Statistical Modeling and Bit Error Rate Analysis for Bio-Sensor Receivers in Molecular Communication

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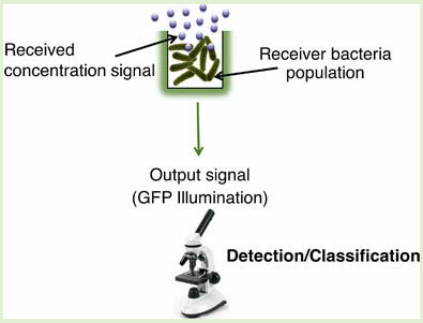
***Abstract*—The behavior of bio-sensor receivers is studied for molecular communication (MC). Bacteria can be engineered as a bio-sensor receiver to produce an output signal, e.g., produce green fluorescent protein, with respect to an external concentration pulse (MC signal). The signal transduction of bacteria, i.e., bacteria response, can be used to detect the pulse-amplitude modulated MC signals. In this work, a statistical model for the bacteria-based bio-sensor receivers is developed. Statistical signal models are useful to evaluate the reliability of the communication systems. The bacteria response is modeled by approximating a first-order model of signal transduction in the linear ramp-up region. The bacteria response is found to be a function of the response rate (linear ramp-up slope) and the time. Bacterial signal transduction is inherently noisy due to the cascades of biochemical reactions to produce the output signal. Therefore, the first-order model is extended incorporating the noise in both the rate and the timing (random delay) of the bacteria response. The bit error rate performance is studied to reveal the impact of the timing noise against the response rate noise. The developed statistical signal model can aid performance evaluation of bacteria-based bio-sensor receivers in MC and biological sensing.**



***Index Terms*—Molecular communication, statistical modeling, bit error rate, bacterial signal transduction, bio-sensor, receiver analysis.**

I. Introduction

SYNTHETIC biology aims to engineer biological systems that can process chemicals, produce food, create sustainable energy, enhance bioremediation, and help biomedical therapies [1]. Engineering of large-scale complex biological systems necessitates the engineering of biological communication techniques leveraging cell signaling mechanisms by taking into consideration the biochemical dynamics of such systems. The interconnection of the engineered biological systems can improve reliability and predictability, as well as expand capabilities of individual engineered biological systems.

With this aim, molecular communication (MC, communication using mass transport and signal transduction mechanisms) is a novel bio-inspired paradigm that can leverage the biochemical signals produced by engineered cells to exchange information [2], [3]. Researchers have been investigating biological communication mechanisms for information transmission among engineered cells and nanomachines in the MC research area. Bacteria is popular for the applications of synthetic biology due to their relatively easy and inexpensive genetic modification and measurement [1], [4]. Engineered bacteria-based bio-sensor systems have been discussed in [5]. A bacteria-based molecular oscillator on a microfluidic chip has been developed in [6]. Bacteria have also been investigated to develop bacteria-based bio-sensor receivers for MC using concentration signals [7]. Bacteria-based bio-sensor receivers can be used as an interface to connect engineered biological systems to outside world by recording the bioluminescence [7]. Molecular source can transmit pulse-amplitude modulated (PAM) concentration signals with a certain level x and composed of a single type of molecule. The bacteria can transduce the molecular signal to green fluorescence protein (GFP), and bacteria illumination can be recorded as the received signal y.

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In the MC literature, there have been efforts to study receiver modeling and performance analysis for molecular sensors that are capable of measuring the level of the received concentration [8], [9]. Modeling and analysis of chemical reactions in MC systems have been often studied in the context of ligand-binding nano-receivers, and receiver design [10]–[14]. The error rate in information reception with bacteria-based bio-sensor receivers has been an open problem. For the development reliable MC systems, the noisy operation of signal transduction in the bacteria-based bio-sensor receivers needs to be incorporated into signal models.

To this end, our objective is to develop a statistical model for bacteria-based bio-sensor receivers capturing the noise in the bacteria response. A statistical model of the received signal can facilitate the characterization of the bit error rate (BER) performance using the detection theory developed for classical communication systems [15]. In [7], it was shown that if the bacteria response is sampled based on slope of the linear ramp-up behavior, statistically better detection performance could be achieved compared to the sampling based on peak value, ramp-down slope, and total response duration. However, to the best of our knowledge, our work here is the first analytical approach to develop a statistical signal model for the bacteria-based bio-sensor receivers that incorporates the response rate and response delay noise effects of signal transduction and its relation to the BER. Ramp-up slope can be a useful feature for machine learning algorithms, specifically in the area of classification. Bacteria response can take up to several hours to finish, while ramp-up slope can make early classification of input concentration signal possible (e.g., timely detection of multi-drug resistant infections). Furthermore, statistical model of ramp-up slope can enable characterization of receiver operating characteristic curves with respect to noise statistics for classification algorithms, and reduce the burden on data collection and experimentation.

