Characterization of Hydrogen Bonding Network in Cadence using Verilog-A

Elitsa E. Gieva

Характеризиране на мрежа от водородни връзки в Cadence чрез Verilog-A.

Преносът на сигнал в мрежите от водородни връзки е изследван с цел използването им в микроелектрониката. Мрежата е екстрахирана от протеина β-лактамаза и включва атоми от основните вериги на протеина и водни молекули. Моделът на протонен пренос във водородните връзки е разработен на основата на теорията на Маркус и е описан с език за описание Verilog-A. Направени са постояннотоков и времеви анализ на мрежата от водородни връзки със системата за проектиране Cadence и сравнение с предишни изследвания в Матлаб.. Изследванията показват, че характеристиките на водородните връзки са сходни с волт-амперните характеристики на вече познати микроелектронни схеми и елементи като диод, тунелен диод или транзистор. Цялата мрежа наподобява микроелектронна схема с два входа и два изхода, която може да пренася сигнал.

In this paper signal transfer (proton transfer) in hydrogen bonding networks is studied for microelectronic applications. The network is extracted from β-lactamase protein and it includes atoms from protein backbone and water molecules. The proton transfer model in hydrogen bonds is developed on the basis of Marcus theory and it is coded in Verilog-A hardware description language for behavioral modeling. DC and transient analyses of the hydrogen bonding network are performed in Cadence and the results are compared to previous Matlab analyses. The simulation shows that the characteristics of the hydrogen bonds are similar to the I-V characteristics of well-known microelectronics elements such as diode, tunnel diode, transistors. The entire network is similar to a microelectronic circuit with two inputs and two outputs and it can be used for signal transfer.

Introduction

The fundamental element of molecular electronics is the molecular device (MD) or the supramolecular device [1], which is an organized molecular system, constructed mainly by organic molecules or biomolecules that have some specific functions in signal detection, process, storage, and transmission through chemical or physical interactions at molecular or supramolecular levels. It can involve chemical information processes, and be relatively easy to realize a large number of links between the molecules. The links can be controlled by the external signals. There are many expected features of molecular computing which directly involve chemical and biological processes. MD may overcome some limitations of the solid-state chips, and can be directly applied to chemical and biological processes. Mainly based on a variety of organic materials, various functional devices can be designed and constructed such as ultrafast charge-transfer systems and three-dimensional storage. Besides, a large number of links between the different molecular units may relatively easily be realized in MD, and the links can be controlled by an external signal. Molecular electronics is a part of bioelectronics

MD could involve chemical information processes with nonlinear dynamic properties, which are important in a biological information system. Sensors can be built as a part of devices for detecting chemical and biological molecular information. The devices can be fabricated through bottom-up route instead of the top-down route. In principle, it has no submicron limitation in the device fabrication. MD can be designed and fabricated to construct molecular information systems based on different computing principles and architectures such as discrete logical computation, non-discrete dynamic evolutionary computation, cellular automation, and artificial neural network, etc. On one hand, the realization of a biocomputing system will be dependent on the development of molecular devices. On the other hand,

making an investigation of the biocomputing principle can help one understand what kind of designs and features a molecular device should have for use in future computers, and guide the device researches in seeking proper molecules and structures to meet the requirement of the computing system.

In this paper signal transfer in a hydrogen bonding networks (HBN) is studied with respect to applications to micro- and nanoelectronics. The network extracted from β-lactamase protein [2] is investigated. The model of proton transfer in hydrogen bonds is developed based on Marcus and electrostatic theories [3]. It has been proved that the proton transfer parameter (the proton current, respectively) and the donor/acceptor electrostatic potentials depend on the pH that changes with the electrostatic potential of the donors and acceptors. Based on its hydrogen bonding network a block-element circuit [4] that models its behavior is coded in Matlab [5]. In the model circuit each donor and acceptor is substituted by electronic block-element; the proton transfer parameter is juxtaposed to electrical current and the electrostatic potential of donor/acceptor atom is juxtaposed to electrical voltage. The preformed static and dynamic simulations showed that the circuit works similarly to real electronic elements like diodes, tunneling diodes and transistors. Logical next step is to make a model of the hydrogen bonding network using CADENCE [6] CAD system using Verilog-A hardware description language [7].

The block-elements that replicate the functions of hydrogen bonding networks are connected in a microelectronic circuit that is analogues to "proton network". Static and dynamic analyses on the analogues circuit are made in Matlab. Matlab is a very convenient tool for model implementation. The Matlab model code can be converted to SPICE-like simulation code for electrical circuits, which can be next applied in CAD design systems such a Cadence.

