Supplementary Material

For 'Mutation detection using thermal-gradient electronic transduction on hairpin-loop sensor'

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1. Introduction of the nanocompartment model

The DNA motif for fabricating DNA nanocompartment comprises two contiguous elements: double-stranded DNA (dsDNA), whose array is responsible for a relatively impermeable membrane, and a single-stranded DNA (ssDNA) serving as skeleton that supports the dsDNA membrane. The DNA terminates on 5′ end with alkanethiol group that immobilizes DNA on gold surface by sulphur-gold bond. Because the diameter of ssDNA is much smaller than that of dsDNA, a compartment with designable effective height can form between the dsDNA membrane and gold surface.

2. Which conditions are known resulting from experiments?

- The height of the container is estimated to be 5 nm .
- The length of PDC-TH on the electrode surface is estimated to be 1.6 nm .
- The mean distance of two neighbor oligonucleotides immobilized on probe electrodes is about 4nm, about twice of the diameter of duplex DNA.
- A certain range of coverage (0.1×10^{-10} ~ 0.5×10^{-10} mol/cm^2) of double-stranded DNA on the electrode surface is a necessary condition for the step effect in i_p-T curves.
- The coverage ratio of PDC-TH versus hairpin on the surface of the electrode is roughly 100:1.

3. Detailed calculation

3.1 Equilibrium constant of chemical reaction between PDC and TH

Control experiments on PDC-modified electrodes reflect the equilibrium movement of chemical reaction between PDC and TH. Set the function $F_c(T)$ stand for the corresponding i_p-T profile.

PDC + TH ←→ PDC-TH

The area density of PDC-TH = Z_C

The concentration of TH = C_{th}

The area density of PDC = σ_c

Z_C should be proportional to $F_c(T)$. So we set $Z_C = k_c F_c(T)$, then the equilibrium constant is expressed by

$$K(T) = \frac{Z_c}{} = \frac{k_c F_c(T)}{}$$

$$K(T) = \frac{1}{(\frac{\sigma_c}{k_c F_c(T)} - 1) \cdot C_{th}^{\lambda}} \qquad (2/3 \le \lambda < 1) \qquad (1)$$

Equation (1) implies that $K(T)$ decrease continuously with increasing temperature.

3.2 Chemical reaction that happened on SAMs

On the SAMs formed by DNA hairpin-loop, the area density of DNA-PDC is denoted by σ_1, the area density of DNA-PDC-TH by σ_{outer}, and the concentration of environmental TH by C_{th}

$$K(T) = \frac{\sigma_{outer}}{}$$

$$\sigma_{outer}(T) = \frac{K(T)\sigma_1 C_{th}^{\lambda}}{1 + K(T) C_{th}^{\lambda}} \qquad (2)$$

Equation (2) implies that σ_{outer} decrease with increasing temperature.

On the SAMs formed by PDC directly bound to surfaces, the area density of PDC is denoted by σ_2, the area density of PDC-TH by σ_{inner}, and the concentration of TH sandwiched in the nanocompartment by $\chi(T)$

$$\sigma_{inner}(T) = \frac{K(T)\sigma_2 \chi^{\lambda}(T)}{1 + K(T)\chi^{\lambda}(T)} \qquad (3)$$

Equation (3) cannot tell us how σ_{inner} varies with temperature.

3.3 When the DNA SAMs close its gate

Before the DNA nanocompartment is switched on, the concentration of TH in the volume of the nanocompartment is approximately equate to the concentration of environmental TH.

Set T_2 represents the temperature at which the DNA nanocompartment is switched on. Since the amount of TH entrapped in the SAMs is assumed invariable after the DNA nanocompartment is switched on, we can get the following equation on the condition of $T < T_2$:

