

Transient Analysis of Electronic Circuit Derived from the Active Site β -lactamase Hydrogen Bonding Network

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Abstract – A Verilog-A circuit derived from a Hydrogen Bonding Network located in the active site of β -lactamase protein is developed for the purposes of microelectronics. The transient circuit analysis showed that the protein is able to process information like conventional the microelectronic circuits. At identical sine signal input, circuit outputs are similar to the outputs of an amplitude limiter, current source, and modulator.

Keywords – Hydrogen bonding network, Verilog-A, proteins, Cadence

I. INTRODUCTION

Bimolecular information processing is of great interest to contemporary electronics [1]. It is brought forth by the functional characteristics of biomolecules and the biochemical and biophysical processes that take place in the biomolecules [2]. These phenomena allow for the construction of elements that could process information [3].

In the present paper we will present the functions of a protein Hydrogen Bonding Network (HBN) and code them in Verilog-A language [4] in Cadence Design Framework [5], [6]. Afterwards, we will examine the circuit properties to process signals.

II. MODEL AND EQUATIONS

Hydrogen Bonding Networks (HBNs) formed in the active site of the β -lactamase protein are shown in Fig. 1 [7].

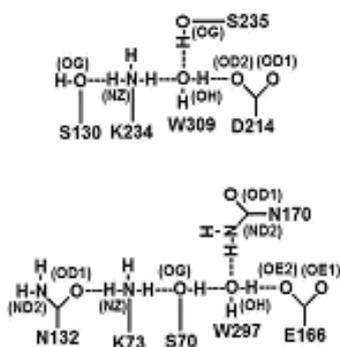


Fig. 1. HBNs in the active site of free enzyme β -lactamase

Charge (proton) transfer is investigated in [8] using the theory of Marcus [9]. The K -parameter of proton transfer is

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calculated by Marcus theory in analogy to the electron transfer parameter for each of the hydrogen bonds. Based on the calculations it is concluded that the higher the K parameter, the easier the transfer between donor and acceptor becomes and hence, the greater the protein current will be. After calculation of K , a block-element for each HBN donor and acceptor is set up and these block-elements are coded in Matlab [10]. Next, AC and DC analyses are performed; the results of these AC and DC analyses are compared to previous Matlab results.

Similarly, we set up a circuit of block-elements in Cadence Design Framework in Verilog-A language (Fig. 2). Here, we take into account the fact that the proton transfer in the two HBNs, viz. nucleophilic and electrophilic HBNs, occurs at the same time. The transfer in the two HBNs is also influenced by the pH of the environment. Hence, the respective electronic circuits are inseparably linked or integrated and so we place the respective block-elements into a common aggregated or integrated equivalent circuit. By analogy to the common pH of the environment, we input identical voltage to the inputs of the equivalent circuit.

In Fig. 2 Uin1 designates the input of the first circuit that is analogical to the “nucleophilic” HBN. In this circuit, the T1 block-element corresponds to the K73NZ lysine. The lysine is strong proton donor so in the equivalent circuit it is interpreted as a voltage controlled current source. The S70OG residue is substituted by the T2 block-element, which is a three-terminal element with identical input and output voltages but different input and output currents.

In the equivalent circuit the water molecule W297 is identified with T3 block-element which has two inputs and one output.

The T4 block-element corresponds to the strong proton acceptor E166 which can form different hydrogen bonds. The T4 is a three-terminal element with one input and one output.

The other block-elements, T5 and T6, correspond to asparagine residue N132 and N170. Asparagines might be simultaneously proton-donors and proton-acceptors, therefore the respective block-elements can alternate the current direction with the S switch in the equivalent circuit.

Uin2 designates the input of the second electrical circuit of the integrated equivalent circuit. This circuit is functionally analogical to the electrophilic HBN which also has three outputs. T10 represents a voltage controlled current source as well because it corresponds to the strong proton donor K234NZ. With this block-element (as with T1) the output voltages are identical to the input voltage and the currents are different.

