Molecular Switches

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A Helical Molecule That Exhibits Two Lengths in Response to an Applied Potential**

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Molecular devices are expected to play an important role in advanced electronics in the form of molecular diodes,[1] molecular transistors,[2] and molecular switches.[3] However, the electron-transfer mechanism of organic molecules on metal surfaces—the most fundamental aspect of molecular devices—still awaits elucidation.[4–6] In an effort to shed light on this issue, we applied helical peptides as mediators for long-range electron transfer,[7] a scaffold for chromophores to accelerate electron transfer,[8] and a viable system for molecular photodiodes.[9]

Stochastic on–off switching phenomena of molecular conductance in organic molecules have been observed in numerous cases through careful observation by scanning tunneling microscopy (STM).[10–13] These phenomena are considered to be caused by fluctuations in the hybridization of the sulfur atom that accompanies the change in molecular orientation. Our focus is on the use of this mechanism in a molecular memory device, because one bit may be recognized by a change in molecular length. For this purpose, however, the molecule should be able to exhibit two distinct lengths in response to outer stimuli. Herein, we propose helical peptides as an appropriate system for the controlled switching of molecular length on a bulk substrate.

Peptides that contain α-aminoisobutyric acid (Aib) have the unique ability to adopt two different helical structures: an α-helical conformation with a short overall length (1.5 Å for each amino acid residue) and a longer 3_{10}-helical conformation (2.0 Å for each amino acid residue).[14,15] Whereas Boc-(Ala-Aib)$_4$-OCH_3 in crystalline form has been reported to adopt a 3_{10}-helical structure, crystals of Boc-(Ala-Aib)$_8$-OCH_3 favor an α-helical structure (Boc = *tert*-butoxycarbonyl).[16] This suggests that an intermediate-length dodecapeptide could have dual α-helical and 3_{10}-helical character. The critical chain length which determines the favored helix type may be an octapeptide, because *para*-bromobenzoyl-(Aib-Ala)$_4$-OCH_3 forms an α helix in the crystalline state.[17] However, the critical chain length is expected to be longer (10 or 12 residues) for the present case, in which the peptides immobilized on gold are examined in air or under ultrahigh vacuum (UHV) because less-polar media tends to favor the formation of 3_{10} helices in peptides, whereas media of higher polarity favors the α-helical conformation, as discussed previously.[16]

In an earlier study, we succeeded in single-molecule observations of upright helical peptides incorporated into an alkanethiolate self-assembled monolayer (SAM) by STM.[18] Notably, these helical peptides display a large dipole moment parallel to the helical axis from the C terminus to the N terminus. Therefore, such peptides should be responsive to an applied electric field. Figure 1a illustrates our experimental design with a helical peptide in which the molecular length is modulated with the applied bias. The helical dodecapeptide is immobilized to the gold surface by the N terminus to expose the negatively charged C terminus at the top. The peptide can be contracted to the α helix by placing the STM tip of negative potential on the peptide C terminus. Alternatively, the peptide favors the 3_{10}-helical conformation by the extension force of the STM tip bearing a

