Detection of Ions and DNA hybridization

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Si ion sensitive FETs and diamond solution gate FETs

For a long time, ion sensitive field effect transistors (ISFETs) have been studied in the field of biosensing application. In general, transistor biosensors not only detect chemical substances and transduce them into electrical signals, but also amplify the signals. The device size can be scale down without reducing sensitivity. Many types of ISFETs have been produced experimentally using Si MOS technology. The modulation doped FETs in III-V compound semiconductors have been also applied to realize ISFETs. In both cases, however, the sensing regions are separated from the transducing and amplifying region by gate insulator or doped layers. These layers are necessary, because carriers should be confined in the buried channels. The performance of sensors such as sensitivity, time response has been affected by the insulator which reduces the surface potential change. Higher gate capacitance is desirable to reflect the charge change in electrical dipole layer of electrolyte solution near the sensing surface. However, the gate capacitance of Si ISFET is small because of the relatively thick insulator above gate oxide (Fi.1(a)) necessary for protecting gate oxide from ion invasion. These insulators are normally Si_3N_4, Al_2O_3, and Ta_2O_3 which have not perfectly dense structure. The target molecules diffuse into them and the time response of the ISFETs become slow.

We have demonstrated a new type of FET sensor without such an interlayer [1-3] (Fig.1(b)). Since the diamond surface is nearly inert to the electrolyte solutions at room temperature and has a wide potential window within which the redox reaction does not occur. The reproducible FET performance can be obtained in a wide pH region where the diamond surface channel is in contact with the electrolyte solution. We call this type of FET as electrolyte solution gate FET (SGFET) (Fig.1(b)).

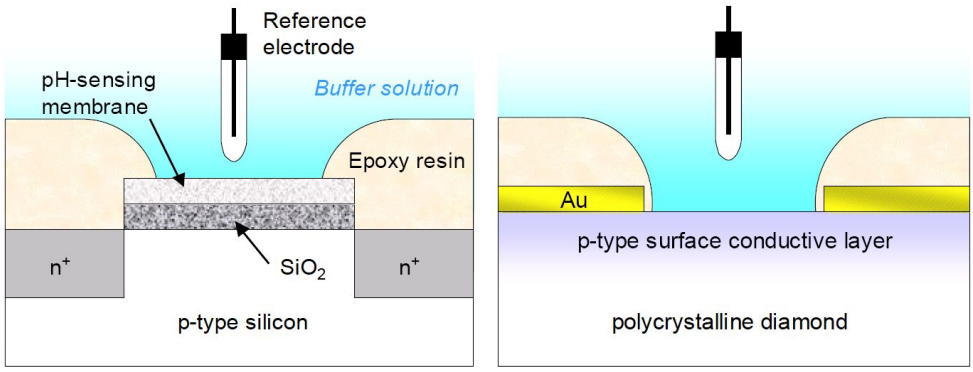

Fig.1. (a) Si ISFET. (b) Diamond SGFET.

Biomolecule Immobilization on Chemically Modified Diamond Surface

The surface chemical modification starts from the H-terminated surface which is a commonly obtained surface after the chemical vapor deposition of diamond with abundant hydrogen atoms in the growth condition. This surface exhibits highly p-type semiconductivity after the adsorption of negatively charged ions such as O_2^- in the air. These ions are attracted by the H-terminated surface because the surface hydrogen atoms are positively charged because of surface H-C dipoles formed by the electronegative difference between hydrogen (2.1 in Pauling unit) and carbon (2.5). The charge density of $H^{\delta+}$–$C^{\delta-}$ dipole is about $1x10^{14}e/cm^2$. This effect is valid in the air or in the electrolyte solutions where halogen ions such as Cl^-,Br^-, and I^- are effectively adsorbed on the H-terminated diamond and detected by the SGFETs down to 10^{-7}M. Negatively charged biomolecules can be also detected if they present in the electric double layer. On the contrary, the pH sensitivity of H-terminated surface is not high because H^+ ions might be repelled by the surface positive charges. For the other positively charged ions such as K^+, Na^+, Ca^{2+}, the surface does not show sensitivity. In the small ions the surface is only sensitive to Cl^-,Br^-, and I^-. These results are summarized in Table 1.

Table 1. Sensitivity of diamond surface termination to charged species in SGFET.

