# Protein Hydrogen Bonding Network Electrical Model and Simulation in Verilog-A

Elitsa Emilova Gieva, Lyuben Mihailov Penov, Rostislav Pavlov Rusev, George Vasilev Angelov and Marin Hristov Hristov

*Abstract* - **Electrical model of proteins in Verilog-A is developed and compared to previous Matlab models. A hydrogen bonding network is modeled as microelectronic circuit consisting of three-terminal block-elements. The results show that in static mode the functionally analogous circuit behaves as a class B amplifier. In dynamic mode the simulations show that the generated curves at the three circuit outputs have different frequency, amplitude, and width; the circuit operates as a signal modulator..**

*Keywords* – **bioelectronics, hydrogen bonds, proton transfer, Verilog-A, Cadence.**

## I. INTRODUCTION

The trends of MOS technology scaling show that soon it would reach the absolute physical limits and state-of-the-art silicon technology will not further match the constantly growing demand for computational performance. A recent innovation in bioelectronics proposes the use of proteins as circuits for signal processing. In analogy to traditional microelectronic four-terminal elements where the input circuit in general influences the output circuit and the electrical current itself is formed by electrons, some protein hydrogen bonds connected in a network could be modeled as four terminal block-elements where the current is formed by proton transfer between donor part and acceptor part of the heavy atoms in the network [1].

This analogy allows us to model the hydrogen bonding network (HBN) by electrical four terminal block-elements. The *I-V* characteristics of each four terminal block-element are proportional to the *K-V* characteristics of the respective hydrogen bonds. The current (*I*) of each block-element represents the proton transfer parameter (*K*) of each hydrogen bond and the voltage (*V*) of each block-element represents the electrostatic potential (El. pot.) [1].

Models of HBN can be coded in general-purpose programming languages or mathematical environments such as Matlab [2] or in hardware description languages such as Verilog-A [3].

Matlab is a general-purpose mathematical computation package widely used in engineering and science. The high speed of calculations is essential for simulations. It is clear that the combined circuit and device optimization is capable of leading to real benefits in both device design and circuit use.

Verilog-A has become increasingly viewed as a leading candidate for device and circuit model development as it is supported in circuit design CAD tools.

Our Verilog-A model uses three-terminal cells and defines all three terminals as "electrical-discipline" input/output ports that have different voltages. Being open-coded the Verilog-A equations can be easily modified or changed. In this way it is possible to handle an open model in a proprietary industry standard CAD tool Cadence Design Framework [4]. In Cadence Spectre simulator we create symbols to each three terminal instance and connect them in a circuit. It should also be mentioned that the design kits used to simulate in Spectre (Spectre cannot work without a design kit) may limit some parameters in simulations as they differ in many ways form one to the other.

## II. HBN AND ITS EQUIVALENT CIRCUIT

The HBN labeled with "M3"of the $\beta$-lactamase protein is modeled in Matlab to perform its DC and transient analysis [1]. Matlab allows to program arbitrary set of equations while SPICE-like circuit simulators are based on the laws of Ohm and Kirchhoff to predicts circuit behavior. To demonstrate that the HBN could be used in microelectronic applications we perform simulations of the four terminal block-elements in the conventional circuit simulator Cadence Spectre.

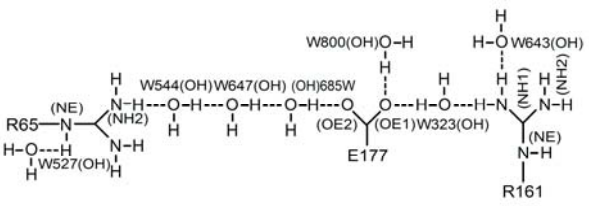



FIGURE 1. HYDROGEN BONDING NETWORK LABELED "M3" OF THE β-LACTAMASE PROTEIN.