In our case the microelectronic circuit is realized in Cadence Spectre. Its output characteristics are similar to the output characteristics of hydrogen bonding networks that include water molecules. The simulations of the modeled circuit in Cadence are comparable to the results obtained with Matlab. The hydrogen bonding network is shown on Figure 1. On Figure 2 it is shown a circuit analogous to the circuit from Figure 1 but realized with block-elements. And the realization of this circuit in Cadence is shown on Figure 3.

Circuits

The network on Figure 1 is extracted from β-lactamase protein and it contains residues from protein and water molecules. The model of proton transfer in hydrogen bonds is developed on the basis of Marcus and electrostatic theories.

The proton current, which flows through hydrogen bonding networks, depends on the change of acidic environment (pH) controlled by the electrostatic potential of donors and acceptors. Thus, we also account for the flow of protons – the proton transfer.

The subject of this paper is the hydrogen bonding network formed between the protein's main chain and the water molecules. The hydrogen bonding network on Figure 1 is taken from [4]; it shows connections between the elements. On Figure 2 is shown microelectronic circuit emulating a hydrogen bonding network from Figure 1.

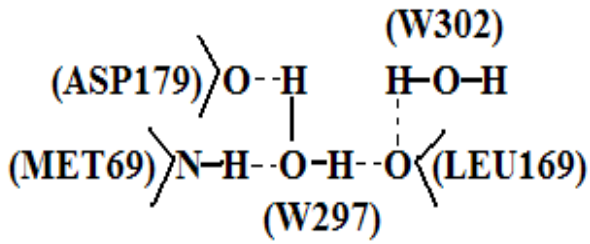


Fig.1. Hydrogen bonding network, where N is nitrogen atom of methionine residue (MET69), O is oxygen atom of water molecules W (297, 302), leucine residue (LEU169) and aspartic acid residue (ASP179).

In this hydrogen bonding network (shown in Figure 1) MET69N and W302O residues have strong proton donor properties and can be compared to voltage/current sources in micro- and nanoelectronics. The LEU169O residue is a strong proton acceptor properties and analogy can be accepted for adder of two signal and output for the circuit. The heavy atoms, forming the hydrogen bonds, are represented by three- and four-terminal networks. Each three-terminal network has equal input and output voltages and different currents.

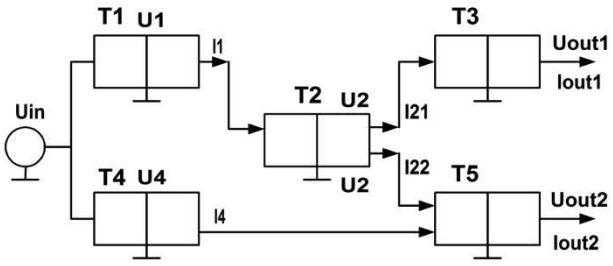


Fig.2. The respective circuit that emulates the function of the network in Fig.1.

On Figure 2 it is illustrated the circuit analogous to the hydrogen bonding network that is realized as combination of thee- and four-terminal block-elements which is investigated in [2]. The *I–V* characteristics of the block-elements are analogous to *K–V* characteristics of the hydrogen bonds in [2]. The current (*I*) of each block-element represents the proton transfer parameter (*K*) of each hydrogen bond and the voltage of each block-element represents the donor (acceptor) electrostatic potential (El. pot. [V]).

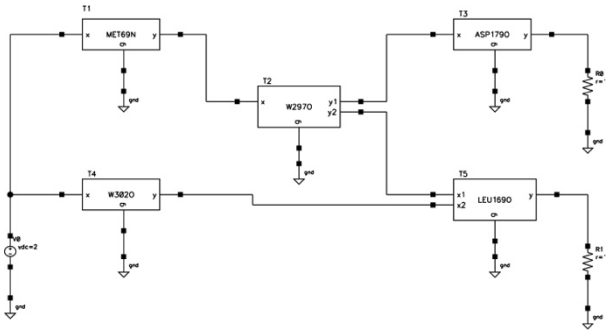


Fig.3. Circuit analogues to previously in Figure 2 but realized in Cadence.

The circuit of Figure 3 is developed in Cadence [7]. It is similar to the circuit from Figure 2. The block-elements are described in Verilog-A hardware description language. The current and voltage relations are expressed by polynomials of different orders. Some of the block-element equations in Verilog-A are given below. The rest of the equations are similar to these.