In this paper, we initially consider a first-order biochemical model of the signal transduction by bacteria. We simplify the model for the linear ramp-up region. We show that bacteria response in the linear ramp-up region is product of the response rate (slope of linear ramp-up) and the time. We extend this model by incorporating the noise factors for the response rate and response delay. We investigate the difference between the exact results and results with Gaussian distribution for noise terms. Gaussian distribution approximation can provide easy way for closed form solutions when the decision variable needs to be analytically incorporated into the statistical analysis (the exact distribution for noise term would require use of numerical techniques or hybrid analysis-simulation for BER analysis). Lastly, we study how BER changes with respect to the response rate and the response delay noises. We compare the impact of the probability distribution and the variance of both noise factors on the BER performance.

The remainder of this paper is organized as follows. In Section II, a deterministic biochemical model of bacterial signal transduction in the linear ramp-up region is obtained. In Section III, the response rate and response delay noises incorporated into received signal model, and the noise distribution is studied. In Section IV, the BER is studied using the developed statistical signal model for the bio-sensor receivers. The conclusions are provided in Section V.

II. Bacteria-Based Bio-Sensor Receivers

The goal of the bacteria-based bio-sensor receiver is to determine from a noise perturbed signal which of the finite set of discrete messages had been sent by the transmitter. We consider the molecular source is releasing concentration pulse with a constant duration. The discrete messages are represented by the amplitude of the transmitted constant-duration concentration pulses, i.e., pulse-amplitude modulation (PAM) is used for information transmission. Concentration pulse is composed of single type of molecules which bacteria cannot synthesize. Therefore, bacteria produce desired output signal for detection only when there is a transmission. Engineered bacteria transduce the concentration pulse to green fluorescence protein (GFP), which can be observed using fluorescence microscopy. Detection of the transmitted message is performed based on the fluorescence microscopy of the bacteria response. The finite-duration concentration pulses can be realized in a microfluidic chip where bacteria-based bio-sensor receiver are placed in chambers attached to the microfluidic channel. Due to the required large pulse duration, i.e., on the order of 10 mins, dispersion and delay in microfluidic channel are inconsequential for bacteria response [16].

A. Efficient Sampling of the Bacteria-Based Bio-Sensor Receiver

There are several challenges for the efficient sampling of the bacteria-based bio-sensor receiver. To detect the transmitted message, given fixed pulse duration, a unique response level (one-to-one input-output relation) is required. Imperfections (noise effects) which are present in the bacteria response level as well as timing issues (randomly varying response beginning, peak instant, and response ending) make it challenging to distinguish which message was transmitted. The presence of noise effects have a detrimental effect on the detection performance and should be minimized. Furthermore, bacteria response can take several hours to complete. In some applications, the timely communication of the transmitted message can be of great importance, such as in the case of real-time monitoring of chemical changes. Therefore, instead of waiting for the bacteria response to finish, it could be critical to decide on the transmitted signal as early as possible or within a delay constraint. Sampling of the ramp-up slope of bacteria response is shown to be less vulnerable to noise and providing the most accurate detection performance compared to sampling of the peak value [7], as well as requiring less observation duration for bacteria response.

B. Background on Step Response of Bacteria-Based Bio-Sensor Receiver

The gene sequence of bacteria can be engineered such that specific proteins can be produced in response to an external molecular signal [17, Chapter 2]. To analytically characterize this signal transduction by bacteria (external signal to output

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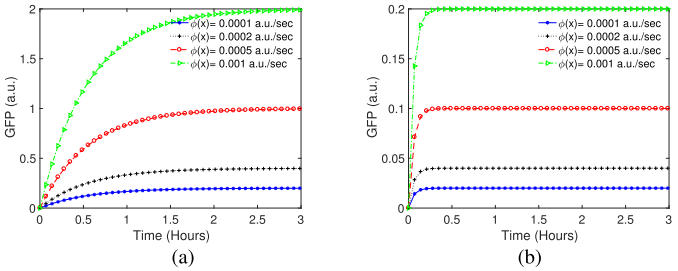

Fig. 1. Theoretical results for rise time transient response of signal transduction by bacteria with various $\phi \triangleright x \triangleleft$ values for $\alpha = 0.0005\text{s}^{-1}$ and $\alpha = 0.005\text{s}^{-1}$ in (a) and (b), respectively.

protein conversion), we use the model of the gene expression from systems biology [17]. For a transmitted pulse level x, the output signal y can be modeled as [17]

$$\frac{\partial y(t)}{\partial t} = \frac{\beta x^n}{\theta_x^n + x^n} - \alpha y(t) \tag{1}$$

where θ_x is the activation coefficient, n determines steepness of the bacteria signal transduction, β is the maximum expression level, and α is the degradation rate of the output signal y. $\beta x^n/(\theta_x^n + x^n)$ is the rate of production for y. $x^n/(\theta_x^n + x^n)$ is the Hill function that scales the maximum expression level β with respect to the input signal x. θ_x determines the activation of expression with respect to the amount of x. Maximum expression level β is reached when input concentration $x \gg \theta_x$. n determines how sensitive the expression level scales with respect to the changes in input signal x.

