Comparison of Branching Hydrogen Bonding Networks with Microelectronic Devices

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Abstract – **Signal transmission (proton transfer) in hydrogen bonding networks is investigated for the needs of microelectronics. Three branching hydrogen bonding networks are extracted from β-lactamase protein. The model of proton transfer in hydrogen bonds is developed on the base of Marcus theory and protein electrostatic theory. The influence over proton transfer parameter caused by the acceptor electrostatic potentials, the sum of protein electrostatic potentials, and cooperative effects are estimated. The obtained hydrogen bond characteristics are compared to the I-V characteristics of known electronic devices. The comparison shows that some characteristics of hydrogen bonds are similar to the I-V characteristics of electron tubes; characteristics of a current source or microelectronics multiplexer and demultiplexer. The investigation demonstrates that the hydrogen bonds are prospective candidates for future microelectronics applications.**

Keywords – **Proton transfer, hydrogen bonding network, electron tubes, multiplexer, demultiplexer**

I. INTRODUCTION

The application of bioorganic molecules such as microelectronic components is a novel direction in science and nanotechnology. Bioobjects such as cytochrome c oxidase [1] and bacteriorhodopsin can be used in memories [2] and other microelectronics devices.

The key information transfer elements in biopolymers are the hydrogen bonds. An interesting analogy between them and known Si-elements is observed. The hydrogen bond has a proton donor and acceptor while the field effect transistor has a source and drain, respectively. In hydrogen bonds, the proton transfer depends on donating and accepting potentials as well as on the surrounding

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potentials. In field effect transistors, the current flow depends on drain, source and gate potentials, respectively.

In analogy to microelectronics circuits, the hydrogen bonds can be cooperated in hydrogen bonding networks (HBN). In this way, the information is transferred by proton current in biopolymers. The first proton transport model systems have been realized with water hydrogen bonding networks [3].

With this regard, the proton transfer in real biological HBN is investigated to find a new microelectronic device. The hydrogen bonds are extracted from TEM1 β-lactamase. The objective of the present paper is to explain i) how the information is transferred in branching hydrogen bonding networks, and the role of water molecules in them, ii) how the proton transfer depends on donor-acceptor potentials, and surrounding residues, and iii) what are the analogies between process of proton transfer in hydrogen bonds and process of current flow in microelectronic devices.

II. MATERIALS AND METHODS

The crystallographic structure of TEM1 β-lactamase (1btl) is taken from Protein Data Bank [4]. It is made by X-ray diffraction at resolution of 1.80 Å. Water layer is added by Vega ZZ [5]. The layer size is 4.5 Å and the maximum heavy oxygen atom overlap is 0.2 Å. The protein-water geometric optimization is performed by NAMD program [6]. The electrostatic potentials and pKa's of ionizable groups are calculated by PHEI server [7]. It is required by hydrogen bonding networks that for every participant both donating and accepting properties are initialized. The hydrogen bonding networks are extracted by WHAT_IF server [8], and additionally the distance between donor and acceptor is restricted to <2.90 Å.

We have developed a custom code for calculation of the proton transfer parameter (K) using the Marcus parameterization [9]. In this parameterization, the cooperative effects and surrounding residue electrostatic effects are taken into account. The K parameter is calculated by:

$$K = \frac{k_B T}{2\pi} \exp\left(-\frac{Eb - h\omega/2}{k_B T}\right) \tag{1}$$

where: K – proton transfer parameter, kB – Boltzmann constant, Eb – energy barrier, h – Planck constant, ω – frequency, T – temperature [K].

The energy barrier is calculated by:

$$Eb = (s_A(R(DA) - t_A)^2 + v_A) + s_B E_{12} + \\ + (s_C \exp(-t_C(R(DA) - 2)) + v_C)(E_{12})^2 \tag{2}$$

where R(DA) is distance between the donating and accepting atoms, E12 is the energetic difference between donating and accepting atoms, the values for other parameters are taken from the same publication [9]. The proton transfer parameter is measured in [J/mol], and the proton current is proportional to K.

III. RESULTS AND DISCUSSION

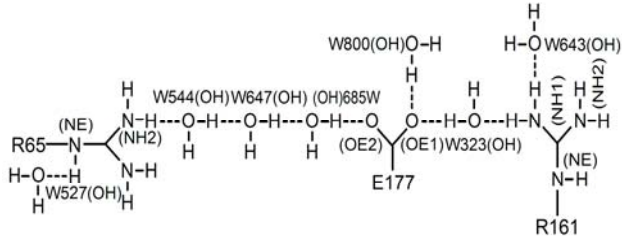Three hydrogen bonding networks are objects of this investigation. They are shown in Figures 1, 2, 3.