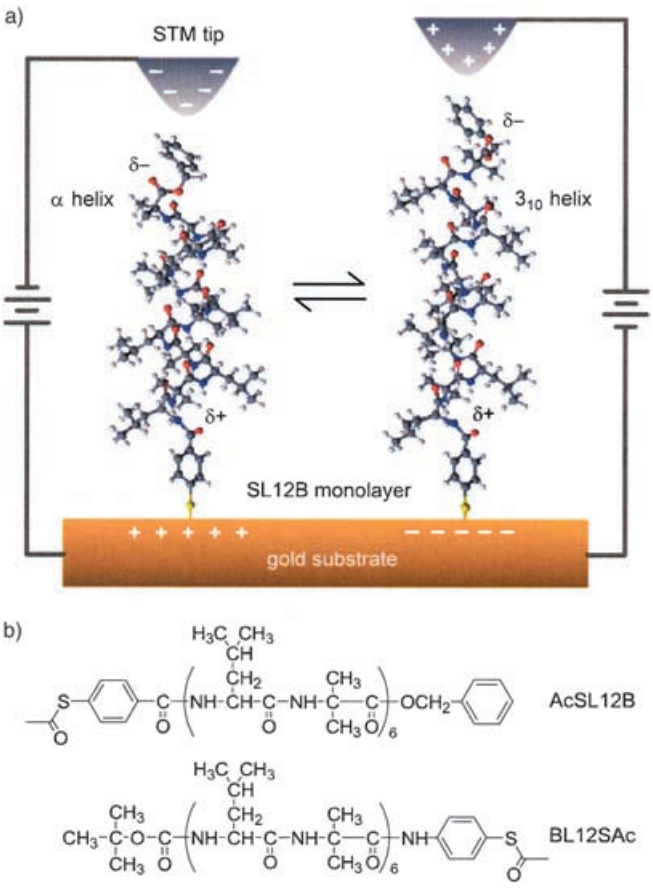

Figure 1. a) Conformational change of a dodecapeptide immobilized onto a gold surface by the N terminus. α Helices and 3_{10} helices are stabilized by applying a positive (left) and negative (right) bias, respectively. b) Structures of the two dodecapeptides used for the work reported herein.

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positive potential. Indeed, we observed conductance switching for the first time in which the apparent molecular lengths are altered as a function of the polarity of the applied bias through the use of the two helical dodecapeptides (Figure 1b). For the experiments reported herein, benzyl ester was used instead of *tert*-butyl ester as the protecting group for the C terminus of the SL12B peptide for synthetic purposes. However, as the size of benzyl ester of SL12B is similar to that of a Boc group in the BL12S peptide, the different terminating groups are not expected to affect the length of the peptides on the substrate.

Conformational energies of the peptide Ac-(Leu-Aib)$_n$-OCH_3 ($n = 4, 6, 8$) in α-helical and 3_{10}-helical conformations are calculated semiempirically. The heats of formation (kcal mol^{-1}) are indicated in the parentheses as follows: Ac-(Leu-Aib)$_4$-OCH_3 α helix (−491.759), 3_{10} helix (−492.390); Ac-(Leu-Aib)$_6$-OCH_3 α helix (−699.056), 3_{10} helix (−697.146); Ac-(Leu-Aib)$_8$-OCH_3 α helix (−907.733), 3_{10} helix (−902.486). The dodecapeptide with the intermediate length exhibits a small energy difference between the α-helical and 3_{10}-helical conformations, which suggests that there is facile exchange between the two helical types.

Characterizations of BL12S in solution and in SAMs on gold were carried out similarly to those of the previous report on SL12B.[18] Circular dichroism (CD) studies of BL12SAc in 2,2,2-trifluoroethanol and reflection–absorption spectroscopy (RAS) of the BL12S SAM revealed its α-helical conformation. From the RAS spectrum, the tilt angle of the helical axis from the surface normal was calculated to be 45° (Supporting Information).[7,9,19,20]

We previously observed single molecules or bundles of SL12B incorporated into dodecanethiolate (C_{12}) SAMs as bright spots by STM under UHV.[18] BL12S in a C_{12} SAM is also observed as bright spots (Figure 2a). Notably, time-resolved STM images of the BL12S molecules clearly show switching. Each circle shown in Figure 2a represents a fixed observation point for the peptide helices. Peptides are observed as bright spots with apparent length differences of 5 Å from the surrounding dodecanethiolate SAM surface (ON state). However, these protrusions stochastically disappeared (OFF state) and reappeared (ON state) over a time span of three to four hours.

The effect of the density of the surrounding alkanethiolate matrix on switching was examined.[10,13] Dodecanethiolate molecules were found to desorb from the gold surface if SAMs were left under UHV ($\approx 10^{-8}$ Pa) for a long period even at room temperature which resulted in a rearrangement of the SAM surface structure.[21] Figure 2b shows a series of STM images of the SL12B/C_{12} SAM after leaving the sample under UHV for a long period. The striped pattern of the matrix monolayer is clearly observable, indicating that the C_{12} molecules lie down on the surface owing to low surface coverage. Under these conditions, the molecular motion of the peptides is allowed more freedom than that of tightly packed peptides in freshly prepared SAMs. The switching behaviors shown in Figure 2b, however, occur at a frequency similar to those shown in Figure 2a; these stochastic switching data are summarized in Table 1. The average number of switching events is nearly the same for the loosely packed SAM as it is for the tightly packed SAM. The surrounding C_{12} molecules do not influence the switching behavior, which suggests that the apparent length change is not a result of the change of the molecular orientation as has been reported for oligo(phenylene ethynylene) groups in alkanethiolate SAMs.[10,13]

The variation of the apparent molecular length of BL12S is plotted as a function of time (Figure 3a). The dodecapep-

