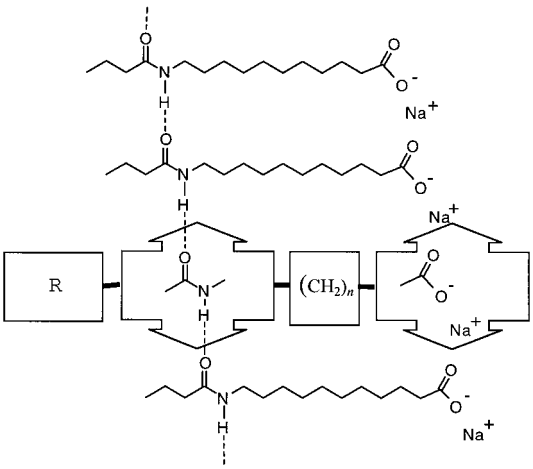

Scheme 3. Illustration of one-dimensional self-aggregation in the case of sodium *N*-acyl aminocarboxylate compound **15**. R represents a pendant aliphatic chain or aromatic group.

prepare in large amounts and at low cost. These features open exciting perspectives toward the development of functional material based on this family of organogelators.

Experimental Section

The synthesis of compounds $\mathbf{1}_n$ and **2**–**16** was performed according to classical procedures and will be published elsewhere. Chemicals and solvents were used as received.

Received: February 23, 2001 [Z16672]

[1] P. Terech, R. G. Weiss, *Chem. Rev.* **1997**, *97*, 3133–3159.
[2] D. J. Abdallah, R. G. Weiss, *Adv. Mater.* **2000**, *12*, 1237–1245.
[3] J. H. van Esch, B. L. Feringa, *Angew. Chem.* **2000**, *112*, 2351–2354; *Angew. Chem. Int. Ed.* **2000**, *39*, 2263–2266.
[4] a) G. Clavier, M. Mistry, F. Fages, J.-L. Pozzo, *Tetrahedron Lett.* **1999**, *40*, 9021–9024; b) D. J. Abdallah, R. G. Weiss, *Langmuir* **2000**, *16*, 352–355.
[5] a) F. S. Schoonbek, J. H. van Esch, R. Hulst, R. M. Kellog, B. L. Feringa, *Chem. Eur. J.* **2000**, *6*, 2633–2643; b) K. Hanabusa, M. Yamada, M. Kimra, H. Shirai, *Angew. Chem.* **1996**, *108*, 2086–2088; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1949–1951; c) M. Jokic, J. Makarevic, M. Zinic, *J. Chem. Soc. Chem. Commun.* **1995**, 1723–1724; d) J.-E. Sohna Sohna, F. Fages, *Chem. Commun.* **1997**, 327–328; e) L. Lu, T. M. Cocker, R. E. Bachman, R. G. Weiss, *Langmuir* **2000**, *16*, 20–34; f) C. Geiger, M. Stanescu, L. Chen, D. G. Whitten, *Langmuir* **1999**, *15*, 2241–2245; g) M. Amaike, H. Kobayashi, S. Shinkai, *Bull. Chem. Soc. Jpn.* **2000**, *73*, 2553–2558; h) J.-L. Pozzo, G. M. Clavier, J.-P. Desvergne, *J. Mater. Chem.* **1998**, *8*, 2575–2577.
[6] J. H. Fuhrhop, J. Köning, *Membranes and Molecular Assemblies: The Synkinetic Approach*, Royal Society of Chemistry, Cambridge, **1994**.
[7] a) L. A. Estroff, A. D. Hamilton, *Angew. Chem.* **2000**, *112*, 3589–3592; *Angew. Chem. Int. Ed.* **2000**, *39*, 3447–3450 and references therein; b) F. M. Menger, K. L. Caran, *J. Am. Chem. Soc.* **2000**, *122*, 11679–11691.
[8] L. Marton, J. W. McBain, R. D. Vold, *J. Am. Chem. Soc.* **1941**, *63*, 1990–1993.
[9] T. Tachibana, T. Mori, K. Hori, *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1714–1719.
[10] P. Terech, D. Pasquier, V. Bordas, C. Rassat, *Langmuir* **2000**, *16*, 4485–4494.
[11] a) S. Bhattacharya, Y. Krishnan-Ghosh, *Chem. Commun.* **2001**, 185–186; b) T. Imae, Y. Takahashi, H. Muramatsu, *J. Am. Chem. Soc.* **1992**, *114*, 3414–3419; c) K. Sakamoto, R. Yoshida, M. Hatano, T. Tachibana, *J. Am. Chem. Soc.* **1978**, *100*, 6898–6902.

