Multiple-valued computing by dipole-dipole coupled proteins

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Summary
We demonstrate through a simple model validated by molecular dynamics-based simulations that terahertz-speed, many-valued logic computations, and digital signal processing, functional for several cycles of operations are potentially possible with electric field-effect, dipole-dipole coupled protein architectures with various dipole moment orientations. Many-valued logic can be applied in various areas, such as artificial intelligence, machine learning, and robotics. Furthermore, programmable logic arrays and field programmable gate arrays can also benefit from its implementation. Even top companies like Intel developed circuits based on such logic (eg, StrataFlash and a NOR flash memory). The present study suggests that multivalued logic states can be stored in a protein with the application of proper external electric fields, and digital signal propagation is potentially achievable using dipole-dipole coupled molecules, placed few nanometers (on the order of 10 nm) apart. Furthermore, we propose a Dronpa protein-based ternary logic gate, suitable for universal ternary logic computations. The architectures are potentially operational at room temperature. The proposed operational principle is not restricted to proteins only; it might be applied in case of other types of molecules or artificial structures exhibiting similar behavior.

KEYWORDS
computing architectures, Coulomb coupling, digital signal processing, Dronpa, many-valued logic, molecular electronics, nanoelectronics, organic electronics, protein, protein model

1 | INTRODUCTION

In multiple-valued (also many-valued or multivalued) logic (MVL) more than two truth values are used in contrast with the Boolean system, where only “true” and “false” (usually denoted as “1” and “0,” respectively) exist. Examples for the most frequently used multivalued logics are three-valued (ternary)\(^1\)\(^2\) and four-valued systems. In the case of the ternary logic system, three truth values exist (“true,” “false,” and “indeterminate”); in the four-valued one, four distinct states are used (“Z,” “X,” “true,” and “false”). Multivalued logic has several useful applications, such as solving problems related to Boolean logic in a more efficient manner (eg, a multiple-output Boolean function can be converted to a single-output, many-valued logic function).\(^3\) Other implementations are related to electronic circuits, which apply more...
discrete signal levels, for example arithmetic circuits, field-programmable gate arrays (FPGA), and multiple-valued memories. Multivalued logic can be considered a combination of binary digital logic, and analog signal processing, which retains the advantages of both (the better noise immunity of binary logic and the greater information content of analog signals).

Several studies discuss the application of many-valued logic in semiconductor-based computing circuits. One can find a detailed historical and technical overview about the application of such logic in VLSI technology, where it is already incorporated in commercially available integrated circuits (especially four-valued logic, since it can be easily connected to the traditional binary systems) in Smith. The application of MVL in computing and digital signal processing integrated circuits can decrease the number of necessary interconnections; furthermore, fewer transistors, gates, and other elements are needed due to the increased efficiency of logic functions. Some disadvantages of MVL are reduced speed and noise margin, but in most cases, the overall parameters of such systems are improved by the implementation of multivalued logic (e.g., in the Intel 8087 coprocessor a quaternary ROM is applied, resulting in around 31% area reduction compared to binary ROM). Current-mode CMOS MVL circuits are compatible with VLSI technology. Kawahito et al. demonstrate a 32 × 32-bit multiplier realized by current-mode CMOS multivalued logic architectures, which clearly indicates the advantages: the size and power dissipation of the chip are half of those of the equivalent binary CMOS multiplier, and its speed is equivalent with that of the fastest binary multiplier.

It is possible to realize many-valued logic circuits by using resonant tunneling diodes (RTD), as well, by taking advantage of their unique current-voltage characteristics. Tristate logic has been demonstrated with the application of vertically integrated silicon-based resonant interband tunneling diodes (RITD). Even a ternary adder based on silicon nanowires has been proposed. The potential suitability of molecules in multivalued logic architectures has also been discussed in various works. de Silva et al. show that based on fluorescent photoionic devices, the implementation of MVL with four distinct logic states is possible, where the input signal is a chemical species (e.g., H+), and the output is fluorescence. Li and Marzari in their paper suggest that tape porphyrins can behave as molecular memory units, suitable for MVL operations.