As an example, encoding of information via the concentration of Acyl Homoserine-Lactone (AHL) molecules can be considered. It is possible to engineer a bacteria population to produce GFP with an intensity (y) that depends on the concentration of AHL molecules (x) [6]. This feature can be added in bacteria that normally do not emit GFP through the configuration of their plasmid [6].

The step response of (1) is obtained as

$$y(t) = \left(\frac{\beta x^n}{\theta_x^n + x^n}\right) \frac{1}{\alpha} \left(1 - e^{-\alpha t}\right). \tag{2}$$

We define the bacteria response rate ϕ based on transmitted pulse level x as

$$\phi(x) = \frac{\beta x^n}{\theta_x^n + x^n}, \tag{3}$$

where function ϕ depends on the empirical parameters θ_x, and β. In case these empirical parameters may not be accessible individually, ϕ can be tabulated for selected pulse levels x. Accordingly, $y(t)$ is rewritten as

$$y(t) = \frac{\phi(x)}{\alpha} \left(1 - e^{-\alpha t}\right). \tag{4}$$

In Fig. 1(a), and Fig. 1(b), we present the bacteria responses with respect to the various $\phi(x)$ values for $\alpha = 0.0005\text{s}^{-1}$ and $\alpha = 0.001\text{s}^{-1}$, respectively (values were taken from [17]). Linear ramp-up slope changes with respect to response rate $\phi(x)$. The bacteria response increases linearly with time around $t = 0$. It should be also noted that the bacteria response stays in the linear region for a short amount of time. For different ϕ values, bacteria response has a different ramp-up slope s in the linear region.

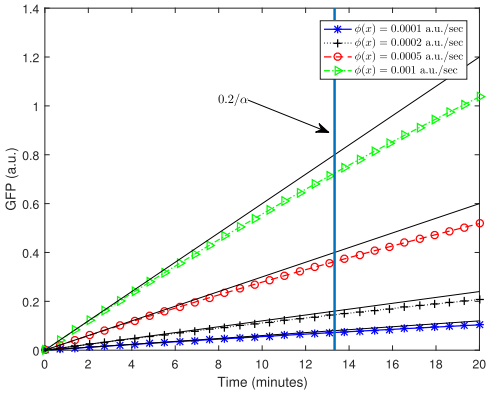

Fig. 2. Error in linear approximation of signal transduction by bacteria with various $\phi \triangleright x \triangleleft$ values for $\alpha = 0.00025\text{s}^{-1}$. Black solid lines denote results with linear approximation and other lines denote exact results.

C. Approximation for Bacteria Response in Linear Ramp-Up Region

Here, we approximate the bacteria response in the linear ramp-up region for $\alpha t \approx 0$ using the first order Taylor series expansion. Using $\exp(-\alpha t) \approx 1 - \alpha t$, y is given by

$$y(t) \approx \phi(x) t. \tag{5}$$

The linear relation between the ϕ and the time enables development of slope-based detection, where the slope of the bacteria response can be used as decision variable to decide on the transmitted pulse level x.

1) Time Where the Approximation Is Reasonable: Let us use more accurate second order Taylor series approximation for $y(t)$ (when $\alpha t \approx 0$),

$$y(t) \approx \phi(x) t - \frac{\phi(x) \alpha t^2}{2}. \tag{6}$$

The error of the linear term (5) compared to the exact value in (4) can then be approximated with

$$\varepsilon(t) \approx -\frac{\phi(x) \alpha t^2}{2}. \tag{7}$$

The error relative to the linear approximation value is

$$\begin{aligned} \varepsilon_r(t) &= \frac{\varepsilon(t)}{\phi(x) t} \\ &= -\frac{\alpha t}{2}. \end{aligned} \tag{8}$$

By requiring that relative error is less than 10%, i.e., $|\varepsilon_r(t)| < 0.1$, we get

$$t \leq \frac{0.2}{\alpha}. \tag{9}$$

Fig. 2 illustrates this limit. Please note that actual experimental results in [7] show that bacteria response can sufficiently change in the time scale of this limit.

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D. Noise in the Response Delay

The bacterial signal transduction involves a series of biochemical reactions. A biochemical reaction can produce fluctuating number of intermediate molecules in short bursts at random time intervals, which need to reach an effective level to activate the next step in the signal transduction pathway. Therefore, there can be large differences in the bacteria response delay, especially across the bacteria population. The random variations in the response rate and the response delay need to be incorporated in the statistical received signal model for the bacteria-based biosensor receiver. The difference of the response beginning and input molecular signal start ($t = 0$) times gives the bacteria response delay. The randomness in response beginning delay was studied based on measurements [7]. The response delay of the bacteria-based biosensor has importance to correctly detect the transmitted concentration pulse level.