A New Method toward Microengineered Surfaces Based on Reactive Coating**

Jörg Lahann, Insung S. Choi, Jinwook Lee, Klavs F. Jensen, and Robert Langer*

The control of engineered microenvironments on device surfaces has been addressed by several approaches including soft lithographic methods, such as microcontact printing (μCP) and micromolding (MIMIC).[1] These procedures have been used for the formation of a wide range of surface patterns, for example protein and cell arrays,[2] and for micro- and nanofabrication of devices. Potential applications include the regulation of cell shapes,[3] the development of microelectronic elements, such as optical displays,[4] circuits, or lasers,[5] and the fabrication of complex three-dimensional microstructures[6] or microfluidic devices.[7] A key step is generally the spatially controlled self-assembly of monolayers on a substrate.[8] Although several systems have been investigated, only assemblies of siloxanes on silicon oxide[9] and of alkanethiolates on gold[10] are widely exploited. Biomedical devices are however mostly manufactured from polymers and metals other than gold. For these materials, the microengineering of patterns is very challenging and only addressed in a few cases.[11] The main limitation is the lack of sufficient and homogeneously distributed functional groups on the substrate surface being necessary for the build-up of further structural elements. Treatment with high-energy sources, such as plasma,[12] laser,[13] or ion beams,[14] has been used to create functionalized surfaces for biomedical systems. Recently, poly(ethylene terephthalate) was surface modified via a multistep synthesis to generate a surface for the μCP of biological ligands.[15] Alternatively, CVD-based polymer coatings were used in order to provide amino- or hydroxyl-functionalized surfaces for the conjugation of biomolecules.[16] Although CVD polymerization has been known for more than 30 years,[17] the exploitation of functionalized [2.2]paracyclophanes for CVD polymerization was realized only recently.[18]

Amino- or hydroxyl-functionalized poly(*para*-xylylene) coatings require an additional activation step for linkage of proteins or ligands. Typically, bivalent spacers, such as hexamethylene diisocyanate, are used for amino- or hydroxyl-functionalized polymers.[16] The additional activation step not only limits the feasibility of microengineering but also causes the contamination of the substrate with organic solvents and volatile chemicals. These contaminations reduce crucial advantages of CVD coatings, such as their low intrinsic cytotoxicity due to the absence of harmful solvents, initiators, or accelerators during polymerization. Therefore, an one-step

[*] Prof. R. Langer, J. Lahann, I. S. Choi, J. Lee, K. F. Jensen
Department of Chemical Engineering
Massachusetts Institute of Technology
Cambridge, MA 02139 (USA)
Fax: (+1) 617-258-8827
E-mail: rlanger@mit.edu

[**] This work was supported by the Fonds der Chemischen Industrie, the National Science Foundation, and the National Institutes of Health.

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coating procedure that provides linkable reactive groups is highly desirable.

