Modeling and simulation of photon-coupled, fluorescent photoswitchable protein logic

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Summary
Today’s society has an ever-increasing demand for smaller-scale, lower-energy-consuming, cheaper, and faster computing and digital signal processing systems. Photon-coupled, fluorescent photoswitchable protein-based architectures are promising candidates for the fulfillment of these requirements. In order to properly design digital circuits based on the aforementioned building blocks, an efficient simulation procedure is needed. We present a simple, differential equation-based model, suitable for the design and simulation of such structures. It characterizes the radiation-induced switching, the form-dependent fluorescence, and the effect of photon coupling in a fast and efficient manner. The applicability of the model is demonstrated through simulations of the OR and NOR logic gates consisting of readily available, fluorescent photoswitchable proteins. It can be a potential design tool for future molecular logic circuitry based on such molecules.

KEYWORDS
logic circuits, molecular electronics, nanoelectronics, organic electronics, photon coupling, photoswitchable protein, protein modeling

1 | INTRODUCTION

In order to adhere to the principles of sustainable development and the demands of society, electronic components with lower energy consumption and dissipation, higher speed, and smaller size than the existing ones must be realized. If we would like to keep up with the present trend, we are about to enter the era of molecular dimensions in this regard; therefore, it is reasonable to assume that molecular electronic devices will play an important role in the future.

Proteins are polymer-based biomolecules with dimensions on the order of few nanometers. Their numerous advantages, such as low cost, remarkable self-assembling properties, availability with various properties, and possibility of the development of artificial proteins with the desired properties indicate that they may serve as building blocks of computing and digital signal processing circuitry of the future.1–4

In previous works, we examined two means by which proteins may be used for computing and digital signal processing applications: One of them is based on structural changes of proteins in response to an external electric field,2 and the other possibility is the application of photoswitchable proteins,3 which can be switched between different forms using appropriate photon pulses. The molecules can be integrated together into logic circuits with the aid of Coulomb2 and photon coupling.3
1.1 | Fluorescent photoswitchable proteins

Fluorescent, reversibly photoswitchable proteins are special kinds of proteins. They can be switched reversibly between different forms with the aid of light with specific frequencies. At least one of their forms exhibits fluorescent properties. The mechanism of photoswitching is generally related to the cis–trans isomerization of the chromophore methylene bridge between the two rings of the chromophore, but in certain cases, structural changes of the chromophore pocket also play an important role in the process.\(^5\)\(^–\)\(^8\) Such molecules are primarily used for biological purposes, such as tracking the movements and interactions of proteins, but they may be suitable for other applications like information storing.\(^8\)\(^–\)\(^10\)

Numerous fluorescent photoswitchable proteins are available, such as the artificially modified versions of the green fluorescent protein obtained from \textit{Aequorea victoria} are photoswitchable,\(^11\)\(^–\)\(^14\) but Kindling fluorescent protein was the first one to exhibit efficient photoswitching.\(^15\) The green fluorescent protein Dronpa,\(^16\) an engineered version from a tetrmeric Pectiniidae coral fluorescent protein, can be switched from its fluorescent (on), resting state to its dark (off) state with a \(\lambda_{\text{off}} = 488\) nm wavelength light. The molecule can be switched back to its fluorescent form in a reversible way by irradiating it with a \(\lambda_{\text{on}} = 405\) nm wavelength radiation. The fluorescent state of Dronpa emits radiation with \(\lambda_{\text{em}} = 517\) nm in response of a \(\lambda_{\text{ex}} = 503\) nm light. Padron,\(^17\) the artificially modified version of Dronpa, exhibits the opposite behavior: Its dark (off) resting form can be switched to its fluorescent one with the aid of a \(\lambda_{\text{on}} = 488\) nm light, and it can be switched back reversibly by a \(\lambda_{\text{off}} = 405\) nm radiation. In the case of Padron, fluorescence with \(\lambda_{\text{em}} = 522\) nm can be induced by an excitation with \(\lambda_{\text{ex}} = 503\) nm.