FIGURE 1. BRANCHING HYDROGEN BONDING NETWORK COMPOSED OF: NH1, NH2, AND NE — NITROGEN ATOMS OF ARGININE RESIDUES R65 AND R161, OE1 AND OE2 — CARBOXYL OXYGEN ATOMS OF GLUTAMIC ACID RESIDUE E177, OH — ARE OXYGEN ATOMS OF WATER MOLECULES (W323, W544, W527, W643, W647, W685 AND W800).
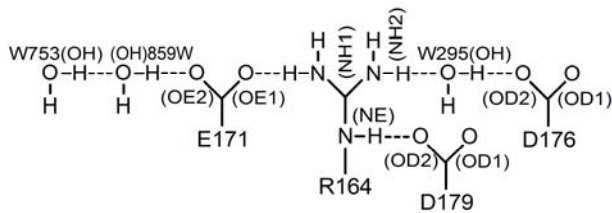

FIGURE 2. BRANCHING HYDROGEN BONDING NETWORK COMPOSED OF: NH1, NH2, AND NE — NITROGEN ATOMS OF ARGININE RESIDUE R164, OE1 AND OE2 — CARBOXYL OXYGEN ATOMS OF GLUTAMIC ACID RESIDUE E171, OD1 AND OD2 - CARBOXYL OXYGEN ATOMS OF ASPARTIC ACID RESIDUES, OH — ARE OXYGEN ATOMS OF WATER MOLECULES (W295, W753 AND 859W).
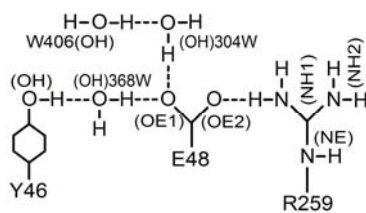

FIGURE 3. BRANCHING HYDROGEN BONDING NETWORK COMPOSED OF: NH1, NH2, AND NE — NITROGEN ATOMS OF ARGININE RESIDUE R259, OE1 AND OE2 — CARBOXYL OXYGEN ATOMS OF GLUTAMIC ACID RESIDUE E48, OH — OXYGEN ATOM OF TYROSINE RESIDUE Y46 AND OH ARE OXYGEN ATOMS OF WATER MOLECULES (W304, W368 AND W406).

In Figure 1, the hydrogen bonding network is branched by R65 and E177 residues. The oxygen atom OE1 of E177 residue forms bifurcate bond with water molecules. In the second network, similar branches are formed by E171 and R164. The difference between R65 and R164 is that the R164 forms three hydrogen bonds. The branch of the third hydrogen bonding network is formed by E48. Its oxygen atom OE1 also forms bifurcate bond. In the three networks,

the water molecules are integrated elements. The side chain residues of protein are bound by them.

For exploring of hydrogen bond properties and characteristics, the pH-varying of medium is used. The variation of pH causes polarization and ionization of the groups to occur. Immediately, the charges of protein-water system are redistributed, and the potentials of all atoms are changed, including explored donor and acceptor atoms. Hence, the proton transfer conditions are changed. The proton transfer parameters (K) versus electrostatic potentials (El. pot.) of hydrogen bonding donors and acceptors are shown in Figures 4 - 7.
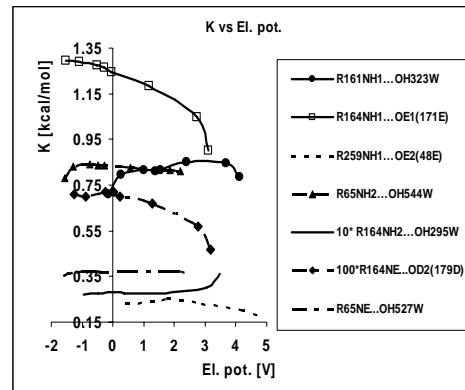