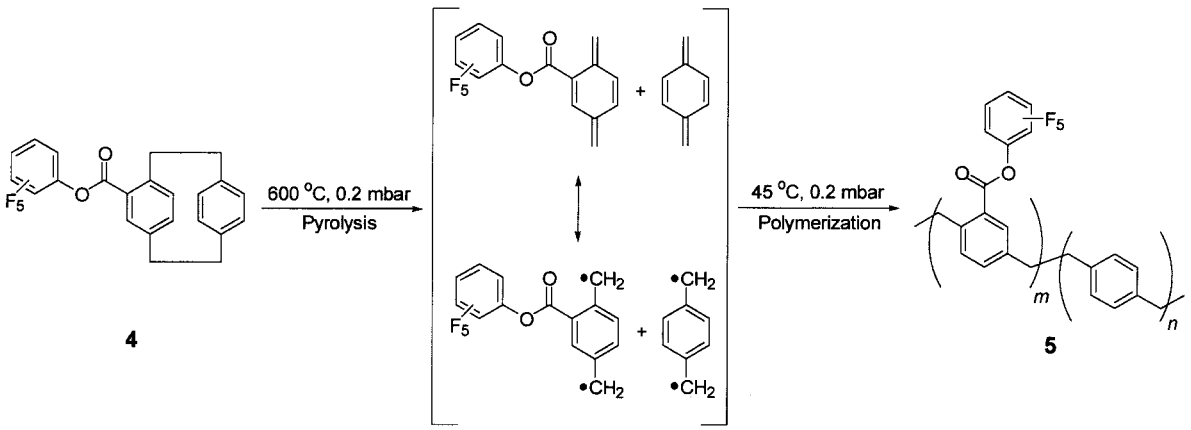
Herein, we report an approach toward engineered microenvironments based on coating with poly(*para*-xylylene carboxylic acid pentafluorophenolester-*co*-*para*-xylylene) (**5**). The technique is applicable to all substrates that are not affected by reduced pressure. For simplicity, we suggest "reactive coating" for polymers like compound **5**. Reactive coating **5** provides active ester groups on the surface being suitable for straightforward linkage of biomolecules presenting amino groups. As a proof-of-principle, we used μCP of biotin-based ligands. The evaluation was done by means of fluorescein-conjugated streptavidin.

[2.2]Paracyclophane-4-carboxylic acid pentafluorophenolester (**4**) was synthesized from [2.2]paracyclophane (**1**) via a three-step synthesis. Friedel–Crafts acylization of **1** with trifluoroacetic acid anhydride using an excess of $AlCl_3$ resulted in 4-trifluoroacetyl [2.2]paracyclophane (**2**) in 92% yield. Hydrolysis of **2** to 4-carboxy [2.2]paracyclophane (**3**) (93% yield) and subsequent conversion with pentafluorophenol trifluoroacetate led to the final product **4**.

CVD polymerization of **4** resulted in a vacuum-deposited film of polymer **5** on the substrate (Scheme 1). Carefully purified **4** (dimer) was sublimated under a reduced pressure of 0.2 mbar at temperatures between 120 and 130 °C. Sublimated **4** was transferred to the pyrolysis zone, which was heated to 600 °C to ensure cleavage of the C–C bonds resulting in the corresponding quinodimethanes (monomers). In the last step, monomers were adsorbed on the substrate at temperatures around 45 °C and spontaneously polymerized. The CVD polymerization of **4** resulted in transparent and topologically uniform polymer films of thicknesses between 90 and 600 nm. The film thickness is mainly determined by the amount of **4** used for polymerization. The thickness of a film produced by the deposition of 30 mg of **4** was determined by means of spectroscopic ellipsometry (SE) to be 190.0($\pm$5.8) nm. Atomic force microscopy was used to characterize the surface topology: The root-mean square roughness was determined to be 0.4 nm (1 μm^2 spot). The reactive coating showed excellent chemical stability in a dry-air environment. No significant change in composition or chemical behavior was found for samples stored under dry air for several weeks as compared to freshly prepared samples.

