

Simulation of Branching Hydrogen Bonding Network in Cadence

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Abstract: Microelectronic circuit based on branching hydrogen bonding network with water molecules is modeled. The hydrogen bonds of the network are presented by electronic block-elements in a microelectronic circuit. These block-elements and their electrical connections are coded in Cadence Spectre simulator where transient and DC analyses are performed. The simulations from Cadence are compared to previously obtained Matlab simulations. The results from the DC analysis show that the circuit behavior is similar to a current source or amplifier. The transient analysis shows that the circuit analogous to the hydrogen bonding network can operate as triangle pulse source.

Key-Words: Hydrogen bonding network, behavioral modeling, Verilog-a, proteins;

1 Introduction

The roadmap of microelectronics leads to miniaturized device sizes and faster signal processing. Bio- and nanoobjects are promising candidates for a basis of such future devices. Bioobjects have formed a separate branch in electronics – bioelectronics. Their target is to use natural and/or synthetic organic compounds as a medium for signal transfer. Bioelectronics focuses on development of new biosensors [1], pH-sensors [2], light sensors [3], etc.

Suitable bioobjects for future investigations and simulations are the proteins and their hydrogen bonding networks [4]. In protein hydrogen bonding network (HBN) the current is formed by protons (rather than the electron current in the conventional microelectronics) and its characteristics depend on the type and structure of the protein. For example the bacteriorhodopsin with its HBN can be used as bioelectronic device [5]. Alike bacteriorhodopsin, other proteins with HBNs can also be used for microelectronic purposes. The first step in their investigation is to model the charge transfer in them. After that, an electrical circuit functionally analogous to the HBN has to be synthesized. In this paper create such electron circuit analogous to HBN and we model its signal transfer characteristics by Verilog-A hardware description language [6].

2 Model and Equations

The hydrogen bonding network (Fig.1) is extracted from β -lactamase protein [7]. It includes atoms from protein side-chain and water molecules. The model of proton transfer in its hydrogen bonds is developed on the basis of Marcus theory [8].

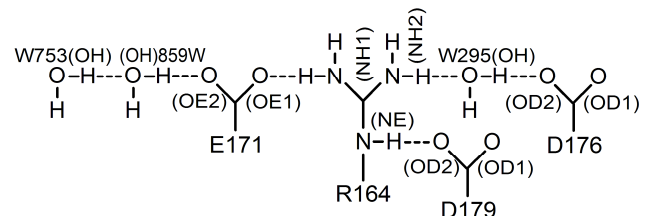


Fig.1. Hydrogen Bonding Network. NH1, NH2, and NE — nitrogen atoms of arginine residue R164, OE1 and OE2 — carboxyl oxygen atoms of glutamic acid residue E171, OD1 and OD2 - carboxyl oxygen atoms of Aspartic acid residues, OH — are oxygen atoms of water molecules (W295, W753 and 859W).

It is proved that the proton transfer parameter (proton current, respectively) depends on the pH which changes the donor/acceptor electrostatic potentials. Based on the HBN, a circuit containing block-elements of each hydrogen bond (Fig.2) is realized in Matlab [9]. This circuit emulates the operation of the HBN.

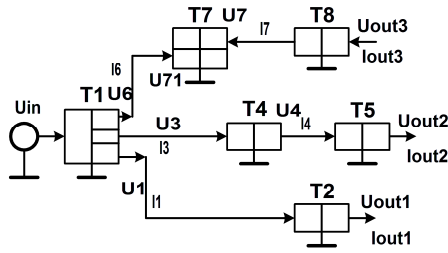


Fig.2. Microelectronics circuit analogous to HBN modeled in Matlab.

In this circuit, each donor and acceptor is juxtaposed by electronic block-element. The proton transfer parameter is presented by electrical current. The atom potentials are introduced by voltages on the block-element electrodes. The static and dynamic analyses in Matlab showed that the behavior of this block-element circuit is similar to the real microelectronic devices [10]. For this reason, we are doing the next step – the model of the hydrogen bonding network is modeled in Verilog-A. The microelectronic circuit analogous to HBN that is input in Cadence [11, 12] is presented on Fig.3.

