Error Probability Bounds for Coded-Index DNA Storage Systems

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Abstract—The DNA storage channel is considered, in which a codeword is comprised of \( M \) unordered DNA molecules. At reading time, \( N \) molecules are sampled with replacement, and then each molecule is sequenced. A coded-index concatenated-coding scheme is considered, in which the \( m \)th molecule of the codeword is restricted to a subset of all possible molecules (an inner code), which is unique for each \( m \). The decoder has low-complexity, and is based on first decoding each molecule separately (the inner code), and then decoding the sequence of molecules (an outer code). Only mild assumptions are made on the sequencing channel, in the form of the existence of an inner code and decoder with vanishing error. The error probability of a random code as well as an expurgated code is analyzed to decay exponentially with the number of molecules (an outer code). Only mild assumptions are made on the sequencing channel, in the form of the existence of an inner code and decoder with vanishing error. The error probability of a random code as well as an expurgated code is analyzed to decay exponentially with the number of molecules (an outer code).

Index Terms—Concatenated coding, data storage, error exponent, DNA storage, permutation channel, reliability function, state-dependent channel.

I. INTRODUCTION

In recent years, the capability of storing information on a Deoxyribonucleic acid (DNA) medium [1] was practically demonstrated by a few working prototypes [2]–[7]. Based on these experimental systems, the possible impairments of this storage channel were characterized in [8], and various authors have proposed and analyzed coding methods for this storage channel [2]–[6], [9]–[14]. In this paper, we propose and analyze a general coding method and a suitable decoder for this storage channel. Our analysis focuses on error probability of such systems, and specifically on its scaling, with respect to (w.r.t.) the parameters of the system. To facilitate this analysis, we consider random, unstructured, codes. Nonetheless, both the codebook ensemble and the decoder take complexity considerations into account, as a step towards effective, practical, implementation of such systems.

A. The DNA Storage Channel Model

Information is stored in a pool of \( M \) short DNA molecules, where each such molecule is comprised of two complementary length \( L \) strands of four nucleotides (Adenine, Cytosine, Guanine, and Thymine). The \( M \) molecules cannot be spatially ordered, and during reading are accessed in uncontrolled manner. Specifically, the \( M \) molecules are sampled from the DNA pool \( N \) times (with replacement), and each of these sampled molecules is sequenced in order to obtain a vector describing the \( L \) nucleotides which were synthesized to this molecule. The set of \( N \) sequenced molecules is the channel output. The sampling mechanism leads to molecule errors, as, e.g. some of the \( M \) molecules might not be read at all (erased).\(^1\) The sequencing mechanism leads to symbol errors, modeled as an \( L \)-dimensional probability kernel \( W^{(L)} \) which specifies the probability of sequencing some \( L \)-symbol vector conditioned that the information synthesized to the molecule was (possibly other) \( L \)-symbol vector.\(^2\)

B. Capacity

The capacity of the DNA channel was first studied in [15], and later on by [16]–[18]. These works assumed that the sequencing channel is memoryless, and specifically, a binary symmetric channel (BSC) in [15]–[17] (with some results generalized to larger alphabet symmetric channels), and general, possibly asymmetric, discrete memoryless channels (DMC) in [18]. A fundamental observation [15] has established that the capacity is positive only when the scaling of the molecule length is \( L = \beta \log M \) with \( \beta > 1 \). In [16], [17] it was observed that the decoder can gain from observing the same molecule multiple times with independent sequencing “noise” realizations, and so the capacity of the DNA channel is related to the binomial (multi-draw) channel [19] (for BSC sequencing channels), and more generally, to information combining [20]–[22]. For the DNA storage channel, the impediment of achieving this capacity is that the decoder does not know the order of the output molecules. To resolve this, [16] proposed a decoder based on (hard) clustering\(^3\) of the \( N \) output molecules, so that with high probability the decoder can identify the output molecules which correspond to the same input input, and thus can exploit this multi-draw BSC to obtain increased capacity. Nonetheless, this requirement for clustering limited the regime of \( \beta \) and the crossover probability, both for the lower bound (achievable) [16] and the upper bound.

\(^1\)In fact, in practice, it might be that a molecule was actually not written at all to the pool, or was erased during storage time.

\(^2\)In fact, in practice, it might be that a molecule was not synthesized to the correct sequence of nucleotides during writing, or because it was corrupted during storage.

\(^3\)The adjective “hard” is in the sense that the clustering is based on thresholding the Hamming distance between molecules.
This was alleviated in [18] which considered general DMCs, and significantly improved the regime in which the capacity bounds are valid.

C. Motivation

In this paper, we focus on an alternative type of schemes and analysis for several reasons: First, the decoder in [18] is computationally intensive, in the sense the even computing the metric for a single codeword requires maximizing over all possible sampling events which has cardinality of $M^N$ (the clustering algorithm of [16] has $O(N)$ metric computation complexity, but as said, it only guaranteed to successfully operate in a restricted regime of $\beta$ and the BSC crossover probability). Second, the results of [15]–[18] all assume a memoryless sequencing channel. As surveyed in [8], a practical sequencing channel might be much more involved, and include, e.g., deletions and insertions in addition to substitution errors. Moreover, constraints on long sequences of homopolymers or constraints on the composition of the nucleotides types in the codeword should practically also be taken into account [23], [24]. Third, as was established in [18] for the $N = \Theta(M)$ case, the error probability is dominated by sampling events, in which some molecules are significantly under-sampled. So, while a codeword is comprised of a total of $ML$ symbols, the error probability decays as $e^{-\Theta(M)}$, rather than the $e^{-\Theta(ML)}$ decay rate expected from a code of blocklength $ML$ used over a standard DMC. This slow decay of the error probability is significant for practical systems of finite blocklength. Fourth, even in the memoryless setting, if the sequencing channel is almost clean, then $C(W) \lesssim \log |\mathcal{X}|$, and in this sense, there is only a marginal gain in capacity due to information combining according to the binomial (multi-draw) channel. For example, if we denote the capacity of the binomial ($multi$-draw) BSC as $C_{w,d}$, where $w$ is the crossover probability and $d$ is the number of independent draws, then $C_{0.01, d} \approx (0.91, 0.97, 0.99)$ bits for $d = 1, 2, 3$, and quickly saturates to its maximal value of $\log_2 |\mathcal{X}| = 1$ bit.

D. Our Contribution

Accordingly, and in the spirit of [16], we consider a simple, yet general, coding method for the DNA storage channel and analyze its error probability. The scheme follows a practical approach to this channel [4]–[6], [10] in which the lack of order of the molecules is resolved by an index. The simplest indexing-based scheme, is based on utilizing the first $\log_2 M$ bits of each DNA molecule to specify its index $m \in [M]$. Whenever there is no noise, the decoder is able to perfectly sort the molecules using the received index. This leads to a rate loss of $1/\beta$, which seems to be an inherent consequence of the lack of order of the molecules in the pool. Nonetheless, if the payload bits (the last $(\beta - 1) \log_2 M$ bits of the molecule) of such encoding are arbitrary, then an erroneous ordering of the molecules can be caused by a single bit flip. This motivated explicit coded-indexing based schemes for noisy sequencing channels [15], [17], [18], [25], [26]. Here, we consider a general, non-explicit coded-indexing scheme, in which the possible molecules of the codeword are chosen from an inner code – a restricted subset $\mathcal{B}_m^{(L)} \subset \mathcal{X}^L$ of all possible molecules. This inner code is further partitioned into $M$ equal cardinality sub-codes $\mathcal{B}_m^{(L)}$, so that the $m$th molecule of a codeword is chosen only from $\mathcal{B}_m^{(L)}$. As before, when there are no sequencing errors, the index $m$ of a sampled molecule is determined by the sub-code $\mathcal{B}_m^{(L)}$ it belongs to. The advantage over uncoded indexing is that the inner code $\mathcal{B}_m^{(L)}$ also protects the index from sequencing errors. The decoder that we consider in this paper is based on a black-box decoder for the inner code $\mathcal{B}_m^{(L)}$. Upon sampling and sequencing $N$ molecules, this decoder uses the inner-code decoder to independently decode each of the sequenced molecule to a valid sequence in $\mathcal{B}_m^{(L)}$. Since the decoder operates on a molecule-by-molecule basis, it is fairly practical ($L = \beta \log M$ is expected to be relatively short, say on the order of $10^2$–$10^3$), and much simpler than the decoder of [18].

After the individual molecule decoding stage, the decoder holds $N$ sequences from $\mathcal{B}_m^{(L)}$, which are partitioned to the $m$ sub-codes $\mathcal{B}_m^{(L)}$. For each $m \in [M]$, the decoder collects the set of inner-code decoded output molecules which belong to $\mathcal{B}_m^{(L)}$ (if there are any), and either chooses from this sub-code a unique molecule, or declares an erasure of the $m$th molecule. An outer-code – which restricts the possible sequences of molecules – is then used to correct possible erasures or undetected erroneous molecules. Specifically, this can be achieved by a simple minimum Hamming distance (on a molecule level) decoder. Therefore, the proposed coded-index based scheme is practical, and its analysis is general, in the sense that very little is assumed on the sequencing channel. It is only required that a proper decoder for an inner code of block-length $L$ exists, such that the error probability decays to zero with increasing $L$. This addresses the first two issues raised above.

As was shown in [18], and will also be apparent from the analysis in this paper, it appears that sequencing errors affect the error probability to much less extent compared to unfavorable sampling events. Indeed, bad sampling events are the origin of the slow $e^{-\Theta(M)}$ decay of the error probability obtained in [18], which assumed $N = \alpha M$ for some fixed $\alpha > 1$. The only way to ameliorate this behavior is by increasing $N$. In accordance, we consider in this paper the scaling $N = \alpha_M M$ where $\alpha_M$ may either be a constant (as in [15]–[18]) or an increasing function of $M$ (though at a rather slow rate). As we shall see, this has a profound effect on the scaling of the decay of the error probability. This addresses the third issue raised above. Furthermore, if indeed the increased capacity of the binomial (multi-draw) capacity is marginal, then increasing $N$ is not useless, since it has an important role in determining the error probability. This addresses the fourth issue discussed above. Our main

\footnote{For comparison $C_{0.11, d} \approx (0.5, 0.71, 0.83, 0.9)$ bits for $d = 1, 2, 3$. See also Fig. 1 in the discussion in Sec. III to follow.}

\footnote{Practically, by a maximum distance separable code [16].}
result pertains to an achievable single-letter bound on the error probability of a coded-index based scheme for the DNA storage channel. It is comprised of both a random coding bound, as well as an expurgated bound, which lead to a decay rate of the error probability of the order $e^{-\Theta(N)}$. An important consequence of this result is that operating at a large covering depth $N/M$ is of importance when low error probability is of interest. This is in contrast to capacity analysis, which, as discussed in [15, Sec. I], it is wasteful to operate at a large covering depth $N/M$ as this only provides marginal capacity gains, but the sequencing costs are large.

E. Comparison With Previous Works

In [16] a coding scheme was proposed which is similarly based on (explicit) coded-indexing and on concatenated coding of outer code aimed to correct erasures, and an inner code aimed to correct sequencing errors. The main difference is, perhaps, that [16] aims to achieve the capacity of the multi-draw channel. To this end, it should be recalled that the encoder does not know in advance how many times each molecule will be sampled, and thus also not the capacity of the effective channel from the input molecule to the corresponding output molecule(s). The scheme [16] incorporates a code over multiple molecules, so that the capacity of the jointly encoded molecules is averaged over the randomness of the sampling operation. Compared to this paper, [16] is based on (hard) output clustering, and so is mainly tailored to the BSC, and positive rate is only achieved when the crossover probability is less than $1/4$. The resulting capacity lower bound tends to capacity bound of [17] only if the crossover probability of the BSC tends to zero (as in our scheme, as the increase in capacity due to multi-draws is marginally small), or if $N/M \to \infty$ (which is indeed better than our scheme in terms of rate, but the improvement in the error probability is not established). As described above, in this paper, we consider general sequencing channels, and focus on error probability analysis and simple decoding, at the price of possible rate loss. We also mention that [27] have studied the coding rate of explicit uncoded indexing compared to optimal codes, under an adversarial channel model (with a different scaling of the molecule size). In our context, the conclusion is that the loss is more profound for small $\beta$.

F. Outline

The rest of the paper is organized as follows. In Sec. II we establish notation conventions, and formulate the DNA storage channel and coded-index based systems. In Sec. III we state our main result, and in Sec. IV we provide the proof, which includes both random coding analysis as well as an expurgated bound. In Sec. V we summarize the paper.

II. PROBLEM FORMULATION

A. Notation Conventions

Random variables will be denoted by capital letters, specific values they may take will be denoted by the corresponding lower case letters, and their alphabets will be denoted by calligraphic letters. Random vectors and their realizations will be super-scripted by their dimension. For example, the random vector $A^K = (A_0, \ldots, A_{K-1}) \in A^K$ (where $K \in \mathbb{N}^+$), may take a specific vector value $a^K = (a_0, \ldots, a_{K-1}) \in A^K$, the $K$th order Cartesian power of $A$, which is the alphabet of each component of this vector. The Cartesian product of $A$ and $B$ (both finite alphabets) will be denoted by $A \times B$. The probability of the event $E$ will be denoted by $\mathbb{P}(E)$, and its indicator function will be denoted by $\mathbb{1}(E)$. The expectation operator w.r.t. a given distribution $P$ will be denoted by $\mathbb{E}[\cdot]$.