Eng. E. Gieva is PhD student at the Department of Electronics and Electronics Technologies, Faculty of Electronic Engineering and Technologies, Technical University of Sofia, 8 Kliment Ohridski blvd., 1000 Sofia, Bulgaria, e-mail: gieva@ecad.tu-sofia.bg

Eng. L. Penov is student at the Department of Electronics and Electronics Technologies, Faculty of Electronic Engineering and Technologies, Technical University of Sofia, 8 Kliment Ohridski blvd., 1797 Sofia, Bulgaria, e-mail: lyubenpenov@gmail.bg

PhD R. Rusev is with the Department of Microelectronics, Faculty of Electronic Engineering and Technologies, Technical University of Sofia, 8 Kliment Ohridski blvd., 1797 Sofia, Bulgaria, e-mail: rusev@ecad.tu-sofia.bg

PhD G. Angelov is with the Department of Microelectronics, Faculty of Electronic Engineering and Technologies, Technical University of Sofia, 8 Kliment Ohridski blvd., 1797 Sofia, Bulgaria, e-mail: gva@ecad.tu-sofia.bg

Prof. PhD M. Hristov is with the Department of Microelectronics, Faculty of Electronic Engineering and Technologies, Technical University of Sofia, 8 Kliment Ohridski blvd., 1797 Sofia, Bulgaria, e-mail: mhristov@ecad.tu-sofia.bg

Figure 1 depicts the structure of the M3 HBN. The analysis of this network reveals that the R65NE and R161NE residues have donor properties. Hence, both of them are modeled as current sources. On the other hand GLU177OG1 is proton acceptor and it corresponds to a circuit output that sums two input signals. The rest of the elements are modeled as three-terminal devices that have equal input and output voltages but different input and output currents.

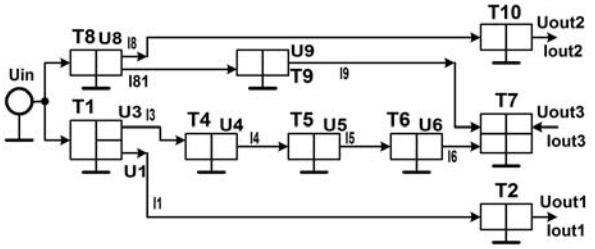



FIGURE 2. BLOCK DIAGRAM OF THE "M3" HBN MODELED IN MATLAB.

All the residua have their own *I-V* characteristics which are described by polynomials. For instance the T6 element – equivalent to HOH685 – has the following equations:

$$U_6 = 0.9419 \times U_5 - 0.0228$$

$$I_6 = 0.7072 \times U_6^3 - 0.5794 \times U_6^2 - 3.3778 \times U_6 + 44.728$$

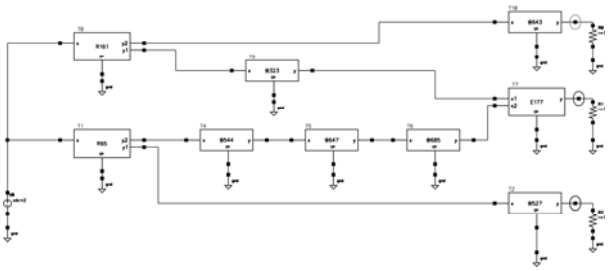


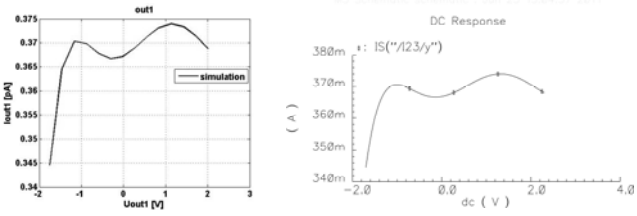
FIGURE 3. BLOCK DIAGRAM IN CADENCE

These polynomials are coded in Verilog-A. Since the Cadence Spectre simulator has native Verilog support the cells with the different polynomials are implemented as device instances to compose the circuit schematic (Figure 3). In Spectre the input signals are given by a "Vdc" or "Vac" sources (standard cells from the design kit) and all outputs have a resistive load in order to calculate the currents.