Equations of block-element T1 analogous to MET69N:

$U_1 = U_{in}$

$I_1 = (-2*10^{-6}*U_1^{6} + 2*10^{-6}*U_1^{5} + 3*10^{-5}*U_1^{4} - 6*10^{-5}*U_1^{3} - 10^{-6}*U_1^{2} + 4*10^{-5}*U_1 + 0.0018)*10^{-12}$;

I_1 and U_1 are output currents and voltages of block-element T_1. He represents three-terminal block-element and is analogues to residues MET69N; here the range of the input voltage is defined by the potential on MET69N.

Verilog-A code:

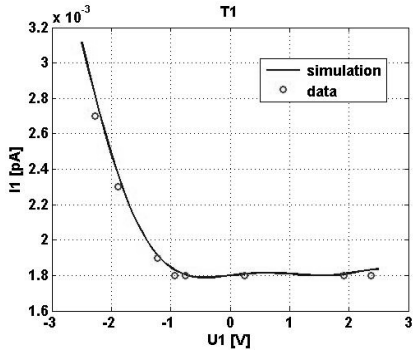
```
// VerilogA for M6, MET69N, veriloga
   `include "constants.h"
   `include "discipline.h"
   module MET69N (x, y, g);
   inout x, y, g;
   electrical x, y, g;
   electrical Vin;
   parameter real R = 1.0;
   analog
      begin
    V(Vin) <+ V(x, g);
    V(y) <+ V(Vin);
    I(x, y) <+ 10e-12*(-2*10e-
6*V(y)*V(y)*V(y)*V(y)*V(y)*V(y)+2*10e-
6*V(y)*V(y)*V(y)*V(y)*V(y)+3*10e-
5*V(y)*V(y)*V(y)*V(y)-6*10e-
5*V(y)*V(y)*V(y)-10e-6*V(y)*V(y)+4*10e-
5*V(y)+0.0018);
      end
   endmodule
```

DC analysis

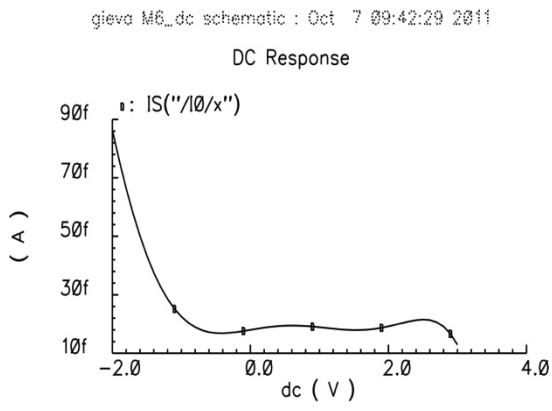
The DC analysis is performed using input voltage from -2 to +3 V in Cadence.

The results are compared to previous investigations of the hydrogen bonding network in Matlab [4].

Output graphics from DC analysis are shown on Figures 4 to 6.



a)

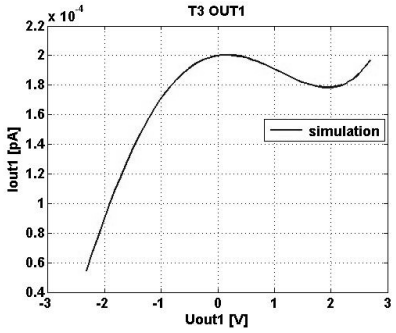


b)

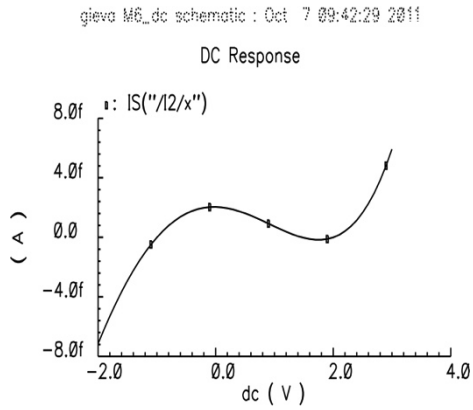
Fig. 4. The output current of block-element T1 verses input voltage.

The simulations show that the results from Cadence simulations are similar to the results from Matlab simulations.

On Figure 4 the graphics of the output currents are similar to the graphics of a diode.



