Digital Operation of Microelectronic Circuits Analogous to Protein Hydrogen Bonding Networks

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Abstract: *Two hydrogen bonding networks with water molecules and branching residues extracted from β-lactamase protein are investigated and their proton transfer characteristics are studied by creating analogous electrical circuits consisting of block-elements. The block-elements and their proton transfer are described by polynomials that are coded in Matlab and in Verilog-A for use in the Spectre simulator of Cadence IC design system. DC and digital pulse analyses are performed to demonstrate that some circuit outputs behave as repeaters while other – behave as inverters. The results also showed that the HBN circuits might behave as a D-latch and a demultiplexer.*

Keywords: *Hydrogen Bonding Networks (HBNs), Proteins, β-lactamase, Behavioral modeling, Verilog-A.*

Introduction

The ongoing trend for increase in signal processing performance requires for introduction of new materials. A promising approach is to study algorithms and methods using bio-objects and their structures by analogy with the nature. Good example of this approach is the use of artificial neuron networks for calculation of complex numerical problems. Another example is the DNA based bio-computing [1].

Bio-objects and bio-structures might be the new elements and devices that could supplement or even replace conventional CMOS microelectronic devices. The aim is to utilize existing and/or synthesized organic compounds as elements, circuits and medium for signal transfer or signal processing. Prospective candidate for signal transfer and signal processing are the proteins and their hydrogen bonding networks [3].

In the present paper, two hydrogen bonding networks (HBNs) extracted from β-lactamase protein [8] and their proton transfer characteristics are studied. The hydrogen bonding networks are selected based on their donor or acceptor residues. Microelectronic circuits analogous to the HBNs are created in Cadence Spectre simulator in order to study their characteristics.

The investigation of transient characteristics of the circuits that are analogous to HBNs showed that the HBNs could process digital signals. It was demonstrated that the input and output currents meet the requirements in digital processing for setting up the circuit operating levels and setting up the levels of logic “0” and logic “1”. The digital simulations disclosed that some circuit outputs operate as repeaters while other outputs operate as inverters. The results also showed that the HBN circuits might operate as a D-latch and a demultiplexer.

Based on the circuit analyses it can be concluded that the HBNs possess the basic properties needed for digital circuitry and hence they might have applications to digital electronics circuits.

Hydrogen bonding networks, models, and equations

Several types of hydrogen bonding networks extracted from the β-lactamase protein are investigated and their transfer characteristics [7] and [6] are shown on Figs. 1 and 2.

The parameter K (dimension of a potential – [J/mol]) is introduced for quantitative estimation of proton current. This parameter is proportional to proton current. The parameter is calculated by software based on Markus approximation following [4]. The program code uses the following equations:

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

where K – speed constant, k_B – Boltzmann constant, Eb – energy of the barrier, h – Plank constant, ω – frequency, T – temperature (in Kelvin). The barrier energy is calculated by:

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

where $R(DA)$ is the distance between donor and acceptor, E_{12} is the difference between the energies of donor and acceptor.

The networks are selected based on the sought types of donor and acceptor residues in order to demonstrate and investigate their typical properties. The following typed of HBNs are selected:

Network 2: network with water molecules, named M2 [7];
Network 4: branching network, named M4 [6].

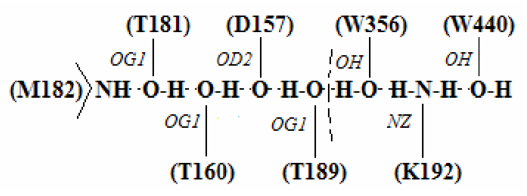

Fig. 1 HBN M2

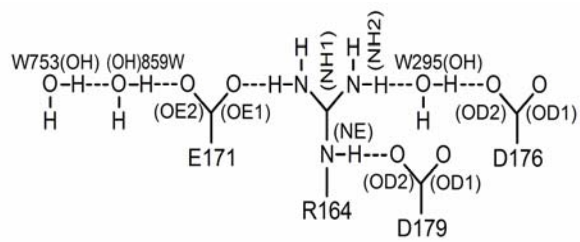

Fig. 2 HBN M4

After analyzing the HBNs and their properties, we create the respective microelectronic block-elements to emulate the HBN operation. The HBN can be divided in separated heavy atoms that participate in hydrogen bonds shown in Fig. 3.

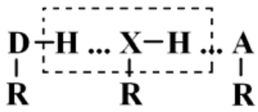

Fig. 3 Sample HBN with conditional separation
of the heavy atoms

In the analogous circuit each heavy atom (which is both donor and acceptor) is designated as a separate block-element, shown in Fig. 4.

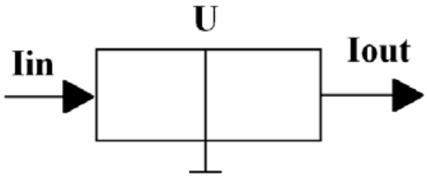

Fig. 4 Block-element that is analogous
to heavy atom from the hydrogen bonding network

Schematically, the acceptor part of the heavy atom is depicted as input part of the block-element in which flows in the input current I_{in}; the acceptor part of the heavy atom is the output of the block-element, where flows out the output current I_{out}. The potentials at the input and the output of the block-element are equal to the potential U of the heavy atom. The magnitude of the input and output currents are proportional to the proton transfer parameter of the hydrogen bonding network where the heavy atom is present.