The aforementioned proteins exhibit typical fluorescent photoswitchable protein-like behavior; however, more exotic ones exist, as well: Proteins in Adam et al.\(^6\) and Brakemann et al.\(^18\) integrate reversible photoswitching with irreversible photoconversion. Brakemann et al.\(^18\) demonstrate a unique switching behavior related to the reversible hydration/dehydration in the imidazolinone ring of its chromophore.

1.2 | Photon-coupled, fluorescent photoswitchable protein-based computing architectures

In previous works, we examined two methods by which proteins can be integrated together to form computing architectures: dipole–dipole coupling\(^2\) and photon coupling.\(^3\) Dipole–dipole coupling, which is a straightforward way to integrate together electric field-effect proteins,\(^2\) suffers certain drawbacks, such as rapid decay with distance and extreme sensitivity to the separation between neighbors. On the other hand, photon coupling between fluorescent photoswitchable proteins provides a stable, robust integration method.\(^3\) The operation of architectures based on the latter method is related to the form-dependent fluorescent radiation of the molecule coupled to the neighboring protein, thereby switching it to another form.

In Rakos et al.,\(^3\) we proposed universal, binary logic architectures based on hypothetical, fluorescent, two-state photoswitchable proteins. Later OR and NOR logic gate architectures consisting of already existing, photon-coupled, fluorescent photoswitchable proteins have been introduced.\(^19\) The detailed description of this work can be found in Section 3. In Rakos et al.,\(^20\) we showed that even multiple-valued computing architectures may be realized with such method. Furthermore, already available, two-state, photon-coupled, fluorescent photoswitchable proteins can be applied for multi-valued computing purposes, as well.\(^21\)

In a previous work, we proposed a simple circuit model for the characterization of two-state photoswitchable proteins.\(^22\) It consists of only a handful of basic electronic components (resistors, capacitors and diodes) but accurately describes the photoswitching behavior. However, fluorescence and photon coupling are not incorporated into the model, although they are essential for the simulation and design of photon-coupled, fluorescent photoswitchable protein-based logic circuits.

In this work, we propose a model consisting of simple differential equations, suitable for the characterization of both the photoswitching behavior and fluorescence combined with photon coupling. Section 2 gives a detailed description of the model, including frequency-selective switching, fluorescence, and photon coupling. In Section 3, we demonstrate the application of the model through simulations of photon-coupled, fluorescent photoswitchable protein-based OR, and NOR logic gates. The discussion and conclusion of the results are provided in Sections 4 and 5, respectively.
2 | FLUORESCENT PHOTOSWITCHABLE PROTEIN MODEL

In order to adequately characterize the behavior of photon-coupled, two-state, fluorescent photoswitchable protein-based computing and digital signal processing architectures, the model must fulfill the following requirements. It needs to be able to simulate switching from form\textsubscript{1} to form\textsubscript{2} and vice versa in response to radiation with specific frequencies and intensities. In its fluorescent form, the molecule must emit light with a well-defined frequency in response to a stimulating radiation. If only one of the forms is stable, the model has to be able to characterize the spontaneous relaxation from the unstable form to the stable, resting one even in the absence of the required switching radiation.

The above requisites can be accomplished if the model consists of the following blocks: frequency-selective parts for passing only those components of the incoming radiation required for switching or excitation of the fluorescent form, a switching block responsible for the characterization of switching between forms, and a fluorescent part providing the fluorescent output radiation of the fluorescent form in response to proper excitation. Furthermore, the fluorescent output radiation of a protein must be coupled to its neighbors. The block diagram of the model is displayed in Figure 1.

