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# A Theoretical Method for Mercury Ion Detection Based on Calculation of T-Hg<sup>2+</sup>-T Configuration Energy

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**Abstract.** The energy value of specific structural unit of T-Hg<sup>2+</sup>-T is calculated theoretically, and the secondary structures of a series of DNA molecules based on T-Hg<sup>2+</sup>-T structure are predicted theoretically with the minimum free energy algorithm. At the same time, Gibbs free energy is thought to have changed before and after hybridization of DNA molecules in the presence and absence of mercury ions. According to the second law of thermodynamics, the trend and direction of the reaction before hybridization were judged. A novel DNA molecule based on T-Hg<sup>2+</sup>-T structure was designed and applied to the detection of mercury ion. It provides a new theoretical design method for the design of mercury ion electrochemical probe in the future.

## 1. Introduction

The introduction of DNA secondary structure is the basis of nanotechnology (such as DNA molecular self-assembly [1] and DNA calculation [1-4]), so the prediction of DNA secondary structure has become one of the main research fields in computational biology. A minimum free energy prediction algorithm was proposed by Zuker [5-22], which consists of two steps. Firstly, a free energy table is established, in which different basic structural units of DNA secondary structure should be assigned different energy values, then minimum free energy of all subsequences is calculated and the results are filled in the free energy table. Secondly, when the free energy is minimum, the secondary structure of DNA is found. In addition, according to the minimum free energy algorithm, the secondary structure of DNA can be found from the minimum free energy of all kinds of stem and ring structures by molecular dynamics method when the combination is optimized, which is the central idea of the minimum free energy algorithm [23]. Based on the minimum free energy algorithm, the method of summing the free energy and taking the smallest value is adopted to the DNA folding algorithm and the optimal structure for the sub-sequences of the predicted sequences will be obtained. There is a high probability that the optimal structure is the real structure of the DNA molecule after being folded.

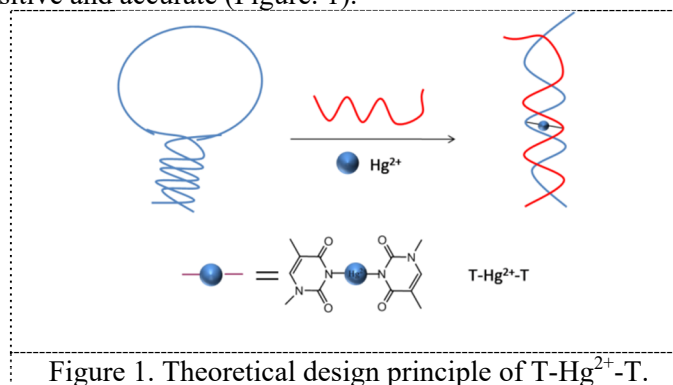
Mercury is a highly toxic pollutant for the global environment. Long-term deposition of mercury ion can lead to irreversible pollution for the soil and water environment. In turn, the microbes that live in aquatic environments can convert inorganic mercury into more toxic organic mercury, which is enriched in the food chain and enters the human body. The mercury that entered human body will accumulate in bones and organs, which can cause serious damage to the brain and nervous system [24]. Therefore, the qualitative and quantitative analysis of mercury ion have great significance to life, environment, medical science, industrial and agricultural production. Up to now, many traditional



methods with different instruments for quantitative analysis of mercury ions in aqueous solution have been reported [25-39].

As early as 1952, Katz found that the dynamic viscosity of natural DNA decreased after adding  $\text{HgCl}_2$  [40], then the hypothesis that mercury ion and thymine formed T- $\text{Hg}^{2+}$ -T structure at the ratio of 1:2 was proposed [41-42]. In 2006, the Ono's team reported more studies which directly confirmed the structure of T- $\text{Hg}^{2+}$ -T base pairs [43-44]. The Ono's team confirmed that mercury ion forms T- $\text{Hg}^{2+}$ -T structure in DNA by means of melting curves, electrospray ionization mass spectrometry and nuclear magnetic resonance spectroscopy. Based on the particularity of T- $\text{Hg}^{2+}$ -T structure, a special DNA sequence can be designed, which can change its secondary structure in the presence of mercury ion. This characteristic is favored by many analytical researchers. Therefore, many researchers combined the coordination of T- $\text{Hg}^{2+}$ -T with electrochemical sensing technology to construct a more convenient and sensitive mercury ion electrochemical sensing system [45-49]. The above design of DNA molecular based on T- $\text{Hg}^{2+}$ -T structure is basically through some empirical results, and has not been discussed in theory. Therefore, from the theoretical point of view, it is necessary to study the design of DNA molecule based on T- $\text{Hg}^{2+}$ -T structure and optimize the whole design process through the corresponding calculation research, so as to find the optimal DNA molecular structure based on T- $\text{Hg}^{2+}$ -T structure.