III. Statistical Model for Bacteria-Based Bio-Sensor Receivers

The detection of molecular signals using bacteria response is a challenging task, since the transmitted molecules are also involved in the signal transduction of the bacteria. To understand the BER performance of various detection schemes, a statistical description of the received signal is needed. A statistical received signal model can enable assessment of BER performance of MC schemes with respect to the noise factors, i.e., response rate and response delay noises.

The analytical model in (5) does not include the noise effects. In this section, a statistical received signal model which incorporates the noise in the response rate and the response delay is developed.

A. Noisy Model for Linear Ramp-Up Region

The noisy bacteria response is caused by intra-cellular dynamics, intercellular variations as well as by environmental variations. The signal transduction of bacteria is composed of multiple biochemical reactions where fluctuating number of intermediate molecules are produced in short bursts at random time intervals. Furthermore, the intermediate signaling molecules in the signaling pathway of bacteria need to reach a sufficient level to start the next biochemical reaction in the signaling pathway. Additionally, variations across the bacteria population as well as the environmental changes can also cause imperfections in the bacteria response. The overall effect of these random variations, i.e., noise, on the output signal y are seen as the variation in the bacteria response rate $\phi(x)$ and response delay (τ_{delay}) [7]. To statistically characterize the received signal from bacteria-based bio-sensor receivers, response rate noise w_{rate} and response delay noise w_{delay} effects need to be incorporated into the received signal model.

We extend the approximation in (5) by incorporating the response rate noise w_{rate}, and the response delay noise w_{delay}. Our model is based on observed behaviour of actual experimental bacteria responses [7].

The noisy received signal is given by

$$y(t) = \begin{cases} [\phi(x) + w_{\text{rate}}] \\ \cdot[(t - \tau_{\text{delay}}) + w_{\text{delay}}] & t \geq \tau_{\text{delay}} - w_{\text{delay}} \\ 0 & t < \tau_{\text{delay}} - w_{\text{delay}} \end{cases} \tag{10}$$

We assume that slope noise has time-invariant statistics. We sample the $y(t)$ after waiting for a duration T_s after beginning of the bacteria response. Following (9), reasonable T_s should satisfy

$$T_s \leq \frac{0.2}{\alpha}.$$

Sampling instant is given by

$$t = \tau_{\text{delay}} + T_{\text{s}}, \tag{11}$$

where τ_{delay} is the bacteria response delay, and T_s is the sampling interval.

Using (11), (10) is re-written as

$$\begin{aligned} y &= [\phi(x) + w_{\text{rate}}][T_{\text{s}} + w_{\text{delay}}] \\ &= \phi(x)T_{\text{s}} + T_{\text{s}}w_{\text{rate}} + \phi(x)w_{\text{delay}} + w_{\text{rate}}w_{\text{delay}}, \end{aligned} \tag{12}$$

when $T_{\text{s}} \geq -w_{\text{delay}}$, and $y = 0$ otherwise.

B. Probability Distributions

Chemical reactions can be modeled as a Poisson process as well as a Gaussian process under certain approximations [18]. A common approach taken to model randomness in chemical reactions is the approximation to the Gaussian process due to the large mean, i.e., large number of molecules entering to the reaction [18].

To analytically study the noise distribution here, the distribution of the the response rate w_{rate} and the response delay w_{delay} noises are taken Gaussian distributed as

$$w_{\text{rate}} \sim \mathcal{N}\left(0, \sigma^2_{\text{rate}}\right), \tag{13}$$

and

$$w_{\text{delay}} \sim \mathcal{N}\left(0, \sigma^2_{\text{delay}}\right). \tag{14}$$

The term $w_{\text{rate}}w_{\text{delay}}$ in (12) becomes a product of independent Gaussian random variables as

$$w_{\text{rate}}w_{\text{delay}} \sim P_{w_{\text{rate}}w_{\text{delay}}}(z), \tag{15}$$

where $P_{w_{\text{rate}}w_{\text{delay}}}(z)$ is as

$$\begin{aligned} &P_{w_{\text{rate}}w_{\text{delay}}}(z) \\ &= \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} \frac{1}{\sqrt{2\pi\sigma^2_{w_{\text{rate}}}}} e^{-\frac{w^2_{\text{rate}}}{2\sigma^2_{w_{\text{rate}}}}} \\ &\quad \cdot \frac{1}{\sqrt{2\pi\sigma^2_{w_{\text{delay}}}}} e^{-\frac{w^2_{\text{delay}}}{2\sigma^2_{w_{\text{delay}}}}} \delta(w_{\text{rate}}w_{\text{delay}} - z)\mathrm{d}w_{\text{rate}}\mathrm{d}w_{\text{delay}}. \end{aligned} \tag{16}$$