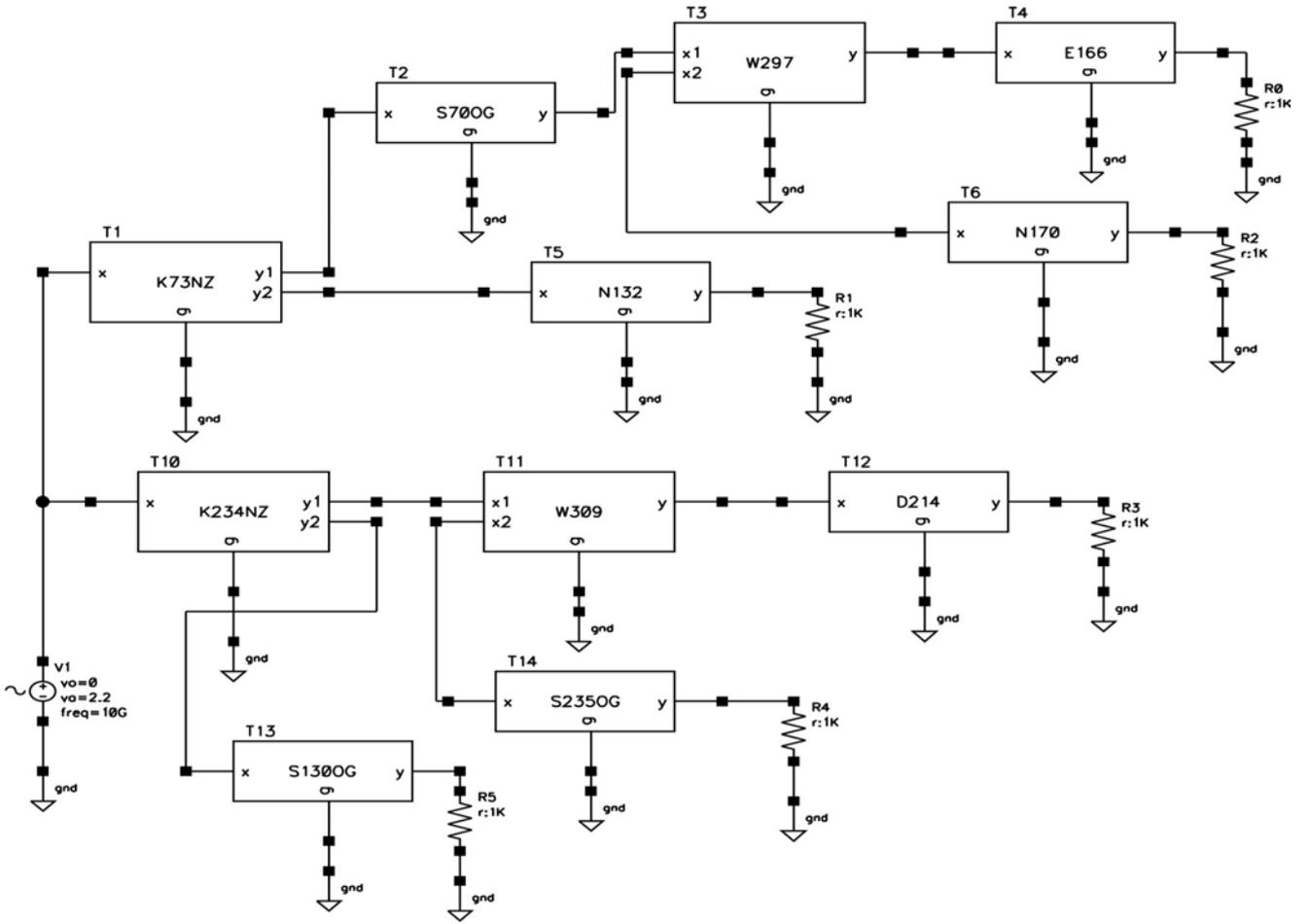


Fig. 2. Equivalent circuit in Cadence Spectre editor.

T11 block-element is analogical to the water molecule W309; the block-element has two inputs and one output.

The D214 residue is juxtaposed to t12 block-element with one input and one output; the latter is the output of the overall circuit.

The three-terminal block-element T13 is similar to S130OG. Its input and output voltages are identical but the currents are different.

The last T14 block-element is functionally analogical to S235OG and it has the same functions as S130OG (and T13 respectively).

Below are listed the equations modeling the equivalent integrated circuit in accordance with the switch position.

Equations 1 and 2 describe the T1 block-element.

$$U_1 = U_{in} \quad (1)$$

$$I_1 = 3 \times 10^{-5} U_1^3 - 5 \times 10^{-5} U_1^2 - 7 \times 10^{-5} U_1 + 0.0013; \quad (2)$$

Equations 3 and 4 describe the T2 block-element.

$$U_2 = 1.0451 \times U_1 - 0.1194; \quad (3)$$

$$I_2 = -0.0236 \times U_2^3 + 0.0379 \times U_2^2 + 0.124 \times U_2 + 1.3046; \quad (4)$$

Equations 5 and 6 describe the T3 block-element.