2.1 | Frequency-selectivity

The frequency-selectivity of switching and fluorescence can be characterized by a second-order bandpass filter. Its transfer function is

\[
H(\omega) = \frac{\omega_0^2 \omega}{(i\omega)^2 + \frac{\omega_0 Q}{\omega} i\omega + \omega_0^2},
\]

where \(\omega\) is the angular frequency, \(i\) is the imaginary, and \(Q\) is the quality factor of the filter. Furthermore, \(\omega_0\) is the angular frequency at which the gain of the filter peaks, in or case the frequencies suitable for switching from form\textsubscript{1} to form\textsubscript{2} and from form\textsubscript{2} to form\textsubscript{1}, respectively, or the fluorescence excitation frequency in the case of fluorescence excitation.

![Block diagram of the two-state, fluorescent, photoswitchable protein model](image-url)
The intensity of the filtered incident radiation can be expressed with the aid of Equation 1:

\[ I_0(t) = \int_0^{\infty} |H(\omega)|I_i(\omega,t)d\omega, \]  

(2)

where \( I_i(\omega,t) \) is the intensity of the incident radiation. Since usually the overall radiation spectrum used for the operation of the circuits consists of discrete elements with specific frequencies, the equation can be expressed in a simpler way:

\[ I_0(t) = |H(\omega_1)|I_{i1}(\omega_1,t) + |H(\omega_2)|I_{i2}(\omega_2,t) + ... \]  

(3)

### 2.2 Switching

Switching between forms occurs when radiation with the proper frequency reaches the protein. The previous subsection described the way to obtain the intensity, \( I_0(t) \), which switches the molecule between forms from the entire incident radiation. In the following, we detail the derivation of the formulas necessary for the characterization of such switching mechanism.

Since \( I_0(t) \) initiates the transition between forms, it is the input variable of the equation, and the output is the form, \( f(t) \) of the protein. If we define \( form_1 \) and \( form_2 \) with \( f = 0 \) and \( 1 \), respectively, switching from \( form_1 \) to \( form_2 \) can be characterized by

\[ v_1(t) \frac{df(t)}{dt} + f(t) = 1, \]  

(4)

where the \( v_1(t) \) variable determines the speed of the transition, and it depends on the intensity of the switching radiation. Since, at least for reasonable intensities, the switching speed depends linearly on the radiation intensity, therefore,

\[ v_1(t) = a_1 - b_1 I_{o12}(t), \]  

(5)

where \( I_{o12}(t) \) is the intensity of the radiation, which switches \( form_1 \) to \( form_2 \), and \( a_1 \) and \( b_1 \) are constants. The two constants can be calculated by the experimental data related to switching using the following equations:

\[ \tau_A = a_1 - b_1 I_{o12A}, \]  

(6)

and

\[ \tau_B = a_1 - b_1 I_{o12B}, \]  

(7)

where \( \tau_A \) and \( \tau_B \) are the time intervals required for switching in the case of \( I_{o12A} \) and \( I_{o12B} \) radiation intensities, respectively.

Similarly, transitioning from \( form_2 \) to \( form_1 \) can be described by

\[ v_2(t) \frac{df(t)}{dt} + f(t) = 0, \]  

(8)

where the \( v_2(t) \) variable determines the speed of the transition. It can be found using

\[ v_2(t) = a_2 - b_2 I_{o21}(t), \]  

(9)
where $Io_{12}(t)$ is the intensity of the radiation, which switches form$_2$ to form$_1$, and the $a_2$ and $b_2$ constants can be determined similarly to Equations 6 and 7.

Putting Equations 4 and 8 together, we get

$$\frac{df(t)}{dt} = (\text{sign}(Io_{12}(t)) - f(t)) \cdot \text{sign}(Io_{12}(t) + Io_{21}(t)).$$

(10)

If only $Io_{12}$ is present, Equation 10 reduces to Equation 4, and the protein switches from form$_1$ to form$_2$. On the other hand, if only $Io_{21}$ is extant, Equation 10 is equivalent with Equation 8, and the molecule transitions from form$_2$ to form$_1$. Equation 10 adequately characterizes switching between two stable forms; however, it cannot be used if both $Io_{12}$ and $Io_{21}$ are present simultaneously. However, in that case, the protein would probably oscillate between forms, and that situation can be avoided during operation of protein-based computing architectures.