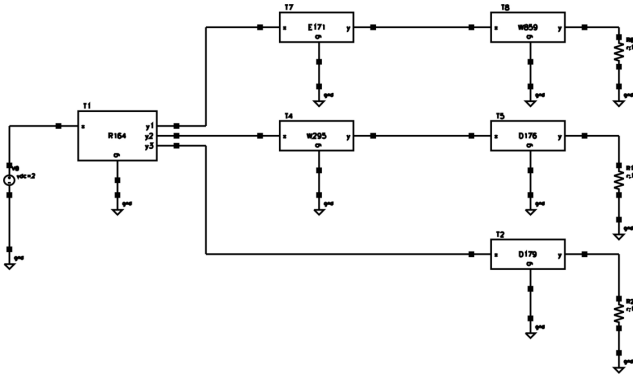


Fig.3. Microelectronics circuit analogous to HBN modeled in Cadence.

Here, the arginine residue R164 is presented by the four terminal block-element (T1). This block-element operates as current source with three outputs because R164 is a strong proton donor. The output currents of T1 are different in magnitude and they are controlled by input voltage of the block-element.

The second block-element T2 appears as the first output of the circuit and it is analogous to the strong proton acceptor – aspartic acid residue D179. The block-elements T4 and T5 are derived from water molecule w295 and aspartic acid residue D176. They are presented like three terminal block-elements. Each of them has identical input-output voltages and different input-output currents. T5 is the second output of the microelectronic circuit.

The block-element T7 originates from the strong proton acceptor E171. E171 simultaneously accept

proton from R164 and water molecule w859. The proton transfer between (w859)OH...OE2(E171) also depends on the OE1 potential. For this reason the output voltage and current (U_7 and I_7 respectively) of the analogous block-element T7 depend on the input voltage U_{71} .

The last circuit output is the block-element T8 analogous to water molecule w859. This block-element is again with three terminals. The input/output voltages are identical but the input/output current are different (similarly to T5 with derived from w295).

The electrical relations between each block-element in the circuit are described by different polynomials.

The equations describing the first block-element T1 are:

$$U_1 = U_{in} \{-1.3 \text{ to } 3.2\} \quad (1)$$

$$I_1 = -5 \times 10^{-5} \times U_1^3 - 8 \times 10^{-5} \times U_1^2 - 2 \times 10^{-5} \times U_1 + 0.0071 \quad (2)$$

The equations for the second output of T1 are:

$$U_3 = 1.0066 \times U_1 - 0.0967 \quad (3)$$

$$I_3 = 0.0005 \times U_3^3 - 0.0006 \times U_3^2 - 0.001 \times U_3 + 0.0279 \quad (4)$$

The equations for the third T1 output:

$$U_6 = 1.0193 \times U_1 + 0.3216 \quad (5)$$

$$I_6 = -0.0072 \times U_6^3 + 0.0069 \times U_6^2 - 0.03 \times U_6 + 1.2646 \quad (6)$$

The equations for T2 are:

$$U_2 = U_{out1} = 0.9994 \times U_1 - 0.3421 \quad (7)$$

$$I_2 = I_{out1} = I_1 \quad (8)$$

The equations for T4 are:

$$U_4 = 0.9802 \times U_3 + 0.4294 \quad (9)$$

$$I_4 = -0.1922 \times U_4^3 + 0.2821 \times U_4^2 + 0.0044 \times U_4 + 1.6922 \quad (10)$$

The equations for block-element T5 witch are the second circuit output:

$$U_5 = U_{out2} = 0.9374 \times U_4 + 1.4074 \quad (11)$$

$$I_5 = I_{out2} = I_4 \quad (12)$$

Equations for the T7 block-element:

$$U_{71} = 1.0387 \times U_6 - 0.5498 \quad (13)$$

$$U_7 = 0.9705 \times U_{71} - 0.5167 \quad (14)$$

$$I_7 = 0.0591 \times U_7^3 + 0.0162 \times U_7^2 - 0.6792 \times U_7 + 4.5597 \quad (15)$$

Equations for the T8 block-element that is the third output of the circuit:

$$U_8=U_{out3} = -0.0437 \times U_7^2 + 1.0318 \times U_7 + 0.4173 \quad (16)$$

$$I_8=I_{out3} = 0.0041 \times U_8^4 - 0.0456 \times U_8^3 + 0.0772 \times U_8^2 + 0.234 \times U_8 + 1.8401 \quad (17)$$