The so constructed block-elements are three- and four-terminal elements that can be used in circuits to simulate the proton transport in hydrogen bonding networks. The relation between the input and output currents can be expressed through the parameter U – the potential of the heavy atom. Similarly can be treated the two- and three terminal block-elements where the currents also can be expressed through the same parameter U.

With the so constructed block-elements, we can model electronic circuits that are functionally analogous to the hydrogen bonding networks. Thus, each circuit could be described in Verilog-A [2] and simulated in Cadence Spectre simulator [9].

Model and equations of the M2 network

To model system is constituted by the HBN shown in Fig. 1 [7], and the proton transfer characteristics of its elements are investigated and described by Markus theory; there are water molecules in the investigated network. The water molecules expand the signal processing possibilities of the circuit.

Based on the M2 network, it is developed a microelectronic circuit [5] shown in Fig. 5; this circuit is coded in Matlab.

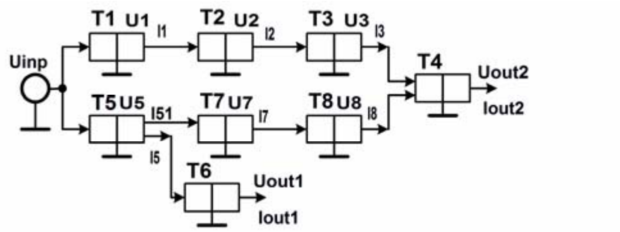

Fig. 5 Microelectronic circuit analogous to HBN coded in Matlab

The microelectronic circuit that is analogous to the HBN is used in Cadence Spectre simulator using Verilog-A (Fig. 6).

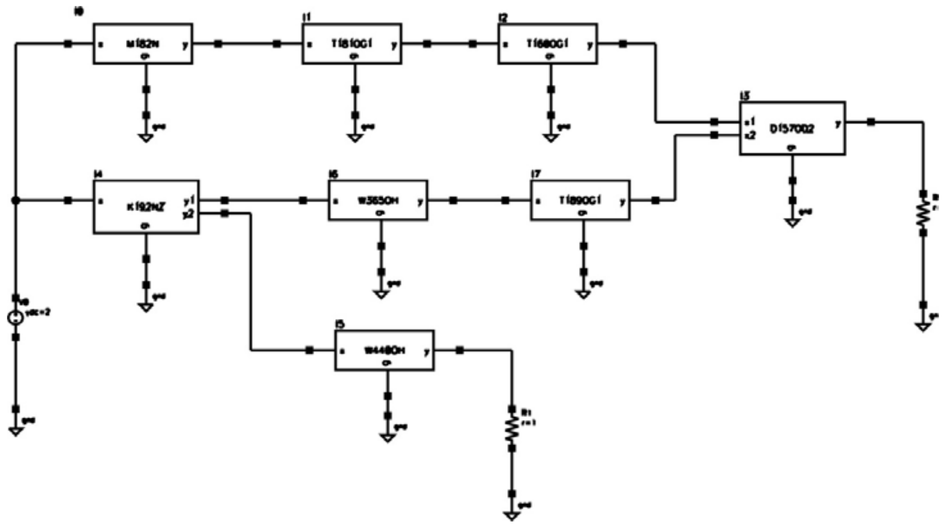

Fig. 6 Microelectronic circuit analogous to HBN coded in Cadence

The block-elements are described using polynomials listed below.

Eqs. (3) and (4) describe block-element T1; it models M182N (Fig. 1). The voltage range is between –2.1 до +2.65 V.

$$U_1 = U_{in} = [-2.1:0.1:2.65] \quad (3)$$

$$I_1 = 7\times10^{-5}\times U_1^4 - 7\times10^{-6}\times U_1^3 - 0.0011\times U_1^2 + 0.0047\times U_1 + 0.2514 \quad (4)$$

The next equations, (5) and (6), describe block-element T3 that models the (T181) OG1 (Fig. 1).

$$U_3 = 1.0248\times U_2 + 0.028 \quad (5)$$

$$I_3 = 0.00019\times U_3^3 - 0.0003\times U_3^2 - 0.0021\times U_3 + 0.0101 \quad (6)$$

The block-element T5 models (K192) NZ (Fig. 1):

$$U_5 = 0.894\times U_1 + 0.2369 \quad (7)$$

$$I_5 = 0.0006\times U_5^4 + 0.9\times10^{-5}\times U_5^3 - 0.0064\times U_5^2 + 0.0061\times U_5 + 0.072 \quad (8)$$

$$I_{51} = -0.0013 \times U_5^5 + 0.0039 \times U_5^4 + 0.0041 \times U_5^3 - 0.016 \times U_5^2 + 0.0045 \times U_5 + 0.057 \quad (9)$$

The block-element T6 models (W440) OH; T6 is the first input of the microelectronic circuit.

$$U_6 = 1.0809 \times U_5 + 0.1706 \quad (10)$$

$$I_6 = I_5 \quad (11)$$

Next is the water molecule (W365) OH described by the block-element T7:

$$U_7 = 1.0004 \times U_5 + 0.1371; \quad (12)$$

$$I_7 = 0.000495 \times U_7^5 - 0.00207 \times U_7^4 - 0.0013 \times U_7^3 + 0.0116 \times U_7^2 - 0.0006 \times U_7 + 0.0353 \quad (13)$$

