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A Workbench for Single Macromolecules

Single macromolecules in controlled molecular environments are the fundamental information processing entities in living systems. They perform with a mind boggling efficiency: Our genome is stored in single polynucleic acids, antibodies recognize single antigens in a body, and proteins detect single photons and convert their energy highly efficient into chemical energy. Since there has been enormous progress in understanding the underlying mechanisms of these processes in recent years, one may ask whether single macromolecules may not also be used for information processing in man-made, *biomimetic systems*. In other words, would the laws of physics allow new bio- and information technologies on the nanometer scale? In order to carry out experiments with single macromolecules we developed a workbench, which allows to move, bend and stretch, to cut and link, as well as to measure properties of single macromolecules at solid-liquid interfaces. It consists of a single crystalline substrate, suitably functionalized with a molecular top layer. Nanostructure and molecular dynamics of the molecular layer, together with the forces exerted by scanning probes, i.e. atomically sharp tips in a scanning tunneling microscope (STM) or a scanning force microscopy (SFM), are employed to control the conformation of macromolecules at surfaces, as well as for metrology. The workbench is used, e.g., to manipulate DNA or to demonstrate a single-molecule chemical field-effect transistor with nanometer-sized gates.

Manipulation of single macromolecules

Scanning probes, i.e. STM- and SFM-tips, have been used to manipulate single atoms [1] and small molecules [2]. Single macromolecules, however, could not be manipulated without breakage [3]. The reason is their friction with the substrate, which increases with the length of the macromolecule, while the force to break a bond in a single chain is independent of the chain length. The interaction with the substrate must therefore be strong enough to immobilize the macromolecule, yet sufficiently weak to avoid breakage during manipulation. We therefore devised a method, which allows us to control this interaction.

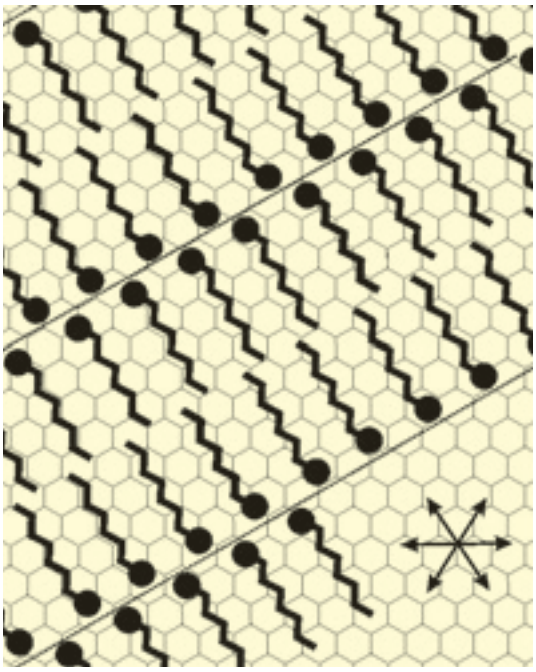


Fig. 1
Schematic of a monolayer of alkane derivatives on graphite. Circles denote head groups and arrows denote the crystallographically equivalent graphite axes with three-fold symmetry.