These equations are coded in Cadence by Verilog-A. Excerpt of the code is given below.

```
// VerilogA for M4, W295, veriloga
`include "constants.h"
`include "discipline.h"
module W295 (x, y, g);
inout x, y, g;
electrical x, y, g;
electrical Vin;
analog
begin
V(Vin) <+ V(x, g);
V(y) <+ 0.9802*V(Vin)+0.4294;
I(x, y) <+ (-0.1922*V(y)*V(y)*V(y) +
0.2821*V(y)*V(y)*V(y) + 0.0044*V(y) +
1.6922)*10e-12;
end
endmodule
```

```
// VerilogA for M4, W859, veriloga
`include "constants.h"
`include "discipline.h"
module W859 (x, y, g);
inout x, y, g;
electrical x, y, g;
electrical Vin;
analog
begin
V(Vin) <+ V(x, g);
V(y) <+ -0.0437*V(Vin)*V(Vin) +
1.0318*V(Vin) + 0.4173;
I(x, y) <+ (0.0041*V(y)*V(y)*V(y)*V(y) -
0.0456*V(y)*V(y)*V(y)+0.0772*V(y)*V(y) +
0.234*V(y)+1.8401)*10e - 12;
end
endmodule
```

3 DC Analysis

The DC analysis is performed by varying $U_{in} = -1.3 \div +3.2$ V. Next, a comparison between the I - V characteristics obtained by Matlab and I - V characteristics obtained by Cadence is done. The characteristics are shown on Figures 4-11. The simulations illustrate that all output voltages are proportional to the input voltage (Fig.4 and Fig.5). U_{out1} and U_{out3} change in the range between -1.5 V to +3.2 V, U_{out2} – in the interval between +0.5 to 4.5 V when U_{in} interval is between -1.3 to +3.2 V. These results are obtained from both simulations in Matlab and Cadence.

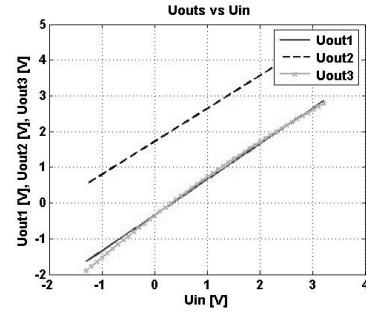


Fig.4. Outputs voltages vs. input voltage in Matlab.

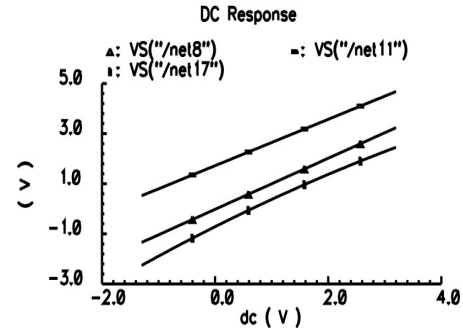


Fig.5. Outputs voltages vs. input voltage in Cadence.

The currents in the different outputs are changing from 10^{-3} to 10^1 pA. The I - V characteristics of first and second outputs are with similar shape (Fig.6-9) but are shifted to each other. For the first output, when output voltage is between -1.5 to 0 V the current does not change. Therefore, this circuit can be used as a current source. When the voltage of the first output is between 0 and +3 V then the current decreases, i.e. the circuit works as an amplifier. Similar conclusions can be drawn also for the second output: when U_{out2} is between +0.5 and +2.5 V then the current does not change (see Fig.8 and Fig.9). When the U_{out2} is between +2.5 and +4.5 V the circuit is similar to an amplifier.

The characteristics from Matlab and Cadence have identical forms but the currents from Cadence simulations have negative values (in contrast to Matlab simulations). This difference originates from the different nature of the simulators used.

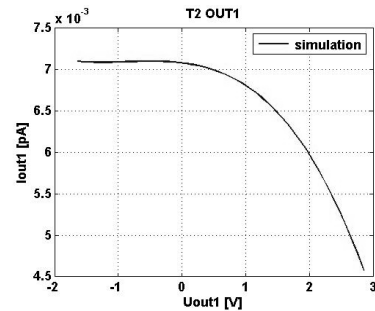


Fig.6. First output characteristics in Matlab.

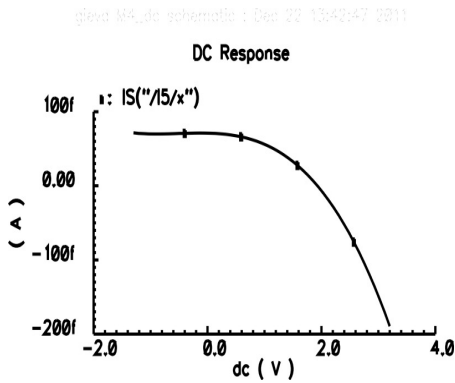


Fig. 7. First output characteristics in Cadence.

