Abstract—In conventional molecular communication (MC) systems, the signaling molecules used for information transmission are stored, released, and then replenished by a transmitter (TX). However, the replenishment of signaling molecules at the TX is challenging in practice. Furthermore, in most envisioned MC applications, e.g., in the medical field, it is not desirable to insert the TX into the MC system, as this might impair natural biological processes. In this paper, we propose the concept of media modulation based MC where the TX is placed outside the channel and utilizes signaling molecules already present inside the system. The signaling molecules can assume different states which can be switched by external stimuli. Hence, in media modulation based MC, the TX modulates information into the state of the signaling molecules. In particular, we exploit the group of photochromic molecules, which undergo light-induced reversible state transitions, for media modulation. We study the usage of these molecules for information transmission in a three-dimensional duct system, which contains an eraser, a TX, and a receiver for erasing, writing, and reading of information via external light, respectively. We develop a statistical model for the received signal which accounts for the distribution of the signaling molecules in the system, the initial states of the signaling molecules, the reliability of the state control mechanism, the randomness of irrepressible, spontaneous state switching, and the randomness of molecule propagation. We adopt a maximum likelihood detector and show that it can be reduced to a threshold based detector. Furthermore, we derive analytical expressions for the optimal threshold value and the resulting bit error rate (BER), respectively. Both the statistical model and BER results are verified by computer simulations. Our results reveal that media modulation enables reliable information transmission, validating it as a promising alternative to MC based on molecule emitting TXs.

I. INTRODUCTION

To facilitate synthetic molecular communication (MC), several modulation schemes for embedding information into molecular signals have been proposed over the last few years [2]. In [3], concentration shift keying (CSK) and molecule shift keying (MoSK), where information is encoded into the molecule concentration and the molecule type, respectively, have been proposed. Additionally, index modulation techniques such as molecular space shift keying [4], [5] have been reported for MC systems with multiple spatially distributed transmitter (TX) locations, where information is embedded into the activation of a single transmitter. Moreover, the authors in [6] proposed molecular type permutation shift keying (MTPSK) where information is encoded into permutations of different molecule types.

For the implementation of these modulation schemes, the signaling molecules are stored, released, and then replenished by the transmitter. However, from a practical point of view, the replenishment of signaling molecules at the TX is difficult to realize, especially at microscale and in medical applications. Therefore, it is desirable to develop alternative concepts for both TX and modulation design that decouple the modulation process from the release of signaling molecules.

Such a decoupling has already been proposed for conventional wireless communication systems in the context of media modulation. Here, information is embedded into the properties of the communication medium, i.e., the carrier signal is not directly modulated [7], [8]. Extending the concept of media modulation to MC, the authors of [9] propose to alter the properties of the channel to embed information. In [10], changing the flow velocity of the medium for modulation is proposed.

In contrast to the channel-based forms of media modulation considered in [9], [10], in this paper, we propose a new form of media modulation, where the properties of signaling molecules already present in the channel are modulated for information transmission via an external stimulus.

In the simplest case, the signaling molecules can be in two different states which can be switched by an external stimulus to encode the information to be conveyed. For media modulation, the signaling molecules may be naturally present in the environment or they may be injected once and then remain in the channel. Media modulation is different from existing modulation schemes as information is not encoded in the molecule concentration, the type of molecule or the releasing transmitter but in the properties of the signaling molecules themselves. Media modulation based MC can overcome several shortcomings of existing MC systems by avoiding repeated injections of signaling molecules, hereby (i) making the replenishment of the TX unnecessary and (ii) reducing the soiling of the channel due to the deposition of signaling molecules after repeated injection. Furthermore, the TX, i.e., the source of the external stimulus, is not placed inside the transmission medium and does not influence molecule propagation. The practical feasibility of media modulation hinges on the availability of suitable switchable signaling molecules, of course. The general concept of this form of media modulation based MC is new and has not been reported in

\footnote{We note that if the signaling molecules degrade in the channel, occasional replenishment of signaling molecules may be necessary. However, even in this case, the number of additional signaling molecules needed is expected to be much lower than for a conventional MC system with molecule emitting TX, provided suitable signaling molecules are chosen.}
the literature, yet. Nevertheless, redox-based MC \cite{11} can be interpreted as an instance of media modulation where signaling particles are switched between two states, the reduced state and the oxidized state. However, the focus of \cite{11} was on the biological and experimental aspects of redox-based MC, while a thorough communication theoretical analysis was not conducted. Furthermore, in biological systems, a natural form of media modulation can be observed during phosphorylation, where a phosphoryl group is added to a protein affecting the properties of the protein. The phosphorylation is mediated by a kinase, a specific type of enzyme, which in turn can be controlled via an external stimulus \cite{12, 13}.

Another promising candidate for signaling molecules for media modulation are photochromic molecules. These molecules can be reversibly interconverted between two states, where the transition between the states is induced by light \cite{14}. Photochromic molecules are well established in molecular devices for information processing \cite[Chap. 10]{14}, but their exploitation for media modulation in synthetic MC systems is new. Photochromic systems facilitate different functionalities including writing, reading, and erasing of information by an external light stimulus.

In this paper, we develop a novel modulation scheme for synthetic MC systems employing photochromic signaling molecules. Hereby, the information is embedded into the state of a photochromic molecule. As photochromic signaling molecule, we exemplarily consider the reversibly photo-switchable green fluorescent protein variant “Dreiklang” (GFPD), whose fluorescence can be reversibly switched by light stimuli of mutually different wavelengths \cite{15}. Fluorescence denotes the ability of a molecule to first absorb light and then radiate light back at a higher wavelength, i.e., with a lower energy, which makes it possible to read out the current state of a GFPD molecule. GFPD has been shown durable, i.e., stable over several photo-switching cycles \cite{15}, which allows the long-term use of GFPD as signaling molecule.

The application of fluorescence has gained significant interest for the design of synthetic MC systems over the last few years \cite{16}–\cite{21}. In the experimental MC system in \cite{16}, a fluorescent dye was employed as information carrier. In order to facilitate long-range information transfer in MC systems, fluorescent carbon quantum dots were investigated as signaling particles due to their concentration dependent emission properties \cite{17}. In \cite{18}, a bacterial receiver (RX) was proposed which produces green fluorescent protein upon the reception of signaling molecules. Similarly, the authors of \cite{19} employed genetically engineered \textit{Escherichia coli} (\textit{E. coli}) bacteria to exhibit fluorescence upon the reception of specific signaling molecules, thereby demonstrating that a chemical transmit signal can be converted to a fluorescence signal at the RX. In \cite{20}, an MC system for generating pulse shaped signals with a NOR logic operation in engineered \textit{E. coli} bacteria was proposed. Hereby, the fluorescence of the yellow fluorescent protein was employed as the pulse signal generated by the NOR gate. The authors in \cite{21} developed a multiple-input multiple-output (MIMO) nano-communication system, where information transmission was based on the exchange of energy levels between fluorescent molecules employed as transceiver nano-antennas. Most of the existing works employ fluorescent nano-antennas. Most of the existing works employ fluorescent molecules because of their easy detectability at the RX. However, to the best of the authors’ knowledge, the encoding of information into the state of a switchable photochromic molecule was not considered so far in the MC literature.

In the MC system proposed in this paper, fluorescent and non-fluorescent GFPD molecules correspond to state A and state B, respectively. The fluorescence of GFPD can be switched on (B → A) and off (A → B) by light stimuli at different wavelengths. Consequently, assuming the GFPD molecules are suspended in a fluid medium as elements of the envisioned synthetic MC system, optical sources emitting light at different wavelengths can be used as TX unit to modulate information (B → A) and eraser (EX) unit to delete the information (A → B). Moreover, a fluorescence detector equipped with a fluorescence-stimulating light source and an optical sensor can be employed as RX.

The main contributions of this paper can be summarized as follows:

- We propose a new form of media modulation for synthetic MC. As information carrier, we employ signaling molecules, which are already present in the channel. These molecules can assume different states which can be reversibly switched and read out by external stimuli. This property allows for information transmission by writing, reading, and erasing information embedded in the molecule state. Hence, this novel concept does not require a TX that stores and releases molecules, and therefore overcomes several drawbacks of existing modulation schemes, e.g., the need for TX replenishment.
- We realize media modulation by employing photochromic molecules for information transmission. The information is conveyed in the state of these molecules, which is either fluorescent or non-fluorescent. Since both the state transitions and the fluorescence are triggered by external light stimuli, we provide an in-depth mathematical investigation of the underlying photochemical processes.
- We develop a statistical model for the received signal which integrates the different sources of randomness present in media modulation based MC systems.
- Based on the statistical model, we derive mathematical expressions for the optimal threshold value of a threshold-based detector and the bit error rate (BER).
- We show that reliable media modulation based MC is feasible and provide insight into the impact of the irradiation power densities, the number of signaling molecules present in the channel, and the channel characteristics, such as the flow velocity, on the BER.

The proposed concept of media modulation was introduced in the conference version \cite{1} of this paper. Here, we significantly extend \cite{1} by investigating the physical properties of the RX and the RX in detail. Furthermore, we include the spontaneous state switching of GFPD molecules in our model. The aforementioned extensions require the development of a more elaborate and comprehensive statistical model as compared to the model proposed in \cite{1}. Based on this new statistical model,
we provide mathematical expressions for the optimal detection threshold of a threshold detector and the BER.

The remainder of this paper is organized as follows. In Section II we introduce the considered MC system and describe the proposed media modulation scheme. In Section III the relevant photochemical processes are studied in detail. In Section IV we derive an analytical end-to-end statistical model for the proposed MC system. Expressions for the detection threshold and the BER are provided in Section V. In Section VI we evaluate the proposed models numerically. Section VII concludes the paper and outlines topics for future work. Note that we use the terms switching and conversion interchangeably.

II. SYSTEM MODEL

In this section, we describe the proposed media modulation based MC system, including the erasure, modulation, propagation, and reception mechanisms, cf. Fig. 1. The system model presented in this section is generic and applicable to different types of photoswitchable fluorescent molecules. The mathematical details of the relevant photochemical processes are given in Section III. In Section VI the model is specialized to GFPD.

