A Unifying Model for External Noise Sources and ISI in Diffusive Molecular Communication

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Abstract—This paper considers the impact of external noise sources, including interfering transmitters, on a diffusive molecular communication system, where the impact is measured as the number of noise molecules expected to be observed at a passive receiver. A unifying model for noise, multiuser interference, and intersymbol interference is presented. Where, under certain circumstances, interference can be approximated as a noise source that is emitting continuously. The model includes the presence of advection and molecule degradation. The time-varying and asymptotic impact is derived for a series of special cases, some of which facilitate closed-form solutions. Simulation results show the accuracy of the expressions derived for the impact of a continuously-emitting noise source, and show how approximating old intersymbol interference as a noise source can simplify the calculation of the expected bit error probability of a weighted sum detector.

Index Terms—Diffusion, intersymbol interference, molecular communication, multiuser interference, noise.

I. INTRODUCTION

Molecular communication is a physical layer design strategy that could enable the deployment of nanonetworks by facilitating the sharing of information between individual devices with nanoscale functional components. It is envisioned that these networks will bring new applications to fields that require diagnostics or actions on a small physical scale, e.g., healthcare and manufacturing; see [1], [2]. Molecular communication relies on molecules released by transmitters as information carriers, and is inspired by the common use of molecules for information transmission in biological systems; see [3].

Passive molecular propagation methods do not require external energy for transport. The simplest such method, free diffusion, randomly moves molecules via collisions with other molecules, and does not require fixed connections between transceivers. However, the design of a communication network that is based on free diffusion faces a number of challenges. The propagation time increases and the reliability decreases as the distance between transceivers increases. Intersymbol interference (ISI) arises if there is no process to degrade information molecules or carry them away from the receiver.

Furthermore, the deliberate release of molecules by the intended transmitter might not be the only local source of information molecules. We refer to other such sources as external molecule sources. External molecule sources can be expected in diffusive environments where nanonetworks may be deployed. Examples include:

- Multiuser interference caused by molecules that are emitted by the transmitters of other communication links. This interference can be mitigated by using different molecule types for every communication link, but this might not be practical if there is a very large number of links and the individual transceivers share a common design.
- Unintended leakage from vesicles (i.e., membrane-bound containers) where the information molecules are being stored by the transceivers. A rupture could result in a steady release of molecules or, if large enough, the sudden release of a large number of molecules; see [4].
- The output from an unrelated biochemical process. The biocompatibility of the nanonetwork may require the selection of a naturally-occurring information molecule. Thus, other processes that produce or release that type of molecule are effectively noise sources for communication. For example, calcium signalling is commonly used as a messenger molecule within cellular systems (see [5], Ch. 16), so selecting calcium as the information carrier in a new molecular communication network deployed in a biological environment would mean that the natural occurrence of calcium is a source of noise.
- The unintended reception of other molecules that are sufficiently similar to the information molecules to be recognized by the receiver. For example, the receptors at the receiver might not be specific enough to only bind to the information molecules, or the other molecules might have a shape and size that is very similar to that of the information molecules; see [5], Ch. 4).

Most existing literature on noise analysis in diffusive molecular communication has considered the noise in the communication link, i.e., via the noisiness of diffusion itself or chemical mechanisms at the receiver, cf. e.g. [6]–[11], without accounting for the impact of external noise sources. The impact of multiuser interference on capacity was evaluated numerically in [12]. Wave theory was used to approximate both ISI and multiuser interference in [13], where ISI was limited to one previous interval and only multiuser emissions in the current transmission interval were considered. In [14], a stochastic model was proposed that included the spontaneous generation of information molecules in the propagation environment.
In this paper, we propose a unifying model for external noise sources (including multiuser interference) and ISI in diffusive molecular communication. We consider an unbounded physical environment with steady uniform flow, based on a system model that we studied in [15], [16] (but where we did not develop any detailed noise analysis; we only assumed that the asymptotic impact of the noise sources was known). The primary contributions of this paper are as follows:

1) We derive the expected asymptotic (and, wherever possible, time-varying) impact of a continuously-emitting noise source, given the location of the source and its rate of emission. By impact, we refer to the corresponding expected number of molecules observed at the receiver, and by asymptotic we refer to the source being active for infinite time. Closed-form solutions are available for a number of special cases; otherwise, the impact can only be found via numerical integration.

2) We use asymptotic noise from a source far from the receiver to approximate the impact of interfering transmitters, thus providing a simple expression for the molecules observed at the receiver due to multiuser interference without requiring the interfering transmitters’ data sequences. The accuracy of this approximation improves as the distance between the receiver and the interfering transmitters increases.

3) We approximate “old” ISI in the intended communication link as asymptotic interference from a continuously-emitting source. We decompose the received signal into molecules observed due to an emission in the current bit interval, molecules that were emitted in recent bit intervals, and molecules emitted in older intervals, where only the impact of the “old” emissions is approximated.

Knowing the expected impact of a noise source enables us to model its effect on successful transmissions between the intended transmitter and receiver. For example, in [15], [16] we assumed that we had knowledge of the expected impact of noise sources in order to evaluate the effect of external noise on the bit error probability at the intended receiver for a selection of detectors. The expected impact of noise sources can also be used to assess different methods to mitigate the effects of noise, e.g., via the degradation of noise molecules as we consider in this paper.

Decomposing the signal received from the intended transmitter enables us to bridge all existing work on ISI by adjusting the number of “recent” bit intervals and deciding how we analytically model the “old” molecules. Most literature on diffusive molecular communication has accounted for only one recent bit interval and ignored the impact of old molecules; see [13], [17]–[19]. More recently, it has become more common to model its effect on successful transmissions between the intended transmitter and receiver. We adapt the noise analysis for asymptotic old ISI and use it to simplify detector performance evaluation in Section V. Numerical and simulation results are described in Section VI and conclusions are drawn in Section VII.

II. System Model

We consider an infinite 3-dimensional fluid environment of uniform constant temperature and viscosity. The receiver is a sphere with radius \( r_{\text{obs}} \) and volume \( V_{\text{obs}} \) (if the transmitter is sufficiently far from the receiver, then the precise shape is irrelevant and we are only interested in \( V_{\text{obs}} \)). As this paper focuses on the impact of unintended sources of information molecules on the observations made at the receiver, the receiver is centered at the origin. Without loss of generality, the intended transmitter is placed at coordinates \( \{-x_1, 0, 0\} \). We assume there is steady uniform flow (or drift) in an arbitrary direction with a velocity component in each dimension, i.e., \( \vec{v} = \{v_x, v_y, v_z\} \).

The receiver is a passive observer that does not impede diffusion or initiate chemical reaction (so that we can focus on the impact of the propagation environment). Its only interaction with the environment is the perfect counting of \( A \) molecules if they are within \( V_{\text{obs}} \); any other molecules that might be present are ignored. \( A \) molecules are the information molecules that can be emitted by the transmitter or by some other sources. In practice, the receiver would observe \( A \) molecules by having them bind to receptors that are on the surface of or inside \( V_{\text{obs}} \).

The expected local concentration of \( A \) molecules at the point defined by vector \( \vec{r} \) and at time \( t \) in molecule-m\(^{-3}\) is \( C_A(\vec{r}, t) \), and we write \( C_A \) for compactness. All \( A \) molecules diffuse independently with constant diffusion coefficient \( D_A \), and they can degrade into a form that cannot be detected by the receiver via a reaction mechanism that can be described as

\[
A \xrightarrow{k} \emptyset, \tag{1}
\]

where \( k \) is the reaction rate constant in s\(^{-1}\). If \( k = 0 \), then this degradation is negligible. Eq. (1) is a first-order reaction, but it can also be used to approximate higher-order reactions or reaction mechanisms with multiple steps. For example,
in our previous work where we considered enzymes in the propagation environment to mitigate ISI, we implicitly used [1] to derive a bound on the expected number of observed molecules; see [23], [24]. First-order reactions have also been used to approximate higher-order reactions in a molecular communication context in [11], where the reactions occurred only at the receiver.

We emphasize that our assumptions include a passive receiver, first-order $A$ molecule degradation throughout the environment, and the constant diffusion of $A$ molecules. These assumptions make our model analytically tractable but ignore the impact of effects including anomalous diffusion, localized chemical reactions, and other interactions between molecules. We are interested in studying such complex systems in our future work.

For clarity of exposition in the remainder of this paper, we convert our system model into dimensionless form. We have used dimensional analysis in our previous work, including [16], [25], because it generalizes our model’s scalability and facilitates comparisons between different dimensional parameter sets. In this paper, dimensional analysis also provides clarity of exposition by reducing the number of parameters that appear in the equations. Unless otherwise noted, all variables that are described in this paper are assumed to be dimensionless (as denoted by a “$\star$” superscript), and they are equal to the dimensional variables scaled by the appropriate reference variables; see [26] for more on dimensional analysis.