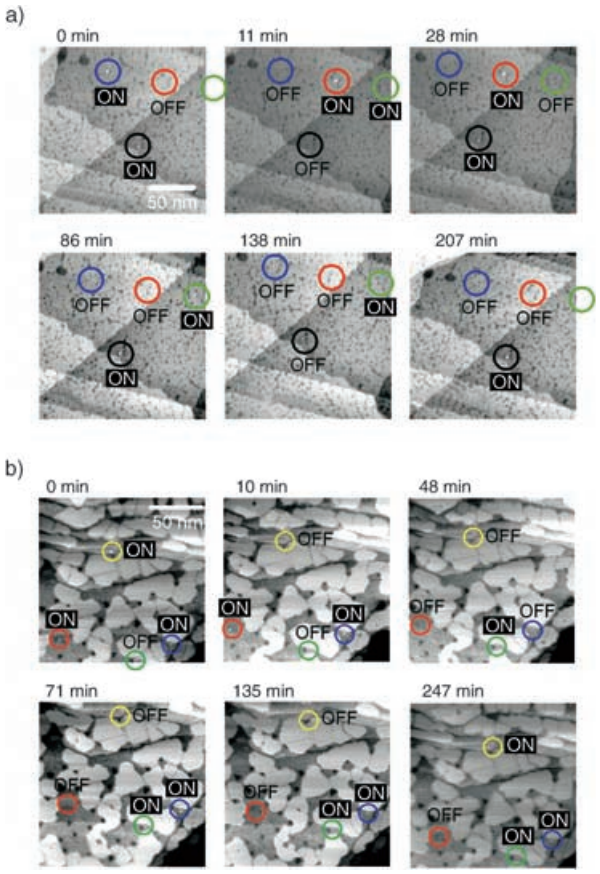

Figure 2. a) STM images of BL12S incorporated into the dodecanethiolate SAM. Images were obtained at a sample bias of 1.4 V and a set-point current of 2.5 pA. b) STM images of SL12B incorporated into the dodecanethiolate SAM after leaving the sample under UHV for a long period (several days). Images were obtained at a sample bias of −1.3 V and set-point current of 5.0 pA.

Table 1: Summary of stochastic conductance switching events.

Parameter	Peptide SL12B		BL12S	
Alkanethiol density	tight	loose	tight	loose
Number of samples	9	6	6	9
Observation time [min]	305	306	207	211
Total number of switching events[a]	36	27	19	14
Average number of switching events [min^{-1} (500×500 nm^{-2})]	0.50	0.85	0.55	0.47

[a] The total number of switching events was counted by all changes from ON to OFF and vice versa observed in the STM images between the two successive scans. Each scan required an average of ≈6 min. With an observation time of 305 min, ≈50 images were recorded.

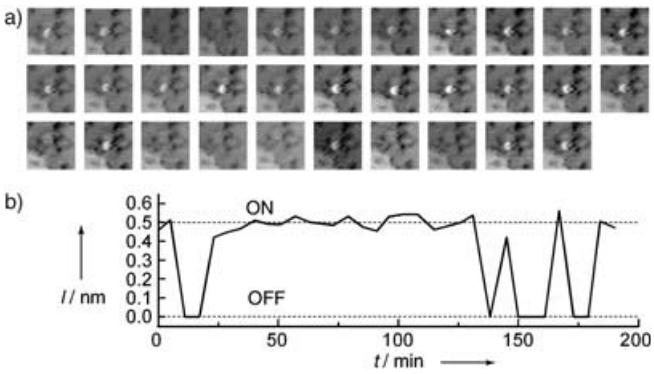

Figure 3. a) Time-lapse STM images (first image, upper left; final image, lower right) of BL12S peptide molecules incorporated into the dodecanethiolate SAM; conditions are the same as those reported in Figure 2. b) Measured molecular length (*l*) for each image in part a).

tide shows two apparent molecular lengths, and the switching occurs stochastically in transition between these two states. As the dodecapeptide is allowed to take both α-helical and 3_{10}-helical conformations, the two states may be explained by an α helix representing the ON state, and a 3_{10} helix corresponding to the OFF state. This interpretation is supported strongly by the length difference of 5 Å between the two states (Figure 3b), which is in agreement with the molecular-length difference between an α helix and a 3_{10} helix.

Because both helix types display a large dipole moment along the helical axis,[22] it is expected that the polarity of the applied voltage between the STM tip and the gold substrate influences the STM image of the peptides.[23,24] BL12S was observed by STM under application of the positive sample bias as described above. When the sample bias was inverted from positive to negative, the bright spots of BL12S disappeared within a few scans, but they reappeared with a return to the positive bias (Figure 4a).