If only one of the forms, e.g. form$_1$ is the stable, resting state of the protein, Equation 10 modifies to

$$\frac{df(t)}{dt} = \text{sign}(Io_{12}(t)) - f(t).$$

(11)

where the constant $c$ determines the speed of spontaneous relaxation from form$_2$ to the stable form$_1$, and it can be obtained from the experimental data.

### 2.3 | Fluorescence

Fluorescent, photoswitchable proteins exhibit fluorescence upon irradiation with specific frequencies, depending on its form. The characterization of the frequency-selectivity of fluorescence excitation has been described in Section 2.1.

If form$_1$ is the fluorescent one of the molecule, the power of its output fluorescent radiant power can be described by

$$P_{fo}(t) = P_{f0}Io(t)(1 - f(t)).$$

(12)

where $Io(t)$ is the intensity of the radiation required for fluorescence-induction, and $P_{f0} = \phi_{fl}A_p$, where $\phi_{fl}$ is the quantum yield of fluorescence and $A_p$ is the irradiated surface of the protein. If form$_2$ is the fluorescent state, the equation to be used is

$$P_{fo}(t) = P_{f0}Io(t)f(t).$$

(13)

### 2.4 | Photon coupling

The output radiation of a fluorescent, photoswitchable protein can influence the states of its neighbors. The intensity of the fluorescent radiation incident on the neighboring molecule can be determined with the aid of the output power described by Equations 12 and 13. If we assume that the protein radiates uniformly in each direction, and its distance from its neighbor is $d$, the coupled radiation on the neighboring molecule is

$$Io(t) = \frac{P_{fo}(t)}{4\pi d^2}.$$

(14)

If the radiation characteristic of the protein is not uniform, Equation 14 should be modified accordingly. However, in the following, we will assume the simple case described by Equation 14.
3 | SIMULATIONS

In order to demonstrate the applicability of our model, in this section, we characterize the photoswitching properties of Dronpa with the aid of our model; furthermore, we present simulations of two, photon-coupled, fluorescent photoswitchable protein-based logic gates. The arrangements examined are the mTFP0.7-Padron-mTFP0.7-based OR gate and the mTFP0.7-Dronpa-mTFP0.7-based NOR gate. We already described their operation principle in Rakos, but simulations characterizing their behavior were lacking so far.

3.1 | Simulation setup

The simulations were performed in GNU Octave using the equations described in Section 2. In order to avoid problems with inaccuracies of the numerical simulations, both the filtered radiation intensities and the forms in the equations were rounded to the second decimal place by using the

$$\text{round}(x/100)/100$$

routine, where $x$ can be either a filtered radiation intensity-component or the instantaneous form of the protein.

The parameters of the corresponding proteins necessary for the simulations were obtained from the literature. The values are displayed in Table 1, where $\lambda_{\text{on}}$ and $\lambda_{\text{off}}$ are the radiation wavelengths necessary to switch the molecule to its fluorescent on state and backwards, respectively; $\lambda_{\text{ex}}$ is the fluorescence excitation wavelength; $\lambda_{\text{em}}$ is the wavelength of the fluorescent radiation emitted by the protein; and $\phi_f$ is the quantum yield of fluorescence. The $P_{f0}$ constants of the proteins necessary for the simulations (see Section 2.3) have been determined using the quantum yields and assuming an irradiated surface of 50 nm$^2$. Since the differential equations used for the simulations require the knowledge of the $a_1$, $b_1$, $a_2$, and $b_2$ constants (see Section 2.2), those must be determined from the experimental data with the aid of the equations outlined in Section 2.2. The data needed are displayed in Table 1, where $\tau_{12,1}$ and $\tau_{12,2}$ are the time intervals required for switching from $\text{form}_1$ to $\text{form}_2$ in the case of $P_{12,1}$ and $P_{12,2}$ incident powers, respectively. From $\text{form}_2$ to $\text{form}_1$, the $\tau_{21,1}$ and $\tau_{21,2}$ intervals in the case of $P_{21,1}$ and $P_{21,2}$ incident powers are applied.