A. Topology

Fig. 1 shows the considered three-dimensional (3-D) straight rectangular duct with height $H$, width $W$, and infinite extent in $z$-direction, which we denote as domain $\Omega$. The duct is filled with a fluid medium, which flows in $z$-direction with constant velocity $v > 0$, i.e., we assume uniform flow, as is widely done in the MC literature [22], cf. Section II-E. Moreover, we assume that the duct surface is impermeable to molecules, i.e., the molecules are reflected at the boundaries of the duct. Additionally, at duct segments $S^{TX}$, $S^{EX}$ and $S^{RX}$ where the EX, TX, and RX are located, respectively, we assume the surface to be transparent to light. The communication process of interest takes place in the subvolume $S = \{ \Omega \cap \frac{Z_{sys} - L_{sys}}{a} \leq z \leq \frac{Z_{sys} + L_{sys}}{a} \}$ of length $L_{sys} = \frac{Z_{sys} - L_{sys}}{a}$ and volume size $V_{sys} = W H L_{sys}$ with unit $m^3$. In the following, all lengths and volume sizes have the units $m$ and $m^3$, respectively. We employ photochromic signaling molecules, which can assume two distinguishable states, state A and state B, and, depending on their state, we refer to them as state A molecules and state B molecules, respectively. The state of a photochromic molecule can be changed by irradiation with light at appropriate wavelength.

We assume that the state of the signaling molecules is random when they arrive at the EX at $z = \frac{Z_{sys} - L_{sys}}{a}$, i.e., with a probability of $P_{in}^{EX} = [0, 1]$ and $1 - P_{in}^{EX}$ a signaling molecule enters the EX in state A and state B, respectively. We assume that $P_{in}^{EX}$ is determined by an external process that cannot be controlled in the considered system. At time $t = 0$, the signaling molecules are assumed to be uniformly distributed in the duct system, i.e., we assume that the signaling molecules had enough time to reach an equilibrium with respect to (w.r.t.) space. The latter assumption requires both identical propagation behavior of state A and state B molecules, cf. Section II-E.

and independence between the state switching processes and molecule propagation, cf. Section III. We assume that $N_{sys}$ signaling molecules are uniformly distributed in subvolume $S$ at time $t = 0$, i.e., we assume that the concentration of the signaling molecules is $C_{sys} = \frac{N_{sys}}{V_{sys}}$, with unit $mol m^{-3}$, where $N_{sys}$ denotes the Avogadro constant. In the following, all concentrations have the unit $mol m^{-3}$.

B. Purification at the EX

We consider a two-dimensional (2-D) EX with area $A^{EX} = L^{EX} W$, which is attached to the surface of the duct at $\frac{Z_{sys} - L_{sys}}{a} \leq z \leq \frac{Z_{sys} + L_{sys}}{a}$, i.e., the EX length is $L^{EX} = \frac{Z_{sys} - L_{sys}}{a}$, cf. Fig. 1. The EX shall ensure that molecules entering subvolume $S$ are in state B, as the TX assumes all molecules are in state B. To this end, the EX constantly radiates light of wavelength $\lambda^{EX}$ and power density $P_{in}^{EX}$ with unit $W m^{-2}$ into volume $S^{EX} = \{ \Omega \cap \frac{Z_{sys} - L_{sys}}{a} \leq z \leq \frac{Z_{sys} + L_{sys}}{a} \}$ of size $V^{EX} = H A^{EX}$. The following, all power densities have the unit $W m^{-2}$. The EX radiation triggers a photochemical reaction at the signaling molecules that switches the state of a signaling molecule from state A to state B with probability $P_{s, EX} \in [0, 1]$.

C. Media Modulation at the TX

We consider a 2-D TX with area $A^{TX} = L^{TX} W$, which is attached to the surface of the duct next to the EX at $\frac{Z_{sys} + L_{sys}}{a} \leq z \leq \frac{Z_{sys} - L_{sys}}{a} = -L^{TX}$, i.e., the TX length is $L^{TX} = \frac{Z_{sys} - L_{sys}}{a}$, cf. Fig. 1. For information transmission, at $t = 0$, the TX radiates light of wavelength $\lambda^{TX}$ and power density $P_{in}^{TX}$ for an irradiation duration of $T_{in}^{TX}$ into volume $S^{TX} = \{ \Omega \cap \frac{Z_{sys} - L_{sys}}{a} \leq z \leq \frac{Z_{sys} + L_{sys}}{a} \}$ of size $V^{TX} = H A^{TX}$. The TX uses ON-OFF keying (OOK) modulation [22] and either radiates with power density $P_{in}^{TX} > 0$ or is inactive, i.e., $P_{in}^{TX} = 0$, representing binary symbols $s = 1$ and $s = 0$, respectively. Assuming appropriate source coding, the empirical frequency of data symbols 0 and 1 will approach 0.5 in the limit of long data transmission, i.e., we assume that the binary information bits 0 and 1 are equiprobable. The TX radiation triggers a photochemical reaction that switches the state of a signaling molecule from state B to state A with probability $P_{s, TX} \in [0, 1]$.

We consider single symbol transmission, i.e., inter-symbol interference (ISI) is assumed to be negligible. We make this assumption to focus on unveiling the properties of the novel modulation scheme proposed. Single symbol transmission can be realized by introducing a guard interval between symbols. The length of the guard interval has to be chosen in accordance with the system properties such that consecutive transmissions do not overlap, which may significantly reduce the achievable transmission rate. If a guard interval cannot be afforded, ISI mitigation techniques as proposed in [23], where light-based eraser units at the RX side are utilized, can be applied.

\footnote{The assumption that the number of signaling molecules in subvolume $S$ is known is similar to the common assumption that the number of molecules released by the TX in conventional MC systems is exactly known [22]. In practice, only the average number of signaling molecules in subvolume $S$, $\langle N_{sys} \rangle$, may be known. Extending the analysis in this paper to this case is an interesting topic for future work.}
D. Detection at the RX

We consider a 2-D RX with area $A_{RX} = l_{RX} W$, which is attached to the surface of the duct at $z = z_{RX}$, i.e., the RX length is $l_{RX} = z_{RX} - z_{RX-a}$. We assume that the TX and the RX are parallel to each other and therefore the distance between the TX and RX centers is $d = \frac{z_{RX} - z_{RX-a}}{2}$. The RX emits light of wavelength $\lambda_{RX-in}$ and can sense light of wavelength $\lambda_{RX-out}$ emitted by the signaling molecules in state A. At fixed sampling time $t_s = \frac{s}{2}$, the RX radiates light of wavelength $\lambda_{RX-in}$ and power density $P_{RX-in}^w$ for a short time duration of $T_{eq}$ into volume $S_{in} = \{\Omega \land z_{RX-a} \leq z \leq z_{RX-b}\}$ of size $V_{RX-in} = \frac{f_{RX-in}^w}{c}$. Here, $t_s$ corresponds to the time a molecule needs to propagate from TX to RX due to uniform flow. The radiated light triggers a fluorescence reaction in state A molecules, i.e., illuminated state A molecules radiate light with wavelength $\lambda_{RX-out}$. This results in a light power density $P_{RX-out}^w$ received at $A_{RX-out}$. We denote the probability to detect a state A molecule at the RX by the abovementioned process as $\Phi_{RX}$.

Remark 1: All considered wavelengths $\lambda_{RX-in}$, $\lambda_{RX-out}$, and $\lambda_{RXi}$ are mutually distinct. For GPPD, the values of these wavelengths are provided in Table I.

E. Molecule Propagation

In both states A and B, the molecules are subject to 3-D Brownian motion characterized by diffusion coefficients $D_A$ and $D_B$, respectively, and flow. The actual flow for the given system structure is laminar, which is for simplicity commonly approximated by uniform flow $\bar{v}$. Hence, we also assume uniform flow with constant flow velocity $v$ in this work. While in general a chemical reaction can result in a change of the molecule structure and size, here we assume $D = D_A = D_B$ for GPPD.

III. PHOTOCHEMICAL PROCESSES

In the proposed system, we employ photochromic molecules as signaling molecules, which can be reversibly switched from state A to state B by external light. This property allows reading, writing, and erasing of information embedded in the state of a molecule by irradiation with light of different wavelengths.

In this section, we mathematically model the photochemical processes, which enable the state transitions and state detection of the signaling molecules. In Section III-A we introduce the general properties and underlying mathematically descriptions of photochemical processes, upon which we build in Section III-B to derive mathematical expressions for the probabilities of, respectively, state switching at the EX and TX, spontaneous state switching in the propagation channel, and detection at the RX via fluorescence. We summarize in Appendix A all simplifying assumptions made to arrive at tractable models and explain the conditions needed for their validity.

A. Quantitative Analysis of a Photoreaction: Absorption and Quantum Yield

Any radiation of light corresponds to a photon flux $q_w^m$ with unit s$^{-1}$, which is given by

$$q_w^m = \frac{P_w^m A^m}{E_w^m},$$

where $m \in \{EX, TX, RX\}$ and $w \in \{in, out\}$ denote the module under investigation and the direction of the radiation w.r.t. the signaling molecules, respectively. In particular, $w = in$ and $w = out$ indicate that the molecule is illuminated and emits light, respectively. Furthermore, due to the use of light with constant radiation wavelength $\lambda_w^m$, each photon $\Phi_w^m$ has the same energy $E_w^m$ [14, Eq. (1.2)]

$$E_w^m = h f_w^m = \frac{h c}{\lambda_w^m},$$

where $h$, $c$, and $f_w^m$ denote the Planck’s constant, the speed of light, and the radiation frequency, respectively.

The general photochemical reaction between a molecule in state $X$ with $X \in \{A, B\}$ and one photon $\Phi_{in,abs}^m$ is defined as follows [14, Eqs. (1.3), (12.18), (12.19)]

$$X + \Phi_{in,abs}^m \xrightarrow{k_{X \rightarrow Y}} Y,$$

and

$$Y + \Phi_{in,abs}^m \xrightarrow{k_{Y \rightarrow X}} X,$$

Figure 1. System model: Signaling molecules are uniformly distributed in a 3-D volume with extent $H$ in y-direction, $W$ in x-direction, and infinite extent in z-direction, resembling an infinite pipe. The molecules propagate by Brownian motion and uniform flow. When signaling molecules enter the EX, their state is random (either A (green) or B (gray)). To reduce randomness, the EX switches the molecules in state A to state B via irradiation of wavelength $\lambda_{EX}$ and measurable light power density $P_{EX-in}^w$. We refer to Figs. 2 and 3 for a detailed description of the photochemical reactions. The variables used in Fig. 1 are defined in Section II and Table I. Table I also lists corresponding default values.
where $k_{X \rightarrow Y}$ and $\overline{k}_{X \rightarrow Y}$ denote the reaction rate constants for yielding a molecule in state $Y$ and state $X$ as reaction product, respectively. Here, all reaction rate constants have the unit $s^{-1}$. In Fig. 2, the corresponding photochemical reactions at EX and TX with $(X, Y, k_{X \rightarrow Y}, \overline{k}_{X \rightarrow Y}) \cong (A, B, k_{A \rightarrow B}, \overline{k}_{A \rightarrow B})$ and $(X, Y, k_{X \rightarrow Y}, \overline{k}_{X \rightarrow Y}) \cong (B, A, k_{B \rightarrow A}, \overline{k}_{B \rightarrow A})$, respectively, are visualized. An important measure of the efficiency of the photochemical reaction in $\mathbb{R}$ is the reaction quantum yield $\varphi_X$, which assumes values between 0 and 1, i.e., $\varphi_X = [0, 1]$, and is defined as the fraction of the reaction rate constants $\mathbb{E}$ Eqs. (12.18), (12.20)]

$$\varphi_X = \frac{k_{X \rightarrow Y}}{k_{X \rightarrow Y} + \overline{k}_{X \rightarrow Y}}. \tag{4}$$

For a constant total number of photons in the system, definition $\mathbb{E}$ is equivalent to the ratio of the change of the concentration of the molecules in state $X$, $dC_X(t)/dt$, in unit time to the change of the concentration of the absorbed photons, $dC^{in, abs}_X(t)/dt$, in unit time, i.e.,

$$\varphi_X = -\frac{dC_X(t)}{dt} / \frac{dC^{in, abs}_X(t)}{dt}. \tag{5}$$

Here, the concentration of absorbed photons, the concentration of molecules in state $X$, and the derivative w.r.t. time are denoted as $dC^{in, abs}_X(t)/dt$, $C_X(t)$ and $dC_X(t)/dt$, respectively. In the extreme case, for $\varphi_X = 1$, each absorbed photon successfully triggers the molecule switching from state $X$ to state $Y$.