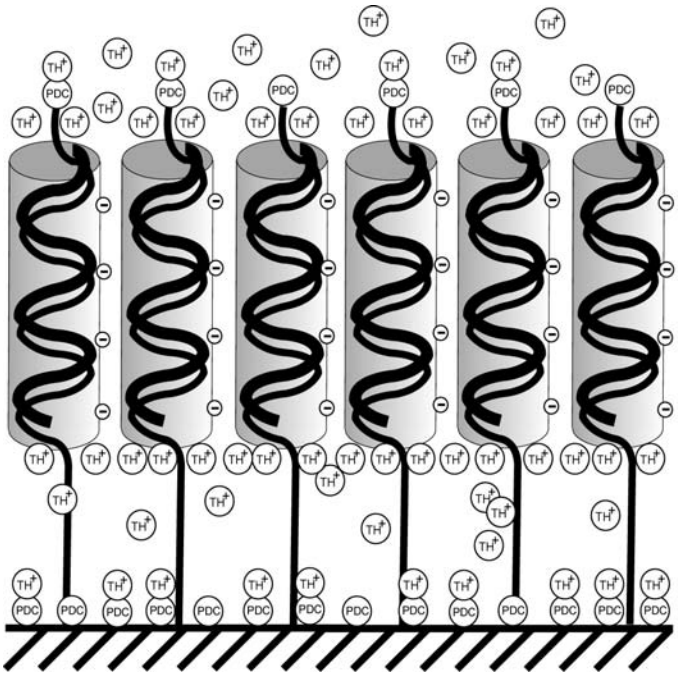
$$\chi(T)d(T) + \sigma_{inner}(T) = C_{th}d_0 + \sigma_{inner}(T_2) \qquad (4)$$

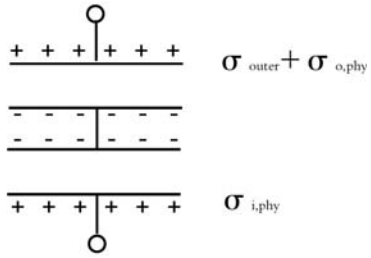
T_2 can be got from the DNA denature profile.

3.4 Capacitance approximation

TH is cation in solution. The oligonucleotide was negative in charge and is electrically conductive in some extent[1-6]. So at the equilibrium state of SAMs on the gold surface, there are approximately two capacitances in series, which responsible for the charge distribution of the SAMs.

Supposing that σ represents the amount of charge per single stranded oligonucleotide, $\sigma_{o,phy}(T)$ and $\sigma_{i,phy}(T)$ represent the surface densities of TH which was absorbed respectively on the outer side and inner side of the double helices membrane by static force, $f_{dDNA}(T)$ represents the percentage of double stranded oligonucleotides on the base of the amount of oligonucleotides on the gold surface, we can get the formula according to charge equilibrium in capacitances:





$$\frac{1+f_{dDNA}(T)}{2}\sigma=\sigma_{outer}(T)+\sigma_{o,phy}(T)+\sigma_{i,phy}(T) \qquad (5)$$

3.5 Characteristic of $\chi(T)$

According to equation (3) and (4), we get:

$$K(T)=\frac{m-\chi(T)d(T)}{\left[\chi(T)d(T)+\sigma_2-m\right]\chi^{\lambda}(T)} \qquad (6)$$
$$m=C_{th}d_0+\sigma_{inner}(T_2)$$

3.6 What will happen about SAMs at the temperature below T_2

Gauss Theorem could calculate the electric field applied on the dsDNA membrane.

$$E=\frac{C_{th}d_0+\sigma_{inner}(T_2)}{\varepsilon}$$

While the forces on dsDNA membrane are in equilibrium, there is

$$(P_{outer}-P_{inner})+\sigma_1 f=\sigma_{o,phy}E$$

$$P_{outer}=C_{th}RT \quad P_{inner}=\chi(T)RT$$

Considering the critical point of temperature, the forces on the ssDNA skeleton begin losing ($f=0$), and the height of the small container has the value of its maximum

($d(T) = d_0$). So, after deduction, we can get:

$$\chi(T) = C_{th} - \frac{\sigma_1 \sigma E}{RT}$$

The critical temperature (T_2) can be got by solving the following equations:

$$\begin{cases} \chi(T) = C_{th} - \dfrac{\sigma_1 \sigma}{RT}\left(\dfrac{C_{th} d_0 + \sigma_{inner}(T_2)}{\varepsilon}\right) \\ K(T) = \dfrac{m - d_0 \chi(T)}{\left[d_0 \chi(T) + \sigma_2 - m\right]\chi^{\lambda}(T)} \end{cases}$$