The equations for the block-element T8 that is analogous to (T189) OG1 are:

$$U_8 = 0.0303 \times U_7^2 + 0.9435 \times U_7 - 0.3204 \quad (14)$$

$$I_8 = -6 \times 10^{-6} \times U_8^5 + 10^{-5} \times U_8^4 + 5 \times 10^{-5} \times U_8^3 - 6 \times 10^{-5} \times U_8^2 - 0.000189 \times U_8 + 0.00064 \quad (15)$$

The second output of the circuit is at block-element T4 that models (D157) OD2:

$$U_4 = 0.9904 \times U_8 + 0.0967 \quad (16)$$

$$I_4 = I_3 + I_8 \quad (17)$$

These equations are coded in Cadence using Verilog-A. Excerpt of the code is listed below:

```
// VerilogA for VerilogA, T160OG1, veriloga
`include "constants.h"
`include "discipline.h"
module T160OG1 (x, y, g);
inout x, y, g;
electrical x, y, g;
electrical Vin;
analog
begin
V(Vin) <+ V(x, g);
V(y) <+ 1.0248*V(Vin)+0.028;
I(x, y) <+ 10e-12*(0.00019*V(y)*V(y)*V(y)-0.0003*V(y)*V(y)-
0.0021*V(y)+0.0101);
end
endmodule

// VerilogA for VerilogA, T181OG1, veriloga
`include "constants.h"
`include "discipline.h"
module T181OG1 (x, y, g);
inout x, y, g;
electrical x, y, g;
electrical Vin;
analog
begin
V(Vin) <+ V(x, g);
```

```
V(y) <+ 0.974*V(Vin)+0.0627;
I(x, y) <+
10e-12*(-6*10e-6*V(y)*V(y)*V(y)*V(y)-
0.00012*V(y)*V(y)*V(y)+0.00035*V(y)*V(y)+0.0013*V(y)+0.0083);
end
endmodule
```

Model and equations of the M4 network

The network on Fig. 2 is extracted from *β*-lactamase protein and includes water molecules and atoms from adjacent chains of the protein. The proton transfer model is developed on the basis of Markus theory [4].

It is proved that the proton transfer parameter (the proton current) depends on the change of pH, which changes the electrostatic potential of donors and acceptors. This HBN is described in Matlab in a circuit consisting of block-elements (Fig. 7).

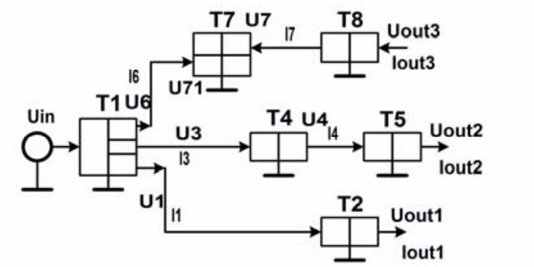

Fig. 7 Functionally analogous to HBN M4 microelectronic circuit consisting of block-elements coded in Matlab

The same circuit is used in Cadence (Fig. 8) but now it is coded in Verilog-A.

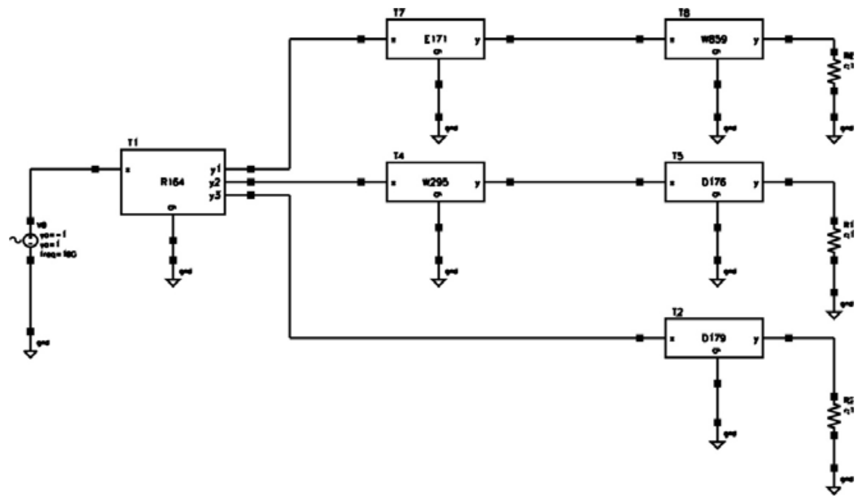

Fig. 8 Functionally analogous to HBN M4 microelectronic circuit in Cadence

The relations between currents and voltages are again described using polynomials.

The output block-element T1 is described by Eqs. (18) and (19)

$U_1 = U_{in}$ {–1.3 to 3.2} (18)

$$I_1 = -5\times10^{-5}\times U_1^3 - 8\times10^{-5}\times U_1^2 - 2\times10^{-5}\times U_1 + 0.0071 \quad (19)$$

The equations for the block-element T2 are:

$$U_2 = U_{out1} = 0.9994\times U_1 - 0.3421 \quad (20)$$

$$I_2 = I_{out1} = I_1 \quad (21)$$

T3 block-element is described by:

$$U_3 = 1.0066\times U_1 - 0.0967 \quad (22)$$

$$I_3 = 0.0005\times U_3^3 - 0.0006\times U_3^2 - 0.001\times U_3 + 0.0279 \quad (23)$$