The elemental composition of **5** was determined by X-ray photoelectron spectroscopy (XPS) to be in good accordance with the theoretical composition. Decomposition of the pentafluorophenol ester group was negligible when pyrolysis temperatures under 600 °C and a working pressure between 0.1 and 0.2 mbar were chosen. At higher pyrolysis temperatures, however, significant loss of fluorine due to decomposition of the pentafluorophenol ester group was detected by means of XPS. The IR spectrum of polymer **5** confirmed the presence of the intact ester bond, as indicated by a characteristic signal at 1762 cm^{-1}. Further evidence is provided by characteristic bands of the C–F stretching vibrations between 997 and 1036 cm^{-1} and of symmetric and asymmetric C-O-C stretching vibrations at 1176 and 1246 cm^{-1}. The reactive coating showed excellent adhesion on various substrates, such as poly(dimethylsiloxane) (PDMS), poly(tetrafluoroethylene), poly(carbonate), chrome nitride, gold, and silicon. Polymer **5** is insoluble in common solvents, such as dimethylformamide, chloroform, acetone, ethanol, or aqueous solutions. Incubation of a gold substrate coated with polymer **5** in an aqueous PBS buffer (pH 7.4) for seven days at room temperature did not affect its mechanical stability. Similarly, the reactive coating showed excellent adhesion after Soxhlet extraction for six hours in acetone. Adhesion of the reactive coating to the gold substrate was examined by gently pressing a 1 cm^2 area of a Scotch tape onto the polymer coating. After subsequently peeling off the tape, the sample was examined by optical microscopy and infrared spectroscopy and was mechanically and chemically intact.

(+)-Biotinyl-3,6,9-trioxaundecanediamine (**6**) was used for μCP of different patterns on gold substrates coated with polymer **5** (Scheme 2). Biotin-based ligands were chosen since biotin is a prototype of a small ligand. Its interaction with streptavidin is characterized by strong noncovalent interaction and allows the facile patterning of streptavidin on the surface. Streptavidin is a widely used immobilization protein that has two pairs of binding sites on opposite faces and therefore represents a universal platform for further patterning of biotin-labeled biomolecules. In this study, fluorescein-labeled streptavidin was used to examine the micropatterns. A



Scheme 1. Reactive coating with polymer **5** by means of CVD polymerization of paracyclophane **4**; polymerization involves quinodimethanes intermediates being in equilibrium with the corresponding diradicals.

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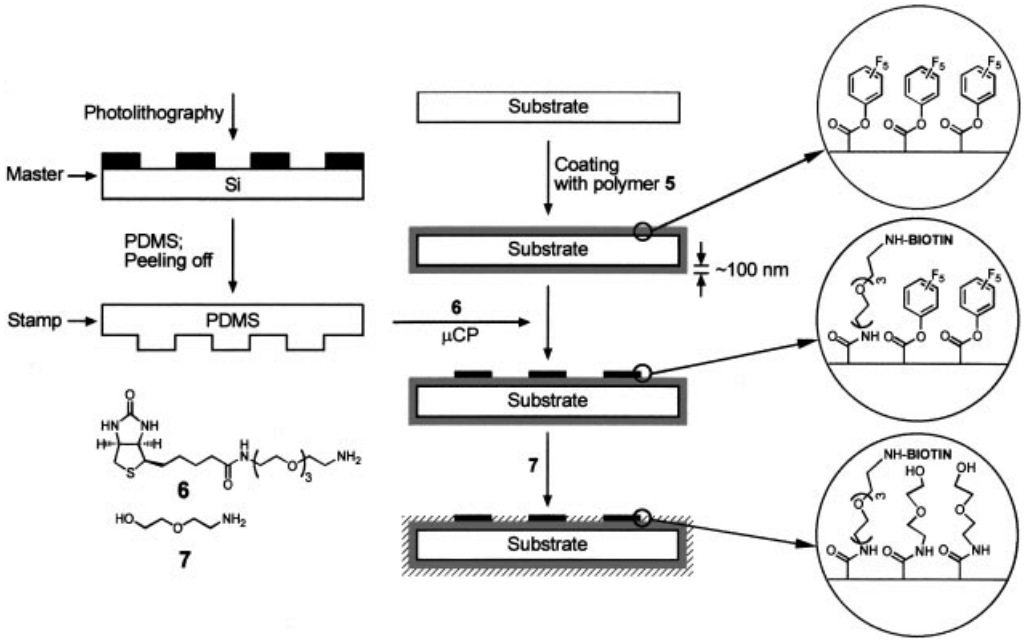

Scheme 2. Spatially controlled surface modification of the reactive coating covering a substrate using μCP. A PDMS stamp, manufactured as a replica from a silicon master, is used for printing ligand **6** onto polymer **5**. The remaining surface area is passivated by reaction with compound **7**.