Not all photons, which are emitted into the fluid medium by the irradiation light, are absorbed. However, only absorbed photons contribute to the photochemical process, of course. Hence, the photon absorption process is detailed next, which characterizes the ratio of the flux of the emitted photon concentration $dC^{in, abs}_X(t)/dt = q^{in}_m V_{NaX}$ Eq. $\mathbb{E}$, to the flux of the absorbed photon concentration $dC^{in, abs}_X(t)/dt$, both with unit mol m$^{-3}$s$^{-1}$. In the following, all concentration fluxes have the unit mol m$^{-3}$s$^{-1}$. Here, $C^{in, abs}_X(t)$ denotes the concentration of the photons emitted by module $m$. The absorption of a photon initiates the photochemical reaction, and is governed by the Beer-Lambert law Eq. (12.21), (12.22)]

$$dC^{in, abs}_X(t) = \frac{P_m^{in}}{E_m^{in} H N_{AV}} \left( 1 - \exp \left( -\log(10) e^m H C_X(t) \right) \right), \tag{6}$$

where $e^m$ denotes the molar absorption coefficient of the signaling molecules in m$^2$mol$^{-1}$ for the wavelength used in module $m$. Note that (6) is independent of $A^m$, and the duct height $H$ is the maximum absolute distance a photon can propagate through the fluid medium.

**Proposition 1:** Given an initial concentration of the molecules in state $X$ of $C_X(t = 0) = C_{X,0}$ at the beginning of the radiation at $t = 0$, the concentration of molecules in state $X$ as a function of the irradiation time is obtained from (6) as follows

$$C_X(t) = \frac{1}{a} \log \left[ 1 - \exp \left( -C_{X,0} a \frac{P_m^{in}}{E_m^{in} H N_{AV}} t \right) \times \left( 1 - \exp \left( a C_{X,0} \right) \right) \right], \tag{7}$$

where $a = \log(10) H e^m$.

**Proof:** Please find the proof in Appendix $\mathbb{E}$.$\blacksquare$

**B. Derivation of Switching and Detection Probabilities**

In the following, we individually model the photochemical processes in each section of the pipe channel, i.e., EX, TX, propagation channel, and RX. We refer to Figs. 2 and 3 for an overview of the possible state conversions.

**1) Photochemical Reaction at EX:** The molecule state switching process at the EX is given by the following chemical reaction, cf. Fig. 2

$$A + \Phi^{EX}_{in,abs} k_{A \rightarrow B} B, \tag{8}$$

**2) Photochemical Reaction at TX:** The molecule state switching process at the TX is given by the following chemical reaction, cf. Fig. 3
i.e., the EX impacts only state A molecules. As described in Section II-B, the EX constantly radiates light into the subjacent volume $S^{EX}$.

Let $C_{A,0}^{EX}$ denote the concentration of molecules in state A at $z = z_0^{EX}$, i.e., at the left boundary of the EX. $C_{A,0}^{EX}$ is random and further specified in Section IV-B1. The concentration of molecules in state A leaving the EX volume $S^{EX}$ is given by $C_{A}^{EX}(T_{S}^{EX})$, i.e., entering volume $S$ at the right boundary of EX at $z = z_S^{EX}$ is given by (7) with $m = EX$, $X = A$, $Y = B$, and $C_{A,0}^{EX} = C_{A,0}^{EX}$. The probability that a given molecule in state A is switched to state B during the time $T_{S}^{EX}$ it spends in $S^{EX}$ is given with Assumption 7 by

$$p_B^{EX} = 1 - \frac{C_{A}^{EX}(T_{S}^{EX})}{C_{A,0}^{EX}}. \quad (9)$$

Remark 2: Due to EX radiation, the probability of a signaling molecule to be in state A decreases as it propagates through EX. Therefore, the probability w.r.t. the position, where a signaling molecule switches its state within EX, is non-constant and decreases with increasing $z$ in EX. However, randomness of the switching position within EX does not impact the molecule propagation, as the characteristics of the molecules in state A and state B are similar, see Section II-B. Hence, we model the switching position due to irradiation at EX to be at $z_S^{EX}$ i.e., the right boundary of EX.

2) Photochemical Reaction at TX: The modulation process at the TX is described by the following chemical reaction, cf. Fig. 2

$$B + \Phi_{in,abs}^{TX} \xrightarrow{k_B^{TX,A}} A, \quad (10)$$

i.e., the TX impacts only state B molecules. In contrast to the EX, which permanently irradiates light, the TX irradiates for a short duration of length $L^{TX}$ if a binary 1 is sent.

Let $C_{B}^{TX}(t = 0) = C_{B,0}^{TX}$ denote the concentration of the molecules in state B in $S^{TX}$ at the beginning of information transmission at $t = 0$. $C_{B}^{TX}(t = 0)$ is random and further specified in Section IV-B2. The concentration of the molecules in state B in $S^{TX}$ as a function of time $C_{B}^{TX}(t)$ follows from (7) with $m = TX$, $X = B$, $Y = A$, $C_{X,0} = C_{B,0}^{TX}$, and Assumption 2. Then, the probability of any molecule in state B in $S^{TX}$ to be switched from state B to state A within the irradiation time $T_{S}^{TX}$ follows as

$$p_A^{TX} = 1 - \frac{C_{B}^{TX}(T_{S}^{TX})}{C_{B,0}^{TX}}. \quad (11)$$

3) Spontaneous Switching: Next to the desired switching processes in EX and TX, photochromic molecules in state B can spontaneously switch to state A without any external trigger, while spontaneous switching from state A to state B is not possible [24]. We model this spontaneous switching with rate constant $k_s$, as a first-order reaction, i.e., $B \xrightarrow{k_s} A$. Hence, the probability $p_{B,SP}$ that a state B molecule has spontaneously switched in time interval $T_{ch}^{sp}(z_\alpha, z_\beta)$ follows as

$$p_{B,SP}(z_\alpha, z_\beta) = 1 - \exp\left(-k_s T_{ch}^{sp}(z_\alpha, z_\beta)\right) = 1 - \exp\left(\frac{T_{ch}^{sp}(z_\alpha, z_\beta)}{T_1/2} \ln(2)\right), \quad (12)$$

where $T_{ch}^{sp}(z_\alpha, z_\beta) = \frac{z_\beta - z_\alpha}{v}$ and $T_{1/2} = \frac{\ln(2)}{k_s}$ denote the average duration a molecule needs to propagate from $z = z_\alpha$ to $z = z_\beta$ and the half-time of molecules in state B, respectively. The half-time specifies the time needed for a reaction to halve the starting concentration. The spontaneous switching can occur anywhere. However, we model it to take place only in the propagation channel between TX and RX, which is an accurate approximation for small EX and TX lengths, respectively, cf. Assumption 3. Therefore, spontaneous switching does not impact the EX and TX processes, respectively.

Moreover, as the propagation properties of state A and state B molecules are identical, the exact position of the spontaneous switching within the propagation channel from TX to RX is insubstantial. Hence, we examine the impact of spontaneous switching only for the signaling molecules which are at RX at the sampling time. In particular, each signaling molecule entering the RX has spontaneously switched with a probability of $p_{B,SP}^{TX} = p_{B,SP}^{TX}(z_S^{EX}, z_0^{EX})$ during propagation from EX to RX.

Remark 3: For achieving reliable information transmission, spontaneous switching is not desirable. In contrast to molecule degradation, spontaneous molecule switching perturbs the communication link as it creates random noise conveying misleading information.

4) Fluorescence at the RX: At the RX, molecules in state A fluoresce in response to irradiation by light of wavelength $\lambda_{in}$. In particular, at the RX, molecules in state A can assume two substates, cf. Fig. 3. The photons emitted by the RX light switch some of the state A molecules temporarily into an excited, non-stable substate of state A, which we denote as substate $A^*$. The non-excited substate of signaling molecules in state A is denoted as ground state $A^G$ for completeness. In the absence of RX irradiation, all state A molecules are in substate $A^G$.

The concentration of molecules in state A in $S^{RX}$ is constant during the fluorescence process of duration $T_{RX}$ according to Assumption 2, i.e.,

$$C_{A}^{RX} = C_{A}^{RX}(t) + C_{A}^{RX}(t), \quad \text{for} \quad t_s \leq t \leq t_s + T_{RX}. \quad (13)$$

Here, $C_{A}^{RX}(t)$ and $C_{A}^{RX}(t)$ denote the concentrations of the signaling molecules in substates $A^G$ and $A^*$, respectively. $C_{A}^{RX}$ is constant during the fluorescence process, but can be different for every transmission, i.e., $C_{A}^{RX}$ is random and further specified in Section IV-B3.

We utilize two time intervals at the RX. Using two time intervals helps to distinguish the photons emitted from the RX from the photons observed by the RX. In particular, the difference between the employed wavelengths at the RX, denoted as Stokes shift, i.e., $\lambda_{RX} - \lambda_{in}$, is small for GFPD, leading to interference issues in practical systems, if they occur simultaneously. In the proposed RX model, in the first time interval of duration $T_{eq}$ the RX irradiates light and excites some of the state A molecules. In the second time interval of duration $T_{obs}$, the excited molecules are counted. Hence, $T_{RX} = T_{eq} + T_{obs}$ follows. Next, the photochemical processes in the individual intervals are detailed.