Block-element T4:

$$U_4 = 0.9802\times U_3 + 0.4294 \quad (24)$$

$$I_4 = -0.1922\times U_4^3 + 0.2821\times U_4^2 + 0.0044\times U_4 + 1.6922 \quad (25)$$

The second output of the circuit, T5 is described by:

$$U_5 = U_{out2} = 0.9374\times U_4 + 1.4074 \quad (26)$$

$$I_5 = I_{out2} = I_4 \quad (27)$$

The equations for the third output T6 are:

$$U_6 = 1.0193\times U_1 + 0.3216 \quad (28)$$

$$I_6 = -0.0072\times U_6^3 + 0.0069\times U_6^2 - 0.03\times U_6 + 1.2646 \quad (29)$$

T7 block-element is described by:

$$U_{71} = 1.0387\times U_6 - 0.5498 \quad (30)$$

$$U_7 = 0.9705\times U_{71} - 0.5167 \quad (31)$$

$$I_7 = 0.0591\times U_7^3 + 0.0162\times U_7^2 - 0.6792\times U_7 + 4.5597 \quad (32)$$

The block-element T8 that is the third output of the microelectronic circuit is described by:

$$U_8 = U_{out3} = -0.0437\times U_7^2 + 1.0318\times U_7 + 0.4173 \quad (33)$$

$$I_8 = I_{out3} = 0.0041\times U_8^4 - 0.0456\times U_8^3 + 0.0772\times U_8^2 + 0.234\times U_8 + 1.8401 \quad (34)$$

The above equations are coded in Cadence using Verilog-A.

```
// VerilogA for M4, D176, veriloga
`include "constants.h"
`include "discipline.h"
module D176 (x, y, g);
inout x, y, g;
electrical x, y, g;
electrical Vin;
analog
begin
V(Vin) <+ V(x, g);
V(y) <+ 0.9374*V(Vin)+1.4074;
I(x, y) <+
10e-12*(-
0.1922*V(Vin)*V(Vin)*V(Vin)+0.2821*V(Vin)*V(Vin)+0.0044*V(Vin)+1.6922);
end
endmodule
```

```
// VerilogA for M4, D179, veriloga
`include "constants.h"
`include "discipline.h"
module D179 (x, y, g);
inout x, y, g;
electrical x, y, g;
electrical Vin;
analog
   begin
   V(Vin) <+ V(x, g);
   V(y) <+ 0.9994*V(Vin)-0.3421;
   I(x, y) <+
   (-5*10e-5*V(y)*V(y)*V(y)-8*10e-5*V(y)*V(y)-2*10e-5*V(y)+0.0071)*10e-12;
   end
endmodule
```

Analyses

DC analysis of the M2 network

The DC analysis with input voltage between –2.1 and +2.65 [V] is performed. The output characteristics of the microelectronic circuit I_{out1}, I_{out2} = f(U_{in}) (Fig. 9 Matlab and Fig. 10 Cadence) are similar with the output characteristics of differential amplifier. With increasing the input voltage the output current of first output decreases, while the current output of the second output increases. Both output currents are positive all the time and they saturated.

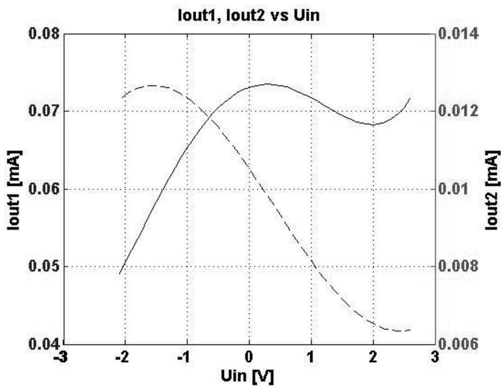

Fig. 9 The output characteristics of the microelectronic circuit, analogous to the network M2

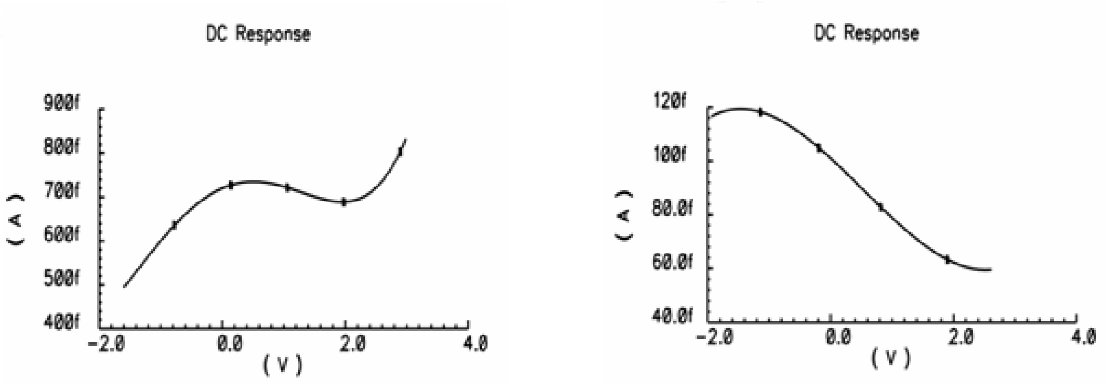

Fig. 10 The output characteristics of the microelectronic circuit, analogous to the network (M2)

The voltage transfer characteristics (Fig. 11) show that both output voltages are linear functions of the input voltage and are shifted to each other.