If technology is intended to keep up with Moore’s law, it is inevitable to reach molecular dimensions regarding basic electronic elements in the not too distant future. By taking into account the above facts related to MVL, it is clear to assume that in the future several potential molecular electronics-based computing architectures can also benefit from the usage of many-valued logic. The application of organic molecules, basic biological building blocks for the possible realization of logic circuits has been suggested by various studies. DNA-related computing architectures have been proposed by Adleman and Boneh et al., and operational DNA-based computing arrangements have been successfully realized previously. Unfortunately, the mechanisms involved in their operation are extremely slow (they can take hours). Neurons have also been suggested for computing circuits; however, their operation is slow (on the order of milliseconds), and their energy consumption is considerable. Several contemporary papers propose devices based on organic molecules, as well: Mahmoud et al. describes a three-leg molecular transistor theoretically suitable for the realization of the NAND gate, and a single-molecule switch based on the motion of a phenyl ring is presented in Kitaguchi et al.

In previous works, we proposed protein-based computing, and signal processing architectures, and discussed the potential advantages of proteins in such applications. Proteins are organic macromolecules with outstanding properties for the aforementioned purposes: one can find plenty of them in nature with various properties, they can be engineered to provide the needed behaviors, theoretically, they can permit the realization of THz-frequency logic circuits, furthermore, they are available at low cost and possess excellent self-assemblying properties. The proposed architectures operate based on switching the individual photoswitchable proteins in the circuit by light with appropriate wavelength (it depends on the type of the protein used; for example, the Dronpa molecule can be switched between forms by λ1 = 405 nm and λ2 = 488 nm) or by the application of well-designed electric fields. The protein elements of the architectures are integrated together with dipole-dipole coupling (the method is described in a detailed way in previous studies and in Section 3 of this paper), since Coulomb coupling, which takes advantage of the interactions between the electronic charges of the neighboring molecules, is a potentially promising way for molecular device integration. The potential application of photon pulse and electric field-effect Coulomb coupled molecular structures for logic computations is not a new idea; it has been discussed extensively in the literature.

In the following, we will demonstrate that based on electric field-induced structural changes in proteins, it is theoretically possible to realize many-valued logic-based computing and digital signal processing circuits using electric field-effect protein architectures. Section 2 provides a brief overview of the mechanisms and describes the proposed model suitable for the characterization of the external electric field-induced behavior of proteins. The methods potentially applicable for the implementation of MVL, and an example for the application of the proposed mechanism, a
ternary universal logic gate are described in Section 3, based on simulations performed using our model. Finally, the
discussion and conclusions are presented in Sections 4, and 5, respectively.

2 | MODEL

According to Xu et al.,38 external electric fields result in structural changes in proteins (the paper discusses this phenomen-
on in the case of protein bovine pancreatic trypsin inhibitor), which do not relax completely after the field is switched off, thereby providing a memory effect. Therefore, such molecules can serve as nonvolatile memory elements (e.g., solid-state device memories) in contrast to volatile memory (e.g., random access memory), which does not retain its memory state. In Rakos,29 we demonstrated the same behavior in the case of Dronpa,39 an artificially developed protein, by performing simulations with the aid of the Not Another Molecular Dynamics Program (NAMD) molecular dynamics simulator software,40 and the Visual Molecular Dynamics (VMD) software package.41 When the molecule is subjected to an external electric field with a certain direction, due to the forces the field exerts on the charges within the protein, it is deformed in that direction, which results in a dipole moment change corresponding to the deformations. As the electric field is turned on (the molecule is energized), the shape of the protein, and the corresponding dipole moment, \( \mu \), will change depending on the direction (the field exerts a torque on the dipole moment, which is perpendicular to the plane defined by the electric field and dipole moment vectors according to the right-hand rule) and magnitude (a higher magnitude results in a greater change in dipole moment) of the field according to

\[
\begin{align*}
\mu_x &= \mu_{0x} + \alpha_x E_x \\
\mu_y &= \mu_{0y} + \alpha_y E_y \\
\mu_z &= \mu_{0z} + \alpha_z E_z
\end{align*}
\]

where \( \mu_{0x}, \mu_{0y}, \) and \( \mu_{0z} \) are the \( x, y, \) and \( z \) components of the dipole moment of the protein prior to the external electric field; \( \mu_x, \mu_y, \) and \( \mu_z \) are the \( x, y, \) and \( z \) components of its final dipole moment under the influence of the field \( E_{xyz} \); and \( \alpha_x, \alpha_y, \) and \( \alpha_z \) are the \( x, y, \) and \( z \) components of its polarizability. After the electric field is switched off, the dipole moment begins to relax back towards its original value; however, it never reaches it, and the difference between the final and original dipole moments also corresponds to the direction and magnitude of the previously applied electric field.29

Our NAMD-based simulations suggest that this phenomenon is still reversible without noticeable degradation even after 10 cycles of switching the molecule between two states. Therefore, we can assume that the MVL computing method based on this mechanism, and will be introduced in the following, can be applied through several cycles of operations.