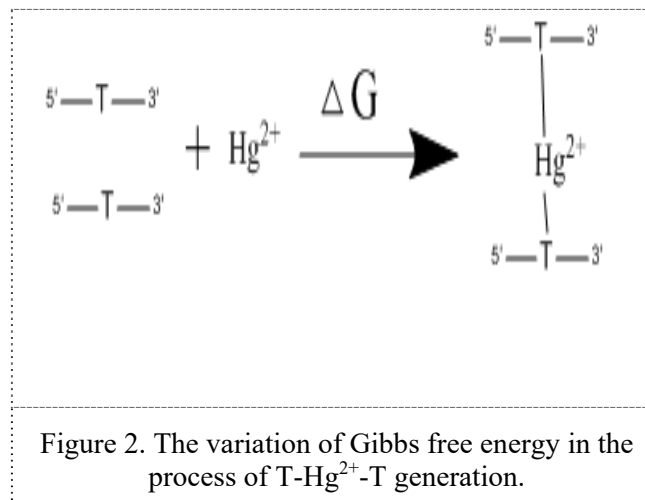
In this study, the energy value of specific structural units of T- $\text{Hg}^{2+}$ -T was calculated by quantum chemistry method, and the secondary structures of a series of DNA molecules based on T- $\text{Hg}^{2+}$ -T structure were predicted theoretically with the minimum free energy algorithm. At the same time, we considered the change of Gibbs free energy before and after hybridization of DNA molecules in the presence and absence of mercury ion. According to the second law of thermodynamics, the trend and direction of the reaction before hybridization were judged. Based on the above principles, an electrochemical probe for mercury ion detection was designed. In the presence of a few mercury ions, this DNA molecule can use the binding force of the T- $\text{Hg}^{2+}$ -T base to replace the natural base, so that the Gibbs free energy of the system can be reduced and the reaction can carry out. Using the principle of this reaction to design new DNA molecules based on T- $\text{Hg}^{2+}$ -T structure will make the detection of mercury ion more sensitive and accurate (Figure. 1).



## 2. Experimental section

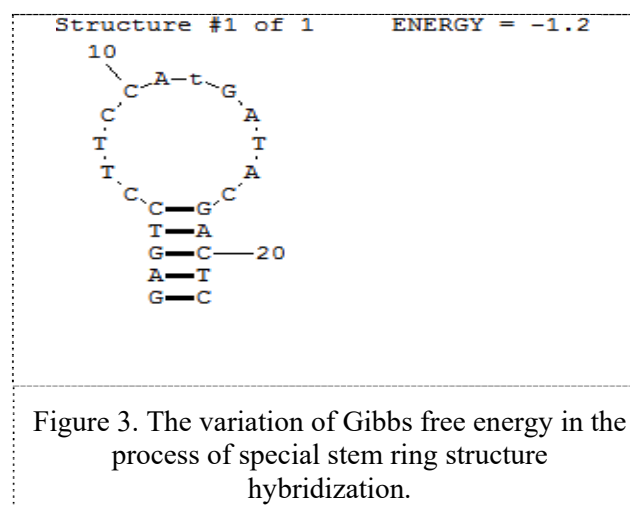
### 2.1. The calculation of the energy change during the formation of T- $\text{Hg}^{2+}$ -T specific structural units

Because the different basic structural units of DNA secondary structure do not include the energy values of T- $\text{Hg}^{2+}$ -T specific structural units in the free energy table of the minimum free energy Zuker algorithm. Therefore, we need to calculate the energy values of diverse T- $\text{Hg}^{2+}$ -T specific structural units firstly, so as to obtain the complete free energy table of the Zuker algorithm. The value of  $\Delta G$  was calculated to be -9.5 kcal/mol during the formation of T- $\text{Hg}^{2+}$ -T specific structural units (Figure 2).