Logarithms and exponents will be understood to be taken to the natural base. The binary entropy function $h_2 : [0, 1] \to [0, 1]$ will be denoted by $h_2(a) := -a \log_2 a - (1-a) \log_2(1-a)$ and the binary Kullback–Leibler (KL) divergence $d_{KL} : [0, 1] \times (0, 1) \to \mathbb{R}^+$ by $d_{KL}(a|b) := a \log_2 \frac{a}{b} + (1-a) \log_2 \left(\frac{1-a}{1-b}\right)$.

The number of distinct elements of a finite multiset $A$ will be denoted by $|A|$. For a positive integer $N$, $[N] := \{0, 1, \ldots, N\}$, where scalar multiplications of these sets will be used, e.g., as $\frac{1}{2}[N+1] = \{0, \frac{1}{2}, \ldots, \frac{N+1}{2}\}$. Throughout, for the sake of brevity, integer constants on large numbers which are inconsequential will be ignored, for example, the number of codewords in a rate $R$ codebook of dimension $K$ will be simply written as $e^{KR}$ (instead of $e^{KR}|$).

B. Formulation of the DNA Storage Channel

In this section, we formulate a DNA storage channel and the corresponding encoders and decoders. The channel will be indexed by the number of molecules $M$ in the DNA pool used to store a message.\(^7\)

1) The Channel Model (Reading Mechanism): A DNA molecule is a sequence of $L \equiv L_M \in \mathbb{N}_+$ nucleotides (symbols) chosen from an alphabet $X$, where in physical systems $X = \{A, C, G, T\}$. In previous works (e.g., [15]–[17]) the binary case $X = \{0, 1\}$ was typically assumed for simplicity, yet here, we do not make any such assumptions. Thus, each molecule is uniquely represented by a sequence $x^L \in X^L$. An input to the DNA channel is a sequence of $M$ molecules, $x^{LM} = (x^L_0, \ldots, x^L_{M-1})$, where $x^L_m \in X^L$ for all $m \in [M]$.\(^8\)

\(^7\)Occasionally, also by quantities which depend on $M$. Specifically, we may index the channels by $N \equiv N_M$, the number of output molecules.

\(^8\)In principle, a codeword is a multiset of $M$ molecules, that is, the order is not specified. However, for analysis it is convenient to assume an arbitrary ordering of the molecules. As evident from the description of the sampling stage, this ordering does not affect the channel output.
Suppose that an input is synthesized into a sequence of $M$ molecules, $x^{LM}$. The DNA storage channel we consider here is parameterized by the number of molecule samples $N \equiv N_M \in \mathbb{N}_+$, and a sequencing channel $W^{(L)} : \mathcal{X}^L \to \mathcal{Y}^{(L)}$. Note that the output alphabet $\mathcal{Y}^{(L)}$ does not have to be the $L$th order Cartesian power of $\mathcal{Y}$. For example, for a deletion/insertion sequencing channel $\mathcal{Y}^{(L)} = \mathcal{Y}^0 \cup \mathcal{Y}^1 \cup \cdots$.

The operation of the channel on the stored codeword $x^{LM}$ is modeled as a two-stage process:

1. **Sampling:** $N$ molecules are sampled uniformly from the $M$ molecules of $x^{LM}$, independently, with replacement. Let $U^N \in [M]^N$ be such that $U_n$ is the sampled molecule at sampling event $n \in [N]$. We refer to $U^N$ as the **molecule index vector**, so that $U^N \sim \text{Uniform}([M]^N)$.

The result of the sampling stage is thus the vector

$$ (x^{L}_{U_0}, x^{L}_{U_1}, \ldots, x^{L}_{U_{N-1}}) \in (\mathcal{X}^L)^N. \quad (1) $$

Let $S^M \in [N]^M$ be such that $S_m$ is the number of times that molecule $m$ was sampled, to wit $S_m = \sum_{n \in [N]} 1\{U_n = m\}$, the empirical count of $U^N$. It holds that $S^M \sim \text{Multinomial}(N; (\frac{1}{M}, \frac{1}{M}, \ldots, \frac{1}{M}))$, and we refer to $S^M$ as the **molecule duplicate vector**.

2. ** Sequencing:** For each $n \in [N]$, $x^{L}_{U_n}$ is sequenced to $Y^{(L)}_n \in \mathcal{Y}^{(L)}$, and the sequencing of $x^{L}_{U_n}$ is independent for all $n \in [N]$. Denoting the channel output by $(Y^{(L)})^N = (Y^{(L)}_0, \ldots, Y^{(L)}_{N-1}) \in (\mathcal{Y}^{(L)})^N$, it thus holds that

$$ P \left[ (Y^{(L)})^N = (y^{(L)})^N \mid x^{LM}, U^N \right] = \prod_{n \in [N]} W^{(L)} \left( y^{(L)}_n \mid x^{L}_{U_n} \right). \quad (2) $$

The channel output is $(Y^{(L)})^N$, where due to the random sampling stage, it is clear that the observed index $n$ of $y^{(L)}_n$ in $(y^{(L)})^N$ is immaterial for decoding.

2) **The Encoder:** A codebook to the DNA storage channel is a set of different possible codewords (channel inputs) $\mathcal{C} = \{x^{LM}(j)\}$. In this work we consider the following restricted set of codebooks, which is based on coded-index:

**Definition 1 (Coded-Index Based Codebooks):** Let $\{B^{(L)}_m\}_{m \in [M]}$ be a collection of pairwise disjoint sets $B^{(L)}_m \subset \mathcal{X}^L$ of equal cardinality, and let $B^{(L)} = \bigcup_{m \in [M]} B^{(L)}_m$ be their union. A DNA storage code is said to be coded-index based if $x^{LM}(j) \in B^{(L)}_m$ for all $m \in [M]$ and all $j \in [\mathcal{C}]$.

To wit, a codeword contains exactly a single molecule from each of the $M$ sub-codes $\{B^{(L)}_m\}_{m \in [M]}$. The identity of the sub-code from which $x^{LM}(j)$ was chosen from is considered an “index” of the molecule, which can be used by the decoder to order the decoded molecules. A coded-index based codebook can be thought of as a concatenated code. The set $B^{(L)}$ is an inner-code, which is used to clean the output molecules from sequencing errors, and the dependency between molecules of different index $m$ can be considered an outer-code which is used to cope with erasures due to the sampling stage, and residual sequencing errors.

3) **The Decoder:** A general decoder is a mapping $D : (Y^{(L)})^N \to [\mathcal{C}]$. In this work we consider the following class of decoders, which are suitable for coded-index based codebooks. The decoder is equipped with an inner-code decoder $D_b : (y^{(L)})^N \to B^{(L)}$ and a threshold $T \equiv T_M$, and processes $(y^{(L)})^N$ in three steps:

1) Correction of individual molecules: The decoder employs the inner-code decoder for each of the received molecules $y^{(L)}_n$, $n \in [N]$, and sets $z^{LM}_n = D_b(y^{(L)}_n)$. Following this stage, it holds that $z^{LM} = (z^{LM}_0, \ldots, z^{LM}_{N-1})$ is such that $z^{LM}_n \in B^{(L)}_m$ for all $n \in [N]$.

2) Threshold for each index: For each index $m \in [M]$, if there exists a $b^L \in B^{(L)}_m$ such that

$$ \sum_{n \in [N]} 1\{z^{LM}_n = b^L\} \geq T $$

then the decoder sets $\hat{x}^{LM}_m = b^L$. That is, $\hat{x}^{LM}_m = b^L$ if $b^L$ is a unique molecule in $B^{(L)}_m$ whose number of appearances in $z^{LM}$ is larger than $T$. Otherwise $\hat{x}^{LM}_m = e$, where $e$ is a symbol representing an erasure.

3) Codeword decoding: Let

$$ j^* = \arg \min_{j \in [\mathcal{C}]} \rho(\hat{x}^{LM}, x^{LM}(j)), \quad (4) $$

where (with a slight abuse of notation)

$$ \rho(\hat{x}^{LM}, x^{LM}) := \sum_{m \in [M]} \rho(\hat{x}^{LM}_m, x^{LM}_m), \quad (5) $$

and

$$ \rho(\hat{x}^{LM}, x^{LM}) := \begin{cases} 1\{\hat{x}^{LM} \neq x^{LM}\}, & \hat{x}^{LM} \neq e, \\ 0, & \hat{x}^{LM} = e. \end{cases} \quad (6) $$

That is, the distance of a codeword $x^{LM}(j)$ to $\hat{x}^{LM}$ has zero contribution from erased molecule indices or if $x^{LM}(j) = \hat{x}^{LM}$, and 1 otherwise.

4) **Assumptions on the Channel Model:**

1) **Molecule length scaling:** $L \equiv L_M = \beta \log M$, where $\beta > 1$ is the molecule length parameter.

2) **Coverage depth scaling:** $N = \alpha M$, where $\alpha M > 1$ is the coverage depth scaling function, and $\alpha M$ is a monotonic non-decreasing function. If $\alpha \equiv \alpha M$ is constant then $\alpha$ is the coverage depth scaling parameter.

The DNA storage channel is thus indexed by $M$ and parameterized by $\alpha M, \beta, \{W^{(L)}\}_{L \in [N_+]}$. The (storage) rate of the codebook $C$ is given by $R = \frac{\log |\mathcal{C}|}{LM \cdot M}$, and the error probability of $D$ given that $x^{LM}(j) \in C$ was stored is given by

$$ pe(C, D \mid x^{LM}(j)) := P \left[ D((y^{(L)})^N) \neq j \mid x^{LM}(j) \right]. \quad (7) $$

Let $\psi_M : \mathbb{N}_+ \to \mathbb{N}_+$ be a monotonic strictly increasing sequence. An error exponent $E(R)$ w.r.t. scaling $\psi_M$ is achievable for channel DNA at rate $R$, if there exists a
sequence \( \{C_M, D_M\}_{M \in \mathbb{N}^+} \) so that the average error probability is bounded as

\[
\liminf_{M \to \infty} \frac{1}{\Psi_M} \log \left[ \frac{1}{|C_M|} \sum_{j \in |C_M|} \text{pe}(C_M, D_M | x^{LM}(j)) \right] 
\geq E(R). \tag{8}
\]

In this paper, we present single-letter expressions for error exponents achieved under coded-index codebook and the class of decoders defined above. Let \( R_b = \frac{\log |B(L)|}{L} \) be the rate of the inner code, and let

\[
\text{pe}_b(B^{(L)}) = \max_{b^L \in B^L} W^{(L)} \left[ D_b(b^{(L)}) \neq b^L \mid b^L \right] \tag{9}
\]

be the maximal error probability of the inner code over the sequencing channel \( W^{(L)} \). We will not make any assumptions regarding the channel \( W^{(L)} \) (e.g., that it is the \( L \)th order power of a DMC \( W : X \to Y \), or that \( W^{(L)} \) is a deletion/insertion channel). Rather instead, we will assume that a suitable sequence of codes can be found, as follows.

5) Assumptions on the Inner Code:

1) Inner code rate: \( R_b = \frac{1}{L} \log |B^{(L)}| > 1/\beta \).
2) Vanishing inner code error probability: \( \text{pe}_b(B^{(L)}) = e^{-\Theta(L^\gamma)} \) where \( \gamma > 0 \).

The cardinality of each sub-code is \( |B_m^{(L)}| = M^{(R_b^L - 1)} = M^{(R_b^L - 1)} \). Thus, for any rate which satisfies the assumption \( R_b > 1/\beta \), the inner sub-code size \( |B_m^{(L)}| \) is strictly larger than 1 for all \( M \) large enough. The assumption on the error probability assures that the error probability at the first decoding step tends to zero as \( L = \beta \log M \to \infty \). Thus, it must hold that \( R_b \) is below the normalized capacity of the channel \( \lim_{L \to \infty} \frac{1}{L} C(W^{(L)}) \), where, in general, the capacity is as given by the \textit{infimum information rate} formula of [28]. For memoryless sequencing channels \( W^{(L)} = W^\otimes L \), and the error probability decays exponentially with \( L \), as \( e^{-E \cdot L} \) where \( E \) is an exponent which depends on the rate of the inner code. Here, however, we consider general sequencing channels, for which the error probability may decay much more slowly with \( L \), even for optimal codes. For concreteness, we have assumed \( \text{pe}_b(B^{(L)}) = e^{-\Theta(L^\gamma)} \), but as we shall see, \( \gamma \) does not affect the achievable exponent, and, in fact, the assumption \( \text{pe}_b(B^{(L)}) = o(1) \) suffices for our next result to hold (but makes the derivations in the proof slightly more cumbersome). Moreover, we do not specify the inner code and the decoder, and they may correspond to any suitable choice.

For example, \textit{polar codes} can be used, which can achieve error scaling of \( e^{-\Theta(\sqrt{N})} \) for standard DMCs [29], [30], and of \( e^{-\Theta(N^{1/3})} \) for channels which include insertions, deletions, and substitutions [31].

In order to derive achievable error probability bounds, we will consider the following random coding ensemble.

\textit{Definition 2 (Coded-Index Based Random Coding Ensemble):} For a given \( \{B_m^{(L)}\}_{m \in [M]} \) (with the notation of Definition 1), let \( C = \{ X_m^{L,M}(j) \} \) be a random code such that \( X_m^{L,M}(j) \) is chosen uniformly at random from \( B_m^{(L)} \), independently for all \( m \in [M] \) and all \( j \in |C| \).