In Rakos,29 we presented an equivalent circuit model suitable for characterizing the observed electric field-induced behavior of proteins and the dipole-dipole interactions between the molecules. However, in the following, we propose a model based on simple differential equations, which is the mathematical equivalent of the circuit model; therefore, it describes the behavior of architectures consisting of proteins characterized by the afore-mentioned effects equally well, without the necessity of an electronics circuit simulator software or time-consuming molecular dynamics-based simulations. Here, we have to emphasize that experimental data or molecular dynamics software-based simulation results of the behavior of the proteins are still required for the determination of the constants in the equations; however, after these values were determined, the model can be applied on an arbitrarily complicated system made of those proteins without the need of time-consuming molecular dynamics software-related simulations on the entire system.

Since the electric field results in structural rearrangements in the protein,38 the electric field-induced characteristics can be modeled as physical deformations of the molecule consisting of two components: a viscoelastic one, which completely returns back to the original state after the field is switched off, and a viscoplastic one, which is conserved.29

The \( x \) component of the viscoelastic-like change of the dipole moment, \( \mu_{ex} \), with respect to its initial state due to the \( x \) component of the external electric field, \( E_x \), can be expressed by

\[
\frac{d\mu_{ex}(t)}{dt} + \frac{\mu_{ex}(t)}{C_{e1x}C_{e2x}} = \frac{E_x(t)}{C_{e1x}},
\]

where the \( C_{e1x} \) and \( C_{e2x} \) constants can be determined from the electric field-induced response of the protein in question obtained either experimentally or with the aid of a molecular dynamics simulator software (in the case of Dronpa...
The viscoplastic-like change of the $x$ component of the dipole moment, $\mu_{px} = \mu_{p1x} + \mu_{p2x}$, can be characterized by

$$\frac{d\mu_{p1x}(t)}{dt} + A_x \frac{\mu_{p1x}(t)}{C_{p1x}C_{p2x}} = \frac{E_x(t)}{C_{p1x}},$$  \hspace{1cm} (3)$$

where

$$A_x = \frac{1}{2}\left(\text{sign}(E_x(t) - \mu_{p1x}(t)/C_{p2x}) + \text{abs}\left(\text{sign}(E_x(t) - \mu_{p1x}(t)/C_{p2x})\right)\right),$$  \hspace{1cm} (4)$$

and

$$\frac{d\mu_{p2x}(t)}{dt} + B_x \frac{\mu_{p2x}(t)}{C_{p1x}C_{p2x}} = \frac{E_x(t)}{C_{p1x}},$$  \hspace{1cm} (5)$$

where

$$B_x = \frac{1}{2}\left(\text{abs}\left(\text{sign}(E_x(t) - \mu_{p2x}(t)/C_{p2x})\right) - \text{sign}(E_x(t) - \mu_{p2x}(t)/C_{p2x})\right).$$  \hspace{1cm} (6)$$

The $C_{p1x}$ and $C_{p2x}$ constants can be obtained from the electric field-generated characteristics of the molecule, as well (in the case of Dronpa $C_{p1x} = 0.037 \frac{D \text{mol} A e}{ps \text{kcal}}$, $C_{p2x} = 153 \frac{D \text{mol} A e}{ps \text{kcal}}$, see details later). Equations (3) and (5) are the modified versions of Equation (2), where the inclusion of $A_x$ and $B_x$ permits the conservation of $\mu_{px}$ after the electric field is turned off (the protein is de-energized), they provide the same result as the two branches consisting of serially connected $R_p$ resistors, $C_p$ capacitors, and oppositely facing diodes in the circuit model of Rakos.\(^2^9\) Finally, the $x$ component of the overall dipole moment of the protein is

$$\mu_x(t) = \mu_{ex}(t) + \mu_{p1x}(t) + \mu_{p2x}(t) + \mu_{0x},$$  \hspace{1cm} (7)$$

where $\mu_{0x}$ is the $x$ component of the initial dipole moment. The $y$ and $z$ components of the dipole moment can be found in a similar way by replacing the indices in Equations (2) to (7).