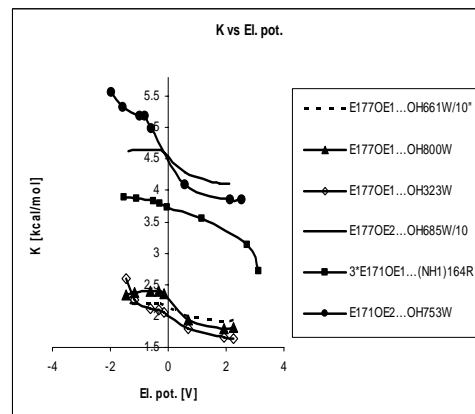FIGURE 4. K VS EL. POT. OF DONOR NITROGEN ATOMS OF ARGININE RESIDUES

FIGURE 5. K VS EL. POT. OF ACCEPTOR OXYGEN ATOMS OF GLUTAMIC ACID RESIDUES.
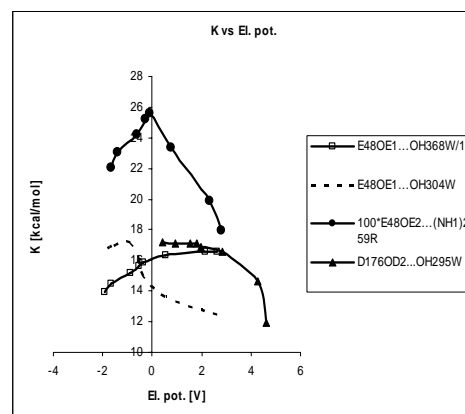

FIGURE 6. K VS EL. POT. OF ACCEPTOR OXYGEN ATOMS OF GLUTAMIC ACID RESIDUES AND ASPARTIC ACID RESIDUE.
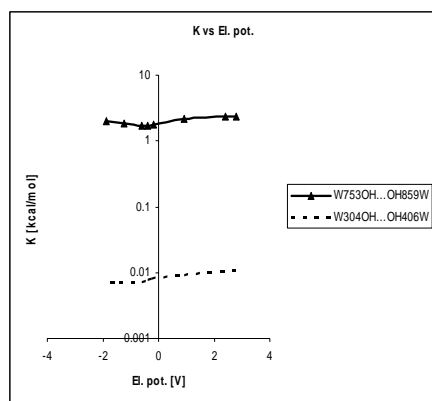
FIGURE 7. K VS EL. POT. OF ACCEPTOR OXYGEN ATOMS OF WATER MOLECULES. THE GRAPHIC IS SEMI-LOGARITHMIC SCALE.

It can be seen that, the electrostatic potential interval is from -2 to +4 [V]. The K-range is large (from 0 to 10^7). If the K-values of identical donor-acceptor pairs W753OH...OH859W and W304OH...OH406W are compared, it can be observed that $K_{W753OH...OH859W}$ is two orders bigger than $K_{W304OH...OH406W}$. The reason of this phenomenon is donor-acceptor atom distances, which are 2.71 Å and 2.83 Å respectively. Similar effects can be observed in other donor-accepting pairs, which are not discussed here. If a comparison of different hydrogen bonds with equal distances between donating and accepting atoms is made, it can be seen that proton transfer parameter depends on the atom nature. For example, the distance between W753OH...OH859W is equal to distance between R164NH1...OE1(171E) (2.71 Å), but K-values are different (see Figures 4 and 7). In some hydrogen bonds (Figure 4, R65NE…OH527W), the proton transfer parameter does not change with changing of the electrostatic potential. The K (El.pot.) characteristics are similar to I-V characteristic of a current source. However, most of the obtained curves have S-form or a combination of S-form curves (see Figures 5, 6 and 7). The curves are similar to Brunger [3] curves of proton current as function of pH, although the authors have used different model for water hydrogen bonding networks. The similar curves are also predicted by Scharnagl and authors [10] in Green Fluorescent Protein using different calculation formalism. On the other hand, the curves are similar to I-V characteristics of 2- or 3-terminal devices. The proton donor and acceptor can be presented as drain and source electrodes. The sum of electrostatic potential in a given hydrogen bond can be presented as gate electrode. Also, the similarities between K (El. pot.) curves and I-V characteristics of electron tubes are explored. In hydrogen bonding network examinations, the residues E48, 171, 177 can sum signals from different network branches. One of the branches terminates with OE1 atom, the other branch terminates with OE2 atom. The oxygen atoms (OE1 and OE2) have strong proton accepting properties. In the first network, OE1 atom of E177 forms two hydrogen bonds with W800OH and W323OH. These bonds have different proton transfer characteristics, despite that the donor and acceptor atoms are identical. Three factors are responsible for this phenomenon: i) charge density redistribution between OE1 and OE2 atoms, ii) cooperative effect in the hydrogen bonding networks, and iii) sum of protein electrostatic potentials in these points.

The influence of these factors is accounted for in the discussed model but their individual contributions can not be obtained. Analogical situation is observed in other two networks which include glutamic acid residue (E residue). The signal transmission in one branch depends on signal transmission in the second branch. The E residues have similar functions as microelectronics multiplexers. The same processes affect arginine residues R65, 161, 164 residues which branch signals by donor atoms NE, NH1 and NH2. The functions of R residues are similar to microelectronic demultiplexers.

IV. CONCLUSION

The study of proton transfer in hydrogen bonds and networks show that the proton transfer parameter depends on donor and acceptor electrostatic potentials, cooperative effects, and the sum of protein electrostatic potential. The obtained curves of proton transfer parameters versus donor and acceptor electrostatic potentials are similar to I-V characteristics of 2- or 3-terminal devices. In addition, some of the characteristics are similar to the I-V characteristics of electro-vacuum devices and current sources. The arginine and glutamine acid residues in hydrogen bonding networks have similar functions as microelectronics demultiplexers and multiplexers.

V. ACKNOWLEDGMENT

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