Research Integration of Nanotechnology and Biotechnology ～ Precise Control of Nano-structures in Bottom-up style using Bio-related Materials ～

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By technical progress of nanotechnology and biotechnology in recent years, the target of research is coming to the similar, nano-molecular complexes, and that the idea to use the function of a bio-system substance for bottom up process in nanotechnology has been emerged. Such concepts are promising to produce novel functions of organic materials. In this paper, we introduce the research of nano-scale construction using DNA tiling technology, which is one of the typical examples of bottom up construction with bio-materials.

1 Introduction

"Nanotechnology" is the general concept of fine process technology with nanometer scale precision in order to extremely utilize various properties of materials. Many researchers have expected this technology as to boost the performance of current electronic devices and technology related to information processing, and research is being carried out actively in various fields.

In terms of miniaturization, tremendous efforts have been devoted to create devices with higher performance and greater energy efficiency through their miniaturization and integration even before the time of nanotechnology. These efforts were generally based on the technological concept known as the "top-down approach" in which macro materials were micro processed, and they were in line with the traditional trend of achieving energy efficiency and greater integration through the miniaturization of devices [1].

NICT has been carrying out research exploring the technological concept known as the "bottom-up construction" which enables us to produce various functional materials and structures from individual atoms and molecules. This method is one of the goals of nanotechnology, and it aims to achieve the ultimate functions for future ICT devices by literally creating the higher structures of materials through manipulation of atoms, the smallest structural units[2].

The bottom-up approach of building up material or device structures through the deliberate manipulation of individual atoms is a ground-breaking idea in that it involves the direct controlling of the position of and bonds between atoms, which are the smallest structural units of materials. However, the created materials are made up of extremely large numbers of atoms, and construction of target structures by gathering each small atom requires a tremendous amount of time and effort[3].

Our research group has been exploring the more practical bottom-up construction by means of self-organization phenomenon observed in nano-sized organic molecules[4]. In the process of bottom-up construction using self-organization phenomena of organic molecules, detailed structures of individual molecule units are designed as a component of structures in order to realize targeted properties, and synthesized by means of organic chemistry method. Following, synthesized organic molecules, as unit parts of target structures, are dispersed onto substrates, and that adjoining units are connected with each other through interaction between neighboring molecule units, which is called a self-organizing phenomena. With this method, higher structures with atomic or molecular scale precision can be created relatively easily, just like building something with LEGO.

By means of the state of arts synthetic technology of organic chemistry, the physical and chemical properties of individual molecule units can be controlled, and that properties of higher structure created by the combination of molecule units is essentially the same as that created

from individual atoms. Furthermore, the interaction between molecule units can be controlled by their shape, polarization, chemical affinity at the interface between neighboring molecules, we can control their manner of self-organization towards higher structures by means of programming their detailed structure and physical properties[4]. According to this technical scheme, it is, in principle, possible to create minute device structures without complicated photolithographic processes, through prior chemical synthesis of parts such as transistors, memories and sensors on single molecular scales, then connecting them with each other through self-organization phenomena.

It is important in using this method to have knowledge of the pattern of manifestation in the self-organization processes of the structure-forming factors programmed into the individual molecular units.

However, there are many unknown factors regarding these mechanisms, and it is important to confirm what kind of structures are actually formed, what their properties are, whether the desired functions and structures can be attained upon actually positioning them on substrates and electrodes, and to ascertain the rules and physical properties pertaining to molecular self-organization in order to accumulate more knowhow and knowledge on controlling them.

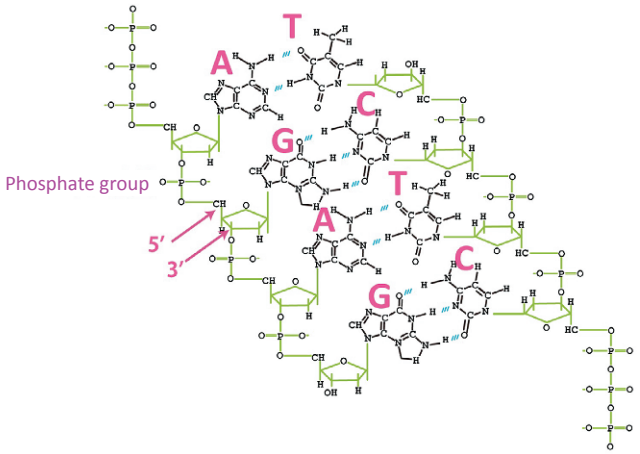

Fig. 1 Diagram of the chemical structure of deoxyribonucleic acid (DNA). The A, T, G and C in the diagram represent adenine, guanine, cytosine and thymine, respectively, on the phosphate group frame

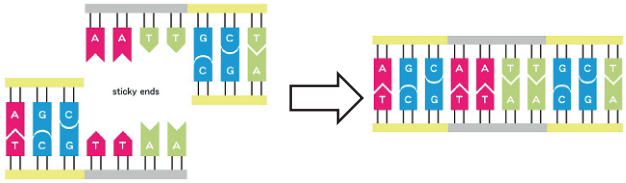

Fig. 2 A conceptual diagram of selective bonding based on complementary base pairs