PDMS stamp was casted from a photolithographically produced silicon master.[19] Prior to use, the PDMS stamp was oxidized by means of an oxygen plasma.[20] Ligand **6** was printed via a PDMS stamp on the substrate surface coated with polymer **5**; the contact time was 60 s. Subsequently, the remaining pentafluorophenol ester groups were treated with 2-(aminoethoxy)ethanol (**7**) to passivate nonprinted areas of the surface. The covalent nature of the linkage of the amino ligands to the reactive coating was examined by IR spectroscopy. After μCP of ligand **6** for 60 s, the IR spectrum of polymer **5** showed characteristic bands at 1653 and 1578 cm^{-1} indicating primary amide bonds. By patterning the substrate into regions that alternately promote or prevent the binding of streptavidin, spatially controlled self-assembly was expected to occur. A patterned substrate was then incubated with fluorescein-conjugated streptavidin in an aqueous phosphate buffer (pH 7.4) containing 0.1 % (w/v) bovine serum albumin and 0.02 % (v/v) Tween 20. Fluorescence microscopy was used to visualize the microengineered patterns. As shown in Figure 1, the fluorescein-labeled streptavidin was spatially restricted to the biotin-coated areas of the substrate surface. Sharp contrasts were observed. Both micrographs demonstrate homogeneity and reproducibility of the reactive coating on the substrate.

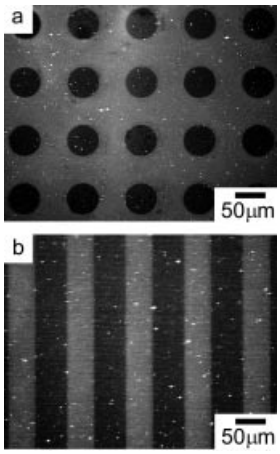

Figure 1. Fluorescence micrographs of fluorescein-labeled streptavidin bound to the ligand **6**, which was patterned onto the reactive coating by μCP. a) Dot profile with a dot radius of 25 μm; b) line profile with a line width of 50 μm.

An unique and basically substrate-independent technique toward reactive coatings has been developed and used for spatially designed microenvironments. The resulting surfaces may have value for several biomedical applications, such as tissue engineering, drug development, or molecular diagnostics.

Experimental Section

2: Trifluoroacetic acid anhydride (6.75 mL, 47.75 mmol) dissolved in dichloromethane (30 mL) was added to a suspension of $AlCl_3$ (5.7 g, 43.13 mmol) in dichloromethane (120 mL) at 0 °C. After 15 min, **1** (5 g, 24.03 mmol) was added while the temperature was held under 5 °C. After stirring for 30 min at room temperature, the reaction mixture was quenched at 0 °C by adding concentrated aqueous HCl (4.4 mL). Extraction with dichloromethane and subsequent column chromatography delivered **2** in 92 % yield. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 2.90-3.25$ (7 H; CH_2), 3.95 (1 H; CH_2), 6.47 (4 H; CH), 6.63 (1 H; CH), 6.78 (1 H; CH), 7.11 (1 H; CH); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): $\delta = 34.54$, 35.07, 35.09, 36.31, 118.47, 130.10, 131.36, 132.42, 132.98, 134.67, 136.96, 138.87, 139.39, 139.92, 140.26, 145.41, 145.21, 182.00; IR (KBr): $\tilde{\nu} = 844$, 986, 1136, 1204, 1708, 2857, 2928, 3047 cm^{-1}; MS (70 eV): m/z: 304 [M^+], 235 [$C_{16}H_{15}CO^+$], 200 [$C_8H_7COCF_3^+$], 131 [$C_8H_7CO^+$], 105 (100) [$C_8H_9^+$], 78 [$C_6H_6^+$], 77 [$C_6H_5^+$].