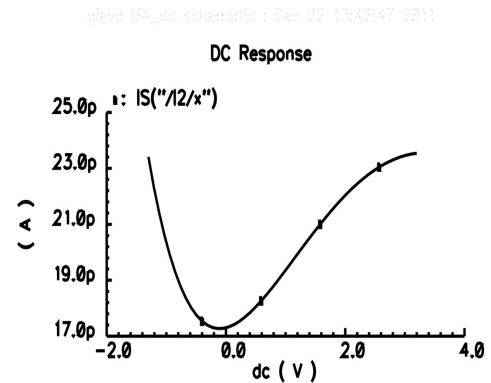


Fig. 11. Characteristics of the third output in Cadence.

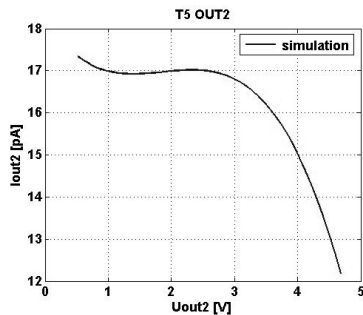


Fig. 8. Characteristics of the second output in Matlab.

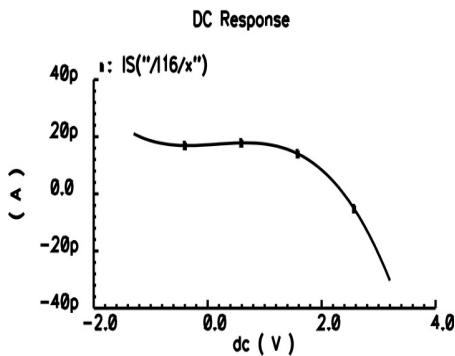


Fig. 9. Second output characteristics in Cadence.

The I - V characteristic of third output is very interesting (Fig. 10 and Fig. 11). It can be split in two parts: 1) when the voltage is between -2 and -0.8 V then output current decreases, 2) when the output voltage is between -0.8 and $+2.8$ V then the current increases. Such output characteristics cannot be found in conventional devices.

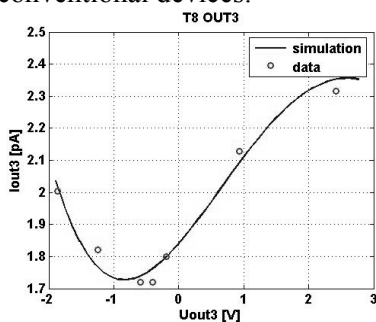


Fig. 10. Characteristics of the third output in Matlab.

4 Transient Analysis

The research of hydrogen bonds shows that the proton transfer takes place for maximal time on the order of 10^{-10} s. Therefore, the analogues microelectronic circuits should operate at very high frequencies (approximately 10 GHz). These conditions are met when performing the simulations in Matlab but in Cadence Spectre the frequencies are on the order of 1 MHz because when simulating in GHz-range the results are seriously distorted (the reason can be traced back to the intrinsic limitations of the design kit models embedded in the Cadence Spectre simulator that we are using in simulations).

Stable operation of the circuit in Matlab is observed when the input voltage is $U_{in} = -1 + \sin(t \times 1.5 \times 10^{11})$. The same input signal form but with different frequency is fed in Cadence Spectre schematic to compare the results when similar voltages are input.

When the input signal in Cadence, shown in Fig. 12, is sinusoidal, the signals at three outputs are triangular pulses shown in Fig. 14-16.

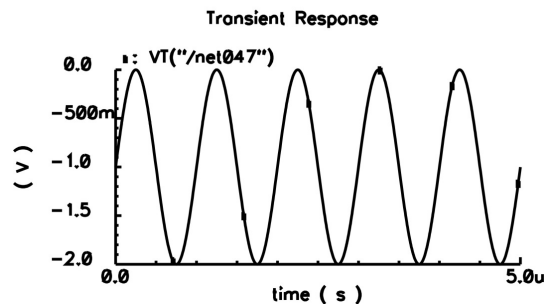


Fig. 12. Input voltage vs. time in Cadence.