Since we could not obtain the quality factors (see Equation 1) from the literature, $Q = 10^6$ has been applied in all cases. Due to the long spontaneous relaxation times to the stable forms of the corresponding proteins, Equation 10 has been used during simulations instead of Equation 11.

| Protein  | $\lambda_{\text{on}}$ (nm) | $\lambda_{\text{off}}$ (nm) | $\lambda_{\text{ex}}$ (nm) | $\lambda_{\text{em}}$ (nm) | $\phi_f$ | Reference     |
|----------|---------------------------|---------------------------|---------------------------|---------------------------|--------|--------------|
| Dronpa   | 405                       | 488                       | 503                       | 517                       | 0.85   | Habuchi et al.$^{23}$ |
| Padron   | 488                       | 405                       | 503                       | 522                       | 0.64   | Fron et al.$^{24}$ |
| mTFP0.7  | 405                       | 458                       | 453                       | 488                       | 0.5    | Ai and Campbell$^{25}$ |

| Protein  | $P_{12,1}$ | $\tau_{12,1}$ | $P_{12,2}$ | $\tau_{12,2}$ | Reference |
|----------|------------|---------------|------------|---------------|-----------|
| Dronpa   | 80 nW$^*$  | 85 ms         | 600 nW$^*$ | 8.6 ms        | Habuchi et al.$^{23}$ |
| Padron   | 80 nW$^*$  | 85 ms         | 600 nW$^*$ | 8.6 ms        | - -       |

| Protein  | $P_{21,1}$ | $\tau_{21,1}$ | $P_{21,2}$ | $\tau_{21,2}$ | Reference |
|----------|------------|---------------|------------|---------------|-----------|
| Dronpa   | 3.6 nW$^*$ | 100 ms        | 36 nW$^*$  | 10 ms         | Habuchi et al.$^{23}$ |
| Padron   | 3.6 nW$^*$ | 100 ms        | 36 nW$^*$  | 10 ms         | - -       |

*The literature specified only the power incident on the sample. We estimated the radiation intensity on the sample using the incident power values, assuming a laser beam diameter of 1.8 mm (Stabilite 2018-RM Ar-Kr ion laser was used in the reference), and a magnification of $\times60$, since the beam has been focused on the sample by a microscope with that magnification.

**Since we could not find the corresponding data in the literature, we assumed a similar behavior to Dronpa, a close relative to Padron.
3.2 Photoswitching of Dronpa

The photoswitching phenomenon of Dronpa was characterized by setting up the model parameters according to the data provided in Habuchi et al.\textsuperscript{23} (see Table 1). Since the literature provided only the power incident on the sample, $P$ instead of the radiation intensity, $I$, in the model equations (see Section 2), we applied $P$ in place of $I$.

The simulations were performed assuming the following conditions: Dronpa is originally in its resting, fluorescent form ($\text{form}_1$). From $t = 1000$ to 2000 ms, a radiation with $P = 80$ nW and $\lambda_{\text{off}} = 488$ nm is subjected to the protein, which switches it to its non-fluorescent form ($\text{form}_2$). From $t = 3000$ to 4000 ms, another radiation with $P = 3.6$ nW and $\lambda_{\text{on}} = 405$ nm is applied, which switches the molecule back to its fluorescent form ($\text{form}_1$). The protein is continuously irradiated by a $\lambda_{\text{ex}} = 503$ nm radiation from $t = 0$ to 4000 ms. Dronpa emits fluorescent radiation with $\lambda_{\text{em}} = 517$ nm only in its fluorescent form. The results of the simulation are displayed in Figure 2. The plots correctly demonstrate both the switching behavior and fluorescence corresponding to the experimental data published in Habuchi et al.\textsuperscript{23}

