced deposition of silver,[9] or the formation of DNA–Pt^{II} adducts as precursors to metal deposition,[10] have brought progress in this direction.

Recently we reported the formation of dimetallic Ag/Au nanowires that were grown on artificial DNA templates by a two-step metalization process.[11] For this purpose, alkyne-modified cytosine nucleobases were incorporated into artificial DNA strands. Sugar molecules carrying azide groups were coupled to these alkyne groups by "click chemistry". The sugar molecules served as localized reducing sites for Ag^+ in a Tollens reaction, forming Ag^0 nucleation centers along the DNA. Subsequent reductive deposition of gold on these metal seeds analogous to the development process in photography yielded nanowires of 10 nm in diameter, as visualized by atomic force microscopy (AFM).

Deeper insight into the process of silver nucleation was obtained by applying artificial diol-modified nucleobases.[12] These diol groups could be cleaved to give mono- and dialdehyde groups, leading to a high density of reducing functional groups capable of Ag^+ reduction which were homogeneously distributed along the DNA double strand. The dialdehyde DNA (daDNA) provided the best density and distribution of Ag seeds, and thus may lead to a homogeneous metal coating in the subsequent Au deposition step for the formation of nanowires.

Although the approach we developed makes it possible to metalize DNA in a programmed manner, the nanowires obtained are structurally highly delicate or even fragile and suffer from the lack of specific binding affinity to a stabilizing substrate, which is an indispensable prerequisite for future integration in electronic devices.

In order to overcome these obstacles a novel type of DNA is needed, which, at the same time, is suitable for programmable metalization and for covalent immobilization on technically relevant substrates, for example, silicon wafers. Furthermore, the DNA should be capable of intermolecular linking, which would allow the formation of multistrands with enhanced structural integrity. At the same time the capability of integration into programmed DNA assemblies should be retained, such that complex architectures can be positioned by utilization of prepatterned functionalized surfaces.

Facing these challenges, we designed a difunctional DNA template by ligation of an immobilization and a metalization sequence. The immobilization sequence consists of a 300 base pair (bp) long alkyne-functionalized DNA sequence which enables the covalent binding to azide-functionalized Si surfaces through copper-catalyzed alkyne–azide cycloaddition (CuAAC), whereas both 900 bp long metalization sequences are based on the diol-nucleobase strategy.[13] This approach can serve two purposes at the same time: 1) the formation of Ag seeds as the first step of a two-step metalization process and 2) the aldehyde-mediated interstrand linking analogous to the glutaraldehyde cross-linking of proteins.[14] We anticipate that this novel type of DNA fulfills the requirements formulated above and should be continuously metalizable up to a length of micrometers.

The difunctional DNA was synthesized by polymerase chain reaction (PCR) of three different fragments: 1) a 900 bp long PCR product (PCR900·**3**, I) comprising a diol-dT (deoxythymine, nucleoside **3**, see the Supporting Informa-

---

[*] Dipl.-Chem. J. Timper, Dipl.-Chem. J. Broda, Dr. M. Noyong, Prof. Dr. U. Simon
Institut für Anorganische Chemie, RWTH Aachen University
and
JARA – Fundamentals of Future Information Technologies
Landoltweg 1, 52074 Aachen (Germany)
E-mail: ulrich.simon@ac.rwth-aachen.de
Dr. K. Gutsmiedl, Dr. C. T. Wirges, Prof. Dr. T. Carell
Department Chemie und Biochemie
Ludwig-Maximilians-Universität
Butenandtstrasse 5–13, 81377 München (Germany)
Prof. Dr. J. Mayer
Gemeinschaftslabor für Elektronenmikroskopie, RWTH Aachen
Ahornstrasse 55, 52074 Aachen (Germany)

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201202401.

tion) instead of natural dT; 2) a 300 bp long PCR product (PCR300·**1**) comprising an alkyne-dT (nucleoside **1**, see the Supporting Information) instead of natural dT; and 3) a 900 bp long PCR product II (PCR900·**3**, II) comprising a diol-dT (nucleoside **3**) instead of natural dT. Both strands were designed so as to have specific restriction sites for BsaI restriction digests to produce specific single-stranded sticky ends on the three PCR fragments. The three PCR products could be selectively ligated by sticky-end ligation to give rise to a 2100 bp long alkyne-diol-DNA (aldo-DNA, **L1**) site-specifically functionalized (**A** in Figure 1; see the Supporting Information).