The distribution of the product of two Gaussian random variables has been studied in [19], [20], [21]. For zero mean w_{rate} and w_{delay}, the distribution of $w_{\text{rate}}w_{\text{delay}}$ is given by

$$P_{w_{\text{rate}}w_{\text{delay}}}(z) = \frac{K_0\left(\frac{|z|}{\sigma_{w_{\text{rate}}}\sigma_{w_{\text{delay}}}}\right)}{\pi\sigma_{w_{\text{rate}}}\sigma_{w_{\text{delay}}}}, \tag{17}$$

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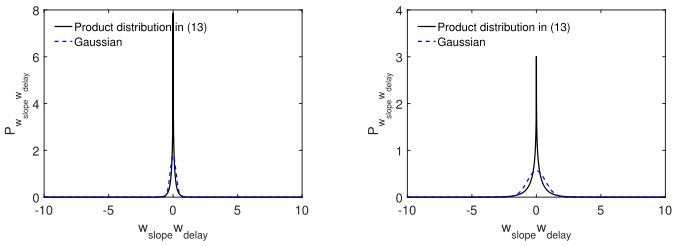

Fig. 3. Comparison of the p.d.f. in (17) and Gaussian p.d.f. with zero mean and variance $\sigma^2_{\text{rate}}\sigma^2_{\text{delay}} = 0.05$ a.u.^{2} in (a), and with zero mean and variance $\sigma^2_{\text{rate}}\sigma^2_{\text{delay}} = 0.5$ a.u.^{2} in (b).

where K_0 is modified Bessel function of the second kind.

In the literature, error probability has been studied analytically for a wide range of Gaussian noise communication systems. Therefore, a Gaussian approximation to the p.d.f. in (17) is useful for the analytical tractability. We compare the distribution of $P_{w_{\text{rate}}w_{\text{delay}}}$ and Gaussian distribution with zero mean and variance $\sigma^2_{\text{rate}}\sigma^2_{\text{delay}}$ in Fig. 3(a) and Fig. 3(b). The $\sigma^2_{\text{rate}}\sigma^2_{\text{delay}}$ is equal to 0.05 a.u.^{2} and 0.5 a.u.^{2} for Fig. 3(a) and Fig. 3(b), respectively. The Gaussian random variable with the same mean and the same variance provides a good approximation of the p.d.f. in (17) for $\sigma^2_{\text{rate}}\sigma^2_{\text{delay}}$ of 0.05 a.u.^{2} with less good fit for 0.5 a.u.^{2}. This does not mean that BER estimation cannot be sufficiently accurate. To check this, in Section IV, we will study the accuracy of the Gaussian approximation in terms of BER.

For the ranges of standard deviation that provide a good approximation, the distribution of $w_{\text{rate}}w_{\text{delay}}$ product can be approximated as zero mean Gaussian random variable with variance $\sigma^2_{\text{rate}}\sigma^2_{\text{delay}}$. The obtained analytical distribution of the $w_{\text{rate}}w_{\text{delay}}$ and the Gaussian approximation to it will be utilized to study statistics of the decision variable in Section IV for BER performance evaluation.

C. Decision Variable

Bacteria response is a function of time. However, it is not required to sample response at all times. For slope calculation, one sample or two samples can be used instead.

1) One-shot Detection: We use the slope s of the linear ramp-up region as the decision variable. From the bacteria response y approximated for the linear ramp-up region in (12), s is obtained as

$$s = \frac{y}{T_{\text{s}}} = \phi(x) + w_{\text{rate}} + \frac{\phi(x)}{T_s}w_{\text{delay}} + \frac{1}{T_s}w_{\text{rate}}w_{\text{delay}}, \quad (18)$$

when $T_{\text{s}} \geq -w_{\text{delay}}$ and $s = 0$ otherwise. In practice, T_{s} is selected as sufficiently large so that the calculated slope will be non-zero.

The slope s can be experimentally obtained via sampling the recorded raw GFP illumination of the bacteria-based biosensor receiver and by using (18). The bacteria illumination can be recorded as the received signal y via fluorescence microscopy. Then, the decision variable s can be obtained via dividing received signal y by T_s.