At the beginning of the read out process at the RX, all state A molecules are in ground substate $A^G$, i.e., $C_{A}^{RX}(t_s) = C_{A}^{RX}$. 


At \( t = t_s \), the RX starts to illuminate \( \text{S}^\text{RX} \) for a duration of \( T_{\text{eq}} \). The irradiation excites molecules in substate \( A^G \), i.e., the RX induces the switching from \( A^G \) to \( A^* \). Subsequently, a molecule in substate \( A^* \) can switch back to substate \( A^G \) and may emit light. In particular, with rate constant \( k_t \), a photon of wavelength \( \lambda_{\text{RX, max}} \) is radiated and with rate constant \( k_{\text{nr}} \), the switching between the substates produces heat instead of a photon, see Fig. 3. Therefore, the aforementioned process can be modeled as follows

\[
\frac{dC_{\text{RX}}^{A^G}(t)}{dt} = (k_t + k_{\text{nr}})C_{A^*}^{\text{RX}} - \frac{dC_{\text{RX}}^{A^G}(t)}{dt},
\]

for \( t_s \leq t \leq t_s + T_{\text{eq}} \), where the absorbed photon concentration flux \( \frac{dC_{\text{RX, abs}}^{A^G}(t)}{dt} \) is obtained from (6) as follows

\[
\frac{dC_{\text{RX, abs}}^{A^G}(t)}{dt} = E_{\text{in}}^{\text{RX}} H_{A^G}(1 - \exp(-\log(10) C_{A^G}^{\text{RX}}(t))) = \text{const.}
\]

Remark 4: We note that during \( T_{\text{eq}} \), a molecule can change its state multiple times from the ground substate to the excited substate and back.

The duration of irradiation \( T_{\text{eq}} \) is chosen such that the state \( A \) substates reach an equilibrium, where on average the number of molecules switched from substate \( A^G \) to substate \( A^* \) equals the number of molecules switched from substate \( A^* \) to substate \( A^G \) in one unit time step. This can be assured for \( T_{\text{eq}} \geq T_{\text{eq,min}} \), where \( T_{\text{eq,min}} \) denotes the minimum irradiation duration needed at the RX to reach the equilibrium. We refer to Appendix C for the derivation of \( T_{\text{eq,min}} \). According to (27), \( T_{\text{eq,min}} \) is inversely proportional to \( k_t + k_{\text{nr}} \), i.e., the equilibrium is reached faster for larger rate constants.

In equilibrium, the concentration of the molecules in substate \( A^G \) in \( \text{S}^\text{RX} \), \( C_{\text{RX}}^{A^G} \), is constant

\[
\frac{dC_{\text{RX}}^{A^G}(t)}{dt} = 0, \quad \text{for} \quad t_s + T_{\text{eq,min}} \leq t \leq t_s + T_{\text{eq}}.
\]

Proposition 2: The equilibrium concentration of state \( A \) molecules in excited substate \( A^* \) is obtained from (14) – (16) as follows

\[
C_{A^*, \text{eq}}^{\text{RX}} = \frac{1}{x_1 - 1} \frac{x_0 x_2 \exp(\frac{x_2}{x_1})}{x_1},
\]

where \( x_0 = \log(10) E_{\text{in}}^{\text{RX}} H_{A^G} \), \( x_1 = \frac{E_{\text{in}}^{\text{RX}} H_{A^G}(k_t + k_{\text{nr}})}{D_{A^G}}, \) and \( x_2 = \exp(-x_0 C_{A^G}^{\text{RX}}) \), respectively.

Proof: Please find the proof in Appendix D.

Thus, the fraction \( p_{A^*} \) of molecules in substate \( A^* \) at equilibrium is given by

\[
p_{A^*} = \frac{C_{A^*, \text{eq}}^{\text{RX}}}{C_{A^G}^{\text{RX}}}. \tag{18}
\]

After the equilibrium is reached, at \( t_{\text{obs}} = t_s + T_{\text{eq}} \) the RX irradiation stops. Hereupon, the number of photons \( N_{\text{RX}}^{\text{obs}} \) caused by the switching from substate \( A^* \) to substate \( A^G \) are counted by the RX for a time interval of \( T_{\text{obs}} \). We assume \( T_{\text{obs}} \gg \frac{1}{k_t} \) to ensure all molecules in substate \( A^* \) have enough time to switch back to the ground substate \( A^G \). Hence, \( N_{\text{RX}}^{\text{obs}} \) can be obtained as follows

\[
N_{\text{RX}}^{\text{obs}} = \frac{T_{\text{obs}}}{k_t} C_{A^G, \text{eq}}^{\text{RX}} \varphi \Phi^\text{RX}, \tag{19}
\]

Finally, given a molecule in excited substate \( A^* \) at \( t_{\text{obs}} \), we count that molecule indirectly by observing the photon, which is emitted with probability \( \varphi \Phi^\text{RX} \) as the molecule switches back from \( A^* \) to \( A^G \). Hence, the probability of a substate \( A^* \) molecule to be detected by the receiver is given as

\[
\varphi \Phi^\text{RX} = \frac{k_t}{k_t + k_{\text{nr}}}. \tag{20}
\]

In summary, a given state \( A \) molecule in \( \text{S}^\text{RX} \) is detected with probability \( \varphi \Phi^\text{RX} \) during \( T_{\text{RX}}^{\text{obs}} \).

IV. ANALYTICAL END-TO-END CHANNEL MODEL

In this section, we provide insight into the propagation of the molecules. In particular, we derive the probability of arrival at the RX for molecules which were within the TX and outside the TX region during modulation, respectively. In addition, the arrival probability for \( s = 0 \), where we do not need to differentiate between inside and outside the TX, is given. These probabilities are referred to as channel impulse responses (CIRs). As the propagation characteristics of state \( A \) and state \( B \) molecules, respectively, are identical, the same applies to their CIRs. Hence, in Section IV-A for derivation of the CIR, the state of the signaling molecule is irrelevant. Moreover, in Section IV-B we develop a statistical model for the number of photons detected by the RX by interpreting the transmission process of the proposed MC system as a multistage stochastic process.

A. Channel Impulse Responses

Here, we derive the probability of arrival at the RX for a molecule with given position \( z \) during modulation. Due to the assumptions of uniform flow and reflective boundaries, and the considered RX model, the molecule propagation in the system proposed in Section II-A can be equivalently modeled as a molecule propagation in an one-dimensional (1-D) domain with infinite extent, i.e., \(-\infty < z < \infty\). We derive the probability that a molecule is inside the RX given that it was inside the TX at position \( z_{\text{TX}} \) at time \( t \in [0, 0 + T_{\text{TX}}^S] \), as a function of time, i.e., the irradiation starts at \( t = 0 \) and stops at \( t = T_{\text{TX}}^S \). We refer to this probability as \( h_0(t) \). In the following, we approximate \( t \in [0, 0 + T_{\text{TX}}^S] \) by \( t = 0 \), cf. Assumption D in Appendix D. The position \( z_{\text{TX}} \) of the signaling molecules is random and uniformly distributed in the TX region \( z_{\text{TX}} \sim U(z_{\text{TX}}^S, z_{\text{TX}}^S) \).

Proposition 3: The probability \( h_0(t) \) that a signaling molecule, whose position is random and uniformly distributed in \( U(z_{\text{TX}}^S, z_{\text{TX}}^S) \), i.e., \( z_{\text{TX}} \leq z_{\text{TX}} \leq z_{\text{TX}} \), at time \( t = 0 \), is inside the RX region, i.e., \( z_{\text{RX}}^S \leq z_{\text{RX}} \leq z_{\text{RX}}^S \), at time \( t \) is given by

\[
h_0(t) = \frac{1}{2} \exp\left(-\frac{a_0^2}{4Dt}\right) + \sqrt{\frac{4Dt}{\pi}} \exp\left(-\frac{a_0^2}{4Dt}\right), \tag{21}
\]
where \( \{ a_0, a_1, a_2, a_3 \} = \{ s^{\text{RX}}_a - vt, s^{\text{TX}}_a - vt, s^{\text{RX}}_b - vt, s^{\text{TX}}_b - vt \} \) and \( \text{erf}(x) \) denotes the Gaussian error function.

**Proof:** Please find the proof in Appendix E.

Similarly, we obtain the probability \( h_1(t) \) that a signaling molecule, which was in \( S^{\text{TX}}_s = S \setminus S^{\text{RX}}_s \) at \( t = 0 \), i.e., not in the TX region during TX irradiation, is inside the RX region as follows

\[
h_1(t) = \frac{1}{2} L^{\text{sys}} \sum_{i=0}^{3} (-1)^{i} \left[ b_i \text{erf} \left( \frac{b_i}{\sqrt{4Dt}} \right) \right]
+ \sqrt{\frac{4Dt}{\pi}} \exp \left( -\frac{b_i^2}{4Dt} \right),
\]

where \( \{ b_0, b_1, b_2, b_3 \} = \{ s^{\text{RX}}_a - vt, s^{\text{TX}}_a - vt, s^{\text{RX}}_b - vt, s^{\text{TX}}_b - vt \} \).

Furthermore, the probability \( h_2(t) \) that a signaling molecule is inside the RX region, if it was in \( S^{\text{TX}}_s = S \) at \( t = 0 \), follows as

\[
h_2(t) = \frac{1}{2} L^{\text{sys}} \sum_{i=0}^{3} (-1)^{i} \left[ c_i \text{erf} \left( \frac{c_i}{\sqrt{4Dt}} \right) \right]
+ \sqrt{\frac{4Dt}{\pi}} \exp \left( -\frac{c_i^2}{4Dt} \right),
\]

where \( \{ c_0, c_1, c_2, c_3 \} = \{ s^{\text{RX}}_a - vt, s^{\text{TX}}_a - vt, s^{\text{RX}}_b - vt, s^{\text{TX}}_b - vt \} \).

Note that \( h_2(t) \) is related to \( h_0(t) \) and \( h_1(t) \) as \( h_2(t) = h_0(t) + h_1(t) \).

**B. Statistical Model**

In this section, we determine the statistics of the number of photons detected by the RX. These photons originate from the fluorescence reaction of state \( \text{A} \) molecules at the RX (see Section III-B4). Fig. 4 shows that there are several possibilities for a signaling molecule to be detected by the RX based on the photon \( \Phi_{\text{out}} \) it emits. In particular, the fate of any individual molecule is characterized by a conglomerate of eight consecutive stochastic processes, where the output of one process is the input of the subsequent process. Each random process has two possible outcomes and therefore can be modeled as a Bernoulli process. This process is repeated for every input molecule. Eventually, each outcome occurrence follows a Binomial distribution, as the input molecules are modeled to be mutually statistically independent. The latter claim is proved in this section. Finally, we determine the probability distribution of the number of photons detected at the RX characterized by the last stochastic process in the proposed system, which is conditional on all previous processes.