3.3 Photon-coupled, fluorescent photoswitchable protein-based OR gate

The OR gate consists of a Padron molecule serving as output, surrounded by two mTFP0.7 proteins corresponding to the inputs. Figure 3 displays the arrangement when $\text{input}_1$ is set to logic “1,” which results in a radiation at the output corresponding to logic “1.” The molecules have been plotted by Visual Molecular Dynamics (VMD)\textsuperscript{27} using the PDB formats of the protein structures obtained from the Protein Data Bank.\textsuperscript{28}

The operation of the gate is based on photon–photon coupling between the neighboring proteins. The input molecules are in their fluorescent forms, and the output protein is originally in its resting, non-fluorescent, dark state. If Padron is irradiated by a $\lambda_{\text{ex}} = 503$ nm readout radiation (which corresponds to the excitation of its fluorescent form, see Table 1), it will not produce an output radiation. Since the absence of radiation corresponds to logic “0,” in this situation, the output is logic “0.” However, if one or both of the inputs are subjected to a $\lambda_{\text{ex}} = 453$ nm radiation (the
excitation wavelength of the fluorescent form of mTFP0.7, see Table 1), which corresponds to logic “1,” the mTFP0.7 molecule produces a radiation with $\lambda_{em} = 488$ nm. Since the 488 nm radiation switches Padron to its fluorescent form, it will produce a $\lambda_{ex} = 522$ nm radiation upon irradiation by a $\lambda_{ex} = 503$ nm readout radiation, which corresponds to logic “1.”

The situation depicted in Figure 3 was simulated using our model. During simulation, the output molecule was continuously irradiated by a $\lambda = 503$ nm radiation, and input$_1$ was subjected by a $\lambda = 453$ nm radiation starting from $t = 1000$ ms. This results in the switching of the output protein to $f = 1$ (form$_2$), which produces a fluorescent radiation due to the $\lambda = 503$ nm readout radiation. The results of the simulation can be observed in Figure 4.

### 3.4 | Photon-coupled, fluorescent photoswitchable protein-based NOR gate

In the case of the NOR gate, the output molecule is Dronpa, surrounded by two mTFP0.7 proteins serving as inputs. Figure 5 displays the arrangement when input$_1$ is set to logic “1,” which results in the absence of fluorescent radiation at the output corresponding to logic “0.”

The operation of the gate is the following: The input mTFP0.7 molecules are in their fluorescent forms, and the output Dronpa protein is originally in its resting, fluorescent form. If Dronpa is irradiated by a $\lambda_{ex} = 503$ nm readout radiation (which corresponds to the excitation of its fluorescent form, see Table 1), it produces an output radiation

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**FIGURE 4** Fluorescent radiant power of input$_1$ (top), form of output (middle), and fluorescent radiant power of output (bottom) in the case of the mTFP0.7-Padron-mTFP0.7 OR gate

**FIGURE 5** Setting input$_1$ of the mTFP0.7-Dronpa-mTFP0.7 NOR gate to logic “1” results in no radiation at the output corresponding to logic “0”
corresponding to logic “1.” However, if one or both of the inputs are subjected to a $\lambda_{ex} = 453$ nm radiation (the excitation wavelength of the fluorescent form of mTFP0.7, see Table 1), which corresponds to logic “1,” the inputs produce a radiation with $\lambda_{em} = 488$ nm. Since the 488 nm radiation switches Dronpa to its non-fluorescent form, it will not produce radiation upon irradiation by a $\lambda_{ex} = 503$ nm readout radiation, which corresponds to logic “0.”