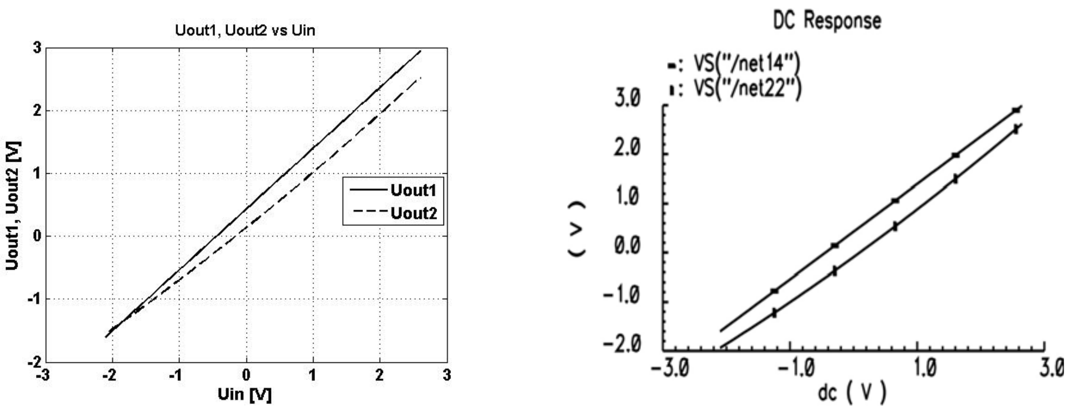

Fig. 11 Outputs voltages vs. input voltage in Matlab and Cadence

Hence, the microelectronics circuit analogous to the HBN with water molecules and protein residues could operate as CMOS differential power amplifier.

DC analysis of the M4 network

The DC analysis is performed by varying U_{in} = –1.3 ÷ +3.2 V. The characteristics are shown on Figs. 12-15. The simulations illustrate that all output voltages are proportional to the input voltage (Fig. 12). Uout1 and Uout3 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.

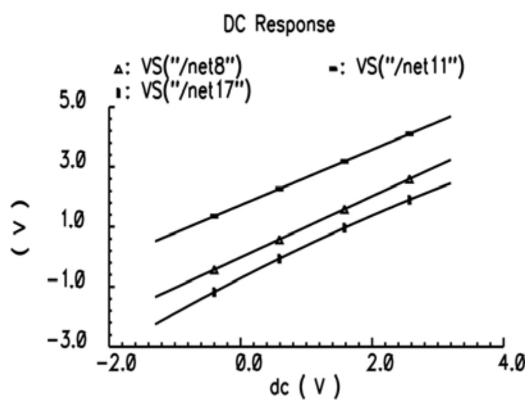

Fig. 12 Outputs voltages vs. input voltage in Cadence

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 (Figs. 13-14) but are shiftes 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 could 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 (current source). When the U_{out2} is between +2.5 and +4.5 V the circuit is similar to an amplifier.

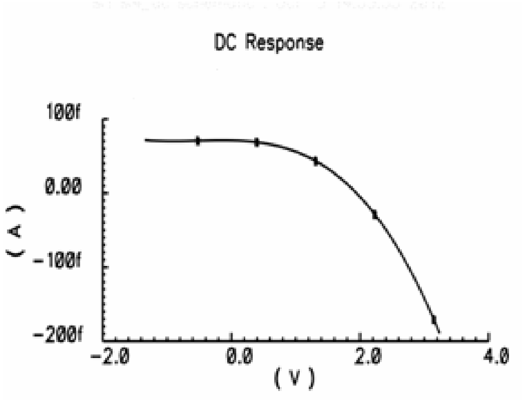

Fig. 13 Characteristics of the first output in Cadence

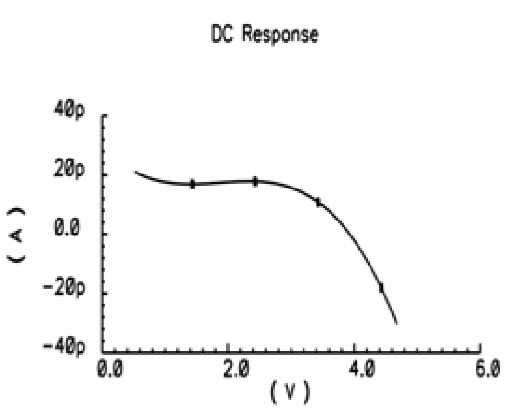

Fig. 14 Characteristics of the second output in Cadence

The I-V characteristic of third output is very interesting (Fig. 15). 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.

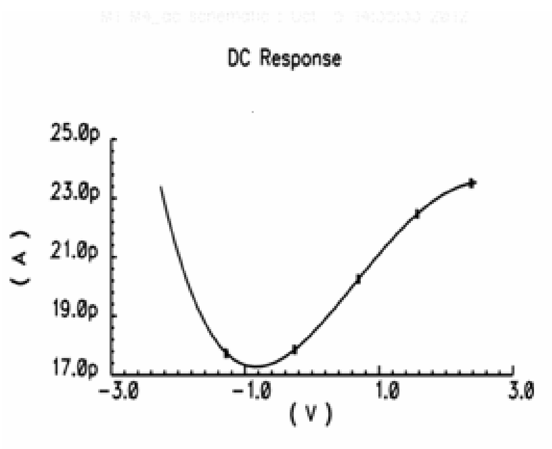

Fig. 15 Characteristics of the third output in Cadence

Digital analysis of the M2 network

Operating levels of the circuit for digital simulation

From the Fig. 16 we see that there are two stable states and a switch between them. We determine the levels for the input and output logic “0” and logic “1”.