On Fig. 13 and Fig. 14 are shown outputs current of the first output of the circuit (Fig. 13 Matlab, Fig. 14 Cadence). The general similarities between the two simulations is the shape of the curves, measurement order of magnitude of current fA and that they are with positive value when was applied negative input voltage. The difference between the

two simulations is in the amplitude of the signal in simulation. The amplitude in Cadence is much greater. Also the value of current in Cadence is almost 10 times higher than in Matlab. Differences have also in the frequency of the signal, but since the input voltages in two simulations are with different frequencies there is no way the current frequencies are the same. The difference in the rates is necessary because different environments for simulations are used. These are the main differences between the two simulations. In Matlab in GHz-range, in Cadence in MHz-range.

There is a difference in the amplitude of the output currents for different simulation environments. The amplitudes in Cadence are many times higher than these in Matlab. This is illustrated in Fig.13 and Fig.14.

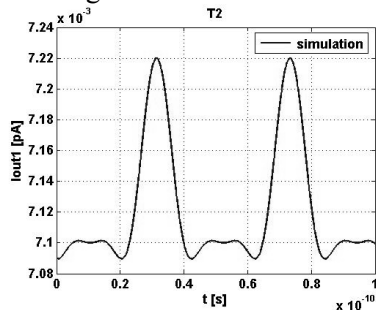


Fig.13. Output current at the first output vs. time in Matlab.

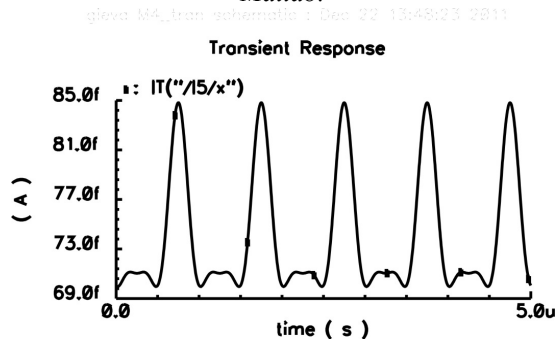


Fig.14. Output current at the first output vs. time in Cadence.

Fig.15 and Fig.16 show the output currents at the second and third outputs of the circuit in Cadence Spectre. Here we observed the same relations between currents and voltages as in the previous case that is why we do not show the respective graphics. In this case there is the same change in the frequency of the output current depending on the frequency of the input voltage. The circuit can be controlled by voltage.

Both I_{out2} and I_{out3} signals have similar form, with magnitudes of the order of pA and have a positive value when to the input is applied negative voltage. Triangular pulses with the same frequency but different amplitude are generated.

The amplitudes of the currents at the three circuit outputs are with different magnitudes at same frequency of 1 MHz. When changing the input voltage frequency, the frequency of the output current also changes. This shows how we can control the output signals.

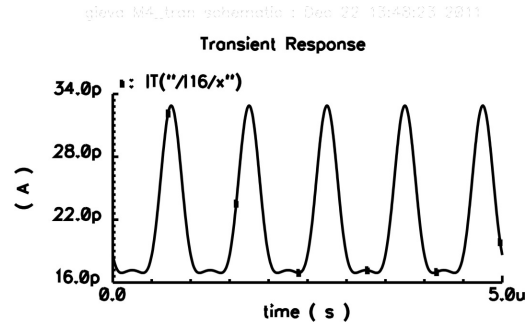


Fig.15. Output current in the second output vs. time in Cadence.

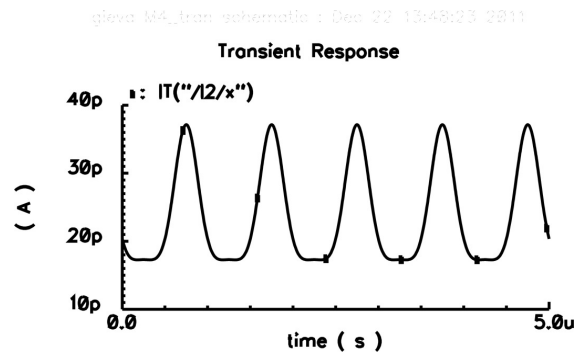


Fig.16. Output current in the third output vs. time in Cadence.