The Verilog-A code corresponding to the T6 element is listed below:

```
// VerilogA for M3, W685, veriloga
`include "constants.h"
`include "discipline.h"
module W685 (x, g, y);
inout x, y, g;
electrical x, y, g;
electrical Vin;
parameter real R = 1.0;
 analog
   begin
   V(Vin) <+ V(x, g);
   V(y) <+ 0.9419*V(Vin)-0.0228;
   I(y) <+ 0.7072*V(y)*V(y)*V(y)-
0.5794*V(y)*V(y)-3.3778*V(y)+44.728;
   end
endmodule
```

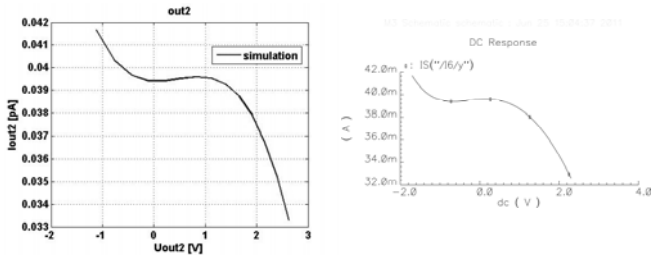
## III. SIMULATIONS AND RESULTS




A) B)

FIGURE 4. DC ANALYSIS OF OUTPUT 1 SIMULATED IN A) MATLAB AND B) CADENCE SPECTRE.

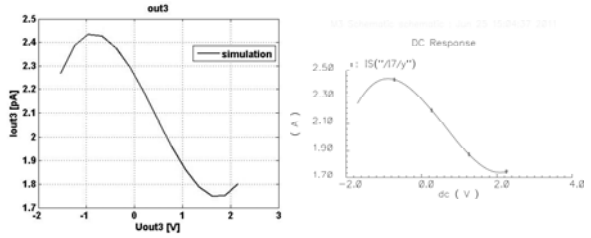
Figures 4A and 4B have similar form. The Maltab simulation however has much less calculated points and slightly differs in both voltage and current ranges. With some approximation this characteristic resembles that of a tunnel diode.




A) B)

FIGURE 5. DC ANALYSIS OF OUTPUT 2 IN A) MATLAB AND B) CADENCE SPECTRE.

The second output (Figure 5A and 4B) exhibits a more steep form than the original Matlab simulation and is displaced about 400 mV toward the negative range of the scale. These characteristics are similar to a class B amplifier.




A) B)

FIGURE 6. DC ANALYSIS OF OUTPUT 3 IN A) MATLAB AND B) CADENCE SPECTRE.

The last output's new simulation with Cadence has shown the two peaks have shifted to the left with a more negative value but with no change to the range of the full graph. This particular *I-V* characteristic is not similar to any known conventional microelectronic device.

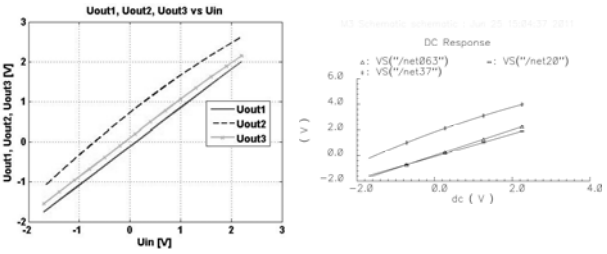



FIGURE 7. DC ANALYSIS OF ALL OUTPUTS VS INPUT IN A) MATLAB AND B) CADENCE SPECTRE.

It should be noted that voltage in all outputs follows the input voltage (Figure 7A and 7B) and results of all simulations show the relation of the current to the input. Only minor deviations are noticeable as the first output has a curved form.

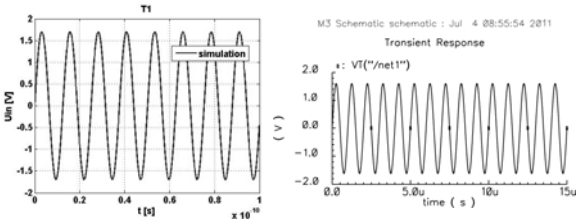



FIGURE 8. TRANSIENT ANALYSIS INPUT IN A) MATLAB AND B) CADENCE SPECTRE.