According to Section III-A, \( N^{\text{sys}} \) signaling molecules are uniformly distributed in \( S \) at time \( t = 0 \). Therefore, each of these signaling molecules has traversed the EX during \( t < 0 \). At \( t = 0 \), the TX radiates light if \( s = 1 \), and the RX counts the signaling molecules in \( S^{\text{RX}} \) at \( t = t_s \) for subsequent detection, cf. Fig. 4.

1) **State Distribution of Molecules entering EX:** All \( N^{\text{sys}} \) signaling molecules have entered EX at \( t < 0 \), but only a subset \( N^\text{RX}_\text{A} \leq N^{\text{sys}} \) entered EX in state \( \text{A} \). In particular, a given signaling molecule entered EX in state \( \text{A} \) with a probability \( p^\text{A}_s \) and with a probability of \( 1 - p^\text{A}_s \) in state \( \text{B} \). Hence, the state in which a molecule enters EX can be modeled as a Bernoulli random variable. Therefore, \( N^\text{RX}_\text{A} \) follows the Binomial distribution

\[
N^\text{RX}_\text{A} \sim \text{Binom}(N^{\text{sys}}, p^\text{A}_s) .
\]

2) **Initial Number of State A Molecules:** When a state \( \text{A} \) molecule propagates through EX, it is switched to a state \( \text{B} \) molecule with probability \( p^\text{AB} \), see 9. From 7 and 9, we observe that \( p^\text{AB} \) depends on the number of nearby state \( \text{A} \) molecules, i.e., the concentration \( C_{\text{A},0} \) of signaling molecules in state A. In particular, for large \( C_{\text{A},0} \), \( p^\text{AB} \) is influenced by the competition of molecules for photons. Therefore, during the switching process, there is a statistical dependence between the states of different molecules and the Binomial distribution does not apply. However, the competition can be neglected for small \( C_{\text{A},0} \). In this case, \( p^\text{AB} \) is constant w.r.t. \( C_{\text{A},0} \), which is what we assume in the following. The validity of this assumption is verified in Section VI-B. Hence, applying Theorem 1 on conditional Binomial distributions in Appendix 8, the overall number of state \( \text{A} \) molecules in \( S \) at \( t = 0 \) follows the Binomial distribution

\[
N^\text{sys}_\text{A} \sim \text{Binom}(N^{\text{sys}}, p^\text{A}_s(1 - p^\text{AB})) .
\]

3) **Number of Molecules at TX:** \( N^\text{sys}_\text{B} = N^{\text{sys}} - N^\text{sys}_\text{A} \) state \( \text{B} \) molecules are uniformly distributed in \( S \) at \( t = 0 \). Hence, \( N^\text{sys}_\text{B} \sim \text{Binom}(N^{\text{sys}}(1 - p^\text{A}_s) + p^\text{A}_s p^\text{AB}) \) follows also a
Binomial distribution, as $N_{\text{sys}}^{B}$ and $N_{\text{sys}}^{A}$ are fully correlated. However, only a subset of the these molecules $N_{B}^{TX} \leq N_{\text{sys}}^{B}$ is in $S^{TX}$ at $t = 0$. In particular, with a probability of $p_{h}^{B}$ a given signaling molecule $M$ is inside the TX volume, i.e., $M \in S^{TX}$ and with a probability of $1 - p_{h}^{B}$ it is outside the TX. The availability of a molecule for information transmission can be modeled as a Bernoulli random variable. Therefore, the total number of state B molecules $N_{B}^{TX}$ available at the TX follows the Binomial distribution

$$N_{B}^{TX} \sim \text{Binom}\left(N_{\text{sys}}^{B} \cdot p_{h}^{B}\right).$$

Eq. (20)

4) Number of Switched Molecules at TX: When a state B molecule is in $S^{TX}$ at $t = 0$, it is switched to a state A molecule with probability $p_{s}^{B}$ within the modulation interval, i.e., with probability $p_{s}^{B} > 0$ and $p_{s}^{B} = 0$ for transmit symbol $s = 1$ and $s = 0$, respectively. From (17), we observe that $p_{s}^{B}$ depends on the initial number of molecules $N_{B}^{TX}$ in $S^{TX}$. However, using the arguments from Section IV-B2 we can assume the conversion probability is independent of $N_{B}^{TX}$. Hence, the number of state A molecules at the TX switched from state B during modulation follows the Binomial distribution

$$N_{B}^{TX} \sim \text{Binom}\left(N_{B}^{TX} \cdot p_{s}^{B}\right).$$

Eq. (21)
A. Optimal Detector

We apply the maximum likelihood (ML) decision rule to obtain an estimate \( \hat{s} \) of the transmit symbol \( s \) as follows \[^{22}\]

\[
\hat{s} = \arg \max_{s \in \{0, 1\}} f_r (r | s)
\]

\[
= \begin{cases} 
1, & \text{if } r \geq \xi \\
0, & \text{otherwise}
\end{cases}
\]

where \( f_r (r | s) \) denotes the probability of observing \( r \) photons given symbol \( s \) was transmitted, which is a Binomial distribution according to \[^{30}\].

In the following, we show that the ML decision rule in \[^{31}\] is equivalent to a threshold detector employing a single decision threshold without any performance loss. The threshold value needed for detection can be computed offline and can then be utilized throughout the communication process. Therefore, the threshold detector reduces the computational complexity for online data detection.

**Proposition 4:** The ML decision rule in \[^{31}\] can be equivalently realized by a threshold detector employing a single decision threshold as follows

\[
\hat{s} = \begin{cases} 
1, & \text{if } r \geq \xi \\
0, & \text{otherwise}
\end{cases}
\]

with threshold \( \xi = [\Theta] \) and \( \Theta \in \mathbb{R}_0^+ \) given by

\[
\Theta = \min \left\{ \frac{-N^{\text{sys}}}{10^{k}}, \frac{-N^{\text{sys}}}{10^{k}}, \frac{-N^{\text{sys}}}{10^{k}} \right\}, \quad \text{if } p_t, s=0 > 0
\]

\[
= \min \left\{ \frac{-N^{\text{sys}}}{10^{k}}, \frac{-N^{\text{sys}}}{10^{k}}, \frac{-N^{\text{sys}}}{10^{k}} \right\}, \quad \text{if } p_t, s=0 = 0
\]

**Proof:** Due to space constraints, we only provide a sketch of the proof. An optimal threshold value exists if for one unique value \( \Theta \in \mathbb{R}_0^+ \) with \( \xi = [\Theta] \) the decision metric given by the ML decision rule in \[^{31}\] equals one, i.e., \( f_r (\Theta | s = 1) = f_r (\Theta | s = 0) \). The uniqueness can be proven by showing that \[^{31}\] is monotonically increasing in \( r \). The value of \( \Theta \) is obtained by solving \( f_r (\Theta | s = 1) = f_r (\Theta | s = 0) \). This completes the proof.

B. Bit Error Rate

The BER of the proposed MC system can be expressed as follows

\[
P_e = \Pr \{ s = 0 \} \Pr \{ \hat{s} = 1 | s = 0 \} + \Pr \{ s = 1 \} \Pr \{ \hat{s} = 0 | s = 1 \}
\]

\[
= \frac{1}{2} \sum_{r=0}^{\xi-1} \left( \frac{N^{\text{sys}}}{r} \right) p_t, s=0(1 - p_t, s=0)^{N^{\text{sys}}-r} + \frac{1}{2} \sum_{r=0}^{\xi-1} \left( \frac{N^{\text{sys}}}{r} \right) p_t, s=1(1 - p_t, s=1)^{N^{\text{sys}}-r}
\]

\[
= \frac{1}{2} \left[ 1 - \sum_{r=0}^{\xi-1} \left( \frac{N^{\text{sys}}}{r} \right) p_t, s=0(1 - p_t, s=0)^{N^{\text{sys}}-r} \right]
\]

\[
= \frac{1}{2} \left[ 1 - \sum_{r=0}^{\xi-1} \left( \frac{N^{\text{sys}}}{r} \right) p_t, s=1(1 - p_t, s=1)^{N^{\text{sys}}-r} \right]
\]

VI. PERFORMANCE EVALUATION

In this section, we first specify the parameter values of GFPD \[^{15}\], which we adopt as a practically feasible option for photoswitchable fluorescent molecules. Then, we evaluate the statistical model in \[^{30}\]. Finally, the dependence of the BER in \[^{34}\] on the various system parameters is evaluated.

A. Choice of Parameter Values

The default values of the adopted system parameters are given in Table \[^{4}\]. These values are used in the following if not specified otherwise. The GFPD specific parameter values are taken from \[^{15}, \{24-28\}]. The parameter values related to the duct are chosen such that they have the same order of magnitude as those of the human cardiovascular system \[^{29}, \text{Chap. 14}\]. Note that all parameters used in this section satisfy the conditions of the assumptions in Appendix A.

To verify the accuracy of the analytical expression for the BER, the probability of drawing a photon \( \theta \), stochastic 3-D particle-based simulation (PBS) was carried out. Note that the probability for states switching \( p^{\text{on}} \), \( p^{\text{off}} \), \( p^{\text{on}} \), and \( p^{\text{off}} \) are calculated based on \[^{9}, \{11\}, \{12\}, \{18\}\], respectively, and are then adopted for PBS. PBS is employed to verify \( p^{\text{on}} \), \( h_0(t_0), h_1(t_0), h_2(t_0) \), and the statistical model derived for the consecutive stochastic processes given in \[^{30}\]. The results from PBS were averaged over 10^4 realizations. In addition, we used Monte Carlo simulation to validate the analytical expression for the BER in \[^{34}\]. Hereby, we randomly generated 10^6 transmit symbols. Next, according to the transmit symbols, values for \( N^{\text{sys}} \) were randomly generated based on the proposed and validated statistical model. Finally, the BER for all possible threshold values up to \( \xi \geq 100 \) was numerically determined and the lowest BER selected.