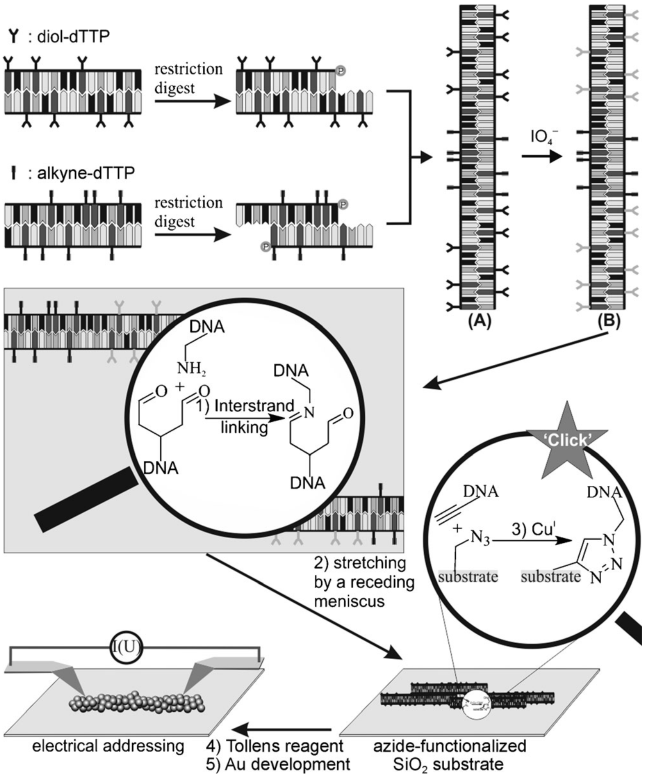

Figure 1. Synthesis of the difunctional DNA template by treatment with restriction digest followed by ligation of three PCR fragments to form alkyne-diol-DNA (aldoDNA, **A**). Subsequent application of periodate solution resulted in alkyne-dialdehyde-DNA (aldaDNA, **B**), which can undergo the two-step metalization process. The aldaDNA exhibits intermolecular coupling (1), and the products are stretched onto an azide-functionalized Si-substrate resulting in micrometer-long DNA multistrands (2). The strands were covalently immobilized by click chemistry (3) and subsequently metalized (4, 5) to form electrically addressable nanowires. dTTP: deoxythymine triphosphate.

In initial tests, we optimized the reaction parameters for the interstrand coupling utilizing 2000 bp daDNA by assuming that subsequent introduction of the immobilization sequence would not greatly influence the coupling and metalization properties.[12] We applied the receding meniscus technique to obtain stretched DNA structures[15] which could be visualized by AFM as micrometer-long structures with the respective orientation. Since the applied daDNA corresponds to a length of about 600 nm, the observed length indicates the formation of daDNA multistrands exhibiting a height profile ranging from 2.5 to 8 nm. We hypothesized that interstrand coupling results from aldehyde–amine condensation to form a Schiff base. For these structures we could already verify the metal deposition (see the Supporting Information).

Next, we optimized the CuAAC immobilization reaction for the aldoDNA. For this purpose, DNA was deposited in a first stretching process, resulting in linear 400 nm long structures (in AFM images) that can be assigned to partly backfolded single DNA strands. In a second stretching step the Cu^I catalyst was applied to covalently bind the aldoDNA to the substrate. Afterwards the DNA could not be removed by thorough rinsing, so we assumed successful covalent binding to the substrate.

To optimize the metalization process for the envisioned synthesis of multistrand DNA-templated conductive nanowires, we studied the metalization process of the individual strands in more detail. Hence, subsequent to the covalent binding we treated aldoDNA with periodate, transforming it into alkyne-dialdehyde-DNA (aldaDNA). This step was followed by Ag staining for 50 s and Au development for 10 s. AFM characterization of the samples revealed bulky structures as well as 5 to 9 nm thick wirelike structures; the latter are thicker than DNA double strands, suggesting the presence of metal-coated DNA (see the Supporting Information).

We then transferred the preparation process onto 40 nm thick SiO_2 membranes so that we could study the metalized structures by scanning transmission electron microscopy (STEM). AFM characterization could be performed next to the membrane windows before and after metal deposition revealing wirelike structures similar to those observed on the Si surfaces.