	H^+	K^+,Na^+	Cl^-,Br^-,I^-	DNA
H-termimated	Low	Low	High	-
O-terminated	Medium	Low	Low	-
NH_2-terminated	High	Low	Low	High

In order to get the pH sensitivity, the H-terminated surface should be partially replaced by O-termination or NH_2 termination, which can attract H^+ to become OH_2^+ or NH_3^+ leading to the repulsion or the reduction of holes in the surface channel. The time response of pH sensitivity shown in Fig. 2 is superior to that of Si based ISFET, because, in Si ISFET, in- and out-diffusion process inevitably takes places in the subsurface region of sensing layer such as Si_3N_4, Al_2O_3, and Ta_2O_3 etc. The hysteresis width which is a measure for time response is one order of magnitude lower than those of membranes used in Si ISFETs, because diamond is a much more densely packed material compared with those of membranes (Table 2).

Enzyme such as urease changing the surrounding pH after reacting with a special substance, e.g. urea, has been immobilized on the partially NH_2 diamond surface exhibiting pH sensitivity (Fig.3). The sensing of such a special substance and transducing of the signals have been successfully obtained in several cases [4].

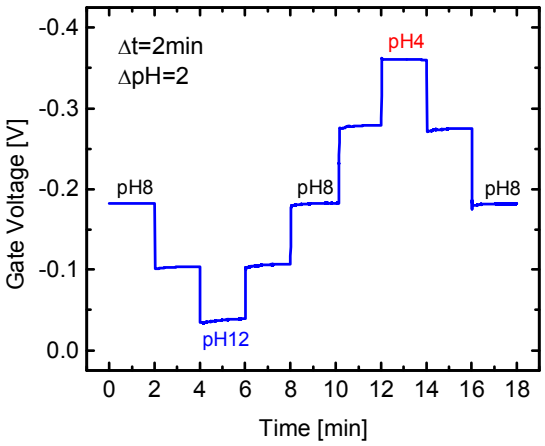

Fig.2. Time response of the pH sensing of a diamond SGFET with partially NH_2 terminated channel.

Table 2. Hysteresis width of pH sensing in several membrane.

pH-sensing membrane	Si_3N_4*	a-Si-H**	Al_2O_3**	Ta_2O_5**	Diamond
hysteresis width (mV)	7.1	9	10	7	0.7

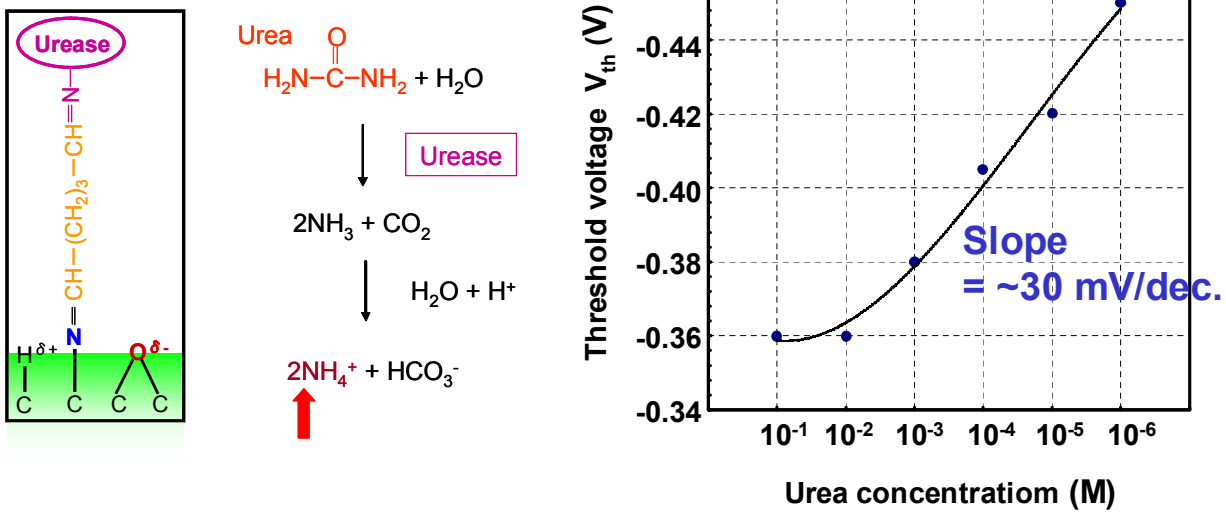

Fig.3. Urea sensing by an urease immobilized SGFET. The concentration of urea can be detected by the pH change provided by the decomposition of urea by urease.