On Fig.14 to Fig.16 it can be observed that the pulses have equal frequency, phase and positive amplitude. All the three pulses have different amplitudes, magnitudes but the same duration of the pulses. On the other hand, we can control the period of the output pulses by changing the period of the input voltage. For example, in Fig.17 it is given the characteristics of I_{out2} versus time obtained by halving the period of the input signal in Cadence Spectre. Similar characteristics were obtained for the other outputs, therefore we show the results only for one output. Comparing Fig.17 with Fig.15 it can be seen that the triangular pulses on Fig.17 are at the higher frequency. This is true for both the simulations in Matlab and in Cadence Spectre. We found that regardless of the simulation environment used the results are the similar. Finally, the circuit can operate as triangular pulse source which can be controlled by changing the period of the input voltage to achieve the desired frequency or amplitude.

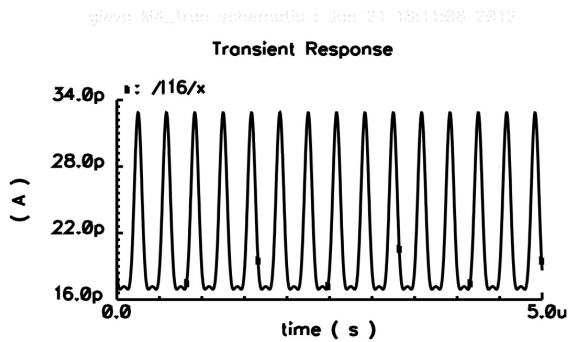


Fig.17. Output current in the second output vs. time in Cadence with different frequency.

5 Conclusion

The microelectronic circuit developed in Cadence Spectre well reproduces the functions of the hydrogen bonding network. The DC analyses showed that the circuit operates as a current source or amplifier. The transient analyses demonstrated that the circuit analogous to the hydrogen bonding network can operate as a frequency controlled triangle pulse source. The third output of the source can work with different amplitudes and widths of the pulses. From the simulations it can be seen that the proteins and their hydrogen bonding networks are promising candidates for future microelectronics devices.

6 Acknowledgment

The research in this paper was carried out within the framework of Contract No. D-002-126/15.12.2008.

References:

- [1] Wolfgang Göpel, *Bioelectronics and nanotechnologies*, Biosensors & Bioelectronics 13 (1998) 723–728
- [2] Paola Fabbri, Francesco Pilati, Luigi Rovati, Ruel McKenzie, Jovan Mijovic, *Optical Materials, Poly(ethylene oxide)–silica hybrids entrapping sensitive dyes for biomedical optical pH sensors: Molecular dynamics and optical response*, Optical Materials 33 (2011) 1362–1369, 2011.
- [3] Sudarshan Rajagopal and Keith Moffat, *Crystal structure of a photoactive yellow protein from a sensor histidine kinase: Conformational variability and signal transduction*, 1649-1654 (2002)
- [4] D. Michael P. Mingos, *Supramolecular Assembly via Hydrogen Bonds I*, Springer Berlin Heidelberg New York, ISSN 1616-8550, 2004.
- [5] Kevin J. Wise, Nathan B. Gillespie, Jeffrey A. Stuart, Mark P. Krebs and Robert R. Birge, *Optimization of bacteriorhodopsin for bioelectronic devices*, 387-394 (2002).
- [6] D. Fitzpatrick, I. Miller, *Analog Behavioral Modeling with the Verilog-A Language*, Kluwer Academic Publishers, New York, Boston, Dordrecht, London, Moscow, 2003, pp 41-86, ISBN: 0-7923-8044-4
- [7] R. Rusev, G. Angelov, T. Takov, B. Atanasov, M. Hristov, "Comparison of Branching Hydrogen Bonding Networks with Microelectronic Devices", Annual J. of Electronics, 2009, Vol.3, No. 2, pp. 152-154. ISSN 1313-1842.
- [8] Markus A., and V. Helms. 2001. *Compact parameter set for fast estimation of proton transfer rates*. J. Phys. Chem. 114: 3
- [9] Matlab website <http://www.mathworks.com>.
- [10] Rostislav Rusev, George Angelov, Elitsa Gieva, Marin Hristov, and Tihomir Takov, *Hydrogen Bonding Network Emulating Frequency Driven Source of Triangular Pulses*", International Journal of Microelectronics and Computer Science, vol.1, No3, 2010
- [11] Radonov R., *Methodology for design with CADENCE* (in Bulgarian), National conference with international participation Elektronika 2008, Sofia, Bulgaria, 29 – 30 May 2008, pp. 182 – 186, ISSN 1313-3985.
- [12] Website Cadence www.cadence.com