We simulated the situation of Figure 5. During simulation, the output molecule was continuously irradiated by a $\lambda = 503$ nm radiation, and input$_1$ was subjected by a $\lambda = 453$ nm radiation starting from $t = 1000$ ms. This results in the switching of the output protein to $f = 1$ (form$_2$), which is non-fluorescent. The results of the simulation can be observed in Figure 6.

4 | DISCUSSION

The simulation results suggest that the proposed model adequately describes the behavior of two-state, photon-coupled, fluorescent photoswitchable protein architectures. It is able to characterize the switching phenomenon, fluorescence, and the effect of photon coupling between individual molecules. However, more experimental data regarding both the individual protein building blocks and protein-based logic circuits would aid the refinement and possible extension of the model in case of proteins with more complex behavior.

The model enables one to design a software suitable for the efficient characterization of complex, photon-coupled, photoswitchable protein circuits. Due to its simplicity, the calculations are very fast even in the case of systems consisting of numerous molecules, which would not be achievable with a conventional protein simulation software. The simulations of the OR and NOR gates (see Sections 3.3 and 3.4) took about 10 s each on an EliteBook 8560p under Windows 10. This amount of time is considerably shorter than in the case of a conventional molecular dynamics software (e.g. NAMD), where calculations even on an individual protein take several hours. Furthermore, such a software is not even capable of simulating interactions with photons in order to characterize photoswitching.

The aforementioned advantages may aid the design of future circuits and complex systems based on the operational principle described in the paper. The model also enables the exploration of other operational principles related to photon-coupled, photoswitchable protein-based systems. Furthermore, it helps in the determination of the optimal properties of protein building blocks needed for specific circuitry.

The main limitation of the model is that the main parameters of the protein building blocks must be obtained experimentally; it is not suitable for their determination of such properties from the structural arrangement of the protein. However, it is intended for the characterization of photoswitchable protein-based systems, not for molecular simulations of individual proteins, and its advantages far outweigh this drawback.

**FIGURE 6** Fluorescent radiant power of input$_1$ (top), form of output (middle), and fluorescent radiant power of output (bottom) in the case of the mTFP0.7-Dronpa-mTFP0.7 NOR gate
Proteins can be selectively fixed on various substrates\textsuperscript{29}; furthermore, present-day nanofabrication tools provide us with the means to arrange macromolecules next to each other with nanometer-scale precision.\textsuperscript{30} In this way, the contemporary nanofabrication methods and equipment already enable the experimental realization and characterization of simple logic structures such as the ones simulated in Section 3; thereby, the model can be tested and refined accordingly. Moreover, our model can assist in the design of more complex logic architectures based on the aforementioned operation principle.

One major drawback of the presently available fluorescent photoswitchable proteins regarding our purposes is their slow response (on the order of milliseconds). Fortunately, individual structural rearrangements in proteins occur within picoseconds.\textsuperscript{2,23,24,31} This indicates that with careful design, artificially developed photoswitchable proteins can operate at that timeframe, opening the door for terahertz-speed, photon-coupled, fluorescent photoswitchable protein-based computing and digital signal processing circuits.

5 | CONCLUSION AND FUTURE OUTLOOK

We presented a model, which can adequately characterize computing, and digital signal processing circuitry consisting of photon-coupled, fluorescent photoswitchable proteins. The model consists of simple differential equations and describes the photoswitching mechanism, fluorescence, and photon coupling between molecules. We illustrated its usability through simulations of OR and NOR logic gates consisting of readily available proteins. Our model may serve as the basis of a design tool for future, terahertz-speed organic molecular logic circuitry based on such proteins. Since, in our opinion, presently available nanofabrication tools and techniques already make it possible to realize these kinds of logic architectures, simple structures of photon-coupled, fluorescent photoswitchable proteins can be realized and tested. The experimental results would be indispensable in the refinement and further development of the model.

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