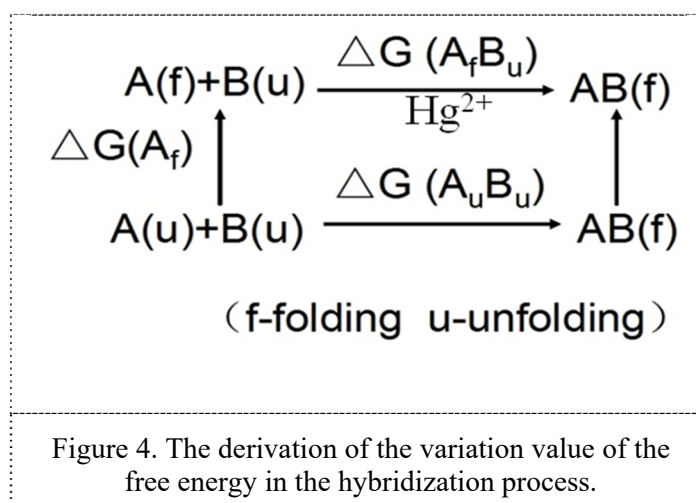
## 2.2. Designing DNA molecule and auxiliary DNA based on T-Hg<sup>2+</sup>-T structure with minimum free energy algorithm

The DNA molecules based on T-Hg<sup>2+</sup>-T structure which have special stem ring structure (including single ring) can be designed by using programmed minimum free energy algorithm software. The auxiliary DNA can partially hybridize with the DNA molecule based on the T-Hg<sup>2+</sup>-T structure and contains a T-T mismatch. Below is the cross process of the GAGTC CTTCC ATGAT ACGAC TCAGTC CTTCC ATGAT ACGAC T, and the  $\Delta G$  is -1.2kcal/mol (Figure 3).



## 2.3. Based on the second law of thermodynamics, the minimum free energy algorithm is used to calculate the energy changes of hybridization process of DNA molecule and auxiliary DNA based on T-Hg<sup>2+</sup>-T structure

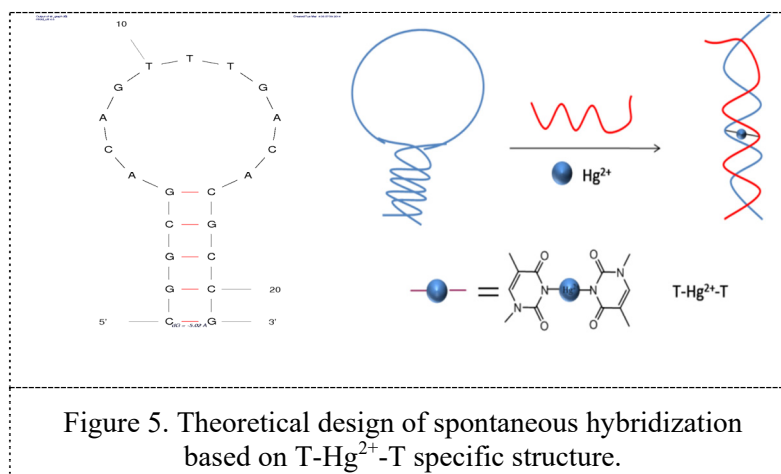
The energy values during the formation of T-Hg<sup>2+</sup>-T specific structural units are calculated by quantum chemistry method, then add the energy values to the free energy table of the minimum free energy algorithm, and the complete free energy table of the Zuker algorithm is obtained. Based on the second law of thermodynamics, the free energy variation of the hybridization process caused by the presence of mercury ion is calculated. We designed a spontaneous hybridization process under the condition of the presence of mercury ion, in which the DNA molecule (A) (based on the T-Hg<sup>2+</sup>-T structure) and the auxiliary DNA (B) could form a T-Hg<sup>2+</sup>-T structure as well as a natural base ligand (Figure 4). The result of spontaneous process will result in the change of DNA molecular configuration based on T-Hg<sup>2+</sup>-T structure.



According to the second law of thermodynamics: the change of Gibbs free energy  $\Delta G(A_fB_u) = \Delta G(A_uB_u) - \Delta G(A_f) < 0$ , the reaction can take place spontaneously (Figure 4).

#### 2.4. A DNA molecular probe with a special sequence is designed based on the above results

Based on the above, a series of DNA molecules and auxiliary DNA with special sequences based on T-Hg<sup>2+</sup>-T structure are designed. In the presence of mercury ion, the Gibbs free energy of the hybridization process is reduced by using the T-Hg<sup>2+</sup>-T bonding force and natural base pairing, which makes the reaction spontaneous. For the DNA molecule (A): A: 5'CGGCGACAGTTTGACGCCG3', the following configuration is formed spontaneously, and its  $\Delta G(A_f)$  is -5.02 kcal/mol (Figure 5).



Then we can design a matching DNA (B): B: 5'TGTCTTTCTGT3', the  $\Delta G(A_uB_u)$  of the hybridization process is -4.35 kcal/mol and the calculated  $\Delta G(A_fB_u)$  is 0.67 kcal/mol ( $\Delta G(A_fB_u) > 0$ ). According to the second law of thermodynamics, the reaction can not occur spontaneously. By adding Hg<sup>2+</sup> to form a specific structure of T-Hg<sup>2+</sup>-T, the  $\Delta G(A_fB_u) < 0$  can be obtained and the reaction will occur spontaneously (Figure 5).