The $C_{ex}$, $C_{e2x}$, $C_{p1x}$, and $C_{p2x}$ parameters can be determined from the experimental or simulated electric field-dependent responses in the following way. In the case of a nonzero, constant external electric field, $E_x$, the viscoelastic part of the $x$ component of the dipole moment is

$$\mu_{ex}(t) = \mu_{ex0}\left(1 - e^{-\frac{t}{\tau_{ex}}}\right),$$  \hspace{1cm} (8)$$

where

$$\mu_{ex0} = E_x C_{e2x}, \quad \tau_{ex} = C_{ex} C_{e2x}.$$  \hspace{1cm} (9)$$

The viscoplastic part of the $x$ component of the dipole moment under the same conditions can be described by

$$\mu_{px}(t) = \mu_{px0}\left(1 - e^{-\frac{t}{\tau_{px}}}\right),$$  \hspace{1cm} (10)$$

where

$$\mu_{px0} = E_x C_{p2x}, \quad \tau_{px} = C_{p1x} C_{p2x}.$$  \hspace{1cm} (11)$$

The time dependence of the $x$ component of the overall dipole moment under the influence of the constant electric field can be calculated with the aid of Equations (8) and (10):

$$\mu_x(t) = \mu_{ex}(t) + \mu_{px}(t) + \mu_{0x}.$$  \hspace{1cm} (12)$$
By leaving the electric field on for a few picoseconds (in the case of the Dronpa molecule, 40 picoseconds are sufficient), the dipole moment saturates (the NAMD-based simulations of Dronpa suggest that this saturation can be considered ideal if noise is neglected). When, after saturation, we turn off the field, the time dependence of the $x$ component of the overall dipole moment is

$$\mu_x(t) = \mu_{px0} + \mu_{ex0} e^{-\frac{t}{\tau_{ex}}}.$$  \hfill (13)

Equation (13) yields

$$\frac{1}{\tau_{ex}} = -\frac{1}{t} \ln \left( \frac{\mu_x(t) - \mu_{px0}}{\mu_{ex0}} \right).$$  \hfill (14)

Equations (10) and (12) result in

$$\frac{1}{\tau_{px}} = -\frac{1}{t} \ln \left( \frac{\mu_{ex}(t) + \mu_{px0} - \mu_x(t)}{\mu_{px0}} \right).$$  \hfill (15)

The $C_{e1x}, C_{e2x}, C_{p1x},$ and $C_{p2x}$ constants can be determined with the aid of Equations (9), (11), (14), and (15). The $y$ and $z$ components of the parameters can be found in a similar way by replacing the indices in the equations above. In the case of the Dronpa molecule, the parameters were calculated using the electric field-induced responses supposing $E_x = -3$ kcal/(molÅe), $E_y = -3$ kcal/(molÅe), and $E_z = -3$ kcal/(molÅe) simulated with the NAMD software are displayed in Table 1 (for a detailed description of the NAMD-based simulations please refer to the Appendix A). The averages and standard deviations were determined from the data of three subsequent NAMD simulations.

3 | ELECTRIC FIELD-EFFECT PROTEIN-BASED MVL

In the following subsections, we show that, based on the electric field-induced characteristics of proteins, many-valued computations are possible by two different means: by assigning logic values either to the magnitudes or to the directions of the dipole moment of the molecule.