2) Two-Sample Detection: We can use two samples for calculating the slope with

$$s = \frac{y - y_1}{T_{\text{s}} - T_{\text{s}_1}}, \quad (19)$$

where y and y_1 are responses at sampling instants (relative to τ_{delay}) T_{s} and T_{s_1}, respectively. We assume that T_{s} is selected as sufficiently large, so that $T_{\text{s}} \geq -w_{\text{delay}}$. For the first sampling instant, it is possible to select for example $T_{\text{s}_1} = 0$. Let us assume $T_{\text{s}_1} = 0$. Now,

$$s = \begin{cases} \phi(x) + w_{\text{rate}} & w_{\text{delay}} \geq 0 \\ \phi(x) + w_{\text{rate}} + \dfrac{\phi(x)}{T_{\text{s}}}w_{\text{delay}} + \dfrac{w_{\text{rate}}w_{\text{delay}}}{T_{\text{s}}} & w_{\text{delay}} < 0 \end{cases} \quad (20)$$

We can see that when the delay noise is positive, the noise terms involving it disappear. The reason is that in the linear region delay does not affect two-sample slope as long as both samples are non-zero. Since delay noise is modeled as Gaussian random variable, this occurs with 0.5 probability. When delay noise is negative, the first sampling interval gives output zero so the result will be the same as in the case of one-shot detection. Note that it is also possible to select $T_{\text{s}_1} > 0$ in which case the delay noise can be better reduced but at the cost of the reduced effective sampling interval.

3) Triggered Detection: In triggered detection, we wait until the output reaches level y_1. Let us denote this time as t_1. Then output is sampled at $t_2 = t_1 + T_{\text{s}}$ and slope is found with

$$s = \frac{y_2 - y_1}{T_{\text{s}}}, \quad (21)$$

where y_2 denotes output at time t_2. By setting output to y_1 and solving (10), we get

$$t_1 = \frac{y_1}{\phi(x) + w_{\text{rate}}} - w_{\text{delay}} + \tau_{\text{delay}}$$

By sampling at t_2, we get

$$y_2 = y_1 + T_{\text{s}}\left(\phi(x) + w_{\text{rate}}\right). \quad (22)$$

Therefore, the obtained slope

$$s = \phi(x) + w_{\text{rate}}. \quad (23)$$

We can see that with triggered detection, the delay noise does not affect at all. This is its benefit compared to two-sample detection that could cancel delay noise only 50% of the time. However, triggered detection depends on the proper choice of the trigger level. Too high trigger level would mean that the second sample may not be taken anymore during the linear region, degrading the slope estimation quality. Also, we can see that obtained slope does not depend on T_{s}. In practice, slope noise may vary with time so that higher sampling intervals do give benefit (as long as we stay in the linear region).

In the next section, we investigate the BER for the bacteria-based bio-sensor receivers.

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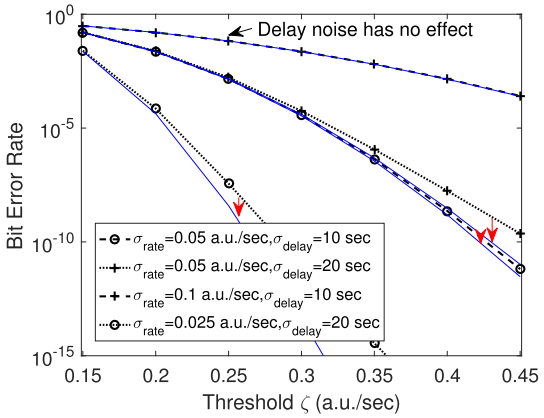

Fig. 4. BER performance when s is obtained using the analytical distribution of $w_{\text{rate}}w_{\text{delay}}$ in (17). Black lines with one-shot detection and blue lines with two-sample detection, $T_s = 10$ minutes, $T_{s_1} = 0$ minutes. Arrows show the two-sample detection corresponding to given one-shot detection curve.

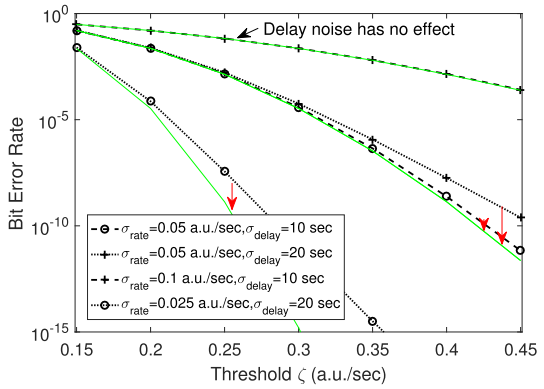

Fig. 5. BER performance. Black lines with one-shot detection (using the analytical distribution of $w_{\text{rate}}w_{\text{delay}}$ in (17)) and green lines with triggered detection found using (28) with (29).

IV. Bit Error Rate Performance

In this section, we study the BER performance using the developed statistical signal model. Two signal levels (x_1 and x_2) are considered to be transmitted. The corresponding signal level to x_1 is taken to be lower than the one for x_2. In the line with signal levels, the bacteria response corresponding to x_1 is lower than x_2.