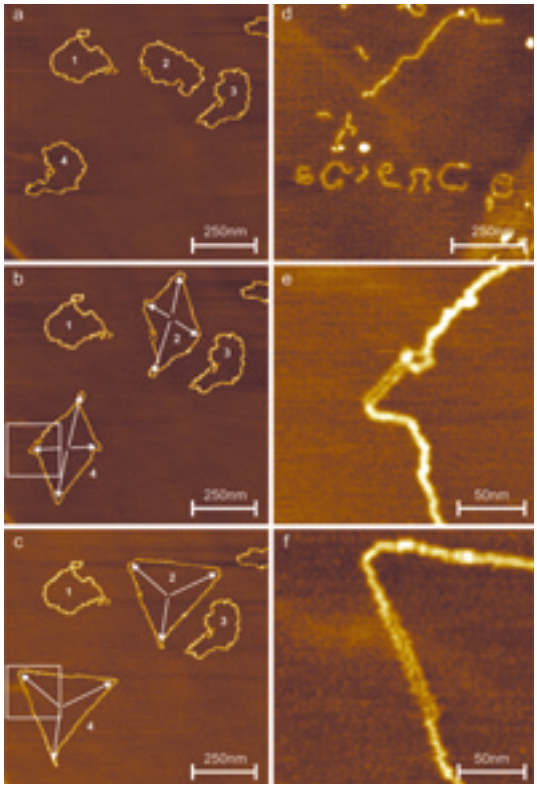


Fig. 2
SFM images of ds-DNA adsorbed on a graphite surface modified with $CH_3(CH_2)_{11}NH_2$ molecules. Manipulation was performed by bringing the tip in contact with the surface and moving it in the desired direction, using home made manipulation hard- and software. (a) ds-plasmid DNA molecules as deposited; (b) after stretching two of them (no. 2 and 4) along the white arrows; (c) after manipulation of the same molecules into triangles; (d) seven letter word written with polydisperse sample of linear ds-DNA; (e) zoom of the square marked in (b), revealing two separated single DNA strands; (f) zoom of the square marked in (c), revealing the same section as in (e) but now with two fully extended single DNA strands.

Long chain alkanes and alkylated small molecules self-assemble in lamellar monolayers on a crystalline substrate like the basal plane of graphite ([4, 5], Fig. 1). Rows of head groups, which may be positively or negatively charged, are separated by rows of hydrophobic alkyl chains. The chemical nature of the head groups and the length of alkyl chains define a surface potential ripple, which may be employed to orient single polymer molecules on a dry surface [6], using the lamellae as soft nanoscopic »rails«. Polyelectrolytes are then adsorbed from aqueous solution to the substrate by applying a droplet to the surface, which is then blown off with air.

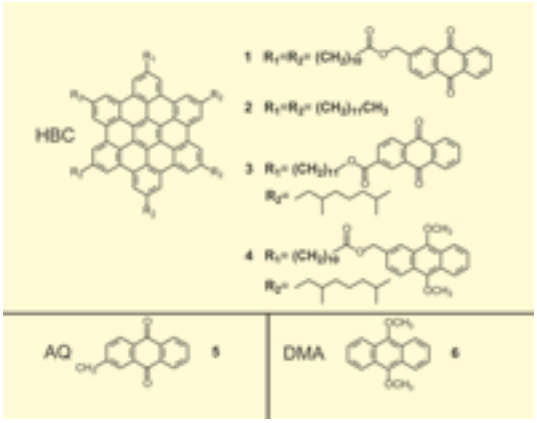
Fig. 2a displays the image of four ds-plasmid DNA molecules adsorbed to a modified graphite substrate [7]. From the digitized images their contour lengths are a little less than expected for a relaxed B-form ds-DNA. The difference is attributed to the non-ideally flat adsorption of some segments. Moreover, there are some short sections, where the double strand has separated into two single strands, which apparently is caused by the interaction with the substrate. In order to stretch subsequently two of the molecules with the SFM the tip was brought into contact and then moved

from within a molecular ring outwards in four directions as marked in Fig. 2b. Subsequent imaging in the tapping mode reveals an increase of the contour lengths of these molecules to about 15 and 22 % more than the fully extended B-form ds-DNA. Fig. 2c displays the same molecules stretched further into a triangular shape with contour lengths corresponding to 24 and 33 % overstretching, respectively.

The manipulation with the SFM tip on properly tailored substrate allows also to displace the whole molecule without its rupture. Free arranging and shaping of polymer molecules is evidenced in Fig. 2d, which displays the arrangement and shaping of seven ds-DNA molecules of a polydisperse sample. Similarly single stranded DNA and also double stranded DNA on molybdenum disulphide have been manipulated. ds-DNA with contour lengths of up to 2 micrometers has been moved as a whole. In all these cases, we attribute the immobilization of the macromolecules to the interaction of the charged polymer backbone with an oppositely charged row of headgroups in the surfactant monolayer like in a polyelectrolyte-amphiphile complex [7].

Prototypical chemical-field-effect transistor with nanometer sized-gates

Besides molecular manipulation, the workbench is also used to measure physical properties on the nanometer scale. Hybrid-molecular diodes [8] with current-voltage characteristics determined by a single nanometer-sized molecule in a well controlled gap can be realised using a scanning tunnelling microscope [9]. Also field effect transistors have been fabricated



Scheme 1
Chemical formulae of the employed materials: hexa-peri-hexabenzocoronene (HBC) decorated with six anthraquinone (AQ) functions (1), hexaalkyl-HBC (2), HBC bearing either one AQ (3) or one 9, 10-dimethoxyanthracene (DMA) function (4), methyl-AQ (5) and DMA (6).

with carbon nanotubes [10, 11] and single molecules [12, 13]. The electrodes, however, were macro- or mesoscopic and not readily scalable to nanoscale dimensions. With our workbench, we developed a prototypical chemical-field-effect transistor (ChemFET), in which the current through a hybrid-molecular diode is modified by nanometer-sized charge transfer complexes (»nanogates«) covalently linked to the molecule in the STM junction [14].