For the input logic “0” the levels are between 0.13 to 0.17 pA, for the input logic “1” the levels are between 0.22 to 0.37 pA.

For the output logic “0” the levels are between 0.142 to 0.158 pA. For the output logic “1” 0.237 to 0.262 pA.

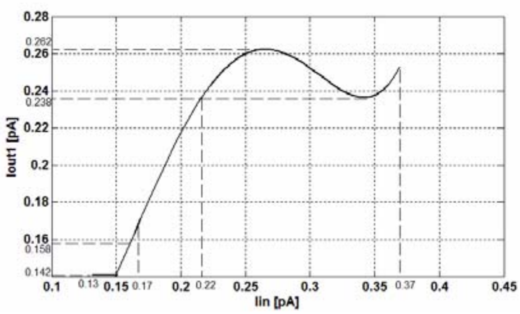

Fig. 16 Transfer characteristic of the first output of the circuit. The output current as a function of the input current.

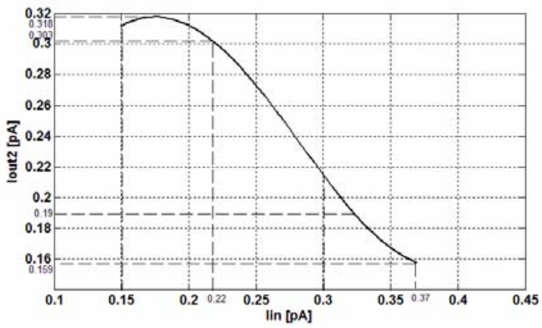

Fig. 17 Transfer characteristic of the second output of the circuit. The output current as a function of the input current.

From the Fig. 17 the logic levels are: For the input logic “0” the levels are between 0.15 to 0.22 pA, for the input logic “1” the levels are between 0.30 to 0.37 pA.

For the output logic “0” the levels are between 0.16 to 0.19 pA. For the output logic “1” 0.305 to 0.32 pA.

From the transfer characteristics (Figs. 16-17) and the determined logic levels it can be seen that the logic is positive and the logic levels follow the input logic levels which is an essential requirement for digital circuitry.

Digital analysis of the second circuit, similar to M2 network

The analysis is performed with clock input signal. The input voltage with amplitude 2 V between –2 to +2 V is shown on Fig. 18.

For input logic "0" level is 0.157 pA, for output logic "1" level is 0.341 pA. For the first output of the circuit the level of the signal for logic "0" is 0.148 pA, and for the output logic "1" the level of the signal is 0.238 pA. For the second output of the circuit the level in the signal for logic "0" is 0.162 pA, and the output logic "1" the signal level is 0.31 pA.

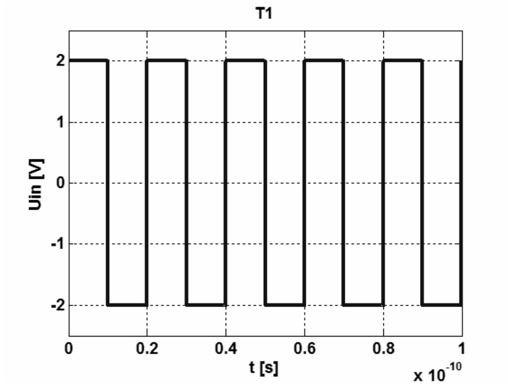

Fig. 18 Input voltage versus time

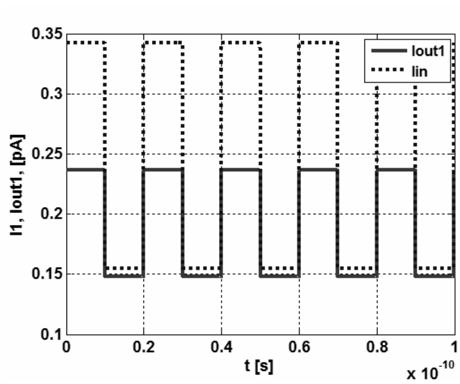

Fig. 19 First output and input current versus time

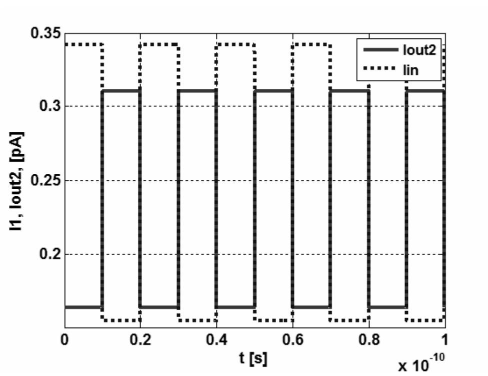

Fig. 20 Second output and input current versus time

Considering the signal in respect of the time from figures 19 and 20 it could be seen that when there is on the input logic "0" on the first output there is logic "0", and on the second a level of logic "1". When there is logic '1' on the input on the first output there is logic "1", and on the second logic "0", which shows that the circuit could work as a D-latch. The first output current I_{out1} answers of the output Q of the D-latch, and the second output current I_{out2} answers to the $\bar{Q}$.