A sine wave (Figure 8) is fed the input for the transient analysis. The range is +/– 1.6 V but Matlab simulations were done at a 10 GHz while those in Cadence – at 1 MHz in order to provide a more realistic result at a typical frequency for real-world devices.

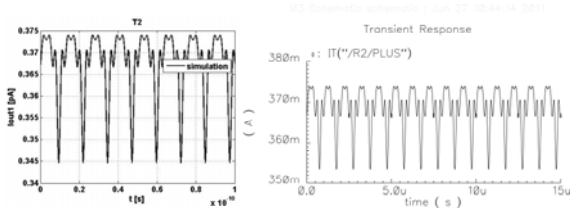



FIGURE 9. TRANSIENT ANALYSIS OF OUTPUT 1 IN A) MATLAB AND B) CADENCE SPECTRE.

As seen on Figures 9A and 9B the Cadence simulation signal from the first output has a smaller secondary component. The ratio of the two main components is higher. Note that the scale of the current in Cadence is many times larger. This is due to the fact that this simulation had a "real-world" load of 1 kΩ connected to the output and thus current size is dictated by Ohm's law.

Figures 10A and 10B illustrate in a similar fashion a higher scale of signals in the Cadence simulation. The component that contains the upper peak is smaller in range augmenting the ratio.

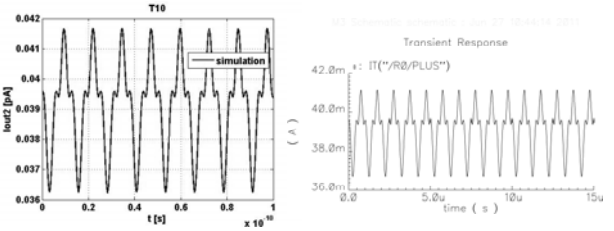



FIGURE 10. TRANSIENT ANALYSIS OF OUTPUT 2 IN A) MATLAB AND B) CADENCE SPECTRE.

The same situation is observed in Figure 11.

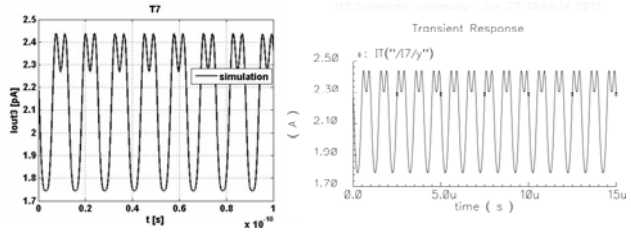



FIGURE 11. TRANSIENT ANALYSIS OF OUTPUT 3 IN A) MATLAB AND B) CADENCE SPECTRE.

The signal forms are similar to a decoder. In the AC domain proteins might be used as a modulator that could be a part of high frequency signal processing devices. It should be noted that at the moment no data is available on the frequency range at witch this protein operates normally.

## IV. CONCLUSION

The presented results from the simulations in Cadence Spectre via Verilog-A code and in Matlab showed similar forms but different in scales. The protein 'circuit' may operate in static mode as a class B amplifier. In dynamic mode it behaves like signal modulator. The results prove that the modeled proteins are relevant to signal processing applications and real-world microelectronic circuits.

## V. ACKNOWLEDGMENT

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## REFERENCES

[1] R. Rusev, G. Angelov, T. Takov, M. Hristov, *Biocircuit for Signal Modulation Based on Hydrogen Bonding Network*, Annual J. of Electronics, Vol.3, No. 2, pp. 155-158. ISSN 1313-1842 (2009).
[2] http://www.mathworks.com/products/matlab/ (2011)
[3] Cadence Design Systems, Inc, *Verilog-A Language Reference Manual Analog Extensions to Verilog HDL Version 1.0* August 1, 1996
[4] http://www.cadence.com/ *Products, Custom IC Design* (2011).