\section{Main Result}

Our main result is as follows:

\textit{Theorem 3:} Let \( m \) sub-codes be given \( \{B_m^{(L)}\}_{m \in [M]} \), and let \( D_b \) be a decoder which satisfies the assumptions on the inner code for \( B^{(L)} = \cup_{m \in [M]} B_m^{(L)} \left( R_b > 1/\beta, \text{pe}_b(B^{(L)}) = e^{-\Theta(L^\gamma)} \right) \). Then, there exists a sequence of codebooks \( C_{\alpha} \) and corresponding threshold-based decoders (as described in Sec. II-B) so that:

- If \( N/M = \Theta(1) \) then

\[
\liminf_{M \to \infty} \frac{1}{M} \log \text{pe}(C_{\alpha}, D_{\beta}) \geq 2 R_b - \frac{R}{R_b} \log R_b - 1/\beta \tag{10}
\]

for any \( R < (R_b - 1/\beta)/(R_b - 1) \).

- If \( N/M = \omega(1) \) then

\[
\liminf_{N \to \infty} \frac{1}{N} \log \text{pe}(C_{\alpha}, D_{\beta}) \geq \left\{- \frac{1}{2} \left[ 2R_b - \frac{R}{R_b} \right] - \frac{M}{N} \leq 4(R_b - 1/\beta) \right. \tag{11}
\]

for any \( R < R_b - 1/\beta \).

The proof of Theorem 3 follows directly by taking the better of a random coding bound (Prop. 9 in Sec. IV-B) and an expurgated bound (Prop. 11 in Sec. IV-C).

6) Discussion:

1) The exponent bound is not continuous in \( N \) (that is, there is a phase transition), and the behavior is markedly different between \( N = \Theta(M) \) and \( N = \omega(M) \). As emanates from the analysis, in both regimes, the threshold is chosen so that \( T = T_M = o(N/M) \). This is because the error probability of the inner code decay to zero as \( e^{-\Theta(L^\gamma)} = e^{-\Theta(\log^2 M)} \), and so the average number of erroneously sequenced molecules is \( o(N/M) \) per molecule. It is plausible that similar bounds can be obtained with a simpler decoder which only checks if there exists a unique molecule of index \( m \), and otherwise declares an erasure (which is equivalent to setting \( T = 1 \)), or a decoder based on majority for each index \( m \). Nonetheless, the insight from the random coding analysis of our general threshold decoder is that even if \( N/M \) is large, there is no gain in setting the threshold to be \( \Theta(N/M) \). This is not obvious \textit{a priori}.

2) The only regime in which the expurgated bound is better than the random coding bound is \( \frac{N}{ML} > 4(R_b - 1/\beta) \). Consequently, in the two other regimes the error probability bound holds for a typical code from the ensemble.

3) The result does not depend on \( \gamma \), the assumed scaling of the inner code error probability (\( \text{pe}_b(B^{(L)}) = e^{-\Theta(L^\gamma)} \)), and manifests the fact that sampling events dominate the error probability, compared to sequencing error events.
4) For the standard channel coding problem over DMCs with blocklength \( N \), the method of types leads to random coding and expurgated bounds which tend to their asymptotic values up to a \( O((\log N)/N) \) term (this can be avoided using Gallager’s method [32, Ch. 5], see also [33, Problem 10.33]). Here, it is evident from the proof that the decay is much slower, and could be as slow as \( O(1/\log M) \). As discussed in [18, Sec. VII] this seems to be an inherent property of this channel.

5) Proof outline: The proof appears in Sec. IV that follows. There, in Sec. IV-A, we analyze the channel operation, and evaluate the probability of events in which either some of the molecules are not sampled enough times, or that there are many sequencing errors (respectively, Lemmas 4, 5 and 7). Using these bounds, we evaluate a large-deviation bound for the number of erasures and undetected errors in the output of the decoder (Lemma 8). Then, in Sec. IV-B we consider the random coding ensemble of Definition II-B.5, and evaluate the probability that a single randomly chosen codeword from this ensemble is decoded instead of the true codeword, conditioning on a specific number of erasures and undetected errors (Lemma 10). This bound uses the erasure/undetected-error probability bounds of Sec. IV-A. A clipped union bound is then invoked to prove the random coding bound. In Sec. IV-C, the expurgated bound is proved by first establishing the existence of a codebook with specific values of distance spectrum, according to the \( \rho \) distance defined in (5) (Lemma 12). The expurgated bound is then proved by upper bounding the error probability of this codebook by the sum of all its pairwise error probabilities.

6) Theorem 3 only provides an achievable bound, and establishing tightness of this bound seems to be a challenging task for the multinomial model assumed here. Recall that the sampling model is such that each molecule from the codeword \( x^L \) is chosen uniformly at random, with replacement. Consequently, the molecule duplicate vector \( S^M \) follows a multinomial distribution. Lemma 5 bounds the probability that \( \sigma M \) molecules have been under-sampled during the sampling stage. The direct analysis of this event under the multinomial distribution of \( S^M \) is difficult. To circumvent this, the proof of the lemma utilizes the Poissonization of the multinomial effect, proposed in [15], [25] to analyze the capacity of the channel. Specifically, the aforementioned probability is upper bounded by the probability of the same sampling event, while replacing \( S^M \) with an independent and identically distributed (i.i.d.) Poisson r.v.’s, \( S_m \sim \text{Pois}(N/M) \), \( m \in [M] \). While this provably upper bounds the error probability, this upper bound is tight at the center of the multinomial distribution, but may be loose at its tails. It is thus anticipated that a lower bound on the error probability would require a direct analysis of the multinomial distribution. Nonetheless, if one adopts a pure Poisson model for the number of times each molecule is sampled, i.e., \( S_m \sim \text{Pois}(N/M) \) i.i.d., then a simple lower bound can be derived using the following considerations. The probability that a molecule is erased is at least \( \mathbb{P}[\text{Pois}(N/M) \leq T] \), and is independent over different molecules. Thus, the error probability of the code is larger than that of the optimal error probability in an erasure channel with erasure probability \( \mathbb{P}[\text{Pois}(N/M) \leq T] \), neglecting undetected errors, which will only increase the error probability (informally speaking). The optimal error exponent for binary erasure channel can then be lower bounded by standard bounds for erasure channel, e.g., the sphere packing bound [32, Thm. 5.8.1], [33, Thm. 10.3].

7) For \( N/M = \Theta(1) = \alpha \), and a DMC sequencing channel \( W \), a lower bound on capacity (which is tight for all \( \beta \) above a critical value depending on \( W \) ), was obtained in [18, Thm. 5]. This lower bound is given by

\[
\max_{P_X \in \mathcal{P}(X)} \sum_{d \in \mathbb{N}^+} \pi_\alpha(d) \cdot I(P_X, W^{\otimes d}) - \frac{1}{\beta} (1 - \pi_\alpha(0)),
\]

where \( \pi_\alpha(d) := \frac{\lambda^{d-\alpha}}{\alpha d!} \) for \( d \in \mathbb{N} \) is the Poisson probability mass function for parameter \( \alpha \), \( I(P_X, V) \) is the mutual information of a channel \( V: A \to B \) with input distribution is \( P_X \), and \( V^{\otimes d} \) is the \( d \)-order binomial extension of \( V \), that is the DMC \( V^{\otimes d}: A \to B^d \) for which

\[
V^{\otimes d}[b_d | a] = \prod_{i=0}^{d-1} V(b_i | a).
\]

From Theorem 3, a lower bound on the maximal rate achieved by the considered scheme is \( (R_b - 1/\beta)(1 - \pi_\alpha(0)) \). To maximize this lower bound, we choose the maximal possible rate for which vanishing inner code error probability can be attained, that is \( R_b = I(P_X, W) \). Thus, the difference between the capacity lower bounds is

\[
\sum_{d \in \mathbb{N}^+} \pi_\alpha(d) \cdot I(P_X, W^{\otimes d}) - I(P_X, W) (1 - \pi_\alpha(0)).
\]

This is expected since our decoder does not combines information from multiple output molecules. The difference (14) for a BSC sequencing channel with crossover probability \( w \), and an optimal input distribution \( P_X = (1/2, 1/2) \) is shown in Fig. 1, as a function of \( \alpha \), for various values of \( w \). As expected, for a low values of \( w = 10^{-3} \), this difference is rather small (at most \( \sim 0.01 \) nats). While the difference is increasing with \( w \), it saturates as a function of \( \alpha \), and can still be low for low values of \( \alpha \) (close to 1). Note also that the difference in (14) is independent of \( \beta \). For the case \( N/M = \omega(1) \) the lower bound on capacity implied by Theorem 3 is \( R_b - 1/\beta \), where \( R_b \) can be chosen to be as large as the normalized capacity of the sequencing channel. Thus, the result agrees with the capacity lower bound of the \( N/M = \Theta(1) \) case, when taking the limit \( N/M \to \infty \).
IV. PROOF OF THEOREM 3

A. Error Events for the Threshold Based Decoder

In the coded-index based coding, each codeword \( x^{LM}(j) \) contains exactly a single molecule from each of the sub-codes \( B^M_m \). The molecule \( x_m^L(j) \) is sampled \( s_m \) times, where \( s^M \in [N]^M \) is the molecule duplicate vector. According to the definition of the decoder, an error in the “inner” decoding of the \( m \)th molecule, that is, \( \hat{x}_m^L \neq x_m(j) \), may occur for several reasons. First, it may occur that the number of times that \( x_m(j) \) was sampled is below the required threshold \( T \), that is, the event \( \mathbb{I}\{s_m \leq T\} \). This is an erasure/undetected-error event caused by non-ideal sampling. Second, it may occur that \( x_m(j) \) was sampled more than \( T \) times, however, sequencing errors have caused the number of appearances of \( x_m(j) \) in \( z^{LN} \) to drop below the threshold \( T \). Third, it may occur that \( x_m(j) \) appears in \( z^{LN} \) more than \( T \) times, yet sequencing errors have caused a different molecule \( \hat{x}_m^L \in B^M_m \) to appear in \( z^{LN} \) more than \( T \) times. If neither of these events has occurred then the molecule \( x_m^L = x_m(j) \) is decoded correctly. Otherwise, the \( m \)th molecule is either erased in the second step of the decoder or is erroneously decoded (which is an undetected error).

For such events to have an effect on the exponential decrease of the error probability after the decoding of the outer code, they must have \( \Theta(M) \) occurrences. In accordance, we analyze in this section the large deviations of the erasure-probability and undetected-error-probability. To this end, we recall that the decoder \( D \) is defined by a threshold \( T \), and we next parameterize this threshold by a parameter \( \tau \in (0, \frac{1}{2}) \), and write

\[
T \equiv T_\tau := \frac{N}{M} \left(1 - \sqrt{2\tau}\right). \tag{15}
\]

Note that the constraint \( \tau < \frac{1}{2} \) assures that \( T_\tau > 0 \). For the analysis, we will use the following notation for random variables that correspond to channel events:

- \( K_m \in [s_m + 1] \) is the number of copies of the molecule \( x_m^L(j) \) that have been erroneously inner-decoded.
- \( K := \sum_{m \in [M]} K_m \in [N + 1] \) is the total number of molecules which have been erroneously inner-decoded.
- \( V_m \in [K + 1] \) is the number of output molecules \( y^L \) that originated from reading a molecule \( x_m^L(j) \) for some \( m' \in [M]\setminus\{m\} \), and that have been erroneously inner-decoded to have index \( m \). Note that \( \sum_{m \in [M]} V_m \leq K \) holds.

With these definitions, the event in which the molecule \( x_m^L \) was not decoded correctly in the second stage of the operation of the decoder is included in a union of the following events:

1) \( S_m < T_\tau \), that is, the molecule have not been sampled enough times in the sampling stage.
2) \( S_m \geq T_\tau \) yet \( S_m - K_m < T_\tau \), that is, the molecule has been sampled enough times in the sampling stage step, but \( K_m \) sequencing errors have caused the number of appearances of \( x_m^L(j) \) to drop below the threshold \( T_\tau \).
3) \( V_m \geq T_\tau \), that is, there are more than \( T_\tau \) molecules with index \( m \), which are not the correct molecule \( x_m^L(j) \).

In correspondence to the three types of events, we define the following sets for the analysis of multiple erasures/undetected-errors:

\[
\mathcal{M}_{sam} := \{m \in [M]: S_m < T_\tau\}, \tag{16}
\]
\[
\mathcal{M}_{cbt} := \{m \in [M]: S_m \geq T_\tau, S_m - K_m < T_\tau\}, \tag{17}
\]
\[
\mathcal{M}_{eat} := \{m \in [M]: V_m \geq T_\tau\}, \tag{18}
\]

where the subscripts are mnemonics to “sampling”, “correct-below-threshold”, “erroneous-above-threshold”. We next make two remarks regarding the definition of the above events:

1) The threshold rule in (3) requires that the number of occurrences of the chosen molecule \( b^L \in B^M_m \) in \( z^{LN} \) is large by at least \( 1 \) over the maximal number of occurrences of other competing molecules in \( B^M_m \). Therefore, given a total of \( K \) sequencing errors (out of \( N \) molecules), there could be at most \( K \) molecules which were sampled a sufficient number of times, i.e., \( S_m \geq T_\tau \), yet sequencing errors have caused the number of appearances of this molecule after the first stage of decoding to drop below the threshold, i.e., the event \( S_m - K_m < T_\tau \). This bound seems rather crude, but will be shown to be effective in what follows.
2) On the face of it, the third error event \( V_m \geq T_\tau \) can lead to a crude upper bound. In typical situations, the \( V_m \) molecules which are erroneously mapped to index \( m \) due to sequencing errors are not likely to be the exact same molecule in \( B^M_m \). However, a more precise analysis of this event would require making assumptions on the structure of the sub-codes \( B^M_m \), which we avoid here altogether. In other words, we take here a worst-case approach, and assume the most unfavorable situation in which the erroneous \( V_m \) molecules from \( B^M_m \) are the exact same molecule, and whenever their number of appearances is larger than \( T_\tau \), an erosion occurs.