3: Compound **2** (5 g, 16.45 mmol) was incubated in aqueous KOH (10 % (w/v), 125 mL) and heated under reflux for 4.5 h. The solid residue was separated by filtration and subsequently washed with chloroform. The organic phase was then extracted with water. Titration of the aqueous phase with concentrated aqueous HCl delivered a precipitate **3** that was purified by recrystallization from a mixture of acetic acid and water (9/1, v/v) (yield 86 %). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 2.86-3.25$ (7 H; CH_2), 4.22 (1 H; CH_2), 6.52 (2 H; CH), 6.59 (3 H; CH), 6.71 (1 H; CH), 7.28 (1 H; CH), 14.03 (1 H; COOH); ^{13}C NMR (100 MHz, DMSO, TMS): $\delta =$ 34.79, 34.81, 34.99, 35.79, 131.45, 131.92, 132.36, 132.99, 133.45, 135.56, 136.23, 136.34, 139.53, 139.72, 139.84, 142.27, 168.47; IR (KBr): $\tilde{\nu} = 867$, 928, 1304, 1686, 2854, 2938, 3010, 3425 cm^{-1}; MS (70 eV): m/z: 252 [M], 148 [$C_8H_7COOH^+$], 105 (100) [$C_8H_9^+$], 104 [$C_8H_8^+$], 91 [$C_7H_7^+$], 78 [$C_6H_6^+$].

4: A solution containing **3** (1 g, 3.94 mmol), pentafluorophenol trifluoroacetate (0.7 mL, 4.07 mmol), and pyridine (0.4 mL, 5.0 mmol) in tetrahydrofuran (10 mL) was stirred at room temperature for 12 h. The solution was concentrated under reduced pressure and the remaining crude product

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was dissolved in ethyl acetate (35 mL). Extraction with ethyl acetate and subsequent column chromatography delivered 1.15 g of product **4** (88%). ^{1}H NMR (300 MHz, $CDCl_3$, TMS): $\delta = 2.92-2.99$ (1H; CH_2), 3.07–3.23 (6H; CH_2), 4.10 (1H; CH_2), 6.51 (1H; CH), 6.54 (1H; CH), 6.60 (1H; CH), 6.65 (1H; CH), 6.68 (1H; CH), 6.81 (1H; CH), 7.39 (1H; CH); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): $\delta = 34.80$, 35.32, 35.45, 36.38, 125.79, 127.50, 131.74, 132.51, 133.28, 133.53, 136.59, 136.81, 138.01, 138.52, 139.71, 139.94, 140.10, 140.12, 140.80, 141.24, 143.50, 145.10, 159.51; IR (KBr): $\tilde{\nu} = 513$, 630, 693, 790, 852, 902, 994, 1040, 1122, 1163, 1255, 1516, 1757, 2853, 2898, 2926, 2955, 3015 cm^{-1}; MS (70 eV): m/z: 418 [M^+], 314 [$C_8H_7CO_2C_6F_5^+$], 251 [$C_{16}H_{15}CO_2^+$], 235 [$C_{16}H_{15}CO^+$], 131 [$C_8H_7CO^+$], 104 (100) [$C_8H_8^+$], 77 [$C_6H_5^+$].

5: Compound **4** was polymerized using a self-designed CVD installation consisting of a sublimation zone, a pyrolysis zone, and a deposition chamber.[21] Compound **4** (30 mg, 0.07 mmol) was placed in the sublimation zone and a sample, such as a gold-coated silicon substrate, was fixed in the deposition chamber at 45 °C. The pressure was adjusted to 0.2 mbar and the pyrolysis zone was heated to 600 °C. Subsequently, **4** was sublimated slowly by increasing the temperature of the sublimation zone from 120 to 130 °C. Under these conditions, the deposition rate was 0.4 Å s^{-1}.

The spectroscopic ellipsometry was done on a variable-angle spectroscopic ellipsometer (J. A. Woollam Inc., USA) using a Cauchy model for curve fitting. AFM studies were conducted in tapping mode on a NanoScope III (Digital Instruments Inc., USA).