The probability of error for x_1, i.e., the received signal is greater than the detection threshold ζ, is

$$P(s > \zeta | x_1) \tag{24}$$

and similarly the error rate for x_2 is given by

$$P(s < \zeta | x_2) \tag{25}$$

The transmission of both signal levels are taken to be equally likely, and hence, the error rate for binary PAM is obtained using (24) and (25) as

$$P_b = \frac{1}{2} P\left(s > \zeta | x_1\right) + \frac{1}{2} P\left(s < \zeta | x_2\right), \tag{26}$$

where ζ is the threshold, which we assume is obtained as

$$\zeta = \frac{\mu_{x_1} + \mu_{x_2}}{2}, \tag{27}$$

where $\mu_{x_1} = \phi(x_1)$ is the mean of the decision variable s when x_1 is transmitted, and $\mu_{x_2} = \phi(x_2)$ is the mean of the decision variable s when x_2 is transmitted. For simplicity, we use this threshold even when the variances for different transmitted levels are unequal.

By using Gaussian approximation, we get

$$P_b = \frac{1}{2} Q\left(\frac{\zeta - \mu_{x_1}}{\sigma_{x_1}}\right) + \frac{1}{2} Q\left(\frac{-\zeta + \mu_{x_2}}{\sigma_{x_2}}\right), \tag{28}$$

where $Q(\cdot)$ denotes the Q-function, and σ_{x_1} and σ_{x_2} are the standard deviations of the decision variable when x_1 or x_2 is sent, respectively.

For example, for triggered detection, only Gaussian rate noise is present so that Gaussian approximation is exact with

$$\sigma_{x_1} = \sigma_{x_2} = \sigma_{\text{rate}}. \tag{29}$$

For one-shot detection, we can approximate noise as Gaussian with

$$\sigma_{x_i} = \sqrt{\sigma_{\text{rate}}^2 + \left(\frac{\phi(x_i)}{T_s}\right)^2 \sigma_{\text{delay}}^2 + \left(\frac{1}{T_s}\right)^2 \sigma_{\text{rate}}^2 \sigma_{\text{delay}}^2}, \tag{30}$$

where $i \in \{1, 2\}$. We can see that standard deviation varies with the transmitted signal level.

For two-sample detection, the variance is the average of the variance in one-shot detection (corresponding to case where delay noise is negative) and triggered detection (corresponding to case where delay noise is positive). We get the standard deviation with

$$\sigma_{x_i} = \sqrt{\sigma_{\text{rate}}^2 + \left(\frac{\phi(x_i)}{T_s}\right)^2 \frac{\sigma_{\text{delay}}^2}{2} + \left(\frac{1}{T_s}\right)^2 \frac{\sigma_{\text{rate}}^2 \sigma_{\text{delay}}^2}{2}}, \tag{31}$$

where $i \in \{1, 2\}$.

A. Simulation Environment

We perform simulations to study BER performance of the bacteria-based biosensor receivers. First, we evaluate the BER using the obtained analytical distribution of the $w_{\text{rate}}w_{\text{delay}}$ in (17). BER results using (17) are presented in Fig. 4. We demonstrate the impact of response rate noise and the response delay noise on the BER performance of the bacteria-based biosensor performance in Fig. 4. In Fig. 5, results are presented for the triggered detection also. They are found with (28) and (29) (Gaussian approximation is exact in this case).

Additionally, we also evaluate the BER performance by approximating the $w_{\text{rate}}w_{\text{delay}}$ as Gaussian distributed. BER results using Gaussian distribution approximation are presented in Fig. 6. The results with Gaussian approximation are obtained by using (28) with standard deviations in (30) and (31).

The results using (28) were obtained using fully closed form equations. The results using (17) were based on hybrid analytical and simulation approach. We simulate the received signal y using (12) for various variances of the noises w_{rate} and w_{delay}. w_{rate} and w_{delay} are taken zero mean. We obtain the decision variable s via dividing received signal y by T_s as in (18).

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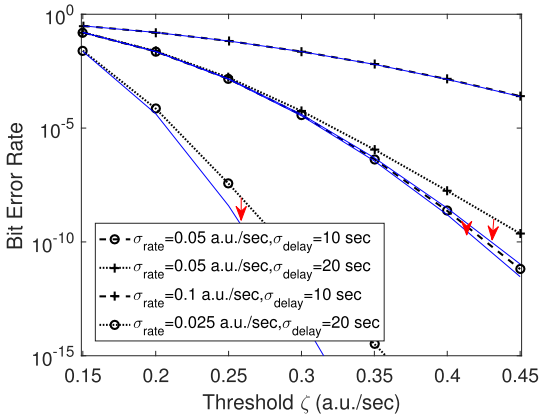

Fig. 6. BER performance when s is obtained by approximating $w_{\rm rate}w_{\rm delay}$ as Gaussian distributed with a mean of zero and a standard deviation of $\sigma_{\rm rate}\sigma_{\rm delay}$. Black lines with one-shot detection and blue lines with two-sample detection, $T_s = 10$ minutes, $T_{s_1} = 0$ minutes. Results found using (28) with (30) and (31).