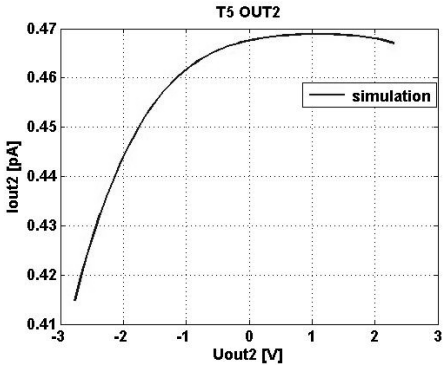
a)



b)

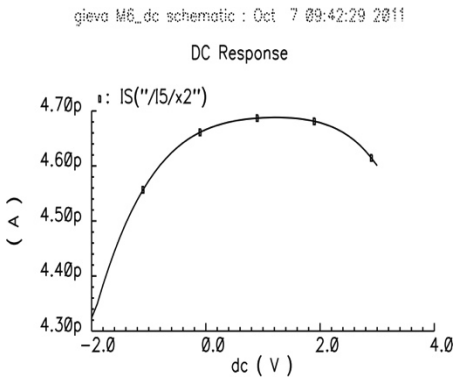
Fig.5. Output current at first output verses time a) in Matlab b) in Cadence.

On Figure 5 the curves of output currents on the one hand are similar to the characteristics of tunneling diode and on the other hand they are similar to single-electron transistors [8].



a)

On Figure 6 the graphics of the output currents are similar to the output characteristics of transistors.



b)

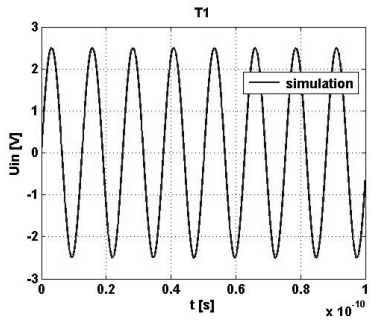
Fig.6. Output current at second output verses time a) in Matlab b) in Cadence.

On all Figures (Figures 4-6) it can be observed that the form of the curves is identical. There is no difference between magnitudes of measurements. The only difference is in the first output of the circuit: the current from Cadence simulation has negative values, while that of Matlab is positive at all time. The difference is due to the simulation environments used. Matlab calculates mathematical models only, while Cadence accounts connections between single block-elements, Kirchhoff's law and Ohm's law, and the need of the load at the output to be able to flow through it the output current and to be measurement. All this differences in the simulations environments lead to differences in the shape of the curves of voltages and currents.

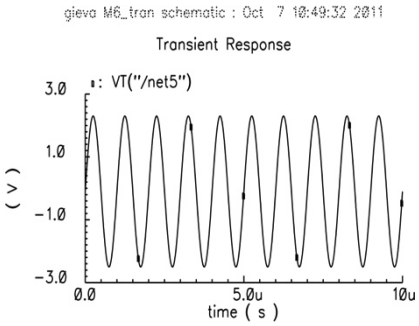
Transient analyses

The transient analysis is performed by feeding sine-shaped input voltage with amplitude of +2.4 [V] and frequency of 1 [MHz]. The Matlab simulation results are taken from [4]. The comparison of Matlab and Cadence results is given in Figures 7 to 11. The maximum operating frequency of the hydrogen bonding network is around 100 GHz like in Matlab simulations but since Cadence uses 0.35 μm technology it restricts the frequency of simulations to 1 [MHz]. That is the basic difference between Verilog-A circuit and the hydrogen bonding network simulated in Matlab.

The input voltage in both simulations (Figure 7a, b) has sinusoidal waveform and equal amplitude, but with different frequency.

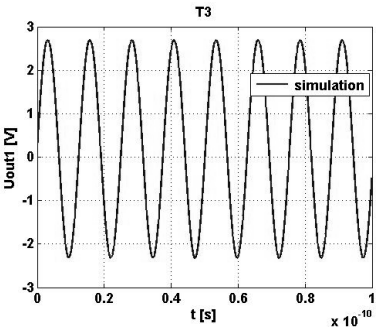


a)

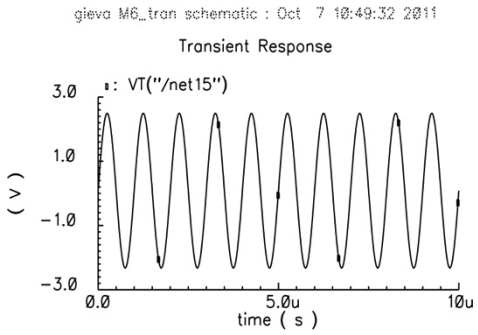


b)

Fig.7. Input voltages verses time a) in Matlab b) in Cadence.