XPS (atomic ratios): F_{1s}/C_{1s}: 31.7% (calcd: 21.7%), O_{1s}/C_{1s}: 7.4% (calcd: 8.7%), C–F/C–C: 28.3% (calcd: 31.3%), C–O/C–C: 5.7% (calcd: 6.3%), C=O/C–C: 5.4% (calcd: 6.3%); IR (grazing angle 85°): $\tilde{\nu} = 658$, 829, 997, 1036, 1176, 1246, 1450, 1471, 1497, 1523, 1762, 2862, 2931, 3025, 3054 cm^{-1}.

Received: February 8, 2001 [Z16580]

[1] Y. Xia, G. M. Whitesides, *Angew. Chem.* **1998**, *110*, 568–594; *Angew. Chem. Int. Ed.* **1998**, *37*, 550–575.

[2] a) E. Ostuni, R. S. Kane, C. S. Chen, D. E. Ingber, G. M. Whitesides, *Langmuir* **2000**, *16*, 7811–7819; b) R. S. Kane, S. Takayama, E. Ostuni, D. E. Ingber, G. M. Whitesides, *Biomaterials* **1999**, *20*, 2363–2376; c) D. Chiu, N. L. Jeon, S. Huang, R. S. Kane, C. J. Wargo, I. S. Choi, D. E. Ingber, G. M. Whitesides, *Proc. Natl. Acad. Sci.* **2000**, *97*, 2408–2413.

[3] a) L. Lu, L. Kam, M. Hasenbein, K. Nyalakonda, R. Bizios, A. Gopferich, J. F. Young, A. Mikos, *Biomaterials* **1999**, *20*, 2351–2361; b) C. S. Chen, M. Mrksich, S. Huang, G. M. Whitesides, D. E. Ingber, *Biotechnol. Prog.* **1998**, *14*, 356–363.

[4] D. C. Duffy, R. L. Jackman, K. M. Vaeth, K. F. Jensen, G. M. Whitesides, *Adv. Mater.* **1999**, *11*, 546–522.

[5] J. A. Rogers, Z. Bao, M. Meier, A. Dodabalapur, O. J. A. Schueller, G. M. Whitesisdes, *Synth. Met.* **2000**, *115*, 1–3.

[6] S. T. Brittain, O. J. A. Schueller, H. Wu, S. Whitesides, G. M. Whitesides, *J. Phys. Chem. B* **2001**, *105*, 347–340.

[7] J. McDonald, D. C. Cooper, J. R. Anderson, D. T. Chiu, H. Wu, O. J. A. Olivier, G. M. Whitesides, *Electrophoresis* **2000**, *21*, 27–40.

[8] a) R. G. Nuzzo, D. L. Allara, *J. Am. Chem. Soc.* **1983**, *105*, 4481–4483; b) E. B. Troughton, C. D. Bain, G. M. Whitesides, R. G. Nuzzo, D. L. Allara, M. C. Porter, *Langmuir* **1988**, *4*, 365–85.

[9] P. M. St. John, H. G. Craighead, *Appl. Phys. Lett.* **1996**, *68*, 1022–1024.

[10] A. Kumar, H. A. Biebuyck, N. L. Abbott, G. M. Whitesides, *J. Am. Chem. Soc.* **1992**, *114*, 9188–9189.

[11] a) A. Schwarz, J. S. Rossier, E. Roulet, N. Mermod, M. A. Roberts, H. H. Girault, *Langmuir* **1998**, *14*, 5526–5531; b) N. Patel, R. Bhandari, K. M. Shakesheff, S. M. Cannizzaro, M. C. Davies, R. Langer, C. J. Roberts, S. J. Tendler, P. M. Williams, *J. Biomater. Sci. Polym. Ed.* **2000**, *11*, 319–331; c) N. Stutzmann, T. A. Tervoort, K. Bastiansen, P. Smith, *Nature* **2000**, *407*, 613–616.

[12] J. Lahann, D. Klee, H. Thelen, H. Bienert, D. Vorwerk, H. Höcker, *J. Mater. Sci. Mater. Med.* **1999**, *10*, 443 448.

[13] J. Heitz, H. Niino, A. Yabe, *Appl. Phys. Lett.* **1996**, *68*, 2648–2650.