Finally, we define the set of erased molecules and the set of molecules with undetected errors as

\[
\mathcal{M}_e := \{m \in [M]: \hat{x}_m^L = e\}, \tag{19}
\]
\[ M_u := \{ m \in [M] : \hat{x}_m^j \neq e, \hat{y}_m^j \neq x_m^j(j) \}, \] (20)
assuming that the jth codeword was stored. Our goal in this section is to bound the probability that \( |M_u| \) is larger than \( \theta M \) for some \( \theta \in [0, 1] \), and the same probability for \( |M_u| \). To this end, we begin by deriving relations between \( |M_{sam}|, |M_{cbt}| \) and \( |M_{eat}| \) to the erasure and undetected error sets.

**Lemma 4:** Let \( \tau \in (0, \frac{1}{2}) \) be given. Then,
\[
|M_u| \leq |M_{sam}| + \left( 1 + \frac{1}{T_e} \right) K \tag{21}
\]
and
\[
|M_u| \leq \frac{K}{T_e}. \tag{22}
\]

**Proof:** The bound (21) is proved by the following chain of inequalities:
\[
|M_u| \leq |M_{sam} \cup M_{cbt} \cup M_{eat}|
\leq |M_{sam}| + |M_{cbt}| + |M_{eat}|
\overset{(a)}{\leq} |M_{sam}| + K + \frac{K}{T_e},
\]
where the inequality follows since both \( |M_{cbt}| \leq K \) and \( |M_{eat}| \leq \frac{K}{T_e} \) must hold at worst case (as discussed informally above). The bound (22) follows immediately from the threshold definition in (15) as
\[
|M_u| \leq |M_{eat}| \leq \frac{K}{T_e}. \tag{26}
\]

The next pair of lemmas is devoted to analyzing the probability that the cardinality of one of the index sets defined in 16, 17, and (18), is larger than some threshold. We begin with the cardinality of \( M_{sam} \).

**Lemma 5:** Let \( \tau \in (0, \frac{1}{2}) \) be given, and let \( x^{LM}(j) \) be a codeword from a coded-index codebook. Let \( \tilde{S} \sim \text{Pois}(N/M) \) and
\[
\varphi_{\tau} := -\frac{1}{N/M} \log P\left[ \tilde{S} \leq T_e \right], \tag{27}
\]
Let \( M_{sam} \) be as in (16). If \( N/M = \Theta(1) \) then
\[
P\left[ |M_{sam}| \geq \sigma M \mid x^{LM}(j) \right] \leq 2(1 + o(1) \cdot \exp \left[ -M \cdot db\left( \sigma \mid e^{-\varphi_{\tau} N/2} \right) \right] \tag{28}
\]
for \( \sigma \in (e^{-\varphi_{\tau} N/2}, 1] \). If \( N/M = \omega(1) \) then
\[
P\left[ |M_{sam}| \geq \sigma M \mid x^{LM}(j) \right] \leq 4e^{-\sigma \tau N[1+o(1)]} \tag{29}
\]
for \( \sigma \in (e^{-\tau N/2}, 1] \).

**Proof:** The molecule duplicate vector \( S^M \) follows a multinomial distribution, and so its components \( S_m \) are dependent random variables. To facilitate the analysis, we use the following well-known fact (e.g., [34, Thm. 5.6]):

**Fact 6 (Poissonization of the Multinomial Distribution):**
Let \( \tilde{N} \sim \text{Pois}(\lambda) \), and let \( \tilde{S}^M \) be a random vector such that \( \tilde{S}^M \sim \text{Multinomial}(\tilde{N}, (p_1, \ldots, p_{M-1})) \) conditioned on \( \tilde{N} \), where \( \sum_{m \in [M]} p_m = 1 \) and \( p_m > 0 \). Then, \( \{\tilde{S}_m \}_{m \in [M]} \) are statistically independent and \( \tilde{S}_m \sim \text{Pois}(p_m \lambda) \) (unconditioned on \( \tilde{N} \)).

Returning to the DNA storage model, let \( \tilde{N} \sim \text{Pois}(\lambda) \) and \( \tilde{S}^M = (\tilde{S}_0, \ldots, \tilde{S}_{M-1}) \sim \text{Multinomial}(\tilde{N}, (\frac{1}{M}, \ldots, \frac{1}{M})) \) conditioned on \( \tilde{N} \). By the above fact, \( \{\tilde{S}_m \}_{m \in [M]} \) are i.i.d. and \( \tilde{S}_m \sim \text{Pois}(\frac{\lambda}{M}) \). Define the event \( \xi_m := \{ \tilde{S}_m < T_e \} \), and similarly the event \( \xi_m := \{ S_m < T_e \} \), where \( T_e = \frac{\lambda}{\varphi_{\tau}} (1 - \sqrt{2/\varphi_{\tau}}) \) is the threshold for some \( \tau \in (0, \frac{1}{2}) \). Thus, clearly, \( T_e \leq E[\tilde{S}_m] = \frac{\lambda}{M} \), and so the expected number of occurrences of the \( m \)th molecule at the output exceeds the threshold for noiseless sequencing.

We begin with the \( N/M = \Theta(1) \) case. In this regime, \( P[\tilde{S}_m < T_e] \) can be computed directly, and it specifically holds by the definition of \( \varphi_{\tau} \) that \( P[\tilde{S}_m < T_e] = e^{-\varphi_{\tau} N/2} \). Next, we derive an inequality which will be used to bound the probability that \( \sum_{m \in [M]} \xi_m \geq \sigma M \). Recall that the sum of two independent multinomial distributions with the same probability parameters \( (p_0, \ldots, p_{M-1}) \) and \( N_1 \) (resp. \( N'_1 \)) trials is distributed as Multinomial\((N_1 + N'_1, (p_0, \ldots, p_{M-1})\)). Thus, if \( N_1 \leq N_2 = N_1 + N'_1 \) then
\[
P \left[ \sum_{m \in [M]} 1 \{ \tilde{S}_m < T_e \} \geq \sigma M \mid \tilde{N} = N_1 \right]
\geq P \left[ \sum_{m \in [M]} 1 \{ S_m < T_e \} \geq \sigma M \mid \tilde{N} = N_2 \right] \tag{30}
\]
holds. A simple application of the law of total expectation then implies that
\[
P \left[ \sum_{m \in [M]} 1 \{ \tilde{S}_m < T_e \} \geq \sigma M \mid \tilde{N} = N \right]
\leq P \left[ \sum_{m \in [M]} 1 \{ S_m < T_e \} \geq \sigma M \mid \tilde{N} \leq N \right]. \tag{31}
\]
Hence, the required probability is bounded as (see also [34, Exercise 5.14])
\[
P \left[ \sum_{m \in [M]} \xi_m \geq \sigma M \right]
= P \left[ \sum_{m \in [M]} 1 \{ S_m < T_e \} \geq \sigma M \right] \tag{32}
= P \left[ \sum_{m \in [M]} 1 \{ \tilde{S}_m < T_e \} \geq \sigma M \mid \tilde{N} = N \right] \tag{33}
\overset{(a)}{\leq} P \left[ \sum_{m \in [M]} 1 \{ \tilde{S}_m < T_e \} \geq \sigma M \mid \tilde{N} \leq N \right] \tag{34}
\leq P \left[ \sum_{m \in [M]} 1 \{ \tilde{S}_m < T_e \} \geq \sigma M \right] \tag{35}
\overset{(a)}{\leq} P \left[ \tilde{N} \leq N \right] \tag{36}
\]
that limit theorem for Poisson random variables which states

\[ \xi \sim \text{Pois}(\lambda) \]

where

\[ \lim_{N \to \infty} \frac{\xi}{N} = \lambda \]

for any \( \lambda > 0 \). Specifically, if \( A \sim \text{Pois}(\lambda) \) then for any \( a < \lambda \) it holds that [34, Thm. 5.4]

\[ \mathbb{P}[A \leq a] \leq \left( \frac{e \lambda}{a} \right)^a e^{-\lambda}. \]  

Then, setting \( a = c\lambda \) for \( c \in [0, 1] \) we obtain

\[ \mathbb{P}[A \leq c\lambda] \leq \left( \frac{e \lambda}{c} \right)^c e^{-\lambda} \]  

(42)

\[ = e^{c\lambda \log(e/c) - \lambda} \]  

(43)

\[ = e^{-\lambda [c \log e - c + 1]} \]  

(44)

\[ \leq \exp \left[ -\lambda \left( c \left( c - 1 - \frac{1}{2}(c-1)^2 \right) - c + 1 \right) \right] \]  

(45)

\[ = \exp \left[ -\lambda \left( (c-1)^2 - \frac{c}{2} \right) \right] \]  

(46)

\[ \leq \exp \left[ -\frac{\lambda}{2} (c-1)^2 \right] \]  

(47)

where (a) follows from \( \log c \geq c - 1 - \frac{1}{2}(c-1)^2 \) for \( c \in [0, 1] \). Then, using (47), we obtain

\[ \mathbb{E}[\xi_m] = \mathbb{P}[\xi_m \leq \tau] \]  

(48)

\[ \leq \exp \left[ -\frac{N}{2M} \left( \frac{T_r M}{N} - 1 \right)^2 \right] \]  

(49)

\[ = \exp \left[ -\tau \frac{N}{M} \right], \]  

(50)

that is, the bound \( \varphi_r \geq \tau \) holds. We then approximate

\[ \exp \left[ -M \cdot d_b \left( \sigma || e^{-\varphi_r N/M} \right) \right] \]  

\[ \leq \exp \left[ -M \cdot d_b \left( \sigma || e^{-\tau N/M} \right) \right] \]  

\[ \leq \exp \left[ -\sigma \tau N \cdot [1 + o(1)] \right], \]  

(51)

(52)

using the asymptotic expansion of the binary KL divergence

\[ d_b(a||b) = -[1 + o(1)] \cdot a \log b \] (see Proposition 13 in Appendix A). The result then follows by an analysis similar to the \( N/M = \Theta(1) \) case above until (40), followed by an application of the bound (52).

In the next lemma, we bound the large deviations of the total number of sequencing errors \( K \). To this end, we first discuss the statistical dependency between sampling events and sequencing errors events. In principle, the random behavior of the sequencing channel is independent of the sampling operation. However, since the error probability of the inner-code \( B^{(L)} \) may be different when conditioned on different codewords, the total number of sequencing errors may depend on the sampling event.\(^9\) Following our general approach in this paper, we avoid assuming any structure on the inner code, and so we make a worst-case approach. Let \( B^L \) be the inner-code codeword which achieves the maximal error probability over all possible codewords of the code \( B^{(L)} \), and let \( Y^{(L)} \) be a random sequenced output given that \( B^L \) was sampled to \( W^{(L)} \). Then,

\[ \text{pe}_b(B^{(L)}) = W^{(L)} \left[ D_b(Y^{(L)} \neq b^L \mid b^L) \right] \]  

(53)

\[ = \max_{b^L \in B^{(L)}} W^{(L)} \left[ D_b(Y^{(L)} \neq b^L \mid b^L) \right]. \]  

(54)

We define by \( \bar{K} \) the total number of molecules which were erroneously sequenced, conditioned on the event that the only sampled molecule is \( \bar{b}^L \). Then, clearly \( \bar{K} \sim \text{Binomial}(N, \text{pe}_b(B^{(L)})) \), and \( \bar{K} \) is independent of the sampling event.

**Lemma 7:** Let \( \bar{K} \) be the total number of erroneously sequenced molecules out of the \( N \) sampled molecules. Let \( U \subset [M]^N \) be an arbitrary sampling event, and assume that

\[ \text{pe}_b(B^{(L)}) = e^{-c \cdot L \xi}. \]  

Then, for any \( \kappa \in (0, 1] \)

\[ \mathbb{P}[K \geq \kappa N \mid U] \leq \exp \left[ -c(1 + o(1)) \cdot \kappa N L \xi \right]. \]  

(55)

**Proof:** Assume that an arbitrary codeword \( x^{(L)} \) has been stored. Let \( E_n = \mathbb{I}[D_b(Y_n^{(L)} \neq x_{U_n}^{(L)}) \] denote the indicator of the event that a sequencing error has occurred in the first stage of the decoder, for the \( n \)th sampled molecule, \( n \in [N] \). Then, conditioned on any sampling event \( U \),

\[ \mathbb{P}[K \geq \kappa M \mid U] \leq \mathbb{P} \left[ \sum_{n \in [N]} E_n \geq \kappa M \mid U \right] \]  

(56)

\[ \leq \mathbb{P} \left[ \bar{K} \geq \kappa M \mid U \right] \]  

(57)

\[ = \mathbb{P} \left[ \bar{K} \geq \kappa M \right], \]  

(58)

where (a) follows from the following consideration: Let \( E^N \in \{0, 1\}^N \) be a sequence of independent Bernoulli trials so that

\[ \mathbb{P}[E_n = 1] = p_n. \]  

Let \( p_{\max} := \max_{n \in [N]} p_n \), and let \( A \sim \text{Binomial}(N, p_{\max}) \). Let \( E^N \in \{0, 1\}^N \) be another sequence of independent Bernoulli trials, statistically independent of \( E^N \),

\(9\)For example, consider the case in which the sub-code \( B^{(L)} \) has a low average error probability compared to the other \( M - 1 \) sub codes \( \{B^{(L)}\}_{m \in [M] \setminus \{1\}} \). In this case, the expected value of the number of sequencing errors conditioned the sampling event \( S_1 = M \) is lower than the unconditional expected value.
so that $\Pr[E_n \lor \tilde{E}_n = 1] = p_{\text{max}}$ for all $n \in [N]$ (concretely, $\Pr[\tilde{E}_n = 1] = \tilde{p}_n = (p_{\text{max}} - p_n)/(1 - p_n)$). Then,
\[
\mathbb{P} \left[ \sum_{n \in [N]} E_n \geq t \right] \leq \mathbb{P} \left[ \sum_{n \in [N]} (E_n \lor \tilde{E}_n) \geq t \right] = \mathbb{P} \left[ A \geq t \right].
\]
(59)

Given (58), we may next analyze the large-deviations of $\tilde{K}$ in lieu of that of $K$. For any fixed $\kappa \in (0, 1]$, the expected number of sequencing errors is
\[
\mathbb{E}[\tilde{K}] = N e^{-c \cdot L^\xi} = o(\kappa N).
\]
(60)
Thus, the event $\tilde{K} \geq \kappa N$ is a large-deviations event. Since $\tilde{K} \sim \text{Binomial}(N, e^{-c \cdot L^\xi})$, Chernoff’s bound implies that
\[
\Pr \left[ \tilde{K} \geq \kappa N \right] \leq \exp \left( -N \cdot d_b \left( \kappa \left\| e^{-c \cdot L^\xi} \right\| \right) \right),
\]
(61)
and the result follows from the asymptotic expansion of the binary KL divergence $d_b(a|b) = -[1 + o(1)] \cdot a \log b$ (see Proposition 13 in Appendix A).