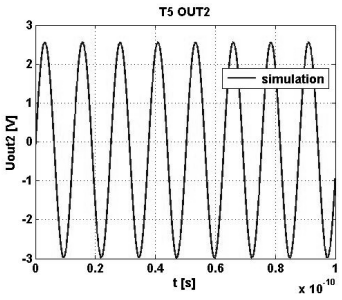


a)

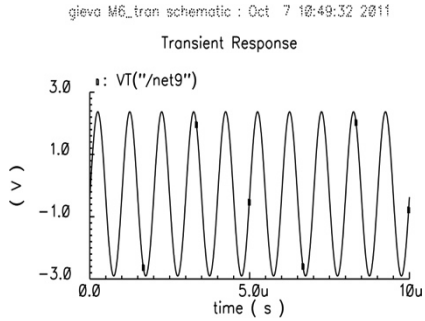


b)

Fig.8. Output voltages at first output verses time a) in Matlab b) in Cadence.



a)

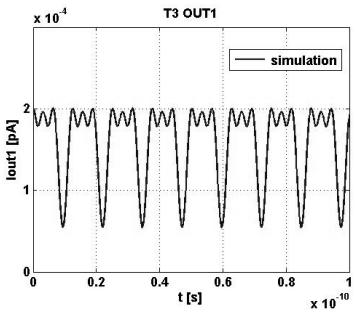


b)

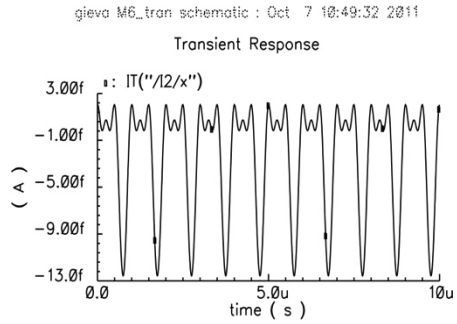
Fig.9. Output voltages at second output verses time a) in Matlab b) in Cadence.

The output voltages from the Cadence simulation are similar to the output voltages from Matlab simulation both in form and value. There is no difference between the graphics (Figures 8 and 9).

The current at the first output from simulation in Cadence (Figure 10b) is with similar shape to the current from Matlab simulation (Figure 10a). The magnitude of values is same, but have differences at negative values appeared in results from simulation in Cadence. The demonstrated difference is due to the simulation environments used. Spectre simulator is unable to override the laws and technology rules of design kit. In Cadence simulation the block-elements are not ideal elements, hence they have intrinsic resistance.

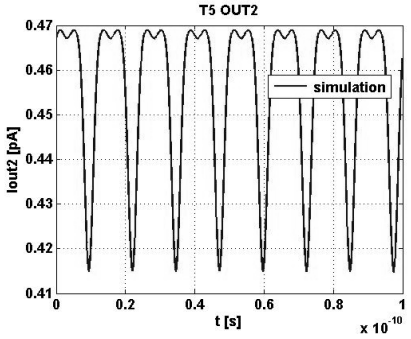


a)

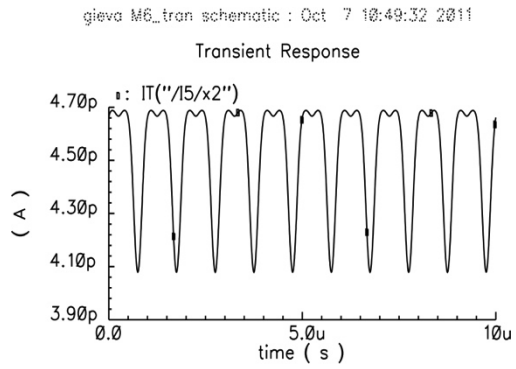


b)

Fig.10. Output current at first output verses time a) in Matlab b) in Cadence.



a)



b)

Fig.11. Output current at second output verses time a) in Matlab b) in Cadence.

The current in the second output of the Cadence circuit (Figure 11b) has the same shape and same order of magnitude like the current in the second output of the Matlab circuit (Figure 11a). In this output the values of current in the both simulations do not differ – they are always positive.

The circuit realized in Cadence behaves like the circuit modeled in Matlab.

Conclusion

The tested circuit in Cadence Spectre simulator represents the properties of a hydrogen bonding network. The developed behavioral model and the performed DC and transient analyses showed that the network is analogous to diode, tunnel diode and transistors. The circuit can successfully transfer signals despite of its extremely small sizes. From the simulation results it can be concluded that proteins and their hydrogen bonding networks are one of the best candidates for future bioelectronic devices.

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