[14] M. Celina, H. Kudoh, T. J. Renk, K. T. Gillen, R. L. Clough, *Radiat. Phys. Chem.* **1998**, *51*, 191–194.

[15] a) Z. Yang, A. Chilikoti, *Adv. Mater.* **2000**, *12*, 413 417; b) Z. Yang, A. M. Belu, A. Liebmann-Vinson, H. Sugg, A. Chilkoti, *Langmuir* **2000**, *16*, 7482–7492.

[16] J. Lahann, W. Plüster, D. Klee, H. Höcker, *Biomaterials* **2001**, *22*, 817–826.

[17] a) W. F. Gorham, *J. Polym. Sci. A* **1966**, *4*, 3027–3039; b) W. F. Gorham, Y. L. Yeh, *J. Org. Chem.* **1969**, *34*, 2366–2370.

[18] a) J. Lahann, H. Höcker, R. Langer, *Angew. Chem.* **2001**, *113*, 746–749; *Angew. Chem. Int. Ed.* **2001**, *40*, 726–728; b) J. Lahann, D. Klee, H. Höcker, *Macromol. Rapid Commun.* **1998**, *19*, 441–444; c) H. Hopf, G. N. Gerasimov, S. A. Chvalun, V. L. Rozenberg, E. L. Popova, E. V. Nikolaeva, E. I. Grigoriev, S. A. Zavjalov, L. I. Trakhtenberg, *Adv. Mater.* **1997**, *3*, 197–200; d) G. N. Gerasimov, E. L. Popova, E. V. Nikolaeva, S. N. Chvalun, E. I. Grigoriev, L. I. Trakhtenberg, V. I. Rozenberg, H. Hopf, *Macromol. Chem. Phys.* **1998**, *199*, 2179–2184; e) E. A. Popova, D. Antonov, E. Sergeeva, E. Vorontsov, A. Stash, V. Rozenberg, H. Hopf, *Eur. J. Inorg. Chem.* **1998**, 1733–1737.

[19] A. Kumar, G. M. Whitesides, *Appl. Phys. Lett.* **1993**, *63*, 2002–2004.

[20] Y. Lan, W. T. S. Huck, X. M. Zhao, G. M. Whitesides, *Langmuir* **1999**, *15*, 1208–1214.

[21] K. M. Veith, K. F. Jensen, *Chem. Mater.* **2000**, *12*, 1305–1313.

Hapten-Functionalized DNA-Streptavidin Nanocircles as Supramolecular Reagents in a Competitive Immuno-PCR Assay**

Christof M. Niemeyer,* Ron Wacker, and Michael Adler

The self-assembly of small building blocks to form structural and functional elements is an important goal of molecular nanotechnology.[1] In this respect, DNA is a promising construction material which has already been employed in the fabrication of nanometer-scale scaffolds and surface architectures,[2] to selectively position proteins[3] and nanoclusters,[4] and to generate mechanical molecular devices.[2] We recently reported the nanostructured oligomeric conjugates **3**, formed by self-assembly of bisbiotinylated DNA **1** and the biotin-binding protein streptavidin (STV) **2** (Scheme 1).[5] Despite its tetravalent binding capacity for biotin, the STV molecules are predominantly present as bi- or trivalent linkers between double-stranded DNA (dsDNA) fragments within **3**. Because of this remaining biotin-binding capacity, the DNA–STV oligomers **3** are powerful reagents for immuno-PCR (IPCR; PCR = polymerase chain reac-

[*] Priv.-Doz. Dr. C. M. Niemeyer, Dipl.-Biol. R. Wacker, Dr. M. Adler
Universität Bremen, FB2-UFT
Biotechnologie und Molekulare Genetik
Leobener Strasse, 28359 Bremen (Germany)
Fax: (+49) 421-218-7578
E-mail: cmn@uni-bremen.de

[**] This work was supported by Deutsche Forschungsgemeinschaft and Fonds der Chemischen Industrie. We thank Priv.-Doz. Dr. L. Chi and S. Gao for scanning force microscopy measurements and Prof. D. Blohm for stimulating discussion and generous support.