3.1 | Dipole moment magnitude-based MVL

A straightforward way to introduce multiple logic to such system is to divide the range of the magnitudes of dipole moments available in the case of the particular protein into well-defined intervals, and assign a certain logic value to each of them. Figure 1 shows a possible assignment of six-valued logic (“value1,” “value2,” “value3,” “value4,” “value5,” and “value6”) in the case Dronpa.\textsuperscript{39} The simulations were performed both with Matlab using the model described in the previous section and with the aid of the NAMD molecular dynamics software\textsuperscript{40} combined with the VMD software package\textsuperscript{41} in order to validate our model. The details and parameters used in the case of simulations with NAMD are identical to those described in Rakos.\textsuperscript{29} The structural data of the dark-state version of the molecule (PDB ID: 2POX)

| Parameter | Average Value (\textit{pskcal} / \textit{DmolÅe}) | Standard Deviation (\textit{pskcal} / \textit{DmolÅe}) | Parameter | Average Value (\textit{DmolÅe} / kcal) | Standard Deviation (\textit{DmolÅe} / kcal) |
|-----------|-----------------------------------------------|-------------------------------------------------|-----------|----------------------------------------|----------------------------------------|
| $C_{e1x}$ | 0.008                                         | 0.0008                                          | $C_{e1x}$ | 192                                    | 10                                     |
| $C_{p1x}$ | 0.037                                         | 0.007                                           | $C_{p2x}$ | 151                                    | 40                                     |
| $C_{e1y}$ | 0.01                                          | 0.001                                           | $C_{e2y}$ | 195                                    | 12                                     |
| $C_{p1y}$ | 0.020                                         | 0.004                                           | $C_{p2y}$ | 147                                    | 16                                     |
| $C_{e1z}$ | 0.01                                          | 0.001                                           | $C_{e2z}$ | 204                                    | 10                                     |
| $C_{p1z}$ | 0.02                                          | 0.005                                           | $C_{p2z}$ | 138                                    | 14                                     |

TABLE 1 | Calculated model parameters in the case of Dronpa
was downloaded from the Protein Data Bank\textsuperscript{42} in PDB format. The electric field at the protein in the $x$ direction is zero from 0 to 4 ps, it is a constant, nonzero value from 4 to 44 ps ($E_1 = 3 \text{ kcal/(molÅe)}$, $E_2 = 2 \text{ kcal/(molÅe)}$, $E_3 = 1 \text{ kcal/(molÅe)}$, $E_4 = -1 \text{ kcal/(molÅe)}$, $E_5 = -2 \text{ kcal/(molÅe)}$, $E_6 = -3 \text{ kcal/(molÅe)}$), from 44 ps, it is zero again.

3.2 Dipole moment direction-based MVL

There is, however, another possibility to realize MVL with electric field-effect proteins, which takes advantage of the fact that the dipole moment changes only at the direction of the applied field. This phenomenon is illustrated by simulating the electric field-induced responses of Dronpa in the case of fields pointing to different directions. Figure 2 presents the results of the simulations. In all of the four cases, the electric field is turned on at 4 ps, and it...
is turned off at 44 ps. If only the x component of the electric field is nonzero \( (E_x = 3 \text{ kcal/(molÅe)}), \) then only the x component of the overall dipole moment \( (\mu_x) \) changes its value; the other two components \( (\mu_y \text{ and } \mu_z) \) remain the same (see upper left graph of Figure 2). A nonzero electric field in the y direction \( (E_y = 3 \text{ kcal/(molÅe)} \) results in an increase of the y component of the dipole moment \( (\mu_y); \) the other components \( (\mu_x \text{ and } \mu_z) \) stay the same (see upper right graph of Figure 2). When the z component of the field is nonzero \( (E_z = 3 \text{ kcal/(molÅe)}), \) only \( \mu_z \) changes (see lower left graph of Figure 2). The afore-described phenomenon can be used for MVL by assigning logic values to certain directions of the dipole moment vector (eg, if only \( \mu_x \) differs from its \( \mu_{x0} \) ground-state value, the other components remain in their ground state, the protein is in a “value0” logic state, if only \( \mu_x \) differs from its \( \mu_{x0} \) ground-state value, the protein is in a “value1” logic state, and when only \( \mu_z \) differs from its \( \mu_{z0} \) ground-state value, the molecule is in a “value−” state) with a certain tolerance.

Since the two methods can be combined together (each logic state can be assigned to a certain dipole moment vector length and direction), the entire dipole-moment space is available; therefore, one can assign a logic value to each section of the available part of the \( \mu_{xyz} \) dipole moment space with an appropriate \( \mu_x \pm \Delta \mu_x, \mu_y \pm \Delta \mu_y, \) and \( \mu_z \pm \Delta \mu_z \) tolerance.