### 3. Results and discussion

#### 3.1. Synthesis and theoretical verification of a new type electrochemical probe for mercury ion

The probe DNA based on T-Hg<sup>2+</sup>-T structure is fixed on the surface of the electrode, and the methylene blue labeled at the end of the electrode is close to the electrode (open state) which can produce a large electrochemical signal. In the presence of mercury-free ion with only auxiliary DNA,

there is no hybridization between probe DNA and auxiliary DNA because of T-T base mismatch. In the presence of mercury ion, the auxiliary DNA formed the T-Hg<sup>2+</sup>-T structure with the probe DNA by hybridization reaction, resulted in the change of the probe configuration. Therefore, due to the electrochemical indicator methylene blue that label on the other end of the probe is far away from the electrode (closed state), the electrochemical response on the electrode surface decreased, so as to achieve the purpose of mercury detection. In this kind of sensor, there is no need to add reagents during the detection, so it is simple to construct and easy to operate. The related results have been verified by experiments [50-51].

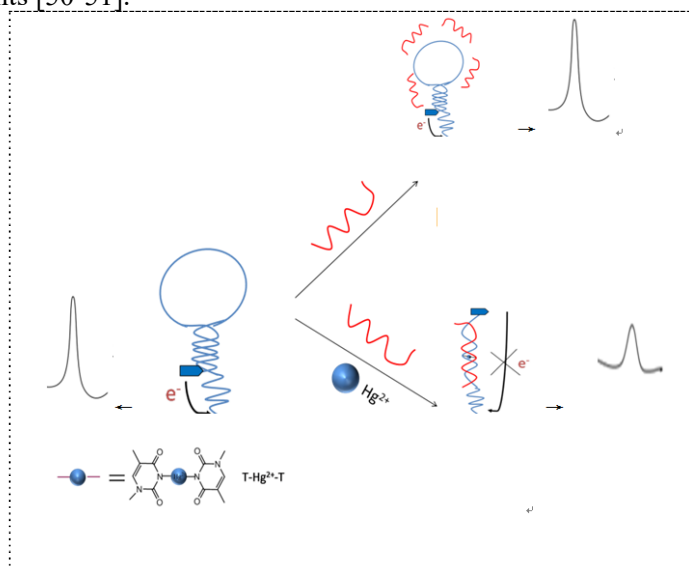


Figure 6. A new type of mercury ion electrochemical probe for mercury ion detection.

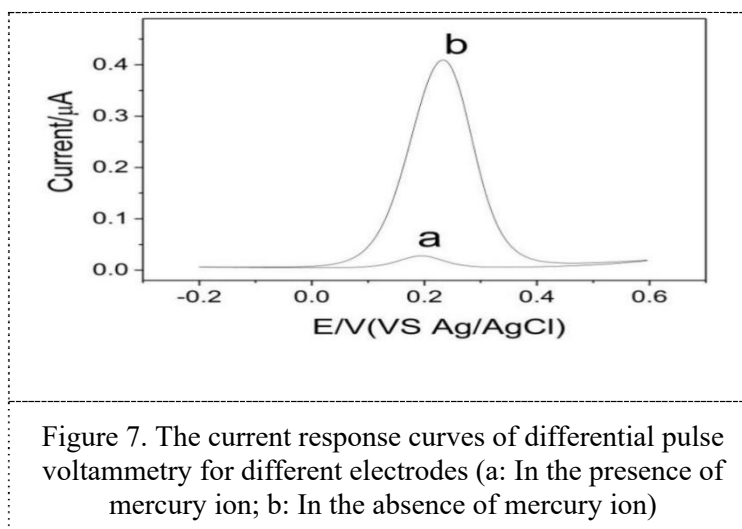


Figure 7. The current response curves of differential pulse voltammetry for different electrodes (a: In the presence of mercury ion; b: In the absence of mercury ion)

### 3.2. Conclusion

Using the energy value of specific structural unit of T-Hg<sup>2+</sup>-T and the minimum free energy algorithm, a new DNA molecule is designed for mercury ion detection. The whole design process was programmed and standardized by corresponding standards to find the optimal DNA molecular sequence based on T-Hg<sup>2+</sup>-T structure and to construct highly efficient and sensitive mercury-ion

electrochemical probe. It provides a new theoretical design method for the design of mercury ion electrochemical probe in the future.

### Acknowledgments

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