If the interaction of the peptide dipole moment with the applied electric field is the origin of this conductance switching, then SL12B, which has an orientation opposite to that of BL12S and which was immobilized to the gold surface by the N terminus, should also show switching behavior, but with the opposite response to the applied bias polarity. Figure 4b shows the bias dependence of the STM images of SL12B. Indeed, SL12B helices were observed as bright spots at the negative sample bias, but nearly all peptides apparently disappeared from the STM image at the positive bias. Taken together, the dodecapeptides take on a physically elongated state upon application of an electric field in accordance with the direction of the dipole moment. The peptide adopts physically shortened state if the applied electric field is opposite in direction to the dipole moment. It is speculated that under a parallel electric field, the peptides are most stable in a 3_{10}-helical conformation (elongated), and under an opposing electric field direction, the peptides are most stable in an α-helical conformation (shortened; Figure 1a).

The dependence of helical peptide conductivity on the applied bias polarity was further investigated by scanning tunneling spectroscopy (STS) at 77 K. Current–voltage (*I–V*) curves of the C_{12} molecules and the peptide helices in the SAMs are shown in Figure 5. The *I–V* curve of the matrix C_{12}

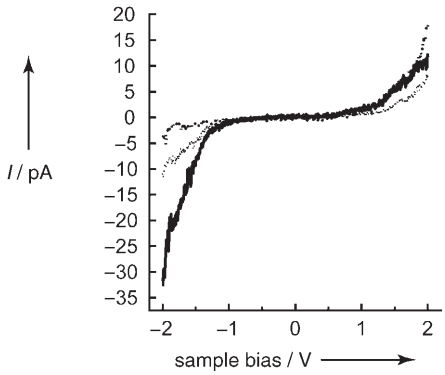

Figure 5. Current–voltage (*I–V*) curves of dodecanethiolate (thin dotted line), BL12S (thick dotted line), and SL12B (thick solid line) acquired at the temperature of liquid nitrogen (77 K). The lines represent the average of 20–30 individual responses.

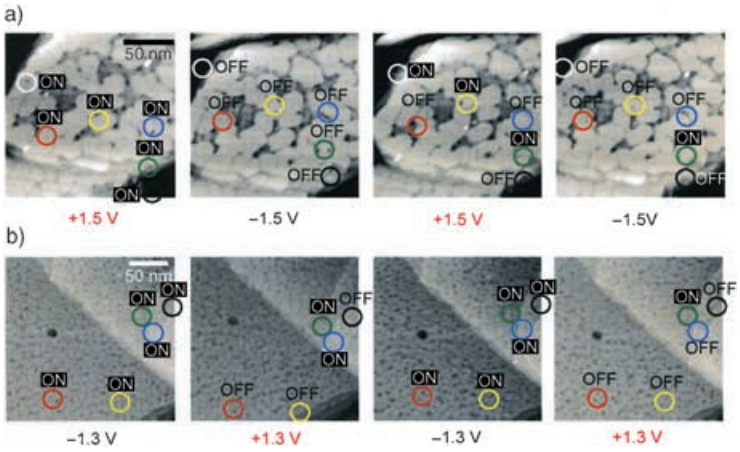

Figure 4. Sequential STM images of a) BL12S (set-point current of 4.5 pA) and b) SL12B (set-point current of 5.0 pA) incorporated into the dodecanethiolate SAM with alternation of the polarity of the applied sample bias voltage.

molecules shows a featureless monotonic increase in the range from −2 to +2 V.[25,26] On the contrary, asymmetric *I–V* responses are observed for the helices. In the case of BL12S, the current increased more dramatically at the positive sample bias than at the negative bias. On the other hand, the current through SL12B increased more strongly at the negative bias than that at the positive bias. Both results indicate that the current through the helix is enhanced by applying the bias voltage such that the direction of the electric field coincides with the helical dipole moment. Therefore, the *I–V* characteristics of the helices also support the interpretation that the helix dipole moment interacts with the external electric field to convert between α-helical and 3_{10}-helical conformations.

In conclusion, we observed conductance switching of peptide helix bundles by STM. The conductance and the

apparent molecular length were observed to undergo stochastic changes with time. The conductance of the helix alternated between two states by changing the polarity of applied bias. This novel behavior can be explained by the conformational change between an α helix and a 3_{10} helix. The helical structure is influenced by the applied electric field as a result of the interaction with the large dipole moment of the helix. This means that the apparent molecular length can be regulated by an external stimulus. The precise control of the switching of the helices is now under investigation.

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