$$U_3 = 1.0179 \times U_2 - 0.039; \quad (5)$$

$$I_3 = 0.0015 \times U_3^3 - 0.0015 \times U_3^2 - 0.0171 \times U_3 + 0.0859; \quad (6)$$

Equations 7 and 8 describe the T4 block-element.

$$U_4 = 0.9703 \times U_3 + 0.0589; \quad (7)$$

$$I_4 = I_3 = I_{out1}; \quad (8)$$

Equations 9 and 10 describe the T5 block-element.

$$U_5 = 0.0457 \times U_1^2 + 1.2273 \times U_1 - 0.8501; \quad (9)$$

$$I_5 = 0 \times U_5 + 0.0001; \quad (10)$$

Equations 11 and 12 describe the T6 block-element.

$$U_6 = 1.0544 \times U_3 - 0.0933; \quad (11)$$

$$I_6 = 0.0058 \times U_6^2 + 0.0367 \times U_6 + 0.7113; \quad (12)$$

Equations 13 and 14 describe the T10 block-element.

$$U_{10} = 0.9701 \times U_1 + 0.2072; \quad (13)$$

$$I_{10} = 4 \times 10^{-5} \times U_{10}^4 - 6 \times 10^{-5} \times U_{10}^3 - 0.0002 \times U_{10}^2 + 0.0004 \times U_{10} + 0.00252; \quad (14)$$

Equations 15 and 16 describe the T11 block-element.

$$U_{11} = 0.9835 \times U_{10} + 0.1438; \quad (15)$$

$$I_{11} = 2 \times 10^{-5} \times U_{11}^3 - 13 \times 10^{-6} \times U_{11}^2 - 0.00015 \times U_{11} + 0.00048; \quad (16)$$

Equations 17 and 18 describe the T12 block-element.

$$U_{12} = 0.9683 \times U_{11} + 0.458; \quad (17)$$

$$I_{12} = I_{11}; \quad (18)$$

Equations 19 and 20 describe the T13 block-element.

$$U_{13} = 1.1009 \times U_{10} - 0.3571; \quad (19)$$

$$I_{13} = 10^{-5} \times U_{13}^4 + 2 \times 10^{-5} \times U_{13}^3 - 8 \times 10^{-5} \times U_{13}^2 + 2 \times 10^{-5} \times U_{13} + 0.0015; \quad (20)$$

Equations 21 and 22 describe the T14 block-element.

$$U_{14} = 1.034 \times U_{11} - 0.1986; \quad (21)$$

$$I_{14} = 0 \times U_{14} + 0.0001; \quad (22)$$

Afterwards, the equations are coded in Verilog-A and implemented in Cadence to perform a dynamic analysis. The excerpt of the code is listed in Fig. 3.

```
// VerilogA for slA, S700G, verilogA
`include "constants.h"
`include "discipline.h"
module S700G(x, y, g);
inout x, y, g;
electrical x, y, g;
electrical Vin;
analog
begin
V(Vin) <+ V(x, g);
V(y) <+ 1.0451*V(Vin)-0.1194;
I(x, y) <+ (-
0.0236*V(y)*V(y)*V(y)+0.0379*V(y)*V(y)+0.124*
V(y)+1.3046)*10e-12;
end
endmodule

// VerilogA for slA, S1300G, verilogA
`include "constants.h"
`include "discipline.h"
module S1300G(x, y, g);
inout x, y, g;
electrical x, y, g;
electrical Vin;
analog
begin
V(Vin) <+ V(x, g);
V(y) <+ 1.1009*V(Vin)-0.3571;
I(x, y) <+ (10e-
5*V(y)*V(y)*V(y)*V(y)+2*10e-5*V(y)*V(y)*V(y)-
8*10e-5*V(y)*V(y)+2*10e-5*V(y)+0.0015)*10e-
12;
end
endmodule
```

Fig. 3. Verilog-A code.

III. TRANSIENT ANALYSIS

The equivalent integrated circuit is functionally analogical to hydrogen bonding networks in the protein's active site. It has 2 inputs and 6 outputs. The transient analysis is performed with sine AC voltage to the two inputs with amplitude between -2.2 and $+2.2$ V and frequency of 1 MHz. The output voltages follow the form and frequency of the input voltage but the currents are different. The current in the first output is shown in Fig. 4. It reveals that the current is positive and modulated. The same relation is observed in Matlab simulations as well [9].