Digital analysis of the M4 network

Operating levels of the circuit for digital simulation

From Fig. 21 it seen, that the output current repeats the input current. The output is repeating the input signal.

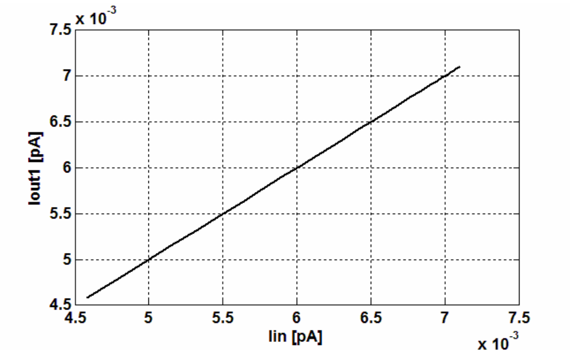

Fig. 21 Transfer characteristic of the first output of the circuit

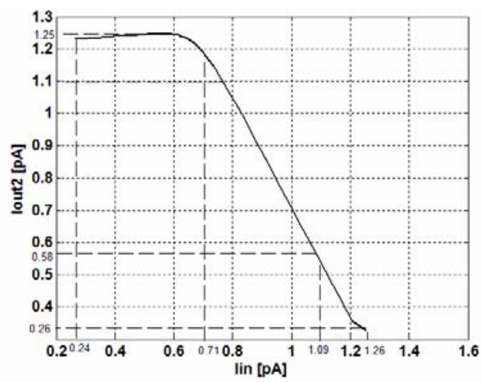

Fig. 22 Transfer characteristic of the second output of the circuit

From the Fig. 22 we see that there are two stable states and a switch between them. We determine the levels for the input and output logic “0” and logic “1”.

For the input logic “0” the levels are between 0.24 to 0.71 pA, for the input logic “1” the levels are between 1.09 to 1.26 pA.

For the output logic “0” the levels are between 0.26 to 0.58 pA. For the output logic “1” 1.10 to 1.25 pA.

From the Fig. 23 the logic levels are: For the input logic “0” the levels are between 2.64 to 3.06 pA, for the input logic “1” the levels are between 3.11 to 3.28 pA.

For the output logic “0” the levels are between 2.66 to 2.90 pA. For the output logic “1” 3.17 to 3.25 pA.

From the transfer characteristics (Figs. 22-23) and the determined logic levels it can be seen that the logic is positive and the logic levels follow the input logic levels which is an essential requirement for digital circuitry.

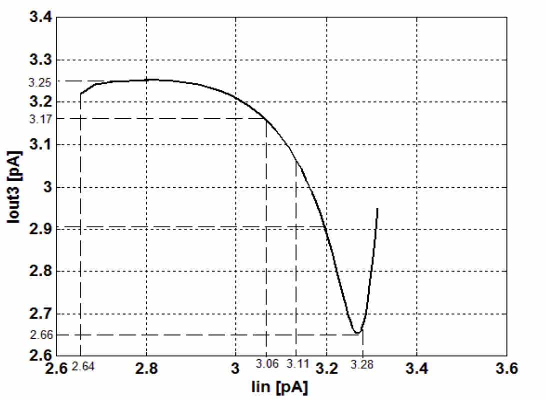

Fig. 23 Transfer characteristic of the third output of the circuit

Digital analysis of the second circuit, similar to M4 network

The analysis is performed with clock input signal. The input voltage between –1.3 to +3.2 V is shown on Fig. 24.

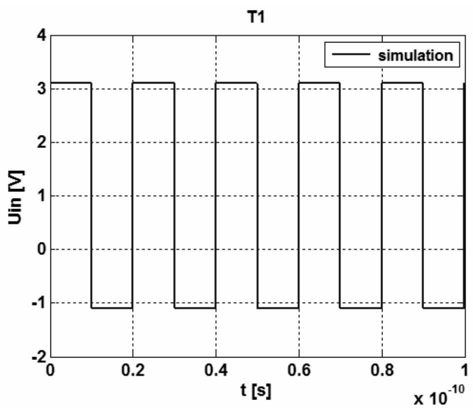

Fig. 24 Input voltage versus time

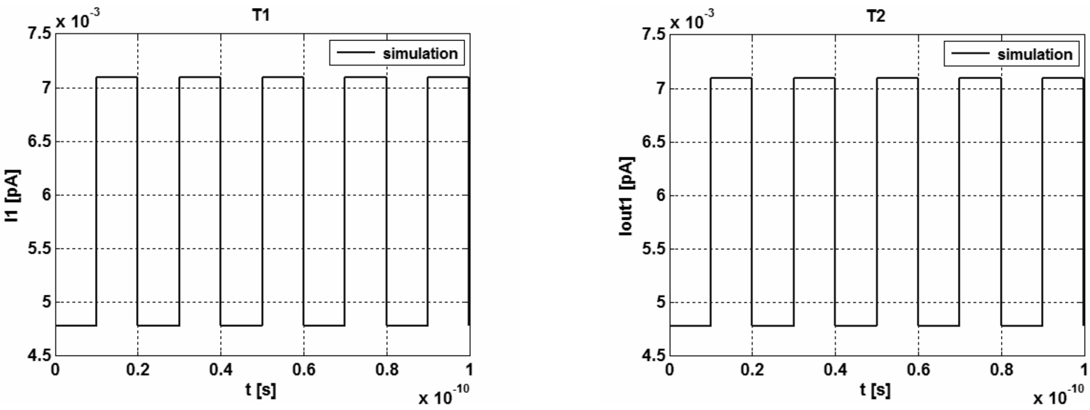

Fig. 25 Iin1 (I1) Input and output currents for the first output of the circuit versus time

Considering the results for the current of the first output and the input current (Fig. 25) it could be noticed that the output current repeats the shape and value the input signal. The first output is buffer in the circuit.