We define reference distance $L$ in m and reference number of molecules $N_{A,REF}$. We also define reference concentration $C_0 = N_{A,REF}/L^3$ in molecule $\cdot m^{-3}$. We then define the dimensionless concentration of $A$ molecules as $C_\star = C_A/C_0$, dimensionless time as $t_\star = DA_t/L^2$, and the dimensionless reaction rate constant as $k_\star = L^2k/DA$. The dimensionless coordinates along the three axes are

$$x_\star = \frac{x}{L}, \quad y_\star = \frac{y}{L}, \quad z_\star = \frac{z}{L},$$

such that they are the dimensional coordinates scaled (i.e., normalized) by the reference distance $L$. Advection is represented dimensionlessly with the Peclet number, $v_\star$, written as [3] Ch. 1

$$v_\star = \frac{vL}{DA},$$

where $v = |\vec{v}|$ is the speed of the fluid. $v_\star$ measures the relative impact of advection versus diffusion on molecular transport. If $v_\star = 1$, then the typical time for a molecule to diffuse the reference distance $L$, i.e., $L^2/DA$, is equal to the typical time for a molecule to move the same distance by advection alone. A value of $v_\star$ much less or much greater than 1 signals the dominance of diffusion or advection, respectively. We saw in [16] that the impact of steady uniform flow on successful communication also depends on the direction of flow, so we define $v^\star_\parallel$ along each dimension as

$$v^\star_\parallel = \frac{v_xL}{DA}, \quad v^\star_{\perp,1} = \frac{v_yL}{DA}, \quad v^\star_{\perp,2} = \frac{v_zL}{DA}.$$  

The dimensionless signal observed at the receiver, $N_{a,obs}(t_\star)$, is the cumulative impact of all molecule emitters in the environment, including interfering transmitters and other noise sources. Due to the independence of the diffusion of all $A$ molecules, we can apply superposition to the impacts of the individual sources, such that the cumulative impact of multiple noise sources is the sum of the impacts of the individual sources. If we assume that there are $U - 1$ sources of $A$ molecules that are not the intended transmitter (without specifying what kinds of sources these are, i.e., other transmitters or simply “leaking” $A$ molecules), then the complete observed signal can be written as

$$N_{a,obs}(t_\star) = N_{a,1}(t_\star) + \sum_{u=2}^{U} N_{a,u}(t_\star),$$

(5)

where $N_{a,1}(t_\star)$ is the signal from the intended transmitter. Without loss of generality (because the impact of multiple molecule sources can be superimposed), we can analyze each $N_{a,u}(t_\star)$ term independently. Thus, for clarity, we assume that the $u$th source is placed at $(-x^\star_u, 0, 0)$, where $x^\star_u \geq 0$. Furthermore, for all molecule sources in (5), the advection variables must be defined relative to the source’s corresponding coordinate frame, such that $v^{\star,u}_\parallel > 0$ always represents flow from the source towards the receiver. By symmetry, and without loss of generality, we can set $v^{\star,1}_{\perp,2} = 0$ and write $v^{\star,1}_{\perp,1} = v^{\star,1}_{\parallel}$, such that $v^{\star,1}_{\parallel}$ represents flow perpendicular to the line between the source and receiver.

In Table I we summarize where the different terms in (5) are analyzed in the remainder of this paper and whether each type of source is treated as continuously-emitting. In Sections III and IV, we model $N_{a,u}(t_\star)$ as a random noise source and as an interfering transmitter, respectively. In Section V we decompose $N_{a,1}(t_\star)$ to approximate old ISI as asymptotic noise.

### III. External Additive Noise

In this section, we derive the impact of external noise sources on the receiver, given that we have some knowledge about the location of the noise sources and their mode of emission. First, we consider a single point noise source placed at $(-x^\star_n, 0, 0)$ where $x^\star_n$ is non-negative (we change the subscript of the source from $u$ to $n$ in order to emphasize that this source is random noise and not a transmitter of information). The source emits molecules according to the random process $N_{A,gen}(t)$, represented dimensionlessly as $N_{a,gen}(t_\star) = L^2N_{A,gen}(t)/(DA_N_{A,REF})$. Assuming that the expected generation of molecules can be represented as a step function, i.e., $\bar{N}_{A,gen}(t) = N_{A,gen}, t \geq 0$, we then

| Component of $N_{a,obs}(t_\star)$ | Source Type | Section | Detailed Form | Emitting Continuously? |
|----------------------------------|-------------|---------|---------------|------------------------|
| $N_{a,1}(t_\star)$              | Random Noise| III     | [3]           | Yes                    |
| $N_{a,gen}(t_\star)$            | Interfering Transmitter | IV     | [25]          | Approximation in [26]  |

**TABLE I**

**DESCRIPTION OF THE TERMS IN 5.**
formulate the expected impact of the noise source at the receiver, \( N_{a_n}^\ast (t^\ast) \). In its most general form, we will not have a closed-form solution for the expected impact of the noise source. Next, we present either time-varying or asymptotic expressions for a number of relevant special cases, some of which are in closed form and others that facilitate numerical integration. While we are ultimately most interested in asymptotic solutions (particularly for extension to the analysis of interference), time-varying solutions are also of interest when they are available because they give us insight into how long a noise source must be “active” before we can model its impact as asymptotic. Time-varying solutions will also be useful when we consider old ISI in Section IV. As previously noted, we can use superposition to consider the cumulative impact of multiple noise sources, as given in (5), where the advection variables \( v^\ast_1 \) and \( v^\ast_\perp \) must be defined for each source depending on its location.

A. General Noise Model

First, we require the channel impulse response due to the noise source, i.e., the expected concentration of molecules observed at the receiver due to an emission of one molecule by the noise source at \( t^\ast = 0 \). This is analogous to the channel impulse response due to an intended transmitter at the same location. The reaction-diffusion differential equation describing the expected motion of \( A \) molecules can be written by applying the principles of chemical kinetics (see [27, Ch. 9]) to (1) and including the advection terms (as in [28, Ch. 4]), i.e.,

\[
\frac{\partial C^\ast}{\partial t^\ast} = \nabla^2 C^\ast - v^\ast_\parallel \frac{\partial C^\ast}{\partial x^\ast} - v^\ast_\perp \frac{\partial C^\ast}{\partial y^\ast} - k^\ast C^\ast, \tag{6}
\]

and it is straightforward (using a moving reference frame) to show that the channel impulse response at the point \( \{x^\ast, y^\ast, z^\ast\} \) due to the noise source at \( \{-x^\ast, 0, 0\} \) is

\[
C^\ast = \frac{1}{(4\pi t^\ast)^{3/2}} \exp \left( \frac{-|r^\ast|^2}{4t^\ast} - k^\ast t^\ast \right), \tag{8}
\]

where \(|r^\ast|^2 = (x^\ast + x^\ast - v^\ast t^\ast)^2 + (y^\ast - v^\ast_\perp t^\ast)^2 + (z^\ast)^2\) is the square of the time-varying effective distance between the noise source and the point \( \{x^\ast, y^\ast, z^\ast\} \).

Unlike an intended transmitter, the noise source is emitting molecules as described by the general random process \( N_{a_n}^\ast (t^\ast) \). We are already averaging over the randomness of the diffusion channel (i.e., we have the expected channel impulse response), so we only consider the time-varying mean of the noise source emission process, i.e., \( N_{a_n}^\ast (t^\ast) \). Thus, the expected impact of the noise source is found by multiplying (8) by \( N_{a_n}^\ast (t^\ast) \), integrating over \( V_{obs}^\ast \), and then integrating over all time up to \( t^\ast \), i.e.,

\[
N_{a_n}^\ast (t^\ast) \int \int \int r^\ast_\parallel^2 N_{a_n}^\ast (\tau) C^\ast_\parallel \sin \theta d\theta d\phi d\nu^\ast_\perp d\tau,
\]

where \( r^\ast_\parallel \) is the magnitude of the distance from the origin to the point \( \{x^\ast, y^\ast, z^\ast\} \) within \( V_{obs}^\ast \). To solve (9), we must also convert \(|r^\ast|^2\) from cartesian to spherical coordinates, which can be shown to be

\[
|r^\ast|^2 = r^\ast_\parallel^2 + x^\ast_\parallel^2 - 2t^\ast x^\ast_\parallel v^\ast_\parallel + 2x^\ast_\perp r^\ast_\parallel \cos \phi \sin \theta - 2t^\ast r^\ast_\parallel (v^\ast_\perp \sin \phi \sin \theta + v^\ast_\parallel \sin \phi \sin \theta) + t^\ast^2 (v^\ast_\parallel^2 + v^\ast_\perp^2), \tag{10}
\]

where \( \phi = \tan^{-1}(y^\ast/x^\ast) \) and \( \theta = \cos^{-1}(z^\ast/r^\ast_\parallel) \). Generally, (9) does not have a known closed-form solution, even if we omit the integral over time. In the following subsection, we present a series of cases for which (9) can be more easily solved (numerically or in closed form), for either arbitrary \( t^\ast \) or as \( t^\ast \rightarrow \infty \). In the asymptotic case, we write \( N_{a_n}^\ast (t^\ast) \bigg|_{t^\ast \rightarrow \infty} = N_{a_n}^\ast \) for compactness. The asymptotic case will also be useful to approximate multiuser interference and old intersymbol interference in Sections IV and V respectively.