IS_HBN slucheIA_Tran schematic : Nov 4 15:20:41 2011

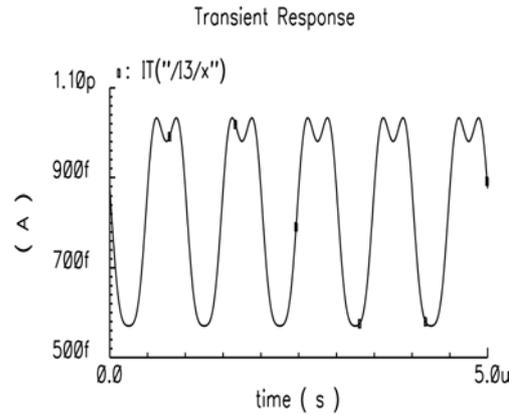


Fig. 4. Output current vs. time relation at output 1.

In Fig. 5 the current versus time relation at output 2 is plotted. Simulations show that this output is similar to the output of a current source, i.e. the current does not depend on voltage changes.

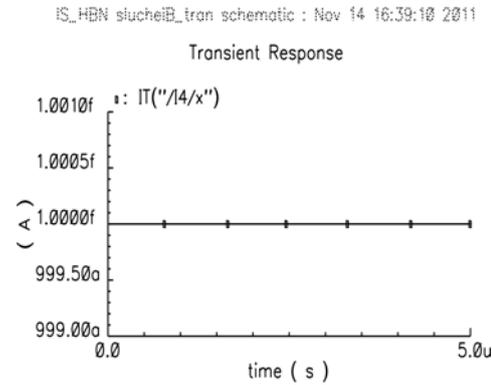


Fig. 5. Output current vs. time relation at output 2.

The output dependence of time at output 3 is given in Fig. 6. The signal here is bottom-limited, i.e. the circuit can operate as amplitude limiter.

IS_HBN slucheIA_Tran schematic : Nov 4 15:20:41 2011

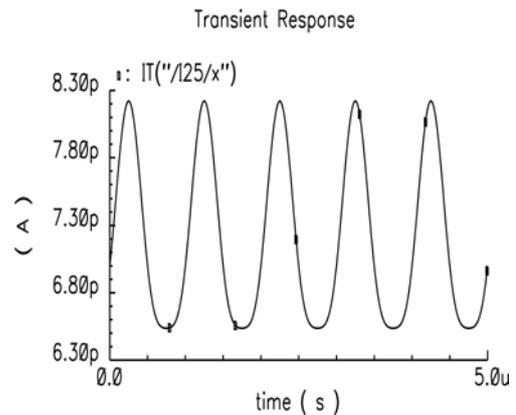


Fig. 6. Output current vs. time relation at output 3.

The other outputs 11 and 12 have differently modulated signals (cf. Fig. 7 and Fig. 8).

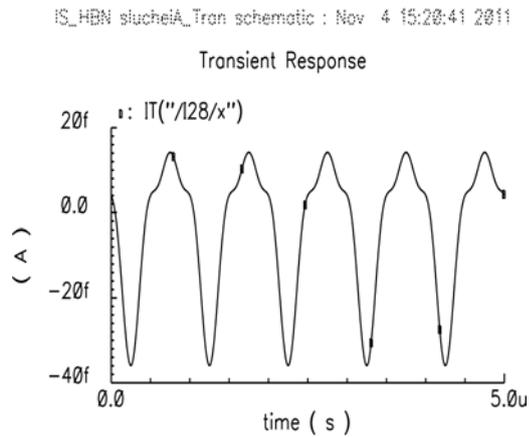


Fig. 7. Output current vs. time relation at output 11.

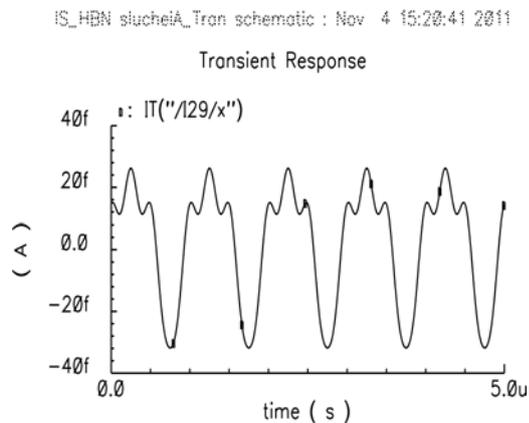


Fig. 8. Output current vs. time relation at output 12.

At the last output 14 we also have a current source with the same magnitude as in Fig. 5, therefore it is not depicted in a figure.

IV. CONCLUSION

The developed equivalent circuit based on HBN in the active site of the protein showed that the protein can process information similarly to the conventional microelectronic circuits. The equivalent circuit outputs has the shape of amplitude limiter, current source, and modulator at identical sine input signal.

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