### 3.3 A protein-based universal logic gate for ternary logic computations

The possibility of storing multiple logic-based values on proteins does not necessarily mean that they are capable of many-valued logic computations. In order to demonstrate that multivalued logic operations are possible with the mechanisms described in Sections 2, 3.1, and 3.2, we present an architecture based on dipole-dipole coupled, electric field-effect Dronpa molecules, which theoretically realizes a universal logic gate suitable for ternary logic operations. The truth table of the gate is displayed in Table 1; we selected it from a list of tables corresponding to universal ternary gates generated by a software available at https://github.com/Strilanc/UniversalTernaryGates.\(^{43}\) The three logic states are represented by “+,” “0,” and “−.”

Dipole-dipole coupling between closely placed neighboring molecules permits the integration of individual proteins into theoretically operational, electric field-effect digital computing circuits.\(^{29,30}\) If the dipole moments of the neighboring molecules are parallel to each other, the magnitude of the electric field \( E \) at the protein induced by its neighbor is

\[
E = \frac{1}{4\pi \varepsilon_0} \frac{\mu}{r^3},
\]

where \( \mu \) is the dipole moment of the neighboring molecule, and \( r \) is the distance between the protein and its neighbor. Since the direction of the field is opposite to that of the dipole moment of the neighboring macromolecule, the dipole moment of the protein will increase/decrease according to the decrease/increase of the dipole moment of its neighbor. In this way, the logic states of the closest neighbors determine the state of the corresponding molecule.

The geometrical arrangement of the proposed logic circuit is represented in Figure 3; the image was prepared using VMD. The arrangement consists of four Dronpa proteins placed in air, we can suppose that each protein is fixed on a substrate; however, this paper is not intended to propose a detailed experimental arrangement. These conditions are strongly idealized; however, simulations with NAMD shows that the electric field-generated behavior of Dronpa is qualitatively similar even if a part of the molecule is fixed and is placed in a medium. The electric fields can be generated using two electrodes with appropriate dimensions, but the details are not examined here. One of the molecules is placed in the middle, surrounded by the other three molecules (input1, input2, and output), each of them located at \( d = 7 \) nm (the minimum possible distance between the centers of two Dronpa molecules) away from the protein in the middle. Since the truth table is asymmetrical (“+” at input1 and “−” at input2 results in a “+,” “0” at input1 and “−” at input2 results in a “0”; however, “−” at input1 and “+” at input2 results in a “0,” and “−” at input1 and “0” at input2 results in a “−”), the two inputs in the arrangement should be also asymmetrical. If we assume that all of the building blocks are made of the same protein (in our case Dronpa), and we keep the distances between input1 and the protein in the middle, and input2 and the protein in the middle the same, one possible solution for asymmetry is to place one of the inputs with an orientation different from the other molecules. Since the polarizability of Dronpa is dependent of the direction of the electric field, such arrangement results in an asymmetrical behavior. In our case, we oriented input1 in a way to provide an external electric field-induced response corresponding to the x direction in Figure 2; all of the other proteins in the architecture are arranged in order to provide responses to the resulting electric fields corresponding to the z direction in Figure 2. In this way, the polarizability of input1 will be larger than that in the case of the other proteins, which provides the desired behavior. Furthermore, in order to avoid the adverse effects of the differences between initial dipole
moments of the proteins ($\mu_A = -100$ D, $\mu_B = \mu_C = \mu_D = -140$ D) on the proper operation of the gate, we set the initial dipole moments of all of the proteins to $-100$ Debyes (this can be achieved by the application of proper electric fields prior to computations).

The simulations were performed with Matlab using the model described in Section 2. The parameters were set according to Table 1 and the other properties of the arrangement described in the previous paragraph. The input molecules were set to the “+” state with the aid of an external electric field of 3 kcal/(molÅe), the “0” state corresponded to the initial dipole moments of the molecules (no electric field was applied), and the inputs were switched to the “−” state with an electric field of $-3$ kcal/(molÅe). The results can be observed in Figure 4. If, in the case of the output protein, we assign the “+” logic state to dipole moment values greater than $-94.6$ D, the “0” state to dipole moments between $-96.39$ and $-94.6$ D, and the “−” state to dipole values lower than $-96.39$ D, the gate operates according to Table 2.