B. Tractable Noise Analysis

For tractability, we will assume throughout the remainder of this section that the expected noise source emission in (9) can be described as a step function, i.e., \( N_{a_n}^\ast (t^\ast) = \frac{L^2 N_{a_n}^\ast}{\left(D_A N_{AREF}\right)} (t^\ast) \geq 0 \). Furthermore, we choose \( N_{AREF} = \frac{L^2 N_{a_n}^\ast}{D_A} \), so that \( N_{a_n}^\ast (t^\ast) = 1, t^\ast \geq 0 \) (the case where the noise source also “shuts off” at some future time, for example when a ruptured vesicle is depleted, is an interesting one that we leave for future work). We note that the emission of molecules by the noise source could then be deterministically uniform, such that the emission process \( N_{a_n}^\ast (t^\ast) \) is in fact \( N_{a_n}^\ast \tau \bigg|_{t^\ast \rightarrow \infty} = N_{a_n}^\ast \) for compactness. The asymptotic case will also be useful to approximate multiuser interference and old intersymbol interference in Sections IV and V respectively.

The solutions to (9) that we present in the remainder of this section follow one of two general strategies. Both strategies reduce (9) to a single integral, which can be solved numerically or reduced to closed form if additional assumptions are made. The first strategy is the uniform concentration assumption (UCA), where we assume that the expected concentration of \( A \) molecules due to the noise source is uniform and equal to that expected at the center of the receiver (i.e., at the origin). This
assumption is accurate if the noise source is sufficiently far from the receiver, such that the expected concentration of \( A \) molecules will not vary significantly throughout the receiver. We studied the accuracy of this assumption for a transmitter using impulsive binary-coded modulation in the presence of steady uniform flow in [16]. Here, applying the UCA means that we do not need to integrate over \( V_{\text{obs}}^* \) and (9) becomes

\[
N_{a,n}^*(t^*) = V_{\text{obs}}^* \int_0^{t^*} C_a^*(r_{\text{eff}}^*, \tau) d\tau,
\]

(11)

where \( r_{\text{eff}}^* = (x_n^* - v_\tau^* \tau)^2 + (v_\tau^* \tau)^2 \) is the square of the effective distance from the noise source to the receiver, and the expected concentration at the receiver is

\[
C_a^*(r_{\text{eff}}^*, t^*) = \frac{1}{(4\pi \tau^2)^{3/2}} \exp \left( -\frac{r_{\text{eff}}^*}{4\tau^2} - k^* t^* \right).
\]

(12)

The second strategy for solving (9) does not apply the UCA, so we include the integration over \( V_{\text{obs}}^* \). We considered that integration (but without the integration over time) for no molecule degradation in [16] and for general advection we could only evaluate the integral over \( r_{\text{obs}}^* \). However, a closed-form solution was possible if \( v_\tau^* = 0 \), which we derived in [16] from the no-flow case presented in [25 Th. 2] via a change of variables. Including the integration over time and the impact of molecule degradation, where \( N_{a,\text{gen}}^*(t^*) = 1, t^* \geq 0 \), in [16] Eq. (17) becomes

\[
N_{a,n}^*(t^*) = \int_0^{t^*} \frac{1}{2} \left[ \text{erf} \left( \frac{r_{\text{obs}}^* - r_{\text{eff}}^*}{2\tau^*} \right) + \text{erf} \left( \frac{r_{\text{obs}}^* + r_{\text{eff}}^*}{2\tau^*} \right) \right] d\tau
+ \frac{1}{r_{\text{eff}}^*} \sqrt{\frac{\tau^*}{\pi}} \exp \left( -\frac{(r_{\text{eff}}^* + r_{\text{obs}}^*)^2}{4\tau^*} \right)
- \exp \left( -\frac{(r_{\text{eff}}^* - r_{\text{obs}}^*)^2}{4\tau^*} \right) \right] \exp (-k^* \tau) d\tau,
\]

(13)

where \( r_{\text{eff}}^* = -(x_n^* - v_\tau^* \tau) \) is the effective distance along the \( x^* \)-axis from the noise source to the center of the receiver, and the error function is [29 Eq. 8.250.1]

\[
\text{erf} (a) = \frac{2}{\sqrt{\pi}} \int_0^a \exp (-b^2) db.
\]

(14)

Eq. (13) can be evaluated numerically but, unlike (11), is valid for any \( x_n^* \) (although special consideration must be made if \( x_n^* = 0 \), i.e., the “worst-case” location for the noise source, and we consider that case at the end of this subsection).

The two strategies that we have presented reduce (9) to a single integral (either (11) or (13)), thereby facilitating numerical evaluation. In the remainder of this subsection, we make additional assumptions that enable us to solve (9) in closed form.

1) Asymptotic Solutions: In the asymptotic case, i.e., as \( t^* \to \infty \), it is straightforward to show that (11) becomes

\[
N_{a,n}^* = \frac{V_{\text{obs}}^*}{4\pi x_n^*} \exp \left( \frac{x_n^* t^*}{2} - \frac{x_n^*}{2} \sqrt{v_\tau^* x_n^* + v_\tau^* + 4k^*} \right),
\]

(15)

where we apply [29 Eq. 3.472.5]

\[
\int_0^\infty \frac{1}{a^{3/2}} \exp \left( -\frac{b}{a} - \frac{c}{a} \right) da = \sqrt{\frac{\pi}{c}} \exp \left( -2\sqrt{bc} \right),
\]

(16)

and recall that \( x_n^* \) is positive.

Remark 1: From (15) it can be shown that, if there is no flow in the \( y \)-direction and no molecule degradation (i.e., \( v_\tau^* = 0 \) and \( k^* = 0 \)), then any positive flow along the \( x \)-direction (i.e., \( v_\tau^* > 0 \)) will not change the asymptotic impact of the noise source. We had expected that this flow would increase the asymptotic impact in comparison to the no-flow case, so this is a somewhat surprising result.

An asymptotic closed-form solution to (13) is possible if we impose \( v_\tau^* = 0 \), such that we are restricted to the no-flow case. If the noise source is also close to the receiver, then this is another “worst-case” scenario because there is no advection to carry the noise molecules away. The result is presented in the following theorem:

\textbf{Theorem 1} \( \left( N_{a,n}^* \right) \text{ in Absence of Flow): The expected asymptotic impact (i.e., as } t^* \to \infty \text{) of a noise source in the absence of flow, whose expected output is } N_{a,\text{gen}}^*(t^*) = 1, t^* \geq 0, \text{ is given by } \)

\[
N_{a,n}^* = \frac{1}{2k^*} \left[ 1 - \frac{1}{x_n^*} \exp \left( -\left| r_{\text{eff}}^* \right| k^* \right) \left( k^* \frac{t^*}{2} + \beta r_{\text{obs}}^* \right)
+ \frac{1}{x_n^*} \exp \left( -r_{\text{sum}}^* k^* \right) \left( k^* \frac{t^*}{2} + r_{\text{obs}}^* \right) \right],
\]

(17)

where \( r_{\text{eff}}^* = r_{\text{obs}}^* - x_n^* - x_n^* \), \( r_{\text{sum}}^* = r_{\text{obs}}^* + x_n^* \), \( \beta = \text{sgn}(r_{\text{obs}}^* - x_n^*) \), and \( \text{sgn}() \) is the sign function.

\textbf{Proof:} Please refer to Appendix [A].

2) Absence of Flow and Molecule Degradation: Time-varying solutions to both (11) and (13) are only possible in the absence of flow and molecule degradation, i.e., if \( v_\tau^* = v_\perp^* = 0 \) and \( k^* = 0 \). If we are using the UCA, then (11) can be combined with [30 Eq. (3.5b)] and we can write

\[
N_{a,n}^*(t^*) = \frac{V_{\text{obs}}^*}{4\pi x_n^*} \left( 1 - \text{erf} \left( \frac{x_n^*}{2\sqrt{\tau^*}} \right) \right),
\]

(18)

Remark 2: We see from (14) that \( \text{erf} (a) \to 0 \) as \( a \to 0 \), and that \( \text{erf} (a) \approx 0.56 \) when \( a = 0.05 \). If the reference distance is chosen to be the distance of the noise source from the receiver, i.e., \( L = x_n \), and if there is no advection or molecule degradation, then from (18) we must wait until \( t^* > 100 \) before the impact is expected to be at least 95\% of the asymptotic impact.