We next utilize Lemmas 5, and 7 to obtain the large-deviations behavior of the cardinality of erasures and undetected errors sets. As will be apparent, the dominating event is $\mathbb{P}[|\mathcal{M}_{\text{sam}}| \geq \sigma M]$ to wit, the probability that the molecules have not been amplified enough times - which is on the exponential order of $N$, compared to the probability evaluated in Lemma 7 which is on the exponential order of $LN = N^\beta \log M$. Therefore, as also discussed in the introduction, for the coded-index based codebooks and the type of decoders studied here, the effect of sequencing errors is much less profound compared to erasures.

**Lemma 8:** Let $\tau \in (0, \frac{1}{2})$ be given. Consider a decoder $D$ for a coded-index based codebook. For the erasure set $\mathcal{M}_e$:
- If $N/M = \Theta(1)$
  \[ -\log \mathbb{P}[|\mathcal{M}_e| \geq \theta M] \geq M \cdot d_b \left( \theta \left\| e^{-\varphi \cdot \frac{M}{N}} \right\| \right) + o(M) \]
  (62)
for all $\theta \in (e^{-\varphi \cdot \frac{M}{N}}, 1]$.
- If $N/M = o(1)$ then
  \[ -\log \mathbb{P}[|\mathcal{M}_e| \geq \theta M] \geq \theta \tau N \cdot [1 + o(1)] \]
  (63)
for all $\theta \in (e^{-\varphi \cdot \frac{M}{N}}, 1]$.

Furthermore, for the undetected error set $\mathcal{M}_u$:
\[ -\log \mathbb{P}[|\mathcal{M}_u| \geq \theta M] \geq c(1 + o(1)) \cdot (1 - \sqrt{2\tau}) \theta NL^\xi. \]
(64)

**Proof:** For any $\theta, \kappa \in \frac{1}{M}$:
\[
\begin{align*}
\mathbb{P}[|\mathcal{M}_e| \geq \theta M] & \leq \mathbb{P} \left[ |\mathcal{M}_{\text{sam}}| \right] \leq \left( 1 + \frac{1}{T_\tau} \right) K \geq \theta M \leq \sum_{\sigma, \kappa \in \frac{1}{M} : \sigma + \kappa \geq \theta} \mathbb{P}[|\mathcal{M}_{\text{sam}}| \geq \sigma M] \\
& \times \mathbb{P} \left[ \left( 1 + \frac{1}{T_\tau} \right) K \geq \kappa M \right] |\mathcal{M}_{\text{sam}}| = \sigma M \leq \sum_{\sigma, \kappa \in \frac{1}{M} : \sigma + \kappa \geq \theta} \mathbb{P}[|\mathcal{M}_{\text{sam}}| \geq \sigma M]
\end{align*}
\]
(65)
\[ \leq \sum_{\sigma, \kappa \in \frac{1}{M} : \sigma + \kappa \geq \theta} \mathbb{P}[|\mathcal{M}_{\text{sam}}| \geq \sigma M]
\]
(66)

where $c > 0$ is the constant for which $p_{\text{th}}(B(L^\xi)) \leq e^{-c \cdot L^\xi}$. We continue to bound the probability of interest for the $N/M = \Theta(1)$ case. Using Lemma 5 in (67) we deduce that
\[
\frac{1}{M} \log \mathbb{P}[|\mathcal{M}_e| \geq \theta M] \geq \min_{\sigma, \kappa \in [0, 1]} \frac{\kappa}{\sigma} \geq d_b \left( \sigma \left\| e^{-\varphi \cdot \frac{M}{N}} \right\| \right) + \kappa \left( 1 + T_\tau \right) L^\xi - O \left( \frac{\log M}{M} \right)
\]
(72)
for all $\sigma \in (e^{-\varphi \cdot \frac{M}{N}}, 1]$. In the last minimization problem, any choice of $\kappa > 0$ will cause the exponent to be $\Theta(L^\xi) = \Theta(\log^\xi M)$ and thus diverge as $M \rightarrow \infty$. Thus, the minimum is obtained for $\kappa = o(1)$ and if $\theta \geq e^{-\varphi \cdot \frac{M}{N}}$ the minimum is obtained at $\sigma = \theta - o(1)$. The claimed result then follows since
\[
d_b \left( \sigma \left\| e^{-\varphi \cdot \frac{M}{N}} \right\| \right) = d_b \left( \theta - o(1) \left\| e^{-\varphi \cdot \frac{M}{N}} \right\| \right) = d_b \left( \theta \left\| e^{-\varphi \cdot \frac{M}{N}} \right\| \right) - o(1)
\]
(73)
holds for any fixed $\tau$, and since $N/M = \Theta(1)$ was assumed. If $\theta \leq e^{-\varphi \cdot \frac{M}{N}}$ then the exponent is $O(\log^\xi M)$. The analysis for the $N/M = \omega(1)$ case is analogous and thus omitted.

Next, the probability that the cardinality of the undetected error set exceeds a certain threshold is bounded as:
\[
\mathbb{P}[|\mathcal{M}_u| \geq \theta M] \leq \mathbb{P} \left[ K \geq (1 - \sqrt{2\tau}) \theta N \right] \leq \exp \left[ -c(1 + o(1)) \cdot (1 - \sqrt{2\tau}) \theta NL^\xi \right].
\]
(76)

where (a) is using Lemma 4, and (b) is by Lemma 7.

**B. Random Coding Analysis**
After analyzing the effect of the channel on the number of erasures and undetected error events at the decoder (the probability that the number of erasures or undetected errors exceeds
\( \theta M \), we turn to the analysis of the average error probability of the random coding ensemble. We let \( \mathbb{P}(C_M, D_M) \) denote the ensemble average over the choice of random codebook \( C_M \) from the ensemble of Definition II-B.5. The random coding bound is as follows:

**Proposition 9 (Random Coding Bound):** Let an inner code be given by \( \{ B_m \} \subset X^L \) for \( m \in [M] \), and let \( D_b \) be a decoder which satisfies the assumption on the inner code at rate \( R_b \). The random coding exponent over the random ensemble from Definition II-B.5, with the decoder described in Sec. II-B is bounded as follows:

- If \( N/M = \Theta(1) \) then
  \[
  - \liminf_{M \to \infty} \frac{1}{M} \log \mathbb{P}(C_M, D_M) \geq d_b \left( 1 - \frac{R}{R_b - 1/\beta} \right) e^{-\frac{R}{R_b - 1/\beta}} \tag{77}
  \]
  for any \( R < (R_b - 1/\beta)(1 - e^{- \frac{R}{R_b - 1/\beta}}) \). If \( N/M = o(1) \) then
  \[
  - \liminf_{N \to \infty} \frac{1}{N} \log \mathbb{P}(C_M, D_M) \geq \left( \frac{1}{M} - \frac{R}{R_b - 1/\beta} \right) \log M \geq 2[R_b - 1/\beta] \tag{78}
  \]
  for any \( R < R_b - 1/\beta \).

In the rest of the section we prove Prop. 9. The next lemma bounds the probability that an erroneous codeword will be decoded conditioned on a given number of channel erasures and undetected errors.

**Lemma 10:** Let \( C \) be drawn from the coded-index based random coding ensemble (Definition II-B.5). Let \( X^L(0) = x^L(0) \) be arbitrary, and let \( X^L(0) \) be the output of the decoder conditioned on the input \( X^L(0) \). Then, for \( \theta_e, \theta_u \in [\frac{1}{2}[M+1] \) such that \( \theta_e + \theta_u \leq 1 \) and any \( j \in [\frac{1}{2}[M+1] \) it holds that

\[
- \frac{1}{M} \log \mathbb{P} \left[ \rho(\hat{X}^L, X^L(j)) \leq \rho(\hat{X}^L, X^L(0)) \bigg| \mathcal{E} \right] \geq (R_b - 1)(1 - \theta_e - \theta_u) \log M - 1 + \frac{\log M}{M}. \tag{79}
\]

where

\[ \mathcal{E} := \{ \mathcal{M}_e = \theta_e M, \mathcal{M}_u = \theta_u M \}. \tag{80} \]

**Proof:** We may assume without loss of generality (w.l.o.g.) that \( \mathcal{M}_e = \theta_e M \) and that \( \mathcal{M}_u = \{(\theta_e + \theta_u)M \} \cap \{\theta_e M\} \). Let \( R_b = \frac{1}{M} \log |B^L| \) be the rate of the inner code. By the definition of the random ensemble, the total number of possibilities to choose the codeword \( X^L(j) \) is \( e^{R_b L/M} \) \( \mathcal{M} = M^{R_b(1-1/\beta)} \) where \( R_b \leq \log |X| \). Let \( \hat{X}^L \) be an arbitrary decoder output such that the event \( \{\mathcal{M}_e = \theta_e M, \mathcal{M}_u = \theta_u M\} \) holds. We next upper bound the number of possible codewords that result a distance \( \rho(\hat{X}^L, X^L(j)) \) that is no larger than \( \rho(\hat{X}^L, X^L(0)) = \theta_u M \) as follows: For the indices \( m \in \mathcal{M}_e \) the choice of \( X^L(m) \) may be arbitrary since it does not affect the distance \( \rho(\hat{X}^L, X^L(j)) \). The number of possibilities to choose molecules for these indices is \( e^{R_b L/M} \) \( \mathcal{M} = M^{\theta_u M(R_b(1-1/\beta)} \). Then, the codeword \( X^L(j) \) will cause an error if the \( \rho \) distance at the remaining set of indices \( [M] \setminus \mathcal{M}_e \) is less or equal to \( \theta_u M \). The number of possibilities for this choice is

\[
\sum_{r=0}^{\theta_u M} \left( \frac{M(1-\theta_e)}{r} \right) \left( \frac{e^{R_b L/M} - 1}{r} \right)^r, \tag{81}
\]

where in the summation above \( r \) is the resulting distance \( \rho(\hat{X}^L, X^L(j)), \) \( M(1-\theta_u) \) is the number of possibilities to choose a subset of cardinality \( r \) from the set of indices \( \{m \in [M] \setminus \mathcal{M}_e : X^L(m) \neq \hat{X}^L \} \), and \( (e^{R_b L/M} - 1)^r \) is the number of ways to choose molecules for these indices. Since the choice of codeword \( X^L(j) \) is uniform over the set of all possibilities, it holds that

\[
\mathbb{P} \left[ \rho(\hat{X}^L, X^L(j)) \leq \rho(\hat{X}^L, X^L(0)) \bigg| \mathcal{M}_e, \mathcal{M}_u \right] \leq \frac{M^{\theta_u M(R_b(1-1/\beta)} \cdot \sum_{r=0}^{\theta_u M} \left( \frac{M(1-\theta_e)}{r} \right) \left( \frac{e^{R_b L/M} - 1}{r} \right)^r} {M^{R_b(1-1/\beta)}}, \tag{82}
\]

\[
\leq \frac{(a) \theta_u M \cdot \left( M(1-\theta_e) \right) \cdot M^{R_b(1-1/\beta)}(\theta_u + \theta_e - 1)M} {M^{R_b(1-1/\beta)}(\theta_u + \theta_e - 1)M}, \tag{83}
\]

\[
\leq \frac{(b) \theta_u M \cdot M(1-\theta_e) \cdot M^{R_b(1-1/\beta)}(\theta_u + \theta_e - 1)M} {M^{R_b(1-1/\beta)}(\theta_u + \theta_e - 1)M}, \tag{84}
\]

\[
\leq \frac{(c) \theta_u M \cdot (\theta_u + \theta_e - 1)M} {M^{R_b(1-1/\beta)}(\theta_u + \theta_e - 1)M}, \tag{85}
\]

where \( (a) \) follows from \( \frac{\theta_u M}{M} - 1 \leq \frac{1}{M} \leq \frac{\theta_u M}{M} = M^{R_b(1-1/\beta)}, \) \( (b) \) follows since the binomial coefficient \( \binom{n}{k} \) is monotonic increasing in \( k \) for \( k \leq n/2 \), \( (c) \) follows from the bound \( \frac{\theta_u M}{M} \leq \frac{1}{M} \). The claim of the lemma follows by rearranging the terms and noting that the bound depends on \( \mathcal{M}_e, \mathcal{M}_u \) only via their respective cardinality \( \theta_e, \theta_u \).