2 Technology for creating large-scale nanostructures with biomaterials

In creating device structures with organic materials, controlling the configuration of molecular units that make up the parts with nanoscale precision is a fundamental subjects in optimizing the performance of organic materials. For example, the properties of π conjugated electron systems, which govern the optical and electronic functions of organic molecules, are known to be greatly dependent on the molecular structure or the higher structure formed by gathering of molecular structures. How these can be controlled with extreme precision and accuracy is one of the keys to improve the performance of organic devices. In other words, it is important to establish fundamental technique to improve the macroscopic functions of parts by controlling the microscopic configuration, spacing and conformation of molecular units, which are the functional units of the parts. However, the typical size of device parts should be around several microns or more, while the size of organic molecular units is no more than several nanometers across. Controlling the configuration of molecular units requires attaining spatial precision on nanometer scales as well as the creation of parts on micron scales.

In order to achieve this, researchers are attempting to make use of structures formed through self-organization by biopolymers such as DNA, as templates for controlling the conformation of molecules[5]. DNA is a nucleic acid composed of deoxyribose, phosphoric acid and bases, and it is a biopolymer that contains genetic information on the organism within its structure (Fig. 1). DNA is made of a combination of nucleotides with four types of bases: adenine (A), guanine (G), cytosine (C) and thymine (T), which form complementary base pairs based on specific combinations such as A-T and G-C, determined by the consistency of their molecular structure and localized polarity (Fig. 2). As a result of this mechanism, DNA rigidly maintains its structural precision in forming a stable double helix of several hundred microns in length. This mechanism will be made use of in forming the template.

3 Construction of "large-scale nanostructure" through DNA tiling

First, several varieties of a single strand of artificially synthesized DNA consisting of around 100 bases are combined and woven into a flat patch shape (DNA tile) of around 10 to 20 nanometers through the self-organization process based on the formation of complementary base pairs. In doing this, single strands of DNA are attached to the edge of each patch as sticky ends with their configuration controlled (programmed) so that counter sticky ends of other tiles will attach themselves complementarily, as shown in Fig. 3(a). Tiles are mass synthesized beforehand and given appropriate heat treatment in a solution. Consequently, the counter sticky ends attached to the edges of DNA tiles connects them together complementary, resulting in the bonding of two DNA tiles (Fig. 3(b)). Furthermore, the successive repetition of the formation of these complementary bonds results in the orderly bonding of DNA tiles, ultimately resulting in the creation of large-scale nanostructures of several microns, which retain spatial precision on a molecular scale. This series of processes is generally known as DNA tiling[5]. Because the configuration of the DNA strand which produces DNA tiles, the basic unit of this large-scale nanostructure, can be designed and synthesized artificially, it is possible to incorporate molecular markers that bond selectively to specific DNA sequences, molecules or structures, into specific locations on each tile. Figure 4 shows an example of the DNA tiling process, in which a biotin molecule has been incorporated into a specific location on a DNA tile as a bonding marker. In this case, a biotin molecule has been attached in a central location on one of DNA tiles programed to produce large-scale structures. The DNA strands have been configured to have sticky ends on each of the tiles as shown in Fig. 4 in order to form large scale structures. Consequently, appropriate heat treatment in a buffer solution is treated to promote their self-organization into "large-scale nanostructures".

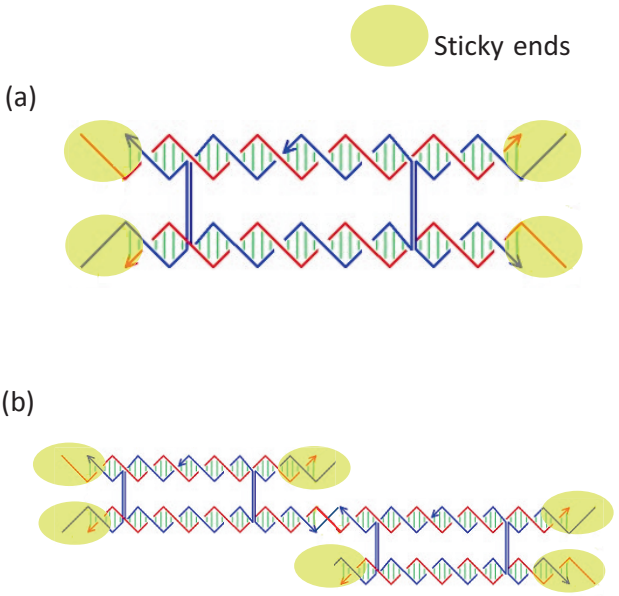

Fig. 3 A conceptual diagram of DNA tiles making use of complementary bonding in DNA (a): A DXAB tile consisting of five single-strand DNAs (b): A diagram showing selective bonding between the sticky ends of a DXAB tile and neighboring tiles