The time-varying solution to (13) is presented in the following theorem:

\textbf{Theorem 2} \( \left( N_{a,n}^*(t^*) \right) \text{ in Absence of Flow and Degradation): The expected time-varying impact of a noise source, whose expected output is } N_{a,\text{gen}}^*(t^*) = 1, t^* \geq 0, \text{ is given in the } \)

\[
\int_0^\infty \frac{1}{a^{3/2}} \exp \left( -\left| r_{\text{eff}}^* \right| k^* \right) da = \sqrt{\frac{\pi}{c}} \exp \left( -2\sqrt{bc} \right),
\]

(16)

and recall that \( x_n^* \) is positive.
absence of flow and molecule degradation by

\[
\overline{N_{an}}(t^*) = \text{erf} \left( \frac{r_{\text{diff}}^*}{2\sqrt{T}} \right) \left[ \frac{r_{\text{diff}}^*}{4} + \frac{r_{\text{diff}}^*}{2} + \frac{r_{\text{diff}}^*}{6} \right] + \text{erf} \left( \frac{r_{\text{sum}}^*}{2\sqrt{T}} \right) \left[ \frac{r_{\text{sum}}^*}{4} + \frac{r_{\text{sum}}^*}{2} + \frac{r_{\text{sum}}^*}{6} \right] + \sqrt{\frac{T}{\pi}} \exp \left( -\frac{r_{\text{diff}}^*}{4T} \right) \left[ \frac{r_{\text{diff}}^*}{2} - \frac{2r_{\text{diff}}^*}{3} + \frac{r_{\text{diff}}^*}{3} \right] + \sqrt{\frac{T}{\pi}} \exp \left( -\frac{r_{\text{sum}}^*}{4T} \right) \left[ \frac{r_{\text{sum}}^*}{2} + \frac{2r_{\text{sum}}^*}{3} - \frac{r_{\text{sum}}^*}{3} \right] - \frac{\beta r_{\text{diff}}^*}{4} - \frac{r_{\text{sum}}^*}{6} - \frac{r_{\text{sum}}^*}{6} - \frac{r_{\text{diff}}^*}{4} \right]. \tag{19}
\]

**Proof:** Please refer to Appendix B.

Although (19) is verbose, it can be evaluated for any non-zero values of \(x_n^*\) and \(t^*\). We consider the case \(x_n^* = 0\) at the end of this subsection. Here, we note that the asymptotic impact of a noise source, i.e., as \(t^* \to \infty\), can be evaluated from (19) using the properties of limits and l’Hôpital’s rule as

\[
\overline{N_{an}}(t^*) = \text{erf} \left( \frac{r_{\text{obs}}^*}{2\sqrt{T}} \right) \left[ \frac{r_{\text{obs}}^*}{4} + \frac{r_{\text{obs}}^*}{2} + \frac{r_{\text{obs}}^*}{6} \right] + \text{erf} \left( \frac{r_{\text{sum}}^*}{2\sqrt{T}} \right) \left[ \frac{r_{\text{sum}}^*}{4} + \frac{r_{\text{sum}}^*}{2} + \frac{r_{\text{sum}}^*}{6} \right] + \sqrt{\frac{T}{\pi}} \exp \left( -\frac{r_{\text{diff}}^*}{4T} \right) \left[ \frac{r_{\text{diff}}^*}{2} - \frac{2r_{\text{diff}}^*}{3} + \frac{r_{\text{diff}}^*}{3} \right] - \frac{\beta r_{\text{diff}}^*}{4} - \frac{r_{\text{sum}}^*}{6} - \frac{r_{\text{sum}}^*}{6} - \frac{r_{\text{diff}}^*}{4} \right]. \tag{20}
\]

**Remark 3:** Eq. (20) simplifies to a single term if the noise source is outside of the receiver, i.e., if \(r_{\text{diff}}^* = r_{\text{obs}}^* - x_n^* < 0\). It can then be shown that \(\overline{N_{an}} = r_{\text{obs}}^* / (3x_n^*)\), which is equivalent to (13) with a spherical receiver in the absence of advection and molecule degradation, i.e., \(v_n^* = v_k^* = k^* = 0\), even though (13) was derived for a noise source that is far from the receiver. Thus, in the absence of advection and molecule degradation, the expected impact of a noise source anywhere outside the receiver increases with the inverse of the distance to the receiver.

3) **Worst-Case Noise Source Location:** Finally, we consider the special case where the noise source is located at the receiver, i.e., \(x_n^* = 0\). Clearly, the UCA should not apply in this case, so we only consider the evaluation of (13). Generally, we need to apply l’Hôpital’s rule to account for \(x_n^* = 0\), and here we do so for three cases. First, if evaluating (13) directly and \(v_n^* = 0\), then l’Hôpital’s rule must be used to re-write the second term inside the curly braces in (13) (i.e., the term with the two exponentials, including the scaling by \(\sqrt{\tau/\pi} r_{\text{diff}}^*\)) as

\[
-\frac{r_{\text{obs}}^*}{(\pi \tau)^{\frac{1}{2}}} \exp \left( -\frac{r_{\text{obs}}^*}{4\tau} \right). \tag{21}
\]

Second, if evaluating (13), which applies asymptotically in the absence of flow, then we can apply l’Hôpital’s rule in the limit of \(x_n^* \to 0\) and write (17) as

\[
\lim_{x_n^* \to 0} \overline{N_{an}} = \frac{1}{k^*} - \exp \left( -r_{\text{obs}}^* \sqrt{k^*} \right) \left( \frac{1}{k^*} + \frac{r_{\text{obs}}^*}{\sqrt{k^*}} \right). \tag{22}
\]

**Remark 4:** From (17) and (22) we see that any increase in \(k^*\) will result in a decrease in the expected number of noise molecules observed, even if the noise source is located at the receiver (i.e., \(x_n^* = 0\)).

Third, the time-varying impact of the “worst-case” noise source in the absence of flow and molecule degradation can be found using repeated applications of l’Hôpital’s rule to (19) as

\[
\lim_{x_n^* \to 0} \overline{N_{an}}(t^*) = \text{erf} \left( \frac{r_{\text{obs}}^*}{2\sqrt{T}} \right) \left[ \frac{r_{\text{obs}}^*}{4} + \frac{r_{\text{obs}}^*}{2} + \frac{r_{\text{obs}}^*}{6} \right] - \frac{\beta r_{\text{diff}}^*}{4} - \frac{r_{\text{sum}}^*}{6} - \frac{r_{\text{sum}}^*}{6} - \frac{r_{\text{diff}}^*}{4} \right]. \tag{23}
\]

This subsection considered a number of solutions to (9), where the expected molecule emission is described as a step function. In Table II, we summarize precisely which conditions and assumptions apply to each equation. We will see the accuracy of these equations in comparison with simulated noise sources in Section VI. In practice, these equations can enable us to more accurately assess the effect of noise sources on the bit error probability of the intended communication link (as we did in [15], [16], where we only assumed that the expected impact of noise sources was known). In the remainder of this paper, we focus on using the noise analysis to approximate some or all of the signal observed by transmitters that release impulses of molecules.

### IV. Multiuser Interference

In this section, we consider the impact of transmitters that are using the same modulation scheme as the transmitter that is linked to the receiver of interest but are sending independent information. Thus, the \(A\) molecules emitted by these unintended transmitters are effectively noise. We begin by presenting the complete model of the observations made at the receiver due to any number of transmitters (independent of whether the transmitters are linked to the receiver). This detailed model is the most comprehensive, so it enables the most accurate calculation of the bit error probability, but it requires knowledge of all transmitter sequences. Then, we apply our results in Section III to simplify the analysis of an interfering transmitter.