We next prove the random coding bound of Proposition 9:

**Proof:** [Proof of Proposition 9] By symmetry of the random coding ensemble w.r.t. the choice of codeword, we may assume w.l.o.g. that \( X^L(0) = x^L(0) \) was stored, and condition on this event. We further condition that \( \hat{X}^L = \hat{x}^L \) was obtained after the first two stages of decoding, and that \( \mathcal{M}_e = \theta_e M \) and \( \mathcal{M}_u = \theta_u M \) for some \( \theta_e, \theta_u \in [0, 1] \). By the clipped union bound and symmetry, the conditional average error probability is

\[
\mathbb{P} \left[ \text{error} \big| X^L(0) = x^L(0), \hat{X}^L = \hat{x}^L \right] \leq 1 + \sum_{j=2}^{e^{R_b L/M}} \mathbb{P} \left[ \rho(\hat{x}^L, X^L(j)) \leq \rho(\hat{x}^L, x^L(0)) \right], \tag{87}
\]

\[
\leq 1 + \sum_{j=2}^{e^{R_b L/M}} \mathbb{P} \left[ \rho(\hat{x}^L, X^L(j)) \leq \rho(\hat{x}^L, x^L(0)) \right], \tag{88}
\]

and so by Lemma 10

\[
- \log \mathbb{P} \left[ \text{error} \big| X^L(0) = x^L(0), \hat{X}^L = \hat{x}^L \right] \geq M \cdot \left[ -1 + (R_b - 1)(1 - \theta_e - \theta_u) \log M - LR \right] + \log M. \tag{89}
\]
where \( G_{R'}(\theta_e, \theta_u) \) was implicitly defined, and where \( R' = R + \frac{1}{\log M} \). Clearly \( R' \geq \frac{1}{\log M} \) must hold, however, we will continue the analysis without this constraint, and then eventually take it into account.

The bound above on the error probability depends on \( \hat{\lambda} N M = \tilde{X} N M(0) \) only via \( \theta_e, \theta_u \), which satisfy the constraint \( \theta_e + \theta_u \leq 1 \). Let \( \overline{\text{pe}}(C_M, D_M) \) denote the ensemble average error probability. Then, it is bounded as

\[
\overline{\text{pe}}(C_M, D_M) \leq \sum_{\theta_e, \theta_u \in [0, \frac{1}{\log M}]} \mathbb{P}[|M_e| = \theta_e M, |M_u| = \theta_u M] e^{-M(G_{R'}(\theta_e, \theta_u) + \log M)}
\]

where \( \sum_{\theta_e, \theta_u \in [0, \frac{1}{\log M}]} \mathbb{P}[|M_e| = \theta_e M, |M_u| = \theta_u M] e^{-M(G_{R'}(\theta_e, \theta_u) + \log M)} \leq M^2 \cdot \max_{\theta_e, \theta_u \in [0, \frac{1}{\log M}]} \mathbb{P}[|M_e| \geq \theta_e M, |M_u| \geq \theta_u M] e^{-M(G_{R'}(\theta_e, \theta_u) + \log M)} \leq M^3 \cdot \exp \left( -c(1 + o(1)) \cdot (1 - \sqrt{2\pi}) \delta N L^2 \right),
\]

where we have utilized Lemma 8. Similarly, the maximum over the second interval, \( \theta_u \in [0, \frac{1}{\log M}] \), is bounded as:

\[
M^3 \cdot \max_{\theta_u \in [0, \frac{1}{\log M}], \theta_e \in [0, \frac{1}{\log M}]} \mathbb{P}[|M_e| \geq \theta_e M, |M_u| \geq \theta_u M] e^{-M(G_{R'}(\theta_u, \theta_e) + \log M)} \leq M^3 \cdot \mathbb{P}[|M_e| \geq \theta_e M, |M_u| \geq \theta_u M] e^{-M(G_{R'}(\theta_u, \theta_e) + \log M)} \leq M^3 \cdot \mathbb{P}[|M_e| \geq \theta_e M, |M_u| \geq \theta_u M] e^{-M(G_{R'}(\theta_u, \theta_e) + \log M)} \leq M^3 \cdot \exp \left( -c(1 + o(1)) \cdot (1 - \sqrt{2\pi}) \delta N L^2 \right),
\]

where the last inequality follows since \( \theta_u \rightarrow G_{R'}(\theta_e, \theta_u) \) is monotonic decreasing. Next, we will evaluate the maximum in (96) over \( \theta_u \in [0, 1 - \delta] \) instead of \( \theta_u \in [0, 1] \). We will eventually take the limit \( \delta \downarrow 0 \), and so the continuity of our exponential bounds implies that the maximum over interval \( \theta_u \in [1 - \delta, 1] \) can be ignored. To further bound this term using Lemma 8, and to obtain the bound on the ensemble average error probability, we separate the analysis to \( N/M = \Theta(1) \) and \( N/M = \Theta(1) \).

Case \( N/M = \Theta(1) \): In this case, Lemma 8 yields

\[
- \log \overline{\text{pe}}(C_M, D_M) \geq \frac{M}{2} \cdot \left( R_b \beta - 1 \right) \cdot (1 - \theta_e - \theta_u) \log M - L \left( R + \frac{1}{L} \right) + \log M \]

where \( \overline{\text{pe}}(C_M, D_M) = M \cdot G_{R'}(\theta_e, \theta_u) - \log M \).

Consider the outer minimization between two terms for any \( \delta > 0 \); While the first term in the minimization is

\[
c(1 + o(1)) \cdot (1 - \sqrt{2\pi}) \delta N (\log M)^2 = \Theta(1),
\]

the second term is

\[
\min_{\theta_e \in [0, 1 - \delta]} d_b \left( \theta_e \mid e^{-\varphi_R \frac{N}{M}} \right) \cdot I \{ \theta_e \geq e^{-\varphi_R \frac{N}{M}} \} + G_{R'}(\theta_e, \delta) = O(1),
\]

as can be obtained by the choice \( \theta_e = 1 - \delta \) (which yields \( G_{R'}(1 - \delta, \delta) = 0 \), and is possibly a sub-optimal choice). Thus, for all large enough \( M \), the minimum between the two terms is obtained by the second term. The exponential bound on the ensemble average error probability is obtained by solving (up to negligible terms)

\[
M \cdot \min_{\theta_e \in [0, 1 - \delta]} \left\{ d_b \left( \theta_e \mid e^{-\varphi_R \frac{N}{M}} \right) \cdot I \{ \theta_e \geq e^{-\varphi_R \frac{N}{M}} \} + G_{R'}(\theta_e, \delta) \right\} = O(1),
\]

and then taking the limit \( \delta \downarrow 0 \). The last minimization has the form

\[
L \cdot \left[ \min_{\theta_e \in [0, 1 - \delta]} f(\theta_e) + g(\theta_e) \right] = O(1),
\]

where

\[
f(\theta_e) := \frac{1}{L} d_b \left( \theta_e \mid e^{-\varphi_R \frac{N}{M}} \right) \cdot I \{ \theta_e \geq e^{-\varphi_R \frac{N}{M}} \}
\]

is a non-negative, monotonic increasing, and convex function, and

\[
\theta_e := (R_b - 1/\beta)(1 - \theta_e - \delta)
\]

is a non-negative, monotonic decreasing and linear (and hence also convex) function. This minimization is solved by a standard procedure which involves finding the minimizer \( \theta_e \) for \( R' = 0 \), the critical rate \( R_c \), which is the minimal rate in which the clipping is active for \( \theta_e \), i.e., \( R_c \) is defined as the unique rate satisfying \( g(\theta_e) = R_c \), and for \( R' > R_c \) by setting \( \theta_e \) to be \( \theta_e, R' \), which is defined as the unique parameter satisfying \( g(\theta) = R' \). The minimizer is then given by \( \theta_e \) for \( R' < R_c \), which yields the linear, unity-slope part of the error exponent function, and by \( \theta_e, R' \) for \( R' > R_c \), which is curved part of the error exponent function. The details appear in Proposition 14, Appendix B.

According to the above procedure, we first find \( \hat{\theta}_e \), the minimizer of at zero rate \( R = 0 \):

\[
\hat{\theta}_e := \arg \min_{\theta_e \in [0, 1 - \delta]} d_b \left( \theta_e \mid e^{-\varphi_R \frac{N}{M}} \right) \cdot I \{ \theta_e \geq e^{-\varphi_R \frac{N}{M}} \} + (R_b \beta - 1)(1 - \theta_e - \delta) \log M.
\]

The minimum value is \( \Theta(1) \) as attained by the possibly sub-optimal choice \( \theta_e = 1 - \delta \). Thus, it must hold that for the minimizer \( \tilde{\theta}_e \)

\[
(R_b \beta - 1)(1 - \tilde{\theta}_e - \delta) \log M = O(1).
\]

and so \( \tilde{\theta}_e = 1 - \delta - c_M \) for some \( c_M = O(1 / \log M) \). Furthermore, since \( \delta > 0 \) will be chosen to arbitrary small, we may further restrict to \( 1 - 2\delta > \max_{\theta \in [0, 1]} e^{-\varphi_R \frac{N}{M}} \). For such restricted \( \delta, \)
it holds that $\mathbb{I}\{1 - \delta - c_M \geq e^{-\varphi_r M} \} = 1$ for all large enough $M$, and the minimal value is then obtained for $c_M$ chosen as

$$\min_{c_M : c_M = O(\log M)} \left\{ d_b \left( 1 - \delta - c_M \| e^{-\varphi_r M} \right) + (R_b \beta - 1) c_M \log M \right\} = d_b \left( 1 - \delta \| e^{-\varphi_r M} \right) + O(c_M \log M). \tag{106}$$

The critical rate $R_{cr}$ is then

$$R_{cr} = g(\hat{\theta}_c) = (R_b - 1/\beta) c_M = o(1). \tag{107}$$

Thus, for any $R' > 0$, and all $M$ sufficiently large, the minimizing $\theta$ is $\theta_{e,R'}$ (and so we are at the curved part of the random coding exponent function), which is the solution to

$$(R_b \beta - 1)(1 - \theta_{e,R'} - \delta) \log M = LR', \tag{108}$$

or, as $L = \beta \log M$,

$$\theta_{e,R'} = 1 - \delta - \frac{R'}{R_b - 1/\beta}. \tag{109}$$

The resulting bound on the random coding error exponent is then

$$- \log \mathbb{P}(C_M,D_M) \geq M \lim_{\delta \downarrow 0} \min_{\theta_{e,R'}} \left\{ d_b \left( \theta_{e,R'} \| e^{-\varphi_r M} \right), \mathbb{I}\{\theta_{e,R'} \geq e^{-\varphi_r M} \} - O(\log M) \right\} = -O(\log M). \tag{110}$$

The condition for a positive exponent in the last display is

$$R' \leq (R_b - 1/\beta) \left( 1 - e^{-\varphi_r M} \right). \tag{112}$$

This exponent is maximized by minimizing $e^{-\varphi_r M}$, that is maximizing $\varphi_r = -\frac{1}{N/M} \log \mathbb{P}(S_m \leq T_r)$. This maximum is clearly obtained by minimizing $T_r = \frac{N}{ML} (1 - \sqrt{2\pi})$, or, equivalently, taking the limit $\tau \uparrow 1/2$. Since $N/M = \Theta(1)$ there exists $\delta^* > 0$ such that for all $\delta \in (0, \delta^*)$ it holds that $T_{1/2 - \delta} < 1$. So, for such $\delta$

$$\varphi_{1/2 - \delta} = -\frac{1}{N/M} \log \mathbb{P}(S_m \leq T_{1/2 - \delta}) \tag{113}$$

$$= -\frac{1}{N/M} \log \mathbb{P}(S_m = 0) = 1. \tag{114}$$

Hence, by taking $\delta \downarrow 0$, which specifically results $\delta < \delta^*$, yields the bound

$$- \lim_{M \to \infty} \frac{1}{M} \log \mathbb{P}(C_M,D_M) \geq \min_{\theta_{e,R'} \in [0,1]} \theta_{e,R'} \frac{N}{ML} \mathbb{I}\{\theta_{e,R'} \geq e^{-\varphi_{1/2 - \delta}} \} + (R_b - 1/\beta (1 - \theta_{e,R'} - \delta) - R'). \tag{115}$$

where (*) follows from $R' = R + \frac{1}{R_b \beta}$, and a first-order Taylor approximation of $d_b(\theta \| e^{-\varphi_r M})$ around $\theta = 1 - \frac{R}{R_b - 1/\beta}$. The claimed bound then follows.