3.4 Impact of the parameters on the performance

Since the model parameters of the molecules fluctuate (see Table 1), and the proteins of the geometrical arrangement cannot be placed exactly 7 nm apart each other, it is important to discuss the influence of slight variations of these parameters on the performance of the logic gate. Our simulations suggest that even larger variations in the model parameters of the protein (eg, one standard deviation difference from the average) would not cause problems with the gate behavior in the case of the first (input$_1$: +, input$_2$: +), second (input$_1$: +, input$_2$: 0), fourth (input$_1$: 0, input$_2$: +), and ninth (input$_1$: −, input$_2$: −) response curves of Figure 4. However, the third (input$_1$: +, input$_2$: −), fifth (input$_1$: 0, input$_2$: 0), sixth (input$_1$: 0, input$_2$: −), seventh (input$_1$: −, input$_2$: +), and eighth (input$_1$: −, input$_2$: 0) curves can tolerate only smaller fluctuations due to the extreme closeness of the final dipole moments to the border between the logic values. Since the parameters depend on the molecule, we can expect that a protein more suitable in this respect than Dronpa may improve such shortcoming, the intention of this paper, however, is to show that the proposed concept works in theory, not to recommend the best available protein building block for such purposes. The aforementioned observations are also valid regarding the errors in positioning of the molecules within the arrangement: the first, second, fourth, and ninth response curves can tolerate larger deviations, but the third, fifth, sixth, seventh, and eight curves...
have significantly lower tolerances (around 1%), which can be compensated for by changing the borders between logic values.

### 3.5 Power consumption

In the following, we give a rough estimation of the power required to switch the protein device described in the previous sections. The energy required for switching is provided by the electric field subjected to the molecule. In order to calculate the needed energy, we envision a simple arrangement consisting of a Dronpa protein between the plates of a parallel-plate capacitor. The energy density of the field, \( \mathcal{W}_E \), arising between the plates assuming a uniform electric field is

\[
\mathcal{W}_E = \frac{1}{2} \varepsilon_0 E^2, \tag{17}
\]

where \( \varepsilon_0 \) is the permittivity of vacuum, and \( E \) is the electric field. The total energy between the plates, \( W_E \), is
where $V$ is the volume between the plates. The power, $P_{\text{switch}}$, required for switching the protein can be described by

$$P_{\text{switch}} = \frac{W_E}{t_{\text{on}}},$$

where $t_{\text{on}}$ is the time duration of the external electric field exerted on the molecule.

If the external electric field on Dronpa is $E = 3 \text{ kcal/(molÅe)} = 1.3 \times 10^9 \text{ V/m}$, the volume between the plates of the capacitor is $V = 3.73 \times 10^{-25} \text{ m}^3$ (the minimal volume required to accommodate the molecule has been estimated by measuring the dimensions of the protein with the aid of VMD), $t_{\text{on}} = 40 \text{ ps}$ then Equations (17) to (19) yields $P_{\text{switch}} = 70.4 \text{ nW}$. This estimated value is significantly lower than the around one milliwatt required for the operation of resonant tunneling diodes.\(^{44,45}\)

4 | DISCUSSION

In Section 3, we proposed two different ways for harnessing the electric field-induced dipole moment characteristics of proteins. This provides one the opportunity to store many-valued logic states in an individual molecule. There is a limit, however, regarding the number of possible values that can be used in such way: as we increase the number of logic states, the signal-to-noise ratio decreases accordingly, which determines the maximum number of states that can be utilized. This can be overcome by reducing the noise of the system or by choosing molecules with greater polarizability (or improving the polarizability of the existing protein).

We showed in Section 3 that, at least theoretically, it is possible to realize all of the different two-input, one-output logic functions in the case of ternary logic, since a universal logic gate can be realized using a Dronpa-based architecture. Although this work did not prove that universality is also valid in the case of other many-valued logic systems, one can expect that at least several logic functions can be implemented with the proposed mechanism in other MVL systems, as well. The application of different types of proteins with various properties in an architecture can further extend the opportunities to design simple architectures with higher MVL-related functionalities.