T_s is taken 10 min. $\phi(x_1)$ is taken as 0.1 a.u./sec, and $\phi(x_2)$ is varied from 0.2 a.u./sec to 0.8 a.u./sec.

B. Results

In Fig. 4, BER results are presented for the case when s is obtained using the hybrid simulation-analytical approach using distribution of $w_{\rm rate}w_{\rm delay}$ in (17). As the difference between transmitted signal levels x_1 and x_2 increases, the BER decreases. Lower variances for $w_{\rm rate}$ and $w_{\rm delay}$ provide better performance. It is observed that noise variances of the response rate and response delay have both detrimental effect on the BER performance. When $\sigma_{\rm rate}$ is doubled from 0.05 to 0.1 a.u./sec for constant $\sigma_{\rm delay} = 10$ sec, BER is severely increased compared to the case when $\sigma_{\rm delay}$ is doubled from 10 to 20 sec for constant $\sigma_{\rm rate} = 0.05$ a.u./sec. Additionally, it is observed from (18) that the selection of a large T_s may alleviate the effect of noise terms $w_{\rm delay}$ and $w_{\rm rate}w_{\rm delay}$ in s. However, one cannot select arbitrarily large T_s, since the ramp-up region is linear for a limited time-interval, which is illustrated in Fig. 1(a) and Fig. 1(b).

The blue lines in Fig. 4 show the results with two-sample detection that can significantly reduce the effect of the delay noise. Since for $\sigma_{\rm rate} = 0.1$ and $\sigma_{\rm delay} = 10$ two-sample detection results exactly correspond to that of the one-shot detection, for this case delay noise does not affect the BER. Similarly, when $\sigma_{\rm rate} = 0.05$ and $\sigma_{\rm delay} = 10$ the delay noise only causes small degradation on the BER. However, for $\sigma_{\rm rate} = 0.05$ and $\sigma_{\rm delay} = 20$, the effect of delay noise is significant. It can be observed that two-sample detection can still give almost the same BER with $\sigma_{\rm delay} = 20$ as with $\sigma_{\rm delay} = 10$. For the case $\sigma_{\rm rate} = 0.025$ and $\sigma_{\rm delay} = 20$, delay noise is also significant and two-sample detection can reduce its effects.

Fig. 5 shows the results with triggered detection. Triggered detection completely removes the delay noise. For example, we can see that results for $\sigma_{\rm rate} = 0.05$ with $\sigma_{\rm delay} = 10$ and $\sigma_{\rm rate} = 0.05$ with $\sigma_{\rm delay} = 20$ are equal, since only delay noise is changing. We can observe by comparing with Fig. 4 that two-sample detection can remove delay noise almost as well as triggered detection without requiring triggering operation.

In Fig. 6, BER results are obtained by approximating $w_{\rm rate}w_{\rm delay}$ as Gaussian distributed with a mean of zero and a standard deviation of $\sigma_{\rm rate}\sigma_{\rm delay}$. BER results in Fig. 6 closely follows the BER results in Fig. 4. Although the presented differences in Fig. 3(a) and Fig. 3(b) for the p.d.f. of $w_{\rm rate}w_{\rm delay}$ using analytical distribution in (17) and Gaussian approximation, BER results obtained using these two distributions follow each other closely in Fig. 4 and Fig. 6. Based on the excellent fit between exact results and results with Gaussian distribution, we conclude that Gaussian distribution approximation for $w_{\rm rate}w_{\rm delay}$ provides easy way for closed form solutions when s needs to be analytically incorporated into the statistical analysis of the MC systems with bacteria-based bio-sensor receivers. Instead, the exact distribution for noise term requires use of numerical techniques or hybrid analysis-simulation for BER analysis.

V. Conclusion

We have studied the development of a statistical signal model for the bacteria-based bio-sensor receivers in MC. A statistical signal model can be useful to evaluate the throughput and the accuracy of MC systems. We, first, analyzed the transient bacteria response to develop a model of signal transduction in the linear ramp-up region. We obtained a statistical received signal model by extending the deterministic model for the slope of the linear ramp-up region to include response rate and response delay noises. The statistical model provided in this work considers the transmission of finite-duration of concentration pulses, i.e., pulse-amplitude modulation, and addresses the effects of noises in the bacteria response delay and the response rate. Then, we studied the distribution of noise terms in the statistical signal model. The excellent fit between exact results and results with Gaussian distribution points out that the Gaussian distribution approximation for noise terms provides a tractable way for closed form solutions when the decision variable statistics need to be analytically computed. Meanwhile, the exact distribution for noise term requires use of numerical techniques or hybrid analysis-simulation for BER analysis. Lastly, the impact of noise variances on the BER performance is investigated. The developed statistical signal model can be useful for the prediction of the detection performance in MC systems with bacteria-based bio-sensor receivers and PAM concentration signals.

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