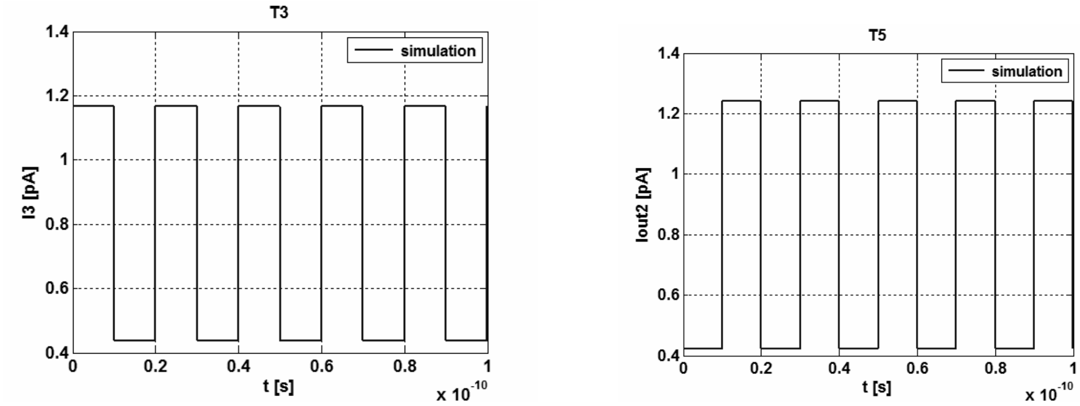

Fig. 26 I_{in2} (I_3) Input and output currents for the second output of the circuit versus time

Considering the results achieved for the current in the second output of the circuit and the input current (Fig. 26), could be noticed logic levels in the input and the output. The input current logic level is "0" = 0.42 pA, and the logic "1" = 1.18 pA. The output current is having logic "0" = 0.42 pA, and level of logic "1" = 1.23 pA.

It can be seen that the logic levels for logic "0" and logic "1" are in the acceptable limits of the output 2. Fig. 27 shows that the output signal inverts the input. The second output operates as an inverter.

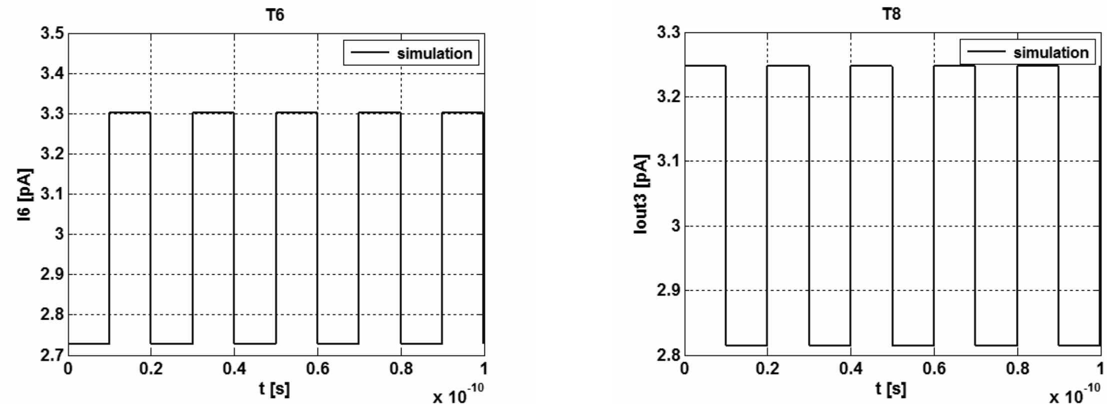

Fig. 27 I_{in3} (I_6) Input and output currents for the third output of the circuit versus time

Considering the results achieved for the current in the third output of the circuit (Fig. 27) and the input current (Fig. 27) could be noticed logic levels for the input and the output current. The input current logic level is "0" = 2.74 pA, and the level logic "1" = 3.30 pA. The output logic "0" = 2.82 pA, and level of logic "1" = 3.25 pA. It can be seen that the logic levels for logic "0" and logic "1" are in the acceptable limits of output 3.

Fig. 27 shows that the output signal inverts the input one. The third output circuit is inverter the same as the second one.

The difference between the second and the third output of the circuit is in the level of the output signal, but both of them work as inverters. The circuit could be operate as demultiplexer.

Conclusion

The investigation of transient characteristics of the circuits that are analogous to HBNs showed that the HBNs could process digital signals. It was demonstrated that the input and output currents meet the requirements in digital processing for setting up the circuit operating levels and setting up the levels of logic “0” and logic “1”. The digital simulations disclosed that some circuit outputs operate as repeaters while other outputs operate as inverters. The results also showed that the HBN circuits might operate as a D-trigger (latch) and a demultiplexer.

Based on the circuit analyses it can be concluded that the HBNs possess the basic properties needed for digital circuitry and hence they might have applications to digital electronics circuits.

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