The key molecule (1, Scheme 1) is an hexa-*peri*-hexabenzocoronene (HBC)-derivative with six strong elec-

Eine »Werkbank« für einzelne Makromoleküle

Die belebte Natur realisiert grundlegende Informationsverarbeitungsprozesse mit einzelnen Makromolekülen und atemberaubender Effizienz: Unser Genom ist in einzelnen Polynukleinsäuren gespeichert, Antikörper erkennen einzelne Antigene im Körper, und Proteine reagieren auf einzelne Photonen und wandeln ihre Energie mit hohem Wirkungsgrad in chemische Energie. Das Verständnis der zugrunde liegenden Mechanismen hat enorme Fortschritte gemacht, so dass man sich die Frage stellen kann, ob einzelne Makromoleküle nicht auch in künstlichen biomimetischen Systemen zur Informationsverarbeitung verwendet werden können. Mit anderen Worten: Erlaubt die Physik neuartige Bio- und Informationstechnologien auf der Nanometerskala? Um Experimente mit einzelnen Makromolekülen durchführen zu können, haben wir eine »Werkbank« entwickelt, die es erlaubt, einzelne Makromoleküle an Fest-Flüssig-Grenzflächen zu bewegen, zu biegen, zu strecken, sie zu schneiden und zu verbinden sowie ihre Eigenschaften zu messen. Sie besteht aus einem einkristallinen Substrat, das mit einer geeigneten molekularen Deckschicht funktionalisiert wird. Struktur und Dynamik der molekularen Schicht auf Nanometer-Skala werden zusammen mit den Kräften von rasternden Spitzen in einem Tunnel- oder Kraftmikroskop benutzt, um die Konformation von Makromolekülen einzustellen, sowie die Moleküle zu vermessen. Kürzlich wurde sie verwendet, um DNS zu manipulieren sowie einen prototypischen monomolekularen chemischen Feldeffekttransistor (ChemFET) mit Nanometer-großen Gate-Elektroden zu demonstrieren.