In the case of Dronpa, a considerably high electric field should be used in order to provide observable results (1 kcal/(molÅe) = 4.3 \times 10^8 \text{ V/m}). If we choose molecules with greater polarizability, the external electric fields needed for proper operation could be reduced. The choice of proteins with better polarizabilities can also increase the dipole-dipole coupling between neighboring proteins within the architectures, which results in better performance, resulting in greater differences between the dipole moment values of the different logic states at the output. Protein engineering can also aid the development of artificial proteins with the desired properties.

The proposed operational principle by which multiple-valued computing is potentially possible is based on changes of the dipole moments of proteins in response to external electric fields and on dipole-dipole interactions between them. Since such behavior is not restricted to proteins, other kinds of molecules, or even other natural or artificial devices demonstrating similar electric field-dependent dipole moment changes might be suitable building blocks for the architectures described in the paper.

5 | CONCLUSION AND FUTURE OUTLOOK

We introduced a simple model based on simple differential equation, suitable for the characterization of the electric field-generated responses of proteins, if preliminary experimental data or molecular dynamics software-based simulation results are available for the determination of the constants related to the molecule in the equations. Furthermore, we showed that the electric field-induced dipole moment changes of proteins make them promising candidates for the realization of multivalued logic-based computing, and digital signal processing circuits. The different logic values can be stored in the proteins by two means: they can be assigned to different dipole moment values of the molecule or to different directions of the $\mu_{\text{xyz}}$ dipole moment vector. The two methods can be combined by assigning each available logic value to a different dipole moment vector length and direction. Based on our model, we also showed that with the aid of dipole-dipole coupling with various dipole moment orientations, many-valued digital signal propagation, and, at least in the case of ternary logic, two-input universal computing architectures are potentially feasible with the
aid of only four proteins. Our simulations suggest that such architectures permit terahertz-frequency operations even at room temperature, functional for several cycles of operations, with significantly lower power consumption than that of existing electronic devices in this field (eg, resonant tunneling diodes). The currently existing, and continuously improving nanofabrication technologies, and self-assembly techniques are indispensable tools for the experimental realization of such structures; however, it is advisable to apply proteins with polarizabilities higher than that of Dronpa, since in that case lower external electric fields are sufficient for proper operation, and the effects are also more pronounced. Moreover, the application of femtosecond spectroscopy can assist in the experimental characterization of the operation of the proposed architectures. Structures other than proteins exhibiting similar electric field-generated responses should also be examined for suitability in the proposed applications.

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**APPENDIX A**

The setup applied for the NAMD-based simulations of this paper is similar to that used in Rakos; however, in the following, we provide its brief description in the present work, as well. The file containing the coordinates of all of the atoms in the molecule necessary for the simulations was obtained from the Protein Data Bank in pdb format. The additional protein structure file (psf), which is also required for the simulations with NAMD was generated from the pdb and par_all27_prot_lipid.prm parameter files with the aid of the Automatic PSF Builder extension of the VMD software. The parameters of the NAMD-based simulations are presented in Table A1.

**TABLE A1**  
NAMD-based simulation parameters (from Rakos)

| Temperature | 300 K |
|-------------|-------|
| Force-field parameters |  |
| Exclude | scaled1-4 |
| 1-4scaling | 1.0 |
| cutoff | 12 |
| switching | On |
| switchdist | 10 |

(Continues)
During simulations, interactions between atoms within 13.5 Å apart from each other were taken into account in order to reduce computational time, which does not result in significant reduction of the accuracy. The molecular dynamics calculations of NAMD were based on Langevin dynamics with 5 ps$^{-1}$ damping coefficient (a standard value often used in NAMD simulations), where the temperature to which atoms are affected was set to 300 K (room temperature).

### TABLE A1  (Continued)

| Parameter                  | Value    |
|----------------------------|----------|
| Temperature                | 300 K    |
| pairlistdist               | 13.5     |
| Integrator parameters      |          |
| timestep                   | 2.0      |
| rigidBonds                 | All      |
| nonbondedFreq              | 1        |
| fullElectFrequency         | 2        |
| stepspercycle              | 10       |
| Constant temperature control|         |
| langevin                   | On       |
| langevinDamping            | 5        |
| langevinTemp               | 300 K    |
| langevinHydrogen           | Off      |

Abbreviation: NAMD, Not Another Molecular Dynamics Program.