#### A. Complete Multiuser Model

Consider from [5] that all \(U\) sources of \(A\) molecules are transmitters with the same modulation scheme. Transmitter \(u\) has independent binary sequence \(W_u = \{W_u[1], W_u[2], \ldots\}\) to send to its intended receiver, where \(W_u[j]\) is the \(j\)th information bit and \(Pr(W_u[j] = 1) = P_1\).
The only receiver that we are concerned with is the one at the origin. The transmitters do not coordinate their transmissions so they all transmit simultaneously, but for clarity of exposition we assume that the transmitters are initially synchronized and begin transmitting at $t^* = 0$. It is also straightforward to add an initial time offset to each transmitter, but we omit that extension in this paper in order to focus on asymptotic multiuser interference. Transmitter $u$ has bit interval $T_{int,u}$ and it releases $N_{AEM,u}^*$ molecules at the start of the interval to send a binary 1 and no molecules to send a binary 0. We model instantaneous molecule releases as approximations of releases that are much shorter than the bit interval; we do not expect that instantaneous releases are practical. Furthermore, we define the dimensionless bit interval $T_{int,u}$ and dimensionless number of emitted molecules $N_{aEM,u}^*$, where we scale the dimensional variables by $D_A/L^2$ and $1/N_{AREF}$, respectively. We note that this binary modulation scheme can be extended to any pulse amplitude modulation scheme, be easily extended to any pulse amplitude modulation scheme, respectively. We note that this binary modulation scheme can be extended to any pulse amplitude modulation scheme, which we have shown in \cite{23} can be accurately approximated as a continuous function so that we can apply the results from our noise analysis. The effective emission rate is $P_jN_{aEM,u}^*$ molecules every $T_{int,u}$ dimensionless time units. If we choose $N_{AREF} = L^2P_jN_{AEM,u}/(T_{int,u}D_A)$, then the emission function of the $u$th transmitter can be approximated as $N_{aEM}^*(t^*) = 1$, $t^* \geq 0$. From \cite{15}, we immediately have the expected asymptotic impact of the noise source, $N_{aEM}^*$, written as

$$N_{aEM}^* = \frac{V_{obs}}{4\pi x_n^*} \exp \left( \frac{x_n^* u_n^*}{2} - \frac{x_n^*}{2} \sqrt{v_n^* - k_n^*} + 4k^* \right),$$  \hspace{1cm} (26)$$

where we recall that, in general, we have adjusted the reference coordinate frame so that the $u$th transmitter lies on the negative $x^*$-axis. The time-varying impact can be found via numerical integration of \cite{11}, or, if $v^*_n = v^*_l = 0$ and $k^* = 0$, i.e., if there is no advection or molecule degradation, via \cite{18}. The complete asymptotic multiuser interference is given by adding \cite{26} for all $U - 1$ interfering transmitters.

We note that \cite{26} is a constant approximation of what is in practice a signal that is expected to oscillate over time. The channel impulse response given by \cite{8} has a definitive peak and tail. The interference can be envisioned as the most recent peak followed by all of the tails of prior transmissions. Even asymptotically, the expected impact at a given instant will depend on the time relative to the interferer’s transmission intervals. So, over time, \cite{26} will both overestimate and underestimate the impact of the interferer. However, we expect that, on average, \cite{26} will tend to overestimate the impact more often. This is because the approximation of molecule emission as a continuous function effectively makes the release of molecules later than they actually are by “spreading” emissions over the entire bit interval instead of releasing all of them at the start of the bit interval. We will visualize the accuracy of \cite{26} more clearly in Section \cite{VI}.

V. ASYMMOTIC ISI

In this section, we focus on characterizing the signal observed at the receiver due to the intended transmitter only. We seek a method to model some of the ISI asymptotically based on the previous analysis in this paper. Specifically, we model $F$ prior bits explicitly (and not as a signal from a continuously-emitting source), and the impact of all earlier bits is approximated asymptotically as a continuously-emitting source. The choice of $F$ enables a tradeoff between accuracy and computational efficiency. We describe the application of our model for asymptotic old ISI to simplify the evaluation of the expected bit error probability of weighted sum detectors, which in general requires finding the expected probability of error of all possible transmitter sequences and taking an average. Other applications of our model for asymptotic ISI are simplifying the implementation of the maximum likelihood detector and in the design of a weighted sum detector with
adaptive weights. Adaptive weighting is physically realizable in biological systems; neurons sum inputs from synapses with dynamic weights (see [32], Ch. 12), but we leave the design of adaptive weighted sum detectors for future work.

A. Decomposition of Received Signal

We now decompose the signal from the intended transmitter, i.e., \( N_{tx}^* (t^*) \) in (5). To emphasize that source 1 is the intended transmitter, we re-write its signal as \( N_{tx}^* (t^*) = N_{tx,cur}^* (t^*) \) and also drop the 1 subscript from its transmission parameters. If we apply the uniform concentration assumption for clarity of exposition, then the expected number of observed molecules due to the intended transmitter, \( \bar{N}_{tx}^* (t^*) \), given the transmitter sequence \( \mathbf{W} \), is

\[
\bar{N}_{tx}^* (t^*) = \sum_{j=1}^{[t^*/T_{int}]} \sum_{j=1}^{[t^*/\tau(j)]} W[j] C_0^* (r_{eff}^* (j), \tau(j)),
\]

where here \( (r_{eff}^* (j))^2 = (x_j^* - v_j^* \tau(j))^2 + (v_j^* \tau(j))^2 \) and \( \tau(j) = t^* - (j - 1)1T_{int} \), i.e., \( (r_{eff}^* (j))^2 \) is the square of the effective distance between the receiver and the transmitter’s jth emission and \( \tau(j) \) is the time elapsed since the beginning of the jth bit interval. For compactness in the remainder of this section, we write \( C_0^* (r_{eff}^* (j), \tau(j)) = C_0^* (j) \). We also note that it is straightforward to relax the uniform concentration assumption and re-write (27) into a more general form, following our analysis in [16]. Similarly to the discussion of \( N_{obs}^* (t^*) \) in Section IV, \( N_{tx}^* (t^*) \) is (dimensionally) a Poisson random variable with time-varying mean \( N_{tx}^* (t^*) \).

We decompose (27) into three terms: molecules observed due to the current bit interval, \( N_{tx,cur}^* (t^*) \), molecules observed that were released within F intervals before the current interval, \( N_{tx,isi}^* (t^*) \), and molecules observed that were released in any older bit interval, \( N_{old}^* (t^*) \). Specifically, (27) becomes

\[
\bar{N}_{tx}^* (t^*) = \sum_{j=1}^{[t^*/T_{int}]} \sum_{j=1}^{[t^*/\tau(j)]} W[j] C_0^* (j) + \sum_{j=1}^{j_c - F - 1} W[j] C_0^* (j) + \sum_{j=1}^{j_c - F - 1} W[j] C_0^* (j) = \bar{N}_{tx,cur}^* (t^*) + \bar{N}_{tx,isi}^* (t^*) + \bar{N}_{old}^* (t^*) \]

(28)

where \( j_c = \lfloor t^*/T_{int} \rfloor + 1 \) is the index of the current bit interval, and we emphasize that each term in (29) is evaluated given the current transmitter sequence \( \mathbf{W} \). The decomposition enables us to simplify the expression for the signal observed due to molecules released by the transmitter if we can write an asymptotic expression for the expected value of \( \bar{N}_{old}^* (t^*) \), i.e., \( \bar{N}_{old}^* \). However, the analysis that we have derived in this paper for the asymptotic impact of signals is dependent on the on-going emission of molecules that began at time \( t^* = 0 \).

We present two methods to derive \( \bar{N}_{old}^* \). First, we begin with the asymptotic expression in (26) for an interferer that is always emitting and then subtract the unconditional expected impact of molecules released within the last \( F+1 \) bit intervals. We then write the expected and time-varying but asymptotic expression for \( \bar{N}_{old}^* (t^*) \) as

\[
\bar{N}_{old}^* (t^*) = \bar{N}_{tx}^* - \bar{N}_{tx,isi}^* (t^*) - \bar{N}_{tx,cur}^* (t^*) \]

(30)

where \( \bar{N}_{tx}^* \) is in the same form as (26), and here \( \bar{N}_{tx,isi}^* (t^*) \) and \( \bar{N}_{tx,cur}^* (t^*) \) do not depend on \( \mathbf{W} \) because they are averaged over the 2 and \( 2^F \) possible corresponding bit sequences, respectively. Eq. (30) is time-varying because the expected impact that we subtract depends on the time within the current bit interval. From (30), \( \bar{N}_{old}^* (t^*) \) is asymptotically a cyclostationary process; the expected mean is periodic with period \( T_{int} \). Although (30) is tractable, it is cumbersome to evaluate (because we need to average the expected impact of molecules released over all \( 2^F+1 \) possible recent bit sequences, including the current bit) and is also not accurate (because (26) is based on continuous emission while \( \bar{N}_{tx,isi}^* (t^*) \) and \( \bar{N}_{tx,cur}^* (t^*) \) are based on discrete emissions at the start of the corresponding bit intervals). A second method to derive \( \bar{N}_{old}^* \) which requires less approximation, is to start with (11) and change the limits of integration over time, i.e.,

\[
\bar{N}_{old}^* (t^*) = \int_{t^* - (j_c - F - 1)T_{int}}^{\infty} V_{obs}^* C_0^* (r_{eff}, \tau) d\tau,
\]

(31)

where \( r_{eff}^2 = (x_j^* - v_j^* \tau)^2 + (v_j^* \tau)^2 \) and, if \( j_c - F - 1 \leq 0 \), then we do not yet have asymptotic ISI. Eq. (31) is also periodic with period \( T_{int} \). A special case of (31) occurs if we have \( v_j^* = v^* = 0 \) and \( \kappa^* = 0 \). In such an environment, we can subtract (18) from the asymptotic expression in (15). Specifically, we can write

\[
\bar{N}_{old}^* (t^*) = \frac{V_{obs}^*}{4\pi x_1^2} \text{erf} \left( \frac{x_1^*}{2\sqrt{t^* - (j_c - F - 1)T_{int}}} \right).
\]

(32)

Depending on the environmental parameters and whether there is a preference for tractability or accuracy, either (30), (31), or (32) can be used for \( \bar{N}_{old}^* (t^*) \) in (29). This asymptotic ISI term is independent of the actual transmitter data sequence \( \mathbf{W} \), so it can be pre-computed and used to assist in applications such as evaluating the expected bit error probability of a weighted sum detector.