STEM images show wirelike metal structures very similar to those found by AFM on the Si wafers. The structures are continuous and only about 10 nm in diameter, with a granular structure still visible. The granularity results from the growth of the seed particles during the development step, which could be verified in a series of STEM images obtained at different stages of development. Statistical analysis of the increase in particle size reveals that the diameter is proportional to the square root of the incubation time and can therefore be adjusted (see the Supporting Information).

Finally we combined the interstrand linking and the covalent immobilization by stretching the aldaDNA on azide-functionalized Si surfaces. This resulted in the desired several-micrometer-long multistrands (Figure 2) which could be fixed by the Cu^I-catalyzed reaction.

These DNA templates could be metalized by applying the procedure described above with a Au development time of 50 s. The structures obtained were stable enough for us to apply our in situ measuring setup for the assessment of the electrical properties.[16] Figure 3 shows three images taken on a micrometer-long and about 80 nm thick nanowire with two measuring tips attached (see the Supporting Information).

$I(U)$ characteristics recorded at tip-to-tip distances of 1.15 μm, 1.25 μm, and 2.32 μm clearly show a linear response over the whole voltage range of ±2 V (Figure 3). While the linear $I(U)$ curves reflect the metallic conductivity, the resistivity varies from 2.3×10^{-5} to 11.3×10^{-5} Ω m. This is

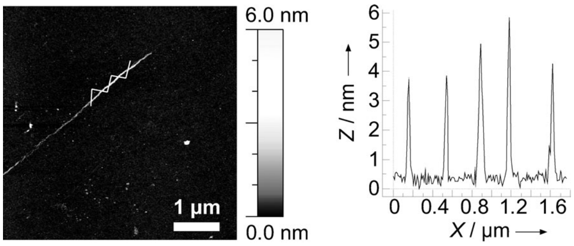

Figure 2. AFM image of the alda-DNA stretched onto an azide-functionalized Si surface and the respective height profile of a line scan.

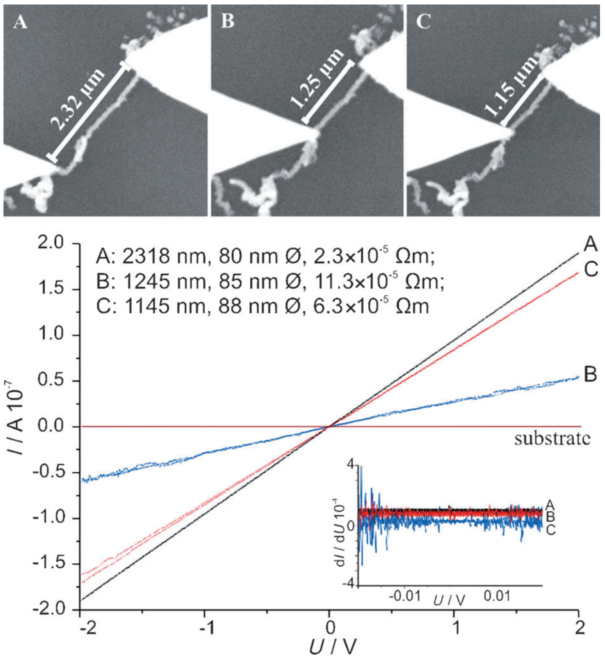

Figure 3. Top: SEM pictures show a strand of metalized DNA with conducting AFM tips in different positions during the contacting process. Bottom: The corresponding *I*(*U*) characteristics were measured in situ and clearly show ohmic behavior. The inset shows the respective d*I*/d*U* curves, representing constant conductivity values within the noise range. Variations in conductivity can be assigned to the quality of the contacts. The *I*(*U*) characteristics correspond to the different positions of the nanomanipulator tips on the DNA-templated Au nanowire. The measurements clearly show linear *I*(*U*) characteristics with no hysteresis. Resistances are independent of the tip-to-tip distances, with the differences resulting from the respective contact quality.

far too low for highly crystalline bulk gold but in agreement with data obtained from polycrystalline nanowires or one-dimensional chains of gold nanoparticles. This is consistent with the granular structure formed in the development process. The variation of the resistivities determined at the three different tip positions may be attributed to different contact areas between the tip and the wire at different points. Nevertheless, the electrical measurements led to resistivity values similar to those reported by other groups.[17]

To summarize, we have reported the design of a difunctional DNA template for the immobilization by click chemistry on functionalized substrates and subsequent controlled metal deposition that leads to metallically conductive nanowires. The metalization process can be controlled with respect to the wire diameter, resulting in continuous metal structures of 10 nm and below. The combined application of the presented metalization and immobilization sequences in complex DNA architectures, for example, DNA origami, present a promising approach for the construction of DNA-templated nanoelectronic circuitry and for molecular lithography.