4 Observation on "large-scale DNA nanostructures"

Figures 5 and 6 show AFM images of a large-scale nanostructure of DNA tiles that has been formed on a mica substrate in a buffer solution. As shown in Fig. 5(a), the surface is flat and appears to have no structures when a relatively wide area of around 2 microns squared is scanned, but further magnifying a part of the scanned area reveals that the surface of the substrate is completely covered with DNA tiles (Fig. 5(b)). A detailed examination reveals the presence of a striped pattern on the surface at

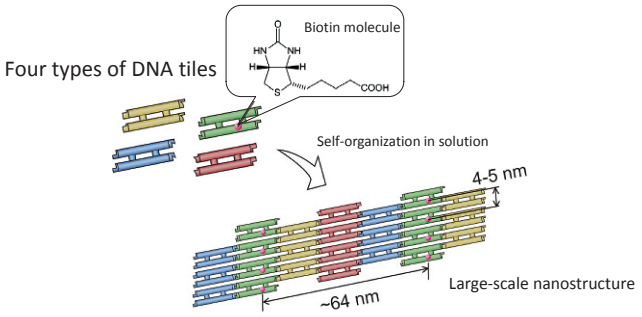

Fig. 4 A diagram showing how a larger structure (large-scale nanostructure) is formed from the bottom up by four types of DNA tiles

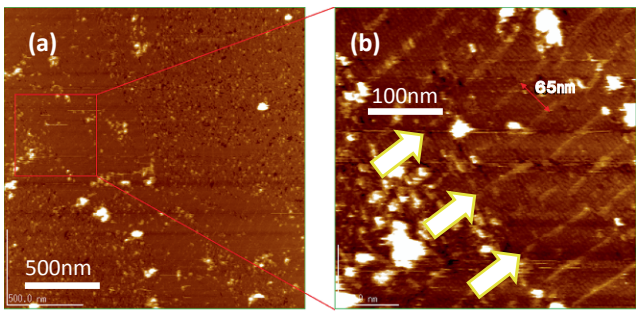

Fig. 5 An AFM image of a large-scale nanostructure in solution formed by DNA tiling (a): The image is 2 microns squared (b): The image is 0.5 microns squared

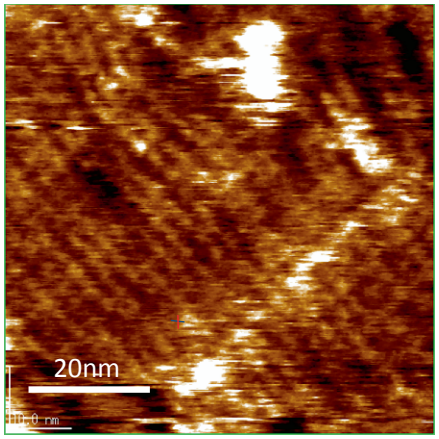

Fig. 6 A high resolution AFM image of the large-scale DNA nanostructure shown in Fig. 5. DNA tiles can be seen arranged in an orderly fashion as shown in the diagram of Fig. 4

around 65 nanometer intervals as indicated by the arrows in the image.

Further examination of this structure reveals that these white parts are the biotin molecules incorporated as markers into one of the four types of DNA tiles that produce the large-scale structure, which revealed that the structure has been formed as programmed beforehand (Fig. 6). As is well known, biotin molecules have a strong tendency to connect with streptavidin specifically. Therefore, this surface composed of DNA tiles can be used as scaffold to locate other devices very precisely in the solution by attaching streptavidin as counter markers on the units. This allows the orderly arrangement of various molecular units, which make up the organic materials on DNA tiles, through self-organization of the molecules with spatial precision on a molecular scale.

This type of configuration control technology is also applicable to the creation of biotype protein device structures such as those using bacteriorhodopsin. Furthermore, adopting the various types of bonding-maker combinations enables the creation of more complex structures, which will bring drastic innovation to the integration process of semiconductor devices[6].

5 Conclusions

Until recently, the terms "nanotechnology" and "biotechnology" were often used in separate situations. Biotechnology is typically thought of as technology used to analyze organisms to gain a better understanding of them, while nanotechnology refers to technology for creating things with greater precision through the enhancement of control over the structure of small objects. However, the progress in recent years of both technologies have brought them into almost the same field of "nanomolecular engineering," and the idea of using nanotechnology to control biotechnology is coming to be real. The DNA tiling which is discussed in this paper is an important fundamental technology for realizing this. The various biomaterials and systems that support life are not powerful, but they skillfully combine simple functions to achieve both the required functions and high levels of efficiency that even outperform existing technology at times. However, not all the mechanisms behind these ingenuities have yet been clarified, and we believe we still have a lot to learn from them. Our goal is to elucidate the mechanisms behind the ingenuity of these biomaterials and systems, and establish technology to simulate and make practical use of them through nanotechnology, as one of the fundamental technologies for realizing the future ICT society.

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