B. Weighted Sum Detection

We focus on a single type of detector at the receiver as a detailed example of the application of an asymptotic model of old ISI. We proposed the family of weighted sum detectors in [13] as detectors that can operate with limited memory and computational requirements. We envision such detectors to be physically practical because they can already be found in biological systems such as neurons; see [32], Ch. 12. Here, we consider weighted sum detectors where the receiver makes \( M \) observations in every bit interval, and we assume that these observations are equally spaced such that the \( m \)th observation in the \( j \)th interval is made at time \( t^*(j,m) = (j + \frac{m}{M}) T_{int} \), where \( j = \{1, 2, \ldots, B\}, m = \{1, 2, \ldots, M\} \).
The dimensionless decision rule of the weighted sum detector in the $j$th bit interval is

$$
W[j] = \begin{cases} 
1 & \text{if } \sum_{m=1}^{M} w_m N_{a_{obs}}(t^*(j,m)) \geq \xi^*, \\
0 & \text{otherwise},
\end{cases}
$$

(33)

where $N_{a_{obs}}(t^*(j,m))$ is the $m$th observation as given by (5), $w_m$ is the weight of the $m$th observation, and $\xi^*$ is the binary decision threshold (we note that we do not need to make the weights dimensionless because they already are). We assume that a constant optimal $\xi^*$ for the given environment (and for the given formulation of ISI when evaluating the expected performance) is found via numerical search.

Given a particular transmitter sequence $W$, we can calculate the expected error probability of a weighted sum detector. The expected probability of error of the $j$th bit, $P_e[j|W]$, is

$$
P_e[j|W] = \begin{cases} 
\Pr \left( \sum_{m=1}^{M} w_m N_{a_{obs}}(t^*(j,m)) < \xi^* \right) & \text{if } W[j] = 1, \\
\Pr \left( \sum_{m=1}^{M} w_m N_{a_{obs}}(t^*(j,m)) \geq \xi^* \right) & \text{if } W[j] = 0.
\end{cases}
$$

(34)

In our previous work in [15], we approximated the expected error probability for the $j$th bit averaged over all possible transmitter sequences, $P_e[j]$, by averaging (34) over a subset of all sequences. An error probability was determined for all $B$ bit intervals of every considered sequence. This analysis can be greatly simplified by evaluating the probability of error of a single bit that is sufficiently “far” from the start of the sequence, i.e., $j \to \infty$, and then model only the most recent $F$ intervals of ISI explicitly and represent all older intervals with $N_{a_{old}}(t^*)$. Furthermore, if the impacts of the external noise sources in (5) are represented asymptotically (whether they are interferers or other noise sources), or if there are no external noise sources present, then we only need to evaluate the expected probability of error of the last bit in $2^{F+1}$ sequences.

The evaluation of (34) depends on the statistics of the weighted sum $\sum_{m=1}^{M} w_m N_{a_{obs}}(t^*(j,m))$. For simplicity, we limit our discussion to the special case where the weights are all equal, i.e., $w_m = 1 \forall m$, such that we can assume that the (dimensional) observations are independent Poisson random variables (we also considered the general case, where we must approximate the observations as Gaussian random variables, in [15]). Then, the sum of observations is also a Poisson random variable. The CDF of the weighted sum in the $j$th bit interval is then [15] Eq. 38

$$
\Pr \left( \sum_{m=1}^{M} N_{a_{obs}}(t(j,m)) < \xi \right) = \exp \left( - \sum_{m=1}^{M} N_{a_{obs}}(t(j,m)) \right) \\
\times \frac{\xi^{\xi-1}}{(\xi-1)!} \left( \sum_{m=1}^{M} N_{a_{obs}}(t(j,m)) \right)^{\xi-1}.
$$

(35)

where, from (5),

$$
N_{a_{obs}}(t(j,m)) = N_{ATX}(t(j,m)) + \sum_{u=2}^{U} N_{A_u},
$$

(36)

and $N_{ATX}(t)$ and $N_{A_u}$ are the dimensional forms of the number of molecules expected from the intended transmitter and $u$th noise source, i.e., $N_{a_{tx}}(t^*)$ of $N_{a_u}$, respectively, and we emphasize that we represent the noise sources asymptotically. We write (35) and (36) in dimensional form to emphasize that the observations are discrete. For the corresponding simulations in Section VI we only consider $U = 1$ to focus on the accuracy of the asymptotic approximation of old ISI, and we evaluate the old ISI as given by (31) or (32) for $k \neq 0$ and $k = 0$, respectively.

VI. Numerical Results

In this section, we present numerical and simulation results to verify the analysis of noise, multiuser interference, and ISI performed in this paper. To clearly show the accuracy of all equations derived in this paper, we simulate only one source at a time, measuring either 1) the impact of a noise source or an interfering transmitter, or 2) the receiver error probability when the intended transmitter is the only molecule source. Our simulations are executed in the particle-based stochastic framework that we introduced in [23], [24]. The $A$ molecules are initialized at the corresponding source when they are released. The location of each molecule, as determined by the uniform flow and random diffusion, is updated every time step $\Delta t$, where diffusion along each dimension is simulated by generating a normal random variable with variance $2D_A \Delta t$. If there is molecule degradation, then every molecule has a chance of degrading in every time step with probability $k \Delta t$. If there is no molecule degradation, then all molecules released are present indefinitely. The signal at the receiver is updated in every time step by counting the number of $A$ molecules that are within $r_{obs}$ of the origin.

Constant environmental parameters are listed in Table III. The chosen values are consistent with those that we considered in [16], where we noted that the value of the diffusion coefficient $D_A$ is similar to that of many small molecules in water at room temperature (see [33] Ch. 5), and is also comparable to that of small biomolecules in blood plasma (see [34]). Most of the results in this section have been non-dimensionalized with the reference distance $L$ depending on the distance from the source of molecules to the receiver. For reference, conversions between the dimensional variables that were simulated and their values in dimensionless form are listed in Table IV.

A. Continuous Noise Source

We first present the time-varying impact of the continuously-emitting noise source that we analyzed in Section III. The times between the release of consecutive molecules from the noise source are simulated as a continuous Poisson process so that the times between molecule release are independent. The expected release rate, $1.2 \times 10^6$ molecule s$^{-1}$.
is chosen so that, asymptotically, one (dimensional) molecule is expected to be observed at the receiver due to a noise source placed 50 nm from the center of the receiver (this distance is actually at the edge of the receiver, cf. Table III). To accommodate the range of distances considered, we adjust the simulation time step $\Delta t$ so that 10 steps are made within every $t^* = 1$ time unit. Simulations are averaged over $10^5$ independent realizations. The specific equations used for calculating the expected values, both time-varying and asymptotically, were chosen as appropriate from Table IV.

In Fig. 1 we show the time-varying impact of the noise source when there is no advection and no molecule degradation, i.e., $v_\parallel^* = v_\perp^* = 0$ and $k^* = 0$. Under these conditions, we have the expected time-varying and asymptotic impact in closed form. For every distance shown, the impact approaches the asymptotic value as $t^* \to 100$, as expected from Remark 3. The expected impact without the UCA is highly accurate for all time, and the expected impact with the UCA shows visible deviation only for $t^* < 1$ when $x_n < 200$ nm, i.e., when the noise source is not far from the receiver. We also observe that the overall impact decreases as the noise source is placed further from the receiver; doubling the distance decreases $\overline{N}_{App}(t^*)$ by about a factor of 8 while the corresponding value of $N_{AppE,u}$, defined as $N_{AppE,u} = L^2 N_{App}/D_A$ and used to convert $N_{App}(t^*)$ into dimensional form, only increases by a factor of 4 (see Table IV). The overall (dimensional) decrease in impact by a factor of 2 is as expected from Remark 3.