Detection of DNA hybridization in electric double layer

The change of electric charge in the electric double layer is very influential in the surface carrier density. When biomolecules are charged negatively and immobilized in the electric double layer, the charge change is detected in the SGFET. The DNAs immobilized on the diamond surface covalently is a good example. When they hybridize with target DNAs at equivalent length, the surface holes can be induced and detected as the drain current increase or the positive shift of the threshold voltage in the p channel SGFET (Fig.4) if the hybridization takes place in the electric double layer. It is clearly and reproducibly observed in the diamond SGFET where the surface has been partially aminated and the probe DNAs have been immobilized. The difference between complementary, 3-base mismatch, and non complementary target DNA has been detected both by the I-V characteristics and the real time shift of the gate voltage keeping the constant drain current [5]. Considering the thickness of electrical double layer controlled by the density of buffer solution, the surface density of probe DNA (immobilized DNA) and the effective charge of DNA are estimated.

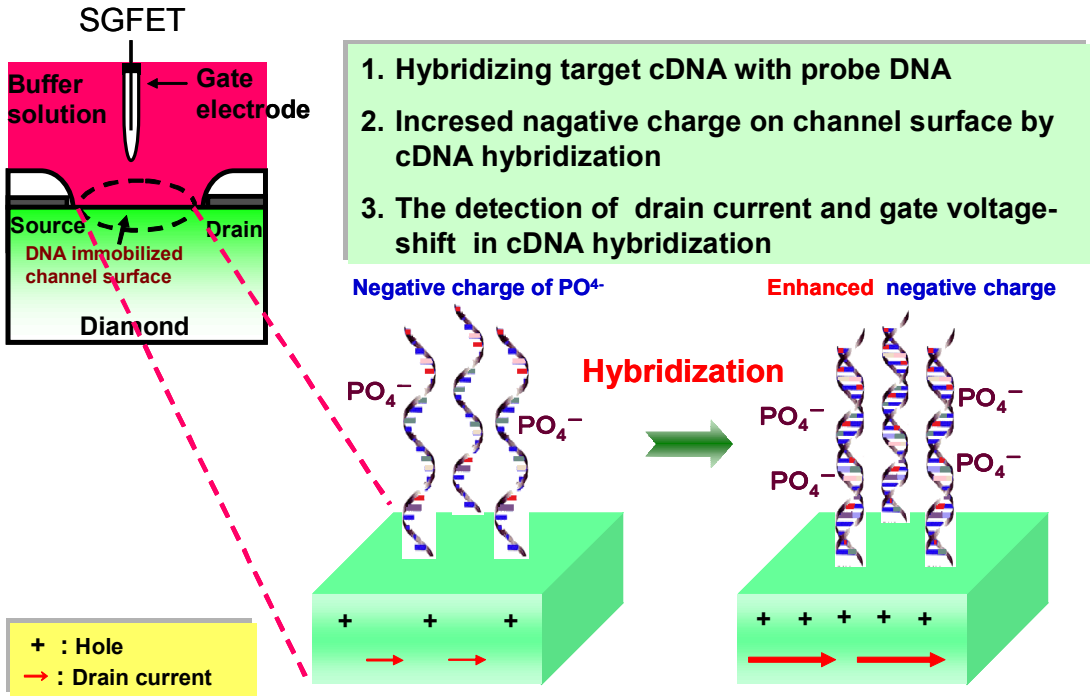

Fig.4. Hybridization of DNA sensed by diamond SGFET, where the single strand DNA are immobilized on the diamond surface. The concentration of target DNA is 0.1nM.

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[2] H.Kanazawa et al., Diamond Relat. Mater. 12, 618 (2003).
[3] K.S.Song et al.,Biosens. Bioelectron. 19, 618 (2003).
[4] K.S.Song et al.,Jpn. J. Appl. Phys., 43,L814 (2004).
[5] K.S.Song, H.Kawarada et al. (submitted).