3.7 $i_p(T)$ in voltammograms

Set $Q(T)$ represent the surface density of the total charges on SAMs. The peak current $i_p(T)$ in voltammograms is proportional to $Q(T)$, that is

$$i_p(T) \propto Q(T)$$

$$\begin{aligned} Q(T) &= (\sigma_{outer}(T) + \sigma_{o,phy}(T) + \sigma_{i,phy}(T))e^{-\beta d(T)} + \sigma_{inner}(T) + \chi(T)d(T) \\ &= \frac{1 + f_{dDNA}(T)}{2}\sigma e^{-\beta d(T)} + \sigma_{inner}(T) + \chi(T)d(T) \end{aligned} \quad (7)$$

4. Discussi

While T>T_2, t

$$Q(T) = \frac{1 + f_{dDNA}(T)}{2}\sigma e^{-\beta d_0} + \sigma_{inner}(T) + C_{th} d_0 \quad (8)$$

ed as:

While T_1<T<T_2, there is $d(T) = d_0$, $f_{dDNA}(T) = 1$. According to the equation (7), we have

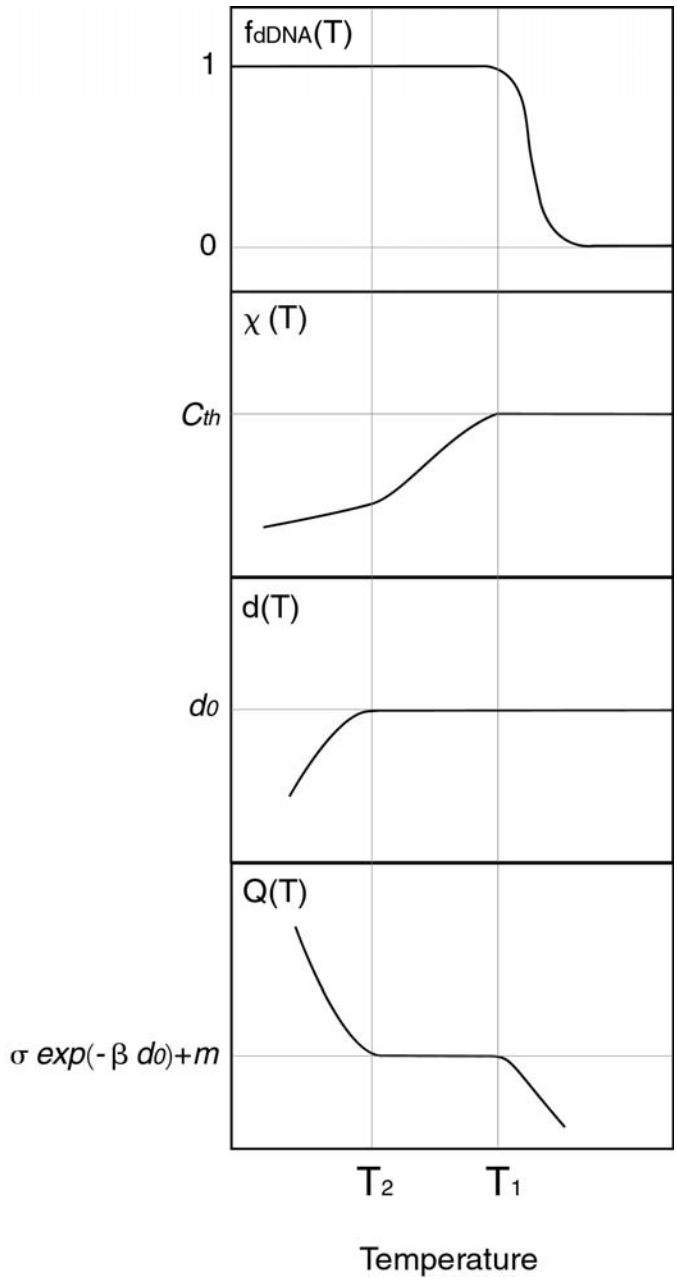
While T<T_1, there is f_d

$$Q(T) = \sigma e^{-\beta d_0} + m \quad (9)$$

tion (7), we have

$$Q(T) = \sigma e^{-\beta d(T)} + m \quad (10)$$

Following figure sets illustrate the changes of $f_{dDNA}(T)$, $\chi(T)$, $d(T)$, and $Q(T)$ with temperature, according to previous analysis.



Reference

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