In Fig. 2 we consider the same environment as in Fig. 1 but here the asymptotic impact is approached about two orders of magnitude faster, as $t^* \to 2$. The asymptotic impact at any distance is also less than half of that observed in Fig. 1 because of the molecule degradation.

In Fig. 3 we observe the impact of a noise source at the “worst-case” location, i.e., $x_n = 0$, and we vary the molecule degradation rate $k^*$. The expressions for the expected time-varying and asymptotic impact are both highly accurate. We see the general trend that the asymptotic impact decreases (as expected by Remark 4) and is reached sooner as $k^*$ increases. Increasing $k^*$ also degrades the signal from the desired transmitter, but this can be good for reducing ISI as we will see in the following subsection. Furthermore, it is interesting that the impact of the noise source can be significantly reduced by increasing the rate of noise molecule degradation, even though the noise molecules are being emitted directly at the receiver. This implies that, if they were not degraded, significantly more
noise molecules would have been observed by the receiver before diffusing away.

In Figs. 4 and 5 we consider the effect of advection on the impact of noise without molecule degradation. For clarity, we observe $x_n = \{0, 100\}$ nm in Fig. 4 and $x_n = \{200, 400\}$ nm in Fig. 5. When $x_n = 0$, only one flow direction is relevant because all flows are equivalent by symmetry. As with molecule degradation, we observe that the presence of advection reduces the time required for the impact of the noise source to become asymptotic, which here occurs by about $t^* = 4$. Flows that are not in the direction of a line from the noise source to the receiver, i.e., $v_1^* < 0$ or $v_1^* \neq 0$ (which we termed “disruptive” flows in [10]), decrease the asymptotic impact of the noise source. However, the flow $v_1^* = 1$ results in about the same asymptotic impact as the no-flow case when $x_n \neq 0$ nm, which we expect from Remark 1 although it might not be an intuitive result.

B. Interference and ISI

We now assess the accuracy of approximating transmitters as continuously-emitting noise sources. First, we observe the impact of an interfering transmitter. Second, we assess the accuracy of evaluating the receiver error probability where we vary the number $F$ of symbols of ISI treated explicitly and approximate all older ISI as an asymptotic noise source. We consider transmitters with a common set of dimensional transmission parameters, as described in Table III.

In Fig. 6 we show the time-varying impact on the receiver of a single interferer using binary-encoded impulse modulation, both with and without molecule degradation, for the interferer placed $x_2 = 400$ nm or $1 \mu$m from the receiver (we emphasize that the only active molecule source is not the intended transmitter by using the subscript 2). At both distances, the same bit interval is used ($T_{int,2} = 0.2$ ms). The expected time-varying and asymptotic curves are evaluating using (11) and (26), respectively. The simulations are averaged over $10^5$ independent realizations, and in Fig. 6 we clearly observe oscillations in the simulated values above and below the expected curves. The relative amplitude of these oscillations is much greater when the interferer is closer to the receiver, and also greater when there is molecule degradation; when $x_2 = 400$ nm and $k^* = 1$, the impact in the asymptotic regime varies from $4 \times 10^{-5}$ to over $6 \times 10^{-4}$, but when $x_2 = 1 \mu$m and $k^* = 0$, the relative amplitude of the oscillations is an order of magnitude smaller. Thus, the impact of an interferer that is sufficiently far from the receiver can be accurately approximated with a non-oscillating function, and an interferer does not need to be transmitting for a very long time to assume that its impact is asymptotic (8 and 50 bit intervals are shown in Fig. 6 for the interferers at 400 nm and 1 \mu m, respectively; the difference is due to plotting on a dimensionless time axis). We note that the relative amplitude of oscillations would also decrease if the interferer transmitted with a smaller bit interval.

In Fig. 7 we measure the average bit error probability of the equal weight detector when $M = 10$ samples are taken...
per bit interval and the optimal decision threshold is found numerically. The receiver is placed $x_1 = 400$ nm from the transmitter and we vary $k^*$ to control the amount of ISI that we expect (since a faster molecule degradation rate means that emitted molecules are less likely to exist sufficiently long to interfere with future transmissions). We do not add any external noise or interference (i.e., there is only one source of information molecules), but we vary the number $F$ of bit intervals that are treated explicitly as ISI, i.e., the complexity of $N_{\text{tx,isi}}(t^*)$, in evaluating the expected error probability. Simulations are averaged over $10^4$ independent realizations, and we ignore the decisions made within the first 50 of the 100 bits in each sequence in order to approximate the “old” ISI as asymptotic. The old ISI, $N_{a,old}(t^*)$, is found by evaluating (31) (or by using (32) when $k^* = 0$), and to emphasize the benefit of including this term we also consider evaluating the expected error probability where we set $N_{a,old}(t^*) = 0$.

We generally observe in Fig. 7 that, as $F$ increases, the expected error probability becomes more accurate because we treat more of the ISI explicitly instead of as asymptotic noise via $N_{a,old}(t^*)$. The exception to this is when $k^* = 0$ and we calculate the expected value using $N_{a,old}(t^*)$. The ISI in that case is much greater than when $k^* > 0$, such that the expected bit error probability is more sensitive to the approximation for $N_{a,old}(t^*)$, which assumes that the release of molecules is continuous over the entire bit interval. This approximation means that the expected “old” ISI is overestimated and a higher expected bit error probability is calculated. When $k^* > 0$, the expected bit error probability tends to underestimate that observed via simulation because the evaluation of the expected bit error probability assumes that all observed samples are independent, but this assumption loses accuracy for larger $M$. Importantly, the expected bit error probability tends to that observed via simulation much faster when including $N_{a,old}(t^*)$, even though it is an approximation. For all values of $k^*$ considered, it is sufficient to consider only 2 or 3 intervals of ISI explicitly while approximating all prior intervals with $N_{a,old}(t^*)$. If we use $N_{a,old}(t^*) = 0$, as is common in the existing literature, then many more intervals of explicit ISI are needed for comparable accuracy ($F = 20$ is still not sufficient if $k^* = 0$, although $F = 5$ might be acceptable if $k^* = 0.2$). Since the computational complexity of evaluating the expected bit error probability increases exponentially with $F$ (because we need to evaluate the expected probability of error due to all $2^{F+1}$ bit sequences), approximating old ISI with $N_{a,old}(t^*)$ provides an effective means with which to reduce the complexity without making a significant sacrifice in accuracy.

VII. CONCLUSION

In this paper, we proposed a unifying model to account for the observation of unintended molecules by a passive receiver in a diffusive molecular communication system, where the unintended molecules include those emitted by the intended transmitter in previous bit intervals, those emitted by interfering transmitters, and those emitted by other external noise sources that are continuously emitting molecules. We presented the general time-varying expression for the expected impact of a noise source that is emitting continuously, and then we considered a series of special cases that facilitate time-varying or asymptotic solutions. Knowing the expected impact of noise sources enables us to find the effect of those sources on the bit error probability of a communication link. We used the analysis for asymptotic noise to approximate the impact of an interfering transmitter, which we extended to the general case of multiuser interference. Finally, we decomposed the signal received from the intended transmitter so that we could approximate “old” ISI as asymptotic interference. We showed how this approximation could be used to simplify the evaluation of the expected bit error probability of a weighted sum detector. Our simulation results showed the high accuracy of our expressions for time-varying and asymptotic noise. We showed that an interfering transmitter placed sufficiently far from the receiver can be approximated as an asymptotic noise source soon after it begins transmitting.
and that approximating old ISI as asymptotic noise is an effective method to reduce the computational complexity of evaluating the expected probability of error. Our future work includes investigating the expected impact of noise sources with random locations, which can be used to model the random generation of noise molecules anywhere in the propagation medium, and using the approximation for asymptotic ISI to design adaptive detectors, where the decision threshold is adjusted based on the knowledge of the previously received information.