B. Evaluation of the Switching Process and the Statistical Model

First, we exemplarily investigate the photochemical reaction at the TX, discussed in Section III-B2 for GFPD. In Fig. \[^{5}\],\(^{3}\) \( p^{\text{on}} \) as defined in \[^{11}\], is shown as a function of input light

\[^{3}\]A more accurate PBS model, which determines \( p^{\text{on}} \), \( p^{\text{off}} \), \( p^{\text{on}} \), and \( p^{\text{off}} \), by simulating the related photochemical processes, does not seem computationally feasible. In fact, a power density of \( 10^{-10} \text{W m}^{-2} \) would require the simulation of approximately 9 \times 10^5 photons per timestep \( \Delta t = 1 \times 10^{-2} \) s, which does not seem possible.
Table I
DEFAULT VALUES FOR SIMULATION PARAMETERS.

| Parameter       | Description                                | Value         | Ref. |
|-----------------|--------------------------------------------|---------------|------|
| $H$, $W$        | Duct height, duct width                    | 0.001 m, 0.001 m | 29   |
| $z_{in}$, $z_{out}$ | Left and right boundary of $S$            | 0 m, 0.5 m     |      |
| $z_{TX}$, $z_{RX}$ | Left and right boundary of EX             | $-0.01$ m, 0 m |      |
| $z_{in}$, $z_{out}$ | Left and right boundary of RX             | 0 m, 0.05 m    |      |
| $v$             | Flow velocity                              | 0.01 m s$^{-1}$| 29   |
| $D$             | Diffusion coefficient                      | $1 \times 10^{-10}$ m$^2$s$^{-1}$ | 25   |
| $N_{S,in}$      | Number of molecules in $S$                 | 1000          |      |
| $p_{S,in}$      | Irradiation power density at $EX$          | $1 \times 10^6$ W m$^{-2}$ | 15   |
| $p_{TX}$        | Irradiation power density at $TX$          | $1 \times 10^6$ W m$^{-2}$ | 15   |
| $p_{RX}$        | Irradiation power density at $RX$          | $1 \times 10^7$ W m$^{-2}$ | 15   |
| $\lambda_{TX}$ | Wavelength to switch GFP at $EX$          | 405 nm         | 15   |
| $\lambda_{RX}$ | Wavelength to switch GFP at $TX$          | $511 \times 10^{-9}$ m | 15   |
| $\lambda_{S,in}$ | Wavelength to trigger fluorescence         | $511 \times 10^{-9}$ m | 15   |
| $\lambda_{S,out}$ | Wavelength of fluorescence                | $529 \times 10^{-9}$ m | 15   |
| $\epsilon_{EX}$ | Molar absorption coefficient @ 405nm      | $1.9 \times 10^3$ mol$^{-1}$ | 26   |
| $\epsilon_{TX}$ | Molar absorption coefficient @ 360nm      | $2.2 \times 10^3$ mol$^{-1}$ | 26   |
| $\phi_{S,in}$  | Molar absorption coefficient @ 511nm      | $8.3 \times 10^3$ mol$^{-1}$ | 15   |
| $\varphi_B$    | Reaction quantum yield $B \rightarrow A$  | $2.4 \times 10^{-2}$ | 27   |
| $\varphi_A$    | Reaction quantum yield $A \rightarrow B$  | $3.4 \times 10^{-3}$ | 27   |
| $\omega_F$     | Fluorescence quantum yield                | 0.47           | 28   |
| $T_{1/2}$       | Half time in state $B$                     | 600 s          | 24   |
| $\tau_A^{*}$   | Excited state lifetime                     | $2.9 \times 10^{-9}$ s | 28   |
| $T_{S,in}^{EX}$ | Irradiation time at $EX$                  | $\frac{T_{S,in}^{TX}}{T_{S,in}^{TX}}$ | 15   |
| $T_{S,in}^{TX}$ | Irradiation time at $TX$                  | $5 \times 10^{-3}$ s | 15   |
| $T_{eq}$        | Irradiation time at $RX$                  | $1 \times 10^{-6}$ s | 15   |
| $T_{obs}$       | Observation duration at $RX$              | $1 \times 10^{-6}$ s | 15   |
| $\epsilon_{eq}$ | Precision error w.r.t. equilibrium concentration | $10^{-6}$ s$^{-1}$ |      |
| $\chi$          | Condition threshold w.r.t. assumptions in Appendix A | 100 |      |
| $\Delta t$      | Time step PBS                             | $1 \times 10^{-2}$ s |      |

(a) [15] reported values between $2 \times 10^4$ W m$^{-2}$ and $4.3 \times 10^4$ W m$^{-2}$.
(b) [15] reported values between $1 \times 10^3$ W m$^{-2}$ and $1.6 \times 10^6$ W m$^{-2}$.
(c) [15] reported values between $8.2 \times 10^3$ W m$^{-2}$ and $4 \times 10^4$ W m$^{-2}$.
(d) No value for 360nm given in literature. Hence, we assume molar absorption coefficient $\epsilon_{360nm} = \epsilon_{365nm}$.
(e) [15] reported values between $1 \times 10^{-7}$ s and $4 \times 10^4$ s.
(f) [15] reported values between $1 \times 10^{-7}$ s and $4 \times 10^4$ s.
(g) [15] reported values between $1 \times 10^{-2}$ s and $1.5 \times 10^{-1}$ s.
(h) $T_{eq,min} \approx 4 \times 10^{-8}$ s for default values, cf. [15]. The maximum value observed for the parameter values used in our simulations was $T_{eq,min} \approx 8 \times 10^{-8}$ s.
(i) $\frac{1}{\omega_F} = \frac{T_{obs}}{\epsilon_{eq}} = 6.18 \times 10^{-9}$ s $\ll T_{obs}$, cf. [15].

power density $P_{S,in}^{TX}$ for irradiation durations $T_{S,in}^{TX} = 5 \times 10^{-3}$ s and $T_{S,in}^{TX} = 5 \times 10^{-5}$ s, respectively. The range of values for $P_{S,in}^{TX}$ considered in this paper is large compared to [15], where power density values ranging from $1 \times 10^3$ W m$^{-2}$ to $1.6 \times 10^6$ W m$^{-2}$ were used for light sources with wavelength $\lambda_{BA}$, cf. Table I. In addition, the authors in [15] show the general feasibility of lasers as light sources, e.g., for imaging. Hence, very high light power density values are in principle possible. Therefore, we also consider larger power density values compared to [15] in this paper. From Fig. 5, we observe that the likelihood of a molecule to switch within the irradiation time is low for small input power density, increases for increasing input power density, and converges to 1 for large values of $P_{S,in}^{TX}$. Furthermore, we observe for a given input power density that a smaller irradiation time $T_{S,in}^{TX} = 5 \times 10^{-5}$ s results in a smaller conversion probability $P_{S,in}^{TX}$. Moreover, Fig. 5 shows that $P_{S,in}^{TX}$ remains unchanged for a wide range of $N_{S,in}^{TX}$. Only for systems with a very large number of signaling molecules, i.e., if $N_{S,in}^{TX} \geq 10^{14}$, a larger input power density is necessary to achieve a given switching.
probability due to the competition of signaling molecules for photons. As the system geometry is identical at EX, TX, and RX, approximating $p_{A}^{TX}$, $p_{A}^{RX}$ and $p_{A}^{OUT}$ as independent from the number of signaling molecules $N_{A}^{TX}$, $N_{B}^{TX}$, and $N_{A}^{RX}$, respectively, as done in Sections IV-B2, IV-B4 and IV-B6, is justified if the number of signaling molecules is sufficiently small. Therefore, as $N_{B}^{TX}$ and $N_{A}^{RX}$ are upper bounded by $N_{B}^{TX} \leq N_{B}^{TX} \leq 10^{14}$ and $N_{A}^{RX} \leq N_{A}^{RX} \leq 10^{14}$ is sufficient to ensure statistical independence of the signaling molecules.

In Fig. 6 we show the probability mass function of the number of received photons $N_{RX}$ according to (30) for $s = 1$ and $s = 0$ and compare it to results from PBS. The corresponding optimal threshold value is highlighted by the vertical dashed line. We observe that the results obtained from PBS and (30), respectively, match, which confirms the statistical model proposed in Section IV-B.

C. Evaluation of BER

In this section, we evaluate the BER for the proposed system. We mainly vary the EX, TX, and RX irradiation power densities, respectively, as this can be easily realized in a practical setup. Moreover, we study the impact of the state probability $p_{A}^{RX}$ of the signaling molecules at the left boundary of EX on the BER. Finally, we show the performance loss caused by spontaneous switching.

1) Impact of TX and RX Irradiation Power Density on BER: In Fig. 7 the BER is shown as a function of the irradiation power density $P_{RX}^{IN}$ for different numbers of signaling molecules $N_{A}^{RX}$ and different RX radiation power densities $P_{RX}^{IN}$. Here, $p_{A}^{RX} = 0$ is assumed. We observe that the BER decreases as $P_{RX}^{IN}$ increases. For $P_{RX}^{IN} > 4 \times 10^{6}$ W m$^{-2}$, the BER approaches an error floor, which is visible for $N_{A}^{RX} \in \{10, 100\}$ for all choices of $P_{RX}^{IN}$, but occurs also for larger $N_{A}^{RX}$ at lower BER values. In particular, for large $P_{RX}^{IN}$ values, $p_{A}^{RX} = 1$ follows, i.e., the conversion at the TX is deterministic. The BER value of the error floor is dependent on the transmittor noise $n^{TX}$, the noise due to spontaneous switching, and the randomness in the detection process. Moreover, we observe from Fig. 7 that the BER decreases as $N_{B}^{TX}$ increases. This is intuitive, as the standard deviation of a Binomial distributed random variable $\sqrt{N_{B}^{TX} \cdot (1-p)}$ normalized to the mean value $N_{B}^{TX}$, i.e., $\sqrt{N_{B}^{TX} \cdot (1-p)} / \sqrt{N_{B}^{TX}}$, converges to zero for $N_{B}^{TX} \rightarrow \infty$. Hence, for increasing numbers of signaling molecules $N_{B}^{TX}$ discriminating between binomial distributions $N_{A}^{RX}$ (s = 1) and $N_{A}^{RX}$ (s = 0) becomes more reliable, which results in a smaller BER. Next, we consider the impact of $P_{EX}^{IN}$. From Fig. 7, we observe that the BER decreases as $P_{EX}^{IN}$ increases. $P_{EX}^{IN}$ impacts the probability $p_{A}^{EX}$ of a state $A$ molecules to be excited by the RX, which is needed for emission of a photon $\Phi_{RX}^{OUT}$. Moreover, we observe that the BERs for $P_{RX}^{IN} = 2 \times 10^{14}$ W m$^{-2}$ and $P_{RX}^{IN} = 2 \times 10^{12}$ W m$^{-2}$ are almost identical. In particular, for $P_{RX}^{IN} = 2 \times 10^{13}$ W m$^{-2}$, $p_{A}^{EX} \rightarrow 1$ follows. Thus, a further increase of the RX irradiation power density can not improve the BER results. We finally note that the numerically and analytically determined BERs perfectly match.

2) Impact of EX Irradiation Power Density on BER: In Fig. 8 we show the BER as a function of the EX irradiation power density for $P_{EX}^{IN} = \{1, 0.5, 0.25, 0.05, 0\}$ and two different TX irradiation power densities. We chose $P_{RX}^{IN} = 2 \times 10^{12}$ W m$^{-2}$ as RX irradiation power density to ensure $p_{A}^{EX} \approx 1$, which eliminates the randomness caused by low RX irradiation power densities.