Received: March 27, 2012

Keywords: click chemistry · conductivity · DNA · nanowires · self-assembly

---

[1] a) E. Winfree, F. Liu, L. A. Wenzler, N. C. Seeman, *Nature* **1998**, *394*, 539–544; b) Y. He, T. Ye, M. Su, C. Zhang, A. E. Ribbe, W. Jiang, C. Mao, *Nature* **2008**, *452*, 198–201; c) Y. Weizmann, A. B. Braunschweig, O. I. Wilner, Z. Cheglakov, I. Willner, *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 5289–5294.
[2] X. Guo, A. A. Gorodetsky, J. Hone, J. K. Barton, C. Nuckolls, *Nat. Nanotechnol.* **2008**, *3*, 163–167.
[3] E. Braun, Y. Eichen, U. Sivan, G. Ben-Yoseph, *Nature* **1998**, *391*, 775–778.
[4] J. Richter, R. Seidel, R. Kirsch, M. Mertig, W. Pompe, J. Plaschke, H. K. Schackert, *Adv. Mater.* **2000**, *12*, 507–510.
[5] R. Seidel, L. C. Ciacchi, M. Weigel, W. Pompe, M. Mertig, *J. Phys. Chem. B* **2004**, *108*, 10801–10811.
[6] C. F. Monson, A. T. Woolley, *Nano Lett.* **2003**, *3*, 359–363.
[7] Q. Gu, C. Cheng, D. T. Haynie, *Nanotechnology* **2005**, *16*, 1358–1363.
[8] a) K. Keren, R. S. Berman, E. Braun, *Nano Lett.* **2004**, *4*, 323–326; K. Keren, M. Krueger, R. Gilad, G. Ben-Yoseph, U. Sivan, E. Braun, *Science* **2002**, *297*, 72–75; b) G. A. Burley, J. Gierlich, M. R. Mofid, H. Nir, S. Tal, Y. Eichen, T. Carell, *J. Am. Chem. Soc.* **2006**, *128*, 1398–1399; c) M. Fischler, U. Simon, H. Nir, Y. Eichen, G. A. Burley, J. Gierlich, P. M. E. Gramlich, T. Carell, *Small* **2007**, *3*, 1049–1055.
[9] L. Berti, A. Alessandrini, P. J. Facci, *J. Am. Chem. Soc.* **2005**, *127*, 11216–11217.
[10] M. Mertig, L. C. Ciacchi, R. Seidel, W. Pompe, *Nano Lett.* **2002**, *2*, 841–844.
[11] Ref. [8c].
[12] C. T. Wirges, J. Timper, M. Fischler, A. S. Sologubenko, J. Mayer, U. Simon, Th. Carell, *Angew. Chem.* **2008**, *121*, 225–225; *Angew. Chem. Int. Ed.* **2008**, *48*, 219–223.
[13] a) V. V. Tsukruk, I. Luzinov, D. Julthongpiput, *Langmuir* **1999**, *15*, 3029–3032; b) N. Balachander, C. N. Sukenik, *Langmuir* **1990**, *6*, 1621–1627.
[14] M. Porro, S. Viti, G. Antoni, M. Saletti, *Anal. Biochem.* **1982**, *127*, 316–321.
[15] a) D. Bensimon, A. J. Simon, V. Croquette, A. Bensimon, *Phys. Rev. Lett.* **1995**, *74*, 4754–4757; b) R. Mehta, M. Rahimi, J. Lund, B. Parviz, *IEEE Trans. Nanotechnol.* **2007**, *6*, 734–736.
[16] a) M. Noyong, K. Blech, A. Rosenberger, V. Klocke, U. Simon, *Meas. Sci. Technol.* **2007**, *18*, N84–N89; b) K. Blech, M. Noyong, F. Juillerat, T. Nakayama, H. Hofmann, U. Simon, *J. Nanosci. Nanotechnol.* **2008**, *8*, 461–465.
[17] a) O. Harnack, W. E. Ford, A. Yasuda, J. M. Wessels, *Nano Lett.* **2002**, *2*, 919–923; b) F. Griffin, A. Ongaro, D. Fitzmaurice, *Analyst* **2004**, *129*, 1171–1175.