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Detection of DNA Molecules Using Insulated Gate Field Effect Transistor and Intercalator

Toshiya Sakata, Hidenori Otsuka and Yuji Miyahara

Biomaterials Research Center, National Institute for Materials Science
1-1, Namiki, Tsukuba, Ibaraki 305-0044, Japan
Phone: +81-29-851-3354 (ext.8198)
FAX: +81-29-851-8291
E-mail: SAKATA.Toshiya@nims.go.jp

1. Introduction

Several types of DNA chips and DNA microarrays have been developed and some of them are used in the field of molecular biology (1). Although most of the current DNA chips and DNA microarrays are based on the fluorescent detection method, amperometric detection methods have been developed in combination with redox reagents (2). We investigated another approach to realize an electrochemical detection for DNA chips and the novel concept of a genetic field effect transistor (FET) is proposed in the present study as a potentiometric detection method for miniaturization of a DNA chip system.

2. Concept of genetic field effect transistor

The conceptual structure of a genetic FET is shown in Fig. 1. Oligonucleotide probes are immobilized on the surface of the gate insulator. When complementary DNA molecules are contained in a sample solution, hybridization occurs at the surface of the gate area. Although DNA molecules are negatively charged in an aqueous solution, it is in general difficult to detect them with field effect devices. One of the reasons for difficulty is that the charge density change as a result of hybridization is small. In the present study, we make use of ionized characteristic of intercalator in an aqueous solution, while it is used as a fluorescent reagent in the conventional methods. Intercalators are ionized and positively charged as shown in Fig. 2, and introduced into double stranded oligonucleotide probes on the gate surface, which leads to increase of the surface charge density. In this way, the signal of hybridization can be enhanced and detected by the use of field effect devices. In order to decrease the background noise such as non-specific adsorption of DNA molecules, chemical modification of the gate surface and differential measurement was carried out.

3. Results and discussion

The field effect transistor was fabricated using the standard integrated circuit technology except for deposition of the gate electrode. The layout of the fabricated device is shown in Fig. 3. Four FETs are integrated in a chip and two of them are used as genetic FETs. The surface of the chip is covered with a Si_3N_4 layer as shown in Fig. 4 Reactive amino groups are generated on the Si_3N_4 surface based on treatment with aminosilane. Amino-modified oligonucleotide probes were attached following surface treatment with glutaraldehyde. Free aldehyde groups were blocked with glycine.

Double-stranded DNA molecules were heat denatured and annealed to the genetic FETs. An intercalator such as ethidium bromide was introduced to the gate surface and the potential difference between the genetic FET and a reference FET was measured. The signal based on the hybridization and introduction of intercalator was obtained.

4. Conclusions

We developed a new method for detecting DNA molecules using FETs and intercalators. Since most of intercalators have charges, the signal based on the hybridization can be enhanced by introducing intercalator into the double stranded DNA. Preliminary experiments showed that the signal based on intercalator could be measured by the use of FETs.

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References

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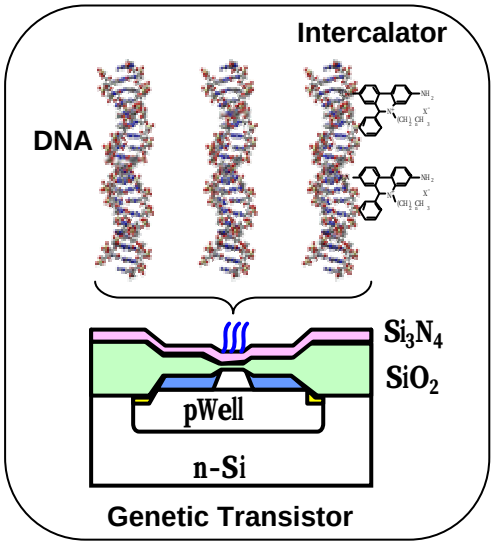

Fig. 1 Concept of genetic FET

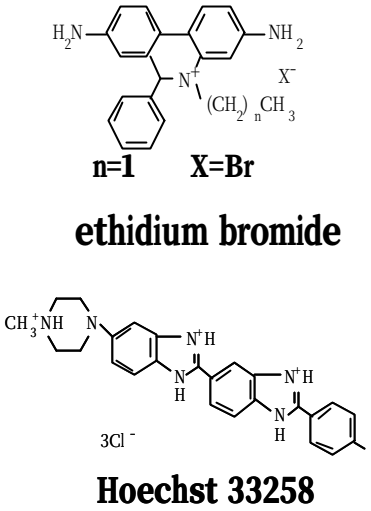

Fig. 2 Chemical structures of typical intercalators

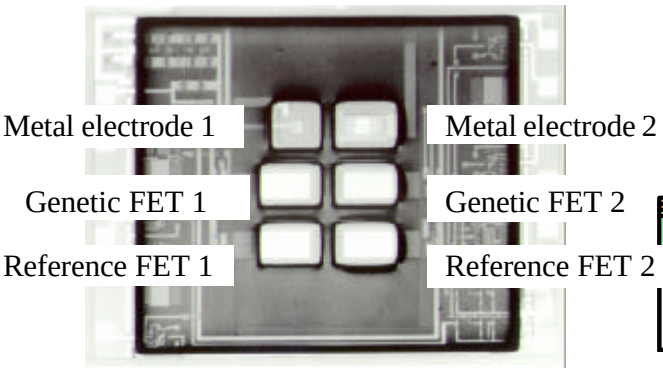

Fig. 3 Photograph of the fabricated field effect transistor

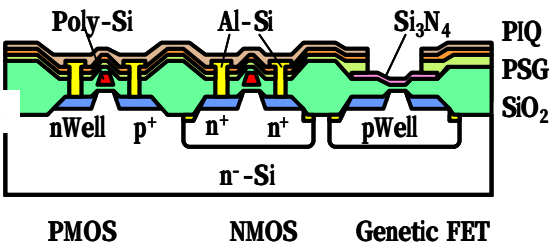

Fig. 4 Cross-section of the fabricated device