Case $N/M = \omega(1)$: As in the previous case, we utilize Lemma 8, and continue bounding (93) separately for the two intervals $\theta_{e} \in [0, \delta]$ and $\theta_{e} \in [\delta, 1]$. The bound (95) remains the same, and this leads to the bound

$$- \log \mathbb{P}(C_M,D_M) \geq \min_{\theta_{e,R'} \in [0,1]} \theta_{e,R'} \frac{N}{ML} \mathbb{I}\{\theta_{e,R'} \geq e^{-\varphi_{1/2 - \delta}} \} + (R_b - 1/\beta (1 - \theta_{e,R'} - \delta) - R'). \tag{116}$$

As in the previous case, the first term in the outer minimization (which is $O\left(\frac{N}{ML} \log N \right)$) is larger than the second term (which is $O\left(\frac{N}{ML} \right)$). Hence, the minimum is obtained by the second term for all large enough $M$, and so the required exponential bound is obtained by solving

$$\min_{\theta_{e,R'} \in [0,1]} \theta_{e,R'} \frac{N}{ML} \mathbb{I}\{\theta_{e,R'} \geq e^{-\varphi_{1/2 - \delta}} \} + (R_b - 1/\beta (1 - \theta_{e,R'} - \delta) - R'). \tag{117}$$

We follow the same procedure as in the $N/M = \Theta(1)$ case. For $R' = 0$, it is required to solve

$$\min_{\theta_{e,R'} \in [0,1]} \theta_{e,R'} \frac{N}{ML} \mathbb{I}\{\theta_{e,R'} \geq e^{-\varphi_{1/2 - \delta}} \} + (R_b - 1/\beta (1 - \theta_{e,R'} - \delta) - R'). \tag{118}$$

We next consider three sub-cases:

- Suppose that $\frac{N}{ML} = o(1)$. Then the term $(R_b - 1/\beta (1 - \theta_{e,R'} - \delta))$ asymptotically dominates and $\theta_{e,R'} \to 1 - \delta$. The critical rate is $R_{cr} = o(1)$, and for any $R' > 0$ and all sufficiently large $M$ so that $R' > R_{cr}$

$$\theta_{e,R'} = 1 - \delta - \frac{R'}{R_b - 1/\beta}. \tag{120}$$

In addition, for $R' \leq (1 - \delta)(R_b - 1/\beta)$ and all large enough $M$, it holds that $\theta_{e,R'} > e^{-\varphi_{1/2}} = o(1)$ and so
the exponent bound is
\[
\left(1 - \delta - \frac{R'}{R_b - 1/\beta}\right)^{-N} \leq ML.
\] (121)
Maximizing the bound by taking \(\tau = 1/2 - \delta\) using \(R' = R + \frac{1}{\beta}\), for all \(R \leq R_b - 1/\beta\), and then taking \(\delta \uparrow 0\) yields the bound
\[
-\lim_{N \to \infty} \frac{1}{N} \log \Pr(\mathcal{C}_{M, D_M}) \geq \frac{1}{2} \left(1 - \frac{R}{R_b - 1/\beta}\right).
\] (122)

- Suppose that \(\frac{N}{ML} = a\) where \(a = \Theta(1)\). At \(R' = 0\) the minimization problem is
\[
\min \theta_{e} \alpha \tau \{\theta_e \geq e^{-\gamma\eta}\} + (R_b - 1/\beta)(1 - \theta_e - \delta)
\]
= \(\min \theta_{e} \alpha \tau \{\theta_e \geq e^{-\gamma\eta}\} - (R_b - 1/\beta)\)\]
+ (R_b - 1/\beta)(1 - \delta).
\] (123)

The minimum is attained at
\[
\tilde{\theta}_e = \begin{cases} 0, & a > \frac{R_b - 1/\beta}{R' - 1/\beta} \\ 1 - \delta, & a < \frac{R_b - 1/\beta}{R' - 1/\beta} \end{cases}
\] (124)
for which \(\mathbb{1}(\theta_{e,R'} \geq e^{-\gamma\eta}) = 1\) for all \(M\) sufficiently large. This yields the exponent
\[
\theta_{e,R'} \alpha \tau \{\theta_{e,R'} \geq e^{-\gamma\eta}\} = \left[1 + o(1)\right] \cdot \mathbb{1}(\theta_{e,R'} \geq e^{-\gamma\eta})
\]
\[
= \left[1 + o(1)\right] \cdot \alpha \tau \left[1 - \delta - \frac{R'}{R_b - 1/\beta}\right].
\] (126)
Maximizing the bounds in both cases by setting \(\tau = 1/2 - \delta\), and then taking \(\delta \uparrow 0\) we obtain the exponent bound
\[
-\lim_{N \to \infty} \frac{1}{N} \log \Pr(\mathcal{C}_{M, D_M}) \geq ML \left[\frac{\alpha}{2} \wedge (R_b - 1/\beta)\right] \left[1 - \frac{R}{R_b - 1/\beta}\right].
\] (127)

- Suppose that \(\frac{N}{ML} = \omega(1)\). Then, at \(R' = 0\) the minimization problem is
\[
\min \theta_{e} \frac{N}{ML} \tau \mathbb{1}\{\theta_e \geq e^{-\gamma\eta}\} + (R_b - 1/\beta)(1 - \theta_e - \delta).
\] (128)
The minimizer is thus \(\tilde{\theta}_e = e^{-\gamma\eta} + o(1) = o(1)\) and at \(R' = 0\) the exponent bound is
\[
(R_b - 1/\beta)(1 - e^{-\gamma\eta} - \delta)
\]
= \(R_b - 1/\beta)(1 - \delta) + o(1)\) \hspace{1cm} (129)
The critical rate is
\[
R_{cr} = (R_b - 1/\beta)(1 - e^{-\gamma\eta} - \delta)
\] (130)
\[
= (R_b - 1/\beta)(1 - \delta) + o(1).
\] (131)

Setting again \(\tau = 1/2 - \delta\), and then taking \(\delta \downarrow 0\) and using \(R' = R + \frac{1}{\beta}\) leads to the exponential bound
\[
-\lim_{N \to \infty} \frac{1}{N} \log \Pr(\mathcal{C}_{M, D_M}) \geq ML \left[\frac{\alpha}{2} \wedge (R_b - 1/\beta)\right] \left[1 - \frac{R}{R_b - 1/\beta}\right].
\] (132)
Summarizing all possible cases leads to the claimed exponential bounds.

\[\mathbf{C.} \text{ Expurgated Bound Analysis}\]

In this section, we improve the random coding bound in some regime of \(N\) via an expurgation argument. Specifically, we establish the following:

\[\text{Proposition 11 (Expurgated Bound): \ Let an inner code be given by } \{B_{m}^{(L)}\} \subseteq \mathcal{X}^{L} \text{ for } m \in [M], \text{ and let } \mathcal{D}_{b} \text{ be a decoder which satisfy the assumptions on the inner code at rate } R_b. \text{ Then, there exists a sequence of coded-index based codebooks } \{\mathcal{C}_M\} \text{ and corresponding decoders (as described in Sec. II-B) such that if } N/(ML) > 4(R_b - 1/\beta) \text{ then}\]
\[
\lim_{N \to \infty} \frac{1}{N} \log \Pr(\mathcal{C}_{M, D_M}) \geq \frac{N}{4} \left[1 - \frac{R}{R_b - 1/\beta}\right],
\] (133)
for any \(R < R_b - 1/\beta\).

We follow the expurgation argument of [35, Appendix]. To this end, we define the distance enumerator of the \(j\)th codeword, \(j \in [C]\), of a coded-index based codebook \(\mathcal{C}\) at relative distance \(\gamma \in \frac{1}{M}[M + 1]\), as
\[
\mathcal{N}_{j}(C, \gamma) := \{\tilde{j} \neq j : \rho(x^{LM}(j), x^{LM}(\tilde{j})) = \gamma M\}.
\] (134)
We begin by proving the existence of a codebook with a specified distance spectrum.

\[\text{Lemma 12: \ Let rate } R \text{ be given, and assume that } \eta \equiv \eta_M = 4/(M/\beta). \text{ Then, there exists a codebook } \mathcal{C}^* \text{ of rate } R - \Theta(1/M) \text{ so that}\]
\[
\mathcal{N}_{j}(C^*, \gamma) \begin{cases} \leq \exp\{ML \cdot (R - (1 - \gamma)(R_b - 1/\beta))\}, & \gamma \geq 1 - \frac{R - \eta}{R_b - 1/\beta} \\ = 0, & \gamma < 1 - \frac{R - \eta}{R_b - 1/\beta} \end{cases}
\] (135)

\[\text{Proof: \ The proof is by random selection over the coded-index based random coding ensemble (Definition II-B.5). We begin by evaluating the expected value of } \mathcal{N}_{j}(C, \gamma) \text{ over the ensemble. By symmetry and the uniformity of the random selection of the codebook, it is clear that we may assume w.l.o.g. that } j = 0, \text{ and that } x^{LM}(0) \text{ is arbitrary. By the definition of the random coding ensemble, the } m\text{th molecule of each codeword } x^{LM}(j) \text{ is chosen uniformly at random from } B_{m}^{(L)}, \text{ whose cardinality is } |B_{m}^{(L)}| = M_{R_b - 1/\beta}^L. \text{ Thus, the probability that } x^{LM}(0) \text{ and } x^{LM}(1) \text{ (or any other } j > 0) \text{ are equal in their } m\text{th molecule is } M^{1 - R_b} = o(1) \text{ (recall the assumption } R_b \beta > 1).\]
Thus, the expected number of identical molecules in $x^{LM}(0)$ and $x^{LM}(1)$ is $M^2 - \rho M \beta = o(M)$. So, the probability that there are $\gamma M$ identical molecules in $x^{LM}(0)$ and $x^{LM}(1)$ is a large-deviations event. Chernoff’s bound then implies

$$
\mathbb{P} \left[ \rho(x^{LM}(0), X^{LM}(1)) = \gamma M \right] = \mathbb{P} \left[ \text{Binomial}(M, M^{1-R_b \beta}) = (1 - \gamma)M \right] 
\leq \exp \left[ -M \cdot d_b \left( 1 - \gamma \left\| M^{1-R_b \beta} \right\| \right) \right]
\leq \exp \left[ -M \cdot \left( 1 + o(1) \right) \cdot (1 - \gamma)(R_b - 1/\beta) \right],
$$

where the last inequality is by the asymptotic expansion of the binary KL divergence $d_b(a||b) = -[1 + o(1)] \cdot a \log b$ (see Proposition 13 in Appendix A). Then, by linearity of expectation

$$
\mathbb{E} \left[ N_0(C, \gamma) \right] = (|C| - 1) \cdot \mathbb{P} \left[ \rho(x^{LM}(1), X^{LM}(2)) = \gamma M \right] 
\leq \exp \left[ M \cdot (R - [1 + o(1)](1 - \gamma)(R_b - 1/\beta)) \right].
$$

Similar bound holds for any $j > 0$. For any $\gamma \in \frac{1}{M}[M + 1]$, denote the event

$$
\mathcal{F}_\gamma := \left\{ \frac{1}{|C|} \sum_{j \in [|C|]} N_j(C, \gamma) \geq e^{M \cdot (R - (1 - \gamma)(R_b - 1/\beta) + \eta/2)} \right\}.
$$

Then, by the union bound and Markov’s inequality,

$$
\mathbb{P} \left[ \bigcup_{\gamma \in \frac{1}{M}[M + 1]} \mathcal{F}_\gamma \right] \leq \sum_{\gamma \in \frac{1}{M}[M + 1]} \mathbb{P} \left[ \mathcal{F}_\gamma \right] \leq M \cdot e^{-ML\eta/2} = e^{-ML\eta/4} = \frac{1}{M},
$$

where the last inequality follows from the choice $\eta = 4/(M\beta)$. So, with probability larger than $1 - \frac{1}{M}$

$$
\frac{1}{|C|} \sum_{j \in [|C|]} N_j(C, \gamma) \leq \exp \left[ M \cdot (R - (1 - \gamma)(R_b - 1/\beta) + \eta/2) \right]
$$

holds for all $\gamma \in \frac{1}{M}[M + 1]$. Let $C'$ be a code which satisfies the property (145) for all $\gamma \in \frac{1}{M}[M + 1]$ whose cardinality is $e^{MLR}$. Then, for any given $\gamma \in \frac{1}{M}[M + 1]$ there must exist a sub-codebook $C''(\gamma)$ of cardinality larger than $(1 - e^{-MLR/2}) \cdot e^{MLR}$ such that

$$
N_j(C''(\gamma), \gamma) \leq \exp \left[ M \cdot (R - (1 - \gamma)(R_b - 1/\beta) + \eta) \right]
$$

holds for any $j \in [|C''(\gamma)|]$. Indeed, assume by contradiction that this is not the case. Then, there exists more than $e^{-MLR/2} \cdot e^{MLR}$ codewords for which $N_j(C', \gamma)$ satisfies the opposite inequality to (146). Summing $\frac{1}{|C''|} \cdot N_j(C', \gamma)$ over these codewords will then lead to a value larger than the right-hand side (r.h.s.) of (145), which is a contradiction. Thus, $C'' := \bigcap_{\gamma \in \frac{1}{M}[M + 1]} C''(\gamma)$ satisfies that

$$
N_j(C'', \gamma) \leq \exp \left[ M \cdot (R - (1 - \gamma)(R_b - 1/\beta) + \eta) \right]
$$

for all $j \in [|C''|]$ and $\gamma \in \frac{1}{M}[M + 1]$. In addition,

$$
|C \setminus C''| = \left| C \cap \bigcup_{\gamma \in \frac{1}{M}[M + 1]} C''(\gamma) \right| = \left| \bigcup_{\gamma \in \frac{1}{M}[M + 1]} C \setminus C''(\gamma) \right| \leq \sum_{\gamma \in \frac{1}{M}[M + 1]} \left| C \setminus C''(\gamma) \right|.
$$

where (a) follows from the union bound, (b) follows since $|C''(\gamma)| \geq (1 - e^{-MLR/2}) \cdot e^{MLR}$ for all $\gamma \in \frac{1}{M}[M + 1]$. Hence,

$$
|C''| \geq (1 - M \cdot e^{-MLR/2}) \cdot e^{MLR}
= (1 - \frac{1}{M}) \cdot e^{MLR}
\geq e^{ML(R - \Theta(1/(ML))},
$$

for all large enough $M$. The proof is completed by noting that since the left-hand side of (147) is integer, it must be zero whenever the r.h.s. is strictly less than 1.