APPENDIX

A. Proof of Theorem 1

The asymptotic integration (i.e., as \( t^* \to \infty \)) in (13) to prove Theorem 1 can be written as the summation of four integrals which can be found by solving the following two integrals:

\[
\int_0^\infty \text{erf} \left( \frac{a}{\tau} \right) \exp(-k^* \tau) \, d\tau, \quad (37)
\]

\[
\int_0^\infty \frac{1}{\tau^*} \exp \left( -\frac{b}{\tau} - k^* \tau \right) \, d\tau, \quad (38)
\]

where \( a \) could be positive or negative and the latter occurs only when \( x_n^* > \tau_{ob}^* \). To solve (37) for \( a > 0 \), we apply the substitution \( c = a/\tau^* \) and use the indefinite integrals [35, Eq. 4.11.14]

\[
\int \text{erf} \left( \frac{c}{\sqrt{2} \tau} \right) \, dc = -\text{erf} \left( \frac{c}{\sqrt{2} \tau} \right) + \frac{1}{\sqrt{\pi}} \int \exp \left( -\frac{c^2}{2} \right) \, dc, \quad (45)
\]

and [29, Eq. 2.325.5]

\[
\int \exp \left( -\frac{c^2}{2} \right) \, dc = \frac{1}{\sqrt{\pi}} \prod_{n=1}^{\infty} \left[ \frac{\sqrt{\pi}}{c^{m-1}} - n \int \exp \left( -\frac{c^2}{2} \right) \, dc \right], \quad (46)
\]

as well as the definition of the error function. It is then straightforward to show that (33) for \( a > 0 \) is solved as

\[
(2a^2 + t^*) \text{erf} \left( \frac{a}{\sqrt{t^*}} \right) + 2a \sqrt{\frac{t^*}{\pi}} \exp \left( -\frac{a^2}{t^*} \right) - 2a^2. \quad (47)
\]

Recalling that \( \text{erf} (\cdot) \) is an odd function, we solve (33) for \( a < 0 \) as

\[
(2a^2 + t^*) \text{erf} \left( \frac{a}{\sqrt{t^*}} \right) + 2a \sqrt{\frac{t^*}{\pi}} \exp \left( -\frac{a^2}{t^*} \right) + 2a^2. \quad (48)
\]

To solve (44), we apply the substitution \( c = \sqrt{b} \tau \), apply (46) twice, and use the definition of the error function. It is then straightforward to show that (44) is solved as

\[
\frac{2}{3} \sqrt{\pi} \exp \left( -\frac{b}{t^*} \right) \left( t^* - 2b \right) + \frac{4}{3} \frac{b^2}{t^*} \sqrt{\pi} \exp \left( -\frac{b}{t^*} \right) \text{erf} \left( \sqrt{\frac{b}{t^*}} \right). \quad (49)
\]

If we take care to consider the sign of \( \tau_{ob}^* - x_n^* \), then we can arrive at (19) by combining (47), (48), and (49).

REFERENCES

[1] I. F. Akyildiz, F. Brunetti, and C. Blazquez, “Nanonetworks: A new communication paradigm,” Computer Networks, vol. 52, no. 12, pp. 2260–2279, May 2008.
[2] T. Nakano, M. J. Moore, F. Wei, A. V. Vasilakos, and J. Shuai, “Molecular communication and networking: Opportunities and challenges,” IEEE Trans. Nanobiosci., vol. 11, no. 2, pp. 135–148, Jun. 2012.
[3] G. A. Truskey, F. Yuan, and D. F. Katz, Transport Phenomena in Biological Systems, 2nd ed. Pearson Prentice Hall, 2009.
[4] A. S. Lodokhin, W. C. Wimley, and S. H. White, “Leakage of membrane vesicle contents: determination of mechanism using fluorescence quenching,” Biophysical J., vol. 69, no. 5, pp. 1964–1971, Nov. 1995.
[5] B. Alberts, D. Bray, K. Hopkin, A. Johnson, J. Lewis, M. Raff, K. Roberts, and P. Walter, Essential Cell Biology, 3rd ed. Garland Science, 2010.
[6] M. Pierobon and I. F. Akyildiz, “Diffusion-based noise analysis for molecular communication in nanonetworks,” IEEE Trans. Signal Process., vol. 59, no. 6, pp. 2532–2547, Jun. 2011.
[7] M. Pierobon and I. F. Akyildiz, “Optimum receiver for molecule shift keying modulation in diffusion-based molecular communication channels,” Nano Commun. Net., vol. 3, no. 3, pp. 183–195, Sep. 2012.
[8] M. Pierobon and I. F. Akyildiz, “Capacity of a diffusion-based molecular communication system with channel memory and molecular noise,” IEEE Trans. Inf. Theory, vol. 59, no. 2, pp. 942–954, Feb. 2013.
[9] H. ShahMohammadian, G. G. Messier, and S. Magierowski, “Nano-machine molecular communication over a moving propagation medium,” Nano Commun. Net., vol. 4, no. 3, pp. 142–153, Sep. 2013.
[11] C. T. Chou, “Noise properties of linear molecular communication networks,” Nano Commun. Net., vol. 4, no. 3, pp. 87–97, Sep. 2013.

[12] M. S. Kuran, H. B. Yilmaz, T. Tugcu, and I. F. Akyildiz, “Modulation techniques for communication via diffusion system in molecular communication,” in Proc. ICST BIONETICS, Jun. 2013, pp. 199–212.

[13] M. Pierobon and I. F. Akyildiz, “Intersymbol and co-channel interference in diffusion-based molecular communication,” in Proc. IEEE ICC MONACOM, Jun. 2012, pp. 6126–6131.

[14] D. Miorandi, “A stochastic model for molecular communications,” Nano Commun. Net., vol. 2, no. 4, pp. 205–212, Dec. 2011.

[15] A. Noel, K. C. Cheung, and R. Schober, “Optimal receiver design for diffusive molecular communication with flow and additive noise,” To appear in IEEE Trans. Nanobiosci., 2014. [Online]. Available: arXiv:1308.0109

[16] ——, “Diffusive molecular communication with disruptive flows,” To be presented at IEEE ICC 2014. [Online]. Available: arXiv:1309.5201

[17] M. S. Kuran, H. B. Yilmaz, T. Tugcu, and I. F. Akyildiz, “Modulation techniques for communication via diffusion in nanonetworks,” in Proc. IEEE ICC, Jun. 2011, pp. 1–5.

[18] M. U. Mahfuz, D. Makrakis, and H. T. Mouthal, “A comprehensive study of concentration-encoded unicast molecular communication with binary pulse transmission,” in Proc. IEEE NANO, Aug. 2011, pp. 227–232.

[19] M. S. Leeson and M. D. Higgins, “Forward error correction for molecular communications,” Nano Commun. Net., vol. 3, no. 3, pp. 161–167, Sep. 2012.

[20] L.-S. Meng, P.-C. Yeh, K.-C. Chen, and I. F. Akyildiz, “Optimal detection for diffusion-based communications in the presence of ISI,” in Proc. IEEE GLOBECOM, Dec. 2012, pp. 3843–3848.

[21] P.-J. Shih, C.-H. Lee, and P.-C. Yeh, “Channel codes for mitigating intersymbol interference in diffusion-based molecular communications,” in Proc. IEEE GLOBECOM, Dec. 2012, pp. 4444–4448.

[22] D. Kilinc and O. B. Akan, “Receiver design for molecular communication,” IEEE J. Sel. Areas Commun., vol. 31, no. 12, pp. 705–714, Dec. 2013.

[23] A. Noel, K. C. Cheung, and R. Schober, “Improving receiver performance of diffusive molecular communication with enzymes,” IEEE Trans. Nanobiosci., vol. 13, no. 1, pp. 31–43, Mar. 2014.

[24] ——, “Improving diffusion-based molecular communication with unanchored enzymes,” in Proc. ICST BIONETICS, Dec. 2012. [Online]. Available: arXiv:1305.1785

[25] ——, “Using dimensional analysis to assess scalability and accuracy in molecular communication,” in Proc. IEEE ICC MONACOM, Jun. 2013, pp. 818–823.

[26] T. Szirmae, Applied Dimensional Analysis and Modeling, 2nd ed. Butterworth-Heinemann, 2007.

[27] R. Chang, Physical Chemistry for the Biosciences. University Science Books, 2005.

[28] H. C. Berg, Random Walks in Biology. Princeton University Press, 1993.

[29] I. S. Gradshteyn and I. M. Ryzhik, Table of Integrals, Series, and Products, 5th ed. London: Academic Press, 1994.

[30] J. Crank, The Mathematics of Diffusion, 2nd ed. Oxford University Press, 1980.

[31] S. Ross, Introduction to Probability and Statistics for Engineers and Scientists, 4th ed. Academic Press, 2009.

[32] P. Nelson, Biological Physics: Energy, Information, Life, updated 1st ed. W. H. Freeman and Company, 2006.

[33] E. L. Cussler, Diffusion: Mass transfer in fluid systems. Cambridge University Press, 1984.

[34] A. A. Merrith and J. L. Lage, “Effect of blood flow on gas transport in a pulmonary capillary,” Journal of Biomech. Eng., vol. 127, no. 3, pp. 432–439, Jun. 2005.

[35] E. W. Ng and M. Geller, “A table of integrals of the error functions,” J. Res. Bur. Stand., vol. 73B, no. 1, pp. 1–20, Jan.-Mar. 1969.

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