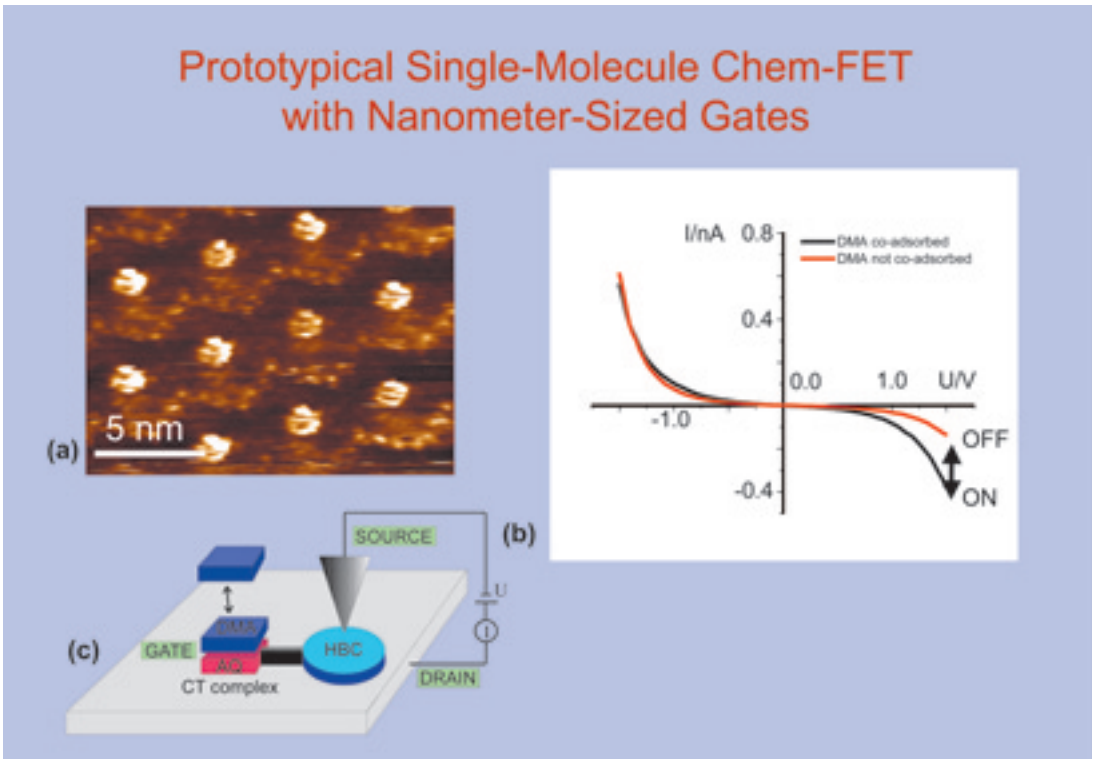


Fig. 3
(a) STM image of a monolayer of 1+6; (b) I-V-characteristic through HBC-cores of 1 with and without coadsorbed donor 6; (c) schematic of a single molecule ChemFET with a charge-transfer complex as a gate [14].

tron acceptor substituents (anthraquinone (AQ)), which can form charge transfer complexes with an electron donor such as 6 (9,10-dimethoxyanthracene (DMA)). Molecules 2–4 were used for control experiments. Scanning tunnelling microscopy and -spectroscopy measurements at the solid-liquid interface [4, 5] were performed with a home-built STM. For scanning tunnelling spectroscopy (STS) the tip was positioned over the region of interest and a voltage ramp with 100 equidistant points between -1.5 and 1.5 V was run with the feedback loop switched off [15].

Fig. 3a displays an STM current image of monolayers obtained from mixed solutions of 1 and the donor DMA 6 with a ten fold molar excess of 6 (further referred to as 1+6). The high resolution image clearly resolves an oblique unit cell with one HBC on each corner and six additional spots arranged in a zig-zag-row between the HBC-cores. AQ and DMA are known to form charge transfer (CT)-complexes in the solid state [16], and we attribute these spots to DMA-AQ-CT-complexes coadsorbed in this arrangement. The new arrangement coexists with the unit cell known of neat 1 where no DMA is co-adsorbed. The key result is presented in Fig. 3b, which displays I–V's through HBC-cores in monolayers of 1+6 measured in the two different unit cells. While the I–V's measured in the unit cell in which no DMA is co-adsorbed are virtually identical to those obtained from neat 1, a much more symmetric I–V is observed through HBCs where DMA-AQ-CT-complexes are coadsorbed in the unit cell. The two I-V-types were observed in the respective domains both within the same and in repeated experiments. Upon shifting the latter I–V by 0.12 V to more positive sample bias and normalising one obtains the first type of I–V.

We attribute this effect to an interface dipole, which causes a shift in the potential given by the Helmholtz equation

$$\Delta\phi = \frac{eN\mu}{\varepsilon_0\varepsilon_r}$$

with dipole strength μ and dipole density *N*.

Conclusions and outlook

We have demonstrated that the interaction between a solid substrate and a polymer chain can be tailored in such a way that synthetic or naturally occurring single macromolecules are immobilized, and on the same

time can be manipulated with a scanning force microscope tip without chain breakage. Combined with spectroscopy of fluorescently labelled single molecules [17, 18] this will provide new opportunities to correlate macromolecular conformation with spectroscopical properties. Precise positioning and stretching of DNA molecules combined with ultra high resolution methods like STM and tip enhanced Raman Scattering (TERS) [19, 20] will provide intriguing new opportunities for direct sequencing of DNA. Moreover, free 2D-molecular shaping should provide a means to fabricate different 2D-molecular architectures, such as electronic circuitry from single macromolecules.

We also demonstrated the modification of current voltage characteristics through a single molecule in an STM junction by nanometer-sized charge transfer complexes covalently linked to this molecule. The effect observed can be explained by a relative shift between the Fermi level of the substrate and the adsorbate's molecular orbitals due to the formation of a dipole at the interface. This set-up can be viewed as a Chem-FET based on a single molecule with an integrated nanometer-sized gate (Fig. 3c), since the charge transfer complexes, responsible for the change in the I–V's, are formed between an acceptor covalently bound to the molecule in the tunnelling junction and a donor coming from the ambient solution. This proof of principle is considered a major step towards monomolecular electronics and highly sensitive electronic molecular probes.

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