First, we consider $P_{RX}^{IN} = 1 \times 10^{6}$ W m$^{-2}$. We observe that for $P_{EX}^{IN} > 0$ the BER decreases as $P_{EX}^{IN}$ increases. In particular, an increase in $P_{RX}^{IN}$ increases the number of state B signaling molecules $N_{B}^{TX}$, which are available for modulation at the TX, cf. (26). Furthermore, we observe that for $P_{EX}^{IN} = 0.05$ and 0.05 the BER improves by a factor of $2 \times 10^{4}$ and $2 \times 10^{6}$, respectively, if $P_{EX}^{IN}$ is increased from $P_{EX}^{IN} = 5 \times 10^{2}$ W m$^{-2}$ to $P_{EX}^{IN} = 5 \times 10^{5}$ W m$^{-2}$. Hence, the actual increase of $N_{B}^{TX}$ due to $P_{EX}^{IN}$ heavily depends on $p_{A}^{EX}$ From that we conclude that for large $p_{A}^{EX}$ i.e., values close to one, an EX is mandatory for the proposed system to ensure reliable
communication, whereas for $p_{A}^{\text{in}}$ close to zero, the EX can be deactivated, e.g., in case of power consumption limitations. Furthermore, for large $P_{\text{in}}^{\text{EX}}$, all signaling molecules exit EX as state B molecules. Hence, the BER is independent of $p_{A}^{\text{in}}$ for large $P_{\text{in}}^{\text{EX}}$ which leads to the error floor in Fig. 8.

Now, we consider the impact of $P_{\text{in}}^{\text{EX}}$. We observe that the BER decreases if $P_{\text{in}}^{\text{EX}}$ is increased from $1 \times 10^6 \text{W m}^{-2}$ to $1 \times 10^7 \text{W m}^{-2}$. However, the BER reduction depends on both $p_{A}^{\text{in}}$ and $P_{\text{in}}^{\text{EX}}$. In particular, an increase of the TX irradiation power density has no visible impact on the BER if $p_{A}^{\text{in}} = 1$ and $P_{\text{in}}^{\text{EX}}$ is small, whereas for $p_{A}^{\text{in}} = 0$ or large $P_{\text{in}}^{\text{EX}}$ we observe a large improvement of the BER.

Finally, we observe that, for very small BERs, the results obtained by Monte Carlo simulation do not perfectly match the analytical results since, in this case, the number of Monte Carlo iterations was too low to obtain numerically stable results.

3) Impact of Spontaneous Switching and Flow Velocity on BER: In the proposed MC system, the state of the signaling molecules is used to encode information. In contrast to MoSK, where the types of molecules employed are assumed to be independent, in media modulation, there exists a dependency between the different states A and B even after the modulation process at the TX due to the spontaneous switching from state B to state A. We show in the following that the amount of noise introduced by the spontaneous switching of GFPD is velocity dependent and results in a performance degradation.

In Fig. 9, the BER is shown as a function of flow velocity $v$ for two different EX irradiation power densities and different spontaneous switching rate constants, which result in different values for $p_{A,\text{SP}}^{\text{in}}$. Here, $p_{A}^{\text{in}} = 0.5$, $T_{S}^{\text{RX}} = 5 \times 10^{-5} \text{s}$, $P_{\text{in}}^{\text{EX}} = 2 \times 10^{12} \text{W m}^{-2}$, $P_{\text{in}}^{\text{TX}} = 1 \times 10^9 \text{W m}^{-2}$, $z_{\text{SP}}^{\text{RX}} = 5 \times 10^{-7} \text{m}$, and $z_{\text{SP}}^{\text{TX}} = 0.405 \text{m}$ are used to satisfy all assumptions detailed in Appendix A.

First, we consider the case with spontaneous switching typical for GFPD according to (12) (solid lines). We observe that the BER has a unique minimum at a particular flow velocity, which we denote by $v_{\text{opt}}$. Increasing and decreasing $v$ compared to $v_{\text{opt}}$ increases the BER. The reason is that a decrease in the flow velocity increases the time a molecule spends in the channel between EX and RX, which leads to an increase of $p_{A,\text{SP}}^{\text{in}}$ and a degradation of information transmission. In contrast, for high velocities, the conversion of state A molecules to state B molecules at EX is insufficient to guarantee conversion of all molecules, as the irradiation duration $T_{S}^{\text{RX}}$ of a molecule inside the EX is short. We also observe from Fig. 9 that an increase in $P_{\text{in}}^{\text{EX}}$ decreases the BER if $v$ is large. In addition, $v_{\text{opt}}$ is larger for higher $P_{\text{in}}^{\text{EX}}$.

Next, we consider $p_{A}^{\text{in}} > 0$. In particular, $p_{A}^{\text{in}} = 0$ is an unrealizable special case for the proposed GFPD as the halftime is not an adjustable property of the signaling molecules, cf. Section III-B3. However, we consider this hypothetical case to gain insight into this specific property of media modulation based on GFPD.

Compared to $p_{A}^{\text{in}} > 0$, for $p_{A}^{\text{in}} = 0$, the unique BER
minimum occurs at a smaller BER and smaller velocity, which we denote as $v_{\text{opt},0}$, i.e., $v_{\text{opt},0} < v_{\text{opt}}$. Decreasing $v$ from $v_{\text{opt},0}$ increases the propagation duration from TX to RX and therefore increases the spatial spread of the modulated signaling molecules due to diffusion. Thus, $\mathbb{E}(N_{s,\text{in}})$ for $s = 1$ decreases, while it remains unchanged for $s = 0$, which increases the BER. For velocities larger than $v_{\text{opt},0}$ the insufficiency at the EX determines the performance and leads to a larger BER. From the BER difference between $p_{s,\text{in}}$ and $p_{s,\text{in}} = 0$ in Fig. 9 we conclude that for small velocities $p_{s,\text{in}}$ is beneficial. These insights motivate the design of new photochromic molecules, whose states are more stable, i.e., which have a smaller spontaneous switching rate constant.

VII. Conclusion

In this paper, we introduced a new form of media modulation for MC, which provides a promising perspective for designing non-invasive MC systems. Media modulation does not require a TX that stores signaling molecules and controls their release. In particular, in media modulation based MC the TX only alters the state of the signaling molecules already present in the channel. We investigated the properties of media modulation for the group of photochromic molecules, whose states can be controlled by external light stimuli. This control mechanism allows for writing, reading, and erasing of information embedded in the molecule state. Furthermore, we studied the usage of these molecules for information transmission in a 3-D duct system with one EX, one TX, and one RX. We developed a statistical model for the received signal taking into account eight consecutive and interdependent random processes. Based on the proposed statistical model, we derived analytical expressions for the optimal threshold value of a threshold based detector and the BER. Our numerical BER results prove that even in the absence of a molecule emitting TX reliable information transmission is feasible. Furthermore, our results reveal that (i) increasing the EX, TX, and RX power densities leads to a BER reduction, (ii) media modulation is negatively affected by TX noise and spontaneous switching in the channel, and (iii) there exists an optimal flow velocity due to the tradeoff between reliable switching at the EX for low velocity values and low spontaneous switching as well as reduced molecule spread in the channel for high velocity values.

In this paper, we focused on media modulation based on the photochromic molecule GFPD. A detailed investigation of signaling molecules which can be switched to more than two states and therefore allow for higher order modulation is an interesting topic for future work. Furthermore, it would be interesting to analyze the applicability of other biological processes, such as phosphorylation, for synthetic media modulation based MC. Moreover, the investigation of potential applications of media modulation in industrial pipelines, biomedical environments, bio-chemical reactors, and microfluidic testbeds seems promising. Also, while a general fair comparison between media modulation and conventional modulation schemes does not seem possible because of the different transmitter and system models, performance and complexity comparisons for concrete application scenarios are important. In addition, while we assumed uniform flow for simplicity of presentation, the extension of the proposed designs and models to laminar, turbulent, and time-varying flows is of high theoretical and practical interest.

APPENDIX

A. Collection of Simplifying Assumptions

Here, we summarize the assumption made in Sections III and IV.

Assumption 1: All signaling molecules are exposed to the irradiation inside EX for $T_{S,EX}^{\text{TX}} = \tau_{\text{opt}}$ seconds. Given the assumed uniform flow, this assumption holds if the molecule movement due to diffusion within EX is negligible, i.e., for large Péclet numbers. Eq. (20) with $\text{Pe} = \frac{\text{EX}}{v_{0,\text{opt}}} > \chi > 1$. Here, for convenience, $\chi$ denotes the threshold that we considered to guarantee $\gg 1$ in the evaluation part in Section VI.

Assumption 2: During one irradiation of length $T_{S,EX}^{\text{TX}}$ molecules do not move into or out of $S_{EX}^{\text{TX}}$, i.e., they are static, and are equally affected by the irradiation. The assumption is valid if the random displacement of a molecule within the irradiation duration $T_{S,EX}^{\text{TX}}$ is much shorter than the TX length $l_{\text{TX}}$, i.e., $\sqrt{2D_{\text{TX}}T_{S,EX}^{\text{TX}}} > \chi > 1$ , where the propagation distance due to diffusion is provided by its standard deviation $\sqrt{2DT_{S,EX}^{\text{TX}}}$.

Assumption 3: Spontaneous switching mainly happens in the propagation channel from TX to RX. This assumption holds true, if $\frac{T_{1/2,EX}^{\text{TX}}}{T_{1/2,EX}^{\text{TX}}} > \chi > 1$ and $\frac{T_{1/2,EX}^{\text{TX}}}{T_{1/2,EX}^{\text{TX}}} = \frac{T_{1/2,EX}^{\text{TX}}}{T_{1/2,EX}^{\text{TX}}} > \chi > 1$, as in this case $p_{s,\text{SP}}^{\text{TX}} \approx 0$ and $p_{s,\text{SP}}^{\text{TX}} \approx 0$ follows.

Assumption 4: The molecules are static during the fluorescence process of duration $T_{S,EX}^{\text{TX}}$, which starts at $t_0$. This assumption is valid, if the duration $T_{S,EX}^{\text{TX}}$ to read out the transmitted information at the RX is short, i.e., $\sqrt{2D_{\text{TX}}T_{S,EX}^{\text{TX}}} > \chi > 1$, cf. condition for Assumption 2.

Assumption 5: $t \in [0, T_{S,EX}^{\text{TX}}]$ is approximated by $t = 0$. This approximation is valid for small $T_{S,EX}^{\text{TX}}$, i.e., when no molecules enter or leave the TX volume $S_{EX}^{\text{TX}}$ during the modulation time length.