We next prove Proposition 11: Proof: [Proof of Proposition 11] Let $\eta = \frac{1}{M}$ be given and assume that $M$ is large enough so that $\eta \in (0, R)$. Further let $C^*$ be a code as guaranteed by Lemma 12 of rate $R' = R - \eta$, and let $D$ be the corresponding decoder, as described in Sec. II-B. By the union bound, for any $j \in [|C^*|]$

$$
\Pr(C^* \in |x^{LM}(j)) \leq \sum_{j \in [|C^*|]\setminus\{j\}} \mathbb{P} \left[ \rho(\hat{x}^{LM}, x^{LM}(j)) < \rho(\hat{x}^{LM}, x^{LM}(j)) \right]
$$

where the last inner summation is over $j \in [|C^*|]\setminus\{j\}; \rho(\hat{x}^{LM}(j), x^{LM}(j)) = \gamma M$.

We next bound the probability in the above summation for some arbitrary pair of codewords $j \neq j$ for which $\rho(\hat{x}^{LM}(j), x^{LM}(j)) = \gamma M$. For the sake of this bound, we assume w.l.o.g. that this pair of codewords has different molecules in the set $[\gamma M]$. In Sec. IV-A we have defined the cardinality of erasure and undetected error events for the entire set of molecules $[M]$ recall the definitions of $M_e$ and $M_u$ in (19) and (20), and here, we consider, in lieu of $M_e$ and $M_u$, a similar sets of indices which are restricted to $[\gamma M]$, to wit,

$$
M_e(\gamma) := \left\{ m \in [\gamma M] : \hat{x}^L_m = e \right\},
$$

Similarly, let

$$
M_u(\gamma) := \left\{ m \in [\gamma M] : (\hat{x}^{LM}, x^{LM}) \right\}.
$$


\[ M_u^{(\gamma)} := \{ m \in [\gamma M] : \hat{x}_m^L \neq e, \hat{x}_m^L \neq x_m^L(j) \}. \] (159)

Analogously to Lemma 4, it then holds that
\[ |M_e^{(\gamma)}| + |M_u^{(\gamma)}| \leq |M_{\text{sam}}^{(\gamma)}| + \left( 1 + \frac{2}{1 - \sqrt{2}\tau} \right) \frac{M}{N} K \] (160)
where
\[ M_{\text{sam}}^{(\gamma)} := \{ m \in [\gamma M] : S_m < T_r \}, \] (161)
and \( K \) is defined, exactly as in the random coding analysis of Sec. IV-B, as the total number of molecules which were erroneously sequenced (even those in \( [M] \setminus [\gamma M] \)). With these definitions, we may further upper bound
\[ \text{pe}(C^*, D \mid x^{LM}(j)) \leq \sum_{\gamma \in [1/M, 1]} N_j(C^*, \gamma) \cdot \mathbb{P} \left[ |M_{\text{sam}}^{(\gamma)}| + |M_u^{(\gamma)}| \geq \frac{1}{2} \gamma M \right] \] (162)
\[ \leq \sum_{\gamma \in [1/M, 1]} N_j(C^*, \gamma) \times \mathbb{P} \left[ |M_{\text{sam}}^{(\gamma)}| + \left( 1 + \frac{2}{1 - \sqrt{2}\tau} \right) \frac{M}{N} K \geq \frac{1}{2} \gamma M \right] \] (163)
\[ \leq \sum_{\gamma \in [1/M, 1]} N_j(C^*, \gamma) \sum_{\sigma, \kappa} \mathbb{P} \left[ |M_{\text{sam}}^{(\gamma)}| \geq \sigma M, K \geq \kappa N \right] \] (164)
\[ \leq \sum_{\gamma \in [1/M, 1]} N_j(C^*, \gamma) \times \sum_{\sigma, \kappa} \mathbb{P} \left[ |M_{\text{sam}}^{(\gamma)}| \geq \sigma M \right] \cdot \mathbb{P} \left[ K \geq \kappa N \right], \] (165)
where the last two inner summations are over \( \sigma \in \frac{1}{2} \cdot [M + 1], \kappa \in \frac{1}{N} \cdot [N + 1] : \sigma + \kappa \left( \frac{N}{M} + \frac{2}{1 - \sqrt{2} \tau} \right) \geq \frac{1}{2} \), and where (*) follows similarly to Lemma 7. We next bound \( N_j(C^*, \gamma) \) by exploiting the guarantees on \( C^* \) (from Lemma 12), and bounds on the probabilities \( \mathbb{P}[|M_{\text{sam}}^{(\gamma)}| \geq \sigma M] \) and \( \mathbb{P}[K \geq \kappa N] \). For the former, it can be easily deduced that the bound of Lemma 5 holds verbatim, and given by
\[ \mathbb{P} \left[ |M_{\text{sam}}^{(\gamma)}| \geq \sigma M \right] \leq 4e^{-\sigma \gamma N} \] (166)
for \( \sigma \in (e^{-\gamma \sqrt{2} / \tau}, 1) \). This is because the reduction in the randomness due to the change from a sum of \( M \) r.v.’s to a sum of \( \gamma M \) r.v.’s is compensated by the increase in the relative probability required to cross the threshold \( \sigma M \). For the latter, we again use Lemma 7 verbatim for \( K \) instead of \( K \).

We next plug in those bounds only the \( N/M = \omega(1) \) case, as similar analysis for the other cases shows that there is no improvement for the \( N/M = \Theta(1) \) case. So, assuming \( N/M = \omega(1) \), the bound is
\[ -\log \text{pe}(C^*, D \mid x^{LM}(j)) \geq ML \cdot \min_{\gamma \in [1 - \frac{R}{R_b - 1/\beta}, 1]} \min_{\sigma, \kappa} \left\{ \sigma \frac{N(1 + o(1))}{ML} + c \cdot \kappa \frac{N}{ML} L^\gamma \right\} - O \left( \frac{1}{M} \right), \] (167)
where the minimization is over \( \sigma \in [0, 1], \kappa \in [0, 1] : \sigma + \kappa \left( \frac{N}{M} + \frac{2}{1 - \sqrt{2} \tau} \right) \geq \frac{1}{2} \) and for \( \sigma \in (e^{-\gamma \sqrt{2} / \tau}, 1) \). Considering the inner minimization for some given \( \gamma \), the minimum must be attained for \( \kappa = 0 \) since \( L^\gamma = \omega(1) \). This leads to the bound
\[ -\log \text{pe}(C^*, D \mid x^{LM}(j)) \geq ML \cdot \min_{\gamma \in [1 - \frac{R}{R_b - 1/\beta}, 1]} \min_{\sigma, \kappa} \left\{ \sigma \frac{N(1 + o(1))}{ML} \right\} + (1 - \gamma)(R_b - 1/\beta) - R' \] (168)
\[ \geq ML \cdot \min_{\gamma \in [1 - \frac{R}{R_b - 1/\beta}, 1]} \left\{ \frac{\gamma(1 + o(1))}{2 \cdot ML} \right\} + (1 - \gamma)(R_b - 1/\beta) - R' \] (169)
for \( \sigma \in (e^{-\gamma \sqrt{2} / \tau}, 1) \). It is evident from that last bound that it is optimal to set \( \tau \uparrow 1/2 \) and so we continue analyzing the bound with this choice, by further restricting to the case \( \frac{N}{ML} > 4(R_b - 1/\beta) \) assumed in the statement of the proposition. Then, the minimizer is obtained for \( \gamma = 1 - \frac{R'}{R_b - 1/\beta} \) and the non-vanishing term is
\[ ML \cdot \frac{\gamma(1 + o(1))}{2 \cdot ML} \geq ML \cdot \frac{(1 - \gamma)(R_b - 1/\beta) - R'}{4(R_b - 1/\beta)} \] (170)
\[ \geq \left( 1 - \frac{R}{R_b - 1/\beta} \right) \frac{N(1 + o(1))}{4} - O \left( \frac{N}{M} \right), \] (171)
where we have used \( R' = R - \eta \) and the assumption that \( \eta = \Theta(1/M) \).

V. Summary

We have considered a simple and general coding scheme for the DNA storage channel and analyzed its error probability. In the analysis of this scheme and in our previous research [18] it was identified that sampling events dominate the error probability, and so lowering the rate of sequencing errors in this scheme is of secondary importance compared to proper sampling of all molecules. This phenomenon resembles wireless fading communication channels [36], in which the transmitted signal experiences both fading (a random gain, or multiplicative noise) and additive noise (typically assumed to be Gaussian). Under common fading models such as Rayleigh, the probability that the random gain is close to zero decays polynomially with the signal-to-noise ratio, and in this event the output signal is “lost”, and so an error is inevitable. This event dominates the error probability, and as a result the error probability decays much slower compared to fixed gain additive noise channels, in which the decay
rate is exponential (e.g., [32, Ch. 7]). Analogously, random sampling events, in which too many molecules are undersampled, dominates the error probability over the sequencing errors.\(^\text{10}\). Hence, since the error probability bound of this paper scales as \(e^{-\Theta(N)}\), and analogously to diversity techniques [36, Ch. 3] in wireless communication, the importance of increasing the coverage depth \(N\) as much as possible.

Nonetheless, as discussed in [15], future systems will aim for faster and cheaper sequencing machines, which inevitably will increase sequencing errors, which even include non-negligible rate of deletions and insertions. Constructing practical coding methods and decoders for this channel, as was studied in [16] and in this paper, is an important avenue for future research.

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APPENDIX A

ASYMPTOTIC EXPANSION OF THE BINARY KL DIVERGENCE

Proposition 13: If \(a \in [0, 1]\) and \(b_n = o(1)\) then
\[
d_{KL}(a||b_n) = -[1 + o(1)] \cdot \log b_n.\]

Proof: It holds that
\[
a \log \frac{a}{b_n} = -[1 + o(1)] \cdot \log b_n = \omega(1)\]
and using the expansion \(\log(1 + x) = x + \Theta(x^2)\) we obtain that
\[
(1 - a) \log \left(\frac{1 - a}{1 - b_n}\right) = (1 - a) \log(1 - a) - (1 - a) \log(1 - b_n)\]
\[
= (1 - a) \log(1 - a) + b_n(1 - a) + \Theta(b_n^2)\]
\[
= [1 + o(1)] \cdot (1 - a) \log(1 - a)\]
\[
= \Theta(1).\]
The result then follows by adding both terms.

APPENDIX B

A MINIMIZATION PROBLEM IN RANDOM CODING EXPONENT BOUNDS

The following provides a general solution for a standard minimization problem that occurs in the derivations of random coding bounds of the error exponent (as developed by Csiszár and Körner [33, Ch. 10]).

Proposition 14: Suppose that \(f(\theta)\) and \(g(\theta)\) are nonnegative and convex functions on \([0, 1]\), and that \(f(\theta)\) is strictly increasing while \(g(\theta)\) is strictly decreasing. Let
\[
\theta_0 = \arg\min_{\theta \in [0, 1]} f(\theta) + g(\theta),
\]
let \(R_{cr} := g(\theta_0)\), and let \(R_{cr}\) be defined by \(g(R_{cr}) = R\) for \(R > R_{cr}\). Then,
\[
\min_{\theta \in [0, 1]} f(\theta) + [g(\theta) - R]_+ = \begin{cases} f(\theta_0) + g(\theta_0) - R, & R \leq R_{cr} \\ f(R_{cr}), & R \geq R_{cr}. \end{cases}
\]

Proof: For \(R = 0\) the minimum is clearly attained for \(\theta_0\). Then, for \(R < R_{cr} = g(\theta_0)\)
\[
f(\theta_0) + [g(\theta_0) - R]_+ = f(\theta_0) + g(\theta_0) - R \quad (B.3)
\]
\[
= \min_{\theta \in [0, 1]} f(\theta) + g(\theta) - R \quad (B.4)
\]
and so \(\theta_0\) is the minimizer for all \(R \leq R_{cr}\). For \(R > R_{cr}\), let us write
\[
\min_{\theta \in [0, 1]} f(\theta) + [g(\theta) - R]_+ = \min_{\theta \in [0, 1]} \left\{ \min_{g(\theta) \leq R} f(\theta), \min_{g(\theta) \geq R} f(\theta) + g(\theta) - R \right\}. \quad (B.6)
\]

Regarding the second inner minimization, that is constrained to \(\{\theta \in [0, 1] : g(\theta) \geq R\}\), we may alternatively inspect the unconstrained minimization, and note that \(\theta_0\), the unconstrained minimizer, satisfies \(g(\theta_0) < R\). The convexity of \(f(\theta) + g(\theta)\) then implies that the solution to the same minimization problem constrained to \(\{\theta \in [0, 1] : g(\theta) \geq R\}\), that is
\[
\min_{\theta \in [0, 1]} f(\theta) + g(\theta) - R \quad (B.7)
\]
can be attained also on the boundary, that is, for \(g(\theta) = R\). Hence, for \(R > R_{cr}\)
\[
\min_{\theta \in [0, 1]} f(\theta) + [g(\theta) - R]_+ = \min_{\theta \in [0, 1]} \left\{ \min_{g(\theta) \leq R} f(\theta), \min_{g(\theta) = R} f(\theta) + g(\theta) - R \right\} \quad (B.8)
\]
\[
= \min_{\theta \in [0, 1]} f(\theta). \quad (B.9)
\]
The monotonicity properties of \(f(\theta)\) and \(g(\theta)\) then imply that the solution is obtained for \(\theta R\) which satisfies \(g(\theta R) = R\).

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