B. Number of Switched Molecules

Eq. (6) can be solved for $C_X(t)$ as follows:

$$\begin{align*}
(6) & \Leftrightarrow (a) \quad \frac{P_m}{E_m H N_{Av}} \varphi_X \, dt = -\frac{1}{1 - \exp(-a C_X(t))} dC_X(t) \\
(6) & \Leftrightarrow (b) \quad \frac{P_m}{E_m H N_{Av}} \varphi_X \, t + c = - \frac{\log(1 - \exp(aC_X(t)))}{a} \\
(6) & \Leftrightarrow (c) \quad \exp(-a \frac{P_m}{E_m H N_{Av}} \varphi_X \, t) (1 - \exp(aC_X(t))) = 1 - \exp(aC_X(t)),
\end{align*}$$

$$\begin{align*}
(35)
\end{align*}$$
where we apply in (a) the substitution $a = \log(10)He^a$ and multiplication with $dt$ and in (b) the integration w.r.t. $t$ and $C_X(t)$. Subsequently, we exploit in (c) $C_X(t = 0) = C_{X,0}$, which yields $c = -\log\left(1 - \exp(a C_{X,0})\right)$. Then, we apply the exponential function to both sides of the equation. Finally, after further rearranging, we apply the natural logarithm function to both sides to obtain (7).

C. Derivation of Minimum Illumination Time at RX to Reach Equilibrium

As (7) denotes the steady-state concentration and does not contain the transient part, we derive the minimum illumination duration $T_{eq,\text{min}}$ necessary to reach the steady state, i.e., the time required for (7) to be valid. To improve readability, we change variables as $t' = t - t_s$. As the solution to the non-linear differential equation defined by (14) and (15) is not straightforward, we approximate the exponential function in (15) by the first two terms of its Taylor series, i.e., $\exp(x) \approx 1 + x$, which leads to

$$\frac{dC_{RX}^{A_G}(t')}{dt'} = (k_t + k_{nr})C_{RX}^{A} - \frac{P_{in}^{RX}}{N_{AV}} \log(10) \frac{C_{RX}^{A}}{C_{RX}^{G}} (t')$$

$$(a) \Rightarrow \frac{dC_{RX}^{A_G}(t')}{dt'} + z_1 C_{RX}^{A_G}(t') = C_{RX}^{A_G} z_1$$

$$(b) \Rightarrow C_{RX}^{A_G}(t') = c_0 \exp(-z_0 t')$$

$$(c) \Rightarrow \frac{dC}{dt'} = C_{RX}^{G} z_1 \exp(z_0 t')$$

$$(d) \Rightarrow C_{RX}^{A}(t') = \exp(-z_0 t') c_1 + C_{RX}^{A_G} z_1$$

$$(e) \Rightarrow C_{RX}^{A_G}(t') = C_{RX}^{A} \left[ \exp(-z_0 t') - \exp(-z_0) \frac{z_1}{z_0} + 1 \right] ,$$

for $t' > 0$, where we substitute in (a) $z_0 = k_t + k_{nr} + \frac{P_{in}^{RX}}{N_{AV}} \log(10)$, $z_1 = k_t + k_{nr}$, and $C_{RX}^{A_G}(t') = C_{RX}^{A} - C_{RX}^{G}(t')$, provide in (b) the homogeneous solution with $c_0 \in \mathbb{R}$, and utilize in (c) the variation of constants, which yields the general solution in (d) with $c_1 \in \mathbb{R}$. Finally, we exploit in (e) that all state A molecules are in state $A^G$ at the beginning of the fluorescence process, i.e., $C_{RX}^{A_G}(t' = 0) = C_{RX}^{A_G}$.

We assume the equilibrium state to be reached, if

$$\left|\frac{dC_{RX}^{A_G}(t')}{dt'}\right|_{t'=T_{eq,\text{min}}} < \frac{\epsilon_{eq}}{N_{AV} \sqrt{\frac{P_{in}^{RX}}{H}}} ,$$

with precision error $\epsilon_{eq}$, which yields

$$T_{eq,\text{min}} \approx -\ln\left(\frac{\epsilon_{eq}}{C_{RX}^{A_G} N_{AV} \sqrt{\frac{P_{in}^{RX}}{H}}}\right) \frac{1}{z_0} .$$

D. Derivation of the Fluorescence Intensity

We insert (15) in (14) and substitute $x_0 = \log(10)C_{RX}^{A_G} N_{AV}$, which in conjunction with (16) yields

$$(k_t + k_{nr})C_{RX}^{A_G,eq} - \frac{P_{in}^{RX}}{N_{AV}} \frac{1 - \exp(-x_0 C_{RX}^{A_G,eq})}{N_{AV}} = 0$$

$$(a) \Rightarrow x_1 C_{RX}^{A_G,eq} = 1 - x_2 \exp\left(x_0 C_{RX}^{A_G,eq}\right)$$

$$(b) \Rightarrow x_0 C_{RX}^{A,G,eq} \exp\left(\frac{x_0 - x_0 C_{RX}^{A,G,eq}}{x_1}\right)$$

$$= \frac{x_0}{x_1} \exp\left(\frac{x_0}{x_1} x_0 C_{RX}^{A,G,eq} - \frac{x_0 x_2}{x_1} \exp\left(\frac{x_0}{x_1}\right)\right)$$

$$(c) \Rightarrow x_0 x_2 \exp\left(\frac{x_0}{x_1}\right)$$

$$= \left(\frac{x_0}{x_1} - x_0 C_{RX}^{A,G,eq}\right) \exp\left(\frac{x_0}{x_1} - x_0 C_{RX}^{A,G,eq}\right)$$

$$(d) \Rightarrow \frac{x_0}{x_1} - x_0 C_{RX}^{A,G,eq} = W \left(\frac{x_0 x_2}{x_1} \exp\left(\frac{x_0}{x_1}\right)\right) ,$$

where we substituted in (a) $x_1 = \frac{P_{in}^{RX} N_{AV} (k_t + k_{nr})}{N_{AV}}$ and $x_2 = \exp(-x_0 C_{RX}^{A,G,eq})$, and used the classification of signaling molecules into substates (13) by $C_{RX}^{A,G,eq} = C_{RX}^{A} - C_{RX}^{A_G,eq}$. Subsequently, we apply in (b) an expansion by factor $\frac{x_0}{x_1} \exp\left(\frac{x_0}{x_1}\right) \exp(-x_0 C_{RX}^{A,G,eq})$. Furthermore, after factoring in (c), we substitute in (d) the Lambert W function $W(\cdot)$ defined as $w \exp(w) = x \Rightarrow W(z) = w$. Finally, further rearranging yields (7).

E. Derivation of Impulse Responses

Because of the assumed uniform flow and the transparent, counting RX, which covers the entire cross-section of the pipe, the received signaling molecule concentration is independent of the $xy$ dimension. Thus, the considered 3-D environment can be equivalently modeled by an unbounded 1-D environment. The 1-D environment is unbounded as the pipe has infinite axial extent. The expected spatio-temporal molecule concentration $P$ in the equivalent 1-D model is characterized by the advection-diffusion equation given as $\partial_t P = D \partial_x^2 P - v \partial_x P$. The solution to this equation is given by $P(t, z^{TX}, z^{RX}) = \frac{1}{4 \pi D t} \exp\left(-\frac{(z^{TX} - z^{RX} - vt)^2}{4 D t}\right)$, i.e., $P(t, z^{RX}, z^{TX})$ denotes the probability that one molecule released at $z^{RX}$ at time $t = 0$ is observed at $z^{RX}$ at time $t > 0$.

The probability of a signaling molecule to be within the RX is obtained by expecting over the release position $z^{RX}$ and integration over the axial extent of the RX as follows

$$h(t) = \mathbb{E}\left\{ P(t, z^{RX}, z^{TX}) dz^{RX}\right\}$$

$$= \int P(t, z^{RX}, z^{TX}) f_{z^{TX}} (z^{TX}) dz^{TX} dz^{RX}$$

$$\Rightarrow (a) \Rightarrow \frac{z^{RX}}{2 \sqrt{D t} \pi} \text{erf}\left(\frac{z^{RX} - z^{TX} - vt}{\sqrt{4 D t}}\right) - \text{erf}\left(\frac{-z^{RX} - z^{TX} - vt}{\sqrt{4 D t}}\right) dz^{RX} ,$$

where $\mathbb{E}\{\cdot\}$ denotes the expectation operator, and we exploit in (a) the uniform distribution of $z^{TX}$, i.e., $f_{z^{TX}} (z^{TX}) = \frac{1}{2 \sqrt{D t}}$. Finally, applying the integral $\int \text{erf}(z) dz = x \text{erf}(x) + \frac{1}{\sqrt{\pi}} \exp(-x^2)$, we obtain (21). This concludes the proof.
F. Distribution of a Doubly Stochastic Binomial Process

Theorem 1: If \( F \) and \( G \) given \( F \) are Binomial distributed random variables, then \( G \) again follows a Binomial distribution, i.e.,

\[
G \sim \text{Binom}\left(n, Pr\{G = m\} = \sum_{k=m}^{n} \frac{n!}{k!(n-k)!} p^k (1-p)^{n-k}
\]

where \( \text{Binom}\left(N, p\right) \) denotes a binomial distribution with parameters \( N \) and \( p \). Here, \( N \) and \( p \) denote the number of trials and the success probability, respectively.

Proof: As \( F \sim \text{Binom}\left(n, p\right) \) and \( G | F \sim \text{Binom}\left(F, q\right) \land F \sim \text{Binom}\left(n, p\right) \), (40)

the total probability of \( G \) is obtained as follows

\[
Pr\{G = m\} = \sum_{k=m}^{n} Pr\{G = m | F = k\} Pr\{F = k\}
\]

\[
= \sum_{k=m}^{n} \binom{n}{k} q^m (1-q)^{n-k} \binom{n}{k} p^k (1-p)^{n-k}
\]

\[
= \sum_{k=m}^{n} \binom{n}{m} \binom{n-m}{k-m} q^m (1-q)^{n-k-m} p^k (1-p)^{n-k-m}
\]

\[
= \binom{n}{m} (qp)^m \sum_{i=0}^{m} \binom{n-m}{i} (p-qp)^i (1-p)^{n-i-m}
\]

\[
= \binom{n}{m} (qp)^m (1-q)^{n-m},
\]

where in (a) we exploit \( \binom{k}{m} \binom{n-m}{k-m} = \binom{n}{m} \binom{n-m}{k-m} \),

in (b) we use \( p^k = p^{k-m} p^m \) and substitute \( i = k - m \), and in (c) we use the binomial identity \( (a+b)^c = \sum_{d=0}^{c} \binom{c}{d} a^{c-d} b^d \). This completes the proof.

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